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Trans-resveratrol metabolism by human faecal microbiota

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Resveratrol has been associated with promoting human health due to antioxidant and anti-inflammatory effects. Inter-individual differences in human metabolism of *trans*-resveratrol exist, and three different metabolites are produced by the gut microbiota, i.e. dihydroresveratrol, 3,4' -dihydroxy-*trans*-stilbene and lunularin. However, little is known about bacterial species involved. Until recently, only two dihydroresveratrol producers had been reported: *Eggerthella lenta* ATCC 43055 and *Bacteroides uniformis* ATCC 8492. While the resveratrol metabolising activity of *E. lenta* ATCC 43055 was confirmed under the conditions used in our laboratory, *B. uniformis* ATCC 8492 could not be affirmed as dihydroresveratrol producer. Furthermore, three other faecal *E. lenta* strains did not convert *trans*-resveratrol. The ability to metabolise *trans*-resveratrol therefore appears to be strain dependent. Additionally, *Slackia equolifaciens* DSM 24851 and *Adlercreutzia equolifaciens* DSM 19450 were identified as dihydroresveratrol producers. In the present study, *Escherichia coli* C3a, *Ruminococcus obeum* DSM 25238 and *Citrobacter freundii* DSM 30039 produced another metabolite of *trans*-resveratrol, i.e. acetyl-resveratrol. In order to investigate the *trans*-resveratrol metabolism in more depth and to identify and isolate additional *trans*-resveratrol metabolising bacterial strains, human faeces was cultivated in brain heart infusion broth under anaerobic conditions at 37°C and subcultured daily into fresh medium for up to 168 h in an effort to reduce the microbial complexity. Resveratrol conversion was monitored by HPLC-DAD. Furthermore, 16 S rDNA-based metagenomic analyses were performed. Subculturing results showed a successive loss of 3,4'-dihydroxy-*trans*-stilbene and lunularin. Bacterial strains were isolated on different media and tested for *trans*-resveratrol metabolism in pure cultures.

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"Tutti fruiti" – fruit and other whole plant foods appear to modulate the human gut microbiome, evidence from *in vitro* and *in vivo* studies.

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Fruit and other whole plant foods have long been considered the base of healthy eating pyramids. Epidemiological studies show that adherence to diets rich in fruit, vegetables and whole grain cereals, and low in red/processed meat are protective against chronic diseases like cardiovascular disease, diabetes, cancer and neurodegeneration. Many of these foods also modulate the human gut microbiota, mediating changes both in microbiome metabolic output (especially quantities and profiles of short chain fatty acids, profiles of deconjugated and secondary bile acids, and small phenolic derivatives of plant polyphenols) and may also modify the relative abundance of important groups of gut bacteria within the gut microbiota. Here we present in vitro data showing that fruits, including apples, raspberries and strawberries can modulate both the composition and metabolic output of the human gut microbiota. Further we present data from our recent human intervention studies confirming that whole grain oats can both reduce circulating cholesterol levels and increase faecal bifidobacteria and lactobacilli. We have also confirmed that increased dietary fruit and vegetables, both flavonoid rich and flavonoid poor, can reduce risk factors of CVD and modulate microbiome composition, as measured by 16s rRNA targeted probes, and metabolic output using metabolomics to track changes in metabolites of both dietary and endogenous origin. Such observations lay the basis for considering whole plant food modulation of the gut microbiome a key ingredient in their ability to protect against chronic, age associated, disease and provides the scientific basis for rational functional food design.

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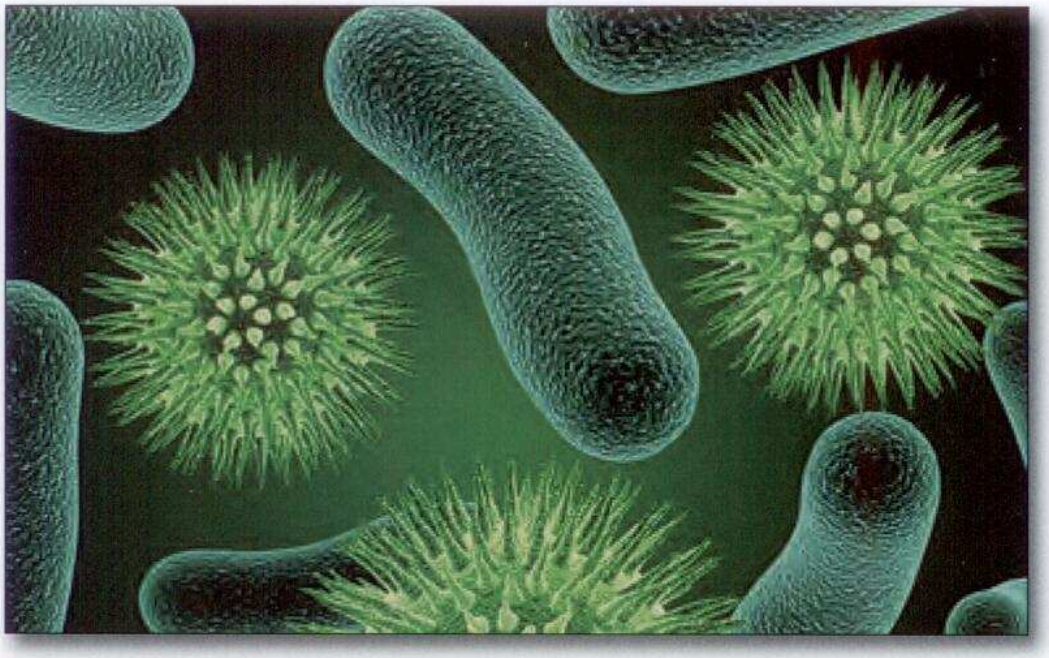

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