(Bicentenary) Influence of gut microbial communities on human health and disease
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Details

Human microbiomes are composed of large amounts of bacterial species and are increasingly recognised to play an essential role to health. Gut microbiota species interact with each other and the host, producing a diverse range of metabolites thereby manipulating and redistributing energy to provide essential functionalities to the human host. Advances in metagenome sequencing and omics analyses have linked gut microbiota with lifestyle, diet, environment, and diseases like cancer, liver cirrhosis, obesity and inflammatory bowel disease. Understanding the mechanisms underlying microbiome composition and function is essential for the development of personalised microbiome-based therapies.

Genome-scale metabolic models (GEMs) are a powerful tool to predict the production of metabolic compounds by various species. They enable prediction of how production rates are affected by changes in environmental conditions, nutrient availability and interactions with other species. Recent advances make GEMs increasingly suited to study communities of multiple organisms. Bacterial abundance data can be derived from meta-genomic experiments and integrated with GEMs to replicate different conditions. Then Flux Balance Analysis (FBA) can be used to predict the flow of metabolites through these metabolic networks, and the metabolic exchange score (MES) enables quantification of metabolic exchanges between species.

In this project, we aim to exploit the wealth of available meta-genomic and metabolic modelling resources to predict interventions that promote a healthy microbiota and reduce resilience of dysbiotic microbiota in patients. The first objective will be to characterise differences between healthy microbiomes and those of patients affected by different diseases. There is strong variability between ‘healthy’ microbiomes depending on a multitude of spatial and temporal factors such as diet, age, physical activity, etc, making it challenging to identify alterations specifically related to disease. We will therefore extend traditional abundance-based analyses by applying network theory methods. We will implement such methodologies to identify not only conserved relationships between bacterial species across healthy microbiomes, but also relationships between network alterations and different disease states.

Then community based GEMs of diseased microbiomes will be reconstructed using the above mentioned resources. FBA simulations will be carried out to gain a mechanistic understanding by analysing how nutrient competition and cooperation by cross-feeding interactions contribute to a healthy phenotype, and by identifying events that trigger a transition to disease. We will be exploiting public metagenomic data as well as data generated by the Coyte (co-supervisor) and Soons labs (external collaborator, University Hospital RWTH Aachen). For example, using metagenomic and meta-transcriptomic data recently generated by the Coyte lab, we will explore whether and how the antibody Immunoglobulin A – which directly binds bacteria within the gut – alters the metabolic interactions occurring between specific microbes in the gut microbiomes of mouse pups and human infants.

The student will receive training in a range of computational biology techniques including metagenome analysis, omics data analysis, network biology, genome-scale metabolic modelling, Python and R programming. We anticipate that the project will result in several publications covering healthy/disease network analysis, genome-scale metabolic modelling and mechanistic understanding of species interactions leading to therapeutic interventions.

Eligibility

Applicants must have obtained or be about to obtain a minimum Upper Second class UK honours degree, or the equivalent qualifications gained outside the UK, in biology, computer science, mathematics or a related subject. Research experience in bioinformatics is desirable.

Before you Apply

Applicants must make direct contact with preferred supervisors before applying. It is your responsibility to make arrangements to meet with potential supervisors, prior to submitting a formal online application.

How to Apply

To be considered for this project you MUST submit a formal online application form – on the application form you must select **FBMH Bicentenary PhD Programme - Full-time.** If you select the incorrect programme your application cannot be considered. Full details on how to apply can be found on the Bicentenary Website

Your application form **must** be accompanied by a number of supporting documents by the advertised deadlines. Without all the required documents submitted at the time of application, your application will not be processed and we cannot accept responsibility for late or missed deadlines. Incomplete applications will not be considered. If you have any queries regarding making an application, please contact our admissions team.

Equality, Diversity and Inclusion

Equality, diversity and inclusion is fundamental to the success of The University of Manchester, and is at the heart of all of our activities. The full Equality, diversity and inclusion statement can be found on the website.

Funding Notes

Studentship funding is for 4 years and covers tuition fees and an annual stipend. This does not include any costs associated with relocation.