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Chemoinformatics in Drug Discovery

Edited by:

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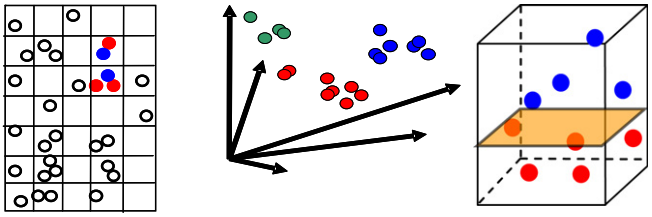
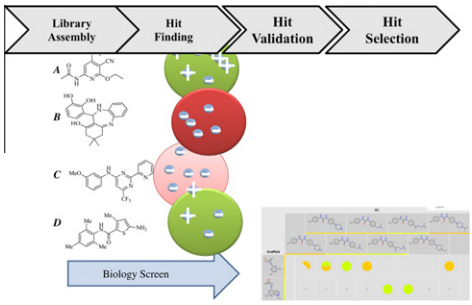
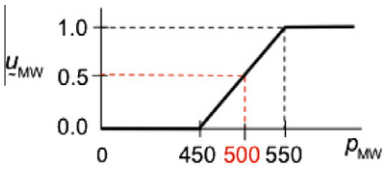
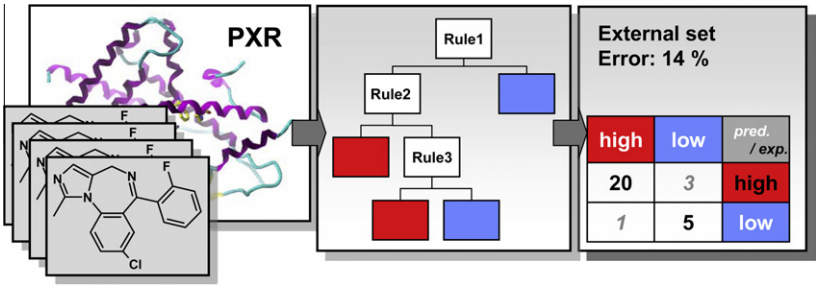
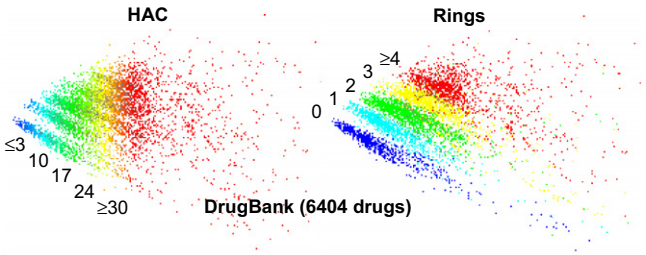


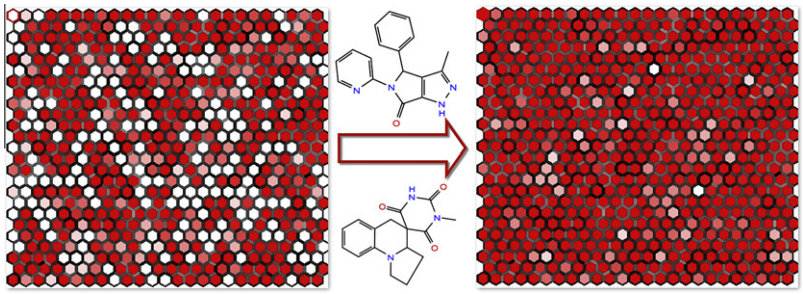
Compound classification approaches are illustrated including (from the left to the right) data set partitioning, an activity-sensitive chemical reference space, and a separating hyperplane in chemical space constructed by a support vector machine algorithm.

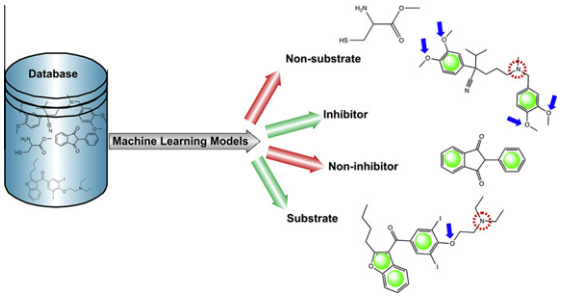


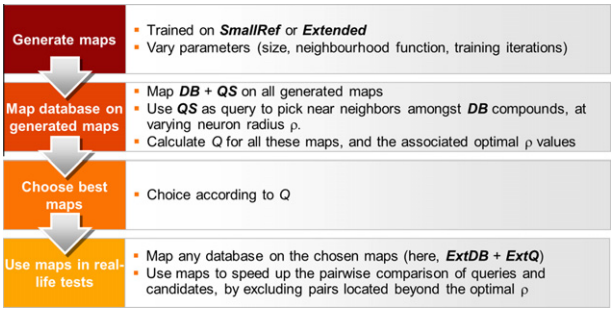


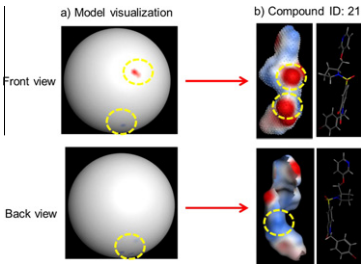




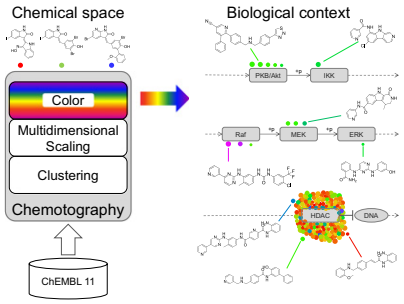


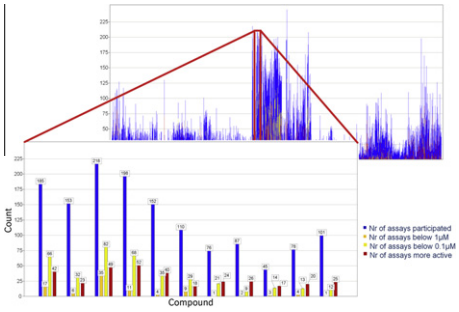


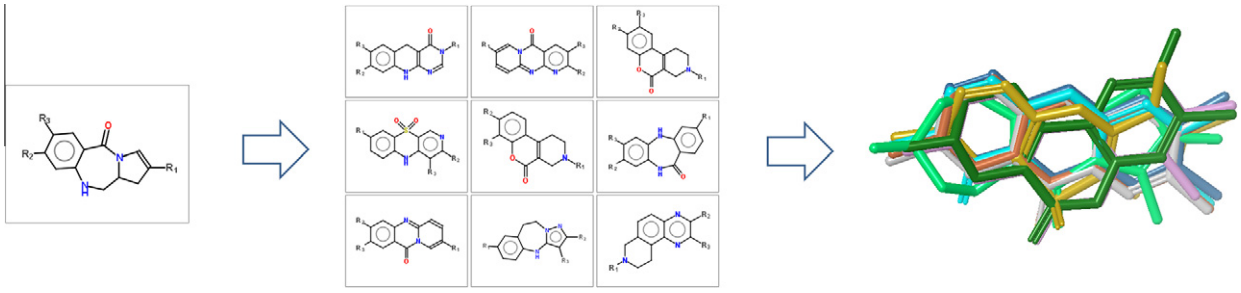


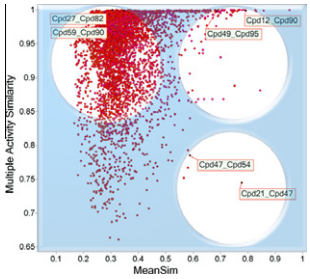


In this study, we perform a QSAR study of caspase-3 inhibitors based on the SSOM technique. The MEP values on the ligand SSOM sphere were used as chemical descriptors. The correlation of the chemical descriptors and the inhibitory activities was investigated by the SVR method. The important MEP descriptors were derived from the final SVR model. Based on the X-ray crystal structure of the protein, the descriptors matched the structural requirements of caspase-3 inhibitors.

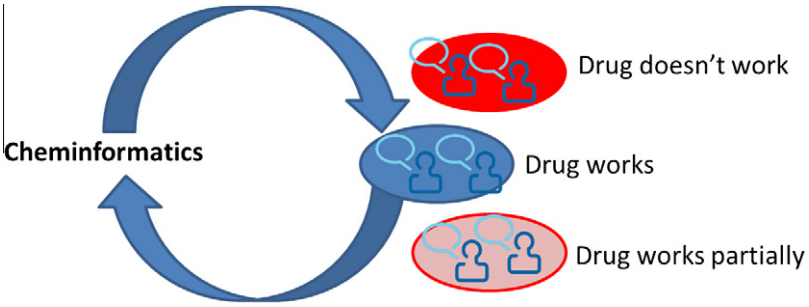




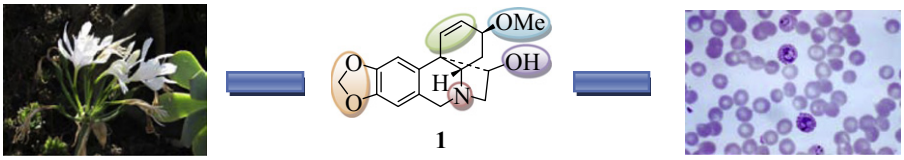




We report the Structure multiple Activity Similarity (SmAS) maps and the Structure multiple Activity Landscape Index (SmALI) as general approaches to explore and quantify the most informative regions of multi-target activity landscapes.



REGULAR ARTICLES



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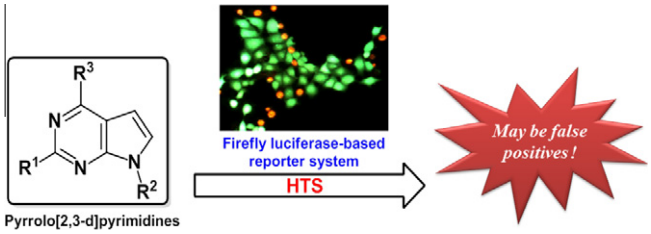
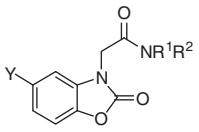
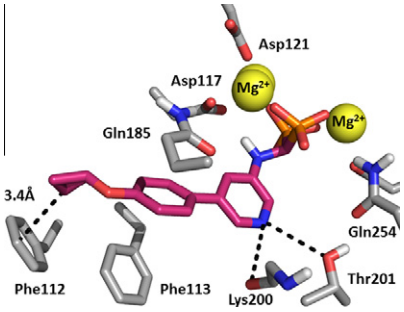
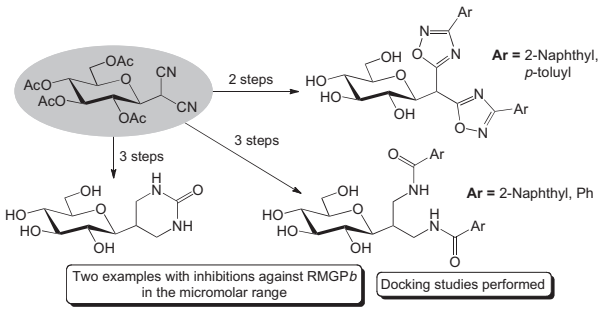


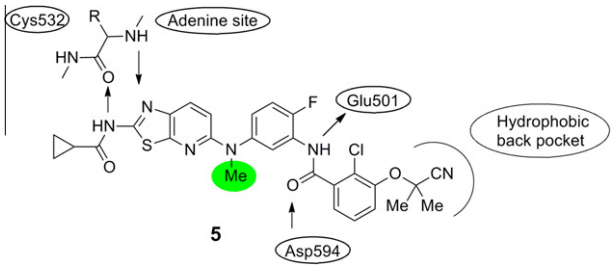


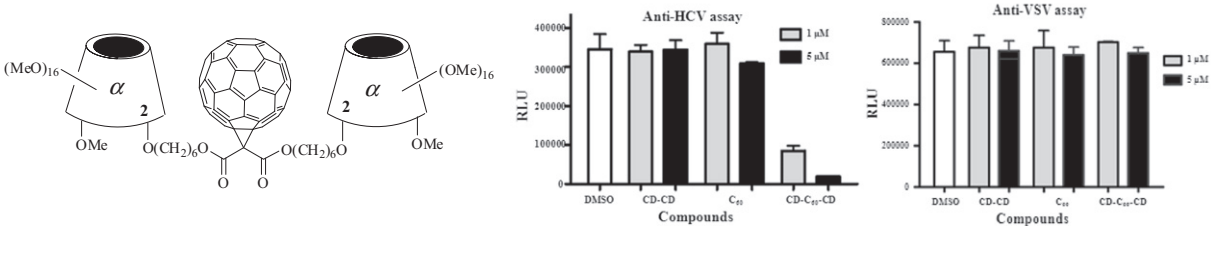
14 (Y = Ph, R^1 = Me, R^2 = Ph) TSPO Ki = 1.6 nM
74 (Y = 3-Py, R^1 = Me, R^2 = Ph) TSPO Ki = 11 nM

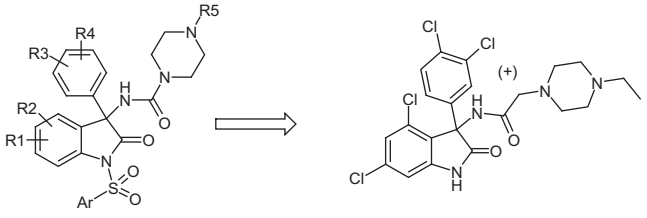
Benzoxazolone derivatives were designed and synthesized as novel TSPO ligands. In view of initial SAR study, we selected compound **14** as lead compound. Further optimization of pharmacokinetic properties of compounds led to discovery of compound **74** which exhibited anxiolytic effect in the rat Vogel model.

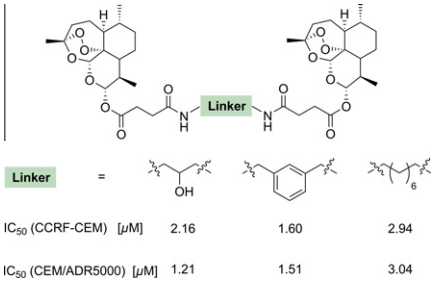


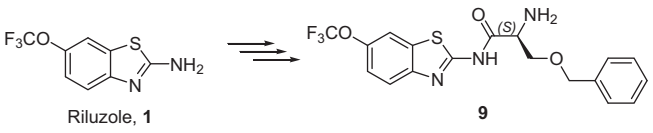












*Corresponding author

Supplementary data available via SciVerse ScienceDirect

COVER

Shown are alternative activity landscape views for a set of adenosine A2 receptor ligands including a similarity-based compounds network (left) and a three-dimensional activity landscape representation (right). An arrow indicates corresponding areas of relatively low SAR information content. On the left, selected compound subsets are encircled. The color code reflects the potency distribution within the data set, ranging from low (green) over intermediate (yellow) to high (red) compound potency. Cover illustration provided by J. Bajorath.

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