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Differentiating the mechanism of lung cell interactions between diesel exhaust particles and carbonaceous fibrous structures

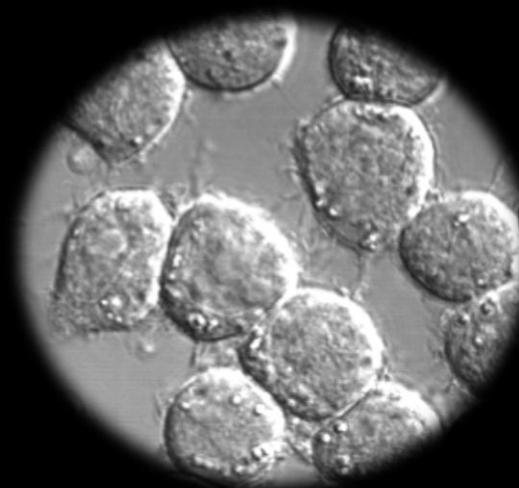
Barbara Rothen-Rutishauser

Co-Chair BioNanomaterials

Adolphe Merkle Institute

University of Fribourg

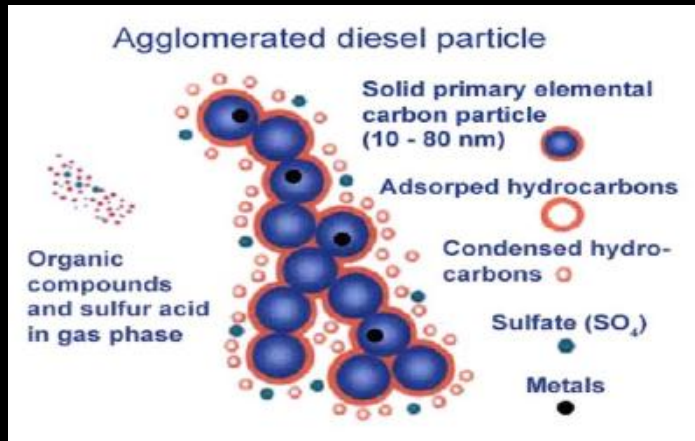
Fribourg, Switzerland



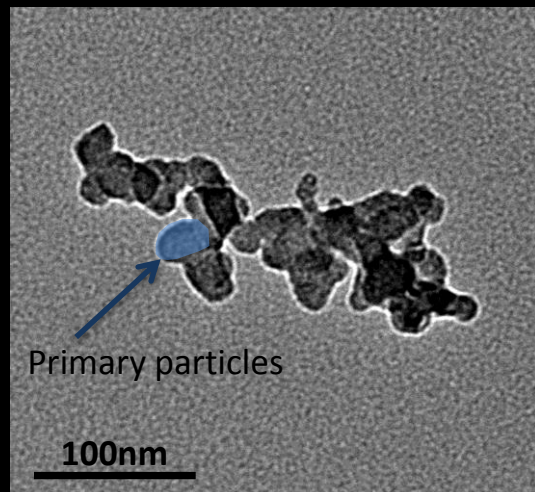


Diesel particles - carbon nanotubes

Diesel exhaust particles

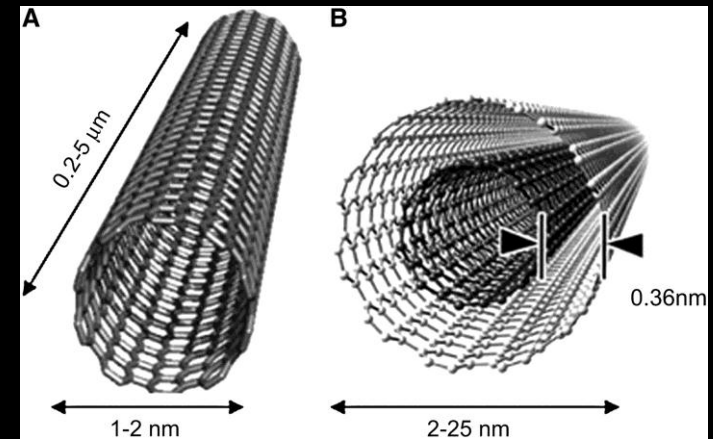


<http://thinkgreen.typepad.com/>

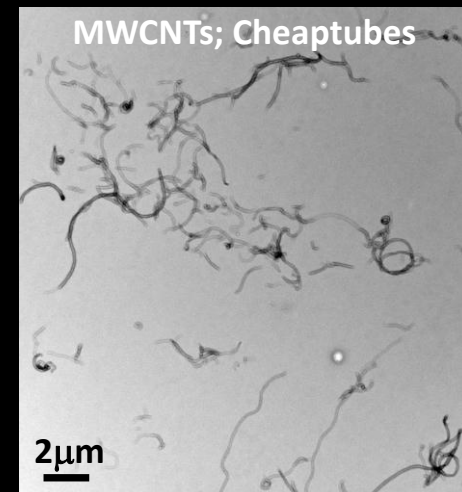
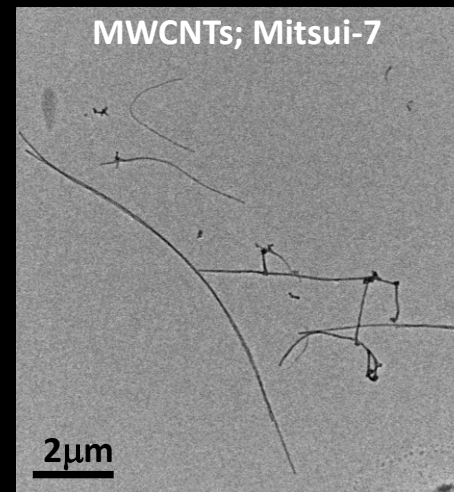


Steiner et al. Arch Tox 2016

Carbon nanotubes



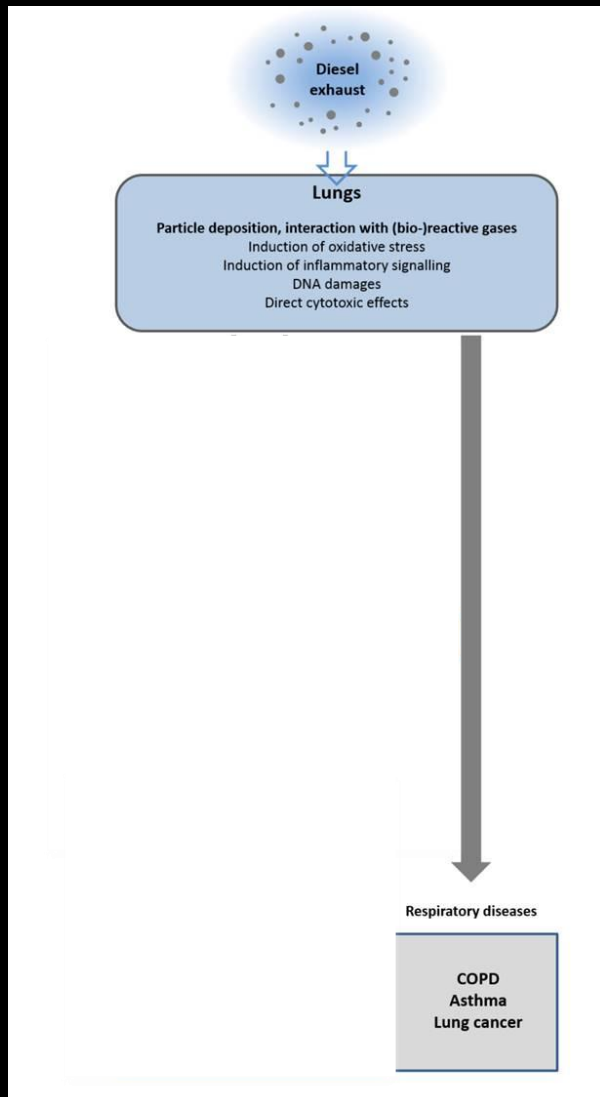
Reilly, J Nucl Med 2007



Chortarea et al. Nanotoxicology 2015



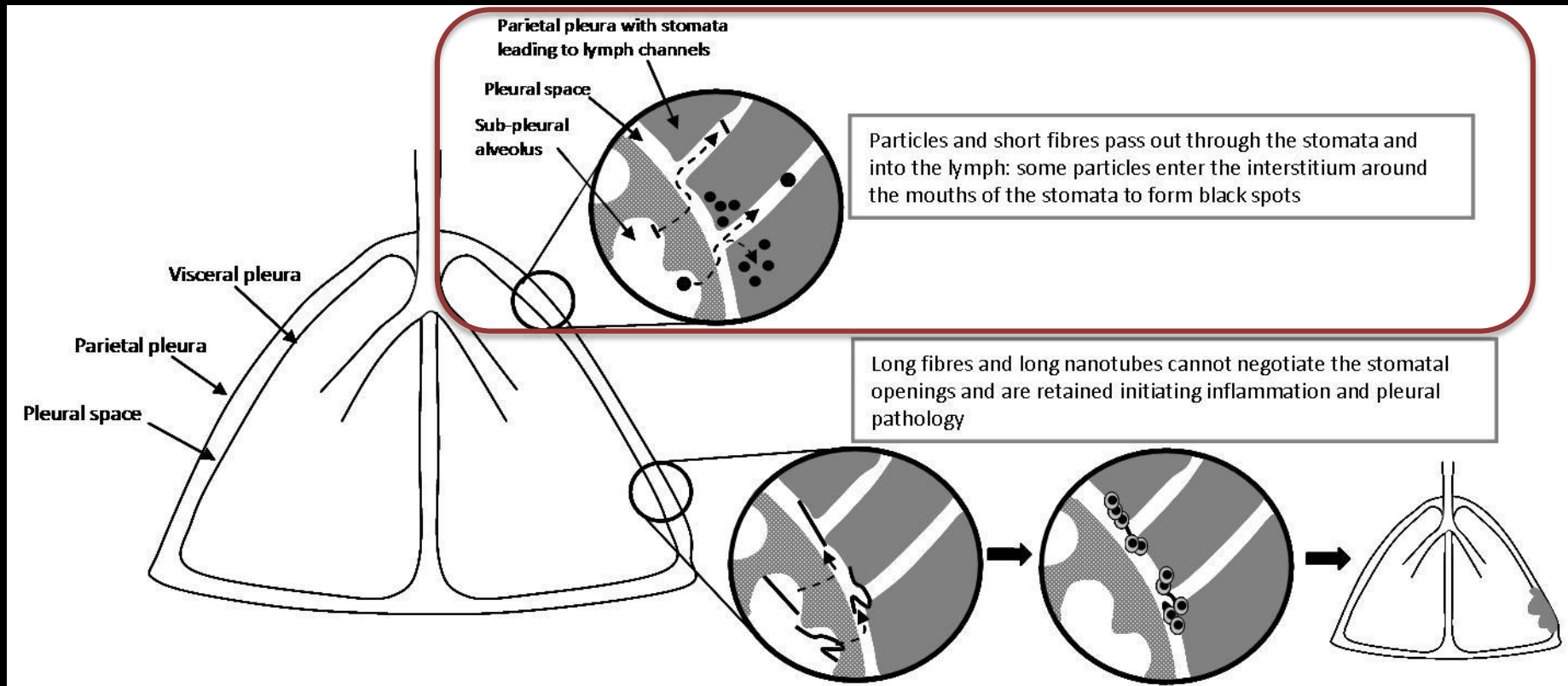
Adverse effects – Diesel exhaust



Steiner et al. Arch Tox 2016



Adverse effects - carbonaceous fibers



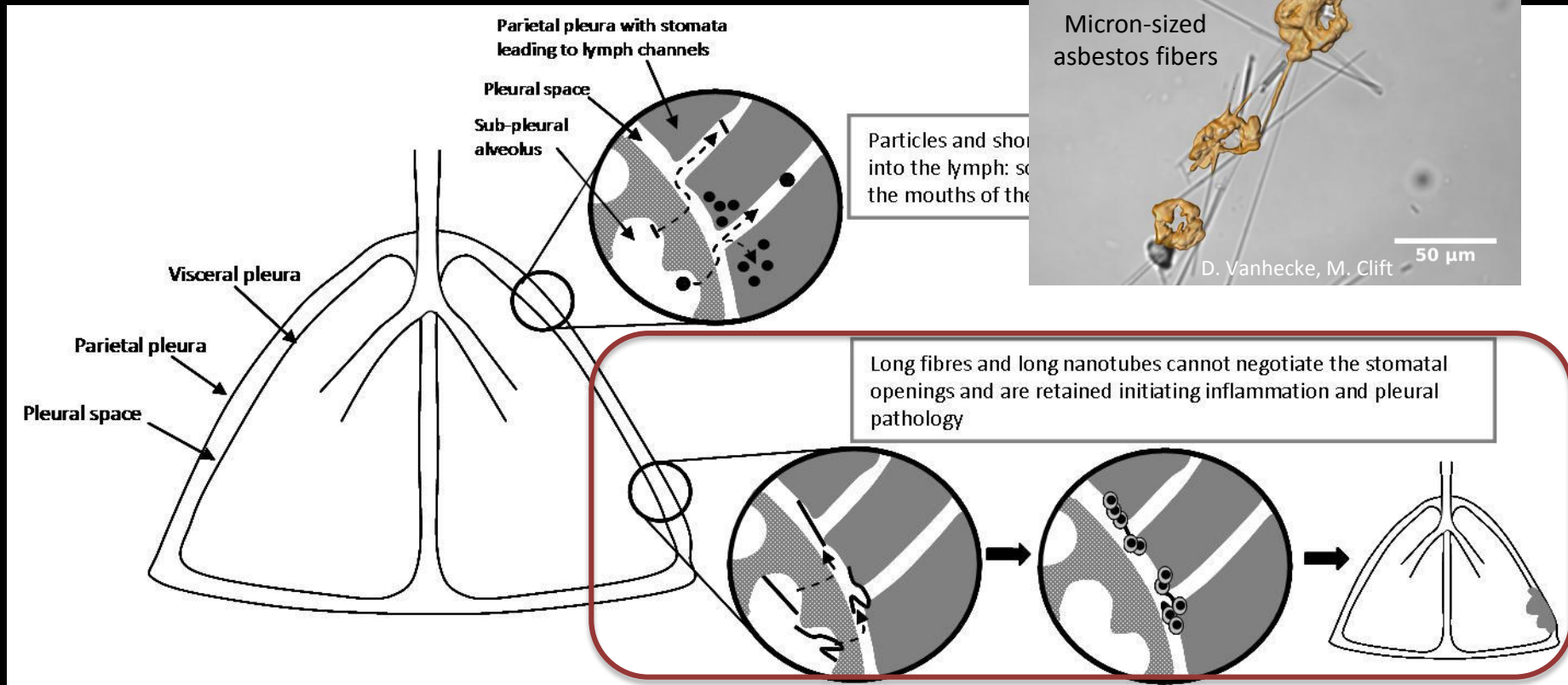
Donaldson et al. Part Fibre Toxicol 2010



Adverse effects - carbonaceous fibers

“frustrated phagocytosis”

Brown et al. Carbon 2007

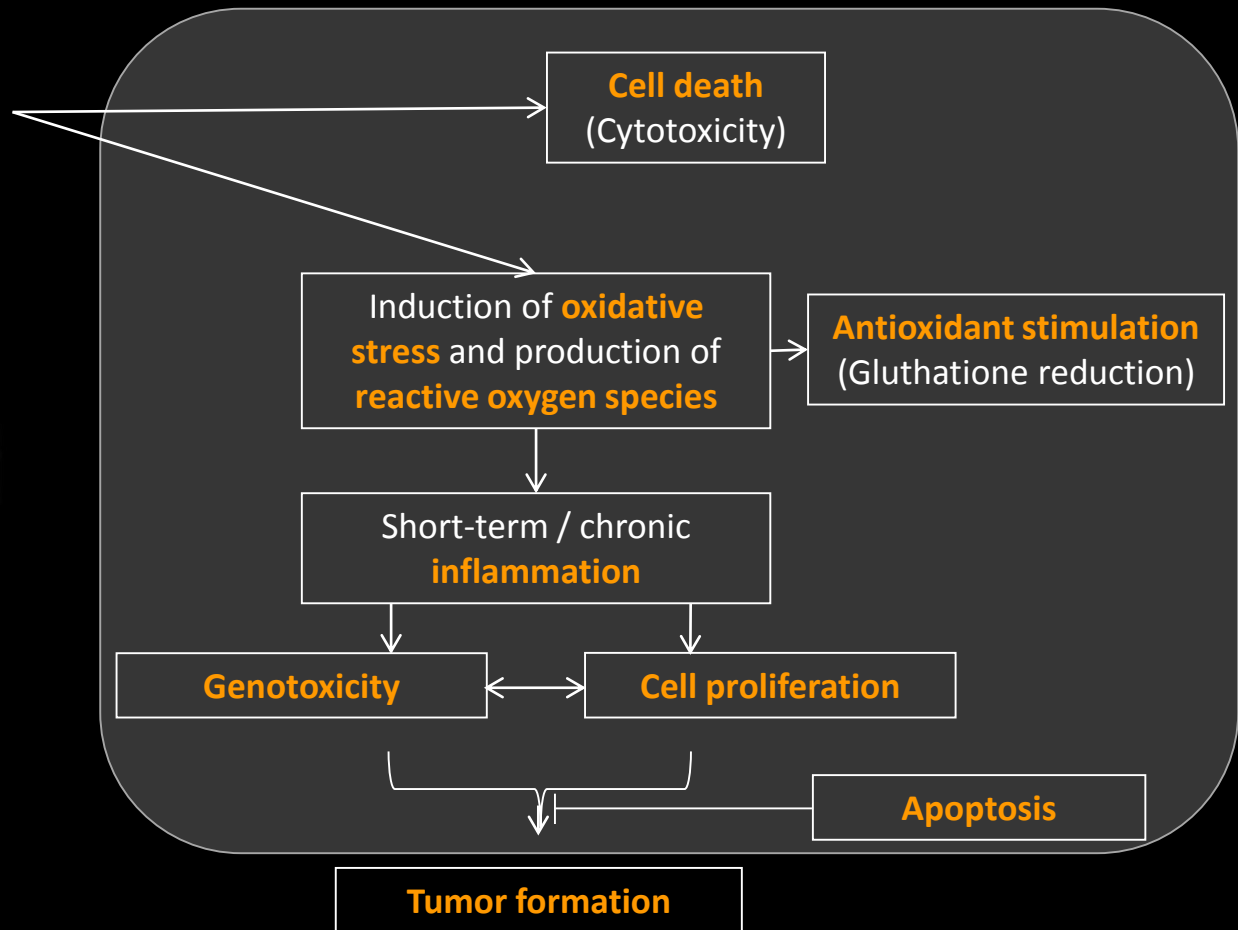
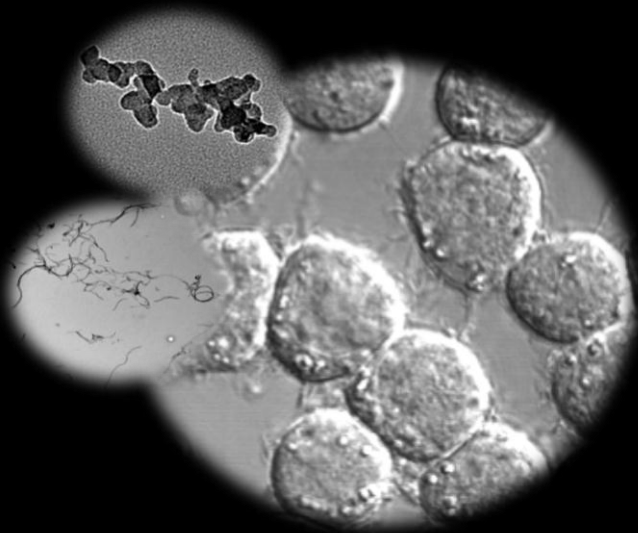


Donaldson et al. Part Fibre Toxicol 2010



Cellular interactions with particles / materials

Nanoparticles – Lung Cell Interactions

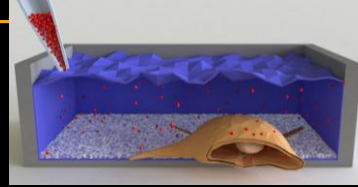


Adapted from Schins et al. Inhalation Toxicology 2007



DEP / CNT interactions with macrophages

Diesel exhaust particles

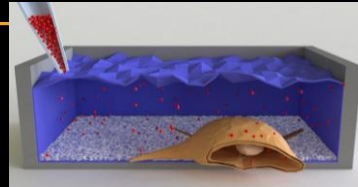


Carbon nanotubes



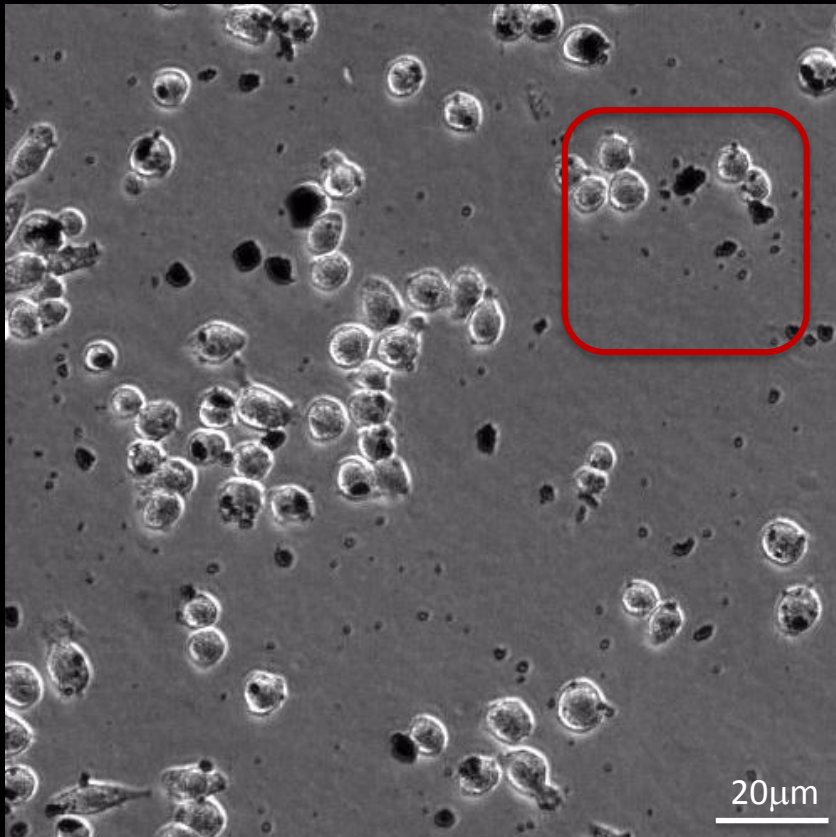
DEP / CNT interactions with macrophages

Diesel exhaust particles



Carbon nanotubes

10 μ g/mL – 48h

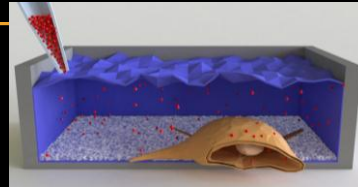


Ch. Bisig / F. Blank



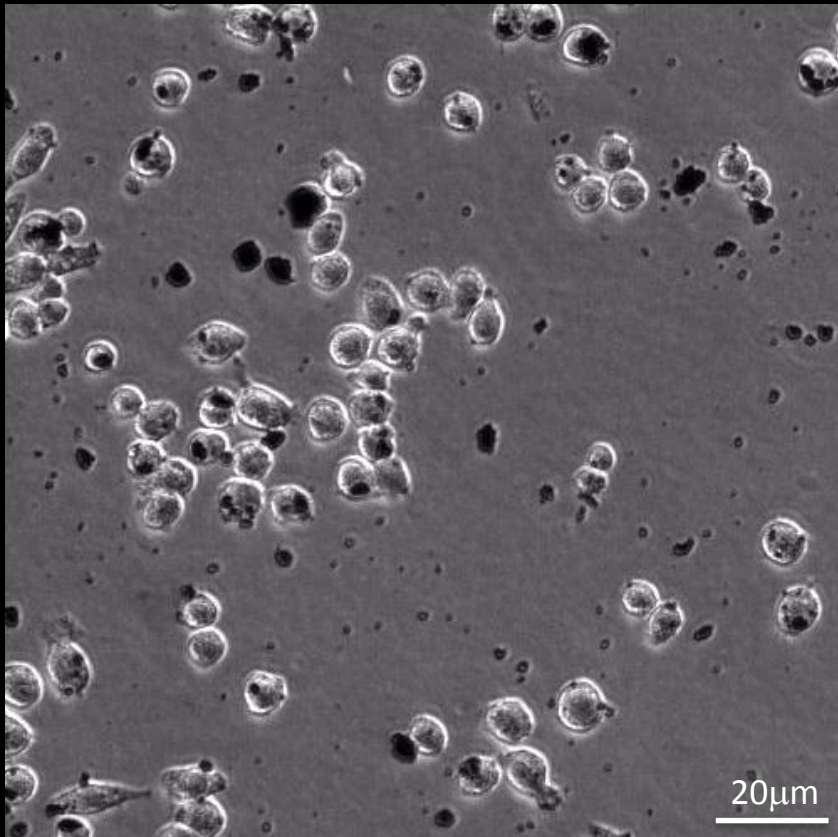
DEP / CNT interactions with macrophages

Diesel exhaust particles

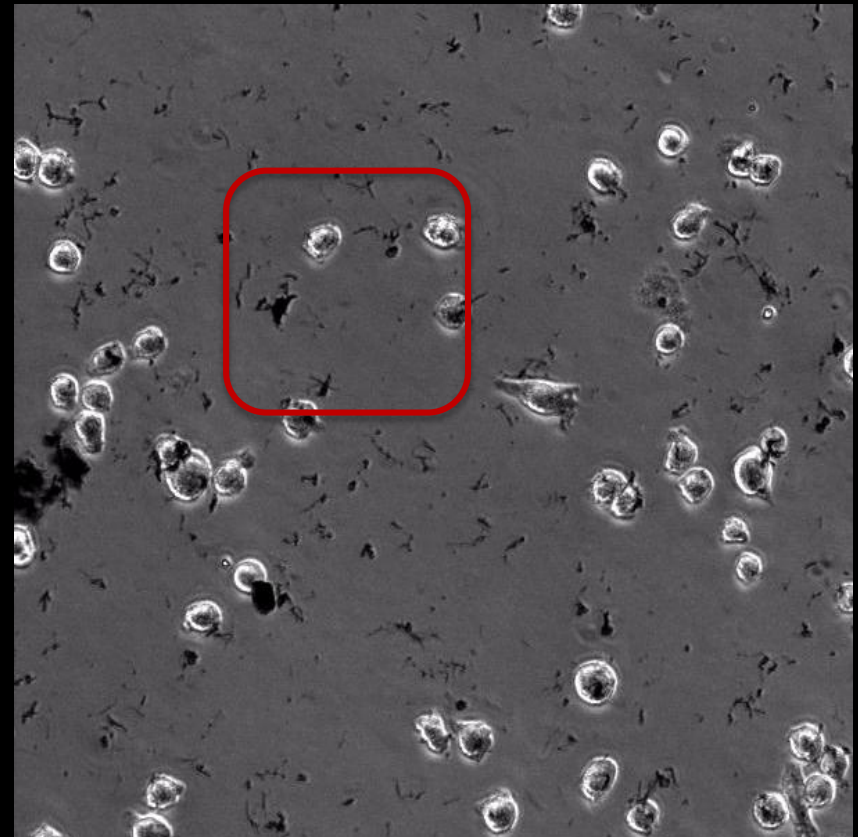


Carbon nanotubes

10 μ g/mL – 48h



5 μ g/mL – 48h



Ch. Bisig / F. Blank

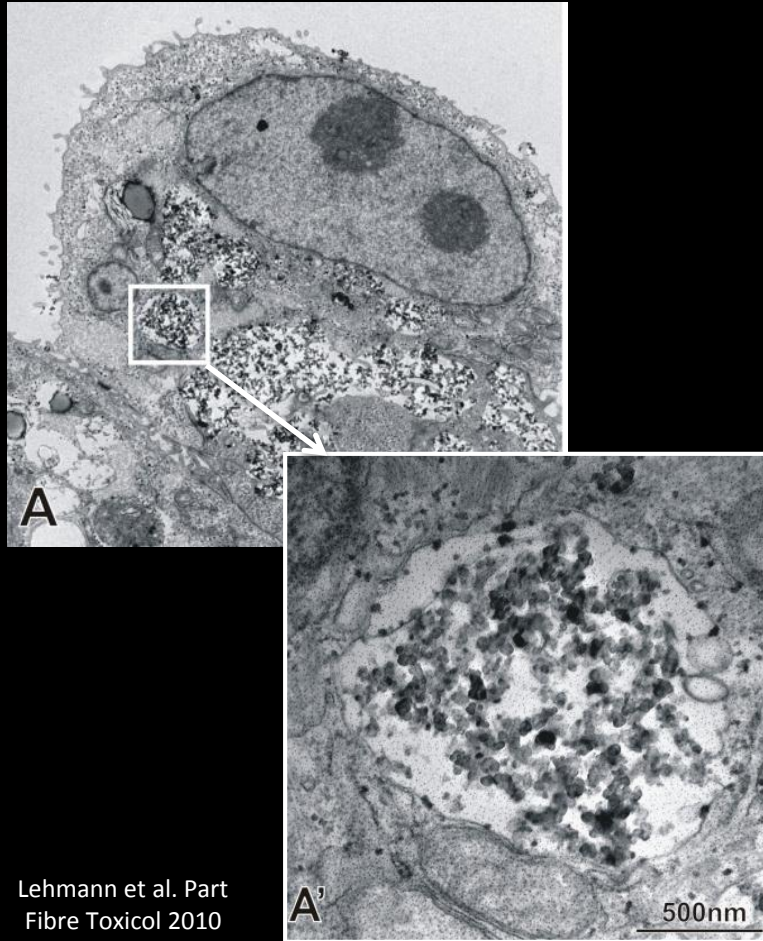


DEP / CNT interactions with macrophages

Diesel exhaust particles

Carbon nanotubes

Macrophage



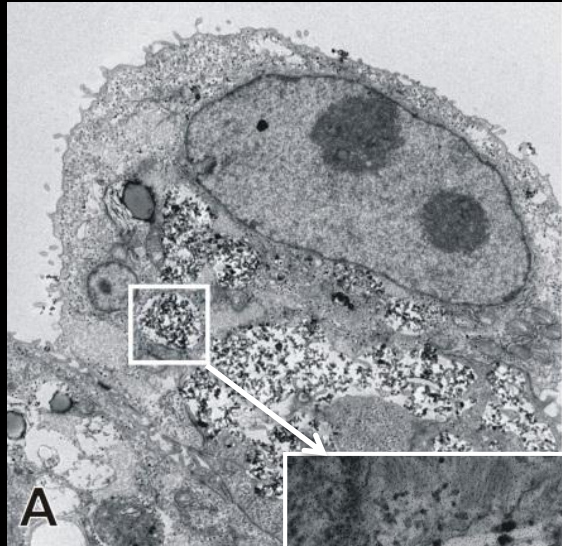
Lehmann et al. Part
Fibre Toxicol 2010



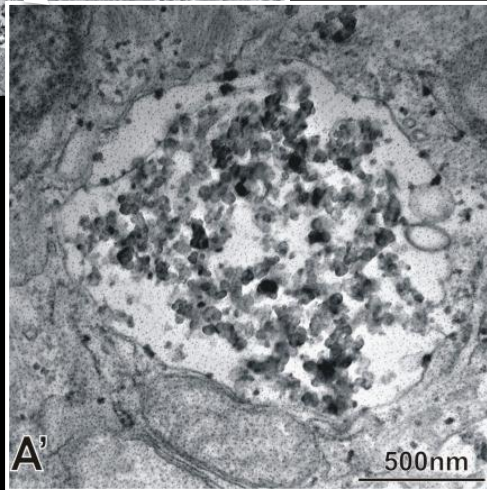
DEP / CNT interactions with macrophages

Diesel exhaust particles

Macrophage



A

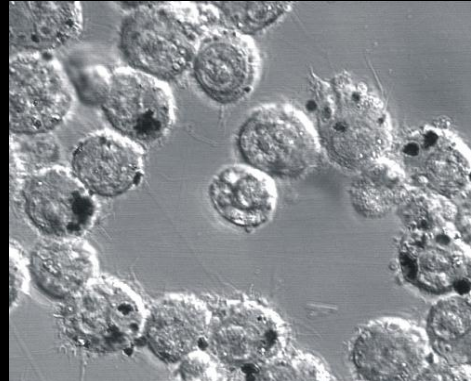


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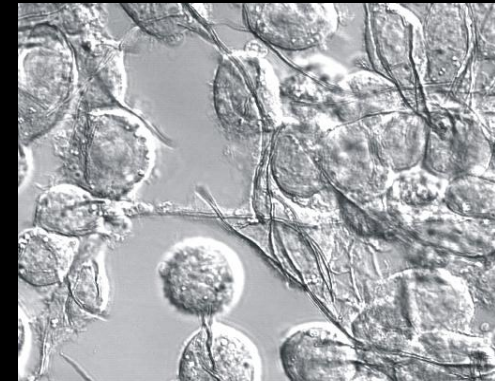
Lehmann et al. Part
Fibre Toxicol 2010

Carbon nanotubes

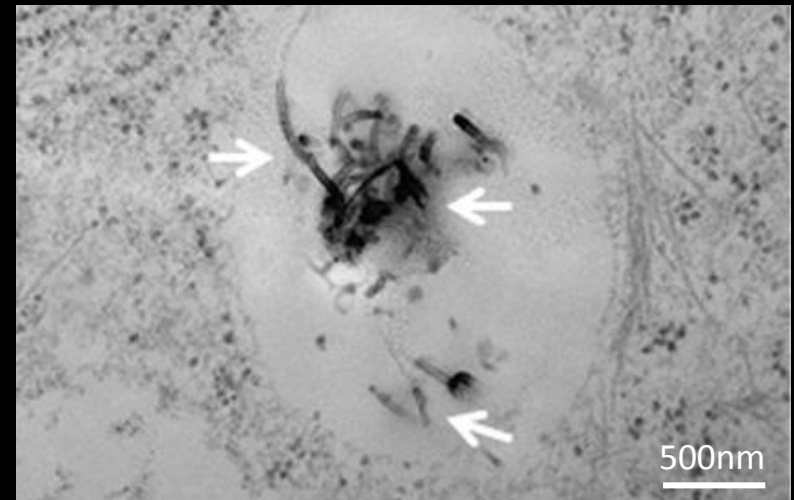
Tangled



Long, Straight



Rothen-Rutishauser et al. Nanotoxicology 2010



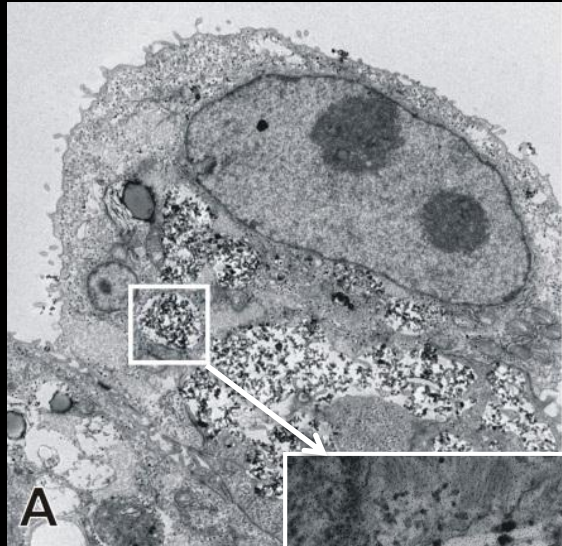
Chortarea et al. Nanotoxicology 2015



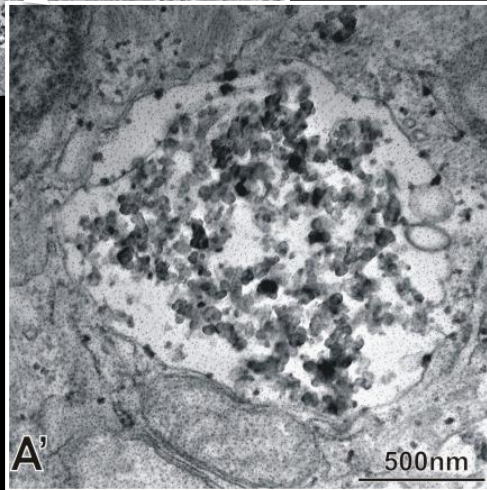
DEP / CNT interactions with macrophages

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Macrophage



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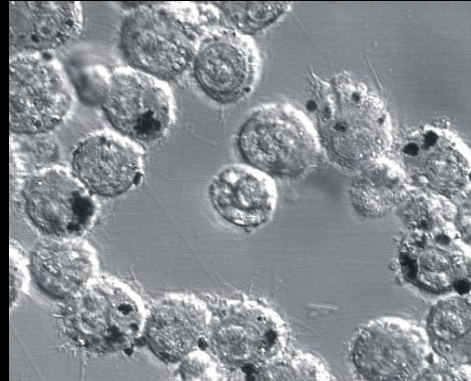


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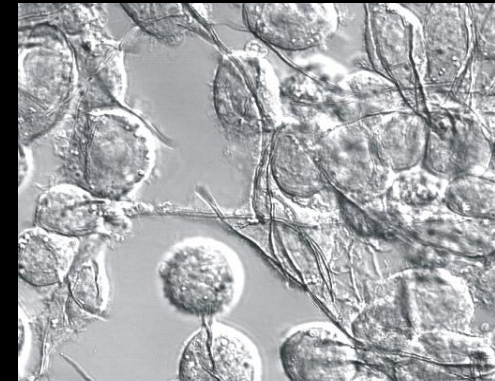
Lehmann et al. Part
Fibre Toxicol 2010

Carbon nanotubes

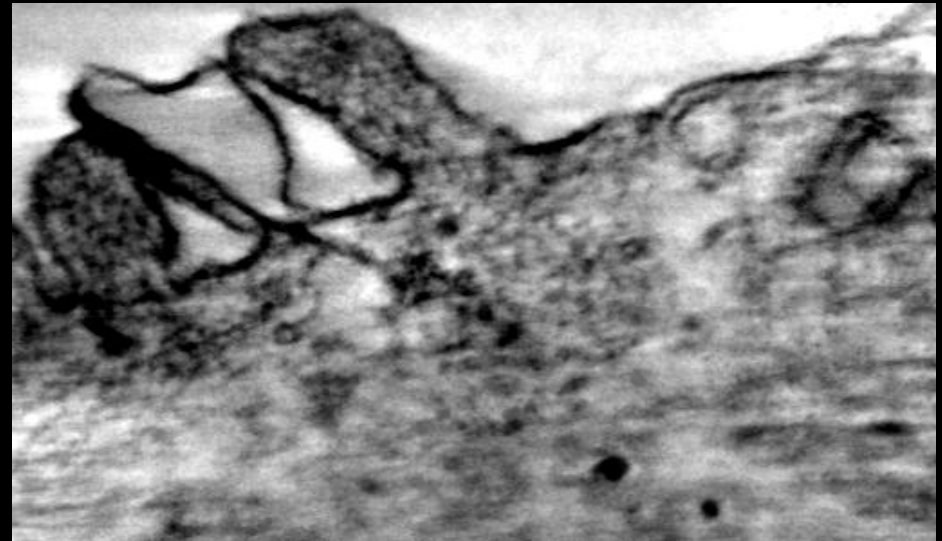
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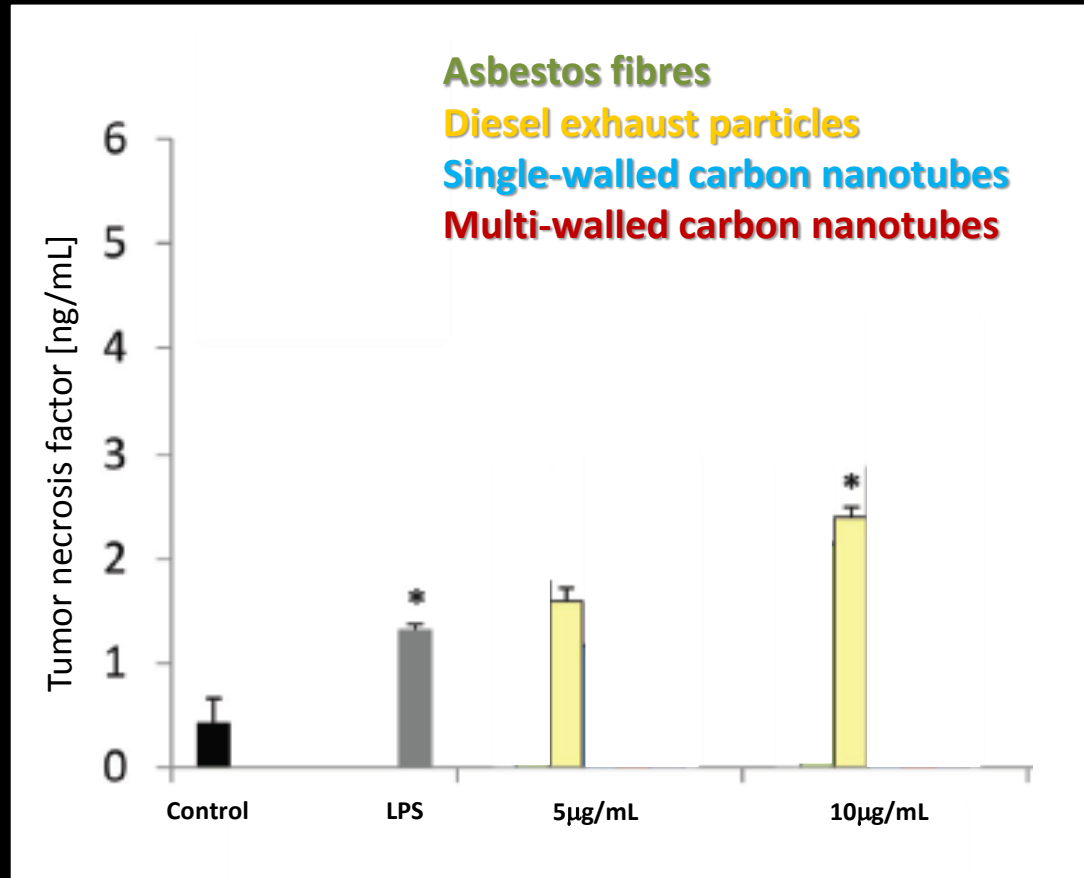


Rothen-Rutishauser et al. Nanotoxicology 2010





DEP / CNT interactions with macrophages



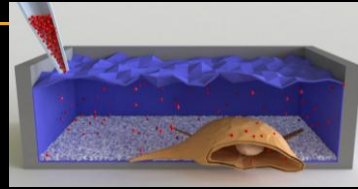
Clift et al. Toxicol Sci 2014



DEP / CNT interactions with macrophages

Diesel exhaust particles

10 μ g/mL – 48h



Carbon nanotubes

5 μ g/mL – 48h

~ 6 months to several years

Ambient urban exposure and occupational exposure

5 mg/m³ respirable nuisance dust / 8h working day (maximum level allowed by Occupational Safety and Health Administration (OSHA))

3x10⁻⁵-5x10⁻³ μ g per h per cm² of lung tissue

2-300 particles per h per (epithelial) cells

Journal of Aerosol Science 42 (2011) 668–692

Contents lists available at ScienceDirect

Journal of Aerosol Science

journal homepage: www.elsevier.com/locate/jaerosci

In-vitro cell exposure studies for the assessment of nanoparticle toxicity in the lung—A dialog between aerosol science and biology ☆

Hanns-Rudolf Paur^a, Flemming R. Cassee^b, Justin Teeguarden^c, Heinz Fissan^d, Silvia Diabate^e, Michaela Aufderheide^f, Wolfgang G. Kreyling^g, Otto Hänninen^h, Gerhard Kasperⁱ, Michael Riediker^j, Barbara Rothen-Rutishauser^k, Otmar Schmid^{g,*}



DEP / CNT – 3D lung model and air-liquid exposures

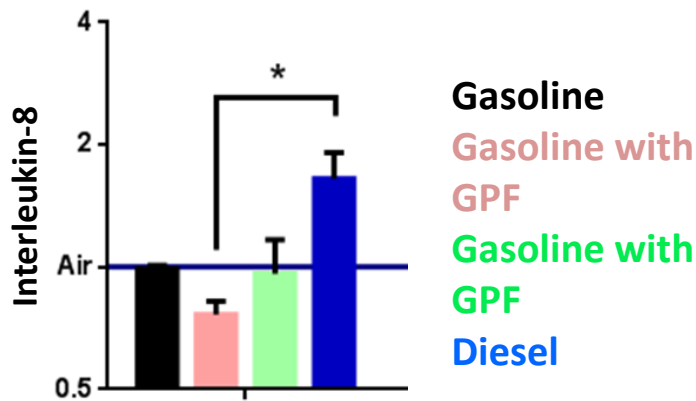
Diesel exhaust particles



Bisig et al. Chimia 2015



Carbon nanotubes



Bisig et al. 2016 submitted

2-300 Partikel per h per (Epithelial) cell

Paur et al. J Aerosol Sci 2011

⇒ 130 -500 Particles /cell

Müller et al. Environ Sci Technol 2009



DEP / CNT – 3D lung model and air-liquid exposures

Diesel exhaust particles

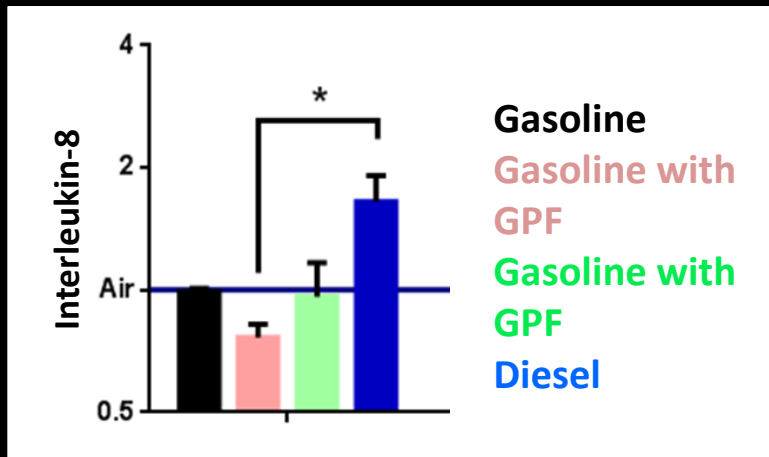


Bisig et al. Chimia 2015

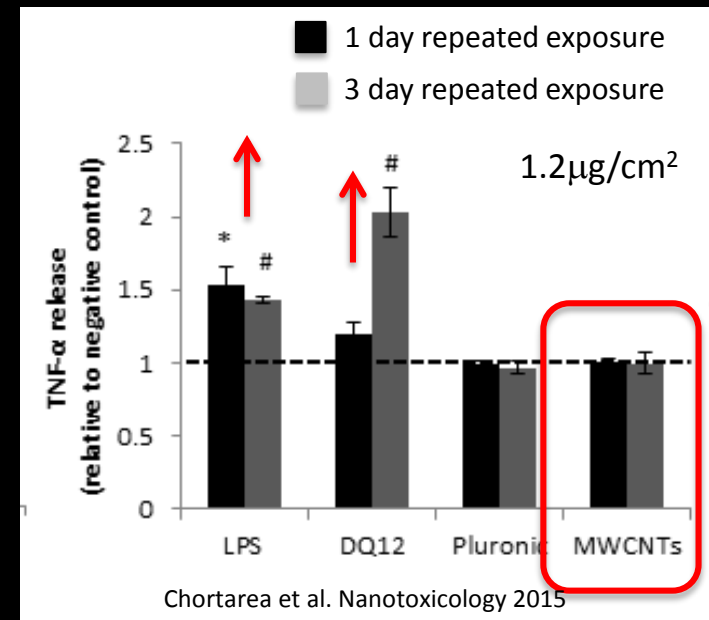


Carbon nanotubes

Lenz et al. Part Fiber Tox 2009



Bisig et al. 2016 submitted

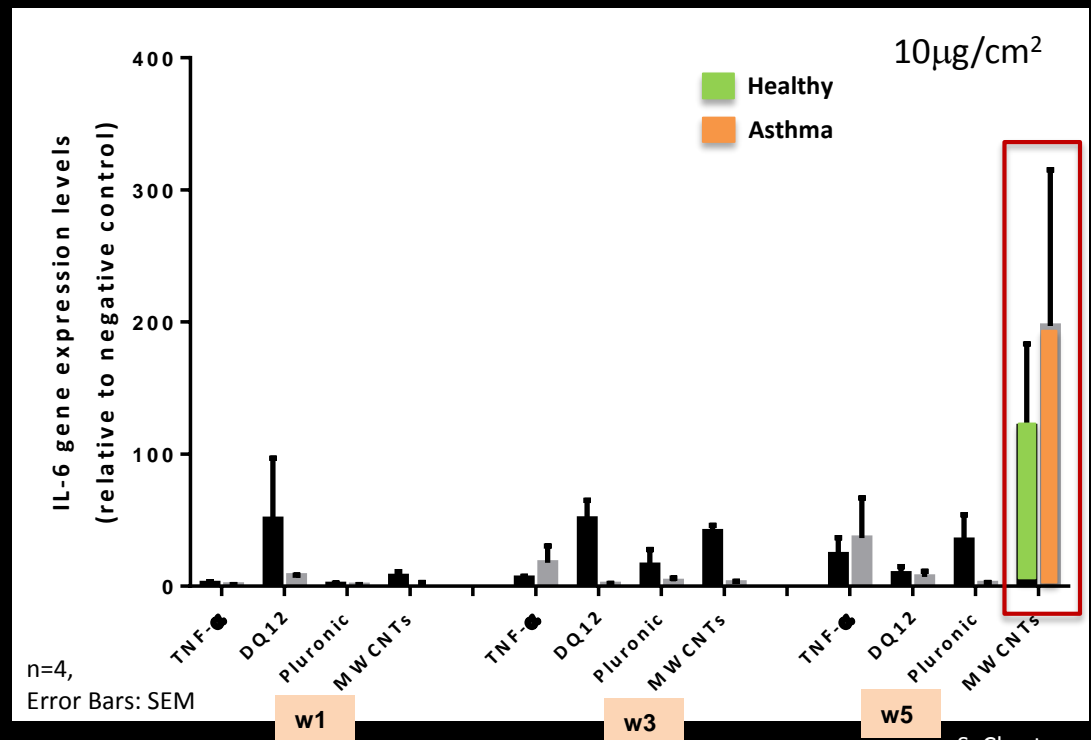
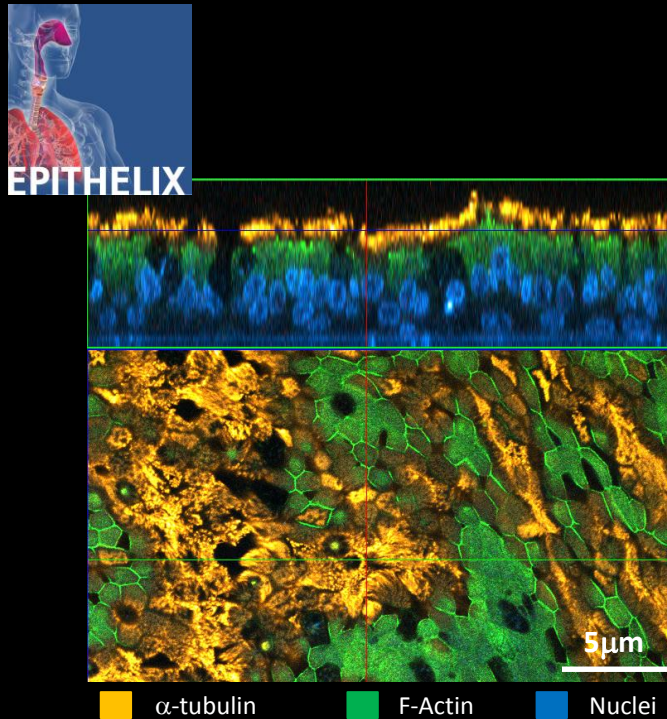


Chortarea et al. Nanotoxicology 2015



DEP / CNT - 3D lung model and air-liquid exposures

Carbon nanotubes

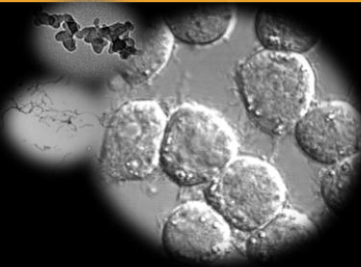


S. Chortarea



...what do we know so far

Diesel exhaust particles



Carbon nanotubes

Diesel particles are taken up by **lung cells** *in vitro*

Condensed compounds such as **semi-volatile** and **non-volatile chemicals** on **particle surface** can access cells

=> Trojan horse effect

Limbach et al. Environ Sci Technol 2007

Adverse effects in lung cells *in vitro* upon exposure to diesel particles / exhaust (**acute exposures**)

Carbon nanotubes are nanofibres, different **physico-chemical characteristics**

Carbon nanotubes are taken up by cells *in vitro*, *i.e.* **inside vesicles, cell membrane penetration**

=> Frustrated phagocytosis

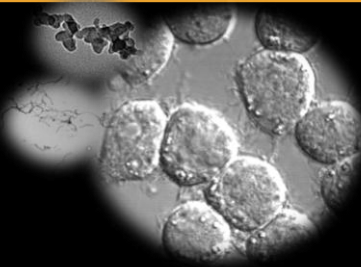
Brown et al. Carbon 2007

Adverse effects in lung cells *in vitro* upon exposure to carbon nanotubes (**acute as well as chronic exposures**)



...and where to go from there

Diesel exhaust particles



Carbon nanotubes

Identify (and eliminate) the **source** of human exposure

Human exposure concentrations

⇒ Realistic cell culture experiments (lower concentrations)

From mono-culture experiments to more **complex lung cell models**

Air-liquid exposures

Acute effects ⇔ **Long-term effects**



Acknowledgments

BioNanomaterials group



S. Chortarea



Ch. Bisig

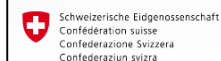


Collaboration partners

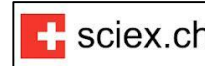
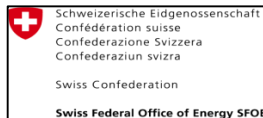
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- Prof. em. Peter Gehr, University of Bern
- Dr. Samuel Constant, EPITHELIX
- Dr. Martin Clift, University of Swansea

EngToxDi Team

- Jan Czerwinski
- Pierre Comte
- Andreas Mayer
- Norbert Heeb



Bundesamt für Umwelt BAFU



Adolphe Merkle Foundation

