Poster

NANOTOXICOLOGY: EXPLORING NEW PARADIGMS IN TOXICOLOGY

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Nanotechnology offers promising opportunities in new materials and biomedical applications among others. The human exposure to larger amounts of naturally produced or intended (chemically or physically prepared) nanoparticles (NP) will become inevitable and previously uncertain risks must be evaluated. As a result, nanotoxicology research is now gaining attention[1]. The aim of this work is to tackle the study from a holisitic perspective, regarding nanomaterials features that can be named as the NP full life cycle, i.e. how they behave far from the synthesis when they are dispersed in the exposure media and finally exposed to humans and environment[2].

It is well known that colloidal particles are systems out of chemical equilibrium, in a metastable phase. Their final fate is the desintegration or agglomeration towards more stable phases. Thus, characterization of NP once produced, as used (administered or other mechanisms of human exposure) and after using is required since physico-chemical changes occur while in solution, what may have a significant impact on observed toxicological responses that go far from the classical paradigms of toxicology. In this scenario we focus our attention on:

Stability of NP: The proper interaction of the NP with biological entities will depend on the stability of the NP in biological media. Consequences of this are of great interest, for instance the higher citotoxicity of unstable colloidal prepararation of NPs are not due to the material but rather its physical state.

The surface of NP: While much of the NPs function is due to their core structure, the surface coating defines much of their bioactivity. NP never travel alone, but they are constantly surrounded by an intended (for further application) or spontaneous due to the environment (the protein-corona[3]) coating. Consequences of this can be the different final bioactivity of NP of the same element depending on among others: 1) Their surface charge: Obviously “positive” NP attach predominantly negative biological surfaces as cell membranes, leading to cell death. 2) The spontaneous coating is not immediate but develops as time progresses with the possibility of differents responses at differents moments of the exposure.

The core of NP: Not for the composition of the NP itself because can be inert or toxic regarding their surface structure as mentioned above but for the release of cations that NP experiment in their full life cycle. Initially, not all of the precursor reagent used to synthesize NP is transformed. After synthesis, additional leakage of cations is observed, usually the leakage is fast in the first few days and then more slowly in the latter days (1% in 100 days of exposure of NP to Cell Culture Medium supplemented with serum). We have observed this pattern for Oxides NP (CeO2, Fe3O4, CoO) and Metallic NP (Au, Ag, Pt), and similar data are being publised for Quantum Dots (CdSe) and Carbon Nanotubes[4]. And this release must be taken into account regarding the toxicity of the material.

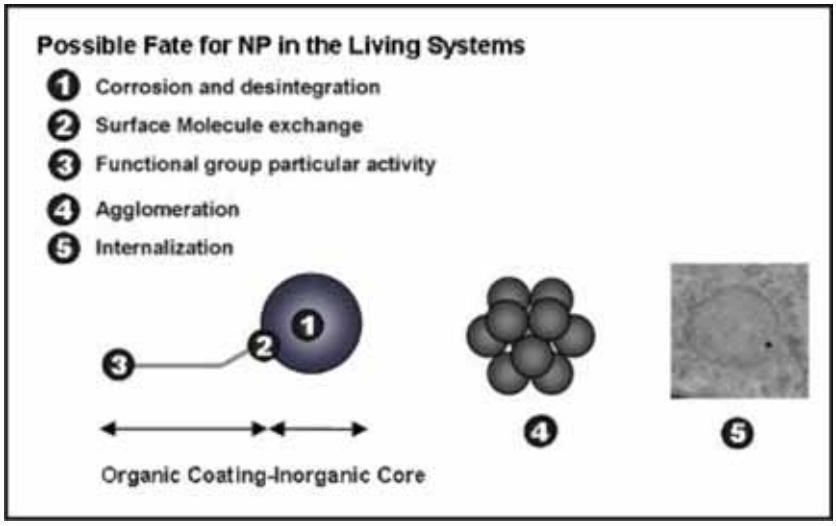
New paradigms in Nanotoxicology: Obviously cells death in the presence of inorganic NP is not the only factor to examine. Other important consideration such as the immunomodulatory effects must be also studied. While inorganic matter is known to be not toxic sometimes, immunogenic leading to sarcoidosis, granulomatosis, asbestosis, silicosis and others are. However in nanometric sizes particles will not follow such pattern since they are easily phagocyted. This new pattern of immune response caused by NP can lead to the possibility of tunning this response[5].

The co-stimulatory effects[6] of NP when they are not toxic for healthy organisms but hazardous in some compromised states should suggest the needs to focus on the efforts on studying nanotoxicolgy in a more compromised cases.

The effect of the solvent itself -where there are presence of stabilizers, surfactants and other molecules required for the NP synthesis – must be considerated and not only used as a control.

Many times the toxic effect is performed as a "catalytic-like" that means inorganic NPs are not deactived when killing the cell (for instance making a hole in cell membrane due to the positive surface charge) and introducing the concept of single particle lethality where in the worse –imaginary- scenario one nanoparticle could kill an organism made of millions of cells.

We work on all these aspects and our results and conclusions will be exposed and discussed.



Regarding the reactivity of a NP inside a biological system one have to take into account: i) degradation of their inorganic core, ii) the surface-molecule substitution and molecule release (phenomenon which can be used at the advantage of the researcher), iii) the particular coating molecule reactivity, iv) NPs stability and agglomeration and the v) NPs internalization.

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