# Mutual inhibition of antifungal and antiviral responses during fungal-viral coinfection

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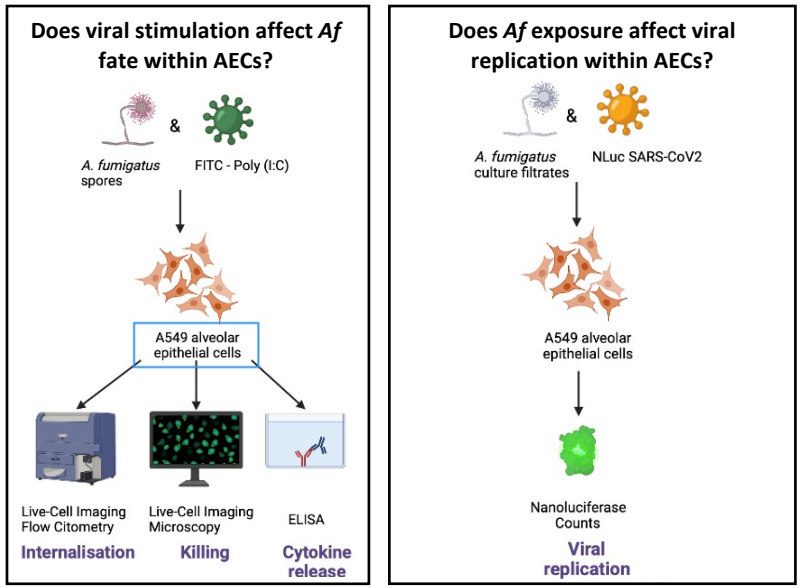
- *Aspergillus fumigatus (Af)* is a causative agent of lethal secondary infections in patients with severe viral infections caused by such as cytomegalovirus, influenza and SARS-CoV2.
- Airway epithelial cells (AECs) play a crucial role in host defence against *Af* by internalising and killing inhaled conidia.
- AECs responses leading to conidia clearance are aberrant in patients susceptible to aspergillosis.

**Hypothesis: Dysregulation of airway epithelial responses during fungal-viral coinfection are a potent driver for aspergillosis**

## Methods




## Results

### Viral mimickers impair antifungal activities of AECs

- Viral stimulation increases *Af* spore uptake by AECs **(FIG. 1A)** while intracellular spore killing was significantly reduced **(FIG. 1B)**.

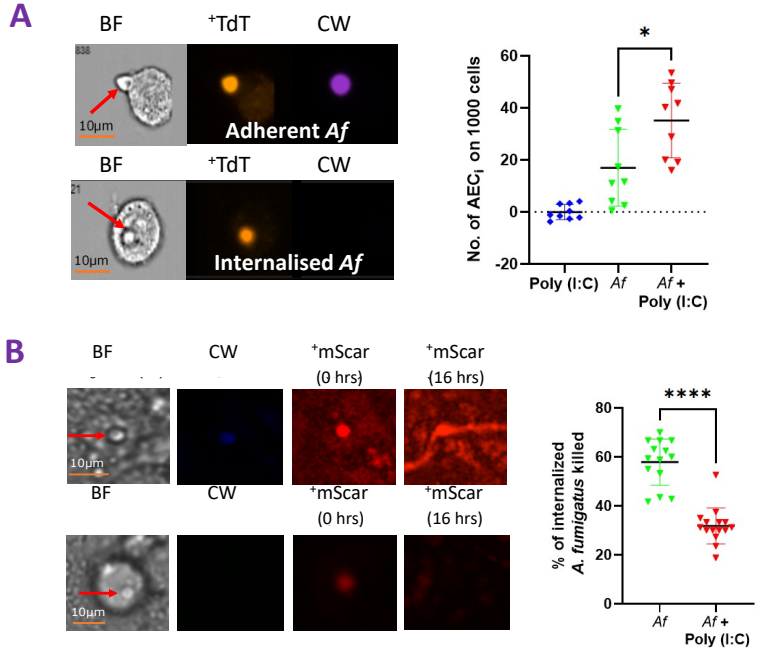



**FIG. 1:** (A) Increased *Af* spores internalisation by AECs in the presence of Poly (I:C) as determined by live cell flow cytometry (B) Live cell imaging microscopy demonstrates decreased intracellular killing of *Af* in the presence of Poly (I:C). * P < 0.05; ****P < 0.0001

### *Af* promote viral replication within AECs

- Exposure of AECs to viral and *Af* challenge abolishes type I Interferon production **(FIG. 2A)**.
- *Af*-induced SARS-CoV2 replication within AECs is strain dependent **(FIG. 2B)**.

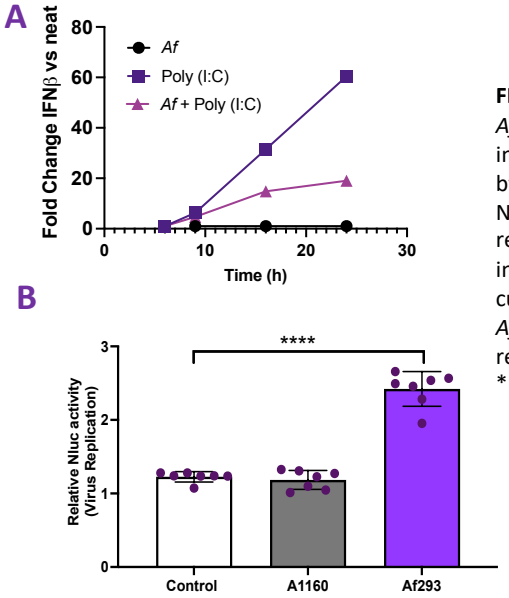



**FIG. 2:** (A) Germinated *Af* spores impair viral–induced IFN responses by AECs (B) Increased Nluc SARS-CoV2 replication within AECs in the presence of culture filtrates from *Af* A1160 and Af293 reference strains. ****P < 0.0001

### Conclusions

i. There is a mutual inhibition of antiviral and antifungal responses of AECs during coinfection.

ii. Some *Af* strains might be better adapted to cause disease in the context of viral infections.

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