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Combinatorial electrospun matrices promote physiologically-relevant cardiomyogenic stem cell differentiation

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Myocardial infarction results in extensive cardiomyocyte death which can lead to fatal arrhythmias or congestive heart failure. Delivery of stem cells to repopulate damaged cardiac tissue may be an attractive and innovative solution for repairing the damaged heart. Instructive polymer scaffolds with a wide range of properties have been used extensively to direct the differentiation of stem cells. In this study, we have optimized the chemical and mechanical properties of an electrospun polymer mesh for directed differentiation of embryonic stem cells (ESCs) towards a cardiomyogenic lineage. A combinatorial polymer library was prepared by copolymerizing three distinct subunits at varying molar ratios to tune the physicochemical properties of the resulting polymer: hydrophilic polyethylene glycol (PEG), hydrophobic poly(ε-caprolactone) (PCL), and negatively-charged, carboxylated PCL (CPCL). Murine ESCs were cultured on electrospun polymeric scaffolds and their differentiation to cardiomyocytes was assessed through measurements of viability, intracellular reactive oxygen species (ROS), α-myosin heavy chain expression (α-MHC), and intracellular Ca^{2+} signaling dynamics. Interestingly, ESCs on the most compliant substrate, 4%PEG-86%PCL-10%CPCL, exhibited the highest α-MHC expression as well as the most mature Ca^{2+} signaling dynamics. To investigate the role of scaffold modulus in ESC differentiation, the scaffold fiber density was reduced by altering the electrospinning parameters. The reduced modulus was found to enhance α-MHC gene expression, and promote maturation of myocyte Ca^{2+} handling. These data indicate that ESC-derived cardiomyocyte differentiation and maturation can be promoted by tuning the mechanical and chemical properties of polymer scaffold via copolymerization and electrospinning techniques.

Biography

Dr. Sung Joined Vanderbilt University as an assistant professor of Biomedical Engineering in 2009. He was a resident faculty member at the New Jersey Center for Biomaterials, Rutgers University from 2006 to 2009. He conducted his postdoctoral and graduate studies at Georgia Institute of Technology (joint program with Emory University School of Medicine) from 2001 to 2006. He had previous master degree training in Medical Engineering and undergraduate training in Biochemistry at Yonsei University in South Korea. His current research is focused on application of advanced combinatorial biomaterial systems for stem cell and vascular engineering.