Reviewer's report

Title: Genome-Wide Methylation Profiling of the Bronchial Mucosa of Asthmatics: Relationship to Atopy

Version: 2 Date: 22 January 2013

Reviewer: Jesús Delgado Calle

Reviewer's report:

Comments to the authors

Although the revised manuscript is considerably better than the original draft and the authors have addressed some of the reviewers' concerns adequately, there are still some key concepts of Epigenetics that are not clearly explained in the manuscript. Especially authors should make an effort to reflect the current knowledge in this field, providing potential readers with correct and useful concepts to understand the conclusions drawn from this study.

Major compulsory revisions

1. Page 11, figure 2C. Figure 2C remains unclear and misleading. This must be corrected. Authors should display the beta values of the 55 loci showing differentially methylated regions instead of the 2904 CpGs sites explored in chromosome 1.

Minor compulsory revisions

2. Abstract: page 3, line 46: 52 or 54 genes?

3. Background.

3.1. Page 4, line 75: Epigenesis must be replaced by Epigenetics. Please check and corrected it throughout the text.

3.2. Page 5, line 79: Besides DNA methylation and histone modifications, include non-coding ARNs as one of the three major epigenetic mechanisms

4. Results.

4.1. Page 11, line 225-228. Authors found 6 loci corresponding to six genes hypermethylated, and 49 loci corresponding to 48 hypomethylated, thus they found a total of 55 differentially methylated loci corresponding to 54 genes. Later, line 238, they use 52 genes for ontology analysis. Is this correct? Where the analysis performed with 52 or 54? Please check the number of loci/genes found throughout the manuscript. The number is not consitent among the different sections.

4.2. Page 11, figure 2C. Figure 2C remains unclear and misleading. This must be
corrected. Authors should display the beta values of the 55 loci showing differentially methylated regions rather than the 2904 CpGs sites explored in chromosome 1.

5. Discussion

5.1. Page 13, line 267. Authors wrote: “...the role of DNA methylation in gene expression is unknown...” This sentence should be deleted. It is known that DNA methylation tends to block gene expression by different mechanisms. Only few examples of gene expression activation by DNA methylation have been described so far.

5.2. Page 13, line 282. Authors wrote: “This suggests that more than 50% of the genes were ready to be express...” Based on the current knowledge, DNA methylation is not the only contributor to gene expression. The sentence should be removed or changed to reflect this concept.

5.3. Page 14, line 304-315. Authors include in these paragraphs information regarding the association of SNPs in two genes, MAP3K5 and CDH1, and atopy and asthma. Please include references of the studies.

6. The text needs several language corrections (grammar and spelling) before being published.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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.