

Poster

A MILLIFLUIDIC GLIOBLASTOMA MODEL TO INVESTIGATE HYPOXIA-DRIVEN SECRETOME REMODELLING AND ITS MODULATION BY PACAP

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Glioblastoma (GBM) remains the most lethal primary brain malignancy, with therapeutic resistance largely driven by glioblastoma stem cells, which reside in specialized tumor niches. This microenvironment is sustained by growth factor and cytokine secretion, which alters the tumor secretome and promotes cancer cell pluripotency, invasiveness, tumor dissemination, and chemotherapy resistance. To investigate these dynamics, we set up a 3D millifluidic platform (MIVO) that replicates the tumor-microcirculation interface. This system features a compartmentalized architecture in which a porous, permeable membrane separates a GBM tumorspheres chamber from a dynamic fluidic compartment, simulating dissemination of the systemic secretome. We validated the platform using immortalized GBM cell lines (T98G, A172 and U118MG). Hypoxia induction via deferoxamine (D-FX) significantly altered the secretome profile in a cell-specific manner, increasing vascular endothelial growth factor (VEGF) in all models and interleukin-1β (IL-1β) levels in A172 and U118MG tumorspheres compared to normoxic controls. PACAP treatment significantly reduced VEGF concentrations in the circulating compartment of all models and brought IL-1β back towards control levels in A172 and U118MG tumorspheres. These data highlight the platform's ability to detect secretome remodelling and its pharmacological modulation. Overall, the 3D millifluidic system captures pathophysiological transitions of the GBM secretome, providing a tool for mechanistic studies and screening of therapeutic agents targeting the hypoxic tumor niche.