Reviewer's report

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

Version: 3
Date: 2 June 2014
Reviewer: Deepa Rastogi

Reviewer's report:

In the manuscript entitled “Human rhinovirus infection causes different DNA methylation changes in nasal epithelial cells from healthy and asthmatic subjects” McErlean et.al. present results on studies investigating differential DNA methylation and its association with differential gene expression in nasal epithelial cells obtained from asthmatic adults as compared to those from healthy adults. As the authors have highlighted, there are limited studies on the epigenetics of asthma and the changes that may be occurring in the setting of a viral illness.

Major Compulsory Revisions
The manuscript is overall well written and their finding of differential methylation at SNORA12 is interesting. However, there are certain concerns:

1. The authors report a 0.5% difference in methylation. It is unclear what is the clinical/ translational significance of such difference. Did the authors address multiple testing in the statistical analysis?

2. The SNORA12 methylation changed in healthy participants but it was not associated with gene expression. Conversely, change in gene expression among asthmatics was not associated with change in methylation. It is unclear having observed these differences, why have the authors combined these groups together (Fig. 6C), which also is notable for a modest correlation coefficient and a p value that approaches significance.

3. Since the authors mention the association of SNORA12 with IFN regulatory factor 4 and NFkB. were gene expression of these inflammatory markers investigated and were there any differences in expression of these molecules?

4. As mentioned in the discussion, the authors did not identify a dominant biological process based on differential DNA methylation. The small sample may have contributed to the lack of observed differences and needs to be included in the discussion as a potential limitation of the study. Further, as mentioned by the authors, the identification of SNORA12 from nasal epithelial cells may be more of a phenomenon of atopy rather than lower airway disease and needs further investigation from lower airway tissue.

Level of interest: An article of limited interest
Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.