All KCTD7 mutations for bi-allelic KCTD7 patients and family members

last updated Jan. 2018

All new and published patient mutations				Patient mutations affecting CpG	Sequenced family members				Predicted effects of patient mutations on disease pathogenesis						# of online tools predicting pathogenicity	Family variants also listed at ExAC				Patient mutations present in ExAC	Allele frequency from ExAC	# mut alleles of seq'd family members at ExAC
									Phenotype predictions				SIFT predictions			ExAC 2016 - Allele number						
Patient number	Zygosity	Nucleotide	Protein		Mother	Father	Other family members	Total with seq data	PolyPhen2	HumDiv	PolyPhen2	HumVar	Score	Prediction	PROVEAN predictions Score Prediction	Nucleotide	Protein	Hetz	Homz			
1	Cmpd het	c.190A>G	T64A		het c.631C>T	het c.190A>G		1	0.999	Probably damaging	0.986	Probably damaging	0	Damaging	-4.693 Deleterious	4 of 4	c.190A>G	T64A	9	0	1	0.00007415	1
				gain CpG													c.192A>G	T64T	7	0			
2	Cmpd het	c.208C>T	R70W	lost CpG	het c.251G>A	het c.208C>T		1	0.998	Probably damaging	0.849	Possibly damaging	0.03	Damaging	-6.175 Deleterious	3 of 4			0	0		0	
				lost CpG					0.615	Possibly damaging	0.166	Benign					c.209G>A	R70Q	2	0		0.00001648	
3	Cmpd het	c.250C>T	R84W	lost CpG	het del Exons3-4	het c.250C>T	1 WT sib	2	1.000	Probably damaging	0.999	Probably damaging	0	Damaging	-4.869 Deleterious	4 of 4	c.250C>T	R84W	1	0	1	0.000008239	2
2	Cmpd het	c.251G>A	R84Q	lost CpG	het c.251G>A	het c.208C>T		1	0.999	Probably damaging	0.969	Probably damaging	0.16	Tolerated	-0.984 Neutral	2 of 4	c.251G>A	R84Q	1	0	1	0.000008239	1
4,5	Homz	c.280C>T	R94W	lost CpG	het c.280C>T	het c.280C>T		2	0.125	Benign	0.094	Benign	0.37	Tolerated	-6.917 Deleterious	1 of 4 ✓	c.280C>T	R94W	1	0	1	0.000008239	2
6,7,8	Homz	c.295C>T	R99X stop		het c.295C>T (2)	het c.295C>T (2)	het c.295C>T	5	Stop		Stop		Stop		Stop	Stop			0	0		0	
																	c.295C>A	R99R	2	0		0.00001648	
9,10	Cmpd het	c.314G>A	G105E		het c.314G>A	het c.341G>A	(1 normal sib)	1	0.588	Possibly damaging	0.475	Possibly damaging	0.97	Tolerated	-2.346 Neutral	0 of 4 ✓			0	0		0	
3	Cmpd het	del Ex3-4	D106 fs		het del Ex3-4	het c.250C>T		1	frameshift		frameshift		frameshift		frameshift	frameshift							
11,12,13	Homz	c.322C>A	L108M		het c.322C>A	het c.322C>A	het c.322C>A	3	1.000	Probably damaging	1.000	Probably damaging	0	Damaging	-1.965 Neutral	3 of 4			0	0		0	
14	Homz	c.334C>T	R112C	lost CpG	het c.334C>T	het c.334C>T		2	1.000	Probably damaging	1.000	Probably damaging	0	Damaging	-7.8 Deleterious	4 of 4	c.334C>T	R112C	2	0	1	0.00001648	2
				lost CpG					1.000	Probably damaging	1.000	Probably damaging					c.335G>A	R112H	1	0		0.000008239	
9,10	Cmpd het	c.341G>A	G114E		het c.314G>A	het c.341G>A		1	0.774	Possibly damaging	0.678	Possibly damaging	0.19	Tolerated	-1.943 Neutral	0 of 4 ✓			0	0		0	
																	c.342G>A	G114G	1	0		0.000008239	
15	Cmpd het	c.343G>T	D115Y		not reported			*	0.142	Benign	0.216	Benign	0.02	Damaging	-2.893 Deleterious	2 of 4			0	0		0	
				lost CpG					0.996	Probably damaging	0.953	Probably damaging					c.361C>T	R121C	8	0		0.0000659	
				lost CpG					0.141	Benign	0.112	Benign					c.362G>A	R121H	3	0		0.00002471	
16,17	Cmpd het	c.362G>T	R121L	lost CpG	het c.704G>C	het c.362G>T	(4 healthy sibs)	1	0.029	Benign	0.097	Benign	0.51	Tolerated	-0.245 Neutral	0 of 4✓	c.362G>T	R121L	1	0	1	0.000008238	1
									0.313	Benign	0.039	Benign					c.457C>G	R153G	1	0		0.000008239	
18	Homz	c.458G>A	R153H	lost CpG	het c.458G>A	het c.458G>A	(1 normal sib)	2	0.939	Possibly damaging	0.229	Benign	0.03	Damaging	-4.638 Deleterious	2 of 4	c.458G>A	R153H	5	0	1	0.00004119	2
19	Cmpd het	c.530G>A	R177H	lost CpG	het c.530G>A	het c.533C>T		1	0.996	Probably damaging	0.661	Possibly damaging	0.07	Tolerated	-1.183 Neutral	1 of 4 ✓			0	0		0	
19	Cmpd het	c.533C>T	A178V	lost CpG	het c.530G>A	het c.533C>T		1	0.901	Possibly damaging	0.277	Benign	0.19	Tolerated	-2.683 Deleterious	1 of 4 ✓	c.533C>T	A178V	3	0	1	0.00002474	1
																	c.534G>A	A178A	5	0		0.00004123	
20,21	Homz	c.536_543 del	V179 fs*22		consanguineous			2	frameshift		frameshift		frameshift		frame shift	frameshift			0	0		0	
22	Cmpd het	c.541C>T	R181W	lost CpG	het c.685G>T	het c.541C>T		1	0.915	Possibly damaging	0.522	Possibly damaging	0.18	Tolerated	-0.995 Neutral	0 of 4✓	c.541C>T	R181W	1	0	1	0.000008245	1
				lost CpG					0.008	Benign	0.004	Benign					c.542G>A	R181Q	2	0		0.00001649	
23,24	Homz	c.550C>T	R184C	lost CpG	het c.550C>T	het c.550C>T	het c.550C>T (2)	4	1.000	Probably damaging	0.985	Probably damaging	0.01	Damaging	-4 Deleterious	4 of 4	c.550C>T	R184C	2	0	1	0.00001649	4
				lost CpG					0.999	Probably damaging	0.98	Probably damaging					c.551G>A	R184H	1	0		0.000008243	
25,26	Homz	c.594delC	I199 fs		het c.594delC (2)	het c.594delC (2)	(1 parent by cons	4	frameshift		frameshift		frameshift		frameshift	frameshift			0	0		0	
27	Cmpd het	c.614C>T	P205L	lost CpG	het c.776T>A	het c.614C>T		1	0.999	Probably damaging	0.997	Probably damaging	0.23	Tolerated	-1.824 Neutral	2 of 4	c.614C>T	P205L	2	0	1	0.00001648	1
1	Cmpd het	c.631C>T	R211X stop	lost CpG	het c.631C>T	het c.190A>G		1	Stop		Stop		Stop		Stop	Stop	c.631C>T	R211X	1	0	1	0.000008238	1
				lost CpG					0.993	Probably damaging	0.565	Possibly damaging					c.632G>A	R211Q	1	0		0.000008238	
				lost CpG					0.996	Probably damaging	0.839	Possibly damaging					c.632G>C	R211P	1	0		0.000008238	
22	Cmpd het	c.685G>T	D229Y		het c.685G>T	het c.541C>T		1	0.999	Probably damaging	0.995	Probably damaging	0.11	Tolerated	-0.549 Neutral	2 of 4			0	0		0	
28,29	Cmpd het	c.685G>T	D229Y		het c.812T>A	het c.685G>T	het c.685G>T	2	0.999	Probably damaging	0.995	Probably damaging	0.11	Tolerated	-0.549 Neutral	2 of 4			0	0		0	
				gain CpG													c.687T>C	D229D	17	0		0.0001401	
30,31	Homz	c.696delT	F232 fs		het c.696delT	het c.696delT		2	frameshift		frameshift		frameshift		frameshift	frameshift			0	0		0	
16,17	Cmpd het	c.704G>C	W235S	gain CpG	het c.704G>C	het c.362G>T		1	0.998	Probably damaging	0.991	Probably damaging	0	Damaging	-10.267 Deleterious	4 of 4			0	0		0	
27	Cmpd het	c.776T>A	V259E		het c.776T>A	het c.614C>T		1	0.421	Benign	0.107	Benign	0	Damaging	-3.492 Deleterious	2 of 4			0	0		0	
28,29	Cmpd het	c.812T>A	L271H		het c.812T>A	het c.685G>T	het c.812T>A	2	0.999	Probably damaging	0.993	Probably damaging	0.3	Tolerated	-0.387 Neutral	2 of 4	c.812T>A	L271H	1	0	1	0.000008269	2
15	Cmpd het	c.818A>T	N273I		not reported			*	0.838	Possibly damaging	0.278	Benign	0.04	Damaging	-1.52 Neutral	1 of 4 ✓			0	0		0	
32	Homz	c.818A>T	N273I		het c.818A>T	het c.818A>T		2	0.838	Possibly damaging	0.278	Benign	0.04	Damaging	-1.52 Neutral	1 of 4 ✓			0	0		0	
33,34,35	Homz	c.827A>G	Y276C		het c.827A>G	het c.827A>G	3 het+1WT sib	6	0.999	Probably damaging	0.990	Probably damaging	0.14	Tolerated	-1.439 Neutral	2 of 4	c.827A>G	Y276C	1	0	1	0.000008294	6
36,37	Homz	c.861_863 del	W289X	gain CpG	consanguineous			2	Stop		Stop		-	Stop/Tolerate	-7.448 Deleterious	Stop						0	
															-15.05 Deleterious		c.863G>A	W288X	1	1		0.000008395	
		30 unique DNA mutations		Total: 25				Total	57								Number of patient mutations in ExAC				14		27
		18 new mutations this study		15 of 30 affect CpG																			
				11 of 12 affect arginines																			

Key:

New KCTD7 patients
Published KCTD7 patients
KCTD7 patient mutations listed in ExAC for >1 individual
Other ExAC mutations at the same codon as patients
Patient mutations listed elsewhere in table (not counted in totals)

ExAC data source:	http://exac.broadinstitute.org/transcript/ENST00000275532
PolyPhen2:	http://genetics.bwh.harvard.edu/pph2/
SIFT:	http://sift.jcvi.org/www/SIFT_enst_submit.html
PROVEAN:	http://provean.jcvi.org/seq_submit.php http://provean.jcvi.org/help.php#protein_batch_input_format

SUMMARY:	Family members	Genotype	Number with EPM3	Description
	41	hetz	0	sequenced parents
	1	hetz	0	sequenced grandparent of patients 23 and 24
	8	hetz	0	sequenced siblings
	2	homoz WT	0	sequenced siblings
	5	rec geneology	0	four parents (families 15 and 25) with known consanguinity
Subtotal	57			All related family members with genetic evidence
	6	ND	0	other known unaffected siblings without sequence data
Exception:	2			Parents of published patient 15 (family 11) have no available sequence data.

NOTES:

Note 1: published patient 13 (family 9) is not known to be related to patients 11 and 12 (family 8) based on further communication with author Gilbert (Seaby et al.).

Note 2: published patients 6, 7 and 8 are from two nuclear families, four parents known to be related.

Note 3: published patients 25 and 26 are reported to have two different sets of parents from different families 18 and 19 (3 were sequenced).