



Genotyping in Inherited Retinal Disease: A single centre retrospective analysis

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Introduction

Inherited retinal diseases (IRDs), though rare, are the leading cause of blindness in the working-age population in the United Kingdom, notable for their clinical and genetic heterogeneity. Current evidence implicates over 300 genes in the pathogenesis of IRDs. A timely genetic diagnosis is essential, enabling accurate prognostication, informed counselling, and where appropriate, guidance on family planning. Furthermore, there is an expanding landscape of clinical trials in a field that has historically been limited in therapeutic options. The aim of this study is to characterise, for the first time, the genotypic and phenotypic spectrum of IRDs within the regional population (Merseyside, Cheshire and neighbourhood), in order to better understand the clinical needs and inform service development, and to explore key research opportunities for those affected.



Fig 1. Fundus autofluorescence image (a) and pseudocolour fundal image (b) of right eye in a patient with Stargardt disease (ABCA4 variants) depicting the hyperautofluorescent properties of the pisciform flecks

Methods

This is a retrospective observational review of patients attending the dedicated IRD clinic at a tertiary NHS hospital in Liverpool (UK) with a confirmed molecular diagnosis obtained between 2018 and mid-2025. Data pertaining to patient demographics, genetic variants and associated clinical presentation was systematically collected from hospital databases after obtaining institutional review board approval. Genetic testing methods employed included the retinal gene panel (targeted next generation sequencing) between 2018 and 2021, and whole genome sequencing (WGS) between 2022 and 2025.

Results

Our cohort comprised of 452 patients who had undergone genotyping, with a slight female predominance (53%) and a mean age of 48.8 years (range 17–96).

A conclusive molecular diagnosis was achieved in 298 patients (66%). Amongst these, approximately two-thirds (68.5%) had retinal dystrophy, the majority of which were non-syndromic (75.5%). Choroidal dystrophy (2.3%) and vitreoretinopathy (1.3%) were rare, with the remaining patients diagnosed with macular dystrophy (27.9%).

ABCA4 (Fig 1) was the most frequently identified gene (17%) across the cohort. In patients with rod-cone and cone-rod dystrophy (both non-syndromic and syndromic), the most commonly implicated genes (Fig 2), in decreasing order, were USH2A (Fig 3), RP1, RPGR, RHO, CRB1 and BBS1.

Geographically, 60% of patients were residents of Liverpool and its surrounding areas, 16% were from Cheshire, and the remainder from other regions in the North-West. Where ethnicity data was available (43%), the majority of patients identified themselves as White British. Within Liverpool, a substantial proportion of patients resided in areas of socioeconomic deprivation.

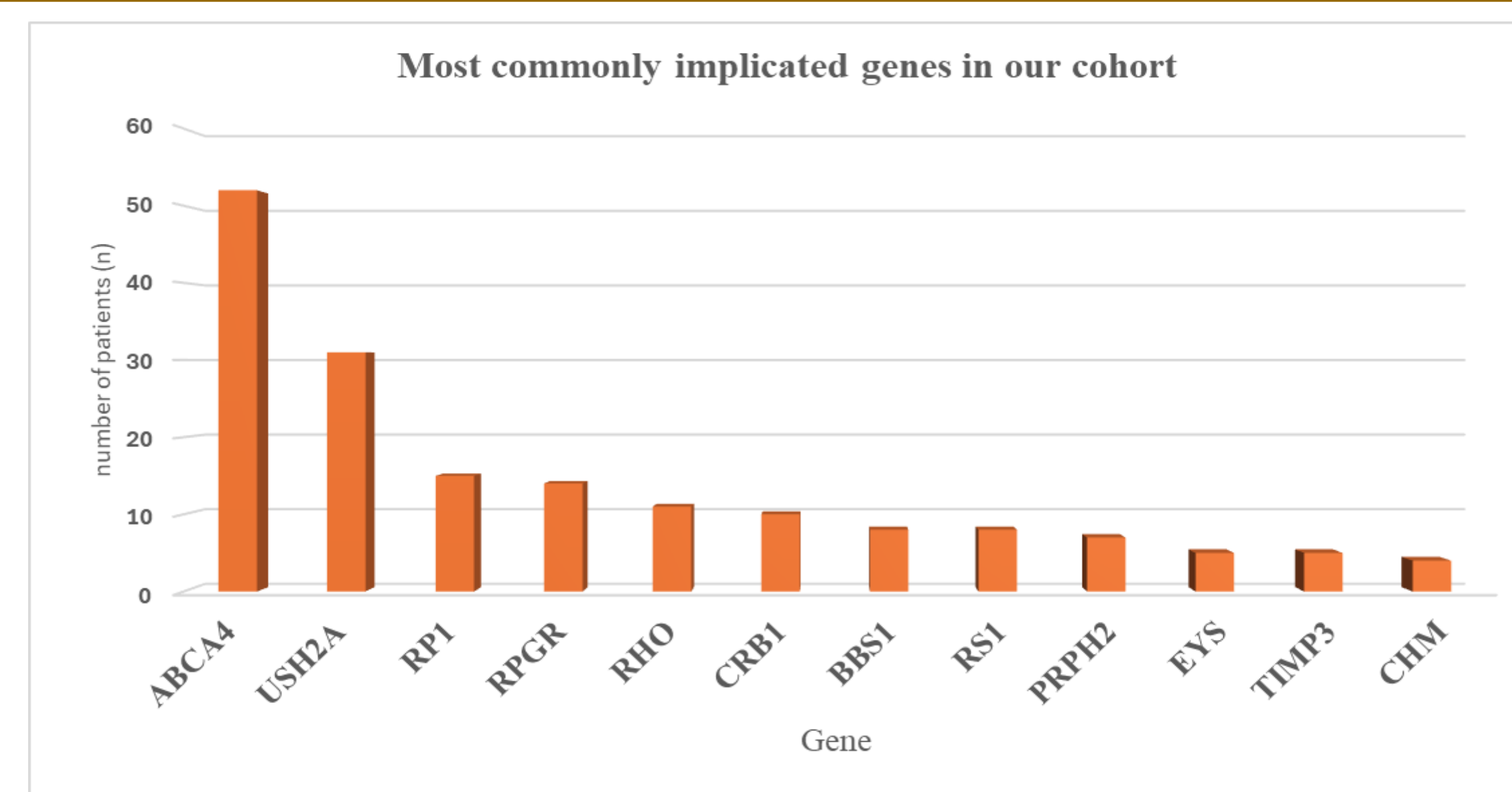


Fig 2. Graphical depiction of the twelve most commonly implicated genes in our cohort

References

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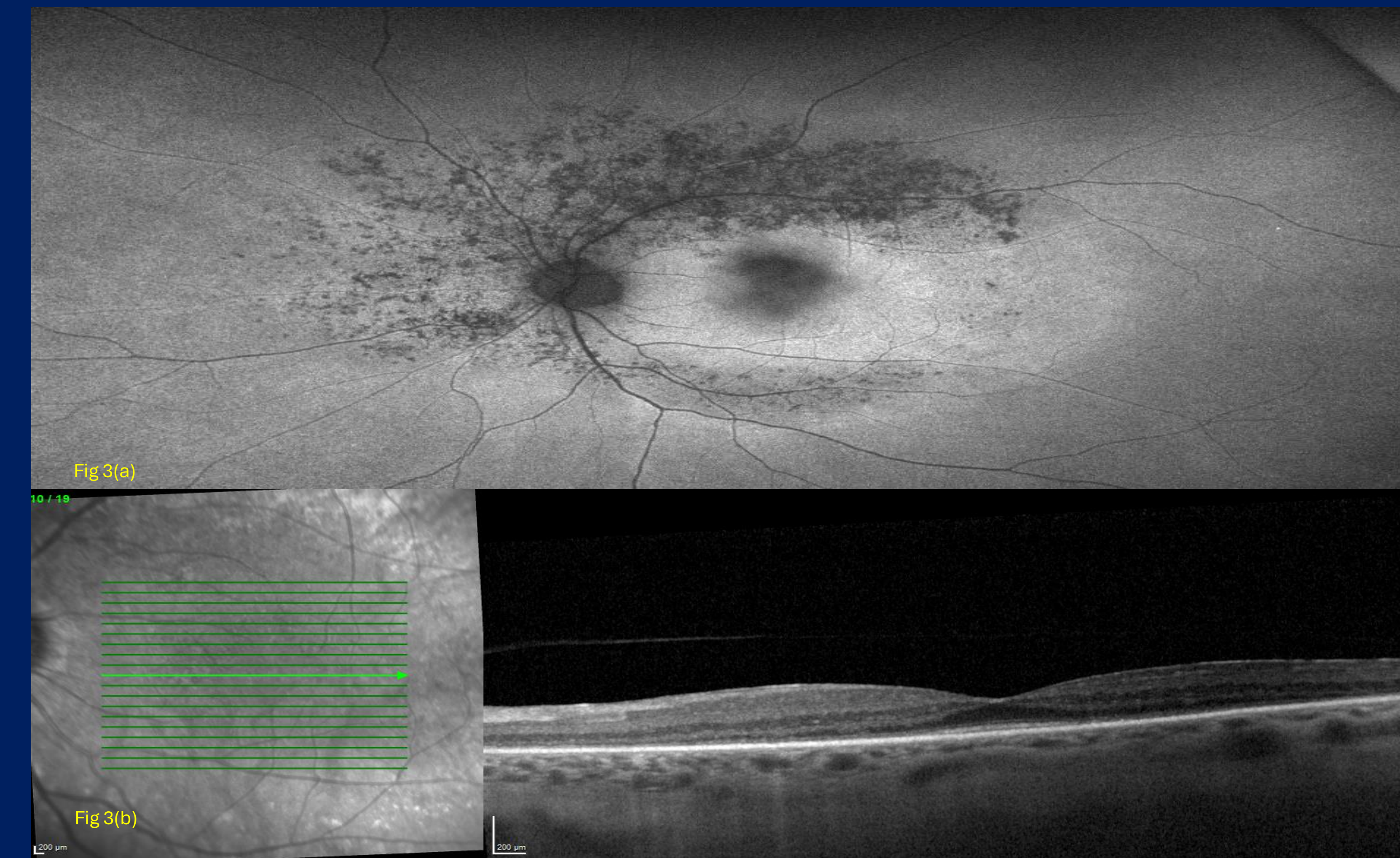


Fig 3. (a) Fundus autofluorescence image of left eye of patient with USH2A variants (b) Foveal OCT image of the same eye depicting extensive loss of ellipsoid zone in keeping with rod-cone dystrophy

Discussion

WGS is known to increase diagnostic yield¹, but almost a third of patients with IRDs unfortunately still do not get a firm genetic diagnosis requiring further work to understand 'negative' results and if the yield rates can be improved². The most common IRDs in the local population related to ABCA4, USH2A, RP1 and RPGR genes resulting in Stargardt disease, Usher's syndrome and non-syndromic retinitis pigmentosa. Our results align with existing evidence on common IRD-associated genotypes within the UK population³. Insights gained from this study will serve to set directions for further development of the regional IRD service including providing informed genetic counselling, accessing emerging treatments, understanding genotype-phenotype correlations and bringing clinical trials to our patients, thereby promoting comprehensive patient care, and prioritising candidate genes and diseases for advancing future research on targeted therapeutic interventions.

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