Mutations in IMGP1 cause autosomal dominant and recessive retinitis pigmentosa

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Abstract

**Purpose**: To identify the causative mutation in a large family with autosomal dominant retinitis pigmentosa (adRP) and consequently to genetically characterize a cohort of RP patients without mutation in known genes.

**Methods**: A large adRP family without mutation in the known RP genes was screened for mutations using whole-exome sequencing (WES). Following the identification of an IMGP1 mutation, additional dominant and recessive RP probands were screened for mutation in this gene by targeted next-generation sequencing (tNGS). Clinical investigations included visual acuity and visual field testing, fundus examination, high-resolution spectral-domain optical coherence tomography (OCT), fundus autofluorescence imaging, full-fields and multifocal electroretinogram (ERG) recording.

**Results**: By WES, a heterozygous splicing mutation in the IMGP1 gene, c.1824+1G>A was identified in a large family with adRP. Three more families with different novel missense mutations were identified. All the variants segregated with the disease phenotype and are predicted to be pathogenic.

**Conclusions**: We identified a novel causative gene, IMGP1, responsible for autosomal dominant and recessive retinitis pigmentosa (RP). IMGP1 was previously associated with vitelliform macular dystrophy (VMD). In conclusion, mutations in the same gene can lead to two clinical entities, RP and VMD as it was reported previously for IMGP2, paralog gene of IMGP1.

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