Fei and colleagues reported an association study between a number of polymorphism markers in VDR, CYP2R1 and GC gene and asthma susceptibility in a Chinese Han cohort (467 cases and 288 unrelated controls). All 8 exons of VDR and all 5 exons of CYP2R1 were sequenced. Two mutations were identified in these regions (variants were specified as rs2228570 in exon 1 for VDR and rs12794714 in exon 1 for CYP2R1). These two variants were later analysed with two other common polymorphisms in the group-specific component (vitamin D binding protein) or GC gene by PCR-RFLP method (rs4588 and rs7041). As a final result, polymorphism markers in GC gene were associated with asthma susceptibility.

Results are interesting, however manuscript need several corrections resulting from the lack of good organisation within each section and/or .

Comments

I- Major Compulsory Revisions

1) Structure of the manuscript

The sentences employed in this manuscript, especially Results and Discussion sections should be reviewed and rearranged in a better way, and authors should replace many simple sentences employed in this manuscript by strong meaning sentences, so they can give a great support to their Hypothesis.
2) Methods
- SNPs selection and genotyping
Authors write they have genotyped two most commonly studied SNPs in the gene GC (rs4588 and rs7041), but this part did not show a clear idea about how SNPs have been selected. Authors should precise whether these two SNPs are a candidate SNPs from previous published studies within different populations, or if they just represent tagSNPs within Chinese population? Authors should clearly describe the basic(s) of their selection.

3) Results
- Characteristics of the subjects
The part of results subtitled “Characteristics of the subjects” should be described in the Methods section and not in the Results section. I would suggest to include this subtitle with the subtitle described previously in the Methods section “Subjects and phenotype definition”, and give it another nomination (for example “Subjects and phenotypical characteristics”…or any other similar proposition).

- Association between polymorphisms in CYP2R1, GC, VDR genes and asthma
In the Results section, Authors have briefly mentioned the different results obtained. However, these results should be described with more details in which separated descriptions of corresponding SNPs association analysis results for each gene are necessary.

3) Discussion
- Vitamin D binding protein
Early in the Discussion section, a writing error in this sentence “We showed that the GC polymorphisms giving rise to the major electrophoretic isoforms of vitamin B binding protein…” should be corrected. “…..vitamin B” should be replaced by “….vitamin D…”.

- Association between GC gene polymorphisms and asthma
Authors state that a significant association were reported between GC gene polymorphisms and asthma, and then used this sentence " …although not 25-OHD concentrations in asthma patients" to support the association obtained. I think that these findings are important (both significant association and concentrations of 25-OHD in asthmatic patients), so supporting them with better organized sentences would be preferable.

- Linkage disequilibrium phenomenon
In the Discussion section, “a linkage disequilibrium phenomenon” is mentioned. To make these findings acceptable, Authors should explain why they consider this phenomenon with non-coding regulatory variant (s). (Is it a deduction from previously studied and analyzed non-coding polymorphisms? Or others?).
II- Minor Essential Revisions:

1) Methods

- SNPs selection and genotyping
I would suggest to summarize all sentences describing any commonly used
Standard method (like PCR, enzymatic restriction… etc.), since authors also
describe all Primers and PCR conditions for amplification in Table 1. However, a
shot description of the different loci and their recognition by restriction
endonucleases would be necessary.

- Table 1
I suggest to add the names of restriction endonucleases used in enzymatic
reactions and their RFLP products in this table.

3) Results
I suggest to eliminate any subtitle in the results section since Authors are
describing one kind of results which is association analysis results in the three
genes. More detailed and clearly separated texts describing these results for
each gene would be understandable.

4) Discussion

- Sequencing all exons of VDR and CYP2R1 genes
In this part, Authors write “…we were able to identify the full range of exonic
genetic variants present in this ethnic group at allele frequencies #0.13%”. I think
that the use of another expression such like variants present in our cohort at
allele frequencies #0.13% “…we have identified…” or start the sentence with
“….identification of …….was possible or successful”. The word "association"
would be preferable.

- SNP nomenclature
Authors write “rs2228570 (also known as Fok1) in VDR”. In this sentence the
name of the restriction endonuclease should be corrected to “FokI” instead of
"Fok1”. However, in the rest of discussion section, I suggest to use the rs# name
to identify this SNP instead of the name “FokI”.

- rs2228570 location
Authors write that “FokI polymorphism is in exon 1 of VDR”. I think that the
location cited here is wrong since rs2228570 (known also as FokI) is located on
exon 2 of the VDR gene. This information should be corrected by authors after
their confirmation.

- References
In the end of discussion section, I think that there is a reference(s) missing for the
studies on transgenic mice. If it is the case, Authors should add this reference
after confirmation.
**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests