3D model systems for cancer biology

VTT offers a miniaturized, three-dimensional screening platform for small compound testing and drug/drug target validation. Standardized experimental conditions have been optimized for rapid drug screening and high-content microscopic imaging. Real-time, live cell microscopy and automated image analysis software solutions provide adequate tools to monitor the dynamics and heterogeneity of cell growth, differentiation, invasion and other highly relevant morphologic features.

Compared to monolayer cell culture, 3D model systems more accurately mimic the complexity of breast and prostate cancer biology, and provide relevant answers related to cancer treatment and drug development. 3D models represent a valid intermediate validation step between primary drug screening and animal experimentation.

**Readout**
- Phase contrast microscopy
- Live-cell imaging
- Confocal microscopy
- Immunofluorescence
- Biomarker expression
- mRNA and protein expression

**All-in-one assays**
- Proliferation
- Apoptosis and cell death
- Growth dynamics
- Cell differentiation & morphogenesis
- Cancer invasion

**Applications**
- Compound screening
- Target validation
- Toxicology
- Basic cell biology
- Co-culture models

Spontaneous transformation of round prostate cancer spheroids (left) with intact basal lamina (red) into invasive structures with simultaneous degradation of the basal lamina (right, day 13).

Small molecule inhibitors can specifically block cancer cell invasion. Untreated cancer cells (left) form characteristic spindle-like filopodia, while treated cells (right) do not develop aggressive features. Image generated by live-cell staining and spinning-disc confocal microscopy.
High content 3D model systems for cancer drug discovery

**Cell lines:** More than 30 normal- and cancer cell lines have been optimized for 3D culture to date. Our panel of models specifically addresses the most relevant problems in oncology: invasive growth and metastasis, proliferation, and cell death. These models address the full spectrum of tumor biology.

**Miniaturization:** Our 3D culture models represent a single miniaturized, high-content screening platform, which is standardized, cost-effective, and flexible for many applications. The modular design allows parallel experimentation, time- and dose-response courses, as well as drug sensitization and synthetic lethality screens.

**Microscopic imaging:** Live-cell imaging enables real-time monitoring of complex organotypic cell cultures for up to 15 days. Live cell staining assures accurate measurements of dynamic cellular features without cell fixation. Morphological changes can be accurately quantified for toxicology and structure-activity relationship studies (SAR), dose response, and EC50 estimations. Confocal microscopy allows us to simultaneously measure multiple relevant endpoints such as biomarker expression, apoptosis, and substructural localization.

**Automated image analysis:** Our software solutions address the specific demands of high-content screening, i.e. acquisition, storage, automated analysis, statistical evaluation and quantification of microscopic images. Panels of diverse morphological features, indicative for tumor cell growth and invasion parameters, are processed. Informative live cell assays (e.g. for apoptosis, proliferation, invasion) are available.

**Drug response:** Miniaturization reduces the cost for screening purposes, and increases the overall throughput. Our settings allow long term exposure e.g. for toxicology and cell differentiation studies. Multicellular organoids formed in 3D assays often respond differently to drugs compared to cells in 2D monolayer culture; drugs that fail in 2D may be effective in 3D. This adds a very relevant layer of information for cancer drug discovery and cell biology.

**Molecular biology and bioinformatic:** Supporting quantitative biochemical methods that complement our phenotypic 3D assays have been established, such as protein, mRNA and miRNA profiling, reversed-phase protein arrays (“lysate arrays”), and quantitative realtime RT-PCR. This is further supported by systems biology and bioinformatics.

**Additional information**
Matthias Nees, Senior Research Scientist
Team Leader
Tel. +358 40 8314 839
matthias.nees@vtt.fi

VTT TECHNICAL RESEARCH CENTRE OF FINLAND