Reviewer's report

Title: A pooling-based genome-wide analysis identifies new potential candidate genes for atopy in the European Community Respiratory Health Survey (ECRHS)

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Reviewer: Florence Demenais

Reviewer's report:

This paper presents a genome-wide association study (GWAS) of atopy and atopic asthma first based on DNA pooling and then on individual genotyping. The most significant and consistent results are obtained with SNPs within SGK493 gene for both atopy and atopic asthma. This gene is a new finding since it has not been previously reported to be associated with asthma or atopy. However, its function is unknown and confirmation is needed.

SNPs within MAP3K5, COL29A1 and COL18A1 genes were reported to be associated with atopy and/or atopic asthma, although the latter results were not always consistent between those obtained from DNA pooling and individual genotyping. Can the authors explain these inconsistencies?

We are concerned with the small sample size for a GWAS: 75 individuals in each of three groups examined (subjects with atopy, subjects with asthma and atopy, controls) using DNA pooling and the replication samples include at most 429 subjects in one group. It would be desirable to increase the sample size of this study or to use other samples for replication.

As pointed out by the authors in the discussion, there is no correction for multiple testing in the analyses carried out at the individual level. Even without that correction, the p-values shown in Table 3 are not really small, except for SGK493 SNPs and one MAP3K5 SNP. This should be indicated in the results which could mainly focus on SGK493.

Since Figure 1 is not easy to read, the pairwise LD measures (D’, r2) among SGK493 SNPs could be indicated in the text. Multiple regression with these SNPs might be performed to determine which SNPs have independent effects. Hapotype analysis might be also carried out.

The discussion regarding genes for which there is no strong evidence of association (eg COL18A1) should be shortened.

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

Quality of written English: Acceptable
**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interest