MCULE KINASE TARGETING LIBRARY

THE MCULE KINASE TARGETING LIBRARY CONTAINS COMPOUNDS WHICH SHOW HIGH MOLECULAR SIMILARITY TO KNOWN ORTHOSTERIC KINASE BINDERS. THE ANNOTATIONS HELP TO FIND MOLECULES MOST SUITABLE FOR SCREENING AGAINST KINASE SUBFAMILIES.

Kinase enzymes belong to phosphotransferases, which catalyzes various biochemical processes via enhancing phosphate group transfer to specific substrate molecules, such as proteins, lipids or carbohydrates. With this funcion kinases play an essential role in the cellular regulatory system by catalyzing phosphorylation, hence their targeting could be an effective therapeutic strategy for various diseases such as cancer, inflammatory, autoimmune, and neurological disorders.

THE LIBRARY WAS GENERATED VIA THE FOLLOWING WORKFLOW:

1. **Experimentally validated bioactivity data from the ChEMBL database.** We have collected activity values of small molecular ligands measured on specific protein kinase targets and their regulatory subunits. The compounds that showed inactivity were excluded just as those which were only active at concentrations greater than 1 μM.

2. **Similarity searches were carried out for each active kinase ligand in the Mcule Database.** The search was performed with a Tanimoto coefficient limit of 0.7 using Mcule's super-fast, in-memory searching service (Mcule BLINK™). The similar compounds (hits) were annotated with the kinase classes that the query structures belong to.

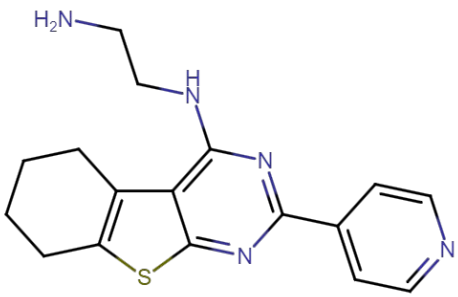
3. **The hits were filtered by a PAINS filter containing 1,000 SMARTS substructure patterns** to exclude compounds containing toxic or promiscuous chemical functions.

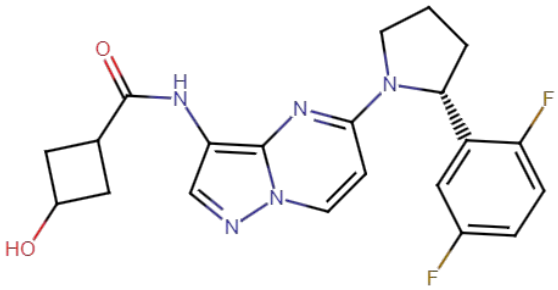
4. **Further filtering was performed to ensure that each hit likely binds to the orthosteric binding site.** Each hit contains a HBD-C-C-HBA substructure (as in adenine) that is crucial for binding to the target protein. Steric hindrance and appropriate orientation of the atoms in the HBD-C-C-HBA chain was also accounted for.

Examples for annotated compounds

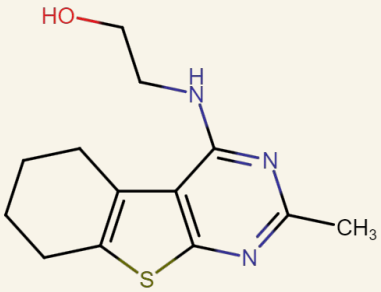
The first row contains ligands obtained from the ChEMBL database that are known to be active on kinase targets. The second row illustrates similar purchasable compounds that are present in the Mcule Database. Consequently, these could potentially serve as candidates for targeting kinases.

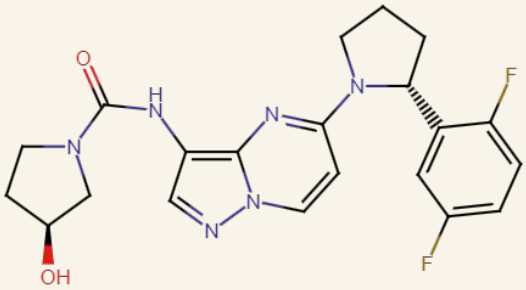
References from ChEMBL



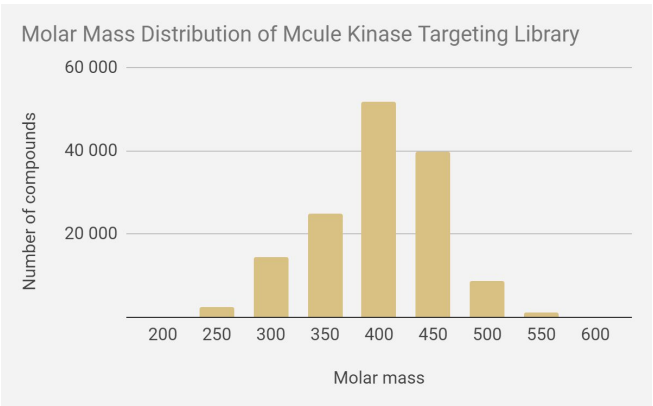


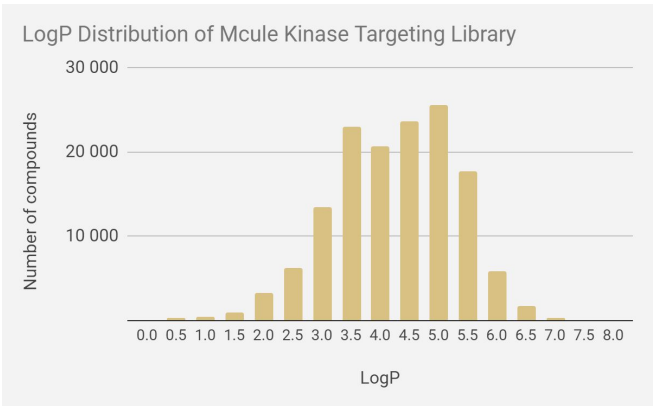
Mcule Kinase Targeting Library members

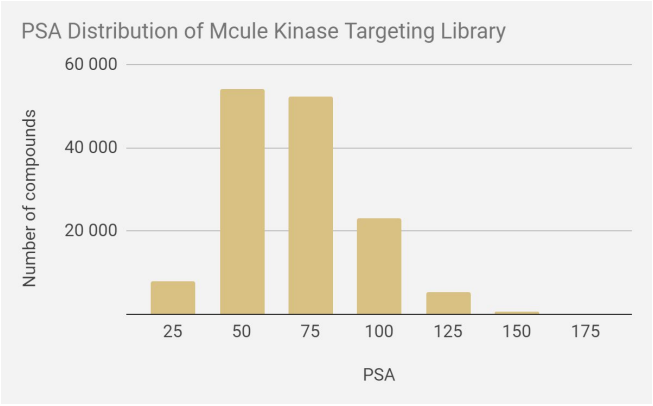


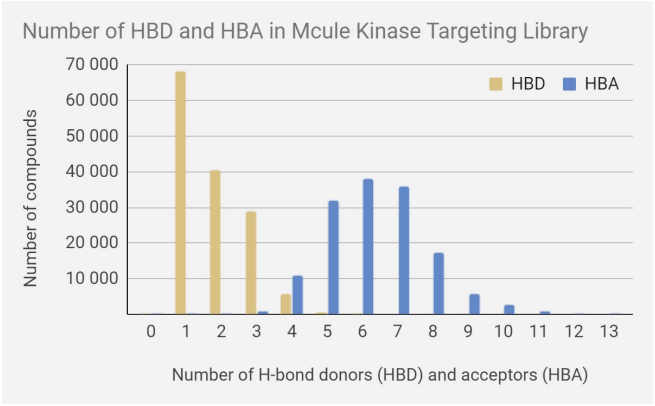


Molar Mass, LogP, PSA distributions and the number of H-bond donors and acceptors of the full Mcule Kinase Library are presented below.









The data files contains the following information:

ID and structure specific info	Property specific info
• Molecule name • SMILES Classification specific info • Protein class levels based on ChEMBL nomenclature (4 ProteinClassification levels)	• mol mass • logP • PSA • H bond donors (HBD) • H bond acceptors (HBA)

To obtain the Mcule Kinase Targeting Library, download the appropriate data file (format: CSV.GZ) from **here**. Here you can find the corresponding documentation for detailed information about the file contents and suggested usage, complete with examples as well.

Did you know?

Mcule provides professional laboratory services including:

- **Mcule Express Compound Inventory System™** - powered by robotized cold room sample storage
- **Mcule Client Portal™** - a cloud-based platform for real-time online sample management
- **Custom formatting** - Solid weighing, robotized dissolution and pipetting
- **Experimental sample characterization** - Structure identity, purity, solubility and reactivity analysis
- **Comprehensive logistic services**- Compound procurement, sample management, customs clearance and worldwide delivery

Mcule provides professional cheminformatics services including:

- **Custom library design** - using a wide range of ligand- and structure-based molecular modeling and cheminformatic approaches including physicochemical property calculations, molecular fingerprint based similarity and substructure searches, diversity selection, similarity clustering, scaffold hopping, toxicity filtering, PAINS and other unwanted substructure filters, molecular docking, etc. Custom library generation workflows can be applied on the Mcule Database or Mcule ULTIMATE database
- **Generation of synthetically feasible chemical universes** - based on specific building blocks and reaction rules

Mcule's Custom Solution Experts are ready to guide you through the selection and ordering process free of charge! If you have any questions or need any help, please feel free to contact us at **support@mcule.com**.