Reviewer's report

Title: Positive Association between Aspirin-Intolerant Asthma and Genetic Polymorphisms of FSIP1: a Case Control Study

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Reviewer: Marek Sanak

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The Authors investigated genetic association between aspirin-induced asthma (AIA) and a structural gene encoding fibrous sheet interacting protein-1 (FSIP1). The study group was large enough to make a statistical inference and the methods used was appropriate. A finding of significant correlation between intronic allele of FSIP1 and AIA is interesting for several reasons. No structural genes were associated with the disease so far, FSIP1 gene is a cell motility gene of unknown exact function, the gene is expressed in respiratory epithelium.

Major comment:

The rationale for investigation of FSIP1 in AIA is quite vague. Definitely it is not the fact, that the gene was discovered as expressed in spermatogenesis. Neither influence of NSAIDs or PAF on spermatocyte mobility is relevant to AIA in the frame of current knowledge on the disease.

The Reviewer suggests to limit copious comments and parallels on male gametes as related to asthma. This sounds oddly and no reproduction defects were ever described in AIA.

Minor remarks:

1. INTRODUCTION: Most noticeable symptoms of AIA include aspirin sensitivity, bronchial asthma, and chronic rhinosinusitis with nasal polyposis [4-6] when non-steroidal anti-inflammatory drugs such as aspirin are ingested. – should be refrased because symptoms persist without ingestion of NSAIDs, while the drugs precipitate bronchoconstriction.

2. A note in proof for expression of FSIP1 in respiratory epithelium is needed. This can be found in GEO set GSE4498 with appropriate publication reference

3. METHODS: The differences in the fall rates in FEV1 following aspirin challenge among the genotypes and haplotypes were examined using logistic model. – this is not clear: a difference is continuous variable, which categorical variables were used exactly?

4. DISCUSSION: rs7179742 SNP is located closer to the gene’s 5’ end. The next gene is only ~20 kb upstream and it is an orphan receptor GPR176. A linkage between SNP and the other gene has to be taken into account.

5. In Table 1 “Fall rate” should be explained in the legend, IgE levels is better described as median and interquartile interval.
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'