Role of epigenetics in gastrointestinal cancers: from mechanisms to therapeutic targets.

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Introduction

Gastrointestinal cancers, including those affecting the oesophagus, stomach, liver, pancreas, colon, and rectum, account for a significant proportion of cancer-related deaths worldwide. Despite advances in diagnosis and treatment, the prognosis for many patients with gastrointestinal cancers remains poor. It has become increasingly evident that genetic alterations alone cannot fully explain the complexity and heterogeneity of these malignancies. Epigenetic modifications, which involve changes in gene expression without altering the underlying DNA sequence, have emerged as crucial players in gastrointestinal cancer development and progression [1].

Epigenetic alterations encompass a diverse array of changes, including DNA methylation, histone modifications, and dysregulation of non-coding RNA molecules. DNA methylation, the addition of a methyl group to the cytosine residue of cpg dinucleotides, is a well-studied epigenetic modification and has been associated with transcriptional repression. Aberrant DNA methylation patterns have been observed in gastrointestinal cancers, leading to the silencing of tumour suppressor genes or the activation of oncogenes [2].

Histone modifications, such as acetylation, methylation, phosphorylation, and ubiquitination, play a pivotal role in regulating chromatin structure and gene expression. Alternate patterns of histone modifications have been linked to gastrointestinal cancer development and progression. Dysregulation of histone-modifying enzymes, such as histone acetyltransferases and histone deacetylases, can disrupt the balance between active and repressive chromatin states, thereby influencing gene expression programmes in cancer cells [3].

Non-coding RNAs, including micrornas (mirnas) and long non-coding RNAs (lncrnas), have emerged as key regulators of gene expression in gastrointestinal cancers. Dysregulated expression of Mirnas has been associated with tumour initiation, metastasis, and drug resistance. On the other hand, lncrnas have been implicated in various aspects of cancer biology, including cell proliferation, apoptosis, and epithelial-to-mesenchymal transition [4].

Understanding the precise mechanisms through which epigenetic alterations contribute to gastrointestinal cancer development and progression is crucial for the identification of novel therapeutic targets. Importantly, the reversible nature of epigenetic modifications makes them attractive candidates for therapeutic intervention. Several epigenetic-targeted therapies, including DNA demethylating agents, histone deacetylase inhibitors, and small-molecule inhibitors of specific epigenetic enzymes, have shown promise in preclinical and clinical settings [5].

Conclusion

In conclusion, epigenetic alterations play a critical role in gastrointestinal cancer initiation, progression, and metastasis. DNA methylation, histone modifications, and dysregulation of non-coding RNAs collectively contribute to the dysregulated gene expression patterns observed in these malignancies. Targeting these epigenetic modifications holds great potential as a therapeutic strategy for gastrointestinal cancers. However, further research is required to unravel the intricate interplay between different epigenetic alterations and to identify patient-specific epigenetic biomarkers that can guide personalized treatment approaches. The continued exploration of epigenetic mechanisms in gastrointestinal cancers will undoubtedly contribute to improved diagnostic and therapeutic strategies, ultimately leading to better patient outcomes.

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