Precision cancer medicine based on 3D drug profiling of patient-derived cancer cell spheroid models

In recent years, personalized medicine has become a much-discussed topic, as it aims to advance health and treat diseases at the individual patient level. Cancer patient -derived cells are in focus in a joint project between the Institute for Molecular Medicine Finland (FIMM), at the University of Helsinki and GrowDex® by UPM Biomedicals.

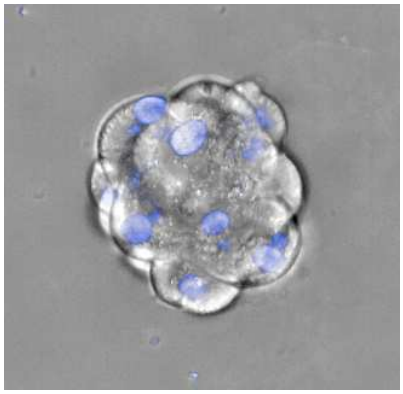
Senior Researcher Vilja Pietiäinen from FIMM (in the middle), Application Scientist Lauri Paasonen (on the right) and Senior Manager Pia Nilsson (on the left) from UPM work closely together in a joint cancer research project.

The joint cancer research project between UPM and FIMM began when UPM established a new innovation department in the Biomedicum research and education centre in Meilahti, Helsinki in 2016. The project focuses on growing patient derived cancer cells in a three-dimensional culture using GrowDex and studying the drug responses of the cancer cells. This exciting research project brings together two growth areas: bioeconomy and personalised medicine.

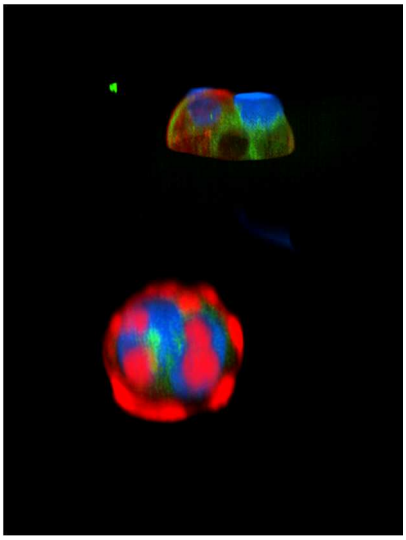
“Fresh cancer tissue samples are obtained directly from clinics and processed to provide patient -derived cells (PDCs). We culture these cancer cells under different conditions in GrowDex hydrogel, for drug testing, among other uses. We are also interested in the mutations of cancer cells,” explains Dr Vilja Pietiäinen, who works as a Senior Researcher at FIMM. FIMM belongs to the recently established Helsinki Institute of Life Science (HiLIFE) that supports high quality life science research across the University of Helsinki. Pietiäinen is a member of a research group led by Professor Olli Kallioniemi.

Additionally, FIMM researchers are trying to understand how cancer begins, the precise point of origin of a patient’s cancer, and how the cancer cells in this patient react to different medicines. “Each patient is different and so is each cancer,” explains Pietiäinen. She adds that UPM’s Biomedicals team was ahead of its time: both personalized medicine and 3D cell culture have now become extremely relevant.

“Major pharmaceutical companies are currently very interested in 3D drug testing. Clearly, they have been waiting for someone to perform academic research in the field and develop new methods. UPM entered the field with perfect timing as interest is clearly increasing day by day,” says Pietiäinen.



Renal carcinoma cells grown as spheroids in GrowDex were stained to detect the nuclei (blue) and imaged with Opera Phenix high-content microscope (40X objective, scale bar 100 µm).



Cancer cells grown in GrowDex were immunostained and imaged with Opera Phenix (40X) objective. Images were further processed for 3D with Volocity software by Lassi Paavolainen. The zoomed-in versions of the original images are shown.

In a talk recently given at Swiss Image-Based Screening Conference, SIBS2017, Pietiäinen presented their drug profiling pipeline and the development of 3D screening methods for patient-derived cancer spheroids from ovarian and renal cancers. They have been able to grow patient - derived cells as spheroids in GrowDex. These spheroids can further be imaged by microscope to investigate the expression of cancer biomarkers or tested for the drug sensitivities. The latest results suggest that the tested 3D models are also applicable in the 384-well drug sensitivity assay, which was set-up with high throughput automation and robotics available at FIMM High Throughput Biomedicine unit. They observed significant differences in the drug responses of patient derived cells in 2D and 3D conditions, suggesting that 3D screening methods are important for representative drug sensitivity profiling of patient derived cancer cells.

Central to the success of this approach is to grow and test the patient derived cells in *ex vivo* conditions mimicking the tumor microenvironment.” Pietiäinen concludes.