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Engineering Pluripotent Stem Cell Fate and Micro-tissue Function

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ABSTRACT

Pluripotent stem cells (PSCs) afford novel avenues for ex vivo modeling and interrogation of human biology as well as potential regenerative therapies due to their innate ability to generate cells of any tissue from all three germ lineages. However, the use of PSCs for such purposes requires robust and reproducible methods of directing differentiation effectively and engineering of multicellular tissue mimetics with the appropriate cellular composition, structure and function. Our laboratory is focused on the development of enabling technologies and platforms to facilitate these goals in order to translate the potential of stem cells into clinically impactful products. We have recently differentiated excitatory (V2a) spinal interneurons from human PSCs by manipulating relevant developmental signaling pathways with small molecules. The V2a interneurons mature to a glutamatergic phenotype in vitro and extend long axon projections (>5mm in 2 weeks) in rostral and caudal directions when implanted into the spinal cord. Thus, hPSC-derived V2a interneurons may be a novel regenerative cell therapy for spinal cord injury as well as serve as a substrate for new drug screening and disease modeling purposes. We have also created 3D cardiac microtissues from hPSC-derived cardiomyocytes (CMs) in combination with different stromal cells (e.g. cardiac fibroblasts, MSCs, etc.) to assess microphysiological function. The source of stromal cells can differentially impact CM gene expression and the electrophysiological properties of 3D multicellular constructs, suggesting that heterotypic interactions can exert a significant influence on CM phenotype. Altogether, these studies demonstrate the utility of hPSC-derived differentiated cells and their potential application as novel mediators and/or substrates for the development of regenerative therapies.

BIO:

Dr. McDevitt is a Senior Investigator at the Gladstone Institute of Cardiovascular Disease and a Professor of Bioengineering and Therapeutics at the University of California, San Francisco. He was previously the founding Director of the Stem Cell Engineering Center at Georgia Tech, the Carol Ann and David D. Flanagan Professor in the Wallace H. Coulter Department of Biomedical Engineering, and a Petit Faculty Fellow in the Parker H. Petit Institute for Bioengineering and Bioscience. Dr. McDevitt has 18 years of experience in biomaterials and tissue engineering research and for the past 14 years has focused primarily on stem cell biology and engineering. The primary objective of Dr. McDevitt's research is to engineer tissues, largely from stem cell sources, for regenerative medicine and in vitro diagnostic applications. Much of the research in the McDevitt laboratory focuses on the application of microtechnologies to engineer 3D environments in order to more effectively control multicellular organization that better recapitulates complex tissue structure and subsequent function. The McDevitt laboratory is interested in using human pluripotent stem cell model platforms to systematically interrogate fundamental mechanisms of morphogenic processes, particularly those associated with critical aspects of human development that can not be probed with any other tangible experimental systems.