Therapeutics for Tuberculosis: Novel Inhibitors of Mycobacterial RNA Polymerase

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Technology description

Invention Summary:Tuberculosis kills nearly 2 million persons each year. One third of the world's population currently is infected with tuberculosis, and the World Health Organization projects that there will be nearly 1 billion new infections by 2020, 200 million of which will result in serious illness, and 35 million of which will result in death. Treatment of tuberculosis infections is slow (minimum treatment period of six months), and treatment of multi-drug-resistant (MDR) and extensively-drug-resistant (XDR) tuberculosis infections is very slow and often ineffective (minimum treatment time of twelve months and mortality greater than 50%).There is an urgent need for new classes of antituberculosis agents, particularly antituberculosis agents that clear infection quickly and are effective against MDR and XDR infections.Rutgers researchers have identified a class of compounds that potently inhibit Mycobacterial RNA polymerase (RNAP) but do not potently inhibit Gram-negative bacterial RNAP or other Gram positive bacterial RNAP: N $^{\alpha}$ -aroyl-N-aryl-phenylalaninamides (AAPs). Rutgers researchers have validated AAPs as lead compounds; have synthesized and evaluated more than 600 novel AAPs; have identified novel AAPs that exhibit improved potencies, physical properties, and pharmacological properties; and have demonstratedin vivoproof of concept in a mouse tuberculosis acute infection model.

Application area

Treatment of tuberculosis, including MDR and XDR tuberculosis
Treatment of non-tuberculosis mycobacterial (NTM) infections, includingMycobacterium aviumcomplex (MAC) infections

Advantages

First-in-class compounds
Novel target and mechanism
Potent selective antimycobacterial activity
Activity against MDR and XDR strains
Activity against both replicating and non-replicating mycobacteria
Rapid sterilizing activity

Additive effects when co-administered with current antituberculosis agents
Suppressed resistance emergence when co-administered with current antituberculosis agents

Institution

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