Human milk oligosaccharides (HMOs) role in neurodevelopment

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Human Milk Oligosaccharides (HMOs): Role in neurodevelopment

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Evolution of Milk: a story 310 million years in making

- Earliest indication in the Pennsylvanian period, approximately 310 million years ago
- Ancestors of mammals laid eggs with parchment-like shells intolerant to desiccation and therefore dependent on glandular skin secretions for moisture
- Today few egg laying mammals still exist
- This skin secretion (intended for moisture and antimicrobial properties) evolved into a nutrient-rich milk long before mammals, taking a role of vehicle of nutrients to the new-borns

Main categories of human milk components

- **Bioactive Components**
  - HMOs
    - Key features: Not digested, No nutritive value, Support microbiota
    - Key functions: SUPPORT BRAIN DEVELOPMENT

- **Nutritive Components**
  - Lactose, Proteins, Fat
    - Key features: Mainly digested, Nutritive value
    - Key functions: SUPPORT HEALTHY GROWTH AND DEVELOPMENT
Gross composition of breast milk

Human breast milk

Solid components

- Proteins (8 g/L)
- HMOs (5-15 g/L)
- Lipids (40 g/L)
- Lactose (70 g/L)

HMOs

- Core structures
  - 5 to 15 g/L in breast milk
  - >130 structures described, of which <20 make up the bulk
  - Most HMOs are not generally present in farmed animal milks
- Fucosyl-HMOs
- Sialyl-HMOs (n=287)

Macro-, micro-nutrients and HMOs

Water

Gross compositional comparison to bovine and formula milk

Adapted from Anna Petherick, Nature volume 468, pages S5–S7 (23 December 2010); Samuel and Binia et al., 2019, Scientific Reports
Which factors influence breastmilk HMO composition?

Maternal parameters

• Genetics (Secretor-, Lewis gene)
• Lactation stage
• Physiological status
• Mode of delivery
• Infant gestational age
• Diet

Important to understand for observational association studies of HMOs with breastfed infant clinical parameters.
2’-Fucosyllactose breast milk levels at 1 month of age is associated with cognitive development at 24 months

Human milk oligosaccharide 2’-fucosyllactose links feedings at 1 month to cognitive development at 24 months in infants of normal and overweight mothers

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Berger et al. PlosOne Feb 2020
Early life supplementation with 2’-Fucosyllactose improves long-term potentiation (LTP) via the Gut-Brain Axis in preclinical model

Dietary 2’-Fucosyllactose Enhances Operant Conditioning and Long-Term Potentiation via Gut-Brain Communication through the Vagus Nerve in Rodents

Vazquez et al. PlosOne Nov 2016
Presence of 6′Sialyllactose during lactation promotes attention and memory in preclinical model

**Spatial memory**  
(Barnes maze)

**Attention**  
(attention set shifting task)

**Myelination**  
(gene expression relative to control)

Hauser et al. ESPGHAN 2019 and unpublished results
HMOs modulation of neurodevelopment: Mode of actions

- **Microbiota**: Modulation of microbiota composition
- **Vagus Nerve**: Modulation of vagal tone by HMOs
- **Myelination**: Modulation of myelination by sialylated HMOs

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Thank you for your attention