Impact of early life factors on the developing gut microbiota and the stress response

Catherine Stanton

18 Oct 2018  Final Conference of MyNewGut
The first thousand days – intestinal microbiology of early life: establishing a symbiosis
Harm Wopereis¹,², Raish Oozeer¹, Karen Knipping¹, Clara Belzer² & Jan Knol¹,²

Microbiota ↔ Immune System

Early microbiota
Allergy
Nutrition
Symbiosis
Infant groups (n = 50 per group):

- INFANTMET: Pre-term (<1500g or <35 weeks)
- INFANTMET: Caesarean section (full term)
- INFANTMET: Natural vaginal delivery (full term)
- MYNEWGUT: Caesarean section (full term)/Antibiotics

Health questionnaire at year 1 and year 2
INFANTMET data to 24 weeks

Hill et al., 2017 Microbiome
INFANTMET data to 4 years

- **Ruminococcaceae**
  - Year 1: 19%
  - Year 2: 32%
  - Year 4: 54%

- **Christensenellaceae**
  - Year 1: 0%
  - Year 2: 2%
  - Year 4: 4%

- **Bifidobacteriaceae**
  - Year 1: 9%
  - Year 2: 4%
  - Year 4: 0%

**Fouhy & Watkins et al. submitted**
Increase in Diversity over Time

Shannon Diversity over time

Hill et al., 2017 Microbiome
Alpha diversity to four years

Alpha diversity: diversity within a sample
Increases with age
Lowest diversity in those born preterm and very preterm

Fouhy & Watkins et al. submitted
Microbiota clustering by age

No clustering by
• delivery mode,
• term (preterm versus full term),
• duration of breastfeeding

Fouhy & Watkins et al. submitted
Recruitment of infants with altered microbiota composition due to C-section delivery at birth, and antibiotic treatment during the first 4 days of life and comparison with healthy controls (INFANTMET)

### Recruitment of MYNEWGUT infant cohort (Task 6.1.)
- 50 subjects recruited
- sequencing samples from week 1 to 24 (30 MNG infants and INFANTMET infants
- Bayleys assessment at year 2:

<table>
<thead>
<tr>
<th>Full Term Infants: C-section delivery and antibiotic treated during the first 4 days of life (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>Stool Samples                                                 X</td>
</tr>
<tr>
<td>Hair                                                          X</td>
</tr>
<tr>
<td>Urine Sample                                                   X</td>
</tr>
<tr>
<td>Saliva Sample                                                  X</td>
</tr>
</tbody>
</table>
Infant gut microbiota: Phylum Level

Average Phylum level abundance Week 1

Average Phylum level abundance Week 4

Data unpublished

www.mynewgut.eu
### Infant gut microbiota: Phylum level

<table>
<thead>
<tr>
<th>Taxonomic Level</th>
<th>Timepoint</th>
<th>Taxon</th>
<th>Comparison</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phylum</td>
<td>Week 1</td>
<td>Bacteroidetes</td>
<td>IM CS vs MNG</td>
<td>0.021</td>
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<td></td>
<td>IM CS vs IM SVD</td>
<td>0.038</td>
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<tr>
<td></td>
<td>Week 24</td>
<td>Saccharibacteria</td>
<td>IM CS vs IM SVD</td>
<td>0.032</td>
</tr>
</tbody>
</table>
Infant gut microbiota: Genus Level

Average Genus level abundance Week 24

- IM CS W24
- MNG W24
- IM SVD W24

- Other
- Akkermansia
- Haemophilus
- Raoultella
- Pantoea
- Klebsiella
- Escherichia-Shigella
- Enterobacter
- Veillonella
- Megalophaga
- Megamonas
- Erysipelotrichaceae Incertae Sedis
- Erysipelatoclostridium
- Flavonifractor
- Peptoclostridium
- Intestinibacter
- Lachnospiraceae [Eubacterium] hallii group
- Roseburia
- Lachnospiraceae UCG-004
- Lachnoclostridium
- Lachnospiraceae Incertae Sedis
- Hungatella
- Blautia
- Anaerospirobacter
- Eubacterium
- Clostridium sensu stricto 1
- Streptococcus
- Lactobacillus
- Enterococcus
- Staphylococcus
- Porphyromonadaceae uncultured
- Bacteroides
- Collinsella
- Rhodococcus
- Bifidobacterium

Data unpublished
Infant gut microbiota at 24 weeks: Genus level

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<th>Comparison</th>
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</thead>
<tbody>
<tr>
<td>Genus</td>
<td>Week 24</td>
<td>Corynebacterium.1</td>
<td>IM CS vs MNG</td>
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<td>IM SVD vs MNG</td>
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<td>Porphyromonadaceae uncultured</td>
<td>IM CS vs IM SVD</td>
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<td>Chryseobacterium</td>
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<td>Lactococcus</td>
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<td>IM CS vs MNG</td>
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<td>Eubacterium</td>
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<td>Flavonifractor</td>
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<td>Caulobacter</td>
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<td>IM SVD vs MNG</td>
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<tr>
<td></td>
<td></td>
<td>Pseudaminobacter</td>
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<tr>
<td></td>
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<td>IM SVD vs MNG</td>
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<td>Burkholderia</td>
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<td>IM SVD vs MNG</td>
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<tr>
<td></td>
<td></td>
<td>Pseudomonas</td>
<td>IM CS vs IM SVD</td>
<td>0.04</td>
</tr>
</tbody>
</table>
Bayley’s Assessment

INFANTMET vs MyNewGut cohort: composite scores.

Cognitive, Language, and Motor composites are clinician-rated.
Social-Emotional and Adaptive composites are calculated based on parent-reports.

Data unpublished
Conclusions

Perinatal factors (gestational age at birth and delivery mode) continue to impact gut microbiota to four years

Discriminative taxa:
Year 1: Escherichia-Shigella and Bifidobacterium
Year 2: Lachnospiraceae_UCG008
Year 4: Christensenellaceae

Antibiotic treatment after C-section birth mode impacts microbiota composition to 24 weeks, but the altered microbiota does not impact motor (fine and gross), language (receptive and expressive) and cognitive development at 2 years
Microbiome Influence on Energy Balance and Brain Development and/or Function Put into Action to Tackle Diet-Related Diseases has received funding from the European Union’s Seventh Framework Programme for research, technological development and demonstration. Grant Agreement no: 613979