Effect of Extracellular Matrix Viscoelasticity on Epithelial-Mesenchymal Transition

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Epithelial cells acquire a mesenchymal phenotype through a process called epithelial to mesenchymal transition (EMT). EMT is marked by a loss of cell-cell adhesions and downregulation of epithelial genes, such as E-cadherin, as well as a gain in migratory ability and upregulation of mesenchymal genes, such as αSMA. EMT is important in development and wound healing, but if dysregulated, EMT contributes to fibrosis and cancer metastasis.

Cell behavior and EMT progression are influenced by the mechanical properties of the surrounding extracellular matrix. Previous in vitro studies have relied on purely elastic hydrogels to mimic the mechanical properties of the extracellular matrix to study EMT and disease progression. However, tissues in our body are not purely elastic, but rather they are viscoelastic. We have previously demonstrated that matrix elasticity regulates gene expression during EMT, but how matrix viscoelasticity impacts the EMT process remains unclear. Here, we synthesized and characterized viscoelastic hydrogels to mimic the viscoelastic properties of healthy and tumor breast tissue. We found that substrate viscoelasticity regulates TGFβ1-induced cell morphology changes and EMT gene expression. We also found that increasing substrate viscoelasticity promotes TGFβ1-induced apoptosis and protects against TGFβ1-induced EMT. Using hydrogels that more closely mimic the mechanical properties of the in vivo cellular microenvironment will improve our understanding of EMT and disease progression.