ACS Infectious Diseases

In This Issue

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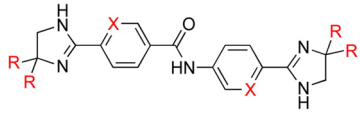
ANTITRYPANOSOMAL TREATMENT FOR MALARIA

The antitrypanosomal activity of diamidines has been well characterized. These compounds continue to show promise against late stage African trypanosomiasis, but the antimalarial potential of diamidines has not been adequately addressed.

In this issue, Wang et al. (DOI: 10.1021/id500034v) show that analogues of diimidazolines also display potent in vitro antimalarial activity in addition to antitrypanosomal activity. Through phenotypic drug discovery study, three new lead compounds with high antiplasmodial selectivity and one lead compound with high antitrypanosomal selectivity were discovered. Importantly, the study demonstrates how small changes in structure lead to rather large changes in antiprotozoal selectivity.

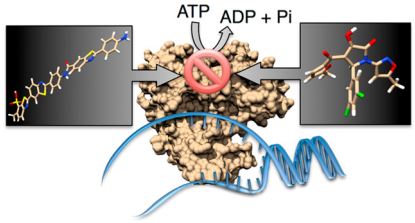


X, R	CH, H	N, H	CH, CH_3
P. falciparum IC_{50}	1.9 nM	28 nM	310 nM
T. b rhodesiense IC_{50}	86 nM	8,300 nM	26 nM
cytotoxicity IC_{50}	68,000 nM	130,000 nM	>150,000 nM

ROBUST ASSAY FOR FLAVIVIRUS INHIBITORS

Flaviviruses comprise a genus of positive sense single-stranded RNA viruses, including yellow fever virus, Dengue virus, and West Nile virus. In the same Flaviviridae family as flaviviruses is hepatits C virus (HCV). With the recent success in development of HCV drugs, it is possible that similar compounds might be useful to treat flavivirus infections, including Dengue virus, which infects an estimated 390 million people each year. The flavivirus nonstructural protein 3 (NS3) is a protease and helicase and shares similarity to its homologue encoded by HCV, making the flavivirus NS3 a promising drug target.

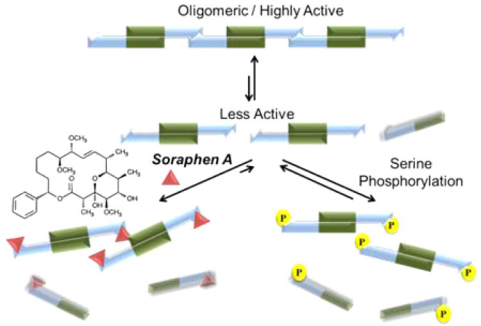
Few flavivirus helicase inhibitors have been reported, due in part to lack of specificity in screening assays. Here, Sweeney et al. (DOI: 10.1021/id5000458) designed a robust dengue virus assay suitable for high-throughput screening to discover inhibitors of Dengue virus replication. One set of compounds were previously designed to target the helicase function of HCV, while another set includes compounds specific for flaviviruses.



SORA, A LIPOGENESIS PROBE

Many viruses, such as hepatitis C virus prompt changes in their hosts. Some viruses generally increase host cell metabolism to meet increased energy demand. Acetyl-CoA carboxylase (ACC), which controls fatty acid biosynthesis, polymerizes to form a catalytic multiprotein complex.

Soraphen A (SorA) is a natural product inhibitor of ACC activity, which acts through disruption of the formation of highly active ACC polymers. Featured on the cover, Singaravelu et al. (DOI: 10.1021/acsinfecdis.5b00019) show that SorA inhibits hepatitis C virus replication in cell culture models. The study demonstrate that SorA lowers cellular lipid levels in hepatoma cells, and shows that SorA could be a valuable probe to study the roles of ACC polymerization and enzymatic activity in viral pathogenesis.



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