# Immune system killer cells increase risk of diabetes

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More than half of the German population is obese. One effect of obesity is to chronically activate the immune system, placing it under continuous stress. Researchers in Jens Brüning's team at the Max-Planck-Institute for Metabolism Research and at the University Hospital Cologne have discovered a subpopulation of immune cells in obese mice and humans that are involved in the development of diabetes. If this immune cell subpopulation could be specifically depleted in humans, the risk for diabetes development in overweight people might be reduced.

The rise of obesity in Germany has resulted in more diabetes and stroke patients. In addition, cancer rates are also increasing, as one effect of obesity is to chronically activate the immune system.

Scientists in Cologne therefore decided to study how the immune system responds to obesity and how related complications arise. This research brought their attention to a subpopulation of immune cells, so called natural killer (NK) cells. Normally the task of NK cells is to fight against virus-infected or malignant cells. In obese mice, however, different genes are activated in a subgroup of NK cells compared to NK cells of normal-weight animals. This specific NK cell subgroup is involved in the increased activation of the immune system leading to more insulin resistance – the precursor of diabetes.

## Diet reduces the risk for diabetes

The composition of NK cells in lean and obese subjects also varies in humans. Killer cells in blood samples from obese patients have a similar genetic profile compared to obese mice. "If our obese patients went on a strict diet, losing up to 30 kilograms, the number of altered killer cells also decreased, as well as the level of systemic inflammation and the risk for diabetes", explains Sebastian Theurich, physician scientist at the Max-Planck-Institute for Metabolism Research and a specialist in haematology and oncology at the Department I for Internal Medicine, University Hospital Cologne

In mice which received a highly fat-enriched diet, the researchers were also able to reduce the risk of diabetes by specific genetic modifications of NK cells, which prevented the development of this altered NK cell subpopulation. Without this NK cell subpopulation, the mice did not gain weight and insulin resistance to the same extent than control animals – notably, despite eating fatty food.

"This subpopulation of killer cells could provide an effective point of attack for new therapeutic approaches if we succeeded to selectively switch them off", explains Theurich. The scientists are therefore hoping to isolate markers that distinguish these specific killer cells from others, which would enable a targeted therapy.

**More information:** Sebastian Theurich et al. IL-6/Stat3-Dependent Induction of a Distinct, Obesity-Associated NK Cell Subpopulation Deteriorates Energy and Glucose Homeostasis, *Cell Metabolism* (2017). DOI: 10.1016/j.cmet.2017.05.018

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