The searching of novel PAM of mGluR III by Virtual Screening of commercial chemical databases

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In recent years the Virtual Screening (VS) has become increasingly popular, as an alternative approach to HTS in the pharmaceutical and academic researches, especially in hit discovery and lead optimization [Shoichet, B. K. Nature, 2004, Vyas, V. Sci. Pharm. 2008]. This *in silico* technology uses high-performance computing to analyze large database of chemical compounds in order to identify possible new ligands of a given target (top-ranked hits) for biological evaluation [Hou, T.; Hu, X. Curr. Pharm. Design, 2004].

Here, we show the implementation of multistep virtual screening workflow to the searching of potentially new Positive Allosteric Modulators (PAM) of mGlu receptors family III. To their construction, a broad range of computational techniques (i.e. 2D fingerprints, 1D molecular descriptors, pharmacophore similarity search, docking and scoring, clustering), machine learning (support vector machines, SVM) and statistical (i.e. PCA and data fusion) methods were applied. The protocol was employed to screen the largest chemical databases (i.e. Enamine, ChemBridge, ChemDiv, UORSY and Vitas-M), containing approximately 5.5 million of tangible compounds.

To improve the global performance parameters of VS, such as efficiency, accuracy and hit rate level, a great effort is being made to develop and validate new tools and methods. Additionally, a web-based interface to the database linking results of different research teams will be shown. Detailed aspects and initial results of this study will be presented.

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