International Journal of Nanomedicine

Dovepress
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ORIGINAL RESEARCH

Daphnia magna and *Xenopus laevis* as in vivo models to probe toxicity and uptake of quantum dots functionalized with gH625

This article was published in the following Dove Press journal:
International Journal of Nanomedicine
4 April 2017
Number of times this article has been viewed

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Abstract: The use of quantum dots (QDs) for nanomedicine is hampered by their potential toxicologic effects and difficulties with delivery into the cell interior. We accomplished an in vivo study exploiting *Daphnia magna* and *Xenopus laevis* to evaluate both toxicity and uptake of QDs coated with the membranotropic peptide gH625 derived from the glycoprotein H of herpes simplex virus and widely used for drug delivery studies. We evaluated and compared the effects of QDs and gH625-QDs on the survival, uptake, induction of several responsive pathways and genotoxicity in *D. magna*, and we found that QDs coating plays a key role. Moreover, studies on *X. laevis* embryos allowed to better understand their cell/tissue localization and delivery efficacy. *X. laevis* embryos raised in Frog Embryo Teratogenesis Assay-*Xenopus* containing QDs or gH625-QDs showed that both nanoparticles localized in the gills, lung and intestine, but they showed different distributions, indicating that the uptake of gH625-QDs was enhanced; the functionalized QDs had a significantly lower toxic effect on embryos' survival and phenotypes. We observed that *D. magna* and *X. laevis* are useful in vivo models for toxicity and drug delivery studies.

Keywords: membranotropic peptide, delivery, blood–brain barrier, nanoparticles, genotoxicity

Introduction

Nanotechnology is rapidly developing and new materials are being produced for a variety of applications. In particular, nanotechnology applied to medicine is expected to bring significant advances in diagnosis and treatment of diseases. The primary goal of research in this field is obtainment of platforms for specific drug delivery and targeting, and reduction of toxicity while preserving the therapeutic effects, safety and biocompatibility.[1]

Metal nanoparticles (MNPs) have been extensively used in medical and biologic research with applications in targeted drug delivery, optical bioimaging and so on.[2–5] With widespread applications, it has become fundamental to investigate their safety and, in fact, the mechanisms triggering their cytotoxicity remain mostly unclear. Toxicity is strictly dependent on internalization pathways, with intracellular aggregation and accumulation into endolysosomal compartments being the leading cause of nanotoxicity, due to nanoparticle (NP) degradation and release of metal ions. Some other possible consequences of exposure to MNPs are production of reactive oxygen species (ROS), genotoxicity and apoptosis, as well as mitochondrial damage and metallic ion production.[6] Size, shape and coating together with dose, route of administration and exposure are key factors that determine the degree of toxicity.

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http://dx.doi.org/10.2147/IJN.S127226