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Exploring the IL-20 Subfamily as a Novel Therapeutic Target in Pancreatic Cancer

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Abstract: *Background*: The interleukin-20 (IL-20) subfamily plays oncogenic roles in various cancers. However, the significance of IL-20 subfamily proteins in pancreatic cancer remains unclear. This study aimed to investigate the role of the IL-20 subfamily in pancreatic cancer. *Methods*: The study used The Cancer Genome Atlas data and the Gene Expression Omnibus database to analyze mRNA levels of IL-20 family members in pancreatic cancer. ICGC clinical data were used to compare clinicopathological features. Lentivirus-transfected cells were used to study the function of the IL-20 receptor subunit (IL20RB) in vitro. *Results*: The IL-20 subfamily receptor IL20RB is highly expressed in pancreatic cancer and positively correlates with poor overall survival. GEO data (GSE 15471) showed that IL20RB expression is higher in pancreatic cancer tissues than in adjacent pancreatic tissues. TCGA and ICGC data indicated that expression of IL20RB is positively associated with advanced tumor stage and lymph node metastasis. Enrichment of upregulated genes in the IL20RB-high expression group showed cancer-promoting pathways in pancreatic cancer. Results from in vitro cell experiments showed that overexpression of IL20RB increases the proliferation and metastasis of pancreatic cancer cells and knockdown of IL20RB produces opposite effects. *Conclusion*: The IL-20 subfamily receptor IL20RB may play a pro-tumorigenic role in pancreatic cancer and is a promising target for treatment.

Keywords: IL-20 subfamily; IL20RB; TCGA; GEO; Pancreatic cancer; Therapeutic target

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1. Background

The IL-20 family (IL-19, IL-20, IL-22, IL-24, and IL26) contains distinct receptor-coding proteins.Unlike other cytokine families, members of the IL-20 family exhibit distinct signaling sequences. IL-22 is primarily responsible for acute responses, while IL-19 and IL-20 are more responsible for chronic inflammation [1,2]. This spatiotemporal expression pattern indicates complementary functions in the tumor microenvironment rather than redundant functions. In particular, soluble receptor IL22BP may not only be a signal inhibitor, but may also contribute to the “molecular boundary” at tumor margins by concentration gradients, thus

restricting the effects of IL-22 spatially. Interestingly, cell ecology, the IL-20 family is also unique to the cell ecologically. Unlike classical immune cytokines, epithelial cells may build bidirectional networks with stromal cells by secreting specific members such as IL-19 and IL-20 [3]. Receptor distribution studies reveal another interesting feature: IL20RA/RB and IL22RA1 show "microenvironmental complementarity," with the former enriched at barrier surfaces and the latter concentrated in secretory epithelia [2,4]. This distribution suggests that IL-20 may guide STAT3 activation towards different downstream modules via different receptor combinations [1,2]. Rapid phosphorylation activates immediate transcriptional programs [5–8], and sustained signaling induces chromatin remodeling [9–11]. This dual regulation may explain why some members of the IL-20 family excel at promoting tumor cell "phenotypic plasticity" [12,13], and why tumors metastasize in IL22RA1-positive tumors [14,15,16]. This may stem from differential stromal remodeling—IL20RA preferentially activates fibroblasts, while IL22RA1 modulates vascular endothelium [17,18,19].

Its specific microenvironment characterizes pancreatic ductal adenocarcinoma (PDAC). As opposed to other gastrointestinal tumors, IL-20 signaling may promote "metabolic reprogramming" rather than just "pro-inflammatory" [20]. Recent results suggest that IL22RA1 sustains stemness [21], but may also modulate autophagic flux to adapt to nutrient-deficient conditions. The interaction between PDAC and IL-20 includes early-stage proliferation driven by IL-19/IL-20, which transitions to IL-22-mediated maintenance of stemness and metastases in advanced stages, and metabolic adaptations such as enhanced glycolysis and autophagy [22]. This pleiotropy makes the IL-20 system a promising therapeutic target, both because it has dual effects on tumor infiltration and microenvironmental support [22]. The study first analyze the IL-20 signaling networks in PDAC bioinformatics, and then validate key molecules experimentally. These goals are (1) to identify therapeutic targets and (2) to develop prognostic biomarker panels. Following biological assays and clinical samples will clarify critical IL-20 signaling nodes in PDAC and provide new insights into the role of pancreatic cancer progression.

2. Methods

2.1. Gene expression analysis and survival analysis

In order to evaluate the expression of IL20RB in pancreatic cancer, the study analyzed the transcriptome data from The Cancer Genome Atlas (TCGA) (http://www.cancer.gov/ccg/research/genome-sequencing/tcga), as well as the gene expression profiles between tumors and normal tissues (http://www.ncbi.nlm.nih.gov/geo/). Differential expression of IL20RB was assessed, and visualizations were created using GraphPad Prism 8. The study also examined the prognosis of IL-20 subfamily genes in pancreatic cancer using the GEPIA platform (http://gepia.cancer-pku.cn/index.html).

2.2. Correlation analysis between IL20RB expression and clinicopathological characteristics

Clinicopathological information on pancreatic cancer patients was obtained from the Cancer Genome Atlas database of 180 eligible patients. Tumor specimens with clinicopathological information ranging from age, gender, TNM stage, lymph node metastases, to incomplete records were included, excluding eight cases. To confirm our findings, the study performed additional correlation analyses between gene expression patterns and clinical characteristics using pancreatic cancer datasets from the International Cancer Genome Consortium (ICGC).

2.3. Analysis of co-expressed genes

Transcriptomic data from the TCGA-PAAD project were obtained from the TCGA portal, and raw sequencing files were processed using the STAR pipeline. Gene expression levels were normalized to TPM and log2(TPM+1) transformed for further statistical analysis. Correlation analyses between IL20RB expression and clinical or biological variables were performed using the R package ggplot2 for visualising results.

2.4. Gene set enrichment analysis (GSEA)

Cancer patients from The Cancer Genome Atlas (TCGA) were classified into high- and low-expression groups for IL20RB based on median expression values. To quantify differences in pathway enrichment, the study performed GSEA using clusterProfiler, with MSigDB Collections (c5.all.v7.5.1.symbols) as the reference database. The study focused on the top 3 highly enriched pathways, with FDR-adjusted p-values less than 0.05. The study further performed functional annotation by studying Gene Ontology (GO) categories and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways using clusterProfiler, and visualized the results with ggplot2.

2.5. Construction of stable transfection tool cells using lentiviruses

The study used three cell lines, PANC-1 and MIA PaCa-2 (human pancreatic cancer cell lines) and 293T (packaging cell line) from the Cell Bank of Type Culture Collection of the Chinese Academy of Sciences in Shanghai, China. Constructions for IL20RB overexpression and shRNA knockdown were custom-designed and synthesized by Guangzhou Ruibo Biotechnology Co., Ltd. Cells were loaded into 6-cm dishes 24 hours prior to transfection. Cells were packed in Viral Packaging using psPAX2 and pMD2.G plasmids (Addgene) and IL20RB constructs at 3:1:4 (psPAX2:pMD2.G:target plasmid), and transfection was performed according to the recommended protocol. Plasmid DNA and Lipofectamine 3000 were diluted separately in 400 L of Opti-MEM medium and added dropwise to 293T cells. After a 6-hour incubation in standard culture (37°C and 5% CO2), the transfection medium was removed and replaced with complete growth medium. Viral particles were harvested from the supernatant 48 hours after transfection. PANC-1 and MIA PaCa-2 cells were transduced with harvested lentiviral particles and successfully transduced cells were selected using 2 g/mL puromycin until stable polyclonal populations were established. This optimized protocol ensures efficient gene delivery and stable cell lines for functional studies.

2.6. Cell proliferation, cloning, migration, and invasion

Cells were seeded in 96-well plates at a density of 2000 cells per well for the CCK-8 viability test (Dojindo, Japan), measured in triplicate. For the colony formation test, cells were seeded in 6-well plates at a density of 5,000 cells per well, cultured 10-14 days at 37°C for 10-14 days, fixed with 4% paraformaldehyde, stained with 0.1% crystal violet (Sigma-Aldrich) and measured using ImageJ software (NIH), performed three times. Cell invasion ability was measured using 8-pore Transwell inserts (Corning) coated with 30 g Matrigel (BD Biosciences). 2105 pancreatic cancer cells were seeded in serum-free medium in the upper compartment, while the lower chamber contained complete medium with 20% FBS as a chemoattractant. After 16 hours at 37°C, invaded cells were fixed in methanol, stained with crystal violet, and counted in three random microscopic fields per insert. Migration experiments were conducted similarly, but without Matrigel coating, while all other conditions remained unchanged. All quantitative experiments contained appropriate controls and were repeated three times to ensure reproducibility, and statistical analyses were performed using GraphPad Prism 8.0 for significance.

2.7. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics (version 25.0) and R software (version 4.2.1). Continuous variables are presented as mean ± standard deviation (SD). Differences in IL20RB expression levels between pancreatic carcinoma tissues and matched normal tissues were evaluated using independent-sample *t*-tests and paired *t*-tests, as appropriate, based on data from The Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO) databases. Associations between IL20RB expression levels and clinicopathological features were assessed using Pearson's chi-square test. Survival outcomes were analyzed using Cox proportional hazards regression models, incorporating both univariate and multivariate analyses. All statistical tests were two-tailed, with significance thresholds set at $*P < 0.05$, $**P < 0.01$, and $***P < 0.001$.

3. Results

3.1. Expression of IL-20 subfamily in pancreatic cancer and normal pancreatic tissues

The TCGA pancreatic cancer RNA-Seq data (**Figure 1A**) show the relative expression of the IL-20 subfamily. The study found that IL10RB, IL20RA, IL20RB, and IL-24 were expressed at higher levels in pancreatic tumors than in normal pancreatic tissues (**Figure 1B**). Box plots show that the expression of IL10RB, IL20RA, and IL20RB in pancreatic tumors was significantly higher than in normal pancreatic tissue. Comparative analysis showed that the expression of IL22RA1 was significantly lower in pancreatic tumors compared with normal pancreatic tissue controls ($p < 0.05$). However, quantitative analyses showed similar expression patterns for the rest of the IL-20 subfamily members in malignant and non-malignant samples. These results suggest that IL10RB, IL20RA and IL20RB may play roles in pancreatic oncogenesis and disease progression, hence require further mechanistic investigation.

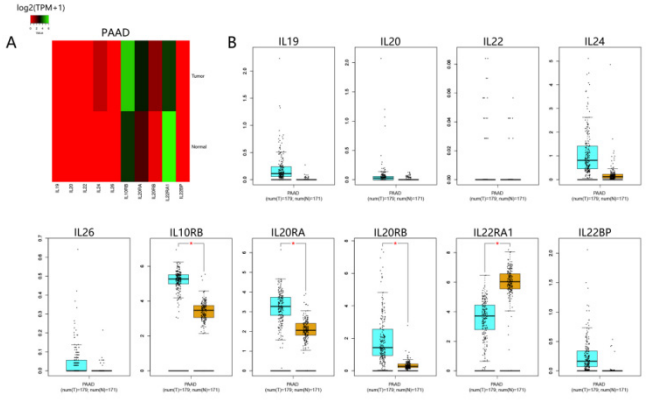

Figure 1. Expression profiling of IL20 subfamily in pancreatic cancer and normal tissues. (A) Heatmap displaying RNA-Seq expression profiles (log2[TPM+1] normalized) of IL20 subfamily members in pancreatic adenocarcinoma (PAAD, n=179) versus normal pancreas tissues (n=171) from TCGA. (B) Boxplots comparing the distribution of normalized IL20 subfamily expression levels between PAAD (red) and normal pancreas tissues (gray).

3.2. Relationship between IL-20 subfamily expression and the prognosis of patients with pancreatic cancer

The study then wanted to investigate how expression of the IL-20 family affects the outcome of patients with pancreatic cancer. The study used Kaplan-Meier survival analysis on 179 pancreatic cancer patients from TCGA. The study classified cases into high- and low-expression groups according to IL-20 subfamily mRNA

levels. Our survival curves (**Figure 2**) showed significantly worse outcomes for patients with high expression (HR=1.8, 95%CI X-X, *P*=0.078) than the low expression group (DFS=1.6, 95%CI X-X, *P*=0.042) than the low expression group. Results for other members of the IL-20 subfamily were not significant. Since only IL20RB was significantly overexpressed in pancreatic cancer tissues and associated with worse prognosis, the study performed bioinformatics analysis on IL20RB.

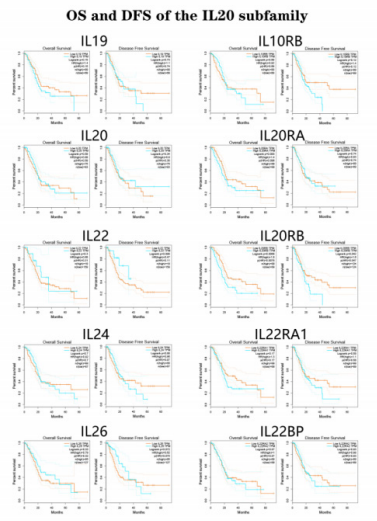

Figure 2. Prognostic significance of IL20 subfamily members in pancreatic cancer. Kaplan-Meier curves demonstrate the independent prognostic values of IL20 subfamily members for (A) overall survival and (B) disease-free survival in PAAD patients (log-rank test, $p < 0.05$ considered statistically significant).

3.3. Expression of IL20RB in pancreatic cancer tissues and adjacent tissues

To confirm the increased expression of IL20RB detected in early analysis, the study investigated independent cohorts of GEO data (GSE15471) of 78 pairs of pancreatic tumors and adjacent normal tissues. Microarray analysis revealed significant overexpression of IL20RB in malignant tissues compared to normal tissues (**Figure 3A-C**), supporting our previous results (**Figure 1B**). This consistent overexpression in different datasets strongly implicates IL20RB in the pathogenesis and progression of pancreatic cancer.

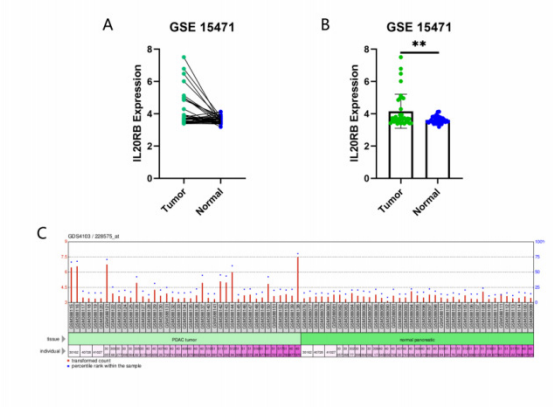

Figure 3. Differential expression of IL20RB in pancreatic cancer tissues. (A-B) Microarray data (GSE15471, n=78) revealed significantly elevated IL20RB expression in pancreatic tumors compared to adjacent normal tissues (***$p < 0.001$). (C) Validation in independent dataset GDS4103 confirmed IL20RB upregulation in tumors.

3.4. IL20RB expression is positively correlated with an advanced stage, lymph node metastasis, and other adverse clinicopathological characteristics of pancreatic cancer

To establish the clinical importance of IL20RB in pancreatic cancer, the study examined its expression levels in multi-institutional data from TCGA and ICGC. Our results showed a progressive increase in IL20RB expression with age, in TNM stage II and stage I tumors (**Figure 4A**), and in lymph node-positive and lymph node-negative tumors (**Figure 4B**). Our results also showed a marked increase in metastatic lesions compared to primary tumors in the ICGC data, suggesting the adverse consequences of high IL20RB expression (**Figure 4C-D**). Univariate analyses showed statistically significant associations with age (P=0.007) and treatment history (P=0.004), borderline correlations with gender (P=0.099), nodal status (P=0.079) and pathological classification (P=0.074) (**Table 1**). **Table 2** shows that IL20RB did not reach statistical significance as an independent prognostic marker in the multivariate Cox regression analysis. These results highlight the potential role of IL20RB overexpression during disease progression and strong correlation with other markers of tumor aggressiveness, suggesting involvement in critical oncogenic pathways that warrant further study. Although our results show clear clinicopathological correlations, independent prognostic significance in the multivariate analysis implies that clinical utility may be context-dependent and may function as part of a more general biomarker panel rather than as an independent prognostic indicator. These results support the growing evidence linking the IL-20 receptor family to pancreatic cancer pathogenesis and lay the foundation for future work on therapeutic targeting of this signaling pathway.

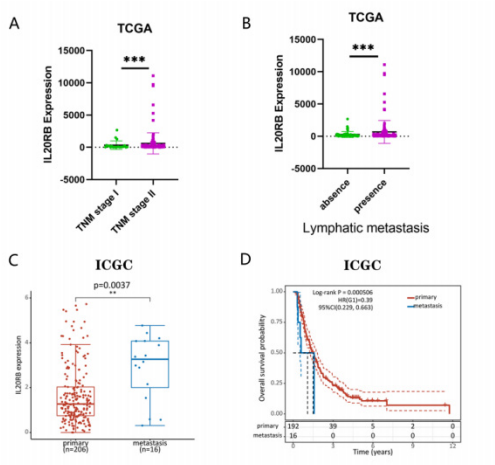

Figure 4. Clinical relevance of IL20RB expression in pancreatic cancer progression. (A) TCGA analysis showed higher IL20RB expression in TNM stage II versus stage I PAAD (*p<0.05). (B) IL20RB expression was elevated in lymph node metastasis-positive cases compared to negative cases (***p<0.001). (C) ICGC data demonstrated increased IL20RB expression in metastatic lesions versus primary tumors, correlating with poorer prognosis.

Table 1. Relationship between IL20RB expression level and clinicopathological variables in pancreatic cancer patients

Variables	IL20RB Expression		χ^2	*P*
	Low (n = 128)	**High (n = 44)**		
Age (years old)				
≤ 55	33(25.80%)	21(47.70%)		
> 55	95(74.20%)	23(52.30%)	7.322	0.007

Variables	IL20RB Expression		χ^2	*P*
	Low (n = 128)	**High (n = 44)**		
Gender				
Male	66(51.60%)	29(65.90%)		
Female	62(48.40%)	15(34.10%)	2.726	0.099
T stage				
T1	24(18.80%)	5(11.40%)		
T2-T4	104(81.30%)	39(88.60%)	1.274	0.259
N stage				
N0	41(32.00%)	8(18.20%)		
N1	87(68.00%)	36(81.80%)	3.083	0.079
TNM stage				
I	16(12.50%)	3(6.80%)		
II-IV	112(87.50%)	41(93.20%)	1.076	0.300
Pathological diagnosis				
PDAC	101(78.90%)	40(90.90%)		
Others*	27(21.10%)	4(9.10%)	3.193	0.074
Tumor site				
Head of pancreas	91(71.10%)	36(81.80%)		
Others**	37(28.90%)	8(18.20%)	1.950	0.163
Treatment				
Pharmacotherapy	67(52.30%)	12(27.30%)		
Radiotherapy	61(47.70%)	32(72.70%)	8.288	0.004

*These include pancreatic acinar cell carcinoma, neuroendocrine carcinoma, and others.

**It includes the body and tail of the pancreas and the whole pancreas.

Table 2. Multivariate analysis of the prognostic factors in pancreatic cancer patients using a Cox regression model

Characteristics		Multivariate analyses		
HR		**95.0% CI**	***P***	
TNM stage	I vs II-IV	1.19	0.525-2.696	0.677
Pathological diagnosis	PDAC vs others	0.635	0.253-1.597	0.335
Tumor site	Head of pancreas vs others	0.564	0.288-1.104	0.095
Treatment	Pharmacotherapy vs radiotherapy	1.62	0.760-3.454	0.212
IL20RB expression	Low vs high	0.546	0.209-1.428	0.217

3.5. Co-expression of IL20RB genes in pancreatic cancer

The study used TCGA datasets to investigate the role of IL20RB function in pancreatic cancer. The study extracted genes with strong positive correlation with the expression of IL20RB (Pearson's R> 0.59). The four strongest association genes were selected for expression scatter plots (**Figure 5A-C**), while the 10 most important correlation genes were used for heatmap and chord diagram visualizations. Validation in an independent GEO cohort (GSE15471) showed that these IL20RB genes were consistently upregulated in pancreatic tumor tissues compared with matched normal controls (**Figure 5D**). The high expression of this IL20RB gene signature was strongly prognostic for patients (**Figure 5E**). Collectively, these results

suggest that IL20RB could work in concert with other molecular networks that facilitate the progression of pancreatic cancer and contribute to adverse outcomes. Permanent overexpression of this gene cluster in malignant tissues and its association with poor survival indicate the clinical importance of the signaling axis in pancreatic cancer biology.

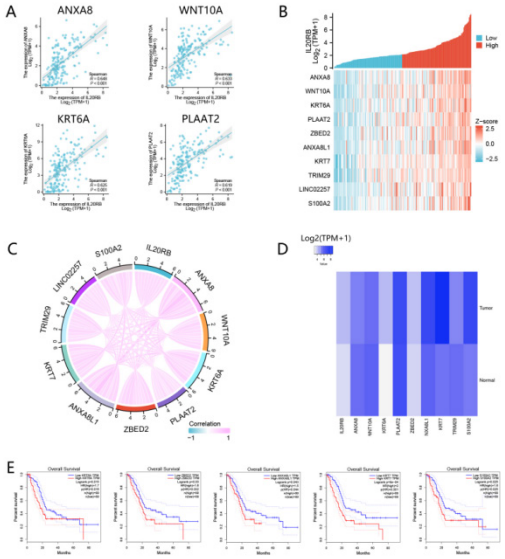

Figure 5. Co-expression network of IL20RB in pancreatic cancer. (A) Scatter plots of IL20RB versus the top four correlated genes. (B) Heatmap of the top 10 co-expressed genes with corresponding correlation coefficients. (C) Chord diagram visualizing correlation strengths between IL20RB and associated genes. (D) Heatmap of log2(TPM+1) normalized expression for IL20RB and co-expressed genes in PAAD versus normal tissues (GSE15471). (E) Survival analysis of IL20RB-coexpressed genes in TCGA cohort.

3.6. Enrichment of upregulated genes in the IL20RB high expression group indicates the associated cancer-promoting pathways

To investigate the potential role of IL20RB in pancreatic cancer, the study performed differential gene expression analysis of low- and high-expression IL20RB samples using TCGA data (**Figure 6A**). The study then performed Gene Set Enrichment Analysis (GSEA) to identify pathways enriched by top-ranked genes in IL20RB high- and low-expression groups, predicting IL20RB signaling pathways (**Figure 6B** and **6C**). KEGG pathways with top-three positive and negative correlations for visualization (all $P < 0.05$). Terms in the high-expression groups that involved immune response and tumorigenesis included SYSTEMIC LUPUS ERYTHEMATOSUS, PROTEASOME, and RIG-I LIKE RECEPTOR SIGNALING PATHWAY. Gene Ontology (GO) and KEGG analysis of significantly different gene sets from samples with different levels of expression identified IL20RB. **Figures 6D and 6E list the** top three components for visualization. Collectively, these results suggest that IL20RB can play a role in the development of pancreatic cancer by activating these signaling pathways.

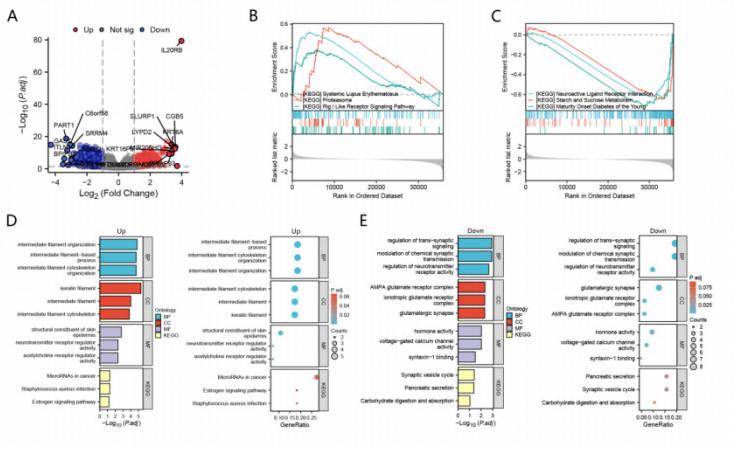

Figure 6. Pathway enrichment analysis of IL20RB-associated genes. (A) Volcano plot of differentially expressed genes between IL20RB-high and -low groups. (B-C) GSEA showing significantly enriched pathways in the IL20RB-high group. (D-E) GO and KEGG analyses of IL20RB-associated gene signatures (FDR<0.05).

3.7. IL20RB promotes the proliferation and metastasis of pancreatic cancer cells in vitro

To functionally characterize the oncogenic role of IL20RB in pancreatic cancer, the study performed in vitro studies to establish stable IL20RB-overexpressing and IL20RB-knockdown models in MIA PaCa-2 and PANC-1 cells. qRT-PCR and Western Blotting were successful in modulating both mRNA and protein levels (**Figure 7A-B**). Functional studies showed that overexpression of IL20RB significantly increased cell proliferation in CCK-8 assays and that IL20RB degradation markedly reduced growth (**Figure 7C**). Consistent with these proliferative effects, colony formation assays showed that IL20RB overexpressing cells had increased clonogenic capacity and IL20RB knockdown cells had reduced colony formation (**Figure 7D**). Metastatic potential studies by transwell assays showed that IL20RB overexpressing cells promoted migration and invasion capabilities, and knockdown impaired these aggressive phenotypes (**Figure 7E**). These functional studies provide compelling experimental evidence that IL20RB plays a key role in pancreatic cancer progression. Consistent effects were observed across several orthogonal assays, including proliferation, clonogenicity, migration, and invasion, strongly supporting its role in pancreatic cancer pathogenesis by increasing both proliferative capacity and metastatic potential in pancreatic cancer cells.

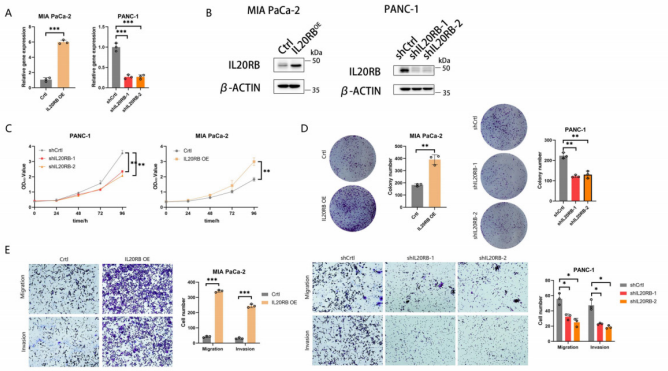

Figure 7. Functional validation of IL20RB in pancreatic cancer progression. (A-B) Successful establishment of IL20RB-overexpressing and -knockdown models in MIA PaCa-2 and PANC-1 cells (qPCR and Western blot confirmation). (C) CCK-8 assays demonstrated enhanced proliferation in IL20RB-overexpressing cells versus suppressed growth in knockdown cells ($p < 0.01$). (D) Colony formation assays showed concordant results. (E) Transwell assays revealed increased migration/invasion capacity with IL20RB overexpression and decreased potential with knockdown (*$p < 0.001$).

4. Discussion

Current studies link the IL-20 subfamily to cancer. Gao et al. (2021)[17] showed that IL20RA activates the JAK1-STAT3-SOX2 pathway, which promotes breast cancer stem cell characteristics and forms a favorable immune environment for tumors. He et al. (2022)[19] showed that IL20RB expression in lung cancer cells activated the downstream JAK1-STAT3 pathway and increased lung cancer cell proliferation in bones, and blockade with an IL20RB neutralizing antibody significantly prevented lung cancer bone metastases. These results show only a small fraction of the role of the IL-20 subfamily.

The study has assessed the clinical value and mechanism of action of the IL-20 subfamily in pancreatic cancer with extensive public data. The study found that:

(1) the members of the IL-20 subfamily (IL10RB, IL20RA, and IL20RB) were highly expressed in pancreatic cancer tissues, but only high expression of IL20RB was associated with poorer prognosis;
(2) The top 10 genes associated with IL20RB were high in PDAC and their expression was associated with poor prognosis;
(3) Functional assays showed that IL20RB improved pancreatic cancer cell proliferation and metastatic potential in vitro.

He and colleagues (2018) first reported elevated IL22RA1 expression levels in pancreatic ductal cancer; this association was clinically significant for poor patient prognosis [21]. IL22RA1/STAT3 signaling promotes pancreatic cancer stemness and indicates a mechanism by which microenvironmental factors can affect pancreatic cancer stemness. In 2020, Lu et al. [22] reported that the elevated levels of IL-20 in tumor tissues of 72 patients with pancreatic cancer were associated with poor OS. Targeting IL-20 not only prolonged survival and reduced PD-L1 expression in mice, but also inhibited tumor growth and inhibited M2-like polarization of macrophages in a mouse model of pancreatic cancer development. The study identified a major role of IL20RB in pancreatic cancer. Previous studies showed that other members of the IL-20 subfamily play a role in pancreatic cancer development. Poor prognosis associated with pancreatic cancer is due to early metastatic dissemination [23-25].

Most patients are diagnosed with advanced-stage disease with lymphatic and distant metastases [26,27], but previous studies have shown other members of the IL20 subfamily. The EMT phenomenon entails dual molecular changes: epithelial marker suppression and mesenchymal marker induction, critically enabling tumor cell invasion and metastasis [28,29,30]. In this study, WNT10A was one of the genes that showed expression patterns that were most highly correlated with IL20RB expression, suggesting that IL20RB may promote the metastasis of pancreatic cancer by affecting the Wnt signaling pathway.

While new insights are provided, this study has several limitations. First, IL20RB expression in clinical pancreatic cancer tissues was not detected in this study, so the study was not able to determine whether IL20RB is expressed at high levels in pancreatic cancer cells. Second, the study only performed bioinformatics analyses of public pancreatic cancer data and a few in vitro experiments. In the future, the study will verify IL20RB role in stimulating proliferation and metastasis of pancreatic cancer cells using clinical data from our hospital and by conducting in vitro experiments. Third, the study did not perform therapeutic experiments on IL20RB in pancreatic cancer cells. Thus, the efficacy of subsequent IL20RB neutralizing antibody therapy has not yet been verified.

5. Conclusion

In summary, the main challenge in pancreatic cancer is finding a suitable therapeutic target and prognostic marker. The study concludes that IL20RB could be a promising prognostic marker and therapeutic target for patients with pancreatic cancer, and we hope that our results will serve as a new reference in basic research and clinical applications for patients with pancreatic cancer. However, new pancreatic cancer targets from the IL-20 family should be investigated in larger patient populations.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Ouyang W, Rutz S, Crellin NK, Valdez PA, Hymowitz SG, 2011, Regulation and Functions of the IL-10 Family of Cytokines in Inflammation and Disease. Annual Review of Immunology, 29: 71–109.

[2] Rutz S, Wang X, Ouyang W, 2014, The IL-20 Subfamily of Cytokines—From Host Defence to Tissue Homeostasis. Nature Reviews Immunology, 14(12): 783–795.

[3] Wolk K, Kunz S, Asadullah K, Sabat R, 2002, Cutting Edge: Immune Cells as Sources and Targets of the IL-10 Family Members? Journal of Immunology, 168(11): 5397–5402.

[4] Blumberg H, Conklin D, Xu WF, et al., 2001, Interleukin 20: Discovery, Receptor Identification, and Role in Epidermal Function. Cell, 104(1): 9–19.

[5] Xue C, Yao Q, Gu X, et al., 2023, Evolving Cognition of the JAK-STAT Signaling Pathway: Autoimmune Disorders and Cancer. Signal Transduction and Targeted Therapy, 8(1): 204.

[6] Hu X, Li J, Fu M, Zhao X, Wang W, 2021, The JAK/STAT Signaling Pathway: From Bench to Clinic. Signal Transduction and Targeted Therapy, 6(1): 402.

[7] Rah B, Farhat NM, Hamad M, Muhammad JS, 2023, JAK/STAT Signaling and Cellular Iron Metabolism in Hepatocellular Carcinoma: Therapeutic Implications. Clinical and Experimental Medicine, 10.1007/s10238-023-01047-8.

[8] Kobayashi Y, Lim SO, Yamaguchi H, 2020, Oncogenic Signaling Pathways Associated with Immune Evasion and Resistance to Immune Checkpoint Inhibitors in Cancer. Seminars in Cancer Biology, 65: 51–64.

[9] Awasthi N, Liongue C, Ward AC, 2021, STAT Proteins: A Kaleidoscope of Canonical and Non-Canonical Functions in Immunity and Cancer. Journal of Hematology & Oncology, 14(1): 198.

[10] Jiang N, Liao Y, Wang M, et al., 2021, BUB1 Drives the Occurrence and Development of Bladder Cancer by Mediating the STAT3 Signaling Pathway. Journal of Experimental & Clinical Cancer Research, 40(1): 378.

[11] Zhao D, Zhang J, Zhang L, et al., 2023, PAFR/Stat3 Axis Maintains the Symbiotic Ecosystem Between Tumor and Stroma to Facilitate Tumor Malignancy. Acta Pharmaceutica Sinica B, 13(2): 694–708.

[12] Hsu YH, et al., 2012, Anti-IL-20 Monoclonal Antibody Suppresses Breast Cancer Progression and Bone Osteolysis in Murine Models. Journal of Immunology, 188: 1981–1991.

[13] Lee SJ, et al., 2013, Interleukin-20 Promotes Migration of Bladder Cancer Cells Through Extracellular Signal-Regulated Kinase (ERK)-Mediated MMP-9 Protein Expression Leading to Nuclear Factor (NF-κB) Activation by Inducing the Up-Regulation of p21WAF1 Protein Expression. Journal of Biological Chemistry, 288: 5539–5552.

[14] Nagakawa H, et al., 2004, Expression of Interleukin-22 in Murine Carcinoma Cells Did Not Influence Tumour

Growth In Vivo but Did Improve Survival of the Inoculated Hosts. Scandinavian Journal of Immunology, 60: 449–454.

[15] Wen Z, et al., 2014, High Expression of Interleukin-22 and Its Receptor Predicts Poor Prognosis in Pancreatic Ductal Adenocarcinoma. Annals of Surgical Oncology, 21: 125–132.

[16] Lim C, Savan R, 2014, The Role of the IL-22/IL-22R1 Axis in Cancer. Cytokine & Growth Factor Reviews, 25: 257–271.

[17] Gao W, Wen H, Liang L, et al., 2021, IL20RA Signaling Enhances Stemness and Promotes the Formation of an Immunosuppressive Microenvironment in Breast Cancer. Theranostics, 11(6): 2564–2580.

[18] Li J, Qin X, Shi J, et al., 2021, A Systematic CRISPR Screen Reveals an IL-20/IL20RA-Mediated Immune Crosstalk to Prevent the Ovarian Cancer Metastasis. eLife, 10: e66222.

[19] He Y, Luo W, Liu Y, et al., 2022, IL-20RB Mediates Tumoral Response to Osteoclastic Niches and Promotes Bone Metastasis of Lung Cancer. Journal of Clinical Investigation, 132(20): e157917.

[20] Siegel RL, Miller KD, Fuchs HE, Jemal A, 2022, Cancer Statistics, 2022. CA: A Cancer Journal for Clinicians, 72(1): 7–33.

[21] He W, Wu J, Shi J, et al., 2018, IL22RA1/STAT3 Signaling Promotes Stemness and Tumorigenicity in Pancreatic Cancer. Cancer Research, 78(12): 3293–3305.

[22] Lu SW, Pan HC, Hsu YH, et al., 2020, IL-20 Antagonist Suppresses PD-L1 Expression and Prolongs Survival in Pancreatic Cancer Models. Nature Communications, 11(1): 4611.

[23] Mizrahi JD, Surana R, Valle JW, Shroff RT, 2020, Pancreatic Cancer. The Lancet, 395(10242): 2008–2020.

[24] Park W, Chawla A, O'Reilly EM, 2021, Pancreatic Cancer: A Review. JAMA, 326(9): 851–862.

[25] Halbrook CJ, Lyssiotis CA, Pasca di Magliano M, Maitra A, 2023, Pancreatic Cancer: Advances and Challenges. Cell, 186(8): 1729–1754.

[26] Strobel O, Neoptolemos J, Jäger D, Büchler MW, 2019, Optimizing the Outcomes of Pancreatic Cancer Surgery. Nature Reviews Clinical Oncology, 16(1): 11–26.

[27] Grodzinski P, Kircher M, Goldberg M, Gabizon A, 2019, Integrating Nanotechnology into Cancer Care. ACS Nano, 13(7): 7370–7376.

[28] Li Z, Yang Z, Liu W, et al., 2023, Disheveled3 Enhanced EMT and Cancer Stem-Like Cells Properties via Wnt/β-Catenin/c-Myc/SOX2 Pathway in Colorectal Cancer. Journal of Translational Medicine, 21(1): 302.

[29] Verstappe J, Berx G, 2023, A Role for Partial Epithelial-to-Mesenchymal Transition in Enabling Stemness in Homeostasis and Cancer. Seminars in Cancer Biology, 90: 15–28.

[30] Garg M, 2017, Epithelial, Mesenchymal and Hybrid Epithelial/Mesenchymal Phenotypes and Their Clinical Relevance in Cancer Metastasis. Expert Review of Molecular Medicine, 19: e3.