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Poster abstract submission

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Presenting author Haftay Tadesse

Presenting author's email haftayt81@gmail.com

Further authors (if any)
Haftay Abraha Tadesse

Affiliation(s)
Mekelle University

Country Ethiopia

Type of organization Academic / research institution

Poster title
Inhibitor Activity and Resistance Mechanism of Compound BTD7 against Mycobacterium tuberculosis

Poster abstract
Tuberculosis remains a global health concern, with the increasing prevalence of multidrug-resistant and extensively drug-resistant tuberculosis undermining the efficacy of current anti-tuberculosis drugs. In light of the stagnant progress in novel tuberculosis drug development over the past five decades, there is an urgent need for innovative therapeutic strategies. This research aimed to characterize the efficacy of the novel compound BTD7 against Mycobacteria and to elucidate its mechanism of action. The M. tuberculosis was subjected to the selection of spontaneous resistant mutants with different concentrations of BTD7. After three rounds of evolution, BTD7-resistant mutants were isolated and subjected to whole-genome sequencing (WGS). The results were confirmed through Sanger sequencing. The novel compound BTD7 demonstrated excellent in vitro activity against M. tuberculosis H37Rv, with a minimum inhibitory concentration (MIC) of 0.0078125μg/mL and macrophage cells of 0.5-1μg/mL. WGS of these mutants identified a common mutation in the essential gene rv0902c, which encodes the histidine kinase PrrB. Specifically, an A266C point mutation was identified, resulting in a non-synonymous amino acid change from Arginine to Leucine at position (A266L) in the sensor histidine kinase PrrB. BTD7 represents a promising new chemical entity targeting the sense of cell membrane of M. tuberculosis. Its potent activity, novel target, and effectiveness against drug-resistant strains warrant its further development as a potential component of new TB drug regimens.

Research topic Microbiology

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