CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
R1006

Project Title:
Recruitment of First-Time, Tenure-Track Faculty Members

Award Mechanism:
Recruitment of First-Time, Tenure-Track Faculty Members

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

Lay Summary:

While some cancers exhibit characteristics of a monolithic disease, the reality is that the vast majority are highly heterogeneous. For example, if a breast cancer tumor is driven by HER2, a protein whose activation leads to cell growth, there is only a 20-30% chance that that patient will respond to Herceptin, a drug that blocks HER2 activation. In this case, even though the same protein drives every tumor, differences in contributions from secondary proteins lead to variations in drug response. To address this, we need a deeper understanding of how growth signals travel from protein to protein to improve clinical treatment. Unfortunately, signaling pathways are complex. Proteins can interact with many partners and drive diverse biological processes. An example is Ras, which controls cell proliferation and fate through interactions with other proteins such as Raf kinase, RalGEF, and PI3K. These critical interactions mediate cell growth, and the genes are frequent targets of mutation in cancer. Because Ras itself has proven difficult to target with drugs, there is great interest in identifying related proteins in this cascade that may represent better therapeutic targets. To better understand the Ras pathway, I developed a novel methodology in my postdoctoral studies to tease apart the pathway into individual components of activity, called the modules of the pathway. This simplified the pathway into individual units that could be linked to outcomes, such as survival in lung adenocarcinomas. I am currently investigating how each module contributes to tumor development, as well as identifying the proteins that drive those activities. In sum, the overarching hypothesis for my investigation is that a deeper understanding of the structure of signaling pathways will result in an improved ability to pinpoint the molecular mechanisms that drive individual diseases, and thus, form the foundation of a rational strategy for selecting clinical treatments.