

LETTER TO THE EDITOR

Role of ORF8a as accessory protein in apoptosis induction in SARS-CoV-2 infection

Dear editor

Recently in a published article in *Reviews in Medical Virology*, Morais da Silva et al., described the different mechanisms that are involved in cell death process such as apoptosis, autophagy, and necrosis which are caused by SARS-CoV-2.¹ The authors reported SARS-CoV and SARS-CoV-2 genomes contain eight accessory genes whose open reading frames are interspersed among the structural genes; two between S and E genes (ORFs 3a and 3b), five are located between the M and N genes (6, 7a, 7b, 8a, 8b) and one within the N gene (9b); in addition, the authors presented ORF8a as one of the accessory proteins in both SARS-CoV and SARS-CoV-2 in fig. 1,¹ although scientific evidence show that genome of SARS-CoV-2 lacks ORF8a.²⁻⁴

The genome of SARS-CoV-2 encodes an intact ORF8; however, in case of SARS-CoV, ORF8 is splitting into two separated ORFs including ORF8a and ORF8b.⁵ ORF8 shares the least homology among all proteins of SARS-CoV and SARS-CoV-2. By direct binding to major histocompatibility complex class I, ORF8 can down-regulate total and surface levels of it; moreover, ORF8 of SARS-CoV-2 degrades major histocompatibility complex class I by the autophagy pathway.⁶ In conclusion, ORF8a is absent in SARS-CoV-2, however, SARS-CoV contains ORF8a and ORF8b.

ACKNOWLEDGEMENT

None.

AUTHOR CONTRIBUTIONS

Milad Zandi conceptualized, edited and supervised the study. Hasan Karami involved in investigation. All authors reviewed and approved the final version of the manuscript.

Milad Zandi^{1,2}

Hassan Karami¹

¹Department of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

²Research Center for Clinical Virology, Tehran University of Medical Sciences, Tehran, Iran

Correspondence

Milad Zandi, Department of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.

Email: Miladzandi416@gmail.com

REFERENCES

1. Morais da Silva M, Lira de Lucena AS, Paiva Júnior SDSL, et al. Cell death mechanisms involved in cell injury caused by SARS-CoV-2. *Rev Med Virol.* 2021. <https://doi.org/10.1002/rmv.2292>
2. Oughtred R, Rust J, Chang C, et al. The BioGRID database: a comprehensive biomedical resource of curated protein, genetic, and chemical interactions. *Protein Sci.* 2021;30(1):187-200.
3. Geng H, Subramanian S, Wu L, et al. SARS-CoV-2 ORF8 forms intracellular aggregates and inhibits IFN γ -induced antiviral gene expression in human lung epithelial cells. *Front Immunol.* 2021;12:2108.
4. Kesheh MM, Hosseini P, Soltani S, Zandi M. An overview on the seven pathogenic human coronaviruses. *Rev Med Virol.* 2021. e2282
5. Mariano G, Farthing RJ, Lale-Farjat SL, Bergeron JR. Structural characterization of SARS-CoV-2: where we are, and where we need to be. *Front Mol Biosci.* 2020;7:344.
6. Zhang Y, Chen Y, Li Y, et al. The ORF8 protein of SARS-CoV-2 mediates immune evasion through down-regulating MHC-I. *Proc Natl Acad Sci.* 2021;118(23).