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A Study of the Intestinal Microbiota in Health and Disease

A thesis presented in partial fulfilment of the requirements for the degree of

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The intestinal microbiota is a massive and complex community, essential to the human host for good health and well-being. However, this population has been associated with gastrointestinal disease, and remains poorly understood. The aim of this study was to develop and validate DNA-based assays for the intestinal microbiota and to apply these methodologies to faecal samples collected from healthy volunteers and patients with gastrointestinal disease. Over 250 faecal samples were analysed using temporal temperature gradient gel electrophoresis (TTGE) and real time PCR. Validated assays had high sensitivity and reproducibility. Healthy individuals displayed a high level of temporal stability during short term studies (≤ 6 weeks) and long term studies (1-4 years). Analysis of faecal samples provided by identical and fraternal twins demonstrated an influence of host genetics over the composition of the predominant bacteria in children. Two intervention studies, bowel lavage and the Atkins' diet, were carried out to monitor the impact of environmental change on the population's stability in healthy volunteers. Following bowel lavage, microbial populations rapidly recovered to control densities, however the stability of the population was disturbed. Introduction of the Atkins' diet, led to a significant change in the composition of the microbial population. A preliminary study of the intestinal microbiota in disease groups was undertaken. Significant differences were detected between inflammatory bowel disease groups and controls. Cluster analysis in these patients indicated a potential association between the composition of the predominant bacterial population and disease localisation. The studies reported here demonstrate that the faecal microbiota in healthy individuals is a highly stable population under the influence of both host genetics and environmental variables, however the population present in patients with inflammatory bowel disease exhibits differences compared to healthy controls.
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