Graphical Abstract

Reshaping the tumor microenvironment with oncolytic viruses, positive regulation of the immune synapse, and blockade of the immunosuppressive oncometabolic circuitry

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In Brief
While the infection of gliomas with oncolytic viruses, such as Delta-24-RGDOX, induces a Th1 phenotype with increased production of IFNγ, viral infection also activates the IFNγ-driven IDO-Kyn-AhR cascade generating immunosuppression via the recruitment of MDSC and CD4+ Treg populations of cells. The addition of IDO inhibitors to virotherapy counteract this immunosuppressive effect by reinforcing the skew from Th1 to Th2 and CD8+ cytotoxic T cells in the tumor microenvironment, leading to glioma eradication.