AUTOIMMUNITY

Gut bacteria keep you healthy

The development of type 1 diabetes in humans and non-obese diabetic (NOD) mice, the mouse model of diabetes, has long been suspected to be influenced by infection. However, the contribution of microorganisms, including commensal bacteria, was not fully understood. Toll-like receptor signalling mediated by the adaptor protein myeloid differentiation primary-response gene 88 (MyD88) is involved in many immune-system functions, including control of responses to commensal bacteria. In this study, the authors investigated the contribution of both MyD88 and microorganisms to the development of diabetes and, surprisingly, observed that commensal bacteria confer protection from disease development.

To examine the role of MyD88 in the development of diabetes, the authors studied a MyD88-deficient NOD mouse strain and observed that, in contrast to MyD88-sufficient NOD mice, MyD88-deficient NOD mice did not develop diabetes when kept in specific pathogen-free conditions. In the MyD88-deficient NOD mice, the lymph nodes that drain the pancreas and intestine had fewer diabetogenic T cells than those from MyD88-sufficient NOD mice, and the few T cells that accumulated showed decreased proliferation and interferon-γ production in response to diabetes-associated peptides. This effect was not observed in T cells from other lymphoid organs and was therefore not systemic. Consequently, the immunosuppressive effect of MyD88 deficiency may be the result of altered responses to bacteria in specific parts of the body, possibly the intestine.

To examine whether the resistance to diabetes development resulted from changes in the responses to intestinal bacteria, the authors treated the MyD88-deficient NOD mice with broad-spectrum antibiotics and observed increased incidence of diabetes. Moreover, MyD88-deficient NOD mice that were raised in germ-free conditions, and therefore completely lacked gut bacteria, had a higher incidence of diabetes and increased levels of pancreatic islet infiltration compared with the MyD88-deficient NOD mice with normal gut flora. Colonization of the germ-free mice with a defined set of normal gut bacteria reduced the incidence of diabetes, which indicates that normal commensal flora might protect against the development of this autoimmune disease.

Interestingly, comparison of the flora from the gut of MyD88-deficient and MyD88-sufficient NOD mice revealed significant differences, which suggests that MyD88 deficiency changes the composition of the gut microbiota. Exposure of the germ-free MyD88-deficient NOD mice to the 'protective' microbiota from the gut of specific pathogen-free MyD88-deficient NOD mice decreased pancreatic islet infiltration by lymphocytes. This result further confirms that commensal gut bacteria have a protective role against type 1 diabetes development that does not depend on MyD88.

This study adds to the beneficial roles that have been ascribed to commensal gut bacteria. Future research will be required to identify the mechanism by which commensal flora can mediate protection, and how this can be used for therapeutic purposes.

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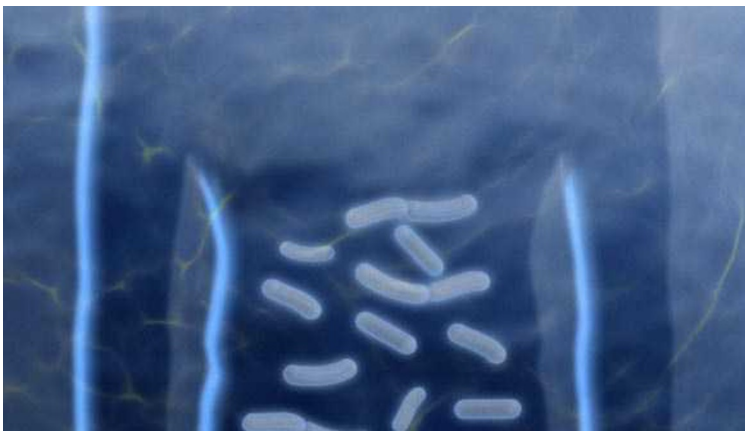

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