

Preface

Ribonucleic acid (RNA) binding proteins currently number in the thousands, and defects in their function are at the heart of diseases such as cancer and neurodegeneration. RNA-binding proteins have become implicated in the intricate control of surprisingly diverse biological settings, such as circadian rhythm, stem cell self-renewal, oncogenesis, and germ cell development.

RNA-binding proteins bind to diverse RNA substrates to mediate aspects of the life cycle of RNA processing, including alternative splicing, stability, export, transport, and translation, as well as the assembly and disassembly of RNA granules. Understanding the roles of RNA-binding proteins requires multidisciplinary approaches: characterization of their targets, single-molecule approaches to unveiling their modes of interaction, and computational considerations of the tremendous amounts of data associated with analysis of their activities.

Given the success of the volume *Systems Biology of RNA Binding Proteins*, I have assembled this second volume with chapters focused on cutting-edge methods to study aspects of RNA-binding protein-RNA function that were not previously covered and introduce the most recent exciting biology related to RNA-binding proteins.

The content of this book surveys a range of genome-wide and systems approaches to studying RNA-binding proteins and the importance of RNA-binding proteins in development, cancer, and circadian rhythm. These chapters provide opportunities for open questions and new areas of inquiry into posttranscriptional processing.

With the combination of high-throughput short-read sequencing with biochemical methods such as RNA immunoprecipitation and RNA cross-linking and immunoprecipitation, transcriptome-wide maps of sites of interaction between RNA-binding proteins and their RNA targets have proved useful in elucidating novel molecular and cellular functions of RNA-binding proteins. Eric Van Nostrand and Stephanie Huelga in my laboratory discuss challenges associated with large-scale identification and analysis of RNA-binding protein-RNA interactions.

RNA does not exist as simple linear sequences in vivo. Gregory and colleagues present a review of genome-wide approaches to determining RNA structure in the

transcriptome. RNA structure discovery is a fundamentally important aspect of understanding the protein-RNA landscape.

With the increasing number of proteins thought to have RNA-binding capacity, Tomas Bos, Julia Nussbacher, and Stefan Aigner in my laboratory review how tethered function assays can be utilized to reveal novel molecular functions of candidate RNA-binding proteins.

To truly understand the stepwise interactions of proteins onto RNA substrates, Moore and Serebrov discuss single-molecule approaches that shed light on deep mechanistic insights into interrogating RNA-binding protein function.

The following chapters deal with exciting areas in biology that have become entwined with RNA-binding proteins.

Circadian control has recently become associated with posttranscriptional control of gene expression. Panda and colleagues recount circadian control of RNA by RNA-binding proteins.

Posttranscriptional and translation regulation is particularly important in germ cell biology. Licatalosi summarizes the role of RNA-binding proteins in male germ cell development.

Ito and colleagues present the importance of RNA-binding proteins in stem cell biology and oncogenesis. Self-renewal of stem cells is key to our understanding of development and cancer. How RNA-binding proteins control stem cell fate and oncogenesis is a topic of hot debate.

Hundley and Washburn feature the roles of RNA-binding proteins in RNA editing. Uncovering how enzymes affect RNA editing is critically important in our dissection of human diseases. It is still unknown how many and which RNA-binding proteins can regulate A-to-I editing *in vivo*.

Bejar clarifies the recent findings that splicing factors are commonly mutated in cancer. Recurrent somatic mutations of genes encoding core subunits of the spliceosome have been identified in several different cancer types and will be discussed in this review, avenues for novel cancer therapeutic strategies.

Calarco and colleagues discuss how tissue-specific alternative splicing is controlled and the utility of the model organism *C. elegans* in aiding in its elucidation.

Leung and Fan present exciting findings of the roles of RNA-binding proteins in RNA granules, particularly in neurodegenerative diseases such as ALS and FTLT.

Massirer and colleagues emphasize the importance of posttranslational modifications on RNA-binding proteins, an area poorly understood but with tremendous potential for understanding diseases such as neurodegeneration.

The contributors of this book are internationally recognized leaders in the arena of technology development, RNA processing, and biology relevant to RNA-binding proteins, and we envision that this book will serve as a valuable resource for both experts and nonexperts. Advanced undergraduate students and entering graduate students in biology, chemistry, molecular engineering, computer science, and bioinformatics, as well as medical students and postdoctoral fellows who are new to the arena of posttranscriptional gene regulation, should find this book accessible. We hope the chapters in this volume will stimulate interest and appreciation of the complexity and importance of posttranscriptional gene regulation to its readers and

even lead them to pose new solutions to the enormous challenges that lie ahead in comprehending how RNA-binding proteins affect gene regulation.

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