Differential response of the bronchial epithelium and macrophages to *Aspergillus fumigatus* allergens

Juan Carlos Soto-Debran¹, Michel Monod², David W Denning¹, Paul Bowyer¹, **Sara Gago¹**

1) University of Manchester, 2) Laussane University Hospital, Correspondence: sara.gago-2@manchester.ac.uk

Background

- Sensitization to fungi can lead to the exacerbation and complication of respiratory conditions such as asthma in predisposed patients.
- Extracellular proteases and toxins from *Aspergillus fumigatus* are involved in host cells activation leading to cell cytotoxicity, generation of cytokines and facilitation of allergic sensitization.
- However, little is known about the normal response to epithelial cells and macrophages to purified fungal allergens.

Methods

- 16HBE bronchial epithelial cells and monocyte-derived macrophages (THP-1) were exposed to *A. fumigatus* spores, crude protein extracts and the recombinant purified allergens Asp f 1, Asp f 5, DppV and AfuS28 for 24 hours.
- Cell damage was measured by lactate dehydrogenase release and epithelial cells desquamation.
- Concentrations of IL-6, IL-8, IL1 β and TNF α in cell culture supernatants were evaluated by ELISA.

Objective:

To describe which specific *A. fumigatus* allergens are able to induce inflammatory responses in epithelial cells and macrophages.

Results

- **FIGURE 1:** Cell damage produced by *Aspergillus fumigatus* proteases, total lysates and hyphae in (A) 16HBE bronchial epithelial cells and (B) THP-1 monocyte-derived macrophages. Damage was measured as percentage of cell detachment and LDH release in bronchial epithelial cells and macrophages respectively. *** P < 0.001, **** P < 0.0001

- *Aspergillus fumigatus* hyphae and Asp f 5 are major drivers of cell damage in both, epithelial cells and macrophages (P < 0.01). **FIGURE 1**

- **FIGURE 2:** TNF- α , IL-8, IL-6 and IL-1 β production by 16HBE bronchial epithelial cells and THP-1 monocyte-derived macrophages challenged with *A. fumigatus* allergens, crude protein extracts and spores. * P < 0.05 ** P < 0.01, *** P < 0.001, **** P < 0.0001- Red = 16HBE bronchial epithelial cells, Blue = THP1 monocyte-derived macrophages

- THP-1 monocyte-derived macrophages secreted more than 4-fold IL1 β , TNF α and IL-6 than unchallenged controls in response *A. fumigatus* spores, Asp f 1 and Asp f 5 (P < 0.01).
- 16HBE bronchial epithelial cells released more than 2-fold IL-6 and IL-8 in response to the purified *A. fumigatus* allergens DppV and Asp f 5 than unchallenged controls (P < 0.001).

CONCLUSIONS:

- The mechanisms of epithelial cell and macrophage activation by fungal allergens are protein-dependent.
- Asp f 5 can activate both epithelial cells and macrophages while Asp f 1 predominantly activates macrophages and DppV epithelial cells.
- Further research is needed to investigate the role of these fungal allergens in modulating the response of the bronchial epithelium and macrophages in patients with fungal allergy.