DANONE RESEARCH & INNOVATION

Infants Gut Microbiota Development & Connection to Immunity:

Rebalancing gut microbiota in C-section born infants to support immune system development.

The gut microbiota is crucial for shaping the immune system, particularly during the first **1000 days of life**, when the infant's immune and GI systems are still immature.[1-2]

70% of immune cells that are part of our immune system are in the gut.[2-4]

C-section delivered infants may have an increased risk of **immune and metabolic diseases later in life** due to compromised and delayed gut microbiota colonization, especially of *Bifidobacterium* and *Bacteroides*.[5-7]

Breast milk plays a vital role in supporting the development of a healthy gut microbiota and immune system.[8-10]

Human Milk Oligosaccharides (HMOs)

- Prebiotic effect [11,12]
- Direct effect on immune cells [14]
- Block route of infection [13]
- Brain building blocks [15]

Bacteria and their metabolites

- Prebiotic and postbiotic effects, for gut and immune benefits[16, 17]

Specialized nutrition strategies, such as those containing a mix of *B.breve* M-16V, can offer an opportunity to restore the compromised gut microbiota in C-section born infants who are not exclusively breastfed.[22,23] This is supported by evidence showing that neither breastfeeding nor formula lacking probiotics effectively prevents delayed Bifidobacterium colonization in this population. [22,24]

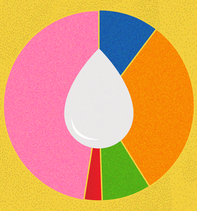
scGOS/lcFOS

- Prebiotic effect[20]
- Immune Modulation[20-21]

B.breve M-16V

- Probiotic effect[12-18]
- Immune Modulation[19]

HUMAN MILK COMPOSITION



RCT 1

STUDY POPULATION: *N=183*

Healthy term infants born by C-section*#: n = 153

STUDY CONCLUSIONS:

This dedicated study on C-section delivered infants showed that the unique synbiotic supplementation restores bifidobacterial levels and promotes gut condition similar to that of vaginally born infants. Additionally, it significantly reduced skin-related disorders, including eczema.[22]

RCT 2

STUDY POPULATION: *N=221*

Healthy term infants born by C-section* subgroup: n = 121

STUDY CONCLUSIONS:

This study confirmed the effect of the unique synbiotic on the gut microbiota, with restoration of bifidobacterial levels and other bacterial species (e.g. *Bacteroides*).[23]

Observational Study

STUDY POPULATION: *N=192*

Healthy term infants born by C-section#: n =121

STUDY CONCLUSIONS:

In a real-world setting, the specific synbiotic supplementation supports the findings of gut microbiota restoration observed in the clinical studies.
Additionally, this unique synbiotic supplementation may potentially support immune development as parent-reported illness episodes were significantly reduced at 12 months (112 infants completed the survey).

*All C-sections were elective *Subjects were mixed-fed

These studies demonstrate the crucial link between infant gut microbiota and immune development. Supplementing C-section born infants who are not exclusively breastfed with a unique synbiotic formula (scGOS/lcFOS and *B.breve* M-16V) can restore *Bifidobacterium* levels to those typically found in vaginally born infants, potentially supporting healthier immune development.

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Mixed-fed infants were included only in RCT1 and the observational study; most subjects received the study product corresponding to their allocated groups in addition to breastfeeding.