

## CTE Design Solutions

- As an engineer you are constantly making design choices - choice for materials, implementation and analysis strategies. A tissue engineer is no different. Let's imagine that you are in a think-tank coming up with new CTE design solutions to a medical problem (sound like a CTE design project?). Comparing chemical and mechanical mechanisms that regulate morphogenesis, please give one advantage of using each when developing an engineered tissue.
- When responding, think about the flip-side of the listed advantage.
- Respond to at least two of your classmates.

Cell differentiation is affected by stretching strategies: frequency, amplitude, duration of stretching cause different cell differentiation. Studies have shown that dynamic compressive strains up to 10% triggers osteogenic differentiation, while 15% and higher strains direct cells towards chondrogenesis [1].

Appropriate mechanical strain promotes osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) while inhibiting differentiation of adipocytes.

Circulating tension promotes endothelial differentiation and angiogenesis of progenitor cells. It also increases expression of smooth muscle cells critical in vascular regeneration engineering. And cyclic stretching without any addition of growth factors induces myogenic differentiation of mesenchymal stem cells (MSC), and leads to mature stem cell-derived cardiomyocytes (hESC-CM) with high beat frequency [1].

- Although, in bioreactors, amplitude, frequency of compression and stretching tensions can precisely be controlled, duration of the mechanical strains highly impacts cellular differentiation. In addition, mechanical properties of biomaterials are often irreversible.
- Lastly, because many critical mechanical parameters of the stimulation have to be controlled; comparison of the results presented in the literature are difficult [1].

Cells migrate in response to gradients of soluble factors such as soluble chemoattractants or surface bound molecules to the substrate (haptotaxis).

Regeneration of tissues is achieved by the buildup of a niche which provides signals to guide the adhesion, migration, proliferation, differentiation of stem cells and apoptosis of cells to desired locations and within specific timings [2]. In wound healing, fibroblasts, leukocytes, and neutrophils are directed by chemotactic factors expressed by macrophages and platelets [3]. Hence the concentration gradient of specific molecules is critical to the design of skin scaffolds. Methods to generate chemical gradients include semi-immersion of substrates, the use of diffusion in which gradient is obtained by depositing two different solutions acting as donor and receptor, selective irradiation by ultraviolet allowing the generation of gradient of different shapes (linear, exponential, sigmoidal, etc.) [4].

- Although, many methods for producing chemical gradients exists, the various techniques and standard to characterize them have major limitations. Fourier transform infrared spectroscopy (FTIR) has detection limitations, and fluorescence labeling provokes changes in chemical composition of the material itself [4].
- Finding an accurate association between molecular and cellular response to chemical gradients remains challenging [3].
- And like in mechanical regulation, timing of experiment is critical: a study using a dynamic hydrogel gel showed that the time window to mechanically induce neurogenesis in neuronal stem cells is between the first 12 to 36 hours of receiving chemical differentiation cues [1].

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