MedicalXpress

Scientists discover new link between bone cells and blood sugar level

February 15 2018

Bone cells do not just form new bone, they also influence blood sugar levels. Leuven scientists have now discovered a new mechanism that controls this link. The metabolism of bone cells determines how much sugar they use; if the bone cells consume more sugar than normal, it can lower the glucose level in the blood. This research may contribute to future therapies for conditions such as osteoporosis and diabetes.

The skeleton is often seen as inert tissue, but this perception is quite wrong. In fact, the skeleton is constantly being renewed: old bone fragments are broken down and new bone matrix is deposited, leading to a completely renewed skeleton every 10 years. There are specific cells that form bone and other cells that resorb it. In diseases such as osteoporosis, the latter cells are too active and too much bone is degraded. Many drugs are aimed at blocking these resorptive cells. Unfortunately, this generally means that their counterparts, the cells responsible for the formation of bone, also stop working. As a consequence, the renewal of bone halts. In addition to bone loss, the quality of the bone also deteriorates. Ultimately, this can lead to painful fractures that are difficult to heal.

To develop new drugs, scientists are investigating how bone-forming cells can be activated. "To achieve this, it is crucial that we understand exactly how these cells work," says professor Christa Maes. "Our research focuses on how these bone cells emerge and form bone at the right sites. A good blood supply is vital for the bone cells to work well. But we do not yet understand the full meaning of the close connection

between blood vessels and bone cells. One aspect is that blood vessels provide oxygen. In this study, we investigated the importance of oxygen by analyzing mice with a mutation that makes their bone cells behave as if they were deprived of oxygen."

The researchers found two consequences. First, the mice formed abnormally heavy bones. Within the bones, they noted that the bone cells absorbed massive amounts of glucose. "That observation is in line with the usual response of cells to oxygen deprivation: they save on the consumption of oxygen by converting glucose to lactate instead of burning the glucose. No oxygen is needed for this conversion, but the downside is that it produces much less energy. In order to generate enough energy, the bone cells in our mice therefore take up much more glucose than normal."

A second and rather unexpected effect was that the mice were lean. "The mice also did not seem to gain weight when they got older, like normal mice do. Still, they ate as much as their normal littermates and were even less physically active. Further research revealed that the mice had low blood sugar levels," says PhD student Naomi Dirckx.

The two effects appeared to be connected: "Mice that had more glucose absorbed into their skeletons showed less glucose circulating in their blood. As such, the altered metabolism in the bone cells caused the mice to have a beneficial whole-body glucose turnover and a lean body. This reveals a new link between bone and the blood glucose level," says professor Christa Maes.

This finding offers new angles for research into conditions such as osteoporosis, diabetes and obesity. "In diabetes, for instance, we see increased blood sugar levels combined with a poor bone quality that easily leads to fractures. With this new knowledge, we can continue working on treatments that could possibly solve both problems, although

this will of course require many more years of research."

More information: Naomi Dirckx et al, Vhl deletion in osteoblasts boosts cellular glycolysis and improves global glucose metabolism, *Journal of Clinical Investigation* (2018). DOI: 10.1172/JCI97794

Provided by KU Leuven