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Advancing stem cell research

Umbilical cord blood stem cells are currently being used to treat more than 75 life-threatening blood and immune disorders. In 2007, Michigan's first public cord bank, jointly sponsored by Oakland University and Beaumont Hospitals, was established. Public cord blood banking will lead to rapid availability of cells and tissues for replacement and regeneration therapy.

The mission of the cord blood bank is to provide additional sources of adult stem cells (SC) for basic research and their application in medicine to develop therapeutics and cures for many otherwise intractable diseases and disorders. Rasul Chaudhry and his colleagues have isolated not only hematopoietic and mesenchymal stem cells but also embryonic-like stem cells from the cord blood samples donated by consented volunteers. New efforts are focused on the renewal and differentiation potential of cord blood SCs and possible uses of these cells to repair damaged nerve fibers, heart muscle and other tissues.

Chaudhry is studying embryonic, adult and induced pluripotent stem cells, focusing on the molecular mechanisms of neurogenesis, osteogenesis and chondrogenesis (the creation of nerves, bone, and cartilage). He is also studying the role of bone morphogenic proteins (BMPs) and sex hormones in early development and differentiation; tissue engineering; and therapeutic applications of SCs for treating spinal cord injuries and neurological diseases, including intervertebral disc (IVD), retinal and nerve degeneration, Multiple Sclerosis, Alzheimer's and Parkinson's diseases.

BMP signaling is involved at multiple levels of regulation. Chaudhry's group has shown that some of the BMPs are specific inducers of embryonic SC differentiation. For example, BMP 2 and BMP 4 induce osteogenic and chondrogenic differentiation, respectively. He has also shown that chemical and microenvironmental cues promote selective differentiation of SCs seeded into biodegradable and biocompatible scaffolds. These studies are aimed at generating vascularized tissue implants for replacement and regenerative therapies.

Recently, Chaudhry and his team have shown that embryonic SC-derived neuroprogenitors transplanted in an animal model proliferated, differentiated and integrated in the diseased retinal tissue. The transplanted cells expressed neural markers such as Nestin, Olig 1, and GFAP. In another study, they have demonstrated chondrogenic derivatives of SCs implanted in the degenerated IVD of a rabbit model survived and differentiated into notochordal- and chondrocyte-like cells and expressed chondro-specific markers such as cytokeratin, vimentin and collagen II. Further studies are underway to devise strategies for restoring physiological function of damaged or degenerated retinas, IVD and other tissues.

Representative Recent Publications

1. Sheikh H, Zakharian K, DeLa Torre RP, Fecek C, Vasquez A, Chaudhry GR, Svinarich DM, Perez-Cruet M. 2009. In vivo intervertebral disc regeneration using stem cell derived chondroprogenitors. *J Neurosurg Spine* 10:265-272.

2. Chaudhry GR, Fecek CM, Lai M, Wu WC, Cheng M, Vasquez A, Pasierb M, Trese M. 2009. Fate of embryonic stem cell derivatives implanted into the vitreous of a slow retinal degenerative mouse model. *Stem Cells Dev* 18:247-258.

3. Fecek C, Yao D, Kaćorri A, Vasquez A, Iqbal S, Sheikh H, Svinarich DM, Perez-Cruet M, Chaudhry GR. 2008. Chondrogenic derivatives of embryonic stem cells seeded into 3D polycaprolactone scaffolds generated cartilage tissue in vivo. *Tissue Eng A.* 14:1403-1413.

4. Yao D, Smith A, Nagarajan P, Vasquez A, Dang L, Chaudhry GR. 2006. Fabrication of polycaprolactone scaffolds using a sacrificial compression-molding process. *J Biomed Mater Res B* 77:287-295.

5. Vasques A, Kaćorri A, Yao D, Perez-Cruet M, Zou Q, Chaudhry GR. 2005. Proliferation of embryonic stem cell-derived neural cells and their growth in biodegradable scaffolds. *J Undergrad Res* 7:300-304.

6. Chaudhry GR, Yao D, Smith A, Hussain A. 2004. Osteogenic cells derived from embryonic stem cells produced bone nodules in three-dimensional scaffolds. *J Biomed Biotech* 2004:203-210.

7. Psaros S, Smith A, Walia SK, Chaudhry GR. 2004. Effect of substituted biphenyls on embryonic stem cell growth. *J Undergrad Res* 6:86-89.

8. Smith A, Sevilla M, Chaudhry GR. 2004. A protein factor supports undifferentiated growth of human embryonic stem cells. *J Undergrad Res* 6:98-102.