Nanoparticle-bio-interactions in the soil nematode *Caenorhabditis elegans*: Silica nanoparticles induce premature aging phenotypes

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Abstract - Nowadays engineered nanomaterials (MNMs) are ubiquitous in the environment and thus in our everyday life. Due to their increased application in medicine, food or catalytic converters MNMs distribute throughout different ecological niches such as waters and soil. We use the soil nematode *C.elegans* to investigate organismal aging processes and show that silica nanoparticles (NPs) induce premature aging phenotype on the molecular and the behavioral level. Nanomaterial exposure occurs via food through the pharynx to the intestinal system and through the vulva to the reproductive system of adult hermaphrodite worms. By confocal microscopy analysis we localize fluorescently labeled NPs in the cytoplasma and cell nucleus of single intestinal and vulval B and D cells. In single cells of the intestinal epithelium silica NPs induce an amyloid-like aggregation of insoluble ubiquitinated proteins. In the living worm distribution of MNMs in respective organs is correlated with alteration of their function. Silica NPs induce an untimely accumulation of insoluble ubiquitinated proteins and reduction of pharyngeal pumping that represent distinct aging phenotypes on the molecular and behavioral level. By comparative analysis of silica, polystyrene and silver NPs we introduce premature onset of protein aggregation and reduced neural behaviors as tools for characterization of nanomaterials (ACS Nano, 2013, 7:10695-703). Our aim in the European Consortium NanoMILE is to screen environmentally relevant nanomaterials for their bio-interactions and effects on organismal aging processes in the nematode *C.elegans*. To this end we measure the lifespan and analyse different behavioral phenotypes which are an indicator of neuronal and cellular functionality. Proteomics are scheduled to identify the underlying signalling pathways.

NanoMILE project / work package 6 (ecotoxicology)

nanomaterial interactions, bioavailability & biological effects *in vivo*

- vehicle exhaust catalysts
- additive in lacquers & coating

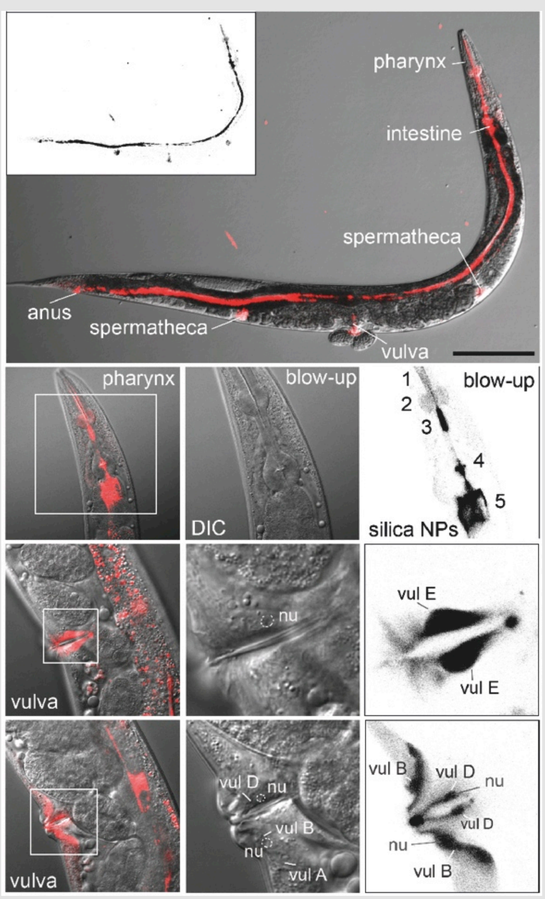
CeO_2 · Ag · ZnO

- UV light scattering additive
- rubber manufacture

- consumer products: detergents, shoes, cosmetics
- surface coating: phones, toys, respirators, water filters

environmental exposure

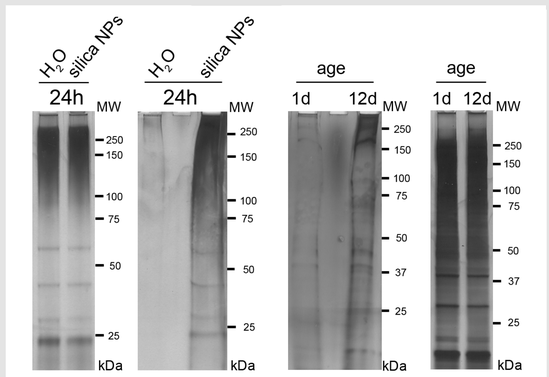
Silica NP-bio-interactions in *Caenorhabditis elegans* - premature aging



Scharf et al.(2013)

Alteration of protein homeostasis

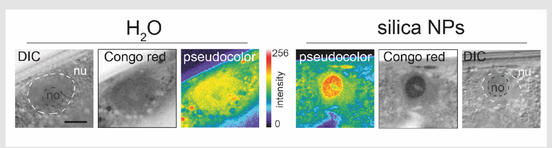
Silica NPs shift protein homeostasis prematurely towards insolubility / protein aggregation.



Scharf et al.(2013)

Silica NPs induce an agglomeration of amyloid-like endogenous proteins in single intestinal cells

The amyloid-dye Congo red visualizes the location of SDS-insoluble, ubiquitinated proteins in single cells of the intestinal epithelium in adult *C.elegans.*

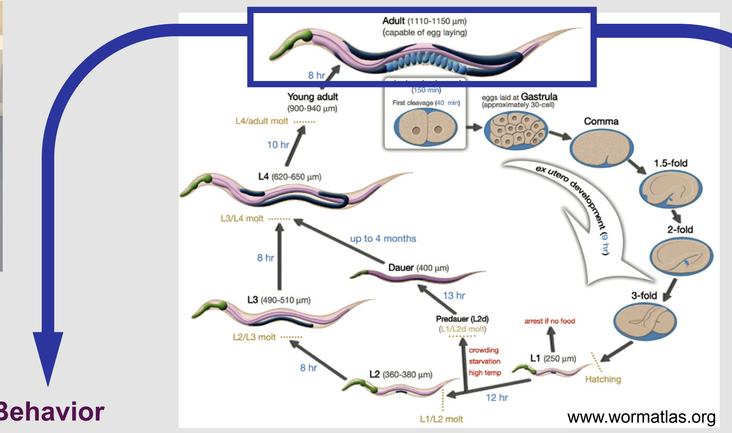


Scharf et al. (2013)

Uptake and distribution of fluorescently labeled silica NPs in *C.elegans*

Distribution of rhodamine labeled silica NPs (red) in the intestinal and reproductive systems of living, adult *C.elegans*. Blow ups show single-cell distribution of silica NPs.

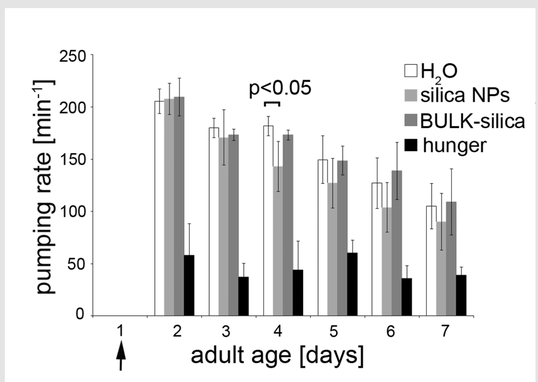
MNM exposure of the soil nematode *Caenrohabditis elegans*



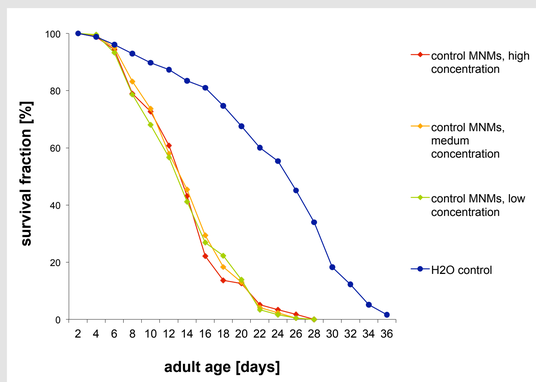
Biochemical assays

Behavior

Lifespan



Scharf et al. (2013)



A.Piechulek

Aims in the European Consortium NanoMILE

***C. elegans* as screening platform of environmentally relevant MNMs for their bio-interactions, investigation tasks:**

- **determination of lifespans / interventions?**
- **impairment/ alteration in behavior phenotypes?**
- **reproduction/ progeny affected?**

➔ **indicators of cellular and neuronal functionality**

analysis of organismal aging

Silica NPs induce premature aging phenotypes

on molecular levels

➔ **accumulation of SDS-insoluble, ubiquitinated proteins**

➔ **agglomeration of amyloid-like proteins in single cells**

on behavioral levels

reduction of pharyngeal pumping

Reference:

•Scharf A., Piechulek A. and von Mikecz A. (2013) Effect of nanoparticles on the biochemical and behavioral aging phenotype of the nematode *Caenorhabditis elegans*. ACS Nano. 7(12):10695-703.