frontiers | Frontiers in Virology

TYPE Editorial
PUBLISHED 14 August 2023
DOI 10.3389/fviro.2023.1270008

OPEN ACCESS

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RECEIVED 31 July 2023
ACCEPTED 07 August 2023
PUBLISHED 14 August 2023

CITATION
Zuñiga S and Corcoran JA (2023) Editorial: Post-transcriptional regulation of viral protein expression and function.
Front. Virol. 3:1270008.
doi: 10.3389/fviro.2023.1270008

Editorial: Post-transcriptional regulation of viral protein expression and function

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KEYWORDS

post-transcriptional, phosphorylation, RNA methylation, epitranscriptomics, non-coding RNA, ribonucleoprotein complexes

Editorial on the research topic
Post-transcriptional regulation of viral protein expression and function

Post-transcriptional regulation includes both RNA and protein modifications, leading to the modulation of protein expression levels or protein functions. These modifications may virtually regulate every cellular process, including DNA repair, transcription, cell cycle, apoptosis, environmental stress response and immune response. The use of systems biology has discovered the extraordinary complexity and the cross-talk between different post-transcriptional modification networks (1). As obligatory intracellular pathogens, post-transcriptional modification networks are common targets for viruses, not only affecting viral protein expression or function, but also providing a fine-tuning for the viral regulation of host cell biology (2). In addition, post-transcriptional modifications during viral infections have attracted increasing interest as a potential target for the development of novel antiviral strategies. In this Research Topic, four groups of authors provide new insights into different aspects of virus-host interactions involving post-transcriptional regulation.

RNA modification, or epitranscriptiomics, is one of the mechanisms for post-transcriptional regulation that is growing in interest, aided by the novel omics technologies facilitating the study of these modifications. Many chemical RNA modifications have been identified to date, playing a relevant role in multiple cellular functions and pathologic processes (3). Some of these modifications, such as N6-methyladenosine (m^6A) are more abundantly described than others, and play different roles during viral infections (4, 5). Two of the contributions in this Research Topic expose how viruses modify cellular RNAs for their own benefit. In Cristinelli et al., the RNA methylation in human immunodeficiency virus (HIV) infected cells is analyzed. The described modifications would lead to the identification of novel virus-host interactions, and these RNA modification pathways may be shared by other viruses. In Talló-Parra et al., tRNA modification is proposed as a novel mechanism shared by RNA viruses to modulate protein expression in their own benefit. Altogether, these works highlight that epitranscriptomic analyses during virus infections may potentially uncover novel targets of therapeutic interventions.

Eukaryotic cell RNA is associated with proteins, forming ribonucleoprotein complexes (RNPs), including stress granules (SGs) and processing bodies (PBs). RNA-protein

interactions leading to RNPs formation represent one of the mechanisms for post-transcriptional regulation of protein expression, as the location of mRNAs in RNPs is a powerful mechanism for the spatial and temporal regulation of RNA processing events in the cell (6). In addition, by sharing components, different RNPs form a large regulatory network in cells. RNA helicases are abundant components of cellular RNPs (7, 8). Virus infection modulates RNA granules at different levels, depending on the different infection mechanisms and virus life cycle. In general, RNP granules can represent an obstacle for virus replication and also serve as sensors to mount the innate immune response. Therefore, viruses have evolved different mechanisms to control the assembly and functions of RNP granules and, in some cases the components of RNPs are co-opted into novel virus-specific structures required for virus replication (9). The interplay between cytoplasmic RNPs, RNA helicases (specially MOV10 helicase), and coronavirus infections was reviewed in (Wang et al.).

Protein phosphorylation is one of the most widespread post-translational modifications found in nature, and is an essential regulatory mechanism in both prokaryotes and eukaryotes (10, 11). In eukaryotic cells, protein phosphorylation plays a key role in the regulation of essential cellular processes, including those related with cell response to viral infection (12). The introduction of systems biology to kinome studies led to the view of complex phosphorylation networks and, in an additional level of complexity, there is a cross-talk with other protein post-translational modification networks (13). Phosphorylation-based networks are very important for the proper functioning of the cell, and are also important targets for human pathogens. Therefore, the study of viral protein phosphorylation is a key aspect in the analysis of virus-host interactions. Several viruses depend on host kinases and phosphatases for the modification of viral proteins involved in key viral functions (10). The role of phosphorylation in the function of viral RNA-dependent RNA-polymerases (RdRps) is reviewed in Duflos and Michiels. Phosphorylation of this essential viral protein could have both positive or negative effects on RdRp activity or its interaction with host proteins. In this review, phosphorylation of viral RdRps as a novel therapeutic target is also explored.

In summary, the works included in this Research Topic are an example of the complex network of interactions that may have different contributions to the outcome of viral infections. Omics approaches have helped to uncover the role of these post-transcriptional modifications in infection, very frequently with some functional redundancy among them, which makes it extremely challenging to untangle these virus-host interaction networks and how they contribute to viral life cycle.

Author contributions

SZ: Conceptualization, Writing – original draft, Writing – review & editing. JC: Writing – review & editing.

Acknowledgments

We would like to thank all of the authors for their insightful contributions. We would also like to thank the reviewers for their constructive suggestions that improved the content of this Research Topic.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The authors declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Publisher's note

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