Biomimetic Tissues: How simple is complex enough?

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Multicellular ecosystems such as biofilms, tissues, and whole organisms operate as highly integrated systems that link physical structure and biological function. In mammalian tissues, structure determines the effectiveness by which muscles generate force, lungs oxygenate blood, or glandular organs produce bile, milk, or saliva. Even at the level of single cells, tissue structure constrains how cells interact with surrounding extracellular matrix, neighboring cells, and physical forces, and these "microenvironmental" cues in turn regulate cell function, such as proliferation, differentiation, migration, and suicide. Understanding the underlying control systems that give rise to these ecosystems is central to our ability to rationally perturb or synthetically design and build them.
Using engineered microenvironments, we have begun to expose the complex interplay that occurs between structure, force, signaling, and function in cells and multicellular systems. We show that these control loops are central to cell and multicellular function and assembly; use these insights to build in vitro organotypic models that mimic native tissue functions; and discuss opportunities and challenges for how to connect these insights to the ultimate translational objectives set by regenerative medicine.