IMMUNOTHERAPY AND OBESITY

Progression of obesity-associated metabolic abnormalities can be reversed by immunotherapy, according to a new study published in *Nature Medicine*. Researchers from the University of Toronto and the Stanford University School of Medicine have identified several populations of T cells as physiological regulators of obesity, fat distribution and insulin resistance.

Winer *et al.* characterized subsets of T cells in the adipose tissue of diet-induced obese mice, leptin-deficient *ob/ob* mice and people with obesity. Specific subsets of T cells accumulated particularly in visceral fat, where interferon γ^+ CD4 $^+$ T cells progressively overwhelmed anti-inflammatory T cells, which prevent metabolic abnormalities during early stages of obesity.

“A severe fat T-cell receptor bias developed, which we could link to progressive insulin resistance and glucose homeostasis,” recounts senior investigator H.-Michael Dosch. “Several strategies were used to confirm and illuminate these processes, including T-cell ablation with anti-CD3 monoclonal antibodies, which mediated surprisingly long-lasting normalization of insulin resistance through several mechanisms readjusting T cell subsets in diet-induced obese and *ob/ob* mice.”

These findings suggest a strong involvement of the cognate immune system in obesity-associated metabolic syndromes. As Dosch points out, “obesity and type 2 diabetes mellitus may be the largest autoimmune disorders yet discovered.”

“Low dose anti-CD3, now in phase III trials in type 1 diabetes mellitus, could become an attractive alternative to invasive bariatric surgery in obese patients at risk for or with overt type 2 diabetes mellitus,” suggests Dosch, even if “treating both diabetes forms with the same modality is, perhaps, counterintuitive.”

Linda Koch

Original article Winer, S. *et al.* Normalization of obesity-associated insulin resistance through immunotherapy. *Nat. Med.* 15, 921–929 (2009).