Molecules and Cells

Editorial

RNA in Biology and Therapeutics

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When the central dogma of molecular biology was proposed over 60 years ago, mRNA was postulated as a transient messenger or an unstable intermediate, carrying information to ribosomes for protein synthesis (Brenner et al., 1961; Crick, 1958; Gros et al., 1961). As investigations on gene expression advanced, the importance of post-transcriptional regulation, the evidences of RNA world and the centrality of RNA have been greatly appreciated (Gilbert, 1986; Sharp, 2009). Accordingly, a mechanistic understanding of RNA metabolism offers new insights on RNA-based technologies and therapeutics (Damase et al., 2021). Specific genes are targeted by guide RNAs (gRNAs) in the CRISPR-Cas genome editing platform, while mRNA expression is modulated by antisense oligonucleotides (ASOs) and RNA interference (RNAi) technologies. These loss-of-function approaches specifically target pathogenic gene expression in diseases and are evolving as promising therapeutics. Similarly, a gain-of-function approach has become an attractive therapeutic modality, remarkably illustrated by the efficacious mRNA vaccine technology introduced during the coronavirus disease 2019 (COVID-19) pandemic. In this special issue on "RNA in biology and therapeutics", we describe how basic concepts of RNA biology are transformed into novel therapeutics (Fig. 1).

In the first article, Dana Carroll (University of Utah) reviews general principles of the CRISPR-Cas genome editing platform and recent advances in base-editing technology. Clinical applications of CRISPR-Cas technology are well summarized, and additional issues around CRISPR-based therapies are also discussed; some of the latter may also apply to other RNA-based therapeutic applications.

Second, Young Jin Kim and Adrian R. Krainer (Cold Spring Harbor Laboratory) introduce ASO technology and elucidate how a deeper understanding of post-transcriptional regulation led to the approval of several ASO drugs. The authors focus on ASO therapies for Cystic Fibrosis which has a significant unmet need for addressing a wide range of disease-causing mutations.

Next, Hyeonseo Hwang et al. (Daehuyn Baek's lab at Seoul National University) review the principles of microRNA (miRNA) targeting and previously utilized determinants for miRNA target prediction. In addition to conventional computational predictions of miRNA target sites, the authors propose novel methods that have not been employed in computational models.

Mingyu Ju et al. (Jinju Han's lab at Korea Advanced Institute for Science and Technology) introduce highly stable circular RNAs as emerging candidates for therapeutics, particularly in mRNA vaccines. The authors start with how endogenous circular RNAs are generated and how they function in gene regulatory networks, then discuss their potential as biomarkers and therapeutic molecules.

Sora Son and Kyuri Lee (Gyeongsang National University) review the recently approved mRNA vaccine platform technology against COVID-19. They describe the principles and technology of mRNA vaccines and provide updates on current clinical trials for other infectious diseases. The basic concepts of RNA delivery methods, such as lipid nanoparticles, are also discussed.

Dawon Hong and Sunjoo Jeong (Dankook University) then introduce emerging issues in the diversity of 3′ untranslat-

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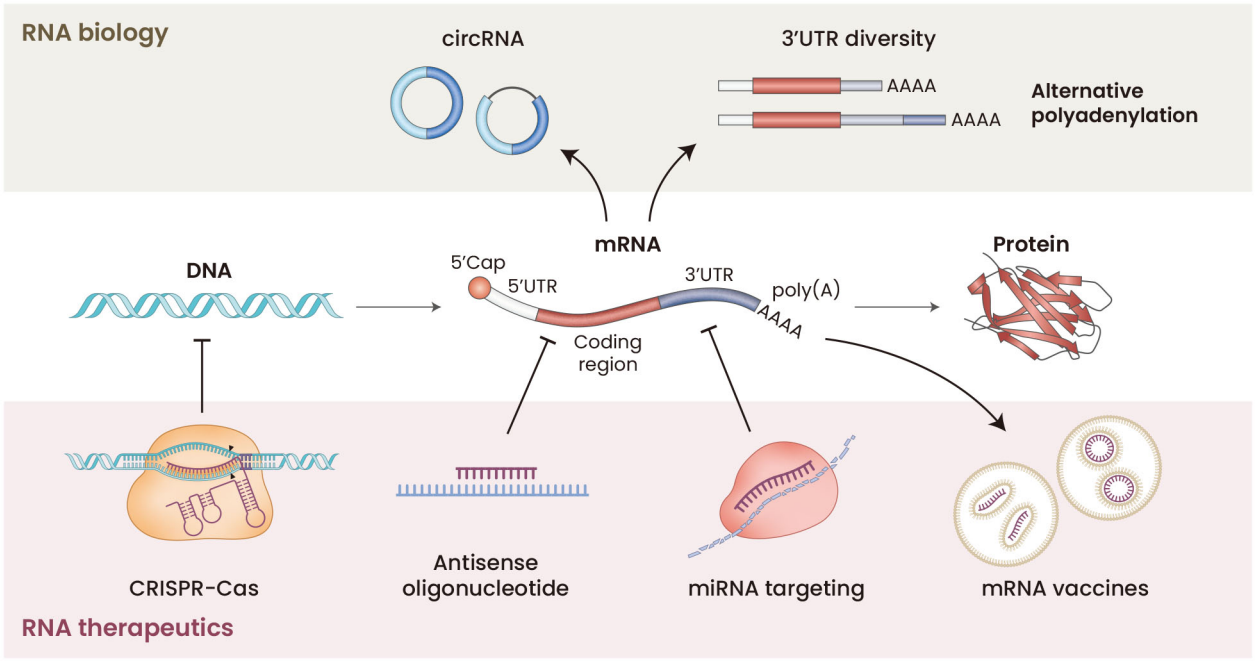

Fig. 1. Summary of the special issues on RNA in biology and therapeutics.

ed regions (3′UTRs) in human mRNA. The authors review the functions, regulation, and biogenesis of dynamic 3′UTR length control and the relevance of 3′UTR diversity to frequent RNA alterations in human cancers.

Finally, Yajing Hao et al. (Xiang-Dong Fu's lab at University of California San Diego) describe the process of 3′ end formation in mRNA and discuss the widespread occurrence of alternative polyadenylation (APA) in higher eukaryotes. Mechanistic details of polyadenylation are also described, and a new model involving post-transcriptional sequential APA is proposed.

The seven reviews in this special issue illuminate how basic RNA biology has contributed remarkably to the development of current RNA-based technologies. With the explosion of RNA data on pathogenic processes, a profound understanding of RNA biology is essential to target and exploit RNAs as novel diagnostics and therapeutics (Huang et al., 2022). Thus, an appreciation of the mRNA is far beyond its original vision in the central dogma and has ushered us to the new and exciting era of "RNA medicine".

CONFLICT OF INTEREST

The author has no potential conflicts of interest to disclose.

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