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Uptake and Transformation of Nanomaterials in Biological Systems Studied by Synchrotron Radiation X-ray Techniques.

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Many nanomaterials are useful in biological detection, diagnosis, and therapy for diseases and have shown great potential for biomedical applications. Therefore, the toxicity of nanomaterials becomes an increasing concern. Both *in vitro* and *in vivo* studies were applied to evaluate the biological consequences of nanomaterials. The underlying mechanisms were investigated including induction of oxidative stress, inflammation and autophagy. The intrinsic physicochemical properties of nanomaterials have a decisive influence on their biological consequences and toxicity. These properties include size, shape, surface charge, chemical composition, surface modification, metal impurities, agglomeration and dispersion, degradation, as well as formation of "protein corona". It is important to obtain a better understanding of the uptake, trafficking, pharmacokinetics, clearance, and role of nanomaterials in biological systems, so their possible undesirable effects can be avoided.

Synchrotron radiation, which is highly polarized, tunable, and concentrated over a small area, plays an indispensable role for nanotoxicology studies [1]. As an example, in our studies, the combination of ICP-MS, μ-SR-XRF and microbeam X-ray absorbance near edge structure (μ-XANES) have simultaneously provided information about the subcellular distribution and chemical species of metal-containing nanoparticles (NP) of interest [2, 3]. For *in vivo* study, both μ-XRF and μ-XANES revealed the distribution and chemical transformation of CdSe@ZnS quantum dots within *C. elegans* [3]. At a single cell level, XRF imaging shows the distribution information of copper nanoparticle inside a macrophage during cellular uptake (Figure 1).

We established techniques to image nanomaterials in single cells and found for the first time the persistent uptake and subcellular distribution of metallofullerenols in macrophages and targeted nanocarriers in cancer cells by taking advantage of synchrotron-based scanning transmission X-ray microscopy (STXM) with high spatial resolution (30 nm) [4, 5]. Figure 2 shows the uptake and intracellular distribution of Gd-containing metallofullerenols (Figure 2A, 2B) [6].

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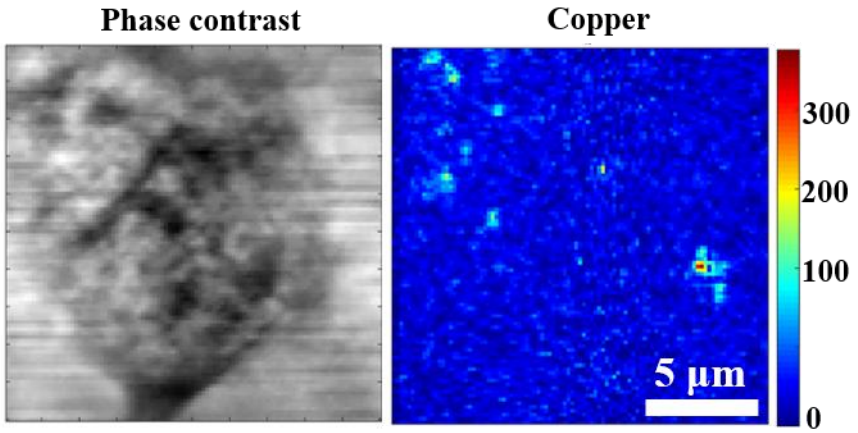

Figure. 1. XRF imaging for copper element in a macrophage when the cells are exposed to 1 µg/mL CuNPs for 6 h.

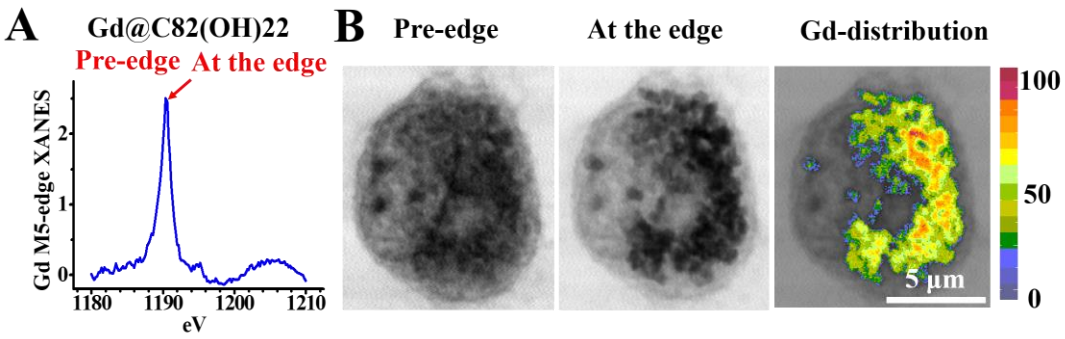

Figure. 2. STXM images of $Gd@C_{82}(OH)_{22}$ NPs in a single cell. (A) Gd M_5-edge XANES spectrum of $Gd@C_{82}(OH)_{22}$. (B) STXM imaging of Gd after the uptake of $Gd@C_{82}(OH)_{22}$ NPs by macrophages.

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