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Editorial: Drug discovery for emerging and neglected tropical diseases: advances, challenges and perspectives

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Editorial on the Research Topic
Drug discovery for emerging and neglected tropical diseases: advances, challenges and perspectives

Neglected tropical diseases (NTDs) comprise a group of 20 human illnesses caused by bacteria, viruses, protozoans, ectoparasites, and venous snakebites. Altogether, NTDs affect over 1.7 billion people worldwide; they are predominantly prevalent in the tropical, low- and middle-income regions of the globe, where the most vulnerable populations live at risk (WHO, 2020). Nonetheless, climate changes and intense human migratory processes accelerate the dissemination of NTDs into non-endemic regions. Furthermore, the COVID-19 pandemic has raised the alert for the emergence of new and the re-emergence of old diseases, mainly because of host-switching events, drug resistance, and failure of public health measures (Morens and Fauci, 2020; The Lancet, 2022).

Besides the massive impacts on the economy, productivity, and social development, the latest records on NTDs indicate that, over 1 year, around 200,000 deaths occur, and the disability-adjusted life years (DALY) sum up to 19 million. In recent years though, we have observed remarkable progress in reducing the global burden for some NTDs, especially under the network of strategic actions managed by the World Health Organization (WHO) in association with governmental and private collaborators. Despite the efforts from several multisectoral initiatives focused on the prevention, control, treatment, and elimination of these maladies, many NTDs still prevail in regions with limited resources (WHO, 2020). Within this period, the field of drug discovery for NTDs has also seen a mix of progressions and drawbacks. There has been an increase in innovative public-private partnerships and the development of important therapeutic alternatives within distinct strategic approaches: drug repurposing [i.e., fexinidazole against human African trypanosomiasis (Kaiser et al., 2011; Bernhard et al., 2022)], new formulations [i.e., paediatric benznidazole against Chagas disease (DNDi, 2021)], drugs combination [i.e., miltefosine-paromomycin combination against visceral leishmaniasis (Musa et al., 2023)]. Nevertheless, several obstacles hamper the discovery and development of new drugs

against NTDs, such as the high biological complexity of the disease, antimicrobial resistance, and financial impediments (De Rycker et al., 2018; Weng et al., 2018; DeWeerdt, 2021; Eisenstein, 2021). Therefore, despite advancements acquired through concerted efforts worldwide, the development of novel or improved treatments remains a relevant need in the continuous fight against NTDs.

In this context, this Research Topic brings together articles covering pivotal aspects of drug discovery and drug development for NTDs, focused on viral and parasitic infections. This Research Topic includes an original article devoted to the identification of novel therapeutic alternatives against *Plasmodium falciparum*. It also contains articles describing and discussing experimental strategies to uncover targets and modes of action of known and new antimicrobials. Lastly, it also includes a review article focused on the valuable lessons gained during the COVID-19 pandemic that could help to face and prevent future arbovirus epidemics.

Chirawurah et al. present follow-up studies to evaluate the potency of three Malaria Box compounds—previously selected as potent antimalarials (Chirawurah et al., 2017)—against a panel of twenty clinical isolates of *P. falciparum*. Using *in vitro* growth inhibitory assays, the authors validated the activity of these compounds and compared their activity with those observed for reference compounds. Most importantly, the article underscored the need to incorporate clinical isolates (including drug-resistant isolates) in antimalarial compound screening activities.

Fairlamb and Wyllie systematically discuss the crucial role of investigating the mode of action in kinetoplastid drug discovery, highlighting the tools currently available for target identification and validation, including genomics, proteomics, and metabolomics, as well as informatic approaches. The authors also provide examples of how to apply these tools to identify and exclude undesirable molecular pathways, detect potential toxic properties, and manage a balanced portfolio of target-based campaigns. Finally, the authors review the primary drug targets (e.g., proteasome and protein kinases) currently in clinical development against *Leishmania* and trypanosomes.

Hauser and Maser described an interesting *in silico* work of an integrative bioinformatic approach that was applied to discover potential targets of suramin, one of the pharmacopoeia's most promiscuous drugs. A list of 44 diverse proteins was identified as potential targets of suramin, presenting common functional motifs. These findings are crucial to understanding the nature of suramin's mechanism of action and, ultimately, to design new and more selective inhibitors.

Rosa-Nunes et al. comprehensively reviewed the scientific and technical advances achieved after the COVID-19 pandemic regarding prophylaxis, antiviral drug development, and immunization strategies. The article exemplifies relevant approaches currently used for disease management, including the use of mRNA-based vaccines and the administration of replication inhibitors (e.g., nucleoside analogues and protease inhibitors). Lastly, the authors discuss how we could explore the lessons learned from the COVID-19 pandemic and how to apply them to control neglected viral infections caused by arboviruses.

As a final remark, this Research Topic shows recent progress in the efforts for the discovery and development of new drugs for NTDs, with emphasis on parasitic and virus infections. Studies such as those collected herein contribute to reducing the existing research gaps that hinder the achievement of more effective and affordable treatments for vulnerable populations worldwide. We thank all the contributors.

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