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Tumor Immunology

Elimination of regulatory T cells is essential for an effective vaccination with tumor lysate-pulsed dendritic cells in a murine glioma model

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Funded by:

- German Research Foundation; Grant Number: GR2089/1-1
- Dutch Cancer Society; Grant Number: KWF 2004-2893

KEYWORDS

glioma • TRP2 • tumor lysate • dendritic cell • regulatory T cell • CD25-depletion

ABSTRACT

Both melanoma and glioma cells are of neuroectodermal origin and share common tumor associated antigens. In this article, we report that the melanocyte differentiation antigen TRP2 (tyrosinase-related protein 2) is not predominately involved in the tumor rejection of a syngeneic murine glioma. Although GL261 glioma cells endogenously expressed TRP2 and were lysed by TRP2 specific cytotoxic T cells (CTLs) *in vitro*, vaccinations with TRP2 peptide-pulsed dendritic cells (DCs) could only induce minor antiglioma responses in a prophylactic setting and failed to work in a stringent setting where vaccine and tumor were administered on the same day. Further analysis revealed that TRP2 is not recognized by bulk CTLs after depletion of regulatory T cells which results in tumor rejections *in vivo*. In contrast to TRP2 peptide-pulsed DC, tumor lysate-pulsed DCs were more potent as a vaccine and completely protected mice from tumor outgrowth in a prophylactic setting. However, the vaccine efficacy of tumor lysate-pulsed DC was not sufficient to prevent the tumor outgrowth when tumors were inoculated the same day. In this case, Treg depletion before vaccination was essential to boost antiglioma immune responses leading to the rejection of 80% of the mice and long-term immunity. Therefore, we conclude that counteracting the immunosuppressive glioma tumor environment *via* depletion of regulatory T cells is a prerequisite for successful eradication of gliomas after targeting multiple tumor antigens by using tumor lysate-pulsed DCs as a vaccine in a more stringent setting. © 2007 Wiley-Liss, Inc.

Received: 19 June 2007; Accepted: 10 October 2007

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