Reviewer’s report

Title: Genetic and functional evaluation of the role of CXCR1 and CXCR2 in susceptibility to visceral leishmaniasis in India

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Reviewer: Marlo Moller

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The manuscript entitled “Genetic and functional evaluation of the role of CXCR1 and CXCR2 in susceptibility to visceral leishmaniasis in India” by Mehrotra and colleagues reports primary and replication genetic studies for visceral leishmaniasis in India. The strength of this study lies in its size and design: both family-based and case-control association study designs were used and the most severe form of the disease was targeted. In the first step, 836 individuals from 176 families were genotyped for 3 tagging SNPs in the CXCR1/CXCR2 region. Replication was done in 941 cases and 942 controls and one SNP (rs3138060) was associated with disease in both sample collections. The same risk haplotype was found to be associated with leishmaniasis in both the family and population samples. In addition, CXCR2 expression was downregulated in pre-treatment compared to post-treatment splenic aspirates, indicating that a lack in expression of CXCR2 may contribute to the disease.

I have general, minor comments:

1. If any heritability studies have been done for VL, what is the % range attributed to the host’s genetic make-up?
2. Given the small odds ratios detected, do the authors consider these SNPs to be major contributors to VL?
3. Is there any reason to believe that population stratification should be corrected for?
4. The samples described in this study could in the future be used in a genome-wide approach.

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests