DIABETES

Gut microbiota improves dysglycaemia

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Immunization with gut microbiota from diabetic mice can induce an adaptive immune response that protects against insulin resistance and dysglycaemia, according to new research. The investigators, building on previous work in which a high-fat diet (HFD) was found to alter the intestinal immune system in the ileum, hypothesized that the ileal microbiota might provide protection from diet-induced diabetes mellitus.

The team first extracted luminal microbiota from the ileum of mice fed an HFD for 4 weeks to induce diabetes-like symptoms. The luminal microbiota were then subcutaneously injected into recipient mice who were allowed to recover for 35 days before being fed an HFD. After 1 month, mice that were immunized with the ileal extracts had better glucose tolerance than nonimmunized control mice that were also fed an HFD. Moreover, the metabolic parameters (hyperglycaemia, hyperinsulinaemia, glucose intolerance and insulin secretion) observed in HFD-fed mice could be reversed by immunization with the ileal microbiota from diabetic mice.

“Extracts from the dysbiotic intestinal microbiota of diabetic mice prevents the occurrence of dysglycaemia and insulin resistance,” explains lead author Céline Pomié. “This process also protects against the development of gut microbiota dysbiosis induced by a fat-enriched diet.”

Interestingly, glycaemic parameters were unaffected in immunized mice that were fed a normal chow diet, and the effect was not observed in mice

immunized with luminal microbiota from germ-free or antibiotic-treated HFD-fed mice.

Markers of inflammation were only minimally changed in the immunized mice, therefore, the team investigated if the adaptive immune system might mediate the protection from dysglycaemia and insulin resistance.

Proliferation of CD4⁺ and CD8⁺ T cells was enhanced in the lymph nodes and spleens of mice immunized with ileum extracts and fed normal chow for 10 days, compared with nonimmunized mice. The team also transferred immune cells from the lymph nodes of immunized mice to nonimmunized mice, who were then fed a HFD. Remarkably, recipient mice were also protected

from dysglycaemia and insulin resistance, which demonstrated that the adaptive immune system has a fundamental role in this process.

The investigators hope their results will lead to a vaccine to prevent the development of diabetes mellitus and obesity. However, more work still needs to be done as Pomié clarifies, “identification of the specific bacterial determinants for effective immunization and, therefore, the development of new vaccine strategy, is required.”

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