Carnot-Pasteur's doctoral school

PhD thesis proposal

Subject:
Metal oxide nanoparticles with a view to medical imaging and therapy: targeting of pathologies thanks to biological molecules

Laboratory:
Laboratory ICB UMR 6303 CNRS – UBFC
Nanosciences' Department/BH2N

PhD thesis supervizors:
Main supervizors: Prof. Nadine MILLOT
Co-supervizors: Dr. Julien BOUDON, Dr. Frederic BOUYER, Dr. Lionel MAURIZI

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Scientific context:
The PhD thesis will be realized within the Nanosciences' department of laboratory ICB of the university of Burgundy (Dijon, France). The successful candidate will be part of the interdisciplinary team BH2N and will work on topics ranging from the development of nanoparticles to toxicity and biocompatibility assaysin collaboration with INSERM teams and hospitals (CHU and CGFL). The objective of this thesis is the improvement of the diagnosis of different pathologies and their treatment by new nanotechnologies.
For several years, the reception team has been synthesizing nanoparticles of metal oxides. Its know-how has led to the development of nanohybrids as biological nanovectors and contrast agents. On the other hand, the team and the laboratory are very well equipped with characterization techniques and have also access to an imaging platform thanks to the CGFL (Centre Georges-François Leclerc).

Description of the scientific project:
The idea is to develop a common functionalization approach for four different types of nanoparticles by controlling the number of active molecules on the surface of the nanoparticles, to control the grafting and stabilization provided by the intermediate functionalization layers on the surface of inorganic cores.
For several years, the host team has developed several types of nanoparticles and their surface modification for various applications: titanate nanotubes with a view to anti-cancer treatment, iron oxide nanoparticles for magnetic imaging and cardiac pathologies, mesoporous silica nanoparticles for controlled drug delivery and, the newest one, tantalum oxide nanoparticles dedicated to tomodensitometry and targeting applications. But the complexity of the grafting of biological molecules (proteins, antibodies, *etc*.) requires an optimization of the surface functionalization of these nanohybrids.
Furthermore, these nanoparticles can be combined to radioelements thanks to the grafting of chelating agents (for use in nuclear imaging: SPECT or PET) and/or combined to magnetic nanoparticles, the magnetic core of which allows their use in magnetic imaging (MRI). With the latter, bimodal imaging can be simultaneously realized thanks to the PET-MRI equipment currently developed (EquipEx IMAPPI).

Finally, in close collaboration with biologists, *in vitro* studies could be realized by cytotoxicity assays on various cell lines and *in vivo* tests on mice will be considered to monitor the biodistribution of these nanohybrids by medical imaging as well as the evaluation of their imaging and therapeutic potentials.

Required skills of the candidate:

We are looking for a graduate student with an inorganic chemist profile with an interest in organic chemistry, a nanoparticle synthesis experience being preferable. The candidate must have good communication skills to work collaboratively on a subject between chemistry and biology. The PhD thesis subject is broken down into two main parts: an inorganic aspect concerning the synthesis of nanoparticles and an organic aspect required for surface modification of nanoparticles. The characterization of nanohybrids will be an important part of the thesis. Therefore, the following characterization techniques must be known, at least theoretically: TGA-MS, FTIR, UV-Vis and Raman spectroscopies, XPS, TEM, XRD, DLS, zetametry. Applicants (for whom English is not the native language) should have a good level in English to read the scientific literature of the subjects, communicate at seminars and write publications.

References:

1. *In vitro* interaction and biocompatibility of titanate nanotubes with microglial cells, S. Sruthi, A. Loiseau, J. Boudon, F. Sallem, L. Maurizi, P. V. Mohanan, G. Lizard, N. Millot, *Toxicol. Appl. Pharmacol.* 353, 74-86 (2018)
2. Cellular interactions of functionalized superparamagnetic iron oxide nanoparticles on oligodendrocytes without detrimental side effects: Cell death induction, oxidative stress and inflammation., S. Sruthi, L. Maurizi, T. Nury, F. Sallem, J. Boudon, J. M. Riedinger, N. Millot, F. Bouyer, G. Lizard, Colloids and surfaces. B, Biointerfaces, 170, 454-462 (2018)
3. Taxane-grafted metal-oxide nanoparticles as a new theranostic tool against cancer: the promising example of docetaxel-functionalized titanate nanotubes in preclinical development on prostate tumors, A. Loiseau, J. Boudon, C. Mirjolet, G. Créhange, N. Millot, *Adv. Healthcare Mater.* 1700245 (2017)
4. Influence of surface charge and polymer coating on internalization and biodistribution of PEG-modified iron oxide nanoparticles, L. Maurizi, A.L. Papa, L. Dumont, F. Bouyer, D. Vandroux, P. Walker, N. Millot, *J. Biomed. Nanotechnol.* 11, 126–136 (2015)