Author's response to reviews

Title: Association of Vitamin D Receptor Apal polymorphism with asthma in the Chinese Han population: a case-control study

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Author's response to reviews: see over
Dear Editors:

On behalf of my co-authors, I am submitting the enclosed articles titled “Association study between Vitamin D Receptor polymorphisms and asthma among the Chinese Han population: a case-control study” for possible publication in BMC Medical Genetics.

Many previous studies suggested that VDR gene is associated with asthma, but the results is inconsistent and needs to be replicated in different population. We genotyped five SNPs located in VDR gene, and found that rs7975232 (ApaI) was significantly associated with asthma in the Chinese Han population with an allelic OR of 1.33 (95% CI: 1.10-1.60), p = 0.009. Our results may be helpful to elucidate the role of VDR in the pathogenesis of asthma.

We certify that we have participated sufficiently in the work to take public responsibility for the appropriateness of the experimental design and method, and the collection, analysis, and interpretation of the data.

We have extensively revised the first version of our manuscript sent on 23 April 2009 and approve it for publication. To the best of our knowledge and belief, this manuscript has not been published in whole or in part nor is it being considered for publication elsewhere.

We would like to address a special thank to both Reviewers for their interesting comments and consideration. Following are the main responses to the concerns:

**Reviewer 1: Giovanni Malerba**

1. Structure of the manuscript including Methods, Results and Discussion sections have been all rearranged and several points have been moved from one section to another.
2. A brief description of the clinical characteristics of the population used in research has been added to the sub-section of Subjects in the Methods section, accompanied by Table 1.
3. SNP selection basis was explained in the Methods. In fact, they were mostly a candidate SNPs from the previous published results on VDR and asthma, since no previous association study between VDR and asthma was done in the Chinese population.
4. Bonferroni correction was applied throughout the manuscript now, in particular for rs7975232 (see Table 4), the only significant association found by this study (P*= 0.045). For the other corrected P* were not applied since the P-values ended up greater than 1.0 for most of them.
5. A more detailed explanation was given to the graphical analysis of genotype frequencies seen with rs7975232 (Figure 1), and this is in the Methods section now.
6. Concerning Z statistics values, we rather preferred removed them from table 4 and just keep a detailed statistical analysis of VDR ApaI site in the Chinese cohort just to make the table interpretable.
7. In the Linkage Disequilibrium part, D’>0.6 was just considered as a highest LD measure obtained after analysis; we also agree that this is not a high LD, so the sentence was corrected.
8. Block B reference was removed both Result and Discussion part.
9. In the SNPs selection sub-section, PCR cycling conditions and tools were removed, so only Primers and Enzymatic restriction was reported.
Reviewer 2: Matthias Wjst
1. Discussion part was revised and many sentences were removed or corrected.
2. More detailed description about the case and control selection was added to Subjects sub-section in the Methods (see also Table 1).
3. Ors were all reported in the text as well as in the tables with 2 decimals.
4. To be honest, it is difficult to answer the question. We just made sure that all the cases and controls are age, sex matched and they are all recruited from the same area.
5. Typing error <Cohn> was corrected to <Crohn>.
6. Different RFLP product lengths are all represented in Table 2 now.
7. No, we did not studied any other asthma association risks, since no other atopy-related diseases or allergy phenotypes were available for our patients.

Best Regards.

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