Let’s discover a new country
Taking advantage of new technologies
Food for the Host and Microbiota
Diet shapes gut microbiota

Impact of the gut microbiome on nutrients & non-nutrients metabolism, and energy availability.

Colette Shortt & Jean-Michel Antoine
## Impact on Nutrients’ bioavailability

<table>
<thead>
<tr>
<th>Bacteroidetes</th>
<th>Proteins</th>
<th>Fats</th>
<th>CHO's</th>
<th>Energy</th>
<th>Non-nutrients</th>
<th>Waste</th>
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<tbody>
<tr>
<td>Firmicutes</td>
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<tr>
<td>ArchaeBacteria</td>
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</tbody>
</table>
Task Force Activity

- Impact of the Gut Microbiome on nutrient and non-nutrient metabolism and energy availability

- One of two reviews:
  1° Systematic review of recent evidence and
  2° review focused on methodologies

- Collaboration between the Functional Food, and the Obesity & Diabetes Task force

Panel members
- Jean-Michel Antoine (Danone)
- Oliver Hasselwander (DuPont)
- Alexandra Meynier (Mondelez)
- Arjen Nauta (Royal Friesland Campina)
- Peter Putz (Ilsi Europe)
- Ian Rowland (University of Reading)
- Colette Shortt (Johnson & Johnson)
- Jonathan Swan (University of Reading)
- Jessica Türck (Yakult Europe)
- Joan Vermeiren (Cargill)
Methodology

• Prospero methodology
• PubMed review
  English
  March 2005-2015
• Selected Key words on
  - Nutrients, non-nutrients
  - Metabolism
  - Gut microbiota

www.crd.york.ac.uk/PROSPERO/
Key word focus for each target

**METABOLISM** or

- Breakdown,
- Degradation,
- Fermentation,
- Digestion,
- Transformation,
- Bioavailability,
- Absorption.

**MICROBIOTA** or

- Bacteria
- Flora
- Microbiome
Nutrient/non-nutrient targets

- Dietary Proteins (83 hits)
- Dietary Fats (63 hits)
- Dietary Carbohydrates (41 hits)
- Resistant Starch OR non-digestible starch (31 hits)
- Dietary Fibre (125 hits)
- Daidzein OR soy protein, equol (49 hits)
- Polyphenols OR phenolic acid*, flavonoid*, stilbene*, tannin*, lignan*, alkylresorcinol*, catechin*, anthocyanin*, quercetin* (181 hits)
**Review process**

*Records identified through database searching (n = 730)

Records screened (n = 730)

Records excluded (n = 533)

Analysis and draft preparation

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**Main reasons for exclusion**

- Non human data: Rumen
- *In vitro* experiment
- Review
- Age below 15 years
- Impact of Diet on Microbiota alone
- « Imprecise » Microbiota

Workshop: critical review and discussion (Dec 3/4)

Redraft

Review and submit to the European Journal of Nutrition

*Conducted by 2 members*
<table>
<thead>
<tr>
<th>Selection</th>
</tr>
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<tbody>
<tr>
<td>Eligibility of articles</td>
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<tr>
<td>Carbohydrates: 16</td>
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<td>Fat: 9</td>
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<td>Fibres: 43</td>
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<tr>
<td>Resistant starch: 7</td>
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<tr>
<td>Polyphenols (incl. Daidzein): 52</td>
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<td>Fibres: 25</td>
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<td>Resistant starch: 7</td>
</tr>
<tr>
<td>Polyphenols (incl. Daidzein): 26</td>
</tr>
</tbody>
</table>
Review strategy
Disappearance data

Energy in → Figure → Energy out

Energy in

Energy out
Review strategy

Amount of Metabolites

Energy in

SCFA
Butyrate
Acetate
Propionate
Out
Review strategy

Consequences: metabolic or others

Energy in
Stakeholder Workshop

Outcomes

• Both manuscripts were critically reviewed
• Networking
• Constructive discussions
• Presentations by leading experts
Key results-preliminary

- Few studies are focusing on the impact of gut microbiota on the metabolism of nutrients and non-nutrients.
- For proteins and digestible carbohydrates no human study matching the selection criteria was retrieved.
- Fibre, RS and Polyphenols most studied
- Lack of harmonisation in methodologies. Difficult to compare study results
- Lack of specificity in relation to taxonomy/nomenclature
Key results: Protein

Protein microbial metabolism

Ammonia → Amines → Phenols → Branched chain fatty acids

Blood → Urine → Faeces
Key results: Carbohydrate

Oligo/polysaccharide microbial metabolism

- Acetate
- Propionate
- Butyrate
- CO₂, H₂, CH₄, H₂S
- Biomass

Blood/lipogenesis
Gluconeogenesis/satiety
Energy-colonocyte
Breath
Faeces
Key results: Polyphenols

Polyphenol microbial metabolism

- Flavonol metabolites
  Hydroxyphenylpropionic acids (3,4-dihydroxyphenylpropionic acid, 3-hydroxyphenylpropionic acid) and hydroxybenzoic acids (3-hydroxybenzoic acid, 4-hydroxybenzoic acid, protocatechuic acid, vanillic acid).
  Additional processing of hydroxyphenylpropionic acids produce hydroxyphenylacetic acids (3,4-dihydroxyphenylacetic acid, 3-hydroxyphenylacetic acid, 4-hydroxy-3-methoxyphenylacetic acid, phenylacetic acid).

- Cocoa flavanol metabolites
  5-(3,4-dihydroxyphenyl)-valerolactone (DHPV) and 4-hydroxy-5-(3,4-dihydroxyphenyl)-valeric acid (4H-DHPVA).

- Daidzein metabolites
  Dihydrodaidzein, equol and O-desmethylandolensin (ODMA).

- Polyphenol metabolites
  4-hydroxyhippurate, m- and p-coumaric acids, ferulic acid and 4-hydroxy-3-methoxyphenylacetic acid.
Human gut microbiota: main phyla and genera

**Firmicutes**
- Clostridium
- Roseburia
- Faecalibacterium
- Blautia
- Dorea
- Lactobacillus
- Peptostreptococcus
- Eubacterium
- Streptococcus
- Staphylococcus
- Butyrivibrio

• **Bacteroidetes**
  - Bacteroides
  - Prevotella

PLUS Archaea
- Methanobrevibacter

And Verrucomicrobia
- Akkermansia

**Actinobacteria**
- Bifidobacterium
- Collinsella

**Proteobacteria**
- Escherichia
- Klebsiella
- Desulfovibrio
Energy microbiota example

red boxes indicate increase
blue boxes indicate decrease
a, data from animal studies; h, data from human studies; p<0.05 for all observations
A challenging field for Nutrition & Health

- How to mix a microbial logic, its kinetics, with our usual human physiology?
- Chicken and egg question: diet, microbes...
- To harmonise markers’ methodologies
- To harmonise microbes classification taking into account their functions
- To consider gut microbiota and nutrition in drug metabolism
New Activity Proposal

Microbiome Human Study Research Guidance

Develop a set of specific guidelines for the design and conduct of human microbiome interventions studies

• Methods and protocols in this field vary, including those used to evaluate microbiota.
• Need for researchers to carefully consider specific factors in study design and execution of human microbiome studies.
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