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Study finds faulty fat sensor implicated in obesity and liver disease

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Defects in a protein that functions as a dietary fat sensor may be a cause of obesity and liver disease, according to a study published in the journal *Nature*, led by researchers at Imperial College London. The findings highlight a promising target for new drugs to treat obesity and metabolic disorders.

The protein GPR120 is found on the surface of cells in the gut, liver and fat tissue and allows cells to detect and respond to unsaturated fatty acids from the diet, especially the omega-3 fatty acids which are believed to have a beneficial impact on health. Scientists found that mice deficient in GPR120 were more prone to developing obesity and liver disease when fed a high-fat diet. They also found that people with a certain mutation in the gene encoding GPR120, which stops the protein from responding to omega-3 fatty acids, were significantly more likely to be obese.

In the gut, when unsaturated fatty acids from food bind to GPR120, this stimulates the release of hormones that suppress appetite and stimulate the pancreas to secrete insulin. When fat cells sense high levels of fat in the blood through GPR120, it stimulates them to divide to produce more fat cells to store all the fat, reducing the risk of fatty liver and furring of the arteries. This mechanism could be an important pathway for bringing about some of the healthy effects of omega-3s.

When they were fed on a high-fat diet, mice that lacked GPR120 not only became obese but also had fatty livers, lower numbers of fat cells,

and poor control of blood glucose. The researchers believe that mice that are deficient in GPR120 have difficulty storing excess fat in fat tissue. Instead, their bodies store fat in areas where it can cause health problems, like the liver, the muscles and in the walls of arteries. In humans, this pattern of obesity is associated with type 2 diabetes and heart disease.

The study involved scientists in the UK, France and Japan. It was led by Professor Philippe Froguel, from the School of Public Health at Imperial College London.

"Being overweight is not always unhealthy if you can make more fat cells to store fat," said Professor Froguel. "Some people seem to be unable to do this, and instead they deposit fat around their internal organs, which is very unhealthy. Our study suggests that in both mice and humans, defects in GPR120 combined with a high-fat diet greatly increase the risk of this unhealthy pattern of obesity. We think GPR120 could be a useful target for new drugs to treat obesity and liver diseases."

The researchers analysed the gene for GPR120 in 6,942 obese people and 7,654 controls to test whether differences in the code that carries instructions for making the protein contribute to obesity in humans. They found that one mutation that renders the protein dysfunctional increases a person's risk of obesity by 60 per cent. The researchers think this mutation mimics the effect of a bad diet lacking in unsaturated omega-3 fat.

More information: A. Ichimura et al. "Dysfunction of lipid sensor GPR120 leads to obesity in both mouse and human." *Nature*, published online 19 February 2012. doi:10.1038/nature10798

Provided by Imperial College London