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Editorial

Stimulating anti-tumor immune response: the problem of regulatory T-cells

Approaches to stimulating an anti-tumor immune response in glioblastoma patients have been a subject of interest in preclinical and clinical brain tumor research for decades. To this end, substantial effort has been directed towards inhibiting regulatory T cells (Tregs), which promote immune tolerance and limit the effectiveness of therapies that depend on evoking an anti-tumor immune response. In the current issue of *Neuro-Oncology*, Wainwright et al. (1) investigate the origin of glioblastoma-associated Tregs, specifically whether they are thymus derived vs. induced; this knowledge may be critically important to developing effective approaches to limiting Treg anti-tumor immunosuppression.

To achieve their objective, the authors used a murine, syngeneic, immunocompetent, orthotopic engraftment model to evaluate the effect of thymectomy on systemically administered anti-Treg CD25 mAb and found that the thymus is necessary for animal subjects to experience a survival benefit from this Treg-depleting treatment. To establish the relevance of the experimental model observations to glioblastoma in patients, a human tumor tissue microarray was examined for expression of the thymus-derived marker Helios in tumor-resident Tregs; the results showed that the majority of tumor-associated T-cells were Helios positive. In total, the results of this elegant study suggest that attempts to suppress Tregs, in association with therapies for evoking patient anti-tumor immune response, need to be targeted to the periphery, where Treg development and expansion predominates. However, since brain tumor patients present with Tregs already infiltrating their malignancy, it may additionally be necessary to target Tregs in the brain. This, in turn, would require the use of Treg-suppressive therapeutics with favorable biodistribution properties.

The featured article emphasizes the increasing interest in exploiting patients' immune responses to combat their disease, while informing us of the complexity of cell types and processes involved in the immune response to cancer. How best to manipulate immune function to achieve improved outcomes in brain tumor patients is certain to remain a subject of keen interest, with innovative approaches such as Treg depletion through antibody administration, providing reason for optimism about the eventual benefits of immunotherapy in neuro-oncology practice.

C. David James,
Executive Editor, SNO

Reference

1. Wainwright DA, Sengupta S, Han Y, Lesniak MS. Thymus-derived rather than tumor-induced regulatory T cells predominate in brain tumors. *Neuro-Oncology* 13:1308–1323, 2011.