Award ID:
RP170074

Project Title:
Molecular Epidemiology And Somatic Alterations Driving Acute Lymphoblastic Leukemia In Down Syndrome

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

Principal Investigator:
Rabin, Karen

Entity:
Baylor College of Medicine

Lay Summary:

Down syndrome results from an extra copy of chromosome 21 and is one of the most common genetic syndromes. Children with Down syndrome have a 10-20 fold increased risk of developing acute lymphoblastic leukemia (ALL), the most common childhood cancer. Even though the success rate today for treating childhood leukemia is high, children with Down syndrome and ALL suffer poorer survival due to increased risk of both relapse and fatal treatment-related complications. The reason for the increased risk of ALL in children with Down syndrome is unknown. Several recent studies have identified genetic risk factors associated with an increased risk of ALL in the general population. In this project, we seek to determine genetic risk factors responsible for the increased risk of ALL in children with Down syndrome. We have preliminary evidence of an increased risk associated with a gene called IKZF1. The goals of our proposal are to explain how variant forms of this gene and others lead to development of ALL in children with Down syndrome. We will do this by studying genetic changes in patient samples, cell lines, and in a mouse model of Down syndrome in which we can genetically alter the cells of the bone marrow and then observe whether these alterations cause the mice to develop leukemia. This project will address the important question of why children with Down syndrome have an increased risk of ALL. We expect to discover genetic changes which will allow us to develop improved treatments for these children, who suffer more severe side effects and poorer survival with current standard chemotherapy. We may also gain knowledge that is broadly applicable to other patients and other types of cancer as well.