The prevalence of allergic diseases, such as food allergy, atopic eczema, allergic rhinitis and asthma, is rising dramatically worldwide. 1,2 CMA is one of the most common allergies in infants and young children, affecting up to 5% of the world population. 3

**The importance of the gut microbiota in early life**

The immune system develops quickly during the first 1000 days of life; it is well known that both the establishment and maintenance of an optimal microbial community is important for the development of the immune system and essential to maintain health, especially in infants and children. 4 Environmental factors such as mode of delivery, diet and use of antibiotics influence the infant gut and immune system. These factors can cause an imbalance of the gut microbiota known as dysbiosis, which impairs the development of the immune system, resulting in a state of inflammation and potentially giving rise to allergic diseases. 5 For this reason, targeting the gut microbiota is suggested to be important in reducing the risk or persistence of allergic diseases like CMA. 6

**Synbiotics** is a combination of pre- and probiotics. 7 Pre- and probiotics can influence the immune system directly or indirectly, via the gut microbiota, and therefore they may play a role in preventing the onset of an allergic disease. 8 The objective of combining pre- and probiotics is to achieve stronger positive effects than with either component alone (synergy). 9

The gut microbiota of infants with allergic conditions is characterized by low levels of Bifidobacteria and Lactobacilli compared with healthy infants. 10 Human milk contains human milk oligosaccharides (HMOs) and live bacteria that are provided at a critical stage in the early development of the gut microbiota. 11 Given the presence and important role of these naturally occurring pre- and probiotics, and recognising that breast feeding is not always possible, there is a compelling rationale to combine pre- and probiotic ingredients (synbiotics) in infant formulas so that functionally it more closely resembles human breast milk. 12

**Synbiotics as a promising approach for CMA**

A growing amount of clinical evidence shows that pre- and probiotics can have beneficial effects in infants at risk of, or living with food allergies. 13-18

Traditional strategies for the dietary management of food allergies such as extensively hydrolysed formula (EHF) or amino acid formula (AAF) have been successful, with most subjects having symptom resolution and achieving oral tolerance with time. However, rising allergy prevalence in the world has led to research on the possibility to further develop effective tolerance to allergens in prevention and dietary management strategies. 19

Supplementation with specific probiotic mixtures and probiotics has been a logical next step in promoting immune system development and balanced gut microbiota as part of strategies for the nutritional management of CMA. 20,21

Nutricia believes that optimal prevention and management strategies combine milk hydrolysate- or amino acid-based formulas with additional ingredients (such as pre- and probiotics). These promote environmental conditions in the gut to train the immune system, supporting the natural development of oral tolerance. Protein hydrolysates may contribute to the induction of oral tolerance via controlled exposure to specific peptides of the allergenic protein. 22

Recognizing the importance of a balanced gut microbiota, and building on the increasing evidence of bacterial presence in human milk, Nutricia is supporting a comprehensive research programme to investigate the efficacy of a specific synthetic mixture of prebiotics (short chain galacto-oligosaccharides (scGOS) or shortchain fructo-oligosaccharides (FOS)) + long chain fructo-oligosaccharides (FOS/FOS) in a 9:1 ratio – and probiotic strain B. breve M-16V.

**Future of allergy management for CMA patients**

The dramatic increase in allergic disease requires a new focus on strategies for the primary prevention and dietary management of food allergy. Increasing insights have highlighted the importance of the gut microbiota for overall health and targeting the gut microbiota appears to be a new way to reduce the incidence and persistence of allergic diseases like CMA.

Nutricia believes that there is a strong rationale for combining pre- and probiotics in the diet of these infants and has an extensive clinical trial programme underway investigating the role of these ingredients in primary prevention and dietary management of CMA.

**References**