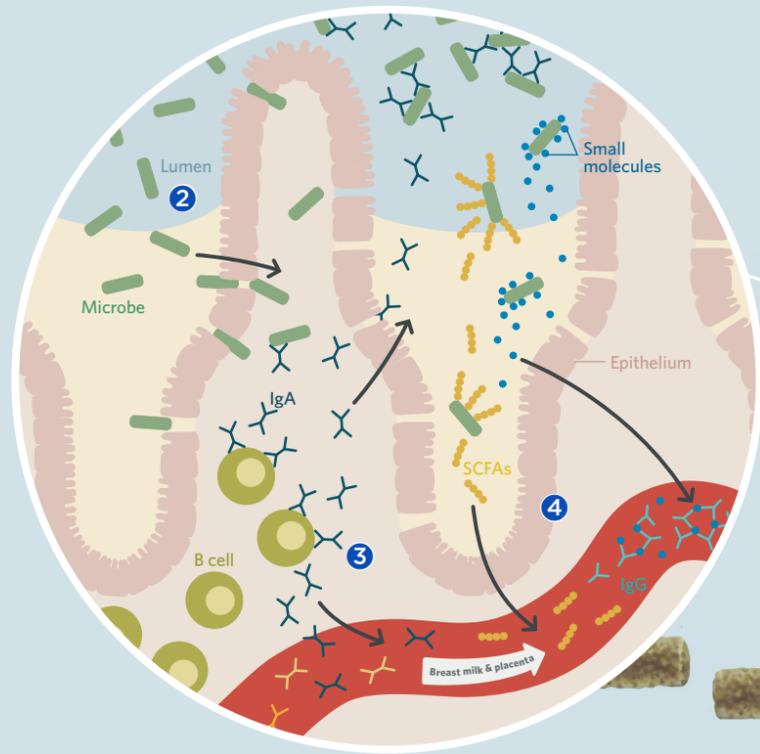


THE MANY EFFECTS OF MICROBES ON OFFSPRING

During pregnancy, the body is subject to numerous changes. The composition of the gut microbiome shifts, metabolism changes, and the gut epithelium becomes more permeable. These alterations facilitate interactions between the immune system and gut microbiota, leading to the production of microbe-specific antibodies that are transferred across the placenta to the developing fetus, and later via the milk to the nursing offspring.

The maternal microbiota, and the external factors that shape it, influence which immunomodulatory metabolites are produced and transferred to offspring, where they support immune education and otherwise influence development, helping to protect offspring from allergic asthma, metabolic syndrome, and likely other inflammatory diseases later in life. After birth, maternally derived antibodies help newborns tolerate the bacterial colonization of their own GI tracts, while simultaneously protecting them from enteric and systemic infections.



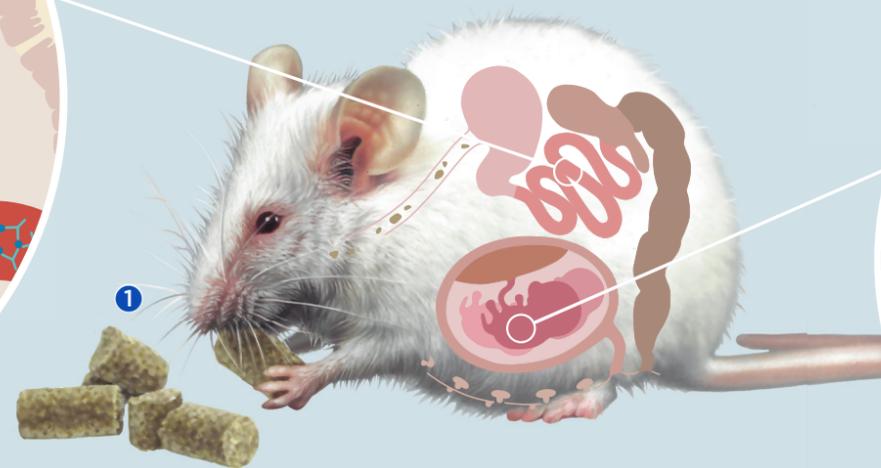
PREGNANT MOUSE

- 1 External factors affect the composition of the maternal microbiota (for example, diet, antibiotics, and other drugs).
- 2 The permeability of intestinal epithelium increases during pregnancy, facilitating interactions between the microbiota and a mother's immune system.
- 3 The maternal microbiota shapes the repertoire of commensal-targeting antibodies, which cross the placenta and are transferred in breast milk to her offspring.
- 4 Gut microbes produce various metabolites, including short-chain fatty acids (SCFAs) and immunomodulatory compounds, some of which are bound by antibodies and transferred to the fetus.



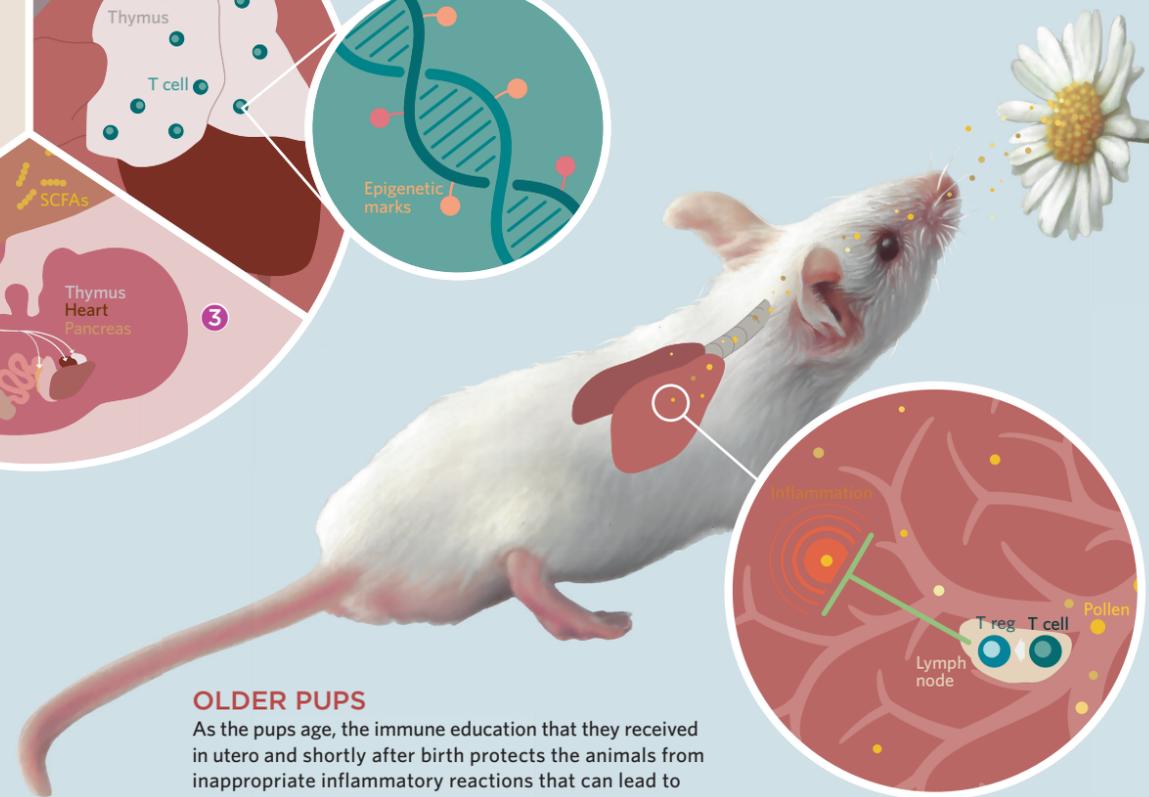
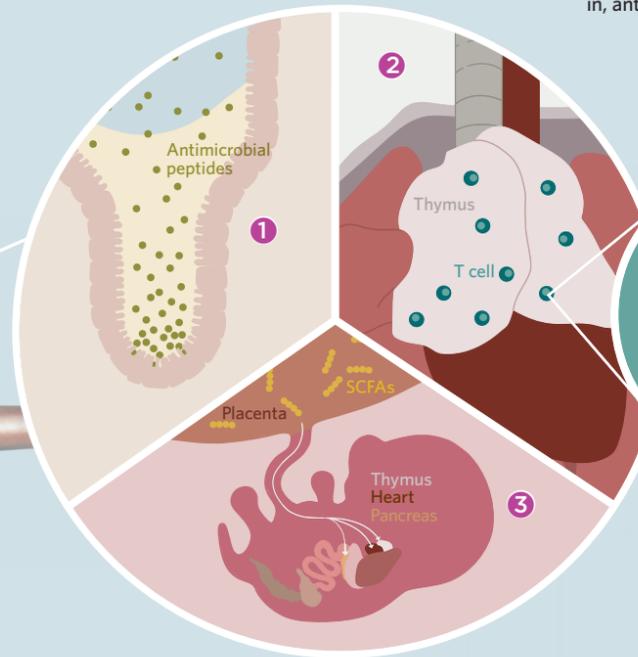
NEONATES

- 1 Commensal-targeting antibodies promote tolerance during bacterial colonization, largely by keeping gut bacteria inside the intestinal lumen or ushering them back in when they do escape.
- 2 If microbes that escape the intestinal lumen are not immediately ushered back in, antibodies from mom tag them for efficient elimination to limit inflammation.



FETUS

- 1 The antibody-mediated transfer of metabolites increases antimicrobial peptide production, which strengthens the epithelial barrier to prepare the gut for microbial colonization.
- 2 SCFAs transferred from mom travel to the fetal thymus, where they trigger epigenetic changes that nudge T cells toward becoming regulatory as opposed to inflammatory later in life.
- 3 SCFAs also have various effects on the heart, pancreas, thymus, and other organs.



OLDER PUPS

As the pups age, the immune education that they received in utero and shortly after birth protects the animals from inappropriate inflammatory reactions that can lead to allergy, metabolic syndrome, or other health consequences.