In vitro model for the prediction of respiratory sensitization of inhaled chemicals and protein allergens

Weber P. 1*, Chary A. 1,2, Saibene M. 1, Serchi T. Cambier S. Moschini E. Contal S. Hennen J. Ezendam J. Blömeke B. Gutleb A.C. Userber P. 1 (1)

¹ Environmental Research and Innovation (ERIN) Department, Luxembourg Institute of Science and Technology (LIST), Luxembourg. ² Department of Environmental Toxicology, Trier University, Germany.

3 Centre for Environmental Protection, National Institute for Public Health and the Environment (RIVM), The Netherlands. * pamina.weber@list.lu

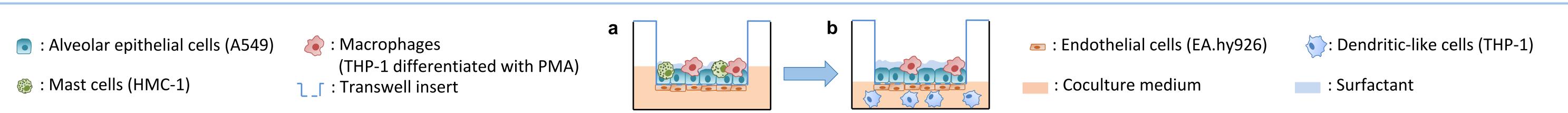
AIM:

- Exposure to chemicals such as acid anhydrides or fragrances can induce respiratory allergies.
- Complex in vitro co-culture systems represent valuable tools to understand the mechanisms involved in lung sensitization.
- At present, no in vitro model is validated to reliably detect chemical respiratory sensitizers.

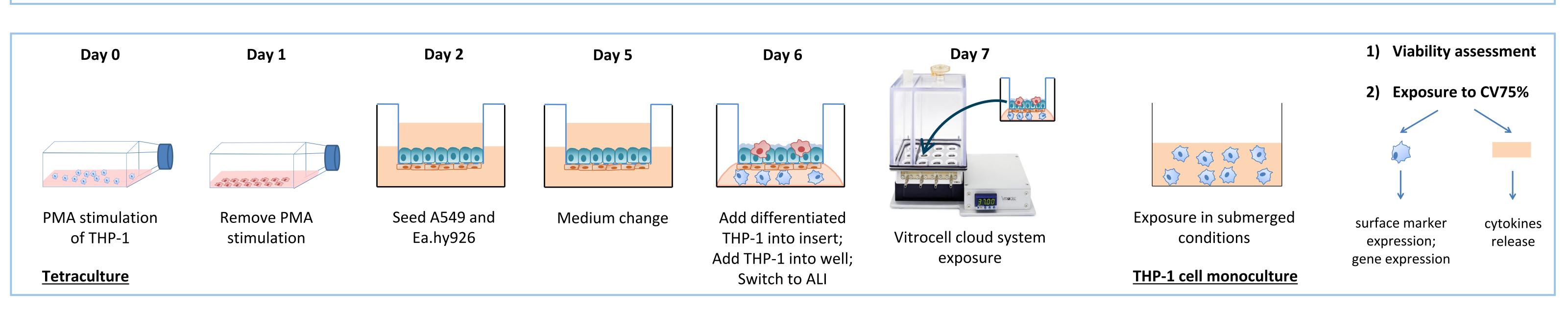
Adaptation of a 3D-co-culture system previously developed by us (Klein *et al.* 2013).

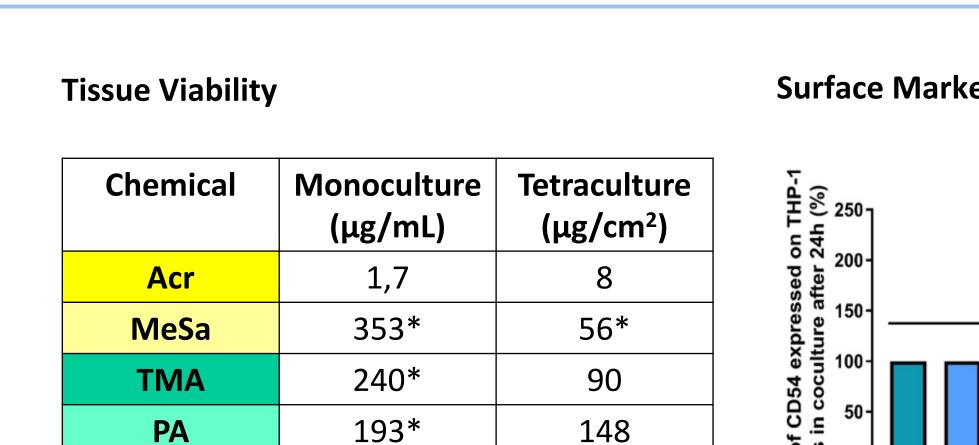
Inclusion of dendritic cells to study respiratory sensitization processes.

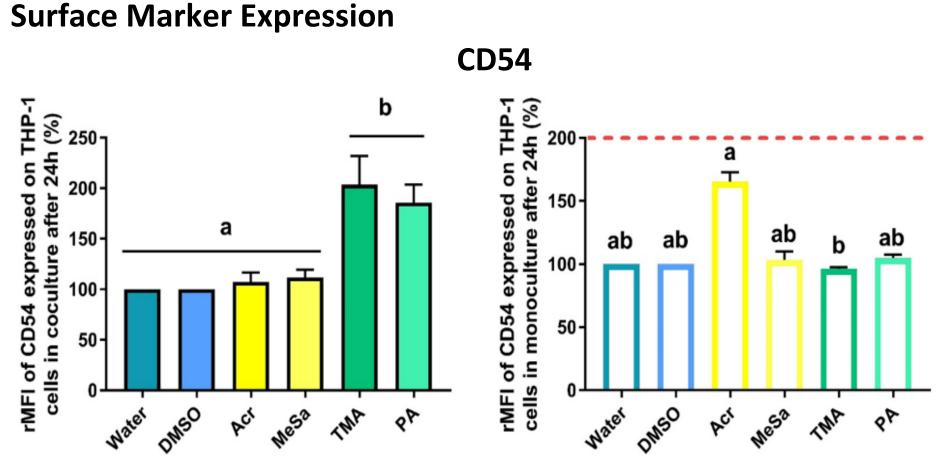
Identification and evaluation of markers to assess the respiratory sensitizing potential of inhaled compounds.

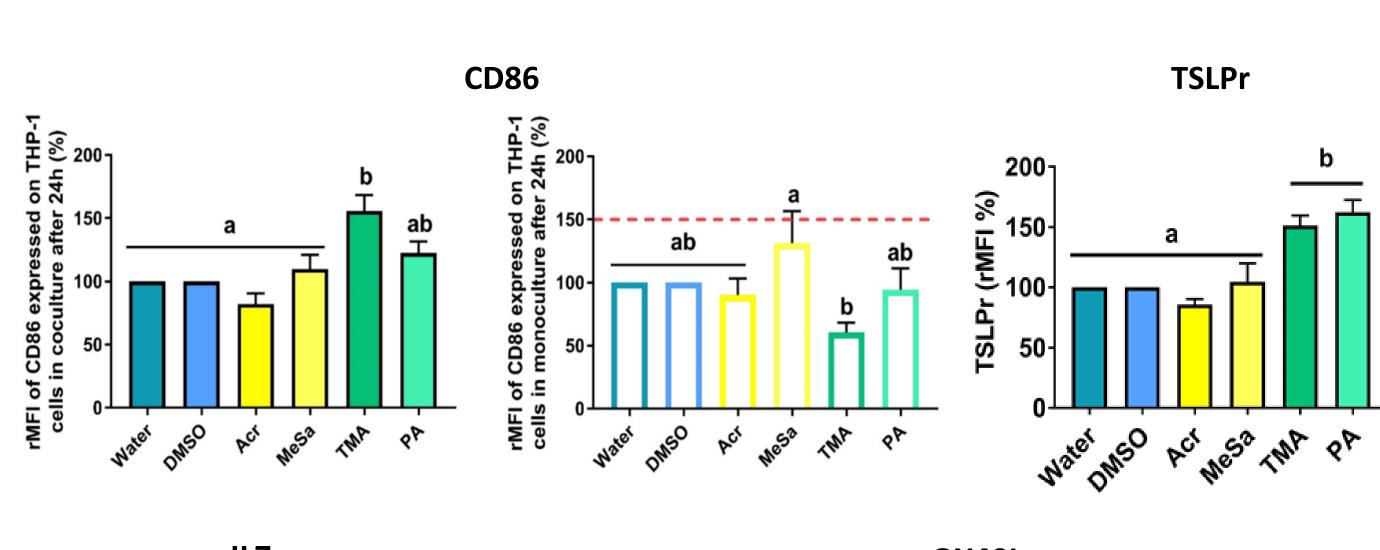


- a) Co-culture system mimicking the alveolar barrier to study cell-to-cell communication and inflammatory effects of NPs at the ALI (Klein et al. 2013, 2017).
- b) Variant of the system to study the sensitizing potential of chemicals at the ALI (Chary et al. 2017, 2019, Patent WO2018/122219 A1).

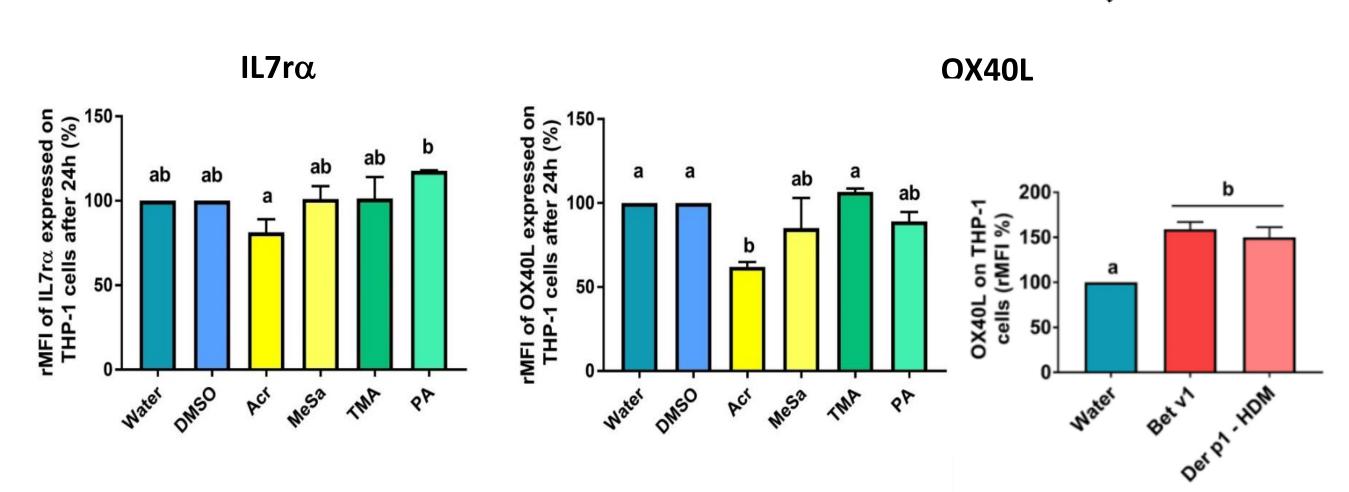








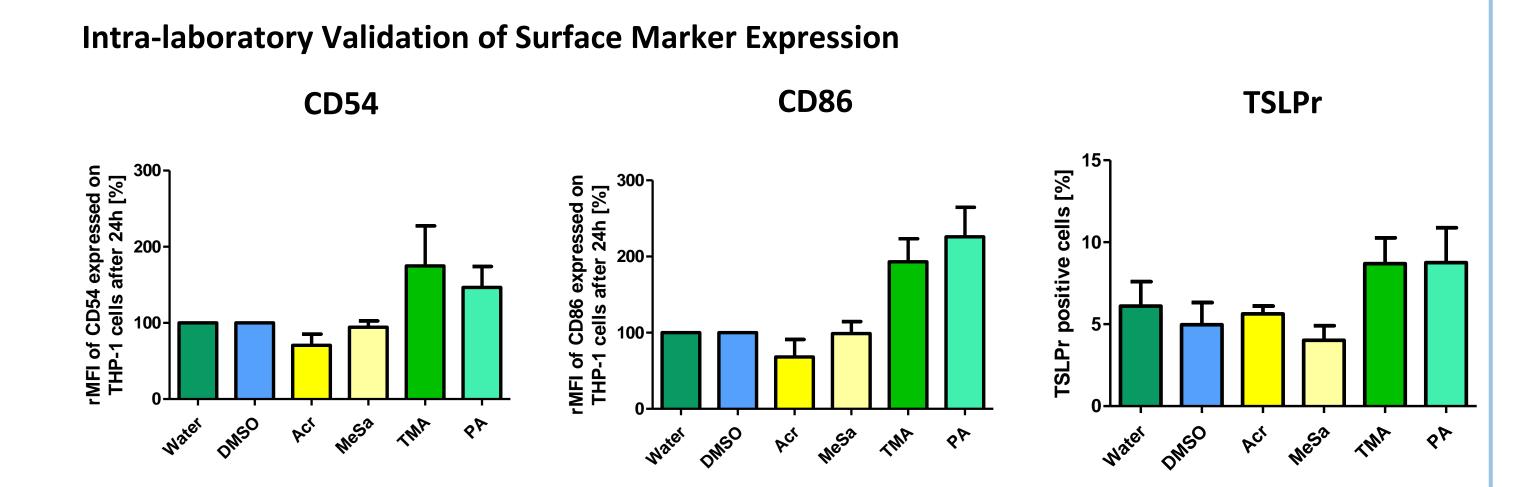
Chemical CCL20 **GM-CSF IL-10** IL-7 MCP-1 **RANTES** 1,3 0,1 0,2 0,2 0,1 Acr 1,6 MeSa 1,1 1,1 3,4 2,6 1,3 1,5 1,5 **TMA** 1,1 2,5 2,4 2 1,2 1,3 PA 1,1



Gene Expression

Cytokines Release

Chemical	CD80	CIITA	G-CFS-R	HLA-DMA	HLA-DRA	IL1R1-1	MAP2K1	MyDD88
Acr	1	-0,4	-0,3	0	0,9	-4,3	-0,3	-0,3
MeSa	2,4	0,6	1,1	1	3,6	-0,3	0,6	0,5
TMA	1,2	-1,8	-0,2	-0,4	0	1,2	0,1	-0,2
PA	0,7	-1,3	0	-0,6	-0,1	1,4	0,1	-0,5



- Better prediction of respiratory sensitizing potential of compounds using THP-1 cells in the tetraculture system compared to monoculture in submerged condition.
- Increased expression of CD54 and CD86 after exposure to the chemical respiratory sensitizers TMA and PA and decreased CD54 expression after exposure to the irritant acrolein:
 - → CD54 and CD86 could be used as a marker to discriminate irritants from chemical respiratory sensitizers!
- Increase of TSLPr expression after exposure to the chemical respiratory sensitizers TMA and PA:
 - → TSLPr could be used as a marker to identify chemical respiratory sensitizers!
- Increased secretion of specific cytokines after exposure to the chemical respiratory sensitizers TMA and PA:
 - → Panel of cytokines is able to identify chemical respiratory sensitizers!
- Increase of OX40L expression after exposure to the protein allergen HDM and Bet v1:

- Klein, S.G., Serchi, T., Hoffmann, L., Blömeke, B., Gutleb, A.C., 2013.
 An improved 3D tetraculture system mimicking the cellular organisation at the alveolar barrier to study the potential toxic effects of particles on the lung. Part. Fibre Toxicol. 10, 31. doi:10.1186/1743-8977-10-31
- Chary, A., Hennen, J., Klein, S.G., Serchi, T., Gutleb, A.C., Blömeke, B., 2018. Respiratory sensitization: toxicological point of view on the available assays. Arch. Toxicol. 92, 803–822. https://doi.org/10.1007/s00204-017-2088-5
- Chary, A., Serchi, T., Moschini, E., Hennen, J., Cambier, S., Ezendam, J., Blömeke, B., Gutleb, A. C., 2019: An in vitro coculture system for the detection of sensitization following aerosol exposure. Altex 36(X), doi:10.14573/altex.1901241. epub
- Patent WO2018/122219 A1
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