SUPPLEMENTARY INFORMATION

Genetic Spectrum of *EYS*-associated Retinal Disease in a Large Japanese Cohort: Identification of Disease-associated Variants with Relatively High Allele Frequency.

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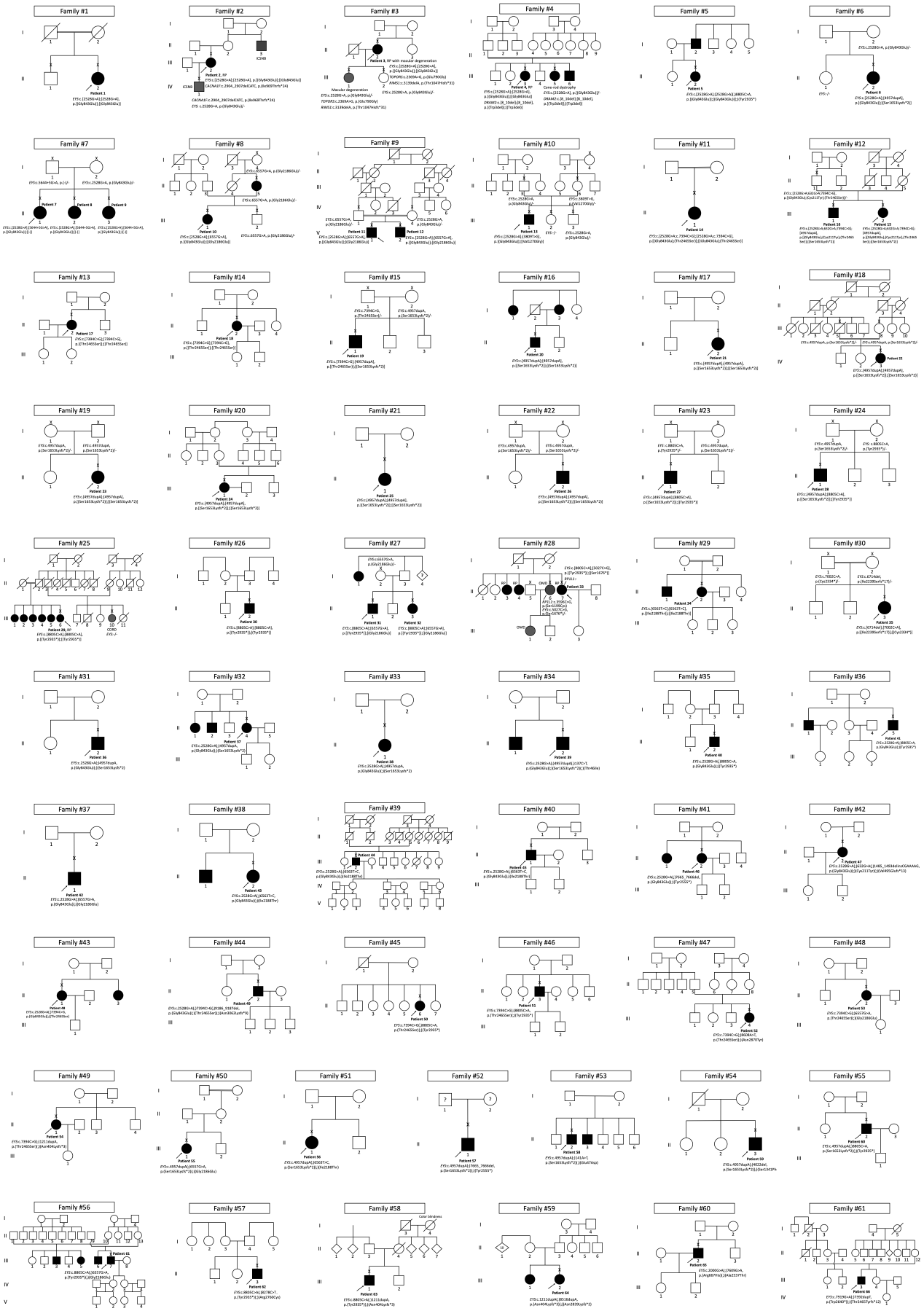
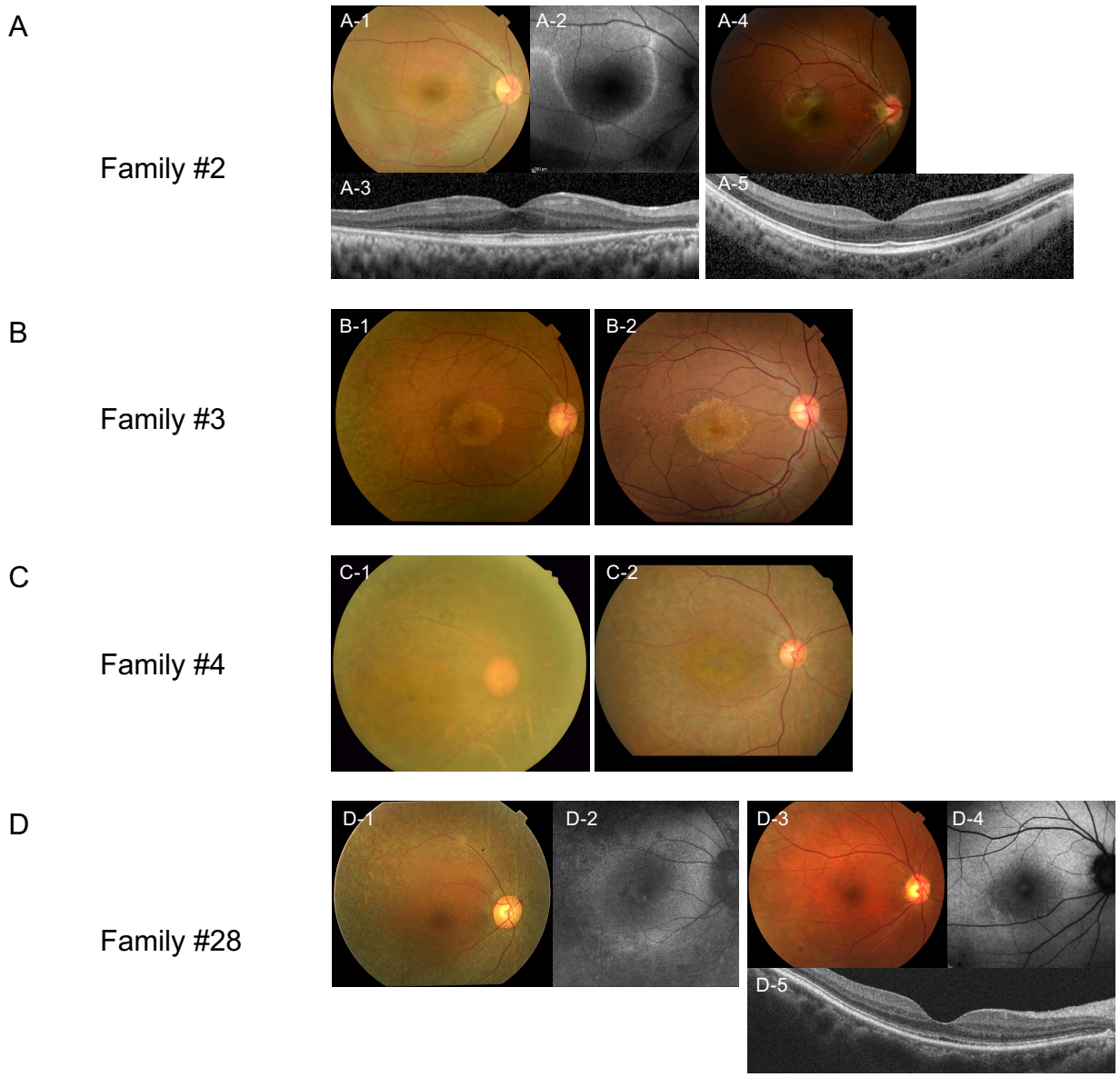


Supplementary Figure S1. Pedigrees of the 61 *EYS*-RD families.
The solid squares (male) and circles (female) represent the affected patients, and unaffected family members are represented by white icons. The rhombus represents subjects with unknown gender. The question mark indicates subjects whose affected/unaffected status is uncertain. The slash symbol indicates deceased individuals. The generation number is shown on the left. The proband of each pedigree is marked by an arrow, and the clinically examined individuals are indicated by a cross.
iCSNB=incomplete congenital night blindness; RP=retinitis pigmentosa; OMD=occult macular dystrophy.



Supplementary Figure S2. Four families with different clinical diagnoses and disease-causing genes.
A (Family #2): The proband (2-III:2) was diagnosed with retinitis pigmentosa (RP) (A-1: fundus photograph; A-2: fundus autofluorescence (FAF); and A-3: optical coherence tomography (OCT)). One homozygous disease-causing *EYS* variant was identified. The affected son (2-IV:1) of this proband shows the phenotype of incomplete congenital stationary night blindness (iCSNB; incomplete type of Miyake; OMIM; 300071) (A-4: fundus photograph; A-5: OCT). One candidate disease-associated variant in the X-linked recessive gene, *CACNA1F* (OMIM; 300110), was identified in 2-IV:1.

B (Family #3): The proband (3-II:2) was diagnosed with macular degeneration with RP-like peripheral changes (B-1: fundus photograph). One homozygous disease-causing *EYS* variant was identified, together with two candidate heterozygous variants in the two autosomal dominant (AD) genes; *TOPORS* (OMIM; 609507) and *RIMS1* (OMIM; 606629). One affected daughter (3-III:1) of this proband has macular degeneration (B-2: fundus photograph). Three heterozygous variants in the *EYS*, *TOPORS* and *RIMS1* genes were identified in 3-III:1. It is still uncertain which (if any) of the two AD genes (*TOPORS* and *RIMS1*) causes the AD macular degeneration.

C (Family #4): The proband (4-III:3) was diagnosed with RP (C-1: fundus photograph). One homozygous disease-causing *EYS* variant was identified, together with one candidate homozygous variant in the autosomal recessive gene; *DRAM2* (OMIM; 613360). The clinical effects by both the *EYS* variant and the *DRAM2* variant can be considered in 4-III:3. One affected sibling (4-III:5) of this proband shows cone-rod dystrophy phenotype (C-2: fundus photograph). This subject has the heterozygous *EYS* variant and the homozygous *DRAM2* variant. The clinical effect only by the *DRAM2* variant is considered in 4-III:5.

D (Family #28): The proband (28-II:7) was diagnosed with RP (D-1: fundus photograph; D-2: FAF). Disease-causing *EYS* variants were identified in a compound heterozygous status. One sibling (28-II:6) was diagnosed with with Occult Macular Dystrophy (OMD; OMIM; 613587) (D-3: fundus photograph; D-4: FAF; D-5: OCT). One daughter (28-III:1) of this sibling (28-II:6) was also diagnosed with OMD. One disease-causing variant in the AD gene, *RP1L1* (OMIM; 608581) was identified in 28-II:6.