[P29] Hit Dexter 2.0: An in Silico Tool for Identifying and Analyzing Frequent Hitters

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High-throughput screening enables the experimental testing of tens of thousands of samples per day.[1] Some of the hits obtained from high-throughput screening may be related to assay interference caused by "bad actors" such as aggregators,[2] pan-assay interference compound (PAINS)[3] or reactive compounds.[4] Few in silico approaches exist that allow the flagging of false-positive assay outcomes. Recently we reported a pair of robust machine learning models ("Hit Dexter") for the prediction of frequent hitters.[5] Frequent hitters are often, but not always, bad actors. In an attempt to develop an approach able to discriminate bad actors from true promiscuous compounds we further developed our machine learning approach. For the assessment of compounds, the new models (implemented in the Hit Dexter 2.0 web service) take the similarity of target proteins into account and make use of predictions from different rule-based and similarity-based approaches. The Hit Dexter 2.0 web service provides a variety of additional analysis tools that in combination allow the discrimination of bad actors and true promiscuous compounds.

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