# Modelling the transformation of adipose-derived stem cells to a cancer-associated fibroblast phenotype within 3D GelMA microgels

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The intricate dynamics of the breast tumour microenvironment, specifically the role of adipose-derived stem cells (ADSCs) in differentiating into cancer-associated fibroblasts (CAFs) and their subsequent contribution to metastasis, represent a significant aspect of breast cancer research [1]. Traditional 2D in-vitro fail to mimic the dynamic interactions and biochemical signalling prevalent in-vivo. Consequently, there is an urgent need for advanced 3D models that more faithfully mimic these conditions, thus providing a more accurate platform for studying the role of ADSCs in cancer progression.

In this study, we utilized jammed suspensions of 3D microscale hydrogels (so called "microgels") [2] to emulate a porous tissue matrix for studying the complex interplay between ADSCs and the tumour microenvironment. Specifically, we focused on how ADSCs contribute to the progression of breast cancer through their transformation into CAFs. 3D gelatin-methacryloyl (GelMA) microgels were used to create a viscous bath with increasing interstitial volume to mimic the densities of healthy and tumour microenvironments (Figure 1A). Invasive and non-invasive breast cancer cell lines, such as MCF7 and MDA-MB-231, were printed and cultured within the 3D microgel-stroma model. The progression of cancer was monitored by assessing α-smooth muscle actin (α-SMA) positive cells, indicating significantly higher CAF appearance within the low interstitial matrix (Figure 1B, C), suggesting a correlation of 3D microenvironment mechano-physical influence in the behaviour of cancer cells.

Together, this work demonstrates how defined microengineered matrices can serve as platforms to evaluate cell behaviour, with scope for translation to in-vitro assays for biological discovery and drug development.

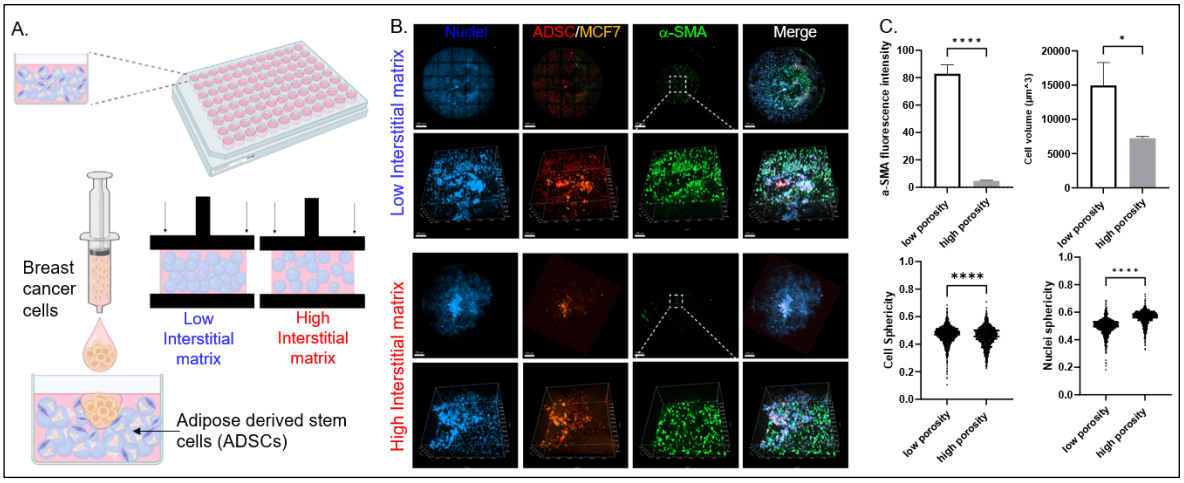


**Figure 1.** A) Schematic of printing process, showing the 2 types of matrices used for the study; B) Immunofluorescence staining showing nuclei counterstained in blue, ADSCs in red, MCF7 in orange, and α-SMA expression in green; Scale bars: 200 μm; C) Quantitative analysis of α-SMA and cell morphometrics in the

**References:**[1] D. Hu, et al. *Cancer Commun.*, **2022**, 42, 401–434; [2] G.Jalandhra**,** et al. *J.Vis. Exp.*, **2022.**