## 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 associated to covid19 severity, interactor, druggable (approved drug available), covid19 (treatment currently being tested in COVID19 patients), cov (similar mechanism in human coronavirus)

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