Development of an alveolar in vitro model to assess the respiratory sensitizing potential to inhaled compounds

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INTRODUCTION

THE GLOBAL BURDEN OF ASTHMA: CURRENT ESTIMATES

334 million people have asthma.

14% of the world’s children experience asthma symptoms.

8.6% of young adults (aged 18-45) experience asthma symptoms.

4.5% of young adults have been diagnosed with asthma and/or are taking treatment for asthma.

The burden of asthma is greatest for children aged 10-14 and the elderly aged 75-79.

Asthma is the 14th most important disorder in the world in terms of the extent and duration of disability.

http://www.globalasthmareport.org
AVAILABLE MODEL TO ASSESS RESPIRATORY SENSITIZATION

→ No existing assay for respiratory sensitization

→ Local Lymph Node Assay (LLNA) used for skin sensitization
ALVEOLAR IN VITRO MODEL TO ASSESS RESPIRATORY SENSITIZATION

Tetraculture system mimicking the alveolar barrier:

Inflammatory effects of NPs at the ALI (Klein et al. 2013)

Sensitizing potential of chemicals and NPs at the ALI

METHODS

Aerosol exposure

24h incubation

Markers

Cytokines: CCL20, GM-CSF, IL-10, MCP-1, RANTES…

Gene expression: IL1R1, CIITA, HLA-DRA, HLA-DMA…

Cell surface markers:
CD54, CD86, TSLPr, IL7ra, OX40L
Expression of CD54 and TSLPr on THP-1 cells in the tetraculture
RESULTS

Chemical respiratory sensitizers: ≠ Chemical respiratory irritants: ≠ Protein allergens:

- CIITA
- IL1R1-1
- TSLPr
- CD54
- IL10
- MCP-1
- GM-CSF

- OX40L
- IL1R1-1
- MCP-1
- GM-CSF
### Fetal Bovine Serum (FBS)

- Essential components for cell proliferation and maintenance (such as hormones, vitamins, growth factors…)
- Obtained from blood of living calf fetus

<table>
<thead>
<tr>
<th>Cell line</th>
<th>Medium</th>
<th>Serum</th>
<th>Supplement</th>
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</thead>
<tbody>
<tr>
<td>A549</td>
<td>DMEM¹</td>
<td>10% (v/v) FBS</td>
<td>10% Penicillin-Streptomycin</td>
</tr>
<tr>
<td>THP-1</td>
<td>RPMI-1640²</td>
<td>10% (v/v) FBS</td>
<td>25 mM HEPES; 50 μM β-mercaptoethanol; 10% Penicillin-Streptomycin</td>
</tr>
<tr>
<td>EA.hy926</td>
<td>DMEM³</td>
<td>10% (v/v) FBS</td>
<td>25 mM HEPES; 10% Penicillin-Streptomycin</td>
</tr>
</tbody>
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**Implementation of 1R principle for an in vitro alveolar model**
THANK YOU
MERCI
VILMOLS MERCI
VIELEN DANK