The first years of a child’s life are critical for growth and development, and despite decades of research, we still do not understand how infant diet shapes a child for both short- and long-term health. The link between food and health is complex, and although breastfeeding is known to have short- and long-term benefits, the relationship between food and the developing neonate is not understood, primarily because in the past there has been a lack of analytical tools. Indeed, most infant studies rely on crude measures of child health such as growth, and absence of obvious disease. While these assessments can reveal rudimentary associations between dietary components and lack of adverse outcomes in the short-term, they do not directly address the impact of food or food components on metabolic health that may have long-term consequences.

Making matters more complex, analysis of food is not trivial. Although decades of research have gone into studying human milk, most research has focused on studying proteins, lipids, and micronutrients. It is now recognized that there are other factors in milk that may be important for infant health, including small-molecule metabolites that include a unique class of sugars known as oligosaccharides. Human milk oligosaccharides, which are complex in structure, act as both food for beneficial bacteria and decoys for pathogens [1], and it is now being shown that they can help build the immune system through modulating CD14 expression and altering plasma cytokine levels [2, 3]. Additionally, there are other metabolites present in milk, and their function is not fully understood, although their expression appears to be controlled through the mammary gland as well [4], and they may have important consequences for the developing neonate. Through the development of modern nuclear magnetic resonance- and mass spectrometry-based metabolomics techniques, we are now in an era where we can measure these small molecules in food, and this will help us understand how food impacts health in an unprecedented way.

Analysis of the infant metabolome has led to important revelations regarding how infant diet impacts development. Breastfed infants...
have been shown to have lower levels of plasma branched-chain amino acids (isoleucine, leucine, and valine), and urea, as well as higher levels of ketone bodies (acetone), acetate, and myo-inositol [5]. Additionally, breastfed infants have lower insulin levels than their formula-fed counterparts 2 h after feeding [5]. High levels of serum branched-chain amino acids and/or insulin activates mechanistic target of rapamycin (mTOR), a serine/threonine kinase that is a master regulator of cell metabolism. mTOR Complex 1 (mTORC1) signaling is particularly important for the control of growth and metabolism of bone, skeletal muscle, the central nervous system, the gastrointestinal tract, blood cells, and other organs. For formula-fed infants, enhanced activation of this pathway may have lasting impacts on overall metabolism and potentially health.

More study of human milk and infant metabolism that incorporates metabolic phenotype (measured through the metabolome of blood, urine, and feces), gut microbial composition and function, as well as genetic (and epigenetic) data will help us understand the purpose of specific milk components, the individual responses to diet, as well as how diet and genetics work together with the gut ecosystem to guide cognitive and metabolic development.

References

2 Goehring KC, Marriage BJ, Oliver JS, et al: Similar to those who are breastfed, infants fed a formula containing 2′-fucosyllactose have lower inflammatory cytokines in a randomized controlled trial. J Nutr 2016;146:2559–2566.