New function for the protein Bcl-xL: It prevents bone breakdown

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In blood cells, the protein Bcl-xL has a well-characterized role in preventing cell death by a process known as apoptosis. However, its function(s) in osteoclasts, cells that slowly breakdown bone (a process known as resorption), has not been determined. In addressing this issue, Sakae Tanaka and colleagues, at The University of Tokyo, Japan, have discovered that not only does Bcl-xL prevent osteoclast apoptosis in mice, it also negatively regulates the bone-resorbing activity of osteoclasts.

To determine the function of Bcl-xL in osteoclasts, the researchers generated mice lacking Bcl-xL only in osteoclasts. As in blood cells, Bcl-xL was shown to promote the survival of osteoclasts. Unexpectedly, however, the mutant mice exhibited marked osteopenia at one year of age.

Further analysis indicated that the reduced bone mass was caused by increased osteoclast-mediated bone resorption and identified a potential underlying mechanism. Specifically, Bcl-xL was found to decrease the production of extracellular matrix proteins, which bind cell surface integrin molecules, leading to the activation of c-Src signaling pathways that are already known to promote osteoclast-mediated bone resorption. Thus, in the absence of Bcl-xL, increased production of extracellular matrix proteins leads to increased osteoclast-mediated bone resorption.

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