Reviewer’s report

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

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Reviewer: Raffaella Buzzetti

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In the present study the Authors investigated whether 6 TLR-4 and 2 TLR-9 gene polymorphisms could be used as genetic markers for the development of Graves' ophthalmopathy (GO) in 471 GD patients from a Taiwan Chinese population. They found that TLR-9 gene polymorphisms were significantly associated with increased susceptibility to GO in male GD patients.

Major Compulsory Revisions

1) The Authors should modify the title of the article “Toll Like receptor gene polymorphism is associated....” in “Toll Like receptor gene polymorphisms are associated....” since they found that two polymorphisms were associated with increased susceptibility to GO in male GD patients.

2) A total of 11 human Toll like receptors have been identified; could the Authors explain clearly why they decided to analyze Toll-Like receptor 4 and TLR-9?

3) In the statistical analysis the Authors reported that “the difference of genotypic and allelic frequencies between GD patients and normal controls........” Could the Authors clarify who are these controls? In patients and data collection their reported information only of GD patients.

4) The Authors should report whether the genotypic and allelic frequencies of the 2 SNPs of TLR9 were in Hardy-Weinberg equilibrium.

5) A power calculation to verify correctness of the results when they stratified in patients with GO and without GO and in male and female and when they performed the haplotype analysis.

6) In statistical section a sentence, to justify why the homogeneity test was used, has to be added.

Minor Essential Revisions

1) In the introduction section the Authors affirm that Toll-Like receptors have been associated with autoimmune thyroiditis. Could they report the specific reference/s?

2) The abstract should follow the Author’s instruction (Background, Results and Conclusions). Also the references should follow the instruction for this specific Journal.
**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

declare that I have no competing interests’