and US projects focused on developing of methodology for modeling toxicity of nanoparticles, including those conducted within the European NanoSafety Cluster and the COST MODENA action, we are now at the stage of collecting first results and conclusions. The most important results and reflections on the further development of computational tools for nanotoxicology will be presented and discussed during the talk. Since calibration and validation of the computational models are impossible without mutual understanding and close collaboration with experimental groups delivering high quality toxicity data, the participation of experimental toxicologists in the talk and discussion is strongly encouraged.

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W02-4
Proteomics approaches for hazard assessment of nanomaterials and for supporting NM classification

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Oxidative stress is considered to be a major paradigm to explain NP toxicity. Here we focused on protein carbonylation as a consequence of oxidative stress for a set of 25 different nanoparticles, used as either plane ("pristine") materials or with different surface coatings. In parallel several *in vitro* and *in vivo* toxicity endpoints have been analyzed. We used well characterized NP of 10 nm (ZrO_2), 15 nm (SiO_2) and 50 or 200 nm (Ag), furnished either with acidic, basic or polymeric functionalities. In addition TiO_2(NM-103,-104,-105), ZnO (NM-110, -111), CNT (NM-400, -401, -402), SiO_2 (NM-200, -203, Ag (NM-300K) $BaSO_4$ (NM-220) and AlOOH were analyzed. In a screening approach we studied time- and dose-dependent carbonylation of all NP in NRK-52E cells via 1D immunoblots. Data were correlated with cytotoxicity (WST-8, LDH assay), ROS formation (DCFDA assay) and surface reactivity (ESR spectroscopy). We applied a 2D-MALDI-MS/MS proteomics approach to identify the modified proteins. For selected NP we also analyzed lung tissues homogenates after intratracheal instillation into rat lungs. In parallel we used proteomics approaches to characterize the NP protein corona in serum as well as in purified native surfactant from pig lungs. Twelve out of 25 NP induced protein carbonylation in NRK-52E cells. The degree of protein carbonylation correlated well with overall *in vitro* toxicity. The 2D approach revealed a complex and distinct pattern of carbonyls. Modified proteins were identified as proteins of cytoskeleton, HSP, or proteins of major cellular pathways (i.e. glycolysis). Carbonyl modifications occurred also in lung tissue homogenates, indicating the relevance of *in vitro* findings. Analysis of poteomics data with hierachical cluster analysis and principal component analysis revealed differential results for the NM with respect to induced carbonyl patterns. Taken together, analysis of protein carbonylation appears useful to describe toxic effects of NP and to better understand underlying molecular mechanisms of toxicity. Furthermore, proteomics data can support NM classification.

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W02-5
Moving towards a safe by design approach for ENM: Linking ENM relevant properties to toxicological concerns

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Within the *Safe by Design concept*, the functionality of a material and its toxicity are considered in an integrated way. The central goal of this presentation is to discuss some fundamental principles of engineered nanomaterials (ENM) interactions with biological systems relevant to human exposure and biological responses. Major factors to consider in the ENM safe-by-design approach are surface modification to reduce the potential hazardous properties of target nanoparticles (NP), compatibility between NP coatings and their matrix, as well as biopersistence, considering the relevant exposure scenarios across the life cycle of the target NP and products. This is a cross-disciplinary field that needs to identify, at earlier stages of the ENM R&D process, the physicochemical properties that may act as good predictors of toxicity, e.g. crystal structure/reactivity, zeta potential/surface charge/dynamic properties. Furthermore, it is also needed to build adequate screening *in vitro* testing strategies (realistic doses, exposure duration and target tissues), incorporating relevant hazard endpoints that can give an insight about the toxicological mode of action (MoA) with relevance to human health and environment, taking into account the uses and applications along the lifecycle (EHS roadmap). These topics will be illustrated by a cytotoxicity and genotoxicity study performed with a set of ENM with identical chemistry but different physicochemical characteristics that highlighted the importance of investigating each ENM individually, instead of assuming a common MoA. The findings, although creating a dilemma for developing criteria for categorization and read-across, are also suggestive of the importance of considering the functionality of a material and its toxicity in an integrated way, enabling a safe-by-design concept. Ultimately, the overall safety data is intended to best support the decision of IND developers and risk managers during the ENM design and development processes.

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Workshop W03: Opportunities to Enhance Quality and Impact of Omics Sciences

W03-1
RNA-sequencing in toxicogenomics

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Till date, microarray-based technologies represent the main analytical platform in toxicogenomics. However, where high throughput sequencing (HTS) methods are technically advancing and costs for HTS are expected to come down on rather short