Immunology

An increase in CD4+CD25+FOXP3+ regulatory T cells in tumor-infiltrating lymphocytes of human glioblastoma multiforme

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The subpopulation of CD4+CD25+ immunoregulatory T (Tr) cells constitutes 5%-10% of CD4+ cells in humans. These cells play a crucial role in the control of tumor immune response. In this study, we evaluated the distribution of Tr cells in tumor-infiltrating lymphocytes of human glioblastoma multiforme and examined the difference between the brain and autologous blood with respect to Tr cells. Glioma samples from 10 patients were classified as WHO grade IV astrocytoma. Control samples were obtained from patients undergoing resection of a seizure focus. The samples were analyzed by flow cytometry to determine the frequency of Tr cells and by real-time PCR for forkhead box P3 (FOXP3) expression. We then examined the expression of CD62L, CD45RO, and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) and assessed the functionality of Tr cells in vitro. There was a significant difference in the number of FOXP3-expressing CD4+CD25+ T cells within glioma-infiltrating lymphocytes as compared to controls (P < 0.01). This difference was further observed in studies of autologous patient blood and control blood. The expression level of FOXP3 mRNA was high in Tr cells and weak in CD4+CD25-T cells. Moreover, the expression of CD62L and CTLA-4 was elevated in glioma Tr cells as compared to that in the controls. These cells were also CD45RO positive. Functional assays confirmed the suppressive activity of Tr cells in patients with glioma. The expression of CD4+CD25+FOXP3+ T cells was significantly higher in patients with glioblastoma multiforme than in controls. This increase in the frequency of Tr cells that display suppressive activity might play a role in modulation of the immune response against glioma. In light of these findings, Tr cells may represent a potential target for immunotherapy of malignant brain tumors.

Key Words: glioma • immunotherapy • regulatory T cells • tumor-infiltrating lymphocyte

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