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Assessment of MUC17 and MUC13 Gene Expression Levels in Tissue Samples of Patients with Colorectal Cancer

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Abstract

Background and Objective: Cancer is a genetically heterogeneous disease and remains one of the leading causes of mortality worldwide. Colorectal cancer (CRC) is the third most common cancer globally and accounts for approximately 38% of gastrointestinal malignancies. It is the most prevalent cancer of the gastrointestinal tract. In men, colorectal cancer ranks third after lung and prostate cancers, while in women it ranks second after breast cancer. The present study aimed to evaluate the expression levels of MUC17 and MUC13 genes in tissue samples from patients with colorectal cancer.

Methods: In this study, tumor tissues and adjacent normal colorectal tissues were analyzed. A total of 30 tumor samples from patients with colorectal cancer and 30 adjacent normal tissue samples were collected from the tumor bank of the Cancer Institute at the Imam Khomeini Hospital Complex from patients undergoing surgical resection. All tissue samples were preserved in liquid nitrogen tanks. After collection, 100 mg of each tissue sample was finely minced using a surgical scalpel and subsequently homogenized using a tissue homogenizer. Total RNA was extracted, and complementary DNA (cDNA) was synthesized. Gene expression levels of MUC17 and MUC13 were then quantified using real-time PCR. The obtained data were analyzed along with patients' clinical information using SPSS software and the t-test statistical method.

Results: Statistical analysis revealed a significant association between the expression levels of the MUC13 and MUC17 genes and the degree of tumor cell differentiation. Additionally, a significant positive correlation was observed between the expression levels of these genes and patient age. A significant difference in the expression levels of MUC13 and MUC17 was also observed between tumor tissues and adjacent normal tissues.

Conclusion: The findings indicate that MUC13 and MUC17 exhibit altered expression patterns between colorectal tumor tissues and adjacent normal tissues, suggesting a potential role for these mucins in colorectal cancer development and progression.

Keywords: Colorectal cancer, CRC, MUC13, MUC17, Real-time PCR

1. Introduction

Colorectal cancer (CRC) is one of the most common malignancies worldwide and represents a major public health concern (1). According to global cancer statistics, CRC ranks among the top three most frequently diagnosed cancers and remains a leading cause of cancer-related mortality. The incidence of colorectal cancer has been increasing in many countries due to aging populations, lifestyle factors, and environmental influences. Despite advances in screening, surgical techniques, and targeted therapies,

CRC continues to impose a substantial clinical burden, highlighting the need for a better understanding of its molecular mechanisms and the identification of reliable biomarkers for early diagnosis and prognosis (2-4).

Colorectal carcinogenesis is a complex, multistep process characterized by the accumulation of genetic and epigenetic alterations that affect oncogenes, tumor suppressor genes, and signaling pathways regulating cell proliferation, apoptosis, and differentiation. In addition to these molecular changes, alterations in the expression of mucin genes have been implicated in the initiation and progression of colorectal tumors. Mucins are high-molecular-weight glycoproteins produced by epithelial cells and play a crucial role in maintaining the protective mucosal barrier of the gastrointestinal tract. Dysregulation of mucin expression has been associated with several gastrointestinal diseases, including inflammatory disorders and malignancies (5-7).

Among the mucin family, membrane-bound mucins such as MUC13 and MUC17 have attracted increasing attention due to their potential role in tumor biology (8) MUC13 is a transmembrane mucin expressed on the apical surface of epithelial cells and is involved in cell signaling, epithelial integrity, and immune responses (9). Aberrant expression of MUC13 has been reported in several cancers, including colorectal, gastric, and pancreatic cancers. Studies have shown that overexpression of MUC13 may promote tumor cell proliferation, invasion, and metastasis through the activation of signaling pathways such as the NF-κB and HER2-related pathways (10, 11).

Similarly, MUC17 is another membrane-bound mucin predominantly expressed in the intestinal epithelium, where it contributes to epithelial protection, restitution, and barrier function (12) Alterations in MUC17 expression have been associated with intestinal inflammation and tumorigenesis. Evidence suggests that MUC17 may influence epithelial cell differentiation and mucosal repair processes, and dysregulation of this gene could contribute to colorectal cancer progression by affecting epithelial homeostasis and cellular signaling pathways (13, 14).

Given the important biological roles of mucins in epithelial protection and tumor progression, investigating their expression patterns in colorectal cancer may provide valuable insights into disease mechanisms and potential diagnostic biomarkers(15). However, the expression patterns and clinical significance of MUC13 and MUC17 in colorectal cancer tissues remain incompletely understood.

Therefore, the present study aimed to evaluate the expression levels of MUC13 and MUC17 genes in tumor tissues and adjacent normal tissues of patients with colorectal cancer using Real-Time PCR and to investigate their potential association with clinicopathological characteristics.

Materials and Methods

Data Collection

Gene expression data for colorectal cancer (CRC) were retrieved from the Gene Expression Omnibus (GEO) database. The microarray dataset GSE44076, containing colorectal cancer and normal colorectal tissue samples, was selected for analysis. The dataset was generated using the Affymetrix Human Genome U219 Array platform.

Gene Expression Analysis

The expression levels of MUC13 and MUC17 were extracted from the dataset and compared between colorectal cancer and normal tissue samples. Differential expression analysis was performed using the GEO2R online tool, which is based on the limma package. Statistical significance was determined using adjusted p-values, and a p-value < 0.05 was considered statistically significant.

MTT Assay

The cytotoxicity of Vitamin C antioxidants on GL261 cells was assessed using the tetrazolium - based (MTT) test. Cells (5x10^4) were seeded in to 96-well plates and allowed to attach for 24 hr, The culture media was then replaced with fresh medium containing various doses of Vitamin C (25, 50, 75, and 100 µg/ml) and the cells incubated for an additional 48 hours. Subsequently, 20 µl of MTT solution (5 mg/ml) was added to each well and incubated for 4 hours. Formazan crystals formed were dissolved in 100 µl DMSO, and optical density was measured at 570 nm using a plate reader (BioTek-ELx800, USA). Cell viability was assessed by comparing treated cells to untreated subgroup (control), and IC50 values were calculated using GraphPad Prism 6 software. All experiments were done in triplicate. The calculated IC50 doses were non-lethal to mice over the 14-day observation period, so the lethal dose was not established for ethical considerations.

Protein–Protein Interaction Network Analysis

A protein–protein interaction (PPI) network was constructed using the STRING database to investigate the functional associations of MUC13 and MUC17 with related proteins in colorectal cancer. The generated network consisted of 11 nodes and 55 edges, indicating extensive interactions among the analyzed proteins. The average node degree was 10, suggesting a high level of connectivity within the network. Furthermore, the average local clustering coefficient was 1.0, demonstrating a highly interconnected network structure.

Compared with the expected number of edges (n = 11), the observed number of interactions (n = 55) was

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significantly higher, indicating that the proteins were biologically connected rather than randomly associated. The PPI enrichment analysis revealed a highly significant interaction enrichment (PPI enrichment p-value < 1.0×10^{-16}), suggesting that these proteins participate in common biological pathways and may have coordinated roles in the development and progression of colorectal cancer.

Collection of Tumor and Adjacent Normal Colorectal Tissues

All tumor and adjacent non-tumor colorectal tissue samples were obtained from Imam Khomeini Hospital Complex, Tehran, Iran. A total of 30 colorectal tumor tissues and 30 matched adjacent normal tissues were collected from patients undergoing surgical resection. The clinicopathological characteristics of the samples, including tumor stage and grade, were obtained from the patients' medical records. All tissue samples belonged to Iranian patients referred to the gastroenterology department of Imam Khomeini Hospital. During surgery, tissue specimens were excised and immediately transferred to liquid nitrogen to preserve RNA integrity. The samples were then transported to the laboratory and stored at −80 °C until further molecular analysis. Each case included paired samples from the same patient, consisting of tumor tissue and corresponding adjacent non-tumor tissue. Clinical and pathological information of the patients included sex, age, tumor location, tumor grade, stage, lymphatic invasion, and vascular invasion, as summarized in Table 1.

Table 1. Tumor and Non-Tumor Colorectal Cancer Samples Used in This Study

BANKING CODE	SEX	AGE	Lymphatic Invasion	Vascular invasion	GRADE	LOCATION	STAGE
1	F	85	yes	Yes	II	COLON	IV
2	F	51	No	No	I	COLON	IIIB
3	M	56	NO	NO	I	COLON	IIA
4	F	78	YES	YES	II	COLON	IIIC
5	F	29	NO	NO	II	RECTUM	IIA
6	F	59	YES	YES	IV	COLON	IIIC
7	F	67	YES	YES	II	COLON	IIIC
8	F	40	NO	NO	II	COLON	I
9	M	47	YES	YES	II	COLON	IIIC
10	M	80	YES	YES	II	RECTOM	IIIC
11	M	55	NO	NO	II	COLON	IIA
12	F	66	NO	NO	I	COLON	IIIA
13	F	59	NO	NO	II	COLON	I
14	F	68	YES	YES	II	COLON	IIIB
15	F	58	NO	NO	II	COLON	IIIC

16	F	61	NO	NO	II	COLON	IIIB
17	M	61	YES	YES	II	COLON	IIIB
18	M	77	YES	YES	II	RECTUM	IIIB
19	M	43	YES	YES	I	COLON	IIIB
20	M	52	YES	YES	II	COLON	IIIB
21	M	73	UNKNOW	YES	I	COLON	IIIB
22	F	31	NO	NO	II	COLON	IIA
23	M	60	YES	YES	II	RECTOM	IIIB
24	M	68	NO	NO	II	COLON	I
25	M	73	NO	NO	I	COLON	IIA
26	F	53	NO	NO	I	RECTUM	I
27	F	45	YES	YES	IV	COLON	IIA
28	F	55	NO	NO	II	RECTUM	IIA
29	F	47	NO	NO	I	RECTUM	O
30	F	50	YES	YES	I	RECTUM	IIA

RNA Extraction and cDNA Synthesis

Approximately 100 mg of each tissue sample was finely minced using a sterile surgical scalpel and then homogenized using a tissue homogenizer. Total RNA was extracted from the homogenized tissues using a standard RNA extraction protocol according to the manufacturer's instructions. The concentration and purity of RNA were evaluated using spectrophotometry. Subsequently, complementary DNA (cDNA) was synthesized from the extracted RNA using a reverse transcription kit following the manufacturer's protocol.

Real-Time PCR Analysis

The expression levels of MUC13 and MUC17 genes were analyzed using quantitative Real-Time PCR (qRT-PCR). The housekeeping gene β-actin was used as an internal control to normalize gene expression levels. PCR reactions were performed using gene-specific primers, and amplification was carried out under standard cycling conditions in a Real-Time PCR system. The sequences of the primers used in this study and the expected product sizes are presented in Table 2. Gene expression levels were calculated using the comparative $2^{-}\Delta\Delta Ct$ method.

Table 2. Primers Used in This Study

Gene	Primer	Sequence (5′–3′)	Product Length (bp)
MUC 17	F	ACCTCAACTCCTACTGTGCC	137
	R	CTCCTCACACAACTCCCCAT	
MUC 13	F	ATGCCTGTAACCAGACTGCG	153
	R	CTTGAGACTGGAAGCAACGC	
B-ACTIN	F	TCAAACAAGCAAATGAGATGTA	149
	R	ACGAAGGCAACAGGTTAA	

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Statistical Analysis

Statistical analysis was performed using SPSS software. Differences in gene expression levels between tumor and adjacent normal tissues were evaluated using the Student's t-test. Associations between gene expression levels and clinicopathological characteristics were also analyzed. A p-value < 0.05 was considered statistically significant. The clinicopathological characteristics of the patients included in this study are summarized in Table 2-6, and the primer sequences used for Real-Time PCR analysis are listed in Table 2-3. Statistical analyses were performed using GEO2R and GraphPad Prism software. Differences between groups were considered statistically significant when $p < 0.05$.

3. Results

Description of Tumor and Non-Tumor Samples

The tumor and adjacent non-tumor samples used in this study were categorized based on their clinical characteristics and pathological reports. Patient information, including age, sex, tumor location, and tumor grade was obtained from pathology records. Accordingly, the samples were classified into four groups: grade I, II, III, and IV. The mean age of the patients was 58.8 years. Among the studied cases, 9 patients (30%) were classified as grade I, 10 patients (33%) as grade II, 2 patients (7%) as grade III, and 8 patients (27%) as grade IV (Figure 1). Levels of circ Expression

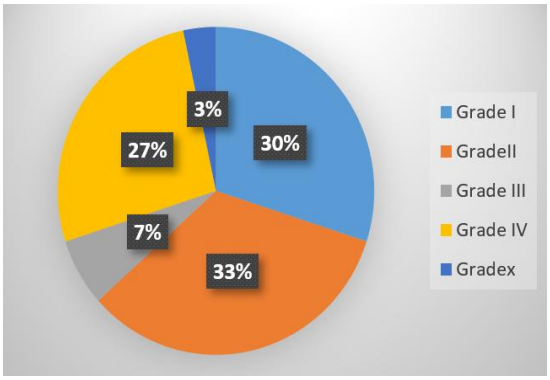


Figure 1. Frequency distribution of the studied samples based on tumor grade

Gene Expression Analysis in Tumor and Non-Tumor Samples

The expression levels of the target genes were examined via real-time PCR. Analysis of the obtained results was performed using fold change. The β-actin gene was used as the reference gene. As the results indicate, the expression level was the same in both tumor and non-tumor colorectal specimens, which means that it is stable among the two groups.

The expression pattern of the investigated genes in tumor versus non-tumor specimens is demonstrated in the relevant figures below. It should be noted that statistical analysis of the data obtained through real-time PCR revealed a significant difference in the expression level of the MUC13 gene in comparison to non-tumor (normal) tissues ($p < 0.05$). Specifically, the difference was about three times higher in tumor tissue.

Likewise, there is a significant difference in the expression level of the MUC17 gene between tumor and non-tumor specimens ($p < 0.05$); however, the difference was two times lower in tumor tissue.

Similarly, a significant difference was observed in the expression level of the MUC17 gene between colorectal tumor tissues and non-tumor samples ($p < 0.05$), indicating an approximately two-fold increase in tumor tissues.

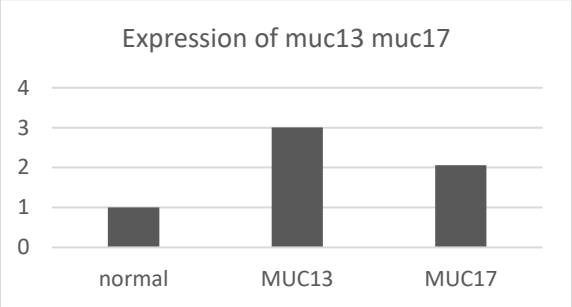
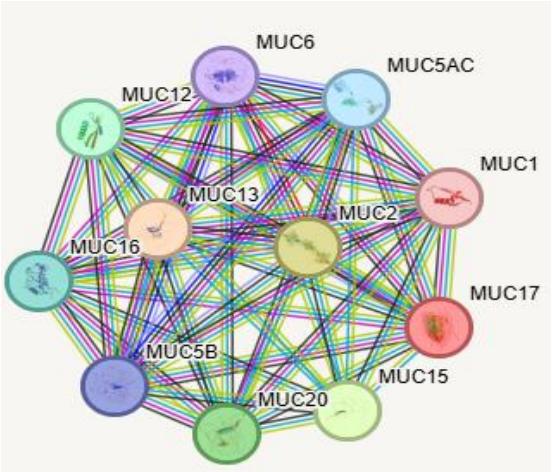


Figure 2. Relative expression analysis of B-actin, MUC13, and MUC17 in colorectal cancer samples.

Protein–Protein Interaction



To investigate the potential interactions of MUC13 and MUC17 with other proteins, a protein–protein interaction (PPI) network was constructed using the STRING database. The gene symbols were uploaded

to STRING, and interactions with a confidence score above the default threshold were included in the network. Functional associations and interaction partners identified by STRING were used to explore the biological roles of MUC13 and MUC17 in colorectal cancer.

4. Discussion

The findings of this study indicate a marked differential expression of MUC13 and MUC17 in colorectal cancer (CRC) tissues relative to adjacent normal mucosa. Quantitative analysis revealed an approximately 150-fold change in MUC13 and a 19-fold change in MUC17. These expression patterns point to a potential involvement of these transmembrane mucins in molecular events associated with colorectal tumorigenesis.

Our results regarding MUC13 are consistent with Sheng et al. (2017), who identified MUC13 as a potent oncogene in CRC that promotes tumor cell survival by activating the NF-κB signaling pathway (10) The dramatic fold-change observed in our samples reinforces the consensus that MUC13 is a highly sensitive marker for malignant transformation in gastrointestinal epithelia (10, 11).

Regarding MUC17, our data showed significant overexpression in tumor tissues ($p < 0.05$), which aligns with the role of membrane-bound mucins in mucosal restitution and their subsequent dysregulation in gastrointestinal malignancies(14). Interestingly, the higher expression of MUC17 in low-grade tumors compared to high-grade ones suggests its expression may be linked to the degree of cellular differentiation, a trend previously noted in studies investigating mucin dynamics during tumor progression (16).

The correlation between the expression of these genes and clinical factors, such as tumor differentiation and age, highlights their potential as diagnostic biomarkers. Given that CRC remains a leading cause of global cancer mortality, the high sensitivity of MUC13 and MUC17 markers could facilitate earlier detection and better pathological stratification.

5. Conclusion

The findings of the present study demonstrate a significant difference in the expression levels of MUC13 and MUC17 genes between colorectal tumor tissues and adjacent non-tumor (normal) tissues. Statistical analysis confirmed this differential expression. Based on these results, these mucins may be considered potential diagnostic biomarkers for colorectal cancer. However, further in vivo studies are required to more comprehensively evaluate their clinical applicability and biological roles in colorectal cancer development and progression.

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Ethical Considerations and Compliance with Ethical Guidelines

The study was conducted in accordance with the ethical principles for medical research involving human subjects as outlined in the Declaration of Helsinki.

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Conflict of interest

The authors declare no conflict of interest.

AI Using Declaration

Chat GPT was used for language and grammar corrections. The final output was read and modified by all authors.

Author's contributions

All authors equally contributed to preparing this article.

Reference

1. Jing Z, Xi Y, Yin J, Shuwen H. Biological roles of pirnas in colorectal cancer. Gene. 2021; **7**69:145063. (DOI: 10.1016/j.gene.2020.145063) (PMID: 32827685)

2. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics 2024. CA Cancer J Clin. 2024; 74(1):12-49. (DOI: 10.3322/caac.21830) (PMID: 38230766)

3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49. (DOI: 10.3322/caac.21660) (PMID: 33538338)

4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics. GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. (DOI: 10.3322/caac.21609) (PMID: 30207593)C:\Users\f.reyhanian\Desktop\10.3322\caac.21609

5. Kufe DW. Mucins in cancer: function, prognosis and therapy. Nature Rev Cancer. 2009; 9(12):874-85. (DOI: 10.1038/nrc2761) (PMID: 19935676)

6. Johansson ME, Larsson JM, Hansson GC. The two mucus layers of colon are organized by the MUC2 mucin, whereas the outer layer is a legislator of host–microbial interactions. Proc Natl Acad Sci USA. 2011;108(supplement_1):4659-65. (DOI:

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10.1073/pnas.1006451107) (PMID: 20615996)
7. Arias-González L, Lucendo AJ. The role of mucins in esophageal inflammatory diseases. J Pers Med. 2026;16(2):93.(DOI: 10.3390/jpm16020093) (PMID: 41745385)
8. Liberelle M, Jonckheere N, Melnyk P, Van Seuningen I, Lebègue N. *Egf*-containing membrane-bound mucins: a hidden targeting pathway. J Med Chem. 2020;63(10):5074-88. (DOI: 10.1021/acs.jmedchem.9b02001) (PMID: 32027502)
9. Segui-Perez C, Stapels DAC, Ma Z, Su J, Passchier E, Westendorp B, et al. MUC13 negatively regulates tight junction proteins and intestinal epithelial barrier integrity via protein kinase C. J Cell Sci. 2024;137(5):jcs261468. (DOI: 10.1242/jcs.261468) (PMID: 38345099)
10.Sheng YH, He Y, Hasnain SZ, Wang R, Tong H, Clarke DT, et al. MUC13 protects colorectal cancer cells from death by activating the NF-κB pathway and is a potential therapeutic target. Oncogene. 2017;36(5):700-13. (DOI:10.1038/onc.2016.241) (PMID: 27399336)
11.Chauhan SC, Ebeling MC, Maher DM, Koch MD, Watanabe A, Aburatani H, et al. MUC13 mucin augments pancreatic tumorigenesis. Mol Cancer Ther. 2012;11(1):24-33. (DOI: 10.1158/1535-7163.MCT-11-0598) (PMID: 22027689)
12.Schneider H, Berger E, Dolan B, Martinez-Abad B, Arike L, Pelaseyed T, et al. The human transmembrane mucin MUC17 responds to tnfα by increased presentation at the plasma membrane. Biochem J. 2019;476(16):2281-95. (DOI: 10.1042/BCJ20190180) (PMID: 31387973)
13.McGuckin MA, Lindén SK, Sutton P, Florin TH. Mucin dynamics and enteric pathogens. Nat Rev Microbiol. 2011;9(4):265-78. (DOI: 10.1038/nrmicro2538) (PMID: 21407243)
14.Senapati S, Sharma P, Bafna S, Roy HK, Batra SK. The MUC gene family: their role in the diagnosis and prognosis of gastric cancer. Histol Histopathol. 2008;23(12):1541-52. (DOI: 10.14670/HH-23.1541) (PMID: 18830939)
15.Wang S, You L, Dai M, Zhao Y. Mucins in pancreatic cancer: a well-established but promising family for diagnosis, prognosis and therapy. J Cell Mol Med. 2020;24(18):10279-89. (DOI: 10.1111/jcmm.15684) (PMID: 32745356)
16.Luu Y, Junker W, Rachagani S, Das S, Batra SK, Heinrikson RL, et al. Human intestinal MUC17 mucin augments intestinal cell restitution and enhances healing of experimental colitis. Int J Biochem cell Biol. 2010;42(6):996-1006. (DOI: 10.1016/j.biocel.2010.03.001) (PMID: 20211273)