The ocular phenotype of IRD secondary to variants in EYS is influenced more by age than by genotype

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1. Background and objectives

Variants in the *EYS* gene account for 5% of cases of inherited retinal degeneration (IRD). Progression of the ocular phenotype is known to worsen with age, but the impact of genotype is not well understood. This project aims to compare the impact of age and variants in the *EYS* gene on phenotypic features of IRD. This will add to existing evidence regarding the relationship between phenotype of IRD and predicted genotype severity, with the hope of informing clinical prognosis of IRDs.

2. Methods

Clinical records, spectral domain OCT, ultrawide field colour and autofluorescence images were used to record age of onset, visual acuity, retinal phenotype and quantitative data on retinal structure. The impact of age and predicted genotype severity was made by comparing the phenotype by age (<40, 40-50 and >50 years) and by predicted genotype severity (most, moderate and least severe).

3. Results

Data was available for 22 patients, of whom 64% were male. Ethnicity was Asian and Caucasian in 13 and 9 cases. Mean age at data collection was 44.

Visual acuity, central 1mm subfield thickness and ellipsoid zone length all had weak, negative associations with age (Figures 1 and 2). No clear association was found for predicted genotype severity. Overall, 30% of eyes had intra-retinal white dots. These were most common in patients aged 40-50 years (11%) and in those with intermediate genotype severity (100%). Intra-retinal pigment migration was not seen before the age of 40 and was most common (100%) in patients aged >50 years. (Figure 3). No association was seen with genotype. (Figure 4) Circumscribed chorio-retinal atrophy was seen in 30% of eyes. It was most common (71%) in patients aged over 50 years and with the least severe genotype (36%).

Figure 1

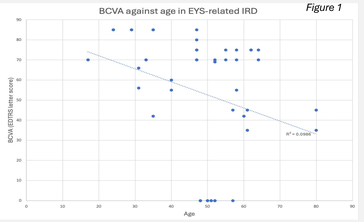


Figure 2

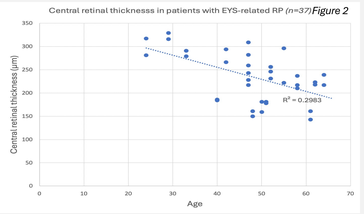


Figure 3

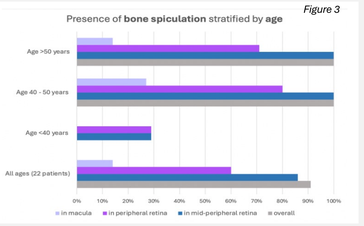
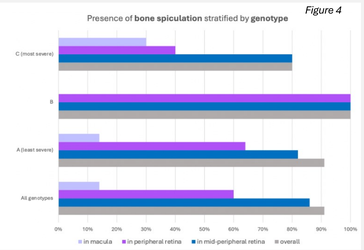


Figure 4



4. Discussion and conclusions

Our findings indicate that predicted genotype severity may not be as robust as age in predicting structure and function in IRDs secondary to variants in the EYS gene. Interpretation of this data is constrained by the methodology of genotype classification and our small sample size. Nonetheless, it underscores the need for larger studies that may help to determine if the EYS genotype can be used to guide consultations about future function, retinal structure and access to research studies. A standardised system is needed to classify the phenotype of IRDs consistently.