

EDITORIAL

Parasites—The importance of time

Kathryn J. Else  | Julie E. Gibbs

Lydia Becker Institute for Immunology and Inflammation & Centre for Biological Timing, Faculty of Biology Medicine and Health, University of Manchester, Manchester, UK

Correspondence

Kathryn J Else, AV Hill Building, Oxford Road, Manchester, M13 9PT, UK.
Email: Kathryn.Else@manchester.ac.uk

Abstract

The special edition of *Parasite Immunology* 'Parasites—The importance of time' embraces the intersection between three established research disciplines—parasitology, immunology, and circadian biology. Each of these research areas has a longstanding history littered with landmark discoveries with the intersect between the three bringing exciting findings and new questions and perhaps even a greater sense of awe in terms of how parasites have evolved to interact and live with their hosts.

KEYWORDS

circadian biology, host-parasite interactions, immunology, parasitology

1 | INTRODUCTION

Parasites date back to the time of the dinosaurs with an awareness of their existence in man evidenced in the records of ancient societies.^{1,2} As parasite lifecycles were uncovered, and understanding of the host–parasite interactions began to grow, the field built towards the discipline of parasite immunology, which explores host immune responses to parasitic infection.

Evolution has supported the formation of timing circuits, which permit organisms to keep track of time in order to adapt physiology to daily changes in the environment (lighting and temperature) driven by the Earth rotating on its axis.³ These clocks imprint 24-hour variation onto a diverse range of processes from conidiation in fungi; leaf movements in plants; and sleep–wake cycles in animals. The clock is preserved from bacteria to plants to humans, and although the fundamental basis of the molecular components of these clocks varies between organisms, the manner in which they are connected together (to form a transcriptional translational feedback loop) is consistent. Additionally, the recent awareness of the potential pervasiveness of nontranscriptional oscillators in prokaryotes and eukaryotes recognizes that there is still a great deal to understand about mechanisms driving 24-hour variation in physiology and behaviour.

2 | RHYTHMS IN PARASITES AND THEIR HOSTS

So what do we know about 24-hour variations in host–parasite relationships? Traits have been recognized for centuries; for example, malaria fever is periodic, implicating daily rhythms in host–parasite interactions.⁴ Further, we can observe rhythms in parasite gene expression, as seen recently in trypanosomes (*Trypanosoma brucei*⁵), malaria (*Plasmodium chabaudi*; *P. falciparum*^{6,7}), and Schistosomes (*Schistosoma mansoni*⁸). However, a greater appreciation of whether daily rhythms in parasites reflect the presence of an intrinsic circadian clock, as demonstrated, for example, for *T. brucei*, what form these clocks may take, and whether they are driven by host rhythms, is required. Indeed, studying circadian rhythms in parasites may allow the discovery of, as yet, unidentified and indeed unique clockwork. Furthermore, over the last 10–15 years, many cells of the host immune system have been discovered to have clocks that regulate the manner in which they respond to immunological challenges including parasites.^{9–12} Thus, time adds a further dimension to host–parasite interactions, and it is critical that we consider clock involvement in order to fully realize the potential of interventions and therapy.

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3 | THE SPECIAL COLLECTION

The special collection provides insight into our current understanding of the role of clocks in parasite immunology. We present a range of articles considering the role of clocks within hosts, vectors, and parasites in directing interactions and influencing the outcome of parasitic relationships with hosts. These specially selected articles cover a diverse range of organisms, offering a fascinating insight into what is known in this field. The issue starts with an article by Ince, which reviews our understanding of biological rhythms in general and introduces the key concepts and nomenclature used within the field. Ince goes on to present the relevance of biological rhythms to parasites and parasite immunology in the context of endogenous rhythms of parasites, parasites that synchronize with their hosts, host rhythmic immune response to infection, and parasite manipulation of host rhythms. Ince concludes her review with a series of thought-provoking questions, answers to which should advance our understanding of parasitology immunology and chronobiology alike.

Following on from Ince, Hunter et al. introduces the reader to the literature describing rhythms in a broad range of parasites: *Leishmania*, *Plasmodium*, *Trypanosoma spp.*, and helminths before concluding with some thoughts on the promises offered by chronotherapy in optimizing drug and vaccine efficacy.

Carvalho Cabral et al. provide an overview of how the host circadian clock regulates immunity to parasitic infections. Clocks in cells of the immune systems are reviewed before the reader is taken on a deep dive into the time of day of infection with *Leishmania spp.* Also covering malaria and helminths, the interplay between host clockwork and parasitic infection is described, and gaps in our knowledge highlighted.

O'Donnell et al. focus on malaria and offers an original research paper exploring whether plasticity in parasite replication rhythms allows the parasite to align with the host feeding-fasting rhythm.

Finally, the special edition concludes with a review article by de Bekker, reminding us of the sheer breadth and scale of clock biology within parasitology. Considering a parasitic fungus and its ability to manipulate host behaviour, evidence is presented which suggests that the fungus can 'corrupt' carpenter ant behavioural plasticity and rhythmicity to enhance transmission.

4 | CONCLUSION

Whilst a significant progress has been made in the field over the last few years, a number of critical questions persist. Perhaps most intriguingly, do all parasites sense time? It is hoped that within the near future we will gain a greater understanding of timing mechanisms within further parasitic organisms, and understand whether

these timers are truly independent of the host. On the flip side, how important are host clocks to parasite survival? Understanding the influence of host clocks on the elimination of parasites from their hosts will add to our knowledge of the importance of timing mechanisms on regulating immunity and will help address the consequence of disruption to host rhythmic behaviour on parasites. One potential outcome of a greater knowledge in this field is the potential to use this information to develop and improve therapeutic approaches.

PEER REVIEW

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ORCID

Kathryn J. Else  <https://orcid.org/0000-0001-6660-055X>

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