RNA BIOLOGY
2017, VOL. 14, NO. 9, 1087–1088
https://doi.org/10.1080/15476286.2017.1358346

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EDITORIAL

Editorial: RNA modifications – what to read first?

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ARTICLE HISTORY Received 20 December 2016; Revised 10 March 2017; Accepted 29 March 2017

Dedication

This special issue is dedicated to my favourite pioneer in the world of nucleic acid modifications. Thank you, Henri Grosjean!

A stupendous boost in the field of nucleic acid modification has recently reached another preliminary climax. So far, the year 2017 experiences multiple capital papers on a monthly basis, with "capital" here referring to the "big 5" journals in the life sciences. When expanding the view to the next tier of journals in the pecking order, even the experienced reader realizes that the flood of high impact papers forces us to make a selection. But where to begin? The field is branching out and interlinking with various domains of the life sciences. In return, a lot of colleagues join us in our fascination for the topic. Obviously, to them, the relative newcomers in the field, a selection of literature is even more difficult. A proven and sensible approach is to start with recent review articles that cover part of the field from certain perspective and typically include developments until a few months ago.

This special issue of RNA Biology provides various entry vectors to current literature of the field of nucleic acid modification. Depending on their personal background, researchers may approach the field according to their preferred perspectives. In the case at hand, several reputed colleagues from the field provide their view on things from different perspectives, e.g. focused on RNA species, on the organism studied, on analytical methods, on a particualar type of modification, on particular families of modification enzymes, on substrate recognition, or in comparison to "the other" nucleic acid, DNA.

A general overview over the recent exciting developments that have boosted the field, primarily by revealing the complexity of mRNA modification, is given by Nachtergaele *et al.*[1] Even more focused , the review by Lence *et al.* discusses components of the mRNA modification system in drosophila.[2] Of note, while most of the exciting recent developments concern mRNA, the notion of new layers of regulation of gene expression by post-transcriptional modification certainly expands to the other known major RNA species, in particular to rRNA and tRNA. The complex rRNA biogenesis is intricately interwoven with modification enzymes, whose roles are not restricted to their catalytic activity. This topic is covered by an insightful review by Sloan *et al.*[3] The catalog of chemically distinct RNA modifications species currently numbers about 150 species[4] which have been discovered in the 3 principal RNA components of the translation system, with tRNA featuring the highest diversity. Most of these have evolved at position 34 in the anticodon loop at the so-called "wobble" position, for reasons that have recently become better understood, as outlined by Schaffrath & Leidel.[5] One particularly exciting aspect of anticodon modifications is their influence on frameshift events, which is discussed by Klassen *et al.*[6]

In addition to these "major RNA players," modifications were detected in many members of the zoo of low abundant RNA species as a consequence of technological breakthroughs in analytical methods. These methods are covered by a series of articles devoted to current developments in modification analytics, including reviews on selective chemical reagents by Heiss & Kellner,[7] on deep sequencing techniques by Schwartz & Motorin,[8] and on antibodies directed against RNA modifications by Federle & Schepers.[9] A research paper by Heiss *et al.*[10] features current progress in mass spectrometry of RNA modifications. Mass spec is an indispensable tool when looking at the atomic details that distinguish modifications from the canonical nucleosides. Analytics like this allow a wider screening for the occurrence of modifications, as is reviewed by Hutinet *et al.*[11] for deazaguanine derivates such as queuine. Also focused on a particular type of modification, and with even more of a biomedical perspective is the review on isopentenyl modifications by Schweizer *et al.*[12]

Overviews centered on enzyme families are given by Rintala-Dempsey & Kothe[13] on stand-alone pseudouridine synthases, by Baiad *et al.*[14] on ADAR enzymes, by Smith[15] on the APOBEC family, and by Jeltsch *et al.*[16] on Dnmt2 enzymes. A ubiquitous aspect in the discussion of an enzyme family is its substrate recognition, and the history of Dnmt2 has a special twist in this respect. Originally thought to be a DNA methyltransferase, it was shown to methylate tRNA, and Kaiser *et al.* now showed in a research paper that, under the right circumstances, it can indeed also modify DNA, at least *in vitro*.[17] As with deazaguanine derivatives such as queosine[11] the borders dissolve between both nucleic acids. It is remarkable, that, while several enzymes cross the border between DNA modification and RNA modification easily, the community has taken several decades to integrate the various perspectives into a "bigger

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picture" of nucleic acid modification that does not care too strictly about the oxidation status of the ribose any more. After all, an advanced aspect of nucleic acid evolution and biogenesis is uridine methylation at C5, and ribose reduction to DNA, which several us consider as a very long, very modified RNA. Accordingly, Traube & Carell illustrate common aspects of modification and de-modification of both nucleic acids.[18]

Acknowlegdements

Efforts to foster nucleic acid modification research in the author's laboratory were and are fostered by the COST action CA16120 "European Epitranscriptomics Network (EPITRANS)" and by the DFG-funded special priority programm SPP1784 "Chemical Biology of Native Nucleic Acid Modifications." Funding for open access was provided by the DFG grant HE3397/13–1.

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