**Laboratoire de Biochimie Théorique**
**I**nstitut de **B**iologie **P**hysico-**C**himique
13, rue Pierre et Marie Curie
75005 PARIS

# *S E M I N A I R E*

## Marc Bianciotto

Sanofi, Vitry-sur-Seine, France

**« Getting to know a biological target : about the structural plasticity of HSP90 and binding kinetics with its ligands »**

Heat Shock Protein 90 (HSP90) is a chaperonne protein which is a major biological target in oncology. In it's N-terminal domain, an ATP-binding pocket is known to be the binding site of several classes of candidate drugs currently in clinical trials, and the clinical efficiency of N-HSP90 ligands have been related to their optimal binding kinetics rather than thermodynamics. It is why we studied this protein in the context of the Kinetics for Drug Discovery (K4DD) consortium. In this talk we will describe the conformational diversity of N-HSP90 bound structures and relate it with the binding kinetics of HSP90 inhibitors from several chemical series. We will present the results of ScaledMD simulations on 27 ligands binding to two different conformations of the human N-HSP90. We propose new analyses of the ligand exit trajectories focusing either on the early or on the late stages of the unbinding event, which provide insight on the factors influencing protein-ligand binding kinetics and possible caveats in its simulation.

## Jeudi 6 février 2020
## 14h30

## SALLE DE CONFERENCE