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3D *in vitro* tissue models integrating microfluidics for drug discovery

The aim of this talk is to introduce a few 3D *in vitro* tissue models for the studies of various diseases. In particular, the focus will be concentrated upon the use of these models in the field of cancer research. As cancer metastasis is responsible for 90% of the cancer related deaths; current drug screening assays, however, are lacking the ability to mimic physiological cancer microenvironments and tumor three-dimensional (3D) structures that may also be critically important in the study and prevention of the various processes in metastasis. Tumor cells cultured in a 3D system as multicellular cancer aggregates (MCA) recapitulate several critical *in vivo* characteristics that allow the study of biological functions and drug discovery. I will introduce a microfluidic system that integrates MCA in a 3D hydrogel scaffold, in close co-culture with an endothelial monolayer, mimicking the in vivo tumor microenvironment. In the design of these studies, the pathophysiology of cancer and mechanisms driving tumor progression are carefully considered by account for the nature of interaction between tumor cells and the surrounding milieu, including tissue microvasculature, growth factors and extracellular matrix (ECM). A microfluidic co-culture platform was designed with improved human umbilical vein endothelial cells (HUVEC) monolayer growth. Lung A549 and bladder carcinoma T24 MCAs were tested. Dose-response assays of four drugs were validated according to their invasive capability to the adjacent 3D matrix. In the absence of HUVECs, T24 MCAs showed dramatic spontaneous dissemination as compared to A549 MCAs. T24 MCAs dispersion inhibition required higher doses of drugs as a single agent and lead to only partial inhibition at 10 µM concentration with a SC inhibitor AZD-0530. The enhanced dispersal observed in the presence of HUVECs is a consequence of the secretion of growth factors including HGF and FGF-2 by endothelial cells. Growth factor production was not affected by addition of AZD-0530. Overall, the above systems demonstrated a new approach in drug screening with the potential to better replicate the in vivo microenvironment. The microfluidic platform provides a new basis for understanding the progression of carcinoma towards dedifferentiated and more malignant states and for the development of future drug discovery.

Biography

Ting Yuan Tu joined the Department of Biomedical Engineering at National Cheng Kung University (NCKU) in 2016 as an Assistant Professor. His PhD work was completed in Singapore-MIT Alliance for Research and Technology Centre in Singapore and received the PhD degree in Mechanobiology from National University of Singapore in 2015. Prior to joining NCKU, he was an Application Scientist at Clearbridge Bio medics (Now Biologics). His current research interest lies in the development of better biomimetic tumor microenvironment for cancer drug discovery, such as *in vitro* tumor models and 3D tumor invasive co-culture microfluidic platforms.

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