Shortlist of human of prospective genetic determinants of COVID19

- 1. Entry, infectivity, spread
- ACE2 Entry receptor (1)
- CD147 Presumtive entry receptor, interacts with S (4)
- TMPRSS2 Proteolitically 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) $_{\blacksquare}$
 - 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 tested in COVID19 patients), cov (similar mechanism in human coronavirus)

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 Th
sen, Jan 2020 Histopatology and genetic susceptibility in COVID-19 pneumonia
 $\verb|https://doi.org/10.1111/ECI.13259|$
- (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.