Automated 3D Cell-Based Assays in Animal-Free Nanofibrillar Cellulose Hydrogels for High-Throughput Screening Analyses

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Plant-based nanofibrillar cellulose (NFC) GrowDex hydrogels made only from NFC and water have shown to provide a biocompatible ECM-like support matrix for multitude cell types that allow free diffusion of small molecules. They are shear thinning and temperature stable; the stiffness can be tuned to apply them to various applications, including automated cell-based assays and clinically relevant cell models for drug discovery and development.

GrowDex hydrogels have shown to be experiment-reproducible support matrices for variety of cell types, enabling spheroid/organoid formation in a defined culture environment. These models provide cost-effective, scalable platforms for high-throughput and high content screening applications: (A) CSC theory proposes a subpopulation of self-renewing cells is responsible for sustaining and propagating tumors. The stemness in spheroids was assessed with human glioblastoma cell line U-251. After 72h culture in transparent anionic GrowDex-T, spheroids were fixed and stained with CSC markers to identify the CSCs in the spheroids. This transparent 3D hydrogel offered an excellent high content imaging and volumetric analysis platform for highly precise quantification of morphology and CSC population in the spheroids. [1] (B) Ex vivo drug screening is used to assess drug efficacy of patient derived vital tumor cells. After preliminary 2D screening of 1160 FDA approved/investigational/preclinical drugs for metastatic urachal carcinoma cells, selected 90 drugs were more closely screened to compare conventional 2D enzymatic assay vs. GrowDex 3D model for drug screening in high-throughput image-based viability assay. All tested models captured the cells' sensitivity to the same drugs that could be associated with the oncogenic mutation specific to this cancer. Specific drug classes showed differences in dose responses 2D vs. 3D. This indicates a need for varied high-throughput modalities for more accurate drug screening methods. [2]

REFERENCES: [1] Y. Meng et al. (2021) Application note: High-content quantitation of cancer stem cells from a glioblastoma cell line cultured in 3D using GrowDex®-T hydrogel at upmbiomedicals.com 9.9.2022 [2] Mäkelä et al. (2020) Ex vivo modelling of drug efficacy in a rare metastatic urachal carcinoma *BMC Cancer* **20**:590.