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How hormones and microbes drive the gender bias in autoimmune diseases

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Females can mount more powerful immune responses than males, but the flip side of this enhanced protection against infections is a greater risk for autoimmune disorders. Shedding light on the underlying causes of the gender bias in autoimmune diseases, a study published by Cell Press August 22nd in the journal *Immunity* reveals that certain gut microbes prevalent in males can help protect them against type 1 diabetes. The study demonstrates that these microbes cooperate with sex hormones to cause this gender bias and provides an important framework that could lead to better treatments.

"The gender bias in major autoimmune diseases is well known but not well understood," says senior study author Alexander Chervonsky of the University of Chicago. "By studying how microbes cooperate with hormones to affect the immune system, we can identify pathways that can be triggered artificially by drugs or manipulations of gut microbes to interfere with the course of autoimmunity."

Sex hormones are known to play an important role in the gender bias of autoimmune diseases. But studies have shown that environmental influences and other non-hormonal factors also make a difference. For instance, animals that lack gut microbes because they were raised in a germ-free environment do not show a pronounced gender bias in type 1 diabetes, which is generally considered to be an autoimmune disorder. Until now, it has not been clear how hormones and microbes work together to influence the gender bias in type 1 diabetes and other autoimmune diseases.

In the new study, Chervonsky and his team found that microbial communities in male and female mice became different once the mice reached puberty, whereas microbes in females and castrated males were more similar to each other. These results suggest that sex hormones contribute to gender-specific changes in microbial communities. When the researchers raised mice in a germ-free environment and then exposed them to different types of bacteria, they discovered that only certain microbes specifically protected males against type 1 diabetes.

Taken together, the findings suggest that hormones and microbes cooperate with each other to protect males against autoimmune diseases. "Our study has helped to establish the general principles of how hormones and microbes interact with the immune system, which is the first significant step to get to the stage of developing new therapies."

More information: *Immunity*, Yurkovetsky et al.: "Gender bias in autoimmunity is influenced by microbiota." dx.doi.org/10.1016/j.immuni.2013.08.013

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