International Journal of Drug Research and Technology

Available online at http://www.ijdrt.com

Commentary

RECENT HIGHLIGHTS IN RESISTANCE AND DRUG DEVELOPMENT AGAINST PROTOZOA

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INTRODUCTION

A selection of the research presented in January at the Keystone Symposium on Drug Discovery for Protozoan Parasites in Santa Fe, New Mexico, is presented in this special issue of IJPDDR. Since its inception, the symposium has been held approximately every two years. Leading researchers from all over the world were able to present data on everything from basic science to clinical trials related to the development of anti-protozoan drugs and drug resistance at the meeting, just as they had in previous years. Malaria was the topic of many talks, as expected, but other protozoan diseases like African sleeping sickness, Chagas disease, leishmaniasis, cryptosporidiosis, and amoebiasis were also discussed. Many of the highlights of the new research presented at the meeting are summarized in this editorial. It is obvious that drug resistance is developing, which has implications for morbidity and mortality; however, other species of malaria parasites have been overlooked.

DESCRIPTION

Kevin Baird, of the Eijkman-Oxford Clinical Research Unit in Indonesia, has been dubbed the neglected malaria parasite despite the fact that this parasite is responsible for between 100 and 400 million infections annually, of which a proportion that is yet unknown is severe 24% and 8% in one Indonesian study. Both primaquine (a hypnozoitocide) and chloroquine (a blood schizontocide) have developed resistance, and for chloroquine, it appears to be widespread throughout Southeast Asia. Sadly, the mechanism of P. falciparum resistance is unknown, unlike chloroquine resistance. New therapies for need to be developed and efforts need to be started and supported. However, any new treatments to take the place of chloroquine must be evaluated in conjunction with primaquine because primaquine is the only medication that can get rid of hypnozoites, which cause relapses. The presented evidence suggests that primaquine can only be effective with the right co-drug. Due to drug resistance and the need to address the various parasite forms that occur throughout the infection's life cycle, new therapies for P. vivax must be pursued as a drug combination endeavor. In this issue of IJPDDR, Kevin Baird discusses the challenges that lie ahead for the discovery of chemotherapeutics and the necessity of developing therapeutic strategies for all malaria species. In addition, any discussion regarding the control and elimination of malaria must include endemic malaria, which is frequently difficult to diagnose and treat ineffectively [1,2].

In a similar vein, the enteric pathogen Cryptosporidium parvum was the subject of a strategy to repurpose FDA-approved drugs for anti-protozoan applications. Kovi Bessof, a researcher at the University of Vermont, created a high-throughput screening platform for C. parvum. He then screened a collection of 727 approved or drug-like molecules, either by themselves or in combination with nitazoxanide, a well-established antibiotic against Cryptosporidium. In immunocompromised C. parvum-infected animals, the hits from this screen are undergoing additional evaluation, either by themselves or in combination. A drug that has been approved for use in rheumatoid arthritis, auranofin, has been shown to have anti-Entamoeba spp. in vitro activity in a presentation by Rosa Andrade from the University of California, San Diego. Auranofin had a much higher cysticidal activity than metronidazole, the standard amoeboide, on Entamoeba invadens cysts, suggesting a potential therapeutic advantage. The IC50 of auranofin against E. histolytica trophozoites was 2 M. Auranofin has the potential to enter clinical studies for amoebiasis much more rapidly than compounds that have not been approved by the FDA.Finally, Anjan Debnath (University of California, San Francisco) investigated Naegleria fowleri, the agent of amoebic meningoencephalitis [3].

A high-throughput in vitro screening platform was developed and tested against a collection of drugs that have been approved by the FDA and are in clinical development. In a mouse model of primary amebic meningoencephalitis, corifungin, a polyene antifungal similar to amphotericin B, was found to have excellent activity (better than amphotericin B). The FDA has granted corifungin Orphan-Drug status for the treatment of primary amebic meningoencephalitis on the basis of these findings.The Australian Army Malaria Institute's Alyson Auliff reported the creation of a transgenic system in which the wild-type and mutant dhfr genes are stably expressed. This system can be used to evaluate the effects of both existing and upcoming antifolate medications. The transgenic expression system has the potential to support drug discovery efforts for specific vivax targets and provide a system to characterize the molecular mechanisms that are responsible for drug resistance due to the difficulties associated with culturing. Karryn Gresty, from the Australian Army Malaria Institute's Pacific Malaria Initiative, wrote about the genotypic and infection monitoring of samples taken from all over the South Pacific. In order to gain a deeper comprehension of the development and dynamics of drug resistance, it is anticipated that the advancement of molecular tools, assays, and culturing methods will soon complement ongoing surveillance efforts [4-6].

CONCLUSION

The Keystone Symposium on "Drug Discovery for Protozoan Parasites" gave people a rare chance to participate in protozoan drug development from all angles. The aim of reducing the burden of protozoan diseases was shared by parasitologists, medicinal chemists, and clinicians from government, industry, and academia. In the process of developing a drug, many issues and obstacles must be overcome; However, this conference facilitated discussions of challenges specific to the development of protozoan drugs. As new collaborations were established and previously unknown data were made public, this conference's momentum will help drug development efforts.

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Received: 2-November-2022, Manuscript No. IJDRT-23-90035; **Editor assigned:** 4-November-2022, Pre QC No. P-90035; **Reviewed:** 17-November-2022, QC No. Q-90035; **Revised:** 23-November-2022, Manuscript No. R-90035; **Published:** 30-November-2022, DOI: 10.37421/2277-1506.2022.11.380

Cite This Article: Tsay W (2022). Recent Highlights in Resistance and Drug Development against Protozoa. ***International Journal of Drug Research and Technology*** Vol. 11(9) 1-3.