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Meta-Analysis Approach of Transcriptome Data to Identify Core Genes Linked To Colorectal Cancer

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Abstract

Despite the known genetic, epigenetic, and transcriptomic alterations, colorectal cancer (CRC) is still one of the major causes of cancer death throughout the world. Recent progress in the field of transcriptome has greatly promoted our understanding regarding the molecular mechanism at the molecular level during CRC progression, which identified several key core genes, such as KRAS, MYC, TP53 and APC, that control oncogenic pathways such as Wnt/β-catenin, PI3K-AKT, inflammatory signaling, etc. The conjoining of transcriptomics with the epigenomics, especially the DNA methylation and histone modifications, has shed more light on tumor suppressor gene silencing and oncogene activation that can serve as potential biomarkers for the early detecting and prognosis of the disease as well as the selection of the therapies. Since much of their development into personalized medicine has been internalized by pharmaceutical companies for proprietary reasons, these markers have not been extracted. New therapeutic interventions involving reversal of the abnormal expression pattern of genes using epigenetic drugs running the gamut of histone deacetylase inhibitors (HDACi's) and DNA methyltransferase inhibitors (DNMTi's) are under investigation. Finally, artificial intelligence (AI) and machine learning is also having a huge role in analyzing large scale transcriptomic data and it is transforming biomarker discovery, treatment selection and predicting patient outcomes, transcriptomic research will lead the personalized view of CRC and will provide a new hope for the early detection, prognosis, and personalized targeted therapy. As such, continuous multi-omics integration, computational biology and clinical validation efforts will be a crucial component in furthering CRC transformation into a renowned disease for which simple management strategies, improved survival and treatment efficacy can all be attained.

Keywords: *Colorectal cancer, transcriptomics, epigenomics, biomarkers, multi-omics, Wnt/β-catenin, PI3K-AKT, DNA methylation, histone modification, artificial intelligence, personalized medicine, targeted therapy, liquid biopsy, single-cell RNA sequencing.*

I. Introduction

A. Background on Colorectal Cancer (CRC)

Widespread CRC marks one of the deadliest cancer associated mortality reasons with continuously rising cases of incidences and high prevalence rates, almost all round the world, and particularly majority of the highly developed countries (Rajamäki et al., 2021). CRC results from an uncontrolled cell growth of the colonic or rectal epithelial cells formed as a tumor. Diet, smoking and inactivity habits as well as environmental issues together lead to CRC pathology but genetic and epigenetic changes present themselves as the main drivers of CRC development. Genetic population of critical tumor suppressor genes and oncogenes is an important factor for development of colorectal cancer. APC and KRAS and TP53 three genetic mutations made the faulty signaling networks superpower the malign cell to spreading and tumor develop (Coppedè et al., 2014).

Genetic and epigenetic alteration of the regulation of gene expression are highly significant in colorectal cancer cells. Epigenetic changes lead to modifications that are not DNA sequencing, but they lead to alterations in chromatin accessibility that are linked to regulation of the expression of genes. DNA methylation and histone modifications, as well as the regulatory effects of non-coding RNA, are the three main epigenetic modifications involved in pathogenesis of CRC (Li et al., 2018). The underlying mechanisms of tumor suppressor gene silencing are hypermethylation of genes such as MLH1 and CDKN2A while oncogene tumor progression is due to hypomethylation events. Histone modifications that function in acetylation and methylation influence chromatin dynamics further, in that they control transcriptional activity (Mack et al., 2018). For finding new targets for gene and epigenetic therapies and raising proper CRC therapy approaches, it is essential to analyze the relationship between genetic and epigenetic factors.

B. Importance of Transcriptome Analysis in CRC

Transcriptome analysis represents an important methodology to tackle disease molecular patterns of colorectal cancer due to the information on gene expression activity during cancer progression development. Using the high-throughput method, researchers can discover genes that are being differently expressed (DEGs) in the entire colorectal cancer development as well as some gene changes associated with progression and metastasis (Zhang et al., 2019). Scientists analyze molecular changes between tumor and normal tissues to identify main biological alterations that contribute to the development of cancer. These analyses helped in discovering essential biomarkers that may be useful for the early diagnosis of CRC as well as for predicting treatment and planning individualized therapeutic developments.

Coding as well as non-coding RNAs, for example long non-coding RNAs (lncRNAs), microRNAs (miRNAs), and circular RNAs (circRNAs), known to play active roles in gene regulation are also obtained by researchers through transcriptome analysis (Esteban-Gil et al., 2019). Abnormal regulation of non-coding RNAs altering signaling networks into cancer promoting and cancer preventing role is found to be the cause of development of CRC based on research findings. However, for the CRC pathogenesis, miR-21 promotes cancer while targeting tumor suppressor genes at the same time and lncRNA HOTAIR cause chromatin remodeling and metastasis.

The breakthrough in research in transcriptomics comes from next generation sequencing (NGS) and microarray technologies for which these tools help researchers acquiring massive RNA sequencing (RNA-seq) datasets. The research datasets allow scientists to know details of temporary change of gene expression and choose new therapeutic candidates. However, to conduct analysis of transcriptomic data, the methods, and computational tools of bioinformatics development are necessary to identify gene coexpression networks and pathway enrichment discovery of learning epigenetic modification interaction (Samadi et al., 2022). The development of transcriptome analysis has significant potential for improving CRC research, and hence, patient-specific precision medicine approaches.

C. Objectives of the Review

The objective of this review is thus to carry out an in depth analysis of colorectal cancer transcriptomic research where different meta analytic techniques have identified important disease relevant genes. The functions of the review are to provide a union of findings of various researches related with transcriptomic for detecting genes that show dysregulations consistently and their possible clinical applications. Integrated studies at high throughput help to conclude on CRC main molecular drivers along with their associated epigenetic modifications in a more powerful way (Mukherjee & Ray, 2023).

Histone modifications and noncoding RNAs are also shown to play significant regulatory roles. While reviewing the regulatory roles, the review also examines the mutual relationship between the transcriptomic changes and epigenetic alterations in colorectal cancer. There is new view on the mechanisms and medicine resistant patterns of CRC development when we look at how epigenetic factors alter transcriptomic changes (Shaath et al., 2019). In this way, the review discusses how the application of transcriptome-based biomarkers could be integrated into CRC clinical practice, e.g., for development of diagnosis procedures, prognosis prediction and treatment strategy.

Finally, the review concludes with an outlook on transcriptomic research with remarks about new technological developments and new approaches for integrating data as well as applications of artificial intelligence in the analysis of transcriptome data. These basic aspects are reviewed in order to improve clinical use of CRC diagnostic and therapeutic approaches to more effectively care for patients.

D. Methodology of the Review

Systematic techniques are used for the diagnosis, selection, and evaluation of appropriate studies about transcriptomics and colorectal cancer to produce a complete and fair synthesis of extant literature in this review. The research was performed via search through various electronic platforms including PubMed, Scopus and Google scholar as well as TCGA, GEO. The research employs databases that provide full access to the high impact of the research article and the data set as well as meta analysis studies focused on transcriptomics and CRC (Hassan, 2019).

The inclusion criteria for selecting studies involved:

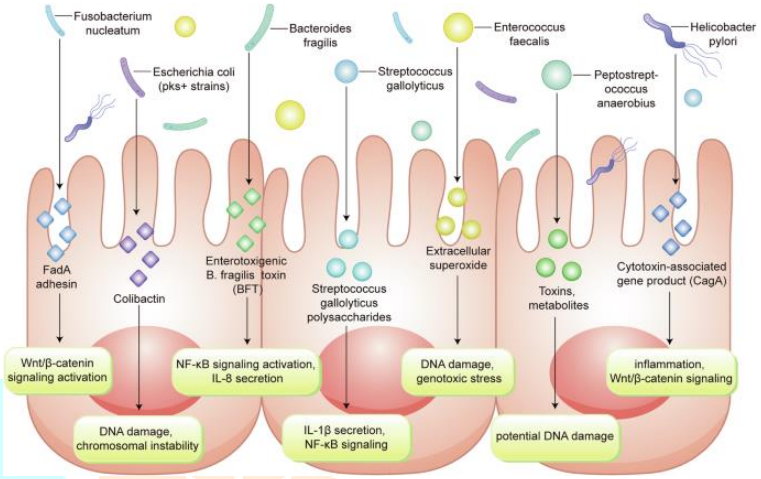
1. Studies published in peer-reviewed journals within the last decade (2013–2024).
2. Research articles that focused on transcriptomic analysis of colorectal cancer, including RNA-seq and microarray studies.
3. Studies that provided meta-analyses of CRC transcriptome data to identify core genes.
4. Papers that integrated transcriptomic findings with epigenetic modifications.
5. Clinical studies that examined transcriptome-based biomarkers for CRC diagnosis and prognosis.

Studies were excluded if they:

- Did not provide sufficient transcriptomic data.
- Focused solely on animal models without human validation.
- Lacked methodological transparency in data analysis.
- Were reviews without original research findings.

The search strategy involved using relevant **keywords and Boolean operators** to refine the results, including:

- "Colorectal cancer transcriptomics"
- "Differential gene expression in CRC"
- "Epigenetics and transcriptome integration in CRC"
- "Meta-analysis of colorectal cancer transcriptomic data"
- "RNA-seq data in colorectal cancer"
- "Biomarkers and transcriptomic profiling in CRC"



II. Colorectal Cancer and Its Molecular Basis

A. Pathophysiology and Genetic Basis of CRC

The development of colorectal cancer (CRC) advances through various genetic and molecular changes and results in uncontrolled growth of cells in either the colon or rectum. Regular cells inside the colon transform into adenomatous polyps that gradually become invasive cancer if healthcare providers do not exert treatment. The development process depends on two forms of mutations that modify regulatory genes which control cell growth and apoptosis and DNA repair activities (Coppedè et al., 2014). CRC growth relies on specific genetic mutations since these alterations provide definite indications of disease progression.

Cell control genes comprise the essential two categories called oncogenes and tumor suppressor genes that control cell activities until mutations in these genes produce cancer development. The cancer progression rate accelerates due to oncogene mutations which enhance cell reproduction and defend cells from apoptotic defeat. Of all the mutated oncogenes in CRC KRAS emerges as the leading case with its ability to activate the mitogen-activated protein kinase (MAPK) signaling pathway. KRAS mutations appear in 40% of CRC patient cases to establish continuous chain reactions leading to continuous cell replication (Rajamäki et al., 2021). The genetic function of phosphatidylinositol 3-kinase subunit gene enables PIK3CA mutations in CRC to create advantages which enhance survival and reprogram cellular metabolism.

Exchange differs from oncogenes as these protective factors maintain proper cell operation and genomic protection mechanisms. CRC development depends on the loss of functionality among these essential genes. Early colorectal tumors experience APC (adenomatous polyposis coli) gene mutation which continues to be one of the commonest abnormalities found in tumor suppressor genes of colorectal tumors. The activation of Wnt/β-catenin signaling occurs due to APC gene mutations that lead to uncontrolled cell proliferation gene transcription. The lack of an active TP53 tumor suppressor gene exists in more than half of CRC cases thus disrupting cellular death and increasing genomic irregularities (Li et al., 2018). Mutations within the SMAD4 pathway make cells misfunction during cell differentiation while also preventing them from carrying out apoptosis properly.

CRC heterogeneity results primarily from two genetic factors involving chromosomal instability (CIN) along with microsatellite instability (MSI). The defective DNA mismatch repair at CIN leads to extensive chromosomal abnormalities and heterozygosity loss while MSI develops from mismatch repair system disorders responsible for elevated mutation quantities. Medical staff now provide precise treatments by recognizing genetic changes within CRC patients according to Zhang et al. (2019).

B. Epigenetic Modifications in CRC

Colorectal cancer development depends significantly on both epigenetic modifications together with genetic mutations in determining its pathway. Epigenetic alteration groups inherit expression changes through hereditary lines without changing DNA base

composition but activate chromatin structure transformations. CRC follows three main epigenetic systems which encompass DNA methylation together with histone modifications and non-coding RNA regulation because these systems regulate the transcription of oncogenes and tumor suppressor genes (Mack et al., 2018).

1. DNA Methylation

Scientists extensively use DNA methylation measures in CRC investigations due to their status as an epigenetic modification. During DNA methylation transcription becomes silent as the process turns CpG dinucleotide cytosines into methylated cytosines. CRC development mainlydepends on normal DNA methylation loss which produces oncogene hypomethylation yet tumor suppressor genes undergo elevated methylation. The DNA repair mechanism along with tumor suppression pathways lose their functionality because promoter hypermethylation blocks genes including MLH1, CDKN2A and RUNX3 (Esteban-Gil et al., 2019). Progressive CRC formation results from DNA methylation decline throughout the whole genome which activates cancer-fostering pathways.

2. Histone Modifications

Histones maintain DNA packaging control through three modifications of post-translational activities which involve acetylation and methylation together with phosphorylation. The biological events of histone acetylation through histone acetyltransferase (HAT) function enable better gene transcription yet histone deacetylation by histone deacetylase (HDAC) causes gene transcription suppression. CRC histone modifications lead to dysfunctional gene expression that alters chromatin structures in an abnormal way. The tumor suppressor gene silencing links to hypermethylated histone H3 with its H3K27me3 mark but H3K9 deacetylation silences regulatory networks controlling cell proliferation (Shaath et al., 2019). Patients with CRC receive effective therapy from HDAC inhibitors because these therapeutic agents normalize gene expression patterns by undoing epigenetic dysregulation.

3. Non-Coding RNAs (miRNA, lncRNA, circRNA)

In CRC research ncRNAs function as vital subjects due to their effect on gene expression regulation. Small molecule microRNAs (miRNAs) control gene expression on a post-transcriptional level through two pathways that degrade or silence mRNA translation. Steady dysregulation of miRNA expression signatures in CRC results in the conversion of oncogenic miR-21 along with a decrease in tumor suppressor miRNA let-7. Both long non-coding RNAs and circular RNAs function through two regulatory mechanisms which include chromatin structure modification and gene expression control. The complex nature of CRC development emerges from research on ncRNA modifications allowing prospects for novel treatment strategies according to Mukherjee & Ray 2023.

C. Current Therapeutic Approaches for CRC

Patients receive collorectal cancer treatments through multiple phases because healthcare practitioners use different therapeutic approaches based on disease progressions and molecular traits. Medical staff design standard CRC treatments through surgery and chemotherapy which must also include immunotherapy following assessments of specific genetic factors and disease progression level for each patient.

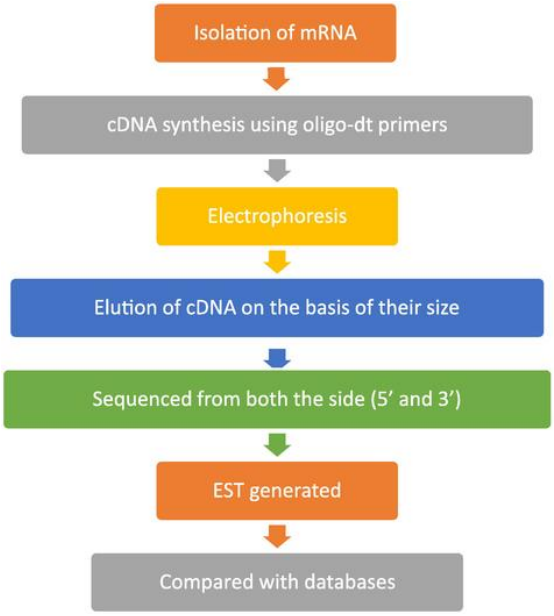
1. Surgery and Chemotherapy

The primary healing method of localized colorectal cancer during initial stages consists of surgical procedures. Patients requiring more advanced cancer treatment scenarios need surgery alongside chemotherapy to help prevent cancer from reappearing. Two commonly utilized chemotherapy treatments for cancer cell control are FOLFOX with its components of 5-fluorouracil and leucovorin together with oxaliplatin and FOLFIRI consisting of these same drugs combined with irinotecan (Nair et al., 2020). Chemotherapy remains effective yet needs improvement of alternative options due to its resistance-causing side effects.

2. Immunotherapy and Personalized Medicine

The revolutionary immunotherapy treatment method provides exceptional benefits to CRC patients who have MSI-H and dMMR positivity. The PD-1/PD-L1 checkpoint pathway in immune inhibitors pembrolizumab and nivolumab enables the body to attack cancer cells better. The available immunotherapy shows limited success for specific patient populations thus molecular profile-based personalized approaches remain necessary (Samadi et al., 2022).

Medical professionals base individualized treatment creation on patient genetic and transcriptomic profile information using personalized medicine strategies. Treatment methods using anti-EGFR drug cetuximab and anti-VEGF drug bevacizumab show advantages for patients who possess wild-type RAS genes because genetic profiling demonstrates its value in improving treatment selection. Emerging biomarkers from advanced transcriptome analysis systems identify new treatment targets which produce improved and precise CRC therapeutic solutions.



III. The Role of Transcriptomics in CRC Research

A. Overview of Transcriptomics Technologies

The analysis of biological samples through Transcriptomics allows scientists to study RNA transcripts for following gene expression patterns and molecular networks that affect colorectal cancer (CRC). Scientists studying CRC through transcriptome profiling receive vital tumor biological understandings that include the detection of differentially expressed genes (DEGs) directing cancer development and spreading (Shaath et al., 2019). The research field of CRC mainly uses microarrays and RNA sequencing (RNA-seq) methodologies while each approach comes with unique capabilities and limitations.

Scientists received the capability of parallel gene detection through hybridization reactions when microarrays emerged as a high-throughput technology (Mack et al., 2018). The execution of this method requires stable cDNA probes attached to solid surfaces which accept RNA molecules bearing fluorescent stain labels. Microarray systems successfully detected CRC-associated expression patterns yet their discovery of new transcripts is restricted because researchers must supply in advance known genomic sequences. False levels of gene expression measurement occur because of probe cross-hybridization combined with background noise according to Li et al. (2018).

RNA molecule characterization within biological specimens has experienced a milestone through next-generation sequencing technology which enables precise complete unfiltered examinations. Through RNA-seq technology scientists can detect coding and non-coding RNAs simultaneously so they can study long non-coding RNAs (lncRNAs) and microRNAs (miRNAs) as well as circular RNAs (circRNAs) during colorectal cancer pathogenesis (Mukherjee & Ray, 2023). The requirement to specify sequences beforehand is not necessary for RNA-seq technology because this technique reveals unidentified RNA molecules and determines splicing alternatives simultaneously. RNA-seq provides various advantages yet researchers must cope with three significant disadvantages that include its high price point and intricate data analysis and absolute need for specialized bioinformatics expertise.

Results produced by CRC researchers reach higher strengths when they combine analysis data across two widely used technologies. The interpretation of transcriptomic data for CRC diagnostic and prognostic biomarker discovery reached new sophistication through the development of bioinformatic tools built with machine learning algorithms and network-based methodologies (Esteban-Gil et al., 2019). Professional transcriptomic technologies continue to advance through better molecular process examination abilities that allow physicians to develop customized medical treatment methods.

B. Key Findings from Transcriptomic Studies in CRC

The transcriptomics research domain delivered vital knowledge about colorectal cancer after identifying patterns that show how malignant tissue disrupts normal tissue patterns during two decades. Transcriptomic investigations focused mainly on identifying differentially expressed genes (DEGs) through their change in expression levels between cancerous and non-cancerous tissue groups. CRC progression involves the essential functions of identified DEGs which alter cell proliferation pathways along with apoptosis and invasion mechanisms as they also manipulate immune evasion functions (Zhang et al., 2019).

Transcriptomic data analysis repeatedly reveals that CRC develops more oncogenes at the same time it loses tumor suppressor genes. Tumor expansion during CRC development depends heavily on three key genes which

are KRAS and MYC and CCND1 because demographic data indicates substantial expression alterations of these genes (Samadi et al., 2022). Metastatic CRC features elevated ZEB1 and SNAI1 expression because these belong to EMT regulatory genes while enabling tumors to spread to different body areas. Genetic mutations together with epigenetic silencing result in downregulation of TP53 and CDKN2A with SMAD4 tumor suppressor genes thus triggering cell cycle control failure with apoptosis dysfunction (Hassan, 2019).

Non-coding RNA regulatory functions together with protein-coding genes determine the natural progression of CRC at significant levels. ócogenic signaling pathways provide transcriptomic evidence showing the repeated changes of microRNAs miR-21, miR-200c, and miR-155 in CRC tissues (Rajamäki et al., 2021). CRC cells express excessive amounts of miR-21 that functions as an oncogenic factor after targeting PTEN and PDCD4 tumor suppressor genes for inhibition to make cells chemoresistant and lead to survival (Li et al., 2018). The change and spread of CRC cells during metamorphosis and metastasis happens with the help of HOTAIR and MALAT1 lncRNAs which modify chromatin structure and regulate gene expression.

Research into molecular CRC subtypes stands vital in transcriptomic investigations because it depends on gene expression signatures to identify such molecular subtypes. Big data transcriptomic analysis through CMS classification organizes CRC tumors into four distinct groups known as CMS1 microsatellite instability immune followed by CMS2 canonical along with CMS3 metabolic and CMS4 mesenchymal types (Mack et al., 2018). The CRC classification system produced by researchers enabled them to understand CRC biological complexity that determines patient survival rates alongside treatment responses. Patients with CMS1 tumors benefit from immunotherapy treatment success because these tumors contain high immune cell infiltration yet CMS4 tumors demonstrate poor outcomes with decreased treatment effectiveness.

Scientific analysis between molecular and clinical data together with transcriptomic results enabled researchers to build survival prediction tools while developing treatment outcome forecasts through gene expression. Personal risk values help physicians plan adjuvant therapy through the gene signature tests named ColoPrint and Oncotype DX Colon Cancer Test (Esteban-Gil et al., 2019). Studies in transcriptomics confirm its capability to enhance CRC evaluation procedures throughout diagnostic operations and therapeutic selection and prognostic forecasting.

C. Meta-Analysis of CRC Transcriptome Data

The research field utilizes meta-analysis as a essential data analysis technique for studying comprehensive transcriptomic information extracted from separate colorectal cancer studies. Meta-analysis enables researchers to enhance research outcomes through an organized approach for combining transcriptomic data from multiple studies while decreasing experimental mistakes (Mukherjee & Ray, 2023). Research analysts can make reliable decisions regarding CRC molecular activities by applying meta-analytical strategies to different patient data sets so they can detect true biological patterns and reduce experimental errors.

The application of meta-analysis to transcriptomic research yields shared dysregulated genes as the main benefit by removing design-specific biases that exist between individual studies. The increased expression levels of MMP9, FN1 and CEACAM5 proved their necessity as biomarkers for CRC development according to findings based on large study databases (Shaath et al., 2019). According to Shaath et al. (2019) the expression levels of SFRP1 CDH1 and TGFBR2 became suppressed during tumor control processes. CRC genetic discovery research provides comprehensive knowledge regarding CRC-modified genes to establish potential new therapeutic possibilities.

The main value of transcriptomic meta-analysis for research includes performing pathway enrichment and network-based analysis. Issue detection within CRC signaling pathways that arise from tissue transformations between normal and cancer-involved colorectal conditions is possible using functional annotation tools Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG). Wnt/β-catenin, PI3K-AKT together with TGF-β represent crucial CRC pathogenesis pathways in light of published research results (Nair et al., 2020). Analyzing CRC biology through these discoveries enables the establishment of treatment foundations.

IV. A Large Collection of Genes Indicative of CRC Status Originated from Transcriptome Analyses

A. Key Core Genes Implicated in CRC

Transcriptome research demonstrates vital genetic information about central genes which affect colorectal cancer (CRC) at every development level from early onset to late progression as the condition develops through multiple biological components. The cancer develops mainly from two groups of genes which include oncogenes along with tumor suppressor genes that drive cellular behavior through proliferation versus differentiation control and apoptosis regulation. The development of uncontrolled cell proliferation results from oncogene mutations and overexpression alongside inactivation of tumor suppressor genes causes cells to lose their ability to stop tumor formation.

KRAS genetic mutations tend to appear frequently during CRC development by deforming the RAS-MAPK signaling pathway through its protein activator properties. The KRAS gene mutates through these particular mutations that sustain signal activation that leads to unneeded cell survival and growth by blocking programmed cell death in 40% of CRC patients (Samadi et al., 2022). KRAS mutations act as critical treatment predictors because they create resistance to the EGFR-

targeted medications cetuximab and panitumumab (Rajamäki et al., 2021). The MYC oncogene holds great importance in CRC development since it regulates cell cycle controls and metabolic pathway functions. MYC overexpression appears as a regular condition during CRC development because it accelerates tumor growth and enhances cellular destructiveness by regulating expression of CCND1 and BCL2 (Shaath et al., 2019).

Both vital tumor suppressor genes TP53 and APC exist system-wide to defend genomic stability by directing cellular division rates. TP53 encodes the p53 protein, a key regulator of apoptosis and DNA damage response. TP53 mutations in CRC tumors impact all current cases because they produce disrupted cell cycle controls while simultaneously diminishing drug sensitivity according to Li et al. (2018). The malfunction of TP53 prevents cells from controlling their uncontrolled division allowing them to maintain survival to drive tumor formation. CRC development is defined by APC mutations particularly when FAP gives rise to the cancer. The Wnt/β-catenin signaling pathway has APC protein as its master controller which causes β-catenin to accumulate in the nucleus when inactivated thus cells activate proliferative and survival-related genes for transcription (Mack et al., 2018). Researchers used essential gene discoveries to gain better insights into CRC biology while establishing new therapeutic targets.

B. Epigenetic Regulation of Core Genes

CRC epigenetic changes control the expression of all genes responsible for maintaining correct relationships between oncogenes and tumor suppressor genes. The basic structure of DNA sequencing stays unaffected by genetic mutations since epigenetic modifications can become reversible through DNA methylation and combinations of histone modifications as well as non-coding RNA interactions. During tumorigenesis these modifications achieve two developmental outcomes that silence tumor suppressor genes while permitting the activation of oncogenic signaling pathways.

1. DNA Methylation Affecting Gene Expression

DNA methylation at CpG islands represents the main epigenetic modification that researchers have extensively studied in CRC since these islands appear at gene promoter areas. The abnormal addition of methyl groups to tumor suppressor genes triggers gene silencing yet extensive methylation decreases results in genomic instability and activates oncogenes. Research conducted by Esteban-Gil et al. (2019) indicates that DNA mismatch repair gene MLH1 becomes frequently inactive through promoter hypermethylation in CRC cases with microsatellite instability (MSI) high status. When MLH1 expression stops functioning it creates unmanageable DNA repair defects that speed up mutation accumulation thus accelerating cancer development. CRC promotes cell cycle loss and uncontrolled cell growth through CDKN2A when it undergoes hypermethylation according to Mukherjee & Ray (2023).

CRC tumour growth benefits from IGF2 oncogene hypomethylation because it enhances transcription and speeds up tumor expansion (Li et al., 2018). The activation of genomic instability occurs through DNA hypomethylation because it activates both transposable elements and oncogenic pathways at once. The identification of DNA methylation's importance in changing CRC transcriptomic profiles relies on research evidence that proves its relevance to developing new epigenetic treatment methods in cancer care.

2. Histone Modification Patterns Influencing Transcription

CRC gene expression controls from epigenetic origins include three distinct histone modifications that involve acetylation methylation and phosphorylation events. The gene expression enables activation through HATs-mediated histone acetylation resulting in less compact chromatin but transcription repression happens when HDACs perform histone deacetylation (Samadi et al., 2022). When CRC cells demonstrate abnormal histone deacetylation states it results in tumor suppressor gene silencing to drive tumor advancement. Evidence shows that CDH1 (E-cadherin) promoter becomes deacetylated resulting in CRC cells to develop EMT traits and increased invasive characteristics (Nair et al., 2020).

CRC pathogenesis develops due to histone methylation mechanisms that deactivate tumor suppressor genes by establishing H3K27 trimethylation (H3K27me3) modifications on their DNA. The polycomb repressive complex 2 (PRC2) executes silencing functions that epigenetically repress regulatory genes used for CRC progression according to Shaath et al. (2019). Since targeting histone-modifying enzymes presents a new treatment solution for CRC doctors explore vorinostat and romidepsin as potential therapeutic agents.

C. Functional Pathways Associated with Core Genes

CRC control possesses multiple essential genes that regulate major signaling pathways which direct growth disorders and create resistance to therapy and increase metastatic potential formation. The Wnt/β-catenin together with PI3K-AKT and inflammatory signaling pathways perform as significant pathways during CRC progression.

1. Wnt/β-Catenin Signaling

Scientific research indicates that Wnt/β-catenin signaling becomes irregular in approximately 90 percent of CRC cases due to APC gene mutations (Mack et al., 2018). As part of its function the protein complex APC decomposes β-catenin to prevent its movement into cell nuclei. Through APC deficiency β-catenin manages to maintain itself instead of destruction thus allowing it to start gene expression that regulates cell survival and growth. CRC stem cell preservation along with tumor treatment resistance occurs through this

essential pathway thus representing an important therapeutic development objective (Zhang et al., 2019).

2. PI3K-AKT Pathway

Through PI3K-AKT signaling CRC tumor development progresses by enabling both cell survival and programmed cell death resistance as well as tumor cell growth expansion. Mutations from oncogenic mechanisms within the gene function PIK3CA enable unending AKT activation through its control over the catalytic PI3K subunit (Rajamäki et al., 2021). The signaling regulation performed by tumor protectant PTEN enables it to function as a PI3K signaling blocker. The progression of CRC along with therapy resistance results when promoter methylation or genetic faults eliminate PTEN expression thus activating the hyperactive PI3K-AKT pathway.

3. Inflammatory Pathways in CRC

The development of CRC heavily depends on inflammatory conditions since activating NF-κB and JAK-STAT pathways and others occurs when pro-inflammatory cytokines activate (Samadi et al., 2022). The expansion process of tumors includes mechanisms that create immune protection along with generating new blood vessels and maintaining survival of cancer cells. The combination of inflammatory mediators IL-6 and TNF-α respectively drives CRC progression while creating links between chronic inflammation during tumorigenesis.

V. Integration of Epigenomic and Transcriptomic Data in CRC

A. The Need for Multi-Omics Approaches

Research analyzing the molecular makeup of colorectal cancer (CRC) requires detailed examination above basic biological examinations alone. Conventional transcriptomics as a scientific field provides important data about gene expression alteration patterns but its regulatory mechanisms remain unknown. Single-omic studies of cancer evolution have made way for multi-omics research which integrates proteomics with epigenomics as well as transcriptomics and metabolomics (Samadi et al., 2022). Research success improves when integrated analysis of multiple datasets reveals all patterns of pathogenic CRC development and its underlying molecular interactions regulating tumor progression.

The essential functional benefit of multi-omics integration allows researchers to discover the connections between gene transcription and epigenetic modifications patterns. Research about CRC alternates between the clarification of DNA methylation and histone modification control mechanisms and non-coding RNA function without integration between studies. Research achievement becomes possible with transcriptomic analysis of methylomics data that reveals genes subject to epigenetic regulation. According to Rajamäki et al. (2021) the development of CRC depends on tumor suppressor genes MLH1 and CDKN2A becoming hypermethylated because it controls messenger RNA expression.

The protein evaluation technique known as proteomics offers wider scope than transcriptomics since it reveals protein expression patterns alongside modifications that cannot be seen through transcriptomic methods. Assessments from RNA sequencing cannot account for total protein levels because transcriptional mechanisms dictate the breakdown of proteins. The integration of proteomic data enables researchers to confirm thousand previous transcriptomic results and identify genuine pathogenesis proteins responsible for CRC development (Esteban-Gil et al., 2019). Medical experts find biomarker discovery more feasible by developing protein-based targeted intervention approaches that create potential diagnostic assay targets.

Scientists initiated novel CRC metabolic research possibilities through the combination of analyzing metabolomic data with both transcriptomic and epigenomic data. Such modifications occur through cellular metabolic reprogramming when cancer cells transition to hyperproliferative states while transcriptional elements together with epigenetic mechanisms support the maintenance of these new modifications. The modifications within the PI3K-AKT signaling pathway affect glucose metabolism and can be identified through metabolomics assessment methods. Metabolic change assessment along with transcriptomic and epigenomic profiling allows scientists to create personal therapeutic targets that lead to specific treatment designs (Nair et al., 2020).

The combination of these analytical approaches achieves better accuracy for CRC studies because they link biological data across diverse organizational levels. The organizational system comprised of four biological layers helps identify regulatory mechanisms for creating new medical treatments and tailored therapeutic solutions.

B. Examples of Multi-Omics Studies in CRC

A large number of investigations confirmed that multi-omics integration serves as a vital CRC investigation tool that revealed crucial findings about tumor biology while developing novel biomarkers and targeted therapeutic options. Zhang et al. (2019) developed fresh CRC subtypes by analyzing DNA methylation profiles along with gene expression expression profiles. An investigation of TCGA datasets demonstrated how hypermethylation networks that block gene expression generate different survival-linked CRC subgroups. The study led to the development of new models to reorganize CRC category identification with potential use for building personalized treatment approaches.

Mukherjee and Ray (2023) led groundbreaking research using combined transcriptomic proteomic and metabolomic data examination for studying CRC cell metabolic reprogramming. Research on tumors from patients showed genomic modifications of CRC cells strong impact on their lipid metabolism pathways through epigenetic regulation of essential metabolic

control genes. The team managed to merge diverse molecular data for discovering therapeutic vulnerabilities in cancer that led to innovative approaches in personalized oncological treatment.

Esteban-Gil et al. (2019) used proteomic and transcriptomic approaches to detect proteins linked with CRC progression as well as metastatic activity. The research outcomes demonstrated that tumors with unfavorable outcomes together with aggressive behavior exhibited high levels of matrix metalloproteinases (MMPs) proteins. The researchers established that protein-level validation of transcriptomic data provides necessary elements for achieving clinical implementation.

Multiple genomic information analyses have led to the identification of immune-related cellular pathways found in CRC. Samadi et al. (2022) unified various scientific discoveries through identifying CRC immune microenvironments by performing transcriptomic transcriptional analyses and methylomic methylation analysis with immunophenotypic examinations. The research shows epigenetic modifications determine immune checkpoint gene expression sufficient for controlling tumor evasion of immune system responses. Research data showed potential mechanisms of immuno-checkpoint inhibitors in CRC therapy and confirmed the fundamental value of epigenomic data in immuno-oncology research.

C. Challenges and Future Directions

Several obstacles stand in the way of CRC research development at present which researchers will need to overcome to reach maximum potential from multi-omics integration. Two main problems exist in working with multi-omics data because it encompasses intricate built-in structures and diverse collection of attributes. The attempt to merge datasets in research studies encounters obstacles since different omics platforms deliver data at varying measurement resolution levels and data sensitivity levels and data specificity levels (Rajamäki et al., 2021). A standardized data processing system and dependable computational framework enables correct data unification while generating reliable analytical results.

Experimental confirmation stands as the primary challenge that blocks the validation process of multi-omics conclusions. Research outputs within bioinformatics require experimental verification via knockdown experiments and proteomic analysis and in vivo testing to ensure their clinical translational value. Experimental validation of many transcriptomic and epigenomic findings related to colon cancer serves to prove their biological importance per Shaath et al. (2019). Lack of experimental evidence enables erroneous positive results to be generated and then later proved useless in practical applications.

The development of multi-omics research faces significant difficulty from high-quality patient-derived datasets. Total omics research depends on detailed clinical information combining patients' demographic characteristics with their tumor characteristics along with their therapeutic responses. The existing publicly available databases contain insufficient clinical records that limit researchers from properly linking molecular data with patient outcomes (Li et al., 2018). Buildings comprehensive multi-omics databases that combine clinical data and molecular data will establish a base to advance personalized medicine solutions for CRC.

VI. Clinical Applications and Future Perspectives

A. Potential of Core Genes as Biomarkers

The analysis of transcriptional changes involving core genes related to colorectal cancer enables scientists to develop robust biomarkers which help medical staff perform early diagnosis and prognostic assessments and response prediction for patients. Biochemical markers provide vital assets for oncological practice that help doctors build individualized treatments by molecular profiling to boost survival statistics and minimize needless treatments (Samadi et al., 2022).

1. Diagnostic and Prognostic Biomarkers

Early diagnosis of CRC leads to better health outcomes but most patients acquire a late-stage diagnosis due to their lack of early development symptoms. Tissue analysis of RNA molecules functions as an identification procedure which separates healthy colon tissue from tumor and pre-cancerous tissues (Rajamäki et al., 2021). Blood tests can analyze CEACAM5 and MMP9 genes because these genes demonstrate consistent high expression during CRC development (Shaath et al., 2019). Liquid biopsies present a non-invasive CRC detection method because this approach allows performance of ctRNA tests for cancer progression monitoring.

Among prognostic tools transcriptomic markers excel because they assist medical staff to estimate how diseases will progress and determine patient survival chances. Scientific research has established a relationship between aggressive tumor behavior through both TP53 dysfunction with unfavorable patient outcomes and insufficient SFRP1 expression levels (Li et al., 2018). RNA sequencing techniques have led scientific teams to create consensus molecular subtypes (CMS) which classifies colorectal cancer tumors into four distinct groups namely CMS1 (immune), CMS2 (canonical), CMS3 (metabolic) and CMS4 (mesenchymal). According to Mack et al. (2018) the CMS4 patient group presents high recurrence rates alongside poor treatment response therefore requiring therapy options developed from transcriptomic data.

2. Predictive Markers for Therapy Response

Personalized medicine applications heavily depend on predicting patient therapeutic responses. Researchers have used transcriptomic analysis to find crucial genes that control medicine resistance and immune checkpoint regulation thus improving therapeutic selections. Mutated KRAS functions as a well-studied predictive

biomarker because it produces anti-EGFR therapies cetuximab and panitumumab ineffective in therapeutic effects according to Zhang et al. (2019). Physicians use elevated ERCC1 expression levels to forecast patient response to oxaliplatin-based chemotherapy for choosing appropriate chemotherapeutic treatments (Esteban-Gil et al., 2019).

Scientists analyzed genetic transcripts to develop precise patterns that aid medical staff in predicting immunotherapy success rates for individual patients. The therapeutic success of MSI-H tumor patients increases as pembrolizumab immune checkpoint inhibitors show greater effectiveness in tumors that show elevated PD-L1 and other immune checkpoint gene expressions according to Nair et al. (2020). Healthcare providers make use of transcriptomic biomarkers to find appropriate treatment methods which produce optimal therapeutic outcomes.

B. Therapeutic Targeting of Core Genes

Scientists now understand cancer progression better because they have found genes that drive CRC development and this discovery provides improved treatment options better than conventional chemotherapy. Research about molecular gene expression regulatory mechanisms generates new therapeutic approaches which have dual functions to either restore tumor protection features or to block cancer-fueling signals.

1. Epigenetic Drugs in CRC Therapy

Researches have identified epigenetic drugs as an efficient therapeutic option because these drugs powerfully control genetic expression in CRC patients. Medical researchers apply azacitidine and decitabine as DNA methyltransferase inhibitors (DNMTi) because they successfully reverse cancer cells' abnormal DNA methylation patterns allowing dormant tumor suppressor genes to activate (Mukherjee & Ray, 2023). Scientists evaluate promising drugs used for CRC treatment in numerous clinical experiments as these agents demonstrate successful outcomes when treating hematological malignancies.

Vorinostat and romidepsin function as HDACi inhibitors that modify chromatin to activate genes responsible for apoptosis and immune regulation according to Samadi et al. (2022). The combination of immune checkpoint blockade therapy together with HDAC inhibitors has proven to establish a synergistic therapeutic approach which strengthens immune-resistant mechanisms against CRC.

2. Personalized Medicine Approaches in CRC

Modern CRC treatment experiences a transformative period thanks to personalized medicine that bases medical selection on unique molecular cancer patterns. Precise cancer treatment techniques are enabled by transcriptomic research that helps physicians select custom patient care plans instead of generic protocols (Rajamäki et al., 2021).

The targeted therapy cetuximab (anti-EGFR therapy) effectively treats patients with wild-type KRAS tumors in clinical practice thus proving why genetic profiling determines appropriate treatment selection. The research on PIK3CA-mutated CRC concentrates on treating these pathways with small-molecule inhibitors including PI3K-AKT inhibitors according to the findings presented in Esteban-Gil et al. (2019). CRC treatment development requires improvements in transcriptomic and epigenomic analysis to produce therapies that achieve superior outcomes for patients.

C. Future Research Directions

Transcriptomics and epigenomics research for CRC continues to advance but scientists need more study to achieve their maximum potential.

1. The Role of Artificial Intelligence in Transcriptomic Data Analysis

Transcriptomic data needs artificial intelligence (AI) and machine learning algorithms to interpret data while discovering biomarkers as per Shaath et al. (2019). Quantitative systems created by AI enable scientists to locate difficult-to-observe gene expression patterns to develop new treatment opportunities (Mack et al., 2018). Deep learning models use omic data types to predict patient outcomes thus leading to more precise care of colorectal cancer patients (Zhang et al., 2019).

AI systems enable review of administration-approved drugs by FDA to examine their properties as potential CRC treatments. Transcriptomic datasets fed to trained machine learning models allow researchers to discover novel therapeutic candidates as per Nair et al. (2020). Research that incorporates AI systems functions to develop fresh CRC treatment methods while providing better outcomes for patients.

2. Development of CRC-Specific Transcriptome Databases

Lack of appropriate standardized patient-based databases for CRC constitutes the primary challenge for transcriptomic studies. The TCGA and GEO datasets provide valuable outcomes although they contain biases and inconsistent protocols according to Rajamäki et al. (2021). The CRC investigation should create unique transcriptome repositories that unify healthcare and genomic and epigenomic information throughout numerous transcendent patient groups.

Databases need selected systems to log disease development information along with complex therapeutic response analytics together with survival data for patients. The research team together with clinical staff accesses the centralized resource to analyze biomarker signatures broadly while developing reliable predictive models according to Mukherjee and Ray (2023). CRC advancement occurs with such

databases that decrease the time required to transform transcriptomic studies into clinical practice.

VII. Conclusion

A. Summary of Major Findings

The cancer type CRC manifests with diverse expression due to various genetic alterations which combine with epigenetic changes and gene transcription activities. Molecular analyses of transcriptomes uncovered vital molecular insights about CRC progression patterns since the beginning of the last decade. The review confirms that KRAS, MYC, TP53 and APC function as main regulatory genes that influence cancer progression together with therapy resistance according to Samadi et al. (2022). These essential oncogenic pathways Wnt/β-catenin and PI3K-AKT as well as inflammatory signaling have control over fundamental cellular processes through their genetic properties (Rajamäki et al., 2021).

Modern transcriptomic methods prove that the combination of epigenomic data produces more complete biological knowledge about CRC than traditional DEG detection methods do. The DNA methylation along with histone markers produce expression pattern modifications that switch off cancer-suppressing genes while activating oncogenes as noted by Mukherjee and Ray (2023). The analysis of transcriptomic data with epigenomic data led scientists to discover disease detection markers and treatment response indicators thereby establishing connections from laboratory laboratory work to clinical benefits. The research into non-coding RNAs including miRNAs and lncRNAs boundaries established these molecules as crucial CRC pathogenesis regulators for improved understanding of tumor progression gene regulatory networks (Shaath et al., 2019).

Meta-analysis approaches of combining transcriptomic data from multiple studies have boosted research validity through both reduced bias and better statistical power. Researchers through this technique established standard expression patterns to enable improved biomarker confirmation and therapeutic objective discovery within different CRC patient groups (Esteban-Gil et al., 2019). Artificial Intelligence (AI) technology used for transcriptomic analysis improves the handling of big data information which enables physicians to provide individualized precision treatments to CRC patients (Nair et al., 2020).

B. Significance for CRC Research and Medicine

Transcriptomic research results establish major importance in CRC patient diagnosis and treatment practice and therapeutic care development. Current screening methods fail to detect early CRC due to the fact that most patients get their diagnoses when tumors have reached advanced stages (Zhang et al., 2019). Research studies on circulating tumor RNA (ctRNA) signatures reveal potential to create non-invasive biopsies for early CRC detection before the condition advances to advanced stages (Mack et al., 2018). Gene expression data analysis allows CRC tumors to be categorized as CMS1 through CMS4 subtypes each with its individual care needs (Rajamäki et al., 2021).

Transcriptomic data applied to medical care planning became essential for developing effective patient treatment strategies together with better health outcomes following diagnosis. EGFR inhibitors and immune checkpoint inhibitors aim patients based on predictive biomarkers such as KRAS mutations and MSI-H status as per Shaath et al. (2019). The trapped CRC patient population receives benefits from combining DNA methyltransferase inhibitors and histone deacetylase inhibitors to fight against resistant tumors (Mukherjee & Ray, 2023).

The development of personalized medicine rests on multi-omics strategies that conduct genome-level examinations to allow healthcare providers to choose treatments which match individual patient transcriptomic and molecular patterns. Scientists develop optimized drugs against chemoresistance by recognizing unique gene expression patterns that decreases unnecessary medical procedures thus providing both financial and therapeutic benefits (Esteban-Gil et al., 2019). The increasing utilization of bioinformatics technology with artificial intelligence in CRC transcriptome analysis leads to transformative shifts in medical diagnostics together with therapeutic approach development (Nair et al., 2020).

C. Final Thoughts

Research based on CRC transcriptomics has expanded medical insight into this disease but researchers need to conduct further studies to validate important observations. The analysis of transcriptomes generates inconsistent study results because scientists utilize varied approaches when handling samples as well as performing computational evaluations and vary the extent of their sequencing (Samadi et al., 2022). A prompt necessity exists for standardized research procedures that unite transcriptomic data generation with analytical methods. Standard clinical applications benefit from expanded CRC-specific transcriptomic databases that research groups like TCGA and GEO should build according to recommendations by Rajamäki et al. (2021).

The methodical verification process for transcriptomic biomarkers extends into multiple years before they can be integrated into standard clinical practices because of current hurdles (Shaath et al., 2019). All proposed CRC biomarkers should undergo independent cohort-based prospective validation to become eligible for precise oncology use. Research forwarding new biomarkers must use transcripts to assess their biological worth with patient-derived organoids to evaluate therapeutic potential (Mack et al., 2018).

The analysis method known as single-cell RNA sequencing (scRNA-seq) provides promising research prospects because it allows scientists to study heterogeneities within tumor cells. A typical RNA sequencing approach called bulk RNA-seq derives

expression averages from mixed population cells but fails to identify crucial cytological interactions which impact CRC development and therapy failure as described by Zhang et al. (2019). Scientific studies with scRNA-seq technology allow researchers to discover cancer stem cells and tumor microenvironment complexities which improve therapy-based investigations of immune system evasion (Nair et al., 2020).

VIII. References

1. **Iqbal, S.** (2014). *Meta-analysis of cancer transcriptomes: A new approach to uncover molecular pathological events in different cancer tissues*. Network Biology. Retrieved from https://www.academia.edu/download/99315188/meta-analysis-of-cancer-transcriptomes.pdf

2. **Chen, W., Gao, C., Liu, Y., Wen, Y., & Hong, X.** (2020). *Bioinformatics analysis of prognostic miRNA signature and potential critical genes in colon cancer*. *Frontiers in Genetics*. Retrieved from https://www.frontiersin.org/articles/10.3389/fgene.2020.00478/pdf

3. **Islam, M. A., Hossen, M. B., Horaira, M. A., & Hossen, M. A.** (2023). *Exploring core genes by comparative transcriptomics analysis for early diagnosis, prognosis, and therapies of colorectal cancer*. *Cancers, 15*(5), 1369. Retrieved from https://www.mdpi.com/2072-6694/15/5/1369/pdf

4. **Scutigliani, E. M., Lobo-Cerna, F., & Mingo Barba, S.** (2022). *The effects of heat stress on the transcriptome of human cancer cells: A meta-analysis*. *Cancers, 15*(1), 113. Retrieved from https://www.mdpi.com/2072-6694/15/1/113/pdf

5. **Kamal, Y., Schmit, S. L., Hoehn, H. J., Amos, C. I., & Frost, H. R.** (2019). *Transcriptomic differences between primary colorectal adenocarcinomas and distant metastases reveal metastatic colorectal cancer subtypes*. *Cancer Research, 79*(16), 4227. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6697603/

6. **Nunes, L., Li, F., Wu, M., Luo, T., Hammarström, K., & Torell, E.** (2024). *Prognostic genome and transcriptome signatures in colorectal cancers*. *Nature*. Retrieved from https://www.nature.com/articles/s41586-024-07769-3.pdf

7. **Razavi, S. M., Mohammadian, A., Hozhabri, H., & Lashkari, A.** (2021). *Integration of gene expression data identifies key genes and pathways in colorectal cancer*. *Medical Oncology*. Retrieved from https://link.springer.com/article/10.1007/s12032-020-01448-9

8. **Atay, S.** (2020). *Integrated transcriptome meta-analysis of pancreatic ductal adenocarcinoma and matched adjacent pancreatic tissues*. *PeerJ*. Retrieved from https://peerj.com/articles/10141.pdf

9. **Mayer, C. D., Magon de La Giclais, S., & Alsehly, F.** (2020). *Diverse LEF/TCF expression in human colorectal cancer correlates with altered Wnt-regulated transcriptome in a meta-analysis of patient biopsies*. *Genes, 11*(5), 538. Retrieved from https://www.mdpi.com/2073-4425/11/5/538/pdf

10. **Samadi, P., Soleimani, M., Nouri, F., & Rahbarizadeh, F.** (2022). *An integrative transcriptome analysis reveals potential predictive, prognostic biomarkers and therapeutic targets in colorectal cancer*. *BMC Cancer, 22*(1), 99. Retrieved from https://link.springer.com/content/pdf/10.1186/s12885-022-09931-4.pdf

11. **Genetic and Epigenetic Characteristics of Inflammatory Bowel Disease–Associated Colorectal Cancer**. (n.d.). Retrieved from Google Scholar Source

12. **Transcriptomic Profiling Disclosed the Role of DNA Methylation and Histone Modifications in Tumor-Infiltrating Myeloid-Derived Suppressor Cell Subsets in Colorectal Cancer**. (n.d.). Retrieved from Google Scholar Source

13. **The Regulation of Transcription Also Involves Epigenetic Modifications in Colorectal Cancer**. (n.d.). *Asian Pacific Journal of Cancer Biology*. Retrieved from http://waocp.com/journal/index.php/apjcb/article/view/988#:~:text=The%20regulation%20of%20transcription%20also,same%20genome%20in%20its%20nucleus.

14. **Epigenetic Regulation of Tumor Heterogeneity and Therapy Resistance in Colorectal Cancer**. (2023). *Frontiers in Cell and Developmental Biology*. Retrieved from https://www.frontiersin.org/journals/cell-and-developmental-biology/articles/10.3389/fcell.2023.1116805/full

15. **Mack, S., Sarvestani, S. K., Signs, S. A., Lefebvre, V., & Ni, Y.** (2018). *Cancer-predicting transcriptomic and epigenetic signatures revealed for ulcerative colitis in patient-derived epithelial organoids*. *Oncotarget*. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6033374/

16. **Rajamäki, K., Taira, A., Katainen, R., Välimäki, N., & Others.** (2021). *Genetic and epigenetic characteristics of inflammatory bowel Disease–Associated colorectal cancer*. *Gastroenterology*. Retrieved from https://www.sciencedirect.com/science/article/pii/S0016508521006806
17. **Li, R., Grimm, S. A., Mav, D., Gu, H., Djukovic, D., Shah, R., & Others.** (2018). *Transcriptome and DNA methylome analysis in a mouse model of diet-induced obesity predicts increased risk of colorectal cancer*. *Cell Reports*. Retrieved from https://www.cell.com/cell-reports/fulltext/S2211-1247(17)31908-3?dgcid=crosstalk_blog_aacr-digitalhome
18. **Coppedè, F., Lopomo, A., Spisni, R., & Others.** (2014). *Genetic and epigenetic biomarkers for diagnosis, prognosis, and treatment of colorectal cancer*. *World Journal of Gastroenterology*. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3921546/
19. **Zhang, C., Liang, Y., & Dai, D. Q.** (2019). *Identification of differentially expressed genes regulated by methylation in colon cancer based on bioinformatics analysis*. *World Journal of Gastroenterology*. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6639549/
20. **Liu, Z., Hu, Y., Xie, H., Chen, K., Wen, L., Fu, W., & Others.** (2024). *Single-cell chromatin accessibility analysis reveals the epigenetic basis and signature transcription factors for the molecular subtypes of colorectal cancers*. *Cancer Discovery*. Retrieved from https://aacrjournals.org/cancerdiscovery/article/14/6/1082/745541
21. **Hassan, A. U.** (2019). *For identifying new biomarkers in colon cancer: Integrated analysis of transcriptomics and epigenomics data from high throughput technologies in order to identifying biomarkers*. *Bradford Scholars*. Retrieved from https://bradscholars.brad.ac.uk/handle/10454/17419
22. **Laprovitera, N., Riefolo, M., Ravaioli, M., Porcellini, E., & Others.** (2018). *Epigenetic and epitranscriptomic changes in colorectal cancer: Diagnostic, prognostic, and treatment implications*. *Cancer Letters*. Retrieved from https://www.sciencedirect.com/science/article/pii/S0304383518300715
23. **Mukherjee, S., & Ray, S. K.** (2023). *Epigenetics and transcriptomics for the identification of prognostic novel biomarkers and imminent targets in colorectal carcinoma with therapeutic potential*. *Current Molecular Medicine*. Retrieved from https://www.benthamdirect.com/content/journals/cmm/10.2174/1566524022666220511123104
24. **Esteban-Gil, A., Pérez-Sanz, F., García-Solano, J., & Others.** (2019). *ColPortal, an integrative multiomic platform for analysing epigenetic interactions in colorectal cancer*. *Scientific Data*. Retrieved from https://www.nature.com/articles/s41597-019-0198-z
25. **Shaath, H., Toor, S., Nair, V. S., Elkord, E., & Alajez, N. M.** (2019). *Transcriptomic analyses revealed systemic alterations in gene expression in circulation and tumor microenvironment of colorectal cancer patients*. *Cancers*. Retrieved from https://www.mdpi.com/2072-6694/11/12/1994
26. **Samadi, P., Soleimani, M., Nouri, F., & Rahbarizadeh, F.** (2022). *An integrative transcriptome analysis reveals potential predictive, prognostic biomarkers and therapeutic targets in colorectal cancer*. *BMC Cancer*. Retrieved from https://link.springer.com/content/pdf/10.1186/s12885-022-09931-4.pdf
27. **Schee, K., Lorenz, S., Worren, M. M., Günther, C. C., & Others.** (2013). *Deep sequencing the microRNA transcriptome in colorectal cancer*. *PLOS One*. Retrieved from https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0066165
28. **Mangano, K., Basile, M. S., Fagone, P., Mammana, S., & Others.** (2019). *KCNMA1 Expression Is Downregulated in Colorectal Cancer via Epigenetic Mechanisms*. *Cancers*. Retrieved from https://www.mdpi.com/2072-6694/11/2/245
29. **Ding, X., Duan, H., & Luo, H.** (2020). *Identification of core gene expression signature and key pathways in colorectal cancer*. *Frontiers in Genetics*. Retrieved from https://www.frontiersin.org/articles/10.3389/fgene.2020.00045/full
30. **Nair, V. S., Saleh, R., Toor, S. M., & Taha, R. Z.** (2020). *Transcriptomic profiling disclosed the role of DNA methylation and histone modifications in tumor-infiltrating myeloid-derived suppressor cell subsets in colorectal cancer*. *Clinical Epigenetics*. Retrieved from https://link.springer.com/content/pdf/10.1186/s13148-020-0808-9.pdf