[P5] Systematic generation of analog relationships of bioactive compounds and promiscuity analysis

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The generation of analogs of active compounds dominates hit-to-lead and lead optimization projects in medicinal chemistry. Most computational approaches applied in the course of chemical optimization attempt to aid in the design of better analogs and/or the exploration of SAR information associated with compound series.

A computational framework is introduced to systematically detect all synthetically accessible analogs of bioactive compounds in databases and determine how their chemical exploration might influence compound promiscuity (i.e., the ability of a compound to interact with multiple targets). For more than a third of all active compounds across 90% activity classes, no analogs were detected. For the majority of compounds with analogs, chemical exploration had no detectable influence on promiscuity. However, for a subset of ~26% of active compounds with analog sets, notable increases in promiscuity were observed, which were mostly due to the presence of single analogs with high degrees of promiscuity.

Bibliography:

[1] D. Dimova, D. Stumpfe, Bajorath. Med. Chem. Commun. 7 (2016) 230-236.