SORLA controls insulin signaling to promote obesity in mice

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Large-scale genetic studies have linked variations in genes and proteins to an increased risk for developing obesity. Determining how these variations alter metabolism to increase body mass may lead to the identification of preventative therapies for obesity and related disorders.

In this month's issue of the *JCI*, research led by Thomas Willnow at the Max Delbrück Center examined how fatty acid metabolism is controlled by differences in the availability of SORLA, a protein that has been identified as an risk factor for both obesity and Alzheimer's disease.

Increasing SORLA levels led to decreased turnover of fat molecules and increased fat accumulation and body mass in mice. In contrast, reducing SORLA levels protected mice against diet-induced obesity.

Finally, the study determined that SORLA's effects on fat metabolism and fat accumulation were due to its ability to regulate insulin signaling.

This work identifies a mechanism for SORLA's association with obesity risk, and suggests that these metabolic changes could also underlie the link between SORLA and the risk for Alzheimer's disease.

More information: Vanessa Schmidt et al, SORLA facilitates insulin receptor signaling in adipocytes and exacerbates obesity, *Journal of Clinical Investigation* (2016). DOI: 10.1172/JCI84708