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: Catherine Laprise

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General comment:

This paper reports results from a pooling-based GWAS for asthma and atopy and represents a cost-effective alternative to the classical GWAS. Essentially, the research used illumina chips containing 300K SNPs to compare a pool of 75 DNAs per group (control, atopic and asthmatic subjects). After the GWAS the study performed genotyping for promising SNPs within genes in the region targeted by the GWAS. Results indicate an association between atopy and SGK493, MAP3K5, COL18A1 and COL29A1 genes. Finally, the literature reports evidence for functional links regarding all associated genes in the context of asthma except for SGK493.

Major comments:

My first comment concerns the pooling itself. It is probably a good alternative to pool samples to reduce budget expenses. However, I think it’s necessary to perform analyses for some groups of samples in order to have an idea of biological variations (for example: analyze three pools of 25 samples per phenotype). It is also important to duplicate some analyses to verify the technical variability.

As the authors note in their discussion, the sample does not reach significant levels to make sure that the association was not a “false positive” one. The authors also note the second major weakness of their design concerning the lack of saturation of the region in term of number of genotyped SNPs. Indeed, I think that the authors need to increase the number of subjects in their association study (or perform a validation of significant association in an independant cohort) as well as the number of SNPs to dissect haplotype.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.