



Shortlist of human of prospective genetic determinants of COVID19

1. Entry, infectivity, spread

ACE2 Entry receptor (1) 


CD147 Presumptive entry receptor, interacts with S (4) 


TMPRSS2 Proteolytically priming of S for membrane fusion, mediates infectivity/ spread (1, 5-7) 

ZDHHC5 GOLGA7-ZDHHC5 acyl-transferase complex interacts with S, could facilitate membrane fusion, mediating infectivity and spread (5, 8) 


2. Replication (ER vesicle trafficking, ERQC)


ERO1B ER Quality Control and UPR mediator, interactor of viral protein Orf8 (5) 


SIGMAR1 ER stress/ UPR/autophagy regulator resident in ER membranes that support viral replication (HCV, human coronavirus 229E), interacts with viral replicase protein Nsp6 (replication machinery complex) (5) 

ATP6AP1 V1-ATPase subunit that mediates late autophagy and endosomal trafficking and interacts with Nsp6 and M, could mediate trafficking needed for viral replication/ infectious virion assembly/maturation in cellular membranes (5) 

3. Antiviral response

RAE1 NUP98-RAE1 complex, known restriction factor for Influenza and other viruses, hijacked by conserved binding motifs in many viruses as an immune evasion strategy, interacts with viral Orf6 protein (5) 

RNF41 E3 Ub-ligase mediating antiviral response via IRF3/TBK1. Interactor of viral protein Nsp15, possibly hijacking of antiviral response (5) 






MBL Polymorphisms on MBL (mannose-binding lectin), antigen presentation, linked to risk of SARS (9) 

HLA HLA-A, B, DR polymorphisms that correlate with susceptibility to SARS-CoV and MERS-CoV (9, 10) 

4. Disease predisposing factors

DPP4 Functional receptor in MERS-CoV in immune cells and mediator of immune response dysregulation in Type II diabetes, disease that poses a major risk of complications in COVID19 (11, 12)

TERT Predisposing factor for lung fibrosis in interstitial fibrosis related to hypersensitivity pneumonitis and collagen vascular disease (13, 14)

variants:  interactor:  druggable: approved drug available  covid19: (treatment currently being proved in COVID19 patients)  sars-cov: (similar mechanism in SARS-CoV) 

References

- (1) Hoffmann, Markus 2020 <https://doi.org/10.1016/j.cell.2020.02.052>
- (2) Renieri A, ACE2 variants underlie interindividual variability and susceptibility to COVID-19 in Italian population. MedRxiv, doi: <https://doi.org/10.1101/2020.04.03.20047977>. (3) Delanghe JR, Speeckaert MM, De Buyzere ML. The host's angiotensin-converting enzyme polymorphism may explain epidemiological findings in COVID-19 infections. Clin Chim Acta. 2020;505:192-193.
- (4) Wang, Ke BioRxiv 2020 SARS-CoV2 invades host cells via a novel route: CD147-spike protein
- (5) Gordon, David E 2020 BioRxiv <https://doi.org/10.1101/2020.03.22.002386>
- (6) Darbani, B. The expression and polymorphism of entry machinery for COVID-19 in human: juxtaposing population groups, gender, and different tissues. Preprints. 2020, 2020040076; doi: 10.20944/preprints202004.0076.v1. (7) Asselta R, Paraboschi EM, Mantovani A, et al. TMPRSS2 variants and expression as candidates to sex and country differences in COVID-19 severity in Italy. MedRxiv: <https://doi.org/10.1101/2020.03.30.20047878>. (8) Petit, C. M. et al. Palmitoylation of the cysteine-rich endodomain of the SARS-coronavirus spike glycoprotein is important for spike-mediated cell fusion. Virology 360, 264-274 (2007). (9) von der Thsen, Jan 2020 Histopathology and genetic susceptibility in COVID-19 pneumonia <https://doi.org/10.1111/ECI.13259>
- (10) Li X, Geng M, Peng Y, et al. Molecular immune pathogenesis and diagnosis of COVID-19. Journal of Pharmaceutical Analysis. 2020; <https://doi.org/10.1016/j.jpha.2020.03.001>. (11) Iacobellis G. COVID-19 and diabetes: Can DPP4 inhibition play a role? Diabetes Res Clin Pract. 2020;162:108125. doi:10.1016/j.diabres.2020.108125
- (12) Ma RCW, and Holt RIG. COVID-19 and diabetes. Diabet Med. 2020; doi: 10.1111/dme.14300.
- (13) Borie R, Le Guen P, Ghanem et al. The genetics of interstitial lung diseases. Eur Respir Rev. 2019;28:190053: <https://doi.org/10.1183/16000617.0053-2019>. (14) Ley B, Torgerson DG, Oldham JM, et al. Rare protein-altering telomere-related gene variants in patients with chronic hypersensitivity pneumonitis. Am J Respir Crit Care Med. 2019;200:1154-1163.