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Session 122
Extracellular Matrix and Cell Signaling I
Presentation 327
Poster Board B279
Halls C-G

Patterning of Multiple Cell Lineages from a Single Stem Cell Population

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Muscle and bone from an ink-jet printer

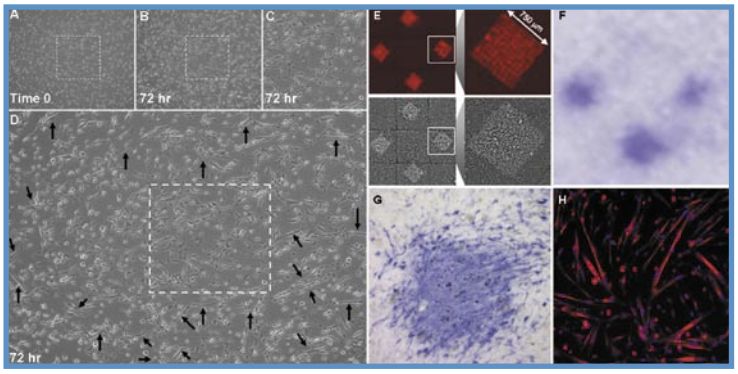
Printed "bio-inks" can pattern multiple cell lineages from a single adult stem cell population

A Pittsburgh-based research team has used an innovative inkjet system to print unique "bio-ink" patterns that directed adult muscle-derived stem cells from mice to differentiate into both muscle cells and bone cells. This is the first report of a system that can pattern the formation of multiple tissues from a single population of adult stem cells.

Bioengineers from Carnegie Mellon University's Robotics Institute and the Institute for Complex Engineered Systems teamed with stem cell biologists from the University of Pittsburgh School of Medicine and Children's Hospital of Pittsburgh to demonstrate the use of ink-jet printing to pattern "bio-inks"—combinations of growth factors to control the fate of stem cells. Working with mice, the Pittsburgh biologists have gained considerable experience in using growth factors to control proliferation and differentiation in populations of "muscle-derived stem cells," or MDSCs. Previous work by University of Pittsburgh researchers has demonstrated the ability of MDSCs to repair muscle in a model for Duchenne Muscular Dystrophy, improve cardiac function following heart failure, and heal large bone defects in the skull. Controlling not only what types of cells differentiate from stem cells, but also gaining spatial control of stem cell differentiation, are important capabilities if researchers are to engineer replacement tissues that might be used in treating disease, trauma, or genetic abnormalities. Spatial patterning of stem cell differentiation through delivery of bio-inks with an ink-jet printer will offer the Pittsburgh researchers a whole new level of complexity and control.

The custom built ink-jet printer, which was developed at Carnegie Mellon, can deposit bio-inks in virtually any design, pattern, or concentration, laying down patterns on fibrin-coated slides placed in culture dishes containing MDSCs. Based on pattern, dose, or factor printed by the ink-jet, the MDSCs could be directed when to differentiate into various cell types (e.g., bone- or muscle-like). Immunocytochemical analyses confirmed that the bio-ink patterns successfully directed differentiation of the MDSCs toward a myogenic or an osteogenic lineage in direct registration to patterns.

The proof-of-concept experiment led to the formation of muscle- and bone-like tissues simultaneously in the same culture dish. The long-term promise of this new technology could be the tailoring of tissue-engineered regenerative therapies. In preparation for preclinical studies, the Pittsburgh researchers are following up this work by combining the versatile ink-jet system with advanced live cell imaging developed at Carnegie Mellon's Robotics Institute and Molecular Biosensor and Imaging Center to further understand how stem cells differentiate into bone, muscle, or other cell types.



Spatial control of muscle-derived stem cell differentiation into multiple cell types using ink-jet printing. A-D) Time-lapse microscopy over 72 hr of MDSCs cultured on BMP-2 printed patterns under myogenic conditions. Muscle-like cells (myotubes) form off BMP-2 pattern; whereas no myotubes are formed on BMP-2 printed pattern. (C) is increased magnification of (B). E) Solid-phase immobilized patterns of fluorescently-labeled BMP-2 are printed using an overprinting strategy to control surface concentrations. F) Dose-dependent differentiation of MDSCs towards the osteogenic lineage shown by ALP activity (purple). G) Increased magnification of spatially-defined osteogenic differentiation of MDSCs controlled by inkjet printing of BMP-2. H) Formation of multinucleated myotubes (nuclei in blue) expressing the muscle-marker myosin heavy chain (red) off BMP-2 pattern under myogenic culture conditions.