The evolving saga of RNAs from bench to bedside

RNAs were initially described to have critical roles in the central dogma of molecular biology long time ago, which were represented by messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA). Gradually, more forms of RNAs have been discovered, such as those involved in the RNA interference (RNAi) pathways that include the exogenous small interfering RNAs (siRNAs) and short-hairpin RNAs (shRNAs), and the endogenous non-coding RNAs [ncRNAs, including microRNAs (miRNAs), small nuclear RNA (snRNA), small nucleolar RNAs (snoRNAs), long noncoding RNAs (lncRNAs), etc.]. RNAi has been utilized for functional genomics studies, where gene-specific RNA sequences are introduced into cells to knockdown gene functions, providing the mechanistic bases for their clinical application.

Thereafter, antisense RNA-based, RNAi-based, and RNA aptamer-based drugs, as well as mRNA-based vaccines have been developed and approved for clinical use, especially against various previously incurable diseases, and in global emergencies like the COVID-19 pandemic. At the same time, with the development of techniques and a deeper understanding of their conserved endogenous activity, various forms of RNAs have been extensively sequenced and analyzed to identify RNAs involved in a given pathway, which help in the diagnosis, treatment, and prognosis prediction of various diseases.

Although the presence/absence or the levels of ncRNAs reflect the disease stages, and siRNAs designed with perfect complementary sequences can effectively bring down target mRNAs, there are still various off-target effects during the application of siRNA. Furthermore, due to the reduction in cost and advancement in sequencing and analysis technologies, the number of newly discovered ncRNAs have been soaring exponentially. In addition, the network of RNAs is more than being a simple loop, but with different levels of feedback and compensation mechanisms that could lead to butterfly effects. Last but not least, the long-term clinical effects of RNA therapy are yet to be investigated.

The purpose of this special issue is to update the comprehensive roles of RNAs in the diagnosis, prophylaxis, treatment, prognosis prediction, and drug resistance of clinical cases using basic, bioinformatics, translational, pharmacological, and clinical experimental methods. This special issue welcomes Original Research and Review manuscripts focused on:

• RNA methodologies in laboratory analysis, bioinformatics, design, produce, discover, and delivery of different types of RNAs in cells, organs or whole organisms with minimal off-target effects

• Specific RNAs identified by high-throughput next generation techniques in case-control studies as causative or modifiers of human diseases that may serve as therapeutic targets

• Animal experimental studies that confirm specific RNAs involvement in inflammatory response, infectious diseases, cancer, genetic, metabolic, neurological, or chronic diseases

• RNA designed for therapeutic interventions against specific targets in experimental and clinical use
• Specific types of RNA sets as unique biomarkers, independent predictors or prognostic factors of human diseases development

Keywords: RNA interference; Diagnosis; RNA therapy; RNA vaccine; antisense RNA

Lead Guest Editor:
Zhongjie Shi, MD, PhD,
Wayne State University, Detroit, USA,
zshi@med.wayne.edu

Guest editor
Ioannis Kosmas, MD, PhD, University of Ioannina, Ioannina, Greece,
kosmasioannis@gmail.com

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