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In vitro studies for the assessment of bio-nano interactions

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Over the past two decades, the rapid application development of nanotechnology reports a massive amounts of information about dangers and benefits of using new nanomaterials. In adaptive nanomaterials science, especially for nanomaterials used in nanomedicine still have been observed some limitations. In order to ensure biosafety of newly developed nanoparticles, their unique features and advanced properties cannot be overtaken by their intrinsic toxicity [1].

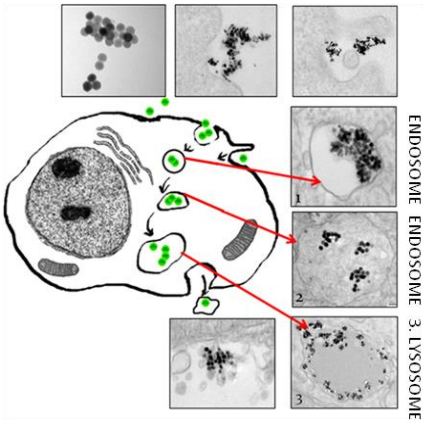

Fig. 1 TEM image of 1µg/ml β-$NaYF_4$:Yb^{3+},Er^{3+} UCNPs inside HeLa cells after 2 hours.

Up-converting nanoparticles (UCNPs) are an emerging class of inorganic optical nanoprobes doped with lanthanide ions. This type of nanoparticles under 980 nm infrared excitation have ability to up-convert long wavelength excitation radiation to short wavelength emission. The UCNPs are also widely characterized by low toxicity, low photobleaching, no visible autofluorescence in biological samples, deep tissue penetration, large anti-Stokes shifts and excellent photostability. These unique features make the nanoparticles have great potential in biomedical application such as bio-detection, drug delivery, cancer therapy or as powerful and non-invasive tool for bio-imaging [2].

The biological and functional interaction of nanoparticles with living cells are often poorly understood. The deep lack of this knowledge is caused mainly by focusing on design new nanoparticles and develop their new potential application in bio-medical field [3].

For this purpose, the all particle-cell interactions including bioavailability, cellular uptake mechanisms, in vitro fate, colocalisation and cytotoxicity of β-$NaYF_4$:Yb^{3+},Er^{3+} up-converting nanoparticles with an average diameter of 20 nm have been investigated. Understanding the interaction of nanoparticles with the cellular membrane is essential in nano-toxicology area. However, internalization of nanoparticles still remains an open question. In our in vitro studies we have analysed short and long term incubation of nanoparticles in human cells by transmission electron microscopy (TEM). The TEM images are provided for observation of a nanoscale materials much more detailed in particular at the subcellular level than conventional light microscopes.

We have observed a rapid nanopraticles' internalisation by active transport and intracellular vesicles containing nanoparticles suggest that UCNPs uptake is correlated with

endocytic pathways. The UCNPs colocalize with the selected cell organelles as early endosomes, late endosomes and lysosomes. The HeLa cells have not shown any cytotoxicity and morphological or ultrastructural changes after treatment with wide range of different UCNPs concentrations. The nanoparticles were never observed in nucleus and mitochondria or free in cytoplasm. In order to verify participation endocytosis in the internalization of nanoparticles into the cells, a number of experiments were carried out when endocytosis is inhibited by various inhibitors. Cells viability studies were also evaluated by a standard colorimetric assays which showed no relevant cytotoxicity.

In vitro studies for the assessment of bio-nano interactions to monitor cells support current and improve future therapeutic strategies with special attention to the use this type of nanoparticles. Their particular potential manifests in modern trend of theranostic which combine both diagnostic and therapeutic capabilities at the same moment.

REFERNCES

[1] H. Su, Y. Wang, Y. Gu, L. Bowman, J. Zhao, & M. Ding, *Journal of Applied Toxicology,* **38** (2018) pp. 3-24.
[2] M. K. Mahata, and K. T. Lee; *Nanoscale Adv*., **1** (2019) pp. 2372- 2381
[3] E. Wysokińska, J. Cichos, A. Kowalczyk, M. Karbowiak, L. Strządała, A. Bednarkiewicz and W. Kałas; *Biomolecules* **9** (2019), pp. 14.