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Belly fat or hip fat -- it really is all in your genes, says UT Southwestern researcher

DALLAS – May 18, 2010 – The age-old question of why men store fat in their bellies and women store it in their hips may have finally been answered: Genetically speaking, the fat tissue is almost completely different.

"We found that out of about 40,000 mouse genes, only 138 are commonly found in both male and female fat cells," said Dr. Deborah Clegg, assistant professor of internal medicine at UT Southwestern Medical Center and senior author of the study appearing in the *International Journal of Obesity*. "This was completely unexpected. We expected the exact opposite – that 138 would be different and the rest would be the same between the sexes."

The study involved mice, which distribute their fat in a sexually dimorphic pattern similar to humans.

"Given the difference in gene expression profiles, a female fat tissue won't behave anything like a male fat tissue and vice versa," Dr. Clegg said. "The notion that fat cells between males and females are alike is inconsistent with our findings."

In humans, men are more likely to carry extra weight around their guts while pre-menopausal women store it in their butts, thighs and hips. The bad news for men is that belly, or visceral, fat has been associated with numerous obesity-related diseases including diabetes and heart disease. Women, on the other hand, are generally protected from these obesity-related disorders until menopause, when their ovarian hormone levels drop and fat storage tends to shift from their rear ends to their waists.

"Although our new findings don't explain why women begin storing fat in their bellies after menopause, the results do bring us a step closer to understanding the mechanisms behind the unwanted shift," Dr. Clegg said.

For this study, researchers used a microarray analysis to determine whether male fat cells and female fat cells were different between the waist and hips and if they were different based on gender at a genetic level.

Because the fat distribution patterns of male and female mice are similar to those of humans, the researchers used the animals to compare genes from the belly and hip fat pads of male mice, female mice and female mice whose ovaries had been removed – a condition that closely mimics human menopause. Waist and hip fat (subcutaneous fat) generally accumulates outside the muscle wall, whereas belly fat (visceral fat), a major health concern in men and postmenopausal women, develops around the internal organs.

In addition to the genetic differences among fat tissues, the researchers found that male mice that consumed a high-fat diet for 12 weeks gained more weight than female mice on the same diet. The males' fat tissue, particularly their belly fat, became highly inflamed, while the females had lower levels of genes associated with inflammation. The female mice whose ovaries had been removed, however, gained weight on the high-fat diet more like the males and deposited this fat in their bellies, also like the males. "The fat of the female mice whose ovaries had been removed was inflamed and was starting to look like the unhealthy male fat," Dr. Clegg said. "However, estrogen replacement therapy in the mice reduced the inflammation and returned their fat distribution to that of mice with their ovaries intact."

Dr. Clegg said the results suggest that hormones made by the ovaries may be critical in determining where fat is deposited. Her overall goal is to determine how fat tissue is affected by sex hormones and whether it would be possible to develop a "designer" hormone replacement therapy that protected postmenopausal women from belly fat and related diseases such as metabolic syndrome.

Researchers from Oregon Health and Science University, Boston University School of Medicine and the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University also contributed to the study. The study was supported by the Society for Women's Health Research.

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