Appendix 4. Candidate list of the compound heterozygous variants.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  | SNP databases | | | | *In silico* analyses | | |  |
| Patient | Gene | Mutation type | Nucleotide change | Predicted effect | Location in gene | Conservation across speciesa | Origin | SNP ID | ExAC | 1000 Genomes | HGVD | ToMmo | SIFT | PoyPhen2 | MutationTaster | Reference |
| JU#1303 | *RPE65* | Missense | c.683A>C | p.Q228P | Exon 7 | Q/Q/Q/Q/Q/Q/Q | Maternal inherit | rs886046510 | 0 | 0 | 0 | 0.0007 | Damaging | probably damaging | Disease causing | This study |
|  |  | Nonsense | c.1028T>A | p.L343\* | Exon 10 | L/L/L/L/L/L/L | Paternal inherit | None | 0 | 0 | 0 | 0 |  |  | Disease causing | Jacobson (2005) Proc Natl Acad Sci U S A 102, 6177 |
| JU#1085 | *RPE65* | Missense | c.683A>C | p.Q228P | Exon 7 | Q/Q/Q/Q/Q/Q/Q | Paternal inherit | rs886046510 | 0 | 0 | 0 | 0.0007 | Damaging | probably damaging | Disease causing | This study |
|  |  | Missense | c.1543C>T | p.R515W | Exon 14 | R/R/R/R/R/R/R | Maternal inherit | rs121917745 | 0.0000165 | 0 | 0 | 0.0005 | Damaging | probably damaging | Disease causing | Kondo (2004) Invest Ophthalmol Vis Sci 45, 4433 |

The nucleotide numbering reflects cDNA numbering with +1 corresponding to A of the ATG translation initiation codon in the reference sequence NM\_000329.2.

a Each denotes human/cow/rat/mouse/chicken/xenopus/zebrafish RPE65 orthologs (sequences selected from the DDBJ/EMBL/GenBank database).

Accession numbers were NM\_000329.2 (human), NM\_174453.2 (cow), NM\_053562.3 (rat), NM\_029987.2 (mouse), NM\_204884.1 (chicken), NM\_001127066.1 (xenopus) and NM\_001113653.1(zebrafish).