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S E M I N A I R E

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Discriminating agonist and antagonist ligands of the Nuclear Receptors using docking and pharmacophores predictions

Nuclear receptors (NRs) are transcription factors naturally switched on and off by small-molecule hormones that monitor a wide range of physiological key functions. A large amount of compounds have been proposed to modulate the activity of NRs, some of them are still marketed, whether to activate (agonist ligands) or inhibit (antagonist ligands) the activity of one or more NRs. The drug discovery process is thus not limited to the search of the best ligand of a given target, but consists in the search of a ligand with a pharmacological profile that his compatible to its target. In this context, the ability to predict the agonist or antagonist behaviour of a NR ligand is of major importance. Despite the elucidation of the molecular bases of agonism and antagonism [1] and several prediction attempts using molecular modeling tools [2-4], discriminating agonist and antagonist ligands based on their sole structure remains a challenge. The performance evaluation of a docking method (Surflex dock [5]) and a 3D pharmacophore modeling method (LigandScout [6]) to discriminate agonist activity from antagonist activity on a public benchmarking dataset dedicated to NRs (NRLiSt BDB [7]) will be presented.

Jeudi 21 avril 2016 - 14h30

Salle de conférence

Bibliographic references:

[1] **Bourguet, W.; et al.** ***Trends Pharmacol Sci*****, 2000. 21(10): p. 381-8**

[2] **Ekins, S.; et al.** ***Journal of Computational Medicine,*** **2013. vol. 2013, Article ID 513537, 8 p**

[3] **Ng, H.W.; et al.** ***BMC Bioinformatics,*** **2014. 15 Suppl 11:S4**

[4] **Politi, R.; et al.** ***Toxicol Appl Parmacol*****, 2014. 280(1):p. 177-89**

[5] **Jain, A. N.** ***J Med Chem,*** **2003. 46(4),:p. 499−511**

[6] **Wolber, G.; Langer, T.** ***J Chem Inf Model*****, 2005. 45(1):p. 160-9**

[7] **Lagarde, N.; et al.** ***J Med Chem*****, 2014. 57(7): p. 3117-25**