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RNA Editing: Breaking the Dogma

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The period between 1983 and 1993 is in the history of molecular biology the "Golden Decade of RNA". In those years, four outstanding discoveries were made violating a central dogma of molecular biology. These discoveries implicated ribonucleic acid as the major subject of interest for many researchers in various fields of modern biology. It was discovered that some RNA molecules called ribozymes possess enzymatic activity and catalyze various biochemical reactions [1, 2]; telomerase, and its RNA component was shown to serve as a template for synthesis of telomeric regions in chromosomes [3]; phenomena of RNA editing [4-7] and RNA interference [8-10] were discovered. Three of these four discoveries led to Nobel Prizes.

In 1986 a group of Dutch researchers reported that kinetoplastid mitochondrial mRNA becomes a valid template for protein synthesis only if certain alterations of its coding nucleotide sequence occurs: after the completion of the transcription process, several uridylic acid residues are incorporated into the mRNA molecule [4]. Namely, the text encoded in the kinetoplast DNA becomes meaningful only after RNA editing. At first, the existence of this exotic process seemed to be limited only to *Protozoa*, which also are known to have deviations in the classical genetic code. However, only a year later similar mechanism of mRNA modification was revealed in mammals too [5]. Furthermore, in two years a perfectly different mechanism of RNA editing was discovered: site-specific deamination of adenine residues converting it into inosine (i.e. into a guanine analog) [6]. Within a short time this novel mRNA editing mechanism was demonstrated to be universal for all living beings. Moreover, it was found that non-coding RNA molecules (tRNA and to a lesser extent, rRNA) are also subjected to a similar process of RNA editing [11]. In recent years, the most intense are studies of editing of small RNAs involved in regulation of gene expression at the translational level [12]. Over time, it was also found that specific site-directed deamination in RNA also occurs for C residues, turning them into U. In addition, another type of RNA editing is a site-directed U-to-C conversion [13].

Regarding protozoan mitochondrial mRNAs, it became clear that beyond insertions of U residues, they can also be edited by site-specific deletions of U residues [13].

More than three thousand papers on RNA editing have been published in the last 25 years. They discuss mechanisms of various types of RNA editing, enzymes and protein factors involved in these processes, and the role of small RNA molecules in the determination of mitochondrial mRNA editing sites. They demonstrate on how RNA editing increases the diversity of proteins in the cell, and why the disruption of RNA editing leads to pathology. More than 500 reviews discuss this vast array of data. Nevertheless, the intensity of research in the field is so high that the availability of reviews of recent papers is still necessary.

This issue of *Biochemistry (Moscow)* presents a collection of review articles focused on the phenomenon of RNA editing; they are contributed by leading scientists in the field. The review by Godfried Sie and Kuchka [14] opens the issue summarizing recent advances in A-to-I RNA editing studies. Of particular interest is data compilation for editing of non-coding RNAs: microRNA, long noncoding RNA, and RNA containing Alu-repeats. Reviews by Barbon and Barlati [15] and by Streit and Decher [16] summarize the data on A-to-I editing events in mRNAs of neuronal receptors and channels, which can affect changes in neuronal excitability. Editing of the coding regions of several mRNAs in neurons is a classic example of RNA editing leading to the translation of alternative isoforms of proteins. Moreover, it now becomes clear that disturbance of editing is directly related to the occurrence of severe CNS pathologies [15, 16].

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A review by Wang [17] summarizes a variety of data on one of the proteins catalyzing A-to-I RNA editing (ADAR1), and it concludes that ADAR1 function is crucial for cell survival. This work suggests the availability of a special signaling pathway connected with the RNA editing process, which regulates programmed cell death. Review articles by Iwamoto et al. [18] and Kiran et al. [19] are devoted to the description of experimental methods developed for the detection of RNA editing events, bioinformatic techniques, descriptions of algorithms, as well as available Internet resources.

A special issue on RNA editing would be incomplete without specific mention of RNA editing in plant organelles and editing events in tRNA. A review article by Castandet and Araya [20] summarizes the current state of knowledge on different types of RNA editing in plant organelles. An article by Su and Randau [21] summarizes data on A-to-I and C-to-U editing of tRNA occurring both in prokaryotes and eukaryotes.

Obviously, RNA editing is a fundamental process that occurs in many species of living beings. RNA editing can lead to the appearance of different protein isoforms. Furthermore, it also changes splicing and RNA interference and affects transcript stability and intracellular localization. We are at the beginning stage of our understanding of how RNA editing is involved in a huge complex of processes including gene expression, regulation of intracellular signal transmission, and genome evolution. Despite a huge amount of available information, researchers still have to answer many emerging questions. Inviting the authors of articles for this issue, we pursued the goal of covering the field broadly (a short review article covering this topic has already been published earlier in *Biochemistry (Moscow)* [22]), as well as to raise interest among scientists with different fields of knowledge.

In conclusion, we would like to thank the authors of the current issue, who kindly responded to the invitation to write a review article, and the Editorial Board of *Biochemistry (Moscow)*, who showed interest in this subject and provided assistance in preparation of this issue. We are also grateful to V. P. Skulachev for his interest, helpful advice, and comments.

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