Reviewer's report

Title: MTTP-297H Polymorphism Reduced Serum Cholesterol but Increased Risk of Non-Alcoholic Fatty Liver Disease

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Reviewer: Ken Sugimoto

Reviewer's report:

The authors investigated the impact of various polymorphisms of MTTP gene on lipid profile and NAFLD and concluded that the CC genotype of Q297H polymorphism was significantly associated with lower LDL-C or non HDL-C and higher risk of NAFLD after adjustments for age, sex and insulin resistance. This study was well designed and clarified the interaction between NAFLD or lipid profiles and MTTP gene polymorphisms using large number of subjects, however, there seems to be several points should be revised and added before the paper would reach the level being suitable for publication in this journal.

Comments:
#Intro, discussion too long, focus on the polymorphisms examining in this study, sex and age, limitation#

1. The authors recruited over a thousand subjects in this study, however, there must be gender bias because the ratio of male was about 90%. Can the authors explain the reason and stress the importance of the current findings without sex bias? The authors should add some explanation about this issue or perform the same analyses after changing the population.

2. The authors recruited the subjects with age 16 to 88 y.o. and mentioned 95% of the recruited subjects were between 25 to 65. The authors should limit the subjects with age 25 to 65 and reanalyze all the data because this study is genetic one.

3. The discussion section seems to be too long, so this section can be shorten. The authors cited too many previous reports supporting the authors’ findings especially in the discussion section. The reviewer knows that there are a few papers talking about the significance of the Q297H polymorphism of MTTP gene, so the authors seemed to do so. On the other hand, there must be some exaggerations in the discussion section to discuss their findings (the latter part of the second and the sixth paragraph). The authors should make it simpler and just speculate the mechanisms underlying the relationship between the polymorphisms of MTTP and the development of NAFLD or low concentration of serum cholesterol.

4. In table 4 & 5, the reviewer is wondering why HOMA-IR was negatively correlated with serum LDL-C or non HDL-C. This might be because the authors exclude the subjects with diabetes and the average of HOMA-IR was within
normal limits. The reviewer would like to know the baseline characteristics of the recruited subjects, so the authors should show it by sex as a table.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**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.