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PDCD10 twists the functions of TGF-β towards cancer-progression in pancreatic cancer

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TGF-β plays a crucial role in the progression of PDAC (Pancreatic ductal adenocarcinoma). Therapies targeting TGF-β signaling hold great outcome in the preclinical and clinical setting. But the Cancer patients who were treated with blockers of TGF-β signaling can experience adverse effects if the function of TGF-β in physiological processes is compromised. Therefore, it is crucial that research can help target the pro-cancer role of TGF-β in PDAC.

PDCD10 expressed higher in the PDAC tumor tissue compared to normal pancreas and is highly correlated to the poor survival. GSEA result implied that expression of PDCD10 is positively related to the TGF-β pathway in PDAC tumor tissue samples from TCGA.

We hypothesized that PDCD10 plays a role in the altered TGF-β signaling in PDAC. To test this hypothesis, we measured the function of TGF-β in cell proliferation and EMT in PDCD10-knockout cell. The results show that PDCD10 can function as a modulator of TGF-β signaling outcomes in pancreatic cancer.

Then, to explore the mechanism of the relationship between the PDCD10 and TGF-β signaling, we tested the expression level of RB and ERK in the TGF-β signaling pathway. Phosphorylation of RB and ERK can be inhibited by the PDCD10 knock-out and the regulation of p-RB is dependent on the SMAD4 pathway. These experiments demonstrate that PDCD10 alter the proliferative function and EMT induction of TGF-β in pancreatic cancer cells.

Results gave the evidence that PDCD10 promote the conversion of TGF-β physiological functions to pro-cancer functions in PDAC. Thus, targeting PDCD10 in PDAC patients could represent a promising target to help overcome the side effect of TGF-β target therapy.