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Introduction

Some of the base, sugar, and phosphate moieties in cellular ribonucleic acids are selectively modified in many instances. These posttranscriptional modifications in nucleic acids have important functions, such as increasing specificity, altering the ability of nucleic acids to base pair, affecting binding of proteins like transcription factors to DNA and thus regulating gene expression, etc. Transfer RNAs have been studied extensively for the function of posttranscriptional modifications. In addition to tRNAs, ribosomal RNAs, messenger RNAs, as well as small RNAs contain posttranscriptional modifications; over 90 different modifications have been identified in different RNAs (3). The fact that approximately 1% of the *E. coli* genome corresponds to the tRNA modifying enzymes and that these genes are retained through evolution would suggest that these modifications are functionally important [reviewed in Bjork et al. (1)]. In one instance, the gene for a tRNA modifying enzyme was shown to be essential for viability. This study showed that the methyluridine found in the conserved TΨC loop of the transfer RNA serves an essential function (6). Although no clear functional role has been suggested for any of the modified nucleotides in rRNA, their importance is evident by models of the *E. coli* ribosome in which the modifications are clustered around the mRNA–tRNA–peptide complex at the catalytic center of the ribosome (2). These suggestions are more relevant in light of Noller's observation that peptidyl transferase activity is unusually resistant to protein extraction procedures, consistent with the hypothesis that rRNA itself is the catalytically active component of the ribosome (5). In one instance, the gene that is responsible for a ribose methylation at a universally conserved nucleotide in peptidyl transfer center of the ribosomal RNA was found to be essential for cell growth (7). These data show that modified nucleotides play important, and some times essential, roles in the rRNA function. While most cellular RNAs contain modified nucleotides, 5S ribosomal RNA from most species does not contain any modified nucleotides. During the last 20 years, there has been a rapid and exciting progress in elucidating the roles of small nuclear RNAs and small nucleolar RNAs (4,8,9). This special issue focuses on the biosynthesis and posttranscriptional processing and modification reactions that occur in small RNAs.

The article by Tschudi and Ullu focuses on the spliced leader RNA and spliceosomal small RNAs with particular emphasis on the mechanism of transcription and cap formation. The splice leader RNA with its unique cap 4 structure provides the 5′ end of all trypanosomal mRNA by *trans*-splicing. In the case of most eukaryotes, the spliceosomal small RNAs are transcribed by RNA polymerase II and the 5′ cap structure is coupled to transcription. The trimethylguanosine cap-containing spliceosomal RNAs of trypanosomes are an unusual example among eukaryotic small RNAs in that they are transcribed by RNA polymerase III. This implies the existence of a distinctive mechanism for capping enzyme selection by the transcriptional machinery.

Elegant work has demonstrated that many snoRNAs guide modification of pre-ribosomal RNAs by base pairing near target sites. Recent discovery that homologs of snoRNAs and associated proteins exist in the domain Archaea indicates that the RNA-guided RNA modification system is of ancient evolutionary origin. Terns' lab, which has been active in understanding the structure and biogenesis of snoRNPs, reviews the multiple mechanisms involved in the synthesis of snoRNAs and discusses in detail the structure and functions of snoRNPs.

All RNA molecules when initiated by an RNA polymerase use a nucleotide 5′ triphosphate as the initiating nucleotide. In some cases like in eukaryotic mRNAs, this 5′ triphosphate of the initiation nucleotide is modified resulting in a cap structure; however, in some cases it is not modified. Richard Maraia's lab showed for the first time that the 5′ triphosphate moiety of the tRNA precursor has a functional role in the processing of rRNAs. The review by Maraia and Intine focuses on the role of La protein in the biogenesis of RNAs transcribed by RNA polymerase III.

While small RNAs may be synthesized by different RNA polymerases, the 3′ end formation is an important metabolic step in small RNA biogenesis. Research work carried out in our lab and many other labs on the 3′ end formation and maintenance of RNA 3′ ends is reviewed by Perumal and Reddy. Generation of the mature 3′ end appears to be very critical because multiple redundant pathways exist in a cell to ensure the process. The correct 3′ end formation has been shown to be important in localization and function of many RNAs, like in nuclear import

for the snRNAs and in base pairing with cognate mRNA for the gRNAs. However, the primary role of the 3′ end sequence of small RNAs appears to be in the maintenance of the integrity of the RNA. Stem–loop structures and long homopolymeric tails are hindrances to the 3′ exonucleolytic complexes. The 3′ ends of RNAs could be protected by their inclusion in ribonucleoproteins. Synthetic reactions like uridylation and adenylation could serve as repair processes to regenerate the 3′ end. Because small RNAs are essential components for many pathways inside the cell, future challenges lie in understanding not only the 3′ end formation mechanisms but also the 3′ end maintenance mechanisms in these RNAs.

Finally, a review by Ravinder Singh looks at the alternate splicing in vertebrates. Alternate splicing generates an enormous repertoire of functional diversity by producing multiple mRNAs and proteins from a single gene. Analysis of genome sequences from several organisms suggests that splicing regulation is likely to provide an important source of functional diversity on more complex organisms. While splice site selection itself is a complex process involving many small RNAs and many proteins, alternate splicing in a tissue-specific manner and at appropriate times is even more complex and highly regulated. This review by Dr. Singh focuses on a few examples involving *Drosophila* pre-mRNA splicing in which the molecular and biochemical basis for splice site selection is better understood.

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