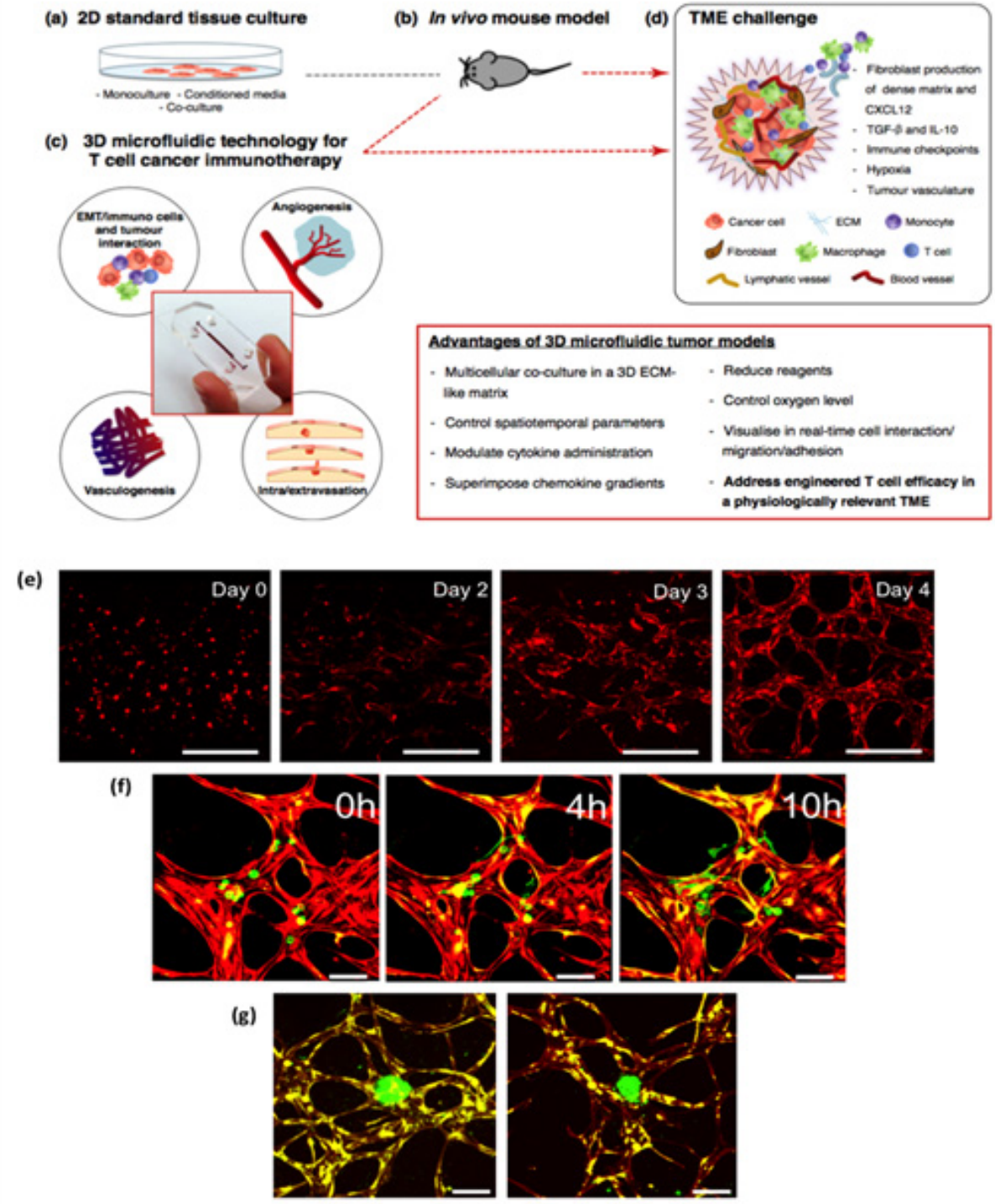
Research

3D tumour microenvironment in vitro models Lab

The group is currently focused on developing and utilizing microfluidic platforms mainly for, but not limited to, cancer research by creating multicellular models with conditions and stimulations that play a fundamental role in specific human tissues.

The powerful microfluidic tool allows the fine tuning of parameters such as: i) co-culture of multiple cell types in 2D and 3D; ii) application of different concentrations and gradients of oxygen; iii) administration of cytokines, chemokines and inflammatory molecules as well as iv) the control of physical parameters, like ECM stiffness and density, to take into consideration the fact that tumour metastasis can seed in different organs or that the TME can be fibrotic and immunosuppressive.

The model represents an efficient preclinical tool to be potentially used during clinical trials to match the optimal drug and technique to individual cancer patients following a personalized medicine strategy.



The Pavesi Lab. in currently focusing on the following topics:

Focus 1: Create a 3D microfluidic model for preclinical evaluation of tumour-specific immunotherapy techniques.

Immunotherapy aims to redirect the patient's immune system to fight against a specific pathology and holds great promise as novel approach in cancer treatment. Our recently developed microfluidics-based assay was successfully able to mimic the conditions of the patient-specific tumour microenvironment and monitor engineered T cell cytotoxicity on hepatocellular carcinoma associated to hepatitis B virus (HBV+ HCC) cells in a 3D extracellular matrix (ECM)-like environment.

Focus 2: Explore epigenetics chemical probes in a 3D TME model

Chemical biology methods using selective, cell-active chemical inhibitors constitute a promising approach for drug development. Chemical probes are small molecules that rapidly and selectively inhibit the target protein in cells. One way to facilitate the discovery of new therapeutics against cancer is to use microfluidic technology mimicking the 3D TME conditions to screen these chemical probes.

Focus 3: Investigate myeloid cells interplay in a 3D TME model

TME is responsible of immune suppression by the synergistic effect of several factors. Some of the most crucial mechanisms are: (a) the presence of cancer associated fibroblasts which regulate ECM and the expression of CXC12, (b) the role of B cells and tumour associated macrophages in T cell recruitment, (c) the production of Indole 2,3-dioxygenase (IDO) that compromise T cell proliferation, (d) the oxygen levels which are correlated with PD-L1 expression and cytokines production, (e) the tumour vasculature that preferentially recruits other immune cells compared to T cells and (f) the nitration of chemokine CCL2 resulting in T cell trapping in the stroma.

By creating a TME model, we recapitulate step by step all these elements. Cancer cell aggregates, T cells, macrophages and B cells can be co-cultured in an optimized matrix composed by a mixture of collagen and fibrin containing also endothelial cells and fibroblast in order to create a vasculature network around the tumour mass model.

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