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MOLECULAR RECOMMENDATION ENGINE FOR MULTI-PROPERTIES OPTIMIZATION

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The attrition rate of drug candidates in development is mainly due to lack of efficacy or off target effects, whereas the main issues during lead optimization phases are usually related the compound's solubility, ADME or toxicity profile. Lead optimization is performed in several steps by introducing or replacing fragments on compounds of interest, monitoring compounds' profile changes and learning. Over several decades, pharmaceutical companies have collected thousands of physicochemical, ADME and pharmacological data which can be used to help designing new compounds. Leach A. *et al.* (2006) highlighted that statistical analyses of pair wised chemical transformations lead to a better understanding of the impact of a transformation on the physicochemical or ADME profile of compounds and could help in faster designing new drugs.

In this work, we present a molecular recommendation engine based on chemical transformations using a graph database. The database gathers internal and external pharmacological, ADME, physicochemical and toxicity data as well as trustful prediction models. Registered compounds are fragmented recursively and linked to fragments together with their scaffold hierarchy.

Several graph-based algorithms are implemented in the database in order to make recommendations for compound design by suggesting fragment replacement, to either improve one or more properties, or identify bioisosteric fragments. Hence, for each suggestion, it provides statistics of the impact of the chemical transformation on compounds' profile, paving the way for multi-objective lead optimization.