Commentary

Ribosome Profiling: A Useful Approach to Discover Hidden Corners of SARS-CoV-2

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Abstract

Following SARS-CoV-2 China epidemic in the December 2019, researches have attended to the genome of novel coronavirus. Hidden corners of SARS-CoV-2, maybe a shiny way to discover its pathogenicity and virulence. To design therapeutic agents, it is critical to map the complete repertoire of viral-translated proteins. Ribosome profiling is considered as a snapshot of all active ribosomes in a cell at a specific time point.

Keywords: Genome, Open Reading Frames, Ribo-seq, SARS-CoV-2

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Coronaviruses (CoVs) are recognized as a single-stranded RNA virus with a genome length from 26 to 32 kilobases, that belongs to the *Coronaviridae* family. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel member of this family, is known as the first global concern since 2019 and still, kills so many people every day (1-4). Since the first days, so many studies focused on its full genome. The SARS-CoV-2 genome displays a body similar to other CoVs. This positive-sense single-stranded RNA (+ssRNA) virus contains a 5′-cap and a 3′-poly-A tail (5, 6). Like the other CoVs, a frameshift mechanism at the 5′-end of SARS-CoV-2 between viral open reading frames (ORFs), including ORF1a and ORF1b, facilitates the synthesis of two polypeptides One of these viral proteases, that named 16 non-structural proteins (Nsp1-16), are necessary for different stages of the virus life cycle (7). These nonstructural proteins are included viral proteases, nuclease, helicase, methyltransferase, RNA-dependent RNA polymerases (1, 8, 9).

Hidden corners pathogenicity and virulence of SARS-CoV-2 are critical points to design effective therapeutic agents. Mapping the complete repertoire of viral-translated proteins is one of these points. The present map of viral translation capacity is according to bioinformatical analysis, and its homology with other CoVs (10). Since the protein profile is various among CoVs, particularly about the accessory proteins, it is essential to describe the exact variety of viral proteins in an open-ended way. Hence, in a recent study, ribosome-profiling methods were used as a high-resolution approach for mapping of coding regions in this RNA virus to precisely account for the canonical viral ORFs in the proteome level to identify viral ORFs (11). Ribosome profiling is also known as ribo-seq is a useful approach that offers *in vivo* genome-wide data on protein synthesis (GWIPS). This technique is established based on deeply sequencing of ribosome protected sequences of mRNA that provides the analysis of ribosome density associate with total RNAs existing in cells. Also, its capacity in high resolution analysis provides a good chance to detailed analysis for individual RNAs (12).

In this technique, mRNA fragments and recovered footprints are transformed into an appropriate feature for massive sequencing. Performing analysis on its outcomes will give us the measured translation capacity of ribosomes at the scale of whole-genome. So ribosome profiling is capable to be utilized for assessing the quantity of viral protein translation. While a large quantity of transcripts in a fraction of polysome is evaluated by microarray techniques or RNA-seq, Ribo-seq method has been identified as a common approach to discovering genes involved in the translation process. Although, ribo-seq previously was applied for polysome analysis in which isolation of protein-coding mRNAs occurs by a gradient of sucrose (13). The actual potential of ribosome profiling is its capability to acquire data on the distinct position by considering ribosome positions on mRNAs, what makes its priority to similar methods. This point is critical for some details. Detection of an mRNA fragment in association ribosomes necessarily does not tell us that our fragment of the mRNA is completely translated. In

other words, ribosomes can associate with an mRNA fragment that do not generate a protein, since translation can't happen at non-coding mRNA (14).

The genome of SARS-CoV-2 encodes at least 13 known open reading frames, organized largely linearly from the 5′ end to the 3′ end (15, 16). However, Salehi et al. (17) reported that the full genome sequence of SARS-CoV-2 has 10 ORFs.

Ribosome profiling as a novel and useful technique can be used to discover hidden corners of pathogens. It is important to map the complete repertoire of viral-translated proteins to design and develop effective therapeutic agents.

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Authors' Contributions

M.Z.; Performed to conception and design and supervised the study. E.B., P.Z.; Contributed to write and draft the manuscript. S.S., M.R.S.; Performed editing. All the authors approving the final version of this paper for submission, also participated in the finalization of the manuscript and approved the final draft.

References

1. Behboudi E, Hamidi-Sofiani V, Zeynali P. Review of therapeutic candidates for the new corona virus (COVID-19). RJMS. 2020; 27(8): 65-77.
2. Wang H, Li X, Li T, Zhang S, Wang L, Wu X, et al. The genetic sequence, origin, and diagnosis of SARS-CoV-2. Eur J Clin Microbiol Infect Dis. 2020; 39(9): 1629-1635.
3. Hosseini P, Dehghan A, Navand AH, Moghadami M, Soltani S, Zandi M. Coronavirus disease 2019 (COVID-19): immune responses, transmission and clinical features: an update. JCMA. 2020; 5(4): 266-268.
4. Zandi M, Rashid S, Nasimzadeh S, Pourhossein B, Fazeli M. A snapshot of different types of under research vaccines against COVID-19: a review. Arch Med Lab Sci. 2020; 6: 1-7.
5. Behboudi E, Hamidi-Sofiani V. New mutations causing the 2019 novel Coronavirus (2019-nCoV) epidemic: letter to the editor. TUMS. 2020; 78(3): 188.
6. Zandi M. ORF8/ORF8a: a difference between SARS-CoV-2 and SARS-CoV. Eur Respir J. 2021: 2102818.
7. Suryawanshi RK, Koganti R, Agelidis A, Patil CD, Shukla D. Dysregulation of cell signaling by SARS-CoV-2. Trends Microbiol. 2021; 29(3): 224-237.
8. Wu A, Peng Y, Huang B, Ding X, Wang X, Niu P, et al. Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in china. Cell Host Microbe. 2020; 27(3): 325-328.
9. Zandi M. Severe acute respiratory syndrome-2 encodes hemagglutinin esterase? Rev Med Virol. 2021: e2294.
10. Michel CJ, Mayer C, Poch O, Thompson JD. Characterization of accessory genes in coronavirus genomes. Virol J. 2020; 17(1): 131.
11. Finkel Y, Mizrahi O, Nachshon A, Weingarten-Gabbay S, Morgenstern D, Yahalom-Ronen Y, et al. The coding capacity of SARS-CoV-2. Nature. 2021; 589(7840): 125-130.
12. Michel AM, Baranov PV. Ribosome profiling: a Hi-Def monitor for protein synthesis at the genome-wide scale. Wiley Interdiscip Rev RNA. 2013; 4(5): 473-490.
13. Larsson O, Sonenberg N, Nadon R. Identification of differential translation in genome wide studies. Proc Natl Acad Sci USA. 2010; 107(50): 21487-21492.
14. Erhard F, Halenius A, Zimmermann C, L'Hernault A, Kowalewski DJ, Weekes MP, et al. Improved Ribo-seq enables identification of cryptic translation events. Nat Methods. 2018; 15(5): 363-366.
15. Malone B, Urakova N, Snijder EJ, Campbell EA. Structures and functions of coronavirus replication-transcription complexes and their relevance for SARS-CoV-2 drug design. Nat Rev Mol Cell Biol. 2022; 23(1): 21-39.
16. Kesheh MM, Hosseini P, Soltani S, Zandi M. An overview on the seven pathogenic human coronaviruses. Rev Med Virol. 2021: e2282.
17. Salehi N, Amiri-Yekta A, Totonchi M. Profiling of Initial available SARS-CoV-2 sequences from Iranian related COVID-19 patients. Cell J. 2020; 22 Suppl 1: 148-150.