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Matrices and Mechanics to Direct hASC Fate

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Functional tissue engineering uses physical stimulation to direct cell populations to produce tissue with anatomically and physiologically correct structures and with material properties similar to native tissue. Adipose-derived stem cells (ASC) are a particularly promising cell source for functional tissue engineering applications due to their multilineage differentiation potential and their abundance and ease of harvest relative to many other cell types. However, mechanobiological understanding of human ASC (hASC) is still emerging and many questions remain to be answered. Approaches and mechanisms associated with physical stimuli-induced hASC lineage specification and functional tissue formation comprise an increasingly active area of investigation and much remains to be learned. A primary objective of the Loboa lab is to understand and elucidate the role of physical stimuli on the mechanobiology of hASC and attempt to optimize these effects for functional tissue engineering using hASC. Both computational and empirical approaches are utilized in our investigations of hASC mechanobiology for tissue regeneration. Methods include: 1) application of external physical stimuli via use of custom bioreactor systems that mimic in vivo physical stimuli; 2) finite element analyses of cell-seeded constructs exposed to mechanical load to determine local stresses and strains associated with global strain applications; 3) investigations of mechanotransduction mechanisms associated with hASC response to physical stimuli; and 4) creation of biomimetic 3D scaffolds to induce hASC proliferation and controlled differentiation. Studies performed with hASC on novel biomaterials developed in our lab have recently led to our further development of biomimetic engineered nanofibrous scaffolds for wound healing applications. Fibrous materials are constructed from biocompatible, biodegradable materials that possess structural and physical similarities to the native extracellular matrix. In addition to mimicking the *in vivo* topographical environment, fibrous materials provide an ideal substrate for bioactive molecule delivery based on their superior surface area to volume ratio (yielding maximum interaction with a surrounding medium), and the ability to generate controlled release kinetics based on biomolecule placement within the fibrous scaffold. Specifically, bioactive dopants can be homogenized within the polymeric matrix of fibrous assemblies, be preferentially located in either the core or shell of a fiber, and unique fiber architectures can also be generated with porous morphologies along the length of the fiber. We have found distinct differences in release profiles as a function of fiber morphology and initial drug concentration that significantly affect human stem cell and human skin cell fate. Using these approaches, we have created novel scaffolds that successfully inhibit and kill multiple bacteria of critical concern in wound healing while also maintaining viability, or in some cases promoting proliferation, of human skin cells.