Title: Exploring the relevance of the mechanical TME in prostate cancer.

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Abstract
Prostate cancer (PCa) is the most prevalent cancer in men and is among the leading causes of cancer related mortality. A large proportion of PCa treatment and research revolves around the function and downstream effects of the androgen receptor (AR). Inhibiting the function of the AR has been the standard of care for patients with advanced prostate cancer for decades. However, our understanding of what factors affect its signalling and enable treatment resistance in patients is underwhelming. Additionally, most current cell models do not represent patients well, as their AR functionality and expression is often altered when moved in vitro. Typically, in vitro studies have been conducted in 2-dimensional cell culture environments, and these systems lack the structural complexity of the original tissue. Our goal is to establish a 3-dimentional culture system for PCa which better mimics the original tissue and further understand what factors in the physical and chemical microenvironment effect PCa cells. Our system is based on encapsulating PCa cells in a hyaluronic acid-based hydrogel with adjustable stiffness and protein composition. By using multiple cell models which simulate the development of treatment resistance in PCa cells, we will be able to identify differences in how they react to environmental changes. Thus far we have identified differential stiffness preferences between naïve and treatment resistant PCa cells. Understanding how these cancer cells interact with the surrounding matrix will allow us to develop more accurate drug screening methods and potentially uncover new cancer mechanism to exploit in treatment.