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Ultra bright magnetic nanoassemblies as theranostic agents

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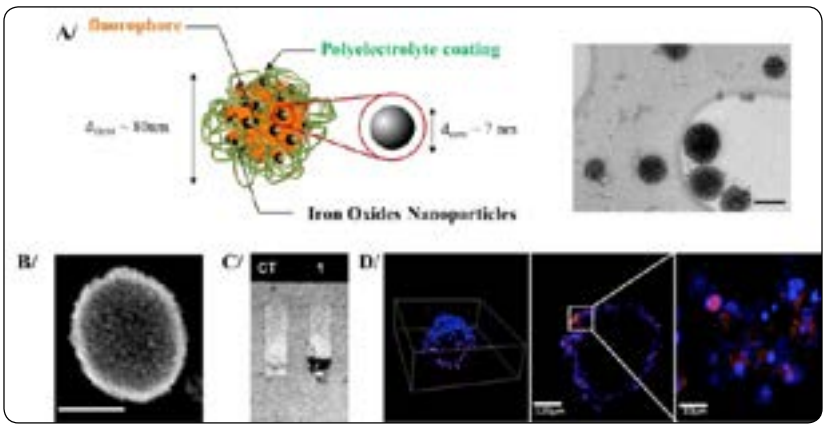
Multifunctional nanoparticles have recently emerged as promising cross-correlated contrast agents for bioimaging and carrier for drug delivery. The combination of magnetic and fluorescent units inside the same assemblies allows *in vitro* fluorescence microscopy (multiplexing, sensitivity and high resolution) and *in vivo* magnetic resonance imaging (MRI) (no penetration limit) with the same nanotools. We report a one-step synthesis to prepare core-shell architectures displaying a high payload of self-assembled magnetic and fluorescent units for improved multimodal tracking. This innovative architecture could contain drug agents for on-demand drug delivery. The multifunctional nanoparticles displayed a core-shell structure. The core consists an ultra-bright fluorescent organic nanoparticle (brightness>10^7 $mol^{-1}Lcm^{-1}$) tightly coated with superparamagnetic iron oxide nanoparticles, known as highly sensitive MRI contrast agents. The closely packed magnetic nanoparticles create strong additivity at the surface (r_2=250 $s^{-1}mmol^{-1}L$), so that large MRI T_2 contrast was obtained with unusually diluted solutions *in vitro* or after intravenous injection in small rodents. Two-photon excited fluorescence imaging could be performed, achieving unprecedented location resolution for agents combining both magnetic nanoparticles and fluorescence properties. Post-functionalization is ensured through an anionic polymer which is readily tailored to ensure furtivity (PEG chain) or active targeting (biotin, protein, etc.) via surface bioconjugation. *In vitro* studies show the importance of the polymer nature on the kinetics of cellular uptake. *In vitro* studies are performed on various cells and demonstrated the non-toxicity of our systems. Endocytosis kinetics was elucidated in mesothelium cancer cells grown as monolayers or multicellular tumor cell spheroids. Compared to numerous architectures like polymersomes or liposomes, the reported innovative nanoassemblies display *in vitro* a very high structural cohesion. The high density of magnetic nanoparticles leads to cooperative dipole effects, so that straightforward comparative investigations at various scales can be achieved using two-photon excited fluorescence imaging and *in vivo* magnetic resonance imaging (MRI).



Recent Publications

1. Faucon A, Benhelli Mokrani H, Fleury F, Dutertre S, Tramier M, Boucard J, Lartigue L, Nedellec S, Hulin P and Ishow E (2017) Bioconjugated fluorescent organic nanoparticles targeting EGFR-overexpressing cancer cells: Dual-color fluorescence correlation spectroscopy for ultra-sensitive detection and clustering upon cell interactions. Nanoscale 9:18094.
2. Linot C, Poly J, Boucard J, Pouliquen D, Nedellec S, Hulin P, Marec N, Arosio P, Lascialfari A, Guerrini A, Sangregorio C, Lecouvey M, Lartigue L, Blanquart C and Ishow E (2017) PEGylated anionic magneto-fluorescent nanoassemblies: Impact of their interface structure on MRI contrast and cellular uptake. ACS Appl. Mater. Interfaces 9:14242.
3. Faucon A, Benhelli Mokrani H, Fleury F, Dubreil L, Hulin P, Nedellec S, Doussineau T, Antoine R, Orlando T, Lascialfari A, Fresnais J, Lartigue L and Ishow E (2016) Tuning the architectural integrity of high-performance magneto-fluorescent core-shell nanoassemblies in cancer cells. J. Coll. Interface Sci. 479:139.
4. Kolosnjaj Tabi J, Javed Y, Lartigue L, Volatron J, Elgrabli D, Marangon I, Pugliese G, Caron B, Figuerola A, Luciani N, Pellegrino T, Alloyeau D and Gazeau F (2015) The one year fate of iron oxide coated gold nanoparticles in mice. ACS Nano 9:7925.
5. Lartigue L, Alloyeau D, Kolosnjaj Tabi J, Javed Y, Guardia P, Riedinger A, Péchoux C, Pellegrino T, Wilhelm C and Gazeau F (2013) Biodegradation of iron oxide nanocubes: High-resolution *in situ* monitoring. ACS Nano 7:3939.

Biography

Lartigue Lenaic has his expertise in size-controlled functionalized magnetic NPs or gold nanoshell and their incorporation in supramolecular fluorescent nano-assemblies. This multimodal nano-assembly was tested as (i) mediator for magnetic hyperthermia and photothermal; (ii) contrast agent for fluorescent imaging, MRI and photoacoustic; (iii) real-time monitoring and on-demand drug delivery system. He received his PhD in 2010 entitled: Synthesis, characterization, functionalization and biomedical applications of iron-based NPs, under the supervision of Dr. Y Guari and Pr. D Gatteschi. Then, he completed two years of Postdoctoral research in the group of Dr. F Gazeau where he studied the physical, magneto-thermal properties and the biotransformation phenomenon of iron oxide NPs. In 2012 he joined the team of Dr. D Alloyeau and synthesized, characterized and studied the biodegradation of iron oxide@gold nano-assemblies. Since September 2013, he was appointed Assistant Professor in the team of Pr. E Ishow. He has co-authored 29 scientific articles on peer reviewed international journals of Chemistry and Physics (h-index ISI Web of Science = 14) and he is currently involved in five research projects in the nanomedicine field including one as coordinator.

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