Author's response to reviews

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

Authors:

Nobuyuki Hamajima (nhamajim@med.nagoya-u.ac.jp)
Mariko Naito (mnaito@med.nagoya-u.ac.jp)
Asahi Hishida (a-hishi@med.nagoya-u.ac.jp)
Rieko Okada (rieokada@med.nagoya-u.ac.jp)
Yatami Asai (yat-asai@sisei.or.jp)
Kenji Wakai (wakai@med.nagoya-u.ac.jp)

Version: 3 Date: 29 January 2011

Author's response to reviews: see over
January 29, 2011

Editor of BMC Medical Genetics

Dear Sir

Thank you again for the helpful comments on the manuscript entitled “Serum uric acid distribution according to \textit{SLC22A12 W258X} genotype in a cross-sectional study for a Japanese general population.”

The manuscript was revised according to the comments, as shown in a separate sheet. The manuscript was then edited carefully by an American-born professional English editor, Mr. John Shields.

I would greatly appreciate it if you would re-consider our revised manuscript as a research article for publication in BMC Medical Genetics.

Sincerely,

Nobuyuki Hamajima, MD, MPH, Ph.D
Department of Preventive Medicine,
Nagoya University Graduate School of Medicine
65 Tsurumai-cho, Showa-ku, Nagoya 466-8550 Japan
Tel. +81-52-744-2133   Fax. +81-52-744-2971
E-mail: nhamajim@med.nagoya-u.ac.jp
Referee 2:

I thank the reviewer again for the comment.

Editorial requests:

Copyedit

- Please get your manuscript copy edited. Perhaps a colleague, preferably a native English speaker, could look it over for you. Alternatively, we can supply the contact details of a professional copy editing service.

I engaged the services of a professional American editor, Mr. John Shields, to have our manuscript edited carefully.

Section Editor comments:

- "The difference in mean SUA between WX and WW genotypes was 2.27 mg/dL in males and 1.19 mg/dL in females (F=45.25, d.f.=1, 5017, p=2E-11)." What does this p-value refer to, the gender x polymorphism interaction?

The p-value refers to the interaction between sex and the genotype (WW and WX).

These statistics were recalculated to confirm, and I realized a slight difference in the estimates because three participants with a creatinine of 2 mg/dL or over were included in the previous analysis. After the exclusion of the three participants, the values were as stated below.

"3.94 mg/dL" in the text and Table 3 was replaced with "3.95 mg/dL."

"The difference in mean SUA between WX and WW genotypes was 2.27 mg/dL in males" was replaced with "The difference in mean SUA between WX and WW genotypes was 2.26 mg/dL in males""

"(F=45.25, d.f.=1, 5017, p=2E-11)" was replaced with "(F=46.99, d.f.=1, 5014, p=8E-12 for the interaction the genotype and sex among 5,018 individuals with WW or WX)."

- "The interaction between sex and the X allele (WX and XX genotypes) was significant; the OR (95% CI) was 0.23 (0.07-0.80) for SUA < 3 mg/dL and 0.17 (0.08-0.35) for SUA < 4 mg/dL." What were the p-values for interaction? How was the interaction tested?

I used the interaction term in the logistic model, as below.

Sex: 0 for males and 1 for females
Genotype: 0 for WW and 1 for WX or XX
Interaction: Sex * Genotype
The results from STATA were per below. The p-values were <0.001. The values were added in the text.

```
.logistic UA3mg age sex SLC22A12X IA_Sex_G if Creatinine<2
Logistic regression                               Number of obs   =       5023
                           LR chi2(4)      =     303.46
                           Prob > chi2     =     0.0000
                           Log likelihood = -358.28723
                           Pseudo R2       =     0.2975
------------------------------------------------------------------------------
UA3mg | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
age |   .9556662   .0120471    -3.60   0.000     .9323435    .9795723
sex |   27.23621   14.15886     6.36   0.000     9.832096    75.44794
SLC22A12X |  106.4962   60.05762     8.28   0.000     35.26196     321.634
IA_Sex_G |   .2318891   .1460906    -2.32   0.020     .0674562    .7971478
------------------------------------------------------------------------------
```

```
.logistic UA4mg age sex SLC22A12X IA_Sex_G if Creatinine<2
Logistic regression                               Number of obs   =       5023
                           LR chi2(4)      =    1132.33
                           Prob > chi2     =     0.0000
                           Log likelihood = -1326.5935
                           Pseudo R2       =     0.2991
------------------------------------------------------------------------------
UA4mg | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
age |   .9692936   .0055772    -5.42   0.000      .958424    .9802866
sex |    22.3986   3.304727    21.07   0.000     16.77387    29.90946
SLC22A12X |   63.6916   13.49573     19.60   0.000     42.04509    96.48128
IA_Sex_G |   .1726661   .0628920    -4.82   0.000       .08456    .3525733
------------------------------------------------------------------------------
```