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Role of oncogenic fusion genes in human cancer

Mutations and chromosome rearrangement are some of the key features of human malignancies. Recently, we discovered a panel of cancer-specific fusion genes that play key roles in human cancer development. One of these fusion genes called *MAN2A1-FER* generated a constitutively activated tyrosine protein kinase. The fusion translocates FER kinase from the cytoplasm to Golgi apparatus. The fusion protein ectopically phosphorylates the N-terminal domain of EGFR, and activates the EGFR signaling pathway in the absence of a ligand. *MAN2A1-FER* has been found in a variety of human malignancies. It transforms immortalized cell lines into highly aggressive cancer cells. Expression of *MAN2A1-FER* produces spontaneous liver cancer in animals. Cancer cells positive for *MAN2A1-FER* are highly sensitive to several tyrosine kinase inhibitors, and can be targeted by genome therapy intervention. Thus, targeting at *MAN2A1-FER* or other oncogenic fusion genes may hold promise to treat human cancer effectively.

Biography

Jianhua Luo has been studying Molecular Pathology related to human malignancies from the last 25 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. In this period, his group has identified and characterized several genes that are related to prostate cancer and hepatocellular carcinoma, including SAPC, myopodin, CSR1, GPx3, ITGA7, MCM7, MT1h and GPC3. He has characterized several signaling pathways that play critical role in prostate cancer development. 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. His group found that patterns of copy number variants of certain specific genome loci are predictive of prostate cancer clinical outcomes, regardless tissue origin. Recently, his group discovered several novel fusion transcripts and their association with aggressive prostate cancer. One of the fusion genes called *MAN2A1-FER*, was found present in 6 different types of human cancers. He later defined a critical *MAN2A1-FER/EGFR* signaling pathway that is essential for *MAN2A1-FER* mediated transformation activity. In addition, his group developed a genome intervention approach to treat human cancers that are positive for fusion gene.

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