

Your Software Partner for Rational Drug Design



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## 17 Million Molecules Screened Against 40 Target Receptors

LASSO Screening on the ChemSpider database will allow you to:

- Find molecules which have a higher likelihood of binding to your targets.
- Find molecules with better selectivity for your target.
- Reduce toxicity issues.

SimBioSys and ChemZoo have teamed up to provide the virtual screening results for 40 target families on the full ChemSpider Library, currently containing over 18 million molecules. Using the LASSO similarity search tool, SimBioSys has screened the ChemSpider database against all 40 target families from the Database of Useful Decoys (DUD) dataset. In addition to allowing instant ranking results for your particular target of interest (retrieving molecules that are likely to be active for your receptor) this matrix of screening results can be used to find molecules that have predicted affinity for your target but low predicted affinity for all other targets. Performing such searches promises to improve selectivity and can be a guide to reducing toxicity concerns.

### Available Screening Results

The 40 Target receptor families included in the screening results available via ChemSpider were taken from the Database of Useful Decoys (DUD)[1]. These targets were chosen to cover a wide range of receptor classes due to their interest in drug discovery. Each target family had 10s to 100s of known active molecules, which were used as the basis for the query files used by LASSO, one query for each family. The similarity screening was performed on the full ChemSpider database across all 40 targets and the similarity scores for each structure/target pair is available via the ChemSpider website. Thus for each structure in the ChemSpider database, you can find its similarity score (based on surface properties) relative to actives of each of the 40 target receptors.

### Retrieving Potential Lead compounds

While this information is very interesting on its own, the real value lies in the searching capabilities of ChemSpider. You are also able to search the ChemSpider database for all molecules with a LASSO similarity score greater than N. [NOTE: The LASSO similarity score ranges from 0 to 1, with 0 being not similar at all, and 1 being very similar to the query set]. This will give you the set of molecules with one being the most similar to the actives used in the query set for that target.

### Selectivity and Toxicity

Selectivity and toxicity are major concerns for drug discovery. By combining search criteria you are able to perform some initial selectivity screens very rapidly using the LASSO screening results and ChemSpider. For example, searching for all structures with a LASSO score better than 0.92 for CDK2 but under 0.3 for all other Kinase receptors would be a good start on finding lead compounds with higher selectivity for CDK2. Requiring poor LASSO scores for all other receptor targets could also help in controlling toxicity or off-target effect.

### Screening Results for Your Target

The LASSO on ChemSpider project currently only contains the screening results for 40 target families. While this is a great first step, there is a good chance your target of interest is not part of this target set. However, you

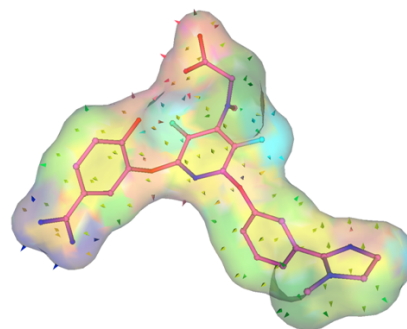
can easily extend this screening dataset with your own internal (or public) data by obtaining a copy of LASSO for yourself and running the screen yourself. Screening with LASSO is very quick (roughly 1 Million Molecules screened in one minute on a standard PC). Therefore, by obtaining LASSO from SimBioSys and the LASSO descriptors from ChemSpider, you can do this screen for your particular target of choice. You could still combine those results with the results available via ChemSpider for selectivity/toxicity concerns.

## About LASSO

LASSO is a similarity searching tool that uses LASSO descriptors to find molecules with diverse chemical scaffolds but similar surface properties. Based on the idea that ligands must have surface properties compatible with the target site in order to bind, LASSO uses a descriptor of Interacting Surface Point Types (ISPT). The LASSO descriptor provides a fuzziness in terms of molecular structure which makes it ideal for scaffold hopping applications. More information about LASSO is available at [www.simbiosys.ca/lasso](http://www.simbiosys.ca/lasso). Additional information is available [here](#).

ISPT descriptor for 1FJS ligand:

0	4	0	0	1	0	4	6	1	0	0	0	8	8	0	0	23	5	2	2	0	6	0
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## About ChemSpider

ChemSpider is a chemistry search engine. It has been built with the intention of aggregating and indexing chemical structures and their associated information into a single searchable repository and making it available to everybody, at no charge. ChemSpider is a value added offering since many properties have been added to each of the chemical structures within the database – structure identifiers such as SMILES, InChI, IUPAC and Index Names as well as many physicochemical properties. The introduction of the LASSO descriptor and associated search capabilities extends the applications of the system further into the world of drug discovery.

## References

- [1] Huang, N.; Shoichet, B. K.; Irwin, J. J., Benchmarking sets for molecular docking. *J Med Chem* 2006, 49, (23), 6789-801.