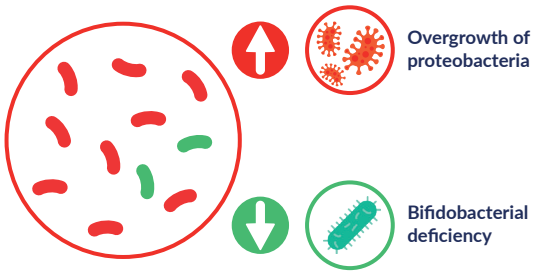
New Insights Into OPTIMIZING GUT HEALTH AND IMMUNITY FOR INFANTS WITH COW'S MILK PROTEIN ALLERGY (CMPA)

DYSBIOSIS



- CMPA in non-breastfed infants is associated with intestinal microbial dysbiosis, characterized by the suppression of infant-type bifidobacteria and the enrichment of potentially pathogenic proteobacteria (e.g., Escherichia coli or Klebsiella).[1,2]
- Human Milk Oligosaccharides (HMO) are complex, non-digestible carbohydrates which are bioactive components found in breast milk. These act as the specific substrate for infant-type bifidobacteria and promote the establishment of other beneficial microbiota in early infancy.
- HMO uniquely support gut and immune health via direct interactions with the gut epithelium and production of specific immune modulating metabolites (e.g., short-chain fatty acids, aromatic lactic acids).[1,2]

SHORT CHAIN FATTY ACIDS AND THEIR ROLE IN GUT AND IMMUNE HEALTH FOR INFANTS

The main short-chain fatty acids

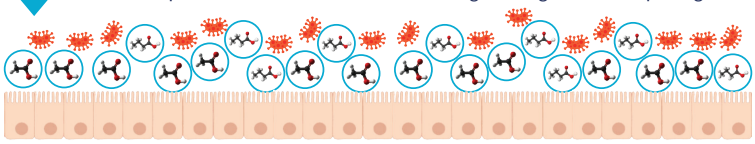
Acetate   Butyrate

- HMO are fermented by infant-type bifidobacteria to lactate and acetate.[1,2]
- Acetate produced by bifidobacteria is converted to butyrate by butyrate-producing bacteria.[1,2]
- Certain bacteria (e.g., Veillonella) can convert lactate to propionate, another beneficial short-chain fatty acid.

Local effect

Systemic effect

pH The presence of acidic metabolites (lactate, acetate, propionate, butyrate) lowers the colonic pH and creates an environment that guards against enteropathogens.[1,2]



Dendritic cell · T cells · Macrophage

Butyrate plays a critical role in promoting early immune development by acting on various immune cells, including dendritic cells and regulatory T cells.[1]

- ↑ Differentiation of regulatory T-cell
- ↓ Inflammation
- ↑ Gut barrier function

Recent studies (CINNAMON and PLATYPUS) in infants with CMPA using hypoallergenic specialty formulas supplemented with two HMO (2'-FL and LNnT) have shown that these HMO can enrich all 4 infant-type bifidobacterial strains and their associated immune-modulating metabolites. This, in turn, can enhance early immune development, strengthen immune protection against infections, and potentially reduce antibiotic use.[1,2,3]

Findings observed in CINNAMON and PLATYPUS

0-6 months of age

Dietary intake:
Hypoallergenic specialty formula containing 2 HMO (2'-FL and LNnT)

Enrichment in HMO-utilizing infant-type bifidobacteria:[1,2]

- *B. longum subsp. infantis*
- *B. breve*
- *B. bifidum*
- *B. longum subsp. longum*

6-12 months of age

Dietary intake:
Hypoallergenic specialty formula with HMO plus complementary feeding

Continued enrichment in bifidobacteria and other bacteria:[1,2]

- *Bacteroides spp.*
- *B. pseudocatenulatum*
- *B. catenulatum subsp. kashiwanohense*
- *Akkermansia muciniphila*
- *Faecalibacterium prausnitzii* (butyrate producer)

Bifidobacteria produce acetate and aromatic lactic acids[1,2]

Immunomodulatory effect

Conversion of acetate to butyrate (cross-feeding) by butyrate producers[1,2]

Impact in infants with CMPA

Partial correction of microbial dysbiosis[1,2]

Age-appropriate microbiome development by 12 months[1,2]

Healthy gut microbiome and immune system is associated with reduction in infections and potential medication use[3]

CONCLUSION

- **Feeding with an HMO-supplemented hypoallergenic specialty formula containing 2′-FL and LNnT in infants with CMPA partially corrected the intestinal microbial dysbiosis by enriching infant-type bifidobacteria and reducing the abundances of proteobacteria.[1,2]**
- **Supplementation with 2′-FL and LNnT contributed to a healthier, age-appropriate gut microbiome[1,2] and promoted immune-modulatory effects, including a lower frequency of respiratory tract infections and otitis media.[3]**

IMPORTANT NOTICE: Mothers should be encouraged to continue breastfeeding even when their infants have cow's milk protein allergy. This usually requires qualified dietary counseling to completely exclude all sources of cow's milk protein from the mothers' diet. If a decision to use a special formula intended for infants is taken, it is important to give instructions on correct preparation methods, emphasizing that unboiled water, unsterilized bottles or incorrect dilution can all lead to illness. Formula for special medical purposes intended for infants must be used under medical supervision.

1. Boulangé CL et al. International Journal of Molecular Sciences. 2023; 24(14):11422 **2.** Gold MS et al., Nutrients 2022;14:2297.
3. Vandenplas Y et al., Nutrients 2022;14:530.

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