Chemistry Central Journal

ChemistryCentral

Poster presentation

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Computer-aided predictions of potential antineoplastic agents

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from 3rd German Conference on Chemoinformatics
Goslar, Germany. 11-13 November 2007

Published: 26 March 2008

Chemistry Central Journal 2008, **2**(Suppl 1):P18 doi:10.1186/1752-153X-2-S1-P18

This abstract is available from: http://www.journal.chemistrycentral.com/content/2/S1/P18

Neoplastic disorders are one of the most widely spread diseases over the world. There are more than 1 million new cases of cancer registered in the world every year. Therefore, searching for new potential antineoplastic agents is very important task. Computer-aided approaches are widely used for this purpose. To find new agents possessing the required activities, we used a computer program PASS. PASS simultaneously predicts more than 2800 pharmacological effects, mechanisms of action and specific toxicities (so called biological activity spectrum) based on structural formula of the compound. As a result, PASS estimates probability of presence of selected biological activities. The method has 93% average accuracy of prediction (leave-one-out cross-validation – LOO CV) and is robust to the incompleteness of data (http://www.ibmc.msk.ru/pass). More than 200 anticancer mechanisms of actions are currently included into PASS knowledgebase. To improve the quality of prediction, we collected more than 5000 chemical compounds with anticancer activities. This data were added to the training set of PASS. The mean accuracy of prediction for anticancer activities was 90% (LOO CV). PASS was applied to analysis of compounds from databases of commercially available samples. We used three databases from ASINEX, ChemBridge and InterBioScreen (IBS) together contained structures of 1565000 compounds. The probability more than 70% of biological activity was used as a criterion for selection of potential anticancer agents. The results of selection are shown in Table 1 below.

We identified more than 230,000 compounds with probability >70% of presence of 148 anticancer activities. Less than 40 compounds for each activity were predicted for 70 activities. Less than 20 compounds for each activity were predicted for 54 activities and less than 10 compounds for 36 activities. These compounds may be tested vs. predicted activities. Additional selection based of ADME properties, drug-likeness etc. is necessary for the remaining compounds.

Acknowledgements

This work is supported by INTAS grant No. 03-51-5218, by European Commission under FP6-Life sciences, genomics and biotechnology for health' contract LSHB-CT-2007-037590 'Net2Drug'.

Table 1

Supplier	Number of Compounds	Number of selected activities	Number of selected compounds
ASINEX	384178	131	69011
CHEMBRIDGE	785622	125	114829
IBS	395200	137	46847