Reviewer’s report

Title: Differential methylation as a diagnostic biomarker of rare renal diseases: a systematic review

Version: 0 Date: 09 Jul 2019

Reviewer: MOHAMED HASHIM ALHAMED

Reviewer's report:

The manuscript represents systematic review of differential methylation as biomarker for rare renal diseases.

Major points:

1. In Background: it would be worth adding information about differential methylation in health and disease

2. To answer 2nd point of aims and objectives, Authors should describe methylation findings in six diseases listed in discussion

3. In this review only 13 articles were found to describe methylation in rare kidney disease! How can you explain this shortage? And what is clinical impact of these findings?

4. Cancer is affected by epigenetics; did you exclude diseases with kidney tumors?

Minor points:

1. In this study, Can we replace rare renal disease by genetics (inherited) renal disease?

2. In abstract, your search was before Sep 2018 then in eligibility criteria (line 126) your search was before Nov 2017. Can you explain?

3. Did you check methylation websites such as genomeweb, epigenesys or EpiSign for methylation in rare renal disease?
Please confirm that you have included your review in the ‘Comments to Author’ box?  
As a minimum standard, please include a few sentences that outline what you think are the authors’ hypothesis/objectives, their main results, and the conclusions drawn. Your report should constructively instruct authors on how they can strengthen their paper to the point where it may be acceptable for publication, or provide detailed reasons as to why the manuscript does not fulfill our criteria for consideration. Please supply appropriate evidence using examples from the manuscript to substantiate your comments. Please break your comments into two bulleted or numbered sections: major and minor comments. 
Please note that we may not be able to use your review if no comments are provided. 
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Yes

Are the methods appropriate and well described to allow independent reproduction of experiments?  
Please state in the ‘Comments to Authors’ box below what you think are the strengths and weaknesses of the methods (study design, data collection, and data analysis), and what is required, if anything, to improve the quality of reporting

Yes

Does the work include the necessary controls?  
If not, please explain in the ‘Comments to Author’ box below.

Yes

Are you able to assess the statistics?
- Are the statistical test(s) used in this study appropriate and well described?
- Is the exact sample size (n) reported for each experimental group/condition (as a number, not a range)?
- Are the description of any error bars and probability values appropriate?
- Are all error bars defined in the corresponding figure legends?
- Has a sample size calculation been included, or a description and rationale about how sample sizes were chosen?
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Are the conclusions drawn adequately supported by the data shown?  
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Please indicate the quality of language in the manuscript:

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I declare that I have no competing interests. This article could be a start point in future research for methylation in rare kidney disease

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