FAM115c that upregulates proliferation and invasion under hypoxia could be a predictive biomarker for pancreatic cancer

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**Background:** In pancreatic cancer whose microenvironment is extremely hypoxic, the analysis of signal transduction under hypoxia is thought to be important. Recently, we have found that the expression of TRP channel-associated factor family, FAM115c, increased under hypoxia in pancreatic cancer. In the present study, the biological significance of FAM115c was investigated in pancreatic cancer, and whether FAM115c could be a new therapeutic target for pancreatic cancer was evaluated.

**Methods:** Three pancreatic ductal adenocarcinoma cell (PDAC) lines (ASPC-1, SUIT-2, and PANC-1) were cultured under normoxia (20%O2) and under hypoxia (1%O2) and were used as target cells. Inhibition or overexpression of FAM115c was performed using FAM115c siRNA and plasmid, respectively. Expression of FAM115c was analyzed by qRT-PCR, western blot and immunohistochemical staining (IHC). Proliferation
was performed by MTT assay. Migration was estimated using time-lapse imaging analysis. Mice xenograft experiments were performed using BALB/c nude mice. Forty surgically resected human pancreatic cancer specimens were used for qPCR experiment and IHC.

**Results:** 1) Expression of FAM115c increased in PDAC under hypoxia compared to normoxia. 2) FAM115c suppression significantly increased migration and invasion in PDAC under hypoxia. 3) FAM115c inhibition significantly increased proliferation in vitro in PDAC under hypoxia. 4) FAM115c overexpression led to decreased proliferation, migration and invasion in PDAC under hypoxia. 5) Tumor volume in mice injected with FAM115c-inhibited PDAC was significantly higher than that in control mice. 6) Signaling from FAM115c was through PI3K and MAPK signaling pathways. 7) FAM115c expression was observed in all 40 patients examined by IHC. 8) In qPCR experiment FAM115c expression correlated with better prognosis in patients with pancreatic cancer.

**Conclusions:** These results suggest that FAM115c upregulates proliferation and invasion in pancreatic cancer under hypoxia and that FAM115c may be a predictive biomarker for better prognosis of patients with pancreatic cancer. FAM115c gene transfer may be a new therapeutic strategy for pancreatic cancer.

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