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EDITORIAL

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Editorial comment "Effect of maternal prebiotic supplementation on human milk immunological composition: Insights from the SYMBA study"

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The first months of life are marked by high immunologic plasticity, which is considered to be a "window of opportunity" for the prevention of allergic diseases. In this regard, nutrition during pregnancy and in infancy seems to play a crucial part.[1,2]

The World Health Organization (WHO) recommends exclusive breastfeeding for the first 6 months of life and continued breastfeeding alongside weaning foods until 2 years of age or beyond,[3] as human milk is the best source of nutrition for infants. While breastfeeding offers numerous benefits, there is ongoing debate about its role in preventing allergic diseases.[1] As human milk has an individually unique composition and contains a large number of immunologically active substances,[4] it is important to identify target immunomodulatory ingredients, which may affect the development of allergic diseases.

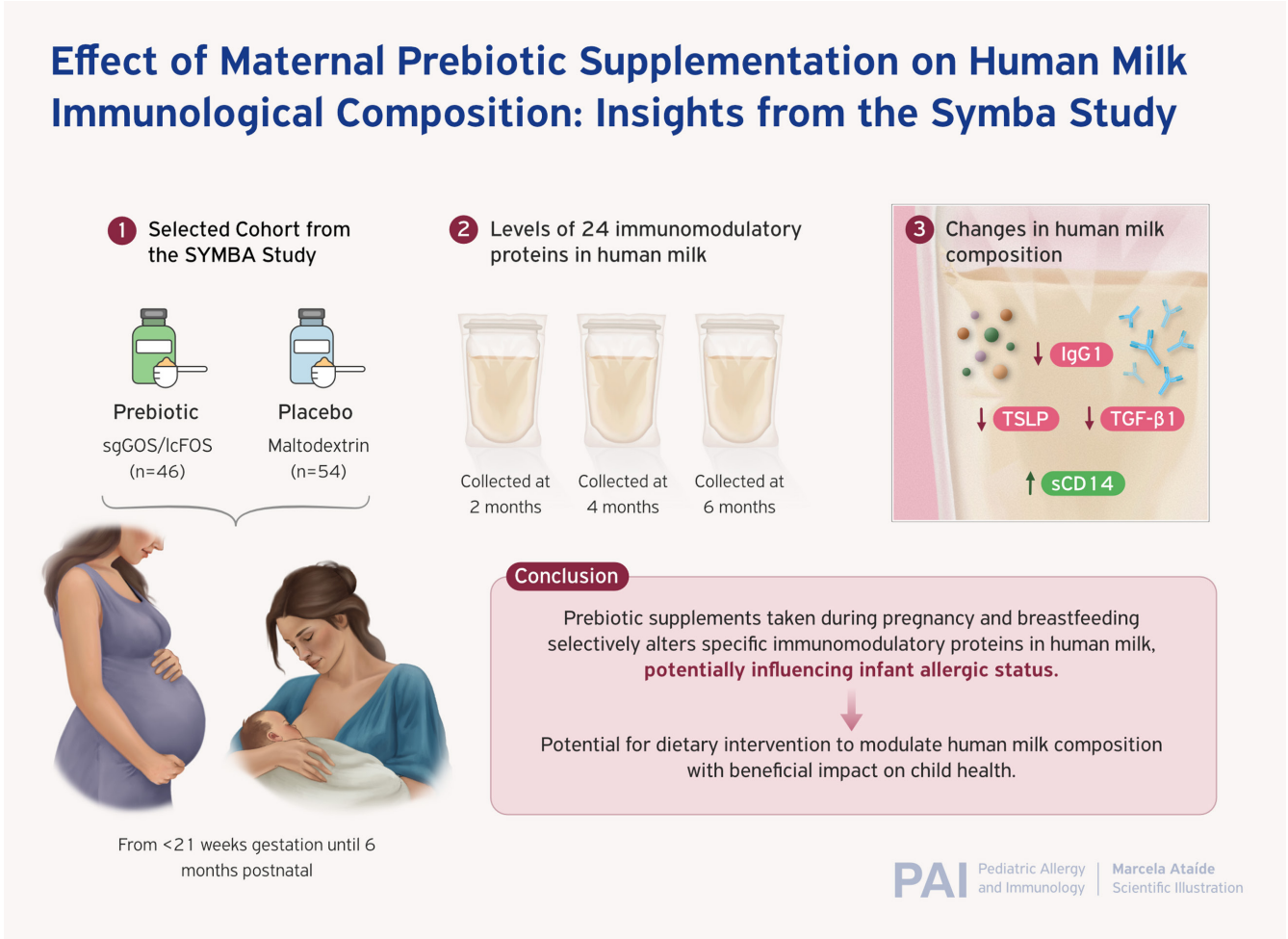
For instance, lower levels of the fatty acids caprylate or acetate could be found to be associated with an increased risk for the development of atopic dermatitis.[5] Moreover, there are hints that modulatory factors of the infant's IgA production in human milk might have allergy-preventive effects.[6]

Furthermore, it has been shown that the maternal microbiome is closely linked with the microbiome in human milk, which significantly influences the development of the newborn's intestinal microbiota. Studies indicate that human milk accounts for about 25%–30% of a child's gut microbiota. A dysbiosis of the intestinal microbiota, in turn, plays a crucial role in the development of asthma and obesity.[4]

Many studies have therefore investigated the allergy-preventive effect of maternal intake of pro- and prebiotics. However, the results are difficult to interpret due to highly heterogeneous methodologies and lack of mechanistic understanding.[7] Remarkably, Ahlberg et al.[8] found that the expression of several immune-related microRNAs in breast milk is influenced by pre- and postnatal supplementation with *Limosilactobacillus reuteri* and that some of them correlated with the fraction of activated and resting regulatory T cells in the children.

As an editor's choice, we highlight results of the SYMBA study by Divakara et al.,[9] which assessed the effects of maternal prebiotic supplementation on the immunomodulatory protein composition of human milk and the risk for the development of allergic diseases in children. This double-blind, randomized placebo-controlled trial involved mothers taking prebiotics from < 21 weeks of pregnancy until 6 months postpartum, during the breastfeeding period. The study included 46 mother–infant pairs receiving prebiotics and 54 receiving a placebo. The levels of 24 immunomodulatory proteins were measured in human milk, collected at 2, 4, and 6 months.

The results showed that commonly detected immunomodulatory proteins in human milk included TSLP, IgA, IgM, IgG2, and IgG3, while others, such as IgG1, IgG4, sCD14, and TGF-β1, were found in over 50% of the samples. Some cytokines, such as TNF-α and IL-5, were less frequently detected, and a few, including IL-10, IL-4, and IL-13, were rarely present. Overall, the prebiotic supplementation did not significantly alter the global immunological composition of human milk. However, a few notable changes were observed. At 2 months postpartum, mothers in the prebiotic group exhibited lower levels of TGF-β1 and TSLP in their milk compared to the placebo group, while the concentration of sCD14 was increased. At 4 months, IgG1 was found to be lower in the prebiotic group. These selective changes highlight that maternal prebiotic consumption may influence specific immunomodulatory factors within human milk, though the broader composition remains unchanged. It is crucial to understand that the definition of "high" or "low" levels of these proteins may vary across time points and populations, and what may be considered "high" at one stage could be viewed as "low" at another, potentially affecting outcomes differently depending on the infant's developmental stage. Although the study



observed changes in certain milk proteins with prebiotic supplementation compared to the placebo group, it was not designed for longitudinal analysis, and direct comparisons between different time points should be made cautiously.

The results of this study align with growing evidence that maternal diet can influence the immunological environment infants are exposed to through breastfeeding.[5,6,8] This study in particular is the first to investigate the effects of maternal prebiotic supplementation, specifically short-chain fructo-oligosaccharides (scFOS), and long-chain galacto-oligosaccharides (lcGOS), during pregnancy and lactation on human milk composition, addressing a notable gap in the existing literature. However, the mechanisms responsible for the observed differences in these key immunomodulatory proteins remain unclear.

These findings underscore the complexity of human milk's immunological profile and the need for further research to determine the clinical relevance of these specific changes, particularly in the context of allergy prevention. Understanding how maternal diet influences the immunomodulatory properties of breast milk could pave the way for new strategies in primary prevention of allergic diseases. Future studies should focus on elucidating the long-term outcomes of these immune shifts and exploring how dietary interventions during pregnancy and lactation can be optimized to support infant health.

CONFLICT OF INTEREST STATEMENT

None.

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