Culprit in reducing effectiveness of insulin identified

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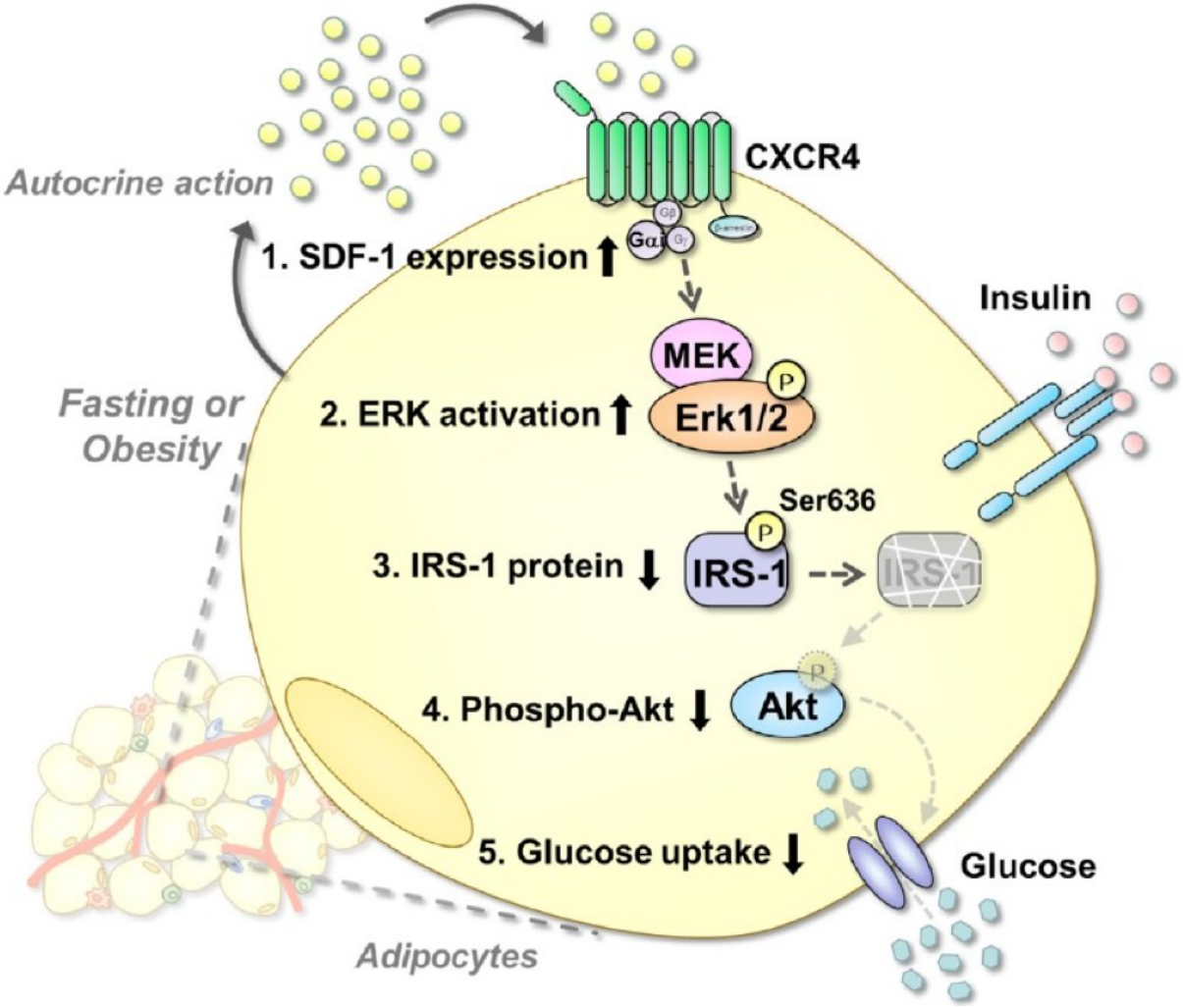

1) Fasting or obesity induces SDF-1 expression in adipocytes. 2) Its autocrine action activates ERK signaling. 3) SDF-1-induced ERK signal concomitantly induces serine phosphorylation of IRS-1 protein, and degrades IRS-1 protein. This attenuates 4) insulin-mediated Akt phosphorylation and 5) glucose uptake.

Credit: Osaka University

Scientists at Osaka University have discovered that Stromal derived factor-1 (SDF-1) secreted from adipocytes reduces the effectiveness of insulin in adipocytes and decreased insulin-induced glucose uptake.

Insulin is a hormone that facilitates glucose uptake. Insulin binds to cellular insulin receptors to activate Insulin Receptor Substrate 1 (IRS-1), taking in sugar through phosphorylation of Akt. If insulin loses its effectiveness, cells in the body become unable to take up glucose, and blood sugar levels rise, leading to diabetes.

A group of researchers led by Atsunori Fukuhara has reported that adipocytokine, or cell signaling proteins secreted by the adipose tissue, played a role in developing obesity. However, it was not known that adipocytokine activated on adipocytes themselves to control insulin sensitivity. SDF-1, one of the adipocytokines, is the most predominantly expressed chemokine; however, its action on glucose uptake in cells had not been analyzed.

Using microarray database analysis, the scientists identified SDF-1 as a factor to enhance expression in adipocytes in both fasting and obese states and found that SDF-1 reduced the effectiveness of insulin in adipocytes. In actuality, in SDF-1 knockout mice, insulin-induced glucose uptake increased (i.e., blood sugar levels decreased), and insulin efficacy improved (i.e., insulin sensitivity was enhanced). Their research results were published in *Diabetes*.

Based on the results of this study, it is expected that insulin sensitivity in adipocytes will increase by inactivating the SDF-1 signaling pathway, which will lead to treatment of obese type 2 diabetes.

More information: Jihoon Shin et al, SDF-1 is an Autocrine Insulin-Desensitizing Factor in Adipocytes, *Diabetes* (2018). DOI: 10.2337/db17-0706