Reviewer's report

Title: Impact of Matrix Metalloproteinase 9 rs3918242 Genetic Variant on Lipid-lowering Efficacy of Simvastatin Therapy in Chinese Patients with Coronary Heart Disease

Version: 0 **Date:** 16 Jun 2016

Reviewer: Duan Liu

Reviewer's report:

In present study, the authors correlated the MMP9 -1562 C>T SNP genotype with lipid-lowering efficacy of simvastatin in Chinese CHD patients. They found that MMP9, as well as LDL-C, were increased in serums from CHD patient carrying TT genotype compared with whom carrying CC genotype. After simvastatin treatment, the authors observed more significant decrease in LDL-C in serums from CHD patient with TT genotype when compared with patient with CC genotype.

Major problems:

1. Based on the observations (the correlation of MMP9 -1562 C>T SNP genotype with % change in LDL-C after simvastatin treatment), the authors stated that " In this study, we showed that MMP-9 1562C>T polymorphism significantly regulated circulating MMP-9, TG and LDL levels, and modulated LDL-C lowering response to simvastatin in Chinese patients with CHD". However, there is no evidence that this SNP can regulate LDL-C or modulate simvastatin LDL-C lowering efficiency. It is just correlation, probably because of LDL-C level was correlated with MMP9 level and MMP9 level was correlated with the SNP genotype. It will not be convincing to claim that a SNP, in which gene is not related to simvastatin PK/PD, can modulate simvastatin LDL-C lowering efficiency without consideration of functional SNPs in the genes (such as SLCO1B1) that involved in the simvastatin PK/PD.

2. It is not surprising that after simvastatin treatment, LDL-C was decreased. Based on the SNP genotype, there is no significant difference in absolute LDL-C levels after simvastatin treatment. The significant larger % change in LDL-C in patients with TT genotype may merely due to a significant higher baseline LDL-C level. However, there is no evidence that MMP9 -1562 C>T variant genotype is a cause of higher baseline LDL-C level, or regulates LDL-C levels.

3. Some of the data are not convincing or not visualized properly. In Table 4, MMP9 levels at week 0 for CT genotype seems more significant than TT genotype since the amount is higher and the n = 69, which is much larger than 7 for TT genotype. The % change for TT

genotype may also significant different from other genotypes. These data, at least for MMP9 and LDL-C, should be showed in figure with x-axle as genotype and y-axle as concentrations, each patient should be dotted and the 95% confidence interval should be showed.

4. Some sentences are not clear and confusing.

Other problems:

1. Many important backgrounds that the authors state in the Introduction has no references;
2. MMP9 1562 (should be "-1562") C>T is not a professional term to refer the SNP. The "rsID" for the SNP should be used;
3. Page 6, line 53. What is the mean for "hand"?
4. Page 7, line 9. What is the mean for "gene frequencies"? That is "minor allele frequency".
5. Table 2 showed that smoking is strongly associated with CHD. It was known that smoking could induce MMP9 expression in lung. Is that also happen in blood? Is smoking a cause of variations in MMP9 level rather than the SNP genotype?
6. Page 9, line 1. Need to specify what is the mean of "improved", plasma lipid increased or decreased?
7. Page 10, line 1. Not clear.
8. Page 11, line 38. The authors cited their previous study (as claimed "our previous….") and labelled [17]. However, reference 17 and present study has no author or affiliation overlaps.
9. Page 12, line 12. "….simvastatin on MMP9 level,…" is not clear.
10. Page 13, line 6. Not appropriate.
11. The quality and resolution of Figure 1 is low.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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I am able to assess the statistics

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