



## AB112. P086. MicroRNA miR-141/200c inhibit proliferation, invasion and metastasis of human pancreatic cancer cells by targeting WIPF1-YAP/TAZ pathway

Yu Pan, Fengchun Lu, Ping Xiong, Zheyang Zhan, Xianchao Lin, Huguang Huang

Fujian Medical University Union Hospital, Fuzhou 350001, China

**Abstract:** MicroRNA-200 gene family (miR-200, including miR-200a, miR-200b, miR-200c, miR-429 and miR-141) is downregulated in some malignancies by heavy CpG island hypermethylation. Its methylation status and function in pancreatic cancer have not been well understood. We have found that miR-200c and miR-141 were hypermethylated in human pancreatic ductal adenocarcinoma compared to the surrounding non-cancerous tissues and this hypermethylation resulted in their silencing, whereas miR-200a, miR-200b and miR-429 were hypomethylated instead. Overexpression of miR-141 inhibited the proliferation of pancreatic

cancer cells. In addition, overexpression of miR-141 or miR-200c suppressed invasion and metastasis of pancreatic cancer cells both in vitro and in mouse model. To understand the mechanism of tumor-suppressive effect of miR-141 or miR-200c, we searched for target genes and identified WIPF1 gene as a direct target of miR-141 and miR-200c. miR-141 and miR-200c bind to the 3'-untranslated region of WIPF1, a gene that binds to the untranslated region of Wiskott-Aldrich syndrome protein that is frequently mutated in Wiskott-Aldrich syndrome, an X-linked recessive disorder. This indicates that WIPF1 may be involved in the oncogenesis of pancreatic ductal adenocarcinoma. We further showed that miR-141 and miR-200c mediated the downregulation of WIPF1 which led to the inactivation of the YAP/TAZ complex. YAP/TAZ complex mediates signal transduction of Wnt/beta-catenin and other key pathways. Taken together, our study shows that miR-141 and miR-200c inhibit the proliferation, invasion and metastasis of pancreatic ductal adenocarcinoma by targeting WIPF1-YAP/TAZ pathway.

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