CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180073

Project Title:
Myeloid support of refractory and aggressive T-ALL at distinct tumor sites

Award Mechanism:
Individual Investigator Research Awards for Cancer in Children and Adolescents

Principal Investigator:
Ehrlich, Lauren

Entity:
The University of Texas at Austin

Lay Summary:

Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy, with the T cell subtype (T-ALL) representing ~15% of pediatric ALL cases. Current chemotherapeutic regimens have improved five-year event-free survival rates to ~80% in children. However, these therapies are toxic, often resulting in life-long morbidities. Furthermore, prognosis is dismal for ~20% of patients who relapse or fail to respond to chemotherapy, as there are no alternative treatments. Therefore, there is an unmet clinical need to develop improved T-ALL therapies.

Despite the fact that molecular changes driving T-ALL have been identified, this knowledge has not yet translated into successful therapeutics. Tumor growth requires not only these molecular changes in tumor cells themselves, but also permissive interactions with support cells in the tumor microenvironment. Despite mutations activating survival and growth programs, T-ALL cells cannot survive on their own in tissue culture. Thus, T-ALL cells must receive extrinsic signals in the body to promote tumor survival. Notably, our lab has recently found that myeloid cells are capable of directly supporting T-ALL growth and survival, suggesting they might be viable therapeutic targets. Thus, we propose to use mouse models and patient samples to determine which myeloid cells and associated signals support multiple subtypes of T-ALL, including aggressive tumors. Because T-ALL disseminates to multiple organs in the body, we will also determine which myeloid cells at multiple tumor sites support tumor growth. Finally, because relapse is a pressing clinical problem, we will determine whether myeloid cells promote survival and growth of chemo-resistant T-ALL cells, which induce relapse. By identifying the myeloid cell types and associated signals broadly required for growth of primary and chemo-resistant T-ALL throughout the body, these studies will identify novel therapeutic targets that could lead to improved patient outcomes.