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Nanotoxicology ten years later: Lights and shadows☆

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ABSTRACT

The mounting societal concerns about possible and maybe even likely adverse effects of nanomaterials are reflected in a large and growing number of publications in the field of nanotoxicology. Indeed, today's search in PubMed reveals >3700 publications on the subject denoted by (toxic + nanomaterials) – quite a growth over the last decade that began with only two dozens of them up-to 2005.

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Nanotoxicology has emerged as a sub-discipline at the interface of toxicology and nano-material science. As a term nanotoxicology was introduced about a decade ago (Shvedova et al., 2010) to reflect the potential uniqueness of the physico-chemical properties of nanoparticles suggesting that their interactions with cells and tissues may be unpredictable. Because cellular molecular machines and man-made nanoparticles have comparable dimensions, one of the popular definitions of nanotoxicology puts emphasis on the possibility of the direct interaction and interference of nanoparticles with the vital cellular processes (Shvedova et al., 2010). In this sense, nanotoxicology is significantly different from the traditional toxicology of fine and ultrafine particles and fibers.

Two major factors make nanotoxicology remarkably important and dictate the necessity of its rapid development: 1) large-scale production of diversified nanomaterials, and 2) remarkable progress in developing newer and newer types of nanomaterials with perplexing and unexpected physical and chemical characteristics (Khan and Shanker, 2015). While the first statement is self-explanatory, the second is supported by the extraordinary high number of discoveries and innovations in the field of nanotechnology. Many studies on graphene have led to the development of graphene-like 2D layered nanomaterials. These new materials, such as boron nitride nano-sheets, graphitic-carbon nitride nano-sheets and transition metal dichalcogenides (e.g. MoS_2 and WS_2) have, in turn, stimulated basic research in physics/chemistry and bioengineering, which has led to numerous interdisciplinary advances in nanoscience and its applications (Yang et al., 2015). For example, optical metasurfaces-patterned arrays of plasmonic nano-antennas that enable the precise manipulation of light-matter interactions are emerging as critical components in many nanophotonic materials, including planar metamaterials, chemical and biological sensors, and photovoltaics (Nemiroski et al., 2014). A new class of superhydrophobic nanomaterials might simplify the process of protecting surfaces from water (Alexander et al., 2015). Tremendous progress has been made in the field of bioapplications of nanomaterials. Among numerous examples one can mention design of magnetic nanoparticles that can attach to cancer cells in the bloodstream and remove them before they establish new tumors or nano-cages that could deliver cancer-killing drugs (Burkert and Star, 2015). Another outstanding example is protein-based biological machines (nano-robots) that can repair DNA damage.

It has been emphasized that nanomedicine and nanotoxicology are two sides of the same coin. Indeed, intentional enhancement with therapeutic and diagnostic goals (theranostic nanomedicine) or unintentional (toxicology) toxicity of nanomaterials may exploit the same mechanisms and affect identical metabolic pathways. Revealing these possible routes and unearthing the mechanisms – these are the major directions of research efforts. There is an ongoing debate as to whether nanoparticles may harbor a specific toxicity due to their size and physic-chemical characteristics that will be associated with 'nano-specific' mechanisms of actions and toxicity action. At present no evidence has been reported supporting the existence of such "mysterious" nano-specific mechanisms of action (Gebel et al., 2014). Of course, ongoing and future research along with new findings are the only productive way to assess risks and potential hazards associated with the use of

☆ *"We cannot solve our problems with the same thinking we used when we created them." Albert Einstein*

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new nanomaterials. Therefore, it is very important, from time to time, to take a break and summarize and re-assess the accumulating data. This is exactly the major goal of the current forum. The breadth and the deepness of today's nanotoxicology studies are astonishing - from plant-mediated biosynthesis of mosquitocidal nanoparticles, using botanical products (Benelli, 2016), to durable oxygen evolution reactions for the aerospace program (Kargar et al., 2015) thus generating new waves of interest in the diversified research audiences: from parasitologists and entomologists to space researchers. With this huge range of contemporary nanotoxicology, it is obvious that reasonable selections had to be made. A good collection of selected reviews and papers has an angle, or way of presenting the most important novel pieces of information and arguments always biased, at least to some extent, by the interests of guest-editors. In this particular forum our choices and focus were made in the following major areas: i) nanotoxicology of human exposures, ii) nanotoxicology vs nanomedicine: commonalities and differences; ii) new mechanisms of nanotoxicity, including biocorona, at cellular and organismal levels; iii) interactions of nanoparticles with the immune system; iv) biodegradation, biopersistence and distribution of nanoparticles in the body; v) applications of computational and systems biology in nanotoxicology; vi) interactions of microbiomes with nanomaterials.

Accordingly, the constellation of papers in this issue includes the first detailed studies with possible profound implications of occupational human exposure to nano-materials discussed in two papers by Iavicoli et al. as well as by Fatkhutdinova et al. Both groups focused their research on the identification and validation of specific biomarkers in exposed workers.

The two hot topics in nanotoxicology: the existence of specific pathophysiologic pathways linked to nanoparticle exposure, and the interplay between nanomedicine and nanotoxicology are extensively reviewed by Kreyling et al., by Riebeling et al., and by Wang and Chen.

The issues related to the effects and dynamics of biocorona in modulation of nanoparticle toxicity and biopersistence are reviewed in the contribution by Westmeier et al. The emergence of new mechanisms of biodegradation vs activation of nanoparticle surface is presented in a hybrid review/research paper by Kagan et al.

Effects and interfacing of nanomaterials with the cells and mechanisms of immune system are presented by Dobrovolskaia et al and special features of the responses elicited by the reproductive system are described by Ema et al.

There are several reviews proposing different new approaches, including systems biology, to considering different aspects of modeling, the diversified relationships between immense variability of physicochemical characteristics of nanoparticles and their biological effects, including the paper by Winkler et al., as well as by Costa and Fadeel, as well as by Oh et al.

The newly emerging field of microbiome/nanoparticle contacts, communications and mutual influences in local and systemic responses is reviewed by Pietroiusti et al.

Finally, we would like to emphasize the inherently collaborative and highly interactive nature of the selected reviews and the global representation of the authorship ranging from Russia and China to US and Western Europe. We believe this reflects a profoundly international character of nanotoxicology as a discipline and we hope that the established and newly emerging productive research connections promise further outstanding developments in this field of toxicological sciences.

Conflict of interest

The authors declare that they do not have any conflict of interest to disclose.

Transparency document

The Transparency document associated with this article can be found, in the online version.

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