The role of epigenetic modifications in cancer: Implications for molecular oncology.

Agata Antczak*

Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, USA

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Abstract

Cancer is a complex disease caused by the accumulation of genetic mutations that lead to uncontrolled growth and proliferation of cells. However, recent research has shown that epigenetic modifications play a critical role in the development and progression of cancer. Epigenetic modifications are changes to the DNA molecule that do not involve alterations to the underlying genetic code. These modifications can affect gene expression and they can be influenced by both genetic and environmental factors. In this article, we will discuss the role of epigenetic modifications in cancer and their implications for molecular oncology.

Keywords: Epigenetics, Cancer, DNA methylation, Histone modification, Oncogenes

Introduction

Epigenetic modifications can occur through various mechanisms, such as DNA methylation, histone modification and non-coding RNA regulation [1]. DNA methylation is a common epigenetic modification that involves the addition of a methyl group to the cytosine nucleotide in DNA. This modification typically occurs at CpG islands, which are regions of DNA that contain a high density of cytosine and guanine nucleotides. Methylation of these CpG islands can silence gene expression by preventing transcription factors from binding to the DNA molecule.

Discussion

Histone modification is another important epigenetic mechanism that regulates gene expression. Histones are proteins that help package the DNA molecule into a compact structure called chromatin. Modifications to histones, such as acetylation, methylation and phosphorylation, can affect the accessibility of the DNA molecule to transcription factors and other regulatory proteins. These modifications can either activate or repress gene expression, depending on their location and the specific modification that occurs [2].

Non-coding RNA molecules, such as microRNAs and long non-coding RNAs, also play a critical role in epigenetic regulation. These molecules can interact with both DNA and RNA to regulate gene expression. MicroRNAs, for example, can bind to specific mRNA molecules and prevent them from being translated into protein. Long non-coding RNAs can interact with chromatin and other regulatory proteins to control gene expression at the transcriptional level.

The dysregulation of epigenetic modifications is a common feature of cancer cells. Aberrant DNA methylation, for example, can lead to the silencing of tumor suppressor genes, which normally help to prevent the development of cancer. Similarly, alterations in histone modification and non-coding RNA expression can contribute to the aberrant expression of oncogenes, which promote cancer development and progression [3].

One of the most well-known examples of epigenetic dysregulation in cancer is the hypermethylation of the CpG island in the promoter region of the tumor suppressor gene p16INK4a. This gene encodes a protein that helps regulate the cell cycle and its silencing is commonly observed in various types of cancer. The hypermethylation of the p16INK4a promoter region prevents transcription factors from binding to the DNA molecule, leading to the downregulation of the gene and the loss of its tumor suppressing activity.

Epigenetic modifications are also involved in the development of drug resistance in cancer cells. For example, the hypermethylation of the MGMT gene promoter region is associated with resistance to chemotherapy drugs such as temozolomide, which is commonly used to treat brain tumors. In these cases, the hypermethylation of the MGMT promoter region prevents the drug from effectively targeting cancer cells, leading to treatment failure and disease progression.

The recognition of the critical role of epigenetic modifications in cancer has led to the development of novel therapeutic strategies targeting these modifications. Epigenetic therapies typically involve the use of small molecules that target specific enzymes involved in epigenetic regulation, such as DNA methyltransferases and histone deacetylases. These drugs can either inhibit or activate these enzymes to modulate the expression of specific genes involved in cancer development and progression [4].

One example of an epigenetic therapy is the use of azacitidine and decitabine, which are DNA methyltransferase inhibitors that are used to treat myelodysplastic syndromes and acute myeloid leukemia. These drugs work by preventing the methylation of DNA, which can lead to the reactivation of silenced tumor suppressor genes and the inhibition of oncogene expression.

Another example of an epigenetic therapy is the use of histone deacetylase inhibitors, such as vorinostat and romidepsin. These drugs work by inhibiting the activity of enzymes that remove acetyl groups from histone proteins, leading to the activation of tumor suppressor genes and the inhibition of oncogene expression.

However, epigenetic therapies can have both beneficial and harmful effects. On the one hand, these therapies can target specific genes involved in cancer development and progression, leading to the inhibition of tumor growth and the improvement of patient outcomes. On the other hand, epigenetic therapies can also have off-target effects, leading to the activation or inhibition of genes that are not directly involved in cancer development [5].

Conclusion

The role of epigenetic modifications in cancer is becoming increasingly recognized as a critical factor in the development and progression of this disease. Aberrant epigenetic modifications can lead to the dysregulation of gene expression, leading to the activation of oncogenes and the silencing of tumor suppressor genes. The development of epigenetic therapies is an exciting area of research that has the potential to revolutionize cancer treatment by targeting specific genes involved in cancer development and progression. However, further research is needed to fully understand the complex interplay between genetic and epigenetic factors in cancer and to optimize the use of epigenetic therapies in the clinic.

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*Correspondence to

Agata Antczak

Department of Periodontics and Oral Medicine,

School of Dentistry,

University of Michigan,

Ann Arbor,

USA

E-mail: *agata.antczak87@umed.lodz.org*