Reviewer’s report

Title: The ACE gene D/I polymorphism as a modulator of severity of cystic fibrosis

Version: 4 Date: 2 July 2012

Reviewer: Frauke Stanke

Reviewer’s report:

2nd Revised version of MS by MS by Marson & colleagues on the role of the ACE D/I polymorphisms in cystic fibrosis

Again, thank you for your time and efforts - the manuscript now displays the observed association of ACE D/I polymorphism with cystic fibrosis disease severity clearly and rightfully notes the limitations of the study due to a selection and recruitment bias, which is an inherent bias to all modifier studies published.

Unfortunately, one major compulsory revision remains:

Prior to publication, please check carefully for the following error which may have occurred during the editing process in the legend to Figure 1: The authors claim that the method for statistical analysis has been changed from parametric t-test to non-parametric Mann-Whitney rank test. This is highly recommended and correct as the box plots in figure 1 show a skewed distribution of the Bhalla score, defining non-normality, hence demanding a non-parametric test.

Surprisingly, all p-values mentioned in the legend to figure 1 are still the same as before, which does not agree with the change of methods. Example: 1st revised version of the manuscript – “…..#T: 1.763 and p: 0.081 *T: 1.267 ¥T:2.538 p:0.015 …” 2nd revised version of the manuscript: “….# p: 0.081 * p: 0.215, ¥ p: 0.015…..” This needs to be corrected – the p-value will change with a change in the evaluation method used.

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

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