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Birth of the Infant Gut Microbiome: Moms Deliver Twice!

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Abstract

The infant gut is rapidly colonized by microbes shortly after birth. In this issue of *Cell Host & Microbe*, Bäckhed et al. (2015) shed new light on the assembly of the infant gut microbiome early in life, and how diet and delivery mode shape this community in a western human population.

After the relative sterility of the uterus, exposure at birth and to the environment results in a rapid colonization of the gut by microbes. Several studies have described this early community assembly (Subramanian et al., 2014; Yatsunencko et al., 2012), and now Bäckhed et al. (2015) analyze the microbiome of a large cohort of Swedish infants to show how specific species in this community colonize the host. By sampling the gut microbiome of these infants and their mothers through the first year of life, the authors identify a number of features contributing to this early assembly. Using shotgun metagenomic sequencing, the authors constructed MetaOTUs (Operational Taxonomic Units [OTUs]), representing functional and taxonomic information from whole genomes, assembled into over 5,500 different bacterial or archaeal genomes. Using this wealth of information, the authors made several key discoveries.

First, while delivery mode has been described as a prime difference in shaping the gut microbiome shortly after birth (Dominguez-Bello et al., 2010), Bäckhed et al. (2015) identified strain-specific links between the mother's fecal microbiome and the infant's microbiome early in life. This link is broken more frequently in children born by cesarean section, and it appears that vaginal delivery provides a source of key gut microbes to the infant gut, not from the vagina, but via a fecal-oral route, in agreement with strain-specific typing methods used in previous studies (Makino et al., 2013; Tannock et al., 1990). Surprisingly, this serves as a way to promote the inoculation of key gut microbes such as *Bifido-bacterium longum*, which is linked with beneficial immune responses early in life (Huda et al., 2014). Bäckhed et al. (2015) showed how vaginal delivery, by comparison to cesarean birth, reduced the stochasticity in the assembly of the neonate gut microbiota. While differences between cesarean and vaginally delivered infants decreased over the course of the first year of life, the gut microbiota of cesarean section-born infants was more heterogeneous as a population than vaginally delivered infants.

After birth, infants fed mother's milk had comparatively reduced alpha diversity (diversity within a sample), as a result of the arsenal of tools that human milk provides to modulate the infant gut microbiota including soluble immunoglobins, lactoferrin, lysozyme as well as an array of structurally complex milk glycans (Pacheco et al., 2015). Bäckhed and coworkers revealed the influence of milk glycans by observing a unique enrichment of specific functional pathways needed to consume these glycans in breast-fed infants. Interestingly, formula-fed infants had more diverse gut microbial communities, but this was typified by higher populations of *Clostridium*, *Franulicatella*, *Citrobacter*, *Enterobacter*, and *Bilophila* relative to breast-fed infants and, functionally, these infants hosted higher proportions of antibiotic resistance genes, especially from γ -*Proteobacteria*. This suggests that there may be previously unconsidered benefits from breastfeeding; including the possibility to reduce exposure to populations of microbes that contribute to the abundance of antibiotic resistance.

As the infants aged, these gut carbohydrate consumption pathways changed to reflect changes in dietary substrates. Over time, with increasing dietary complexity at 12 months of age, the metabolic networks in the gut of these infants similarly increased in complexity as the number of taxa increased. However, in a surprising development, it was the cessation of breastfeeding, rather than introduction of novel foods, that coincided with the transition to a more "adult-like" microbiome.

Despite the increasing understanding of how host-microbe interactions in the gut shape so many aspects of human development, it is still surprising to observe a concerted process that facilitates the inter-generational transfer of microbes from mother to infant. Further, the active suppression of community diversity by the constellation of microbially active factors in breast milk represents an interesting evolutionary model on a guided process of gut colonization. Given how western lifestyles such as formula feeding, a highly processed diet, antibiotic use, sanitized water, and waste disposal have likely changed the composition of human gut microbiomes, it is especially timely to consider how that early gut microbiome is passed from one generation to the next. Indeed, Bäckhed et al. (2015) ponder, how this early relationship contributes to the "priming" of the gut microbiome, and how trajectories established in early life may shape later gut microbial populations—questions especially pertinent given the increasing prevalence of "western" diseases such as atopy and allergy. How a healthy microbiome is established with potentially life-long consequences is just one more lesson we clearly need to learn from our Mothers.

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