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Compounds for HTS
Chemical building blocks
Fragment libraries
Targeted libraries
Drug discovery services

RETINOIC ACID RECEPTOR-RELATED ORPHAN RECEPTOR GAMMA (RORγ) TARGETED LIBRARY

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OTAVA offers a high quality Retinoic Acid Receptor-related (RAR-related) Orphan Receptor-gamma Targeted Library. It is a special screening collection containing drug-like compounds with predicted affinity to RORγ. This library provides an excellent basis for drug discovery projects related with inflammatory, immune and skin diseases.

The library consists of **1,326 compounds***.

All compounds are:

- **in stock**; available amounts: 1 – 50 mg
- **Drug-like only**; reactive, pan-assay interference (PAINS), redox-active and aggregator compounds were removed from the library.

QA/QC passed:

- minimal purity of compounds is **90%**;
- by **NMR** and/or **GC/LC/MS**
- **NMR spectra are available** upon request

Frendly packing services:

- **Cherry-picking is available**
- Supplied as dry powder or DMSO solution**
- Packaging in deep-well plates or barcoded vials***
- **Weighing out is free**

*Please note that the library does not contain known inhibitors. The compounds were selected with computational approach and are intended for screening projects

**there is additional fee for preparation of the solution

***4 ml amber glass vials or Deep-well plates: Matrix cat# 4247 (1.4 mL, Blank, Polypropylene, Round Bottom Tubes) w/CapMats. Or plates and vials provided by customer.

Target engagement:

The Retinoic Acid Receptor-related Orphan Receptor-gamma plays an important role in metabolism, inimmunity and circadian rhythm. Abnormal functioning of RORγ is associated with inflammatory, immune and skin diseases including psoriasis. Antagonists and inverse agonists of this receptor may have therapeutic potential in the treatment of such diseases.

The summary of the library characteristics:

	Minimum	Maximum	Average value
Molecular Weight	217.3	500	380,5
Number of Hydrogen Bond Donors	0	4	1
Number of Hydrogen Bond Aceptors	1	9	4,5
Number of Rotatable Bonds	0	11	5
CLogP	-0,4	5	3
Number of Rings	2	6	3,4
Polar Surface Area	29,1	172,6	84,9

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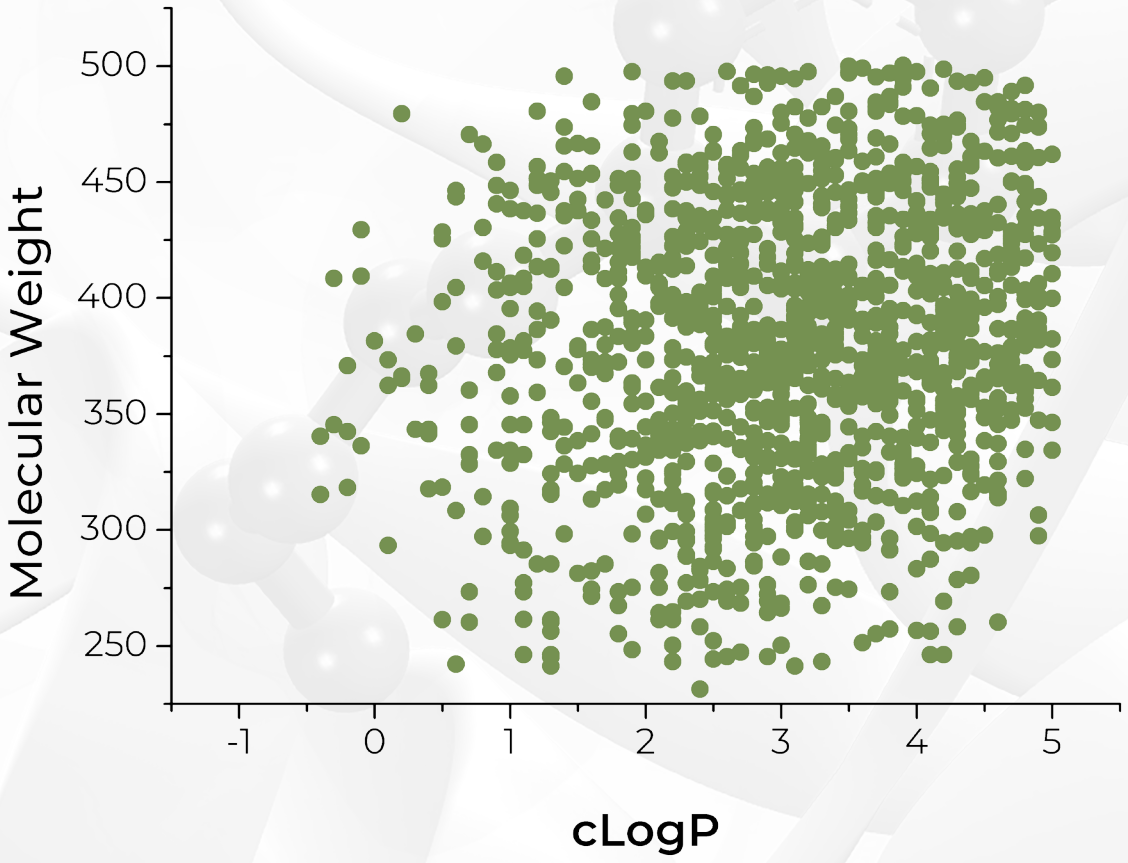
Distribution of physicochemical properties of compounds in the library:

100% Drug-like

47% Lead-like



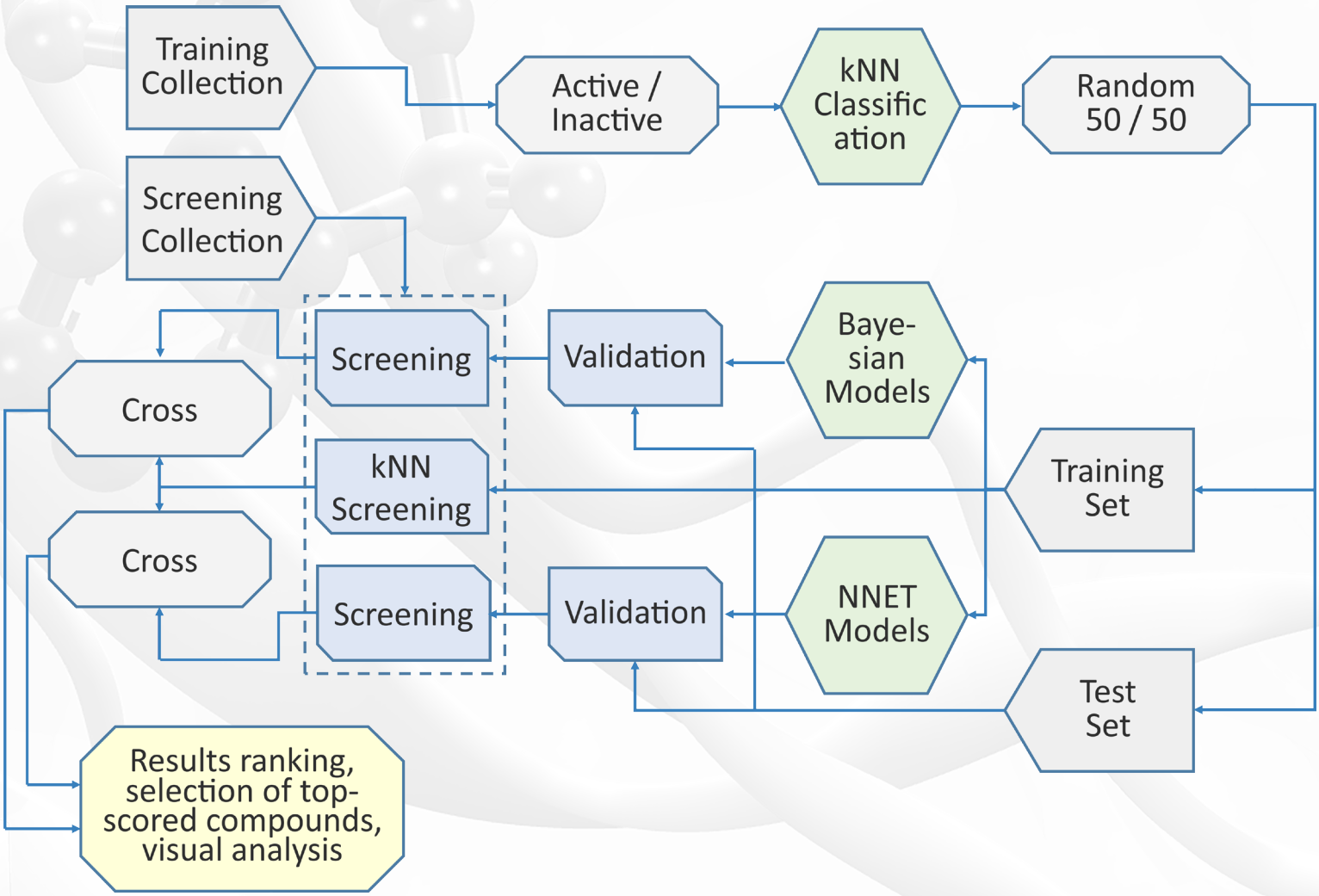
Design speciality:

Library has been carefully designed with combination of ligand-based and receptor-based virtual screening methods - machine learning (artificial neural networks, Bayesian statistics and k-nearest neighbors algorithm (k-NN)) and molecular docking (see Scheme 1 and 2).

For library design known RORγ antagonists and inverse agonists were clustered into four clusters. Compounds of each cluster were classified as active or inactive using k-NN based on molecular fingerprints to achieve more homogeneous sets and then randomly divided into training and test sets. The training sets were used for development and parameterization of artificial neural networks and for Bayesian modeling (both methods based on molecular descriptors, such as number of hydrogen donors and acceptors, PSA, LogP, molecular weight, number of rotatable bonds, number of rings and different fingerprints, topological descriptors and other). The test sets were used for validation of neural networks and Bayesian models. Also the training sets were used for compounds selection with k-NN algorithm (based on fingerprints ECFP4, FCFP4, ECFP6, FCFP6). Top-scored compounds obtained from application of these methods were crossed with top-scored compounds obtained with molecular docking (PDB ID: 4NIE). Final selection of compounds has been made with inspection of intermolecular hydrophobic contacts and hydrogen bonds with key ligand-binding domain residues. The combination of artificial neural networks, Bayesian statistics, k-NN algorithm and molecular docking should allow increasing the number of active compounds identified during screening.

Scheme 1. Application of receptor-based design of targeted library

Scheme 2. Application of machine learning for design of targeted library



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Custom synthesis

Molecular modeling

Amyloids detection

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