Title: Defining Next Generation Stem Cell Mechanics Studies for Prospective Guidance of Lineage Commitment

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Recent studies from our group, subjecting live stem cells to controlled stress-strain states, demonstrate significant correlations between controlled delivery of mechanical cues, changes in stem cell shape and structure, and emergent lineage commitment. We have begun to probe this so-called mechanome by (i) delivering libraries of strains to the surface of stem cells through exposure to controlled normal and shear stresses and (ii) deterimining libraries of stresses and strains conducive to achieving target cell fates. The current study tests this approach parametrically, to assess the sensitivity of normal and shear stresses as well as strains at the cell-fluid interface to estimates of cell mechanical properties. In addition, the current study examines the capacity of experimentally controlled parameters to modulate normal and shear stresses-strains experienced at the cell-fluid interface. While an accurate estimation of the cell's elastic modulus is critical for exact measurements of cell surface stresses and strains, results indicate than an accurate estimation of the cell's Poisson's ratio is less critical. Furthermore, application of low pressure gradients to cells at high density maximizes precise delivery of a range of mechanical cues. While next stage experiments can begin to map the stem cell mechanome, modifications to the current experimental setup will enable delivery of stresses with a greater range in magnitude and higher precision. Overall, the results of this study demonstrate the regions of the mechanome that can be experimentally assessed with currently available, pressurized cell perfusion devices, as well as the precision of these measurements, through the control of cell seeding density, pressure gradients, and fluid viscosity.