Reviewer's report

Title: Whole genome methylation array analysis reveals new aspects in Balkan Endemic Nephropathy etiology

Version: 5 Date: 7 June 2013

Reviewer: S. V. M. Maharaj

Reviewer's report:

OVERALL
This MS will make an excellent addition to the field of nephropathy, as it addresses an important subject of world-wide interest, i.e., BEN, and contributes to the emerging field of epigenetics. Moreover, as far as I know, it will be the first paper (when published) in the peer-reviewed literature that directly addresses the links between DNA methylation (or any epigenetic modification for that matter) and BEN.

Below please find my suggested revisions. I would not consider any as major, however, I do consider #1-4 essential, and #5 discretionary.

REVISIONS
#1: There is an amazing amount of spelling, grammar, and typo mistakes throughout the text. Though I began keeping track in an effort to help, they are too numerous to cite (especially given that according to the review guidelines I must not use page and line numbers). This may seem like a minor comment, except for what it indicates. How did this MS, given all these authors, i.e., 17, get to this stage (i.e., external peer-review) with all these mistakes? Not even a spell check was conducted. It is so overt, e.g., could it be that even “Danube” which appears from the get-go, in the 1st paragraph of the Abstract, is spelled incorrectly? I hate to have to say it, but it is natural to now wonder: What else is wrong? What else did these 17 authors fail to do? What else were they not conscientious and careful about that I cannot check—their procedures in the laboratory that all the data are dependent upon? I suggest that all authors go through the MS, double-checking for all possible mistakes (not just spelling, etc.), and report back to Dr. Toncheva with all their corrections.

#2: The English is not exactly perfect, however, all readers should understand that English is not the authors' first language. The authors should endeavor to correct the English, however, as it stands, there is no instance where I could not understand what they meant scientifically.

#3: A section "Limitations" needs to be added where the authors discuss in detail the limitations (comprehensive, please) of this study and its possible impact on their results and therefore conclusions. Suggestions for topics to address include the: patient selection criteria; different diagnostic criteria used for the different cohorts; different DNA extraction methods used; processing and pooling of
samples; BATUMAN assay; designed software.

#4: bp and PBS need to be defined, and reference #33 is incomplete (i.e., there is no journal, etc).

#5: This MS represents a key contribution to the subject of BEN etiology, and the authors now appear poised for many further studies. I think it would be of interest to colleagues to read at the end of the MS about their other in-progress and/or future research plans on epigenetic modifications as related to BEN.

CONCLUSIONS

I am sure that the authors can be trusted to make the revisions, therefore, I recommend publication (after it is revised), and there is no need for me to see it again. Thank you very much for the opportunity to review the MS.

Level of interest: An article of outstanding merit and interest in its field

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

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.