

A novel high-throughput solution for screening compounds with a light-crosslinked VersaGel 3D tumour culture model and automated high-content imaging

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In order to screen using a model that closely mimics the in vivo tumor microenvironment, but in a microplate, cancer cells and spheroids may be cultured and imaged in a three-dimensional (3D) matrix. In these experiments we paired a novel light-cross linkable 3D cell culture platform, VersaGel<sup>®</sup> and Symphony<sup>®</sup>, with high-content imaging to demonstrate a 3D assay amenable to high-throughput screening. It incorporates a straightforward workflow to grow and treat cancer cells or spheroids embedded in an ECM hydrogel, VersaGel, in a standard 96-well format, and subsequently image the culture using the ImageXpress<sup>®</sup> Micro Confocal High-Content Imaging System. Cells may be stained before or after embedding in the gel, and imaged live or after fixing with standard methods. Here we present results of optimized spheroid growth of different cancer cells lines in three different VersaGel stiffnesses and further treatment with chemotherapeutic compounds. In experiments with only 1-4 spheroids/well, QuickID was performed, whereby the entire plate was rapidly scanned at low magnification and then only fields of view containing a spheroid were automatically re-imaged at a higher magnification and with multiple z planes. Alternatively, a 2D projection image was sometimes generated for simple analyses such as viability or apoptosis. Together, VersaGel/Symphony and the ImageXpress Micro Confocal system provide a powerful solution for drug screening in a 3D ECM hydrogel culture system.