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Microarray analysis to explore the effect of CXCL12 isoforms in a pancreatic pre-tumor cell model

CXCL12 isoforms in a pancreatic pre-tumor cell model

Yan-Dong Miao, Jiang-Tao Wang, Xiao-Long Tang, Deng-Hai Mi

Abstract

C-X-C motif chemokine ligand 12 (*CXCL12*) expression was significantly lower in tumor samples than in corresponding normal samples. *CXCL12* expression was significantly positively related to the infiltration levels of T cells, DCs, iDCs, cytotoxic cells, TFH cells, mast cells, B cells, Th1 cells, NK cells, pDCs, neutrophils, and T helper cells (Spearman correlation coefficient >0.5, P < 0.001) and negatively correlated with the infiltration level of NK CD56bright cells. In addition, pancreatic hTERT-HPNE cells treated with three diverse *CXCL12* isoforms exhibited changes mainly in the regulation of the EMT activation pathway.

Key Words: *CXCL12*; Pancreatic cancer; Splicing isoforms; Bioinformatics analysis; tumor microenvironment; pathway.

Miao YD, Wang JT, Tang XL, Mi DH. Microarray analysis to explore the effect of *CXCL12* isoforms in a pancreatic pre-tumor cell model. *World J Gastroenterol* 2021; In press

Core Tip: *CXCL12* expression was significantly lower in tumor samples than in normal samples. *CXCL12* expression was significantly positively associated with the infiltration levels of 12 immune cells, especially T cells, which may encourage further exploration of the effect of *CXCL12* in PDCA immunotherapy. In addition, treating pancreatic hTERT-HPNE cells with three diverse *CXCL12* isoforms mainly affected the regulation of the EMT activation pathway.

TO THE EDITOR

We read with interest the article by Cecati, Monia *et al.* [1]. They investigated the specific roles of α , β , and γ C-X-C motif chemokine ligand 12 (*CXCL12*) isoforms in pancreatic ductal adenocarcinoma (PDAC) onset by microarray analysis of hTERT-HPNE cells

cured by three diverse isoforms of *CXCL12*, which indicated that *CXCL12* isoforms have different roles in PDAC pathogenesis.

We appreciate the unique perspective provided by the authors' exploration of the roles of the different isomers of *CXCL12* in PDAC. However, the results might be made more meaningful if the authors built on this by presenting the differential expression of *CXCL12* in normal and tumor tissues of PDCA as a whole, such as through a bioinformatics analysis of PDCA cases in The Cancer Genome Atlas (TCGA) database or their own data. We discovered that the *CXCL12* expression was significantly lower in tumor samples than in normal samples (Figure 1A). Detailed statistical results are described in Table 1.

The tumor microenvironment (TME), mediated by interactions between stromal cells and pancreatic epithelial/carcinoma cells, is essential for PDCA progression and has been associated with failure of chemotherapy, radiotherapy, and immunotherapy [2]. The formation of the microenvironment requires interactions between pancreatic cancer cells and stromal cells. A pancreatic cancer microenvironment composition that favors demyelination and immunosuppression is related to poor prognosis [3]. Although immunotherapy has transformed cancer therapy, patients with PDCA rarely respond to these regimens, and this failure is attributed to poor infiltration and activation of T cells in the TME. We found that *CXCL12* expression was positively correlated with the level of infiltration of 22 immune cells, especially T cells (Fig. 1B, C), which may encourage further exploration of the effect of *CXCL12* in PDCA immunotherapy. Detailed information on the correlation between *CXCL12* expression and immune cell infiltration is shown in Table 2.

We agree with Cecati, Monia *et al*, who reported that all *CXCL12* isoforms influenced cell migration, adhesion, and cytoskeleton-associated gene expression. In our study, we found that treating pancreatic hTERT-HPNE cells with three diverse *CXCL12* isoforms mainly affects the regulation of the EMT activation pathway (Figure 1 D, E, F), which confirms that the work done by Cecati, Monia *et al*. is worthy of recognition and that

our findings can be a supplement to their study. In the future, we should investigate the role played by *CXCL12* in the PDCA immune microenvironment in depth.

STATISTICAL ANALYSIS

Software: R (version 3.6.3) was used to perform statistical analysis and visualization results. Differential expression of *CCXL12* between pancreatic cancer tissues and normal tissues was adopted by the Wilcoxon rank-sum test and visualized results using R-package "ggplot2". Immune cell algorithm: ssGSEA (built-in algorithm of GSVA package [6]). Correlation test using Spearman's correlation coefficient. Pathway analysis was performed by the online tool GSCALite (<http://bioinfo.life.hust.edu.cn/web/GSCALite/>) [7].

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