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Engineering Cell Adhesion for Organ Design

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The construction of multi-layered, multi-functional "organoids" for implantation is an important goal for tissue engineering. Achievement of this goal would be greatly facilitated by the development of a simple set of rules defining the spatial relationships established between groups of cells as they interact in three-dimensional space. The practical application of principles underlying embryonic development to tissue engineering is of fundamental importance to this process. We have previously demonstrated that embryonic tissues share common properties with viscoelastic fluids and that embryos use these properties to self-assemble into complex three-dimensional structures. We have developed a simple set of rules describing this self-assembly behavior based on the premise that embryos mimic the behavior of immiscible fluids and that the spatial relationships adopted by different tissues arise as a consequence of differential adhesion, measured as tissue surface tension (TST). We have applied the concept of tissue fluidity to demonstrate that (1) TST can be used to predict and control the spatial relationship between different embryonic tissues and also between genetically engineered cells, (2) competition between cell-cell and cell-substratum adhesion can strongly influence the ability of tissues to interact with biomaterials such as co-polymers of DTE and PEG, and (3) a tissue's liquid properties can be altered not only through direct manipulation of cadherin-based intercellular cohesion but also by manipulation of key ECM molecules such as fibronectin. Collectively, our data strongly suggest that the principles underlying tissue liquidity can be effectively applied in tissue engineering. Application of these principles will make the engineering process more predictable and controllable and will facilitate the rational design of multifunctional organoids that can be either implanted into or "home" to a specific site of the body.