

Preface

Henri Grosjean

Naturally occurring RNA always contains numerous biochemically altered nucleotides. They are formed by enzymatic modification of the primary transcripts during the complex RNA maturation process designated *RNA modification*. To date, more than 100 structurally distinguishable modified nucleosides originating from different types of cellular RNAs and from many organisms of the three biological domains (Bacteria, Archaea, and Eukarya) have been identified. Also, an enzymatic process leading to the replacement of one base by another, hence changing the meaning of the genetic information (*RNA editing*), has been observed in most, if not all higher eukaryotic cells (from unicellular protozoa to man). A large number of enzymes catalyzing the formation of these modified nucleosides or converting one canonical base into another at the posttranscriptional level have been studied for many years, but only recently, have systematic and comparative studies begun. However, the functions of individual enzymes and/or the modified/edited nucleosides in RNA have remained largely ignored. The purpose of this book is to provide advanced information on this huge family of RNA modification, including the associated editing machinery, while offering the reader some perspective on the significance of such modifications in *fine-tuning the structure and functions of mature RNA molecules* and hence the ability to influence the efficiency and accuracy of genetic expression.

The first attempt to assemble into one book the most important information related to both modification and editing of RNA was in 1998 (Modification and Editing of RNA, H Grosjean and R Benne, eds, ASM Press, Washington DC, 596 pages, 1998). The objective was mainly to provide information on various types of RNA modification and editing enzymes identified at that time, and to describe the techniques used for their detection. In less than a decade, the information about this large family of enzymes has about doubled and new ideas concerning the role of modified/edited nucleosides have emerged. In the present volume, outstanding scientists who are actively working on RNA modification/editing processes have provided up-to-date information about these intriguing cellular processes that have been generated over the course of millions of years in all living organisms. The goal of this volume is to demonstrate that these so-called '*minor*' nucleosides encountered in RNA are in fact of '*primary*' importance for RNA function at many different levels of cellular metabolism.

The various review chapters in this book are organized in the following manner. After a first general introduction to the problems of RNA modification and editing, two chapters review the biogenesis and functions of modified/edited nucleosides in the anticodon of tRNA and their roles for precise decoding of the genetic information in bacteria, eukaryotes, and in eukaryotic mitochondria. The next chapter describes the tRNA modification enzymes and their physiological roles in budding yeast, and the following one focuses on the biosynthesis, struc-

ture, and function of a well-conserved methyladenosine tRNA derivative in the three Life Domains. The next three reviews deal with the biosynthesis and function of internal adenosine modifications in eukaryotic mRNA, with modifications in snRNA in relation to snRNPs biogenesis and with the role of a conserved pseudouridine on the structure of the spliceosomal pre-mRNA site, respectively. Then follows a chapter describing the discovery, gene organization, protein components, assembly-organization, putative functions and evolutionary aspects of the RNA-guide modification machinery in Eukarya and Archaea. The role of several conserved rRNA modifications in ribosome biogenesis and functioning of cell-specific rRNA methylations in certain bacteria as a cellular self-defense mechanism against drugs and antibiotics are presented in two independent chapters. The next chapter analyzes the role of modified nucleotides in tRNA on recoding mRNA during translation on the ribosome involving frameshift and readthrough stop codons. Two other chapters deal with the problem of understanding the function of adenosine and cytidine deaminases (RNA Editing) acting on mRNA, and also, as in the case of cytidine deaminases, on DNA in mammalian cells. The problem of RNA and DNA modification in the HIV-1 life cycle and of the role of a ribose methylation in a very special tRNA involved in the incorporation of selenocysteine in response to a stop codon during translation in animal cells are treated in the last two chapters.

Topics such as the functional aspects of RNA editing by insertion/deletion of base(s), utilizing different types of enzymatic machinery as those discussed in this volume, are not covered herein, but can be found in a book edited by BL Bass (RNA Editing, *Frontiers in Molecular Biology* series, Oxford University Press, Oxford, 2001, 181 pages) or in an excellent review article by JM Gott and RL Emeson (Functions and mechanisms of RNA Editing, *Annu Rev Genet* 2000, vol 34: 499-531). For those interested in the methods used for detection and evaluating RNA modification and editing, the book recently edited by JM Gott is an excellent source (RNA interference, Editing, and Modification: Methods and Protocols, *Methods in Mol Biol*, 2004, Humana Press, Totowa, New Jersey, vol 265, 435 pages). The reader is also directed to a description of the cytidine deaminases involved in eukaryotic mRNA and DNA modification (Wedekind et al., *Trends in Genetics* 19:207-216, 2003).

Each review has been written and illustrated for being accessible to a large audience of readers, not only specialists in the field, but also for advanced students or researchers who want to learn more about recent progresses in RNA modification and editing. The book is well referenced up to the end of 2004 and should serve as an invaluable reference tool for researchers, teachers, and students alike as well as for planning future research seeking answers to the many questions that remain unsolved.

I would like to thank each author individually for their excellent contributions, and the series editor Stefan Hohmann, for his editorial skills and great assistance, together with the Springer-Verlag editing office during the assembly of this volume. I apologize to the colleagues in Gif-sur-Yvette for any inconvenience that may have arisen from my spending more time in preparing this book than initially anticipated.

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