

Study in mice discovers injection of heat-generating cells reduces belly fat

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The injection of a tiny capsule containing heat-generating cells into the abdomens of mice led those animals to burn abdominal fat and initially lose about 20 percent of belly fat after 80 days of treatment.

Researchers conducting the study were surprised to see that the injected [cells](#) even acted like "missionaries," converting existing belly [fat cells](#) into so-called thermogenic cells, which use fat to generate heat.

Over time, the mice gained back some weight. But they resisted any dramatic [weight gain](#) on a high-fat diet and burned away more than a fifth of the cells that make up their visceral fat, which surrounds the organs and is linked to higher risk for [Type 2 diabetes](#), cancer and [heart disease](#).

The scientists took advantage of the heat-generating properties of a so-called good fat in the body, [brown fat](#), to cut back on the white fat cells that compose the visceral fat that tends to accumulate in the belly.

The scientists combined those brown fat thermogenic cells with genetically modified cells missing an enzyme that leads to visceral fat growth. The engineered cells were placed inside a gel-like capsule that allowed for release of its contents without triggering an [immune response](#).

"With a very small number of cells, the effect of the injection of this capsule was more pronounced at the beginning, when the mice

dramatically lost about 10 percent of their weight. They gained some weight back after that. But then we started to look at how much visceral fat was present, and we saw about a 20 percent reduction in those lipids. Importantly, other nontreated peripheral or subcutaneous fat, which has some beneficial [health effects](#), remained the same. That's what we want," said Ouliana Ziouzenkova, assistant professor of [human nutrition](#) at Ohio State University and lead author of the study.

"We observed the mice for 80 days after injection and the capsule didn't break or cause any scarring or [inflammation](#). This suggests it's a clean, safe potential therapy for obesity," added Ziouzenkova, also an investigator in Ohio State's Comprehensive Cancer Center and the Center for Clinical and Translational Science. Studies in larger animals would be needed before trials in humans could begin, she said.

If this were someday approved for humans, Ziouzenkova said such a therapy would be best suited to patients who develop visceral fat with aging, aren't able to exercise and shouldn't dramatically reduce their calories because that can cause the loss of beneficial subcutaneous fat. She also noted that anti-obesity drugs for humans currently on the market can reduce body weight by about 10 to 15 percent, but also have side effects.

The research is published in a recent issue of the journal *Biomaterials*.

A year ago, Ziouzenkova's lab identified an enzyme in mice that relates to fat accumulation after consumption of a high-fat diet, and she recently published a paper indicating that mice lacking that enzyme could stay lean even while eating excess fat. She applied those findings in this work by using the genetically modified cells that are missing that enzyme to potentially help boost the ability of brown fat cells to burn up visceral fat.

For this study, she collaborated with Ohio State chemists to create the capsules. They are composed of alginate-poly-L-lysine, a compound that creates enough of a barrier to encapsulate cells without signaling the immune system that it should react to a foreign object in the body, while also enabling nutrient supply to the encapsulated cells for their long-term survival.

The researchers used three groups of normal mice for the study, feeding them all a high-fat diet for 90 days. After that, five mice received no treatment, five were treated with empty capsules and five received an injection of active capsules containing genetically engineered cells. The capsules were injected into two areas of visceral fat in their abdomens.

The mice continued to eat a high-fat diet for another 80 days. The mice receiving no treatment continued to gain weight in those 80 days, while the mice receiving thermogenic cells lost weight for 23 days and then began to gain it back, eventually maintaining a steady weight even after continuing to eat excessive saturated fat. Mice receiving empty capsules also lost some weight, but the researchers determined in a separate pilot study that the sham injections did not reduce visceral fat.

The researchers examined visceral fat pads from the mice and determined that overall, [lipid](#) content was at least 20 percent lower in mice treated with active capsules compared to the placebo injection group of mice.

A closer look at exactly what was going on in the animals' cells showed that the injected cells produced high levels of a protein called Ucp1, which burns fat, suggesting that this protein assisted in the visceral fat reduction.

By tagging the injected cells with a fluorescent protein, the scientists could use imaging technology to track the cells in the body; this not only

benefited the research, but also provides a way to safely remove these capsules if needed, Ziouzenkova noted.

"The injected cells were perfectly inversely correlated with lipids – so the more injected cells we have capable of burning fat, the more fat gets burned," she said. "These injected cells worked almost like missionaries, starting to convert host cells and turning them into thermogenic cells."

Because that creation of heat could be uncomfortable inside a human body, the researchers analyzed the treated [mice](#) further to see if the thermogenesis in the belly would produce effects similar to hot flashes.

"Heat production was higher in injected animals, but it was not dramatically higher. So there is some kind of response, but it seems not to be at a magnitude impairing a patient's well-being," Ziouzenkova said. "The animals were also moving less than noninjected animals, but in spite of that, they were still able to lose visceral [fat](#). Their glucose tolerance improved, as well, which is probably related to reduced [visceral fat](#)."

Ziouzenkova said she hopes to design additional capsules to target a variety of diseases beyond [obesity](#).

Provided by Ohio State University

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