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Meiotic cohesin subunits are frequently expressed in cancers as Cancer-Testis (CT) Genes, and are potentially linked to the onset and proliferation of tumor cells. However, the roles of CT genes, and mei-Cohesin components in particular, in cancer were not studied in depth. In order to address this gap in research we took two approaches : the epigenomics of mei-Cohesin in normal primate testis and the reconstitution of mei-Cohesin complexes in somatic cell lines, both normal and transformed. Applying a novel ChIP-ChEP-seq method in Macaca fascicularis testis, we elucidated the overlapping pattern of mei-Cohesin binding to germline chromosome arms and centromeric repeats for SMC1b, STAG3, RAD21L and REC8 subunits. We also uncovered the rules guiding the cohabitation of mei-Cohesins with BORIS/CTCFL and CTCF-containing regulatory sites controlling gene expression and 3D chromatin structure during the spermatogenesis. Finally, by reconstituting REC8 and RAD21L based mei-Cohesin complexes in human somatic cell lines, we discovered the governing principles for mei-Cohesin binding to chromatin. The introduction of particular combinations of mei-Cohesin subunits into such a system was setting up a potential competition with somatic cohesin complex based on RAD21, resulting in chromosome instability phenotype. As a result of this work, we elucidated the potential biological roles of mei-Cohesin expressed as CT genes in cancer cells.

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Life span-resolved nanotoxicology identifies nuclear amyloid, altered metabolism and neurodegenerative processes in the *nematode Caenorhabditis elegans*

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Along with the expanding application of engineered nanomaterials (ENMs), there is a growing concern over their adverse toxicological effects on human health and the environment upon release and exposure. ENMs are increasingly used in consumer products, as food additives and in drug delivery. To keep up with the fast pace of ENM development, medium to high throughput methodology is required to understand the bioavailability and long-term effects related to ENMs. For the analysis of ENM-long-term effects, we use the invertebrate Caenorhabditis elegans which lives for only 3-4 weeks and is a realistic target organism of ENMs in the environment as well as a top animal model in the laboratory. We exposed adult worms with environmentally relevant ENMs such as silver, silica, ZnO, CeO2 and polystyrene (nano plastics) in liquid media with bacteria in 96-well microtiter plates. The microhabitat in 96-well microtiter plates apparently excluded cultivation stress and thus, enabled analyses

of ENM-bio-interactions over the entire life span. Age-resolved analysis identified especially middle-aged worms as vulnerable target group to certain ENMs. In vulnerable groups, the distribution of ENMs throughout the cytoplasm and the cell nucleus in single intestinal and vulval cells as well as in the pharyngeal tissue was correlated with functional alterations. Nano silica induces nuclear amyloid and perturbs the peptide metabolism in intestinal cells. Global protein is reduced which promotes a 'petite' phenotype. Consistently, mass spectrometry analysis identifies a silica NP-induced aggregome network that contains predominantly the gene ontology (GO) groups of proteostasis, metabolic processes, rRNA processing and translation. Among the molecular ENM-effects, nano silica-exposed worms show an early onset of age-associated stigmata including widespread protein aggregation and premature neurodegeneration of serotonergic and dopaminergic neurons. Impaired neurosignaling is related with reproductive and locomotion defects. All age-related defects result in reduced fitness and health span which normally occur in old worms but are prematurely induced by certain ENMs like nano silica. System biology-based analyses have the potential to identify common pathways of nanoparticle-bio-interactions across species from worm via other taxa to human and thus, to evaluate the risk of nano silica to human health.

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The cell nucleus as sensor of environmental pollution: Amyloid, neurodegeneration and aging

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Two major environmental challenges are predominant - climate change and the biodiversity crisis. Also, pollutants are distributed globally. We identified the cell nucleus as a sensitive sensor for bio-effects of pollutants such as mercury and nanoparticles. Our investigations focus on the role of pollutant-induced nuclear amyloid formation in neural signaling, neurotoxicity and accelerated aging in the nematode Caenorhabditis elegans. Methods: At present, the majority of investigations on the toxicology of pollutants address short-term effects. While this approach allows for the identification of uptake pathways, exposition and acute toxicity, xenobiotic-organism interactions that manifest later in an adult life are missed. To characterize effects of pollutants over the entire life span, all analyses are performed in the nematode C. elegans. Results: We show that mercury and nano silica effect widespread protein aggregation. Proteomic profiling revealed that both pollutants promote segregation of proteins belonging to the gene ontology (GO) group of 'protein folding, proteolysis and stress response' to an SDS-resistant aggregome network. Candidate proteins in this