A mother's genes can influence the bacteria in her baby's gut

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Credit: Vera Kratochvil/Public Domain

Researchers at UC Davis have found that a gene, which is not active in some mothers, produces a breast milk sugar that influences the

development of the community of gut bacteria in her infant. The sugars produced by these mothers, called "secretors," are not digested by the infant, but instead nourish specific bacteria that colonize the babies' guts soon after birth.

Mothers known as "non-secretors" have a non-functional fucosyltransferase 2 (FUT2) gene, which alters the composition of their breast milk sugars and changes how the microbial community, or microbiota, of their infants' guts develop.

The research may have applications in a clinical setting for protecting premature infants from a range of intestinal diseases including necrotizing enterocolitis (NEC), a condition that is the second most common cause of death among premature infants in the United States.

The researchers emphasized that the finding does not suggest that breast milk from mothers without an active copy of the gene is less nourishing or healthy. Rather, it conveys the subtle and elegant choreography of one part of the human microbiome: The relationships between the mothers' genetics, the composition of her breast milk and the development of her infant's gut microbiota. It also reveals clues for enriching desirable bacteria in populations at risk of intestinal diseases—such as preemies.

"In no way is the nonsecretor mother's milk less healthy, and their babies are at no greater risk," said David Mills, Peter J. Shields Endowed Chair in Dairy Food Science at UC Davis and senior study author. "What this work does show us is that the mother's genotype matters, and that it influences the breast milk, which clearly drives the establishment of microbes in the intestines of their babies."

The research examining the differences in infant gut microbial populations arising from differences in human milk oligosaccharides (sugars), "Maternal Fucosyltransferase 2 Status Affects the Gut

Bifidobacterial Communities of Breastfed Infants," is published online today in the journal *Microbiome*, a BioMed Central journal.

Varieties of *Bifidobacterium* inhabit the gastrointestinal tracts and mouths of mammals and are one of the major genera of bacteria that make up the microbial community of the infant colon. The relationship between human genetics, breast milk and *Bifidobacterium* appears to have developed throughout mammalian evolution.

Development of a healthy gut microbiota can have a lifelong effect on health, and early intervention in the establishment of that microbiota could have lifelong positive effects: The early establishment of bifidobacteria has been shown to be associated with improved immune response to vaccines, development of the infants' immature immune system, and protection against pathogens.

Bifidobacterium are known to consume the 2'-fucosylated glycans (sugars) found in the breast milk of women with the fucosyltransferase 2 mammary gene. The study found that, on average, *Bifidobacterium* were established earlier and more frequently in infants fed by women with an active copy of the gene, the secretors, than without one, the non-secretors.

The authors found that the intestinal tracts of infants fed by non-secretor mothers are delayed in establishing a bifidobacteria-dominated microbiota. The delay, the authors said, may be due to difficulties in the infant acquiring a species of bifidobacteria that is geared toward consuming the specific milk sugar delivered by the mother.

The research was conducted using milk samples from 44 mothers in the UC Davis Foods for Health Institute Lactation Study and fecal samples from their infants at four different time points. The researchers determined the secretor status of the mothers: 12 were non-secretor and

32 were secretor mothers. They also measured the amount and type of breast milk sugars left over in the infant's feces, and measured the amount of lactate (a beneficial molecule produced by bifidobacteria) in the infant's feces.

The researchers determined that more infants fed by secretor mothers had high levels of bifidobacteria—60 percent of infants versus 37.5 percent at day 6 and 80 percent versus 50 percent at day 120—and that infants who had more bifidobacteria had lower amounts of milk sugars left over and higher amounts of lactate in their feces.

One question that remains is whether this pattern holds true in infants living in other places.

"We are beginning to observe that infants from different parts of the world have different patterns of colonization by microbes," said lead study author Zachary T. Lewis, a postdoctoral fellow.

"The types and levels of bacteria encountered by infants in developing countries is different from the types and levels of bacteria encountered by the babies in our UC Davis cohort, and that might account for some of the differences," he said.

Maternal secretor status is likely only one of the many factors that influence the infant gut microbiota, Lewis said. The researchers will explore this question further in future studies.

The researchers said that understanding the mechanism behind the observed secretor/non-secretor differences may prove critical to compensating for it in situations where the infants are vulnerable, such as by providing carefully chosen pre- or probiotics. For example, prebiotics and probiotics frequently are given to premature infants to protect them against NEC, which causes portions of the bowel to

necrotize, or die.

"This work significantly advances our efforts to decipher how human milk amazingly orchestrates colonization of the infant gut by helpful bacteria, which then protects and guides intestinal development in the early stages of life. Understanding this incredible sequence of events will provide examples for how to repair this process where it has been disrupted, such as in premature infants or colicky babies," Mills said.

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