



OPEN ACCESS

EDITED AND REVIEWED BY

Jeroen P. J. Saeij,
University of California, Davis, United States

*CORRESPONDENCE

Jayaraman Tharmalingam
✉ jayaraman.ntr@gmail.com

RECEIVED 25 August 2023

ACCEPTED 30 August 2023

PUBLISHED 11 September 2023

CITATION

Tharmalingam J, Brehm K, Kundu S,
Młocicki D and Paredes R (2023) Editorial:
Host-pathogen interaction in
cestodes infection.
Front. Cell. Infect. Microbiol. 13:1283267.
doi: 10.3389/fcimb.2023.1283267

COPYRIGHT

© 2023 Tharmalingam, Brehm, Kundu,
Młocicki and Paredes. This is an open-access
article distributed under the terms of the
[Creative Commons Attribution License
\(CC BY\)](#). The use, distribution or
reproduction in other forums is permitted,
provided the original author(s) and the
copyright owner(s) are credited and that
the original publication in this journal is
cited, in accordance with accepted
academic practice. No use, distribution or
reproduction is permitted which does not
comply with these terms.

Editorial: Host-pathogen interaction in cestodes infection

Jayaraman Tharmalingam^{1*}, Klaus Brehm², Suman Kundu³,
Daniel Młocicki⁴ and Rodolfo Paredes⁵

¹Wisconsin Institute for Discovery, University of Wisconsin-Madison, Madison, WI, United States,

²Institute of Hygiene and Microbiology, Julius-Maximilians-University of Würzburg, Würzburg, Germany,

³Department of Microbiology, Immunology and Biochemistry, University of Tennessee Health Science Center (UTHSC), Memphis, TN, United States, ⁴Department of General Biology and Parasitology, Medical University of Warsaw, Warsaw, Poland, ⁵Laboratorio de Medicina Veterinaria, Escuela de Medicina Veterinaria, Facultad de Ciencias de la Vida, Universidad Andres Bello, Santiago, Chile

KEYWORDS

cestode, echinococcus, cysticercosis, host - pathogen interactions, parasite antigen

Editorial on the Research Topic

Host-pathogen interaction in cestodes infection

Host-pathogen interaction is a complex process specifically during infection with multicellular parasites such as cestodes. Every year, millions of people become infected, and thousands of deaths occur due to this. The World Health Organization listed many of the cestode infections under Neglected Tropical Diseases (NTDs) to address the urgent need to prevent the infection. Number of the NTDs causes millions of Disability Adjusted Life Years (DALYs) and cost billions of dollars in morbidity and mortality associated with diseases every year (Engels and Zhou, 2020). For thousands of years, tapeworms co-evolved with many of its intermediate and definite hosts (including humans) and this complicated and undermined the host response to cestode infections. The complexity of cestodiasis is one of the major reasons for a sustained infection burden worldwide, even though effective treatments are available. The most serious pathological changes during cestode infections are related formation space-occupying metacestodes in diverse of the hosts vital organs and such fatal infections cause neurocysticercosis, cysticercosis, coenurosis, echinococcosis, and sparganosis. In many cases metacestodes are formed by Vesicle Fluid (VF) filled in a space occupying Vesicle Tissue (VT).

Neurocysticercosis is a cestode *Taenia solium* metacestode infection of the human central nervous system. Cyst antigens differentially activate the host immune responses in endemic regions, and thousands of people are exposed to infective antigens, but very few people develop diseases (Jayaraman et al., 2011). Similarly, host immune responses that alter the nature of *Echinococcus* cyst antigens dominate the development of clinically pathogenic diseases. Understanding cestode cyst antigens and host immune responses against those antigens is vital for preventing and eliminating fatal cestode infections. The scientific research section “Host-pathogen interactions in cestode infections” in Frontiers in Cellular and Infections Microbiology and four of the published research articles in this section cover various aspects of metacestode antigens and host interactions in

echinococcosis. Prevention of many of the NTDs is achievable by developing accurate and affordable diagnostic tests. In the case of cestodiasis, including echinococcal diseases, diagnostics based on host humoral immune responses against metacestode antigens are highly effective for early diagnosis and treatment as well as for treatment effectiveness evaluation.

When the intermediate host swallow the infective eggs containing hexacanth larvae, these penetrate intestinal tissues, migrate, and undergo transformation into metacestode stage as a form of cyst (*Echinococcus*, *Taenia*), which may be found in different tissues and organs of the host. Host immune responses are an important determining factor for the establishment of cyst infections. Host recognition of cyst antigens and antigenic proteins vary based on many factors: cestode species, the location of cyst antigens, the excretory and secretory nature of the antigens, and host immune response modulated by and for cyst responses.

The nature of cyst antigens varies between different species of the cestode, and identification of species-prevalent and species-specific antigens improve the prevention of spread of the infection. Basharat et al., research on genetic variation of echinococcosis in an endemic region in Pakistan established the importance of identification of species and immunogenicity against infection. Most of the cyst infections were noticed in the liver and more than 85% of these infections are caused by *Echinococcus granulosus* sensu stricto. Authors reinstated other studies finding that the major source of cystic echinococcus around the world was domestic animal trades between many of the infection endemic countries.

Host immune response against cestodes did not depend on specific species, but within species metacestodes proteins played a major role in affecting host immune responses. Müller et al., in this section try to characterize the location-specific protein in metacestodes of *Echinococcus multilocularis*, a causative agent of alveolar echinococcosis. Authors found many parasite proteins differentially present between vesicle fluid and vesicle tissue, and they found more than 93% of proteins made up of AgB subunits. Characterization of antigen AgB has higher values, as AgB of *Echinococcus* is important for host immune modulation and plays a major role in serodiagnosis of *Echinococcus* infection. Also, authors showed that AgB proteins are involved in lipid transportation from the host to metacestodes to reduce the metabolic burden of the metacestode.

Cestode infections are preventable if they are diagnosed early in a community and when infection monitoring is carried out. Screening of seroprevalence of antigens in primary and intermediate hosts enhances the prevention of community spread of the infection. Kronenberg et al., developed a monoclonal antibody assay for diagnosis of different stage-specific antigens in *Echinococcus*. Clinical relevance of Em18 antibodies is important and is used to interpret the outcome of the treatment for alveolar echinococcus (Hotz et al., 2022). Kronenberg et al., showed that their monoclonal antibodies (mAb Eg2) are reactive to antigen from both the germinal layer and the protoscoleces in both alveolar and cystic echinococcosis.

Host cellular immune response against parasites is an important factor to limit the infection and eliminate the parasite.

In the case of alveolar echinococcosis, however, the immune response of the intermediate host is gradually skewed towards an immunosuppressive environment during infiltrative parasite growth within the liver. Kaethner et al. report how this immune response might influence the differentiation of the *Echinococcus multilocularis* metacestode towards the next larval stage, the protoscolex. These authors showed that *E. multilocularis* expresses a complex TGF- β signaling system which responds to both host and parasite TGF- β ligands. Furthermore, they demonstrate that functional parasite TGF- β signaling is necessary for protoscolex formation initiated by stem cells located in the germinative layer. Since high concentrations of host TGF- β are accumulating around parasite lesions at late stages of alveolar echinococcosis, the immune response of the intermediate host might therefore be a trigger telling the parasite when to differentiate into the infective form for the definitive host.

Within this Research Topic, all four articles established the importance of host-parasite interactions in echinococcosis, which continues to be an important health and life-threatening problem for many people, especially in endemic areas. Researchers indicate the usefulness of serological diagnostic and molecular methods in the identification, diagnosis and prevention of infections. They point to the molecular mechanisms underlying the formation of larvae, and those that are key to better understanding the biology of cestodes and their interaction with the host.

Author contributions

JT: Writing – original draft, Writing – review & editing. KB: Writing – original draft, Writing – review & editing. SK: Writing – original draft, Writing – review & editing. DM: Writing – original draft, Writing – review & editing. RP: Writing – original draft, Writing – review & editing.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

- Engels, D., and Zhou, X.-N. (2020). Neglected tropical diseases: an effective global response to local poverty-related disease priorities. *Infect. Dis. Poverty* 9 (1), 10. doi: 10.1186/s40249-020-0630-9
- Hotz, J. F., Peters, L., Kapp-Schwörer, S., Theis, F., Eberhardt, N., Essig, A., et al. (2022). Evaluation of serological markers in alveolar echinococcosis emphasizing the correlation of PET-CTI tracer uptake with RecEm18 and echinococcus-specific IgG. *Pathogens* 11 (2), 239. doi: 10.3390/pathogens11020239
- Jayaraman, T., Prabhakaran, V., Babu, P., Raghava, V. M., Rajshekhar, V., Dorny, P., et al. (2011). Relative seroprevalence of cysticercus antigens and antibodies and antibodies to taenia ova in a population sample in south India suggests immunity against neurocysticercosis. *Trans. R. Soc. Trop. Med. Hygiene* 105 (3), 153–159. doi: 10.1016/j.trstmh.2010.10.007