

# **Nanoparticle Interactions with Biomolecules: Implications for Disposition**

Nanomaterials: Environmental Risks and Benefits and Emerging  
Consumer Products

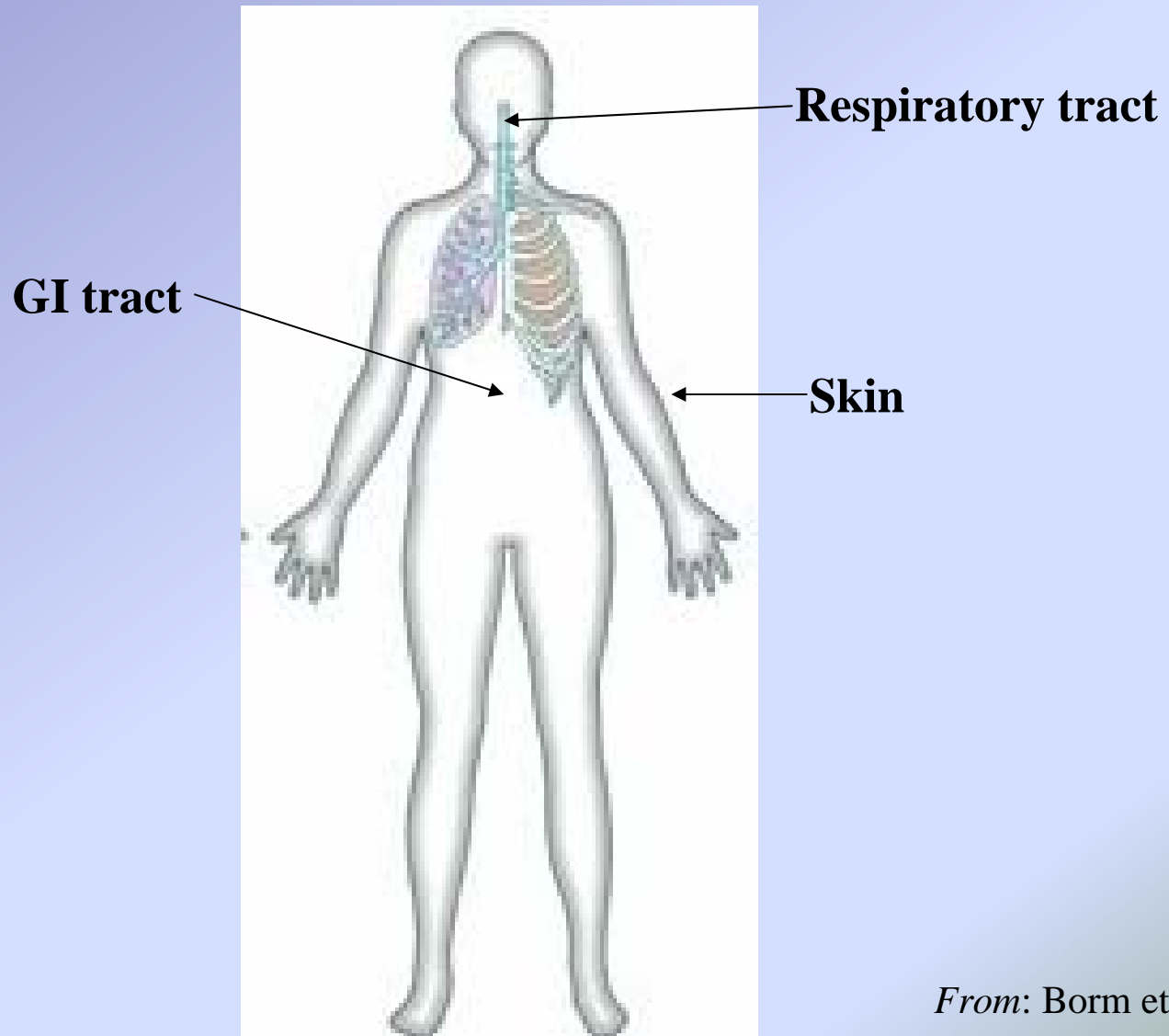
NATO-OTAN Advanced Research Workshop

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**Alison Elder**

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University of Rochester

# Exposures to Nanomaterials: Most Likely Routes

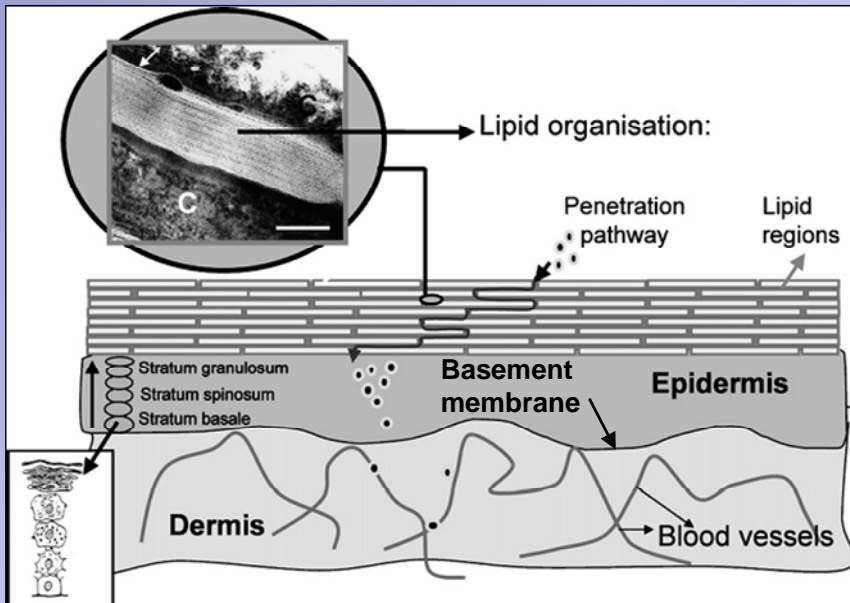


# Gastrointestinal Tract

- Data suggests that persorption of particles can occur.
  - Persorption of micron-sized “insoluble” PVC particles (Volkheimer, 1975).
  - About 0.0001% Pu dioxide GI tract absorption in humans (Stather et al., 1979).
  - No absorption of orally-administered poorly-soluble 15 nm  $^{192}\text{Ir}$  particles from GI tract (Kreyling et al., 2002).
- Tissue distribution of colloidal Au nanoparticles is size-dependent following exposures in drinking water for 7 days (Hillyer and Albrecht, 2001).

*Does particle density play a role?*

# Skin Architecture



From: Bouwstra et al., 2006

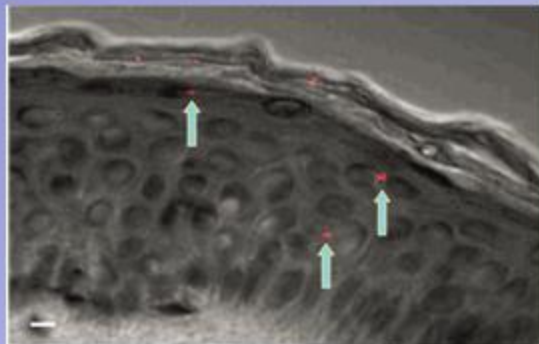
## Key Considerations for Studies of Nanomaterials Interactions with Skin

- Surface pH of  $\sim 5.0$
- Lipid lamellae of stratum corneum

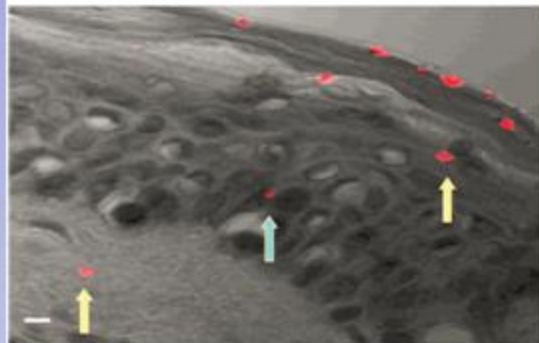
**Main question:** Can nanoparticles breach the stratum corneum and under what conditions?

# Considerations Regarding Nanomaterials

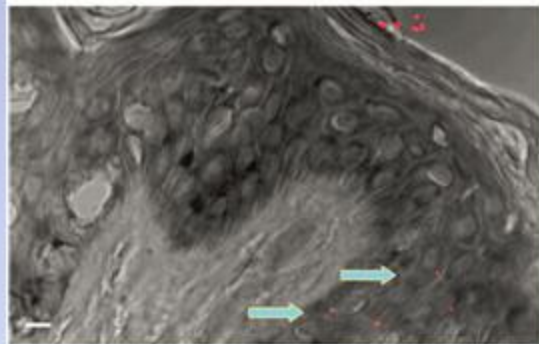
## Absorption through Skin: *Particle Size*



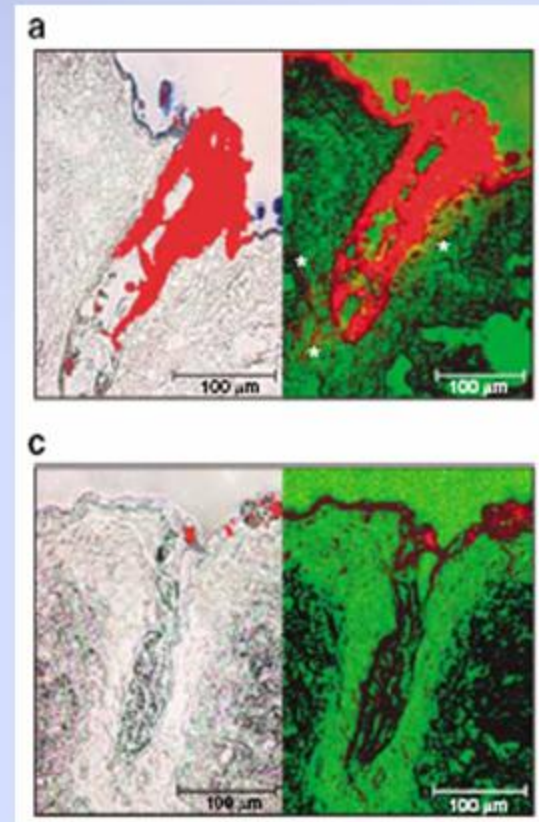
1  $\mu\text{m}$  beads,  
30 mins



1  $\mu\text{m}$  beads,  
60 mins



0.5  $\mu\text{m}$  beads,  
30 mins



40 nm beads,  
~16 hrs

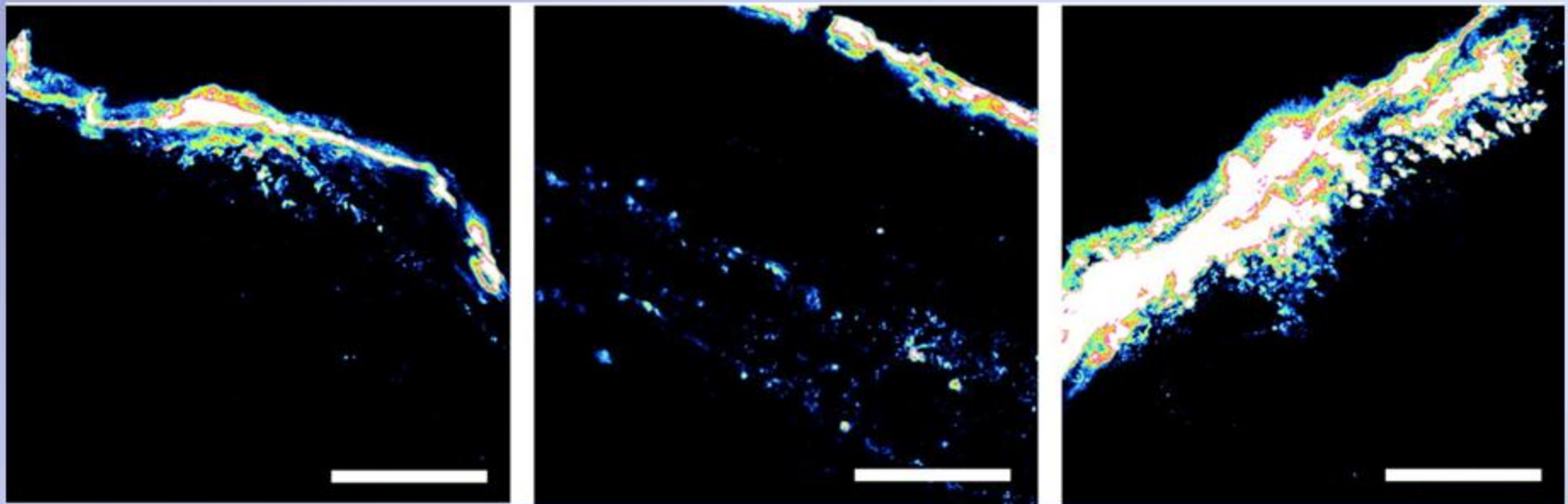
750 nm beads,  
~16 hrs

# Considerations Regarding Nanomaterials Absorption through Skin: *Surface Charge*

PEG

PEGamine

COOH



Scale bar, 50  $\mu\text{m}$

# Respiratory Tract

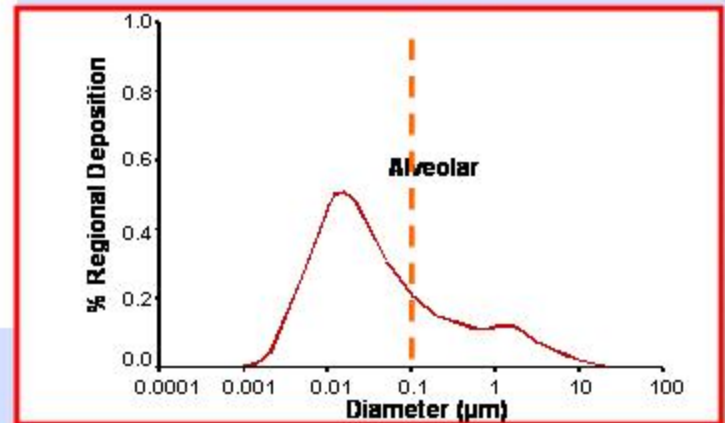
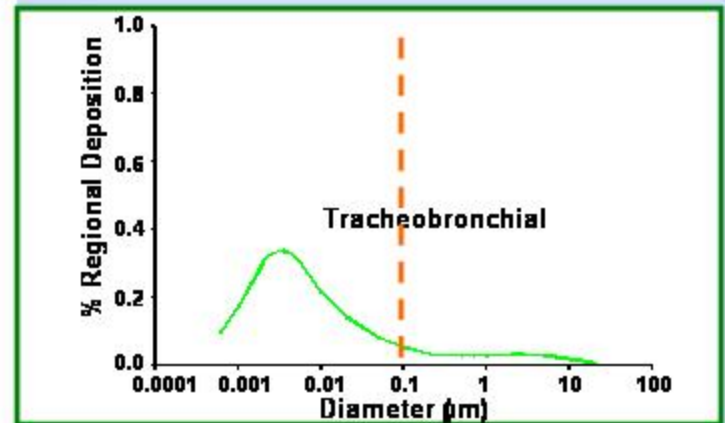
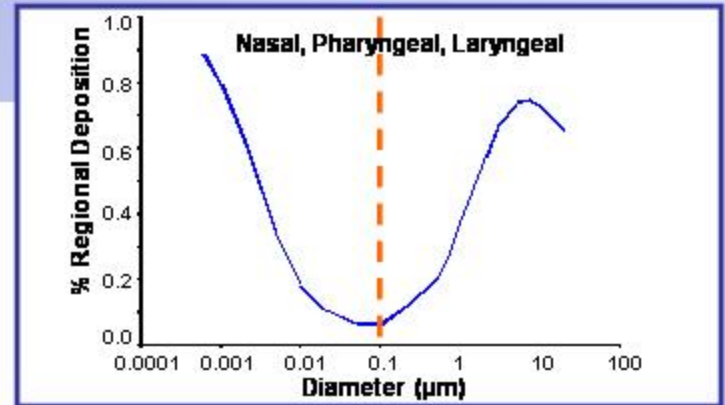
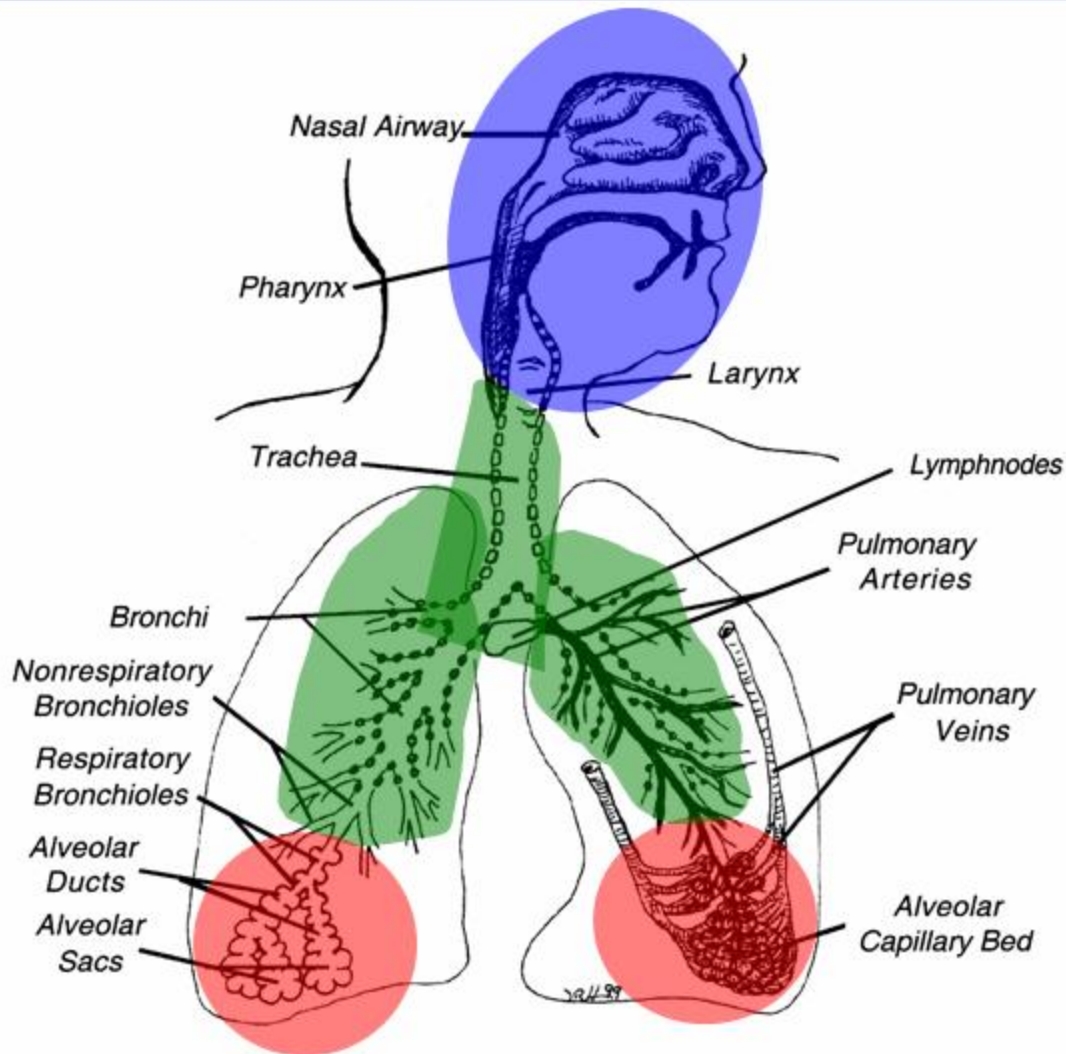
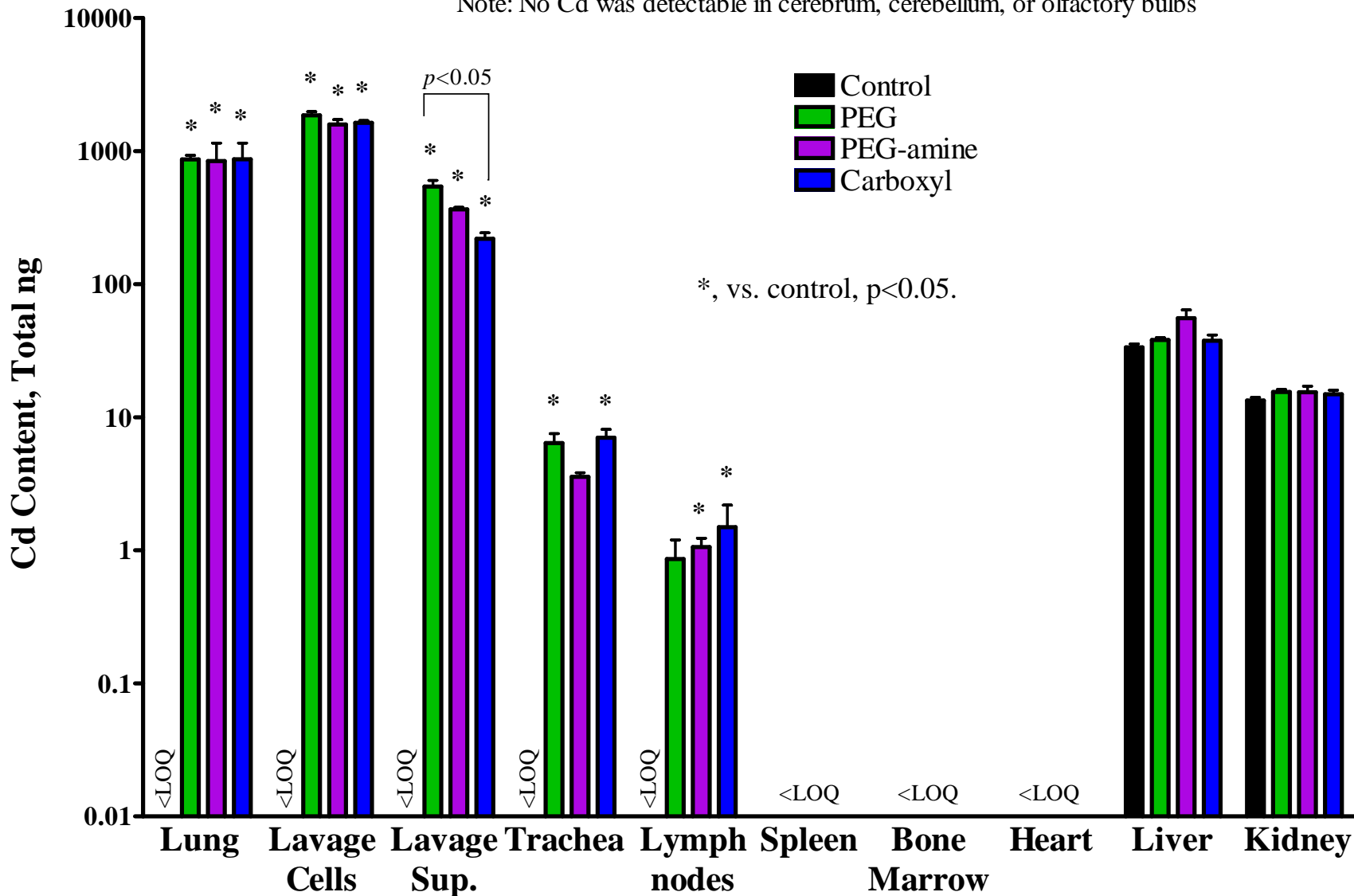


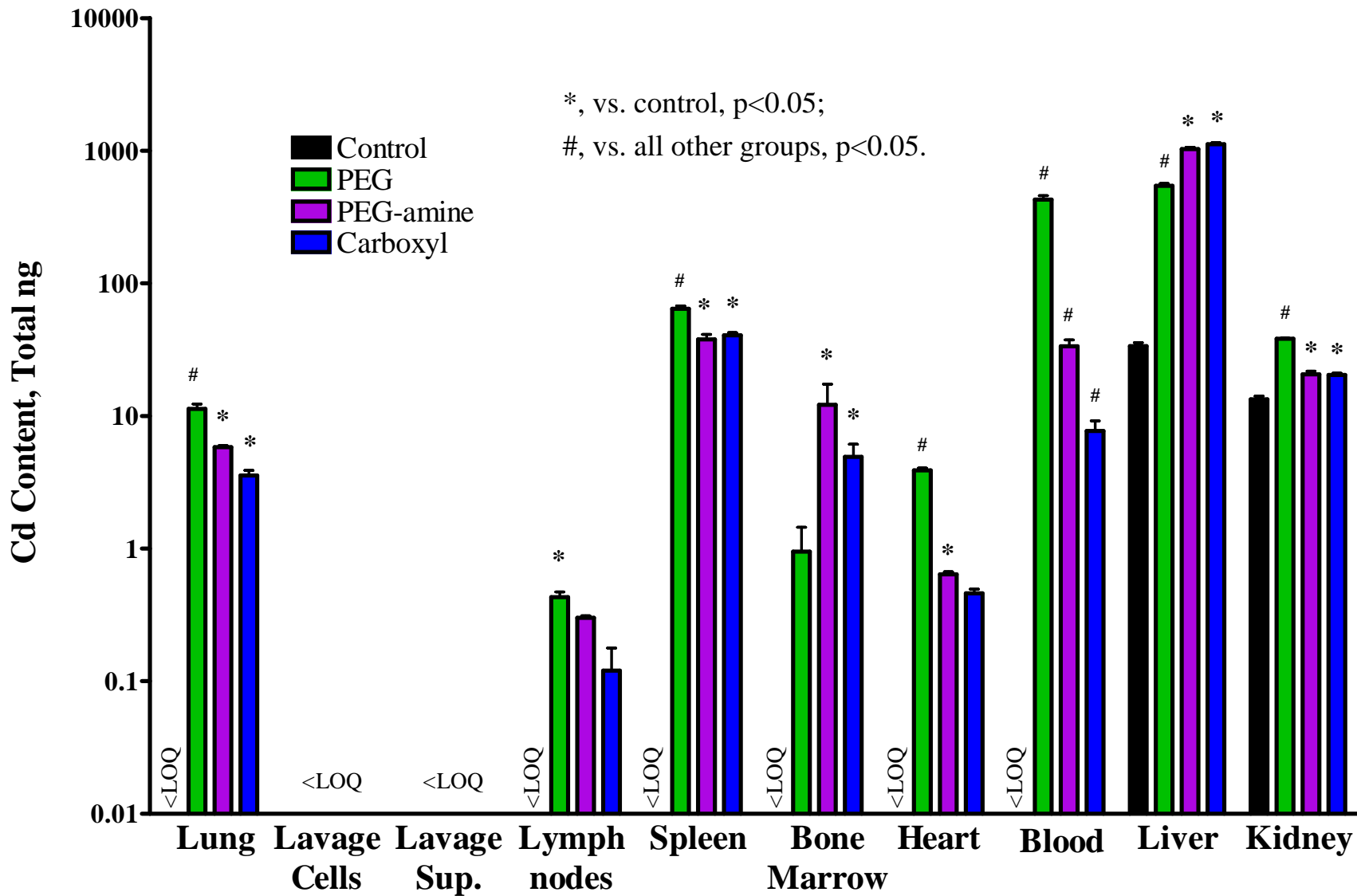
Figure courtesy of J. Harkema; adapted from ICRP, 1994

# Tissue Cadmium Content 24 hrs following Intratracheal Microspray Exposure of Surface-Modified QDots (Rats, 5 $\mu\text{g}$ Cd sprayed in 3x50 $\mu\text{l}$ )

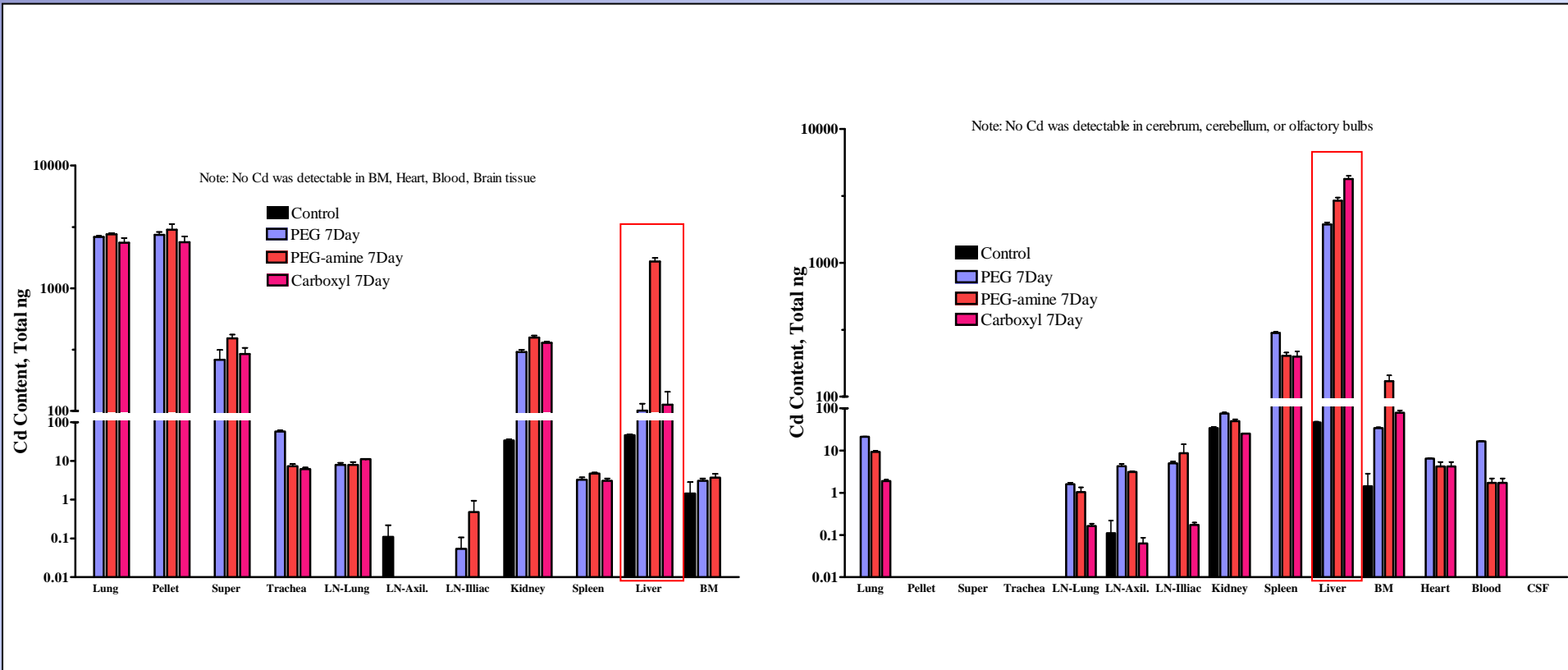
Note: No Cd was detectable in cerebrum, cerebellum, or olfactory bulbs



# Tissue Cadmium Content 24 hrs following Intravenous Exposure to Surface-Modified QDots (Rats, 1.7 $\mu\text{g}$ Cd injected in 200 $\mu\text{l}$ )



# Tissue Cd Levels 7 Days after Exposure

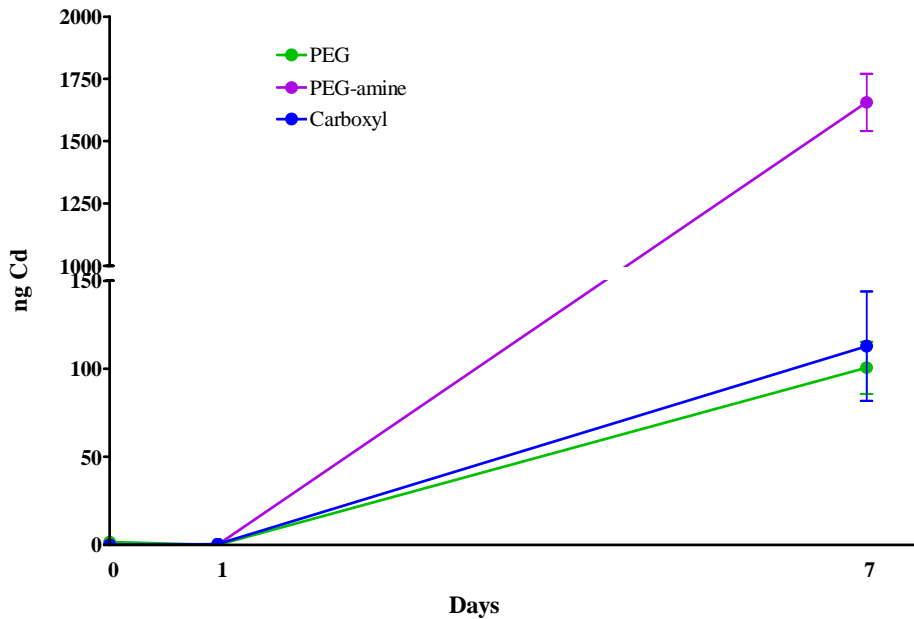


**Intratracheal Microspray**

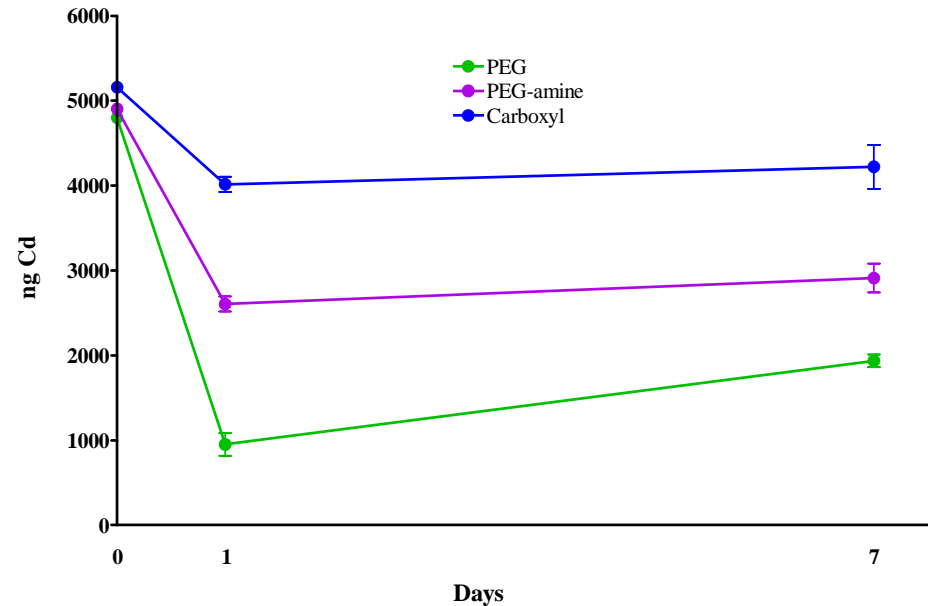
**Intravenous Injection**

# Liver Cd Levels: Comparison of Exposure Route (and Surface Coating)

Intratracheal



Intravenous

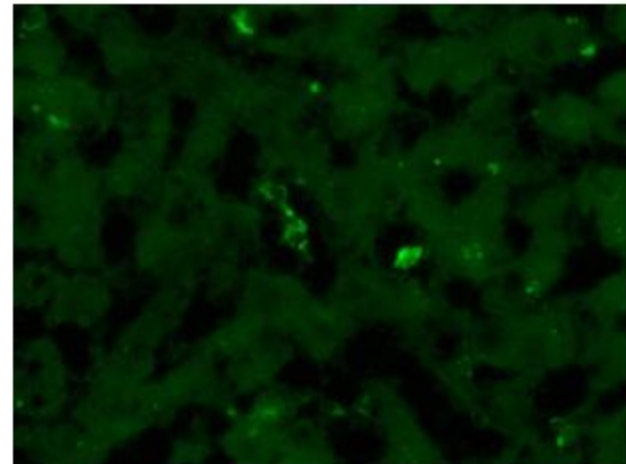
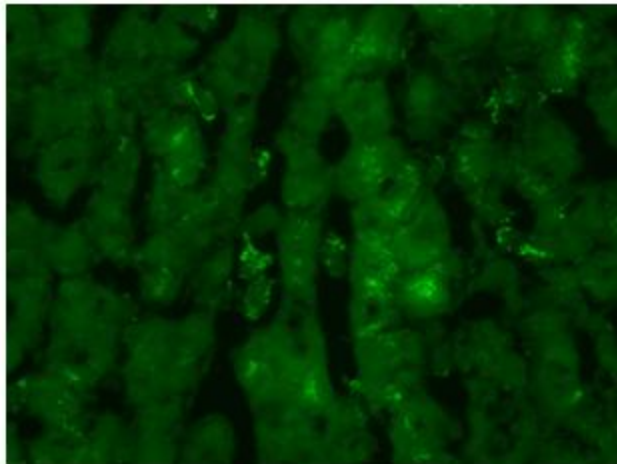


# Retention of Quantum Dots in Liver Tissue after IV injection

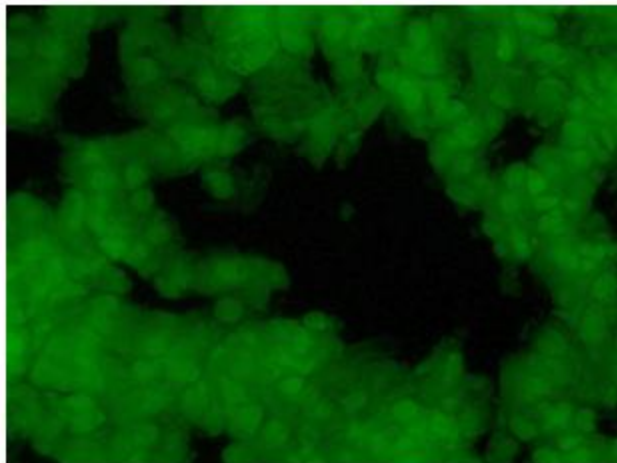
PEGamine-coated QDs

Carboxyl-coated QDs

1 Day

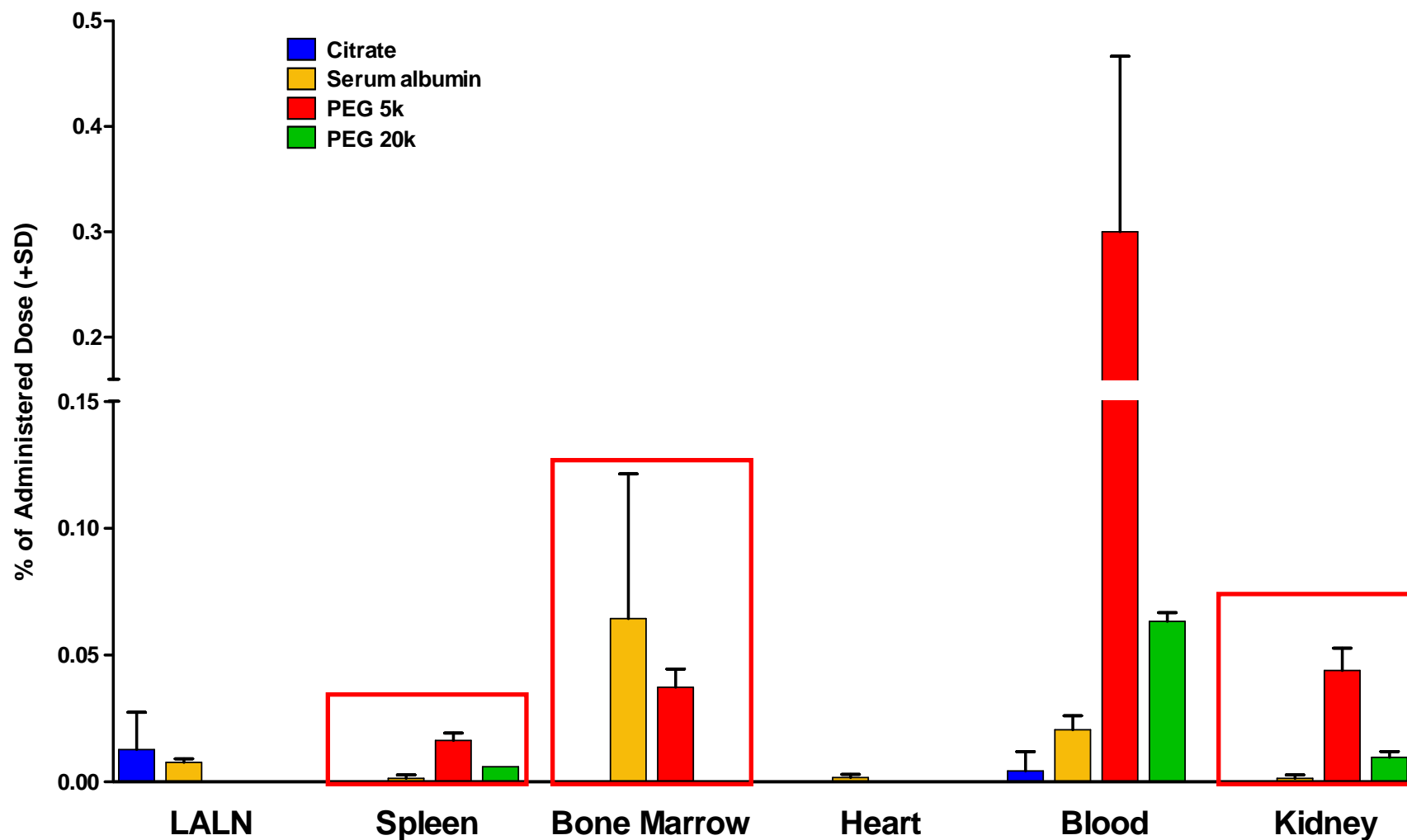


7 Days

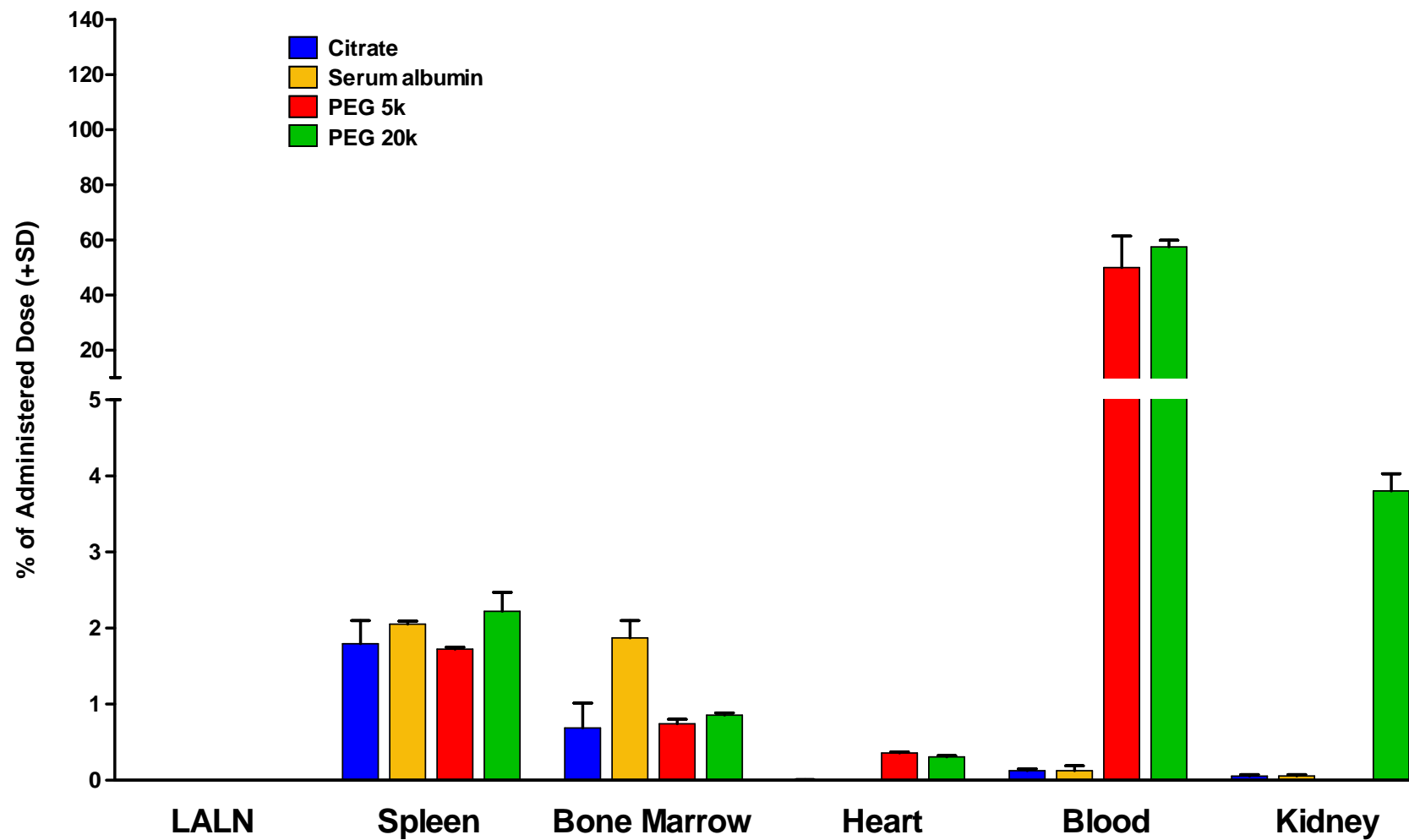


10  $\mu$ m frozen sections  
Magnification, 60x

# Tissue Au Content 24 hrs following Intratracheal Microspray Exposure to Colloidal Au Nanoparticles with Different Surface Coatings

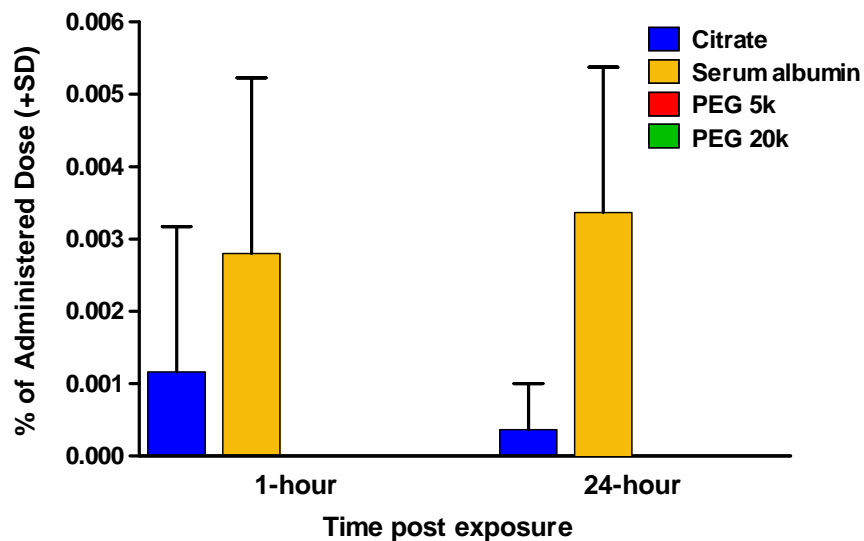


# Tissue Au Content 24 hrs following Intravenous Exposure to Colloidal Au Nanoparticles with Different Surface Coatings

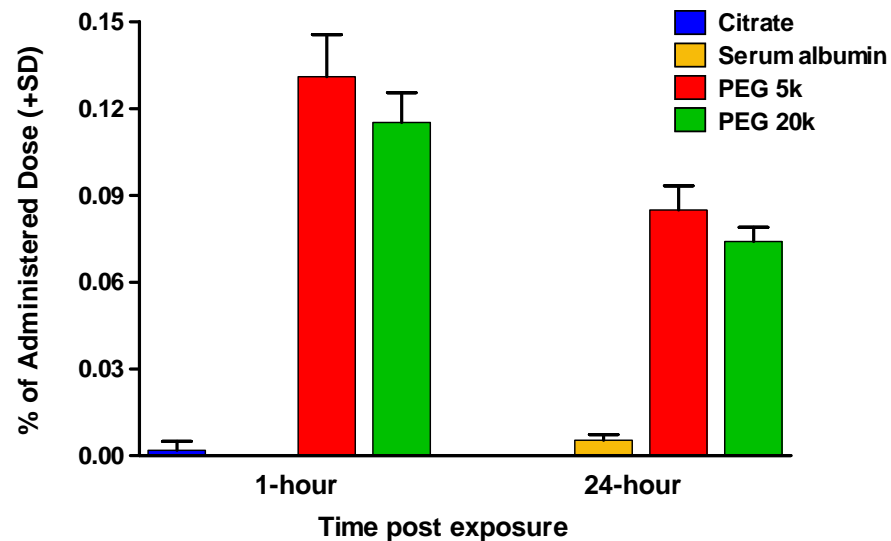


# Translocation of Nanogold to the Brain

5nm Gold, surface modified:  
Au in brain after ITM Exposure



5nm Gold, surface modified:  
Au in brain after IV Exposure



# Key Cross-Cutting Themes

- Nanoparticle physicochemical characteristics
- Properties of portal of entry
- Integrity of barrier
- Responses caused by NP-cell interactions (e.g. inflammation) are likely to affect biodistribution

# Acknowledgements

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**Questions?**

# Summary of Results

1. Nanoparticles delivered via the lower respiratory tract are translocated to extrapulmonary tissues
  - Dependent on particle physicochemical characteristics.
2. Nanoparticles can be retained in small amounts by the brain following a single exposure
  - Dependent on particle physicochemical characteristics and portal of entry.

# Considerations Regarding Nanomaterials Absorption through Skin

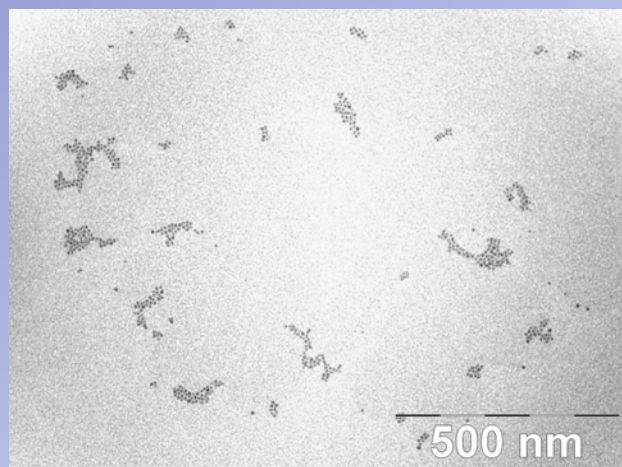
- Penetration via hair follicles
- Health or condition of skin
  - UV radiation, tape stripping facilitate particle access to hair follicles (Sincai et al., 2007; Vogt et al., 2006).
  - No penetration without flexion (Tinkle et al., 2003).
- Nanoparticle size
  - Positively-charged polystyrene beads (20-40 nm) found in follicles at level of epidermis, dermis – particles over 200 nm did not penetrate (Alvarez-Román et al., 2004; Vogt et al., 2007).
  - Small percentage of dextran beads penetrate to level of dermis – size cut-off between 1 and 2  $\mu\text{m}$  (Tinkle et al., 2003).

# Study Design:

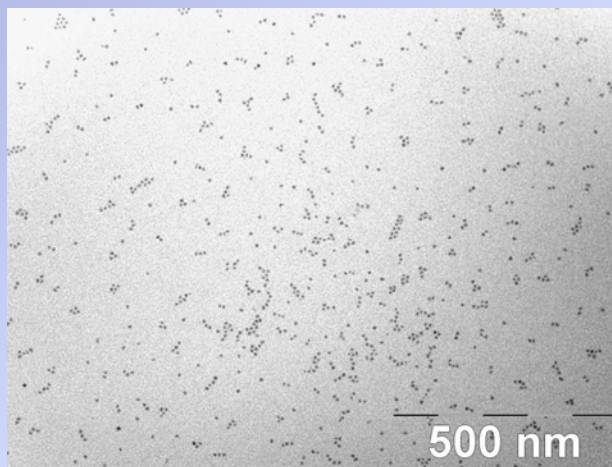
## Nanoparticle Characteristics

- Characteristics of the QDots:
  - CdSe/ZnS core-shell particles coated with polymer, ~5 nm core-shell diameter (Invitrogen) – 565 nm emitters
  - PEG, PEG-amine, or carboxyl conjugated surfaces
- Characteristics of colloidal Au particles:
  - 5 nm primary particle size (Ted Pella, Inc.)
  - Coated with albumin, 5 kDa PEG, or 20 kDa PEG

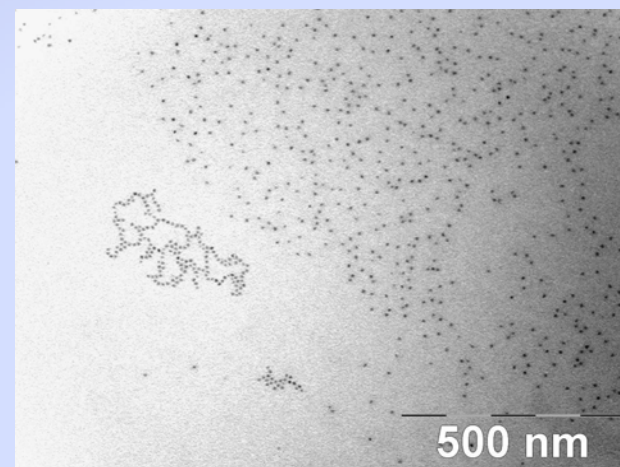
## CdSe-ZnS Quantum Dots in 0.9% Saline



**PEGylated**  
**23 nm**

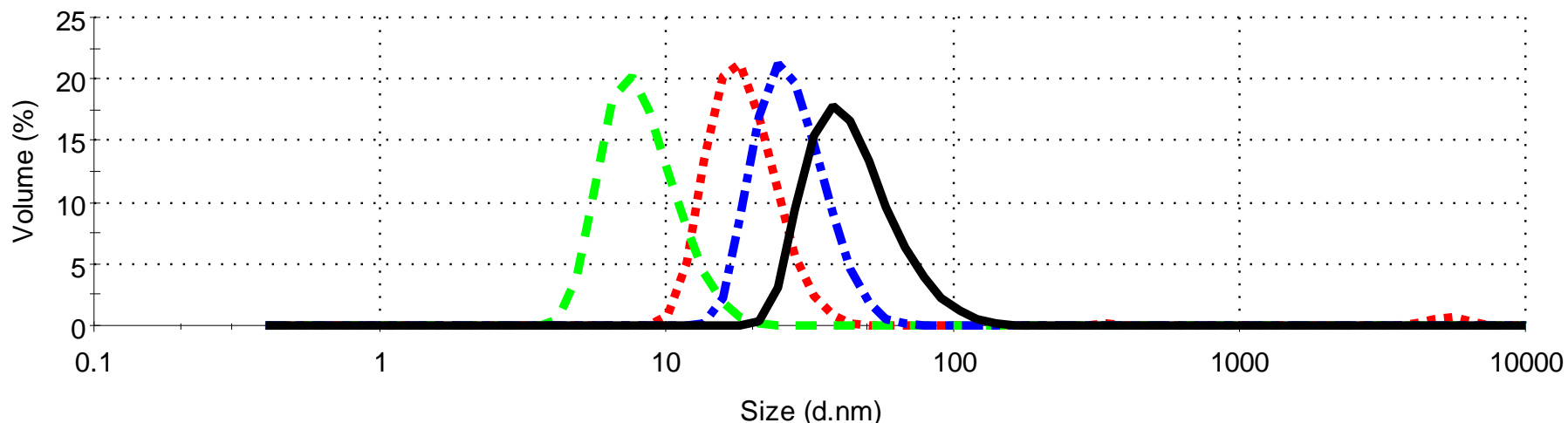


**PEGamine**  
**17 nm**



**Carboxylated**  
**13 nm**

# Hydrodynamic Radii of Colloidal Gold Nanoparticles (5 nm)



Surface Coating	Peak Mean
--- Citrated Au	8 nm
--- RSA-Au	19 nm
- · - PEG (5K)-Au	28 nm
— PEG (20K)-Au	47 nm

*from: Dr. A. Rinderknecht*

# Study Design:

## Nanoparticle Exposures

- Exposures to QDots (dose expressed as Cd content):
  - Intratracheal microspray (5  $\mu\text{g}$  Cd/150  $\mu\text{l}$  saline)
  - Intravenous injection (1.7  $\mu\text{g}$  Cd/200  $\mu\text{l}$  saline)
- Exposures to colloidal Au:
  - Intratracheal microspray (50  $\mu\text{g}$ /150  $\mu\text{l}$  saline)
  - Intravenous injection (15  $\mu\text{g}$ /200  $\mu\text{l}$  saline)