Reviewer's report

Title: MiR-146a G/C rs2910164 variations in South African Indian and Caucasian patients with psoriatic arthritis

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Reviewer: Elena Lopez-Isac

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SUMMARY
Maharaj et al. assess the possible role of MiR-146a G/C rs2910164 variant in the susceptibility to psoriatic arthritis (PsA) in a case-control study of 117 South African Indian and Caucasian PsA patients. They also perform stratified analyses according to several clinical characteristics relevant for the disease. MiR-146a G/C rs2910164 was weakly but significantly associated with PsA. Despite the novelty of the study, the study has some limitations and weaknesses.

MAJORS
1. The main limitation of the present study is the low sample size in their case-control cohorts, which may give rise to a lack of statistical power to detect true association signals. Moreover, the authors should calculate and show the overall statistical power of the present study.

2. The study is performed in case-control cohorts that comprise South African Indian and Caucasian individuals. According to the description of their results, they did not perform the association studies in each cohort followed up by meta-analysis. It is well known that allele frequencies vary across populations; therefore, a proper case-control matching is essential in order to avoid spurious associations. I would recommend performing the association analyses in each cohort separately (according to their ancestry) and then perform a trans-ethnic meta-analysis.
3. In addition, it would be important to know whether the authors evaluated the ancestry match between cases and controls. How was this analysis performed? Did they have self-reported ancestry information?

4. Methods: in line 3 of 'Statistical analysis', authors stated that 'Genotype and allele frequencies were calculated using the Chi squared and Fisher's exact tests, respectively.' I understand that they are referring to the estimation of the differences in the rs2910164-C allele frequency between cases and controls. Please clarify and correct this point. Moreover, they have applied different statistical tests for the stratified analysis but it is not clear which of the test have been specifically used in each sub-analysis. Therefore, this section should be explained in a more detailed way.

5. Table 1. The header of table 1 is confusing. I would recommend the inclusion of a column indicating the sample size, and a second column showing the allele frequencies. In addition, what is the p-value of 0.0542 referring to?

6. According to their results, the rs2910164-C allele is more frequent in cases than controls, thus we could expect a risk OR for the C allele; however, the authors report a protective OR of 0.6274. Please clarify and correct this point.

7. In my opinion, the aim and scientific meaning of the stratified analyses from Tables 4, 5 and 6 is not clear. The authors aim to evaluate the possible association between the rs2910164 genotypes with clinical parameters, splitting the patients according to different conditions in each of the clinical parameters. This leads to smaller subgroup of cases, which arises concerns about the statistical power and the statistically significant findings, since they may represent spurious associations (performing multiple comparisons increases the false positive findings). Therefore, taking into account that these secondary analyses from Tables 4, 5 and 6 are not the main aim of the study, I would suggest excluding them in order to make clear the results from the manuscript.
8. If authors aimed to evaluate the possible functional implication of rs2910164 in the susceptibility to PsA, the analysis of the MiR-146a expression level and its correlation with rs2910164 genotypes would be interesting.

9. I would suggest that the conclusion of the abstract should be toned-down.

MINORS
1. Please indicate 'rs2910164' when referring to the SNP, and specify the allele when necessary as well. This should be reviewed throughout the manuscript.
2. Please change the running title to a one more appropriate according to the findings of the manuscript.
3. There is a grammar mistake in the title: 'variations'.

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.
Yes

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.
Not relevant to this manuscript

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