Research 'paves the way' for early interventions to prevent childhood inflammatory diseases

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A study of newborn infants has identified a compound produced by gut bacteria that appears to predispose certain infants to allergies and asthma later in life.

"We have discovered a specific bacterial lipid in the neonatal gut that promotes immune dysfunction associated with allergic asthma and can be used to assess which babies are at risk of developing the disease in childhood" said study senior author Susan Lynch, Ph.D., a professor of medicine at UCSF. "This finding paves the way for early-life gut microbiome interventions to prevent these diseases from developing."

Lynch's lab has previously shown that one-month-old infants with unhealthy gut microbial ecosystems—more like a weedy lot than a well-functioning garden—are at increased risk of developing asthma later in childhood. They have also shown that a specific fatty molecule, or lipid, called 12,13-diHOME, found at high concentrations in the feces of these babies, reduced the number and activity of a key group of immune cells called regulatory T cells (Tregs) that normally suppress allergic inflammation.

In their newest study, published July 22, 2019 in *Nature Microbiology*, research led by MD/PHD candidate Sophia Levan set out to test whether this bacterial molecule might directly drive the risk of asthma and allergy in young infants. First, they showed that injecting 12,13-diHOME into the gut of mice reduced Treg cell numbers in the animals' lungs, and that this molecule alters Treg and other immune cell function at a molecular level.

To understand where this pro-inflammatory lipid was coming from, the

researchers studied the microbial genes present in stool samples from 41 one-month old infants collected as part of the racially and ethnically diverse WHEALS (Wayne County Health, Environment, Allergy and Asthma Longitudinal Study) cohort in Detroit. They found that the number of copies of three bacterial genes for 12,13 DiHOME or the concentration of the lipid itself in the babies' stool samples predicted which infants went on to develop allergy by age two or asthma by age four. They then replicated this finding in the stool samples of an independent cohort of 50 one-month-olds based in San Francisco.

"While these findings need to be replicated in an even larger study group, the fact that these two cohorts collected in demographically different populations in very different cities showed the same results gives us confidence that the association between this bacterial lipid and childhood asthma and allergy risk may generalize to a broader population," Levan said.

The researchers emphasize that 12,13-diHOME is likely just one of many microbial-derived products that contribute to early-life immune dysfunction and susceptibility to childhood allergy and asthma.

"This is likely just one component of a complex microbiome-immune interaction in young infants that promotes allergy and asthma development in childhood," Lynch said. "But it is a first step towards a more mechanistic understanding of the suite of microbial products that increase susceptibility to allergies and asthma during childhood."

More information: Elevated faecal 12,13-diHOME concentration in neonates at high risk for asthma is produced by gut bacteria and impedes immune tolerance, *Nature Microbiology* (2019). DOI: 10.1038/s41564-019-0498-2