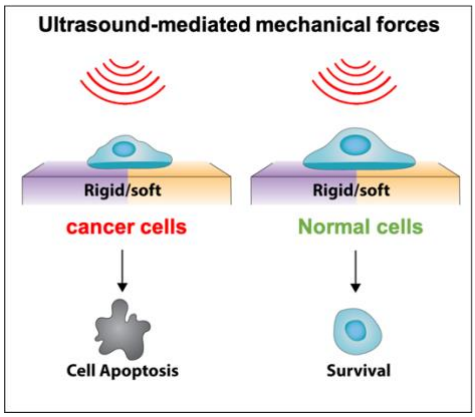
Elucidating the role of dynamic confinement in mechanical force-induced cancer cell killing

Background

Cancer cell invasion to neighboring tissues is an important step in the process of metastasis.[1] During cancer cell invasion, cancer cells migrate through '3D channel-like tracks' present in interstitial extracellular matrix (ECM) of tissues.[2] Cancer cell migration through these confined channel-like tracks leads to confinement-induced cell deformation. This cell deformation changes several biomechanical properties of the cancer cell including cell contractility, adhesion size and distribution and expression level of mechanosensitive channels.[3] Recently the field has learnt that cancer cells are mechanosensitive and undergo apoptosis (programmed cell death) when subjected to physiologically relevant mechanical forces.[4-6] Also, recent findings suggest that cell deformation contributes to the mechanical force-induced cancer cell killing.[3, 7] Thus, in this project, we are interested to address a question, **does cell deformation caused due to confinement promote the mechano-induced cancer cell killing?** If yes, which deformation mediated-biomechanical properties play key role in promoting mechano-induced cancer cell killing?



Experimental design

We will engineer PDMS elastomer-based microfluidic channel platform to mimic the 3D channel-like tracks present in ECM. Also, we will fabricate the custom-built ultrasound device to apply ultrasound-mediated mechanical forces on the cells. Cancer cells will be treated with mechanical force during their migration through confined channels with varying width to measure the level of apoptosis as a function of level of confinement. Cell and molecular biology techniques along with high-resolution imaging will be implemented to characterize the biomechanical properties of the cells and to establish the link between the confinement induced-cell deformation and the mechano-induced cancer cell killing.

Ajay Tijore,
Mechanobiologics Lab
Centre for Biosystems Science and Engineering
Indian Institute of Science, Bangalore

Experimental design schematic

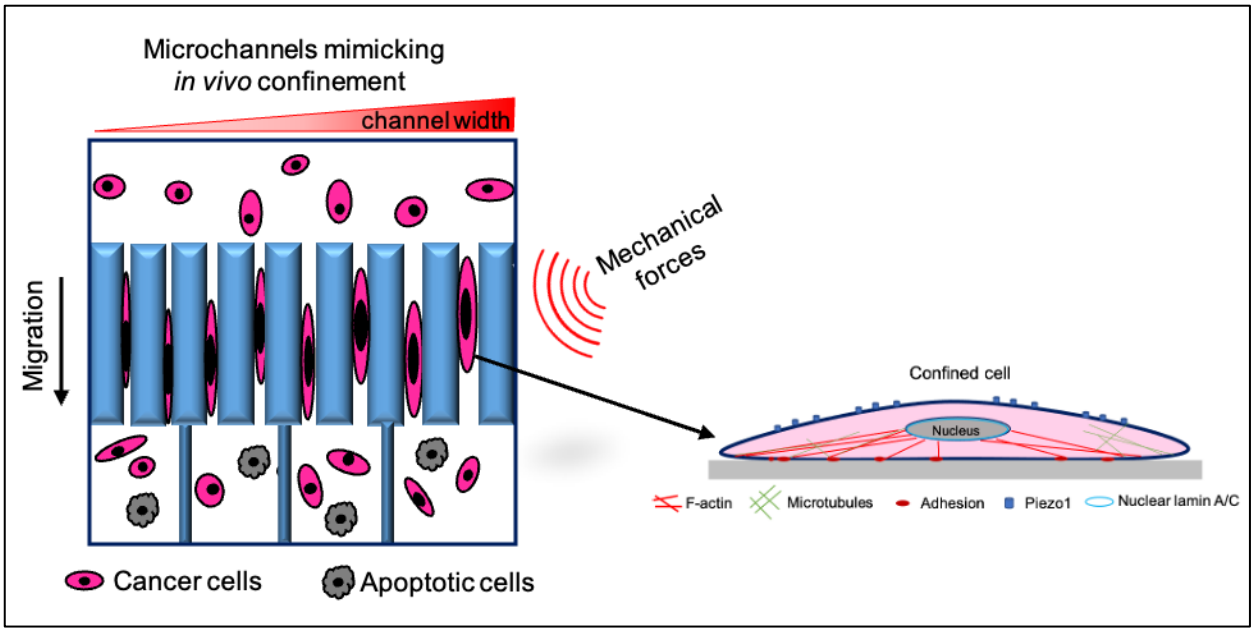


Figure: 3D microchannel platform to study the effect of mechanical forces on cancer cells during their migration through confined microchannels and identifying the molecular and mechanical properties of the cell involved in mechano-induced cancer cell killing

Significance of the study

This study will help us to optimize the ultrasound parameters to maximize killing of highly invasive and metastatic cancer cell types which are in the stage of spreading to other tissues.

Collaboration

This work will be done in collaboration with **Prof Andrew Holle**, Mechanobiology Institute, NUS, Singapore.

Reference

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Ajay Tijore,
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