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Versatile surface engineering of ultra-small γ-maghemite nanoparticles: siRNA-mediated gene silencing applications

Iron oxide nanoparticles (NPs) have been quite widely used in numerous biotechnology applications (magnetism-driven cell separation, magnetic field-guided drug/gene delivery, non-invasive tissue MRI, and anti-cancer hyperthermia). Serious drawbacks dealing with NP fabrication, i.e., both detrimental NP aggregation and controlled NP surface functionalization versatility are extremely challenging issues calling for innovative solutions. Our recent work in the field led to the discovery of a novel method/concept for the (i) aggregation control of ultra-small hydrophilic super-paramagnetic maghemite (γ-Fe_2O_3) NPs and for (ii) its successful use for NP functionalization toward siRNA-mediated gene delivery/silencing applications. This nanofabrication method does not make use of any surface-passivating organic species. Indeed, the controlled high-power ultrasound-assisted metal Ce(III/IV) cation doping of the surface of 45/50 nm-sized (DLS) maghemite NPs strongly modified the NP surface charge to highly positive values (+41.0 - +50.0 mV range) of potential. Such a $Ce^{3/4+}$ cation-doping process enabled (i) an effective charge control of NP aggregation, (ii) the full NP water compatibility for biological applications and finally (iii) the development of quite versatile surface engineering chemistries using the known rich $Ce^{3/4+}$ complex coordination chemistry for any biomolecule or organic species (polymer) binding. This new NP "inorganic" stabilization and surface functionalization method afforded optimized (i) ultra-small core $Ce^{3/4+}$-doped γ-Fe_2O_3 NPs and (ii) various functional polycationic branched 25 kDa b-PEI polymer-based decorated NPs for siRNA/microRNA *in vitro/in vivo* delivery applications. In addition, various effective chemical strategies for NP toxicity mitigation will be described for *in-vivo* end-user applications dealing with siRNA/microRNA delivery.

Biography

Jean-Paul Lellouche received his diploma of Engineer in Organic Chemistry from the Ecole Supérieure de Chimie Industrielle de Lyon (ESCIL, Lyon, France) in 1978. He leads a laboratory dedicated to Nano(bio)technology and Polymer Science. His current R&D activities includes R&D developments in the Materials Science field interfacing with nano(bio)technology, i.e., conducting functional polymers, (b) chemically modified hard nanoscale fillers, (c) UV-photoreactive nano(micro)particles (surface nano(micro) structuration of polymeric coatings, metallic catalytic particles), (d) antibacterial organic/inorganic nanoparticles (NPs), and (e) innovative surface modifications of iron oxide (magnetite/maghemite) NPs towards gene silencing (siRNA/microRNA in vitro/*in vivo* delivery).

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