Peer Community In Infections

Preliminary population genetic analysis of Trypanosoma lewisi

Annette MacLeod *based on reviews by Gabriele Schönian and 1 anonymous reviewer*

A recommendation of:

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Development of nine microsatellite loci for Trypanosoma lewisi, a potential human pathogen in Western Africa and South-East Asia, and preliminary population genetics analyses

Adeline Ségard, Audrey Romero, Sophie Ravel, Philippe Truc, Gauthier Dobigny, Philippe Gauthier, Jonas Etougbetche, Henri-Joel Dossou, Sylvestre Badou, Gualbert Houéménou, Serge Morand, Kittipong Chaisiri, Camille Noûs, Thierry deMeeûs*(2022) Zenodo, 6460010, ver. 3 peer-reviewed and recommended by Peer Community in Infections*

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Recommendation

Trypanosoma lewisi is an atypical trypanosome species. Transmitted by fleas, it has a high prevalence and worldwide distribution in small mammals, especially rats [1]. Although not typically thought to infect humans, there has been a number of reports of human infections by *T. lewisi* in Asia including a case of a fatal infection in an infant [2]. The fact that the parasite is resistant to lysis by normal human serum [3] suggests that many people, especially immunocompromised individuals, may be at risk from zoonotic infections by this pathogen, particularly in regions where there is close contact with *T. lewisi*-infected rat fleas. Indeed, it is also possible that cryptic *T. lewisi* infections exist but have hitherto gone undetected. Such asymptomatic infections have been detected for a number of parasitic infections including the related parasite *T. b. gambiense* [4].

Despite the fact that *T. lewisi* parasites pose a risk to human health, very little is known about their population structure, reproductive mode, population size or dispersal. In the article [5], Ségard et al. presented the first attempt at examining the population structure of the parasite. They developed microsatellite markers and used them to analyse a small set of samples from West Africa and Southeast Asia. Although the number of microsatellite markers is not very high and they encountered problems of PCR amplification especially of the southeast Asian samples, they did provide preliminary data that hints at a clonal population structure with rare recombination and suggests population subdivisions occurring at a scale that is equal, and probably smaller than a

neighborhood of several houses with a short generation time. These are very interesting preliminary findings that will need to be validated using a larger cohort with more markers or by whole genome sequencing.

References

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[3] Lun Z-R, Wen Y-Z, Uzureau P, Lecordier L, Lai D-H, Lan Y-G, Desquesnes M, Geng G-Q, Yang T-B, Zhou W-L, Jannin JG, Simarro PP, Truc P, Vincendeau P, Pays E (2015) Resistance to normal human serum reveals Trypanosoma lewisi as an underestimated human pathogen. Molecular and Biochemical Parasitology, 199, 58–61. https://doi.org/10.1016/j.molbiopara.2015.03.007

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[5] Ségard A, Roméro A, Ravel S, Truc P, Gauthier D, Gauthier P, Dossou H-J, Sylvestre B, Houéménou G, Morand S, Chaisiri K, Noûs C, De Meeûs T (2022) Development of nine microsatellite loci for Trypanosoma lewisi, a potential human pathogen in Western Africa and South-East Asia, and preliminary population genetics analyses. Zenodo, 6460010, ver. 3 peer-reviewed and recommended by Peer Community in Infections. https://doi.org/10.5281/zenodo.6460010

Conflict of interest:
The recommender in charge of the evaluation of the article and the reviewers declared that they have no conflict of interest (as defined in the code of conduct of PCI) with the authors or with the content of the article.

Reviews

Evaluation round #1

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Author's Reply, 17 Sep 2022

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Decision by Annette MacLeod, posted 13 Jun 2022

I think this manuscript will be much improved by adopting the revisions suggested by the reviewers.

Reviewed by Gabriele Schönian, 11 May 2022

This is an interesting study investigating for the first time, at least to my knowledge, the population structure of T. lewisi from West Africa and Southeast Asia using microsatellite markers. The manuscript is well written and all experimental procedures are clearly described.

This study has some limitations, which have been discussed in-depth by the authors. The number of microsatellite markers is not very high and, moreover, there was a problem of amplification of these markers especially in the southeast Asian samples. The sampling procedure also needs to be improved in future studies. Nevertheless, the approach proposed here for population genetic studies in this parasite seems to be promising for future research.

I have only one remark. Is it possible to give more information on the location of the 9 microsatellite markers in the parasite's genome, such as on which chromosome and where exactly on a given chromosome? This could perhaps be added to Table 1.

Reviewed by anonymous reviewer, 02 Jun 2022

Development of nine microsatellite loci for Trypanosoma lewisi, a potential human pathogen in Western Africa and South-East Asia, and preliminary population genetics analyses

Overall Decision: revise

In this paper the authors set out to develop a system of microsatellite genetic (MS) markers for the understudied parasite Trypanosoma lewisi to provide a tool for investigating population genetic parameters. Overall, the paper describes some ambitious work which successfully establishes a key set of MS markers. These markers were successfully used on a wide range of samples although amplification problems were found with a subset of samples. The paper reports the outcomes of population genetic analyses on samples that were successfully amplified.

Overall the paper is well constructed, the study conducted in a robust manner and the conclusions are justified by the results. The authors should be congratulated on the detail and robustness with which they describe and conduct the bioinformatic analyses. Due to the constrictions in the number and range of samples used, the authors describe their studies as a preliminary attempt to determine some of the population genetic parameters – this is indeed true but does not deflect from the value of this paper.

I have some comments which the authors need to address.

1. There are errors in syntax and grammar throughout the manuscript that should be addressed. I appreciate the challenges of scientific writing in a non-native language but I would recommend a thorough editing to bring the language in the manuscript up to the professional standard it deserves.

2. In the materials and methods can you please Indicate whether the study has had ethical approval and if so provide an ethical statement, and reference number.

3. Experimental animals were used, so could you please provide details of how they were maintaned and under what ethical/licensing regulations they were used.

4. Lines 108 – 112. These are rather old references to infection parameters. It would be preferable to also reference something more recent. For example, a more recent study – see ref later - has determined detailed parameters for the cell cycle and includes data on the timing of infection in mammals (rats) in vivo (Figure S1). (Zhang X, Li SJ, Li Z, He CY, Hide G, Lai DH, Lun ZR. Cell cycle and cleavage events during in vitro cultivation of bloodstream forms of Trypanosoma lewisi, a zoonotic pathogen. Cell Cycle. 2019 Mar;18(5):552-567. doi: 10.1080/15384101.2019.1577651. Epub 2019 Feb 20. PMID: 30712435; PMCID: PMC6464594.)

5. Line 130 - 136. In addition to the references provided. There should be a brief description of the methods used (e.g. primers used, cycling conditions etc.) to avoid readers having to trawl back through other papers.

6. Line 139. Which strain(s) was/were used in the sequencing project to detect the microsatellites? You state that some of the amplification problems might be due to primer mismatches - did you sequence any of the South East Asian strains to determine whether the Primer sequences were correctly represented in those genomes?

7. Line 139. Generally, in the interests of repeatability, more detail is required to describe the sequencing methods. Are the data from the sequencing project deposited on public databases? Provision of accession numbers etc. is required.

8. The bioinformatic analyses are well described.