PROTEO
FONCTION | STRUCTURE INGÉNIERIE DES PROTÉINES

CONFÉRENCE

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Mercredi le 27 avril 2011 à 9h30
Auditorium COPL (salle 1168)
Centre d'optique, photonique et laser, Université Laval

An Example of a Challenging Drug Discovery Chemical Space: Protein-Protein Interfaces

Successes in inhibiting Protein-Protein Interaction (PPI) depend on several constraints such as biophysical parameters (size of the interface), conceptual parameters (existence of 'reference' compounds) and chemical parameters (chemical space/specific databases available). One of the main impediments in the drug discovery process targeting this type of interface relates to the absence of specific databases. This obstacle certainly represents an exciting challenge, in the next decade, for the chemo-informatic community and for medical application purposes.

Our group is mainly focusing on the **analysis of the basic principles and parameters that govern protein-protein recognition**. This fundamental research has permitted us to i) develop innovating protocols allowing PPI inhibitions, such as the 2P2I approach[1] and ii) to analyze and classify PPI's to eventually propose **focused databases** dedicated to this attracting class of targets[2].

This conference will focus in a first on the particular chemical space that represent PPI's and on the possibility to cluster protein-protein interfaces and thus to consequently propose new focusing databases. We will highlight in a second part of the conference recent successes in Protein-Protein inhibition and demonstrate the importance of taking into account molecular motions in the hit identification process.
We will give some insights to these challenging questions:

- Can we define chemical databases dedicated to PPI's?
- Can we extract druggable from non druggable interfaces?
- Is the Ro5 a barrier to further PPI inhibitors development?
- What are the next challenges for Structure-based Drug Design?

1- Betzi, S., Restouin, A., Arold, ST., Parrot, I., Guerlesquin, F., **Morelli, X***. and Collette, Y*. (2007) *Protein-Protein Interaction Inhibition (2P2I) combining High Throughput and Virtual Screening: Application to the HIV-1 Nef protein.* Proc Natl Acad Sci U S A. 2007 Dec 4;104(49):19256-61.

2- Bourgeas, R., Basse, MJ. **Morelli, X*.** and Roche P*. (2010) Atomic Analysis of Protein-Protein Interfaces with Known Inhibitors: The 2P2I Database. PLoS ONE 5, e9598

Cordiale bienvenue à toutes et à tous!

Hôtes : Patrick Lagüe (PROTEO) et Jacques Corbeil (CRCHUL)