

Jährliche Fortbildung VPB  
Berner REHA Zentrum Heiligenschwendi  
27. August, 2009

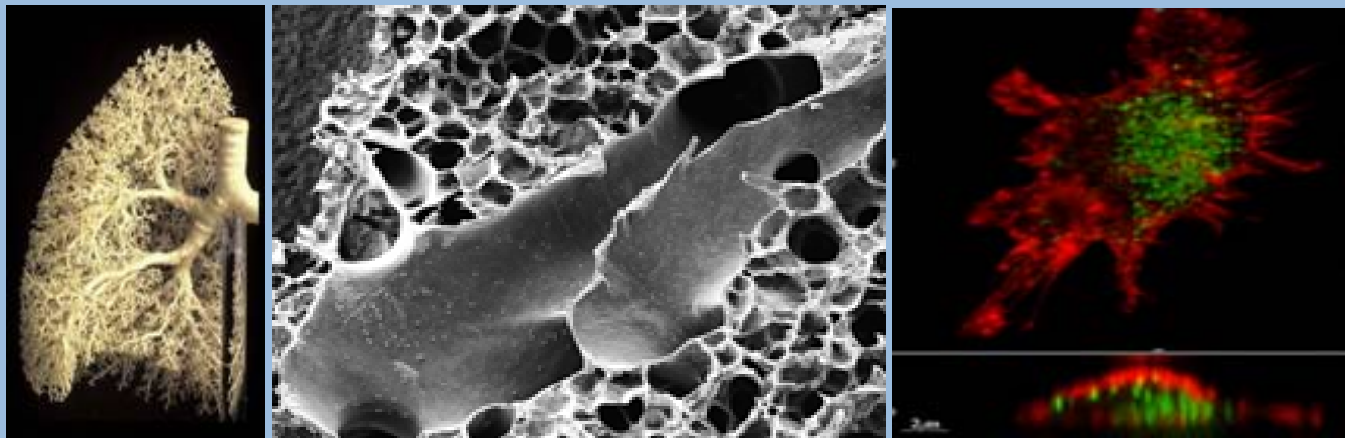
*u<sup>b</sup>*

b  
UNIVERSITÄT  
BERN

Institut für Anatomie

# DAS SCHICKSAL VON FEINSTAUB- PARTIKELN IM RESPIRATIONS- TRAKT – DIE ANATOMISCH-FUNK- TIONELLE PERSPEKTIVE

Peter Gehr  
Institut für Anatomie  
Universität Bern  
Bern  
Schweiz

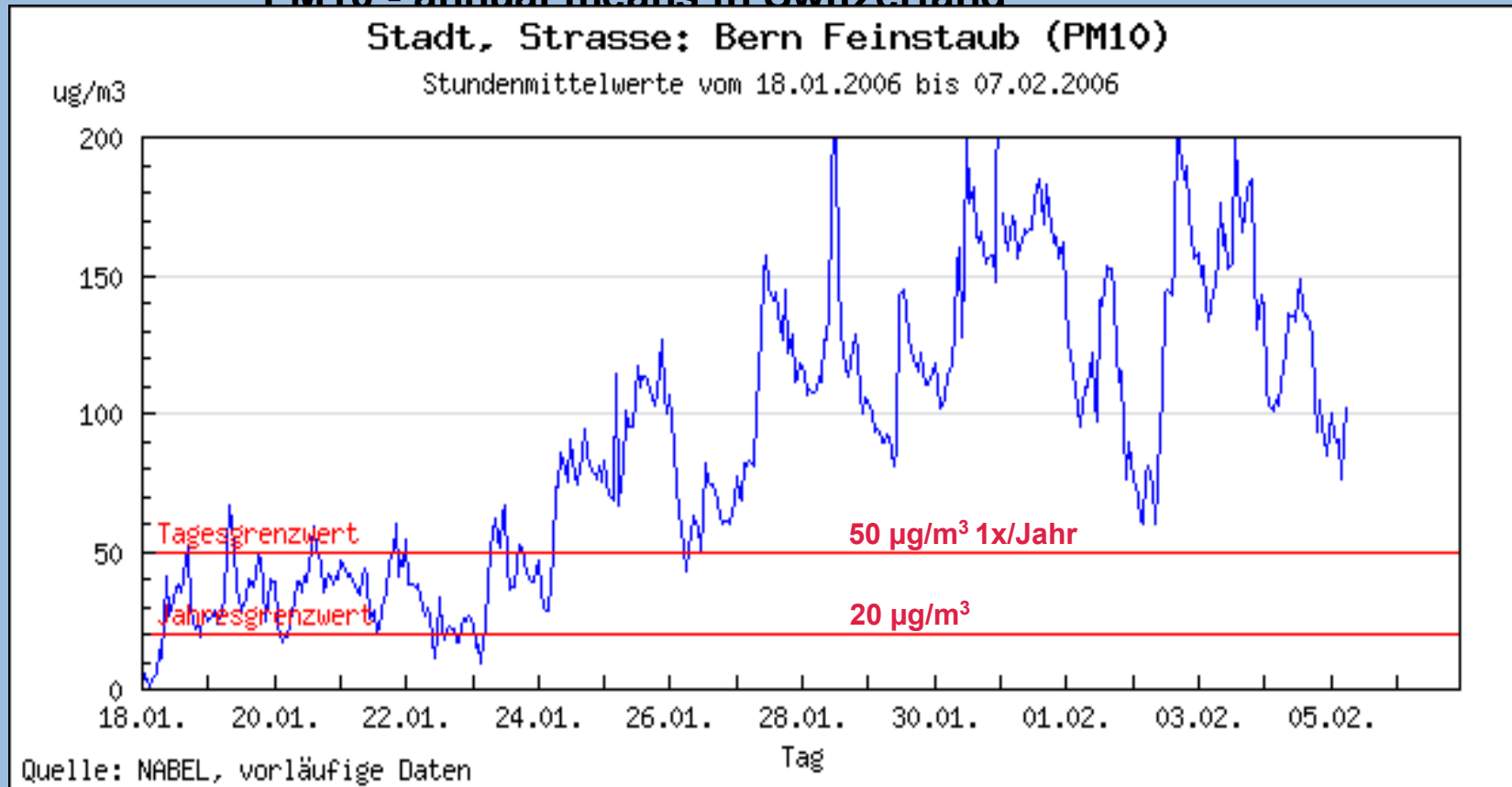


# Smogstaubkonzentration 2006

## PM10 - annual means in Switzerland

Stadt, Strasse; Bern Feinstaub (PM10)

Stundenmittelwerte vom 18.01.2006 bis 07.02.2006

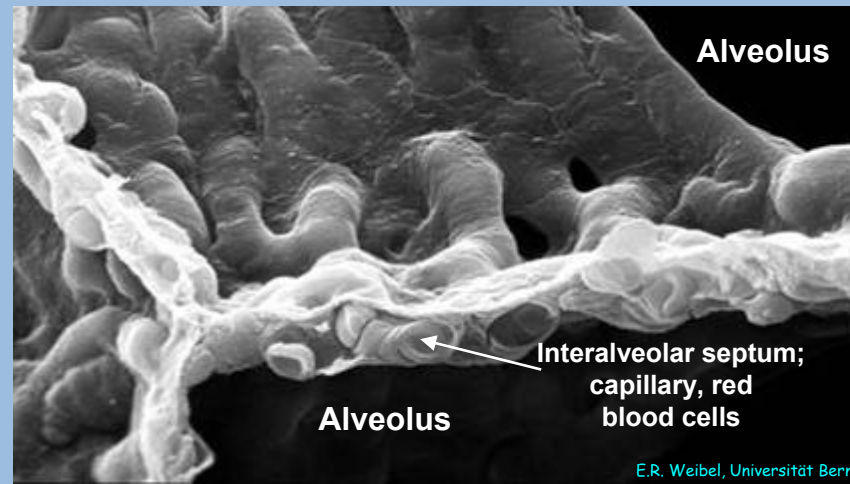
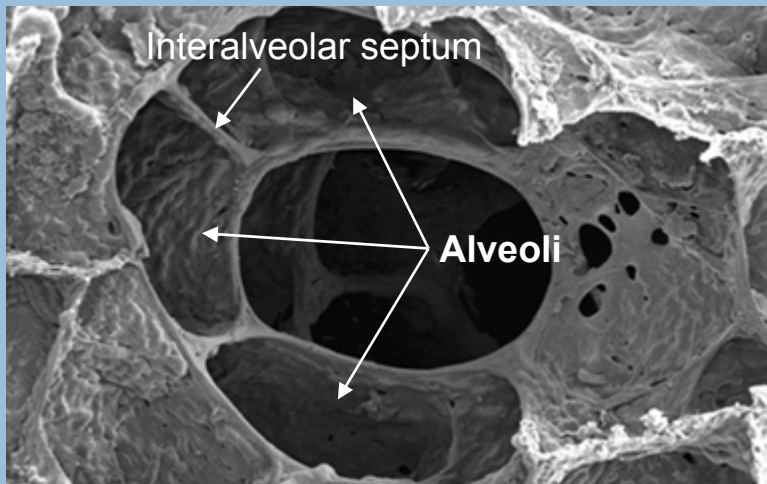
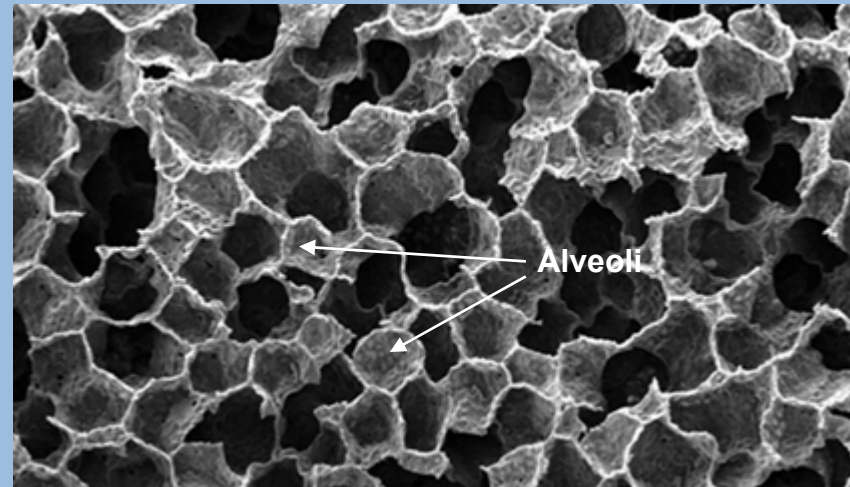
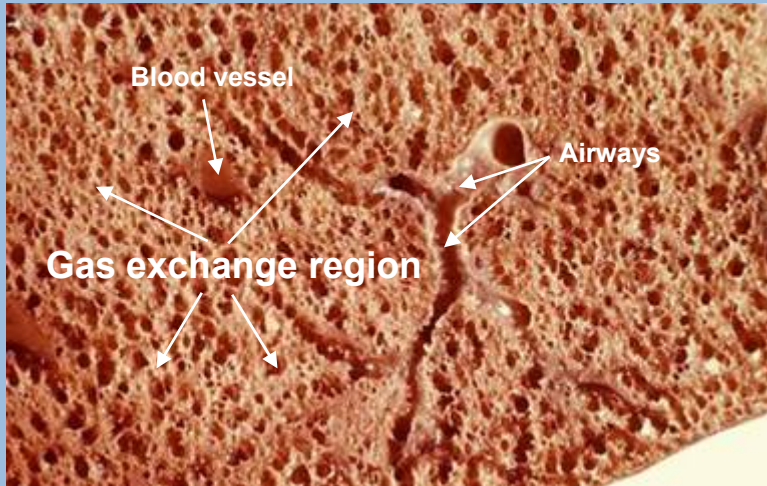


Zusätzliche Todesfälle bis 6%, d.h. bis 12 pro Tag oder 40-70 während der Smogperiode Januar-Februar 2006

P. Straehl, BAFU Abt.  
Luft-reinhaltung und NIS  
P. Straehl  
BAFU  
Abt. Luft-reinhaltung und NIS

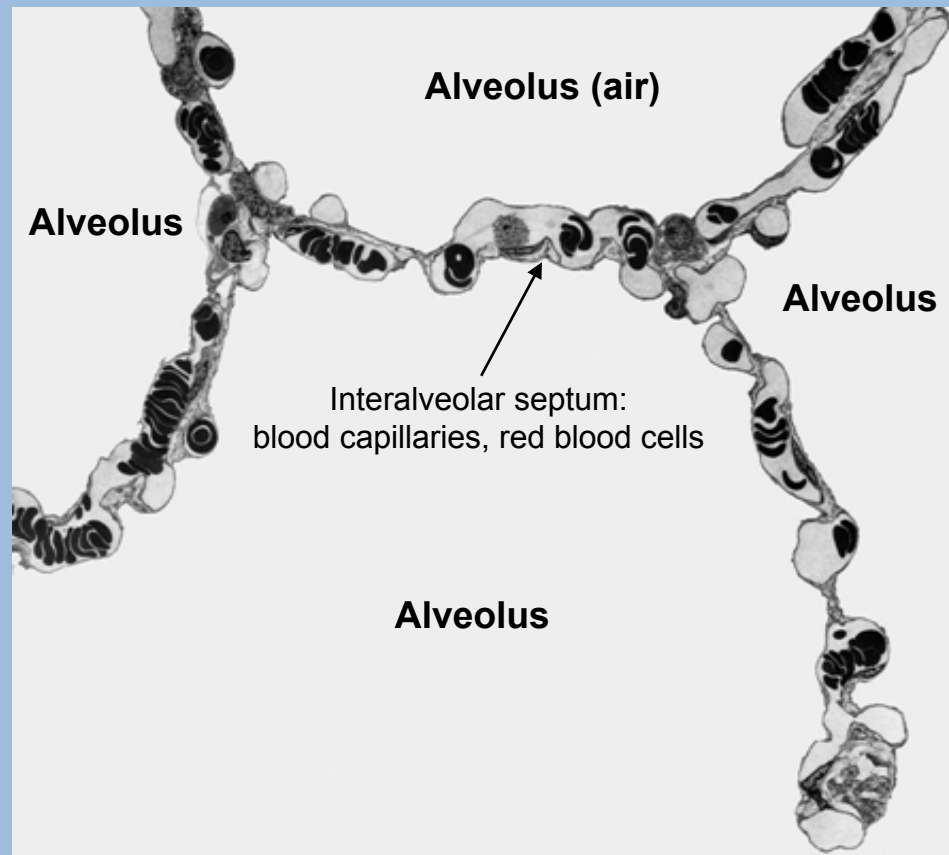
# THE HEALTHY LUNG

(SCANNING ELECTRON MICROSCOPY)



# THE HEALTHY LUNG

(TRANSMISSION ELECTRON MICROSCOPY)



500 millions alveoli  
(M. Ochs, Inst. für Anat., Univ. Bern)  
diameter 1/4mm  
gas exchange region  
80-90%

**alveolar surface area 140 m<sup>2</sup>**



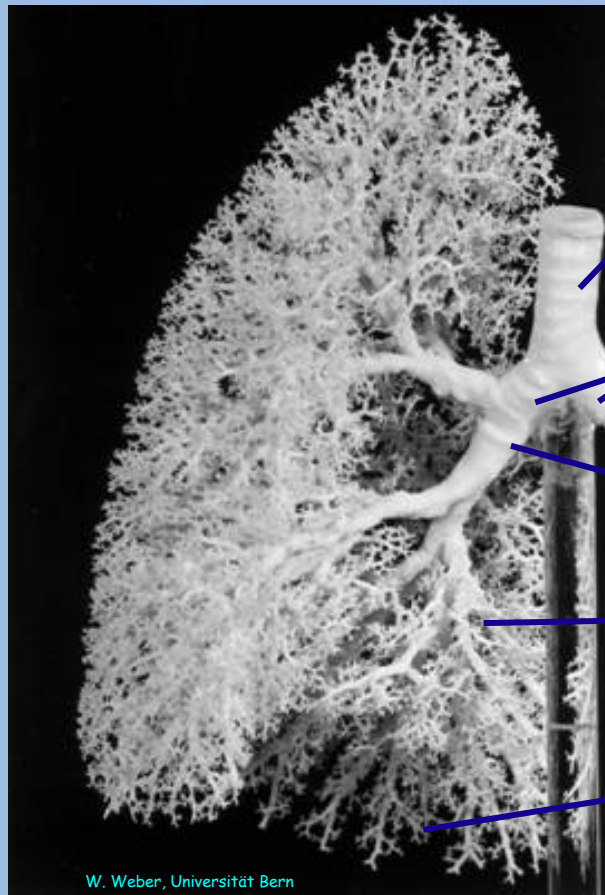
**Capillary blood volume**  
**210cm<sup>3</sup>**



**Red blood cell**  
**in blood capillary**

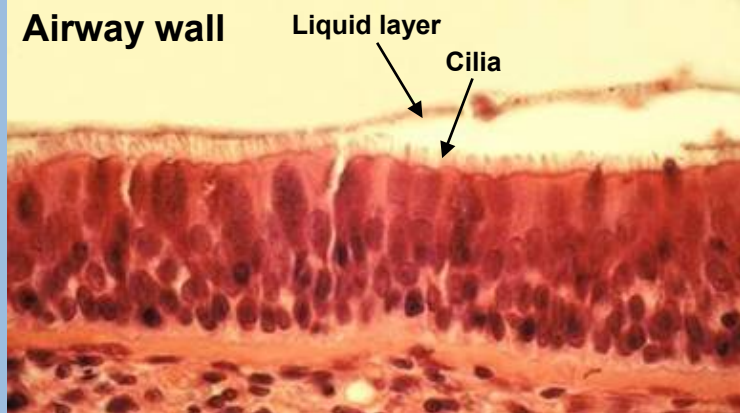
**Air-blood tissue barrier**  
**<1µm**

# THE AIRWAY TREE AS A PARTICLE FILTER

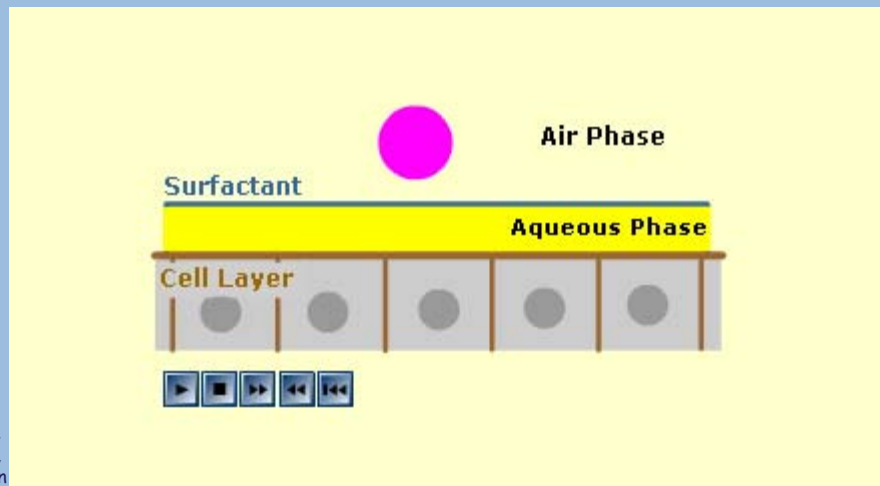


W. Weber, Universität Bern

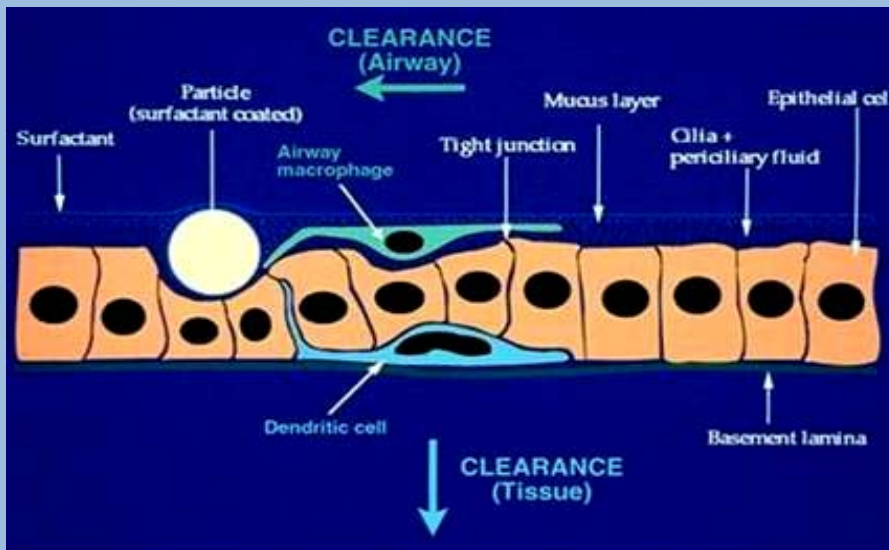
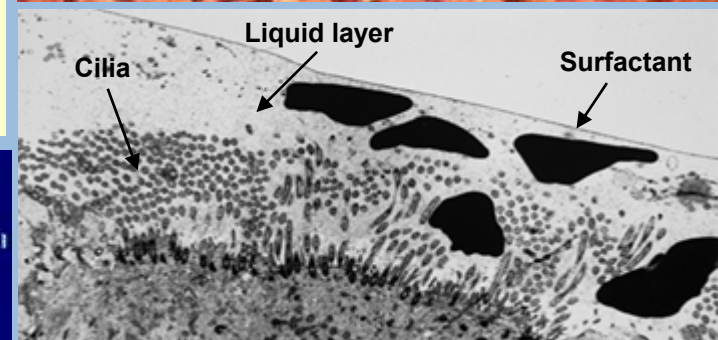
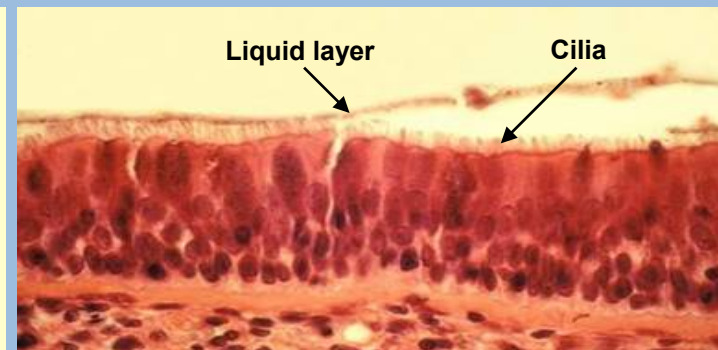
- Trachea
- Main Bronchi
- Bronchi
- Bronchioli
- Alveoli (not seen)



# PARTICLE DISPLACEMENT



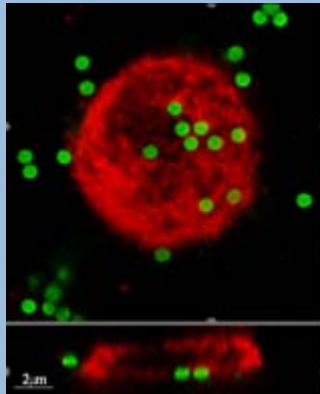
S. Schürch,  
S. Tschanz,  
Universität Bern



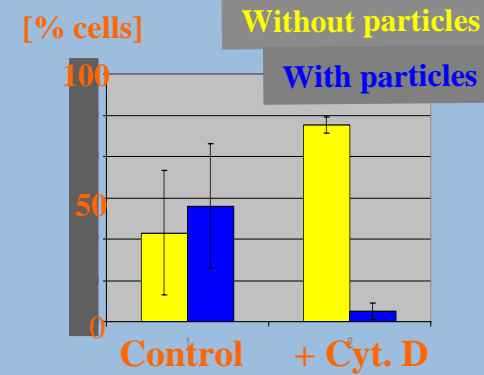
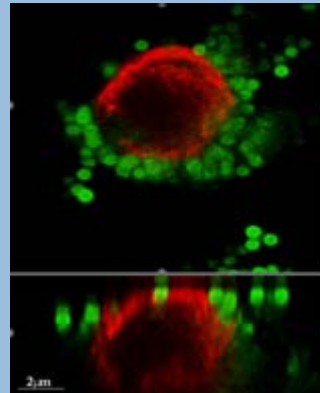
# MACROPHAGES *in vitro* (LASER SCANNING MICROSCOPY)

■ F-Actin  
■ 1 μm (fine) Polystyrene particles

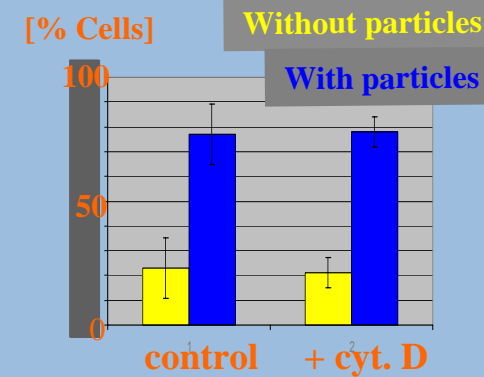
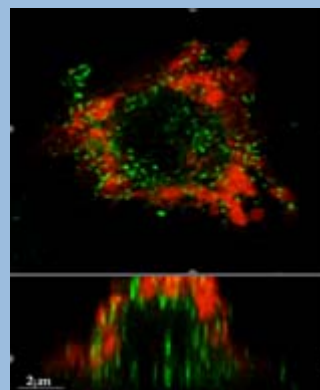
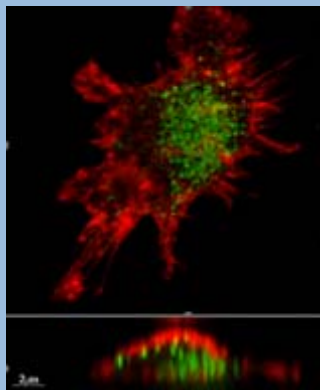
Control



+ Cytochalasin D

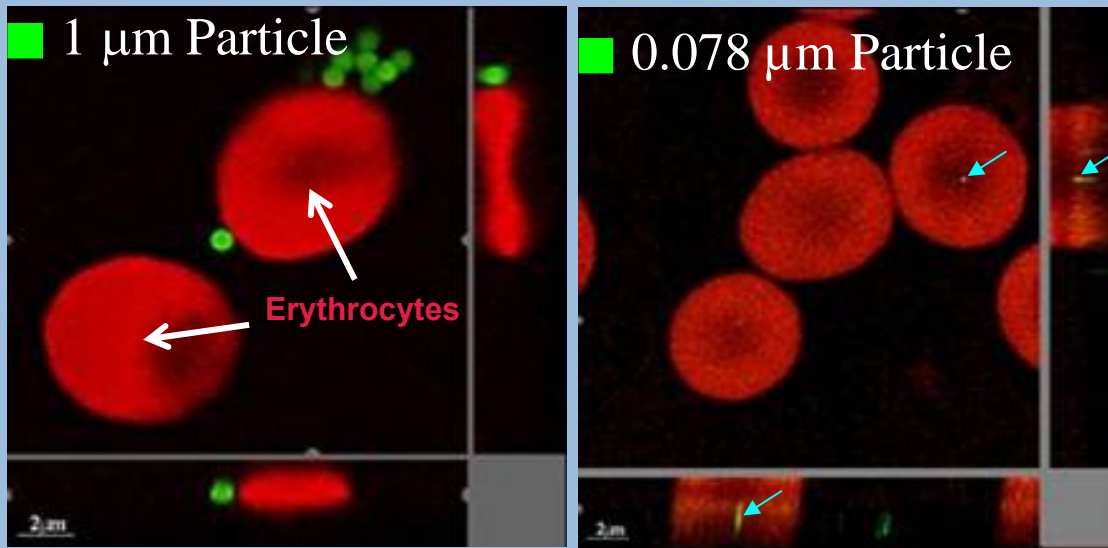


■ 0.078 μm (ultrafine) Polystyrene particles

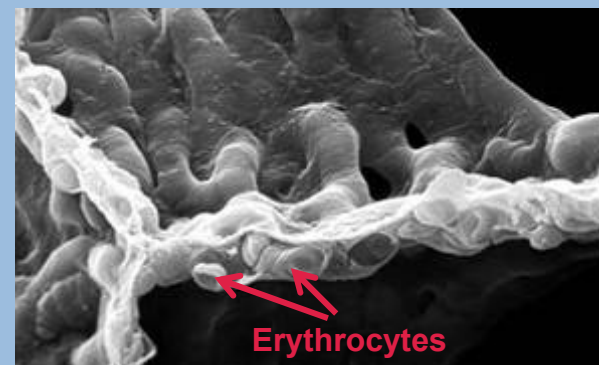
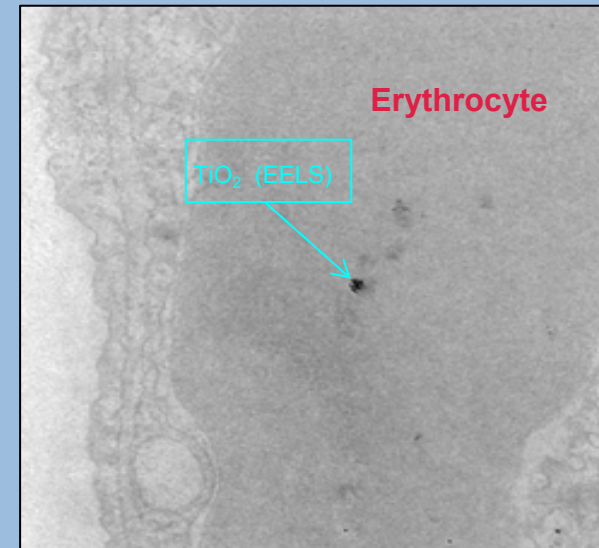


# ERYTHROCYTES WITH POLYSTYRENE PARTICLES

Autofluorescence      Fluorescent Polystyrene Particles



B. Rothen-Rutishauser  
In: Geiser et al.,  
EHP 113: 1555-1560, 2005



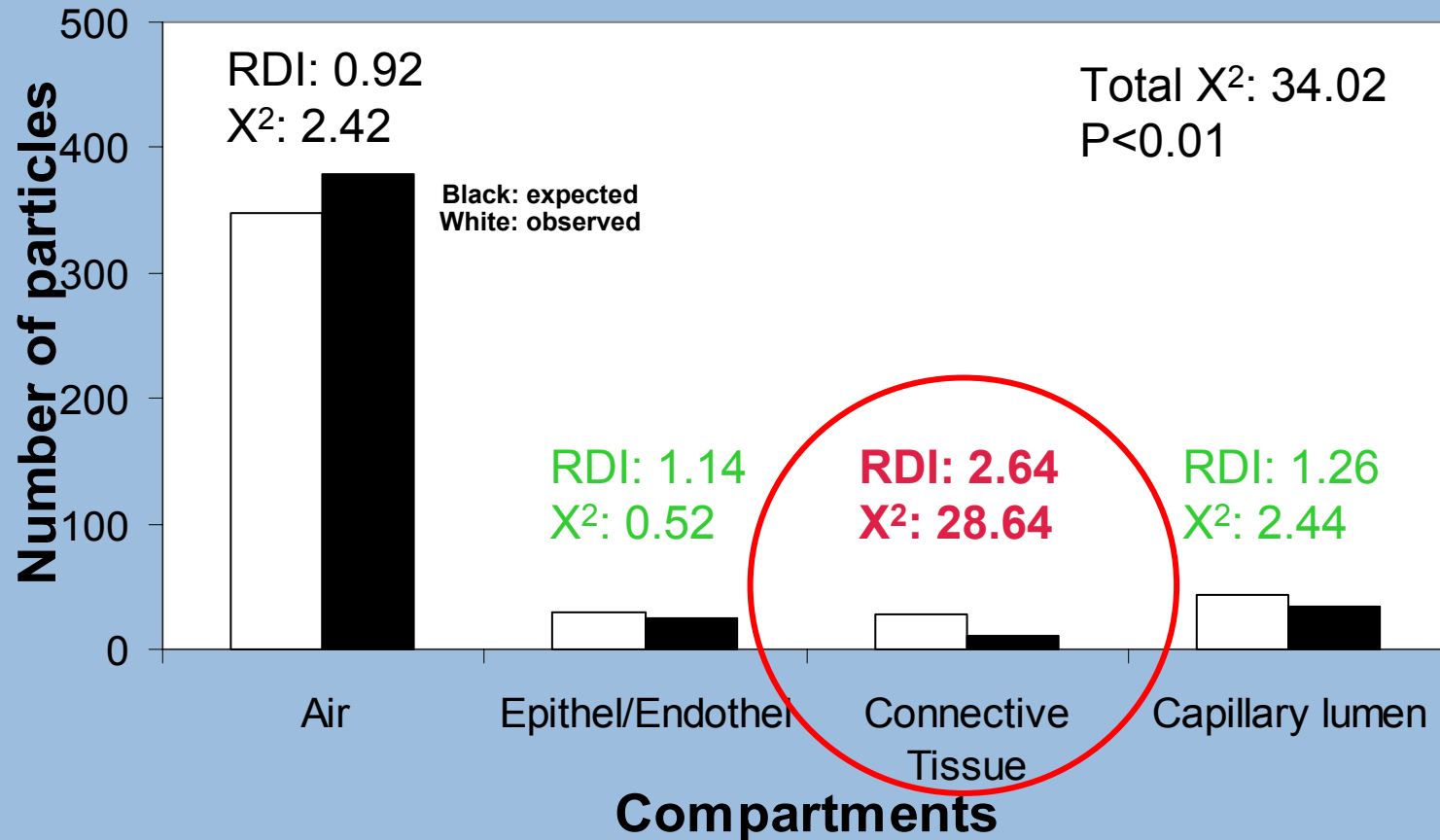
# STEREOLOGICAL ANALYSIS: PARTICLE TRAFFICKING



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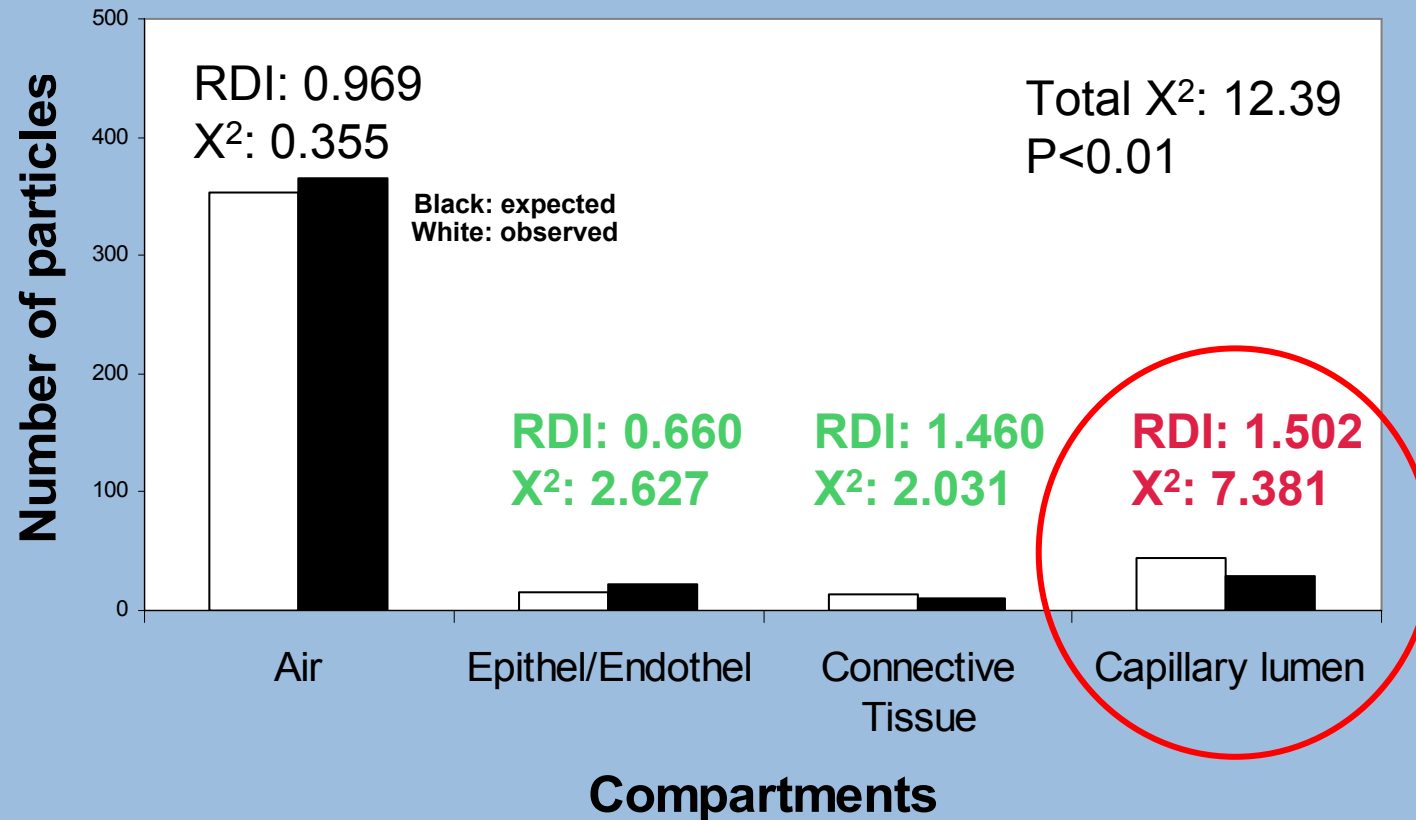
Comparison between observed and expected particles at  
1h after exposure



Mühlfeld et al., Part. Fibre Toxicol. 4: 7, 2007

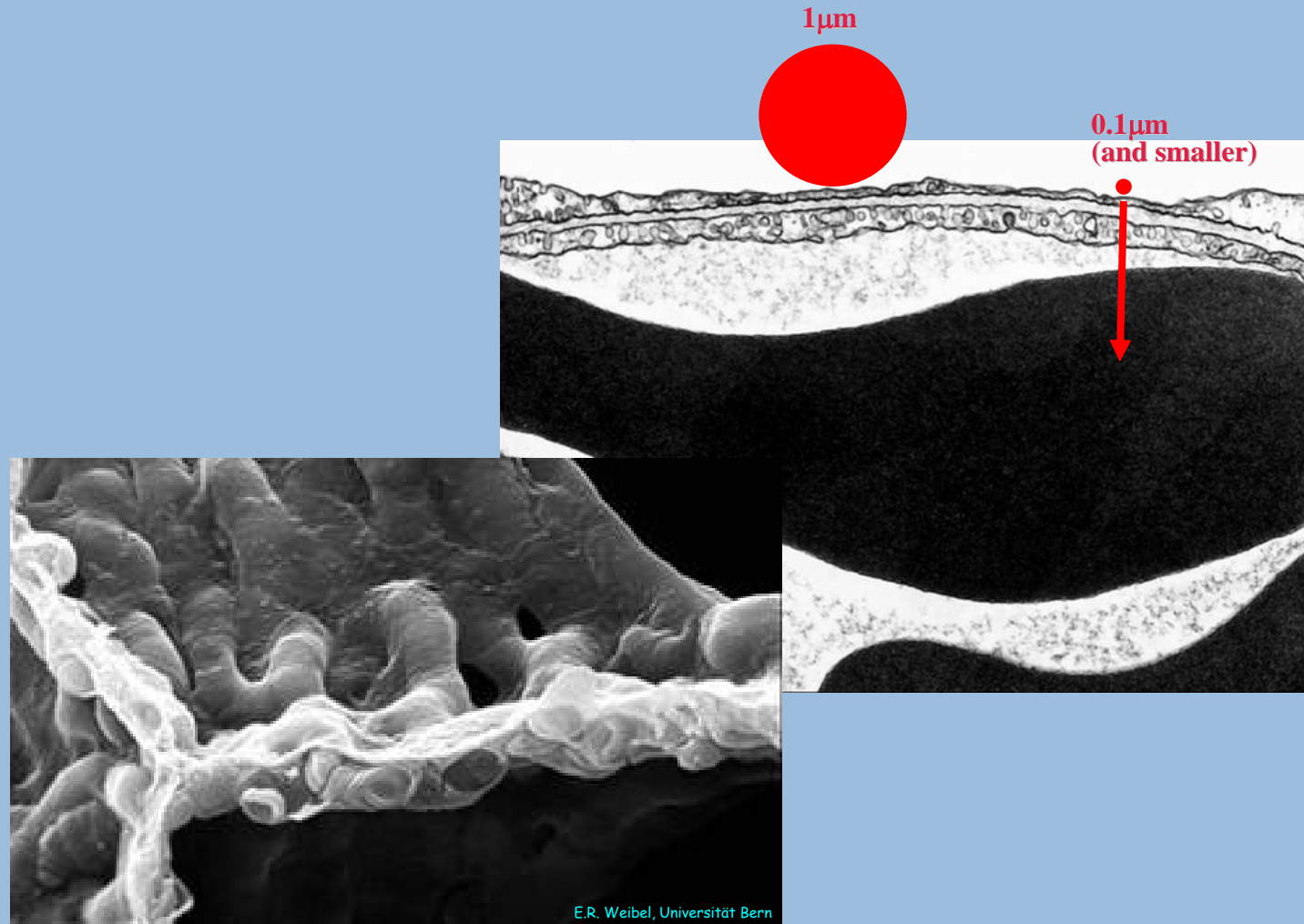
# STEREOLOGICAL ANALYSIS: PARTICLE TRAFFICKING

Comparison between observed and expected TiO<sub>2</sub>-particles at 24h after exposure

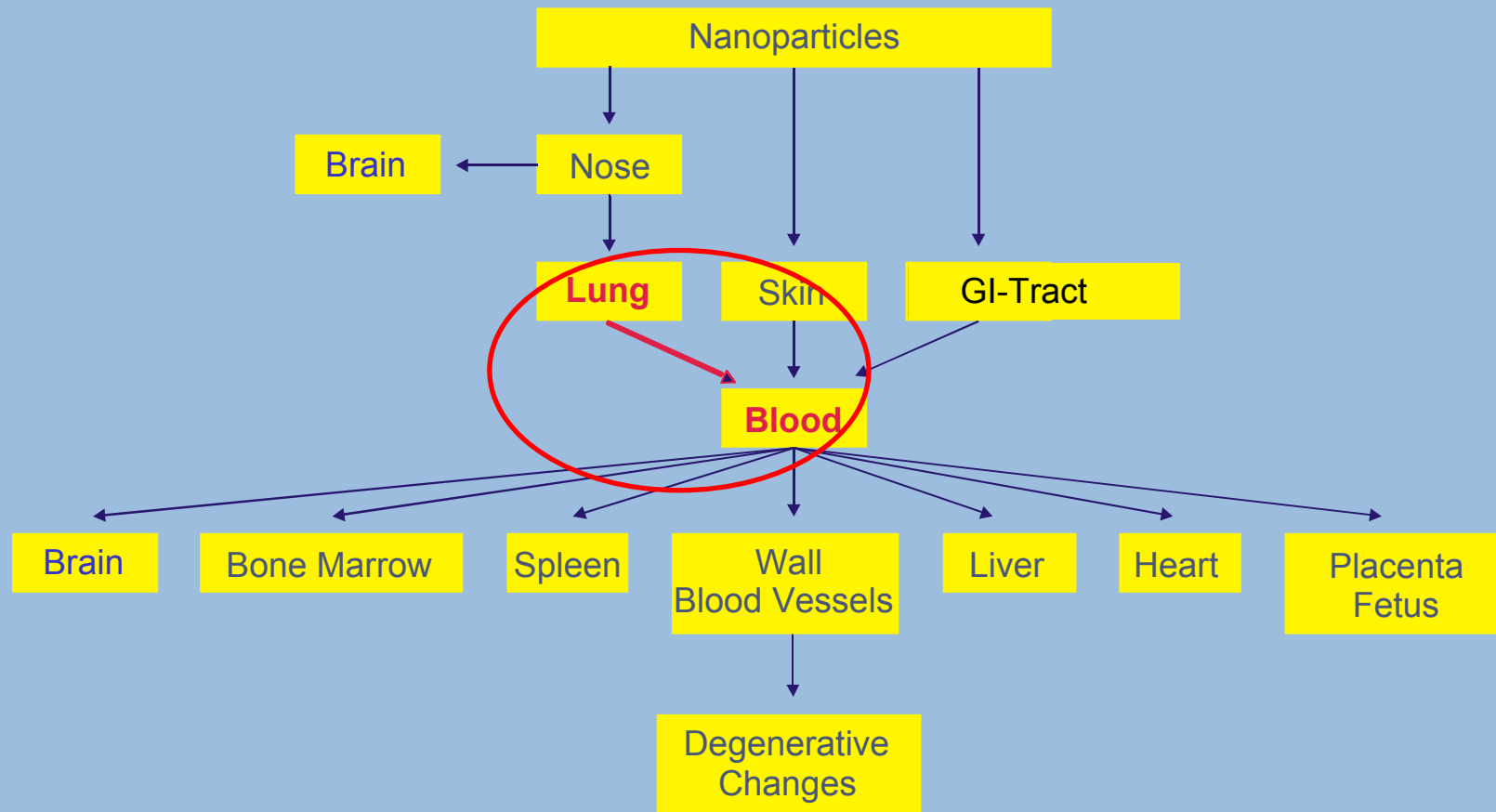


# AIR-BLOOD TISSUE BARRIER:

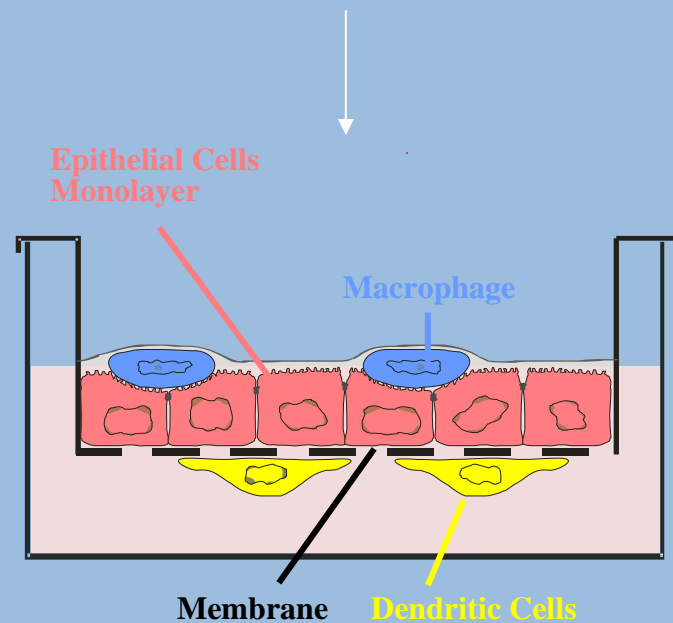
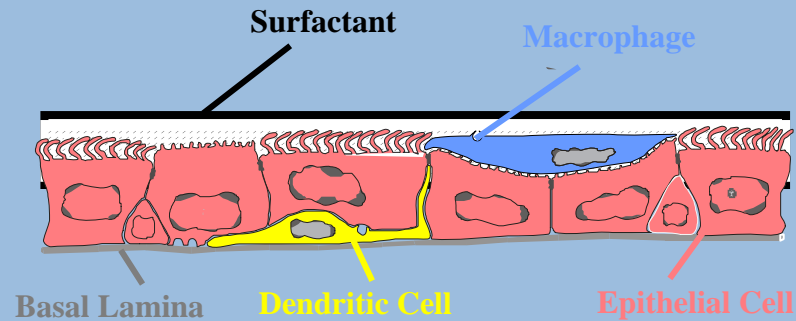
NANOPARTICLES (<0.1 $\mu\text{m}$ ) ONLY MAY PENETRATE INTO THE BLOOD



# TRANSLOCATION

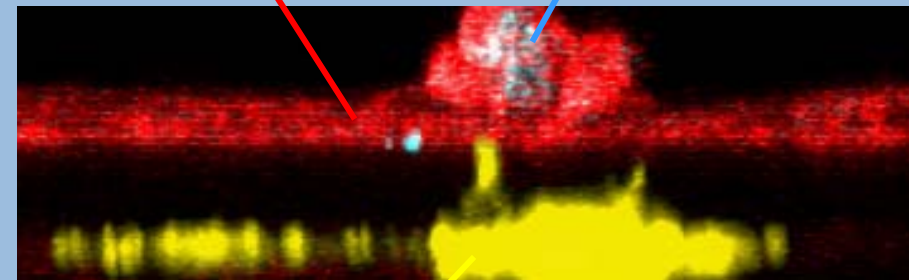


# EPITHELIAL AIRWAY WALL – AN *in vitro* SYSTEM



**Epithelial cell monolayer  
(A549 or 16HBE cells)**

**Macrophage**



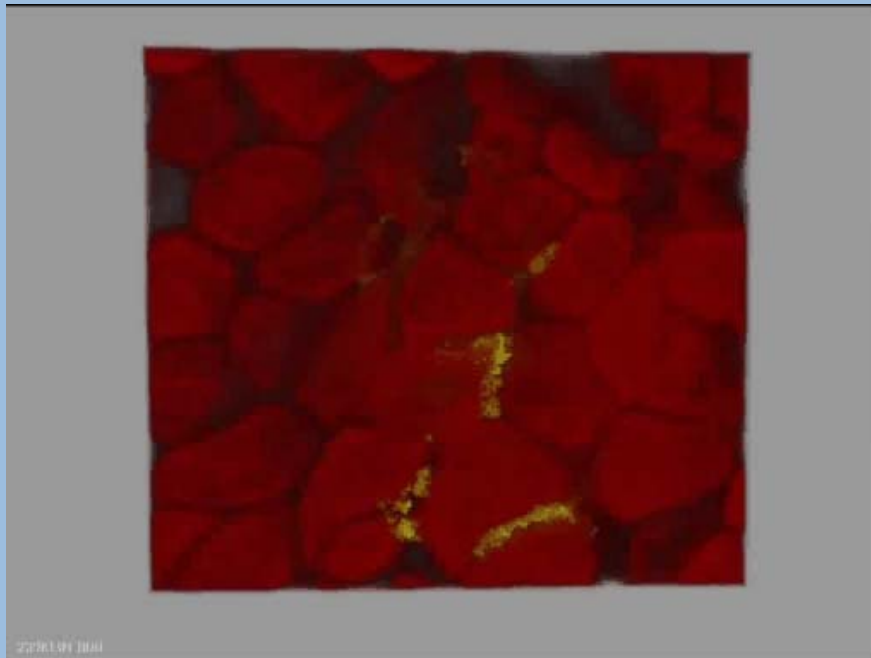
**Dendritic cell**

(Rothen-Rutishauser et al., *Am. J. Respir Cell Mol. Biol.* 32: 281-899, 2005)  
(Rothen-Rutishauser et al., *Expert. Opin. Drug Metab. Toxicol.* 4: 1075-1089, 2008)

# MORPHOLOGY OF THE TRIPLE CELL CO-CULTURES

## *In vivo* (rat lung)

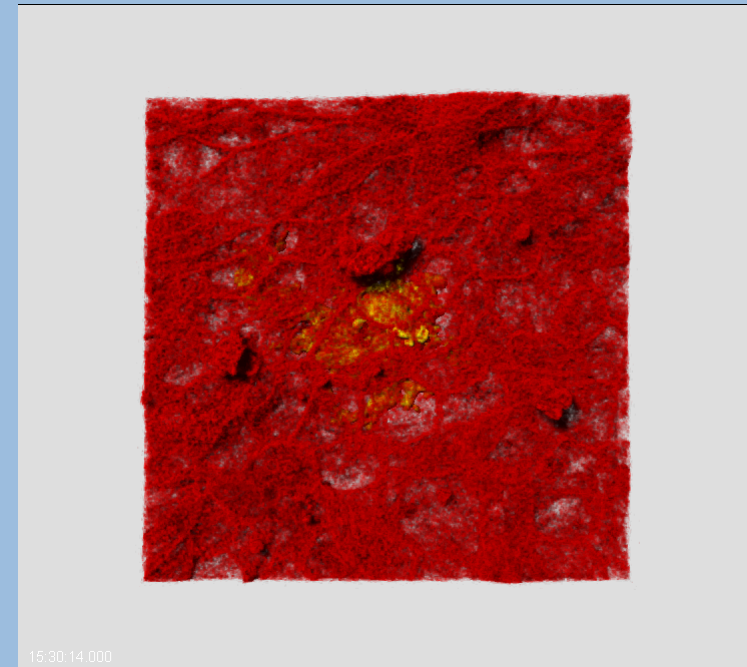
- Epithelial cells (Cytokeratin)
- Dendritic cells (MHC II)



F. Blank  
Rothen-Rutishauser *et al.*, Invited Review,  
*Exp. Opin. Drug Metabol. Toxicol.* 2008

## *In vitro* (3D model)

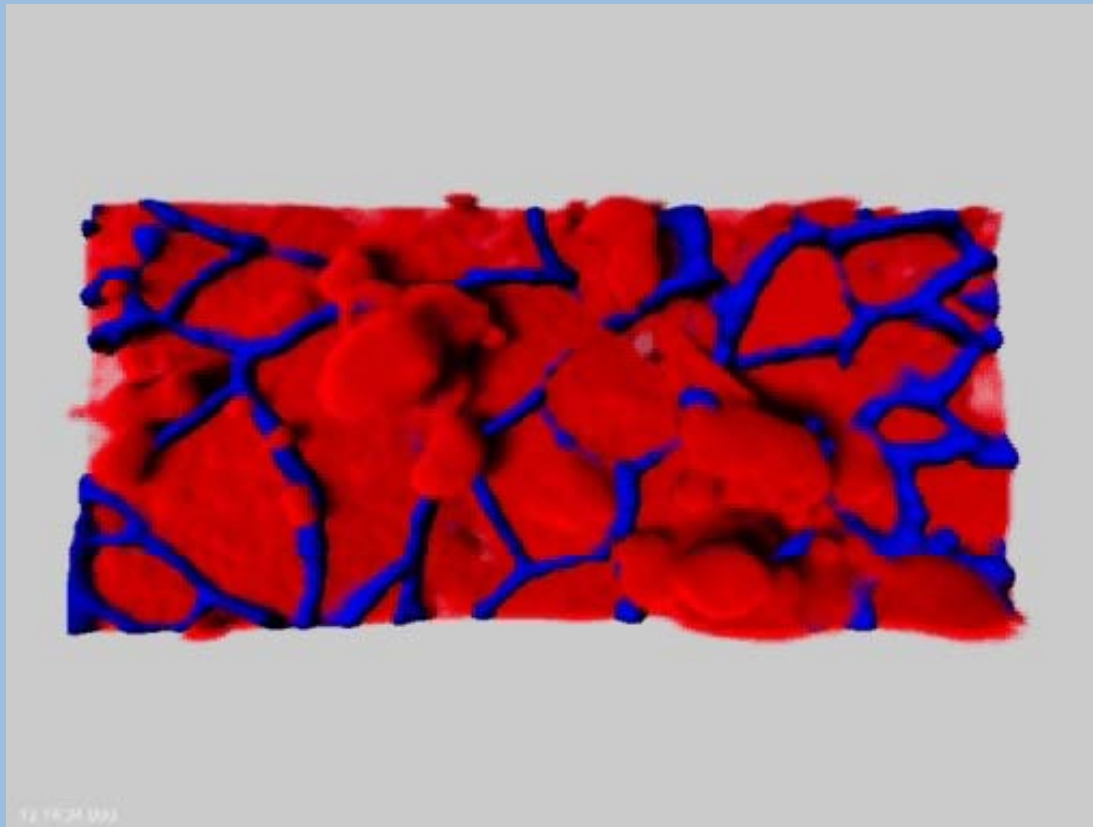
- Epithelial cells (F-Actin)
- Dendritic cells (CD86)



15:30:14.000

# CYTOPLASMIC PORCESSES OF DENDRITIC CELLS, TIGHT JUNCTIONS

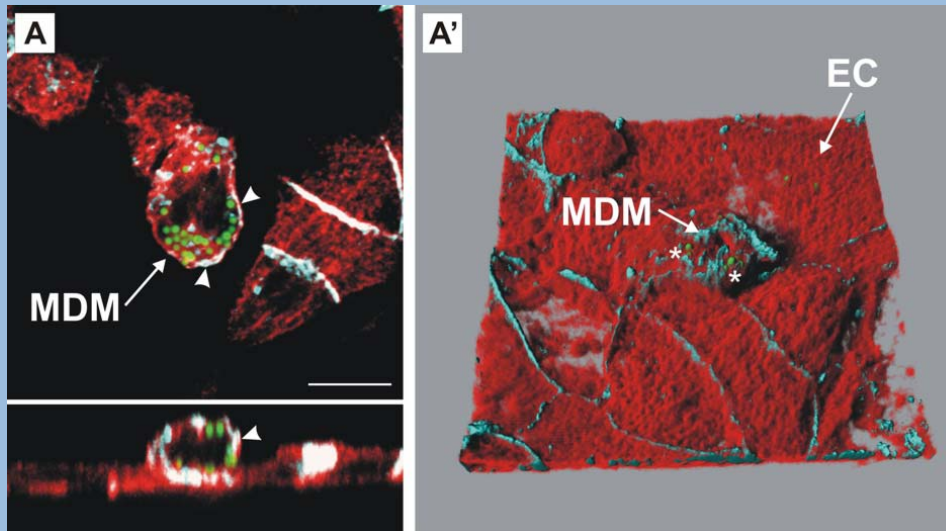
**Dendritic cells** penetrate through **tight junctions (Occludin)**  
of the **epithelium**



F. Blank, Institute of Anatomy, University of Bern

# ZO-LIKE CELL JUNCTIONS

LSM

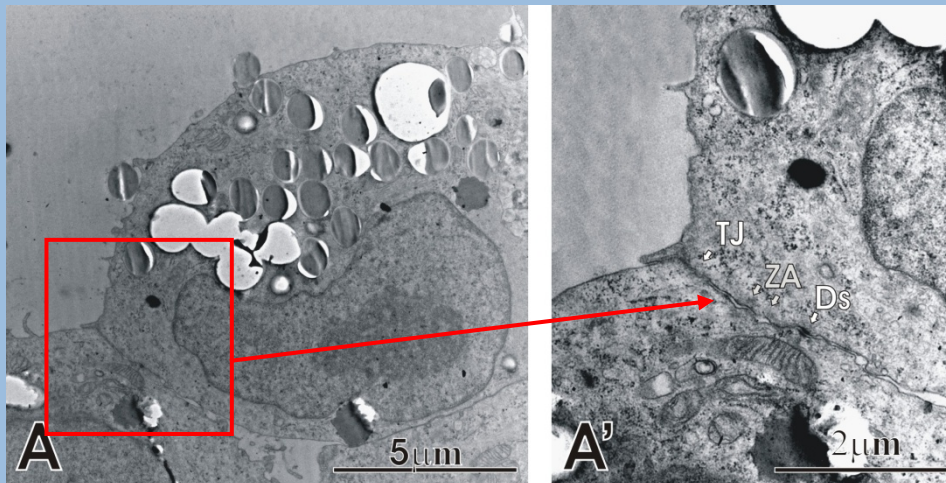


Triple-Cell Co-Culture  
(16HBE14o)

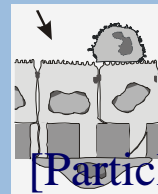
- F-Actin
- 1µm Particles
- Occludin

F. Blank

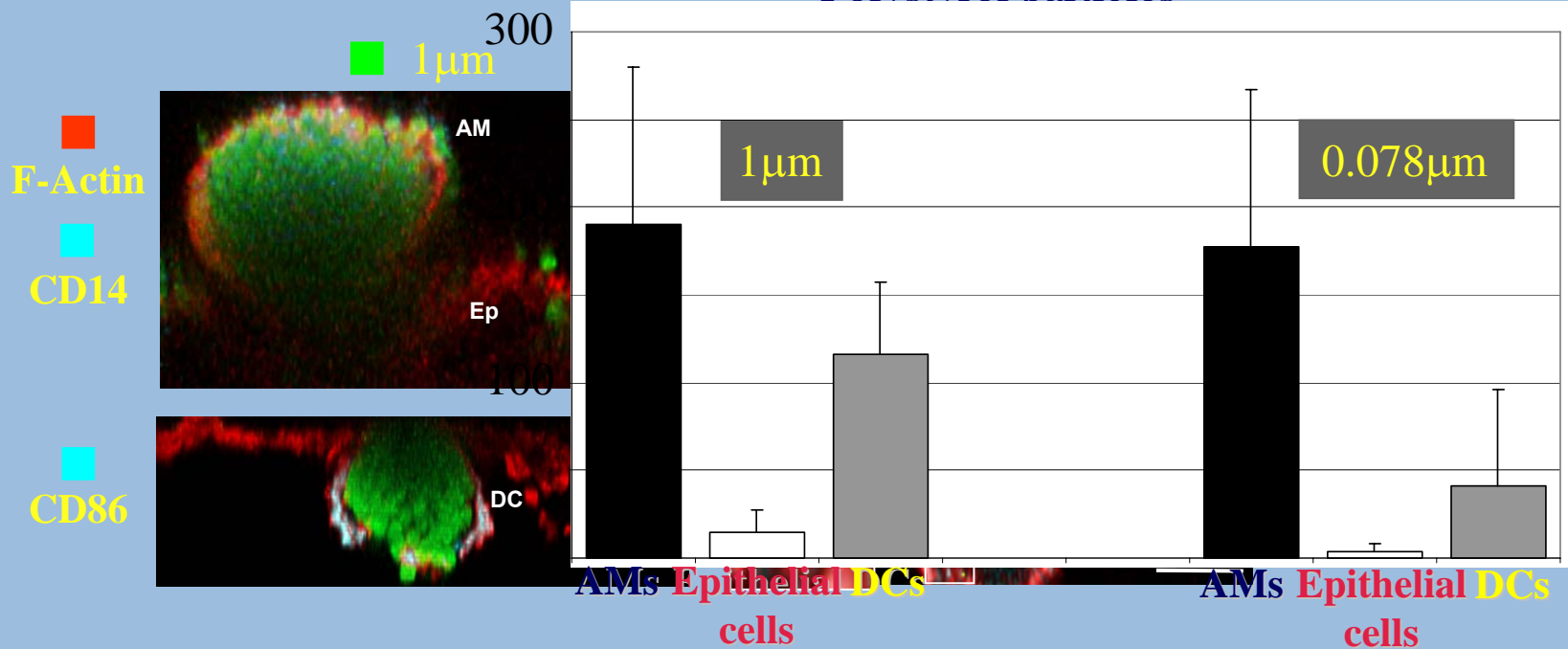
TEM



# INTRACELLULAR PARTICLE LOCALISATION AND QUANTIFICATION



[Particle number/cell]  
Polystyrol particles

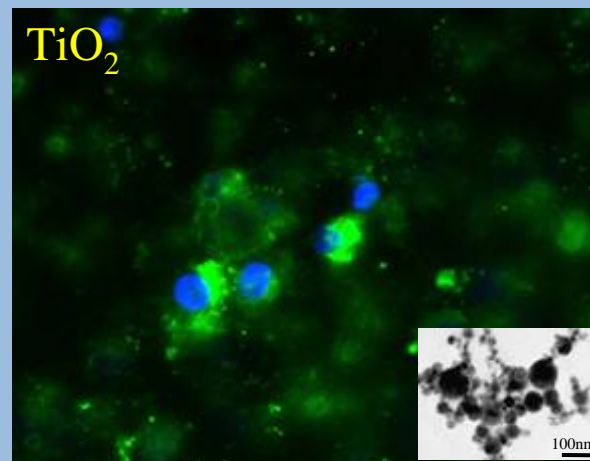
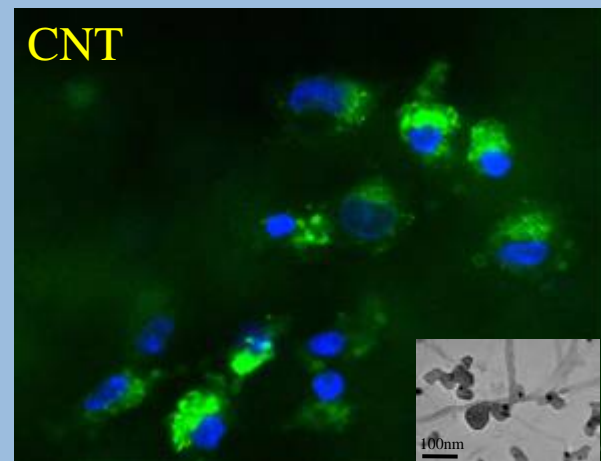
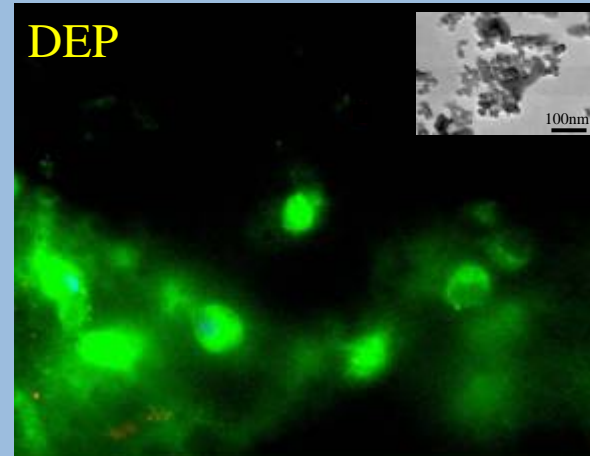
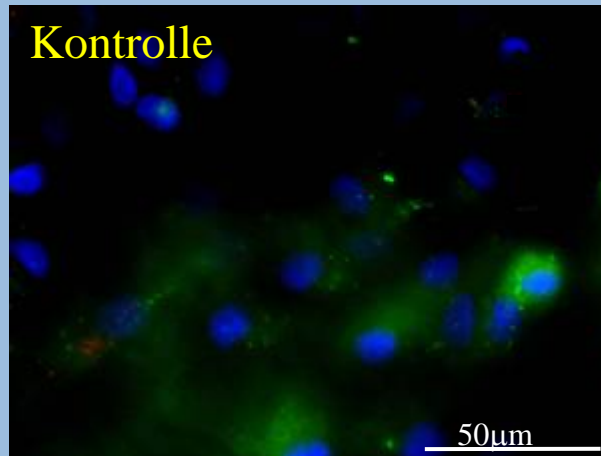


B. Rothen-Rutishauser, University of Bern

# CELLULAR REACTION: OXIDATIVE STRESS (ROS, REACTIVE OXYGEN SPECIES)

■ ROS

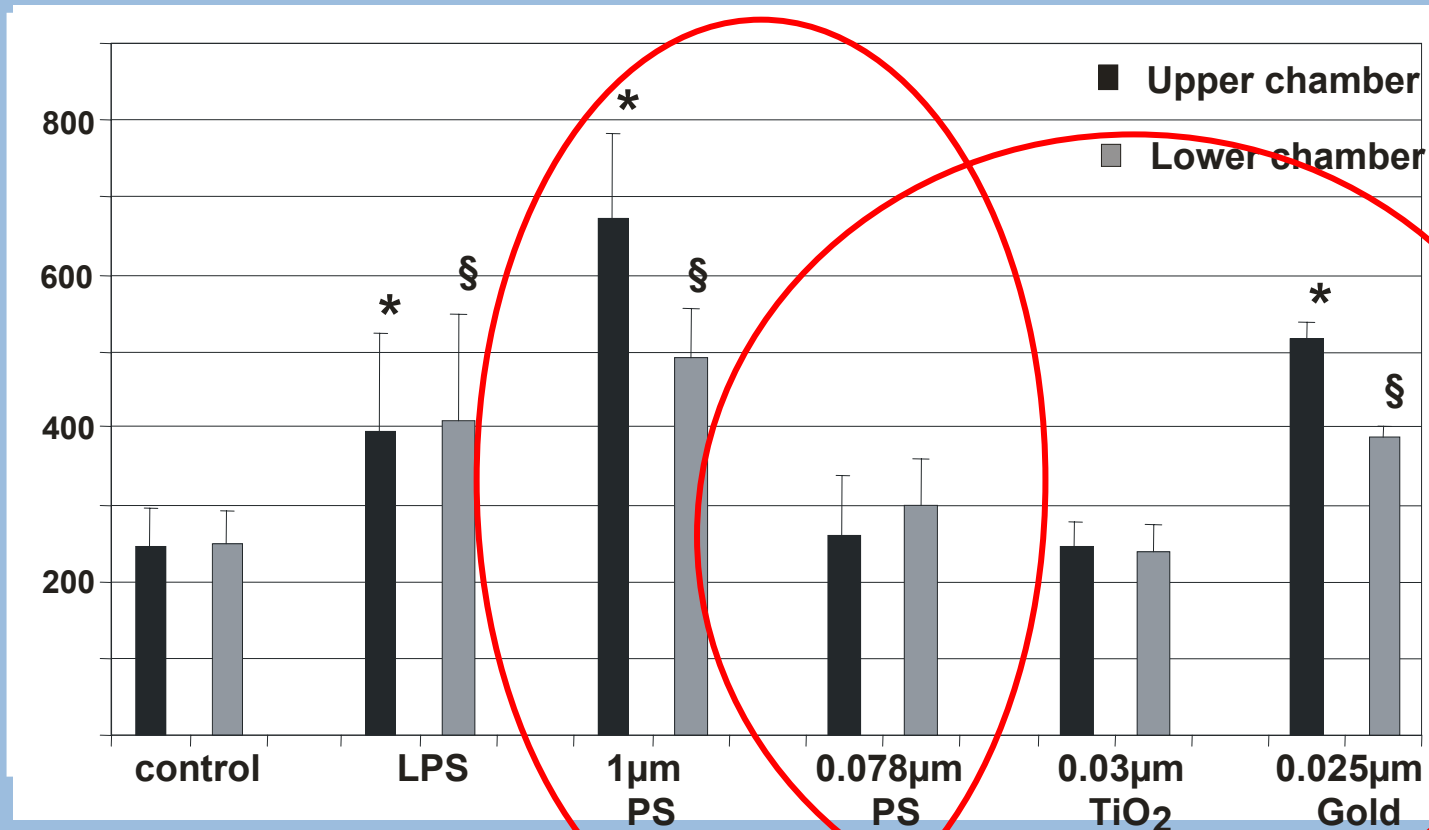
■ Zellkern



L. Müller, University of Bern

# Cellular reaction:

## Pro-inflammatory chemokine (TNF-α)

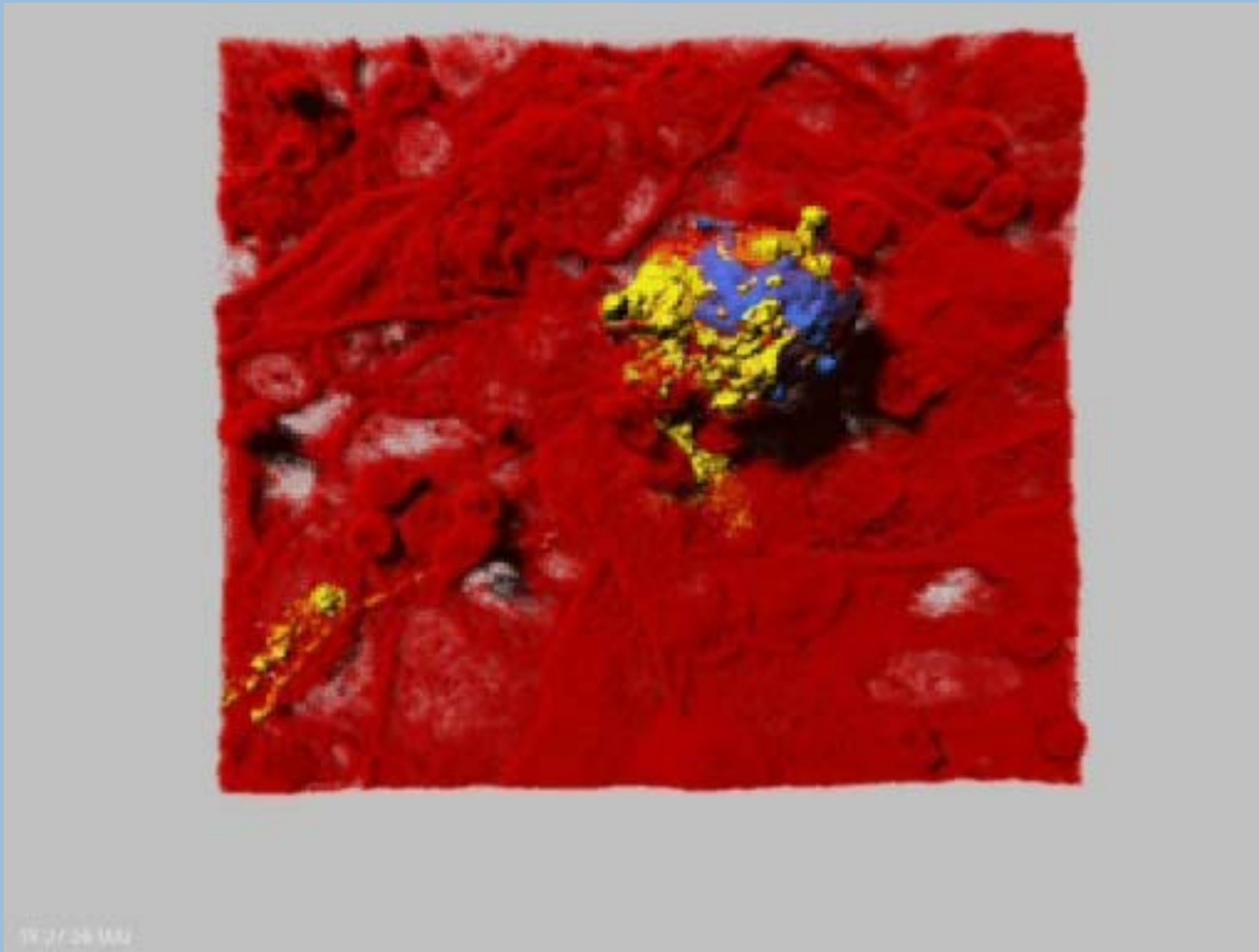


# INTERACTION OF DENDRITIC CELLS WITH MACROPHAGES

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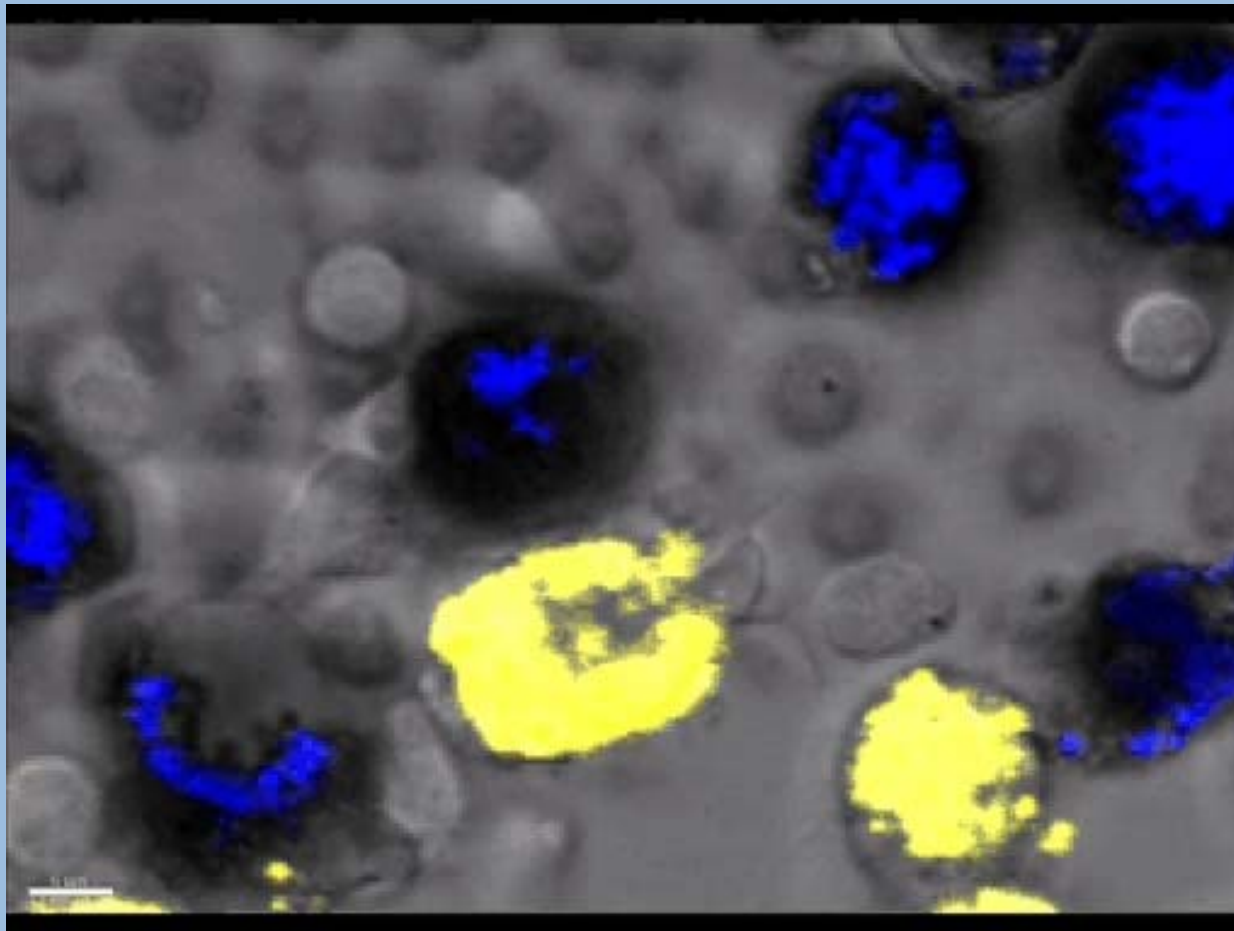
Blank et al., AJRCMB 36: 669-677, 2007

# DENDRITIC CELLS APPROACH PARTICLE LOADED MACROPHAGES

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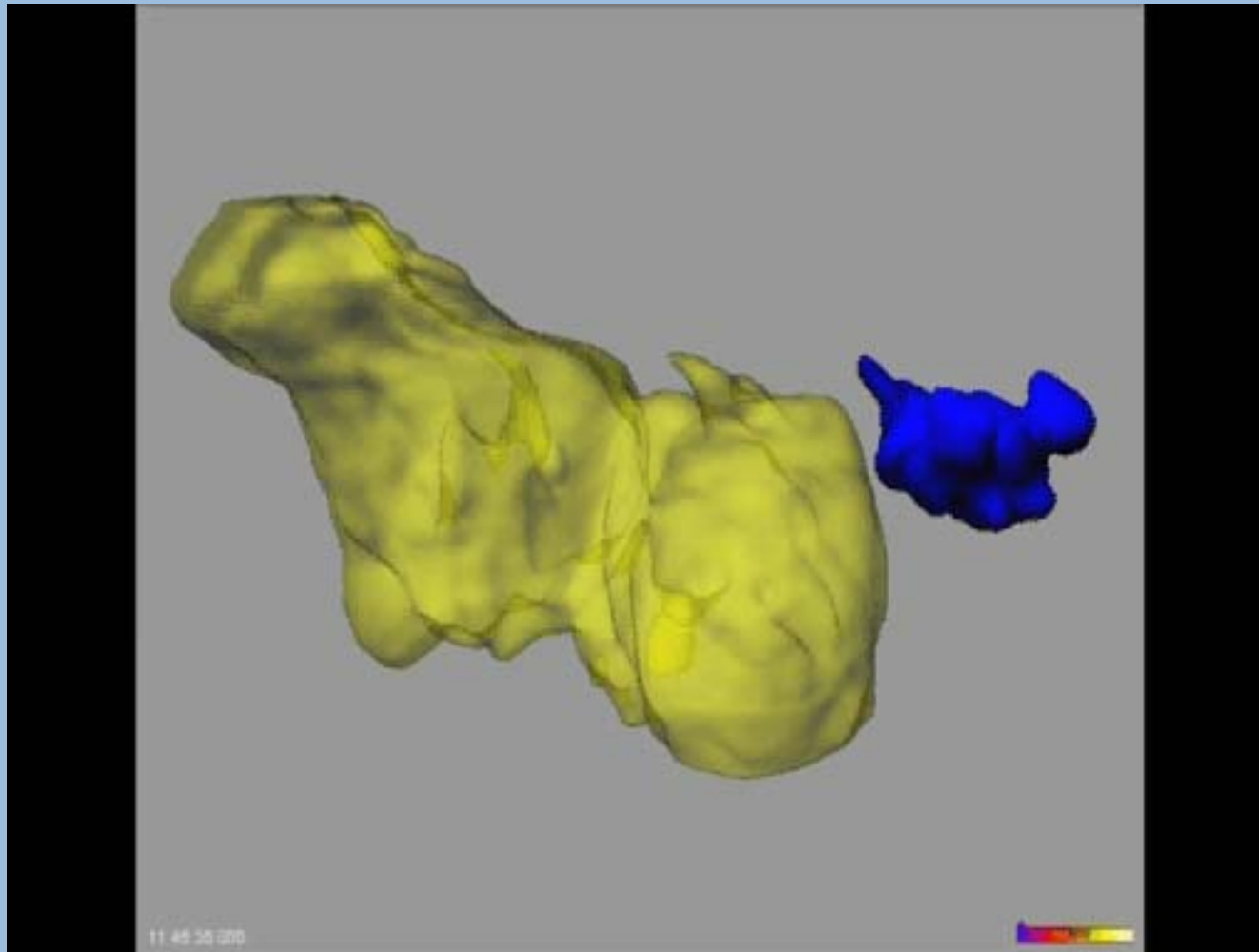
F.Blank, B. Rothen, University of Bern

# PARTICLE TRANSFER FROM MACROPHAGES TO DENDRITIC CELLS

*u*<sup>b</sup>

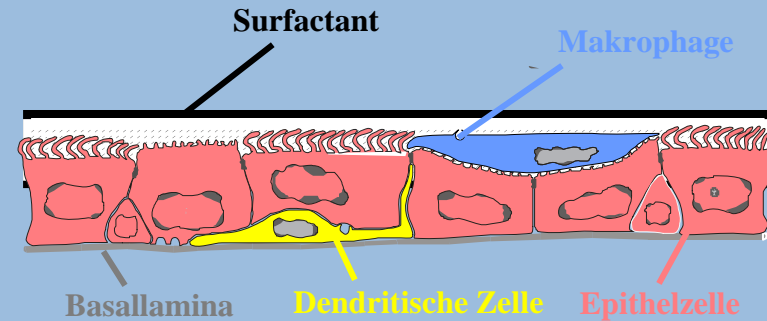
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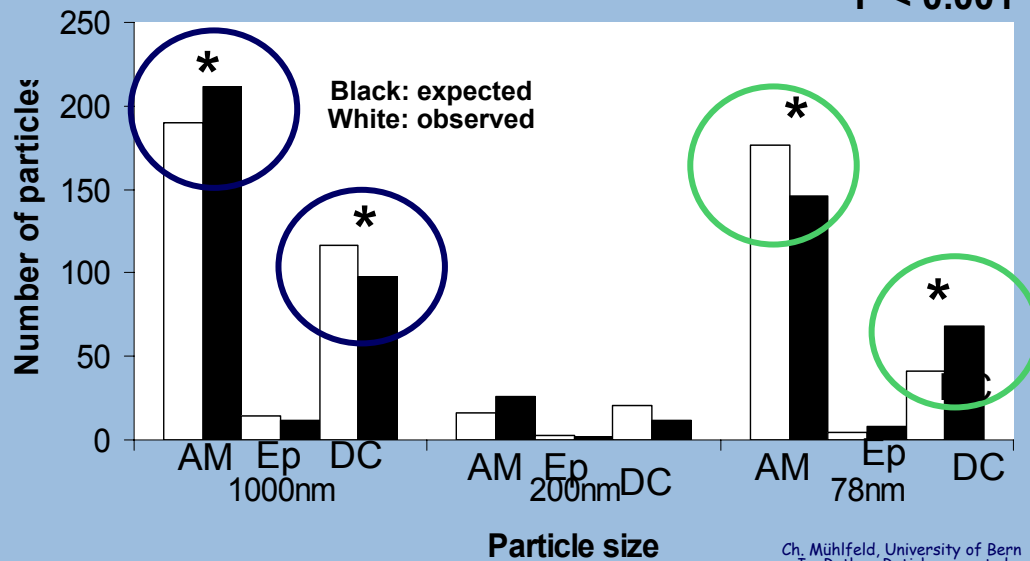
F.Blank, B. Rothen, University of Bern

# Erläuterungen zum „particle trafficking“



Observed and expected numbers of particles taken up by the three different cell types

$\chi^2 = 35.2$   
 $P < 0.001$



- Feine Partikel: Weniger in AM, da AM Partikel an DC abgeben
- Nanopartikel: Mehr in AM, da AM dem Aerosol eine grössere Fläche bieten

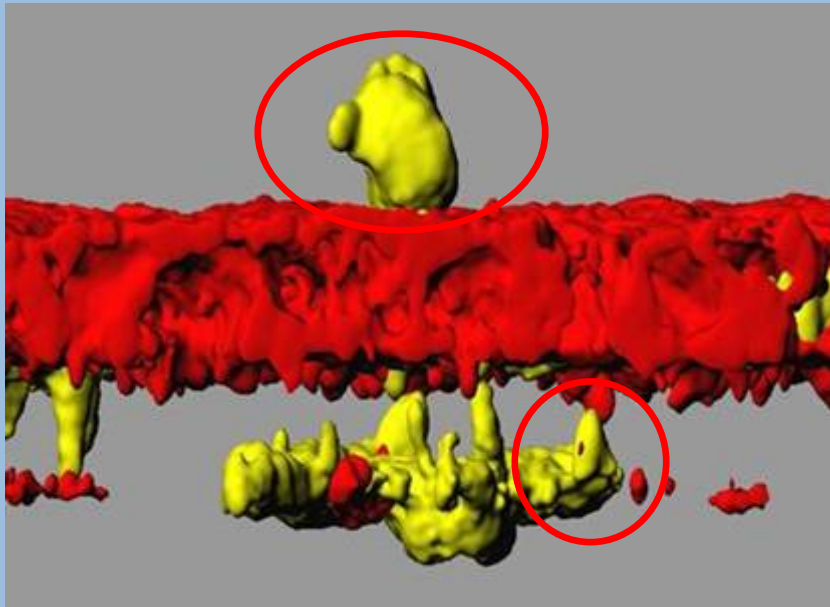
Ch. Mühlfeld, University of Bern  
In: Rothen-Rutishauser et al.,  
Part. Fibre Toxicol., 4: 9, 2007

# INTERPLAY OF MAKROPHAGES AND DENDRITIC CELLS

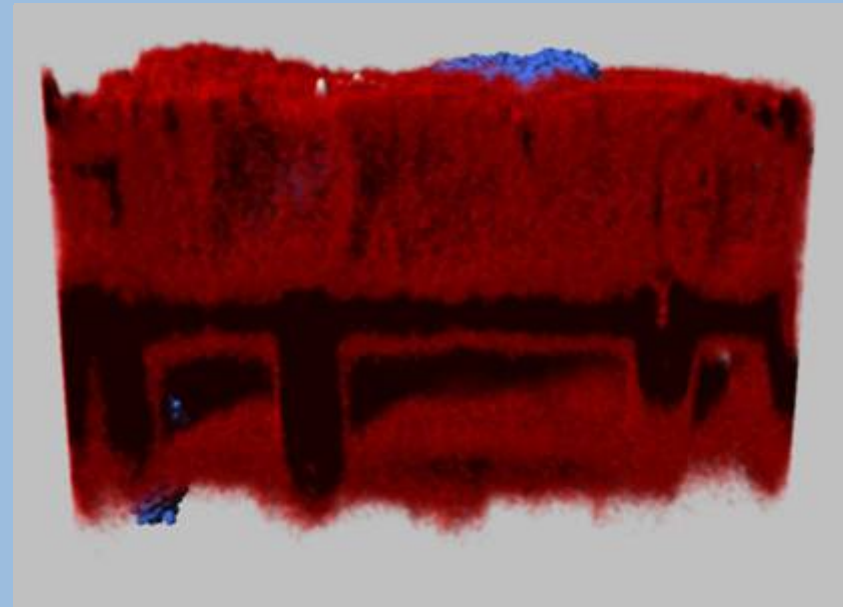
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Blank et al., AJRCMB 36: 669-677, 2007



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Fabian Blank

## University of Giessen, Germany

Christian Mühlfeld

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Helmholtz Centre: Munich  
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