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Abstract

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Project Title: T CELL IMMUNITY TO POLYOMA VIRUS-INDUCED TUMORS

Abstract: DESCRIPTION (Adapted from the Applicant's Abstract): Cytotoxic T lymphocytes (CTL) play a role in host defense against neoplastic cells. Analysis of their immunoregulation and effector mechanism is limited by (a) unknown tumor- specific antigens, (b) experimental tumor models that do not reflect "naturally-occurring" neoplastic disease and (c) polyclonal CTL responses. Polyoma virus is a natural mouse pathogen capable of inducing a diverse variety of epithelial and mesenchymal cell-derived tumors which are the same cell types giving rise to the majority of human tumors. Inbred mouse strains vary in their susceptibility to polyoma tumorigenesis. Resistance to polyoma tumors is mediated by T-cells, with no apparent contribution from antiviral antibody. A subset of H-2k mouse strains that carry an endogenous superantigen encoded by the Mtv-7 provirus are susceptible to polyoma tumorigenicity. Polyoma-specific CD8+ CTL in the resistant H-2k Mtv-7- mice appear to express Vb6-T-cell receptor (TCR), which are deleted in H-2k Mtv-7+ mice. The principal investigator will test the hypothesis that immunity to polyoma tumors is dominated by an oligoclonal CD8+Vb6+ CTL response directed to a single viral epitope. Aim 1 is to determine whether polyoma-specific CD8+Vb6+ CTL protect H-2k mice from polyoma tumors. The investigators have isolated anti-polyoma CTL clones from resistant H-2k mice and found them to be CD8+Vb6+. These CTL clones will enable the principal investigator to determine the antigenic diversity of polyoma tumors. The final aim is to compare TCR sequences of CD8+Vb6+ CTL lines which recognize the same viral peptide-MHC complexes to determine the extent of conservation of the other TCR domains, particularly the CDR3 regions. The availability of an oligoclonal, monospecific anti-tumor CTL response in vivo will permit detailed investigation of the induction, immunoregulation and tumoricidal mechanism(s) of this T-cell subset, and thereby facilitate development of immunotherapeutic strategies to neoplastic disease.

Thesaurus Terms:

Polyomavirus, cytotoxic T lymphocyte, host organism interaction, immunoregulation, microorganism immunology, neoplasm /cancer, neoplasm /cancer immunology, virus disease, virus related neoplasm /cancer
CD8 molecule, T cell receptor, cell population study, cell transplantation, disease /disorder

model, neoplasm /cancer immunotherapy, nonhuman therapy evaluation, protein structure
function, virus antigen
laboratory mouse, tissue /cell culture, transgenic animal

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