

Abstract Submitted
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Mechanoregulatory tumor-stroma crosstalk in pancreatic cancer: Measurements of the effects of extracellular matrix mechanics on tumor growth behavior, and vice-versa, to inform therapeutics¹

JONATHAN CELLI, DUSTIN JONES, HAMID EL-HAMIDI, GWENDOLYN CRAMER, WILLIAM HANNA, ANDREW CAIDE, SEYEDEHROJIN JAFARI, University of Massachusetts Boston — The rheological properties of the extracellular matrix (ECM) have been shown to play key roles in regulating tumor growth behavior through mechanotransduction pathways. The role of the mechanical microenvironment may be particularly important tumors of the pancreas, noted for an abundance of rigid fibrotic stroma, implicated in therapeutic resistance. At the same time, cancer cells and their stromal partners (e.g. tumor associated fibroblasts) continually alter the mechanical microenvironment in response to extracellular physical and biochemical cues as part of a two-way mechanoregulatory dialog. Here, we describe experimental studies using 3D pancreatic cell cultures with customized mechanical properties, combined with optical microrheology to provide insight into tumor-driven matrix remodeling. Quantitative microscopy provides measurements of phenotypic changes accompanying systematic variation of ECM composition in collagen and laminin-rich basement membrane admixtures, while analysis of the trajectories of passive tracer particles embedded in ECM report dynamic changes in heterogeneity, microstructure and local shear modulus accompanying both ECM stiffening (fibrosis) processes, and ECM degradation near invading cells.

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