Reviewer's report

Title: Serum uric acid distribution according to SLC22A12 W258X genotype in a cross-sectional study for a Japanese general population

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Reviewer: Atsuo Taniguchi

Reviewer's report:

URAT1 is a most important transporter of uric acid. W258X on SLC22A12 is a major cause of renal hypouricemia in Japanese. The authors examined the effect of SLC22A12 W258X genotype on serum uric acid levels (SUA) in Japanese. It is a very interesting study, however, I would like to point some problems.

Major Compulsory Revisions

1. The authors indicated that distribution of SUA between individuals with WW and WX was different (Table 2). However, the distribution of factors that exert effect on SUA (BMI, age, triglyceride, blood sugar, etc.) may be different between groups. The authors should show that the frequencies of these factors in individuals with WW or WX as much as possible.

2. The authors stated that “The effect of X allele on SUA was significantly larger in males than in females” in the first paragraph of Discussion. However, is it correct? It is well known that females show lower SUA because of the uricosuric action of estrogen. I think that the SUA-lowering-effect of X allele in males is similar to that in females, but the effect looks stronger in males because of the lower levels of estrogen in males.

3. The authors described that SLC22A12 258X seemed to be a major contributor of SUA levels in Japanese. The authors clearly showed that the distribution of SUA in individuals with WW was different from that in individuals with WX. However, the proportion of individuals with X allele is too small. The data provided here is not sufficient to show that 258X is a “major” contributor of SUA in Japanese.

Minor Essential Revisions

1. Background line 6: The authors have to check the sentence “… and physical conditions the factors associated…”

Discretionary Revisions

1. It is interesting that the SUA distribution of WW females is similar to that of WX males. It may suggest that the effect of X allele on SUA is comparable to the effect of estrogen. It is better to discuss that point in Discussion section.

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.