

High-Throughput LSFM Imaging Of 3D-3-Culture Models To Unveil Macrophage Plasticity In The Tumour Microenvironment

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Drug screens on complex cell models and organisms are a key factor to understand and treat human diseases. However, fast and effective conclusions have been hindered by the lack of robust and predictable models amenable to high-throughput (HT) analysis. Recently, important advances have been made towards the development of 3D co-culture models using distinct cell types that better recapitulates its in vivo features. These models bridge the gap between adherent cell culture and animal models, providing a powerful in vitro model for preclinical research.

A major hurdle, hampering the widespread utilization of complex in vitro models, is the lack of robust imaging tools. Light sheet fluorescence microscopy (LSFM) has been proposed to overcome those limitations [1, 2]. Few years ago, we created the first flow cytometry system based on LSFM, SPIM-Fluid [3, 4], allowing the massive interrogation of a large set of biological parameters in hundreds of 3D cell cultures, thus providing statistical relevance. Now we have developed a new LSFM platform, Flexi-SPIM, which combines automatic fluidic loading of the samples and traditional scanning, overcoming the limitations of previous systems while keeping its HT capabilities.

Using Flexi-SPIM, we are able to image more than 150 sample in only two imaging sessions of complex 3D-3 culture models including a co-culture of tumour cell spheroids of a non-small cell lung carcinoma cell line (tdTomato); cancer-associated fibroblasts (GFP) and a monocytic cell line (THP-1) (Cell tracker) in alginate capsules [5]. We observed phenotypic changes over time as well as how myeloid cells infiltrate into the tumour spheroids and display an immunosuppressive phenotype typical of tumour-associated macrophages.

Ref

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