CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140468

Project Title:
Targeting of Chronic Lymphocytic Leukemia by Designer T Cells

Award Mechanism:
Individual Investigator

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

Lay Summary:

Immunotherapy was named as Breakthrough of the Year for 2013. One reason for this accolade is the spectacular clinical responses achieved after infusion of tumor-specific T cells in some patients with leukemias and lymphomas arising from cancerous B cells. The T cells were rendered specific for the molecule CD19, which is expressed on most malignant B cells. This was achieved through the insertion of a chimeric antigen receptor (CAR) that signals genetically modified T cells to kill upon docking with CD19. Infusions of CD19-specific CAR+ T cells resulted in eradication of tumor cells that had otherwise been refractory to treatment with conventional therapies. Our immunotherapy program at MD Anderson Cancer Center has successfully infused CD19-specific T cells after hematopoietic stem-cell transplantation (HSCT) resulting in complete responses in patients with leukemias and lymphomas. However, these recipients suffer from damage to their normal B cells thus compromising their immune system. This was expected as CAR+ T cells will not distinguish between targeting CD19 expressed on malignant versus normal B cells. Therefore, we developed T cells with alternative specificity for a molecule called ROR1 (receptor tyrosine kinase-like orphan receptor 1) that is only found on cancerous B cells and especially those malignant B cells that give rise to chronic lymphocytic leukemia (CLL). We seek to adapt our existing infrastructure to target ROR1 on CLL rather than CD19 on CLL with the anticipation this will improve safety. In addition to testing, for the first time, the ability of ROR1-specific CAR+ T cells to safely target CLL, we propose a trial that advances the field of immunotherapy by infusing T cells after chemotherapy, thereby avoiding the complications and expense of HSCT. In summary, CPRIT will fund next-generation studies seeking to evaluate an investigational therapy for CLL and paving the way for infusing CAR+ T cells to treat ROR1+ malignancies other than CLL.