IOWA STATE UNIVERSITY
Department of Chemical and Biological Engineering

Graduate Seminar Series 2018-2019

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University of Buffalo, State University of New York

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171 Durham Center

Iowa State University

Resetting the Aging Clock: Reprogramming Stem Cell Rejuvenation for Enhanced Tissue Regeneration

Cardiovascular disease is the leading cause of mortality worldwide. Regarded as the therapeutic gold standard, treatment with autologous grafts suffers from several technical and patient-related risks. Tissue engineered small diameter blood vessels may provide a promising alternative solution as replacement grafts. In this study, we employed adult and induced pluripotent stem cells to engineer fully functional vascular grafts that were implanted into the arterial circulation of a physiologically relevant ovine animal model, where they remained patent and underwent successful remodeling. In addition, we engineered cell-free (off-the-shelf) vascular grafts that were implanted successfully into the arterial system of adult as well as neonatal sheep. Most notably, as the animals grew, the grafts increased in size (length and diameter), demonstrating their potential application for treatment of congenital pediatric disorders.

During the course of our studies using mesenchymal stem cells (MSC) to engineer vascular grafts, we observed MSC originating from older donors suffer from limited proliferative capacity and significantly reduced myogenic differentiation potential. This is a major concern, as the patients most likely to suffer from cardiovascular disease and therefore in need of vascular grafts are elderly. Notably, we developed a strategy to reverse the proliferation and differentiation potential of MSC from adult donors as well as to restore of ECM synthesis and contractile function.

In the second part of my presentation, I will focus on deriving neural crest stem cells (NC) and their derivatives from neonatal and adult epidermis. NC cells are induced by signaling events at the neural plate border during development of vertebrate embryos. Initially arising within the central nervous system, NC cells subsequently undergo epithelial-to-mesenchymal transition and migrate into the periphery, where they differentiate into diverse cell types. We discovered that NC can be derived from postnatal human epidermal keratinocytes (KC) without genetic modification or reprogramming to the pluripotent state. Genome-wide transcriptome analyses showed that KC-derived NC cells are similar to NC cells derived from human embryonic stem cells. Moreover, KC-NC give rise in vitro and in vivo to NC derivatives such as peripheral neurons, melanocytes, Schwann cells and mesenchymal cells (osteocytes, chondrocytes, adipocytes, and smooth muscle cells). Lineage tracing studies by implantation of KC-NC into chick embryos confirmed the NC phenotype of these cells in an in vivo setting. This work represents a paradigm shift as it demonstrates that the epidermis is a novel source of abundant, readily accessible, autologous stem cells for treatment of neurodegenerative diseases, for which cell sourcing remains a severe impediment hampering cell therapy approaches.

Stelios T. Andreadis received his M.S. (Applied Mathematics) and Ph.D. degree in Chemical Engineering from the University of Michigan studying the dynamics of retroviral gene transfer for gene therapy. He then pursued postdoctoral training at the Center for Engineering in Medicine at Harvard Medical School, where he worked in the areas of gene therapy, tissue engineering and regenerative medicine. Currently he serves as SUNY Distinguished Professor of Chemical and Biological Engineering, Biomedical Engineering and Member of the Center of Excellence in Bioinformatics and Life Sciences at the University at Buffalo, State University of New York. He is also the Director of the Stem Cells in Regenerative Medicine (SCiRM) Training Program that was recently funded by NYSTEM to train students in stem cell biology and bioengineering and applications of stem cells in regenerative medicine. He served as CBE department Chair for two terms from 2012 to 2018.

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