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Finnish twin study yields new information on how fat cells cope with obesity

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The mechanisms by which obesity leads towards metabolic co-morbidities, such as diabetes mellitus, are poorly understood and of great public health interest. A study led by Matej Oresic from VTT Technical Research Centre of Finland suggests that adaptation of fat cell membranes to obesity may play a key role in the early stages of inflammatory disorders.

Millions of adults are diagnosed as obese each year, worldwide. Many of these people suffer from a disorder known as metabolic syndrome, which includes symptoms such as hypertension and elevated blood cholesterol. They are also at risk of developing additional diseases such as heart disease and diabetes mellitus. Obesity may in fact be a major cause of all these problems—the question is, why? Kirsi H. Pietiläinen (Obesity Research Unit, Helsinki University Central Hospital), Antonio Vidal-Puig (University of Cambridge), Matej Orešič and colleagues set out to address this question in their paper published on June 7th in the online, open access journal *PLoS Biology*.

The team used lipidomics to study the fat tissue biopsies among several sets of monozygotic twins. In each twin pair, one twin was obese (but not morbidly obese) while the other twin exhibited a normal body mass index. Because monozygotic twins share the same DNA and early upbringing, the impact of these factors on adult body mass phenotypes is accounted for, leaving other factors such as adult diet and lifestyle choices as the major variables.

When the authors compared dietary intake within twin sets they found that obese twins had lower amounts of polyunsaturated fatty acids in their diets than their non-obese counterparts. The kinds of fats a person eats can affect what types of lipids are present in the body. Unexpectedly, the authors found the obese people had higher amounts of certain types of lipids containing polyunsaturated fatty acids in their adipose tissues than their non-obese twins.

This finding is interesting because cell membranes are primarily composed of lipids, and different lipids can alter a membrane's physical properties, such as its fluidity. When the authors used computers to model the effect of these different lipids on adipose cell membranes, they found that the new lipids observed in the cells of the obese twins balanced each other in such a way that overall membrane fluidity was unaffected. The authors concluded that lipid-content changes in obese individuals might actually be an adaptation that serves to preserve membrane function as the cells expand. Additional analyses suggested that this adaptation can only go so far, and breaks down in the morbidly obese.

The authors also conducted a statistical network analysis to attempt to identify the regulatory mechanisms underpinning the changes and found the gene encoding the fatty acid elongase Elovl6 might be involved in fatty acid remodelling in obese people. Indeed, when the researchers reduced Elovl6 expression in an adipocyte cell line, they found the cells could no longer maintain the right level of the adaptive lipids observed in obese twins.

Collectively, the authors' data point to some of the mechanisms the body may use to adapt to excess fat. These results may also help to explain why obese people are at risk of developing inflammatory disorders such as diabetes mellitus: the kinds of lipids that accumulate in the adipocytes of obese people are precursors for compounds that are known to

aggravate the immune system. These findings, while needing to be validated by further studies, nonetheless represent a valuable angle from which to approach the problem.

More information: Pietiläinen KH, Róg T, Seppänen-Laakso T, Virtue S, Gopalacharyulu P, et al. (2011) Association of Lipidome Remodeling in the Adipocyte Membrane with Acquired Obesity in Humans. *PLoS Biol* 9(6): e1000623. doi:10.1371/journal.pbio.1000623