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EDITED AND REVIEWED BY
Sam C. Wassmer,
University of London, United Kingdom

*CORRESPONDENCE
Alena Pance
✉ a.pance@herts.ac.uk

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Editorial: Women in malaria research

Alena Pance^{1*}, Elena Gómez-Díaz² and Sarah Reece³

¹School of Health, Medicine and Life Sciences, University of Hertfordshire, Hatfield, United Kingdom, ²Institute of Parasitology and Biomedicine Lopez-Neyra, Spanish National Research Council, Granada, Spain, ³School of Biological Sciences, University of Edinburgh, Edinburgh, United Kingdom

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Editorial on the Research Topic Women in malaria research

The existence and importance of malaria is recognised throughout the history of humanity, with evidence of its symptoms dating back to ancient Egyptian times. But it was not until 1880 when Laveran discovered that malaria, or ‘mal’aria’ (bad air) as it was known, is caused by *Plasmodium* parasites. This was the beginning of a scientific journey to understand, prevent, and treat the disease. With science and education being mostly male endeavours at the time, it is unsurprising that the field, as many, was propelled by male scientists. Nevertheless, prominent women started influencing the malaria world fairly early on. As early as the late 19th century, Anna Fraentzel Celli, within the Italian School of Malariology, advocated public health education, aiming to prevent malaria and other infectious diseases. In the 1930s–1940s, Ann Bishop worked extensively on chemotherapy for malaria and drug resistance, while Ernestine H.B. Thurman led a vector control programme in the US. By the mid-20th century, Mabel Josephine Mackerras was working on the mosquito stages of *Plasmodium* parasites, their transmission, and measures to control them. At the same time, Ruth Nussenzweig pioneered antimalaria vaccination by demonstrating that mice are protected by injection of attenuated sporozoites, an approach still pursued today to prevent the human disease. The last decade witnessed the first malaria-related Nobel Prize awarded to a woman. Tu Youyou was recognised for identifying and isolating the active ingredient from the Chinese medicinal plant *Artemisia annua*, called artemisinin, the most effective treatment for malaria infections to this day.

Over the last century of intense research, much progress has been achieved in terms of understanding parasite (Figure 1), vector, and host biology; host–parasite interactions; transmission; and population dynamics. The advent of next-generation sequencing, single-cell and stem cell technologies, gene editing, and imaging, together with advances in computational biology, has significantly transformed the field and opened multiple new areas of study. Together with this technological advancement, the last decade has seen more attention paid to the hidden parasite variability in endemic areas, and with this, the necessity of having more representative reference genomes and more realistic models for laboratory experiments. Enormous databases of field parasite isolates and vectors from all over the world now exist (MalariaGen) that provide a detailed picture of their striking biology and diversity. This also allowed important advances in understanding the disease itself, including mechanisms of infection, intrahost adaptation, and transmission dynamics,

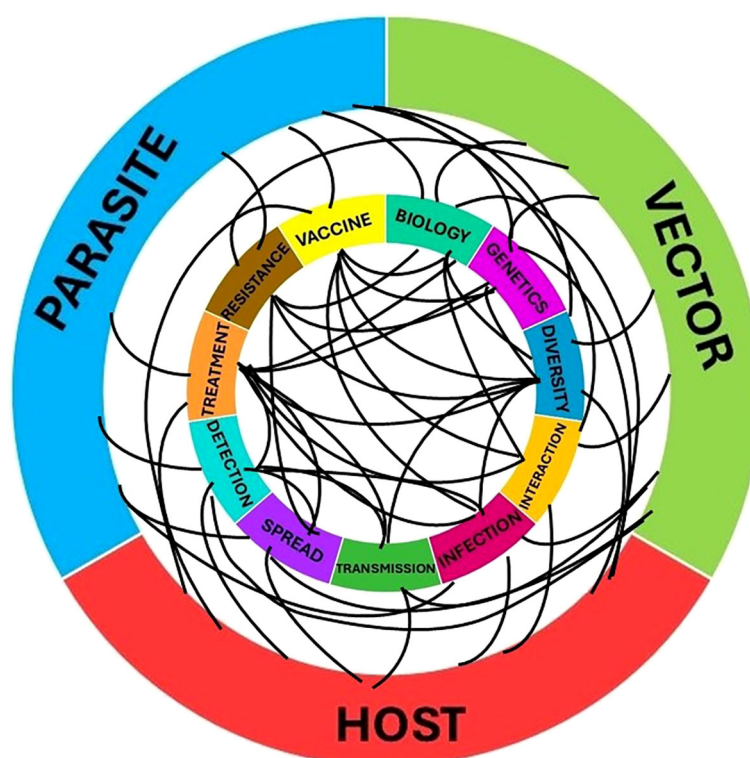


FIGURE 1

Areas of malaria research. Malaria control involves intense research of all three components of the disease: parasite, vector, and host. In each case, the biology, genetics, and diversity are paramount to find novel and effective strategies of prevention, detection, and treatment. Integration and development in all these intertwined areas is required to bring malaria control and eradication.

and with this, more comprehensive knowledge about malaria epidemiology and control. Finally, with efforts reaching a plateau in malaria control and the continuous emergence and spread of resistance to antimalarials and insecticides all over the world, research and development of next-generation drugs and vaccines and a better understanding of immunity to malaria are hot priority areas.

Involvement of women in all these aspects of malaria research has steadily increased in number and importance over the last decades. The aim of this Research Topic is to showcase the varied work of female scientists in all areas of malaria research.

One of the areas that has exploded, in terms of applying the entire portfolio of novel technologies, is the vector. New knowledge about their basic biology, ecology, and adaptation potential is becoming more and more critical in the context of climate change and globalisation. Aligned with this need is the number of articles addressing it within this topic. On one hand, a better understanding of regulatory mechanisms of gene expression, such as alternative splicing, and the identification of candidate genes and regulatory sequences could offer novel strategies for vector control (Diaz-Terenti et al.). Of critical importance is the development of the parasite within the vector, and Oke et al. reveal that oocyst development is highly adapted to the nutritional state of the mosquito (Oke et al.). Furthermore, models integrating parasite stages within the host and the vector link gametocyte density in the host to transmission potential after vector passage, allowing more

realistic estimations of parasite transmission potential (Hoi et al.). Diversity of the circulating parasites is greatly determined by the rate of transmission, and variation in the mosquito population shapes malaria transmission, seasonal persistence, and geographical range. Not only the genetic diversity of the major species of mosquitoes harbouring the parasite but also the number of species capable of transmitting the disease contribute to the persistence and spread of malaria. Hence, tools targeting specific genes or gene drive strategies need to take into account genetically divergent species to be effective (St. Laurent). The evaluation of control measures for the determination of the evolution of resistance among mosquito populations relies on the capture of field mosquitoes at different stages. A mathematical model assessed the value of adult-capture as a tool to monitor insecticide resistance, showing that this approach is effective and relatively easy to apply (Holmdahl et al.).

Most clinical repercussions of malaria infection are due to the erythrocytic stages of the parasite. Novel technologies such as optical tweezers provide detailed insight into the infection of erythrocytes, showing membrane rigidification as the parasite grows, and also of surrounding uninfected erythrocytes in the culture. Interestingly, widely used antimalarials increase the rigidity of infected erythrocytes but only when the parasite strains are sensitive to the particular drug (Dorta et al.). While mathematical models of blood infection dynamics are very useful, measuring erythrocyte and reticulocyte densities revealed that novel

formulations are needed to reflect them more accurately (Peters et al.). Comparison of Poisson with non-parametric methods to estimate multiplicity of infection concluded that the model to use will depend on the transmission characteristics, such that overdispersed distribution is well represented by non-parametric methods, while if not highly overdispersed, a Poisson model is appropriate (Kayanula and Schneider). The development of the parasite in the blood is highly synchronous, which is characteristic of the *Plasmodium* genus and important for disease progression and control. An analysis using a model that takes into account population dynamics and infection kinetics to quantify synchrony showed that strains and environments can be compared in this way, informing evolutionary drivers and the role of synchrony in disease (Greischar et al.).

The tools available to control malaria include diagnostic methods to detect the disease, targeting the infection in patients with drug combinations as well as preventing infection mainly through vaccine development and vector control (Figure 1). All these tools are constantly challenged by the genetic diversity of parasites and vectors as well as drug resistance and environmental factors. Indeed, evaluation of rapid diagnostic test (RDT) accuracy in Uganda showed a high proportion (approximately 20%) of false positive results. This level of sensitivity risks inappropriate treatment and underdiagnosis of other illnesses highlighting the need for constant improvement and updating of diagnostic tools (Mortazavi et al.). One of the novel options to assess drug resistance, Ion Torrent deep sequencing, can effectively assess the haplotypes of the most important drug resistance genes and even detect changes in allele frequency throughout the infection. This could be a straightforward technique to monitor drug efficacy (Kale et al.). Even comparison of reference genomes of *Plasmodium vivax*, focussing on drug resistance genes, revealed allelic variations between them that should be taken into account when establishing detection and vaccine development strategies for this species of parasite (Tamang et al.).

The strategy that has proven most effective to control and reduce transmission of malaria has been the distribution of insecticide-impregnated bed nets. However, the efficacy of bed nets has been declining due to resistance. A measure to counter this is next-generation bed nets with pyrethroid second chemistry. Assessment of three WHO-recommended classes of these dual-active nets showed that they outperform the traditional ones. However, variability in outcomes across Africa points to the need for a regional approach for the best control strategy (Böhmert et al.). Similarly, the local approach to control malaria was also highlighted by Skinner et al., who used statistical modelling to analyse the effect of local climate and spatial variations in factors such as land use, entomological features, temperature, and rainfall on malaria transmission. Finally, all measures to control the disease have to include local communities to understand the specific needs and

requirements for any strategy to be effective, as described by the 'One Health' approach (Knudson Ospina et al.).

This Research Topic is only a small sample of the amazing work of women in the efforts to bring malaria under control. It demonstrates the extensive involvement of women scientists in innovative and important work across the breadth of malaria research, unravelling unknowns and discovering new approaches. The hope is that this small insight will serve as inspiration to women to continue their efforts and encourage men and academic institutions to support, value, celebrate, and disseminate their contributions.

Author contributions

AP: Conceptualization, Visualization, Writing – original draft, Writing – review & editing. EG-D: Conceptualization, Writing – original draft, Writing – review & editing. SR: Conceptualization, Writing – original draft, Writing – review & editing.

Conflict of interest

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