Editing the flow of information

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The central dogma of molecular biology states that genetic information stored in DNA is transcribed and subsequently translated into proteins. The information should thereby be copied from DNA into RNA without changes to the information.1 The relatively constant number of genes among eukaryotes of different complexity has, however, challenged this concept of a rigid flow of information. For quite some time now alternative splicing and post-translational protein modifications have been recognized as means to diversify genetic information and protein function, thereby contributing to cellular and organismic complexity. The recognition of RNA editing as a major player in the alteration of genetic information has only occurred in recent years.

First discovered more than 25 y ago, RNA-editing has long been believed to be an oddity of nature restricted to biological niches such as trypanosome mitochondria or plant organelles. Even when RNA-editing was discovered in metazoan nuclear RNA in the late '80s and early '90s it was still believed to be a rare event.2,3 Only with the onset of powerful bioinformatics combined with next generation RNA sequencing the full extent of RNA editing was recognized.4-6 Today, in the human transcriptome hundreds of thousands of editing combination are detected, leading to a transcriptome variability that may reach similar levels or even outnumber that generated by alternative splicing. The large number of detected editing events makes a prediction of their functional consequences virtually impossible.

As different as the organisms in which RNA editing has been detected are the underlying machineries. Two basic types of RNA-editing can be distinguished. On the one hand, nucleotide conversion is achieved by deaminating cytosines or adenosines to generate uridines or inosines, respectively. On the other hand, nucleotide insertion and deletion events are the predominant type of RNA-editing found in organellar RNA.

Also, depending on the organism, the machineries involved in RNA-editing are sometimes known in much detail, while in other cases only candidate genes have been identified.

Besides the study of the machineries involved, their spatio-temporal regulation, their specific targeting, and the consequences of editing pose obvious open questions.

The current book on RNA editing covers several aspects of RNA editing in 10 chapters. Overall, the book has a clear emphasis on adenosine-deamination type editing mediated by ADARs. Five chapters deal with this type of RNA editing in one way or another. Here, the impact of adenosine deamination on both coding and non-coding transcripts, the interaction with the immune system, but also the detection of edited nucleotides, are the focus of several chapters. The focus on adenosine deamination type editing certainly reflects recent progress but also controversies in the study of adenosine deamination-type editing.

The book does a very good job in summarizing controversial findings such as those on the potential impact of inosines found in RNAs: inosine containing RNAs have been shown to be specifically degraded,7,8 can be nuclear retained,9,10 can be impaired in their association with ribosomes,11,12 and may finally antagonize interferon signaling.13 Putting all these aspects nicely together in one chapter clearly illustrates the many loose ends in this exciting story.

A very timely chapter discusses the recent advancement in the detection of editing events using high-throughput technologies. Various approaches to detect editing events at an ever-increasing sensitivity are being discussed. Most importantly, problems that may emerge due to computational mapping errors are put nicely together as a warning against the over-interpretation of deep sequencing data.14

Two chapters are devoted to the complex machineries involved in kinetoplastid mitochondrial RNA-editing. Of all RNA editing types, this U insertion/deletion type editing has been studied the longest.15 The complexes and machineries involved are therefore well studied. However, the interaction of the machineries, their evolutionary origin, and their involvement in other RNA-processing events are still being investigated. Recent findings are discussed as well as new structural data on editing complexes.

tRNAs are a seemingly endless research field for RNA-biologists. Not surprisingly, they are probably the richest source for the study of RNA modification and editing events. A chapter is devoted to the many modifications and editing events found in these small RNAs. Their function and the mystery of the machineries that need to specifically recognize minor differences on different tRNA substrates are showing the limits of today’s understandings.

Recent developments in C to U deamination by APOBECs have shown the existence of multiple cytidine deamination events in 3’ UTRs of several mRNAs.16 This exciting finding, and the cell biological functions of the APOBEC accessory factors are discussed together with APOBECs function(s) as candidate mutators of DNA.

Lastly, a chapter on editing events in the mitochondria of Physarum polycephalum summarizes the existence of at least three distinct editing events in these organelles. Recent progress in
the understanding of the underlying machineries using model-editing substrates are put together.

While the book tries to give a comprehensive view on RNA editing, researchers focusing on green biology may be disappointed. No chapter on RNA editing events in plant organelles can be found.

Also, tremendous progress has been made in targeting genomic editing events to specific sites by using plant and prokaryotic machineries of TALENs and CRISPR.17,18 Excitingly, proof of principle studies have been done for a potentially less harmful “transcriptome cure” by directing RNA modification and editing machineries to specific sites in RNA.19,20 A perspective on these emerging topics might also have been an exciting addition.

Overall, the book gives a nice perspective on RNA editing for those working or teaching in the expanding field of deamination-type editing with a clear focus on mammals. Here, the book will be useful for a wide readership and should be recommended to your librarian. However, the book falls a bit short when it comes to other (vegetarian) types of RNA-editing and therapeutic uses of RNA editing.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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