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NMR-Based Metabolomic Analyses

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Abstract

Silica nanoparticles are increasingly used in the biomedical fields due to their excellent solubility, high stability and favorable biocompatibility. However, despite being considered of low genotoxicity, their bio-related adverse effects have attracted particular concern from both the scientific field and the public. In this study, human cervical adenocarcinoma cells (HeLa line) were exposed to 0.01 or 1.0 mg/mL of hydrophilic silica nanoparticles. The 1H NMR spectroscopy coupled with multivariate statistical analysis were used to characterize the metabolic variations of intracellular metabolites and the compositional changes of the corresponding culture media. At the early stage of silica nanoparticles-exposure, no obvious dose–effect of HeLa cell metabolome was observed, which implied that cellular stress-response regulated the metabolic variations of HeLa cell. Silica nanoparticles induced the increases of lipids including triglyceride, LDL, VLDL and lactate/alanine ratio and the decreases of alanine, ATP, choline, creatine, glycine, glycerol, isoleucine, leucine, phenylalanine, tyrosine, and valine, which involved in membrane modification, catabolism of carbohydrate and protein, and stress-response. Subsequently, a complicated synergistic effect of stress-response and toxicological-effect dominated the biochemical process and metabolic response, which was demonstrated in the reverse changes of some metabolites including acetate, ADP, ATP, choline, creatine, glutamine, glycine, lysine, methionine, phenylalanine and valine between 6 and 48 h post-treatment of silica nanoparticles. The toxicological-effects induced by high-dosage silica nanoparticles could be derived from the elevated levels of ATP and ADP, the utilization of glucose and amino acids and the production of metabolic end-products such as glutamate, glycine, lysine, methionine, phenylalanine, and valine. The results indicated that it is important and necessary to pursue further the physiological responses of silica nanoparticles in animal models and human before their practical use. NMR-based metabolomic analysis helps to understand the biological mechanisms of silica nanoparticles and their metabolic fate, and further, it offers an ideal platform for establishing the bio-safety of existing and new nanomaterials.

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