Analysis of potential androgenic effect of a large set of environmental chemicals based on docking approaches.

Dafniet, B.,[1*] Petitjean, M.,[1] Audouze, K.,[2] Taboureau, O.[1*]
[1] *Equipe CMPLI, Unité INSERM U1133, Unité de biologie fonctionnelle et adaptative (CNRS UMR 8251), Université Paris Diderot Paris 7, 35 rue Hélène Brion 75013, Paris, France*
[2] *Groupe SysTox, Equipe METATOX, INSERM UMR-S 1124, Université de Paris, Paris, France*

*Corresponding authors: *bryan.dafniet@univ-paris-diderot.fr, olivier.taboureau@univ-paris-diderot.fr*

The androgen receptor (AR) is a nuclear receptor that plays an important part in the development of male primary and secondary sex characteristics as its main ligands are testosterone and dihydrotestosterone[1]. Perturbation of AR function is recognized to play a role in diseases such as prostate cancer, Kennedy's disease, androgen insensitivity syndrome and endocrine disruption[2].

In this study, we decided to assess the androgenic effect (agonist or antagonist) of a large set of environmental chemicals (55k) using *in silico* approaches as a potential nontesting alternative method for predictive toxicology. Receptors co-cristallized with steroid-like compounds and selective androgen receptor modulators (SARM)[3] have been selected from the PDB (6 X-rays in total) and virtual screening with Autodock Vina[4] of agonist and antagonist compounds mixed with inactive ones has been performed to suggest chemicals with androgenic effect and also to determine keys residues in the mode of binding. The software was able to sort correctly the agonist compounds in 3 out of the 6 PDB tested. The 3 receptors giving the worst results were the ones co-crystallized with the SARM. We also tested, with the same protocol, the impact of two SNPs within this dataset to see if the mutations were inducing or preventing a possible interaction with these 55 000 compounds. The results of the virtual screening obtained on the wild-type and mutated AR will be discussed on the poster.

References:

[1] Sinisi A.A. ; Pasquali D., et al. J. Endocrinol. Investig., 2003, 26 (3 Suppl), 23–28
[2]Eisermann K., Wang D., et al. Transl. Androl. Urol. 2013 2, 137–147
[3] Mohler M.L., Bohl C.E., et al. J. Med. Chem. 2009 52 (12), 3597-3617
[4] Trott, O., Olson, A.J., J. Comput. Chem. 2010, 31, 455-461