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Engineering functional blood vessels from human diabetic induced pluripotent stem cells (iPSC)

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Human iPSC derived vasculogenic cells may offer a long sought solution for obtaining large numbers of autologous cells sufficient for tissue engineering and opportunities to model vascular disease in a dish. We report a novel approach for the derivation of endothelial precursor cells from hips cells using triple combination of selection markers: CD34, neuropilin-1 (NP-1) and KDR, and an efficient 2-D culture system for hiPS cell-derived endothelial precursor cell expansion. Functionality of blood vessels in cranial window models of severe combined immunodeficient (SCID) mice was determined by non-invasive longitudinal *in vivo* multiphoton laser scanning microscopy for parameters that included red blood cell (RBC) velocity, blood flow and permeability to bovine serum albumin. We successfully generated endothelial cells from hiPS cells obtained from healthy donors and formed stable functional blood vessels *in vivo* - lasting for 280 days in SCID mice. The RBC velocities of engineered blood vessels were comparable to normal endogenous host vessels (1.36±0.3 mm/s), and demonstrated a higher permeability as compared to endogenous vessels. We also generated mesenchymal precursor cells (MPCs) from hiPS cells in parallel. Moreover, we successfully generated functional blood vessels *in vivo* using these endothelial cells and mesenchymal precursor cells derived from the same hiPS cell line. In parallel, we have isolated hiPSC-derived ECs and PVCs from type-1 diabetes and maturity-onset diabetes of the young (MODY) cases. The T1D-iPS engineered blood vessels were functional for 4 months *in vivo* while MODY-iPS-ECs failed to form functional blood vessels. Human iPSC-derived vasculogenic cells may be an abundant source to examine vascular defects of diabetes in a dish.

Biography

Rekha Samuel is a Pathologist working at the Centre for Stem Cell Research (CSCR), Christian Medical College, India. She did her Post-doctoral Training in Dr. Rakesh K Jain's Laboratory at Massachusetts General Hospital, Boston, on an overseas fellowship that was funded by the Department of Biotechnology, Government of India. She is the Principal Investigator of the Vascular Biology Laboratory at the CSCR. Her current research focuses on examining the Microvascular Defects of Type 2 Diabetes using the Gestational Diabetes Mellitus Placenta. She has recently been awarded the European Foundation of Study for Diabetes/ Sanofi 2015 grant.

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