HCMV promotes GBM pathogenesis. HCMV utilizes multiple mechanisms to promote oncogenesis and subvert the host anti-tumor immune function. HCMV envelope glycoprotein B (gB) attaches to and activates PDGFRα signaling. HCMV gene products IE1 and US28 drive multiple cellular pathways important in gliomagenesis such as PI3-K/AKT, pSTAT3, and GSK3-β. The STAT3 pathway is a master regulator of glioma proliferation, apoptosis, angiogenesis, invasion and tumor stem cell maintenance. Other HCMV gene products, and the cmvIL-10 cytokine, lead to further expression of host factors like IL-10 and TGFβ which subvert host anti-tumor immune responses.

Immune Evasion

A critical component in inflammation-associated malignancies like gliomas is the loss of normal antitumor immune function in the tumor microenvironment. In addition to the tumor-promoting effects of HCMV infection of monocytes / macrophages, expression of HCMV gene products by GBM cells could dramatically alter the host’s immune response to tumor. A variety of tumor-derived factors contribute to the emergence of complex local and regional immunosuppressive networks, including VEGF, IL-10, TGF-β, and PGE-2. Cytotoxic T lymphocyte (CTL; CD8+) and NK cell responses are critical effectors of normal host antitumor immunosurveillance. Through millions of years of co-evolution with the host, HCMV has evolved multiple strategies to allow persistent viral infection through a complex array of immune evasion strategies. Several HCMV gene products are expressed as immediate early and early viral genes to block the host-cell MHC class I antigen expression, which is required for CD8+ cytotoxic