

2016-09

# Innovation and model organisms for the environmental hazard assessment of engineered nanomaterials

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<http://hdl.handle.net/10026.1/10550>

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10.1016/j.toxlet.2016.06.1192

Toxicology Letters

Elsevier BV

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lays now in the development of predictive methods for the assessment of nanomaterial hazards and risks. Even though no definite solutions so far are available, the current attempts focus on the generation of validated in vitro methods with the potential for long-term hazard assessment of well characterized and carefully grouped ENM in which organ-on-a-chip and in vitro models validated by using in vivo models, and consequent use of in silico methods are crucial.

Supported by EU FP7 NANOSOLUTIONS Project.

<http://dx.doi.org/10.1016/j.toxlet.2016.06.1190>

### S06-2 Immunotoxic and pulmonary effects of engineered nanomaterials



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Engineered nanomaterials (ENM) have characteristics that are unique to material offering numerous possibilities to improve the properties of old products and create completely new ones. The rapidly expanding use of ENM will bring hundreds of millions of people in contact with ENM during the next few years. Due to the worldwide use of nanotechnologies, it is crucial to acquire up-to-date knowledge on health effects to avoid any potential risks.

Some of the properties that make ENM so unique and beneficial for technological applications may also endanger human health through the potential induction of cytotoxicity, inflammation and even cancer. These features include a large surface area to mass ratio, increased surface reactivity, altered physico-chemical properties, electrical conductivity, or changes in the crystalline structure of the ENM.

Evidence already exists that exposure to certain type of ENM elicit adverse health effects in experimental models, thus justifying the precautionary approach in assessing risks of ENM. Such effects include the ENM induced pulmonary inflammation in experimental animals. In addition, recent observations reveal that needle-like fibrous CNT may induce asbestos-like granuloma formation and increase the likelihood of mesotheliomas in tumor prone mouse strain. In addition to healthy individuals, a large part of the population has impaired health conditions that may make them more susceptible to develop health problems from ENM exposure.

In this presentation recent understanding on the immunotoxic and pulmonary effects of ENM will be discussed. It will be also discussed how exposure to ENM affects on vulnerary population such as patients with allergic diseases.

<http://dx.doi.org/10.1016/j.toxlet.2016.06.1191>

### S06-3 Innovation and model organisms for the environmental hazard assessment of engineered nanomaterials



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The utility of standard ecotoxicity tests for the hazard assessment of engineered nanomaterials (ENMs) has been discussed, with recommended modifications to the tests. ENMs have provided the opportunity to take a fresh look at the testing strategy,

novel organisms and innovative approaches for hazard assessment. Information on ecotoxicity is currently biased towards standard OECD test organisms (e.g., algae, *Daphnia*, zebrafish), with data lacking on many other organisms. The key practical challenges for environmental hazard assessment include: (i) developing screening methods to manage the large number of potential ENMs; (ii) providing new endpoints that can inform on the relationship between ENM physico-chemistry and ecotoxicity; (iii) identifying ecologically sensitive organisms; and (iv) facilitating predictive toxicology for future innovations. Several screening approaches are proving useful including the Minimum Inhibitory Concentration (MIC) assay with *E. coli* and a revised fish early life stage test. Traditional endpoints such as mortality, reproduction and growth remain relevant, but newer molecular approaches enable data on biological effects to be merged with physico-chemistry, and used for predictive modelling. The NANOSOLUTIONS project is using genomics and proteomics in a systems biology approach with a range of organisms including *E. coli*, earthworms, *C. elegans*, and the zebrafish. The data shows that ENMs can be ranked by toxicity, but the relationship between physico-chemistry and toxicity is both material and test organism-dependent. The data are revealing new proteins, and although a single, novel, nano-specific endpoint remains elusive, the patterns of the biological responses are sometimes predictive of the materials and their chemistry.

<http://dx.doi.org/10.1016/j.toxlet.2016.06.1192>

### S06-4 Developmental toxicity of engineered nanomaterials



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Study of air pollution indicates that minute particles may adversely interfere with pregnancy and fetal development. As engineering of nanoparticles have emerged, so has concern that these might interfere with reproductive and developmental functions. This is because nanotechnology may potentially increase the overall particle burden in air and introduce particles with novel characteristics and surface reactivity. To evaluate safety for pregnant women, we have studied developmental toxicity of engineered nanoparticles (ENPs), following exposure of pregnant mice by inhalation (ENPs of titanium dioxide and carbon black), or by intratracheal instillations (multiwalled carbon nanotubes). Our findings indicate that ENPs may introduce physiological changes in organ function in the offspring that manifest in life after birth, rather than fetotoxicity and malformations. Especially the nervous, immune, and male reproductive systems seemed sensitive to insult due to maternal exposure to ENPs during pregnancy at exposure levels close to common 8 hr time weighted occupational exposure limits. It follows that the potential for developmental hazard warrants characterization. At present, the applied methodology does not always reflect state-of-the-art and the diversity in study designs hampers deduction of general rules as to developmental toxicity. Also, functional outcomes (other than male reproductive function) are rarely addressed in developmental studies of