Antituberculosis Library

Designed with receptor-based approach, this library comprises potential drug candidates possessing activity towards InhA enzyme, *M. tuberculosis*-specific protein responsible for bacteria cell wall synthesis but not present in mammals.

The structure of InhA protein and the binding mode of its known inhibitors were studied based on the analysis of crystal structure records in PDB. This information has given us a detailed understanding of the protein-ligand interaction mechanism.

Next, the Life Chemicals HTS Compound Collection was processed according to ADME requirements, and all undesirable chemical groups were filtered out. The resulting drug-like set of compounds was screened by molecular docking using Glide program (Schrödinger software). 3FNH and 2H7I PDB entries were selected for the docking studies due to the most favorable ligand binding and high resolution of the crystal structures. The referent set of active ligands [1-2] was used for evaluation of the docking procedure. The presence of the NAD^+ coenzyme was taken into account in virtual screening as it is involved in ligand binding. After the docking, the compounds have been selected by ligand efficacy and comparison with binding mode of the referent inhibitors.

A set of **3,625** potential antituberculosis agents capable of binding with InhA protein was obtained (Fig.1).

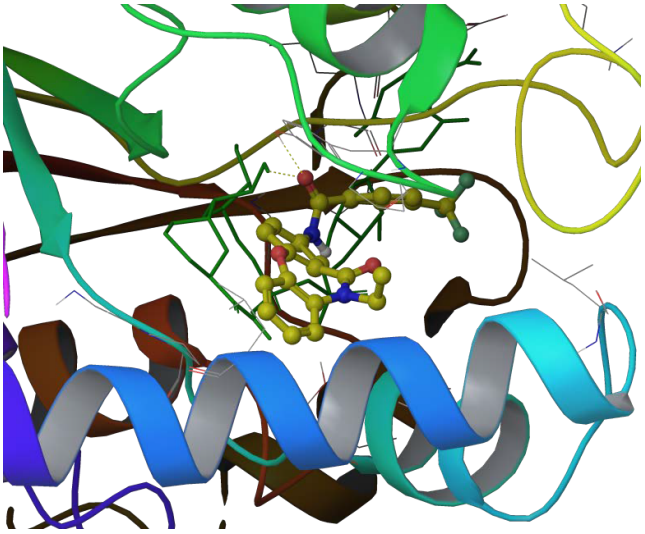

Fig. 1. Ligand F2269-0132 forms a strong hydrogen bond with Tyr158 and protein coenzyme NAD+. High hydrophobic interaction observed between fused aromatic rings and large hydrophobic pocket of InhA.

References

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