

Extracellular adenosine promotes cell migration/invasion of Glioblastoma Stem-like Cells through A₃ Adenosine Receptor activation under hypoxia

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Glioblastoma (GBM) is the brain tumor with the worst prognosis composed of a cell subpopulation called Glioblastoma Stem-like Cells (GSCs) responsible for tumor recurrence mediated by cell invasion. GSCs persist in a hypoxic microenvironment which promotes extracellular adenosine production and activation of the A₃ Adenosine Receptor (A₃ AR), therefore, the aim of this study was to determine the role of extracellular adenosine and A₃ AR on GSCs invasion under hypoxia. GSCs were obtained from a U87MG cell line and primary cultures of GBM patients, and then incubated under normoxia or hypoxia. Gene expression was evaluated by RNAseq, RT-qPCR, and western blot. Cell migration was measured by spreading and transwell boyden chamber assays; cell invasion was evaluated by Matrigel-coated transwell, ex vivo brain slice, and in vivo xenograft assays. The contribution of A₃ AR on cell migration/invasion was evaluated using the A₃ AR

antagonist, MRS1220. Extracellular adenosine produc