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Mechanical 3D nanoenvironment for glioma progression models

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Abstract

Glioblastoma Multiform (GBM) is the most common malignant brain neoplasm, an aggressive and invasive form of brain cancer. Gliomas, which originate from undifferentiated glial cells, retain stem-like potential during the progression of the disease. Additionally, they can perpetuate by self-renewal and from new neoplasms that preserve the phenotypic heterogeneity of the parent tumour, which contains tumorigenic and non-tumorigenic populations. This phenomenon of tumour non-homogeneity is difficult to study of the native body. Innovative in vitro and in vivo models need to be able to recreate the phenotypic mosaicism of GBM and provide mechanical microenvironment associated with native tissue. Gel hybrids for encapsulating the cells by dipping a porous rod into a cell-alginate solution or into cellular alginate solution (as the niche for cancerous invasion) followed by the crosslinking with the bivalent cation solution were built. Then these encapsulated cell constructs were coated using patented electro-spinning/ nanofiber coating technique to provide an adhesive, strengthening nano-topography exterior similar to that of a native tissue. The hydrogel surrounds the cells and provides with a soft mechanical environment comparable to that of the brain. Successful growth spread and invasion of originally (interior) seeded cells into to outer a cellular space was confirmed. The volumetrically distributed layered structure of the scaffold allowed us to distinguish and isolate cells that grow as secondary tumour and thus individually migrating cells from the originally seeded population. Differential gene expression analysis of the subpopulations reveal that the initial line add secondary populations indeed exhibit exclusive gene amplifications. Additionally, an evidence of the direct influence of mechanical nano-environment in glioma progression was obtained. This demonstrates the scaffolds' potential applicability for the therapy testing against GBM. The proposed method allows creation of an affordable inexpensive and completely artificial 3D model for GBM growth; the method provides cells into the mechano-biological environment similar to that of native brain while allowing the easy observation through the construct's layers for the tracking of cancerous growth.

Biography

Kalle Levon graduated with a Doctor Degree from University of Tokyo in 1986 after obtaining MSc and BSc degrees in Chemistry from Helsinki University. He has been an assistant, associate and full professor at Polytechnic University, Brooklyn since 1989 and also the Vice-Dean and Vice Provost of Research and Intellectual Property starting an incubator in NYC already in 2003. He has published over 130 publications, over 30 patents.

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