Early prebiotic supplementation induces long-lasting consequences on microbiota composition and metabolic health of adult pigs consuming an unbalanced diet.

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Food transition and evolution of non-communicable chronic diseases

**Quantity, quality and structure of food**

- **Carbohydrates**
- **Lipids**
- **Proteins**

**Lack of exercise**

**Family environment**

- Perinatal nutrition

**Increased prevalence of obesity and associated metabolic disorders**

**Overweight and obesity**

- 1980: 857 millions
- 2014: 1,9 milliards (dont 600 millions d’obèses)

**Diabetes**

- 1980: 4,7 millions
- 2014: 8,5 millions

(\% world population ; INSEE & OMS)
Developmental origins of health and disease (DOHaD): Barker’s hypothesis

Importance of the early nutritional environment

Critical developmental window

Conception – Gestation – Birth – 2 years = 1000 days

Adult health

% adult population with intolerance to glucose or diabetes

Hales et al., 1991

Birth weight

< 2.5 - 2.94 - 3.40 - 3.85 - 4.30 > 4.31
The gut microbiota: an actor of metabolic programming

- Complex interactions with host
The gut microbiota: an actor of metabolic programming

Establishment during early life and consequences later in life

Cox et al., 2014

- Control
- Antibiotic

Diet rich in lipids

Hallam et al., 2013 & 2014

- Control
- High-protein
- Prebiotic 22%

Prebiotics: A beneficial nutritional strategy for adult health?
**Prebiotics – scFOS**

« The selective stimulation of growth and/or activity of one or a limited number of bacteria in the gut microbiota that confers health benefits to the host » (Roberfroid et al. 2010)

Direct effects of scFOS:

- ↑ Beneficial bacteria Bifidobacteria & Lactobacilli, and SCFA production (Saulnier et al., 2008; Le Blay et al., 2003)

- ↓ Adiposity and inflammatory markers (Shinoki et al., 2011)

- ↑ GLP-1 secretion (Kaji et al., 2011) and insulin sensitivity (Respondek et al., 2008 and 2010)

**scFOS: Long-term effects when consuming during early life?**
Objective

scFOS

Microbiota

Glucose metabolism
Experimental design

Control diet = CTRL

scFOS-supplemented diet = scFOS

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>Gestation</th>
<th>Lactation</th>
<th>Post-weaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>-28</td>
<td>0</td>
<td>+28</td>
<td>+56/77</td>
</tr>
</tbody>
</table>

Diets

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>High-Fat (HF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digestible energy, MJ</td>
<td>13,43</td>
<td>14,99</td>
</tr>
<tr>
<td>% digestible energy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>蛋白质</td>
<td>23,5</td>
<td>17,9</td>
</tr>
<tr>
<td>脂质</td>
<td>7</td>
<td>22,6</td>
</tr>
<tr>
<td>碳水化合物</td>
<td>69,5</td>
<td>59,5</td>
</tr>
</tbody>
</table>

* Microbiota analysis
* Microbiota analysis
* Blood, intestinal contents, tissues and organs
Microbiota – Bacterial composition

**Phylum**

- **D+190: Standard diet**
  - CTRL n=6
  - scFOS n=6

- **D+253: HF diet**
  - CTRL n=6
  - scFOS n=6

**Genus**

- **16S rRNA sequencing**

- **Perinatal scFOS: ↑ Prevotella**
Microbiota – Metabolic activity

Faecal SCFA

Gaz chromatography

Faecal metabolome

Liquid chromatography coupled to mass spectrometry (LC/MS)

<table>
<thead>
<tr>
<th></th>
<th>scFOS vs CTRL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isobutyric acid</td>
<td>↑</td>
</tr>
<tr>
<td>Hydroxy-methyl butyric acid</td>
<td>↑</td>
</tr>
<tr>
<td>Taurocholic acid</td>
<td>↑</td>
</tr>
<tr>
<td>L-Threonine</td>
<td>↑</td>
</tr>
<tr>
<td>Glycerol</td>
<td>↑↓</td>
</tr>
</tbody>
</table>

Perinatal scFOS: ↑ Fermentative metabolites and bile acids
Microbiota

what are the consequences for adult metabolic health?
Entero-insular axis and glucose homeostasis

**Nb GLP-1 secreting L cells (caecum)**

- **CTRL**
- **scFOS**

![Graph showing Nb GLP-1 secreting L cells comparing CTRL and scFOS](image)

**Plasma GLP-1**

- **CTRL**
- **scFOS**

![Graph showing Plasma GLP-1 comparing CTRL and scFOS](image)

- **D+274**
- **n=11 CTRL**
- **n=13 scFOS**
- *** P < 0.05**
- **+ P < 0.10**
Entero-insular axis and glucose homeostasis

**Nb GLP-1 secreting L cells (caecum)**

- **CTRL**
- **scFOS**

**Insulin content**

**Pancreas**

**Plasma GLP-1**

- **CTRL**
- **scFOS**

$n=11$ CTRL
$n=13$ scFOS

* $P < 0.05$
+ $P < 0.10$
**Entero-insular axis and glucose homeostasis**

**Nb GLP-1 secreting L cells (caecum)**

<table>
<thead>
<tr>
<th>CTRL</th>
<th>scFOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

* *P < 0.05*

**Insulin content Endocrine tissue**

**Pancreas**

**Adipose tissue**

**Muscle**

**Perinatal scFOS**:
Stimulation of capacity to secrete GLP-1 and improvement of pancreas sensitivity to glucose (Le Bourgot et al., in preparation)
Plasmatic metabolome

- PLS-DA discriminating both groups \((LC/MS)\)

LysoPC: identified as a potential plasma marker of obesity and metabolic disorders \((\downarrow)\)

(Zhao et al., 2010; Barber et al., 2012; Yea et al., 2009)

Perinatal scFOS: \(\uparrow\) LysoPC (18:0) = improvement of glucose control
Microbiota

scFOS: 0.15 to 0.33% of the diet = physiological dose

Conclusion

Metabolic adaptation

Sustained effect on microbiota

Stimulation of entero-insular axis (GLP-1)
Thank you for your attention

QUESTIONS?