

High Intelectin-I Expression Associated with Aggressive Tumor Behavior and Worse Survival in Rectal Cancer

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Background: Multimodal treatment involving preoperative chemoradiotherapy (CRT) followed by surgery is the current standard of care for rectal cancer. Despite advancements, the risk of recurrence, metastasis, and decreased survival remains high. This study aims to evaluate potential biomarkers to stratify prognosis in patients with rectal cancer undergoing preoperative CRT and surgery.

Methods: Through data mining of receptor-binding pathways in a published transcriptome for rectal cancer cases, ITLN1 was identified as the most relevant gene associated with poor response to chemoradiation (GO:0005102). Rectal cancer specimens (n = 343) collected between 1998 and 2017 were analyzed for ITLN1 expression using immunohistochemistry. The association between ITLN1 protein expression and clinicopathological features was assessed using Pearson's chi-square test. Survival outcomes based on ITLN1 expression were evaluated using the Kaplan–Meier method and compared with Log rank tests.

Results: ITLN1 immunoreactivity was significantly elevated in rectal tumor tissues. High ITLN1 expression was strongly associated with adverse clinicopathological features, including advanced post-treatment tumor status (T3–4; p = 0.001), post-treatment nodal status (N1–2; p < 0.001), vascular invasion (p = 0.017), perineural invasion (p = 0.001), and a lower degree of tumor regression (p = 0.009). Uni- and multivariable analyses revealed that high ITLN1 expression correlated with poorer disease-specific survival, local recurrence-free survival, and distant metastasis-free survival compared to low ITLN1 expression.

Conclusion: Elevated ITLN1 expression is significantly associated with aggressive tumor behavior and unfavorable survival outcomes in rectal cancer. These findings highlight ITLN1 as a potential prognostic biomarker and provide a foundation for future research into its role in rectal cancer progression and treatment response.

Keywords: ITLN1, rectal cancer, chemoradiotherapy, regression, survival

Introduction

Colorectal cancer remains one of the most common malignancies worldwide, ranking as the third leading cause of cancer-related deaths globally.¹ Despite standardized treatment protocols, which include preoperative chemotherapy and radiation followed by surgery, patients continue to face significant risks, with recurrence and metastasis rates ranging between 10% and 20%.^{2,3} Identifying prognostic biomarkers using modern genetic databases could help clinicians tailor therapeutic strategies to improve patient outcomes and prolong survival.

In this study, we conducted an analysis of a publicly available transcriptomic dataset for rectal cancer (GSE35452) sourced from the Gene Expression Omnibus at the National Center for Biotechnology Information (GEO, NCBI, Bethesda, MD, USA). Our analysis identified intelectin-1 (ITLN1) as the most significantly upregulated gene associated with receptor binding (GO:0005102). ITLN1, also known as omentin-1, is a galactose-binding lectin typically expressed in the heart, small intestine, and colon.^{4,5} Its expression often increases during gastrointestinal infections, and recent studies suggest its involvement in carcinogenesis across various cancer types.^{6–9} In colorectal cancer research, Katsuya et al demonstrated that ITLN1 plays a role in tumor suppression, with its retention associated with a more favorable prognosis.¹⁰ Conversely, Feng et al reported that elevated plasma ITLN1 levels in a cohort of 319 colorectal cancer patients correlated with higher recurrence rates and poorer survival outcomes.¹¹ Despite these findings, the clinical relevance of ITLN1 expression in rectal cancer patients undergoing preoperative chemoradiotherapy (CRT) has not yet been established.

To address this gap, we investigated ITLN1 expression in 343 tissue samples from rectal cancer patients treated with preoperative CRT. We explored its correlation with clinicopathological parameters, tumor regression grade, and survival outcomes.

Materials and Methods

Ethics Approval and Consent to Participate

This study followed the Declaration of Helsinki (revised in 2013) and was approved by Chi Mei Medical Center (IRB: CMFHR10801-001). All patients provided their written informed consent.

Analysis of the Published Transcriptome Dataset

To identify genes predictive of response to preoperative CRT, we analyzed data from a publicly available transcriptome database comprising 46 rectal cancer patients (GSE35452; GEO, NCBI, Bethesda, MD, USA). Gene expression profiles were generated using Affymetrix Human Genome U133 Plus 2.0 arrays and analyzed with Nexus Expression 3 statistical software (BioDiscovery, Hawthorne, CA, USA) without preselection. Tumors were classified as either “responders” or “non-responders”, focusing on genes associated with receptor binding (GO:0005102). Genes meeting the criteria of a p -value < 0.01 and a log2-transformed expression difference of at least ± 0.1 -fold were selected for further analysis. Further survival analysis was performed to assess the prognostic significance of this gene.

Patient Clinicopathological Characteristics

We retrospectively analyzed tissue specimens from 343 patients newly diagnosed with rectal adenocarcinoma. These patients were treated at Chi Mei Medical Center between 1998 and 2017, with follow-up extending until December 31, 2022. Tumor staging was performed according to the 7th edition of the American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) system, utilizing diagnostic methods such as endoscopic ultrasound, abdominal computed tomography, and magnetic resonance imaging. Patients with disease classified as clinical stage T3 or N1 or higher received preoperative CRT consisting of 5-fluorouracil-based chemotherapy combined with radiotherapy. Following surgical resection, patients underwent regular post-treatment monitoring until death or their last follow-up appointment.

Histopathologic Evaluation and Immunohistochemistry

Histological assessment of tumor specimens was independently performed by two pathologists, Dr. Li and Dr. Chen. To ensure unbiased evaluation, these assessments were conducted without access to any patient-related information. Tumor

response to preoperative CRT was assessed using the standardized 5-point tumor regression grading system described by C Rödel et al^{12,13}. Tumor shrinkage status were categorized as follows: grade 0 for no observed regression; grade 1 for minor regression (dominant tumor mass with fibrosis in 25% or less of the tumor mass); grade 2 for moderate regression (fibrosis in 26% to 50% of the tumor mass); grade 3 for good regression (fibrosis outgrowing the tumor mass, indicating more than 50% tumor regression); and grade 4 for total regression (no viable tumor cells, only fibrotic tissue).

For immunohistochemical analysis, initial tumor biopsy specimens underwent routine deparaffinization, rehydration, heating, quenching, and epitope retrieval, following previously described protocols. Tissue sections were then incubated for one hour with a primary antibody specific to ITLN1 (ab118232). Detection of ITLN1 immuno-expression was performed using a secondary antibody, followed by hematoxylin counterstaining. The level of ITLN1 protein expression was quantified using the H-score method, calculated as: $H\text{-score} = \sum P_i (i + 1)$, where P_i represents the percentage of tumor cells stained at varying intensities (0% to 100%), and i denotes the immunostaining intensity (0 to 3+). ITLN1 expression levels were classified as high (equal to or above the median H-score) or low (below the median H-score).

Statistical Analysis

All statistical analyses were conducted using SPSS version 22.0 (IBM Corporation, Armonk, NY, USA), with a p-value < 0.05 considered statistically significant. The primary endpoints of the study included 5-year disease-specific survival (DSS), local recurrence-free survival (LRFS), and metastasis-free survival (MeFS) rates. Survival time was defined as the interval from the date of diagnosis to the last follow-up, recurrence, metastasis, or death. Events were classified as valid if deaths were cancer-related, while deaths from other causes were treated as censored in the analysis. Associations between ITLN1 expression and clinicopathological features were assessed using the chi-square test. Survival outcomes were analyzed using the Kaplan–Meier method, with comparisons made via Log rank tests. Multivariable analyses were performed using Cox proportional hazards regression to identify independent prognostic factors.

Results

Up-Regulation of ITLN1 Gene Expression Associated with Poor Response to CRT

Through the analysis of gene expression levels in the public dataset GSE35452, which includes 46 rectal cancer cases treated with CRT, we focused on probes targeting genes involved in receptor-binding pathways (GO:0005102). Comparative analysis between responder and non-responder groups identified ITLN1 as significantly correlated with inadequate response to CRT, demonstrating a pronounced log₂-transformed fold difference in expression. These findings suggest that high ITLN1 expression in rectal cancers predicts poor response to CRT treatment, making it a compelling candidate for further analysis (Table 1; Figure 1).

Demographics of Study Population

The patient and tumor variables of the 343 enrolled patient are summarized in Table 2. The cohort included 223 (65%) males and 120 (35%) females, with a median age of 64 years (range, 22–88 years). The pre-treatment tumor was advanced (T3–4) in 210 patients (61.2%), and 144 patients (41.9%) had nodal status (N1–2). Vascular or perineurial invasion was observed in 38 patients (10.8%). Following the resection of tumor specimens post chemoradiotherapy (CRT), the observed responses were categorized as poor (Tumor Regression Grade, TRG 0–1, indicating less than 25% response) in 73 patients (21.3%), moderate (TRG 2–3) in 248 patients (72.3%), and complete (indicating no visible tumor in the rectal wall; TRG 4) in 22 patients (6.4%).

Association Between ITLN1 Expression and Clinicopathological Factors

To further investigate the clinical significance of ITLN1 expression in rectal cancers, we used immunohistochemical staining to determine its expression levels in a valid cohort (N=343). Immunohistochemical staining of ITLN1 was performed and scored, with H-scores varying from 105 to 320 (median, 200) (Figure 2). High ITLN1 expression was significantly related to post-treatment tumor status (T3–4; $p = 0.001$), post-treatment nodal status (N1–2; $p < 0.001$),

Table I Summary of Differentially Expressed Genes Associated with Receptor Binding (GO: GO:0005102) in Relation to Response to CCRT in Rectal Carcinoma

Probe	Log ratio	P-value	Gene Symbol	Gene Name	Biological Process	Molecular Function
223597_at	1.3196	0.0094	<i>ITLN1</i>	intelectin 1 (galactofuranose binding)	signal transduction	GPI anchor binding, receptor binding, sugar binding
206422_at	1.2432	0.0065	<i>GCG</i>	glucagon	G-protein coupled receptor protein signaling pathway, cell proliferation, feeding behavior, signal transduction	hormone activity, receptor binding
205141_at	0.8389	0.0006	<i>ANG</i>	angiogenin; ribonuclease; RNase A family; 5	actin filament polymerization, activation of phospholipase A2, activation of protein kinase B, angiogenesis, cell communication, cell differentiation, cell migration, diacylglycerol biosynthetic process, homeostatic process, mRNA cleavage, multicellular organismal development, negative regulation of protein biosynthetic process, negative regulation of smooth muscle cell proliferation, ovarian follicle development, phospholipase C activation, placenta development, positive regulation of endothelial cell proliferation, positive regulation of phosphorylation, positive regulation of protein secretion, rRNA transcription, response to hypoxia	DNA binding, actin binding, copper ion binding, endonuclease activity, heparin binding, hydrolase activity, nuclease activity, nucleic acid binding, pancreatic ribonuclease activity, protein binding, rRNA binding, receptor binding, ribonuclease activity
206023_at	0.8363	0.0076	<i>NMU</i>	neuromedin U	G-protein coupled receptor protein signaling pathway, digestion, neuropeptide signaling pathway, regulation of smooth muscle contraction, signal transduction	receptor binding
203726_s_at	0.5308	0.0094	<i>LAMA3</i>	laminin; alpha 3	cell adhesion, cell surface receptor linked signal transduction, epidermis development, keratinocyte differentiation, regulation of cell adhesion, regulation of cell migration, regulation of embryonic development	protein binding, receptor binding, structural molecule activity
201012_at	0.4402	0.0035	<i>ANXA1</i>	annexin A1	anti-apoptosis, arachidonic acid secretion, cell cycle, cell motility, cell surface receptor linked signal transduction, inflammatory response, keratinocyte differentiation, lipid metabolic process, peptide cross-linking, regulation of cell proliferation, signal transduction	calcium ion binding, calcium-dependent phospholipid binding, phospholipase A2 inhibitor activity, phospholipase inhibitor activity, phospholipid binding, protein binding, protein binding; bridging, receptor binding, structural molecule activity

(Continued)

Table 1 (Continued).

Probe	Log ratio	P-value	Gene Symbol	Gene Name	Biological Process	Molecular Function
220785_at	0.3868	0.001	UTS2	urotensin 2	blood pressure regulation, muscle contraction, synaptic transmission	hormone activity, receptor binding
240042_at	0.3474	0.0042	FIBCD1	fibrinogen C domain containing 1	signal transduction	receptor binding
206549_at	0.1723	0.0021	INSL4	insulin-like 4 (placenta)	cell proliferation, cell-cell signaling, female pregnancy, multicellular organismal development, signal transduction	hormone activity, insulin-like growth factor receptor binding, receptor binding
205609_at	-0.2653	0.0037	ANGPT1	angiopoietin 1	angiogenesis, cell differentiation, multicellular organismal development, signal transduction, transmembrane receptor protein tyrosine kinase signaling pathway	receptor binding
210683_at	-0.1394	0.0051	NRTN	neurturin	MAPKKK cascade, nerve development, nervous system development, neural crest cell migration, neurite development, transmembrane receptor protein tyrosine kinase signaling pathway	growth factor activity, receptor binding

vascular invasion ($p = 0.017$), and perineurial invasion ($p = 0.001$). High ITLN1 expression also correlated positively with poor tumor regression after CRT ($p = 0.009$) (Table 2). These findings indicate that ITLN1 expression correlated with rectal tumor behavior and chemoradiation sensitivity.

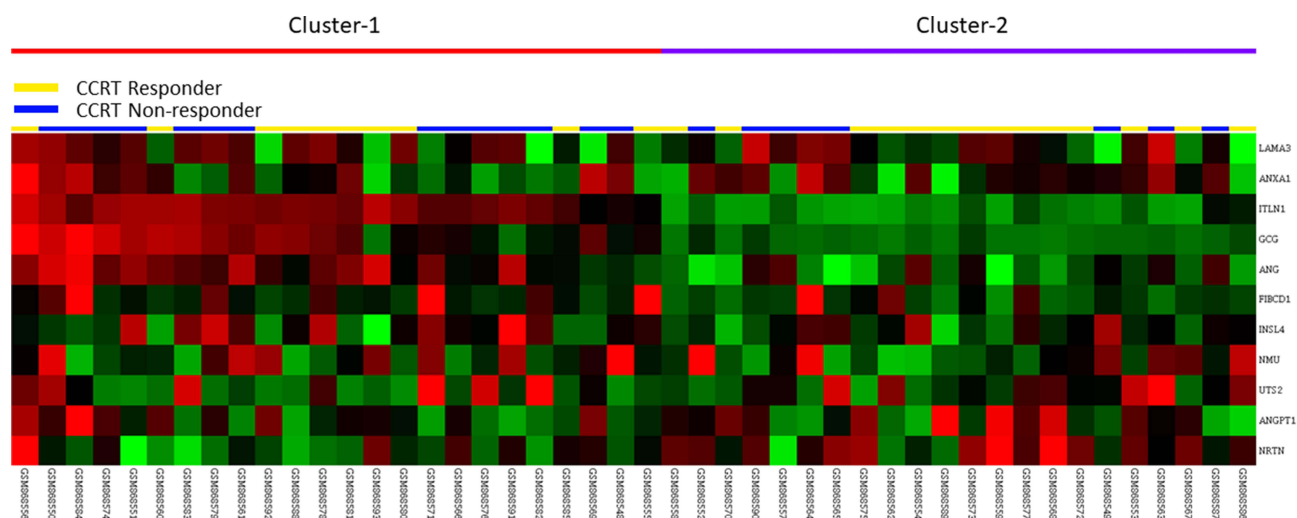


Figure 1 An investigation of gene expression in rectal cancer patients responsive versus non-responsive to chemoradiotherapy (CRT) was conducted using a published transcriptomic dataset (GSE35452). The clustering analysis focusing on genes associated with receptor binding revealed intelectin-1 (ITLN1) as the most notably up-regulated gene in CRT-responsive patients. The heatmap displays tissue specimens from responders (yellow lines) and non-responders (blue lines), illustrating the expression levels of up-regulated gene as red and down-regulated genes as green, respectively. Genes with unaltered mRNA expression are depicted differently within the spectrum.

Table 2 Associations and Comparisons Between ITLN1 Expression and Clinicopathological Factors in 343 Rectal Cancer Patients Receiving Neoadjuvant CCRT

Parameter		No.	ITLN1 Expression		p-value
			Low Exp	High Exp.	
Gender	Male	120	52	68	0.076
	Female	223	119	104	
Age	<70	217	110	107	0.684
	≥70	126	61	65	
Pre-Tx tumor status (Pre-T)	T1-T2	133	72	61	0.207
	T3-T4	210	99	111	
Pre-Tx nodal status (Pre-N)	N0	199	106	93	0.137
	N1-N2	144	65	79	
Post-Tx tumor status (Post-T)	T1-T2	155	92	63	0.001*
	T3-T4	188	79	109	
Post-Tx nodal status (Post-N)	N0	225	128	97	<0.001*
	N1-N2	118	43	75	
Vascular invasion	Absent	305	159	146	0.017*
	Present	38	12	26	
Perineurial invasion	Absent	305	162	143	0.001*
	Present	38	9	29	
Tumor regression grade	Grade 0–1	73	26	47	0.009*
	Grade 2–3	248	130	118	
	Grade 4	22	15	7	

Note: *, statistically significant.

Association Between ITLN1 Expression and Patient Survival

We conducted a survival analysis with three distinct endpoints to evaluate the prognostic significance of ITLN1 expression in rectal cancer patients following preoperative CRT. Univariate analysis revealed that clinicopathologic parameters, including post-treatment tumor status, post-treatment nodal status, vascular invasion, perineural invasion, tumor regression grade (TRG), and ITLN1 expression, were significantly associated with at least one of the following survival outcomes: DSS, LRFS, and MeFS (Table 3; Figure 3). Multivariate analysis using the Cox proportional hazards model identified post-treatment tumor status, perineural invasion, TRG, and ITLN1 expression as independent prognostic factors for survival (Table 4). High ITLN1 expression was associated with worse DSS (hazard ratio [HR], 4.878; 95% confidence interval [CI], 2.978–7.978; $p < 0.001$), LRFS (HR, 9.539; 95% CI, 3.264–27.877; $p < 0.001$), and MeFS (HR, 9.654; 95% CI, 4.250–21.929; $p < 0.001$). These results reveal the prognostic value of ITLN1 expression levels in patients with rectal cancer receiving preoperative CRT and subsequent surgery.

Discussion

The adipokine ITLN1, which is expressed in human omental adipose tissue, is known to regulate insulin action and participate in immune defense against microorganisms and lung inflammatory diseases.^{4,5,14} The abnormal activation of ITLN1 is known to be involved in carcinogenesis.^{6–9,15} In our study, elevated ITLN1 expression was closely associated

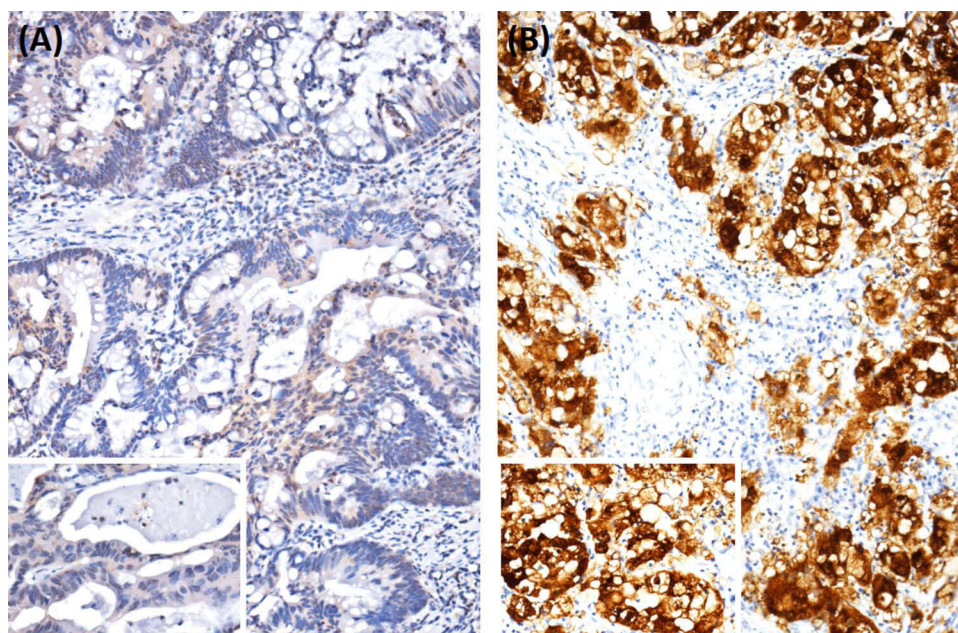


Figure 2 Immunohistochemical staining was conducted to assess intelectin-1 (ITLN1) levels in rectal cancers. Representative images depict low expression (A) and high expression (B) of ITLN1 in pre-treatment specimens of rectal cancers.

with aggressive tumor behavior, poor response to preoperative CRT, and worse patient outcomes. To the best of our knowledge, this is the first study to document ITLN1 expression in rectal cancer following CRT. Additionally, we identified several clinicopathological features that serve as predisposing factors associated with survival outcomes. These findings suggest that ITLN1 may be a useful prognostic biomarker for predicting survival in patients with rectal cancer. The novel insights from this study enhance our understanding of the role of ITLN1 in rectal cancer prognosis.

Accumulating evidence suggests that obesity promotes carcinogenesis in several cancers, including breast, colorectal, pancreatic, and prostate cancer.^{16–19} Factors such as insulin and adipokines may play a significant role in this process.^{6,20,21} ITLN1, also known as omentin-1, is an adipokine with depot-specific characteristics, showing elevated expression and release from visceral fat depots compared to subcutaneous adipose tissue. Although the effects of ITLN1 on tumorigenesis and progression are still unknown, ITLN1 is suspected of playing a critical role in the relationship between obesity and colorectal cancer.^{20,22,23}

While many hypotheses have been proposed to explain the relationship between cancer development and ITLN1 expression, conflicting results from clinical studies have left the precise role of ITLN1 unclear. Serial analysis of gene expression revealed high levels of ITLN1 in malignant pleural mesothelioma, with 28 of 53 specimens and all 4 cell lines showing elevated expression.^{7,24,25} Positive ITLN1 immunostaining was observed in epithelioid-type malignant pleural mesothelioma, but not in pleura-invading lung adenocarcinomas or reactive mesothelial cells near lung adenocarcinomas, suggesting that ITLN1 could serve as a diagnostic marker for malignant pleural mesothelioma. Another study found aberrant ITLN1 expression in gastric cancer tissues, with expression levels positively correlating with the degree of gastric infiltration, lymph node metastasis, and distant metastasis, suggesting a potential tumor-suppressor role for ITLN1 in gastric cancer.²⁶ Furthermore, introducing exogenous ITLN1 into prostate cancer DU145 cells, which naturally express low levels of ITLN1, led to a significant reduction in *in vitro* cell viability. Conversely, knockdown of ITLN1 in prostate cancer cells resulted in increased tumorigenicity and *in vivo* growth, supporting its potential role as a tumor suppressor in prostate cancer.²⁷ In a matched case-control study of 41 renal cell carcinoma patients and 42 healthy controls, Shen et al found significantly lower plasma ITLN1 levels in renal cell carcinoma patients ($p < 0.001$).⁸ In contrast, Fazeli et al observed higher plasma ITLN1 concentrations in colorectal cancer patients compared to controls.²⁸ Two recent studies from Turkey and Poland also reported higher plasma ITLN1 levels in prostate cancer patients compared to those with benign prostatic

Table 3 Univariate Log-Rank Analysis for Important Clinicopathological Variables and ITLN1 Expression

Parameter		No. of case	DSS		LRFS		MeFS	
			No. of event	p-value	No. of event	p-value	No. of event	p-value
Gender	Male	223	42	0.9755	9	0.2176	25	0.3460
	Female	120	21		26		37	
Age	<70	217	34	0.0728	23	0.9398	38	0.5771
	≥70	126	29		12		24	
Pre-Tx tumor status (Pre-T)	T1-T2	133	15	0.0074*	13	0.6695	18	0.0663
	T3-T4	210	48		22		44	
Pre-Tx nodal status (Pre-N)	N0	199	31	0.0932	19	0.4755	30	0.0697
	N1-N2	144	32		16		32	
Post-Tx tumor status (Post-T)	T1-T2	155	13	<0.0001*	8	0.0020*	15	<0.0001*
	T3-T4	188	50		27		47	
Post-Tx nodal status (Post-N)	N0	225	31	0.0022*	18	0.0434*	32	0.0077*
	N1-N2	118	32		17		30	
Vascular invasion	Absent	305	50	0.0023*	28	0.0379*	50	0.0136*
	Present	38	13		7		12	
Perineurial invasion	Absent	305	51	0.0180*	33	0.4263	53	0.1782
	Present	38	12		2		9	
Tumor regression grade	Grade 0–1	73	28	<0.0001*	14	0.0017*	25	<0.0001*
	Grade 2~3	248	34		21		36	
	Grade 4	22	1		0		1	
ITLN1 expression	Low Exp.	171	8	<0.0001*	4	<0.0001*	7	<0.0001*
	High Exp.	172	55		31		55	

Abbreviations: DSS, disease-specific survival; LRFS, local recurrence-free survival; MeFS, metastasis-free survival; *, statistically significant.

hyperplasia.^{29,30} In our study, we observed a positive correlation between ITLN1 expression and rectal cancer status, as well as aggressive tumor behavior. These findings suggest that ITLN1 could serve as a valuable biomarker for rectal cancer progression.

Notably, our results indicate that high ITLN1 expression correlated significantly with a poor response to CRT, DSS, LRFS, and MeFS in rectal cancer. However, two studies report contrary findings, suggesting that higher ITLN1 expression is linked to a better prognosis in colorectal cancer.^{10,31} This discrepancy may be due to the complex metabolic processes within different tumor sites/types, variations in study populations, study designs, treatment regimens, and sample sizes.³² Moreover, while our study used immunohistochemical staining of tissue specimens to assess ITLN1 expression, other studies have measured plasma levels, which can be highly variable. Thus, the combination of data mining from a public gene database followed by validation with clinical tissue samples in our study offers a novel and meaningful contribution to understanding ITLN1's role in rectal cancer.

To date, the specific pathogenic mechanisms underlying the role of ITLN1 in tumorigenesis remain unclear. ITLN1 may promote tumor initiation and progression in response to chronic inflammation within the tumor microenvironment. Zhang and Zhou reported that ITLN1 regulates p53 protein levels by decreasing p53 deacetylation and increasing its

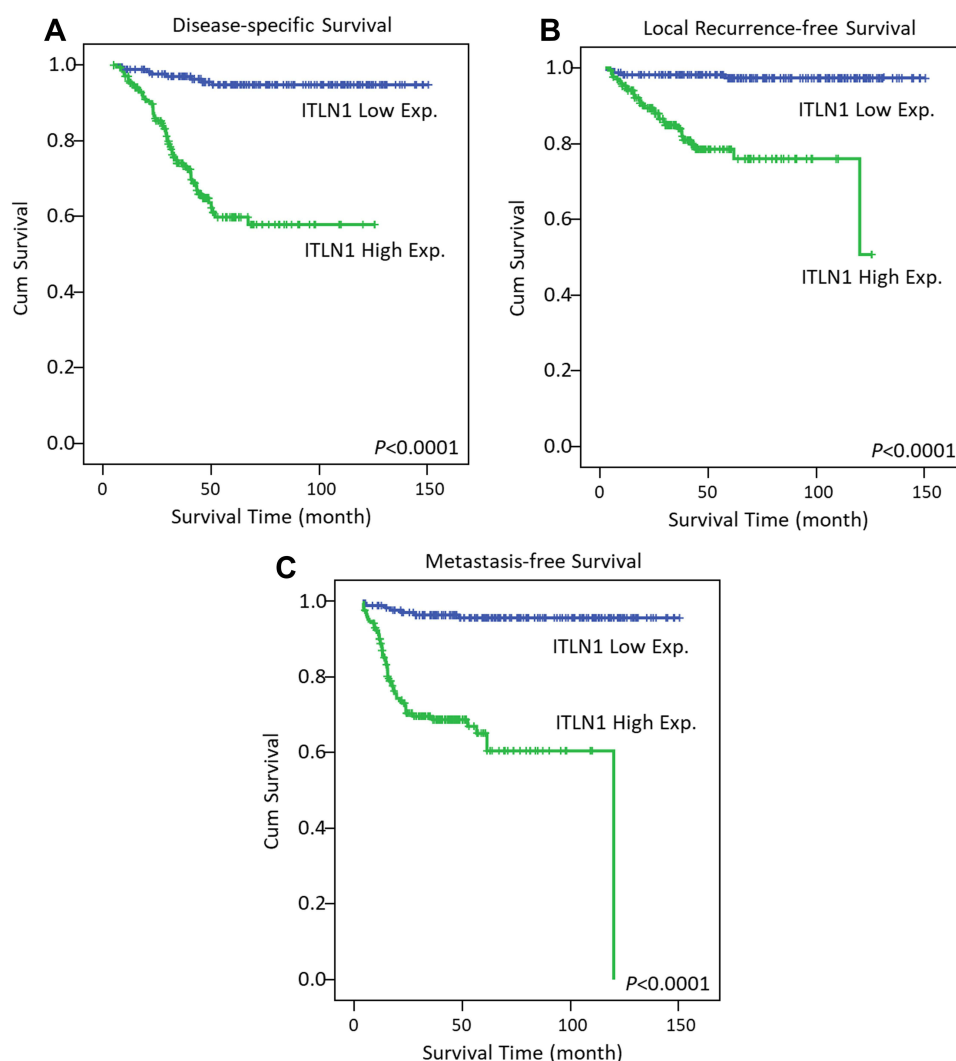


Figure 3 Kaplan-Meier survival curves plotted to predict survival. Using the Log rank test, rectal cancer patients with high expression of ITLN1 had an inferior disease-specific survival (**A**), local recurrence-free survival (**B**) and metastasis-free survival (**C**).

stability in hepatocellular carcinoma cells.³³ In addition, ITLN1 has been shown to induce apoptosis by increasing the Bax/Bcl-2 ratio and inhibiting caspase-3 activation. In colorectal cancer, ITLN1 may influence the PI3K/Akt signaling pathway, which subsequently modulates eNOS activity, contributing to cancer cell proliferation.³⁴ Pothuraju et al demonstrated that ITLN1 activation of the Akt signaling pathway enhances cell proliferation, metabolism, and vascular permeability, potentially promoting tumor metastasis.³⁵ These findings suggest that ITLN1 may play a significant role in enhancing the metastatic potential of tumor cells, thereby shortening patient survival. However, further investigations are needed to elucidate the precise mechanisms through which ITLN1 contributes to rectal cancer pathogenesis and progression.

Several limitations should be mentioned here. First, our analysis included only rectal cancer patients who underwent preoperative CRT, which limits the generalizability of our findings to patients who did not receive CRT. Second, our cancer registry database lacks certain prognostic information, such as mesorectal fascia involvement and the mutational status of key tumor-related genes. Addressing these factors in future studies will be crucial for a more comprehensive survival analysis and understanding of ITLN1's role in rectal cancer.

Table 4 Multivariate Analysis

Parameter	DSS			LRFS			MeFS		
	H.R	95% CI	p-value	H.R	95% CI	p-value	H.R	95% CI	p-value
ITLN1 high expression	4.874	2.978–7.978	<0.001*	9.539	3.264–27.877	<0.001*	9.654	4.250–21.929	<0.001*
Tumor regression grade	1.675	1.134–2.475	0.010*	2.008	1.025–3.937	0.042	1.904	1.152–3.155	0.012*
Post-Tx tumor status (Post-T)	1.728	1.076–2.777	0.024*	2.250	0.964–5.252	0.061	1.932	1.020–3.656	0.043*
Pre-Tx tumor status (Pre-T)	1.366	0.887–2.104	0.157	-	-	-	-	-	-
Post-Tx nodal status (Post-N)	1.031	0.669–1.589	0.889	1.137	0.559–2.314	0.724	1.018	0.587–1.766	0.948
Vascular invasion	1.361	0.805–2.3300	0.250	1.793	0.743–4.328	0.194	1.435	0.732–2.816	0.293
Perineurial invasion	1.050	0.611–1.807	0.859	4.695	1.076–220.408	0.040*	0.820	0.687–3.049	0.330

Note: *, statistically significant.

Abbreviations: DSS, disease-specific survival; LRFS, local recurrence-free survival; MeFS, metastasis-free survival.

Conclusion

The study results suggest that identifying high ITLN1 expression in rectal cancer patients could aid in distinguishing and stratifying those at high risk following CRT. The observed inverse association between ITLN1 expression, tumor regression, and survival outcomes highlights its potential as both a prognostic biomarker and a therapeutic target for rectal cancer.

Abbreviations

CRT, chemoradiotherapy; ITLN1, intelectin 1; AJCC, American Joint Committee on Cancer; TRG, tumor regression grade; DSS, disease-specific survival; LRFS, local recurrence-free survival; MeFS, metastases-free survival; HR, hazard ratio; CI, confidence interval.

Data Sharing Statement

The datasets are available from the corresponding author upon reasonable request.

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Disclosure

The authors report no conflicts of interest in this work.

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