

Master assignment:

The effect of cellular interactions on cell behavior in cellular spheroids and organoids

It is well known that three-dimensional (3D) cell culture is more biomimetic than two-dimensional (2D) cell culture. In conventional monolayer culture cells are cultured on supraphysiological stiff plastic. This culture system provides very different cues to the cells as compared to those provided by native tissues. Examples are differences in cell-cell contact, cell-matrix interaction, matrix stiffness and tissue-specific cell organization. As such, three-dimensional cell culture - like spheroids, organoids or hydrogel culture – was developed, mimicking the native tissue to a larger degree. Not surprisingly, 3D cell culture elicits more biomimetic cell behavior. However, still little is known about the intracellular processes evoked by the presence or absence of certain cues, eventually leading to the more biomimetic cell behavior.

This assignment focusses on studying the intracellular processes leading to the more biomimetic cell behavior. More specifically, you will investigate the effect of cell-cell interactions or cell-biomaterial interactions on cell behavior. The focus can be chosen depending upon personal preferences.

Techniques

You will perform amongst others conventional monolayer and advanced 3D stem cell culture (i.e. spheroids, organoids, hydrogels), biofabrication of microwells, biochemical assays, microscopy and fluorescent confocal microscopy and (basic) image analysis.

This assignment will equipped you with a broad range of different techniques relevant for tissue engineering.

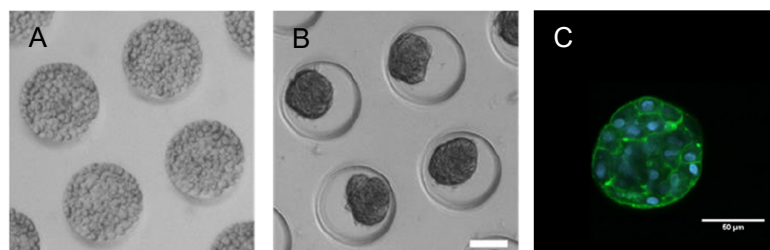


Figure 1: Images of (A) cells in microwells directly after seeding, (B) after 24 hours, aggregate formation is visible, and (C) confocal image of an aggregate (nuclear staining (blue) + membrane staining (green)). The cell-cell contact is clearly visible.

Relevant literature:

1. Pampaloni F, Reynaud EG, Stelzer EH. *The third dimension bridges the gap between cell culture and live tissue*. Nat Rev Mol Cell Biol. 2007;8(10):839-845. DOI: 10.1038/nrm2236
2. Leijten J, Teixeira LS, Bolander J, Ji W, Vanspauwen B, Lammertyn J, et al. *Bioinspired seeding of biomaterials using three dimensional microtissues induces chondrogenic stem cell differentiation and cartilage formation under growth factor free conditions*. Sci Rep. 2016;6:36011. DOI: 10.1038/srep36011
3. Guo M, Pegoraro AF, Mao A, Zhou EH, Arany PR, Han Y, et al. *Cell volume change through water efflux impacts cell stiffness and stem cell fate*. Proc Natl Acad Sci U S A. 2017;114(41):E8618-E8627. DOI: 10.1073/pnas.1705179114

4. Bao M, Xie J, Katoele N, Hu X, Wang B, Piruska A, et al. *Cellular Volume and Matrix Stiffness Direct Stem Cell Behavior in a 3D Microniche*. ACS Applied Materials and Interfaces. 2019;11(2):1754-1759. DOI: 10.1021/acsami.8b19396

Daily supervisor: Marieke Meteling

Principle investigator: Jeroen Leijten