Preface

Ribonucleases continue to attract much interest and investigation in the basic and translational science arenas. Our present understanding of ribonuclease structures, mechanisms, and functions emerged from a myriad of pioneering investigations that employed (as well as led to the development of) diverse experimental approaches. These studies have shed light on the fundamental aspects of biological catalysis and protein folding and ribonuclease function in post-transcriptional regulatory pathways. Indeed, multiple volumes would be needed to provide a comprehensive coverage of ribonucleases. It is instead the intent of this single volume to present a focused collection of reviews on the major groups of ribonucleases, and how their structures and mechanisms relate to biological function. The first three chapters by D'Alessio, Rosenberg, Vilanova, and coauthors focus on the fascinating family of vertebrate secreted ribonucleases, within which pancreatic ribonuclease A has served as the founding member. The extraordinary functional and evolutionary diversity of these enzymes is discussed along with their promise as anticancer agents. The chapters contributed by MacIntosh, Ivanov, Anderson, Meyers, and coauthors focus on the ribonuclease T2 family enzymes. Here, only recently has there been an appreciation gained of the central involvement of T2 family members in stress responses, host defense, and strategies of viral infection. The chapter by Tong and coauthors examines the structures and functions of 5′–3′ exoribonucleases, and the chapter by Arraiano and coauthors provides a comprehensive review of the diverse group of 3′–5′ exoribonucleases. The multisubunit RNA exosome, with its 3′–5′ exonuclease (and endonuclease) activity, is examined by Hopfner and Hartung, with a special focus on how specificity and regulation can be achieved in an otherwise nonselective manner of RNA breakdown. Condon and Gilet address the mechanistically and functionally intriguing metallo-β-lactamase family enzymes and their roles in processing tRNAs, mRNAs, and snRNAs. The structure, mechanism, and diverse functions of the double-strand-specific ribonuclease III is reviewed by Nicholson, and Hollis and Shaban next discuss the structures and functions of the ribonucleases H that cleave the RNA strand in RNA–DNA duplexes. Krasilnikov provides an in-depth examination of

the ribonucleoprotein ribonucleases P and MRP, their central cellular roles in tRNA and rRNA processing, and the functions of the RNA and protein subunits in the catalytic mechanism. The chapter by Lönnberg addresses the inherent reactivity of RNA toward metal ions, and summarizes studies of small molecule ribonuclease mimics that exhibit diverse structures. Finally, Scheraga reviews pioneering experimental studies on protein folding that have employed pancreatic ribonuclease A as the primary model. What is evident from these chapters is the integral involvement of ribonucleases in a broad array of physiological processes, and that the simple act of cutting an RNA molecule, either internally or by removal of one or more nucleotides from either end, has profound effects on cell phenotype. Finally, detailed knowledge of ribonuclease structure, catalytic mechanism, and interacting partners are spurring new approaches to the treatment of disease. It is hoped that this volume will inform and stimulate further investigations of ribonucleases and their involvement in cellular pathways.

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