AB110. P084. OGDHL inhibits human pancreatic ductal adenocarcinoma progression and is regulated by microRNA-214/TWIST1 negative feedback pathway

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Abstract: Oxoglutarate dehydrogenase like (OGDHL) is involved in tricarboxylic acid cycle and was reported as a candidate tumor suppressor in some other tumors. We first explored the mechanisms of OGDHL in human pancreatic ductal adenocarcinoma (PDAC) progression. OGDHL is frequently down-regulated in human PDAC and predicted poor prognosis. OGDHL suppresses PDAC growth though G1 cell cycle arrest both *in vivo* and *in vitro* and OGDHL also inhibits migration and invasion ability of PDAC both in vivo and in vitro. Compared with non-tumor tissues, PDAC tissues showed down-regulation of OGDHL and up-regulation of miR-214 and TWIST1. The results showed that OGDHL is a target gene of miR-214 and always negatively regulated by miR-214 and the decrease expression level of OGDHL was on account of the increased expression level of miR-214 in PDAC. In addition, TWIST1 is frequently up-regulated in PDAC and induces miR-214 expression. However OGDHL could inhibit TWIST1 expression via both promoting ubiquitin-mediated proteasomal degradation of HIF1a and regulating AKT pathways. The effect of OGDHL/HIF1a/TWIST1/miR-214 signaling pathway in pancreatic carcinogenesis and metastasis were also determined both *in vivo* and *in vitro*. A combination of down-regulation OGDHL and over-expression miR-214 and TWIST1 predicts a poorer overall survival in PDAC patients. Finally, we demonstrated that the relationship of expression among OGDHL, miR-214 and TWIST1 may be a significant predictor of prognosis in PDAC patients. It is a novel pathway in OGDHL-regulated inhibition of PDAC tumorigenesis and metastasis. It may be a brand new targeted therapy in PDAC through OGDHL, TWIST1, miR-214, and HIF1a for prevention, treatment and prognosis.

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