BIOENGINEERING SEMINAR

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Seminar Hall, 1st floor, Chemical Engineering Building

Particle Engineering of Stem Cells using Surface Modified Drug Delivery Systems for Phenotype Control & Targeted Cancer Therapy

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Mesenchymal stem cells (MSCs) are attractive candidates to bring about repair and regeneration owing primarily to their immunomodulatory secretome. Each year, multiple MSC-based clinical trials are investigated and the major unmet need is controlling the secretome post-transplantation. We demonstrate a novel particle engineering approach of MSCs to attenuate undesirable pro-inflammatory secretome. Under inflammatory stimulus (TNF-α) MSCs secrete significantly augmented levels of pro-inflammatory mediators. To sustainably reduce secretion of these mediators, we developed poly-L-lactide-co-glycolide (PLGA) based microparticles for controlled release of a small molecule inhibitor of NF-κB signalling. The microparticles were surface modified with poly-L-lysine (PLL) to facilitate increased internalization in MSCs. Preconditioning MSCs with the inhibitor followed by TNF-α activation failed to attenuate pro-inflammatory secretome. Conversely, intracellular release of the inhibitor from microparticles in TNF-α activated MSCs significantly attenuated pro-inflammatory secretome for at least six days *in vitro. Secretome from particle engineered MSCs significantly reduced migration of human monocytes in vitro and relevant to diseases such as atherosclerosis and cardiac fibrosis. This microparticle engineering approach may have great implications in the development of MSC secretome as therapeutic in particular and for controlling stem cell phenotype post-transplantation in general.*

MSCs are also known to be tumor tropic and hence could be developed as targeted delivery vehicles to metastatic tumor sites. In particular, prostate cancer metastasis necessitates efficient targeting of anti-cancer drugs while reducing host systemic toxicity. Prostate specific antigen (PSA) is highly expressed in the extracellular space within prostate cancer and absent in blood and other tissues and thus is an important therapeutic candidate. In this study, we developed PLGA-based microparticles loaded with a PSA-cleavable prodrug. The microparticles were surface modified using chitosan or multiple lipid bi-layers. Surface modification altered the surface charge and in addition, prevented initial burst release of the highly potent prodrug and maximized internalization of microparticles in MSCs without affecting viability for at least 4 days *in vitro. Maintaining MSC viability is extremely critical to allow homing to tumors and releasing the prodrug at the target site. Hence this particle-in-cell engineering approach may be developed as a platform technology for targeted delivery of cancer therapeutics.*

About the speaker:

Dr. Sudhir Ranganath is an IUSSTF Postdoctoral Fellow at Brigham & Women's Hospital, Harvard Medical School, USA. Under this fellowship he was a postdoctoral fellow at the Institute for Stem Cell Biology (inStem) and JNCASR, India. He was previously a Singapore Biomedical Research Council (BMRC) research fellow. He received his B.E in Chemical Engineering from Bangalore University, M.Sc and PhD in Chemical & Biomolecular Engineering from the National University of Singapore (NUS). His research is at the interface of biomaterials, drug delivery and stem cell bioengineering with applications in cancer treatment and regenerative medicine. He has published in international journals such as Cell Stem Cell, Biomaterials and Pharmaceutical Research. His future interests are to develop cell-inspired targeted drug delivery systems, small molecule-based cell bioengineering and study cell-particle(biomaterial) interaction using tools such as chemical engineering of cells and high throughput screening.