Tailoring magneto-fluorescent nanoassemblies with tunable cell interactions for sensitive and spatially resolved multimodal bioimaging

Joanna Boucard¹, Christophe Blanquart², Thibaut Blondy², Lénaïc Lartigue¹, Eléna Ishow¹

¹ Université de Nantes, CEISAM-UMR CNRS 6230, 44322 Nantes, France ²Université de Nantes, IRS-UMR CNRS 1232, 44322 Nantes, France

E-mail: joanna.boucard@univ-nantes.fr

Nanomedicine has recently appeared as a promising field of research at the interface of nanosciences and medicine, promoting the design of bright and multimodal tools for improved diagnostics in terms of reliability and drug administration follow-up. In this context, hybrid nanoassemblies, combining fluorescence and magnetism, enable interesting cross-correlated *in cellulo* and *in vivo* imaging potentialities.

We have thus built fluorescent organic nanospheres (FONs) amenable to be coated with an outer shell of iron oxide nanoparticles^[1] that can themselves complex polyelectrolytes to achieve high colloidal stability in physiological conditions. FONs display a bright and non-photobleachable emission signal that can be tailored from 610 to 675 nm. These properties make them attractive as ~100 nm-sized labelling agents for *in vitro* bioimaging. Moreover, all components (fluorescent core, magnetic shell and polymer shell) are self-assembled in a non-covalent fashion, which affords straightforward modularity according to the desired properties.

Three different fluorophores have been synthesized to generate FONs, differing by their functional moieties R (Fig. 1) in terms of hydrophilicity, hydrophobicity or metal chelating ability. FONs made out of anionic metal chelating moieties exhibited selective interactions with gram-positive bacteria that light up, whereas no such effect could be observed with fluorophores containing hydrophilic or hydrophobic moieties.

The polyelectrolyte shell around the hybrid FONs coated with iron oxide nanoparticles could be modified to study the interactions with malignant pleural mesothelioma (MPM) cells. Preferential accumulation in MPM cells was detected for nanoassemblies coated with a hydrophilic shell. Their subsequent pegylation exerted no deleterious impact on their internalization rate, making these systems attractive for further *in vivo* cancer cell uptake. All these studies pave the way toward theranostic potentialities where improved targeting and anticipated toxicity side-effects are highly requested.^[2]

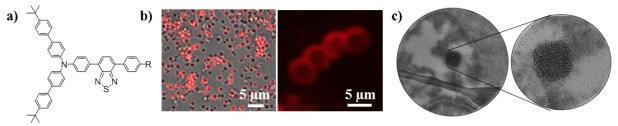


Figure 1. a) Structure of FON fluorescent precursors with variable functional group R. b) Fluorescence confocal microscopy of Staphylococcus aureus (Gram +) bacteria with anionic chelating FONs. c) TEM image of hybrid FONs in harvested mouse liver after intraveinous injection.^[3]

Funding: Région Pays de la Loire, RFI LUMOMAT, ONASSIS project.

Acknowledgement: Julien Poly (IS2M-UMR CNRS 7361, University of Haute-Alsace, Mulhouse, France), Jérôme Fresnais (PHENIX-UMR CNRS 8234, University of Paris 6, Paris, France), Marie-Pierre Fontaine-Aupart, Rym Boudjemaa (ISMO-UMR CNRS 8214, University of Paris-Sud, Orsay, France)

References:

- [1] A. Faucon et al., Phys. Chem. Chem. Phys., 2013, 15, 12748-12756.
- [2] A. Faucon et al., *Adv. Health Mater.*, **2015**, 4, 2727-2734.
- [3] A. Faucon et al., J. Mater. Chem. C, 2013, 1, 3879