An Overview of PseudoUridine Modification in RNAs

It is an efficient way to regulate molecular function by applying specific chemical modifications on biological molecules. This article highlights the current heated pseudoUridine modification in RNA, which suggests new possibilities for novel drug or vaccine discovery.

An Introduction to PseudoUridines

PseudoUridine (Ψ) is a post-transcriptional RNA modification that alters RNA-RNA and RNA-protein interactions and affects gene expression. PseudoUridine modification is also named "fifth base" since it is the earliest and most abundant RNA modification among the 170+ types of known RNA modifications.

Messenger RNA pseudouridylation was recently discovered as a widespread and conserved phenomenon, but the mechanisms responsible for selective and regulated pseudouridylation of specific sequences within mRNAs still remain unknown.

A recent influx of information about Ψ is providing structural insights and new experimental tools as well as helpful data about the intriguing pattern of occurrence of Ψ in various RNA species (tRNA, rRNA, snRNA, snoRNA, *etc.*). The unusual mode of selection of U residues for conversion to Ψ, and, most importantly, possible biological roles of Ψ in RNA are being explored more thoroughly.

Distribution and Localization of PseudoUridines in Different Classes of RNA

Transfer RNAs

Ψ is found in almost all tRNAs, notably as the universal Ψ55, after which the TΨC stem-loop is named. Other locations at which Ψ occurs in all three domains of life (archaebacteria, eubacteria, and eukaryotes) as well as in organelles (mitochondria and chloroplasts) include the D stem and the anticodon stem and loop.

Ψ greatly contributes to the stabilization of the specific structural motifs in which it occurs: for example, the TΨC loop, the D stem, the anticodon stem, and the anticodon loop.

Small Nuclear and Nucleolar RNAs

In eukaryotes, Ψ is found in the major spliceosomal snRNAs and in the minor vertebrate variants responsible for AU/AC intron splicing. These Ψ residues are often phylogenetically conserved but with organism- or taxa-specific variations; nearly all are located in functionally important regions that participate in the intermolecular RN-RNA or RNA-protein interactions involved in the assembly and functioning of the spliceosome.

Ribosomal RNAs

PseudoUridine modifications in rRNA are frequently found in the large and small subunits of rRNA, and are mainly distributed in some functionally important regions, such as the peptidyl transferase center (PTC), decoding center, and A-site finger region (ASF). It may exert effects on the folding of rRNA, the assembly of ribosomes, and the maintenance of the corresponding high-level structure.

Messenger RNAs

As revealed by massive studies, pseudouracilylation of mRNA has three main functions: changing codons, enhancing transcript stability, and stress response. Catalyzed by pseudouracil synthases (PUS), mRNA pseudouracil modification can change the chemical structure of uracil nucleotides (U) to form pseudouracil nucleotides. Researchers have also verified that the injection of *in vitro* transcribed mRNA containing pseudoUridine modification is more likely to see increased translation rate and stability, bringing great breakthroughs in mRNA therapy and vaccine development.

Although pseudoUridine is the first modified nucleoside discovered in RNAs, and is the most abundant, its biosynthesis and biological roles have remained poorly understood. Therefore, much work has to be done for further exploration of its properties, functions, and applications.