

## MIT finds genetic clue to bone and fat production

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MIT researchers have identified a gene that helps control the balance between bone and fat in the human body, a discovery that could pave the way for the prevention of childhood obesity and the treatment of osteoporosis.

The findings will be published in the Aug. 12 issue of Science.

Researchers at MIT's Center for Cancer Research found that a gene called TAZ works to control the destiny of adult bone marrow stem cells, also known as mesenchymal stem cells (MSCs). MSCs have the potential to form a number of different cell types, including bone, fat and muscle.

"We show that a single molecule helps turn one set of genes on to form bone and another set of genes off to inhibit fat formation in MSCs," said Michael Yaffe, the Howard and Linda Stern Professor of Biology and senior author of the paper. "This result suggests a potential new approach to combating various human diseases that result from a disruption in the balance between bone and fat."

The research presents several therapeutic opportunities, including the possibility that once isolated from the bone marrow, MSCs could be useful for healing bone fractures.

"One could also imagine developing a drug to stimulate TAZ activity, which may promote bone growth in elderly patients with osteoporosis," Yaffe said. "And because of the simultaneous inhibitory effect of TAZ



on fat cell development, the same drug might also be used to prevent childhood obesity."

It would also be interesting to investigate whether TAZ activity is defective in bone tumors, and in bone-like tumors that form from fat cells, the researchers said. Modulating TAZ activity could be an effective approach to treating these tumors.

The researchers studied the function of TAZ in cultured MSCs and in animals. MSCs comprise a small percentage of bone marrow cells, about 0.01 percent.

The researchers' most stunning result came when they injected one- to two-cell zebrafish embryos with short strands of RNA that blocked expression of the TAZ gene.

"When we knocked out TAZ in zebrafish, the embryos died when they were just 8 days old, and they had failed to form any bones at all," said postdoctoral fellow Jeong-Ho Hong, the lead author on the paper. Therefore, depletion of TAZ within the body completely impaired bone development. When TAZ was depleted in MSCs grown outside the body in culture, those cells readily turned into fat.

The research was borne out of a collaboration between Yaffe, who also holds appointments in the Broad Institute and in the Department of Surgery at Beth Israel Deaconess Medical Center; Harvard Medical School; the CCR labs of Nancy Hopkins, Amgen Professor of Biology, and Phillip Sharp, Institute Professor of biology; and the lab of Bruce Spiegelman at the Dana-Farber Cancer Institute and Harvard Medical School.

MIT CCR researchers Michael T. McManus, Adam Amsterdam and Ralitsa Kalmukova, Harvard Medical School researchers Eun Sook



Hwang of the Harvard School of Public Health, Yu Tian and Thomas Benjamin of the Department of Pathology, and Elisabetta Mueller and Bruce M. Spiegelman of the Dana-Farber Cancer Institute and the Department of Cell Biology also contributed to this work.

Source: MIT

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