Researchers identify how stressed fat tissue malfunctions

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Ben-Gurion University of the Negev (BGU) researchers, in a collaboration with colleagues from the University of Leipzig, Germany, have identified a signaling pathway that is operational in intra-abdominal fat, the fat depot that is most strongly tied to obesity-related morbidity.

The paper was just published in the Endocrine Society's the Journal of Clinical Endocrinology and Metabolism (J. Clin. Endocrinol. Metab. 2009; 94:2507-251)

"Fat tissue in obesity is dysfunctional, yet, the processes that cause fat tissue to malfunction are poorly understood -- specifically, it is unknown how fat cells 'translate' stresses in obesity into dysfunction," said Dr. Assaf Rudich, senior lecturer from the Department of Clinical Biochemistry at Ben-Gurion University.

Fat tissue is no longer considered simply a storage place for excess calories, but in fact is an active tissue that secretes multiple compounds, thereby communicating with other tissues, including the liver, muscles, pancreas and the brain. Normal communication is necessary for optimal metabolism and weight regulation. However, in obesity, fat (adipose) tissue becomes dysfunctional, and mis-communicates with the other tissues. This places fat tissue at a central junction in mechanisms leading to common diseases attributed to obesity, like type 2 diabetes and cardiovascular diseases.

Fat tissue dysfunction is believed to be caused by obesity-induced fat

tissue stress: Cells over-grow as they store increasing amounts of fat. This excessive cell growth may cause decreased oxygen delivery into the tissue; individual cells may die (at least in mouse models), and fat tissue inflammation ensues. Also, excess nutrients (glucose, fatty acids) can also result in increased metabolic demands, and this in itself can cause cellular stress.

The BGU and Leipzig teams established a setup for collecting fat tissue samples from people undergoing abdominal surgery. The team identified a signaling pathway that is operational in intra-abdominal fat, the fat depot that is most strongly tied to obesity-related morbidity.

The degree of activation of a signaling pathway from these individuals was compared with those of leaner people, those with obesity predominantly characterized by accumulation of "peripheral" fat, and those with obesity with predominant accumulation of fat within the abdominal cavity.

They discovered that the signaling pathway was more active depending on the amount of fat accumulation in the abdomen, and that it correlated with multiple biochemical markers for increased cardio-metabolic risk. Moreover, the expression of one of the upstream signaling components, a protein called ASK1, predicts whole-body insulin resistance (an endocrine abnormality that is strongly tied to diabetes and cardiovascular disease), independent of other traditional risk factors.

Researchers also demonstrated that although non-fat cells within adipose tissue express most of this protein in lean persons, the adipocytes themselves increase its expression by more than four-fold in abdominally-obese persons.

"The importance of this study is not only in contributing to the understanding of adipose tissue dysfunction in obesity, but as a

consequence, may provide important leads for novel ways to prevent the dangerous consequences, such as type 2 diabetes, of intra-abdominal fat accumulation," states Dr. Iris Shai, a BGU researcher at the S. Daniel Abraham International Center for Health and Nutrition and Soroka University Medical Center in Beer-Sheva, Israel.

Source: American Associates, Ben-Gurion University of the Negev (news : web)