Research Doctorate (Ph.D.) in Chemical Sciences
32nd Cycle – Academic Year 2016/2017

Tutor:

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Project Information

1 - Title

Structural and thermodynamic characterization of the protein-ligand interaction for a rational design of new compounds with enhanced ability to modulate the activity of two crucial target proteins, such as CDC25B and prothrombin.

2 - Key words

Cancer, Thrombosis, Crystallography, Calorimetry, Drug-design

3 - Abstract

The objective of the project is the design based on structural data of highly effective ligands of two proteins involved in severe human diseases. Indeed, the research, focused on CDC25B phosphatase and prothrombin, is aimed at discovering/assessing possible selective therapeutic and diagnostic applications. CDC25 phosphatases play critical roles in the regulation of the eukaryotic cell cycle. Due to their overexpression and correlation with poor prognosis in many diverse cancers, CDC25 phosphatases are attractive targets for anticancer drug development. An analysis of the interaction between CDC25B and both reversible and irreversible inhibitors, which already displayed efficacy against melanoma cells, is in program.

Furthermore, a characterization of the binding between prothrombin and DNA-aptamers will be performed. Prothrombin is the precursor of thrombin, the key enzyme in the blood coagulation. A way to control coagulation is to inhibit prothrombin activation by prothrombinase, by using bi-modular aptamers against prothrombin. The study on both proteins includes a combined spectroscopic, calorimetric and crystallographic approach.