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Small RNA function of epigenetic modifications: A review

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ABSTRACT

Small RNA widely exists in one of the main function regulation of gene expression in an organism, rather than direct protein synthesis of RNA. SiRNA and mirnas are important for both small RNA, and play irreplaceable function. Both can inhibit the expression of mRNA, but methods of action vary, siRNA is mainly led by RNAi (RNA interference) to gene silencing; Micrornas in cell proliferation, differentiation and other activities play a key role in regulation. SiRNA and biosynthesis of mirnas are introduced in this paper, siRNA and microRNA mediate gene silencing mechanism, as well as siRNA in yeast, plants, and the human body by triggering the change of the epigenetic modifications regulating gene expression model, the mechanism of siRNA and mirnas is discussed in the end for the influence of disease treatment and drug research and development.

Keywords: small RNA function; epigenetic modifications; gene expression

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INTRODUCTION

In eukaryotes, nucleosome histone modification is changing structure of chromatin, adjusting the important mechanism of gene transcription, all kinds of histone modify as epigenetic information by the activation of specific factors and inhibiting factor identification, without altering the DNA sequence that phenotype changed, forming the so-called the histone code. The previous research show that histone H3 N end nine Lys methylation play a key role to prevent the transcription of chromatin activity [1, 2, 3, 4]. On the contrary, in yeast, worms, fruit flies and mammals, Lys of methylation of histone H3 nine is widely spread on the active gene transcription chromatin,5,6,7,8 [4]. Correspond to H3K9Me, the DNA in plants and some mold is also 5 - methyl cytosine, thus more inhibition gene transcription.

Eukaryotes chromatin include euchromatin and heterochromatin, often being accompanied by low histone acetylation on the heterochromatin and high levels of H3K9Me characteristics, and DNA in plants and mammals heterochromatin is often in high methylation status [1,5,6]. Also, the methylation of histone H3 in heterochromatin of some conservative protein combination is necessary, such as, heterochromatin protein 1 HP1 [7,8]. Although some pathways of heterochromatin formation has been concentrated, the initial steps of the process is still vague. Now, specific non-coding RNA molecules is considered in the process of inducing the formation of heterochromatin [9,10,11]. Especially dsRNA, also called "short RNA", the activity of chromatin is an RNA molecule involved in epigenetic regulation

1. Small rnas biosynthesis
1.1 The miRNA biosynthesis
Micrornas biosynthesis mechanism have been elucidated recently, mainly being produced by RNA polymerase transcription. Transcription starting product is a very large RNA precursors, known as pri - miRNAs. And then within the nucleus: pri- micrornas RNase , Drosha, double-stranded RNA and protein Pasha (also known as DGCR8) are modified by shear and form about 70 nucleotides of pre-miRNAs, are fold it into the rules of pin structure. Then about 70 nucleotides of pre-micrornas via RAN GTP depend on Exportin5 outside the nucleus, the

produced cytoplasm belongs to another kind of RNase □ Dicer further shear processing, form of about 22 nucleotides long double-stranded micrornas. Mature miRNA and miRISC complex are combined with exercise of transcriptional regulation.

Drosha exists in the nucleus, or at least consists of two parts. The larger compounds include a series of RNA related proteins, such as RNA helicase, protein and RNA double-stranded, a new type of various ribonucleoprotein and Ewings sarcoma protein family [12]. And smaller compounds include Drasha, double chain binding protein, DGCR8 (also called Drasha) [13,14,15,16].

1.2 siRNA biosynthesis

Biosynthesis of siRNA are from Dicer for shear double-stranded RNA precursor, without the need for Drasha [17,18]. Double-stranded RNA precursor can be derived from the body, can also be derived from in vitro. In human body, it can be through the chain of justice, two-way transcription antisense strand synthesis. Exogenous, ia probably from RNA virus infection, such as plants, man-made foreign interference of RNAi into fragments, RNA paired with endogenous can lead to the degradation of endogenous RNA.

2. dsRNA mediated gene silencing mechanism

In 1998, dsRNA molecules are injected nematode, it is found that it can effectively restrain homologous gene expression, these phenomenon are called RNA interference named RNAi [19,20]. And then also in plants, fungi, protozoa, it can be found this phenomenon [21,22,23]. However, the molecular mechanism of RNA interference is mainly in the fruit fly cell extracts [24,25,26,27,28] and mammalian cells.

2.1 siRNA mediated gene silencing mechanism

SiRNA mediated gene silencing mechanism of specific is as following: long chain dsRNA is RNase □ Dicer family, the nuclease shear growth degree of 20 -- 25 nucleotides short dsRNA. This short is known as siRNA interference RNA. It has exposed in the ends of the chain of highlight of 3 '- OH, and phosphorylation of 5' end respectively. Then, a chain of siRNA with RNA induces silence complex RISC, under the action of RISC, the chain and its homologous mRNA match combination. RISC can shear mRNA in particular by siRNA target sequence, resulting that the mRNA degrade. But if in the case of siRNA and mRNA incomplete matching, mRNA cannot be cut, but after combination of mRNA and ribosomes, the translation process of blocking siRNA directly leads to the translation of mRNA block, the mechanism of this process is not clear at present.

2.2 miRNA mediated gene silencing

Small RNA is a source of siRNA, and the other different sources is the so-called miroRNA, it also can inhibit the expression of genes. It is derived from this kind of small RNA ribozymes Dcier shearing hairpin structure of animals and plants genome encoding RNA precursors. But, in different sources and siRNA, the regulation of mRNA and siRNA are similar, it is usually combined with the mRNA 3 'UTR- on the complementary sequence, when miroRNA completely complements mRNA in block under the condition of the translation of mRNA [29,30].

3. Small rnas with heterochromatin formation

3.1 Small RNA and yeast heterochromatin formation model

A siRNA related histone modification is reported in literatures in fission yeast, supachai, panitchpakdi, and rombe heterochromatin centromere region [31]. The centromeric chromatin area is rich in H3K9Me and Swi6 protein. Swi6 protein is a kind of HP1 proteins presenting in the yeast belonging to many cells (chromatin protein 1) [32], centromeric chromatin contains a lot of repeat sequences, this area is often considered as transcriptional activity area. The dsRAN hand is repeated by the DNA sequence and double-stranded DNA transcription; DsRNA, on the other hand, also can pass the single-strand RNA as a template in the guidance of RNA RNA polymerase (RdRp) synthesis. Then dsRNA has Dicer shored of siRNA. SiRNA hand in RISC (RNA induce silence compounds), under the action of a line proteins group, they will be able to match exactly with the mRNA in complete matching area, mRNA cut the lead to the degradation of mRNA.

3.2 Plant DNA methylation and RNAi mechanism model

In plants, RNA depended on DNA methylation is more widespread than RNA depending on the methylation [33]. However, RNA depending on DNA methylation is antiviral properties and its regulation in plants has a vital role.

3.3 The treatment of application of RNAi

RNAi has the following important characteristics: (1) the RNAi is mediated double-stranded RNA transcription after gene silencing mechanism; (2) the RNAi specify; (3) the efficiency of RNAi; (4) high penetrability of RNAi. The study of RNAi in vivo and in vitro have showed that RNAi has a good prospect of application in cancer therapy, a variety of cancer gene can be used as a target, designed the corresponding siRNA RNAi, to close the cancer gene

mutation or gene silencing. Using RNAi technology improves tumor sensitivity, radiation or drugs is another RNAi technology applied for tumor treatment. SiRNA against hepatitis virus can effectively inhibit HBV and HCV viral replication and transcription of RNA molecules, eventually reduce the virus antigen expression, RNAi technology for disease resisting viral hepatitis provides a new method for gene therapy. In a series of recent study, siRNA has successfully used in mammalian cells to prevent human immunodeficiency virus (HIV) infection. In addition, RNAi has inhibition of poliovirus infections and the role of resisting the SARS virus.

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