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Supplementary Data

Mutations in the Recessive Deafness Locus *LOXHD1*

Cause Dominant Late-Onset Fuchs Corneal Dystrophy

S. Amer Riazuddin, David S. Parker, Elyse J. McGlumphy, Edwin C. Oh, Benjamin W. Iliff, Thore Schmedt, Ula Jurkunas, Robert Schleif, Nicholas Katsanis, and John D. Gottsch

Table S1. Quantitative RT-PCR of LOXHD1 in Cultured Human Corneal Endothelial Cells

cDNA Source	**LOXHD1 C_T**	**GAPDH C_T**	**β-Actin C_T**	**δC_T *LOXHD1*-*GAPHD***	**δC_T *LOXHD1*- β-Actin**
Cultured human corneal endothelial cells	34	15	16	19	18

Quantitative RT-PCR was performed in triplicate using cDNA reverse transcribed from RNA from cultured human corneal endothelial cells. The mean threshold cycle (CT) value for each target (Loxhd1) and endogenous reference (GAPDH & β-actin), representing the PCR cycle at which the ABI 7900 HT Detection System first detects a noticeable increase in reporter florescence above baseline signal, was calculated for each group. The δCT values for each target were determined by subtracting the mean of the endogenous reference (GAPDH & β-actin), value from the mean LOXHD1 value. Note: all values are obtained after averaging the results of three independent experiments.

Table S2. Characteristics of *LOXHD1* Variants Identified in (A) Late-Onset FCD Cases and (B) Ethnically Matched Control Samples

A.

No	Mutation (DNA)	Mutation (Protein)	Presence in Ethnically Matched	Evolutionary Conservation in *LOXHD1* Orthologs	PolyPhen2 Predictions
1	c.159T>G	p.Asp53Glu	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Do, Co, Hr, Ca, Do, He, Op, Pl	unknown
2	c.242G>A	p.Ser81Asn	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, Sh, El, Am, Op, Pl	unknown
3	c.469C>T	p.Arg157Cys	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, Sh, El, Am, Op, Pl	unknown
4	c.1570C>T	p.Arg524Cys	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
5	c.1639C>T	*p.Arg547Cys	0 in 384 Control chromosomes	Hu, Rh, Mr, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, El, Op, Pl	Probably damaging
6	c.1759C>T	p.Arg587Trp	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, El, Op, Pl	Probably damaging
7	c.1945G>A	p.Asp649Asn	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, El, Op, Pl	Benign
8	c.2251C>T	p.Arg751Trp	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
9	c.2359C>T	p.Arg787Cys	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
10	c.3874C>T	p.Leu1292Phe	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
11	c.5224G>A	p.Glu1742Lys	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Possibly damaging
12	c.5272A>T	p.Thr1758Ser	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Possibly damaging
13	c.5398C>T	p.Arg1800Trp	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
14	c.5953G>C	p.Glu1985Gln	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Possibly damaging
15	c.6112C>A	p.His2038Asn	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Possibly damaging
16	c.1904T>C (NM_001145472)	p.Leu635Pro	0 in 384 Control chromosomes	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op	Possibly damaging

B.

No	Mutation (DNA)	Mutation (Protein)	Evolutionary Conservation in *LOXHD1* Orthologs	PolyPhen2 Predictions
1	c.166G>A	p.Gly56Ser	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
2	c.3940A>T	p.Thr1314Ser	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
3	c.4526G>A	p.Gly1509Glu	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
4	c.5005G>A	p.Gly1669Arg	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
5	c.5024G>A	p.Arg1675His	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
6	c.5087T>G	p.Val1696Gly	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
7	c.5173G>A	p.Gly1725Arg	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging
8	c.5869G>A	p.Glu1957Lys	Hu, Ch, Or, Rh, Ba, Mr, Bu, Mo, Ra, Ka, Gu, Ra, Pi, Do, Co, Hr, Ca, Do, Mi, He, Sh, El, Am, Op, Pl	Probably damaging

H: human; Ch: Chimp; Or: Orangutan; Rh: Rhesus; Ba: Baboon; Mr: Marmoset; Bu: Bushbaby; Mo: Mouse; Ra: Rat; Ka: Kangaroo_rat; Gu: Guinea_pig; Ra: Rabbit; Pi: Pika; Do: Dolphin; Co: Cow; Hr: Horse; Ca: Cat; Do: Dog; Mi: Microbat; He: Hedgehog; Sh: Shrew; El: Elephant; Am: Armadillo; Op: Opossum; Pl: Platypus. * represent the mutation segregating in family "HU."
Note: The DNA mutation numbering system used is based on cDNA sequence.