Mini Review

Recent Updates in Heterogenous Nuclear (hn) RNA

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Abstract

   Ribose nucleic acid (RNA) is a new molecule of hope that arises from ribosomes. RNA is a dynamic molecule that possess the diverse functions and properties. Heterogenus nuclear RNA (hn-RNA) also known as precursor mRNA have vital role in biological process. The branch dealing with the varied role of pre-mRNA is known as epitranscriptome can be used as a marker for disease prognosis. The expression of these pre-mRNA is various diseases are different and this property can be widely exploited in the disease pathogensis and complications.

   Keywords: Disease; RNA; mRNA

Introduction

   Ribose nucleic acid (RNA) is a known to be a fascinating molecule ever. The ribosome is the nurturing mother of RNA. RNA possesses structural properties as shown for rRNA core. Furthermore, RNA also has protein binding properties like rRNA-protein interactions that can be used for protein translation process [1]. Endless properties of RNA also include enzymatic action. So, RNA is a dynamic molecule with varied functions and properties. During the translation process, the non-coding RNA perform decoding (tRNA) and rRNA (amino acid polymerization) [2]. A great statement made by Francis Crick's 'central dogma' of molecular biology it is stated that RNA molecules serve to initiate protein synthesis, decode mRNA and form protein. Apart from RNA molecule the precursor mRNA (pre-mRNA) also known as heterogenous nuclear RNA (hnRNA) also plays a vital role in the biological system [3].

   This hnRNA serve as a single premature single strand of mRNA. Transcription enables the DNS template in the cell nucleus to synthesised pre-mRNA. Pre-mRNAs include two types of segments exons and introns. Exons showed hierarchy in final mRNA, while introns are removed under splicing process by the spliceosome.

Characteristics of hnRNA

   First, hnRNA is 4-10 times complex than mRNA [4].

- Spliceosome process the hnRNA.
- The term hnRNA is often used just for the unprocessed primary transcripts.

Precursor mRNA processing in eukaryotes

   The pre-mRNA and hnRNA derived eukaryotic sources are extensively edited prior to translation [5]. The additional makeover of eukaryotic mRNA impart longer half-life compared to prokaryotic mRNA. Moreover, the pre-mRNAs are incorporated firstly in RNA-stabilzing proteins (RSPs) in order to protect precursor-mRNA from degradation during its processing and oozing out of nucleus. Among the most important steps of stabilizing the pre-mRNA, the three predominant steps includes addition of signalling factors at the 5' and 3' ends followed by stabilising proteins and elimination of intervening sequences that are irrelevant to their corresponding amino acids [6].

5' Capping of pre-mRNA

   Post synthesis of pre-mRNA, a 7-methylguanosine capping at the 5' end of the progressive transcript by a enzyme system 5'-to-5' phosphate linkage is performed. This mechanism prevents the further degradation of the nascent mRNA. Additionally some of the initiation factors involved in protein synthesis recognise this aforesaid cap that assist in translation by ribosomes.

3' Poly-A Tail of pre-mRNA

Endonuclease comprising of protein complex cleave the pre-mRNA between an AAUAAA consensus sequences and a GU-rich sequence [7]. This mechanism enable the release of functional pre-mRNA from rest of the transcript. Another enzyme complex called poly (A) polymerase (PAP) cleaves the functional pre-mRNA and immediately add the 200 A nucleaotides which later on form poly A tail at the 3' end of the cleaved pre-mRNA. This addition of A nucleotides protect the mRNA from further degradation and assist in exporting the pre-mRNA into the cytoplasm.

Insights of pre-mRNA splicing

RNAseq-mediated deep mining of the cellular transcriptome leads to the possibility of defining all alternative RNA splicing (differential removal of introns from pre-mRNAs) events that can occur to individual pre-mRNAs. This has led to the realisation that more than 90% of human pre-mRNAs are alternatively spliced, while the average pre-mRNA gives rise to around seven different alternative mRNA species. Splicing is controlled by RNA secondary structure, the strength of 5′ and 3′ splice sites, splicing enhancer and silencer sequence elements, exon/intron architecture and transcription by RNA polymerase II. However, we do not understand the relative contributions of each of these to determining the final splicing pattern of any one pre-mRNA in development, differentiation or disease. Generation of a 'splicing code' that will allow prediction of splicing outcomes from RNA sequence is a major goal of current research. Directly related to this, transcriptome-wide elucidation of RNA–protein interactions through HITSCLIP (high-throughput sequencing of RNA by cross-linking immunoprecipitation)[8] and related techniques has allowed the identification of hundreds of new RNA-binding proteins that may control splicing and other events in RNA regulation. Despite identification, the roles of many of these proteins are still to be elucidated. Have we abandoned our search for mechanisms of RNA regulation in favour of documenting the complexity of the components of the regulatory machinery? A refocusing on mechanisms of gene regulation will bring new discoveries such as the recent finding that splicing factors regulate transcription elongation.

Epi-transcriptome a marker for disease prognosis

Another exciting new field of pre-RNA research is the RNA 'epi transcriptome' and its roles in posttranscriptional regulation in development and disease. RNA can be modified by the addition of over 100 different chemical groups, thus creating an even more complex diversity of epigenetic modification with potentially more functions than that which occurs on DNA. Although such modifications are common on non-coding RNAs such as rRNAs, tRNAs and hnRNAs, RNA modifications are also present on mRNAs, and these could change their coding potential. Although some pre-RNA modifications have been known for decades, such as tRNA pseudo uridylation, the recent explosion in their study has been brought about by the discovery of a number of molecules that can add and remove modifications and, more importantly, decode them into functional messages.

Defects in these pathways lead to loss of embryonic development and differentiation and congenital defects. It is likely that such modifications change the RNA secondary structure and/or impact on RNA–protein interactions and recent data show that they can alter RNA nuclear export, stability and translation. However, further studies are required to fully explore this exciting new area of RNA research.

Conclusion

The hnRNA research is still need extensive analysis so that hn-RNA molecule can be used in curing and therapeutic approach of several diseases associated with protein translation and defects.

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