

Repair cartilage potentially can heal horribly broken bones

May 11 2016



New ways to regenerate bone emerge from the adult zebrafish face. (Sandeep Paul and Seth Ruffins)

Stem cells could one day be stimulated to make a special type of cartilage to help repair large, hard-to-heal bone fractures – a potential boon for doctors treating big-money athletes, USC researchers say.

Gage Crump, senior author, and his colleagues used the regeneration of zebrafish jawbone to show that the processes required for embryonic development are not necessarily repeated during regeneration of damaged body parts like fractured bones. The study was published online in *Development* last month.

"An exciting finding from our work is that, somewhat counterintuitively, cartilage is critical for healing full-thickness bone injuries," said Crump, associate professor of stem cell and regenerative medicine at the Keck School of Medicine of USC. "By understanding how this bone-producing cartilage is generated in the simpler zebrafish model, we hope to find ways to create more of this unique cartilage tissue in patients to better heal their bones."

Zebrafish are vertebrates that have bones like humans but differ because they have the remarkable ability to regenerate many of their organs. When human bones fracture, a limited cartilage callus forms and is replaced by bone that bridges small but not large gaps. In zebrafish, however, the researchers found that the cartilage callus continued to expand and filled very large bone gaps. Remarkably, this cartilage then changed into bone throughout the large lesion.

Why the discovery matters

Today people who have severe bone fractures may have a surgeon insert metal pins and plates to help set bone, undergo [bone grafts](#) or buy into the still-developing practice of adding [stem cells](#) to the injured area to rush recovery.

About 6 million people in the United States break a bone each year, according to the American Academy of Orthopaedic Surgeons. Although most people recover fully, about 300,000 are slow to heal or do not heal at all with traditional methods. Complications include post-traumatic arthritis, growth abnormalities, delayed union and misaligned union.

How cartilage gives rise to bone repair

The surface of bones has a thin lining of stem cells that help maintain [bone mass](#) throughout life. USC researchers identified a gene, called indian hedgehog a (ihha), responsible for giving the OK to stem cells to shift from making bone to making cartilage that will repair broken bones. Zebrafish lacking this gene are unable to make cartilage in response to bone injury, and they heal poorly.

"Traditionally, the therapeutic approach to healing bone has been to use [bone cells](#) or [bone](#)-like materials," said Francesca Mariani, study co-author and assistant professor of cell and neurobiology at Keck Medicine of USC. "This work suggests that, at least for large-scale repair, stimulating stem cells to make a special kind of [cartilage](#) might be more effective."

More information: Sandeep Paul et al. Ihha induces hybrid cartilage-bone cells during zebrafish jawbone regeneration, *Development* (2016). [DOI: 10.1242/dev.131292](https://doi.org/10.1242/dev.131292)

Provided by University of Southern California

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