ACS Infectious Diseases

In This Issue

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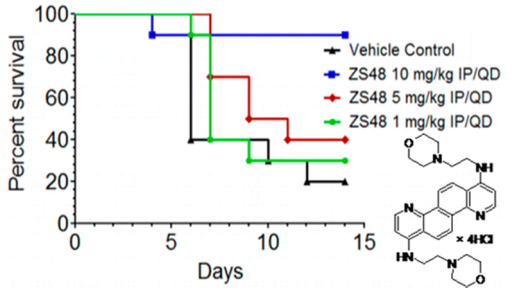
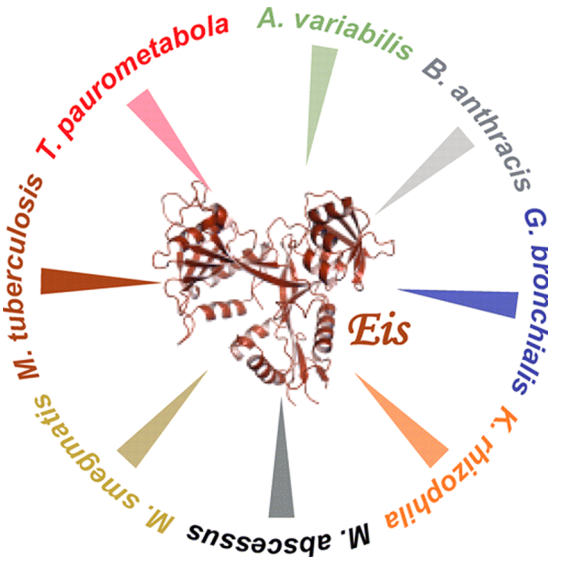
DEVELOPING SMALL-MOLECULE INHIBITORS TO FIGHT EBOLA



There are presently no FDA-approved therapeutics for treatment of Ebola virus infections. The recent outbreak of Ebola virus in West Africa has demonstrated a need for the development of antivirals that are effective against Ebola virus.

A class of small-molecule inhibitors, diazachrysenes, previously demonstrated inhibitory activity against Ebola virus in vitro. In this issue, Selaković et al. (DOI: 10.1021/acsinfecdis.5b00028) develop a series of diazachrysene compounds with improved in vitro activity compared to the predecessor compounds. They demonstrate these small molecules are nontoxic and metabolically stable and provide excellent protection against Ebola virus in mouse models of infection.

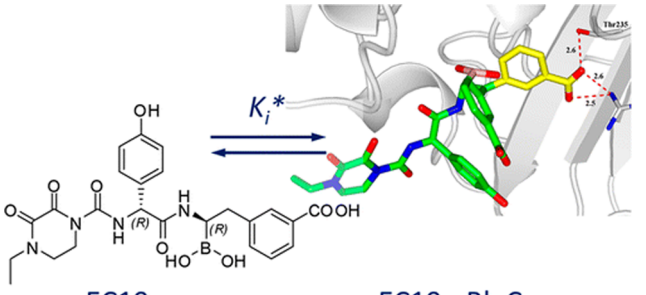
EIS-LIKE PROTEINS DISCOVERED BEYOND *MYCOBACTERIUM TUBERCULOSIS*



Aminoglycosides are a class of broad-spectrum antibiotics that are used as a second-line therapy for treatment of *M. tuberculosis* infections. Although many bacteria possess enzymes capable of modifying aminoglycosides at a single site, *M. tuberculosis* has been found to express an enhanced intracellular survival (Eis) protein capable of modifying aminoglycosides at multiple sites.

Here, Green et al. (DOI: 10.1021/acsinfecdis.5b00036) identify a number of homologues of the *M. tuberculosis* Eis protein in a wide variety of both pathogenic and nonpathogenic bacteria. After cloning and expressing these homologues in vitro, kinetic studies are conducted to assess the ability of these enzymes to modify aminoglycosides and other antibiotic substrates. Finally, the authors demonstrate the ability to broadly inhibit these Eis-like proteins.

TARGETING BlaC OF *MYCOBACTERIUM TUBERCULOSIS*



The β-lactamase BlaC of *M. tuberculosis* presents an important barrier to effective treatment of tuberculosis with β-lactam antibiotics. Identifying effective inhibitors of BlaC would open the possibility for the use of β-lactams as therapeutics against *M. tuberculosis* infection.

In this work, Kurz et al. (DOI: 10.1021/acsinfecdis.5b00003) investigate the ability of boronic-acid containing compounds with structural similarity to β-lactams to inhibit BlaC. The authors synthesize and screen a panel of boronic acid transition-state inhibitors (BATSIs) to identify a lead compound exhibiting slow, time-dependent inhibition of BlaC. The structure–function analysis conducted here may serve as a platform to guide further rational design of BATSIs for the inhibition BlaC.

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