Early childhood gut microbiome shapes immune defence

A study in children living in Finland, Russian Karelia and Estonia supports the hypothesis that the early childhood gut microbiota plays a significant role in the development of immune-mediated disorders, such as type 1 diabetes and allergies.

A University of Helsinki research group led by Professor **Mikael Knip**, working together with a Broad Institute research group led by Professor **Ramnik Xavier**, has found that if a child's intestinal microbiome during the first years of life consists of species with low immunostimulatory capacity, his or her immune defence system will not develop normally.

This observation was made in the DIABIMMUNE study coordinated by the University of Helsinki examining the development of immune-mediated diseases in Finland, Russian Karelia and Estonia. These three geographically and genetically relatively similar countries vary greatly in terms of standard of living and prevalence of immune-mediated diseases. For example, type 1 diabetes and certain other immune-mediated disorders are approximately six times rarer in Russian Karelia than they are in Finland. According to the hygiene hypothesis, the increased prevalence of immune-mediated diseases in the Western world has to do with a lack of early microbe contacts, which leads to abnormal maturation of the immune system.

Recent research does indicate that gut microbiota may be a key factor in susceptibility for autoimmune diseases and allergies.

The children in the birth cohort (n=222) of the DIABIMMUNE study were observed from birth until age three, and monthly stool samples were collected to analyse their gut microbiota. The researchers found that the lipopolysaccharides derived from the microbiota in Finnish and Estonian children came from *Bacteroides* microbes, while in children from Russian Karelia, they most commonly came from the *Escherichia Coli* bacteria (*E. Coli*).

The effects of the lipopolysaccharides from *Bacteroides* on the children's innate immunity are weaker than those from *E. Coli*.

The intestinal microbes in Finnish and Estonian children produced lipopolysaccharides more actively than those in Russian children, leading to a relatively large amount of *Bacteroides*-derived lipopolysaccharides, which have a weaker immunostimulatory effect. In animal testing, the lipopolysaccharides produced by *E. Coli* protected genetically susceptible mice from diabetes, unlike those produced by *Bacteroides*.

"These results from the DIABIMMUNE study provide us with new information on the mechanisms through which the gut microbiota can render a person susceptible or resistant to immune-mediated diseases. If the link between the changes in gut microbiota and the development of immune-mediated illnesses can be confirmed in future studies, we may be able to develop new, effective ways to prevent chronic immune-mediated diseases in persons who are at risk for such disorders," says Professor Mikael Knip.

In addition to researchers from the University of Helsinki and the Broad Institute, the study involved researchers from the Helsinki University Hospital, Aalto University, the University of Turku, the Finnish National Institute for Health and Welfare, the University of Tartu, Petrozavodsk State University, the Ministry of Health and Social Development in the Republic of Karelia as well as the Novartis Institute for Biomedical Research. The primary funders for the study were the EU (7^{th} framework programme), the Academy of Finland and the Juvenile Diabetes Research Foundation. The research results have been published in the internationally esteemed *Cell* publication series.

“We have long been aware of the fact that children who live on farms have fewer allergies than other children. Early exposure to certain micro-organisms seems to benefit the immune system and increase protection against allergies and autoimmune disorders," explains doctoral student Tommi Vatanen from the Department of Information and Computer Science, Aalto University and the Broad Institute of MIT and Harvard.