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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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ABSTRACT

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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TABLE OF CONTENTS

ABSTRACT..... I

ACKNOWLEDGEMENTS..... II

TABLE OF CONTENTS IV

LIST OF FIGURES X

LIST OF TABLES XIII

CHAPTER 1: INTRODUCTION 1

1.1 THE INTESTINAL MICROBIOTA..... 1

1.1.1 Historical Background..... 1

1.1.2 The Resident microbial Population 1

1.1.3 The Intestinal Habitat 2

1.1.4 Distribution within the Gastrointestinal Tract 3

1.1.5 Colonisation of the Large Intestine 7

1.1.6 Characteristics of the Faecal Microbiota 8

1.1.7 The Role of the Microbiota in Host Physiology..... 9

1.1.8 Fermentation by the Intestinal Microbiota 10

1.1.9 Dynamics of Methanogen and Sulfate Reducing Bacteria Populations 12

1.2 THE IMMUNE SYSTEM AND THE INTESTINAL MICROBIOTA 15

1.2.1 Innate Immunity 15

1.2.1.1 Toll-Like Receptors..... 16

1.2.2 Aquired Immunity 17

1.2.2.1 Gut Associated Lymphoid Tissue 17

1.2.2.2 IgA..... 19

1.2.3 Immune Tolerance to the Intestinal Microbiota 20

1.3 THE INTESTINAL MICROBIOTA AND DISEASE 22

1.4 METHODS FOR STUDYING THE MICROBIOTA..... 25

1.4.1 Temporal Temperature Gradient Gel Electrophoresis..... 26

1.4.2 Real Time Polymerase Chain Reaction..... 29

1.5 AIMS OF THE THESIS..... 31

CHAPTER 2: MATERIALS AND METHODS..... 33

2.1. Ethical Approval 33

2.2 Microbial DNA FROM FAECAL SAMPLES..... 33

2.2.2 Collection and Homogenisation of Faecal Samples 33

2.2.3 Faecal DNA Extractions..... 33

2.3 PCR-TTGE 34

2.3.1 Amplification of Bacterial 16S ribosomal RNA Genes 34

2.3.2 TTGE Conditons 35

2.3.3 Staining TTGE Gels 35

2.3.4 TTGE Quality Control	35
2.3.5 TTGE Gel Band Purification.....	36
2.3.6 TTGE Profile Analysis.....	36
2.4 REAL TIME PCR.....	37
2.4.1 Reagents and Conditions.....	37
2.4.2 Quantitation Using External Standards	38
2.4.3 Quality Control.....	39
2.4.4 Statistical Anlysis	39
2.5 SEQUENCING.....	39
CHAPTER 3: OPTIMISATION AND VALIDATION OF METHODS	40
3.1 ABSTRACT.....	40
3.2 INTRODUCTION.....	41
3.3 MATERIALS AND METHODS.....	44
3.3.1 Volunteers/DNA Extractions/PCR-TTGE/Real Time PCR/Sequencing.....	44
3.3.2 Gel Staining Methods.....	44
3.3.2.1 Ethidium Bromide Staining.....	44
3.3.2.2 Silver Staining Method 1 (Cairns, 1994).....	44
3.3.2.3 Silver Staining Method 2.....	44
3.3.2.4 Silver Staining Method 3.....	45
3.3.3 T7 Endonuclease I Digestion	45
3.3.4 Mung Bean Nuclease Digestion	45
3.3.5 Re-conditioning PCR	45
3.3.6 Elongation PCR.....	46
3.3.7 BACTERIAL DNA SAMPLES	46
3.3.8 Preparation of External Standards for Real Time PCR	46
3.4 RESULTS	48
3.4.1 Optimisation of DNA Extractions from Faecal Samples	48
3.4.2 Optimisation and Application of TTGE	49
3.4.2.1 Effect of Template Amount on TTGE Profiles	49
3.4.2.2 Specificity of PCR-TTGE Assay.....	50
3.4.2.3 Reproducibility of the PCR-TTGE Assay	51
3.4.2.4 Sensitivity of the PCR-TTGE Assay.....	52
3.4.2.5 TTGE Gel Staining.....	53
3.4.2.6 Identification of TTGE Gel Artefacts.....	54
3.4.2.7 Construction of a Bacterial Ladder.....	56
3.4.3 Optimisation of Real Time PCR Assays	57
3.4.3.1 Primers	57
3.4.3.2 Specificity of Primer Sets.....	59
3.4.3.3 Real Time PCR Product Stability.....	60
3.4.3.4 Preparation of External Standards	61
3.4.3.5 Amplification Efficiencies of External Standards and Faecal Genomic DNA	61
3.4.3.6 Quantitation of Template DNA	63
3.4.3.7 Quantitation Parameters	63
3.5 DISCUSSION	67
CHAPTER 4: LONG AND SHORT TERM STABILITY OF THE FAECAL MICROBIOTA	72
4.1 ABSTRACT.....	72
4.2 INTRODUCTION.....	73

4.3 METHODS	74
4.3.1 Volunteers	74
4.3.1.1 Volunteers for PCR-TTGE Study	74
4.3.1.2 Volunteers for Real Time PCR Study	74
4.3.2 Breath Methane Measurements	74
4.3.3 Faecal DNA Extraction/PCR-TTGE/Real Time PCR/Sequencing	74
4.4 RESULTS	75
4.4.1 Application of PCR-TTGE to Assess Variability in the Faecal Microbiota between Different Individuals	75
4.4.2 Application of PCR-TTGE to Assess Temporal Variation in the Bacterial Population	76
4.4.2.1 Short Term Stability of the Bacterial Population's Composition	76
4.4.2.2 Long Term Stability of the Bacterial Population's Composition	77
4.4.3 Application of Real Time PCR to Assess Carriage and Temporal Variation of Methanogen and Sulfate Reducing Bacteria Populations	78
4.4.3.1 Carriage Rates and Densities of Methanogens and Sulfate Reducing Bacteria in New Zealand Adults	78
4.4.3.2 Comparison of Real Time PCR and Breath Methane Testing	79
4.4.4 Application of Real Time PCR to Assess Temporal Variation in Bacteria Populations	81
4.4.4.1 Short Term Variability in the Densities of Bacteria	81
4.4.4.2 Long Term Variability in the Densities of Bacteria	81
4.4.5 Temporal Stability of Methanogen and Sulfate Reducing Bacteria Populations	81
4.4.5.1 Short Term Stability of Methanogen Populations	82
4.4.5.2 Long Term Stability of Methanogen Populations	82
4.4.5.3 Short Term Stability of Sulfate Reducing Bacteria Populations	83
4.4.5.4 Long Term Stability of Sulfate Reducing Bacteria Populations	83
4.5 DISCUSSION	85
 CHAPTER 5: INFLUENCE OF HOST GENETICS OVER THE COMPOSITION OF THE FAECAL MICROBIOTA	 89
5.1 ABSTRACT	89
5.2 INTRODUCTION	90
5.3 MATERIALS AND METHODS	92
5.3.1 Volunteers	92
5.3.2 Twin Zygosity	92
5.3.3 Faecal DNA Extraction/PCR-TTGE/Real time PCR/Sequencing	92
5.4 RESULTS	93
5.4.1 Comparison of the preDominant Bacterial Population in Related and Unrelated Individuals	93
5.4.2 Concordance Rates for the Carriage of Methanogens and Sulfate Reducing Bacteria in Identical and Fraternal Twins	98
5.5 DISCUSSION	101
 CHAPTER 6: RECONSTITUTION AND STABILITY OF THE FAECAL MICROBIOTA AFTER INTESTINAL LAVAGE	 107
6.1 ABSTRACT	107
6.2 INTRODUCTION	108
6.3 METHODS	109
6.3.1 Volunteers	109
6.3.2 Intestinal Lavage	109
6.3.3 Faecal DNA Extraction/PCR-TTGE/Real time PCR/Sequencing	109

6.4 RESULTS	110
6.4.1 Quantitation of Bacterial Densities in Faeces and Faecal Lavage Fluid Samples	110
6.4.2 Analysis of Bacterial TTGE Profiles Before and After Lavage	111
6.4.2.1 Band Comparisons between Samples Collected from the Same Individual	111
6.4.2.2 The Effect of the Frequency of Bowel Movements on TTGE Profile Variability	112
6.4.2.3 Sequencing Variable TTGE Bands in One Healthy Volunteer	113
6.4.2.4 Effect of Lavage on Predominant Bacterial Populations in the Seven Days Post Lavage ..	114
6.4.2.5 Effect of Lavage on Community Richness	116
6.4.3 Impact of Lavage on Population Densities	117
6.4.3.1 Bacterial Densities in Control and Post Lavage Samples	117
6.4.3.2 Methanogen Densities in Control and Post Lavage Samples	118
6.4.3.3 Sulfate Reducing Bacteria Densities in Control and Post Lavage Samples	119
6.5 DISCUSSION	121
 CHAPTER 7: COMPOSITION AND STABILITY OF THE FAECAL MICROBIOTA AFTER DIETARY CHANGE	 124
7.1 ABSTRACT	124
7.2 INTRODUCTION	125
7.3 METHODS	127
7.3.1 Volunteers and Sample Collection	127
7.3.2 The Atkins' Diet	127
7.3.3 Faecal DNA Extraction/PCR-TTGE/Real time PCR/Sequencing	127
7.4 RESULTS	128
7.4.1 volunteer Drop-out and Compliance	128
7.4.2 The Effect of the Atkins' Diet on Blood and Weight Measurements	128
7.4.3 Bacterial TTGE Profiles during Consumption of a Western Diet and Consumption of the Atkins' Diet	131
7.4.4 Analysis of TTGE Profiles with Sorenson's Similarity Co-efficient	132
7.4.5 Analysis of TTGE Profiles with the Shannon's Indices	135
7.4.6 Bacterial Densities in Faecal Samples Collected while Consuming a Western Diet and while Consuming the Atkins Diet	135
7.4.7 Methanogen Densities in Faecal Samples Collected while Consuming a Western Diet and while Consuming the Atkins Diet	135
7.4.8 Sulfate Reducing Bacteria Densities in Faecal Samples Collected while Consuming a Western Diet and while Consuming the Atkins Diet	136
7.5 DISCUSSION	138
 CHAPTER 8: THE FAECAL MICROBIOTA IN INFLAMMATORY BOWEL DISEASE	 141
8.1 ABSTRACT	141
8.2 INTRODUCTION	142
8.3 MATERIALS AND METHODS	144
8.3.1 Volunteers	144
8.3.2 Faecal DNA Extraction/PCR-TTGE/Real time PCR/Sequencing	144
8.3.3 Cluster Analysis and Statistics	144
8.4 RESULTS	145
8.4.1 Comparisons of preDominant Bacterial Population Similarities Amongst Different Patient Groups	145
8.4.2 Clustering Analysis of Similarity Data from Inflammatory Bowel Disease Patients	146
8.4.3 Community Richness Amongst Inflammatory Bowel Disease Patients and Controls	150

8.4.4 Carriage Rates of Methanogens and Sulfate Reducing Bacteria	150
8.4.5 Population Densities of Bacteria, Methanogens and Sulfate Reducing Bacteria	152
8.5 DISCUSSION	154
CHAPTER 9: CONCLUDING COMMENTS	161
APPENDIX A: SORENSON'S SIMILARITY CO-EFFICIENTS.....	167
A.1 Unrelated Volunteers from Chapter 4	167
A.2 Short Term Stability Data from Chapter 4	167
A.3 Long Term Stability Data from Chapter 4.....	168
A.4 Twins and Unrelated Controls from Chapter 5.....	168
A.5 Intestinal Lavage Data from Chapter 6.....	169
A.6 Western Diet Data from Chapter 6	170
A.7 Atkins' Diet Data from Chapter 6	170
A.8 Diarrhoea Predominant IBS Data from Chapter 8.....	171
A.9 Constipation Predominant IBS Data from Chapter 8	171
A.10 Mixed IBS Data from Chapter 9	172
A.11 Diverticular Disease Data from Chapter 9.....	172
A.12 Ulcerative Colitis Data from Chapter 9.....	173
A.13 Crohn's Disease Data from Chapter 9.....	173
A.14 Controls	174
APPENDIX B: SHANNON'S INDICES.....	175
B.1 Twins and Unrelated Controls Data from Chapter 5	175
B.2 Intestinal Lavage Volunteers Data from Chapter 6	179
B.3 Western Diet Data from Chapter 7	182
B.4 Atkins' Diet Data from Chapter 7	183
B.5 Disease Group Patients Data from Chapter 8	184
APPENDIX C: BACTERIAL DENSITIES.....	188
C.1 Carriage Rate Data for 12 Healthy Volunteers in Chapter 4	188
C.2 Short Term Stability Data from Chapter 4.....	188
C.3 Long Term Stability Data from Chapter 4.....	189
C.4 Intestinal Lavage Data from Chapter 6.....	189
C.4 Western Diet Data from Chapter 7	191
C.5 Atkins' Diet Data from Chapter 7	191
C.6 Disease Groups Data from Chapter 8	192
APPENDIX D: METHANOGEN DENSITY	194
D.1 Carriage Rates Data for 12 Volunteers in Chapter 4	194
D.2 Short Term Stability Data for Chapter 4	194
D.3 Long Term Stability Data for Chapter 4.....	194
D.4 Intestinal Lavage Data for Chapter 6.....	195
D.5 Western Diet Data for Chapter 7	195
D.6 Atkins' Diet Data for Chapter 7	195
D.7 Disease Groups Data for Chapter 8	196
APPENDIX E: SULFATE REDUCING BACTERIA DENSITIES	197
E.1 Carriage Rates Data for 12 Volunteers in Chapter 4.....	197
E.2 Short Term Stability Data for Chapter 4.....	197
E.3 Long Term Stability Data for Chapter 4	197
E.4 Intestinal Lavage Data for Chapter 6.....	198
E.5 Western Diet Data for Chapter 7.....	198
E.6 Atkins' Diet Data for Chapter 7.....	199
E.7 Disease Groups Data for Chapter 8.....	199

APPENDIX F: SEQUENCING DATA FOR *AKKERMANSIA MUCINIPHILA* 200
 F.1 Identity of Bacteria TTGE Bands from Chapter 3 200
 F.2 Bacteria plasmid clone from Chapter 3 200
 F.3 Intestinal Lavage Chapter 6, Volunteer 4 201
 F.4 Intestinal Lavage Chapter 6, Volunteer 7 201
 F.5 Intestinal Lavage Chapter 6, Volunteer 8 202
 F.6 Western Diet Chapter 7, Volunteer 6 203

APPENDIX G: LOW CARBOHYDRATE MEALS 205

APPENDIX H: PRECISION CALCULATIONS FOR REAL TIME PCR ASSAYS 206

APPENDIX I: PUBLICATIONS ARISING FROM THIS THESIS 208

REFERENCES 209

LIST OF FIGURES

Figure 1.1	Gastrointestinal anatomy and intestinal cross section	3
Figure 1.2	Dendritic cells sample luminal antigen directly	19
Figure 1.3	Effect of increasing denaturant on double stranded DNA in TTGE gels	28
Figure 1.4	Increasing fluorescence during real time PCR	30
Figure 3.1	Biochemical pathway for the production of H ₂ S	43
Figure 3.2	Effect of DNA extraction lysis time on TTGE gel profiles	48
Figure 3.3	Effect of DNA template amount of TTGE gel profiles	49
Figure 3.4	Specificity of bacterial 16S rRNA gene primer set	50
Figure 3.5	Identification of TTGE bands by sequencing	51
Figure 3.6	Reproducibility of TTGE gel profiles	52
Figure 3.7	Sensitivity of TTGE	53
Figure 3.8	Different gel staining methods	54
Figure 3.9	Treatment of PCR products to minimise chimeras, heteroduplexes and single stranded DNA in TTGE gel profiles	55
Figure 3.10	Bacterial DNA ladder for TTGE gels	56
Figure 3.11	Specificity of primer sets specific for methanogens and sulfate reducing bacteria	59
Figure 3.12	Comparison of detection methods for non-specific products in real time PCR	60
Figure 3.13	Amplification efficiencies of plasmid and genomic DNA	62
Figure 3.14	Detection limits of real time PCR assays	64
Figure 3.15	Precision of real time PCR assays	66
Figure 4.1	TTGE profiles of unrelated individuals	75
Figure 4.2	Short term intra-individual variability in TTGE profiles	76

Figure 4.3	Long term intra-individual variability in TTGE profiles	77
Figure 5.1	Correlation between children's age and number of TTGE bands	93
Figure 5.2	Correlation between children's age and Shannon's indices	94
Figure 5.3	TTGE gel profiles of identical, fraternal twins, and unrelated pairs	94
Figure 5.4	Box whisker plots of Sorenson's similarity co-efficients for identical twins, fraternal twins, and unrelated pairs	95
Figure 5.5	Correlation between age and Sorenson's similarity co-efficients in fraternal twins	98
Figure 6.1	Comparison of bacterial densities in faecal samples and faecal lavage fluid samples	110
Figure 6.2	Photograph of the bowel following intestinal lavage	111
Figure 6.3	TTGE profiles of samples collected in the lavage study	112
Figure 6.4	Sequencing of band changes in post lavage TTGE profiles	114
Figure 6.5	Trend lines of Sorenson's similarity co-efficients post lavage	115
Figure 6.6	Box whisker plot of Sorenson's similarity co-efficients determined in the lavage study and the normal temporal stability of the population	116
Figure 6.7	Bacterial density before and after intestinal lavage	118
Figure 6.8	Methanogen densities before and after intestinal lavage	119
Figure 6.9	Sulfate reducing bacteria densities before and after intestinal lavage	120
Figure 7.1	Examples of TTGE profiles following introduction of the Atkins' diet	131
Figure 7.2	Sequencing of TTGE band changes in Atkins' diet Volunteer 6	132
Figure 7.3	Box whisker plot of Sorenson's similarity co-efficients during consumption of normal Western diets and introduction of the Atkins' diet	133
Figure 7.4	Sorenson similarity co-efficients with respect to time during consumption of normal Western diets and introduction of the Atkins' diet	134
Figure 7.5	Methanogen densities in Volunteer 2 during consumption of a normal Western diet, and introduction of the Atkins' diet	136
Figure 7.6	Sulfate reducing bacteria densities during consumption of normal Western diets, and introduction of the Atkins' diet	137

Figure 8.1 Box whisker plot of Sorenson's similarity co-efficients determined for inflammatory bowel disease patients, control disease groups, and healthy controls	146
Figure 8.2 Cluster analysis of Crohn's disease patients' TTGE profiles with respect to disease localisation	148
Figure 8.3 Cluster analysis of ulcerative colitis patients' TTGE profiles with respect to disease localisation	149
Figure 8.4 Carriage rates of methanogens and sulfate reducing bacteria amongst different disease groups and healthy controls	152

LIST OF TABLES

Table 1.1 Bacteria commonly isolated from the intestine using culture studies	5
Table 1.2 Uncultivated and novel bacteria isolated from the intestine using molecular methodologies	6
Table 2.1 Bacterial 16S rRNA gene primers for TTGE	34
Table 2.2 Primer sets for real time PCR	38
Table 3.1 Alignment of sulfate reducing bacterial DNA sequences against the primer APSf	57
Table 3.2 Alignment of archaeobacterial DNA sequences against the primer Arch806r	58
Table 4.1 Carriage rates and quantitation of methanogens and sulfate reducing bacteria in healthy New Zealand adults	80
Table 4.2 Short term stability of methanogen populations	82
Table 4.3 Long term stability of methanogen populations	83
Table 4.4 Short term stability of sulfate reducing bacteria populations	83
Table 4.5 Long term stability of sulfate reducing bacterial populations	84
Table 5.1 Similarity, age, diet, gender data for identical twins, fraternal twins, and unrelated control pairs	97
Table 5.2 Sequence data for methanogens and sulfate reducing bacteria isolated from twins	99
Table 5.3 Concordance and discordance for carriage of methanogens and sulfate reducing bacteria	100
Table 6.1 Sorenson's similarity co-efficients from lavage study TTGE gels	115
Table 6.2 Shannon's indices for control and post lavage samples	117
Table 7.1 Blood chemistry and weight before and after the Atkins' diet	130
Table 8.1 Shannon's indices determined from TTGE profiles of different disease groups	150
Table 8.2 Density of methanogens and sulfate reducing bacteria in disease groups	153