Award ID:
RP120046

Project Title:
Mining the oncogenome: Functional genomics approaches for screening mutation drivers of pancreatic ductal adenocarcinoma.

Award Mechanism:
Individual Investigator

Principal Investigator:
Scott, Kenneth L

Entity:
Baylor College of Medicine

Lay Summary:

A major emphasis in cancer research is focused on identifying early cancer indicators, or biomarkers, and other genes directly responsible for causing tumors that may serve as targets for new cancer therapies. Large-scale efforts toward sequencing the DNA of tumors have uncovered the enormous complexity of cancer genomes. Using such knowledge in the clinic will require new strategies to assess the functional significance of individual DNA mutations in genes. Recently we developed a screening platform that permits the over-expression of large numbers of genes to assess their ability to promote cancer. This approach successfully identified multiple melanoma genes whose expression drives metastasis and designates tumors that are most aggressive. The goal of this proposal is to use an expanded version of this screening platform, which now consists of over 18,000 human genes, to identify new DNA mutations that influence progression of pancreas cancer. We will collaborate with the Baylor College of Medicine Human Genome Sequencing Center to assemble a high confidence list of over 300 candidate mutations identified in the genomes of pancreas tumors. We will use an innovative strategy to model these mutations into our large gene collection, and the resulting mutant genes will be used in genetic screens to identify and validate those mutations that promote tumor formation and metastasis. In summary, our goal is to employ an innovative over-expression platform enabling functional screening of DNA mutations found in pancreas tumors. These studies promise to make a major impact on cancer gene discovery, as the insight and technology gained from this project will be widely applicable to research involving many cancer types. In addition, our studies may uncover new detection biomarkers and drug targets critically needed for patients suffering from pancreas cancer who currently have no other effective treatment options.