

Forum

The era of reference genomes in conservation genomics

Giulio Formenti,^{1,29}
 Kathrin Theissing,^{2,3,4,29}
 Carlos Fernandes,^{5,6,29}
 Iliana Bista,^{7,8}
 Aureliano Bombarely,⁹
 Christoph Bleidorn,¹⁰
 Claudio Ciofi,¹¹
 Angelica Crottini,¹²
 José A. Godoy,¹³
 Jacob Höglund,¹⁴
 Joanna Malukiewicz,¹⁵
 Alice Mouton,¹⁶
 Rebekah A. Oomen,^{17,18}
 Sadye Paez,¹ Per J. Palsbøll,^{19,20}
 Christophe Pampoulie,²¹
 María J. Ruiz-López,¹³
 Hannes Svardal,²²
 Constantina Theofanopoulou,¹
 Jan de Vries,²³
 Ann-Marie Waldvogel,²⁴
 Guojie Zhang,^{25,26}
 Camila J. Mazzoni,²⁷
 Erich D. Jarvis,¹
 Miklós Bálint,^{2,4,28,*}
 European Reference Genome Atlas (ERGA) Consortium^{30,31}



Conservation, genomics, and reference genomes

In 2020 both the United Nations Biodiversity Summit and the European Environment Agency emphasized the accelerating global loss of biodiversity (<https://www.un.org/pga/75/united-nations-summit-on-biodiversity/>; <https://www.eea.europa.eu/highlights/latest-evaluation-shows-europes-nature>). We are in the sixth mass extinction. Although the primary route to preserving biodiversity comprises protection of species and restoration of habitats and ecosystems, genomics provides a rapidly expanding array of novel tools to characterize biodiversity and assist such conservation efforts. The need for immediate actions that help to reverse the current biodiversity decline has prompted national and international initiatives aimed at expanding the genomic reference resources available for biodiversity research and conservation across the tree of life (Box 1). Many of these efforts collectively contribute to the Earth BioGenome Project (EBP) that aims to catalog and characterize the genomes of all of Earth's eukaryotic biodiversity. A large and inclusive community of scientists has recently gathered as the European hub of the EBP to promote the generation of a European Reference Genome Atlas (ERGA; www.erga-biodiversity.eu). This initiative is building a pan-European open access infrastructure to streamline ethical and legally compliant sample and metadata collection [1], sequencing and **assembly** (see Glossary) [2], annotation [3], and release in public archives of high-quality genomic information, thus creating reference genomes for a wide variety of eukaryotic species (Box 1).

Reference genomes, by which we mean highly contiguous, accurate, and annotated genome assemblies, greatly enhance genomic studies, both experimentally and analytically [2,4]. A reference genome is a point representation of the structure and organization of the genome of a species. Similarly to type specimens in taxonomy, reference

Glossary

Assembly: a chromosome-level contiguous sequence of all chromosomes, often aided by genetic maps or other information.
Evolutionary distinct and globally endangered (EDGE) species: species of high conservation priority.
Genetic rescue: a mitigation strategy for restoring intraspecific genetic diversity and reducing extinction risks in small, isolated, or inbred populations through induced gene flow.
Heterozygote advantage: when a heterozygous genotype has a higher relative fitness compared to a homozygous dominant or homozygous recessive genotype.
Hybridization: interbreeding of individuals from genetically distinct lineages.
Inbreeding depression: reduced fitness in offspring as a result of inbreeding – mating between closely related individuals.
Introgression: gene flow between hybridizing populations or species by backcrossing hybrids with one or both parental populations.
Metagenomics and metatranscriptomics: sequencing of DNA or RNA-derived cDNA extracted from environmental and bulk samples.
Outbreeding depression: reduced fitness in offspring from mating between genetically divergent individuals.
Pangenome: the entire set of DNA sequences (or genes) of a species represented by the core genome and the accessory genome.
Phylogenomics: the inference of the phylogenetic relationships among different lineages of organisms from genome-wide data.
Reference genome: a contiguous and accurate genome assembly representative of a species in which the coordinates of genes and other important features are annotated. Current definitions of reference genome quality are given in [2] and <https://www.earthbiogenome.org/assembly-standards>.

genomes serve as the standard for subsequent genomic studies [5]. To cost-efficiently unravel the genomic diversity of species, multiple conspecific individuals can be resequenced and aligned to available reference genomes instead of being assembled *de novo*. Thus, reference genomes provide a comprehensive and fundamental framework onto which genomic variation can be mapped to characterize and ultimately aid in preserving genetic diversity [4]. To this end, special attention should be paid to the origin of the individuals used as the reference because, if these are excessively divergent from the populations under study, this could compromise subsequent

Progress in genome sequencing now enables the large-scale generation of reference genomes. Various international initiatives aim to generate reference genomes representing global biodiversity. These genomes provide unique insights into genomic diversity and architecture, thereby enabling comprehensive analyses of population and functional genomics, and are expected to revolutionize conservation genomics.

Box 1. Sequencing the tree of life

International initiatives aimed at generating genomic resources, and particularly reference genomes, have flourished in recent years. Some focus on specific taxa, such as the Vertebrate Genomes Project, Bird Genome 10K Project, Bat1K Project, Global Invertebrate Genomics Alliance, 10 000 Plant Genomes Project, and 1000 Fungal Genomes project. Others focus on geographic regions, such as the California Conservation Genomics Project, Darwin Tree of Life for Britain and Ireland, Catalan Initiative for the Earth BioGenome Project in the Catalan territories, Endemixit in Italy, Norwegian Earth Biogenome Project, and SciLifeLab in Sweden, on applications such as the LOEWE Translational Biodiversity Genomics in Germany, or on ecological systems such as the Aquatic Symbiosis Genomics project. Collectively part of the Earth BioGenome Project (EBP), in Europe these initiatives are organized under the umbrella of the European Reference Genome Atlas (ERGA).

A genome atlas of European biodiversity

ERGA is a pan-European scientific response to the current threats to biodiversity. Approximately one fifth of the ~200 000 eukaryotic species present in Europe can be inferred to be at risk of extinction according to the International Union for Conservation of Nature (IUCN) Red List classification (this estimate only considers the assessed species; <https://www.iucn.org/regions/europe/our-work/biodiversity-conservation/european-red-list-threatened-species>).

ERGA aims to generate reference genomes of European eukaryotic species across the tree of life, including threatened, endemic, and keystone species, as well as pests and species important to agriculture, fisheries, and ecosystem function and stability. ERGA builds upon current genomic consortia in EU member states, EU Associated Countries, representatives of other countries within the European bioregion, and international collaborators. These reference genomes will address fundamental and applied questions in conservation, biology, and health. ERGA seeks to alert the EU about the potential of conservation genomics, and particularly the role of reference genomes, in biodiversity assessment, conservation strategies, and restoration efforts.

analyses. To overcome this issue, multiple conspecific genomes [6] can now be summarized in the **pangenome** of a species [7].

Until recently reference genomes have only been available for a handful of model organisms. Thanks to the consolidated and standardized efforts of international genome initiatives, the situation is rapidly changing. Recent technological advances provide a general strategy for generating chromosome-scale reference genomes for all organisms across the tree of life [2]. These advances rely on a combination of single-molecule long-read sequencing [either PacBio Single Molecule Real-Time (SMRT) sequencing or Oxford Nanopore Technologies (ONT) sequencing] and/or linked reads [(e.g., transposase enzyme linked long-read sequencing (TELL-seq) or single-tube long fragment read (stLFR) sequencing] for contig assembly, optical mapping, and/or proximity ligation followed by high-throughput sequencing (Hi-C) for scaffolding [2].

Decreasing costs, improved scalability, and increasing quality of sequencing technologies, combined with better algorithms

and advances in computational power [2], facilitate the establishment of reference genomes across the full spectrum of biodiversity. Importantly, reference genomes are fundamental for a comprehensive and accurate characterization of genomic information, for instance of structural features that cannot be inferred from fragmented genomes or reduced-representation sequencing approaches (Figure 1). Therefore, reference genomes coupled with resequencing data should become a standard in conservation genomics, facilitated by constantly evolving analytical methods.

Key contributions of reference genomes in conservation genomics**The full spectrum of genomic diversity**

Reference genomes provide a view of the architecture of the genome, comprising both genic and intergenic regions. These include repetitive regions, some of which are challenging to assemble, such as segmental duplications, centromeres and telomeres, satellites, and mobile elements. Population genomics guided by reference genomes aids the identification of classical genetic variants, such as SNPs and copy number variants (CNVs), as well as

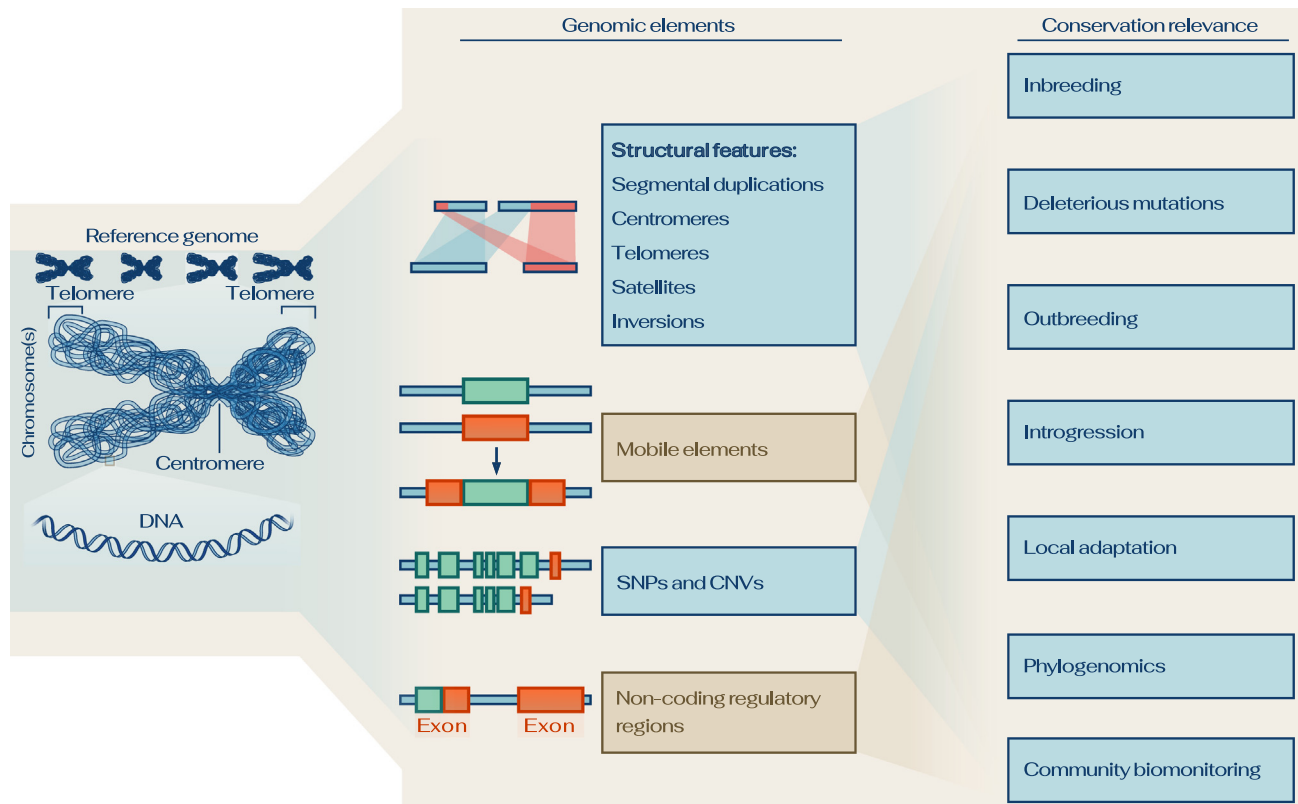
structural variants that are particularly difficult to detect in fragmented and incomplete reference genomes alone, but are potentially important in adaptation to environmental change [8].

Inbreeding and deleterious mutations

Assessments of inbreeding have long informed conservation and breeding programs, guiding genetic crosses and translocations of individuals. Although often estimated from a few loci, understanding the genetic architecture and accurately quantifying inbreeding and **inbreeding depression** require a genome-wide perspective, encompassing for example the number of genes involved, the presence of alleles with large effects, the role of deleterious recessive alleles, and **heterozygote advantage** [9]. Although several questions remain, multiple studies have showcased the power of population genomics guided by reference genomes to identify runs of homozygosity as a means to estimate inbreeding, as well as to reveal the dynamics and fate of deleterious variation in threatened species (e.g., [10]).

Outbreeding and introgression

Mating between individuals from genetically distinct lineages may lead to **outbreeding depression** due to chromosomal or genic incompatibilities, epistatic interactions, disruption of interactions between co-adapted genes, or the introduction of maladaptive variants into local populations. Population genomics guided by reference genomes greatly aids the disentanglement of these phenomena [11]. **Hybridization** is a common evolutionary process that, through **introgression**, can promote the spread of adaptive variation and speciation. Anthropogenic hybridization and introgression, however, can be major threats to biodiversity and evolutionary heritage. Reference genomes facilitate the characterization of introgression patterns and dynamics as well as of admixture proportions, particularly of introgressed tracts along individual genomes [12].



Trends in Ecology & Evolution

Figure 1. Reference genomes offer an (almost) complete record of the genome of a species. They characterize genomic information more thoroughly than fragmented genomes can. Importantly, they reveal structural features which often remain elusive in fragmented genome sequences. These features are relevant for conservation genomics applications. Abbreviations: CNV, copy number variants; SNP, single nucleotide polymorphism.

Local adaptation and genetic rescue

The use of reference genomes in population genomics facilitates the identification of traits under natural selection that form the basis and architecture of local adaptations, and ultimately of speciation. Reference genomes provide the functional and genomic contexts for regions influenced by selection, thereby enabling association of such loci with phenotypes important to adaptation and resilience. Identifying locally adapted variants can inform definitions of conservation units and identify optimal source populations for translocations to support **genetic rescue** [13].

Phylogenetic diversity and phylogenomics

Phylogenetic diversity is essential for ecosystem stability and resilience, and is used to delineate evolutionarily distinct

components of biodiversity to guide conservation priorities [e.g., **evolutionary distinct and globally endangered (EDGE) species**] [14]. Genome-scale analyses based on hundreds or thousands of loci have become the gold standard for phylogenetic inference by capturing the evolutionary histories of the targeted taxa. Reference genomes serve as the basis for **phylogenomic** analyses because they greatly improve orthology inference at the DNA and protein levels, while also facilitating inferences based on genome organization.

Structure and function of communities

Reference genomes are particularly important in **metagenomics** and **metatranscriptomics** where total DNA, or complementary DNA (cDNA) derived

from RNA, from entire communities is sequenced to understand community composition, abundance, function, and dynamics. Facilitated by the availability of reference genomes, metagenomics and metatranscriptomics have been mostly applied to microbial community samples. Eukaryotic reference genomes allow DNA/cDNA reads to be assigned to higher taxa within environmental samples, leading to a more complete characterization of communities from environmental DNA (eDNA) and RNA (eRNA). This approach represents a novel means to track changes in the composition, structure, and functioning of eukaryotic communities, and thus support the biomonitoring and management of taxonomic and functional diversity in entire ecosystems.

A collective effort to conserve biodiversity

Conservation efforts need to account for genomic diversity to optimize management strategies. Accounting for genomic diversity will aid in maintaining population viability and preserving adaptive potential to respond to environmental change. The availability of reference genomes will provide a solid, quantitative, and comparable foundation for biodiversity assessments, conservation, management, and restoration.

Author contributions

Giulio Formenti, Kathrin Theissinger, and Carlos Fernandes led the writing of the manuscript. Details on contributions to the initial discussion, to literature survey, drafting, reviewing of the manuscript and design of the figure can be found in the Supplemental information online.

Acknowledgments

We thank Fabien Condamine, Love Dalén, Richard Durbin, Bruno Fosso, Roderic Guigó, Marc Hanikenne, Alberto Pallavicini, Olga Vinnere Pettersson, Xavier Turon, and Detlef Weigel for their contributions to the manuscript, as well as the whole ERGA community for their ongoing support. We refer to the supplemental information online for acknowledgements for individual authors.

Declaration of interests

The authors declare no conflicts of interest.

Supplemental information

Supplemental information associated with this article can be found online at <https://doi.org/10.1016/j.tree.2021.11.008>.

- ¹¹ University of Florence, Department of Biology, Via Madonna del Piano 6, Sesto Fiorentino (FI) 50019, Italy
- ¹² CIBIO/InBio, Centro de Investigação em Biodiversidade e Recursos Genéticos, Rua Padre Armando Quintas, 7, 4485-661, Portugal
- ¹³ Estación Biológica de Doñana, Consejo Superior de Investigaciones Científicas, Av. Américo Vespucio, 26, 41092, Spain
- ¹⁴ Dept. of Ecology and Genetics, Uppsala University, Norbyvägen 18D, 75246, Sweden
- ¹⁵ German Primate Center, Kellnerweg 4, 37077 Göttingen, Germany
- ¹⁶ InBios - Conservation Genetics Lab, University of Liege, Chemin de la Vallée 4, 4000, Belgium
- ¹⁷ Centre for Ecological and Evolutionary Synthesis, University of Oslo, Blindernveien 31, 0371 Oslo, Norway
- ¹⁸ Centre for Coastal Research, University of Agder, Gimlemoen 25j, 4630 Kristiansand, Norway
- ¹⁹ Groningen Institute of Evolutionary Life Sciences University of Groningen Nijenborgh, 9747, AG, Groningen, the Netherlands
- ²⁰ Center for Coastal Studies, 5 Holway Avenue, Provincetown, MA 02657, USA
- ²¹ Marine and Freshwater Research Institute, Fornubúðir, 5, 220 Hanafjörður, Iceland
- ²² Department of Biology, University of Antwerp, Groenenborgerlaan 171, 2020, Belgium
- ²³ University of Göttingen, Institute for Microbiology and Genetics, Dept. of Applied Bioinformatics, Goettingen Center for Molecular Biosciences (GZMB), Campus Institute Data Science (CIDAS), Goldschmidtstr. 1, 37077, Germany
- ²⁴ Institute of Zoology, University of Cologne, Zùlpicherstrasse 47b, D-50674, Germany
- ²⁵ Villum Center for Biodiversity Genomics, Section for Ecology and Evolution, Department of Biology, University of Copenhagen, Denmark, Build 3, Universitetsparken 15, Copenhagen 2100, Denmark
- ²⁶ China National Genebank, BGI-Shenzhen, Jinsha Road, Dapeng District, Shenzhen 518083, China
- ²⁷ Leibniz Institute for Zoo and Wildlife Research (IZW), Alfred-Kowalke-Str 17, 10315 Berlin, Germany
- ²⁸ Institute for Insect Biotechnology, Justus-Liebig University Gießen, Heinrich-Buff-Ring 26-32, 35392 Giessen, Germany
- ²⁹ Joint first authors.
- ³⁰ This work originates from a collective effort within the ERGA Consortium (Box 1).
- ³¹ Consortium author information: Giulio Formenti, Kathrin Theissinger, Carlos Fernandes, Iliana Bista, Aureliano Bombarely, Christoph Bleidorn, Fedor Čiampor, Claudio Ciofi, Angelica Crottini, José A. Godoy, Jacob Hognlund, Joanna Malukiewicz, Alice Mouton, Rebekah A. Oomen, Sadye Paez, Per Palsboll, Christophe Pampouille, María José Ruiz-López, Hannes Svardal, Constantina Theofanopoulou, Jan de Vries, Ann-Marie Waldvogel, Goujie Zhang, Camila J. Mazzoni, Erich Jarvis, Miklós Bálint, Sargis A. Aghayan, Tyler S. Alioto, Isabel Almudi, Nadir Alvarez, Paulo C. Alves, Isabel R Amorim, Agostinho Antunes, Paula Aribas, Petr Baldrian, Paul R Berg, Giorgio Bertorelle, Astrid Böhne, Andrea Bonisoli-Alquati, Ljudevit L Boštjančič, Bastien Boussau, Catherine M Breton, Elena Buzan, Paula F Campos, Carlos Carreras, L. Filipe Castro, Luis J. Chueca, Elena Conti, Robert Cook-Deegan, Daniel Croll, Mónica V Cunha, Frédéric Delsuc, Alice B. Dennis, Dimitar Dimitrov, Rui Faria, Adrien Favre, Olivier D. Fedrigo, Rosa Fernández, Gentile Francesco Ficetola, Jean-François Flot, Toni Gabaldón, Dolores R. Galea Agius, Guido R. Gallo, Alice M. Giani, M. Thomas P Gilbert, Tine Grebenc, Katerina Guschanski, Romain Guyot, Bernhard Hausdorf, Oliver Hawiltschek, Peter D Heintzman, Berthold Heinze, Michael Hiller, Martin Husemann, Alessio Iannucci, Iker Irisarri, Kjetill S Jakobsen, Sissel Jentoft, Peter Klinga, Agnieszka Kloch, Claudius F Kratochwil, Henrik Kusche, Kara KS Layton, Jennifer A Leonard, Emmanuelle Lerat, Gianni Liti, Tereza Manuosaiki, Tomas Marques-Bonet, Pavel Matos-Maraví, Michael Matschiner, Florian Maumus, Ann M. Mc Cartney, Shai Meiri, José Melo-Ferreira, Ximo Mengual, Michael T. Monaghan, Matteo Montagna, Robert W Mysajek, Marco T Neiber, Violaine

- Nicolas, Marta Novo, Petar Ozretić, Ferran Palero, Lucian Pârvulescu, Marta Pascual, Octávio S. Paulo, Martina Pavlek, Cinta Pegueroles, Loïc Pellissier, Graziano Pesole, Craig R Primmer, Ana Riesgo, Lukas Rüber, Diego Rubolini, Daniele Salvi, Ole Seehausen, Matthias Seidel, Simona Secomandi, Bruno Studer, Spyros Theodoridis, Marco Thines, Lara Urban, Anti Vasemägi, Adriana Vella, Noel Vella, Sonja C Vernes, Cristiano Vernesi, David R Veites, Robert M Waterhouse, Christopher W Wheat, Gert Wörheide, Yannick Wurm, and Gabrielle Zammit.
- Affiliations: Giulio Formenti, The Rockefeller University, 1230 York Avenue, New York, NY 10065, USA; Kathrin Theissinger, LOEWE Centre for Translational Biodiversity Genomics (LOEWE-TBG), Georg-Voigt-Str. 14-16, 60325 Frankfurt/Main, Germany, University of Koblenz-Landau, Institute for Environmental Sciences, Fortstrasse 7, 76829 Landau, Germany, Senckenberg Biodiversity and Climate Research Centre, Georg-Voigt-Str. 14-16, 60325 Frankfurt/Main, Germany; Carlos Fernandes, CE3C - Centre for Ecology, Evolution and Environmental Changes, Departamento de Biologia Animal, Faculdade de Ciências, Universidade de Lisboa, 1749-016 Lisboa, Portugal, Faculdade de Psicologia, Universidade de Lisboa, Alameda da Universidade, 1649-013 Lisboa, Portugal; Iliana Bista, University of Cambridge, Department of Genetics, Downing Street, CB2 3EH, Wellcome Sanger Institute, Hinxton, CB10 1SA, UK, Naturalis Biodiversity Center, Darwinweg 2, Leiden, 2333 CR, The Netherlands; Aureliano Bombarely, Università degli Studi di Milano, Via Celoria 26, 20133 Italy; Christoph Bleidorn, University of Göttingen, Department of Animal Evolution and Biodiversity, Untere Karspüle, 2, 37073 Germany; Fedor Čiampor, Plant Science and Biodiversity Centre, Slovak Academy of Science, Dúbravská cesta 9, 845 23 Bratislava, Slovakia; Claudio Ciofi, University of Florence, Department of Biology, Via Madonna del Piano 6, Sesto Fiorentino (FI) 50019, Italy; Angelica Crottini, CIBIO, Centro de Investigação em Biodiversidade e Recursos Genéticos, InBio Laboratório Associado, Campus de Vairão, Universidade do Porto, 4485-661 Vairão, Portugal, Departamento de Biologia, Faculdade de Ciências, Universidade do Porto, 4099-002 Porto, Portugal, BIOPOLIS Program in Genomics, Biodiversity and Land Planning, CIBIO, Campus de Vairão, 4485-661 Vairão, Portugal; José A Godoy, Estación Biológica de Doñana, Calle Americo Vespucio 26, 41092 Spain; Jacob Hognlund, Dept. of Ecology and Genetics, Uppsala University, Norbyvägen 18D, 75246, Sweden; Joanna Malukiewicz, German Primate Center, Kellnerweg 4, 37077, Germany; Alice Mouton, InBios - Conservation Genetics Lab, University of Liege, Chemin de la Vallée 4, 4000, Belgium; Rebekah A Oomen, Centre for Ecological and Evolutionary Synthesis, University of Oslo, Blindernveien 31, 0371 Oslo, Norway, Centre for Coastal Research, University of Agder, Gimlemoen 25j, 4630 Kristiansand, Norway; Sadye Paez, The Rockefeller University, 1230 York Avenue, New York, NY 10065, USA; Per Palsboll, Groningen Institute of Evolutionary Life Sciences University of Groningen Nijenborgh, 9747 AG Groningen, The Netherlands, Center for Coastal Studies, 5 Holway Avenue, Provincetown, MA 02657, USA; Christophe Pampouille, Marine and Freshwater Research Institute, Fornubúðir, 5,220, Hanafjörður, Iceland; María José Ruiz-López, Estación Biológica de Doñana, Consejo Superior de Investigaciones Científicas, Av. Américo Vespucio, 26, 41092, Spain, CIBER Epidemiología y Salud Pública (CIBERESP), Spain; Hannes Svardal, Department of Biology, University of Antwerp, Groenenborgerlaan 171, 2020, Belgium; Constantina Theofanopoulou, Rockefeller University, 1230 York Ave, New York, NY 10065, USA; Jan de Vries, University of Goettingen, Institute for Microbiology and Genetics, Dept. of Applied Bioinformatics, Goettingen Center for Molecular Biosciences (GZMB), Campus Institute Data Science (CIDAS), Goldschmidtstr. 1, 37077, Germany; Ann-Marie Waldvogel, Institute of Zoology, University of Cologne, Zùlpicherstrasse 47b, D-50674, Germany; Goujie Zhang, Villum Center for Biodiversity Genomics, Section for Ecology and Evolution, Department of Biology, University of Copenhagen, Build 3, Universitetsparken 15, Copenhagen, 2100, Denmark, China National Genebank, BGI-Shenzhen, Jinsha Road,

- Dapeng District, Shenzhen 518083, China; State Key Laboratory of Genetic Resources and Evolution, Kunming Institute of Zoology, Chinese Academy of Sciences, Jiaochang East Road, Wupan District, Kunming, Yunnan 650223, China; Camila J Mazzoni, Leibniz Institute for Zoo and Wildlife Research (IZW), Alfred-Kowalke-Str 17 10315 Berlin, Germany; Berlin Centre for Genomics in Biodiversity Research (BeGenDiv), Koenigin-Luise-Str 6-8, 14195 Berlin, Germany; Erich Jarvis, The Rockefeller University, 1230 York Avenue, New York, NY 10065, USA; Miklós Bálint, LOEWE Centre for Translational Biodiversity Genomics (LOEWE-TBG), Georg-Voigt-Str. 14-16, 60325 Frankfurt/Main, Germany; Institute for Insect Biotechnology, Justus-Liebig University Gießen, Heinrich-Buff-Ring 26-32, 35392 Giessen, Germany; Senckenberg Biodiversity and Climate Research Centre (SBK-F), Georg-Voigt-Str. 14-16, 60325 Frankfurt/Main, Germany; Sargis A Aghayan, Chair of Zoology, Yerevan State University, 1 Alex Manoogian, Yerevan, 0025, Armenia; Tyler S Alliot, CNAG-CRG, Centre for Genomic Regulation (CRG), Barcelona Institute of Science and Technology (BIST), Baldiri i Reixac 4, 08028 Barcelona, Spain; Isabel Almuñi, Department of Genetics, Microbiology and Statistics and IRBio, Universitat de Barcelona, Av. Diagonal 643, 08028 Barcelona, Spain; Nadir Alvarez, Geneva Natural History Museum, 1 route de Malagnou, 1208 Geneva, Switzerland, University of Geneva, Department of Genetics & Evolution, University of Geneva, 4 Boulevard d'Yvoy, 1205 Geneva, Switzerland; Paulo C Alves, CIBIO/InBIO, University of Porto, Campus of Vairão, 4485-661, Vila do Conde, Portugal, Dep Biology, Faculty of Sciences, University of Porto, R Campo Alegre, s/n, 4169-007 Porto, Portugal, Wildlife Biology Program, University of Montana, Missoula, MT 59812, USA; Isabel R Amorim, e3c – Centre for Ecology, Evolution and Environmental Changes / Azorean Biodiversity Group and Universidade dos Açores, Universidade dos Açores, Rua Capitão João d'Ávila, Pico da Urze, 9700-042 Angra do Heroísmo, Azores, Portugal; Agostinho Antunes, CIMAR/CIMAR, Interdisciplinary Centre of Marine and Environmental Research, University of Porto, Terminal de Cruzeiros do Porto de Leixões, Av. General Norton de Matos, s/n, 4450-208 Porto, Portugal, Department of Biology, Faculty of Sciences, University of Porto, Rua do Campo Alegre, s/n, 4169-007 Porto, Portugal; Paula Arribas, Instituto de Productos Naturales y Agrobiología (IPNA-CSIC), S.C. La Laguna, 38206, Spain; Petr Baldrian, Institute of Microbiology of the Czech Academy of Sciences, Videnska 1083, Praha 4 14220, Czech Republic; Paul R Berg, University of Agder, Centre for Coastal Research, 25, Universitetsveien, Kristiansand N-4630, Norway, Norwegian Institute for Water Research (NIVA), 21, Gaustadalléen, Oslo N-0349, Norway; Giorgio Bertorello, Department of Life Sciences and Biotechnology, 46, via Borsari, Ferrara 44121, Italy; Astrid Böhne, Centre for Molecular Biodiversity Research, Zoological Research Museum Alexander Koenig Bonn, Leibniz Institute for Animal Biodiversity, Adenauerallee 160, 53113 Bonn, Germany; Andrea Bonisoli-Alquati, California State Polytechnic University, Pomona, 3801 W Temple Avenue, Pomona, CA 91767, USA; Ljudevit L Boštjančić, LOEWE Centre for Translational Biodiversity Genomics, Senckenberg Biodiversity and Climate Research Centre, Georg-Voigt-Str. 14-16, 60325 Frankfurt/Main, Germany; Bastien Boussau, UMR5558, CNRS, Université Lyon 1, Université de Lyon, Bât. Grégor Mendel, 43 bd du 11 novembre 1918, Villeurbanne, France 69622; Catherine M Breton, Alliance Bioversity CIAT, Europe – Montpellier Office, Bioversity International France, Parc Scientifique Agropolis II, 34397 Montpellier Cedex 5, France, French Institute of Bioinformatics (IFB) – South Green Bioinformatics Platform, Bioversity, CIRAD, INRAE, IRD, F-34398 Montpellier, France; Elena Buzan, University of Primorska, Faculty of Mathematics, Natural Sciences and Information Technologies, Glagoljaška 8, 6000 Koper, Slovenia, Environmental Protection College, Trg mladosti 7, 3320 Velenje, Slovenia; Paula F Campos, CIMAR, Interdisciplinary Centre of Marine and Environmental Research, University of Porto, Terminal de Cruzeiros do Porto de Leixões, Avenida General Norton de Matos, Matosinhos 4450-208, Portugal; Carlos Carreras, Department of Genetics, Microbiology and Statistics and IRBio, Universitat de Barcelona, Av. Diagonal 643, 08028 Barcelona, Spain; L. Filipe Castro, Interdisciplinary Centre of Marine and Environmental Research, Avenida General Norton de Matos, S/N, Matosinhos 4450-208, Portugal, Faculty of Sciences University of Porto, Rua Campo Alegre s/n, Porto 4169-007, Portugal; Luis J Chueca, University of the Basque Country (UPV/EHU), 7, Paseo de la Universidad, Vitoria-Gasteiz 01006, Spain, LOEWE-Centre for Translational Biodiversity Genomics (LOEWE-TBG), 25, Senckenberganlage, Frankfurt am Main 60325, Germany; Elena Conti, University of Zurich, Department of Systematic and Evolutionary Botany, 107 Zollikerstrasse, Zurich 8008, Switzerland; Robert Cook-Deegan, Arizona State University, 1800 I (Eye) Street, NW, Washington, DC 20006, USA; Daniel Croll, University of Neuchâtel, 11, Emile-Argand, Neuchâtel CH-2000, Switzerland; Mónica V Cunha, Centre for Ecology, Evolution and Environmental Changes (CE3C), Campus da Faculdade de Ciências da Universidade de Lisboa, C2 Building, Campo Grande 1749-016, Lisboa, Portugal, BiolSI- Biosystems and Integrative Sciences Institute, Campus da Faculdade de Ciências da Universidade de Lisboa, Teclabs Building, Campo Grande, 1749-016 Lisboa, Portugal; Frédéric Delsuc, Institut des Sciences de l'Evolution de Montpellier (ISEM), CNRS, IRD, EPHE, Université de Montpellier, Place Eugène Bataillon, 34095 Montpellier, France; Alice B Dennis, University of Potsdam, Institute for Biochemistry & Biology, Karl-Liebknecht-Str. 24-25, House 26, Room 2.77, 14476 Potsdam, Germany; Dimitar Dimitrov, Department of Natural History, University Museum of Bergen, University of Bergen, P.O. Box 7800, 5020 Bergen, Norway; Rui Faria, CIBIO, Centro de Investigação em Biodiversidade e Recursos Genéticos; InBIO, Laboratório Associado, Universidade do Porto, Campus Agrário de Vairão, Rua Padre Armando Quintas N7, 4485-661 Vairão, Portugal; Adrien Favre, Senckenberg Research Institute and Natural History Museum, 25 Senckenberganlage, Frankfurt/Main D-60325, Germany; Olivier D Fedrigo, The Rockefeller University, 1230 York Avenue, New York, NY 10065, USA; Rosa Fernández, Institute of Evolutionary Biology (CSIC-Universitat Pompeu Fabra), 37-49 Passeig marítim de la Barceloneta, Barcelona 08003, Spain; Gentile Francesco Ficetola, Università degli Studi di Milano, Via Celoria 10, 20133 Milano Italy, Univ. Grenoble-Alpes, F-38000 Grenoble, France; Jean-François Flot, Université libre de Bruxelles (ULB), C.P. 160/12, Avenue F. D. Roosevelt 50, 1050 Brussels, Belgium; Toni Gabaldón, Barcelona Supercomputing Centre (BSC-CNS), Jordi Girona, 29, 08034 Barcelona, Spain, Institute for Research in Biomedicine (IRB), Carrer de Baldri Reixac, 10, 08028 Barcelona, Spain, Catalan Institution for Research and Advanced Studies (ICREA), Passeig Lluís Companys 23, 08010 Barcelona, Spain; Dolores R Galea Agius, Centre of Molecular Medicine and Biobanking, Tal-Oroqqa, Msida, MSD2080, Malta, G.F. Abela Junior College, Department of Biology, Gużé Debono Square, Msida MSD 1252, Malta; Guido R Gallo, Department of Biosciences, University of Milan, Milan, Italy, 26, Via Celoria, Milan 20133, Italy; Alice M Giani, Weill Cornell Medicine, 1300 York Ave, New York, NY 10065, USA; M. Thomas P Gilbert, Center for Evolutionary Hologenomics, The GLOBE Institute, The University of Copenhagen, 5A, Oester Farimagsgade, Copenhagen, 1353, Denmark, University Museum, NTNU, 47B, Erling Skakkes gate, Trondheim, Norway; Tine Grebenc, Slovenian Forestry Institute, Večna pot 2, SI-1000 Ljubljana, Slovenia; Katerina Guschanski, The University of Edinburgh, Institute of Evolutionary Biology, School of Biological Sciences, Ash worth Laboratories, Charlotte Auerbach Road, Edinburgh, EH9 3FL, UK, Uppsala University, Department of Ecology and Genetics/Animal Ecology, Norbyvägen 18D, SE-752 36 Uppsala, Sweden; Romain Guyot, Institut de Recherche pour le Développement, 911, ave Agropolis, Montpellier, 34394, France; Bernhard Hausdorf, Leibniz Institute for the Analysis of Biodiversity Change, Zoological Museum Hamburg, Martin-Luther-King-Platz 3, 20146 Hamburg, Germany; Oliver Hawlitschek, Leibniz Institute for the Analysis of Biodiversity Change, Zoological Museum Hamburg, Martin-Luther-King-Platz 3, 20146 Hamburg, Germany; Peter D Heintzman, The Arctic University Museum of Norway, UiT - The Arctic University of Norway, P. O. Box 6050, Langnes, Tromsø, N-9037, Norway; Berthold Heinze, Austrian Research Centre for Forests (BFW), 8, Seckendorff-Gudent Weg, Vienna, 1130, Austria; Michael Hiller, LOEWE Centre for Translational Biodiversity Genomics, Senckenberganlage 25, 60325 Frankfurt, Germany, Senckenberg Society for Nature Research, Senckenberganlage 25, 60325 Frankfurt, Germany, Goethe-University, Faculty of Biosciences, Max-von-Laue-Str. 9, 60438 Frankfurt, Germany; Martin Husemann, Leibniz Institute for the Analysis of Biodiversity Change, Zoological Museum Hamburg, Martin-Luther-King-Platz 3, 20146 Hamburg, Germany; Alessio Iannucci, University of Florence, Department of Biology, Via Madonna del Piano 6, Sesto Fiorentino (FI) 50019, Italy; Iker Irisarri, University of Goettingen, 1 Goldschmidtstr., Goettingen, 37077, Germany, Campus Institute Data Science (CIDAS), Goettingen, Germany; Kjetill S Jakobsen, Centre for Ecological and Evolutionary Synthesis (CEES), Dept. of Biosciences, University of Oslo, PO Box 1066 Blindern, NO-0316 Oslo, Norway; Sissel Jentoft, University of Oslo, Department of Biosciences, Centre for Ecological and Evolutionary Synthesis (CEES), Blindernveien 31, 0371 Oslo, Norway; Peter Klinga, Technical University in Zvolen, Faculty of Forestry, Department of Phytology, 24, T.G. Masaryka, Zvolen, 960 01, Slovak Republic, DIANA – Carpathian Wildlife Research, 47, Mládežnícka, Banská Bystrica 974 04, Slovak Republic; Agnieszka Kloch, Institute of Functional Biology and Ecology, Department of Ecology, University of Warsaw, Faculty of Biology, Ilii, Miecznikowa 1, 02-096 Warszawa, Poland; Claudius F Kratochwil, Institute of Biotechnology, HiLIFE, University of Helsinki, 1, Viikinkaari, Helsinki, 00790, Finland; Henrik Kusche, Leibniz Institute for the Analysis of Biodiversity Change, Zoological Museum Hamburg, Martin-Luther-King-Platz 3, 20146 Hamburg, Germany; Kara KS Layton, University of Aberdeen, Zoology Building, Tillydrone Ave, University of Aberdeen, Aberdeen, AB24 2TZ, UK; Jennifer A Leonard, Estación Biológica de Doñana (EBD-CSIC), Avd. Americo Vespucio 26, Seville, 41092, Spain; Emmanuelle Lerat, Université de Lyon, Université Lyon 1, CNRS, Laboratoire de Biométrie et Biologie Evolutive, UMR 5558, Bat. Mendel, 43 bd du 11 novembre 1918, 69622 Villeurbanne cedex, France; Gianni Liti, Université Côte d'Azur, CNRS, INSERM, IRCAN, 28 Avenue de Valombrose, 06107 NICE Cedex 2, France; Tereza Manousaki, Hellenic Centre for Marine Research (HCMR), Institute of Marine Biology, Biotechnology and Aquaculture (IMBBC), Former U. S. Base of Gournes, P.O. Box 2214, 71003, Heraklion, Crete, Greece; Tomas Marques-Bonet, Institute of Evolutionary Biology (UPF-CSIC), PRBB, Dr. Aiguader 88, 08003, Spain, Catalan Institution of Research and Advanced Studies (ICREA), Passeig de Lluís Companys, 23, 08010 Barcelona, Spain, CNAG-CRG, Centre for Genomic Regulation (CRG), Barcelona Institute of Science and Technology (BIST), Baldiri i Reixac 4, 08028 Barcelona, Spain; Pável Matos-Maraví, Biology Centre of the Czech Academy of Sciences, Institute of Entomology, Branišovská 1160/31, 37005 České Budějovice, Czech Republic; Michael Matschner, University of Oslo, 1, Sars' gate, Oslo, 0562, Norway; Florian Maumus, Université Paris-Saclay, INRAE, URGI, 78026, Versailles, France; Ann M Mc Cartney, National Institute of Health, 49 Convent Drive, Bethesda, MD 20892, USA; Shai Meiri, Tel Aviv University, School of Zoology, the Steinhardt Museum of Natural History, 12 Klausner street, Tel Aviv 6997801, Israel; José Melo-Ferreira, CIBIO, Centro de Investigação em Biodiversidade e Recursos Genéticos, InBIO Laboratório Associado, Universidade do Porto, 7, Rua Padre Armando Quintas, Vairão, 4485-661, Portugal, Departamento de Biologia, Faculdade de Ciências da Universidade do Porto, s/n, Rua do Campo Alegre, Porto 4169-007, Portugal; Ximo Mengual, Centre of Taxonomy and Evolutionary Research, Zoological Research Museum Alexander Koenig Bonn, Leibniz Institute for Animal Biodiversity, Adenauerallee 160, 53113 Bonn, Germany; Michael T Monaghan, Leibniz Institute of Freshwater Ecology and Inland Fisheries (IGB), 301, Müggelseedamm, Berlin, 12587, Germany, Institut für

Biologie, Freie Universität Berlin, 1-3, Königin-Luise-Str., Berlin 12489, Germany; Matteo Montagna, Dipartimento di Scienze Agrarie e Ambientali - Università degli Studi di Milano, 2, Via Celoria, Milan, I-20133, Italy; BAT Center - Interuniversity Center for Studies on Bioinspired Agro-Environmental Technology, University of Napoli Federico II, 100, Via Università, Portici I-80055, Italy; Robert W Mysłajek, University of Warsaw, Faculty of Biology, Institute of Functional Biology and Ecology, Department of Ecology, Biological and Chemical Research Centre, 101 Zwirki i Wigury, Warszawa, 02-089, Poland; Marco T Neiber, Leibniz Institute for the Analysis of Biodiversity Change, Zoological Museum Hamburg, Martin-Luther-King-Platz 3, 20146 Hamburg, Germany; Violaine Nicolas, Institut de Systématique, Evolution, Biodiversité (ISYEB), Muséum national d'Histoire naturelle, CNRS, Sorbonne Université, EPHE, Université des Antilles, CP51, 57 rue Cuvier, 75005 Paris, France; Marta Novo, Complutense University of Madrid, José Antonio Novás, 12, Madrid, 28040, Spain; Petar Ozretić, Ruder Bošković Institute, Bijenička cesta 54, Zagreb, 10000, Croatia; Ferran Palero, Institut Cavanilles de Biodiversitat i Biologia Evolutiva (ICBIBE), Universitat de Valencia, Carrer del Catedratic José Beltrán Martínez 2, 46980 Paterna, Spain; Lucian Pârvolescu, Department of Biology-Chemistry, Faculty of Chemistry, Biology, Geography, West University of Timisoara, 16A Pestalozzi St., Timisoara, 300115, Romania; Environmental Advanced Research Institute, West University of Timisoara, Vasile Pârvan 4 Bd., Timisoara 300223, Romania; Marta Pascual, Department of Genetics, Microbiology and Statistics and IRBio, Universitat de Barcelona, Av. Diagonal 643, 08028 Barcelona, Spain; Octávio S Paulo, cE3c - Centre for Ecology, Evolution and Environmental Changes, Departamento de Biologia Animal, Faculdade de Ciências, Universidade de Lisboa, P-1749-016, Lisboa; Martina Pavlek, Ruder Bošković Institute, Bijenička cesta 54, Zagreb, 10000, Croatia; Cinta Pegueroles, Department of Genetics, Microbiology and Statistics and IRBio, Universitat de Barcelona, Av. Diagonal 643, 08028 Barcelona, Spain; Loïc Pellissier, ETH Zürich, Landscape Ecology, Institute of Terrestrial Ecosystems, Department of Environmental Systems Science, ETH Zürich, Zürich, Switzerland, Swiss Federal Institute for Forest Snow and Landscape Research WSL, Unit of Land Change Science, Swiss Federal Institute for Forest, Snow and Landscape Research WSL, Birmensdorf, Switzerland; Graziano Pesole, Department of Biosciences, Biotechnologies and Biopharmaceutics, University of Bari "A. Moro", Campus "E. Quagliariello", via Orabona, 4, 70126 Bari, Italy, Institute of Biomembranes, Bioenergetics and Molecular Biotechnologies, Consiglio Nazionale delle Ricerche, Campus "E. Quagliariello", via Orabona, 4, 70126 Bari, Italy, Consorzio Interuniversitario Bioteconologia, via Flavia, 23/1, 34148 Trieste, Italy; Craig R Primmer, Organismal and Evolutionary Biology Research Program, University of Helsinki, PO Box 56, 00014, University of Helsinki, Finland, Institute of Biotechnology (HiLIFE), University of Helsinki, PO Box 56, 00014, Finland; Ana Riesgo, Museo Nacional de Ciencias Naturales - CSIC, C/

José Gutiérrez Abascal, 2, Madrid, 28028, Spain, Natural History Museum of London, Cromwell Road, SW7 5BD London, UK; Lukas Rüber, Naturhistorisches Museum Bern, 15 Bernastrasse, Bern, 3005, Switzerland, Aquatic Ecology and Evolution, Institute of Ecology and Evolution, University of Bern, 6 Balzerstrasse, Bern 3012, Switzerland; Diego Rubolini, Dipartimento di Scienze e Politiche Ambientali, Università degli Studi di Milano, Via Celoria 26, Milano, I-20133, Italy; Daniele Salvi, Department of Health, Life & Environmental Sciences - University of L'Aquila, Via Vetoio snc, 67100 L'Aquila-Coppito, Italy; Ole Seehausen, Institute of Ecology and Evolution, University of Bern, Baltzerstrasse 6, 3012 Bern, Switzerland, Eawag Swiss Federal Institute for Aquatic Science & Technology, Seestrasse 79, 6047 Kastanienbaum, Switzerland; Matthias Seidel, Leibniz Institute for the Analysis of Biodiversity Change, Zoological Museum Hamburg, Martin-Luther-King-Platz 3, 20146 Hamburg, Germany; Simona Secomandi, Department of Biosciences, University of Milan, Milan, Italy, 26, Via Celoria, Milan 20133, Italy; Bruno Studer, Molecular Plant Breeding, Institute of Agricultural Sciences, ETH Zurich, Universitaetstrasse 2, 8092 Zurich, Switzerland; Spyros Theodoridis, Senckenberg Biodiversität und Klima Forschungszentrum: Frankfurt, DE, 25 Senckenberganlage, Frankfurt am Main 60325 Germany; Marco Thines, Goethe University, Institute of Ecology, Evolution and Diversity, Max-von-Laue-Str. 13, Frankfurt am Main, 60438, Germany, Senckenberg Biodiversity and Climate Research Centre (SBIK-F), Senckenberganlage 25, Frankfurt am Main 60325, Germany, LOEWE Translational Biodiversity Genomics, Georg-Voigt-Str. 14-16, Frankfurt am Main 60325, Germany; Lara Urban, Department of Anatomy, University of Otago, 270 Gt King Street, Dunedin, 9016, New Zealand; Anti Vasemägi, Department of Aquatic Resources, Swedish University of Agricultural Sciences, 2, Stångholmsvägen, Drottningholm, 178 93, Sweden, Chair of Aquaculture, Institute of Veterinary Medicine and Animal, Estonian University of Life Sciences, 56A, Kreutzwaldi, Tartu 51006, Estonia; Adriana Vella, Conservation Biology Research Group, University of Malta, Taq-Qroq, Msida, MSD2080, Malta; Noel Vella, Conservation Biology Research Group, University of Malta, Msida, MSD2080, Malta; Sonja C Vernes, School of Biology, The University of St Andrews, St Andrews, Fife, UK, Max Planck Institute for Psycholinguistics, Wundtlaan 1, Nijmegen, the Netherlands; Cristiano Vernesi, Forest Ecology, Research and Innovation Centre-Fondazione Edmund Mach, 1, via Edmund Mach, San Michele all'Adige, 38010, Italy; David R Vieites, Museo Nacional de Ciencias Naturales -CSIC, Calle José Gutiérrez Abascal 2, 28006, Madrid, Spain; Robert M Waterhouse, Department of Ecology and Evolution, University of Lausanne, 1015 Lausanne, Switzerland, Swiss Institute of Bioinformatics, 1015 Lausanne, Switzerland; Christopher W Wheat, Department of Zoology, Stockholm University, 18B, Svante Arrheniusväg, Stockholm, S-10691, Sweden; Gert Wörheide, Ludwig-Maximilians-Universität München, Dept. of Earth and Environmental Sciences, Palaeontology & Geobiology, Richard-Wagner-Str. 10, Munich, 80333, Germany, Ludwig-Maximilians-Universität München, GeoBio-

Center, Richard-Wagner-Str. 10, Munich 80333, Germany, SNSB - Bavarian State Collections for Palaeontology and Geology, Richard-Wagner-Str. 10, Munich 80333, Germany; Yannick Wurm, Queen Mary University of London, Mile End Road, London, E5 8HS, United Kingdom, Alan Turing Institute, London NW1 2DB, UK; Gabrielle Zammit, Department of Biology, University of Malta, Biomedical Sciences Building, MSD2080, Msida, Malta, Centre for Molecular Medicine and Biobanking, Biomedical Sciences Building, MSD2080 Msida, Malta

*Correspondence: miklos.balint@senckenberg.de (M. Balint). <https://doi.org/10.1016/j.tree.2021.11.008>

© 2021 Published by Elsevier Ltd. This is an open access article under the CC BY IGO license (<http://creativecommons.org/licenses/by/3.0/igo/>).

References

- Shaw, F. *et al.* (2020) COPO: a metadata platform for brokering FAIR data in the life sciences. *F1000Res* 9, 495
- Rhie, A. *et al.* (2021) Towards complete and error-free genome assemblies of all vertebrate species. *Nature* 592, 737–746
- Howe, K.L. *et al.* (2021) Ensembl 2021. *Nucleic Acids Res.* 49, D884–D891
- Brandies, P. *et al.* (2019) The value of reference genomes in the conservation of threatened species. *Genes (Base)* 10, 846
- Balouz, S. *et al.* (2019) Is it time to change the reference genome? *Genome Biol.* 20, 159
- Valiente-Mullor, C. *et al.* (2021) One is not enough: on the effects of reference genome for the mapping and subsequent analyses of short-reads. *PLoS Comput. Biol.* 17, e1008678
- Llamas, B. *et al.* (2019) A strategy for building and using a human reference pangenome. *F1000Res* 8, 1751
- Mérot, C. *et al.* (2020) A roadmap for understanding the evolutionary significance of structural genomic variation. *Trends Ecol. Evol.* 35, 561–572
- Kardos, M. *et al.* (2016) Genomics advances the study of inbreeding depression in the wild. *Evol. Appl.* 9, 1205–1218
- Dussex, N. *et al.* (2021) Population genomics of the critically endangered kākāpō. *Cell Genomics* 1, 100002
- Leitwein, M. *et al.* (2021) Associative overdominance and negative epistasis shape genome-wide ancestry landscape in supplemented fish populations. *Genes (Base)* 12, 524
- Rogers, J. *et al.* (2019) The comparative genomics and complex population history of *Papio* baboons. *Sci. Adv.* 5, eaau6947
- Flanagan, S.P. *et al.* (2018) Guidelines for planning genomic assessment and monitoring of locally adaptive variation to inform species conservation. *Evol. Appl.* 11, 1035–1052
- Owen, N.R. *et al.* (2019) Global conservation of phylogenetic diversity captures more than just functional diversity. *Nat. Commun.* 10, 859