International Research Journal of Biochemistry and Bioinformatics Vol. 13(3) pp. 1-3, June, 2023
Available online http://www.interesjournals.org/IRJBB

Review Article

DNA Methylation in the Epigenetic Hierarchy

Rafael Albert*

Catholic University of Louvain, Belgium

*Corresponding Author's E-mail: albertrafael@rediff.com

Received: 02-Jun-2023, Manuscript No. IRJBB-23-103027; Editor assigned: 05-Jun-2023, PreQC No. IRJBB-23-103027 (PQ); Reviewed: 19-Jun-2023, QC No. IRJBB-23-103027; Revised: 23-Jun-2023, Manuscript No. IRJBB-23-103027 (R); Published: 30-Jun-2023, DOI: 10.14303/2250-9941.2023.57

Abstract

DNA methylation is a heritable epigenetic mark in which DNA methyltransferases (DNMTs) covalently transfer a methyl group to the C-5 position of the DNA cytosine ring. Cytosines are methylated in plants either in symmetrical circumstances (CG or CHG) or in asymmetrical contexts (CHH, where H is A, T, or C). Gene expression can alter in heritable ways that the DNA sequence does not encode. Characterising epigenetic modifications throughout healthy development and in disease states like cancer has advanced significantly in the last ten years. The epigenetic landscape, which includes DNA methylation, the histone code, non-coding RNA, and nucleosome placement, has become more complex sequence (Obembe et al., 2015). DNA methylation, which the DNA methyltransferases (DNMTs) catalyse, is recognised as a crucial factor in the epigenetic silencing of transcription because it serves as a persistent restrictive mark. Through the interaction of DNMTs with other modifications and with elements of the machinery mediating those marks, DNA methylation may cooperatively control the chromatin state. The relationships between DNA methylation and other epigenetic markers will be thoroughly discussed in this review, along with the molecular processes of transcriptional repression in development and cancer.

Keywords: DNA methylation, DNA methyltransferase, Epigenetics, Chromatin, Histone code, epigenetic

INTRODUCTION

The science of genetics focuses on heritable variations in gene function or activity that result from direct alterations to the DNA sequence. Point mutations, deletions, insertions, and translocations are examples of these modifications. Contrarily, epigenetics is the study of heritable changes in gene function or activity that are unrelated to alterations in the DNA sequence. Although almost every cell in an organism has the same genetic makeup, not every kind of cell expresses every gene at once. Epigenetic processes, in a larger sense, mediate the varied gene expression patterns in a range of cells and tissues in multicellular animals (Ashaye et al., 2006).

DNA methylation is an epigenetic process that occurs in the mammalian genome and involves adding a methyl group to the cytosine's C5 position to create 5-methylcytosine. DNA methylation controls gene expression by either attracting proteins that are involved in gene repression or by preventing transcription factor(s) from binding to DNA. A dynamic process involving both de novo DNA methylation and demethylation causes the pattern of DNA methylation in the genome to alter during development. As a result, differentiated cells produce a constant and distinctive DNA methylation pattern that controls the transcription of genes specific to various tissues. The process of DNA (de) methylation and how it interacts with other epigenetic factors including histone modifications and noncoding RNAs. It's interesting to note that postmitotic neurons continue to produce DNA methyltransferases and DNA demethylation-related proteins (Ebeye et al., 2007). In addition, neuronal activity can alter DNA methylation patterns in response to physiological and environmental cues. For healthy cognitive function, DNA methylation must be precisely regulated. Mental impairment is, in fact, a frequent side effect when DNA methylation is changed as a result of developmental mutations or environmental risk factors, such as drug exposure and neurological damage. The study of DNA methylation is still providing a detailed and intricate picture of how epigenetic genes are regulated in the central nervous system and offers potential therapeutic options for the treatment of neuropsychiatric illnesses (Yunusa et al., 2018).

DNA methylation is a heritable epigenetic mark in which DNA methyltransferases (DNMTs) covalently transfer a methyl group to the C-5 position of the DNA cytosine ring. Cytosines are methylated in plants either in symmetrical circumstances (CG or CHG) or in asymmetrical contexts (CHH, where H is A, T, or C). Anywhere throughout the genome in animals, cytosines are methylated. While up to 25% of total DNA methylation can be found in non-CpG contexts in embryonic stem cells (ESCs), more than 98% of DNA methylation in somatic cells takes place in a CpG dinucleotide environment. Typically, DNA methylation is altered during zygote development and subsequently restored in the embryo around the time of implantation. Most DNA methylation plays a crucial role in a number of crucial processes, such as genomic imprinting, X-chromosome inactivation, and suppression of repetitive element transcription and transposition. DNA methylation also aids in the development of illnesses like cancer when it is mismanaged (Saif et al., 2015).

A family of DNMTs, including DNMT1, DNMT2, DNMT3A, DNMT3B, and DNMT3L, controls the methylation of DNA. In vitro, DNMT1 selectively methylates hemimethylated DNA, and during S phase, it is localised to replication foci. As a result, during DNA replication, DNA methylation patterns are copied to the daughter strands by the suggested maintenance methyltransferase. At around day E9, mouse models with both Dnmt1 alleles removed are embryonally fatal. Aspartic acid transfer RNA's anticodon loop contains cytosine-38, which is methylated by DNMT2 instead of DNA. DNMT3A and DNMT3B favour unmethylated CpG dinucleotides and carry out de novo methylation throughout development, in contrast to DNMT1 (Mohamed 2017). Dnmt3b deletion promotes embryonic mortality at E14.5 to E18.5 while Dnmt3a knockout mice die at around 4 weeks of age. Although DNMT3L lacks catalytic activity, it exhibits similarity to DNMT3A and DNMT3B and helps the de novo methyltransferases by improving their capacity to attach to the methyl group donor, S-adenosyl-L-methionine (SAM), and enhancing their activity in vivo. While heterozygous embryos produced from homozygous Dnmt3L-null oocytes die around E9 and have reduced maternal methylation imprints and biallelic expression of imprinted genes typically expressed solely from the allele of paternal origin, Dnmt3L homozygous-null animals are alive (Olusegun et al., 2019). In order to methylate certain portions of the genome, notably repetitive sequences, cooperation between several DNMTs is necessary. In DNA synthesis, it has long been thought that DNMT1 primarily serves as a "maintenance" methyltransferase, whereas DNMT3A and DNMT3B function as "de novo" enzymes throughout development. A growing body of research suggests that DNMT1 may also be necessary for the de novo methylation of genomic DNA and that DNMT3A and DNMT3B participate in replication-related maintenance methylation (Hend et al., 2014).

A family of DNA methyltransferases (Dnmts) transfers a methyl group from S-adenyl methionine (SAM) to the fifth carbon of a cytosine residue to generate 5mC, which is the result of DNA methylation. De novo Dnmts are Dnmt3a and Dnmt3b, which may add a new methylation pattern to DNA that has not been altered. The DNA methylation pattern from the parental DNA strand is copied onto the freshly created daughter DNA strand by Dnmt1 during DNA replication, on the other hand. The development of an embryo involves all three Dnmts in great detail. When cells reach their final stage of differentiation, Dnmt expression is significantly decreased. This seems to indicate that postmitotic cells have a persistent DNA methylation pattern. However, postmitotic neurons in the mature mammalian brain continue to produce high quantities of Dnmts, suggesting that these molecules may have a unique function in the brain (Nwangwa et al., 2016).

Through patterns of depolarization, neurons respond to their surroundings by relaying information and encoding a response. In recent years, it has become more and more clear that changes in gene expression following depolarization are accompanied by modifications of the epigenetic environment, including changes in the DNA methylation pattern. There must be both active DNA methylation and demethylation in the neuronal genome for the DNA methylation pattern to be changed. However, it is unknown of any enzymes that can directly cleave the methyl group off 5mC. The recent discovery of 5-hydroxymethyl-cytosine (5hmC) in postmitotic neurons raises the possibility that 5hmC functions as an intermediary in the DNA demethylation process.

The repetitive modification of the brain's microenvironment can also affect DNA methylation. This microenvironment is repeatedly susceptible to extraordinary, synchronised neuronal activity in recurrent seizures. Electric convulsive stimulation, which was discovered to cause changes in the DNA methylation pattern throughout the whole genome, is one technique to duplicate this atypical brain activity. Similar to how cocaine affects neural function, frequent drug use alters it. Use of cocaine alters Dnmt3a expression in the nucleus accumbens and promotes spine development. Additionally, regular cocaine use raises MeCP2, which raises Bdnf expression. Drug exposure, as well as brain activity, can occasionally contribute posttranslational changes to MeCP2 and other methylation machinery parts. The significance of DNA methylation in the majority of mental diseases is less evident, despite the fact that DNA methylation is obviously changed in the disorders listed above due to mutations, incorrect methylation, or repetitive modification of the microenvironment. Nevertheless, there is growing proof that several mental diseases are linked to aberrant DNA methylation patterns. For instance, maternal neglect throughout early life was enough to cause DNA methylation to change in a mouse model's brain. The glucocorticoid receptor's expression was decreased by maternal neglect because of increased methylation in the receptor's promoter. Unexpectedly, this change in DNA methylation pattern

persisted throughout maturity, resulting in a stronger stress response. Similar to the rat model, childhood maltreatment causes increased methylation of the glucocorticoid receptor promoter and decreased expression in humans. In addition, persons with bipolar illness and schizophrenia are shown to have abnormal DNA methylation patterns (Morteza et al., 2013).

CONCLUSION

We are firmly in an epigenetic age after the genetic era, which culminated with the sequencing of the human genome, thanks to recent developments and large continuing research activities focused at characterising the epigenome and its control. The study of heritable changes in gene expression that take place without alterations in the core DNA sequence is referred to as "epigenetics," which literally translates to "outside conventional genetics." Mammalian development and cell proliferation depend on epigenetic alterations; however these modifications are disturbed in mature mammals due to random events or environmental variables. Alterations in transcriptional states brought on by epigenetic process disruption can result in malignant cellular transformation. Environmental influences have the potential to change epigenetic states, which is likely to result in the emergence of aberrant or diseased phenotypes. Epigenetic alterations, such as DNA methylation, posttranslational modifications of histone proteins, noncoding RNAs, and nucleosome placement along the DNA, are responsible for maintaining a specific epigenetic state. This brings up two broad inquiries: What functions do these epigenetic markers serve, and how do they coordinate throughout healthy development and become disorganised during disease? DNA methylation, which is known as a crucial regulator of transcriptional stability, creates a quiet chromatin state by working with other proteins that alter nucleosomes. Our knowledge of the complete epigenome will thus be improved by analysis of DNA methylation patterns. It is obvious that the integration of DNA methylation with other epigenetic alterations is a complicated process that depends on the cooperation of many different elements, many of which are yet unknown.

REFERENCES

1. Obembe AO, Ofutet EO, Okpo-ene AI, Okon VE, Eyong EE (2015). The Effect of Aqueous Extract of Xylopia Aethiopica (Nigro Pepper) On Some Haematological Parameters in Albino Rats. World Journal of Pharmaceutical Research. 4: 2576-2583.
2. Ashaye OA, Taiwo OO, Adegoke GO (2006). Effect of local preservative (Aframomumdanielli) on the chemical and sensory properties of stored warakanshi. Afr J Agric Res. 1: 10-16.
3. Ebeye OA, Emore E, Enaibe BU, Igbigbi PS (2007). Histopathological effect of piper guinese extract on Wistar rats. J biol sci. 7: 1484-1487.
4. Yunusa H, Hassan Z, Deepika V (2018). Preserving or Poisoning: A Case of Dried-Beans from Nigeria. International Journal of Management Technology and Engineering. 7: 2249-7455.
5. Saif Q, Ruhi K, Aparna S (2015). Aluminium phosphide induced acute kidney injury. The Egyptian Journal of Internal Medicine. 27: 115.
6. Mohamed SA (2017). Nephroprotective Effect of Melatonin against Aluminum Phosphide Induced RenalTissue Damage in Rats. Journal of Bioscience and Applied Research. 3: 252-272.
7. Olusegun KA, Emmanuel BO, Gbadebo EA, Jelili AB, Adedoja DW (2019). Mitigation of Aluminium Phosphide-induced Hematotoxicity and Ovarian Oxidative Damage in Wistar Rats by Hesperidin. American Journal of Biochemistry. 9: 7-16.
8. Hend MT, Omnia EK, Hekmat MT, Amira A (2014). Potential anti-inflammatory effect of lemon and hotpepper extracts on adjuvant-induced arthritis in mice. The Journal of Basic Applied Zoology.
9. Nwangwa JN, Udefa AL, Anyaibe SC, Iragunima AS, Eze NC (2016). Comparative Effect of Chilli Pepper (Capsicum frutescens) Extract and Capsaicin on Some Haematological Parameters and Serum Electrolytes in Albino Wistar Rats. International Blood Research Reviews. 6: 1-8.
10. Morteza RT, Alireza B, Afshin S, Maryam NN, Hannan E, et al (2013). Alteration in Liver Enzymes in Aluminum Phosphide Poisoning a Retrospective Study. Iranian Journal of Toxicology. 7:1-4.