GI tract bacteria may protect against autoimmune disease

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This image shows Dr. Ulrike Rolle-Kampczyk, Helmholtz Association of German Research, during the analysis of a coupled system of a Acquity-UPLC with a Q-Trap mass spectrometer. Credit: Photo: André Künzelmann/UFZ

Early life exposure to normal bacteria of the GI tract (gut microbes) protects against autoimmune disease in mice, according to research published on-line in the January 17 edition of *Science*. The study may also have uncovered reasons why females are at greater risk of autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, and lupus compared to males.

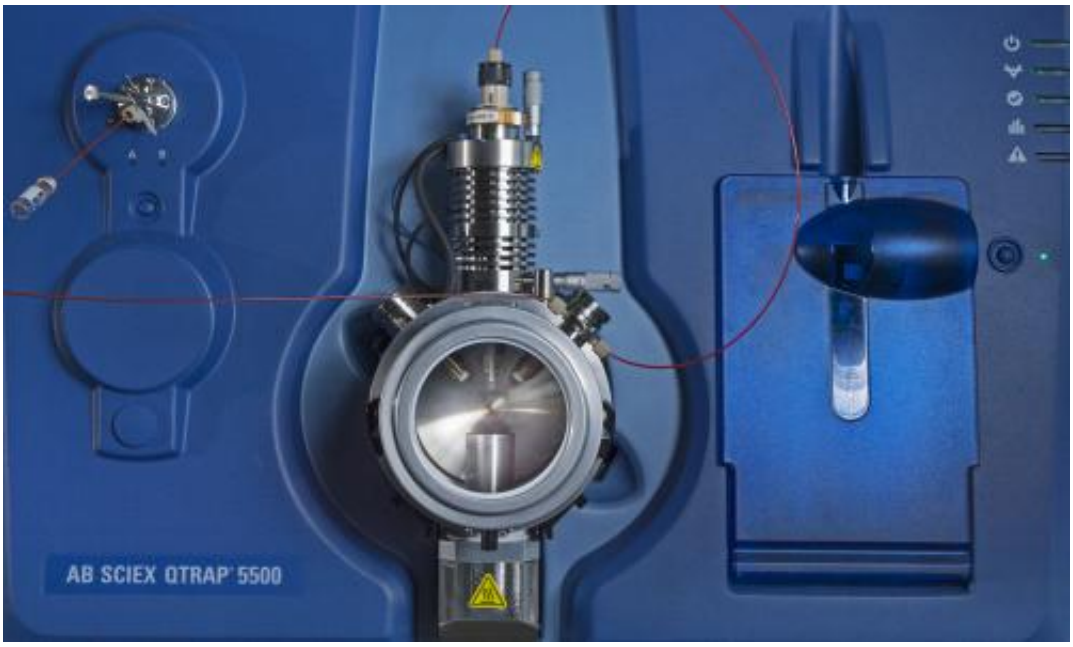
Researchers from The Hospital for Sick Children (SickKids) found that when female mice at high risk of autoimmune (type 1) diabetes were exposed to normal gut bacteria from adult male mice, they were strongly protected against the disease. In this type of mouse strain, more than

85% of females develop autoimmune diabetes due to strong genetic risk factors. In contrast, only 25% of the females developed the disease after they were given normal male gut microbes early in life.

"Our findings suggest potential strategies for using normal gut bacteria to block progression of insulin-dependent diabetes in kids who have high genetic risk," says principal investigator Dr. Jayne Danska. She is Senior Scientist in Genetics & Genome Biology at SickKids and Professor in the Departments of Immunology and Medical Biophysics at the University of Toronto.

A second unexpected finding was the effects of the gut microbe treatments on sex hormones. "We were surprised to see that when young female mice received normal gut microbes from adult males, their testosterone levels rose. We then showed that this hormone was essential for the gut microbe treatment to protect against the disease. It was completely unexpected to find that the sex of an animal determines aspects of their gut microbe composition, that these microbes affect sex hormone levels, and that the hormones in turn regulate an immune-mediated disease," says Dr. Danska.

She adds, "We don't know yet how transfer of male gut microbes into females increases their testosterone, or how this process protects against autoimmunity. This study opens up a new research arena to explore the clinical potential of altering the gut microbe community to prevent or treat immune-mediated diseases."



The consequences of the transplanted intestinal bacteria were examined for the metabolism of mice by mass spectrometry at the Helmholtz Centre for Environmental Research (UFZ) in Leipzig. Credit: Photo: André Künzelmann/UFZ

The hygiene hypothesis

The findings support the 'hygiene hypothesis,' which suggests that the dramatic increase in autoimmune and inflammatory diseases over the past 50 years results from changes in our exposure to microbes. Gut microbes are essential for normal development and training of the immune system, for extracting nutrients from our food, and for protecting us from some infectious diseases. "Our gut microbial community is an essential part of ourselves – bacterial cells outnumber human cells in our bodies by more than ten to one – and we live with them as partners," explains Dr. Danska.

Previous research has shown that children living on farms, exposed to a

denser and more complex microbial environment, have fewer immune-mediated diseases compared to their village or urban-dwelling peers.

Today's publication is the first to identify a difference between normal gut microbes in males and females reared in identical conditions, and to show that transfer of male-sourced gut bacteria protects against autoimmune disease in females with high genetic risk.

"Our findings point to a direct relationship between normal gut microbe composition and prevention of autoimmune disease. From these discoveries we can move on to characterize the relationships between gut microbes, sex hormones, and ways to control unwanted immune responses," says Dr. Danska.

Implications for diabetes and other autoimmune diseases

The researchers' success in preventing type 1 diabetes from developing in high-risk mice suggests that similar approaches may be applicable in preventing and treating other immune diseases, particularly those showing a female sex bias, Dr. Danska says.

More information: Janet G. M. Markle, Daniel N. Frank, Steven Mortin-Toth, Charles E. Robertson, Leah M. Feazel, Ulrike Rolle-Kampczyk, Martin von Bergen, Kathy D. McCoy, Andrew J. Macpherson, Jayne S. Danska (2012): Sex Differences in the Gut Microbiome Drive Hormone-Dependent Regulation of Autoimmunity. SCIENCE, 17 January 2013, DOI: 10.1126/science.1233521

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