CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120108

Project Title:
Improving on Anti-CTLA-4 Therapy

Award Mechanism:
Individual Investigator

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

Lay Summary:

Successful immunotherapy for the treatment of cancer will require agents that target mechanisms responsible for regulating T cell responses. Previously, an antibody that targets an inhibitory molecule on T cells known as cytotoxic lymphocyte antigen-4 (CTLA-4) was found to enhance anti-tumor responses in mouse models of cancer. Subsequently, anti-CTLA-4 antibody was tested in clinical trials in cancer patients. Since the antibody targets a T cell specific molecule, and not a tumor specific molecule, many different types of cancer can potentially be treated with anti-CTLA-4. The first Phase III clinical trial in patients with metastatic melanoma was recently completed and showed a survival benefit for patients who received anti-CTLA-4 therapy. The FDA approved anti-CTLA-4 for the treatment of patients with melanoma on March 25, 2011. Anti-CTLA-4 is also being tested in patients with prostate and lung cancer in additional clinical trials. Although anti-CTLA-4 has been successful in treating some patients, it is not effective in all patients. Anti-CTLA-4 provides benefit, consisting of complete or partial regression of disease or stability of disease for 6 months or greater, to approximately 20-30% of treated patients. In order to improve the benefit of anti-CTLA-4 therapy, we propose to test combination treatment with anti-CTLA-4 and agents that target another T cell specific molecule known as inducible costimulator (ICOS). Our preliminary data in mouse models indicate that combination therapy with anti-CTLA-4 plus agents that target the ICOS pathway improves anti-tumor responses and survival. We also propose to define genetic pathways that predispose to successful anti-tumor responses with anti-CTLA-4 thereby allowing for appropriate selection of patients to receive treatment. Our studies will generate data that can be used to potentially improve the clinical efficacy of anti-CTLA-4 therapy.