ACS Infectious Diseases

In This Issue

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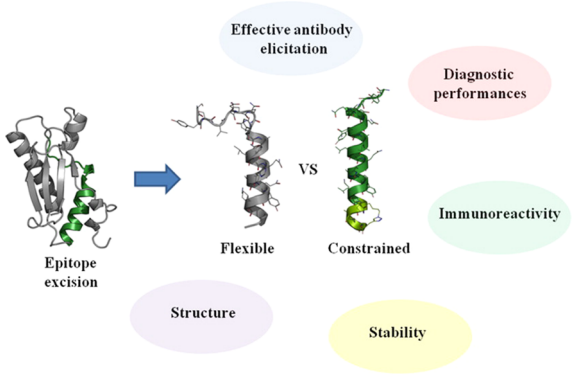
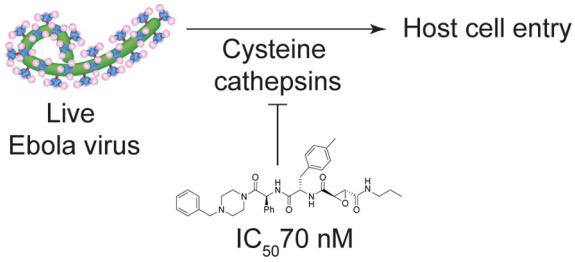
IMPROVING THE USE OF PEPTIDES IN VACCINE AND DIAGNOSTIC DEVELOPMENT



Burkholderia pseudomallei is the causative agent of melioidosis, a severe disease endemic to subtropical regions of Asia and South America. Melioidosis infections not only are associated with high mortality but also are difficult to diagnose as no effective molecular diagnostic is available. Recently, an immunoreactive α-helical epitope from *B. pseudomallei* was identified as a promising candidate for the development of a meliodosis vaccine and also has potential applications for diagnostic development.

In the article featured on the cover, Gori et al. (DOI: 10.1021/acsinfecdis.5b00118) observe that the α-helical structure of the epitope is not conserved as a free peptide and investigate how structural engineering of the flexible synthetic epitope using a stapling strategy impacts the immunological properties of the epitope. The authors evaluate the structurally stabilized variant for diagnostic-oriented immunoreactivity and the ability to elicit cross-reactive antibodies against the native antigen. This work highlights the potential for the use of peptide stapling in epitope stabilization for application in vaccine and diagnostic development, providing promise for the effective prevention and diagnosis of diseases such as melioidosis.

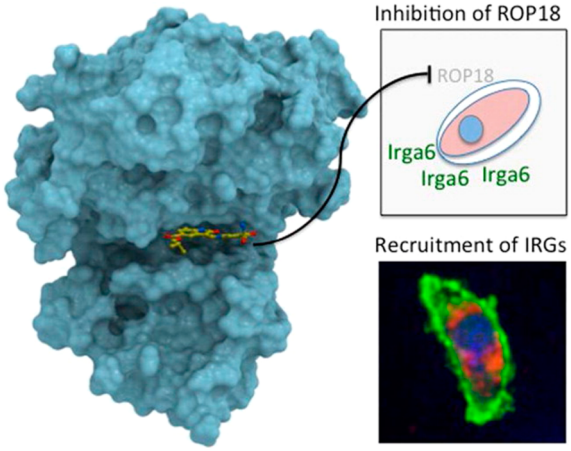
TARGETING HUMAN PROTEASES TO STOP FILOVIRUS SPREAD



Filoviruses, including Ebola virus and Marburg virus, pose a serious threat to human health as sporadic outbreaks of these viruses have demonstrated high mortality rates, and no effective therapeutics against these agents have been validated. As the viral coat proteins require processing by lysosomal cathepsins, targeting these host-derived proteases presents an appealing strategy for the development of antifilovirus agents. Unfortunately, it has been demonstrated that the activity of specific cathepsins is redundant and a broad spectrum inhibitor would be necessary to adequately prevent viral processing.

In this issue, Wouter et al. (DOI: 10.1021/acsinfecdis.5b00130) design and synthesize highly potent, cell-permeable, broad spectrum cathepsin inhibitors. The authors demonstrate the efficacy of these cathepsin inhibitors in blocking host cell entry of Ebola virus and Marburg virus. The small molecules designed here serve as ideal lead compounds for advancement in animal studies of infection and present hope for the identification of a viable therapeutic agent to block spread and prevent mortality in infected individuals.

DEVELOPING KINASE INHIBITORS AS ANTI-INFECTIVES



Toxoplasma gondii is a protozoan parasite that is among the most common human parasites in the developed world. Although acute disease caused by *T. gondii* is generally mild, the parasite can enter a stage of latent infection which may present serious or even fatal complications in situations of weakened immunity. Current therapies targeting *T. gondii* suffer from an inability to clear chronic infections, drug tolerance, and adverse side effects, so the development of antiparasitic agents able to overcome these limitations is needed. As kinase inhibitors have demonstrated success in therapeutic development for human diseases including cancer, their potential as anti-infectives against eukaryotic organisms including *T. gondii* has been proposed.

Here, Simpson et al. (DOI: 10.1021/acsinfecdis.5b00102) conduct a high-throughput screening of small molecules to identify inhibitors of *T. gondii* virulence factor rhoptry kinase 18 (ROP18). From this screening, the authors identify chemical scaffolds exhibiting a potent inhibition of ROP18. The lead compounds identified here present promise for the further development of kinase-directed agents against *T. gondii*.

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