UT SOUTHWESTERN MEDICAL CENTER NEWS

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**EMBARGOED UNTIL 1 P.M. CDT THURSDAY, SEPT. 18, 2008**

# 'Baby' fat cells may be key to treating obesity, say researchers at UT Southwestern

DALLAS – Sept. 18, 2008 – Immature, or "baby," fat cells lurk in the walls of the blood vessels that nourish fatty tissue, just waiting for excess calories to help them grow into the adult monsters responsible for packing on the extra pounds, UT Southwestern Medical Center researchers have found in mice.

Researchers have long known that such cells were probably located near blood vessels, but they didn't know exactly where. Discovering their existence, their identity and their lair may direct future research to find ways to stop these cells from creating undesired fat – or to use these immature cells for such clinical treatments as filling in a woman's breast after a lumpectomy.

"There's both intellectual and clinical importance in this discovery," said Dr. Jonathan Graff, associate professor of developmental biology and molecular biology at UT Southwestern and senior author of the study, which appears in today's online edition of the journal *Science.* "Identifying the progenitor cells and finding where they live gives us an exciting therapeutic opportunity.

"Since we can now isolate the progenitor cells, we can interrogate them molecularly and gain insight not only into how they function but also how to harness their powers to help in a variety of human conditions. And because we have found their location, we might be able to develop therapies that can help people with obesity, diabetes or other metabolic challenges."

Dr. Graff said it might soon be possible to isolate immature cells from each person's own fat and move those cells into other parts of the body, where they might be medically useful. For example, progenitor fat cells from the belly or thighs could be moved to a soldier's wounds or scars from breast cancer surgery. These cells might even be moved for purely cosmetic reasons, say, to give someone smaller hips or bigger lips.

Ordinarily, the progenitor cells, called adult stem cells, create new fat cells in several situations, such as when the young body is growing and needs to form fat cells. They are also necessary when weight is stable; as fat cells die and must be replaced by new ones, as with most tissues in the body. When caloric intake exceeds use, however, not only do existing fat cells get larger to store more fat, but progenitor cells also create entirely new fat cells.

(MORE)

To locate the progenitor cells, the researchers engineered mice so that the stem cells would glow green, making them easy to follow as they transformed from progenitors into fully developed fat cells.

The researchers found that the progenitor cells were embedded within the walls of the blood vessels that run through fat tissue.

"They're not just attached to the vessel wall, they're an integral part of it," Dr. Graff said.

This arrangement makes sense, Dr. Graff said, because it allows the cells to respond to the nutrients such as glucose that are present in the blood after a meal. When they sense excess caloric intake, they drift out of the vessel walls and mature into fat cells. This helps to ensure that they reside in the appropriate location among other fat cells.

The green glow also allowed the researchers to separate the progenitor cells from other cells using a technique that isolates only the glowing cells.

They then grew the cells in culture to analyze some of their properties and found that the progenitor cells have a distinct set of molecules on the surface, which could allow the cells to be isolated easily for transplant or study.

In future research, the scientists plan to characterize the cells more fully and to isolate the progenitors just by removing unwanted fat. These cells then can be moved to other locations in that same person for reconstructive purposes, to treat a variety of diseases, and also paradoxically to treat obesity and diabetes.

Other UT Southwestern researchers involved in the study were lead author Dr. Wei Tang, postdoctoral fellow in developmental biology; graduate student Daniel Zeve; Dr. Jaemyoung Suh, postdoctoral researcher in developmental biology; Dr. Bob Hammer, professor of biochemistry; Dr. Michelle Tallquist, assistant professor of molecular biology; Dr. Darko Bosnakovski, former postdoctoral research fellow in developmental biology; and Dr. Michael Kyba, former assistant professor of developmental biology.

The study was funded by the National Institutes of Health and the Excellence for Education Foundation.

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