THREE-DIMENSIONAL CULTURE SYSTEMS FOR TRANSLATIONAL BIOMEDICINE

Our research focuses on developing advanced three-dimensional (3D) culture systems that more accurately recapitulate the physiological microenvironment compared to conventional two-dimensional models. By integrating spheroid and hydrogel-based platforms, we investigate fundamental cellular mechanisms and their therapeutic potential across diverse applications.

A) 3D spheroids and hydrogel-based cultures for enhancing the therapeutic properties of multipotent mesenchymal stromal cells (MSCs).

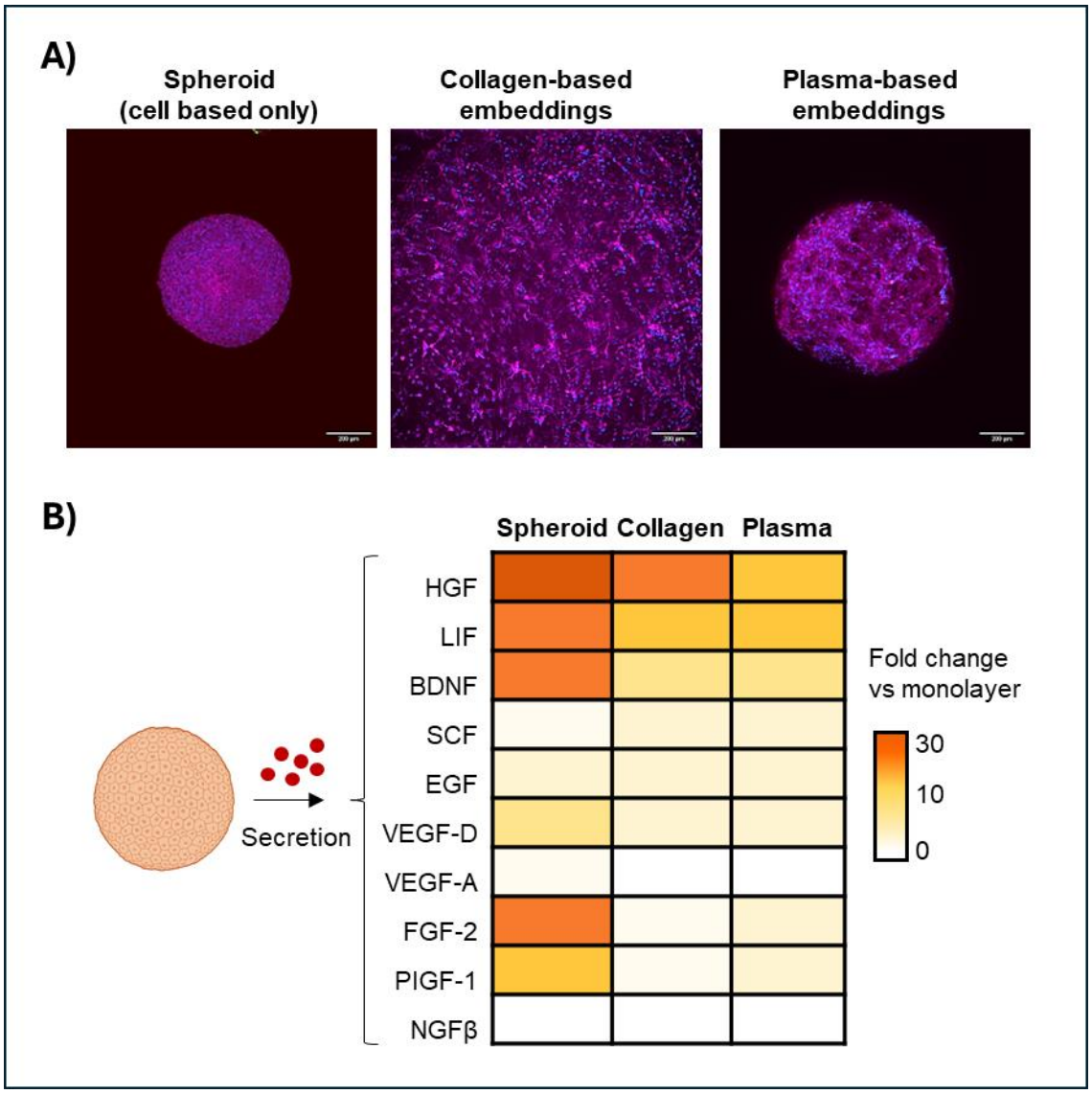

Figure 1. We investigate the 3D architecture and functional properties of MSCs within hydrogel-free spheroids and biomaterial-guided spheroidal constructs (A - staining by phalloidin / DAPI), employing collagen and human plasma-based matrices as clinically-relevant embedding systems. We observed enhanced paracrine activity of MSCs across all established 3D culture systems compared with 2D monolayers (B, multiplex assay), with spheroidal cultures exhibiting the most pronounced effect.

B) Adipose tissue microvascular fragments (MVF) as a tool for pre-vascularization of tissue engineered constructs

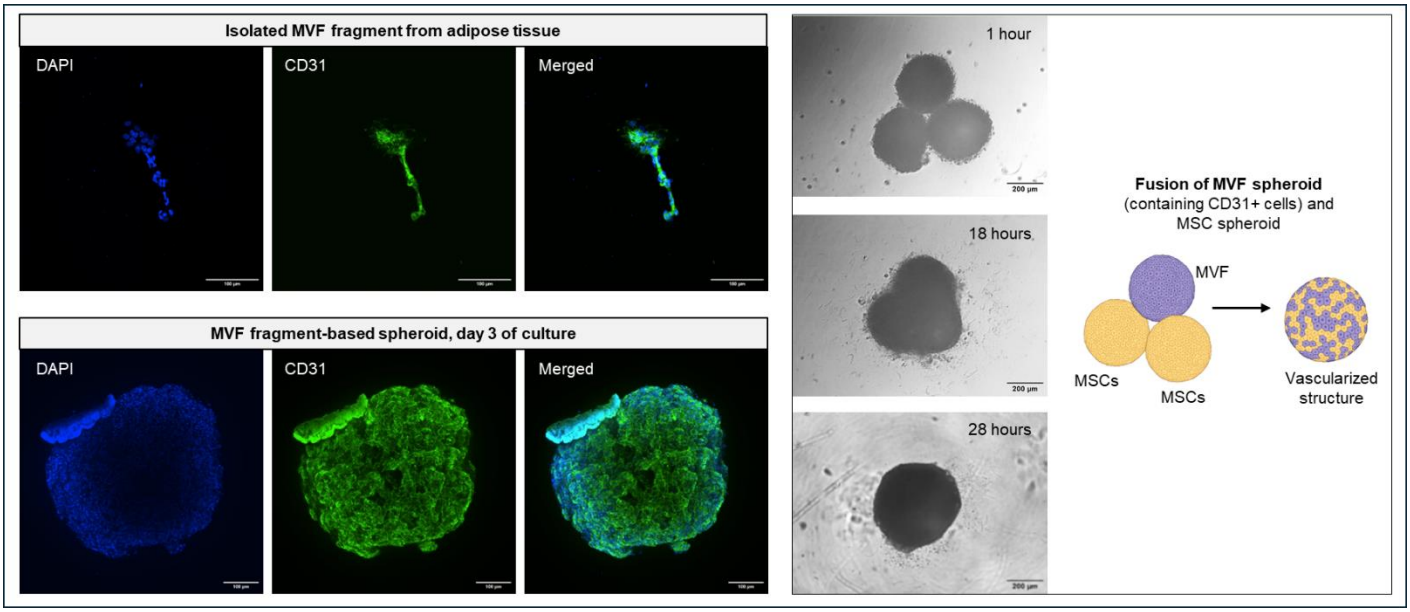

Figure 2. We isolated adipose tissue–derived microvascular fragments (MVFs) and analysed their endothelial compartment by CD31 expression (upper row). We then established 3D culture conditions that preserved endothelial phenotype within the fragments (lower row). Using a fusion-based approach, we generated pre-vascularized 3D constructs containing MVFs together with other cell types, such as MSCs prior to or following differentiation.

C) Multicellular 3D spheroids for cancer research and modelling

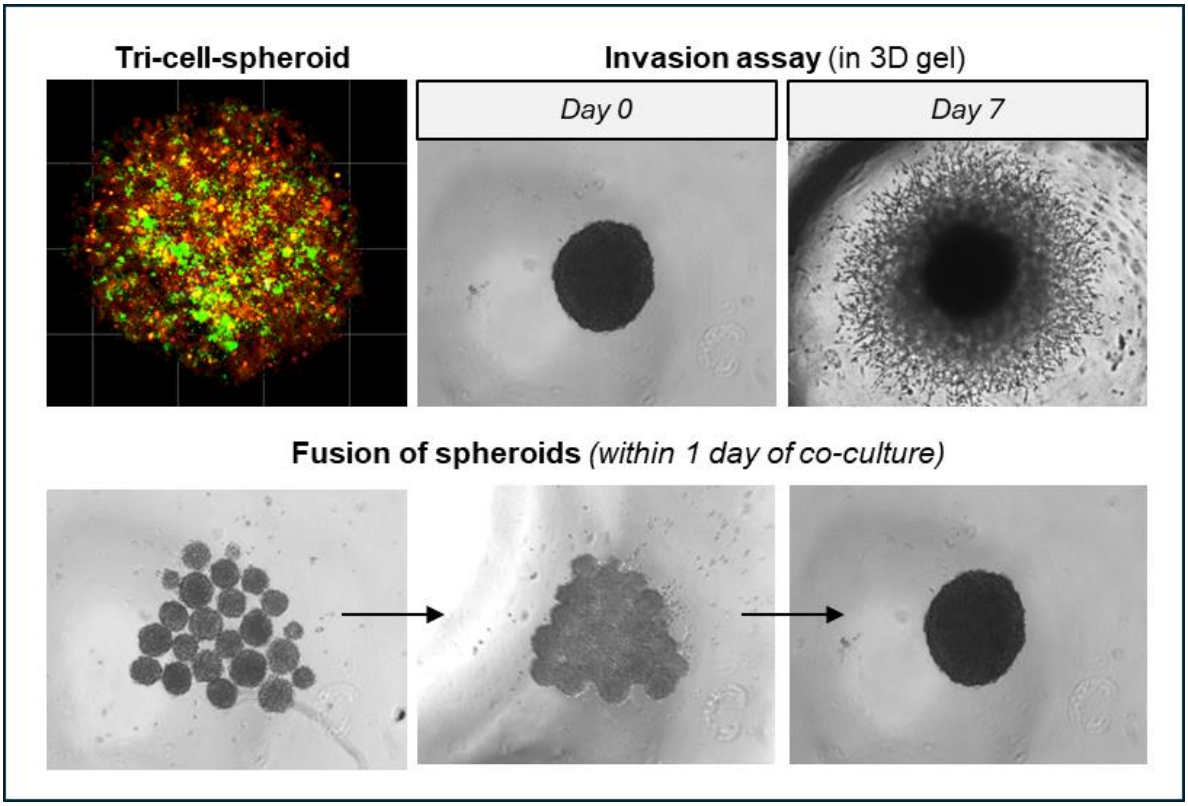

Figure 3. We develop 3D spheroid-based models and culture approaches to study cell–cell interactions within the tumour microenvironment, as well as tumour growth and invasion under anti-cancer treatment. Using hydrogel-free and hydrogel-based spheroids, we establish advanced systems containing endothelial cells, astrocytes, and glioblastoma cells to more accurately recapitulate the glioblastoma microenvironment. We

further apply fusion strategies and 3D hydrogel invasion assays to investigate the impact of therapies on the functional performance of cancer cells.

D) Bioreactors and mini-fluidic systems

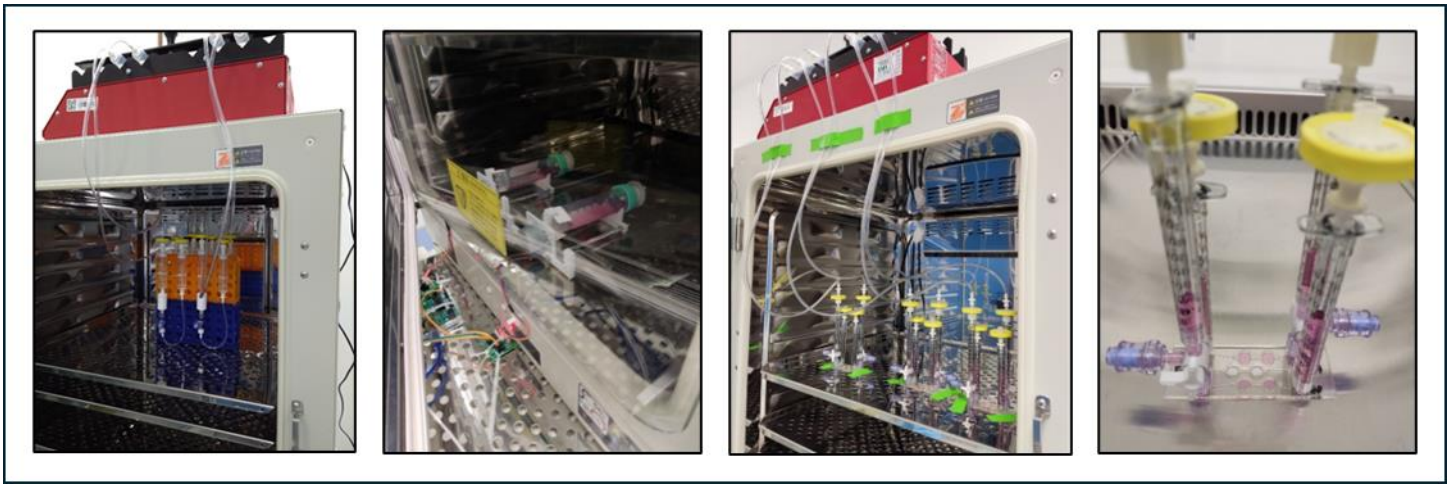

Figure 4. We establish easy-to-use, adjustable, and disposable closed bioreactor systems to introduce dynamic conditions into 3D cultures, thereby enhancing their physiological relevance. These systems include (from left to right) an oscillating perfusion bioreactor for cell-seeded porous scaffolds, a rotating bioreactor, and a mini-fluidic platform for studying paracrine interactions of cells within a 3D environment.

E) Biopreservation of 3D cultures

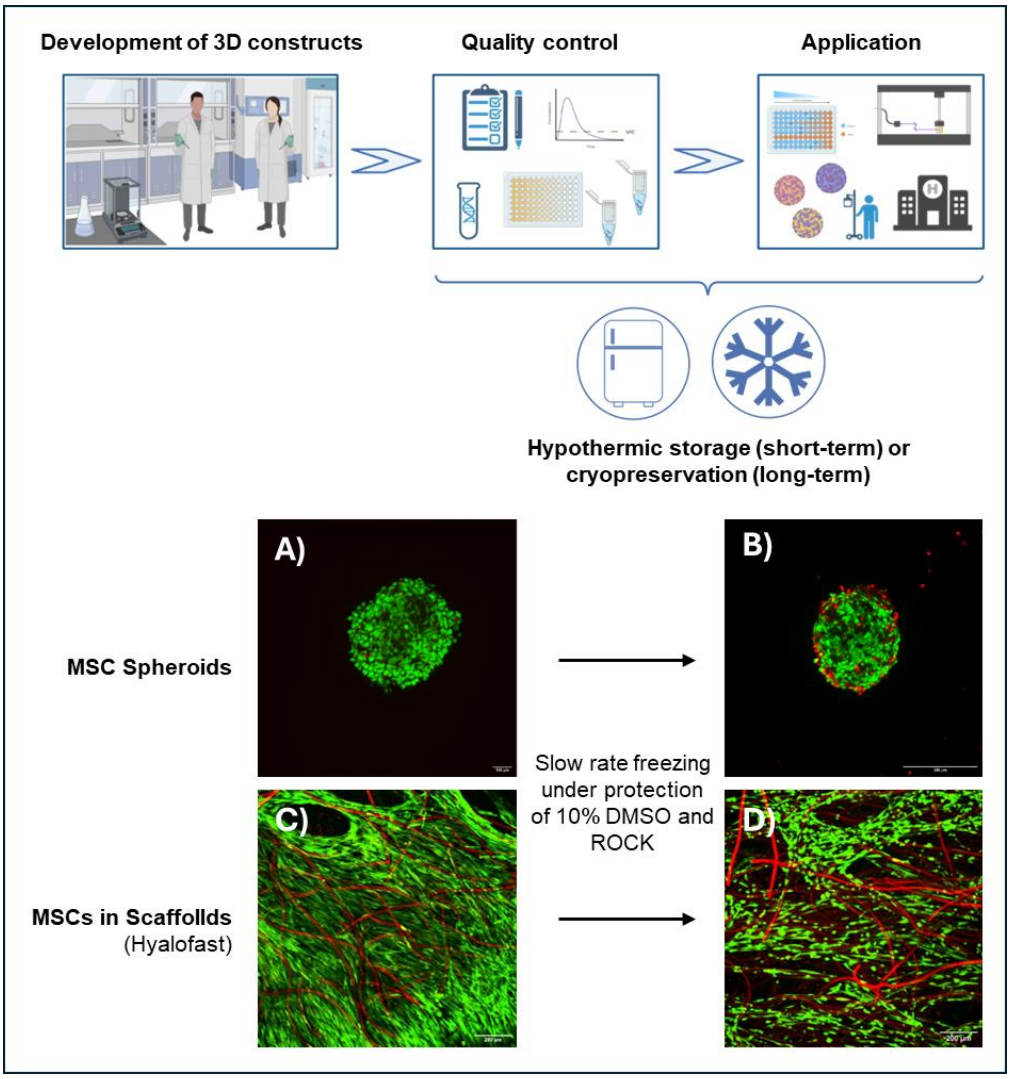

Figure 5. Conventional cryopreservation protocols, originally developed for simple cell suspensions, are not directly applicable to complex 3D culture systems. We are adapting and optimizing cryopreservation procedures for 3D constructs, enabling preservation of structural integrity and high post-thaw viability. Representative images (Live/Dead staining) illustrate MSC viability in spheroids and Hyalofast scaffolds before (A, C) and after cryopreservation (B, D).