POSTDOCTORAL POSITION AT THE INTERFACE OF PHYSICAL-CHEMISTRY/PHOTOBIOLOGY FOR THE DEVELOPMENT OF ANTICANCER PHOTOTHERANOSTIC NANOPARTICLES

Job type: Postdocoral fellowship (funded by Lorraine Université d'Excellence (LUE))
Period: 24 months
Start date: September 2022
Salary: From 28 to 35 k€ per years

- **Information related to the host laboratories:**

Laboratories:
1. Laboratoire Lorrain de Chimie Moléculaire (L2CM, UMR 7053), http://www.l2cm.univ-lorraine.fr/l2cm/, Boulevard des Aiguillettes B.P. 70239 - 54506 Vandoeuvre les Nancy Cedex France
2. Centre de Recherche en Automatique de Nancy (CRAN, UMR 7039, http://www.cran.univ-lorraine.fr/, Campus Sciences BP 70239 54506, Vandœuvre-lès-Nancy

Description:
1. The L2CM is a mixed research unit (UMR7053) between CNRS and University of Lorraine, which integrates around 70 members geographically distributed between Nancy (Faculté des Sciences et Technologies, Campus Brabois Santé) and Metz (Institut de Chimie, Physique et Matériaux). The objectives of the laboratory are to explore and develop synthetic methods for innovative molecules and molecular materials for applications in various domains towards chemistry (drug design, catalysis), physics (energy, materials) and biology (drug delivery, imaging, therapy). These research activities are conducted within two teams (HeMaf and MolSybiO) and are supported by numerous synthesis and characterization technics integrated into internal platforms (SynBion, Photons, MassLor) and partnership.
2. Created in 1980, CRAN is a joint research unit shared by the University of Lorraine and the CNRS (attach to INS2I and INSIS). It also hosts researchers from the Lorraine Cancer Institute (ICL) and the University Regional Hospital (CHRU). The laboratory conducts interdisciplinary research associating automation, signal and image processing with biology and medicine. For several years, CRAN/ICL researchers have been conducting multidisciplinary research aimed at increasing the effectiveness of therapeutic strategies that exploit the interactions of light with biological tissue.

Supervisors of the postdoc:
Yann Bernhard (MCF, team MolSyBiO, L2CM) and Henri-Pierre Lassalle (MCF, team BioSIS, CRAN)

- **Research topic of the postdoc:**

Keywords:
Photobiology, physical-chemistry, organic nanoparticles, photophysical characterization, biological chemistry, cellular biology, nanotheranostics, photothermal therapy, fluorescence imaging, photoacoustic imaging.

Context and research objectives:
Over the last decade, photothermal therapy (PTT) have attracted increasing attention as a potential alternative to other classical therapeutic approaches. It involves molecules or nanoparticles absorbing photons upon NIR irradiation and generating heat through non-radiative relaxation pathways. To help the clinical translation of PTT, which is currently limited to a few early phase pilot trials, highly challenging research aspects concern the development of theranostic nanoparticles that provide

efficient photothermal therapeutic effect in combination with comprehensive image-guiding strategy by fluorescence/photoacoustic imaging (PAI).
Indocyanine Green (ICG) is so far the only FDA-approved dye for fluorescent application, and therefore stays on the frontline for fast pre-clinical and clinical PTT evaluation.[1] Unfortunately, at the molecular scale it exhibits limited PTT efficiency, accumulation at tumor site, and bio/photo-stability. Therefore, its formulation in supramolecular assemblies is of particular significance to improve its pharmacokinetics and PTT performances.[2,3] In this context, our group is exploiting the physico-chemical engineering of ICG into so-called J-type aggregates (i.e. Indocyanine green J-aggregates, IJA), which demonstrates better PTT efficiency and response as contrast agent in PAI, as compared with ICG.[4-8] However, because IJA quickly disassemble in complex biological media, research efforts are dedicated to the stabilization of IJA by appropriate formulation. In continuity with our ongoing research work, the project aims at 1) improve the comprehension of IJA chemical nature and structure at both molecular and self-assembled scale; 2) develop outperforming innovative IJA-based nanoparticles; 3) engineers these nanoparticles to incorporate a second fluorophore (*e.g.* commercial cyanines) for additional imaging outcomes, to targets *in vivo* intelligent fluorescent organic nanoparticles for dual image (PTT/PAI) -guided PTT strategy.

Job description:
We offer a two-years postdoc position to work on the chemical to in vivo development of ICG-based phototheranostic nanoparticles as mentioned above. Within the frame of this project, both the physico-chemical (nanoparticles formulation, chemical and photophysical analysis) and the biological (in cellulo and in vivo phototherapeutic activities evaluation) aspects will be investigated. A good expertise in photochemistry/photobiology will be required and valued by combination with high expertise in chemistry, physico-chemical engineering, photophysics and cellular/small animal biological studies of L2CM and CRAN. As a postdoctoral researcher, you will be attached to both laboratories, which are located in Vandoeuvre-les-Nancy, France. You will be supervised by Y. Bernhard at L2CM and H-P Lassalle at CRAN.

Mission and specific responsibilities: You will be responsible and/or participate to the following tasks:
- Study of the structure and nature of IJA and its degradation products at molecular and self-assembled scale using chemical analysis technics (HPLC, NMR, Mass spectrometry).
- Preparation and characterization of fully organic IJA-based nanoparticles using physico-chemical engineering (e.g. surfactant-based nanoparticles, polymeric micelles, liposomes, nanoparticles constructed by electrostatic interactions) - Bringing forward ambitious and realistic design of new theranostic nanoparticles
- Assessment of photophysical properties of nanoparticles by photophysical technics (spectroscopy, fluorimetry, photothermal production setup)
- Investigation of photothermal activity, (photo)chemical stability in biological environments, evaluation of dark/photo toxicities, cellular uptakes/localization (FaDU cancer cell model and 3D cell models).
- In vivo investigation on mouse models bearing head and neck tumors (in vivo/ex vivo distribution, photothermal treatment, imaging using bimodal fluorescence/photoacoustic imaging equipment) – A formation for in vivo working with small animal models will be provided within the postdoc.
- Participation in the supervision of PhDs, engineers, and trainees - restoring the results, communication at international conferences, participation in writing of manuscripts.

- **<u>Candidate profile and application form:</u>**

You should hold a PhD in photobiology with prior experience in cell biology and at the interface with physical-chemistry/photophysics. Additional experience in formulation/nanoparticle synthesis and characterization, fluorophore synthesis and characterization (spectrofluorimetry, HPLC) or in vivo fluorescence/photoacoustic imaging would be appreciated. Creativity, autonomy and strong reliability

are highly required, together with strong interest in multidisciplinary approach. This project will give great opportunities to develop/extend competences in photophysics, physical chemistry, cell biology and associated characterization techniques with cutting-edge equipment. You are expected to be highly motivated and possess great team spirit to take advantages to work in a leading research environment and potentially make breakthrough innovation in cancer treatments. All applicants must be able to communicate fluently in English. Applications should be sent to Yann Bernhard (yann.bernhard@univ-lorraine.fr) and Henri-Pierre Lassalle (henri-pierre.lassalle@univ-lorraine.fr). It should include a detailed CV and a cover letter highlighting how you meet the criteria.

References:

(1) Jung, H. S.; Verwilst, P.; Sharma, A.; Shin, J.; Sessler, J. L.; Kim, J. S. Organic Molecule-Based Photothermal Agents: An Expanding Photothermal Therapy Universe. *Chem. Soc. Rev.* **2018**, *47* (7), 2280–2297. https://doi.org/10.1039/C7CS00522A.

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