**An oncolytic herpesvirus to counteract Glioblastoma Stem Cells function**

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Glioblastoma Multiforme (GBM) is one of the most lethal cancer of the central nervous system, with a usually poor prognosis due to high frequency of recurrence. “Glioblastoma Stem-like Cells (GSCs)” is a GBM sub-population identified as the main promoter of tumor reformation. The signaling regulated by the CXCR4/CXCL12 axis has been shown to have an important role in promoting GSCs survival and functions. The oncolytic herpes simplex viruses (oHSVs) are a promising anti-cancer therapeutic agent. The oHSVs efficacy relies on their inner oncolytic capacities but also on their capacity to activate an anti-tumor microenvironment. The virotherapy impact can be improved by “arming” the virus, inducing the infected cells to express an exogenous gene.

We have engineered an attenuated oHSV “armed” with a mutated form of CXCL12, called “P2G”, shown to act as an antagonistic inhibitor of CXCR4. oHSV-P2G has demonstrated to efficiently infect human primary GBM cells, to induce the expression and secretion of P2G, and to antagonize the CXCR4/CXCL12 signaling pathway. The impact of HSV-P2G on GSCs CXCR4-dependant features, were analyzed by infecting GBM cells by oHSV-P2G or treating them with conditioned media containing P2G. We showed that these treatments have a significant impact on GSCs self-renewal capacities, measured by tumorospheres and clonogenic assays and on their migration abilities, measured by spheroid migration and transwell assays. The P2G-virotherapy effect, which is correlated with the level of expression of CXCR4 measured by FACS is higher than the one observed with a non-armed oHSV. Moreover, HSV-P2G has shown to decrease the expression of neural stem markers in GBM neurospheres.

Our *in vitro* results show that HSV-P2G has a high impact on GSCs features. oHSV-P2G efficacy will be further analyzed in a murine syngeneic model of GBM, with a special focus on the tumor growth and aggressiveness features.