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Human lung cell co-cultures – state of the art

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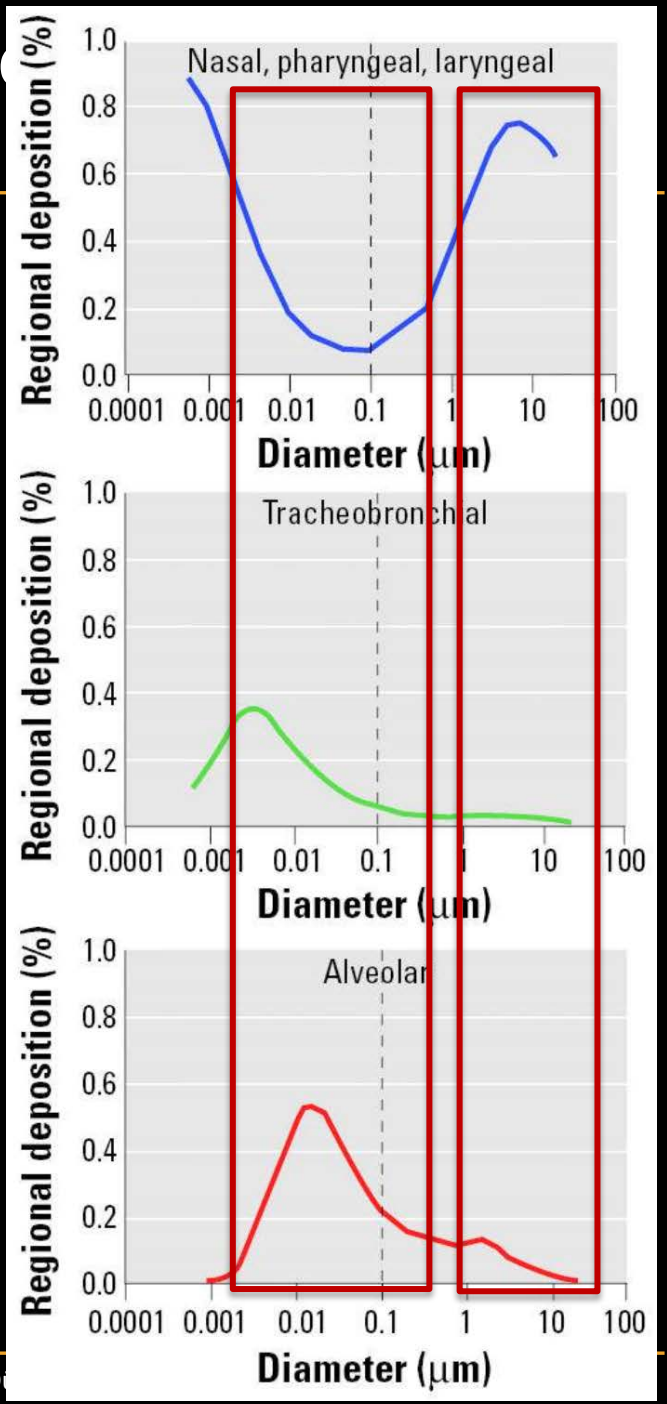
University of Fribourg
Fribourg, Switzerland

Inhalation of particles / aer

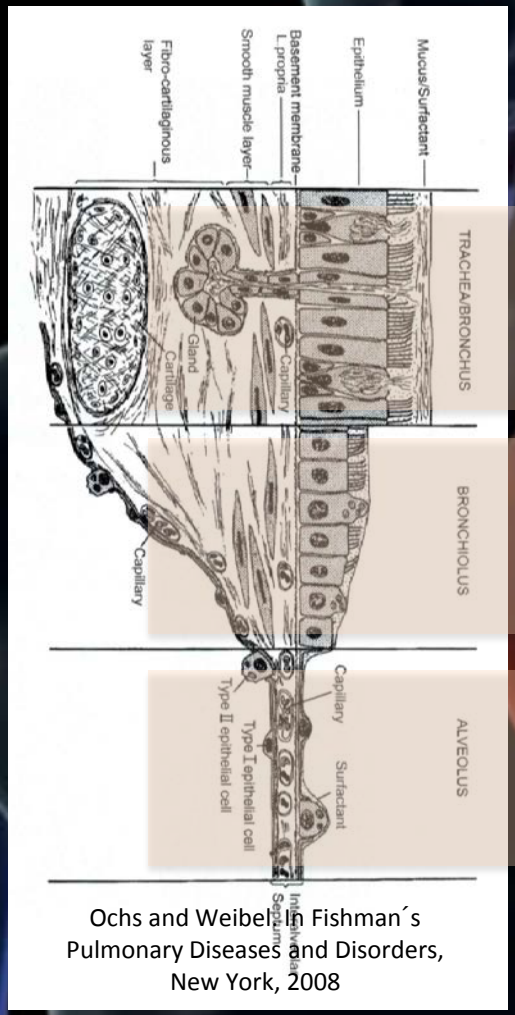
Predicted fractional deposition

Lungs and Breathing - 3D Medical Animation || ABP ©



Oberdörster et al.
Environ Health Perspect (2005)

The human lung structure



Ochs and Weibel in Fishman´s Pulmonary Diseases and Disorders, New York, 2008

Pseudostratified epithelium with ciliated epithelial cells / secretory cells

Ciliated, columnar to cuboidal epithelial cells / secretory cells

Thin, outspreaded epithelial cells / secretory cells

How to chose a cell model to study effects of particles?

Human primary cells	Human cell lines
3D Human airway epithelial models*	• Calu-3 • 16HBE14o- • BEAS-2B • NCL-H441 (Clara cell phenotype)
3D Human small airway epithelia*	
Primary alveolar type I-like cells	• A549 epithelial type II cells • Immortalized human ATII cells with ATI phenotype**

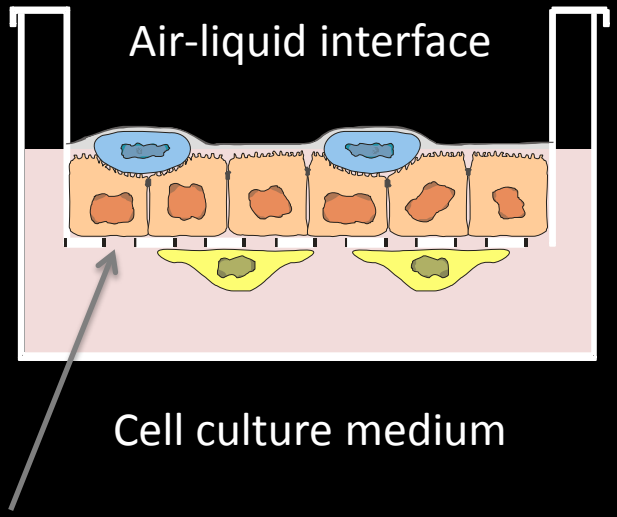
- Co-cultures
- Diseased cells
- Alveolar ventilation
- Flow

* Commercially available (*e.g.* Epithelix, MatTek)

** Kemp et al. Am J Respir Cell Mol Biol (2008); Kuehn et al. ALTEX (2016) (also commercially available)

Air-liquid cultures

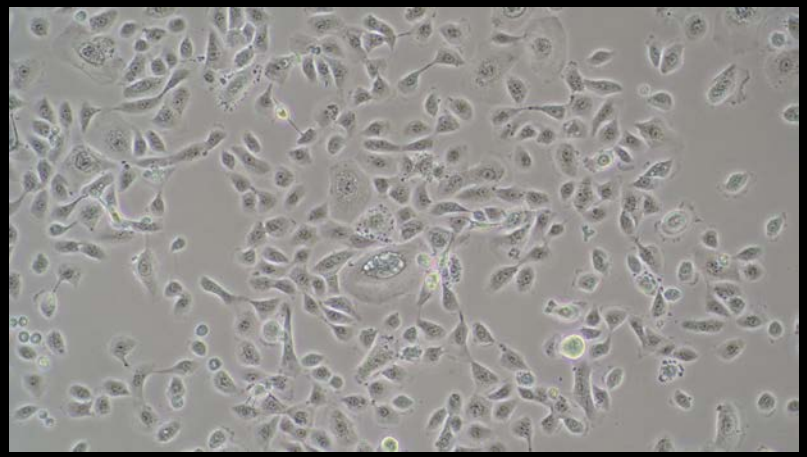
http://www.modefica.com.br/pele-humana-laboratorio-alternativa-testes-em-animais/#.Wqhbe43ruk8



Voisin et al. Bull Eur Physiopathol Respir (1977)

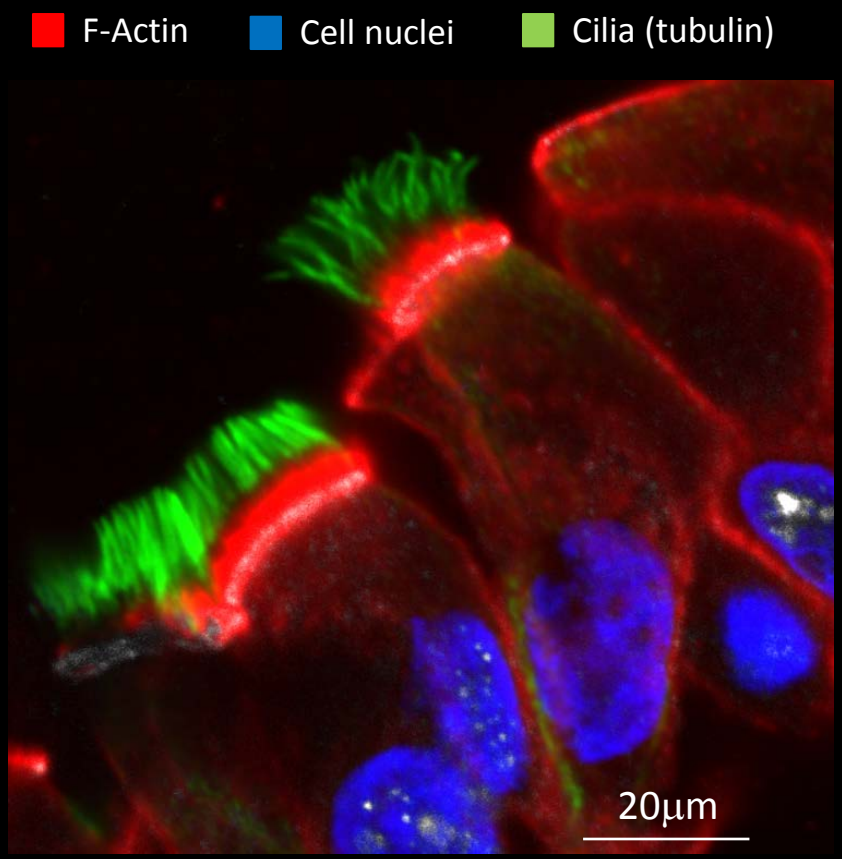
Primary nasal / bronchial cells

http://campus.uni-muenster.de/fileadmin/einrichtung/pcd/Download/cytobrush_muenster.pdf



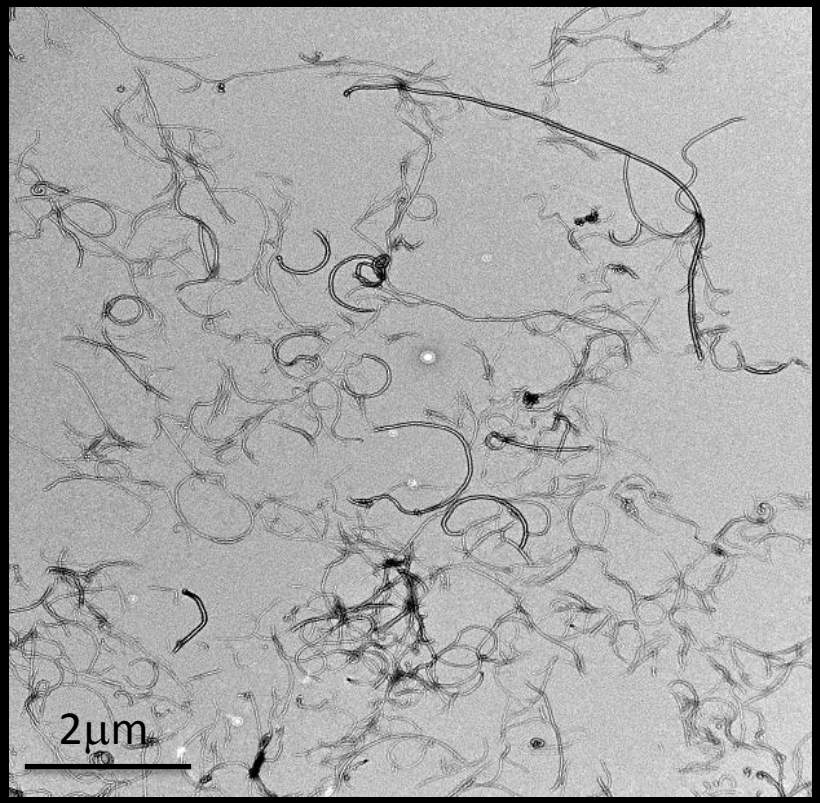
Primary human nasal epithelial cells

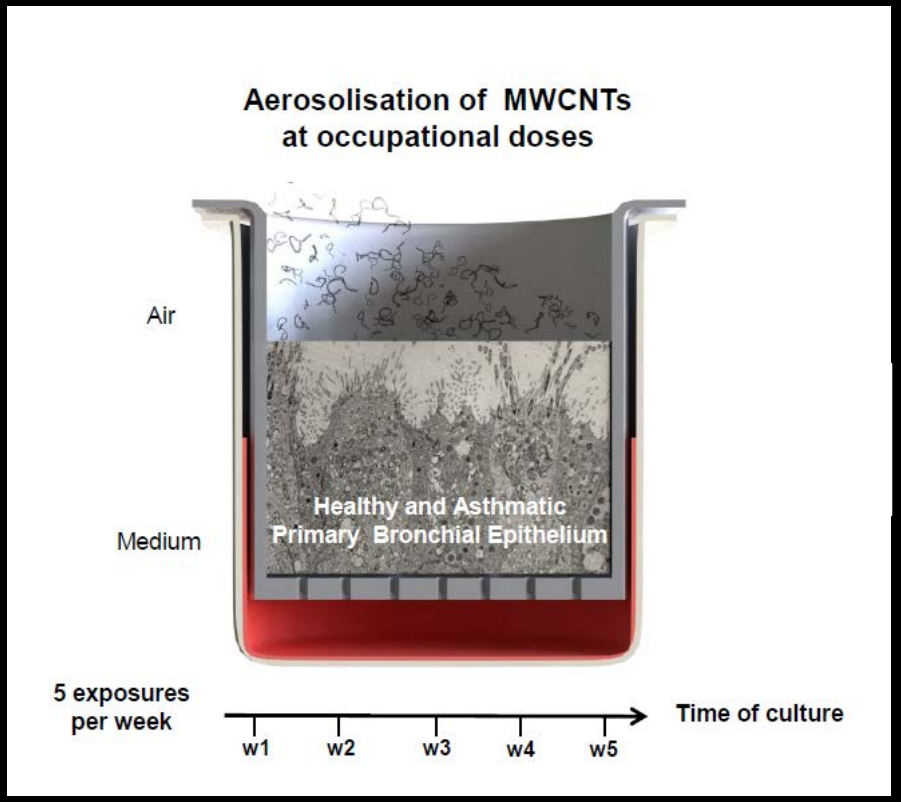
S. Beyeler and F. Blank, DKF, University of Bern



F. Blank, A. Beer, University of Bern, Switzerland

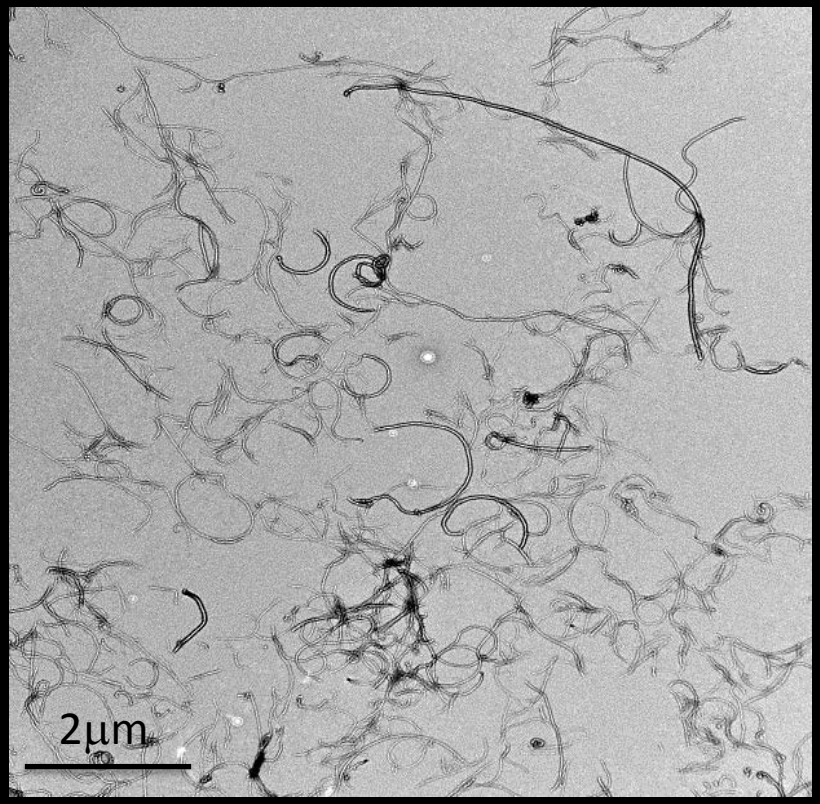
Primary nasal / bronchial cells





Chortarea et al. ACS Nano 2017

Primary nasal / bronchial cells



Chortarea et al. ACS N

ALTERNATIVE CELL-BASED METHODS TO ASSESS HAZARDS OF EXHAUSTS

14:05	**Human lung cell co-cultures – state of the art** B. Rothen-Rutishauser, AMI
14:30	**Lung cell responses upon diesel and GDI vehicle exposures** C. Bisig, AMI
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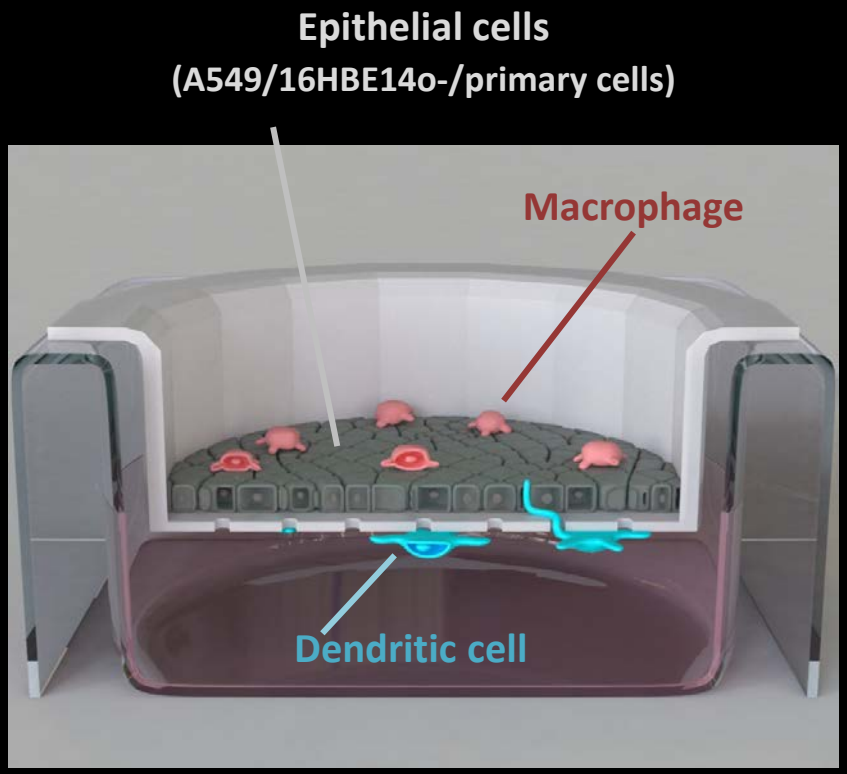
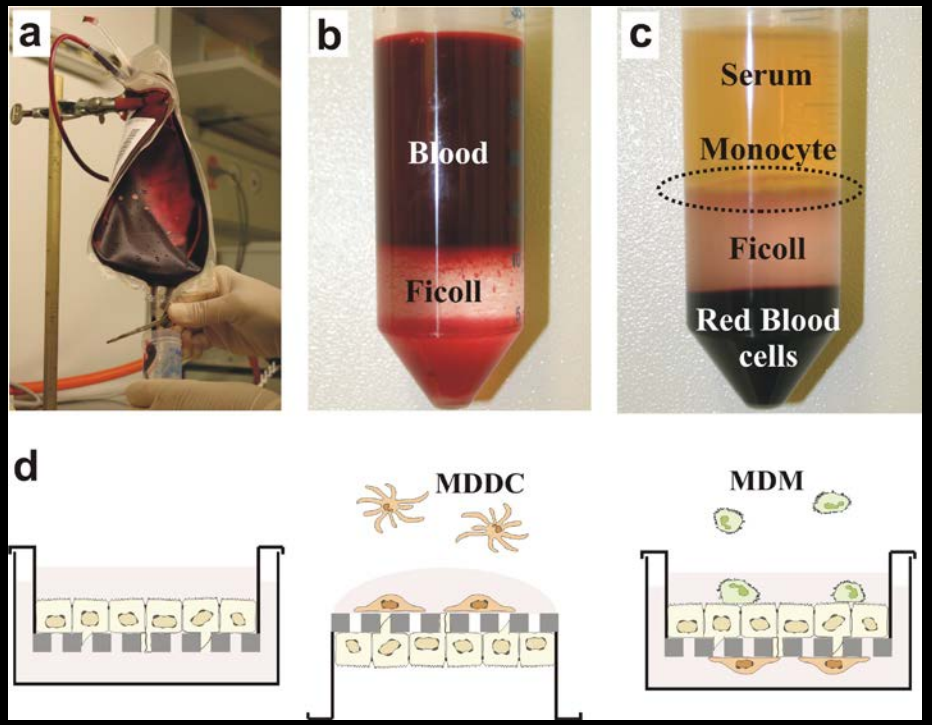
3D human lung epithelial tissue barrier model

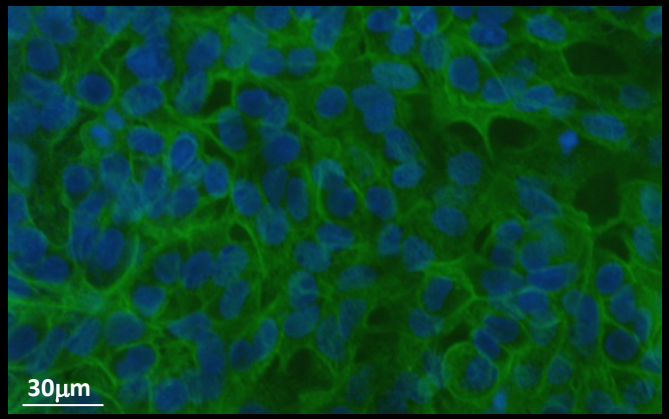


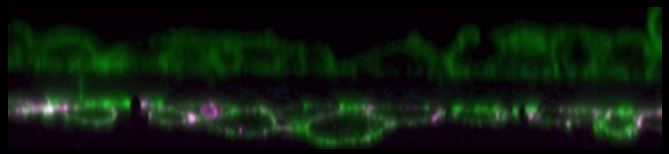


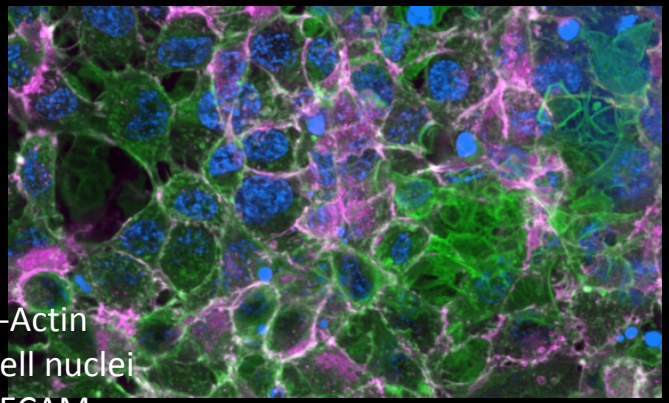
Fytianos et al. Nanomedicine (Lond) 2016
Rothen-Rutishauser et al. Am J Respir Cell Mol Biol 2005;
Blank et al. Am J Respir Cell Mol Biol 2007
Rothen-Rutishauser et al. Review, Exp Opin Drug Metab Toxicol 2008
Lehmann et al. Eur J Pharm Biopharm 2010

Lung co-cultures

Epithelial and endothelial cells

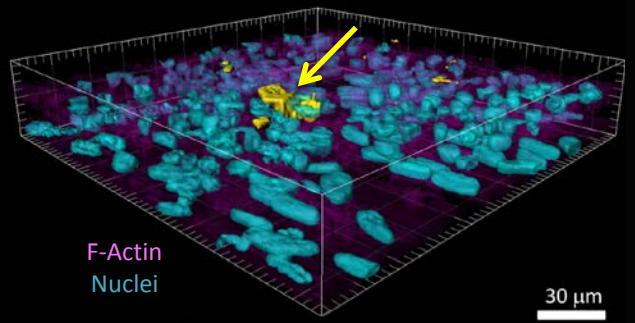




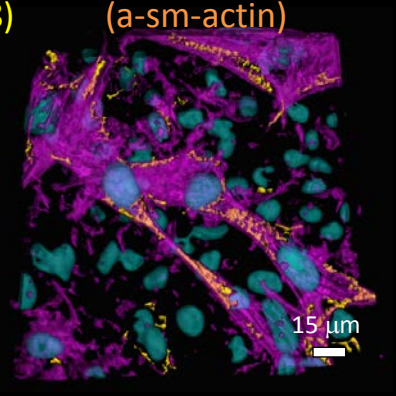


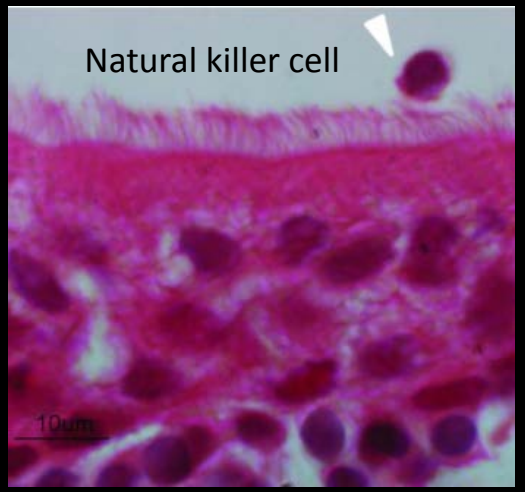
Jud et al. BioResearch (2015)

Macrophages (CD68)



Fibroblasts (a-sm-actin)



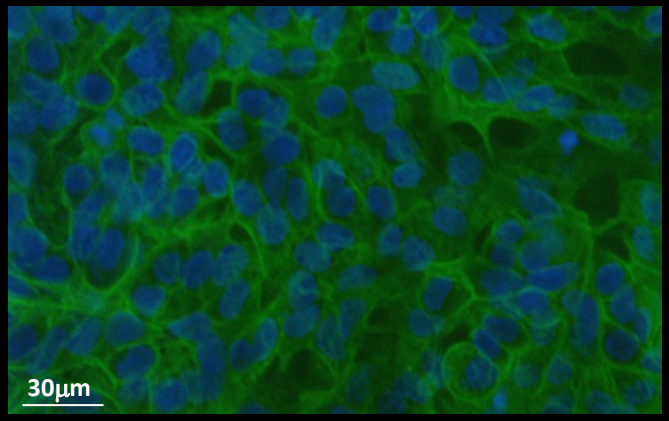


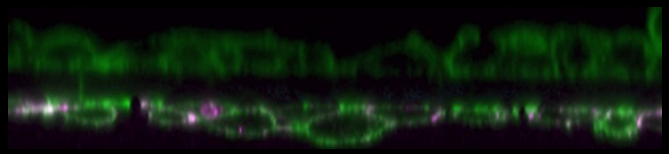
Müller et al. Am J Physiol Lung Cell Mol Physiol (2013)

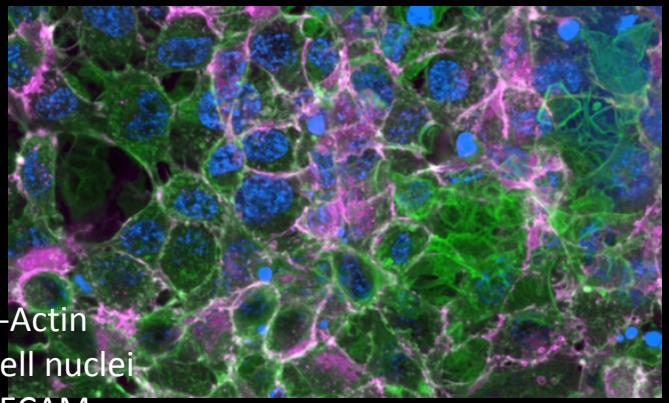
Nasal epithelium

Lung co-cultures

Epithelial and endothelial cells

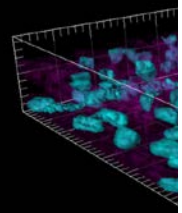






F-Actin
Cell nuclei
PECAM

Jud et al. BioResearch (2015)



F-Actin
Nuclei

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Alveolar ventilation

RESEARCH ARTICLE

Reconstituting Organ-Level Lung Functions on a Chip

Dongeun Huh[1,2], Benjamin D. Matthews[2,3], Akiko Mammoto[2], Martín Montoya-Zavala[1,2], Hong Yuan Hsin[2], Donald E. Ingber[1,2,4,*]

+ Author Affiliations

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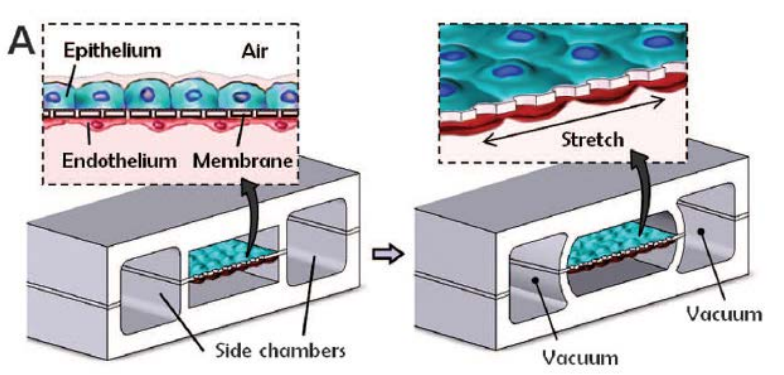
Science 25 Jun 2010:
Vol. 328, Issue 5986, pp. 1662-1668
DOI: 10.1126/science.1188302

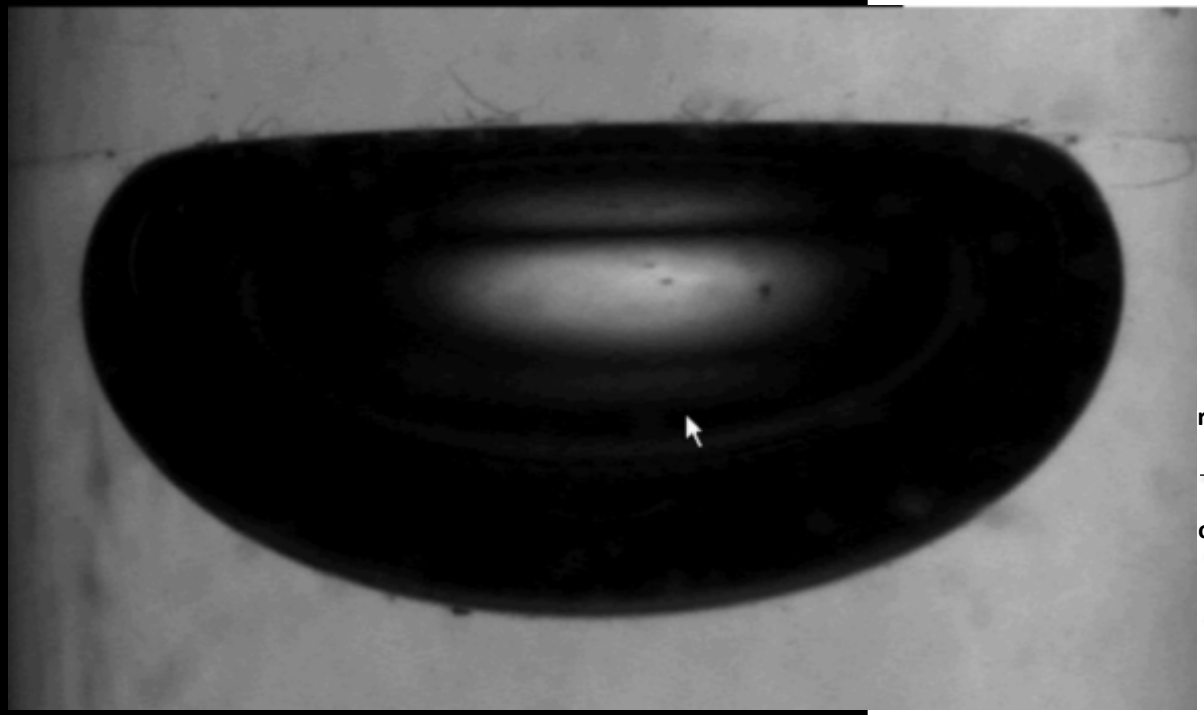


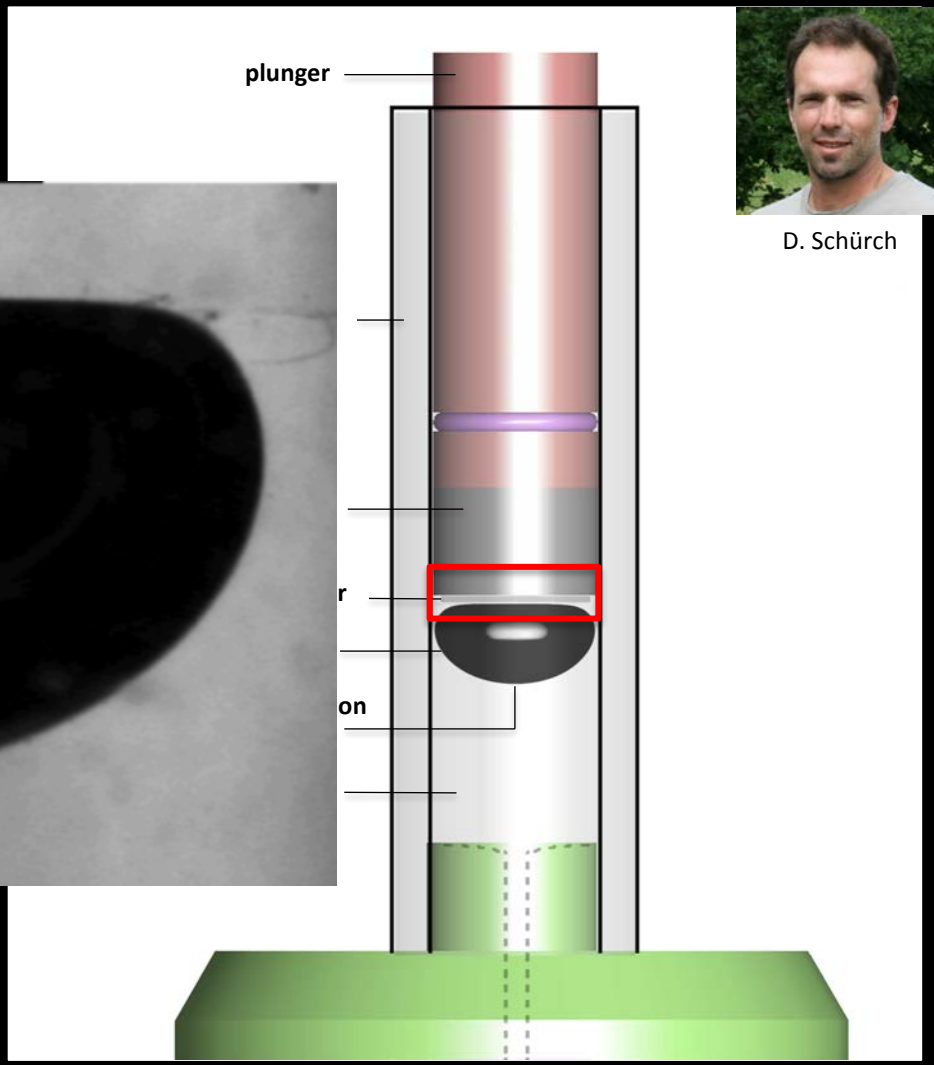
AlveoliX
In-vitro models inspired by nature

D. Schürch

Schürch et al. Langmuir 2014

Alveolar ventilation





D. Schürch

Schürch et al. Langmuir 2014

Conclusions

3D lung models

- Represent more physiologically relevant situations
- Structural-functional characterisation
- Mechanistic studies
- There is not one optimal model yet for all questions

Air-liquid exposures mimicking realistic inhalations of particles / toxicants / drugs

More complex models including

- Optimal **ECM** / **Membrane**
- **Breathing** patterns
- (blood) **Flow**

Outlook

Establishing a battery of innovative, **next generation safety testing tools** to more accurately predict the adverse effects caused by **long-term nanomaterial exposure** in humans and the environment

PATROLS
Advanced Tools for NanoSafety Testing

Understanding the effects of different classes of **air pollutants** on both the cutaneous responses and biomechanical properties to provide **innovative solutions for a better skin protection** against environmental stressors

CITYCARE

Acknowledgments

BioNanomaterials group

AMI members

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University of Fribourg

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- P. Gehr / F. Blank, University of Bern
- MatTek Corporation
- Epithelix
- Peta International Science Consortium

PATROLS
Advanced Tools for NanoSafety Testing
RUN4SCIENCE
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