Reviewer’s report

Title: Association of matrix metalloprotease 1, 3, and 12 polymorphisms with rheumatic heart disease in a Chinese Han population

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Reviewer: Angelica Beate Winter Boldt

Reviewer’s report:

In the abstract: "genetic factors" is too generic. Why it is important to investigate matrix metalloproteinases and no other genes from the immune response, for example (as those cited in the introduction)? Why only those three polymorphisms?

Introduction: The authors mention that MMP promoter polymorphisms alter gene expression, but fail to indicate the location of the investigated SNPs (in the promoter region). The relevance of these three polymorphisms is not clear: why not others? Why not polymorphisms of MMP2, whose expression increases with periostin (Hakuno et al. 2010)? Why not MMP9, whose levels increase in RHD patients with more than 30 years of age (Lee et al. 2006)? In conclusion, gene and polymorphism description is rather poor and fail to set the basis for interpreting the results. Most of the description found in the discussion should be moved to the introduction, in order to clarify these points. The possible impact of other MMPs must be included in the discussion.

Material and Methods: The authors tried to "pair" controls and patients for sex and age, but how was their socioeconomic status, known to be highly influential in the susceptibility to RHD? Were all participants from the same ethnic group (Han, Yunnan)? Regarding age, p value mentioned in the first Results section was close to significance. Please correct all associations for this factor (and possibly others), using logistic regression. Results would be highly enriched with real-time RT-PCR quantification of mRNA expression (since the original hypothesis for the inclusion of these SNPs is that they alter gene expression!), ELISA and/or immunohistochemical analysis.

Results: first section would be more appropriate in the Mat & Meth description of study participants. It is not clear what is meant with the allele nomenclature (1G?, 2G?). There are other, less stringent ways to correct for multiple comparisons (why Bonferroni and not FDR?). Although the association with the 2G/2G genotype ends up without significance, the authors still maintain the association statement for this genotype. Without age correction, the results are not reliable.

Table 1: use Courier new font for DNA sequences

Discussion: as mentioned before, most sentences must be moved to the introduction, in order to understand the rationale of the study.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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Acceptable

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