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The regulation mechanism of HEATR1 on the chemosensitivity of gemcitabine in pancreatic cancer

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Introduction : Our team discovered a chemosensitivity related gene of gemcitabine called HEATR1(HEAT repeat containing 1) and published the research on Cancer Research in 2016. Here our team aim to discover the novel functional genes correlated with HEATR1 in sensitizing pancreatic cancer cells to gemcitabine.

Methods : We first knocked down HEATR1 expression in pancreatic cancer cell line PANC-1 (HEATR1-KD) with gemcitabine treatment. Total RNAs were subjected to gene chip analysis to find out differential expression genes (DEGs) (Fold change >1.5 and P value < 0.05) between two groups (HEATR1 KD vs NC). DEGs were further analyzed and 30 genes were selected. Selection principles were 1) Literature review was carried out to ensure selected DEGs were not reported with functions previously in pancreatic cancer; 2) Trans-membrane protein encoding genes were ruled out as their low knock-down efficiency; 3) Fold change of selected DEGs were larger than 2. These 30 selected genes were tested their expression levels in HEATR1-KD PANC-1 cells using quantitative PCR. Among the top 20 genes with high expression levels were subjected to high content screening (HCS) in HEATR1-KD cells to testify whether they could affect cell proliferation activity when knock down their expressions, with or without gemcitabine treatment respectively.

Results : Our study proposed that silencing ZNF185 could coordinate with gemcitabine to attenuate cell proliferation ability, while silencing ZNF185 alone did not affect cell viability. Meanwhile, ZNF185 fold change was 4.52 in gene chip analysis.

Conclusions : ZNF185 may play a significant role in pancreatic cancer cells responding to HEATR1 mediated chemotherapeutic sensitivity.

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