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The Origin of Nanotoxicity: Physical Damage

Mingyuan Li[1], Zhiping Li[1], Zhenbo Yang[2] and Xingguo Mei[1]*

[1]Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Beijing, 100850, PR China

[2]Pharmacy Department, No. 261 Hospital of PLA, Beijing, 100850, PR China

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*For Correspondence

Xingguo Mei, Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences , N0. 27 Taiping Road, Haidian District, Beijing, 100850, PR China, Tel: 86-01066932644

E-mail: ddsnano@126.com

INTRODUCTION

Now safety concern of *in vivo* nano-carriers toxicity is apparently hindering the extensive applications of nanotechnology in medical sciences. Many studies on the effects of nanomaterials in vitro and in vivo have been published, and revealed that nanomaterials including carbon nanotubes, fullerenes, quantum dots (for example CdS) and oxide nanoparticles (NPs) (for example ZnO, CuO and TiO2) exhibited various toxic effects on biological system. More importantly, they can cause lung inflammation, liver injury, kidney failure, or even fatality [1]. Compared with non-biodegradable nanomaterials, the same nano sized drug carriers prepared by biodegradable ones, such as albumin (Abraxane®) and phosphatides (Doxil®) used in human being approved by FDA, are fairly safe [2-4].

The physical damage is defined as a force interaction between objects that causes a structure alteration and steric hindrance of organs, cells or molecular structures, leading to the functional disorders and disability. Physical damage is basically a physical interaction between two objects rather than a chemical reaction between two molecules. The physical contacting of NPs with the organs, tissues or cells could be the cause of the damage, while oxidative stress and inflammation could be the consequences.

On a microscopic level, non-biodegradable particles can produce cell damage by physical blockage of micro-circulation, membrane structure destruction, and getting stuck in sites of macromolecules that lead to cell dysfunction and acute or chronic inflammation since they in most cases will not be involved in the metabolic process on a molecular basis [5]. The physical damage caused by nanoparticles is mainly owing to the facts that: 1) these NPs are inert and with poor solubility; 2) these NPs will accumulate in the body and locomote from one cell or tissue to another, thus causing continuous physical damages since there are no enzymatic systems in the liver or other tissues for their metabolism. Based on the above facts, we can easily access to the images of nanotubes poke through or particles stuck in cells [6]. These NPs will stay from first to last as particle, get harsh to organelles, cells and tissues and cause long-term, transferable and unpredictable damage, which is difficult to be compensated [7-10]. So unbiodegradable and incompatible NPs turn extremely danger to body. Unlike these NPs, biodegradable NPs are dragged down easily by body fluid, cell phagocytosis and enzymes digestion to participate in molecular metabolism and excreted [11]. Consequently physical damages caused by the biodegradable NPs are almost absent or reversible since the body could repair these physical damages except that the dose of NPs is out of the tolerable range of organisms. In summary, the physical damage is perhaps the main reason why there is such a big gap in toxocity between unbiodegradable and biodegradable NPs.

Physical damage plays an important role in body trauma as exhibited in **Figure 1**, and nano size is a bridge between bulk and atom or molecule [12]. The physical damages caused by various NPs (characterized by the shape, size, surface properties, and kinds of materials) can be divided into three categories according to the manner of the mechanical interactions, that is, adhesion, card inlay and puncture [13,14]. Adhesion here refers to the adherence of NPs on the target surface, which can lead to changes of membrane structures or denature of macromolecular proteins on surface. Card inlay refers to the insertion or imbedding of NPs into the active aperture or channel of large biological molecules e. g. protein channel, which is matched with NPs in size or shape.

Puncture in this commentary means that nanoparticle, due to the shape, size, and rigidity bind and then pierce the structure such as cell membranes, cell junctions and so on. All of these actions can evolve enough and cause further oxidative stress and inflammation, organ failure or other damage phenomenon.

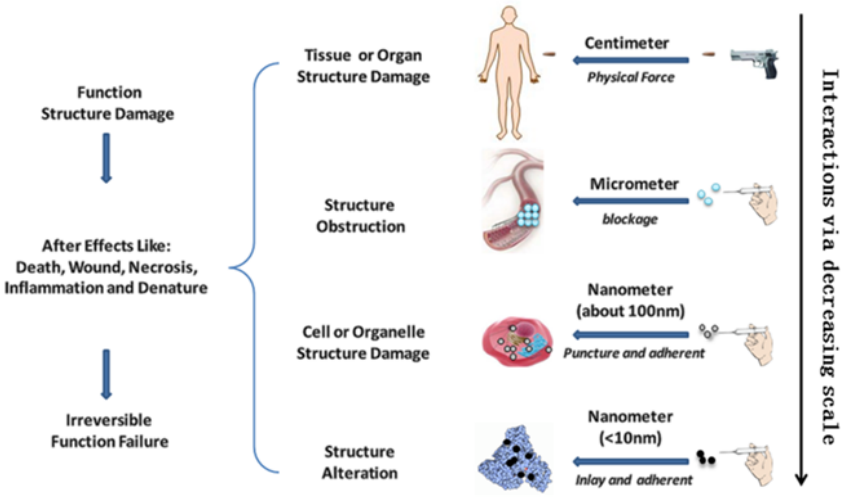

Figure 1. Physical interaction force varied from general to nano in scale, consequently, posing sabotaged function structure corresponding to its level.

In sum, physical damage including adhesion, card inlay and puncture is considered as the toxicity origin of undegradable NPs in this commentary. The perspective of physical damage in nanotoxicity is proposed first to consummate the whole theory system. When consider introducing nanomaterials in vivo, biodegradability and biocompatibility are primary demand and standpoint. Furthermore, the recognition of the origin of nanotoxicity will help us to design more effective drug delivery NPs against various diseases.

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