PANCREATIC CANCER

The Hippo Transducer TAZ Promotes Epithelial-Mesenchymal Transition and Progression in Pancreatic Cancer

Dacheng Xie[1], Jiujie Cui[2], Tian Xia[3], Zhiliang Jia[2], Keping Xie[2], Yong Gao[1], and Ming Quan[1,2]

[1]Department of Oncology, Shanghai Tongji University Affiliated East Hospital, Shanghai, People's Republic of China; [2]Department of Gastroenterology, Hepatology and Nutrition, The University of Texas MD Anderson Cancer Center, Houston, Texas; and [3]Department of Gastroenterology, Shanghai Changhai Hospital, Second Military Medical University, Shanghai, People's Republic of China

Background: Transcriptional co-activator with PDZ binding motif (TAZ) is one of the transducers of the Hippo pathway and promotes cancer development and progression. However, the expression and roles of TAZ in pancreatic cancer has not been revealed. In our current study, we determined the roles and underlying mechanisms of elevated expression and activation of TAZ in pancreatic cancer development and progression.

Methods: The mechanistic role of TAZ and Hippo signaling in promotion of PDA growth and progression was examined using cell culture, molecular biology and mouse models; and the relevance of our experimental and mechanistic findings were validated using human PDA tissues.

Results: We found that the expression of TAZ was significantly increased in pancreatic cancer tissues as compared to normal pancreas tissues. Further analysis the correlation of TAZ expression with TMA clinicopathologic parameters, we found that the expression of TAZ was positively associated with tumor differentiation. However, the expression of TAZ was not correlated with pancreatic cancer TNM stages in our study. TAZ expression was elevated in pancreatic cancer cell lines as compared to pancreatic ductal epithelial cells. TAZ activation in pancreatic cancer cells promoted pancreatic cancer cells proliferation, migration, invasion and epithelial to mesenchymal transition (EMT). Further mechanism studies demonstrated that aberrant expression and activation of TAZ in pancreatic cancer cells was due to suppression of Merlin expression, which was a positive upstream regulator of the Hippo pathway, and the oncogenic function of TAZ in pancreatic cancer was mediated by the TEAD family transcription factors.

Conclusions: TAZ functioned as a tumor oncogene and promoted pancreatic cancer EMT and progression. TAZ could be a potential target for designing effective therapeutic strategies. Therefore, we not only identified a novel molecular mechanism underlying pancreatic cancer development and progression, but also found a new promising target for early detection and treatment of pancreatic cancer.