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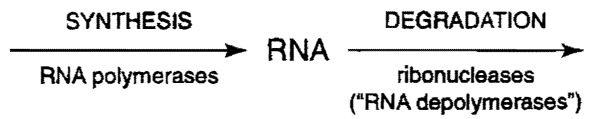
BOOK REVIEW

Ribonucleases: Structures and functions, edited by Giuseppe D'Alessio and James F. Riordan, 1997. New York: Academic Press. 670 pp. $125.00.

Like all biomolecules, RNA is both a product and a substrate. RNA synthesis (that is, transcription) is catalyzed by RNA polymerases in a process that is regulated by elaborate control mechanisms. RNA degradation is catalyzed by ribonucleases, which were known originally as "RNA depolymerases."



Our understanding of ribonucleases is simultaneously more advanced and more primitive than is our knowledge of RNA polymerases. Advanced, because ribonuclease A (RNase A) was one of the first enzymes to be discovered (in 1920), isolated (1938), and crystallized (1939), and has contributed many paradigms to protein science and enzymology. Primitive, because ribonucleases have important and, until recently, unappreciated roles in post-transcriptional control as well as in other biological processes. With this dichotomy of understanding, now is the perfect time to devote a volume solely to ribonucleases. Giuseppe D'Alessio and James F. Riordan have done just that, editing a book of 19 chapters entitled: *Ribonucleases: Structures and Functions.*

The book begins with a discussion of the gallery of *Escherichia coli* ribonucleases. These enzymes provide the best opportunity for understanding how ribonucleases regulate RNA levels by the degradation of RNA. The prevailing question is: how do ribonucleases distinguish between mRNAs destined to have half-lives that range from seconds to days? Exciting progress is being made in answering this question in bacteria (Chapter 1), as well as in yeast (Chapter 18), plants (Chapter 5), and mammals (Chapters 16 and 17). It is noteworthy that Chapter 16 is the first comprehensive review of the fascinating enzyme RNase L, which relies on RNA effectors with $2' \rightarrow 5'$ internucleotide linkages.

Several of the ribonucleases secreted by microbes have been studied in detail. Lacking the complexities imposed by disulfide bonds and *cis* prolyl peptide bonds, barnase has yielded much important information about rudimentary aspects of protein folding. These data and the tight interaction of barnase with its natural inhibitor protein, barstar, provide the gist of Chapter 2. Barnase belongs to the RNase T_1 superfamily of enzymes. Recent advances in the enzymology of this superfamily are presented in Chapter 3. The structures and functions of α-sarcin and the related *Aspergillus* toxins restrictocin and mitogillin are recapped lucidly in Chapter 4.

RNase A has been the most studied enzyme of the 20th century. These studies have generated many paradigms in biochemistry and biophysics. The voluminous amount of information available on RNase A is nicely summarized in the 111 pages of Chapters 9–11, which respectively focus on the biochemistry, X-ray crystallography, and NMR spectroscopy of this venerable enzyme.

The amino acid sequences of RNase A homologs have been obtained from over 40 different vertebrates, and these sequences have been aligned and subjected to parsimony analysis. The resulting phylogeny provides a model system for elaborating the consequences of molecular evolution in vertebrate taxa. For example, putative ancestors of modern pancreatic ribonucleases have been produced to address issues in the evolution of vertebrate physiology. The evolution of the RNase A superfamily is described from different angles in Chapters 7 and 8.

The functions typically ascribed to ribonucleases are to process and turnover cellular RNA, and to degrade dietary RNA. Yet, some ribonucleases appear to have quite different biological roles. For example, ribonucleases can be cytotoxic because cleaving RNA renders its encoded information indecipherable. In 1963, a dimeric homolog of RNase A was discovered in the seminal fluid of bulls. Subsequently, this homolog was shown to be toxic to mammalian cells at low levels. Both the structure and function of this most distinct member of the RNase A superfamily are described with eloquence in Chapter 12. Like bovine seminal ribonuclease, homologs of RNase A from the *Rana* genus of frogs are active antitumor agents. One of these *Rana* ribonucleases, onconase, is now in the midst of a Phase 3 clinical trial. The use of an RNase A homolog as a cancer therapeutic is a wonderful story, which is told in Chapter 15. Finally, the state of research on S-RNases, which somehow prevent a plant from fertilizing its own flowers, is rendered in Chapter 6.

Five homologs of RNase A have been identified in humans. Three of these homologs have unusual properties. Angiogenin is a plasma enzyme that promotes neo-vascularization. Eosinophilic leukocytes contain eosinophil-derived neurotoxin (EDN), which is neurotoxic, and eosinophil cationic protein (ECP), which has helminthotoxic and anti-bacterial activities. The biochemical basis for these complex biological effects is unclear. Current knowledge on the eosinophilic ribonucleases and angiogenin is described in Chapters 13 and 14, respectively. This area is destined to be one of the most exciting in ribonuclease research.

The book ends with a review of the ribonuclease inhibitor (RI) protein, which forms a tight complex with RNase A and other pancreatic ribonucleases. An analogy to the barnase·barstar complex is useful. Barnase and RNase A are secreted enzymes, but barstar and RI are cytosolic proteins. Both complexes have K_d values near 10^{-14} M, and known three-dimensional structures. Both complexes could serve their host organisms by regulating adventitious ribonucleolytic activity. Indeed, the production of barnase is toxic to a bacterial cell unless barstar is present. The anal-

ogous and more challenging experiment has not yet been done with RNase A and RI. Current knowledge of the biochemistry and physiology of RI is provided in Chapter 19.

This book is attractive. The printing is clear, and illustrations are of high quality. Seven pages have superb color figures. Each chapter ends with references (through 1996) that include titles, and the book ends with a comprehensive index. The editors keep the presentation uniform, with only insignificant glitches.

The chapters of this book were written by an impressive international field of ribonuclease experts. Accordingly, this book is extremely comprehensive. I can detect only a few gaps in the coverage. For instance, little information is provided on the folding and stability of RNase T_1 and its homologs. Also absent is mention of the biotechnological applications of ribonucleases, such as in the ribonuclease protection assay and in the control of gene expression by RNase H and antisense nucleic acids. An update on RNase S, which is the noncovalent complex between the S-protein and S-peptide fragments of RNase A, could have been interesting. Ribozymes are beyond the scope of this book.

Ribonucleases: Structures and Functions would be an extremely valuable addition to the personal library of anyone doing research on any ribonuclease. Moreover, because the influence of ribonuclease research is so extensive, this book would also be a useful resource to many who work on protein folding, protein structure, enzymology, protein–RNA interactions, or the post-translational control of gene expression. In addition, this book would be a most appropriate acquisition for a campus library. Although I am surprised that a volume devoted to ribonucleases did not appear sooner, I am delighted that such a splendid one is available now.

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