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British Society for Parasitology

Spring Meeting

Aberystwyth

2018

Including:

BAVP—Joint meeting

Tryp & Leish Symposium

1872 PRIFYSGOL ABERYSTWYTH UNIVERSITY

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Disabled Access to Penglais Campus

SY23 3FL

KEY

- Building entrance with disabled access
- Toilet for disabled
- Disabled parking place

Facilities

1 **Reception/ Enquiries** - *SY23 3FL*

2 **Aberystwyth Arts Centre** - *SY23 3DE*
- Great Hall
- Theatre
- Visitors' Car Park

3 **Parry-Williams Building** - *SY23 3AJ*
- Theatre Film & Television Studies
- Mercator

4 **Hugh Owen Library** - *SY23 3DZ*
- Library and Information Services

Hugh Owen Building - *SY23 3DY*
- Centre for Welsh Language Services
- English & Creative Writing
- History & Welsh History
- Modern Languages
- Welsh and Celtic Studies
- A12 and A14 Lecture Theatres

5 **Llandinam Building** - *SY23 3DB*
- Geography & Earth Sciences
- Computer Science
- International English Centre

6 **Cledwyn Building** - *SY23 3DD*
- Academic Quality and Records Office
- Admissions
- International Office
- Communications, Marketing & Public Affairs

7 **Physical Sciences Building** - *SY23 3BZ*
- Mathematical & Physical Sciences

8 **Edward Llwyd Building** - *SY23 3DA*
- Biological Sciences (IBERS)

9 **Sports Centre** - *SY23 3AR*
- Sports Hall
- Swimming Pool
- All Weather Sports Pitch

10 **Sports Cage**

11 **Design & Print Services** - *SY23 3UG*

12 **Student's Union** - *SY23 3DX*
- Careers Service

13 **Brynamlwg** - *SY23 3AP*
- Staff, Sports & Social Club

23 **Carwyn James Building** - *SY23 3FD*
- Sport & Exercise Science

24 **International Politics Building** - *SY23 3FE*

25 **Visualisation Centre** - *SY23 3BF*
- Vice Chancellor's Office
- Planning Office
- Research, Business & Innovation

26 **Student Welcome Centre** - *SY23 3FB*
- Finance Office
- Student Support
- Student Wellness Centre
- Post Room

27 **New IBERS Building**
IBERS Rural Studies

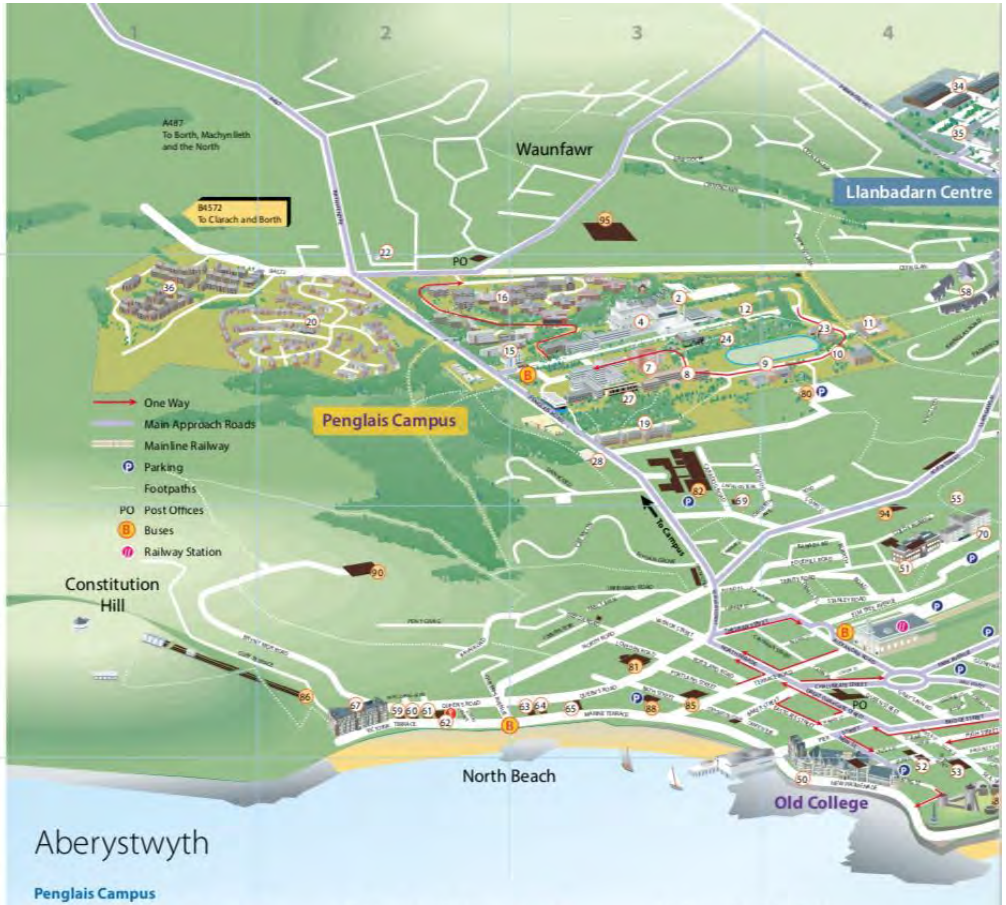
28 **Penglais Day Nursery**

30 **Penbryn 5** - *SY23 3UX*
- Education and Lifelong Learning
- Psychology
- Welsh for Adults

Halls and Residences

15 **Penbryn Halls** - *SY23 3BY*
- Conference Office
- Catering Office
- 'Nightline'

19 **Neuadd Pantycelyn** - *SY23 3BX*



Aberystwyth

Penglais Campus

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Welcome

We are delighted to welcome you to Aberystwyth and to Aberystwyth University for the 2018 Spring Conference of the British Society for Parasitology. The BSP Spring meeting was last held at Aberystwyth in 1986, so we look forward to making 2018 a memorable meeting for you all. This conference will be a perfect opportunity to develop collaborations and share knowledge for the goal of controlling parasitic diseases. We have several diverse and interesting sessions and themes, symposia and workshops including the:

- Trypanosomiasis & Leishmaniasis Symposium
- British Ecological Society Symposium on Ecological Parasitology
- British Association for Veterinary Parasitology symposium on Veterinary Parasitology
- NC3Rs sponsored Workshop on *in vitro* Technologies in *Cryptosporidium* Research.

The conference oral sessions will be held on Penglais Campus, starting at 8.45am on Monday morning with Plenary Talks at the Arts Centre Great Hall (please see maps in delegate bags).

As well as a packed academic program we have a busy social program for delegates and accompanying families starting on Sunday evening with a Welcome Reception at Old College on the seafront (close to the pier). This is followed by a Public Lecture ‘Invasion of the parasites. *A Hospital for Tropical Diseases Production*. Coming soon to a theatre near you' by Professor Peter Chiodini. During the Poster Sessions on Monday and Tuesday evening we have specially designed parasite beers for delegates from Penlon Brewery. On Monday evening we are hosting a Science Café event at the Arts Centre ‘Parasites: the Good, the Bad and the Ugly’, plus the Young Parasitologist Party at Y Consti. On Tuesday evening we have the Conference Dinner, and the after dinner Ceilidh.

Aberystwyth is situated on the beautiful West coast of Wales and there are lots of tourist attractions for delegates and their families to do and explore in the surrounding area (see guide to attractions in the delegate bags).

BSP Spring 2018 Conference Organisers

Justin Pachebat (Lead Organiser)

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Jo Hamilton

Russ Morphew

Karl Hoffmann

Organising Committee and Session Organisers

Justin Pachebat (Lead Organiser, IBERS, Aberystwyth University)

Jo Hamilton (Organiser, IBERS, AU)

Russ Morphew (Organiser, IBERS, AU)

Karl Hoffmann (Organiser, IBERS, AU)

Siwan Griffiths (Conference Office, AU)

Peter Brophy (IBERS, AU)

Iain Chalmers (IBERS, AU)

Kathy Geyer (IBERS, AU)

Joe Ironside (IBERS, AU)

Claire Risley (IBERS, AU)

Martin Swain (IBERS, AU)

Hefin Williams (IBERS, AU)

Julian Fuller (BSP)

Richard Wall (Bristol University)

Shona Wilson (Cambridge University)

Jo Cable (Cardiff University)

Anna Paziewska - Harris (Cardiff University)

Rachel Chalmers (Cryptosporidium Reference Unit, Public Health Wales)

Mark Field (Dundee University)

Paul Horrocks (Keele University)

Helen Price (Keele University)

Alvaro Acosta - Serrano (Liverpool School of Tropical Medicine)

Lisa Reimer (LSTM)

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Julius Hafalla (London School of Hygiene & Tropical Medicine)

Shahid Khan (Leiden University Medical Centre, Holland)

Damer Blake (Royal Veterinary College)

Claire Alexander (Scottish Microbiology Reference Laboratories)

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Brief history of Aberystwyth University

Aberystwyth University was established as the University College of Wales in 1872 with twenty-six students. Based in an old hotel in the seafront it offering a variety of courses including chemistry. In 1884, the first female student was enrolled; in 1891 the Department of Agriculture was established, followed by the Department of Dairy Science in 1901; in 1918 after university authorities refused funding the Chair of Zoology R.D. Laurie and his colleagues built their own Zoology Department. In the 1960’s the University built the Penglais Campus where this meeting is being held.

Parasitology in Aberystwyth

There is a long history of parasitology at Aberystwyth. Dr Florence Gwendoline Rees (later becoming Prof. Rees; right) joined Aberystwyth University (AU) in 1930 and subsequently spent the rest of her professional career here, helping establish AU as a centre of excellence for parasitological research. Among her many achievements, Florence was a founding member of the British Society for Parasitology (BSP) where she later served as the president from 1974 to 1976. At the same time she was an honorary fellow of the American Society for Parasitology (ASP), the Chairman of the editorial board of Parasitology (1970-81) and the first Welsh woman to become a fellow of the Royal Society. Her research was in the area of helminthology, concentrating on the systematics, comparative functional anatomy, histology and life cycles of trematodes and cestodes. The work of Florence was important in defining the relationship between parasites and their invertebrate intermediate hosts. Her papers were meticulously researched and illustrated with elaborate line drawings. During her time with AU, Florence was joined by several prominent parasitologists, including Dr John Barrett (later becoming Prof. Barret; below).

Prof. Gwendolen Rees

Prof. John Barret

Starting his research with AU in 1973, John was keen to study helminth

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biochemistry with an emphasis on comparative energy metabolism and detoxification mechanisms. He was awarded the C. A. Wright medal from the BSP in 1985 and the Bueding-von Brand medal from the ASP in 2001. In 1991 he was elected Dean of Science and over the next three years was instrumental in steering the Faculty in its move to modularity and a two semester teaching year. In 2000, John was successively appointed Pro Vice-Chancellor of two different posts, the second one of which he held until his retirement in 2006. Shortly after, he became the president of the BSP from 2006 to 2008 and kept in touch with research activities in parasitology at AU until his death in 2011. As a hallmark of John's legacy, Aberystwyth University's Barret Centre for Helminth Control (BCHC) established in 2016, bears his name.

In 2007, AU recruited three new research scientists; Prof. Peter Brophy from Liverpool University, Prof. Karl Hoffmann from the University of Cambridge and Prof. Chris Thomas from Durham University. In 2008, they formed the Parasitology and Epidemiology (PE) Group within the Institute of Biological, Environmental and Rural Sciences (IBERS). By engaging in basic-science-, co-evolutionary driven- and systems-based- investigations, the PE group collectively addresses some of the world's major health problems caused by important biomedical and veterinary pathogens. In 2016, the BCHC was created and brings together an internationally-recognised team to lead the research community in the fight against parasitic worms causing agricultural, veterinary and biomedical diseases. It is one of ten Interdisciplinary Research Centres based at AU and is composed of members from IBERS and the Institute of Mathematics, Physics and Computer Science (IMPACS). The research at BCHC spans a variety of disciplines and is funded by the likes of Innovate UK, the Wellcome Trust, Life Sciences Research Network Wales (LSRNW), the BBSRC and the Welsh Government.

In 2018 the strong and vibrant PE group consists of investigators with expertise in gene level investigations, application of single-molecule and functional genomics-based technologies, high-throughput compound screening, biomarker discovery, host-parasite interactions, immunological investigations, evolutionary studies, ecological epidemiology, mathematical modelling, GIS, satellite and aerial remote sensing and climate modelling. They are supported by advanced microscopy and bio-imaging, genomics and bio-informatics facilities, as well as the BCHC, and the Roboworm high throughput drug discovery platform . Our studies consider a range of infectious diseases caused by viruses, bacteria, protozoa, microsporidia and helminths.

In 2018, AU will accept it's first cohort of MRes students in Parasite Control, a one year PG course providing a range of vocational skills for professional employment or further post-graduate PhD studies in Parasitology or related disciplines (i.e. infectious diseases, public health, epidemiology, etc.). An aspect of this course that uniquely positions itself from other Masters level Parasitology courses in the UK is the 12-month dissertation project. Working under the supervision of active researchers in the field, students will collaboratively develop a

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research project on diverse topics such as (but not inclusive) intermediate host and vector control, anthelmintic drug and target discovery, biomarker identification, visual cue selection for arthropod vectors, mathematical modelling of disease transmission, host responses to parasite biomolecules, parasite and host population studies and functional genomics manipulation of parasites.

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About the BSP

Today many researchers and students are very passionate about the fascinating world of infectious diseases, parasites, their complex lifestyles and their associated impact on people and livelihoods.

To draw attention to the unique importance of parasitology as a distinct discipline within biology, The British Society for Parasitology was formed in 1962 from the Parasitological Section of the Institute of Biology. Today the Society is the central networking and meeting point for many professional and amateur parasitologists throughout the UK and across the world.

Did you know that the UK leads Europe – and Europe leads the world – in parasitology research? No European country publishes more parasitology research than the UK, and UK papers were cited more than those from any other country in the past 5 years (2011-2016, data from Elsevier SciVal, see News item for more details.)

As the leading academic society for a country preeminent in parasitology, the remit of the BSP is broad. It promotes and supports the academic study of parasitology in all its many guises. This can be from experimental to theoretical approaches as applied to infection biology and disease research, or from ecological to medical and veterinary studies in global health and international aid. Each year students are given financial support to attend BSP meetings and scholarship schemes are in place to support fieldwork and training events.

The membership of the BSP stands at around 800 in number. Approximately a third of members are from overseas locations. Highlights of the annual BSP calendar include the annual residential meetings in spring and autumn which are focused upon general and specialist aspects of parasitology. Written academic outputs include special issues or supplements in a variety of scientific journals and books.

The BSP Society is a charitable company and managed by the BSP Council. This comprises a President, Honorary Officers and ordinary Council Members, who together act as Company Trustees. Co-opted members of Council also include representation from the student membership and other learned societies where clear synergies are apparent.

The BSP Council 2017-18

Professor Mark Taylor - Council President (2016-2018)
Professor of Parasitology at Liverpool School of Tropical Medicine
Prof Maria-Gloria Basanez - Vice-President (2016-2018)

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Professor of Neglected Tropical Diseases at Imperial College London

Professor Damer Blake - Honorary Meetings Secretary (2016-2019)

Professor of Parasite Genetics at the Royal Veterinary College

Dr Paul Denny - Honorary Treasurer (2016-2019)

Director of Postgrad Research at Durham University

Professor Paul Horrocks - Honorary General Secretary (2016-2019)

Professor in Molecular Parasitology at Keele University

Dr Catherine Merrick - Honorary Communications Secretary (2015-2018)

Senior Lecturer in Biology at Keele University

Dr Alvaro Acosta-Serrano - Ordinary Council Member (2016-2018)

Senior Lecturer in Parasite and Vector Biology, Liverpool School of Tropical Medicine

Professor Jo Cable - Ordinary Council member (2015-2018)

Professor of Parasitology at Cardiff University

Dr Helen Price - Ordinary council member (2016-2019)

Lecturer in the Centre for Applied Entomology and Parasitology (CAEP) at Keele University

Dr Paul McVeigh - Ordinary council member (2016-2019)

Research fellow at Queen's University, Belfast

Dr Justin Pachebat - Ordinary council member (2016-2019)

Senior Lecturer in Microbial Genomics at Aberystwyth

Ms Alison Mbekeani - Student representative

PhD student at Durham University

Mr Tom Pennance - Student representative

PhD student at the Natural History Museum and Cardiff University

BSP AGM

This is the first year of the CIO Charitable Incorporated Organisation. The new status allows us to use more modern forms of communication, to and from the membership. Below is the link to the accounts for 2017; it should be noted they differ a little in their form from the old charity but we have wherever possible attempted to replicate the approach taken in previous accounts

http://bsp.uk.net/wp-content/uploads/2018/03/Signed-2017-Accounts.pdf

Student travel awards are given at the end of the AGM.

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General Meeting information

Reception and Registration

BSP Registration and Welcome Reception

Sunday conference registration will be at Old College (on the seafront) between 14:00 to 20:00.
Monday to Wednesday conference registration will be at the Students Union building from 08:00.

On Sunday evening between 18:30 and 20:00 there is a Welcome Reception at Old College with finger buffet and drinks. This will be followed by a family friendly Public Understanding of Science lecture by Professor PeterChiodini 'Invasion of the parasites. *A Hospital for Tropical Diseases Production*. Coming soon to a theatre near you'.

The Conference programme starts on Monday at 8.45 in the Great Hall, Arts Centre. Other facilities that will be made available at the reception desk will include:

- Urgent message pickup
- Conference organising committee contact details
- Internet access codes
- An information board
- Tourist Information

Delegates who have booked university accommodation (rooms at Pentre J Morgan) should pick up their room keys from the Porter's Lodge,(Aberystwyth University Penglais Campus main entrance).

On Sunday coaches will be available to shuttle delegates from Aberystwyth Railway Station to Old College and to the Porters lodge for key collection and Pentre J Morgan.

On Monday to Wednesday coaches will collect delegates from Aberystwyth Town Centre in the morning and drop off in the evening.

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On Wednesday afternoon from 16:00 a coach will collect delegates from outside IBERS, Penglais Campus and drop off at Aberystwyth train station.

Presentations

Information for Oral Presentations

Loading of oral presentations will take place in the lecture theatre appropriate to the session, and there is a desktop computer provided.

Please ensure that your presentation is loaded by 8.45am at the latest if you are presenting in the morning sessions or by 1.45pm if you are presenting in the afternoon sessions.

There will be a student volunteer in each room who will help you load your presentation and assist you if any problems arise with the A/V equipment.

Speakers are respectfully requested to keep to their time slot so that delegates who wish to move between sessions can do so.

All presentations should be as follows
30 mins – 25 mins oral with 5 mins for questions.
15 mins - 10-12 mins oral with 3-5 mins for questions
10 mins – 7-8 mins oral with 3-2 mins for questions.

Information for Poster Presentations

Posters will be displayed in the Students Union Building, next to the Arts Centre.

Posters should be A0 size (841 mm wide x 1189 mm high) in portrait format, and be no larger than 900 mm wide x 1200 mm high).
You will find Velcro coins on the board ready to attach your poster. Please put up your poster on Monday before the first poster session and remove it on Wednesday afternoon.

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There are two poster sessions during the conference: Monday from 17:45 to 19:15 (odd poster board numbers), and Tuesday from 17:45 till 19:15 (even poster board numbers). Presenters should stand by their poster during these times.

Delegates will receive a drinks voucher for each poster session: these can be exchanged for a soft drink, a glass of wine or a bottle of locally brewed beer (Penlon Brewery).

Social Programme and Trade Fair

Welcome Reception & Public Lecture: Sunday

Delegates and their families are invited to attend the Welcome Reception at Old College on Sunday evening from 18:30 to 20:00. Old College is located on the seafront (close to the pier). Canapes and refreshments will be provided. Welsh Singers Bois-y-Fro will be performing during the Welcome Reception. During the reception their will be a presentation to recipients of the Rhiannon Powell Science Bursary, set up in memory of Rhiannon by her daughters, Kay and Suzanne. Rhiannon was a proud Biological Sciences alumna who valued education, furthering the academic cause and inspiring and supporting the scientists of tomorrow.

After the welcome reception delegates are invited to stay at Old College to attend a Public Lecture at 20:00 by Professor Peter Chiodini ‘Invasion of the parasites. *A Hospital for Tropical Diseases Production*. Coming soon to a theatre near you'.

A coach to return delegates to the Pentre Jane Morgan accommodation on Penglais Campus will be available from outside the Pier/Chinese Restaurant on the Promenade from 21:00

Arts Centre Cinema

Delegates and their families are invited to use the Arts Centre Cinema.
During the conference (Monday – Wednesday) the cinema will be offering tickets at a discounted rate of £4.50 to delegates and accompanying family members for the following films:

MONDAY 2.30pm: Peter Rabbit (PG)
MONDAY 5.45pm: The Phantom Thread (15)
TUESDAY 1.45pm: Peter Rabbit (PG)

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TUESDAY 4.00pm: Peter Rabbit (PG) - (this screening subtitled for hard of hearing)
TUESDAY 6.15pm: Peter Rabbit (PG)
WEDNESDAY: 12.00pm: Peter Rabbit
WEDNESDAY: 2.30pm: Phantom Thread (15)

We are also offering classic parasite films for delegates to watch for free on Monday and Tuesday evenings. On Monday at 20:30 we will be showing X Files - Host' followed by John Carpenters 'The Thing'. On Tuesday at 20:30 we will be showing 'X Files - Ice' followed by 'Aliens'.

Photography Exhibiton & Wellcome Trust Films

Photographs and images submitted for the BSP photograph competition in the two categories:

1) My Favourite Parasite
2) Parasitology and Me

These will be displayed on screens opposite the Arts Centre Great Hall. We will be showing a selection of Wellcome Trust parasite related documentaries in the audio visual Pod next to the Great Hall.

BES Special Interest Group Social: Monday from 19:15

The BES SIG social will be at the Royal Pier, Marine Terrace, Aberystwyth SY23 2AZ http://www.royalpier.co.uk from 19:15 to 20:15.

Aberystwyth Science Café : Monday from 19:30

The BSP are proud to invite delegates to attend a special Aberystwyth Science Café in the Arts Centre Theatre Bar. '*Parasites: the Good, the Bad and the Ugly*' featuring Professors Alex Loukas, Peter Preiser and Rachel Chalmers. Professor Sheena Cruickshank will be chairing the event.

Young Parasitologists Party

This year's YPP will be held at Y Consti, a cliff side restaurant overlooking the town and sea. A ride to the top of the cliff on the Aberystwyth Cliff Railway will also be included.

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The cliff railway station couldn’t be easier to find - head to the promenade and walk north (with the sea on your left) when you reach the end of the promenade look to your right and there it is! Some of the conference helpers will be at the Cliff Railway station to greet you.

ABERYSTWYTH SCIENCE CAFÉ

&

THE BRITISH SOCIETY FOR PARASITOLOGY

are proud to present

Parasites:

THE GOOD

THE BAD

AND THE UGLY

7:30 pm, Monday 9th April 2018

Aberystwyth Arts Centre, Theatre Bar

(Free event, open to the public)

Professor Alex Loukas, James Cook University, Australia, researches vaccines for human parasitic infections and novel anti-inflammatories for the treatment of autoimmune and allergic disorders, including inflammatory bowel disease.

Professor Peter Preiser, Nanyang Technological University (NTU), Singapore, specialises in the study of the malaria parasite and leads the NTU team that discovered a route to a possible vaccine for malaria.

Professor Rachel Chalmers, Consultant Clinical Scientist and Head of the NHS Wales Cryptosporidium Reference Unit, provides specialist detection and advisory services for the management of national and international outbreaks of cryptosporidiosis.

Barrett Centre for Helminth Control

FUGI

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Timetable in Brief

Plenary (Great Hall, Arts Centre)

Sunday 8th

Public Understanding of Science - 20:00 to 20:30 (30 mins)

A15772 - *Invasion of the Parasites, a hospital for tropical diseases production. Coming soon to a theatre near you.* (Peter Chiodini)

Monday 9th

Plenary Sessions (Great Hall, Arts Centre)

Plenaries 08:45 to 10:45

08:45 *Welcome*

09:15 - Plenary I - *Hookworms and their secreted proteins as a novel anti-inflammatory modality* (Alex Loukas) (45 mins)

10:00 - Plenary II - *The evolution of sociality and division of labour in trematode parasites* (Robert Poulin) (45 mins)

Tryps & Leish Sessions

Tryps & Leish Therapeutics, diagnostics & epidemiology I – Sponsored by Elsevier - (Stream 1 - Edward Llwyd 0.26 Biology Main - Edward Llwyd 0.26 Biology Main) 11:15 to 12:45

Chair - Prof Mark Field

11:15 - *Drug target deconvolution in the kinetoplastids* (Susan Wyllie) (30 mins)

11:45 - *The structure of serum resistance-associated protein and its implications for human African trypanosomiasis* (Sebastian Zoll) (15 mins)

12:00 - *Mode of action of the anti-trypanosomal benzoxaborole AN7973* (Christine Clayton) (15 mins)

12:15 - *Trypanosoma brucei 20S proteasome homology modeling and validation of compound interaction assist in designing novel proteasome inhibitors* (Srinivasa P S Rao) (15 mins)

12:30 - *Trypanosomes and their bloody matrix: microfluidic separation approaches* (Axel Hochstetter) (15 mins)

Tryps & Leish Cell & Molecular Biology I - (Stream 1 - Edward Llwyd 0.26 Biology Main) 14:00 to 15:30

Chair - Prof Wendy Gibson

14:00 - *Co-transcriptional nuclear export of trypanosome mRNAs* (Susanne Kramer) (30 mins)

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14:30 - *Towards a whole genome CRISPR-CAS9 loss of function screen to study the mode of action and resistance to drugs in Leishmania* (Ana Maria Mejia) (15 mins)

14:45 - *Gluconeogenesis in bloodstream-form Trypanosoma brucei* (Julie Kovarova) (15 mins)

15:00 - *Global gene expression analysis during the Trypanosoma cruzi life cycle identifies regulatory RNA Binding Proteins involved with metacyclogenesis and parasite virulence* (Santuza Maria Teixeira) (15 mins)

15:15 - *Co-localisation of two simultaneously active VSG expression sites in 'double-expresser' T. brucei strains* (James Budzak) (15 mins)

Tryps & Leish Therapeutics, diagnostics & epidemiology II - (Stream 1 - Edward Llwyd 0.26 Biology Main) 16:15 to 17:45

16:15 - *Towards the next generation of drugs for African trypanosomiasis* (Pascal Mäser) (30 mins)

16:45 - *Rapid accumulation of suramin in bloodstream form trypanosomes leads to differentiation related metabolic switching* (Mark Field) (15 mins)

17:00 - *More than immune evasion – a variant surface glycoprotein causes in vitro suramin resistance in Trypanosoma brucei* (Natalie Wiedemar) (15 mins)

17:15 - *Minor groove binders as antitrypanosomal agents for animal African trypanosomiasis* (Federica Giordani) (15 mins)

17:30 - *Dīvide et īmpera: Chromosome segregation in Trypanosoma brucei, a target deconvolution view.* (Manuel Saldivia) (15 mins)

Ecological Parasitology Sessions

Ecological Parasitology I - (Stream 4 - Edward Llwyd 0.01) 11:15 to 12:45

11:15 - *Throwing the baby out with the bath water: impact of parasite control treatments on non-target organisms* (Rachel Paterson) (30 mins)

11:45 - *Are parasites stressful?* (Katie O'Dwyer) (15 mins)

12:00 - *Effects of host's altered food ration on host-parasite interaction in changing environment* (Saman Yaqub) (15 mins)

12:15 - *Warming can alter host behaviour to the same extent as behaviour-manipulating parasites* (Maureen Williams) (15 mins)

12:30 - *Human history, drugs and climate shape the global diversity of Haemonchus contortus populations* (Guillaume Sallé) (15 mins)

Ecological Parasitology: Eco-Immunology. - (Stream 4 - Edward Llwyd 0.01) 14:00 to 15:30

14:00 - *Food and environmental temperature predominantly drive immune allocation and infection resistance in wild fish* (Joe Jackson) (30 mins)

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14:30 - *The Immune State of Wild Mice, Mus musculus domesticus* (Mark Viney) (15 mins)

14:45 - *Fungal communities in the Field Vole (Microtus agrestis) and their possible impact on host immunology and disease risk* (Anna Thomason) (15 mins)

15:00 - *Assessing the Darwinian costs of mounting an adaptive immune response* (Dominik Schmid) (15 mins)

15:15 - *Taking a step into the unknowns of myoxozoan genomics: Sequencing and functional characterisation of a myxozoan micro-exon gene* (Jason Holland) (15 mins)

Ecological Parasitology: Multi-species Interactions - (Stream 4 - Edward Llwyd 0.01)16:15 to 17:45

16:15 - *Unravelling Interactions Between Schistosomes, the Microbiome and Anti-Helminthic Drugs in a Ugandan Field Setting* (Lauren Carruthers) (15 mins)

16:30 - *The effect of endemic macroparasite on the quality and quantity of an epidemic parasite* (Oluwaseun Somoye) (15 mins)

16:45 - *Strongyloides stercoralis infection in humans and its association with increased gut microbial diversity* (Timothy Jenkins) (15 mins)

17:00 - *Social stress alters transcriptomic responses to infection and dysregulates molecular body clocks* (Amy Ellison) (15 mins)

17:15 - *Murine schistosomiasis quantitatively and qualitatively modifies the intestinal microbiota* (Laura Peachey) (15 mins)

Protozoa Sessions

Protozoa: Cell Biology & Immunology I - Sponsored by William Powell - (Stream 2 - Llandinam A6) 11:15 to 12:45

Chair - Dr Tony Holder

11:15 - *Immune-mediated control of Toxoplasma in human cells* (Eva Frickel) (30 mins)

11:45 - *Functional characterization of mitochondrial translation components in the early diverging eukaryote Toxoplasma gondii.* (Alice Lacombe) (15 mins)

12:00 - *Development of modified organoid culture protocols for interrogation of interactions between Toxoplasma gondii and the intestinal epithelium* (Janine Coombes) (15 mins)

12:15 - *Serotyping and genotyping studies reveal indigenous atypical type II Toxoplasma strains are associated with symptomatic infection of patients in Australia* (John Ellis) (15 mins)

12:30 - *Apicomplexan C-mannosyltransferases modify adhesins of the TRAP family* (Andreia Albuquerque-Wendt) (15 mins)

Protozoa: Drug Discovery & Resistance - (Stream 2 - Llandinam A6) 16:15 to 17:45

16:15 - *Antimalarial pharmacology of primaquine: Attempting to solve a 70 year-old puzzle* (Giancarlo Biagini) (30 mins)

Go to here for the 'at a glance' view of the conference

16:45 - *RecQ helicases in the malaria parasite Plasmodium falciparum affect genome stability, gene expression patterns and DNA replication dynamics* (Catherine Merrick) (15 mins)

17:00 - *Artemisinin resistance? Mind the traffic ...* (Colin Sutherland) (15 mins)

17:15- *Repositioning of synthetic emetine analogues as potential anti-malarial drugs and use of molecular modelling tools to aid in drug discovery* (Priyanka Panwar) (15 mins)

17:30 - *Exploring the potential of autophagy as a novel drug target: SK1.49 as a chemical probe of autophagy in Plasmodium falciparum* (Paul Horrocks) (15 mins)

Helminth Sessions

Helminths: Drug Discovery & Resistance I - Sponsored by Life Sciences Research Network Wales - (Stream 3 - Physics 0.15 Main) 11:15 to 12:45

11:15 - *Targeting epigenetic mechanisms for drug development against Neglected Parasitic Diseases: the A-ParaDDisE project and beyond* (Raymond Pierce) (30 mins)

11:45 - *Targeting the histone methylation machinery in Schistosoma mansoni* (Gilda Padalino) (15 mins)

12:00 - *Curcumin induced biochemical and tegumental surface changes in a digenetic fluke : Clinostomum complanatum* (Lubna Rehman) (15 mins)

12:15 - *Computationally-Guided Drug Repurposing Enables the Discovery of Kinase Targets and Inhibitors as New Schistosomicidal Agents* (Nicholas Furnham) (15 mins)

12:30 - *In silico profiling and prediction of putative neuropeptide ligand-receptor interactions in parasitic nematodes* (Fiona Mc Kay) (15 mins)

Helminths: Molecular Communication – Sponsored by Zoetis- (Stream 3 - Physics 0.15 Main) 14:00 to 15:30

14:00 - *Small RNAs in nematode-host interactions* (Amy Buck) (30 mins)

14:30 - *Nematode microRNAs – roles in development and host-parasite interactions* (Collette Britton) (15 mins)

14:45 - *Characterisation of Schistosoma mansoni Larval Extracellular Vesicle protein 1 (SmLEV1) an immunogenic, schistosome-specific, protein exhibiting developmentally regulated alternative splicing* (Thomas Gasan) (15 mins)

15:00 - *Optimisation Of Parasitic Extracellular Vesicle Purification for Downstream Analysis To Understand Their Role Within Drug Exposure* (Chelsea Davis) (15 mins)

15:15 - *MiR-277/4989 regulate transcriptional landscape during juvenile to adult transition in the parasitic helminth Schistosoma mansoni* (Anna Protasio) (15 mins)

15 :30 - *Wormbase Parasite* (Kevin Howe) (10 mins)

Go to here for the 'at a glance' view of the conference

Helminths: Intermediate host - parasite interactions. Sponsored by Zoetis - (Stream 3 - Physics 0.15 Main) 16:15 to 17:45

Chair - Dr Jim Collins

16:15 - *First contact - Release of schistosome exosome-like extracellular vesicles during early intramolluscan larval development* (Tim Yoshino) (30 mins)

16:45 - *Comparing the population genetic structure of snail hosts and their schistosome parasites in Northern Senegal* (Tine Huyse) (15 mins)

17:00 - *Snail infection / pre-patent surveillance approach for intestinal schistosomiasis control and elimination programs: Tanzania* (Tom Pennance for Bonnie Webster) (15 mins)

17:15 - *Farewell to the God of Plague: Conquering schistosomiasis in China; the last mile* (Don McManus) (15 mins)

17:30 - *Experimental evaluation of behavioural changes in gilt-head seabream infected with brain-encysted metacercariae of Cardiocephaloides longicollis* (Trematoda, Strigeidae) (Ana Born-Torrijos) (15 mins)

Clinical Parasitology Session

Clinical Parasitology - (Stream 2 - Llandinam A6) 14:00 to 15:30

14:00 - Toxoplasma and transplants: forewarned is forearmed (Roger Evans) (20 mins)

14:20 - Life as a clinical parasitologist (Peter Chiodini) (20 mins)

14:40 - *Prevalence of malaria, urinary schistosomiasis, typhoid fever and hepatitis b virus co-infection among school children in Ogbese, Ise-Ekiti, South-Western, Nigeria.* (Charles Ayorinde) (10 mins)

14:50 - *Epidemiology of Trichomonas vaginalis infection among infertile women in Gaza city, Palestine* (Adnan Al-Hindi) (10 mins)

15:00 - *A rapid ATP bioluminescence assay for antimicrobial susceptibility testing of Acanthamoeba; cysts and trophozoites* (Chidi Ahamuefula) (10 mins)

15:10 - *Treatment of individuals living with neurocysticercosis and HIV/AIDS: a systematic review* (P Jewell) (10 mins)

15:20 – *Designing antifilarial drug trials using clinical trial simulators: the case of river blindness* (Martin Walker) (10 mins)

Workshops

In vitro Technologies in Cryptosporidium Research: Workshop 1 - (Stream 5 - IBERS New Build 0.33) 11:15 to 12:45

11:15 - *Introduction to the 3Rs* (NC3Rs representative) (10 mins)

Go to here for the 'at a glance' view of the conference

11:25 - Topic 1: *Advances in In vitro culture of Cryptosporidium* (Nigel Yarlett) (50 mins)

12:15 - Topic 2: *Genetic stability of parasites in the in vitro cultures* (30 mins)

In vitro Technologies in Cryptosporidium Research Workshop 2 - (Stream 5 - IBERS New Build 0.33) 14:00 to 15:30

14:00 - Topic 3: *Culturing from clinical and veterinary material; sample biobanks* (30 mins)

14:30 - Topic 4: *Potential novel approaches and future developments in Cryptosporidium in vitro cultures* (30 mins)

15:00 - Topic 5: *Genetic manipulation and drug target screening* (30 mins)

Commercialising Research Workshop - (Stream 5 - IBERS New Build 0.33) 16:15 to 17:45

16:15 - *Developing drugs for developing world diseases: The role of patents* (Katherine Ellis) (30 mins)

16:45 - *The challenges of commercialisation and industry adoption of novel parasite diagnostic tools* (Greg Mirams) (30 mins)

Poster Session I

17:45 – Odd Numbered posters with drinks in the Student Union (90 mins)

Social and Housekeeping

10:45 – *Tea and Coffee Break* : In Students Union (30 mins)

12:45 – *Lunch Break* : In Students Union (75 mins)

15:30 – *Tea and Coffee Break* : In Students Union (45 mins)

19 :15 –BES SIG social :At the Royal Pier, Marine Terrace, Aberystwyth SY23 2AZ (60 mins)

19 :30 – Science Cafe The Good, the Bad, and the Ugly with Professors Alex Loukas, Peter Preiser, Rachel Chalmers : In Arts Complex

20 :00 – Young Parasitologists Party : Constitution Hil take cliff Railway

Tuesday 10th

Plenary Sessions

Plenary III/IV - (Great Hall, Arts Centre)11:15 to 12:45

11:15 - *Genetic modification of Plasmodium for malaria vaccine development* (Shahid Khan) (45 mins)

12:00 - *Tsetse and trypanosomes* (Wendy Gibson) (45 mins)

Go to here for the 'at a glance' view of the conference

Tryps & Leish Sessions

Tryps & Leish Cell & Molecular Biology II - (Stream 1 - Edward LIwyd 0.26 Biology Main) 09:00 to 10:30

09:00 - *Post-transcriptional regulation of the Trypanosoma brucei cell cycle* (Michael Urbaniak) (30 mins)

09:30 3 - *In Vitro Characterization of a compound capable of arresting T. Cruzi cell cycle without affecting parasite viability* (Adalberto Miguel de Araújo Júnior) (15 mins)

09:45 - *Decoding the network of Trypanosoma brucei proteins that determines sensitivity to apolipoprotein-L1* (Sam Alsford) (15 mins)

10:00 - *Chemical-mediated transfection meets Parasitology: Trypanosomatids as proof-of-concept for the technology* (Francisco Olmo) (15 mins)

10:15 - *ERAD and disposal of misfolded GPI-anchored proteins in Trypanosoma brucei* (Calvin Tiengwe) (15 mins)

Host / Vector Parasite Interactions Sessions

Host /Vector- Parasite Interactions I - (Stream 1 - Edward LIwyd 0.26 Biology Main) 14:00 to 15:30

14:00 - *The cell cycle and the distinct antioxidant defence mechanisms of Trypanosoma rangeli* (Edmundo Grisard) (30 mins)

14:30 - *Complementary paths to Chagas disease elimination: the impact of combining vector control with aetiological treatment* (Maria-Gloria Basanez) (15 mins)

14:45 - *Parallel sexual and parasexual population genomic structure in Trypanosoma cruzi* (Philipp Schwabl) (15 mins)

15:00 - *Revisiting the intracellular cycle of Trypanosoma cruzi in chronically infected animals* (Martin Taylor) (15 mins)

15:15 - *Fatal progression of experimental visceral leishmaniasis is associated with secondary infection by commensal bacteria and severe anaemia* (Michael Lewis) (15 mins)

Host /Vector- Parasite Interactions II - (Stream 1 - Edward LIwyd 0.26 Biology Main)16:15 to 17:45

16:15 - *A second uninfected blood meal in sand flies promotes reverse metacyclogenesis and Leishmania replication* (Jesus Valenzuela) (30 mins)

16:45 - *The mRNA-bound proteome of Leishmania is stage-regulated with little correlation to transcriptome or whole proteome expression* (Pegine Walrad) (15 mins)

17:00 - *Differential expression of Vitamin D related genes in Macular vs. Polymorphic Post Kala-azar Dermal Leishmaniasis* (Srija Moulik) (15 mins)

17:15 - *Comparative metabolism of Trypanosoma brucei brucei and the livestock trypanosome T. congolense* (Pieter Steketee) (15 mins)

Go to here for the 'at a glance' view of the conference

17:30 - *Curative Benznidazole treatment in the acute stage of Trypanosoma cruzi infection prevents the development of chronic cardiac fibrosis* (Amanda Francisco) (15 mins)

Ecological Parasitology Sessions

Ecological Parasitology II - (Stream 4 - Edward LIwyd 0.01) 09:00 to 10:30

09:00 - *The world in an oyster - biological invasions and their impact on parasite-host interactions* (David Thieltges) (30 mins)

09:30

A15315 - *The role of the urban environment in shaping parasite communities of red foxes in Edinburgh* (Lisa Gecchele) (15 mins)

09:45 - *Ecological and population-level drivers of gastrointestinal parasitism in the Genus Papio: a meta-analysis* (Cassandra Raby) (15 mins)

10:00 - *Parasite-mediated effects of an invasive fish on native brown trout* (Paula Tierney) (15 mins)

10:15 - *Infected crayfish play it safe: Aphanomyces astaci reduces crayfish movement on land* (Rhidian Thomas) (15 mins)

Ecological Parasitology: Molecular Ecology and Evolution of Parasites - (Stream 4 - Edward LIwyd 0.01) 14:00 to 15:30

14:00 - *Determinants of genetic structure and diversity patterns in parasite population* (Isabel Blasco-Costa) (30 mins)

14:30 - *Xenomonitoring of schistosomiasis transmission on Pemba Island* (Zanzibar) (Tom Pennance) (15 mins)

14:45 *Totiviruses, parasites and everything else* (Ahmad Garziz) (15 mins)-

15:00 - *Parasitic feminisation of crustaceans* (Joseph Ironside) (15 mins)

15:15 - *Patterns of genetic variation in the parasitic nematode Strongyloides ratti* (Rebecca Cole) (15 mins)

Ecological Parasitology: Aquatic Parasitology I - (Stream 4 - Edward LIwyd 0.01) 16:15 to 17:45

16:15 - *Parasite resistance: from genes to ecosystems* (Chrisophe Eizaguirre) (30 mins)

16:45 - *The ecological role of trematode parasites in aquatic food webs: a case study in a subarctic lake* (Miroslava Soldanova) (15 mins)

17:00 - Vertical transmission and drivers of myxozoan distributions (Paolo Ruggeri) (15 mins)

17:15 - The global success of monogeneans: more than just a fluke (Jo James) (15 mins)

17:30 - *Rapid test to detect the infection load of the parasite, Anguillicola crassus, in the European eel, Anguilla anguilla* (Michele De Noia) (15 mins)

Go to here for the 'at a glance' view of the conference

Veterinary Parasitology Sessions

Veterinary Parasitology - Diagnostics & Therapeutics - (Stream 5 - Physics 0.11 A) 09:00 to 10:30

09:00 - *Current innovations in parasite diagnostics – what does the future look like?* (Greg Mirams) (30 mins)

09:30 - *Molecular detection of fancy birds parasites for clinical diagnosis and epidemiology* (Muhammad Fiaz Qamar) (15 mins)

09:45 - *On the importance of validating diagnostic RT-PCR assays for Dientamoeba fragilis and other gastrointestinal pathogens of human and veterinary importance* (John Ellis) (15 mins)

10:00 - *Isolation and characterization of novel reagents using phage display technique for detection of pathogenic Acanthamoeba* (Tim Paget) (15 mins)

10:15 - *Evaluation of oxfendazole in the treatment of zoonotic Onchocerca lupi infection in dogs* (Vito Colella) (15 mins)

Veterinary Parasitology Symposium - Arthropod Ectoparasites and Vectors Sponsored by MSD Animal Health- (Stream 5 - Physics 0.11 A) 14:00 to 15:30

14:00 - *Thelazia callipaeda: from oriental to European eyeworm* (Domenico Otranto) (30 mins)

14:30 - *Molecular Epidemiology of Tick-Borne Haemoparasites in Nigerian Sheep* (Babagana Mohammed Adam) (15 mins)

14:45 - *Ecological niche modelling of Phortica variegata and the potential for Thelazia callipaeda introduction to the UK* (John Graham-Brown) (15 mins)

15:00 - *The Prevalence and distribution of Babesia and Borrelia pathogens in ticks infesting domestic dogs in the UK* (Swaid Abdullah) (15 mins)

15:15 - *Optimisation of an on-hen feeding device for all hematophagous life stages of poultry red mite: a tool for mite control evaluation* (Francesca Nunn) (15 mins)

Veterinary Parasitology Symposium - Livestock Parasitology - (Stream 5 - Physics 0.11 A) 16:15 to 17:45

Chair - Prof Joanne Webster

16:15 - *Back to the Drawing Board - Basic Science improving Prospects for Control of Liver Fluke in Ruminants* (Grace Mulcahy) (30 mins)

16:45 - *The impact of acute and chronic infections by parasitic helminths on the faecal microbiota of UK Thoroughbred horses* (Laura Peachey) (10 mins)

16:55 - *The clinical importance of Fasciola hepatica infection in horses* (Alison Howell) (10 mins)

17:05 - *Neuropeptide Biology in Fasciola hepatica* (Duncan Wells) (10 mins)

17:15 - *Biomarkers of triclabendazole efficacy against Fasciola hepatica* (Clare Collett) (10 mins)

17:25 - *Examining the presence and function of tuft cells in ovine abomasum tissue following parasitic nematode infection* (Katie Hildersley) (10 mins)

Go to here for the 'at a glance' view of the conference

Public Understanding of Science Session

Public Engagement with Science - (Stream 2 - Llandinam A6) 09:00 to 10:30

09:00 - *From Parasites to Public Engagement and Impact* (Sheena Cruickshank) (30 mins)

09:30 - (30 mins) *Ticks: getting the bite right* (Richard Wall)

10 :00 - (30 mins) *The challenge of Malaria* (Paul Horrocks)

Protozoa Sessions

Protozoa: Cell Biology & Immunology II - Sponsored by William Powell - (Stream 2 - Llandinam A6) 14:00 to 15:30

14:00 - *Host cell cytosolic immune response during Plasmodium liver stage development* (Volker Heussler) (30 mins)

14:30- *Malaria parasite cycling: in and out of erythrocytes* (Tony Holder) (30 mins)

15:00 - *Comparative pathogenicity of Brazilian, Caribbean and European isolates of Toxoplasma gondii* (Clare Hamilton) (15 mins)

15:15 – *Cancelled* (Nana Efua) (15 mins)

Protozoa: Cell Biology & Immunology III - Sponsored by Life Sciences Andoh Research Network Wales- (Stream 2 - Llandinam A6) 16:15 to 17:45

16:15 - *Pre-Clinical and Early Clinical Evaluation of a Plasmodium berghei Sporozoite-Based Malaria Vaccine* (Miguel Prudencio) (30 mins)

16:45 - *Differential location and interactions of PfRH1 processing products during merozoite invasion* (Peter Preiser) (30 mins)

17:15 - *Plasmodium falciparum infected erythrocytes from cerebral malaria cases bind preferentially to brain microvascular endothelium; a study in Malawian children* (Janet Storm) (15 mins)

17:30 - *IgG and IgE responses to Plasmodium falciparum and intestinal parasites antigens in Mozambican children* (Rebeca Santano) (15 mins)

17:45 - *Magnitude of the inflammatory response to parasite infection differentiates calf and adult bovine monocytes* (Parul Sharma) (15 mins)

Helminth Sessions

Helminths: Immuno-modulation - (Stream 3 - Physics 0.15 Main) 09:00 to 10:30

09:00 - *Helminths and other environmental factors shaping the immune response: consequences* (Maria Yazdanbakhsh) (30 mins)

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09:30 - *Antigenic cross-reactivity between Schistosoma mansoni and allergens: a possible alternative explanation for the hygiene hypothesis* (Mike Doenhoff) (15 mins)

09:45 - *Unravelling early host intestinal epithelia interactions with whipworms using intestinal organoids* (Maria Adelaida Duque-Correa) (15 mins)

10:00 - *Antigenic targets of IgG1-associated anti-fecundity immunity against Schistosoma haematobium* (Rebecca Oettle) (15 mins)

10:15 - *Infection-state independent moderation of Th2 inflammation and inflammatory-associated lymphatic remodelling by tetracyclines in pre-clinical lymphatic filariasis pathology models* (Stephen Cross) (15 mins)

Helminths: Drug Discovery & Resistance II - Sponsored by Life Sciences Research Network Wales - (Stream 3 - Physics 0.15 Main) 16:15 to 17:45

16:15 - *Genetic and molecular basis of triclabendazole resistance in Fasciola hepatica* (Jane Hodgkinson) (30 mins)

16:45 - *Development of a long-term Brugia malayi lymphatic endothelial cell co-culture system and its validation as an alternative to in vivo screening for anti-Wolbachia drug assessment* (Amy Marriott) (15 mins)

17:00 – *Cancelled* (Abdollah Rafiei) (15 mins)

17:15 - *G-quadruplexes in the parasitic platyhelminth Schistosoma mansoni: identification and anthelmintic drugability* (Holly Craven) (15 mins)

17:30 - *Anthelmintic action of triclabendazole in vivo in juvenile tropical liver fluke, Fasciola gigantica: a scanning and transmission electron microscope study* (Ahammed Shareef) (15 mins)

17 :45 - *The first industrial scale screen of 1.3 million compounds against Wolbachia identifies five promising new leads for the treatment of lymphatic filariasis and onchocerciasis* (Rachel Clare) (15 mins)

Omics Session

Omics I –Sponsored by Wormbase Parasite- (Stream 3 - Physics 0.15 Main) 14:00 to 15:30

14:00 - *'Drugging' Liver Fluke into the 21st Century* (Aaron Maule) (30 mins)

14:30 - *G protein-coupled receptors (GPCRs) in the liver fluke, Fasciola hepatica* (Paul McVeigh) (15 mins)

14:45 - *Determining anti-glycan antibody responses to Haemonchus contortus Barbervax vaccine using glycan array screening* (Eve Hanks) (15 mins)

15:00 - *Chromatin structure changes are essential for life cycle progression of the human parasite Schistosoma mansoni* (Christoph Grunau) (15 mins)

Go to here for the 'at a glance' view of the conference

Poster Session II

17:45 – Odd Numbered posters with drinks in the Student Union (120 mins)

Social and Housekeeping

10:30 – *Tea and Coffee Break* : In Students Union (45 mins)

12:45 – *Lunch Break* : In Students Union (75 mins)

12:45 – Meet the Editors Workshop : LOCATIoN ?(75 mins)

12 :45 – WormbaseWorkshop : LL Computer Room B23 (100) (75 mins)

15:30 – *Tea and Coffee Break* : In Students Union (45 mins)

20 :00 – BSP Conferrence Dinner – Arts Centre

Wednesday 11th

Plenary Sessions

Wright Medal Lecture - (Great Hall, Arts Centre) 11:45 to 12:30

11:45 - *Trypanosomes get under your skin* (Annette MacLeod) (45 mins)

BSP Annuel General Meeting

12 :30 – Collect travel awards after AGM

Host / Vector- Parasite Interactions Sessions

Host -Vector- Parasite Interactions III - (Stream 1 - Edward LIwyd 0.26 Biology Main) 14:15 to 15:45

14:15 - *Follow the light: a trypanosomes' journey into the tsetse ectoperitrophic space* (A Acosta-Serrano) (30 mins)

14:45 - *Characterisation of genes important for the successful life cycle completion of Trypanosoma brucei in the tsetse (Aitor Casas-Sanchez) (15 mins*

15:00 - *Shape-shifting trypanosomes from the tsetse proventriculus (Lori Peacock) (15 mins)*

15:15 - *Swim like your lifecycle depends on it: The impact of motility on the survival of Leishmania parasites (Rachel Findlay) (15 mins)*

15:30 - *Ecology of cutaneous leishmaniasis in Ochollo, a hotspot in Southern Ethiopia* (Myrthe Pareyn) (15 mins)

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Ecological Parasitology Sessions

Ecological Parasitology: Aquatic Parasitology II - (Stream 4 - Edward Llwyd 0.01) 09:30 to 11:00

09:30 - *Pathogens associated with aquaculture may have wider ecosystem impacts* (Sarah Culloty) (30 mins)

10:00 - *Spatio-temporal variation of trematode parasites community in Cerastoderma edule cockles from Ria de Aveiro (Portugal)* (Luísa Magalhães) (15 mins)

10:15 - *Fussy Fluffy Fiend? Investigating Host-Specificity of Saprolegnia parasitica Isolates* (Emily Matthews) (15 mins)

10:30 - Can parasites be a drag? Impact of Argulus fish lice on host swimming performance (Rhiannon Hunt) (15 mins)

10:45 - *Use of in vivo fluorescent dyes to determine the infectivity and penetration pattern of Cardiocephaloides longicollis (Trematoda, Strigeidae) into the gilt-head seabream* (Gabrielle van Beest) (15 mins)

Ecological Parasitology: Ecological Modelling - (Stream 4 - Edward Llwyd 0.01) 14:15 to 15:45

14:15 - *Understanding transmission dynamics in multihost communities* (Andy Fenton) (30 mins)

14:45 - *Cancelled*

15:00 - *The impact of exposure heterogeneity on onchocerciasis transmission and control/elimination* (Jonathan Hamley) (15 mins)

15:15 - *Biodiversity dilution and amplification effects in tick-borne diseases: an eco-epidemiological modelling approach* (Flavia Occhibove) (15 mins)

15:30 - *Macroparasites are indirect drivers of hantavirus transmission* (Joanne Lello) (15 mins)

Veterinary Parasitology Sessions

Veterinary Parasitology Symposium - Wildlife Parasitology - (Stream 5 - Physics 0.11 A) 09:30 to 11:00

09:30 - *Microclimatic influences on availability of gastrointestinal nematode larvae of livestock under global warming* (Eric Morgan) (30 mins)

10:00 - Multi-locus sequence typing of Neospora caninum (John Ellis) (15 mins)

10:15 - Parasites of badgers in the Republic of Ireland- an untold story (Rachel Byrne) (15 mins)

10:30 – *Cancelled (Amna Arshad Bajwa)* (15 mins)

10:45 - *The toad fly Lucilia bufonivora: its evolutionary status and molecular identification* (Gerardo Arias Robledo) (15 mins)

Veterinary Parasitology Symposium - Sheep Scab - (Stream 5 - Physics 0.11 A) 14:15 to 15:45

14:15 - *Psoroptes ovis - a cause of significant disease in sheep and cattle* (Sian Mitchell) (30 mins)

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14:45 - *Treatment strategies for sheep scab: an economic model of farmer behaviour* (Emily Nixon) (15 mins)

15:00 - *The prevalence and distribution of sheep scab in Wales: a farmer questionnaire survey* (Hannah Rose Vineer) (15 mins)

15:15 - *Resistance to macrocyclic lactones, in Psoroptes ovis sheep scab mites* (Richard Wall) (15 mins)

Vector / Parasite Interactions Session

RES Vector - Parasite - Microbiome Interactions and Interventions Sponsored by The Royal Entomological Society- (Stream 2 - Llandinam A6) 09:30 to 11:00

Sponsored by the Royal Entomological Society.

09:30 - *Employing Anopheles microbiota for Plasmodium-blocking* (George Dimopoulos) (30 mins)

10:00 - *Attach and infect – Identification of a mosquito receptor for the Plasmodium ookinete* (Florian Brod) (15 mins)

10:15 - *Exploring the salivary N-glycome of bloodfeeding arthropods and their relevance in pathogen transmission* (Karina Mondragon-Shem) (15 mins)

10:30 – *Cancelled* (Alaa Al-Khafaji) (15 mins)

Protozoa Session

Protozoa: Cryptosporidium & Giardia Sponsored by PLos NTDs - (Stream 2 - Llandinam A6) 14:15 to 15:45

14:15 - *Recent advances in Giardia and Cryptosporidium genotyping* (Karin Troell) (30 mins)

14:45 - *Mining the Genome of Cryptosporidium to Elucidate Transmission Cycles* (Arthur Morris) (15 mins)

15:00 - *Acute Symptoms and Long-term sequelae of Human Cryptosporidiosis – a prospective study* (Bethan Carter) (15 mins)

15:15 - *Giardia duodenalis in Ugandan children: field application of recombinase polymerase amplification and determination of assemblages* (Tapan Bhattacharyya) (15 mins)

15:30 - *Giardia Secretome Highlights Secreted Tenascins as a Key Component of Pathogenesis* (Kevin Tyler) (15 mins)

Helminth Sessions

Helminths: Cell & Molecular Biology - (Stream 3 - Physics 0.15 Main) 09:30 to 11:00

Chair - Prof Tim Yoshino

09:30 - *Molecular analysis of schistosome reproductive develo*pment (Jim Collins) (30 mins)

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10:00 - *SGTP4–mediated glucose uptake in Schistosoma mansoni is regulated through Akt/PKB signalling* (Anthony Walker) (15 mins)

10:15 - *Somatic genome editing in the multicellular blood fluke Schistosoma mansoni* (Paul Brindley) (15 mins)

10:30 - *A propeptide 'clamp' mechanism is required for inhibition of Fasciola hepatica Collagenolytic Cathepsin L3* (Carolina De Marco Verissimo) (15 mins)

10:45) - *Maternal nematode infection induces transcription of Long-term potentiation in the postnatal brain via Wnt signaling* (Manjurul Haque) (15 mins

Helminths: Epidemiology & Field Work – Sponsored by Elsevier - (Stream 3 - Physics 0.15 Main) 14:15 to 15:45

14:15 - *Epidemiology and Evolution of zoonotic schistosomiasis in Africa: challenges for reaching the WHO elimination targets* (Joanne Webster) (30 mins)

14:45 - *Schistosoma mansoni praziquantel treatment: low coverage driven by systematic non-compliers or systematically not offered?* (Poppy Lamberton) (15 mins)

15:00 - *Impact of malaria coinfections on S. mansoni clearance, intensity and reinfection rates* (Rachel Francoeur) (15 mins)

15:15 - *Alternative strategies for onchocerciasis elimination in loiasis co-endemic areas: test-and-treat with doxycycline in combination with targeted vector control in South West Cameroon* (Louise Hamill) (15 mins)

15:30 - *Elimination within reach: lymphatic filariasis persists in rural Ghana due to sub-optimal intervention coverage and adherence* (Corrado Minetti) (15 mins)

Omics Session

Omics II - (Stream 1 - Edward Llwyd 0.26 Biology Main) 09:30 to 11:00

Chair - Dr Martin Swain

09:30 - *Helminth glycans at the host-parasite interface* (Cornelis Hokke) (30 mins)

10:00 - *Deciphering gonad-transcriptomes in Schistosoma mansoni provides novel and exploitable insights for basic and applied research* (Christoph G. Grevelding) (15 mins)

10:15)- *Regulation of RNA-binding protein stability and function by PRMT7-dependent arginine methylation in Leishmania* (Tiago Ferreira) (15 mins

10:30 - *Population genomics of Guinea worm eradication* (James Cotton) (15 mins)

10:45 - *Details Matter - Consistent, comparative and evidence-based genome annotation and re-annotation for the closely-related species, Cryptosporidium parvum, C. hominis and C. tyzzeri reveal surprising similarities and differences* (Jessica Kissinger) (15 mins)

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Social and Housekeeping

11:00 – *Tea and Coffee Break* : In Students Union (45 mins)

13:00 – *Lunch Break* : In Students Union (75 mins)

List of oral abstracts by time

Sunday 8th

Pleanary

Public Understanding of Science - 20:00 to 21:00 (30 mins)

Prof Peter Chiodini, *UCL Hospital for Tropical Diseases*

Invasion of the parasites, a hospital for tropical diseases production. Coming soon to a theatre near you - *A15772*

The public has a fascination with parasites and the diseases they may cause, so there is much demand for articles, lectures and documentaries on parasitology. But there is a thin line between the educational and sensational aspects of this discipline. This lecture will look at how parasites are portrayed in the media and examine how closely that matches reality. Despite such a high level of interest, public engagement in the UK is seriously lacking in crucial areas, to the detriment of individual patients and the public health. Individual cases will be used to illustrate the point.

Monday 9th

Plenary Session

09:15 - Plenary I - (45 mins) (Great Hall, Arts Centre)

Prof Alex Loukas, *Professorial Research Fellow, James Cook University*

Hookworms and their secreted proteins as a novel anti-inflammatory modality - *A15210*

A Loukas[1];

[1] James Cook University, Australia

Hookworms possess potent immunoregulatory properties. Support for this notion comes from immuno-epidemiological observations in hookworm-endemic countries, clinical trials involving experimental infection of volunteers with hookworms, and studies with animal models of inflammatory diseases. As proof-of-concept for the therapeutic benefits of helminth therapy, we have completed a small open label clinical trial using trace gluten

consumption coupled with hookworm as an immunoregulatory agent to treat coeliac disease. Beyond our expectations, the treatment resulted in improved gluten tolerance, improved coeliac disease activity measurements and increased regulatory T cell (Treg) numbers in the intestinal epithelium. Despite the promising efficacy of live helminth therapy, the approach has major drawbacks for wide-spread implementation. Central to the hookworm's ability to modulate inflammation is the excretory/secretory (ES) component, the parasite's public face of the host-pathogen interactome. We have characterised the hookworm secretome using genomics and targeted proteomics of the ES proteins and secreted vesicles. At least one family of abundant ES proteins with therapeutic properties in mouse models of asthma, colitis and rheumatoid arthritis has been identified, and one of these proteins (AIP-2) is undergoing further development in partnership with pharma as a novel biologic for treating autoimmune diseases.

10:00 - Plenary II - (45 mins) **(Great Hall, Arts Centre)**

Prof Robert Poulin, *Professor of Zoology, Otago University*

The evolution of sociality and division of labour in trematode parasites - *A15209*

R Poulin[1];

[1] Otago University, New Zealand

Social organisation involving division of labour is a phenomenon we generally associate with humans and colonial insects like ants, bees and termites. One of the most remarkable discoveries regarding parasite biology in recent years has been the recognition that this same kind of division of labour occurs in clonal colonies of trematode parasites within their snail intermediate hosts. In several trematode species, the life stages (rediae) occurring in snails come in two morphologically and functionally distinct forms: a reproductive caste ensuring the production of infective stages (cercariae) released from the snail, and a soldier caste consisting of much smaller and more mobile individuals that defend the colony, by attacking and killing trematodes of other species that attempt to colonise the same snail. I will first present an overview of this division of labour, summarise its phylogenetic occurrence among trematode taxa, and propose a simple evolutionary model to explain its stepwise evolution from an ancestral state where all rediae are identical. Then, I will discuss our recent *in-vivo* and *in-vitro* experiments exploring adaptive responses in the social organisation of trematodes. These experiments investigated whether trematode colonies adjust their caste ratio (number of soldiers versus number of reproductives) in the face of competition from other trematodes or other external threats. Also, we investigated phenotypic plasticity at the individual level, to test whether members of one caste can pick up the functions of the other caste when the latter's numbers are low. Overall, these studies reveal a level of complex social organisation comparable to that in higher organisms.

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Tryps & Leish Sessions

Tryps & Leish Therapeutics, diagnostics & epidemiology I - (Stream 1 - Edward Llwyd 0.26 Biology Main)11:15 to 12:45

Chair - Prof Mark Field

Invited Speaker -11:15 - (30 mins)

Dr Susan Wyllie, *Independent Investigator, University of Dundee*
Drug target deconvolution in the kinetoplastids - *A15151*

S Wyllie[1];
[1] University of Dundee, UK

Dr Susan Wyllie has more than 15 years of experience studying kinetoplastid biology. Specifically, her research has focused on determining the mechanisms of action and mechanisms of resistance of drugs targeting kinetoplastid parasites. Her talk will detail her recent work leading the Mode of Action Group at the University of Dundee. Specifically, she will detail the groups: -Use of complementary methodologies in the fields of genomics, chemical proteomics and cell biology to determine the modes of action and specific molecular targets of phenotypically-active compounds -Development of new genetic and cell biology tools to facilitate the study of drug mechanism of action in the kinetoplastids -Functional characterisation of novel targets -Development of novel cell-based assays to exploit high value drug targets

11:45

Dr Sebastian Zoll, *Postdoctoral Research Associate, University of Oxford*
The structure of serum resistance-associated protein and its implications for human African trypanosomiasis - *A15220*

S Zoll[3]; H Lane-Serff[1]; S Mehmood[4]; C V Robinson[4]; M Carrington[2]; M K Higgins[3];
[1] Medimmune, UK; [2] University of Cambridge, UK; [3] University of Oxford, Department of Biochemistry, UK; [4] University of Oxford, Physical and Theoretical Chemistry Laboratory, UK

Only two trypanosome subspecies are able to cause Human African Trypanosomiasis. To establish an infection in human blood, they must overcome the innate immune system by resisting the toxic effects of the trypanolytic

factors TLF1 and TLF2. These lipoprotein complexes contain an active component, apolipoprotein L1, ApoL1, a pore-forming protein that causes trypanosome cell death by a yet not well-characterised mechanism. One of the two human infective subspecies, *Trypanosoma brucei rhodesiense,* differs from non-infective trypanosomes solely by presence of the serum-resistance-associated protein, SRA, which binds directly to ApoL1 and blocks its pore-forming capacity. Since this interaction is the single critical event that renders *T. b. rhodesiense* human infective, detailed structural information that allows identification of binding determinants is crucial to understand immune escape of the parasite. This will ultimately create the input needed to drive the development of therapeutics as there is no current vaccine and existing drugs have severe side effects. Here we present the crystal structure of SRA and reveal the adaptations that occurred as it diverged from other trypanosome surface molecules to neutralise ApoL1. In order to determine the binding region with ApoL1 we carried out hydrogen-deuterium exchange mass spectrometry (HDX-MS) using recombinantly expressed proteins. To confirm and to further delineate the region of SRA identified as a hot-spot for ApoL1 binding in HDX-MS, mutational analysis was used. The binding affinities of wild-type and mutant SRAs to ApoL1 were then studied using microscale thermophoresis. Our mapping of residues important for ApoL1 binding revealed that the interaction is likely to be predominantly electrostatic in nature. These results give molecular insight into the SRA ApoL1 interaction, which is at the heart of human sleeping sickness.

12:00

Prof Christine Clayton, *Professor, ZMBH*

Mode of action of the anti-trypanosomal benzoxaborole AN7973 - *A15296*

D Begolo[8]; F Giordani[7]; I Vincent[7]; M Witty[5]; T Rowan[4]; Z Bengaly[2]; K Gillingwater[6]; Y Freund[1]; M P Barrett[7]; C Clayton[3];

[1] Anacor Pharmaceuticals, United States; [2] CIRDES, Burkina Faso; [3] DKFZ-ZMBH Alliance, Germany; [4] GALVmed, UK; [5] Global Alliance for Livestock Veterinary Medicine, UK; [6] Swiss Tropical and Public Health Institute, Switzerland; [7] Wellcome Trust Centre for Molecular Parasitology, University of Glasgow, UK; [8] ZMBH - Heidelberg University, Germany

In the past few years several million compounds have been tested for selective toxicity towards kinetoplastids, and thousands have shown activity. To develop such compounds, it is useful to know the mode of action. Characterization of cells that become resistant after RNAi has proven extremely useful in identifying mechanisms of uptake or intracellular activation, but not, so far, in identifying molecular targets.
The benzoxaborole compound AN7973 was considered for development for cattle trypanosomiasis, and a similar compound, AN5568, is in phase II trials for sleeping sickness. We investigated the mode of action of AN7973 using

multiple methods, including metabolome analysis and measurements of macromolecular biosynthesis. Treatment of *Trypanosoma brucei* with AN7973 inhibited *trans* splicing within 1h, as judged by increases in partially processed tubulin mRNAs, reduced levels of mRNA, and loss of the Y-structure splicing intermediate. Methylation of the spliced leader precursor RNA was not affected, suggesting a direct effect on processing machinery. The trypanosomes also accumulated perinuclear granules typical for splicing inhibition. Prolonged selection of trypanosomes in AN7973 resulted in only 1.5-fold resistance: while the genomes of the parasites had numerous changes, none was indicative of a primary target.
The cleavage and polyadenylation factor CPSF3 is a known oxaborole target in *Plasmodium* and *Toxoplasma* and there was a *CPSF3* gene duplication in a published line with mild resistance to a different oxaborole. We found that the EC_{50} for AN7973 in *T. brucei* was increased three-fold by ectopic expression of *T. brucei* CPSF3, indicating a possible role for CPSF3 as a target.
Several other benzoxaboroles showed effects similar to those of AN7973, but metabolic changes, splicing inhibition, granule formation, and resistance after CPSF3 expression did not always correlate and there was no obvious structure-function relationship. Our results suggest that inhibition of mRNA processing, perhaps via inhibition of CPSF3, contributes to the anti-trypanosomal activity of several benzoxaboroles.

12:15

Dr Srinivasa P S Rao, *Investigator, Novartis Institute for Tropical Diseases*

Trypanosoma brucei 20S proteasome homology modeling and validation of compound interaction assist in designing novel proteasome inhibitors - *A15298*

S Rao[3]; L Tian[1]; [2]; H Koh[1]; [2]; V Manoharan[1]; [2]; C Yen-Liang[3]; J Jiricek[3];
[1] Novartis, China; [2] Novartis, Singapore; [3] Novartis Institute for Tropical Diseases, United States

Phenotypic high through put screening resulted in identification of triazolopyrimidine (TP) class of inhibitors that are active against all kinetoplastids. Whole genome sequencing of resistant *T. cruzi* mutants against these inhibitors showed single nucleotide polymorphism (F24L and I29M) in β4 sub-unit of 20S proteasome. The proteasome sequence is very well conserved across 3 different kinetoplastids. Ectopic expression of β4 F24L and I29M mutations in *T. brucei* resulted in significant shift in IC50 against TP series compounds, thus validating proteasome as the target. In the present study, we developed *T. brucei* 20 S proteasome homology model by using human 20S proteasome template (PDB: 4R67). The differential IC50 data for multiple compounds generated using proteasome mutants helped in visualizing binding pocket between β4 and β5. Further, the model showed a few possible new interactions namely, S96 with flourophenyl group, Y113 and G129 form hydrogen bonds with amide group and one of the 2 nitrogens in the TP core probably interacting with the T1 of β5 subunit. The TP compounds have low

solubility and low brain penetration. The homology model is helping medicinal chemists to design new compounds. In parallel, β4 mutants (F24L and I29M) are assisting in "on target lead optimization" of compounds having core and side-chain modifications in order to optimize for better pharmacological properties. Further validation of probable β5 interactions is being investigated.

12:30

Dr. Axel Hochstetter, *Honorary Research Associate, University of Glasgow*

Trypanosomes and their bloody matrix: microfluidic separation approaches - *A15300*

A Hochstetter[1];

[1] University of Glasgow, UK

Humans and animals alike suffer from diseases caused by African trypanosomes. These protozoan parasites dwell in their hosts' adipose tissue and body fluids. Trypanosomes propel themselves using a single, mostly sheathed flagellum, which also plays key roles in immuno-evasion and differentiation throughout their life cycle.
Diagnosis of human African Trypanosomiasis (HAT) requires the positive identification of *Trypanosoma brucei spp.* in the bloodstream, which can be very challenging with samples of low parasitaemia, as for example in peripheral blood samples. Therefore, separating trypanosomes from other cells in their matrix (especially red blood cells) can be of pivotal importance for successful diagnosis of HAT. By increasing our knowledge on physicochemical properties of trypanosomes – and their importance for pathogenicity – we can adapt more and more microfluidic-based approaches to isolate the parasitic flagellates from red blood cells or other particles. Recent advances in interdisciplinary research have led to multiple microfluidics-based approaches – i.e. Dielectrophoresis, deterministic lateral displacement, and optical traps – to separate trypanosomes from (artificially) infected blood samples and to isolate single trypanosomes for analyses including drug screening.

Tryps & Leish Cell & Molecular Biology I - (Stream 1 - Edward Llwyd 0.26 Biology Main) 14:00 to 15:30

Chair - Prof Wendy Gibson

Invited Speaker 14:00 - (30 mins)

Dr Susanne Kramer, *Junior PI, Biozentrum, Lehrstuhl für Zell-und Entwicklungsbiologie, Universität Würzburg*

Co-transcriptional nuclear export of trypanosome mRNAs - *A15176*

C Goos[1]; M Engstler[1]; F Butter[2]; **S Kramer**[1];

[1] Biozentrum, Lehrstuhl für Zell-und Entwicklungsbiologie, Universität Würzburg, Germany; [2] Institute of Molecular Biology, Germany

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mRNA export is tightly regulated in eukaryotes. Several control systems are in place to ensure that only fully processed mRNA can leave the nucleus. Trypanosomes lack homologues to most proteins that control mRNA export in yeast, have highly unusual symmetrical nuclear pores and unspliced mRNAs are detectable in the cytoplasm. Thus, trypanosomes may have either no quality control system for mRNA export, or the system is not tight. We visualised mRNAs during nuclear export by intra-molecular multi-colour smFISH. We found that neither transcription, nor splicing needs to be completed for the start of nuclear export. However, unspliced transcripts are enriched in trypanosome-unique granules at the cytoplasmic site of the nuclear pores that resemble stress granules in protein composition, but depend on active transcription rather than translation. Taken together, our data indicate that trypanosomes lack important nuclear export control checkpoints present in other eukaryotes. Trypanosomes process their mRNAs by trans-splicing and have almost no introns: a tight quality control system may therefore not be necessary.

14:30

Dr Ana Maria Mejia , *Postdoctoral fellow, Université Laval*

Towards a whole genome CRISPR-CAS9 loss of function screen to study the mode of action and resistance to drugs in *Leishmania - A15518*

A MejiaP LeprohonC FernandezM Ouellette
[1] Université Laval , Canada

Leishmaniasis is a group of diseases caused by different species of protozoan parasites belonging to the genus *Leishmania*, which produce extensive morbidity and mortality in humans. Although there are some drugs available to treat these diseases, several problems associated with the uses of these drugs such as the high toxicity and the appearance of resistance are commonly reported. Thus, the development of new techniques, which are scalable to the entire genome, to understand the mechanisms of action and resistance of new and old drugs are necessary. We generated a new strategy to study the whole ORFome of *Leishmania* parasites using CRISPR-Cas9. To test our approach, first we designed a vector compatible with illumina sequencing to express the gRNA in *L. infantum* parasites expressing Cas9. As a proof of principle, we chose 4 candidates genes: miltefosine transporter (MT), aquaglyceroporin 1 (AQP1), nucleoside transporter (NT1) and thymidine kinase (TK), the disruption of which were shown to lead to the acquisition of resistance to the drugs miltelfosine, trivalent antimony SbIII, tubercidin, and 5-Fluorouracil, respectively. For each gene we designed a total of 6 gRNA (24 in total) that were pooled. After validating the diversity of this small library, the pool of gRNA was transfected in Cas9-expressing *L. infantum* promastigotes that were then independently selected for each drug using concentrations equivalent to 2.5x and 5x

the IC_{50}. In all cases we obtained parasites growing under drug pressure while mock-transfected parasites failed to grow. Sequencing the gRNA vector recovered from these parasites confirmed the targeting of the expected gene for each drug: MT-targeting gRNA for miltefosine-selected parasites, AQP1-targeting gRNA were recovered from SbIII-selected parasites, and so on. Gene deletions were confirmed by PCR, even for genes located on polyploid chromosomes. Following this proof of principle, we have now synthesized 48.000 gRNA. This library will be transfected in *Leishmania* which will be selected with drugs for whole genome loss of function screens.

14:45

Dr Julie Kovarova, *postdoctoral research assistant, University of Dundee*

Gluconeogenesis in bloodstream-form *Trypanosoma brucei* - *A15519*

J Kovarova[2]; M P Barrett[3]; D Horn[1];

[1] Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee, UK; [2] University of Dundee, UK; [3] Wellcome Centre for Molecular Parasitology, UK

The *Trypanosoma brucei* genome contains two glucose transporter gene types, each present in five copies organized in an array. Trypanosoma hexose transporter 1 (THT1) dominates in the bloodstream stage, whereas THT2 is procyclic specific. These transporters are thought to be the sole route of glucose supply for glycolysis in bloodstream form cells, while the need for a distinct transporter in the insect-stage has remained mysterious. We prepared RNAi constructs targeting each group of transporter genes specifically, or both simultaneously. We also tagged and localised a copy of each group to facilitate monitoring of knockdown; both proteins were localised to the plasma membrane, as expected. In the bloodstream form, THT1 knockdown lead to a growth defect, but the defect was more severe following THT1-THT2 double knockdown. In contrast, knockdown of both transporters in the procyclic stage resulted in only a minor growth defect. These outcomes are consistent with an exquisite dependence on glycolysis for ATP production in bloodstream-form cells; glucose is considered to be the only carbon source used by this life cycle stage. Somewhat surprisingly, the severe growth defect in bloodstream-form cells was rescued by supplementation of glycerol in the growth media. Subsequent metabolomics analysis demonstrated that these bloodstream-form cells take up and metabolise glycerol, using it for the synthesis of fructose 6-phosphate, and to fuel the tricarboxylic acid cycle. To our knowledge, this is the first observation of gluconeogenesis in bloodstream-form *T. brucei*. Glycerol may be a physiological substrate for gluconeogenesis in natural host tissues.

15:00

Dr Santuza Maria Teixeira, *Professor, Federal University of Minas Gerais*

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Global gene expression analysis during the *Trypanosoma cruzi* life cycle identifies regulatory RNA Binding Proteins involved with metacyclogenesis and parasite virulence - *A15583*

B M Valente[2]; T S Tavares[2]; W Goes[2]; V G Silva[2]; A E Oliveira[2]; C L Campos[2]; F S Pais[1]; T A Bellew[3]; N M El-Sayed[3]; **S Teixeira**[2];
[1] Centro de Pesuisas Rene Rachou, Brazil; [2] Federal University of Minas Gerais, Brazil; [3] University of Maryland College Park, United States

Trypanosoma cruzi, the causative agent of Chagas disease, has three distinct developmental stages that are programed to rapidly respond to environmental changes within the vertebrate and invertebrate hosts. Its population is comprised of a highly heterogeneous pool of strains that exhibit a wide-range of biological characteristics such as distinct morphology, growth rate, curves of parasitemia, virulence and sensitivity to drugs. Unlike other eukaryotes, *T. cruzi* protein-coding genes are transcribed into polycistronic pre-mRNAs that are subsequently processed into mature, monocistronic mRNAs through coupled "trans-splicing" and poly-adenylation reactions. Because of this, control of gene expression relies on post-transcriptional mechanisms mainly affecting steady-state levels and translation rates of mature mRNAs. We performed whole transcriptome analysis comparing *in vitro* cultured epimastigotes, trypomastigotes and intracellular amastigotes from two cloned strains, named CL Brener and CL-14, which showed highly distinct virulence phenotypes. Our RNA-seq data revealed common changes in gene expression in both parasites strains, reflecting their capacity to adapt their energy metabolism, oxidative stress responses, cell cycle control and interactions with cellular components within the distinct host environments. However, differences observed in the transcriptomes from both strains also indicated that the avirulent phenotype of the CL-14 strain may be due to reduced expression of genes encoding surface proteins that are associated with intracellular amatigote-trypomastigote differentiation. Since RNA-seq analyses also revealed significant changes in the expression of genes encoding RNA binding proteins (RBPs), we decided to characterize two novel RBPs that may act as regulatory factors involved in post-transcriptional control of gene expression during the life cycle of the two *T. cruzi* strains. Transcript levels of one RBP, named TcRBP99, are up-regulated 25-fold in epimastigotes of the CL Brener strain whereas the second RBP, named TcRBP300, presents constitutive expression in the virulent CL Brener but is highly up-regulated in trypomastigotes of the avirulent CL-14 clone. To investigate the role of these RBPs, we generated CL Brener epimastigote cell lines in which the TcRBP99 gene was disrupted as well as CL-14 knockout (KO) mutants for TcRBP300 gene. Analyses of mutant parasites revealed a role for TcRBP99 as a main factor controlling the expression of genes involved with epimastigote proliferation and differentiation since TcRBP99 KO cells grew slowly and presented increased capacity to differentiate into metacyclic trypomastigotes compared to wild type CL Brener epimastigotes. RNA-seq analyses of TcRBP99 KO mutants showed reduced levels of epimastigote-specific transcripts compared to wild type parasites and co-immunoprecipitation assays

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confirmed the mRNA binding capacity of TcRBP99 to a transcript encoding a protein involved with differentiation. A role for the TcRBP300 related to parasite virulence is currently been investigated in infection assays with CL-14 KO mutants as well as with transfected CL Brener cell lines over-expressing this gene.

15:15

Mr James Budzak, *PhD student, Imperial College London*
Co-localisation of two simultaneously active VSG expression sites in 'double-expresser' *T. brucei* strains - *A15615*

J Budzak[1]; L E Kerry[1]; C Davies[1]; A Aristodemou[1]; B Wickstead[2]; K Witmer[1]; B Hall[1]; M Kushwaha[1]; M Povelones[1]; G Rudenko[1];
[1] Imperial College London, UK; [2] Queen's Medical Centre, University of Nottingham, UK

The African trypanosome *Trypanosoma brucei* is coated with a dense layer of antigenically variable Variant Surface Glycoprotein (VSG) when in the bloodstream of the host. Although a single trypanosome has thousands of VSG genes, only one is expressed at a time in a stringently monoallelic fashion from one of about 15 telomeric expression sites (ES)s. The active ES is transcribed by RNA polymerase I (RNA pol I), which normally exclusively transcribes rDNA. ES transcription occurs in an extra-nucleolar body called the Expression Site Body (ESB). In order to investigate the restriction operating on monoallelic exclusion, we have generated cell lines in which the VSG221 and VSGV02 ESs were simultaneously selected for using drug selection markers. In addition, there is an *eGFP* gene in the VSG221 ES, and an *mCherry* gene in the VSGV02 ES, allowing ES activity to be monitored using flow cytometry. These 'double expresser' (DE) cell lines appear to continuously switch back and forth between the two ESs. We next introduced an RNAi construct into the DE KW01 cell line, allowing inducible knock-down of eGFP and mCherry. This allows us to transiently 'defluoresce' the cells and further analyse ES expression using an epitope tagged Pol I subunit or by DNA or RNA FISH experiments.
Interestingly, mNeonGreen tagged RNA pol I showed that around 64% of the DE KW01 trypanosomes contain only one ESB, 29% have no ESB, and 7% have two. DNA-FISH experiments showed that in 57% of all cells, both ESs either co-localise or are within 250 nm of each other. In contrast, in the parental 'single expresser' trypanosomes, only 3% of the two ESs are this close to each other. In order to monitor transcriptional activity in these DE lines, we used Stellaris RNA-FISH to detect nascent transcripts from both dynamically active ESs. We find that trypanosomes predominantly transcribe either one or the other ES. However strikingly, in cells where transcripts from both ESs are detected (about 20% of total cells), nascent transcripts from both ESs localise in close proximity in the nucleus. These data therefore show that ES double expression results in two active ESs sharing the same sub-nuclear location, presumably allowing the two ESs to occupy the same ESB. Although simultaneous

transcription of two ESs appears possible, transcriptional activation of only a single ES is highly favoured. This argues that monoallelic exclusion places a physical restriction on the number of ESs that can be simultaneously activated at any one time in the nucleus.

Tryps & Leish Therapeutics, diagnostics & epidemiology II - (Stream 1 - Edward LIwyd 0.26 Biology Main) 16:15 to 17:45

Invited Speaker 16:15 - (30 mins)

Assoc Prof Pascal Mäser, *Swiss Tropical and Public Health Institute*
Towards the next generation of drugs for African trypanosomiasis - *A15178*

P Mäser[1];
[1] Swiss Tropical and Public Health Institute, Switzerland

The incidence of human African trypanosomiasis being at a historic low, the elimination of the disease as a public health problem may finally be tangible - but only with a new, safe and uncomplicated treatment option. There is no shortage of potential drug targets. *Trypanosoma brucei* possesses numerous biochemical peculiarities that are essential to the parasite but absent in mammalian cells, i.e. trypanothione metabolism, the kinetoplast, the glycosomes and RNA editing. However, target-based approaches have so far not yielded novel drug candidates. The molecules that progressed to the clinical phases of development (pafuramidine, fexinidazole and the benzoxaborole SCYX-7158) had been discovered in cell-based screens. I shall compare the different approaches and present new strategies towards the next generation of drugs for human African trypanosomiasis.

16:45

Prof Mark Field, *Professor, University of Dundee*
Rapid accumulation of suramin in bloodstream form trypanosomes leads to differentiation related metabolic switching - *A15373*

M Zoltner[1]; G D Campagnaro[4]; M Cero[7]; A Burrell[2]; S Vaughan[2]; C Gadelha[5]; K F Leung[3]; M P Barrett[8]; H de Koning[4]; **M Field**[6];
[1] Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee, UK; [2] Department of Biological and Medical Sciences, Oxford Brookes University, Oxford, UK; [3] Department of Pathology, University of Cambridge, UK; [4] Institute of Infection, Immunity and Inflammation, University of Glasgow, UK; [5] Queen's Medical

Centre, University of Nottingham, Nottingham, UK; [6] University of Dundee, UK; [7] University of Glasgow , UK; [8] Wellcome Trust Centre for Molecular Parasitology, University of Glasgow, UK

Suramin, a key trypanosomiasis drug developed over a century ago, remains in the clinic for treatment of early stage disease, while its mode of action is elusive. Recent studies suggest a prominent role of endocytosis for suramin uptake and an apparent receptor function of invariant surface protein 75 (ISG75). We demonstrate here that suramin is taken up rapidly and accumulates to high intracellular concentrations, dependent on ISG75 abundance. Furthermore, we investigated how suramin impacts the global proteome and metabolome at various timepoints. Suramin treatment perturbs the mitochondrial membrane potential within hours, preceding a drop of cellular ATP-levels and a build-up of intracellular pyruvate. Global proteomics analysis of suramin treated cells revealed significant upregulation of enzymes of the tricarboxylic acid cycle, proline dehydrogenase, glutamate dehydrogenase, pyruvate dehydrogenase and mitochondrial metabolite transporters, suggesting a dramatic switch of mitochondrial metabolism. Also among the upregulated cohort are proteins involved in differentiation to stumpy form, including PAD isoforms and PIP39. Notably, the vast majority (>90%) of upregulated (>2 fold) proteins were previously described to be more abundant in the procyclic form when compared to the bloodstream form proteome. Our results demonstrate that suramin accumulation by endocytotic uptake is highly efficient, amounting to higher intracellular concentrations than previously assumed, indeed likely sufficient to act as micromolar inhibitor. The observed metabolic switching indicates the possibility that the suramin mode of action relies on trapping the parasite between life cycle stages.

17:00

Ms Natalie Wiedemar, *PhD student, Swiss Tropical and Public Health Institute*
More than immune evasion – a variant surface glycoprotein causes *in vitro* suramin resistance in *Trypanosoma brucei - A15648*

N Wiedemar[2]; M Zwyer[2]; M Zoltner[1]; F E Graf[2]; E Ndomba[3]; C Kunz Renggli[3]; M Cal[3]; R S Schmidt[3]; T Wenzler[3]; M C Field[1]; P Mäser[3];
[1] Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee, UK; [2] Swiss Tropical and Public Health Institute, Basel, Switzerland; [3] Swiss Tropical and Public Health Institute, Basel, Switzerland, Switzerland

Suramin is the drug of choice to treat the first stage of the acute form of sleeping sickness, caused by *T. brucei rhodesiense*. Despite its use for a century, knowledge about the drug is still limited. Investigating drug resistance mechanisms can help to identify the target, transport and mode of action of a drug. For suramin, we observed the

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emergence of a high resistance in a *T. b. rhodesiense* strain (STIB900) after exposure to the drug for only few days. Here we investigate the genetic and biochemical mechanisms behind this phenomenon.
A fresh STIB900 clone was exposed to suramin *in vitro* and four independently selected, resistant derivatives were generated. They were phenotypically characterized and mRNA sequencing was carried out to find differentially expressed genes between suramin sensitive and resistant cells. The identified candidate gene was validated by reverse genetic *in situ* gene replacement. And the effect on endocytosis of different substrates was investigated by FACS and fluorescence microscopy.
Suramin resistant derivatives were obtained after 6 days of selection and showed a resistance factor around 100-fold compared to the sensitive parent clone. They were cross-resistant to trypan blue and had a mild growth defect. Gene expression analysis revealed a switch to the same *variant surface glycoprotein* (*VSG*), termed VSG^{Sur}, in all the resistant derivatives. No other genes were differentially expressed between resistant and sensitive cells. We then introduced VSG^{900}, which was expressed in the sensitive parent clone, into the active expression site of one resistant derivative, and thereby replaced VSG^{Sur}. Through this manipulation, the cells completely lost their resistance. Complementary, the introduction of VSG^{Sur} into the active expression site of *T. b. brucei* 2T1 cells led to suramin resistance. Upon expression of VSG^{Sur}, uptake of trypan blue was reduced, and uptake of low density lipoprotein and transferrin were highly reduced.
Here we describe a previously unknown *VSG* (VSG^{Sur}), which causes a strong suramin resistance. The expression of VSG^{Sur} not only confers resistance, but also alters the uptake of a number of substrates including nutrients, thus supposedly has a major impact on the biology of the cells.

17:15

Dr Federica Giordani, *Research assistant, University of Glasgow*

Minor groove binders as antitrypanosomal agents for animal African trypanosomiasis - *A15678*

F Giordani[6]; K Gillingwater[4]; A I Khalaf[5]; F J Scott[5]; C J Suckling[5]; L J Morrison[3]; H P de Koning[2]; R Peter[1]; M Witty[1]; M P Barrett[6];
[1] GALVmed, UK; [2] Institute of Infection, Immunity and Inflammation, University of Glasgow, UK; [3] Roslin Institute, UK; [4] Swiss Tropical and Public Health Institute, Switzerland; [5] University of Strathclyde, UK; [6] Wellcome Centre for Molecular Parasitology, Institute of Infection, Immunity and Inflammation, University of Glasgow, UK

Current treatments for animal African trypanosomiasis (AAT) suffer from many limitations including limited efficacy, narrow safety range and, of particular concern, a rise in drug resistance. No new compounds have been introduced in over 50 years, limiting the control options for this livestock disease, which remains a major scourge for African farmers. With the establishment of dedicated public-private partnerships and expanded international interest, the

development of drugs for AAT is back on the agenda. We are developing a novel class of anti-infective compounds called S-MGBs (Strathclyde Minor Groove Binders), which have great promise as veterinary trypanocides. The compounds are cidal against all of the three main *Trypanosoma* species causing AAT, an important property as in the field mixed infections with *T. congolense*, *T. vivax* and *T. b. brucei* are common and species diagnosis is seldom carried out before treatment. Lead candidates are curative in trypanosome-infected mice and, notably, do not show any cross-resistance to the diamidine and phenanthridine drugs currently licensed for AAT. Investigations into S-MGBs mode of action revealed perturbations to the integrity and function of nucleic acids, including an increase in cellular nucleotide content and partial inhibition of DNA synthesis upon treatment. Accumulation of parasites with multiple kinetoplasts, nuclei and flagella was also observed, indicative of a cytokinesis block. Although the S-MGBs concentrate within the nucleus and kinetoplast, they also localise to other cellular compartments which may offer further clues into their mode of action.

17:30

Mr Manuel Saldivia, *Research Associated, University of York*
Dīvide et īmpera: Chromosome segregation in *Trypanosoma brucei*, a target deconvolution view - *A15732*

M Saldivia[2]; S Rao[1]; J C Mottram[2];
[1] Novartis Institute for Tropical Diseases, United States; [2] University of York, Centre for Immunology and Infection, UK

Protein kinases (PKs) are attractive drug targets since they play an essential role in signaling pathways for growth and differentiation and, more importantly, are amenable for inhibition by small-molecules. Protozoan PKs differ significantly from those in mammalian systems making them attractive for selective drug targeting. A focused high-throughput screening effort to identify growth inhibitors against *Trypanosoma brucei* using Novartis kinase inhibitor library led to identification of multiple potent hits. Further bio-centric characterization of these hits resulted in identification of non-cytotoxic, cidal chemical scaffold with favorable drug-like properties.
One of the major challenges for progressing hits to lead obtained from phenotypic screens is the identification of the target that is responsible for the phenotypic effect. We have used a *T. brucei* gain of function library of essential PKs to identify and validate an essential protein kinase as the target for one of these compound series. The inhibition of this PK dramatically compromises the cell cycle progression of parasites. The PK is a component of the kinetochore and its inhibition via chemical or genetic perturbation leads to disruption of kinetochore assembly. We have thus identified a novel mechanism of action and a novel drug target for African trypanosomes and a new chemical tool for investigation the biology of the parasite.

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Ecological Parasitology Sessions

Ecological Parasitology I - (Stream 4 - Edward Llwyd 0.01) 11:15 to 12:45

Invited Speaker 11:15 - (30 mins)

Dr Rachel Paterson, *Ser Cymru II - Marie Sklodowska-Curie Actions COFUND fellow, Cardiff University*

Throwing the baby out with the bath water: impact of parasite control treatments on non-target organisms - *A15189*

R Paterson[1];

[1] Cardiff University, UK

Invasive parasites and pathogens are major threats to aquatic biodiversity. However, management strategies directed towards invasive parasite control may detrimentally impact non-target species. For example, the widespread use of the aquatic pesticide rotenone in Norwegian waterways to eradicate the invasive salmonid parasite *Gyrodactylus salaris* has the potential to inadvertently alter beneficial interactions between native parasites and their hosts. Utilising a multi-lake Norwegian system, I demonstrate how native parasite communities of Arctic charr *Salvelinus alpinus* and brown trout *Salmo trutta* populations have responded to a catchment-wide rotenone treatment program. Results indicate approximately 50% of native parasite species are present three years following the rotenone application, however the abundance of most species remains low. This study also suggests that rotenone may have greater impacts on native parasite species with direct lifecycles and those which utilise copepods as intermediate hosts, compared to species utilising snail intermediate hosts. The implications of short- and long-term alterations to native parasite and fish communities are discussed.

11:45

Dr Katie O'Dwyer, *Assistant Lecturer*

Are parasites stressful? - *A15608*

K O'Dwyer[2]; M Forbes[1]; F Dargent[1]; J Koprivnikar[3];

[1] Carleton University, Canada; [2] Galway-Mayo Institute of Technology, Ireland; [3] Ryerson University, Canada

Parasite infections are generally considered ‘stressful’ to their vertebrate host species, although the role of

parasites as a physiological stressor is unclear. Stress hormone responses of vertebrates to parasites appear contradictory in the literature, hence, our overall aim in this study was to assess variation in stress hormone responses across vertebrate species, with a focus on glucocorticoid responses following experimental infections. Our meta-analysis encompassed 31 parasite species, 32 host species, and 146 effect sizes. We found that glucocorticoids in the infected groups, relative to the control groups, showed an overall increase in response to parasite infection, when based on the largest effect size observed for studies with single and multiple samples taken. We next investigated the effect of time since infection on the glucocorticoid response using those studies that had multiple glucocorticoid measurements for varying time periods following infection. Glucocorticoids are associated with important anti-inflammatory responses and increasing glucocorticoids following experimental infections would demonstrate an acute stress response to parasite infection in vertebrates in general, but this relationship could change under the chronic stress possibly imposed by some parasite infections. Furthermore, we present results showing that glucocorticoid responses following the time course post infection appears to depend on the type of parasite considered.

12:00

Miss Saman Yaqub, *PhD student, University of Leicester, UK*

Effects of host's altered food ration on host-parasite interaction in changing environment - *A15590*

S Yaqub[2]; W Norton[2]; I Barber[1];

[1] Nottingham Trent University, UK; [2] University of Leicester, UK

The effects of anthropogenic global warming on host-parasite interactions can have considerable ecological implication and have gained much attention. In addition, the consequences of multiple stressors associated with global temperature change has also been subject to recent study. However, far less is known about the interaction between temperature change and altered food availability on subsequent host-parasite biology. Here, we outline a study designed to examine the effects of interaction between global warming and altered ration of the three-spined stickleback fish host - *Gasterosteus aculeatus* on the fitness of a cestode parasite – *Schistocephalus solidus.* Sticklebacks were either parasite-exposed or sham exposed by feeding with infected or non-infected copepods respectively and held at either 15 C or 20 C for eight weeks. During this period fish were fed either 8% or 16% body weight per day. Every two-week fish was weighed to recalculate food ration. At the end of study, the infection status of all fish was determined, and mass of plerocercoids was quantified and indices of fish health and immune status calculated. The plerocercoids of *S. solidus* recovered from infected fish were cultured by using *in vitro* techniques to measure parasite fecundity. Our results show host's growth and body condition were enhanced at cooler temperature, whereas warmer temperature favours accelerated growth of *S. solidus* plerocercoids and

bigger worms have produced more eggs. The effects of host ration found to be non-significant on host parasite biology, thus suggesting that 8% body weight was adequate to sustain parasite growth even at the warmer/higher temperatures. Furthermore, our results indicate that the effects of warmer temperatures on parasite growth may be unlikely to be diminished even if available food is reduced. In this talk I will discuss the possible implications of these findings on the ecology of host-parasite interactions in changing environment.

12:15

Ms Maureen Williams, *Ph.D. Student, Trinity College Dublin*

Warming can alter host behaviour to the same extent as behaviour-manipulating parasites - *A15564*

M Williams[1]; C V Holland[1]; I Donohue[1];
[1] Trinity College Dublin, Ireland

While parasitic relationships are globally ubiquitous, the impact of parasitic infection, particularly in the light of a warming climate, is only now becoming clear. Warming temperature is likely to influence host-parasite relationships, especially in cases where parasites are known to modify the behaviour of their hosts. We explore whether parasitism and warming interact to modify energy flow in ecosystems by comparing individual energy budgets of the gammerid amphipod *Gammarus duebeni* infected with the acanthocephalan parasite *Polymorphus minutus* with those of uninfected individuals across a broad range of ecologically relevant temperatures. By combining individual energy budgets with experiments on behavioural manipulation across the same temperature range, we see a clear pattern where temperature moderates individual physiology, infection status influences feeding preferences, and both parasitism and temperature modify anti-predator behaviour. These findings highlight the importance of the non-trophic effects of parasites in modifying energy flow through ecosystems and affirm the need for experimental and field studies of the impact of temperature in a warming world.

12:30

Dr Guillaume Sallé, *Scientist, INRA*

Human history, drugs and climate shape the global diversity of *Haemonchus contortus* populations - *A15649*

G Sallé[1]; S R Doyle[4]; J Cortet[1]; J Cabaret[1]; R Beech[2]; J Gilleard[3]; M Berriman[4]; N Holroyd[4]; J A Cotton[4];
[1] INRA, France; [2] Institute of Parasitology, McGill University, Canada; [3] University of Calgary, United States; [4] Wellcome Trust Sanger Institute, UK

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We have analyzed the global diversity of *Haemonchus contortus* populations, the most pathogenic gastro-intestinal nematode of ruminants, using low-coverage whole-genome sequencing of 265 individual males from 19 populations sampled from 13 countries. Both high nucleotide diversity (23,868,644 autosomal SNPs) and rapid decay of linkage disequilibrium with physical distance (0.09 to 0.33 at 2 Kbp) were consistent with a large effective population size (Ne) which varied between populations from 10^5 to 15 x 10^6 individuals. A mitochondrial sequence phylogeny of individual worms supported an out-of-Africa hypothesis, followed by radiations in Oceania and Western Europe. Close genetic relationships were observed between Caribbean and western African populations mirroring slave trade movements. A weak phylogeographic signal (Mantel's test r=0.14, P=0.003) combined with admixture between geographically remote populations is consistent with modern sheep movement. A scan for genes under diversifying selection in African populations demonstrated enrichment for genes involved in neurogenesis and response to biotic stimuli such as heat acclimation. The region surrounding the beta-tubulin locus displayed a strong reduction in genetic diversity, presumably due to exposure to benzimidazoles. Genetic differentiation between ivermectin-resistant and –susceptible populations revealed multiple candidate regions in line with a polygenic architecture of ivermectin resistance. In contrast, comparing populations from different climatic conditions revealed two major candidate genes associated with climatic adaptation, which have orthologs associated with resistance to dessication in insects or adaptation to hot environment in *C. elegans*. Our results give the first global picture of genome-wide diversity in this key veterinary nematode parasite and provide valuable insights into the key factors underpinning adaptation of a parasitic nematode to a range of environmental pressures.

Ecological Parasitology: Eco-Immunology. - (Stream 4 - Edward Llwyd 0.01) 14:00 to 15:30

Invited Speaker 14:00 - (30 mins)

Prof Joe Jackson, *University of Salford*

Food and environmental temperature predominantly drive immune allocation and infection resistance in wild fish - *A15190*

J Jackson[2]; I Friberg[2]; N Masud[1]; A Stewart[3]; J Cable[1];

[1] Cardiff University, UK; [2] University of Salford, UK; [3] University of Surrey, UK

It is increasingly recognized that immunity in vertebrates is highly plastic and driven by the environment. Many studies have found piecemeal effects of individual environmental variables on immunity, but we lack a quantitative, mechanistic understanding of how different environmental players combine to regulate immune allocation and defence against infection in real-world situations. Using a systems biology-like approach and a combination of

intensive field monitoring at multiple sites, mesocosm experiments and laboratory experiments, we have begun to dissect the main environmental variables that drive immune allocation and defence in wild 3-spined sticklebacks (*Gasterosteus aculeatus*). We have chosen this natural system because it allows us to work with genuinely wild animals in the field and with animals as close to a wild phenotype as realistically achievable in experiments (wild fish that very easily acclimate to semi-natural mesocosms or laboratory tanks). Importantly, we focus on seasonal effects as a proxy for environmental effects in general. Season reflects a major environmental axis that tends to influence all individuals in a population the same way - and whose effects may thus be appropriately addressed at a population level. Based on our field monitoring and matched experiments we have very firm results indicating that temperature drives much of the seasonal immune variation and variance in disease resistance observable in the field - up to about 50% in more stable still-water habitats. We report further experimental results demonstrating a major effect of season-specific diet that qualitatively re-capitulates immunophenotypic changes seen seasonally in the field. When these effects and thermal effects (both estimated in the experiments) are quantitatively combined with field records of diet and temperature, using an inverse modelling approach, we are able to predict the great majority of seasonal immune variance in still-water natural habitats.

14:30

Prof Mark Viney, *., University of Bristol*

The immune state of wild mice, *Mus musculus domesticus - A15202*

M Viney[3]; S Abolins[3]; L Lazarou[3]; E C King[1]; P Drescher[3]; J Hafalla[1]; E Riley[2];
[1] London School of Hygiene and Tropical Medicine, UK; [2] Roslin Institute, UK; [3] School of Biological Sciences, University of Bristol, UK

Most of what we know about mammalian immunology; and so immunoparasitology; is based on studies of laboratory rodents. In contrast, the immune state of wild animals is largely unknown. To properly understand parasites, we need to know the actual immune environment in which they live and evolve in the wild. We have investigated the immunobiology of wild house mice; the same species as the laboratory mouse; as an example of a wild mammal, characterising their adaptive humoral, adaptive cellular and innate immune state. We find that wild mouse cellular immune systems are in a highly activated (primed) state, compared with those laboratory mice. We find that wild mice have a population of highly activated myeloid cells not present in laboratory mice. In contrast to the activated cellular state, we find that *in vitro* cytokine responses to pathogen-associated ligands are generally lower in cells from wild mice, probably reflecting the importance of maintaining immune homeostasis in the face of intense antigenic challenge in the wild. We have also discovered how immune variation is structured among mouse populations, finding that there can be extensive immune discordance among neighbouring populations. Finally, we

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have identified the principal factors that underlie the immunological differences among mice, showing that individuals' body condition promotes, and age constrains, immune state, while factors such as microparasite infection and season are comparatively unimportant. Together these results reveal the actual immune environment that parasites experience during their daily lives. These results raise questions about the utility of laboratory rodent models in immunoparasitological research.

14:45

Miss Anna Thomason, *Research Assistant / PhD Student, University of Salford*

Fungal communities in the Field Vole (*Microtus agrestis*) and their possible impact on host immunology and disease risk - *A15542*

A Thomason[3]; R Antwis[3]; M Begon[1]; J Bradley[2]; I Friberg[3]; S Paterson[1]; J Jackson[3];
[1] University of Liverpool, UK; [2] University of Nottingham, UK; [3] University of Salford, UK

Variability in the way individuals in a population respond to infection can influence the wider dynamics of infectious disease. For example, an individual host's characteristics may lead it to be a "super-spreader", responsible for a large amount of transmission. Each host balances investing energy into immunity and investing energy into other processes that increase fitness, such as foraging or mating. An immune strategy of completely eradicating an infection may not be the most beneficial for host fitness, in a wild situation where there is finite energy. Due to this balance, as well as other genetic, biological and environmental factors, there are variations in the way individuals respond to an infection.

Laboratory studies into immunity, although critical for our understanding of immunology, are not reflective of wild situations mainly due to the stressor free conditions the animals are kept in. Therefore, with newly developed techniques, there has been an upwards trend in researching immunology in the natural environment, or 'eco-immunology'.

Current research into eco-immunology has brought to light that the amount of immunological variation between individuals is greater than previously thought. What drives this variation is not fully understood, especially what components of the environment are responsible for determining the nature of immune investment. Recently bacterial communities (microbiota) have been identified as playing a key part in immune modulation. However, bacteria are only part of an extended gut ecosystem, which also contains a range of eukaryotes (fungi, protozoa, helminths) that might influence the outcome of interactions with the immune system.

The present study provides a preliminary assessment of the importance of the fungal component of the gut microbiota. Communities of fungi in faeces of individual *Microtus agrestis* (Field Vole) have been characterised using next generation sequencing (MiSEQ) and in the future, will be analysed in conjunction with data on host

immune expression (measured through qPCR analysis). The purpose is to understand how fungal communities may influence a host individual's immune expression, and how this impacts on other host factors and infectious disease susceptibility.

15:00

Mr Dominik Schmid, *PhD, Queen Mary University London*

Assessing the Darwinian costs of mounting an adaptive immune response - *A15717*

D Schmid[2]; M Milinski[1]; C Eizaguirre[2]; M Kalbe[1];

[1] Max Planck Institute for Evolutionary Biology, Germany; [2] Queen Mary University London, UK

In vertebrates, the adaptive immune system evolved to maximise protection and minimise immunological costs upon repeated parasites exposure. At high risk of recurring infections, the costs of immune activation of a specific response should be offset by the benefits of parasite resistance. Yet, under low parasite pressure the physiological costs of acquired immune responses may outweigh their benefits. Such conditional cost/benefit trade-offs should ultimately translate into Darwinian fitness. Here, we experimentally triggered an immune response in three-spined sticklebacks by injecting antigens derived from common parasites, while simultaneously avoiding the costs of infection. Antigen and control-injected fish were then allowed to naturally reproduce in either parasite-free or parasite-rich mesocosms. As predicted, exposure to parasites significantly decreased fish reproductive success. Furthermore, immune activation by antigen treatments conferred parasite-specific resistance and most importantly, Darwinian fitness increased under natural parasite exposure. Following our hypothesis, mounting an adaptive immune response significantly reduced the individual lifetime reproductive success of uninfected fish. These findings provide experimental evidence of the intricate cost/benefit balance of acquired immune responses. They also provide explanations for the observed variation in immune-competence across connected populations or related species inhabiting environments with distinct parasite pressure.

15:15

Dr Jason Holland, *Senior Research Fellow, University of Aberdeen*

Taking a step into the unknowns of myoxozoan genomics: Sequencing and functional characterisation of a myxozoan micro-exon gene - *A15792*

J W Holland[4]; S Yoon[4]; M Faber[4]; H Hartikainen[3]; B Abos[1]; I Estensoro[2]; C Bailey[5]; K A Veenstra[4]; A Alnabulsi[4]; T Wang[4]; C Tafalla[1]; C J Secombes[4];

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[1] Centro de Investigación en Sanidad Animal, Spain; [2] Institute of Aquaculture Torre de la Sal, Spain; [3] Institute of Aquatic Ecology, Switzerland; [4] University of Aberdeen, UK; [5] University of Bern, Switzerland

The Myxozoa represents a large group of enigmatic endoparasites sharing morphological features with bilateria, protists, and cnidarians. Due to their extreme sequence diversity, precise phylogenetic placement has only recently been resolved placing them firmly in the phylum, cnidaria. Our work has focused on *Tetracapsuloides bryosalmonae,* a myxozoan that cycles between an invertebrate host (colonial bryozoans) and salmonid fish causing proliferative kidney disease (PKD) in the latter. The chronic pathology associated with PKD is refractory towards pro-inflammatory mechanisms, although eliciting dominant anti-inflammatory activities, and dysregulated B and T cell responses. Our recent investigations have focused on putative *T. bryosalmonae* virulence factors to attempt to unravel host immune evasion mechanisms exploited by the parasite.

A unique form of antigenic diversification that differs to classical antigenic variation, has been described in schistosomes based on the variant expression of proteins encoded by micro-exon genes (MEGs). MEGs are stage-specific intrinsically disordered secreted proteins associated with external parasite surfaces that are likely to be in contact with the host immune system. Unlike other micro-exon containing genes, > 75% of the coding region of MEGS consists of very short exons that undergo alternative splicing to yield an array of protein variants. It has been postulated that protein variants may have numerous host-derived binding partners and so may represent an important form of immune evasion. Indeed, recently a MEG has been shown to potently suppress pro-inflammatory mechanisms via interaction with the human calcium binding protein, S100A9.

Here we report the sequencing and characterisation of the first non-helminth MEG (*Tb*-MEG1). The 264 amino acid open reading frame of the full length molecule is encoded by 65 exons, with only 5 exons > 30 bp. The predicted structure of *Tb*-MEG1 is consistent with schistosome MEGs in possessing a signal peptide, a mature protein largely consisting of an intrinsically disordered loop, and an alpha helix tail at the C terminal encoded by the largest exon (145 bp). The intrinsic loop is characterised by the presence of a tandem repeat region. Predominantly expressed in the fish host at both transcriptional and protein levels, we have uncovered numerous cDNA variants expressed in infected fish based on alternative splicing in the repeat region. Consistent with schistosome MEGs and other surface proteins involved in protein-protein interactions, the repeat region possesses 10 putative O-linked glycosylation sites and 4 sulphated tyrosines. By immunohistochemistry we have demonstrated the protein to be endogenously expressed in and on the surface of parasites within the kidneys of infected fish. Intriguingly, the protein has also been found to envelope clusters of lymphoid-like cells, a phenomenon also observed in kidney cells incubated with recombinant *Tb*-MEG1. We have also demonstrated a potent *Tb*-MEG1-specific antibody response in parasite-infected farmed rainbow trout that has been corroborated using a lab-based challenge model. Current studies are in progress to establish host binding partners of *Tb*-MEG1, the modulation of host immune gene expression by recombinant *Tb*-MEG1, and its immune protective efficacy as both DNA and protein-based

vaccines. Overall, the discovery and characterisation of *Tb*-MEG1 may provide insights into host immune evasion mechanisms exploited by myxozoan parasites whilst having major implications concerning the evolution of antigenic diversity in metazoan parasites.

Ecological Parasitology: Multi-species Interactions - (Stream 4 - Edward Llwyd 0.01)16:15 to 17:45

16:15

Miss Lauren Carruthers, *PhD Research Student, University of Glasgow*
Unravelling interactions between schistosomes, the microbiome and anti-helminthic drugs in a Ugandan field setting - *A15101*

L V Carruthers[1]; C Rowel[2]; D Ajambo[2]; A Nakasi[2]; A Atuhaire[2]; F Besigye[2]; M Arinaitwe[2]; A Wamboko[2]; M Adriko[2]; C L Faust[1]; E Tukahebwa[2]; P H Lamberton[1];
[1] Institute of Biodiversity, Animal Health and comparative Medicine, and Wellcome Centre for Parasitology, University of Glasgow, UK; [2] Vector Control Division, Ministry of Health, Uganda

Schistosomiasis is a neglected tropical disease that infects millions of people globally, mainly in developing countries. In the Mayuge district of Uganda, the prevalence of schistosomiasis has been increasing in some communities even with over a decade of annual mass drug administration interventions. We aim to further understand schistosomiasis to help improve treatment success and disease control. The role of the microbiome in health and disease is becoming increasingly apparent and correlations between gut bacterial structure and helminth infection have been demonstrated both in laboratory and natural settings. The influence the gut microbiome may have on treatment efficacy has been reported for a wide variety of drugs. This research therefore aims to address whether associations between schistosomes, the bacterial gut microbiome and anti-helminthic drugs are present in a community highly endemic with schistosomiasis and whether these interactions are important when considering control and treatment options for the disease. Since the field setting is a challenging environment in which to undertake research, an initial pilot study has been undertaken to compare stool 16S rRNA microbiome sequencing profiles of three children at time point zero and determine how these profiles vary with storage technique used and time to taken to freeze. Stool was stored raw, in RNAlater and in ethanol and then frozen on dry ice at doubling time increments at 0, 1, 2, 4, 8, 16 and 32 h post collection. These children were tested for schistosomiasis, soil-transmitted helminth infections and malaria. Initial study findings will be discussed.

16:30

Mr Oluwaseun Somoye, *Research student, Cardiff University*

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The effect of endemic macroparasite on the quality and quantity of an epidemic parasite - *A15670*

O Somoye[1]; J Cable[1]; J Lello[1];
[1] Cardiff School of Biosciences, Cardiff University, UK

Given the ubiquity of endemic coinfection with epidemic infection in natural populations, determining the impacts the endemic parasites may have on epidemic parasite transmission is essential. During coinfection, interspecific parasite interactions, whether direct or indirect, could impact on the quality and quantity of parasite transmission stages. Using a model host (the German cockroach) its endemic gut protozoan (*Gregarina blattarum*) and the epidemic entomopathogenic nematode, *Steinernema carpocapsae*, we assessed the impact of varying levels of endemic infection upon the quality and quantity of the transmission stages of *S. Carpocapsae*. We hypothesized that the lipid resource, which we have previously shown mediates the interaction between the two parasites species, would decrease in *S. carpocapsae* in relation to the level of gregarine infection within the host impacting both the number and quality of emerging infective juveniles (IJs) of the nematode. We exposed specific parasite free cockroaches to different numbers of gregarine gametocysts (0 to 20) and subsequently exposed them to the epidemic *S. carpocapsae*. We then monitored, host time to death, number of emerging IJs with time and the lipid levels within the IJs. Our results suggest that the level of endemic infection has substantial effects on transmission potential. We present these results and discuss their implication for epidemic transmission.

16:45

Mr Timothy Jenkins, *PhD, Mr*
Strongyloides stercoralis infection in humans and its association with increased gut microbial diversity - *A15592*

T P Jenkins[4]; F Formenti[1]; C Piubelli[1]; C Castro[2]; F Perandin[1]; D Buonfrate[1]; J Griffin[2]; D Otranto[3]; Z Bisoffi[1]; C Cantacessi[4];
[1] Centre for Tropical Diseases, Sacro Cuore-Don Calabria Hospital, Negrar, Verona, Italy; [2] Department of Biochemistry, Metabolomics Facility, University of Cambridge, UK; [3] Department of Veterinary Medicine, University of Bari, Valenzano, Italy; [4] Department of Veterinary Medicine, University of Cambridge, UK

Data from recent studies support the hypothesis that infections by human gastrointestinal (GI) helminths impact, directly and/or indirectly, on the composition of the host gut microbial flora. However, to the best of our knowledge, these studies have been conducted in cohorts of human volunteers from helminth-endemic areas and infected by multiple species of parasites or with underlying gut disorders, which, in most cases, impaired an unbiased

assessment of the sole effects of GI parasites on the gut microbial profiles. Exploring the impact that single species of GI helminths exert on the gut microbial composition of otherwise healthy human volunteers may help disentangle the causality of parasite-microbiota relationships. Thus, in this study, we explored the impact of natural infections by the parasitic nematode *Strongyloides stercoralis* on the gut microbiota and the metabolic profiles of a cohort of otherwise healthy individuals from northern Italy, pre- (*S+*) and post- (*St*) anthelmintic treatment with ivermectin and compared the findings with data obtained from a cohort of uninfected individuals (*S-*) from the same geographical area. Bioinformatics and biostatistical analyses of bacterial 16S rRNA gene data revealed a significantly increased microbial alpha diversity (*P* 0.03) and decreased beta diversity (*P* 0.04) in the gut microbial profiles of *S+* subjects compared to *S-*. In *St* subjects, gut microbial alpha diversity was higher than in *S-* and lower than in *S+* subjects, while beta diversity was lower than in *S-* and higher than in *S+* subjects, albeit not significantly. Amongst others, populations of bacteria belonging to the Order Pseudomonadales (genus *Pseudomonas*) and genus Bacteroides were significantly more abundant in the microbiota of *S-* subjects compared to both *S+* and *St* subjects. Conversely, Leuconostocaceae, Paraprevotellaceae and *Peptococcus* were significantly increased in the microbiota from *S+* subjects compared to *S-*. The gut microbiota of *St* was characterized by a higher abundance of *Lachnobacterium* and *Roseburia* compared to *S-*, and of bacteria of the order Enterobacteriales compared to *S+* subjects. Metabolomic analysis using nuclear magnetic resonance (NMR) and gas chromatography revealed significant differences in the abundance of selected faecal metabolites between subject groups. For instance, levels of acetate were significantly higher in the faecal metabolome of *S-* compared to *S+* subjects (*P* 0.03), whilst those of alanine, formate and leucine were higher in *S+* compared to *S-* subjects (*P* 0.05, *P* 0.03 and *P* 0.05, respectively). The saturated fatty acid C15:0 ante (pentadecanoic acid) was significantly increased in faecal samples from *St* compared to S+ subjects (P 0.02).

17:00

Dr Amy Ellison, *Postdoc fellow, Cardiff University*

Social stress alters transcriptomic responses to infection and dysregulates molecular body clocks - *A15124*

A Ellison[1]; T Uren-Webster[2]; O Rey[2]; C Garcia de Leaniz[2]; S Consuegra Del Olmo[2]; P Orozco-terWengel[1]; J Cable[1];

[1] Cardiff School of Biosciences, Cardiff University, UK; [2] Swansea University, UK

Stress can have profound effects on vertebrate immunity. Stress-induced changes in immune functions are typically orchestrated via hypothalamic–pituitary–adrenal (HPA) axes, particularly glucocorticoids hormones. However, glucocorticoid release and levels of immune activity exhibit diel variation, driven by the molecular

circadian clock. Therefore, it is increasingly apparent that understanding this complex three-way interaction of stress, circadian rhythms and immunity, is pivotal to managing disease risks. Here, utilising a whole-transcriptome sequencing approach, we demonstrate that social stress in tilapia (*Oreochromis niloticus*) due to sub-optimal stocking conditions increases susceptibility to the oomycete *Saprolegnia parasitica*, via altered transcriptional responses to infection. Tilapia held at low densities have increased expression of genes related to stress, likely due to increased aggressive interactions. When challenged with *Saprolegnia*, low density fish exhibit reduced expression of inflammatory gene responses and higher levels of adaptive immune gene suppression, resulting in significantly higher mortality rates. In addition, *Saprolegnia* infection substantially perturbs expression of circadian clock genes and low density (high stress) fish have higher levels of molecular clock dysregulation. Our results reveal the impact of chronic social stress on transcriptional responses to infection and highlight the need to incorporate circadian infection biology into our understanding of disease dynamics in animals.

17:15

Dr Laura Peachey, *Research Fellow, University of Cambridge*

Murine schistosomiasis quantitatively and qualitatively modifies the intestinal microbiota *- A15597*

L E Peachey[5]; T P Jenkins[5]; N Ajami[1]; [2]; A S MacDonald[6]; M H Hsieh[3]; P Brindley[4]; C Cantacessi[5]; G Rinaldi[7]; [1] Alkek Center for Metagenomics and Microbiome Research, Baylor College of Medicine, UK; [2] Alkek Center for Metagenomics and Microbiome Research, Baylor College of Medicine, United States; [3] Biomedical Research Institute, Rockville, Maryland, United States; [4] George Washington University, United States; [5] University of Cambridge, UK; [6] University of Manchester, UK; [7] Wellcome Trust Sanger Institute, UK

Schistosomiasis is one of the most prevalent neglected tropical diseases. In spite of the extensive contribution of intestinal, liver and urogenital disease, little is known of the impact of schistosomes (blood flukes) on the composition of the commensal microbial flora of the vertebrate host. In particular, bacterial taxa with putative roles in the pathophysiology and immunology of schistosome infection and disease have yet to be identified. In this study, we characterised fluctuations in the composition of the microbial flora of the murine small (SI) and large intestine (LI) at two time-points, day 28 (D28) and day 50 (D50) post-infection with cercariae of *Schistosoma mansoni*. Bioinformatics analyses of microbial community high-throughput sequence data revealed an overall reduction in alpha diversity of the gut microbiome in *S. mansoni*-infected mice at D50 post-infection (SI P=0.006; LI P=0.02), alongside a significant increase in microbial beta diversity (SI P=0.004; LI P=0.008). Microbial composition analyses between groups showed expanded populations of *Akkermansia muciniphila* (phylum Verrucomicrobia) in the SI and LI of *S. mansoni*-infected mice at D28 and D50. Conversely, lactobacilli increased at D28 in the LI of *S. mansoni* infected mice, whilst at D50, infection was associated with changes in the relative

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abundance of a number of taxa. Amongst these, Turicibacterales were markedly reduced in the schistosome-infected mice compared with the uninfected counterparts. These findings demonstrate a significant dysbiosis in the gut microbial flora of mice at D50 post-infection with *S. mansoni*, at which time, parasite eggs are migrating across the intestinal wall. Observations of this study support a role for gut microbiota in the pathophysiology of schistosomiasis, and set a basis for future investigations of the mechanisms underlying the complex relationships among infection with parasitic worms, commensal flora, host immunity and disease outcome.

Protozoa Sessions

Protozoa: Cell Biology & Immunology I - Sponsored by William Powell- (Stream 2 - Llandinam A6) 11:15 to 12:45

Chair - Dr Tony Holder

Invited Speaker 11:15 - (30 mins)

Dr Eva Frickel, *Group Leader, Francis Crick Institute*

Immune-mediated control of *Toxoplasma* in human cells - *A15885*

B Clough[1], A Johnston[1], D Fisch[1], J Wright[1], **E-M Frickel**[1]

[1]Host-Toxoplasma Interaction Laboratory, The Francis Crick Institute, London, UK

Certain intracellular pathogens avoid host cytosolic cellular defence mechanisms by residing inside pathogen vacuoles (PVs). The Frickel Lab studies human host defence against the protozoan parasite *Toxoplasma gondii*. *Toxoplasma* always leads to chronic infection and has a seroprevalence in man of 30 percent. Infection with *Toxoplasma* leads to the rapid production of IFNγ, a proinflammatory cytokine that upregulates host defence mechanisms that target the pathogens. We study how IFNγ-mediated ubiquitin- and guanylate binding protein (GBP)-driven mechanisms target *Toxoplasma*. These mechanisms remodel pathogen vacuoles (PVs) within host cells to limit *Toxoplasma* replication and mediate parasite killing. For example, human primary endothelial cells target *Toxoplasma* PVs with ubiquitin to cause parasite death by acidification in the cell's endo-lysosomal system. In epithelial cells and macrophages, GBPs are responsible for *Toxoplasma* replication restriction. In order to classify the host response to *Toxoplasma* in an unbiased and high content fashion we have recently developed an artificial intelligence-driven image analysis pipeline. Using this tool, we are now in the position to rapidly classify host defence mechanisms to Toxoplasma in a variety of human cell types.

11:45

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Miss Alice Lacombe, *PhD student, University of Glasgow*

Functional characterization of mitochondrial translation components in the early diverging eukaryote *Toxoplasma gondii - A15294*

A Lacombe[1]; J Tottey[1]; J Ovciarikova[1]; L Sheiner[1];

[1] Wellcome Trust Centre for Molecular Parasitology, University of Glasgow, UK

Apicomplexan parasites are unicellular eukaryotes. Being early diverging organisms they often possess the universally conserved core of global eukaryotic machineries. Yet, being parasites they often possess unique functions. Studying fundamental mitochondrial biology in these organisms leads to definition of the ancestral core of eukaryotic pathways while simultaneously aiding the identification of new targets for drug development against diseases like malaria. Organelle translation has been a focus for the latter in recent years.

Due to extreme gene transfer to the nuclear genome, the apicomplexan mitochondrial genome encodes only three proteins: COXI, COXIII and COB. Indirect evidence suggests that translation of these proteins in the mitochondrion is active and essential [1], but it is not clear what the ribosome composition is. For example, many of the mitochondrial ribosome 30S subunit components are missing in apicomplexan and it has been proposed that the presence of other proteins, that are not widespread amongst eukaryotes, like S22, S29 and S35, may compensate [2].

Via a new bioinformatics screen [3], we identified candidate components of the apicomplexan mitochondrial translation pathway. Gene tagging and immunofluorescence confirmed the mitochondrial location of 12 out of 15 proteins tested. Conditional knockdown of three of the corresponding genes individually confirmed an expected growth defect upon the depletion of each gene. However, despite growing slowly, *Toxoplasma* lacking the mitochondrial ribosomal S35 subunit could survive continuously in culture. Moreover, mitochondrial functions like protein import remain unaffected. These surprising findings argue against the current model and raise the question of whether mitochondrial translation is in fact not essential for *Toxoplasma.*

[1] Pino P, Aeby E, Foth BJ, Sheiner L *et al*; 2010 Mol Microbiol. 2010 May; 76(3):706-18 [2] Gupta A *et al*; Open Biol. 2014 May; 4(5): 140045 [3] Sheiner L *et al*; PLoS Pathog. 2011 Dec; 7(12):e1002392.

12:00

Dr Janine Coombes, *Lecturer, University of Liverpool*

Development of modified organoid culture protocols for interrogation of interactions between *Toxoplasma gondii* and the intestinal epithelium *- A15473*

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L Luu[2]; N Randle[2]; S D Armstrong[2]; J Wastling[1]; **J L Coombes**[2];
[1] Keele University, UK; [2] University of Liverpool, UK

When transmitted through the oral route, *Toxoplasma gondii* first interacts with its host at the small intestinal epithelium. This interaction has the potential to shape the course of the systemic immune response, and may be an attractive target for prophylactic therapy in livestock. However, we understand surprisingly little about the molecular pathways governing the interactions between *T. gondii* and the intestinal epithelium.
The *in vitro* 3D culture of intestinal epithelium as organoids (or "mini-guts") shows great promise for modelling infection. Organoids retain key architectural features of, and contain all of the major differentiated epithelial cell types found in, the intestinal epithelium. However, current protocols yield cultures with an enclosed luminal space that precludes the large-scale application of infectious agents to the apical surface of the epithelium.
Here, we have adapted organoid culture protocols to generate collagen-supported semi-monolayer cultures with an exposed lumen for practical application of pathogens. These cultures retain epithelial polarization, and the presence of fully differentiated epithelial cell populations with host-defensive function, such as goblet and Paneth cells. They are susceptible to infection with, and support replication of, *T. gondii*.
Using quantitative label-free mass spectrometry, we show that infection of the intestinal epithelium in our model is associated with upregulation of host lipid biosynthesis pathways, including isoprenoid biosynthesis. While *T. gondii* can synthesise isoprenoid precursors in the apicoplast, optimal survival and growth relies on the use of host cell isoprenoids. Consequently, host isoprenoid biosynthesis may represent an attractive drug target.
In conclusion, our adapted semi-monolayer model offers a tractable tool for understanding how interactions between *T. gondii* and the host intestinal epithelium influence the course of infection.
This work was funded by a Biotechnology and Biological Sciences Research Council Tools and Resources Development Fund grant (BB/M019071/1)

12:15

Prof John Ellis, *Professor of Molecular Biology, University of Technology Sydney*
Serotyping and genotyping studies reveal indigenous atypical type II *Toxoplasma* strains are associated with symptomatic infection of patients in Australia - *A15506*

M S Johnson[5]; **J T Ellis**[5]; R Lee[3]; D Stark[2]; M Reichel[1]; M Grigg[4];
[1] College of Veterinary Medicine and Life Sciences, City University of Hong Kong, China; [2] Department of Microbiology, St Vincent's Hospital, Sydney, Australia; [3] Institute of Clinical Pathology & Medical Research, Westmead Hospital, Westmead, NSW, Australia, Australia; [4] Laboratory of Parasitic Diseases, National Institutes of Health, NIAID, United States; [5] School of Life Sciences, University of Technology Sydney, Australia

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Toxoplasma gondii is a common intracellular parasite that has the ability to infect any warm-blooded animal or bird, including people.. Human infection is widely distributed throughout the world with prevalence rates of between 10 – 90% reported from different countries. Infection by *T. gondii* is usually benign and self-limiting, but severe and possibly life threatening disease does occur in immune-compromised patients or if acquired during pregnancy. Studies focussed on strain type relative to disease outcome in humans have identified some strain-type specific disease associations; the most striking of these is the association of atypical strains on severe ocular disease outcomes in South America. In order to investigate human toxoplasmosis and strain diversity in Australia we examined clinical material from *Toxoplasma* infected patients from various locations to determine both *Toxoplasma* prevalence and the infective strain-type. Whilst overall prevalence appears to be dropping in comparison to historical reports, our longitudinal analysis over a 40 year time span suggests a shift of age where peak prevalence plateaus from 30 -40 years olds through to those who are older than 70 years of age, indicative of a birth cohort effect. Furthermore, examination of sera by serotyping indicates an abundance of Type II strains are infecting the human population. Investigation by High Resolution Multi Locus Sequence Typing (MLST) PCR shows that many of these Type II infections in humans contain drifted alleles that are unique to the Australian continent.

12:30

Mrs Andreia Albuquerque-Wendt, *PhD student, Medical School of Hannover*

Apicomplexan C-mannosyltransferases modify adhesins of the TRAP family - *A15319*

A Albuquerque[2]; C Hoppe[2]; G Bandini[3]; D Leon[1]; A Shcherbakova[2]; F Buettner[2]; L Izquierdo[4]; C Costello[1]; H Bakker[2]; F Routier[2];

[1] Boston University School of Medicine, United States; [2] Hannover Medical School, Germany; [3] Henry M. Goldman School of Dental Medicine, United States; [4] Instituto de Salud Global de Barcelona, Spain

C-mannosylation is a poorly known posttranslational modification of proteins which differs from other types of glycosylation by the carbon-carbon bond that links the anomeric carbon of the mannose residue to the indole C2 carbon of tryptophan. This modification is characteristically found in WXXW/C motifs, present in thrombospondin type-1 repeat domains (TSR) and type 1 cytokine receptors in metazoans. This modification is catalyzed by C-mannosyltransferases of the DPY19 family located in the endoplasmic reticulum and it affects the folding and secretion of several proteins. Interestingly, orthologues of the encoding gene were found in the genome of apicomplexan parasites. Considering that apicomplexans share the same recognition motif as mammals, over 30

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C-mannosylated proteins might be present in these parasites. Recently, the micronemal adhesion thrombospondin-related anonymous protein (TRAP) was shown to be C-hexosylated in *Plasmodium falciparum* sporozoites. Here, we demonstrate that also the micronemal protein MIC2 secreted by *Toxoplasma gondii* tachyzoites is C-hexosylated. When expressed in a cell line deficient in C-mannosylation, *P. falciparum* and *T. gondii* DPY19 homologues are able to modify TSR domains of the micronemal adhesins TRAP/MIC2 family, known to be integral components of the glideosome and therefore of paramount importance for the parasite motility and invasion. Furthermore, we observed a decreased amount of recombinant MIC2 secretion in absence of C-mannosylation, suggesting this modification might play an important role for the proper folding of this protein. *In vitro*, the apicomplexan enzymes can transfer mannose to a WXXWXXC peptide. Since one or more TSR domains are commonly found in several surface proteins of apicomplexan parasites, C-mannosylation may be a common modification in this phylum. Since this protein is predicted to be expressed at many parasite stages, we suggest it plays an important role in infection.

Protozoa: Drug Discovery & Resistance - (Stream 2 - Llandinam A6) 16:15 to 17:45

Invited Speaker 16:15 - (30 mins)

Prof Giancarlo Biagini, *Liverpool School of Tropical Medicine*

Antimalarial pharmacology of primaquine: Attempting to solve a 70 year-old puzzle - *A15185*

G Biagini[1]; G Camarda[1]; S March[1]; R Priestley[1]; A Saif[1]; A Miller[1]; P Jirawatcharadech[1]; M H Wong[1]; S Leung[1]; D Baker[1]; P Alano[1]; M J Paine[1]; S Bhatia[1]; P M O'Neill[1]; S A Ward[1];

[1] Liverpool School of Tropical Medicine, UK

Primaquine (PQ) is an 8-aminoquinline class FDA-approved drug on the World Health Organization's (WHO) List of Essential Medicines, and is currently the only registered drug available for radical cure of relapse malaria showing activity against Plasmodium vivax and P. ovale dormant liver stages. PQ is also active against *P. falciparum* liver stages and against the sexual gametocyte stages of Plasmodium species, making this drug available for prophylaxis and in transmission blocking strategies such as in elimination programmes. However, its widespread use in mass drug administration intervention is limited due to severe side effects occurring in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Despite being in use for some 70 years, PQ mechanism of action is still poorly understood. Metabolic activation has long been known to be required for PQ to gain activity, and recently CYP2D6 enzyme has been shown to be required to achieve *P. vivax* radical cure in humans. It is hypothesised CYP2D6 mediates the generation of hydroxylated metabolites, which in turn could exert the anti-parasitic effect via a redox cycling mechanism. Here, by using a chemical biology approach we provide the first

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direct definitive evidence of the role of hydroxylated and quinoneimine primaquine metabolites in anti-gametocyte and liver stage inhibitory activity. Furthermore, we present biochemical evidence consistent with a mechanism of action whereby redox cycling of catalytic quantities of PQ metabolites can generate pharmacologically-relevant levels of hydrogen peroxide (H2O2) which lead to parasite killing. Finally, we demonstrate how redox cycling of PQ metabolites by host enzymes leads to the selective killing of malaria parasite gametocytes and liver stages. The identification of the biochemical events responsible for the anti-parasite activity of primaquine not only answers to a long-asked question, but also opens the way to the possibility of designing new 8AQs with improved therapeutic profiles.

16:45

Dr Catherine Merrick, *Senior Lecturer, Keele University*

RecQ helicases in the malaria parasite *Plasmodium falciparum* affect genome stability, gene expression patterns and DNA replication dynamics - *A15611*

A Claessens[2]; L M Harris[1]; S Stanojcic[3]; L Chappell[4]; A Stanton[1]; N Kuk[3]; P Veneziano-Broccia[1]; Y Sterkers[3]; J C Rayner[4]; C J Merrick[1];

[1] Keele University, UK; [2] Medical Research Council Unit, The Gambia, Gambia; [3] University of Montpellier and Centre Hospitalier Universitaire, France; [4] Wellcome Trust Sanger Institute, UK

The malaria parasite *Plasmodium falciparum* has evolved an unusual genome structure. The majority of the genome is relatively stable, with mutation rates similar to most eukaryotic species. However, some regions are very unstable with high recombination rates, driving the generation of new immune evasion-associated *var* genes. The molecular factors controlling the inconsistent stability of this genome are not known. We have studied the roles of the two putative RecQ helicases in *P. falciparum*, *Pf*BLM and *Pf*WRN. When *Pf*WRN was knocked down, recombination rates increased four-fold, generating chromosomal abnormalities, a high rate of chimeric *var* genes and many microindels, particularly in known 'fragile sites'. This is the first identification of a gene involved in suppressing recombination and maintaining genome stability in *Plasmodium*. By contrast, no change in mutation rate appeared when the second RecQ helicase, *Pf*BLM, was mutated. At the transcriptional level, however, both helicases evidently modulate the transcription of large cohorts of genes, with several hundred genes – including a large proportion of *var*s – showing deregulated expression in each RecQ mutant. Aberrant processing of stalled replication forks is a possible mechanism underlying elevated mutation rates and this was assessed by measuring DNA replication dynamics in the RecQ mutant lines. Replication forks moved slowly and stalled at elevated rates in both mutants, confirming that RecQ helicases are required for efficient DNA replication. Overall, this work identifies the *Plasmodium* RecQ helicases as major players in DNA replication, antigenic diversification and

genome stability in the most lethal human malaria parasite, with important implications for genome evolution in this pathogen.

17:00

Dr Colin Sutherland, *Professor of Parasitology, London School of Hygiene & Tropical Medicine*
Artemisinin resistance? Mind the traffic ... - *A15485*

R C Henrici[1]; C J Sutherland[1];
[1] London School of Hygiene & Tropical Medicine, UK

Artemisinin susceptibility in *Plasmodium falciparum* is modulated by mutations in the gene pfk13, which encodes a kelch propeller domain protein of unknown function. Reduced susceptibility is demonstrated *in vitro* by elevated parasite survival after short exposures to physiologic concentrations of drug in the early ring stage. Using CRISPR-Cas9 genome editing, we provide the first evidence of a similar but K13-independent *in vitro* artemisinin resistance caused by a single base change in locus encoding the AP-2 adaptor complex mu-subunit (*pfap2mu*). Through extensive fluorescence and electron microscopy and proteomics, our functional characterisation of PfAP2mu validates that gene as encoding a clathrin-independent, non-canonical AP-2 trafficking factor that interacts with K13 and other important factors at a distal face of the ER and is essential for asexual parasite survival. We show that disruption of trafficking in early rings initiates an ER-based stress response that underlies artemisinin resistance and induced dormancy. A model depicting a role for ER trafficking components in ring-stage artemisinin action is proposed and implications for controlling multi-drug resistance in natural parasite populations will be discussed.

17:15

Miss Priyanka Panwar, *PhD student, University of Salford*
Repositioning of synthetic emetine analogues as potential anti-malarial drugs and use of molecular modelling tools to aid in drug discovery - *A15787*

P Panwar[2]; M Abubakker[2]; K K Burusco[1]; R Bryce[1]; N Nirmalan[2];
[1] University of Manchester, UK; [2] University of Salford, UK

Drug resistance has emerged towards all antimalarials in use including the Artemisinin-based combination therapies. There is a pressing need for novel anti-malarial treatments but long development timelines cripple the process of drug discovery. An alternative to *de novo* drug design is offered by drug repositioning to help reduce the

long timescale involved in bringing a drug to market. Natural products have been a reliable source of anti-malarial treatments. Emetine dihydrochloride, an anti-amoebic compound, has been identified to be a potent inhibitor of the multi-drug resistant strain K1 of *Plasmodium falciparum* (IC_{50}: 47nM) and shows ideal pharmacokinetic matching and synergy with atovaquone. The use of emetine has been prevented by its emetic and cardiotoxic effects. However, synthetic analogues of emetine hydrochloride have been claimed to be less cardiotoxic than the parent compound. Using *in-silico* modelling methods, synthetic emetine analogues were found to have the potential for retaining the anti-malarial activity. The results were verified experimentally. Emetine and its analogues were found to have a multi-modal mechanism of action. A huge investment of time and resources are needed for high throughput screening and *in-silico* virtual screening provides an inexpensive alternative to filter through large libraries of compounds. Virtual screening of FDA approved library of drugs was carried out to identify synergies and propose anti-malarial combination therapy between these drugs and synthetic emetine analogues.

17:30

Prof Paul Horrocks, *Professor, Institute for Science and Technology in Medicine*
Exploring the potential of autophagy as a novel drug target: SK1.49 as a chemical probe of autophagy in *Plasmodium falciparum - A15752*

I Ali[3]; J Reynisson[1]; P Roepe[2]; **P Horrocks**[3];
[1] Auckland University, New Zealand; [2] Georgetown University, United States; [3] Keele University, UK

Macroautophagy is an evolutionarily conserved survival process of eukaryotes that supports cellular survival during stress, an exemplar being during nutrient limitation. A key marker of this process is the lipidation of Atg8 with phosphatidylethanolamine (PE) by the E2-conjugating enzyme Atg3 and inclusion of Atg8-PE into autophagososmes that deliver cytoplasmic cargo to lysosomes for degradation and recycling of macromolecules. The cascade of the canonical regulatory and effector proteins for macroautophagy is incomplete in *Plasmodium falciparum*, leading to speculation around whether canonical autophagy exists in this parasite. PfAtg8 has, however, been implicated in recycling of specialist organelles, vesicular trafficking and apicoplast function.
A screen of a library of compounds that act as modulators of macroautophagy in human cell lines as inhibitors of the Atg8-Atg3 interaction have been evaluated here for their potential as antiplasmodial agents. We identify SK1.47 and SK1.49 as having a rapid cytocidal activity against trophozoite-stage intraerythroctic parasites with a potency (EC_{50}) in the 1µM range. Both compounds show selectivity against parasites compared to the human HepG2 line. Proof-of-concept as inhibitors of autophagy was shown when both compounds inhibit the formation and distribution of PfAtg8-labelled vesicles on induction of starvation. We also report molecular modelling and structure activity relationship studies that describe a key scaffold to be developed in follow on work. Whilst not a

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lead for development at this stage - SK1.49, the more potent of these two compounds, is available as a chemical probe to explore the potential of autophagy-related processes in the parasite as a novel drug target.

Helminth Sessions

Helminths: Drug Discovery & Resistance I - Sponsored by Life Sciences Research Network Wales - (Stream 3 - Physics 0.15 Main) 11:15 to 12:45

Invited Speaker 11:15 - (30 mins)

Dr Raymond Pierce, *Directeur de Recherches CNRS, CIIL, Pasteur Institute of Lille*
Targeting epigenetic mechanisms for drug development against Neglected Parasitic Diseases: the A-ParaDDisE project and beyond - *A15204*

R Pierce[1];
[1] CIIL, CNRS UMR 8204, France

Introduction: The "writers", "erasers" or "readers" of epigenetic marks on chromatin are attractive targets for drug development in numerous pathologies, including neglected parasitic diseases. Parasite-selective inhibitors may be designed to exploit key differences in parasite enzymes compared to human orthologues. Moreover, species-specific sensitivities to the blocking of a particular enzyme activity can be exploited. These strategies were pursued during the A-ParaDDisE project, funded by the EC, involving research teams in Europe, Brazil and Australia, targeting schistosomiasis, leishmaniasis, Chagas disease and malaria.
Methods: Target validation by gene or transcript knockdown and phenotypic screening with inhibitors allowed prioritization of enzymes for target-based screening. Production of active, recombinant proteins, structural studies and assay development permitted both high-throughput and *in silico* compound screening. Hits prioritized on the basis of potency of enzyme inhibition and selectivity for the parasite followed bio-guided optimization steps to generate lead compounds for ADME studies and pre-clinical *in vivo* testing.
Results: Both phenotypic and target-based screening strategies generated a large number of hits. Leads were selected on the basis of their low toxicity, bio-availability and *in vivo* efficacy. The structure-based optimization of inhibitors of the validated therapeutic target *Schistosoma mansoni* histone deacetylase 8 (SmHDAC8) proved the concept that parasite selectivity can be achieved. Investigation of the interactome of SmHDAC8 indicates key roles in cytoskeletal integrity and cell division.
Conclusion: Enzymes involved in epigenetic processes are valid therapeutic targets for parasitic diseases and selective inhibitors are currently under development as drug leads.

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11:45

Miss Gilda Padalino, *PhD, Aberystwyth University*

Targeting the histone methylation machinery in *Schistosoma mansoni - A15646*

I W Chalmers[2]; K Hoffmann[2]; A Brancale[3]; **G Padalino**[1];

[1] Aberystwyth University, UK; [2] IBERS, Aberystwyth University, UK; [3] School of Pharmacy and Pharmaceutical Sciences, Cardiff University, UK

Dis-regulation of epigenetic processes is responsible for many human diseases (including cancer, diabetes and obesity). This realization had led to increasing numbers of drug discovery projects targeting the responsible epigenetic components, which has contributed to a substantial increase in the number of approved epi-drugs available. Epigenetic pathways have also been recently identified as crucial components in the developmental progression of parasitic helminths, in particular *Schistosoma mansoni*, the causative agent of schistosomiasis. We, therefore, hypothesised that schistosome proteins involved in epigenetic processes could be suitable targets for the development of next-generation anthelmintics.

This study investigated the histone post-translational methylation machinery in schistosome and it was conducted in two parts. Firstly, the schistosome components involved in protein methylation (histone/protein methyltransferases, HMTs) and demethylation (histone/protein demethyltransferases, HDMs) pathways were identified and structurally characterized. This led to the classification of 26 HMTs and 13 HDMs, which included all the previously identified members as well as 4 new proteins (2 HMTs and 2HDMs). Interestingly, some of these proteins included parasite-specific features (such as extended loops), which could be explored in detail for the development of selective anti-schistosomals. Secondly, these epigenetic components were further studied using an integrated biological&hypen;chemical approach to identify new chemical identities with anthelmintic activity. Here, *in vitro* screens against larval schistosomula and adult schistosomes confirmed interesting anti-parasitic activity (phenotype, motility and egg laying defects) of some compounds selected by the *in silico* approach. RNAi-based functional genomics experiments and post-translational histone modification analyses confirmed the mechanism of action of some of these compounds and the suitability of their targets for progression. For a particular HMT (Smp_138030), this led to the further identification of structural analogues with increased anti-schistosomal potency. Collectively, these results reveal how complementary biological, chemical, structural and functional genomic approaches can be used to identify promising starting points for further chemical optimization of novel anthelmintics targeting schistosome epigenetic components.

Further exploitation of such approaches may identify an efficient alternative to the current treatment for schistosomiasis and a description of our ongoing work in such a direction will be provided.

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12:00

Miss Lubna Rehman, *Research Scholar, Aligarh Muslim University*
Curcumin induced biochemical and tegumental surface changes in a digenetic fluke: *Clinostomum complanatum - A15509*

L Rehman[1]; R Ullah[1]; A Rehman[1]; S M Abbas Abidi[1];
[1] Aligarh Muslim University, India

Alternative therapeutic approaches are being considered very important due to the emerging drug resistance against the commonly used anthelmintics. Curcumin a biologically active ingredient of *Curcumin longa* may turn out to be a promising compound as anthelmintic whose therapeutic potential in different ailments is known through various *in vitro* and *in vivo* experiments. In the present study “Curcumin” was assessed for its anthelmintic potential against a model digenean trematode, *Clinostomum complanatum* also a potent zoonotic parasite. The adult worms normally infect the pharyngeal region of ardeiid birds and their excysted progenetic metacercarial form with quiescent gonads infects *Trichogaster* sp. and other economically important fishes and the reports of acute pharyngitis, laryngitis and eye infection in human also been reported.
Progenetic metacercariae of *Clinostomum complanatum* were collected from, *T. fasciatus* and *in vitro* incubated in different concentration of curcumin along with control group without the test drug. Worm motility was observed post incubation every 30 minutes till 6 hours. Worms were further processed for tegumental surface changes, production of reactive oxygen species, reduced Glutathione assay, glutathione-s- transferases and superoxide dismutase activity. Polypeptide profile of somatic and *in vitro* released excretory/secretary products of the treated parasites was generated to evaluate the anthelmintic potential of curcumin.
Concentration dependent inhibition in the worm motility was observed. Treatments of worms with curcumin influenced the production of ROS and altered levels of detoxification and antioxidant enzymes and the tegumental surface structures as revealed by scanning electron microscopy, coupled with the changes in the proteolytic activity which might affect the virulence and the successful establishment of the parasite within the host. Based on the present results it is indicated that the anthelmintic potential of curcumin could be further validated using molecular tools and more species of the trematodes before taking up the *in vivo* investigations.

12:15

Dr Nicholas Furnham, *Associate Professor, London School of Hygiene and Tropical Medicine*
Computationally-guided drug repurposing enables the discovery of kinase targets and inhibitors as new schistosomicidal agents - *A15513*

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S Giuliani[2]; A C Silva[4]; J V Borba[4]; P I Ramos[1]; R A Paveley[2]; E N Muratov[5]; C H Andrade[4]; **N Furnham**[3];
[1] Instituto Gonçalo Moniz, Fundação Oswaldo Cruz (FIOCRUZ), Brazil; [2] London School of Hygiene & Tropical Medicine, UK; [3] London School of Hygiene and Tropical Medicine, UK; [4] Universidade Federal de Goiás, Brazil; [5] University of North Carolina, United States

The development of novel therapeutics is urgently required for diseases where existing treatments are failing due to the emergence of resistance. This is particularly pertinent for parasitic infections of the tropics and sub-tropics, referred to collectively as neglected tropical diseases, where the commercial incentives to develop new drugs are weak. One such disease is schistosomiasis, a highly prevalent acute and chronic condition caused by a parasitic helminth infection, with three species of the genus Schistosoma infecting humans. Currently, a single 40-year old drug, praziquantel, is available to treat all three infective species, but its use in mass drug administration is leading to signs of drug-resistance emerging. To meet the challenge of developing new therapeutics against this disease, we developed a novel computational drug repurposing pipeline supported by high-content phenotypic screening. The approach highlighted several protein kinases as interesting new biological targets for schistosomiasis as they play an essential role in many parasite's biological processes. Focusing on this target class, we also report the first elucidation of the kinome of *Schistosoma japonicum*, as well as updated kinomes of *S. mansoni* and *S. haematobium*.In comparison with the human kinome, we explored these kinomes to identify targets of existing inhibitors which are unique to Schistosoma species, allowing us to identify novel targets and suggest approved drugs that might inhibit them. These include previously suggested Schistosomicidal agents as well as new inhibitors, and 22 newly identified targets. Additionally, the primary and secondary targets in Schistosoma of those approved drugs are also suggested, allowing for the development of novel therapeutics against this important yet neglected disease.

12:30

Miss Fiona McKay, *PhD student, Queen's University Belfast*
In silico profiling and prediction of putative neuropeptide ligand-receptor interactions in parasitic nematodes - *A15719*

F Mc Kay[1]; L Atkinson[1]; C McCoy[1]; N J Marks[1]; A G Maule[1]; A Mousley[1];
[1] Queen's University Belfast, UK

Nematode parasites impact health and agriculture worldwide, where increasing reports of anthelmintic failure underscore the need for novel discovery programmes. The nematode neuropeptide system has been highlighted as a novel source of anthelmintic targets with neuropeptide G-protein coupled receptors (GPCRs) emerging as

primary targets. Nematode neuropeptide GPCRs receive input from neuropeptide ligands to control a range of muscle- and chemosensory-based activities that are pertinent to the biology and survival of nematodes. Anthelmintic exploitation of neuropeptide GPCRs requires knowledge of neuropeptide and neuropeptide-GPCR complements across key nematode parasites, and an understanding of neuropeptide-receptor interactions.

The increased availability and quality of 'omics' datasets in parasitic nematodes has enabled the identification of neuropeptides and neuropeptide GPCRs in key parasite species, however the complexity of the neuropeptidergic signalling system in nematode parasites makes identifying neuropeptide-GPCR interactions difficult. Indeed, there are >250 neuropeptide ligands that have the potential to interact with ~150 neuropeptide GPCRs in parasite species. The available neuropeptide-receptor interaction data, derived from *Caenorhabditis elegans* reverse pharmacology approaches, highlight a few receptor interactions that have been functionally corroborated *in vivo*. However, interpretation of the available data is limited by the use of an incomplete ligand-library, and its relevance to ligand-receptor interactions in parasitic nematodes, where disparity exists in neuropeptide/receptor localisation for some targets.

This study provides data on the Neuropeptide-like protein (NLP) profile across 8 key nematode parasite species to complete the portfolio of putative interacting ligands [FMRFamide like peptide (FLP) and neuropeptide GPCR data are available for these species], and using an *in silico* bioinformatics approach, aims to predict ligand-receptor interactions that are possible *in vivo*. These predictions are aided by analyses of RNA-Seq expression data for key lifestages, sexes, and tissue-types where interaction potential is greater for ligands and receptors that are expressed in the same lifestages, sexes, and tissues at the same time.

Helminths: Molecular Communication –Sponsored by Zoetis - (Stream 3 - Physics 0.15 Main) 14:00 to 15:30

Invited Speaker 14:00 - (30 mins)

Dr Amy Buck, *University of Edinburgh*

Small RNAs in nematode-host interactions - *A15188*

F Chow[5]; G Koutsovoulos[3]; C O Vazquez[6]; J R Bermúdez Barrientos[6]; D Laetsch[3]; S Kumar[4]; J Claycomb[2]; M Blaxter[1]; C A Goodger[6]; **A Buck**[7];

[1] Centre for Immunity, Infection and Evolution, School of Biological Sciences. University of Edinburgh, UK; [2] Department of Molecular Genetics, University of Toronto, Canada; [3] Institute of Evolutionary Biology and Centre for Immunology, Infection and Evolution, University of Edinburgh, UK; [4] Institute of Immunology & Infection

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Research, University of Edinburgh, UK; [5] Institute of Immunology and Infection Research, University of Edinburgh, UK; [6] Langebio – Cinvestav, Irapuato, GTO, Mexico; [7] University of Edinburgh, UK

RNA interference pathways underpin defence and adaptation strategies in nematodes, but their roles in parasitism are largely unexplored. We previously showed that the gastrointestinal nematode *Heligmosomoides polygyrus bakeri* (Hpb) exports small RNAs in extracellular vesicles that are internalized by mouse cells, and these suppress host immune responses *in vitro* and *in vivo*. We further showed that raising antibodies against the EVs confers protection to infection, suggesting EVs are an important mechanism of host modulation. Here we report the full spectrum of small RNAs in these vesicles, based on a new assembly and annotation of the Hpb genome. The dominant class of RNAs in EVs is siRNAs generated by RNA-dependent RNA polymerases inside the nematode and there is a specific enrichment in siRNAs derived from novel repetitive and transposable elements. Small RNA sequencing of mouse epithelial cells following EV treatment suggests a selective subset of the nematode siRNAs and miRNAs are present at functionally relevant concentrations and may interact with host genes with high degrees of complementarity. We further characterize one specific vesicular Argonaute protein that is highly conserved in the parasitic species but rapidly diverged in free-living *Caenorhabditis* and confirm its presence in other parasitic strongyle extracellular products. Our findings point to selectivity in the loading of newly evolved siRNAs in EVs from nematode parasites and suggest a novel Argonaute protein may mediate this.

14:30

Dr Collette Britton, *University Reader, University of Glasgow*

Nematode microRNAs – roles in development and host-parasite interactions *- A15595*

C Britton[1]; A D Winter[1]; N D Marks[1]; H Y Gu[1]; K Maitland[1]; V Gillan[1]; E Devaney[1];

[1] Institute of Biodiversity, Animal Health and Comparative Medicine, University of Glasgow, UK.

The mechanisms regulating development and survival of parasitic helminths within their hosts are not well understood. We are examining microRNAs in parasitic nematodes to investigate potential roles in development and immune modulation. microRNAs (miRNAs) are small (~22 nucleotide) non-coding RNAs that regulate gene expression at the post-transcriptional level. They are expressed in a diverse range of organisms from viruses to humans. We previously identified 192 miRNAs in the ovine gastrointestinal nematode *Haemonchus contortus* and, using microarray analysis, have begun to examine the functions of these. Two miRNAs are enriched in the infective L3 larval stage and genetic knockout of the homologous miRNAs in the free-living nematode *Caenorhabditis elegans* prevents arrest as dauer stage larvae, considered analogous to parasite infective L3. The two miRNAs are predicted to suppress metabolic processes associated with development and may act in parallel

to the insulin-signaling pathway to regulate developmental progression. In contrast to the L3 stage, many novel miRNAs are upregulated in the L4 and adult stages of *H. contortus*. Using small RNA sequencing we have identified that some of these are present in excretory-secretory (ES) products and in extracellular vesicles (EVs) released from L4 and adult worms *in vitro*. Secreted miRNAs can also be detected in abomasal tissue from H. contortus infected sheep and we speculate that these may modulate immune outcome. Our results indicate that miRNAs play important roles in development and in host-parasite interactions and identify miRNAs and the pathways they regulate as potential targets of parasite control.

14:45

Mr Thomas Gasan, *PhD Student, Aberystwyth Univerisy*
Characterisation of *Schistosoma mansoni* Larval Extracellular Vesicle protein 1 (SmLEV1) an immunogenic, schistosome-specific, protein exhibiting developmentally regulated alternative splicing - *A15619*

T A Gasan[1]; S Wilson[2]; J M Wawrzyniak[2]; E Tukahebwa[3]; K Hoffmann[1]; I W Chalmers[1];
[1] IBERS, Aberystwyth University, UK; [2] University of Cambridge, UK; [3] Vector Control Division, Ministry of Health, Republic of Uganda, Uganda

As an integral component of cellular communication, Extracellular Vesicles (EVs) have been described in both protozoa and metazoan parasites. Both larval schistosomula and mature adult Schistosoma mansoni worms release pre-packaged EVs, but to what end? Identifying and characterising proteins within schistosome EVs will aid in discernring their function(s) and may help develop potential schistosomiasis control strategies. To this end, this project aims to characterise the most abundant EV protein in the tissue-migrating schistosomula stage - *Schistosoma mansoni* Larval Extracellular Vesicle protein (SmLEV1). Comparative sequence analysis demonstrates that while SmLEV1 has orthologs in all published *Schistosoma* genomes, it lacks any homologs outside of the genus, nor has any characterised protein domains. By employing qRT-PCR, we discovered differential expression of SmLEV1 across the schistosome lifecycle, with peak expression in cercariae as well as male biased expression in sexually reproductive adults. Importantly, SmLEV1 exhibits developmentally regulated alternative splicing during infection of the mammalian host. Specifically cercariae displayed a significantly different population of isoforms, with over twice the level of exon-5 expression, when compared with adult worms, but only two-thirds the expression of exon-8. Recombinant expression of SmLEV1.3, the most abundant isoform in cercariae, has enabled investigation of the host's response to SmLEV1, in both the mouse model and endemic human populations. Interestingly, preliminary serological analysis from *S. mansoni* infected individuals shows a strong IgG1 response against SmLEV1 with minimal antigen-specific IgG4 and IgE measured; this finding is

congruent to antibody responses generated against other surface/secreted schistosome proteins (e.g. SmLy6A, D, and SmTSP-2). Collectively, these results point to SmLEV1 being an abundant, novel schistosome-specific, secreted protein (within EVs). Finally a murine model vaccination trial has been conducted to investigate the potential protective capabilities of an SmLEV1 vaccine.

15:00

Miss Chelsea Davis, *PhD student, Aberystwyth University*

Optimisation of parasitic extracellular vesicle purification for downstream analysis to understand their role within drug exposure - *A15723*

C N davis[1]; R M Morphew[1]; P M Brophy[1];

[1] Aberystwyth University - IBERS, UK

Robust protocols for the isolation of parasitic extracellular vesicles (EVs) away from other excretory-secretory (ES) products are necessary for downstream functional studies and applications such as vaccine and diagnostic development. The most widely used purification method of EVs in parasite biology is currently differential centrifugation (DC). Outside of parasite biology, size exclusion chromatography (SEC) has been adopted to purify EVs. However, there is no agreed research community ‘gold standard’ of EV isolation from parasitic helminths. In this case study, Fasciola hepatica from natural populations were cultured in order to collect EVs and evaluate a SEC or DC approach to EV purification focusing on the properties of EV preparations. Transmission electron microscopy and atomic force microscopy demonstrated that EVs prepared by SEC were both smaller in size and diversity than EV populations resolved by DC. Protein concentration and Western blotting indicated that SEC purification realised a high EV purity to free ES protein yield ratio compared to DC approaches. Proteomic analysis highlighted an increased diversity of protein identifications and unique peptide hits in EVs isolated by DC compared to SEC. In contrast, transcription and ribosome GO terms, following gene enrichment analysis, demonstrated significantly less gene enrichment in DC purified EVs compared to SEC purified EVs, while translation was enriched to a greater extent in DC purified EVs compared to SEC purified EVs. This data suggests that DC and SEC purification methods do not isolate equivalent EV population profiles and caution should be taken in the choice of EV purification utilised with functional assays incorporated into the isolation pipeline. Thus, this research highlights SEC methods with functional assays as the methodology of choice for parasite EV studies and application development.

Following EV purification analysis, we further aimed to determine the role of parasite EVs during drug exposure, given that investigations upon the EVs and drugs have been limited to cancer chemotherapy and antibiotic resistance research. Therefore, natural populations of F. hepatica were cultured in lethal and sub-lethal doses of

triclabendazole, and active metabolites, in order to SEC purify EVs and evaluate their production, morphological characteristics and drug metabolite content. TEM micrographs demonstrated that all drug exposure EV samples had similar morphology despite disruption to the tegument. qNano particle analysis identified that drug exposure samples produced at least five times more EV concentration than drug exposure controls, where drug dose or drug metabolite did not significantly affect EV production. Particle diameter analysis also showed that only under lethal doses of TCBZ-SO did parasites produce smaller EVs. Using mass spectrometry and qNano particle analysis, drug concentrations in EVs were found in all TCBZ and TCBZ-SO drug exposure samples, although little was identified in TCBZ-SO2 drug exposure samples. Quantification of drug contained within EVs suggests that drug uptake is passive. Interestingly, alternative TCBZ was observed in TCBZ-SO drug exposure samples. This data suggests that EVs may have a metabolic role when parasites are subjected to drug exposure. In this study, it is likely that EVs were utilised to remove drug metabolites from the parasite's microenvironment, to maintain parasite survival. Further research upon the biological role of EVs in parasite environments could provide insight into improving drug control strategies and possibly drug resistance scenarios.

15:15

Dr Anna Protasio, *Post-doctoral fellow, NCBS-Instem-Cambridge Fellowship*
MiR-277/4989 regulate transcriptional landscape during juvenile to adult transition in the parasitic helminth *Schistosoma mansoni - A15778*

A Protasio[1];
[1] NCBS-Instem-Cambridge Fellowship, UK

Schistosomes are parasitic helminths that cause schistosomiasis, a disease affecting circa 200 million people, primarily in underprivileged regions of the world. *Schistosoma mansoni* is the most experimentally tractable schistosome species due to its ease of propagation in the laboratory and the high quality of its genome assembly and annotation. Although there is growing interest in microRNAs (miRNAs) in trematodes, little is known about the role these molecules play in the context of developmental processes. We use the completely unaware ªmiRNA-blindº bioinformatics tool Sylamer to analyse the 3'-UTRs of transcripts differentially expressed between the juvenile and adult stages. We show that the miR-277/4989 family target sequence is the only one significantly enriched in the transition from juvenile to adult worms. Further, we describe a novel miRNA, sma-miR-4989 showing that its proximal genomic location to sma-miR-277 suggests that they form a miRNA cluster, and we propose hairpin folds for both miRNAs compatible with the miRNA pathway. In addition, we found that expression of sma-miR-277/4989 miRNAs are up-regulated in adults while their predicted targets are characterised by significant down-regulation in paired adult worms but remain largely undisturbed in immature "virgin" females.

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Finally, we show that sma-miR-4989 is expressed in tegumental cells located proximal to the oesophagus gland and also distributed throughout the male worms' body. Our results indicate that sma-miR-277/4989 might play a dominant role in post-transcriptional regulation during development of juvenile worms and suggest an important role in the sexual development of female schistosomes.

15 :30

Mr Kevin Howe, *EMBL-EBI*

Wormbase Parasite - *A15913*

K Howe[1];

[1] European Bioinformatics Institute, UK

WormBase ParaSite is an open access resource providing genome sequences, genome browsers, semi-automatic annotation and comparative genomics analysis for nematode and platyhelminth parasites (helminths).

Helminths: Intermediate host - parasite interactions – Sponsored by Zoetis - (Stream 3 - Physics 0.15 Main) 16:15 to 17:45

Chair - Dr Jim Collins

Invited Speaker 16:15 - (30 mins)

Prof Tim Yoshino, *Professor, Parasitology, University of Wisconsin-Madison*

First contact - Release of schistosome exosome-like extracellular vesicles during early intramolluscan larval development - *A15198*

T Yoshino [1]

[1] University of Wisconsin-Madison, USA

Schistosome miracidia transform to primary sporocysts soon after entry into the snail intermediate host. This event is characterized by the shedding of ciliated epidermal plates concurrently with the formation of the sporocyst tegumental syncytium. During this transformation process a diverse array of larval proteins (larval transformation proteins or LTP) are released into surrounding snail tissues, thereby representing the first major source of host-interactive molecule. Previous proteomic analyses of whole LTP released *in vitro* by transforming *S. mansoni* miracidia included several marker proteins typically found in exosome-like extracellular vesicles (ELVs). Because ELVs have not been investigated in early developing schistosome larvae, we proceeded to isolate ELVs from LTP (24-hr cultures) and characterize their proteomic profile. Isolated nanoparticles exhibited mean and mode

diameters of 130 and 66 nm (NanoSight LM10), respectively. Protein comparisons between ELV-enriched samples and LTP-depleted or ELV-wash fractions revealed an enrichment of known exosome-associated proteins. Among the 25 most common proteins associated with exosomes (exoCarta), 10 were present in ELVs isolated from 24h *S. mansoni* LTP, including tetraspanin/CD63 receptor, annexin, enolase, GAPDH and others. Additional proteins involved in cell signaling, RNA metabolism, transcriptional regulation, cell cycle regulation, and stress response were also identified. Fluorescent-labeled ELVs bound to, and were internalized by, a subset of circulating *Biomphalaria glabrata* snail hemocytes, as well as to cells of the *B. glabrata* embryonic (Bge) cell line. Studies are currently in progress to further characterize ELVs released during early larval development and their potential roles in regulating snail cell/parasite interactions.

16:45

Dr Tine Huyse, *senior researcher - parasitologist, Royal Museum for Central Africa*
Comparing the population genetic structure of snail hosts and their schistosome parasites in Northern Senegal - *A15788*

T Huyse[4]; N Boon[1]; N Smitz[4]; A Di Scicio[4]; B Kanage[6]; D Faye[5]; F Volckaert[6]; K Polman[3]; F Van den Broeck[2];
[1] Belgian Scientific Institute for Public Health, Belgium; [2] Institute of Tropical Medicine, Antwerp, Belgium; [3] Institute Tropical Medicine, Antwerp, Belgium; [4] Royal Museum for Central Africa, Belgium; [5] Sante Plus Dakar, Belgium; [6] University of Leuven, Belgium

The epidemiology of schistosomiasis in northern Senegal is changing. *Schistosoma mansoni* was the dominant parasite at the onset of the epidemic in the early nineties, but has nowadays in many places been overtaken by the urinary species *S. haematobium*. Moreover, molecular analyses revealed that children were infected with *S. haematobium* x *S. bovis* hybrids, the latter being a livestock parasite. Here we want to compare the population genetic structure of the two main schistosome species and their respective snail host species in order to understand the role of vector co-adaptation, colonization history and hybridization on schistosome transmission dynamics.
Our results revealed limited *S. haematobium* gene flow between the Middle Valley and the other regions in Northern Senegal, as is the case for one of the bulinid snail hosts. This contrasts with the panmictic population structure found for both *S. mansoni* and the snail host *B. pfeifferi.* We discuss this contrasting resultin relation to the presence and genetic constitution of the intermediate snail hosts, and the colonisation history of the parasites. We found no evidence that hybridization influenced the genetic make-up of *S. haematobium* populations in Senegal. Human schistosomes with a *S. bovis* mitochondrial haplotype could not be differentiated from schistosomes with a *S. haematobium* mitochondrial haplotypeas revealed by 17 nuclear microsatellite markers. In

addition, no first generation hybrids were found. This suggests limited gene flow between human and cattle parasite populations, and that hybridization does not lead to a barrier breakdown between both species in this area.

17:00

Tom Pennance for Dr Bonnie Webster, *Natural History Musuem*
Snail infection / pre-patent surveillance approach for intestinal schistosomiasis control and elimination programs: Tanzania

B Webster[2]; D Rollinson[2]; **T Pennance**[2]; F Allan[2]; A Emery[2]; A Gouvras[2]; K Poulton[2]; E Lugli[2]; S Kinung'hi[1]; T Angelo[1];
[1] National Institute for Medical Research, Dar es Salaam, Tanzania; [2] Natural History Museum, UK

From a global health perspective, the Neglected Tropical Disease (NTD), human schistosomiasis, is the most important water-borne parasitic disease. It is a chronic and debilitating disease caused by infections with trematodes of the genus Schistosoma, which are highly endemic in many subtropical and tropical regions. The parasites, 'schistosomes', have a two-host lifecycle with an asexual stage in particular species of fresh water snail vectors and a sexual stage living in the blood vessels of their human hosts. Whilst Mass Drug Administration (MDA) with praziquantel, behavioural change, education and snail control are having a major impact on schistosomiasis transmission, further research into schistosome transmission biology together with more tailored tests and tools for transmission monitoring and surveillance are required to help achieve these ambitious goals. Additionally, schistosomiasis transmission is highly dynamic with water resource development/management, climate change and the high mobility/migration of people all being important factors that can dramatically and rapidly affect the spread, intensity and introduction/re-introduction of the disease, exacerbating the requirement for accurate ways to monitor transmission. Molecular vector (mainly insects) xenomonitoring is a powerful tool for monitoring the transmission of several parasitic infections. Detection of infection/transmission of schistosomes in snail intermediate hosts (vectors) has primarily relied on morphological methods based on observed parasite emergence but this method lacks sensitivity (very few snails are observed shedding), specificity (animal and human schistosome cercariae can not be easily morphologically identified) and is a highly labour intensive process. Here we will report on the development of a molecular assay for the xenomonitoring of S. mansoni, which causes human intestinal schistosomiasis, in Biomphalaria spp snails in Mwanza Tanzania and how this has been applied to investigate transmission dynamics in different endemic settings in the Mwanza region. Biomphalaria snails were collected from multiple water contact sites from 3 low transmission areas and 1 high transmission area in Mwanza. Snail were checked for patent infections by cercarial shedding and all negative snails were preserved

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for molecular xenomonitoring. Up to 10% more snails were found to be infected following the molecular xenomonitoring analysis and this varied by location and site. Our data shows that even in low transmission settings xenomonitoring methods can be used to detect and monitor transmission but specificity and sensitivity of the assays is important due to multiple other trematode infections existing in such settings.

17:15

Professor Don McManus, *Lab Head and Senior Scientist, QIMR Berghofer Medical Research Institute*

Farewell to the God of Plague: Conquering schistosomiasis in China; the last mile - *A15123*

D P McManus[4]; C A Gordon[4]; P He[3]; G M Williams[5]; Y S Li[4]; Y Wang[3]; J Hu[3]; D J Gray[1]; A G Ross[2]; D Harn[6];
[1] Australian National University, Australia; [2] Griffith University, Australia; [3] Hunan Institute of Parasitic Diseases, China; [4] QIMR Berghofer Medical Research Institute, Australia; [5] The University of Queensland, Australia; [6] University of Georgia, United States

Schistosomiasis in the People's Republic of China (PRC) goes back to antiquity but, in the last 65 years, the Chinese government has made great strides in its control so that elimination is now the final declared goal by 2020. The control strategy aims to eliminate the role of bovines and humans as the sources of infection for intermediate host snails as a pre-requisite for transmission interruption. Due to inadequacies in diagnosis and surveillance, *Schistosoma japonicum* infection rates are underestimated, and areas of transmission risk go undetected so the likelihood of elimination by 2020 is questionable.
We are evaluating (2016-2020) the National Schistosomiasis Control Programme in 16 sentinel villages in the Dongting (Hunan province) and Poyang (Jiangxi province) Lakes areas of the P.R. China using newly developed and field-verified loop-mediated isothermal amplification (LAMP) (for oncomelanid snails)- and real-time polymerase chain reaction (PCR)-based (for humans and animals) diagnostic techniques alongside the currently implemented methods. In a pilot study, we evaluated the qPCR assay using 633 human stool samples collected from five villages in Hunan, Anhui, Hubei, and Jiangxi provinces, and 182 bovine (70 cattle and 112 buffalo) stool samples obtained from four villages in Hunan, Anhui, and Jiangxi provinces in the PRC. All stool samples were subjected to the miracidium hatching test (MHT) (a diagnostic procedure used in the National Schistosomiasis Control Programme) and the qPCR assay. Samples positive by MHT were subjected to either the Kato-Katz technique for humans, or the formalin-ethyl acetate sedimentation-digestion （FEA-SD) procedure for bovines, to determine infection intensities.
The qPCR assay exhibited a high level of sensitivity in the detection of *S. japonicum* infections. With both the human and bovine samples, a significantly higher prevalence was determined using the qPCR assay (11.06% humans, 24.73% bovines) than with the MHT (0.93% humans, 7.69% bovines). The animal contamination index

(calculated using data obtained with the qPCR technique) for all positive bovines was 27, 618, 000 eggs per day, indicating a considerable amount of environmental egg contamination that would be underestimated using less sensitive diagnostic procedures. The qPCR assay we have tested is applicable for monitoring the Schistosomiasis Control Programme in the PRC and can be used as a future field diagnostic and surveillance tool in low-transmission zones where schistosomiasis elimination is targeted and for monitoring post-intervention areas to verify that elimination has been maintained.

17:30

Dr Ana Born-Torrijos, *Institute of Parasitology, Biology Centre, ASCR*

Experimental evaluation of behavioural changes in gilt-head seabream infected with brain-encysted metacercariae of *Cardiocephaloides longicollis* (Trematoda, Strigeidae) - *A15511*

G S van Beest[1]; F E Montero[1]; J A Raga[1]; **A Born-Torrijos**[2];
[1] Cavanilles Institute for Biodiversity and Evolutionary Biology, Science Park, University of Valencia, Spain; [2] Institute of Parasitology, Biology Centre of the Czech Academy of Sciences, eské Budějovice, Czech Republic

Trophically transmitted parasites may increase their transmission efficiency by altering the behaviour of infected hosts, thus increasing their susceptibility to predation by next hosts. The strigeid trematode *Cardiocephaloides longicollis* (Rudolphi, 1819) Dubois, 1982 parasitises 31 fish species, including the gilt-head seabream (*Sparus aurata* L.), one of the most important fish in Mediterranean aquaculture. Actually, this parasite has recently been found in gilt-head seabreams from aquaculture facilities, with a prevalence of infection up to 54%. The cercariae penetrate the skin and migrate into the brain, where they encyst as metacercariae, and the definitive hosts, seabirds, become infected by consumption of infected fish. It is commonly believed that the parasite larvae can cause significant alterations in fish behaviour, thus increasing their transmission to the definitive host, as evidenced in other brain-infecting trematodes (e.g. *Euhaplorchis californiensis*). However, the behavioral pathology suggested to be provoked by *C. longicollis* has never been experimentally studied. In this study, an experiment to detect differences in the behaviour of infected and uninfected fish was performed. First, 14 fish were experimentally infected with 180 cercariae of *C. longicollis*, emerged from their first intermediate host, the snail *Nassarius reticulatus*. Preliminary assays showed an infection success around 50%, so that a high number of metacercariae should be accumulated in the fish brain. Furthermore, behaviour experiments were run 6 months post-infection to ensure that metacercariae were infective. Fish were placed in a plexiglass tube (200 cm height, 30 cm diameter) where an effective light-dark gradient was generated. The water column was vertically divided into 20 cm sections and the position of each fish at 1-min intervals for 30 minutes every 2 hours during 3 days was recorded in three assays, i.e. control (i.e. uninfected), infected and mixed fish group. Preliminary results show significant differences

in the distribution of control and infected fish along the sections in the tube, in both separated and mixed groups, suggesting a different use of the space, and thus behaviour. This may indicate that encysted metacercariae might provoke this behavioral alteration in infected fish within the tube associated to a neuronal disorder. Despite of the fact that most metacercariae infect the optical lobes, this behaviour might not be a consequence of a decrease of light perception, as infected fish occupied generally deeper and so darker positions. However, other aspects of fish vision to be important in the nervous control of behaviour or the host´s antipredator responses, such as visual acuity, could be affected, which has to be further studied.

This study was supported by projects MSM200961706 (Czech Academy of Sciences), AGL2015-68405-R (MINECO/FEDER, UE), Prometeo/2015/018 and Revidpaqua ISIC/2012/003 (Valencian Regional Government).

Clinical Parasitology Session

Clinical Parasitology - (Stream 2 - Llandinam A6) 14:00 to 15:30

Invited Speaker 14:00 - (20 mins)

Dr Roger Evans, *Consultant Clinical Scientist, NHS*

Toxoplasma and transplants: forewarned is forearmed - *A15213*

R Evans[1];

[1] National Health Service, UK

Toxoplasmosis in the immunocompromised host can have serious consequences and, if not recognised, a fatal outcome. The number of patients undergoing haemopoietic stem cell transplant has increased dramatically in the last few years in the UK. This procedure greatly suppresses the patient's immune system making them vulnerable to infections, such as toxoplasmosis. This talk presents the clinical presentations, predisposing risks and diagnosis of this disease in these patients. Prophylaxis and treatment are also discussed.

Invited Speaker 14:20 (20 mins)

Prof Peter Chiodini, *UCL Hospital for Tropical Diseases*

Life as a clinical parasitologist - *A15172*

Until 2014, I was the only Consultant Parasitologist in the entire NHS and there are still only 1.25 of us. My clinical cases can be acquired in any part of the World, temperate or tropical and represent a wide range of protozoal and helminthic parasites. This lecture will cover a selection of challenging cases from the Hospital for Tropical Diseases and how they are managed.

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14:40

Charles Ayorinde Ologunde , *Lecturing, research on tropical parasites and implementation of health policies, The Federal Polytechnic Adoekiti*

Prevalence of malaria, urinary schistosomiasis, typhoid fever and hepatitis b virus co-infection among school children in Ogbese, Ise-Ekiti, South-Western, Nigeria - *A15133*

C A Ologunde[1];

[1] The Federal Polytechnic, Ado-Ekiti, Nigeria

Malaria, Schistosomiasis, Typhoid fever and Hepatitis are some of the causes of morbidity and mortality in tropical Africa. This study was carried out in Ogbese, Ise-Ekiti, South-Western, Nigeria to determine the prevalence and co-infection rate of Malaria, Urinary Schistosomiasis, Typhoid fever and Hepatitis B among school children between the ages of 4 -15. The study design and sampling methods were based on standard procedure as recommended by World Health Organization (WHO). A total of 200 pupils were enrolled in the study. The prevalence of Malaria, Urinary Schistosomiasis, Typhoid fever and Hepatitis were 78%, 68%, 54% and 6.5% respectively. The rate of double, triple and quaternary co-infections were 75(37.5%), 62(31%) and 3(1.5%) respectively. The discovery that three (3) out of the 200 pupils were infected concomitantly with Malaria, Schistosomiasis, Typhoid fever and Hepatitis shows a total and complete public health programme failure in most developing countries like Nigeria. The roles of sex, age and blood group on this observed multiparasitism were also discussed. Further studies is required to understanding the complex immune interactions involved in this multiparasitism and its effect on the outcome of disease presentation with the aim of designing control interventions.

14:50

Prof Adnan Al-Hindi, *Dean, Faculty of Health Sciences, Islamic University-Gaza, Faculty of Health Science*

Epidemiology of *Trichomonas vaginalis* infection among infertile women in Gaza city, Palestine - *A15491*

A Al-Hindi[2]; A Al Maqadma[1];

[1] Faculty of Medicine, Islamic University of Gaza, Palestinian Territory; [2] The Islamic University, Gaza, Palestinian Territory

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Objectives: The present study was conducted to determine the prevalence and risk factors associated with Trichomoniasis infection among infertile women in Gaza city, Palestine.
Materials and methods: A descriptive analytical cross sectional study was conducted between December 2013 to April 2014 in Al Basma medical center in Gaza city. A total of 120 endocervical swabs were collected from females attending the center for management of delayed conception. The samples were processed using PCR technique with Tv1-Tv2 primers. A structured questionnaire was conducted with all participants regarding sociodemographic data, risk factors and symptomatology.
Results: The prevalence of *T. vaginalis* was 5.8%. Statistical significant relation (P 0.01) was found between infection and age of patient, age at marriage, no history of previous vaginal infection and inguinal erythema. Higher infection rate was found among women who were unemployed, of preparatory educational level, from Mid zone, living in crowded house and married to smoker husband.
Conclusion: We concluded that the prevalence of Trichomoniasis is attributed to iatrogenic causes mainly not to personal hygiene. We recommend more hygienic measures inspection in Gynecology clinics in Gaza Strip.
Clinical significance: Avoidance of iatrogenic contamination with *Trichomonas vaginalis* should be considered among Gynaecologists, so, this will decrease the transmission.
Keywords: *Prevalence, Trichomonas vaginalis, infertility, Gaza, PCR.*

15:00

C Ahamuefula *Professor of Medical Microbiology, University of Sunderland*

A rapid ATP bioluminescence assay for antimicrobial susceptibility testing of *Acanthamoeba*; cysts and trophozoites - *A15635*

C Ahamuefula[1]; K Salaman[1]; L Bingle[1]; T Paget[1];
[1] University of Sunderland, UK

Introduction: *Acanthamoeba* is a genus of free living but opportunistic amoebae usually found in soil, fresh water and many other habitats. *Acanthamoeba* exist in two morphologically forms; a motile reproductive trophozoites and a dormant yet viable cyst. The most common type of infections caused by this organism is a keratitis that up until recently was associated with poor hygiene by contact lens users. In the UK there are currently no licenced anti-amoeba drugs for the treatment of this infection. Such infections are currently managed using biocides such as polyhexanide (polyhexamethylene biguanide), chlorhexidine and propamidine isetionate; however failure to kill the cyst forms have been implicated in resistance and reinfection. Development of drugs for the treatment of this infection requires use of appropriate assay methods that can be used for both morphological forms and can be

adapted for high throughput screening. In this work we have shown that and ATP viability assay is a sensitive, reproducible assay that can be used for both cysts and trophozoites forms

Method: In this study an ATP- based antimicrobial susceptibility assay for *Acanthamoeb*a cells was developed by optimising cell lysis and assay conditions. For both life cycle forms the assays were similar in that the compounds were incubated with cells, however after incubation, trophozoites were lysed using conventional detergent lysis methods and for cysts, the cyst wall was enzymatically lysed with lysozyme (lysis was confirmed using TEM). After lysis ATP was measured using the luciferase+ luciferin assay. For our assay development two biocidal compounds were used as our test compounds; Povidone-iodine (PvP-1) and Menadione

Results: Results shows a concentration dependent inhibition of *Acanthamoeba* cells in both the cysts and the trophozoites, but with different MIC values. We were able to extrapolate the minimal inhibitory concentration for PVP by taking RLU values where linearity of our plot stops. These MIC values have RLU similar to control wells were no drug was added. From our data and as supported by previous work using PVP on Acanthamoeba cysts and trophozoites the minimal inhibitory concentration for the cysts is about 1 % (w/v), and about 0.06 % (w/v) for the trophozoites. Menadione showed inhibition of *Acanthamoeba* cyst and trophozoites at 0.06mM concentration and inhibition was concentration dependent. The data generated by this assay has shown remarkable reproducibility and the results obtained are similar to those reported by other researchers.

Conclusion: From our results, this optimised ATP bioluminescence assay showed a good correlation with the conventional plate microscopy count method and the resazurin assay. Both of these methods however have limitations, growth based microscopy show high levels of variation and the resazurin assay does not work for cyst forms and requires large numbers of trophozoites. This method can be engineered into a HTS assay and would be an invaluable tool in the search for new anti-amoebic drugs.

15:10

Paul Jewell, *Imperial College London, Faculty of Medicine*

Treatment of individuals living with neurocysticercosis and HIV/AIDS: a systematic review - *A15651*

P Jewell[1]; A Abraham[3]; V Schmidt[3]; J Bustos[4]; H H Garcia[4]; M A Dixon[1]; M Walker[2]; M G Basáñez[1]; A S Winkler[3];
[1] Imperial College London, UK; [2] Royal Veterinary College, UK; [3] Technical University of Munich, Germany; [4] Universidad Peruana Cayetano Heredia, Peru

Background: Neurocysticercosis (NCC), due to infection with immature stages (cysts) of the pork cestode *Taenia solium*, is the single most important risk factor for acquired epilepsy worldwide and has a substantial global disease burden. Many regions endemic for NCC are also endemic for HIV/AIDS, yet literature on HIV and NCC co-infection is sparse, and there is no current treatment guidance for this large population group.

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To map the currently available literature on NCC and HIV co-infection, with particular focus on clinical characteristics, diagnostic outcomes and treatment of these patients, as well as interactions between anthelmintic, antiepileptic and antiretroviral medications.

Methods: The systematic literature review methodological framework and PRISMA guidelines were followed. A total of 13,777 records identified through database searching and 45 additional records from other sources, were reduced to 57 included studies after a standardised selection process. Included studies were analysed for data relating to the study aims.

Results: One experimental study was identified, of poor methodological quality, which demonstrated improved outcomes in treating intraventricular NCC with raised intracranial pressure with albendazole vs. ventriculoperitoneal shunt insertion plus praziquantel, in a cohort of HIV-positive patients. Twelve observational studies were identified, none of which discussed treatment. Prevalence of NCC was shown to be similar in HIV-positive and -negative populations, with no significant association with CD4 count. Of the 26 cases of HIV and NCC co-infection extracted from 21 case series and case reports, 10 (38%) were from Latin America, 8 (31%) from sub-Saharan Africa and 6 (23%) from the Indian sub-continent. Fourteen suffered with seizures (54%), 12 with headaches (46%) and 10 (38%) had focal neurological deficits. Five (19%) were treated surgically, 15 (58%) received albendazole and 3 (12%) received praziquantel. Four cases could be considered a form of immune reconstitution inflammatory syndrome. Fifteen patients were reported to have clinically improved, and 2 patients died, 1 due to an adverse response after receiving albendazole. No other adverse responses to treatment were reported.

Conclusions: This review highlights the current gaps in the literature on NCC and HIV co-infection. Updated evidence to guide treatment of NCC and HIV co-infection is lacking and further studies are warranted. We will discuss issues relating to *T. solium*-NCC diagnosis and highlight a pressing research gap on the pharmacovigilance of drug interactions between anthelmintics, antiretrovirals and antiepileptics.

15:20

Dr Martin Walker, *Lecturer Epidemiology, Royal Veterinary College*

Designing antifilarial drug trials using clinical trial simulators: the case of river blindness - *A15579*

M Walker[3]; J Hamley[2]; P Milton[2]; F Monnot[1]; B Pedrique[1]; M G Basáñez[2];

[1] Drugs for Neglected Diseases initiative, Switzerland; [2] Imperial College London, UK; [3] Royal Veterinary College, UK

Lymphatic filariasis (elephantiasis) and onchocerciasis (river blindness) are neglected tropical diseases (NTDs) targeted for elimination by mass (antifilarial) drug administration. These drugs are predominantly active against the

microfilarial progeny of the adult worms. New drugs or combinations of existing drugs are needed to improve patient therapies in the clinical setting and to enhance the effectiveness of public health interventions in transmission hotspots where elimination is unfeasible by 2020/2025. Several novel therapies and new regimens are currently in pre-clinical and clinical testing. Clinical trial simulators project patient outcomes to assist with the design of clinical trials. They are used in the pharmaceutical sector but have not been widely applied in the NTD domain, where their resource-optimising payoffs could be highly beneficial. Using river blindness as an example, we demonstrate the utility of clinical trial simulation using a novel individual-based onchocerciasis transmission model that projects trial outcomes of a hypothetical macrofilaricidal drug. We identify key design decisions that influence the power of phase II/III trials, including infection status-based recruitment criteria and follow-up times after treatment for measuring different infection indicators. We discuss how target product profiles must be carefully formulated to ensure they are demonstrable in a clinical trial's framework.

Workshops

Commercialising Research Workshop - (Stream 5 - IBERS New Build 0.33***) 16:15 to 17:45***

Invited Speaker 16:15 - (30 mins)

Dr Katherine Ellis, *Patent Attorney, Williams Powell*

Developing drugs for developing world diseases: the role of patents - *A15173*

K Ellis[1];

[1] Williams Powell, UK

Patents reward inventors (or often, their employers) by granting a time-limited monopoly on their invention in return for disclosing details of their idea to the public. Such reward is crucial in the pharmaceutical sector in view of the cost of bringing a drug through pre-clinical and clinical trials and eventually to market. The possibility of owning the rights to, and charging a premium for, life-saving medical treatments is, however, not without controversy. Should researchers seek patent protection for promising candidates for treating developing world diseases? How can patents be used to ensure both inventors and society at large benefit from innovations? And what steps should you take to ensure your potential inventions are properly protected?

Invited Speaker 16:45 - (30 mins)

Greg Mirams, *Techion Group Ltd*

The challenges of commercialisation and industry adoption of novel parasite diagnostic tools - *A15893*

G Mirams[1]

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[1] Techion Group Ltd, New Zealand.

The primarily challenge to the adoption of a new diagnostic approach is the natural human reluctance to accept and embrace change. This reluctance to change is heightened due to the complex nature of the issue and the traditional mindset of influencers that support industry stakeholders. These stakeholders are changing and increasingly wanting robust and timely parasite diagnostic information which traditional diagnostic services struggle to provide. A new diagnostic approach may have a strong and compelling list of advantages over traditional methods, yet adoption and commercial success is often slow and constrained. To overcome this reluctance to change, the parasitology community needs an openness and awareness of their changing world, the value proposition for a new approach must be compelling, early adoption needs to be well supported to build user confidence. The collaborative use of a new approach builds positive user experiences and if shared effectively, encourages more new users. The need for more robust, timely, expertise supported parasite diagnostic information has never been more relevant, yet the challenge of slow adoption of these new technologies threatens to limit our ability to more effectively manage and control parasitism in 2018 and beyond.

In vitro Technologies in Cryptosporidium Research: Workshop 1 - (Stream 5 - IBERS New Build 0.33) 11:15 to 12:45

Invited Speaker 11:15 - (90 mins)

Prof Nigel Yarlett, *PACE University*

Advances in *in vitro* culture of *Cryptosporidium - A15184*

N Yarlett[1];

[1] PACE University, USA

Long term *in vitro* growth of *Cryptosporidium parvum* has proved difficult with the majority of *in vitro* studies being performed in 2-3 days, after which time they fail to propagate in *in vitro* or *in vivo*. Using a hollow fiber bioreactor (HFB) to grow human intestinal epithelial cells we can simulate *in vivo* conditions by providing oxygen and nutrients to host intestinal cells from the basal surface, while permitting the establishment of a low redox, high nutrient environment on the apical surface. When inoculated with 10^5 *C. parvum* (Iowa isolate) oocysts the bioreactor produces 10^8 oocysts per ml (20 ml extra-capillary volume) and has been maintained for over 2 years. *In vivo* infectivity studies using a TCR-α-immune deficient mouse model showed that oocysts produced from the bioreactor at 6, 12 and 18 months are indistinguishable from the parent Iowa isolate used to initiate the culture. In addition, the HFB produced oocysts have similar percent excystation profiles to the parent Iowa isolate. The technique provides for the first time the opportunity to perform long term *in vitro* studies with *Cryptosporidium parvum*.

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In vitro Technologies in Cryptosporidium Research Workshop 2 - (Stream 5 - IBERS New Build 0.33) 14:00 to 15:30

14:00 - (90 mins) As above

Tuesday 10th

Plenary Sessions

Plenary III/IV - (Great Hall, Arts Centre)11:15 to 12:45

11:15 - (45 mins)

Dr Shahid Khan, *Associate Professor, Leiden University Medical Center*
Genetic modification of *Plasmodium* for malaria vaccine development - *A15505*

Genetic manipulation of *Plasmodium* parasite has considerably improved our understanding of parasite gene function and revealed many novel host-parasite interactions underlie malaria pathology. Genetically modified malaria-parasites are now also being used directly as vaccines against malaria and the LUMC were one of first groups to develop the concept of immunization with genetically attenuated parasites (GAPs). Together with our partners we have established a roadmap that goes from GAP immunization studies in rodent models, through pre-clinical testing and into vaccine manufacture and Phase 1/2 clinical evaluation. We are currently engaged in GAP vaccine trials that are now being conducted in volunteers in the Netherlands. The procedures for GAP selection and testing as well as the safety and efficacy trial will be presented. In addition, we are creating transgenic malaria parasites that express foreign genes (e.g. fluorescent and luminescent proteins) that are also being used to advance malaria sub-unit vaccine development. How transgenic malaria parasites are used, *in vitro* and *in vivo*, to determine protective efficacy of different *Plasmodium* antigens and vaccination strategies and to determine immunological correlates of protection will be discussed. Chimeric rodent parasites expressing *P. falciparum* or *P. vivax* antigens are also being used to evaluate and rank order human malaria vaccines before their advancement to clinical testing and will also be described.

Invited Speaker 12:00 - (45 mins)

Prof Wendy Gibson, *University of Bristol*
Tsetse and trypanosomes - *A15174*

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W Gibson[1];
[1] University of Bristol, UK

When Bruce first implicated tsetse flies as the carriers of pathogenic trypanosomes in 1895, he did not appreciate that the trypanosomes undergo a cycle of development inside the fly rather than just being transmitted mechanically from animal to animal. By the 1970's the complexity of the developmental cycle of *Trypanosoma brucei* had been revealed by light and electron microscopy and it was thought that most of the details were known. Now fluorescent proteins have opened a new window on the development of trypanosomes inside the fly. By genetically engineering trypanosomes to express fluorescent proteins, we can directly observe these parasite cells inside the fly. Even a single trypanosome can be seen. This approach has allowed us to track the trypanosomes as they migrate through the alimentary tract of the fly and identify the developmental stages found in different organs. We can analyse how different strains and species interact along their shared migration routes. By tagging stage-specific genes, we can locate particular life cycle stages in the fly and for example pinpoint the location where genetic exchange takes place.

Tryps & Leish Sessions

Tryps & Leish Cell & Molecular Biology II - (Stream 1 - Edward LIwyd 0.26 Biology Main) 09:00 to 10:30

Invited Speaker 09:00 - (30 mins)

Dr Michael Urbaniak, *Lecturer, Lancaster University*

Post-transcriptional regulation of the *Trypanosoma brucei* cell cycle *- A15182*

M Urbaniak[1];
[1] Division of Biomedical and Life Sciences, Faculty of Health and Medicine, Lancaster University, UK

The cell division cycle of *Trypanosoma brucei* is highly organised and tightly controlled, reflecting the need to co-ordinate not only nuclear division, but also the division and segregation of the mitochondrial kinetoplast DNA and its single copy organelles such as the ER, Golgi and flagellum. The temporal control of protein involved in the regulation and progression of cell cycle is essential to ensure correct growth and division, and cell cycle arrest is required for pre-adaption for transmission between hosts. Regulation of the eukaryotic cell cycle is achieved through control at multiple levels including transcriptional regulation, and despite a paucity of transcription factor mediated gene expression, *T. brucei* regulates it transcript abundance over the cell cycle [1]. We are taking an unbiased approach to investigate the role of dynamic phosphorylation in the *T. brucei* cell cycle by conducting global quantitative proteomic analysis of synchronised cell populations. We have optimised a centrifugal counter-flow elutriation protocol for both Pcf and Bsf cells that yields viable and proliferative cells that maintain

synchronicity into subsequent cell cycles [2]. SILAC isotopic labelling of these synchronised cells has allowed us to generate quantitative temporal profiles of protein and phosphorylation site abundance that provide an insight into the role of dynamic phosphorylation in the post-transcriptional regulation of cell cycle control. 1. Archer, S.K., *et al*., The cell cycle regulated transcriptome of *Trypanosoma brucei*. PLoS One, 2011. 6(3): p. e18425. 2. Benz, C., *et al*., Cell cycle synchronisation of *Trypanosoma brucei* by centrifugal counter-flow elutriation reveals the timing of nuclear and kinetoplast DNA replication. Sci Rep, 2017. 7(1): p. 17599.

09:30

Mr Adalberto Miguel de Araújo Júnior, *PhD student, Federal University of São Paulo*

In vitro characterization of a compound capable of arresting *T. cruzi* cell cycle without affecting parasite viability - *A15633*

A M Araújo-Júnior[2]; S Schenkman[2]; C B Moraes[1]; L H Freitas-Junior[1];

[1] Biomedical Sciences Institute/USP, Brazil; [2] Federal University of São Paulo, Brazil

Little is known about what proteins regulate intracellular development of *Trypanosoma cruzi* in the mammalian cell. The present investigation has studied and characterized the intracellular development of *T. cruzi* considering a chemical biology approach. We have identified, from a high content screening campaing, a small molecule capable of arresting the intracellular development of *T. cruzi,* seemingly without affecting parasite or host cell viability. The functional characterization of compound activity showed that: (i) the intracellular development arrest phenotype is not restricted to a host cell type; (ii) the compound is able to inhibit the replication of other *T. cruzi* strains belonging to different Tc groups of clinical relevance (Y, Sylvio X10/1 and CL Brener strain); (iii) the arrest can be reversed upon compound removal, at which point intracellular amastigotes resume their cycle, differentiating to trypomastigotes; (v) the compound did not show cytotoxicity for distinct host cells (U2OS, LLC-MK2, NRK-52E and BHK-51) for up to 200 µM for 48 h; and (vi) while the epimastigote form of *T. cruzi* can also be arrested without loss of viability, the compound displayed a concentration-dependent cidal activity against bloodstream forms of *Trypanosoma brucei* and promastigote forms of *Leishmania donovani* (DD8 strain), without causing arrest. Altogether, these results suggest that this compound acts via a regulator of cell cycle that can specifically cause arrest in *T. cruzi* and not in other trypanosomatids. Future experiments will focus on target deconvolution and molecular characterization of the target, aiming at unveiling the parasite proteins that regulate *T. cruzi* parasite cell cycle and intracellular development in the host cell.

09:45

Dr Sam Alsford, *Associate Professor, London School of Hygiene and Tropical Medicine*

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Decoding the network of *Trypanosoma brucei* proteins that determines sensitivity to apolipoprotein-L1 - *A15638*

R B Currier[1]; **S Alsford**[1];
[1] London School of Hygiene and Tropical Medicine, UK

In contrast to *Trypanosoma brucei gambiense* and *T. b. rhodesiense*, *T. b. brucei* is lysed by apolipoprotein-L1 (apoL1)-containing human serum trypanolytic factors (TLF), rendering it non-infectious to humans. While the mechanisms of TLF1 uptake, apoL1 membrane integration, and *T. b. gambiense* and *T. b. rhodesiense* apoL1-resistance have been extensively characterised, our understanding of the range of factors that drive apoL1 action in *T. b. brucei* is limited. Selecting our bloodstream-form *T. b. brucei* RNAi library with recombinant apoL1 identified an array of factors that supports the trypanocidal action of apoL1, including six ubiquitin modifiers and several proteins putatively involved in membrane trafficking. Most prominent amongst these novel apoL1 sensitivity determinants was a putative ubiquitin ligase. Intriguingly, while loss of this ubiquitin ligase reduced parasite sensitivity to apoL1, its loss enhanced parasite sensitivity to TLF1-dominated normal human serum, indicating that free and TLF1-bound apoL1 have contrasting modes-of-action. Indeed, loss of the known human serum sensitivity determinants, p67 (lysosomal associated membrane protein) and the cathepsin-L regulator, ‘inhibitor of cysteine peptidase’, had no effect on sensitivity to free apoL1. Our findings highlight a complex network of proteins that influences apoL1 action, with implications for our understanding of the anti-trypanosomal action of human serum.

10:00

Dr Francisco Olmo, *Research Fellow, London School of Hygiene and Tropical Medicine*
Chemical-mediated transfection meets Parasitology: Trypanosomatids as proof-of-concept for the technology - *A15687*

F Olmo[1]; C Rotger[2]; M C Taylor[1]; F Orvay[2]; A Costa[2]; J M Kelly[1];
[1] London School of Hygiene and Tropical Medicine, UK; [2] Universitat de les Illes Balears, Spain

Electroporation is the only technique routinely used to transfect trypanosomatids. However, the procedure has limited efficiency and flexibility, for example, taking up to 6 weeks to establish a genetically transformed culture of *Trypanosoma cruzi*. We have developed a new method of transfection, using a non-viral, toxicity-free chemical carrier, which is able to efficiently package DNA into globular particles (visible under atomic force microscopy). The DNA-carrier complex is efficiently internalized without damaging the parasite or disrupting the cell cycle. The procedure involves a very straightforward 3-step protocol, without the need for expensive devices, reagents and

cuvettes, and can generate >3000 stable transformants per microgram of plasmid DNA. The approach has been applied to several intra and extra-cellular trypanosomatid species using both episomal and integrative vectors. Parasites expressing RFP/GFP are visible within 6 hours and they can be cultured under drug selection to generate stably transformed lines. This approach has great potential to help address new and important biomedical questions, related to pathogenesis, drug-resistance and parasite latency. Recently obtained results also suggest that the technique will be more widely applicable to other pathogens.

10:15

Mr Calvin Tiengwe, *Research fellow, SUNY Buffalo*

ERAD and disposal of misfolded GPI-anchored proteins in *Trypanosoma brucei - A15694*

C Tiengwe[1]; J D Bangs[1];
[1] University at Buffalo (SUNY), United States

Misfolded secretory proteins are generally retrotranslocated from the ER and degraded in the proteasome by ER-associated degradation (ERAD). However, in yeasts and mammals, where glycosylphosphatidylinositol (GPI) anchors are forward trafficking signals, misfolded GPI-anchored proteins are preferentially delivered to the vacuole/lysosome for disposal. Using the phylogenetically ancient parasite *Trypanosoma brucei* as a model system, we test the universality of this process with a misfolded subunit of the transferrin receptor (TfR). TfR is a heterodimer of GPI-anchored ESAG6 and non-GPI ESAG7. When expressed with ESAG7, misfolded ESAG6 assembles into heterodimers, but are non-functional for Tf binding. When expressed alone, misfolded ESAG6 is N-glycosylated and GPI-anchored, but accumulates in the ER as monomers/aggregates. Treatment with MG132, a proteasome inhibitor, generates a protected polypeptide that is full length, soluble, cytosolic, and de-N-glycosylated. This protected polypeptide is non-reactive with anti-CRD antibody, a GPI-specific reagent, indicating that GPI destruction precedes delivery to the proteasome. The trypanosome GPI anchor is a forward trafficking signal, thus the dynamic tension between ERAD and ER exit favors degradation by ERAD. These results differ markedly from the standard eukaryotic model systems and may indicate an evolutionary advantage related to pathogenesis.

Host / Vector Parasite Interactions Sessions

Host /Vector- Parasite Interactions I - (Stream 1 - Edward Llwyd 0.26 Biology Main) 14:00 to 15:30

Invited Speaker 14:00 - (30 mins)

Prof Edmundo Grisard, *Professor of Cellular and Molecular Parasitology, Universidade Federal de Santa Catarina*

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The cell cycle and the distinct antioxidant defence mechanisms of *Trypanosoma rangeli - A15771*

E Grisard[1];
[1] Universidade Federal de Santa Catarina, Brazil

The proliferation of the non-virulent protozoan *Trypanosoma rangeli* within its mammal hosts is controversial. Although increasing number of parasites are observed in experimental infections, there are no clues on the parasite replication sites and, thus, little is known how this species deal with the host’s defences. Assessment of cell cycle-associated proteins in *T. rangeli* revealed that the Polo-like kinase mRNA is up-regulated in proliferating epimastigotes, being a marker for cytokinesis. Although showing distinct expression levels and activity among *T. rangeli* strains from distinct genetic lineages, expression and enzymatic activity of the *T. rangeli* arginine kinase (TrAK) is down-regulated in blood trypomastigotes and up-regulated in epimastigotes, which may indicate a low or even absent replication of the bloodstream forms. These results allowed us to estimate that *T. rangeli in vitro* cell cycle takes ± 20.6 hours. The *in vitro* differentiation to infective trypomastigotes was assessed using distinct techniques. Along the classical morphological changes of the nucleus, kinetoplast and flagellum, increased mRNA levels of KMP-11, spermidine synthase (SpdS) and histidine ammonia lyase (HAL) were observed in epimastigotes while dihydrolipoamide dehydrogenase (DHLADH), mitochondrial HSP70 (mtHSP70), mitochondrial RNA binding protein 2 (MRP2), SS and a protein of unknown function revealed to be differentially expressed at the protein level between life-cycle stages during differentiation. A comparative *in silico* analysis of the genes related to the parasite antioxidant defence mechanisms, have shown that *T. rangeli* genome lacks the genes coding for cysthatione synthase (CS), ornithine decarboxylase (ODC), glutamylspermidine synthase (GspS), ascorbate peroxidase (AP) and one out of the three isoforms (“C”) of glutathione peroxidase (GP). However, multiple copies of cystathionine β-synthase (CβS) and GP isoform “A” were observed. Functional rescue of the CS activity in *T. rangeli* via heterologous expression of the *L. amazonensis* CS have doubled the epimastigotes survival rates when exposed to both oxidative (H2O2) and nitrosative (SNAP) stress if compared to wild-type parasites. Likewise, overexpression of a homologous trypanothione reductase (TR), which is present as a single copy gene on the haploid genome and shows reduced expression level in trypomastigotes, has also increased the parasite resistance to oxidative stress. We have also noticed that endogenous H2O2 production is higher in *T. rangeli* than *T. cruzi* epimastigotes. Taken together, our results seem to indicate that evolution of the *T. rangeli* antioxidant defence mechanisms is highly influenced by specific adaptations to the distinct biological life cycle within the insect vectors. Funding: CNPq, CAPES, FINEP and STINT

14:30

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Prof Maria-Gloria Basanez, *Chair Neglected Tropical Diseases, Imperial College London, Faculty of Medicine*

Complementary paths to Chagas disease elimination: the impact of combining vector control with aetiological treatment - *A15653*

Z M Cucunubá[1]; P Nouvellet[5]; J K Peterson[3]; S M Bartsch[2]; B Y Lee[2]; A P Dobson[4]; **M G Basáñez[1];**
[1] Imperial College London, UK; [2] John Hopkins Bloomberg School of Public Health, United States; [3] University of Pennsylvania, United States; [4] University of Princeton, United States; [5] University of Sussex, UK

BackgroundThe World Health Organization's 2020 goals for Chagas disease are: (1) interrupting vector-borne intra-domiciliary transmission, and (2) having all infected people under care in endemic countries. Insecticide spraying has proved efficacious for reaching the first goal, but active transmission remains in several regions. For the second, treatment has mostly been restricted to recently infected patients, who comprise only a small proportion of all infected individuals. The current fraction of people in endemic areas that has access to screening and treatment amounts only to c. 1%.

Methods We extended our previous dynamic transmission model to simulate a domestic Chagas disease transmission cycle (with human and reservoir hosts and triatomine vectors), and used the model to examine the effects of both vector control (through indoor residual spraying of insecticides, IRS) and aetiological treatment of those infected with *Trypanosoma cruzi*, on achieving one of the operational criteria proposed by the Pan American Health Organization for intra-domiciliary, vectorial transmission interruption (i.e., reaching <2% seroprevalence in children <5 years of age). A range of endemicity levels (from low endemicity to very high endemicity) was simulated by increasing the carrying capacity of the domiciliated vectors. An external force of infection was included to account for the contribution of sylvatic transmission.

Results Depending on the level of endemicity, an antivectorial (IRS) intervention that decreases vector density by 90% annually would achieve the transmission interruption criterion in 2-3 years (low endemicity) to >30 years (very high endemicity). When this strategy is combined with annual aetiological treatment (leading to parasitological cure) in 10% of the infected human population, the seroprevalence criterion would be achieved in 1 year (low endemicity) or 11 years (high endemicity).

Conclusions Combining highly effective vector control with aetiological (trypanocidal) treatment in humans would substantially reduce time to transmission interruption as well as infection incidence and prevalence (in human, reservoir and vector populations). However, the success of vector control may depend, among other things, on prevailing vector species, and many technical issues surrounding the application of insecticide to human dwellings. It will also be crucial to improve the coverage of screening programmes of the human population, the performance of the diagnostic tests to detect and confirm Chagas disease, the proportion of people treated, and the efficacy of

trypanocidal drugs. While screening and access to treatment can be incremented as part of strengthening the health systems response, improving diagnostics performance and drug efficacy will require strong commitment and investment in research and development (R&D) of novel diagnostic and therapeutic tools.

14:45

Mr Philipp Schwabl, *cruzi repro, University of Glasgow*
Parallel sexual and parasexual population genomic structure in *Trypanosoma cruzi- A15594*

P Schwabl[1]; M S Llewellyn[1]
[1] University of Glasgow, UK

The unicellular eukaryote *Trypanosoma cruzi*, parasitic agent of Chagas disease, was once held up as a paradigm for clonal evolution. In later years, limited evidence emerged of recombination in the field and laboratory. The mechanisms and extent of genetic exchange in *T. cruzi*, however, remain very little understood. Here, we present evidence from 83 sequenced *T. cruzi* genomes that coincident meiotic and para-sexual mating cycles drive genetic structure among sympatric populations. In one section of the 100 km^2-study region, host and vector-isolated strains carry single-nucleotide-polymorphisms at Hardy-Weinberg frequencies and under linkage decay consistent with widespread meiosis-like genetic exchange. At adjacent sites, populations exhibit near-maximal excess-heterozygosity throughout the genome. Haplotype structure, mitochondrial and ploidy analyses suggest that these heterozygous groups originate from a para-sexual genome fusion event. Based on measurements of shared segment similarity, distribution and length, we give frequency estimates for these recombination processes and discuss their epidemiological and evolutionary implications.

15:00

Dr Martin Taylor, *Associate Professor, London School of Hygiene and Tropical Medicine*
Revisiting the intracellular cycle of *Trypanosoma cruzi* in chronically infected animals - *A15700*

M C Taylor[2]; A Ward[2]; A F Francisco[1]; S Jayawardhana[2]; M Lewis[1]; J M Kelly[1];
[1] Department of Pathogen Molecular Biology, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT., UK; [2] London School of Hygiene and Tropical Medicine, UK

Trypanosoma cruzi causes a chronic life-long infection. Parasites are rarely observed in the blood and infected patients may routinely be PCR-negative. Highly sensitive bioluminescence imaging (BLI) has allowed us to establish the GI tract as the major reservoir site in murine models of chronic *T. cruzi* infections. However, BLI is

limited in its ability to identify parasites at a cellular level. To circumvent this, we generated trypanosomes expressing a luciferase-mNeonGreen fusion protein, such that parasites were both highly bioluminescent and fluorescent. In acutely infected mice many organs are infected and nests of amastigotes are readily identified in the heart, the adipose tissue and in other organs. In chronically infected animals, where parasites are mainly restricted to the GI tract, there were very few nests, with infections generally restricted to single or low numbers of amastigotes per cell. However, some of the nests detected in the chronic phase contained extremely large numbers of parasites. Using a combination of TUNEL assays for kDNA replication, and EdU labelling, we have been able to examine the replication of the parasites in the chronic phase. This has demonstrated that in all phases of the infection parasite replication within a single infected cell is asynchronous, regardless of the number of parasites within the nest. Differentiation from amastigote to trypomastigote also appears to be asynchronous and multiple morphological forms can exist within a single nest, including epimastigote-like cells and amastigotes with protruding flagella.

15:15

Dr Michael Lewis, *Assistant Professor, London School of Hygiene and Tropical Medicine*
Fatal progression of experimental visceral leishmaniasis is associated with secondary infection by commensal bacteria and severe anaemia - *A15711*

M D Lewis[2]; A Paun[1]; A R Romano[1]; H Langston[2]; D L Sacks[1];
[1] Laboratory of Parasitic Diseases, National Institutes of Health, NIAID, United States; [2] London School of Hygiene and Tropical Medicine, UK

The canonical target organs for *Leishmania donovani* are spleen, liver, bone marrow and lymph nodes. Using qPCR and histology we observed that in the hamster, a model of progressive, fatal VL, the GI tract was also a site of intense parasitism. GI infection was not detected in mice, in which VL is much less severe. We therefore reasoned that the host-microbiota homeostasis could be perturbed by *L. donovani* in hamsters, and that this could contribute to VL outcome. To address this, we induced intestinal dysbiosis using broad spectrum antibiotic treatment prior to and during *L. donovani* infection in both hamsters and mice. This treatment had no impact in the mouse model. Treated hamsters had delayed onset and progression of weight loss, and significantly less severe hepatosplenomegaly. Antibiotic-treated hamsters also had a significant survival advantage compared to untreated controls. However, parasite loads in the liver and spleen were not significantly different between groups and they did not correlate with progression. Only marginal differences in immune response profiles were observed. Protection from VL in antibiotic-treated hamsters was associated with reduced susceptibility to secondary bacterial infection, revealed through immunohistochemical detection of lipopolysaccharide in the liver. Further

multiparametric analysis of blood biomarkers identified anaemia as the strongest overall correlate of VL progression. Therefore, VL in the hamster model is associated with bacterial sepsis and severe anaemia, potentially linked to parasitism of the GI tract. We conclude that these factors, rather than *L. donovani* parasite loads, are the main drivers of fatal VL disease progression.

Host /Vector- Parasite Interactions II - (Stream 1 - Edward Llwyd 0.26 Biology Main)16:15 to 17:45

Invited Speaker 16:15 - (30 mins)

Dr Jesus Valenzuela, *Senior Investigator, NIAID*

A second uninfected blood meal in sand flies promotes reverse metacyclogenesis and *Leishmania* replication - *A15183*

M Valenzuela[1];

[1] National Institute of Allergy and Infectious Diseases, USA

Tiago Donatelli Serafim, Iliano V. Coutinho-Abreu, Fabiano Oliveira, Claudio Meneses, Shaden Kamhawi and Jesus G. Valenzuela.

Vector Molecular Biology Section, Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, Maryland 20852, USA.

Disease vectors transmit pathogens as they blood feed, and most vectors take multiple blood meals during their lifetime. Here, we show a remarkable ramification of a subsequent uninfected blood meal for a *Leishmania*-infected sand fly. Within 24h after uninfected blood feeding by a sand fly carrying a mature infection, 93% of *Leishmania* metacyclics, previously considered a terminally differentiated infectious stage, dedifferentiate to a replicative form we term "retroleptomonad". This new replicative phase results in an amplification of metacyclics, and reveals an unidentified recurrent metacyclogenesis cycle that increases sand fly infectivity with every blood meal, including non-infectious blood meals. On the other hand, in the absence of a second blood meal the majority of *Leishmania* infections acquired by feeding on an infected host are lost. Together, these findings highlight the relevance of multiple blood meals for vector-borne pathogens that exceed facilitation of contact between insect and host. They reveal a novel and fundamental role for multiple blood meals in establishing the pathogen, and most importantly in perpetually enhancing infectivity of the insect vector. These findings also place readily available blood sources as a critical element of vector-borne pathogen transmission, a new concept of consequence for vector-borne diseases.

16:45

Dr Pegine Walrad, *Research Lecturer, University of York*

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The mRNA-bound proteome of *Leishmania* is stage-regulated with little correlation to transcriptome or whole proteome expression - *A15618*

L M de Pablos[1]; T R Ferreira[1]; A A Dowle[1]; S Forrester[1]; K Newling[1]; **P B Walrad**[1];
[1] University of York, UK

Leishmania species parasite infections, termed the leishmaniases, cause significant global infectious disease burden. The lifecycle of the parasite embodies three main stages that require precise coordination of gene regulation to survive drastic environmental shifts transitioning from sandfly to mammalian hosts. Constitutive transcription in these kinetoplastid parasites is overwhelmingly reliant on post-transcriptional mechanisms, yet strikingly few *Leishmania trans*-regulator proteins are known. Utilizing optimised crosslinking and in-depth, quantified mass spectrometry, we present a comprehensive analysis of over 1,400 mRNA binding proteins (mRBPs) and over 2,400 whole cell proteins from the three main lifecycle stages. Supporting the validity of this RBPome, Gene Ontology (GO) analysis reveals significant enrichment of RNA binding and gene regulation terms and endogenously-tagged candidate mRBPs exhibit stage-specific expression and associate with mRNA. Important findings from this work include a low correlation between protein and transcript expression, stage-specific variation in protein expression versus mRNA binding potential, and a modulation of mRNA binding protein enrichment during the *Leishmania* parasite lifecycle. Our results indicate that in *L. mexicana* parasites, RNA levels are not a strong predictor of whole cell expression or RNA binding potential of proteins. Our study is the first at its depth in kinetoplastid parasites and provides novel, quantified insight into *trans*-regulatory mRNA:Protein (mRNP) complexes that drive *Leishmania* lifecycle progression to human infectious stages.

17:00

Miss Srija Moulik, *Ph. D student, Institute of PG Medical Education and Research*
Differential expression of Vitamin D related genes in macular vs. polymorphic post Kala-azar dermal leishmaniasis - *A15140*

S Moulik[1]; A Dighal[1]; R Sengupta[1]; D Mukhopadhyay[1]; S Mukherjee[1]; S J Choudhuri[2]; M Chatterjee[1];
[1] Institute of PG Medical Education and Research, India; [2] Ranaghat SD Hospital, Kolkata, India

Background: Indian Post kala-azar dermal leishmaniasis (PKDL) is the cutaneous aftermath of visceral leishmaniasis (VL) that manifests as macular or polymorphic PKDL in the ratio of 1:10. However, ensuing the ongoing active surveillance for PKDL as part of the Leishmaniasis elimination programme, a substantial increase in the proportion of macular PKDL has been established. The lesional distribution of polymorphic cases is

predominantly in sun-exposed areas whereas it is disseminated in the macular variant, suggesting a differential role for Vitamin D. Accordingly, this study aimed to delineate the status of Vitamin D_3 expressing genes in peripheral blood and dermal lesions of patients with polymorphic vs. macular PKDL.

Methods: Patients clinically diagnosed with PKDL were recruited from active field surveys conducted in VL endemic districts of West Bengal. Blood and dermal biopsies were collected at disease presentation. Upon ITS-1 PCR positivity, parasite load was quantified, and mRNA expression of Vitamin D receptor (*VDR*), 25-Hydroxyvitamin D_3 1-alpha-hydroxylase (*CYP27B1*), *LL-37* (cathelicidin) and *β-actin* was measured by qPCR in PBMC of PKDL cases (n 20, macular: polymorphic, 1:1) and VL (n 6) along with reverse transcriptase-PCR from dermal biopsies (n 10, macular: polymorphic 1:1). Plasma levels of 25(OH) Vitamin D_3 was measured by sandwich ELISA at disease presentation (n 23, macular: polymorphic 11:12).

Results: As compared to healthy controls, plasma 1α,25-dihydroxyvitamin D3($1,25D_3$) levels were significantly raised in the polymorphic variant and positively correlated with parasite load at disease presentation. In circulating monocytes, irrespective of the variant, the mRNA expression of VDR (responsible for nuclear signaling of 1,25D3), *CYP27B1* (converts vitamin D to its active form, 1,25D3) and *LL-37* was significantly increased, and they positively correlated with parasite load. Additionally, Plasma $1,25D_3$ positively co related with mRNA expression of *CYP27B1* and *LL37*. In dermal lesions, normal skin demonstrated expression of *VDR* but *CYP27B1* and *LL37* was not detectable. The mRNA expression of *CYP27B1* was significantly raised in both variants, but an increase of *LL37* was restricted to the polymorphic cases. The mRNA expression of Vitamin D related genes in circulating monocytes of VL patients was comparable with healthy individuals.

Conclusion: In PKDL, the enhanced polarization of monocytes-macrophages towards alternate activation accounted for the enhanced expression of Vitamin D related genes *VDR*, *CYP27B1* and *LL37* in both variants in their peripheral blood. Importantly, in dermal lesions which are the site of the disease, an increase in the mRNA expression of *VDR*

17:15

Dr Pieter Steketee, *Research Fellow, The Roslin Institute*

Comparative metabolism of *Trypanosoma brucei brucei* and the livestock trypanosome *T. congolense* - *A15706*

P C Steketee[1]; F Achcar[4]; J Iremonger[1]; F Giordani[4]; S Jayaraman[1]; K CrouchE Paxton[1]; A Donachie[4]; H de Koning[4]; C J Suckling[3]; M P Barrett[4]; L J Morrison[1];

[1] Roslin Institute, UK; [2] University of Glasgow , UK; [3] University of Strathclyde, UK; [4] Wellcome Trust Centre for Molecular Parasitology, UK

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The protozoan livestock parasite, *Trypanosoma congolense*, is a primary causative agent of animal African trypanosomiasis (AAT), also known as Nagana. This disease is responsible for a significant socio-economic burden across sub-Saharan Africa, with annual cattle deaths in excess of 3 million. There are limited chemotherapeutics to combat AAT, and with drug resistance emerging to the majority of compounds available, there is a dire need for novel trypanocides. Whilst the closely related trypanosomatid *T. brucei* has been the subject of much attention over the past century, the livestock trypanosomes, including both *T. congolense* and *T. vivax*, have been relatively ignored, partially due to an inability to culture the parasites in a laboratory environment. Hence, biological understanding of these pathogens remains limited. Using metabolomics (liquid chromatography-mass spectrometry) and RNAseq, we have compared the metabolism of *T. congolense* with *T. brucei*, and have identified both similarities and important differences. Analyses suggest that glycolysis remains active in *T. congolense*, but is geared towards acetate production. In contrast to *T. brucei*, the primary metabolic outputs of *T. congolense* are acetate, succinate and malate, suggesting that *T. congolense* bloodstream form bears similarities, albeit on a metabolic level, to that of both bloodstream and procyclic form *T. brucei*. This information is aiding our attempts to develop novel *in vitro* culturing strategies for the livestock trypanosomes.

17:30

Dr Amanda Francisco, *Research Fellow, London School of Hygiene and Tropical Medicine*
Curative Benznidazole treatment in the acute stage of *Trypanosoma cruzi* infection prevents the development of chronic cardiac fibrosis - *A15666*

A F Francisco[1]; S Jayawardhana[1]; M C Taylor[1]; M Lewis[1]; J M Kelly[1];
[1] Department of Pathogen Molecular Biology, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT., UK

The insect-transmitted protozoan parasite *Trypanosoma cruzi* is the causative agent of Chagas disease (CD), and infects 5-8 million people in Latin America. CD is characterised by an acute phase, which is partially resolved by the immune system, but then develops as a chronic infection. Approximately 30% of those infected with *T. cruzi* develop chronic stage pathology, but this can take decades to become symptomatic. Because of this, and with difficulties in demonstrating parasitological cure, it has been difficult to assess the extent to which anti-parasitic therapy can prevent the development of pathology. We sought to address this question using highly sensitive bioluminescent imaging methodology and murine models BALB/c and C3H/HeN infected with CL Brener and JR strain, respectively. We monitored heart inflammation and fibrosis, two widely markers of cardiac pathology. This *in vivo* imaging procedure has a limit of detection of 100-1000 parasites, and facilitates the real-time tracking of

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parasite burden in individual mice during chronic infections. These experiments demonstrated that curative benznidazole treatment early in murine *T. cruzi* infections prevents the development of cardiac fibrosis. Treatment during the chronic stage can also block pathology, but the effectiveness of this varies between infection models. If these findings are extendable to humans, it will imply that widespread chemotherapeutic intervention targeted at early stage infections could play a crucial role in reducing CD morbidity at a population level.

Ecological Parasitology Sessions

Ecological Parasitology II - (Stream 4 - Edward Llwyd 0.01) 09:00 to 10:30

Invited Speaker 09:00 - (30 mins) **Dr David Thieltges**, *Senior Scientist, NIOZ Royal Netherlands Institute for Sea Research*

The world in an oyster - biological invasions and their impact on parasite-host interactions - *A15181*

D Thieltges[1];

[1] NIOZ Royal Netherlands Institute for Sea Research, Netherlands

Biological invasions often result in dramatic impacts on native biota in recipient ecosystems and it is now increasingly recognised that they can also affect parasite-host interactions and diseases. In this presentation, I will give a conceptual overview of the different mechanisms of how invaders can affect diseases in invaded ecosystems and I will illustrate them with results of recent investigations on the invasion impacts of Pacific oysters. This marine bivalve has been introduced worldwide for aquaculture purposes and has become one of the most notorious invader in global coastal waters. The findings presented in this talk will highlight the intricate ecological complexity of the impacts of biological invasions on parasite-host interactions and diseases in recipient ecosystems.

09:30

Miss Lisa Gecchele, *PhD Student, The University of Edinburgh*

The role of the urban environment in shaping parasite communities of red foxes in Edinburgh - *A15315*

L V Gecchele[1]; A B Pedersen[1]; M Bell[1];

[1] The University of Edinburgh, UK

Urbanisation affects both the abiotic and biotic properties of ecosystems and have a profound impact on ecological processes. Although urban areas have green spaces that provide habitat for wildlife, these areas are often highly fragmented and frequently disturbed. Urban environments can also have high availability of resources and lack

many common competitors and predators, which can positively impact wildlife species. Urban environments can be particularly challenging for carnivore species, given the high rate of conflict with humans. While many studies have focused on how the urban environment can directly affect the ecology of wildlife species, much less is known about how urban habitats affect species interactions, specifically between hosts and their parasite communities. Previous research has shown that urban environment can have an effect on parasite prevalence and species richness of carnivores; however most of these studies have not taken into account the spatial heterogeneity of urban environments, which can be important for parasite transmission and persistence.

Here we investigate how fine-scale variation in urban environment influences gastrointestinal parasite infection risk and community structure in the red fox (*Vulpes vulpes*) population across the city of Edinburgh. We surveyed all green spaces across the city to determine the influence of both socio-economic and ecological variables on parasite prevalence and diversity. We found that the presence and abundance of fox faecal samples was non-uniformly distributed; ecological, rather than socio-economic, variables such as the size of the green area and the presence of other wildlife were significant predictors of scat deposition patterns in urban foxes. In addition, the presence of roe deer (*Capreolus capreolus*) was positively correlated with the parasite species richness of specific sites. These results highlight the importance of "pockets of wilderness" within urban areas for wild foxes and could have wider implication for the management of urban carnivores.

09:45

Miss Cassandra Raby, *PhD student, University of Liverpool*

Ecological and population-level drivers of gastrointestinal parasitism in the Genus *Papio*: a meta-analysis - *A15628*

C L Raby[2]; G Cowlishaw[1]; A C Fenton[2]; X A Harrison[1];

[1] Institute of Zoology, UK; [2] University of Liverpool, UK

Emerging infectious diseases are a threat to human health and wildlife populations. Non-human primates are of particular interest due to their close phylogenetic relationship to humans, shared parasites, and their own extinction risk from novel pathogens. We use baboons (*Papio*) as a model primate species, since they are widely spread across the African continent, and regularly live beside and interact with rural and urban human populations, making them important to human health research.

This study presents the first investigation into key drivers of parasites across baboon species and populations. We reviewed data from 45 study sites detailing parasite abundance across five baboon species, to investigate the key environmental and population-level drivers influencing their macroparasite communities. We found that the assemblages of parasite species are indistinguishable across all African baboons. These assemblages differ across NDVI gradients, latitudinal gradients, and temperature gradients. Despite this, there were no significant

correlations between parasite richness and the environmental variables, or between baboon troops. We explored variables important to the presence of key microparasites (*Balantidium coli* and *Giardia*) and macroparasites (*Trichuris* spp*, Oesophagostamum* spp*, Streptopharagus* spp*,* and *Physaloptera* spp), with a range of correlated variables emerging. When exploring across-population patterns of parasites, there are key environmental conditions relating to the assemblages of parasites. We can explore this further to consider how environmental change, or mitigation strategies, will influence the presence of parasite species.

10:00

Ms Paula Tierney, *PhD student, Zoology Department, Trinity College*

Parasite-mediated effects of an invasive fish on native brown trout - *A15699*

P A Tierney[2]; J M Caffrey[1]; C V Holland[2];
[1] Inland Fisheries Ireland, Ireland; [2] Trinity College Dublin, Ireland

The role of parasites in biological invasions is becoming increasingly recognised. The differential effects of parasites on native and invasive hosts can amplify or mitigate the negative impacts of invaders on native hosts, thereby mediating the effects of invasions and altering invasion outcomes. The common dace (*Leuciscus leuciscus*) was first introduced to Ireland in 1886 and remained confined to a single catchment until 1980. By 2015, dace had invaded the two largest catchments in Ireland and had the highest density of all fish species in the upper River Barrow, some 200 kilometres away from the initial point of introduction. Its rapid spread has raised concerns over potential impacts on sympatric native freshwater fish, particularly given the dearth of information on its parasite fauna. In the first comprehensive study of the parasite community of invasive dace in Ireland, we compared the helminth parasite communities of long-established and recently established populations of dace with native brown trout (*Salmo trutta*) from the same sites. Our results show that while dace acquired acanthocephalan parasites, the parasites did not reach sexual maturity in the invasive fish. Brown trout from sites with a longer-established dace population had a lower infection burden of acanthocephalans, indicating that by taking up but not distributing infective stages of the parasite, the invasive fish may be diluting acanthocephalan infection in brown trout. However, while heavy acanthocephalan infection can cause severe damage to host fish, a decline in this dominant parasite group may alter the structure of brown trout parasite communities and disrupt native host-parasite dynamics.

10:15

Mr Rhidian Thomas, *PhD student, Cardiff University*

Infected crayfish play it safe: *Aphanomyces astaci* reduces crayfish movement on land - *A15489*

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J R Thomas[1]; C Robinson[2]; A Ellison[1]; E Matthews[1]; S W Griffiths[1]; S Consuegra[2]; J Cable[1];
[1] Cardiff University, UK; [2] Swansea University, UK

Parasites can play a key role during the spread of invasive, non-native species, especially when invaders transmit parasites to native species. Parasites can also influence the behaviour of invaders, which can mediate their impact and spread in invaded ecosystems. The invasive North American signal crayfish (*Pacifastacus leniusculus*) has caused mass mortalities of native European crayfish species, primarily through the spread of crayfish plague (*Aphanomyces astaci*). This oomycete pathogen is fatal to all European crayfish species, though North American crayfish are generally considered to be largely resistant carriers. Such a chronic infection, however, could affect invasive crayfish by altering their behaviour. Here, we tested the effect of crayfish plague on signal crayfish behaviour. Overall, infected crayfish spent significantly less time out of water, were less active during the day and were less likely to display an escape response when infected. In management terms, this study shows that crayfish plague affects invasive crayfish to a greater extent than previously considered, which could contribute to observed signal crayfish declines in commercially harvested stocks.

Ecological Parasitology: Molecular Ecology and Evolution of Parasites - (Stream 4 - Edward Llwyd 0.01) 14:00 to 15:30

Invited Speaker 14:00 - (30 mins) *Determinants of genetic structure and diversity patterns in parasite population* (Isabel Blasco-Costa)

Ms Isabel Blasco-Costa, *Research Scientist, Natural History Museum of Geneva, Switzerland*
Determinants of genetic structure and diversity patterns in parasite population - *A15206*

I Blasco-Costa[1];
[1] Natural History Museum of Geneva, Switzerland

Since the advent of molecular data, studies examining genetic variation within parasite species and populations have gathered little attention. Only recently, understanding how parasite species are subdivided has extended outside the medically or veterinary relevant species allowing a wide comparative approach. These new model systems provide a unique opportunity to test how general predictions borrowed from population genetics theory of free-living organisms apply to a broad range of parasite species. Furthermore, disentangling the contribution of multiple variables unique to the diversity of life histories of parasitic species may widen the knowledge and generality of the theoretical principles. In this talk I will first review and summarise the current state of the field.

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Then, I will present new comparative data from different parasite-host systems examining the role of several life history and environmental variables in structuring genetic diversity of parasite species. I will discuss our results and future research venues in the light of the new opportunities arising from genomic approaches.

14:30

Mr Tom Pennance, *PhD Student, Natural History Museum*

Xenomonitoring of schistosomiasis transmission on Pemba Island (Zanzibar) - *A15727*

T Pennance[2]; J Cable[1]; D Rollinson[2]; F Allan[2]; B Webster[2];
[1] Cardiff School of Biosciences, Cardiff University, UK; [2] Natural History Museum, UK

Urogenital schistosomiasis, a snail-borne disease caused by infection with *Schistosoma haematobium*, accounts for more than 110 million cases of human schistosomiasis in sub-Saharan Africa alone. Zanzibar (Unguja and Pemba Island) is endemic for urogenital schistosomiasis but is now targeted for elimination through the 'Zanzibar Elimination of Schistosomiasis Transmission' (ZEST). However new measures are required to evaluate 'true' elimination (cessation of *Schistosoma* transmission), when it is finally reached. Snail xenomonitoring has been suggested as an alternative method to assess levels of transmission/freshwater-schistosome-contamination and certify eventual elimination. Two morphologically similar species of freshwater snail, *Bulinus globosus* and *B. nasutus*, are linked with *S. haematobium* transmission on Pemba Island, however the latter is widely regarded as naturally refractory to schistosome infection in this setting. The development of sensitive and specific xenomonitoring molecular markers may therefore offer a more efficient approach to evaluate these two *Bulinus* species individual roles in transmitting *Schistosoma* spp. in Pemba Island. Here we report on the development of protocols for the xenomonitoring of *Schistosoma* infection in *Bulinus* in Pemba Island. Snails have been collected over 3 times points in up to 11 shehias (smallest administrative region) of 4 differing transmission statuses. Transmission status categories were developed from results of the annual ZEST *S. haematobium* prevalence surveys between 2012 and 2016 with shehias grouped in either 1 of 4 categories: persisting hot-spots (high prevalence areas with persisting high prevalence of >10%), declining hot-spots (high prevalence areas with decline to <10% by 2016), low non-responders (prevalence persisting at <10%) and low decliners (starting <10% prevalence and declining to <1%). In each shehia, human freshwater contact sites were mapped, and snail surveys conducted at each site involving searching and collecting *Bulinus* and recording ecological characteristics. Snails were checked for shedding schistosomes (patent infections) and any cercariae were molecularly identified by amplifying and sequencing the mitochondrial cytochrome oxidase subunit 1 (cox1) and internal transcribed spacer 1 (ITS 1+2) DNA regions. All snails were then fixed in absolute ethanol for morphological and molecular identification to differentiate *B. globosus* and *B. nasutus* and for xenomonitoring. Different primer combinations are

currently being developed to amplify snail and schistosome DNA in a single reaction, to confirm *Bulinus* species and pre-patent schistosome infections. Initial results have been surprising, in that although *S. haematobium* cercariae have been identified shedding from *B. globosus*, the new emergence of *S. bovis*, a parasite of cattle, also identified from multiple shedding *B. globosus* complicates the development of the xenomonitoring tool that now requires an increased specificity to differentiate these two species of schistosome. Not only this, but the confirmed presence of *B. nasutus* in identified transmission areas, questions their individual involvement in transmission. Our data therefore shows the necessity for the molecular identification and the development of species-specific molecular xenomonitoring tools of the snails and their schistosomes to truly evaluate the levels of human schistosome transmission/contamination. Without such specificity the transmission of *S. bovis* will be misidentified and assumed to be *S. haematobium*.

14:45

Mr Ahmad Garziz, *PhD, Bangor University*
Totiviruses, parasites and everything else - *A15095*

A A Garziz[1]; H R Braig[1];
[1] Bangor University, School of Biological Sciences, UK

Totiviridae are unsegmented, icosahedral dsRNA viruses which display a fascinating diversity of hosts, a disparity of host effects, and a divergence of transmission strategies. Hosts include human parasites like *Giardia*, plant parasitic oomycetes, fungi and yeasts, red macroalgae (seaweed), terrestrial crustaceans like woodlice, insects like flies, mosquitoes, ants and wasps, marine crustaceans like shrimp, but also fish, fresh water snails that are intermediate hosts to parasites, and plants like papaya, notoginseng, maize, and wild petunias. In *Leishmania* and *Trichomonas*, the viruses increase the virulence of the parasites (hypervirulence), while in Victoria blight of oats it reduces the virulence of the fungus (hypovirulence). In salmon, smelt, and shrimp, it causes myocarditis and myonecrosis, in golden shiners it is asymptomatic. In *Leishmania* and many fungi and some plants, it is non-infectious and vertically transmitted, while in *Giardia*, fish, shrimps, and papaya, it is horizontally transmitted. Using PCR with degenerate primer sets, we are trying to explore the taxonomic boundaries of the vertically transmitted viruses in parasites to estimate the evolutionary age of first infection, the virulence in *Giardia*, and the evolutionary origin of dsRNA viruses in arthropods, especially sand flies, which are vectors of *Leishmania*.

15:00

Dr Joseph Ironside, *Senior Lecturer, Aberystwyth University*
Parasitic feminisation of crustaceans - *A15907*

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J Ironside[1];
[1] Aberystwyth University, UK

Within populations of the amphipod crustaceans *Orchestia gammarellus* and *O. aestuarensis*, a proportion of females produce thelygenic (female-only) broods which often contain intersexual individuals. This phenomenon is associated with the presence of two parasites, the paramyxid *Paramarteilia orchestiae* and the microsporidian *Dictyocoela cavimanum*, which frequently co-infect the same host. In order to determine which of the parasites causes feminisation, *Orchestia* were resampled from the type locality of *P. orchestiae* in France and from another population at Dale in the UK. Breeding experiments indicated that female *O. gammarellus* infected with *P. orchestiae* produced a significantly higher proportion of female and intersex offspring than uninfected females, even in the absence of *D. cavimanum*. Although *D. cavimanum* also displays a female-biased prevalence in *Orchestia* populations, this is due to co-infection with *P. orchestiae*, indicating that the paramyxid, rather than the microsporidian, is the cause of feminization in these *Orchestia* populations.

15:15

Miss Rebecca Cole, *PhD Student, University of Bristol*
Patterns of genetic variation in the parasitic nematode *Strongyloides ratti - A15271*

R Cole[1]; N Holroyd[2]; M E Lotkowska[2]; A Tracey[2]; M Berriman[2]; M Viney[1];
[1] School of Biological Sciences, University of Bristol, UK; [2] Wellcome Trust Sanger Institute, UK

We have been investigating the population genetics of *Strongyloides ratti*, a nematode that infects brown rats (*Rattus norvegicus*). Population genetic analysis can reveal a species’ population biology, and can be used to predict population-level responses to selection pressures. Nevertheless, very little is known about the population genetics of parasitic nematodes, especially those that infect wild animals
We have sequenced the whole genomes of individual *S. ratti*, sampled non-destructively from three wild rat populations. So far, results show strong genetic differentiation among *S. ratti* sampling sites. We detect a low level of gene flow among parasite populations, likely mediated by occasional long-range dispersal of rat hosts. We have serendipitously detected evidence of mitochondrial heteroplasmy in these parasite populations.
There is an uneven distribution of polymorphic sites within the *S. ratti* genome, possibly reflecting the action of selection. Loci putatively associated with the parasitic lifestyle have been detected in *S. ratti*. It will be interesting to see whether these genes share concerted patterns of selection, which could reflect ongoing adaptation of parasitic traits.

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This work is revealing how genetic variation is distributed in *S. ratti* at three levels - within individual genomes, within populations, and among sampling sites.

Ecological Parasitology: Aquatic Parasitology I - (Stream 4 - Edward LIwyd 0.01) 16:15 to 17:45

Invited Speaker 16:15 - (30 mins)

Dr Chrisophe Eizaguirre, *Reader in Evolutionary and Conservation Genetics, Queen Mary, University of London*

Parasite resistance: from genes to ecosystems - *A15193*

C Sagonas[1]; F Brunner[2]; **C Eizaguirre**[1];

[1] Queen Mary, University of London, UK; [2] University of Liverpool, UK

Parasites are ubiquitous. They impact both ecological dynamics as well as adaptive evolution of their hosts. Focusing on a series of infection experiments using the three-spined stickleback as a model host species, we will report about various molecular bases of resistance whether genetics or epigenetics. Furthermore, we describe how parasites and the evolution of parasite resistance in this fish host can mediate eco-evolutionary feedbacks altering prey communities impacting the selection pressure on subsequent host generations. Given the high parasite abundance in natural populations, and the rapid evolution of resistance, we argue that the neglect of parasites in ecosystem studies is unwarranted since they act as cryptic but crucial part in eco-evolutionary dynamics.

16:45 –

Mrs Miroslava Soldanova, *PhD, Biology Centre, Czech Academy of Sciences*

The ecological role of trematode parasites in aquatic food webs: a case study in a subarctic lake - *A15559*

M Soldánová[5]; A Born-Torrijos[5]; J Schwelm[1]; G S van Beest[2]; T Vyhlídalová[4]; E H Henriksen[3]; R Knudsen[3]; R Kristoffersen[3]; P A Amundsen[3];

[1] Aquatic Ecology and Centre for Water and Environmental Research, University of Duisburg-Essen, Essen, Germany; [2] Cavanilles Institute for Biodiversity and Evolutionary Biology, Science Park, University of Valencia, Spain; [3] Department of Arctic and Marine Biology, Faculty of Biosciences, Fisheries and Economics, UiT The Arctic University of Norway, Tromsø, Norway; [4] Faculty of Science, University of South Bohemia in Ceské Budějovice, Czech Republic; [5] Institute of Parasitology, Biology Centre of the Czech Academy of Sciences, Ceské Budějovice, Czech Republic

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Recent attempts for the inclusion of parasites in food webs have shown parasites to be significant structuring forces that could potentially increase important properties of trophic networks. Understanding ecosystem processes and functioning inherently requires the assessment of the ecological role of parasites in food webs, particularly the quantification of parasite-predator-prey relationships. However, recent findings are based on topological food webs, and the energetic aspect in terms of strength of trophic links between parasites and free-living organisms remains to be tested. Digenean trematodes are essential components of aquatic food webs potentially affecting multiple trophic levels within an ecosystem. The aim of this study is to investigate the ecological role of trematodes in trophic interactions and their biomass contribution to energy flow in the food web of a subarctic freshwater system. From Lake Takvatn in northern Norway, a highly resolved parasite-inclusive topological network has been established, and trematodes, the most diverse parasite taxon in this ecosystem, represent an excellent model system to address the general questions on trematodes’ ecological relevance in food webs. During two extensive sampling periods in August and October 2017, we performed a series of field and laboratory experiments to quantify and evaluate the strength of trophic interactions between the trematode free-living stage, the cercariae, and several predatory organisms by obtaining data for estimation of three main ecological aspects: (i) cercarial emission, output rates and biomass, (ii) survival rates of cercariae, and (iii) predation rates on cercariae from direct and indirect (i.e. concomitant predation) consumption by different predators. Model organisms comprised trematodes of three genera, one invertebrate predator (amphipod) and three vertebrate species (fish). Our preliminary results on the mean daily output rates and chronobiology in cercariae emergence suggest an adaptive response to the unique subarctic light and climatic conditions (photo- and thermoperiod). High survival rates of cercariae at low temperatures indicate the existence of compensation mechanisms of trematodes for a narrow temporal transmission window in subarctic areas. Part of the cercarial biomass serves as food resource for non-host species in the Takvatn ecosystem, as evidenced by the frequent direct consumption of cercariae by amphipod and fish predators. An additional proportion of the trematode population was excluded via concomitant predation, when trematodes were consumed along with their snail hosts. This indicates that parasite-predator-prey interactions could have strong knock-on effects on trematode population dynamics, transmission success and infection levels in downstream hosts. Collectively, our preliminary estimates of trematode biomass and its loss within the lake ecosystem provide empirical evidence that parasites play a significant ecological role in ecosystem energetics and thereby ecosystem processes. Our data underline the importance of studying the role of both parasites and ambient environment on the energy flow and functioning of food webs in general.

17:00

Dr Paolo Ruggeri, *PostDoc PDRA NERC Hydroscape, Natural History Museum*

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Vertical transmission and drivers of myxozoan distributions - *A15582*

P Ruggeri[1]; B Okamura[1];
[1] Natural History Museum, UK

Myxozoans are a group of endoparasitic cnidarians with complex life cycles, exploiting invertebrates and vertebrates (usually fish) as definitive and intermediate hosts, respectively. It is now known that covert myxozoan infections are vertically transmitted to dormant overwintering stages (statoblasts) of bryozoan hosts. After statoblast dormancy is broken overt infection development triggered in newly hatched bryozoans enables transmission to fish hosts via infectious spores. In at least one system such vertical transmission is substantial - up to 45% of statoblasts produced by the bryozoan *Fredericella sultana* are infected by the myxozoan *Tetracapsuloides bryosalmonae*. Here we investigate whether myxozoan infections are vertically transmitted to statoblasts in a contrasting system along with potential drivers of variation in infection prevalence.
The bryozoan *Cristatella mucedo* produces hooked statoblasts that float upon release, unlike the adherent statoblasts produced by *F. sultana*. Previous research has demonstrated metapopulation dynamics with local *C. mucedo* populations undergoing extinction and (re)colonization. Infections by the myxozoan *Buddenbrockia bryozoides* have been hypothesized to contribute to local extinctions of *C. mucedo* while colonisation has been strongly linked with transport of statoblasts by waterfowl. We collected 1349 *C. mucedo* statoblasts from 48 sites in four regions of the United Kingdom representing lowland agricultural (Norfolk and Northern Ireland), upland (Cumbria), and urbanized (Greater Glasgow) landscapes. In each region we collected samples from hydrologically connected, semi-connected and isolated sites. Following DNA extraction, statoblasts were screened for myxozoan DNA using targeted primers for a portion of the 18S rRNA gene. We also genotyped each statoblast using 10 microsatellite markers in order to characterise patterns of infection in highly clonal bryozoan populations. Our results provide evidence for vertical transmission with infected statoblasts detected in 37 of 48 populations. For infected populations the mean infection prevalence 0.20 (SD 0.12, range 0.3 - 43%; n 37). Such vertical transmission may enable myxozoan infections to be spread to new sites by waterfowl vectors along with their bryozoan hosts. Infection prevalence was significantly greater in populations from Norfolk and Northern Ireland suggesting that agricultural environments may favour parasites as a result of nutrient- enhanced primary production and hence more food for suspension-feeding bryozoan hosts. Hydrological connectivity exerted no apparent effect on infection prevalence, thus the spread of infection may be achieved by other processes (e.g. waterfowl movements). Finally, we obtained evidence for disproportionate infections of common host clones. This result suggests that Red Queen dynamics may often characterise even relatively ephemeral local populations. There was no correlation between the number of host clones and infection prevalence. Our investigations provide

evidence that vertical transmission of myxozoans appears to be a common strategy that creates a reservoir for fish disease, and they identify both landscape and invertebrate host genotype as drivers of infection prevalence.

17:15

Dr Jo James, *Technical Officer, Environment Agency*
The global success of monogeneans: more than just a fluke - *A15679*

J James[3]; A J Reading[3]; J Cable[2]; R Britton[1]; G Paladini[4]; C F Williams[3];
[1] Bournemouth, UK; [2] Cardiff School of Biosciences, Cardiff University, UK; [3] Environment Agency, UK; [4] Institute of Aquaculture, University of Stirling, Facultry of Natural Sciences, UK

Over the last 30 years, the recorded parasite diversity of British freshwater fish has significantly increased as a consequence of greater detection efforts and the introduction of new species with global fish movements. For those managing freshwater environments understanding changes in the parasitological fauna represents a significant challenge, and there is a need to balance surveillance efforts with risk of disease. Globally, the Monogenea are among the most successful and widespread group of aquatic parasites, which have the potential to cause significant fish mortalities. However, our current estimate of mongenean diversity is thought to be a gross underestimate. Here, we highlight current issues with detecting and identifying monogeneans, and use *Pellucidhaptor pricei, Thaprocleidus vistulensis* and *Gyrodactylus sprostonae* as examples of recent additions to the British parasitological fauna. We also discuss the potential implications of these and other newly emerging monogeneans for British freshwater fisheries.

17:30

Mr Michele De Noia, *PhD, glasgow University*
Rapid test to detect the infection load of the parasite, *Anguillicola crassus*, in the European eel, *Anguilla anguilla - A15777*

M De Noia[1], J Kaufmann[1]; P McGinnity[1]; M S Llewellyn[2]
[1] Marine Institute, Ireland; [2] University of Glasgow , UK

Anguillicola crassus is a nematode parasite of the swim bladder originally endemic to Japanese eels, *Anguilla japonica*. *A. crassus* was introduced into Europe in the 80’s since when it has spread widely and is thought to contribute to the rapide decline in the European eel. Currently, the only way to detect the parasite is to dissect the eel. We are developing a non-lethal rapid test based on presence/absence of eggs and L2 larvae in the faecal

material. A faecal wash had been performed on c.60 European eels in the Burrishoole catchment in Ireland. qPCR primers were designed based on CO1, 18s specific genes and transcriptome available in the literature. Primers were tested using pure *A. crassus* DNA and and related nematodes to establish the specificity. To validate the test 24 eels were fecal sampled, euthanized, dissected, and the number of worms counted in the swim bladder. The rapid test is in an optimisation phase and we hope will be a valulable tool for fisheries managers hopeing to interrupt transmission of the parasite.

Veterinary Parasitology Sessions

Veterinary Parasitology - Diagnostics & Therapeutics - (Stream 5 - Physics 0.11 A) 09:00 to 10:30

Invited Speaker 09:00 - (30 mins)

Greg Mirams, *Techion Group Ltd*
Current innovations in parasite diagnostics – what does the future look like? - *A15308*

G Mirams[1]
[1] Techion Group Ltd, New Zealand.

Many institutes and commercial organisations around the world are working on new and innovative parasite diagnostic tools. The reality is that few of these innovations will ever be commercially developed and fewer still will reach commercial adoption. Parasite diagnostics is a technically challenging and complex area, however most new diagnostics tools will fail due to an inability to provide an integrated, end to end solution. An integrated solution needs to connect the sample collection, processing, analysis, reporting, interpretation and most importantly, an ability to deliver this information to those on the front line of parasite management. Regardless of the technology used to analyse a sample, future parasite diagnostic approaches will be transformed by utilising the combined power of collaboration and cloud computing. By working more collaboratively, science and commercial entities can deliver an integrated and powerful platform that enables easily access to live data, linked and supported by expertise that will empower decision makers to make faster, more informed and accurate disease management decisions.

09:30

Prof Muhammad Fiaz Qamar, *Chairman, University of Veterinary & Animal Sciences*
Molecular detection of fancy birds parasites for clinical diagnosis and epidemiology - *A15049*

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M F Qamar[1]; K A Ali[1]; M Zaman[1]; F Atif[1];
[1] University of Veterinary & Animal sciences, Lahore, Pakistan

The parasitic infections are significantly increasing especially over the past few years. The faecal and blood smears microscopic examination are routinely used protocol for detection of parasites. As microscopically, we can differentiate the genus and their related species, so more accurate diagnosis can be made through real-time PCR assay. The technique was used for DNA extracted whole-blood specimens for detection of parasites. This method was more sensitive, rapid, and precise for parasitic finding in fancy birds and human being specimens.
New diagnostic tools for the detection of fancy birds parasites are essential for the monitoring of altering epidemiology of parasites, mainly among urban areas. This Real-time PCR along with microscopy aim for the identification of parasites in fancy birds. These molecular techniques aid in diagnostic methods for further research about the detrimental effects of parasitic infestation on birds and human beings.
Methods: A comparison of conventional microscopy and real-time PCR assay was carried out for the comparison of detection rate of parasites from blood and faecal materials gathered from the 6 different species of birds and human beings. Real-time PCR optimization and cycle threshold was performed to compare the sensitivity and specificity of faecal microscopy and PCR. A species-specific PCR assay was used to categorize the contribution of different parasitic speciesin infections.
Conclusions: Although microscopy is widely used routine practice in field conditions for the quick diagnosis of infestation clinically but molecular diagnostics approaches like PCR present a more sensitive source of identification of parasites. Probable role of these parasitic infections to fancy birds and human beings is serious to evaluate and determine so it is necessary to be performed. The possible applications of the concerned technique in certain epidemiological research and strategic planning for control programmes will also be addressed. The main aim of this study was to determine a parasitic species, prevalence and infection rate in selected fancy birds. We will correlate our data with morphologic findings for different parasite developmental stages, host phylogeny, and overall taxonomic relations within different fancy birds.

09:45

Prof John Ellis, *Professor of Molecular Biology, University of Technology Sydney*
On the importance of validating diagnostic RT-PCR assays for *Dientamoeba fragilis* and other gastrointestinal pathogens of human and veterinary importance *- A15553*

R Gough[2]; **J T Ellis**[2]; J Barratt[2]; J Harkness[1]; D Marriott[1]; D Stark[1];
[1] Department of Microbiology, St Vincent's Hospital, Sydney, Australia; [2] School of Life Sciences, University of Technology Sydney, Australia

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Dientamoeba fragilis is a trichomonad parasite that resides in the human bowel and it remains unclear whether there is a need to diagnose and treat human infections. Patients infected with *D. fragilis* experience a range of symptoms including abdominal pain, diarrhoea, fatigue and flatulence, lasting in some cases for many years. Drug treatment is typically offered to such patients and symptoms normally clear quickly. Microscopy has proved really inefficient as a means of detecting *D. fragilis* in faecal specimens, and so real time PCR methods have emerged as the gold standard methods for diagnosing infections. Despite their use in diagnostic laboratories, there remains the need to ensure these tests are vigorously validated and the EasyScreen™ Enteric Parasite Detection Kit (Genetic Signatures, Sydney, Australia) is arguably the most extensively validated of these tests. We have benchmarked the EasyScreen assay for specificity and sensitivity for both faecal samples from animals and humans and compared it to other commonly used assays. The results show that the EasyScreen assay should be considered the gold standard for real time PCR detection of *D. fragilis* and other gastrointestinal parasites.

10:00

Prof Tim Paget, *Professor of Medical Microbiology, University of Sunderland*
Isolation and characterization of novel reagents using phage display technique for detection of pathogenic *Acanthamoeba - A15634*

K Salman[1]; O Oyeniyi[2]; L Bingle[2]; T A Paget[2];
[1] Sunderland university, UK; [2] University of Sunderland, UK

Background: *Acanthamoeba* is a free-living opportunistic protozoan that can cause serious human infections, the most common being *Acanthamoeba* Keratitis (AK). Early diagnosis and fast treatment are required for good prognosis, however the lack of good tools for rapid identification oftecn cause significant delay in treatment.Current methods of detection involve culture and microscopy. These methods are time consuming, laborious, and open to error. The development of a rapid, simple detection method for *Acanthamoeba* is thus important.
Phage display is a technology that allows the presentation of peptides and proteins including antibody fragments on the surface of filamentous bacteriophage. The genes encoding the variable domains of antibodies (scFv) and a linker are fused to the g3p gene in the genome of the filamentous phage. In our system the scFv is displayed as a fusion to g3p (pIII) protein at the tip of the phage.
The aim of this study is to Isolate antibody fragments that can be used to detect *Acanthamoeba* from clinical samples. It is hoped that these antibodies provide the reagents to establish a specific and rapid detection assay for *Acanthamoeba*.

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Methods: *Sequence analysis of selected clones*: Nine clones identified from earlier experiments were cultured in 2xTY broth containing 100 µg/ml ampicillin and 4 % glucose and incubated overnight at 37°C. The diversity of these clones was determined by PCR screening . Recombinant clones were screened by amplifying the scoff insert using primers LMB (CAGGAAACAGCTATGAC) and fd-SKEQ1 (GAATTTTCTGTATGAGG). and the products sequenced

Screen of clones by soluble ELISA: The same clones that sequenced were used to produce soluble antibody fragments, briefly, each colony was grown at optimal condition until and then induced by adding 1 mM Isopropyl-ß-D-thiogalactopyranoside (IPTG) and further incubated for overnight at 30C and 250 rpm. Cultures were centrifuged and supernatants (soluble fractions) were used in ELISA assay. Binding of soluble scFvs with to *Acanthamoeba* was detected with the HPR-peroxidase and mouse monoclonal antibody 9E10.

Results: All sequenced clones were used to identify framework and complementarity-determining regions (CDRs) in the VH chain, and compare their amino acids sequence to the germ line using BLAST (http://www.ncbi.nlm.nih.gov/BLAST). Nucleotide sequence alignment and homology searches were performed with Clustal Omega software. Although there were some differences in the CDRs amino acids sequence, these clones were 95% identical. ELISA results indicated that the nine selected clones have produced soluble fragments as they showed a high absorbance reading in comparison with control.

Conclusion: From our initial work we have identified 9 clones that show significant binding to Acanthamoeba using ELISA, flow cytometry and fluorescent microscopy.

We believe that these novel reagents are suitable candidates as potential tools for Acanthamoeba diagnosis due to cost effectiveness and ease of production. Such reagents may also have potential for use in targeting therapeutic drugs.

10:15

Dr Vito Colella, *PhD Candidate, University of Bari*

Evaluation of oxfendazole in the treatment of zoonotic *Onchocerca lupi* infection in dogs - *A15684*

V Colella[3]; C Maia[2]; A Pereira[2]; I Scandale[1]; D Otranto[3];

[1] Drugs for Neglected Diseases initiative, Switzerland; [2] Universidade Nova de Lisboa, Portugal; [3] University of Bari, Italy

The genus *Onchocerca* (Spirurida, Onchocercidae) is well known mainly for *Onchocerca volvulus* which is estimated to infect at least 37 million people globally, as well as for including zoonotic species. Among these, *Onchocerca lupi* has been reported in dogs and cats from several European countries and, recently, also in the

U.S. and Canada. In humans, *O. lupi* displays a marked neurotropism and patients require neurosurgical intervention because of nematodes localisation in the cervical spine of infant, children and adults. Though the severe outcomes of the infection in humans and the high prevalence in dogs from endemic countries have been recognised, a proper treatment regime for curing this parasitic infection is lacking, being the surgical removal of the parasitic nodules the therapy of choice in canine patients. Hence, there is an unmet medical need for treatment of this zoonotic disease in both humans and animals. In this study, we evaluated the efficacy of oxfendazole under two treatment regimes in the reduction of ocular lesions and skin-dwelling microfilariae (mfs) of *O. lupi* in naturally infected dogs. Eleven out of the 21 client-owned dogs (21/123; 17.1%) positive for skin-dwelling *O. lupi* mfs, were enrolled in the efficacy study and were treated with oxfendazole (50 mg/kg) per OS once a day for 5 (G2) or 10 (G3) consecutive days or were left untreated (G1). The efficacy of oxfendazole in the reduction of *O. lupi* mfs was evaluated by microfilarial count and by assessing the percentage of mfs reduction and mean microfilaricidal efficacy, whereas the efficacy in the reduction of ocular lesions was evaluated by ultrasound imaging. All dogs were subjected to follow-ups at 30 (D30), 90 (D90) and 180 (D180) days post-treatment. The percentage of reduction of mfs was 78% for G2 and 12.5% for G3 at D180. The mean microfilaricidal efficacy of oxfendazole in the treatment of canine onchocercosis by O. lupi at D30, D90 and D180 was 41%, 81% and 90%, in G2 and 40%, 65% and 70%, in G3, respectively. Retrobulbar lesions did not reduce from D0 to D180 in control group (dogs in G1), whereas all treated dogs (in G2 and G3) had slightly decreased ocular lesions. Percentage of reduction of ocular lesions by ultrasound examination was 50% and 47.5% in G2 and G3 at D180, respectively. Despite the decrease in ocular lesions in all treated dogs, oxfendazole was ineffective in reducing ocular lesions and skin-dwelling *O. lupi* mfs in a six-month follow-up period. In this study, we discuss the need for more reliable diagnostic techniques and efficient treatment protocols to better plan future intervention strategies.

Veterinary Parasitology Symposium - Arthropod Ectoparasites and Vectors sponsored by MSD Animal Health- (Stream 5 - Physics 0.11 A) 14:00 to 15:30

Invited Speaker 14:00 - (30 mins)

Prof Domenico Otranto, *Professor, University of Bari*

Thelazia callipaeda: from oriental to European eyeworm - *A15208*

D Otranto[1];

[1] University of Bari, Italy

Amongst vector borne helminths (VBH), the eyeworm *Thelazia callipaeda* is an emergent zoonotic agent of concern to the public health of several European regions. Adult nematodes live in the orbital cavities and associated host tissues of dogs and cats, foxes, wolves, rabbits and humans, causing ocular disease. One of the

peculiarities of the life cycle of *T. callipaeda* is that its vector, *Phortica variegata*, is a zoophilic fruit fly. Indeed, unlike almost all other arthropod vectors of pathogens, only *P. variegata* males feed on lachrymal secretions of animals, ingesting first-stage larvae (L1). In the vector, larval development through to infective L3 occurs within 14-21 days from experimental infestation; larvae may also survive in overwintering flies (for up to 6 months) before being transmitted to a receptive host. Although *T. callipaeda* has not been reported from the US, *P. variegata* collected in the US can successfully transmit the parasite. At the time when vector identity and biology were elucidated, the infection was confined to remote poor settings in southern Italy; nevertheless, ecological niche models predicted that large areas of Europe (including the United Kingdom) are suitable for the development of the vector, thus highlighting the potential risk of *T. callipaeda* spreading to other European countries. Indeed, whilst *T. callipaeda* had exclusively been reported from easternmost countries until two decades ago, it has now been described in both animals and humans from Italy, France, Switzerland, Germany, Belgium, Spain, Bosnia and Herzegovina, Croatia, Hungary, Serbia, Bulgaria, Romania, and Greece. Thus, this parasite can be considered as an emergent vector-borne pathogen in Europe, and zoonotic infections have been diagnosed on several occasions in European endemic areas. In the UK, the infection has been reported in animals with a history of travel were found positive for *T. callipaeda* and, after ten years since the predictive model was published, a recent updating and re-assessment of that model suggested the presence of suitable conditions for *P. variegata* in previously undocumented regions of the UK, therefore highlighting the possibility for further spread of the infection. Off-label topical administration of ivermectin may result in irritation of the ocular tissues, and it is therefore discouraged in veterinary practice. Milbemycin oxime/praziquantel tablets as well as the imidacloprid 10% and moxidectin 2.5% spot-on formulation have shown to significantly reduce infection rates in naturally infected dogs.

14:30

Mr Babagana Mohammed Adam, *PhD Candidate, University of Salford*
Molecular epidemiology of tick-borne haemoparasites in Nigerian sheep - *A15581*

B Adam[5]; V Lorusso[3]; [4]; M Wijnveld[1]; [2]; K Bown[5]; R Birtles[5];
[1] Centre for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Austria, Austria; [2] Centre for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Austria, UK; [3] Global Research & Medical Division, Vetoquinol, Paris, France, France; [4] Global Research & Medical Division, Vetoquinol, Paris, France, UK; [5] University of Salford Tick Infections (USALTI) Group, School of Environment and Life Sciences, University of Salford, UK

Background: Tick-borne diseases (TBDs) caused by bacteria, rickettsiae and protozoa impose a serious constraint to livestock health and production in sub-Saharan Africa (SSA) including Nigeria. Thus far, research

focusing on TBDs in livestock from SSA in general and Nigeria, in particular, has majorly focused on large ruminants such as cattle with limited attention paid to small ruminants. In Nigeria, diagnosis of TBDs in livestock is essentially based on clinical signs, microscopic examination of blood smears and/or lymph node biopsies and serological methods for the detection of antibodies, with negligible use being made of sensitive molecular tools. The aim of this study was, therefore, to update the existing knowledge on the occurrence of TBDs-causing pathogens of veterinary and zoonotic importance in domestic ruminants from North-Western Nigeria, focusing on the so far more neglected species of sheep.

Methods: In July 2016, 257 whole blood samples were collected from sheep in Kachia grazing reserve Kaduna State, North-Western Nigeria. Detection of TBD-causing microorganisms pathogens was conducted by means of PCR-based reverse line blotting (RLB) targeting a six genera of microorganisms including bacteria (i.e. *Ehrlichia* spp., *Anaplasma* spp., *Rickettsia* spp. and *Bartonella* spp.) and apicomplexan protozoa (*Theileria* spp. and *Babesia* spp.)

Results: 75.1 % (193/257) of sampled animals were found infected, with 21.7% (42/193) of them being positive for single infections and the great majority of them (78.2%, 151/193) being affected by multiple infections. *Theileria equi*-like was the most prevalent microorganism detected (66.3%), followed by *Rickettsia* spp. (20.2%), *Anaplasma centrale* (17.5%), *Theileria velifera* (12.1%), *Theileria* spp. (10.8%), *Ehrlichia* sp.Omatjenne (10.1%), *Ehrlichia/Anaplasma* spp. (10.1 %), *Theileria mutans* (8.9%), *Theileria* sp.MSD4 (5.8%), *Bartonella* spp. (3.1%), *Babesia bovis* (2.7%), *Babesia* spp.(1.25%), *Babesia caballi* (0.45%), *Ehrlichia ruminantium* (0.4%), and *Rickettsia* spp. of the "thypusgroup" (0.4%). Lambs were found significantly less infected than juvenile and adult sheep.

Conclusions: This survey ascertained the presence of haemoparasites of bacterial and parasitic (protozoal) aetiology, of veterinary and medical importance, in sheep from North-Central Nigeria. The rather high infection rates detected for several *Theileria* and *Ehrlichia* spp. and the broad diversity of pathogen species suggests their possible involvement in disease condition and serious production losses, especially when animals are subjected to stress (e.g. in case of drought and/or fodder shortages). The detection of several zoonotic agents (i.e. *Rickettsia* spp. and *Bartonella* spp.) warrants further characterisation.

14:45

Dr John Graham-Brown, *PDRA, Infection Biology, University of Liverpool*

Ecological niche modelling of *Phortica variegata* and the potential for *Thelazia callipaeda* introduction to the UK - *A15643*

J Graham-Brown[3]; J Palfreyman[4]; C Caminade[1]; P Gilmore[5]; D Otranto[2]; D J Williams[3];

[1] Department of Epidemiology and Population Health, Institute of Infection and Global Health, University of Liverpool, UK; [2] Dipartimento di Medicina Veterinaria, University of Bari, Italy, UK; [3] Infection Biology, Institute of

Infection and Global Health, University of Liverpool, UK; [4] Institute of Veterinary Science, University of Liverpool, UK; [5] Liverpool Veterinary Parasitology Diagnostics, University of Liverpool, UK

Male fruitflies of the species *Phortica variegata* (Drosophilidae, Steganinae) are the intermediate host and vector of the zoonotic nematode *Thelazia callipaeda* (Spirurida, Thelaziidae). Whilst not currently endemic, recent evidence suggests a growing threat of *T. callipaeda* to UK animal and public health through infection of animals and humans whilst travelling abroad. Furthermore, presence of *P. variegata* in the UK has been confirmed on multiple occasions suggesting introduction of *T. callipaeda* is possible, although the current geographic distribution of *P. variegata* in the UK is unclear.
Ecological niche models have been used previously to predict the distribution of *P. variegata* in Europe and Italy. These results have been largely validated by the subsequent geographic spread of *T. callipaeda* across mainland Europe. We re-visited this analysis using up-to-date information to predict the current UK distribution of *P. variegata* and determine the likelihood of introducing autochthonous transmission of *T. callipaeda*. Our results suggest *P. variegata* presence in the south of England, including regions where this species has not previously been documented. Subsequent field sampling resulted in recovery of *P. variegata* at two locations, with suitable habitat identified at four others. Our results indicate a risk to the UK of *T. callipaeda* introduction. Surveillance of sylvatic definitive host species in locations with confirmed *P. variegata* presence is advised to monitor for evidence of autochthonous *T. callipaeda* transmission. Further work is planned to validate and improve the accuracy of this UK model through collection of additional field data.

15:00

Dr Swaid Abdullah, *Research Associate, University of Bristol*
The Prevalence and distribution of *Babesia* and *Borrelia* pathogens in ticks infesting domestic dogs in the UK - *A15118*

S Abdullah[3]; C Helps[1]; S Tasker[1]; H Newbury[2]; R Wall[3];
[1] Molecular Diagnostic Unit, Langford Vets and School of Veterinary Sciences, University of Bristol, UK; [2] MSD Animal Health, UK; [3] School of Biological Sciences, University of Bristol, UK

A large-scale survey was undertaken to assess the prevalence and distribution of *Babesia* and *Borrelia* pathogens in ticks infesting domestic dogs in the UK. This involved the recruitment of 1094 veterinary practices over a period of 16 weeks. Participating practices randomly examined 5 dogs for ticks each week and sent a clinical history along with any ticks to the investigators. A total 12,096 dogs were examined during this period. The ticks were

identified to species. The overall prevalence of tick attachment was 30%. The relatively high prevalence may have been inflated by the method of participant recruitment.
For pathogen analysis DNA was extracted from 4,750 ticks collected over the first 13 weeks and were subjected to PCR and sequence analysis to identify *Babesia* and *B. burgdorferi* (s.l.) species. From 4,737 ticks, *B. burgdorferi* (s.l.) was detected in 94 (2.0%). Four *Borrelia* genospecies were identified: *Borrelia garinii* (41.5%), *Borrelia afzelli* (31.9%), *Borrelia burdorferi* (s.s.) (25.5%) and *Borrelia spielmanii* (1.1%). One *Rhipicephalus sanguineus*, from a dog with a travel history outside the UK, was positive for *B. garinii*. Seventy ticks (1.5%) were positive for *Babesia* spp.: 84.3% were *Babesia venatorum*, 10.0% were *Babesia vulpes* sp. nov., 2.9% were *Babesia divergens/capreoli* and 1.4% were *Babesia microti*. One isolate of *Babesia canis* was detected in a *D. reticulatus* tick from a dog that had recently travelled to France. The prevalence of *Babesia* spp.and *B. burgdorferi* (s.l.) did not differ significantly between different regions of the UK. The results map the widespread distribution of *B. burgdorferi* (s.l.) and *Babesia* spp. in ticks in the UK and highlight the potential for the introduction and establishment of exotic ticks and tick borne pathogens.

15:15

Dr Francesca Nunn, *postdoc, Moredun Research Institute*
Optimisation of an on-hen feeding device for all hematophagous life stages of poultry red mite: a tool for mite control evaluation - *A15496*

F Nunn[1], K Bartley[1]; F Turnbull[1]; H Wright[1]; A J Nisbet[1];
[1] Moredun Research Institute, UK

Poultry red mites (prm) are small and highly mobile blood feeding ectoparasites that live off-host, only seeking a bird to rapidly engorge every few days. Prm are therefore difficult to contain in a controlled experimental environment that allows natural feeding on the host and *in vitro* feeding techniques have been previously employed to overcome containment issues (e.g. Mcdevitt *et al*., 2006). The *in vitro* feeding technique for the preliminary screening of prm vaccine candidates in small scale trials was refined by Bartley *et al*., 2015 but has several drawbacks, including a high background mite mortality and a high variability in feeding rates, requiring a technical and experimental replication to overcome this and it requires invasive blood sampling of hens. In addition, previous studies have shown that vaccine efficacy measured using the *in vitro* feeding device is not always translated into mite population reduction in field trials (Bartley *et al*., 2017) leading to false indications of the potential of a vaccine. A prototype 'on-hen' *in vivo* mite feeding device for adult mites was therefore developed as an alternative to the *in vitro* assays for more accurate pre-screening of potential novel interventions before embarking on field studies. This is an important development in reduction and refinement of animals and in keeping with 3r's approaches. The

device consisted of a sealed 250µm aperture mesh pouch containing pre-starved, adult mites. They were applied to the (plucked) skin of the hen's thigh and secured with medical tape and elasticated bandage. Fed adult mites were recovered from the device, enumerated and maintained to monitor mortality and fecundity. This on-hen device resulted in a consistent feeding rate of 50% of adult mites following a 3h feeding period and only a low background mite mortality was observed. Here we describe the optimisation of the feeding device for protonymph, deutonymph and adult life stages. Preliminary studies evaluated three nylon meshes (75µm, 120µm, 125 µm aperture), three polyester meshes (68 µm, 105 µm and 120 µm aperture) and two device designs. The best device and two mesh sizes (105 µm and 120 µm) were further adjusted and evaluated for feeding and survival rates among the three life stages, hen welfare and comfort, mite recovery from the devices. The 105µm provided the best interface for each life stage resulting in a mean feeding rate up to 10% for protonymphs, 26% for deutonymphs and 59% for adults with both aperture size and mesh thickness affecting feeding of the juvenile life stages. The most successful design was employed in a mite conditioning study to maximise feeding rates with an optimised regime of one week at room temperature (rt) and two weeks at 4oc for both adults and protonymphs and one week at room temperature (rt) and one week at 4 Cfor deutonymphs. This device represents a high hen-welfare method of allowing mites to feed on the live host whilst maintaining prm containment and has great potential as a tool to allow feeding of nymph and adult life stages to evaluate systemic prm controls (e.g. Vaccines, systemic acaricides).

References: Bartley K., Wright HW., Huntley JF., Manson ED., Inglis NF., Mclean K., Nath M., Bartley Y., Nisbet AJ. 2015. Identification and evaluation of vaccine candidate antigens from the poultry red mite (Dermanyssus gallinae). Int j parasitol. 45:819-30. Bartley K., Turnbull F, Wright HW., Huntley JF., Palarea-Albaladejo J., Nath M., Nisbet AJ. 2017. Field evaluation of poultry red mite (Dermanyssus gallinae) native and recombinant prototype vaccines. Vet parasitol. 244: 25-34. Mcdevitt R., Nisbet AJ., Huntley JF. 2006. Ability of a proteinase inhibitor mixture to kill poultry red mite, dermanyssus gallinae in an in vitro feeding system.

Veterinary Parasitology Symposium - Livestock Parasitology - (Stream 5 - Physics 0.11 A) 16:15 to 17:45

Chair - Prof Joanne Webster

Invited Speaker 16:15 - (30 mins)

Prof Grace Mulcahy, *UCD Conway*

Back to the drawing board - basic science improving prospects for control of liver fluke in ruminants - *A15195*

G Mulcahy[3]; Y Fu[3]; A Garcia-Campos[3]; L Garza-Cuartero[3]; M Sekiya[3]; S N O'Neill[2]; J P Dalton[1]; T Geurden[4];

[1] Queen's University Belfast, UK; [2] School of Biotechnology, Dublin City University, UK; [3] School of Veterinary

Medicine and Conway Institute, University College Dublin, UK; [4] Veterinary Medicine Research and Development, Zoetis Inc, Belgium

Liver fluke infection - fasciolosis - is one of the problematic conditions where the search for a commercially-viable vaccine still continues. In spite of intensive work over many years by several laboratories, and repeated demonstration as "proof of principal" that partial protection is achievable, significant hurdles remain to be overcome.

These include consistency in achieving protection in repeated trials, as well as variations in fluke burden stemming from both parasite strain differences and host factors. In addition, the "extreme immunoregulation" induced by infection with *Fasciola hepatica* makes achieving vaccine-mediated protection an even tougher target.

Our laboratory has recently therefore "taken a step back", in an attempt to better understand both parasite-mediated immunoregulation and the nature of protective and non-protective immune responses to the parasite in ruminants.

Our approaches have included looking at the host immune transcriptome at acute and chronic stages of infection, examining the differences between vaccine-induced responses and responses to infection, as well as seeking to understand the role of glycans in host-parasite interaction.

Examination of the transciptome of ovine peripheral blood mononuclear cells (PBMC) reveals a large number of differentially-expressed genes at both acute and chronic stages of infection. Pathway analysis of the response sheds light on the suppression of IFN-γ and parasite-specific IgG2 during infection, as well as alteration of macrophage metabolic pathways and activation of death receptors. In contrast, initial analysis of the bovine transcriptome indicates a more muted response during the acute stage of infection, and reflecting the different disease phenotype in sheep vs cattle.

In comparing responses of ruminants to infection (non-protective) and vaccination (partially protective), we have known for some time that high-titre, high-affinity antibody to specific antigens is required for protection, and that a mixed, rather than a skewed Th2/Treg response is required. Extending these studies to the fine-specificity of the response to a target antigen, FhCL1, we have observed areas of this ES protein that may be serving as decoy antigens, and others which are associated with protective responses.

An effective liver fluke vaccine would further animal health and welfare as well as public health. Despite the difficulties inherent in pursuing this goal, we are encouraged that the Back to the Drawing Board approach we have adopted will pave the way for smart vaccines capable of inducing protective responses while neutralizing non-protective elements.

16:45

Dr Laura Peachey, *Research Fellow, University of Cambridge*

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The impact of acute and chronic infections by parasitic helminths on the faecal microbiota of UK Thoroughbred horses - *A15729*

L E Peachey[1]; R A Molena[1]; T P Jenkins[1]; C Cantacessi[1];
[1] University of Cambridge, UK

Increasing evidence supports the occurrence a myriad of interactions between gastrointestinal (GI) helminths and the host gut commensal flora, with likely implications on host local and systemic immunity and metabolic potential. However, thus far, whether parasite-associated changes in the composition of the host gut microbiota are depending on the infection status (acute *versus* chronic) remains unclear. A better understanding of these mechanisms is nonetheless crucial, particularly in livestock species, as this knowledge will represent the basis for the development of novel parasite control methods based on the manipulation of the host gut flora. Therefore, in this study, we assessed the impact of acute and chronic infections by an important group of equine GI helminths (i.e. the cyathostomins) on the faecal microbiota of two cohorts of Thoroughbred (TB) horses from the same stud farm prior to and following treatment with a commonly used anthelmintic (i.e. ivermectin). The first cohort was composed of young-stock (between 12-16 months of age, ‘acute group’), whereas the second cohort was composed of broodmares (between 4 and 18 years of age, ‘chronic group’). Individual faecal samples were collected from all study animals at day 0 and ivermectin was administered immediately after sample collection. Sampling was repeated 2 and 14 days post-anthelmintic treatment. High-throughput sequencing of microbial 16S rRNA amplicons and subsequent bioinformatics and statistical analyses revealed global changes of the faecal microbiota that could be correlated with burden of infection (as estimated by faecal egg counts) in both yearlings and broodmares. For instance, higher infection burdens were associated with reduced microbial alpha diversity in yearlings, whilst the opposite was observed in broodmares. In addition, in yearlings, cyathostomin infection was associated with significant alterations of the relative abundance of major bacterial phyla with roles in carbohydrate and protein metabolism and GI inflammation. Conversely, in broodmares, helminth infection was associated with the expansion of lower level taxa with roles in methane metabolism and fibre digestion. The changes described above were reversed by anthelmintic treatment in the yearlings, but not in the broodmares. Observations from this study support the hypothesis that cyathostomin infection may be associated with dysbiosis in young animals with little acquired immunity to infection. The implications of this acquired knowledge on future studies aimed at reducing the pathology associated with cyathostomin infection via the manipulation of the gut microbiota will be discussed.

16:55

Dr Alison Howell, *PDRA, University of Liverpool*

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The clinical importance of *Fasciola hepatica* infection in horses - *A15600*

A K Howell[1]; F Malalana[1]; J E Hodgkinson[1]; N J Beesley[1]; H Clough[1]; D Archer[1]; D J Williams[1];
[1] University of Liverpool, UK

Fasciola hepatica is recognised as a parasite affecting grazing animals, and reports of clinically affected horses appear in the literature. Our study, which was funded by the Animal Welfare Foundation, aimed to establish the extent of the problem, to assist with diagnosis and ultimately to improve the welfare of horses. Firstly, we undertook a prevalence survey in abattoir horses, with *F. hepatica* infection status determined by both liver inspection and excretory-secretory antibody ELISA. Of 342 horses examined, four (1.1%) were positive for adult flukes in the liver, whilst 26 (7.6%) tested positive on ELISA. Secondly, we conducted a case control study of horses with and without liver disease from the UK horse population, to determine whether *F. hepatica* was a cause of liver disease in horses. Of 277 horses recruited into the study, 17 (6.1%) tested positive for liver fluke on ELISA. Horses with liver disease were significantly more likely to test positive for liver fluke than controls. Thirdly, using flukes (n=123) collected from horses at abattoir, we performed microsatellite analysis. This showed that these flukes were likely to have come from the same population as flukes derived from cattle and sheep. Our results show that *F. hepatica* is causing clinically important morbidity in horses, and should be considered as a differential diagnosis in cases of liver disease in at-risk horses.

17:05

Mr Duncan Wells, *PhD Student, QUB*
Neuropeptide biology in *Fasciola hepatica* - *A15722*

D J Wells[1]; P McVeigh[1]; E McCammick[1]; P McCusker[1]; E Robb[1]; M P Evans[1]; E Gardiner[1]; A Mousley[1]; N J Marks[1]; A G Maule[1];
[1] Queen's University Belfast, UK

Increasing resistance to existing flukicides continues to compromise the sustainable control of liver fluke. New flukicides are needed to suppress the impact of fluke infections in animals and humans. G-protein coupled receptors (GPCRs) are established targets for drugs used in human medicine. Within the GPCR complement of the liver fluke, *Fasciola hepatica*, at least 47 are putative peptide receptors with many of the associated ligands likely to be neuropeptides (npps). Neuropeptidergic-signalling systems are evolutionarily ancient and have been shown to play key roles in a variety of fundamental processes including motility, reproduction and development. Here we report the *in silico* discovery of the putative npp gene complement of *F. hepatica*. Thus far, we have

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identified 37 putative npp genes by using a combination of degenerative search strings involving common npp motifs as well as using reciprocal BLAST searches using previously identified putative npp genes as queries against genomic and transcriptomic datasets. Using the 'new Tuxedo' package (HISAT2, Stringtie and Ballgown), we have assessed the expression of these genes across the intra-mammalian life stages. Further, we have optimised a planarian wholemount in situ protocol for *F. hepatica* and used it to examine the spatial expression patterns of putative neuropeptide-F/Y-like gene transcripts. We show that these have distinct expression patterns suggesting differential functions. Expression and localisation information will be used to underpin functional genomics approaches such as RNA interference (RNAi) to generate functional data and, where possible, ligand-receptor pairings. These will provide impetus to anthelmintic/flukicide discovery efforts.

17:15

Miss Clare Collett, *PhD Student, Aberystwyth University*

Biomarkers of triclabendazole efficacy against *Fasciola hepatica - A15589*

C F Collett[1]; R M Morphew[1]; G Parry[2]; P M Brophy[1];
[1] Aberystwyth University, UK; [2] Hybu Cig Cymru Meat Promotion Wales, UK

The liver fluke, *Fasciola hepatica*, is a zoonotic, food borne parasite and growing threat to global food security and public health. Current fasciolosis diagnosis is confined to complex laboratory methods, with no penside options for the farmer towards infection intensity or drug efficacy determination. In the absence of fluke vaccines, disease management relies on triclabendazole (TCBZ) despite widespread TCBZ resistance (TCBZ-R), as it is the only flukicidal compound active against pathogenic juveniles and long-lived adult flukes. There is mounting pressure to develop rapid diagnostics to measure fluke presence and drug efficacy. To this end, we have progressed with the discovery of a panel of TCBZ-associated secreted biomarker candidates. *In vitro* TBCZ response phenotypes and non-specific fitness-associated markers have been characterised and the recombinant expression in progress for eight diagnostic contenders for infection identification, post-TCBZ fluke survival (TCBZ-R) and successful TCBZ-specific treatment. Cathepsin L proteases are robust indicators of fluke presence, whereas inactive cathepsin L zymogens are conversely untapped biomarkers for fluke death and drug efficacy diagnoses, whereby they are non-specifically released by TCBZ-exposed susceptible adult flukes. Other candidates of the TCBZ-associated diagnostic phenotypes include survival proteins: calreticulin, enolase and glyceraldehyde-3-phosphate dehydrogenase; and susceptibility proteins: actin, deglycase DJ-1, gelsolin and triose phosphate isomerase. Recent developments in the biomarker validation pipeline shall be presented, reporting the progress of this broad panel of fluke and TCBZ efficacy diagnostic candidates.

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17:25

Miss Katie Hildersley, *PhD Student, Moredun Research Institute*
Examining the presence and function of tuft cells in ovine abomasum tissue following parasitic nematode infection - *A15660*

K Hildersley
[1] Moredun Research institute, UK

There is increasing interest in tuft cells due to their proposed function in sensing environmental changes in the gut lumen, and in initiating the Type 2 T helper (Th2) immune response to gastro-intestinal parasite infections in mice. Specific tuft cell markers have been identified and have demonstrated the expansion of tuft cells over the course of an infection, as part of a ‘feed-forward loop’ with Group 2 Innate Lymphoid Cells (ILC2). The aim of this project was to determine whether murine tuft cell markers were also expressed in the abomasum epithelium of sheep and if so, whether an expansion of the cells expressing these markers was observed during infection with the ovine gastro-intestinal nematode *Teladorsagia circumcinta*. Antibodies to the murine tuft cell markers POU2F3, Gfi1b, DCLK-1 and TRPM5 were evaluated using immunohistochemistry techniques on ovine tissues. Anti-POU2F3 and anti-Gfi1b were found to give a strong specific signal on putative tuft cells throughout the gastro-intestinal tract. The percentages of POU2F3+ epithelial cells in the ovine abomasum over the course of a *T. circumcinta* infection showed similar increases to those seen in the mouse, suggesting that the POU2F3+ cells in the ovine abomasum are tuft cells. In addition, we have identified a high number of POU2F3+ cells in abomasal epithelium tissue of sheep infected with the related nematode *Haemonchus contortus.* Further investigations are underway to assess the specificity of anti-DCLK-1 and anti-TRPM5 for putative ovine tuft cells, and to determine whether all putative ovine tuft cells express the same markers. This project has taken the first steps in identifying markers of ovine tuft cells, enabling further investigation of the importance of these cells in the ovine Th2 response to parasitic nematode infections.

Public Understanding of Science Session

Public Engagement with Science - (Stream 2 - Llandinam A6) 09:00 to 10:30

Invited Speaker 09:00 - (30 mins)

Prof Sheena Cruickshank, *Professor of public engagement and biomedical sciences, University of Manchester*
From parasites to public engagement and impact - *A15152*

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S Cruickshank[1];
[1] University of Manchester, UK

Public engagement describes the many ways in which our research and knowledge is shared with the public. Importantly engagement is a two-way, interactive process of listening to others - regardless of whether we aim to inspire, consult, or collaborate with the public - our overall purpose is to generate mutual benefit. For researchers there are many benefits of public engagement including: expanding our awareness through debating and discussing our work; reflecting on our approach to research and developing new avenues and opportunities; acquiring alternative sources of funding; improving our communication skills; and reinvigorating our enthusiasm for our research. But with the competing pressures for our time, how can we do quality public engagement and can our engagement contribute to the "impact" agenda? Along with my research group, I have spent more than 10 years developing public engagement tools and resources for work around parasitology and immunology. For example, we created a mobile resource called the Worm Wagon to explore our research into parasitic worm infections with community groups and have we used a variety of approaches including sci-art, participative workshops, and citizen science. In this talk I will share the successes and challenges of my public engagement work and provide some top tips for developing effective and impactful public engagement with research.

09:30 - (20 mins) *Ticks: getting the bite right* (Richard Wall)
10 :00- (20 mins) *The challenge of Malaria* (Paul Horrocks)

Protozoa Sessions

Protozoa: Cell Biology & Immunology II - Ponsored by William Powell - (Stream 2 - Llandinam A6) 14:00 to 15:30

Invited Speaker 14:00 - (30 mins)

Dr Volker Heussler, *Bern University*
Host cell cytosolic immune response during *Plasmodium* liver stage development - *A15200*

V Heussler [1]
[1] Bern University, Switzerland

Plasmodium parasites are the causative agent of malaria and are transmitted by *Anopheles* mosquitoes. Before the clinically relevant blood stage, the parasites infect hepatocytes where they reside in a special compartment called parasitophorous vacuole (PV). We use the rodent malaria model parasite *Plasmodium berghei* to investigate

the liver stage. A host cell autophagy-related process plays an important role in the control of liver stage *Plasmodium* parasites. Previously, we have shown that autophagy markers, like LC3, localise to the PV membrane (PVM) in early liver stages. It has been found that viable parasites can exclude LC3 from the PVM by membrane shedding. To prove membrane shedding by biophysical means, we expressed parasite and host cell PVM proteins tagged with photo-convertible fluorescent proteins and analyse their localization before and after photo-conversion. Intravital imaging of mice infected with fluorescent *P. berghei* parasites support these *in vitro* obtained data.

Invited Speaker 14:30 - (30 mins)

Dr Tony Holder, *Senior Group Leader, The Francis Crick Institute*

Malaria parasite cycling: in and out of erythrocytes - *A15890*

A A Holder[1]

[1]The Francis Crick Institute, London, UK

The malaria parasite's cycle of replication and proliferation in the asexual blood stage of the life cycle alternates between intracellular and extracellular phases, with the extracellular merozoite being very short lived. Each cycle, the parasite has to elaborate and assemble a new food vacuole and all the subcellular structures necessary for merozoite invasion of an erythrocyte as well as discarding or disassembling them once their function has been fulfilled. Whilst we know quite a bit about the importance of gene expression in these processes, the role of protein modification and degradation is less well understood. The transition from schizont to merozoite is accompanied by extensive protein phosphorylation and ubiquitylation. We suggest that phosphorylation provides a rapid and dynamic way to control protein function and that ubiquitylation prepares merozoite proteins for rapid degradation once their function is completed, enabling reuse of scarce resources in the early intracellular parasite.

15:00

Dr Clare Hamilton, *Research Scientist, Moredun Research Institute*

Comparative pathogenicity of Brazilian, Caribbean and European isolates of *Toxoplasma gondii* - *A15645*

C M Hamilton[1]; L Black[1]; S Oliveira[3]; A Burrells[1]; P M Bartley[1]; F Chianini[1]; E A Innes[1]; P J Kelly[2]; F Katzer[1];

[1] Moredun Research institute, UK; [2] Ross University School of Veterinary Medicine, United States; [3] Universidade de São Paulo, Brazil

Toxoplasma gondii is a ubiquitous protozoan parasite capable of infecting all warm-blooded animals, including humans. Disease outcome can vary depending on a number of factors, including genetic diversity of the infecting

strain. The aim of this study was to investigate the pathogenicity of eight genotypically distinct isolates of *T. gondii*. Eight groups of 15 Swiss Webster mice were inoculated intraperitoneally with 200 *T. gondii* tachyzoites (one isolate per group) &hypen; six were atypical isolates previously isolated from free-roaming chickens in St. Kitts (Caribbean), one isolate was the Type II Moredun strain (M4) and one isolate was an atypical Brazilian strain (Brl). Mice were monitored for signs of toxoplasmosis and euthanized when they reached a defined end point or at 4 weeks post-infection. Percentage mortality was recorded for 10 mice per group, and 5 mice per group were euthanized at day 8 p.i. and tissues were collected for parasite quantification, histopathology and RNA extraction and quantification of cytokines. Three of the isolates were acutely virulent for mice (100% mortality), 3 isolates were moderately virulent (30-70% mortality) and 2 isolates were non-virulent (0-20% mortality). The acutely virulent and moderately virulent strains had Type I and Type III ROP5 alleles, respectively, which are associated with virulence. Mice infected with acutely virulent isolates had significantly higher levels of parasite DNA in their lungs at day 8 p.i., and also had more severe pathology.

15:15

Miss Nana Efua Andoh,
Cancelled

Protozoa: Cell Biology & Immunology III - Sponsored by Life Sciences Research Network Wales- (Stream 2 - Llandinam A6) 16:15 to 17:45

Invited Speaker 16:15 - (30 mins)

Mr Miguel Prudencio, *Group Leader, IMM Lisboa*
Pre-clinical and early clinical evaluation of a *Plasmodium berghei* sporozoite-based malaria vaccine - *A15201*

A M Mendes[1]; M Machado[2]; N Gonçalves-Rosa[2]; I Reuling[2]; L Foquet[2]; C Marques[2]; A M Salman[2]; A S Yang[2]; C C Hermsen[2]; B Jiménez-Díaz[2]; S Viera[2]; \ M Santos[2]; I Albuquerque[2]; S N Bhatia[2]; I Angulo-Barturen[2]; G Leroux-Roels[2]; C J Janse[2]; S M Khan[2]; M M Mota[2]; R W Sauerwein[2]; **M Prudencio**[2];
[1] IMM Lisbo, Portugal; [2] IMM Lisboa, Portugal

There is a pressing need for safe and highly effective *Plasmodium falciparum* (Pf) malaria vaccines. The circumsporozoite protein (CS), expressed on sporozoites and during early hepatic stages, is a leading target vaccine candidate and a crucial protective antigen in whole-sporozoite malaria vaccination. We describe a novel

malaria vaccination platform using transgenic sporozoites of rodent *P. berghei* (Pb) parasites for expression and delivery of PfCS (PbVac). We show that both wild-type Pb and PbVac sporozoites unabatedly infect and develop in human hepatocytes while unable to establish an infection in human red blood cells. In a rabbit model, similarly susceptible to Pb hepatic but not blood infection, we show that PbVac elicits cross-species cellular immune responses and PfCS-specific antibodies that efficiently inhibit Pf sporozoite liver invasion in human hepatocytes and in mice with humanized livers. Thus, PbVac is safe and induces functional immune responses in preclinical studies. An extensive pre-clinical assessment of PbVac's safety was conducted, warranting the evaluation of this vaccine candidate in a first-in-human study. Early results from this ongoing Phase I/IIa clinical trial will also be presented.

Invited Speaker 16:45 - (30 mins)

Prof Peter Preiser, *Director of NTU Integrated Medical, Biological & Environmental Life Sciences (NIMBELS), Nanyang Technological University*

Differential location and interactions of PfRH1 processing products during merozoite invasion - *A15211*

P Preiser[1]; A X Gao[1]; K Gunalan1[2]; S L Yap[1];

[1] Division of Molecular Genetics & Cell Biology, School of Biological Sciences, Nanyang Technological University, Singapore; [2] Laboratory of Malaria and Vector Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, United States

Invasion of the host red blood cell by the merozoite is a complex process involving a range of parasite ligand - host receptor interactions. The reticulocyte binding like protein homologues (RH) of *Plasmodium falciparum* play a critical role in host cell recognition and parasite signaling events during invasion. Along with all other RH proteins PfRH1 is extensively and sequentially processed during maturation and merozoite release. We have generated a panel of monoclonal antibodies against different regions of PfRH1 to investigate the fate of the different processing fragments during merozoite maturation and invasion. Using a combination of Immunofluorescents assays (IFA), Proximity Ligation Assays (PLA) and Fluorescence Resonance Energy Transfer (FRET) by acceptor bleaching we are able to establish protein co-localization data at the low nanometer scale. We obtain clear evidence that the different PfRH1 processing products interact with different parasite proteins during invasion. In particular we can demonstrate that a specific part of PfRH1 interact with AMA1 but note EBA175 in the junction of invading merozoites. Interestingly, we can obtain no evidence that EBA175 and AMA1 co-localize at any time in merozoites or during the invasion process. Taken together our data provides first clues on the biological role of RH protein processing during invasion.

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17:15

Dr Janet Storm, *PDRA, Liverpool School of Tropical Medicine*

Plasmodium falciparum infected erythrocytes from cerebral malaria cases bind preferentially to brain microvascular endothelium; a study in Malawian children - *A15616*

J Storm[4]; J Jespersen[2]; K Seydel[1]; T Szestak[4]; M Mbewe[5]; N Chisala [5]; P Phula[5]; C Wang[2]; T Taylor[1]; C Moxon[3]; T Lavstsen[2]; A Craig[4];

[1] Blantyre Malaria Project, College of Medicine, University of Malawi, Malawi; [2] Centre for Medical Parasitology, University of Copenhagen, Denmark; [3] Institute of Infection and Global Health, University of Liverpool, UK; [4] Liverpool School of Tropical Medicine, UK; [5] Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Malawi

Cerebral malaria (CM) is one of the manifestations of severe malaria and a major cause of death in children in Sub-Saharan Africa. CM is characterised by a *Plasmodium falciparum* infection and unarousable coma and brain swelling in children is strongly associated with fatal outcome. Post mortem studies have shown an association between brain haemorrhages and sequestration of *P. falciparum* infected erythrocytes (IE) to microvascular endothelium in the brain. The mechanisms linking IE sequestration to the development of CM are not fully understood, but it is clear that both host and parasite factors play important roles. The major mediator of parasite adhesion is *P. falciparum* erythrocyte membrane protein 1 (PfEMP1), a variant surface antigen expressed on the IE surface. Specific PfEMP1 variants have been identified in children with CM and show binding to receptors expressed on brain microvascular endothelial cells (MEC), such as endothelial protein C receptor (EPCR) and Intercellular Adhesion Molecule 1 (ICAM-1).

It remains unclear why a child develops CM at a particular time, as the vast majority of *P. falciparum* infections do not lead to CM. We investigated if the pathogenesis of CM is driven by parasite variants that preferentially bind brain MEC and thereby increase the recruitment of IE to the brain. We determined the cytoadherence properties of IE from children with CM, using the IE of children with uncomplicated malaria (UM) as comparator. In addition, associations between the binding phenotype and the expression of particular PfEMP1 variants with binding to the putative receptors EPCR, ICAM-1 and CD36 were assessed. During 3 malaria seasons in Malawi, IE were obtained from carefully characterised paediatric CM and UM cases. The IE were used with minimal *in vitro* expansion, to retain the PfEMP1 variant expressed, and binding to primary MEC, derived from brain or dermis, was determined using a micro-channel flow adhesion assay. Inhibitory antibodies and recombinant protein were used to assess the differential role of receptors and *var* transcripts were identified by qPCR and associated with binding phenotype.

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The data, for the first time, provide direct evidence of preferentially binding of IE from CM patients to brain MEC. This binding is associated with specific PfEMP1 variants expressed, and provides a mechanism by which increased sequestration in the brain leads to CM.

17:30

Ms Rebeca Santano, *PhD student, Barcelona Institute for Global Health*

IgG and IgE responses to *Plasmodium falciparum* and intestinal parasites antigens in Mozambican children - *A15915*

R Santano[1]; F Góngora[1]; I Cuamba[2]; M Vidal[1]; B Grau[1]; R Aguilar[1]; C Jairoce[2]; J Muñoz[1]; A Nhabomba[2]; G Moncunill[1]; C Dobaño[1];
[1] Barcelona Institute for Global Health, Spain; [2] Centro de Investigação em Saúde da Manhiça (CISM), Mozambique

Exposure to multiple parasites in African children leads to harboring two or more simultaneous infections, which can generate immune responses with different profiles that may impair the ability of the immune system to fight one of the coexisting pathogens. Intestinal parasites mainly induce T_H2 (and IgE) responses, whereas immunity to *Plasmodium falciparum* is acquired through a T_H1 (and IgG) profile. We have previously found that T_H2 cytokines are associated with lack of protection of the antimalarial vaccine RTS,S and that CSP, the main component of RTS,S, and MSP-2, a *P. falciparum* blood stage antigen, induce elevated levels of IgE. In the case of MSP-2, high IgE levels are associated with the development of malaria. We hypothesize that the induction of T_H2 cytokines and specific IgE against *P. falciparum* antigens is due to an immune deviation caused by previous or current infections with intestinal parasites. In order to investigate the possible role of parasite co-infections on immune deviation, multiplex suspension array technology with a panel of antigens of *P. falciparum* (AMA_1, EXP-1, EB - - A140, LSA-1, MSP-1, MSP-2, MSP-5), *Giardia lamblia* (VSP_3) and *Cryptosporidium parvum* (Cp_{17}) was used to measure the levels of IgG and IgG_{1-4} in Mozambican children between 2 and 10 years old, for which their infection status for malaria and intestinal helminths and protozoa was known. We will present results on the influence of intestinal parasites on the response to malaria antigens in terms of IgG and its subclasses. We have observed a tendency to have reduced antibody levels in the co-infections groups in comparison with single infection with malaria for most antigens. Future studies will increase the sample size of helminthic gut infections and malaria groups. Ongoing analyses include IgE assessment with an expanded panel including helminth antigens and in samples from malaria vaccine studies and severe malaria studies.

17:45

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Dr Parul Sharma, *Student, University of Nottingham*
Magnitude of the inflammatory response to parasite infection differentiates calf and adult bovine monocytes - *A15551*

P Sharma[2]; S Egan[2]; R Flynn[1];
[1] University of Liverpool/ Institute of Infection and Global Health/ Department of Infection Biology, UK; [2] University of Nottingham, UK

Monocytes are pivotal due to the links they form between the innate and adaptive immune response and are one of the first immune cells encountered by intra-cellular parasites during infection. Our previous data confirmed that neonatal monocytes have a higher level of secretion of IL-1β and TNF-α in response to LPS, IFN-γ and Alum, than adult derived monocytes. Here, we attempted to resolve if this age related difference was maintained in the context of *in-vitro* infection with *Neospora caninum* infection.
N. caninum (NCLiv-1) was maintained in VERO cell lines and purified CFSE labelled parasites used to infect naïve $CD14^{+}$cells which were purified by magnetic cell separation. The number of parasitized monocytes was determined after infection or co-culture with autologous NK-cells culture. CD80 expression was determined as a marker of cellular activation, by flow cytometry. These results reveal a greater reduction of parasitaemia in neonates with higher levels of IL-1β and IL-6 during *N. caninum* infection compared to adult cattle. Neonatal NK-cells also display enhanced cytotoxic activity, measured through perforin and granzyme production after co-culture with *N. caninum* infected monocytes. Complementary gene array analysis was also performed which suggests that during infection, neonates have a greater magnitude of response and a more complex network of upregulated genes are altered. Overall our comparisons show that there is a fundamental difference in the steady-state and in the response to intracellular parasite infection in neonatal monocyte led inflammatory responses.

Helminth Sessions

Helminths: Immuno-modulation - (Stream 3 - Physics 0.15 Main) 09:00 to 10:30

Invited Speaker 09:00 - (30 mins)

Prof Maria Yazdanbakhsh, *Leiden University Medical Center*
Helminths and other environmental factors shaping the immune response: consequences - *A15205*

M Yazdanbakhsh[1];
[1] Leiden University Medical Center, Netherlands

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Intense exposure to microorganisms and parasites changes the immunological landscape. Using mass cytometry, which allows the characterization of the peripheral blood mononuclear cells by more than 35 antibodies, it has been possible to show that not only large differences exist in the adaptive immune system but also the innate immune cells are affected profoundly in rural areas of the developing world. The consequences of such differences in "normal immunological profile" that is seen in areas where exposure to microorganisms and parasites is high is thought to result in lower prevalence of disorders such as allergies and diabetes, but at the same time might contribute to poorer responses to certain vaccines. Focusing on helminth infections, which skew immune responses towards Th2 and lead to increase in regulatory immune cells, it has been possible to show a negative association between helminths and allergic response to environmental allergens. More recently, elegant studies in murine models have indicated that Th2 and regulatory responses are important for control of insulin sensitivity and helminth infected animals are protected against the development of insulin resistance. Population studies and clinical trials conducted in areas where helminth infections are highly prevalent have shown a negative association between helminths and insulin resistance. Currently, helminth derived antigens are being identified that can replicate the effect seen by the whole parasite on glucose metabolism. Such compounds, acting via the immune system or directly on tissues can form the basis of novel therapeutics for a number of inflammatory disease. However, the specificity of their effect will have to be engineered so that detrimental effects such as attenuation of vaccine responses are circumvented.

Invited Speaker 09:30 - (15 mins)

Prof Mike Doenhoff, *Associated member of staff, University of Nottingham*

Antigenic cross-reactivity between *Schistosoma mansoni* and allergens: a possible alternative explanation for the hygiene hypothesis - *A15186*

M Doenhoff[1]

[1] University of Nottingham, UK

Allergies and other disorders of the immune system have recently increased markedly, particularly in economically advanced countries. The 'hygiene hypothesis' ascribes this to reduced exposure to microbial and parasitic infections and consistent with this, some people with helminth infections are protected against allergic disorders. It has been known for some time that glycoproteins of invertebrates and plants are antigenically cross-reactive due to their carrying carbohydrate epitopes in common (cross-reactive carbohydrate determinants - CCDs). In preliminary experiments we found that rabbit IgG antibodies raised against *Schistosoma mansoni* egg antigens reacted in

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Western immunoblots with a wide range of molecules in different plants and invertebrates known to be causes of allergy. We have investigated this antigenic cross-reactivity with respect to: (i) determining whether the rabbit anti-*S. mansoni* antibodies cross-reacted with known allergens in the plant and invertebrate extracts; and (ii) determining which *S. mansoni* egg antigens may have induced the allergen cross-reactive antibodies. Allergen molecules which have been found to be reactive in immunoblots with rabbit anti-*S. mansoni* antibodies include: Hev b 7 in rubber latex, Ara h 1 in peanut, 5 different known allergens in Timothy grass and birch tree pollens, Der f 15 from the house dust mite *Dermatophagoides farinae*, a Per a 3 homologue from cockroach and honey bee venom phospholipase A. The rabbit IgG antibodies reactive with the above-mentioned allergens were purified by elution from immunoblotted allergen using low pH buffer. These acid-eluted antibodies reacted with three immunodominant *S. mansoni* egg antigens IPSE/alpha-1, omega-1 and kappa-5 (though the reactivity with IPSE/alpha-1 may be due to its ability to complex non-immunologically with immunoglobulins). If the results are substantiated with similar observations using sera from schistosome-infected humans, they may offer an explanation for the hygiene hypothesis in terms of schistosome-induced IgG anti-CCD antibodies 'blocking' the reactivity of allergenic IgE antibodies

09:45

Dr Maria Adelaida Duque-Correa, *NC3Rs Fellow, Wellcome Sanger Institute*
Unravelling early host intestinal epithelia interactions with whipworms using intestinal organoids - *A15781*

M A Duque-Correa[2]; F Schreiber[2]; A Roustant[2]; T Mkandawire[2]; D A Goulding[2]; R K Grencis[1]; M Berriman[2];
[1] University of Manchester, UK; [2] Wellcome Sanger Institute, UK

Whipworms *(Trichuris trichiura)* are soil-transmitted helminths and the etiologic agent of the human disease, trichuriasis. Whipworms live preferentially in the caecum of their hosts where they tunnel through epithelial cells and cause inflammation potentially resulting in colitis. Despite extensive research, the early whipworm interactions with host intestinal epithelial cells (IECs) determining parasite establishment or expulsion remain unclear. Here, we investigate novel interactions of whipworms with the host IECs during the first events of infection. Imaging caecum of *T. muris* -infected mice (a mouse model of *T. trichuira* infection in humans) after three hours, one day and three days post infection has revealed whipworm larvae (L1) infecting the epithelium at the base of the crypts of the intestine of mice. These images suggest a close interaction between the L1 larvae and the host goblet cells. Based on these data, we hypothesize that targeted infection of goblet cells by L1 larvae can support parasite growth and establishment in the host, potentially by the degradation of mucus. To further understand this critical early colonisation event, we are using intestinal organoids as a replacement model of the murine infections that are

currently used. Organoids are a novel *in vitro* system generated from human and mouse primary tissues and recapitulating their architecture and cellular composition. Intestinal organoids are three-dimensional cell clusters generated from gut tissue showing similar characteristics and function to the gut. Thus far, we have developed and established protocols for generating and differentiating intestinal organoids, derived from either mouse caecum or human inducible pluripotent stem cells; hatching *T. muris* and *T. trichiura* eggs; and microinjecting organoids with *T. muris* and *T. trichuira* L1 larvae. Using whipworm-infected organoids, we are performing microscopy studies to identify the intestinal epithelial cell type targeted by the whipworm and visualise active infection. Moreover, we are performing transcriptomic experiments and planning proteomic, flow cytometry and cytokine analysis to discover host IECs-whipworm interactions and evaluate IECs responses to whipworm larvae infection.

10:00

Miss Rebecca Oettle, *PhD Student, University of Cambridge*
Antigenic targets of IgG1-associated anti-fecundity immunity against *Schistosoma haematobium* - *A15384*

R C Oettle[3]; I W Chalmers[1]; M Sacko[2]; S Wilson[3];
[1] Aberystwyth University - IBERS, UK; [2] Institut National de Recherche en Santé Publique, Mali; [3] University of Cambridge, UK

Schistosomiasis is a parasitic disease resulting from trematode worm infection. *Schistosoma haematobium* is the most prevalent causative organism, representing 112 million infections, the majority of which occur in sub-Saharan Africa. Severe morbidity results from immunopathogenic responses to eggs laid by adult worms. Sequelae include haematuria, squamous cell carcinoma of the bladder and female genital schistosomiasis, the latter being associated with an increased risk of human immunodeficiency virus (HIV) infection.
Significant progress has been made towards the control of schistosomiasis through mass annual preventative chemotherapy with praziquantel, however praziquantel does not prevent the frequent reinfection that results from ongoing exposure. Individuals therefore remain at risk of accumulating high worm burdens and tissue damage associated with eggs produced by mature female worms. There is therefore an ongoing need for research into alternative means of disease control.
Vaccines offer one conceivable solution since there is emerging evidence for slow acquisition of natural immunity to schistosomiasis. *S. haematobium* transmission is understood to be governed by immunity to reinfection (evidenced in all three species of schistosomes important to human health) and additionally, by a second means of immunity that modulates the number of eggs that mature female worms lay, known as worm fecundity. This immunity is also exhibited in closely-related schistosome infections of veterinary importance.

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It has been demonstrated in a Malian cohort that the development of anti-fecundity immunity is associated with an IgG1 immune response. In the absence of a published protein microarray for *S. haematobium*, we used a conventional proteomic approach to explore the antigen recognition profile of IgG1 in this previously characterised cohort of individuals from Mali, known to have high levels of infection intensity.
2D-Western blots were probed with sera from individuals from the cohort who demonstrate reduced egg to worm ratios, suggestive of reduced female worm fecundity. Proteins spots that were identified as differentially immunoreactive to the sera of cases compared to matched controls were subsequently sent for MS analysis. A review of associated literature and bioinformatic analysis was performed on those significant protein identifications. Antigens that have previously been identified as having vaccine potential were identified, including 28kDa glutathione-S transferase, in addition to a number of proteins previously uncharacterised. The majority of proteins identified were cytosolic and a number had previously been identified as present in the tegument, extracellular vesicles or excretory/secretory products of schistosomes. Functional analysis indicated significant enrichment of proteins associated with energy metabolism, protein folding and reproductive processes.

10:15

Dr Stephen Cross, *PDRA, Liverpool school of tropical medicine*
Infection-state independent moderation of Th2 inflammation and inflammatory-associated lymphatic remodelling by tetracyclines in pre-clinical lymphatic filariasis pathology models - *A15702*

S D Cross[1]; J Furlong-Silva[1]; A Fanthome[1]; H Tyrer[1]; J Archer[1]; A Steven[1]; D Cook[1]; M Taylor[1]; J Turner[1];
[1] Liverpool School of Tropical Medicine, UK

Lymphatic filariasis (elephantiasis) is the third major cause of global disability and the number one causative agent of non-hereditary lymphoedema (LE). An anti-morbidity effect of the second-generation tetracycline, doxycycline (DOX), has been promoted in filarial lymphoedema which is disassociated from active filarial infection, anti-*Wolbachia* activity or more broad-spectrum antibiotic effects. Here, we utilise *in vitro* and in vivo preclinical models of human filarial infection and vascular remodelling to interrogate the direct anti-lymphangiogenic effects of treatment with DOX or the related second-generation tetracycline, minocycline (MIN).
Two weeks following subcutaneous hind-limb infections of *B. malayi* infectious stage (L3) larvae, extensive lymphatic remodelling in limb superficial dermal lymphatic system could be visualised using intra-vital Near Infra-Red optical bioimaging. Further, impaired lymphatic drainage/back-flow from the site of infection was evident by Evans Blue dermal retention. Significant increases in vascular endothelial growth factor (VEGF)C was detectable in circulation following infection. In mice receiving human dose bioequivalent DOX (40mg/kg bid) for two weeks co-incident with infection, the extent of aberrant lymphatic remodelling and impaired lymphatic function were reduced.

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This ameliorating effect on lymphatic pathology was not due to anti-*Wolbachia* efficacy of DOX because larval recovery rates were similar between DOX and vehicle treated animals at 2 weeks and TLR6-/- mice deficient in the *Wolbachia* innate inflammatory pathway exhibited a similar degree of remodelling and lymphatic insufficiency. Further, evidence against an 'off-target', broad spectrum anti-microbial effect of DOX in modifying pathology was evident by observing a similar degree of lymphatic pathology in vehicle and oral amoxicillin (dose) treated mice. We explored a direct mechanism of tetracyclines attenuating lymphangiogenesis using longitudinal *in vitro* human endothelial cell imaging. We determined that DOX and MIN are effective inhibitors of VEGFA or C-induced endothelial cell proliferation. This effect was more selective for lymphatic endothelial cells versus blood endothelial cells and was dose dependent with effects manifest after concentration exposures 6 micromolar. Preliminary data indicates at these dosages, DOX interferes with intracellular calcium levels, suggesting a calcium-binding anti-proliferative mode-of-action.

Helminths: Drug Discovery & Resistance II - Sponsored by Life Sciences Research Network Wales - (Stream 3 - Physics 0.15 Main) 16:15 to 18:00

Invited Speaker 16:15 - (30 mins)

Prof Jane Hodgkinson, *Professor of Molecular Veterinary Parasitology, UOL*

Genetic and molecular basis of triclabendazole resistance in *Fasciola hepatica- A15175*

J Hodgkinson[1];
[1] University of Liverpool, UK

The liver fluke, *Fasciola hepatica*, has a substantial impact on the health and welfare of livestock, particularly cattle and sheep and is recognised by WHO as an important zoonosis. With predictions for further increases in prevalence due to a changing climate, increased animal movement and changes in land management *F. hepatica* infection is set to have a greater impact on livestock productivity and human health in future. This is compounded by the problem of triclabendazole (TCBZ) resistance, the only drug to target the highly pathogenic juvenile fluke migrating through the liver.
This paper will report a series of studies we have taken to better understand the genetic basis of TCBZ resistance in *F. hepatica*. We have used single miracidial:snail infections of *F. hepatica* to generate and characterise clonal parental lines of TCBZ-resistant (TCBZ-R) and TCBZ-susceptible (TCBZ-S) liver fluke. These parental clones have been used to generate a cross between TCBZ-R and –S parasites and, given that *F. hepatica* is hermaphrodite, a panel of neutral microsatellite markers was used to track those F1 parasites that undergone cross fertilization. By comparing the frequency of SNP alleles derived from the resistant parental clone and linked to the TCBZ

resistance loci in pooled, phenotyped F2 recombinants we have localised six regions of the genome under selection. Using a sequence capture approach we have identified SNP markers in loci under selection and we are currently genotyping ~750 F2 liver fluke to establish if TCBZ resistance is a dominant or recessive trait. In addition this work will highlight our enhanced *F. hepatica* genome draft, our work to generate a genetic linkage map and our plans to finer-scale map resistance loci using field isolates.

16:45

Miss Amy Marriott, *PhD Student, Liverpool School of Tropical Medicine*

Development of a long-term *Brugia malayi* lymphatic endothelial cell co-culture system and its validation as an alternative to *in vivo* screening for anti-*Wolbachia* drug assessment - *A15556*

A E Marriott[1]; J Archer[1]; A Steven[1]; M J Taylor[1]; J D Turner[1];
[1] Liverpool School of Tropical Medicine, UK

Filarial parasites are the causative agents of lymphatic filariasis (LF) and onchocerciasis. Current elimination programmes rely on up to 12 annual mass drug administrations with standard anti-filarial drugs which target the microfilarial (mf) stage of infection. There is therefore a need to identify new short-course curative drugs (macrofilaricides) in order to accelerate elimination time frames. A promising drug target is the filarial endosymbiotic bacteria, *Wolbachia*, which can be depleted with antibiotics to initiate blockade of embryogenesis, permanent sterilisation and slow, safe killing of adult parasites.
Reproductively active adult female parasites have a limited life-span in culture, therefore filarial drug screens assessing both *Wolbachia* depletion and blockade of embryogenesis rely on *in vivo* models. Here, we have developed a long term *in vitro* co-culture system to maintain adult female stages of the human lymphatic filariae, *Brugia malayi,* using primary human lymphatic endothelial cells (LEC).
We examined motility and survival (n 12), uterine release (n 6), metabolic activity (n 10) and *Wolbachia* titres (n 10) of 3-6 month old mature female *B. malayi* following aseptic isolation from infected immunodeficient mice and cultured over periods up to 28 days. Readouts were compared against freshly isolated *ex vivo B. malayi* or human embryonic kidney (HEK) cell monolayer co-cultures as non-specific feeder cells. When cultured on LEC monolayers, female *B. malayi* retained full motility on average for 14 days. This compared with 8 days for corresponding cell-free LEC culture medium or HEK monolayers. Survival reduced below 80% at 22 days in LEC co-cultures compared with 16 days for LEC culture medium or HEK monolayers. Uterine release of motile mf was sustained till day 10 in LEC co-cultures compared with 5 days for LEC culture medium. Metabolic activity was not statistically different in 14 day LEC co-cultured *B. malayi* compared with *ex vivo* worms, whereas 14 day cell-free LEC culture medium or HEK monolayer cultured worms showed significant ($P<0.0098$) metabolic

decline. *Wolbachia* titres remained similar in 14 day LEC co-cultured *B. malayi* compared with *ex vivo* controls. Having verified LEC co-cultures stably supported *B. malayi* and *Wolbachia* viability over 14 days, we assessed *Wolbachia* reductions and dynamics after treatment with physiologically relevant doxycycline exposures. Doxycycline induced significant ($P<0.0001$) 79-84% reductions in *Wolbachia* after continuous treatment for 7 or 14 days whilst drug removal after 7 days led to non-significant 54% reduction after 7 days washout. Thus, we have robustly validated an *in vitro* co-culture system which may be used to examine anti-*Wolbachia* agents for superiority compared with doxycycline.

17:00

Prof Abdollah Rafiei,
Cancelled

17:15

Miss Holly Craven, *PhD Student, Aberystwyth Univeristy*
G-quadruplexes in the parasitic platyhelminth *Schistosoma mansoni*: identification and anthelmintic drugability - *A15724*

H Craven[1]; H Whiteland[1]; M Swain[1]; L Hurley[2]; K F Hoffmann[1];
[1] Aberystwyth University, UK; [2] University of Arizona, United States

Guanine rich sequences of DNA can fold into alternative structures called G-Quadruplexes (GQs) and form *in vivo* in single cell as well as multicellular organisms. *Schistosoma mansoni* is a multicellular parasitic platyhelminth and a causative agent of schistosomiasis, which affects some 200 million people annually. New *S. mansoni* drugs and therapeutic targets are urgently needed as potential for resistance to the current chemotherapy, praziquantel, increases. As GQs have been targeted in drug development pipelines ranging from cancer to human African trypanosomiasis (HAT or sleeping sickness), they could provide a new target for progressing novel anti-schistosomal agents. Here, computational methodologies to identify putative quadruplex structures (PQS) within the *S. mansoni* genome were performed. The genome was searched for sequences that satisfy the algorithm $(G_3N_{1-7}G_3N_{1-7}G_3N_{1-7}G_3N_{1-7})n$ using Quadparser software. A total 1,145 PQS were established (409 in intragenic regions, 370 in intergenic regions). Cross referencing sequences with the annotated genome illustrated that of the 409 PQS found in intragenic regions, 354 occurred within introns and only 40 were found within exons. When stringency was relaxed to N_{1-20}, total PQS increased to 7,913 (2,576 within intragenic regions, 2,874 within intergenic regions), with 2,149 mapped to introns and 293 found in exons. A list of putative quadruplex sequences most likely to fold *in vivo* are currently being assessed. Roboworm, our in-house, high-throughput screening

platform was utilised to assess anthelmintic efficacy of Quarfloxin, a compound known to bind GQs and affect rRNA biogenesis, on *Schistosoma* larva (schistosomula). After 72 hours, significant reduction in viability measures were detected in schistosomula dosed with quarfloxin ($IC_{50motility}$ 1.42 µM; $IC_{50phenotype}$ 1.45 µM). Quarfloxin efficacy was further assessed on adult worm (and 3 week juvenile) parasites, and was found to impair adult parasite motility up to 5 µM, with a greater observed effect on males than females. However, oviposition in females was disrupted up to 0.625 µM. < p> This work represents the first evidence of PQS within the *S. mansoni* genome and the first to test GQ targeting molecules on the parasite. While the mechanism of quarfloxin action against *S. mansoni* must be confirmed (inhibition of PolI and/or PolII transcription), this exciting preliminary data suggests that GQs could be targeted in developing alternative routes of treatment for a neglected tropical disease.

17:30

Dr Ahammed Shareef, *Assistant Professor, PSMO College*
Anthelmintic action of triclabendazole *in vivo* in juvenile tropical liver fluke, *Fasciola gigantica*: a scanning and transmission electron microscope study - *A15731*

P A Ahammed Shareef[2]; D R S.M.A. Abidi[1];
[1] Aligarh Muslim University, India; [2] PSMO College, India

Fasciolosis, caused by *Fasciola hepatica* (temperate species) and *Fasciola gigantica* (tropical species), is a serious veterinary disease and zoonotic infection worldwide. Triclabendazole (TCBZ) is the drug of choice to treat *Fasciola* infection due to its potent efficacy against both juvenile and adult liver flukes. In the present study, the effect of *in vivo* treatment with TCBZ on immature *F. gigantica* was investigated. Five goats were infected with 150 *F. gigantica* metacercariae each by oral gavage and four of them were treated with a single oral dose of TCBZ at 10 mg/kg at four weeks post-infection. They were euthanized at 0 (untreated), 24, 48, 72 and 96 hours post treatment. Juvenile flukes were recovered from the livers and processed for scanning electron microscopy (SEM) and transmission electron microscopy (TEM).
In control flukes, the SEM shows normal morphology and TEM reveals normal ultrastructure. No noticeable changes were observed at 24 h post-treatment. By 48 h post-treatment, there were some tegumental blebbing, swelling and deposition of secretions displayed by the SEM of flukes and moderate level of disruption to the basal infoldings, mitochondria, musculature, nuclei and, formation of vacuoles and reduced number of T1 and T2 secretory bodies were observed by TEM. At 72 h post-treatment, SEM displayed severe disruption and dislodging of spines, sloughing off the tegument to expose basal lamina and isolated lesions to expose underlying musculature. The TEM revealed complete sloughing off the tegument to expose basal lamina, severe disruption of circular and longitudinal muscle fibres, mitochondria, nuclei and granular endoplasmic reticulum were observed. By

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96 h post-treatment, SEM of the flukes showed extremely severe disruption and, the tegument was completely sheared off and deeper lesions to expose underlying musculature. The ultrastructural changes were at their most advanced level, including severe disruption to basal lamina, circular and longitudinal muscle fibres, mitochondria, nuclei and degeneration of a substantial area of cytoplasm. This is the first *in vivo* study describing the TCBZ action in juvenile *F. gigantica* at SEM and TEM level.

17:45

Ms Rachel Clare, *RA and part time PhD, LSTM*
The first industrial scale screen of 1.3 million compounds against *Wolbachia* identifies five promising new leads for the treatment of lymphatic filariasis and onchocerciasis - *A15720*

R H Clare[1]; N Berry[2]; D Hong[2]; K L Johnston[1]; L Ford[1]; D A Cook[1]; J Archer[1]; A Steven[1]; G Nixon[2]; P M O'Neill[2]; M J Taylor[1]; S A Ward[1];
[1] Liverpool School of Tropical Medicine, UK; [2] University of Liverpool, UK

A screening campaign through a partnership between the anti-*Wolbachia* consortium (A·WOL) and AstraZeneca has identified 5 novel areas of diverse chemical space with enhanced activity against *Wolbachia*, an essential bacterial endosymbiont of filarial parasites. This was accomplished through the first industrial scale screening of 1.3 million of AstraZeneca's compounds against *Wolbachia*, using a fully automated intracellular whole cell assay. Following a primary screen at 10µM, ~20,000 hits were triaged through chemoinformatic analysis to select 58 clusters in distinct areas of chemical space. Representatives from all 58 clusters were tested *in vitro* using microfilariae (Mf), resulting in 10 clusters demonstrating potent *Wolbachia* reduction after 6 days exposure. When tested in a Mf time kill assay, five of these clusters showed a superior rate of kill compared to all other A·WOL drugs with activity demonstrable at less than 1 day exposure. These chemotypes, are extremely promising new leads for safe macrofilaricides against lymphatic filariasis and onchocerciasis.

Omics Session

Omics I - (Stream 3 - Physics 0.15 Main) 14:00 to 15:30

Invited Speaker 14:00 - (30 mins) '

Prof Aaron Maule, *Academic, Queen's University Belfast*
'Drugging' liver fluke into the 21st century - *A15179*

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A Maule[2]; P McVeigh[2]; E McCammick[2]; E Robb[2]; W Hussain[1]; E Gardiner[2]; D Wells[2]; M Tsifaki[2]; A Margariti[2]; A Mousley[2]; N J Marks[2];

[1] Institute for Global Food Security, Queen's University Belfast, UK; [2] Queen's University Belfast, UK

Liver fluke species are pervasive parasites, renowned for undermining the productivity of farmed ruminants and for causing a neglected tropical zoonosis. Despite their sustained economic toll on agricultural production systems, a restricted panel of effective flukicides and mounting evidence for widespread drug resistance, research resources/tools for *Fasciola* species parasites have languished in the 20th Century, hindering the biological scrutiny needed to underpin drug and vaccine target discovery and validation. Further, after infection peak virulence associates with the migrating juvenile, a stage that has defied biological interrogation based on the challenge of juvenile worm recovery from infected livers at appropriate scale. The last decade has seen a slow, but remarkable progression in the resources and tools available for liver fluke, promoting confidence that these can help advance the development of new control agents. Coincident with liver fluke definitive host promiscuity is the largest helminth genome reported to date that along with improving transcriptomic resources provide new opportunities for *in silico* discovery. Gene silencing is robust during *in vitro* maintenance for diverse target genes and a growing panel of bioassays boast refined phenotypic readouts. In vitro maintenance supports long-term laboratory culture, facilitating experimentation on the juvenile, the key life stage for control. Here we will consider how these new tools are supporting advances in our understanding of two elements core to juvenile liver fluke biology: (i) their stem cell-like neoblasts that support the rapid growth and development displayed by migrating worms. These cells drive fluke virulence, offer important new avenues for control and potential tools for the heterologous expression of target genes; (ii) their neurobiology that underpins the sensory and motor coordination needed to support migration from the intestine to the bile ducts. The importance of nerve/muscle targets to nematode parasite control supports the hypothesis that fluke nerve and muscle cells are likely to provide a rich source of flukicide targets.

This work reported here has been supported by BBSRC (BB/H009477/1, BB/K009583/1), NC3Rs (NC/N001486/1), Merial and Boehringer Ingelheim Animal Health.

14:30

Dr Paul McVeigh, *Senior Research Fellow, Queen's University Belfast*

G protein-coupled receptors (GPCRs) in the liver fluke, *Fasciola hepatica - A15607*

P McVeigh[1]; D Wells[1]; E McCammick[1]; P McCusker[1]; J E Hodgkinson[2]; S Paterson[2]; A Mousley[1]; N J Marks[1]; A G Maule[1];

[1] Queen's University Belfast, UK; [2] University of Liverpool, UK

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GPCRs are established drug targets in human medicine. Despite their considerable appeal as anthelmintic targets, poor understanding of GPCR diversity and function in parasitic helminths has thwarted progress towards GPCR-targeted anti-parasite drugs. To facilitate GPCR research in the liver fluke, *Fasciola hepatica*, we have generated the first profile of GPCRs from the *F. hepatica* genome. Our dataset describes 147 high confidence GPCRs, representing the largest cohort of GPCRs, and the largest set of *in silico* ligand-receptor predictions, yet reported in any parasitic helminth. All GPCRs fall within the established GRAFS nomenclature, comprising three glutamate, 135 rhodopsin, two adhesion, five frizzled, one smoothened, and one secretin GPCR. Amongst rhodopsins were 18 highly diverged receptors that maintained core rhodopsin signatures, but lacked significant similarity with non-flatworm sequences, providing a new sub-group of potential flukicide targets. Seventy-six orthologous sequences in other flatworm genomes identified these as new members of existing groups (PROF1/Srfb, Rho-L, Rho-R, Srfa, Srfc) of flatworm-specific rhodopsins. These receptors imply flatworm specific GPCR functions, and/or co-evolution with unique flatworm ligands, and could facilitate the development of selective anthelmintics. Liver fluke homologues of deorphanised rhodopsins displayed sequence conservation of ligand binding domains. These data enabled high confidence ligand-receptor matching of 17 receptors activated by acetylcholine, neuropeptide F/Y, octopamine or serotonin. RNA-Seq analyses showed expression of 101 GPCRs across various developmental stages, with the majority expressed most highly in the pathogenic, intra-mammalian, juvenile parasites. These data identify a broad complement of GPCRs in *F. hepatica*, including rhodopsins likely to have key functions in neuromuscular control and sensory perception, as well as frizzled and adhesion/secretin families implicated, in other species, in growth, development and reproduction. This catalogue of liver fluke GPCRs provides new opportunities to study flatworm biology and to advance anthelmintic discovery. Ongoing work aims to localise sites of GPCR gene expression through in situ hybridisation and investigate GPCR functions through RNA interference (RNAi).

14:45

Mrs Eve Hanks, *PhD student, University of Glasgow*

Determining anti-glycan antibodies responses to *Haemonchus contortus* Barbervax vaccine using glycan array screening - *A15375*

E Hanks[3]; A Van Diepen[1]; D Smith[2]; G F Newlands[2]; S Burgess[2]; D P Knox[2]; A J Nisbet[2]; T N McNeilly[2]; C Hokke[1]; C Britton[3];

[1] Leiden University Medical Centre, Netherlands; [2] Moredun Research institute, UK; [3] University of Glasgow , UK

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Haemonchus contortus is a highly pathogenic, blood feeding gastrointestinal nematode of small ruminants. High levels of protective immunity can be achieved against challenge infection by vaccinating sheep with the native *H. contortus* gut glycoprotein vaccine Barbervax. Previous studies have shown that vaccination induces high antibody titres to two main glycoproteins present in Barbervax, aminopeptidase H11 and the H-gal-GP complex. Approximately 90% of the antibody reactivity is targeted towards glycan components of these glycoproteins. To identify the specific glycan structures recognised by host antibody following vaccination, glycan array screening was carried out. Arrays were printed with Barbervax glycans fractionated by HPLC and screened with serum from 56 vaccinated lambs, predominantly from field trials carried out in Australia. These lambs all showed high levels of anti-Barbervax IgG based on ELISA titre at peak *H. contortus* challenge. From the serum recognition profiles, we identified a number of glycans that were recognised consistently by serum from these lambs. We examined any relationships between level of IgG binding to specific glycan fractions and three measures of protection to *H. contortus* infection: mean faecal egg count throughout the trials, antibody titre at peak challenge and change in haemoglobin level during the trials. We identified a small number of glycan fractions which were significantly related to protection. Synthetic glycans were also included on the arrays and synthetic LDNF was strongly recognised by some of this cohort. Further work is underway to determine the structures of the immunogenic Barbervax glycans and to examine whether specific glycans of interest may be involved in inducing protective immunity. This is important in identifying the mechanisms of vaccine-induced immunity to *H. contortus* and in development of a future synthetic vaccine.

15:00

Prof Christoph Grunau, *Group leader, UMR5244 University of Perpignan/CNRS*

Chromatin structure changes are essential for life cycle progression of the human parasite *Schistosoma mansoni - A15472*

R Augusto[2]; D Roquis[3]; A Taudt[4]; K Geyer[1]; G Padalino[1]; K F Hoffmann[1]; N Holroyd[6]; M Berriman[6]; B Aliaga[5]; C Chaparro[2]; **C Grunau**[5];

[1] Aberystwyth University, UK; [2] IHPE, France; [3] IRHS, France; [4] University of Groningen, Netherlands; [5] University of Perpignan via Domitia, France; [6] Wellcome Trust Sanger Institute, UK

Schistosoma mansoni is a parasitic flatworm and causative agent of intestinal schistosomiasis, a neglected tropical disease affecting 67 million people worldwide. The parasite has a complex life cycle involving two obligate consecutive hosts (a cold-blooded snail and a warm-blooded mammal). We show here that the chromatin structure of five different developmental stages is characterized by specific changes in posttranslational histone modifications, in particular methylation of H3K4, H3K27 and H4K20. E.g. bivalent methylation in H3K4me3 and

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H3K27me3 at transcription start sites (TSS) of genes is a landmark of cercaria. In addition to specific modifications around genes, repetitive sequences undergo characteristic changes in their chromatin structure during the lifecycle. Trimethylation of H3K27 at TSS is found in sporocysts and pharmacological inhibition of G9a/GLP and EZH2 histone methyltransferase orthologs in *S. mansoni* efficiently blocked miracidia to sporocyst transition. Consequently, histone methylation emerges as suitable target for control of schistosomiasis.

Wednesday 11th

Host / Vector- Parasite Interactions Sessions

Host -Vector- Parasite Interactions III - (Stream 1 - Edward LIwyd 0.26 Biology Main) 14:15 to 15:45

14:15

Dr A Acosta-Serrano, *Liverpool School of Tropical Medicine*

Follow the light: a trypanosomes' journey into the tsetse ectoperitrophic space

A Acosta-Serrano[1];

[1] Liverpool School of Tropical Medicine, UK

The tsetse peritrophic matrix (PM) is a chitinous structure that surrounds the bloodmeal and forms a physical barrier for ingested pathogens, like trypanosomes. To establish an infection and avoid harmful factors present in the bloodmeal, sub-species of Trypanosoma brucei colonise the tsetse ectoperitrophic space (ES), which is located between the PM and the gut epithelium. Although unproven, and despite the fact that T. brucei parasites do not express chitinases, it is generally accepted that after stumpy trypanosomes differentiate into early procyclic cells within the anterior midgut, the parasites reach the tsetse ES by direct penetration of the PM. Here we re-visited this event by employing several microscopy techniques, including confocal and serial block face-scanning electron microscopy that allowed 3D-reconstructions of trypanosome-infected tissues. We found no evidence supporting direct crossing of the tsetse PM by procyclic trypanosomes. Instead, early procyclic trypanosomes first colonise the proventriculus (place of PM synthesis), where they can either reach the ES or become trapped in pockets between PM layers, which move along the entire gut as the PM gets remodeled.

14:45

Mr Aitor Casas-Sanchez, *PhD Student, Liverpool School of Tropical Medicine*

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Characterisation of genes important for the successful life cycle completion of *Trypanosoma brucei* in the tsetse - *A15793*

A Casas-Sanchez[1]; C Cansado-Utrilla[1]; L Lopez-Escobar[1]; P B Walrad[2]; A Acosta-Serrano[1];
[1] Liverpool School of Tropical Medicine, UK; [2] University of York, Centre for Immunology and Infection, UK

Trypanosoma brucei undergoes a complex life cycle progression in the tsetse vector. The parasite encounters many challenges involving migration and colonization of several tsetse tissues, which are accompanied by a series of developmental changes. After the "stumpy" form differentiates into the procyclic stage, it is assumed that the parasite first colonises the midgut (MG) ectoperitrophic space and then invades the proventriculus (PV) or cardia, where transformation into epimastigotes occurs. The last step of the journey involves migration to and establishment of a salivary gland (SG) infection to ensure transmission of infectious metacyclic trypomastigotes. In order to understand what parasite genes are important for a successful life cycle completion in the fly, we used RNA-seq to compare the gene expression profiles of a fly-transmissible strain with that of a trypanosome strain that is unable to progress beyond the PV. Overall, we found 786 and 867 genes that were significantly up-regulated or down-regulated in the transmissible strain, respectively, compared with the impaired one. Among the top up-regulated genes we identified several encoding metabolic enzymes (i.e. folate transporters and glutamate dehydrogenase) and RNA-binding proteins (RBPs), including RBP6, whose overexpression in procyclics leads to the differentiation up to the metacyclic stage *in vitro* (Kolev *et al.* 2012). To validate the role of these genes in parasite development in the fly, we overexpressed them in procyclic trypanosomes and characterized their phenotypes *in vitro. In vivo* studies are on their way to determine if the overexpression of these genes rescues the limited infectivity of the impaired strain in the tsetse.

15 :00

Dr Lori Peacock, *Research associate, university of bristol*
Shape-shifting trypanosomes from the tsetse proventriculus - *A15504*

L Peacock[2]; C Kay[3]; M Bailey[1]; W Gibson[3];
[1] Bristol Veterinary School, University of Bristol, UK; [2] School of Biological Sciences & Bristol Veterinary School, University of Bristol, UK; [3] School of Biological Sciences, University of Bristol, UK

Like *Trypanosoma brucei,* the livestock pathogen *Trypanosoma congolense* savannah undergoes a complex life cycle in the tsetse vector, involving morphological and metabolic changes that adapt the cells for survival in different niches within the host insect. In *T. brucei* the trypomastigote-epimastigote transition is achieved by an

asymmetric division of proventricular trypanosomes. As *T. congolense* makes the same trypomastigote-epimastigote transition in moving from the midgut to the fly mouthparts, we have searched for the analogous stage. We find that in *T. congolense*, the long proventricular trypomastigotes undergo extensive cell remodelling before repeated asymmetric divisions yielding small daughter cells. In *T. brucei* there is a single asymmetric division, resulting in one long and one short epimastigote. Thus, despite its close evolutionary relationship with *T. brucei* and shared developmental route within the insect vector, *T. congolense* is markedly divergent from its sister species.

15:15

Miss Rachel Findlay, *PhD Student, University of York*

Swim like your lifecycle depends on it: The impact of motility on the survival of *Leishmania* parasites - *A15593*

R C Findlay[2]; H Gadelha[4]; M E Rogers[1]; L G Wilson[5]; P B Walrad[3];
[1] London School of Hygiene & Tropical Medicine, UK; [2] University of York, UK; [3] University of York, Centre for Immunology and Infection, UK; [4] University of York, Department of Mathematics, UK; [5] University of York, Department of Physics, UK

Motility of *Leishmania* spp. parasites is essential for survival during host transitions and is important for lifecycle progression. The presence of an anterior flagellum appendage allows parasite movement. This oscillating flagellum creates the force which pulls the promastigote through changing environments. As the environmental conditions of the parasite change, it morphologically transforms to optimise its survival.
During the host transition, from female phlebotomine sandfly vector to mammalian host, the egestion from the sandfly bite is highly enriched in metacyclic promastigotes (86-98%). This is due to the highly viscous promastigote secretory gel (PSG) creating a 'sieve' to block earlier lifecycle stages. The details of how the metacyclics are capable of swimming through this substance compared to other stages remains obscure but is fundamentally linked to infectivity and is the focus of our investigation.
We have adapted a unique method of high-speed, three-dimensional imaging called digital inline holographic microscopy (DIHM) allowing us to examine the movements of *Leishmania mexicana* promastigotes. The data produced can be used to numerically refocus and create a high resolution reconstruction of parasite movement at different length scales. We have tracked both procyclic and metacyclic promastigote parasites over multiple frames to gain information on the swimming patterns of these cells. This revealed how the parasite and host cells interact with each other and their environments in three-dimensions.

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Three-dimensional tracking of promastigotes demonstrates stage-specific differences in swimming behaviour in biologically-relevant environments. Using this technique we have revealed that the mammalian-infective promastigotes are more capable of swimming in highly viscous solutions such as PSG.
Additionally, the DIHM technique has allowed us to investigate how the different stages of *Leishmania* promastigotes are capable of taxis, including whether human-infectious stage parasites can recognise and are drawn toward phagocytic host cells.
DIHM has allowed us to mathematically quantify the relationship between the active bending of the flagellum and cell movements in response to the PSG environment of the phlebotomine sandfly midgut versus the presence of mammalian host macrophages. These swimming parameters have helped to determine which factors of promastigote movement are essential for it to respond and thrive within distinct environmental pressures.

15:30

Miss Myrthe Pareyn, *PhD student, Universiteit Antwerpen*

Ecology of cutaneous leishmaniasis in Ochollo, a hotspot in Southern Ethiopia - *A15647*

M Pareyn[3]; E Van den Bosch[3]; N Girma[1]; N van Houtte[3]; G Van der Auwera[2]; H Leirs[3];
[1] Arba Minch University, Ethiopia; [2] Institute of Tropical Medicine, Antwerp, Belgium; [3] University of Antwerp, Belgium

Ochollo is a village in the mid-highlands of Southern Ethiopia where cutaneous leishmaniasis (CL) forms a major health concern. The past decades, the high CL burden attracted several researchers to this area, conducting basic research on the players of transmission. The assigned vector for transmitting *Leishmania aethiopica* in Ochollo is *Phlebotomus pedifer*. Hyraxes, living on cliffs and in caves near human settlements in close contact with *P. pedifer*, are suspected to be the reservoir hosts. Since the transmission dynamic of *Leishmania* is somewhat unique to every region, a detailed description on the ecology of the different players of transmission needs to be established prior to attempting a control program to decrease the disease burden.
The general aim of this study is to extensively investigate the ecology of CL in Ochollo. More specific, the potential small mammal reservoirs, vectors and parasites of CL and the environmental characteristics (biotic and abiotic) they are associated with will be established.
A monthly sand fly sample collection was carried out from March 2017 until February 2018 in different habitats (caves, stone fences, tree crevices) using CDC miniature light traps and sticky traps. Temperature and humidity data were recorded by loggers on an hourly basis for one year in the different habitats. Furthermore, hyraxes and rodents were trapped at different locations and ear, spleen and blood samples were taken. The presence of *Leishmania* DNA among the different sand fly, hyrax and rodent species was demonstrated by screening for kDNA

using a real-time PCR. To determine the *Leishmania,* sand fly and small mammal species of the kDNA positive specimens, conventional PCRs targeting ITS-1, COI and CytB were performed respectively. PCR products were sequenced and examined by BLAST.
17% of the hyraxes was found infected with *L. aethiopica,* while only one out of 196 rodents, *Mus mahomet,* was kDNA positive. The prevalence of the (different) *Leishmania* species will be established among the variety of sand fly species and the potential seasonal dynamics in infectivity of different sand fly species and their ecological niche will be obtained. Finally, blood meal sources of fresh fed sand flies will be determined to establish the feeding preferences of the sand fly species.
This study will provide information about the sand fly and small mammal species that might play a role in CL transmission in Southern Ethiopia. Accordingly, the epidemiological relevance of the potential vectors and reservoirs will be assessed, as well as their ecological niche. This information will be used to prepare ecological niche models that will make predictions of the CL distribution at present and under changing environmental and land use circumstances, based on all players of transmission in this area.

Plenary Sessions

Wright Medal Lecture - (Great Hall, Arts Centre) 11:45 to 12:30

Invited Speaker 11:45 - (45 mins)

Dr Annette MacLeod, *Wellcome Senior Fellow, University of Glasgow*
Trypanosomes get under your skin - *A15177*

A MacLoed[1];
[1] University of Glasgow., UK

Human African trypanosomiasis, or sleeping sickness, is a neglected tropical disease which has been targeted by the World Health Organisation WHO for elimination as a public health problem by 2020. However, although over the last 10 years the number of annual reported cases has shown a steady decline, major challenges are still ahead to reach the 2020 goal, and even greater challenges to completely block transmission. Among these is the existence of natural genetic variation in both the host and parasite, and overlooked reservoirs of the causative agent, *Trypanosoma brucei gambiense*. Here I will discuss some of the progress we have made in understanding genetic variation and disease transmission, and how we can exploit this knowledge to combat sleeping sickness once and for all.

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BSP AGM

Ecological Parasitology Sessions

Ecological Parasitology: Aquatic Parasitology II - (Stream 4 - Edward Llwyd 0.01) 09:30 to 11:00

Invited speaker 09:30 - (30 mins)

Prof Sarah Culloty, *University College Cork*
Pathogens associated with aquaculture may have wider ecosystem impacts - *A15194*

S Culloty[1];
[1] University of Cork, Ireland

Mortality events in cultured bivalves, related to disease can be significant. Viruses, bacteria and protistans have been associated with various diseases, many of which cause significant losses not just in Europe but globally. The origins of many of these pathogens and the associated diseases they cause have not been determined. As the host species are economically significant, the focus of much of the research has been on reducing economic losses. However, methods to screen and detect parasites have become more sensitive in recent years allowing more opportunities to understand the infection paths and the potential routes for dissemination of parasites. The life cycles of many parasites have multiple stages and multiple hosts indicating that transmission within aquatic systems is ongoing and dynamic. Screening for parasites within aquatic systems indicates that other species within the ecosystem may act as reservoirs, carriers or alternate, intermediate or final hosts. Examples from some of the study systems which are currently being focussed on, suggest that spread of parasites to other hosts and other trophic levels may be possible via a range of routes, and so may ultimately have wider ecosystem impacts, some of which we are only beginning to understand.

10:00

Mrs Luísa Magalhães, *PhD student, University of Aveiro*
Spatio-temporal variation of trematode parasites community in *Cerastoderma edule* cockles from Ria de Aveiro (Portugal) - *A15550*

L Magalhães[1]; S Correia[1]; X de Montaudouin[2]; R Freitas[1];
[1] University of Aveiro, Portugal; [2] University of Bordeaux, France

Cerastoderma edule (edible cockle) is among the most exploited bivalves in Europe playing an important socio-

economic role. Cockles are keystone species living in estuaries and lagoons. They act as ecosystem engineers and occupy a crucial position within food webs. In fact, cockles contribute to biodiversity and ecosystem resilience, and therefore the identification of environmental factors that control their population dynamics, including parasitism, is of utmost importance. Trematodes are the most prevalent macroparasites of cockles being able to exert an impact both at the individual and population levels. Therefore, it is of prime relevance to recognize and understand the parasite-host system dynamics in order to better predict potential conservation threats to bivalve populations and to maximize the success of stock and disease episodes management.
Cockle monitoring was conducted in 2012 and 2016, in six and eight stations, respectively, distributed by two channels from the Ria de Aveiro coastal lagoon, northwest of Portugal. Cockles were sampled in one single occasion in 2012 and seasonally in 2016. The tested hypothesis is that the trematode community in cockles was spatially and seasonally heterogeneous but stable over time.
The main result showed that despite a relative homogeneity of the parasite community structure in cockles, the among-years heterogeneity of trematode communities was higher than among-sites and among-seasons heterogeneity rejecting the postulated hypothesis. It was demonstrated that (1) spatially, despite an overall channel difference and a slight downstream-upstream gradient, mean parasite species richness per cockle and mean metacercariae abundance per cockle displayed low values. This scarcity of trematode parasites in the Ria de Aveiro was linked to the success of infection processes, which appears to be related to the more or less sheltered status of the habitat. In inner areas of coastal ecosystems with more continental influence (which is the case of the present study area), more pronounced seasonal variation of temperature and salinity, less hydrodynamics and lower water mass turnover, and sometimes seagrass occurrence and salt marsh proximity, trematode parasite abundance is often low. Conversely, more oceanic influenced habitats with more buffered temperature and salinity fluctuations, and higher hydrodynamics features are generally characterized by higher metacercariae abundance. (2) Seasonally, and conversely to what is generally expected, there was no evident modification in the sampled trematode community, a possible direct consequence of trematode scarcity found in the Ria de Aveiro. (3) Interannually, there was a worrisome loss of trematode diversity and prevalence which consequently indicates an important loss of overall diversity and/or environmental conditions reflecting the negative effects of global and local changes.

10:15 –

Miss Emily Matthews, *PhD student, -*

Fussy fluffy fiend? Investigating host-specificity of *Saprolegnia parasitica* isolates *- A15690*

E Matthews[1]; A Ellison[1]; J Cable[1];

[1] Cardiff School of Biosciences, Cardiff University, UK

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The freshwater oomycete *Saprolegnia parasitica* is responsible for crippling damage to both the aquaculture industry and wild fish stocks. This fungal-like pathogen releases infective zoospores which germinate upon location of a fish host. The resulting mycelial hyphae colonise the host epidermal tissues before penetrating the muscle and blood layers. The chemotactic responses exhibited by *S. parasitica* zoospores greatly impact their ability to successfully locate a host. Chemotaxis is described as the movement of a cell/organism in response to an increasing or decreasing concentration gradient of a particular substance. It has been previously demonstrated that *S. parasitica* zoospores exhibit strong chemotactic activities towards amino acids. To date, no study has investigated whether *S. parasitica* zoospores exhibit varying chemotactic responses to the skin of different fish species. Such *in vitro* investigations represent a solid foundation for examining whether a host preference exists between *S. parasitica* isolates. The current study utilises both *in vitro* and *in vivo* methods to examine the zoospore chemotactic activities of four *S. parasitica* isolates. While crude *in vitro* methods do indicate that there are isolate-specific differences in zoospore chemotactic activity, these host preferences are not well demonstrated in lab-based challenge experiments.

10:30

Rhiannon Hunt, *PhD Student, Cardiff University*

Can parasites be a drag? Impact of *Argulus* fish lice on host swimming performance - *A15212*

A Stewart[1]; R Hunt[1]; R Mitchell[1]; V Muhawenimana[2]; C Wilson[2]; J Jackson[3]; J Cable[1];
[1] Cardiff School of Biosciences, Cardiff University, UK; [2] Cardiff University, School of Engineering, UK; [3] University of Salford, UK

When examining the consequences of infection, focus is often placed upon the pathological effects. Some parasites can drastically alter the shape of their host, and in doing so may have an additional physical impact. Ectoparasitic fish lice have been a problem in marine farms for decades, with freshwater lice (*Argulus* spp.) rising in concern over the past decade. *Argulus* lice can alter the profile of fish due to their relatively large size and consequently could exert a physical effect on their hosts. Here, using *Argulus foliaceus* on the model three-spined stickleback (*Gasterosteus aculeatus*), we examine both physical (including form drag and mass) and pathological effects of infection. Impact was assessed using both sustained (prolonged swimming within an open channel flume) and burst (C-start) swimming performance tests on hosts before, immediately after and days after infection to separate the physical and pathological effects. We then questioned the overall impact of *Argulus* on fish swimming performance and effect of large parasites on their hosts. Considering the economic cost of parasites, an understanding of the consequences of infection is essential to reduce loss.

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10:45

Gabrielle van Beest, *Universitat de Valencia*

Use of *in vivo* fluorescent dyes to determine the infectivity and penetration pattern of *Cardiocephaloides longicollis* (Trematoda, Strigeidae) into the gilt-head seabream - *A15512*

G S van Beest[1]; F E Montero[1]; M Villar-Torres[1]; J A Raga[1]; A Born-Torrijos[2];
[1] Cavanilles Institute for Biodiversity and Evolutionary Biology, Science Park, University of Valencia, Spain; [2] Institute of Parasitology, Biology Centre of the Czech Academy of Sciences, eské Budějovice, Czech Republic

The trematode parasite *Cardiocephaloides longicollis* (Rudolphi, 1819) Dubois, 1982 (Digenea, Strigeidae) is widespread in marine ecosystems along European coastlines, especially in the Mediterranean. Its metacercariae parasitise, among other fishes, the gilt-head seabream (*Sparus aurata* L.), one of the most important marine species in Mediterranean aquaculture, with prevalence up to 54 %. *Cardiocephaloides longicollis* has a three-host life cycle. The cercariae penetrate the skin and migrate into the fish brain, where they encyst as metacercariae. The cysts are supposed to cause significant alterations in fish behaviour, possibly increasing their transmission to the definitive host.

For the study of the infectivity and penetration pattern of *C. longicollis* in fish second intermediate host, different experimental assays were performed. First, the effects of two *in vivo* fluorescent dyes on survival and activity of labelled cercariae were tested. Thereafter, an experimentally designated dose of one of the dyes helped to determine the penetration points of *C. longicollis* into *S. aurata*. Finally, the effect of both dyes on the infectivity capacity of labelled cercariae was tested.

Two different fluorescent dyes were tested: (1) 5(6)-carboxyfluorescein N-hydroxysuccinimidyl ester (CFSE), which stains intracellular amines in life cells and concentrates in the acetabular gland of the cercariae, and (2) Hoechst 33342 (NucBlue), which specifically stains DNA, i.e. the nuclei of life or fixed cells. Three different ascending concentrations were tested for each dye (CFSE at 20 µM, 50 µM and 100 µM, and NucBlue at1 drop/ml, 2 drops/ml and 3 drops/ml), and their effect on cercarial activity was recorded during 24 hours, showing no differences between concentrations and unlabelled cercariae. Additionally, intermediate doses of both dyes were selected based on labelling efficacy over time, to test the effect of dyes on cercarial activity and survival during the first five hours post labelling (hpl), i.e. the time during which cercariae should be highly efficient during penetration. Intermediate doses of CFSE enabled a quick and accurate location of the cercariae on the host body surface without affecting cercarial survival. Results suggest a centralisation of the larvae around the facial areas of the fish. Furthermore, in order to evaluate the post-labelling infectivity of the larval trematodes, labelled and control cercariae were used to infect *S. aurata*. The water where the fish were infected was analysed to count the tails as

cercariae lose them when penetrating the host. Additionally, 20 days post infection, fish brains were examined for metacercariae, showing no significant differences between the number of metacercariae developed from NB-labelled and control cercariae. In contrast, the number of metacercariae developed from CFSE-labelled cercariae was significantly lower compared to the control treatment.
In conclusion, the *in vivo* fluorescent dye CFSE appears to be the most adequate labelling treatment in experimental assays studying the infectivity capacity and penetration strategy of cercariae of *C. longicollis*.
This study was supported by projects MSM200961706 (Czech Academy of Sciences), European Centre of IchthyoParasitology, Centre of excellence program of the Czech Science Foundation; project No. P505/12/G112, AGL2015-68405-R (MINECO/FEDER, UE), Prometeo/2015/018 and Revidpaqua ISIC/2012/003 of the Valencian Regional Government.

Ecological Parasitology: Ecological Modelling - (Stream 4 - Edward Llwyd 0.01) 14:15 to 15:45

Invited Speaker 14:15 - (30 mins)

Prof Andy Fenton, *Professor, University of Liverpool*
Understanding transmission dynamics in multihost communities - *A15192*

A Fenton[2]; S M Withenshaw[2]; A Pedersen[1];
[1] Institute of Evolutionary Biology and Centre for Immunology, Infection and Evolution, University of Edinburgh, UK; [2] Institute of Integrative Biology, University of Liverpool, UK

Vector-borne pathogens (VBPs) are a major source of disease, suffering and economic loss. The epidemiology of VBPs can be complex as transmission arises from interactions between the pathogen, and potentially many vector and definitive host species. Furthermore, while many vector and pathogen species can infect multiple host species in the host community, their abilities to infect those different hosts can vary between the pathogen and vectors. Given these complexities, well-informed theory is needed to understand VBP dynamics in multihost-multivector-multipathogen systems. However, data on how different host species contribute to pathogen transmission are needed to inform these models, but are often lacking. Most studies of VBP dynamics in natural systems rely on purely observational data, which can reveal patterns of pathogen-vector-host co-associations, but cannot show definitively the roles that different species play in pathogen transmission. Hence, mathematical models of VBP transmission in multi-host communities remain poorly informed. We present results from a large-scale experiment conducted on a natural multihost-multipathogen-multivector system, which we use to inform a mathematical model to infer rates of within- and between-species transmission. Our study focuses on woodland small mammal communities dominated by wood mice (*Apodemus sylvaticus*) and bank voles (*Myodes glareolus*). Each species

hosts multiple flea species, which vector a range of apparently host-specialist and host-generalist pathogens (primarily *Trypanosoma* and *Bartonella*). We used targeted treatments with the insecticide Fipronil to interfere with vector (and hence VBP) transmission from one or other host species, and monitored changes in VBP prevalence in the drug-target and non-target host species. We then used these data to fit epidemiological models to infer differential rates of host use by the fleas, and the consequences for within-and between-species transmission. We show that cross-species transmission is much rarer than suggested by observational data, such that each host species has a relatively host-specific flea population, and even when vector sharing does occur, host-pathogen compatibility barriers further restrict cross-species transmission. Overall this combination of experimental perturbation and tailored mathematical models provides a powerful means to infer pathways of within- and between host species transmission that would not be possible with observational data alone

14:45

Miss Emma Davis, *PhD student, University of Warwick*

Cancelled

15:00

Dr Jonathan Hamley, *Imperial College London, Faculty of Medicine*

The impact of exposure heterogeneity on onchocerciasis transmission and control/elimination - *A15733*

J Hamley[1]; M Walker[2]; P Milton[1]; M G Basáñez[1];
[1] Imperial College London, UK; [2] Royal Veterinary College, UK

Background: Onchocerciasis (river blindness) has been proposed, by the World Health Organization's 2012 roadmap on neglected tropical diseases, for elimination in selected African countries by 2020 (and in 80% of endemic countries by 2025). To investigate the feasibility of elimination with current interventions (mainly mass annual or semi-annual distribution of the microfilaricidal drug ivermectin), onchocerciasis transmission models have been developed and refined to understand the factors determining the ability of control programmes to achieve interruption and elimination of transmission. Factors thus far identified include: a) the level of initial (pre-control) endemicity; b) the magnitude of transmission intensity and biting rate by local simuliid vector species (particularly in the absence of vector control); c) the duration of the programme, the therapeutic coverage achieved and maintained, and d) the level and nature of treatment adherence (random vs. systematic non-compliance). However, when developing individual-based versions of the models, it must be taken into account that individuals in a host population frequently differ in their exposure to infection. The level of exposure heterogeneity plays a

central role in the distribution of parasites amongst individuals, and this distribution, in turn, determines the levels of infection prevalence, infection intensity, and the overall contribution of parasite population regulatory processes to the stability and resilience of the infection to interventions. Large variation between hosts in the number of vector bites they receive will result in high levels of parasite overdispersion. At a given prevalence, a population of highly aggregated parasites will require increased levels of mass drug administration (MDA), or the deployment of other (including targeted) interventions, in comparison to those with low aggregation, to suppress transmission.

Methods: We use an individual-based version of our model, EPIONCHO-IBM, which tracks individual humans and accounts for the age-structure of adult worms and microfilariae, allowing for senescence in parasite mortality and fecundity. In line with deterministic EPIONCHO, we account for various density-dependent processes in parasite establishment and vector survival. The goal of this work is to explore how existing data on the relationship between infection prevalence and vector biting rate can be used to incorporate exposure heterogeneity into EPIONCHO-IBM, and explore how this can influence trends in (parasitological, serological and entomological) markers of infection following long-term ivermectin treatment as well as the dynamics of recrudescence after treatment cessation.

Results and Conclusions: Individual host variation in exposure to vectors is a crucial determinant of epidemiological dynamics during and after the treatment phase of a programme. Analyses of prevalence-vector biting rate data indicate that strong heterogeneity is necessary to stabilise low levels of infection prevalence. Levels of worm overdispersion were in broad agreement with those of other studies using different types of (parasitological) data and more severe than values used by other models predicting the probability of elimination. Areas of low pre-intervention prevalence and high exposure heterogeneity may experience infection recrudescence faster than areas of high pre-intervention prevalence but low exposure heterogeneity, for a given MDA duration and coverage. There is a pressing need to identify, gather, and analyse data on distributions of infection in host populations and their determinants (e.g. proximity to vector breeding sites, behavioural, occupational, immunological factors), to better parameterise parasite transmission and control/elimination models.

15:15

Miss Flavia Occhibove, *PhD student, Aberystwyth University*

Biodiversity dilution and amplification effects in tick-borne diseases: an eco-epidemiological modelling approach. - *A15474*

F Occhibove[1]; K Kenobi[1]; C Risley[1];

[1] Aberystwyth University, UK

Tick-borne diseases include several of high importance both for human health and for conservation; furthermore,

ticks can bridge host populations and these diseases have therefore been a matter of huge interest in the context of the nexus between wildlife disease ecology and public health.
In particular, rodent-tick disease systems, due to the rodent biology/ecology and the common host-generalism of the ticks, have been extensively studied to identify the connection between biodiversity and disease transmission. There has been widespread debate on the relative importance of the dilution versus amplification effects; i.e. does higher biodiversity decrease or increase disease transmission?
This eco-epidemiological modelling study aimed to investigate dilution/amplification in two different host-parasite-pathogen systems by varying community composition in order to highlight its effects on model outputs such as vector numbers and disease prevalence in the presence of parameter variation.
The model employed consisted of a deterministic single-vector multi-host compartmental model, also including ecological relationships with non-host species such as competition and predation, in order to describe disease transmission in a hypothetical Welsh woodland rodent community. The dilution effect was investigated by assembling a progressively more complex community. The two systems chosen for the analysis were *Ixodes ricinus*-Lyme disease and *I. trianguliceps*-Babesiosis.
Sensitivity analysis was performed on parameters that were hypothesised to affect model outputs but could not be directly estimated (e.g. efficiency in transmission/competence, host-vector encounter rate, feeding/moulting probability of success).
To improve model predictions, where relevant, parameters were estimated from field data. Rodent live-trapping was conducted in Welsh woodlands across two seasons for three consecutive years.
Modelling results confirmed that community composition and inter-specific dynamics strongly affect disease transmission; hence, in similar studies, the inclusion of ecological relationships within models would be expected to obtain more realistic predictions. The parameters most affecting the systems were among those where estimation in the field was more difficult, demonstrating that more empirical research is needed to reduce parameter uncertainty.
Finally, dilution or amplification effects might not be mutually exclusive and their detection depends on the result under consideration, which has to be selected according to the aim of the eco-epidemiological study (e.g. public health or wildlife management/conservation). In the presented Lyme disease case, for example, more complex communities have fewer infected rodents (i.e. evidence for the dilution effect); however, increasing the number of species in the community led to an increase in the number of infectious nymphs, the metric mostly used as a proxy of human disease risk, amplifying it.

15:30

Dr Joanne Lello, *Senior Lecturer, Cardiff University*

Macroparasites are indirect drivers of *Hantavirus* transmission - *A15786*

Go to here for the ‘at a glance’ view of the conference

J Lello[1]; R Rosà[2]; G Marini[2]; A Konecny[3];
[1] Cardiff University, UK; [2] Fondazione Edmund Mach, Italy; [3] Masaryk University, Czech Republic

Macroparasite species are responsible for endemic infections in almost all animal species (including humans). An increasing number of studies demonstrate the capacity of such macroparasites to alter the dynamics of coinfecting microparasite populations via within-host processes (e.g. resource competition, alteration of host immune response). There also exists a large body of theoretical and empirical evidence demonstrating that macroparasites can alter host demography; through effects on host fecundity and survival. However, the potential for such demographic change to alter the course of microparasite infections has only been explored in a single theoretical study. Here we present the first study providing empirical evidence that a macroparasite, *Heligmosmoides polygyrus*, of wild mice, *Apodemus flavicollis*, could be driving the dynamics of a zoonotic microparasite, *Hantavirus*, via such changes in host demography. We then explore this relationship using a theoretical model parameterized from our empirical data and consider the implications of host and parasites control measures on viral transmission.

Veterinary Parasitology Sessions

Veterinary Parasitology Symposium - Wildlife Parasitology - (Stream 5 - Physics 0.11 A) 09:30 to 11:00

Invited speaker 09:30 - (30 mins)

Prof Eric Morgan, *Professor, Queen's University Belfast*
Is wildlife relevant to helminth control in livestock? - *A15180*

E Morgan[1]
[1] Queen’s University Belfast, UK;

Many helminth species can infect both wild and domestic animals, but the scale of cross-transmission and its relevance to parasite control on farms is highly uncertain. In the face of this uncertainty, it is easy and common to assume that wild hosts with high parasite prevalence act as sources of infection. This presentation sets out some approaches to disentangle the complexities of host species range, spatial overlap and climatic influences on parasite transmission, to predict risks of cross-infection. Thus, bipartite networks show promise for assessing degree of overlap in helminth fauna between wild and domestic hosts where sampling effort is uneven between host species. Further, formalising empirical knowledge of factors influencing transmission within mechanistic simulation models can help to assess directions and key times of spill-over between host populations. This

approach has been applied to nematodes of saiga antelopes in Kazakhstan, and diverse ungulate assemblages in Botswana. By predicting key points of transmission, rational attenuation measures can be put in place, and consequences of spill-over managed without resorting to radical and ineffective interventions. In the UK, increasing deer numbers along with the discovery of anthelmintic-resistant nematodes in deer, raise the possibility that wildlife are important vectors of drug resistance between farms; although, they might equally serve as refugia for drug-susceptible nematodes. The quantitative frameworks outlined for other systems might contribute to balanced assessments of the risks of helminth infections in wildlife for farming, and to design appropriate mitigation measures in a diverse and multi-purpose farming landscape.

10:00

Prof John Ellis, *Professor of Molecular Biology, University of Technology Sydney*

Multi-locus sequence typing of *Neospora caninum* - *A15507*

L Calarco[1]; J Barratt[1]; **J T Ellis**[1];
[1] School of Life Sciences, University of Technology Sydney, Australia

Comparative studies have shown extreme differences in pathogenicity between isolates of the parasite *Neospora caninum* which causes abortion in cattle. These observations led to the hypothesis that intrinsic genetic differences may exist amongst *N. caninum* isolates that contribute to phenotypic differences. To investigate this, the present study employed a pipeline for the identification of single nucleotide polymorphisms (SNPs) in the *N. caninum* genome using RNA-seq data. RNA-seq data from two phenotypically different isolates of *N. caninum*; NC-Liverpool and NC-Nowra, were analysed using VarScan 2 to identify genetic differences between the two, using an assembled transcriptome from NC-Liverpool as a reference. PCR and DNA sequencing of SNP-containing loci were then used to extend the SNP data to additional *N. caninum* isolates in order to investigate patterns of genetic diversity within the species. Variant analysis identified 3130 SNPs of high confidence, and Sanger sequencing of PCR amplicons captured 56 variants, confirming 86% of these as true variants, supporting the accuracy of the variants called using the pipeline. The multilocus sequence typing results for ten isolates of *N. caninum* revealed a population structure reflecting two main clades that contain geographically dispersed isolates. The link to parasite virulence will be discussed.

10:15

Miss Rachel Byrne, *Postgraduate student, Trinity College Dublin*

Parasites of badgers in the Republic of Ireland- an untold story - *A15295*

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R Byrne[1]; C V Holland[1]; N Marples[1];
[1] Trinity College Dublin, Ireland

The European badger (*Meles meles*) is Ireland's largest terrestrial carnivore. It was first identified as a wildlife reservoir of bovine tuberculosis (bTB) in Ireland in 1972, generating an increased research focus on the badgers' behaviour and ecology to aid bTB control. However, the helminth parasite community of the Irish badger has been continuously overlooked and under-researched, despite the established links between macroparasites and immune suppression and immunodulation.
We are the first to describe the parasite community of the Irish badger, with an emphasis on helminth species. We sampled Western counties and Eastern counties, male and female badgers, and bTB positive and negative badgers, allowing the effects of all these factors to be interrogated.
Of the 289 badgers sampled there was a prevalence of 61% for hookworm infection. The average worm burden was 22.5 with a range of 1-500 worms. As seen in many other hosts there was an aggregated distribution of helminths with a small number of individuals harbouring the majority of worms. Little diversity within the helminth parasite community was observed. This is surprising given that badgers are fossorial feeders, eating in and around soil, and many helminth species are transmitted through faecal contaminated soil.
Additionally, as part of this project both gross organ dissection and faecal egg counts were used as diagnostic tools. In contrast to what is observed in humans, as the intensity of worm burden increased so did the number of eggs shed by the adult hookworm with egg per gram counts of over 3000 being recorded. Given the rarity of having both egg count data and adult worm burden, this presented the unique opportunity to evaluate the sensitivity of faecal egg counts. For the diagnosis of hookworm infection, faecal egg counts had a low sensitivity when compared to the diagnostic gold standard of adult worm burden.
The parasite communities of Irish badgers' present challenges and opportunities for wildlife management, farmers and ecologists. A further understanding of the interplay between parasitic and bTB infection in the context of Ireland and its badger population is necessary for future management of bTB and co-infected helminth parasite outbreaks.

10:30

Miss Amna Arshad Bajwa,
Cancelled

10:45

Mr Gerardo Arias Robledo, *PhD student, University of Bristol*
The toad fly *Lucilia bufonivora*: its evolutionary status and molecular identification - *A15317*

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G Arias Robledo[3]; T Stark[2]; R Wall[3]; J Stevens[1];
[1] Biosciences, University of Exeter, UK; [2] RAVON, Netherlands; [3] School of Biological Sciences, University of Bristol, UK

The blowfly genus *Lucilia* is composed largely of saprophages and facultative myasis agents, including the economically important species *Lucilia cuprina* and *Lucilia sericata*. Only one species is generally recognised as an obligate agent of myiasis, *Lucilia bufonivora* Moniez, and this is an obligate parasite of toads. *Lucilia silvarum* (Meigen), a sister species, behaves mainly as a carrion breeder, however, it has also been reported as a facultative parasite of amphibians. Morphologically, these species are almost identical and historically this has led to misidentification, taxonomic ambiguity and a paucity of studies of *L. bufonivora*. In this study, dipterous larvae were analysed from toad myiasis cases from the UK, The Netherlands and Switzerland, together with adult specimens of fly species implicated in amphibian parasitism: *L. bufonivora*, *L. silvarum* and *Lucilia elongata*. Partial sequences of two genes, COX1 and EF1α, were amplified. Seven additional blowfly species were analysed as outgroups. Bayesian inference trees of COX1, EF1α and a combined-gene dataset were constructed. All larvae isolated from toads were identified as *L. bufonivora* and no specimens of *L. silvarum* were implicated in amphibian myiasis. This study confirms *L. silvarum* and *L. bufonivora* as distinct sister species and provides unambiguous molecular identification of *L. bufonivora*.

Veterinary Parasitology Symposium - Sheep Scab - (Stream 5 - Physics 0.11 A) 14:15 to 15:45

Invited Speaker 14:15 - (30 mins)

Dr Sian Mitchell, *Veterinary Investigation Team Lead, APHA*

Psoroptes ovis - a cause of significant disease in sheep and cattle - *A15196*

Psoroptes ovis is a significant ectoparasite causing disease in sheep in the UK for many years (sheep scab). The history of the disease in the UK and details of its pathogenicity and diagnosis will be given, as a background to other talks later in this session. The APHA, is a government funded agency of Defra and the Welsh Government with regional laboratories in England and Wales. We are tasked with veterinary scanning surveillance, that is the timely detection and investigation of animal-related New & Re-emerging Threats (NRTs), including changes to patterns & trends of endemic diseases. Action can then be taken by farmers, their vets and/or government to manage and control these threats and diseases. As part of this activity, APHA, together with our collaborators in the University of Bristol, undertook investigations into inefficacious treatment of sheep scab and this has resulted in concerning but not unexpected findings. Details will be presented later in the session, but the background to our

investigations will be given. Finally, *Psoroptes* sp. mites have been detected in cattle in the UK, Ireland and Europe causing severe disease. Information about these cases will also be given.

14:45

Mrs Emily Nixon, *PhD Student, University of Bristol*

Treatment strategies for sheep scab: an economic model of farmer behaviour - *A15111*

E Nixon[1]; R Wall[1]; H Rose Vineer[1];
[1] University of Bristol, UK

Ovine psoroptic mange (sheep scab) is a debilitating and damaging condition caused by a hypersensitivity reaction to the faecal material of the parasitic mite *Psoroptes ovis*. Farmers incur costs from the use of prophylactic acaricides and, if their sheep become infected, they incur the costs of therapeutic treatment plus the economic loss from reduced stock growth, lower reproductive rate, wool loss and hide damage. The unwillingness of farmers to use routine prophylactic treatment has been cited as a primary cause of the growing incidence of sheep scab in the United Kingdom (UK) since the disease was deregulated in 1992. However, if farmers behave rationally from an economic perspective, the optimum strategy that they should adopt will depend on the risk of infection and the relative costs of prophylactic versus therapeutic treatment, plus potential losses. This calculation is also complicated by the fact that the risk of infection is increased if neighbours have scab and reduced if neighbours treat prophylactically. Hence, for any farmer, the risk of infection and optimum approach to treatment is also contingent on the behaviour of neighbours, particularly when common grazing is used. Here, the relative economic costs of different prophylactic treatment strategies are calculated for upland and lowland farmers and a game theory model is used to evaluate the relative costs for a farmer and his/her neighbour under different risk scenarios. The analysis shows that prophylaxis with organophosphate (OP) dipping is a cost effective strategy, but only for upland farmers where the risk of infection is high. In all other circumstances prophylaxis is not cost effective relative to reliance on reactive (therapeutic) treatment. Hence, farmers adopting a reactive treatment policy only, are behaving in an economically rational manner. Prophylaxis and cooperation only become economically rational if the risk of scab infection is considerably higher than the current national average, or the cost of treatment is lower. Should policy makers wish to reduce the national prevalence of scab, economic incentives such as subsidising the cost of acaricides or rigorously applied financial penalties, would be required to make prophylactic treatment economically appealing to individual farmers. However, such options incur their own infrastructure and implementation costs for central government.

15:00

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Dr Hannah Rose Vineer, *Senior Research Associate, University of Bristol*
The prevalence and distribution of sheep scab in Wales: a farmer questionnaire survey - *A15738*

H Rose Vineer[2]; R Wall[1]; **C A Chivers**[2];
[1] School of Biological Sciences, University of Bristol, UK; [2] University of Bristol, UK

Outbreaks of ovine psoroptic mange in the U.K. have increased 100-fold since its deregulation in 1992, with the highest prevalence in Wales, a region of high sheep density. A cross-sectional, retrospective, questionnaire-based survey of 7500 members of the association of Welsh lamb and beef farmers (Welsh Lamb and Beef Producers Ltd (WLBP)) was used to investigate the prevalence and distribution of sheep scab in this region in 2015. The survey was completed by 14.0% (n = 972) of potential respondents. Scab outbreaks were reported on 15.8% (n = 154) of farms in 2015. However, 29.0% (n = 282) of farms reported at least one scab outbreak and 2.4% (n = 23) of farms had experienced between six and 10 outbreaks in the previous 10 years. Most outbreaks occurred during September-January (83.0%, n = 150), and were clustered around Brecon (mid-Wales) and Bangor (North Wales). Farmers who used common grazing were significantly more likely to report scab outbreaks in the previous 10 years than farmers who did not. No quarantine procedures for sheep bought in were used by 29.0% (n = 262) of farmers. Future research should be directed towards the development of localized management programmes, with a particular focus on areas of common grazing.

15:15

Prof Richard Wall, *Professor, University of Bristol*
Resistance to macrocyclic lactones, in *Psoroptes ovis* sheep scab mites - *A15665*

E Doherty[3]; S Burgess[2]; S Mitchell[1]; **R Wall**[3];
[1] APHA Camarthen, UK; [2] Moredun Research institute, UK; [3] University of Bristol, UK

Ovine psoroptic mange (sheep scab) is an infection of substantial economic and animal welfare concern in the UK. Its prevalence has increased rapidly over the last 20 years and management is dependent on a small number of acaricidal compounds, many of which are also used to control a range of other endo- and ectoparasites. Here, the effects of the macrocyclic lactone (ML) moxidectin were as considered using *in vitro* assays against mites from four farm populations where persistent treatment failure had been reported: two in west Wales, one from the England/Wales border and one in Herefordshire. The data demonstrate resistance in mites from all four farms. This is the first quantitative evidence of ML resistance in *Psoroptes* mites in the UK. Given the similarities in their mode of action it is highly likely that cross-resistance across the range of this class of compound will be found. The

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development of resistance to moxidectin is of considerable concern given the already high prevalence of scab infection in some regions; major difficulties in scab management should be anticipated if ML resistance becomes widely established in the UK.

Vector / Parasite Interactions Session

RES Vector - Parasite - Microbiome Interactions and Interventions - Sponsored by The Royal Entomological Society - (Stream 2 - Llandinam A6) 09:30 to 11:00

Invited Speaker 09:30 - (30 mins)

Prof George Dimopoulos, *Professor, Johns Hopkins University, Bloomberg School of Public Health*
Employing *Anopheles* microbiota for *Plasmodium*-blocking - *A15197*

G Dimopoulos [1]
[1] Johns Hopkins University, Bloomberg School of Public Health, USA

Malaria is the world's more serious vector-borne disease with a tremendous loss of life and socioeconomic impact. A major problem in malaria control efforts is the parasite's resistance to drugs, thereby rendering the development of new therapeutic and transmission-blocking agents an urgent need. We have identified a *Chromobacterium* sp (Csp_P) from field-derived mosquito midgut microbiota that exerts broad spectrum anti-pathogen and entomopathogenic activity. Csp_P is capable of rapidly colonizing/infecting the mosquito midgut, leading to a drastically shortened mosquito lifespan, and it renders *Anopheles* resistant to infection with the human malaria parasite *Plasmodium falciparum* by interfering with infection of the midgut epithelium. A Csp_P - produced metabolite also inhibit sexual and asexual stages of *Plasmodium in vitro*, thereby rendering it interesting as a possible lead compound for transmission blocking and therapeutic agent/drug development.

10:00

Mr Florian Brod, *PhD student, University of Oxford*
Attach and infect – Identification of a mosquito receptor for the *Plasmodium* ookinete - *A15641*

F Brod[4]; A Nobrega Pitaluga[2]; K Miura[3]; S Tapanelli[2]; W de Jongh[1]; C A Long[3]; G K Christophides[2]; S Biswas[4];
[1] ExpreS2ion Biotechnologies, Denmark; [2] Imperial College London, UK; [3] NIH: NIAID, United States; [4] University of Oxford, UK

The passage through the mosquito vector is a natural bottleneck in the malaria parasite's lifecycle, and therefore an attractive intervention target. Upon ingestion of *Plasmodium* gametocytes by a mosquito as part of a blood

meal, male and female gametocytes fuse to form a zygote which then matures into the motile ookinete. The ookinete penetrates the mosquito peritrophic matrix, followed by specific attachment to and traversal of the mosquito midgut epithelial cell layer. A number of proteins on the surface of the ookinete and the mosquito midgut epithelium have been suggested to be involved in this process, but whether specific protein-protein interactions facilitate attachment and invasion, and which proteins could form putative ligand receptor pairs, has not yet been comprehensively investigated. Identification of ligand-receptor interactions is often complicated due to low affinities which prevent them from being detected by conventional interaction screens. To overcome this problem, a library of ookinete and mosquito midgut surface proteins was generated to screen for interactions between *Plasmodium falciparum* and *Anopheles gambiae* using an avidity based extracellular interaction screen (AVEXIS), an assay specifically designed to detect low affinity interactions. This identified a highly conserved mosquito protein as a putative receptor for the well characterised transmission blocking antigen Pfs28. The protein comprises two transferrin like domains, and is expressed in high levels in the midgut and malpighian tubules in both male and female mosquitoes. The interaction was extensively characterised *in vitro*, which revealed that both transferrin like domains are required together to facilitate binding to Pfs28. A dissociation constant of 13 μM was determined by surface plasmon resonance, indicating the interaction could be functionally relevant at physiological concentrations. Preliminary *in vivo* studies on the effect of RNAi knock-down of the putative Pfs28 midgut receptor in *A. gambiae* on susceptibility to *P. falciparum* confirmed this hypothesis and suggests an important role for these proteins in midgut invasion by the ookinete. The interaction between Pfs28 and its midgut receptor is the first interaction between proteins of the ookinete and the mosquito midgut identified in *P. falciparum* invasion and establishment in *A. gambiae*. It could therefore provide a foundation for further efforts to unravel this still largely uncharacterized process and to guide the development of new interventions that could interfere with it.

10:15

Ms Karina Mondragon-Shem, *PhD Student, LSTM*

Exploring the salivary N-glycome of bloodfeeding arthropods and their relevance in pathogen transmission - *A15791*

K Mondragon-Shem[1]; K Wongtrakul-Kish[3]; R Araujo[4]; A Marques[4]; D Spencer[3]; R Kozak[3]; S Yan[5]; K Paschinger[5]; I Wilson[5]; M E Rogers[2]; M H Pereira[4]; A Acosta-Serrano[1];

[1] Liverpool School of Tropical Medicine, UK; [2] London School of Hygiene & Tropical Medicine, UK; [3] Ludger Ltd., UK; [4] Universidade Federal de Minas Gerais, Brazil; [5] University of Natural Resources and Life Sciences, Austria

The saliva of haematophagous arthropods is a cocktail of substances meant to facilitate bloodfeeding, by counteracting the host's healing processes. These salivary components can also elicit significant immune

responses, and while most research has focused on the salivary proteins, the sugars that modify them remain overlooked. Glycans influence a protein's biological role, and so can be partially responsible for the saliva's modulatory effects before, during and after pathogen transmission; furthermore, they can induce severe allergic reactions in some people. In some cases, salivary glycosylation pathways could influence viral glycosylation before transmission to the next host. In this work we studied the salivary glycome *Amblyomma cajennense*, *Anopheles gambiae*, *Aedes aegypti*, *Glossina morsitans*, *Lutzomyia longipalpis* and *Rhodnius prolixus*. To characterise the sugar structures in saliva we used a glycomics approach that included analyses by HPLC in combination with highly sensitive LC-MS/MS. Our work shows that the salivary glycoproteins of all these vectors are mostly composed of mannose-type sugars, with differences mainly in abundance of the various structures, as well as the presence of some hybrid sugars. Overlay work using recombinant fractions of human mannose receptors showed that salivary glycoproteins are positively recognised, which hints at *in vivo* interactions with macrophages and dendritic cells. These interactions may be responsible for the saliva-specific immune responses that affect the process of pathogen infection; additionally, they can have a role in the clearance (half-life) of the salivary glycoproteins themselves. Finally, the similarities of the sugars found indicate suggests the presence of conserved pathways of salivary protein glycosylation.

10:30

Mrs Alaa Al-Khafaji,
Cancelled

Protozoa Session

Protozoa: Cryptosporidium & Giardia –Sponsored by PLos NTDs- (Stream 2 - Llandinam A6) 14:15 to 15:45

Invited Speaker 14:15 - (30 mins)

Dr Karin Troell, *National Veterinary Institute, Sweden*
Recent advances in *Giardia* and *Cryptosporidium* genotyping - *A15203*

K Troell [1]
[1] National Veterinary Institute, Sweden

Giardia duodenalis and *Cryptosporidium* spp. are intestinal protozoan parasites of humans and other mammals, and are common causes of diarrheal disease worldwide. Both parasites are genotyped to determine species, but also to perform epidemiological studies, source tracking, and outbreak investigations. For *Giardia*, either single-gene PCR typing or multi-locus sequence typing (MLST) are used for genotyping. The variability of the traditionally

used markers (gdh, tpi and bg) are often high enough to discriminate subtypes of assemblage B isolates, but when applied on assemblage A isolates, low resolution is obtained. Recently, a set of six novel MLST markers were published, based on several whole genome sequences, and that can be used on Assemblage A isolates. These markers were shown to give a considerably higher resolution than the three commonly used loci, and were proven useful to discriminate between samples that were otherwise genotyped as identical. After species determination based on 18S sequencing sometimes, *Cryptosporidium* can be further subtyped using partial sequencing of the highly variable surface antigen gp60. However, this marker has limitations and a robust multi-locus typing scheme is desired. Recently a set of markers that can be used for fragment analysis was suggested for *C. parvum*. Similarly, a sequencing-based MLST scheme has been developed based on whole genomes sequences of many *C. parvum* isolates of both human and animal origin. An amplicon-based MLST scheme has been developed for the prevalent gp60 subtype, IbA10G2; this subtype that has previously proven difficult to type further as the variability on genome level is very low. In summary, genotyping of isolates contributes to the identification of parasite sources and routes of transmission. A well-designed multi-locus scheme should take into account recombination and needs to include unlinked markers, preferably located on different chromosomes. To maximise time and cost efficiency, it is useful to use a diversity index calculation to avoid using markers that provide redundant information.

14:45

Mr Arthur Morris, *PhD Candidate, Aberystwyth University*

Mining the genome of *Cryptosporidium* to elucidate transmission cycles - *A15783*

A Morris[1]; M Swain[2]; J A Pachebat[2]; R M Chalmers[4]; G Robinson[3];
[1] Aberystwyth University, UK; [2] Aberystwyth University - IBERS, UK; [3] *Cryptosporidium* Reference Unit, Public Health Wales, UK; [4] *Cryptosporidium* Reference Unit, Swansea, UK

In Wales there are ~300 reported cases of cryptosporidiosis per year, outbreaks of which can have significant health and economic impacts. The cause of cryptosporidiosis is the apicomplexan *Cryptosporidium*, a protozoan parasite with a complex life cycle. In the UK most cases of Cryptosporidiosis are caused by *C. parvum* or *C. hominis*. While self-limiting after prolonged duration of symptoms (2-3 weeks) in immunocompetent hosts, severely immunocompromised patients suffer severe, sometimes life threatening disease. Although all ages can be affected, cryptosporidiosis is most common in young children. In the developing world *Cryptosporidium* is one of the main causes of childhood morbidity. A recent large-scale study has evaluated the aetiology, burden and clinical syndromes of moderate-to severe diarrhoea in >20,000 children across seven sites in sub-Saharan Africa and South Asia and identified *Cryptosporidium* as one of the four highest contributors to diarrheal diseases worldwide

in children <5 years of age. Because of this, there is a growing need to develop novel prevention strategies in combating the spread of this parasite.

Currently, *Cryptosporidium* sp. subtyping is carried out via interrogation of a highly repetitive (Variable Number Tandem Repeat) region within the gp60 surface glycoprotein gene. This has furnished epidemiological studies with higher resolution data with which to investigate the transmission of *Cryptosporidium* throughout a population. However, recombination events at the gp60 locus have been demonstrated, due to the sexual nature of the *Cryptosporidium* life cycle. This proves to be a potential confounding issue in *Cryptosporidium* subtyping, and therefore epidemiological investigation. Here we present a bioinformatics tool developed to allow for the *in silico* automation of novel VNTR biomarker identification, with the intention of developing a more robust single or multi locus VNTR subtyping paradigm. Using this tool, 370 VNTR's were identified within coding regions in a dataset of 8 *C.parvum* genomes, of which 97 were seen to be polymorphic, and therefore suitably discriminatory. This data is useful for developing novel prevention strategies to be employed in the battle against cryptopsoridiosis.

15:00

Miss Bethan Carter, *Medical Student, Swansea University*

Acute symptoms and long-term sequelae of human cryptosporidiosis – a prospective study - *A15693*

B Carter[4]; R E Stiff[2]; B Mason[3]; H Hutchings[4]; A P Davies[4]; R M Chalmers[1];

[1] Cryptosporidium Reference Unit, Swansea, UK; [2] Health Protection, Public Health Wales NHS Trust, UK; [3] Public Health Wales Carmarthenshire, Wales, UK; [4] Swansea University Medical School, UK

Introduction: *Cryptosporidium* is the most common protozoal cause of acute gastroenteritis in the UK with between 3,500 and 5,500 laboratory-confirmed cases reported annually in England and Wales from 2013 to 2015. Cryptosporidiosis in immunocompetent patients is characterized by gastrointestinal symptoms that include a sudden-onset, profuse, watery diarrhoea which may be accompanied by abdominal pain or cramps, vomiting and weight loss. Other, more non-specific symptoms include malaise, fatigue, fever, nausea and muscle weakness. More than 90% of human cryptosporidiosis cases in developed countries can be attributed to just two *Cryptosporidium* species; *Cryptosporidium parvum*, a zoonotic species, and *Cryptosporidium hominis*, an anthroponotic species.

Relatively little is known about the longer term health effects of *Cryptosporidium* infection, with some potential sequelae identified and substantiated by solitary case reports. However, there is growing evidence to suggest that, rather like some bacterial causes of gastroenteritis, *Cryptosporidium* infection may have long-term consequences.

Aims: To investigate long-term health sequelae after resolution of acute cryptosporidiosis.

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Methods: This was a prospective study of cases aged >6 months old and resident in Wales, with laboratory confirmed cryptosporidiosis, genotyped at the Cryptosporidium Reference Unit, Swansea between July 2013 - July 2015. Participants self-reported symptoms, and clinician-diagnosed conditions, at three time points: within 2 weeks of laboratory diagnosis (baseline), at 3 months, and 12 months. To identify cases with symptoms consistent with irritable bowel syndrome (IBS) specifically, the standard Rome III criteria were used.
Results: Over the two-year recruitment period, 515 cases were contacted by our study team, 52% of which were < 18 years old. The predominant *Cryptosporidium* species identified was *C. parvum* (n 300) followed by *C. hominis* (n 200), *C. cuniculus* (n 9), *C. felis* (n 3), *C. hominis* & *C. parvum* (n 2) and *C. ubiquitum* (n 1). The response rate at baseline was 40%; 205 patients agreed to participate in our study. Long-term sequelae analysis was performed on 89 complete data sets (i.e. baseline, 3 month and 12 month questionnaires all returned). In the 12-month follow up period, 6 participants (8%) of developed Irritable Bowel Syndrome (IBS) according to Rome III criteria, while 34 participants (44%) reported IBS-like symptoms. Statistically significant new symptoms self-reported between 3 - 12 months post-infection included: fatigue (35%), abdominal pain (25%), nausea (24%), headache (24%), loss of appetite (21%), joint pain (21%), blurred vision (13%) and eye pain (10%).
At baseline, 205 patients (40%) agreed to participate in our study. Long-term sequelae analysis was performed on 89 complete data sets (i.e. baseline, 3 month and 12 month questionnaires all returned).

In the 12-month follow up period, 6 participants (8%) developed Irritable Bowel Syndrome (IBS) according to Rome III criteria, while 34 participants (44%) reported IBS-like symptoms.
Statistically significant new symptoms self-reported up to 12 months post-infection included: fatigue (35%), abdominal pain (25%), nausea (24%), headache (24%), loss of appetite (21%), joint pain (21%), blurred vision (13%) and eye pain (10%).

In the 12 months following resolution of acute illness, the self-reported symptoms nausea (RR: 0.07, 95% CI: 0.02 - 1.04, p = 0.05), abdominal pain (RR: 0.60, 95% CI: 0.06 - 6.44, p = 0.99), loss of appetite (RR: 0.89, 95% CI: 0.11 - 7.20, p = 0.99), fatigue (RR: 0.59, 95% CI: 0.20 - 1.69, p = 0.42), blurred vision (RR: 0.60, 95% CI: 0.18 - 2.05, p = 0.48) and eye pain (RR: 0.87, 95% CI: 0.21 - 3.56, p = 0.99) were less likely to be reported following *Cryptosporidium parvum* infection than *Cryptosporidium hominis* infection. Joint pain was more likely to be reported following C. parvum infection (RR: 4, 95% CI: 0.56 - 30.19, p = 0.14). However, none of these species differences were statistically significant.
15:15

Dr Tapan Bhattacharyya, *Research Fellow, London School of Hygiene & Tropical Medicine*
Giardia duodenalis in Ugandan children: field application of recombinase polymerase amplification and determination of assemblages - *A15703*

Go to here for the ‘at a glance’ view of the conference

T Bhattacharyya[3]; S Molina[3]; B Webster[5]; H Al Shehri[1]; S Allen[1]; J R Stothard[2]; M A Miles[4]; A Bustinduy[3];
[1] Liverpool School of Tropical Medicine, UK; [2] Liverpool School of Tropical Medicine / UoL, UK; [3] London School of Hygiene & Tropical Medicine, UK; [4] London School of Hygiene and Tropical Medicine, UK; [5] Natural History Museum, UK

Purpose of research. *Giardia duodenalis* is a worldwide gastro-intestinal protozoan pathogen. Symptomatic giardiasis afflicts around 200 million people in Asia, Africa and Latin America with around 500,000 new cases per year. Sensitive and specific DNA-based identification in resource-limited settings may enhance diagnosis, which currently relies on microscopy or antigen test of stool. Here we apply isothermal recombinase-polymerase amplification (RPA) to identify *Giardia* by specific β-giardin DNA sequences in human faecal samples from an endemic setting, and in addition we perform intra-species assemblage typing.
Principal results. n 238 of faecal samples collected from schools around Lake Albert, Uganda, were successfully DNA extracted. Results obtained to date reveal that n 21/122 were positive by initial qPCR screening for the presence of *Giardia* DNA, and that n 20/79 were positive by RPA during the optimisation phase. In addition, n 30 were typed by qPCR of the triose phosphate isomerase gene as assemblage A, n 15 as Assemblage B, and n 14 as mixed assemblage infection
Major conclusions. This is the first application of RPA to field samples from Uganda or Africa; with further refinement, it can be adapted to a point-of-care, rapid, sensitive and specific test for the diagnosis of *Giardia* in faecal samples. The *Giardia* assemblages identified from human faecal samples expand the knowledge of circulating assemblages in Uganda, and can be used as the basis for association studies of symptomatic giardiasis.

15:30

Mr Kevin Tyler, *Senior Lecturer, University of East Anglia*
Giardia secretome highlights secreted tenascins as a key component of pathogenesis *- A15351*

A Dubourg[2]; D Xia[3]; M Bouzid[2]; J Wastling[1]; P Hunter[2]; **K M Tyler**[2];
[1] Keele University, UK; [2] Norwich Medical School at UEA, UK; [3] Royal Veterinary College, UK

Giardia is a protozoan parasite of public health relevance that causes gastroenteritis in a wide range of hosts. Two genetically distinct lineages (assemblages A and B) are responsible for the human disease. Although it is clear that differences in virulence occur, pathogenesis and virulence of *Giardia* remains poorly understood.

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The genome of *Giardia* is believed to contain ORFs that could encode as many as 6,000 proteins. By successfully applying quantitative proteomic analyses to the whole parasite and to the supernatants derived from parasite culture of assemblages A and B, we confirm expression of ~1,600 proteins from each assemblage, the vast majority of which being common to both lineages. To look for signature enrichment of secreted proteins, we considered the ratio of proteins in the supernatant compared with the pellet, which defined a small group of enriched proteins, putatively secreted at a steady state by cultured growing trophozoites of both assemblages. This secretome is enriched with proteins annotated to have N-terminal signal peptide. The most abundant secreted proteins include known virulence factors such as cathepsin B cysteine proteases and members of a *Giardia* superfamily of cysteine rich proteins that comprises VSPs, HCMPs and a new class of virulence factors, the *Giardia* tenascins. We demonstrate that physiological function of human enteric epithelial cells is disrupted by such soluble factors even in the absence of the trophozoites.
In conclusion, we are able to propose a straightforward model of *Giardia* pathogenesis incorporating key roles for the major *Giardia* derived soluble mediators.

Helminth Sessions

Helminths: Cell & Molecular Biology - (Stream 3 - Physics 0.15 Main) 09:30 to 11:00

Chair - Prof Tim Yoshino
Invited Speaker 09:30 - (30 mins)

Dr Jim Collins, *UT Southwestern Medical Center*
Molecular analysis of schistosome reproductive development *- A15199*

J Collins [1]
[1] UT Southwestern Medical Center, Texas, USA

Schistosomiasis is a neglected tropical disease that affects hundreds of millions of the world's poorest people. The pathology of schistosomiasis stems from the fact that these parasites lay hundreds-to-thousands of eggs per day while living in the vasculature. Therefore, understanding the mechanisms that control the development and maintenance of the schistosome reproductive system could present new opportunities to limit the spread of the disease and blunt the pathology caused by the parasite. Interestingly, female schistosome sexual development depends of constant physical contact with a male worm. Although this phenomenon was described almost 100 years ago, there are few molecular insights into how this process is regulated. A major stumbling block for addressing this issue is that the reproductive system of female schistosomes degenerates within days of being removed from the host. Therefore, detailed studies of schistosome reproduction have not previously been possible

using molecular approaches. To address this issue we have developed a novel media formulation that supports male-induced female sexual development and long-term egg production *in vitro*. Using this media we have discovered a role for a parasite-specific nuclear receptor that is essential for female reproductive development. We are exploring the model that this receptor is activated in females upon pairing with a male worm. We are hopeful the application this new media, together with modern approaches, will allow us to address how female schistosome reproductive development is controlled on a molecular level.

10:00

Prof Anthony Walker, *Professor of Cell Biology, Kingston University*
SGTP4–mediated glucose uptake in *Schistosoma mansoni* is regulated through Akt/PKB signalling - *A15281*

M Mckenzie[1]; R S Kirk[1]; **A J Walker**[1];
[1] Kingston University, UK

In the blood fluke *Schistosoma mansoni*, the facilitated glucose transporter SGTP4 is expressed exclusively in the apical double-bilayer membranes of mammalian-resident life stages, and is surface exposed. This transporter imports glucose from the host blood to support the growth, development and reproduction of the parasite. However, the molecular mechanisms that underpin SGTP4-mediated glucose uptake are not understood. Here, through biochemical characterization/functional confocal microscopy mapping of *S. mansoni* Akt/Protein kinase B (PKB), we discover a crucial role for Akt/PKB signalling in this process. We find that Akt/PKB, which could be activated by molecules such as host insulin and L-arginine, was active in the tegumental layer of both schistosomules and adult worms. Blockade of Akt/PKB blunted the expression and evolution of SGTP4 at the surface of the host-invading larval parasite life-stage, and suppressed SGTP4 expression in the tegument of adult worms. Concomitant glucose uptake by the parasite was also significantly attenuated in both scenarios. These findings shed light on crucial mechanistic signalling processes that underpin the energetics of glucose uptake in schistosomes. Given that the adult worms consume their dry weight in glucose every five hours, our results highlight the potential for targeting tegumental glucose transport signalling processes for parasite elimination.

10:15

Dr. Paul Brindley, *Professor, George Washington University*
Somatic genome editing in the multicellular blood fluke *Schistosoma mansoni* - *A15379*

Go to here for the 'at a glance' view of the conference

W Ittiprasert[3]; V Mann[3]; S Karinshak[3]; T Tanno[4]; G Rinaldi[6]; A Coghlan[6]; P Driguez[6]; M Mentink-Kane[2]; C Hokke[5]; K Hoffmann[1]; M Berriman[6]; **P Brindley**[3];
[1] Aberystwyth University - IBERS, UK; [2] Biomedical Research Institute, Rockville, Maryland, United States; [3] George Washington University, United States; [4] Institute of Human Virology, University of Maryland, United States; [5] Leiden University Medical Centre, Netherlands; [6] Wellcome Trust Sanger Institute, UK

We investigated the feasibility of programmed genome editing in schistosomes. Soluble egg antigen (SEA) and excretory-secretory (ES) products of the egg of *Schistosoma mansoni* contain a glycoprotein T2 family ribonuclease termed omega-1 (ω1). Following release from the egg, ω1 instructs antigen presenting cells to induce naïve CD4+ T cells to mature into T helper 2 (Th2) effectors that, in turn, ultimately drive the immunological phenotype characteristic of schistosomiasis. Schistosome eggs were either transiently exposed to recombinant Cas9 complexed with a synthetic guide RNA (sgRNA) of 20 nt complementary to exon 1 of ω1 by electroporation, or infected with pseudotyped lentivirus encoding Cas9 and the sgRNA, the latter undertaken to prolong expression of and exposure to sgRNA/Cas9 in the schistosome tissues. Subsequently, the eggs were transduced with single stranded deoxynucleotide bearing 5'- and 3'- homology arms of 50 nt each matching the predicted Cas9-catalyzed double stranded break (DSB) in ω1 and a central transgene that included six stop codons. Levels of ω1-encoding mRNA were reduced up to 83%, indicative that programmed Cas9 cleavage had mutated the ω1 gene and the DSB in schistosome chromosomes had been resolved by non-homologous end joining (NHEJ) and/or homology direct repair (HDR). Analysis assisted by the CRISPResso pipeline of sequence reads of amplicons spanning the predicted DSB site revealed ~5% of the reads (read depth, 2×10^6) were mutated by insertions, deletions and/or substitutions, with an efficiency for HDR of 0.18% insertion of the donor transgene. Ribonuclease activity of SEA from ω1-mutated eggs was diminished markedly and SEA from ω1-mutated eggs failed to induce pronounced secretion of Th2 cytokines, IL-4, IL-5 and IL-13 *in vitro*, in comparison to wild-type SEA. To conclude, programmed genome editing was functional and facile in schistosomes, Cas9-catalyzed chromosomal breakage was repaired by NHEJ and/or HDR, and mutation of ω1 impeded the capacity of schistosome eggs to establish macrophage polarization of inflammation response and polarize CD4+ T cells into Th2 effectors.

10:30

Dr Carolina De Marco Verissimo, *Research Fellow, Queen's University Belfast*
A propeptide 'clamp' mechanism is required for inhibition of *Fasciola hepatica* Collagenolytic Cathepsin L3 - *A15612*

I Pritsch[1]; I Tikhonova[2]; H Jewhurst[2]; O C Drysdale[2]; K Cwiklinski[2]; M Molento[1]; J P Dalton[2]; **C M Verissimo**[2];
[1] Department of Basic Pathology, Federal University of Parana, Brazil; [2] Queen's University Belfast, UK

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Cysteine proteinases are important *Fasciola hepatica* virulence molecules. Among the various cathepsins that *F. hepatica* expresses, cathepsin L3 (FhCL3) secreted by the newly excysted juveniles (NEJs) is of special interest due to its central role in host invasion. Its unique collagenolytic activity facilitates the rapid passage of the NEJ through the host gut wall. To protect cells and tissues integrity cathepsins are initially produced as inactive zymogens whereby the enzyme-specific N-terminal propeptide (pp) is responsible for regulating the catalytic activity. Accordingly, it has been suggested that propeptides represent a structural template on which to develop specific cathepsin inhibitors. Here, differential immunolocalization of the FhCL3 zymogen and its pp in NEJ's and immunoblotting of NEJ excretory-secretory products show that most of FhCL3 zymogen is releasing the pp in the parasite gut. We also investigated the inhibitory properties and mechanisms of FhCL3 propeptide (ppFhCL3), revealing that it is a highly potent and selective inhibitor of *F. hepatica* cathepsin L's. Using 3-D structural data we made amino acids substitutions in the ppFhCL3 at residues that we found are involved in interaction within the propeptide bind loop (PBL) of the mature enzyme ($Tyr^{46}Lys^{47}$/$Ala^{46}Ala^{47}$) or within the active site (Leu^{66}/Gly^{66}). Our enzyme kinetics and inhibitory studies unveiled a 'clamp' mechanism that is required for the proper binding and inhibitory activity of the pp to FhCL3. In summary, our results give remarkable insights regarding the propeptide-cathepsin interaction and open up the possibility of exploring these features in order to design new and selective inhibitors for *F. hepatica* cathepsins.

10:45

Mr Manjurul Haque, *PhD Student, McGill University*

Maternal nematode infection induces transcription of Long-term potentiation in the postnatal brain via Wnt signaling - *A15696*

M Haque[2]; K G Koski[3]; M E Scott[1];

[1] Institute of Parasitology, McGill University, Canada; [2] McGill University, Canada; [3] School of Human Nutrition, McGill University, Canada

Background: Development of the mammalian brain initiates at early pregnancy and continues postpartum through neural differentiation, migration and synaptogenesis until early adulthood. Maternal intestinal nematode infection has been shown to alter fetal brain gene expression in mice and here we used next generation RNA sequencing to determine whether this maternal influence continues postpartum.

Methods: Timed-pregnant CD1 mice were either infected with four doses of 100± 3 Heligmosomoides bakeri larvae (gestation day [GD] 7, 12, 17, postpartum day [PPD] 3) or intubated four times with distilled water (n 5 / group). On PPD 7, six pups were randomly selected from each litter, livers and brains were collected, and pup sex

was determined by PCR. Brain RNA was extracted and sequenced in the illumina Hi-seq sequencer from one male pup per litter. HTSeq was used to count expressed transcripts and differential expression of genes was determined by edgeR. The Protein-protein interaction networks of the differentially expressed genes were generated by functional exploration against KEGG pathway database.
Results: Using a P value cut-off of 0.05 and log2 fold-change cut-off of 1, a total of 5736 differentially expressed genes were recorded. Among them, 2751 were up-regulated and 2985 were down-regulated. Pathway analysis revealed upregulation of a number of favorable pathways. Long-term potentiation (LTP) was of particular interest as synaptogenesis is one of the main events in postnatal brain development. Our data showed up-regulation of all five sequential pathways and receptors required for synaptic plasticity and LTP: Wnt signaling, N-methyl D-aspartate receptors (NMDARs), Ca+ signaling, ras-MAPK signaling, and α-amino-3-hydrozy-5-methylisoxazole-4-propionic acid receptors (AMPARs). On the other hand, several pathways that respond to stress and inflammation were down-regulated including p53 signaling and cytokine-cytokine receptor interaction, suggesting that maternal nematode infection might provide a less stressful inflammatory milieu during postnatal brain development.
Conclusion: Exposure to maternal nematode infection altered the postnatal brain gene expression which may have a positive impact on postnatal brain development, synaptic plasticity and LTP. **Funding:** NSERC

Helminths: Epidemiology & Field Work - Sponsored by Elsevier- (Stream 3 - Physics 0.15 Main) 14:15 to 15:45

Invited Speaker 14:15 - (30 mins)

Prof Joanne Webster, *Royal Veterinary College*

Epidemiology and evolution of zoonotic schistosomiasis in Africa: challenges for reaching the WHO elimination targets' - *A15187*

J Webster[1]
[1] Royal Veterinary College, UK

Schistosomiasis (or Bilharzia), is a serious disease of humans and animals caused by schistosome parasitic worms, inflicting suffering on poor rural communities in many parts of the developing world, with the greatest burden within sub-Saharan Africa. Schistosomes are transmitted through eggs passed in stool or urine, depending on the parasite species, which then infect snails in freshwater. The mammalian definitive host, be it human, livestock and/or wildlife, becomes infected when entering freshwater containing infected snail intermediate hosts. Anthropogenic change, through natural phenomena or human interventions such as dam constructions, changes in agricultural practices or drug treatments, impact the dynamics and distribution of this disease, with subsequent

effects upon human and animal health. Such changes can increase opportunities for schistosome species of both humans and animals to be found in the same geographical area and in the same host type. Furthermore, human and animal schistosomes can pair to produce viable zoonotic hybrid infections, which can subsequently infect both humans and their animals. Focusing within Niger and Senegal, we are performing research to elucidate for the first time how common these hybrid schistosomes are in humans and animals, what harm they might do to their hosts, how easily they might spread, how they respond to drug treatment, and ultimately how we can control and prevent them.

14:45

Dr Poppy Lamberton, *Senior Lecturer, University of Glasgow*
Schistosoma mansoni praziquantel treatment: low coverage driven by systematic non-compliers or systematically not offered? - *A15139*

M Adriko[2]; C L Faust[1]; L V Carruthers[1]; M Arinaitwe[2]; E Tukahebwa[2]; **P H L Lamberton**[1];
[1] Institute of Biodiversity, Animal Health and comparative Medicine, and Welcome Centre for Parasitology, University of Glasgow, UK; [2] Vector Control Division, Ministry of Health, Uganda

In 2002 Uganda began praziquantel Mass Drug Administration (MDA) in *Schistosoma* endemic communities across 79 districts. The World Health Organization recommends community-wide treatment in areas where prevalence in school-aged children (SAC) is >50%, aiming to reach >75% of SAC and adults/year in these areas. Most mathematical models assume the untreated proportion are randomly distributed. While others assume a small proportion are systematic non-compliers, and the rest are randomly distributed. MDA coverage is often only reported at a district level. To address a gap in our understanding of individual's annual and lifetime treatment, we undertook detailed mapping and household surveys in two villages, Bugoto A and B, in Mayuge District, Uganda, a high endemicity area (92% SAC infected, 2017) on the shores of Lake Victoria which has received community-wide MDA for 15 years. From Feb-March 2017, a total of 676 households (>90%) and all associated pit latrines were GPS mapped. Comprehensive data on praziquantel coverage, socio-economic indicators, and other individual-level risk factors were collected from 3,335 individuals. Praziquantel uptake was low compared to other studies, especially among adults, with an overall 2016 coverage of 35% (61% in SAC). Only 70% of SAC and 50% of adults had ever taken praziquantel. Side effects were rarely the reason for not taking it. Most untreated individuals were either not offered the drug, not bothered, or absent from the village during MDA. Other risk factors linked with never being treated included living in Bugoto A (the predominantly lakeside, fishing community, with higher infection levels), being >15y, and not sleeping under a mosquito net. To our knowledge, this is the first study to record lifetime coverage, reporting chronically untreated individuals, who, contrary to expectation are rarely

systematic non-compliers but are better described as systematically not-offered. This has implications for human disease reservoirs and ethical issues associated with morbidity. Improved interventions may be able to better reach these people and easier to implement than side effects education.

15:00

Ms Rachel Francoeur, *PhD Student, Rachel Francoeur*
Impact of malaria coinfections on *S. mansoni* clearance, intensity and reinfection rates - *A15598*

R Francoeur[1]; A Wamoko[2]; P H Lamberton[1];
[1] Institute of Biodiversity, Animal Health and comparative Medicine, and Wellcome Centre for Parasitology, University of Glasgow, UK; [2] Vector Control Division, Ministry of Health, Republic of Uganda, Uganda

Schistosomiasis and malaria are the two most significant human parasitic diseases. Schistosomiasis is a commonly occurring neglected tropical disease with over 240 million people infected globally. In 2016, there were 216 million cases of malaria worldwide resulting in an estimated 731,000 deaths. Praziquantel is the standard chemotherapeutant in treating schistosomiasis however, in certain endemic hotspots, despite over a decade of mass drug administration (MDA), infection intensities and prevalence remain higher. Past studies indicate a correlation between increased risk of malaria contraction in individuals with schistosomiasis. However, it is unknown if malarial infections play a role in susceptibility to reinfection with schistosomiasis, nor whether drug efficacy is influenced. This study investigates the impact of malaria coinfections on *Schistosoma mansoni* includinginfection intensity, clearance post treatment, and reinfection rates.Samples were obtained from 197 school children aged 6-14 in the Mayuge district of Uganda who were tested for *S. mansoni* and *Plasmodium falciparum*. Infection data were obtained using Kato-Katz for *S. mansoni* egg counts and RDT tests for *P. falciparum*. Results from regression analysis will be presented on correlations between co-infected individuals, clearance, and reinfection rates compared with those infected with only *S. mansoni*. These results will contribute to a broader biostatistical study looking at host factors that influence *S. mansoni* clearance.

15:15

Dr Louise Hamill, *Post-doctoral researcher, Liverpool School of Tropical Medicine*
Alternative strategies for onchocerciasis elimination in loiasis co-endemic areas: test-and-treat with doxycycline in combination with targeted vector control in South West Cameroon - *A15726*

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L Hamill[1]; R Ekenya[2]; P W Ndongmo[2]; B Ndzeshang[2]; D Nkimbeng[2]; A Amuam[2]; J D Turner[1]; P A Enyong[2]; S Wanji[2]; M J Taylor[1];
[1] Liverpool School of Tropical Medicine, UK; [2] University of Buea, Cameroon

Community Directed Treatment with ivermectin (CDTi) is the current mainstay for onchocerciasis control. In addition, sustained annual or biannual use of CDTi has delivered onchocerciasis elimination in specific focal settings, and reduced prevalence of disease in others. However, in areas where *Onchocerca volvulus* infection overlaps with the related filarial parasite, *Loa loa,* ivermectin cannot be safely implemented at scale, since individuals with high *L. loa* parasitaemias can suffer from severe adverse events (SAEs), including coma and death. Readily implementable alternative strategies to CDTi are therefore needed in loiasis co-endemic areas of Central Africa if 2025 elimination targets are to be achieved. The COU**NTD**OWN consortium is trialling co-implementation of 5-week 100mg/day doxycycline (a macrofilaricidal antibiotic that targets *O. volvulus* obligate symbiotic bacteria *Wolbachia*), alongside focal vector control to reduce *Simulium* blackfly biting rate in the Meme river basin, South-West Cameroon. Further, societal and health economic data are being captured to analyse acceptability and feasibility of the approach. Here we present the study design and results from baseline parasitological surveys, including self-reported adherence to ivermectin, community microfilarial load, prevalence of *O. volvulus* skin microfilariae, prevalence of *L. loa*, blackfly cytospecies and susceptibility testing.

15:30

Dr Corrado Minetti, *PDRA, Liverpool School of Tropical Medicine*
Elimination within reach: lymphatic filariasis persists in rural Ghana due to sub-optimal intervention coverage and adherence - *A15516*

C Minetti[3]; E J Tettevi[1]; F Mechan[3]; J M Prada[4]; B Idun[1]; N K Biritwum[2]; M Y Osei-Atweneboana[1]; L J Reimer[3];
[1] Council for Scientific and Industrial Research Water Research Institute, Ghana; [2] Ghana Health Service, Ghana; [3] Liverpool School of Tropical Medicine, UK; [4] University of Surrey, UK

Despite the progress achieved in scaling-up mass drug administration (MDA) for lymphatic filariasis (LF) in Ghana, communities with persistent LF still exist despite over 10 years of community treatment. To assess the status of disease elimination and understand the adherence to interventions including MDA and insecticide treated nets, we conducted a parasitological and epidemiological study in people 16y of age and older from eight villages still under MDA in the Northern and Western Regions. We used a stochastic model (TRANSFIL) to assess the expected microfilaria prevalence under different MDA coverage scenarios using available historical data on one community. Prevalence of filarial antigen ranged 0 to 29.2% and the prevalence of night blood microfilaria (mf) was estimated

to range from 0 to 5.5%. Median mf density was 67 mf/ml (range: 10-3,560). Antigen positivity was positively associated with male sex but negatively associated with participating in MDA the previous year. Male sex was also associated with a decreased probability of participating to MDA and both owning and using a bed net. Using one community as an example, the model simulations suggested that the MDA coverage was slightly lower than reported. There is a need for an integrated quantitative and qualitative research approach to identify the variations in prevalence, associated risk factors and intervention coverage and use levels between and within regions and districts. Such knowledge will help target resources and enhance surveillance to the communities most at risk and to reach the 2020 LF elimination goals in Ghana.

Omics Session

Omics II - (Stream 1 - Edward Llwyd 0.26 Biology Main) 09:30 to 11:00

Chair - Dr Martin Swain

Invited Speaker 09:30 - (30 mins)

Prof Cornelis Hokke, *Professor of Glycobiology of Host-Pathogen Interaction, Leiden University Medical Center*

Helminth glycans at the host-parasite interface - *A15207*

C Hokke[1];

[1] Leiden University Medical Center, UK

Helminths express an abundance of proteins and lipids with specific and complex glycosylation patterns. Glycomics studies of helminth glycosylation are providing more and more insights into glycan and glycoconjugate expression of different helminth species. Schistosomes are one of the best studied parasitic helminths with respect to structural as well as functional glycomics. In the mammalian host antigenic glycans of larvae, worms and eggs of schistosomes induce specific antibodies to numerous glycan motifs, and glycans initiate or modulate innate immune responses and cellular uptake of glycoconjugates via host lectins. In the intermediate snail host specific glycans of miracidia and sporocysts interact with glycan-binding proteins in the hemolymph determining aspects of snail-schistosome compatibility. To provide a clear map of schistosome glycosylation in support of functional studies of host-parasite glycobiology we applied mass spectrometric (MS) glycomics approaches to determine the expression profiles and structural identity of hundreds of glycans expressed during the schistosome life cycle. Striking shifts and switches in the expression of putative functional glycan motifs during during worm and egg development were identified suggesting various roles of glycans and associated anti-glycan responses during infection. In addition, we have generated a microarray of hundreds of N-, O-, and lipid-glycans covering the entire

glycome of *S. mansoni*. The constructed glycan microarray was used to determine IgG and IgM to each glycan in a number of human and animal infection cohorts. Using clear examples I will discuss how glycan motifs contribute to immunological properties of schistosome antigens, such as the immunomodulatory omega-1 glycoprotein. Also, based on cross-sectional and longitudinal glycan screens of antibodies in sera from natural and experimental schistosome infections, I will discuss the potential of antibodies against schistosome-specific Fucα1-2Fucα1-3-R glycan motifs in the development of glycan targets for vaccines and diagnostics. Glycomics-driven studies of helminths and helminth infections provide clear contributions to the development of novel therapeutics and control tools.

10:00

Professor Christoph G Grevelding, *Professor for Parasitology, Justus-Liebig-University Giessen*
Deciphering gonad-transcriptomes in *Schistosoma mansoni* provides novel and exploitable insights for basic and applied research - *A15668*

C G Grevelding[4]; S Hahnel[3]; S Langner[4]; T Quack[4]; C Dissous[1]; N J Wheeler[2]; T A Day[2]; P McVeigh[6]; A Wangwiwatsin[7]; N Holroyd[7]; M Berriman[7]; P Ribeiro[5]; Z Lu[7];
[1] CIIL- Center for Infection and Immunity of Lille Inserm U1019, CNRS UMR 8204, Institut Pasteur Lille, France; [2] College of Veterinary Medicine, Iowa State University, United States; [3] Department of Molecular Biosciences, Northwestern University, United States; [4] Institute of Parasitology, BFS, Justus-Liebig-University Giessen, Germany; [5] Institute of Parasitology, McGill University, Montreal, Canada; [6] Queen's University Belfast, UK; [7] Wellcome Trust Sanger Institute, UK

As one of the exceptional biological features of schistosomes, the adult female achieves sexual maturation only if it is constantly paired with the male. Although the male is sexually mature before pairing, it is assumed that the male-female interaction of schistosomes is a bidirectional process. However, not much is known about the complexity of pairing-dependent gene expression, especially with respect to the gonads. Based on a recently established isolation approach for complete reproductive organs, we performed comparative transcriptomics with RNA of ovaries and testes from both paired and unpaired adult *S. mansoni*. By RNA-seq we identified transcripts of >7,000 genes in the gonads of both sexes. Although transcript levels of the majority of these genes (>4,000) were pairing-unaffected in both gonads, transcripts of 243 (testes) and 3,600 (ovaries) genes occurred pairing-dependently. Among these, 309 and 42 differentially transcribed genes showed ovary-specific and testis-specific transcriptional activity, respectively.
Detailed bioinformatics analyses provided new insight into the role of the *S. mansoni* kinome, which consists of 357 kinases. Of these 268 protein kinases (pks) and 83 non-protein kinases (non-pks) are transcribed in adult

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S. mansoni. Remarkably, many of the adult-stage pk and non-pk genes exhibited a pairing-dependent and gonad-preferential transcript occurrence. This highlights the importance of kinases in the reproductive development of this parasite. In schistosomes GPCRs represent the largest receptor family comprising 115 receptors in *S. mansoni*. Of these 60% are transcribed in adults, covering all classes of the phylogenetic analyses. Furthermore, we obtained new insights into the potential roles of GPCRs in the male-female interaction, including participation in both gonad-specific functions, and in gonad-unrelated, pairing-dependent processes. Finally, a first GPCR-selective *in silico* comparison to *Fasciola* genome data revealed a high congruence between both GPCR*omes*.
Importantly, kinases and GPCRs represent interesting molecules as they are potentially druggable targets. New targets are urgently needed in the face of drug resistance and an alarmingly limited repertoire of available drugs to fight schistosomes and other parasitic worms. Therefore, the work reported here has relevance for both basic and applied parasitology research.

10:15

Dr Tiago Ferreira, *PDRA, University of York*

Regulation of RNA-binding protein stability and function by PRMT7-dependent arginine methylation in *Leishmania - A15530*

T R Ferreira[3]; A A Dowle[2]; E V Alves-Ferreira[3]; T R Larson[2]; A K Cruz[1]; P B Walrad[3];
[1] University of São Paulo, Brazil; [2] University of York, UK; [3] University of York, Centre for Immunology and Infection, UK

Protein aRginine MethylTransferases (PRMTs) catalyse arginine methylation in various cellular processes. The chromatin modifier PRMT7 is the only Type III PRMT found in higher eukaryotes and a restricted number of unicellular eukaryotes. *Leishmania major* PRMT7 is a cytoplasmic protein implicit in pathogenesis with unknown substrates. Using comparative methyl-SILAC proteomics for the first time in protozoa, we identified 40 putative targets, including 17 RNA-binding proteins (RBPs) hypomethylated in PRMT7 null mutants. *In vitro,* PRMT7 can modify RBPs Alba3 and RBP16 as direct substrates. *In vivo* PRMT7 knockout reduces both RBP16 protein half-life and Alba3 mRNA-binding capacity. RNA immunoprecipitation (RIP) analyses demonstrate PRMT7-dependent methylation promotes Alba3 association with target transcripts and consequent stability of *delta-amastin* surface antigen. These results highlight a novel role for PRMT7-mediated arginine methylation of RBP substrates, suggesting a post-translationally-directed regulatory pathway controlling gene expression and virulence in *Leishmania*. This work introduces *Leishmania* PRMTs as epigenetic regulators of mRNA metabolism with novel mechanistic insight into the functional manipulation of RBPs by methylation.

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10:30

Dr James Cotton, *Senior Staff Scientist, Wellcome Trust Sanger Institute*
Population genomics of Guinea worm eradication - *A15709*

C Durrant[7]; N Holroyd[7]; E A Thiele[5]; [6]; S R Doyle[7]; G Sallé[2]; A Tracey[7]; G Sankaranaranayan[7]; M Lotkowska[7]; E Ruiz-Tiben[3]; [4]; M Eberhard[1]; M Berriman[7]; J A Cotton[7];
[1] Centers for Disease Control and Prevention, United States; [2] INRA, France; [3] The Carter Center, UK; [4] The Carter Center, United States; [5] Vassar College, UK; [6] Vassar College, United States; [7] Wellcome Trust Sanger Institute, UK

Historically, Guinea worm - *Dracunculus medinensis* - was one of the major parasites of humans. It is also one of the best known, and has been known since antiquity. Today, Guinea worm is on the brink of eradication, as control efforts have reduced the burden of disease from millions of infections per year in the 1980s to only 30 human cases reported globally last year. Despite this enormous success of the control efforts to date, one major complication has arisen, as last year there were 817 dogs in Chad reported to be infected with this previously apparently anthroponotic parasite. In an effort to shed light on the peculiar epidemiology of Guinea worm in Chad, we have generated a reference genome for *Dracunculus medinensis* and a related species, and genomic sequence data for worms from dog and human infection. We show that the same population of worms are causing both infections, can confirm transmission between host species and detect signs of a population bottleneck due to the eradication efforts. The diversity of worms in Chad appears to exclude the possibility that there were no, or very few, worms present in the country during a 10-year absence of reported cases.

10:45

Dr Jessica Kissinger, *Professor & Director, IOB, University of Georgia*
Details matter - Consistent, comparative and evidence-based genome annotation and re-annotation for the closely-related species, *Cryptosporidium parvum*, *C. hominis* and *C. tyzzeri* reveal surprising similarities and differences - *A15756*

R P Baptista[1]; Y Li[1]; A Sateriale[2]; B Striepen[2]; **J C Kissinger**[1];
[1] University of Georgia, United States; [2] University of Pennsylvania, United States

New genome sequences for parasites in the genus *Cryptosporidium* are emerging with regularly. However, because of insufficient starting material, non-clonal infections, the use of short-read sequencing technologies and poor availability of experimental resources needed for validation, fundamental gaps in our characterization of the

genome sequence exist. We do not have complete chromosomal assemblies with confirmed genome structure for each species, we lack experimentally confirmed gene content/annotation and most importantly, we lack information on gene function. Our aim has been to generate the best possible structural and functional genome annotation for three closely related species of *Cryptosporidium*, *C. parvum* strain IOWA, a patient isolated strain, *C. hominis* 30976 and the new *Cryptosporidium* mouse model species, *C. tyzzeri,* using all available public data. Using ESTs, cDNA, RNA-Seq, mass spectrometry proteomics data, synteny and gene orthology information, we trained three different gene prediction tools and all data were added as evidence tracks in WebApollo2 for manual curation of all three genome sequences. Relative to the previous genome annotations available for *C. parvum* IOWA and *C. hominis* TU502 genome, > 1,500 changes to the structural annotation have been made. These changes are related to altered gene boundaries, such as adding UTRs, altering the start codon and updating or adding intron features, as well as adding > 50 new RNA-seq supported genes to the annotation. More than 800 evidence-supported introns have been added to each genome sequence annotation and and alternative splicing is detected. Many previously annotated single-copy genes are shown to be multi-copy and copy number variation is detected between the species. The functional analysis was greatly improved and domains have been identified in many uncharacterized proteins and 98 additional transporters have been identified. Although the number of characterized proteins is greatly improved, approximately ~35% of the annotated genes in each species are still characterized as hypothetical. Additional experimental data are essential for bettering our understanding of *Cryptosporidium*. The new annotations have been submitted prepublication to CryptoDB.org and GenBank to facilitate immediate access by the research community.

Posters

Miss Shradha Maharjan, *Student, Kingston University*

Poster 1 : Host-parasite signalling through lipid rafts in the human parasite *Schistosoma mansoni*

S Maharjan[1]; R S Kirk[1]; S P Lawton[1]; A J Walker[1];
[1] Kingston University, UK

Lipid rafts are microdomains present in plasma membranes that are rich in cholesterol and sphingolipids. As lipid rafts are thought to play an important role in signal transduction, the presence of lipid rafts in the tegument of *Schistosoma mansoni* schistosomules (somules) and their potential role in molecular communication with the host

was investigated. Twenty-four hour *in vitro*-cultured somules were stimulated with human epidermal growth factor (EGF) and stained for lipid rafts. Confocal laser scanning microscopy revealed that lipid raft clusters were present in the tegument of somules and were preferentially localized towards the anterior cone of the parasite. Furthermore, a number of lipid raft-associated proteins were detected by western blotting/immunofluorescence including flotillin, Ras, and Gq that were predominantly expressed in the parasite tegument; Ras and Gq were also localised in structures like the acetabulum and cephalic ganglia. Epidermal growth factor receptors (EGFRs) were mapped on somules using fluorescence-labelled EGF and were discovered towards the anterior cone of the parasite, consistent with the localisation of lipid rafts. Next, detergent resistant membranes were prepared and proteomic analysis carried out to reveal which proteins are present in these structures. A total of 287 proteins were identified in both triton-insoluble (TI) and triton-soluble (TS) fractions, of which 41 were specifically identified in the TI fraction only. Current experiments on the effect of raft disruption using methyl-beta-cyclodextrin (MBCD) on signalling pathways suggest that cholesterol levels modulate phosphorylation/activation of protein kinase C (PKC), extracellular signal-regulated kinase (ERK), p38 mitogen-activated protein kinase (p38 MAPK) and Akt pathways. Future work aims to further characterise the lipid rafts and elucidate their importance to schistosome survival and host-parasite interactions.

Dr Janine Coombes, *Lecturer, University of Liverpool*

Poster 2 : Developing a 3D intestinal epithelium model for studying gastrointestinal infections of livestock species

H Derricott[2]; L Luu[2]; N Randle[2]; S D Armstrong[2]; B J Campbell[2]; C A Duckworth[2]; J Wastling[1]; **J L Coombes**[2]; C Hartley[2];

[1] Keele University, UK; [2] University of Liverpool, UK

Infections of the gastrointestinal tract cause serious economic and welfare issues in agriculture, and carry a risk of zoonotic transmission. A better understanding of the earliest post-infection events occurring at the intestinal epithelium is required to develop novel therapeutics and vaccines that would address concerning rises in anti-microbial resistance. The *in vitro* 3D culture of intestinal epithelium isolated from mice or humans as organoids (or "mini-guts") has generated a large volume of data on epithelial development, physiology, and disease in the species. However, the potential importance of organoid cultures in veterinary health and zoonotic disease research has been largely overlooked. By modifying and refining protocols for the culture of murine organoids, we have successfully established porcine and bovine intestinal organoids, which remain viable and regenerate in culture for a period of several months. Importantly, we were able to utilize tissue obtained from abattoirs that would otherwise be considered a waste-product of food production, providing an accessible, ethically-sound and continuous source

of material. Further, we demonstrated that our organoid cultures are susceptible to infection by *Toxoplasma gondii* and *Neospora caninum*, and show host-species specific responses. In conclusion, our 3D organoid models offer a long term, renewable resource for investigating species-specific intestinal infections with a variety of pathogens.*This work was funded by a Biotechnology and Biological Sciences Research Council Tools and Resources Development Fund grant (BB/M019071/1)*

Dr Rowaida Bakri, *Assistance Professor, Umm-Al- Qura University*

Poster 3 : Subtyping identification of *Blactocystis* sp. isolated from symptomatic and asymptomatic individuals in Makkah, KSA

R Bakri[1];

[1] Umm-Al- Qura University, Saudi Arabia

Background: *Blastocystis* is a group of cosmopolitan gastrointestinal parasite of humans and a wide variety of animals. These anaerobic protozoans include more than 17 specific small-subunit ribosomal RNA subtypes, of which nine are found in humans with a variable geographical distribution. Until now, no study has described the *Blastocystis* subtypes present in Saudi Arabia.

Methods: In total, 1,262 faecal samples were collected from patients with gastrointestinal complaints and asymptomatic individuals visiting two major hospitals. All samples were analysed by F1/R1 diagnostic PCR, microscopy and culture methods. The subtypes of *Blastocystis* sp. isolates were determined by the sequenced-tagged site (STS)-based method.

Results: One-hundred-thirty-three positive cases were detected by F1/R1 diagnostic PCR, of which 122 were also positive by the culture method and 83 by direct microscopy. The sensitivities of direct microscopy and the culture method were 62% and 92%, respectively. Subtype (ST3) was the most prevalent (80.5%), followed by ST1 (14.5%) and ST2 (5%). ST4, ST5, ST6 and ST7 were not detected in this study. ST3 infections were significantly predominant ($P < 0.05$) among symptomatic patients.

Conclusions: To our knowledge, this study provides the first run-through information on *Blastocystis* sp. epidemiology in Makkah city, revealing a rather moderate prevalence of 10.5% and the presence of three subtypes, ST1, ST2, and ST3. ST3 was the most predominant, particularly among symptomatic patients

Keywords: *Blastocystis* sp, Sequence-Tagged Sites (STS) PCR, Subtyping, Makkah city

Ms Claire Beaufay, *PhD student, UCL/LDRI/GNOS*

Poster 4 : Evaluation of antitrypanosomal activity and selectivity of natural and semi-synthetic triterpenic derivatives

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C Beaufay[3]; J Bero[3]; N Bonneau[3]; C Girardi[3]; M Sanchez[1]; A Leverrier[1]; R Frédérick[2]; J Palermo[1]; J Quetin-Leclercq[3];
[1] Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina; [2] UCL/LDRI/CMFA, Belgium; [3] UCL/LDRI/GNOS, Belgium

Human African trypanosomiasis, so called sleeping sickness, is a parasitic infection endemic in 36 African countries with about 3,000 new cases registered each year and 13 million people at risk of infection in 2015 [1]. This neglected disease, due to *Trypanosoma brucei*, may evolve into a neurological disease and be lethal if non treated. A promising source of new active compounds, as alternative to limited and toxic actual medications, could be natural compounds [2, 3] such as bioactive pentacyclic triterpenes [4] some of them being identified in a Beninese traditionally used plant, *Keetia leucantha* [5].
The purpose of this work was 1-to study structure-activity relationships with other triterpenic derivatives identified in the *Keetia* gender, semi-synthetized or commercialized to define structural key positions and improve selective activity and 2- to evaluate the *in vivo* activity of plant extract and the most promising compounds. Tests were performed on *Trypanosoma brucei brucei* (strain 427) and selectivity measured on the mammalian WI38 cells. Preliminary structure-activity relationships allowed us to observe that, for acids, the more hydroxylated, the less active they are with potential impact of configuration (α2 versus β23). A ketone and a shift of the double bond lead to a decrease of activity. Furthermore, ursane derivatives seem more active than oleanane ones as suggested in literature. For esters, the position of esterification seems to be important. Indeed, C-28 esters are significantly less active than their corresponding acids. C-27 esters isolated from *Keetia leucantha* are more active than acids but activities still stay moderate to low. For esterification on position 3, a similar or higher activity is mostly observed with even a significant increase for oleanane esters. However, ursolic acid and two esters, hydrocinnamic and ortho-fluorophenylpropionic, as well as *Keetia leucantha* twigs dichloromethane extract didn't show any parasiteamia inhibition or survival impact in an aggressive *in vivo* model. We have now to evaluate the activity of these compounds and other derivatives on *Plasmodium* and *Leishmania*.

Dr Corinna Benz, *Research Associate, Lancaster University*
Poster 5 : *Trypanosoma brucei* cycling sequence binding proteins?

C Benz[1]; M D Urbaniak[1];
[1] Lancaster University, UK

Gene expression control in *Trypanosoma brucei* is predominantly posttranscriptional and can be exerted on many

levels, ranging from the efficiency of trans-splicing and polyadenylation, regulation of mRNA export, localisation and stability to translational efficiency and finally protein modification and stability. RNA-binding proteins are key players in regulating several of these aspects of gene expression control and thus play particularly important roles in the parasite. But is this also true for regulation of gene expression during the cell cycle? In the insect trypanosomatid *Crithidia fasciculata* a cycling sequence binding protein complex II (CSBPII) has been identified. CSBPII consist of the RNA-binding proteins RBP33, RBP45 and a poly(A) binding protein and has been reported to regulate expression of S-phase transcripts. These transcripts share a common hexamer motif in their untranslated regions important for CSBPII binding. We wondered if the homologous TbRBP33 and TbRBP45 play a similar role in cell cycle dependent mRNA regulation in *T. brucei*. Hence we investigated expression of these two RBPs and their potential targets during the trypanosome cell cycle, assayed their essentiality using RNAi and attempted to identify interaction partners by immunoprecipitation. Results of these experiments will be presented.

Miss Teteh Champion, *PhD student, University of Glasgow*
Poster 6 : Characterising and curbing environmental contamination by *Schistosoma mansoni*.

T S Champion[3]; S Connelly[1]; C Smith[1]; C Rowel[4]; M Adriko[4]; P H Lamberton[2];
[1] Infrastructure and Environment,School of Engineering, University of Glasgow, UK; [2] Institute of Biodiversity, Animal Health and comparative Medicine, and Wellcome Centre for Parasitology, University of Glasgow, UK; [3] Institute of Biodiversity, Animal Health and comparative Medicine, University of Glasgow, UK; [4] Vector Control Division, Ministry of Health, Republic of Uganda, Uganda

Preventative chemotherapy with praziquantel is the mainstay of control programs for schistosomiasis and has proved to be cost-effective for morbidity control. However, integrating additional interventions that can affect the free-living stages of the schistosome's lifecycle, could help interrupt parasite transmission. Environmental contamination by human excreta facilitates contamination of freshwater sources and the subsequent hatching of miracidia and their invasion of susceptible snail hosts. Similarly, human exposure to cercariae-contaminated freshwater enables the progression of the schistosome to the next stage of its lifecycle.
The aims of my PhD are to characterise the level and distribution of *Schistosoma mansoni* (*S. mansoni*) environmental contamination and, assess the potential for environmental engineering interventions to reduce this contamination. Environmental DNA (eDNA) methodology will be used to examine the distribution of *S. mansoni* in soil proximal to pit latrines and open defecation sites. The contamination of water contact sites will also be investigated, and PCR will be used to detect eDNA from these soil and freshwater samples. Following the characterisation of the eDNA distribution, site appropriate engineering interventions will be assessed for their

potential to reduce the survival of the free-living stages of *S. mansoni* lifecycle. I will present the key aims, methods and preliminary results of this work.

Miss Alessandra Crusco, *PhD student, Aberystwyth University*
Poster 7 : Design, synthesis and anthelmintic activity of 7-keto-sempervirol analogues

A Crusco[1]; A D Westwell[2]; K F Hoffmann[1];
[1] Aberystwyth University, UK; [2] Cardiff University, UK

The plant-derived, diterpenoid 7-keto-sempervirol was recently reported to display moderate activity against larval stages of *Schistosoma mansoni* (IC_{50} = 19.1 uM) and *Fasciola hepatica* (IC_{50} = 17.7 uM). These related parasitic blood and liver flukes are responsible for the neglected tropical diseases schistosomiasis and fascioliasis respectively. As both diseases are predominatly controlled by single-class chemotherapies, praziquantel for schistosomiasis and triclabendazole for fascioliasis, the discovery of new anti-flukicidal drugs is imperative should parasite resistance against the current drugs develop. In this study, we aimed to increase the potency of 7-keto-sempervirol by total synthesis of 30 structural analogues. Subsequent screening of these new diterpenoids against juvenile and adult lifecycle stages of both parasites as well as the human HepG2 liver cell line and the bovine MDBK kidney cell line revealed structure-activity relationship trends. The most active analogue, **7d**, displayed improved dual anthelmintiv activiy over 7-keto-sempervirol (IC_{50} 6 uM for larval blood flukes; IC_{50} 3 uM for juvenile liver flukes) and moderate selectivity (SI 4-5 for blood flukes, 8-13 for liver flukes compared to HepG2 and MDBK cells respectively). Phenotypic studies using scanning electron microscopy revealed substantial tegumental alterations in both helminth species, supporting the hypothesis that the parasite surface is one of the main targets of this chemical family. Further modifications of **7d** could lead to greater potency and selectivity metrics resulting in a new class of broad-spectrum anthelmintic.

Dr Rachel Currier, *Postdoctoral researcher, Heidelberg University Biochemistry Center*
Poster 8 : Characterizing the unusual function of thioredoxin 2 - an essential mitochondrial protein in *Trypanosoma brucei*

R B Currier[1]; A Leroux[2]; K Ulrich[3]; N Dirdjaja[1]; R L Krauth-Siegel[1];
[1] Biochemie-Zentrum der Universität Heidelberg, Germany; [2] Biomedicine Research Institute of Buenos Aires, Argentina; [3] University of Michigan, United States

Trypanosomatids possess a unique redox metabolism based on the trypanothione/trypanothione reductase

system. The majority of reactions are mediated by tryparedoxin, the main oxidoreductase found in the parasite cytosol, however maintenance of the thiol-redox homeostasis in the mitochondrion is not yet fully understood.

The *Trypanosoma* genome encodes two thioredoxin-type proteins, Trx1 and Trx2. Previous studies showed that Trx1 functions as a conventional oxidoreductase, whereas the role of Trx2, a protein unique to Kinetoplastids, is currently unknown. As thioredoxin reductases have not been identified in Kinetoplastid organisms, the trypanothione system is the only known source of reducing equivalents for any type of oxidoreductases.

Here, we report that Trx2 is a mitochondrial protein and is essential for proliferation of both bloodstream and procyclic *T. brucei* parasites. Depletion of Trx2 in procyclic cells causes a proliferation defect which is overcome after approximately 8 days of RNAi induction. Remarkably, this is not due to reappearance of the protein suggesting that this occurs via a compensatory mechanism involving the over-expression of a protein with a similar function. Interestingly, this mechanism is accelerated following heat stress.

Conditional knock-out cell lines expressing a mutant Trx2 which lacks all five cysteine residues are viable and proliferative, and show no differences in response to heat shock or oxidative stress compared to wild type cells. We also demonstrate that recombinant Trx2 as well as the 5-cysteine mutant protein both inhibit, instead of accelerate, protein precipitation in the insulin reduction assay. These findings suggest that the primary role of *T. brucei* Trx2 may be a chaperone function that is independent of its thiol redox activity.

Miss Annabelle Dairain, *PhD student, University of Bordeaux*

Poster 9 : Does parasitism interfere with trace metal sensibility? A case of study in a bioturbator species

A Dairain[2]; A Legeay[2]; A Ciutat[1]; P Gonzalez[1]; M Baudrimont[2]; O Maire[2]; P Y Gourves[2]; G Daffe[1]; X de Montaudouin[2];
[1] CNRS, France; [2] University of Bordeaux, France

Bioturbating species are benthic organisms living in the sediment. Through their fossorial life style, bioturbators deeply alter the physical and biochemical properties of sediments and thus are defined as important ecosystem engineer species. Within bioturbators, thalassinidean mud shrimp are considered as among the most influential organisms in marine soft-bottom environments because of the significant roles they play on benthic habitats shaping, nutrient cycling and structuring of benthic communities.
The influence that mud shrimp have on their environment is related to the magnitude of their bioturbation activities and thus to their physiological state. Among factors impairing the fitness of organisms, parasitism is now well

established. Mud shrimp are no exception: they host a bopyrid parasite, which are recognized to alter the physiological state of their host and to reduce the magnitude of mud shrimp's bioturbation activities.
In addition to parasitism, mud shrimp could naturally undergo a variety of others stressors which may interact. For example, anthropogenic trace metals are of major concern in marine environments. Pollutants are recognized to have widespread impacts on organisms with some of them highly toxic from the cell levels (alteration of gene expression) to modification of organism's behavior. However, studies evaluating both influence of parasitism and trace metals on organisms are still scarce, and none has been conducted on bioturbating species.
The present study aimed in evaluating the interactive effect of trace metal contamination (cadmium used as a model contaminant) and parasitism (bopyrid isopod *Gyge branchialis*), alone, and in combination on the mud shrimp *Upogebia* cf. *pusilla* over a 14-days *ex-situ* experiment. Kinetics of trace metal bioaccumulation was determined in the abdominal muscle and hepatopancreas of mud shrimp. In addition, the impact of trace metal contamination and parasitism were investigated at the cellular levels (study of gene expression) in both organs and on the behavior of mud shrimp (quantification of bioturbation activities).
Over 14 days of experiment, mud shrimp showed significant Cd bioaccumulation in both organs with parasite presence impairing contaminant bioaccumulation in the mud shrimp's hepatopancreas. In addition, parasitism and trace metal contamination interfered with genetic expression. However, there was no clear impact of both stressors on mud shrimp's bioturbation activities.

Prof Ahmed Daoud, *Prof. of clinical Parasitology, Tanta University Faculty of Medicine*
Poster 10 : Is there relationship between *Toxoplasma gondii* IgG seropositivity and idiopathic Parkinsonism and does it have correlation with cortisol blood level ?

A Daoud[1];
[1] Tanta University Faculty of Medicine, Egypt

Background: some researches linked between latent toxoplasmosis and neurological diseases, now the main interest is the propable relation between toxoplasmosis and neurological diseasesas epilepsy and Parkinsonism.
Aim: To detect the incidence of *Toxoplasma gondii* infection in patients idiopathic Parkinsonism and correlate it to their blood level of cortisol.
Materials and Methods: This study was conducted on 30 idiopathic Parkinson's Patients, 30 psychiatric Patients, 30 apparently healthy individuals. All subjects were submitted to a questionnaire, detection of anti-*Toxoplasma* IgM, anti-*Toxoplasma* IgG and cortisol level by ELISA.
Results: of the 90 cases; 41.11% and 1.11% were positive for anti-*Toxoplasma* IgM and IgG, respectively. The percentage of positive anti-*Toxoplasma* IgG cases was in healthy group (46.67%) followed by Parkinsonism group

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(43.3%). Mean cortisol level higher in Pakinson's group than other groups but still within normal levels. Contact to cats, drinking unfiltered water and consuming unwashed raw vegetables were significantly higher in *Toxoplasma* IgG seropositive Parkinson's patients. Highest anti-*Toxoplasma* IgG positive casaes in Parkinson's group were detected in stage 3 of the disease.

Conclusion: A high *Toxoplasma* seropositivity in association with Parkinsonim. *Toxoplasma gondii* oocyst may be was the most propable main mode of transmission of *T. gondii* in idiopathic Parkinson's patients. *Toxoplasma gondii* may worsen idiopathic Parkinsonism. Cortisol level was higher in Parkinson's patients, still it showed no significant relationship with *T. gondii* seropositivity.

Miss Carys Davies, *PhD student, Imperial College London*

Poster 11 : Whole genome RNAi library screens identify repressors of metacyclic VSG expression site transcription in bloodstream form *T. brucei*

C Davies[1]; E Lockyear[1]; G Sioutas[1]; H Sidhu[1]; S Alsford[2]; B Wickstead[3]; B S Hall[1]; G Rudenko[1];
[1] Imperial College London, UK; [2] London School of Hygiene and Tropical Medicine, UK; [3] University of Nottingham, UK

Trypanosoma brucei relies on an elegant system of antigenic variation to survive extracellularly in the bloodstream of its mammalian host. Strict mono-allelic expression of the protective variant surface glycoprotein (VSG) is crucial to this process. VSG is always expressed from a telomeric expression site, of which there are two types: bloodstream form (BES) and metacyclic form (MES), which are each utilised at different life cycle stages. We would like to identify factors that play a role in keeping the MESs silent in bloodstream form trypanosomes. Do the same key players regulate both types of expression sites or do MESs have their own distinct set of regulatory machinery? To tackle this unanswered question, we have carried out whole genome RNAi library screens. These were performed using a trypanosome line containing a puromycin resistance gene integrated behind a silent MES promoter. RNAi mediated knock down of genes involved in silencing MESs would lead to increased expression of puromycin resistance protein. We successfully performed three whole genome RNAi screens at three different concentrations of puromycin.

High throughput RITseq analysis allowed us to identify a number of candidate genes, many of which were picked up in multiple screens. These candidates have been validated as having a role in ES regulation using a cell line with a reporter GFP gene in a silent MES. This allowed us to measure fluorescence intensity following RNAi knockdown. These analyses have resulted in us identifying an MES silencing candidate which we call SAP, due to the presence of a predicted SAP DNA binding domain (Tb927.10.4440). SAP domain containing proteins are typically chromatin associated and have been implicated in the organisation of chromatin domains within

chromosomes. Knock-down of SAP results in derepression of multiple MESs as monitored by qPCR. We have also shown that SAP is essential for normal growth in bloodstream form trypanosomes. SAP localises in the nucleus, with enrichment at the nuclear periphery.
Further characterisation of these candidate genes will provide more insight into the transcriptional regulation occurring at MESs, and potentially all telomeric VSG expression sites. Understanding the monoallelic expression in this organism is crucial to understanding its success as a parasite.

Mr Obiora Eneanya, *Doctoral Student , Imperial College London*
Poster 14 : Modelling the environmental limits of Lymphatic filariasis in Nigeria

O Eneanya[1]; O Cano[2]; T Garske[1]; C Donnelly[1];
[1] Imperial College London, UK; [2] London School of Hygiene & Tropical Medicine, UK

Lymphatic filariasis (LF) is a mosquito-borne parasitic disease and a major cause of disability worldwide. It is one of the neglected tropical diseases identified by the WHO for elimination as a public health problem by 2020. Maps of disease distribution and environmental suitability are a necessary tool to delineate endemic foci and target scarce control resources. Here, we used pre-intervention occurrence data from 717 out of a possible 774 implementation units (IUs) collected during extensive mapping surveys by the Health Ministry. Using an ensemble of machine learning modelling algorithms (generalised boosted models (GBM) and random forest (RF)), we predicted the ecological niche of LF at a spatial resolution of 1 km. By overlaying modelled population distribution maps, we estimated population living in LF risk areas on a cell-by-cell scale. Our maps demonstrate that there is a heterogeneous distribution of LF across Nigeria, with large portions of northern Nigeria having more environmentally suitable climate able to drive disease transmission. Here we estimated that approximately 92 million individuals are at risk of transmission. Machine learning and ensemble modelling are a powerful tool to map disease risk, and are known to construct more accurate predictive models while decreasing the uncertainty of single models. We hope that this map will help target and assess the potential impacts of LF control measures.

Mr Matt Evans, *PhD student , Queen's University Belfast*
Poster 15 : Neoblast-like cells of *Fasciola hepatica*

M P Evans[1]; E Gardiner[1]; M Tsifaki[1]; P McVeigh[1]; E McCammick[1]; N J Marks[1]; A Margariti[1]; A G Maule[1];
[1] Queen's University Belfast, UK

The liver fluke, *Fasciola hepatica*, exerts a significant burden on global livestock production and poses an

emerging threat to human health. Combining this with the increasing resistance to triclabendazole, the frontline drug, makes the search for new flukicides critical to efforts to combat the disease. The stem cells of the liver fluke, similar to the neoblasts that give planarians their regenerative ability, could be valuable sources of novel drug targets that disrupt the growth and development of the parasite in the mammalian host. Using transcriptomic datasets generated from schistosomes, we have identified 92 homologues of the 128 genes down-regulated in irradiated schistosomes (i.e. those in which proliferative cells were destroyed), and show that the majority of these show up-regulation in *in vivo* parasites versus parasites cultured *in vitro*, correlating with our growth-rate dynamics data. We also demonstrate for the first time the use of fluorescence activated cell sorting (FACS) to investigate cell populations of the fluke at a single-cell level and show that we can obtain a single cell suspension of *F. hepatica* cells that includes viable proliferating cells. With further optimization and in combination with stem-cell ablation techniques including irradiation and anti-proliferative drugs, this technique will facilitate the isolation of neoblast-like cells from the fluke and seed omics approaches to interrogation of their biology.

Miss Nadin Fathallah, *PhD Student, Lancaster University*

Poster 16 : Correlating *Trypanosoma brucei* localisation with neuropsychiatric symptoms in the rodent model

N A Fathallah[1]; J K Whittingham-Dowd[1]; R Hughes[1]; N Dawson[1]; M D Urbaniak[1];
[1] Lancaster University, UK

Trypanosoma brucei is an extracellular protozoan parasite that causes Human African Sleeping Sickness (HAT). Trypanosomes are thought to be found in two major niches during mammalian host infection; in the blood and lymphatic system during the early stage infection, and later in the central nervous system (CNS). This later stage is characterised by neuropsychiatric symptoms and sleep disorders that occur through an undefined mechanism. Trypanosomes cultured *in vitro* significantly deplete tryptophan from the media, using it in both protein synthesis and transamination reactions.[1] As well as forming an essential component of the kynurenine pathway, with both neurotoxic and neuroprotective branches, tryptophan is also the precursor serotonin and melatonin which are implicated in sleep regulation. [2]

Parasite localisation to other tissues types has often been overlooked; however Trindade and colleagues [3] recently documented the presence of trypanosomes in extravascular adipose tissue, and Capewell and colleagues demonstrated the skin to be a significant anatomical reservoir. [4]

Working with a well-established murine model of infection using red-shifted luciferase expressing parasites (REF[5]), our *ex vivo* imaging data reveals parasite sequestration to many organs during early stage infection not previously documented. In addition, we identified localisation to the CNS during the early stage infection in a subset of

animals. HPLC-based metabolomics analysis has been used to determine tryptophan uptake and metabolism during the course of infection.

This preliminary data raises some interesting points regarding tropism, or lack of it, during *Trypanosoma brucei* infection in the mammalian host. Our current work aims to relate parasite localisation to specific areas within the brain, with altered brain function, metabolism and translationally relevant behavioural changes in the mouse model. This is a clinically relevant area of research which remains to be well defined.

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Mrs Caroline Fenn, *Lab manager/GLP study director, Ridgeway Research Ltd*

Poster 17 : Comparison of hepatic, pathology and antibody response in lambs challenged with identical *Fasciola hepatica* infections

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The Differential outcomes of *Fasciola hepatica (Fh)* infection on the liver pathology and blood chemistry in naturally infected ruminants are well known. In addition, hepatic and peritoneal changes and immune response have been recorded in vaccination trials following artificial challenge infections. However, the variety and range of effects of fascioliosis on individuals is not well characterised. This study aimed to measure this variation using commercially reared Texel X lambs given a defined challenge of *F. hepatica* isolate. In total, 15 female and 2 male (castrated) lambs having no previous exposure to liver fluke, were each challenged with 200 metacercariae from a confirmed TCBZ susceptible *F. hepatica* isolate. During the 12 weeks of infection animals maintained reasonable body condition and showed no clinical signs. At post mortem, data was collected for body weights, liver weights, numbers of adult fluke, and liver condition was scored. Images of liver pathology were also recorded. Blood samples were collected for liver enzyme analysis and antibody response testing. Results demonstrated an average

infection rate of 51% (range 19.5 to 83.5%) with high levels of liver enzymes; GGT up to 13 times the normal range and GLDH up to 40 times the normal range. Liver morphology scores revealed moderate adverse changes in 3 of the animals, the remaining 14 exhibiting mild changes. Thus, the study confirmed variation in individual host responses in a challenge that could lead to chronic *F. hepatica* infection, with no apparent correlation between, or trends in, the levels of fluke infection and pathological, biochemical or antibody responses. Future studies will repeat the experiment with significantly lower *F. hepatica* infection levels in order to delineate individual response profiles.

Mr. Cyril Hammoud, *PhD student, Royal Museum for Central Africa*

Poster 18 : Untangling the drivers of parasite diversity along gradients of natural and anthropogenic variables in a tropical crater-lake system (Kasenda, Uganda)

C Hammoud[3]; T Huyse[3]; D Verschuren[1]; B Van Bocxlaer[1]; C Albrecht[2];
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Biodiversity loss caused by human activities threatens the capacity of ecosystems worldwide to provide essential ecological services. Hence, a growing effort is directed at understanding the consequences of anthropogenic disturbances for biodiversity. Parasitic organisms have so far been widely overlooked in this effort, even though parasitism is the most common feeding strategy on Earth. One group of parasites with high societal relevance are the trematodes, flatworms utilizing snails as intermediate hosts to infect vertebrate species, including humans, as final host. Trematodes cause important human diseases such as schistosomiasis, a neglected tropical disease affecting more than 200 million people. Here we aim to document the patterns and processes governing the local and regional diversity of trematodes infecting the hosts of schistosomiasis - *Bulinus* and *Biomphalaria* snails - in a crater-lake district in western Uganda which bridges the temperature threshold of schistosomiasis presence. As these lakes cover a wide gradient of human-impact intensity, this crater-lake system represents a natural laboratory to analyze the impact of both natural and anthropogenic environmental variation on trematode diversity within and among lakes. In order to tackle existing difficulties in detecting and identifying trematode infections in snails, we are developing a multiplexing and pooling techniques by means of next-generation-sequencing. This genotyping by targeted sequencing allows to simultaneously amplify loci for host and parasite, which will increase the genomic coverage and thus the power to infer population dynamic processes, population genetic structure, genetic diversity and phylogeography.

Mr Daniel Horton, *PhD student, Brunel University London*

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Poster 19 : Epigenetic modifications in the *Biomphalaria glabrata* snail induced by *Schistosoma mansoni*

D A Horton[1]; G Rinaldi[3]; P Driguez[3]; H D Arican-Goktas[1]; M Knight[2]; J M Bridger[1];
[1] Brunel University London, UK; [2] George Washington University, United States; [3] Wellcome Trust Sanger Institute, UK

The spatial organisation of the genome of the interphase nuclei is highly regulated, with chromosomes and genes occupying specific regions of the nuclei to which they can be reproducibly localised. However, when cells react to sudden changes in their environment, i.e. when they are exposed to external stimuli, genes and/or whole chromosomes can be actively and rapidly relocated, this mechanism is associated with regulating of gene expression. We have shown that *Schistosoma mansoni*, a blood fluke that infects a quarter of a billion people globally, induces this mechanism in its intermediate snail host *Biomphalaria glabrata*. Subsequent gene repositioning is followed by upregulation of gene expression, which seems to be necessary for infection establishment. In particular, heat shock protein 70 (*hsp70*) locus which has been shown to relocate in susceptible but not resistant strains of *B.glabrata* when exposed to the parasite, can also be induced to move by heat shock making *B.glabrata* an invaluable model for exploring the mechanisms behind gene migration. We now have evidence that *B.glabrata* nuclear myosin is required to permit the movement, as inhibition of nuclear myosin blocks gene movement in the heat shock model. Understanding the mechanisms behind this parasite induced relocation and subsequent gene upregulation through nuclear signalling, chromatin remodelling and chromatin dynamics will allow us to uncover the complex co-evolved host-parasite relationship with the main goal of discovering novel strategies for infection control.

Miss Rachel Hutchinson, *PhD Student, University of Bristol*

Poster 20 : Characterising *Trypanosoma suis*, a neglected livestock pathogen

R Hutchinson[2]; L Peacock[1]; C Kay[2]; W Gibson[2];
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Trypanosoma suis Ochmann 1902 is a tsetse-transmitted pathogen of pigs in sub-Saharan Africa. The importance of *T. suis* as the missing link between *T. brucei* and *T. congolense* was recognised in the 1950s, but this obscure parasite of pigs remained undetected for nearly 60 years, until 2015 when a *T. brucei*-like trypanosome found in tsetse midguts collected from Tanzania matched *T. suis* on archival Giemsa-stained slides from the 1950s using

two independent species-specific PCR tests1. *T. suis* has an ITS-1 region similar in length to *T. simiae*, which may explain why *T. suis* has escaped detection in the past. We have optimised culture conditions for *T. suis* and are developing a molecular toolbox for this organism, adapting resources available for other trypanosome species. Transfection with a fluorescent protein gene will allow us to detect the trypanosome by fluorescence microscopy inside the tsetse fly vector and follow its developmental cycle. Historical observations indicate that *T. suis* colonises the salivary glands and the proboscis of the tsetse fly, an intriguing amalgamation of the strategies employed by its closest relatives, *T. brucei* and *T. congolense*.

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Miss Shiromani Jayawardhana, *Scientific Officer, London School of Hygiene & Tropical Medicine*
Poster 21 : Recrudescence of *Trypanosoma cruzi* infection following sub-curative benznidazole treatment during the acute and chronic stages

S Jayawardhana[1]; A F Francisco[1]; M C Taylor[1]; M Lewis[1]; J M Kelly[1];
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Chagas disease is caused by the protozoan parasite *Trypanosoma cruzi* and is a major source of morbidity in Central and South America. The nitroheterocyclic compounds benznidazole and nifurtimox are the current front-line drugs. Recently, we generated a *T. cruzi* strain expressing a bioluminescent/fluorescent fusion protein. When used to infect mice, this reporter strain enables *in vivo* bioluminescent imaging and tracking of the parasite burden in whole animals, and in organs and tissues, and facilitates detection of individual fluorescent parasites in tissue sections at a cellular level. This model was used to assess the recrudescence of *T. cruzi* infections following sub-optimal treatment with benznidazole, in both the acute and chronic stages. The results reveal that no specific tissue or organ acts as a reservoir of infection, acting as a site where parasites are able to survive drug treatment. Morphologically unusual forms of the parasite were identified in multiple tissue types. TUNEL assays, which provide a read-out of kDNA replication, identified surviving parasites that had both replicative and non-replicative status following benznidazole treatment. These experiments demonstrate that the technology outlined here can be used to provide new insights into drug activity in an *in vivo* context, as well as being a valuable tool for exploring the pathogenesis of *T. cruzi* infections.

Dr Ruth Kirk, *Associate Professor, Kingston University*
Poster 22 : Itchy and scratchy? An investigation of human cercarial dermatitis in the UK

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R J Micallef[1]; R S Kirk[1];
[1] Kingston University, UK

Human cercarial dermatitis (CD) or cercariosis is a cutaneous allergic response caused by repeated penetration of avian and mammalian schistosome cercariae and possibly non-schistosomatid cercariae. It is an emerging and re-emerging disease frequently reported in Europe and the USA in association with recreational lakes inhabited by snail intermediate hosts and waterfowl definitive hosts for *Trichobilharzia* spp. There is insufficient information about the occurrence and causative agents of CD in the UK and the condition is under-diagnosed due to confusion with insect bites and lack of a reporting system. Reports of CD in the UK are increasing in frequency via social media, partly due to the popularity of open water swimming, although the full extent of CD as a health issue is not known. This is the first study in the UK to explore occurrence of CD and its impacts on open water swimmers. Following ethical approval from Kingston University Ethics Committee, open water swimmers were contacted via swimming clubs and on social media to complete a 14-question survey on Survey Monkey on CD and open water swimming behaviour during 2016. A total of 62 responses (61% female: 39% male, age range: <25 to >76) were received. Self-diagnosed reports of CD were recorded from 38 sites, mainly in England, comprising freshwater lakes and rivers except for one marine site in Cornwall. Interestingly, not all swimmers experienced symptoms at known CD sites and they reported symptoms from April to November, beyond the usual seasonal period of cercarial emergence. CD does not discourage open water swimming for the majority due to strong motivators for the sport. Multiple preventative measures and treatments were undertaken, mainly following advice from friends, pharmacies and the internet. Wet suits were not worn by the majority and do not appear to be effective in preventing CD. The efficacy of removing snail intermediate hosts at one site is currently being tested and more demographic data will be needed in future studies to identify reasons for variable responses to exposure.

Ms Isabel Blasco-Costa , *Research Scientist, Natural History Museum of Geneva, Switzerland*
Poster 23 : A functional trait framework to study diversity of helminth parasites

C Llopis-Belenguer[2]; J A Balbuena[2]; K Lange[1]; F de Bello[3]; **I Blasco-Costa**[4];
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Traditionally, Taxonomic Diversity (TD) is used to measure diversity, mainly as richness or abundance of species present in a given sample. The greatest limitation of TD metrics is that they consider species as equivalent entities, with no consideration of their phylogenetic relationships and functional role in the community. To tackle this issue,

it has been proposed to incorporate phylogenetic and functional distances between species when measuring diversity. Thus, Functional Diversity (FD) is based on estimating diversity in a community using distances between functional traits of species (i.e. phenotypic traits that impact fitness of individuals via their effects on growth, reproduction and survival). It has been shown that studies of FD can unveil the processes that determine species composition in ecosystems and the responses of organisms to different factors. However, despite the promise of FD approaches and the ubiquity of parasites in ecosystems, very few studies have concentrated in communities of these organisms. We aim to develop a practical framework of functional traits of aquatic helminth parasites ready for application in FD studies. Furthermore, to show the usefulness of our list of functional traits, we calculated TD and FD of the helminth parasite fauna (Monogeneans, Trematodes, Nematodes and Acanthocephalans) of the flathead grey mullet (*Mugil cephalus*) from three habitats: one marine and two brackish. For TD and FD analyses, we measured diversity at alpha (individual host) and beta (locality) levels of organisation using the Rao quadratic entropy index. In our case study, we determined the assembly of the parasite species at host and locality levels. Moreover, we define the heterogeneity of the community composition in terms of both parasite species and functional traits. We expect that our framework of functional traits would inspire future FD analyses of parasite communities.

Miss Ana Moro Bulnes, *Cytidine deaminase in T. brucei, Instituto Parasitología y Biomedicina López-Neyra*

Poster 24 : Cytidine deaminase in *Trypanosoma brucei*: a mitochondrial enzyme involved in *de novo* biosynthesis of pyrimidines

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Trypanosoma brucei possesses the metabolic machinery for *de novo* synthesis of pyrimidine nucleotides but also has the capacity to obtain pyrimidines from the host via the salvage pathway. This parasite lacks the dCMP deaminase responsible for dUMP formation present in mammalian cells however it does contain a putative cytidine deaminase (TbCDA). We previously reported that *T. brucei* deoxyuridine triphosphate nucleotidohydrolase null mutants are thymidine (dThd) auxotrophs although 5-methyl-2â€™-deoxycytidine (5mdC) can also support growth presumably through deamination to yield dThd thus suggesting an important role of TbCDA in pyrimidine nucleoside homeostasis.We have characterized recombinant TbCDA and show that it catalyzes deamination of cytidine (Ctd) or deoxycytidine (dCtd) to uridine (Urd) and deoxyuridine (dUrd) respectively. TbCDA is also capable of deaminating several nucleoside analogues, such as 5mdC. In agreement with this observation, *T. brucei* bloodstream forms overexpressing TbCDA are hypersensitive to the analogue 5fdC. Cellular localization studies

revealed that TbCDA is a mitochondrial enzyme in both procyclic and bloodstream forms of the parasite. RNAi-mediated depletion of the enzyme in *T. brucei* bloodstream forms resulted in defective growth in the absence of external pyrimidines. The defective growth phenotype is reversed by dThd supplementation further supporting the notion that TbCDA has an important role in providing dUrd for *de novo* dTMP biosynthesis.

Mr Martin Mutuku, *Research Officer, Kenya Medical Research Institute*

Poster 25 : Comparative efficiency of *Biomphalaria pfeifferi* and *B. sudanica* as intermediate host snails for *Schistosoma mansoni* in Kenya

M Mutuku[1]; I Mwangi[1]; E Lelo[1]; J Kinuthia[1]; G Maina[1]; H Ochanda[2]; G Mkoji[1];
[1] Kenya Medical Research Institute, Kenya; [2] The University of Nairobi, Kenya

In Kenya, an estimate of 6 million people are infected with schistosomiasis with >30 million people at risk of infection. *Schistosoma mansoni* is commonly transmitted by *Biomphalaria pfeifferi*, an inhabitant of streams and small water bodies, and *B. sudanica*, which is mostly found along lakeshores, mainly in Lake Victoria. Recent studies have accentuated the role of infected snails in maintaining transmission as some snails can survive for over a year shedding cercariae daily. We sought to determine if these two snail species may differ with respect to the efficiency with which they support *S. mansoni* infections. We exposed field-derived *B. pfeifferi* (Kirinyaga, central Kenya) and *B. sudanica* (Kisumu, western Kenya) to *S. mansoni* derived from human subjects from Kirinyaga or Kisumu. The reciprocal cross infection design allowed us to ascertain if local adaptation effects might influence infection outcomes. Juvenile (<6 mm shell diameter), young adult (6-9 mm) and adult snails (> 9 mm) were exposed, all to one miracidium/snail. Overall, *B. pfeifferi* consistently had higher infection rates than *B. sudanica* (39.6 - 80.7% vs. 2.4 - 21.5%), regardless of the source of *S. mansoni* or the size of the snails used. Allopatric *B. pfeifferi - S. mansoni* combinations had higher infection rates than sympatric combinations while *B. sudanica* showed the opposite trend. Infection rates were inversely proportional to snail size. Mean daily cercariae production was greater for *B. pfeifferi* exposed to sympatric than allopatric *S. mansoni* (62 –2465 and 100 – 1232, respectively), and this trend increased with snail size. Overall mean daily cercariae production amongst all *B. sudanica* was low (50–590) with no significant differences between sympatric or allopatric combinations, or among the different snail sizes ($p < 0.05$). In conclusion *B. pfeifferi* is more likely to become infected and to shed more cercariae than *B. sudanica,* suggesting that the per snail risk of perpetuating transmission in Kenyan streams and lacustrine habitats may differ considerably, with noteworthy implications for understanding transmission dynamics and planning control efforts.

Mrs Adefunke Ogunkanbi, *PhD Student, University of Manchester*

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Poster 26 : Gut dwelling helminths drive intestinal regulation through direct induction of host TGF-β

A Ogunkanbi[2]; **J L Pennock**[2]; B Eldakhakhny[1];
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Gut dwelling helminths infect approximately 1.45 billion people globally with children being the most infected. Chronic infection with helminths is associated with a local Th1 response regulated by the induction of immunoregulatory cytokines such as IL-10 and TGF-β. Evidence to date demonstrates that helminths themselves can encode TGF-β receptor ligands to modulate immune response and enhance their survival, although little is known about *Trichuris spp*. Given the impact of *Trichuris* as iatrogenic treatment for inflammatory diseases, we were interested to better understand the direct immunoregulatory mechanisms induced by these helminths *in vivo*. Here we show that infection with *Trichuris muris* drives systemic host TGF-β in a dose responsive manner, independently of the adaptive immune response. Furthermore, *in vivo* administration of worm homogenate drives serum TGF-β in uninfected mice, demonstrating that immunoregulation is not related to intestinal damage. We demonstrate using *in vitro* approaches that a novel *Trichuris muris* homologue induces host TGF-β through interaction with the TGF-βR complex, and that this is sufficient to regulate DSS-induced colitis. These data complement and extend our current understanding of helminth immunoregulation and broaden the scope for potential therapeutics for regulation of intestinal inflammation.

Mr Ewan Parry, *PhD Student, University of York*

Poster 27 : Investigating developmental regulators of infectious *Leishmania* parasites

E Parry[1]; J Mottram[1]; P B Walrad[1];
[1] University of York, Centre for Immunology and Infection, UK

The leishmaniases, the infections caused by *Leishmania* parasite species, represent the second largest burden of parasitic disease in the world. Despite this, available treatments are limited; partly due to our incomplete knowledge of the molecular and genetic mechanisms that conduct these parasites through their complex, dixenous lifecycle. Constitutive transcription of polycistrons suggests that post-transcriptional regulators like mRNA-binding proteins (mRBPs) play a prominent role in *Leishmania* gene regulation. The Walrad lab has recently isolated the mRNA-bound proteome of the three main lifecycle stages in *Leishmania*. This dataset has been analysed for candidate mRBPs with a putative involvement in parasite differentiation. By tagging and genetically manipulating levels of prioritised mRBPs, we hope to screen for key regulators which play essential roles in lifecycle progression, infectivity and virulence characterised using a range of bespoke techniques. The fundamental

dependence of kinetoplastid parasites on post-transcriptional control also makes *Leishmania* an ideal model for the study of RNA-binding protein function, providing valuable insight to the broader field of *trans*-regulators. Immunoprecipitation (IP) and *in situ* hybridization (FISH) will be used to identify and visualise target mRNAs and protein cofactors that form mRNP 'regulon' complexes. Visualisation of mRNP complexes could provide *in vivo* data on cellular localisation dynamics in response to key environmental shifts and stress. Isolation of vital gene regulatory pathways could aid in the design of anti-leishmanial therapeutics.

Dr Anna Paziewska-Harris, *Postdoctoral fellow, Cardiff University*

Poster 28 : High-throughput *in vitro* culture system for *Cryptosporidium* oocysts: replacing animals in research

A Paziewska-Harris[1]; R Thomas[1]; J Cable[1];
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Cryptosporidium is a water-borne pathogen, which poses a major threat to animal health and welfare, and to public health, because there is no proper treatment and no immediate prospect of vaccine development. The increasing attention has focussed substantially more funding to develop drugs to eliminate *Cryptosporidium* as a human pathogen. Lack of proper *in vitro* culture system for Cryptosporidium maintenance and oocyst production means that recent increase in funding will dramatically increase animal use in this research field. A promising new method of rearing *Cryptosporidium* in the hollow fibre system (Morada *et al.* 2016) claims to generate up to 10^8 *Cryptosporidium* oocysts per day. If this can be adapted into a routine methodology, the output of oocysts would meet the needs of the research community without using calves or other live animals. We are aiming at establishing the method at Cardiff University, and then making this supply available to other European *Cryptosporidium* laboratories. Before the technique can be adopted as the method of choice for *Cryptosporidium* oocyst supply, it is imperative that we (a) demonstrate the reliability of the method for the growth of different *Cryptosporidium* species and variants, including the human-infecting forms, and (b) assure the genetic stability of parasites grown in this system for many generations, relative to parasites reared in calves. The technology can be used by basic scientists; parasitologists, microbiologists, biochemists, pharmacologists and geneticists interested in cell-cycle control and the search for drugs against *Cryptosporidium*, and it will surely benefit veterinarians, medical practitioners and water treatment companies.

Dr Gabriel Rinaldi, *Senior Staff Scientist, Wellcome Trust Sanger Institute*

Poster 30 : Using CRISPR-Cas9 to develop a selectable marker for schistosome transgenesis

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G Rinaldi[1]; M Lotkowska[1]; P Driguez[1]; G Sankaranarayanan[1]; A Coghlan[1]; M Berriman[1];
[1] Wellcome Trust Sanger Institute, UK

Schistosomiasis is a neglected tropical disease affecting >200 million people worldwide. Genome sequences for several Schistosoma species are available, including a high quality annotated reference for *Schistosoma mansoni*. There is now an urgent need to develop a functional toolkit to translate these data into new biological insights and targets for intervention. The eggs of *S. mansoni* can be transduced using mammalian retroviruses. Transgenes can be stably integrated into chromosomes and transmitted through the germline as stable transgenic lines. However, in the absence of a robust selection protocol for transgenic parasites, transgenic organisms become diluted among non-transformed parasites and eventually lost in successive generations. A sulfotransferase (ST) has been identified as the gene contributing to resistance against Oxamniquine (OXA), an anthelmintic with schistosomicidal activity against *S. mansoni*. Here, we target the sulfotransferase locus using CRISPR-Cas 9 and introduce transgenes in to the germ line of *S. mansoni*, to obtain stable transgenic lines resistant to OXA. Sensitivity to OXA was analysed in eggs and sporocysts, the two key developmental stages suitable for development of germline transgenesis, given the high germline to soma cell ratio present in these stages. Although the eggs were resistant to OXA at the tested concentrations, sporocysts displayed a hypermotile phenotype followed by increasing mortality in a concentration-dependent manner. RNAi experiments against ST in sporocysts cultured in the presence of OXA were performed to investigate the presence of a rescue phenotype, i.e. OXA-resistant sporocysts. In addition, we have designed three ST-specific gRNAs and transfected eggs and sporocysts with fluorescently-labelled ribonucleoprotein complex comprising CRISPR-Cas9 and gRNA. From these transfected parasites, we used PCR-amplicon sequencing to quantify insertions and deletions in the ST locus, and qRT-PCR to determine the extent to which gene expression was perturbed. Donor DNA cassettes for CRISPR-Cas9 mediated Homology Directed Repair knock-in experiments in the ST locus, and retrovirus expressing Cas9 and ST-specific gRNAs are underway. Retroviral-based approaches coupled with genome editing, driven by CRISPR-Cas9, promise exciting new opportunities to explore the functional genomics investigations of this neglected tropical disease parasite.

Mr Eljelani Salim, *Salford University*

Poster 31 : Occurrence of *Cryptosporidium* and *Eimeria* infections in UK sheep

E Salim[1]; R J Birtles[1]; D R Brooks[1];
[1] University of Salford, UK

The protozoan parasites *Cryptosporidium* spp. and *Eimeria* spp. infect a wide range of animals across the world.

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Although the public and veterinary health significance of these parasites are different, they continue to remain infection challenges to the farming industry. As such, we investigated the occurrence of *Cryptosporidium* spp. and *Eimeria* spp. in sheep at two farm locations in North West England using a combination of classical parasitological and molecular approaches.

Throughout 2015-16, we collected a total of 552 faecal samples from female Swaledale and Texel sheep reared at two farms in South Cumbria. DNA extractions were performed on the sheep faeces and the presence of *Cryptosporidium* spp. and *Eimeria* spp. was confirmed by PCR amplification of the respective 18S rRNA gene. In total, 110 samples (20%) were confirmed to be infected with *Cryptosporidium* spp. and 99 of these were typed to species level. The most common (n 65) 18S rRNA sequence corresponded to *C. xaio*/*C. bovis* and further analysis of the actin gene sequence confirmed that 42 of these were *C. xaio* infections. Also identified were *C. ubiquitum* (n 24), *C.* sp. (n 9) and *C. parvum* (n 1). Further analysis of the *C. ubiquitum* isolates by PCR amplification of the gene encoding GP60 confirmed that they were all subtype XIIa, which is a broad host range parasite. Infections in 70 of the 110 PCR-positive samples were also confirmed following staining and microscopy. A qPCR-based approach targeting the 18S rRNA gene was then utilized to assess parasite infection loads. The maximum, minimum and mean *Cryptosporidium* spp. infection loads (oocysts g^{-1} faeces) were confirmed as 43,000, 10 and 5,000 respectively.

A subset of 158 faecal DNA extractions were PCR screened for *Eimeria* spp. infection and 78.4% were confirmed positive. DNA sequencing of these 18S rRNA amplicons confirmed the dominance of *E. crandallis* (71%); other species identified were *E. ahsata* (27%) *E. faurei* (2%).

Overall, the data confirms that different *Cryptosporidium*and eimerian species are present in UK sheep at high prevalence levels and hence co-infections were also commonly observed (52%). The data allows for some potentially interesting associations between the parasite infections and intrinsic/extrinsic factors to be further investigated.

Dr Claudia Schaffner, *Postdoctoral associate, University of Edinburgh*

Poster 33 : Pharmacological inhibition of the vacuolar ATPase in bloodstream form *Trypanosoma brucei* rescues genetic knockdown of mitochondrial gene expression

C Schaffner-Barbero[3]; M Miskinyte[3]; D Horn[2]; J Mottram[4]; A Schnaufer[1];

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The survival of *Trypanosoma brucei* depends on maintenance and function of the mitochondrial genome (kinetoplast, or kDNA). However, a single point mutation in subunit γ of the mitochondrial F1FO ATPase can

abolish the requirement of kDNA for survival of the bloodstream form of the parasite (Dean *et al*. 2013), and it was found that genetic or chemical inhibition of the vacuolar ATPase (V-ATPase) could have a similar effect (Baker *et al*. 2015). Here we present detailed studies of the effects of V-ATPase inhibitors on parasite growth after genetic or chemical interference with kDNA function. We found that treating bloodstream form *T. brucei* cells with bafilomycin A1 fully rescued loss of viability induced by depletion of the essential RNA editing ligase REL1 via genetic repression ('conditional knock-out'; (Schnaufer *et al*. 2001). This confirmed a connection between V-ATPase function and kinetoplast dependency and suggests that V-ATPase inhibitors could be used as chemical tools in the study of kinetoplast biology. We also confirmed attenuation of the growth defect caused by isometamidium concentrations known to induce kDNA loss (Baker *et al*. 2015), although the rescue was only partial and not equivalent to the compensatory effect afforded be subunit γ mutations. Surprisingly, this rescue was not robustly replicated when using the chemically related compound ethidium bromide. In addition, bafilomycin A1 could not rescue from kDNA loss induced by RNAi-mediated knock-down of essential proteins PNT1 or TAC102 (Grewal *et al*. 2016; Trikin *et al*. 2016). Work is ongoing to investigate these unexpected findings in more detail.

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Miss Eman Shakir, *PhD student , Kingston University*

Poster 34 : Cell signalling during male-female interactions by *Schistosoma mansoni*

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E Shakir[1]; R Kirk[1]; G Rinaldi[2]; A J Walker[1];
[1] Kingston University, UK; [2] Wellcome Trust Sanger Institute, UK

Eukaryotic protein kinases have been well conserved through evolution and the genome of *Schistosoma mansoni* encodes over 250 of these regulatory proteins. To further understand protein kinase signal transduction and function during male-female interactions of *S. mansoni*, we investigated the temporal effects of excreted-secretory molecules produced by adult male worms over 20 h culture on protein kinase activities in female worms, and *vice versa*. Western blotting with anti-phospho tyrosine/serine/threonine antibodies revealed that the phosphorylation status of multiple proteins changed over 60 min in response to exposure to secretory molecules released from worms of the opposite sex. This finding encouraged us to test for activation of specific pathways in worms in response to these secretory molecules using antibodies that react specifically with activated protein kinase C (PKC), extracellular signal-regulated kinase (ERK), p38 mitogen-activated protein kinase (p38 MAPK) or protein kinase A (PKA). Exchange of male/female culture media between groups of single sex worms resulted in the rapid activation of protein kinase pathways, particularly the ERK and p38 MAPK pathways where activation was seen as early as 5 min. Immunofluorescence and confocal laser scanning microscopy revealed that activation occurred in different structures including the parasite tegument. The motility of the parasites was also enhanced in response to the opposite-sex media. The secreted molecules were next biotinylated and fluorescence confocal laser scanning microscopy revealed that the secreted adult male molecules bound the surface of females and *vice versa*. This study is the first to report that male-female secretory molecules influence signal transduction mechanisms in worms of the opposite sex. Future studies aim to further characterise the importance of the excretory-secretory molecules in *S. mansoni* male-female interactions.

Miss Marianne Silva, *PhD student, Swiss TPH*
Poster 35 : Metronidazole in mono- and combined therapy against *Trypanosoma cruzi* - a drug repurposing strategy for Chagas disease

M R Simões-Silva[1]; J S De Araújo[1]; G M Oliveira[1]; K C Demarque[1]; R B Peres[1]; I D'Almeida-Melo[1]; D G Batista[1]; C F Da Silva[1]; C Cardoso-Santos[1]; P B Da Silva[1]; M M Batista[1]; M T BahiaM N Soeiro[1];
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Chagas disease (CD) is a life-threatening neglected pathology caused by the protozoan *Trypanosoma cruzi*, mostly asymptomatic in the acute and chronic phases, even though a significant number of patients progress to cardiac and/or digestive forms, that affects the life quality and induce high mortality rates. The treatment demands long periods of administration of nifurtimox or benznidazole (Bz), along with the occurrence of severe side effects,

besides both being inactive upon the late chronic stage and the occurrence of naturally resistant parasite strains. The limitations evidence the need of new and alternative treatments for CD. Drug repurposing and combined therapy are strategies applied for other pathologies including the neglected diseases. These approaches are less time-consuming and reduce costs during the drug screening process and may help addressing the issue in a rational way. Metronidazole (Mtz) is a nitroimidazolic derivative in the market with broad-spectrum antimicrobial activity and important safety profile, and thus, represents a reasonable candidate for pre-clinical *in vitro* tests upon *Trypanosoma cruzi*, as well as *in vivo* experimental mice model, in mono- and combined schemes. While Bz is active against intracellular amastigotes and bloodstream trypomastigotes of *T. cruzi* in a low micromolar range (2.51 and 11.5 mM, respectively), Mtz presents low activity with EC50 > 200mM. Mtz shows no cytotoxicity profile against mammalian host cells up to 200 mM. Its combination with Bz in fixed-ratio proportions although did not provide cell cultures sterile cidality, the potency of Bz was promoted by the addition of Mtz. *In vivo* toxicity assays confirmed absence of adverse effects since no histopathological neither biochemical alterations were found up to 2000 mg/kg. *In vivo* studies using Swiss Webster male mice infected with 10^4 bloodstream forms of Y strain showed that Mtz administered up to 1000 mg/kg in monotherapy scheme did not lead to reduction of the parasitemia while Bz given at its optimal dose (100 mg/kg) completely suppressed the parasite load at the peak. Nevertheless, the doses of 250 and 500 mg/kg of Mtz could prolong animal survival, hence being determined for use in combination with suboptimal dose of Bz (10 mg/kg). These treatments were not able to reduce parasitemia, but 250 mg/kg Mtz + 10 mg/kg Bz prevented mortality in 70% of the animals and protected the cardiac electric alterations induced by the parasite infection, whilst the standard therapy with Bz was not effective in producing the same protection. The present work highlights the importance of the rational, cheap and fast approaches of drug repurposing and combined therapy for CD, aiming to accelerate the search for alternative treatments for this silent pathology. Supported by FAPERJ, CNPq, Fiocruz and STI.

Miss Kirstin Spence, *PhD Student, University of York*

Poster 36 : Investigating the molecular machinery that controls autophagy during *Leishmania* spp. differentiation

K Spence[2]; N J Bryant[1]; P B Walrad[2];

[1] University of York, UK; [2] University of York, Centre for Immunology and Infection, UK

Autophagy is an important degradation system by which cells recycle unwanted or damaged cytoplasmic material. During times of stress and cellular differentiation this process is upregulated. Macroautophagy (the main autophagy pathway) begins with formation of a phagophore, a double membranous structure, that expands to

engulf cellular components, becoming an autophagosome. This autophagosome then fuses with the lysosome to deliver its contents for degradation and subsequent recycling.
Many of the pathways and components involved in autophagy and membrane fusion events are highly conserved in eukaryotic organisms. Observations in yeast and mammalian systems could therefore provide insight into the roles and mechanisms of related proteins found in the medically-important *Leishmania* parasite.
Research will characterise the interactions of the Tlg2 t-SNARE protein and its partner SM protein Vps45 in *Leishmania* spp. and determine whether, as is observed in yeast, they play a role in autophagy. Autophagy has previously been shown to be critical for *Leishmania* differentiation into human-infectious forms. A better understanding of the molecular mechanisms underlying these processes could potentially prime development of therapeutic strategies to combat leishmaniasis.
Preliminary evidence from genetic experiments examining phenotypic outcomes relevant to lifecycle progression and infectivity of the parasites will be presented. Functional homology experiments will examine whether *Leishmania*-derived Tlg2 can rescue *tlg2Δ* mutant yeast and demonstrate conservation of autophagic pathways

Mr Doko-Miles Thorburn, *PhD Candidate, Queen Mary University of London*
Poster 38 : Do parasites maintain extreme polymorphism in their host's immune genes?

D M Thorburn[3]; K Sagonas[3]; T B Reusch[1]; M Milinski[2]; C Eizaguirre[3];
[1] Geomar Helmoltz-Zentrum für Ozeanforschung, Germany; [2] Max Planck Institute for Evolutionary Biology, Germany; [3] Queen Mary University of London, UK

One of the central questions in evolutionary biology is to explain the mechanisms that maintain genetic diversity within and among populations. Parasites are ubiquitous, and are arguably one of the most important selection pressures which organisms face. In response to the costs of parasitism, hosts have evolved a variety of genetically encoded and complex immune defence mechanisms. It is often claimed that as a response to parasite-mediated balancing selection, the immune genes are among the most variable genes in jawed vertebrates. Because the current understanding of the maintenance of polymorphism mostly comes from empirical evidence on a limited number of candidate loci, the claim is mostly unsubstantiated. Here, we followed a genome-wide approach to detect genomic regions of increased polymorphism in populations of *Gasterosteus aculeatus* fish from diverse European and North American water bodies covering a large part of the species distribution. Based on >60 high quality genomes, we will report about genomic regions under balancing selection, and the diverse rate of polymorphism based on gene functions. Overall, out study highlights evidence for the maintenance of polymorphism of diverse functions evolving under different selection pressures, including parasitism.

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Dr Anna Trenaman, *Postdoctoral Research Assistant, University of Dundee*
Poster 39 : A high-throughput genetic screen for regulatory 3’-untranslated regions in African Trypanosomes

A Trenaman[1]; R Wall[1]; D Horn[1];
[1] University of Dundee, UK

African Trypanosomes constitutively transcribe the majority of their genome in a polycistronic manner and have expanded their repertoire of RNA-binding proteins (RBPs), in order to modulate gene expression. Many of these RBPs are thought to act by binding 3' untranslated regions (UTRs) in the mRNA. Indeed, abundant stage-specific surface proteins are known to be subject to this form of regulation. Relatively few UTRs have been shown to play such a role, however, and the sequences responsible remain largely uncharacterised. We aim to identify these regulatory UTRs on a genome-wide scale and to improve our understanding of these trypanosome-specific adaptations. We assembled a reporter construct comprising a dual positive/negative selectable marker cassette, containing a blasticidin deaminase/thymidine kinase fusion gene. A small set of reference UTRs were used to validate the reporter system. We then assembled a *Trypanosoma brucei* genome-scale library by cloning genomic DNA fragments (1 - 3 kbp) immediately downstream of the reporter gene. The plasmid library has been used to assemble a *T. brucei* library and we have applied both positive (Blasticidin) and negative (Ganciclovir) selection to the library. These two screens have initially been performed in bloodstream form *T. brucei* with the aim of identifying 3’-UTRs associated with increased or reduced reporter gene expression, respectively. We are currently running a deep-sequencing step designed to quantify the relative contributions of several thousand UTRs.

Ms Suzan Trienekens, *PhD Student, University of Glasgow*
Poster 40 : Identifying individual risk behaviours and community-level contributions to reinfection with *Schistosoma mansoni* in school-aged children in rural Uganda

S Trienekens[1]; C L Faust[1]; L Pickering[2]; F Besigye[4]; L Mujumbusi[3]; E Nalwadda[3]; C Rowel[4]; P H Lamberton[1];
[1] Institute of Biodiversity, Animal Health and comparative Medicine, and Wellcome Centre for Parasitology, University of Glasgow, UK; [2] Institute of Health & Wellbeing, College of Social Sciences, University of Glasgow, UK, UK; [3] Medical Research Council, Uganda Virus Research Institute, Entebbe, Uganda, Uganda; [4] Vector Control Division, Ministry of Health, Republic of Uganda, Uganda

Globally, over 200 million people are infected with *Schistosoma* parasitic helminths, and 400 million are at risk of

infection, with school-aged children (SAC) disproportionately affected. The World Health Organization identified Uganda as one of the ten priority countries, highly endemic for schistosomiasis, with an estimated 4 million people infected. The national control programme focusses on mass drug administration (MDA) with praziquantel. However, MDA coverage is only ~37% of SAC and even fewer community members, and hotspots with high prevalence remain. SAC are also found to become rapidly reinfected after treatment and mean infection intensities and associated morbidity continue to be high. My interdisciplinary study aims to use ethnographic and population genetics in conjunction with standard epidemiological methods to better understand how, why and where certain children in Mayuge District become rapidly reinfected with *S. mansoni* after treatment. Observational ethnographic appraisals of rapidly reinfected and non-infected children and focus group
s with parents on water contact attitudes and practices will be undertaken. These methods will help elucidate group and/or individual behaviours that affect children's risk of reinfection and how such risks might be reduced. Concurrently, intermediate snail hosts will be collected from key water contact sites identified through the ethnographic appraisals. DNA will be extracted from *S. mansoni* cercariae shed from these snails and will be compared to DNA from *S. mansoni* miracidia found in previously collected samples from SAC and community members to understand better who is driving these reinfections. Analyses of collected data and interpretation of results will help provide recommendations for improvements to the national control programme with the aim to reduce *Schistosoma* reinfection in Uganda. I will present my study plan as well as preliminary observations from Bugoto from Nov 2017 and March 2018.

Ms Miriam Yague Capilla, *PhD Student, Instituto Parasitologia y Biomedicina Lopez-Neyra*
Poster 41 : Novel nucleotidases involved in *Trypanosoma brucei* pyrimidine homeostasis

M Yagüe Capilla[1]; V M Castillo-Acosta[1]; M Valente[1]; C Bosch-Navarrete[1]; L M Ruiz-Perez[1]; D González-Pacanowska[1];
[1] Instituto de Parasitologia y Biomedicina 'Lopez-Neyra', CSIC. Granada, Spain

Nucleotide metabolism has been an area of interest for the discovery of novel targets against many diseases since a balanced pool of deoxyribonucleotides is required for correct DNA replication and repair. Particularly relevant for cell survival is the maintenance of a balanced dUTP/dTTP ratio in the pyrimidine pool as several DNA polymerases cannot distinguish between the two nucleotides and incorporate indiscriminately one or the other depending on their availability. We have previously shown that thymidine kinase (*Tb*TK) has a major role in the maintenance of the dUTP/dTTP ratio and the response to genotoxic agents in bloodstream forms of *Trypanosoma brucei*. We reported that *Tb*TK was essential for parasite viability, both *in vitro* and *in vivo* thus demonstrating that phosphorylation of deoxyuridine and/or thymidine is important for the maintenance of the dTTP pool even in the

absence of a source of extracellular pyrimidines. These observations indicated a role of the enzyme in *do novo* synthesis and pointed towards the existence of an intracellular deoxynucleoside pool available for phosphorylation. Here we have aimed at characterizing nucleotidases involved in the generation of intracellular nucleosides important for thymidylate *de novo* biosynthesis. We present data for HD domain containing nucleotidases with regard to their intracellular localization, role in cell viability, nucleotide pools and cell cycle progression and propose this class of enzymes as relevant players in nucleotide homeostasis in trypanosomes.

Dr Alena Zíková, *Group leader, Biology Centre, Institute of Parasitology*
Poster 42 : Mitochondrial metabolic remodeling during *Trypanosoma brucei* developmental differentiation

E Doleželová[3]; M Dejung[2]; B Panicucci[3]; C Janzen[1]; F Butter[2]; **A Zíková**[3];
[1] Department of Cell and Developmental Biology, Biocenter, University Wuerzburg, Germany; [2] Institute of Molecular Biology, Germany; [3] Institute of Parasitology, Biology Centre, ASCR, Czech Republic

The *Trypanosoma brucei* mitochondrion undergoes extensive structural and metabolic remodeling during the parasite´s life cycle since the insect stage fully relies on oxidative phosphorylation (OXPHOS) to produce ATP while the mammalian bloodstream stage generates ATP by aerobic glycolysis. This complex developmental differentiation is exemplified during the flagellated protist's migration from the tsetse fly midgut to the salivary glands, a process that can now be mimicked *in vitro* by overexpressing a single RNA binding protein. Here we demonstrate that the mitochondrial membrane potential and reactive oxygen species are increased at the early transition stages. Meanwhile, respiratory complexes III and IV become reduced and the electron flow is redirected from the OXPHOS pathway to an alternative oxidase. This coincides with the increased abundance of respiratory complex II and proline degradation enzymes that may act to provide ATP by substrate phosphorylation. Molecular triggers for this metabolic rewiring are being explored.

Dr. Paul Brindley, *Professor, George Washington University*
Poster 44 : Diminished hepatobiliary disease during infection with CRISPR/Cas9-gene-edited *Opisthorchis viverrini* liver flukes

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P Arunsan[3]; **W Ittiprasert**[1]; V Mann[1]; S Chaiyadet[3]; M Smout[2]; J Sotillo[2]; A Loukas[2]; P Brindley[1]; T Laha[3];
[1] George Washington University, United States; [2] James Cook University, Australia; [3] Khon Kaen University, Thailand

Infections with several flatworm parasites also represent group 1 biological carcinogens, i.e. definite causes of cancer. Infection with the food-borne liver fluke *Opisthorchis viverrini* causes cholangiocarcinoma, bile duct cancer. Whereas the causative agent for most cancers, including CCA in the West, remains obscure, the principal risk factor for CCA in Thailand has long been established - infection with *O. viverrini*. We utilized this established link between infection and cancer to explore the molecular carcinogenesis of *O. viverrini*-induced CCA. Here we report a gene-editing protocol for *O. viverrini* to enable in-depth investigation of pathogenesis and carcinogenesis. We targeted the Ov-grn-1 gene of *O. viverrini* for knockout by deletion mutation of the coding region of the gene. Both adult and infective larval flukes (newly excysted juveniles, or NEJ) were transfected with a plasmid encoding a guide RNA sequence specific for 20 nucleotides 5'- to a prototypic adjacent motif in exon-1 of the Ov-grn-1 gene and also encoding the Cas9 nuclease of *Streptococcus pyogenes*. Illumina based deep sequencing of amplicon libraries from genomic DNAs from the parasites demonstrated the presence of Cas9-catalyzed indels within the Ov-grn-1 locus, and tandem analyses by RT-PCR and western blots revealed rapid depletion of Ov-grn-1 transcripts and liver fluke granulin. Infection of hamsters with CRISPR/Cas9-edited NEJ enabled studies of liver fluke infection and biliary tract disease in hamsters. Following introduction of CRISPR/Cas9 nuclease plasmid into NEJ, marked reduction of Ov-grn-1 gene transcripts was evident within days. When hamsters were infected with the gene-edited NEJ, liver fluke infection established within the biliary tract. The findings demonstrated transfection of NEJ with the gene editing plasmid, that gene knockout abolished expression of Ov-grn-1 by >95%, and infectivity of wild type (WT) and Ov-grn-1knockout gene-edited NEJ for hamsters. Ov-grn-1-/- knockout flukes induced significantly less pathology in the hamster bile ducts. Ov-grn-1-/- parasites were infectious, colonized the biliary tract, grew and developed, were active and motile, and induced a clinically relevant pathophysiological tissue phenotype that significantly differed from WT liver flukes.

Dr Wannaporn Ittipraser, *Research Assistant Professor, The George Washington University*
Poster 45 : Diminished hepatobiliary disease during infection with CRISPR/Cas9-gene-edited *Opisthorchis viverrini* liver flukes

W Ittiprasert[1];
[1] The George Washington University, United States

Infections with several flatworm parasites also represent group 1 biological carcinogens, i.e. definite causes of

cancer. Infection with the food-borne liver fluke *Opisthorchis viverrini* causes cholangiocarcinoma, bile duct cancer. Whereas the causative agent for most cancers, including CCA in the West, remains obscure, the principal risk factor for CCA in Thailand has long been established &hypen; infection with *O. viverrini*. We utilized this established link between infection and cancer to explore the molecular carcinogenesis of *O. viverrini*-induced CCA. Here we report a gene-editing protocol for *O. viverrini* to enable in-depth investigation of pathogenesis and carcinogenesis. We targeted the *Ov-grn-1* gene of *O. viverrini* for knockout by deletion mutation of the coding region of the gene. Both adult and infective larval flukes (newly excysted juveniles, or NEJ) were transfected with a plasmid encoding a guide RNA sequence specific for 20 nucleotides 5'- to a prototypic adjacent motif in exon-1 of the *Ov-grn-1* gene and also encoding the Cas9 nuclease of *Streptococcus pyogenes*. Illumina based deep sequencing of amplicon libraries from genomic DNAs from the parasites demonstrated the presence of Cas9-catalyzed indels within the *Ov-grn-1* locus, and tandem analyses by RT-PCR and western blots revealed rapid depletion of *Ov-grn-1* transcripts and liver fluke granulin. Infection of hamsters with CRISPR/Cas9-edited NEJ enabled studies of liver fluke infection and biliary tract disease in hamsters. Following introduction of CRISPR/Cas9 nuclease plasmid into NEJ, marked reduction of *Ov-grn-1* gene transcripts was evident within days. When hamsters were infected with the gene-edited NEJ, liver fluke infection established within the biliary tract. The findings demonstrated transfection of NEJ with the gene editing plasmid, that gene knockout abolished expression of *Ov-grn-1* by >95%, and infectivity of wild type (WT) and *Ov-grn-1*knockout gene-edited NEJ for hamsters. *Ov-grn-1*$^{-/-}$ knockout flukes induced significantly less pathology in the hamster bile ducts.*Ov-grn-1*$^{-/-}$ parasites were infectious, colonized the biliary tract, grew and developed, were active and motile, and induced a clinically relevant pathophysiological tissue phenotype that significantly differed from WT liver flukes.

Mr EduBiel Alpizar Sosa, *DVM, PhD, University of Glasgow*

Poster 46 : Polyene resistance in *Leishmania* probed with metabolomics and genomic approaches

E A Alpizar[2]; A Pountain[2]; M P Barrett

[1] University of Glasgow , UK; [2] University of Glasgow, Institute of Infection, Immunity & Inflammation,, UK

Drugs targeting ergosterol have been used for decades to treat Leishmaniasis. Nonetheless, their mechanism of action is not fully understood. An Omics approach was taken to probe the development of resistance to several polyene compounds in Leishmania. spp.. Drug resistant clones of *L. mexicana, L. infantum* and *L. tarentolae* were selected in increasing concentrations of drug, then analysed using genomic (NGS), transcriptomic (RNA-seq, qPCR) and metabolomics approaches (LC-MS and GC-MS). Key changes were observed in metabolites related to energy metabolism and the synthesis of sterols. CRISPR Cas9 is now being used to probe further some of the mutations identified as contributing to their role in drug resistance.

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Mr Simão Correia, *Master student, University of Aveiro*

Poster 47 : Patterns of trematode parasites communities in *Cerastoderma edule* cockles from Portugal aquatic systems

S Correia[1]; L Magalhães[1]; X de Montaudouin[2]; R Freitas[1];

[1] University of Aveiro, Portugal; [2] University of Bordeaux, France

The edible cockle, *Cerastoderma edule,* is a widely distributed bivalve along the European aquatic systems. This species displays an important ecological and socio-economic role, being the most exploited bivalve in Portugal. Cockles act as first and/or second intermediate host for several trematode species. Trematodes are the most abundant and common macroparasites in coastal waters, displaying a complex life cycle alternating, generally, between three hosts. Trematodes, as parasites in general, present a key structuring role in communities, imposing adverse impacts on the host population dynamics. Therefore, it is of upmost importance to recognize the diversity and abundance of the species infecting cockles. In this way, the present study aimed to i) provide the first survey of trematodes infecting *C. edule* in several Portuguese aquatic systems and ii) correlate the infection level to environmental parameters (water temperature and salinity, sediment median grain size and organic matter, tidal regime and coastal system type).

Cockles monitoring was conducted from July to October 2016 in six Portuguese aquatic systems. A total of 10 species of trematodes were observed infecting cockles as first and second intermediate host. Despite the main results showed a heterogeneous trematode community among aquatic systems, two groups were identified, differing in terms of species richness and trematode mean abundance. The first group, including lower abundance values, was composed by the only subtidal area and by a lagoon characterized by low water exchanges. The second group, mainly characterized by a higher abundance of trematodes, highly correlated to the prevalence of the trematode *Parvatrema minutum*, was composed by lagoons and estuaries with significant water exchanges. These results emphasized the importance of biotic and abiotic habitat characteristics in determining the trematode distribution with more oceanic influenced areas, characterized by lower water temperature variation and higher hydrodynamic features presenting higher infection level. On the other hand, more sheltered areas, with lower water exchanges, despite the higher water temperatures reached, were characterized by lower abundance of trematodes.

In conclusion, this study suggested that one of the most limiting factor for trematode infection in *C. edule* populations was the more or less sheltered status of the habitats. Moreover, this work highlighted the ubiquity of trematode parasites in the different lagoons and argued in the necessity to incorporate them in ecological studies, in particular due to their potential negative impact on host populations.

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Dr Stephen Chiweshe, *Research Fellow, Stephen Chiweshe*
Poster 48 : A trypanosome expressed small non-coding RNA as a diagnostic marker

S M Chiweshe[2]; P C Steketee[2]; S Jayaraman[2]; E Paxton[2]; H Erasmus[1]; M Labuschagne[1]; F E Grey[2]; L Morrison[2];
[1] Clinvet Research Innovation, South Africa; [2] Roslin Institute, UK

African trypanosomiasis is a protozoan disease that affects humans (Human African Trypanosomiasis – HAT) and livestock (Animal African Trypanosomiasis – AAT) in sub-saharan Africa. There is a significant need in both HAT and AAT for improved diagnostics, in particular a specific and sensitive trypanosome-derived marker of active infection. This is particularly the case in AAT, where most diagnosis is currently symptomatic or reliant upon microscopy. Small non-coding RNA (ncRNA) are being utilised as biomarkers in a range of diseases. We have identified a small ncRNA encoded by the trypanosomes that is secreted/excreted at high levels in infected animals. The ncRNA is conserved between *T. brucei, T. congolense* and *T. vivax*, albeit with sufficient nucleotide differences to allow design of a diagnostic test that differentiates between species. Using quantitative reverse transcription polymerase chain reaction (qRT-PCR) assay, we show that active infection can be detected with high levels of sensitivity and specificity in cattle infected with all three African trypanosome species, and signal rapidly disappears after successful drug treatment. Strikingly, when parasitaemia is non-detectable by the microscopic means, we are able to detect the small ncRNA at high levels. This detection is lost following drug treatment of infected cattle. Additionally, we show that this small ncRNA can be detected using serum as the qRT-PCR substrate, increasing potential field applicability. As the biomarker is pathogen expressed, this ncRNA has significant potential utility as a diagnostic marker for active infection of AAT and HAT.

Dr Achim Schnaufer, *MRC Senior Research Fellow, University of Edinburgh*
Poster 49 : Trypanosome mitochondrial DNA: the importance of networking for getting ahead in life

S Cooper[1]; C E Dewar[1]; A Ivens[1]; A MacLeodN Savill[1]; **A Schnaufer**[1];
[1] Institute of Immunology & Infection Research, University of Edinburgh, UK; [2] University of Glasgow , UK

Function of the single mitochondrion of the sleeping sickness parasite *Trypanosoma brucei* shows striking regulation during the complex life cycle, with oxidative phosphorylation only active in the insect vector, the tsetse fly. Four out of the five mitochondrial respiratory chain protein complexes (complex I, NADH:ubiquinone oxidoreductase; complex III, cytochrome bc_1 complex; complex IV, cytochrome *c* oxidase; complex V, F_1F_O ATP synthase) are composed of both nuclearly and mitochondrially encoded subunits. Thus, while the slender

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bloodstream stage of *T. brucei* requires only two mitochondrially encoded proteins (F_1F_0 ATP synthase subunit *a* and subunit RPS12 of the mitochondrial ribosome), the procyclic insect stage in thought to require at least five. Trypanosome mitochondrial DNA (the kinetoplast) is organised as a massive network of intercalated 'maxicircles' and 'minicircles' - the most complex mitochondrial genome known. Maxicircles are the equivalent of mtDNA in other eukaryotes, while minicircles encode a vast number of short guide RNA (gRNA) molecules, typically of 40-60 nt length, that specify extensive post-transcriptional RNA editing of maxicircle-encoded mRNAs. The exact number of different types of minicircles per *T. brucei* kinetoplast was unknown, but most have predicted 100-300 distinct classes. As the procyclic insect stage requires more mitochondrially encoded gene products than the bloodstream stage, it is also expected to depend on a larger number of gRNA species, and therefore a more complex mitochondrial genome, but this has not been formally tested.
Using next-generation sequencing we have now determined the complete mitochondrial genome content of pleomorphic strain *T. brucei* EATRO 1125 (AnTat 1.1 90:13) and annotated the encoded genes using RNA-seq. We have identified 391 unique minicircles of varying copy numbers, assembled into a network of ~10,000 individual minicircle molecules per cell. Encoded within these minicircles we have identified 1035 distinct species of gRNA that cover virtually all known editing events in this organism ('canonical' gRNAs), at considerable redundancy. In addition, we have identified 225 expressed gRNA-like molecules ('non-canonical' gRNAs) of unknown function. We also have obtained conclusive evidence that *T. brucei* loses minicircle classes when grown as bloodstream stage parasite (i.e. independent of oxidative phosphorylation) and that during sexual recombination of the organism in the tsetse fly a new hybrid mtDNA network is generated that is composed of the parental networks in equal parts. Thus, highly unusual in nature, mtDNA inheritance in *T. brucei* is biparental.

Miss Zandile Nare, *PhD Student, Institute of Immunology and Infection Research, University of Edinburgh*

Poster 50 : RNA Editing Ligase 1 (REL1) drug discovery and characterisation of REL1/REL2 structure-activity relationships

Z Nare[1]; M F Sardis[1]; S Zimmermann[1]; A Schnaufer[1];
[1] Institute of Immunology and Infection Research, University of Edinburgh, UK

Trypanosomatids utilise a unique method of post transcriptional modification known as uridylyl (U) insertion/deletion RNA editing to produce mature mitochondrial mRNAs. This conversion is catalysed by the RNA editing core complexes (RECCs) of which there are three distinct classes. The RECCs are comprised of a set of twelve common proteins including the enzymes RNA editing ligase 1 (REL1) and RNA editing ligase 2 (REL2). RNA editing involves endonucleolytic cleavage, insertion and/or deletion of a number or uridine nucleotides (Us)

and ligation of the edited RNA either by REL1 or REL2. *In vivo* studies have shown that REL1 is essential for the survival of bloodstream forms of *T. brucei* while no negative effects have been observed following REL2 downregulation by RNAi-mediated knockout. Although REL1 and REL2 have a high degree of sequence similarity (41% sequence identity and 55% similarity) biochemical studies have shown that there are significant differences in their activities. It remains unclear why TbREL1 is essential for parasite survival in the bloodstream while TbREL2 is not. Previous work in our lab has led to the development of a high throughput screening (HTS) assay compatible with 384-well and 1536-well microplate formats that has been used successfully for the identification of inhibitors of TbREL1. We will report our progress of the following: (1) identification and characterisation of inhibitors of different trypanosomatid REL1 orthologues including *T. brucei*, *T. cruzi*, *T. vivax* and *L. donovani*, (2) development and optimisation of a surface plasmon resonance based assay as a secondary assay for the validation of small molecule inhibitors of TbREL1, (3) development of an expression and purification protocol for trypanosomatid REL2 orthologues for use in structural and functional studies and as complementary tools for REL1 drug discovery.

Dr Achim Schnaufer, *MRC Senior Research Fellow, University of Edinburgh*

Poster 51 : Mitochondrial retrograde signalling in *Trypanosoma brucei*

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In organisms such as yeast, mammals and plants, 'mitochondrial retrograde signalling' pathways, including the 'unfolded protein response (UPR^{mt}), convey information on the functional status of this organelle to the nucleus and modulate expression of nuclear genes accordingly[1,2,3]. Although successful completion of the life cycle of *Trypanosoma brucei* depends on stringent regulation of mitochondrial activity, it is not known if similar signalling pathways exist in these parasites. As *T. brucei* differentiates from the slender bloodstream form via the transmission competent stumpy form to the procyclic insect form it undergoes dramatic remodelling of its morphology and metabolism, including mitochondrial activity. For example, respiratory complexes III (cIII, cytochrome bc_1 complex) and IV (cIV, cytochrome *c* oxidase), composed of both mitochondrially and nuclearly-encoded subunits, are repressed in slender forms but fully active in procyclic forms. As a first step towards exploring potential retrograde signalling pathways in *T. brucei* we have compared the transcriptome of strain EATRO 1125 (AnTat1.1 90:13[4]) with a genetically engineered derivate devoid of mitochondrial DNA (akinetoplastic, or AK cells), before and after differentiation from slender to stumpy forms. Our main findings are: (i) In control ('WT') and AK parasites, 242 and 433 genes, respectively, showed significant upregulation in stumpy forms (we considered a difference of 2-fold with a p-value 0.05 as significant). 102 upregulated genes were

shared, including genes previously reported to be upregulated in stumpy cells such as PIP39 (Tb927.9.6090), dihydrolipoyl dehydrogenase (Tb927.11.16730) and EP1 procyclin (Tb927.10.10260). The upregulation of other procyclins was much less pronounced in AK stumpy cells compared to WT stumpy cells and data from the literature. This is perhaps a reflection of the reduced life span of AK stumpy cells[5]. On the other hand, 10 hypothetical proteins showed more than 4-fold upregulation exclusively in stumpy AK cells.
(ii) As reported before[6,7], genes involved in the glycolytic pathway were generally downregulated in stumpy cells. We also observed robust downregulation in stumpy cells of numerous histones and of two genes involved in kDNA maintenance, mitochondrial DNA ligase LIG k alpha (Tb927.7.610) and cysteine peptidase PNT1 (Tb927.11.6550).
(iii) When we compared slender AK vs. WT cells we observed only 27 robust changes (either up or down), which mostly concerned genes annotated as 'pseudogene', or 'hypothetical unlikely', including a putative UDP-Gal or UDP-GlcNAc-dependent glycosyltransferase pseudogene that was ~5-fold increased in AK slender cells. The same mRNA was ~3-fold increased in AK stumpy cells compared to WT stumpy cells. Other changes in AK stumpy cells concerned a hypothetical protein (~3-fold upregulated) and a putative adenylosuccinate lyase (~3-fold downregulated), but overall we observed only a limited number of robust changes (13 up, 9 down), including the decreased levels of procyclin mRNAs mentioned above.
In summary, our transcriptomic studies suggest that absence of the mitochondrial genome has a surprisingly limited effect on levels of nuclearly encoded mRNAs in bloodstream stage *T. brucei*.

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Prof. Omar Triana-Chavez, *Professor, Universidad de Antioquia*

Poster 53 : Functional genomics of hypothetical proteins in *Leishmania panamensis*: towards the discovery of new vaccines candidates

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Cutaneous leishmaniasis, is a disease complex with high incidence in Colombia, caused mainly by parasites of the

species *Leishmania panamensis*. To date, an efffective vaccine for leishmaniasis is not available and drug treatments have many complications. Therefore, it is necessary to make a rational search of vaccine candidates and new drugs, which requires information of the genome and transcriptome of this parasite. The purpose of this study was to compare the transcriptome between amastigotes and promastigotes from *L. panamensis* to identify stage-specific expressed genes and new vaccine candidates. We found 123 up-regulated and 127 down-regulated transcripts in amastigotes. Comparative analysis with genomes of other species and *in silico* analysis allowed us to select twenty conserved genes highly immunogenic. The biological characterization and cell localization of two of these proteins, LPAL13_270024700 and LPAL13_220016330, were evaluated in both stages. The first one, was a hypothetical protein with a BAR domain that is located in the promastigotes flagellum and in the flagellar pocket of amastigotes. This protein was overexpressed in promastigotes, and showed higher expression in highly virulent *L. panamensis* strains. In the other side, the protein LPAL13_220016330 presented a MAK16-L28e family domain and a nuclear localization signal (NLS), with a conserved zinc motif and phosphorilation target to CK2 kinase. The expression analysis showed that the amastigotes have higher expression by qRT-PCR and Western blot. Furthermore, the protective efficacy of both proteins in J774 cells and mice was evaluated using recombinant proteins with and without encapsulation in MPGE-PLA nanoparticles, and DNA vaccines as antigens. Interestingly, the cells J774 pre-treated with LPAL13_270024700 protein decreased significantlly the number of intracellular amastigotes. Moreover, a high protection was observed in *L. panamensis* infected BALB/C mice. Thus, the results indicate that hypothetical proteins are promising source of new candidates to develop vaccines against leishmaniasis. Further studies to evaluate the possible mechanism of protection of these genes should be performed.

Dr Juan Macedo, *Postdoc, London School of Hygiene and Tropical Medicine*

Poster 54 : Decoding the regulators of ribosomal DNA transcription in *Trypanosoma brucei*

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Uniquely, amongst eukaryotes, *Trypanosoma brucei* RNA polymerase I (RNAPI) generates a subset of mRNAs. The most important of these gives rise to the highly abundant variant surface glycoprotein (VSG), the major surface protein of the pathogenic form of *T. brucei*, and key mediator of antigenic variation. Research on RNAPI transcriptional regulation in *T. brucei* has focused on understanding its role in monoallelic *VSG* transcription. However, relatively little attention has been paid to the regulation of ribosomal DNA (*rDNA*) array transcription. Our previous findings have suggested that only a subset of *rDNA* arrays are active and that changes in *rDNA* transcriptional activity may have an impact on *VSG* transcription. We aim to identify and characterize the *trans-*

acting factors that regulate *rDNA* transcription in *T. brucei*, thereby ensuring optimal rRNA and VSG mRNA production. We have generated a set of reporter cell lines incorporating a neomycin phosphotransferase (*NPT*) gene either immediately downstream of an ectopic or native *rDNA* promoter (proximal) or adjacent to the *5.8S* sequence within an *rDNA* array (promoter distal). Consistent with the previously identified expression variability seen between *rDNA* spacers, we observed variable reporter expression between arrays, whether the reporter was integrated in a promoter-proximal or -distal position. To enable the identification of factors responsible for *rDNA* array transcriptional repression, we introduced the RNAi library into a subset of our reporter lines and screened for enhanced resistance to G418, leading to the identification of several candidate factors. Efforts to validate these putative novel *rDNA* transcriptional regulators are currently underway.

Helen Whiteland, *PDRA, Aberystwyth university*

Poster 55 : The dual anthelmintic potential for triterpenoids in the treatment of blood and liver flukes

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The ability to rapidly identify chemotherapies with activity against a diverse range of disease-causing pathogens is a major driving force in drug discovery. For example, compounds with dual activity against both liver and blood flukes could improve the economic and biomedical burdens associated with the neglected infectious diseases schistosomiasis and fascioliasis. In the UK alone, infection with *Fasciola hepatica* (liver fluke) leads to the loss of over £300 million per annum in the livestock sector. Furthermore, chronic infection with *Schistosoma* (blood fluke) worms results in the deaths of 200,000 people per annum. In the absence of immunoprophylactic vaccines, these figures clearly demonstrate an urgent need to maintain existing or identify new chemotherapies for sustaining anthelmintic control.

For *F. hepatica* control, triclabendazole (TCBZ) is the only drug on the market that kills both adult and juvenile stages of the parasite. In schistosomiasis, praziquantel (PZQ) is the only registered drug active against all human-infective schistosome species. Unfortunately, PZQ is ineffective against juvenile worms, often requiring repeat treatment in endemic areas. Furthermore, TCBZ resistant (or less susceptible) liver flukes have been found in all continents where fascioliasis is endemic and there is increasing concern that PZQ insensitive (or resistant) blood flukes could also be developing. Therefore, single-compound fascioliasis and schistosomiasis control strategies are unlikely to be sustainable presenting a strong impetus for identifying new anthelmintics.

In this study, we continued our search for anthelmintic products derived from plants. Specifically, we screened twenty triterpenoids for activity against juvenile and adult lifecycle stages of both liver and blood fluke parasites. Of these twenty, one compound had an overlapping effect on both parasites in all stages of the lifecycle examined.

This compound, 700015, resulted in gross disruption to the tegument of both species and affected both neoblast proliferation as well as oviposition within *S. mansoni* adult worms. Initial investigations into cell cytotoxicity suggests that this compound is not particularly cytotoxic to bovine MDBK or human HepG2 cells. We have demonstrated that naturally derived triterpenes have the potential as future drug candidates to treat both liver and blood flukes.

Prof Hoda Elfayoumi, *Professor parasitology, Faculity of Science Beni-suef University*
Poster 56 : *Rhabdias bufonis* (Nematoda: Rhabdiasidae) from the lung of the African common toad, *Amietophrynus regularis* (Bufonidae) in Egypt. A new data on the basis of light and scanning electron microscopic study

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Rhabdias bufonis (Rhabdiasidae) is one of the highly pathogenic nematode parasites infecting the lung of amphibians. The present study introduces the morphological description of this nematode isolated from the lung of the African common toad, *Amietophrynus regularis* collected from its natural habitat; the damp, moist fields and gardens at Giza governorate, Egypt. The study based on the data obtained from light and scanning electron microscopic examination. 14 out of 40 (35%) of the examined specimens were found to harbor a large number of this parasite. All of the recovered worms were females5.2-12.5 mm (8.8 mm) long and 0.2-0.7 mm (0.5 mm) wide at mid body. The anterior end was blunted while the posterior one was tapered. The body covered by a delicate inflation of the cuticle strongly folded on its surface. The SEM study presented new details regarding the cephalic end of this nematode which was not identified in the previous studies, of them, a slit-like mouth surrounded by two pairs of lateral papillae and two amphids. Also, three pairs of cuticular inflation supporting the area around mouth opening

Dr Wafa Al-Kandari, *Associate Professor, Kuwait University*
Poster 57 : Molecular characterization of *Acanthoparyphium* sp. (Trematoda: Himasthilidae) by mitochondrial genome from Kuwait Bay

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Echinostomes of the family Himasthlidae are common parasites in birds and mammals including humans world-

wide. Advanced molecular techniques are required for the accurate and reliable identification of these parasites, for understanding its life cycle and host parasite interactions. Mitochondrial genome consists of many molecular markers making it an excellent candidate for trematode identification. These molecular markers can be used for many diagnostic purposes as well as phylogenetic studies. This study is the first molecular study done on whole mitochondrial genome of *Acanthoparyphium* sp. isolated from Kuwait Bay using Next generation Sequencing technique. It employs phylogenetic analysis on the whole mitochondrial genome for the accurate identification and comparison of the *Acanthoparyphium* sp. isolated from Kuwait Bay with members of the superfamily Echinostomatidea found in the world. The phylogenetic analyses confirmed its position within the Himasthlidae family and within the genus *Acanthoparyphium*.

Miss Claudia Andrew, *Student, Aberystwyth University*

Poster 58 : Exploring the Glutathione transferase (GST) family in *Schistosoma mansoni*: Extracellular vesicle expression

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Schistosomiasis causes 280,000 deaths per year in sub-Saharan Africa exclusively. Subsequently, the World Health Organisation (WHO) reported that 206 million people required treatment for schistosomiasis in 2016.Globally, a third of all infections are due to *Schistosoma mansoni*. At present, control is heavily focused on the administration of anthelmintics, an approach not regarded as sustainable. Thus, research is targeted towards the development of novel vaccines including those based on recombinant proteins. The glutathione transferase (GST) protein family has long been identified as a source of such vaccine candidates to eradicate schistosomiasis. However, the mechanism of action is poorly understood and the complete understanding of the GST family itself is lacking. Thus, vaccine trials incorporating GST components have stalled. The aim of the current study was to utilise high resolution proteomics technology supported by in depth bioinformatics, to explore the full capacity of the GST family in *S. mansoni*. Bioinformatic characterisation of the *S. mansoni* genome revealed 3 classes of GST (Mu, Microsomal, and Omega) with multiple members within the Mu class. Following GST affinity purification, using glutathione agarose, high resolution proteomics in combination with Western blotting has confirmed the presence of both sigma and mu class GSTs in the adult soma. In addition, we have explored GST expression associated with extracellular vesicles (EVs). EVs were purified from adult excretory/secretory products using size exclusion chromatography. Transmission electron microscopy with target GST gold labelling has been established to investigate sigma class GST expression on the surface of S. mansoni EVs. This study has deepened our

understanding of the GST family in S. mansoni and will assist the development of an improved schistosomiasis vaccine based on GST.

Dr Achim Schnaufer, *Reader in Parasite Biology, University of Edinburgh*

Poster 59 : Trypanosome mitochondrial DNA: the importance of networking for getting ahead in life

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Function of the single mitochondrion of the sleeping sickness parasite *Trypanosoma brucei* shows striking regulation during the complex life cycle, with oxidative phosphorylation only active in the insect vector, the tsetse fly. Four out of the five mitochondrial respiratory chain protein complexes (complex I, NADH:ubiquinone oxidoreductase; complex III, cytochrome bc_1 complex; complex IV, cytochrome *c* oxidase; complex V, F_1F_O ATP synthase) are composed of both nuclearly and mitochondrially encoded subunits. Thus, while the slender bloodstream stage of *T. brucei* requires only two mitochondrially encoded proteins (F_1F_O ATP synthase subunit *a* and subunit RPS12 of the mitochondrial ribosome), the procyclic insect stage in thought to require at least five. Trypanosome mitochondrial DNA (the kinetoplast) is organised as a massive network of intercalated 'maxicircles' and 'minicircles' - the most complex mitochondrial genome known. Maxicircles are the equivalent of mtDNA in other eukaryotes, while minicircles encode a vast number of short guide RNA (gRNA) molecules, typically of 40-60 nt length, that specify extensive post-transcriptional RNA editing of maxicircle-encoded mRNAs. The exact number of different types of minicircles per *T. brucei* kinetoplast was unknown, but most have predicted 100-300 distinct classes. As the procyclic insect stage requires more mitochondrially encoded gene products than the bloodstream stage, it is also expected to depend on a larger number of gRNA species, and therefore a more complex mitochondrial genome, but this has not been formally tested.
Using next-generation sequencing we have now determined the complete mitochondrial genome content of pleomorphic strain *T. brucei* EATRO 1125 (AnTat 1.1 90:13) and annotated the encoded genes using RNA-seq. We have identified 381 unique minicircles of varying copy numbers, assembled into a network of ~10,000 individual minicircle molecules per cell. Encoded within these minicircles we have identified 1035 distinct species of gRNA that cover virtually all known editing events in this organism, at considerable redundancy. In addition, we have identified 225 expressed gRNA-like molecules of unknown function. We also have obtained conclusive evidence that *T. brucei* loses minicircle classes when grown as bloodstream stage parasite (i.e. independent of oxidative phosphorylation) and that during sexual recombination of the organism in the tsetse fly a new hybrid

mtDNA network is generated that is composed of the parental networks in equal parts. Thus, highly unusual in nature, mtDNA inheritance in *T. brucei* is biparental.

Anna Kildemoes, *PhD student, University of Copenhagen*

Poster 60 : Host immunopathology in response to *Schistosoma mansoni* infection in mice with altered gut microbial composition

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Chronic infection with the parasitic blood fluke, *Schistosoma mansoni*, present the most severe pathology related to egg-induced host immune responses and fibrosis development. Commensal gut microbial composition influences host immune homeostasis and hence potentially affects systemic immunopathology induced by pathogens such as *S. mansoni.* Both humans and experimental models show metabonomic changes related to gut microbial and liver metabolism associated with *S. mansoni* infection. These points towards a role for gut microbiota in *S. mansoni* pathology regulation via the host immune response. To investigate whether different gut microbial compositions would result in differences in pathology induced by *S. mansoni* eggs, a controlled mouse model combining antibiotics treatment and infection was established. The commensal gut microbial composition was altered by oral administration of ampicillin/vancomycin and combined with subsequent *S. mansoni* infection in a C57BL/6-NTAC mouse model. Here egg-induced hepatomegaly and relative degree of inflammation were quantified in liver and ileum tissues by stereological principles. A significantly lesser degree of inflammation in liver tissue in the combined antibiotics treated and *S. mansoni* infected group compared to the infected only group was seen. This difference in degree of inflammation was not observed in ileum tissue and could not be explained by infection burden. Furthermore, differences in liver panel parameters, number of collagen depositions and cytokines (IFN-ɣ, IL-33) underscore an altered response to *S. mansoni* eggs in the liver when the gut microbial composition is strongly altered before infection. Our results implicate a role for intestinal immune milieu influenced by gut microbial composition in liver pathology development and hence morbidity. Further research is necessary to determine whether more subtle alterations of gut microbial compositions by factors such as diet, other infections, food-associated antibiotics or drugs facilitate a strong enough change in immune milieu to affect systemic pathology.

Mr Ibrahim Alfayez, *PhD student, University of Glasgow*

Go to here for the 'at a glance' view of the conference

Poster 61 : An investigation of 5-fluorouracil resistance in kinetoplast parasites

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Kinetoplastid parasites are a widespread group of flagellated protozoan pathogens and the defining feature of these parasites is the presence of a large mitochondrial DNA region known as the 'kinetoplast'. The most common human diseases caused by kinetoplastid parasites are: 1) African trypanosomes (African sleeping sickness), 2) *Leishmania* species (leishmaniasis) and 3) *Trypanosoma cruzi* (Chagas' disease). The two types of nucleotides in the cell are purine and pyrimidine which have a very significant role in nucleic acid synthesis (DNA and RNA) and the metabolism of prokaryotic and eukaryotic cells. Kinetoplastid parasites are capable of salvage as well as synthesis of pyrimidine nucleotides. Kinetoplastid protozoa express many such membrane transport proteins which enable them to take up nutrients, efflux metabolites, regulate physiological concentrations, translocate various molecules, and import or export drugs. Resistance to 5-fluorouracil (5-FU) was generated in both *T. b. brucei* BSF s427- wild type and *Leishmania mexicana* promastigotes, yielding clonal lines Tbb-5FURes and Lmex-5FURes, respectively. The gene family encoding pyrimidine nucleobase transporters in kinetoplast parasites has not yet been discovered. We try to identify these using the antimetabolite 5-FU as a probe. Previous work in our laboratories (RNA-seq and RIT-seq) analyses of 5-FU resistant cell lines has identified candidate genes for pyrimidine transporters, including genes annotated as cation transporters (*Tbb-CATs*), fatty acid desaturase (*Tbb-FAD* and *Lmex-FAD*) and glucose transporters (*2A*, *1B* and *1E*). Apart from some glucose transporters, none of these potential transport genes have been previously characterised in protozoa and as such they are of interest in their own right as well. The main aim of this study therefore is to identify the gene(s) encoding the protozoan transporters of pyrimidines, particularly uracil, and assess candidate genes that may be involved in transport of, or sensitivity to, 5-FU. For this we will use reverse genetics approaches such as knockout constructs, targeted RNAi, and overexpression of the target genes. We determined the sensitivity of the 5-FU and 6-Azauracil (6-AU) in a sKO of *Tbb-CATs* and *T. b. brucei 427 WT* with the use of alamar blue drug sensitivity assay, and found no significant difference. We were unable to make a full double knockout for the CATs, as this led to the death of the cells, showing that their function is essential for the growth of BSF *T. b. brucei in vitro*. Also, the effect of increased gene expression of *Tbb-FAD* in Tbb-5FURes and *Lmex-FAD* inLmex-5FURes on 5-FU and 6-AU sensitivities were analysed using the alamar blue assay. Results showed no significant differences in the EC_{50} values of 5-FU and 6-AU between the overexpressing cell lines and the control lines. Efforts to identify the pyrimidine transporter genes are presently ongoing and identification of these genes will significantly improve our understanding of drug and nutrient transporters of kinetoplast parasites.

Go to here for the 'at a glance' view of the conference

Mrs Diane Anderson-Aidoo, *PhD Student, University of Aberdeen*
Poster 62 : *In vitro* models of macrophage activation in *Trypanosoma brucei* infection

D Anderson-Aidoo[1]; J M Sternberg[1];
[1] University of Aberdeen, UK

Pathogenesis in African trypanosome infection is associated with a dysregulation of inflammatory regulation and an over-activation of type 1 macrophage responses. This is driven in part by components of the variant surface antigen, though other factors have been implicated. The mechanisms of this process are poorly understood. The requirement for MyD88 signalling provides circumstantial evidence of TLR signalling, but no direct evidence has been presented for this. We are developing experimental platforms to define the interaction of trypanosomes with innate immune receptors, with the aim of identifying key immunomodulatory parasite components. In an *in vitro* system using murine macrophage like RAW264 cells, we demonstrate that culture adapted *T.brucei*, conditioned medium and lysate caused upregulation of inflammatory cytokine production (specifically TNF-α and IL-6). We confirmed these findings in RAW264 reporter cells that express alkaline phosphatase after PRR signalling leading to NF-KB activation. We also have used TLR overexpressing HEK reporter cells to demonstrate that the parasites trigger signalling via TLR4 and TLR2 *in vitro*. We will use this system to identify the ligands involved in these responses.

Mr Santiago Chavez Garcia, *Research Assistant, Facultad de Ciencias*
Poster 63 : Gene expression remodeling at the G1/S transition of the *Trypanosoma cruzi* cell cycle

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The mechanism governing gene expression regulation along the proliferative cycle of *Trypanosoma cruzi* are still poorly understood. In view of the biological and therapeutic relevance of the parasite replication we sought to apply RNA-seq approaches to identify global gene expression patterns during the progression of the parasite cell cycle. For that purpose, we deep sequenced the polyA-RNAs (transcriptome) and the ribosome footprints (translatome) of different cell cycle phases. We analyzed epimastigotes of a TcI strain synchronized with hydroxyurea, obtaining cell populations in G1, S and G2/M phases (at 70% enrichment). We extracted RNA and prepared RNA-seq libraries for NGS. We found 305 differentially expressed mRNAs (DEGs) (fold change>1.5, p-value <0.01) in the

total RNA fraction. These transcriptomic changes involve proteins dedicated to carbohydrates metabolism and energy production at G1-phase (70 genes), DNA and chromatin replication at S-phase (97 genes) and microtubules-based movement at G2/M-phase (138 genes). For the ribosome profiling, we only studied the G1-S transition. Interestingly, translational regulation affects more than 1150 genes at >2.0-fold change, 20% and 80% of which were up-regulated in G1 and S-phase respectively. Enriched molecular functions in the latter dataset include ribosome synthesis, nucleotide metabolism and microtubule dynamics. We found specific sequence and structural RNA motifs in the UTRs, including the known CS sequence responsible for the periodical expression of some mRNAs. Several known as well as novel RNA binding proteins are found to periodically modify the abundance of their mRNA; indeed, some are predicted to bind the enriched RNA sequence motifs.

Dr Gregorio Perez Cordon, *Research Scientist, Cryptosporidium Reference Unit, PHW*
Poster 64 : Developing a multilocus variable number tandem repeat analysis scheme for *Cryptosporidium parvum* subtyping

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Cryptosporidium parvum is a protozoan parasite that infects a wide range of animals and humans typically causing a diarrhoeal disease, which can lead to death especially in immunocompromised individuals. The robust nature of *Cryptosporidium* oocysts enables the parasite to be transmitted through multiple routes from diverse hosts. Thus, in order to assess risks of infection, investigate outbreaks, and apply appropriate interventions, tracking sources of contamination and routes of transmission is of paramount importance. In the absence of a multilocus genotyping scheme, subtyping *C. parvum* isolates has been mainly restricted to the DNA sequence analysis of a gene encoding a 60 KDa glycoprotein (gp60). Although this marker provides some discrimination and inference of linkage to point source contamination, the recombinant nature of this parasite observed both experimentally and in nature demands a multilocus-based method for more accurate discrimination. Whole genome sequencing would provide the ultimate determination of variation, but for *Cryptosporidium* it is a time consuming and expensive approach to be implemented routinely in clinical laboratories and for inter-laboratory surveillance. It has been shown that multilocus genotyping based on genetic loci containing a variable number of tandem repeats, can enable rapid characterization of outbreak isolates and infer linkage.
During an expert workshop on *Cryptosporidium* genotyping hosted by the Robert Koch Institute, Berlin, 2016, the criteria to develop a harmonised approach to intra-species differentiation in *Cryptosporidium* were established. Based on these criteria we interrogated the *C. parvum* Iowa II reference genome with Tandem Repeat Finder software in order to identify variable number tandem repeats loci (VNTR) suitable for fragment sizing by most

fragment sizing platforms: VNTR loci containing repeats 6 bp in tandem and providing an amplicon size < 300 bp including 50bp flanking the repeat region at both sides for the location of primers. Twenty eight markers were identified initially (Tandem Repeats Finder, New York) and subsequently showed multiple alleles in seven of our own *C. parvum* genomes. From these, seven markers were selected for *in vitro* evaluation based on their higher variability. PCR primers were designed and fragment sizes estimated for 20 *C. parvum* samples using a QIAxcel Advanced (Qiagen) machine, run under optimised conditions, and compared with sequencing. Estimated fragment sizes were confirmed in most samples. When repeatability and reproducibility was investigated using triplicate PCR reactions of four samples on two occasions, discrepancies were observed in a small number of reactions but were resolved readily. However, when applied to a larger validation panel of 268 *C. parvum* samples representing spatio-temporal variation, outbreaks and sporadic infections of humans and animals, 5% PCR reactions were not detectable, and a further 5% provided inconsistent and unresolvable ambiguous sizes especially in the 6 bp repeat markers; consequently, MLGs could not be assigned to 48 % samples. To improve accuracy and reliability, the validation panel is under re-evaluation using labelled primers for fragment sizing on a different platform (3500 Genetic Analyzer, Applied Biosystems™), using multiplexed PCRs for an economic approach. This should enable full-scale validation according to internationally accepted methods for evaluation of microbial typing schemes: typability, discriminatory power, epidemiological concordance and efficiency, and the results will be presented at the conference.

Mrs Samia Alghamdi, *PhD student, Infection Biology Institute of Infection & Global*

Poster 65 : The first investigation of ectoparasites on rodents from the 'Asir region of Saudi Arabia

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Background: Rodents have become increasingly recognised as hosts of ectoparasites and reservoirs of numerous human diseases including scrub typhus (*Orientia* spp.), bartonellosis (*Bartonella* spp.), hantaviruses, Lyme disease (*Borrelia burgdorferi* complex), and plague (*Yersinia pestis*).
Objectives: This study aimed to define the taxonomic diversity and bacterial microbiome of ectoparasites collected from wild rodents in the 'Asir Region of southwestern Saudi Arabia, with a main focus on chigger mites (family Trombiculidae), the vectors of scrub typhus.
Methods: Wild rodents were trapped in scrubland across one site on the slopes of the Asir Mountains in 2016 (Al Ous') and four sites in 2017 (Al Ous', Al Jarf, Alogl and Wosanib). Rodents were euthanized prior to examination

and all ectoparasites were collected and stored in absolute ethanol. A 10% subsample of ectoparasites was selected from each rodent for mounting in Berlese fluid and morphometric examination.
Results A total of 7,802 ectoparasites were obtained from 74 rodent specimens, comprising 6,135 chigger mites, 119 fleas in one species (Parapulex chephrenis), 770 ticks of at least two species (Haemaphysalis erinacei and Rhipicephalus spp.), 589 lice in two species (Polyplax brachyrrhyncha and Polyplax oxyrrhyncha), and 189 gamasid mites(species to be determined). The rodents belonged to three species: Acomys dimidiatus, Myomys yemeni and Meriones rex. Based on the morphology of the scutum (or dorsal shield), chiggers were assigned to subgenera and provisionally into 17 species, including three putative new species: Neotrombicula sp. n., Microtrombicula aff. machadoi, and Schoutedenichia sp. n. The most abundant chigger species were Ericotrombidium kazeruni, Schoutedenichia aff. geckobia and Ascoschoengastia browni. The site with the highest mean chigger infestation (139) was Al Ous', and the host species with the greatest mean infestation rate (114) was the Eastern spiny mouse (A. dimidiatus). Conclusion: This is the first survey of rodent ectoparasite diversity performed in the 'Asir Region of Saudi Arabia. Following DNA extractions, 16S rRNA amplicon sequencing will be applied to pools of different chigger species and other ectoparasites to identify potentially zoonotic bacteria and other arthropod symbionts that may be circulating within the 'Asir region.

Miss Kezia Whatley, *Research Assistant*

Poster 66 : Roboworm 3: Development of an automated drug screening platform for *Fasciola hepatica*

K Whatley[1]; J Tomczak[2]; H Whiteland[1]; K F Hoffmann[1];
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At least 2 billion people worldwide are carrying a parasitic helminth infection resulting in chronic illness, and morbidity, equating to > 55 million disability adjusted life years (DALYs). The domestic livestock industry is also affected, with >£110 million lost in revenue per annum and £360 million spent on preventative anthelmintics in the EU alone. Current chemotherapeutic options for helminth infections in both human and veterinary medicine are limited. With building concern that helminths may be losing sensitivity or building resistance to these treatments, new cost effective, strategic routes for drug discovery are needed.
The Roboworm platform is a high-throughput, high content screening system. Through the Welsh government funded Life Sciences Bridging Fund, this system has been adopted to assess whether it is possible to build an image analysis model based on the phenotype of newly excysted juvenile (NEJ) stage of helminth parasite *Fasciola hepatica* in collaboration with commercial partner Informatics Unlimited.
In order to capture a wide variety of phenotypes expressed by drug treated NEJs, 25 parasites per well were cultured in 10uM of model compounds (Artesunate, Nitroxynil, Clorsulon, Closantel, Auranofin) along with the

current Fascioliasis treatment option, Triclabendazole, and negative control DMSO. Following 72 hours culture, NEJs were imaged at a 10x magnification (9 tiles per well). Following image capture, NEJs were segmented, individually scored as affected, unaffected or ignored, with additional subcategory considerations of image clarity, contrast and segmentation being noted.
Individual field-of-view (FOV) images were first stitched together into well images using a novel algorithm that addresses uneven illumination across individual FOV images. The obtained well images were then processed using a sequence of morphological, thresholding and segmentation operations to extract individual parasite images. The resulting objects were then assessed for their quality and a set of 75 histogram-based, texture and morphological descriptors were calculated for individual parasite images. They were next randomly split into a training and tests sets which were used to build and validate a Bayesian classification model that distinguishes between healthy and treated parasites.
Current results and planned improvements of this automated anthelmintic screening system for *F. hepatica* NEJs will be presented.

Linda Anagu, *Researcher , Keele University*
Poster 67 : Stress, sirtuin, and severe malaria

L Anagu[1]; C J Merrick[1];
[1] Keele University, UK

The mutually exclusive expression of *var* genes in blood-stage *P. falciparum* parasites is a major virulence factor in *falciparum* malaria. This depends partly upon sirtuin deacetylase enzymes - as has been shown by mutagenesis studies disrupting the sirtuin genes in cultured parasites. Furthermore, a field study of direct patient isolates previously showed that high expression of sirtuins correlates with high expression of severe-disease-associated *var* genes, and this, in turn, correlates with stress factors in the human host: high fever and hyperlactatemia. Our present work seeks to determine cause-and-effect in this relationship: can host stress factors actually cause increased sirtuin expression; and hence potential changes in virulence gene expression? To investigate this, cultured parasites were exposed to heatshock and/or lactate, and sirtuin expression was assessed by RTPCR. We previously showed that in the laboratory line 3D7, heatshock, but not lactate alone, can lead to increased expression of sirtuin RNA. We have now extended this work to several recently-lab-adapted field strains, to establish the generality of the phenomenon, and have begun to investigate the associated *var* gene expression profiles. This work ultimately aims to improve our understanding of how *P. falciparum* can respond to variable conditions in its human host.

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Mr Gustavo Campagnaro, *PhD student, University of Glasgow*
Poster 68 : Characterisation of *Trypanosoma cruzi* Equilibrative Nucleoside Transporters by expression in a genetically adapted *Trypanosoma brucei* cell line

G D Campagnaro[1]; H P De Koning[1];
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Trypanosoma cruzi, the causative agent of Chagas' disease, is a kinetoplastid parasite endemic to the American continent and infects around 6 to 7 million people. As a kinetoplastid, *T. cruzi* is unable to synthesise its own purines and relies on salvage from the host, but its transport mechanisms have not yet been characterised. In other protozoa, purine uptake is mediated by Equilibrative Nucleoside Transporters (ENTs). To investigate whether this is also the case in *T. cruzi*, its four ENT genes (provisionally named TcrNBT1, TcrNBT2, TcrNT1 and TcrNT2) were cloned and expressed in a *Trypanosoma brucei* procyclic cell line from which a cluster of three high-affinity nucleobase transporters was deleted (TbNBT-KO), and which displayed reduced (~86%) [^{3}H]-Hypoxanthine uptake. TcrNBT1 was shown to be a very high affinity oxopurine nucleobase transporter with a K_m of 93.8 ± 4.7 nM for hypoxanthine and a K_i of 121.9 ± 22.4 nM for guanine, while the K_i for adenine was determined as 3.7 ± 0.5 µM. TcrNBT1 harboured lower affinity for purine nucleosides and poor affinity for pyrimidines. In contrast, TcrNT1 was found to be a high-affinity guanosine/inosine transporter with a K_m of 1.0 ± 0.03 µM for inosine and a K_i of 0.92 ± 0.2 µM for guanosine. Interestingly, TcrNT1 showed higher affinity for hypoxanthine (K_i = 23.9 ± 5.5 µM) than for adenosine (K_i = 38.9 ± 5.8 µM) and virtually no affinity for other purines or pyrimidines. Different from TcrNB1 and TcrNT1, TcrNT2 turned out to be a high-affinity thymidine transporter (K_m = 223.5 ± 7.1 nM), displaying some affinity for uridine and cytidine, (K_i values of 66 ± 6 and 728 ± 70 µM, respectively), but barely sensitive to inhibition by pyrimidine nucleobases or purines. At present, only TcrNB2 is still undergoing characterisation. We propose TbNBT-KO as system for rational characterisation of ENT genes, and established the kinetic parameters of some *T. cruzi* purine and pyrimidine transport systems. The results indicate that, surprisingly, this parasite has a preference for oxopurines over aminopurines.

Dr Kathryn Huson, *Research Fellow, Queen's University, Belfast*
Poster 69 : Novel eggshell biochemistry of rumen flukes

K M Huson[1]; N A Oliver[1]; M W Robinson[1];
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Paramphistomosis, caused by *Calicophoron daubneyi,* is an emerging disease of ruminant livestock in the UK and Ireland. With only one drug (oxyclozanide) currently proven to be effective against both the adult and juvenile parasites there is a clear need to identify new control strategies to combat rumen fluke infection. *C. daubneyi* produce thousands of eggs per day, to complete their life-cycle, thus eggshell formation may represent a promising target for therapeutic intervention. Most trematode eggshells (including those of the liver fluke *Fasciola hepatica*) are formed by tyrosinase-mediated cross-linking of modified tyrosine (L-DOPA) residues present in the vitelline proteins. However, our histochemical analysis and UV fluorescence microscopy suggests that the composition of the eggshell proteins and the chemical nature of their cross-links are distinct in *C. daubneyi*. In addition, *C. daubneyi* eggshells were resistant to the de-tanning agent sodium hypochlorite (which readily dissolved *F. hepatica* eggshells) but were solubilised by the reducing agent DTT. Finally, sequence analysis of *C. daubneyi* vitelline proteins revealed that the percentage of tyrosine residues present had approximately halved in *C. daubneyi* compared to sequences from related fluke species, and a similar percentage of cysteine residues had been introduced, whereas no cysteine is present in the vitelline protein sequences from these other trematodes. In some instances the cysteine residues had directly replaced tyrosine where known L-DOPA modifications involved with cross-linking occur. Taken together, our data suggest that *C. daubneyi* eggshells may be stabilised by disulfide cross-links rather than cross-linking of L-DOPA residues as seen in other trematodes.

Ms Julia Halder, *Research Assistant, Imperial College London*

Poster 70 : Decreasing the impact of Chagas disease through modelling: The DICTUM framework for retrieving, collating, and analysing serosurvey data for Chagas disease across Latin America

J B Halder[1]; Z M Cucunubá[1]; D Prociuk[1]; P Nouvellet[2]; M G Basáñez[1];
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In order to assess progress towards interruption of intra-domiciliary transmission of *Trypanosoma cruzi* in the 21 endemic countries of Latin America, understanding the historical exposure to infection is paramount. Serological surveys can provide useful insight if the serological data are age-structured, because the force-of-infection (FoI) can then be estimated retrospectively according to the ages of the serosurvey participants. Following on from previous analyses of data from Colombia [1], which allowed understanding of the spatio-temporal profiles of the FoI, we sought to expand this work across Latin America to support the endemic countries' goals. The first stage was to search the published literature systematically and to construct a framework for collating, harmonising, and preparing for analysis, serological survey data which can be used to model the FoI.
We conducted a literature search, across PubMed, Embase, LILACS, Global Health, CAB Abstracts and Web of

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Science, to find and retrieve published serosurvey data for the 21 endemic countries. Gaps in the published, retrievable literature were identified. We constructed standardised data extraction forms, and have collated data for a subset of these countries. The serosurvey results were harmonised and stored, with survey and source meta-data, in a relational database. The total number of serosurveys stored currently is 241. This includes, from the literature search: 27 from Brazil, 48 from Argentina, 31 from Mexico, 19 from Bolivia, six from Guatemala, and one from Costa Rica, alongside 109 datasets from the Colombia study, which had been collated from published and unpublished literature [1]. The database facilitates the retrieval of data for use in catalytic models to reconstruct estimates of the FoI through time and space. Model outputs, primarily the FoI estimates (median and Bayesian credible intervals), are also stored in the database ready for further analyses such as obtaining estimates of disease burden.

The work was funded by the Neglected Tropical Diseases Modelling Consortium (NTD-MC). [1] Cucunubá ZM, Nouvellet P, Conteh L, *et al.* Modelling historical changes in the force-of-infection of Chagas disease to inform control and elimination programmes: application in Colombia. BMJ Glob Health 2017;2:e000345.

Mr Benjamin Hulme, *PhD Student, Aberystwyth University*

Poster 71 : Characterisation of a functional α-N-acetylgalactosaminidase (α-NAGAL) in the parasitic blood fluke *Schistosoma mansoni*

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α-galactosidase (α-GAL) and α-N-acetylgalactosaminidase (α-NAGAL) are two glycosidases responsible for maintaining normal cellular homeostasis by preventing the accumulation of glycan substrates on proteins and lipids. Mutations in the genes encoding both enzymes lead to neurological and neuromuscular impairments seen in both Fabry disease and Schindler/Kanzaki disease. This current study investigates whether the parasitic blood fluke *Schistosoma mansoni,* responsible for the neglected tropical disease schistosomiasis, also contains enzymatically active α-GAL and α-NAGAL proteins. As infection, parasite maturation and host interactions are all governed by carefully-regulated glycosylation processes, inhibiting *S. mansoni*'s α-GAL and α-NAGAL activities could lead to the development of novel chemotherapeutics. Sequence and phylogenetic analyses of platyhelminth α-GAL/α-NAGAL protein types showed that one particular *S. mansoni* protein (Smp_089290) to be quite distinct from other putative α-GAL/α-NAGAL members and the only *S. mansoni* protein to contain the functional amino acid residues necessary for α-GAL/α-NAGAL substrate cleavage. By homology modelling, the predicted three-dimensional structure of Smp_089290 exhibited folds and secondary features similar to those described for human α-GAL/α-NAGAL proteins. Both α-GAL and α-NAGAL enzymatic activities in adult *S. mansoni* worms were

significantly higher in females compared to males ($p<0.05$; α-NAGAL > α-GAL), which was consistent with Smp_089290's female biased gene expression. While siRNA-mediated knockdown of Smp_089290 in adult male worms caused a slight decrease in α-GAL activity, α-NAGAL activity was significantly reduced in these same samples when compared to control male worms (*siLuc* treated males; $p<0.01$). Similarly, a significant reduction in α-NAGAL activity was also exhibited in adult female worms treated with the same Smp_089290-specific siRNA when compared to *siLuc* treated females ($p<0.05$). Based on these enzymatic and functional genomics results, Smp_089290 acts predominantly as a α-NAGAL (hereafter termed SmNAGAL) in schistosome parasites. Whole-plate motion-based screening of si*Smnagal* treated males and females revealed a significant decrease in motility when compared to *siLuc* treated controls ($p<0.05$). Inhibition of SmNAGAL activity could lead to glycan substrate accumulation which cause adult schistosomes to experience severe neuromuscular/motility defects consistent with the phenotypes observed in Fabry and Schindler/Kanzaki diseases. Interestingly, whole mount *in situ* hybridization (WISH) analysis of adult male schistosomes revealed *Smnagal* staining throughout the tegmental cells lining the esophagus as well as within neurons (including the cephalic ganglian). Further investigations quantifying glycan accumulation of si*Smnagal* treated worms (males and females) will increase our understanding of this schistosome gene product in normal developmental processes and reveal phenotypes useful for drug development efforts.

Mr Hajri Alshehri, *phd, Liverpool School of Tropical Medicine*

Poster 72 : Molecular detection of equine trypanosomosis from Riyadh region, Saudi Arabia

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This is a cross-sectional study carried out to detect possible trypanosomes infecting horses and donkeys in Riyadh region, Saudi Arabia. Blood were collected from of 368 horses and 142 donkeys, DNA extraction and subsequently subjected to catch –all ITS1-PCR followed *T. evansi* species specific RoTat1.2-PCR. The universal ITS1-PCR showed that horses were more infected with *T. evansi* 12 (3.26%) than donkeys 4 (2.81%). However, application of RoTat 1.2-PCR revealed, RoTat 1.2 VSG gene was absent in 3 and 1 positive ITS1-PCR samples of horses and donkeys respectively. This could be explained by circulation of *T. evansi* type B in Saudi Arabia. Thereafter, risk analysis revealed that *T. evansi* was more prevalent in females of both animal species 9 (3.73%) and 3 (3.44%) than males 1(1.81%) and 3(2.36%) respectively. Whereas, elder animals of age more than five years have had

higher *T. evansi* prevalence 8 (5.25%) and 4(4.3%) than the younger ones that of less than 5 years. However, the results show no significant effects of sex and age on the prevalence of Trypanosomosis in horses (p 0.4810 and p 0.0664) and donkeys (p 0.5673 and p 0.1408), respectively. It is concluded that, *T. evansi* is more prevalent in horses than in donkeys and that the females and animal elder than 5 years have had higher parasite load in both animal species. Moreover, None RoTat1.2 gene *T. evansi* type B is circulating in Saudi Arabia though this needs additional confirmation step. To our knowledge, this is the first study demonstrating *T. evansi* type B out of Africa.

Miss Zandile Nare, *PhD Student, Institute of Immunology and Infection Research, University of Edinburgh*

Poster 73 : Towards new drugs for trypanosomatid diseases based on specific high-affinity inhibitors for RNA editing ligase 1

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Messenger RNA editing by uridylyl insertion/deletion is a unique process in kinetoplastid mitochondria and therefore a potential drug target (Read, Lukeš and Hashimi, 2016). We previously showed that knock-down of RNA editing ligase 1 (REL1), an essential component of ~20S editosome, is lethal in *Trypanosoma brucei* (Schnaufer *et al*., 2001). REL1 is highly conserved throughout trypanosomatids, which, together with what is known about mitochondrial biology in these organisms, suggests an essential function in other pathogens like *T. vivax*, *T. congolense*, *T. cruzi* and *Leishmania* spp. as well. The crystal structure of the catalytic domain of TbREL1 (Deng *et al*., 2004) shows a unique active centre with a well-defined ATP binding site. Together with the low sequence and structural similarity between REL1 and DNA ligases (which represent the closest mammalian homologs), this suggests the feasibility of developing highly specific REL1 inhibitors with little side effects. Recently, we developed a new REL1 activity assay suitable for high-throughput screening (HTS) and a proof-of-concept screen against the LOPAC library resulted in a hit rate of 1.7% and identified interesting REL1 inhibitors such as suramin and the flavonoid myricetin (Zimmermann *et al*., 2015). Here we report results from HTS screening campaigns of diversity and kinase inhibitor-focused compound libraries at the Dundee Drug Discovery Unit and the European Screening Centre Newhouse and subsequent hit optimisation efforts that led to the identification of several promising compound series with potency up to an IC50 of 20 nM. Furthermore, we have expressed REL1 orthologs from four kinetoplastid parasites, *T. cruzi*, *T. congolense*, *T. vivax* and *L. donovani*, in *Escherichia coli* cells and purified all

proteins in soluble form. REL1 enzymes from *T. cruzi*, *T. vivax* and *L. donovani* are functional in the HTS activity assay and some TbREL1 inhibitors show similar potency against these orthologs. Aided by the orthologous proteins we are continuing the lead development of the initial hits and analogues and will present findings on structure-activity relationships, biophysical characterization by Differential Scanning Fluorimetry and Microscale Thermophoresis, and activity against parasites.

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Mr Adam Burgess, *MRes Student, Aberystwyth University*

Poster 74 : Extracellular-vesicle/Tegumental Unknown protein (ETU): characterising proteins of unknown function in *Schistosoma mansoni*

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Proteins of unknown function are commonly found in genomic, transcriptomic and proteomic studies of parasites. Notably, many of these proteins possess limited homologies that are often restricted to parasitic species, highlighting these proteins as potential intervention targets. One of these unknown proteins, Smp_075420, has been found to be present in extracellular vesicles and the tegument of the parasitic trematode *Schistosoma mansoni*. Therefore this protein has been named, *S. mansoni* Extracellular vesicle/Tegumental Unknown protein -1 (SmETU-1). Through extensive genomic searches, PCR cloning, transcription analysis, homolog searches and phylogenetics we describe the current knowledge of how widespread the ETU family are within parasite species. We find nine family members within *S. mansoni* (SmETU-1-9) with differing expression patterns across the parasite lifecycle and homologs in key platyhelminth species but not outside this phylum. Importantly, searches of published proteomic data find that the association of this novel protein family with Extracellular vesicles continues outside of the schistosome genus. Finally recombinant expression of SmETU-1 has been carried out for the purposes of testing serological immunogenicity in infected mouse and human studies via ELISA. These show antibody responses to this unknown protein are present in both experimental models and natural infection in endemic

communities. In future, we aim to use localisation experiments such as whole-mount *in situ* hybridisation and additional functional and immunological studies to characterise this novel protein family further.

Ms Rachel Francoeur, *PhD Student, Rachel Francoeur*
Poster 75 : Impact of malaria coinfections on *S. mansoni* clearance, intensity and reinfection rates

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Schistosomiasis and malaria are the two most significant human parasitic diseases. Schistosomiasis is a commonly occurring neglected tropical disease with over 240million people infected globally. In 2016, there were 216 million cases of malaria worldwide resulting in an estimated 731,000 deaths. Praziquantel is the standard chemotherapeutant in treating schistosomiasis however, in certain endemic hotspots, despite over a decade of mass drug administration (MDA), infection intensities and prevalence remain higher. Past studies indicate a correlation between increased risk of malaria contraction in individuals with schistosomiasis. However, it is unknown if malarial infections play a role in susceptibility to reinfection with schistosomiasis, nor whether drug efficacy is influenced. This study investigates the impact of malaria coinfections on *Schistosoma mansoni* includinginfection intensity, clearance post treatment, and reinfection rates.Samples were obtained from 197 school children aged 6-14 in the Mayuge district of Uganda who were tested for *S. mansoni* and *Plasmodium falciparum*. Infection data were obtained using Kato-Katz for *S. mansoni* egg counts and RDT tests for *P. falciparum*. Results from regression analysis will be presented on correlations between co-infected individuals, clearance, and reinfection rates compared with those infected with only *S. mansoni*. These results will contribute to a broader biostatistical study looking at host factors that influence *S. mansoni* clearance.

Dr Patrick Driguez, *postdoc, Henry Patrick Driguez*
Poster 76 : Studying the translatome of *Schistosoma mansoni* using ribosome profiling

P Driguez[1]; G Rinaldi[1]; K Rawlinson[1]; M Berriman[1];
[1] Wellcome Trust Sanger Institute, UK

Schistosomes infect over 200 million people and are one of the leading causes of morbidity and disability in developing countries. These helminths have a complex life cycle that involves a clonal stage in the snail host, a sexually-differentiated stage in the mammal host and dramatic transitions between free-swimming and parasitic

stages. There is indirect evidence that post-transcriptional regulation is responsible for controlling some of these changes over the parasite life cycle. For example, transcription is halted in the cercarial stage and despite no initial increase in mRNA transcription after transformation into schistosomulum, protein synthesis expands. It is not known if protein translation is regulated via mRNA sequestration, ribosome pausing or other mechanisms. In addition, current proteomics methods are not yet sensitive enough to detect all proteins synthesised during stages of the schistosome life cycle. To address these deficiencies we have commenced the first ribosome profiling studies in the schistosomes. Our first ribosome profiling libraries, using a ligation-free method across a broad range of *S. mansoni* life cycle stages, have footprints that map well to the CDS region, show codon periodicity, and correlate with published RNA-seq studies. Our next step will be to closely examine the cercaria-schistosomulum and miracidium-sporocyst transitions at the mRNA, ribosome footprint and protein levels using RNA-seq, ribosome profiling and quantitative proteomics (LC-MS/MS with TMT labelling). In addition, using a similar approach, we are also examining differences between male and female adult worms and the regulation of clock genes in a circadian rhythm study. Once better understood, post-transcriptional regulators or stage critical proteins could make attractive drug and therapeutic targets for schistosomiasis.

Dr Florian Noulin, *research associate, Keele University*

Poster 77 : Investigating the role of RNA G-quadruplex structures in *Plasmodium falciparum* gene expression

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Nucleic acids (DNA and RNA) can form several different secondary structures and these can influence general gene expression. Among these structures, one that has recently gained the spotlight is the G-quadruplex (G4). G4s are formed by the stacking of guanine quartets and they have well-established roles at the DNA level in controlling gene expression, genome stability and telomere maintenance. 'rG4s' have recently been identified at the RNA level in several model systems including human cells. G4 structures have been identified by our group and others at the DNA level in *Plasmodium falciparum* using bio-informatics algorithms and structure-specific antibodies. In view of the important A/T bias of this parasite genome, the presence of such G-rich motifs might indicate that they are maintained in the genome to play specific regulatory roles. This is particularly intriguing because almost half of the predicted G4 motifs in the genome are associated with the major virulence gene family *var*. The *var* genes are a group of nearly 60 genes coding for the Pfemp1 protein that is involved in immune evasion and malaria pathogenicity. Interestingly, only one *var* gene is express at the time while the others are silenced. The presence of G4 motifs in the neighborhood of these genes could be one of the keys to understand

the fine regulation of this family. Building upon our work on DNA G4s, we have now identified putative G4 structures at the RNA level in *Plasmodium falciparum*. This was achieved by structure-specific sequencing of the transcriptome using a technique called rG4-seq. Among the genes with rG4s, genes encoding DNA binding proteins, as well as *var* virulence genes, are over-represented. We decided to investigate the influence of these rG4s on gene expression at the RNA and protein levels. For this, we are focusing on several different rG4-containing genes, including *var* genes and the gene encoding histone H4. By treating parasites with a drug, carboxypyridostatin (cPDS), that targets and specifically stabilizes rG4 structures we are able to observe an influence of these structures on the studied genes in presence of the drug. We believe that rG4s may play a role in gene expression at both RNA and protein levels. Further studies involving reporter genes are planned to better investigate their role.

Dr. Zhigang Lu, *Computational Biologist, Wellcome Trust Sanger Institute*
Poster 78 : High-quality genome annotation for the V7 assembly of *Schistosoma mansoni*

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We introduce here a high-quality annotation towards the upgrade of genome sequence V5.2 to V7.0 for *Schistosoma mansoni*. As a result of moving from a very fragmented assembly to a very contiguous assembly and comparing the results of direct annotation-transfer (using RATT) and gene finding (using Augustus based on RNAseq evidence), > 740 previously incomplete or absent gene models are now correctly resolved and about 850 spurious gene models have been deleted. The structures of about 1000 gene models have changed (> 20% difference) and about 800 novel genes have been discovered. All the above-mentioned gene models have been manually examined and curated using WebApollo. Furthermore, the use of Pacbio Iso-Seq reads supported the predictions of alternative splicing, and it has been possible to accurately annotate UTRs, which were previously lacking in V5.2. Besides, more than 70 genes have at least 2 copies in the new genome and several protein families are found to be extended.

Miss Sheila Macharia, *PhD Student, University of Manchester*
Poster 79 : Investigating the role of eosinophils in barrier function in infection

S Macharia[1]; S Cruickshank[1]; K J Else[1]; R Forman[1];
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Eosinophils are non-dividing, fully differentiated granule containing cells that form part of the local cellular pool in the gut during homeostasis. However, during inflammatory conditions such as allergic diseases and parasitic infections. , the numbers of eosinophils increases. Eosinophil numbers then subsequently decrease upon the resolution of infection, however, a small number remain within the gut. Despite this knowledge, the role of eosinophils in both the maintenance of gut homeostasis and the development or resolution of inflammation is poorly understood. Our previous work suggested that they have differing functions in small intestine vs large intestine therefore in this study we looked at large and small intestinal inflammation. Additionally the loss of eosinophils in the gut has been shown to result in gut dysfunction and leaky gut syndrome but the exact mechanisms are unclear.

Using C57BL/6 mice and eosinophil deficient ΔdblGATA mice we have studied the role of eosinophils in a high dose *Trichuris muris* infection. In the current study we have demonstrated the changes in the eosinophil population and localisation of this cell type within the gut at day 0, 14, 21 and 35 post-infection. We observed that a proportion of these cells are located close to epithelial cells. Additionally, we investigated eosinophils in the context of *Trichinella spiralis* infection. We found that eosinophil numbers and localisation were similar to those in T. muris infected mice. Taken together this data suggests that eosinophils may be interacting with the epithelial cells to mediate healthy gut function. We now aim to look at tight junction distribution to look at changes in gut barrier function in eosinophil deficient mice.

Given this interaction between the eosinophil and epithelial cells we are now investigating the properties of eosinophils *in vitro* using an eosinophil cell line and different inducers of activation including *T. muris* derived products. Through this we therefore hope to further elucidate the role of eosinophils in gut barrier function.

Mrs Woyneshet Gelaye Yalew, *Lecturer , Bahir Dar University*

Poster 80 : New foci for cutaneous leishmaniasis - Ankesha district, Amhara region, Ethiopia

W Yalew[1];

[1] Bahir Dar University, Ethiopia

Background: Cutaneous leishmaniasis is found in more than 80 countries in the world. With estimated 29 million people at risk and 20,000 to 40, 000 new cases per year Ethiopia is one of the ten high burden countries. From studies so far in more than 90% of the cases *Leishmania aethiopica* is incriminated as the causative species.
Objective: The aim was to investigate cutaneous lesion outbreak in Ankesha district, Awi zone, Amhara region.
Methods: A preliminary rapid assessment survey was done from November 2013 to January 2014. **37** cases and 74 apparently healthy individuals were interviewed. Skin slit lesion sample was taken from 25 cases. Identification

of *Leishmania* parasite was done by smear microscopy and culture. PCR; restriction fragment length polymorphism was done for species identification.

Results: Two clinical form of CL were observed; 33 (89%) localized cutaneous leishmaniasis and 4 (11%) diffused cutaneous leishmaniasis. All of CL lesions were observed on the exposed parts of the body such as the face and upper and lower limbs. 16 samples were positive by smear and culture. 6 samples were typed as *L. aethiopica.* The community did not know the cause, transmission and prevention mechanism of CL.

Lessons and Recommendations: We confirmed that the cause of cutaneous lesions among the residents of Sositu Gimjabet kebele, Ankesha district is cutaneous leishmaniasis. The average duration of lesion in the 37 participants was three month showing the probability that CL appeared in this kebele recently. None of the interviewees had knowledge about the cause of CL. The presence of CL in Ankesha was not known before thus underlining the need for further survey to certain the claim of new outbreak, and identify associated risk factors to designed efficient and effective control.

Key words: Cutaneous leishmaniasis, Ankesha, Ethiopia

Mr Aboagye Kwarteng Dofuor, *Mr., University of Ghana*

Poster 81 : Antitrypanosomal effects of *Zanthoxylum zanthoxyloides* extracts on African trypanosomes

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African trypanosomiasis is a disease caused by the parasitic protozoa of the *Trypanosoma* genus. Despite several efforts at chemotherapeutic interventions, the disease poses serious health and economic concerns to humans and animals of various sub-Saharan African countries. Commercially available drugs have reported cases of undesirable side effects, drug resistance, and difficulty in regimen application. Moreover, even though studies have reported antitrypanosomal activities of different plant extracts in several parts of the world**,** action mechanisms of these extracts remain poorly understood. *Zanthoxylum* is a widely distributed plant genus with several pharmacological and phytochemical properties. The aim of this study was thus to determine the effect of active fractions of the plant species *Zanthoxylum zanthoxyloides* (root) on the cell cycle, cell morphology and induction of cell death of *Trypanosoma brucei*. While fractions moderately induced apoptosis-like cell death, they significantly affected the cell cycle of the parasite. Moreover, fractions strongly affected the parasite's cell morphology. Results suggest that *Zanthoxylum zanthoxyloides* (root) have potential chemotherapeutic effects on African trypanosomes with implications for novel therapeutic interventions in African trypanosomiasis.

Dr Josephine Forde-Thomas, *Research Assistant, Aberystwyth University*

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Poster 82 : Identification of novel anti-schistosomal compounds using an automated high-throughput platform

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Schistosoma mansoni is a parasitic trematode that contributes to the infectious human disease schistosomiasis which affects in excess of 240 million people worldwide. Currently a single chemotherapeutic agent, praziquantel (PZQ), has been identified to combat this disease. However, PZQ is ineffective against juvenile worms, often necessitating repeated treatment. With no anti-*Schistosoma* vaccine on the horizon, mass drug administration programs form the only line of defence in controlling this disease.
This project is focused on identifying novel chemotypes with anti-schistosomal activity. Our workflow initially screens compounds against schistosomula larvae using our automated high-throughput platform (Roboworm). Hits from these larval screens are subsequently taken forward for screening against juvenile and adult worms.
We initially screened 12,672 compounds from the Global Health Chemical Diversity Library (GHCDL) against schistosomula and identified 214 hits. These initial hits were reconfirmed and the chemical space around these hits expanded in a second round of screening against larval stage schistosomula. Confirmed hits were then subjected to mass spectrometry analysis and 9 compounds were ultimately taken forward for testing in juvenile and adult worms.
Juvenile and adult worms screens were conducted in parallel at a single point concentration of 20mM. Against juvenile worms, 2 out of the 9 compounds were hits. Upon titration, these two hits continued to show significant activity down to 5mM. Of the 9 identified hit compounds, 3 were also hits against the adult worms. However, 2 of these demonstrated differential activity towards male and female worms. Only one compound was found to have activity against both sexes at 20mM. This hit was also one of the compounds effective against juvenile worms. These initial results represent promising progress in the development of a new treatment options for this disease.

Mr James Iremonger, *PhD student, Roslin Institute, University of Edinburgh*
Poster 83 : Mitochondrial acetate production in *Trypanosoma congolense*

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Pathogenic animal trypanosomes infecting livestock have a significant economic and social impact in endemic

areas. *Trypanosoma congolense*, which is particularly pathogenic in cattle, is currently controlled with chemotherapy and chemoprophylaxis, however, existing compounds are losing efficacy due to the emergence of drug-resistant parasites. Therefore, probing metabolic pathways will assist the development of *in vitro* culture methods, vital to the discovery of novel trypanocidal compounds. Our current understanding of the mitochondrial metabolism of trypanosomatids is mostly derived from studies involving *T. brucei*. However, our preliminary data show that the central carbohydrate metabolism of *T. brucei* differs to that of other, lesser studied livestock trypanosome species such as *T. congolense* and *T. vivax*. For example, *T. congolense* was shown to consume glucose at lower rates *in vitro* than *T. brucei*, and untargeted metabolomic analyses showed that less pyruvate is excreted as a metabolic end-product. Here, we investigate the source of mitochondrial acetate production in bloodstream form *T. congolense* IL3000 and *T. brucei* 427. Acetate was found to be excreted by *T. congolense* at significantly higher rates than *T. brucei* (138.0 vs. 16.6 nM/min/10^8 cells). ^{1}H-NMR spectrometry revealed the primary sources of acetate production in *T. congolense* to be glucose-derived pyruvate and L-threonine. *In vitro* drug inhibition assays showed *T. congolense* to be more sensitive than *T. brucei* to inhibition with the pyruvate transport inhibitor UK5099, and the pyruvate dehydrogenase inhibitor arsenite (59.9 nM vs. 134.6 nM; 139.9 μM vs. 292.0 μM), suggesting an increased dependence on the mitochondrial acetate pathway in *T. congolense*. Together, these data suggest that bloodstream form *T. congolense* display similar metabolic characteristics to procyclic (insect-stage) *T. brucei*. This strengthens the previous observation that mitochondrial metabolism is distinctly different between *T. congolense* and *T. brucei*.

Ms Tegwen Marlais, *PhD student, London School of Hygiene & Tropical Medicine*
Poster 84 : Comparative 'Omics' identification of coproantigens for diagnosis of *Strongyloides stercoralis* infection

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Background:*Strongyloides stercoralis* is a soil transmitted helminth with potential to cause fatal hyperinfection if not successfully treated. It is therefore important both to diagnose strongyloidiasis and to confirm cure after treatment. Diagnosis currently requires *Strongyloides*-specific methods that vary in sensitivity and are slow to give a result or unable to determine cure. An ideal alternative would be an antigen detection rapid diagnostic test (RDT) for application at point-of-care and capable of confirming cure.
Methods: We analysed open access transcriptomic, genomic and proteomic data and searched published literature on *S. stercoralis* and *S. ratti*, a parasite of rodents, to identify proteins that are likely to be *Strongyloides*-specific,

antigenic and detectable in stool. Proteins expressed in the gut-dwelling life stages of the nematode were compared, using phylogenetic trees, with homologues from 14 other helminth species and humans. *Strongyloides*-specific protein regions were then mapped onto 3D models and analysed for predicted epitopes. The excretory/secretory (E/S) proteome of *S. ratti* was used to identify *S. stercoralis* E/S homologues. Genomes of 3 *Strongyloides* species were mapped to the *S. ratti* reference in order to reveal variants in genes of interest. Datasets were cross-referred to build evidence for strong candidate antigens.

Results: Transcriptomic data revealed 328 proteins differentially expressed in gut-dwelling versus non-gut dwelling life stages of *S. stercoralis*. Over 50 *S. stercoralis* proteins from seven protein families contained species-specific sequences as revealed by phylogenetic comparison with outgroups and by sequence alignments. In total, 125 epitope regions were predicted in proteins expressed by gut-stage *S. stercoralis*. *Strongyloides* unique, predicted epitope peptides of selected proteins were 3D mapped to the surface of the molecules and revealed adjacent amino acid residues that may form conformational diagnostic epitopes.

Conclusion: The comparative 'omics' approach used here for the first time for *Strongyloides* has identified numerous candidate antigens that should be investigated as targets for a *S. stercoralis* coproantigen assay. Furthermore, online analytical tools and the increasing wealth of open access data on multiple helminth and other parasites means that this approach can be applied more widely to diagnostics discovery and development.

Dr Katerina Doleckova, *Research Associate, Keele University, School of Life Sciences*

Poster 85 : In search for new treatments of camel trypanosomosis (surra)

K Doleckova[2]; H Hameed[1]; R Nash[3]; P D Horrocks[1]; H Price[4];

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Trypanosoma evansi is a protozoan parasite causing surra, a debilitating veterinary disease, found worldwide and affecting a range of domestic livestock including cattle, horses and camels. The disease causes major socio-economic losses especially among pastoralists and farming populations, who heavily rely on their animals as a main source of income. Current treatments for surra have limited efficacy and can cause severe toxicity and the emergence of drug resistance to all available treatments highlight the need to identify new drugs.

This work is part of our project on surra in Egyptian camels, financed by Newton-Mosharafa fund, with one of the aims to initiate work to develop new lead compounds against *T. evansi* parasite.

PhytoQuest library is a proprietary set of ca 1000 molecules from different chemical classes, isolated from temperate zone plants. It represents a novel source of potentially new biologically active compounds - typically,

temperate zone plants have been overlooked in search of antiparasitic activities, unlike the plants from subtropical and tropical regions, which have been used in traditional medicine to cure parasitic diseases for centuries.
We screened a subset of compounds from PhytoQuest library against culture adapted *T. evansi* using a phenotypic 72 h AlamarBlue assay with the aim to identify hit compounds, with high efficacy and selectivity. We obtained IC50 values for the hit compounds and determined cytotoxicity using the mammalian cell line HepG2 to ascertain parasite selectivity. In total, we screened 547 compounds, out of which we identified 12 compounds with IC50 values of 1 µM against *T. evansi*.
In summary, we identified several promising natural products with the potential to be new chemical starting points for drug discovery efforts for surra disease.

Dr Sarah Berry, *Post-Doc, University of Keele*

Poster 86 : Functions of the BBSome protein complex in the protozoan parasite *Leishmania mexicana*

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The neglected tropical disease leishmaniasis is caused by infection with the protozoan parasite *Leishmania spp*, with an estimated 1 million new cases per year. The *Leishmania* parasite cycles between a procyclic promastigote stage in the sandfly vector; a host-infective metacyclic promastigote stage which is transferred from vector to mammalian host during a bloodmeal; and an intracellular amastigote stage which resides inside host macrophages. The BBSome is a protein complex which is associated with molecular trafficking to/from primary cilia and flagella in other eukaryotes. Previous work (Price *et al* 2013) showed that deletion of one of the subunits, *BBS1,* from *L. major* severely reduces parasite virulence in mice. We hypothesise that the *Leishmania* BBSome is involved in the transportation of macromolecules to the parasite cell surface. We are testing this hypothesis by creating transgenic parasite cell lines with disrupted BBSome function. We will analyse the effect these changes have on the distribution of macromolecules, including proteins, on the cell surface. This work will initially involve biotinylation and streptavidin pull down of cell surface proteins, which will be analysed by mass spectrometry for differences in protein expression. This will lead on to the analysis of global protein distribution within the cell using LOPIT (Localisation of Organelle Proteins by Isotope Tagging) – a mass spectrometry-based technique that allows the subcellular location of large numbers of different proteins to be mapped.

Prof Paul Horrocks, *Professor, Institute for Science and Technology in Medicine*

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Poster 87 : Evaluating the antiparasitic activity of the Phytopure library: natural products isolated from temperate zone plants

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There is an urgent need to identify and evaluate novel chemical scaffolds to seed the drug discovery pipeline for parasitic diseases to meet the challenges of emerging resistance, toxicity and costs of current treatment. Whilst there is a significant investment in international efforts to screen massive small-chemical libraries, this search also encompasses the evaluation of natural products often identified from traditional medicines. Here we report the screen of a proprietary library of purified natural products, the PhytoPure library, that are predominantly sourced from temperate zone plants. As traditional medicines of tropical parasitic diseases focus on the local flora, the antiparasitic activity of temperate zone plants is relatively under evaluated. The Phytopure library screened here consists of 643 purified products (ie not plant extracts, which are mixes of active and inactive components), two thirds of which are novel, and the remaining one third not otherwise commercially available. These compounds have also been selected on the basis of their development potential: they have a high degree of functionality and physiochemical properties that meet Lipinski's rules-of-five. We report here activity screens against intraerytrocytic *Plasmodium falciparum*, blood-stream form of *Trypanosoma brucei* and axenic *Leishmania mexicana*. Activity was confirmed by the determination of the EC_{50} and compared to the CC_{50} against HepG2 cells to explore their selectivity. In total, 33 compounds with EC_{50} <2µM were identified. Of these, three closely related sesquiterpenes (701155, 701157 and 701158) exhibited significant activity against all three parasite species trested. Seven compounds showed activity against both kinetoplastid parasites with 4 compounds showing *T. brucei* and *P. falciparum*.

Mr Jaksha Chandrathas, *PhD Student, Life Sciences - Keele University*
Poster 88 : ARF regulating proteins as novel drug targets against Kinetoplastids

J P Chandrathas[1]; H Price[1];
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Several members of the ADP-ribosylation factor (ARFs) family of the small GTPases are known to be essential for viability in *T. brucei* bloodstream form cells. However, the molecular interactions of these proteins have not been fully characterised in *T. brucei* and there is a high level of identity shared between *T. brucei and human* ARF

protein sequences, thus impacting on their potential as drug targets. An alternative method of indirectly targeting of ARFs may be through their regulators, the guanine nucleotide exchange factors (GEFs) and GTPase activating proteins (GAPs). These regulating molecules are responsible for maintaining the active/inactive state ARFs and are highly divergent in *T. brucei*. The aim of this study is to identify ARF regulators in *T. brucei* and to investigate whether they are essential in the parasite using RNAi. Further studies will determine which ARFs are regulated by these proteins, towards development of an assay for inhibitor screening. Two TbGEFs and Two TbGAPs have been identified using bioinformatics and through RNAi studies it was determined that TbGEF3 is essential for bloodstream form *T. brucei* viability. Following RNAi knockdown, cells exhibited the Big Eye phenotype, suggesting a defect in endocytosis. Flow cytometry was used to demonstrate that RNAi of TbGEF3 has a cytotoxic effect on BSF *T. brucei*, thus indicating an essential role of this protein in parasite viability.

Dr Karolina Subrtova, *Postdoc, University of Edinburgh*

Poster 89 : F1-ATPase as a drug target in parasitic trypanosomatids

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Improved drug therapy against trypanosomatid infections is urgently needed[1,2].The mitochondrial F_oF_1-ATP synthase represents an attractive drug target for the following reasons: i) The structure and composition of this large multisubunit complex in trypanosomatids significantly differs from its mammalian counterpart as it includes 13 unique proteins with no homology outside the Euglenozoa group (the functions of these components remain to be elucidated)[3,4]. The catalytic core F_1-ATPase itself involves an additional subunit, p18, again with unknown function. Moreover, the essential α subunit is proteolytically cleaved into two separate polypeptides that remain associated with the complex, a feature that appears to have no parallel in any other group of organisms[5–7]. Thus, despite the ubiquitous presence of this enzyme in all domains of life, it should be feasible to develop inhibitors that are specific for the trypanosomatid enzyme. ii) The absence of the traditional respiratory chain inthe infective bloodstream stage of *Trypanosoma brucei* (and potentially in other trypanosome species as well) requires this enzyme to continuously operate as an ATP-hydrolysis driven proton pump to generate the essential mitochondrial potential ($\Delta\psi_m$)[8–10]. The mechanism of maintaining the$\Delta\psi$m is even more unique in non-tsetse transmitted, dyskinetoplastic subspecies *T. b. evansi* and *T. b. equiperdum*, which lack functional mitochondrial DNA and maintain the $\Delta\psi_m$ using the hydrolytic activity of the F_1-ATPase coupled to the electrogenic exchange of ATP^{4-}/ADP^{3-} by the ATP/ADP carrier[10]. The aim of this project was to perform a pilot medium throughput screening campaign to identify small molecule inhibitors of *T. brucei* F_1-ATPase activity. Active, tagged F_oF_1-ATP synthase was purified from insect

stage *T.brucei* by affinity chromatography and used to develop a robust ATPase enzymatic screening assay. The ADP Hunter Plus kit (DiscoverX) was optimized to meet screening requirements set by the European Lead Factory[11]. The fluorescence based endpoint assay had excellent performance during the robustness testing, consistently generating a Z' value 0.6, and a signal to background ratio of 2.6. DMSO tolerance was 2.5%. A pilot screen of 7623 compounds from four drug libraries (NIH Clinical Collection, Selleckchem FDA approved drug library, BioAscent and GSK Kinase Inhibitor Compounds) identified 54 primary hits with inhibition of pIC_{50} > 4.3 and no off-target interference against the ADP hunter assay components. Twenty compounds from the BioAscent library that achieved the highest medicinal chemistry scores (1 and 2 - excellent or good candidates) were chosen for follow up studies. As a first step we retested the compounds using a modified Pullman ATPase assay that couples the production of ADP to the oxidation of NADH via the pyruvate kinase and lactate dehydrogenase reactions[12]. Out of the twenty selected hits, two compounds showed inhibition of ATPase activity in low micromolar range (pIC_{50} values of 5.4 and 5.6, respectively). These hits are currently being tested in cell viability assays to elucidate their trypanocidal potential. 1) Cullen, D. R. *et al.* (2017) 2) Giordani, F. *et al.* (2016) 3) Zikova, A. *et al.* (2009) 4) Perez, E. *et al.* (2014) 5) Speijer, D. *et al.* (1997) 6) Nelson, R. E. *et al.* (2004) 7) Gahura, O. *et al.* (2018) 8) Nolan, D. P. *et al.* (1992) 9) Vercesi, A. E. *et al.*(1992) 10) Schnaufer, A. *et al.* (2005) 11) McElroy, S. P. *et al.* (2017) 12) Pullman, M. E. et (1960)

Mr Numair Masud, *PhD student , Cardiff University*

Poster 90 : Transport stress impacts infection trajectories in an ornamental fish

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The transport of fish in aquaculture and the ornamental trade exposes fish to multiple stressors that can cause mass mortalities and economic loss. Previous research on fish transport has largely focused on chemical stress related to deterioration in water quality. For many small ornamental fish, however, water quality remains stable during routine transport leaving mechanical stress as a neglected stressor when studying fish welfare. Elevated stress induces immunosuppression, which increases the chance of contracting infections and reducing the rate of recovery. Here, using two experimental infection protocols, we investigate how parasite infections prior to and after simulated transport impacts infection trajectories of the ectoparasitic *Gyrodactylus turnbulli*. Guppies (*Poecilia reticulata*) that were exposed to infection before simulated transport suffered significantly higher parasite burden compared to fish that were not transported. In constrast, fish exposed to parasites after transport did not suffer a significant increase in parasites. This increased disease susceptibility due to fish infections prior to transport

demonstrates the potential to mitigate the impact of parasites on stock survival and we suggest improvements for reducing parasite burden on stock survival.

Dr Kathy Geyer, *Postdoctoral Research Assistant, Aberystwyth University*
Poster 91 : Crucial Role of SmMBD2/3 and SmCBX during schistosome neoblast proliferation and oviposition

S Munshi[1]; D Phillips[1]; N Fernandez-Fuentes[1]; **K Geyer**[1]; K F Hoffmann[1];
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We have previously confirmed the presence of the epigenetic mark 5-methylcytosine (5mC) in the genome of the medically important blood fluke *Schistosoma mansoni*, as well as identified the core DNA methylation machinery components DNA methyltransferase 2 (SmDNMT2) and methyl-CpG binding domain protein (SmMBD2/3). While we demonstrated that SmDNMT2 is responsible for the establishment of this DNA modification, we did not further pursue the role of SmMBD2/3 during schistosome epigenetic processes. MBD proteins represent the readers of metazoan DNA methylation systems and specifically bind to methylated loci via a conserved N-terminal 5mC-binding domain. This event catalyses the recruitment of further co-repressors, thereby leading to a transcriptionally silent chromatin state. In *S. mansoni*, previous bioinformatics-led characterisation of the metazoan MBD family suggested that SmMBD2/3 is a functional member. Here we confirm that this schistosome protein is indeed a functional candidate by validating binding affinity of rSmMBD2/3 to a methylated substrate as well as demonstrating its primary nuclear localisation. A subsequent yeast-two-hybrid (Y2-H) screen identifies the heterochromatin-associated SmCBX (S. mansoni chromobox protein) as a putative interaction partner of SmMBD2/3 and whole mount fluorescent *in situ* hybridisation (WISH) further confirms the co-expression of these proposed binding partners throughout mesenchymal-, germ- and proliferating somatic stem cells (PSCs or neoblasts). Interestingly, RNAi-mediated knockdown of Smmbd2/3 and Smcbx results in PSC proliferation defects as well as reproductive deficiencies. Our data collectively suggest that SmMBD2/3 represents a functional epigenetic reader capable of binding to 5mC and its physical interaction with the repressor SmCBX further suggests a role for these partners in heterochromatin formation and regulation of gene expression. Additionally, the observed reductions in both PSC proliferation and egg laying, following Smmbd2/3 and Smcbx knockdown, demonstrates a pivotal role for these gene products in schistosome development, transmission and immunopathology progression.

Miss Gloria Amegatcher, *PhD Student, University of Edinburgh*
Poster 92 : Mitochondrial retrograde signalling in *Trypanosoma brucei*

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In organisms such as yeast, mammals and plants, ‘mitochondrial retrograde signalling’ pathways, including the ‘unfolded protein response (UPRmt), convey information on the functional status of this organelle to the nucleus and modulate expression of nuclear genes accordingly1,2,3. Although successful completion of the life cycle of *Trypanosoma brucei* depends on stringent regulation of mitochondrial activity, it is not known if similar signalling pathways exist in these parasites. As *T. brucei* differentiates from the slender bloodstream form via the transmission competent stumpy form to the procyclic insect form it undergoes dramatic remodelling of its morphology and metabolism, including mitochondrial activity. As a first step towards exploring potential retrograde signalling pathways in *Trypanosoma brucei* we have compared the transcriptome of strain EATRO 1125 (AnTat1.1 90:134) with a genetically engineered derivate devoid of mitochondrial DNA (akinetoplastic, or AK cells), before and after differentiation from slender to stumpy forms. Our main findings are: (i) In control (‘WT’) and AK parasites, 242 and 433 genes, respectively, showed significant upregulation in stumpy forms (we considered a difference of $\geq$ 2-fold with a p-value $\leq$ 0.05 as significant). 102 upregulated genes were shared, including genes previously reported to be upregulated in stumpy cells such as PIP39 (Tb927.9.6090), dihydrolipoyl dehydrogenase (Tb927.11.16730) and EP1 procyclin (Tb927.10.10260). The upregulation of other procyclins was much less pronounced in AK stumpy cells compared to WT stumpy cells. On the other hand, 10 hypothetical proteins showed more than 4-fold upregulation exclusively in stumpy AK cells. (ii) Genes involved in the glycolytic pathway were generally downregulated in stumpy cells. We also observed robust downregulation in stumpy cells of numerous histones and of two genes involved in kDNA maintenance, mitochondrial DNA ligase LIG k alpha (Tb927.7.610) and cysteine peptidase PNT1 (Tb927.11.6550). (iii) When we compared slender AK vs. WT cells we observed only 27 robust changes (either up or down), which mostly concerned genes annotated as ‘pseudogene’, or ‘hypothetical unlikely’, including a putative UDP-Gal or UDP-GlcNAc-dependent glycosyltransferase pseudogene that was ~5-fold increased in AK slender cells. The same mRNA was ~3-fold increased in AK stumpy cells compared to WT stumpy cells. Other changes in AK stumpy cells concerned a hypothetical protein (~3-fold upregulated) and a putative adenylosuccinate lyase (~3-fold downregulated), but overall we observed only a limited number of robust changes (13 up, 9 down), including the decreased levels of procyclin mRNAs mentioned above. In summary, our transcriptomic studies suggest that absence of the mitochondrial genome has a surprisingly limited effect on levels of nuclearly encoded mRNAs in bloodstream stage *T. brucei*.

Miss Rachael Magwaza, *PhD student, University of Manchester*
Poster 93 : Design, synthesis and evaluation of novel leads for drug-resistant malaria

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R Magwaza[1]; S Alnabalsi[2]; B Hussein[2]; I Russo[2]; S Freeman[2];
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Malaria is caused by parasite infection of the genus *P*lasmodium. Human infection is caused by one of five *Plasmodium* species including *falciparum*, *malaria*, *knowlesi*, *vivax* and *ovale. P. falciparum* is associated with the most severe form of malaria and responsible for approximately 400 000 deaths per year. A number of antimalarial drugs are currently used to treat malaria. However, *P. falciparum*, which is responsible for mortality especially in Eastern and Southern Africa, has developed resistance to all currently used drugs. Hence, there is a great need for the development of new drugs for malaria. Here, we report non-symmetrical furan-amidines as novel antimalarial leads. The non-symmetrical furan-amidines were originally designed and shown to be inhibitors of NRH:quinone oxidoreductase 2 (NQO2), a potential therapeutic target in cancer chemotherapy. The malaria parasite *P. falciparum* contains an enzyme that has similar activity to NQO2, called *P*fNDH2, therefore the non-symmetrical furan-amidines were tested against *Plasmodium.* The most active furan-amidines showed IC_{50} values in the nanomolar range for the inhibition of *P. falciparum* erythrocyte development. Interestingly, upon screening, the non-symmetrical furan-amidines showed very low binding affinities towards DNA in comparison to the known symmetrical furan-amidine (DB75), which is a known DNA intercalator. This confirmed that the non-symmetrical furan-amidines are not DNA intercalators. Synthesis of further novel non-symmetrical furan-amidines and their target identification is ongoing.

Dr Jessica Kissinger, *Professor & Director, IOB, University of Georgia*
Poster 94 : EuPathDB: Free, online genomics resources for eukaryotic pathogens and their hosts

J C Kissinger[1]; EuPathDB Team[2];
[1] University of Georgia, United States; [2] University of Pennsylvania, United States

The Eukaryotic Pathogen Database Resources (EuPathDB, https://eupathdb.org) is a family of free, online resources that facilitate the discovery of meaningful biological and clinical relationships from large volumes of data. This platform supports hypothesis driven research and places the power of bioinformatics in the hands of the scientific community by combining pre-analyzed Omics data with advanced search capabilities, powerful data visualization and analysis tools. EuPathDB supports over 170 species within Amoebazoa, Apicomplexa, Chromerida, Diplomadida, Trichomonadida, Kinetoplastida, oomycetes and fungi. For these organisms, EuPathDB integrates a wide range of data including genome sequence and annotation, transcriptomics, proteomics, epigenomics, metabolomics, population resequencing of clinical and field isolates, and host-pathogen interactions.

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Data are analyzed using standard workflows and an in-house pipeline generates data including domain predictions, GO term associations, and orthology profiles across all genomes. These pre-analyzed data are easily accessed in a graphical interface that compiles data into record pages (genes, pathways, etc.) and provides tools to search and visualize the data. Our unique search strategies system offers over 100 preconfigured searches that query individual datasets. Searches can be combined into strategies that easily merge evidence from diverse data types and across organisms. Analysis tools enhance the search strategy system and include dynamic data visualization, comparative genome and population genetics tools, functional or pathway enrichment, and a Galaxy instance for the analysis of primary data. This platform has recently expanded to incorporate data from systems biology programs and clinical studies such as the International Centers of Excellence in Malaria Research. User support includes an email help desk (help@eupathdb.org), social media, YouTube tutorials, and a global program of workshops. Please stop by our poster for a demonstration.

Examples of recent additions and highlights:

- Private Galaxy Workspace: Perform analysis of your own data and then easily port alignments to EuPathDB GBRowse to privately view against data already integrated into EuPathDB. Includes preloaded genomes and preconfigured RNA seq and variant calling workflows.
- New Database: ClinEpiDB (https://clinepidb.org) hosts clinical and epidemiological data for the infectious disease research community.
- Circadian Rhythm Analysis: *T. brucei* 927 Bloodstream and procyclic form transcriptomes during a 48-hour time-course of alternating temperatures or at constant temperature.
- Improved Annotation: GO Slim data integrated for all genomes.
- Knockout Phenotypes: PlasmoGEM knockout vectors were used to measure growth rate phenotypes in mice for 2,578 *P. berghei*genes. Gene record pages contain tabulated and graphical data.
- Cellular localization of gene products: *T. brucei* 927 cellular localization images for 3180 genes from the TrypTag project. Search for genes based on GO annotation.
- Translational Efficiency: T. cruzi transcriptome and translatome of epimastigotes and metacyclics.
- Stage Specific Expression: L. mexicana transcriptomes of promastigote and amastigote stages.
- Host-Pathogen Interactions: Paired host (mouse) and parasite (T. gondii) transcriptomes during infection of mouse neurons, astrocytes, fibroblasts and skeletal muscle cells. Interrogate parasite data in ToxoDB.org and mouse data in HostDB.org

Miss Maria Ines Neves, *PhD Student, The Royal Veterinary College, University of London*

Poster 95 : Re-evaluating density-dependent fecundity in human *Schistosoma mansoni* infections using novel molecular techniques: implications for control and elimination

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M I Neves[1]; C M Gower[1]; J P Webster[1]; M Walker[1];
[1] The Royal Veterinary College, UK

The stability of parasite populations may be regulated by density-dependent processes occurring at different stages of their life cycle. Understanding how such mechanisms affect the transmission dynamics of parasites is essential to inform control strategies, to predict resilience to interventions and to develop robust mathematical models. In diecious helminth infections, density-dependent fecundity describes the reduction in egg production by female worms in high worm burden within-host environments. For human schistosomiasis, unlike intestinal worms, investigating density-dependent fecundity is hampered by the inaccessibility of adult worms within hosts, due to the intravascular location of the parasite. Hence, whether density-dependent processes regulate the fecundity of schistosomes is contested, with the total evidence base to date generated from a single human autopsy study providing data on *Schistosoma mansoni* worm burdens and associated faecal egg counts. Furthermore, analyses of these data by various have reached contradictory conclusions. We used a novel multiplexed microsatellite-derived dataset, in which adult worm burdens of *S. mansoni* were estimated indirectly from genetic data, via parentage analysis, of *S. mansoni* miracidia obtained from children undergoing long term preventive anti-schistosome chemotherapy in Tanzania. Using associated parasitological data on eggs excreted per gram of faeces, we re-examined the longstanding and controversial issue of density-dependence in *S. mansoni*. We used Bayesian statistical techniques to highlight uncertainties in the density-dependent relationship, while showing that indirect genetically-based techniques can be useful for estimating adult worm burdens. We discuss the implications of our results in the context of developing *S. mansoni* transmission models, and the feasibility of schistosomiasis control and elimination.

Charles Ayorinde Ologunde, *Lecturing, research on tropical parasites and implementation of health policies, The Federal Polytechnic Adoekiti*
Poster 96 : Schistosomiasis in Ogbese-Ekiti, re-infection after successful treatment with praziquantel

C A Ologunde[1];
[1] The Federal Polytechnic, Ado-Ekiti, Nigeria

Urinary schistosomiasis infection is one of the major public health problem facing developing countries with school age children at greater risk. Previous studies showed that Ogbese-Ekiti is endemic for urinary schistosomiasis. The impact of chemotherapy was evaluated using praziquantel (40mg/kg body weight) on *S. heamatobium* among school pupils in Ogbese-Ekiti, Ekiti State, Nigeria. Urine samples were collected between the hours of 7.00am and 10.00am. The number of eggs in 10ml of each urine sample was calculated from the mean of two counts. At

baseline, one hundred and seventy two (172) pupils were screened for eggs of the *S. heamatobium* out of which 75.6% were positive with high egg intensity ranging between 40780 eggs/10ml of urine. Out of the one hundred and seventy two screened, thirty subjects with high egg intensity (440-780 eggs/10ml of urine) were treated with praziquantel in January 2009. After 10 days post treatment, the urine samples of the thirty subjects were negative for *S. heamatobium*. The subjects were monitored monthly for re-infection for seven consecutive months (February – August). Re-infection was first noticed in May.

Ms Alison Mbekeani, *Research Assistant, University of Durham*
Poster 97 : Protozoa are a global burden - and need new treatments and novel drug targets

A J Mbekeani[1]; V C Kalel[1]; E Ruiz[1]; W Stanley[1]; M Meissner[1]; W Schliebs[1]; R Erdmann[1]; E Pohl[1]; P Denny[1];
[1] Durham University, UK

The use of natural products (NP) for treating protozoan infections could be dated back to 1631 in Rome, where cinchona tree bark was used to cure malaria. The discovery of new NP, in the treatment of protozoan diseases is absolutely vital for many of these vaccine deficient protozoan infections. The assessment of NP against Cutaneous Leishmaniasis, was explored using a library of NP screened against the mammalian stage of *L. mexicana* in *in vitro* assays. In addition we also explored the use of a NP, Aureobasidin A and its five derivatives against *T. gondii* Type I and Type II. Investigating a drug target in *T. gondii*, we focused on the presence of peroxisomes within *T. gondii* using Pex proteins. The experimental approach taken involved characterization of putative TgPex5 and it's associated putative protein ligand TgSCP2. TgSCP2 with a C-terminal Peroxisomal Targeting Signal 1 (PTS1) binds TgPex5, whilst the N-terminal of TgPex5 binds TgPex7. Using molecular biology, reverse genetics and protein characterization, we show that pull-down assays, localisation of TgSCP2, and complementation of TgPex5 and TgPex7 in yeast and human expression systems, we are able to compile evidence to prove or refute the presence of peroxisomes within *T. gondii*.

Mr David Cutress, *PhD, Aberystwyth University - IBERS*
Poster 98 : Towards validation of an immune suppressor protein from liver fluke as a drug target

D Cutress[1]; R Morphew[1]; D Browne[2]; P M Brophy[1];
[1] Aberystwyth University - IBERS, UK; [2] Cardiff University, UK

The Liver flukes, *Fasciola hepatica* and *F. gigantica* are zoonotic parasitic flatworms of significant health and economic interest. Predictions on livestock production estimates losses at over $3 billion annually in reduction in

meat, milk and other agriculturally significant yields. The WHO has also designated fascioliasis, liver fluke disease, as a neglected food borne human disease with up to 17 million infections and up to 200 million people living in areas at risk. In absence of vaccines, the current mainstay treatment is Triclabendazole (TCBZ); the only drug effective against both juvenile and adult flukes. However, evidence of TCBZ resistance is now confirmed worldwide and new chemical compounds are being discovered or designed and synthesised to novel protein targets in liver flukes to combat increasing TCBZ resistance. Sigma class glutathione transferases (GSTs) aka prostaglandin D synthases offers a key target, due to well characterised role in immune modulation and limited relationship to host orthologues and potential roles in specific life cycle stages. Drug synthesis and testing has been performed using both recombinant and purified native enzyme extracts in order to validate this approach. Transcript analysis has uncovered another protein with suggested prostaglandin D synthase properties within *F. hepatica* proteome. Using various techniques this protein has been analysed structurally and functionally to determine the role played. Phylogenetic analysis of the GST clade across trematodes and free living helminths highlighted interesting factors in relation to extracellular vesicle content in their suggested role of host parasite interaction which requires further exploration.

Ms Rebeca Santano, *PhD student, Barcelona Institute for Global Health*

Poster 99 : IgG and IgE responses to *Plasmodium falciparum* and intestinal parasites antigens in Mozambican children

R Santano[1]; F Góngora[1]; I Cuamba[2]; M Vidal[1]; B Grau[1]; R Aguilar[1]; C Jairoce[2]; J Muñoz[1]; A Nhabomba[2]; G Moncunill[1]; C Dobaño[1];

[1] Barcelona Institute for Global Health, Spain; [2] Centro de Investigação em Saúde da Manhiça (CISM), Mozambique

Exposure to multiple parasites in African children leads to harboring two or more simultaneous infections, which can generate immune responses with different profiles that may impair the ability of the immune system to fight one of the coexisting pathogens. Intestinal parasites mainly induce T_H2 (and IgE) responses, whereas immunity to *Plasmodium falciparum* is acquired through a T_H1 (and IgG) profile. We have previously found that T_H2 cytokines are associated with lack of protection of the antimalarial vaccine RTS,S and that CSP, the main component of RTS,S, and MSP-2, a *P. falciparum* blood stage antigen, induce elevated levels of IgE. In the case of MSP-2, high IgE levels are associated with the development of malaria. We hypothesize that the induction of T_H2 cytokines and specific IgE against *P. falciparum* antigens is due to an immune deviation caused by previous or current infections with intestinal parasites. In order to investigate the possible role of parasite co-infections on immune deviation, multiplex suspension array technology with a panel of antigens of *P. falciparum* (AMA$_1$, EXP-1, EB - - A140, LSA-

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1, MSP-1, MSP-2, MSP-5), *Giardia lamblia* (VSP_3) and *Cryptosporidium parvum* (Cp_{17}) was used to measure the levels of IgG and IgG_{1-4} in Mozambican children between 2 and 10 years old, for which their infection status for malaria and intestinal helminths and protozoa was known. We will present results on the influence of intestinal parasites on the response to malaria antigens in terms of IgG and its subclasses. We have observed a tendency to have reduced antibody levels in the co-infections groups in comparison with single infection with malaria for most antigens. Future studies will increase the sample size of helminthic gut infections and malaria groups. Ongoing analyses include IgE assessment with an expanded panel including helminth antigens and in samples from malaria vaccine studies and severe malaria studies.

Dr Sonia Boughattas, *PostDoc, Qatar University*

Poster 101 : Molecular identification and characterizations of *Cryptosporidium* spp. among food-handlers in Qatar

S Boughattas[3]; D Al-Sadeq[3]; A Sharma[3]; W Abu-Alainin[1]; A Ismail[2]; **M Abu-Madi**[3];
[1] Hamad Medical Corporation, Qatar; [2] Medical Commission, Qatar; [3] Qatar University, Qatar

The World Health Organization (WHO) has identified *Cryptosporidium* spp. as globally the most common diarrhea-causing protozoan. The protozoan is the second most important cause of moderate-to-severe childhood diarrhea in developing countries whereas, in high-income countries it is an under-recognized pathogen in sporadic gastroenteritis. Humans can acquire *Cryptosporidium*infections through person-to-person transmission, zoonotic transmission, and waterborne/foodborne transmission. The potential for foodborne transmission of the protozoan parasite *Cryptosporidium* spp. is widely acknowledged. In this case, the role of food handlers is very important because they can make unsafe and hazardous foods for consumption. Indeed, outbreaks of Cryptosporidiosis Linked to a Foodhandler have been already observed in schools and in university campus. Since unhygienic preparation, storage and handling of food by infected individuals are a major cause for food-borne diseases, food handlers need to be screened before they are allowed to work in food establishments such as restaurants, hotels, food stores, factories or as helpers and cooks in private houses. Moreover, changes in nutritional habits have resulted in increased consumption of undercooked or raw foods, exposing consumers to parasites that proper food processing would otherwise reduce or eliminate. The aim of this study was to assess the prevalence of *Cryptosporidium* infection and its molecular characterization among foodhandlers in Qatar to check the relative importance of this transmission route in the epidemiology of cryptosporidiosis.
Stool samples were collected from workers related to food services. Samples were then subjected to DNA extraction and Real Time PCR detection. The positive RT-PCR products for *Cryptosporidium* spp. were analyzed by RFLP to identify the *Cryptosporidium* species. Specimens that contained *Cryptosporidium parvum* or

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Cryptosporidium hominis were further subtyped by DNA sequencing of the PCR product of the gp60 gene. The parasite was identified in 2.9% of the samples by RT-PCR targeting the 18S rRNA. PCR-RFLP analysis revealed distinctive banding patterns. The majority of isolates (45.45%) were identified as *C. parvum*. 9% were positives for *C. hominis*, 27.27% were *C. parvum* + *C. hominis*, and 18.18% were *C. parvum* + *C. meleagridis*. All *C. parvum* isolates were classified as allele IId and were assigned as IIdA20G1. The identified *C. hominis* subtype was the less common IeA12G3T3 subtype. The predominance of the zoonotic subtype families of *C. parvum* IId in the Middle Eastern regions suggests that animal-to human transmission may be a common transmission route of *Cryptosporidium*. However, this postulation may be premature in view of findings of studies conducted in Kuwait. The very limited molecular heterogeneity among the isolates reported in the present study may be due to a common origin of the infection and/or the infection was due to epidemic clone. Having anthroponotic *Cryptosporidium* strain predominance with no association between Cryptosporidium prevalence and animal contact in our study population reveals that population dynamics influence the transmission pattern of the parasite in Qatar. The role of foreign workers from Asia and Africa as a source of *Cryptosporidium* spp. infection in Arab countries has been suggested. Regarding the complications of cryptosporidiosis, the importance of its eradication / control becomes more evident.

Ms Aver Hemben, *Cranfield University*

Poster 102 : Screen-printed electrodes for malaria detection

A M Hemben[1]; I E Tothill[1];
[1] Cranfield University, UK

Malaria is a disease caused by *Plasmodium* parasite and transmitted by adult female *Anopheles* mosquitoes. Malaria affects approximately 50% of the world's population causing millions of deaths every year. Mostly affected are pregnant women and children under 5 years of age. Despite control efforts the disease continues to affect productivity. This can be minimised by early detection of the disease. Methods for malaria detection include blood film microscopy, immunochromatographic, serological and molecular tests. Blood film microscopy shows the highest sensitivity and specificity when used by trained personnel with reliable instruments. It is however time-consuming and cannot be applied as a point -of-care diagnostic method. Therefore, a simple, fast and reliable method of detection such as biosensors is needed.
Two electrochemical biosensors (immunosensors) for malaria biomarkers *Plasmodium falciparum* histidine rich protein 2 (*Pf*HRP 2) and parasite L-Lactate dehydrogenase (LDH) were developed for the detection and quantification of *Plasmodium* species. The methods were based on screen-printed gold electrodes (SPGEs) and sandwich assay comprising a 'capture antibody' immobilised on the SPGEs and a detector monoclonal antibody

conjugated to the enzyme HRP for signal generation. Enhancement of the sandwich assays by the use of gold nanoparticles (AuNP) was also investigated.
The biosensors developed for *Pf*HRP 2 can detect sub-microscopic *Plasmodium* infection with a limit of detection (LOD) as low as 2.14 ng mL^{-1} and 2.95 ng mL^{-1} in buffer and serum assays respectively. When AuNPs were used to enhance the assays, the LODs were lowered to 36 pg mL^{-1} and 40 pg mL^{-1}. Lactate dehydrogenase (LDH) showed LODs of 1.80 ng mL^{-1} and 0.70 ng mL^{-1} in buffer and serum assays. By using AuNP, the LODs were lowered to 19 pg mL^{-1} and 23 pg mL^{-1}. Further investigation will look at possible use of graphene SPEs (Rashid Solutions, UK) to replace gold based SPEs for sensor performance.

Mrs Andreia Albuquerque-Wendt, *PhD student, Medical School of Hannover*

Poster 103 : Apicomplexan C-mannosyltransferases modify adhesins of the TRAP family poster version

A Albuquerque[5]; C Hoppe[2]; G Bandini[3]; D Leon[1]; A Shcherbakova[2]; F Buettner[2]; L Izquierdo[4]; C Costello[1]; H Bakker[2]; F Routier[2];
[1] Boston University School of Medicine, United States; [2] Hannover Medical School, Germany; [3] Henry M. Goldman School of Dental Medicine, United States; [4] Instituto de Salud Global de Barcelona, Spain; [5] Medizinische Hochschule Hannover, Germany

C-mannosylation is a poorly known post-translational modification of proteins which differs from other types of glycosylation by the carbon-carbon bond that links the anomeric carbon of the mannose residue to the indole C2 carbon of tryptophan. This modification is characteristically found in WXXW/C motifs, present in thrombospondin type-1 repeat domains (TSR) and type 1 cytokine receptors in metazoans. This modification is catalyzed by C-mannosyltransferases of the DPY19 family located in the endoplasmic reticulum and it affects the folding and secretion of several proteins. Interestingly, orthologues of the encoding gene were found in the genome of apicomplexan parasites. Considering that apicomplexans share the same recognition motif as mammals, over 30 C-mannosylated proteins might be present in these parasites. Recently, the micronemal adhesion thrombospondin-related anonymous protein (TRAP) was shown to be C-hexosylated in *Plasmodium falciparum* sporozoites. Here, we demonstrate that also the micronemal protein MIC2 secreted by *Toxoplasma gondii* tachyzoites is C-hexosylated. When expressed in a cell line deficient in C-mannosylation, *P. falciparum* and *T. gondii* DPY19 homologues are able to modify TSR domains of the micronemal adhesins TRAP/MIC2 family, known to be integral components of the glideosome and therefore of paramount importance for the parasite motility and invasion. Furthermore, we observed a decreased amount of recombinant MIC2 secretion in absence of C-mannosylation, suggesting this modification might play an important role for the proper folding of this protein. *In*

vitro, the apicomplexan enzymes can transfer mannose to a WXXWXXC peptide. Since one or more TSR domains are commonly found in several surface proteins of apicomplexan parasites, C-mannosylation may be a common modification in this phylum. Since this protein is predicted to be expressed at many parasite stages, we suggest it plays an important role in infection.

Mrs Justyna Nalepa-Grajcar, *PhD Student, Aberystwyth University*

Poster 104 : Genomic and computational analysis of *Toxoplasma gondii* direct from clinical samples using selective genome whole-genome amplification (SWGA)

J Nalepa-Grajcar[1]; M Swain[1]; J A Pachebat[1]; S J Hadfield[2]; E Guy[2];
[1] Aberystwyth University - IBERS, UK; [2] Toxoplasma Reference Unit (TRU), Public Health Wales NHS Trust, UK

Toxoplasma gondii is a protozoan parasite which infects approximately one third of the world's population. Infection usually results in mild symptoms or is asymptomatic; however, severe, life threatening disease can occur in immunocompromised individuals and, if acquired during pregnancy may result in foetal abnormalities or death. The *Toxoplasma* Reference Unit (TRU) investigates *Toxoplasma* infection in patients from England and Wales, and provides advice on patient management and risk reduction. A cost-effective method of performing whole genome sequencing on *Toxoplasma* is highly desirable. This would have a significant impact on rapid diagnosis and molecular typing, which in turn would support enhanced molecular surveillance and promote effective management of clinical infections. Whole genome sequencing (WGS) of *T. gondii* has been successful using parasites cultured in laboratory animals. For human clinical samples, however, the technology is limited because the relative levels of host genomic DNA are much higher than those of the pathogen. Selective Whole Genome Amplification (SWGA) is a new technique that has been successfully employed to specifically amplify the Malaria parasite, *Plasmodium* spp., directly from clinical blood samples. The technique involves searching both the parasite genome and the human genome for short, e.g. 6 to 12 nucleotide, motifs that are much more common in the parasite genome than in the human genome. These motifs can be then used as oligonucleotide primer targets for the whole genome amplification reaction, thus enriching the target organism DNA concentration. The successful outcome of this project will allow analysis of *Toxoplasma* genome sequences directly from human clinical samples, opening a valuable collection of DNA extracts and original clinical samples with accompanying clinical data for analysis. These resources would enable significantly more in-depth investigations, improving our understanding of the epidemiology, virulence and other traits of this important human pathogen, thus assisting in developing strategies for treatment, surveillance and infection prevention. The successful development of this method will also make an

important contribution to the '3Rs' (Replacement, Refinement and Reduction in the use of animals in research) by precluding the need for *in vitro* isolation of *Toxoplasma* from clinical specimens prior to WGS.

Miss Margherita Mainiero, *PhD student, University of Bristol*

Poster 105 : The toxic effect of essential oils on mites

M Mainiero[1]; L Ellse[1]; R Wall[1];
[1] School of Biological Sciences, University of Bristol, UK

As reports of resistance to conventional synthetic pesticides and repellents to control veterinary ectoparasites are increasing, their use is becoming increasingly problematic. Possible alternatives are the plant-derived essential oils. The objective of this study was to determine the toxic effects of essential oils on parasitic and economically important pest mites: the stored food mite *Tyrophagus longior* and the red poultry mite *Dermanyssus gallinae*. Seven essential oils and oil components (2-undecone, α-methyl-trans-cinnamaldehyde, methyl trans-cinnamate, ethyl cinnamate, benzyl alcohol, *Melaleuca viridiflora* and *Mentha spicata*) were used for a series of *in vitro* experiments. Contact and vapour toxicity were tested by exposing the mites to a concentration of 5%, 2.5%, 1.25% or 0.625% (V/V) in ethanol for a period of 24h. The residual activity of the oils was determined by leaving bioassays of the 5% (V/V) concentration to air-dry for 1, 2, 6, 24, 72 hours and subsequently exposing the mites to them for a 24h period. The repellency of the oils at 5%, 2.5%, 1.25% or 0.625% (V/V) concentrations was also tested, as was the synergistic effect of vanillin when added to 5% dilutions of the oils. Overall, the results were comparable between the two mite species, with benzyl alcohol and α-methyl-trans-cinnamaldehyde showing the most potential with a mortality rate of 80% or higher, although the toxicity was less marked with *D. gallinae*. In conclusion, these *in vitro* assays demonstrated that there is indeed some merit to this line of research, however this study is only a first step towards creating an efficient alternative to synthetic pesticides.

Dr Juan Balbuena, *Associate Professor, ICBiBE, University of Valencia*

Poster 106 : Random Tanglegram Partitions (Random TaPas): a novel approach to cophylogenetic relationships between hosts and parasites

J A Balbuena[3]; C Llopis-Belenguer[3]; O A Pérez-Escobar[2]; **I Blasco-Costa**[1];
[1] Muséun d'Histoire Naturelle - Ville de Genève, Switzerland; [2] Royal Botanic Gardens Kew, UK; [3] University of Valencia, Spain

Cophylogeny attempts to estimate the past relationships between ecologically linked groups of organisms, such as

hosts and parasites, based on comparison of their phylogenetic relationships. A central assumption is that congruence between the phylogenies of hosts and their parasites indicates a shared evolutionary history. However, perfect phylogenetic congruence is rarely observed, because several eco-evolutionary processes promoting incongruence can act concurrently. This often leads to situations that can be described as coevolutionary Gordian knots. Whereas event-based approaches focus on disentangling the knots, we propose here an Alexandrian solution: Random Tanglegram Partitions (Random TaPas). Random TaPas is particularly intended for analysis and visualization of large, entangled cophylogenetic settings. Given a tanglegram, consisting of two phylogenies, representing each the relationships among hosts and parasites, and the information of associations them across both phylogenies, Random TaPas resorts to recursive random partitions to establish heuristically (1) to which extent the relationships observed are due to cospeciation, (2) which individual host-parasite associations taxa contribute most to cospeciation and (3) whether cospeciation events are evenly distributed or concentrated in parts of the phylogenies. A desirable property of Random TaPas is that it can explicitly take into account phylogenetic uncertainty in the analysis. We assessed the performance of Random TaPas with simulated coevolutionary histories built using a varying number of common coevolutionary events (cospeciation, lineage duplication, failure-to-diverge, loss, spreading and host switching) and demonstrate its applicability with a real dataset.

Miss Parul Sharma, *Student, University of Nottingham*

Poster 107 : Magnitude of the inflammatory response to parasite infection differentiates calf and adult bovine monocytes

P Sharma[2]; S Egan[2]; R Flynn[1];

[1] University of Liverpool/ Institute of Infection and Global Health/ Department of Infection Biology, UK; [2] University of Nottingham, UK

Monocytes are pivotal due to the links they form between the innate and adaptive immune response and are one of the first immune cells encountered by intra-cellular parasites during infection. Our previous data confirmed that neonatal monocytes have a higher level of secretion of IL-1β and TNF-α in response to LPS, IFN-γ and Alum, than adult derived monocytes. Here, we attempted to resolve if this age related difference was maintained in the context of *in-vitro* infection with *Neospora caninum* infection.

N. caninum (NCLiv-1) was maintained in VERO cell lines and purified CFSE labelled parasites used to infect naïve $CD14^+$cells which were purified by magnetic cell separation. The number of parasitized monocytes was determined after infection or co-culture with autologous NK-cells culture. CD80 expression was determined as a marker of cellular activation, by flow cytometry. These results reveal a greater reduction of parasitaemia in neonates with

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higher levels of IL-1β and IL-6 during *N. caninum* infection compared to adult cattle. Neonatal NK-cells also display enhanced cytotoxic activity, measured through perforin and granzyme production after co-culture with *N. caninum* infected monocytes. Complementary gene array analysis was also performed which suggests that during infection, neonates have a greater magnitude of response and a more complex network of upregulated genes are altered. Overall our comparisons show that there is a fundamental difference in the steady-state and in the response to intracellular parasite infection in neonatal monocyte led inflammatory responses.

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This 1 year course leads to an internationally recognised MRes qualification that provides training for those wishing to pursue a career in parasitology. You will gain expert knowledge in the detection, prevention and control of protozoan, metazoan animal and human pathogens, and be trained in biochemistry, molecular biology, whole organism/cell culture and manipulation, bioinformatics, proteomics, transcriptomics, genomics, functional genomics, drug discovery, vaccinology, biomarker discovery, genetics/epigenetics, epidemiology, vector/intermediate host biology and ecology.

Why study Parasite Control at Aberystwyth?

Parasitism is the most successful lifestyle on the planet and leads to diverse and highly-damaging infectious diseases of agricultural, veterinary and biomedical significance. A greater understanding of the parasite species responsible for these conditions and the means by which they are controlled is a priority for scientists, health care professionals and farmers in the 21st Century. For example, parasitic worms infect greater than 1 billion people worldwide with some species causing between $700 million-$1 billion USDs in economic losses per annum. The development of novel, creative and integrated control strategies are urgently needed to combat the growing threat of changing parasite distributions due to climate change, human migration, animal transportation and farming practices. This MRes course will provide you with a range of vocational skills and prepare you for professional employment or further post-graduate PhD studies in parasitology or related disciplines e.g. infectious diseases, public health and epidemiology.

IBERS maintains an excellent internationally-recognised reputation in parasitological research that has existed since the 1930s. Recent appointments and University investments have increased critical mass in parasitology leading to the formation of the Parasitology and Epidemiology Research Group (in 2007) and the Barrett Centre for Helminth Control (in 2016). The creation of both research groupings has facilitated greater interactions with animal health and pharmaceutical/biotech companies as well as increased research grant capture derived from government, research council and charitable funding bodies.

Why study at Aberystwyth?

With 360 members of staff (principle investigators, technicians and post-doctoral fellows), 1350 undergraduate students and more than 150 postgraduate students, IBERS is the largest research and teaching institute within Aberystwyth University. Excellence in teaching was recognised by outstanding scores in the National Student Satisfaction Survey (NSS 2017) and being awarded University of the Year for Teaching Quality by the Times and Sunday Times Good University Guide 2018. Employability data from the Recent Destinations of Leavers from Higher Education (DLHE, 2017) shows that 97% of IBERS graduates were in work or further study six months after leaving Aberystwyth University. The economic and social impact of IBERS research was recognised in 2011 when IBERS won the national BBSRC Excellence with Impact Award.

How is the course structured?

This course is uniquely different from other Masters level parasitology courses in the UK as it includes a 12-month dissertation project (Semesters 1-3). Working under the supervision of active researchers in the field, you will develop a research project on diverse topics such as intermediate host and vector control, anthelmintic drug and target discovery, biomarker identification, visual cue selection for arthropod vectors, mathematical modelling of disease transmission, host responses to parasite biomolecules, parasite and host population studies and functional genomics manipulation of parasites. A list of available projects and supervisors will be advertised closer to the start of each academic year. Your supervisor/supervisory team will mentor you in hypothesis and discovery driven experimental design, provide training in lab-based and computer-assisted methodologies, arrange instruction in analytical techniques, aid in the trouble-shooting of experimental challenges, assist you in the interpretation of results and prepare you for successful oral presentations. You will also be guided in how to most efficiently communicate your results during the dissertation write-up. It is expected that during this year long research project you will become an expert in your topic.

MRes Parasite Control

Please note: The modules listed below are those currently intended for delivery during the next academic year and may be subject to change. They are included here to give an indication of how the course is structured.

- MRes Dissertation
- Research Methods in the Biosciences
- Infection and Immunity
- Hot Topics in Parasite Control

Employability

This course is an ideal training programme for those wishing to:

- Pursue PhD studies
- Work in industry, charities or funding bodies
- Improve animal and human health
- Influence governmental policies

Go to here for the ‘at a glance’ view of the conference

Timetable at Glance

Sunday 8th April

14.00 - 20.00	Registration, Old College
18.30 - 20.00	Welcome Reception - Drinks & Finger Buffet, Old College
20.00 - 21.00	Public Understanding of Science Event, Peter Chiodini (UCL HTD,) Old College

Monday 9th April

	Edward Llwyd 0.26 Bio Main	Llandinam A6	Physics 0.15 Main	Edward Llwyd 0.01	IBERS New Build 0.33
8.30 - 8.45	Welcome Address V-C, Great Hall, Arts Centre				
8.45 - 9.15	Professor Karl Hoffmann, Great Hall, Arts Centre				
9.15 - 10.00	Plenary Lecture I. Alex Loukas (James Cook University), Great Hall, Arts Centre				
10.00 - 10.45	Plenary Lecture II. Robert Poulin (Otago University), Great Hall, Arts Centre				
10.45 - 11.15	Coffee Break, Students' Union				
11.15 - 12.45	Sponsor - Elsevier Tryps & Leish: Therapeutics, Diagnostics & Epidemiology 1. Susan Wyllie (Dundee)	Sponsor - Williams Powell Protozoa: Cell Biology & Immunology I. Eva Frickel (Crick)	Sponsor - Life Sciences Research Network Wales Helminths: Drug Discovery & Resistance 1. Raymond Pierce (Pasteur)	Sponsor - BES Ecological Parasitology : Ecological Parasitology I. Rachel Paterson (CRIPES, Cardiff)	NC3Rs Workshop : *In vitro Technologies in Cryptosporidium Research. Nigel Yarlett (PACE University)*
12.45 - 14.00	Lunch, Students' Union		Careers Networking Session. Elsevier. Katherine Ellis. Peter Chiodini. Greg Mirams. Organisers Joanne Hamilton & Helen Price. Location		
14.00 - 15.30	Tryps & Leish : Cell & Molecular Biology. S Kramer (Wuertzberg)	Clinical Parasitology. Roger Evans (Raigmore Hospital), Peter Chiodini (UCL HTD	Helminths: Molecular Communication. Amy Buck (Edinburgh University), Kevin Howe (Wormbase)	Sponsor - BES Ecological Parasitology: Eco-Immunology. Joe Jackson (Salford)	NC3Rs Workshop : *In vitro Technologies in Cryptosporidium Research. Cont.*
15.30 - 16.15	Coffee Break, Students' Union				
16.15 - 17.45	Sponsor - Elsevier Tryps & Leish : Therapeutics, Diagnostics & Epidemiology II. Pascal Mäser (Swiss TPH)	Sponsor -Life Sciences Research Network Wales Protozoa: Drug Discovery & Resistance. Giancarlo Biagini (LSTM)	Helminths: Intermediate host - parasite interactions. Tim Yoshino (University of Wisconsin-Madison)	Sponsor - BES *Ecological Parasitology: Multi-species interactions.*	Commercialising Research Workshop - Katherine Ellis(Patent Attorney), Greg Miriams(Techion)

Go to here for the ‘at a glance’ view of the conference

17.45 - 19.15	Poster Session 1, Students' Union with drinks	
20.00 - late	*Young Parasitologists Party - Constitution Hill*	*Science Café Event- Arts Centre Theatre Bar. Peter Preiser, Alex Loukas and Rachel Chalmers ‘Parasites: The Good, the Bad and the Ugly’*

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Tuesday 10th April

	Edward Llwyd 0.26 Bio Main	Llandinam A6	Physics 0.15 Main	Edward Llwyd 0.01)	Physics 0.11 A
09.00 - 10.30	Tryps & Leish : Cell & Molecular Biology. Mick Urbaniak (Lancaster)	Public Understanding of Science. Sheena Cruickshank (Manchester), Peter Chiodini (UCL HTD)	Sponsor - Williams Powell Helminths: Immuno-modulation. Maria Yazdanbakhsh (Leiden University Medical Center); Mike Doenhoff (Nottingham)	Sponsor - BES Ecological Parasitology : Ecological Parasitology II. David Thieltges (Royal Netherlands Institute for Sea Resaerch)	Sponsor - Techion BAVP-BSP Veterinary Parasitology -Diagnostics & Therapeutics. Greg Mirams (Techion, NZ)
10.30 - 11.15	Coffee Break, Students' Union				
11.15 - 12.00	Plenary Lecture III. Shahid Khan (Leiden University Medical Centre) Malaria Transfection Technologies and Vaccines, Great Hall, Arts Centre				
12.00 - 12.45	Plenary Lecture IV. Wendy Gibson (University of Bristol), Great Hall, Arts Centre				
12.45 - 14.00	Lunch, Students' Union			Elsevier Meet The Editors Workshop Near SU	WormBase Training Session LL Computer Room B23 (100)
14.00 - 15.30	Tryps & Leish : Host - Vector - Parasite Interactions I. SPBz Speaker: Edmundo Grisard (Fed. University Santa Catarina, Brazil)	Sponsor - Williams Powell Protozoa: Cell Biology & Immunology II. Volker Heussler (Bern)	Sponsor - WORMBASE Omics I: Aaron Maule (QUB)	Sponsor - BES Ecological Parasitology: Molecular Ecology & Evolution of Parasites. Dr Isabel Blasco-Costa (Natural History Museum of Geneva, Switzerland)	Sponsor - MSD Animal Health BAVP-BSP Veterinary Parasitology - Arthropod Ectoparasites and Vectors. Domenico Otranto (Bari, Italy)
15.30 - 16.15	Coffee Break, Students' Union				
16.15 - 17.45	Tryps & Leish : Host - Vector - Parasite Interactions II. Jesus Valenzuela (NIAID)	Sponsor - Williams Powell Protozoa: Cell Biology & Immunology III. Miguel Prudencio (IMM Lisbon) & Peter Preiser (NTU Singapore)	Sponsored by Life Sciences Research Network Wales. Helminths: Drug Discovery & Resistance II. Jane Hodgkinson (Liverpool)	Sponsor - BES Ecological Parasitology: Aquatic Parasitology I. Christophe Eizaguirre (QMUL)	Sponsor - Ridgeway Research. BAVP-BSP Veterinary Parasitology Symposium - Livestock Parasitology. Grace Mulcahy (UCD)
17.45 - 19.15	Poster Session 2 & Drinks, Students' Union				
20.00 -late	Conference Dinner & Party, Great Hall, Arts Centre				

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Wednesday 11st April

	Edward Llwyd 0.26 Bio Main	Llandinam A6	Physics 0.15 Main	Edward Llwyd 0.01	Physics 0.11 A
09.30 - 11.00	Sponsored by WORMBASE. Omics II. Ron Hokke (Leiden University Medical Center)	Sponsor - Royal Entomological Society. Vector - Parasite - Microbiome Interactions and Interventions. George Dimopoulos	Helminths: Cell & Molecular Biology. Jim Collins (UT Southwestern Medical center)	Sponsor - BES Ecological Parasitology Symposium: Aquatic Parasitology II. Sarah Culloty (University College Cork)	BAVP-BSP Veterinary Parasitology - Wildlife Parasitology. Eric Morgan (Queens University Belfast)
11.00 - 11.45	Coffee Break, Students' Union				
11.45 - 12.30	CA Wright Medal Lecture Annette MacLeod (Glasgow), Great Hall, Arts Centre				
12.30 - 13.00	BSP AGM, Great Hall				BAVP AGM
13.00 - 14.15	Lunch, Student's Union				
14.15 - 15.45	Tryps & Leish : Host - Vector - Parasite Interactions III: Alvaro Acosta-Serrano (LSTM)	Sponsor - PLOS NTDs Protozoa: Cryptosporidium & Giardia. Karin Troell (Nation Veterinary Institute, Sweden)	Sponsor - Elsevier Helminths: Epidemiology & Field Work. Joanne Webster (RVC)	Sponsor - BES Ecological Parasitology: Ecological Modelling. Andy Fenton (Liverpool)	BAVP-BSP Veterinary Parasitology Symposium - Sheep Scab. Sian Mitchell (APHA).