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Identification Of Novel Homozygous Deletion Of The Plakophilin-1 Gene Through Illumina Next Generation Sequencing In An Indian Patient With EDSF Syndrome

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Abstract

A rare autosomal recessive disorder ectodermal dysplasia-skin fragility (EDSF) syndrome causes skin fragility, persistent cheilitis, palmoplantar keratoderma, aberrant hair growth, and nail dystrophy. Plakophilin-1 gene mutations, which induce desmosomal abnormalities and poor intercellular cohesion between epidermal cells, are the root cause of EDSF syndrome. Here, we present information on a 7-year-old Indian girl with EDSF syndrome who has a new homozygous deletion of the PKP1 gene. Our research adds to the body of knowledge on PKP1 mutations and highlights the use of crucial part that PKP1 plays in the development and maintenance of the epidermal desmosomes. In addition, for the first time, we describe the change in gene and protein sequences of PKP1 at c.1333delC (p.Arg445Alafs*56) with ultrastructural alterations of the skin and curly hair in patients with EDSF syndrome.

Categories: Dermatology, Genetics, Pediatrics
Keywords: desmosomes, skin fragility, autosomal recessive, pkp1, ectodermal dysplasia

Introduction

An autosomal recessive illness known as ectodermal dysplasia-skin fragility (EDSF) syndrome (OMIM #604536) causes skin fragility, persistent cheilitis, palmoplantar keratoderma, aberrant hair growth, and nail dystrophy. Plakophilin-1 is a protein that is encoded by the PKP1 gene, and it has been discovered that these mutations account for EDSF syndrome. There have been a total of 21 people with EDSF syndrome recorded till date around the world in various groups since McGrath's initial case report in 1971. Plakophilins (PKP) are essential structural elements of desmosomal adhesion and are critical for controlling desmosomal signalling and turnover [1]. The suprabasal epidermis is the primary site of expression for the three known isoforms (PKP1, PKP2, and PKP3), with PKP1 playing a critical role in controlling cell migration, desmosome assembly, and desmosomal protein content.

Case Presentation

A couple from Indian family from Telangana state have a history of multiple abortions. After 11 miscarriages a baby was born in 2015 and the wife was pregnant with 14 weeks foetus in her womb. Their daughter, who is 7-year-old is presenting with dermatological problems including bleeding lesions, delicate nails with hard and fissured skin of the palms and soles, lusterless and pulkable thin hair and lack of sweating. Perioral fissuring and cheilitis were prominent. Scaly hyperkeratotic plaques were symmetrically distributed over the extensor surface of his elbows and knees. Yellowish, thickened fingernails and toenails were evident. Diffuse hyperkeratosis with deep fissures was present on his palms and soles (Fig-1). The oral mucosa was normal, but irregular teeth arrangement was noticed. WES trio has been recommended rule out recurrence in subsequent pregnancies and they been evaluated for the gene variations related to the reported phenotype.

Methodology

Targeted sequencing and mutation analysis was performed by Polymerase Chain Reaction (PCR) followed by automated DNA sequencing of the amplicon using BigDye ABI Genetic Analyzer 3500DX platform [2]. The raw data obtained is subsequently analyzed for the nucleotide variants. Sanger sequencing of genomic DNA for PKP1 mutations were used to examine novel, unrelated instances of EDSF syndrome [3].

Electrophoretogram analysis for chromosome specific markers through Quantitative fluorescence PCR (QF-PCR)

Quantitative fluorescence PCR (QF-PCR) is a reliable molecular method for rapid aneuploidy diagnosis [4]. DNA was isolated from the given sample using a commercial kit according to manufacturer's instructions. Multiplex PCR amplification of short tandem repeat (STR) markers using fluorescent tagged primer was carried out using a commercial kit according to manufacturer's instructions. The resulting fragments were analysed on the genetic analyser for visualization and quantification. The copy number of respective chromosome is quantified by calculating the relative allele ratio. Analysed region includes: D13S742, D13S634, D13S628, D13S305, D13S1492, D18S978, D18S535, D18S386, D18S976, GATA178F11, D21S1435, D21S11, D21S1411, D21S1444, D21S1442, D21S1437.

Diagnostic findings not related to phenotype

To find the variants of other genes that are unrelated to the detected abnormality, sequencing of the protein coding regions approximately 30Mb of the human exome (targeting approximately 99% of regions in CCDS and Ref Seq) and complete mitochondrial genome sequencing was performed using Illumina next generation sequencing (NGS) systems at a mean depth of 80-100X with percentage of bases covered at 20X depth >90% in the target region and the depth for mitochondrial genome at 1000-2000X.

Sequencing of the protein coding regions approximately 30Mb of the human exome (targeting approximately 99% of regions in CCDS and Ref Seq) and complete mitochondrial genome sequencing was performed using Illumina next generation sequencing (NGS) systems at a mean depth of 80-100X with percentage of bases covered at 20X depth >90% in the target region and the depth for mitochondrial genome at 1000-2000X. In some cases, due to the complexity of the sequence, not all variants in the flanking regions are able to be analysed. A base is considered to have sufficient coverage at 20X and an exon is considered fully covered if all coding bases plus three nucleotides of flanking sequence on either side are covered at 20X or more. GATK best practice framework was followed for variant identification. Duplicate reads identification and removal, Base quality recalibration and re-alignment of reads based on indels were done using DRAGEN BIO IT platform [2]. Quality checks (QC) will be performed on all VCF files to exclude variants where sequencing is of poor quality. Additional QC metrics includes total homozygous and heterozygous calls (SNVs and indels), proportion of variant calls that were common, number of variants falling into different annotated consequence categories, number of extreme heterozygotes (alternate allele proportion 0.8). Variant annotations will be done using published databases like OMIM, GWAS, GNOMAD, 1000 Genome etc [5-7]. Non-synonymous and splice site variants will be used for clinical interpretation. Silent variations that do not result in any change in amino acid in the coding region are not reported. Golden helix Varseq 2.2.4 was used for variant annotation, analysis and reporting [8].

Discussion

Ectodermal dysplasia/skin fragility syndrome is caused by homozygous or compound heterozygous mutation in the plakophilin-1 gene (PKP1) on chromosome 1q32. Ectodermal dysplasia/skin fragility syndrome

(EDSFS) is an autosomal recessive genodermatosis characterized by widespread skin fragility, alopecia, nail dystrophy, and focal keratoderma with painful fissures. Hyohidrosis and cheilitis are sometimes present [3, 4, 9].

Skin biopsies were taken from the scalp and the hyperkeratotic plaque on the right ankle. The histological changes were similar, revealing hyperkeratosis, focal thickening of the granular layer, widened intercellular spaces, isolated dyskeratotic cells and striking paranuclear eosinophilic masses within the upper epidermal layers. The formation of suprabasal splits within the follicles were evident. (Fig. *2*).

Cortical cells that were fragmented, abnormally curling hair, and morphogenic abnormalities were all found. An analysis of the scalp's histopathology revealed hyperkerat

PKP1 chr1:201289495delC - Likely Pathogenic

The frameshift deletion NM_001005337.3(PKP1):c.1333delC (p.Arg445Alafs*56) has not been reported previously as a pathogenic variant nor as a benign variant, to our knowledge. The p.Arg445Alafs*56 variant is novel (not in any individuals) in gnomAD. The p.Arg445Alafs*56 variant is novel (not in any individuals) in 1kG. This variant is predicted to cause loss of normal protein function through protein truncation caused a frameshift mutation. The frame shifted sequence continues 56 residues until a stop codon is reached. This variant is a frameshift variant which occurs in an exon of PKP1 upstream of where nonsense mediated decay is predicted to occur. There is another pathogenic loss of function variant 169 residues downstream of this variant, indicating that the region is critical to protein function. The p.Arg445Alafs*56 variant is a loss of function variant in the gene PKP1, which is intolerant of Loss of Function variants, as indicated by the presence of existing pathogenic loss of function variant NP_001005337.1:p.Q614*. For these reasons, this variant has been classified as Likely Pathogenic. The same variant in heterozygous state was detected in father (KT41398134-FB) and mother (KT41398134-MB) (Table-1).

Sanger sequencing data (electropherogram) for the provided prenatal sample showing nucleotide change at chr1: c.1333delC, (p.Arg445Alafs*56) in PKP1gene (Figure-3).

QF-PCR reveals that no other chromosomal abberations

Electrophoretogram analysis for chromosome specific markers indicates a normal complement of 13, 18, 21 and sex chromosomes (Figure-4). No pathogenic variants in genes that are unrelated to the patient's phenotype were detected in this individual (Table-2)

Sample	Gene & Transcript	Variant	Location	Zygosity	Inheritance
Daughter (7 yys)	PKP1 NM_001005337.3	c.1333delC (p.Arg445Alafs*56)	Exon 7	Homozygous	Autosomal Recessive
Foetus (14 weeks 2 days)	PKP1	c.1333delC (p.Arg445Alafs*56)	Not yet known	Present (Heterozygous)	Autosomal Recessive

TABLE 1: PKP1 chr1:201289495delC - Likely Pathogenic

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Figure-1

FIGURE 1: clinical presentation of the patient with ED. The index patient is indicated by an arrow

Figure-2

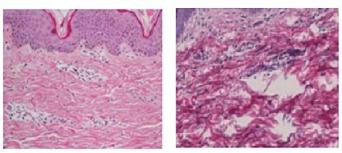

FIGURE 2: Histology of skin biopsies of the patient with ED

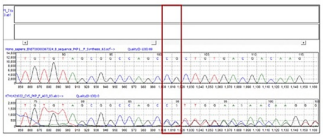

Fig1: Sanger sequencing data (electropherogram) for the provided prenatal sample showing **nucleotide change** at **chr1: c.1333delC, (p.Arg445Alafs*56)** in ***PKP1*** gene.

FIGURE 3: Sanger sequence data of nucleotide change at chromosome-1 PKP-1 gene at c1333delc

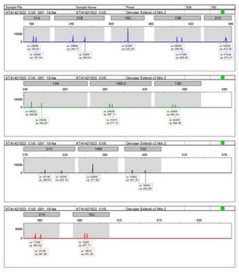

FIGURE 4: QT-PCR analysis for chromosomal abberations

Further, the chorionic villus sample of 14 weeks foetus was evaluated for the gene variations related to the reported phenotype. The results of laboratory tests, electrocardiography, chest computed tomography, abdominal and urinary ultrasonography, and ultrasonic cardiogram were normal (Table-3)

List of Syndromes	Aneuploidy
Pataus syndrome (Trisomy 13)	Not Detected
Edward syndrome (Trisomy 18)	Not Detected
Downs syndrome (Trisomy 21)	Not Detected
Gonosomal Aneuploidy	Not Detected
Maternal Cell Contamination	No significant MCC Detected

TABLE 2: Chromosome specific marker analysis

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Conclusions

To summarize, ED is an uncommon genetic skin condition. We present the case of the second known Indian individuals affected by ED, which can be attributed to a deletion and frame shift mutation in the PKP1 gene. This finding strengthens the existing understanding of the role of PKP1 mutations in the development of ED and contributes to the growing collection of PKP1 mutation data.

Appendices

Gene	Percentage of Coding Region Covered	Gene	Percentage of Coding Region Covered	Gene	Percentage of Coding Region Covered
AAAS	100	AAGAB	100	ABAT	100
ABCA1	100	ABCA12	100	ABCA3	100
ABCA5	100	ABCB11	100	ABCB4	100
ABCB6	100	ABCC6	100	ABCC8	100
ABCC9	100	ABCD1	100	ABCG5	100
ABCG8	100	ABHD5	100	ABL1	100
ACAD9	100	ACADVL	100	ACAN	96.85
ACAT1	100	ACD	100	ACO2	100
ACP2	100	ACP5	100	ACTA2	100

ACTB	100	ACTC1	100	ACTG1	100
ACTG2	100	ACTL6A	100	ACTL6B	100
ACTN1	100	ACVR1	100	ACVRL1	100
ADA	100	ADA2	100	ADAM10	100
ADAM17	100	ADAMTS10	100	ADAMTS13	100
ADAMTS2	100	ADAMTS3	100	ADAMTSL1	100
ADAMTSL2	100	ADARB1	100	ADAT3	100
ADCY5	100	ADGRE2	100	ADH5	100
ADNP	100	AEBP1	100	AFF3	100
AFF4	100	AGA	100	AGBL5	100
AGGF1	100	AGO2	99.34	AGPAT2	100
AGXT	100	AHI1	100	AHSG	100
AIFM1	100	AIMP1	100	AIMP2	100
AIP	100	AIRE	100	AK9	98
AKR1D1	100	AKT1	100	AKT2	100
ALAS2	100	ALDH2	100	ALDH3A2	100
ALDOA	100	ALDOB	100	ALG11	100
ALG12	100	ALG3	100	ALG8	100
ALG9	100	ALKBH8	100	ALMS1	100
ALOX12B	100	ALOXE3	100	ALPK1	100
ALS2	100	ALX1	100	ALX4	100
AMACR	100	AMMECR1	100	AMN	100
ANAPC1	100	ANGPT1	100	ANGPTL6	100
ANK1	100	ANKRD11	100	ANKRD17	100
ANO6	100	ANOS1	100	ANTXR1	100
ANTXR2	100	AP1B1	100	AP1G1	100
AP1S1	100	AP1S2	100	AP1S3	100
AP2M1	100	AP3B1	100	AP3B2	100
AP3D1	100	APC	100	APC2	100
APCDD1	100	APOA1	100	APOA5	100
APOB	100	APOC2	100	APOE	100
APP	100	AQP5	100	AR	100
ARFGEF2	100	ARHGAP31	100	ARID1B	100
ARID2	100	ARL13B	100	ARL2BP	100
ARL3	100	ARL6	100	ARL6IP6	100
ARMC5	100	ARMC9	100	ARNT2	100
ARSB	100	ARSG	100	ARVCF	100
ARX	100	ASAH1	100	ASL	100
ASPRV1	100	ASXL1	100	ASXL3	100
ATG7	100	ATIC	100	ATL1	100
ATL3	100	ATM	100	ATP10A	100
ATP11C	100	ATP1A3	100	ATP2A2	100
ATP2C1	100	ATP6AP1	100	ATP6AP2	100
ATP6V0A2	100	ATP6V1A	100	ATP6V1B2	100
ATP6V1E1	100	ATP7A	100	ATP7B	100
ATP8B1	100	ATR	100	ATRIP	100
ATRX	100	ATXN10	100	ATXN7	100
AUTS2	100	AXIN2	100	AXL	100
B2M	100	B3GALNT2	100	B3GAT3	100
B3GLCT	100	B4GALNT1	100	B4GALT1	100
B4GALT7	98.58	B4GAT1	100	B9D1	100
B9D2	100	BAAT	100	BANF1	100
BAP1	100	BAZ1B	100	BBS10	100
BBS12	100	BBS2	100	BBS4	100
BBS7	100	BBS9	100	BCAS3	100
BCL11B	100	BCL2	100	BCL6	100
BCL7B	100	BCO1	100	BCOR	100
BCORL1	100	BCR	100	BCS1L	100
BEST1	100	BHLHA9	100	BICRA	100
BIRC3	100	BLM	100	BLOC1S6	100
BMP15	100	BMP2	100	BMP4	100
BMPER	100	BMPR1B	100	BMPR2	100
BNC1	100	BPGM	100	BPTF	100

BRAF	100	BRCA1	100	BRCA2	100
BRCC3	100	BRD4	100	BRF1	100
BRIP1	100	BRSK2	100	BSCL2	100
BTD	100	BTK	100	BTNL2	100
BUB1	100	BUB1B	100	BUD23	100
C12ORF4	100	C1QTNF5	100	C1R	100
C1S	100	C2	100	C2CD3	100
C4A	100	C5	100	C9ORF72	100
CA4	100	CACNA1A	100	CACNA1B	100
CACNA1D	100	CACNA1F	100	CACNA1G	100
CACNA1H	100	CACNA1I	100	CACNG2	100
CALR	100	CAMK2A	100	CAMK2B	100
CANT1	100	CAP2	100	CAPN15	100
CAPN5	100	CARD11	100	CARD14	100
CARD9	100	CARMIL2	100	CASK	100
CASP10	100	CASP14	100	CASP8	100
CASR	100	CAST	100	CASZ1	100
CAT	100	CAV1	100	CAVIN1	100
CBL	100	CC2D1A	100	CC2D2A	100
CCBE1	100	CCDC103	100	CCDC115	100
CCDC141	100	CCDC22	100	CCDC32	73
CCDC39	100	CCDC40	100	CCDC47	100
CCL2	100	CCM2	100	CCNK	100
CCNO	100	CCR1	100	CCR6	100
CCT5	100	CD109	100	CD19	100
CD28	100	CD36	100	CD3D	100
CD3E	100	CD3G	100	CD4	100
CD79A	100	CD79B	100	CD81	100
CD96	100	CDAN1	100	CDH1	100
CDH11	100	CDH15	100	CDH2	100
CDH3	100	CDK10	100	CDK13	100
CDK19	100	CDK4	100	CDK5	100
CDKL5	100	CDKN1A	100	CDKN1B	100
CDKN1C	100	CDKN2C	100	CDON	100
CDSN	100	CENPE	100	CENPJ	100
CENPT	100	CEP120	100	CEP152	100
CEP19	100	CEP290	100	CEP55	100
CEP57	100	CERKL	100	CERS3	100
CFI	100	CFTR	100	CHAMP1	100
CHD1	100	CHD2	100	CHD7	100
CHKB	100	CHMP1A	100	CHMP2B	100
CHN1	100	CHRNA1	100	CHRNA7	100
CHRNB1	100	CHRND	100	CHRNE	100
CHRNG	100	CHST14	100	CHST8	100
CHSY1	100	CIB1	100	CIC	100
CIDEC	100	CIITA	100	CISD2	100
CITED2	100	CKAP2L	100	CLCN2	100
CLCN3	100	CLCN7	100	CLDN1	100
CLDN10	100	CLEC7A	100	CLIP1	100
CLIP2	100	CLMP	100	CLPX	100
CLRN1	100	CLTC	100	CNBP	100
CNGA1	100	CNGB1	100	CNGB3	100
CNKSR2	100	CNOT2	100	CNOT3	100
CNP	100	CNPY3	100	COG4	100
COG5	100	COG6	100	COG7	100
COG8	100	COL11A2	100	COL12A1	100
COL14A1	100	COL18A1	100	COL1A1	100
COL1A2	100	COL25A1	100	COL2A1	100
COL3A1	100	COL4A1	100	COL4A2	100
COL4A5	100	COL5A1	100	COL5A2	100
COL6A1	100	COL6A2	100	COL6A3	100
COL7A1	100	COLEC10	100	COLGALT1	95.08
COMT	100	COPB1	100	COQ2	100
COX10	100	COX14	100	COX4I2	100

COX5A	100	COX7B	100	CPA1	100
CPLX1	100	CPOX	100	CRADD	100
CRBN	100	CREBBP	100	CRIPT	100
CRKL	100	CRLF1	98.27	CRX	100
CRYAB	100	CSGALNACT1	100	CSNK2A1	100
CSPP1	100	CSRP3	100	CST3	100
CST6	100	CSTA	100	CSTB	100
CTBP1	100	CTC1	100	CTCF	100
CTLA4	100	CTNNA1	100	CTNNB1	100
CTNND1	100	CTNND2	100	CTNS	100
CTSA	100	CTSB	100	CTSC	100
CUBN	100	CUL4B	100	CUX1	100
CUX2	100	CWC27	100	CXCR4	100
CYB5A	100	CYB5R3	100	CYBA	100
CYFIP2	100	CYLD	100	CYP11A1	100
CYP11B1	100	CYP11B2	100	CYP19A1	100
CYP1B1	100	CYP27A1	100	CYP4F22	100
CYP7A1	100	CYP7B1	100	CYSLTR2	100
D2HGDH	100	DACT1	100	DAG1	100
DALRD3	100	DAXX	100	DCAF17	100
DCC	100	DCDC2	100	DCHS1	100
DCPS	100	DCT	100	DDB1	100
DDB2	100	DDC	100	DDIT3	100
DDX11	100	DDX3X	100	DDX41	100
DDX58	100	DDX6	100	DEF6	100
DENND5A	100	DEPDC5	100	DES	100
DGUOK	100	DHCR24	100	DHCR7	100
DHFR	100	DHODH	100	DHPS	100
DHX30	100	DHX37	100	DHX38	100
DIAPH1	97.93	DICER1	100	DIP2B	100
DIS3L2	100	DKC1	100	DLG4	100
DLK1	100	DLL1	100	DLL4	100
DLST	100	DLX3	100	DLX4	100
DLX5	100	DMD	100	DMPK	100
DMRT3	100	DMXL2	100	DNAAF1	100
DNAAF2	100	DNAAF3	100	DNAAF4	100
DNAAF5	100	DNAH11	100	DNAH5	100
DNAI1	100	DNAI2	100	DNAJC13	100
DNAJC19	100	DNAJC21	100	DNAJC30	100
DNAL1	100	DNASE1	100	DNASE1L3	100
DNM1	100	DNM2	100	DNMT3A	100
DOCK3	99.74	DOCK6	100	DOCK8	100
DOK7	100	DPAGT1	100	DPF2	100
DPH1	100	DPM1	100	DPM2	100
DPYS	100	DPYSL5	100	DRC1	100
DSC2	100	DSC3	100	DSE	100
DSG1	100	DSG2	100	DSG3	100
DSG4	100	DSP	100	DST	100
DTNBP1	100	DUOX2	100	DUOXA2	100
DUSP6	100	DVL3	100	DYNC1H1	100
DYNC2H1	100	DYNC2LI1	100	DYRK1A	100
DZIP1L	100	EBP	100	ECHS1	100
EDA	100	EDA2R	100	EDAR	100
EDC3	100	EDN1	100	EDN3	100
EDNRA	100	EDNRB	100	EED	100
EEF1A2	100	EFEMP1	100	EFEMP2	100
EFL1	100	EFNB1	100	EFTUD2	100
EGFR	100	EHMT1	100	EIF2AK3	100
EIF2AK4	100	EIF4G1	100	EIF4H	100
EIF5A	100	ELANE	100	ELMO2	100
ELN	100	ELOVL4	100	ELP1	100
EMC10	100	EMD	100	ENG	100
ENPP1	100	EOGT	100	EP300	100

EPAS1	100	EPB41L1	100	EPB42	100
EPCAM	100	EPG5	100	EPHB4	100
EPHX2	100	EPM2A	100	EPOR	100
ERAP1	100	ERBB4	100	ERCC1	100
ERCC2	100	ERCC3	100	ERCC4	100
ERCC8	100	ERGIC1	100	ERLIN2	100
ERMARD	100	ESCO2	100	ESR1	100
ETFA	100	ETFB	100	ETFDH	100
ETHE1	100	ETV6	100	EVC	100
EVC2	100	EXOC2	100	EXOC6B	100
EXOSC2	100	EXOSC3	100	EXPH5	100
EXT1	100	EXT2	100	EXTL3	100
EYA1	100	EYS	100	EZH2	100
EZR	100	F10	100	F11	100
F12	100	F13A1	100	F2	100
F7	100	F8	100	F9	100
FAH	100	FAM111A	100	FAM111B	100
FAM161A	100	FAN1	100	FANCA	100
FANCB	100	FANCC	100	FANCD2	100
FANCE	100	FANCG	100	FANCI	100
FANCL	100	FANCM	100	FAR1	100
FARSA	100	FAS	100	FASTKD2	100
FAT4	100	FBLN1	100	FBLN5	100
FBN1	100	FBP1	100	FBXO31	100
FBXW11	100	FCGR2B	100	FDFT1	100
FDPS	100	FDXR	100	FECH	100
FERMT1	100	FERMT3	100	FEZF1	100
FGA	100	FGB	100	FGD1	100
FGF10	100	FGF12	100	FGF13	100
FGF14	100	FGF17	100	FGF20	100
FGF23	100	FGF3	100	FGF9	100
FGFR1	100	FGFR3	100	FGFRL1	100
FGG	100	FHL1	100	FHL2	100
FIG4	100	FITM2	100	FKBP10	100
FKBP14	100	FKBP6	100	FKRP	100
FKTN	100	FLCN	100	FLI1	100
FLII	100	FLNA	100	FLNB	100
FLRT1	100	FLRT3	100	FLT4	100
FLVCR2	100	FMR1	100	FN1	100
FOS	100	FOXC1	100	FOXC2	100
FOXE1	100	FOXF1	100	FOXG1	100
FOXL2	100	FOXN1	100	FOXP1	100
FOXP3	100	FOXRED1	100	FRAS1	100
FREM1	100	FREM2	100	FRG1	100
FRMPD4	100	FRRS1L	100	FSCN2	100
FSHB	100	FSHR	100	FTL	100
FTO	100	FUS	100	FUT8	100
FUZ	100	FYB1	100	FZD2	100
FZD4	100	FZD6	100	G6PC3	100
G6PD	100	GABRA1	100	GABRA2	100
GABRA3	100	GABRA5	100	GABRB2	100
GABRB3	100	GABRG2	100	GALC	100
GALK1	100	GALM	100	GALNT3	100
GAN	100	GAS8	100	GATA1	100
GATA2	100	GATA3	100	GATA4	100
GATA5	100	GATA6	100	GATAD1	100
GBE1	100	GCDH	100	GCLC	100
GDF11	100	GDF3	100	GDF5	100
GDF6	100	GFI1B	100	GFM1	100
GGCX	100	GHR	100	GIGYF2	100
GINS1	100	GJA1	100	GJB2	100
GJB6	100	GLA	100	GLB1	100
GLE1	100	GLI1	100	GLI2	100

GLI3	100	GLRX5	100	GLS	100
GMPPA	100	GMPPB	100	GNA11	100
GNA14	100	GNAO1	100	GNAQ	100
GNAS	100	GNB2	100	GNE	100
GNPTAB	100	GNRH1	100	GNRHR	100
GNS	100	GP1BA	100	GP1BB	100
GP6	93.51	GP9	100	GPC3	100
GPC4	100	GPC6	100	GPI	100
GPKOW	100	GPNMB	100	GPR101	100
GPR143	100	GPR35	100	GPX4	100
GREM1	100	GRHL2	100	GRIA3	100
GRIA4	100	GRIK2	100	GRIN1	100
GRIN2B	100	GRIN2D	100	GRIP1	100
GRM1	100	GRM7	100	GSC	100
GSN	100	GTF2E2	100	GTF2H5	100
GTF2I	100	GTF2IRD1	100	GTF2IRD2	100
GTPBP2	100	GTPBP3	100	GUCA1A	100
GUCA1B	100	GUCY2D	100	GUF1	100
GUSB	100	GYPC	100	HAMP	100
HAND2	100	HAVCR2	100	HBA1	100
HBA2	100	HBB	100	HBG1	100
HBG2	100	HCCS	100	HCN1	100
HDAC4	100	HDAC6	100	HDAC8	100
HEPHL1	100	HERC2	100	HESX1	100
HEXB	100	HEY2	100	HFE	100
HGD	100	HGSNAT	95.65	HHAT	100
HIC1	100	HINT1	100	HIRA	100
HIVEP2	100	HLA-B	100	HLA-C	100
HLA-DPA1	100	HLA-DPB1	100	HLA-DQA1	100
HLA-DQB1	100	HLA-DRA	100	HLA-DRB1	100
HLCS	100	HMBS	100	HMGA2	100
HMOX1	100	HNF1A	100	HNF1B	100
HNF4A	100	HNMT	100	HNRNPH2	100
HNRNPK	100	HOXA11	100	HOXA13	100
HOXC13	100	HPD	100	HPDL	100
HPGD	100	HPS3	100	HPS4	100
HPS5	100	HR	100	HS3ST6	100
HS6ST1	100	HSD17B10	100	HSD3B7	100
HSPA9	100	HSPG2	100	HTRA2	100
HTT	100	HUWE1	100	HYAL1	100
HYDIN	100	HYLS1	100	HYOU1	100
ICOS	100	IDH1	100	IDH2	100
IDH3A	100	IDH3B	100	IDS	100
IDUA	100	IFIH1	100	IFNG	100
IFNGR1	100	IFT122	100	IFT140	100
IFT172	100	IFT27	100	IFT43	100
IFT52	100	IFT57	100	IFT74	100
IFT88	100	IGF1	100	IGF1R	100
IGF2	100	IGHMBP2	100	IGLL1	100
IHH	100	IKBKB	100	IKBKG	100
IKZF1	100	IKZF3	100	IL10RA	100
IL10RB	100	IL11RA	100	IL12A	100
IL12B	100	IL12RB1	100	IL17F	100
IL17RA	100	IL17RC	100	IL17RD	100
IL18BP	100	IL1RAPL1	100	IL1RN	100
IL2RB	100	IL2RG	100	IL31RA	100
IL36RN	100	IL4R	100	IL6	100
IL6ST	100	IL7	100	IL7R	100
IMPDH1	100	IMPG1	100	IMPG2	100
ING1	100	INPP5K	100	INPPL1	100
INSR	100	INTU	100	IPO8	100
IQSEC1	100	IQSEC2	100	IRAK1	100
IREB2	100	IRF4	100	IRF5	100
IRX5	100	ITCH	95.46	ITGA2	100

ITGA2B	100	ITGA3	100	ITGA6	100
ITGB2	100	ITGB4	100	ITGB6	100
ITPR2	100	IVD	100	IYD	100
JAG1	100	JAK2	100	JAK3	100
JAM2	100	JARID2	100	JRK	100
JUP	100	KANK2	100	KANSL1	100
KAT6A	100	KAT8	100	KATNB1	100
KCNA1	100	KCNA2	100	KCNB1	100
KCNJ11	100	KCNJ2	100	KCNJ5	100
KCNJ6	100	KCNJ8	100	KCNK4	100
KCNK9	100	KCNN4	100	KCNQ1	100
KCNQ2	100	KCNQ3	100	KCNQ5	100
KCTD1	100	KDM4B	100	KDM5C	100
KDM6A	100	KDM6B	100	KDR	100
KDSR	100	KEAP1	100	KIAA0586	100
KIAA0753	100	KIAA1549	100	KIF12	100
KIF15	100	KIF1A	100	KIF22	100
KIF23	100	KIF3B	100	KIF5A	100
KIF7	100	KIRREL3	100	KISS1	100
KISS1R	100	KIT	100	KITLG	100
KIZ	100	KLC2	100	KLF1	100
KLF13	100	KLHL24	100	KLHL7	100
KMT2A	100	KMT2C	100	KMT2D	100
KMT2E	100	KNG1	100	KNL1	99.51
KNSTRN	100	KPNA3	100	KRAS	100
KREMEN1	100	KRIT1	100	KRT1	100
KRT10	100	KRT13	100	KRT14	100
KRT16	100	KRT17	100	KRT18	100
KRT2	100	KRT25	100	KRT4	100
KRT5	100	KRT6A	100	KRT6B	100
KRT6C	100	KRT71	100	KRT74	100
KRT8	100	KRT81	100	KRT83	100
KRT85	100	KRT86	100	KRT9	100
KYNU	100	LACC1	100	LAMA1	100
LAMA3	100	LAMA4	100	LARGE1	100
LARP7	100	LCA5	100	LCP2	100
LDHA	100	LDLR	100	LEMD2	100
LEMD3	100	LETM1	100	LHB	100
LHCGR	100	LHX3	100	LIFR	100
LIG4	100	LIMK1	100	LINS1	100
LIPC	100	LIPE	100	LIPH	100
LIPT2	100	LMAN1	100	LMAN2L	100
LMBRD1	100	LMBRD2	100	LMF1	100
LMNB1	100	LMNB2	100	LMX1B	100
LONP1	100	LOX	100	LPAR6	100
LPIN2	100	LPL	100	LRAT	100
LRBA	100	LRP1	100	LRP2	100
LRP4	100	LRP5	100	LRPPRC	100
LRRC32	100	LRRC8A	100	LRRK2	100
LSS	100	LTBP1	100	LTBP2	100
LTBP3	100	LTBP4	100	LYZ	100
LZTFL1	100	LZTR1	100	MAB21L1	100
MADD	100	MAF	97.12	MAFB	100
MAGEL2	100	MALT1	100	MAN1B1	100
MAN2B1	100	MANBA	100	MAOA	100
MAP1B	100	MAP2K1	100	MAP2K2	100
MAP3K1	96.36	MAP3K7	100	MAPK1	100
MAPK8IP3	100	MAPRE2	100	MASP1	100
MAT2A	100	MAX	100	MBD5	100
MBOAT7	100	MBTPS2	100	MC2R	100
MC4R	100	MCCC2	100	MCFD2	100
MCM4	100	MCOLN1	100	MCTP2	100
MDH2	100	MDM2	100	MECR	100

MED12	100	MED12L	100	MED13	100
MED13L	100	MED23	100	MED25	100
MED27	100	MEFV	100	MEGF8	100
MEIS2	100	MEN1	100	MEOX1	100
MERTK	100	METTL23	100	METTL27	100
MFAP5	100	MFRP	100	MGAT2	100
MGMT	100	MGP	100	MID1	100
MITF	100	MKKS	100	MKRN3	100
MKS1	100	MLH1	100	MLH3	100
MLPH	100	MLX	100	MLXIPL	100
MMADHC	100	MMP1	100	MMP14	100
MMP2	100	MMP23B	100	MNX1	100
MOGS	100	MORC2	100	MPDU1	100
MPEG1	100	MPI	100	MPLKIP	100
MPV17	100	MRAP	100	MRAS	100
MRM2	100	MRPS22	100	MS4A1	100
MS4A2	100	MSH2	100	MSH3	100
MSH6	100	MSL3	100	MSMO1	100
MSN	100	MST1	100	MSTO1	100
MSX1	100	MSX2	100	MTFMT	100
MTHFD1	100	MTTP	100	MTX2	100
MUSK	100	MVD	100	MVK	100
MYBPC3	100	MYC	100	MYD88	100
MYH11	100	MYH3	100	MYH6	100
MYH7	100	MYH9	100	MYLK	100
MYO18B	100	MYO5A	100	MYO5B	100
MYO9A	100	MYOD1	100	MYT1L	100
NAA10	100	NAA20	100	NABP1	100
NADSYN1	100	NAGA	100	NAGLU	100
NALCN	100	NANS	100	NAXD	100
NBAS	100	NBEA	100	NBEAL2	100
NBN	100	NCAPG2	100	NCF1	100
NCF4	100	NCKAP1L	100	NDE1	100
NDN	100	NDNF	100	NDP	100
NDST1	100	NDUFA1	100	NDUFA10	100
NDUFA12	100	NDUFA2	100	NDUFA4	100
NDUFA6	100	NDUFA9	100	NDUFAF1	100
NDUFAF2	100	NDUFAF3	100	NDUFAF4	100
NDUFAF5	100	NDUFAF6	100	NDUFAF8	100
NDUFB10	100	NDUFB11	100	NDUFB3	100
NDUFB9	100	NDUFS1	100	NDUFS3	100
NDUFS4	100	NDUFS6	100	NDUFS7	100
NDUFS8	100	NDUFV1	100	NDUFV2	100
NECAP1	100	NECTIN1	100	NEDD4L	100
NEK1	100	NEK9	100	NELFA	100
NEMF	100	NEPRO	100	NEU1	100
NEUROD2	100	NEXN	100	NF1	100
NF2	100	NFE2L2	100	NFIX	100
NFKB1	100	NFKBIA	100	NGLY1	100
NHLRC1	100	NHP2	100	NIPAL4	100
NIPBL	100	NKX2-5	100	NLRC4	100
NLRP1	100	NLRP12	100	NME8	100
NNT	100	NOD2	100	NOG	100
NONO	100	NOP10	100	NOTCH1	100
NOTCH2	100	NOTCH3	100	NOVA2	100
NPAP1	100	NPC1	100	NPC2	100
NPHP1	100	NPHP3	100	NPM1	100
NPR2	100	NPRL2	100	NPRL3	100
NR0B1	100	NR1H4	100	NR2E3	100
NR3C1	100	NR5A1	100	NRL	100
NSD1	100	NSD2	100	NSDHL	100
NSMCE2	100	NSMF	100	NSUN2	100
NTHL1	100	NTNG2	100	NTRK2	100

NUBPL	100	NUMA1	100	NUP107	100
NUP188	100	NUP62	100	NUP85	100
NUP88	100	NUS1	100	NUTM1	100
NXN	100	OCA2	100	OCLN	100
OCRL	100	ODC1	100	OFD1	100
OGT	100	OPA1	100	OPHN1	100
ORC6	100	OSMR	100	OTUD5	100
OTUD6B	100	OTULIN	100	OTX2	100
P4HA2	100	PACS1	100	PACS2	100
PAFAH1B1	100	PAH	100	PAK3	100
PALB2	100	PALLD	100	PANK2	100
PARK7	100	PARN	100	PAX1	100
PAX3	100	PAX6	100	PAX8	100
PCCA	100	PCCB	100	PCDH19	100
PCGF2	100	PCK1	100	PCNA	100
PCNT	100	PCSK1	100	PDCD10	100
PDE10A	100	PDE11A	100	PDE4D	100
PDE6A	100	PDE6B	100	PDE6G	100
PDE8B	100	PDGFB	100	PDGFRB	100
PDHA1	100	PDHB	100	PDHX	100
PDP1	100	PDSS2	100	PEPD	100
PERP	100	PEX1	100	PEX12	100
PEX13	100	PEX16	100	PEX2	100
PEX26	100	PEX3	100	PEX5	100
PEX6	100	PEX7	100	PFKM	100
PGAP1	100	PGAP2	100	PGAP3	100
PGM3	100	PHACTR1	99.71	PHF6	100
PHF8	100	PHIP	100	PHOX2B	100
PIEZO1	100	PIEZO2	100	PIGA	100
PIGB	100	PIGF	100	PIGG	100
PIGL	100	PIGN	100	PIGO	100
PIGP	100	PIGQ	100	PIGS	100
PIGT	100	PIGU	100	PIGW	100
PIGY	100	PIK3C2A	100	PIK3CA	100
PIK3R1	100	PITX1	100	PITX2	100
PKDCC	100	PKHD1	100	PKP1	100
PLA2G7	100	PLAA	100	PLAG1	100
PLAGL1	100	PLCB1	100	PLCB4	100
PLCD1	100	PLCG2	100	PLEC	100
PLG	100	PLIN1	100	PLK4	100
PLOD2	100	PLOD3	100	PLP1	100
PLVAP	100	PLXND1	100	PML	100
PMM2	100	PMS1	100	PMS2	100
PNKD	100	PNKP	100	PNPLA1	100
PNPLA6	100	PNPT1	100	POC1A	100
PODXL	100	POFUT1	100	POGLUT1	100
POLA1	100	POLD1	100	POLE	100
POLG	100	POLG2	100	POLH	100
POLR1B	100	POLR1C	100	POLR1D	100
POLR3H	100	POLR3K	100	POMC	100
POMGNT2	100	POMK	100	POMP	100
POMT1	100	POMT2	100	POP1	100
POR	100	PORCN	100	POT1	100
POU1F1	100	POU2AF1	100	PPARG	100
PPM1D	100	PPP1CB	100	PPP1R17	100
PPP1R21	100	PPP2R1A	100	PPP2R3C	100
PPP2R5D	100	PPP3CA	100	PQBP1	100
PRCD	100	PRDM12	100	PRDM5	100
PRICKLE1	100	PRICKLE2	100	PRKACA	100
PRKACG	100	PRKAG2	100	PRKAR1A	100
PRKCD	100	PRKCSH	100	PRKD1	100
PRKG2	100	PRKRA	100	PRLR	100
PRMT7	100	PRNP	100	PROC	100
PROK2	100	PROKR2	100	PROM1	100

PROP1	100	PROS1	100	PRPF31	100
PRPF4	100	PRPF6	100	PRPF8	100
PRPH2	100	PRPS1	100	PRR12	100
PRSS1	100	PRSS12	100	PRTN3	100
PSAT1	100	PSEN1	100	PSMB10	100
PSMB8	100	PSMB9	100	PSMC3	100
PSMC3IP	100	PSMD12	100	PSMG2	100
PSTPIP1	100	PTCD3	100	PTCH1	100
PTDSS1	100	PTH1R	100	PTPN11	100
PTPN23	100	PTPN3	100	PTS	100
PUF60	100	PURA	97.83	PUS1	100
PUS3	100	PUS7	100	PYCR1	100
RAB11A	100	RAB11B	100	RAB23	100
RAB27A	100	RAB39B	100	RAB3GAP1	100
RAB7A	100	RABL3	100	RAC1	100
RAC2	100	RAD21	100	RAD51	100
RAD51C	100	RAF1	100	RAG1	100
RAG2	100	RAI1	100	RALGAPA1	100
RANBP2	100	RAPSN	100	RARA	100
RASA1	100	RASA2	100	RASGRP1	100
RASGRP2	100	RAX2	100	RB1	100
RBBP8	100	RBCK1	100	RBM10	100
RBM28	100	RBPJ	100	RDH11	100
RDH12	100	RDH5	100	RECQL4	100
REEP6	100	REV3L	100	RFC2	100
RFT1	100	RFWD3	100	RFXANK	100
RFXAP	100	RHAG	100	RHBDF2	100
RHO	100	RHOA	100	RHOH	100
RIN2	100	RINT1	100	RIPK1	100
RIPK4	100	RLBP1	100	RLIM	100
RNASEH2A	100	RNASEH2B	100	RNASEH2C	100
RNF113A	100	RNF125	100	RNF13	100
RNF168	100	RNF213	100	ROGDI	100
ROM1	100	ROR2	100	RORB	100
RP1	100	RP1L1	100	RP2	100
RP9	100	RPGRIP1	100	RPGRIP1L	100
RPL10	100	RPL15	100	RPL18	100
RPL21	100	RPL27	100	RPL31	100
RPL35	100	RPL35A	100	RPS14	100
RPS15A	100	RPS17	100	RPS19	100
RPS20	100	RPS23	100	RPS26	100
RPS28	100	RPS29	100	RPS6KA3	100
RPS7	100	RRAS	100	RRAS2	100
RREB1	100	RRM2B	100	RS1	100
RSPH1	100	RSPH3	100	RSPH4A	100
RSPH9	100	RSPO4	100	RSRC1	100
RTL1	100	RTN2	100	RTTN	100
RUNX1	100	RUNX2	100	RUSC2	100
RYR1	100	SAG	100	SALL1	100
SALL4	100	SAMD9	100	SAMHD1	100
SASH1	100	SATB1	100	SATB2	100
SBDS	100	SBF2	100	SCAPER	100
SCARB2	100	SCN10A	100	SCN11A	100
SCN1A	100	SCN1B	100	SCN2A	100
SCN3A	100	SCN4A	100	SCN5A	100
SCN8A	100	SCN9A	100	SCNN1A	100
SCNN1B	100	SCNN1G	100	SCO2	100
SDCCAG8	100	SDHA	100	SDHAF2	100
SDHD	100	SDR9C7	100	SEC23A	100
SEC23B	100	SEC63	100	SEMA3A	100
SEMA3E	100	SEMA4D	100	SEMA5A	100
SEPSECS	100	SERPINA1	100	SERPINA12	100
SERPINB7	100	SERPINB8	100	SERPINE1	100

SERPINF2	100	SERPING1	100	SET	100
SETBP1	100	SETD1A	100	SETD1B	100
SETD2	100	SETD5	100	SETX	100
SF3B1	100	SFTPB	100	SFTPC	100
SGCD	100	SGSH	100	SH2B1	100
SH2B3	100	SH3PXD2B	100	SHOX	100
SHROOM4	100	SIAH1	100	SIK3	100
SIL1	100	SIM1	100	SIN3A	100
SIN3B	100	SIX1	100	SIX5	100
SKIV2L	100	SLC10A1	100	SLC12A2	100
SLC12A3	100	SLC12A6	100	SLC13A5	100
SLC16A2	100	SLC17A5	100	SLC17A9	100
SLC19A3	100	SLC1A2	100	SLC1A3	100
SLC1A4	100	SLC20A2	100	SLC24A5	100
SLC25A1	100	SLC25A11	100	SLC25A13	100
SLC25A20	100	SLC25A3	100	SLC25A4	100
SLC26A2	100	SLC26A4	100	SLC27A4	100
SLC2A10	100	SLC2A2	100	SLC30A9	100
SLC33A1	100	SLC34A2	100	SLC35A1	100
SLC35A2	100	SLC35C1	100	SLC39A13	100
SLC39A14	100	SLC39A4	100	SLC40A1	100
SLC44A1	100	SLC45A2	100	SLC46A1	99.15
SLC4A1	100	SLC51A	100	SLC51B	100
SLC5A5	100	SLC5A7	100	SLC6A1	100
SLC6A19	100	SLC6A3	100	SLC6A8	100
SLC7A7	100	SLC9A7	100	SLCO1B1	100
SLCO2A1	100	SLFN14	100	SLITRK1	100
SLURP1	100	SLX4	100	SMAD2	100
SMAD3	100	SMAD4	100	SMARCA2	100
SMARCA4	100	SMARCAD1	100	SMARCAL1	100
SMARCB1	100	SMARCC2	100	SMARCD1	100
SMARCD2	100	SMARCE1	100	SMC1A	100
SMCHD1	100	SMG9	100	SMO	100
SMOC1	100	SMPD1	100	SMPD4	100
SMS	100	SNAI2	100	SNAP25	100
SNAP29	100	SNCA	100	SNRNP200	100
SNRPN	100	SNX10	100	SNX14	100
SON	100	SOS1	100	SOS2	100
SOST	100	SOX11	100	SOX18	100
SOX2	100	SOX3	100	SOX4	100
SOX6	100	SOX9	100	SP110	100
SPAG1	100	SPARC	100	SPATA5	100
SPATA5L1	100	SPATA7	100	SPECC1L	100
SPG11	100	SPIDR	100	SPINK1	100
SPINK5	100	SPINT2	100	SPOP	100
SPP1	100	SPR	100	SPRED1	100
SPRED2	100	SPRY4	100	SPTAN1	100
SPTB	100	SPTBN1	100	SPTLC1	100
SPTLC2	100	SRA1	100	SRC	100
SRCAP	100	SRD5A3	100	SREBF1	100
SRP54	100	ST14	100	ST3GAL3	100
ST3GAL5	100	STAG1	100	STAG2	100
STAMBP	100	STAR	100	STAT1	100
STAT2	100	STAT3	100	STAT4	100
STAT5B	100	STEAP3	100	STIM1	100
STK11	100	STK36	100	STK4	100
STS	100	STUB1	100	STX11	100
STX1A	100	STX3	100	STXBP1	100
STXBP2	100	SUCLA2	100	SUCLG1	100
SUFU	100	SUGCT	100	SULT2B1	100
SUMF1	100	SUOX	100	SUPT16H	100
SURF1	100	SUZ12	100	SYK	100
SYNCRIP	100	SYNE1	100	SYNE2	100
SYNGAP1	100	SYNJ1	100	SYT1	100

TAB2	100	TAC3	100	TACO1	100
TACR3	100	TAF1	100	TAF6	100
TALDO1	100	TANC2	100	TAOK1	100
TAP1	100	TAPBP	100	TASP1	100
TAT	100	TBC1D20	100	TBCD	100
TBCK	100	TBL1XR1	100	TBL2	100
TBX1	100	TBX15	100	TBX2	100
TBX20	100	TBX3	100	TBX4	100
TBX6	100	TBXA2R	98.66	TCAP	100
TCF12	100	TCF20	100	TCF3	100
TCF4	100	TCIRG1	100	TCOF1	100
TCTN1	100	TCTN2	100	TECPR2	100
TECR	100	TEK	100	TELO2	100
TERF2IP	100	TERT	100	TET2	100
TFAP2A	100	TFE3	100	TFR2	100
TFRC	100	TG	100	TGDS	100
TGFB1	100	TGFB3	100	TGFBR1	100
TGFBR2	100	TGM1	100	TGM3	100
TGM5	100	THOC2	100	THOC6	100
THPO	100	THRA	100	THSD1	100
TIMMDC1	100	TINF2	100	TJP2	100
TKT	100	TLK2	100	TLL1	100
TLR4	100	TMC6	100	TMC8	100
TMEM107	100	TMEM126A	100	TMEM126B	100
TMEM127	100	TMEM138	100	TMEM216	100
TMEM231	100	TMEM237	100	TMEM260	100
TMEM270	100	TMEM43	100	TMEM67	100
TMEM94	100	TMEM98	100	TMPO	100
TMPRSS6	100	TMTC3	100	TNFAIP3	100
TNFRSF10B	100	TNFRSF11A	100	TNFRSF11B	100
TNFRSF13B	100	TNFRSF13C	100	TNFRSF1A	100
TNFRSF4	100	TNFSF11	100	TNFSF15	100
TNIK	100	TNNC1	100	TNNI2	100
TNNI3	100	TNNT3	100	TNPO3	100
TNRC6B	100	TNXB	100	TOM1	100
TOP3A	100	TOPORS	100	TOR1A	100
TP53	100	TP63	100	TPI1	100
TPM1	100	TPM2	100	TPO	100
TPP2	100	TRAF3IP2	100	TRAF6	100
TRAF7	100	TRAIP	100	TRAK1	100
TRAPPC11	100	TRAPPC4	100	TRAPPC9	100
TREX1	100	TRH	100	TRHR	100
TRIM37	100	TRIO	99.72	TRIP12	100
TRIP13	100	TRIP4	100	TRMT1	100
TRMT10A	100	TRMU	100	TRNT1	100
TRPM1	100	TRPM3	100	TRPM4	100
TRPS1	100	TRPV3	100	TRRAP	100
TSC1	100	TSC2	100	TSEN2	100
TSEN34	100	TSEN54	100	TSHB	100
TSHR	100	TSPAN12	100	TSPEAR	100
TSR2	100	TTC26	100	TTC37	100
TTC5	100	TTC7A	100	TTC8	100
TTI2	100	TTN	100	TTPA	100
TUB	100	TUBB	100	TUBGCP6	100
TULP1	100	TUSC3	100	TWIST1	100
TWIST2	100	TXN2	100	TXNDC15	100
TXNL4A	100	TXNRD2	100	TYR	100
TYRP1	100	UBA1	100	UBA5	100
UBAC2	100	UBAP1	100	UBE2A	100
UBE3A	100	UBE3B	100	UBE4A	100
UBR1	100	UBR7	100	UCHL1	100
UCP2	100	UFSP2	100	UGDH	100
UGP2	100	UMPS	100	UNC13D	100

UNC45A	100	UNC80	100	UQCC2	100
UQCRFS1	100	USB1	100	USF3	100
USP18	100	USP53	100	USP8	100
USP9X	100	UVSSA	100	VAC14	100
VAMP1	100	VAMP7	100	VDR	100
VEGFC	100	VHL	100	VIPAS39	100
VPS13A	100	VPS13B	100	VPS13C	100
VPS33B	100	VPS35	100	VPS37A	100
VPS37D	100	VPS51	100	VPS53	100
VSX1	100	VWF	100	WAS	100
WASF1	100	WBP11	100	WDFY3	100
WDPCP	100	WDR1	100	WDR19	100
WDR35	100	WDR45	100	WDR73	100
WDR81	100	WFS1	100	WIPF1	100
WIPI2	100	WNK1	100	WNT10A	100
WNT10B	100	WNT5A	100	WNT7A	100
WRAP53	100	WRN	100	WT1	100
WWOX	100	XIAP	100	XPA	100
XPC	100	XPNPEP2	100	XRCC2	100
XRCC4	100	XYLT1	100	XYLT2	100
YIF1B	100	YWHAE	100	YWHAG	100
YY1	100	ZAP70	100	ZBTB16	100
ZBTB20	100	ZC3H14	100	ZC4H2	100
ZEB2	100	ZFHX2	100	ZFHX4	100
ZFPM2	100	ZFYVE26	100	ZIC1	100
ZIC2	100	ZIC3	100	ZMPSTE24	100
ZMYM2	100	ZMYND10	100	ZNF292	100
ZNF341	100	ZNF407	100	ZNF408	100
ZNF462	100	ZNF469	100	ZNF513	100
ZNF592	100	ZNF699	100	ZNF711	100
ZNFX1	100	ZPR1	100	ZSWIM6	98.88

TABLE 3: Expression analysis of other genes in ED

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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