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ORF8a as a viroporin in SARS-CoV-2 infection?

The seventh human coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is described as the causative agent of coronavirus infectious disease (COVID-19) [1]. Since the first detection of SARS-CoV-2 in late December 2019 [2], the virus and ongoing COVID-19 pandemic have spread across the globe, killing more than 4 million individuals in the past 18 months. Highly efficacious vaccines generated by biotech and pharma remain the only solution to this international crisis.

The SARS-CoV-2 harbors a positive-sense single-stranded RNA in order of 5′-replicase (ORF1a/b)-S-E-M-N-poly(A)-3′, also the SARS-CoV-2 genome contains several ORFs at its 3′ portion which encodes accessory proteins including ORF3a, ORF3b, ORF6, ORF7a, ORF7b, ORF8, ORF9b, ORF9c as well as ORF10 [3,4]. The scientific evidence shows that the genome of SARS-CoV-2 lacks ORF8a [5–8].

Indeed, both ORF8a and ORF8b are absent in SARS-CoV-2 because of a 29-nucleotide deletion that inactivates the formation ORF8ab tandem [9], while ORF8a and ORF8b are present in SARS-CoV [5,10]. In SARS-CoV, ORF8 splitting into two separated ORFs (ORF8a and ORF8b) [11]. In addition, ORF3b of SARS-CoV is longer than its ortholog in SARS-CoV-2 [8,12].

The SARS-CoV-2 encodes an intact ORF8, which among all the viral proteins of SARS-CoV-2 and SARS-CoV shares the least homology [13]. The ORF8 protein, one of the accessory proteins of SARS-CoV-2, can downregulate surface and total levels of MHC-1 by direct binding and can also degrade MHC-1 by the autophagy pathway [13]. In addition, the ORF8 protein prevents antigen presentation system and CTL-mediated killing of cells that infected with SARS-CoV-2 [14,15].

I have recently read with interest an article by Ni Zhao et al. the authors reported that SARS-CoV-2 can encode a set of accessory proteins, including two ion-channel proteins known as viroporins (open reading frame 3a (ORF3a) and ORF8a) [16], while according to scientific evidence, SARS-CoV-2 lacks ORF8a, and this protein (ORF8a) has no role in SARS-CoV-2 infection.

Declaration of Competing Interest

The author reports no declarations of interest.

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