MAR15-2014-020248

Abstract for an Invited Paper
for the MAR15 Meeting of
the American Physical Society

Protein-engineered block-copolymers as stem cell delivery vehicles

SARAH HEILSHORN, Stanford University

Stem cell transplantation is a promising therapy for a myriad of debilitating diseases and injuries; however, current delivery protocols are inadequate. Transplantation by direct injection, which is clinically preferred for its minimal invasiveness, commonly results in less than 5% cell viability, greatly inhibiting clinical outcomes. We demonstrate that mechanical membrane disruption results in significant acute loss of viability at clinically relevant injection rates. As a strategy to protect cells from these damaging forces, we show that cell encapsulation within hydrogels of specific mechanical properties will significantly improve viability. Building on these fundamental studies, we have designed a reproducible, bio-resorbable, customizable hydrogel using protein-engineering technology. In our Mixing-Induced Two-Component Hydrogel (MITCH), network assembly is driven by specific and stoichiometric peptide-peptide binding interactions. By integrating protein science methodologies with simple polymer physics models, we manipulate the polypeptide chain interactions and demonstrate the direct ability to tune the network crosslinking density, sol-gel phase behavior, and gel mechanics. This is in contrast to many other physical hydrogels, where predictable tuning of bulk mechanics from the molecular level remains elusive due to the reliance on non-specific and non-stoichiometric chain interactions for network formation. Furthermore, the hydrogel network can be easily modified to deliver a variety of bioactive payloads including growth factors, peptide drugs, and hydroxyapatite nanoparticles. Through a series of *in vitro* and *in vivo* studies, we demonstrate that these materials may significantly improve transplanted stem cell retention and function.