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Fewer blood vessels in adipose tissue could explain higher risk of diabetes

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Type 2 diabetes normally occurs in late middle age, but the reason is still unclear. An international team of researchers led from Karolinska Institutet have, in experiments on mice, shown that adipose tissue develops fewer blood vessels in middle age – which could explain why the risk of developing the disease increases at this stage in life. The researchers are confident that the discovery, which is published in the journal *PNAS*, opens the door for a whole new treatment strategy for type 2 diabetes, in which drugs that modulate vessel formation can be used to prevent the disease from occurring.

It is already known that the risk of developing type 2 diabetes increases sharply in late middle age, but the reasons are unclear. Researchers have now examined healthy mice in different age groups and found that the number of blood vessels in white adipose tissue varies over a lifetime. Blood vessel production in mice reaches its lowest point just after the halfway point in a mouse's life. Coincidentally, this is also when the adipose cells in mice secrete the least amount of Vascular Endothelial Growth Factor (VEGF), a protein that regulates vessel formation. Researchers therefore believe that VEGF controls vessel formation in adipose tissue and that fewer vessels are consistent with a higher risk of type 2 diabetes.

Another experiment involved the examination of mice, which after being given fatty food had developed obesity and reduced insulin sensitivity, which is a precursor of type 2 diabetes. The researchers gave the mice a drug that blocked VEGF production, thereby preventing the vessels from

forming. There are drugs already available today that are approved for treating several forms of cancer and an eye disease in accordance with this principle. After the treatment, the mice developed fewer blood vessels in their adipose tissue, which was what the researchers had expected. What they did not expect, however, was that the insulin sensitivity of the mice also improved.

Complex pattern

"This is a complex pattern of causes that we do not yet fully understand, and which requires further studies. But we do see an opening for a new treatment strategy that could improve low insulin sensitivity by blocking VEGF production. We now wish to move forward and try to gain a better understanding of the causes. We also plan to conduct experiments on mice with developed type 2 diabetes to see if it is possible to treat more manifest diseases using same principle," says Yihai Cao, Professor at the Department of Microbiology, Tumour and Cell Biology.

More information: Jennifer Honek, Takahiro Seki, Hideki Iwamoto, Carina Fischer, Jingrong Li, Sharon Lim, Nilesh J. Samani, Jingwu Zang, and Yihai Cao. "Modulation of age-related insulin sensitivity by VEGF-dependent vascular plasticity in adipose tissues" *PNAS* 2014 ; published ahead of print September 30, 2014, DOI: 10.1073/pnas.1415825111

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