DNA methylation is an epigenetic mechanism known to affect gene expression. DNA methylation (5 mC) is formed by the addition of a methyl group to the 5' position of cytosine residues within a CpG dinucleotide context in mammalian DNA. The majority of CpG sites are highly methylated in the mammalian genome, with the exception of CpG islands which are largely unmethylated.

Genome-wide demethylation happens in totipotent cells. This is followed by de novo methylation where tissue-specific genes undergo demethylation in their cell type of expression.

DNA methylation is maintained during DNA replication of somatic cells. When the literature refers to DNA methylation as heritable it generally refers to heritability across cell divisions, not transgenerational. Some regions of the methylome vary across cell divisions, not heritable.

DNA methylation and disease

Alterations in DNA methylation are associated with numerous diseases, including cancer, cardiovascular diseases, metabolic disorders, and neurodegenerative diseases. DNA methylation can affect gene expression and lead to changes in gene expression.

Therefore, identifying therapies that inhibit these epigenetic changes are of great interest.

Cancer

Abnormal DNA methylation has been implicated as one of the mechanisms underlying normal tissue development, progression and recurrence. Abnormal gene expression due to hypermethylation of CpG islands, which can lead to cancer cell survival, is a common mechanism in tumors through the inhibition of tumor suppressor genes.

Most CpG islands are found in almost half of all human genes.

Promoter regions

Promoter regions are DNA sequences that define the transcriptional start sites of genes. These regions are typically situated several hundred bases upstream of the transcriptional start sites. Promoters are very important; they initiate transcription and are a target of various epigenetic modifications.

Enhancers

Enhancers are short (20–500 bp) DNA sequences that interact with transcription factors and coregulate transcription at distant loci through chromatin remodeling. Enhancers can be found throughout the genome, in intergenic regions, but some are also found within genes.


The relationship between DNA methylation and specific elements of the mammalian genome

1. CpG islands
   - CpG islands or CG islands are regions in the mammalian genome that are densely methylated. These regions are typically located within promoters and associated with transcriptional silencing.

2. Enhancers
   - Enhancers are DNA sequences that can increase or decrease gene expression by interacting with transcription factors and coregulating transcription at distant loci. They can be found throughout the genome, in intergenic regions, but some are also found within genes.

3. Enhancers
   - Enhancers are short (20–500 bp) DNA sequences that interact with transcription factors and coregulate transcription at distant loci through chromatin remodeling. Enhancers can be found throughout the genome, in intergenic regions, but some are also found within genes.

4. Enhancers
   - Enhancers are short (20–500 bp) DNA sequences that interact with transcription factors and coregulate transcription at distant loci through chromatin remodeling. Enhancers can be found throughout the genome, in intergenic regions, but some are also found within genes.

5. DNase hypersensitivity sites
   - DNase hypersensitivity sites (DHSs) are short nucleotide regions of the genome that are extremely sensitive to cleavage by the DNase I enzyme and often associated with transcription start sites.

6. CpG islands
   - CpG islands or CG islands are regions in the mammalian genome that are densely methylated. These regions are typically located within promoters and associated with transcriptional silencing.

References