CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180435

Project Title:
Fasting-induced inhibition of leukemia development

Award Mechanism:
Individual Investigator

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

Lay Summary:

Acute lymphoblastic leukemia (ALL), which includes B cell and T cell subtypes (B-ALL and T-ALL), is the most common form of cancer in children and also occurs in adults. Although treatment of pediatric ALL is highly effective, a sizeable number of patients are non-responders. The prognosis for adult ALL patients is significantly worse than for pediatric ALL patients. Additionally, some types of ALL have a much poorer prognosis than others. New therapeutic targets and approaches are needed to effectively treat ALL. Using mouse tumor models, we demonstrated that fasting alone robustly inhibits the development of both B-ALL and T-ALL, but not acute myeloid leukemia (AML). Mechanistically, we found that a low level of a protein - leptin receptor (LepR) - is essential for the development of ALL, and that fasting inhibits ALL development by increasing LepR and its downstream proteins. Moreover, expression of LepR signaling-related genes correlated well with the prognosis of B-ALL patients, and fasting effectively inhibited B-ALL growth in an animal model. We hypothesize that the effects of fasting on tumor growth are cancer-type dependent, and elavation of LepR expression can effectively block devlopment of both B-ALL and T-ALL. We proposed three specific aims to test this hypothesis. In Aim 1, we will clarify the contributions of oncogene driver and cells of origin to the distinct effects of fasting on different types of leukemia. In Aim 2, we will test whether potential fasting-mimicking molecules that we identified act as an effective alternative for the antitumor effects of fasting in the treatment of ALL. Finally, we will determine whether fasting can inhibit human ALL development using patient samples in Aim 3. Our study will lead to development of novel fasting and fasting-mimicking strategies for treating human leukemia.