Summary

Gliomas are the most frequent primary brain tumors, and for highly malignant gliomas (World Health Organization grade III and IV) there is no available effective therapeutic procedure; patients survive an average of about a year even with multidirectional therapies. Although gliomas are immunogenic tumors, they are not efficiently eliminated by the immune system. Previously, the following irregularities in immune response in glioma patient immunity have been described: low peripheral T cell counts, decreased delayed-type hypersensitivity reactions to recall antigens, and defective mitogen-induced blastogenic responses by peripheral blood mononuclear cells. The modulation and downregulation of T cell functions by numerous immunosuppressive cytokines and factors released by malignant gliomas have already been described by many authors. However, even after the neutralization of these factors, efficient immune response is not generated. Moreover, some types of gliomas and other cancers metastasizing to the brain do not secrete immunosuppressive molecules, yet efficacious immune response is still not observed, which implies that more factors are involved in the process.

One of the main signaling pathways important in the development of an immune response is triggered by the interaction of the appropriate receptorson T cells with B7 molecules that function as immune checkpoints. Key regulators of immune activation and tolerance are the CTLA-4 and PD-1 molecules (Cytotoxic T Cell Antigen 4 and Programmed Death Receptor 1, respectively) belonging to the B7-1 / B7-2-CD28 superfamily. The expression of immune checkpoints in tumor cells creates the possibility of interaction not only with immune cells, but also with each other, maximizing the effect of immunosuppression.

These molecules are also expressed on the surface of cancer cells, including human glioblastoma. The results of this study do not confirm the relationship between the tumor grade and the level of CTLA-4 or PD-1 expression.The immune microenvironment of glioblastoma is very complex, but under an immune checkpoint approach, along with other factors that modulate the immune response, may be the key to improving survival in patients with this cancer. Analysis of the cytokine profile released by immune cells, supplemented with the assessment of proliferation and survival of human glioblastoma cells, showed potential therapeutic possibilities with the use of CTLA-4 or PD-1 inhibitors.