Evidence of horizontal gene transfer between human maternal microbiome and infant gut microbiome

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Researchers have discovered a new mode of vertical mother-to-infant microbiome transmission, where microbes in the maternal gut shared

genes with microbes in the infant gut during the perinatal period starting immediately before birth and extending thought the first few weeks after birth. This horizontal gene transfer allowed maternal microbial strains to influence the functional capacity of the infant microbiome, in the absence of persistent transmission of the microbial strains themselves.

Such a large-scale integrative analysis, presented December 22 in the journal *Cell*, provides a series of high-resolution snapshots of gut colonization dynamics that influence infant development both before and after birth.

"This is the first study to describe the transfer of mobile genetic elements between maternal and infant microbiomes," says senior study author Ramnik Xavier of the Broad Institute of MIT and Harvard. "Our study also, for the first time, integrated gut microbiome and metabolomic profiles from both mothers and infants and discovered links between gut metabolites, bacteria and breastmilk substrates. This investigation represents a unique perspective into the co-development of infant gut microbiomes and metabolomes under the influence of known maternal and dietary factors."

Gut bacteria promote the maturation of the immune system in part through the production of microbial metabolites. The development of the infant gut microbiome follows predictable patterns, starting with transmission of microbes from the mother at birth. In addition to immune system maturation, microbial metabolites also influence early cognitive development.

The perinatal period represents a critical window for cognitive and immune system development, promoted by maternal and infant gut microbiota and their metabolites. Nevertheless, the co-development of microbiomes and metabolomes during the perinatal period and the determinants of this process are not well understood.

To address this knowledge gap, Xavier and his colleagues tracked the co-development of microbiomes and metabolomes from late pregnancy to one year of age using longitudinal multi-omics data from a cohort of 70 mother-infant dyads. They discovered large-scale mother-to-infant interspecies transfer of mobile genetic elements, frequently involving genes associated with diet-related adaptations.

Infant gut metabolomes were less diverse than maternal metabolomes but featured hundreds of unique metabolites and microbe-metabolite associations not detected in mothers. Metabolomes and serum cytokine signatures of infants who received regular, but not extensively hydrolyzed, formula were distinct from those of exclusively breastfed infants.

"The infant gut harbored thousands of unique metabolites, many of which were likely modified from breastmilk substrates by gut bacteria," says Tommi Vatanen, co-first author on the study along with Karolina Jabbar, both of the Broad Institute of MIT and Harvard. "Many of these metabolites likely impact immune system and cognitive development."

Pregnancy was associated with an increase in steroid compounds, including gonadal hormone derivatives and intermediates of bile acid biosynthesis, several of which were independently linked to impaired glucose tolerance. Although infant gut metabolomes were less diverse than maternal metabolomes, the researchers detected more than 2,500 infant-unique metabolomic features. Moreover, they identified numerous infant-specific associations of bacterial species and fecal metabolites, including neurotransmitters and immune modulators.

"We were surprised to find that maternal gut bacteria that were rarely observed in infants contributed to the infant gut microbiome structure," says Xavier. "We also found evidence that prophages—dormant bacteriophages, or viruses that reside on bacterial genomes—contribute

to the exchange of mobile genetic elements between maternal and infant microbiomes."

The authors say that the maternal microbiome may shape the infant gut microbiome through horizontal gene transfer, apart from classical vertical transmission of strains and species. Moreover, the identification of distinctive metabolomic profiles and microbe–metabolite interactions in the infant gut constitutes a platform for further study of microbial contributions to infant development.

One study limitation was that the researchers did not consider changes in diet and lifestyle between pregnancy and the postpartum period, which may have affected microbiome and metabolome alterations. In future studies, they plan to further explore linkages between bacteria and metabolites and investigate strain-specific bacterial metabolic output using isolated bacteria in vitro.

"Taken together, our integrative analysis expands the concept of vertical transmission of the gut microbiome and provides new insights into the development of maternal and infant microbiomes and metabolomes during late pregnancy and early life," Xavier says.

More information: Ramnik J. Xavier, Mobile genetic elements from the maternal microbiome shape infant gut microbial assembly and metabolism, *Cell* (2022). DOI: 10.1016/j.cell.2022.11.023. www.cell.com/cell/fulltext/S0092-8674(22)01467-2

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