Reviewer’s report

Title: Eight previously unidentified mutations found in the OA1 ocular albinism gene

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Reviewer: Valeria Marigo

Reviewer’s report:

General
The paper by Mayeur et al. describes the identification of new mutations in the OA1 gene causing Ocular albinism type 1. The authors analyzed 37 patients from 9 families and two sporadic cases by genetic molecular analysis. They identified 8 new mutations and two previously identified mutations. These data may be important for molecular diagnosis of this disease.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
Some aspects of the paper should be amended. Because of the frequency of intragenic deletions in the OA1 gene, above all in the American population, it is unclear whether in the 27 patients, in which they did not detect mutation, possible rearrangements of the genomic locus have been considered (have all the PCR fragments been detected in these patients and was the sequence wt?). Furthermore, it is not clear whether the fundus of the mother has been analyzed for all of them confirming the mosaic pattern characteristic of OA1 and, without doubt, diagnosis of Ocular albinism type 1.
Secondly, at page 7 and 9 the description of mutation T166N is not correct. The authors state that the T166 is conserved among all tetrapods while their figure shows that T166 is present only in the human OA1 protein not even in mouse (so also the Pfam software does not show conservation among mammals in fact the mouse is a mammal). So I believe that this is not a matter of software but this amino acid is not conserved in evolution.
At page 7 the authors describe the effects of p.G58fsX29 saying:” preventing any functional interaction of the OA1 receptor with its ligand”. This is a supposition because no biochemical data have ever been forwarded on interaction of OA1 with its ligand. Truncation of the protein may cause protein degradation, mislocalization and probably no function, however the statement that this interferes with interaction between receptor and ligand may be misleading suggesting that the interaction has been characterized.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
Different panels and different figures show sequence analysis of either the carrier females of the family or the patients. The author should describe in detail in figure legend the individual from which the sequence derives.

Some inaccuracies should also be corrected:
1- Page 2: Albinism causes foveal hypoplasia not macular hypoplasia
2- Page 2: No data show that OA1 is not characterized by hypopigmentation of the choroids but just of the retinal pigment epithelium.
3- Page 3: Macromelanosomes have never been shown in the uvea of OA1 patients (O’Donnell 1976).
4- Page 13- the second author is missing from reference 4
Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests