The Role of F11R in Pancreatic Cancer Malignancy and Its Clinical Implication as a Therapeutic Target

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Medical Genetics

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F11R (-/-); pancreatic cancer; genome editing; malignancy degree; cellular behavior
Abstract

Background The F11 receptor belongs to the immunoglobulin superfamily and is expressed in epithelial and endothelial cells. F11R mediates the formation of tight junctions between the epithelium and endothelium, and participates in the invasion and metastasis of tumor cells. We have previously shown that the F11R gene is closely related to KRas (P = 0.76), a known therapeutic target for pancreatic cancer (PCa). In recent years, it has been found that F11R is expressed in different tumors and has biological effects. However, according to different tumor cases, different cell lines and experimental conditions, the regulatory results and mechanisms of F11R on tumor are different, even contradictory, and the expression, clinical significance and biological mechanism of F11R in tumor tissues have not been reported in detail.

Results To investigate the role of F11R in carcinogenesis of PCa and the potential of F11R as a therapies target for PCa, we silenced F11R (-/-) in the PCa cell line PANC-1 (known to express high levels of KRas) using lentiviral approaches. We found that F11R silencing led to decreased cell proliferation, a loss of cell invasiveness, reduced colony forming ability, cell cycle arrest in G1 phase, cells apoptosis enhanced, and ros enhanced. In vitro data showed that inhibition of F11R decreased proliferation and invasiveness of cancer cells. The present results suggest that F11R may be a promising therapeutic target for PCa.

Conclusions This study used bioinformatics combined with gene chip data to find the gene F11R, which is closely related to KRAS gene, and we used lentivirus to package shRNA plasmid to interfere with the gene F11R in pancreatic cancer panc-1 cells. A series of biobehavioral studies indicated the biobehavioral function and malignancy of panc-1 in pancreatic cancer cells with negative regulation of F11R gene. Based on this, we need to continue to clarify the expression of F11R gene in clinical case samples to determine whether F11R gene can be a new therapeutic target for pancreatic cancer.

Full-text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF from the Manuscript Files section below.

Figures
Figure A: Box plot showing the distribution of a variable in PAAD with statistics (num(T)=179; num(N)=171).

Figure B:

- **Cancer stages**
  - Expression of F11R in PAAD based on individual cancer stages

- **Tumor grade**
  - Expression of F11R in PAAD based on tumor grade

- **Patient's age**
  - Expression of F11R in PAAD based on patient's age
Bioinformatics analysis of F11R about pancreatic cancer. A: Bioinformatics analysis showed that the expression of F11R in pancreatic cancer was higher than that of normal tissue (P < 0.05). B: Data from the TCGA database showing the variable expression of F11R in pancreatic cancer tissue from different stages, different grades and different age. C: Data from the TCGA database showed that low expression of F11R prolongs the OS of pancreatic cancer patients.
F11R expression in pancreatic cancer cell lines and PCa pathological specimens. A: q-PCR showed that F11R is highly expressed in 5 (PANC-1, MIA paca-2, bxpca-3, cfpac-1, SW1990) pancreatic cancer cell lines. B: Immunohistochemical staining of F11R in pathological specimens of pancreatic cancer showed that the expression of F11R was 86%.
Knockout of PANC-1 F11R following lentivirus transfection. A: PANC-1 cells were transfected with control and F11R -/- lentiviruses for 72 h. GFP fluorescence showed an infection efficiency \( \geq 90\% \). B: PANC-1 cells infected with the indicated lentiviruses for 72 h were assessed for F11R expression by western blot analysis. F11R expression in the F11R -/- group was significantly reduced.
Cells proliferation assays. FigA: Cell proliferation in the F11R -/- group was significantly slower than the blank control and NC groups. FigB: The number of clones in the negative control group (NC) was 78.32% which decreased to 15.24% in the RNAi-GFP group. These results suggest that F11R silencing significantly inhibits the clonal formation of PANC-1 cells (* represent P<0.05).
Flow cytometry analysis. Transfection increased the number of cells in the G0/G1 phase. Cytotoxicity was significantly higher in F11R -/- cells compared to control or NC groups. F11R silencing led to further G0/G1 phase arrest. (* represent P<0.05)
Apoptosis assessments. The number of apoptotic cells significantly increased following F11R silencing (lower right quadrant), as did the number of necrotic cells (upper right quadrant).

Results as shown in the figure, the proportion of apoptotic cells in the untreated group was 0.74%, and the proportion of apoptotic cells in the early stage of RNAi-GFP was 1.86%, showing no statistical difference compared with the untreated group. The proportion of RNAi-F11R apoptotic cells in F11R -/- cells was 15.85%. Compared with untreated group and NC group, the proportion of dead cells in F11R -/- cells increased, with statistically significant differences. (* represent P<0.05)
Figure 7

PANC-1 cell migration and invasion in vitro. In the F11R -/- group, the number of cells Transwell assay significantly decreased, indicating a loss of invasion. Cell numbers were calculated using ImageJ. Transwell assays showed that the number of migrating cells significantly decreased following F11R silencing. (* represent P<0.05)
ROS production in PANC-1 cells. Fluorescence intensity represents intracellular ROS levels. ROS production was assessed through comparison of the fluorescent intensities of DCFH-DA staining in Control, NC and F11R groups. (* represent P<0.05)