MODELLING THE INTERACTION OF STEROID RECEPTORS WITH ORGANIC POLYCHLORINATED COMPOUNDS

Pasqualina D'Ursi[a], Erika Salvi[a], Paola Fossa[b], Luciano Milanesi[a], Ermanna Rovida[a] and Luisa Mosti[b]

[a]CNR - Istituto di Tecnologie Biomediche, Via Fratelli Cervi 93, Segrate (Mi) – Italy
[b]Università di Genova - Dipartimento di Scienze Farmaceutiche,Viale Benedetto XV 3, Genova - Italy

The organic polychlorinated compounds like dichlorodiphenyltrichloroethane (DDT) with its metabolites (p,p'-DDT, o,p'-DDT, p,p'-DDE and p,p'-DDD), polychlorinated biphenyls (PCBs) and, more recently, polybrominated diphenyl ethers (PBDEs) are present in atmospheric particulate as persistent contaminants. They have been recognized to have detrimental health effects both on wildlife and humans acting as endocrine disrupters chemicals (EDC) due to their ability of mimicking the action of the steroid hormone and thus interfering with hormone response. They are responsible of a long list of very serious human and animal health problems, including cancers, infertility, osteoporosis, depression, cardiovascular diseases and deformities of the reproductive organs [1, 2]. There are several experimental evidences that they bind and activate human steroid receptors [3], however molecular data of the interaction of these compounds with biological targets are still lacking. In order to better understand the ability of various EDC to interact with the receptor hormone binding pocket, we have simulated by docking approach the molecular models of the complexes between some DDT and PCB derivatives and estrogen (hERα), progesterone (hPR) and androgen (rAR) receptors. The results of our investigation allow to describe a wide pattern of interactions between EDC ligands and steroid receptors, suggesting that their action can be brought about by a possible combined effect.

[1] Colburn T., vom Saal F. S., Soto A. M. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. *Environ. Health Perspect. 101*, 378–384, 1993.
[2] McKinney J. D., Waller C. L. Polychlorinated biphenyls as hormonally active structural analogues. *Environ. Health Perspect. 102*, 290–297, 1994.
[3] Scippo M. L., Argiris C., Van De Weerdt C., Muller M., Willemsen P., Martial J., Maghuin-Rogister G. Recombinant human estrogen, androgen and progesterone receptors for detection of potential endocrine disruptors. *Anal. Bioanal. Chem. 378*, 664-669, 2004.