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A Review of Genetic and Epigenetic Regulation in Gastric Cancer

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Abstract Gastric cancer a leading cause of cancer-related deaths worldwide, necessitating a comprehensive understanding of its underlying mechanisms. This study explores the genetic and epigenetic regulation in gastric cancer, highlighting the critical roles of oncogenes, tumor suppressor genes, and chromosomal aberrations. Genome-wide association studies (GWAS) are discussed for their contributions to identifying genetic predispositions. Additionally, the study delves into epigenetic mechanisms, including DNA methylation, histone modifications, and non-coding RNAs, and their impact on gene expression. The interplay between genetic and epigenetic changes is examined, emphasizing the interaction effects and the benefits of integrated genomic and epigenomic approaches. Clinical implications are addressed, focusing on diagnostic and prognostic biomarkers, therapeutic targets, and the potential for personalized medicine. The study also considers the challenges and limitations in studying gastric cancer, such as its complexity, technical constraints, and biological variability. Future directions point to the promise of emerging technologies, integrative and multi-omics approaches, and global epidemiological studies in advancing the understanding and treatment of gastric cancer. The study concludes by summarizing key findings and underscoring the importance of ongoing research in this field.

Keywords Gastric cancer; Genetic regulation; Epigenetic mechanisms; Biomarkers; Personalized medicine

1 Introduction

Gastric cancer (GC) is one of the most prevalent and deadly malignancies worldwide, ranking as the fourth most common cancer and the third leading cause of cancer-related deaths globally (Ebrahimi et al., 2020). The incidence of GC is particularly high in developing countries, where over 70% of new cases and deaths occur (Qu et al., 2013). Despite advancements in diagnosis and treatment, the prognosis for GC remains poor, largely due to late-stage diagnosis and the complex, heterogeneous nature of the disease (Puneet et al., 2018).

The pathogenesis of gastric cancer involves a multifaceted interplay between genetic mutations and epigenetic alterations. Genetic mutations, such as those in the *TP53*, *CDH1*, and *KRAS* genes, have long been recognized as critical drivers of GC (Yoda et al., 2015). However, recent research has highlighted the significant role of epigenetic mechanisms, including DNA methylation, histone modifications, and non-coding RNAs, in the regulation of gene expression and tumor progression (Nemtsova et al., 2021; Capparelli and Iannelli, 2022). Epigenetic changes are heritable yet reversible, making them attractive targets for therapeutic intervention (Puneet et al., 2018; Ebrahimi et al., 2020). For instance, aberrant DNA methylation in the promoter regions of tumor suppressor genes can lead to their inactivation, contributing to oncogenesis (Qu et al., 2013). Similarly, histone modifications and chromatin remodeling can alter the expression of genes involved in cell cycle regulation, apoptosis, and metastasis (Kang et al., 2014; Kang et al., 2017).

This study aims to provide a comprehensive overview of the current understanding of genetic and epigenetic regulation in gastric cancer. By synthesizing findings from recent studies, we seek to elucidate the molecular mechanisms underlying GC pathogenesis and progression. The study will cover key genetic mutations and epigenetic alterations, their clinical implications, and potential therapeutic strategies targeting these molecular changes. Through this analysis, we hope to identify gaps in the current knowledge and suggest directions for future research, ultimately contributing to the development of more effective diagnostic and therapeutic approaches for gastric cancer. Understanding the genetic and epigenetic landscape of gastric cancer is crucial for improving patient outcomes. This study will explore the intricate regulatory networks that drive GC,

highlighting the importance of integrating genetic and epigenetic data to advance the field of cancer research and treatment.

2 Genetic Insights in Gastric Cancer

2.1 Oncogenes and tumor suppressor genes

Gastric cancer (GC) development is significantly influenced by the interplay between oncogenes and tumor suppressor genes. Oncogenes, when mutated or overexpressed, can drive the proliferation and survival of cancer cells. Conversely, tumor suppressor genes, which normally function to inhibit cell growth and promote apoptosis, can contribute to cancer progression when inactivated.

Recent studies have identified several key oncogenes and tumor suppressor genes involved in GC. For instance, the gene *PRKAA1*, which is part of the PI3K-Alt-mTOR-signaling pathway, has been highlighted as a potential target for drug development due to its significant role in oncogenic processes (Lee et al., 2022). Additionally, the lncRNA lncPSCA has been characterized as a novel tumor suppressor whose expression is regulated by genetic variants associated with GC risk. This lncRNA interacts with DDX5, promoting its degradation and thereby activating *p53* signaling genes (Zheng et al., 2021).

Moreover, the role of epigenetic mechanisms in the regulation of tumor suppressor genes has been increasingly recognized. Promoter methylation is a common mechanism of tumor suppressor gene inactivation in GC, with several genes identified through genome-wide methylation screening showing potential as diagnostic or prognostic biomarkers (Otani et al., 2013).

2.2 Chromosomal aberrations

Chromosomal aberrations, including deletions, amplifications, and translocations, are common in GC and contribute to the dysregulation of oncogenes and tumor suppressor genes (Flavahan et al., 2017). These genetic alterations can lead to the loss of tumor suppressor genes or the gain of oncogenes, thereby promoting cancer development and progression. A comprehensive study on the mutational profiling of epigenetic regulation genes in GC revealed significant associations between specific chromosomal aberrations and reduced overall survival in patients. For example, mutations in the genes *KMT2D*, *KMT2C*, *ARID1A*, and *CHD7* were found to be mutually exclusive and correlated with poor prognosis, particularly in patients with distant metastases or tumors with signet ring cells (Nemtsova et al., 2021).

2.3 Genome-wide association studies (GWAS)

GWAS have been instrumental in identifying genetic variants associated with GC risk. These studies have uncovered numerous single nucleotide polymorphisms (SNPs) and genes that contribute to the genetic predisposition to GC. A systematic review of GWAS on GC identified 226 SNPs located in 91 genes, with 44 genes showing significant associations with GC. Among these, 12 genes were identified as expression quantitative trait loci (eQTL), indicating their potential regulatory roles in GC development. Notably, genes such as *PRKAA1*, *THBS3*, and *EFNA1* were found to be involved in key signaling pathways like PI3K-Alt-mTOR and p53, highlighting their importance in GC pathogenesis (Figure 1) (Lee et al., 2022).

The research of Lee et al. (2022) illustrates the complex biological pathways involved in the mechanisms of gastric cancer, highlighting key proteins and interactions within the PI3K-Akt-mTOR signaling pathway. This pathway is central to cell growth, proliferation, and survival, making it a critical target in cancer research. Genes such as *THBS3*, *EFNA1*, and *PRKAA1* play pivotal roles in this pathway. *THBS3* and *EFNA1*, through their interactions with integrins and receptor tyrosine kinases (RTKs), initiate downstream signaling that activates PI3K, leading to the phosphorylation and activation of Akt. Akt activation subsequently influences several cellular processes by regulating mTOR, which is involved in protein synthesis, autophagy, and cell survival. MUC1 interacts with other significant proteins like ICAM-1, CD11b, EGFR, Src, and CTNNB1, integrating into the PI3K-Akt-mTOR signaling network and further influencing cancer cell behavior. Additionally, the image shows how external factors such as Helicobacter pylori infection and interactions with eosinophils and other immune components contribute to the inflammatory and pro-apoptotic environment, promoting gastric cancer

progression. Understanding these pathways and interactions is crucial for developing targeted therapies for gastric cancer.

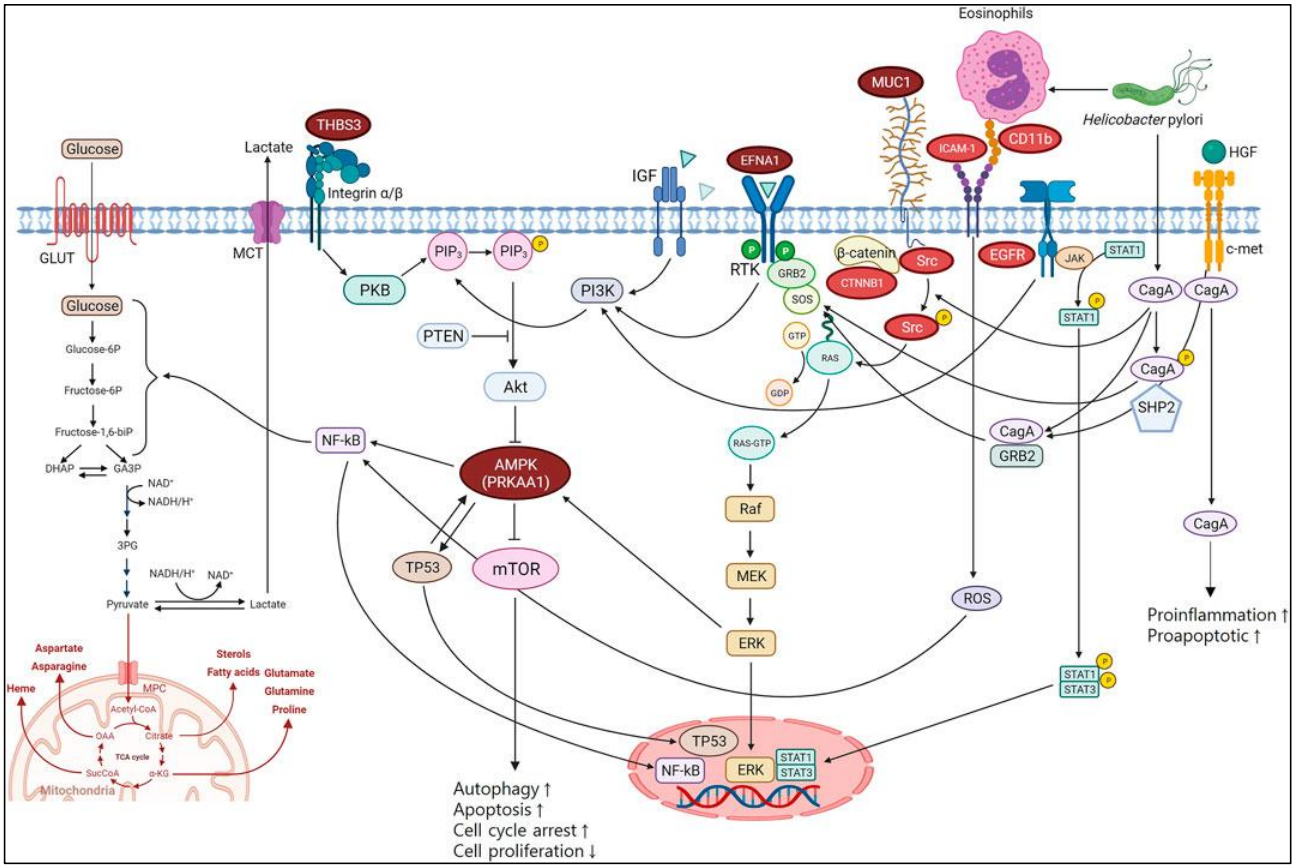

Figure 1 Biological pathways of gastric cancer mechanisms (Adopted from Lee et al., 2022)

Image caption: *THBS3*, *EFNA1*, and *PRKAA1* are involved in PI3K-Alt-mTOR-signaling pathway which is the key pathway associated with gastric cancer. MUC1 interacted with ICAM-1, CD11b, EGFR, Src, and CTNNB1 in PPI network is a regulator of the PI3K-Alt-mTOR-signaling pathway. PPI, protein-protein interaction (Adopted from Lee et al., 2022)

Furthermore, a meta-analysis of GWAS and prospective cohort studies demonstrated that genetic risk models, such as polygenic risk scores, can effectively stratify individuals based on their risk of developing GC (Tuan et al., 2021). The study of Jin et al. (2020) also emphasized the potential of lifestyle modifications to mitigate the genetic risk of GC, suggesting that individuals with a high genetic risk could substantially reduce their risk by adopting a healthy lifestyle.

In summary, the genetic landscape of GC is shaped by a complex interplay of oncogenes, tumor suppressor genes, chromosomal aberrations, and genetic variants identified through GWAS. Understanding these genetic insights is crucial for developing targeted therapies and improving the prognosis of GC patients.

3 Epigenetic Mechanisms in Gastric Cancer

3.1 DNA methylation

DNA methylation is a critical epigenetic modification that involves the addition of a methyl group to the cytosine residues in CpG dinucleotides, leading to gene silencing. In gastric cancer, aberrant DNA methylation patterns are frequently observed and are associated with the inactivation of tumor suppressor genes and the activation of oncogenes (Biswas and Rao, 2017). This epigenetic alteration is considered a hallmark of gastric cancer and plays a significant role in its pathogenesis (Ebrahimi et al., 2020). Studies have shown that hypermethylation of promoter regions in tumor suppressor genes can lead to their silencing, contributing to cancer development and progression (Qu et al., 2013). Additionally, global hypomethylation can activate oncogenes, further promoting malignancy (Puneet et al., 2018). The potential of DNA methylation as a

biomarker for early detection and prognosis of gastric cancer has been extensively explored, with promising results (Toiyama et al., 2014).

3.2 Histone modifications

Histone modifications, including methylation, acetylation, phosphorylation, and ubiquitination, play a crucial role in the regulation of gene expression by altering chromatin structure and accessibility. In gastric cancer, dysregulation of histone modifications has been implicated in the aberrant expression of genes involved in cancer progression (Dawson and Kouzarides, 2012). For instance, histone deacetylation can lead to the repression of tumor suppressor genes, while histone methylation can either activate or repress gene expression depending on the specific residues modified (Perri et al., 2017). The therapeutic potential of targeting histone modifications has been recognized, with histone deacetylase inhibitors showing promise in preclinical and clinical studies (Jin et al., 2021). These inhibitors can reactivate silenced tumor suppressor genes and inhibit cancer cell growth, offering a novel approach to gastric cancer treatment.

3.3 Non-coding RNAs

Non-coding RNAs (ncRNAs), including microRNAs (miRNAs) and long non-coding RNAs (lncRNAs), are key regulators of gene expression at the epigenetic level. In gastric cancer, ncRNAs have been shown to play significant roles in tumorigenesis, metastasis, and drug resistance (Toiyama et al., 2014). miRNAs can function as oncogenes or tumor suppressors by targeting mRNAs for degradation or translational repression (Zhou et al., 2017). Dysregulation of miRNAs in gastric cancer can lead to the aberrant expression of genes involved in cell proliferation, apoptosis, and metastasis (Puneet et al., 2018). Similarly, lncRNAs can modulate gene expression through various mechanisms, including chromatin remodeling, transcriptional regulation, and post-transcriptional processing (Zhou et al., 2018). The epigenetic regulation of lncRNAs and their involvement in gastric cancer pathogenesis highlight their potential as therapeutic targets and biomarkers for diagnosis and prognosis.

The understanding of epigenetic mechanisms such as DNA methylation, histone modifications, and non-coding RNAs in gastric cancer has provided valuable insights into the molecular underpinnings of this malignancy (Calcagno et al., 2013). These epigenetic alterations not only contribute to cancer development and progression but also offer potential avenues for novel therapeutic interventions and biomarker discovery.

4 Interplay Between Genetic and Epigenetic Changes

4.1 Interaction effects

The interplay between genetic and epigenetic changes in gastric cancer (GC) is a complex and multifaceted process. Genetic mutations and epigenetic modifications often co-occur and influence each other, contributing to the pathogenesis and progression of GC. For instance, mutations in genes involved in epigenetic regulation, such as *KMT2D*, *KMT2C*, *ARID1A*, and *CHD7*, have been found to be mutually exclusive (Figure 2), suggesting a potential compensatory mechanism among these genes (Nemtsova et al., 2021). These mutations are significantly associated with reduced overall survival in patients with metastases and tumors with signet ring cells, highlighting their clinical relevance.

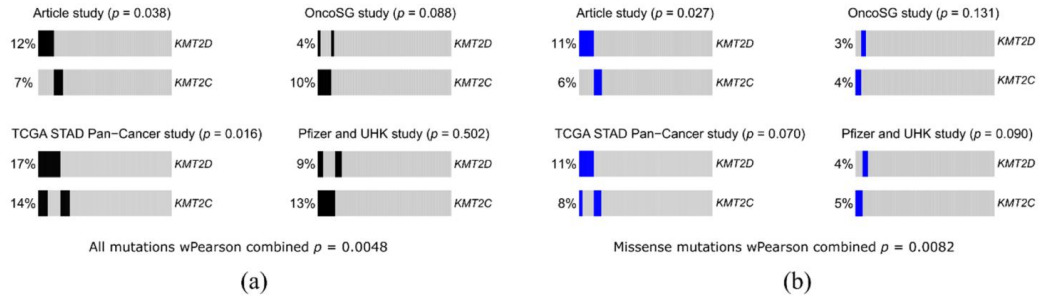

Figure 2 Analysis of mutual exclusivity of *KMT2D* and *KMT2C* mutations on the data presented in gastric cancer mutation databases (Adopted from Nemtsova et al., 2021)

Image caption: Portions of samples without mutations in *KMT2D* or *KMT2C* are shown in grey; (a) analysis of all types of mutations, excluding amplification and deep deletions, portions of samples with mutations in *KMT2D* or *KMT2C* are colored black; (b) analysis

of missense mutations only, portions of samples with missense mutations in *KMT2D* or *KMT2C* are colored blue (Adopted from Nemtsova et al., 2021)

The research of Nemtsova et al. (2021) provides an analysis of the mutual exclusivity of KMT2D and KMT2C mutations in gastric cancer based on multiple studies. The left panel (a) examines all types of mutations, showing that mutations in *KMT2D* and *KMT2C* rarely co-occur within the same sample, as indicated by the combined wPearson p-value of 0.0048. Notably, the TCGA STAD Pan-Cancer study reports the highest mutation rates for *KMT2D* (17%) and *KMT2C* (14%). The right panel (b) focuses on missense mutations, demonstrating a similar pattern of mutual exclusivity with a combined wPearson p-value of 0.0082. The Article study shows significant results with 11% of samples having *KMT2D* missense mutations and 6% with *KMT2C* missense mutations. These findings suggest that mutations in *KMT2D* and *KMT2C* are functionally redundant, indicating that either mutation can drive the oncogenic process in gastric cancer, but their co-occurrence is rare. This mutual exclusivity points to distinct but overlapping pathways in cancer development, which could inform targeted therapeutic strategies.

Epigenetic alterations, such as DNA methylation and histone modifications, can also affect the expression of genes involved in key cancer-related pathways. For example, the WNT pathway can be activated by mutations in *CTNNB1* and by aberrant methylation of its negative regulators, such as DKK3, NKD1, and SFRP1 (Yoda et al., 2015). Similarly, the AKT/mTOR pathway is influenced by mutations in *PIK3CA* and *PTPN11*, as well as by epigenetic changes. These interactions underscore the importance of considering both genetic and epigenetic factors in understanding GC.

4.2 Integrated genomic and epigenomic approaches

Integrated genomic and epigenomic approaches have provided valuable insights into the molecular mechanisms underlying GC. By combining genetic and epigenetic data, researchers can identify comprehensive profiles of alterations that drive cancer development and progression. For instance, an integrated analysis of cancer-related pathways in GC revealed that genes involved in these pathways are more frequently affected by epigenetic alterations than by genetic mutations (Yoda et al., 2015). This finding suggests that epigenetic changes play a predominant role in the dysregulation of these pathways.

Moreover, the use of next-generation sequencing and DNA methylation arrays has enabled the identification of specific epigenetic markers that can serve as potential targets for diagnosis and therapy. For example, aberrant DNA methylation in the promoter regions of tumor suppressor genes is a well-defined hallmark of GC and can be used for early detection and prognosis (Qu et al., 2013; Ebrahimi et al., 2020). Additionally, the inhibition of BET bromodomain proteins, which are epigenetic regulators, has shown promise as a therapeutic approach in GC, particularly in cases with specific genetic and epigenetic alterations (Kang et al., 2017).

The interplay between genetic and epigenetic changes in GC is a critical area of research that holds promise for improving our understanding of the disease and developing more effective diagnostic and therapeutic strategies. By integrating genomic and epigenomic data, researchers can uncover the complex mechanisms driving GC and identify novel biomarkers and targets for clinical application.

5 Clinical Implications

5.1 Diagnostic and prognostic biomarkers

The identification of reliable biomarkers for gastric cancer (GC) is crucial for early diagnosis and prognosis. Several studies have highlighted the potential of genetic and epigenetic markers in this regard. For instance, a seven-gene signature (FBN1, MMP1, PLAU, SPARC, COL1A2, COL2A1, and ATP4A) has been identified as having significant prognostic value, with high-risk patients showing worse survival outcomes (Wang et al., 2018). Additionally, epigenetic alterations such as DNA methylation and histone modifications are being developed as biomarkers for early detection and prognosis of gastrointestinal cancers (Figure 3), including GC (Wong et al., 2019; Grady et al., 2020). Long non-coding RNAs (lncRNAs) and circular RNAs (circRNAs) have also emerged as promising biomarkers due to their stable expression and regulatory roles in cancer progression (Naeli et al., 2020; Askari et al., 2023).

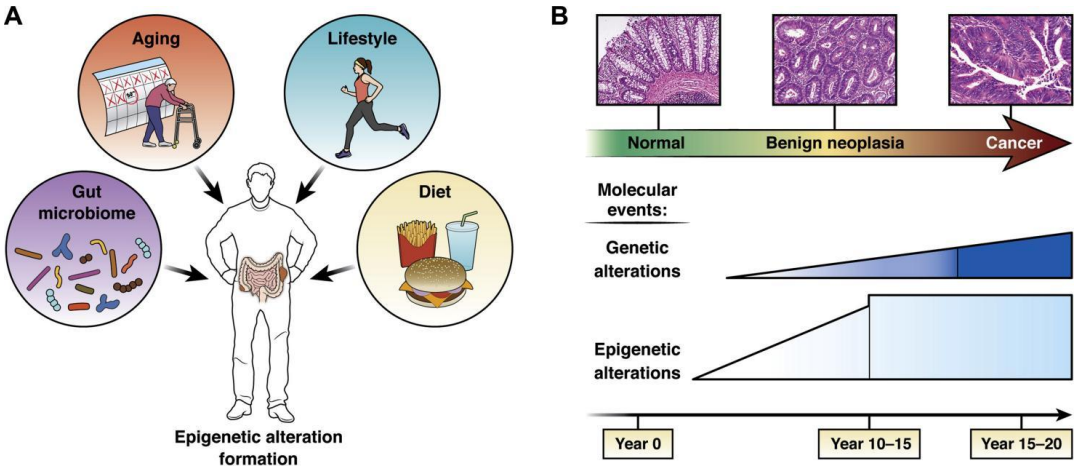

Figure 3 Schematic diagram showing factors that influence epigenetic alteration formation and the timing of epigenetic alteration formation in GI tract cancer formation (Adopted from Grady et al., 2020)

The research of Grady et al. (2020) illustrates the factors influencing the formation of epigenetic alterations in gastrointestinal (GI) tract cancer and their progression over time. Panel A highlights key contributors to epigenetic changes, including aging, lifestyle, diet, and the gut microbiome. These factors interact with an individual's genetic material, leading to modifications that can predispose cells to cancerous transformations. Panel B presents the timeline of cancer development, from normal tissue through benign neoplasia to malignant cancer. It emphasizes the molecular events involved, distinguishing between genetic and epigenetic alterations. Genetic changes accumulate gradually over time, becoming more significant in later stages of cancer progression. In contrast, epigenetic alterations start early and increase steadily, playing a crucial role in the initial stages of tumorigenesis. The diagram underscores the importance of lifestyle and environmental factors in the early stages of cancer development, highlighting potential intervention points for prevention and early detection through lifestyle modifications and monitoring of epigenetic markers.

5.2 Therapeutic targets

Epigenetic dysregulation is a hallmark of GC, and targeting these alterations offers new therapeutic opportunities. BET inhibitors, which target bromodomain and extra-terminal domain proteins like BRD4, have shown efficacy in inhibiting GC cell growth by down-regulating oncogenes such as *c-Myc* (Kang et al., 2017). Furthermore, targeting specific epigenetic mechanisms, such as DNA methylation and histone modifications, has been proposed as a strategy to overcome GC heterogeneity and improve treatment outcomes (Canale et al., 2020). The identification of TGFβ1 and VEGFB as potential therapeutic targets in the tumor microenvironment further underscores the importance of epigenetic regulation in GC therapy (Cai et al., 2020).

5.3 Personalized medicine

The heterogeneity of GC necessitates personalized treatment approaches. Genetic and epigenetic profiling can help tailor therapies to individual patients. For example, the GPSGC model, which integrates gene expression data with clinical variables, provides a personalized risk assessment and helps in selecting targeted therapies (Cai et al., 2020). The use of lncRNAs and circRNAs as biomarkers can also guide personalized treatment strategies by identifying specific molecular alterations in each patient (Zhou et al., 2018). Additionally, the development of epigenetic drugs, such as BET inhibitors, offers personalized therapeutic options based on the specific epigenetic landscape of the tumor (Kang et al., 2017).

6 Challenges and Limitations

6.1 Complexity of gastric cancer

Gastric cancer (GC) is a highly heterogeneous disease, characterized by a multitude of genetic and epigenetic alterations that complicate its diagnosis and treatment. The intricate interplay between genetic mutations and epigenetic modifications, such as DNA methylation, histone modifications, and non-coding RNAs, contributes to the complexity of GC (Nemtsova et al., 2021; Tang et al., 2022). This heterogeneity is further exacerbated by the

diverse environmental factors and the presence of different molecular subtypes within the same tumor, making it challenging to develop universal therapeutic strategies (Capparelli and Iannelli, 2022). The complexity of GC necessitates a comprehensive understanding of the molecular mechanisms underlying its pathogenesis to identify effective biomarkers and therapeutic targets (Yoda et al., 2015; Khorasani et al., 2021).

6.2 Technical limitations

The study of genetic and epigenetic regulation in GC is hindered by several technical limitations. High-throughput sequencing technologies, while powerful, often generate vast amounts of data that require sophisticated bioinformatics tools for analysis and interpretation (Kang et al., 2017). Additionally, the detection of epigenetic modifications, such as DNA methylation and histone modifications, demands highly sensitive and specific assays, which can be technically challenging and costly (Ebrahimi et al., 2020). The variability in sample quality and the need for large, well-characterized cohorts further complicate the identification of consistent and clinically relevant biomarkers (Canale et al., 2020). Moreover, the integration of multi-omics data to provide a holistic view of the genetic and epigenetic landscape of GC remains a significant challenge (Zhou et al., 2018).

6.3 Biological variability

Biological variability poses a significant challenge in the study of GC. The genetic and epigenetic landscape of GC can vary widely between patients, and even within different regions of the same tumor (Nemtsova et al., 2021; Capparelli and Iannelli, 2022). This intra-tumor heterogeneity can lead to differential responses to treatment and complicate the identification of universal biomarkers (Canale et al., 2020). Additionally, the dynamic nature of epigenetic modifications, which can be influenced by environmental factors and therapeutic interventions, adds another layer of complexity to the study of GC (Qu et al., 2013). Understanding the biological variability and its implications for disease progression and treatment response is crucial for the development of personalized therapeutic strategies.

7 Future Directions

7.1 Emerging technologies

The landscape of gastric cancer research is rapidly evolving with the advent of new technologies that promise to enhance our understanding and treatment of this malignancy. High-throughput sequencing technologies, such as next-generation sequencing (NGS), have revolutionized the field by enabling comprehensive profiling of genetic and epigenetic alterations in gastric cancer (Yoda et al., 2015). These technologies facilitate the identification of novel biomarkers and therapeutic targets, which are crucial for early diagnosis and personalized treatment strategies. Additionally, the development of small molecule inhibitors targeting specific epigenetic regulators, such as BET inhibitors, has shown promising results in preclinical models of gastric cancer (Kang et al., 2017). These inhibitors work by preventing the binding of BET proteins to acetylated histones, thereby inhibiting the transcriptional activation of oncogenes like *c-Myc*, which are critical for cancer cell survival and proliferation.

7.2 Integrative and multi-omics approaches

Integrative and multi-omics approaches are essential for a holistic understanding of gastric cancer. These approaches combine data from genomics, epigenomics, transcriptomics, proteomics, and metabolomics to provide a comprehensive view of the molecular alterations driving gastric cancer. For instance, the interplay between metabolic dysregulations and epigenetic modifications has been shown to contribute significantly to tumor progression (Crispo et al., 2019). By integrating multi-omics data, researchers can identify key regulatory networks and pathways that are disrupted in gastric cancer, leading to the discovery of novel therapeutic targets. Moreover, bioinformatics tools and algorithms are being developed to integrate and analyze these complex datasets, which will enhance our ability to infer the functional roles of specific genetic and epigenetic alterations in cancer (Kagohara et al., 2018).

7.3 Global and epidemiological studies

Global and epidemiological studies are crucial for understanding the diverse etiological factors contributing to gastric cancer across different populations. These studies can provide insights into the genetic and epigenetic variations that influence cancer susceptibility and progression in various demographic groups. For example, the

prevalence of specific gene methylation patterns and histone modifications may vary between populations, affecting the efficacy of targeted therapies (Qu et al., 2013). Large-scale epidemiological studies can also identify environmental and lifestyle factors that interact with genetic predispositions to influence gastric cancer risk. By integrating data from global studies, researchers can develop more effective prevention and treatment strategies tailored to specific populations, ultimately improving patient outcomes on a global scale.

The future of gastric cancer research lies in the integration of emerging technologies, multi-omics approaches, and global epidemiological studies. These strategies will provide a deeper understanding of the genetic and epigenetic mechanisms underlying gastric cancer, paving the way for innovative therapeutic interventions and personalized medicine.

8 Concluding Remarks

The research on genetic and epigenetic regulation in gastric cancer (GC) has revealed significant insights into the mechanisms driving this malignancy. Key findings include the identification of somatic mutations in epigenetic regulation genes such as *KMT2D*, *KMT2C*, *ARID1A*, and *CHD7*, which are associated with reduced overall survival and metastasis in GC patients. DNA methylation, particularly in promoter regions, has been highlighted as a critical epigenetic modification leading to the inactivation of tumor suppressor genes and the activation of oncogenes, contributing to gastric carcinogenesis. Additionally, the PI3K/Akt/mTOR signaling pathway has been identified as a significant player in GC pathogenesis, with potential for targeted pharmacologic interventions. The role of BET inhibitors in targeting epigenetic regulators like BRD4 has also shown promise as a therapeutic approach.

Continued research in the field of genetic and epigenetic regulation in gastric cancer is crucial for several reasons. Firstly, understanding the intricate mechanisms of epigenetic alterations can lead to the identification of novel biomarkers for early diagnosis and prognosis, which is essential given the typically late diagnosis and poor prognosis associated with GC. Secondly, exploring the therapeutic potential of targeting epigenetic modifications, such as DNA methylation and histone modifications, can pave the way for the development of more effective and personalized treatment strategies. Furthermore, investigating the interplay between genetic mutations and epigenetic changes can provide a comprehensive understanding of GC pathogenesis, potentially leading to the discovery of new drug targets and the improvement of existing therapies.

In conclusion, the integration of genetic and epigenetic research holds significant promise for advancing our understanding and treatment of gastric cancer. The identification of key epigenetic alterations and their impact on gene expression and tumor behavior underscores the potential of epigenetic therapies in improving patient outcomes. As research progresses, it is imperative to continue exploring the molecular underpinnings of GC and to translate these findings into clinical practice. By doing so, we can move closer to achieving more effective diagnostic tools and therapeutic options, ultimately improving the prognosis and quality of life for patients with gastric cancer.

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Conflict of Interest Disclosure

The author affirms that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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