

Obesity without the health problems? There could be a way

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Obesity is linked to the widespread epidemics of diabetes and heart disease that plague society, but a lesser-known fact is that the weight can also lead to autoimmune disease. Now, researchers have new information about how that damaging immune response happens and how it might be stopped, published on April 4 in *Cell Reports*.

The key, they show, may be to block an important element known as AIM (for apoptosis inhibitor of macrophage) in the bloodstream and, ultimately, the production of antibodies that attack the self.

The discovery is especially notable because the team of researchers, from the University of Tokyo and led by Toru Miyazaki, previously discovered AIM, linking it to the inflammation that comes with obesity. They also showed that its suppression could help prevent obesity-associated diabetes and atherosclerosis. Their new work extends those benefits of AIM suppression to include autoimmune disease.

"Our report for the first time explains how obesity causes an initial <u>autoimmune response</u>, namely production of multiple antibodies against self-antigens, and also defines a key molecule in this autoimmune process," Miyazaki said.

The researchers found that a natural immunoglobulin called IgM rises in the blood of mice fed on a high-fat diet. The rise in IgM results as <u>fatty</u> acids stimulate particular <u>immune cells</u>. Furthermore, IgM binds to AIM, and this complex is retained in the blood rather than excreted in urine.



The researchers propose that the prolonged presence of IgM-AIM in the blood may contribute to the production of auto-antibodies. Correspondingly, they find that <u>obese mice</u> lacking AIM are protected from that harmful autoimmune response.

"Suppression of AIM appears to intercept two different obesity-associated pathological immune responses, namely, chronic inflammation based on innate immunity and autoantibody production based on humoral immunity," the researchers wrote. "Thus, AIM inhibition potentially could be used as a therapy to prevent not only insulin resistance and metabolic disorders but also autoimmunity under obese conditions."

Miyazaki's team says that human studies are needed to pursue the development of a new AIM-targeted obesity therapy.

More information: *Cell Reports*, Arai et al.: "Obesity-associated autoantibody production requires AIM to retain IgM immune complex on follicular dendritic cells." dx.doi.org/10.1016/j.celrep.2013.03.006

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