CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
DP150056

Project Title:
New antibody therapy for treating leukemia

Award Mechanism:
Bridging the Gap: Early Translational Research Awards

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Acute myeloid leukemia (AML) is the most common acute leukemia affecting adults. Despite continuous treatment, the majority of the patients relapse within 5 years. Leukemia stem cells (LSCs) may be responsible for the relapse of disease following a remission brought about by conventional chemotherapy, and new molecular targets and therapeutic approaches need to be identified to effectively inhibit LSC activity. Our research has indicated that several members of the inhibitory receptor LILRB family supports the self-renewal and survival of human leukemia cells. We found that several members of the LILRB family are highly expressed on AML cells and their expression negatively correlates with the overall survival of human AML patients. LILRB+ primary human AML cells are enriched for AML stem cell (AML-SC) activity. Interestingly, the deletion of individual LILRB in the mouse does not cause defects in normal hematopoiesis. In contrast, the disruption of several LILRB in human and mouse leukemia cells blocked leukemia development. Moreover, inhibition of LILRB stimulates body immunity and indirectly boosts anti-tumor effects. Therefore LILRB signaling represents an ideal target for treating AML. Most importantly, we developed an anti-LILRB monoclonal antibody that strikingly blocks human AML development in various xenografted mouse models. Here, we propose to develop therapeutic anti-LILRBs for clinical applications. In Aim 1, we will develop additional anti-LILRB mAbs that inhibit human AML development, and determine the physical, biochemical, and functional properties of neutralizing antibodies. In Aim 2, we will develop humanized anti-LILRB antibodies that can be used in the future clinical trials. In Aim 3, we will initiate early stage preclinical development of the lead antibody. Our proposed blockade of LILRB signaling may prove to be an effective strategy for elimination of leukemia stem cells and lead to complete remission of patients.