

UFIPOLNET
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Health effects of inhaled ultrafine particles in the lungs and secondary target organs like brain and heart.

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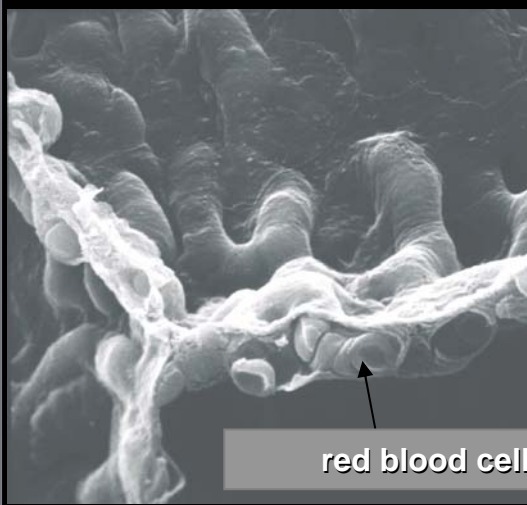
Kreyling@gsf.de; www.gsf.de/ihb; <http://www.gsf.de/neu/aerosols>;

- **Translocation and accumulation of nanoparticles (NP) in secondary target organs of rats after inhalation of**
 - **iridium (Ir); macroscopic view**
 - **elemental carbon (EC); macroscopic view**
 - **titanium dioxide (TiO₂) NP; microscopic view**
- **Systematic studies in rats on the effect of NP parameters on systemic translocation and secondary target organ accumulation**
- **Toxicology: biological response to NP surface area**

Alveolar epithelium

Ultrafine

alveolar wall



Immune system

Monocyte

PMN

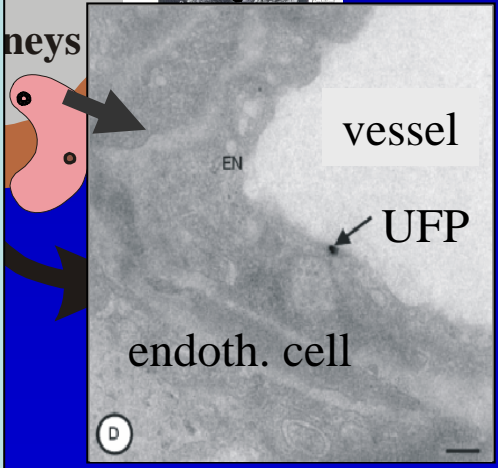
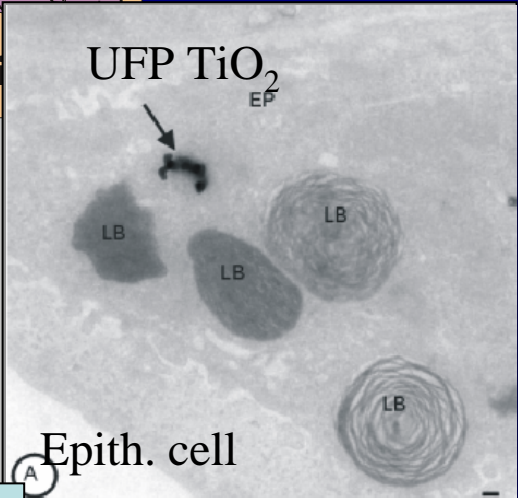
heart

brain

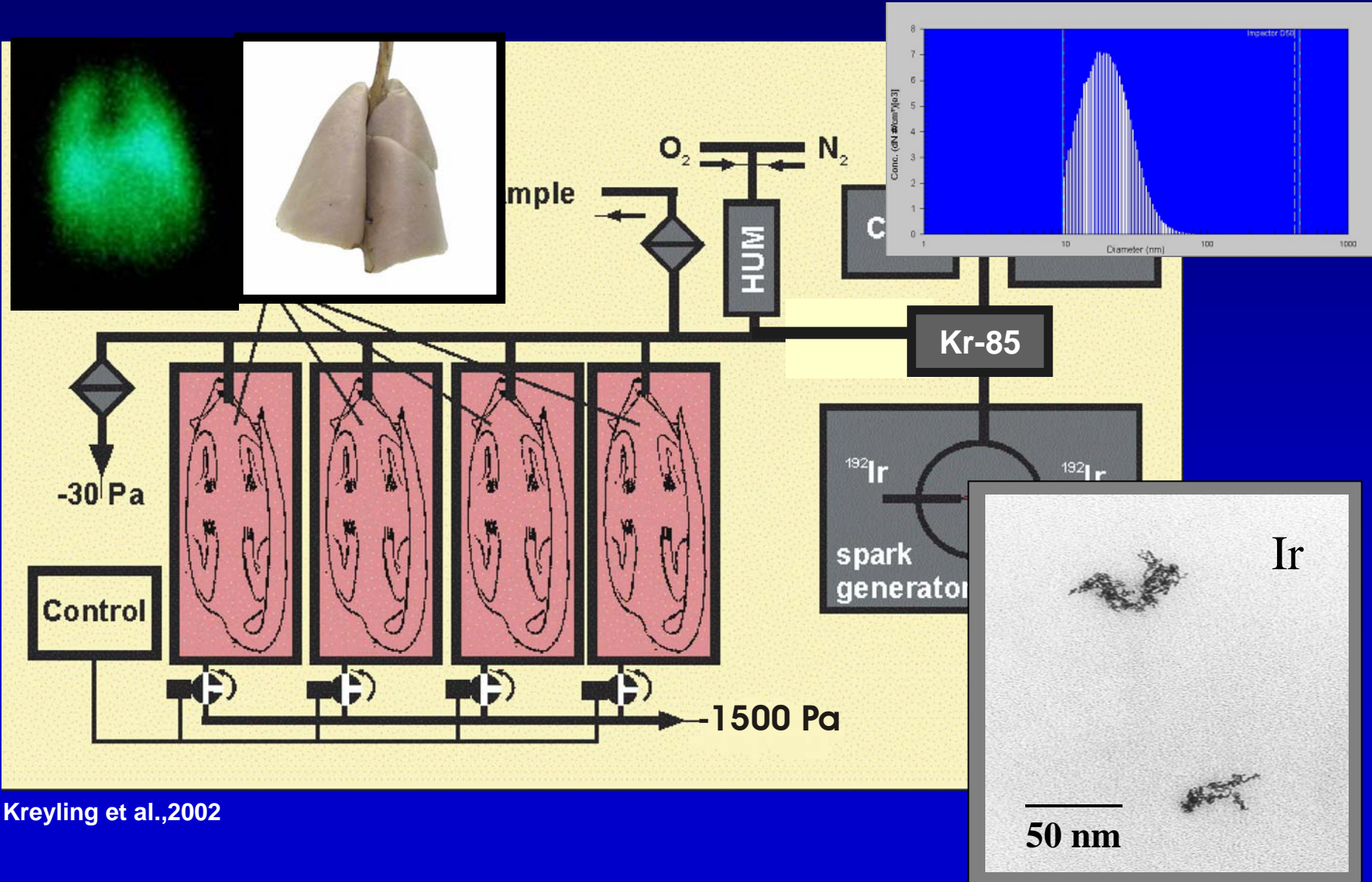
Macroscopic view
 NP content in organs + tissues

Microscopic view: in which cells?
 parenchymal immuno-competent

Where in cells?
 cytoplasm vesicles/organelles nucleus



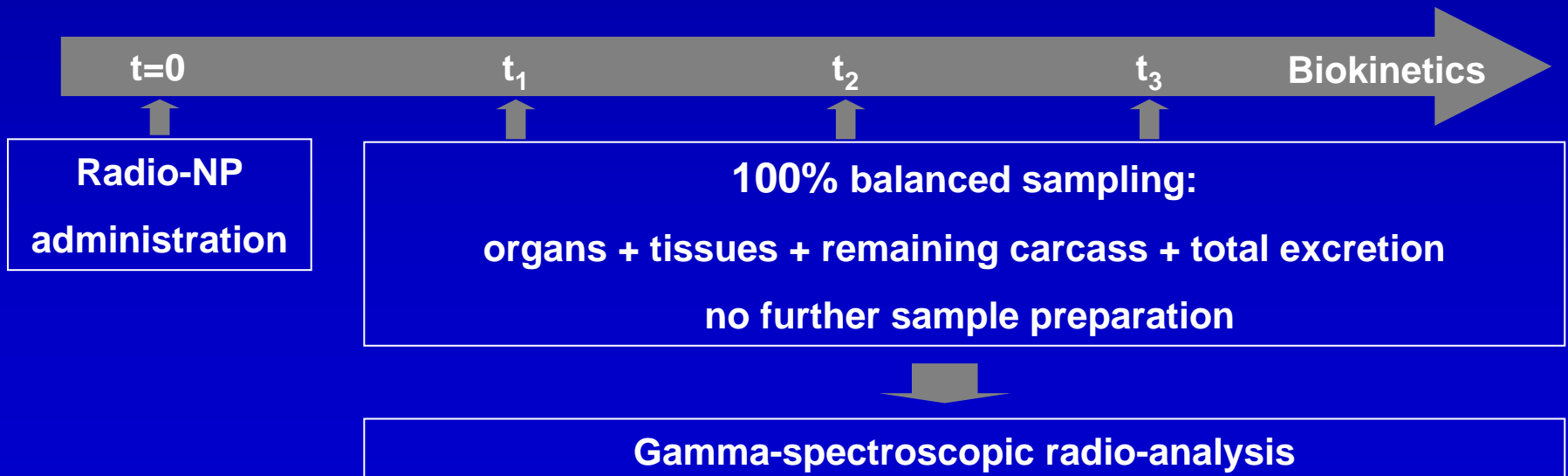
Ventilation-inhalation system of Ir-NP



Intubation ventilation

Nose-only inhalation

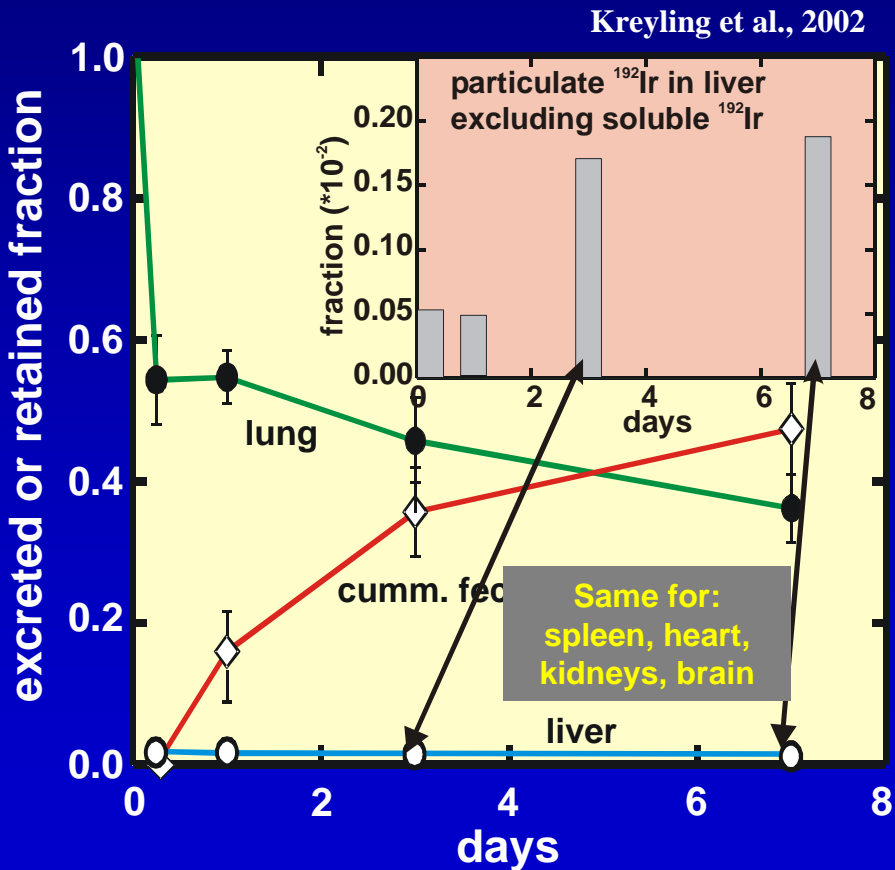
Intra-tracheal instillation



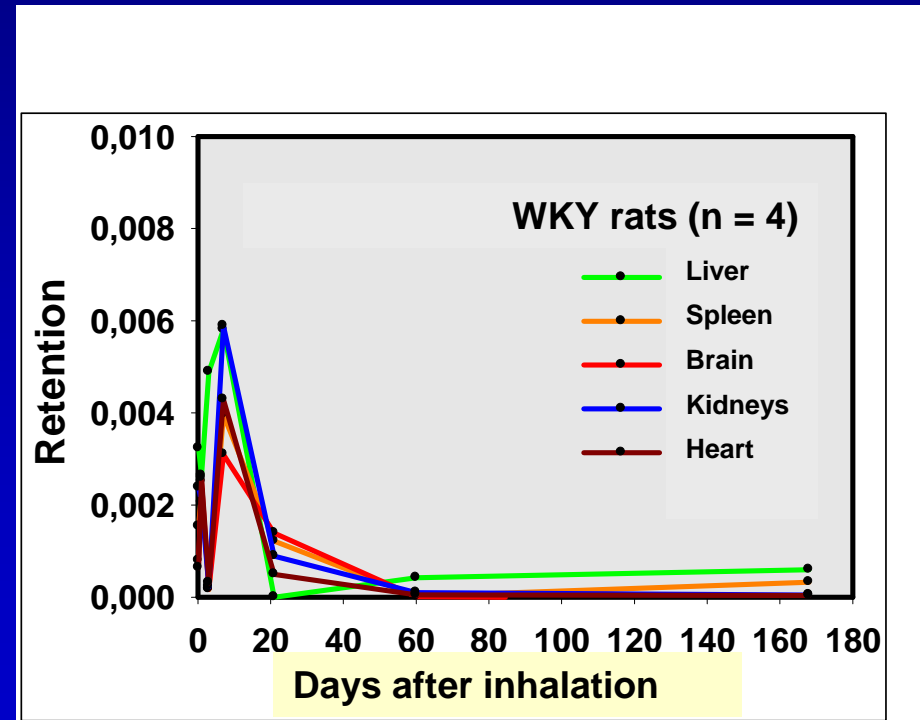
Systemic translocation of nanoparticles towards secondary target organs

WKY rat, ^{192}Ir NP, 1 hr exposure
 15 nm CMD, 10^7 cm^{-3} , 0.2 mg/m^3

Long-term translocation kinetics
 same exposure



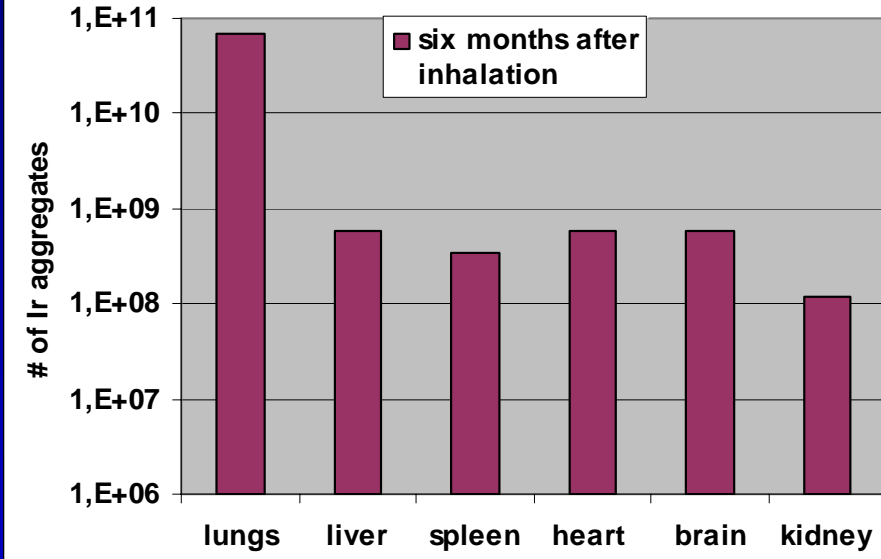
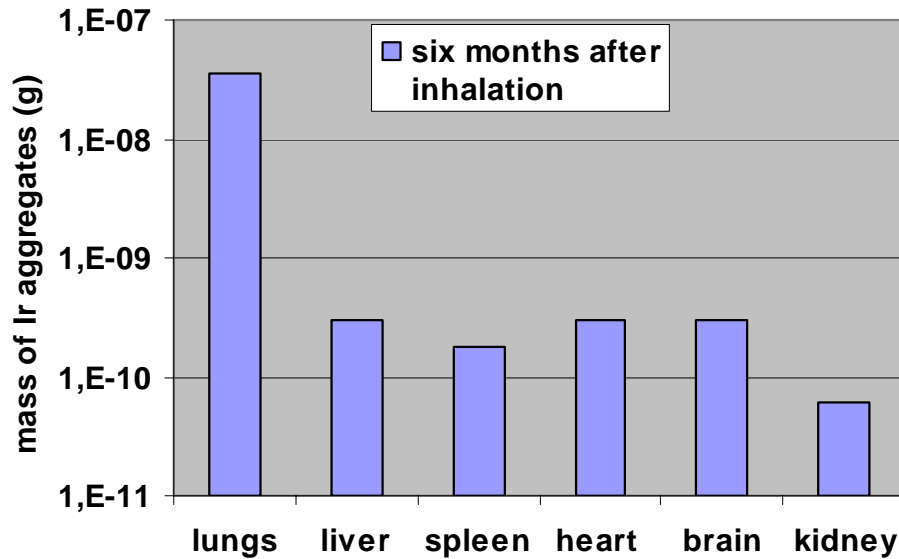
Semmler et al., 2004



There is little but persistent translocation of Ir-NP towards secondary target organs

Systemic translocation of nanoparticles towards secondary target organs

WKY rat, ^{192}Ir NP, 1 hr exposure
 15 nm CMD, 10^7 cm^{-3} , 0.2 mg/m^3



Primary particles ~ 2 nm
 Specific surface area $1200 \text{ m}^2 / \text{cm}^3$
 Zeta potential - 20 mV
 SIMS-TOF surface analysis IrO_2

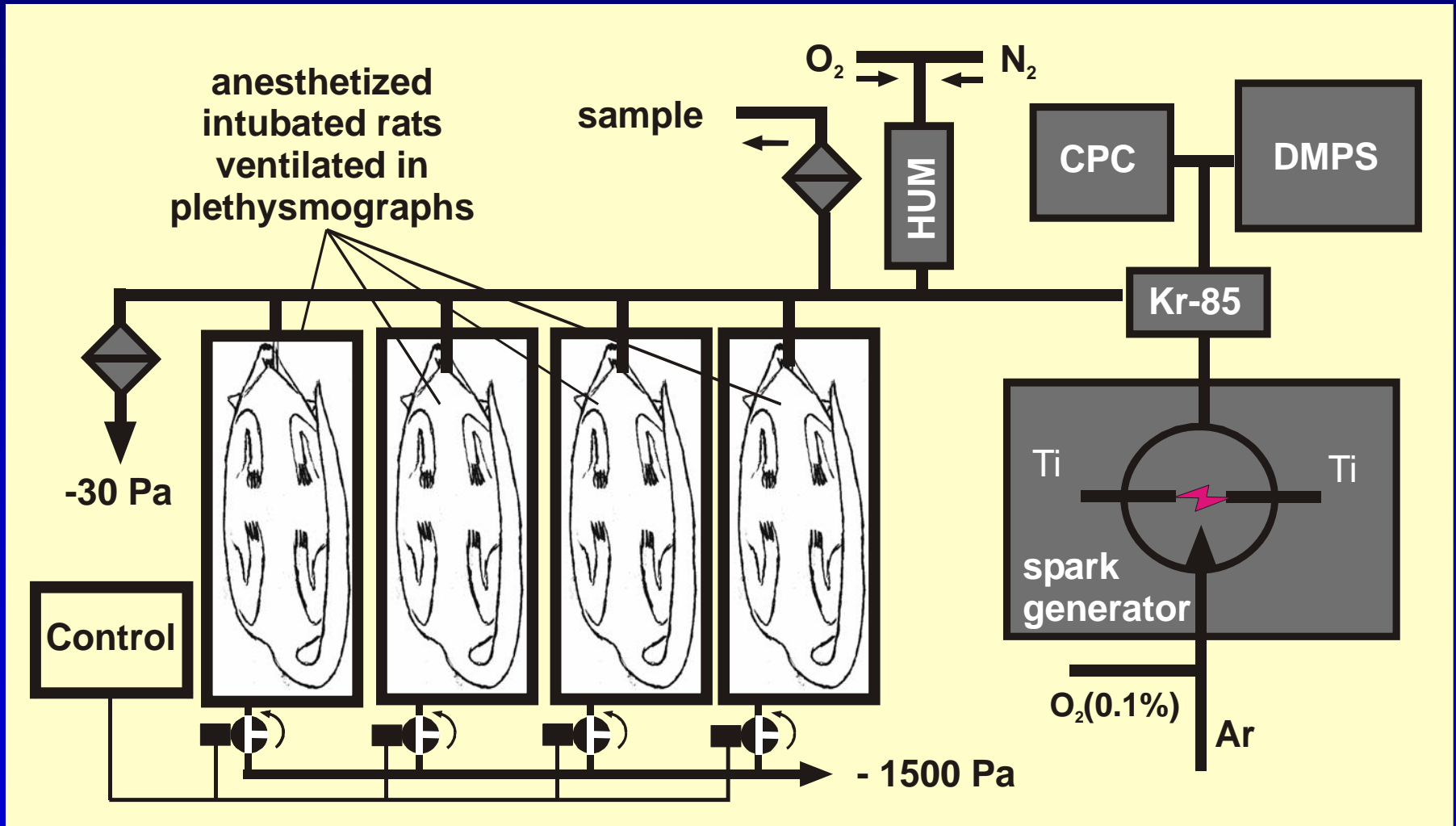
Unexpected high NP numbers in secondary target organs including heart and brain after six months which are not considered to be exposed to particulate foreign bodies.
 Do these many NP cause harm?

Systemic translocation of nanoparticles towards secondary target organs

Human dose estimate during continuous exposure applying rat translocation dynamics determined for Ir UFP:

NC (UFP) (10^5 p/cm ³)	10^{11} p/m ³
Daily inhaled volume	10 m ³
Deposition fraction	0.3
Insoluble UFP fraction	0.1
Translocated fraction to brain, heart	0.001 (of lung deposit)
Retained UFP number in brain, heart	$\sim 10^{10}$ UFP/year
Estimated surface area	$\sim 10^{-1}$ mm²
(5 nm assumption)	

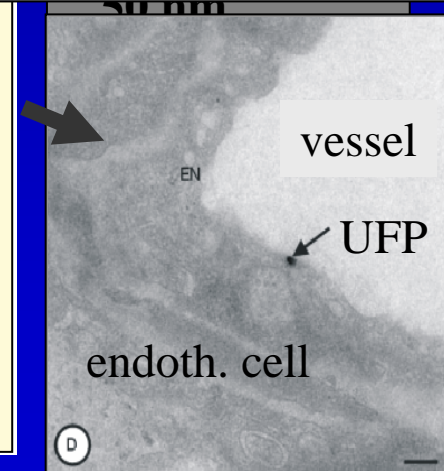
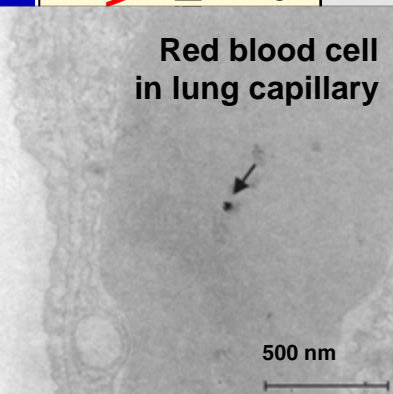
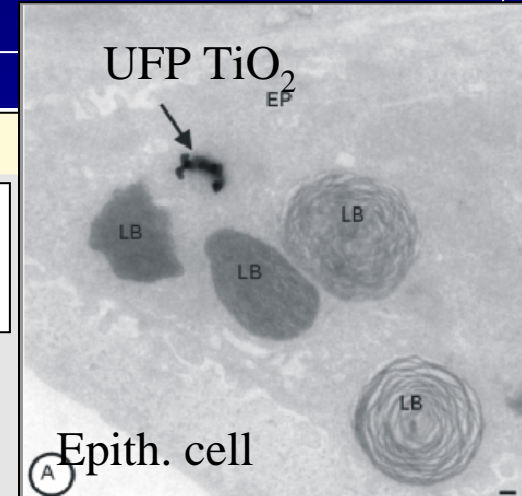
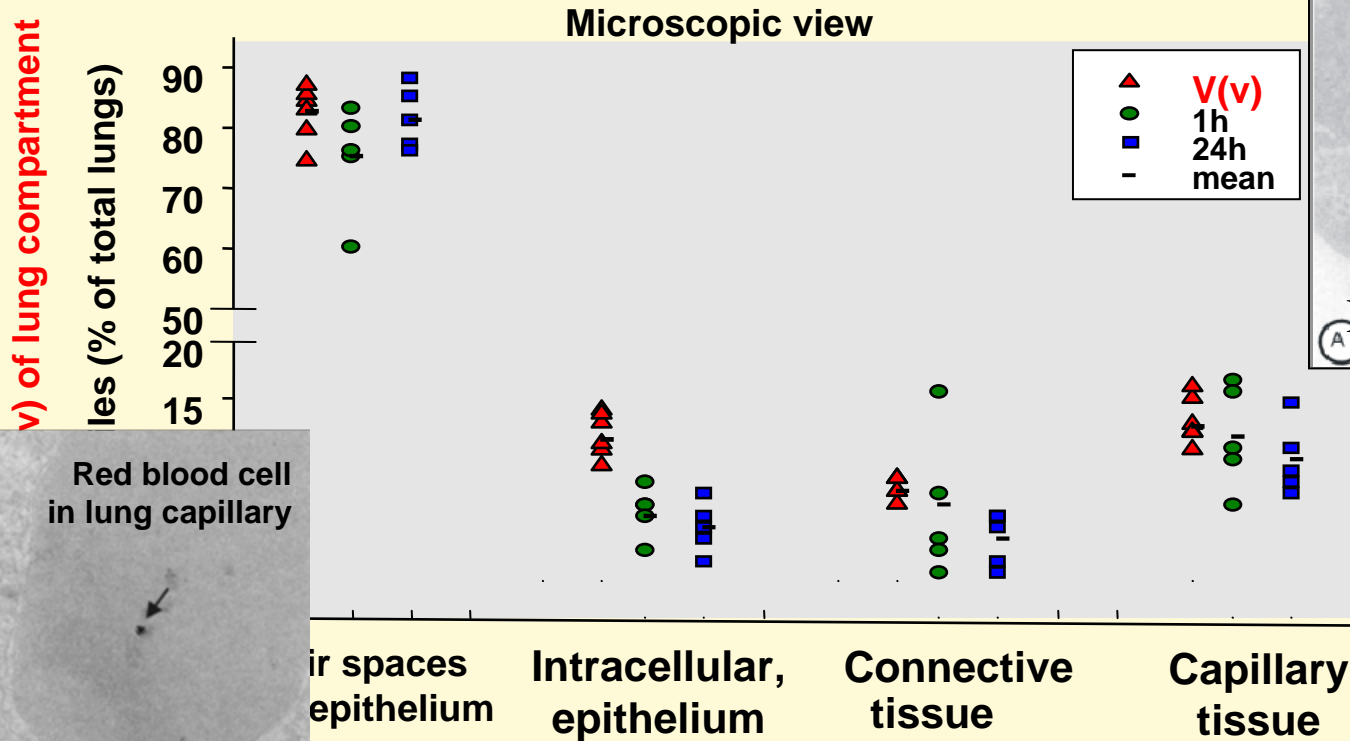
Morphological characterisation of NP distribution in the lungs



Intubated ventilated WKY rat,
TiO₂ NP, 1 hr exposure
22 nm CMD, 10⁷ cm⁻³, 0.1 mg/m³
morphometry 0 + 24 h after inhalation

→ Rapid translocation of ~ 20% NP fraction
→ Volume proportional translocation: by which mechanism?

M. Geiser et al., EHP 2005



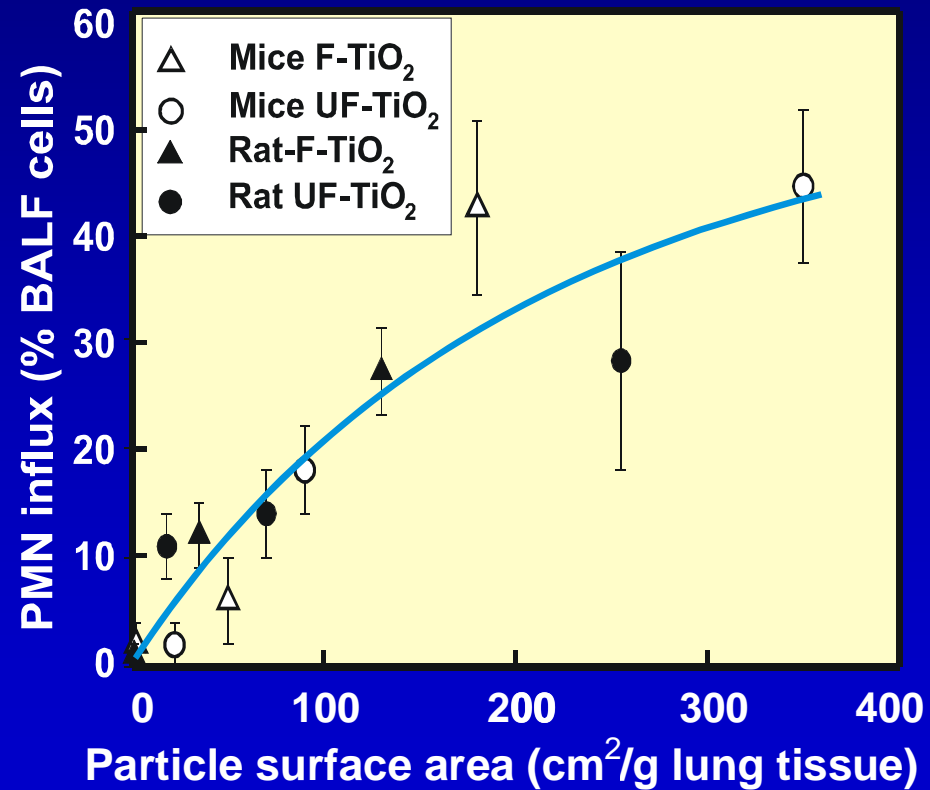
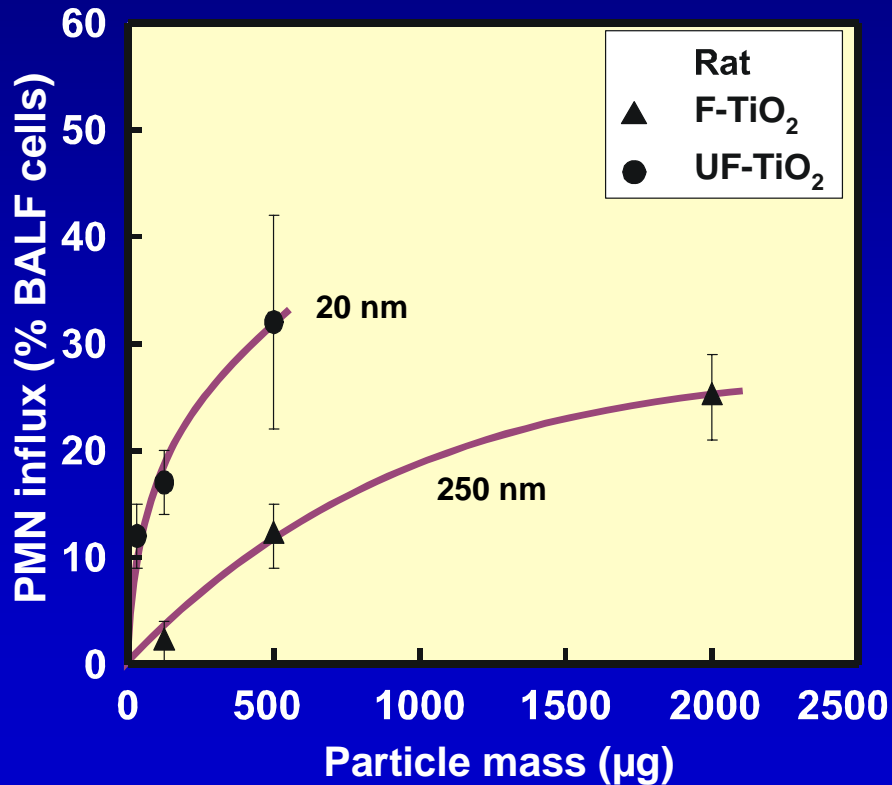
Systemic translocation depends on NP material + particularly its surface

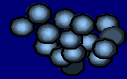
Toxicology: biological response to NP surface area

Surface area of NP is associated with inflammatory response

Influx of neutrophils (PMN) : indicator of inflammation

Instillation of ultrafine UF-TiO₂ (20 nm) or fine F-TiO₂ (250 nm) into rat lungs

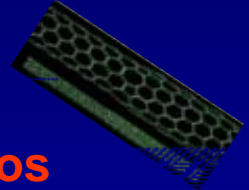




reactive surfaces of
low-solubility particles:
structure + compounds
(TiO₂, elemental carbon)

organic
compounds
(Diesel exhaust
particles, DEP)

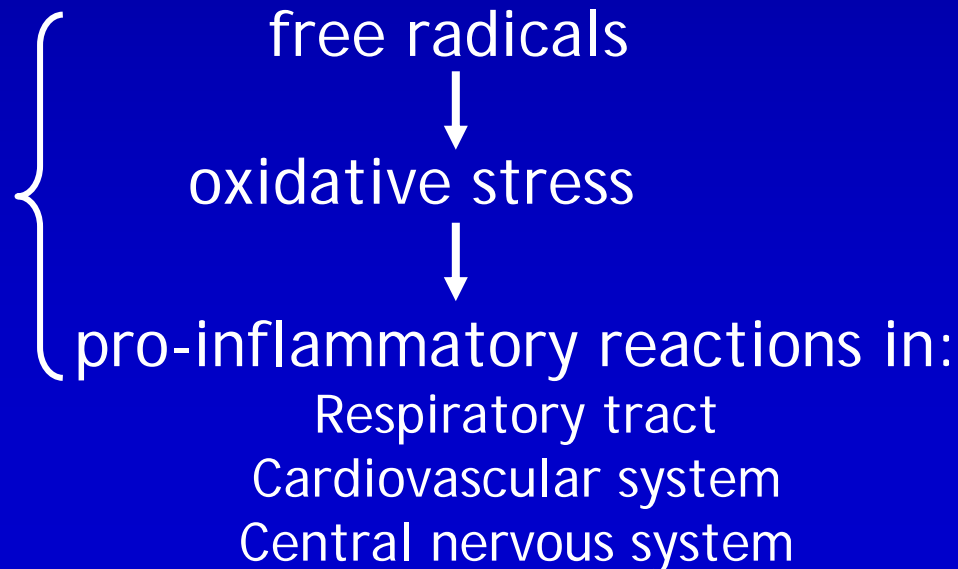
nanotubes??
extremely thin + long,
biopersistent as asbestos



transition metals:
Zn, V, Fe, Ni, Cr,
(welding fume)



**NP interaction with
biological systems:
body fluids, cells,
tissues, organs**



- Six months after a single 1-hour inhalation iridium NP were found at elevated number concentrations in 2nd target organs such as liver, spleen, heart, brain, etc.
- While 20 nm Ir and 25 nm carbon and 18 nm gold NP show similar translocated fractions, 22 nm TiO₂ NP seem to be much more translocated towards circulation
- Translocation and uptake in secondary target organs is strongly NP size dependent
- Biological inflammatory response is strongly driven by NP parameters like metals, organics and the NP surface area and its biologically active sites

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Thank you!

