CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP150316

Project Title:
T-cell activating immunotherapy for indolent B-cell malignancies

Award Mechanism:
Individual Investigator

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

Lay Summary:

Chronic lymphocytic leukemia (CLL) and follicular lymphoma (FL) are the most common slow-growing B-cell lymphomas worldwide that are currently incurable. The observation of long-term remissions with allogeneic stem cell transplantation or genetically modified T-cell therapy suggested that agents that activate T cells against the tumor could be highly effective therapies for these patients. In the current proposal, we will test three novel strategies to activate T cells. These approaches will be evaluated in a mouse model that mimics human CLL. Therefore, following completion of this project, we expect to translate our findings for testing in patients with CLL, FL, and other B-cell lymphomas.

In Aim 1, we will develop a novel vaccine formulation using a novel tumor antigen called TCL1 that was recently identified by us. In Aim 2, we will combine the TCL1 vaccine with agents called immune checkpoint inhibitors that block mechanisms that help the tumor evade the immune system. In Aim 3, we will combine the vaccine and immune checkpoint inhibitors with a drug called ibrutinib that causes tumor cell death by blocking an enzyme called BTK. In addition, ibrutinib has also been shown to block another enzyme called ITK, which in turn leads to activation of T cells against the tumor. Therefore, the combination of these three agents is expected to activate T cells against the tumor by three complementary mechanisms.

In the long term, this combination approach may potentially improve remission duration and chance of cure without increasing toxicity in these patients. Development of such non-toxic approaches is highly desirable for these patients as most of them are elderly. Although we will test these strategies in a CLL mouse model, the results are broadly applicable because 1) TCL1 may serve as vaccine candidate for CLL, FL, and other B-cell lymphomas, 2) immune checkpoints are similar between these tumors, and 3) ibrutinib is effective in most B-cell lymphomas.