Cheminformatics at geneXplain GmbH

Introducing PASS and PharmaExpert
geneXplain GmbH

We can explain your genes and put bricks together...

- Gene regulation
- Biomarkers
- Drug activity
- Network modeling

Products
- bioinformatics and systems biology: geneXplain platform
- bioinformatics and NGS: IMC and GenomeTraveler
- cheminformatics: PASS, PharmaExpert, GUSAR
Bioinformatics, Systems Biology, NGS

- geneXplain platform
  - collection, storage and analysis of experimental data
  - network clustering and search for master regulators
  - features: graphical programming of workflows and the possibility to write new scripts and add-ons

- IMC
  - handling whole genome data
  - supports: feature mapping and annotation
  - PCR primer calculation

- GenomeTraveler
  - handling of next generation sequencing (NGS) data
  - genome analysis
  - all functions of IMC
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PharmaExpert
- General
- Key Data
- Activity Types and Relationships
- Summary

Why You Should Give PASS and PharmaExpert a Try
PASS

Prediction of Activity Spectra for Substances
PASS...

- does computational predictions of biological activity spectra for drug-like compounds.
- uses 2D chemical structures from SD or MOL files.
- predicts activities qualitatively.
- gives probability estimates for every prediction.
- has an average prediction accuracy of 95%.

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Key Data

- included SAR base constructed from a training set with 250,407 substances and 69,950 MNA descriptors
  - drugs
  - drug-candidates
  - pharmacological substances

- 4,444 biological activities can be predicted
  - 498 pharmacotherapeutic effects
  - 3,378 biochemical mechanisms
  - 351 possible toxic and side effects
  - 116 possible antitargets/offtargets
  - about 300 terms related to metabolism, transport and gene expression

- mathematical algorithm based on Bayesian estimates of probabilities

MNA Descriptors

Multilevel Neighborhood of Atoms

MNA/0: -C

MNA/1: -C(CN-H-C)

MNA/2: -C(C(C-C)N(CC-C)-H(-C)-C(-C-O-O))

Biological Activity Prediction

The predicted activity spectrum is displayed with probability values for each activity:

- Pa, the probability to be active, and
- Pi, the probability for the structure to be inactive.

predicted activity spectrum

53 of 4130 Possible Activities at Pa > 0.500

- 0.982 0.002 Hepatic disorders treatment
- 0.811 0.003 Lipotropic
- 0.790 0.002 Gastrointestinal motility stimulant
- 0.785 0.002 Antiemphysemic
- 0.787 0.004 Chronic obstructive pulmonary disease treatment
- 0.780 0.002 Free radical scavenger
- 0.766 0.002 Expectorant
- 0.724 0.002 Mucolytic
- 0.735 0.015 Muramoyltetrapeptide carboxypeptidase inhibitor
- 0.728 0.013 Proteasome ATPase inhibitor
- 0.686 0.011 Radioprotector
- 0.662 0.004 Thiopurine S-methyltransferase inhibitor
Substructures and Activity Spectra

All substructures have a positive impact on the activity “dizziness” (green).

Many atoms have a negative impact on the activity “peptide agonist” (red).
Summary

Estimate the general biological potential of chemical compounds.

Discover the impact of separate atoms on a particular activity.

PASS is an easy to use tool to predict biological activity spectra of substances qualitatively.

Discover new potential activities for known substances.

Use the default SAR base or create your own.
PharmaExpert

A useful extension for PASS
PharmaExpert...

- works with PASS prediction results as SD files.
- analyses mechanism-effect relationships.
- identifies drug-drug interactions for pairs of molecules.
- searches for structures with required activity profile(s).
- finds molecules that act on multiple targets.

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Key Data

- 11,049 mechanism-effect relationships (MER)

- manually curated MER base containing 7,723 activities
  - 5,753 mechanisms of action
  - 715 pharmacological effects
  - 998 toxic and side effects
  - 133 antitargets
  - about 500 terms related to metabolism, gene expression and transporters
Activity Types and Relationships

- Mechanisms and their subclasses
- Effects caused by these mechanisms
- Classification relationships
- Mechanism-effect relationships
Summary

Select compounds with desirable and without toxic effects.

Use the comparative analysis of compounds.

PharmaExpert helps searching, sorting and analyzing the activity data obtained by PASS.

Assess drug-drug interactions.

Select compounds with multiple mechanisms leading to the same effect.
Why You Should Give PASS and PharmaExpert a Try

Advantages of the Software
Evaluate Drug-Like Compounds

- estimation of the general biological potential of drug-like chemical compounds, including newly synthesized and virtually designed substances
- discovery of new potential activities of known compounds
- dissecting the impact of separate atoms and groups on a particular activity
- selection of compounds with desirable activities and without adverse or toxic effects
- selection of compounds with multiple mechanisms of action
- comparative analysis of compounds
- assessing drug-drug interactions with regard to their pharmacokinetic, pharmacodynamic and adverse effects
Advantages of PASS/PharmaExpert

- Only the structural formula of a compound is required to predict its biological activity spectrum.
- Analysis options and filters help restricting the number of tested compounds and direct further experimental evaluations.
- The software is installed locally and runs on any ordinary PC.
- A proprietary SAR base can be created to generate a user-specific version of PASS.
- The algorithm is fast, 50,000 compounds can be screened in ten minutes.
- PASS is widely accepted by the community: applications of PASS are cited in over 200 independent publications, and in about 40 of them PASS predictions are experimentally verified.
  - A list of all third-party publications about PASS can be found here: http://www.genexplain.com/sites/default/files/PASS%20-%20third-party%20publications.pdf