Reviewer's report

Title: Identification of a novel homozygous nonsense mutation in EYS in a Chinese family with autosomal recessive retinitis pigmentosa

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Reviewer: Guillermo Antinolo

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In the present article, Huang et al. report a new truncating mutation in Eyes Shut Homologue (EYS) in a consanguineous Chinese family affected by severe autosomal recessive retinitis pigmentosa (arRP). Firstly, they employ linkage and haplotype analysis for the identification of EYS as the causal gene following sequence analysis to identify the disease-causing variation. The candidature of the identified mutation as the genetic event triggering the pathogenic mechanism of such retinal dystrophy phenotype is supported by the truncating nature of the change, which would lead to the translation of EYS into a significantly shorter protein. This, together with the family segregation of the variation consistently with the consanguinity of the family, and its absence in 200 control individuals, makes the authors to conclude that p.E1836X is the pathogenic variation that triggers the disease in this family.

Minor Essential Revisions

1. The authors present their results as the first independent confirmation of the two original reports of mutations in EYS as the cause of RP, as well as the first report of a mutation identified in the Chinese population. However, during the running month, two papers have been published reporting a wider spectrum of EYS mutations in different populations, including mutations in a Chinese family. Therefore, we suggest that the authors include a ‘Note Added in Proof’ referencing these recent reports.

2. The manuscript is poorly written. We strongly recommend a native-English revision of the language that would greatly improve the quality and comprehension of the content.

3. Given the importance of RP phenotype characterisation when presenting results based on a single family, we suggest that Table 1 is included within the manuscript data and not as supplementary information.

4. The authors should revise the current number of arRP loci, which is incorrect as described in the manuscript.

5. Regarding the prevalence of the genes implicated in arRP, they should include some references, especially of recent reviews on the subject.
6. In page 3, line 19, the term differentiation is incorrectly used. The authors should employ other terms such as ‘classification’, and the like.

7. We have found some disorder in the references numbering, for example, in page 4, line 4, Barragan et al. is reference 11 and not 10.

8. When describing the identification of EYS and its structure in page 4, lines 6-10, the authors should reference Abd El-Aziz et al., 2008 (4).

9. In page 6, line 14, the authors describe the visual acuity in the three affected individuals as limited to hand movements. However, in Table 1, which they refer in this line, they use this term for the description of the visual acuity only in family member II5. They should try to keep the consistency by using a different term or sentence to report the visual acuity in the manuscript text.

10. We recommend that the authors include the mutation state of family member III1 in the results text, given that they are showing the corresponding chromatogram information in Figure 3.

11. There is a depiction error in Figure 1 regarding the genetic markers employed for the analysis. Whereas the figure legend describes the haplotype as conformed of SNPs (rs) and homozygous, the figure depicts microsatellite markers showing heterozygosity around EYS region.

12. In the discussion section, authors hypothesise that EYS may also play an important role in the cataractogenesis of patient II5. To our view, this conclusion is too speculative, and should be supported by additional evidence.

The article describes an interesting novel mutation in EYS as the cause of the disease in a consanguineous Chinese family affected by arRP. Interestingly, this mutation has not been found in any of the recent reports on EYS prevalence in different populations including the Chinese one. Furthermore, this finding supports the hypothesis of a global EYS involvement in the disease development of the arRP, confirming the initial linkage data in populations of different ancestral origins. Therefore, we find this manuscript appropriated to be published in BMC Medical Genetics upon addressing the previously enumerated comments as revisions.

**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:**
I declare that I have no competing interests