

[CLS] 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. **[SEP]**