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Targeting cancer specific fusion genes

Chromosome rearrangement is one of the hallmarks of human malignancies. Recently, we discovered a panel of fusion genes that are widely present in a variety of human cancers. One of these fusion genes called *MAN2A1-FER* has shown cancer driver activity in multiple malignancies both in animals and human. Other fusion genes also appear to play critical roles in the human cancer development. Due to high frequency of these fusion genes in cancer samples, targeting at these fusion genes may achieve effective control of human cancers. In this study, we develop a genome targeting strategy to insert an artificial gene device into the chromosomal breakpoints of cancer genome using CRISPR-cas9 genome editing system. Genome targeting at the chromosomal breakpoint of fusion genes produced high rate of insertion of suicide gene into the cancer genome, while had minimal impact on cells that do not contain the fusion gene breakpoint. Treatment of animals xenografted with cancer cells containing fusion genes using this genome targeting approach resulted in partial remission of the cancers and zero mortality. In contrast, all control animals quickly succumb to these xenografted cancers. Thus, genomic targeting may hold promise as an effective treatment for human cancers.

Speaker Biography

Jianhua Luo has been studying molecular pathology related to human malignancies from the last 28 years. Currently, he is a Professor of Pathology and Director of High Throughput Genome Center at University of Pittsburgh. In the last 17 years, he has been largely focusing on the genetic and molecular mechanism of human prostate and hepatocellular carcinomas. He is one of the pioneers in utilizing high throughput gene expression and genome analyses to analyze field effects in prostate cancer and liver cancer. He is also the first in using methylation array and whole genome methylation sequencing to analyze prostate cancer. Recently, his group discovered several novel fusion transcripts and their association with aggressive prostate cancer. Overall, these findings advance our understanding of how cancer develops and behaves and lay down the foundation for better future diagnosis and treatment of human malignancies.

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