

Transmaternal Helicobacter pylori exposure reduces allergic airway inflammation in offspring through regulatory T cells **BACKGROUND** Transmaternal exposure to tobacco, microbes, nutrients, and other environmental factors shapes the fetal immune system through epigenetic processes. The gastric microbe *Helicobacter pylori* represents an ancestral constituent of the human microbiota that causes gastric disorders on the one hand and is inversely associated with allergies and chronic inflammatory conditions on the other. **OBJECTIVE** Here we investigate the consequences of transmaternal exposure to *H. pylori* in utero and/or during lactation for susceptibility to viral and bacterial infection, predisposition to allergic airway inflammation, and development of immune cell populations in the lungs and lymphoid organs. **METHODS** We use experimental models of house dust mite- or ovalbumin-induced airway inflammation and influenza A virus or *Citrobacter rodentium* infection along with metagenomics analyses, multicolor flow cytometry, and bisulfite pyrosequencing, to study the effects of *H. pylori* on allergy severity and immunologic and microbiome correlates thereof. **RESULTS** Perinatal exposure to *H. pylori* extract or its immunomodulator vacuolating cytotoxin confers robust protective effects against allergic airway inflammation not only in first- but also second-generation offspring but does not increase susceptibility to viral or bacterial infection. Immune correlates of allergy protection include skewing of regulatory over effector T cells, expansion of regulatory T-cell subsets expressing CXCR3 or retinoic acid-related orphan receptor γ , and demethylation of the forkhead box P3 (FOXP3) locus. The composition and diversity of the gastrointestinal microbiota is measurably affected by perinatal *H. pylori* exposure. **CONCLUSION** We conclude that exposure to *H. pylori* has consequences not only for the carrier but also for subsequent generations that can be exploited for interventional purposes.