Reviewer's report

Title: Immuno-epidemiology of human Schistosoma haematobium infection: preferential IgG3 antibody responsiveness to a recombinant antigen dependent on age and parasite burden.

Version: 1 Date: 9 May 2006

Reviewer: Daniel Colley

Reviewer's report:

General

This is an interesting and well written manuscript that explores the human immune responses against a newly cloned Schistosoma haematobium antigen termed Sh13. As such, it adds to the useful data regarding potential protective responses against individual antigens during schistosomiasis.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The anti-SWAP data (Fig. 3c) are somewhat confusing, in that the ELISA values for all isotypes are quite low, and are non-existent for IgG3 and IgG4. Many investigators do see anti-SWAP responses by these isotypes. Perhaps the reason the data are negative and low in this manuscript is due to the use of only 1 ìg/ml of SWAP used to coat the plates. In this reviewer’s experience, 10 ìg/ml or even 25 ìg/ml is often used, which then detects reasonable to high levels of almost all isotypes. SWAP is indeed a highly complex, crude mixture of many antigens. This may mean that to get sufficient antibodies binding against any one component you need to coat the plates with a higher quantity than a purified or recombinant protein. Because the data in Fig. 3c are very low or negative, and because this might be due to a methodological reason (low concentrations used to coat the plates), the authors should consider qualifying or eliminating these data. In this reviewer’s opinion, the currently presented data do not instill sufficient confidence to warrant their inclusion.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

None

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Discretionary Revisions (which the author can choose to ignore)

1. Page 4, first line. The authors should consider providing a reference for the statement “the evidently short duration of protective responses,” because this reviewer knows of no published basis for this statement in regard to human schistosomiasis.
2. The lack of a detectable IgM response would seem to preclude problems that might have been encountered by using an E. coli-expressed protein in the authors’ ELISAs, but they might consider noting this in their Materials and Methods section, just to assure readers that they did not experience difficulties due to anti-LPS and other such reactions.
3. Page 9, 2nd & 3rd lines from the bottom. The authors indicate that both the prevalence and intensity of infection rise and decline, and while Fig. 3a seems to agree with this statement in regard to the intensity of infection, there is doubt in this reviewer’s mind about the statistical significance of the purported decline after ages 11-12 in the prevalence of infection. It is suggested that the authors either confirm the statistical significance of the indicated decline in prevalence, or change the sentence to reflect that while intensity declines, prevalence does not.
4. Page 11, last line & Fig. 4c. It is possible that this reviewer simply does not sufficiently understand the statistical analyses presented, but it is suggested that the authors clarify whether the negativity that develops in the analysis is statistically sound; since the p value associated with that negativity (Fig. 4c) appears to be 0.158.
5. In several places in the Discussion the authors indicate that the relationship between age groups and anti-Sm13 IgG3 responses suggest that exposure to adult worms is important in this, and could have something to do with the development of resistance. Based on the mean longevity of adult S. haematobium
worms, this reviewer suggests that it is equally plausible that the relationship is not just with having adult worms, but also with having some dying adult worms and reacquisition of new adult worms (albeit fewer due to resistance) through re-infection. There have been several publications that suggest that dying adult worms might be important/responsible for the induction of resistance (essentially all of these are cited by the authors), and it is suggested that the data in this manuscript are consistent with this interpretation, since young, untreated children may well not have yet been exposed to antigens from dying adult worms. Perhaps the authors would care to expand their interpretations in this vein.

What next?: Accept after discretionary revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.