



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
DP150093

Project Title:
Targeting an Elusive Foe: Development of K-Ras Inhibitors

Award Mechanism:
Bridging the Gap: Early Translational Research Awards

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

Lay Summary:

The United States National Cancer Institute estimates that there will be close to 1.7 million new cancer cases and 585,720 cancer-related deaths in 2014. Activating mutations of a key enzyme in humans, called K-Ras, are known to occur in about 25% of all human cancers. Combining these two statistics, we estimate that about 400,000 US citizens will be affected by one or another form of K-Ras-related cancers this year alone. Currently, there are no drugs that can directly act on mutated K-Ras to stop its cancer-causing activities. As a result, K-Ras-related cancers remain untreatable, including some of the deadliest such as pancreatic cancer. In fact, the prognosis of K-Ras-associated cancers is often dismal. Clearly, anti-K-Ras medications would save millions of lives and have a huge market potential. We have decided to attack this elusive foe by assembling a team of experts from diverse fields and adopting a strategy that combines theory, physics-based computations, high-end biophysical, biochemical and biological experiments. Our goal is to rationally design and develop compounds that directly attack misbehaving mutant K-Ras. Specially, we plan to perform additional characterization of compounds that have exhibited promising therapeutic potential in our initial studies, and to generate and optimize new leads until a clinically viable developmental drug is found. Because we build on innovative conceptual and technical capabilities that our team has developed over several years, we have the opportunity few others possess to overcome many of the historical challenges that have prevented direct inhibition of K-Ras. Thus, the proposed work will advance laboratory discoveries to clinically and commercially viable outcomes, thereby breaking new grounds in cancer therapy with profound benefit to millions of people suffering from the many diverse Ras-related carcinomas.