

Insulin Transcription Factor PDX1 Promotes Liver Tumorigenesis

Chacko Jacob, Tinghan Zhao, X. F. Steven Zheng
Rutgers, The State University of New Jersey

Pancreatic and duodenal homeobox 1 (PDX1) is a protein that is primarily known for its function as an insulin transcription factor. While PDX1 expression is normally restricted to pancreatic beta cells in adult animals, PDX1 has also been found to be expressed in several cancers of non-pancreatic origin, including colorectal, stomach, and liver cancers. However, it is still unclear if and how PDX1 regulates the development of these cancers. The purpose of this study is to determine whether aberrant PDX1 expression promotes liver tumorigenesis. My analysis of liver cancer patient survival data from The Cancer Genome Atlas (TCGA) shows that the survival rate of patients with high PDX1 mRNA expression was significantly decreased compared to that of patients with low PDX1 mRNA expression. To further understand the role of PDX1 in liver tumorigenesis, I performed in vitro and in vivo experiments using cultured liver cancer cell lines and a mouse hydrodynamic transfection (HDT) liver tumor model. Western blot analysis confirms PDX1 expression in liver cancer cell lines, especially in the Huh7 cell line. Furthermore, I ectopically expressed PDX1 in combination with the oncogenes AKT and NRAS in mouse livers through the HDT method. Liver tumor development was observed in the AKT/NRAS/PDX1 group, but not in the AKT/NRAS control group. These results provide evidence for the role of PDX1 in promoting liver tumorigenesis. In the future, I plan to perform more in vitro and in vivo experiments to verify the above results and to investigate the mechanism by which PDX1 drives liver tumorigenesis. Supported by SURF and NIH grants DK124897 and R25ES020721.

