Chemistry and Modelling for Protein Recognition

UMR9187 / U1196 – Chemistry and Modelling for the Biology of Cancer (CMBC)

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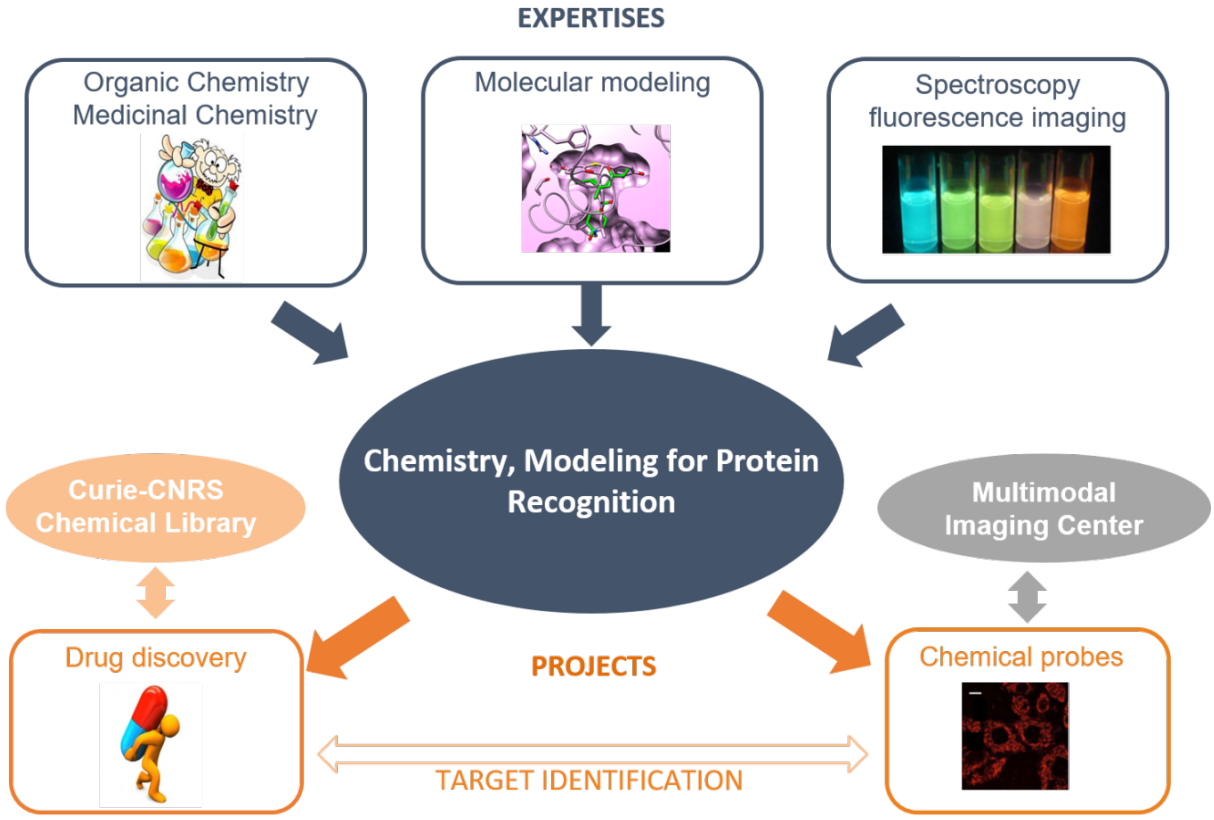
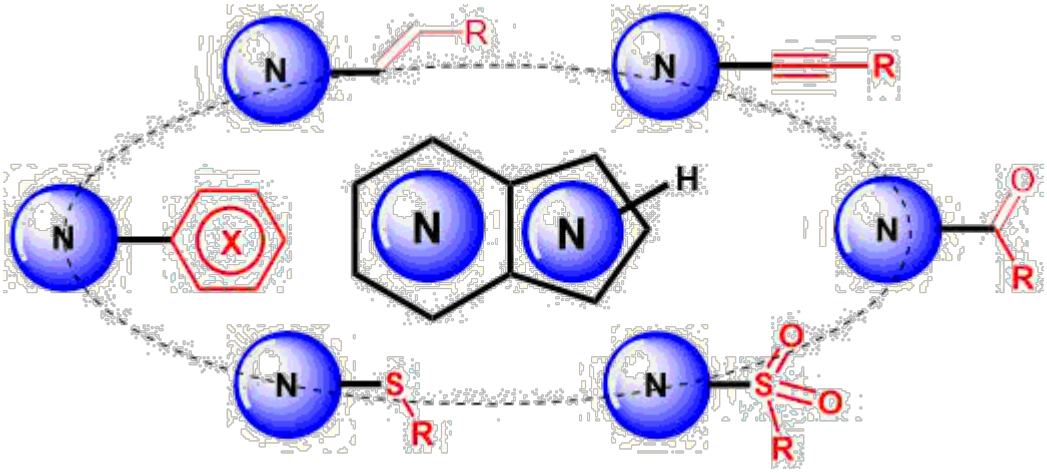
Our scientific goal is to provide, via organic chemistry and synthesis, small molecules as druggable candidates and chemical tools for a better understanding of biological processes in the field of cancer. The discovery of new molecules interacting with living organisms benefits from the team's expertise in modeling and molecular dynamics.

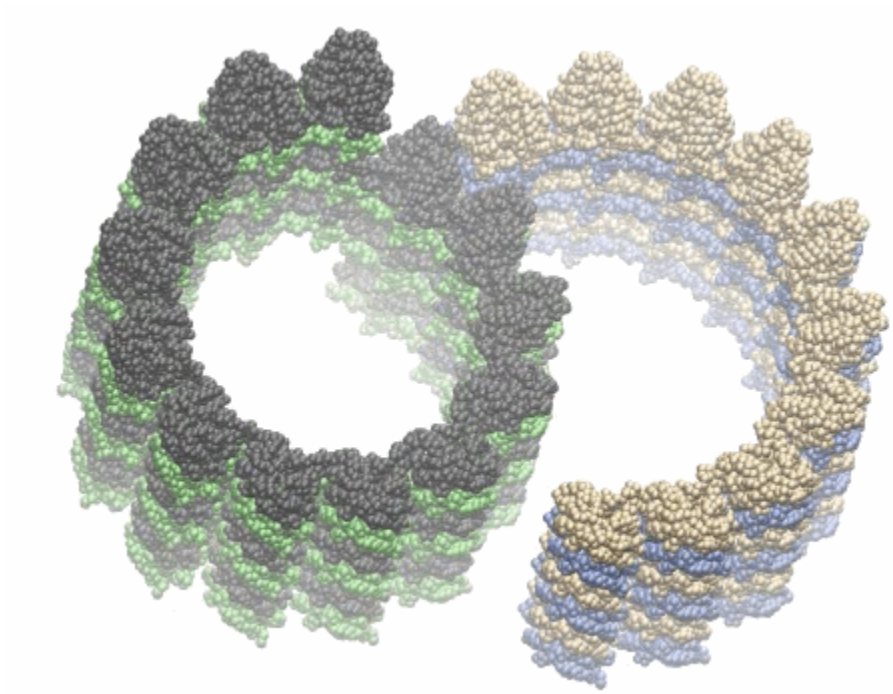


In parallel with these drug discovery projects, we are continuing to develop and optimize methods in organic chemistry in order to introduce molecular diversity and open new chemical space and on normal modes in order to implement...



Thanks to the drug discovery expertise acquired through the collaboration with the biotech Abivax and through the development of ATP competitive kinase inhibitors, the team is developing medicinal chemistry on innovative projects in oncology in collaboration with biologists from Institut Curie. Our research focusses on non-ATP competitive inhibitors of kinase of the TAM family and on a receptor coupled to protein G identified as a potential target of melanoma. For these goals, the screening of the Curie-CNRS chemistry library is an asset to identify hits that require further hit-to-lead optimization.

The questions of subcellular detection, localization and quantification in cellular medium of small molecules are crucial in their development as chemical tools or as drugs. Therefore, we also pursue our efforts on development of new fluorophores for cellular subcompartments labelling as well as biosensors for protein labeling.



Internal motions of a microtubule doublet.
Flagellar microtubule doublet (MTD) assembly *in vitro* reveals a regulatory role of tubulin C-terminal tails. In support of the *in vitro*experiments, we performed molecular simulations that showed that all MTD tails are not equivalent in this regulation (Science 363, 285-288 (2019)). In the movie presented here, we display four essential motions of MTD in the absence of the tubulin tails. These motions correspond to the four lowest-frequency normal modes.

Key publications

Year of publication 2020

Breton-Patient C., Naud-Martin D., Mahuteau-Betzer F., Piguel S. (2020 Oct 14)
Three-component C-H bond sulfonylation of imidazoheterocycles via visible-light organophotoredox catalysis.
European Journal of Organic Chemistry : Accepted Article : DOI : 10.1002/ejoc.202001219

Marchand A., Beauvineau C., Teulade-Fichou M.P., Zenobi R. (2020 Oct 14)
Competition of ligands and the 18-mer binding domain of the RHAU helicase for G-quadruplexes – orthosteric or allosteric binding mechanism?
Chemistry – A European Journal : Accepted article : DOI : 10.1002/chem.202004040

Leandro H. Zucolotto Cocca, Luis M. G. Abegão, Lucas F. Sciuti, Roxane Vabre, Jonathas de Paula Siqueira, Kenji Kamada, Cleber R. Mendonca, Sandrine Piguel, and Leonardo De Boni (2020 Jun 11)
Two-Photon Emissive Dyes Based on Push–Pull Purines Derivatives: Toward the Development of New Photoluminescence Bioprobes
The Journal of Physical Chemistry C : 124 : 12185-12864 : DOI : 10.1021/acs.jpcc.0c01859

Rahima Chennoufi, Ngoc-Duong Trinh, Françoise Simon, Guillaume Bordeau, Delphine Naud-Martin, Albert Moussaron, Bertrand Cinquin, Houcine Bougherara, Béatrice Rambaud, Patrick Tauc, Céline Frochot, Marie-Paule Teulade-Fichou, Florence Mahuteau-Betzer & Eric Deprez (2020 Apr 23)
Interplay between cellular uptake, intracellular localization and the cell death mechanism in triphenylamine-mediated photoinduced cell death
Scientific Reports : 10 : 6881 : DOI : 10.1038/s41598-020-63991-9

Julie Le Bescont, Chloé Breton-Patient et Sandrine Piguel (2020 Apr 16)
Unconventional Reactivity with DABCO-Bis(sulfur dioxide): C–H Bond Sulfenylation of Imidazopyridines
European Journal of Organic Chemistry : 2020 : 2101-2109 : DOI : 10.1002/ejoc.202000112

Year of publication 2019

Mouawad L., Beswick V., Jamin N., Montigny C., Quiniou E., Barbot T. (2019 Dec 18)
Deciphering the mechanism of inhibition of SERCA1a by sarcolipin using molecular simulations
bioRxiv : DOI : 10.1101/2019.12.17.879825