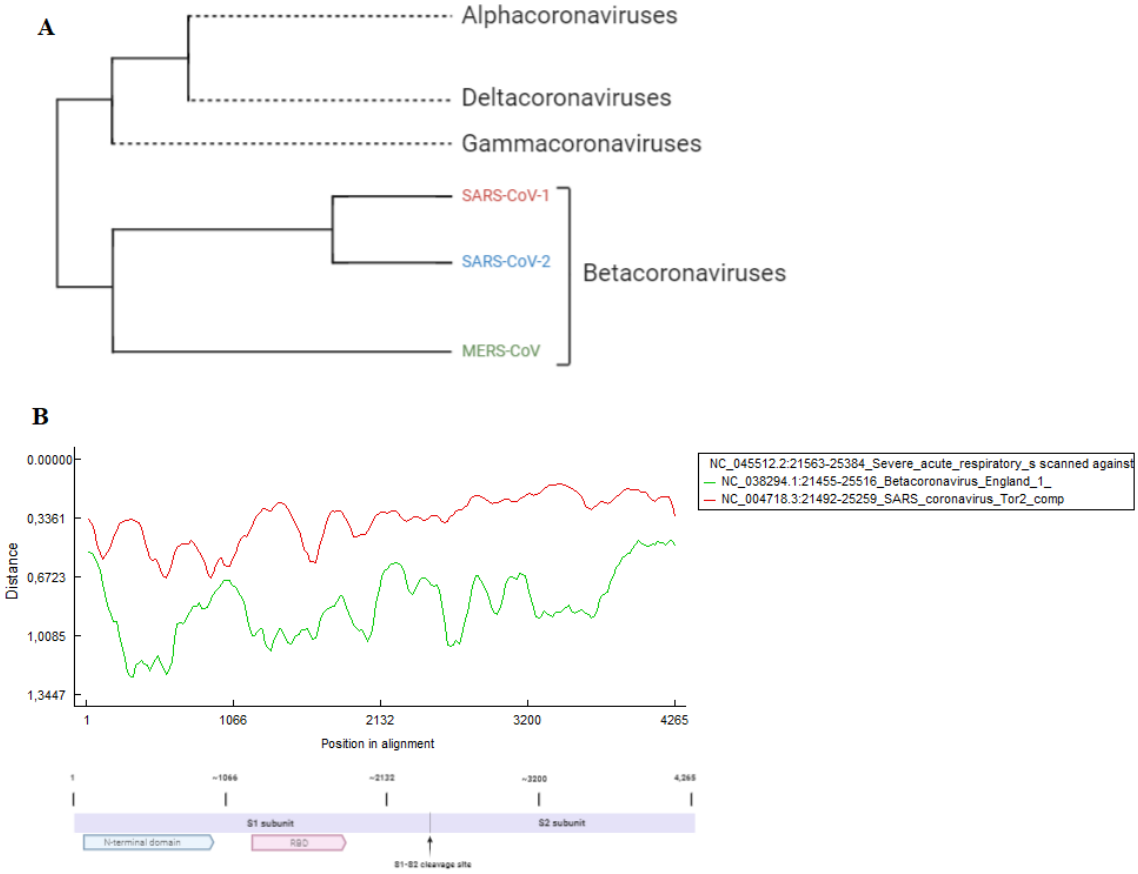
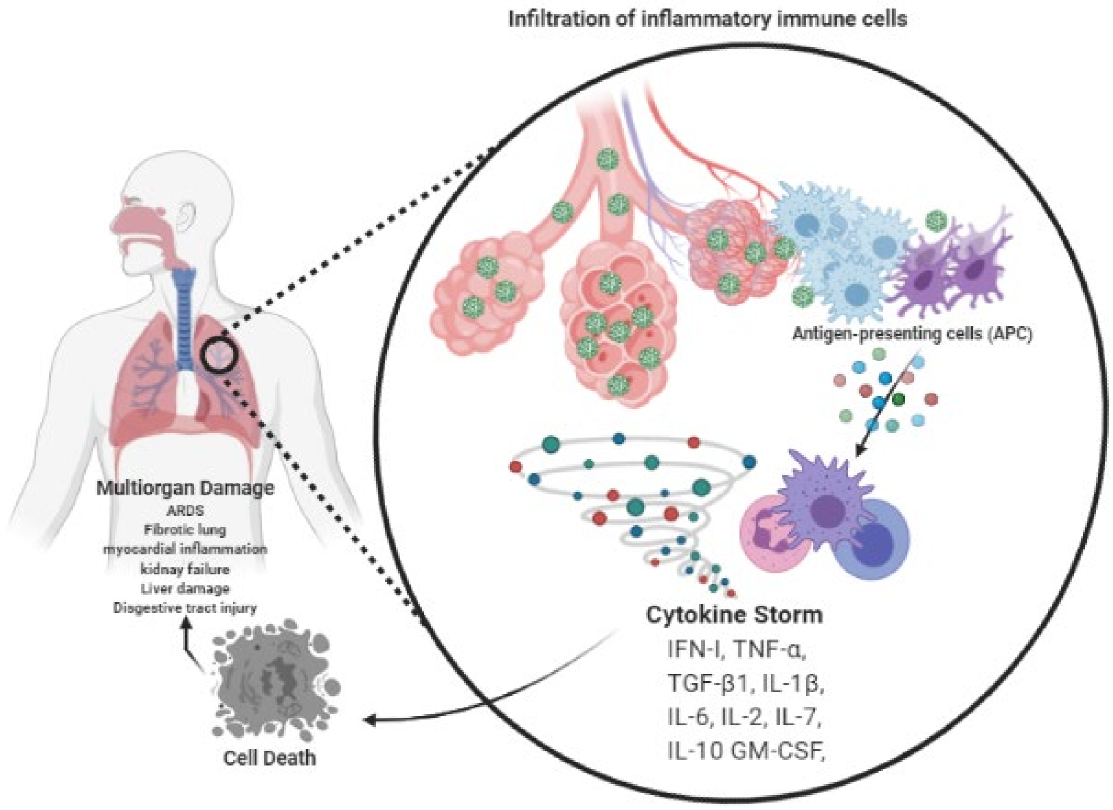
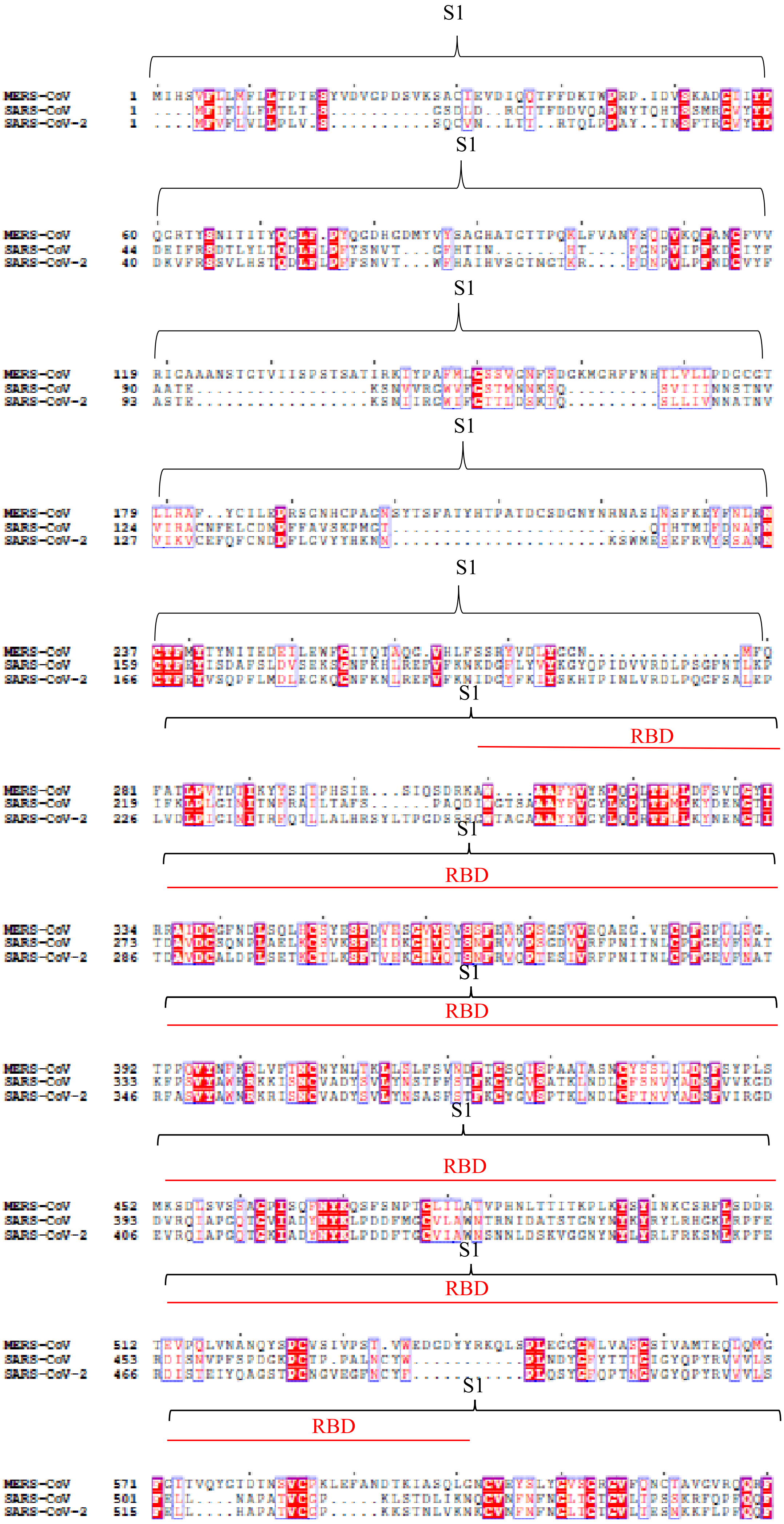
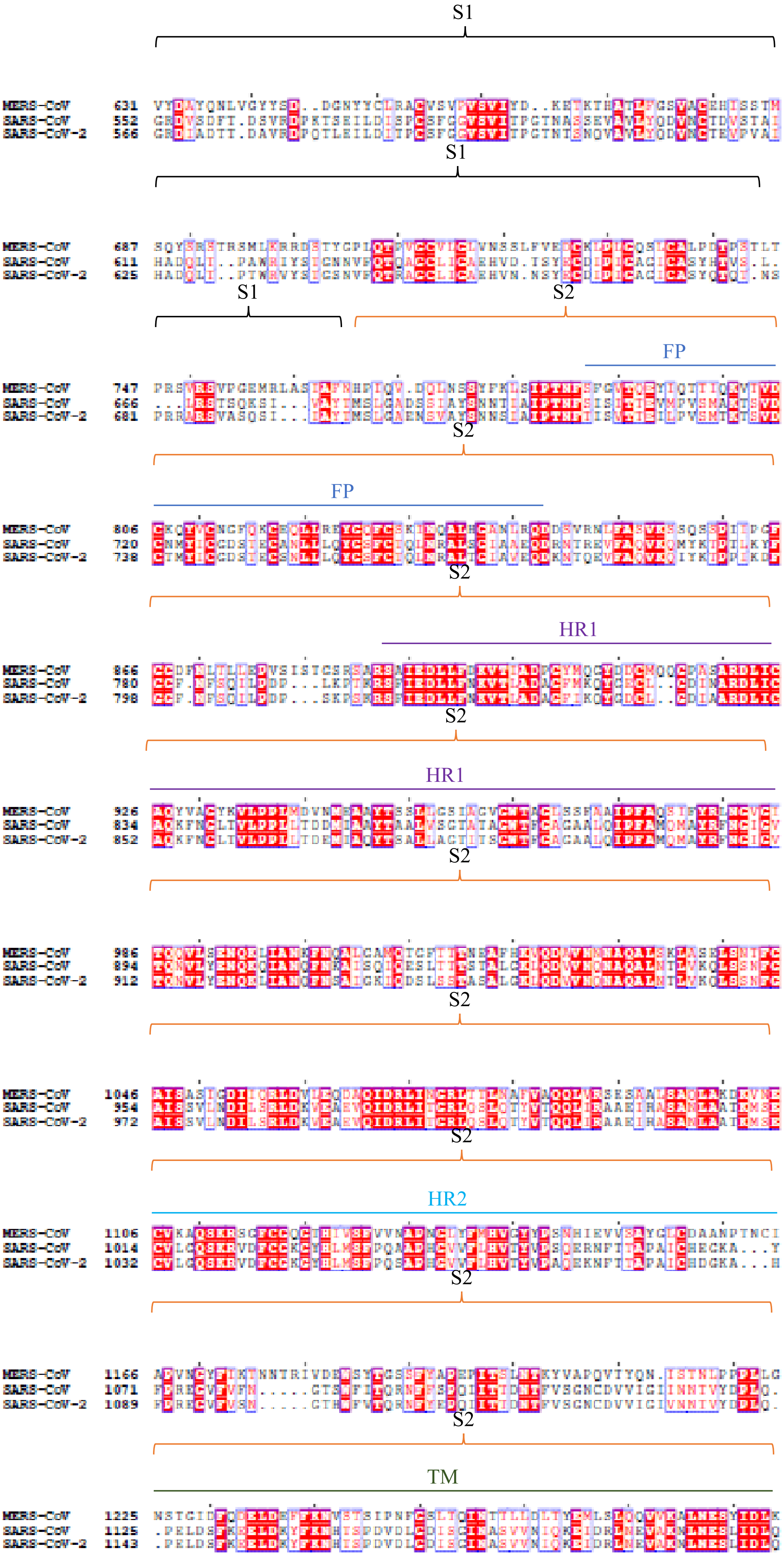


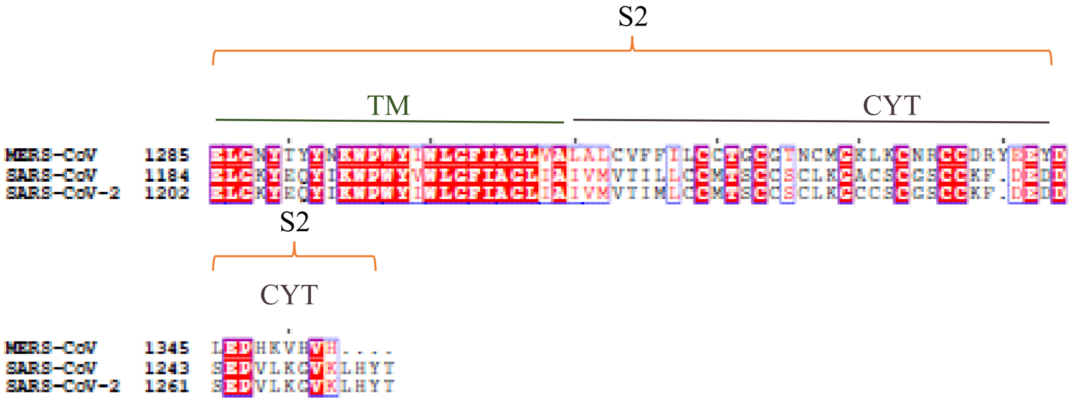
**Supplementary Figure 1** – Evolutionary divergence between SARS-CoV-2, SARS-CoV and MERS-CoV. **(A)** SARS-CoV-2 is closer related to SARS-CoV than MERS-COV, all of them in the same evolutive branch of Betacoronaviruses group. Phylogenetic tree adapted from Tang et al. [114]. **(B)** Genetic distance Spike gene comparing SARS-CoV-2 (NC_045512.2) against SARS-CoV (NC_004718.3) and MERS-CoV (NC_038294.1), proving the evolutive distance among them. The distance analysis was performed using the RDP4 package. Created with BioRender.com.



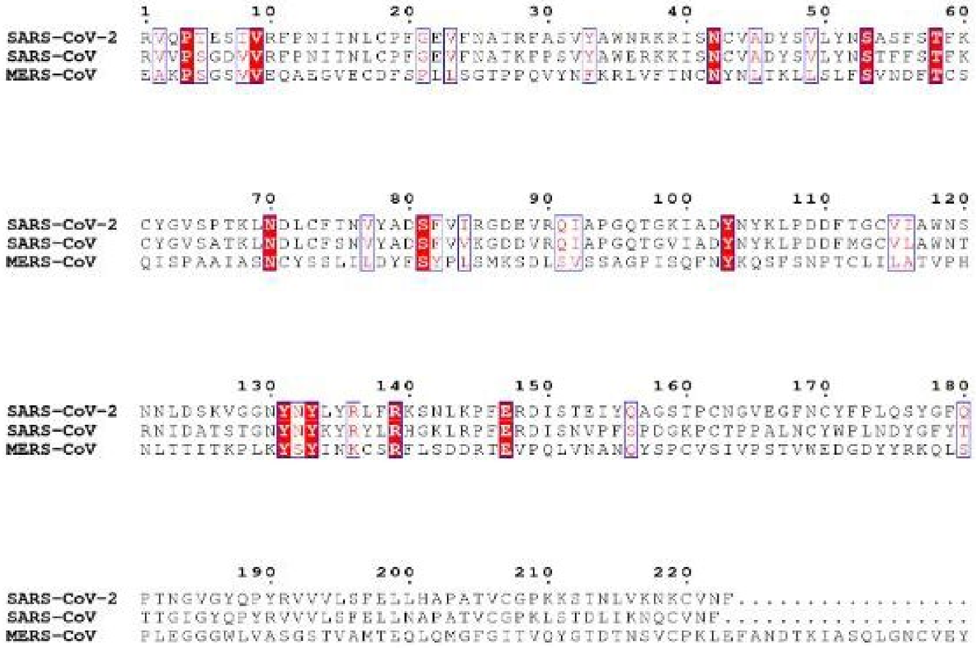
**Supplementary Figure 2** – Short overview of critical role of immune system in the COVID-19 pathogenesis. The presence of SARS-CoV-2 in the alveolar environment induces the infiltration of inflammatory immune cells. Thus, antigen-presenting cells (APC) release cytokines and chemokines that increases the production and releasing of cytokines by the immune system cells, provoking the cytokine storms. The consequence of this event is the cell death of affected tissue with multi organ damage. Created with BioRender.com.


S1
RBD
MERS-CoV
SARS-CoV
SARS-CoV-2
1
60
44
40
119
90
93
179
124
127
237
159
166
281
219
226
334
273
286
392
333
346
452
393
406
512
453
466
571
501
515


S1
MERS-CoV 631
SARS-CoV 552
SARS-CoV-2 566
S1
MERS-CoV 687
SARS-CoV 611
SARS-CoV-2 625
S1
S2
FP
MERS-CoV 747
SARS-CoV 666
SARS-CoV-2 681
S2
FP
MERS-CoV 806
SARS-CoV 720
SARS-CoV-2 738
S2
HR1
MERS-CoV 866
SARS-CoV 780
SARS-CoV-2 798
S2
HR1
MERS-CoV 926
SARS-CoV 834
SARS-CoV-2 852
S2
MERS-CoV 986
SARS-CoV 894
SARS-CoV-2 912
S2
MERS-CoV 1046
SARS-CoV 954
SARS-CoV-2 972
S2
HR2
MERS-CoV 1106
SARS-CoV 1014
SARS-CoV-2 1032
S2
MERS-CoV 1166
SARS-CoV 1071
SARS-CoV-2 1089
S2
TM
MERS-CoV 1225
SARS-CoV 1125
SARS-CoV-2 1143



**Supplementary Figure 3 -** Alignment of the entire sequence of spike protein from the three pandemic coronaviruses deposited in the UniProt database: SARS-CoV-1 (accession number P59595); MERS-CoV (accession number K9N5Q8); SARS-CoV-2 (accession number P0DTC2). The alignment was performed using the ESPript 3.0 tool (http://espript.ibcp.fr/ESPript/ESPript/). S1: subunit 1 from spike protein; S2: subunit 2 from spike protein; RBD: receptor-binding domain; FP: fusion peptide; HR1: heptapeptide repeated sequence 1; HR: heptapeptide repeated sequence 2; TM: transmembrane domain; CYS: cytoplasmic domain.



**Supplementary Figure 4 -** Alignment of the RBD domain sequence extracted from S protein entire sequence from the three pandemic coronaviruses deposited in the UniProt database: SARS-CoV-1 (accession number P59595); MERS-CoV (accession number K9N5Q8); SARS-CoV-2 (accession number P0DTC2). The alignment was performed using the ESPript 3.0 tool ([http://espript.ibcp.fr/ESPript/ESPript/](http://espript.ibcp.fr/ESPript/ESPript/)).