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Identification of mutations in *UBIAD1* following exclusion of coding mutations in the chromosome 1p36 locus for Schnyder crystalline corneal dystrophy

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Purpose: To identify the genetic basis of Schnyder crystalline corneal dystrophy (SCCD) through screening positional candidate genes and *UBIAD1*, in which mutations have been associated with SCCD, in affected families.
Methods: The coding region of each of the 16 positional candidate genes for which mutation screening has not been previously reported was screened with polymerase chain reaction (PCR) amplification and automated sequencing in four affected individuals from two families with SCCD. In addition, the coding region of *UBIAD1*, located just outside of the originally described SCCD candidate interval on chromosome 1p36, was directly sequenced in affected and unaffected individuals from three families with SCCD.
Results: Eighteen novel and 15 previously reported sequence variants were identified in 10 of the 16 positional candidate genes. Only two of the sequence variants segregated with the affected phenotype in either of the families screened. Both were novel single nucleotide polymorphisms (SNPs) predicted to result in synonymous amino acid substitutions in different predicted genes. However, one of these SNPs was also identified in control individuals, and the other SNP was not predicted to alter splicing. Screening of *UBIAD1* revealed a different missense mutation in each of the three unrelated probands that was screened: p.Asn102Ser, p.Arg119Gly, and p.Leu121Val. Screening of the affected and unaffected relatives of the probands in whom the p.Asn102Ser and p.Leu121Val mutations were identified demonstrated that each mutation segregated with the affected phenotype. None of the three missense mutations was identified in 110 control individuals.
Conclusions: No presumed pathogenic coding region mutations were identified in the genes mapped to the candidate region for SCCD. However, missense mutations in *UBIAD1*, located just outside of the originally described SCCD fine mapped region, were identified in each of the three families with SCCD, confirming that mutations in *UBIAD1* are associated with SCCD.

Schnyder crystalline corneal dystrophy (SCCD; OMIM 121800) is an autosomal dominantly inherited disorder that is characterized by corneal stromal cholesterol deposition, most commonly in an axially distributed, annular or discoid pattern with prominent arcus lipoides. While affected individuals demonstrate a higher prevalence of hypercholesterolemia than that observed in the general population, the majority of affected individuals do not have elevated serum cholesterol levels [1]. Affected individuals often require corneal transplantation for visual rehabilitation although laser phototherapeutic keratectomy has been reported to be of benefit in patients with corneal opacification primarily involving the anterior stroma [2,3].

The search for the genetic basis of SCCD began over 10 years ago with the performance of a genome-wide linkage analysis in two large affected families of Scandinavian descent [4]. Significant evidence of linkage to chromosome 1p24.1-p36 (now defined as 1p36.2-p36.3) was obtained in each family with haplotype analysis defining a 16 cM candidate interval [5]. Fine mapping of this candidate region in these and 11 other affected families refined the SCCD locus to a 2.32 Mbp interval, containing 31 known and predicted genes (build 35.1) [5]. We have previously reported the absence of coding region mutations in 15 of the positional candidate genes in two families with SCCD [6]. Subsequently, we proceeded to screen the remaining positional candidate genes mapped to the 2.32 Mbp interval between the D1S1160 and D1S1635 markers. Although a large number of novel and previously identified sequence variants were identified in these genes, each was considered a polymorphism due to nonsegregation with the affected phenotype in the family identified with it and/or due to identification of the sequence variant in control individuals.

Recently, Orr and colleagues [7] identified five different presumed missense mutations in the UbiA prenyltransferase domain containing gene (*UBIAD1*) in five families with SCCD. While *UBIAD1* is located 368 Kbp centromeric to the D1S1635 marker that defines the centromeric border of the 2.32 Mbp fine mapped interval for SCCD, it is located within an overlapping 1.3 Mbp candidate interval identified through the performance of linkage and haplotype analysis by Orr and colleagues in a large family with SCCD [7]. As screening of *UBIAD1* in the families linked to the original 2.32 Mbp fine

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mapped interval for SCCD has not been reported, it remains to be determined whether the location of *UBIAD1* outside of the original fine mapped interval is indicative of a phenotyping error, a genotyping error, or possible genetic heterogeneity [7]. The latter explanation is supported by previous reports of inherited disorders such as autosomal dominant hearing loss and X-linked recessive retinitis pigmentosa associated with mutations in different genes that have been mapped to the same chromosomal locus [8,9]. Therefore, after screening the genes mapped to the original 2.32 Mbp fine mapped interval for SCCD, we performed screening of *UBIAD1* in three families with SCCD. Our identification of three missense mutations, two of which have been previously reported in families with SCCD, confirms that mutations in *UBIAD1* are associated with SCCD and provides additional evidence against genetic heterogeneity in SCCD.

METHODS

The researchers followed the tenets of the Declaration of Helsinki in the treatment of the subjects reported herein. Study approval was obtained from the Institutional Review Board at the University of California, Los Angeles (UCLA IRB Number 94-07-243-22, 94-07-243-22B, and 94-07-243-24B).

Patient identification and DNA collection: Members of three families diagnosed with SCCD were examined by one of the authors (A.J.A.). A slit lamp examination was performed to establish each individual's affected status (affected or unaffected). Two of the families have been reported previously, one of Irish descent (Family 1) and the other of Egyptian ancestry (Family 2) [6], while a third unrelated proband of African American ancestry has not been previously reported (Family 3). The diagnosis of SCCD was made in each family based on the presence of bilateral, axially-distributed, discoid or annular corneal stromal opacification and arcus lipoides in the corneal periphery with or without subepithelial crystalline deposits (Figure 1). After informed consent was obtained, affected and unaffected individuals were enrolled in the study.

DNA previously collected from 110 unrelated individuals without evidence of SCCD served as control samples.

Phlebotomy was performed for the majority of patients and saliva collection kits (Oragene; DNA Genotek Inc., Ontario, Canada) and buccal epithelial swabs (CytoSoft™ Cytology Brush; Medical Packaging Corporation, Camarillo, CA) were used for DNA collection from patients in whom phlebotomy could not be performed. Genomic DNA was prepared from the peripheral blood leukocytes and buccal epithelial cells using the FlexiGene DNA (Qiagen, Valencia, CA) and QIAamp DNA Blood Mini Kits (Qiagen), respectively.

Polymerase chain reaction amplification: Polymerase chain reaction (PCR) amplification of each positional candidate gene was performed using DNA from two affected individuals in Family 1 and in Family 2. When a sequence variant was identified in both individuals in either one or both families and was neither observed in a simultaneously analyzed control specimen nor a previously reported single nucleotide polymorphism (SNP; dbSNP section of the NCBI database), DNA from the other family members was analyzed to determine if the identified variant segregated with the affected phenotype. If so, at least 100 DNA specimens from individuals without SCCD were screened for the sequence variant.

Primers were designed using Primer3 software to bind to untranslated regions approximately 60-80 bases from the intron-exon boundaries (sequences available upon request). The coding regions were amplified by PCR using a 25 µl reaction volume that contained 50 mM Tris-HCl (pH 9.0, 25 °C), 20 mM NH_4Cl, 2.5 mM $MgSO_4$, 200 µM of each dNTP, 0.5 M Betaine, 2.5 µl DMSO, 150 mM Trehalose, 0.002% Tween-20, 0.12 µM of each primer, 0.5 units of REDTaq Genomic DNA Polymerase (Sigma-Aldrich, St. Louis, MO), and approximately 60 ng of genomic DNA. Thermal cycling was performed in an iCycler Thermal Cycler (Bio-Rad, Hercules, CA).

Primer3 software was used to custom design primers for the two coding exons of *UBIAD1*: 2F-CTC GTG GGG TGT AAG ACC CAC TT, 2R-GCG GCT TAA ATT AGA AAG CCA CCT; 3F-AGT GCC CAC CTG CAC AGT CTA AG, 3R-CAA ACT GGG CAG CTC CTT TAC AA. Each reaction was performed in a 25 µl mixture containing 50 mM Tris-HCl (pH 9.0, 25 °C), 20 mM NH_4Cl, 2.5 mM $MgSO_4$, 0.2 mM of each dNTP, 0.5 M Betaine, 0.12 µM of each primer, 0.5 units of REDTaq Genomic DNA Polymerase (Sigma-Aldrich), and approximately 60 ng of genomic DNA. Thermal cycling was performed in an iCycler Thermal Cycler (Bio-Rad).

DNA Sequencing: Purification of the PCR products and DNA sequencing was performed as described previously [6]. Nucleotide sequences, read manually and with Mutation Surveyor v2.2 (Softgenetics, State College, PA), were compared to published cDNA sequences for each gene (Table 1).

RESULTS

Screening of positional candidate genes: Eighteen novel and 15 previously reported sequence variants were identified in the coding regions of 10 of the positional candidate genes while no sequence variants were identified in the coding regions of the remaining six positional candidate genes (Table 2). Only two of the identified sequence variants were found to be present in both affected members of either family, were not identified in a simultaneously analyzed control individual, and subsequently demonstrated segregation with the affected phenotype in the family in which it was identified: c.772A>G (p.Thr258Ala) in *LOC644896* and c.396G>A (p.Ala132Ala) in *LOC729124*. Both of these sequence variants were identified in the heterozygous state in each of the three affected individuals in Family 2 but neither was present in an unaffected individual from this family nor in any members of Family 1. One hundred and ten additional unrelated control individuals of western European (70), Asian (13), Hispanic (12), African American (10), and unknown (5) ancestry were screened for these variants: the *LOC644896* p.Thr258Ala missense variant was identified in two individuals while the *LOC729124* p.Ala132Ala synonymous substitution was not identified in any of the control individuals. Analysis of the *LOC729124* wild type sequence and the mutant *LOC729124* sequence containing the c.396G>A substitution with the splice

site recognition software NNSplice (donor and acceptor score cutoff 0.40) revealed identical splicing profiles with neither a gain nor a loss of a splice acceptor or donor site in the mutant sequence. Each of the other identified sequence variants was considered a polymorphism as each failed to segregate with the affected phenotype in the family in which it was identified and/or was also identified in a simultaneously analyzed control individual (Table 2).

UBIAD1 *screening:* A different missense mutation was identified in each of the three probands in whom *UBIAD1* screening was performed. In Family 1, p.Ser75Phe (c.224C>T) and p.Asn102Ser (c.305A>G) were present in the heterozygous state in the affected proband, five other affected family members, and another individual of an undetermined affected status. Neither missense variant was identified in the only unaffected family member available for screening (Figure 2A). In Family 2, p.Leu121Val (c.361C>G) was identified in the proband and two other affected individuals but was absent in an unaffected family member (Figure 2B). The p.Ser75Phe (c.224C>T) variant was also identified in the proband, her affected sister, and her unaffected son but was not present in the proband's affected daughter. In Family 3, the proband demonstrated a p.Arg119Gly missense mutation (c.355A>G) although no family members were available to determine segregation (Figure 2C). While the p.Asn102Ser, p.Leu121Val, and p.Arg119Gly missense mutations were not identified in 110 control individuals, the p.Ser75Phe variant was identified in four unrelated controls out of 110.

DISCUSSION

The identification of three missense mutations (p.Asn102Ser, p.Arg119Gly, and p.Leu121Val) in highly conserved *UBIAD1* in three affected probands, with segregation of p.Asn102Ser and p.Leu121Val with the affected phenotype in two of the families. provides additional evidence that SCCD is caused by mutations in *UBIAD1*. Two of these mutations, p.Asn102Ser and p.Arg119Gly, were recently reported by Orr and colleagues [7] in two of the five families with SCCD that were screened. In both of these previously reported families, the mutation segregated with the affected phenotype as the p.Asn102Ser mutation did in the family that we report. It is therefore reasonable to assume that the p.Arg119Gly mutation would also segregate with the affected phenotype in the family that we report if additional family members had been available for examination and *UBIAD1* screening. However, it is unlikely that the families we report share a common ancestral mutation with the previously reported families as we identified the p.Asn102Ser mutation in a family of Irish descent while Orr and colleagues identified this mutation in an Italian family [7]. Similarly, we identified the p.Arg119Gly mutation in an African American individual while Orr and colleagues identified this mutation in a large family from Nova Scotia, of possible Spanish ancestry [7].

The p.Leu121Val mutation has not been previously reported and is presumed to be pathogenic as it segregated with the affected phenotype in Family 2 and was the only coding region sequence variant other than p.Ser75Phe identified in the affected individuals in this family. Additionally, this mu-

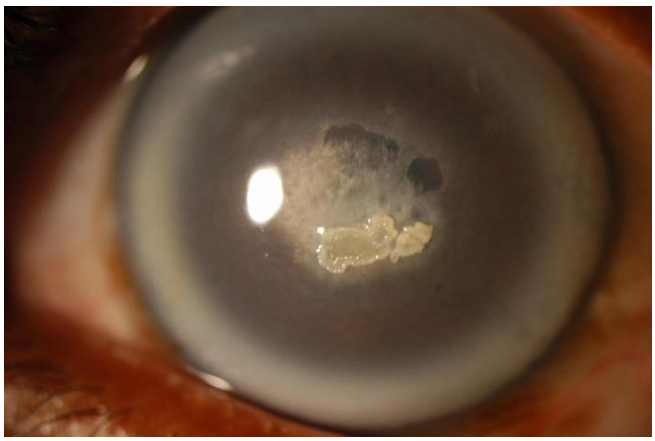

Figure 1. Schnyder crystalline corneal dystrophy. Slit lamp photomicrograph of the proband from a previously unreported family with SCCD demonstrates dense arcus lipoides and central corneal opacification secondary to superficial and subepithelial crystalline deposits. Photograph courtesy of Dr. Sadeer Hannush.

Table 1. Schnyder crystalline corneal dystrophy candidate genes

Gene (symbol)	*mRNA accession number*
Apoptosis-inducing TAF9-like domain 1 (*APITD1*)	variants NM_199294, NM_199295 & NM_198544
carbonic anhydrase VI (*CA6*)	NM_001215
castor homolog 1 zinc finger (*CASZ1*)	NM_017766
microRNA 34a (*MIRN34A*)	AL591166
nicotinamide nucleotide adenylyltransferase 1 (*NMNAT1*)	NM_022787
arginine-glutamic acid dipeptide repeats (*RERE*)	variants NM_012102, NM_001042681 & NM_001042682
solute carrier family 2 member 5 (*SLC2A5*)	NM_003039
facilitated glucose transporter member 7 (*SLC2A7*)	NM_207420
ubiquitination factor E4B (*UBE4B*)	NM_006048
LOC645010 (*FLJ16126*)	NM_001039777
hypothetical protein RP13-15M17.2 (*LOC199953*)	NM_001010866
protein similar to ribosomal protein L9 (*LOC642740*)	XM_927197
protein similar to 60S ribosomal protein L7 (*LOC644896*)	XR_018436
hypothetical protein LOC7227721 (*LOC7227721*)	XM_001123441
hypothetical protein LOC729124 (*LOC729124*)	XM_001129378
hypothetical protein LOC729158 (LOC729158)	XM_001129511
UbiA prenyltransferase domain containing 1 (*UBIAD1*)	NM_013319

Names and mRNA accession numbers of sixteen positional candidate genes for Schnyder crystalline corneal dystrophy and *UBIAD1*.

Table 2. Coding region sequence variants identified in positional candidate genes for Schnyder crystalline corneal dystrophy

Gene	*Nucleotide change*	*Amino Acid change*	*RefSNP #*	*Affecteds*	*Unaffecteds*	*Controls*
APITD1	c.853C>T	Ala129Ala	rs628462	1/2 Family 1 1/2 Family 2	-	0/1
	c.898T>C	Ser144Ser	rs666103	2/2 Family 1 2/2 Family 2	-	1/1
CA6	c.188C>T	Thr55Met	rs2274327	4/4 Family 1 1/2 Family 2	1/2 Family 1	0/1
	c.226A>C	Met68Leu	rs2274328	4/4 Family 1 1/2 Family 2	2/2 Family 1	1/1
	c.233G>C	Gly70Ala	rs2274329	4/4 Family 1 0/2 Family 2	2/2 Family 1	1/1
	c.252G>C	Gly76Gly	rs2274330	4/4 Family 1 0/2 Family 2	2/2 Family 1	1/1
CASZ1	c.2365A>G	Ser661Ser	rs284294	1/2 Family 1 2/2 Family 2	-	1/1
	c.2950G>A	Ala856Ala	rs284299	0/2 Family 1 2/2 Family 2	-	1/1
	c.3229T>C	Phe949Phe	rs778228	0/2 Family 1 2/2 Family 2	-	1/1
LOC199953	c.105C>T	Leu32Leu	None	2/2 Family 1 2/2 Family 2	-	1/1
LOC644896	c.772A>G	Thr258Ala	None	0/2 Family 1 3/3 Family 2	0/1 Family 2	2/101
LOC729124	c.396G>A	Ala132Ala	None	0/2 Family 1 3/3 Family 2	0/1 Family 2	0/101
LOC729158	c.286G>A	Gly96Ser	None	1/2 Family 1 0/2 Family 2	-	0/1
RERE	c.645_659delGG ACAAAGACAA AGA	Asp4_Lys8del	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.685C>T	Arg17X	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.691C>T	Arg19Trp	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.697C>T	Arg21X	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.838G>A	Ala68Thr	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.861T>C	Asp75Asp	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.879A>G	Lys81Lys	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.884A>C	Lys83Thr	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.912T>C	Gly92Gly	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.945G>T	Val103Val	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.982C>T	Arg116Trp	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.998C>T	Pro121Leu	None	2/2 Family 1 2/2 Family 2	-	1/1
	c.3000A>G	Pro788Pro	rs13596	2/2 Family 1 3/3 Family 2	1/1 Family 1 1/1 Family 2	0/1
	c.3111G>A	Pro825Pro	rs2784735	2/2 Family 1 3/3 Family 2	1/1 Family 1 1/1 Family 2	0/1
	3582G>A	Ser982Ser	None	0/2 Family 1 1/2 Family 2		0/1
	c.4581A>G	Arg1315Arg	rs521047	2/2 Family 1 3/3 Family 2	1/1 Family 1 1/1 Family 2	0/1
	c.4587G>T	Arg1317Arg	rs11121172	2/2 Family 1 3/3 Family 2	1/1 Family 1 1/1 Family 2	0/1
SLC2A7	c.818G>A	Arg273Gln	rs12402973	1/2 Family 1 0/2 Family 2	-	0/1
UBE4B	c.2012G>C	Leu442Phe	None	0/2 Family 1 1/2 Family 2	-	0/1
	c.3251T>C	Ser855Ser	rs2273299	0/2 Family 1 1/2 Family 2	-	1/1

Sequence variants are documented at the nucleotide and amino acid levels, and the RefSNP number provided for previously identified polymorphisms. The number of affected and unaffected individuals in each family in which the variants were identified is shown, as is the number of control individuals in whom each variant was identified.

tation is not reported as a known SNP in either the HapMap or NCBI SNP databases (dbSNP Build 127) and was not identified in the 110 control individuals that were screened. Although codon 121 is not located in one of the predicted nine transmembrane regions of the encoded protein, it is located within the predicted prenyltransferase functional domain (InterPro) and occurs in a highly conserved amino acid residue across vertebrate and invertebrate orthologs of *UBIAD1* [7]. The other missense variant identified, p.Ser75Phe, is not presumed to be a pathogenic mutation despite its segregation with the affected phenotype in Family 1 as it did not segregate with the affected phenotype in Family 2 and was identified in unaffected control individuals in this study and a previously one [7].

While a sequence variant in two of the positional candidate genes that were screened, *LOC644896* and *LOC729124*, segregated with the affected phenotype in Family 2, the identification of the missense variant in *LOC644896* in unaffected control individuals and the demonstration that the synonymous substitution in *LOC729124* does not alter splicing indicate that these are not pathogenic variants. Additionally, even though nonsense mutations typically produce a truncated, nonfunctional protein product, the two nonsense changes observed in *RERE* were considered nonpathogenic polymorphisms as each was identified in affected and unaffected individuals in Families 1 and 2 as well as in a control individual. Frequently observed, nonpathogenic nonsense changes have been previously described in several genes including *RP1* (OMIM 603937), which is associated with autosomal dominant retinitis pigmentosa [10-12].

UBIAD1 is variably expressed in a wide variety of tissues, but its expression as measured by expressed sequence tag (EST) counts is higher in the eye than in any other tissue (UniGene's EST ProfileViewer). Although *UBIAD1* has been found to be expressed in the adult human cornea (NEIBankLibrary NbLib0073), the mechanism by which mutations in *UBIAD1* result in corneal cholesterol deposition is not immediately clear. It is interesting to note that mutations in another gene coding for a prenyltransferase that is overexpressed in the eye, Rab escort protein 1 (REP1; OMIM 300390), are responsible for another inherited ocular disorder, choroideremia [13]. Although the role of *REP1* in the retinal pigment epithelial cells and photoreceptors has not been elucidated, it is thought that the loss of function of the encoded protein could lead to defects in intracellular vesicular trafficking [13]. Orr and colleagues [7] hypothesized that

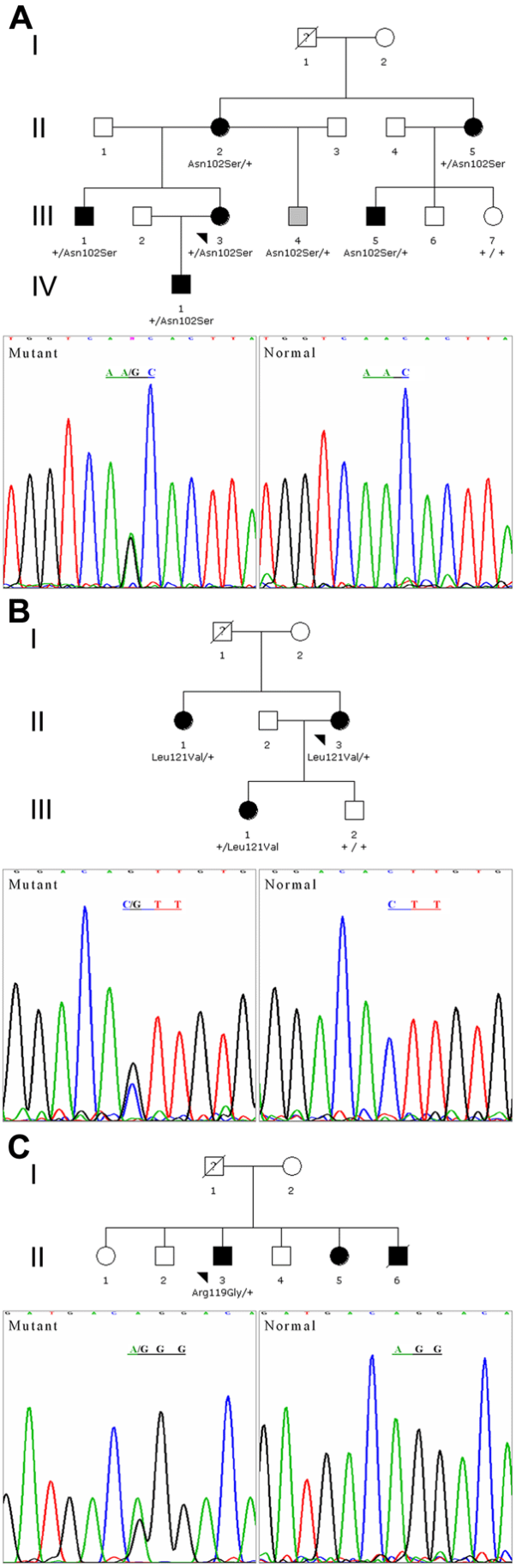

Figure 2. Pedigrees of three families with Schnyder crystalline corneal dystrophy. **A**-**C**: In each pedigree, black filled symbols represent affected individuals, symbols filled with gray represent individuals of indeterminate phenotype, and the unfilled symbols represent unaffected individuals based on examination or history. Question marks indicate individuals of unknown affected status. Below the symbol for each individual in whom DNA collection and *UBIAD1* screening was performed, the presence of the wild type allele (designated by the + symbol) or the mutant allele is indicated. Chromatograms demonstrating the identified mutation and the wild-type DNA sequence are shown beneath each pedigree.

UBIAD1 may play a role in the intracellular localization of other proteins via prenylation of these proteins. The missense mutations that Orr and colleagues and we have identified in the prenyltransferase domain of *UBIAD1* may therefore interfere with intracellular transport, resulting in the accumulation of various metabolic substances such as lipids in tissues where the gene is highly expressed, such as the eye. The use of RNA interference targeting of *UBIAD1* transcript in cultured human keratocytes or the development of a knock-in animal model of SCCD will hopefully clarify the role of *UDIAD1* in the cornea and the mechanism by which the identified missense mutations in *UDIAD1* result in corneal cholesterol deposition.

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REFERENCES

1. Bron AJ, Williams HP, Carruthers ME. Hereditary crystalline stromal dystrophy of Schnyder. I. Clinical features of a family with hyperlipoproteinaemia. Br J Ophthalmol 1972; 56:383-99.
2. Koksal M, Kargi S, Gurelik G, Akata F. Phototherapeutic keratectomy in Schnyder crystalline corneal dystrophy. Cornea 2004; 23:311-3.
3. Meier U, Anastasi C, Failla F, Simona F. [Possibilities of therapeutic photokeratotomy with the excimer laser in treatment of Schnyder crystalline corneal dystrophy]. Klin Monatsbl Augenheilkd 1998; 212:405-6.
4. Shearman AM, Hudson TJ, Andresen JM, Wu X, Sohn RL, Haluska F, Housman DE, Weiss JS. The gene for schnyder's crystalline corneal dystrophy maps to human chromosome 1p34.1-p36. Hum Mol Genet 1996; 5:1667-72.
5. Theendakara V, Tromp G, Kuivaniemi H, White PS, Panchal S, Cox J, Winters RS, Riebeling P, Tost F, Hoeltzenbein M, Tervo TM, Henn W, Denniger E, Krause M, Koksal M, Kargi S, Ugurbas SH, Latvala T, Shearman AM, Weiss JS. Fine mapping of the Schnyder's crystalline corneal dystrophy locus. Hum Genet 2004; 114:594-600.
6. Aldave AJ, Rayner SA, Principe AH, Affeldt JA, Katsev D, Yellore VS. Analysis of fifteen positional candidate genes for Schnyder crystalline corneal dystrophy. Mol Vis 2005; 11:713-6.
7. Orr A, Dube MP, Marcadier J, Jiang H, Federico A, George S, Seamone C, Andrews D, Dubord P, Holland S, Provost S, Mongrain V, Evans S, Higgins B, Bowman S, Guernsey D, Samuels M. Mutations in the UBIAD1 gene, encoding a potential prenyltransferase, are causal for Schnyder crystalline corneal dystrophy. PLoS ONE 2007; 2:e685.
8. Meindl A, Dry K, Herrmann K, Manson F, Ciccodicola A, Edgar A, Carvalho MR, Achatz H, Hellebrand H, Lennon A, Migliaccio C, Porter K, Zrenner E, Bird A, Jay M, Lorenz B, Wittwer B, D'Urso M, Meitinger T, Wright A. A gene (RPGR) with homology to the RCC1 guanine nucleotide exchange factor is mutated in X-linked retinitis pigmentosa (RP3). Nat Genet 1996; 13:35-42.
9. Souied E, Kaplan J, Soubrane G, Coscas G. [Retinitis pigmentosa]. J Fr Ophtalmol 1997; 20:461-86.
10. North KN, Yang N, Wattanasirichaigoon D, Mills M, Easteal S, Beggs AH. A common nonsense mutation results in alpha-actinin-3 deficiency in the general population. Nat Genet 1999; 21:353-4.
11. Germain DP. Pseudoxanthoma elasticum: evidence for the existence of a pseudogene highly homologous to the ABCC6 gene. J Med Genet 2001; 38:457-61.
12. Zhang X, Yeung KY, Pang CP, Fu W. [Mutation analysis of retinitis pigmentosa 1 gene in Chinese with retinitis pigmentosa]. Zhonghua Yi Xue Yi Chuan Xue Za Zhi 2002; 19:194-7.
13. Alory C, Balch WE. Organization of the Rab-GDI/CHM superfamily: the functional basis for choroideremia disease. Traffic 2001; 2:532-43.

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