UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: Kristen Holland Shear
214-648-3404
kristen.hollandshear@utsouthwestern.edu

UT Southwestern researchers identify protein that may explain 'healthy' obesity

DALLAS – Jan. 29, 2009 – Mice whose fat cells were allowed to grow larger than fat cells in normal mice developed "healthy" obesity when fed a high-fat diet, researchers at UT Southwestern Medical Center found in a new study.

The fat but healthy mice lacked a protein called collagen VI, which normally surrounds fat cells and limits how large they can grow, like a cage around a water balloon. The findings appear online and in a future edition of *Molecular and Cellular Biology*.

"The mice lacking collagen VI fared much better metabolically than their counterparts that retained this particular collagen," said Dr. Philipp Scherer, director of the Touchstone Center for Diabetes Research at UT Southwestern and the study's senior author. "The mice without collagen VI don't develop inflammation or insulin resistance. They still get obese, but it's a 'healthy' obesity."

When people take in more calories than needed, excess calories are stored in adipose or fatty tissue. The fat cells are embedded in and secrete substances into an extracellular matrix, a type of connective tissue that provides support to fat tissue, like scaffolding. Collagen VI is one component of the extracellular matrix. Too much of this connective tissue prevents individual cells from expanding and can lead to fibrosis and eventually inflammation.

Inflammation is thought to be an underlying cause of metabolic disorders in humans, said Dr. Scherer. Large fat cells are often considered a bad omen, he said, because they typically lead to increased cell death and systemic insulin resistance. Under normal circumstances, fat cells continue to grow until they reach a point where the extracellular matrix they've built around themselves is so strong that it's no longer flexible.

"In this particular case, however, the large fat cells are not as inflamed as they would normally be," Dr. Scherer said. "Fat cells that lack collagen VI can grow to a huge size without becoming inflamed, suggesting that collagen VI directly affects the ability of fat cells to expand."

Dr. Scherer said the current finding is clinically relevant and probably will translate well from

(MORE)

the mice to humans. "Our study highlights the fact that collagen VI, and possibly other extracellular matrix constituents, are extremely important in modulating fat-cell physiology," he said.

The next step is to determine precisely how collagen VI functions in the body.

"We need to get a better grip on targets that may allow us to interfere in this process. Unfortunately collagen VI can't be knocked out in humans, but we may be able to manipulate it," Dr. Scherer said.

Other UT Southwestern researchers involved in the study were Dr. Zhao Wang, postdoctoral researcher in internal medicine, as well as volunteer faculty members Drs. Nicola Abate and Manisha Chandalia, who are now on staff at the UT Medical Branch at Galveston. Scientists from the Albert Einstein College of Medicine, Merck Research Laboratories and the University of Padua in Italy also participated.

The work was supported by the National Institutes of Health.

Visit http://www.utsouthwestern.org/endocrinology to learn more about UT Southwestern's clinical services in endocrinology, including diabetes treatment.

###