BOOK REVIEWS

Transfer RNA

tRNA. Structure, Biosynthesis, and Function. DIETER SÖLL and UTTAM L. RAJBHANDARY, Eds. ASM Press, Washington, DC, 1994. ix, 572 pp., illus. $99.

If 40 years of transfer RNA (tRNA) research have taught us anything, it is that this small molecule can play a powerful and complex role in the economy of the cell. Simply put, tRNA makes possible the accurate synthesis of cellular proteins, in conjunction with the ribosome, by mediating the orderly addition of amino acids to growing polypeptide chains in response to genetic instructions encoded in messenger RNA. But the simplicity of this description of tRNA function belies the large number of intermolecular interactions that tRNA must undergo to accomplish its central role in gene expression. At the same time, tRNA has become a paradigm for the study of RNA structure at the level of sequence, secondary structure, and three-dimensional conformation as well as for the investigation of specific RNA-RNA and protein-RNA associations. It is precisely the world of tRNA interactions that the present volume brings into focus through a series of robust and comprehensive reviews that detail the intricate and subtle relationships between tRNA structure and tRNA function.

The life of a tRNA molecule is dominated—and defined—by interactions with a large number of other molecules, mostly but not exclusively proteins. It is in fact likely that tRNAs spend almost all of their time in complexes with one or another cellular component. In their incredible journey these molecules must come in contact with processing nucleases that liberate them from larger precursor transcripts, modifying enzymes that introduce a variety of different base or backbone substituents at specific locations, aminoacyl-tRNA synthetases that ligate them to their cognate amino acids, and elongation factors that transport the aminoacylated tRNAs to their sites of utilization on the ribosome. There, after their anticodons interact with complementary codons in the mRNA, they bind successively to the A, P, and E sites as they deliver their amino acids to the nascent protein chains and exit for recycling. Finally, there are repair enzymes such as nucleotidyl transferase that can restore the universal 3′-CCA sequence and scavenging enzymes such as peptidyl-tRNA hydrolase that release nascent polypeptide chains from peptidyl-tRNA molecules that have been prematurely released from the ribosome. In a few cases, specific synthases even remodel the aminoacyl moiety of aminoacyl-tRNA before it is incorporated into the protein chain.

The principle that ties these phenomena together is tRNA "identity," a theme that pervades nearly all of the chapters of this volume either explicitly or implicitly. Originally, this term was used to denote the "positive" elements of tRNA structure that allow recognition and aminoacylation by cognate aminoacyl-tRNA synthetases together with "negative" elements that prevent aminoacylation by noncognate aminoacyl-tRNA synthetases. The notion of tRNA identity has now become far broader, encompassing various sets of partially overlapping structural determinants that mediate recognition of, discrimination by, and interaction with a number of other macromolecules and macromolecular complexes. Some of these sets distinguish a very small group of tRNAs, such as those that accept one kind of amino acid or contain a very specific base modification, while others delineate much wider tRNA classes. For instance, the features recognized by ribonuclease P, the 5′ processing enzyme, and nucleotidyl transferase, the 3′ repair enzyme, are presumed to be common to all tRNAs. It hardly needs mentioning that such patterning is a remarkable feat for molecules that average only 75 to 85 nucleotides in length and all fit roughly the same three-dimensional mold.

Over 15 years have passed since the varied threads of tRNA research have been woven together in a single work. The earlier efforts, edited by Altman in 1978 and by Schimmel, Söll, and Abelson in 1979, were landmarks in their time. However, the intervening years have seen the introduction of numerous new tools of investigation—genetic, biochemical, and biophysical—and a vast expansion of the structural database. The present volume chronicles the resulting advances in nearly all aspects of tRNA research: biosynthesis and regulation of expression, post-transcriptional cleavage, splicing and modification, structure and coding properties, recognition by aminoacyl-tRNA synthetases, configuration of tRNA-synthetase complexes, and interactions with the protein synthesis apparatus.

In the new telling of the tRNA story old principles are reaffirmed, fresh ones are revealed, and a number of enigmas emerge. A central tenet, that the overall shape of virtually all tRNAs adheres to the familiar L-shaped pattern despite differences in size and secondary structure, receives strong support from many quarters. The canonical three-dimensional structure nonetheless allows sufficient conformational flexibility to satisfy the various functional demands to which tRNA is subject. In addition, the essential role of aminoacylation in maintaining the accuracy of translation is amply confirmed. It is also clear that the interaction of tRNA with the ribosome is complex, involving several binding sites and, in all likelihood, cyclical changes in tRNA conformation. Finally, our faith in the fundamental universality of the genetic code remains unshaken, as the alterations in codon usage found in particular organisms and organelles almost certainly reflect a divergence from the norm occasioned by special evolutionary circumstances.

More recently, it has become apparent that the specificity and accuracy of interaction between mRNA codon and tRNA anticodon depends on numerous factors that transcend the rules of canonical Watson-Crick base pairing. The particular codons that a given tRNA is able to translate, for example, can be restricted or expanded by base modification within or adjacent to the anticodon. This observation provides at least one rationale for the substantial resources cells devote to post-transcriptional alterations of tRNA structure. Moreover, there is good evidence that conformational changes in other parts of the tRNA can modulate its interaction with mRNA. Decoding is influenced as well by the specific mRNA sequence context in which a given codon occurs, by alterations in the ribosomal RNA, and by the special apparatus that promotes the initiation of polypeptide chain synthesis. The past few years have also seen an unprecedented increase in our understanding of the way in which tRNAs interact with their cognate aminoacyl-tRNA synthetases and with elongation factor Tu, owing both to crystallographic studies on the corresponding complexes and to the definition of the features of tRNA architecture that these proteins recognize. The former studies have demonstrated an unanticipated flexibility in tRNA molecules that permits remarkable distortions within the anticodon loop and the 3′ end of the acceptor stem when bound to the enzyme. In addition, the mechanisms that regulate the expression of the aminoacyl-tRNA synthetases have proved to be sur-

prisingly diverse, providing several instructive examples of autogenous control at the translational level. Yet another discovery of note is that ribonuclease P, the enzyme that cleaves the leader sequence from the 5′ end of precursor tRNA, is a ribonucleoprotein and, even more astonishing, that it is the RNA component that is catalytically active, at least in vitro.

Many mysteries about tRNA remain, however, from the extra base pair in the aminoacyl acceptor stem of histidine-specific tRNAs to the oddly truncated tRNA species found in certain mitochondria. In addition, the function of most base modifications outside the anticodon loop is still unknown, although there is evidence that some serve as sensors of environmental stress. It has also been suggested that besides its role in tRNA transport, EFTu—as well as its eukaryotic counterpart eIF-1α—may be in a position to report on the status of the translational machinery to other parts of the cell. One may hope that these and other puzzles will be resolved before the next tRNA book appears.

The present work is well produced, with a pleasing two-column layout, an easy-to-read typeface, abundant illustrations, an adequate index, and a minimum of typographical errors. It will unquestionably become a basic primer in the field of RNA structure and function and will surely find a prominent place on the bookshelves of those who study and teach the molecular biology of tRNA.

Robert A. Zimmermann
Department of Biochemistry and Molecular Biology, University of Massachusetts, Amherst, MA 01003, USA

■

Also Noteworthy

Cephalopod Neurobiology. Neuroscience Studies in Squid, Octopus, and Cuttlefish. N. JOAN ABBOTT, RODDY WILLIAMSON, and LINDA MADDOCK, Eds. Oxford University Press, New York, 1995. xviii, 542 pp., illus. $125 or £70.

Noting that cephalopods are of neurobiological interest both because of their own highly developed (by invertebrate standards) capabilities and because they provide useful preparations for the study of more general processes, the editors describe the present work as "a book to be enjoyed by both vertebrate and invertebrate neuroscientists, and by anyone interested in the basic principles that control neural function." The book attempts no synthesis of cephalopod neurobiology but sets forth 32 papers on specific research topics, including some advances in technique. An

The squid *Loligo pealei* with egg mass. [Steinhart Aquarium; Andrew J. Martinez]

opening group of four papers deals with squid axon structure, biochemistry, and transport, including an account of the cytoskeleton and a discussion of the nervous system of *Loligo pealei* as a model of organelle motility. An ensuing nine papers deal with squid axon ion channels. Three each are then devoted to interactions between squid axons and Schwann cells and the squid giant synapse. Broadening the range of genera considered is a group of three papers on neuromuscular control, with emphasis on the chromatophore system, unique to the Cephalopoda. A group of six papers on the central nervous system includes accounts of diffusion characteristics of extracellular space, electrophysiological recording, cerebrovascular organization and dynamics, the blood-brain barrier, and the two interacting memory systems (visual and touch) that make learning possible. The final four papers in the book take up sensory function—visual pigments and olfactory physiology in squid and muscular function and the organs (statocysts) that facilitate balance and orientation in Cephalopoda generally. The book, which had its origins in a symposium held in Plymouth, England, at an unspecified date, has an international authorship, with contributions from Western Europe, North and South America, and Japan as well as the United Kingdom. Each paper has an abstract, and a subject index is provided.

Katherine Livingston

The Cortical Neuron. MICHAEL J. GUTNICK and ISTVAN MODY, Eds. Oxford University Press, New York, 1995. xvi, 406 pp., illus. $75 or £49.50.

This book is a presentation of state-of-the-art research about neurons and local neuronal circuits in the mammalian cortex. A compilation of 22 chapters by 33 authors that had its origin in a symposium honoring the 60th birthday of David Prince, an early pioneer in the study of cortical neurons as related to epilepsy, it addresses a wide range of topics. A general overview by Prince is followed by sections on cellular and synaptic properties of cortical neurons, neurons in networks, development of cortical neurons, and cortical neurons in disease. Because of Prince's interest in epilepsy this disease is emphasized more than others. One of the striking features of epileptic seizures is that they are sudden and often occur in what would otherwise appear to be normally functioning individuals. During a seizure cortical neurons undergo sudden depolarizations and rapid firings followed by relatively normal modes of activity. In studying cortical neurons in animal models of epilepsy much is therefore learned about normal neurophysiology, and basic research in cortical electrophysiology owes a great deal to this disease. In addition to epilepsy, there are a number of other important themes that permeate the book, including synaptic plasticity, neurotransmitter function, and local circuit inhibition. Gutnick and Crill provide a particularly nice review of the basic electrophysiology of cortical neurons and of the differences between regular spiking, fast spiking, and intrinsic bursting neurons. The chapter by Bush and Sejnowski is noteworthy for its presentation of a scheme for simplifying computer models of single cortical neurons for use in more complex neuronal network models. Overall, the book provides a valuable "snapshot" of various aspects of neuroscience research related to cortical neurons.

Daniel Johnston
Division of Neuroscience, Baylor College of Medicine, Houston, TX 77030, USA

■

Books Received

Aspartic Proteinases. Structure, Function, Biology, and Biomedical Implications. Kenji Takahashi, Ed. Plenum, New York, 1995. xxiv, 629 pp., illus., + plates. $39.50. Advances in Experimental Medicine and Biology, vol. 362. From a conference, Gifu, Japan, Sept. 1993.

At Home in the Universe. The Search for Laws of Self-Organization and Complexity. Stuart Kauffman. Oxford University Press, New York, 1995. xii, 321 pp., illus. $25.

At the Nuclear Crossroads. Choices about Nuclear Weapons and Extension of the Non-Proliferation Treaty. John B. Rhinelander and Adam M. Scheinman, Eds. Lawyers Alliance for World Security, Washington, DC, and University Press of America, Lanham, MD, 1995. xvi, 113 pp., illus. $37.50; paper, $21.50.

Atlas of Human Cross-Sectional Anatomy. With CT and MR Images. Donald R. Cahill, Matthew J. Orland, and Gary M. Miller. 3rd ed. Wiley-Liss, New York, 1995. xii, 312 pp. $159.95.

Atlas of the Human Brainstem. George Paxinos and Xu-Feng Huang. Academic Press, San Diego, 1995. Variously paged. Spiralbound, $99.

Copepoda. Introduction to the Copepoda. B. H. Dussart and D. Defaye. SPB Academic, Amsterdam, 1995. viii, 277 pp., illus. Paper, $69. Guides to the Identification of the Microinvertebrates of the Continental Waters of the World, 7.

The Coronaviridae. Stuart G. Siddell, Ed. Plenum, New York, 1995. xviii, 418 pp., illus. $89.50. Viruses.

Cosmic Questions. Galactic Halos, Cold Dark Mat-