Breast vs. bottle feeding in rhesus monkeys

September 4 2014, by Carole Gan

(Medical Xpress)—Infant rhesus monkeys receiving different diets early in life develop distinct immune systems that persist months after weaning, a study by researchers from UC Davis, the California National Primate Research Center (CNPRC) at UC Davis and UC San Francisco has shown.

The study, which compares breast- and bottle-fed infants, appears online today (Sept. 3) in *Science Translational Medicine*.

While the researchers expected different diets would promote different intestinal bacteria (microbiota), they were surprised at how dramatically these microbes shaped immunologic development. Specifically, breast-fed macaques had more "memory" T cells and T helper 17 (TH17) cells, which are known to fight salmonella and other pathogens.

These differences persisted for months after the macaques had been weaned and placed on identical diets, indicating that variations in early diet may have long-lasting effects.

"We saw two different immune systems develop: one in animals fed mother's milk and another in those fed formula," said Dennis Hartigan-O'Connor, a CNPRC scientist in the Infectious Diseases Unit and Reproductive Sciences and Regenerative Medicine Unit, and an assistant professor in the Department of Medical Microbiology and Immunology at UC Davis.

Lasting differences

"But what's most startling is the durability of these differences. Infant microbes could leave a long-lasting imprint on immune function," he said.

Previous research has highlighted the relationship between breast milk, microbiota and the developing immune system. For example, sugars in breast milk help grow specific bacteria, which in turn support certain immune cells. This new study is an important step towards understanding how these separate pieces link together and how they might influence the immune systems response to infections or vaccinations.

Macaques are born with virtually no TH17 cells, and must develop them during the first 18 months of life. Hartigan-O'Connor and other researchers have noted that some macaques develop large TH17 populations, while others have few of these cells. This could profoundly affect the animals' ability to fight infection, particularly SIV, the simian strain of HIV.

To understand this variability, the investigators followed six breast- and six bottle-fed rhesus macaques from age five months to 12 months. At

six months, they found significant differences in the two groups' microbiota.

Diverse microbiota

Specifically, the breast-fed macaques had larger numbers of the bacteria prevotella and ruminococcus, while the bottle-fed group had a greater abundance of clostridium. Overall, the microbiota in breast-fed macaques was more diverse than in the bottle-fed group.

The big surprise came when examining their immune systems. By 12 months, the two groups showed significant contrasts, with the differences centered on T cell development. The breast-fed group had a much larger percentage of experienced memory T cells, which are better equipped to secrete immune defense chemicals called cytokines, including TH17 and interferon-producing cells.

"This is the first time researchers have shown that these immunologic characteristics may be imprinted in the first new months of life," said Amir Ardeshir, the study's first author. "Our study suggests that the gut microbiota present in early life may leave a durable imprint on the shape and capacity of the immune system, a programming of the system if you will."

Further investigation may have identified chemicals that drive these differences. For example, arachidonic acid, which stimulates the production of TH17 cells and is found in macaque breast milk, was tightly linked to TH17 cell development. Previous studies have suggested it can influence T cell development. The researchers caution that these chemicals must be tested in larger studies to understand their effects.

While this research provides a fascinating window into immune cell development in macaques, Hartigan-O'Connor cautions that it doesn't

prove the same mechanisms exist in people. The lab is planning similar studies in humans to test that hypothesis. In addition, this study does not prove a link between breastfeeding and better health.

"There's a developmental shape to the immune system that we don't often consider," Hartigan-O'Connor said. "It's dramatic how that came out in this study. There's a lot of variability in how both people and monkeys handle infections, in their tendency to develop autoimmune disease, and in how they respond to vaccines. This work is a good first step towards explaining those differences."

Provided by UC Davis