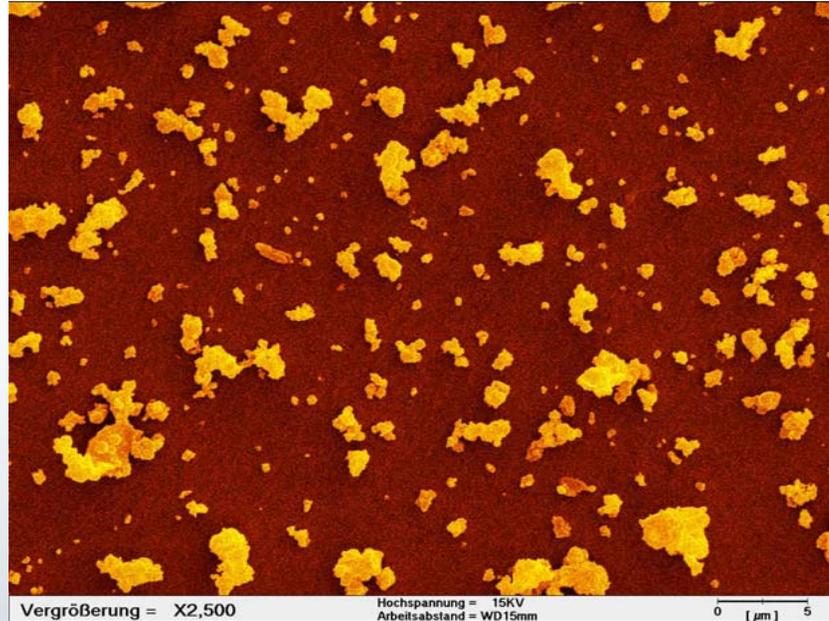


10th ETH-Conference on Combustion Generated Nanoparticles



Ultrafine Dust and Nanoparticles: Hazard Identification in vitro

Harald F. Krug & Silvia Diabaté
Forschungszentrum Karlsruhe
Institute of Toxicology and Genetics

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Fahrverbot, Rußfilter, City-Maut



DAS FEINSTAUB GESPENST

JOHANNES PAUL II.
SEIN LETZTER KAMPF

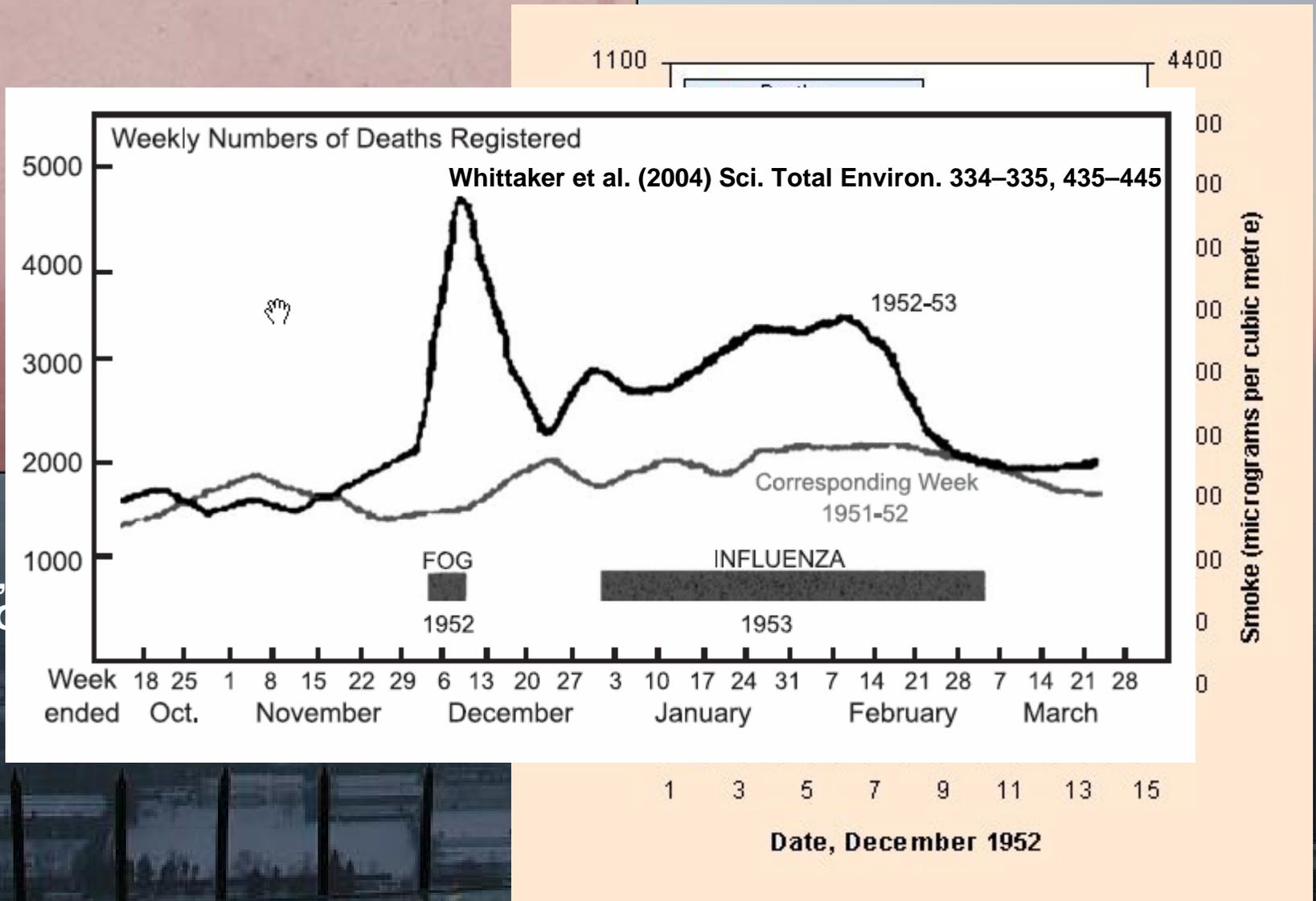


Vergrößerung = X2,500

Hochspannung = 15KV
Arbeitsabstand = WD15mm

0 [µm] 5

The London Smog Disaster, Dec. 3.-11., 1952



Comparison of Time-Series Study Estimates of the Total Mortality RR of a 100 µg/m³ PM₁₀ Increase

Study Area (Reference)	Mean PM ₁₀ (µg/m ³)	Maximum PM ₁₀ (µg/m ³)	100 µg/m ³ RR	100 µg/m ³ (95%CI)
Utah Valley, UT (Pope et al., 1992)	47	297	1.16* ^{☐☐}	(1.10-1.22)
St. Louis, MO (Dockery et al., 1992)	28	97	1.16* [☐]	(1.01-1.33)
Kingston, TN (Dockery et al., 1992)	30	67	1.17* [☐]	(0.88-1.57)
Birmingham, AL (Schwartz, 1993)	48	163	1.11* ^{☐☐☐}	(1.02-1.20)
Athens, Greece (Touloumi et al., 1994)	78	306	1.07* [☐] 1.03** [☐]	(1.05-1.09) (1.00-1.06)
Toronto, Canada (Özkaynak et al., 1994)	40	96	1.07* [☐] 1.05** [☐]	(1.05-1.09) (1.03-1.07)
Los Angeles, CA (Kinney et al., 1995)	58	177	1.05* [☐] 1.04** [☐]	(1.00-1.11) (0.98-1.09)
Chicago, IL (Ito, et al., 1995)	38	128	1.05** [☐]	(1.01-1.10)
Santiago, Chile (Ostro et al., 1995)	115	367	1.08* [☐] 1.15* ^{☐☐☐}	(1.06-1.12) (1.08-1.22)

* Single pollutant model (i.e., PM₁₀)

** Multiple pollutant model (i.e., PM₁₀ and other pollutants simultaneously)

☐ One-day mean PM₁₀-concentration employed

☐☐ Multiple-day mean PM₁₀-concentration employed

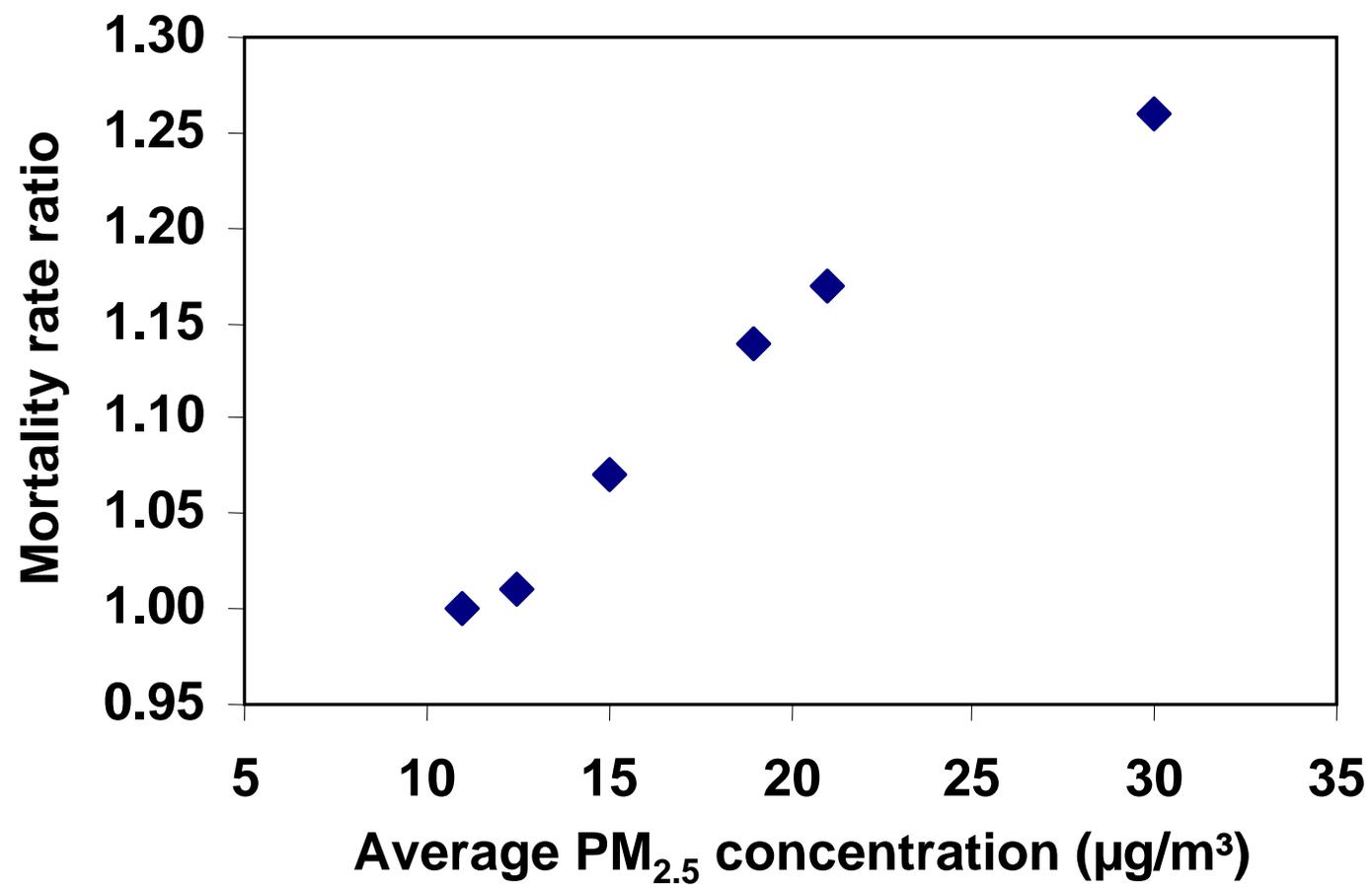
PM₁₀ = particulate matter < 10 µm

Meta-Analysis of Epidemiological Studies



- Introduction
- Cellular Responses
- In vitro Exposure
- Hypothesis

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Estimated city-specific mortality rate ratios adjusted for age, sex, smoking, education, and body mass index, plotted against mean PM_{2.5} concentrations in six U.S. Cities.

From: Dockery et al. (1993) New Engl. J. Med. 329: 1753-1759

The U.S. Environmental Protection Agency Particulate Matter Health Effects Research Centers Program: A Midcourse Report of Status, Progress, and Plans

Morton Lippmann, Mark Frampton, Joel Schwartz, Douglas Dockery, Richard Schlesinger, Petros Koutrakis, John Froines, Andre Nel, Jack Finkelstein, John Godleski, Joel Kaufman, Jane Koenig, Tim Larson, Dan Luchtel, L-J. Sally Liu, Günter Oberdörster, Annette Peters, Jeremy Sarnat, Constantinos Sioutas, Helen Suh, Jeff Sullivan, Mark Utell, Erich Wichmann, and Judith Zelikoff

Environ Health Perspect 111:1074–1092 (2003)

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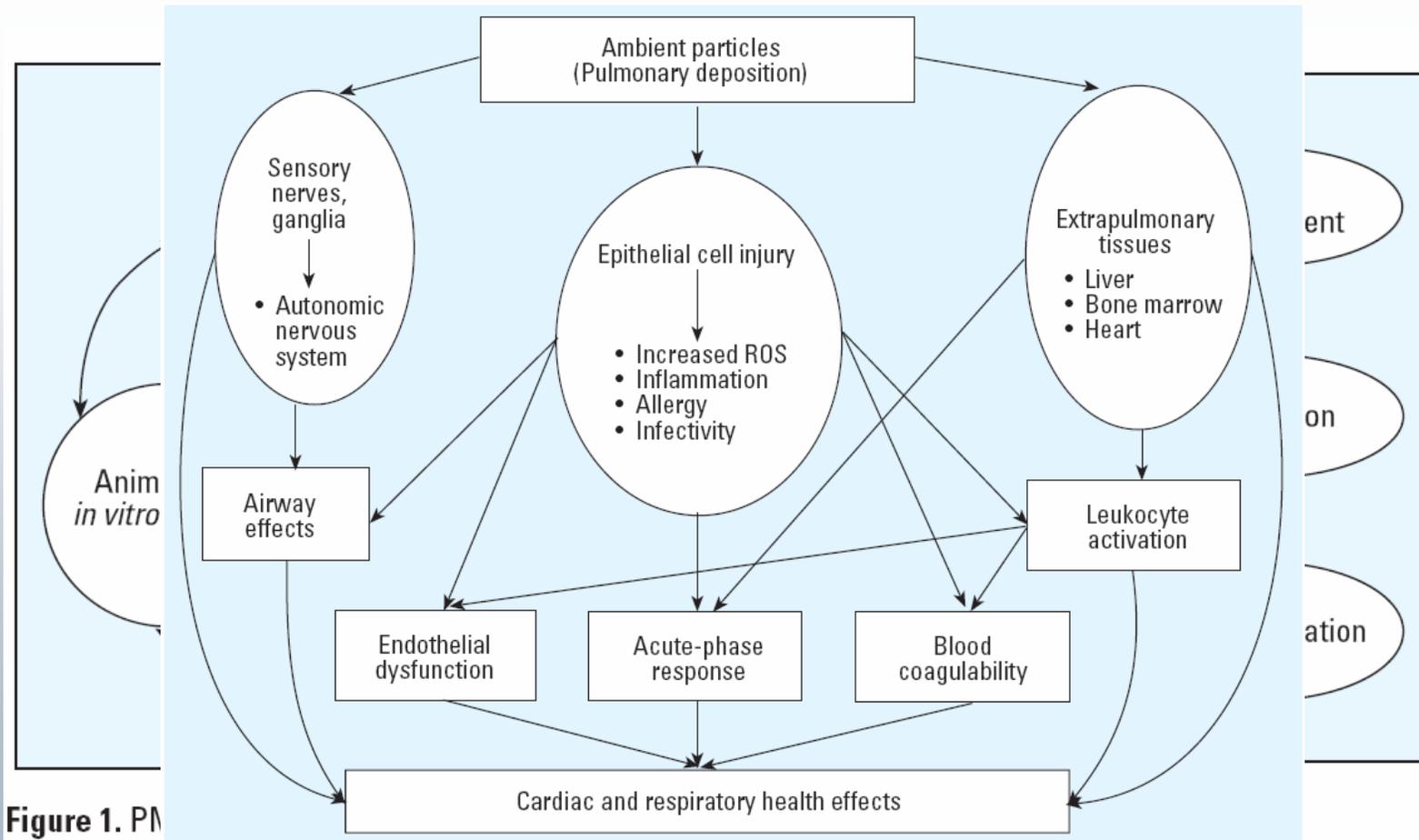
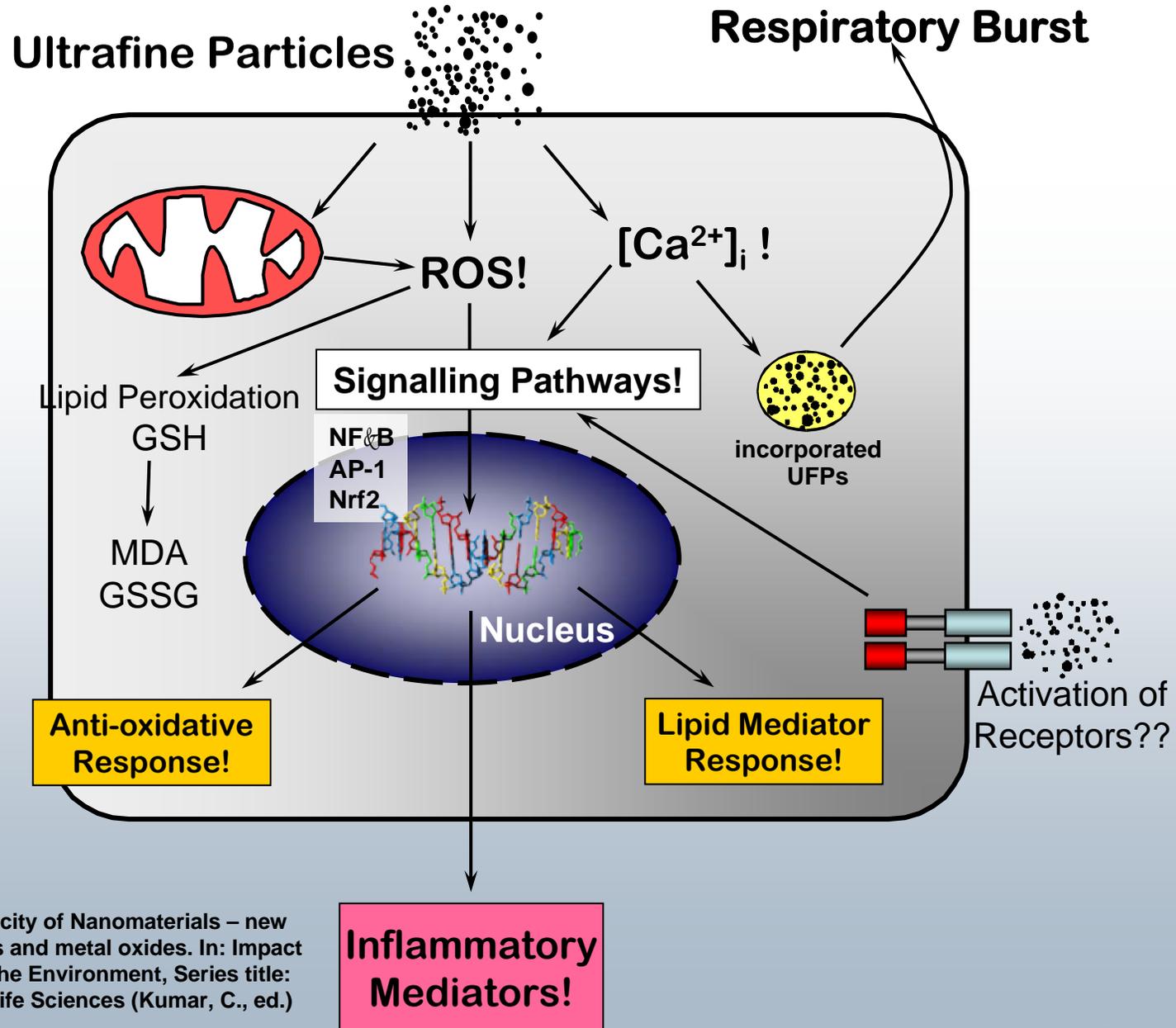


Figure 1. PM

Figure 2. Hypotheses for health effects of PM.

Cellular Responses to UFP



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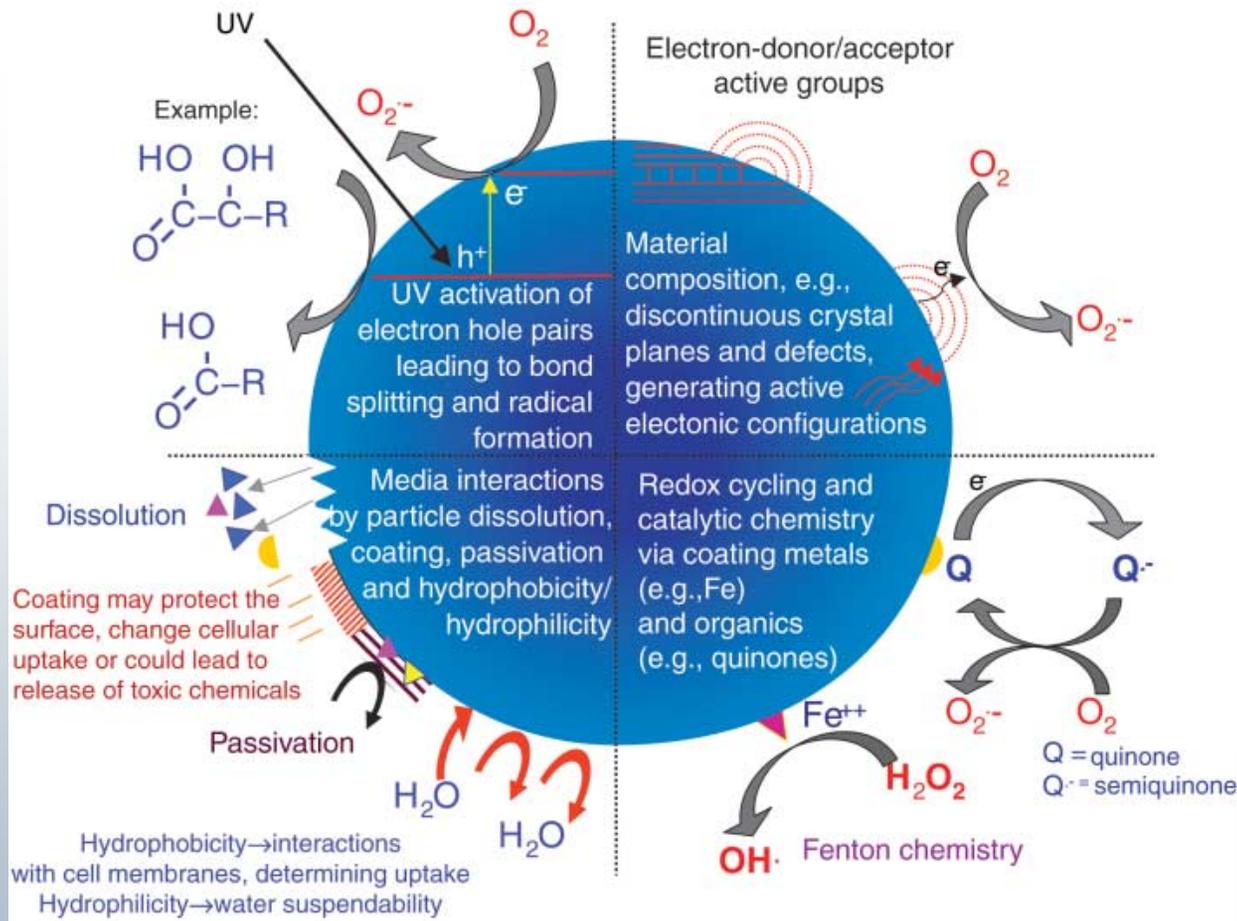


Krug et al. (2006) Toxicity of Nanomaterials – new carbon conformations and metal oxides. In: Impact of Nanomaterials on the Environment, Series title: Nanotechnology for Life Sciences (Kumar, C., ed.) Wiley-VCh, Weinheim

Particle Properties



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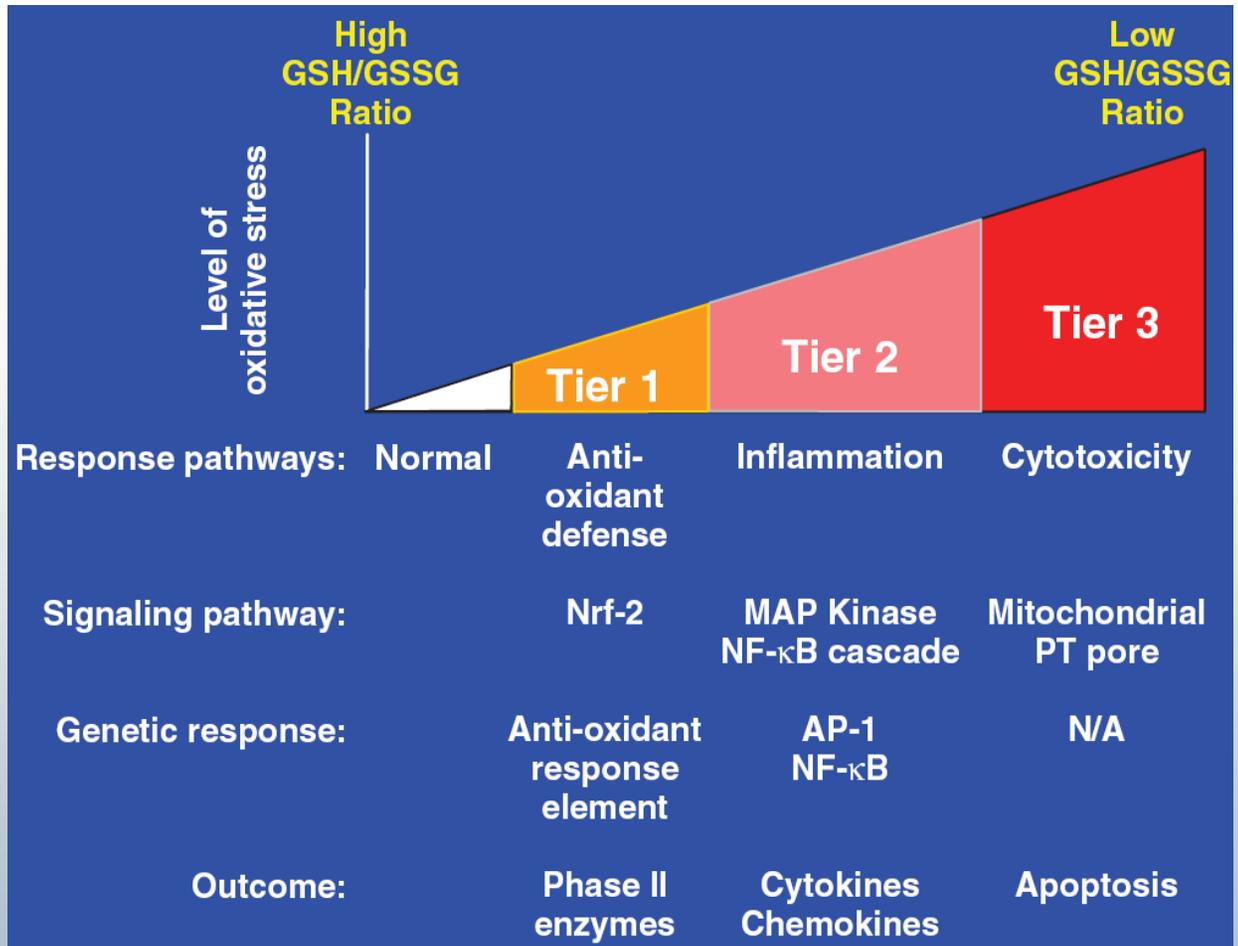


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Nel et al. (2006) Science 311: 622-627

The Hierarchical Oxidative Stress Model



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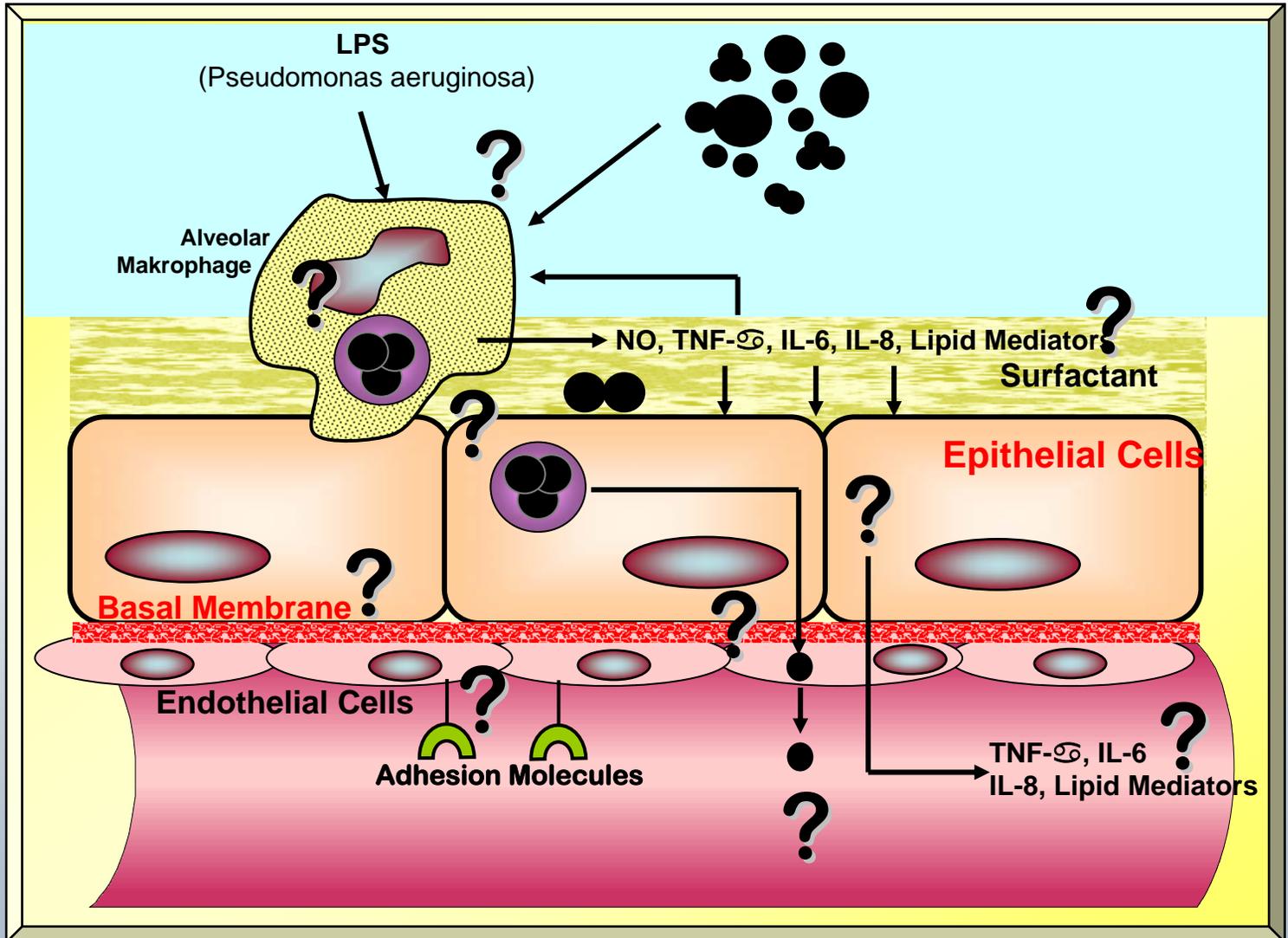
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Nel et al. (2006) Science 311: 622-627

Situation in the Lung

Fate of Particles



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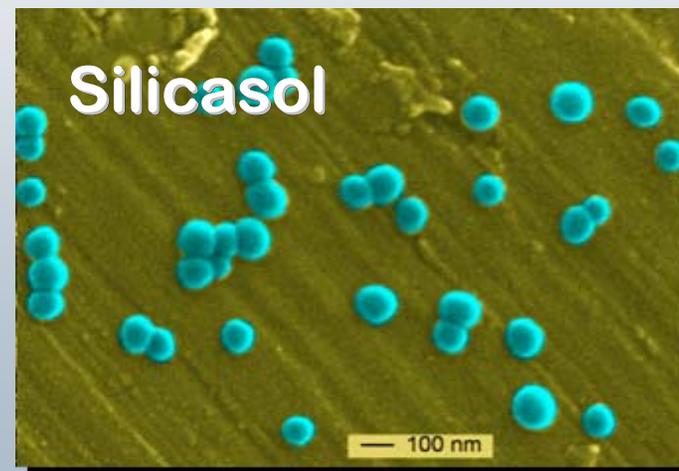
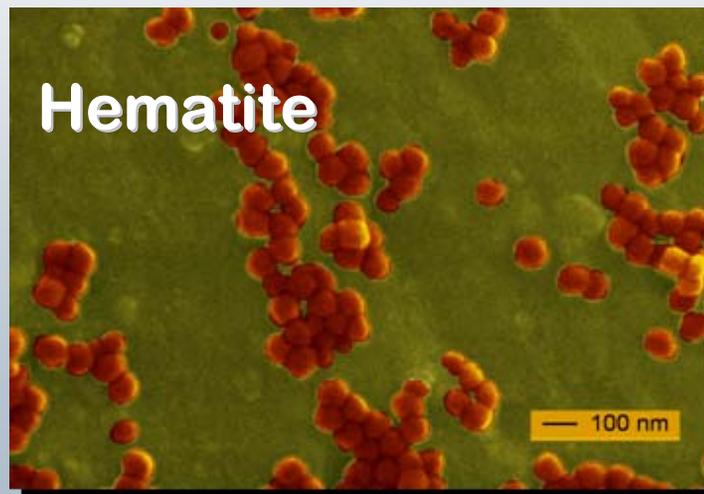
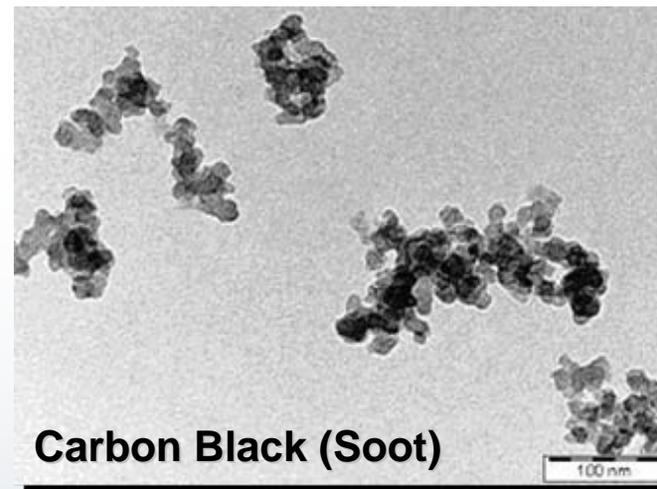
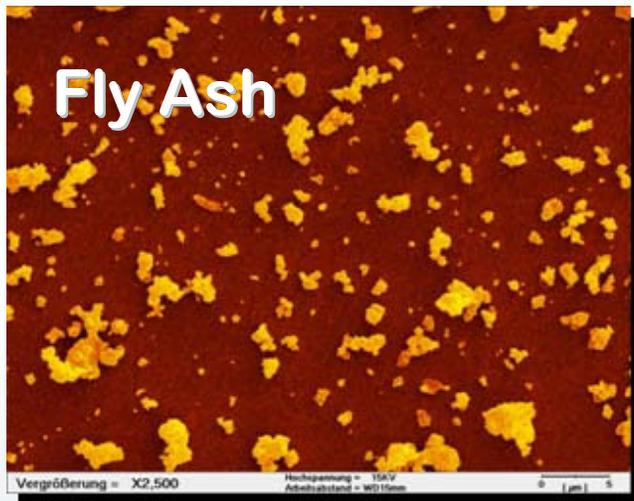
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Ultrafine Particles - Nanoparticles



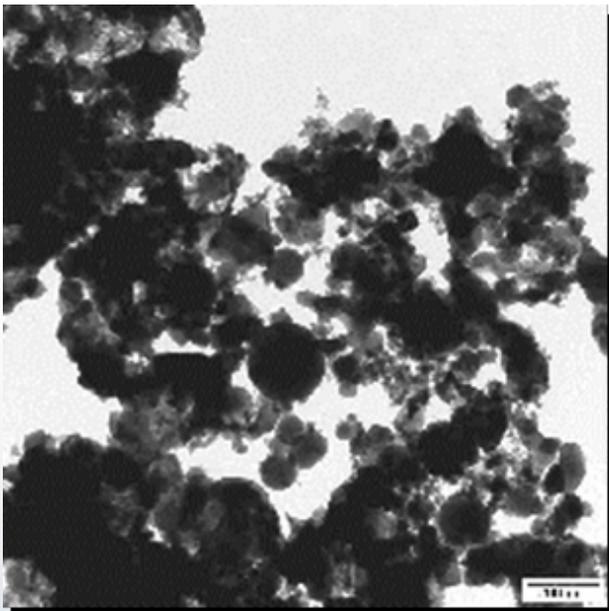
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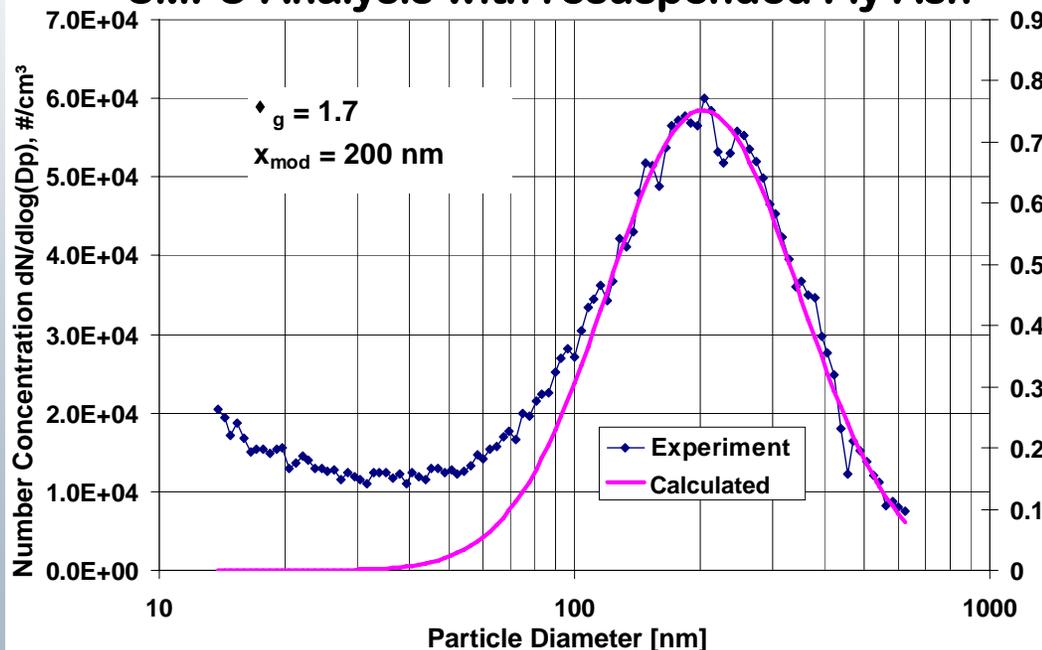
Fly Ash as Model Particles for *Real-Life* Emissions



Medium Mass of the Components [% of total Mass]:

- ca. 75 % Sulfates and Chlorides of Na, K and Ca
- ca. 6 % Metals (Cd, Cu, Fe, Pb, Sb, Sn, Ti, Zn)
- ca. 1 % Carbon
- ca. 70% are watersoluble Constituents (pH 7,4)

SMPS-Analysis with resuspended Fly Ash



Diabaté et al. (2002) Int. J. Hyg. Environ. Health 204: 323 - 326

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Nanotoxicology Exposure System

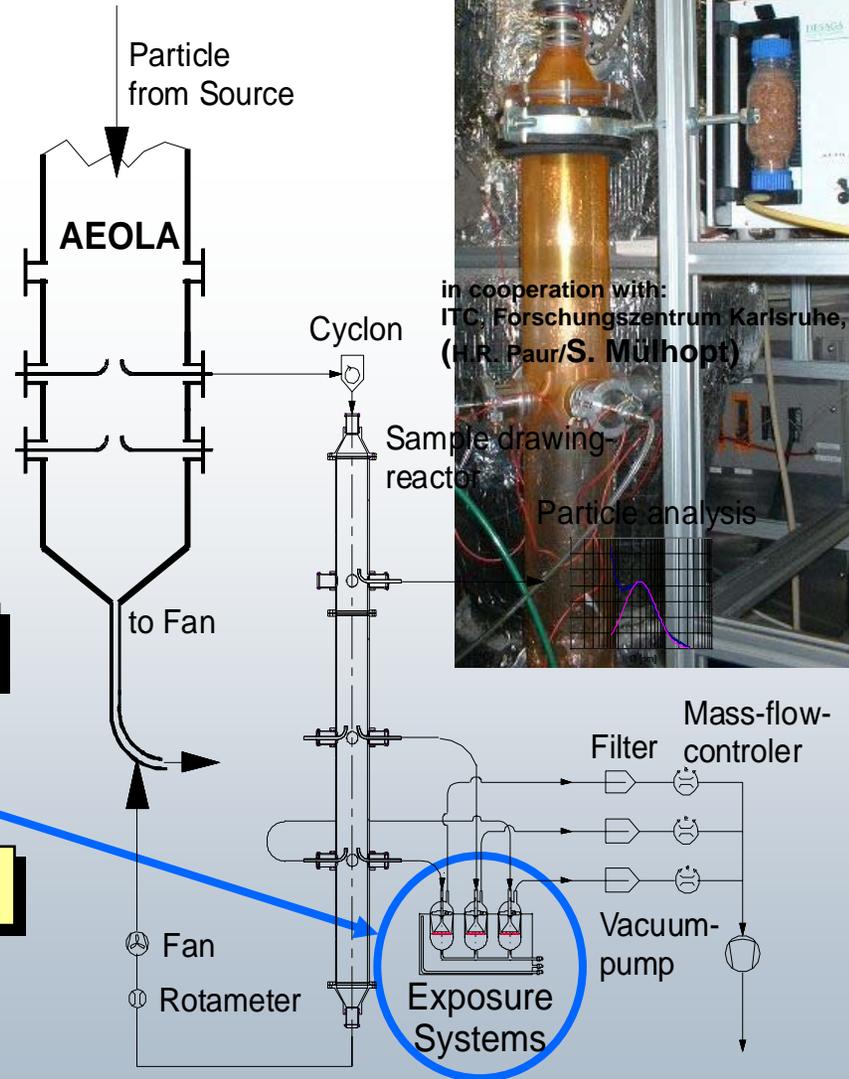
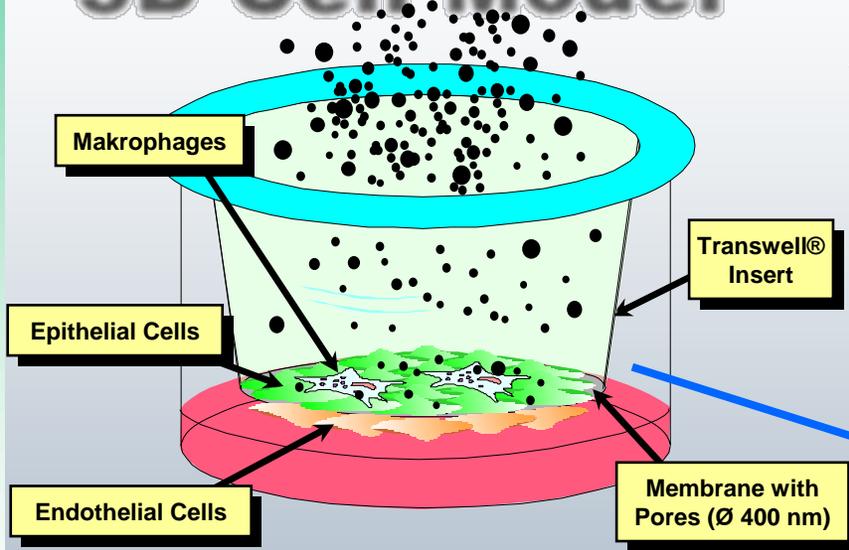


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3D Cell Model



in cooperation with:
ITC, Forschungszentrum Karlsruhe,
(H.R. Paur/S. Mülhaupt)

Particle analysis

Mass-flow-controller

Filter

Vacuum-pump

Exposure Systems

Particle from Source

AEOLA

Cyclon

Sample drawing reactor

to Fan

Fan

Rotameter

3D-Cell Model

Exposure to Particles at the Air-Liquid-Interface

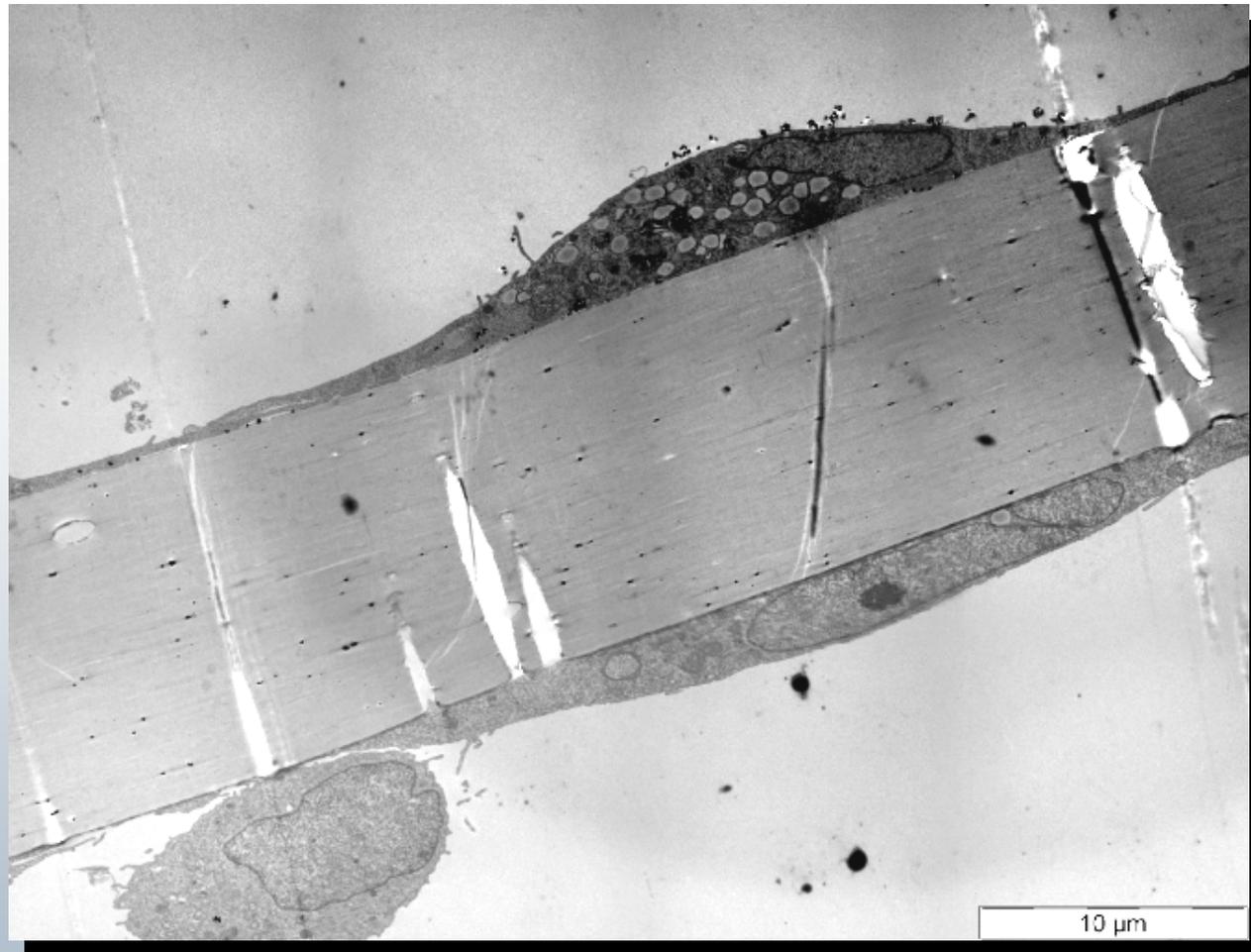


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The Cultex/FZK-System



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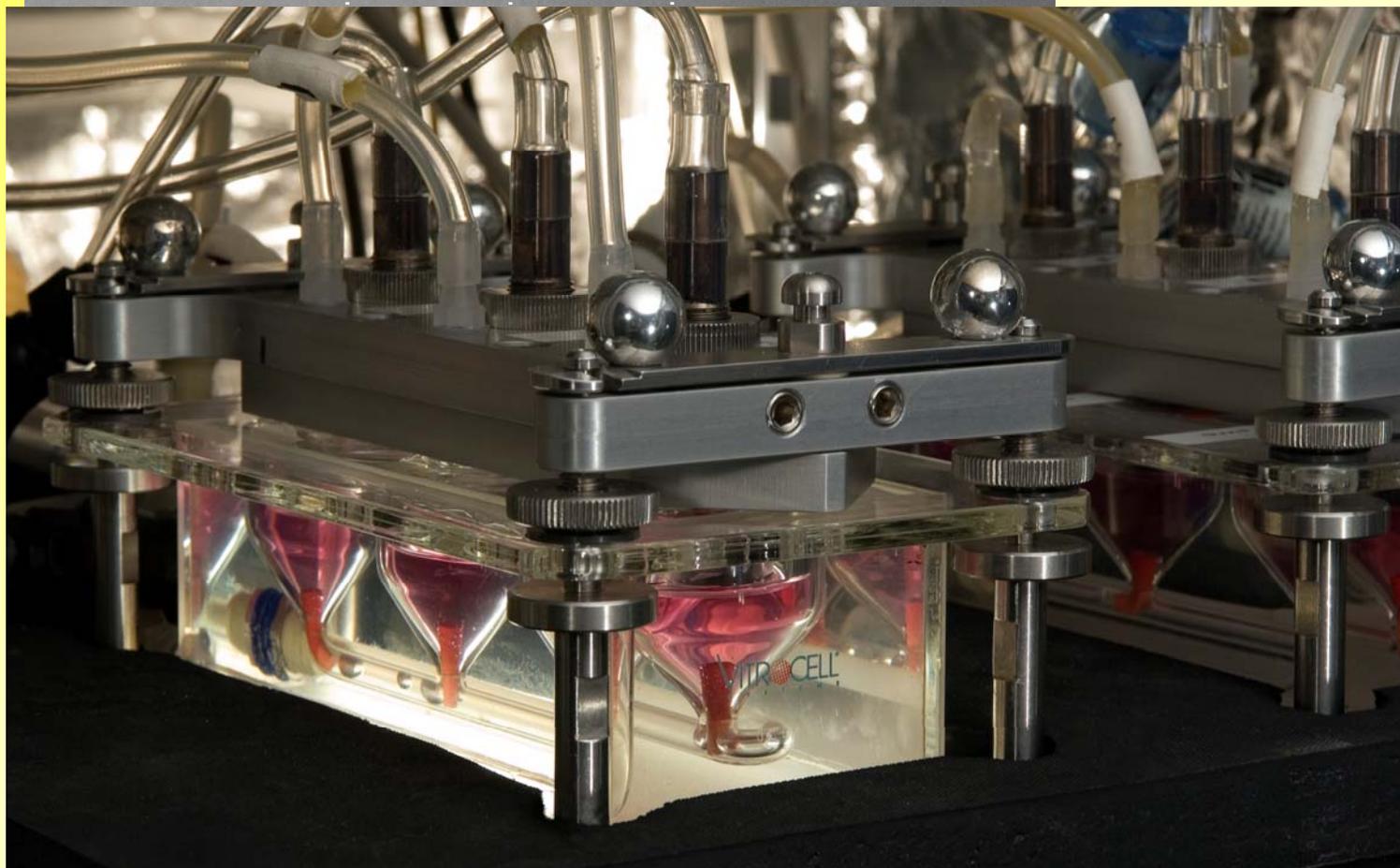
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Gas inlets



www.vitrocell.com



Survivaltime during Air-Exposure

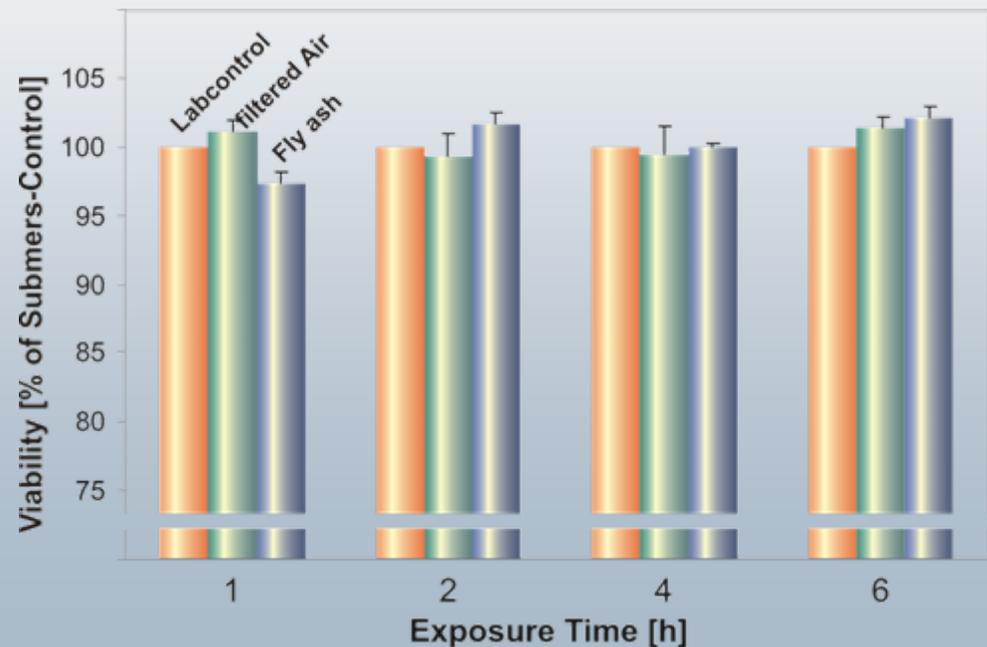
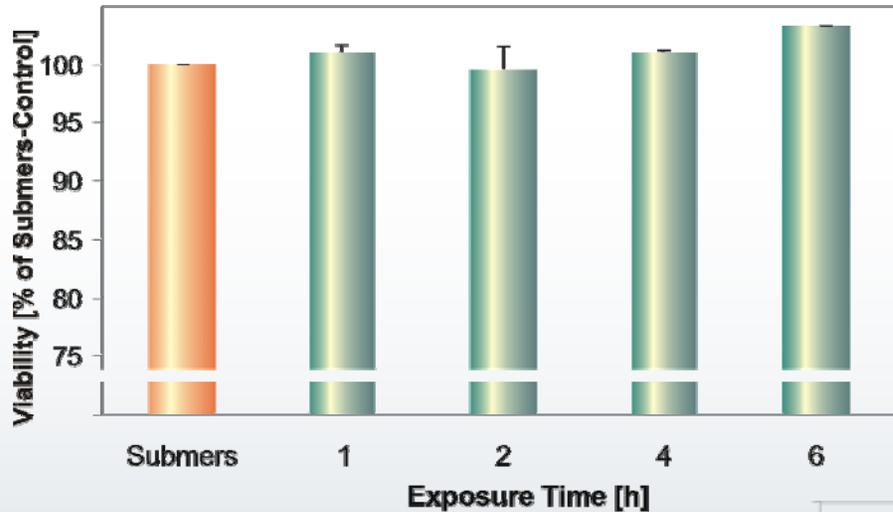


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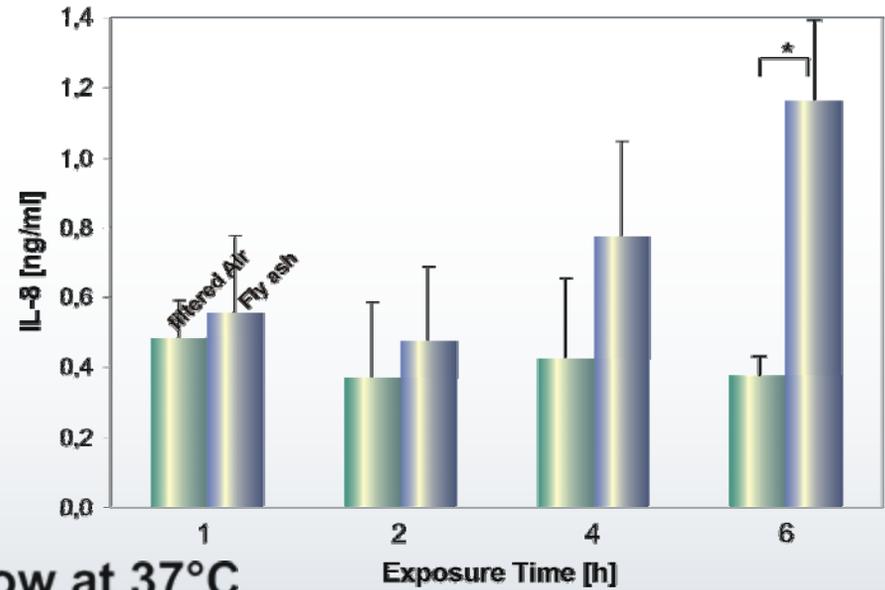
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Lab Air without Flow

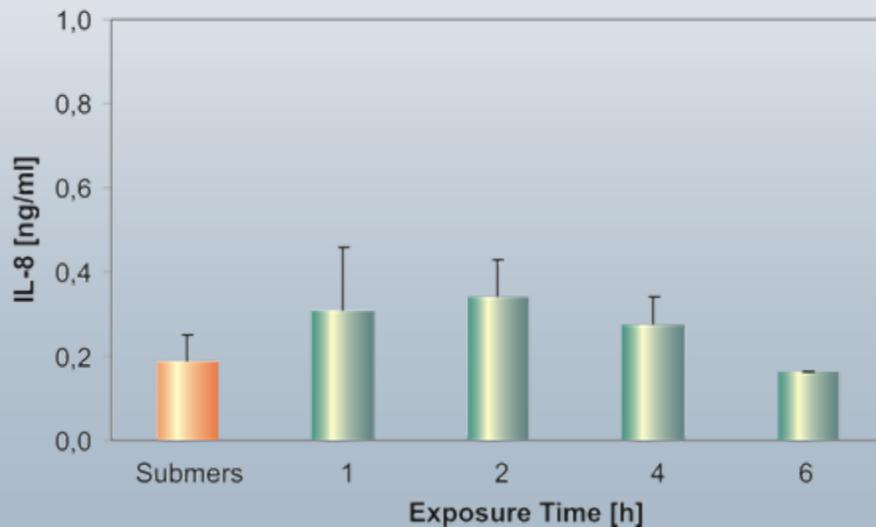


Interleukin-Production after Fly Ash Exposure

Exposure to air flow at 100 ml/min +/- fly ash



Exposure to lab air without flow at 37°C



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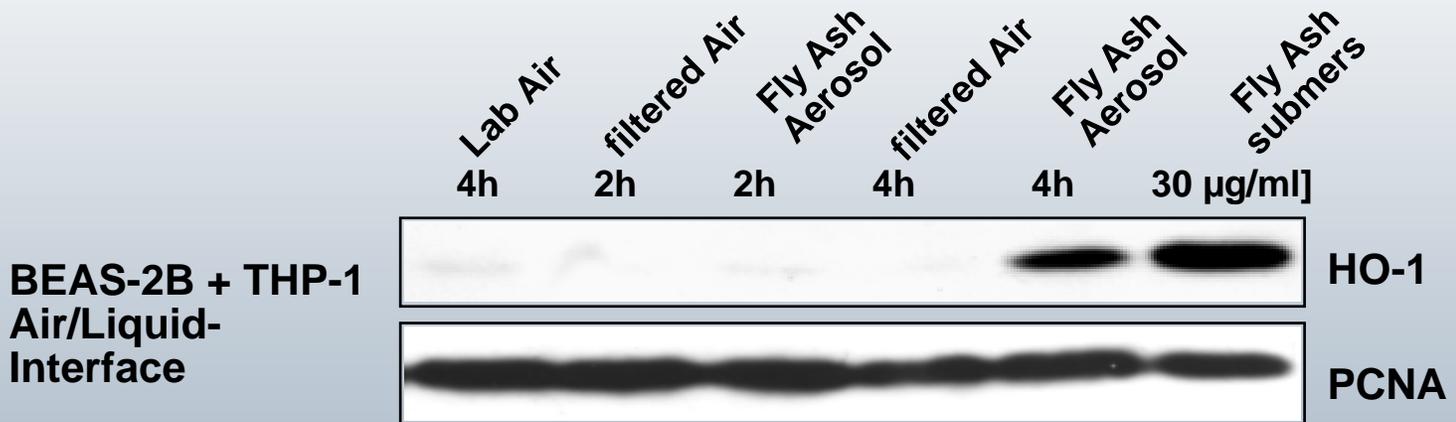
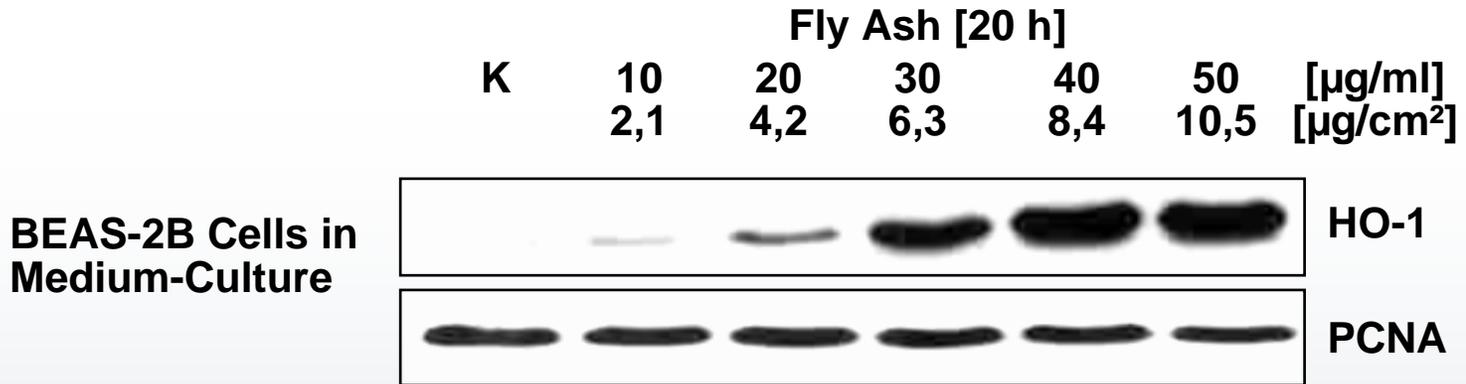
Induction of Hemoxygenase-1

Antioxidative Protection

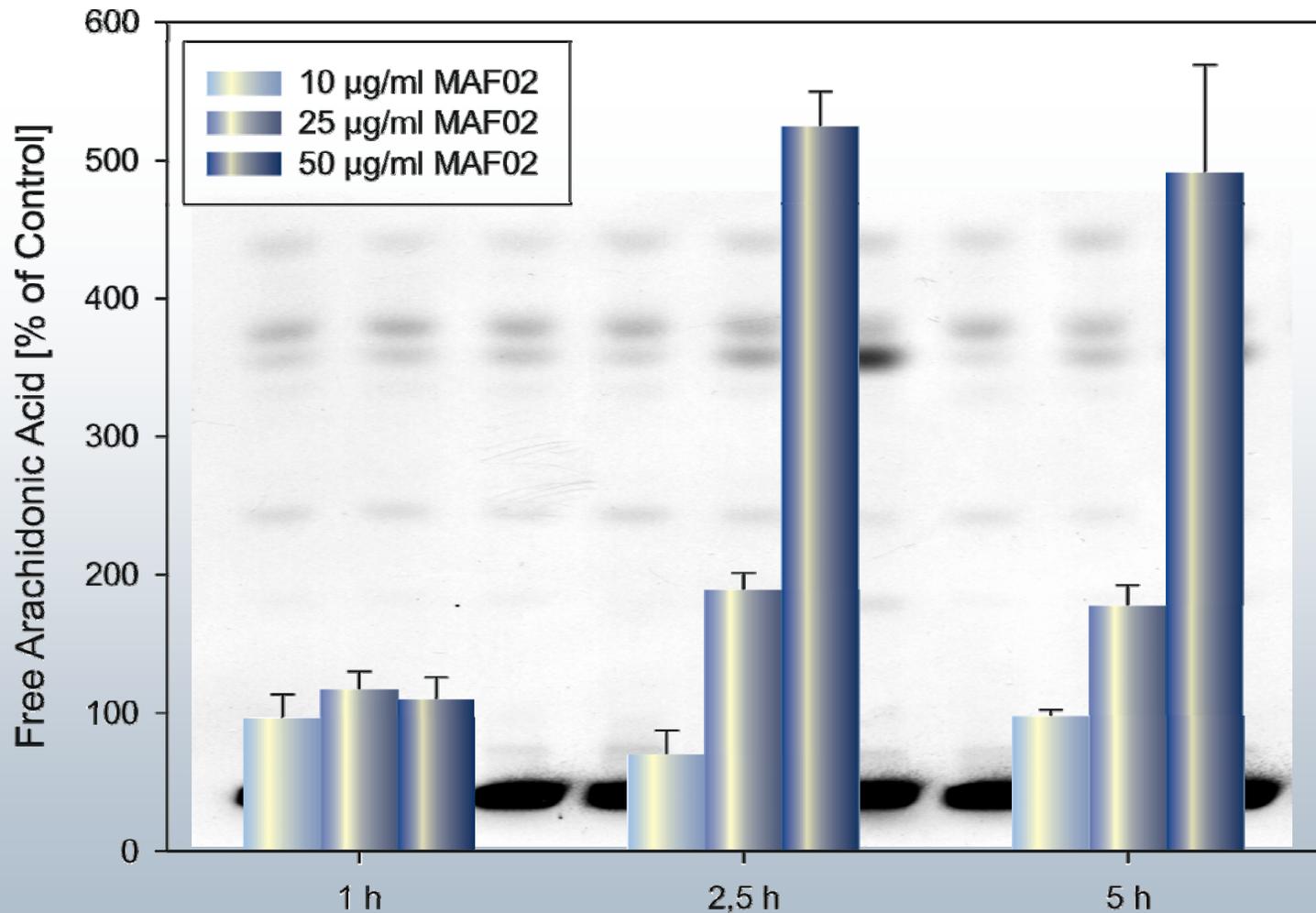


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Fly Ash induces Arachidonic Acid Release in RAW264.7 Macrophages



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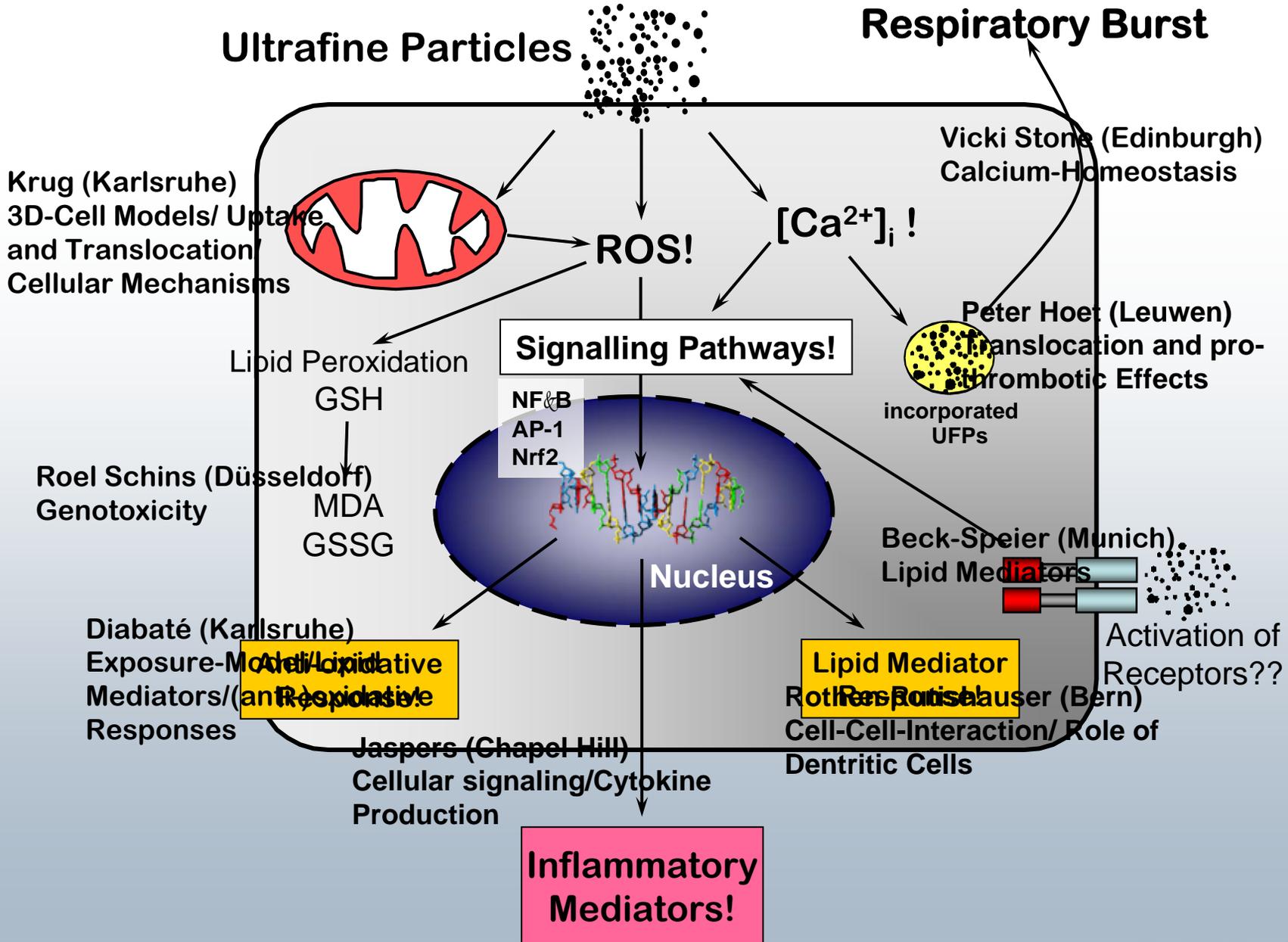
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In Vitro Studies by

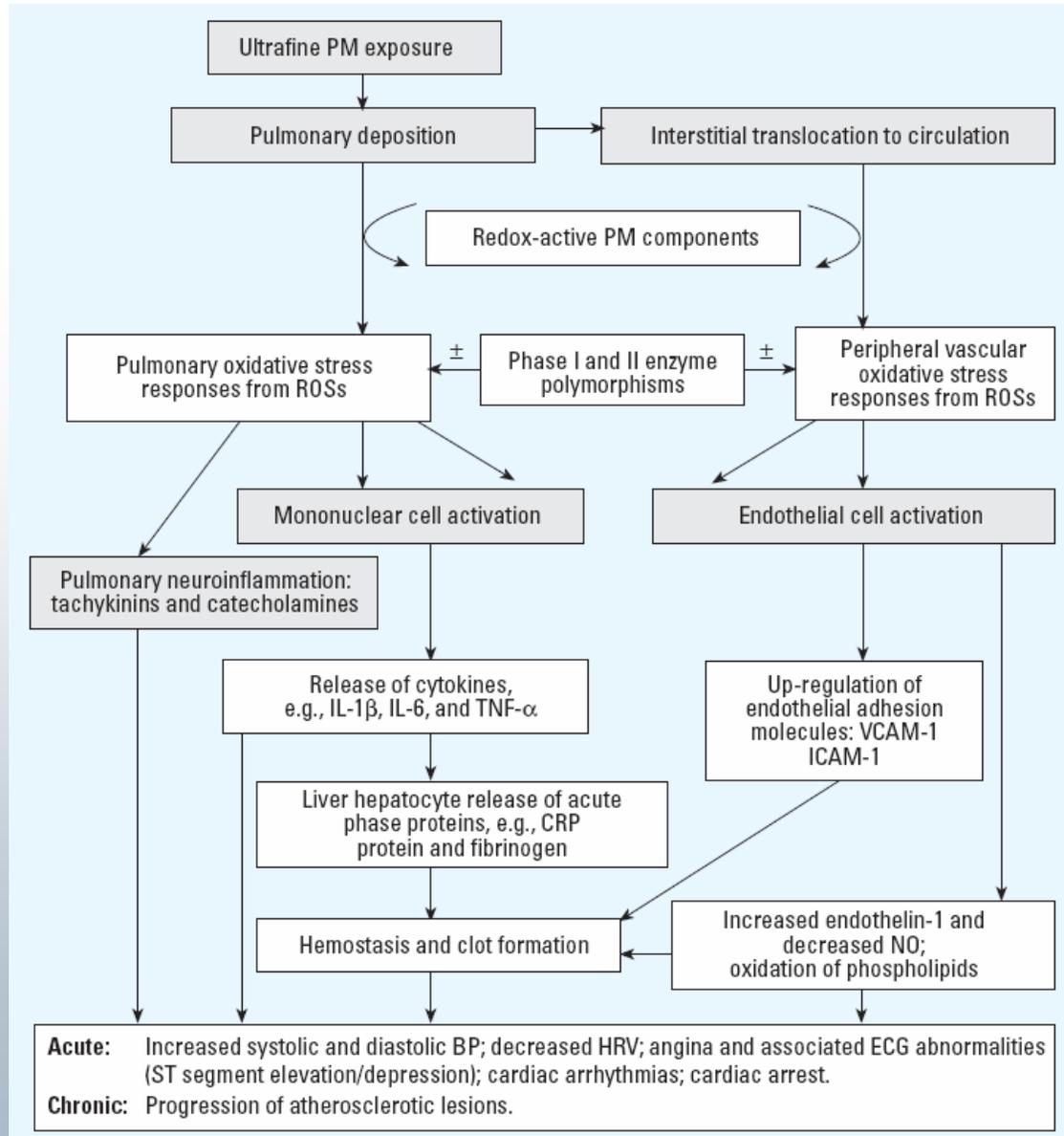


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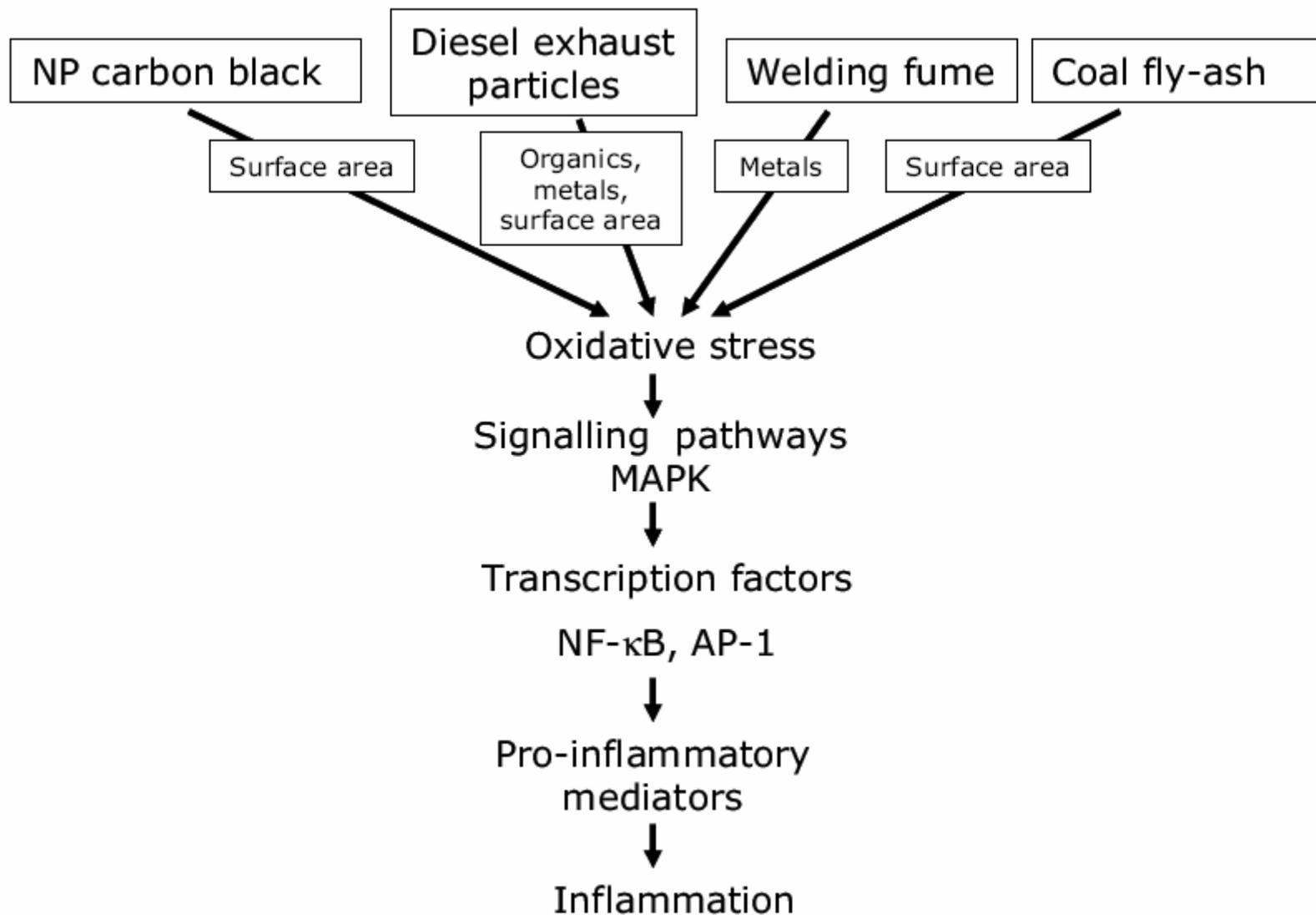
Hypothesized pathways leading to adverse cardiovascular health effects from exposure to UFPs



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Donaldson et al. (2005) Particle&Fibre Toxicol. 2 (doi:10.1186/1743-8977-2-10)

Characteristics of Combustion Derived Nanoparticles (CDNP)



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Table I: Characteristics of the CDNP considered in this review

CDNP	Origin	Reported health effects	
		animals	humans
Diesel exhaust particles	Combustion of diesel oil	Inflammation, fibrosis, cancer,	Inflammation, cancer?
Welding fume	Welding processes	Inflammation; translocation of metals to the brain	Metal fume fever, fibrosis, cancer, bronchitis
Fly-ash	Combustion of coal or oil	inflammation	no data available
NP Carbon black	Combustion of heavy fuel oil	Inflammation, lung cancer; translocation of particles to the brain	no data available

Donaldson et al. (2005) Particle&Fibre Toxicol. 2 (doi:10.1186/1743-8977-2-10)

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V. Dixit - University of Michigan
J. Blenis - Harvard Medical School
D. Green - La Jolla

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