Breastfeeding is well-known to provide short- and long-term health benefits, but the complex interaction between the mother's milk and the neonate remains to be fully understood. This involves exploring the effect of gastrointestinal digestion of the milk on its structural transitions and their impact on the breakdown of macronutrients. Understanding how the composition of human milks from different stages of lactation influence the milk digestibility will help to fully realise how metabolism is established in early life, as well as how all these aspects can potentially prevent the development of chronic diseases later in life. This is important for advancing the knowledge regarding the healthy development of a full-term infant. This is crucial for understanding transitions of macronutrients delivered with the milk to the digestive system of preterm neonates, for whom every single day of their early lives can impact on long-term health conditions.

The biochemical composition and structure of human milk varies considerably between different stages of lactation. Compositional/structural differences are also evident when the milks produced by mothers of full-term and preterm infants are compared. The two effects have been believed to be in line with the specific needs of a developing infant under any given set of circumstances. The human milk has been the subject of many research studies, including those looking at its digestibility. However, the majority of existing research has either focused on developing/validating *in vivo* (animal) and *in vitro* models of the human infant digestion, or on characterising digestion of the milk that is easily accessible for research – the mature milk produced by mothers of children born at term. There are no available results of large-scale comparative studies that would look comprehensively at differences in digestibility of human milks produced under the different sets of circumstances described above. This presents a serious gap in the fundamental knowledge and a limitation for a knowledge-based design of new nutritional supplements of the milk for personalised needs of infants in situations when mother's milk is not available.

We will test four different types of human milk in this project: the colostrum and the mature milk obtained from mothers of preterm infants, as well as the colostrum and the mature milk from mothers of full-term infants. The milks will be subjected to simulated infant digestion conditions, involving the aspects of the gastric phase separation and the dynamic transition of digesta into the small intestine with further digestion. The gastrointestinal fate of human milk will be closely monitored by advanced analysis of proteins, lipids and saccharides during the digestion to identify and explain any digestion-dependent differences between the four types of milk.

By using the diverse types of real human milk and by applying the physiologically relevant model of infant digestion, we aim to deliver, for the first time, robust and extensive scientific data on how the lactation stage can influence the human milk digestion and nutrient bioaccessibility in preterm and full-term infants.

Apart from revealing fundamental aspects the human milk digestion patterns, we will also test the gastrointestinal behaviour of conventional infant formulas. This is in order to emphasise any differences relative to the behaviour of human milk. It is also to produce a comprehensive scientific evidence we will use in the mathematical modelling that would support any future design of such human milk supplements for feeding preterm and full-term infants at different stages of their development.