Targeted Project / AY 2026 -2027

Retracing the evolution and host adaptation of the human gut microbiome

Project Reference: TRG-VET-AA26

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Main BBSRC strategic theme: Understanding the rules of life

Secondary BBSRC strategic theme: Bioscience for an integrated understanding of health

Project outline:

The human gut microbiome is comprised of a diverse community of microbial species known to contribute to many aspects of human health and disease, including colorectal cancer, inflammatory bowel disease, metabolic diseases, and even mental illness. Therefore, new therapies are being developed to promote the intestinal colonization and engraftment of gut species deemed beneficial to health. However, the ecological rules and biological mechanisms required by bacteria to colonize the intestinal tract remain largely unknown, which has hampered the success of approaches aimed at modulating the composition of the host microbiome for improved health. Research into the identities and functions of the gut microbiome is currently limited due to difficulties in culturing thousands of gut bacterial species under laboratory conditions. However, using large-scale metagenomic techniques, our lab in collaboration with the European Bioinformatics Institute (EMBL-EBI) has assembled >400,000 microbial genomes from various environments and hosts, including the human gut, skin, oral cavity, mouse gut, bovine gut, soil and marine environments. These datasets now provide a unique opportunity to identify host-specific features of the microbiome and better understand the ecological and evolutionary principles that govern the assemblage and structure of the human intestinal microbiome.

This project aims to improve our understanding of the relationship and co-evolution between hosts and their microbiomes to discover biological features required for human colonization and adaptation. In turn this will open newfound opportunities to develop targeted microbiome-based therapeutics to promote the successful intestinal engraftment of bacterial species beneficial to health. The project will be structured around three main aims:

1. Identify host-specific genomic signatures of the human gut microbiome

A comprehensive analysis of available genomes and metagenomes from 13 environments and hosts (including human gut, skin, oral cavity, mouse gut, bovine gut, soil and marine environments) will first be performed. Bioinformatics approaches combining metagenomics, machine learning, ecological modelling and metabolic prediction will be used to infer host-associated taxonomic and functional signatures at a community level. This will reveal combinations of species and functions that are either host-specific or host-generalists.

2. Track the evolutionary history and adaptation of human gut species
A genome-wide analysis will be further undertaken specifically on the most prevalent and abundant human gut species, compared with those with varying degrees of host tropism. Pan-genome patterns and nucleotide-level polymorphisms will be investigated between strains to identify mutational hotspots and genes under positive or negative selection. Functional prediction of candidate genes and mutations will be performed to generate testable hypothesis.

3. Gain new mechanistic insights into the biological features essential for human gut colonization
Biological insights from aims 1 and 2 will be tested experimentally in collaboration with Dr Virginia Pedicord (Department of Medicine). The student will learn and apply diverse experimental techniques in immunology and molecular biology, including in vitro culturing, organoids and animal models. This may involve for instance, comparing the metabolic capabilities of candidate bacterial species with different host specificities; assessing bacterial adhesion to human intestinal epithelial cells; and comparing microbial colonization success in humanized (i.e., with human faecal microbiota) versus wildtype mice.