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Researchers get important glimpse into microbiome development in early life

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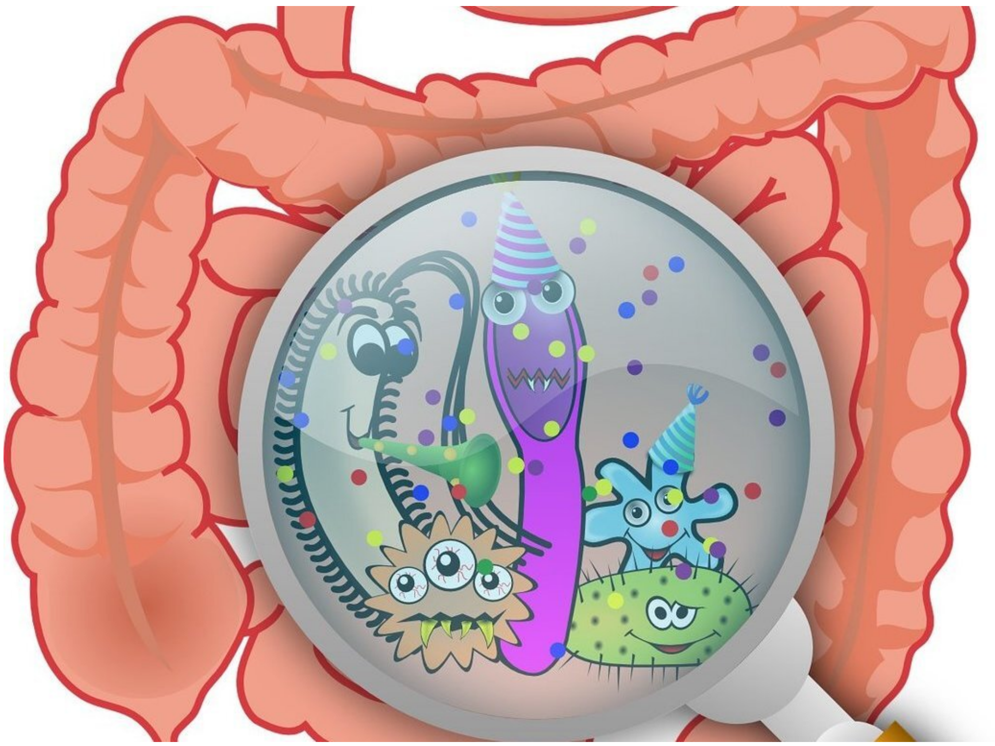

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A team of researchers at Children's Hospital of Philadelphia (CHOP) has characterized how the gut microbiome develops in the first hours of infancy, providing a critical baseline for how changes in this environment can impact health and disease later in life. The findings were published online by the journal *Nature Microbiology*.

While researchers understand the important connection between the many species of bacteria in the gut microbiome and human health, how these species emerge in infancy and what functions they serve are not fully understood.

"Eventually, the gut in children will hold hundreds of different species of bacteria, but at birth, there might only be 10 or fewer species," said Kyle Bittinger, Ph.D., the Analytics Core Director of the Microbiome Center at CHOP and first author of the study. "We wanted to understand why those particular bacteria are the first to emerge and what they are doing in those first hours of life."

The study team focused on three species of bacteria—Escherichia coli, Enterococcus faecalis, and Bacteroides vulgatus—because to date those species have been observed in the highest number of babies. They analyzed the genomes of these bacteria to determine why they are growing in infants. Additionally, the team characterized the proteins and metabolites, or small molecules, that were present in the microbiome at this stage of development.

One of the challenges for collecting this information is that for the first several hours of life, any DNA collected from a stool sample is not from the bacteria but from the infant itself. The researchers did not see bacteria emerge in detectable concentrations until the infants were about 16 hours old.

The study team found evidence that the initial environment of the gut microbiome is anaerobic, contrary to the prevailing model which holds that the gut becomes anerobic only after bacteria grow and consume oxygen. The evidence came from observing the order in which amino acids were consumed by bacteria.

The study team also observed that metabolite levels were generally consistent with the detection of bacteria. Molecules typically produced by gut bacteria, like acetate and succinate, went up in samples where bacteria were detected. Additionally, the levels of select proteins went down in samples containing bacteria, suggesting that bacteria might have been consuming those proteins to promote growth.

Analysis of the three bacterial species studied in these infants revealed that multiple strains of each bacterium were already emerging.

"With the information we have, as we continue to follow these infants, we can track them and see how long these early strains of bacteria linger," Bittinger said. "We can then see the consequences of this initial chemical activity in later samples and hopefully pinpoint early changes that might impact health later in childhood."

The researchers hope to use the study findings to determine how the development of the gut microbiome may influence excess weight gain. The infants involved in this study will be followed through the first two years of life. Additionally, all 88 infants involved in the study are African American, a population for whom childhood obesity is a growing concern.

"There are remarkably few studies that have looked at infant growth patterns in African Americans," said Babette Zemel, Ph.D., the Associate Program Director of the Center for Human Phenomic Science, the Director of the Nutrition and Growth Laboratory, an academic investigator with the Healthy Weight Program at CHOP, a research professor of pediatrics at the Perelman School of Medicine at the University of Pennsylvania, and senior co-author of the study. "With this important first piece in the puzzle, we can follow these healthy term infants and learn what a normal growth pattern looks like so that, in the future, we may be able to intervene when changes in the microbiome can adversely affect children."

More information: Kyle Bittinger et al, Bacterial colonization reprograms the neonatal gut metabolome, *Nature Microbiology* (2020). DOI: 10.1038/s41564-020-0694-0

Provided by Children's Hospital of Philadelphia