Reviewer's report

Title: Human rhinovirus infection causes different DNA methylation changes in nasal epithelial cells from healthy and asthmatic subjects

Version: 3
Date: 5 June 2014
Reviewer: Nelis Soto-Ramirez

Reviewer's report:

The authors investigated the involvement of epigenetic mechanisms on virus-induced asthma exacerbations. To this end, the authors profiled “DNA methylation of primary nasal epithelial cells (NEC) from asthmatics and healthy individuals infected in vitro with human rhinovirus (HRV)”. Interestingly, they found that HRV influence changes in both global and loci-specific DNA methylation in NEC from asthmatic individuals. The findings of this study are of great interest in the area of epigenetics and asthma research and offer new insights to further explore epigenetic mechanisms by which respiratory viruses cause asthma exacerbations. Some major and minor revisions are needed.

Major Compulsory Revisions:
1. In the method section (page 9) you mention that you presented either the top n = 10 most positive or negative loading probes because you couldn’t find in the literature a consistent component loading cutoff. Please discuss this issue in the discussion section of the manuscript and potential limitations for this approach.
2. A detail explanation of the results regarding Table 2 was not presented in the manuscript. Please include this in the results section.
3. The authors did not mention whether the results were influenced by gender. Please provide information on this.
4. Page 7; lines 95 to 97: Provide the methods for lung function measurements, allergic sensitization, and methacholine challenge.

Minor Essential Revisions:

Abstract:
1. Page 3; lines 36 and 39: Include a comma before the word “respectively”.

Introduction:
2. Page 5; line 69: Please, provide a reference for this sentence.

Methods:
3. Page 7; line 90: What kind of advertisements did the authors used?
4. Page 7; line 94: Please include the name of the study clinic (University clinic?)
5. Page 8; line 116: You wrote the following: “DNA from all cultures in Population 1 (Table 1) were used global methylation profiling”. Please include the word “for” after “used”. 
6. Page 9; line 140: Please, spell out the abbreviations “PC1”, “PC2”, and “PC4”. Is there any PC3?

Results:
7. Page 12; line 189: Do you mean population 2? If yes, please revise.
8. Page 13; line 204: Add a comma before the word “respectively”.
9. Page 14; line 225: Please include in parenthesis: (population 2).

Discussion:
10. Page 15; line 235: Delete the comma
11. Page 15; line 237: Do you mean “such as”?
12. Page 15; line 238: Provide a reference for the following statement: “…DNA methylation in the airway epithelium of asthmatics.”
13. Page 15; line 238: Edit “et. al” to “et al.”

References:
14. Some of the references are not formatted according to the journal guidelines. Please, revise.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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