Stem Cells and Forces

Forces are generated and resisted in biology across many magnitudes and length scales, from actomyosin motors to the loading from gravity. Analogous to how stem fate is controlled by intrinsic and extrinsic biochemical factors, mechanical cues which result from both intrinsic cell-generated forces and externally applied forces control the function and fate of stem cells. The adhesion of cells to the extracellular matrix (ECM), and cell-cell junctions, transmit forces to and between cells, and control intracellular mechanical signaling pathways. Understanding how mechanical forces regulate stem cell behavior can lead to new strategies for regenerative medicine. There has been tremendous interest in the role of substrate stiffness on cell behavior, from the perspective that this controls the resistance to cell intrinsic forces, but historically the field has ignored that tissues are typically viscoelastic. It has now been demonstrated that the stiffness of biomaterial substrates, and their viscoelasticity, has dramatic effects on stem cell spreading, proliferation and fate. These relationships are increasingly being exploited to promote tissue regeneration from stem cells.

In order to harness the full power of stem cells, we must overcome key obstacles of poor survival and limited integration. This is particularly important in the central nervous system where the neural circuitry needs to be restored to regain function. While the immune system is a key contributor to poor survival, other factors contribute to cell death, such as anoikis (lack of adhesion) and an inhibitory microenvironment. To overcome some of these issues, we've investigated survival factors for co-delivery with cells – these include biomaterials, growth factors and cell adhesion molecules that promote survival, integration and endogenous tissue repair.

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