The influence of habitual dietary intake on the responsiveness of the gut microbiota to a dietary intervention

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

of

Doctor of Philosophy

in

Nutritional Science

at Massey University, Manawatu, New Zealand

Genelle Rose Healey

2017

Abstract

Preliminary evidence suggests that inter-individual variability in gut microbiota response to a dietary intervention is influenced by baseline gut microbiota composition. Differing habitual dietary intakes lead to distinctions in baseline gut microbiota composition making it plausible that habitual dietary intake may also influence gut microbiota response. Prior to conducting this research no studies had been undertaken to determine whether habitual dietary intake has an impact on gut microbiota responsiveness. Therefore, the aim of this research was to investigate the influence habitual dietary intake has on gut microbiota response to a dietary intervention.

Initially, secondary data analysis was conducted to determine whether there was any support for the hypothesis that individuals with differing habitual dietary intakes would have gut microbiota that respond in a distinctive manner to a dietary intervention. The secondary data analysis results demonstrated that dietary groups rich in dietary fibre had the greatest impact on gut microbiota responsiveness. An *in vitro* three-stage colonic model system study was conducted to determine whether media with differing fermentable carbohydrate (i.e. dietary fibre) contents influenced gut microbiota response to an inulin-type fructan prebiotic. It was demonstrated that differing prebiotic driven changes in organic acids and bacterial taxa occurred between the low (LFC) and high fermentable carbohydrate (HFC) content media. The results of the secondary data analysis and *in vitro* study provided evidence to suggest that a human intervention study was warranted. A randomised, double-blind, placebo-controlled, cross-over, human intervention study in 34 healthy participants was undertaken to determine whether habitual dietary fibre intake influenced gut microbiota response to an inulin-type fructan prebiotic. The results of the human intervention study demonstrated that the low habitual

dietary fibre (LDF) group harboured gut microbiota that were less responsive to the inulin-type fructan prebiotic than the high habitual dietary fibre (HDF) group.

Future studies which aim to modulate the gut microbiota via dietary change or to determine the prebiotic potential of a novel fermentable substrate should take habitual dietary fibre intakes into consideration when recruiting participants or analysing the data. This will help reduce the confounding influence of inter-individual variability in gut microbiota responsiveness and ensure the true efficacy of a dietary intervention is demonstrated.

Acknowledgements

I would like to take the opportunity to thank the following individuals and organisations who contributed to making the completion of this thesis possible:

- My PhD supervisors, Professor Jane Coad, Associate Professor Rinki Murphy, Dr Louise Brough and Dr Chrissie Butts for the greatly appreciated guidance and continued support provided throughout my PhD;
- Professor Kevin Whelan for providing expertise relating to the fructan food frequency questionnaire and feedback on the study protocol and human intervention study manuscripts;
- Dr Paul Blatchford and Dr Doug Rosendale for providing microbiological support and expertise, particularly during the *in vitro* three-stage colonic model system study. Dr Paul Blatchford also provided much appreciated bioinformatic support during my PhD;
- Halina Stoklosinski for undertaking all the organic acid analysis;
- Duncan Hedderley for his statistical expertise and support;
- Anne Broomfield for her much appreciated help during the human intervention study and Ying Jin for being available to take blood samples from my study participants;
- My husband David, who constantly helped, supported and encouraged me throughout my PhD. I am truly grateful for his love and belief in me.
- My family, friends and colleagues at The New Zealand institute for Plant & Food Research Limited who were always there to support me and provide advice and encouragement when needed;

- The validation and human intervention study participants for their time and commitment;
- Massey University and The New Zealand institute for Plant & Food Research Limited for providing financial and resource support throughout my PhD;
- Ministry of Business, Innovation and Employment for providing financial support to The New Zealand institute for Plant & Food Research Limited which was used in part to fund my PhD research.

Table of Contents

List of Appendices

List of Tables

List of Figures

List of Abbreviations

AA	African Americans
AC	African children
AMER	Typical American style dietary pattern
ANOVA	Analysis of variance
BMI	Body mass index
BodPod	Air displacement plethysmography
CD	Crohn's disease
CHO	Carbohydrate
CNAQ	Comprehensive nutrition assessment questionnaire
CRON	Plant-rich, calorie-restricted diet with optimal nutrient composition
D	Donor
DFI-FFQ	Dietary fibre intake short food frequency questionnaire
DNA	Deoxyribonucleic acid
EC	European children
EI:BMR	Energy intake: basal metabolic rate
FFQ	Food frequency questionnaire
FI-FFQ	Fructan intake food frequency questionnaire
FISH	Fluorescence *in situ* hybridisation
FMP	Fermented milk product
FODMAP	Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols
GC	Gas chromatography
GI	Gastrointestinal
GLP-1	Glucagon-like peptide-1
HFC	High fermentable carbohydrate medium
HDF	High habitual dietary fibre
HMP	Human Microbiome Project
HNRU	Human Nutrition Research Unit
IBD	Inflammatory bowel disease
IBS	Irritable bowel syndrome
IP1	Intervention phase 1

IP2	Intervention phase 2
LFC	Low fermentable carbohydrate medium
LDF	Low habitual dietary fibre
LPS	Lipopolysaccharide
MetaHIT	Metagenomics of the Human Intestinal Tract
MGC	Microbial gene count
MoH	Ministry of Health
NA	Native Africans
NCD	Non-communicable disease
NS	Not specified
NZ	New Zealand
OTU	Operational taxonomic units
PANDASeq	Paired-end assembler for DNA sequencing
PCR	Polymerase chain reaction
PICRUSt	Phylogenetic investigation of communities by reconstruction of unobserved states
PS	Prudent style
PYY	Peptide YY
QIIME	Quantitative Insights Into Microbial Ecology
qPCR	Quantitative real-time polymerase chain reaction
SCFA	Short-chain fatty acid
SD	Standard deviation
T2DM	Type 2 diabetes mellitus
TE	Total energy
UC	Ulcerative colitis
VAS	Visual analogue scales
WS	Western style