Gut Health and the Elderly Microbiome

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(+ the work of thousands of scientists in US and abroad)

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“microbiome”
“microbial organ”
“human superorganism”
“good germs”
“our second genome”
Microbiota acquired anew each generation.

1) Infants obtain inoculum from mother or environment.
2) Microbial succession over ~1-2 yrs.
3) Microbiome becomes "adult-like" in ~1-2 yrs.

Palmer et al. (2007)
Koenig et al. (2010)
### Development of the immune system

<table>
<thead>
<tr>
<th>Age</th>
<th>Maternally-acquired (passive) immunity</th>
<th>Adaptive immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>newborn</td>
<td>Maternal immune properties transferred <em>in utero.</em></td>
<td>Infant begins producing antibodies.</td>
</tr>
<tr>
<td>three month old</td>
<td>Antibodies at 15-20% of adult levels.</td>
<td></td>
</tr>
<tr>
<td>one year old</td>
<td>Normal antibody levels.</td>
<td></td>
</tr>
</tbody>
</table>
We co-evolved with our microbiome: Immune system cannot mature without specific bacteria.

Some microbes induce host pro-inflammatory response to protect against infection.

Others microbes induce host anti-inflammatory response to restore immune system balance.

Cross section of gut epithelium and bacterial community. (blue = gut wall cells green = mucous layer yellow and fuschia = bacteria)

micrograph from Earle et al. (2015)
We co-evolved with our microbiome: Microbial colonization requires specific host receptors.

ex. A particular bacterium (B. fragilis) orients to specific mucosal components in gut.
And, human genetics shape the gut microbiome.

Goodrich et al. (2014)
Microbiota and host *interact* to regulate human health.

- ‘educates’ the immune system to recognize self from nonself,
- digests the ‘indigestables’ (ex. plant material, host cells, mucous),
- produces energy substrates for host cells (ex. SCFAs),
- metabolizes drugs,
- produces beneficial compounds (ex. vitamins, antimicrobials)
- produces signaling molecules which interact with the host,
- communicates with the brain
Though the human microbiome is a fixed feature, it is also a variable trait.

- Between generations
- Throughout our lifetimes
- Between health and disease

Unlike the human genome, the microbiome is naturally mutable.
The environment matters. Diet is an environmental factor which regulates the microbiome.

South Dakota Hutterites

Communal lifestyle
Grow own food
Fresh produce in the summer
Canned foods in the winter

Davenport et al. (2014)
Welcome to ELDERMET

Scientists working at University College Cork, Cork University Hospital, and Teagasc, Moorepark have created the ELDERMET project. This project is funded by the Government of Ireland through the Department of Agriculture, Food and the Marine (DAFM), and the Health Research Board, through the Food-Health Research Initiative.

Why ELDERMET?

There are 10-100 trillion microbes in the human intestine. 10 times more bacterial cells in intestine than human cells in body meaning 100 times more bacterial genes than human genes in your body!
Environnent matters: microbiome composition separates elderly based upon where they live.

Elderly subject coding:

**Green**: community
**Yellow**: day hospital
**Orange**: rehabilitation
**Red**: long-stay

**Purple**: young healthy (control subjects)
Environment matters: microbiome composition in elderly tied to their dietary habits

Claessen et al., 2012

Microbiome composition in the elderly subjects

Green: community
Yellow: day hospital
Red: long-stay
**Environment matters: Dietary fiber and the elderly microbiome** (data taken from Claessen et al. 2012)

<table>
<thead>
<tr>
<th>Association</th>
<th>Long-Term Care (&gt;6 Weeks)</th>
<th>Rehabilitation Care (&lt;6 Weeks)</th>
<th>Day Hospital</th>
<th>Community Dwellers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: low fat/high fiber</td>
<td>DG3, DG4 predominate</td>
<td>Variable&lt;sup&gt;a&lt;/sup&gt;</td>
<td>DG1, DG2 predominate</td>
<td>DG1, DG2 predominate</td>
</tr>
<tr>
<td>2: moderate fat/high fiber</td>
<td></td>
<td>Intermediate&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Intermediate&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Lowest</td>
</tr>
<tr>
<td>3: moderate fat/low fiber</td>
<td></td>
<td>Intermediate&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Intermediate&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Normal function predominate</td>
</tr>
<tr>
<td>4: high fat/low fiber</td>
<td>Highest</td>
<td>Impaired function and frailty predominate</td>
<td>Variable&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Variable&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**Inflammatory markers (tumor necrosis factor-α, IL-6, IL-8, C-reactive protein)**

- Highest
- Intermediate<sup>b</sup>
- Intermediate<sup>c</sup>
- Lowest

**Functional status and frailty**

- Impaired function and frailty predominate
- Intermediate<sup>c</sup>
- Intermediate<sup>c</sup>
- Normal function predominate

**Microbiota**

- Bacteroidetes predominate
- Variable<sup>d</sup>
- Variable<sup>d</sup>
- Firmicutes predominate

**Predominating phyla**

- DG = diet group; IL = interleukin.
- Contents of table are adapted from reference 30.
- <sup>a</sup> Dietary patterns were variable between subjects in rehabilitation care (<6 weeks).
- <sup>b</sup> Inflammatory markers for subjects in rehabilitation care (<6 weeks) and day hospital subjects fell in an intermediate range between levels seen in long-stay and community dwellers.
- <sup>c</sup> Functional status and frailty measures showed a spectrum between community dwellers and long-stay subjects. Rehabilitation and day hospital subjects showed greater variability of function than community dwellers, who had a predominance of normal function, and long-stay subjects, who had a predominance of impaired function and frailty.
- <sup>d</sup> Predominance of Bacteroidetes and Firmicutes varied more in rehabilitation and day hospital subjects than in long-stay and community dwellers, who were more defined with respect to predominance of phyla.
Expanding classification of dietary fiber; now proposed as a prebiotic*

**Prebiotic**: A non-digestible compound which, through microbial metabolism, modulates the composition, and/or activity of gut microbiota. This change in microbial composition or activity confers health benefit to host.

Prebiotic

Specifics of this definition:

✓ Shifts focus on the role of the gut microbiota to the effect of the compound (causality)

✓ Not restricted to carbohydrates

✓ Requirement for beneficial host physiological effect retained.
Though the human microbiome is a fixed feature, it is also a variable trait.

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Unlike the human genome, the microbiome is naturally mutable.
FastTrack Action Committee – Mapping the Microbiome (FTAC-MM)

✓ President’s OSTP chartered the FTAC-MM

FTAC-MM definition: The microbiome is the multi-species community of microbes in a specific environment. Microbiome research is the study of these communities with regard to phylogenetic and genetic composition, structure and function and interactions with their hosts or in ecosystems using genome-enabled technologies.
Questions?

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additional slides
Changes in the microbiome and appearance of modern diseases?

Increase in immune disorders over last ~60 yrs.
Practices in modern society may be leading to an impoverished microbiota.

Contemporary practices:
- sanitation
- fresh food
- clean water
- bathing
- antibiotic use
- caesarean birth
- formula feeding
- Hg amalgams
- diet changes
- etc.

Postulated systematic loss of microbiota inocula each generation.

"Healthy Brazilian Amerindians and African Malawians have 30% more microbes in their microbiomes than so-called healthy Americans" (M. G. Dominguez-Bello, NYU 2014)
The list of potential microbiome-associated diseases/disorders is growing.

**Brain/behavior:** general *brain function*, epilepsy, Alzheimer’s, psychiatric disorders

**Heart:** cardiovascular diseases

**Gut:** irritable bowel disease (IBD), ulcerative colitis, Crohn’s disease, GERD, necrotizing enterocolitis (NEC)

**Cancers:** esophageal cancer, colorectal cancer, Hodgkin’s lymphoma, cervical cancer, liver cancer, gastric cancer

**Systemic:** obesity, metabolic syndrome, rheumatoid arthritis, multiple sclerosis, autism, type 1 diabetes, type 2 diabetes

**Skin:** eczema, psoriasis, acne

**Lung:** asthma, cystic fibrosis

**Vagina:** bacterial vaginosis, preterm birth

**Liver:** non-alcoholic liver disease (NAFLD), alcoholic steatosis