PLENARY PRESENTATIONS

Harnessing Engineered Cell and Tissue Adhesion for Medical Applications

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This talk will explore technologies that are currently being developed in the Karp Lab to tackle numerous medical problems, namely: sealing tissues/closing wounds, achieving long term local drug delivery for treatment of diseases such as inflammatory arthritis, and development of surfaces to separate cells for disposable point of care diagnostics. In addition, an mRNA transfection strategy using cells for targeted delivery of biologics will be discussed, as will approaches to engineer cells with an intracellular depots of phenotype altering agents that can be used for drug delivery or programming cell fate via both intracrine-, paracrine-, and endocrine-like mechanisms. The talk will examine methods to enhance the engraftment of infused stem cells through a surface engineering approach to induce a robust rolling response and the potential of nano-engineered sensors immobilized on the cell surface that can be used to detect signals within the cellular nano-environment with unprecedented spatial and temporal resolution that should be useful for elucidating niche biology *in vivo* and for drug discovery.

Biofunctional Hydrogels for Cell Delivery and Tissue Repair

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Hydrogels, highly hydrated cross-linked polymer networks, have emerged as powerful synthetic analogs of extracellular matrices for basic cell studies as well as promising biomaterials for regenerative medicine applications. A critical advantage of these artificial matrices over natural networks is that bioactive functionalities, such as cell adhesive sequences and growth factors, can be incorporated in precise densities while the substrate mechanical properties are independently controlled. We have engineered poly(ethylene glycol) [PEG]-maleimide hydrogels to incorporate VEGF as supportive matrices to improve pancreatic islet vascularization and engraftment. PEG-maleimide

were functionalized with RGD peptide and VEGF and cross-linked into a hydrogel by addition of collagenase-degradable peptides. These hydrogels supported *in vitro* islet survival, insulin production, and intra-islet endothelial cell sprouting. Importantly, islets delivered within these functionalized hydrogels exhibited improved engraftment, vascularization and insulin production compared to islets delivered within other hydrogels and without a hydrogel carrier. In another application, we functionalized hydrogels with the integrin-specific, collagen-mimetic triple helical peptide GFOGER to promote osteogenic differentiation and bone repair. Human mesenchymal stem cells adhered well and maintained viability on both RGD and GFOGER hydrogels. However, alkaline phosphatase activity and mineralization was higher on GFOGER-hydrogels than on RGD-hydrogels. GFOGER-functionalized hydrogels significantly enhanced bone volume and mass in critically sized, segmental bone defects in murine radii compared to other hydrogels and empty defects. These studies establish these maleimide-cross-linked hydrogels as promising biomaterial carriers for cell delivery, engraftment and enhanced tissue repair.

Bioactivation and Morphology of Biomaterials as Complementary Triggers for Regenerative Medicine

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Biointerface engineering of classical biomaterials such as orthopedic implants for specific bioactivation and optimized tissue ingrowth has initially directed biomaterials research. With the onset of tissue engineering, the aim to structurally and morphologically mimic the native environment of cells, the so-called extra-cellular matrix (ECM), has become a major research focus. In the ECM of connective tissue, cells adhere to polymeric protein fibers that serve as their mechanical scaffold. This interaction of cells with the ECM is highly regulated and controlled. Hence, together with degradability, both the activation of specific cell/material interactions and a three-dimensional environment that mimics the ECM biochemically and structurally are core challenges for advanced tissue engineering scaffolds. Nowadays, regenerative medicine has turned into the focus of biomaterials research, and many classical paradigms are challenged. The strategy of *in situ* tissue engineering starts to replace the classical approach of initial biopsies with subsequent *in vitro* culture of cell-scaffold constructs, and the use of 3D printing technologies allows the direct generation of hierarchical tissue-like structures. This also facilitates the design of *in vitro* tissue models, taken into account that dynamic co-culture systems are available that facilitate *in vitro* tissue ripening. The lecture will guide us through this development using the work performed in my department as examples. Special focus will be given to the changing role of surface activation of biomaterials and the promise of stringent morphology control for *in situ* regenerative materials, as well as the use of 3D printing technologies for bio-fabrication of tissue-like structures.