



Review

Forensic DNA methylation profiling—Potential opportunities and challenges

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ABSTRACT

Investigating the DNA sequence is the most powerful tool that can be employed in forensic genetics for the identification of an individual, or to determine specific ethnic and phenotypic characteristics. However, there are also other heritable changes in gene function or cellular phenotype which are caused by mechanisms other than differences in the DNA sequence itself. Over the last decade it has become evident that epigenetic markers can be of substantial forensic significance. The determination of possible alterations in DNA methylation patterns could aid various forensic investigations, such as differentiating monozygotic twins, identifying the tissue source or determining the age of tissue donors. This review aims to give a brief overview of the possible advantages of forensic DNA methylation profiling and sheds light on the limitations of this approach.

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1. Introduction

1.1. The epigenome

Epigenetics refers to the study of heritable alterations in gene function or cellular phenotype caused by mechanisms other than

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Epigenetics

A mechanism used to regulate gene activity independently from DNA sequence by deciding which genes are on or off

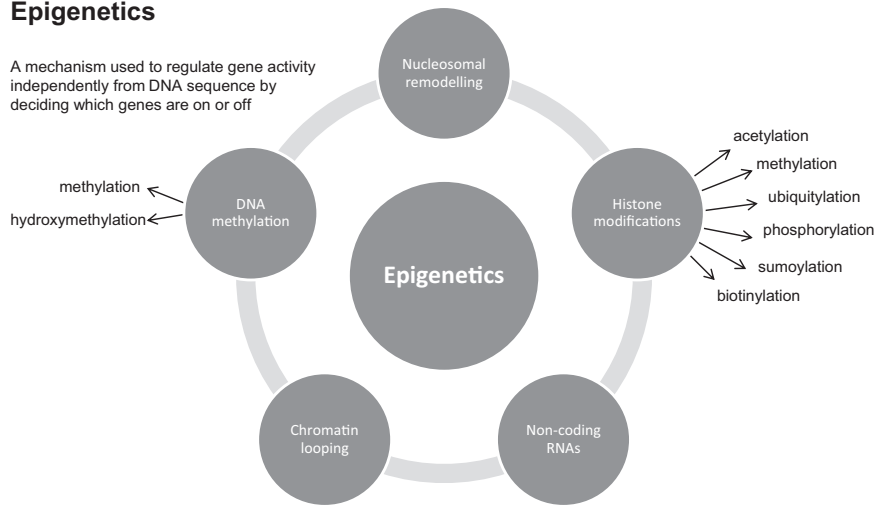


Fig. 1. Different epigenetic mechanisms involved in gene regulation.

changes in the DNA sequence itself (Fig. 1). It involves functionally relevant modifications, such as DNA methylation and histone modifications, both of which play a significant role in regulating gene expression without altering the DNA. The molecular basis of epigenetics is complex and primarily involves alterations in the activation of particular genes. In addition, the chromatin proteins associated with DNA may be activated or silenced and therefore ensure that each cell expresses only the genes that are necessary for an activity [1,2]. The term 'epigenome' is a parallel to the word 'genome' and refers to the overall epigenetic status of a cell.

Epigenetic patterns are preserved during cell division just as the DNA sequence is inherited from one generation to the next; however, they can change over an individual's lifetime [3]. Epigenetic changes have been observed to occur in response to environmental exposure

and can be affected by various factors such as diet and smoking [4]. Imprinting, gene silencing, X chromosome inactivation, reprogramming and carcinogenesis are all examples of epigenetic processes. A very important cell function that is regulated by epigenetic mechanisms in mammals is cell differentiation, where stem cells become fully differentiated cells during embryogenesis [4].

1.2. DNA methylation and gene regulation

In the human genome, DNA methylation is a vital biochemical process for normal development. It involves the addition of a methyl group ($-\text{CH}_3$) at the 5' position of cytosine residues in CpG dinucleotides (Fig. 2a). The absence of CpG methylation has only been observed in embryonic stem cells [5]. When taking the

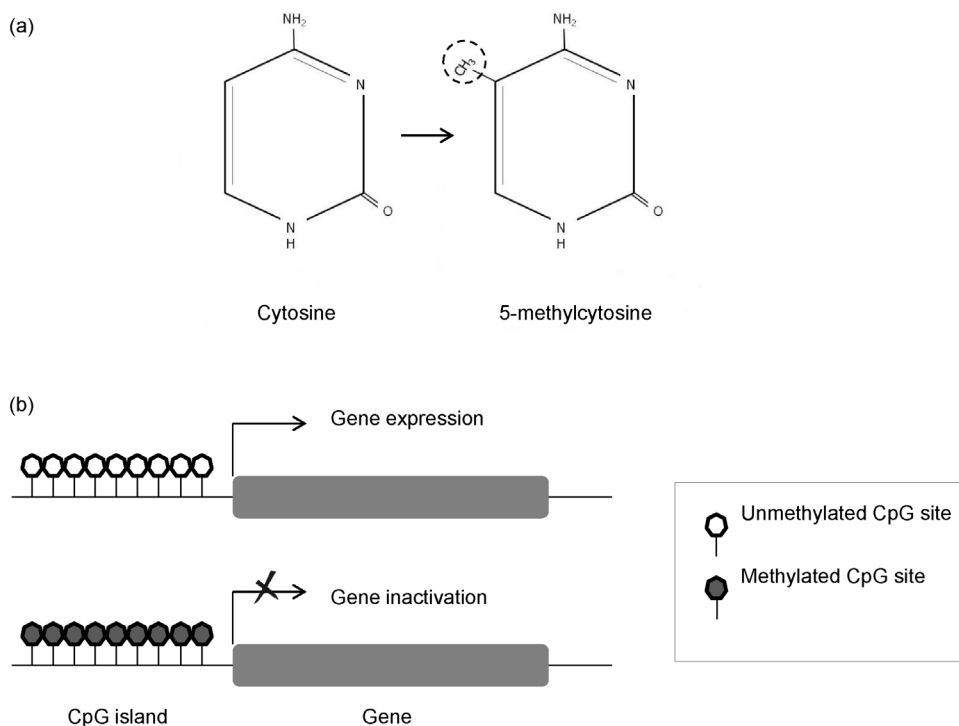


Fig. 2. (a) DNA methylation on cytosine. (b) Schematic representation of a typical gene containing a CpG island. In most cases, when the CpG island is unmethylated allows for gene expression; however, when it is methylated, the gene becomes inactive.

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