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CORRESPONDENCE

A retinitis punctata albescens family with biallelic mutations in retinaldehyde-binding Protein 1

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To the Editor:

Retinitis punctata albescens (RPA, OMIM#136880) is an autosomal recessive hereditary disease characterized by subretinal punctate yellow–white deposits, progressive night blindness, and visual field reduction. This disease was first described by Mooren in 1882 and named by Lauber in 1910. RPA has an incidence of 1/800,000 people worldwide, and mutations at retinaldehyde-binding protein 1 (*RLBP1*) gene were reported only in about 1% of patients affected by autosomal recessive forms [1]. RPA can also be caused by mutations in Rhodopsin (*RHO*), Retinol Dehydrogenase 5 (*RDH5*), Peripherin 2 (*PRPH2*), and Lecithin Retinol Acyltransferase (*LRAT*) genes. However, different mutations in *RLBP1* gene can lead to multiple phenotypes as fundus albipunctatus (FA), Newfoundland rod-cone dystrophy (NFRCD) and Bothnia retinal dystrophy [2].

In this study, we report a consanguineous family with RPA (Fig. 1a). And the cases harboring biallelic mutations in *RLBP1* (Fig. 1b). Both the patients of this family were referred to our hospital for night blindness. They had typical RPA characteristics. Best corrected visual acuity was decreased, accompanied by red and green weakness. Fundus evaluation showed bilateral pigment epithelial changes and numerous yellow–white punctate deposits at the level of the retinal pigment epithelium around vascular arcades, without central macular involvement (Fig. 2a). Visual field measurements showed peripheral visual field defect (Fig. 2d). The electroretinogram measurements showed significantly decreased responses. The spectral-domain optical coherence tomography showed that the ellipsoid zone is rough and fractured (Fig. 2b). Fundus fluorescein angiography showed retinitis pigmentosa-like changes in the middle and peripheral

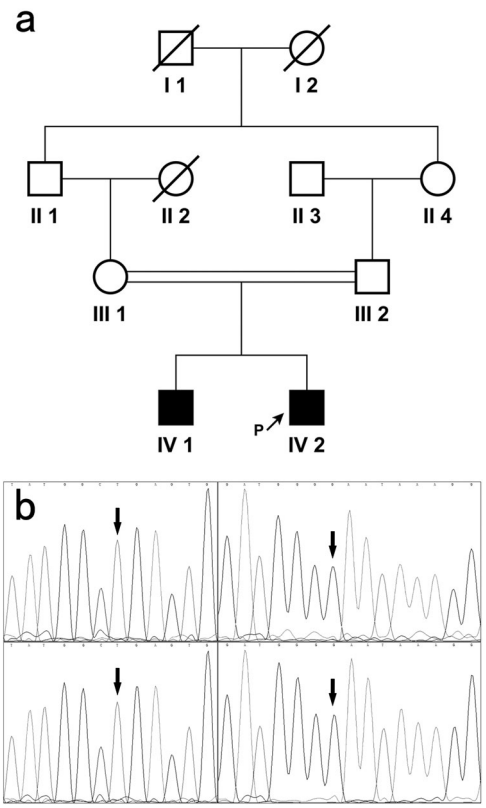

Fig. 1 Familial pedigree and partial electropherograms of *RLBP1*. **a** Familial pedigree. The arrow 'P' indicates the proband (IV 2). Empty squares and circles symbolize undiseased men and women, respectively. Full fill indicates the retinitis punctata albescens patients. Slash indicates died individuals. **b** Partial electropherograms of *RLBP1*. The arrows indicate affected nucleotide. Left, two electropherograms showing the homozygous condition for c.466C > T mutation. Right, two electropherograms showing the homozygous condition for c.*167T > G mutation.

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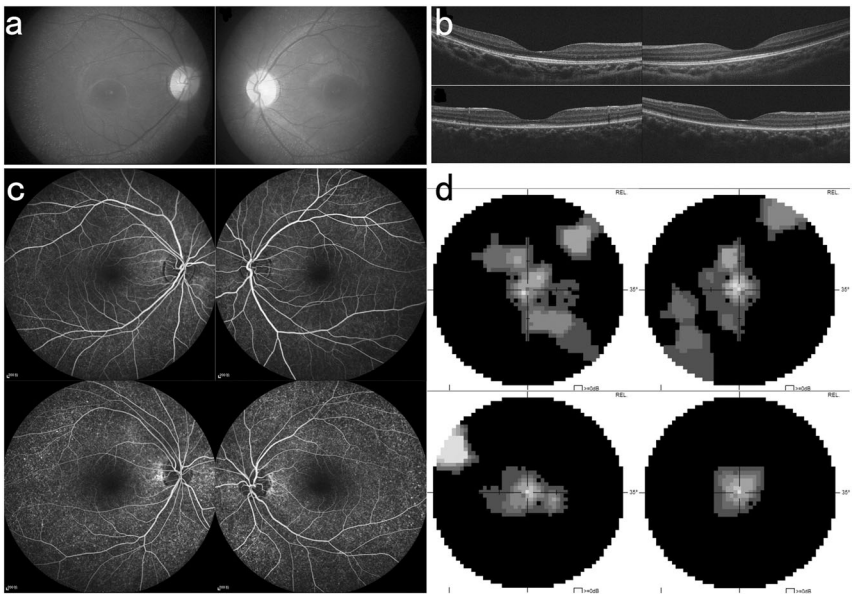

Fig. 2 Imaging results of patients. a Fundus photograph shows bilateral pigment epithelial changes and numerous yellow–white punctate deposits at the level of the retinal pigment epithelium around vascular arcades. **b** SD-OCT shows the rough and fractured ellipsoid zone. **c** FFA shows multiple point intense fluorescence in the middle and peripheral retina. **d** Visual field shows irregular defect of peripheral visual field.

retina (Fig. 2c). Two homozygous mutations (c.466C > T and c.*167T > G) were identified in *RLBP1* (Fig. 1b).

RLBP1 is the most common causative gene in RPA, so we performed genetic testing of the *RLBP1* gene in two patients [3]. Both patients with two homozygous mutations were identified in *RLBP1*, c.466C > T, and c.*167T > G. The mutation c.466C > T is located in the sixth exon of *RLBP1*. The p.R156X(c.466C > T) mutation is expected to produce an unstable transcript that will be degraded by nonsense-mediated decay [4]. If somehow the mutant mRNA escapes nonsense-mediated decay, the protein thus produced will lack the 161 amino acids of the C-terminal domain [5]. The mutation c.*167T > G is located in the 3′ UTR region of *RLBP1*, however, its role is unclear. This mutation suggested in Clinvar that it may be associated with FA, Retinitis Pigmentosa, and NFRCD, but the risk of disease was assessed as benign (one star).

Naz et al. reported a FA family caused by the *RLBP1* c.466C > T mutation [5]. Although the family of our study also carried the *RLBP1* c.466C > T mutation, but the patients was clearly diagnosed with RPA. The family that *RLBP1* c.466C > T mutation led to RPA was reported for the first time. We hypothesize that the cause of RPA in this family may be that mutation c.*167T > G enhances the pathogenic role of c.466C > T and thus leads to changes in patient phenotype. Of course, the assumption needs further evidence.

In summary, through the observation of the family, we learned about a new type of RPA pathogenic gene.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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