Author's response to reviews

Title: Immune markers characteristic for asymptotically infected and diseased Entamoeba histolytica individuals and their relation to sex

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Version: 2
Date: 3 July 2014

Author's response to reviews: see over
Dear Prof. Kremsner,

Please find enclosed our manuscript, entitled

“Immune markers characteristic for asymptotically infected and diseased *Entamoeba histolytica* individuals and their relation to sex”,

which we would like to submit as a full-length article in *BMC Infectious Diseases*.

Very little is known about the immune response in invasive amebiasis and so far, it is an unresolved enigma why an infection with *Entamoeba histolytica* occurs equally in males and females but the liver manifestation of the disease predominates in adult men. In the present study, we investigated the humoral immune responses, including total IgG, IgG subclasses, and IgA, to proteinaceous and non-proteinaceous *E. histolytica* antigens, as well as serum cytokine and chemokine levels in what we believe to be one of the best and most comprehensive large cohort of male and female patients with amebic liver abscess. In addition, we had available sera from a unique group of individuals asymptotically infected with *E. histolytica*, of both sexes. All samples were obtained from residents living in an area of amebiasis endemicity in central Vietnam. Sensitive stool-PCR amplification was previously used to confirm *E. histolytica* infection in the cohort of asymptomatic individuals. This clearly distinguished asymptomatic *E. histolytica* carriers from subjects infected with the *Entamoeba dispar*, which has been responsible for many study errors in the past. Although there are limitations in the study concerning sample sizes, especially in the female ALA patients, which is a intrinsic problem of the disease, we assume that this study can give possibly first clues to sex differences in the outcome of a disease and encourage further immunological work on human amebiasis.

However, our investigation generated several statistically robust data that allowed, for the first time, insights into the complexity of the immune response associated with resistance and susceptibility to disease in the context of sex difference. We believe that our findings will be of great interest to researchers and clinicians working in the fields of infectious diseases in general and perhaps in diseases where sex differences occur.

The manuscript has not been submitted or accepted for publication elsewhere. All authors have seen
and approved the content and have contributed significantly to the work.

We suggest

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We look forward to hearing from you at your earliest convenience.

Yours sincerely,

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