MATERNAL EXPOSURE TO A WESTERN-STYLE DIET CAUSES DIFFERENCES IN INTESTINAL MICROBIOTA COMPOSITION AND GENE EXPRESSION OF SUCKLING MOUSE PUPS

AN OBSERVATIONAL STUDY

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Note: for non-commercial purposes only
INTRODUCTION

• Long-lasting effects of nutritional interventions during early life have become increasingly evident: nutritional programming

• Effects of maternal nutrition on the offspring and its developing intestinal system are still underexplored

STUDY QUESTION

• What is the effect of *indirect* exposure to a (maternal) high-fat diet during the perinatal period on the gene expression in the colonic wall and the microbiota development in the offspring?
STUDY DESIGN

Pre-treatment 6 wks

Gestation 3 wks

Lactation 2 wks

Mating

Birth

Termination

L - Low fat diet (10 En% fat, 18 mg cholesterol/kg)

W - Western-style diet (45 En% fat, 197 mg cholesterol/kg)

Now:

- 2-wk-old pups (both sexes): colonic content and wall
- colonic wall: transcriptome analysis/gene expression
- colonic content: microbiota composition (16S rRNA gs)
- integrative analysis of colonic wall + content data

@ PN 14
COLONIC LUMINAL CONTENT: DEEP SEQUENCING

- Verrucomicrobia
- Tenericutes
- Proteobacteria
- Actinobacteria
- Firmicutes
- Bacteroidetes

Relative abundance (%)

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Relative abundance (%)
REDUNDANCY ANALYSIS (RDA) ON INDIVIDUAL MICROBIOTA COMPOSITION: clustering on DIET (P-1) and LITTER (P-2)

Axis P1: separation L from W diet offspring
Axis P2: clustering of the litters (in W<L)
No sex-differences
Maternal diet affects sex-specifically colonic gene expression in the offspring.
COLONIC WALL ANALYSIS

Sexually dimorphic gene expression (FC>1.2)

- **up-regulated**
  - ♂ (27)
  - ♀ (99)

- **down-regulated**
  - ♂ (38)
  - ♀ (62)

### Similar gene expression
- 
  - Olfr78
  - Pdk4

### Differential gene expression
- 
  - Ceacam2
  - Ly86
  - Gpd1

Expression levels (Log2)

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DANONE NUTRICIA
Early Life Nutrition
Integration: top-500 expression-affected genes in the colon wall and top-16 (>0.1%) microbiota families found in colonic content of the 2-week-old mice (♂ + ♀) separation into two equal main clusters with crosswise reverse correlation.
Integration: top-500 expression-affected genes in the colon wall and top-16 (>0.1%) microbiota families found in colonic content

Quantified Correlation

Network Analysis

strongest correlations with only a few microbiota groups, large overlap in genes
DISCUSSION

Note: maternal feces nor milk composition were analysed!

Mechanism of action? Correlations are causal relations?
- Pattern recognition receptors (PRRs) e.g. Toll-like receptors
- Anxa13 gene product interaction with bacterial adhesion factors
- Fermentation products (e.g. SCFAs, ethanol, inflamm. mediators)

CONCLUSIONS

- Maternal diet during the perinatal period affects both gene expression and microbiota composition in the colon of 2-week-old offspring
- In line with the DOHaD concept, food choices of soon-to-be and lactating mothers are important for the developing offspring
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