Abstract

In 1890, Coley observed that cancer patients who developed infections had smaller tumors. From this, he developed Coley’s toxin and treated tumors with injections of infectious materials. In 1960s, Mahaley used monoclonal antibodies to treat central nervous system (CNS) tumors, that research and clinical investigations in brain tumor immunotherapy became a serious undertaking.

There are several different approaches to immunotherapy, include the following:

- Antibody-directed therapies
- Cytokine-mediated therapies
- Cellular therapies
- Vaccines

High-grade gliomas are notable for marked cellular heterogeneity, which accounts for the failure of therapy. Immune therapeutics had previously been underused in patients with low-grade gliomas. These patients are usually less immune suppressed and are less likely to respond to chemotherapy and radiation because their tumor is less rapidly dividing than a malignant glioma. Given the underlying biology, combination therapy will ultimately become the mainstay of therapy. Recent strides have been made in improving survival in these patients with both chemotherapy and immunotherapy. This may be the case when chemotherapy is delivered during the effector phases. However, these two forms of therapy may actually be synergistic in nature when appropriately administered. The proper combination of both chemotherapeutic agent and time of administration will maximize efficacy of treatment and offer an additional regimen for patients, especially those with heterogeneous types of tumors such as glioblastoma multiform, who are not likely to respond to single-agent modality treatments. Immunotherapies for gliomas appear promising, but the unique characteristics of the CNS tumors need to be considered for rational design of therapeutics. Novel approaches to antitumor immunotherapy need to be independently and thoroughly evaluated against tumors within the CNS despite successes with these techniques outside the CNS. Identification of tumor-associated antigens provide selective targeting to the gliomas with a theoretical decreased risk for induction of autoimmunity. Many of the previous attempts to treat glioma patients with immunotherapies, such as lymphocyte transfer, vaccination with glioma cells, and the use of some cytokines, have not met with significant success. Emerging concepts within the field of immunology, advances in molecular technique, and a greater understanding of the interaction between the CNS and the immune system provide background for more rational and hope-fully more efficacious treatments.

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*Corresponding Author: Mohammad Faraji Rad
E-mail: farajirad@yahoo.com