
Preface

The year 2017 is the 40th anniversary of the landmark discovery of splicing by the laboratories of Richard J. Roberts and Phillip A. Sharp. At the time, it was unclear whether splicing was a rare event or a common phenomenon. With the completion of the Human Genome Project, we now know that splicing is a nearly universal mechanism for human mRNA maturation. More importantly, the great majority of human genes produce multiple mRNA isoforms through alternative mRNA processing, including alternative splicing and alternative polyadenylation. These alternative mRNA processing events are highly regulated in a tissue- and/or developmental stage-dependent manner. Aberrant regulation of mRNA processing has been causally linked to or implicated in many human diseases. Forty years of basic research into mRNA processing have culminated in another landmark event: the first antisense oligo that alters the splicing pattern of a human gene has been granted accelerated approval by the Food and Drug Administration for treating spinal muscular atrophy!

It is an exciting time to be studying mRNA processing. The vast majority of alternative mRNA processing events has remained an unexplored territory. The recent discovery of circular RNAs generated by “back-splicing” revealed a whole new type of mRNA processing. New technologies are being developed at a breathtaking rate that provides us with a broader and deeper view of the world of mRNA processing. For example, high-throughput sequencing methods provide an unbiased picture of mRNA processing of any biological samples under any condition. Metabolic labeling coupled with high-throughput sequencing can trace the life of all mRNAs, from synthesis, processing to degradation. For any specific mRNA processing event, high-throughput screens can be employed to sift through the entire genome to look for regulators. For any specific regulator that binds to RNA, we can map all of its RNA interactions in vivo in one experiment. Bioinformatic tools not only help reveal global trends and regulatory mechanisms but also predict mRNA processing alterations under different conditions. In addition to these tools for global analyses, the “old school” in vitro assays have also been developed for in-depth analyses of individual mRNA processing events. Innovative methods have been developed for purifying mRNA processing complexes that are suitable for functional and structural studies. Single particle methods enable us to follow individual mRNA processing reactions in real time. With such a wide range of available methodologies, it can be a daunting task for scientists in the mRNA processing field to pick and choose a method that is most suitable to their specific problems. In this volume, we have assembled a series of the most commonly used and state-of-the-art methodologies in the field of mRNA processing. It is our hope that these protocols will be helpful for researchers to explore the wonderful world of mRNA processing.

With all of these exciting new developments, I believe that the mRNA processing field is poised to enter an explosive growth period. If the past 40 years is any indication, the best is yet to come! Good luck with your experiments!

Irvine, CA, USA

Yongsheng Shi

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