SORBONNE UNIVERSITÉ

CHINA SCHOLARSHIP COUNCIL

Appel à projets
Campagne 2022
https://www.sorbonne-universite.fr

Title of the research project :

Design, synthesis and evaluation of functionalized silica nanoparticles for multim

Thesis supervisor (HDR) :

Name : DELSUC Surname : Nicolas

Title : Dr

email : nicolas.delsuc@sorbonne-universite.fr

Professional adress :
(site, dresse, bulding, office…)
ENS, Dpt of Chemistry, 24 rue Lhomond, 75005 PARIS

Research Unit

Name : Biomolecules Laboratory

Code *(ex. UMR xxxx)* : UMR7203

Doctorate School

Thesis supervisor's doctorate school (candidate's futur doctoral school) : ED406

PhD student currently supervised by the thesis supervisor (number, year of the first inscription) :

1 PhD student (2019)

SORBONNE UNIVERSITÉ

Joint supervisor :

Name : POLICAR Surname : Clotilde

Title : Pr

email : clotilde.policar@ens.psl.eu

Professional adress :
(site, dresse, bulding, office…)
ENS, Dpt of Chemistry, 24 rue Lhomond, 75005 PARIS

Research Unit

Name : Biomolecules laboratory

Code *(ex. UMR xxxx)* : UMR7203

École doctorale

Joint supervisor's doctorate school : Or, if non SU :

ED406

PhD student currently supervised by the joint supervisor (number, year of the first inscription) :

1 PhD student (2020)

Joint supervisor :

Name : BALFOURIER Surname : Alice

Title : Dr

email : alice.balfourier@ens.psl.eu

Professional adress :
(site, dresse, bulding, office…)
ENS, Dpt of Chemistry, 24 rue Lhomond, 75005 PARIS

Research Unit

Name : Biomolecules laboratory

Code *(ex. UMR xxxx)* : UMR7203

École doctorale

Joint supervisor's doctorate school : Or, if non SU :

ED406

PhD student currently supervised by the joint supervisor (number, year of the first inscription) :

0

Design, synthesis and evaluation of functionalized silica nanoparticles for multimodal imaging in unconventional modalities (IR and X-fluorescence imaging).

Bio-imaging, by enabling the visualization of biomolecules of interest, has proven to be highly informative in the study of biological processes. Although fluorescence microscopy is probably one of the most used techniques, alternative methods of imaging, providing complementary information, are emerging. In this context, metal complexes represent valuable platforms for multimodal imaging, since they may combine interesting spectroscopic features and biologically relevant functionalization on a single molecular core. In particular, d^6 low-spin rhenium tri-carbonyl complexes display unique luminescence and vibrational properties, and can be readily functionalized. Vibrational spectroscopy is attractive for bio-imaging [1–3]. As it involves no electronic transition, no photobleaching is induced, contrary to what is observed with organic fluorophores in the visible or UV excitation range (with excitation in electronic excited states whose reactivity may lead to non-fluorescent species) [4–6]. Each chemical function exhibits its own IR signature, and the IR-spectrum of a cell is the superimposition of complex IR-patterns due to the absorption of endogenous biomolecules [7]. Synchrotron-based X-ray micro-fluorescence (SXRF) and absorbance microspectroscopies have also been used for the detection of metal centers in biological samples [8,9]. Using synchrotron-based X-fluorescence microspectroscopy (SXRF-MS), the simultaneous collection of data for a large range of elements is carried out, provided their edge energy is lower than the incident energy. For both micro-spectroscopies, probes tagging specific organelles are still missing and their availability would contribute substantially to the development of these two unconventional bio-imaging techniques.

We have previously shown that $[ReCl(CO)_3(pyta)]$ can be used as multimodal probes for imaging by UV-vis fluorescence, IR and X fluorescence.[6,9–14] In the mid IR range, the CO coordinated to the Re core absorb the energy at ca 2000 cm^{-1}, an energy at which biological media are transparent (no energy absorbed). Upon excitation of the vibrational levels of the coordinated CO, the unique relaxation path is the released of heat, with no reactivity associated with electronic excited state and hence, no photobleaching of the probe.

The development of IR-probes is a real challenge in the emerging field of IR-imaging with a key issue of sensitivity. We thus want to investigate the opportunity to incorporate these $[ReCl(CO)_3(pyta)]$ into silica nanoparticles to obtain a high density of probes and hence improved significantly the sensitivity. Silica nanoparticles (SiNPs) are well spread materials that are easy to synthesize, easy to modify and are biocompatible. In this context, the aim of this research project is to design, synthesize and study silica-based nanoparticles which contain

a [$ReCl(CO)_3$(pyta)] complex for multimodal imaging, including mid IR mapping, classical fluorescence and X-fluorescence.

This thesis projects will explore different ways to prepare with high reproducibility monodisperse [$ReCl(CO)_3$(pyta)] functionalized SiNPs (ReSiNPs). We will investigate coating of the complex at the surface of the SiNPs or co-polymerization of a silica precursor functionalized with [$ReCl(CO)_3$(pyta) with tetraethoxysilane in order to reach the higher local concentration of $Re(CO)_3$. ReSiNPs will be studied in cells in order to evaluate their toxicity and sensitivity of the detection in the IR. In parallel to those studies, we will also investigate classical fluorescence imaging, as a control, and X-fluorescence synchrotron-based imaging working at the Lß-edge of Re (~10.15 and 10.28 keV), as we have previously performed with protein tagged with a similar (pyta)$Re(CO)_3$ probe.[9] We will then functionalize the SiNPs with targeting peptidyl moieties in order to achieve the targeting of specific organelles,[15–17] to provide a range of new IR and X-fluorescence dyes for bio-imaging. This project, if successful, will have a high impact for the communities involved in bio-imaging, opening new opportunities with unconventional modalities such as IR and X-fluorescence.

Provisional duration and timetable of the PhD student:

Year1:

Synthesis of various functionalized rhenium complexes and silica precursors

Preparation and optimization of silica nanoparticles. Characterization, evaluation of Re content and IR-signature

Year2

Studies in cells: optimization of the conditions for cellular experiments: size of the NPs, incubation concentration, incubation time…

Year3

Evaluation of the sensitivity in the IR and in X-fluorescence. IR-imaging and X-fluorescence mappings.

Year4

Functionalization of the surface with targeting peptides and imaging screening in cells