PhD position in Organic/Polymer Chemistry: Adaptative organic nanoparticles based on polymer-fluorophore conjugates for phototheranostic applications

Job type: 3-years PhD thesis (funded by Lorraine University)
Period: 36 months
Start date: 01/10/2022

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

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

Description:
The L2CM is a mixed research unit (UMR7053) between CNRS and University of Lorraine, which integrates around 70 members localized in 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.

Supervisors of the PhD thesis:
Andréea Pasc (Prof., team MolSyBio, L2CM) – PhD Director
Yann Bernhard (MCF, team MolSyBio, L2CM) – PhD co-director

- **Research topic of the PhD:**

Keywords:
Organic synthesis, fluorescent probes, polymer synthesis, photophysics, physical-chemistry, organic photothermal agent, stimuli-responsive polymers, 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.[1] It involves molecules or nanoparticles absorbing photons upon light-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 intelligent theranostic (i.e. combination of therapy and diagnostic) systems that provide efficient photothermal therapeutic effect in combination with comprehensive image-guiding strategy by fluorescence/photoacoustic imaging (PAI).
In this context, our group is interested in the use of Aggregation-Induced-Emission organic fluorescent dyes (AIE-dyes). These dyes present fluorescence capabilities when they are in an aggregated state, as well as heat production capability when the aggregation is reduced (because the molecular motion is permitted, favoring non-radiative relaxation pathway).[2] Therefore, they can be very effective for fluorescence imaging, or for photothermal therapy and photoacoustic imaging, depending on the aggregation state. However, alternating between these two states by transformation around the dye environment (*i.e.* switch between aggregate and non-aggregate state), to benefit from both properties in an intelligent manner, is an underexplored promising strategy,[3] which will be targeted during this thesis.

The main objective of this PhD project is to synthetize AIE-dyes and to attach them to side-chain/end-chain of stimuli-responsive amphiphilic polymers in order to obtain structures able to 1) self-assemble in aqueous solution and 2) switch between the two aggregation states as a function of the stimuli to achieve both photothermal and fluorescence properties in controlled manner. The final aim is to elaborate a polymeric one-component system capable to autonomously adapt from the diagnostic to the therapeutic needs via the state change strategy.

PhD work description:
This thesis position will be dedicated to 1) the multistep organic synthesis of fluorescent dyes with aggregation induced emission properties and bearing a functionality to attach them to polymeric carrier, 2) the preparation of polymers with tailored properties (amphiphilicity, stimuli-responsiveness) and side-chain or end-chain functionality to attach the AIEgen-dye, 3) the evaluation of self-assembly properties and characterization of the formed nanoparticles at nanoscale, 4) the evaluation of photophysical properties of dyes, dye-polymer conjugates and dyes nanoparticles, 4) the exploration of properties toward *in vivo* applications (photothermal production efficiency, photoacoustic response).
In the framework of this project, competences in organic synthesis, polymer synthesis, photophysics and physical-chemistry and associated characterization techniques will be developed. The project is focusing on a multidisciplinary research area of great interest in academia and truly represents an opportunity for highly motivated graduate students. The selected candidate will also have the opportunity to interact proactively with a network of collaborators and will have the opportunity to use modern synthesis and characterization tools.

- **Candidate profile and application form:**

You should hold a Master/engineer degree in chemistry with specialization in organic chemistry. Prior experience in polymer chemistry, fluorophore chemistry or organic nanoparticle synthesis would be appreciated. Creativity, autonomy, reliability and organization skills are highly required, together with strong interest in multidisciplinary approach. Candidates are expected to be highly motivated and possess great team spirit to take advantage of the work in a leading research environment and potentially make breakthrough innovation. Applications should be sent to Yann Bernhard (yann.bernhard@univ-lorraine.fr). It should include a detailed CV, a cover letter highlighting how you meet the criteria, and your M1/M2 (or equivalent) grades reports.

References:

(1) Li, X.; Lovell, J. F.; Yoon, J.; Chen, X. Clinical Development and Potential of Photothermal and Photodynamic Therapies for Cancer. *Nat. Rev. Clin. Oncol.* **2020**, *17* (11), 657–674. https://doi.org/10.1038/s41571-020-0410-2.

(2) Wang, J.; Li, J.; Wang, L.; Han, T.; Wang, D.; Tang, B. Z. AIEgen-Based Polymer Nanocomposites for Imaging-Guided Photothermal Therapy. *ACS Appl. Polym. Mater.* **2020**, *2* (10), 4306–4318. https://doi.org/10.1021/acsapm.0c00712.

(3) Li, J.; Wang, J.; Zhang, J.; Han, T.; Hu, X.; Lee, M. M. S.; Wang, D.; Tang, B. Z. A Facile Strategy of Boosting Photothermal Conversion Efficiency through State Transformation for Cancer Therapy. *Adv. Mater.* **2021**, *33* (51), 2105999. https://doi.org/10.1002/adma.202105999.