Nuclear Receptors Targeted Library

Nuclear receptors are a class of proteins that are responsible for sensing steroid and thyroid hormones and some other molecules. In response, these receptors work with other proteins to regulate the expression of specific genes, thereby controlling the development, homeostasis, and metabolism of the organism.

Nuclear Receptor Targeted Library by Life Chemicals comprise compounds selected with protein-ligand docking method. For this purpose we have applied Glide software from Schrödinger. Using available crystal structures of nuclear receptors (Estrogen, Androgen, Progesterone, Glucocorticoid, Mineralcorticoid, RAR, RXR, PXR, ROR (-α/γ), LXR, PPAR, Thyroid hormone receptors), a number of H-bond and hydrophobic constraints were assigned, that in combination with electrostatic maps of the binding sites have been used as docking/screening models (Fig. 1). To estimate the efficiency of the docking procedure, each model was validated using a reference set (50 to 1,107 compounds, depending on the target) with known nuclear receptor antagonist activity (IC_{50} lower than 1 μM) as well as a random set of inactive compounds, both extracted from the ChEMBL database.

As a result, *in-silico* HTS of all compounds from Life Chemicals Stock Collection selected about **5,100** compounds which were ranked as based on docking score values obtained from a reference set docking. Finally, compounds with unwanted structures were filtered off using the PAINS filter.

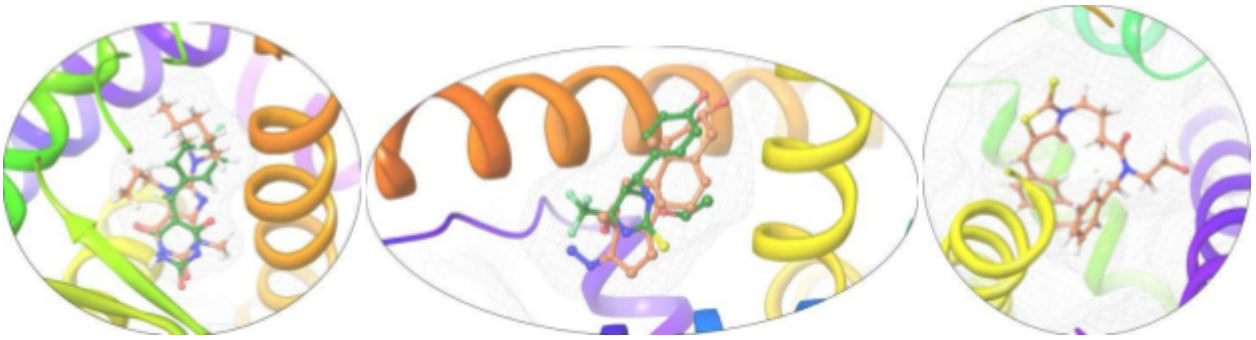

Fig. 1. Ligand positions and conformations generated as based on docking results. As an example, estrogen (left), progesterone (middle) and PXR (right) receptors were taken to show localization of ligand molecules from Life Chemicals Stock Collection in the receptor binding sites.