Editorial: Approaches for Development of New Antiprotozoan Drugs

Protozoan parasites such as *Trypanosoma cruzi*, *Leishmania* spp, and *Plasmodium* spp have ancient histories of co-evolution and complex interactions with their mammalian hosts. In order to survive against hostile environments created by the host's defense mechanisms highly adapted parasites have been selected, possessing biologic, metabolic and enzymatic features that allow them to survive and multiply within the mammalian host. Although these unique features may represent obstacles for parasite eradication, they may also be the key for development of chemotherapeutics with selective action. The development of new drugs with high efficacy and low toxicity against these protozoan parasites is of great need on account of the high toxicity of many of the available drugs and to the appearance of drug-resistant parasite strains.

The diseases caused by these parasites are neglected in terms of investments for drug development because they are endemic in developing countries. Although a significant amount of basic research is carried out aiming to identify new anti-protozoan molecules, only few candidate drugs have entered clinical studies and even less became available to patients due to gaps in the pipeline of drug development. Since the identification of hits and lead compounds is a critical step towards progression in the drug development pipeline, the use of combined strategies may facilitate the identification of promising compounds and their mechanism of action.

The present issue brings reviews focused on different approaches and strategies than can be employed for the development of chemotherapy for diseases caused by protozoan parasites. Cruz and collaborators also highlight the need for integrated partnerships and networks between scientists in academic institutions and industry for drug development against parasitic diseases, and the importance of initiatives such as the one aiming to produce transgenic parasites, e.g. *Leishmania* and *Plasmodium*, better suited for HTS platforms in order to accelerate the screening of antiparasitic drugs.

Several metabolic pathways important for the protozoan parasites have been identified as potential drug targets. Azevedo Jr. and Soares discuss about three identified targets, protein kinases, chorismate synthase, and purine nucleoside phosphorylase, focusing on the main features that can be explored in virtual screening initiatives.

Compounds to be screened can be obtained from natural sources of by synthesis. Here, Queiroz and colleagues highlight the importance of plants as a rich source of new molecules with pharmacological properties, which can be more efficiently explored in the development of new antiparasitic drugs by combined approaches which allows distinguishing between already known bioactive compounds and new molecules directly in crude plant extracts, accelerating the discovery of compounds of interest. Regarding the synthesis of active compounds, Moreira and co-workers comment on approaches used for the design of new potential anti-*T. cruzi* agents by using modern concepts of medicinal chemistry, and show that, although we are still far from being able to design compounds with the desired features, lessons can be learned from already published studies which may enhance the chances of success.

The main bioinformatics tools available for drug discovery and development are discussed by Azevedo Jr and collaborators, showing the potential of computational methods in drug discovery and development. The current status of efforts to develop genomic databases for protozoan parasites is also reviewed by Timmers and co-workers. In addition, Vannier-Santos and De Castro describe how alterations induced by antiparasitic compounds may help in the identification of subcellular targets for drug development in protozoan parasites and of the mechanism of action of drugs.

Infection with *Plasmodium* spp is an interesting example of how complex the interaction of the host and the parasite can be, opening several possibilities of intervention. Different experimental models and screening assays for drug screening in malaria have been developed, allowing the identification of drug candidates against different forms of the parasites, as commented by Krettli and co-workers. Interaction studies of ligands with validated protein targets for antimalarial drug development are highlighted in the review of Azevedo and co-workers. In addition, Bustamante and co-workers discuss about the identification of molecular markers of parasite drug resistance, which may be helpful for the future development of new antimalarials.

A significant proportion of drug candidates fail in other parameters than efficacy. In this issue, Nogueira and collaborators review the importance of early evaluation of toxicity and selection of lead compounds with physicochemical parameters that will benefit orally bioavailable drugs, which are crucial for patients' compliance and cost effectiveness, as well as for successful pharmacology.

Finally, I would like to thank the authors for their valuable contribution with dedication and hard work to this special issue, which hopefully will be of usefulness to researchers engaged in the task of developing new drugs for neglected diseases.

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