

Sujet de stage de Master 2 Recherche (Année 2023/2024)

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NMR study of G-quadruplex motifs in a context of malaria control

Résumé du projet

Guanine-rich DNA and RNA sequences can fold into non-canonical four-stranded secondary structures called G-quadruplexes (G4). The genome of the *Plasmodium falciparum* parasite responsible for malaria is characterized by an extremely AT-rich sequence (>80%). However, some regions of the parasite genome have the potential to form G4 structures. In addition, certain G4-specific ligands show high effective activity against parasite, causing a drastic reduction in the mitochondrial DNA copy relative to the overall amount of parasite genomic DNA. As part of an ANR project (D. Gomez, IPBS & F. Benoit-Vical, LCC), we aim to develop new ligands as antimalarial drugs acting by stabilizing the G4 structures present in the mitochondrial genome of *Plasmodium falciparum*.

The aims of the internship will be to use ^1H NMR to monitor G4 structuring of DNA sequences present in the mitochondrial genome of *Plasmodium falciparum*. We will then study the ability of these sequences to bind G4s ligands *in vitro*, using two main techniques (NMR and ITC calorimetry). ^{19}F and Thallium NMR experiments (Coll. P. Berthault, CEA) are also envisaged.

Skills to be acquired during the internship

- Recording of proton NMR spectra (600 and 700 MHz spectrometers)
- Assignment of ^1H NMR spectra of oligonucleotides
- NMR titration experiments (NMR plateau, CEA Saclay) and ITC calorimetry (PIM platform, Orsay).

Team references on the topic

Kotras, C., Fossépré, M., Roger, M., Richeter, S., **Gervais, V.**, Gerbier, P., Ulrich, S., Surin, M., and Clément S. (2019) A cationic tetraphenylethene as a light-up supramolecular probe for DNA G-quadruplexes, **Frontiers in Chemistry**

Drozd, W., Walczak, A., Bessin, Y., **Gervais, V.**, Cao, X. Y., Lehn, J. M., Ulrich, S., and Stefankiewicz, A. R. (2018) Multivalent Metallosupramolecular Assemblies as Effective DNA Binding Agents. **Chemistry** 24:10802-10811

Gervais, V., Campagne, S., Durand, J., Muller, I., and Milon, A. (2013) NMR studies of a new family of DNA binding proteins: the THAP proteins. **J. Biomol. NMR** 56: 3-15