

Genome-wide DNA methylation variations upon engineered nanomaterials and their implications in nanosafety assessment

Subject Code: B07

With the support by the National Natural Science Foundation of China, the National “973” Program, and the Strategic Priority Research Program of the Chinese Academy of Sciences, the research team led by Prof. Liu Sijin (刘思金) at the State Key Laboratory of Environmental Chemistry and Ecotoxicology, Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, uncovered the fingerprint signature of genomic DNA methylation upon exposure to sub-lethal engineered nanomaterials (ENMs), which was published in *Advanced Materials* (2016, DOI: 10.1002/adma.201604580).

Given the novel and unique physicochemical properties of ENMs, traditional toxicity assays that were originally developed for bulk materials or chemicals may not be suitable for reliable detection of nanotoxicity and nanoimpact assessment, due to the low sensitivity of the methods, especially under low-dose exposure. Thus, more sensitive methodologies are needed to evaluate their safety profiles. DNA methylation is an early sensitive parameter in response to a wide range of exogenous and endogenous stimuli including ENMs. However, there is limited understanding on this front, and, to address this issue, they performed DNA methylation sequencing at base-pair resolution in lung A549 and kidney HEK293T cells upon diverse ENM exposure. Exposure of silver nanoparticles and graphene oxide led to significant increases in the global 5-mC level, which was however to a much less extent for gold nanoparticles, carbon nanotubes, nano-TiO₂ and nano-ZnO. Furthermore, physicochemical properties, such surface modification, affected ENM-induced DNA methylation variations. Through gene functional mapping, significant perturbations in cellular processes and signaling pathways could be ascribed primarily to DNA methylation alterations. Supported by gene expression and toxicological/physiological evaluations, adverse outcome pathways, adaptive cell survival and compensatory effects were identified due to the genome-wide DNA methylation changes. Thus, ENM-induced DNA methylation variations represent a more sensitive fingerprint analysis of their direct and indirect effects that may be overlooked by the traditional toxicity assays, and the understanding on the structure-activity relationship for DNA methylation changes induced by ENMs would open a new path for their safer design.

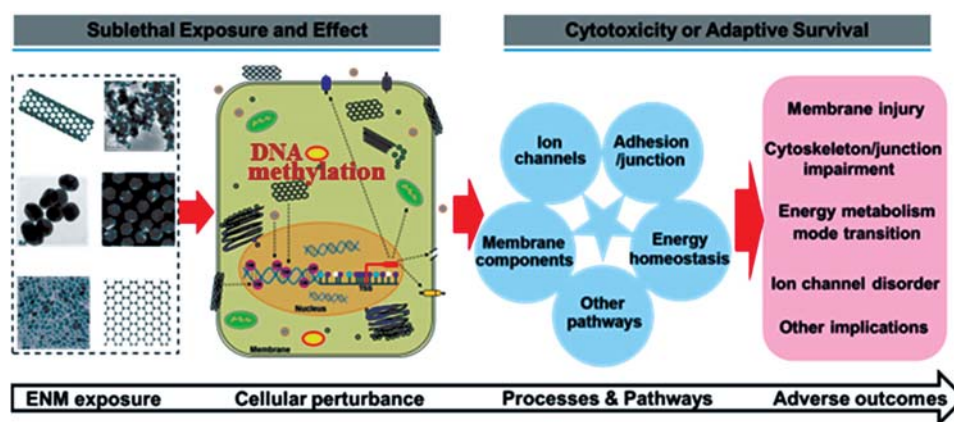


Figure Sublethal exposure of engineered nanomaterials (ENMs) induces alterations of various cellular processes due to DNA methylation changes.