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The physiological breast-milk proteins S100A8 and S100A9 promote an eubiotic gut state in infants

Keywords: Microbiome, breast milk proteins, calprotectin, immune development, dysbiosis-linked disease, Sepsis, NEC

INVENTION NOVELTY

Instantly after birth, every newborn is exposed and must adapt to a variety of pathogenic and non-pathogenic microorganisms. Feeding a newborn with mother's milk supports the immune system to adopt to the environmental change and to establish a health promoting microbiome. However, preterm birth and other circumstances may prevent breast-feeding, and necessitate substitute nutrition lacking important maternal factors. Application of the physiological proteins S100A8 and S100A9, also called calprotectin, which are highly abundant in human breast milk, primes the newborn immune system for the adaptation to an extrauterine microbial environment, aid to promote an eubiotic infant gut state, and prevent the development of sepsis and NEC.

VALUE PROPOSITION

Formula nutrition is based on milk preparations originating from cow, goat or soy and lack maternally derived developmental and immunological factors. Newborns fed with these products lack the supply of S100A8 and S100A9 which are important factors to build a health promoting microbiome. Compensation of calprotectin deficiency in the nutrition of neonates offers the great potential to prevent the development of sepsis and NEC which can arise from a disbiotic gut state.

TECHNOLOGY DESCRIPTION

The S100 calcium binding proteins S100A8 and S100A9, and their extracellular dimeric complex, S100A8–A9, also known as calprotectin, are expressed by lamina propria macrophages in intestinal tissues from infants at higher levels than in intestinal tissues from adults and are, additionally, found in high amounts in human breast milk. High fecal levels of S100 proteins, from 30 days to 1 year of age, were associated with higher abundance of beneficial Actinobacteria and Bifidobacteriaceae, and lower abundance of Gammaproteobacteria, particularly opportunistic Enterobacteriaceae, in the neonate's gut microbiome. In term infants, fecal S100A8-A9 levels are significantly higher during the first 3 months of life compared with normal adult values and normalize along with weaning until the end of the first year. In preterm infants, initial fecal S100A8-A9 levels are significantly lower than in term infants but increase during the first month of life. Breast milk is one important source of fecal S100A8-A9 in newborns and supplements the natural low S100A8-A9 production by macrophages. The clinical relevance is corroborated by strong associations of neonatal fecal S100A8-A9 deficiency with dysbiosis-linked diseases like NEC, sepsis, and obesity, which can experimentally be prevented by a single nutritional supply of S100A8 at birth.

COMMERCIAL OPPORTUNITY

In-licensing or collaboration for further development is possible.

DEVELOPMENT STATUS

Pre-clinical data available.

PATENT SITUATION

Patents have been granted in Europe (EP 3534931, national validation in DE, CH, FR and GB), USA (US 11,253,570 B2) and China (ZL 2017 8 0065576.8) with priority of 2016. Patent application in Canada is pending.

FURTHER READING

- Ulas T, Pirr S, Fehlhaber B, Bickes MS, Loof TG, Vogl T, Roth J, Viemann D et al. 2017. S100-alarmin-induced innate immune programming protects newborn infants from sepsis. *Nat Immunol*. 2017 Jun;18(6):622-632. doi: 10.1038/ni.3745. Epub 2017 May 1. Erratum in: Nat Immunol. 2017 Sep 19;18(10):1173. PMID: 28459433.
- Willers et al. 2020. S100A8 and S100A9 Are Important for Postnatal Development of Gut Microbiota and Immune System in Mice and Infants. *Gastroenterology*. 10.1053/j.gastro.2020.08.019

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- Viemann 2020. S100-Alarmins Are Essential Pilots of Postnatal Innate Immune Adaptation. *Front Immunol.* 10.3389/fimmu.2020.00688
- Pirr 2017. High Amounts of S100-Alarmins Confer Antimicrobial Activity on Human Breast Milk Targeting Pathogens Relevant in Neonatal Sepsis. *Front Immunol*. 10.3389/fimmu.2017.01822.