1) What mediates anti-fungal allergic disease?

- The fungus Aspergillus fumigatus (Af) is a major pathogen of the human airways. Af-sensitisation can lead to fungal allergic airway disease which accounts for 90% of the 500,000 annual asthma related deaths.

Hypothesis: Myeloid innate cells dictate the type-2 and type-17 balance that mediates anti-Af sensitisation that underpins all asthma disease.

2) Does repeated exposure to live Aspergillus spores induce type-2 and type-17 allergic inflammation?

Repeated exposure to Aspergillus drives type-2/type-17 inflammation:

- WT mice were exposed to Af fumigatus spores (Af, strain: D410, 4 x 10⁸ spores per dose) or PBS, and BAL or lung tissue cells were harvested as indicated.

3) Is anti-Af dependent on DC/MΦ to mediate type-2 and type-17 CD4+ T cell responses?

- CD11c+ cells are required to mediate anti-Af type-2/type-17 inflammation. Mice were exposed to Af spores (i.n.) and harvested at d5.

4) Are distinct DC subsets important for anti-Af type-2 vs type-17 allergy?

5) Does type-2/type-17 inflammation underpin human anti-fungal allergic disease?

Patient groups:
- Healthy (no asthma)
- Mild Asthmatics
- Severe Asthmatics
- ABPA

Tissue collection: Sputum, Cellar tissue

Experimental plan:
- Assessed by flow cytometry. Dead cells, doublets and CD45- cells excluded. Bar graphs show mean ± SEM (n=3-4 per group).

6) Summary

Figure 3. Single-cell RNAseq reveals a MOL2+ DC cluster that mediates anti-Af type-2, but not type-17, allergic responses.

- Single-cell (CD11c+MH-2+) libraries from indicated mice were generated (10x platform).
- BAL cells and lung CD4+ T cell cytokine production from Af-exposed and MOL2+ cell deleted mice.