Fat cells reach their limit and trigger changes linked to type 2 diabetes

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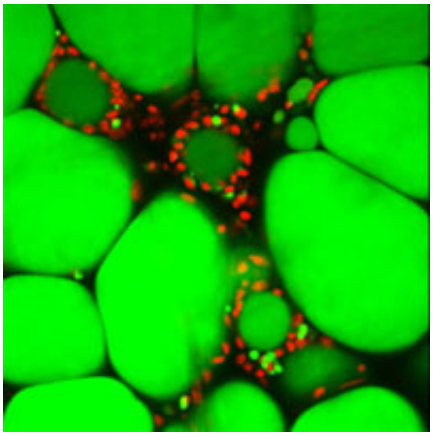

(PhysOrg.com) -- Scientists have found that the fat cells and tissues of morbidly obese people and animals can reach a limit in their ability to store fat appropriately. Beyond this limit several biological processes conspire to prevent further expansion of fat tissue and in the process may trigger other health problems.

Research funded by the Biotechnology and Biological Sciences Research Council (BBSRC), the Medical Research Council (MRC) and the European Union Sixth Framework Programme, shows that a protein called secreted frizzled-related protein 1 (SFRP1) is produced by fat cells and may be involved in changes to our metabolism that could increase the risk of diabetes and cardiovascular disease. The work was

carried out at the University of Cambridge and will be published in a future edition of the *International Journal of Obesity Research.*

Professor Antonio Vidal-Puig from the Institute of Metabolic Science, University of Cambridge, said: "We have known for some time that many obese individuals are at greater risk of developing diabetes, cardiovascular disease and also cancer. But this is not true for all obese people."

Dr Jaswinder Sethi, also from the Institute of Metabolic Sciences, added: "What we still do not fully understand, is how the expansion of fat tissue is regulated in healthy people and how this process of regulation might be different in those obese people who have health problems such as the metabolic syndrome."

One hypothesis is that storing surplus fat in itself may not lead to metabolic syndrome but there may be a maximum limit of how much fat a person can store safely before the body's natural responses lead to the debilitating chronic health problems often associated with obesity.

Dr Sethi continued, "To investigate this we have been using a combination of molecular cell biology, human gene profiling and mouse genetics as tools to understand what is happening as fat cells and tissues develop and then, in some very obese people, lose their normal process of regulation."

The researchers have found that the level of SFRP1 increases as fat cells and tissues increase in volume until it peaks at about the point of mild obesity. There is evidence that SFRP1 is involved in recruiting new fat cells, thereby facilitating the expansion of fat tissue up until this point where it peaks.

"SFRP1 seems to be very closely linked to some sort of tipping point,

after which the way in which our fat tissue is regulated changes significantly and there are knock-on consequences to our wider metabolism. We think that in very obese people this may be an early event that triggers metabolic syndrome and the chronic health problems associated with it, such as diabetes and cardiovascular disease," said Dr Sethi.

The fat tissue of people who are obese and also have diabetes shows signs of not being regulated as it usually would be. In this tissue, the researchers also see the levels of SFRP1 begin to fall so as to prevent further expansion of the tissue. It is this fall in SFRP1 that has knock-on effects on metabolism that may in part explain the link between morbid obesity and metabolic syndrome.

The researchers believe that SFRP1 works in concert with other molecules to respond to the availability, or not, of energy. Together these molecules also determine to what extent our fat tissue can continue to expand as we consume more calories than we burn.

Professor Douglas Kell, BBSRC Chief Executive said: "Research such as this leads to better understanding of the biochemistry that drives normal human physiology. In particular we can see how we usually respond to extremes brought on by the various onslaughts of our lifestyles and environments. Increasing our understanding of the fundamentals of metabolic signalling is an important part of working towards an increase in health span to match our increasing life spans."

Provided by University of Cambridge