Transcriptional profiling of immune and inflammatory responses in the context of SARS-CoV-2 fungal superinfection in a human airway epithelial model

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Context

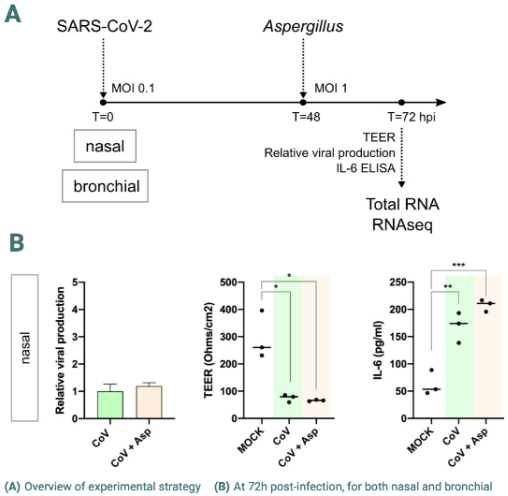
- Fungal superinfections can affect the course and severity of respiratory viral infections

- Several reports indicating high prevalence of Aspergillus superinfections associated with COVID-19

=> Reasons for increased vulnerability to Aspergillus in COVID-19 patients?

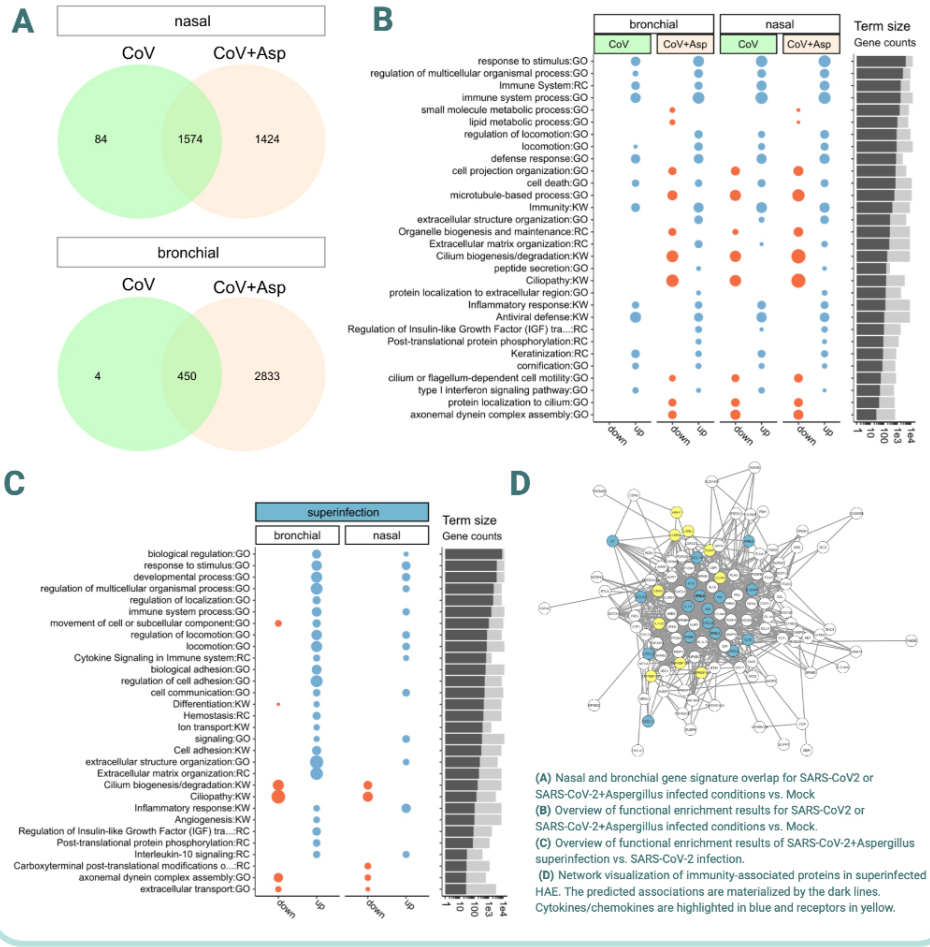
=> Contribution of Aspergillus to SARS-CoV-2 related lung inflammation and COVID-19 pathophysiology?

Experimental strategy



(A) Overview of experimental strategy **(B)** At 72h post-infection, for both nasal and bronchial HAE model, the relative viral production (intracellular) was determined using RTqPCR, and the impact of infection on epithelium integrity was monitored by measure of the transepithelial resistance (TEER Ohms/cm2). IL-6 was measured at the apical using a specific ELISA assay.

Results



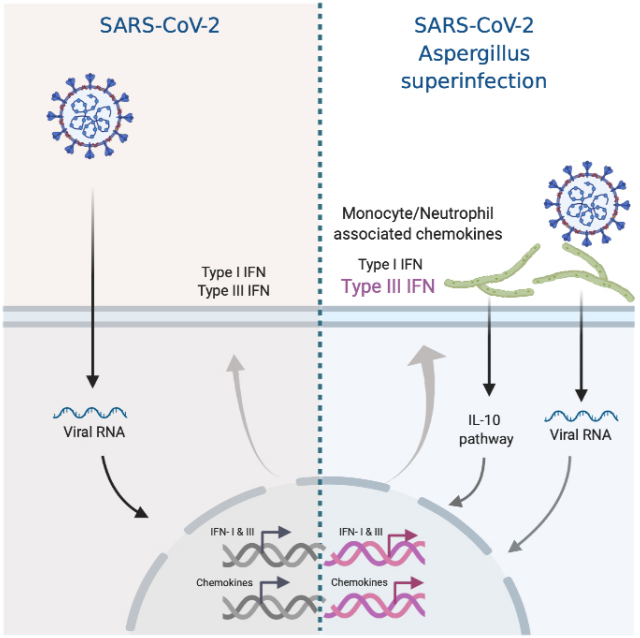
(A) Nasal and bronchial gene signature overlap for SARS-CoV2 or SARS-CoV-2+Aspergillus infected conditions vs. Mock
(B) Overview of functional enrichment results for SARS-CoV2 or SARS-CoV-2+Aspergillus infected conditions vs. Mock.
(C) Overview of functional enrichment results of SARS-CoV-2+Aspergillus superinfection vs. SARS-CoV-2 infection.
(D) Network visualization of immunity-associated proteins in superinfected HAE. The predicted associations are materialized by the dark lines. Cytokines/chemokines are highlighted in blue and receptors in yellow.

Key findings

Unique transcriptional footprints of superinfection
- imbalanced type I/type III IFN
- monocyte and neutrophil associated chemokines

SARS-CoV-2 -induced immunomodulation
=> Favorable context for severe forms of Aspergillosis

Treatments targeting COVID-19 inflammatory response
=> Counter-productive for the management of Aspergillosis?



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The authors declare that they have no conflict of interest.
Preprint available: **https://www.biorxiv.org/content/10.1101/2020.05.19.103630v1**