

Editorial

The Concerns on Biosafety of Nanomaterials

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INTRODUCTION

Nanomaterials, with sizes range from 0.1 to 100 nm, are similar to many biomacromolecules and organelles. When the size of a material decreases to nanometer level, small size effect, surface effect, quantum size effect and quantum tunneling effect will play significant roles, and enable nanomaterials with new properties, such as the increasing hardness and strength, super paramagnetism, strong surface adsorption capacity, chemical reactivity and quantum properties.

Today, various kinds of nanomaterials have been used in commercial and industrial products. ZnO and TiO₂ nanoparticles are widely used on cellulosic fabrics for UV-protection purpose [1,2]. A lot of cosmetics and skin products contain ZnO and TiO₂ nanoparticles as sun-screening active ingredients [3,4], together with nano silver, gold and other inorganic nano-structured materials to gain antimicrobial activity [5-7]. Nanoscale CeO₂ can serve as fuel additives and reduce fuel consumption, CO₂ emissions, and particulate emissions [8,9]. Al₂O₃ nanoparticles are widely used in plastic, rubber and ceramic to reinforcing and toughening the products. Nanotechnology and nanomaterials are also very promising in improving the diagnosis, treatment and monitoring of many diseases. Studies have shown that incorporation of nanotechnology in medicine increases solubility, stability, targeting, biocompatibility, permeability and controllability of drugs and vaccines [10-12].

Despite the increasing interest and effort in the development and application of nanomaterials, there are increasing concerns about their potential toxicity. In fact, the number of nanomedicine being approved for clinical is limited [13,14]. A lot of uncertainties remain as how nanoparticles interact with biomacromolecules after entering into the human body; how they accumulate, degrade and finally leave the body; how different organs, tissues and the circulation system are affected. There are reports that nanomaterials can cause damage to cells by generating reactive oxygen species which will result in DNA damage, lipid peroxidation and protein denaturation [15-17]. In addition, proteins and nucleic acids may stick to nanoparticles upon their entrance into the cells [18-22], interfering metabolic pathways and ultimately cell death.

A number of *in vivo* and *in vitro* studies have been performed to assess the potential toxicity of nanomaterials. At cellular level, methods that are generally used include cell morphology analysis,

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tissue staining, cell viability assay, ROS analysis, NO assay, LDH or MTT assay, cell cycle analysis and cytokine (IF8, IL-6 or TNF-alpha etc.) release test. These assays are carried out to explore how the size, shape, and surface properties of nanoparticles affect cell viability and their *in vivo* distribution, cellular uptake, subcellular location, metabolism and degradation [10,20,23-26]. *In vivo* studies showed that nanomaterials can accumulate in many organs, for instance, liver, spleen, lung or kidney, depending on their characteristics and how they are administrated [27]. Oxidative stress are detected in cells exposed to nanomaterials such as Ag [28], Au [29], copper and copper oxide [30], TiO₂ [31], ZnO [32], CeO₂ [33], Al₂O₃ [34], carbon nanotube [35,36] and et al. Recently, genomic and proteomic technologies have also been applied to study the biological effects and toxicity of nanomaterials [37]. These high throughput analysis provide a more comprehensive view of how molecules in the biological network response to the presence of nanoparticles. Genomic instability [38-40], inflammatory response [41,42], apoptosis [43], protein phosphorylation [44,45] are found to be affected by exposure to nanomaterials.

Despite the efforts on the studies of nanomaterial safety, there remain a lot of problems. Firstly, these studies are not systematic, most studies use only one cell line or one tissue of the animal models. The methods reported are different and therefore no comparisons can be made among different materials and studies. Secondly, most studies report observations on cellular or tissue level, there are still not enough studies on how nanomaterials interact with biomolecules and finally the mechanism leads to toxicity or biological effects. The third concern is that among these studies there are contradictory results in the evaluation of toxicity of the same kind nanomaterials. One example is that nano Au was observed to show both causing oxidative stress [46] and anti-oxidative stress [47,48]. And this happens to CeO₂ [49] and carbon nanotube [50] too. Factors including different concentration, administration procedures, fabrication and processing of nanoparticles and other details can all lead to inconsistent results.

As a new area and many nanomaterials are newly engineered, standardized preparation and characterization methods of many nanomaterials are not available. With the development of nanomaterials and nanotechnology, there is a great need to set up regulations and standards based on comprehensive studies on biosafety and bioeffects of nanomaterials. It is critical to develop a systematic and standardized method that is accurate and repeatable for the analysis of the biological effects and safety of nanomaterials at tissue, cell and molecular levels. The method should start with a comprehensive and detail characterization of each nanomaterial before *in vitro/vivo* analysis, which includes dimensions, compositions, purity, surface charges et al. The method should be applicable to the analysis of most nanomaterials. In addition, a series of dosage and exposure time to nanomaterials should be designed to monitor the effects. This will allow comparisons of toxicity of different nanomaterials to same cells and tissues, and therefore facilitate the standardized regulations for nanomaterial safety.

With the increasing interest in nanomaterials and concern of their biological effects and safety, more efforts are being invested in these fields of studies. It is promising that in the near future a systematic and accurate method to evaluate the safety of nanoparticles will be developed and consents on by fields of nanomaterials. This will in turn improve the regulations and standards of nanomaterials preparation, processing, characterization and application.

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