« PROPOSITION DE STAGE ET/OU DE THESE »

Laboratoire : ***Laboratoire d'Optique et Biosciences***

Adresse : ***Ecole Polytechnique, 91120 Palaiseau***

Directeur du laboratoire : ***François Hache***

Équipe de recherche (si pertinent) : Dynamique interne des protéines

Responsable de l'équipe : ***Marten VOS***

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N° et intitulé de l'Ecole Doctorale de rattachement : ***INTERFACES***

Profil recherché : ***formation (bio)physique ou physico-chimie avec intérêt pour biophysique moléculaire***

Possibilité de poursuite en thèse : OUI -

Si oui financement envisagé : ***bourse ED***

Titre du stage : Light-induced reaction mechanisms in flavoproteins

Résumé :

Flavins are colored cofactors of numerous proteins. They can undergo a wide variety of redox and protonation states and are therefore often involved in biochemical electron and proton relay reactions, interacting with substrate molecules and/or with the protein environment, in particular with aromatic amino acid residues. Some flavoproteins are naturally light sensitive and act as photosensors or even photoenzymes, but in many other flavoproteins light absorption leads to ultrafast non-physiological photochemical reactions that can be exploited to probe the environment and the dynamics of the active site. We develop methods using femtosecond transient fluorescence and transient absorption spectroscopy, in combination with molecular dynamics simulations, to investigate such processes in both photoactive and non-photoactive flavoproteins. Recently, we have for instance been able to characterize the extremely flexibility of the important potential drug-target enzyme ThyX (*1*) and been able to spectroscopically identify a novel instable but physiologically relevant tyrosine radical species in another flavoprotein (*2*). The present M2 project aims at an initial characterization of photochemical processes and active site dynamics in an important human protein, lysine-specific histone demethylase 1 (LSD1), a flavoenzyme that plays a role in a number of biological processes including cancerogenic cell proliferation. Tutoring for the spectroscopic aspects as well as for the biochemical aspects is provided. The associated thesis project will also aim at investigating the physiological photocycle of a recently discovered algae photoenzyme, fatty acid photodecarboxylase of potential biotechnological interest (*3*). . This project, financed by ANR, represents a number of challenging experimental hurdles, related to the irreversible nature of the photoreaction.

1. Laptenok, S. P., Bouzhir-Sima, L., Lambry, J.-C., Myllykallio, H., Liebl, U., and Vos, M. H. (2013) Ultrafast real time visualization of the active site flexibility of the flavoenzyme thymidylate synthase ThyX, ***Proc. Natl. Acad. Sci. U.S.A.*** *110*, 8924-8929.
2. Nag, L., Sournia, P., Myllykallio, H., Liebl, U., and Vos, M. H. (2017) Identification of the $TyrOH^{\bullet+}$ Radical Cation in the Flavoenzyme TrmFO, ***J. Am. Chem. Soc.*** *139*, 11500-11505.
3. Sorigué, D., Légeret, B., Cuiné, S., Blangy, S., Moulin, S., Billon, E., Richaud, P., Brugière, S., Couté, Y., Nurizzo, D., Müller, P., Brettel, K., Pignol, D., Arnoux, P., Li-Beisson, Y., Peltier, G., and Beisson, F. (2017) An algal photoenzyme converts fatty acids to hydrocarbons, ***Science*** *357*, 903-907.