Safer-by-Design strategies in GUIDEnano

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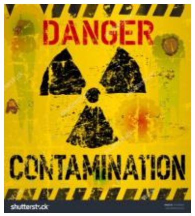
NANOSAFE 2016

Grenoble, 7-10 November

Safety by Design

Human learning: Trial-and-error approach + bad decision

Synthesis of product



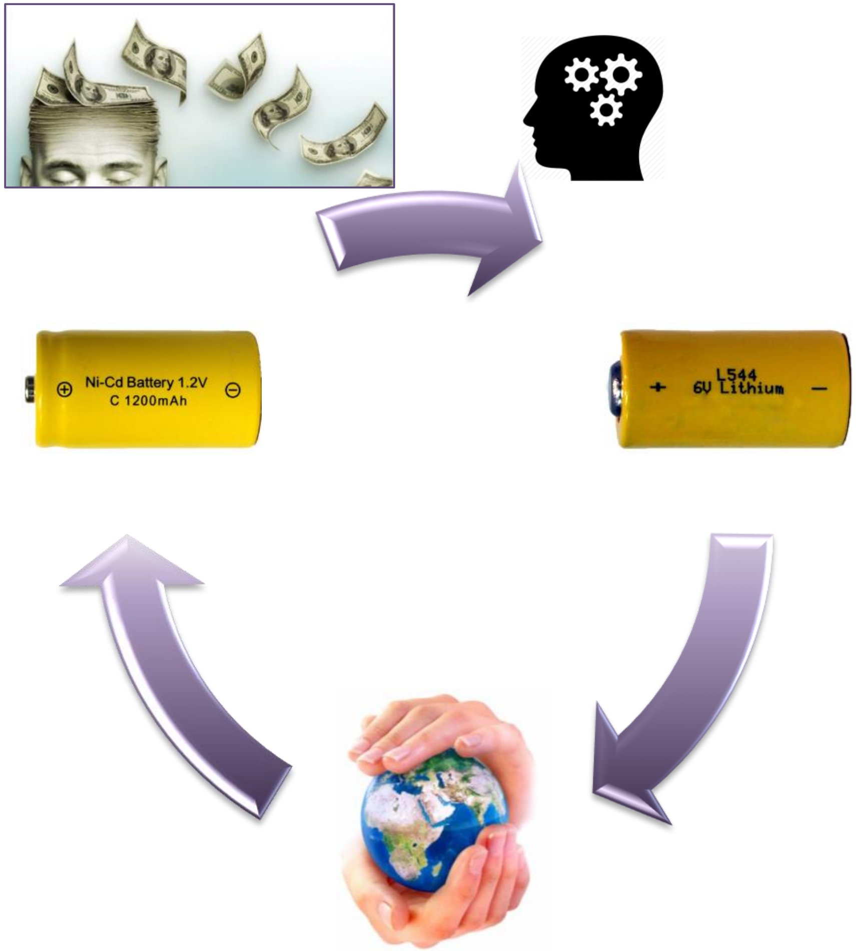
Toxic metals and environmentally unfriendly

Change the regulatory rules

Design safer product

Safety by Design

Synthesis of product with toxic metals and environmentally unfriendly



Design safer product

1. Safety is addressed at the design stage of a process or product rather than tested after their development
2. Not develop toxic technologies
3. Design or re-design protocols to avoid make mistakes

State of the art

FUTURE NANO NEEDS

GUIDEnano

nanoSAFE'16

BIO NANONET

NANoREG A common European approach to the regulatory testing of nanomaterials

NANOSOLUTIONS

NanoReg2

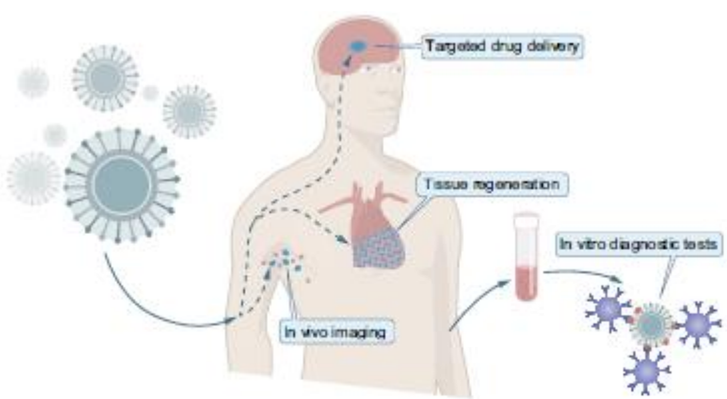
NanoFASE

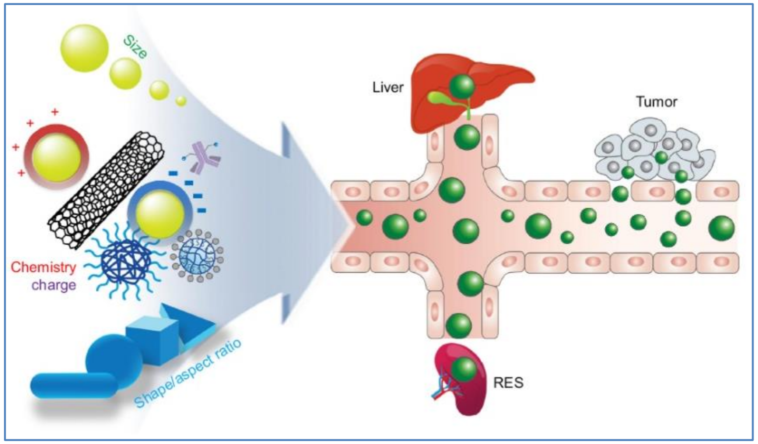
NanoMILE

nanopolytox

NanoSafety Cluster

Nanosafety: towards safer design of nanomedicines





Int. J. Nanomedicine. **2015**,10,3989-4008
Angew. Chem. Int. Ed. **2014**, 53,2-18
http://www.safenano.org

Safer by Design strategies

Developed to modulate the main factors determining safety of NMs:

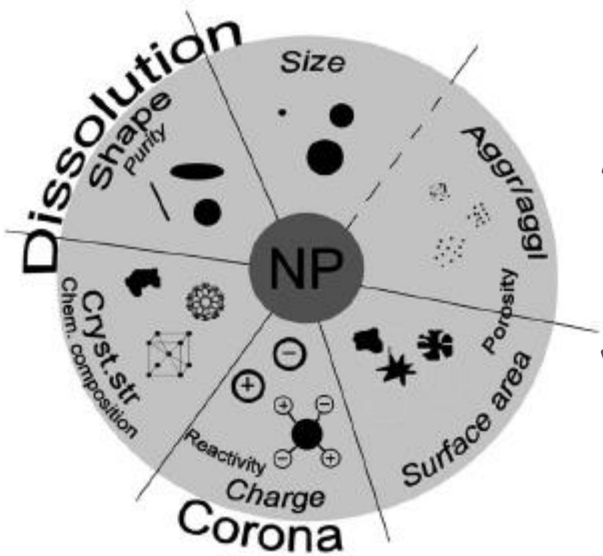
- Intrinsic toxicity
- Release/bioavailability potential
- Persistence

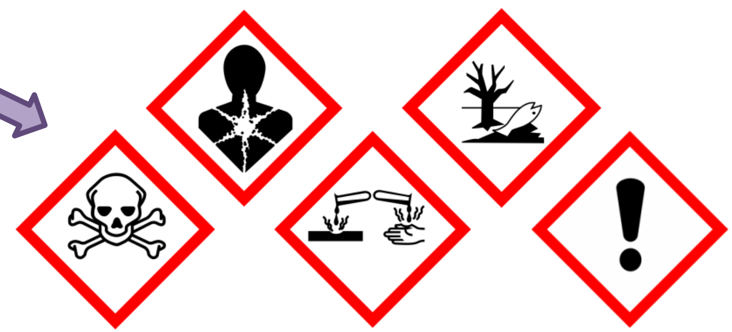
To reduce toxicity of NMs:
- **Shape** and **size** modifications
- Increase in **hydrophilicity** to decrease the potential to cross biological membranes
- Changing **oxidation state** to mitigate reactivity

To reduce release of NMs from their matrices:
- Induction of strong **Van der Waals** and **covalent bonding** between the NMs and their matrices
- Development of barriers by multilayer approaches (multilayer films) or **multicoating** approaches
- Self-healing pairs of NM/matrix by **ionic approach** to avoid release of NMs

To reduce persistence of NMs:
- Induction of self-assembly of NMs to increase the coalescent character of the NMs in **aqueous media** or at high temperatures to promote the **sintering** into microaggregates
- Development of **new** high **biodegradable** NMs under certain temperature or oxidative conditions

Physico-chemical Characteristics of NMs

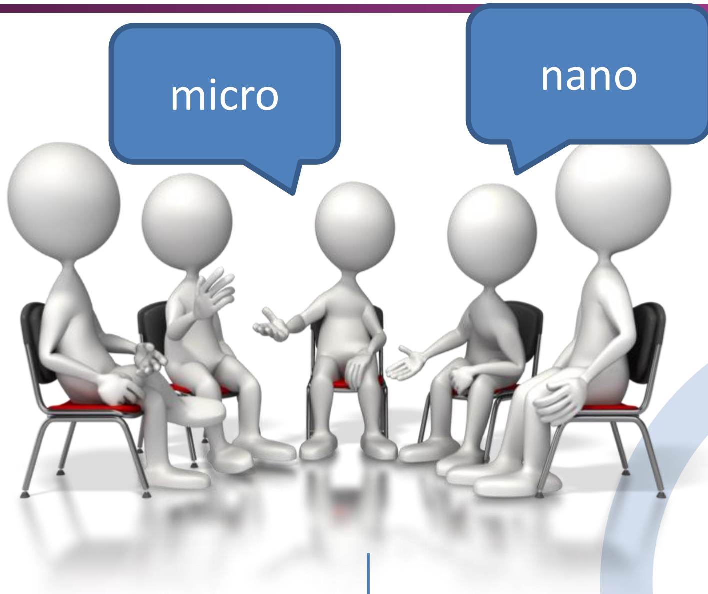




- Green Chemistry
- Design to avoid changes in the activity or properties
- Proper and extense physico-chemical characterization

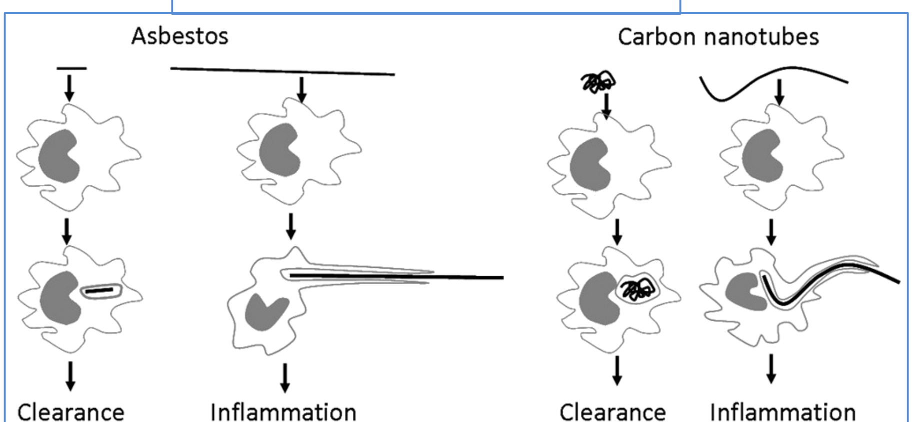
Environ. Sci.: Processes Impacts, **2013,** 15, 23

Reducing toxicity of NMs

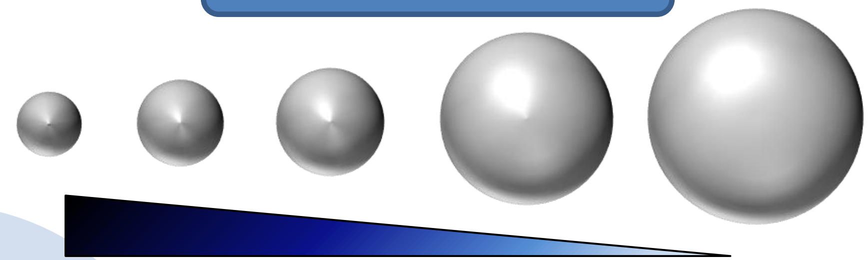


Size ≥ 10 µm

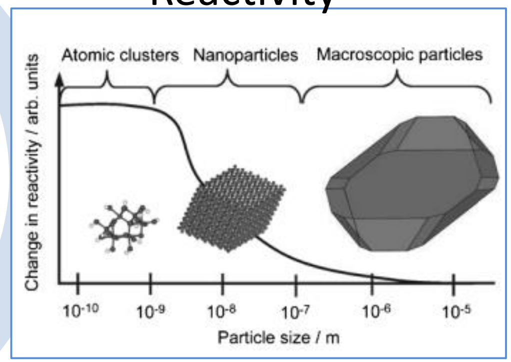
Frustrated phagocytosis



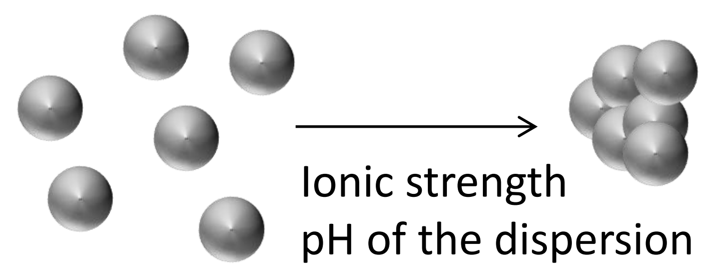
Size modifications



Reactivity



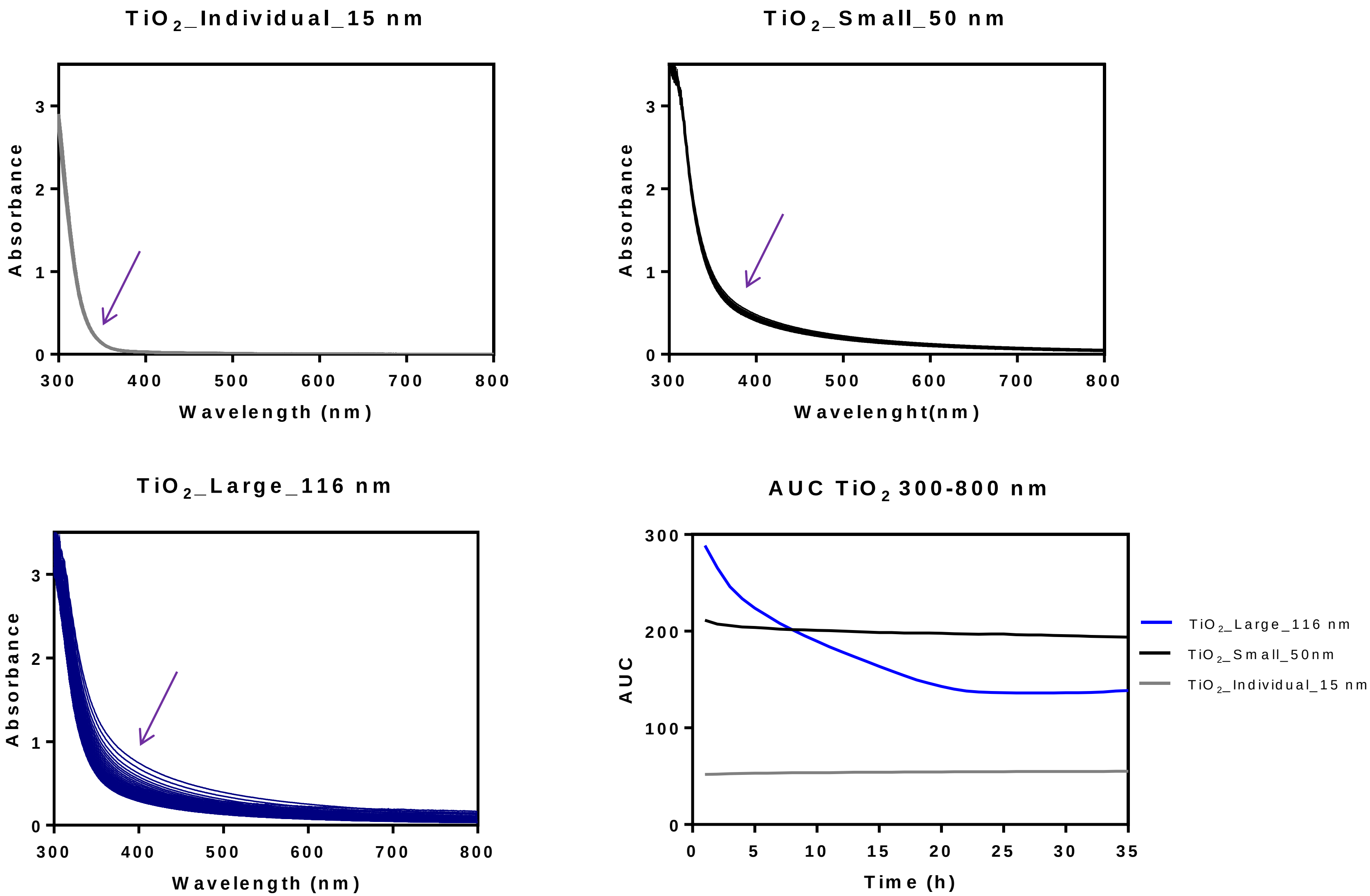
Control of Nanoparticle aggregation



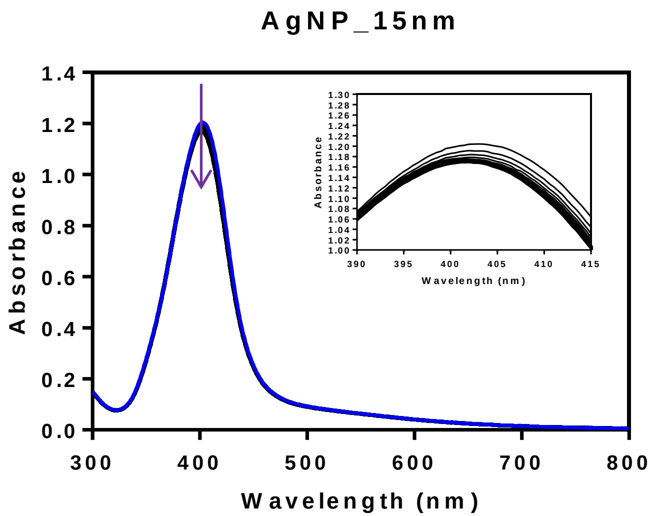
Ionic strength
pH of the dispersion
Surface charge

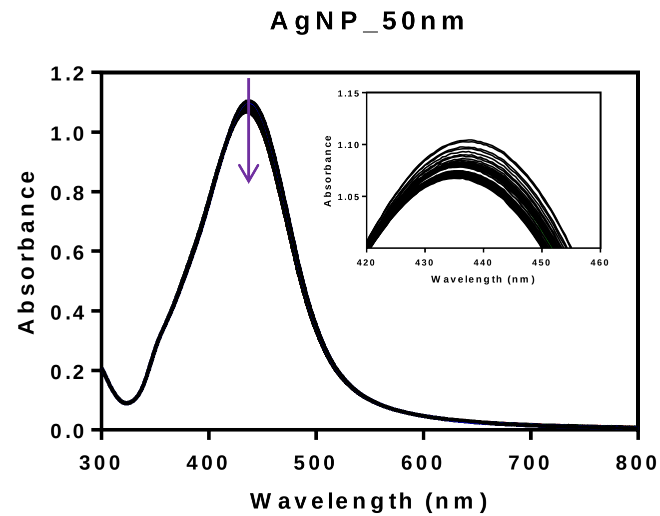
J. Environ. Sci. Health Part A, **2009**, 44, 1485–1495
Particle and Fibre Toxicology, **2010**, 7:5

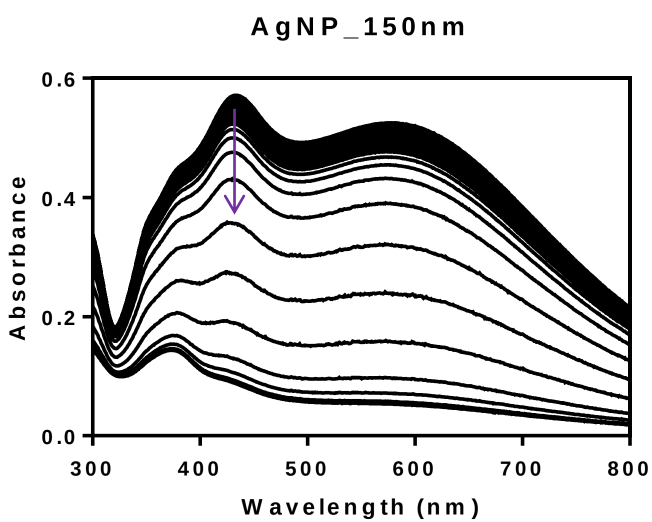
Sedimentation of TiO_2

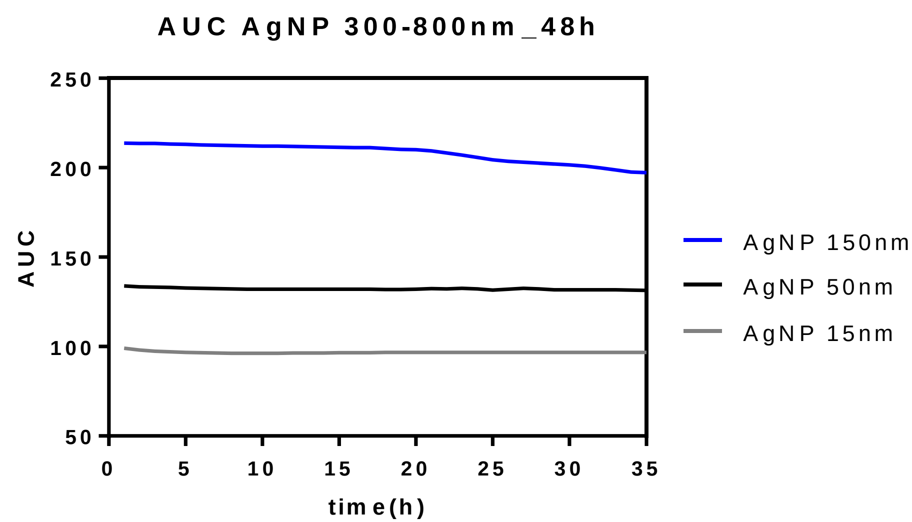


Sedimentation of Ag









Reducing release of NMs

Risk assessment: The release of NMs from their matrices. **Objective:** avoid the release of the NM or release as ions. **Procedure:** Protect the NP using polymer coatings (PVP)

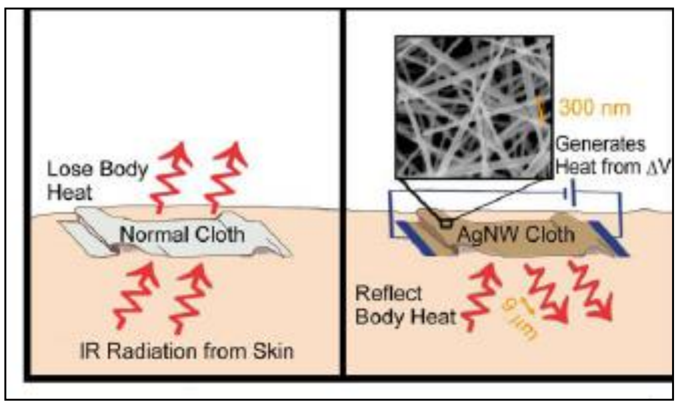
NANO LETTERS

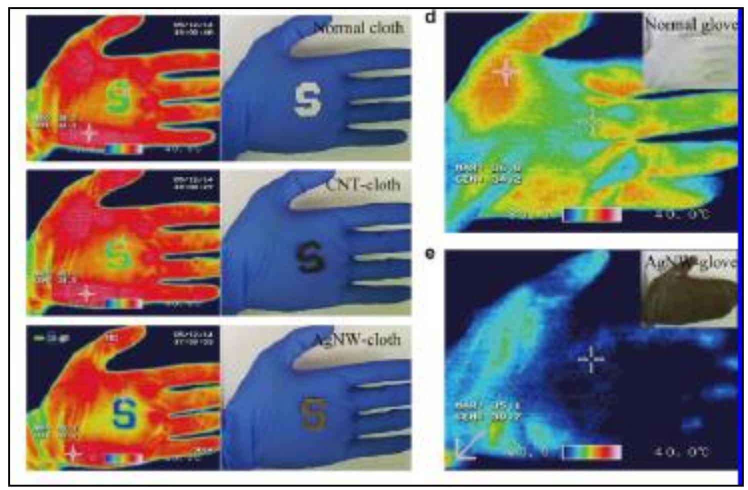
Letter

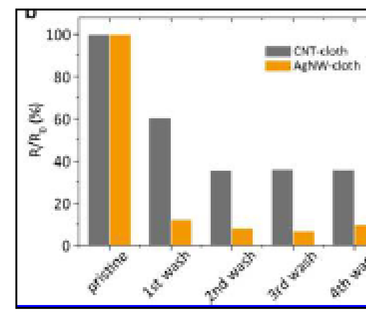
pubs.acs.org/NanoLett

Personal Thermal Management by Metallic Nanowire-Coated Textile

Po-Chun Hsu,[†] Xiaoge Liu,[‡] Chong Liu,[†] Xing Xie,[§] Hye Ryoung Lee,[∥] Alex J. Welch,[†] Tom Zhao,[†] and Yi Cui[*,†,⊥]







AgNW-cloth overall emissivity is much less than that of normal cloth and provides great insulation against radiative heat loss (higher IR reflectance and thermal insulation capability)

Nano Lett., **2015**, *15* (1), 365–371

Reducing release of NMs

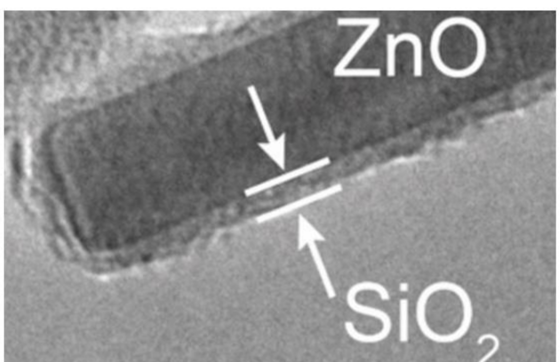
Risk assessment: The ion release is more toxic than the NP. **Objective:** avoid the degradation of the NM. **Procedure:** Protect the NP using coating ligands

Toxicology Letters 208 (2012) 286–292

Toxicity of silver nanoparticles—Nanoparticle or silver ion?

"Several studies have shown that AgNP suspensions are toxic. However, there have been no systematic studies, which analyze to which degree varying amounts of silver ions present in AgNP suspensions contribute to their toxicity"

Safer-by-design nanostructured materials



- ZnO NPs absorb UV wavelengths ranging from 280 to 400 nm (ideal component in cosmetic creams and sunscreens)

- Generation of reactive oxygen species (ROS) which led to DNA damage, cell viability reduction, and apoptosis (released ions and direct particle interactions with cells)

- SiO_2 shell exhibits less DNA damage in comparison to the uncoated ones

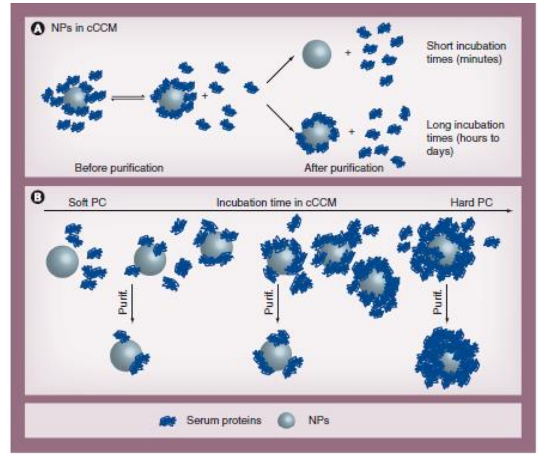
- Minimizing the ZnO nanoparticle dissolution and direct contact with the cells inhibiting toxicity

Environ Sci Nano., **2014,** 1(2), 144–153.

Reducing persistance of NMs

Controlling and monitoring the evolution of NMs

• The addition of protective agents to avoid the spontaneous transformation of NMs, for instance using albuminization strategy.

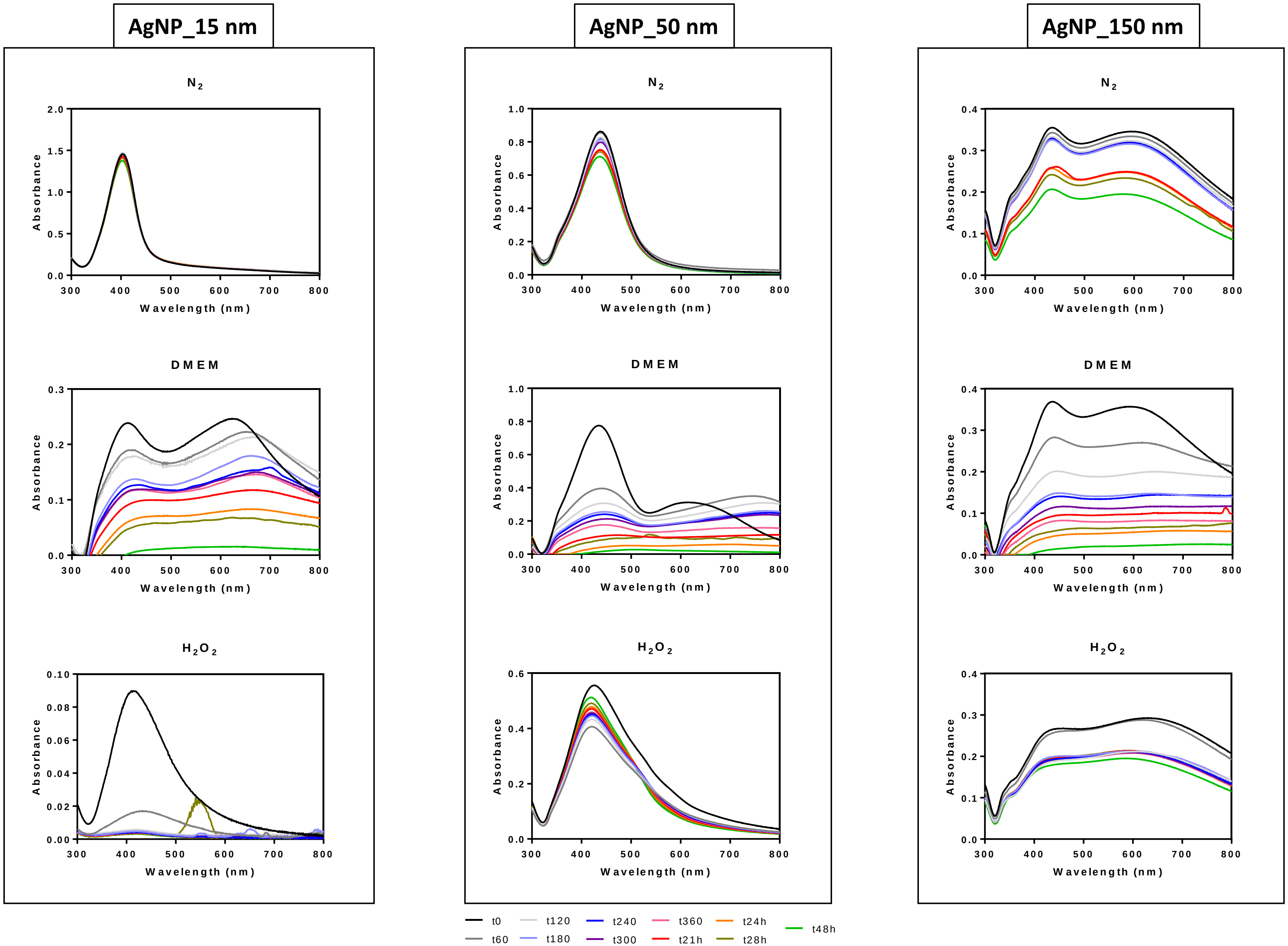


• Studying the transformation of NMs and their corresponding toxicity by changing the NM composition, such as Ag^+ and Ag_2S in the presence of S^{2-} ions.

Nature Nanotechnology, **2009,** 4, 546 – 547
J. Nanobiotechnol, **2015**, 13, 84

Corrosion of Ag

Development of biodegradable NMs under certain temperature or oxidative conditions



Conclusions

✓ **Safer** not Safe or safety by design

✓ **Proper** and extense **characterization** of NMs to obtain an optimal design

✓Controlling and monitoring our NMs **“from cradle to grave”**

✓ Controlling the size, shape, possible oxidation states during lifecycle….

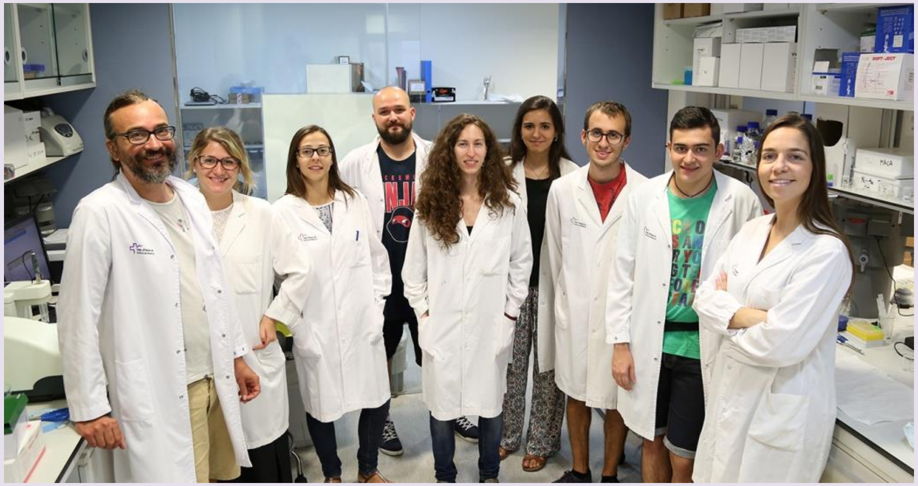
✓ Controlling the release of the NM from the solid/of the ions from the NM

✓ Controlling the persistance of NMs: transformation, corrosion,…

✓ Solid is a **friend**, aqueous solution is an **ally** but airborne is the **enemy**

✓ **Safety** aspects should inform about the design of a product or process at the **inception point**, along with other key concepts such as function, quality and cost

Acknowledgment



Design and Pharmacodynamic of Nanoparticles Group

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