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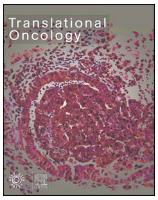

Epigenetic modifications: Key players in cancer heterogeneity and drug resistance

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ABSTRACT

Cancer heterogeneity and drug resistance remain pivotal obstacles in effective cancer treatment and management. One major contributor to these challenges is epigenetic modifications - gene regulation that does not involve changes to the DNA sequence itself but significantly impacts gene expression. As we elucidate these phenomena, we underscore the pivotal role of epigenetic modifications in regulating gene expression, contributing to cellular diversity, and driving adaptive changes that can instigate therapeutic resistance. This review dissects essential epigenetic modifications - DNA methylation, histone modifications, and chromatin remodeling - illustrating their significant yet complex contributions to cancer biology. While these changes offer potential avenues for therapeutic intervention due to their reversible nature, the interplay of epigenetic and genetic changes in cancer cells presents unique challenges that must be addressed to harness their full potential. By critically analyzing the current research landscape, we identify knowledge gaps and propose future research directions, exploring the potential of epigenetic therapies and discussing the obstacles in translating these concepts into effective treatments. This comprehensive review aims to stimulate further research and aid in developing innovative, patient-centered cancer therapies. Understanding the role of epigenetic modifications in cancer heterogeneity and drug resistance is critical for scientific advancement and paves the way towards improving patient outcomes in the fight against this formidable disease.

Abbreviations

CircRNA	Circular RNA
CRC	Colorectal cancer
DNMT	DNA methyltransferase
LIF	Leukemia inhibitory factor
LncRNA	Long non-coding RNA
MiRNA	MicroRNA
NcRNA	Non-coding RNA
NK	Natural Killer cell
PiRNA	PIWI-interacting RNA
SiRNA	Small interfering RNA
TME	Tumor microenvironment
DNMT	DNA methyltransferase
MDR1	Multidrug resistance 1
HDACs	Histone deacetylases
PRC2	Polycomb repressive complex 2
NEAT1	Nuclear paraspeckle assembly transcript 1

Introduction

Epigenetic modifications have emerged as key players in the unfathomable complexities of cancer biology, driving an astounding degree of heterogeneity and leading to the frustrating challenge of drug resistance [1,2]. As the scientific community works tirelessly to unravel the mysteries of cancer, it is increasingly clear that understanding cancer at the molecular and cellular level is a critical endeavor that stands at the frontline of our battle against this relentless disease [3]. Cancer is not a single disease but a collection of diverse conditions, each with a distinct genetic and epigenetic landscape [4]. The vast heterogeneity seen in

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