Human embryonic stem cell -- derived bone tissue closes massive skull injury

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There are mice in Baltimore whose skulls were made whole again by bone tissue grown from human embryonic stem cells (hESCs).

Healing critical-size defects (defects that would not otherwise heal on their own) in intramembraneous bone, the flat bone type that forms the skull, is a vivid demonstration of new techniques devised by researchers at John Hopkins University to use hESCs for tissue regeneration.

Using mesenchymal precursor cells isolated from hESCs, the Hopkins team steered them into bone regeneration by using “scaffolds,” tiny, three-dimensional platforms made from biomaterials.

Physical context, it turns out, is a powerful influence on cell fate. Nathaniel S. Hwang, Jennifer Elisseeff, and colleagues at Hopkins demonstrated that by changing the scaffold materials, they could shift mesenchymal precursor cells into either of the body’s osteogenic pathways: intramembraneous, which makes skull, jaw, and clavicle bone; or endochondral, which builds the “long” bones and involves initial formation of cartilage, which is then transformed into bone by mineralization.

Mesenchymal precursor cells grown on an all-polymer, biodegradable scaffold followed the endochondral lineage. Those grown on a composite scaffold made of biodegradable polymers and a hard, gritty mineral called hydroxyapatite went to the intramembraneous side.

Biomaterial scaffolds provide a three-dimensional framework on which cells can proliferate and differentiate, secrete extracellular matrix, and form functional tissues, says Hwang. In addition, their known composition allowed the researchers to characterize the extracellular microenvironmental cues that drive the lineage specification.

The promise of pluripotent embryonic stem cells for regenerative medicine hangs on the development of such control techniques. Left to themselves, hESCs in culture differentiate wildly, forming a highly mixed population of cell types, which is of little use for cell-based therapy or for studying particular lineages.

Conventional hESC differentiation protocols rely on growth factors, co-culture, or genetic manipulation, say the researchers. The scaffolds offer a much more efficient method.

As a proof of principle, Hwang and colleagues seeded hESC-derived mesenchymal cells onto hydroxyapatite-composite scaffolds and used the resulting intramembraneous bone cells to successfully heal large skull defects in mice. The Hopkins researchers believe that this is the first study to demonstrate a potential application of hESC-derived mesenchymal cells in a musculoskeletal tissue regeneration application.

Source: American Society for Cell Biology