CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160188

Project Title:
Regulation of infiltration and function of tumor-resident CD8 T cells by IL-15

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Cancer patients vary considerably in their responses to cancer therapies. Recent studies have found that patients with tumors containing cytolytic T cells have significantly better clinical outcomes. This provides evidence that one's own cytolytic T cells are capable of effective tumor clearance. Unfortunately, it is not clear how sufficient numbers of T cells are generated in tumors. Excitingly, the presence of the T cell growth factor, Interleukin-15 (IL-15) within tumors has recently been shown to be associated with increased T cell numbers within tumor, increased patient survival, and lower rate of relapse. Overall, this is compelling evidence that IL-15 is critical for generating tumor-infiltrating T cells. But how IL-15 is regulated within the tumor and its exact functions on those T cells is not known. Based on our expertise in the area and our prior research, we hypothesize that IL-15 mediates multiple important functions in tumor-infiltrating T cells that include attracting T cells into the tumor as well as stimulating their growth, survival, and tumor-killing activity. Our proposed studies will identify the precise roles of IL-15 in the tumors using elegant mouse models that allow dissection of immune cell activities in ways not feasible using cultured human cells. Also, our data suggest a unique, potent form IL-15 is expressed within the tumor by immune stimulation. Our proposed studies will confirm this unique control of IL-15 thereby identifying novel approaches to enhance IL-15 responses within the tumor. These studies revealing the mechanisms that mediate cytolytic T cell infiltration and their growth is significant to multiple cancers as studies have found that immune cell infiltration is an important prognostic criterion in colorectal cancer, melanoma, breast, and brain cancer. Overall, this research will lead to knowledge that can be used to identify novel therapeutic strategies to enhance effective cytolytic T cell responses against tumors.