Abstract

Living cells sense, exert and respond to physical/mechanical stimuli and transform them into biological response within their microenvironment as a part of their normal physiology. Mechanical signals communicate via mechanosensing and mechanotransduction regulate cellular behavior leading to biochemical and structural modifications. Monitoring cellular behaviors i.e. growth, migration and proliferation becomes a crucial factor in determining cell and tissue interaction. Mechanobiology of cell responding to microenvironment has profound impact on several biological processes such as wound healing, angiogenesis and metastasis. Quantitative analysis of mechanobiology is essential to perceive or predict pathophysiological event at cellular level and help in disease control process. The present dissertation aims to model soft elastomeric matrix with physical and topographical variation to interact with different cells and study the role of microenvironment on biomechanics. Using microfabrication technology, formation of tailor made elastomeric matrix to act as cell culture platform coupled with various microscopy modalities like SEM, AFM, etc. accomplish this investigation on four different cell lines: 3T3 fibroblast, HaCaT keratinocyte, MCF-7 and MDA-MB 231 (breast cancer). Culture of fibroblast and keratinocyte cell on PDMS surface of variable stiffness underscores the influence of surface physico-mechanical properties in cell-substrate interaction. In order to estimate cell elasticity, stiffness, adhesive force and traction force, AFM analysis was performed to map nanomechanical attributes of different cell lines cultured on diverse microenvironment and analyzed cellular biophysical properties. High aspect ratio microstructured platform realized on PDMS elastomer of different stiffness by replica moulding process was used to study cell traction force. A novel force sensor model along with python based algorithm has been developed to identify cell anchoring location and estimate traction force. Measurement of mechanical properties was also employed to appraise the effect of doxorubicin drug on breast cancer cells that results in decrement of mechanical attributes of cell. Differentiation in biomechanics between healthy, cancer and drug treated cell was evidenced in expression of their morphology, cytoskeleton rearrangements, nanomechanical features, deflection of pillar and cell adhesion site to pillar. Entire study paved the path in developing smarter bio-matrix with tunable textural, mechanical and compositional attributes for biomedical applications.

Keywords: Cell mechanics, PDMS film, Surface modification, Healthy & Cancer cells, AFM, Micropillar.