Engineered Cellular Microenvironments Decoupling Cell-Cell and Cell-Matrix Interactions

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In their native microenvironment, cells receive multitude of physical, mechanical and chemical cues from their extracellular matrix (ECM) (cell-matrix adhesions, integrin adhesions) and neighboring cells (cell-cell adhesions, cadherin adhesions), which are critical to regulate their behavior during tissue development and healing. These cues are tightly regulated with high spatial precision at different contact interfaces, to direct cellular functions and cell fate decisions. Recapitulating native spatial characteristics in vitro has become an important strategy in regenerative medicine to generate biomaterials that are close mimics of the native tissue and particularly interesting to target anisotropic tissues (e.g., skeletal muscle and cardiac muscle). In this work, we aim to develop 3D biomaterials strategy for e.g., cardiac-like tissue engineering by incorporating mechanical anisotropy and a regulated formation of cell-cell and cell-matrix adhesions in spatially and mechanically defined matrices. For this purpose, we will use poly (acryl amide) based hydrogel systems enabling orthogonal coupling chemistries, to immobilize ligands specifically targeting integrin and cadherin adhesions with spatial segregation. This platform also presents the ability to separately control mechanical properties of both contact interfaces. Progenitor cell response to defined physical and biochemical cues will be investigated to reveal parameters for functional tissue formation. Finally, this highly tailorable biomimetic material system will not only enable us to develop new biomaterials for regenerative medicine, but can serve as a tool to study fundamental aspects of cellular behavior in both development and disease.