Master « In Silico Drug Design »

Second Year

OFFER AN INTERNSHIP
Academic Year 2016/2017

Send to Mrs Pr Camproux
anne-claude.camproux@univ-paris-diderot.fr

Name of the head of laboratory or company: Prof. Maurizio Sironi

Adress : Via Golgi 19, 20133, Milano

E-mail : maurizio.sironi@unimi.it

Name of training supervisor: Dott. Stefano Pieraccini

Phone number : +390250314248
Fax : +300250314300
E-mail : stefano.pieraccini@unimi.it

Specialty training : Research x☐ Professional ☐

a few key words to describe the subject of training : tubulin, binuclear compounds, protein-protein interactions, antibody-drug conjugates.

Title of internship: Molecular modeling of binuclear tubulin targetting compounds

this subject is a first step towards a thesis: No

Short texte describing your project

Microtubules are the target of many anticancer drugs that exert their cytotoxic action during the cell-division process. Molecules such as Taxol, vinca alcaloids, colchicinoids and other compounds interfere with microtubule dynamic instability, either by stabilizing or destabilizing them. Despite the excellent results obtained with these drugs, their success has been limited by the onset of multidrug resistance in tumour cells during the treatment and by the significant adverse effects. The combination of drugs often provides enhanced efficacy and reduced the development of adaptive resistance compared to monotherapies. In this context, bifunctional drugs, whose components bind to separate sites allowing a multiple effect and increasing their pharmacological activity, represent an interesting and promising class of tubulin targetted agents. In particular, bivalent compounds formed by two tubulin targeting molecules connected by a linker could have a great pharmacological potential. The internship project aims at the design of vinblastine based binuclear compounds active as microtubule destabilizing agents. In particular, vinblastine and modified vinca alkaloids will be *in silico* linked to different microtubule destabilizing agents whose binding site is located in close proximity to the vinca site, and the binding performances of the obtained hybrid compounds, as well as the linker effect, will be evaluated by docking and molecular dynamics simulations. The

possibility of the conjugation of this class of molecules with antibodies and the required chemical modifications will be also considered.

Send by e-mail : anne-claude.camproux@univ-paris-diderot.fr