Priority Research Programme
Foods for improving gut function and comfort

Are microbes the missing piece of the gut comfort puzzle?

Wayne Young
Senior Scientist, AgResearch
Foods for gut function and comfort

- Complementary feeding for immune protection
- Fibres for sustained energy release

- A2 Milk for gut comfort
- Building immune defence
- Natural milk for allergy management
- Greenshell™ mussels to manage inflamed joints
Irritable Bowel Syndrome is the ideal model for developing future foods with clinical evidence to support claims for healthy people.
Microbiome and gut comfort

- Gut microbiota modulates mechanisms underlying gut comfort;
  - Motility
  - Immune system
  - Barrier function
  - Gut-brain axis
- Food is the obvious choice to fine-tune the microbiome for health conscious consumers

Microbiome and gut comfort

- Altered microbiota associated with perturbed gut function, including irritable bowel syndrome (IBS)

- Changes differ between studies, e.g. Firmicutes, *Faecalibacterium*, *Blautia*, bifidobacteria, methanogens, *Prevotella*

- For food to be effective, we need to know where we are coming from and where we are going

Which bacteria are present?

- To date, most IBS microbiome studies have been based on 16S rRNA gene amplicon sequencing.
- Relatively easy to do.
- Only provides taxonomy (who is there?)
Our whole systems approach to High-Value Nutrition science

**Our biology**
- Organ networks
- Cellular networks
- Molecular networks
- Genetic interaction

**Our environment**
- Where we live
- Cultural backgrounds
- Social networks
- Food choices

Our research focuses on understanding biological processes as complex integrated systems. Nutrition to keep us healthy and well requires an holistic approach.
What are the bacteria doing?

- We want to know what the bacteria are capable of doing
- Sequencing all DNA in the community (the metagenome) provides this insight

Metagenomic sequencing gives insight into what the community is doing
Metagenomic sequencing of COMFORT cohort faecal microbiome

- Faecal microbiome analysed by shotgun metagenome sequencing using Illumina NextSeq 500 paired-end 2x150 bp (APC/Teagasc)
- 112 samples sequenced
  - 41 case-controls
  - 9 IBS constipation (IBS-C)
  - 22 IBS diarrhoea (IBS-D)
  - 10 IBS mixed (IBS-M)
  - 16 functional constipation (FC)
  - 5 functional diarrhoea (FD)
  - 9 not determined
What did we find?
Alpha diversity
(how many different types)

- IBS groups have lower alpha diversity than controls (P=0.05)
Microbiome composition

Genus level

Highly variable

No obvious division immediately apparent between case-controls and IBS subtypes
Gene functions

Level 1

Less variation between subjects
No obvious division apparent between case-controls and IBS subtypes
Are there differences in microbiome composition and function?

- Standard statistical methods show few differences between case-controls and IBS subtypes
- Machine learning methods (e.g. PLS-DA, SVM, random forest) could help to separate groups
Partial least squares discriminant analysis (PLS-DA)

Taxonomy

Gene function

- IBS-C
- IBS-D
- IBS-M
- CONTROL
What are the taxa and gene functions that lead to separation in PLS-DA models?

Genera include *Roseburia*\(^1\), *Streptococcus*, *Prevotella*\(^{1,2}\), *Bifidobacterium*\(^3\)

- Complex carbohydrate fermenters.
- Some generally thought of as “good” bacteria, but appear to be higher in IBS groups

What are the taxa and gene functions that lead to separation in PLS-DA models?

- Functions include those related to carbohydrate and protein metabolism
- Aligns with taxonomy data
How robust is the separation between groups? Support vector machines (SVM)

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How robust is the separation between groups?

Support vector machines (SVM)

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Improved predictive power with gene function
How robust is the separation between groups?

Support vector machines (SVM)

Combined taxonomy and gene function

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Predictive power further improved by combining taxonomy with gene function
Can we classify the undefined samples?

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Time will tell if these predictions are accurate
Conclusions

- Microbiome composition and function appear be different between controls and IBS subtypes, more pronounced with IBS-D
- Add to predictability of existing biomarkers?
- Carbohydrate fermentation appears to play a role
- Some ostensibly “good” bacterial increased in IBS
- What we need to know is “what they are doing”?

→ Clinical and systems approach will de-risk developing new foods with validated gut health benefits that will be highly desirable and sought after by healthy consumers
Research Team and collaborators

Programme Leader/Principal Investigator
- Nicole Roy, AgResearch, Riddet Institute

Principal Investigator, clinical
- Richard Gearry, University of Otago

Associate Investigators, biomarkers
- Metabolites: Karl Fraser, AgResearch
- Microbiota: Wayne Young, AgResearch
- Immune: Oliver Grasser, Malaghan Institute
- Proteins: Janine Cooney, Plant and Food Research

Collaborator
- Sequencing: Paul Cotter, APC/Teagasc