3D-dimensional patient-derived cell culture models for therapeutic screening: preclinical efficacy of a novel sigma receptor modulator in glioblastoma

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Human glioblastoma multiforme (hGBM) is the most malignant and aggressive primary adult brain tumor. The current treatment strategy consists of multimodal therapy including surgery and concurrent adjuvant radiotherapy in combination with chemotherapy. However, median survival is still only 12-15 months, making an improvement in treatment efficacy an important challenge. The identification of hGBM stem-like cells (hGSCs), considered potentially responsible for hGBM initiation, maintenance and propagation, represents a promising cellular target for more effective and personalized therapies. There is increasing evidence that sigma receptors S1R and S2R, a class of orphan receptors, both highly expressed in the central nervous system and involved in different degenerative and neuropsychiatric diseases, play a significant role in cancer biology. Thus, RC-106 a novel modulator of both SR subtypes, could represent a promising approach for the treatment of hGBM. We developed an in vitro 3D cell culture model from patient-derived hGSCs to analyze the antitumor activity of RC-106. 3D cell cultures were obtained using a Rotatory Cell Culture System (RCCS) (Synthecon Inv., Houston, TX, USA) and pellet culture system. Growth and morphology of the 3D tumor cultures were monitored by open-source AnaSP and ReViSP software tools. The efficacy of RC-106 was measured after a 48-h and 72-h treatment. The treatment of RC-106 led to a significant reduction in the growth of hGSC spheroids. Our findings suggest that the 3D cell culture model is a good tool for drug testing and that RC-106 represents the lead compound of a new class of SR modulators potentially useful for the treatment of hGBM.