Ben-Gurion University of the Negev
Blaustein Institutes for Desert Research
The Swiss Institute for Dryland Environmental and Energy Research
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Using NMR-fragment based and computational chemistry for the development of novel antibacterial agents targeting the ribosomal PTC of M. tuberculosis

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Abstract:

We have developed new lead compounds that target the ribosomal peptidyl transferase center (PTC) of M. tuberculosis, a pathogenic bacterium that kills more than 1.5 million people worldwide every year. For this purpose, we used a fragment-based screening workflow in which the first step was the novel exploitation of NMR transverse relaxation times (T2) to identify fragment molecules that bind specifically to RNA hairpin 91 in the ribosomal PTC of M. tuberculosis. This initial screening was followed by computational optimization of the fragment molecules into larger molecules with drug-like properties. Specifically, a virtual filtration followed by a high-throughput docking procedure yielded drug-sized molecules. A machine-learning model predicted two molecules that exhibited IC50 values superior to that of chloramphenicol, an antibiotic drug that acts on the ribosomal PTC.

Date & Location:

Monday, April 6, 2021, 11:00

YDSEEP WEEKLY SEMINAR 2020-2021