Reviewer's report

Title: Whole-exome sequencing of a pedigree segregating asthma

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Reviewer: Tara Matise

Reviewer's report:

This article describes the use of whole-exome sequencing in a single family to identify novel family-specific variants that may contribute to asthma in this family. The article is clear and well-written and the research is novel, interesting and well-described. I make the following comments:

Major Compulsory Revisions:

1. Methods: Although substantial details were given of the home interviews, a little additional detail about the phenotype is warranted.

For example, it was not specified whether the initial diagnosis of asthma was confirmed or substantiated by the findings of the home interview. It is worth noting that for one of the 2 affected children their age at diagnosis could not be confirmed. Considering that this child had no need of medication in the previous 12 months, additional details from the interview that confirm this subject's diagnosis would be helpful.

Discretionary Revisions:

2. Results: It would be helpful, if space allows, to summarize the specifics from the functional prediction analysis that indicate the 4 novel variants are likely to be functional - the information can be found in Table 4 but a few sentences with specific details given in the text would enhance the manuscript.

3. Results: The following sentence could be written more explicitly which would make it more clear:

³We then looked at variants where the two affected children and the mother had at least one minor allele, but the unaffected children and the father had zero (affected individuals were heterozygous) or one (affected individuals were homozygous) minor allele.²

4. Some acronyms were not defined

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