Reviewer’s report

Title: Association between Insertion/Deletion Polymorphism in Angiotensin-Converting Enzyme Gene and Acute Lung Injury/Acute Respiratory Distress Syndrome: A Meta-Analysis

Version: 1 Date: 2 March 2012

Reviewer: Carlos Flores

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The study by Matsuda et al. entitled “Association between Insertion/Deletion Polymorphism in Angiotensin-Converting Enzyme Gene and Acute Lung Injury/Acute Respiratory Distress Syndrome: A Meta-Analysis” describes the first meta-analysis done for the ACE I/D polymorphism in ALI/ARDS susceptibility and mortality. Despite the small sample size, particularly where the association was found, the analyses have been well executed and appropriately explained. The manuscript merits being published, although some modifications need to be done. Particularly:

Major compulsory revisions:

1. The authors need to include power calculations for their analyses and discuss the possibility that associations with susceptibility truly exist but not detected because of the limited sample size. A further discussion regarding power limitations needs to be included.

2. Main text and Figures (including supplementary ones): There is no way for the reader to deduce which allele, D or I, is the allele at risk in Asians. For example, should one conclude from Figure 1 that the Insertion allele is the allele at risk for ALI mortality in Asians? Please, modify all figures and indicate to which allele correspond the ORs reported.

3. It is not described how the authors performed the adjustment for multiple testing using the FDR. Was it done considering all study p-values generated or was it performed for p-values for each sub-analysis assessing ALI susceptibility vs. healthy controls, ALI susceptibility vs at risk controls and mortality? Please specify it in the methods section.

4. There is an incongruence of studies used for meta-analysis. In the results section, the first paragraph of page 9 mentions the use of data from references 23, 27-29, while later on (page 10, both paragraphs; page 11, second paragraph) another reference, ref. 30, is mentioned. Please, clarify.

Discretionary Revisions:

1. Results. Please state the exact p-values for associations instead of using a “less than” symbol (pages 11 and 12).

2. Results. Page 11. Please, rephrase the sentence “The disequilibrium of gene
distribution, including ACE, among different ethnicities is well known.” I assume that what the authors want to indicate is that the linkage disequilibrium in the ACE gene is expected to vary considerably between Asian and European populations so that it justifies the stratified analyses.

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

**Quality of written English:** Acceptable

**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.