Identifying Disease-Associated Microorganisms of a Microbiome

HUDSON INSTITUTE OF MEDICAL RESEARCH

Researchers at the Hudson Institute of Medical Research have developed a new culture-based metagenomics approach enabling high resolution and elimination of human DNA contamination

Gastrointestinal microbiota plays significant roles in health and disease

Microbiota in the gastrointestinal tract can drive disease or be affected in a way that results in deleterious effects to the host. Inflammatory Bowel Disease (IBD), which includes Crohn's Disease and Ulcerative Colitis, involves aberrant immune responses to environmental conditions, which includes commensal microbiota of the GIT. IBD affects 1 in 250 people in Australia; patients experience severe impairments in quality of life, education, and employment. Current treatments require long-term immune suppression, which carries variable efficacy and cancer risks.

Manipulation of the GIT microbiota through faecal microbial transplant (FMT) is emerging as a potential treatment for IBD. However, it is costly, difficult to ensure similar efficacy across patient pools, and may carry disease risks. These limitations highlight the great clinical potential of identifying specific, causative bacteria to formulate more precise treatment methods or biomarkers for disease.

Current metagenomics analyses of microbiota are limited by low resolution and human DNA contamination

Typically, metagenomics analysis is performed using 16S rRNA ribosomal profiling or whole genome shotgun metagenomics sequencing. 16S rRNA sequencing only amplify bacterial specific rRNA genes, but cannot distinguish between genetically similar organisms such as pathogenic and commensal E. coli species. Whole genome shotgun sequencing is capable of analysing all DNA within a sample, but results in significant, unwanted sequencing of human and other host DNA, particularly with specific sample types such as biopsies.

Unique discovery method

Our team have previously developed novel methods for culturing human GIT bacteria from faecal samples. Building upon these technical advances, our project team have developed new methods to culture microbiota from biopsy samples to enable high-resolution metagenomics sequencing with minimal human DNA contamination. This method has high potential in providing significant commercial and R&D value in assisting candidate discovery and clinical screening. Our novel approach involves culturing biopsies on broad-spectrum YCFA agar, which allows for microbiota growth, and subsequent extraction and metagenomic sequencing of human DNA-depleted samples. Our combination of culturing methods with metagenomic sequencing allows for the generation of adequate total raw read counts while eliminating eukaryotic DNA contamination. The project team validated this method in a study with 70 paediatric patients, and were able to identify 2,487 distinct isolates from gastrointestinal biopsies.

IP position

PCT Filed (WO2021163758), currently at National Stage.

Countries filed: AU, EP, US

Key steps

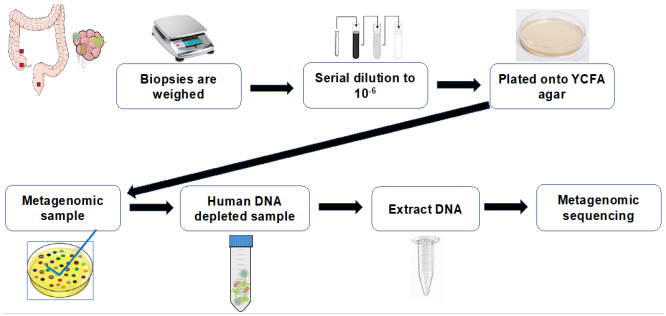

Figure 1. Schematic representation of methods used to culture from mucosal biopsy samples to obtain a eukaryotic DNA-depleted metagenomics sample for sequencing

Project team

This project is led by the combined research and clinical expertise of A/Prof Samuel Forster of the Hudson Institute of Medical Research, and Dr. Edward Giles of the Monash Children's Hospital.

A/Prof Forster leads the Microbiota and Systems Biology Laboratory within the Centre of Innate Immunity and Infectious Diseases. A/Prof Forster works to understand the role of gastrointestinal microbiota and identify ways to modify these microbial communities to improve human health. A/Prof Forster is a leading expert in this field, and his discoveries have been featured in prestigious journals including Nature, Nature Microbiology, and Nature Immunology.

Dr. Giles is a consultant gastroenterologist at the Monash Children's Hospital and a world-leading expert in paediatric Inflammatory Bowel Disorder. Dr. Giles is also a research fellow at the Hudson Institute, and is the current President of the Australian Society of Paediatric Gastroenterology.

Dr. Gemma D'Adamo completed her PhD under the supervision of A/Prof Forster and Dr. Giles in the Microbiota and Systems Biology Laboratory. She is a co-inventor of this method.

Contact us

e: commercialisation@hudson.org.au
t: +61 3 8572 2555
w: https://hudson.org.au/commercialisation/