

## In vitro biocompatibility study of sub-5 nm silica-coated magnetic iron oxide fluorescent nanoparticles for potential biomedical application

Mario Ledda <sup>a</sup>, Daniela Fioretti <sup>a</sup>, Sabrina Foglia <sup>b</sup>, Massimiliano Papi <sup>c</sup>, Giovanna Iucci <sup>d</sup>, Giovanni Capellini <sup>d</sup>, Maria Grazia Lollo <sup>a</sup>, Settimio Grimaldi <sup>a</sup>, Monica Rinaldi <sup>a#</sup> and Antonella Lisi <sup>a#</sup>

<sup>a</sup> Institute of Translational Pharmacology (IFT), Department of Biomedical Sciences, National Research Council (CNR), Rome, 00133, Italy

<sup>b</sup> Institute of Materials for Electronics and Magnetism (IMEM), Department of Engineering, ICT and technologies for energy and transportation, National Research Council (CNR), Parma, 43124, Italy

<sup>c</sup> Institute of Physics, Catholic University of the Sacred Heart, Rome, 00168, Italy

<sup>d</sup> Department of Science, University Roma Tre, Rome, 00146, Italy

<sup>#</sup>These authors shared senior authorship

e-mail: Antonella.lisi@ift.cnr.it

Keywords: ultra-small Fe<sub>3</sub>O<sub>4</sub> nanoparticles; superparamagnetic; functionalization; nanomedicine

Nanoparticles (NPs) made up of components between 1 nm and 100 nm in size and specifically magnetic iron oxide nanoparticles (IONPs), approved by Food and Drug Administration (FDA) [1], have been extensively studied and have attracted much interest for their intriguing properties employable in a wide range of biomedical applications (Figure 1).

NPs are used for diagnosis, prevention and treatment of diseases as much as for tissue engineering and regenerative medicine applications. These implementations demand the cross communication among different disciplines for the success of new therapies in restoring and regenerating the normal function of damaged cells, organs and tissues.

The scientific rationale for the present multidisciplinary study is suggested by the need to design innovative and safe strategies to deal with human diseases.

We synthesized and characterized ultrafine 3 nm superparamagnetic water-dispersible nanoparticles, prepared by an “arrested precipitation strategy”. By a facile and inexpensive one-pot approach, nanoparticles were coated with silica to prevent their degradation/aggregation and to increase their surface functionalization, and contemporarily labelled with fluorescein isothiocyanate (FITC) dye to visualize their intracellular localization.

The resulting new sub-5 nm silica-coated magnetic iron oxide fluorescent (sub-5 SIO-FI) nanoparticles were tested in CaCo-2 cell line, a well characterized model of the intestinal epithelium, commonly used for biopharmaceutical evaluations as well in toxicity studies either as differentiated or undifferentiated cells [2].

We studied sub-5 SIO-FI nanoparticles cellular uptake and intracellular localization. Furthermore, we investigated if their uptake affected CaCo-2 cell morphology, growth, viability, cell cycle distribution, as well as transcriptional, translational and secretory activities, in a dose-dependent manner. To further shed light on their biocompatibility, the effect of the sub-5 SIO-FI nanoparticles on CaCo-2 cell differentiation and pro-inflammatory response was analysed.

Overall, these results showed the in vitro biocompatibility of the sub-5 SIO-FI nanoparticles promising their safe employ for diagnostic and therapeutic biomedical applications.

Since their magnetic nature, our nanoparticles could be easily in vivo directed toward the desired tissues/organs to shuttle drugs upon the application of an external static magnetic field. They could be used as efficient vehicles for drug/gene delivery for antitumoral therapies, enhancing the efficacy of treatments with reduced systemic toxicity. Moreover, these nanoparticles can maintain the ability to act as antennae in an external alternating magnetic field to convert electromagnetic energy into heat, to synergize the action of the shuttled drugs with hyperthermia [3].

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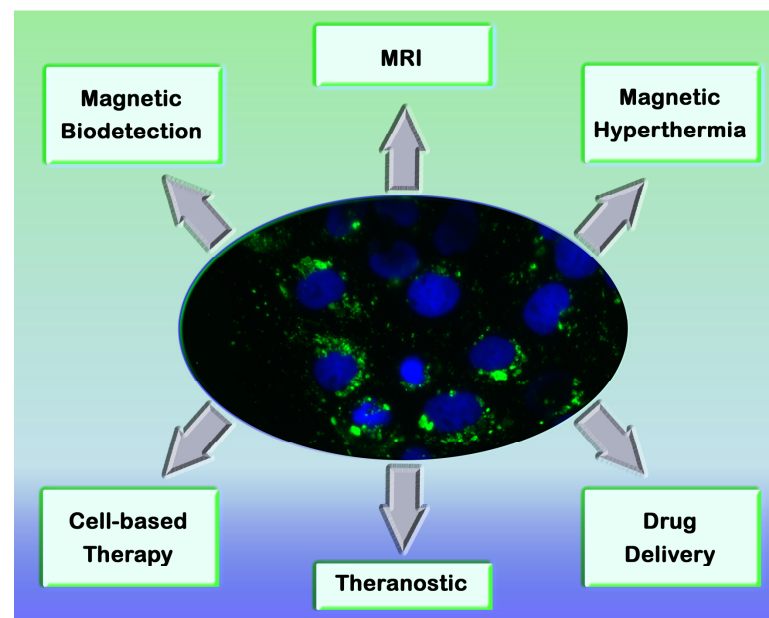


Figure 1. Magnetic nanoparticles cellular internalization and biomedical applications.