Controlling iPSC behaviour in 3D microtissues using tunable microgels

AIM

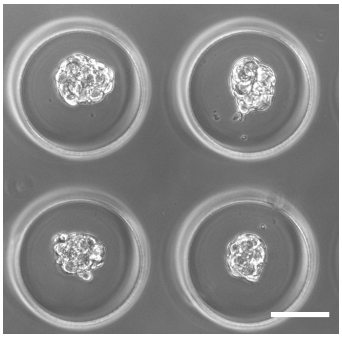
Engineer advanced microgels with cell-like properties to control the fate and behavior of 3D iPSC cultures.

INTRODUCTION

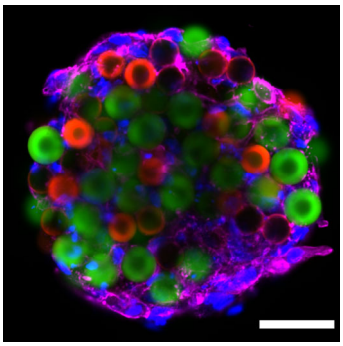
Induced pluripotent stem cells (iPSCs) technology is of high interest for regenerative medicine and human disease modeling. 3D cell culture is essential in mimicking the complexity of the *in vivo* situation. However, incorporating iPSCs into biomaterials to create 3D cultures has proven to be challenging using conventional culturing techniques (e.g. hydrogel encapsulation). Although aggregating iPSCs into material-free cellular microtissues allows for 3D cultures, this approach lacks controllable material-cell interactions that can predictable guide cell behavior. Consequently, the control over 3D iPSC cultures has remained limited.

Recently, our group has developed a microfluidic platform to produce tunable cell-adhesive microgels that can be incorporated in stem cell microtissues (Figure 1 and 2). These microgels offer a high degree of control over their physical and chemical properties, which can be leveraged to tune stem cell behavior. We hypothesize that incorporating these microgels into these microtissues will offer the desired cell-material interaction to guide the fate of iPSCs and thus the behavior of the microtissues. Custom modifications of these cell adhesive microgels would enable the controlled study of specific interactions within 3D iPSC/microgel aggregates.

In this project, the student will design and investigate 3D iPSC culture in stem cell microtissues. For example, microgels will be functionalized with various cell-adhesion mimicking peptides, tunable mechanical moieties and growth factor binding compounds. Specifically, the effect of these microgels on iPSC behaviour (e.g. viability, differentiation, pluripotency) will be investigated.



3D culture of cell-microgel aggregates with stem cells.



3D microaggregate of stem cells and microgels.

GOALS

1. Produce cell-sized microgels using an advanced droplet microfluidic system
2. Functionalize microgels with biofunctional moieties
3. Optimize iPSC culture in both 2D and 3D platforms
4. Combine microgels with iPSCs in 3D co-cultures
5. Steer and evaluate the behaviour of iPSC in 3D stem cell aggregates

TECHNIQUES

The student will learn several state-of-the art techniques, including droplet microfluidics, enzymatic hydrogel crosslinking, (3D) stem cell culture, iPSC culture, qPCR, immunohistochemistry, and confocal fluorescence imaging and apply this skill set in a top-level institute.

RELEVANT LITERATURE

1. Kamperman, T., *Microgel Technology to Advance Modular Tissue Engineering*, in *Developmental BioEngineering*. 2018, University of Twente. p. 174.
2. Barcelona-Estaje, E., Dalby, M. J., Cantini, M., Salmeron-Sanchez, M., You Talking to Me? Cadherin and Integrin Crosstalk in Biomaterial Design. *Adv. Healthcare Mater.* 2021, 10, 2002048
3. Kamperman, T., Koerselman, M., Kelder, C. *et al.* Spatiotemporal material functionalization via competitive supramolecular complexation of avidin and biotin analogs. *Nat Commun* **10,** 4347 (2019)
4. Rao, V., Wechsler, M.E., Anseth, K.S., *et al*, Granular PEG hydrogels mediate osteoporotic MSC clustering via N-cadherin influencing the pro-resorptive bias of their secretory profile, *Acta Biomaterialia,* 145, 77-87 (2022)

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