Missense mutations at homologous positions in the fourth and fifth laminin A G-like domains of eyes shut homolog cause autosomal recessive retinitis pigmentosa

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Purpose: To describe two novel mutations in the eyes shut homolog (*EYS*) gene in two families with autosomal recessive
retinitis pigmentosa (arRP) from Pakistan and Indonesia.

Methods: Genome-wide linkage and homozygosity mapping were performed using single nucleotide polymorphism microarray analysis in affected members of the two arRP families. Sequence analysis was performed to identify genetic changes in protein coding exons of *EYS.*

Results: In the Indonesian and Pakistani families, homozygous regions encompassing the *EYS* gene at 6q12 were identified, with maximum LOD scores of 1.8 and 3.6, respectively. Novel missense variants in the *EYS* gene (p.D2767Y and p.D3028Y) were found in the Pakistani and Indonesian families, respectively, that co-segregate with the disease phenotype. Interestingly, the missense variants are located at the same homologous position within the fourth and fifth laminin A G-like domains of EYS.

Conclusions: To date, mostly protein-truncating mutations have been described in *EYS*, while only few patients have been described with pathogenic compound heterozygous missense mutations. The mutations p.D2767Y and p.D3028Y described in this study affect highly conserved residues at homologous positions in laminin A G-like domains and support the notion that missense mutations in *EYS* can cause arRP.

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