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2004 Program
New Investigator (3-year project)

Project Title: Mechanism of Down-regulation of XIAP Induced by Purine Analogues

Project Summary: Cigarette smoking is associated with an approximately 50% increase in leukemia risk. Longtime cigarette smokers have a significantly elevated risk for all leukemias, chronic myelogenous leukemias, and chronic lymphocytic leukemias. In addition, passive exposure during childhood to a parent's smoking increases a child's risk of leukemia and lymphoma during adulthood. Recent studies suggest that cigarette smoke has a deleterious effect on the survival of acute myeloid leukemia (AML) by shortening complete remission duration and subsequent survival. Despite progress in the field of leukemia, the prognosis of Adult T-cell leukemia (ATL) remains poor, mainly because of its resistance to conventional, as well as high-dose, chemotherapy and resistance to cellular death (apoptosis). Thus, the need for drug(s) that kills these cells is apparent. Understanding the mechanisms of roscovitine-induced apoptosis and identifying the alternate survival pathway in MT-2 cells will facilitate the design of novel therapeutics against leukemia and human cancers. This proposal focuses on the mechanisms of chemoresistance of cancers including leukemias, specifically relating to defects in the apoptosis program that is induced by anticancer drugs.