Reviewer’s report

Title: Genetic variation of Glucose Transporter-1 (GLUT1) and nephropathy in 10,278 Caucasian and African-Americans: a case-control study in the Atherosclerosis Risk in Communities (ARIC) Study

Version: 1 Date: 19 January 2010

Reviewer: Shiro Maeda

Reviewer’s report:

Hsu et al. examined the association of SNPs in GLUT1 with albuminuria in 8,122 European American subjects and in 2,156 African American subjects. They selected 6 SNPs for the stage 1 analysis, and identified modest association of rs841847 (Enh2) with albuminuria (micro + macro) in European American subjects with type 2 diabetes, but not in subjects without diabetes. Then they selected this SNP for further analysis (stage 2), and the authors could observe the same trend of the association of this SNP with albuminuria in European subjects with type 2 diabetes. They further demonstrated that the effect of Enh2 might be interacted with elevated plasma insulin concentration in European American subjects without diabetes. The authors could not identify any effects of the GLUT1 SNPs on albuminuria in the African American population. The authors have performed important attempt, and provided interesting information, but there are several concerns in the present form.

Major Compulsory Revisions

Although the authors reported that the rs841847 (Enh2) was significantly associated with albuminuria in European subjects with type 2 diabetes, the number of subjects with type 2 diabetes was too small to lead correct conclusion. In addition, because the authors examined 6 SNPs using several models, the authors need to perform a correction of multiple testing errors with an appropriate way; the present associations seem not to overcome Bonferroni’s correction that is considered too conservative for the present analysis.

Classification of albuminuria was based on single measurements of ACR in the present study. This may be leading incorrect conclusions in case that an association between variations and phenotypes exhibits a borderline value as shown in the present study.

The interactive effect of rs841847 (Enh2) with insulin sensitivity (plasma insulin concentrations) on albuminuria has considerable interest, but it is not clear why the authors exclude subjects with microalbuminuria from the analysis.

I recommend the authors to examine the association of GLUT1 SNPs with quantitative traits related to renal function (e.g, ACR, s-Cr, BUN) in the ARIC population.
Minor Essential Revisions

Because white population is not exactly the same as Caucasian, the description needs to be unified.

The description for unit of plasma insulin concentration (in the results section; mg/dl) is probably wrong.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.