

DNA Methylation

Introduction

DNA methylation is a crucial epigenetic modification that regulates gene expression without altering the actual DNA sequence. It involves the addition of a methyl group ($-CH_3$) to the cytosine base of DNA, typically at CpG sites (cytosine followed by guanine). This modification plays a significant role in gene regulation, development, and disease.

Mechanism of DNA Methylation

1. Enzymes Involved

DNA methylation is catalyzed by a group of enzymes known as DNA methyltransferases (DNMTs):

DNMT1: Maintains methylation patterns during DNA replication.

DNMT3A and DNMT3B: Establish new methylation patterns during development.

2. CpG Islands and Gene Regulation

CpG sites are often clustered in CpG islands, found in gene promoter regions.

Methylation of CpG islands typically leads to gene silencing, preventing RNA polymerase from transcribing genes.

Unmethylated CpG islands allow genes to remain active and be expressed.

3. Role in Chromatin Structure

Methylated DNA interacts with methyl-CpG binding proteins (MeCPs), which recruit histone modifiers.

This leads to chromatin condensation, making genes inaccessible for transcription.

Functions of DNA Methylation

1. Gene Regulation and Development

Controls tissue-specific gene expression during embryonic development.

Ensures cell differentiation, allowing specialized cell functions.

2. X-Chromosome Inactivation

In females, one of the two X chromosomes is silenced through DNA methylation, preventing gene overexpression.

3. Genomic Imprinting

Some genes are expressed only from the maternal or paternal allele due to DNA methylation.

Example: IGF2 gene is methylated on the maternal allele, silencing it.

DNA Methylation and Diseases

1. Cancer and Abnormal Methylation

Hypermethylation of tumor suppressor genes leads to gene silencing and uncontrolled cell growth.

Hypomethylation causes genomic instability, increasing mutation rates.

2. Neurological Disorders

Abnormal methylation patterns are linked to Alzheimer's disease, autism, and schizophrenia.

3. Aging and DNA Methylation

DNA methylation patterns change with aging, affecting gene expression and cellular function.

Scientists use epigenetic clocks to estimate biological age based on methylation levels.

DNA Methylation in Biotechnology and Medicine

1. Epigenetic Therapies

Drugs like azacitidine (Vidaza) and decitabine are used to reverse abnormal DNA methylation in cancer.

2. DNA Methylation in Diagnostics

Methylation patterns serve as biomarkers for cancer detection (e.g., MGMT methylation in brain tumors).

3. Role in Stem Cell Research

DNA methylation is manipulated to reprogram cells into induced pluripotent stem cells (iPSCs).

Conclusion

DNA methylation is a powerful epigenetic mechanism that regulates gene expression, ensuring proper development and cellular function. While essential for normal biology, its dysregulation can lead to severe diseases, including cancer and neurological disorders. Understanding DNA methylation has opened new

doors in epigenetic therapy, diagnostics, and regenerative medicine, making it a key area of research in modern biology.