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THREE DIMENSIONAL *IN VITRO* MODELS FOR STUDYING CANCER ANGIOGENESIS

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Introduction: Hydrogels prepared from star-shaped poly(ethylene glycol) (PEG) and maleimide-functionalized heparin provide a potential matrix for use in developing three dimensional (3D) models. We have previously demonstrated that these hydrogels support the cultivation of human umbilical vein endothelial cells (HUVECs). We extend this body of work to study the ability to create an extracellular matrix (ECM)-like model to study breast and prostate cancer cell growth in 3D. Also, we investigate the ability to produce a tri-culture mimicking tumour angiogenesis with cancer spheroids, HUVECs and mesenchymal stem cells (MSCs).

Materials and Methods: The breast cancer cell lines MCF-7 and MDA-MB-231, and prostate cancer cell lines LNCaP and PC3, were seeded into starPEG-heparin hydrogels and grown for 14 days to analyze the effects of varying hydrogel stiffness on spheroid development. Resulting hydrogel constructs were analyzed *via* proliferation assays, light microscopy and immunostaining. Cancer cell lines were then seeded into starPEG-heparin hydrogels functionalized with growth factors as spheroids with HUVECs and MSCs and grown as a triculture. Cultures were analyzed *via* immunostaining and observed using confocal microscopy.

Results: Cultures prepared in MMP-cleavable starPEG-heparin hydrogels display spheroid formation in contrast to adherent growth on tissue culture plastic. Small differences were visualized in cancer spheroid growth between different gel stiffness across the range of cell lines. Cancer cell lines were able to be cocultivated with HUVECs and MSC. Interaction was visualized between tumours and HUVECs *via* confocal microscopy. Further studies intend to further optimize and mimic the ECM environment of *in situ* tumour angiogenesis.

Discussion: Our results confirm the suitability of hydrogels constructed from starPEG-heparin for HUVEC and MSC co-cultivation with cancer cell lines to study cell-cell and cell-matrix interactions in a 3D environment. This represents a step forward in the development of 3D culture models to study the pathomechanisms of breast and prostate cancer.