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https://t.co/DF40S9biYF

Unfortunately the observed ORF8 inactivation or the nsp6 SGF deletion are both indicative of T cell depletion, yet the deletion of HV and Y suggest functional B cell immunity—specifically the HV deletion is not observed in the patient nor the ORF8

@BallouxFrancois Deactivation. The nsp6 SGF is located in an ER exposed loop that is conserved even in long passage within immunocompromised patients. The loop likely interacts with nsp3 and help antagonizing cellular autophagy. And human-like B cell immunity does not cause deletion here.

@BallouxFrancois Cellular autophagy help display peptides on MHC class II molecules, and ORF8 removed MHC class I molecules. The loss of both functions suggest the host cytotoxic T cell immunity is not functional yet the S deletions are consistent with B cell immunity in an altered host

@BallouxFrancois Environment. As the long covid-associated immnocompromisation was not found to cause either SGF deletions (or any deletions) in ORF1ab nor does it inactivate ORF8, Cytotoxic T cells are functional enough in these patients to require both functions to remain intact.

@BallouxFrancois It can not be HIV since that https://t.co/yKJIxeSzlf depletes helper T cells instead of cytotoxic T cells https://t.co/h0aN2vnkLk ,ironically creating a patient condition that is B-cell deficient but not T-cell deficient.

@BallouxFrancois It just happened that CD8 knockout mice are https://t.co/AAz9fV5p4A “deficient in functional cytotoxic T-cells; however, helper T-cell development and function is comparable to normal.” And are models for both vaccination and challenge trials for LAV vaccines due to specific

@BallouxFrancois Serum B-cell immunity associated with these animals. Combined with evidence of accelerated viral dynamics evident of a non-human host, and the observation that P681H, that is not observed in immunodeficient patient passage but mimics the S1-S2 sequence of MHV, removing a heparan

@BallouxFrancois Sulfate binding motif in the S1-S2, https://t.co/nBCMX6RPGD
Which happened to be a requirement for human infection fitness,
https://t.co/Ytdb1hkZdU
Also suggest a mouse host (which hosts non-Heparan sulfate binding MHV A59 and other non-cell passaged MHV strains)

being likely.

@BallouxFrancois https://t.co/k1ViIDUHCq
Notice that for this other case the same kind of deletion—multiple AAs in the S position 144 and no deletion at S position 69-70, and a single deletion in the nsp1 removing a single Methionine residue, was found. This indicate functional B and T cell

@BallouxFrancois Immunity during passage, and the nsp6 SGF and ORF8 are likewise kept intact. The S1-S2 continues to bind Heparan Sulfate in this case, confirming it’s importance for fitness of infection in the human host. In this case the N501Y did not occur.

@BallouxFrancois The persistent infected immunocompromised patient scenario simply don’t fit with the UK isolate’s heightened sensitivity to cytotoxic T cell and evasion of B cell immunity. The GTNGTKR glycan loop being affected also suggest CTLR being different jn the passage host than humans.

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