Application of a Maximum Common Substructure Concept to Library Design

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High- Throughput-Screening (HTS) has become the ultimate method for the discovery of new active compounds. However, the major drawback that interferes with the HTS-ideal is the high number of stable drug candidates. The exact number is not known, but the lowest estimate is that there exist at least 1013 stable candidates. That means, even if 1 million compounds are screened per day, 27000 years would be needed per target. Therefore a rational preselection of compounds to be screened is of utmost importance.

Therefore the objective of this project was the rational assembly of a screening collection enriched with bioactive and chemical diverse drug-like compounds for HTS. The assembled screening collection should be suitable for the discovey of a maximum number of hits for a variety of different protein classes. Therefore numerous self-written filters as well as commercial software tools have been applied for the rational assembly of a bioactive and diverse screening collection, namely:

- removal of compounds containing reactive, unstable and pharmaceutical negligible groups in order to avoid false positive hits
- selection of a diverse subset of compounds containing bioactive substructures in order to enrich the final assembly with putative bioactive compounds
- consideration of Lipinskis “Rule of 5” to ensure drug-likeness