CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140553

Project Title:
Translational Discovery of Resistance Genes and Cancer Gene Functions

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

Most cancer deaths result not from cancer itself but from cancers that have evolved resistance to our chemotherapies. Resistance is caused by mutations in genes. Some of these mutations are present in tumors before chemotherapy is undertaken, making particular therapies doomed to failure in some tumors before they are started. If we could distinguish which tumors were already resistant to specific drugs, we could give the right drugs for each patient. Ineffective drugs allow development of more resistances to additional therapies as cancers continue to grow, mutate and evolve. The goal of this project is to identify which genes cause resistance to one of the most commonly used anti-cancer drugs, 5-FU, so that in future, we will be able to check these genes in tumors in patients before treatment begins, and then customize treatments to avoid drugs that cannot work on tumors with particular mutations. This would improve the chance of successful cancer eradication dramatically. The approach to finding resistance mutations used in this project is unique in that the researchers will harvest two preexisting resources that allow the discovery of resistance genes much faster than usual: first, the fact that even simple organisms like bacteria have versions of the human resistance genes that work similarly. Second, many resistance genes has been discovered in E. coli bacteria that indicate which human genes are likely to cause resistance to 5-FU. This project decodes the gene sequences of those human resistance candidates in specimens of resistant tumors to determine whether those genes really are the culprits 5-FU resistance in cancer. The bacterial resource is a tool that tells the investigators which human genes to investigate; then the investigation is done in human cancer tissue and cancer-model cell lines. The resistance genes discovered will provide a map for future testing of patients' tumors before treatment to diagnose which tumors will respond to which drugs.