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Targeting of CXCR4+ Glioblastoma initiating cells with a retargeted oncolytic herpesvirus

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Multiform Glioblastoma (GBM) is the most aggressive primary brain tumor in adults. Despite improvement of treatments (usually surgical resection followed by radio- and/or chemotherapy), glioblastoma patients have a poor prognosis, mainly due to recurrences of the tumor. It has been recently shown in an orthotopic xenograft model that

GBM cells can escape the tumor mass and specifically invade the subventricular zones (SVZ) of the adult brain. This migration is mediated by a CXCL12 gradient that attracts GBM cells, which have been shown to express CXCR4 (one of the two CXCL12 receptors). In addition, these CXCR4+ cells share characteristics with stem cells and are thus considered as GBM-initiating cells responsible for the recurrences. They appear therefore as a target of choice for therapeutic approaches. Oncolytic Herpes simplex virus (oHSV) has been shown to have potent oncolytic effects against tumor cells of different origin, including GBM. We have engineered a herpesvirus, which specifically targets CXCR4+ cells and is armed with genes inducing the extrinsic or/and intrinsic apoptosis signaling pathways. The specificity and efficacy of these engineered oHSV are currently evaluated in vitro in monolayers and 3D cultures and will be soon characterized in vivo in an orthotopic xenograft model of GBM.
