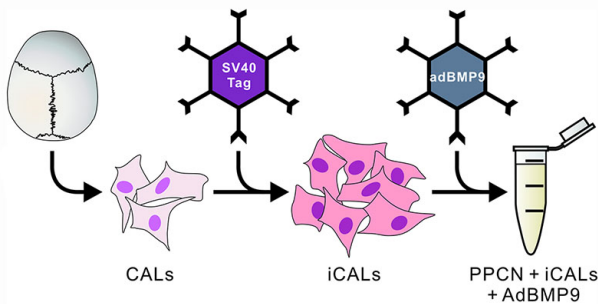


New material regrows bone: Procedure could potentially treat patients with injuries to the skull

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A schematic representation of the experimental design. Credit: Northwestern University

A team of researchers repaired a hole in a mouse's skull by regrowing "quality bone," a breakthrough that could drastically improve the care of people who suffer severe trauma to the skull or face.

The work by a joint team of Northwestern University and University of Chicago researchers was a resounding success, showing that a potent combination of technologies was able to regenerate the skull [bone](#) with supporting blood vessels in just the discrete area needed without developing scar tissue—and more rapidly than with previous methods.

"The results are very exciting," said Guillermo Ameer, professor of biomedical engineering at Northwestern's McCormick School of Engineering, and professor of surgery at Feinberg School of Medicine.

Supported by the China Scholarship Council, National Institute of Dental and Craniofacial Research, Chicago Community Trust, and National Center for Advancing Translational Sciences, the

research was published last week in the journal *PLOS One*. Russell Reid, associate professor of surgery at the University of Chicago Medical Center, is the article's corresponding author. Reid, his long-time collaborator Dr. Tong-Chuan He, and colleagues in Hyde Park brought the surgical and biological knowledge and skills. Zari P. Dumanian, affiliated with the medical center's surgery department, was the paper's first author.

"This project was a true collaborative team effort in which our Regenerative Engineering Laboratory provided the biomaterials expertise," Ameer said.

Injuries or defects in the skull or facial bones are very challenging to treat, often requiring the surgeon to graft bone from the patient's pelvis, ribs, or elsewhere, a painful procedure in itself. Difficulties increase if the injury area is large or if the graft needs to be contoured to the angle of the jaw or the cranial curve.

But if all goes well with this new approach, it may make painful bone grafting obsolete.

In the experiment, the researchers harvested skull [cells](#) from the mouse and engineered them to produce a potent protein to promote [bone growth](#). They then used Ameer's hydrogel, which acted like a temporary scaffolding, to deliver and contain these cells to the affected area. It was the combination of all three technologies that proved so successful, Ameer said.

Using calvaria or skull cells from the subject meant the body didn't reject those cells.

The protein, BMP9, has been shown to promote bone cell growth more rapidly than other types of BMPs. Importantly, BMP9 also appeared to improve the creation of blood vessels in the area.

Being able to safely deliver skull cells that are capable of rapidly regrowing bone in the affected site, in vivo as opposed to using them to grow bone in the laboratory, which would take a very long time, promises a therapy that might be more "surgeon friendly, if you will, and not too complicated to scale up for the patients," Ameer said.

The scaffolding developed in Ameer's laboratory, which is a material based on citric acid and called PPCN-g, is a liquid that when warmed to body temperature becomes a gel-like elastic material. "When applied, the liquid, which contains cells capable of producing bone, will conform to the shape of the bone defect to make a perfect fit," Ameer said. "It then stays in place as a gel, localizing the cells to the site for the duration of the repair." As the bone regrows, the PPCN-g is reabsorbed by the body.

"What we found is that these cells make natural-looking bone in the presence of the PPCN-g," Ameer said. "The new bone is very similar to normal bone in that location."

In fact, the three-part method was successful on a number of fronts: The regenerated bone was better quality, the bone growth was contained to the area defined by the scaffolding, the area healed much more quickly, and the new and old bone were continuous with no scar tissue.

The potential, if the procedure can be adapted to treat people that suffered trauma from car accidents or aggressive cancers that have affected the skull or face, would be huge, and give surgeons a much-sought-after option.

"The reconstruction procedure is a lot easier when you can harvest a few cells, make them produce the BMP9 protein, mix them in the PPCN-g solution, and apply it to the bone defect site to jump-start the new bone growth process where you want it." Ameer said.

Ameer cautioned that the technology is years away to being used in humans, but added, "We did show proof of concept that we can heal large defects in the skull that would normally not heal on their own

using a protein, cells and a new material that come together in a completely new way. Our team is very excited about these findings and the future of reconstructive surgery."

More information: Zari P. Dumanian et al, Repair of critical sized cranial defects with BMP9-transduced calvarial cells delivered in a thermoresponsive scaffold, *PLOS ONE* (2017). [DOI: 10.1371/journal.pone.0172327](https://doi.org/10.1371/journal.pone.0172327)

Provided by Northwestern University

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