

## Human Breast Milk Microbiome: An Editorial

Michael Naafs, A. B.

*Department of Medicine, Naafs International Health Consultancy, Netherlands*

**\*Correspondence to:** Dr. Michael Naafs, A. B., Department of Medicine, Naafs International Health Consultancy, Netherlands.

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### Abstract

Human milk oligosaccharides (HMOs) are believed orchestrating the whole process of translocating bacteria of the mother's gut microbiome to breast milk and shape the infants' gut microbiome. HMOs are involved in modulating the infants' innate immune system and to prevent bacterial infections. Paradoxically, they can enhance rotavirus replication and symptomatic rotavirus infection, which could lead to better performance of live-attenuated rotavirus vaccines in the future. Bioactive HMOs, exosomes and milk microbiota play an important role in the establishment of the neonatal microbiome. The role of microbial endocrinology in the breast milk microbiome is unknown yet.

### Introduction

The human milk is not only a source of vitamins and nutrients but also of commensal bacteria, the breast milk microbiome. The microbiota associated to the human breast milk are believed to modulate the infants' innate immune system and contribute to the 'initial' intestinal microbiota of infants [1]. The development of the infants' innate and oral mucosal immune system is a miracle itself, preventing massive infections and allergic reactions to every new microbe or antigen [2].

The components of breastmilk that promote healthy infant growth and interact with breast milk microbiota are largely unknown. Sialylated milk oligosaccharides for example, promote microbiota-dependent growth in models of infant undernutrition [3].

Human milk oligosaccharides (HMOs) are believed orchestrating the whole process of translocating bacteria of the mother's gut microbiome to breast milk and its dynamic transfer to the infant. The synthesis of the HMOs is partially determined by the maternal genotype. HMOs are thought to play a role in preventing pathogenic bacterial adhesion by multiple mechanisms besides providing nutrition for the microbiome [4].

Extravesicular vesicles (EVs), including exosomes, carry a diverse cargo including mRNA, mtRNA and cytosolic and membrane-bound proteins which are readily detectable in human breast milk. Strongly implicated in cell-cell signalling EVs may play a further role in the development of the infant microbiome. Human breast milk microbiota, bioactive HMOs and EVs have an emerging role in the establishment of the neonatal microbiome and potential for modulation of the neonatal immune system development.

If you think you got it and HMOs play only a protective role in neonatal infections by shaping the infants' microbiota, you are probably wrong. A recent publication sheds a new light on the role of HMOs in understanding of rotavirus infections in the new born that could improve the performance of live, attenuated rotavirus vaccines [5].

Ramani *et al* asked themselves why some neonatal rotavirus infections are symptomatic and others not? The amount of virus in the new born or the genome of the virus could not be linked to the presence of symptoms in new-borns. In the lab the researchers investigated then whether components of the mother's breast milk could inhibit infection of MA104 cells, a well-established model of rotavirus infection. Unexpectedly and in contrast with the general belief they discovered that specific HMOs enhanced infection of cells in culture with the neonatal rotavirus strain [5].

Returning to the field, the investigators found that some specific HMOs are present in the milk of mothers of new-borns with symptomatic rotavirus infection. In addition, they found an association between the microbiome in the mother's milk and gastrointestinal symptoms in the new born, which prompted new questions.

Most interesting these sugars also increased the replication of the rotavirus attenuated- live vaccine that is similar to the neonatal virus studied by the investigators. Enhanced virus replication can potentially translate into a more effective immune response against the virus, which could lead to better protection for the infant [5].

Last but not least the influence of hormonal changes on the breast milk microbiome has been hardly or not investigated. Microbial endocrinology of the microbiome is an intriguing emerging field of research [6]. With all the hormonal changes that take place during and around pregnancy and breastfeeding, new and exciting results in breast milk research can be expected, as well as for subsequent improving of breast milk formula.

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## Conclusion

It is obvious research is not finished with the breast milk microbiome and milk formula yet, and exciting results are to be expected in the near future.

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