# Epigenetics

Subjects: Genetics & Heredity

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Changes in gene expression/phenotype without underlying DNA modification.

DNA methylation | Heart failure | TET enzymes

## 1. Introduction

Epigenetics refers to changes in phenotypes without changes in genotypes, a concept first described by Waddington in 1942[1]. Subsequent research has shown that epigenetic modifications can occur as a result of at least three different mechanisms: (i) genomic DNA methylation, (ii) modification of DNA interacting proteins, and (iii) microRNAs. Various types of genomic DNA (gDNA) methylation are known. The most important one is probably methylation of cytosine in the 5C position. This creates 5-Methylcytosine (5mC) via de novo methyltransferases (DNMTs), and the 5mC is then converted to 5hmC via ten-eleven translocation methylcytosine dioxygenase (TET) enzymes, where the C is followed by a guanine (G) and separated by a phosphate (CpG).

Higher levels of DNA methylation lead to chromatin condensation, for example, as observed during X-chromosome inactivation transposon silencing and genomic imprinting[2]. Until recently, 5mC was thought to be a stable modification of DNA and was expected to remain unchanged throughout the life of a fully differentiated somatic cell. However, it has now been discovered that 5mC can be oxidized to 5hmC[3]. Recent studies have shown that the enrichment of 5hmC on the gene body has been associated with activation of transcription[3][4][5][6][7][8] and TET-mediated 5mC oxidation regulates the activity on the transcription start site (TSS)[4][9][10] and active enhancers. Epigenetic studies of human hearts have reported altered 5mC in chronic heart failure. However, our knowledge with regard to the underlying molecular mechanisms in CVD remains incomplete, despite the observation that DNA methylation appears to regulate CVD development.

## References

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