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Regulatory mechanism of dynamic changes in nuclear ultrastructure on cellular transcriptional activity

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Abstract:

This study focuses on the regulatory mechanism of dynamic changes in the ultrastructure of the nucleolus on cellular transcriptional activity. It elaborates on the structure and function of the nucleolus, the concept of cellular transcriptional activity, and its regulation methods. The dynamic changes in the ultrastructure of the nucleolus, as well as various regulatory mechanisms of cellular transcriptional activity, are analyzed in depth. The direct and indirect regulatory mechanisms of dynamic changes in the ultrastructure of the nucleolus on cellular transcriptional activity are explored.

Keywords:

Nucleolus
Ultrastructure
Dynamic changes
Cellular transcriptional activity
Regulatory mechanism

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1. Introduction

In the complex regulatory network of cellular life activities, the relationship between the ultrastructure of the nucleolus and cellular transcriptional activity is crucial. Deeper exploration of the regulatory mechanisms of dynamic changes in the ultrastructure of the nucleolus on cellular transcriptional activity not only helps to reveal the basic principles of cellular operation but also provides a theoretical foundation for overcoming related diseases. This study will delve into this topic.

2. Overview of the Nucleolus and Cellular Transcriptional Activity

2.1 Structure and Function of the Nucleolus

The nucleolus is not a static structure, and its composition can vary significantly depending on the species of cells and their physiological metabolic state [1]. The nucleolus is the most prominent structure in the interphase nucleus of eukaryotic cells. It usually appears as one or more strongly refractive spherical bodies without a membrane structure. It mainly consists of the fibrillar center (FC), dense fibrillar component (DFC), and granular component (GC). Its primary function is to participate in ribosome biogenesis, a process that includes the synthesis and processing of rRNA and the assembly of ribosomal subunits.

2.2 Concept and significance of cellular transcriptional activity

2.2.1 Definition of cellular transcriptional activity

Cellular transcriptional activity refers to the ability and efficiency of transcribing genes into RNA in a cell. It is a dynamic process that is precisely regulated by a variety of factors and can be measured by a variety of indicators, such as the rate of transcription of a particular gene and the abundance of transcription products. Gene transcription in cells is a key step in the transmission of genetic information, which converts genetic information in DNA into RNA molecules to provide templates for subsequent protein synthesis [2]. There are significant differences in the transcriptional activity of different types of cells in different physiological states, which determines the function and phenotype of the cells.

2.2.2 Regulation of cellular transcriptional activity

The regulation of cellular transcriptional activity is a complex and delicate process involving regulatory mechanisms at multiple levels. Transcription factors bind to specific DNA sequences in the promoter regions of genes, recruit transcription-related proteins such as RNA polymerase, and form transcription initiation complexes, thereby initiating the transcription process. The activity and expression levels of transcription factors are regulated by a variety of factors, including intracellular signal transduction pathways, post-transcriptional modifications, etc. [3].

3.Dynamic changes in cell nucleolus ultrastructure

3.1 Changes in the cell cycle

In the early G1 phase, the cell nucleolus is small, the structure is relatively simple, and the boundary between the fibre centre and dense fibre components is less clear. As the cell enters the late G1 phase, the nucleolus begins to gradually increase in size, rRNA transcriptional activity is enhanced, and the boundaries of the fibre centre and dense fibre components become more obvious. This is because the cell needs to prepare for the upcoming DNA replication and protein synthesis in G1 phase, thus rRNA synthesis and ribosome assembly activities increase [4]. Entering S phase, DNA replication begins, the size and morphology of the nucleolus is relatively stable, but the transcriptional activity of rRNA is still active, and the components in the nucleolus continue to participate in the process of ribosome biogenesis, providing enough ribosomes for cell division.In G2 phase, the nucleolus further increases in size and granular components, indicating that the process of assembly of the ribosomal subunits is accelerated. This is due to the fact that the cell needs a large number of ribosomes to synthesise proteins during G2 phase in preparation for the upcoming cell division.In M phase, the nucleolus gradually disintegrates as the chromosomes coalesce, and the structures of the fibre centre, dense fibre component and granular component gradually disappear.This is due to the fact that the cell needs to reallocate its resources to processes such as chromosome segregation and cell division in the process of cell division. When the cell enters the G1 phase of the next cell cycle, the nucleolus begins to reassemble again, gradually restoring its normal structure and function.

3.2 Changes during cell differentiation

The process in which a cell changes from an undifferentiated state to a differentiated state with a specific function is called cell differentiation, during which the ultrastructure of the nucleus pulposus also undergoes adaptive changes. During neuronal differentiation, as neural stem cells gradually differentiate into mature neuronal cells, the size of the nucleolus decreases, and rRNA synthesis and ribosomal subunit assembly activities are correspondingly weakened. Because the main function of mature neural cells is to transmit and process neural signals, the protein synthesis requirement is relatively stable and does not require a large number of ribosomes. In undifferentiated cells such as embryonic stem cells, which have a large and complex nucleolus, rRNA synthesis and ribosome assembly activities are vigorous, which is to meet the needs of rapid cell proliferation and differentiation [5]. During muscle cell differentiation, the structure and function of the nucleolus also change. As muscle cells mature, the nucleolus adjusts the level of rRNA synthesis and ribosome assembly to adapt to the specific protein synthesis needs of muscle cells, such as synthesising large amounts of muscle-specific proteins such as actin and myosin.

4. Mechanisms regulating cellular transcriptional activity

4.1 Transcription factors and transcriptional activity regulation

To ensure the accuracy and adaptability of gene transcription, the activity of transcription factors is regulated in a variety of ways. Covalent modification is one of the important ways to regulate the activity of transcription factors, and common covalent modifications include phosphorylation, acetylation and methylation. The binding ability to DNA and transcriptional activation of certain transcription factors are altered upon phosphorylation. Phosphorylation can regulate gene transcription by activating or inhibiting the activity of transcription factors. Transcription factors can also regulate their activity by interacting with other proteins, which can be either coactivators or co-inhibitors [6]. Co-activators can bind to transcription factors to enhance their transcriptional activation, while co-repressors can bind to transcription factors to inhibit their transcriptional activity. In the transcriptional regulation of certain genes, transcription factors need to form complexes with coactivators to effectively bind to DNA and initiate transcription. The expression levels of transcription factors are also tightly regulated, and intracellular signal transduction pathways can control the amount of transcription factor expression by regulating the transcription and translation processes of transcription factor genes. When cells are stimulated by growth factors, the intracellular signalling pathway will activate the expression of relevant transcription factor genes, thus increasing the level of transcription factors and promoting the transcription of genes related to cell proliferation and differentiation.

4.2 Chromatin structure and regulation of transcriptional activity

4.2.1 Chromatin remodelling and transcriptional activity

Chromatin remodelling is a process in which the structure and composition of chromatin are altered, thereby affecting gene accessibility and transcriptional activity. Chromatin remodelling complexes are a class of protein complexes that can use the energy provided by ATP hydrolysis to change the position and structure of nucleosomes, with two main modes of action: one is to slide the nucleosome so that the position of the nucleosome on the DNA is shifted, thereby exposing or masking the regulatory elements of genes; the other is to change the composition of the nucleosome, for example, by replacing the histone variant, thus affecting the chromatin structure and function. When chromatin remodelling complexes move nucleosomes away from the promoter regions of genes, transcription factors and RNA polymerases are more likely to bind to DNA, thereby facilitating gene transcription [7]. In contrast, when chromatin remodelling complexes move nucleosomes to cover the promoter regions of genes, binding of transcription factors and RNA polymerases is impeded and gene transcription is inhibited.

4.2.2 Histone Modifications and Transcriptional Activity

Histone modification is one of the important modes of chromatin structure regulation and has a profound effect on transcriptional activity. Common histone modifications include methylation, acetylation and phosphorylation. Different histone modification sites and modification states have different functions. Methylation of the lysine 9 site of histone H3 is usually associated with gene silencing, and this modification can make the chromatin structure more compact and hinder the binding of transcription factors to DNA. Methylation of the lysine 4 site of histone H3, on the other hand, is associated with gene activation, which can loosen the chromatin structure and facilitate the binding of transcription factors and the initiation of transcription. Acetylation of histones is also an important modification. Acetylation can neutralise the positive charge of histones, weaken the interaction between histones and DNA, and make the chromatin structure more open, thus facilitating the binding of transcription factors to DNA and the initiation of transcription.

5.Regulation mechanism of cellular transcriptional activity by dynamic changes in nucleolus ultrastructure

5.1 Direct regulation mechanism

5.1.1 Interaction between nucleolus ultrastructure and transcription machinery

The fibre centre (FC), as a storage site for rRNA genes,

has a special association with the core component of the transcription machinery, RNA polymerase I. RNA polymerase I is responsible for the transcription of rRNA genes, and it needs to be accurately localised to the rDNA region of the fibre centre in order to initiate the transcription process [8]. In this process, the fibre centre provides a stable binding platform for RNA polymerase I, allowing efficient assembly of the transcription initiation complex. At the same time, some specific proteins within the fibre centre may be involved in the recruitment and activation of RNA polymerase I, ensuring efficient rRNA gene transcription.

The dense fibre component (DFC) surrounds the fibre centre and is a key site for rRNA transcription and initial processing. It not only accumulates a large number of rRNA molecules being transcribed, but also contains numerous protein factors associated with transcription and processing. These protein factors work in concert with RNA polymerase I to carry out a series of processing modifications in conjunction with rRNA transcription.

The granule component (GC) consists of ribosomal subunit precursor particles at different stages of processing, and its interaction with the transcriptional machinery is mainly reflected in its effect on post-transcriptional events. As rRNA completes its initial processing in the DFC, progressively more mature rRNA is translocated into the granule component, where it binds to ribosomal proteins translocated in from the cytoplasm and assembles into ribosomal subunits [9]. This process does not occur in isolation, but there is a feedback regulatory mechanism with transcriptional activity. When ribosomal subunit assembly proceeds smoothly, it transmits signals to the transcription machinery and promotes the continued transcription of rRNA genes; conversely, if ribosomal subunit assembly is abnormal, it may inhibit the activity of the transcription machinery and reduce the synthesis of rRNAs, thus maintaining a balance between the transcription and translation processes in the cell.

5.1.2 RNA Processing and Transcriptional Activity in the Nucleolus

After rRNA is transcribed to generate the initial transcript (pre-rRNA), it needs to undergo a series of complex processing steps to become mature rRNA and participate in ribosome assembly. These processing steps include shearing, modification, etc., each of which exerts feedback regulation on transcriptional activity.

During the shearing process, the pre-rRNA is cleaved into different fragments by specific nucleases, removing non-coding regions and generating the individual components of the mature rRNA. If there is an abnormality in the shearing process, such as reduced or absent nuclease activity, resulting in pre-rRNAs not being sheared properly, a large amount of unprocessed rRNAs can accumulate. these unprocessed rRNAs can bind to transcription factors or RNA polymerase I, forming a negative feedback regulatory mechanism that inhibits the transcription of rRNA genes. This is because there is a monitoring mechanism in the cell, when unprocessed rRNA accumulates to a certain level, the cell will sense this abnormal situation and avoid wasting too much resources on rRNA synthesis that cannot be processed properly by inhibiting transcription.

5.2 Indirect regulatory mechanisms

5.2.1 Nucleolus signalling pathway and regulation of transcriptional activity

The nucleolus is involved in many important signalling pathways, which indirectly and profoundly affect cellular transcriptional activity by regulating the dynamics of nucleolus ultrastructure.

The mTOR signalling pathway is a key intracellular nutrient-sensing and growth-regulating pathway, which is closely linked to the nucleolus function. When nutrition is sufficient, mTOR is activated, which regulates the size and activity of the nucleolus through signal transduction and promotes rRNA synthesis and ribosomal subunit assembly in the nucleolus [10]. p53, as a tumour-suppressor protein, is activated when the cell is subjected to stress stimuli, such as DNA damage, and activated p53 enters the nucleolus and interacts with proteins in the nucleolus to affect the structure and function of the nucleolus. In addition to these two signalling pathways, the nucleolus is also involved in a variety of signalling pathways such as Wnt, MAPK, etc., which regulate the dynamic changes in the ultrastructure of the nucleolus by different mechanisms, resulting in a complex regulation of cellular transcriptional activity.

5.2.2 Effect of nucleolus-chromatin interaction on transcriptional activity

Spatially, some regions of chromatin bind to the

nucleolus to form nucleolus-associated chromatin regions (NADs), which are rich in rRNA genes and genes related to transcriptional regulation. Interaction between nucleoli and NADs can alter chromatin structure: it may either loosen chromatin to facilitate DNA binding by transcription factors and RNA polymerase and promote gene transcription, or it may result in chromatin condensation and inhibit transcription.

The nucleolus recruits histone-modifying enzymes, such as histone methyltransferases and acetyltransferases, to specific chromatin regions. These enzymes modify histones, alter chromatin charge and structure, and affect the ability of transcription factors to bind to DNA, thereby regulating transcription, as histone acetyltransferases promote transcription and methyltransferases may inhibit transcription.

6. Conclusion

Dynamic changes in the ultrastructure of the nucleolus finely regulate cellular transcriptional activity by a variety of mechanisms, both direct and indirect. This study has deepened our knowledge of cellular life activities. In the future, we need to further explore the complex mechanisms, which will contribute to the development of cell biology and open up more possibilities for the diagnosis and treatment of related diseases.

Disclosure statement

The author declares no conflict of interest.

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