

Lead optimisation with LIGTOR and PRODRG

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PRODRG[1][2] is a tool for the generation and manipulation of small molecule data. It can be used to produce topologies for diverse compounds, thus enabling their use in various other software packages. Another application of PRODRG is the rapid and systematic modification of existing compounds, both by adding/removing functional groups and by regenerating coordinates guided by user-provided restraints. As such PRODRG can be employed in ligand design applications not only to prepare compounds for use with docking programs, but also to flexibly generate combinatorial libraries for in silico screening.

A new program, LIGTOR, adds a simple ligand docking step to the ‘PRODRG pipeline’. It optimises the conformation of a PRODRG-generated ligand in the context of a receptor site as described by a set of grid maps calculated using the AutoDock 3 force field[3]. Starting from a protein-ligand complex, the combination of PRODRG and LIGTOR allows the rapid screening of derivatives for improved binders. Several screening protocols and their application to *Aspergillus fumigatus* chitinase B[4] are described.

References

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