Overview of Nanosafety in Europe 2015 – 2025

U.S. – EU Bridging nanoEHS research efforts: A Joint Workshop

Arlington, Virginia

Dec 2-3, 2013

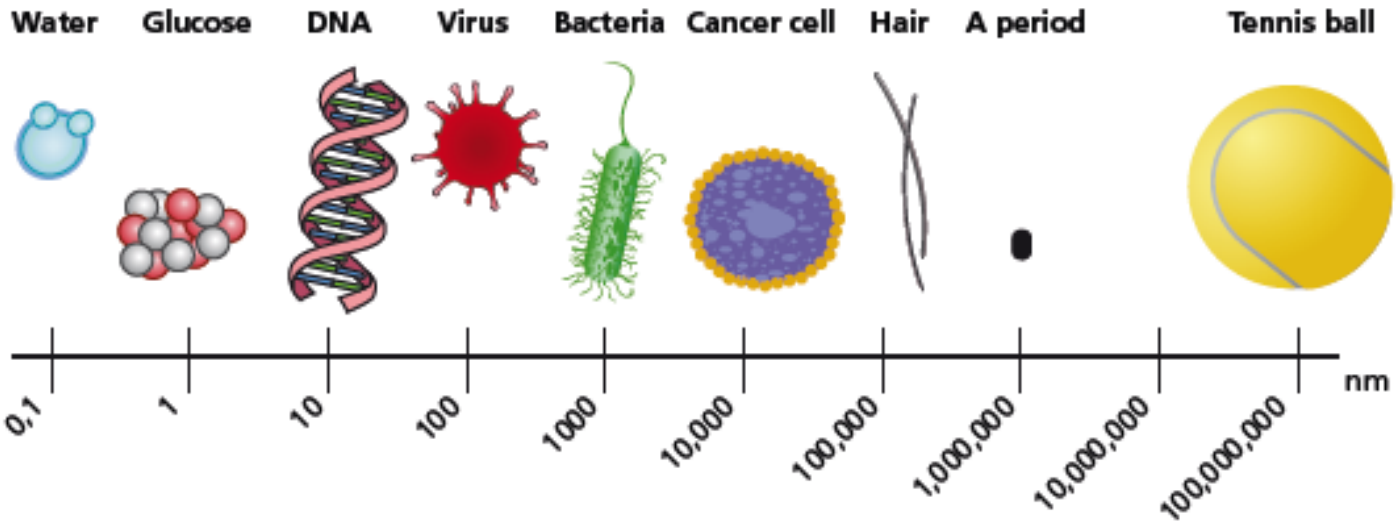
Kai Savolainen

Finnish Institute of Occupational Health

Nanosafety Research Centre

us – eu bridging nanoEHS research efforts

Size of objects in a nanometer scale



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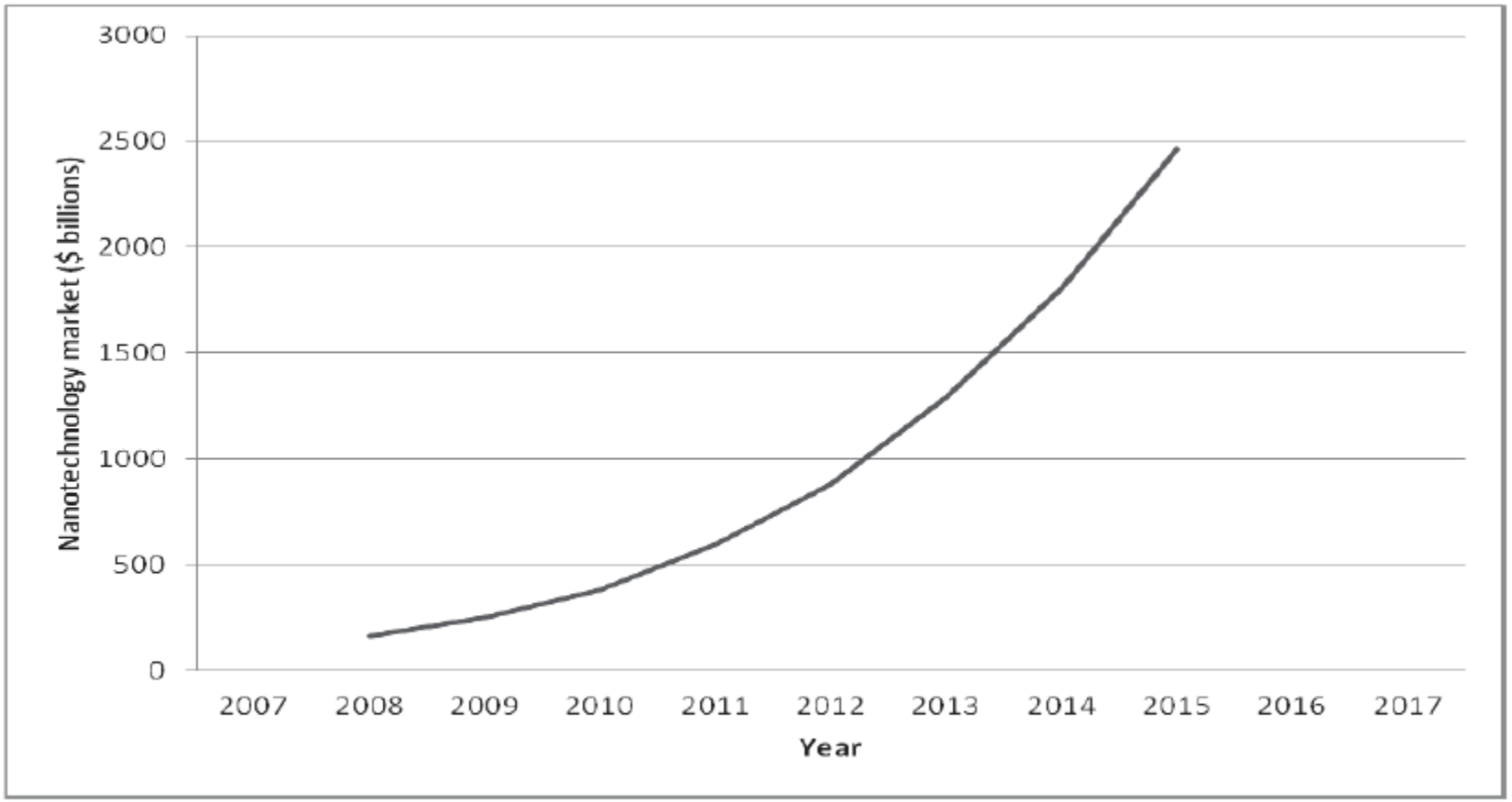

FIGURE 3-4 Projection of the size of the nanotechnology market. Source: Data from Lux 2009.

NRC 2012: A Research Strategy for Environmental, Health, and Safety Aspects of Engineered Nanomaterials

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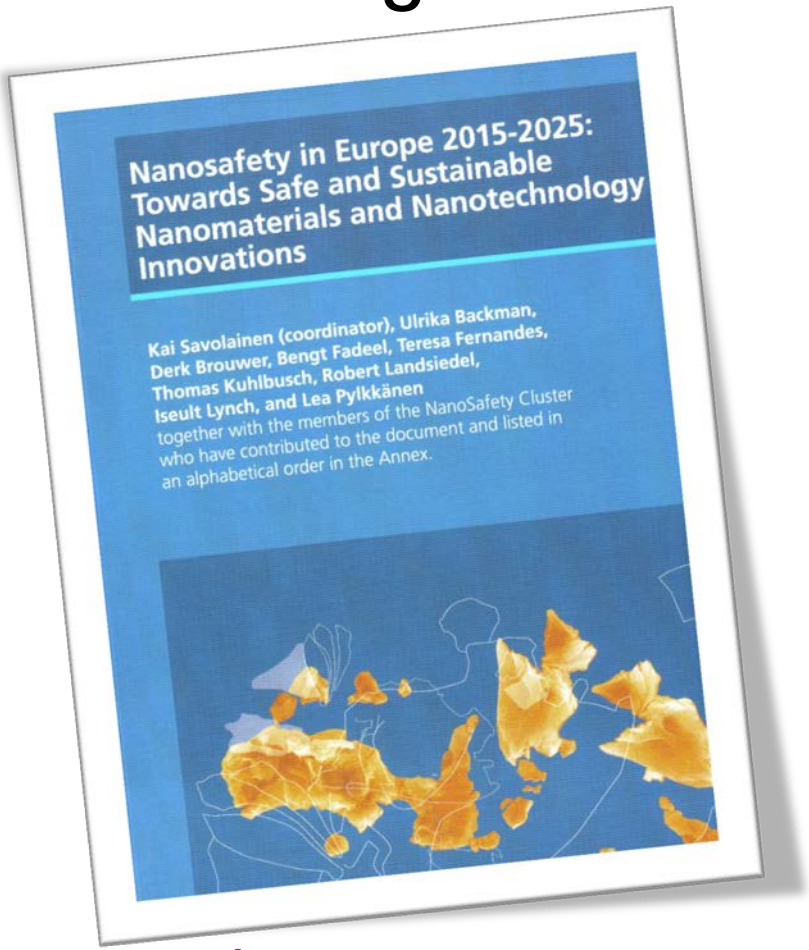
EU Nanosafety Cluster's Strategic Research Agenda Document



Research on ENM exposure & toxic mechanisms as well as research to develop tests serving regulations are in focus – the European approach is to merge these approaches

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Research of nanosafety, and regulation of their safe use in the EU

- European nanosafety scientists have pooled their resources by joining the NanoSafety Cluster (NSC) for better coordination and to reduce the duplication of work
- The EU Commission has supported the activity but the NSC is *a priori* a bottom-up activity to amplify research on nanosafety in projects
- Development of regulations is a top-down rather than a bottom-up issue organized in the EU currently under the NANOREG Project

Research of nanosafety in the EU and regulation of their safe use in EU

- NANOREG utilizes results of ongoing EU nanosafety projects, and supports the development new regulations by providing new data, SOPs and validated methods
- A European mega-trend is to develop the risk assessment process to become quicker, more affordable and less laborious with less steps
- NANOREG & the ongoing research projects enable continuation of the current approach, and enable developing novel RA concepts

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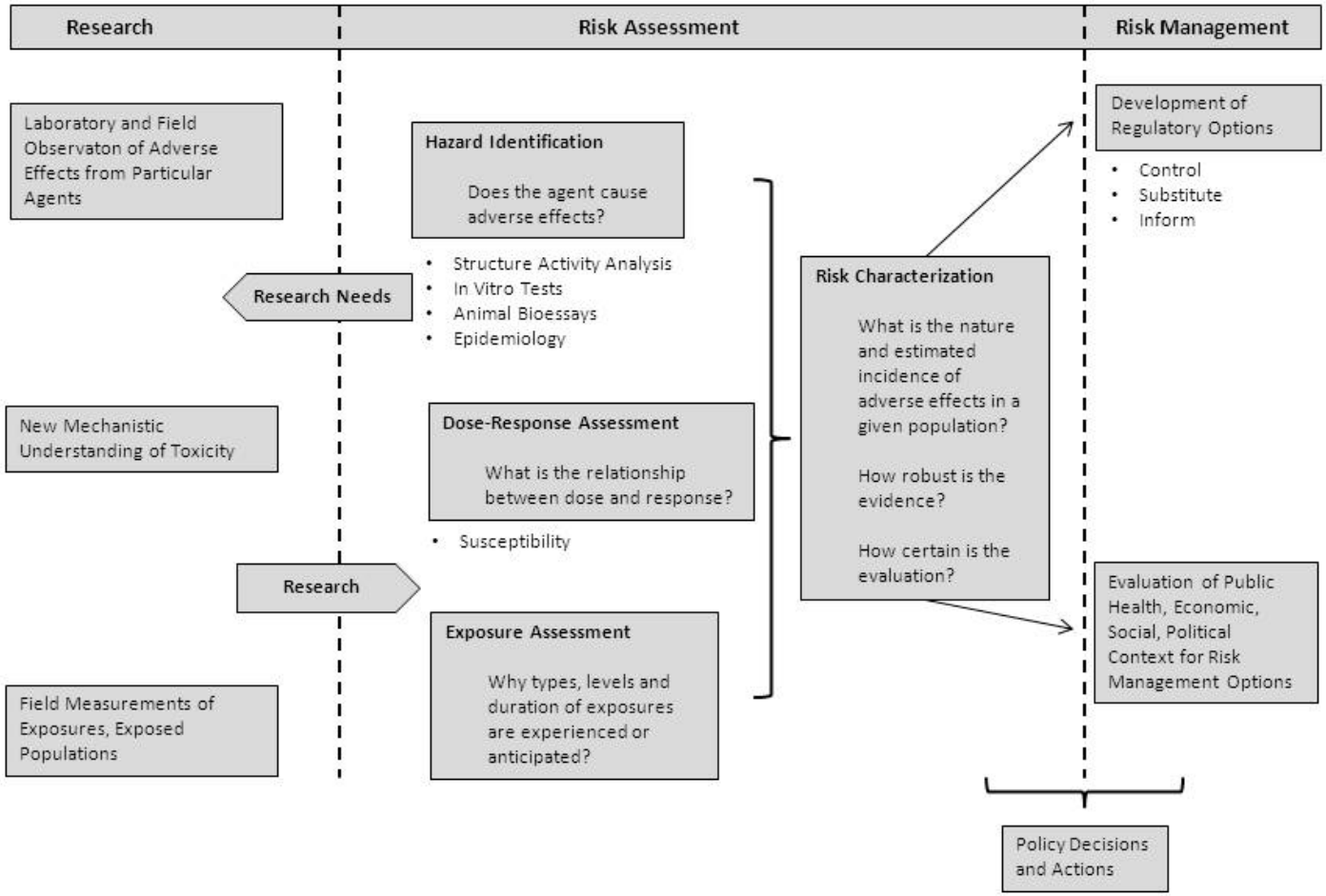
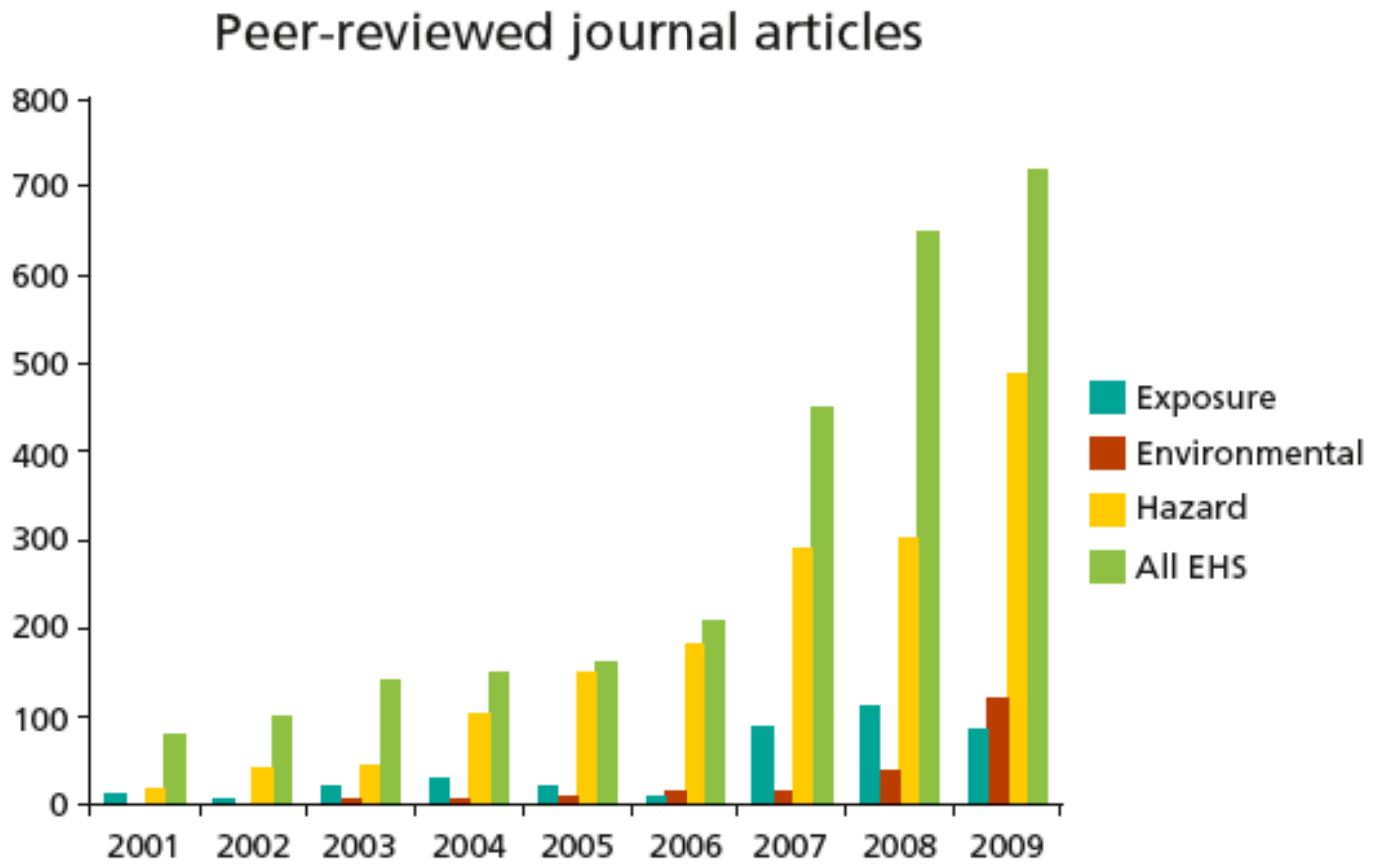
In the future, an affordable, quick and reliable risk assessment of engineered nanomaterials is required

- Current means to assess risks of engineered nanomaterials (ENM) tend to be increasingly obsolete, expensive, slow and their reliability (in the regulatory setting) has been questioned: this situation should be remedied as quickly as possible and resources put to it
- The existing ENM risk assessment (RA) paradigm relies on the one by the National Research Council in 1983 even though it has been amended several times over the years

Four key-steps of risk assessment



Systematic research supporting RA is lacking – important role for NANOREG for improving the situation



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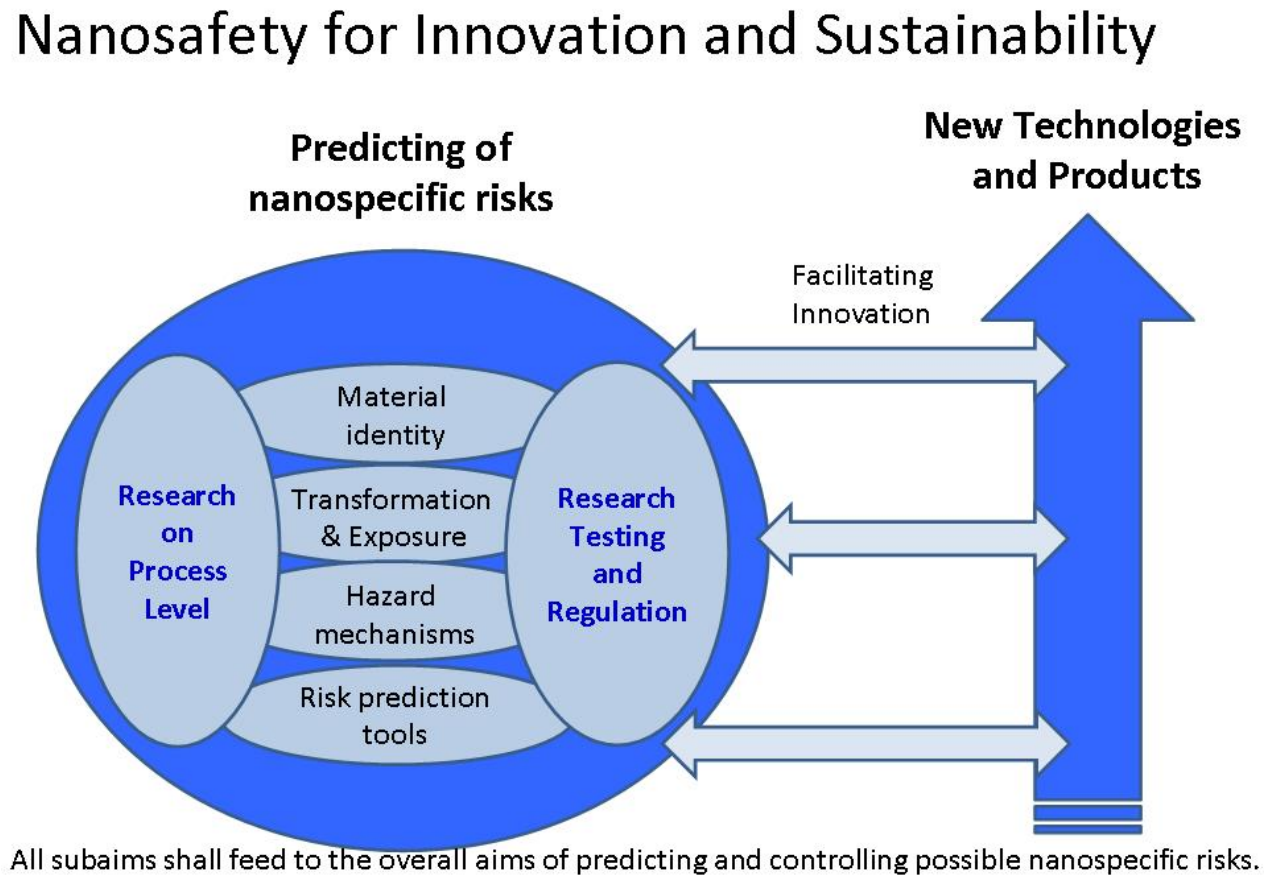
Proceeding towards knowledge on ENM toxicity and coming up with tests serving regulations and innovations



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Promoting nanotechnology innovations through reducing and preventing risks of ENM

- Safety research is critical for nanotechnology
- For successful nanotechnology, it is also important to create means to prevent unacceptable risks:
  - occupational exposure levels, ventilation solutions, PPE's, banning, labelling, classification – support modification of policies
- This also requires nanosafety (nanotoxicology) research illustrated on the previous slide
- Preventing of and dealing with unacceptable ENM risks is crucial to include in future projects

EU Nanosafety Cluster's Strategic Research Agenda: Contents

Main themes of EU funded nanosafety research

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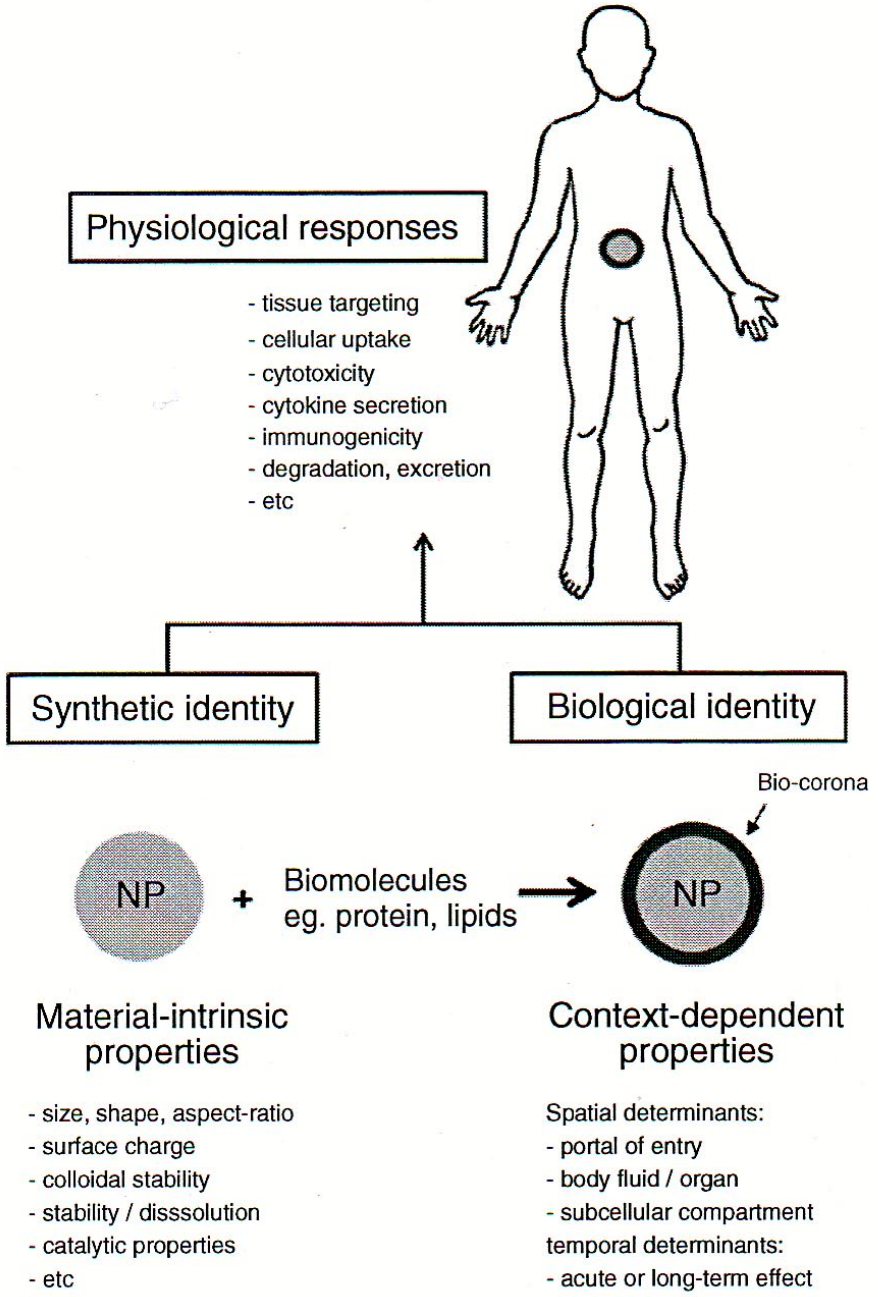
Engineered nanomaterials: Molecular interactions of ENM

- penetration of membranes and other biological barriers
- induction of nano-specific effects enabling ENM grouping
- understanding for a foundation for predictive material characteristic assessment
- developing models for both mammalian and environmental species

Synthetic and biological identities of nanomaterials

Fadeel B et al. Brigde over troubled waters: understanding the synthetic and biological identities of engineered nanomaterials. WIREs Nanomed Nanobiotechnol 2013, 5:111-129.



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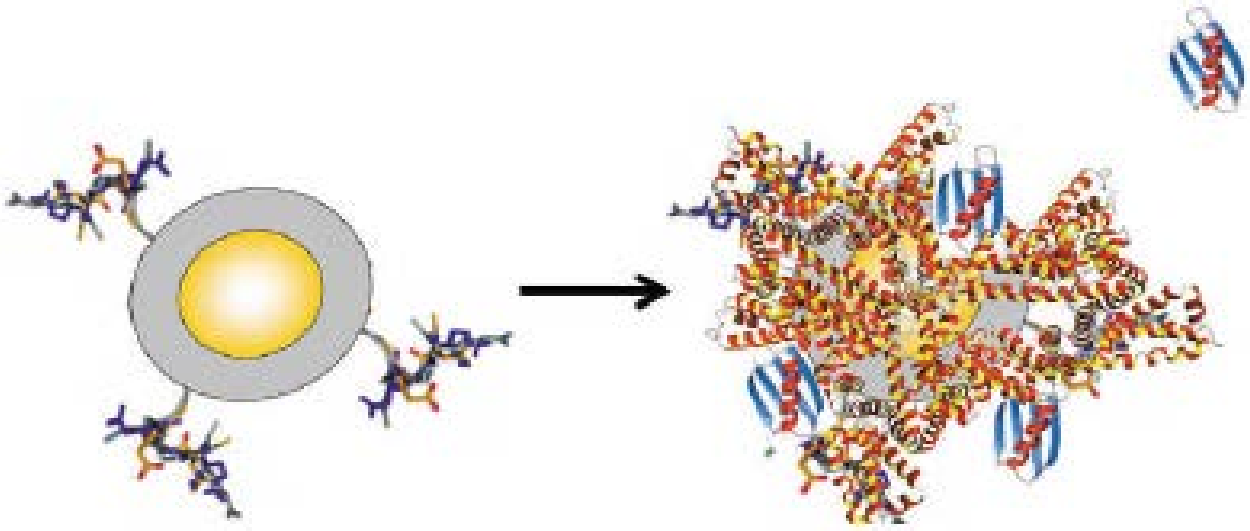
Nanomaterial characterization and nano-bio-interactions (Monopoli et al., Nature Nanotechnol., 2012)



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Grouping of nanomaterials is a crucial step to speed up ENM risk assessment

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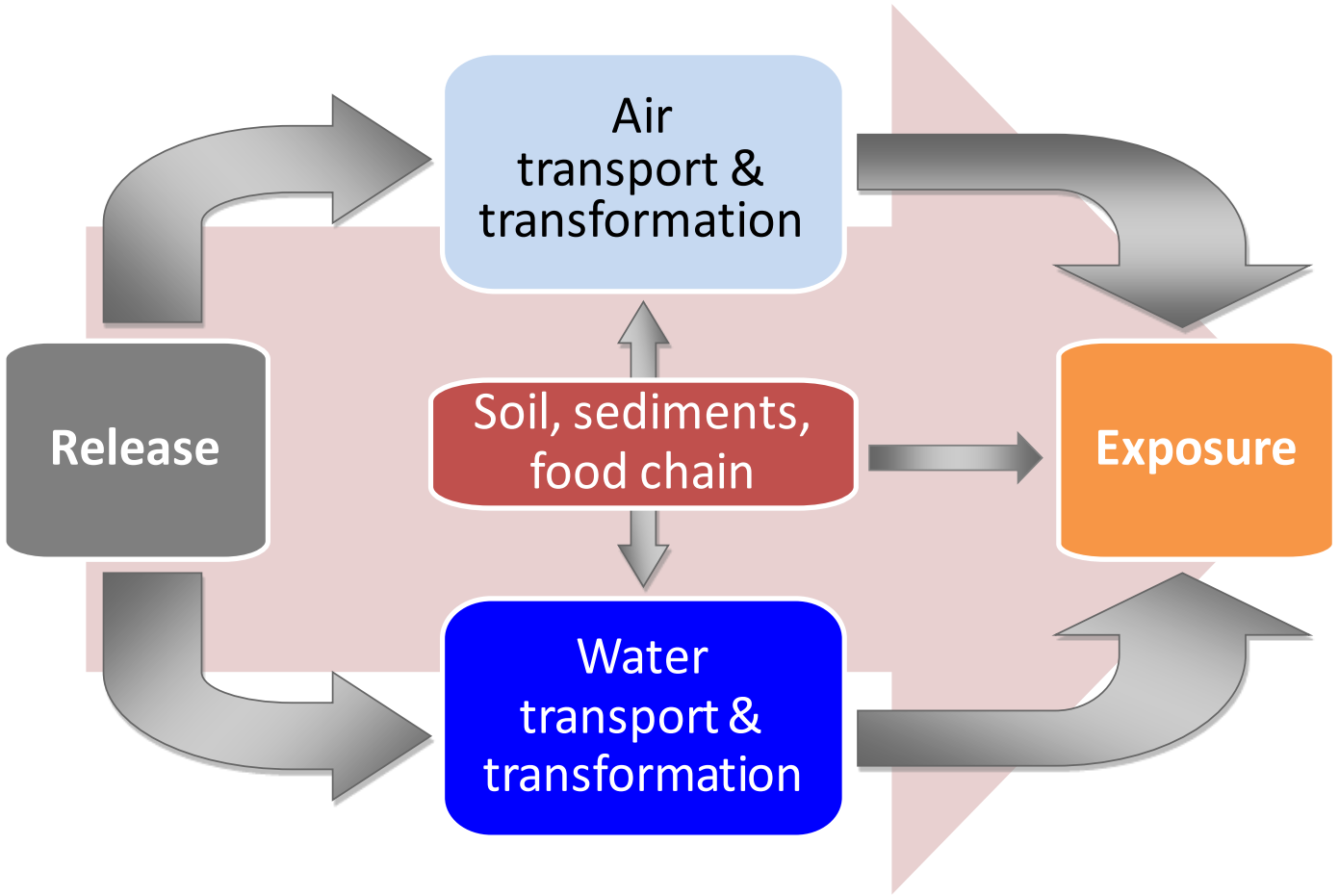
Nanomaterials from release to exposure



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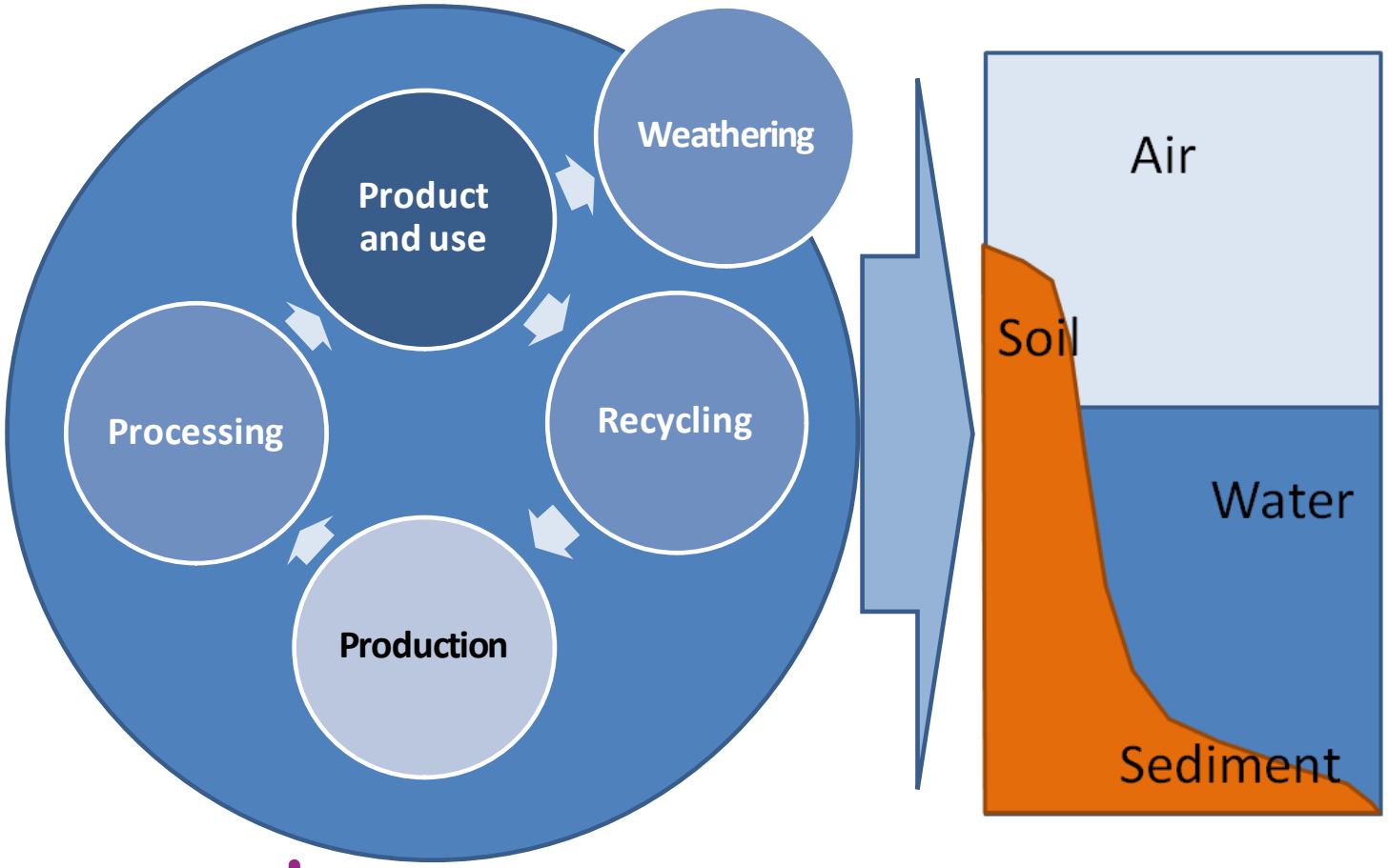
Nanomaterial life-cycle and release



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Transformation of ENM aerosol

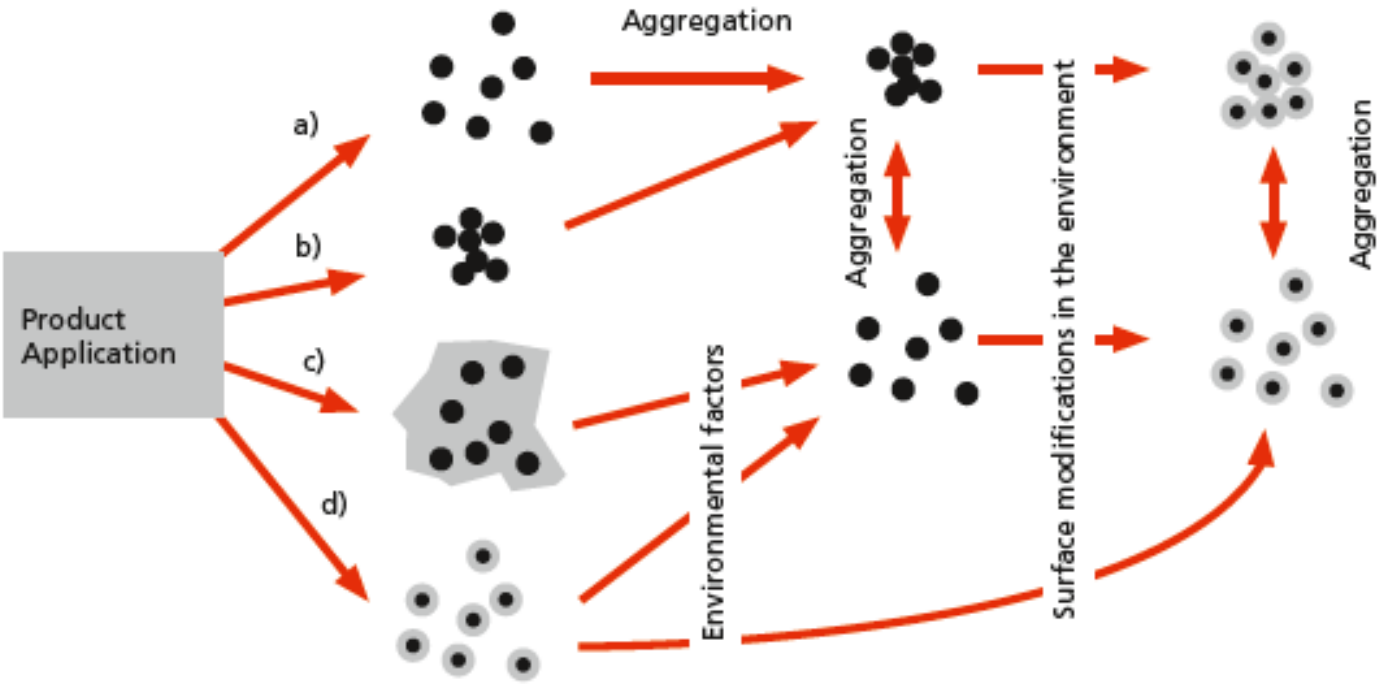

Figure 4.8. Release of nanoparticles (NP) a) as free NP; b) as aggregated NP; c) of NP bound in a matrix; d) as functionalised NP. Environmental factors influence agglomeration and deagglomerations (from Nowack & Bucheli, 2007).

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Assessment of exposure to ENM at a workplace

Figure 4.14.
Exposure assessment during liquid flame spray process
(Photo by Joonas Koivisto, FIOH)

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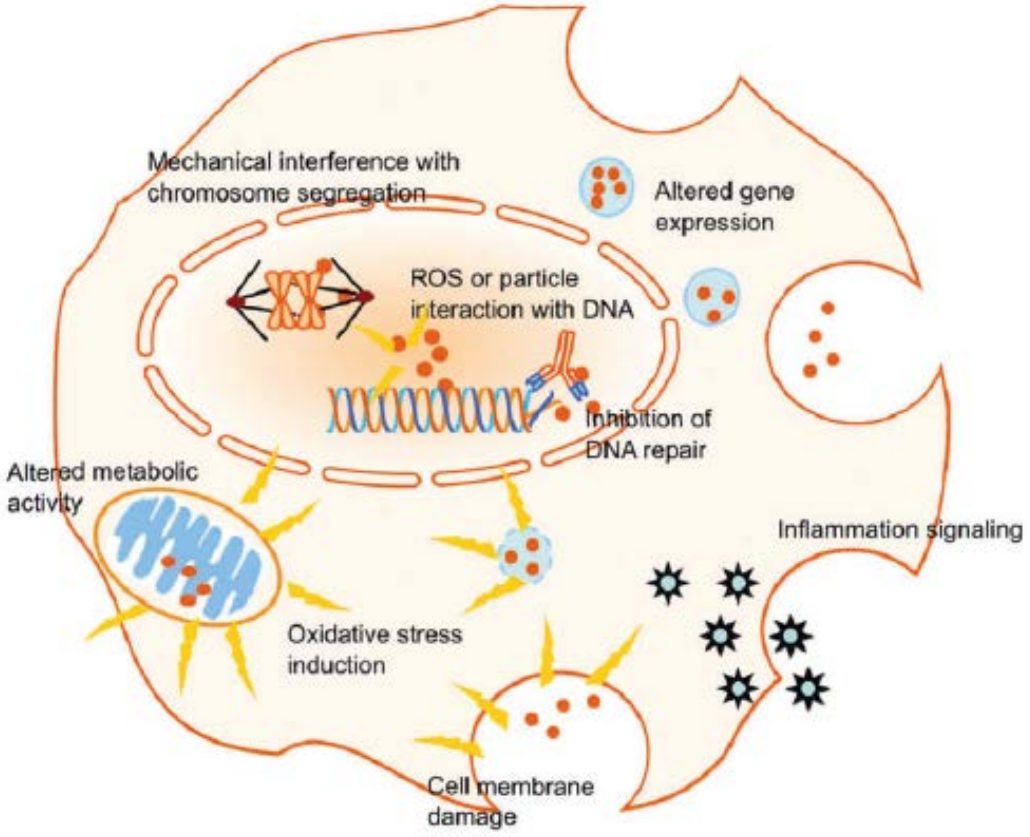
Interactions of ENM with living organisms – assessment of ENM hazards

Figure 4.9. Possible interactions of ENM with the cell and subcellular structures. (adapted from Colognato et al. 2012 with permission).



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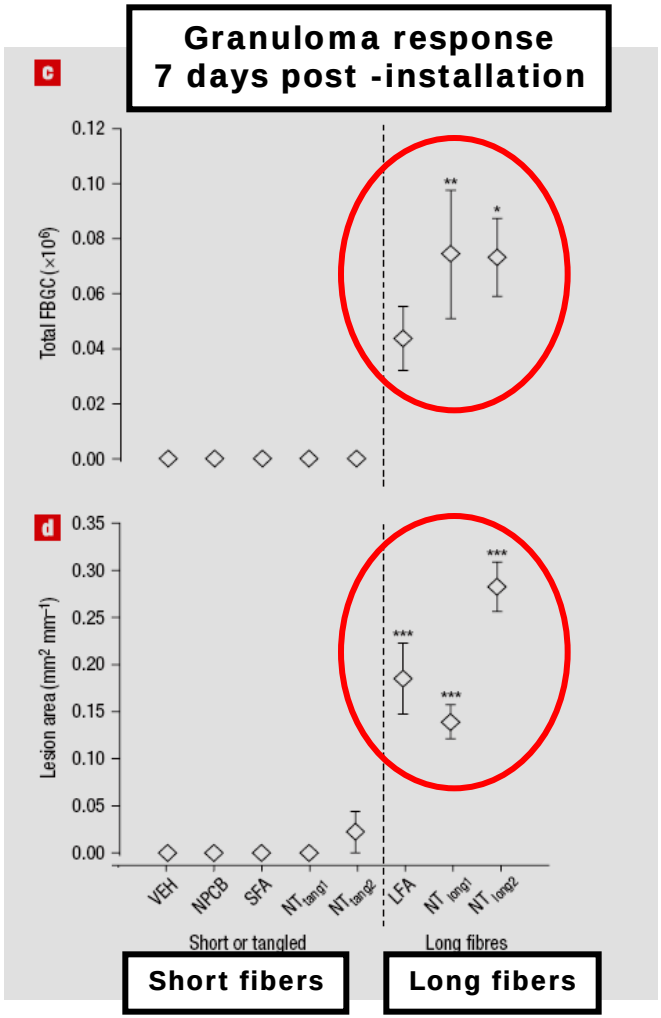
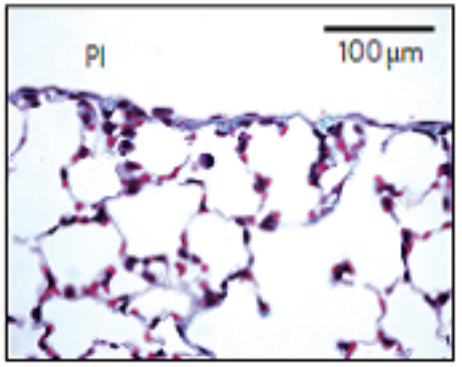
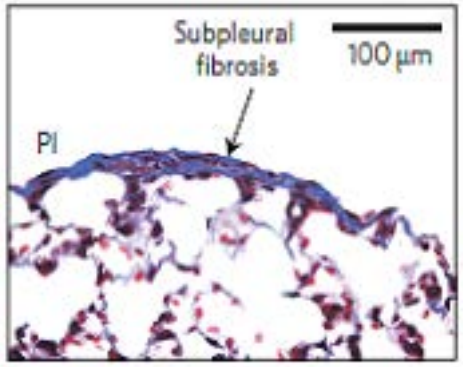
Granuloma formation and subpleural fibrosis after exposure to long rod-like CNT





saline aerosol-exposed

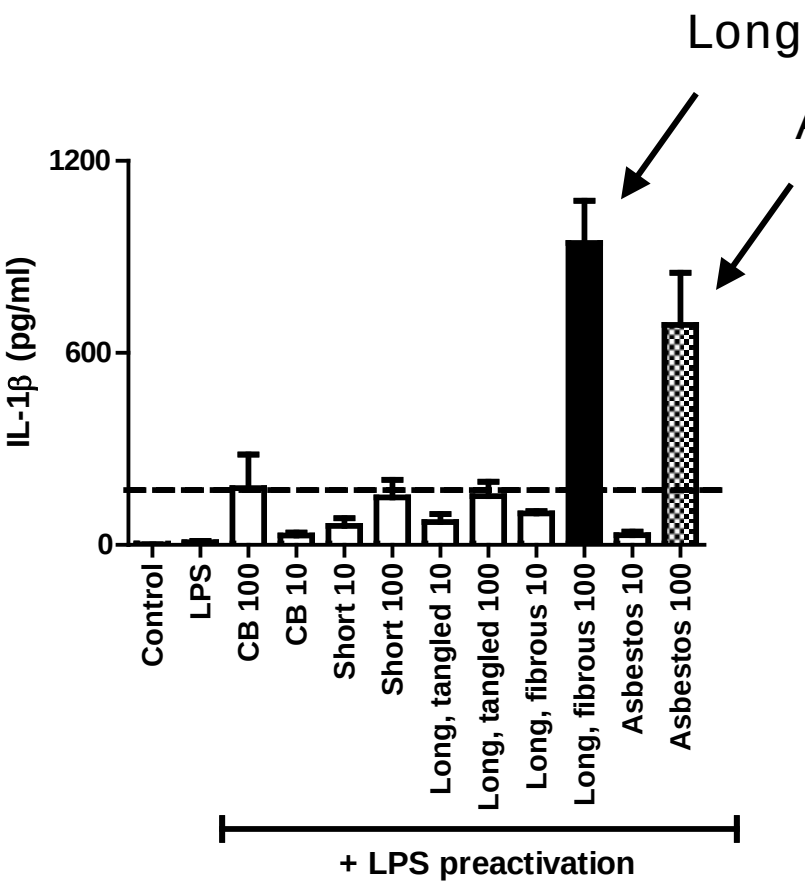


MWCNT exposed mice
2 weeks after inhalation

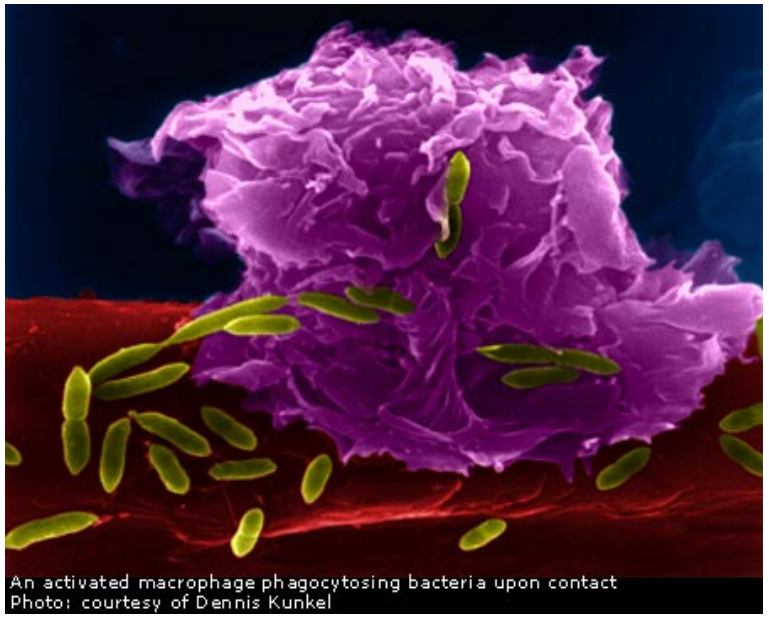
Poland et al. Nature Nanotechnology. 2008 Jul;3(7):423-8.

Ryman-Rasmussen et al. Nature Nanotech. 4(11):747-751 (2009)

Long, fibrous MWCNT induce IL-1β secretion primary macrophages



Monocyte derived macrophages



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Conclusions

- Fibrous CNT activates the NLRP3 inflammasome and induce robust secretion of IL-1β cytokine
- Mechanisms of fibrous CNT and asbestos fibers induced IL-1β secretion is identical

✓ **Concern about possible health effects of long fibrous CNT**

Risk assessment and management

- A goal is to develop predictive methods for predictive hazard assessment which together with exposure data enables predictive risk assessment
- Another goal is to develop nano-specific bio-indicators of exposure to enable workplace surveys and epidemiological studies to support risk assessment and management

Predicting ENM risks through predictive exposure assessment

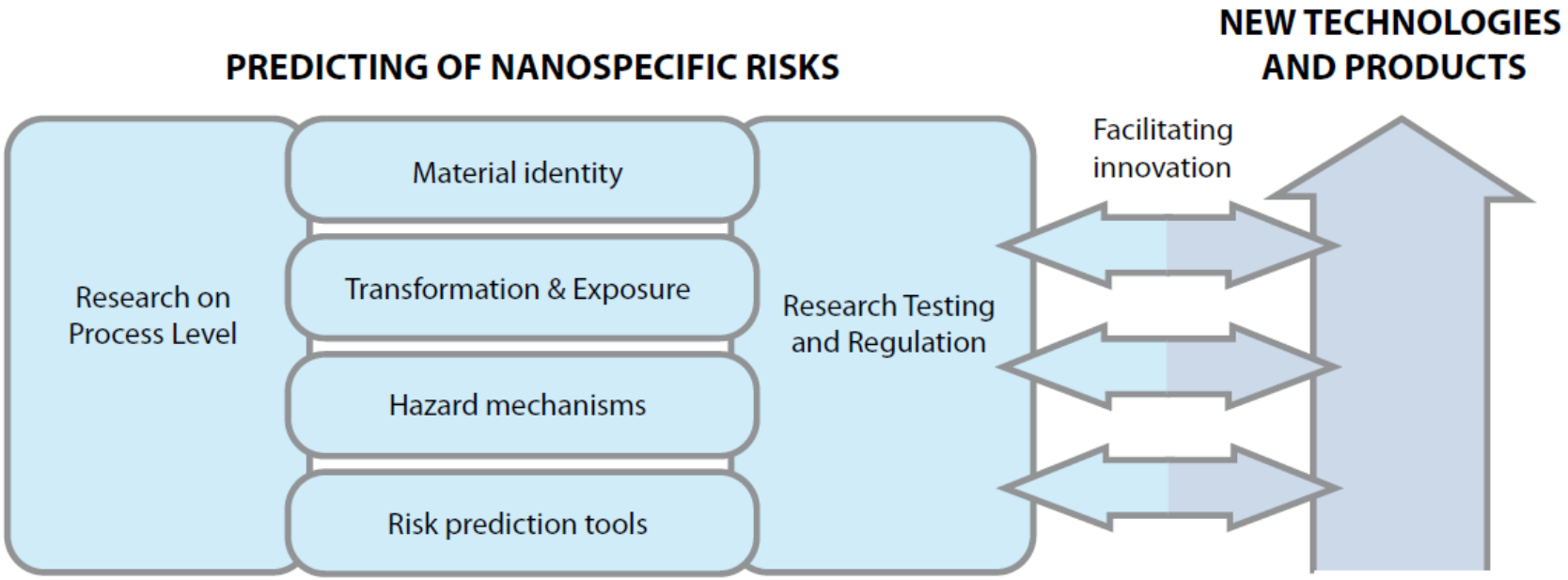
- Exposure indicators are useful when they predict harms of ENM
- For this, the associations between the synthetic identify and bio-identity of ENM and associated hazards have to be identified
- Understanding ENM in-depth could help to merge their exposure and hazard assessment

Requirements for affordable, reliable, quick & predictive risk assessment of ENM – fill the gaps

- Bio- & synthetic identity – role of corona
- Bio-kinetics – passing membranes
- Release, transformation, exposure
- Hazard mechanisms to group and classify
- Merging of exposure and hazard assessment
- Quicker, affordable and equally reliable risk assessment & management

Key challenges to promote the safety of ENM and nanotechnologies: Themes for the future

Nanosafety for Innovation and Sustainability



All subaims shall feed to the overall aims of predicting and controlling possible nanospecific risks.

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Translation of mechanistic hypothesis-driven research into RA-driven research

- Including regulatory and innovation-driven issues on board of research projects with a space for creative and wild ideas
- Systematic building of hazard- and exposure-related databases to support building of regulations
- Effective use of validated methods based on omics technologies, systems biology and bioinformatics to speed up RA

SENN2015

International Congress
on Safety of Engineered
Nanoparticles
and Nanotechnologies
12-15 April 2015,
Helsinki, Finland

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The Congress is organized by the
Finnish Institute of Occupational Health

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