

Toxicity mechanism of low doses of NaGdF₄:Yb³⁺,Er³⁺ upconverting nanoparticles in activated macrophage cell lines.

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Streszczenie

Gadolinium-doped nanoparticles (NPs) are regarded as promising luminescent probes. In this report, we studied details of toxicity mechanism of low doses of NaGdF₄-based fluorescent nanoparticles in activated RAW264.7, J774A.1 macrophages. These cell lines were specifically sensitive to the treatment with nanoparticles. Using nanoparticles of three different sizes, but with a uniform zeta potential (about -11 mV), we observed rapid uptake of NPs by the cells, resulting in the increased lysosomal compartment and subsequent superoxide induction along with a decrease in mitochondrial potential, indicating the impairment of mitochondrial homeostasis. At the molecular level, this led to upregulation of proapoptotic Bax and downregulation of anti-apoptotic Bcl-2, which triggered the apoptosis with phosphatidylserine externalization, caspase-3 activation and DNA fragmentation. We provide a time frame of the toxicity process by presenting data from different time points. These effects were present regardless of the size of nanoparticles. Moreover, despite the stability of NaGdF₄ nanoparticles at low pH, we identified cell acidification as an essential prerequisite of cytotoxic reaction using acidification inhibitors (NH₄Cl or Bafilomycin A1). Therefore, approaching the evaluation of the biocompatibility of such materials, one should keep in mind that toxicity could be revealed only in specific cells. On the other hand, designing gadolinium-doped NPs with increased resistance to harsh conditions of activated macrophage phagolysosomes should prevent NP decomposition, concurrent gadolinium release, and thus the elimination of its toxicity

Słowa kluczowe

gadolinium, nanoparticles, Upconversion, Macrophages, lanthanides, fluorescent, Toxicity, cytotoxicity, Mitochondria, contrast agents

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