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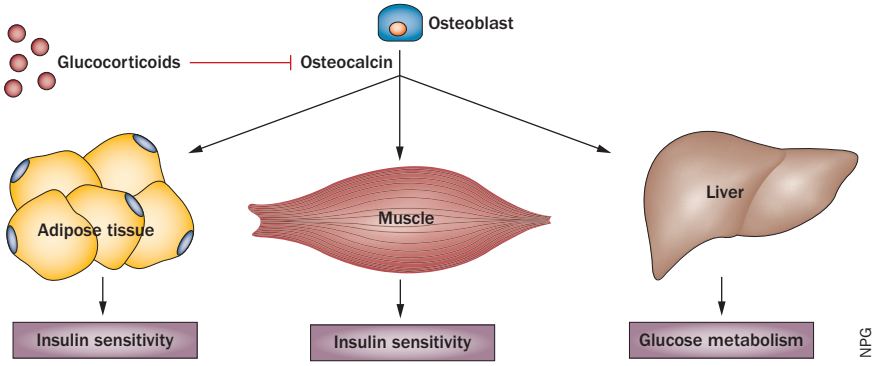
BONE

Bare bones of glucocorticoid effects on metabolism

Long-term treatment with glucocorticoids is widely known to be associated with the development of metabolic disorders including insulin resistance, diabetes mellitus and weight gain; however, the mechanisms underlying these adverse effects remain unclear. New research suggests that osteoblasts, through the production of osteocalcin, have a pivotal role to play.

Using a transgenic mouse model in which a glucocorticoid-inactivating enzyme is expressed exclusively in osteoblasts, Markus Seibel and colleagues found that transgenic mice were protected from the weight gain associated with administration of exogenous corticosterone. Glucocorticoid-induced insulin resistance and glucose intolerance were similarly attenuated in the transgenic mice compared with wild-type mice.

In line with these observations, serum levels of osteocalcin were substantially suppressed in wild-type mice, but to a much lesser extent in transgenic mice. "The osteoblast was protected from the effects of glucocorticoids," explains Seibel, "maintaining its function of making and secreting osteocalcin."



Further establishing the link between the skeleton and fuel metabolism, the researchers showed that gene therapy to induce production of osteocalcin in wild-type mice prevented the effects of glucocorticoids on glucose metabolism. "Animals expressing osteocalcin in the liver did not develop diabetes or obesity when treated with corticosteroids," reports Seibel. "This strongly suggests that osteocalcin is one of the main signals that links osteoblasts and bone to systemic fuel metabolism."

Together, the results point to a key role for the skeleton, and the function of osteoblasts in particular, in the adverse effects of glucocorticoids on metabolism.

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Original article Brennan-Speranza, T. C. *et al.* Osteoblasts mediate the adverse effects of glucocorticiods on fuel metabolism. *J. Clin. Invest.* doi:10.1172/JCI63377