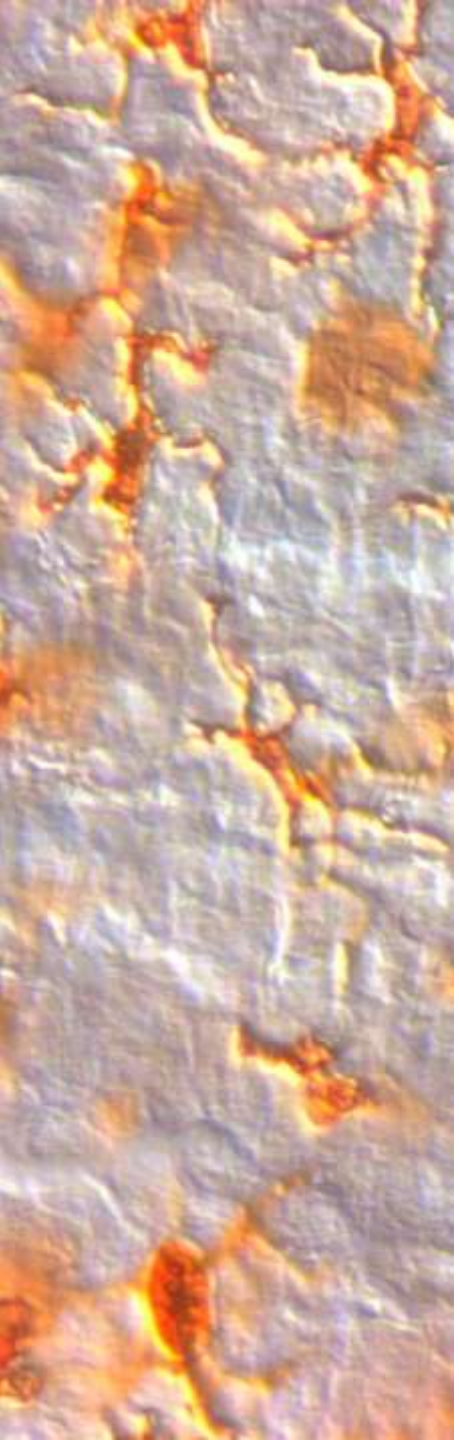

ESR12 (WP3):

The role of flame retardants in indoor dust in potentiating allergic responses to inhaled allergens

Collaboration AMC and VU:

Leonie van Rijt, PhD
AMC Amsterdam
The Netherlands

Timo Hamers, PhD
IVM VU Amsterdam
The Netherlands

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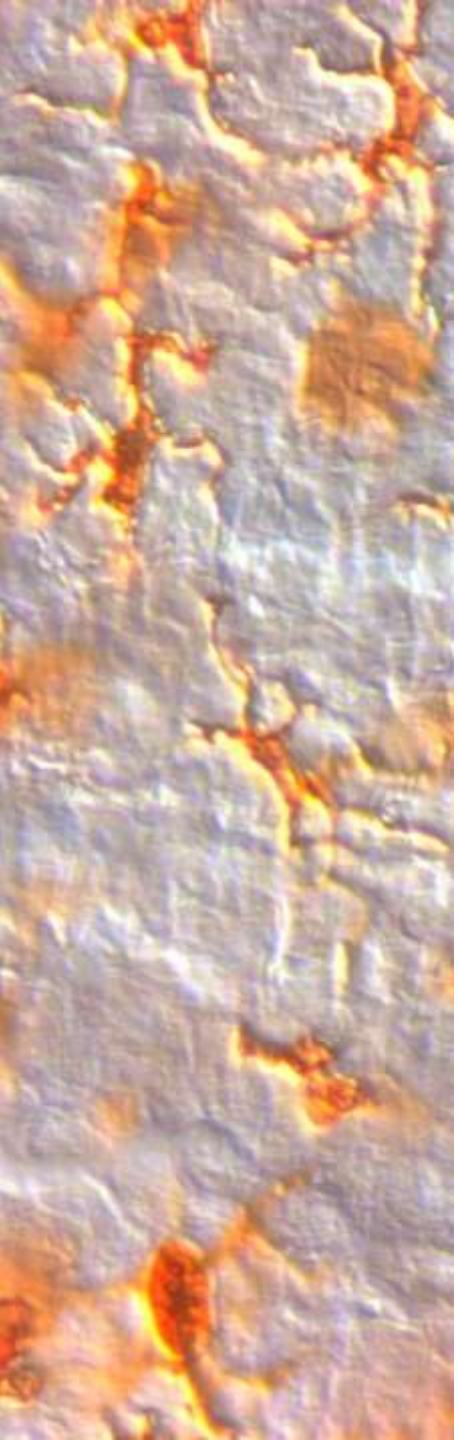

Rationale:

*House dust mite allergen one of the most common allergens for the induction of allergy

*A tremendous increase in allergy the last decades → exact cause is still unknown (hygiene hypothesis, pollutants..)

*In allergy the immune system reacts with an aberrant immune response to allergens

*Allergen presenting cells process many signals and skew the allergen specific T cells in a specific subset

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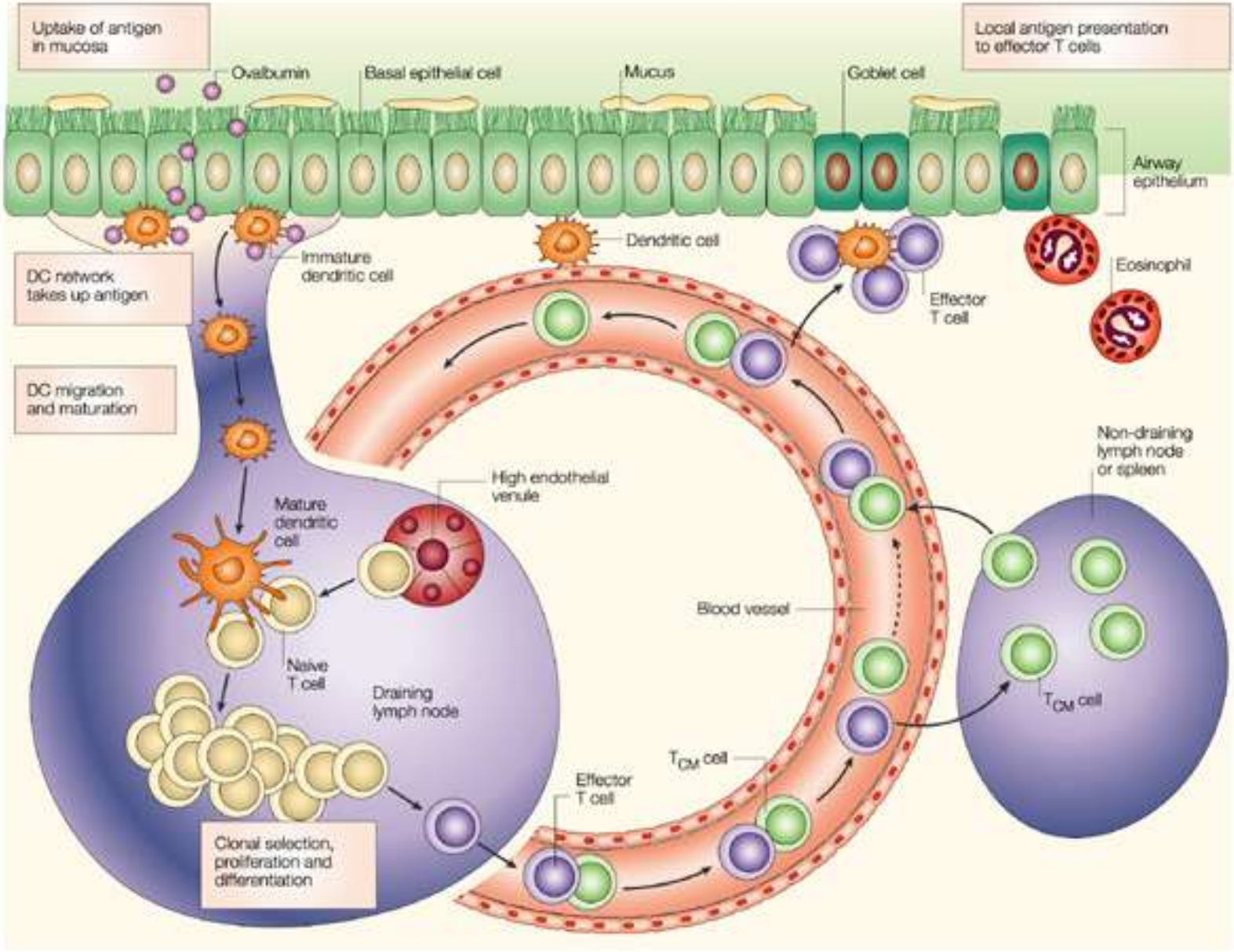
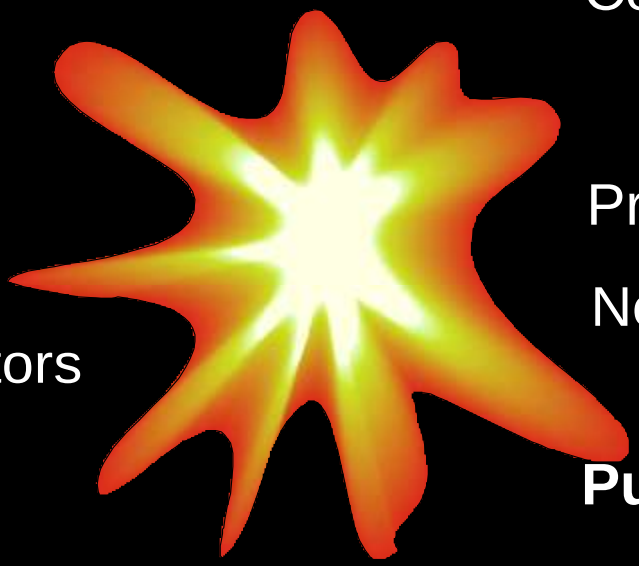

Uptake of antigen in mucosa
Local antigen presentation to effector T cells
Ovalbumin
Basal epithelial cell
Mucus
Goblet cell
Airway epithelium
Dendritic cell
Immature dendritic cell
Eosinophil
DC network takes up antigen
Effector T cell
DC migration and maturation
Non-draining lymph node or spleen
High endothelial venule
Mature dendritic cell
Blood vessel
Naive T cell
Draining lymph node
T_{CM} cell
T_{CM} cell
Effector T cell
Clonal selection, proliferation and differentiation

Innate sensing of danger : DC express ancient receptors

Toll like receptors 1-9

Protease activated receptors

Complement receptors



Prostanoid receptors

Neuropeptide receptors

C-type lectin receptors
- Dectin
- MMR
- DEC-205
- BDCA-2
- ....

Purinergic receptors

Receptors X for
uric acid
heat shock proteins
....

Aryl hydrocarbon receptor
Estrogen receptor

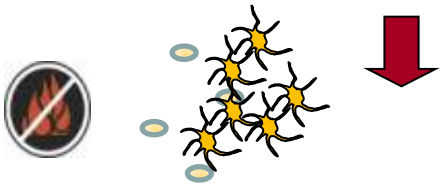
Microbial patterns

Damage associated patterns

Experimental setup

Bone marrow isolation + 10 days GMCSF

Dendritic cells; pulse with antigen (OVALBUMIN)
Expose to flame retardant



FACS analysis for molecules involved in
T cell interaction + supernatant for cytokine production

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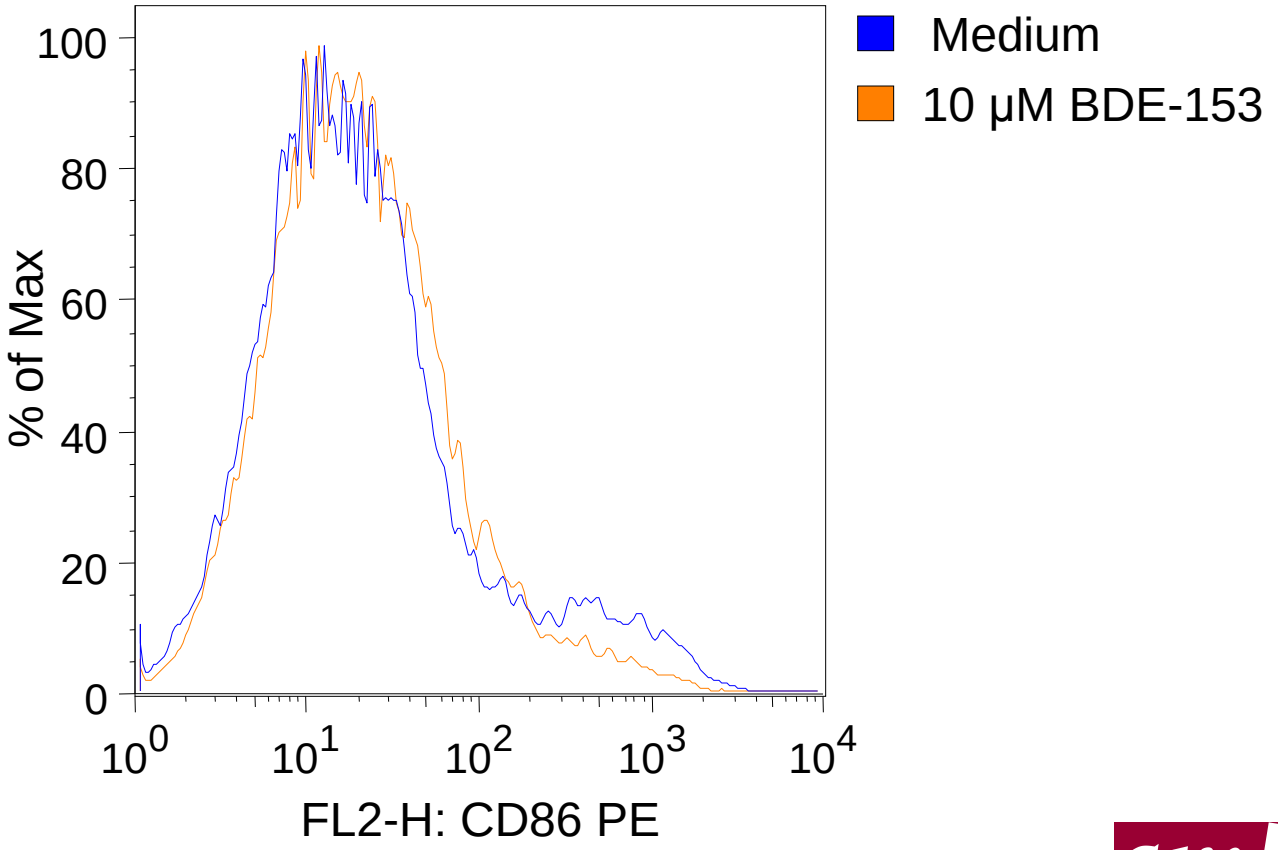
Preliminary results: BDE-153

Effect on dendritic cell phenotype



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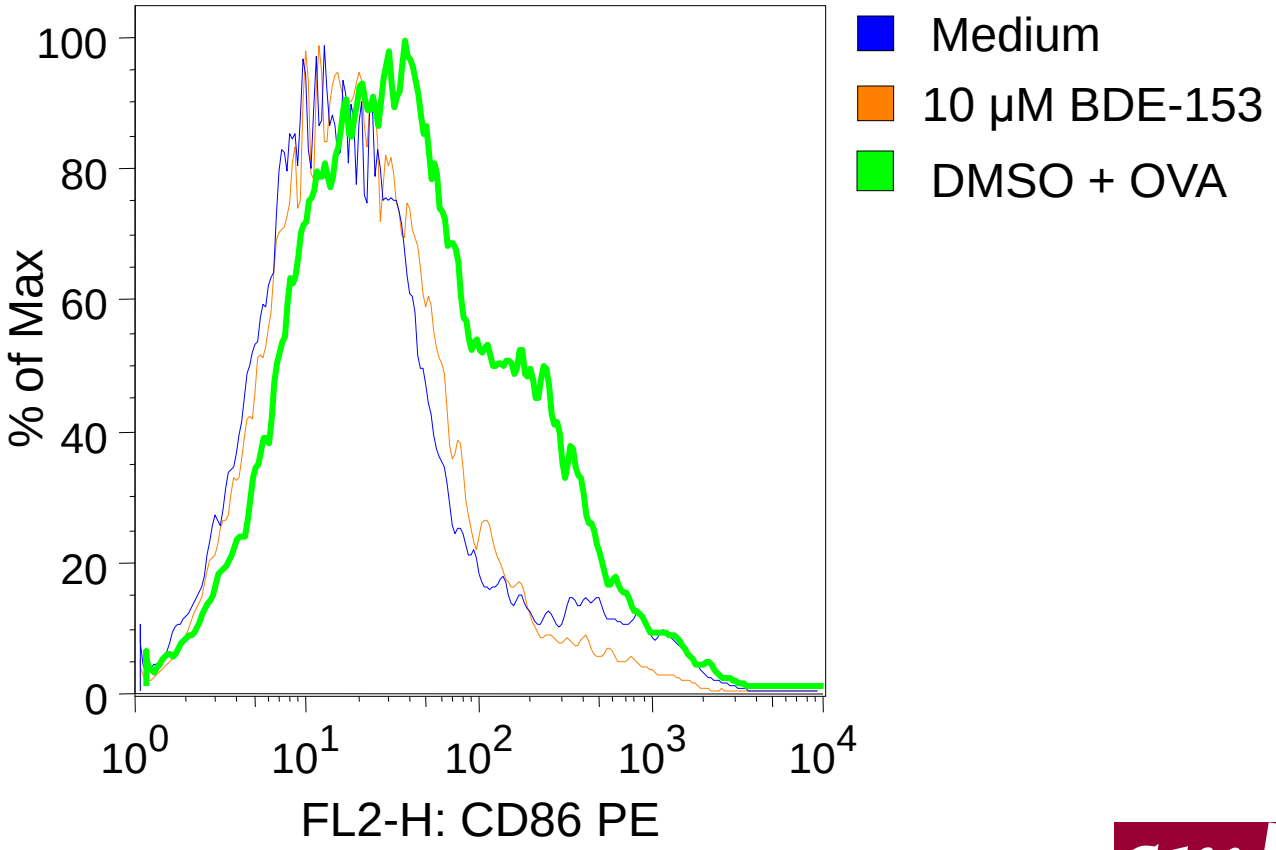
Preliminary results: BDE-153

Effect on dendritic cell phenotype



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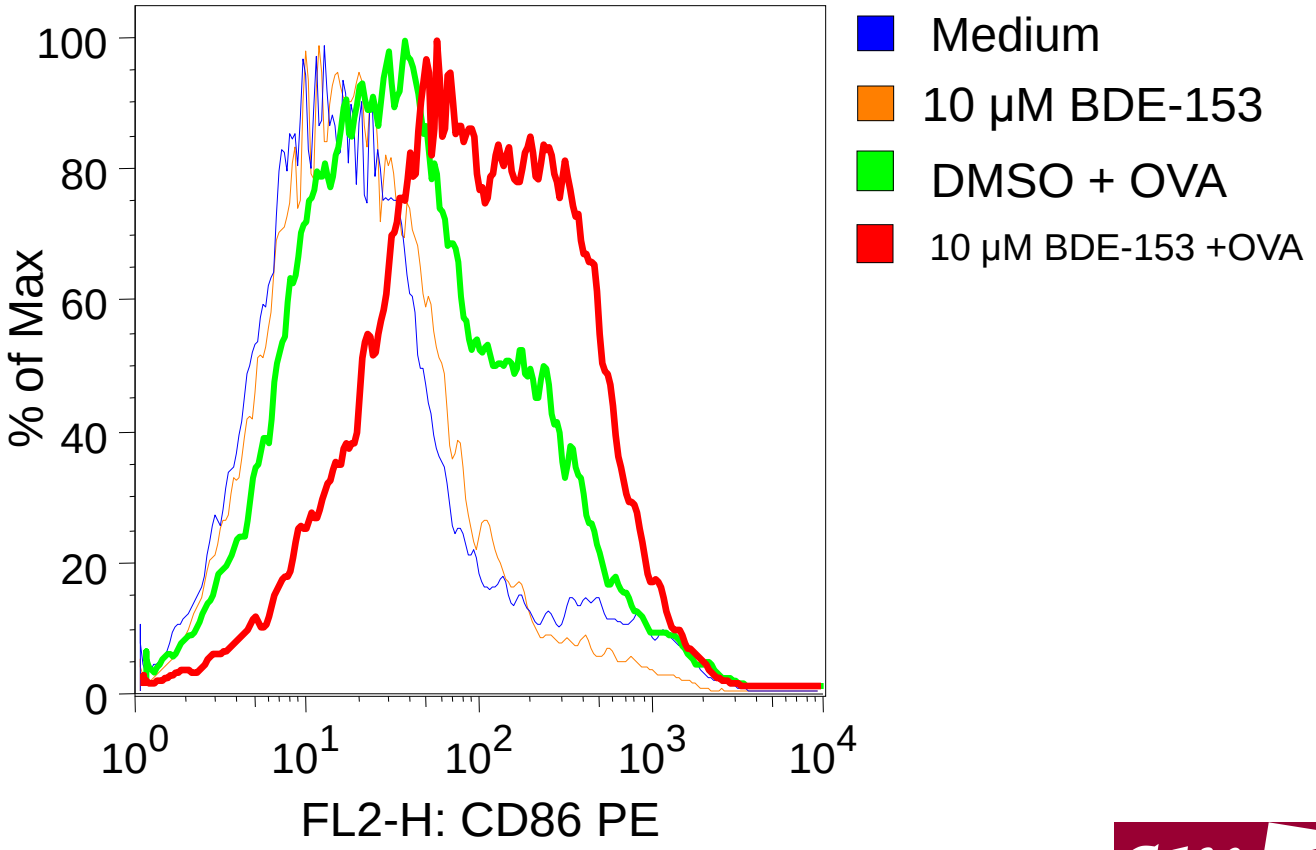
Preliminary results: BDE-153

Effect on dendritic cell phenotype



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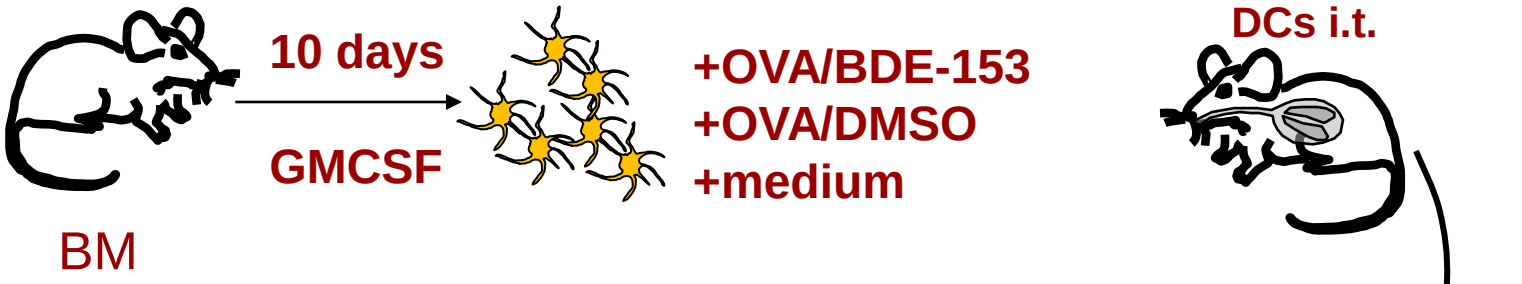
Does BDE-153 aggrevate the adaptive immune response to inhaled OVA via enhanced maturation of DCs?



BAL
Airway histology
Serum IgE
Ex vivo restimulation of LN

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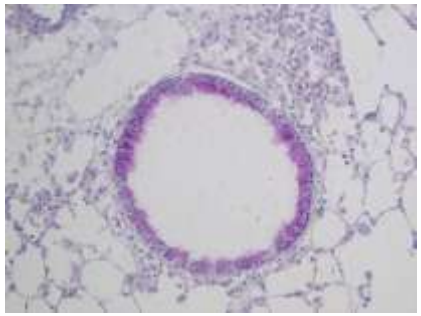
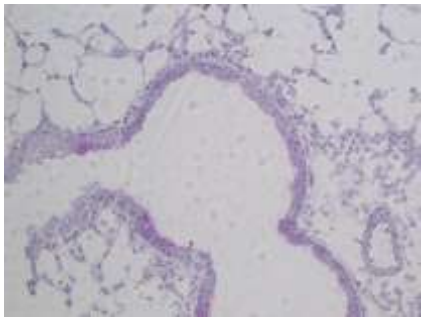
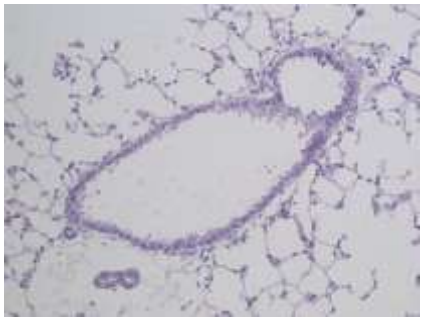
Lung histology



OVA BDE-153



OVA DMSO



medium

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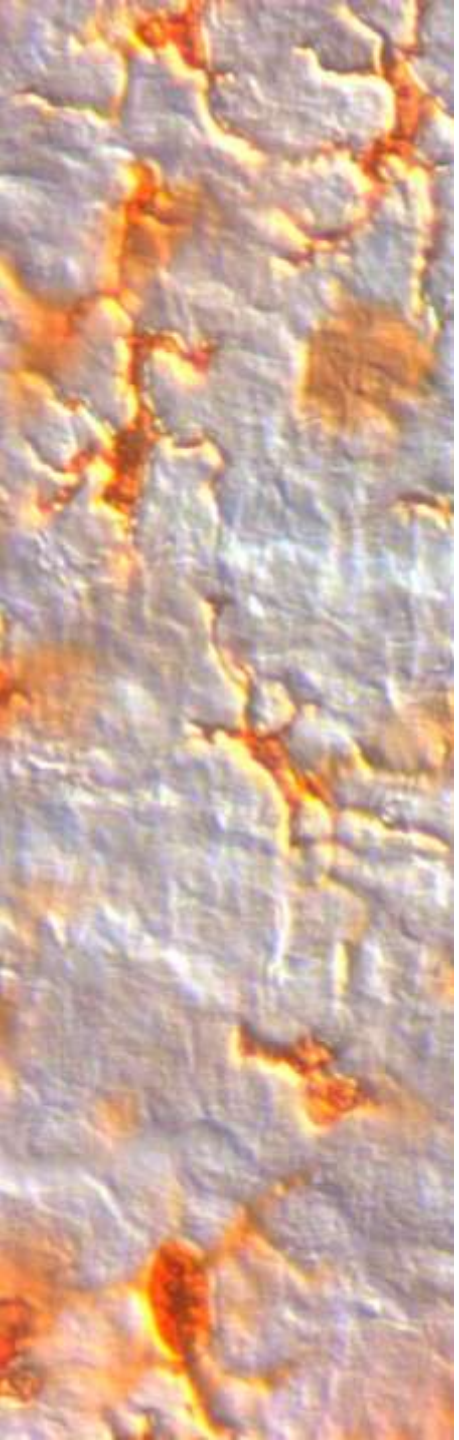

Researcher recruitment:

-Placed an additional advert at *"www.academic transfer.nl"* and AMC vacancy site

-Response:

- via academic transfer 7 candidates
- via EU website 4 candidates

-Overall:

- 1 suitable candidate (Reka Nemes, Hongary)

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