Reviewer’s report

Title: Toll-Like Receptor Gene Polymorphisms are Associated with Susceptibility to Graves’ Ophthalmopathy in Taiwan Males

Version: 4 Date: 3 August 2010

Reviewer: Holger Kirsten

Reviewer’s report:

The authors responded in detail to all my questions. Thank you for their effort! However, there are some issues, which should be clarified before the manuscript should be published.

Major Compulsory Revisions:

1. There are some questions from the reviewers where the authors provided answers to the reviewers, but did not include this information in the modified manuscript. In my opinion, also these answers will improve the readers understanding of this publication. Therefore, I strongly suggest, if possible, including all answers at least in part within the modified manuscript. Note that supplemental information can be included, as an example, table 1a within the document “answers to the reviewers” would be a very valuable supplemental table.

2. When the authors were asked to provide power calculation, I referred to design power - so given allele frequencies of the investigated SNPs within the population (e.g. from HapMap) and the size of the cohorts/sub cohorts, it should be calculated, which allele frequency or odds ratio can be observed at a certain statistical level. In case of a non-significant observation, this will provide the reader with a quantitative estimate of the effect size which still might existent but could not be detected. In addition, observable effect sizes from such a design power calculation can be compared with reported effect sizes from other studies to justify study design.

Minor Essential Revisions

1. In the revised manuscript, the authors now comment on reported genetic association relevant to their work in more detail. However, they only provide references for association of genes with GD in general. To my understanding, the aim and the focus of this paper actually is GO. The authors stated, that to their knowledge, there is no study on TLR4 and TLR9 in GO. I suggest, in addition, it should be stated within the manuscript, whether there are published studies on association of other genes than TLR4 and TLR9 with GO.

Discretionary Revisions

1. The authors deleted within the material and method the last part of the
sentence
“The difference of genotypic and allelic frequencies distributions between GD patients with and without ophthalmopathy ‘and between GD patients and normal controls’ were analyzed by the #2 test or Fisher exact test.” Actually, within table S2 they compared GD patients with HapMap individuals with just these tests, so they might still include something like …and between GD patients and individuals from HCB-HapMap…

**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.