Post Doctoral fellow position in Chemical Biology of Nucleic Acids

A two-years post-doctoral position is currently available in the laboratory of Chemistry, Modelling and Imaging for Biology (CMIB) In the team of Dr. Marie-Paule Teulade-Fichou (http://CMIB.curie.fr) Institut Curie. The laboratory is located at the research center of the Institut Curie on the campus of Orsay (Paris-Saclay University- south of Paris, France). Read more ...

Our group works on the design of compounds targeting non-B nucleic acid structures and certain kinases involved in cancer. The group has a broad expertise in bio-organic chemistry and optical spectroscopy with a strong background in supramolecular chemistry and molecular recognition. Our final aims are to open new perspectives in the discovery of anticancer drugs and mechanistic tools.

Context : Our current interest is focused on the design of new nucleic acid targeted compounds for anticancer research and for elucidating DNA-related molecular basis of cancer. It is well recognized that DNA sequences containing repeats of heterocyclic bases are highly susceptible to aberrant replication and perturbation of other DNA-related processes such as recombination and transcription. These dysfunctions may lead ultimately to modifications of the genetic material) and may have a role in explaining mechanisms linked to cancer development or more largely be involved in pathogenic rearrangements genome-wide. Repeat-containing DNA
domains are highly prone to form non-canonical secondary structures due to self-assembly of bases via various H-bonding modes (mismatched pairs, base-triplets or quartets). The generated structures (mismatched sites, hairpins, triplex, quadruplex) are known (for some) or suspected (for others) to be involved in genetic instability and in pathogenic dysfunctions. 

**Our team is interested** in the recognition of these non-canonical structures locally formed in DNA by means of specifically designed small molecules (i.e. ligands) that will bind the target structure with high specificity. The primary objectives of this research are two-folded, firstly to provide structure probes usable in various in vitro and cellular models for exploring the polymorphism of DNA; secondly to provide functional probes reporting or acting on the target structure (fluorescent signalling, covalent crosslinking). Of note the design and synthesis of targeted fluorescent molecules compatible with cellular imaging represents a subtopic of our research tightly intertwined with the structure-targeting topic. The final objectives of this research are to create new chemical biology tools for studying and controlling the formation of the target structures as well as their processing by proteins. Ultimately we aim at the discovery of better targeted (regiospecific) DNA interactive agents that may become clinical drugs for anticancer chemotherapy.

**Our specific approaches** towards the identification of active scaffolds are based on rational design (shape complementarity- topology adaptation) and on screening methods. Thus we developed home-made assays amenable to high-throughput screening. These are combined with the use of state of the art optical spectroscopy (UV-Vis, fluorescence, circular dichroïsm) and biochemical methods (gel electrophoresis, pull down assay) for quantitative evaluation of NA-ligands interactions. We also intend to a deep understanding of non-covalent interactions at the atomic level by means of molecular modelling analyses.

**Publications clés**

Année de publication : 2019


**Probing Ligand and Cation Binding Sites in G-Quadruplex Nucleic Acids by Mass Spectrometry and Electron Photodetachment Dissociation Sequencing**
*bioRxiv* : Early view : [DOI : 10.1101/563627](https://doi.org/10.1101/563627)


**Mannose distribution in glycoconjugated tetraphenylporphyrins governs their uptake mechanism and phototoxicity**
Sondes de structures et sondes photoactivables pour les acides nucléique et les kinases

UMR9187 / U1196 – Chimie, modélisation et imagerie pour la biologie

Morgan Pellerano, Delphine Naud-Martin, Florence Mahuteau-Betzer, Marie Morille, May Catherine Morris (2019 Feb 15)

**Fluorescent biosensor for detection of the R248Q aggregation-prone mutant of p53.**


El Hassen Mokrani, Abderrahmane Bensegueni, Ludovic Chaput, Claire Beauvineau, Hanane Djeghim, Liliane Mouawad (2019 Feb 7)

**Identification of New Potent Acetylcholinesterase Inhibitors Using Virtual Screening and In Vitro Approaches.**

*Molecular informatics* : Early view : [DOI](https://doi.org/10.1002/minf.201800118)

Coralie Caron, Xuan N T Duong, Régis Guillot, Sophie Bombard, Anton Granzhan (2019 Feb 6)

**Interaction of Functionalized Naphthalenophanes with Abasic Sites in DNA: DNA Cleavage, DNA Cleavage Inhibition, and Formation of Ligand-DNA Adducts.**


Delphine Naud-Martin, Corinne Landras-Guetta, Daniela Verga, Deepanjan Ghosh, Sylvain Achelle, Florence Mahuteau-Betzer, Sophie Bombard, Marie-Paule Teulade-Fichou (2019 Jan 26)

**Selectivity of Terpyridine Platinum Anticancer Drugs for G-quadruplex DNA.**

*Molecules (Basel, Switzerland)* : 24 : 404 : [DOI](https://doi.org/10.3390/molecules24030404)