Brain cancer immunoediting: novel examples provided by immunotherapy of malignant gliomas.


Abstract
A number of studies in murine models have suggested that the immune system may edit different tumors by forcing their expression profiles so that they escape immune reactions and proliferate. Glioblastoma (GB), the most frequent and aggressive primary brain tumor, provides a good example of this, thanks to the production of numerous immunosuppressive molecules (with TGF-β being of paramount importance), downregulation of the MHC complex and deregulation of the potential for antigen presentation by the surrounding microglia. Given that surgery, radiotherapy and chemotherapy with available protocols have limited effects on the survival of GB patients, different immunotherapy strategies have been developed, based on the use of dendritic cells, antibodies and peptide vaccination. Presently, bevacizumab, a humanized anti-VEGF antibody, provides the most successful example for immune-based treatment of GB, however, its action is limited in time, as the often tumor relapses due to still undefined immunoediting mechanisms. Altered function of EGF receptor-driven pathways is common in GB and is most frequently due to the presence of a deleted form named EGFRvIII, providing a unique cancer epitope that has been targeted by immunotherapy. A recent trial of GB immunotherapy based on vaccination with the EGFRvIII peptide has shown clinical benefit: interestingly most GBs at relapse were negative for EGFRvIII expression, a relevant, direct example of cancer immunoediting. Investigations on the mechanisms of GB immunoediting will lead to an increased understanding of the biology of this malignancy and hopefully provide novel therapeutic targets.

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