

How does obesity cause disease in organs distant from those where fat accumulates?

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Barcelona, Spain: Obesity is on the rise throughout the world, and in some developed countries two-third of the adult population is either overweight or obese. This brings with it an increased risk of serious conditions such as heart disease, stroke, cancer and osteoarthritis. Many of these conditions do not appear to affect the parts of the body where the excess fat accumulates, but rather to involve body systems that are remote from the fat accumulation. Now an international group of scientists has taken an important step towards understanding the links between obesity and the related, yet physically distant, diseases it causes, the annual conference of the European Society of Human Genetics will hear today.

Ms Taru Tukiainen, D.Sc., a postdoctoral researcher working at the Institute for Molecular Medicine Finland (FIMM), Helsinki, Finland and colleagues from the UK and US, set out to study the relationship between [body mass index](#) (BMI), a common-used way of measuring obesity, and gene expression in 44 different tissue types, including some that are rarely accessible in large sample sizes, for example the brain and internal organs. "Most tissue sampling is invasive, but we were able to use the GTEx* dataset of tissues from autopsy donors, and therefore sample a far wider range than is usually possible," Ms Tukiainen explains. "This is the first time that such changes in human tissue function in response to alterations in BMI have been explored among so many body systems simultaneously."

The researchers found simultaneous changes in response to obesity in

almost all the tissues studied. "These results show that obesity really is a systemic condition, and particularly a condition of systemic inflammation. Interestingly, though, the changes in tissue function appeared to be only partially shared between different types of tissues; some tissues clearly act in pairs with one half of the pair compensating for - or enhancing - the dysfunction of the other. For instance, adipose tissue and adrenal glands, which are both organs secreting hormones essential to metabolism, often react to changes in BMI in completely opposite ways, including a decrease in metabolic activity in the former and an increase in the latter," Ms Tukiainen will say.

Although lifestyle changes are the most effective way to combat obesity, they can be hard work and difficult to maintain. Therefore the biological processes identified by the researchers may help the treatment of obesity by identifying potential drug targets, and particularly tissue-specific targets, they say. The results may also help to distinguish groups of individual who are at higher risk of developing complications, and lead toward personalised care.

"Our research highlights the burden of overweight and obesity on the digestive system. Although this is unsurprising, given the role of digestive system tissues in food processing, we found alarming links between BMI-related changes in different parts of the digestive tract and genes implicated in some diseases, for example Crohn's disease.

"An association between two variables does not necessarily imply there is a causal link and, from the gene expression results alone, we cannot tell which is driving which. Do changes in BMI or changes in gene expression come first? We can, however, address the potential causes by using genetic variants known to be associated with BMI in combination with our data on gene expression," says Ms Tukiainen.

Large-scale genome-wide association studies have already identified

nearly 100 genetic variants that influence BMI. Analyses by the group that interpret this information further have shown that many of these [gene expression](#) changes, particularly in adipose tissue, appear to be caused by increased BMI.

"I believe that our work adds to the weight of evidence, and provides hypotheses for other researchers to follow up in the hope of being able to translate the results into ways of preventing and treating the very serious complications of [obesity](#)," Ms Tukiainen will conclude.

More information: *GTEx is a dataset consisting of thousands of tissue samples in which the RNA from each sample has been sequenced to measure gene expression. Because it is not a dataset collected specifically for obesity research, the donors are representative of the population as a whole, and the obesity epidemic is clearly reflected in that only 31% of GTEx donors are of normal weight; the remainder are either overweight or obese.

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Provided by European Society of Human Genetics

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