Nature Reviews Endocrinology **10**, 639 (2014); published online 19 August 2014; doi:10.1038/nrendo.2014.148

IMMUNOLOGY

IL-22 AND METABOLIC DISEASE

New research published in *Nature* reveals a novel role for IL-22 in regulating metabolism.

IL-22 is required for host innate immunity, maintenance of epithelial integrity in the gut and regulation of the commensal bacterial population. Given the associations between altered intestinal microbiota, chronic low-grade inflammation and development of metabolic disorders, researchers from Genentech in South San Francisco, CA, USA, hypothesized that IL-22 signalling might contribute to regulation of metabolic functions via modulation of mucosal immunity.

The research team, led by senior investigator Wenjun Ouyang, used leptin-receptor-deficient (*db/db*) mice and leptin-deficient (*ob/ob*) mice combined with a mouse model of *Citrobacter rodentium* infection (in which IL-22 is indispensable for mucosal defence) to assess the relationship between IL-22 and obesity. The obese mice succumbed to infection within 2 weeks of inoculation, in stark contrast to lean control mice, all of which survived. IL-22 production and adaptive antibody responses were impaired in the obese mice.

Knockout mice lacking the IL-22 receptor that were fed a high-fat diet (HFD) developed more severe features of the metabolic syndrome, with increased body weight, glucose intolerance and insulin resistance, than wild-type controls. Treatment of HFD-fed mice or *db/db* mice with exogenous IL-22-Fc resulted in reduced body weight and epididymal fat-pad mass, lowered blood glucose levels in fed and fasting conditions, as well as decreased glucose intolerance and insulin resistance in these animals compared with untreated controls. Treatment with IL-22-Fc also enhanced mucosal immunity and reduced metabolic endotoxiemia and the expression of adipocyte-derived proinflammatory genes. Moreover, peptide YY levels were increased, which resulted in a concomitant reduction in food intake by these animals.

"IL-22 not only enhances intestinal barrier integrity and maintains homeostatic interactions with microflora, but also directly mediates several essential functions linked to metabolism, including modulating lipid metabolism in adipose tissue and reducing food consumption," summarizes Ouyang.

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Original article Wang, X. *et al.* Interleukin-22 alleviates metabolic disorders and restores mucosal immunity in diabetes. *Nature* doi:10.1038/nature13564