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LIPIDS

Adipose lipid turnover—a new target in metabolic disease

Lipid turnover in adipocytes differs between healthy individuals and those with obesity or hyperlipidemia, reveal findings of a study published in *Nature*. Arner *et al.* show that triglyceride content is renewed six times during the average 10-year life span of human fat cells and that the rates of triglyceride storage are increased and their removal is decreased in humans with obesity compared with healthy individuals. "By contrast, storage and removal rates are reduced in non-obese individuals with hyperlipidemia, the most common form of hereditary dyslipidemia," explains Peter Arner from the Karolinska University Hospital in Sweden. "These findings provide evidence that the lipid storage and removal capacities of fat cells have different roles in health and disease pathology."

The investigators had previously determined that the turnover rate of fat cells is similar between lean and obese individuals. As the size of the fat mass is a product of the number of cells and their lipid content, Arner and colleagues next studied the rate of lipid storage and removal from adipocytes and whether this rate differs in healthy individuals and those with obesity or dyslipidemia. Adipocytes were, therefore, isolated from subcutaneous abdominal depots of about 100 adults with differing metabolic profiles, on the basis of buoyancy using standard methods.

"The novel aspect of our study was the use of radiocarbon dating to determine the age of the lipid," recounts senior investigator Kirsty Spalding. "Nuclear bomb testing during the cold war caused a rapid increase in ^{14}C levels in the atmosphere, and following a partial test ban treaty signed in 1963, ^{14}C levels in the atmosphere have been decreasing exponentially ever since." As a result, the age of cells or of lipids can be determined by measuring the ratio of the radioactive isotope ^{14}C to the abundant, stable isotope ^{12}C, without having to administer any toxic compounds to an individual.

Until now, lipid turnover in adipocytes was viewed primarily as a pivotal part of energy balance (deposition of excess calories and mobilization thereof when needed). This study shows that lipid turnover has effects on health beyond the regulation of energy balance. Moreover, Arner and co-workers demonstrate that metabolic alterations in adipocytes (increased lipid storage in combination with decreased removal capacity) contribute to the development of obesity. "This process facilitates development of obesity if the changes are primary and, if secondary, accelerates further development of excess fat accumulation and/or makes it more difficult to lose the fat upon slimming efforts," comments Arner.

Finally, the researchers implicate metabolic alterations in lipid turnover in the pathology of familial combined dyslipidemia, which is associated with a high risk of lethal coronary heart disease early in life and has no known cause. "We generate for the first time direct *in vivo* proof that a disturbance in adipocyte metabolism underlies this condition, and we offer a disease model which could be used to develop causal pharmacological therapy," concludes Arner.

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Original article Arner, P. *et al.* Dynamics of human adipose lipid turnover in health and metabolic disease. *Nature* doi:10.1038/nature10426