

ORIGINAL RESEARCH ARTICLE

Association of *TYK2* rs2304256 and rs12720270 single-nucleotide polymorphisms with COVID-19 severity

Supplementary Files

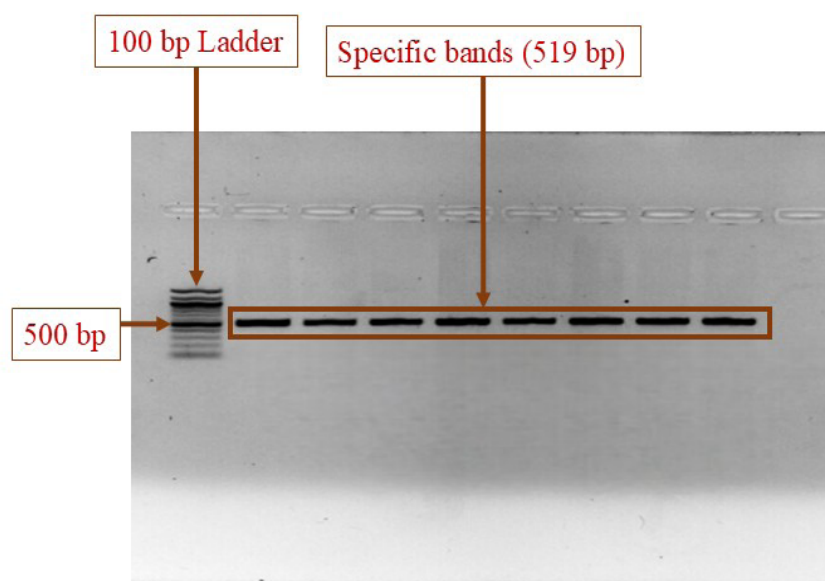


Figure S1. A representative photograph of agarose gel electrophoresis of the purified polymerase chain reaction product. Gel images were captured using Quantity One software. The “100 bp ladder” refers to the complete molecular weight marker containing multiple DNA fragments of different sizes. The 500 bp marker band is indicated for reference.

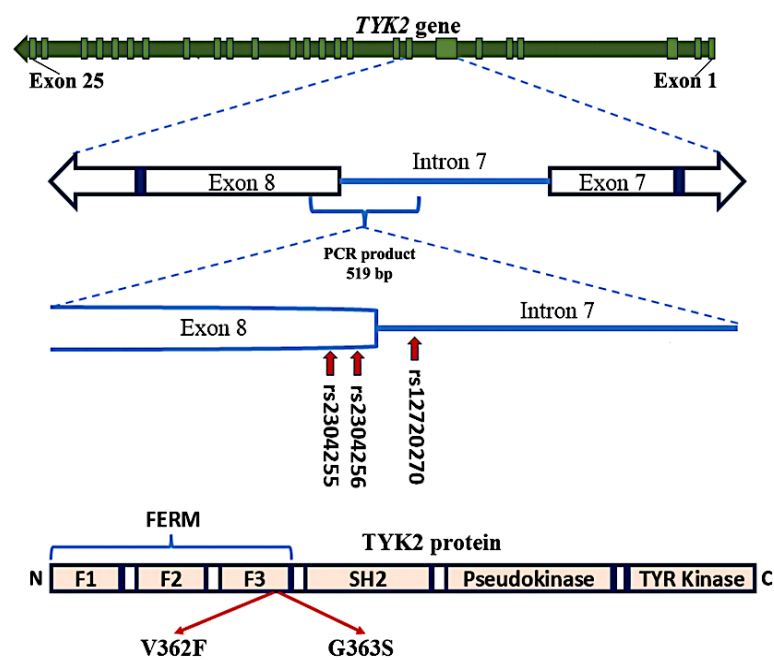


Figure S2. The locations of the variations in the *TYK2* gene and specific amino acid changes in the encoded protein. The top panel shows the *TYK2* gene structure, including exon 7, exon 8, and intron 7. The middle panel highlights a 519 bp polymerase chain reaction (PCR) product spanning exon 8 and intron 7, clearly marking the positions of rs2304255 and rs2304256 within Exon 8, and rs12720270 within Intron 7. The bottom panel shows the TYK2 protein and its key functional domains. Red arrows indicate the locations of the missense variants leading to amino acid changes V362F and G363S within the protein. Adapted with permission from Zabihi Rizi *et al.*¹ Copyright © 2023, The Author(s), under exclusive license to Springer-Verlag GmbH Austria, part of Springer Nature.

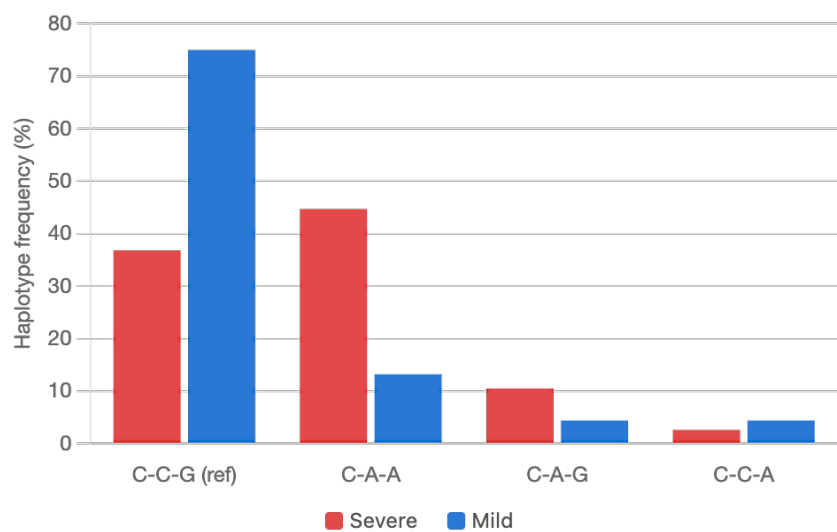


Figure S3. *TYK2* haplotype frequencies by COVID-19 severity. Frequency of the four major three-locus haplotypes (rs2304255–rs2304256–rs12720270) among severe and mild COVID-19 patients, based on expectation–maximization–estimated haplotype assignments. The reference haplotype C-C-G is markedly depleted in severe cases (36.8% vs. 75.0% of alleles), while the C-A-A haplotype is enriched (44.7% vs. 13.2%), consistent with a protective and risk-associated haplotype, respectively.

Table S1. Haplotype frequencies and association with COVID-19 severity (dominant model)

Haplotype (rs2304255–rs2304256–rs12720270)	Frequency	Score	<i>p</i> -value
C-C-G (reference)	0.543	−3.946	0.00008
C-A-A	0.295	4.256	0.00002
C-A-G	0.082	1.601	0.109
C-C-A	0.038	−0.546	0.585

Notes. T-A-A and T-C-A (combined frequency 4.1%) fell below the threshold for individual haplotype scoring but were included in the global test.

Reference

1. Zabihi Rizi F, Ghorbani A, Zahtab P, *et al.* TYK2 single-nucleotide variants associated with the severity of COVID-19 disease. *Arch Virol.* 2023;168(4).
doi: 10.1007/s00705-023-05729-2