Aspergillus fumigatus strains are adapted to the lung environment in a case of chronic pulmonary aspergillosis

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Background

- Chronic pulmonary aspergillosis (CPA) is a neglected lung condition caused by colonisation of the lungs by the opportunistic fungus *Aspergillus fumigatus*.
- CPA affects more than 3 million people worldwide carrying 5-year mortality ranging from 30-70%.
- CPA is associated with greater morbidity and mortality than invasive aspergillosis.
- Because of the frequency of relapse, antifungal treatment is often long-term leading to negative side effects and the development of resistance.

Objective:

The aim of this study was to investigate in host adaptation of *Aspergillus fumigatus* in CPA.

Methods

- Thirty *Aspergillus fumigatus* isolates were recovered from a CPA patient from 2008-2014.
- Whole genome sequencing was performed to identify phylogenetic association between strains over time.
- An *in vitro* model using alveolar epithelial cells (A549) was used to describe fluctuations in the response of the lung epithelium to five of the *A. fumigatus* isolates recovered from the CPA patient compared to 3 *A. fumigatus* strains normally used as a wild type in infection studies (A1163, ATCC 90240 and ATCC 46645).
- Differences in epithelial cell detachment, fungal burdens and cytokine production (IL-8 and IFN γ) were evaluated.

Results

- Aspergillus fumigatus* strains isolated from the CPA patient were grouped into a common clade, although there was genetic variability within strains (FIGURE 1).

- Epithelial cell desquamation of A549 cells exposed to *A. fumigatus* strains derived from the CPA case, was 20 % higher than controls ($P < 0.01$). (FIGURE 2)

Figure 2: Percentage of epithelial cell detachment in A549 cells challenged with 8 different *A. fumigatus* strains for 24 h. ** $P < 0.01$

- Fungal burdens were 5-10 times higher in A549 cells challenged with *A. fumigatus* CPA strains than controls ($P < 0.05$). (FIGURE 3)

- IL-8 and IFN γ concentrations in cell supernatants from A549 cells challenged with *A. fumigatus*-CPA strains were lower than in those challenged with control strains ($P < 0.01$). (FIGURE 4)

Figure 4: IL-8 and IFN γ levels secreted by A549 cells in response to 8 different *A. fumigatus* strains for 24 h. ** $P < 0.01$

CONCLUSIONS:

- Aspergillus fumigatus* strains involved in a single case of CPA are phylogenetically associated.
- The strains isolated from the CPA-case were able to produce a higher percentage of epithelial cell damage than *A. fumigatus* strains used as controls. Therefore decreasing the ability of the epithelium to function as a physical barrier and, facilitating *A. fumigatus* growth and limiting the immune host response.
- Further research is needed to characterise the virulence properties of these strains.