Translating Gut Microbiome Structure to Function: Insights from Dietary Fibre
The meeting so far:

The Ecosystem

Physiology and Life cycle

Health and Disease
Gut Microbiome and Health
Fibre and its benefits

- Bowel cancer
- Inflammatory Bowel diseases
- Irritable bowel syndrome
- Regularity
  - Faecal bulking
  - Water content
- Diarrhoea
- Cardiovascular disease
- Neurodegenerative diseases
Fibre and Gut Health

Fibre – many components

**Short Chain CHO**
Highly fermentable

- **Effects**
  - Laxation - Weak
  - Transit – No effect
  - Microbe - Prebiotic
  - SCFA – Very Rapid
  - Gas - High

**Long Chain CHO**
Highly fermentable

- **Effects**
  - Laxation - Mild
  - Transit – No effect,
  - Microbe – Diversity up
  - SCFA – Rapid
  - Gas - Moderate

**Long Chain, Intermediate Fermentable**

- **Effects**
  - Laxation - Good
  - Transit – Speeds up,
  - Microbe – Diversity up
  - SCFA – Moderate
  - Gas - Moderate

**Long chain slowly fermentable**

- **Effects**
  - Laxation - Good
  - Transit – No effect,
  - Microbe – Diversity up
  - SCFA – low
  - Gas - Medi/high

Adapted from Gibson et al. Internal Med. J. (2013) 43: 1067
Different fermentation products

- Fructo-oligosaccharide → Acetate
- Galacto-oligosaccharide → Lactate
- Resistant starch → Butyrate
- Arabinoxylan → Propionate
- Cellulose → Not fermented
# Resistant starch

<table>
<thead>
<tr>
<th>Type of resistant starch</th>
<th>Source</th>
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</thead>
<tbody>
<tr>
<td>RS1 – physically inaccessible</td>
<td>Whole or partly milled seeds or grains</td>
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<tr>
<td>RS2 – resistant granules</td>
<td>Raw starches (e.g. banana), high amylose starches</td>
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<tr>
<td>RS3 – retrograded</td>
<td>Cooked and cooled rice, potato</td>
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<tr>
<td>RS4 – chemically modified</td>
<td>Food ingredients</td>
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</tbody>
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Butyrate in humans

Inter-individual variation greater than intra-individual variation

A subset of individuals have very low butyrate concentrations

A subset of individuals have very high butyrate concentrations
Butyrate levels are modified by RS

In most instances the faecal butyrate concentration is increased by high RS diets.

In the subset of individuals which have very high faecal butyrate concentrations high RS diets actually decrease butyrate concentrations.
Enhancing fatty acid delivery

Starplus
- Vehicle for short-chain fatty acid delivery to the colon

Patents:
PCT/AU94/00713. Fatty acid delivery system
PCT/AU00/00792. Nasogastric Formulations

Adapted from Gibson et al. Internal Med. J. (2013) 43: 1067
SCFA and gut barrier function

Gut microbes needed for Treg expansion

Atarashi et al. Science (2011) 331:337
Butyrate enhances Treg expansion

A High fibre diet increases Treg abundance in the colonic lamina propria

Butyrate is the strongest inducer

Butyrate acts through HDAC activity

ChIP-seq
Anti- H3Ac

ChIP QPCR

Butyrate also acts through dendritic cells

Bacteria, Butyrate, Tregs and Inflammation

Baas SciBX©2013) 5: 7-9
Adapted from Furusawa e.al. Nature (2013) 504:446-450
Butyrate ameliorates colitis

The Future?

- SCFA and other conditions:
  - IBD
  - IBS
  - Allergies
  - CVD
- Other substrates
- A paradigm for other bioactive metabolites.
Thank you

Dr Trevor Lockett
Research Scientist

t  +61 2 9490 5140
e  trevor.lockett@csiro.au

Acknowledgements

• Prof Koji Hase and his team
• Dr Julie Clarke
• Dr David Topping