Reviewer's report

**Title:** Genetic variants associated with circulating MMP1 levels near matrix metalloproteinase genes on chromosome 11q21-22 in Taiwanese: interaction with obesity

**Version:** 2  **Date:** 3 December 2012

**Reviewer:** Mateusz Kurzawski

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**Major Compulsory Revisions**

1. It is a lot data in the literature suggesting that BMI cut-off points for defining overweight and obesity in asians should be generally lower than values used in caucasians (25 kg/m2 and 30 kg/m2). Among other reports, Deurenberg-Yap et al (2000) gives BMI=27.5kg/m2 as a cut-off value for obesity in singaporean chines. However, I did not find a clear definition of obesity defined as >25kg/m2 in the paper by Tan et al. which is given as reference in the methods section. In fact, Tan concludes that waist circumference may be more useful in identifying individuals with the metabolic syndrome in Asia than BMI. Please provide additional references for your cut-off value selection.

2. How many of the subjects were obese? (numbers of subjects in each group should be given. Without that one doesn't know if lack of significance of MMP1 polymorphisms is not a result of small number of obese subjects;

3. I am a little confused by tha statement in conclusion: "our evidence suggested an association between MMP1 gene polymorphisms, MMP1 levels, and various diseases" as presented data does not refere to any disease - there is no analysis of MMP1 polymorphism nor level in relation to any disease. Moreover, all the diseases previously associated with MMP1 genotype were among the exclusion criteria: "Exclusion criteria included a history of myocardial infarction, stroke or transient ischemic attack, cancer, and current renal or liver disease." I feel that this statement should be modified.

**Minor Essential Revisions**

1. How were haplotypes compared? carriers to non-carriers? or number of selected haplotype as a variable (1, 2 or 3)? In my opinion the resuts would be more clear to interpret if carriers of each haplotype were compared to the same reference group (best - homozygotes for the most frequent haplotype).

2. It is mentioned that SNPs were selected 'due to previous reports showing an association with MMP1 gene expression/level'. Among GWAS by Cheng et al. there was one more SNP associated with MMP1 levels: rs12289128. Why it has been not included in the current study together with two other SNPs (rs495366 and rs11226373)?
Discretionary Revisions

1. References’ list: please check for duplicated references, e.g. 20 and 37

2. Last paragraph of Backround: 'six closely linked SNPs’ - should be: "five closely linked SNPs’; Genomic DNA Extraction and Genotyping: 'Six SNPs were analyzed' - again five are described

3. Table 2: TaqMan SNP Genotyping Assays - Assay IDs should be given

4. Supplementary Table 1 could be replaced by a figure presenting the pairwise linkage disequilibrium coefficient r2 and D’ in the way it is usually presented in literature

5. SNPs described as -519A>G and -340T>C in discussion: please try to provide rs IDs for them. Have they been investigated in the current study?

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: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests