



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP120076

Project Title:  
Novel mechanisms leading to telomere dysfunction and cancer  
predisposition

Award Mechanism:  
Individual Investigator

Principal Investigator:  
Bertuch, Alison A

Entity:  
Baylor College of Medicine

### Lay Summary:

Telomeres are protective structures at ends of our chromosomes. In dyskeratosis congenita (DC), people lack the ability to maintain their telomeres properly due to a mutation in one of several genes that guide cells in making telomere maintenance factors. As a result, people with DC have unstable chromosomes. These unstable chromosomes lead to other genetic changes that drive the development of cancer. Consequently, people with DC have a lot of cancer. For example, about half of those surviving to their mid 40's will have or had cancer, particularly of the tongue or leukemia. Although a bone marrow transplant can prevent the development of leukemia, there are no therapies that can prevent the development of the other cancers in DC patients. We want to develop ways to stabilize telomeres in people with DC so they can lead healthy lives. Hampering our effort is the fact that the gene mutated is known in only about 50% of cases. In this research, we will identify the other gene mutations that can result in DC. To do this, we have determined every mutation present in two children with DC. Now, we will prioritize the mutations and determine which one causes their disease. We are also studying Familial Platelet Disorder with Propensity to Myeloid Leukemia (FPD/AML), a genetic syndrome that also frequently results in leukemia. Although it is known that a gene called RUNX1 is mutated in FPD/AML patients, why leukemia occurs isn't clear. We recently found that the telomere lengths in a child with FPD/AML were very short, as seen in DC. This led us to think that maybe very short telomeres are common in FPD/AML, and they might contribute to the development of leukemia (as in DC). Therefore, we will determine whether short telomeres are common in FPD/AML, and, if so, if this is due to a reduction in certain telomere maintenance factors. We will also determine if some people who are thought to have a condition resembling DC may in fact have mutations in RUNX1 and FPD/AML.