EUROPEAN RESPIRATORY journal

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Early View

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Please cite this article as: Zandi M. ORF8/ORF8a: a difference between SARS-CoV-2 and SARS-CoV. *Eur Respir J* 2021; in press (https://doi.org/10.1183/13993003.02818-2021).

This manuscript has recently been accepted for publication in the *European Respiratory Journal*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJ online.

Title: ORF8/ORF8a: A difference between SARS-CoV-2 and SARS-CoV

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Recently in a published article in European respiratory journal, the authors reported ORF8a has a role in SARS-CoV-2 infection(1). In figure 1, the authors stated ORF7a, ORF8a and ORF9b locate within the mitochondria and can inhibit RIG1- MAVS dependent interferon signaling, enhance viral replication and disrupt mitochondrial function(1), although based on scientific evidence, SARS-CoV-2 lacks ORF8a(2-4).

The genome of SARS-CoV-2 contains several accessory genes in the 3′-end of genome that codes nine accessory proteins (3a, 3b, 6, 7a, 7b, 8, 9b, 9c and 10) which are involved in SARS-CoV-2 infection(5) (Fig. 1). SARS-CoV-2 ORF8 is a 121-amino acid protein which contains an N-terminal signal sequence which followed by a predicted Ig-like fold. ORF8 protein has a signal sequence for import into ER to interact with proteins of host cell(6). ORF8a is absent in SARS-CoV-2 because of a 29-nucleotide deletion that inactivates the formation ORF8ab tandem. ORF8 splitting into two separated ORFs (ORF8a and ORF8b) in SARS-CoV.

An intact ORF8 is encoded by SARS-CoV-2 that shares the least homology among SARS-CoV-2 and SARS-CoV proteins(7). SARS-CoV-2 encodes two viral proteins with ion channel activity (viroporin): 3a and E (8), but SARS-CoV encodes three: proteins 3a, E, and 8a(9). In SARS-CoV, ORF8 gene encodes two proteins, ORF8a and ORF8b, which characterize proteins of 39 and 84 aa, respectively(10). ORF8a can induce apoptosis by a mitochondrion-dependent pathway(11).

SARS-CoV-2's ORF8 has several function during infection. ORF8 can disrupt IFN-I signaling when exogenously overexpressed in cells, it also downregulates levels of MHC-1 through direct binding(6), however this process is not observed for ORF8a and ORF8b, furthermore, ORF8 degrades MHC-1 via the autophagy pathway.

In conclusion, one of the differences between SARS-CoV-2 and SARS-CoV is ORF8/ORF8a, which presented SARS-CoV-2's genome encodes an intact ORF8, however, SARS-CoV encodes two proteins, ORF8a and ORF8b.

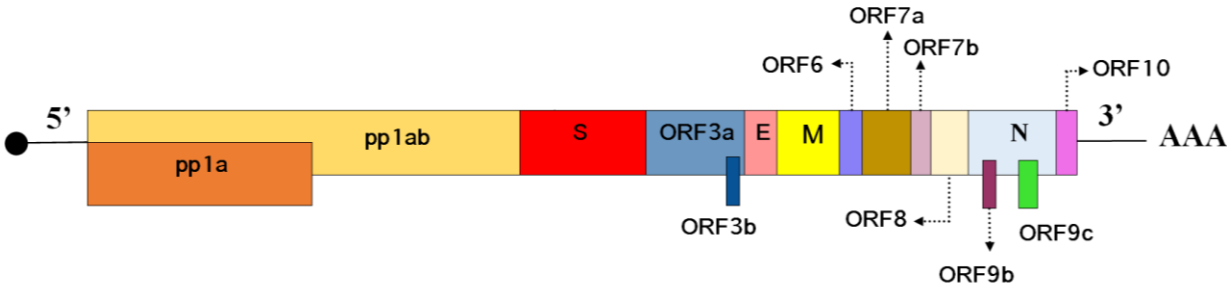

Figure1. SARS-CoV-2 genome

Conflict of interest: Milad Zandi declares no conflict of interest for this article

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