Antibodies in breast milk help newborn mice tolerate good gut microbes

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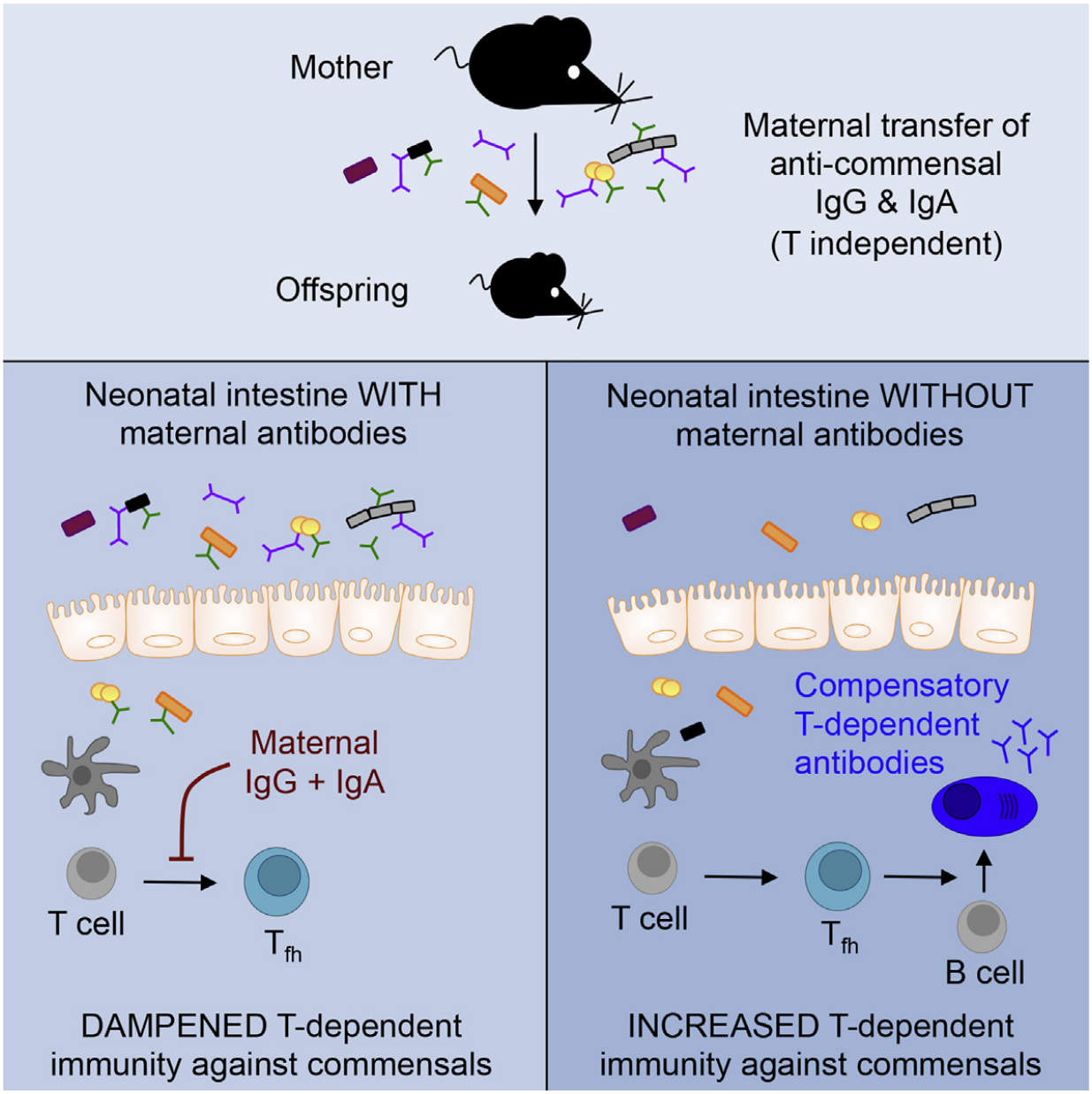

This visual abstract depicts how maternally acquired, commensal-specific IgG antibodies coordinate with IgA to limit mucosal T cell responses and reinforce intestinal immunity in mouse neonates. Credit: Koch et al./Cell 2016

From the moment of birth, a newborn's gut is colonized by a diverse array of microbes that aid digestion and boost immunity. But it has not been clear how the newborn's immune system learns to tolerate the majority of these foreign species rather than attacking them as hostile invaders. In a mouse study published May 5 in *Cell*, researchers reveal that immunoglobulin G (IgG) antibodies acquired from breast milk help dampen immune responses to newly acquired microbes early in life.

Abnormal immune responses that reduce tolerance to beneficial gut microbes can lead to inflammatory bowel disorders such as ulcerative colitis and Crohn's disease. Previous studies have suggested that immunoglobulin A (IgA) antibodies supplied by breast milk are primarily responsible for teaching the neonatal immune system to tolerate gut microbes early in life. By contrast, maternally acquired immunoglobulin G (IgG) antibodies are mainly thought to be critical for protecting newborns against a variety of pathogens.

The *Cell* paper challenges this dogma, revealing that IgG antibodies from breast milk establish appropriate immune responses to a diverse array of gut microbes in newborns. "The findings show that the antibody response to the gut microbiota is more complex than previously appreciated and reveal a broader function for maternal IgG antibodies in helping to establish proper immune function early in life," says study first author Meghan Koch of the University of California, Berkeley.

The researchers found that healthy mice produce IgG antibodies that recognize a broader spectrum of bacteria than do IgA antibodies,

suggesting that IgG antibodies expand recognition of gut microbes by the immune system. Additional experiments revealed that IgG antibodies were present in mice as early as 2 weeks of age and were acquired from mothers after birth rather than in the uterus. These antibodies played a critical role in dampening immune response against gut microbes in newborn mice.

To expand on this work, the researchers plan to investigate how IgG antibodies establish appropriate immune responses to gut microbes. They will also examine the role of IgG antibodies in long-term intestinal health. For example, it's possible that infants breastfed by antibody-deficient mothers are more susceptible to intestinal inflammation, but it is too early to tell if this is the case.

"The findings suggest that profiling the antibody response in humans may be useful for characterizing the immune response to gut microbes," says senior study author Gregory Barton of the University of California, Berkeley. "This information could then be used to assess an individual's risk for inflammatory intestinal disorders and to implement therapeutic interventions at early disease stages."

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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