



## PredictFX

### Benefits

- Identify potential safety risks much earlier in discovery or development phase
- Focus chemistry efforts on areas with the best chance of pre-clinical and clinical safety
- Enhance predictive models by easily incorporating proprietary in-house data
- Predict a wide variety of off-target biological activities
- Rescue lost investment by identifying a new therapeutic application for a failed development candidate
- Integrates into in-house IT/IS systems so that any scientist can make off-target predictions
- Developed at Chemotargets S.L., a spin-off of Jordi Mestres' lab at IMIM, leaders in predictive safety

## Identify and address safety issues earlier in the drug discovery process

Nearly half of drug candidates entering into pre-clinical development will be lost due to lack of safety. PredictFX™ is a modeling and simulation suite that provides improved opportunities to identify, monitor, and address safety issues earlier in the process by predicting the off-target pharmacology and associated side effect profile of a small molecule from its 2D chemical structure.

Using PredictFX, scientists engaged at any stage of the drug discovery and development process can identify safety risks, thus better managing attrition. Based on off-target predictions, chemistry efforts can be focused and targeted on the areas with the best chance of success in preclinical and

clinical safety, and biological and safety evaluation can be focused on the areas of greatest risk.

Scientists can easily enhance predictive safety models further with PredictFX by incorporating in-house chemical and biological data to ensure the models cover their company's proprietary chemical space, and that poor compounds are recognized early, reducing attrition effects in the preclinical safety stage.

Additionally, PredictFX can be used in the context of drug repurposing to identify new therapeutic applications for a failed development candidate, thus rescuing lost investment.

## Who should use PredictFX

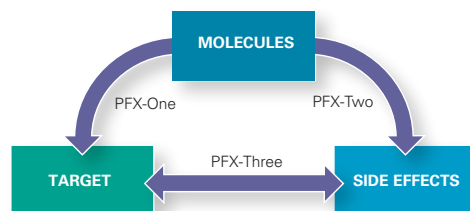
- Scientists involved in drug design for Hit Identification and Lead Optimization
- Scientists responsible for safety aspects of drug discovery
- Discovery Informatics Group responsible for delivering predictive models to discovery scientists
- Scientists involved with target deconvolution of bioactive small molecules identified from phenotypic screens
- Drug Repurposing Group

## About PredictFX

PredictFX considers drug selectivity and safety from multiple viewpoints. The PredictFX suite reveals the relationships between the chemical structure, the pharmacological profile, and the resultant side effect profile.

The PredictFX suite consists of three (3) modules:

- PFX-One: From a 2D chemical structure, predicts the profile of affinities against a panel of biological targets.
- PFX-Two: From a 2D chemical structure, predicts the profile of pharmacologically-relevant side effects.
- PFX-Three: Predicts the link between side effects and target profile.



## About PFX-One

PFX-One uses both chemical structure and biological activity data to generate its predictive models. First generating an optimal set of molecular descriptors from the 2D chemical structure, PFX-One uses these descriptors to identify molecular neighbors from which target affinities are then predicted.

PFX-One allows the prediction of affinity profiles on 4,790 targets, covering all major protein families of therapeutic interest. For each target, a ligand-based model is derived from molecules with known affinity data using a combination of descriptors, and a list of targets and the predicted affinities for each compound processed is returned.

The suite will be completed with PFX-Two, which predicts the side effect profile associated to known and/or predicted affinities for protein targets, and PFX-Three, which closes the triad by returning those causal links identified between targets and side effects.

## System Requirements

PredictFX is supported for Red Hat Enterprise Linux 5 and 6, and requires OpenBabel v2.2.+ to be installed as a prerequisite.

## References

### Linking Pharmacology to Clinical Reports: Cyclobenzaprine and Its Possible Association With Serotonin Syndrome.

Mestres J, Seifert S, Oprea T. Clin Pharmacol Ther. 2011 Oct 5. doi: 10.1038/clpt.2011.177. [Epub ahead of print]

### Multi-targeted activity of maslinic acid as an antimalarial natural compound.

Moneriz C, Mestres J, Bautista JM, Diez A, Puyet A. FEBS J. 2011 Aug;278(16):2951-61. doi: 10.1111/j.1742-4658.2011.08220.x. Epub 2011 Jul 7.

### Chemical probes for biological systems.

Garcia-Serna R, Mestres J. Drug Discov Today. 2011 Feb;16(3-4):99-106. Epub 2010 Nov 18.

### Ligand-based approaches to in silico pharmacology.

Vidal D, Garcia-Serna R, Mestres J. Methods Mol Biol. 2011;672:489-502.

### Anticipating drug side effects by comparative pharmacology.

Garcia-Serna R, Mestres J. Expert Opin Drug Metab Toxicol. 2010 Oct;6(10):1253-63. Review.

### In silico directed chemical probing of the adenosine receptor family.

Areias FM, Brea J, Gregori-Puigjané E, Zaki ME, Carvalho MA, Domínguez E, Gutiérrez-de-Terán H, Proença MF, Loza MI, Mestres J. Bioorg Med Chem. 2010 May 1;18(9):3043-52. Epub 2010 Mar 27.

### The topology of drug-target interaction networks: implicit dependence on drug properties and target families.

Mestres J, Gregori-Puigjané E, Valverde S, Solé RV. Mol Biosyst. 2009 Sep;5(9):1051-7. Epub 2009 Jul 8.

### A ligand-based approach to mining the chemogenomic space of drugs.

Gregori-Puigjané E, Mestres J. Comb Chem High Throughput Screen. 2008 Sep;11(8):669-76. Review.

### Data completeness--the Achilles heel of drug-target networks.

Mestres J, Gregori-Puigjané E, Valverde S, Solé RV. Nat Biotechnol. 2008 Sep;26(9):983-4.