CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100429

Project Title:
Regulation of Ash2L and MLL oncoproteins by PRMT-mediated methylation in normal cells and acute leukemias

Award Mechanism:
Individual Investigator

Principal Investigator:
Dent, Sharon

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

Lay Summary:

The mixed lineage leukemia (MLL) gene is disrupted by chromosomal translocations in > 50% of acute leukemias in infants and ~10% of acute myeloid leukemias (AMLs) in children and adults. These MLL mutations are linked to very poor patient prognosis. The MLL protein is required for normal blood cell formation, and it functions as an enzyme that changes the way DNA is folded inside of the cell nucleus. This function governs gene expression during blood development, and it is disrupted by the MLL mutations that occur in leukemias. MLL associates with other proteins to achieve its functions in normal cells. One of these proteins, Ash2L, also has oncogenic properties. How Ash2L is regulated, or how it effects MLL activity, is not known. We recently discovered that Ash2L is itself methylated by another kind of enzyme family, the protein arginine methyltransferases (PRMTs). Proposed studies will test our hypothesis that PRMTs modify Ash2L to regulate MLL functions in normal cells and during oncogenesis. Proposed studies will define the significance of PRMT-mediated methylation of Ash2L in regards to MLL activity, cellular transformation, and tumor formation. In the long term, these studies may identify new targets for small-molecule based therapies directed towards PRMTs or Ash2L to improve patient survival.