Austin Journal of Anatomy

Austin Publishing Group

Open Access Full Text Article

Editorial

Biotransformation of Nanomaterial is Pivotal for Nanotoxicology Research

Michael T Tseng*

Department of Anatomical Sciences & Neurobiology, University of Louisville, USA

***Corresponding author:** Michael T Tseng, Department of Anatomical Sciences & Neurobiology, School of Medicine, University of Louisville, Louisville, Kentucky, USA

Received: May 22, 2014; **Accepted:** May 26, 2014; **Published:** May 26, 2014

Editorial

New material synthesis through manipulation of atoms has spurred interest in nanotechnology development for more than five decades [1]. Materials with at least one dimension sized from 1 to 100 nanometers have been manufactured with enhanced physical strength and greater chemical reactivity than their larger-scale counterparts. At this dimension, some material properties are governed by the laws of atomic physics. Today nanotechnology touches nearly all aspects of our lives and for biomedical researchers nanotechnology holds the promise of new drug formulation and new approaches of molecular targeting therapies [2,3]. Other discoveries in nanotechnology that influence agricultural developments, environmental sciences, and for material science advancement including nanocomposites have been made [4,5].

Nanomaterial for medical applications alone has been projected, with a compound annual growth rate of 13.5%, to surpass $100 billion in 2014 [6]. However, challenge simposed by technical limitations have allowed the successful emergence of only a few nano-therapeutics that included doxorubicin-loaded liposomes, paclitaxel micelles and albumin-bound paclitaxel nanoparticles as well as few injectable materials. It should be noted that most materials currently used for gene delivery or with good photo-electric properties designs have limited therapeutic applications due to the systemic toxicity concerns. Natural materials with little inherent toxic components could offer superior alternatives in the future. CNS disorders, such as inflammation and psychosis may be ameliorated by brain targeting nanoparticles [2,3,7]. Systemic released microvesicles and exosomes, nanoparticles containing small RNAs, mRNA and proteins may be used to affect cells at distant sites. Through autocrine, paracrine, and endocrine signaling these vesicles may be regarded as a component of a newly identified intercellular communication system [8,9]. Investigations on the edible nanoemulsion-based delivery systems could further enhance the bioavailability of these encapsulated substances [10]. Future studies on the nanoemulsion- induced exosomes release from the gastrointestinal tract could offer valuable clues on the additional functional importance of these nanoparticles.

Despite the plethora of benefits, potential toxicity of biomaterials remains a concern and the bioretention of nanomaterial necessitates regulatory oversight. Inadvertent exposures to nanomaterials through inhalation, ingestion, penetration of dermal layers, or deliberate parenteral administration may result in subsequent systemic distribution through the circulatory system. Indeed, the increased production of nanomaterial, especially carbon nanotubes has raised concerns over potential risks of adverse human health effects [11]. Titanium dioxide nanoparticles, considered as biologically inert, have been extensively used as additives in sunscreen products, antimicrobial, bio-medical ceramic and implanted biomaterials, plastic packaging, and self-cleaning sanitary ceramics. Their widespread use has raised the question of potential adverse effects and health risks to workers as well as to the general population. As a matter of fact, in vitro and in vivo studies have showed toxic effects such as chronic pulmonary inflammation, changes in gene expression including apoptosis-related genes and inflammatory genes, and promotion of oxidative stress and DNA damage responses [12]. Cerium oxide nanoparticle (CeO_2 NP), another metal oxide, has expanded beyond its traditional role as polishing agents to be found in television tubes components, in precision optics materials and in various consumer products including semiconductors. The use of cerium oxide as a fuel borne catalyst improves fuel burning efficiency; as a result, CeO_2 NP are directly released into the environment with no clear impact on human health [13]. However, a recent study showed combined nanoceria with diesel exhaust nanoparticles from diesel engine induced pulmonary fibrosis and renewed concerns for its safety [14]. In the agricultural arena, untransformed CeO_2 NPs are up taken and stored in a variety of plants including soybean, corn, cucumber, tomato, and cilantro. While majority of the CeO_2 NPs absorbed in hydroponics plants remains in the nascent form, a small percentage is biotransformed to $CePO_4$ and to cerium carboxylates [15].Owing to its natural multivalent state, nanoceria has been proposed as a novel therapeutic strategy to cerium neurodegenerative diseases in human including oxidative stress-mediated ocular diseases such as age-related macular degeneration and retinal angiomatous proliferation [16]. As a redox mediator ceria can bind reactive oxygen species reversibly. Internalized nanoceria elicits responses with both therapeutic effects and as oxidative stress inducer [17,18]. Experimental exposure of high iv dose of nanoceria quickly saturated elements of the reticuloendothelial system in liver and spleen, together with sustained proliferation of T lymphocytes, resulted in the formation of granuloma in the rat [19]. The behavior of CeO_2 NP in plants may undergo biotransformation with the assistance of PO_4 and other organic acids, to modulate their toxicity potential [15]. Regarding the biotransformation of nanoceria in mammalian system, a recent report examined the fate of nanoceria while being retained in the hepatic phagolysosomes and found the release of a secondary plum of the CeO_2 NPs.These very small 1-3 nm CeO_2 NPs are known to reduce free radical formation [20]. The in situ formation and release of secondary CeO_2-plum signifies the discharge of cerium ions

Citation: Tseng MT. Biotransformation of Nanomaterial is Pivotal for Nanotoxicology Research. Austin J Anat. 2014;1(1): 1004.

from the iv-infused ceria in the liver for systemic distribution. Aside from the obvious implication in the principal of administration, delivery, metabolism and elimination (ADME) for nanomaterial, the observed in situ biotransformation appeared to play a functional role in oxidative stress reversal found in the rat brain [21]. Perhaps due to their miniature dimension, migration pathway from cell cytoplasm interior to extracellular domains remains to be identified for this nanomaterial; nevertheless, biotransformation clearly is a pivotal bioprocessing junction for many of the newly manufactured nanomaterial.

Applying the principal of ADME, a framework can be developed for analyzing and evaluating the biological impact of nanomaterial to safeguard cell, tissue, and organisms. Tiered toxicity testing involving cell-free, cellular and in vivo methodologies have been developed with endpoints relating to induction of oxidative stress, inflammation, geno toxicity and others to determine the safe levels for human exposure. Parallel structural biology analysis using advanced instrumentation for image generation reaching near-atomic resolution should be encouraged in future studies in risk assessment of nanomaterial and for their beneficial applications.

References

1. Feynman R. There's plenty of room at the bottom. Caltech Engineering and Science. 1960; 23: 22-36.
2. Fazil M, Md S, Haque S, Kumar M, Baboota S, Sahni JK, Ali J. Development and evaluation of rivastigmine loaded chitosan nanoparticles for brain targeting. Eur J Pharm Sci. 2012; 47: 6-15.
3. Gao H, Pang Z, Jiang X. Targeted delivery of nano-therapeutics for major disorders of the central nervous system. Pharm Res. 2013; 30: 2485-2498.
4. Sharma AK, Khare P, Singh JK, Verma N. Preparation of novel carbon microfiber/carbon nanofiber-dispersed polyvinyl alcohol-based nanocomposite material for lithium-ion electrolyte battery separator. Mater Sci Eng C Mater Biol Appl. 2013; 33: 1702-1709.
5. Morales MI, Rico CM, Hernandez-Viezcas JA, Nunez JE, Barrios AC, Tafoya A, et al. Toxicity assessment of cerium oxide nanoparticles in cilantro (Coriandrum sativum L.) plants grown in organic soil. J. Agric. Food Chem. 2013; 61: 6224-6230.
6. BCC Research. "Nanotechnology in Medical Applications: The Global Market," 2010.
7. Kim ID, Shin JH, Kim SW, Choi S, Ahn J, Han PL, et al. Intranasal delivery of HMGB1 siRNA confers target gene knockdown and robust neuroprotection in the postischemic brain. Mol Ther. 2012; 20: 829-839.
8. Alvarez-Erviti L, Seow Y, Yin H, Betts C, Lakhal S, Wood MJ. Delivery of siRNA to the mouse brain by systemic injection of targeted exosomes. Nat Biotechnol. 2011; 29: 341-345.
9. Zhang HG, Grizzle WE. Exosomes: a novel pathway of local and distant intercellular communication that facilitates the growth and metastasis of neoplastic lesions. Am J Pathol. 2014; 184: 28-41.
10. McClements DJ, Xiao H. Potential biological fate of ingested nanoemulsions: influence of particle characteristics. Food Funct. 2012; 3: 202-220.
11. Hamilton RF Jr, Wu Z, Mitra S, Shaw PK, Holian A. Effect of MWCNT size, carboxylation, and purification on in vitro and in vivo toxicity, inflammation and lung pathology. Part Fibre Toxicol. 2013; 10: 57.
12. Silva RM, Teesy C, Franzi L, Weir A, Westerhoff P, Evans JE, et al. Biological response to nano-scale titanium dioxide (TiO2): role of particle dose, shape, and retention. J Toxicol Environ Health A. 2013; 76: 953-972.
13. Cassee FR, van Balen EC, Charanjeet Singh C, Green D, Muijser H, Weinstein J, et al. Exposure, health and ecological effects review of engineered nanoscale cerium and cerium oxide associated with its use as a fuel additive. Critical Reviews in Toxicology. 2011; 41: 213–229.
14. Ma JY, Young SH, Mercer RR, Barger M, Schwegler-Berry D, Ma JK, et al. Interactive effects of cerium oxide and diesel exhaust nanoparticles on inducing pulmonary fibrosis. Toxicol Appl Pharmacol. 2014; 278:135-47.
15. Zhang P, Ma Y, Zhang Z, He X, Zhang J, Guo Z, et al. Biotransformation of ceria nanoparticles in cucumber plants. ACS Nano. 2012; 6: 9943-9950.
16. Kyosseva SV, Chen L, Seal S, McGinnis JF. Nanoceria inhibit expression of genes associated with inflammation and angiogenesis in the retina of Vldlr null mice. Experimental Eye Research. 2013; 116: 63–74.
17. Chen J, Patil S, Seal S, McGinnis JF. Rare earth nanoparticles prevent retinal degeneration induced by intracellular peroxides. Nat Nanotechnol. 2006; 1: 142-150.
18. Eom HJ, Choi J. Oxidative stress of silica nanoparticles in human bronchial epithelial cell, Beas-2B. Toxicol In Vitro. 2009; 23: 1326-1332.
19. Tseng MT, Fu Q, Lor K, Fernandez-Botran GR, Deng ZB, Graham U, et al. Persistent Hepatic Structural Alterations Following Nanoceria Vascular Infusion in the Rat. Toxicol Pathol. 2013; 00: 1-13.
20. Pirmohamed T, Dowding JM, Singh S, Wasserman B, Heckert E, Karakoti AS, et al. Nanoceria exhibit redox state-dependent catalase mimetic activity. Chem Commun (Camb). 2010; 46: 2736-2738.
21. Graham UM, Tseng MT, Jasinski JB, Yokel RA, Unrine JM, Davis BH, et al. In vivo processing of ceria nanoparticles inside liver: Impact on free radical scavenging activity and oxidative stress. ChemPlusChem. doi: 10.1002/cplu.201402080.

Austin J Anat - Volume 1 Issue 1 - 2014
ISSN : 2381-8921 | www.austinpublishinggroup.com

Citation: Tseng MT. Biotransformation of Nanomaterial is Pivotal for Nanotoxicology Research. Austin J Anat. 2014;1(1): 1004.