Breastfeeding is good for yet another reason, researchers discover

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New study finds antibodies in breast milk help shape newborns' immune systems. (Credit: iStockphoto)

A mother's breast milk supports immune responses in her newborn that help the infant's gut become a healthy home to a mix of bacterial species, thanks in part to newly identified antibodies from the mother, according to a study by UC Berkeley researchers.

Scientists believe the gut is sterile and bacteria -free at birth, when suddenly the infant is exposed to bacteria from the wider world. The body learns to tolerate many bacterial species, and the relationship is regarded as mutually beneficial—in exchange for free meals, gut bacteria aid digestion, help prevent infection and enhance immune function.

The new study sheds light on how immune antibodies from breast milk interact with the just-forming immune system of the newborn to help shape lifelong immune responses that are key for establishing boundaries and balance between gut microbes and the mammalian host. If this balance fails to become established or later falters, chronic inflammatory conditions, such as Crohn's disease or ulcerative colitis, may result.

A healthy relationship between host and bacteria is deemed to be "commensal," essentially meaning that neither is harmed.

In their studies of mice, Gregory Barton, the Class of '36 Chair in the Department of Molecular and Cell Biology, and post-doctoral fellow Meghan Koch, found that three specific types of antibodies, called Immunoglobulin A (IgA), Immunoglobulin G2b (IgG2b), and immunoglobulin G3 (IgG3), are present in breast milk and promote peace between the immune system and common gut-dwelling bacteria by putting the damper on inflammatory responses.

"This study provides real evidence that breast milk is important for a newborn's health," said Koch, who designed and conducted most of the experiments. "Breastfeeding helps to instruct the newborn's immune system on how to appropriately respond to non-pathogenic bacteria, many of which may reside in the gut for a lifetime."

Barton, Koch and their colleagues published their findings in the May 5, 2016 issue of the journal *Cell*.

IgA antibodies in milk had been identified earlier, but thought mainly to function to fight pathogens and to prevent bacteria from penetrating the gut wall and entering the circulation. IgG antibodies had been known to enter the infant in utero, and to help fight infection.

There are other components in breast milk known to shape the composition of the gut microbiota. As evidence for a long and evolving relationship between mammals and gut microbes, scientists

previously identified sugars in breast milk that commensal bacteria can derive energy from, but which are indigestible to the infant.

In addition, there are other molecules in breast milk, made by the mother's immune system, that promote tolerance for commensal microbes while keeping them in the gut and away from the rest of the body.

The UC Berkeley scientists detected IgG2b- and IgG3-triggered immune responses directed toward commensal bacteria in two-week-old mice. These responses waned after three weeks, and grew stronger again in older mice. "The presence of these antibodies in young mice suggested that, like IgA, they are maternally derived," Koch said.

When she genetically eliminated maternal-derived IgG2b, IgG3 and IgA antibodies, the mice were more susceptible to inflammatory responses caused by commensal microbes.

Barton said the distinctive immune responses by the newborn's immature immune system were "surprising." The researchers found that the antibody responses against the gut microbiota did not depend on arousing the T helper cells that are the foot soldiers of the evolutionarily advanced "adaptive" immune system, but instead relied on signaling by the earlier-evolved, innate immune system.

The immune responses may serve to set up the immune system to eliminate commensal bacteria that might escape the gut and enter the circulation, without triggering an overwhelming inflammatory response, Barton said.

"What we have learned is that it is important for the immune system to recognize and to make an immune response to microbiota in the gut, but this response is qualitatively different than the immune response to pathogens," Barton said.

"We identified breast milk as a primary source of IgG antibodies that are directed against commensal bacteria early in life and demonstrated that this maternally acquired, anti-commensal IgG helps dampen T-helper-cell-driven immune responses against newly encountered microbes."

"While our study demonstrates the importance of commensal-specific IgG antibodies when acquired maternally, it is certainly possible that they serve important functions in adults, as well," he added.

More information: *Cell*, Koch et al.: "Maternal IgG and IgA Antibodies Dampen Mucosal T Helper Cell Responses in Early Life" www.cell.com/cell/fulltext/S0092-8674(16)30500-1 , DOI: 10.1016/j.cell.2016.04.055

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