ACS Infectious Diseases

In This Issue

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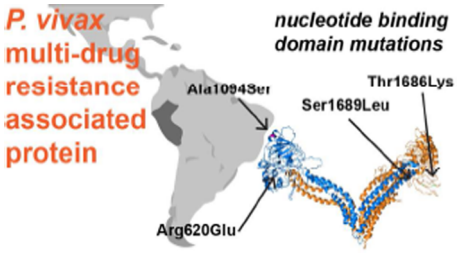
INVESTIGATING THE BASIS OF MALARIA DRUG RESISTANCE IN THE PERUVIAN AMAZON



Malaria is a life-threatening parasitic disease endemic to sub-Saharan Africa and regions of Asia and Latin America. Although several species are known to cause malaria in humans, the most widespread form of the disease is caused by the parasite *Plasmodium vivax*. Unfortunately, investigations of *P. vivax* biology are hampered by a lack of sustainable culture systems which would allow manipulation of the parasite in the laboratory. As such, few molecular markers of drug resistance have been identified.

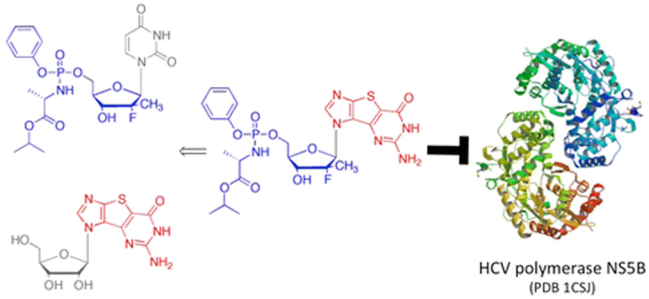
To circumvent the impediments relating to the lack of appropriate culture system, Flannery et al. (DOI 10.1021/acsinfecdis.5b00049) use a population-based approach to map genes involved in drug resistance. Using next-generation sequencing, the authors investigate polyclonality and inbreeding of *P. vivax* samples from the Peruvian Amazon and present evidence of recent evolution in known drug resistance genes.

BRINGING EBOLA RESEARCH OUT OF CONTAINMENT

The current outbreak of Ebola virus in West Africa is unprecedented in scope and demonstrates a dire need for antiviral therapies effective against this emerging pathogen. Although a clear need exists for the development of novel therapeutics targeting Ebola virus, handling of live Ebola virus must be conducted in high-containment facilities (biosafety level 4), thus restricting research to a small number of facilities worldwide.

Here, Edwards et al. (DOI 10.1021/acsinfecdis.5b00053) adapt an established minigenome assay that does not require live virus or handling in high containment to establish a high-throughput screen for small molecule inhibitors of Ebola virus. Following screening of a large number of compounds, the authors confirm the efficacy of the new high-throughput screening assay by testing hit compounds against live Ebola virus. The screening method developed here provides the scientific community with a greater capacity to screen for novel Ebola therapeutics without the requirement of high-containment.

USING SOFOSBUVIR'S SUCCESS TO GUIDE THE DESIGN OF HEPATITIS C THERAPIES



Hepatitis C virus (HCV) is a blood-borne virus capable of causing chronic infections that result in serious long-term health problems. Recently, Sofosbuvir, a nucleotide analogue that acts by inhibiting HCV RNA polymerase, was developed and approved for use in combination therapy for treatment of HCV infection. Sofosbuvir combination therapy has demonstrated excellent efficacy in the clinic. In the laboratory, tricyclic expanded purines have also demonstrated promising efficacy against HCV.

In this issue, Chen et al. (DOI 10.1021/acsinfecdis.5b00029) design and synthesize a series of novel tricyclic expanded purine nucleosides that have incorporated the 2′,2′-Me/F modification found in Sofosbuvir's sugar. Although the novel compounds demonstrated antiviral activity against HCV, their activity was not superior to that of Sofosbuvir. Nonetheless, the synthesis of these compounds provides a novel platform for further development of compounds with improved efficacy against HCV.

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