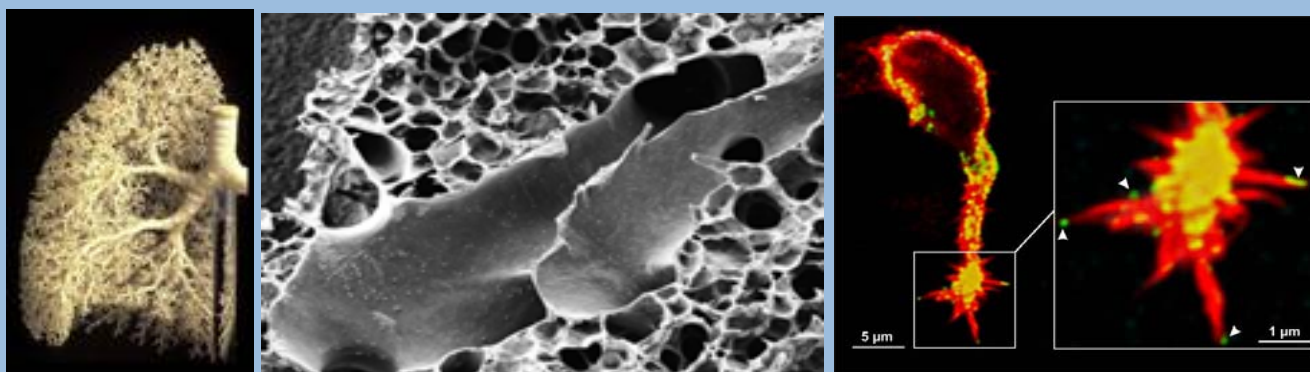


Intergovernmental Forum on Chemical Safety, IFCS  
Forum VI, Nanotechnology and manufactured  
nanomaterials: Opportunities and challenges  
Dakar, Senegal  
26 September, 2008

# THE INTERACTION OF MANUFACTURED NANOMATERIALS WITH OUR ORGANISM – EXAMPLE LUNG

Peter Gehr, PhD  
Professor and Chair  
Institute for Anatomy  
University of Bern  
Bern  
Switzerland



# HEALTHY LUNG – FINE DUST LUNG



Boehringer Ingelheim

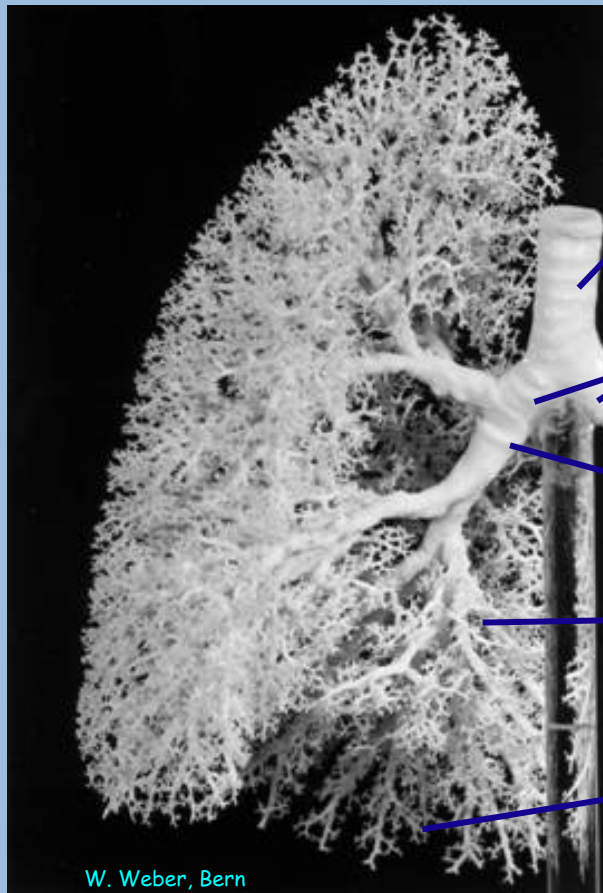


Boehringer Ingelheim

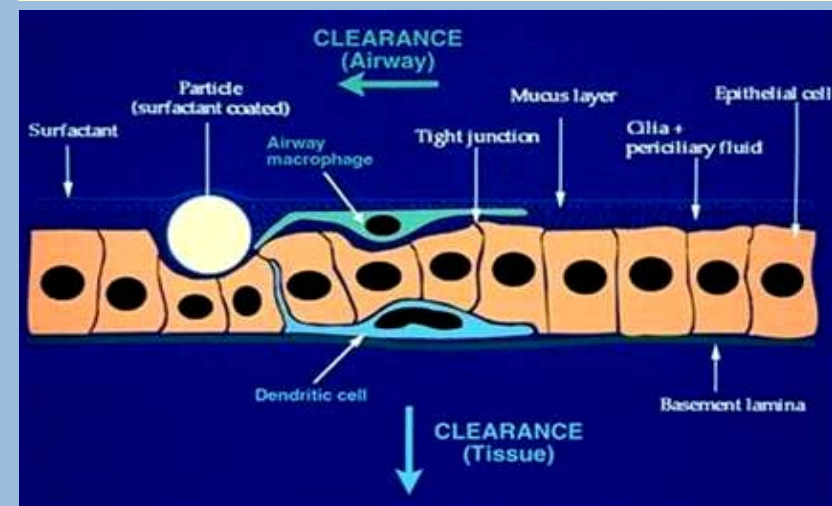
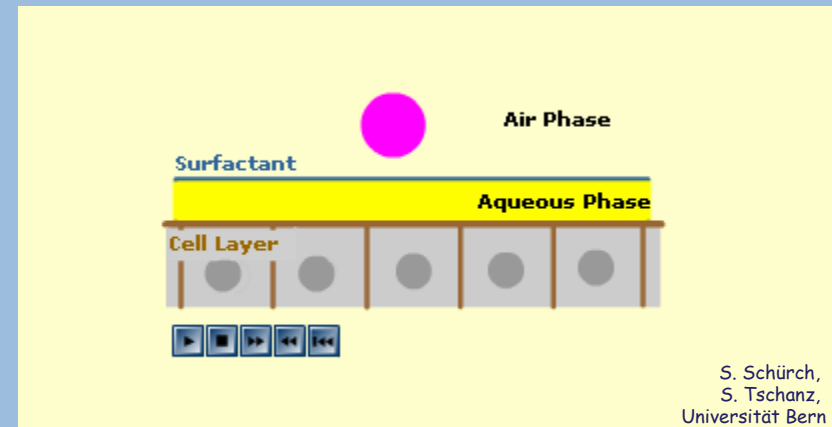


Burkhardt, Institute for Pathology, University of Bern

# THE AIRWAY TREE AS A PARTICLE FILTER



Trachea  
Main Bronchi  
Bronchi  
Bronchioli  
Alveoli  
(not seen)

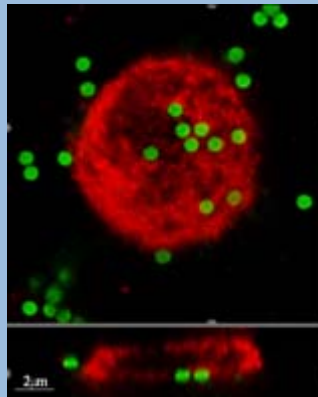


# MACROPHAGES *in vitro* (LASER SCANNING MICROSCOPY)

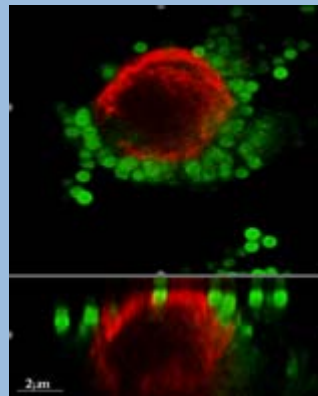
■ F-Actin

■ 1 μm  
(fine)  
Polystyrene  
particles

Control



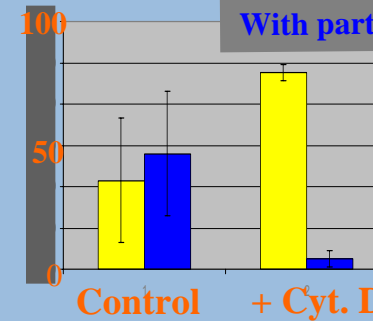
+ Cytochalasin D



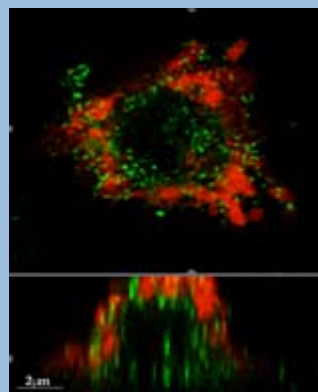
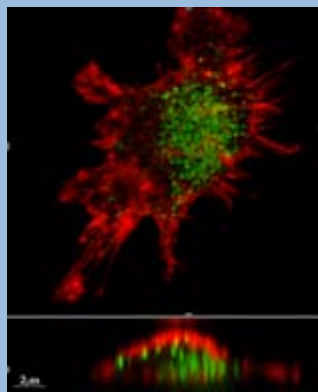
[% cells]

Without particles

With particles



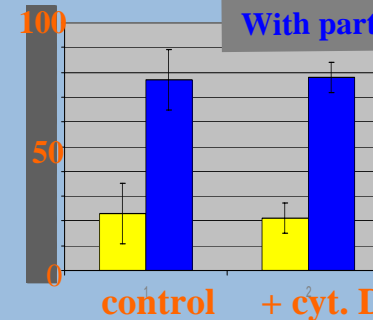
■ 0.078 μm  
(ultrafine)  
Polystyrene  
particles



[% Cells]

Without particles

With particles

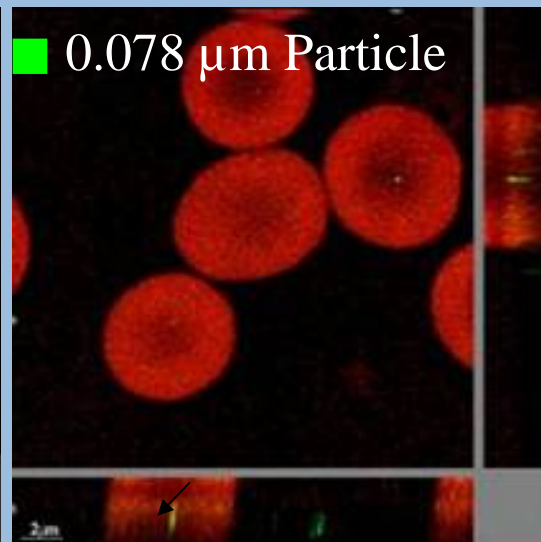
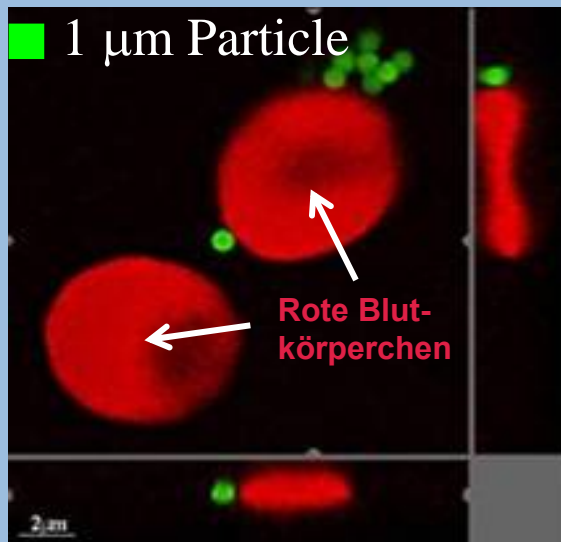


B. Rothen-Rutishauser, University of Bern

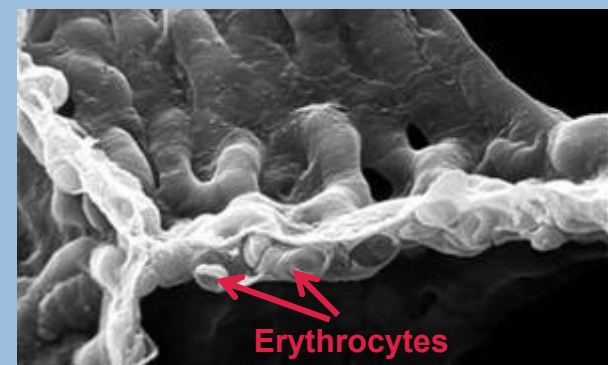
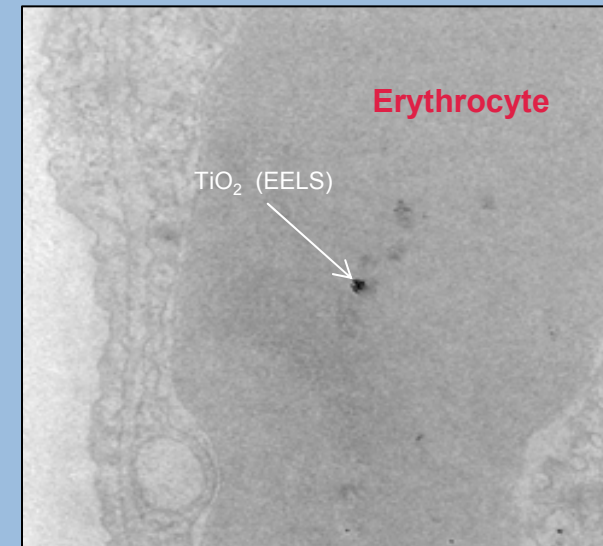
# ERYTHROCYTES WITH POLYSTYRENE PARTICLES

Autofluorescence

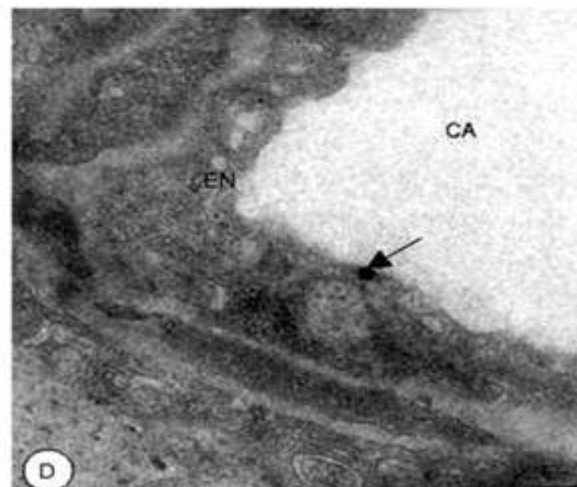
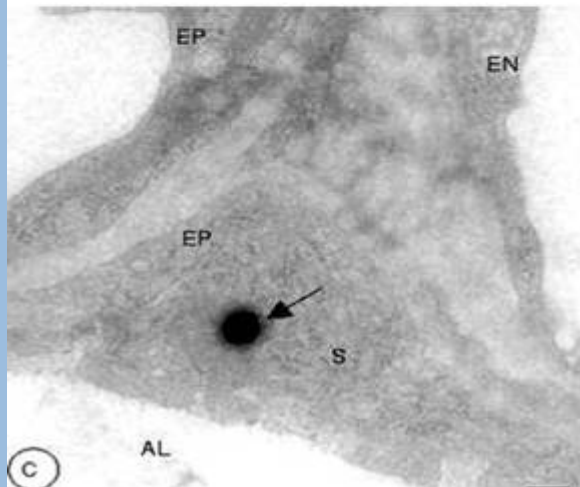
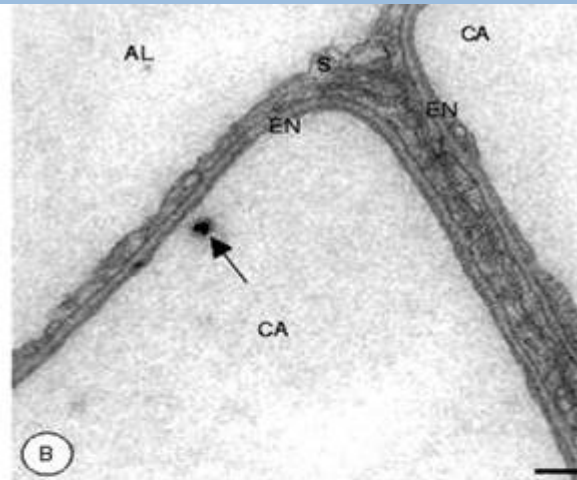
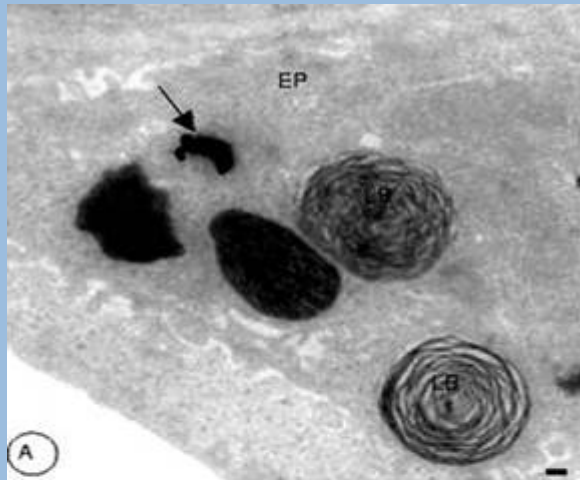
Fluorescent Polystyrene Particles



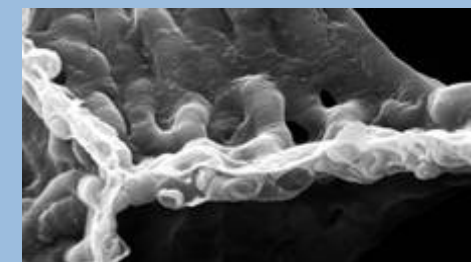
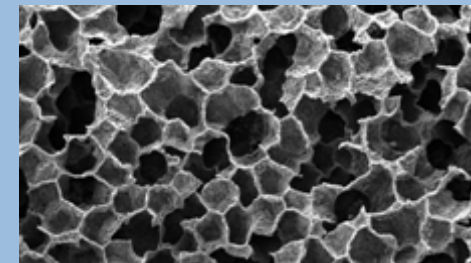
B. Rothen-Rutishauser  
In: Geiser et al.,  
EHP 113: 1555-1560, 2005



# ULTRAFINE TiO<sub>2</sub> PARTICLES IN THE GAS EXCHANGE REGION OF THE HAMSTER LUNG

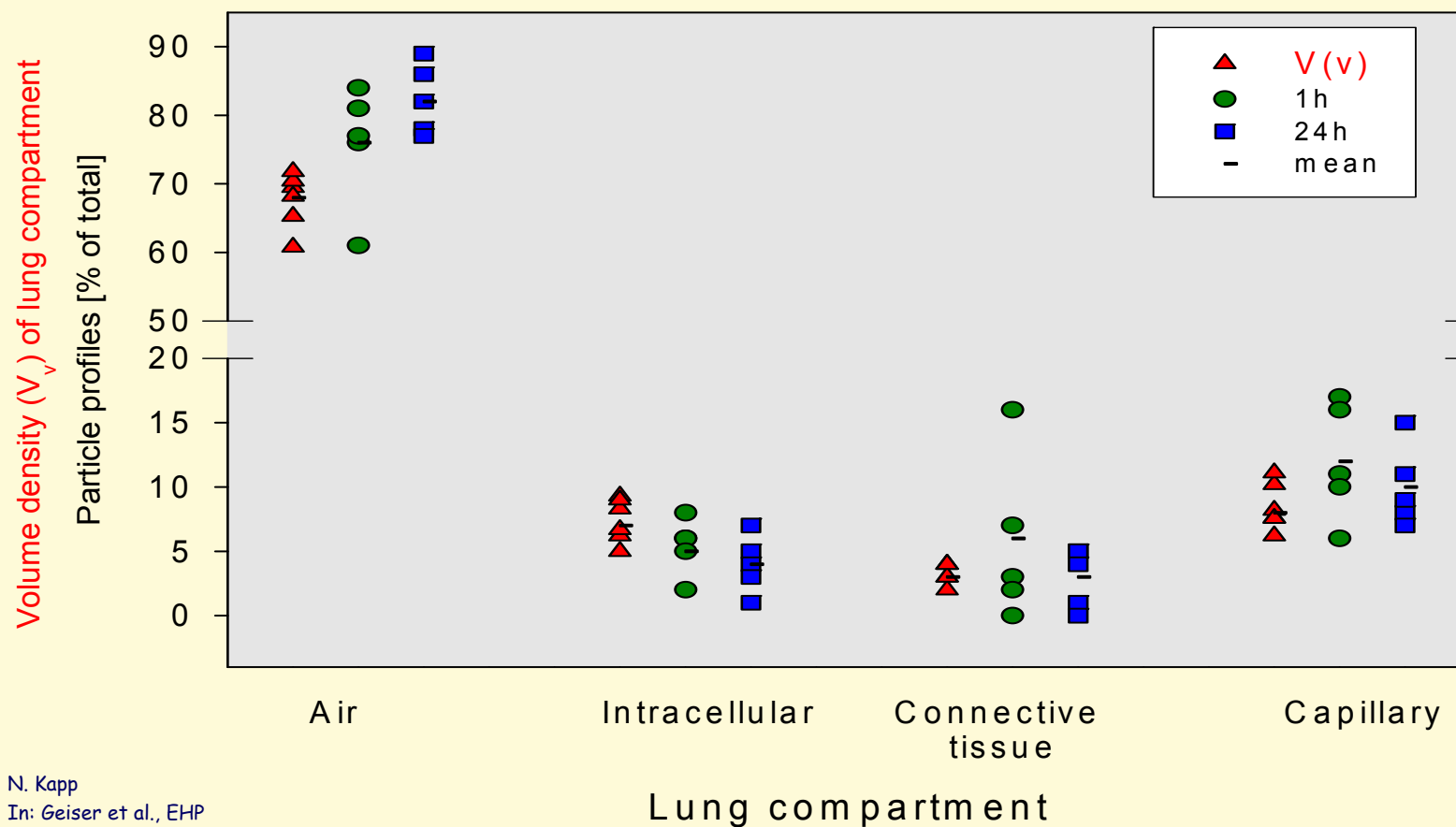


## Human Lung



Kapp et al., MRT 36/5, 2004

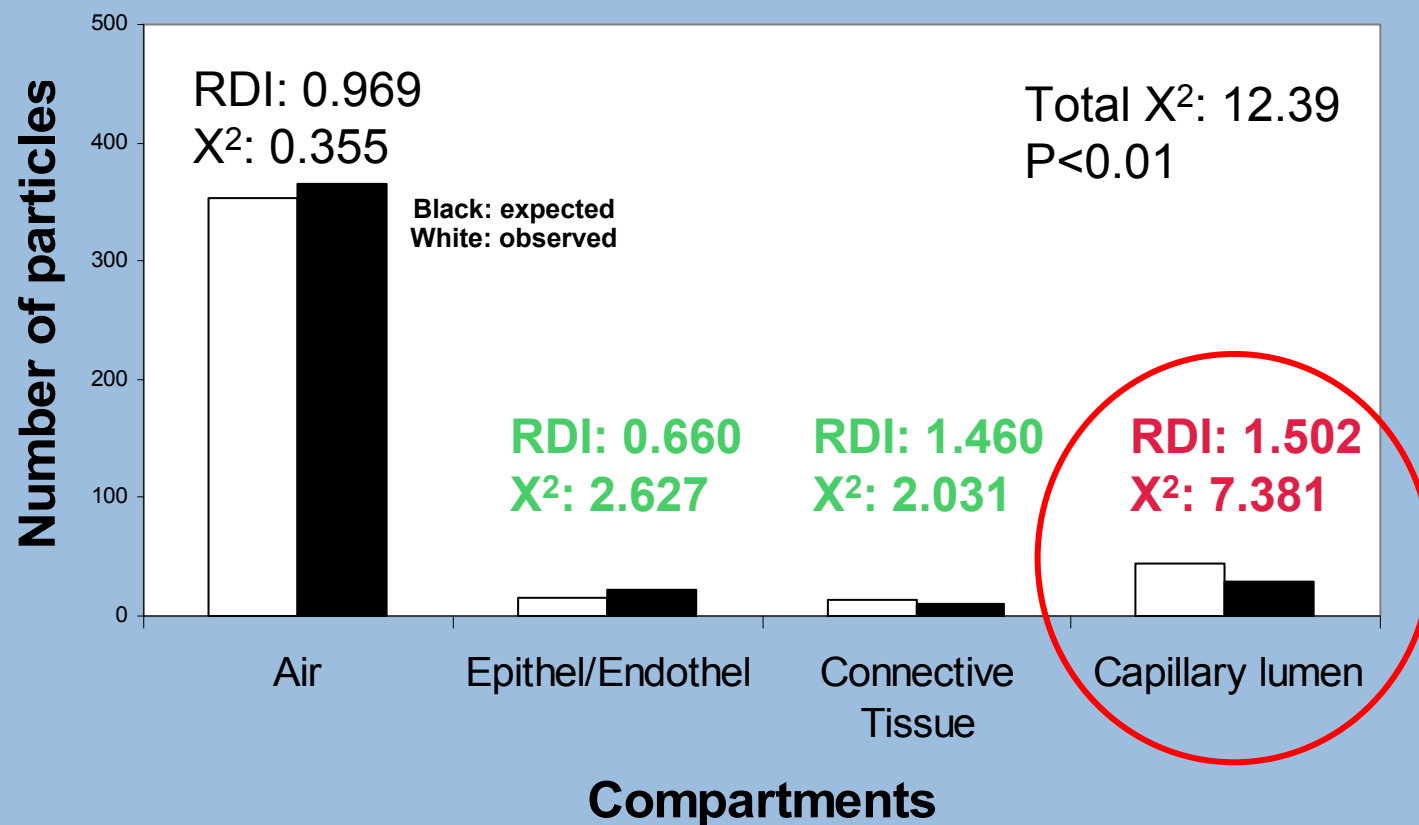
# DISTRIBUTION OF ULTRAFINE $\text{TiO}_2$ PARTICLES IN HAMSTER LUNGS



N. Kapp  
 In: Geiser et al., EHP  
 113: 1555-1560, 2005

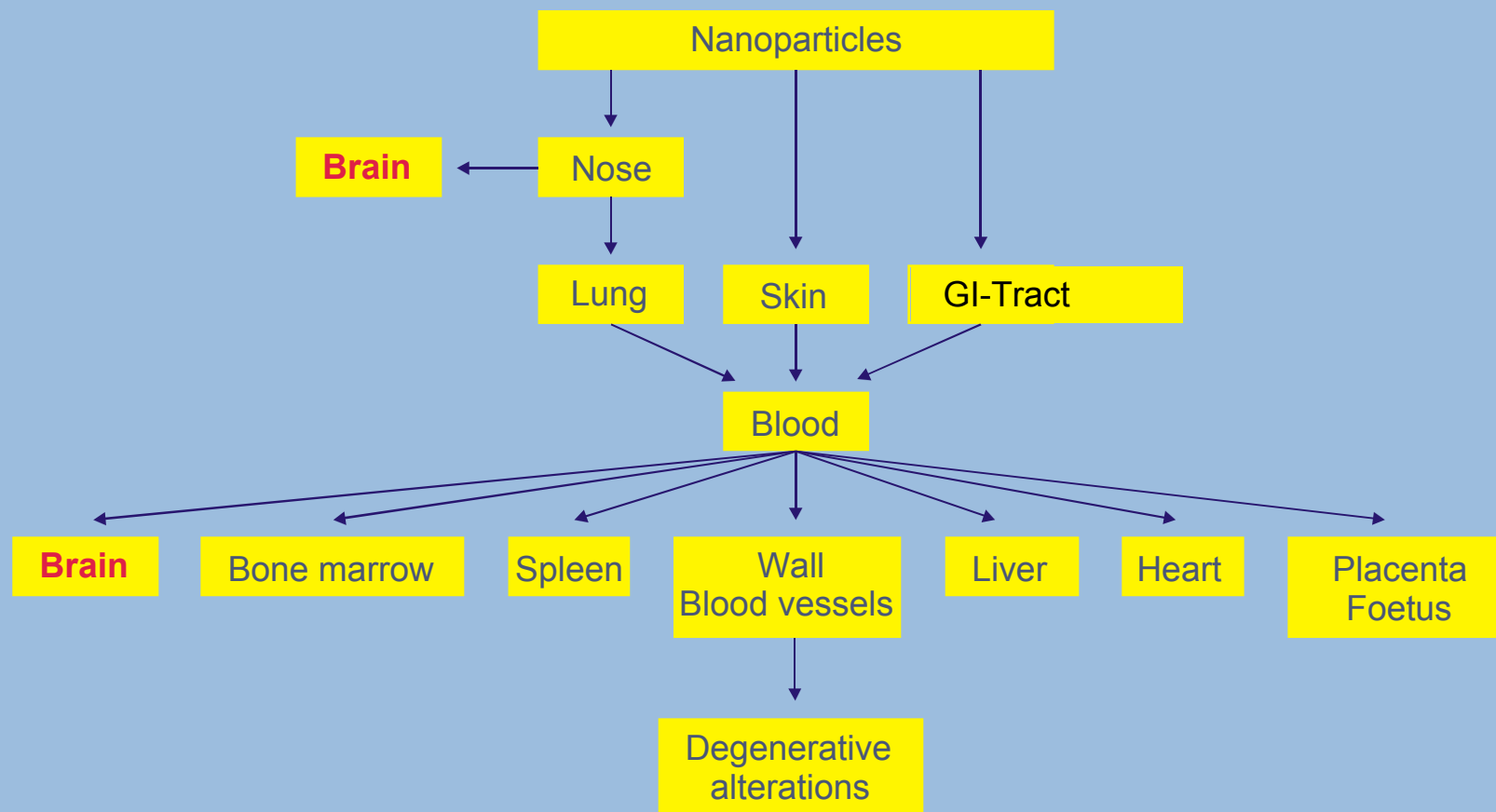
# STEREOLOGICAL ANALYSIS: PARTICLE TRAFFICKING

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

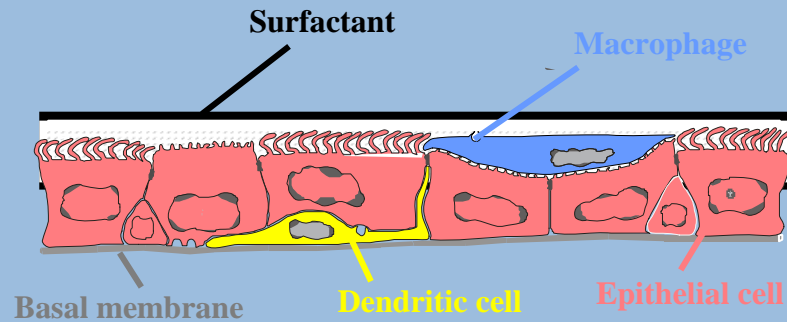


# Translocation

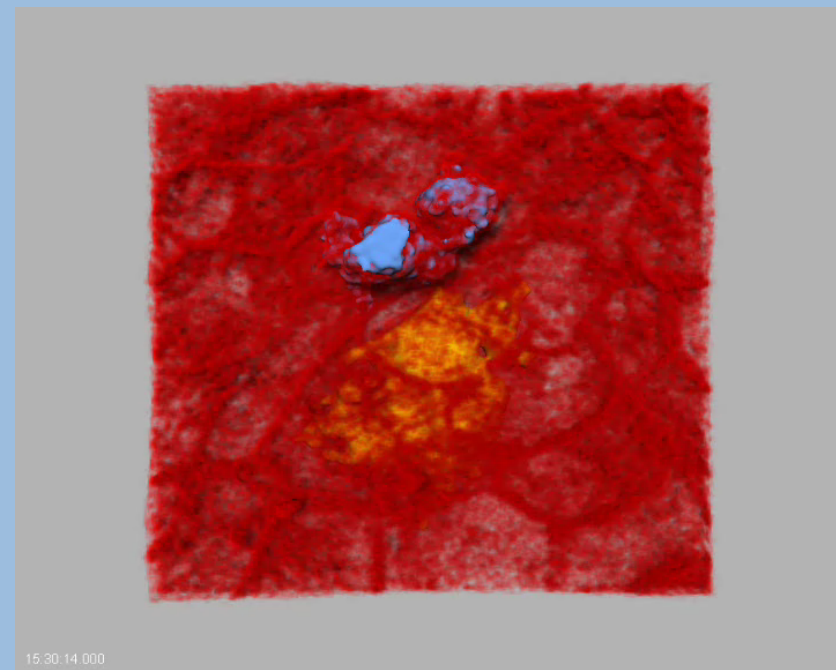
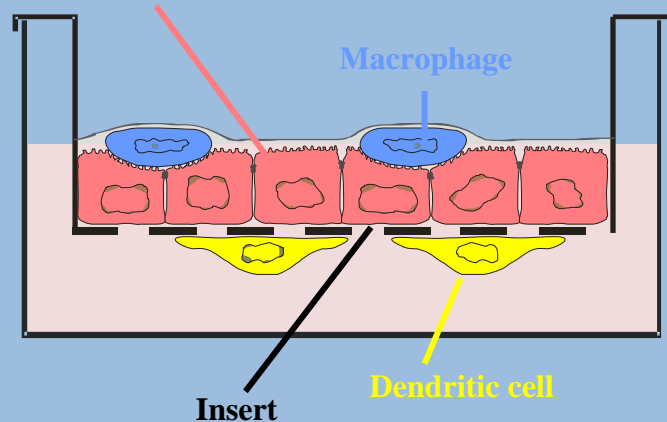
Distribution of nanoparticles in the organism



# EPITHELIAL AIRWAY WALL – *in vitro* SYSTEM



Epithelial cell  
monolayer



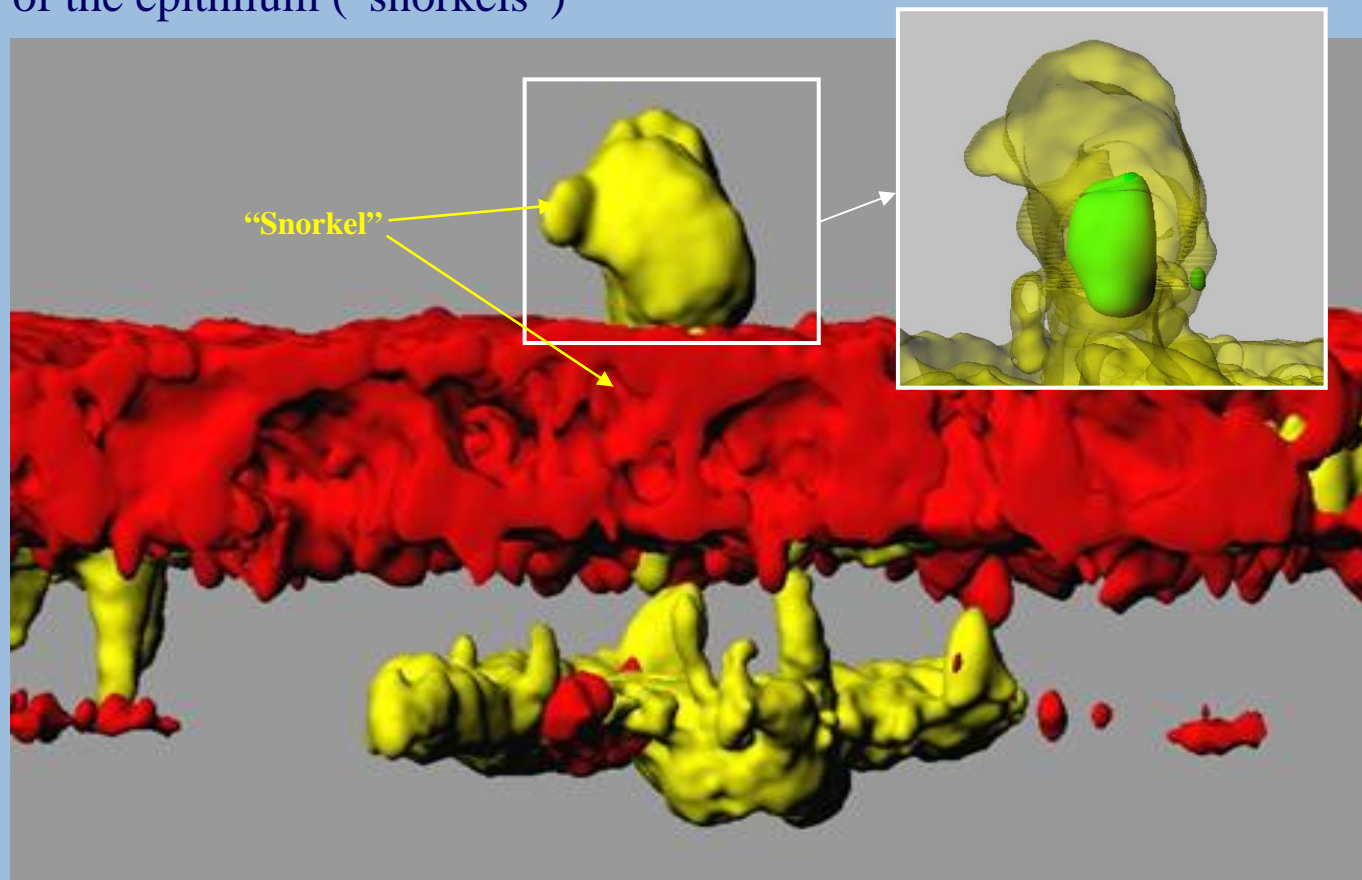
F. Blank, Institute for Anatomy, University of Bern

(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)

# PARTICLE TRANSLOCATION

**DCs** extend transepithelial processes towards the “luminal side” of the epithelium (“snorkels”)

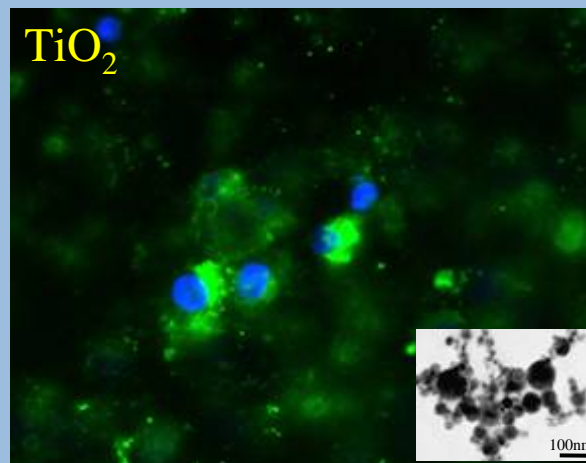
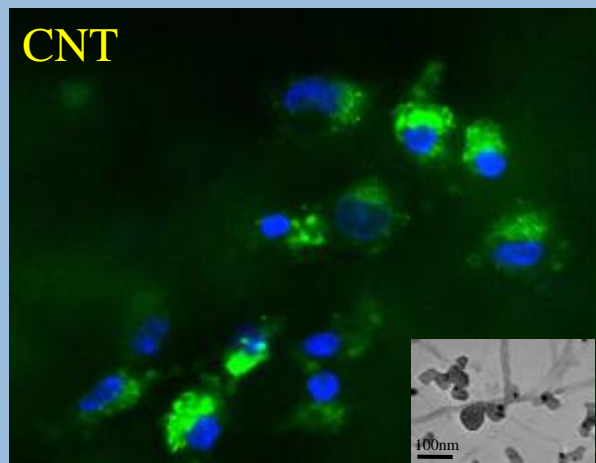
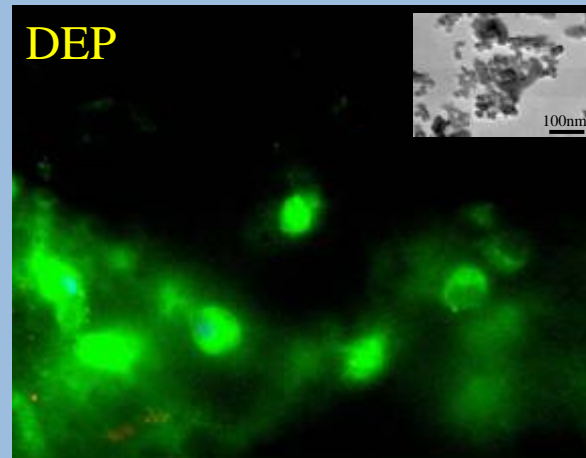
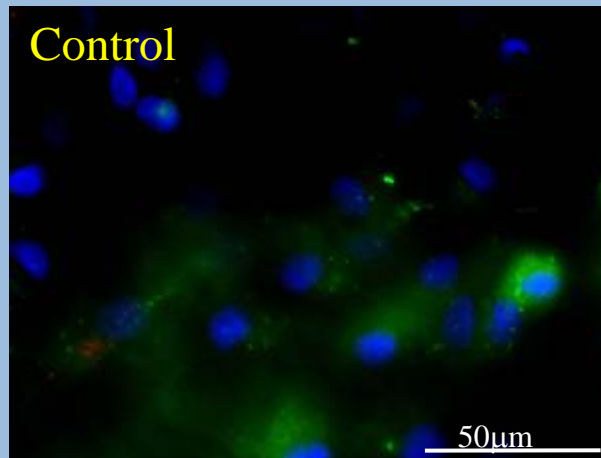


Blank et al., 2007, *Am. J. Respir. Cell Mol. Biol.* 36: 669-77.

# CELLULAR REACTIONS (OXIDATIVE STRESS: ROS)

■ ROS

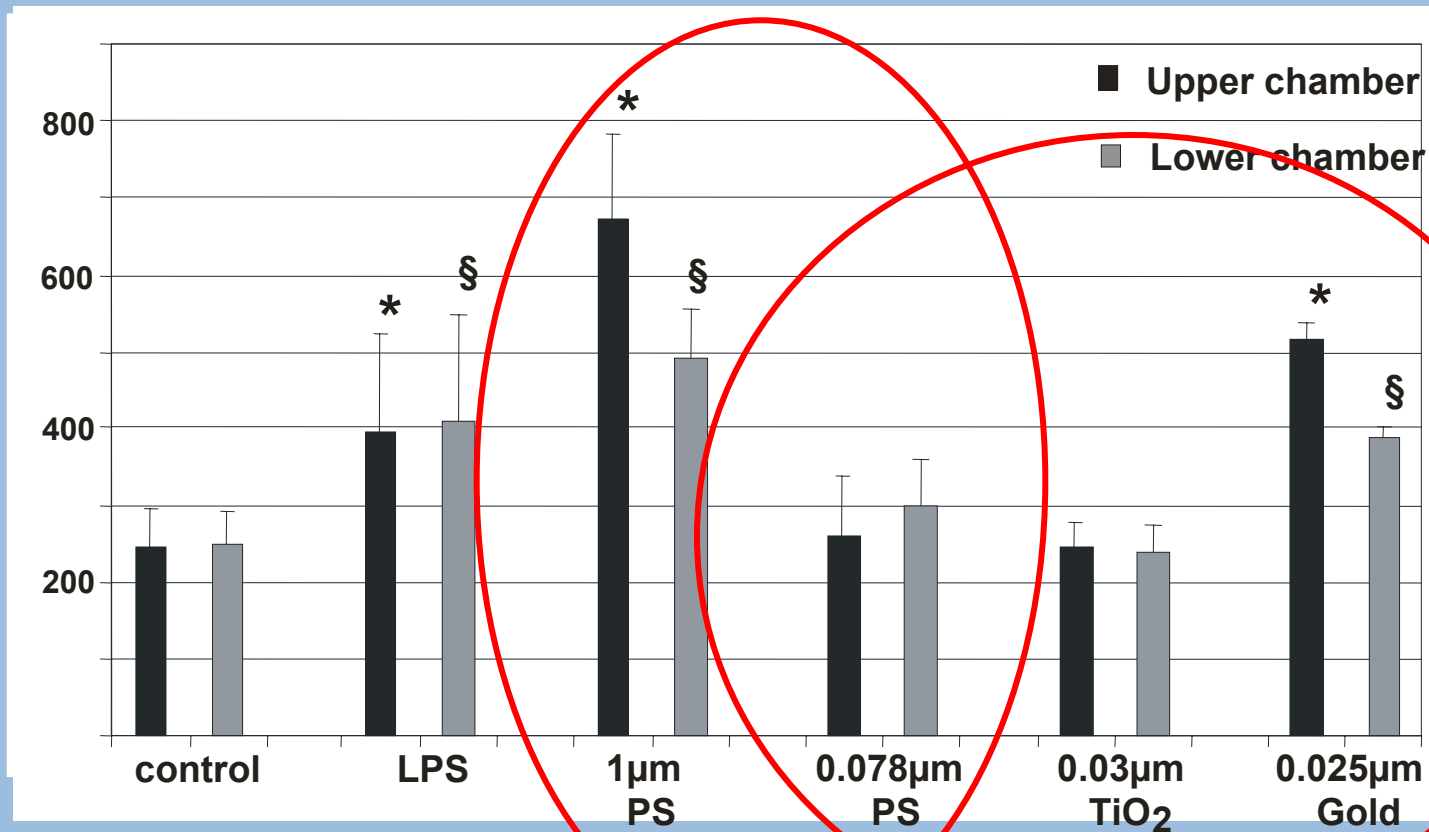
■ Cell Nuclei



L. Müller, University of Bern

# CELLULAR REACTIONS

(PRO-INFLAMMATORY CHEMOKINE TNF- $\alpha$ )



# CONCLUSIONS

- M. nanoparticles may penetrate cells and tissue
  - M. nanoparticles may enter the capillary blood vessels in the lungs
  - M. nanoparticles may be transported by the blood stream to other organs
  - M. nanoparticles may cause oxidative stress in cells
  - M. nanoparticles may cause inflammatory reactions in cells
- **M. nanoparticles have the potential for adverse health effects**

# TEAMS AND SUPPORT

## Institute of Anatomy, University of Bern:

Barbara Rothen-Rutishauser  
Fabian Blank  
Christian Mühlfeld  
Loretta Müller  
Andrea Lehmann  
Christina Brandenberger



Sandra Frank  
Beat Haenni  
Barbara Tschirren  
Andrea Stokes  
Claudia Haller



## Universities of Calgary and Bern:

Samuel Schürch



## Further Collaborations:

University Hospital Bern  
ETH Zürich  
EMPA St.Gallen/Dübendorf  
IST Lausanne  
Helmholtz Munich

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