Title: Development of 3D scaffold for the analysis of tumour growth-induced stress on cell behaviour

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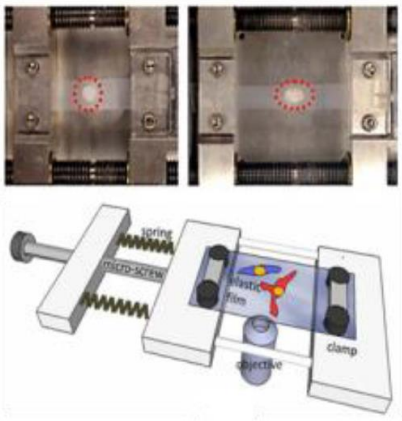
Project background:

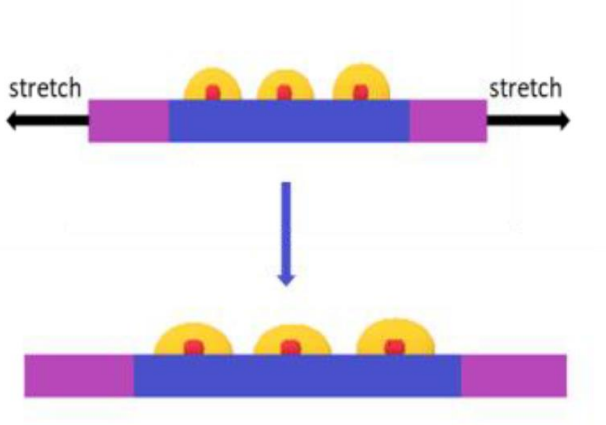
Emerging research is revealing the far reaching impact of solid stresses developed in the tumour environment as solid tumours grow in mechanically resistive surroundings. Distinct to other biophysical cues such as tissue rigidity, solid stress has been found to influence phenomena ranging from cancer cell proliferation to drug efficacy. Studies have shown that distribution profiles of solid stress are complex – uniform compression within the tumour itself, but simultaneous tension and compression peritumourally. While the effects of intratumoural compression are already the focus of numerous studies, the effect of peritumoural tension on stromal cells remains unknown. This project therefore seeks to contribute to efforts to elucidate the underlying mechanisms by which mechanical stress evolution influences cancer progression, particularly the stromal response to tumour growth.

Project aims:

The research group is analysing the effects of tension on stromal cells found within the tumour microenvironment. To do so, cell-seeded hydrogels are to be stretched using a novel 3D printed bioreactor. Currently, the focus is on stretching cells seeded in 2D. Cells are however known to behave structurally and functionally different when seeded in 2D versus 3D which more closely mimics their natural environment. The aim of this project is therefore to analyse the effect of tension on cancer associated cells when seeded in 3D.

Example of stretching device:





Research plan:

The successful applicant is to start by reviewing existing 3D scaffolds for cell culture and develop a tailored protocol for a scaffold that enables stretching of cells and mimics the stress state within the tumour environment through the use of a 3D printed bioreactor. Subsequently, the scaffold is to be synthesised through the developed protocol and have its mechanical material properties characterised (e.g. Young's modulus, nonlinearity, stress relaxation, ultimate tensile stress). Finally, cancer associated cells are to be encapsulated in the scaffold and the effect of tensile stress on their behaviour is to be evaluated within the context of tumour development.

Skills - skills that the student will develop during the project:

This project is highly multidisciplinary in nature and as such will require the development of diverse skills in multiple fields. An ability to review and link the current literature across diverse fields will be a requirement throughout the project. Development of lab techniques needed to synthesise cell culture scaffolds and an understanding of their underlying biochemistry will undoubtedly be core to the proposed work. In addition, the applicant will be expected to use material testing tools that characterise the scaffold mechanical properties and analyse the resulting data. Finally, wet lab techniques that include cell culture and methods to analyse cell behavioural response to external biophysical cues will enable the evaluation of novel mechanotransduction processes at the heart of tumour development.

References

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