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Immunology

Induction of Potent Antitumor Immunity by Intratumoral Injection of Interleukin 23–Transduced Dendritic Cells

Jinwei Hu<sup>1</sup>, Xiangpeng Yuan<sup>1</sup>, Maria L. Belladonna<sup>3</sup>, John M. Ong<sup>1</sup>, Sebastian Wachsmann-Hogiu<sup>2</sup>, Daniel L. Farkas<sup>2</sup>, Keith L. Black<sup>1</sup> and John S. Yu<sup>1</sup>

<sup>1</sup> Maxine Dunitz Neurosurgical Institute and <sup>2</sup> Department of Surgery, Cedars-Sinai Medical Center, Los Angeles, California and <sup>3</sup> Department of Experimental Medicine, University of Perugia, Perugia, Italy

Requests for reprints: John S. Yu, Maxine Dunitz Neurosurgical Institute, Cedars-Sinai Medical Center, Suite 800 East, 8631 West 3rd Street, Los Angeles, CA 90048. Phone: 310-423-0845; Fax: 310-423-0810; E-mail: [yuj@cshs.org](mailto:yuj@cshs.org).

Dendritic cells (DCs) are potent antigen-presenting cells that play a critical role in priming immune responses to tumor. Interleukin (IL)-23 can act directly on DC to promote immunogenic presentation of tumor peptide *in vitro*. Here, we evaluated the combination of bone marrow–derived DC and IL-23 on the induction of antitumor immunity in a mouse intracranial glioma model. DCs can be transduced by an adenoviral vector coding single-chain mouse IL-23 to express high levels of bioactive IL-23. Intratumoral implantation of IL-23–expressing DCs produced a protective effect on intracranial tumor–bearing mice. The mice consequently gained systemic immunity against the same tumor rechallenge. The protective effect of IL-23–expressing DCs was comparable with or even better than that of IL-12–expressing DCs. IL-23–transduced DC (DC-IL-23) treatment resulted in robust intratumoral CD8<sup>+</sup> and CD4<sup>+</sup> T-cell infiltration and induced a specific TH1-type response to the tumor in regional

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lymph nodes and spleen at levels greater than those of nontransduced DCs. Moreover, splenocytes from animals treated with DC-IL-23 showed heightened levels of specific CTL activity. *In vivo* lymphocyte depletion experiments showed that the antitumor immunity induced by DC-IL-23 was mainly dependent on CD8<sup>+</sup> T cells and that CD4<sup>+</sup> T cells and natural killer cells were also involved. In summary, i.t. injection of DC-IL-23 resulted in significant and effective systemic antitumor immunity in intracranial tumor–bearing mice. These findings suggest a new approach to induce potent tumor-specific immunity to intracranial tumors. This approach may have therapeutic potential for treating human glioma. (Cancer Res 2006; 66(17): 8887-96)

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