Interestingly, sequence data of polymerase chain reaction from this organism showed this isolate to be more similar to *R seeberi* from a canine sample than that of other human isolates. This patient did not have any dogs at home. As such, these data suggest that the genus *Rhinosporidium* may possess isolates capable of infecting multiple host types.

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**Novel Compound Heterozygous Mutations in CERKL Cause Autosomal Recessive Retinitis Pigmentosa in a Nonconsanguineous Chinese Family**

Retinitis pigmentosa (RP) (OMIM 268000) is characterized by night blindness, progressive constriction of the visual fields, and fundus changes, including bony spicule pigmentation. To date, a number of RP loci or genes have been reported. One of the autosomal recessive RP (arRP) loci, RP26, was mapped to chromosome 2q31-q33 in 1998. The disease-causing gene at this locus has been recently identified as the *CERKL* gene (ceramide kinase–like) (GenBank NM_201548), encoding a 532–amino acid protein that shares 29% identity with ceramide kinase. Only 3 *CERKL* mutations have been reported, including p.E257X in Spanish families, and p.P106S in a consanguineous Pakistani family, and a splicing mutation in Yemeni Jewish families. We now report 2 novel compound heterozygous mutations in *CERKL*, c.156_157insT and c.758delT, which were found in a nonconsanguineous Chinese family with arRP. Our data indicate that compound heterozygous mutations of *CERKL* can cause RP.

Methods. A family with arRP was enrolled in a study in China and diagnosed by clinical and ophthalmological examinations. Peripheral blood was collected and genomic DNA was isolated. Linkage and haplotype analyses were carried out with microsatellite markers flanking 21 known arRP loci, including RP26. After the pathogenic gene was mapped to chromosome 2q31-q33, all 13 exons of *CERKL* were sequenced using both forward and reverse polymerase chain reaction primers as described. To discern 2 mutant alleles in the proband, polymerase chain reaction products of exon 1 and exon 5 of *CERKL* were cloned using the pGEM-T Easy Vector System (Promega Corp, Madison, Wisconsin) and multiple clones were sequenced.

Results. The nonconsanguineous Chinese family with arRP includes 5 siblings. Both parents and their 2 daughters do not show any RP symptoms, but 3 sons are affected with RP (Figure 1). The proband (III:3) had night blindness at age 18 years and progressively lost visual acuity. Funduscopic examinations revealed attenuation of the retinal arteries and bony spicule pigmentation in the midperipheral retina but normal color of optic discs. A bull’s-eye–like appearance in the macular region was observed (Figure 1). Family members...
Asp G
G
T
G
G
A
to arg.

Ser G
G
G
Leu G
A
to ilu.

G
A
I
T
G
G
A
A
to c.758delT.

A
G
G
G
A
A
to stop.

G
A
G
A
T
to thr.

Lys G
G
G
G
A
A
to arg.

G
T
G
to glu.

G
T
G
G
A
G
T
T
T
T
G
G
G
A
A
Stop
Thr
G
A
A
G
A
G
T
A

III:2 and III:4 had similar RP features, including onset of nystagmus at about age 20 years. Currently, visual acuity in all 3 affected individuals is severely limited to the hand movement level, and no additional symptoms or ocular defects were observed.

Linkage and haplotype analysis mapped the disease-causing gene to RP26 (Figure 1). Direct DNA sequencing identified 2 compound heterozygous mutations, c.156_157insT in exon 1 and c.758delT in exon 5 of CERKL (Figure 2). The mother carried the c.156_157insT mutation and the father carried the c.758delT mutation. The 3 affected brothers carried both mutations, whereas the 2 unaffected sisters inherited both normal alleles from their parents. The c.156_157insT mutation introduces a stop codon at position 53 of CERKL, causing a prematurely truncated CERKL protein with only 52 amino acids. Mutation c.758delT causes a frameshift and substitutes 6 amino acids, 253-METDRI-258, by abnormal RKQTES and results in a truncated CERKL protein with only 258 amino acid residues. Neither mutation was detected in 100 healthy Chinese Han control subjects.

Comment. CERKL is a novel gene that has been recently associated with arRP. To date, only 3 mutations have been reported, including E257X, P106S, and a splicing mutation, all in consanguineous families.2,4,6 Interestingly, no significant clinical difference has been found among the patients with the 3 CERKL mutations. The patients with RP in this study have RP features and symptoms similar to those in the patients with the 3 reported CERKL mutations. In this study, we identified 2 compound heterozygous mutations in the CERKL gene, c.156_157insT and c.758delT, in a nonconsanguineous family with arRP. To our knowledge, this is the first report of compound heterozygous mutations of CERKL that cause arRP. Our results expand the spectrum of CERKL mutations causing arRP to the Chinese population.

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