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: Rob WJ Collin

Reviewer's report:

Huang et al. describe the identification of the first nonsense mutation in EYS causative for arRP in the Chinese population. The identification and causality of the mutation is clear-cut and the clinical data are well-presented. However, a number of issues need to be addressed that will improve the quality of the paper.

Major compulsory revisions:

1) The mutation is present in a homozygous manner in affected family members born from a consanguineous marriage. The haplotype analysis shown in figure one however suggests that the mutation is present on two different alleles (only one marker is homozygous in all affected members). Either the homozygous region flanking the mutation is relatively small, or the mutation occurs on two different haplotypes which might suggest that this mutation might be more frequently present in the Chinese population. The distance between the markers flanking the EYS gene (D6S257 and D6S460) is 24 Mb of genomic DNA. The authors should analyze more markers in close proximity of the EYS gene, to see whether the mutation is present on the same or on two different haplotypes.

2) Based on studies performed by others, the frequency of EYS mutations in recessive RP patients is relatively high (5-10%). Here, the authors describe a single mutation in a Chinese family. Do the authors have DNA of other Chinese RP patients? If so, have they been analyzed (either by linkage or sequence analysis) for mutation in EYS? If not, I think the authors should test these for mutations in the EYS gene, at least starting with the mutation that was identified here. Data about the prevalence of EYS mutations in the Chinese RP population would definitely strengthen the manuscript.

3) The authors claim to be the third group (after the two initial papers identifying the EYS gene) that present mutations in EYS. However, a paper just appeared in IOVS describing several novel mutations in EYS by Abd El-Aziz et al., (Manuscript iovs.09-5109, published on March 17, 2010). Please refer to this paper.

Minor essential revisions:

1) Add page numbers.

2) Abstract, conclusions: EYS encodes the orthologue and not the homologue of Drosophila spacemaker. Please correct.
3) Background section, first page: RP; OMIN should say OMIM
4) Background section, second page: ‘…which is predicted to be a 3,145 amino acid’. The protein has 3,165 amino acids. Please correct.
5) Background section, second page: ‘…from Spanish and Dutch…’ Please add the word ‘origin’.
6) Results, second page: ‘To identify the disease causing EYS mutation..’.
   Please remove EYS.
7) Discussion, first page: ‘EYS is a multi-domain protein with 3,1645 amino acids and containing…’ Please remove 'with 3,1645 amino acids and' as this has been stated in the previous sentence.
8) Discussion, second page: Upon mentioning the previously identified mutations, remove the family names. This has no additive value at all.
9) Discussion, second page: Be straight in mutation nomenclature throughout the manuscript, use either single-character or three-character amino acid codes, but not both.
10) Discussion, second page: Elaborate on the recently published paper by Abd El-Aziz et al., as they also identify missense mutations.
11) Discussion, third page: …from two different families with mutation p.Pro3156X…” should state ‘with mutation p.Tyr3156X’
12) Discussion, third page: ‘..in the cataractogenesis in addition to the retinas.’ Replace retinas by retinal dystrophy.
13) Figure legends, figure 1: There is no description of the genomic positions of the markers in the legend. In addition, add which genome browser working draft was used to extract positions.
14) Figure legends, figure 2: Briefly describe the findings of the ERG recordings in the legend.
15) Figure legends, figure 3: I think exon 2 is a typo, and should state a different exon.

Discretionary revisions:
1) Figure 3: Adding the amino acids encoded by the triplets of nucleotides above the sequence chromatogram would improve the figure.

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