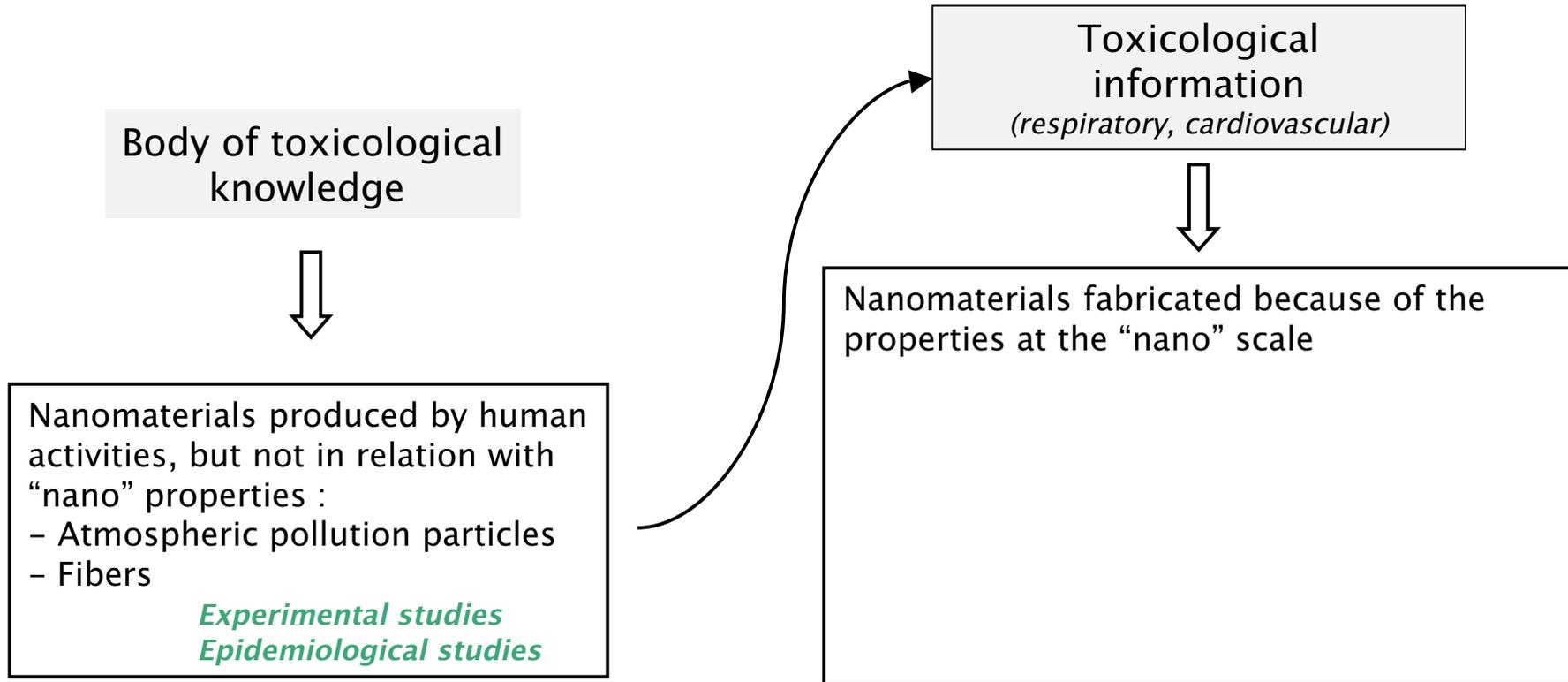


State of the art related to toxicity aspects of nanomaterials

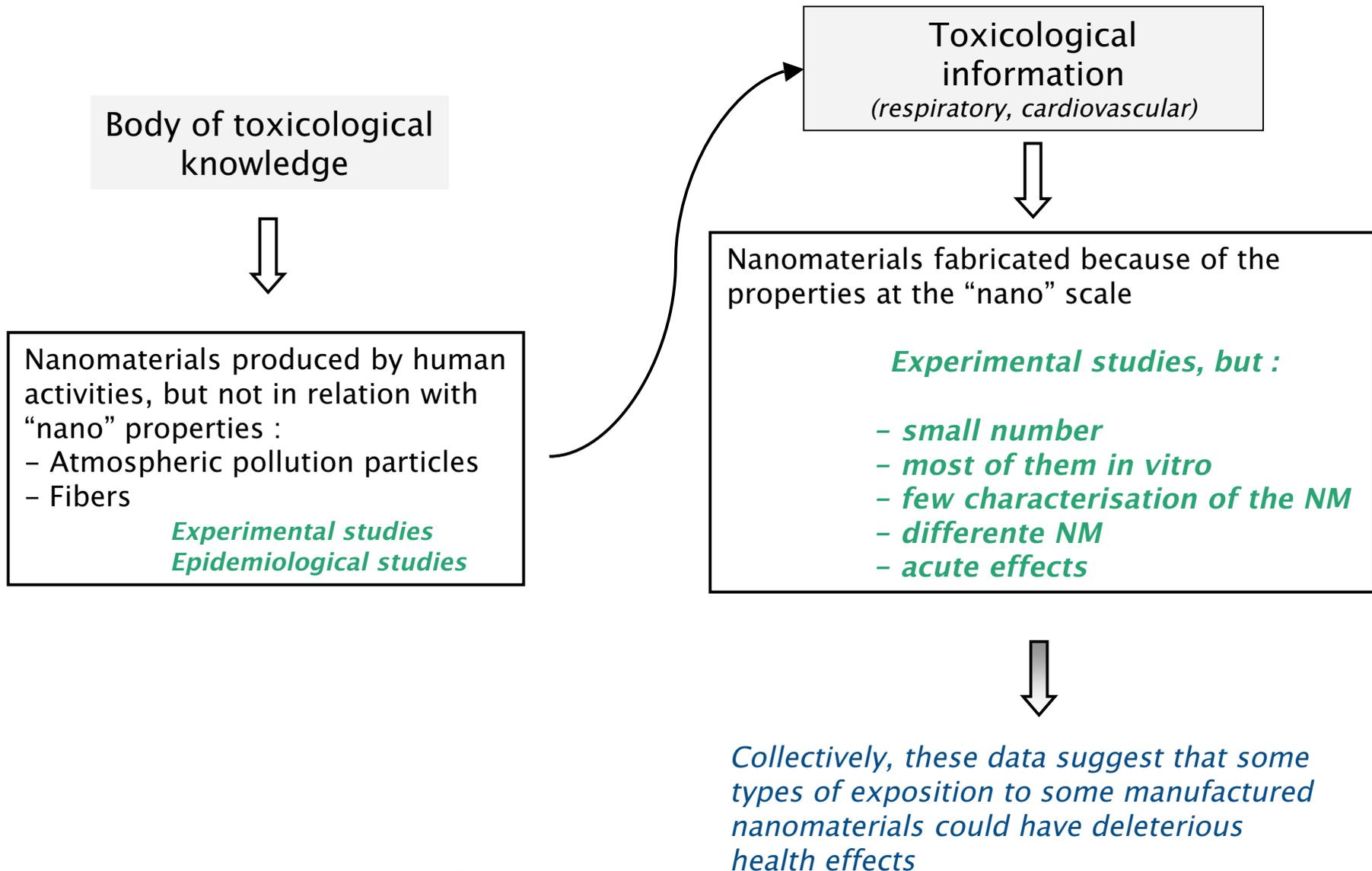
Sophie Lanone, Jorge Boczkowski

UMR 700 (Inserm–Université Paris 7)

General concepts



General concepts



Determinants of the potential toxicologic effects of manufactured nanomaterials

- **Exposition factors**
 - Sources : aerosols, solutions
 - Route of entry : respiratory system, skin, gastro-intestinal
 - Magnitude and duration of exposition
- **Factors concerning the exposed organism**
 - Individual susceptibility : disease states
 - Interaction of nanomaterials with body components : proteins (pulmonary surfactant, transferrin) Cooper et al. *Int. J. Radiat. Biol. Relat. Stud. Phys. Chem. Med.* 1979, 36:453-66
 - Evolution of nanomaterials once they enter into the body
- **Factors concerning the nanomaterials: physico-chemical characteristics**

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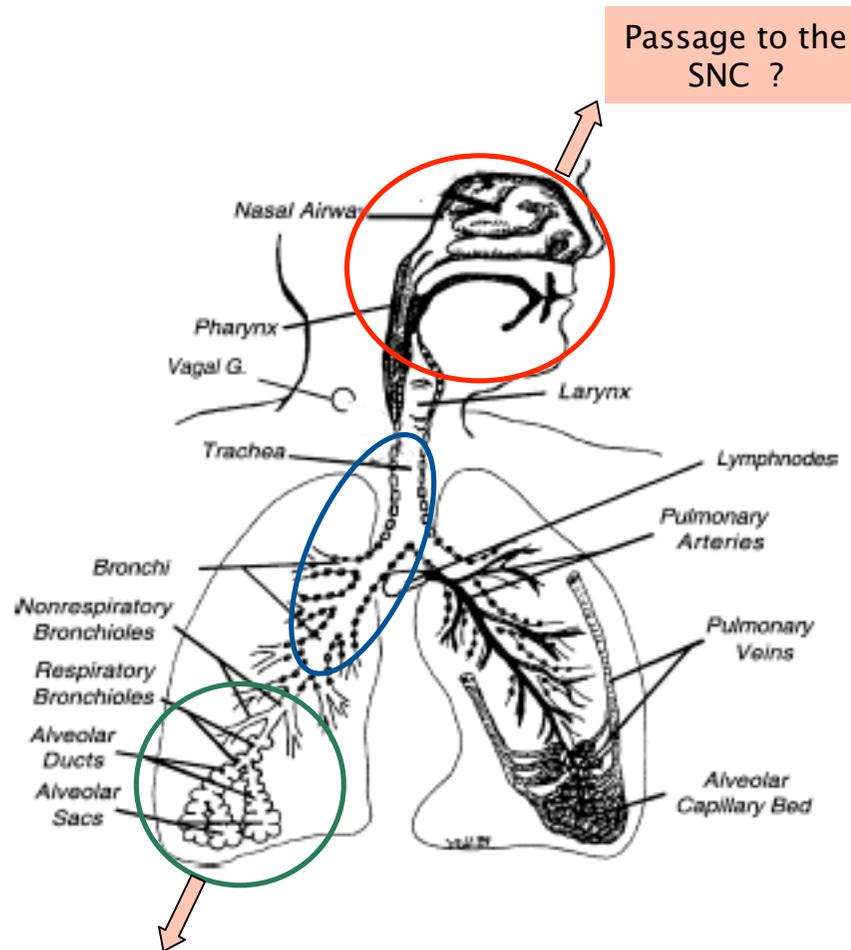
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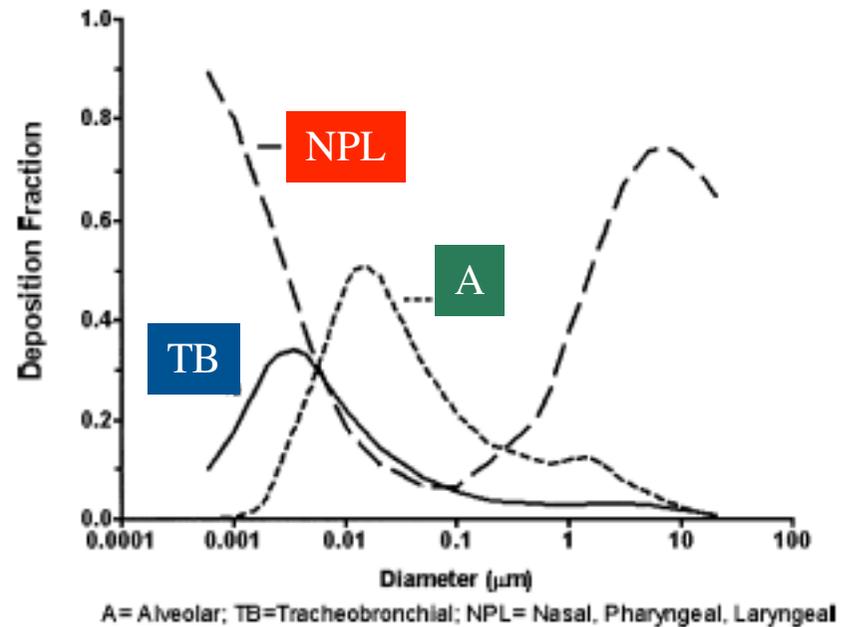
Respiratory exposure

Airways anatomy



Systemic translocation ?

Size of particles and site of deposition



The deposition site depends on :

- particle's size and shape,
- airways geometry, and
- ventilatory mode

Witschger O et Fabries JF. INRS, *Hygiène et sécurité au travail* , 2005
 Oberdorster G et al. *Inhal. Toxicol.* 2004, 16:437-445
 Borm PJ et al. *Partic Fiber Toxicol.* 2006, 3:11

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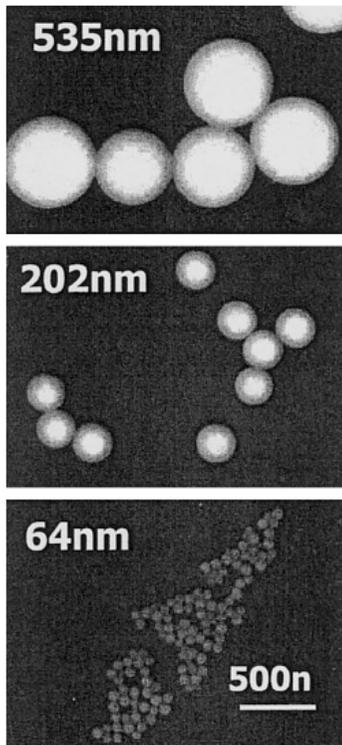
Factors concerning the nanomaterials

- **The size** : détermine
 - surface area,
 - cellular localization (internalization),
 - localization in the body (resp. system, skin),
 - pulmonary and central nervous system translocation

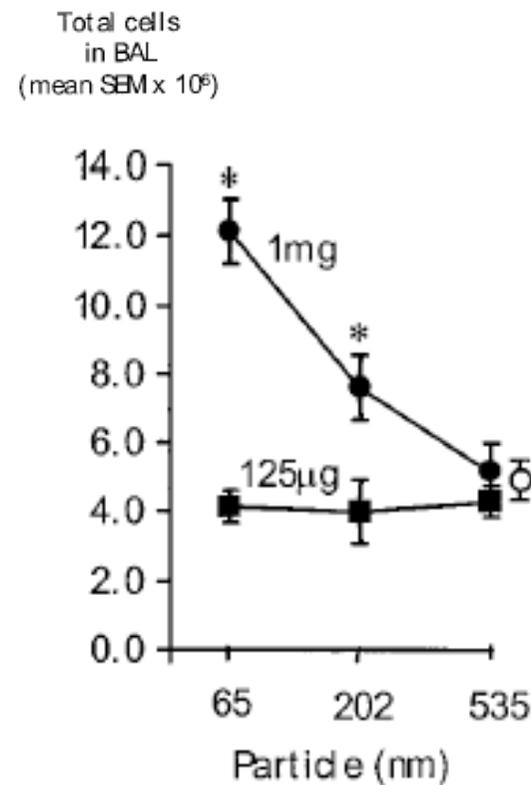
Particles size determines their inflammatory properties

Polystyrene particles, different diameters, IT instillation in rats. Animals examined at 24h.

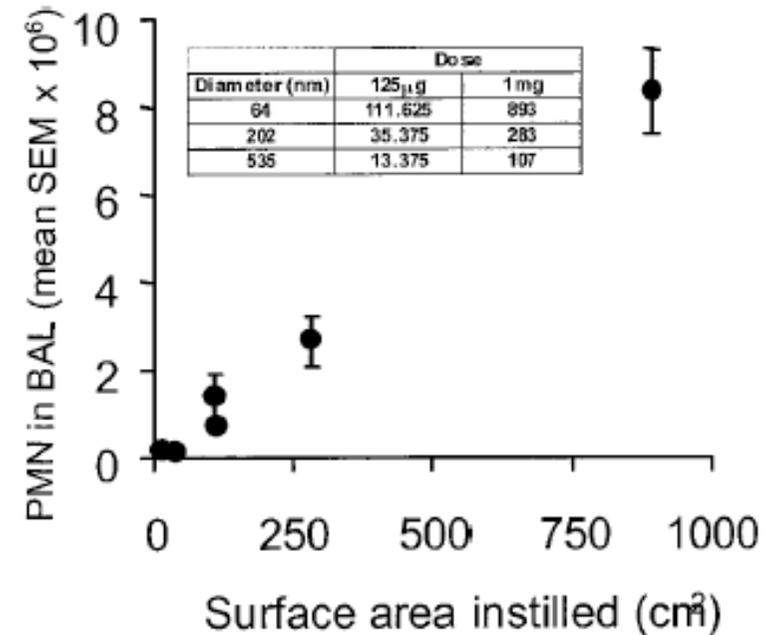
Particles



BAL inflammatory cellularity



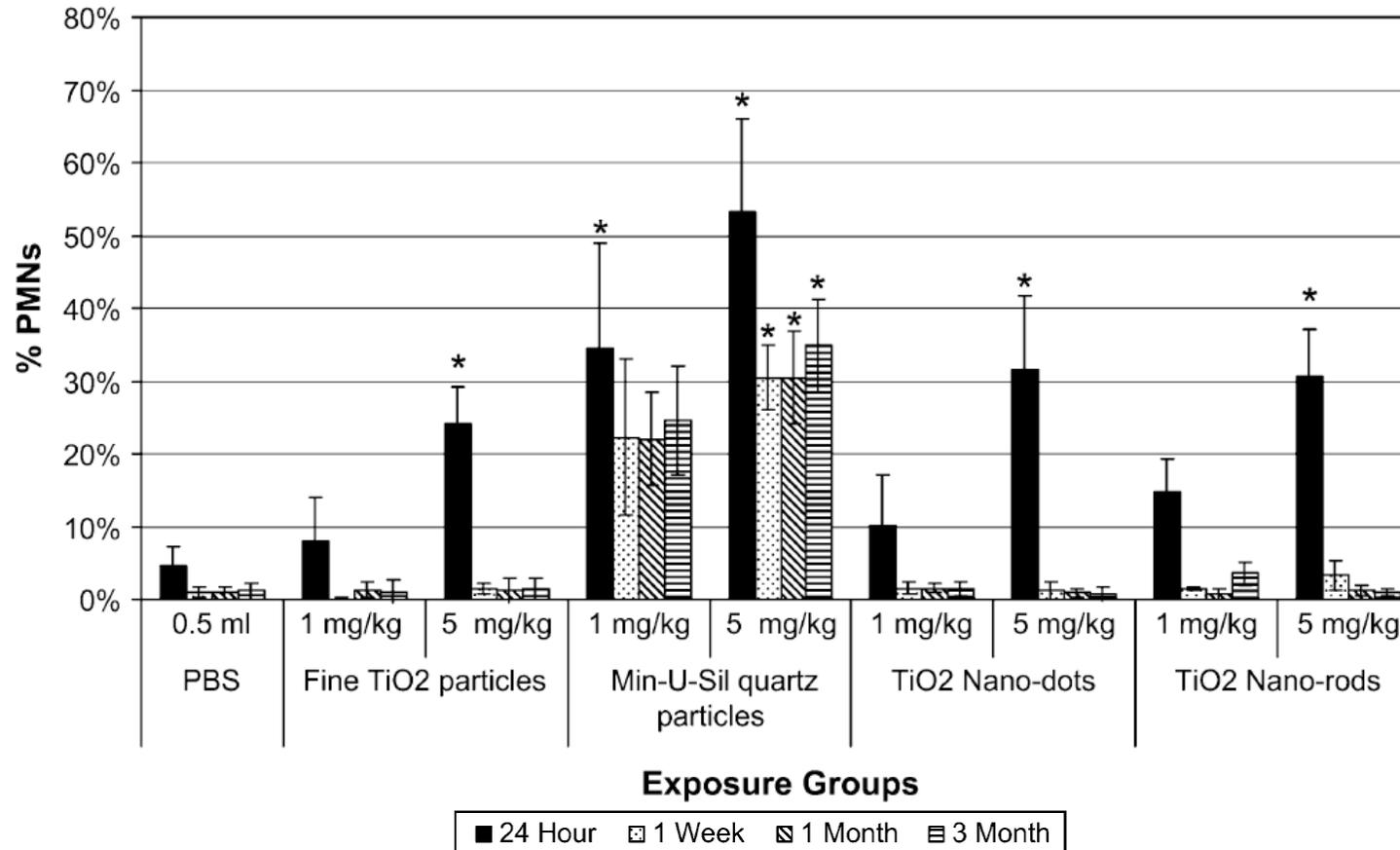
Inflammatory cellularity vs surface



But...other factors exist !!!

TiO₂ particles, IT instillation in rats. Animals examined à 24h.

Percent Neutrophils in BAL Fluids of Rats exposed to Fine and Nano-sized TiO₂ Particulates (Second Study)



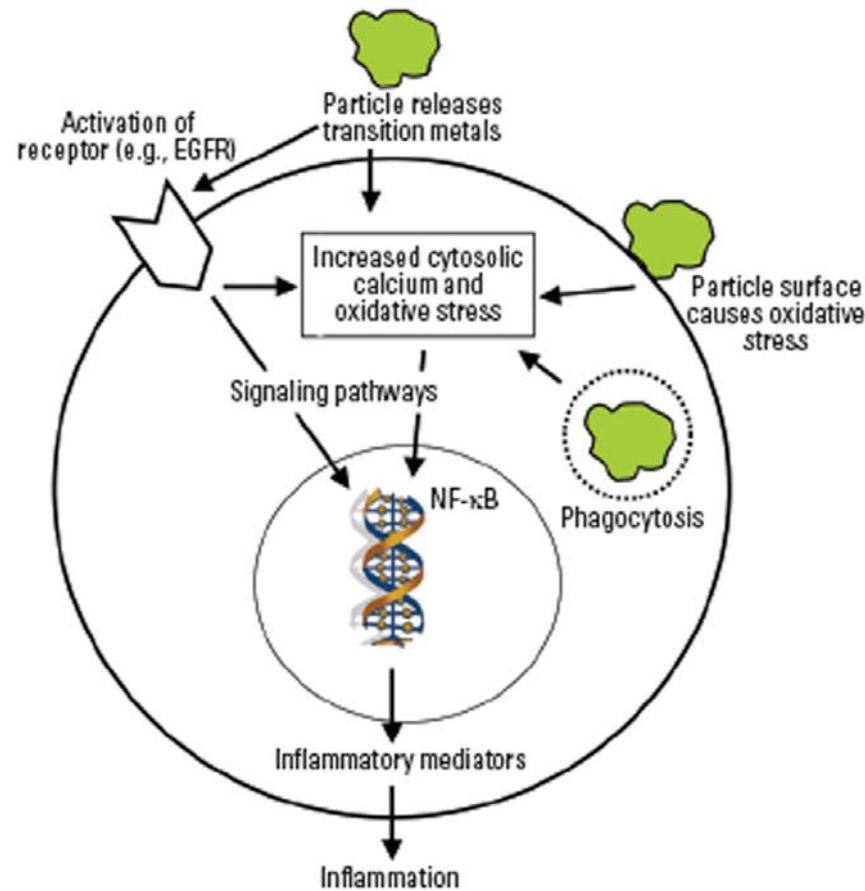
Determinants of the potential toxicologic effects of manufactured nanomaterials

Factors concerning the nanomaterials

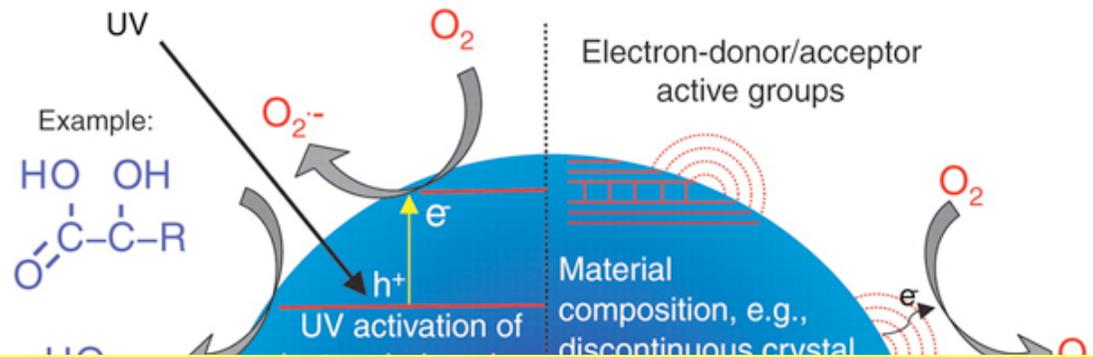
- **The size** : détermine
 - surface area,
 - cellular localization (internalization),
 - localization in the body (resp. system, skin),
 - pulmonary and central nervous system translocation
- **Surface phenomena** : area, reactivity, treatment ;
- **Chemical composition**, including transition metals and the capacity to generate reactive oxygen species ;
- **The shape** ;
- **Solubility** and the capacity to form aggregates and/or agglomerates and the shape of these aggregates/agglomerates
- **Charge** ;
- **Photoreactivity** ;
- **Cristaline structure** ;
- **The number** of particles ;
- and other parameters :
 - methods de fabrication and stockage ;
 - ageing of particles

Molecular mechanisms probably involved in the toxicological effects of nanomaterials

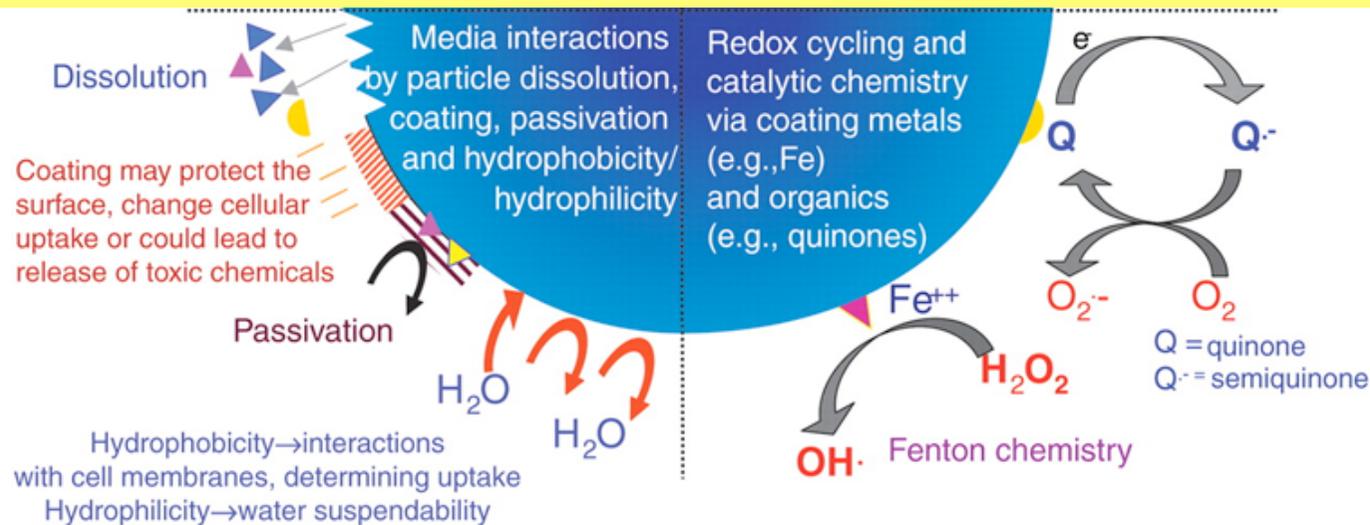
Oxidative stress and inflammation are the most frequently cited mechanisms



Molecular mechanisms involved in reactive oxygen species production



Utilization of the capacity of nanomaterials to produce reactive oxygen species as an indicator of potential toxicity ?



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PubMed data

Participants

Lyes Tabet, Cyril Bussy, Sophie Lanone, Jorge Boczkowski

INSERM U700

Ghislaine Lacroix

Ineris

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