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Funding Source: NSF-REU Program in Biosystems Modeling and Analysis

From tissue liquidity to vascular printing

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Over the last decades, many tissues have been shown to share common properties with liquids: tissue fragments round up as liquid drops and fuse with similar kinetics of liquids. Also of interest is the phase separation phenomenon undergone by mixed cell populations of different adhesiveness mimicking the "breaking" of a dispersion or emulsion of two immiscible liquids. For a system to show such behavior it must (1) be composed of many subunits that (2) cohere while (3) being mobile. These are the defining characteristics of a liquid. In ordinary liquids the subunits are molecules and the mobility is Brownian. Rearranging cell populations also possess these same three properties that underlie liquid behavior, but their subunits are living cells whose mobility may be either active, driven by intracellular forces, or passive, pulled by external forces.

In the present study, we used tissue-liquidity to generate microtissue droplets of smooth muscle cells, fibroblasts and endothelial cells that can serve as minimal building units for vascular tissue-engineering. Size-specific spheroids of SMCs and fibroblasts were first generated by cell aggregation in P96 well plates. As the extracellular matrix content of the vessel wall is essential for obtaining adequate mechanical properties in tissue-engineered vascular grafts, those tissue droplets were then matured over 4 weeks in the presence of ascorbic acid or TGF-β1 and insulin, and then analyzed at various times by histology in order to assess collagen and elastin production. At last, straight and branching tubes of different diameters were achieved by the fusion of CHO cells tissue spheroids deposited by hand or by a bioprinter. In conclusion, we show that the understanding of the physical mechanisms underlying tissue organization can be easily applied in the field of tissue-engineering.