PEG-Methylsulfone (MS) Based Hydrogels for 3D Culture of Invasive Breast Cancer Organoids: Studying the Effects of Biochemical and Biophysical Cues on Organoid Response

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Breast cancer invasion is accompanied with changes in biochemical and biophysical (mechanics, architecture) properties of complex native extracellular matrix (ECM).[1] Understanding the effects of ECM derived cues on cancer cell response is critical to discover possible interventions. Thus, engineering in vitro 3D models to systematically study cell-matrix interactions has been an important focus in the field. To this hand, synthetic poly(ethylene) glycol (PEG) based 3D hydrogels introduce tunability to individually tailor cell-instructive matrix properties.[1] Here, we use 3D PEG-MS hydrogels, that are crosslinked with cell-degradable peptide crosslinkers, to encapsulate PyMT breast cancer organoids, with non-invasive luminal and invasive basal cells that show mechanosensitivity. We individually tune the biochemical cues by using specific cell-adhesive peptide ligands from fibronectin, collagen I or laminin 5. We control the degree of crosslinking and network mechanics via polymer (PEG) density. We investigate the invasive potential of organoids in different matrices by studying the positioning of basal cells, nuclear localization of mechanosensitive proteins, organoid growth and morphology. We finally aim to translate our knowledge to gradually design more complex biomimetic cancer microenvironments via combinatorial cues and control over matrix architecture next to mechanics.

References

1 Holle, A. W., Young, J. L. & Spatz, J. P. In vitro cancer cell-ECM interactions inform in vivo cancer treatment. *Advanced drug delivery reviews* **97**, 270-279, doi:10.1016/j.addr.2015.10.007 (2016).