MolScore Antivirals

Expert system for antiviral research

==> Hit detection & validation

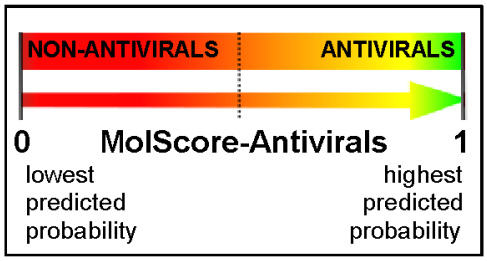
==> Lead selection & prioritisation

The expert system discriminates between antivirals and non-antivirals. MolScore-Antivirals identifies novel antiviral substances at the earliest stage through analysing the chemical structure of a drug candidate, its ADMET characteristics and its molecular targets. The chemical space of antivirals is different to that of common drugs. Extremely large structure-activity relationships (SAR) and structure-property relationships (SPR) with up to tens of thousands compounds allow the estimation of useful antiviral chemical space.

Application & Advantages

- Selects compounds from external suppliers before purchase or synthesis
- Focuses screening campaigns against viral diseases
- Validates hits from primary screening
- Selects and prioritises promising antiviral drug candidates for further development
- Prioritises derivatives even of different lead structures
- Simple usage and integration of results

MolScore-Antivirals calculates the probability of having antiviral activity and is defined as a value between 0 and 1. This value correlates with the predicted probability of a substance becoming a successful antiviral drug.

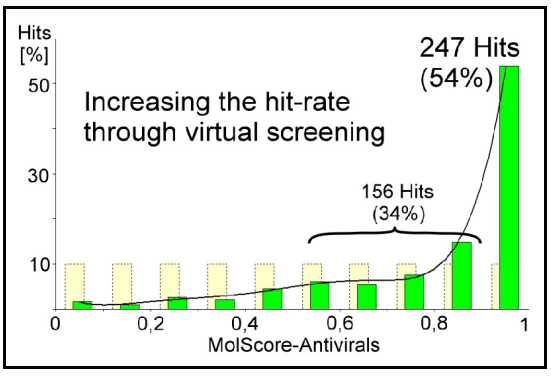


MolScore-Antivirals evaluates drug-candidates at an early state in order to reduce the costs and time for the development of new antiviral drugs.

The expert system combines different strategies and methods of drug research, so that structural patterns of virus-specific inhibitors but also structural patterns of target-specific inhibitors will be detected, for example:

- Inhibitors of viral genome replication (integration, transcription)
- Entry-, Uncoating- and Assembly-Inhibitors
- Inhibitors of viral protein synthesis and of protein modification
- Virus specific protease inhibitors (HIV, hepatitis C, SARS-CoV, etc.)
- Neuraminidase inhibitors (influenza viruses)
- Reverse transcriptase inhibitors (retro-viruses)
- Inhibitors with currently unknown mechanism of action

The high quality of prediction on new compounds was confirmed through an comparison with experimental screening results. MolScore-Antivirals priorities suitable antiviral substances, so only a part has to be screened experimentally:



41632 substances have been experimentally screened, whereby 1,1% of the substances possessed antiviral activity (459 hits).

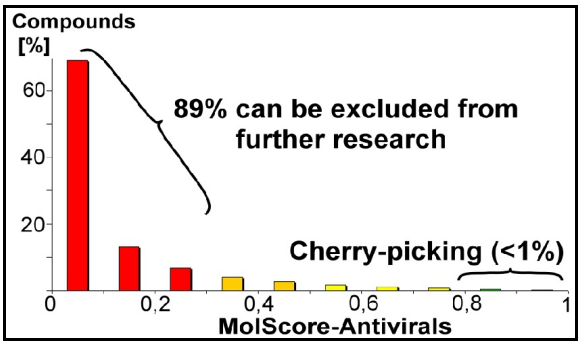
By using MolScore-Antivirals only 12,5% of the compounds have to be screened to yield more than half of the hits (247 hits).

Further screening of 28% yields to 88% of the overall hits (403 hits).

As a result, up to 77% of costs (purchase of substances, screening-costs) can be saved.

Hit detection & validation

The expert system identifies compounds which are not useful for further development. To provide an example we have analysed a commercial available library composed of 200.000 compounds.



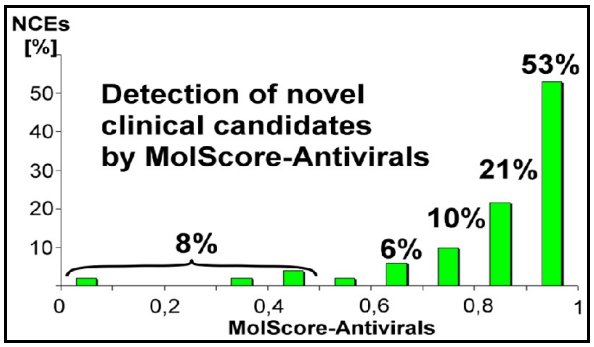
More than 89% of the examined compounds don´t fit into the chemical space of antivirals and can be filtered out. Less than 1% of the compounds had a MolScore-Antivirals result higher than 0,8 and can be selected for further research ("cherry-picking").

In general about 60-95% of molecules can be filtered out by MolScores-Antivirals depending on molecular patterns and properties of each molecule.

MolScores-Antivirals focuses screening campaigns and validates results from primary screening.

Lead selection & prioritisation

MolScores-Antivirals detects and prioritises suitable candidates for clinical development. The expert system has been validated with novel antiviral compounds which are now in clinical trials.



92% of diverse clinical candidates have been correctly classified as antivirals, which are suitable for further development into drugs.

This validation demonstrates the excellent prediction capability of MolScore-Antivirals to detect antiviral clinical candidates. These results are in accordance with previous obtained results (quality of prediction in the range of 88-95%).

Oral bioavailability knowledge base and prediction

Oral bioavailability is one of the most important properties in drug development. Low oral bioavailability in clinical trials is a major reason for drug candidates failing to reach the market.

PharmaInformatic develops and licenses PACT-F, the largest knowledge base on bioavailability worldwide. PACT-F contains experimental bioavailability results of clinical trials in humans and preclinical trials in animals. The results and conditions of those trials have been taken manually from more than 5000 scientific research articles related to bioavailability.

The knowledge base has been used to develop the expert system IMPACT-F, which estimates oral bioavailability in humans much more precisely compared to animal trials. Predictions of IMPACT-F are reliable and were as accurate as the common deviation between individual humans taking part in the same clinical trial (inter-subject variability in humans).

About PharmaInformatic

PharmaInformatic is a German biotech company, which provides ADME/Tox knowledge bases and expert systems to improve drug discovery and development. The company was founded in 2004 by Dr Wolfgang Boomgaarden. Before he founded the company, he worked as a professor in bioinformatics in Emden, Germany.

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