[P26] NRLiSt BDB : the manually curated Nuclear Receptors Ligands and Structures Benchmarking Database

Nathalie Lagarde[1], Nesrine Ben Nasr[1], Aurore Jérémie[1], Hélène Guillemain[1], Vincent Laville[1], Taoufik Labib[1], Jean-François Zagury[1], Matthieu Montes[1]

[1]Laboratoire Génomique Bioinformatique et Applications, Equipe d'accueil EA4627, Conservatoire National des Arts et Métiers, 292 rue Saint Martin, 75003 Paris, France.

Nuclear receptors (NRs) are transcription factors naturally switched on and off by small-molecule hormone [1] and constitute an important class of drug targets. We created the most exhaustive NR-focused benchmarking database to date, the NRLiSt BDB (NRs Ligands and Structures Benchmarking DataBase) [2]. The 9905 compounds and 339 structures of the NRLiSt BDB are ready for structure-based and ligand-based virtual screening. The NRLiSt BDB originality lies in that datasets were constructed according to the pharmacological profile of ligands, leading to the formation of two datasets for each proposed target, one agonist and one antagonist.
In the present work, we detail the protocol used to generate the NRLiSt BDB and its features and the website we created to freely provide the NRLiSt BDB to the scientific community (http://nrlist.drugdesign.fr). We presented also the enrichment performances obtained with a docking method, Surflex-dock, used to study whether and how our construction choices impact the quality of the benchmarking dataset. We demonstrated the influence of the ligand bound on the docking performances and provided some clues to guide target structures selection: agonist-bound structures should be used for the identification of agonist ligands and antagonist-bound structures for the identification of antagonist ligands, if available.

Since extensive and manually curated experimental data about NR ligands and structures is provided in the NRLiSt BDB, it should become a powerful tool to assess the performance of virtual screening methods on NRs, assist the understanding of NR's function and modulation and support the discovery of new compounds targeting NRs. The rational protocol develop to construct the NRLiSt BDB could also serve as guidelines for future benchmarking datasets.

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