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 – uB
Nanosciences' Department

PhD thesis supervisors:
Main supervisor: Dr. Julien BOUDON
Co-supervisor: Prof. Nadine MILLOT

Informations de contact :
julien.boudon@u-bourgogne.fr, +33 (0)3 80 39 59 42
nadine.millot@u-bourgogne.fr, +33 (0)3 80 39 59 37
Website: ICB/Nanosciences

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 Nanosciences' department and will work on topics ranging from the development of nanoparticles to toxicity and biocompatibility assays, from the state of the art to specific tests using characterization platforms. *In vitro* and *in vivo* experiments are realized in collaboration with biological or medical research teams (O. Micheau, INSERM, C. Mirjolet, Centre Georges-François Leclerc CGFL and imaging platform, EquipEx IMAPPI).
For several years, the host team has been synthesizing nanoparticles of metal oxides. Its know-how has led to the development of nanohybrids as biological nanocarriers and contrast agents. On the other hand, the team and the laboratory are very well equipped with characterization techniques (Arcen Carnot platform).
The objective of this PhD thesis is the improvement of the diagnosis of different pathologies and their treatment by new nanotechnologies.

Description of the scientific project:
The idea is to develop a common functionalization approach for two different types of nanohybrids by controlling the number of active molecules at the surface of the inorganic cores along with their stabilization, achieved by tuning the grafting of intermediate functionalization layers.
The research team has already developed many types of nanoparticles and their surface modification for various applications and among them: titanate nanotubes with a view to anti-cancer treatment, iron oxide nanoparticles for magnetic imaging and treatment of neurological disorders and cardiac pathologies and, the newest one, gold nanoparticles dedicated to both phototherapy and immunotherapy as well as targeting applications. But the complexity of the grafting of biological molecules (proteins, antibodies, *etc*.) on these nanohybrids requires an optimization of the surface functionalizations, those being brought by customized molecules in collaboration with the institute of molecular chemistry (C. Goze, ICMuB).
Finally, in close collaboration with biologists, *in vitro* studies will 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.

This PhD thesis and its applications will be an opportunity to strengthen the collaboration started with the Belgian team of Dr. S. Penninckx (Jules Bordet's institute).

Required skills of the applicant:

We are looking for a graduate student with an inorganic chemist profile and with an interest and possibly experience in organic chemistry and/or biology, a nanoparticle synthesis experience being preferable but not mandatory. The applicant 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 as well. 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 (to 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 related to the subject:

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. Innovative Magnetic Nanoparticles for PET/MRI Bimodal Imaging, G. Thomas, J. Boudon, L. Maurizi, M. Moreau, P. Walker, I. Severin, A. Oudot, C. Goze, S. Poty, J.-M. Vrigneaud, F. Demoisson, F. Denat, F. Brunotte, N. Millot, *ACS Omega* 4, 2637-2648 (2019)
3. Titanate Nanotubes Engineered with Gold Nanoparticles and Docetaxel to Enhance Radiotherapy on Xenografted Prostate Tumors, A. Loiseau, J. Boudon, A. Oudot, M. Moreau, R. Boidot, R. Chassagnon, N. M. Saïd, S. Roux, C. Mirjolet, N. Millot, *Cancers*, 11, 1962 (2019)
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)
5. *In vivo* protein corona on nanoparticles: does the control of all material parameters orient the biological behavior? N. Singh, C. Marets, J. Boudon, N. Millot, L. Saviot, L. Maurizi, *Nanoscale Adv.*, 3, 1209-1229 (2021)
6. Titanate nanoribbon-based nanobiohybrid for potential applications in regenerative medicine, L. Maurizi, V. Bellat, M. Moreau, E. De Maistre, J. Boudon, L. Dumont, F. Denat, D. Vandroux, N. Millot, *RSC Adv.*, 12, 26875 (2022)