"Silica nanostructures toxicity assessment and their potential for biomedical applications"

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Silica nanoparticles are widely used in various industrial fields and recently, they have been exploited also for biomedical research. The impact of SiO_2NPs on human health and the environment is thus of great interest. Nowadays, the overall evaluation of the toxicity/biocompatibility of SiO_2NPs is extremely difficult, owing to controversial results in the literature and to the lack of standard procedures and/or insufficient characterization of the nanomaterials in biological systems. Therefore the biocompatibility needs to be documented in greater detail. In this study we evaluated the toxicity of different silica nanostructures, both pure and quantum dots (QDs)- or iron oxide-doped, and studied their potential applications in gene delivery. We performed a systematic *in vitro* study to assess the biological impact of pure SiO_2NPs, by investigating 3 different sizes (Fig.1) and 2 surface charges in 5 cell lines. We analyzed the cellular uptake and distribution of the NPs along with their possible effects on cell viability, membrane integrity and generation of reactive oxygen species (ROS). We observed that all the investigated SiO_2NPs do not induce detectable cytotoxic effects (up to 2.5 nM concentration) in all cell lines (Fig.2a). Once having assessed the biocompatibility of SiO_2NPs we evaluated their potential in gene delivery, showing their ability to bind, transport and release DNA, allowing the silencing of a specific protein expression (Fig.2b)[1]. The biocompatibility of SiO_2NPs and their gene carrier performance were also evaluated and confirmed in primary neuronal cells[2]. Finally, we investigated the toxicity of silica nanoparticles doped with iron oxide nanocrystals. We tested nanoparticles with two surface charges in two cell lines by evaluating their effect on cell viability, cell membrane integrity and induction of ROS. We found that SiO_2NPs doped with iron oxide nanoparticles do not induce detectable cytotoxic effects up to 1 nM concentration (Fig.3b) with negatively charged NPs exerting the higher toxicity. This is likely associated to the nanoparticles degradation in lysosomal environment.
Overall, we demonstrate that SiO_2 nanostructures are quite safe *in vitro* and have promising potential in biomedical applications.

References:

1. M.A. Malvindi et al., *Nanoscale*, 2012, 4; 4(2), 486-495.
2. G. Bardi et al., *Biomaterials*, 2010, 31, 6555-6566.

Images:

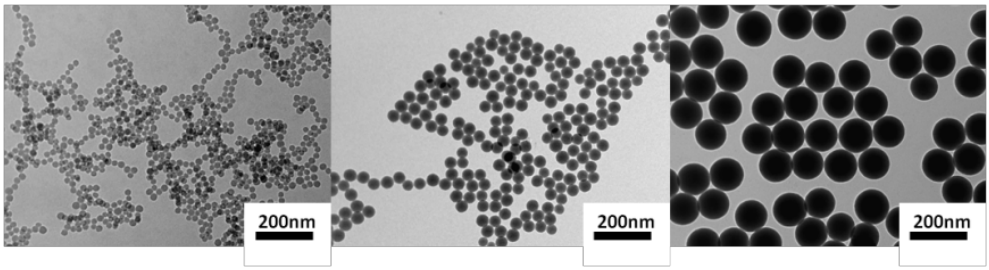

Fig.1 Representative TEM images of three sizes of SiO_2NPs: 25, 60 and 115 nm.

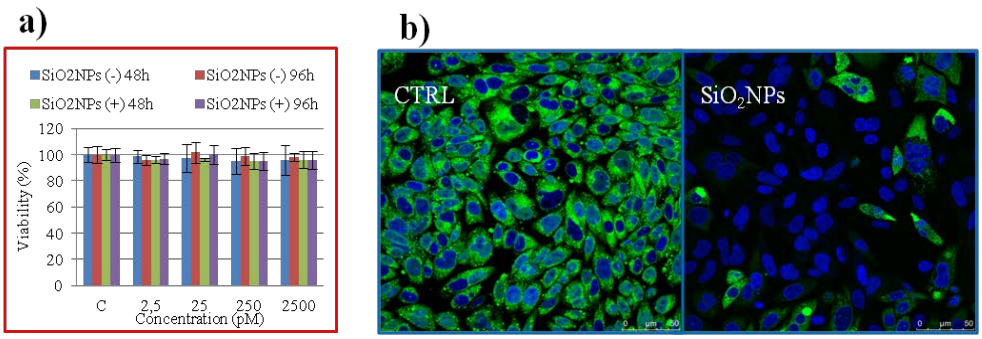

Fig.2 a) Viability of A549 cells 48 and 96 h after the exposure to increasing doses evaluated of 25 nm SiO_2NPs by the WST-8 assay; b) In v*itro* silencing of tGFP expression.

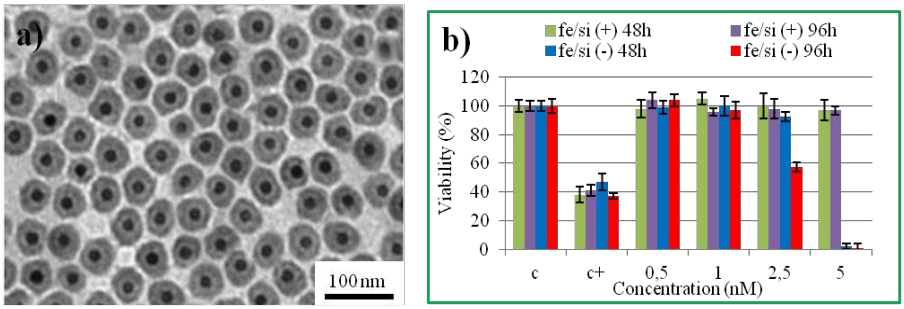

Fig.3 a) SiO_2NPs doped with iron oxide NPs; b) Viability of A549 cells 48 and 96 h after the exposure to increasing doses of SiO_2NP doped with iron oxide NPs evaluated by the WST-8 assay; c) Iron release in lysosomal environment.