# PhD thesis: Validation and optimization of new fluorogenic probes for DNA-PAINT super-resolution imaging

The emergence of super-resolution microscopies has profoundly transformed research in cell and molecular biology by making it possible to visualize structures and organelles below the light diffraction limit. The main variants, namely PALM (photoactivatable and photoconvertible localization microscopy) and dSTORM (direct stochastic optical reconstruction microscopy) super-localization microscopes are particularly efficient, allowing resolutions of about 20 to 30 nanometers. However, one of the main limitations of these approaches is the control of the stochastic blinking of the fluorescent markers. An interesting variant is the DNA-PAINT microscopy (point accumulation for topographic imaging at the nanoscale) which exploits the transient hybridization of short fluorescent DNA strands (imaging DNA strands) to a complementary strand linked to a target. The imaging DNA transiently bound to the complementary strand generates localized photon fluxes contrasting with the background noise of the diffusing molecules in the field of view. The activation / deactivation process is therefore mainly controlled by the diffusion of the imaging DNA and its dissociation constant with its complementary strand. The objective of this thesis is to reduce the background noise of the freely diffusing imager strands DNA by labelling them with fluorogenic probes, which are almost non-fluorescent in single strand DNA, but which become highly fluorescent once annealed with the target strand. This project, supported by the Agence Nationale pour la Recherche (ANR), will be carried out in Yves Mély's laboratory (Strasbourg), in collaboration with Alain Burger's team. The first objective of the candidate will be to characterize and validate these DNAs in a single molecule mode. The best fluorogenic imaging DNA strands will then be used to locate and image by DNA-PAINT a target mRNA in cellular samples.

This project is intended for a student (biophysicist, physico-chemist or biologist) who wishes to work on innovative microscopy approaches. A good knowledge of fluorescence microscopy and/or spectroscopy and a strong willingness to invest in these areas would be an asset.

Interested candidates are invited to send their i) curriculum vitae, ii) transcript of M1 and M2 marks and iii) contact information for at least one referee by email to yves.mely@unistra.fr.

Laboratoire de Bioimagerie et Pathologies (LBP) UMR 7021 CNRS
Faculté de Pharmacie
74 route du Rhin
67401 Illkirch
http://www-lbp.unistra.fr/rubrique3.html

Deadline for application: 25 May 2019.
Start date: no later than October 2019.
Duration: 3 years.
Funding : ANR fellowship.