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A Novel Compound Heterozygous Mutation in the Cellular Retinaldehyde-binding Protein Gene (*RLBP1*) in a Patient With Retinitis Punctata Albescens

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PURPOSE: To describe a patient with retinitis punctata albescens (RPA) associated with compound heterozygosity for two novel mutations in the *RLBP1* encoding cellular retinaldehyde-binding protein (CRALBP).

DESIGN: Observational case report.

METHODS: The proband underwent a complete ophthalmic examination and leukocyte genomic DNA samples were obtained from him and his parents. The *RLBP1* exons were analyzed by direct sequencing of PCR-amplified fragments.

RESULTS: The patient had a clinical phenotype suggestive of slowly progressive RPA, characterized by numerous yellow-white dots in the fundus. The *RLBP1* sequence analysis revealed a novel compound heterozygotic mutation of Gly145Asp and Ile200Thr transmitted from the

mother and father, respectively. Analysis of 100 control chromosomes showed no individuals with these sequence alterations.

CONCLUSIONS: Only eight *RLBP1* mutations have been reported to date, and here we describe two novel mutations. These additional mutations will aid ongoing functional studies and add to our understanding of the molecular pathology pertaining to *RLBP1*-associated retinopathies. (Am J Ophthalmol 2004;138:171-173. © 2004 by Elsevier Inc. All rights reserved.)

MUTATIONS IN THE GENE (*RLBP1*) ENCODING THE CELLULAR retinaldehyde-binding protein (CRALBP) cause autosomal recessive progressive retinopathy, variously termed as retinitis pigmentosa (RP), Bothnia dystrophy (BD), retinitis punctata albescens (RPA), and Newfoundland rod-cone dystrophy (NFRCD).¹⁻⁴ The *RLBP1*-related retinopathies are characterized with subretinal punctate white-yellow deposits and clinical manifestations similar to that of RP. Fundus albipunctatus (FA) is an apparently stationary night blindness characterized by similar white-yellow deposits. A recent study revealed that the same *RLBP1* mutation may cause FA in the first two to three decades of life and RPA in the fourth to fifth decades, suggesting that some young patients with seemingly stationary night blindness may eventually develop a progressive-atrophic phenotype.⁵ The distinctions among FA, RPA, BD, NFRCD, and RP are poorly defined and depend on the age of onset, age at diagnosis, progression rate, and severity.

Cellular retinaldehyde-binding protein is expressed in retinal pigment epithelium (RPE) and Müller cells and plays a fundamental role in the visual cycle. The retinoid-binding domain is located within the C-terminal part, between residues 120 to 313.⁶ Eight different *RLBP1* (chromosome 15q26) mutations have been reported, including 4 missense, 2 frameshift, and 2 splice site alter-

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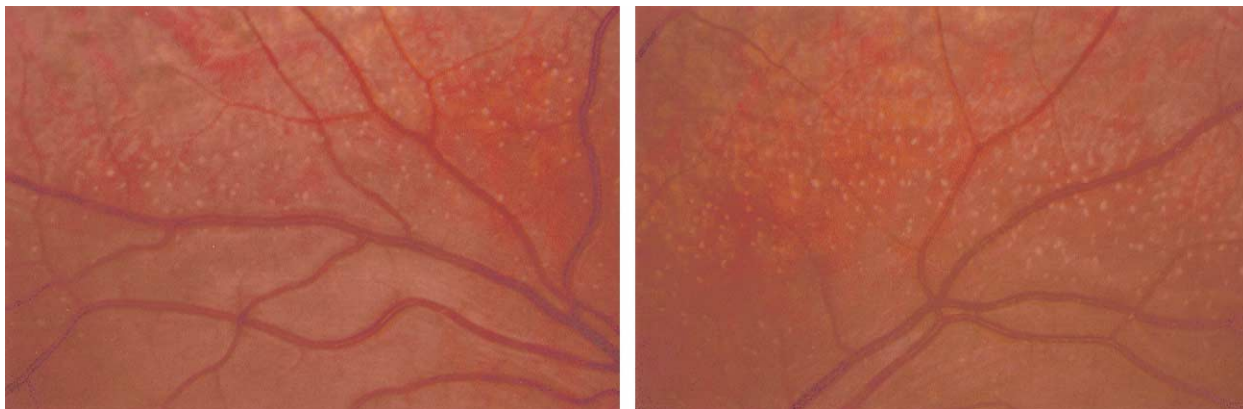


FIGURE 1. Fundus photographs of the proband showing bilateral pigment epithelial changes and numerous yellow-white punctate deposits at the level of the retinal pigment epithelium around vascular arcades, without central macular involvement (data not shown).

intraocular pressures and anterior segment findings were within normal limits. Fundus examination revealed extensive subretinal yellow-white dots along the vascular arcades and retinal pigment epithelium changes in the mid and far peripheries. Full-field electroretinography demonstrated markedly diminished scotopic and mildly reduced photopic responses, with normal implicit times. At ages 16 and 17 years, the patient had enlarged blind spots and mild constriction of peripheral vision. At his most recent visit (age 17), the midperipheral retinas showed progressive areas of retinal pigment epithelium atrophy with continued presence of yellow-white dots in the perimacular areas and far peripheries (Figure 1).

Genomic DNAs were isolated from blood samples from the patient and his parents. Mutation screening was performed with direct PCR sequencing of *RLBP1* coding exons and flanking intronic regions (the primers were generously provided by Dr Thaddeus P. Dryja, Ocular Molecular Genetics Institute, Harvard Medical School, Boston, Massachusetts).³ A novel compound heterozygotic mutation of Gly145Asp (exon 5, GGT>GAT) and Ile200Thr (exon 6, ATT>ACT) was identified (Figure 2, top). The region surrounding those residues is conserved across human, bovine, and mouse CRALBP orthologues, suggesting that these substitutions are likely to have functional significance (Figure 2, bottom). These nonconservative changes fall within the critical C-terminal protein region and are predicted to disrupt normal function. Analysis of the parents' DNAs confirmed that the two alterations in the proband's DNA were located on different alleles, consistent with recessive disease. Analysis of 100 control chromosomes revealed no individuals with similar alterations (heterozygous carrier frequency: <1/50). A female control subject was found to be a heterozygous carrier for another novel and potentially pathogenic, nonconservative sequence alteration (Glu125Lys).

A mild RPA phenotype, as described here, may be observed in some young patients with *RLBP1* defects. However, the current published data are insufficient to infer a meaningful genotype-phenotype correlation. The phenotypic variability reported for the same mutations^{1,4,5} suggests that other genetic or environmental factors may modify the clinical state. Identification of these novel mutations contribute to the structure-function studies that may guide future therapeutic efforts in these patients.

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Extraction of Endocapsular Tension Ring After Phacoemulsification in Eyes With Pseudoexfoliation

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PURPOSE: To describe an easy and effective surgical technique for removing the endocapsular tension ring (CTR) after phacoemulsification.

DESIGN: New surgical technique.

METHODS: One 10-0 polypropylene suture needle is passed through the hole at one end of the CTR. Then, the CTR is introduced into the capsular bag before phacoemulsification. If the posterior capsule ruptures, the CTR can be removed by pulling the suture toward the corneal incision and rotating the CTR to remove it.

RESULTS: We performed this technique in 23 cases with a risk of zonular damage and did not encounter complications at any point in the procedure.

CONCLUSIONS: We recommend this procedure in eyes with risk of zonular dialysis and posterior capsule rupture, especially in advanced pseudoexfoliative cataracts or if the surgeon has limited experience with these cases. (*Am J Ophthalmol* 2004;138:173–175. © 2004 by Elsevier Inc. All rights reserved.)

VARIOUS CASES OF ENDOCAPSULAR TENSION RING (CTR) dislocation into the vitreous have been reported recently.^{1–3} The CTR is a useful device to manage the integrity of the capsular bag during cataract surgery; however, if the posterior capsule breaks and the CTR

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