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Review on Regulation of Epigenetic Mechanism

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Abstract

The transfer of genetic information from the archival copy of DNA to the transient messenger RNA, often followed by the creation of protein, is represented by transcription, translation and subsequent protein modification. Despite having fundamentally the same DNA, every cell in an organism has a different kind and function due to qualitative and quantitative variations in gene expression. Therefore, differentiation and development depend on the regulation of gene expression. Although it is believed that epigenetic mechanisms such as DNA methylation, histone modification and different RNA-mediated processes primarily affect gene expression at the level of transcription, other stages of the process (such as translation) may also be regulated by epigenetic factors. The following will describe how epigenetics works on different circumstances, their role in various diseases and disorders.

Keywords: Gene expression• Transcription• Epigenesis• Genome

Introduction

The study of heritable and stable variations in gene expression that result from changes to the chromosome rather than the DNA sequence is known as epigenetics. Despite not changing the DNA sequence directly, epigenetic mechanisms can control gene expression by chemically altering DNA bases and altering the chromosomal superstructure, which is the structure in which DNA is packaged. A positively charged histone protein octamer that contains two copies of the histone proteins H2A, H2B, H3 and H4 is wrapped around negatively charged DNA. The fundamental component of chromatin, the nucleoprotein complex is a nucleosome. A continuous DNA polymer's linker DNA connects the nucleosomes and histone protein H1 stabilises the complex. A chromosome is created as a result of chromatin gathering. There are two types of chromatin on chromosomes: loose, transcriptionally active euchromatin and compact, inactive heterochromatin. The formation of either the open euchromatin state, which promotes gene expression by allowing transcription factors and enzymes to interact with the DNA, or the closed heterochromatin state, which inhibits gene expression by preventing the start of transcription, can be caused by chemical changes to histone proteins. The transfer of genetic information from the archival copy of DNA to short-lived messenger RNA, usually followed by the creation of protein, is represented by transcription, translation and subsequent protein modification. Despite having fundamentally identical DNA, all cells in an organism have various kinds and activities due to qualitative and quantitative variations in gene expression. Control of gene expression is therefore necessary for differentiation and development. As cells split during mitosis, the gene expression patterns that distinguish differentiated cells are formed during development. Thus, in addition to receiving genetic information, cells also inherit information known as epigenetic information that is not encoded in the DNA nucleotide sequence. "The study of mitotically (and maybe meiotically) heritable changes in gene expression that are not driven by changes in DNA sequence," according to the definition of epigenetics.

DNA methylation, histone modification and non-coding RNA (ncRNA)-associated gene silencing are three distinct epigenetic mechanisms. DNA methylation is the process of adding a methyl group directly to a cytosine nucleotide within a cytosine-guanine sequence (CpG), which is frequently surrounded by other CpGs, forming a CpG island. This process is catalysed by DNA methyltransferase enzymes. Common sites for epigenetic DNA methylation include CpG islands, particularly those found in promoter regions. In fact, it has been noted that CpG islands include over 70% of gene promotor regions. A promoter region's methylated cytosines draw in gene suppressor proteins and lessen the interaction of the DNA with transcription factors. The nucleosome tightness hinders transcriptional machinery from interacting with the DNA since cytosine methylation also promotes the establishment of heterochromatin. As a result, DNA methylation in promoter regions silences genes. Frequently, tumour development is accompanied by pronounced hypomethylation of proto-oncogenes and hypermethylation of tumour suppressor genes in cancers. Additionally, the imprinting of the genome, the X chromosome and tissue-specific gene regulation are all significantly influenced by this epigenetic mechanism.

Histone protein post-translational changes represent the second epigenetic process. The DNA-histone connections in nucleosomes are modified by enzyme-catalyzed processes such as acetylation, methylation, phosphorylation and ubiquitylation. Histone acetylation frequently takes place at positively charged lysine residues, weakening the connections between DNA and histones and opening up the chromatin to allow transcription. For instance, the acetylation of histone 3's lysines 9 and 27 (designated as H3K9ac and H3K27ac, respectively) is correlated with the activation of transcription. Since histone methylation does not alter the protein's charge and can involve the addition of 1-3 methyl groups to lysine and 1-2 methyl groups to arginine, it is a more complicated process. For instance, trimethylation of lysine 27 on histone 3 (H3K27me3) connects with transcription repression, whereas lysine 4 on histone 3 (H3K4me) is related with transcription activation. A negative phosphate group is added to the histone tail during histone phosphorylation, but little is known about its use outside of the role that H2A(X) phosphorylation plays in the response to DNA damage and subsequent repair. Lysine residues on histones are subjected to the insertion of a large ubiquitin molecule. Histones like H2AK119ub, which is linked to gene silencing and H2BK123ub, which is involved in transcription, are examples of histones that have become ubiquitylated. In contrast to histone acetylation, which has a relatively simple impact on gene expression, other histone modifications have complex consequences and are significantly influenced by the state of surrounding DNA molecules. Non-coding RNA-associated gene silencing is the epigenetic mechanism that has lately been fully understood. Non-coding RNAs (ncRNAs) are functional RNA molecules that undergo transcription but do not undergo protein translation. Although ncRNA molecules were often thought to be a waste product of the genome, current research indicates they play a critical role in epigenetic gene expression and are likely responsible for the stark differences in phenotype between species and within human groups.

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MicroRNAs (miRNA) and short interfering RNAs (siRNA), which have less than 30 nucleotides and long non-coding RNAs (lncRNA), which have 200 nucleotides or more, are examples of notable ncRNA molecules. Although the full scope of ncRNAs' involvement in epigenetics is yet unknown, there is evidence that they play a role in histone modifications, DNA methylation and gene silencing in addition to gene silencing. It has been demonstrated that the development of heterochromatin is a mechanism by which siRNAs and lncRNAs control gene expression.

Literature Review

How does methylation of cytosine affect the expression of genes? Numerous methods are proposed to explain how DNA methylation results in transcriptional silence. One process is site-specific transcription factor interaction by DNMTs, leading to promoter area methylation. The subsequent assembly of proteins that recognise methylated DNA at these sites is caused by this site-specific methylation. These assemblies then directly affect the transcriptional machinery's subsequent actions or change the structure of the chromatin, which has an impact on regular gene expression mechanisms. Site-specific DNA methylation at promoters as a result of the direct interaction of DNMTs with transcription factors, which interact with DNA at specific locations, is thought to play a significant role in the regulation of gene expression. Data on particular interactions between different transcription factors and DNMTs exist, notwithstanding their limitations. There are several different DNA methyl-binding proteins (MBPs), which are categorised into related "families" based on structural similarities. The proteins MBD1, MBD2, MBD3, MBD4 and MECP2 all share a DNA-binding domain known as the methylated DNA-binding domain, or MBD. The MBD1-3 proteins are transcriptional repressors that function in a variety of ways, attracting histone deacetylases and co-repressors as a result. The activation of histone deacetylases causes a distinctive compaction of DNA, which culminates in the recognisable remodelling of chromatin. Thymidine glycosylase repair enzyme MBD4 is involved.

It is not linked to transcriptional inactivation and probably plays a part in lowering methylcytosine's mutagenic potential. The MBD family member with the greatest characterization is likely MECP2. Through its second functional domain, a transcriptional repression domain, it binds methylated CpG and suppresses transcription over several hundred base pair distances. This repressor domain enlists various co-repressor complexes or the co-repressor Sin3 complex, which contains histone deacetylases 1 and 2. As an alternative, MECP2 can change the compaction of chromatin by attaching to nucleosomes and linker DNA, creating a physical barrier to the transcriptional machinery. A common zinc finger domain is seen in the proteins Kaiso, ZBTB4 and ZBTB38, which make up the second family of MBPs. This family of proteins has a variable nucleo/cytoplasmic distribution and is thought to react to intracellular signalling, particularly the Wnt pathway. According to a recent study, Kaiso can control transcriptional activity by influencing the development of the -catenin and histone deacetylase 1 (HDAC1) complexes and interacting with transcription factors including LEF1 and its homologs. UHRF1 and UHRF2 (also known as ICBP90 and NIRF, respectively) are members of the third family of methyl DNA-binding proteins and they are able to identify and bind semi-methylated DNA thanks to their SET- and RING finger-associated domains (SRA proteins). When SRA proteins bind to methylated DNA, DNMT1 is directed to these locations, further altering DNA methylation and attracting more MBPs and the related activities.

As a result, methyl-binding proteins respond to the DNA's methylation status at particular locations, which are frequently linked to gene promoters. These methyl-binding proteins seem to work by enticing other enzymes, like histone deacetylases, which, as will be discussed in the sections that follow, also play significant roles in the epigenetic regulation of gene expression. In eukaryotic cells, DNA and histone proteins combine to form chromatin, which is the environment in which transcription occurs. The nucleosome, which is the fundamental building block of chromatin, is an octamer made up of two molecules of each of the four conventional histone molecules (H2A, H2B, H3 and H4), around which 147 base pairs of DNA are wrapped. Between the nucleosomes, another kind of histone (linker histone, H1) links to the DNA.

Regulatory Gene Mechanism

The creation and maintenance of neural networks in the brain, as well as higher-order brain activities like cognition and behaviour, appear to depend on epigenetic mechanisms, according to new research. The aetiology or pathophysiology of several ailments, as well as the response to treatments, are now recognised to be affected by defects in epigenetic pathways. Numerous studies link epigenetic dysfunctions to psychiatric and neurological diseases like Alzheimer's disease, frontotemporal lobar degeneration, depression and schizophrenia as well as neurodevelopmental disorders like Rett syndrome, Fragile X and Rubinstein-Taybi syndrome. Epigenetic pathways also play a role in the inheritance of illnesses across families as a result of the environment's transgenerational impact on brain and body functions. Less is known about RNA-based mechanisms of epigenetic regulation than about those based on DNA methylation and histones. The role of RNA in controlling the monoallelic expression of imprinted genes (see the Barlow article in this issue) and the inactivation of the X chromosome (see the Wutz article in this issue) is well known, but more recent research has linked RNA-based mechanisms to broader epigenetic regulation. TRNAs, rRNAs, small nuclear RNAs (snRNAs) and short nucleolar RNAs are among the long-known non-coding infrastructural RNAs (snoRNAs). These take part in translation and splicing and recognise RNA substrates based on their sequences while also acting as catalysts.

Some of them may play regulatory roles in addition to their infrastructure-related ones. For instance, U1 snRNA controls the activity of RNA polymerase II's transcription initiation through its interaction with the transcription initiation factor TFIIH. The bulk of the genome, according to more recent research, is transcribed into RNA transcripts, the majority of which do not code for proteins. These non-coding RNAs (ncRNAs) are categorised typically based on length, subcellular location, orientation with regard to the closest protein-coding gene, and/or function and range in size from extremely tiny molecules to extremely massive transcripts (if known). Small (less than 200 nt and generally much shorter) and long (more than 200 nt and frequently much longer) species are two categories for ncRNAs that are frequently employed in classification. Small ncRNAs, which include microRNAs, short interfering RNAs, PIWI-interacting RNAs and repeat-associated RNAs (rasiRNAs), as well as other less well-known species, are often produced from larger RNA precursor molecules by cleavage with RNAse III-family enzymes (mainly Drosha and Dicer). Long ncRNA precursors or introns with incorrect hairpin structures are the source of miRNAs, which are about 22 nucleotides long (of coding or non-coding genes). In addition to their infrastructure-related functions, some of them might also fulfil regulatory ones. For instance, U1 snRNA interacts with the transcription initiation factor TFIIH to regulate the activity of RNA polymerase II's transcription initiation. According to more recent studies, the majority of the genome is translated into RNA transcripts, the majority of which do not code for proteins. These non-coding RNAs (ncRNAs) range in size from extremely minute molecules to extremely enormous transcripts and are often categorised based on length, subcellular location, orientation with respect to the closest protein-coding gene, and/or function (if known). Two categories for ncRNA species that are widely used in classification are little (less than 200 and typically much shorter) and long (more than 200 nt and frequently much longer) species. They typically base-pair with exact matches to their target mRNAs and drive them for degradation; but, if they base-pair with less complementarity, they may also suppress translation.

The role of siRNAs in transcriptional gene silencing is well understood in plants, where the siRNA directs DNA methylation to genomic areas similar to the siRNA sequence. This function is particularly important for silencing transposable elements. SiRNA-directed transcriptional gene suppression in Saccharomyces pombe and likely in mammals, requires the activation of histone methyltransferases and the production of heterochromatin. In male germ cells and oocytes, piRNAs, which are between 28 and 33 nucleotides in length, connect with PIWI-family proteins. They appear to be processed via a Dicer-independent (but poorly understood) route from single-stranded precursors. The '21U' RNAs of Caenorhabditis elegans and the rasiRNAs of Drosophila seem to correspond to piRNAs. For the viability of the germline, these RNAs are crucial for controlling the activity of transposable elements in the Drosophila, Caenorhabditis elegans, fish and mammalian germ lines. The

phenotypic of offspring is altered by maternal piRNAs deposited in Drosophila oocytes in a heritable way; hence, these piRNAs may function as carriers of epigenetic inheritance.

An growing number of research have found epigenetic processes for cell development. It highlights how crucial chromatin remodelling, noncoding RNA-mediated regulation of chromatid DNA and covalent alteration of DNA and histones are for the proper patterning of various cell types. The effects of epigenetic control on transcription are multifaceted since they affect not only on/off regulation but also kinetics and robustness moderation, preservation of transcriptional status and responsiveness or insensitivity to external transcriptional stimuli. The maintenance of differentiation, the development of effector functions and plasticity of immune cell biology are all coordinated by epigenetic changes.

Role of Epigenetics

Normal endocrine physiology and the emergence of endocrine disorders like type 2 diabetes and obesity both depend heavily on epigenetic processes. Understanding the relationship between neuroendocrine function and epigenetic mechanisms can help in the development of new therapeutic approaches and provide insight into the underlying biological causes of various illnesses. During development, in reaction to environmental variables and endocrine disruptors, in endocrine cancer, during endocrine therapies, etc., DNA methylation regulates hormonal responses at several levels. It is evident that the onset of obesity is a considerably more complex combination of numerous coexisting elements than a simple overshoot of calories in against calories out. There is strong evidence connecting epigenetic processes to the control of metabolic pathways that result in obesity and type 2 diabetes. Particularly in foetal development, where exposure to an excess or deficiency of energy and some nutrients results in altered chromatin structure and DNA alteration, affecting the expression of important genes, the importance of the timing of such events cannot be neglected. The observations in animals detailed here give new information on the significance of this epigenetic change in the operation of the endocrine glands and in the response of target tissues to hormones, even though many aspects of the endocrine system epigenetics are still unclear.

Despite the fact that DNA methylation and histone changes do not work separately, epigenetic mechanisms are frequently explored in isolation. A greater understanding of key epigenetic interactions, their function in disease etiopathology and assistance in developing therapeutic options would be provided by concurrent investigations on these various levels of epigenetic modification. Additionally, more research is needed to properly understand epigenetic mechanisms such ubiquitination, sumoylation, RNA- and polycomb-based mechanisms. Unresolved issues include the distribution of miRNAs to specific regions. In many vertebrate species, DNA methylation plays a role in the sex-determination process by controlling the expression of genes connected to sex-determination networks. The connection between invertebrate epigenetics and sex determination, however, has remained obscure. People respond to adversity in a variety of ways, with a sizable percentage of people exhibiting psychological resilience. According to one proposed molecular pathway, epigenetic processes, unfavourable and traumatic experiences might become physiologically ingrained and contribute to individual variances in resilience. However, little is understood about how epigenetics contributes to the growth of psychological toughness. In this Review, we offer a fresh conceptual framework for the various roles played by epigenetic pathways in psychological adaptability.

In the past, it was believed that epigenetic mechanisms, which control gene activity in the central nervous system, were only relevant to disease or developmental processes. Recent research contends that these mechanisms, particularly DNA covalent modification and posttranslational modifications of histones, are labile throughout life and are affected by experiences. Exciting new research has shown that experience-induced changes in adult brain function and behaviour depend on epigenetic regulation of genes. Direct cardiac reprogramming, a promising treatment approach for heart disorders, also entails extensive epigenetic alterations during the conversion of cell fate. With the help of computational analyses of multi-omics data, it will be possible to thoroughly understand epigenomic changes and identify important epigenomic signatures in cardiac development, reprogramming and diseases. This will lead to new understandings of the epigenetic mechanisms regulating cell plasticity and will inspire creative new therapeutic approaches for cardiovascular diseases.

Epigenetics and Gene Expression

The transfer of genetic information from the archival copy of DNA to the transient messenger RNA, often followed by the creation of protein, is represented by transcription, translation and subsequent protein modification. Despite having fundamentally the same DNA, every cell in an organism has a different kind and function due to qualitative and quantitative variations in gene expression. Therefore, differentiation and development depend on the regulation of gene expression. Although it is believed that epigenetic mechanisms such as DNA methylation, histone modification and different RNA-mediated processes primarily affect gene expression at the level of transcription, other stages of the process (such as translation) may also be regulated by epigenetic factors. Without changing their DNA sequence, cells go through significant morphological and functional changes during differentiation and development. Epigenetic mechanisms set up and maintain the underlying modifications of gene expression patterns. Early mechanistic understandings resulted from the fact that the degree of DNA methylation in a gene's promoter region correlates with both gene activity and repression states. In vertebrate cells, DNA methylation is a post-replication alteration that primarily affects CpG dinucleotides and only takes place at the C5 position of cytosine residues (5mC).

Here, distinct DNA methylation patterns are established during differentiation and maintained over numerous cell division cycles by three primary DNA methyltransferases (Dnmt1, 3a and 3b). At least three protein families identify CpG methylation, which in turn attracts histone modifying and chromatin remodelling enzymes, converting DNA methylation into repressive chromatin structures. DNA methylation has now been associated in various ways with a wide variety of histone modifications. Accurate gene transcription control in response to the right environmental signals is necessary for the development and operation of the CNS. Precise brain gene regulation is mediated by epigenetic mechanisms, such as DNA methylation, histone changes and other chromatin-remodeling activities. Not only is DNA methylation and histone modification essential for brain cell development, but it is also essential for high-order cognitive processes like learning and memory [1-5].

Conclusion

Because it may be possible to control gene expression without altering the DNA sequence, which would probably raise ethical and safety issues if applied to people, epigenetics is a promising area of study. Pharmacology has shown the most promise as a means of treating disorders whose epigenetic regulation has been altered. Previous medication clinical studies that aimed to stop cancer-related epigenetic changes were successful. Numerous illnesses linked to genomic imprinting, including cancer, are brought on by dysregulated epigenetic pathways. Epigenetic mechanisms, particularly in imprinted genes where only one paternal chromosome is expressed, can cause disease but they are also essential for proper cell function. The epigenome differs from cell to cell and is plastic, changing over time and in response to exposure to the environment. This is in contrast to the genome, which is almost similar in all vertebrate cells and stable throughout an individual's lifetime. Long-term variations in gene expression patterns provide an alluring biological foundation for the theory that environmental exposure events during a person's prenatal or postnatal development are the cause of adult disease. Because of this, research into the epigenetic control of gene expression will not stop.

References

1. Bonasio, Roberto, Shengjiang Tu and Danny Reinberg. "Molecular signals of epigenetic states." *Science* 330 (2010): 612-616.

2. Mikkelsen, Tarjei S., Jacob Hanna, Xiaolan Zhang and Manching Ku, et al. "Dissecting direct reprogramming through integrative genomic analysis." *Nature* 454 (2008): 49-55.

3. Yang, Xiangzhong, Sadie L. Smith, X. Cindy Tian and Harris A. Lewin, et al. "Nuclear reprogramming of cloned embryos and its implications for therapeutic cloning." *Nat Genet* 39 (2007): 295-302.

4. Keefer, C. L. "Lessons learned from nuclear transfer (cloning)." *Theriogenology* 69 (2008): 48-54.

5. Yamanaka, Shinya and Helen M. Blau. "Nuclear reprogramming to a pluripotent state by three approaches." *Nature* 465 (2010): 704-712.

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