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Development of a DNA vaccine for treatment of an intracerebral tumor

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Abstract

Antigenic differences between normal and malignant cells of the cancer patient form the rationale for clinical immunotherapeutic strategies. Because the antigenic phenotype of neoplastic cells varies widely among different cells within the same malignant cell-population, immunization with a vaccine that stimulates immunity to the broad array of tumor antigens expressed by the cancer cells is likely to be more efficacious than immunization with a vaccine for a single antigen. A vaccine prepared by transfer of DNA from the tumor into a highly immunogenic cell line can encompass the array of tumor antigens that characterize the patient's neoplasm. Poorly immunogenic tumor antigens, characteristic of malignant cells, can become strongly antigenic if they are expressed by highly immunogenic cells. A DNA-based vaccine was prepared by transfer of genomic DNA from a breast cancer that arose spontaneously in a C3H/He mouse into a highly immunogenic mouse fibroblast cell line, where genes specifying tumor-antigens were expressed. The fibroblasts were modified in advance of DNA-transfer to secrete an immune augmenting cytokine and to express allogeneic MHC class I-determinants. In an animal model of breast cancer metastatic to the brain, introduction of the vaccine directly into the tumor bed stimulated a systemic cellular anti-tumor immune response measured by two independent *in vitro* assays and prolonged the lives of the tumor-bearing mice. Furthermore, using antibodies against the various T-cell subsets, it was determined that the systemic cellular anti-tumor immunity was mediated by $CD8^+$, $CD4^+$ and NK/LAK cells. In addition an enrichment strategy has also been developed to increase the proportion of immunotherapeutic cells in the vaccine which has resulted in the development of enhanced anti-tumor immunity. Finally regulatory T cells ($CD4^+CD25^+$Fox $p3^+$-positive) were found to be relatively deficient in the spleen cells from the tumor-bearing mice injected intracerebrally with the enriched vaccine. The application of DNA-based genomic vaccines for the treatment of a variety of brain tumors is being explored.

Biography:

Terry Lichtor completed his MD and PhD degree at the University of Chicago. Dr. Lichtor currently is a practicing neurosurgeon with research interests including the development of immunotherapeutic strategies for treatment of brain tumors, passive immunotherapy for treatment of Alzheimer's disease and the development and application of a non-invasive MRI technique for measurement of intracranial pressure and brain compliance.

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