Ching-Chieh Weng et al., J Cell Sci Ther 2018, Volume 9
DOI: 10.4172/2157-7013-C2-045

Genetically engineered mouse models recapitulating KLF10 loss in late-stage of PDAC and evoke PDAC lung metastasis

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Pancreatic Ductal Adenocarcinoma (PDAC) is a highly aggressive and lethal malignancy, which is characterized by activating Kras mutations and inactivation of the p53-Arf pathway in virtually all cases. Kruppel-like transcription factor 10 (KLF10), also referred to as TIEG1, plays essential roles in mediating TGFβ signaling and has been shown to function as a tumor suppressor in multiple cancer types. However, its roles in mediating cancer development and progression *in vivo* have yet to be fully characterized. Here, we have employed two well-characterized Pdx-1Cre LSL-KrasG12D and Pdx-1Cre LSL-KrasG12D p53L/L PDAC models to ablate KLF10 expression and determine the impact of KLF10 deletion on tumor development and progression. We demonstrate that loss of KLF10 co-operates with KrasG12D leading to an invasive and widely metastatic phenotype of PDAC. Mechanistically, loss of KLF10 in PDAC is shown to increase distant metastases and cancer stemness through activation of SDF-1/CXCR4 and AP-1 pathways. Furthermore, we demonstrate that targeting the SDF-1/CXCR4 pathway in the context of KLF10 deletion substantially suppresses PDAC progression suggesting that inhibition of this pathway represents a novel therapeutic strategy for patients with this disease.

Biography

Ching-Chieh Weng is pursuing his Ph.D. in Biomedical Science Institute from National Sun Yat-Sen University, Taiwan. He has finished his M.S. in Biomedical Science Institute from National Sun Yat-Sen University, Taiwan. He was awarded twice for Outstanding Paper Award in 27th JACBS (2012) and 30th JACBS (2015). His expertise in evaluation and passion in creating new genetically engineered mouse models.

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