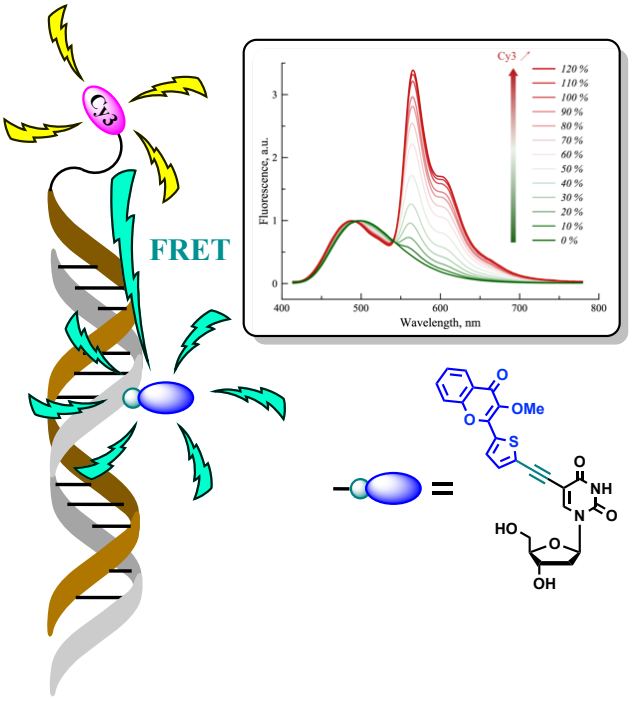
PROPOSAL FOR A RESEARCH INTERNSHIP
(Master 2R 2017-2018, 6 months)

Title of the Research Training: Development of a fluorescent assay to investigate the interactions of MITF with DNA and their inhibition

Host Team: « Bioactive Molecules Team », Direction: R. BENHIDA
Laboratory « Chemistry Institute of Nice » (ICN), UMR CNRS 7272

Proposal:

To study the interactions of DNA / protein assemblies, sensitive tools are required. In this context, our team develops different fluorescence-based approaches to investigate these interactions. Promising results were obtained with innovative fluorophores synthesized in our laboratory to circumvent the limited sensitivity of common dyes, classically employed for this purpose. Based on these emissive tools, a fluorescent assay to detect and quantify the binding of a transcription factor called MITF to its DNA target will be developed. MITF is the conductor of melanocyte homeostasis. It is involved in the development of metastatic melanoma, one of the most aggressive and deadly cancers for humans. Despite recent therapeutic advances, a large number of patients are resistant to the available treatments and therefore, relapse. This brief overview highlights the need for new therapeutic solutions. Our objective is concomitantly to propose and validate new fluorescent biosensors capable of demonstrating MITF inhibitors. Achieving this step is a prerequisite to medicinal chemist to detect drug candidates as a potential therapeutic option in the treatment of metastatic melanoma.



The research that will be entrusted to the trainee in charge of this project will consist initially in the synthesis of the emissive dyes, their incorporation into DNA and the photophysical characterization of the labeled sequences. The resulting fluorescent probes, presenting the most appropriate spectroscopic properties for the development of an efficient biosensor, will then be used to detect MITF inhibitors. The implementation of this fluorescent assay will correspond to the second part of his work.

Used techniques: Organic Synthesis, Standard Purification (Flash & HPLC), NMR, UV, Fluorescence

Technical skills: The applicant should be a motivated organic chemist with good knowledge in synthesis and structural analysis (NMR, MS). A first background in laboratories (extraction, chromatography…) as well as an interest for the interface of chemistry with biology would be appreciated.

Keywords: Organic Synthesis – Heterocycles – Nucleosides – DNA –UV/Fluorescence Characterization
Manager(s) of the training: Prof Alain BURGER & Dr Benoît MICHEL

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Possible subsequent PhD financial support: Various fellowships
Salary during the research period: 520 euros per month (for 6 months, from January 2018)
Supporting Program: Grant IDEX Academy 4 « Complexity and diversity of living organisms : Dual Master Funding »