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Study suggests link between metabolic disease, bone mass in mice

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A new study by Johns Hopkins researchers has found that insulin, the sugar-regulating hormone, is required for normal bone development and that it may provide a link between bone health and metabolic disease, such as diabetes.

The study, headed by Thomas Clemens, Ph.D., the Lewis Cass Spencer Professor of Orthopaedic Surgery, and published online in the journal *Cell,* identified a unique communication between bone and pancreas cells through which insulin signaling in osteoblasts — cells responsible for bone development — promotes postnatal bone accumulation and, at the same time, stimulates cells to make a bone protein called osteocalcin. This protein regulates insulin secretion to control blood glucose levels.

The researchers examined mutant mice lacking insulin receptors in their osteoblasts and found that they had low circulating osteocalcin, reduced bone formation and fewer osteoblasts compared to normal mice. Surprisingly, as the mutant mice aged, they became fat and developed high blood sugar accompanied by severe glucose intolerance and insulin resistance, hallmarks of diabetes in people.

When the researchers infused the mutant mice with osteocalcin, the symptoms of metabolic disease improved. These results led the team to conclude that insulin action in bone provides a critical signal that links metabolism and metabolic disease with bone heath.

"These findings will have an immediate impact on our understanding of

insulin's involvement in normal bone development and provide a theoretical guide to new approaches for the treatment of bone disease and diabetes," says Clemens, director of Johns Hopkins' Center for Musculoskeletal Research. "This research may also be a first step in explaining a possible correlation between bone health and other metabolic diseases such as osteoporosis."

More research is needed because many questions remain, added Clemens. Do osteoporosis drugs affect osteocalcin and insulin production or change blood sugar? Could osteoporosis drugs help patients with diabetes?

"This study," Clemens says, "is really just the beginning. The next step is to conduct studies in humans."

More information: Ferron et al.: “Insulin Signaling in Osteoblasts Integrates Bone Remodeling and Energy Metabolism.” Publishing in Cell 142, 296-308, July 23, 2010. DOI:10.1016/j.cell.2010.06.003

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