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Supplemental Data

Recessive Mutations in *ELOVL4* Cause Ichthyosis, Intellectual Disability, and Spastic Quadriplegia

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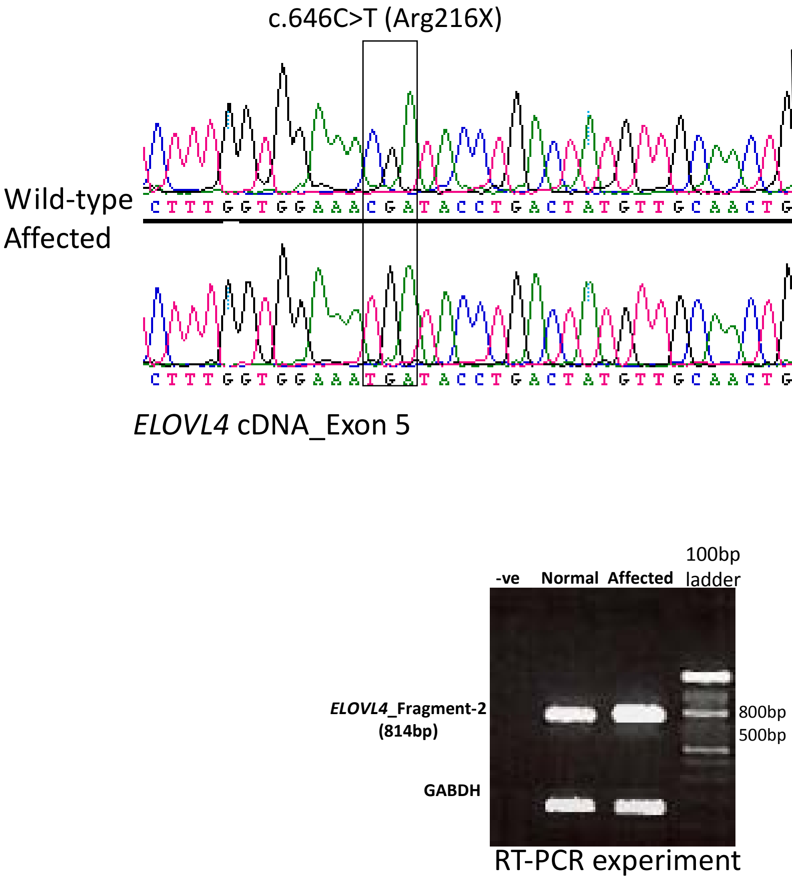

Figure S1. RT-PCR on Person 1's fibroblasts showing normal abundance of *ELOVL4* RNA which is confirmed to harbor the nonsense mutation as shown in the sequence chromatogram.

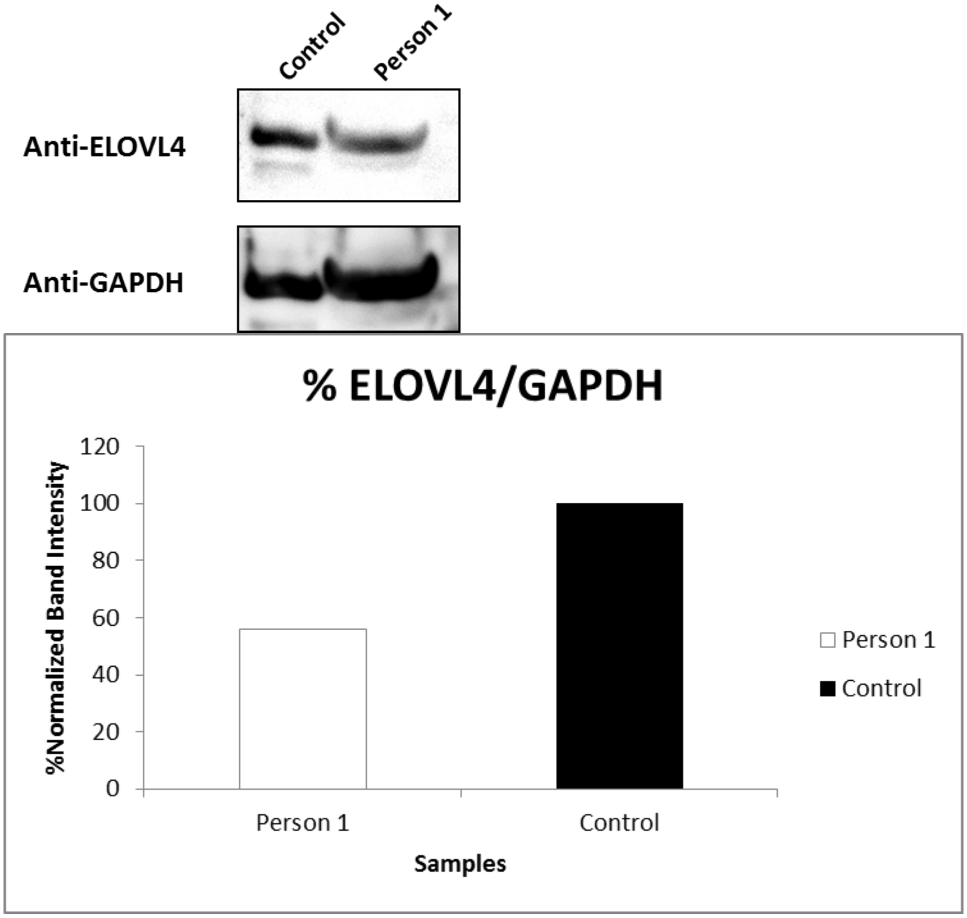

Figure S2. Western blot analysis using ELOVL4 antibody showing reduced abundance of the protein in Person 1 compared to control.

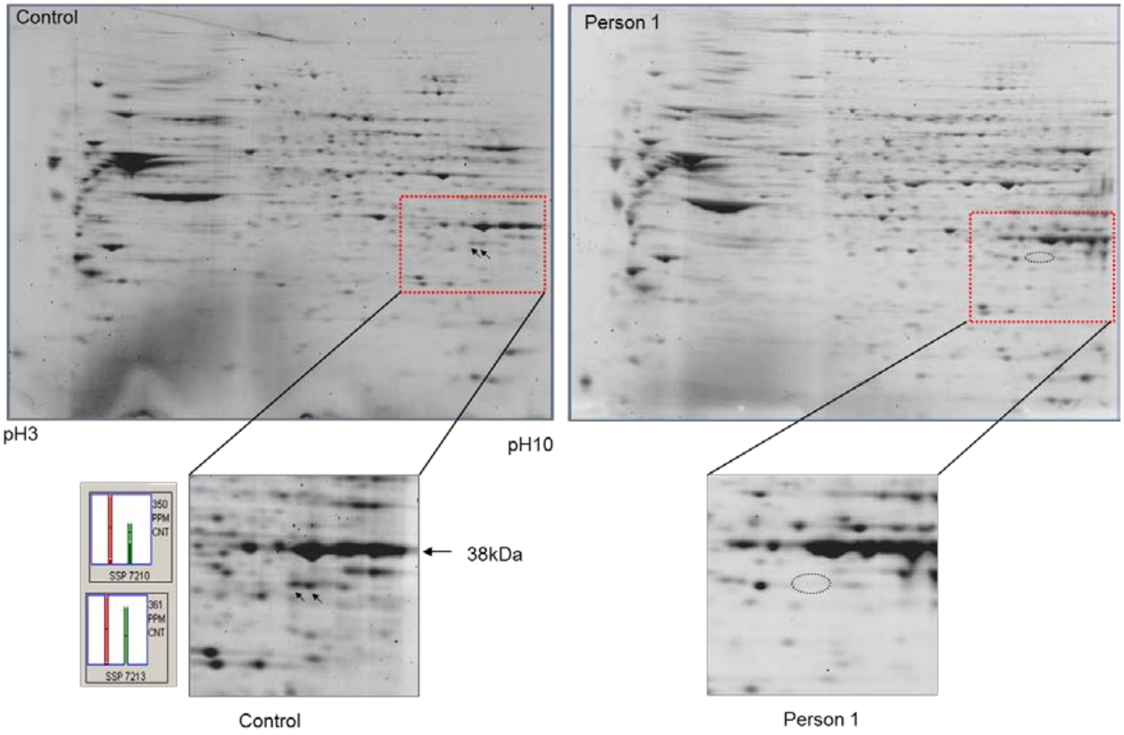

Figure S3. Representative 2-De gels derived from control and Person 1 samples. Whole cell extracts were separated by electrophoresis using IPG 3-10 nonlinear gradient strips in the first dimension and 12.5% homogeneous criterion precast SDS-polyacrylamide gels in the second dimension. Insets are gel segments from basic portion of each gel in the 31-38 kDa molecular mass range showing differentially expressed protein spots (Red bar= control, Green bar = Person 1). Gels were stained with Sypro Ruby fluorescent stain and scanned with Typhoon Trio Imager.

Table S1. Summary of autozygome analysis of Person 1

Order	ROH Coordinates	# Genes	Length (bp)
1	chr6:10000000-99000000	1198	89,000,001
2	chr10:109600000-113200000	27	3,600,001
3	chr10:33400000-36200000	20	2,800,001
4	chr12:23600000-41000000	106	17,400,001
5	chr13:54400000-57000000	8	2,600,001
6	chr16:2700000-6800000	105	4,100,001
7	chr17:22800000-28000000	142	5,200,001
8	chr19:4100000-12500000	318	8,400,001
9	chr21:24800000-37000000	180	12,200,001

Table S2. Filtration strategy used in this study

ROH	location	gene ID	A.A> change	Other Saudi exomes	PolyPhen-2 prediction	comments
chr6:10,000,000-99,000,000	17400067	RBM24 _CCDS4538.1	'Ile105Thr'	No	possibly damaging with a score of 0.553	
	17741012	NUP153	'Ser=>Cys'	Yes		
	24531897	MRS2	'Arg=>His'	Yes		
	26032113	SLC17A2_CCDS4567.1	'Gly10Asp'	No	benign with a score of 0.020	
	26305063	HIST1H3D_CCDS4590.1	'Arg132His'	No	possibly damaging with a score of 0.778	not exp in Eye or brain,but in skin
	28228923	ZNF192_CCDS4645.1	'Gly296Ser'	No	benign with a score of 0.067	
	28441932	ZKSCAN3	'Thr=>Ser'	No	probably damaging with a score of 1.000	not in skin but in Eye and Brain
	29664134	OR2H2	'Val=>Ala'	No	benign with a score of 0.260	
	30234156	TRIM10_CCDS34375.1	'Thr252Met'	No	probably damaging with a score of 0.996	exp only in heart, kidney, and liver
	30234204	TRIM10	'Ile=>Thr'	No	benign with a score of 0.206	
	30234264	TRIM10	'Arg216Lys'	No	benign with a score of 0.000	
	30234282	TRIM10_CCDS34375.1	'Gln210Leu'	No	benign with a score of 0.000	
	30242966	TRIM15	'Thr=>Met'	No	benign with a score of 0.000	
	31345812	HLA-C	'Met=>Val'	Yes		
	31346008	HLA-C	'Met=>Val'	Yes		
	31346238	HLA-C	'Pro=>His'	Yes		
	31346936	HLA-C	'Leu=>Trp'	Yes		
	31347781	HLA-C	'Gly=>Ala'	Yes		
	31430959	HLA-B	'Val=>Ile'	Yes		
	31431316	HLA-B	'Ile=>Val'	Yes		
	33144413	HLA-DPA1	'Thr=>Pro'	Yes		
	38921390	DNAH8_CCDS4838.1	'Glu1419Asp'	No	benign with a score of 0.032	
	39375468	KCNK17_CCDS4842.1	'Pro238Ala'	No	probably damaging with a score of 0.987	Not conserved in mouse and Dog, and not expressed in Eye, Brain or Skin
	41108675	UNC5CL_CCDS4847.1	'Arg292His'	No	probably damaging with a score of 0.998	not exp in either skin or eye
	42821532	TBCC_CCDS4872.1	'Glu86Asp'	No	probably damaging with a score of 0.996	in most of tissues
	51605462	PKHD1	'Arg=>Leu'	Yes		
	80,685,879	ELOVL4	CGA=>TGA' (p.R216X; c.646C>T)	No		high exp in Eye, Brain, and skin
	88,372,460	ORC3L	Base=A (+2) (spliceSite_INDEL)	Yes		
chr10:109,600,000-113,200,000	No novel homozygous variants					
chr10:33,400,000-36,200,000	34440159	PARD3	c.4015G>C; p.V1339L	No	probably damaging with a score of 0.988	in most of tissues, BUT in the knock-out mice showed: mortality/aging, cardiovascular, growth/size, nervous system, limbs/digits/tail, homeostasis, embryogenesis. It did not present any phenotype (s) in vision or skin.
chr12:23,600,000-41,000,000	26726071	ITPR2	Base= + ACTC (spliceSite_INDEL (-3))	Yes		
	52734373	HOXC4	I134V	Yes		not exp. In skin
chr13:54,400,000-57,000,000	No novel homozygous variants					
chr16:2,700,000-6,800,000	No novel homozygous variants					
chr17:22,800,000-28,000,000	No novel homozygous variants					
chr19:4,100,000-12,500,00	5817736	FUT5	'His=>Arg'	Yes		
	6684582	GPR108	'Thr241Met' (CCDS42479.1)	No	probably damaging with a score of 1.000	in most of tissues, BUT not consreved in checken, Rat, and Pongo
	9186252	OR7D4	'Arg=>Trp'	Yes		
	10224251	MRPL4	'Lys=>Thr'	Yes		
	10609382	SLC44A2	'Glu=>Gln'	Yes		
chr21:24,800,000-37,000,000	30,835,852	KRTAP19-6	Base=G	Yes		
	32,925,799	SYNJ1	Base=AGTATT (+2) (CCDS33539.1), frameshift-INDEL	No		in most of tissues, but not in skin
	33,870,566	SON	Base=A	Yes		in most of tissues
	31175500	KRTAP11-1	'Arg=>Gln'	Yes		
	31448587	TIAM1	'Arg1007His' (CCDS13609.1)	No	probably damaging with a score of 1.000	in most of tissues
	33847913	SON	'Met=>Ile'	Yes		

We were left with the three variants below:

TBCC (MS): NM_003192.2: c.258G>T, p.Glu86Asp

ELOVL4 (NS): NM_022726.2:c.646C>T, p.R216X

TIAM1 (MS): NM_003253.2:c.3020G>A, p.Arg1007His

Table S3. gDNA primers for ELOVL4 and cDNA primers for ALDH3A

ELOVL4 gDNA ID	Forward	Reverse	Ta (°C)
ELOVL4_Ex-1	CTTTCTCCCGGGAACCTT	CGGATCAGATTAACCAGTGC	59
ELOVL4_Ex-2	TTTTTTGTTGGGACTCAAAGG	TTCAATGCCAGAACAGCTAA	59
ELOVL4_Ex-3	AGCAATCGGAATGCATGA	ACCCGTAGTCCCAGCTACTT	59
ELOVL4_Ex-4	CCATGGAGAGATGCTTAGGTT	GGAAATGATTAACCATGAAAGC	59
ELOVL4_Ex-5	ATCTAGCTTAATCTGAAGGGAAAA	GATTTGCTGGGACCAATAAG	59
ELOVL4_Ex-6	CATGGGAGCCAGAAAACA	ACATCTGGGTATGGTATTAACACTT	59
ALDH3A2_cDNA_1	GAGTGAATTGTGGCTGTGG	CCCGTATAGAAAATGTGGTCA	58
ALDH3A2_cDNA_2	GCCTTCTGAACTGAGTGAAAA	CTCCACTGGATGTCTCATCA	58
ALDH3A2_cDNA_3	TGAAAAATGTAGATGAGGCCATAA	GGCAACTTTTATTAATGATGAATGG	58