Methods in ENZYMOLOGY

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tRNA-DERIVED RNAs

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METHODS IN ENZYMOLOGY

TRNA-derived RNAs

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Preface

In the 1950s, transfer RNAs (tRNAs) have emerged as a central class of RNA molecules playing key roles in protein synthesis. tRNAs are best known as adaptor molecules helping to decode the genetic information of mRNA triplet codons by the ribosome and delivering amino acids to the extending polypeptide chain during mRNA translation. Historically, tRNAs were among the first recognized noncoding RNA (ncRNA) playing fundamental roles in RNA metabolism. Although mainly recognized for their role in protein biosynthesis, tRNAs have also emerged on the stage of RNA biology in the last ~15 years as a rich source for small ncRNA processing products, named tRNA-derived RNAs (tDRs).

In the 1970s, tRNA breakdown products were detected in urine and serum of cancer patients. These fragments were considered as simple degradation byproducts with no biological function that are formed naturally during the tRNA lifecycle, and were considered valuable cancer biomarkers. Fortunately, with the availability of high-throughput RNA sequencing approaches, tDRs were frequently detected in small ncRNA sequencing projects focused on e.g. microRNA profiling. It became clear that tDRs are produced from both precursor and mature tRNAs by enzyme-mediated cleavage at specific sites of the RNA molecules, mainly in the loop regions. Consequently, tDRs can be further classified into more narrow subcategories based on the cleavage sites that produce tDR molecules containing either the 5′, the 3′, or internal regions of pre-tRNAs/tRNAs. Due to dedicated research in various model organisms spanning all three domains of life, it was demonstrated that some of the identified tDRs possess physiological, mainly regulatory, functions and can thus be considered genuine ncRNA riboregulators. What is intriguing is that all these heterogeneous tDRs are implicated in various biological processes, and the list of their potential functions and their modes of action continued to grow in the past years. Even more importantly, connections between human disease and tDR (mis) regulation have emerged, which warrants further studies of the molecular mechanisms underlying tDR functions and their potential therapeutic use. Thus it can be concluded that a growing fraction of the initially considered meaningless tRNA-derived fragments possess physiological roles in cell biology, likely in all kingdoms of life.

The research on tDRs is still in its infancy. There are obvious gaps in our understanding about biogenesis of tDRs, the interacting proteins, and

their biological functions in different domains of life. The understanding that tDR production is tightly regulated and is conserved throughout evolution has triggered multiple laboratories worldwide to uncover their functional roles in cellular physiology. In turn, such interest has created a strong demand in developing experimental tools and novel approaches to study their biogenesis, chemical composition, structure and dynamics, interaction with proteins, and biological functions. In this volume of *Methods in Enzymology*, we assembled 21 chapters that cover a broad range of experimental concepts and biocomputational tools for gaining insight into the multifaceted biology of tDRs in bacteria, mitochondria, plants, single cellular eukaryotes, and mammalian cells. These chapters describe in details essential tools and methods to characterize and investigate this versatile class of ncRNA molecules.

We are thankful for the phenomenal positive responses from the contributors of this volume whose strict adherence to the deadlines and the uniformly high quality of the submitted material allowed us to edit this book series in an adequate timeframe. We also thank Elsevier's editorial and production stuff for the help in the preparation of this volume. We hope that this volume will stimulate future studies on the manifold roles of tDRs in different biological contexts, as it did for both of us.

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