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Data set analysis for the calculation of the QSAR models predictive efficiency based on activity cliffs

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The activity cliff concept is of high relevance for medicinal chemistry. Herein, we explore a concept of "data set modelability", i.e., a priori estimate of the feasibility to obtain externally predictive QSAR models for a data set of bioactive compounds. This concept has emerged from analyzing the effect of so-called "activity cliffs" on the overall performance of QSAR models. Some indexes of "modelability" (SALI, ISAC, and MODI) are known already. We extended the version of MODI to data sets of compounds with real activity values. We chose out of 5231 compounds from CHEMBL database, for which activity regarding CA2 protein (Inhibitory activity against human recombinant carbonic anhydrase II) was calculated. The data set divided into some samples, containing 100 and 50 compounds in each. There are 19 real-valued descriptors for each compound in CHEMBL that we used in the calculations. The predictive efficiency of QSAR models is expressed as the correct classification rate by SVM algorithm, which compared with the results of the other two algorithms: algorithm MODI and Voronin algorithm modified by the authors. Comparative analysis of the results performed using Pearson's correlation coefficient square. Our study showed an extreme lack of evaluation of predictive efficiency of data set only based on "activity cliffs". In the development of more accurate methods that allow to evaluate the possibility of building of effective models on the data samples, it is necessary to take into account other properties of the sample, and not only the presence (and number) of "activity cliffs".

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VERO stable cell lines expressing full-length human epidermal growth factor receptors 2 and 3: Platforms for subtractive phage display

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Cross-talk between human epidermal growth factor receptor 2 and 3 (HER2 and HER3) may potentially contribute to therapeutic resistance in human breast cancer. Subtractive phage display allows highly specific selection for antibody fragments directed against cells surface HER2 and HER3. The strategies to select conformation- and activation-specific antibodies against HER2 and HER3 require tightly regulated HER2 and HER3 expressing cells that allow controlled activation/inactivation of these receptors during panning procedures. To achieve this, first, we found that VERO cell line is an appropriate cell line for heterogeneous expression of HER2 and HER3, and then we established a panel of VERO stable cell lines expressing high levels of HER2 and HER3 alone and in combination. The cell line established here; not only provided platforms for phage display-based methods but also could be used in any HER-related studies and drug discovery.

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