FBVS, a novel design to identify small molecules to various targets

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Technology

Dr. Akabayov and his team developed new method to discover small molecules leads that binds desire target macromolecules, using the combination of NMR-fragment based screening and machine learning-based computational optimization to enhance binding and inhibition of the target. The method was named **"Fragment based virtual screening, FBVS"**. The leads being examined and verified using relevant factional assay. This method is more efficient, less expensive and faster than the traditional medicinal chemistry used today for drug discovery. This method can be applied for various targets, such as enzyme, protein, RNA and more. The proof of concept was extensively studied in the lab for the DNA primase from bacteriophage T7. Moreover, few of the molecules discovered also inhibits the Tuberculosis primase. Similarly, the methodology was applied to identify new bactericidal lead compounds that target ribosomal peptidyl transferase center (PTC). Using NMR-fragment based screening they identified fragment molecules that bind specifically to unique RNA hairpin in the ribosomal PTC. The initial screening against the ribosomal PTC of the pathogenic bacterium *Mycobacterium tuberculosis* was performed by NMR T2 relaxation – a novel fragment screening approach– which was found to be effective for performing fragment screening for RNA targets. After the initial screening they employed computational optimization, in which the fragment molecules found by NMR were developed into larger molecules with drug like properties.

Applications

New methodology that can be used to facilitated and improved drug discovery for various macromolecules. Few lead compounds were identified as potential candidates for treating Tuberculosis.

Advantages

- New platform for drug discovery
- High-throughput screening
- Can be used for various target macromolecules, such as enzyme, protein, RNA and more
- Faster than traditional medicinal chemistry
- Reduce risk and cost
- More relevant heats
- Combines tools from different disciplines in drug development that bypasses many of the limitations of current drug discovery
- FBVS enable the isolation of inhibitors against targeted pathways that cannot be adapted for HTS and therefore considered as "undruggable" targets in potentially any biochemical pathway.

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