

Reviewer's report

Title: A novel HSF4 gene mutation (p.R405X) causing autosomal recessive congenital cataracts in a large consanguineous Pakistani family

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Reviewer: Colin E. Willoughby

Reviewer's report:

This paper reports a novel nonsense mutation in HSF4 in a Pakistani family with autosomal recessive congenital cataracts. Eight mutations have been previously reported and this is the first nonsense change: p.R405X. The paper is well written but the clinical phenotype reported is limited. Unfortunately, the lens phenotype/ataract morphology is unknown which is a common problem in many previous studies in this field. Few other clinical features are presented like visual acuity and whether the eyes show microcornea or microphthalmia. A number of weaknesses need to be addressed (MAJOR COMPULSORY REVISIONS):

1. Markers : the markers used should be stated including their genetic and physical distance in relation to HSF4 should be stated. A table showing the LOD score versus recombination fraction for each marker should be shown.
2. The NM or Genbank ID for HSF should be given. This is particularly relevant when reporting the nucleotide position of the mutation which should be number from the ATG and the reference sequence given. In the results line 8 the authors should state that the mutation lies in exon 11.
3. Restriction digest: in the methods the authors should state the expected fragments for the wild-type and mutant allele. Figure 1 is weak : all the lanes should be number with the individual pedigree ID as the lane for III:3 could represent I:1. The product sizes (648, 403, 248 and 148bp) should be highlighted on the gel. The band for 148bp is poor especially for III:3 and II:4.
4. Controls: even though the mutation segregates and has a major effect on the protein must studies would report negative findings in ethnically matched controls. Are this family Afghans or Pakistani? Has implications for the title and the type of controls required.
5. Conclusion: the conclusion is weak and unimaginative.

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