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Genomic markers of prostate cancer

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Despite a high incidence, only a fraction of men diagnosed with prostate cancer (PCa) develop metastases and even fewer die from the disease. The majority of prostate cancers remain asymptomatic and clinically indolent. The precise mechanisms for the development of progressive, clinically relevant PCa remain elusive. Recently, we found large numbers of copy number variations in the blood, benign prostate tissues and prostate cancer samples from prostate cancer patients. Interestingly, the sizes of CNVs in the blood samples of prostate cancer patients are highly correlated with the clinical outcomes in terms of prostate cancer recurrence and prostate cancer related death. Using least square regression model, we achieved 75% accuracy in predicting prostate cancer recurrence after radical prostatectomy using CNV information from the blood samples of prostate cancer patients, significantly higher than the prediction rates generated by Gleason scores or Nomogram. When blood CNV is combined with the status of Nomogram and fusion gene, the accurate prediction rate is 87.6%. The blood CNV prediction model is of particular interest, since it offers an alternative in predicting prostate cancer clinical courses when radical prostatectomy is not performed, and nomogram information cannot be obtained. As a result, we conclude that the formation of large size germline CNVs predisposed patients to aggressive prostate cancer clinical courses.

Biography

Dr. Luo been studying molecular pathology related to human malignancies in the last 23 years. Currently, he is a Professor of Pathology and Director of High Throughput Genome Center at University of Pittsburgh. In the last 13 years, Dr. Luo has been largely focusing on 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, including Myopodin-ILK-MCM7 inhibitory signaling, myopodin-zyxin motility inhibition pathway, CSR1-CPSF3 and CSR1-XIAP apoptotic pathways, MT1h-EHMT1 egigenomic signaling, ITGA7-HtrA2 tumor suppression pathway, GPx3-PIG3 cell death pathway, and AR-MCM7 oncogenic pathway. 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, Dr. Luo's 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 behaves, and lay down the foundation for better future diagnosis and treatment of human malignancies.

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