PharmaExpert

This is an optional extension of the PASS system, allowing for a systematic data mining and biological interpretation of PASS results.

PharmaExpert analyzes mechanism-effect relationships, identifies the probable drug-drug interactions for pairs of molecules, and searches for molecules acting on multiple targets. The software can also help to identify molecules with desired activities and without toxic or side effects.

The analysis is based on a "mechanism-effect(s)" relationship knowledgebase (MER base) that is collected by experts from literature of more than 15 years.

PASS

The acronym PASS stands for "Prediction of Activity Spectra for Substances". Upon entering a structural formula of a chemical substance, the program returns the potential biological activities of this compound.

PharmaExpert allows to:

- Select compounds with required therapeutic, but without adverse effects;
- Comparatively analyze compounds with similar structures;
- Select compounds with multiple mechanisms of action;
- Assess drug-drug interactions with regard to their pharmacokinetic, pharmacodynamic, and adverse effects.

PharmaExpert

About geneXplain

GeneXplain's mission is to provide a comprehensive platform for bioinformatic, systems biological and cheminformatic tools. The raison d'être of this platform is to assist translational research in the life sciences, mainly in the context of personalized medicine and pharmacogenomics. We intend to make our expertise available to academic and commercial partners in collaborative research projects.

To achieve this, geneXplain offers:

- The geneXplain platform providing a large number of bioinformatic and systems biological data analysis workflows. Unique is geneXplain's Upstream Analysis for causal interpretation of expression data.
- TRANSFAC®, the most comprehensive database on eukaryotic transcription regulation. TRANSFAC® is now also available under the geneXplain platform, providing the most comprehensive collection of TF DNA-binding profiles.
- TRANSPATH®, one of the largest pathway/network databases presently available, particularly well suited for geneXplain's proprietary *Upstream Analysis*.
- HumanPSD, a rich information resource connecting pathways with targets, drugs and clinical trials.

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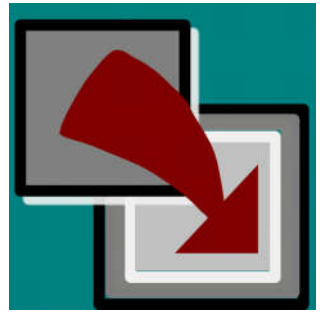
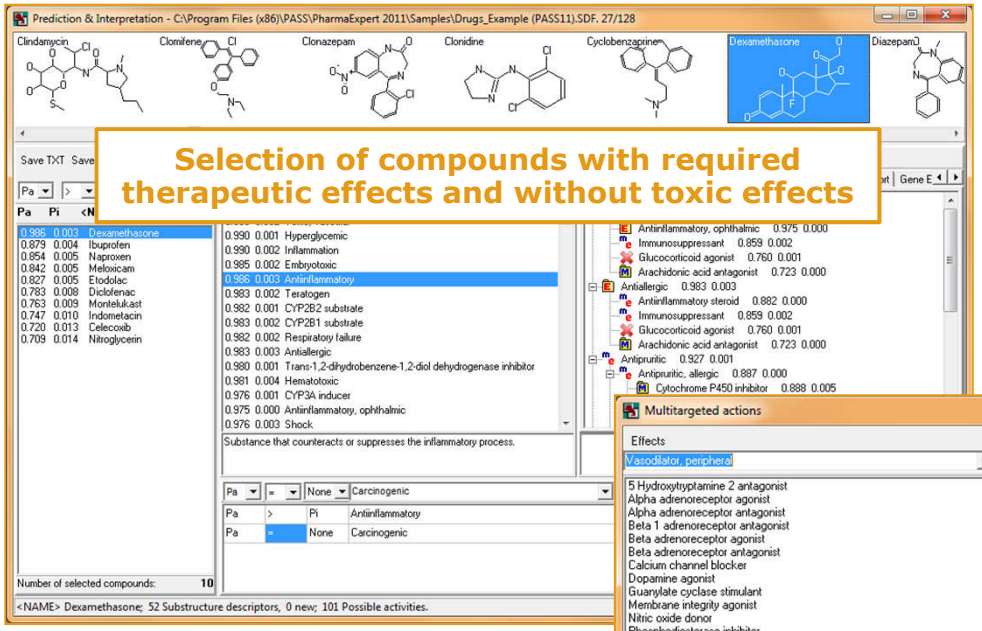
PharmaExpert

The tool for estimation of safety and efficacy of new pharmaceutical agents



geneXplain

PharmaExpert - a tool for the estimation of safety and efficacy of new pharmaceutical agents



How to select the most promising compounds among those predicted to interact with the selected target(s) and to cause the required pharmacotherapeutic effect(s)?

The current version, **PharmaExpert2017**, as a pharmacological knowledge-based tool, provides *in silico* screening of compounds using either the PASS predictions or GUSAR predictions of their biological activities.

PASS and PharmaExpert: The optimal combination

In a first step, PASS has predicted biological activities for chemical compounds based on a library containing more than **1,025,000** structures (known drugs and drug-like compounds).

As the next step, PharmaExpert selects those chemical compounds that exhibit the required biological activity spectra with low probability of adverse or toxic effects.

Out of the thousands of biological activities predicted by PASS, PharmaExpert identifies rational combinations of multi-targeted action and finds the suitable pharmaceutical agents among commercially available chemical compounds.

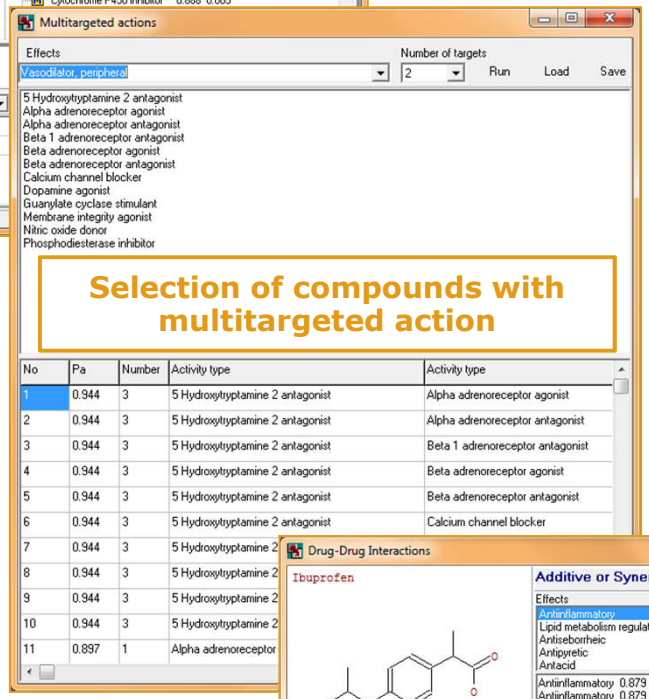
Mechanism-effect relationships

PharmaExpert comes with a database, manually curated by experts, containing mechanism-effect relationships (MER), which is used to analyze the PASS prediction data.

In the current version, the MER base includes **6233** mechanisms of action, **710** pharmacological effects, **995** toxic and side effects, **175** antitargets, **343** metabolic effects, **113** effects on transporters, and **2523** effects on gene expression.

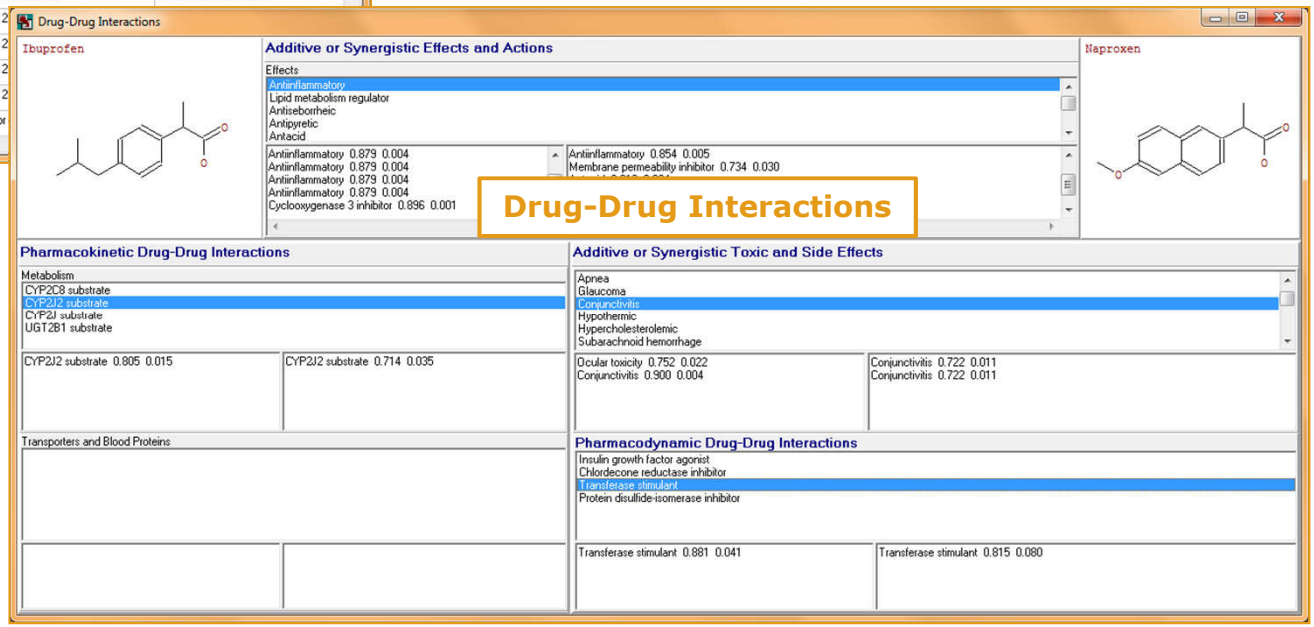
Search function

The search mask of PharmaExpert allows to find any number of desired activities with specified thresholds of the probability to be active (Pa). At the same time, it is possible to exclude unwanted activities by simply minimizing their Pa.



Multitarget selection

With PharmaExpert it is possible to identify substances with multitargeted actions. Simply choose a desired effect and a number of mechanisms that should lead to it will be displayed automatically. The software will then return a list of substances displaying more than one mechanism leading to the effect.



Drug-drug interactions

PharmaExpert provides a comfortable interface to reveal the most important types of drug-drug interactions for pairs of pharmaceutical agents.

A dedicated option allows to classify interactions of the compounds with metabolic enzymes and protein transporters, thus facilitating the estimation of *pharmacokinetic drug-drug interactions*.

Pharmacodynamic interactions are estimated with respect to molecular targets and pharmacotherapeutic effects.

Synergistic or additive effects of two compounds are provided for *adverse and toxic effects* as well.

A slide show with screenshots can be found on our homepage (www.genexplain.com) and also on our Facebook account (www.facebook.com/genexplain), and recommendations from experts for the PASS software can be found on our LinkedIn profile (http://www.linkedin.com/company/genexplain/products).