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JOURNAL OF Immunotherapy

In Vivo Vaccination With Tumor Cell Lysate Plus CpG Oligodeoxynucleotides Eradicates Murine Glioblastoma.

Basic Studies

Journal of Immunotherapy. 30(8):789-797, November/December 2007.
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Abstract:
Dendritic cell (DC) vaccines have shown antitumor activity in experimental glioma models and in human glioma patients. The typical approach has been to generate the vaccine ex vivo, by pulsing DCs with tumor lysate or peptides, then administering the DCs back into the patient. This process requires significant expertise and expenses in DC generation. Immature DCs which present antigens to T cells in the absence of appropriate costimulatory signals can lead to induction of immune tolerance. Recent studies have shown that coadministration of toll-like receptor 9 agonists, CpG oligodeoxynucleotides, can promote DC vaccines to break immune tolerance to tumor antigens. We investigated the therapeutic efficacy of in vivo DC activation, by directly administering glioma cell lysate with CpG oligodeoxynucleotides (CpG/lysate), in glioma-bearing mice. Subcutaneous vaccination with CpG/lysate induced a significant increase ($P<0.05$) in the number of total T cells and activated DCs in lymph nodes draining the vaccination site as compared to mice treated with CpG or tumor lysate alone. Mice vaccinated with CpG/lysate exhibited over 2 times greater median survival than mice in the control groups ($P<0.05$). Up to 55% of mice vaccinated with CpG/lysate were rendered tumor-free as assessed by survival and bioluminescent imaging. Splenocytes taken from mice vaccinated with CpG/lysate elaborated significantly more IFN-[gamma] production and displayed greater tumor cell lysis activity compared with the control groups ($P<0.05$). These results suggest direct vaccination with CpG/lysate provides an alternative and effective approach to induce host antitumor immunity and warrants clinical investigation in the immunotherapy of cancer.