



CANCER PREVENTION & RESEARCH
INSTITUTE OF TEXAS

Award ID:
RP180769

Project Title:
A Novel Anti-BCR-ABL Approach for Leukemia Therapy

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Rao, Hai

Entity:
The University of Texas Health Science Center at San Antonio

Lay Summary:

Our long-term goal is to elucidate the function of proteasome-mediated protein degradation in health and diseases. The goal of this proposal is to develop small molecules that would promote rapid degradation of BCR-ABL, a key factor in chronic myelogenous leukemia (CML) and acute lymphocytic leukemia (ALL). Specifically, we will design and evaluate novel compounds that exploit the cell's own degradation pathway to eliminate the BCR-ABL protein kinase. Small molecules designed will bring BCR-ABL to the proteasome for destruction selectively. The study would lead to new anti-BCR-ABL drugs to CML and ALL patients.

Our destruction-based approach significantly reduces the risk that acquired secondary mutations/defects develop over time and also phenotypes are reversed. This modified method is orthogonal to other approaches and overcomes limitations of existing strategies with significantly improved properties, likely leading to broader application, better efficacy and control. Our approach requires only transient drug-target binding without the need of direct inhibition of substrate activity. Since this strategy could be easily adapted to other cancers, the work proposed here may lead to a new anti-cancer approach in general and could have a major impact on existing targeted therapies.