Abstract

Glioblastomas (GBM) are the most malignant brain tumors, which are thought to originate from neoplastic transformation of glial cells. These tumors are characterized with highly infiltrative growth, neovascularization, and radio- and chemoresistance. In spite of current therapy including surgical resection of the tumor and chemo/radio therapy, patient's prognosis is still poor and median survival is about 15 months. Certain non-tumor cells present in the GBM microenvironment participate in tumor progression using mechanisms contributing to the local and systemic immunosuppression. Critical roles in the immune escape of GBM have the regulatory T-cells (Tregs), the tumor-associated macrophages (TAMs) and the myeloid-derived suppressor cells (MDSCs). Immunosuppressive mechanisms in GBM are conducted through direct cell-mediated contacts and soluble mediators secreted by tumor-associated cells into the local tumor microenvironment and circulating blood. Both these processes may inhibit immune response mounted against cancer cells. Certain cancer associated cells and secreted mediators are distributed by peripheral blood and potentiate systemic immunosuppression in the GBM host organism. Gaining knowledge about these mechanisms may reveal to possible targets for GBM immunotherapy. For instance, therapeutic targeting of immune checkpoint molecules such as CTLA-4 and PD-L1 by inhibitors are now in the phase of clinical testing.

Key words

glioblastoma multiforme; tumor microenvironment; immunosuppression; immunotherapy; hypoxia; immune checkpoint molecules, Tregs, TAMs, MDSCs,