MedicalXpress

Lean despite many calories

June 8 2015

Metabolism experts are increasingly convinced that obesity and many of the pathogenic changes it entails, such as Metabolic Syndrome and type 2 diabetes, are a result of chronic inflammatory processes in fatty (adipose) tissue. The adipose tissue of obese people exhibits higher-than-normal quantities of almost all types of immune and inflammatory cells.

"We are quite convinced that immune cells play a role in the pathogenic consequences of obesity," says Professor Hans-Reimer Rodewald of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ). "But apart from that, little is understood so far about the exact processes that lead to disruptions in metabolism." However, Rodewald's team has now been able to take a first step towards answering this question: the researchers have identified an enzyme in immune cells that is required for metabolically linked pathogenic processes to unfold.

The enzyme, called Kit, is involved in the development of blood and immune cells, as well as stem cells. Dr. Dario Gutierrez, first author of the current publication, compared mice that had functioning Kit with animals in whose cells the enzyme had been turned off.

When the researchers fed all of the animals a fat-rich diet, the mice with Kit deficiency were protected from obesity and insulin resistance. By contrast, the mice with functioning Kit gained weight and were affected by the associated metabolic disorders.

Apart from its functions in immune cells, Kit also plays a role in many processes that are independent of the immune system. For example, it

regulates liver function and impacts the central nervous system and insulin secretion. However, the DKFZ scientists showed in subsequent experiments that the culprits responsible for obesity and resulting metabolic disorders are immune cells that express Kit, not the effects that are independent of the immune system. "Now we know the key molecule involved in the development of pathogenesis. But we still have to find out which of the various immune cell types are actually involved," says Rodewald.

The Kit enzyme is a member of the large family of receptor tyrosine kinases, for which many highly specific inhibitors have already been developed. Drugs called kinase inhibitors are used to slow down cellular growth in many cancers. Imatinib, for example, is used in the treatment of specific types of leukemia (for example, chronic myeloid leukemia, or CML) and tumors of the gastrointestinal tract. "Interestingly, a case was reported where type 2 diabetes regressed during treatment with Imatinib. This finding suggests that Kit and Metabolic Syndrome might also be linked in humans," Rodewald hypothesized.

More information: Dario A. Gutierrez, Sathya Muralidhar, Thorsten B. Feyerabend, Stephan Herzig and Hans-Reimer Rodewald: Hematopoietic Kit deficiency, rather than lack of mast cells, protects mice from obesity and insulin resistance. *Cell Metabolism* 2015, DOI: 10.1016/j.cmet.2015.04.013

Provided by German Cancer Research Center