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Molecules, Stem Cells and Bone Growth

Small molecule with an appropriate scaffold potently induced mesenchymal stem cells to generate bone cells useful for spinal fusion. The paper was featured in *Tissue Engineering.*

San Diego, California – December, 2020. Medicinal chemists and biologists at the Human BioMolecular Research Institute (HBRI), in San Diego, CA, and University of California, San Diego (UCSD), in San Diego, CA, respectively, have reported on a technology to robustly produce human bone cells from stem cells. This may have importance for spinal fusion and addressing other bone cell disease drug discovery efforts.

Despite success of bone grafts, treatment of large or complex bone defects remains a challenge. Autograft bone harvest limitations include prolonged recovery time, increased surgical blood loss, and pain. Use of autologous bone may be compromised by underlying bone or metabolic disorders that limit patient eligibility. Allografts may be applicable to individuals with underlying conditions, but allograft comes with safety concerns. Now, the ability to produce unlimited numbers of human bone cells creates a new paradigm for addressing bone defects and bone disease. Writing in December, 2020, in the journal *Tissue Engineering,* the authors describe a robust way to create human bone cells. With this new method, researchers also showed transplantation of this mixture into the spine resulted in efficient spinal fusion in rats after only 28 days.

The method combines a derivative of a small molecule from the curcumin family applied to human bone marrow-derived mesenchymal stromal cells (hBMSCs) in the presence of an appropriate tricalcium phosphate (TCP) scaffold to robustly generate bone cells for noninvasive therapy for spinal fusion. The technique can be adapted to other bone defects or bone diseases with potentially less side effects than current standard of care.

The approach provides an efficient biocompatible scaffold for delivery of a potentially clinically useful system applicable in patients.

"*The technology will lead to bone disease treatment applications that may prove efficacious in clinical trials, resulting in greater patient tolerance, and less side effects*"… explains co-author Dr. John Cashman. "*As stem cell drug development progresses, and less toxic approaches become available, patients will benefit from improved safety, less side effects and possibly with significant cost-savings."*

How the technology works

Chemists and biologists at HBRI and UCSD are among the first group to apply small molecules and an osteogenic scaffold in the presence of human mesenchymal stromal cells to generate bone cells. The researchers showed that after transplantation into rats, the strategy was useful for spinal fusion.

Treatment of hBMSCs with a curcuminoid compound in the presence of a TCP ceramic increased osteogenic target gene expression over time. After 8 days in cell culture in the presence of curcuminoid and TCP ceramic, osteogenesis of hBMSCs, including proliferation, differentiation, and mineralization was observed. No evidence of chondrogenic or adipogenic potential using this protocol was observed. Transplantation of curcuminoid/TCP-treated hBMSC mixtures into the spine of immunodeficient rats showed that it achieved spinal fusion and provided greater stability of the spinal column than untreated hBMSC-TCP implants or TCP alone implants. On the basis of histological analysis, greater bone formation was associated with curcuminoid/TCP-treated hBMSC implants manifested as contiguous growth plates with extensive hematopoietic territories.

Publication

"Role of Curcuminoids and Tricalcium Phosphate Ceramic in Rat Spinal Fusion." Daniel A. Ryan, Jiongjia Cheng, Koichi Masuda, and John R. Cashman, *TISSUE ENGINEERING*: Part C, Volume 26, Number 11, 577-589 (2020).

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About Human BioMolecular Research Institute

The Human BioMolecular Research Institute is a non-profit research institute conducting basic research focused on unlocking biological and chemical principles related to diseases of the human brain, human bone, cardiovascular disease and cancer. The Institute conducts fundamental studies of central nervous system disorders, bone, heart

disease and cancer including stem cell approaches and translates findings into new drug development to address human illness. In addition, the institute promotes scientific learning through community service and public access by disseminating information and sharing research with collaborators, colleagues and the public. For more information, visit www.HBRI.org.

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