Reviewer's report

Title: Leukotriene B4 receptor locus gene characterisation and association studies in asthma

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Reviewer: Kelan Tantisira

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In this manuscript, Tulah and colleagues seek to understand the role of LTB4 receptor genetic variation on asthma susceptibility and on lung function within asthma. Following a nice characterization of the receptor structure itself, they report genotyping of a subset of resequenced SNPs and lack of association of these variants with asthma and FEV1 in asthmatics.

Major Comments:

1. SNP Selection - Despite this methods section, it is unclear if all of the common variation within this region (understandably, rare variants were not included) is actually covered by the selected SNPs for two reasons:
   a). While the authors refer to use of 1000 genomes data to evaluate dbSNP variants, it is unclear how these are incorporated into the genotyping selection, if at all. There are 100 annotated dbSNP variants, of which several have MAFs in excess of 5% but do not appear to be represented in the genotyped variants.
   b). Based on figure 3, the LD metric used to determine the selected SNPs appears to be D'. For association testing, R-square values have consistently been cited as a better metric to use.

The authors should address each of these issues in SNP inclusion criteria or state that there are limitations to their genotyping schema.

2. The authors list very little in the way of details in regard to the clinical cohorts, and do not detail any potential confounders or details of multivariable analyses within their methods or results sections. In addition to traditional covariates, information related to atopic status and/or controller medication administration would appear to be crucial in the interpretation of the association results data (especially the FEV1 and severity analyses). Have these been done?

Minor Comments:

1. Given that only common (and not complete common) variation was the focus of the association analyses, it is premature to state the conclusions that "LTB4R polymorphisms are not susceptibility markers" (or severity/lung function markers).
2. The lung function analyses demonstrate z-scores and betas in the same direction for the family and population based analyses. What happens when the evidence from the cohorts is combined?
3. Given #2 above, since there is a consistent direction, but no significant
association within a cohort, despite the power calculations provided, it should be
stated that there may be a subtle effect that the current study is underpowered to
detect.

4. For the lung function analyses, it should also be noted by the authors that the
FEV1 was relatively normal in all populations. Therefore, a ceiling effect might
have helped to prevent the detection of a significant association.

5. Given that spirometry was obtained, did the authors consider evaluating other
measures of lung function (e.g. FEV1/FVC)? This would help to make the story
more complete.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a
statistician.

**Declaration of competing interests:**

No competing interests.