Immune-checkpoint blockade and active immunotherapy for glioma.

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Abstract
Cancer immunotherapy has made tremendous progress, including promising results in patients with malignant gliomas. Nonetheless, the immunological microenvironment of the brain and tumors arising therein is still believed to be suboptimal for sufficient antitumor immune responses for a variety of reasons, including the operation of "immune-checkpoint" mechanisms. While these mechanisms prevent autoimmunity in physiological conditions, malignant tumors, including brain tumors, actively employ these mechanisms to evade from immunological attacks. Development of agents designed to unblock these checkpoint steps is currently one of the most active areas of cancer research. In this review, we summarize recent progresses in the field of brain tumor immunology with particular foci in the area of immune-checkpoint mechanisms and development of active immunotherapy strategies. In the last decade, a number of specific monoclonal antibodies designed to block immune-checkpoint mechanisms have been developed and show efficacy in other cancers, such as melanoma. On the other hand, active immunotherapy approaches, such as vaccines, have shown encouraging outcomes. We believe that development of effective immunotherapy approaches should ultimately integrate those checkpoint-blockade agents to enhance the efficacy of therapeutic approaches. With these agents available, it is going to be quite an exciting time in the field. The eventual success of immunotherapies for brain tumors will be dependent upon not only an in-depth understanding of immunology behind the brain and brain tumors, but also collaboration and teamwork for the development of novel trials that address multiple layers of immunological challenges in gliomas.