Designing Materials and Constructing Tissues for Cardiovascular Regenerative Medicine

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The range of materials that are mechanically compatible with cardiovascular and other soft tissues to provide temporary structural support during regenerative processes has historically been limited. To address this need as well as to directly evaluate new approaches to relieve cardiovascular tissue failure, our group has focused on developing a series of biodegradable thermoplastic elastomers based on poly(ester urethane)ureas (PEUUs) that possess elastomeric behavior. The ability to solvent-process these materials has allowed the formation of a variety of scaffold types. The PEUUs incorporate polyester soft segments that, with variable incorporation of polyether segments, can be tuned for faster hydrolysis. Enzymatically labile peptide sequences have also been incorporated into the polymer backbone to introduce specific enzymatic sensitivity (e.g. elastase degradation). Processing PEUUs with thermally induced phase separation leads to the formation of a scaffold with interconnected pores that can be seeded to high cellular densities with vacuum techniques. This method also allows protein-polymer composites to be generated that facilitate controlled release. PEUUs have been processed with electrospinning to create fibrillar scaffolds in which mechanical anisotropy results by altering processing parameters to control fiber alignment. This anisotropy can approximate that observed physiologically in, for instance, heart valve leaflets. The electrospinning method has been combined with cellular electrospraying to create a means for generating elastic, highly cellularized scaffolds in relatively short time periods. The resulting constructs can also be designed to exhibit controlled anisotropy that is reflected in the cellular and polymeric components. The array of materials and tissue constructs described above have been evaluated in a variety of settings including in vivo models for pediatric cardiac reconstruction, fasciotomy repair, vascular replacement and ischemic cardiomyopathy. This work is facilitated by the collaborative design of the McGowan Institute for Regenerative Medicine at the University of Pittsburgh.