CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120867

Project Title:
An NMR resource for enhancing the discovery of novel cancer therapeutics at the University of Texas Health Science Center at San Antonio

Award Mechanism:
Shared Instrumentation Awards

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

Lay Summary:

Standard chemotherapeutic agents function by indiscriminately killing rapidly growing cells, which are both cancer cells and normal cells. In contrast, targeted therapies block molecules that act on the specific pathways and processes used by cancer cells to grow and divide - they are less toxic than chemotherapies and offer many benefits, including enhanced quality of life and improved safety. Unfortunately, the discovery of novel targeted therapies remains stubbornly slow. The goal of this proposal is to implement an innovative new structure-based approach for drug discovery, known as fragment-based drug discovery or FBDD. FBDD uses a spectroscopic technique called NMR to identify drug-like chemical pieces (fragments) that interact with cancer targets at sites critical for function. Although individual fragments tend to interact weakly and are not therapeutically effective, the site-directed information provided by NMR for these weakly binding fragments is exceptionally valuable. This information guides the design of larger molecules that combine relevant features and form strong interactions with the target at the precise position that is expected to have a therapeutic effect. This circumvents several of the obstacles that hinder drug development using conventional methods and is being widely embraced in both industry and academia. An FDA-approved drug for treating malignant melanoma was recently developed by FBDD - the development cycle took only 6 years, compared to the average of 16 years for drugs developed by other methods. The instrumentation requested in this proposal will provide essential enhancements needed to enable FBDD using our NMR spectrometer. The enhanced NMR capabilities will be used to develop novel targeted therapies against several established cancer targets, including heat shock proteins, growth factors, matrix proteinases, and others that have essential roles in promoting the growth and metastasis of cancer cells.