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Expression of GALNT5 in Pancreatic carcinoma and its association with clinical and pathological features and prognosis

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SUMMARY: ***Background and Objective:*** *To explore the association between the expression, infiltration of immune cells, mechanism, and prognostic status of peptide N-acetylgalactosaminotransferase 5 (GALNT5) in pancreatic ductal cancer (PDAC) by Bioinformatics, and to verify the association between GALNT5 expression and clinical and pathological features with clinical data, aiming to find a new direction for immunotherapy and prognosis of PDAC clinical cases.* ***Method:*** *(1) Bioinformatics: The association of GALNT5 expression, prognosis, and immune microenvironment in PDAC tumor tissues was analyzed by using transcriptome sequencing data from the TCGA database, GTEx database, and GSE183795 microarray data from the GEO database. (2) Basic experiments: Pancreatic carcinoma microarray was adopted to further immunohistochemistry to verify the expression pattern of GALNT5 protein in PDAC tumor tissues and its association with clinical and pathological features.* ***Results:*** *The findings of bioinformatics demonstrated that GALNT5 was an up-regulated gene in ductal adenocarcinoma tissues (log2FC=2.609, P=0.026) compared with normal pancreatic tissues, and its expression in PDAC tumor tissues was substantially higher than that in non-tumor tissues (P<0.05), the OS (HR=1.6, P=0.038) and DFS (HR=1.8, P=0.012) of clinical cases with high expression of GALNT5 PDAC were lower than those of clinical cases with low expression. The expression of GALNT5 in pathological stage T3/4 was substantially higher than that in the T1/2 stage in PDAC clinical cases (P=0.0049). The prediction of the survival rate of GALNT5 in PDAC clinical cases is low, but the prolonged prognostic survival of PDAC clinical cases is better predicted. The analysis of infiltration of immune cells demonstrated that GALNT5 was negatively correlated with the infiltration levels of activated B cells, naïve CD8 T cells, and effector memory CD4 T cells (P<0.05), while it was positively correlated with NK cells (P<0.05). The findings of the GSEA enrichment analysis demonstrated that GALNT5 may be associated with the cell cycle and TGF-β signaling pathway in PDAC. (2) Immunohistochemistry results: 84 cases of Pancreatic carcinoma and 79 cases of para-tumor tissues were obtained by staining Pancreatic carcinoma tissue chip. The results demonstrated that 65 cases (77.38%) of GALNT5 were highly expressed in PDAC tumor tissues and 42 cases (53.16%) were highly expressed in para-tumor tissues, and the expression of GALNT5 in Pancreatic carcinoma tissues was statistically significant (X^2=10.586, P=0.001). The expression of the GALNT5 gene was not statistically significant with the age, gender, tumor location, tumor stage, T stage, lymph node metastasis, distant metastasis, nerve invasion, differentiation degree, and tumor diameter in PDAC clinical cases (P>0.05). The Kaplan-Meier method was adopted to plot the survival probability curves between the GALNT5 high-expression group and the low-expression group, and the Log-rank test demonstrated that there was no significant difference in OS and DFS survival between the two groups (P=0.256,*

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P=0.29> 0.05). ***Conclusion:*** *GALNT5 is highly expressed in PDAC and is associated with poor prognosis in clinical cases. The mechanism of GALNT5 in PDAC affecting tumorigenesis and development may be associated with immune regulation, cell cycle, and TGF-β signaling pathway. GALNT5 may be a potential therapeutic target or biomarker for PDAC.*

KEYWORDS: *PDAC; GALNT5; Bioinformatics; tumor immune microenvironment; prognosis.*

1 Preface

Pancreatic carcinoma constitutes one of the most aggressive tumors in the digestive system, with a 5-year survival rate of only 13% [1]. According to the latest report from China Cancer Center, in 2022, Pancreatic carcinoma ranked 10th in incidence and 6th in cancer-specific mortality in China [2]. The American Cancer Society reports that Pancreatic carcinoma is is the third most common cause of death in the USA, with an approximate 66,440 newly diagnosed cases and 51,750 deaths in 2024 [3]. Currently, radical resection is considered the only effective method for clinical cases with Pancreatic carcinoma to achieve a cure and long-term survival [4]. However, due to its high malignancy and rapid progression, early clinical symptoms are often non-specific, and most clinical cases are diagnosed at an advanced stage, leading to a radical resection rate of less than 20% [5, 6]. In addition to radical resection, other treatment options for Pancreatic carcinoma include neoadjuvant therapy, adjuvant therapy, targeted therapy, and immunotherapy, which aim to increase the radical resection rate and improve patient outcomes [7, 8]. Research on immunosuppressants has confirmed that PD-1/PD-L1 inhibitors can effectively regulate the tumor immune microenvironment and restore the anti-tumor immune activity of T cells [9, 10]. Research on bone marrow-derived suppressor cells (MDSCs) has shown that targeted inhibition of MDSCs can significantly enhance the anti-tumor efficacy of PD-L1 monoclonal antibodies [11]. Early clinical trials demonstrated that dendritic cell vaccine depending on WT1 peptide and MUC1 antigen could effectively improve the long-term prognosis of clinical cases with postoperative chemotherapy Pancreatic carcinoma (PDAC) [12]. In terms of biomarker research, research depending on glycolysis related score (GRS) model suggests that Pancreatic carcinoma clinical cases with high GRS score usually have worse prognosis [13, 14].

With the continuous development of sequencing technology, tumor genomics research has expanded from tumor cells themselves to the level of tumor microecology, significantly deepening our understanding of tumor biological mechanisms [15, 16]. The GALNT family is a core enzyme class that mediates O-glycosylation modification of mucin type proteins, catalyzing the covalent linkage of N-acetylglucosamine with protein serine/threonine residues, and closely related to the expression of tumor associated carbohydrate antigens such as Tn antigen [17]. The GALNT family plays a key regulatory role in the occurrence and development of various malignant tumors: (1) GALNT6 can promote tumor metastasis by enhancing the level of mucin O-glycosylation [18]; (2) GALNT2 can significantly enhance the invasive ability of colorectal cancer cells [19]; (3) GALNT14 can serve as a potential biomarker for predicting the efficacy of various tumors [20]; (4) The absence of GALNT3 can trigger abnormal O-glycosylation modification of ErbB family proteins, which in turn affects tumor cell proliferation and therapeutic response [21]; (4) The feature model constructed depending on GALNTs can serve as a novel prognostic biomarker for low-grade gliomas [22].

GALNT5 is a member of the GALNT glycosyltransferase family, with its coding gene located on chromosome 2q24.1. The expressed product is N-acetylglucosamine transferase 5 (NAGT5), which catalyzes the initial step of O-glycosylation of mucin type. In various tumors,

GALNT5 shows a significant upregulation trend in tumor tissues and can promote tumor cell proliferation and metastasis. In cholangiocarcinoma, high expression of GALNT5 is closely related to tumor occurrence and development. Silencing GALNT5 can significantly reduce VBG expression and inhibit the proliferation, migration, and invasion ability of cholangiocarcinoma cells. Inhibition of GALNT5 can weaken the proliferation and migration ability of pancreatic adenocarcinoma (PAAD) cells, and induce ferroptosis of tumor cells.

The aim of this work is to systematically elucidate the association between GALNT5 expression levels and the immune microenvironment, clinical pathological characteristics, and prognosis of Pancreatic carcinoma (PDAC) clinical cases, in order to provide new theoretical basis and potential strategies for the clinical prognosis evaluation and targeted therapy of PDAC.

2 Materials and Methods

2.1 Research Data

Using the Cancer Genome Atlas (TCGA) database (https://portal.gdc.cancer.gov), we collected transcriptome data from 178 PAAD tumor samples and 4 normal tissue samples. We analyzed the transcriptome and proteome data from the TCGA, GEO, and GTEx databases using R language software (version 4.4.1), the GEPIA data platform, the STRING database, and cytoscape software.

2.2 Differential Expression and Prognostic Analysis of GALNT5

Using the GEPIA data platform, which is depending on data from the TCGA and GTEx databases, the study analyzes the expression of GALNT5 in PDAC tumor tissues and non-tumor tissues, as well as the prognostic analysis of high and low GALNT5 expression groups. GEPIA (Gene Expression Profiling Interactive Analysis) is an efficient and feature-rich online tool for gene expression analysis. It provides deep visualization of gene expression data from the TCGA and GTEx databases, including differential expression analysis between cancer and non-tumor tissues, pathological staging analysis, and patient survival analysis.

2.3 Protein-Protein Interaction Network

Depending on the median expression levels of GALNT5, tumor samples in the TCGA database were divided into high and low expression groups for differential gene analysis. Genes with logFC values of 2 and $P<0.05$ were selected as differentially expressed genes to investigate the protein interactions among these genes. During the analysis, a confidence threshold of 0.7 was set, and the network was visualized using Cytoscape software (version 3.9.1).

2.4 Genetic enrichment analysis

This study used the median expression level of GALNT5 to categorize tumor samples in the GEO database into high and low expression groups. Differential expression analysis was conducted using R, with logFC set to 1 and $P<0.05$ as the criteria for identifying differentially expressed genes. The identified genes were then subjected to Gene Ontology (GO) enrichment analysis and Gene Set Enrichment Analysis (GSEA) using R.

2.5 Immunohistochemical Staining

Immunohistochemical staining was performed by Dako's fully automated immunohistochemical staining system.

2.5.1 Immunohistochemical Staining Protocol

(1) Wax removal: The Pancreatic carcinoma tissue was placed in an oven for 63℃ of wax removal for 1 h. Then, the tissue chip was placed in an automatic staining machine for xylene 2 cylinders, each for 15 min; 100% alcohol 2 cylinders, each for 7 min; and 90% alcohol, 80% alcohol, and 70% alcohol each for 5 min.

(2) Antigen repair: put the slide into the antigen repair instrument, select the program and start the repair. After the repair is complete, put it in distilled water at room temperature and let it cool naturally for more than 10 min.

(3) Primary antibody incubation: PBS buffer was washed; GALNT5 primary antibody was diluted at 1:200, added to the primary antibody, and incubated overnight in 4℃ refrigerator;

(4) Secondary antibody incubation: remove the slide from the refrigerator, reheat at room temperature for 45 min, and clean the slide with PBS buffer;

(5) The slide was placed in DAKO fully automatic immunohistochemistry instrument, and the corresponding program was selected according to "Autostainer Link 48 User Guide" to run blocking, secondary antibody binding and DAB coloring programs;

(6) Sulfanilamide re staining: Sulfanilamide staining for 1 min, immersed in 0.25% hydrochloric acid alcohol (400ml70% alcohol +1ml concentrated hydrochloric acid) for about 10s, and rinsed with tap water for 5 min.

(12) Mounting: the slide is dried at room temperature and mounted with neutral resin;

(13) Microscopic observation and photography;

(14) Image collection, staining and scoring were combined with clinical data for statistical analysis.

2.5.2 Immunohistochemical Staining Scoring Systems

The immunohistochemical staining score was performed by senior physicians in the Department of Pathology at XXXXX Hospital. The scoring follows: When performing immunohistochemical staining scoring on tumor cells under an optical microscope, the final staining score is determined by multiplying the proportion of tumor-positive cells (A) by the staining intensity score (B) (A×B), as follows:

(1)Tumor positive cell percentage score (A) is classified into five levels depending on the proportion of positive cells. Specifically, a score of 0 is awarded when the proportion of positive cells is ≤5%; 1 for 6% to 25%; 2 for 26% to 50%; 3 for 51% to 75%; and 4 for>75%.

(2)Staining intensity score (B): According to the degree of coloration of positive cells in the pathological section, it was divided into four grades. No coloration was rated as 0 points; light yellow was rated as 1 points; brown yellow was rated as 2 points; brownish brown was rated as 3 points.

(3)The final staining score is obtained by multiplying the above two scores, that is, A x B, and the total score of this product is 12 points. When A x B> 6 points, it is judged as high expression; when A x B ≤ 6 points, it is judged as low expression.

2.6 Statistical analysis

All statistical analyses were conducted using R language software (version 4.4.1), the GEPIA data platform, and the SPSSAU online analysis platform. For normally distributed data, the mean ± standard deviation was used, and t-tests were employed for inter-group comparisons. For non-normally distributed data, the median (Q) was used, and rank-sum tests were used for inter-group comparisons. For categorical data, the number of cases or percentage (n%) was used, and chi-square tests or Fisher exact probability methods were employed.

3 Results

3.1 Differential Analysis Between PDAC Tumor tissues and Non-tumor tissues

The transcriptome expression data were divided into two groups: Pancreatic carcinoma (PDAC) tissue and normal tissue, for differential analysis. The differential gene (DEG) screening was conducted using log2FC = 1 and P <0.05 as criteria, and a volcano plot (Figure 2) was created. The log2FC of GALNT5 was found to be 2.609, with an Adjusted P value of 0.026, indicating a significant expression difference between the two groups. These results indicate that the GALNT5 gene is upregulated in PDAC tissue relative to normal tissue.

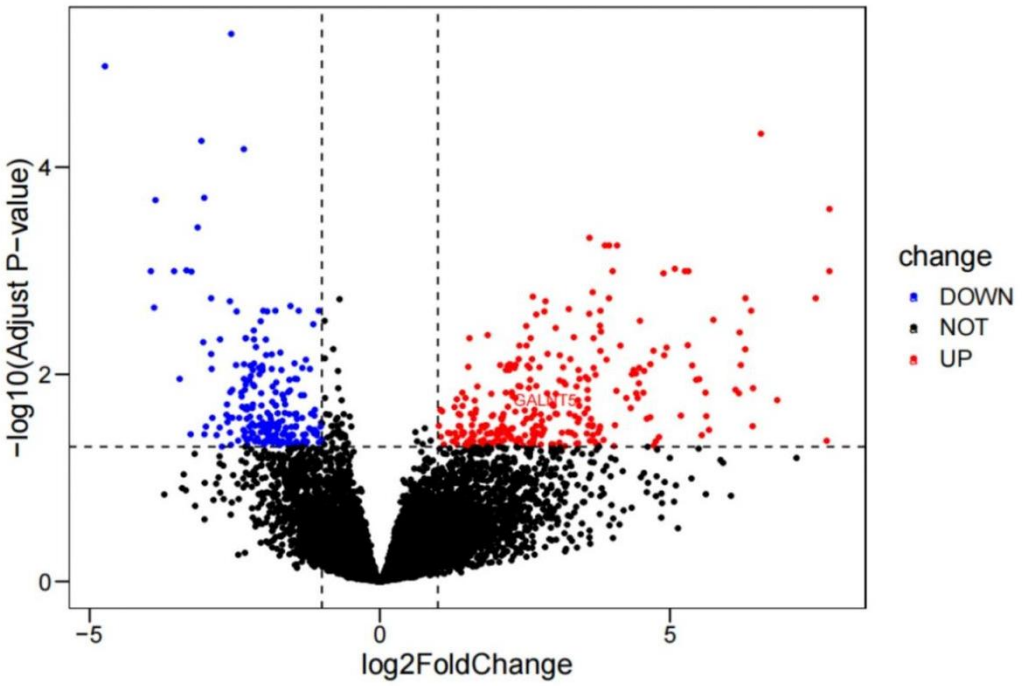

Figure 2: Volcano diagram of differential genes between cancer and non-tumor tissues

3.2 Expression in Tumor and Non-tumor tissues and Prognostic Significance

GALNT5 is an upregulated gene in Pancreatic carcinoma (PDAC) tissues. According to the GEPIA search results, the TCGA and GTEx databases collectively contain 179 PDAC cancer tissue samples and 171 normal pancreatic tissue samples. The analysis revealed that GALNT5 expression levels in PDAC tumor tissues are substantially higher than in non-tumor tissues (Figure 3A). Further analysis explored the relationship between GALNT5 expression levels and the overall survival (OS) and disease-free survival (DFS) of PDAC clinical cases. The study found that the OS and DFS of pancreatic ductal adenocarcinoma patients in the GALNT5 high expression group were significantly shortened relative to the low expression group (HR=1.6, P=O.O38, HR=1.8, P=0.013, Figure 3B, C)

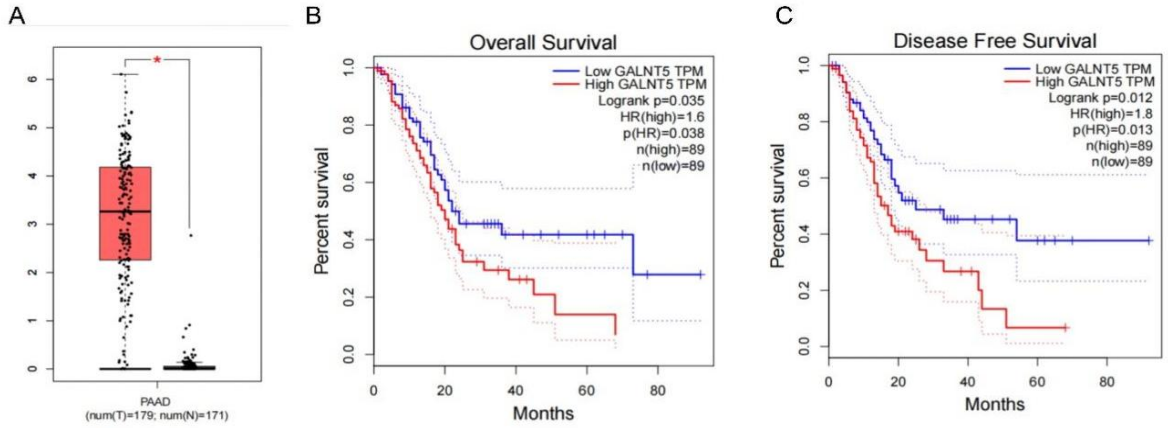

Figure 3: Expression and prognosis of GALNT5 gene. A: Expression of GALNT5 in PDAC tissues and non-tumor tissues; B: OS survival curve of GALNT5 expression; C: DFS survival curve of GALNT5 expression

3.3 Survival Prediction Efficacy of GALNT5 Expression

We conducted a survival rate prediction evaluation and plotted the corresponding ROC curve. The results indicate that the OS for PDAC clinical cases has a low predictive power (AUC=0.613) (Figure 4A). Additionally, as the prognostic survival of PDAC clinical cases increases, the prediction accuracy for patient survival rates improves (Figure 4B).

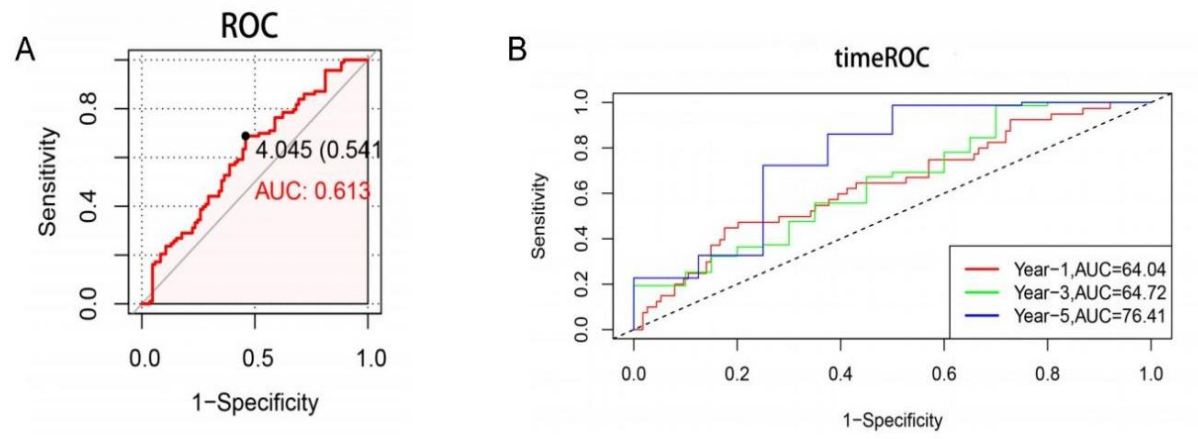

Figure 4: ROC curve of OS assessment. A: ROC curve of GALNT5 and total OS of clinical cases; C: TimeROC curves of GALNT5 versus 1-year, 3-year, and 5-year OS of clinical cases

3.4 Protein interaction network

To explore the core genes associated with GALNT5, the median expression level of GALNT5 (M=4.315) was adopted to divide the PDAC gene expression dataset. The results indicate that the core genes associated with GALNT5 in PDAC include CPA1, CELA3A, CEL, SNAP25, CTRB1, PNLIP, CTRB2, CLPS, and ALB (Figure 5).

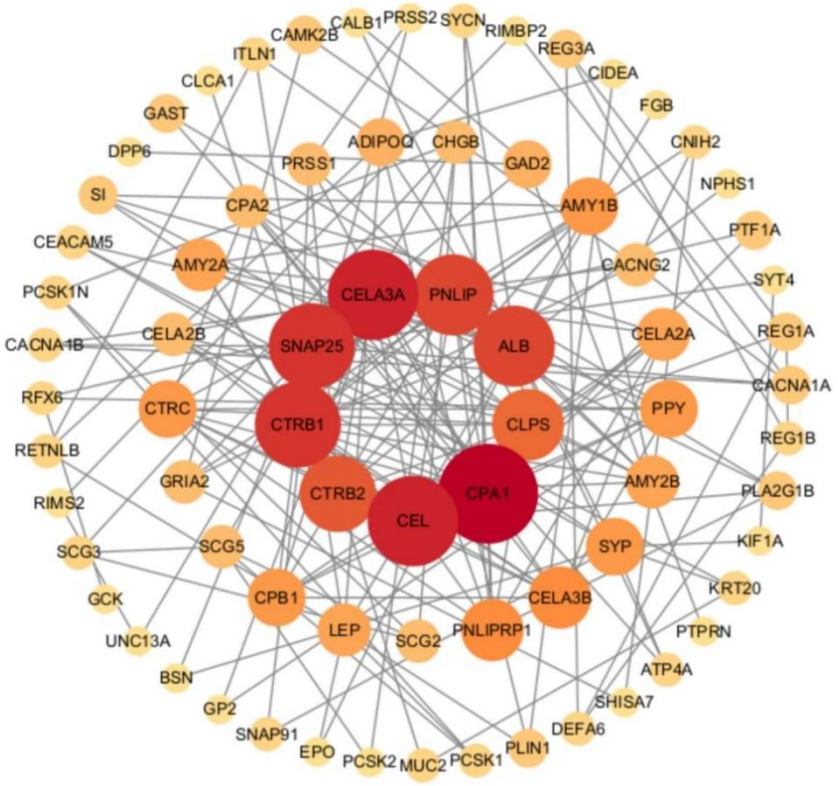

Figure 5: Protein-protein interaction network analysis of GALNT5

4 Gene Set Enrichment Analysis

To further elucidate the role of GALNT5 in the development and progression of PDAC and the signaling pathways involved, the PDAC gene expression dataset from the GSE183795 database was divided into a low-expression group (70 samples) and a high-expression group (69 samples) depending on the median expression level of GALNT5 (M=7.00). Gene expression differential analysis was conducted using log2FC = 1 and P <0.05 as screening criteria to identify differentially expressed genes. These genes were then analyzed using R for GO enrichment and GSEA enrichment. The GO function results (Figure 6A) show that biological processes (BP), cellular components (CC), and molecular functions (MF) were enriched separately. BP was mainly enriched in cell matrix adhesion, cell basal adhesion, tissue homeostasis anatomical structure homeostasis, and epithelial structure maintenance. CC was mainly enriched in the apical part of cells, apical plasma membrane, cell base, and basolaminal membrane. MF was mainly enriched in endopeptidase activity, serine endopeptidase activity, serine peptidase activity, and serine hydrolase activity. The GSEA results demonstrated that the high-expression samples of GALNT5 were enriched in apoptosis, cell cycle, and TGF-β signaling pathway (Figures 6B, C).

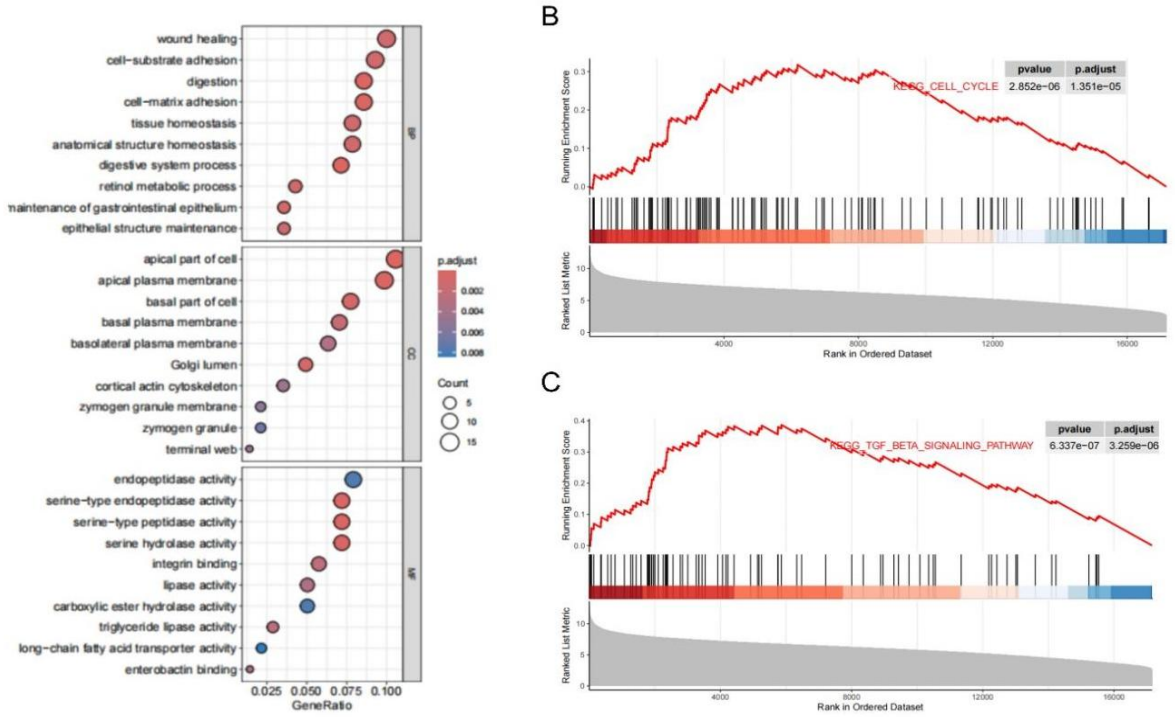

Figure 6: GALNT5 GO and GSEA enrichment analysis. A: GO enrichment analysis; B: KEGG_CELL_CYCLE; C: KEGG_TGF_BETA_SIGNALING_PATHWAY

5 Signal pathway analysis

GALNT5 is potentially linked to the cell cycle and the TGF-β signaling pathway. The results demonstrated that GALNT5 is positively correlated with cell cycle-promoting proteins such as CDK1, SFN, CDC25C, MAD2L1, and BUB1 (Figure 7A). It is also positively correlated with TGF-β signaling pathway-promoting proteins like BMP2, BMP4, and RHOA, but negatively correlated with TGF-β signaling pathway-inhibiting proteins such as MYC, LEFTY1, and LEFTY2 (Figure 7B).

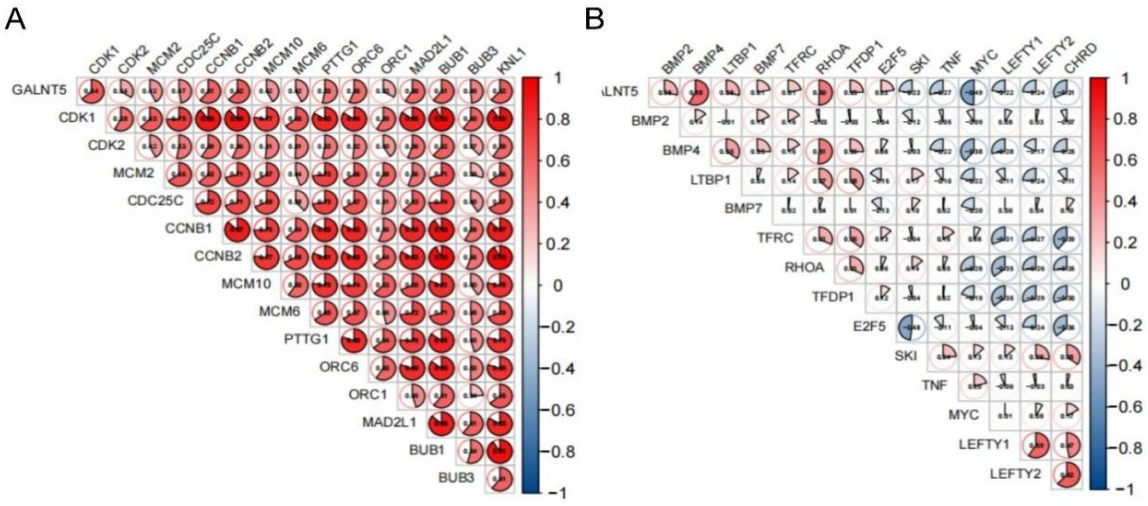

Figure 7: Association heat map of GALNT5 with mechanism. A: KEGG_CELL_CYCLE; B: KEGG_TGF_BETA_SIGNALING_PATHWAY

6 Tumor Immunological Characteristics Analysis

6.1 Tumor Immune Microenvironment (TIME) Scoring

In the tumor immune microenvironment (TIME) of PDAC, the remodeling of the extracellular matrix makes it difficult for tumor cells to interact with immune cells, thereby limiting the migration and infiltration of immune cells into the tumor region [23]. The results show that relative to the GALNT5 low-expression group, the GALNT5 high-expression group has substantially higher tumor purity and a relatively lower proportion of stromal cells and immune cells (Figure 8). This difference may be associated with the remodeling of the tumor stromal microenvironment, which in turn affects the tumor's invasiveness and immune escape ability. Therefore, the high expression of GALNT5 may weaken the anti-tumor effects of immune cells by altering the cellular composition of the tumor stromal microenvironment, potentially becoming one of the key factors contributing to poor patient outcomes.

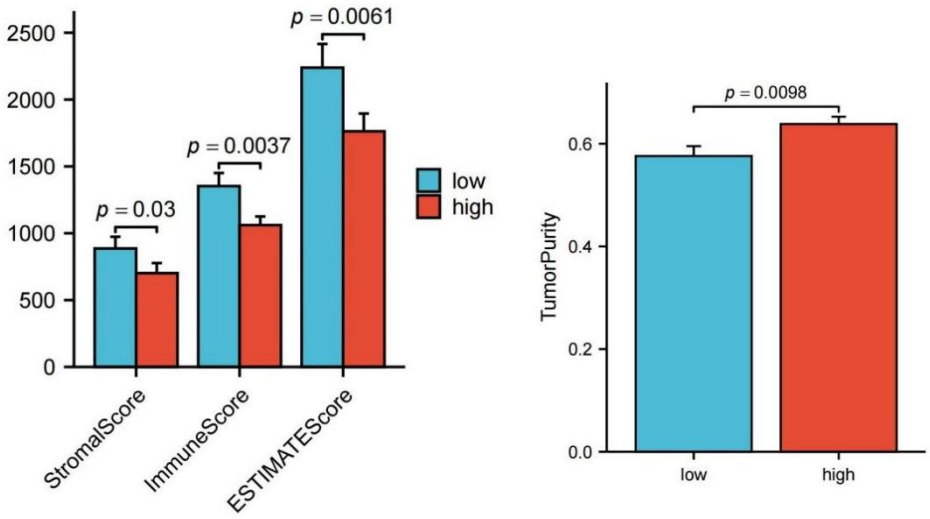

Figure 8: Immune score and tumor purity analysis of high and low expression groups

6.2 Infiltration of immune cells Level

The previous analysis indicates that high GALNT5 expression is associated with lower immune components in TIME, but the specific immune cells involved remain unknown. The infiltration of CD56dim natural killer (NK) cells was relatively higher in the GALNT5 high-expression group (Figure 9A). Further association analysis demonstrated that GALNT5 is negatively correlated with activated B cells, naive CD8 T cells, and effector memory CD4 T cells, while it is positively correlated with CD56dim natural killer (NK) cells (Figure 9B-E).

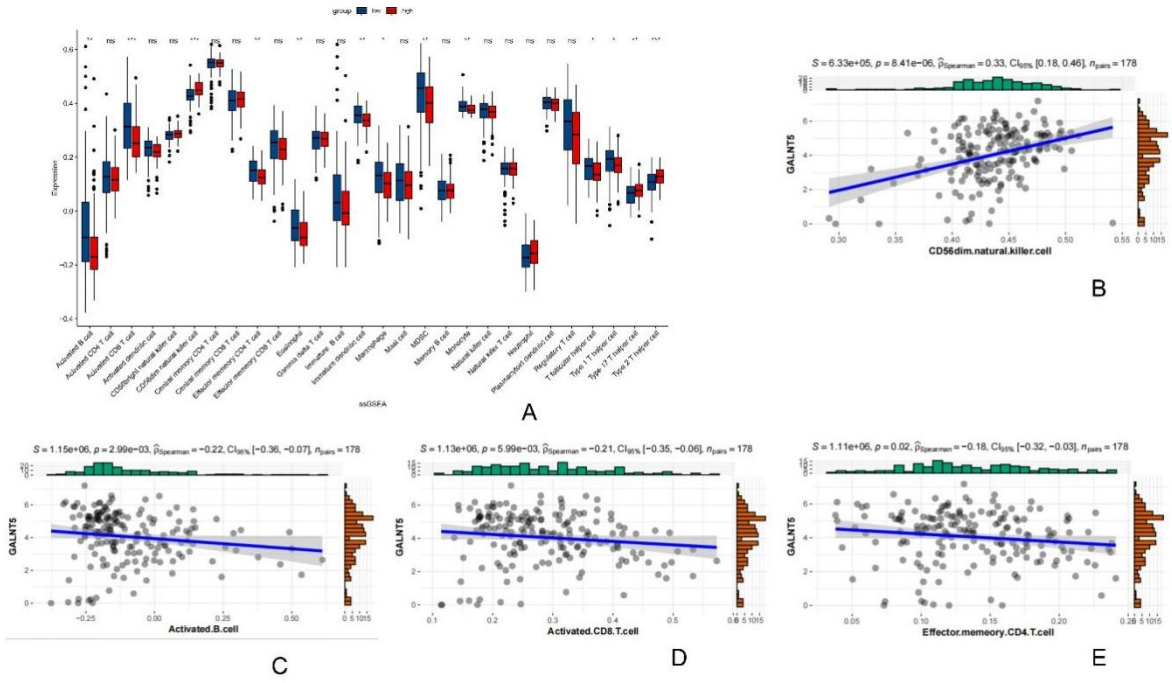

Figure 9: GSVA and association analysis. A: Analysis of the infiltration degree of high and low expression of GALNT5 in 28 immune cells; B: Association between GALNT5 and NK cells; C: Association of GALNT5 with activated B cells; D: Association between GALNT5 and naïve CD8 T cells; E: Association of GALNT5 with effector memory CD4 T cells

7 Immunohistochemical (IHC) Results

7.1 Expression Level of GALNT5 in Pancreatic carcinoma (PDAC)

This study conducted immunohistochemical staining and scoring on Pancreatic carcinoma tissue chips, ultimately identifying qualified pathological sites: 84 cases of Pancreatic carcinoma (PDAC) and 79 cases of para-tumor tissues. The results demonstrated that in PDACs, GALNT5 positive expression was mainly found in the cytoplasm (Figure 10). Among the 84 PDACs, 65 cases (77.38%) had high GALNT5 expression, while 19 cases (22.62%) had low expression. In the 79 para-tumor tissues, 42 cases (53.16%) had high GALNT5 expression, and 37 cases (46.84%) had low expression. The difference in GALNT5 expression between PDACs and para-tumor tissues was statistically significant (X2=10.586, P=0.001) (Table 1).

Table 1: Expression of GALNT5 in PDAC and para-tumor tissues

	N(case)	GALNT5 Highexpression	GALNT5 Lowexpression	X^2	p-value
CTs[n(%)]	84	65(77.38)	19(22.62)	10.586	0.001
Cancerous tissue[n(%)]	79	42(53.16)	37(46.84)		

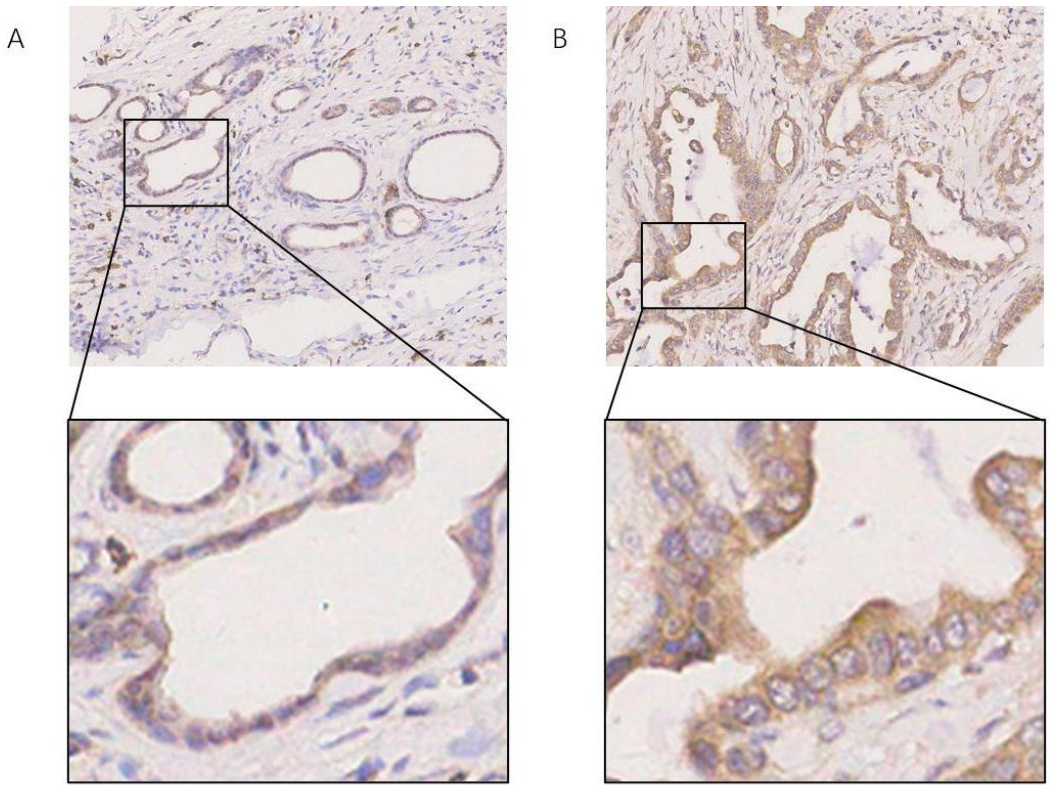

Figure 10: IHC image of GALNT5 in paracancerous tissue and PDAC tissue (2000x). A: paracancerous tissue; B: cancer tissue

7.2 GALNT5 expression in pancreatic cancer

The immunohistochemical results of Pancreatic carcinoma were analyzed with the clinical and pathological characteristics of clinical cases in the chip, suggesting that the expression of GALNT5 gene was not correlated with age, sex, tumor location, tumor Stage, T stage, lymph node metastasis, distant metastasis, neural infiltration, differentiation degree and tumor diameter ($P>0.05$) (Table 2).

Table 2: Relationship between GALNT5 expression and clinical and pathological features in PDAC

	Examples (n)	Expression levels of GALNT5 protein		X^2	p-value
		Low expression	High expression		
Gender[n(%)]				2.200	0.138
man	52	9(17.31)	43(82.69)		
woman	32	10(31.25)	22(68.75)		
Age(year) [n(%)]				0.247	0.619
>60	44	9(20.45)	35(79.55)		
≤60	40	10(25.00)	30(75.00)		
Location of the tumor				0.001	0.980
head of pancreas	40	9(22.50)	31(77.50)		
Non-head of the pancreas	44	10(22.73)	34(77.27)		
Tstages[n(%)]				0.611	0.434
T1/2	51	13(25.49)	38(74.51)		
T3/4	33	6(18.18)	27(81.82)		
lymphatic metastasis [n(%)]				1.549	0.213
None	47	13(27.66)	34(72.34)		
have	37	6(16.22)	31(83.78)		
It's moving away in the distance[n(%)]				1.661	0.197
None	69	18(26.09)	51(73.91)		
have	15	1(6.67)	14(93.33)		
Stage				1.666	0.197
I/II	56	15(26.79)	41(73.21)		
III/IV	28	4(14.29)	24(85.71)		

Table 2: Relationship between GALNT5 expression and clinical and pathological features in PDAC (continued table)

	Examples(n)	Expression levels of GALNT5 protein		X^2	p-value
		Low expression	High expression		
Nerve infiltration				3.565	0.059
None	51	8(15.69)	43(84.31)		
have	33	11(33.33)	22(66.67)		
Tumor diameter				0.034	0.854
>4	28	6(21.43)	22(78.57)		
≤4	56	13(23.21)	43(76.79)		
Degree of differentiation				0.006	0.937
Moderate to high differentiation	68	16(23.53)	52(76.47)		
poorly differentiated	16	3(18.75)	13(81.25)		

7.3 Impact of GALNT5 Expression Level on Prognosis in Pancreatic carcinoma

Kaplan Meier method was adopted to plot the survival probability curves of clinical cases with overexpressed and under expressed of GALNT5. The results of the log rank test showed that there was no significant statistical difference in the overall survival (OS) and disease-free survival (DFS) prognosis survival rates between the two groups of patients (P=0.256, P=0.29, both P>0.05).

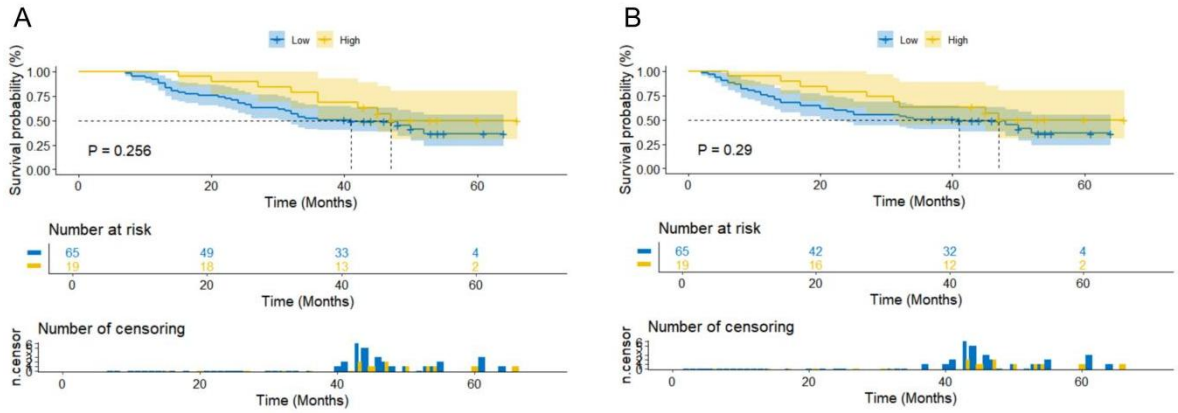

Figure 11: Survival probability curves of clinical cases with Pancreatic carcinoma in tissue microarray. A: OS B: DFS

8 Discussion

Pancreatic carcinoma often presents with abdominal pain as its initial symptom, characterized by high malignancy, rapid progression, and a poor prognosis, accounting for about 10% of all gastrointestinal cancers[24]. It is also known as the 'king of cancers.' With advancements in treatment concepts and models, as well as the continuous development of new technologies, the shift from open to minimally invasive Pancreatic carcinoma surgery has significantly improved tumor resection rates and perioperative safety[25]. However, despite these advancements, the potential for surgical methods to improve long-term patient outcomes remains limited[26]. Therefore, current research should focus on breakthroughs in early diagnosis, targeted therapy, and immunotherapy. Future research should aim to identify new therapeutic targets in the field of targeted therapy for Pancreatic carcinoma.

This study systematically analyzed the expression characteristics, infiltration of immune cells levels, molecular regulatory mechanisms, and clinical prognostic value of GALNT5 in Pancreatic carcinoma (PDAC) tissues. GALNT5 showed a significant upregulation trend in PDAC tissues relative to normal pancreatic tissues. High expression of GALNT5 was significantly correlated with poor prognosis in PDAC clinical cases, and its predictive power for survival outcomes gradually improved with prolonged follow-up time. Immunohistochemistry and clinical pathological analysis have confirmed that there is a statistically significant difference in the 3-year survival rate between clinical cases with high and low expression of GALNT5, with substantially higher survival rates in the low expression group. GALNT5 may play a key role in promoting the development of PDAC and has potential value as an independent prognostic marker for PDAC.

Depending on the STRING database, GALNT5 interaction core genes were screened, and it has been confirmed that CPA1 can be used as a diagnostic marker of pancreatic acinar cell

carcinoma [27], and may promote the occurrence and development of Pancreatic carcinoma by inducing pancreatic cell endoplasmic reticulum stress [28]; SNAP25 can enhance the proliferation, migration, and invasion ability of non-small cell lung cancer cells by activating the MEK/ERK signaling pathway [29]; SYT4 can bind with SNAP25 to promote vesicle exocytosis, thereby mediating the resistance of prostate cancer cells to enzalutamide [30]; CTRB1 is associated with the risk of Pancreatic carcinoma, and its abnormal expression may affect the disease process [31].

The GO enrichment analysis indicates that BP is primarily enriched in cell matrix adhesion, cell basement adhesion, tissue homeostasis, and epithelial structure maintenance. These processes suggest that tumor cells may undergo epithelial-mesenchymal transition and enhanced adhesion, which can promote tumor cell invasion and immune evasion. CC is mainly enriched in the cell apex, apical plasma membrane, cell base, and basal plasma membrane. The enrichment of CC suggests that it may be associated with changes in cell polarity. MF is primarily enriched in endopeptidase activity, serine endopeptidase activity, serine peptidase activity, and serine hydrolase activity. Tumor cells can degrade and remodel the extracellular matrix components by secreting endopeptidases, creating favorable conditions for their invasion and metastasis. Serine enzymes may interfere with the recognition and attack of tumor cells by immune cells by regulating the expression of cell surface molecules, thereby helping tumor cells evade immune surveillance. The enrichment of cell matrix adhesion and endopeptidase activity suggests that there may be matrix remodeling in the tumor stromal microenvironment, which could affect the infiltration of immune cells, consistent with the lower proportion of immune cells in the microenvironment mentioned earlier. GSEA enrichment analysis revealed that GALNT5 plays a role in the cell cycle and TGF-β signaling pathways within PDAC. Further association analysis demonstrated that GALNT5 is positively correlated with proteins that promote the cell cycle and TGF-β signaling pathway, and negatively correlated with proteins that inhibit this pathway. This suggests that GALNT5 may promote tumor cell proliferation by activating cell cycle-related proteins, and may inhibit immune cell activity or promote the epithelial-mesenchymal transition of tumor cells, leading to tumor metastasis by affecting the TGF-β signaling pathway.

In summary, this study utilized a public database to identify the high expression of GALNT5 in PDAC and confirmed its high expression in Pancreatic carcinoma (PDAC) through immunohistochemistry (IHC). The analysis of immunohistochemical results and clinical pathological data demonstrated that there was a statistically significant difference in 3-year survival rates between clinical cases with high and low GALNT5 expression, with the low-expression group showing a higher survival rate. However, no significant association was found between GALNT5 expression and factors such as gender, age, tumor location, tumor size, TNM stage, neural invasion, or prognostic survival. This may be due to the small sample size and the use of polyclonal antibodies in immunohistochemistry, which requires further expansion of the clinical sample size and the use of monoclonal antibodies for further experimental research. Additionally, this study has some limitations. While it used bioinformatics analysis and immunohistochemistry to explore the mRNA and protein levels of GALNT5 in PDAC, it lacked further validation through Western blotting, RT-qPCR, and cell function experiments. The potential mechanisms of GALNT5 in PDAC are only preliminarily explored and lack experimental verification, necessitating further research.

9 Conclusion

GALNT5 is highly expressed in PDAC, which is a risk factor for PDAC prognosis and is

associated with poor PDAC prognosis. Its mechanism in PDAC may be associated with immune infiltration, cell cycle, and TGF-β signaling pathway. GALNT5 may become a potential therapeutic target or biomarker for PDAC.

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