CNRS Ph.D. in the frame of French-Japanese International Research Project NANO-SYNERGETICS

Title: *"Nano-Synergy between fluorescent proteins and metallic nanoparticles to design new nano-probes for super-resolution imaging"*

Background: Fluorescence microscopy has become one of the most widely used techniques for in vivo imaging after the 2014 Nobel Prize for nanoscopy, which allows imaging of cells with spatial resolutions of the order of a few tens of nanometers. Reversibly photoswitchable fluorescent proteins (RSFPs) have been widely applied in super-resolved fluorescence microscopy, such as reversible saturable optical fluorescence transition (RESOLFT), a super-resolved microscopy technique that allows for a significant reduction in the illumination intensities and in photobleaching. However, their photo-physical properties are not yet optimal because it is difficult to control the brightness, the fluorescence quantum yield and the photo-switching efficiency by a directed mutation. It is therefore necessary to develop new probes and to study their photo-physical properties in order to enable their practical application in nano-imaging.

Goal: This project is based on recent results obtained by members of LASIRE (ANR BioXFEL, coll. Dr. M. Weik, CEA, IBS) that determine some intrinsic factors controlling the photo-switching parameters of RSFPs used in super-resolution microscopy (Nat. Chem. 2018, Nat. Comm. 2020). These results led to the synthesis of new mutants for nano-imaging. Moreover, members of PPSM have shown (Chem. Comm. 2014) that it is possible to modulate the photo-switching efficiency of photochromic molecules using plasmonic units. We therefore propose within this Ph.D. to develop and study novel hybrid nanoparticles based on new RSFPs and metallic nanoparticles.

Job Description: The Ph.D. deals with the synthesis of new hybrid bio-nanoparticles (RSFP-metallic nanoparticles), the characterization of their photo-dynamics (photo-conversion, brightness, study of photo-stability, multivariate analysis) as well as the enhanced resolution that is possible to reach in nanoscopy for these new NPs isolated and internalized within cells. The work covers preparation of nanomaterials and characterization by optical spectroscopy and fluorescence microscopy.

Environment: The Ph.D. thesis will be hosted in Lille in the DyNaChem team of LASIRE (http://lasir.cnrs.fr/dynachem/) which gathers spectroscopists and chemometricians interested in nanometric imaging of photo-active systems. It will be conducted in collaboration with the PPSM Laboratory (ENS Paris-Saclay), and the Dynamics and kinetics of molecular processes Group (Institut de Biologie Structurale, CEA, IBS), within the frame of the CNRS French-Japanese International Research Project NANO-SYNERGETICS (http://www.nanosynergetics.cnrs.fr/). The Ph. D. work will be directed by Dr. Michel Sliwa (DyNaChem) and co-supervised by Dr. Olivier Devos (DyNaChem) and Dr. Guillaume Laurent (PPSM). The Ph.D. student will be located in LASIRE and research stays are planned in ENS Paris-Saclay (PPSM) and in Japan (Osaka Univ., Pr. H. Miyasaka).

Candidate profile: Candidates should have a Master in (bio-)physical-chemistry with a background in photochemistry, photobiology, or optical spectroscopy. He / She should be highly motivated to work in an international and interdisciplinary project with skills in the manipulation of nanoparticles, proteins, fluorescence microscopes and optical spectroscopy.

Contract / Salary: The position is intended as full-time appointment for a duration of 3 years. The Ph. D. salary is fixed according to CNRS regulations (2135 € gross income per month). Recruitment will be done through the CNRS website (https://emploi.cnrs.fr/) for an expected starting date of October 2020.

References: J. Woodhouse, […], M. Sliwa, J.-P. Colletier, I. Schlichting, M. Weik, *Nat. Comm.*, **2020**, *11*, 741; N. Coquelle, M. Sliwa, […], M. Weik, *Nat. Chem.* **2018**, *10*, 31;; K. Ouhenia-Ouadahi, R. Yasukuni, P. Yu, G. Laurent, […], K. Nakatani, R. Métivier, *Chem. Commun.*, **2014**, *50*, 7299.

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