Protein could be key for drugs that promote bone growth

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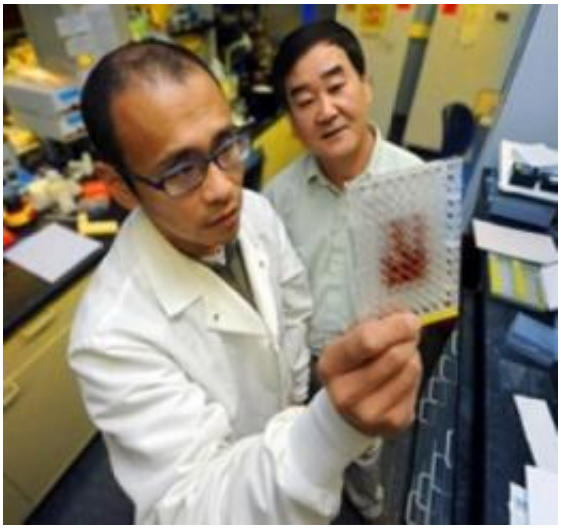

Georgia Health Sciences University researchers have developed a mouse that errs on the side of making bone rather than fat, which could eventually lead to better drugs to treat inflammatory diseases such as rheumatoid arthritis. Dr. Xingming Shi, bone biologist at the GHSU Institute of Molecular Medicine and Genetics and Graduate Student Guodong Pan say the key to the body developing bone instead of fat is a small protein called GILZ. Credit: Phil Jones

Georgia Health Sciences University researchers have developed a mouse that errs on the side of making bone rather than fat, which could eventually lead to better drugs to treat inflammatory diseases such as rheumatoid arthritis.

Drugs commonly used to treat those types of conditions – called glucocorticoids – work by turning down the body's anti-inflammatory response, but simultaneously turn on other pathways that lead to bone loss. The result can lead to osteoporosis and an accumulation of marrow fat, says Dr. Xingming Shi, bone biologist at the GHSU Institute of Molecular Medicine and Genetics.

The key to the body developing bone instead of fat, a small protein called GILZ, was shown in cell cultures in 2008. Now, with work by GHSU Graduate Student Guodong Pan, the work has been replicated in an animal model. Pan received the American Society for Bone and Mineral Research's Young Investigator Award for his work at the society's annual meeting Oct. 12-15 in Minneapolis.

Bone and marrow fat come from the same biological precursor – mesynchymal stem cells. "The pathways for bone and fat have a reciprocal relationship, so we needed to find the key that disrupts the fat production pathway, which would then instead encourage bone growth," Shi says.

GILZ, Shi and Pan say, was already a known mediator of the anti-inflammatory response of glucocorticoids, and the protein also mediates bone production. Shi's early research had shown that glucocorticoids enhance bone formation in the lab because of a short "burst" of GILZ.

The protein works by inhibiting the way cells regulate fat production and turn on fat-producing genes, Shi says. "When you permanently express GILZ, the fat pathway is suppressed, so the body chooses to produce bone instead."

"We found that when we overexpressed the protein in these mice, it increased bone formation," Pan added. "This supports our original

hypothesis that GILZ mediates the body's response to glucocorticoids and encourages bone growth." In fact, the genetically modified mice showed a significant increase in bone mineral density and bone volume as well, he found.

"That means GILZ is a potential new anti-inflammatory drug candidate that could spare people from the harmful effects associated with glucocorticoid therapy," Pan said

Long-term goals, Shi said, are developing the GILZ-like pill that is anti-inflammatory and protects or even increases bone production.

Provided by Georgia Health Sciences University