Jianhua Luo, J Stem Cell Res Ther 2017, 7:9 (Suppl)
DOI: 10.4172/2157-7633-C1-028

Jianhua Luo

University of Pittsburgh School of Medicine, USA

Novel ectopic signaling of *MAN2A1-FER* fusion protein

Cancer remains one of the most lethal diseases for human. Oncogenic fusion gene is one of the fundamental mechanisms driving the progression of human cancers. *MAN2A1-FER*, a fusion gene between the mannosidase domain of *MAN2A1* and tyrosine kinase domain of *FER*, was found in 6 different types of human malignancies. *MAN2A1-FER* fusion translocated *FER* domain from cytoplasm to golgi apparatus, and led to phosphorylation of N-terminus of EGFR and activation of EGFR signaling pathway. Expression of *MAN2A1-FER* generated dramatic increase of growth and invasion of cancers, while removal of *MAN2A1-FER* through knockout generated significant lower level of growth and metastasis. The presence of *MAN2A1-FER* increased the sensitivity of human cancers to *FER* kinase inhibitor crizotinib or EGFR kinase inhibitor canertinib. Hydrodynamic tail-vein injection of *MAN2A1-FER* gene resulted in rapid development of liver cancer in mice with somatic Pten deletion. Taken together, we concluded that *MAN2A1-FER* fusion gene is one of the key drivers for human cancer development.

Biography

Jianhua Luo has been studying molecular mechanism related to human malignancies since last 24 years. Currently, he is a Professor of Pathology and Director of High Throughput Genome Center at University of Pittsburgh. In the last 16 years, he has been largely focusing on genetic and molecular mechanism of human prostate cancer and hepatocellular carcinomas. He has characterized several signaling pathways that play critical role in prostate cancer development, including Myopodin-ILK-MCM7 inhibitory signaling, myopodin-zyxin motility inhibition pathway, CSR1-CPSF3, CSR1-SF3A3 and CSR1-XIAP apoptotic pathways, MT1h-EHMT1 egigenomic signaling, ITGA7-HtrA2 tumor suppression pathway, GPx3-PIG3 cell death pathway, AR-MCM7 and MCM7-SF3B3 oncogenic pathways. He proposed prostate cancer field effect in 2002. 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 found that patterns of copy number variants of certain specific genome loci are predictive of prostate cancer clinical outcomes, regardless tissue origin. His discovery of several novel fusion transcripts and their association with aggressive prostate cancer has brought significant new insight into the field of prostate cancer research. Overall, these findings advance our understanding on how cancer develops and behave and lay down the foundation for better future diagnosis and treatment of human malignancies..

luoj@msx.upmc.edu

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