Centre for BioSystems Science and Engineering

THESIS COLLOQUIUM

at 04:00 PM on May 08, 2017
MRDG Seminar Hall

Engineering 3D Organotypic Models for the Study of Breast Cancer Metastasis

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Breast cancer is the most common type of cancer and cancer-related morbidity in women, worldwide. Metastasis, or, the spreading of the primary tumor to other vital organs is the major cause of mortality in breast cancer. Therefore, understanding the mechanisms that lead to metastasis becomes critical to design and develop effective treatment strategies. The platforms currently adopted to study breast cancer biology involve culturing breast cancer cells in two-dimensional tissue culture polystyrene dishes (2D-TCPS), or, propagate the tumor cells as xenografts in mice. While the conventional two-dimensional (2D) cell culture systems fail to mimic in vivo signaling due to the planar architecture and inappropriate substrate stiffness, animal based xenograft models are expensive and time consuming.

The aim of this work was to develop models to study breast cancer biology using three-dimensional (3D) tissue scaffolds that would overcome the disadvantages of the two systems and better mimic the tumor in vivo. In the first part of the work, 3D scaffolds with modulus of 7 kPa that is mechano-mimetic of the metastatic breast tumor were prepared using poly (□-caprolactone) (PCL). MDA-MB- 231 metastatic breast cancer cells cultured on these scaffolds formed 3D networks and eventually formed tumoroids and had increased metastatic potential of invasion, progression and colonization, compared to the cells cultured on 2D TCPS dishes. On comparison of the miRNA profiles of these cells with those from breast cancer patients, it was observed that the cells in 3D scaffolds had better positive correlation to cancer cells in vivo, for every tumor tissue compared, than the cells cultured in 2D TCPS dishes. This data showed that the cells cultured in scaffolds can better mimic the cells in vivo that cells cultured on 2D TCPS dishes.

In the last part of the work, fibrous scaffolds of PCL were fabricated for the study of breast cancer associated fibroblasts (CAFs). The CAFs cultured on the fibrous PCL matrices acquired myo-fibroblastic properties similar to the activati observed by cancer cells in vivo. Also the CAFs cultured on fibrous scaffolds were better able to promote tumor progression and invasion, by secretory factors and by evoking an inflammatory response, compared to the cells cultured in 2D TCPS dishes.

Taken together, polymer based synthetic matrices for the two major cell types present in metastatic breast cancers, viz., epithelial cells and the stromal fibroblasts were developed. These matrices mimic the mechanical properties of the tumor tissue and the cells cultured on these matrices better mimic cells in vivo. These matrices could be used as ideal culture platforms to study the biology of breast cancer metastasis; useful in analyzing the drug response, which could lead to improved treatment strategies.

Poster presentation depicting short snippets from this work will start from 3:30 PM

For more information and artwork depicting the research (http://www.be.iisc.ernet.in/seminars.html)