

Role of fluid imparted shear stress on progression of bone metastasis of prostate cancer in porous 3D scaffolds

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Abstract:

The bone site is a favored niche for prostate cancer metastasis. Prostate cancer bone metastasis often results in skeletal impairment and high mortality. The progression of metastasis and consequent influence on both the bone site as well as the tumor itself, is of immense medical interest. The mechanical cues caused by interstitial blood flow have bone remodeling and cancer promigratory roles. The influence of the shear stresses due to the fluid flow through the hierarchical bone porosities on metastasized prostate cancer is not well understood.

We have developed a 3D invitro tissue engineered scaffold based humanoid testbed of prostate cancer bone metastasis^{1,2} using sequential seeding with human mesenchymal stem cells and prostate cancer cells. Nanoclay based bone mimetic scaffolds are designed to provide the remodeling bone niche that prostate cancer cells migrate to. Through the use of a specially designed perfusion bioreactor, the 3D *in vitro* model enables evaluation of effect of fluid derived shear stress on prostate cancer bone metastasis. The computational fluid dynamics studies indicate a uniform fluid dispersion and a varying fluid velocity within the scaffold. Concurrently, scanning electron microscopy studies show a uniform and directional distribution of human mesenchymal stem cells and varying prostate cancer tumor morphology on the dynamically cultured scaffolds. These studies suggest that the shear forces exerted by fluid flow may be used to influence bone metastasis.

¹ MD S Molla, D. R. Katti, K. S. Katti, (2018) In vitro design of mesenchymal to epithelial transition of prostate cancer metastasis using 3D nanoclay bone-mimetic scaffolds, Journal of Tissue Engineering and Regenerative Medicine. Volume12, Issue3 Pages 727-737. doi: 10.1002/term.2492.

² MS S Molla, D. R. Katti, J. Iswara, R. Venkatesan, R. Paulmurugan, K. S. Katti, Prostate Cancer Phenotype Influences Bone Mineralization at Metastasis: A Study Using an In Vitro Prostate Cancer Metastasis Testbed, Journal of Bone and Mineral Research Plus (WOA), Vol. 00, No. 00, Month (2019), 1–14. DOI: 10.1002/jbm4.10256