Glioma 261

Glioma 261 (GL261) is a frequently used murine glioma model. It was induced via intracranial injection of methylcholanthrene followed by serial intracranial and subcutaneous transplantations of tumor fragments into syngeneic C57BL/6 mice.

By the mid-1990s, multiple groups had established a permanent cell line from the tumor.

GL261 tumors resemble ependymoblastomas on histology but show many characteristics of glioblastoma phenotypes. They contain activating mutations of the K-ras as well as mutations of p53, resulting in high expression of c-myc. GL261 tumors also highly express MHC I, explaining their partial immunogenicity and have limited expression of MHC II, B7-1, and B7-2. The tumors are invasive, are not known to be metastatic, and do not spontaneously regress.

Other immunocompetent murine models used to study GBM include GL26, CT-2A, SMA-560, and 4C8.

Cui et al demonstrate in vitro, GL261 and CT-2A GBM-like tumors steer macrophage polarization towards a M2-like phenotype for fostering an immunosuppressive and proangiogenic niche, which is consistent with human brain tumors.

They distinguished that GBM and M2-like immunosuppressive macrophages promote angiogenesis, while M1-like pro-inflammatory macrophages suppress angiogenesis, which they coin “inflammation-driven angiogenesis.”

They observed soluble immunosuppressive cytokines, predominantly TGF-β1, and surface integrin (αvβ3) endothelial-macrophage interactions are required in inflammation-driven angiogenesis.

They demonstrated tuning cell-adhesion receptors using an integrin (αvβ3)-specific collagen hydrogel regulated inflammation-driven angiogenesis through Src-PI3K-YAP signaling, highlighting the importance of altered cell-ECM interactions in inflammation. To validate the preclinical applications of our 3D organoid model and mechanistic findings of inflammation-driven angiogenesis, Cui et al. screened a novel dual integrin (αvβ3) and cytokine receptor (TGFβ-R1) blockade that suppresses GBM tumor neovascularization by simultaneously targeting macrophage-associated immunosuppression, endothelial-macrophage interactions, and altered ECM. Hence, they provide an interactive and controllable GBM tumor microenvironment and highlight the importance of macrophage-associated immunosuppression in GBM angiogenesis, paving a new direction of screening novel anti-angiogenic therapies [1].

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Cui X, Morales RT, Qian W, Wang H, Gagner JP, Dolgalev I, Placantonakis D, Zagzag D, Cimmino L, Snuderl M, Lam RHW, Chen W. Hacking macrophage-associated immunosuppression for regulating glioblastoma angiogenesis. Biomaterials. 2018 Feb 2;161:164-178. doi: 10.1016/j.biomaterials.2018.01.053. [Epub ahead of print] PubMed PMID: 29421553.