Reviewer's report

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

**Version:** 1  **Date:** 28 September 2011

**Reviewer:** Mridula Bose

**Reviewer's report:**

Major essential revision:

1. The selection of such a small number of loci for such big sample size is surprising. Robust justification is needed. How and why were only these rsIDs selected for analysis? Give specific reasons.

2. In the title: Only population from BIHAR is considered and that cannot serve as representative of all of INDIA. It should read something like north India or north-east India as per IGVDB. Analyses must be done keeping the a/m database as reference.

3. In methods: although the selection of tag SNPs is described selection of only three loci for such a sample size is surprising. Given the fact that Sequenom platform was used inclusion of more loci in the study could have generated some more interesting unexplored data. This is not acceptable and needs justification.

4. It should be made clear whether strand conversion was done before haplotype analysis as the SNPs lie on different strands. If no, then these haplotypes are not possible. Needs clarification.

5. The major issue of population stratification that can be a serious confounding factor in genetic studies has not been addressed which is a serious drawback as there are different religious groups involved in the population included in the study. Kindly perform this analysis.

6. The role of CXCR1 and 2 are very confusing. Association found in CXCR1 and downregulation expression of CXCR2 does not necessarily imply a role of CXCR2 and not of CXCR1. Moreover only a tiny fraction 19 samples used for expression analysis as against considerably larger samples used for genetic study. Therefore to discredit genetic study saying that the association could reflect some LD effect and the expression analysis has binding is not acceptable.

Minor essential revision:

1. The research question are not well formulated and findings are not suitably explained.

2. The study is concluded in a haphazard manner and needs to be concluded better, specifically and clearly.

3. Define nuclear families? Because a good part of analysis is depends on the
relevant definition.

4. Why was qRT PCR done on such a small number of samples? This number is too small given the fact that the inference it draws and the number of cases the authors had access to.

5. In abstract results include “using FBAT”. Details must be given in the methodology.

6. Introduction: “Genetically regulated variability in the immune system”; Modify the sentence.

7. xi. While mentioning the power of study authors say that the “the 313 VL trios had #95% power to detect an odds ratio #2 at P=0.01 for markers with MAF#0.1, and 49% power for an odds ratio of 1.5” since most of the detected odds ratio is in this range of 1.5 and none greater than 2; justify only 49% power of study.

8. The name of the country should be mentioned along with the products.

9. In methods: while mentioning the softwares write it fully as: GraphPad Prism (version 5.00 for Windows, Graph Pad Software, San Diego California USA, www.graphpad.com)

10. p values are one tailed or two tailed? Write clearly.

11. The major issue of population stratification that can be a serious confounding factor in genetic studies has not been addressed which is a serious drawback as there are different religious groups involved. Kindly perform this analysis.

12. In discussion the authors mention that same blood marriages are very common in this population but that is true only for Muslim families not the majority of Hindus. Such statement should be removed or detailed analysis must be included to justify the statement.

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

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

"I declare that I have no competing interests"