Reviewer's report

Title: Associations of ECP (eosinophil cationic protein)-gene polymorphisms to allergy, asthma, smoke habits and lung function in two Estonian and Swedish sub cohorts of the ECRHS II study

Version: 2 Date: 1 March 2010

Reviewer: Guicheng Zhang

Reviewer's report:

Jönsson et al investigated the associations of three SNPs in ECP gene with asthma, smoke habits and lung function in the two populations: Estonian and Swedish. They concluded that ECP-genotypes may play an important role in the processes of allergic diseases including asthma. This study also showed inconsistencies for the polymorphisms of the ECP gene with asthma like phenotypes such as the association for the G allele of rs2073342 with allergic asthmatics (authors’ previous publications red 8) and with no-allergic asthma in the present study and the opposite effect of -38 (A>C) polymorphism in this study and the publication of ref 7. As gene by environment interactions are important for asthma pathogenesis and an opposite effect has been reported in a Karelian population (Allergy. 2009 Sep;64(9):1333-41) for several polymorphisms with asthma phenotypes, this study can address this more in the data analysis and discussion. There are several major and minor concerns for the manuscript.

Major concerns:
1. Interaction terms should be examined of the genotypes and ethnic groups, gender and smoke habit using appropriate statistical strategies;
2. The haplotype between the three SNPs of ECP gene should be constructed and investigated in terms of the associations with asthma like phenotypes;
3. Regression strategies can be employed to adjust for confounders for some analyses.

Minor concerns:
1. How was the ‘symptomatic sample’ selected in the Estonian and Swedish sub-cohorts?
2. It is better to present the major findings in a table for a comparison between the cohorts of Sweden and Estonia.
3. Table 5, it may be easy to understand giving the prevalence of these conditions rather than prevalence of genotypes.
4. For some tests (for example in Table 5 allergic asthma vs non-allergic asthma) of differences in proportions, Fisher’s exact tests should be employed due to small sample size.
5. For Fig 1, the readers may also be interested in the associations with lung
function for smoking women, woman never-smokers and man never-smokers for a comparison.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.