CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140500

Project Title:
Toward the Cure of Myelodysplastic Syndrome: Interfering With Innate Immunity Alterations in Human and Mouse Systems

Award Mechanism:
Individual Investigator

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

Lay Summary:

The myelosdysplastic syndromes (MDS) are a group of leukemias that affect older individuals. This disease results in progressive anemia, low platelets and increased risk of infections and transformation to acute myelogenous leukemia. At the present time there is no cure for this disease, except for the rare patient that is a candidate for transplantation. Most patients will eventually die from complications of MDS. A decade ago, several new agents with activity in MDS were developed. These included the hypomethylating agents and lenalidomide. Despite this progress, we have not been able to develop any further therapies for these patients in the last five years and their prognosis remains dismal, particularly for those not benefitting from hypomethylating agents. Research in this disease, with an objective to develop new therapeutic agents, is limited by lack of complete understanding of the molecular bases of the disease, lack of cell lines and until recently access to representative animal models. Our group has observed that alterations in immune system and inflammation contribute to MDS and resistance to hypomethylating agents. More recently, we have developed what we think is the most representative mouse model of MDS. Here we propose the first systematic analysis of innate immune/inflammatory alterations in MDS. This will be performed both in a large cohorts of human MDS patients and in mouse models that carry different MDS-associate molecular lesions. We propose to perform: #1) the first global analysis of key innate immune/inflammatory alterations in MDS; #2) study their interaction with other known molecular lesions in MDS; #3) study how innate immunity/inflammation alters blood formation; and #4) evaluation inhibitors of inflammation as therapy for MDS. We believe that the results from this proposal will significantly improve our understanding of MDS and will result in the development of new therapeutic targets for MDS.