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. SARS-CoV-2
B. Aspergillus
C. MOI 0.1
D. MOI 1
E. Y45
F. Y72
G. TEER
H. Relative resistance
I. Total RNA
J. RNASeq

(A) Overview of experimental strategy. (B) At 72 h post-infection, for both nasal and bronchial HAE model, the relative viral production (Transwell) was determined using RT-qPCR and the impact of infection on epithelial integrity was monitored by measuring the transwell resistance (TEER; Ohms/cm²). IL-8 was measured at the apical using a specific ELISA assay.

Results

A. nasal
B. bronchial
C. CoV
D. CoV-Asp
E. Total RNA
F. RNASeq

(A) N statistical samples were analyzed. (B) Bar plots showing the relative viral production (Transwell) for both nasal and bronchial HAE model. (C) IL-8 levels were measured at the apical using a specific ELISA assay.

Key findings

Unique transcriptional footprints of superinfection
- Imbalanced type I/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?