Reviewer's report

Title: Genetic polymorphisms and risk of recurrent wheezing in pediatric age

Version: 3  Date: 23 June 2014

Reviewer: Paul Robinson

Reviewer's report:

This is an interesting study of infants presenting with LRTI induced wheeze where the associations with genetic polymorphisms are investigated. The relationship between these and common viral aetiologies is also explored. This is an area of research interest, and the findings are variably in agreement/conflict/add to the existing literature. I feel the paper would benefit from some additional details, and enhanced discussion of how this paper adds to the current literature so the reader can better understand the current status of these tests. Some of the statements about identifying early asthma seem premature and overstated given the conflicting nature of the literature outlined in the discussion and the fact that asthma is not one of the outcomes measured by this group.

Major compulsory revisions

Pg 6 – please insert the inclusion criteria used, rather than just referencing if possible. This helps the reader understand the population recruited.

I am impressed that no-one approached declined participation for a study that was intensive in nature. It required blood testing, regular follow up, diary completion, telephone contact weekly and review when unwell. Is this really true that no-one declined? It appears that no-one dropped out of the study/failed to complete all measurements. Please add details regarding these aspects and the completeness of the data collected.

pg 7 - Which outpatient clinic were the controls selected from? Please describe this in more detail. The impression the reader gets is that these controls were recruited at 2 years of age or older and the parents recalled whether the child had a wheezing illness related to LRTI during the first two years. If this is the case then this is an important difference to the prospectively closely followed index cases. Please can the authors clarify this aspect and also add this to the limitations discussion.

Statistics used

- were any adjustments made for the fact that multiple comparisons were being made across this cohort? I can not see this stated in the methods

- How was the sample size calculated? – no power calculation is provided by the authors and as stated in the discussion this study contained smaller numbers than others in the literature.
When was the blood taken for genetic polymorphism analysis? This is not stated in the methods. Can you please add the details about this aspect.

The authors state that some of their findings are not in agreement with the existing literature (NFKBIB) whilst others are in agreement with some but not all studies (CTLA4). Can the authors please offer some suggestions as to why the existing data might conflict? For example, could this reflect study numbers etc?

Given the conflicting literature I think it is highly speculative at this stage to state that these SNIPs may be useful for early identification of recurrent wheezers – I would prefer authors to reduce the prominence of these type of statements and focus on the fact that further large studies are required to confirm whether these findings are true associations.

Minor essential revisions

P 11 ln 254 – need to reference this statement where discussing previous study findings. This approach should be applied throughout the paper

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

**Quality of written English:** Acceptable

**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