DOI:10.31557/APJCC.2026.11.4.605

RESEARCH ARTICLE

KRAS, IGF2bp2 Genes Elevated in Positively Stained CDX2 and CK20 Colon Adenocarcinoma Tissues

Ban Hatam Kareem*, Hydar Muhsin Khalfa

Department of Biology, Faculty of Science, University of Kufa, Iraq.

Abstract

Introduction: Colon cancer is one of the most common malignancies worldwide, ranking third in incidence and second in cancer-related deaths. This study aimed to evaluate the histological and molecular changes associated with colon cancer, focusing on molecular markers related to chemotherapy resistance. **Materials and Methods**: The study included 60 paraffin-embedded tissue samples from patients histologically diagnosed with colon adenocarcinoma, as well as 10 normal tissue samples as controls. All samples underwent routine histological examination using hematoxylin and eosin (H&E) staining to assess the overall histological structure, and Giemsa staining was used to examine nuclear changes in cancer cells. Immunohistochemical (IHC) assays using CDX2 and CK20 markers were performed to confirm the colonic origin of the tumors. Quantitative polymerase chain reaction (qRT-PCR) was also used to assess the gene expression levels of KRAS and IGF2BP2. **Results:** The results showed clear histological changes in the affected colon and rectal tissues, characterized by glandular distortion and increased cellular irregularity, along with nuclear clumping in cancer cells compared to control samples. The study also demonstrated a strong positive immunoreactivity for both CDX2 and CK20, the signature immunophenotype of colon cancer. **Conclusion:** Furthermore, a significant increase in the gene expression levels of KRAS and IGF2BP2 was observed, suggesting their potential role in tumor progression and their association with chemotherapy resistance mechanisms.

Keywords: Colorectal cancer- CDX2- CK20- KRAS- IGF2bp2

Asian Pac J Cancer Care, **11 (4)**, 605-612 Submission Date: 04/02/2026 Acceptance Date: 05/15/2026

Introduction

Colon cancer is the second most common cause of death worldwide, and colon cancer (CC) ranks third in prevalence and second in cancer-related deaths. CC originates in the colon or rectum and is influenced by genetic mutations, lifestyle, and diet [1].

CDX2 gene and transcription factor caudal-type homeobox gene 2 which is normally expressed in colonic epithelium and plays important role in development of intestine in embryo [2]. CDX2 positivity was defined as moderate nuclear staining in at least 5% of tumor cells. Stage 1 tumors were more likely to be CDX2 positive, and CDX2 positivity was associated with improved survival in this study. In a series of 44 patients from the United States, CDX2 positivity, defined as nuclear staining in 25% or more of tumor cells, was present in 59.1% of cases [3]. CDX2 is highly expressed in normal colonic and rectal epithelium, but its levels are reduced in a subset of colorectal cancers. It has been identified as a predictive biomarker for response to chemotherapy in stage II and III colorectal cancer. Additionally, in stage IV colorectal cancer, the absence of CDX2 expression predicted poor patient survival [4].

Cytokine keratins (CKs, keratins) are a class of intermediate filament proteins that includes those of type I (CK9-CK20) along with type II (CK1-CK8) proteins, according to the traditional classification. They control growth, proliferation, migration, apoptosis, immunity, and other aspects of cellular metabolism, as well as providing structural support to epithelial cells. Cytokine keratin expression is typically maintained by cancer cells; therefore, CK-specific antibodies are widely used in routine pathological diagnostics to determine the origin of a tumor, particularly in metastases [5].

Major recent advances in understanding the genetic

Corresponding Author:
Dr. Ban Hatam Kareem
Department of Biology, Faculty of Science, University of Kufa, Iraq.
Email: banh.aljahawi@student.uokufa.edu.iq

basis of cancer have been built on the foundations of familial, epidemiological, cellular, and molecular genetic studies. These studies have shown that cancer is often associated with errors in the expression of genes normally assigned to regulate cell function. These genes belong to a class known as recessive genes or tumor suppressor genes [6].

Aside from promoting tumorigenesis, mutant KRAS can also affect the tumor microenvironment (TME) by regulating cytokine release, recruiting immune cells to tumor sites to enhance inflammatory responses, and facilitating immune escape. This phenomenon has been observed in pancreatic, colon, and lung cancers harboring KRAS mutations. Mechanistically, the oncogenic variant of KRAS activates inflammatory cytokines, chemokines, and subsequent signaling pathways to promote tumor progression and invasion [7].

High expression of IGF2BP2 in tumors negatively affects patient prognosis and plays an important role in regulating the tumor immune microenvironment and immune checkpoints. Therefore, the IGF2BP2 gene family has the potential to be used as a biomarker for early cancer diagnosis and detection, as well as a target for immunotherapy. In summary, conducting comprehensive cancer analyses of IGF2BP2 can help understand their mechanisms in various tumors, providing new insights and strategies for tumor prevention and treatment [8]. The aim of this study is to investigate the relationship between the immunohistochemical expression of diagnostic CDX2 CK20 and genetic expression of KRAS and IGF2bp2 in colorectal adenocarcinoma.

The aim of this study is to investigate the relationship between the immunohistochemical expression of diagnostic CDX2 CK20 and genetic expression of KRAS and IGF2bp2 in colorectal adenocarcinoma.

Materials and Methods

A total of 60 paraffin embedded blocks containing fine needle aspiration tissues from patients suspected clinically confirmed colorectal adenocarcinoma as per the histopathological report between the periods of October and November 2025 from histopathology laboratories in Al-Najaf Al-Ashraf, Iraq. Tissues were sectioned by rotary microtome (5µm thick sections) and sections were stained with hematoxylin and eosin.

Immunohistochemistry of CD2 and CK20

CDX2 and Ck20 antibodies were purchased from (BIO SB) was carried out using manufacturer protocol. Paraffin blocks tissues were sectioned and processed accordingly for H and E and immunohistochemistry. Charged Slides were marked with hydrophilic pen and Antibodies were applied at a dilution of 1:50 and incubated for 2 hours at room temperature. Slides were then washed with PBS 3 times for 2 minutes. Reagent 1 Bio SB (polymer helper) was applied to the slides and incubated for 20 minutes at room temperature and then washed with PBS 3 times for 2 minutes. Reagent 2 Bio SB (polyperioxidase-anti-mouse/rabbit IgG) is then added and slides were incubated at room temperature for 20 minutes and slides were washed with PBS 3 times for 2 minutes. Slide colour development was carried out using DAB (3,3 diaminobenzidine) and slides were washed with deionized water. Slides were counterstained using haematoxylin stain. Mounting medium was applied before a cover slip was attached to each slide.

Immunohistochemical score

Positive stained cells were counted using image j, image processing software to identify and count the number of positively stained cells. Positive cells were counted and intensity of staining recorded. Each immunohistochemical slide was examined for 10 fields at a magnification of 100 X and mean data was recorded. Immuno reactive score (IRS) was worked out according to the following table and represented by plus system according to (20). Aperio image scope (leica) Image analysis software was used to identify positively stained cells.

Quantitative real-time polymerase chain reaction

Gene Expression for KRAS, IGF2bp2 and housekeeping GAPDH gene are examined by Quantitative Reverse Transcriptase - PCR (qRT-PCR) techniques.

Total RNA Extraction

RNA was extracted from a total of 60 FFPE embedded colorectal tissues using a commercial purification system (abm's ExCellen CT Lysis Kit canada). A total of 2.0 g of tissued was processed accordingly following manufacturer instructions.

Estimation of RNA Concentration and Purity

A Nanodrop spectrophotometer (biodrop/thermofischer) was used to determine the concentration and purity of RNA. A purity of 40–50 ng/µL was considered acceptable in this study.

cDNA Synthesis

Program the thermal cycler so that cDNA synthesis is followed immediately by qPCR amplification Table 1.

Table 1. cDNA Synthesis Programme

Step	Temperature	Duration	Cycle (s)
cDNA Synthesis	57°C	55 mins	1
Pre-Denaturation	95°C	7 mins	1
Denaturation	95°C	25 secs	40
Annealing	57 °C - 72°C	60 secs	1
Melt Curve	30 min		

Table 2. The Reaction Mixture for each qRT-PCR Tube

	Reaction Volume	
Component	50 µl	Concentration
Total RNA	2.5 µl	50 ng/ µl
EVA Green qPCR Master Mix	25 µl	1X
qRT-PCR Enzyme Mix	0.5 µl	1X
Forward Primer	2 µl	25 picamole
Reverse Primer	2 µl	25 picamole
DPEC-DW	18 µl	-

Table 3. Primers and Their Sequence for the Examined Genes

Gene name	Product size (bp)	Product size (bp)	Reference
	(5'-----3')		
KRAS	F: CAGTAGACACAAAACAGGCTCAG	134bp	(NCBI)
	R: TGTCGGATCTCCCTCACCAATG		
IGF2BP2	F:GTTGGTGCCATCATCGGAAAGG	171bp	(NCBI)
	R:TGGATGGTGACAGGCTTCTCTG		
GAPDH	F:CTGAGAACGGGAAGCTTGTC	154	(NCBI)
Glyceraldehyde-3-Phosphate Dehydrogenase	R: TGCAAATGAGCC CCA GCC TTC TC		

Quantitative Real-Time PCR (qRT-PCR)

Preparation of KRAS, IGF2bp2 and housekeeping gene primers

These primers (IDT DNA, USA) were provided in lyophilized form, dissolved in sterile deionized distilled water to give a final concentration of 100 picomole/ µl as recommended by provider and stored in a deep freezer until use.

Detection of Gene Expression by (qRT-PCR) system

Detection of gene expression by Abm's One-Step EVA Green qRT-PCR Kit, is a complete qPCR system containing all necessary reagents for both reverse transcription and PCR amplification to occur in a single qPCR reaction tube.

Dnase preparation

Dnase enzyme is added to degrade the DNA. Dnase is prepared as follows according to manufacturer instructions (promega. USA).15 µl of the above mixture is added to 1 µl of extracted RNA and placed in water bath at 85 C° for 7 min to inactivate the Dnase enzyme.

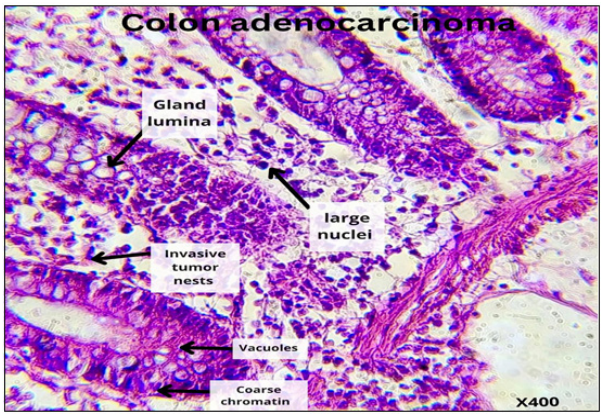

Figure 1. Colon Adenocarcinoma Tissue Showing Glandular Lumina, Large Hyperchromatic Nuclei, Invasive Tumor Nests, Cytoplasmic Vacuoles, and Coarse Chromatin at ×400 Magnification.

Expression by (qRT-PCR) system for KRAS, IGF2bp2 and GAPDH

The reaction mixture is made in a qRT-PCR tube on ice for every gene Table 2 each reaction was repeated 3 times.

Primer design KRAS, IGF2bp2 and GAPDH Receptor genes

Primers for KRAS, IGF2bp2 Receptor genes and housekeeping gene GAPDH (glyceraldehyde's 3-phosphate dehydrogenase) Table 3.

Statistical analysis

Data was analyzed by Graphpad prism v6, data were offered as the mean. Statistical analysis of variance to compare between groups were tested by one-way Anova (F-test). Unpaired T test was used to compare between groups. A level of statistically significant determination by P-value < 0.05, (Motulsky, 2003). Graphs were represented using Microsoft Excel 2010.

Results and Discussion

Histopathological findings (Figure 1 and 2).
Immunohistochemical (Figure 3-8).
Gene Expression (Figure 9).

Discussion

The results of this study revealed a histological section of well-differentiated adenocarcinoma in the colon and rectum, characterized by microscopic evidence. Figure 1

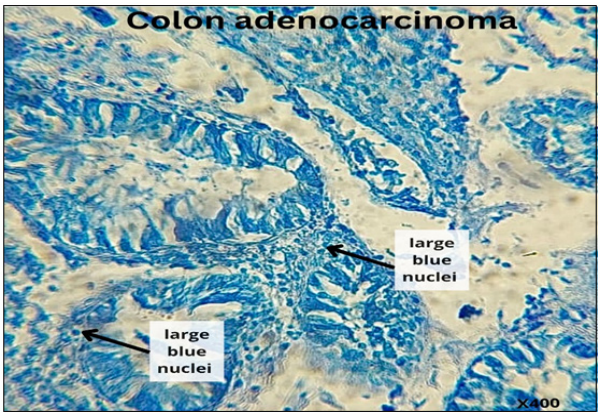

Figure 2. Giemsa Stains of Colon Adenocarcinoma Showing Irregular Glandular Arrangements with Large, Deeply Stained Blue Nuclei at 400x.

shows hematoxylin and eosin-stained tissue sections, magnified 400 times, showing a clear disruption in glandular organization, which characterizes colorectal adenocarcinoma. Irregularly shaped glands were observed, consisting of transformed epithelial cells with large, hyperchromatic nuclei, coarse chromatin, and prominent nucleoli. Vacuoles were also found in some cells, reflecting myosin secretion. Gastric tumor foci penetrating the surrounding connective tissue were also observed, confirming the malignant nature of the lesion. The sections stained with James staining at 400 magnification (Figure 2) showed dark blue staining of the tumor cells' nuclei, reflecting increased DNA density and high nuclear activity. The large, irregularly shaped nuclei also indicate a high degree of malignancy in thyroid cancer. The glands appeared irregular with a decrease in cavity formation and clear nuclear congestion, indicating loss of polarity and differentiation, two hallmarks of malignant transformation.

The results of this study agree with the findings of the Ilie et al. [9] study, where most cases of glandular cancer consist of branched and complex glandular structures with irregular cavities, primarily composed of columnar cells, and sometimes acinar-shaped cells located on a basal membrane. Tumorous glands show empty cavities or cavities occupied by necrotic cells, cytoplasmic fragments, nuclear remnants, and fibrous material, referred to as "contaminated necrosis". The tumor's epithelial tissue often appears columnar or pseudostratified, with cytoplasm of varying abundance and heterogeneity, and large, poorly stained nuclei, or vesicular nuclei, or one or more small nuclei.

However, in the immunohistochemical staining (Figure 3), a tissue section of well-differentiated glandular cancer in the colon and rectum is shown, stained with the chemical immunomarker CDX2 and examined at a magnification of 400 times. In Figure (A), the arrow head (→) indicates the brown staining in the nuclei of the tumor's epithelial cells, indicating the specific binding of antibodies to the CDX2 subtype within the cell nuclei, and highlighting the areas that show positive expression of CDX2. Figure (B) shows the same section after digital analysis using specialized software, providing a more accurate assessment of the intensity of the staining. In the analytical map, the yellow/brown areas indicate positively stained cells, while the blue areas represent tissues that do not show expression of CDX2.

For the comparison group (Figure 4), a histological section of a control sample of colon and rectal tissue, stained with the chemical immunostaining CDX2 and examined at a magnification of 400 times. In Figure (C), the arrow head (→) indicates the absence of staining in the nuclei of epithelial cells in the normal section, indicating that the antibody does not bind to the CDX2 subtype within the cell nuclei, thus indicating areas that do not show expression of CDX2. Figure (D) shows the same section after digital analysis using a specialized program, providing a more accurate estimate of the intensity of staining. In the analytical map, the yellow/light brown areas indicate cells stained with a specific antibody, while the blue areas represent tissues that do not show expression of CDX2. This digital analysis shows the spatial distribution of immunostaining cells and improves the identification of cancer cells within the same area.

The intensity of the immunohistochemical staining for the CDX2 protein is shown in (Figure 5), indicating a clear increase in cancerous tissues compared to healthy tissues. The average intensity of staining in normal tissues was 142, while it significantly increased in colorectal cancer tissues to 923. This sharp increase in the intensity

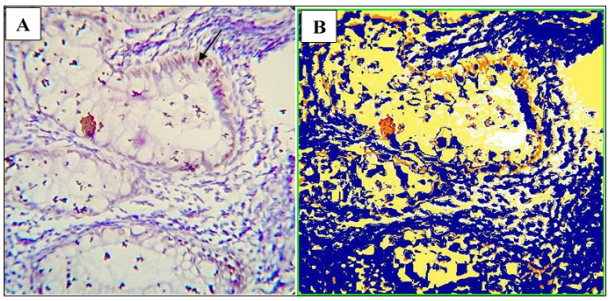

Figure 3. A Histological Section of Well-differentiated Colorectal Adenocarcinoma Stained with CDX2 Using the IHC Method at 400X Magnification. Image (A) shows arrow head (→) indicates the brown staining in the tumor epithelial cells, while Image (B) shows the digital analysis of the same section with identification of positive areas and staining intensity.

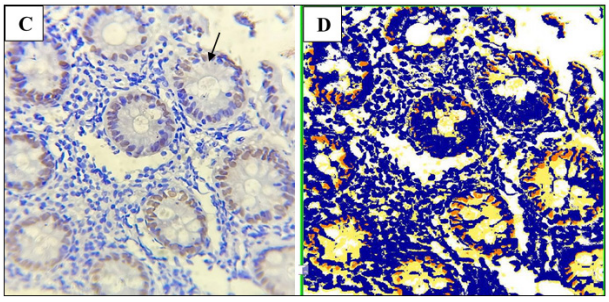

Figure 4. A Histological Section from a Control Sample of Colorectal Tissue Stained with CDX2 Using the IHC Method at 400X Magnification. Image (C) shows the staining of normal epithelial cells, while image (D) shows the digital analysis of the same section with identification of positive areas and staining intensity.

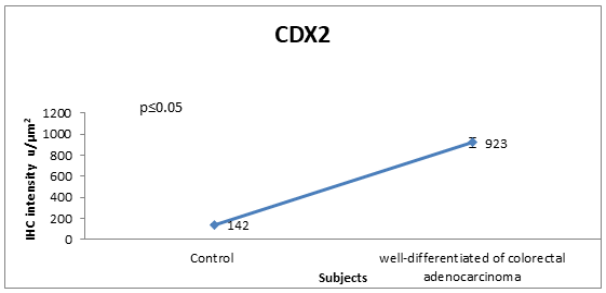

Figure 5. CDX2 Staining Intensity Average IHC Staining, Control 142, well-differentiated colorectal adenocarcinoma 923, p-value < 0.05.

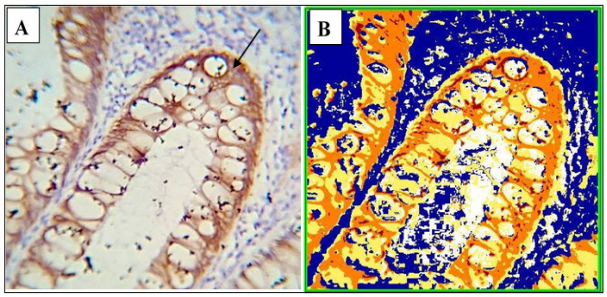

Figure 6. A Histological Section of Well-differentiated of Colorectal Adenocarcinoma Stained with CK20 Dye Using IHC Method at 400× Magnification. Image (A) shows arrow head (→) indicates the brown staining in the cytoplasm of tumor epithelial cells, while Image (B) shows the digital analysis of the same section with identification of positive areas and staining intensity.

of staining of the tissue immunomarker CDX2 in cancer cells is consistent with it being a specific marker for differentiated cells of intestinal origin, and it shows high expression levels in colorectal cancer. The $p < 0.05$ value indicates that the difference between the two groups is statistically significant.

Our results agreed with the study by Ilie-Petrov et al., [10], the natural mucous membrane of the colon was used as a positive internal reference in the analysis of the intensity of the immunohistochemical expression of the CDX2 protein at the tumor level. In addition, only the nuclear expression of the CDX2 protein in cancer cells was considered. The decision to focus exclusively on the nuclear expression of the CDX2 protein stems from its role as a nuclear transcription factor, which is extremely important in regulating gene expression within intestinal epithelial cells. The evaluation of the expression of the CDX2 protein included an assessment of both the intensity of nuclear staining and the proportion of stained nuclei. The evaluation was conducted at a magnification of 40x to observe the details of the nuclei accurately and ensure a precise measurement of the intensity of staining.

The positivity of the CDX2 protein was recorded using a semi-quantitative method to assess the intensity of staining and the proportion of cells that showed positivity.

As shown in the study by Reehorst et al. [11], the analysis of CDX2 gene expression in a group of primary and metastatic tumors revealed a wide range of nuclear expression levels, with a significant increase in expression in well-differentiated/moderately-differentiated (low-grade) tumors compared to poorly differentiated (high-grade) tumors, as previously reported. In contrast, no difference in the overall expression levels of the CDX2 gene was observed between matched primary and metastatic tumors, while a strong positive correlation was found in the expression levels of the CDX2 gene between matched individual cases of primary and metastatic tumors, collectively indicating the stability of CDX2 gene expression between matched primary and metastatic lesions.

As shown in (Figure 6), a tissue section of well-differentiated colonic rectal adenocarcinoma, stained with an immunohistochemical marker (IHC), was examined at a magnification of 400 times. In Figure (A), the arrowhead (→) indicates the specific immune reaction between the antibodies in the cytoplasm of cancer cells and the CK20 antigen, which appears in a light brown color. Figure (B) shows the same section processed with a specialized program to distinguish positively stained areas and determine their intensity more accurately, highlighting yellow/brown areas as positively stained cells, while blue areas represent tissues negative for CK20 expression. This evaluation facilitates the distribution of immunohistochemically stained cells within the same field.

In (Figure 7), a tissue section from a control sample of the colon and rectum stained with immunohistochemistry (IHC) and examined at 400x magnification is shown. In Figure (C), the arrow head (→) indicates a weak or absent specific immune reaction between the antibody in the cell cytoplasm and the immunohistochemical marker CK20. In Figure (D), the same section was processed using a specialized image analysis program to distinguish positive areas and determine their intensity more accurately. The blue areas indicate healthy tissue and a negative result, which facilitates the evaluation of the distribution of immunostaining cells within the same field.

(Figure 8) shows a diagram of the intensity of immunohistochemical staining for CK20 with a clear increase in the tumor tissue compared to the control sample. The intensity of immunohistochemical staining in the control group was 142 , while it significantly increased in cancer cells to 923. This increase indicates a higher

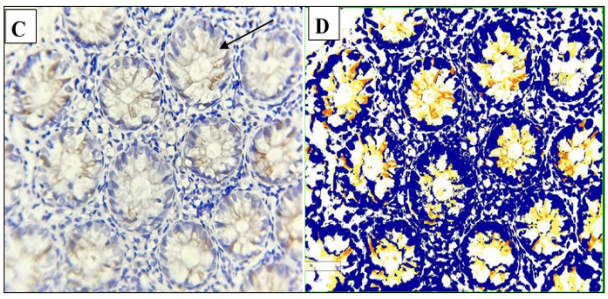

Figure 7. A Histological Section from a Control Sample of Colorectal Tissue, Stained with CK20 Using the IHC Method at 400x Magnification. Image (C) arrowhead (→) shows weak or indistinct staining in the cytoplasm of epithelial cells, consistent with the normal expression of healthy samples, while image (D) shows the numerical analysis of the same section with positive areas identified and staining intensity measured.

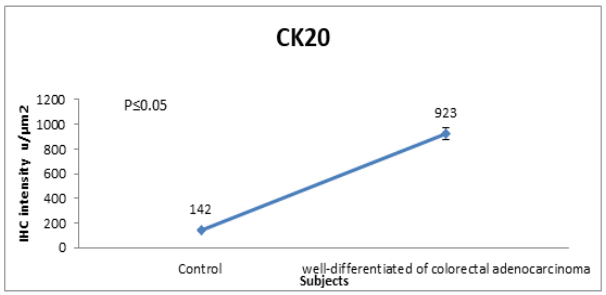

Figure 8. CK20 Staining Intensity, Average IHC Staining, Control 142, well-differentiated colorectal adenocarcinoma 923, p≤0.05

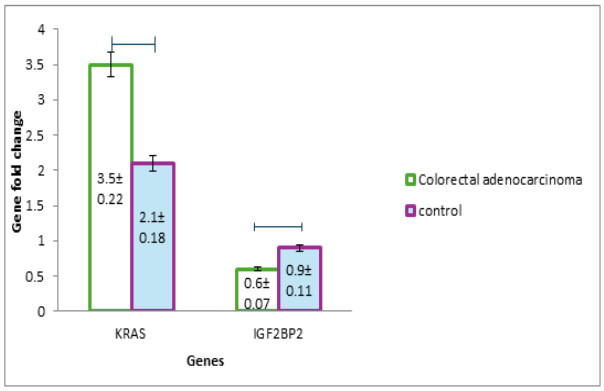

Figure 9. Gene Fold Change of KRAS and IGF2BP2 (SE) in Colorectal Adenocarcinoma and Control Subjects. A statistically significant (p= 0.04) increase in gene fold change of both KRAS and IGF2BP2 (p=0.05) genes which may indicate a cellular genetic change I response to immune expression changes seen in histological analysis.

level of expression of the immunohistochemical marker CK20 in cancer cells, which is consistent with its role as an immunohistochemical marker for the differentiation of colorectal cancer. The P value was less than 0.05, indicating a statistically significant difference between the two groups.

A study by Rezaei et al. [12], demonstrated that cytokeratin's, a family of intermediate filament proteins, are essential components in the structure of epithelial cells. Among them, cytokeratin 20 (CK20) has received significant attention as a potential biomarker for colorectal cancer, due to its role in distinguishing between different subtypes of intestinal epithelial cells. Therefore, our study aimed to investigate the relationship between the immunohistochemical expression of CK20 and diagnostic factors for colorectal adenocarcinoma.

In a study conducted by PraSanna et al. [13], a loss of CK20 gene expression, in contrast to the positive expression of CK7, was observed in some cases of colorectal cancer. The significance of this abnormal expression remains unclear. In primary colorectal cancer, the CK20 gene expression was positive in 62.5% of cases, while the CK7 gene expression was positive in 5.6%. In cases of nodal metastases, the proportion of positive CK20 and CK7 gene expression was 63.5% and 4.1%, respectively. The reason for the unusual immunohistochemical staining of CK20 and CK7 remains unclear. Recent molecular studies have classified colorectal cancer into microsatellite stable tumors and microsatellite unstable tumors. Other studies have examined the CK20/CK7 gene expression in 44 cases of colorectal cancer and its relationship with molecular subtypes, concluding that a decrease or complete absence of CK20 is a characteristic of colorectal cancer caused by microsatellite instability (MSI).

Genetic expression, (Figure 9) shows that the KRAS gene expression increases by approximately 5.83 times in colon and rectal tissue compared to healthy tissue. This indicates a significant increase in KRAS gene expression in the cancerous sample (colon and rectum). KRAS is a well-known oncogenic gene involved in cell signaling and proliferation, and its increased expression is often associated with cancer development. Similarly, the IGF2BP2 gene expression increases by approximately 2.33 times in colon and rectal tissue compared to healthy tissue. IGF2BP2 (insulin-like growth factor 2 mRNA binding protein) is typically associated with tumor growth promotion, and its moderate increase in expression here suggests that it may also play a role in this specific case of colorectal cancer.

Both KRAS and IGF2BP2 show increased expression in the colon and rectal sample, indicating that they are potential targets or indicators in this case, with a notable increase in KRAS expression. Genetic changes could have a direct realtion to immune expression of CK20 and CK7.

In a study by Pandin et al. [14], it was reported that KRAS gene mutations are responsible for resistance to specific cancer treatments, and are associated with a more invasive tumor phenotype and worse prognoses. The location of the tumor was also linked to clinical outcomes; some analyses suggested that patients with tumors on the left side of the body have better survival rates than those with tumors on the right side. These two variables - the status of the KRAS mutation and the location of the tumor - have emerged as key indicators of treatment response in recent years.

As explained in a study conducted by Su et al. [15], mutations in the KRAS gene are among the most common mutations in cancer, especially in cancers driven by the RAS gene, where KRAS mutations play a significant role. The G12 and G13 sites are KRAS mutation sites that play a crucial role in tumor resistance, which can lead to continuous activation of the KRAS protein and affect other signaling pathways, thereby enhancing tumor development and drug resistance. The study found that DNA damage repair and KRAS mutations are closely related.

As a study by Kendzia et al. [16] demonstrated a decade ago, the presence of autoantibodies against IGF2BP2 was detected in the serum of patients with colon cancer. At the same time, reports indicated that IGF2BP2 enhances the proliferation of colon and rectal cancer cells through multiple mechanisms. Moreover, it has been linked to a poor prognosis in patients with colon and rectal cancer. However, the data regarding the impact of IGF2BP2 on chemotherapy resistance in colon cancer are still insufficient.

In a study conducted by Liu et al. [17], the survival rate

of colorectal cancer patients with high levels of IGF2BP2 was shorter. After inhibiting IGF2BP2, the viability, proliferation, and migration of HCT-116 and SW480 cells decreased. The gene expression of MYC, TGF-β, and IL-10 significantly decreased in the IGF2BP2-inhibited group, while the gene expression of TNF-α increased. The level of MYC protein and its mRNA stability significantly decreased.

The noticeable increase in gene fold change of both KRAS and IGF2BP2 may directly influence the expression of CDX2 and CK20 which may in turn lead to a more aggressive form colorectal cancer. The current study lacks the more molecular evidence to establish the relationship between genetic markers and histopathological changes in colorectal adenocarcinoma.

In conclusions, the results of the current study indicate an increase in the gene expression of the studied genes, which leads to poor prognosis, as shown by other studies. This may significantly affect the cells' response to chemotherapy and subsequent resistance to it.

Originality Declaration for Figures

All figures included in this manuscript are original and have been created by the authors specifically for the purposes of this study. No previously published or copyrighted images have been used. The authors confirm that all graphical elements, illustrations, and visual materials were generated from the data obtained in the course of this research or designed uniquely for this manuscript.

Acknowledgments

Statement of Transparency and Principles

• The authors declare no conflict of interest.

• The study was approved by the Research Ethics Committee of the authors' affiliated institution.

• The study data are available upon reasonable request.

• All authors contributed to the implementation of this research.

References

1. Yang Z, Cespedes-Acuña CL, Yang Z, Abu Bakar MZ, Chan KW, Deng X. Plant Foods and Their Bioactives as Dietary Enhancers for Colon Cancer Treatment with 5-Fluorouracil. Food Reviews International. 2025 07 04;41(5):1390-1439. https://doi.org/10.1080/87559129.2024.2446366
2. Mishra A, Singh KJ, Gahlot GPS, Pal S. Prognostic Significance of Caudal-type Homeobox Gene 2 and Sex-determining Region Y-Box 2 Immunohistochemistry Markers in Gastric Cancer – A Clinicopathological Study. Journal of Marine Medical Society. 2025 04;27(1):32. https://doi.org/10.4103/jmms.jmms_18_24
3. Voutsadakis IA. Gastric Adenocarcinomas with CDX2 Induction Show Higher Frequency of TP53 and KMT2B Mutations and MYC Amplifications but Similar Survival Compared with Cancers with No CDX2 Induction. Journal of Clinical Medicine. 2024 Dec 15;13(24):7635. https://doi.org/10.3390/jcm13247635
4. Ribeirinho-Soares S, Pádua D, Amaral AL, Valentini E, Azevedo D, Marques C, Barros R, et al. Prognostic significance of MUC2, CDX2 and SOX2 in stage II colorectal cancer patients. BMC cancer. 2021 04 06;21(1):359. https://doi.org/10.1186/s12885-021-08070-6
5. Nada A, Alkhatib A, Abdelmalik F, El-Abd M, Elabd NS, Abdel-Latif HE. Bile level of cytokeratin 7 as a diagnostic marker for cholangiocarcinoma: a case-control study in Egyptian patients. Egyptian Liver Journal. 2024 06 15;14(1):46. https://doi.org/10.1186/s43066-024-00353-4
6. Hansen MF. Genetic predisposition and cancer. In developmental biology and cancer (pp. 277-312). Crc press. 2024.
7. Wang Y, Bui TA, Yang X, Hutvagner G, Deng W. Advancements in gene therapies targeting mutant KRAS in cancers. Cancer Metastasis Reviews. 2025 01 17;44(1):24. https://doi.org/10.1007/s10555-025-10243-9
8. Zeng F, Chen L, Li J, Yu W, Sa N, Zhang K, Qu C, Wen D. A pan-cancer analysis reveals the oncogenic and immunological role of insulin-like growth factor 2 mRNA-binding protein family members. Discover Oncology. 2025 03 15;16(1):323. https://doi.org/10.1007/s12672-025-02077-2
9. Ilie DS, Mitroi G, Păun I, Ţenea-Cojan TS, Neamţu C, Totolici BD, Sapalidis K, et al. Pathological and immunohistochemical study of colon cancer. Evaluation of markers for colon cancer stem cells. Romanian Journal of Morphology and Embryology = Revue Roumaine De Morphologie Et Embryologie. 2021;62(1):117-124. https://doi.org/10.47162/RJME.62.1.11
10. Ilie-Petrov A, Cristian D, Grama fa, Chitul A, Blajin A, Popa A, Mandi D, et al. Evaluation of the Immunohistochemical Scoring System of CDX2 Expression as a Prognostic Biomarker in Colon Cancer. Diagnostics. 2024 05 15;14(10):1023. https://doi.org/10.3390/diagnostics14101023
11. Reehorst CM, Mooi JK, Uy CJ, Needham KA, Ellis S, Luk IY, Jenkins LJ, et al. Differentiation grade is highly concordant between matched primary and metastatic colorectal cancer. Clinical & Experimental Metastasis. 2025 Oct 17;42(6):61. https://doi.org/10.1007/s10585-025-10380-z
12. Rezaei R, Kheradmand P, Bagheri S, Mansouri E. Investigating the Relation between Immunohistochemical Expression of Cytokeratin 20 and Clinicopathological Factors Determining Colorectal Adenocarcinoma Prognosis.. Iranian Journal of Gastroenterology & Hepatology (GOVARESH). 2023 Oct 01;28(3):183.
13. Prasanna K, Palaniappan V, Kumar S, Ravi S. (2024). Analysing immunohistochemical co-expression of cdh17, ck7 and ck20 in lower gastrointestinal tumours: A cross-sectional study. National journal of laboratory medicine.13(04):17-23.
14. Pandin AR, Parewangi ML, Bakri S, Rasyid H, Minhajat R. Survival Rate of Colorectal Cancer Patients Receiving Chemotherapy based on Tumor Location and K-Ras Gene Mutation Status: A Systematic Review. Asian Pacific Journal of Cancer Biology. 2025 Nov 26;10(4):1087-1093. https://doi.org/10.31557/apjcb.2025.10.4.1087-1093
15. Su Q, Wang K, Liao R, Zhang H, Wang B. Dissecting the METTL3/STC2 axis in colorectal cancer: implications for drug resistance and metastasis. Cell Biology and Toxicology. 2025 06 10;41(1):100. https://doi.org/10.1007/s10565-025-10043-5
16. Kendzia S, Franke S, Kröhler T, Golob-Schwarzl N, Schweiger C, Toeglhofer AM, Skofler C, et al. A combined computational and functional approach identifies IGF2BP2 as a driver of chemoresistance in a wide array of pre-clinical models of colorectal cancer. Molecular Cancer. 2023 05 30;22(1):89. https://doi.org/10.1186/s12943-023-01787-x

17. Liu T, Han C, Hu C, Mao S, Sun Y, Yang S, Yang K. Knockdown of IGF2BP2 inhibits colorectal cancer cell proliferation, migration and promotes tumor immunity by down-regulating MYC expression. Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi = Chinese Journal of Cellular and Molecular Immunology. 2023 04;39(4):303-310.