Probing geometric confinement and oxygen gradients in epithelial-to-mesenchymal transitions using microengineered matrices

*Harry Zhou, Thomas G. Molley, Kristopher A. Kilian**

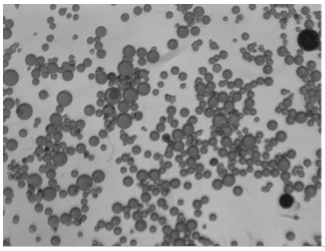
UNSW Sydney,

New South Wales 2052

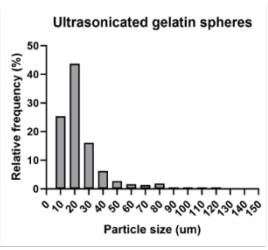
University of New South Wales

Sydney, New South Wales, Australia

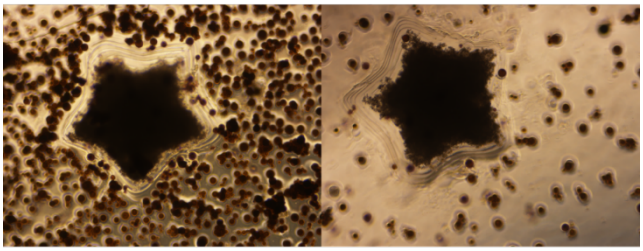
Presenting: z5036672@ad.unsw.edu.au Corresponding: k.kilian@unsw.edu.au



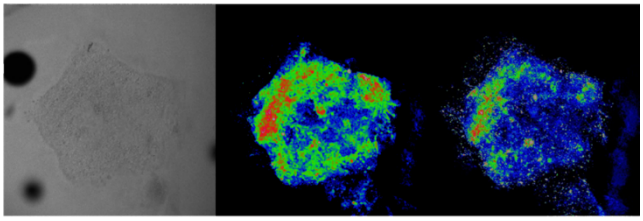
Microcapsules under 4x



Microcapsule size distribution



Hypoxic microcapsules embedded platform with HepG2 star shape aggregate



HCC38, 2mg of 100u microcapsules embedded, Brightfield

HCC38, 2mg of 100u microcapsules embedded, Hif-1a

HCC38, 2mg of 100u microcapsules embedded, CD133

Tissue hypoxia has been considered a critical component of the tumor microenvironment (TME), with relationships to the epithelial-mesenchymal transition (EMT), which leads to tumor plasticity and metastasis. Within the solid tumor comprised of billions of cells, the oxygen level will be gradually decreased as the distance to the blood vessel increases. However, growing cells in the lab generally will incubate them under global normoxia conditions. Based on this, we developed a novel hypoxic microcapsules-embedded hydrogel platform for studying the relationship between EMT progress and cancer stemness derived by low oxygen conditions.

The Hypoxic microcapsule as an advanced oxygen scavenging tool significantly reduces the oxygen level from the microcapsule position in a spatial gradient.[1] To template tissue-mimetic structures, we used a micro-mould template where populations of cells could be cultured within a defined volume (Figure). After 3 days of culture, the presence of hypoxic regions fostered by the embedded microcapsules led to increased expression of HIF-1α and the stemness marker CD133.

In summary, the data indicates that hypoxic conditions derived from microcapsules can spatially enhance the stemness markers and hypoxic-related marker. Since the size of the microcapsules can be easily tuned, this platform can enable studies of matrix mechanics, confinement and oxygen tension, which will prove useful for evaluating the tole of these parameters in regulating hypoxic-related diseases.

References:

1. Molley, T. G. *et al.* Gas-modulating microcapsules for spatiotemporal control of hypoxia. *Proc Natl Acad Sci U S A* **120**, e2217557120 (2023).