

MECHANICS MATTERS TO CELLS: LENGTH & TIME SCALES FOR HOW TISSUE CELLS FEEL AND RESPOND TO THE STIFFNESS OF THEIR SUBSTRATE

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Normal tissue cells are generally not viable when suspended in a fluid and are therefore said to be anchorage dependent. Such cells must adhere to a solid, but a solid can be as rigid as glass or softer than a baby's skin [1]. The behavior of some cells on soft materials is characteristic of important phenotypes; for example, cell growth on soft gels of agarose has been used for many years to identify cancer cells. However, an understanding of how tissue cells — including stem cells, myocytes of various types [2, 3], osteoblasts in our lab — sense matrix stiffness is just emerging with quantitative studies of cells adhering to gels (or to other cells) with which elasticity can be tuned to approximate that of tissues. A key question to better understand is how far cells feel and what time scales of material visco-elasticity are influential. The answers should reflect the key roles in molecular pathways played by adhesion complexes and the actin-myosin cytoskeleton, whose contractile forces are transmitted through transcellular structures. Ultimately, this feedback of local matrix stiffness on cell state likely has important implications for development, differentiation, disease, and regeneration.

References

- [1] D.E. Discher, P. Janmey, Y-L. Wang. Tissue cells feel and respond to the stiffness of their substrate. *Science* 310: 1139-1143 (2005).
- [2] A. Engler, M. Sheehan, S. Sen, C. Bonnemann, H.L. Sweeney, and D.E. Discher. Myotubes Differentiate Optimally on Substrates with Tissue-like Stiffness: Pathological Implications of Stiff or Soft Microenvironments. *Journal of Cell Biology* 166(6): 877-887 (2004).
- [3] A. Engler, L. Bacakova, C. Newman, A. Hategan, M. Griffin, and D.E. Discher. Substrate compliance versus ligand density in cell on gel responses. *Biophysical Journal* 86: 617-628 (2004).

Keywords

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