Feverish writing

A couple of years ago, the Medicines for Malaria Venture partnered with IUPHAR to fund the building of a new data portal on to the Guide to PHARMACOLOGY database. This portal was intended to make data on antimalarial drugs as accessible as possible to malaria researchers. Part of the point of this is that different research communities tend to think, and to organize information, in different ways. While dyed-in-the-wool pharmacologists may focus at once on ligands, receptors and binding affinities, malaria specialists tend to focus on parasite species and life-cycle stages of those parasites as they breed in an infected person. Jane and Simon, working in this group, therefore constructed a portal based around these things, and it became the already much-used Guide to MALARIA PHARMACOLOGY (see links section at the end).



One of the first things that Jane had to do, working with MMV (especially with their Brice Campo), was to assemble a large team of expert advisors who, between them, know pretty much all there is to know about antimalarial pharmacology. Having these people on hand, or at least on-screen because they are scattered all over the world, was amazing. During the planning of the project, someone – and I really don't remember who it was at this stage – had the idea of giving the group one last task: to write a comprehensive and up-to-date review of the state-of-the-art in antimalarial drugs, in the problems of resistance, and in the most promising future directions. This was to be an official IUPHAR review, published in the British Journal of Pharmacology.

The search for drugs against malaria has a long history, from the use of natural barks and plant teas, to identification of their key ingredients such as quinine, to the manufacture of entirely synthetic drugs. The task has never been easy: malaria parasites are, like us, eukaryotic and share much of our biochemistry. It is therefore much harder for researchers to find biochemical pathways of the parasite to attack without attacking the same pathways in the human host. In addition, malaria has proved very good at evolving resistance to once-effective drugs and the modern method is to attack it with several new drugs at once, to lower the chances that any parasites can become resistant to, say, three drugs at the same time.

All of this means that there are many sections of our review, each focusing on a potential drug target in some stage of the parasite life-cycle, and on the various chemicals that seem to show promise agains that target, many in clinical trials or even in use. This was not a short piece of writing – we ended up citing literally hundreds of references, so many we required a special dispensation to go beyond the normal maximum-reference-number rule of the journal in fact. We hope we captured everything that is really important, but apologize to anyone whose work we just could not fit in.

Having 27 authors brought with it the advantage of a great deal of knowledge. It also brought a formidable problem of organization to ensure that that everyone contributed what they know best, leaving no gaps but also avoiding repetition. Jane more than earned her status as first author in coordinating all of this, again with considerable help from Brice, who appears as second author (me? I come last! My main contribution was the short section on the history of the field). After some months, and several cycles of revision it all came together, and the peer reviewers were finally satisfied that all of their suggested changes were made. Should you want to read it, it is available on open-access (see links below).

Jamie Davies, Edinburgh, June 2023

Links:

Medicines for Malaria Venture <u>https://www.mmv.org/</u> Guide to PHARMACOLOGY <u>https://www.guidetopharmacology.org/</u> The paper: <u>https://bpspubs.onlinelibrary.wiley.com/doi/10.1111/bph.16144</u>