

Bankhead-Coley Cancer Research Program

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*2007 Program
New Investigator (3-year project)*

Project Title: The Mechanisms of TAL1/SCL-Induced Leukemogenesis

Project Summary: Leukemia is a severe malignant blood disease. Activation of the TAL1/SCL (for stem cell leukemia) gene, a transcription factor required for normal blood cell development, has been frequently associated with a specific form of leukemia called T-cell acute lymphoblastic leukemia (T-ALL). The disease affects children and young adults; there are very few effective treatments for this disease, and most attempted treatments have a high risk of failure. Our preliminary results indicated that the function of TAL1 in blood cell development is modulated by its binding partners, called co-regulators. To better understand the function of TAL1 protein in blood cell development and how its function is modulated by the interacting partners, we purified and isolated the TAL1-associated proteins. We found that two TAL1 interacting proteins contain specific enzymatic activities that add or remove a methyl group to a group of specific DNA interacting proteins termed histones, which have been shown to have an important function in regulating chromatin structure and gene expression. In this grant, we are investigating how these histone-modifying enzymes regulate TAL1-directed gene expression. Furthermore, this study will explore how the TAL1-associated histone-modifying enzymes alter TAL1 function in blood cell growth and differentiation and whether inappropriate TAL1-co-regulators' interactions influence leukemia development. Given that the activation of the TAL1 gene is frequently accompanied by the formation of T-cell leukemia, these studies will provide a new insight into the development of TAL1-induced leukemia. This information will eventually aid the design of new therapeutic approaches to treat blood diseases such as leukemia.