

Supplementary Material

Supplementary tables:

Table S1

Table S2

Table S3

Table S4

Table S1. Forward and reverse primers sequences and additional data for sanger sequenced genes.

Patient	Gene	Sequenz Primer Forward	GC %	Sequenz Primer Reverse	GC %	Product size	Annealing Temp in °C
VCK 1	<i>FAT1</i>	ACATGACTTTCGTTTCATG GTTCT	39.10	GGACCAAATGGTGGGAG GAG	60.00	398	59
VCK 4	<i>FAT1</i>	GCTGGCGTATGCTACAG AGG	60.00	TGGACAGAATTTGTAACC TCACTG	41.70	750	60
VCK 6	<i>GLI1</i>	GGAACCTACAGCCAGTG TCC	60.00	TGCGATCTGTGATGGATG AGA	47.60	962	59
VCK 3	<i>AXIN1</i>	CCTCAGCACACGCTGTACG	63.16	GTGTCACAAGCTGCCTCC C	63.16	139	60
VCK 3	<i>DNAH2</i>	TCATCACCCACCATCTA CTCAG	50.00	CGCCGTTGATGAGGGTC	64.71	136	60
VCK 4	<i>IQCE</i>	GGTTCAGTGTCTCTTTTC TGGG	50.00	TGTGATCTGACTGGCTCT GC	55.00	139	60
VCK 4	<i>PGK2</i>	ATTGACAGGACCATGAG CCA	50.00	CGGATGCTTTATGGGGCA GA	55.00	761	60
VCK 5	<i>FAT2</i>	CCGTCTCCATGACCGTA AAG	55.00	ATCAAGGCAACAGACAG TGG	50.00	139	60
VCK 5	<i>FAT4</i>	TGATAACAACCCCATCT TTGC	42.86	CACCTGTGACAGAGTCTA TCCG	54.55	185	60
VCK 5	<i>CATSP ERG</i>	ACACGAGCACCTACTGCAAC	55.00	CCCACCCAGTAGGGCAG	70.59	128	60
VCK 5	<i>EFHC1</i>	GCCAAGTTGAACTCCCT ACTTTTAG	44.00	GATAGTAATGAATGATGT AGGTCCG	40.00	137	60
VCK 10	<i>KREME N2</i>	GCAGTAACCCAGACGGT GAC	60.00	GTTCCACCTCTGTCCAG C	63.16	127	60
VCK 10	<i>AP2A2</i>	GTCTCATTGCCTGTGCTG TC	55.00	GTGCAGCTTCAGGAGCC	64.71	168	60
VCK 10	<i>EZR</i>	TCCTGACTTGCCTTCTTA TCC	47.62	CTCTCTCTCTCACGCAGG TG	60.00	124	60
VCK 11	<i>CCDC6 3</i>	CTGCTGAAGCTGGCTGA GAG	60.00	TCTCCATGTCGTTGTTGAG C	50.00	118	60
VCK 11	<i>DNAH1 1</i>	TCAGAAATTCTTGAGAA ACCCC	40.91	CCATAATCAATATGCTGC CG	45.00	164	60
VCK 11	<i>NPHP4</i>	CACACGAGCCAGGAGG C	70.59	CAAAGGTGTCTTCGTGCT GC	55.00	141	60
VCK 13	<i>PLCB3</i>	TTCTATACCCAGCCAGAGCC	55.00	CAGGACCTGCTGCTGCC	70.59	138	60
VCK 13	<i>CACNA 1F</i>	AACCGGATCCCAGGAA GTAG	55.00	TTCCATCATGAAGGCTCT GG	50.00	137	60
VCK 13	<i>POC1A</i>	GATGACGGGTGAACCCA C	61.11	GCAGGAGTGTGGAGTCTG TG	60.00	140	60
VCK 14	<i>OFD1</i>	TTTAGTCTGTGGAATA GACACAT	37.50	GCTTTCGGTCATAGGTCT CCT	52.38	196	60
VCK 14	<i>AES</i>	GAGGCTTCGGCTCCACC	70.59	tcacaagaatgGCTTCCCTC	50.00	406	60
VCK 14	<i>CACNA 1F</i>	GCCCTCTTCAGCCATAG AAC	55.00	GAAGCAGCAGATGGAGG AAG	55.00	118	60
VCK 15	<i>GNAT2</i>	ATCATAGGCACTGAGGG CTG	55.00	ATGAAAATAGCTGCTTCT TCCC	40.91	129	60
VCK 15	<i>ABCA4</i>	CCAGCCCAGGAGACTGA G	66.67	AGATGCCAAGGTGGTGAT TC	50.00	126	60
VCK 15	<i>SCNN1 A</i>	GCTGGAGGCCACGCTAC	70.59	CAGCTCCTTCACCACTCT CG	60.00	136	60
VCK 15	<i>TULP4</i>	GTCCTCTCCCTGACCGA AAG	60.00	CCTCCTTCTTCACTTTGCC C	55.00	133	60
VCK 16	<i>CTBP1</i>	ACTGGGACAGAGGCTGCTC	63.16	ACTGTGGCCTTCTGCGAC	61.11	177	60
VCK 16	<i>DNAH2</i>	TCATCACCCACCATCTA CTCAG	50.00	CGCCGTTGATGAGGGTC	64.71	136	60
VCK 16	<i>SPTBN 5</i>	CCTCTTCCCAGTGACCT G	63.16	TTCAAGGCCTGAGAAGC AAG	50.00	123	60

VCK 16	<i>TTL3</i>	GTGGTGAGTGTGGGCAG TC	63. 16	AGTAGCAGCGTGGGAAG AAG	55. 00	130	60
VCK 17	<i>IFT57</i>	GTGTTCCACAATGCCAA TTC	45. 00	TGGGCTTAAGACAAAGTG AGG	47. 62	182	60
VCK 17	<i>FAT4</i>	AAAAGCCAATGATCAA GCTG	40. 00	CTGATGGGTCTGCAGCAA G	57. 89	134	60
VCK 17	<i>CABYR</i>	CACATCTTTGAAAGGTC AGCC	47. 62	TCCTGCCAGTATTGTCA GAG	52. 38	135	60
VCK 17	<i>PKD1L 1</i>	GCCAAATGCAGAAGAC AAGG	50. 00	GATGCCTGTTTGGGACA AG	50. 00	152	60
VCK 18	<i>LRP5</i>	GCCTGGCTGAGTATTTCC CTT	52. 38	CGGTCCAGTAGAGGTTTC GG	60. 00	383	60
VCK 18	<i>CC2D2 A</i>	TTTTCTTAGAGTCCTGAT CCTGTT	40. 00	TCCATCAGACAGGTTTG GG	50. 00	140	60
VCK 18	<i>DNAH1</i>	GGCTACTGCAGGACCAA GTG	60. 00	TCCATGCAGCGCTTGAG	58. 82	127	60
VCK 18	<i>KIF19</i>	CACTGATCCTGCCCTTT C	57. 89	CCATCTTTGCCATGGGTG	55. 56	141	60
VCK 18	<i>PCDHB 8</i>	CTTCTCGGTGCTCCTGTT CG	60. 00	GAAAACAAGACAAATAC TATGGGCA	36. 00	414	60
VCK 18	<i>PKHD1 L1</i>	TACGGTCACACTCCCTG ATG	55. 00	TCAGCATTCCAAATTC CAC	38. 10	334	60
VCK 18	<i>RP1L1</i>	TACGCTACTCTCCCTGA GC	60. 00	ACTCAGGCCTCTGGGAGC	66. 67	140	60
VCK 18	<i>TCTN3</i>	GGTTGGTTTGTCCTCAA CTG	50. 00	GTCCTAAACATATTCGGC CC	50. 00	133	60
VCK 19	<i>LRP2</i>	GTGCGTCTCGTTTATCA GC	50. 00	CATTAGTAGGAAAATTGA TGCCTAC	34. 62	208	60
VCK 19	<i>ALMS1</i>	GAGTCTGAAATTAGGAG AGCTGTG	45. 83	AAGCGGTGCTGAGATA CAC	55. 00	281	60
VCK 19	<i>CENPJ</i>	CATACCACTCTTGCTCT GGC	52. 38	TCTTAGGTGATAATCTTGT GTTGG	37. 50	178	60
VCK 19	<i>DNAH1 0</i>	CCAGAACCTTGAAAATC CACC	47. 62	CTCTTGAAATCGGAGGAT GG	50. 00	115	60
VCK 19	<i>PKD1</i>	GCGTGAAAGTTGTGTGTC ACC	55. 00	ACATCACGTGGACCTTCG AC	55. 00	333	60
VCK 20	<i>CSNK1 G1</i>	AGCATTGAAACAAAGCC CTC	45. 00	CGGAGAGATGATTTGGA AGC	50. 00	120	60
VCK 20	<i>FAT4</i>	TGAAAACACACTTACTG GAACAG	39. 13	CACCTGTGACAGAGTCTA TCCG	54. 55	137	60
VCK 20	<i>APC2</i>	CACAGTCTCCCTTGTGTC CC	60. 00	GGTGGAGCTCCTCACTGT C	63. 16	130	60
VCK 20	<i>MMP7</i>	CTCATCGAAGTGAGCAT CTCC	52. 38	TTCTAGCCTCAATAATCG TATAAACTG	33. 33	190	60
VCK 20	<i>C2CD3</i>	GCCTTGATGGAACCTGA AAC	50. 00	GGGGACATTCCITACAAT CC	50. 00	272	60
VCK 20	<i>DNAH5</i>	CTGAAATTAGGGCAGGG AAC	50. 00	CAGGTGCCTTCTACCAA TG	55. 00	140	60
VCK 20	<i>DNAH1 1</i>	TGATAGAGGGAAGGAC CCAC	55. 00	ACATGTTGCATGGCATCT TC	45. 00	141	60
VCK 20	<i>SPEF2</i>	ATACAGCAGGCCAGAC AACC	55. 00	CATTAACAATTTCCGCCG TC	45. 00	137	60
VCK 20	<i>TCTEX 1D4</i>	TTTTGCAGAATTGGACTC CC	45. 00	TGCAGTGTGGTGCTGGG	64. 71	175	60
VCK 21	<i>IFT88</i>	TCAGAATTTTAAAGCTA ATCCATGTC	30. 77	CAGATTTGGTGCCATGCT C	52. 63	141	60
VCK 21	<i>DNAH1</i>	CCGAGTACGAGTGCTTC CAG	60. 00	AAGAGGAAGGTGATGGG TAGG	52. 38	121	60
VCK 21	<i>MAK</i>	CGGATTCATTACTCTTGC CC	50. 00	TTCAACAAGGAAGTCATT TCAATC	33. 33	132	60
VCK 22	<i>PTCH2</i>	CCTTCTACCCAGAGCTG TTCC	57. 14	GGGATCCAGAGACATTGT GG	55. 00	119	60
VCK 22	<i>SPEF2</i>	CATGTTCCGCATGAAAA GG	47. 37	CAAAATATAGCTTTGTTT ACCACG	33. 33	191	60

Table S2: Genetic variants in Shh-signalling pathway genes with predicted damaging potential in patient cohort, “-” shows no prediction was possible because of the frameshift or nonsense character of the genetic variant.

Gene	Variant	gnomAD allele frequency	PPH2	SIFT	Provean	Affected Patient
<i>GLI1</i>	c.3307delA p.N1103T fsTer7	~0.000006	-	-	-	VCK6
<i>PTCH2</i>	c.203G->T p.A68D	~0.00001	Probably damaging	Damaging	Deleterious	VCK22
	c.247C->T p.E83K	~0.00003	Probably damaging	Damaging	Deleterious	VCK1
<i>IFT172</i>	c.3400G->A p.R1134W	~0.0002	Probably damaging	Damaging	Deleterious	VCK1
<i>IFT57</i>	c.1119C->A p.L373F	~0.0001	Probably damaging	Damaging	Deleterious	VCK17
<i>IFT88</i>	c.884G->C p.G295A	Unknown	Probably damaging	Damaging	Deleterious	VCK21
<i>LRP2</i>	c.2356C->T p.V786I	~0.000008	Probably damaging	Tolerated	Neutral	VCK19
<i>CSNK1G1</i>	c.745G->A p.L249F	Unknown	Probably damaging	Damaging	Deleterious	VCK20
<i>DZIP1</i>	c.1033C->G p.D345H	Unknown	Probably damaging	Damaging	Deleterious	VCK2
<i>IQCE</i>	c.1045A->G p.K349E	Unknown	Probably damaging	Damaging	Deleterious	VCK4
<i>OFD1</i>	c.974_975insT p.E326*	Unknown	-	-	-	VCK14

Table S3: Genetic variants in Wnt-signalling pathway genes with predicted damaging potential in patient cohort, “-” shows no prediction was possible because of the frameshift or nonsense character of the genetic variant.

Gene	Variant	gnomAD allele frequency	PPH2	SIFT	Provean	Affected Patient
FAT1	c.4433 A->G p.I1478T	~0.00009	Possibly damaging	Damaging	Deleterious	VCK1
	c.12899 G->A p.A4300V	~0.00001	Probably damaging	Tolerated	Neutral	VCK4
FAT2	c.4028G->A p.S1343F	~0.000004	Probably damaging	Damaging	Deleterious	VCK5
FAT4	c.6532G->A p.A2178T	~0.0002	Possibly damaging	Damaging	Deleterious	VCK5
	c.4543G->A p.V1515M	~0.00005	Probably damaging	Damaging	Neutral	VCK17
	c.6562C->T p.Q2188Stop	Unknown	-	-	-	VCK20
APC2	c.1463G->A p.R488H	~0.0001	Probably damaging	Damaging	Deleterious	VCK20
MMP7	c.487G->A p.H163Y	~0.000004	Probably damaging	Damaging	Deleterious	VCK20
LRP5	c.1192C->T p.R398C	~0.00007	Probably damaging	Damaging	Deleterious	VCK18
CTBP1	c.204_205insA p.G69Rfs*78	~0.00002	-	-	-	VCK16
PLCB3	c.3418G->C p.E1140Q	~0.0002	Probably damaging	Tolerated	Neutral	VCK13
AXIN1	c.1378G->A p.R460W	~0.00005	Probably damaging	Damaging	Neutral	VCK3
SOX7	c.203C->T p.G68E	~0.00001	Probably damaging	Damaging	Deleterious	VCK6
KREMEN2	c.326T->G p.I109S	Unknown	Probably damaging	Damaging	Deleterious	VCK10
AP2A2	c.742A->G p.T248A	~0.000004	Probably damaging	Tolerated	Deleterious	VCK10
AES/TLE5	c.200C->T p.W67Stop	~0.00003	-	-	-	VCK14
GNAT2	c.633C->G p.W211C	Unknown	Probably damaging	Damaging	Deleterious	VCK15

Table S4: Genetic variants in ciliary genes with predicted damaging potential in patient cohort, “-” shows no prediction was possible because of the frameshift or nonsense character of the genetic variant.

Gene	Variant	gnomAD allele frequency	PPH2	SIFT	Provean	Affected Patient
ABCA4	c.3292G->A	~0.00002	Probably damaging	Damaging	Deleterious	VCK15
	p.R1098C					
ALMS1	c.770T->G	Unknown	Probably damaging	Damaging	Deleterious	VCK19
	p.I257S					
BBS10	c.1838T->C	~0.00003	Probably damaging	Damaging	Deleterious	VCK8
	p.Y613C					
C2CD3	c.519G->T	~0.00002	-	-	-	VCK20
	p.Y173Stop					
CABYR	c.941G->A	~0.000008	Probably damaging	Damaging	Neutral	VCK17
	p.G314D					
CACNA1F	c.761A->G	~0.00006	Probably damaging	Damaging	Deleterious	VCK13
	p.I254T					
	c.1234C->T	~0.00002	Probably damaging	Damaging	Deleterious	VCK14
	p.E412K					
CATSPERG	c.3193C->T	~0.00003	Probably damaging	Damaging	Deleterious	VCK5
	p.R1065W					
CC2D2A	c.3055C->T	~0.0001	-	-	-	VCK18
	p.R1019Stop					
CCDC63	c.983C->T	Unknown	Probably damaging	Damaging	Neutral	VCK11
	p.A328V					
CENPJ	c.3532G->A	~0.000008	-	-	-	VCK19
	p.R1178Stop					
CNGB3	c.1582C->A	~0.00001	-	-	-	VCK6
	p.E528Stop					
DNAH1	c.7441G->A	Unknown	Probably damaging	Damaging	Deleterious	VCK18
	p.V2481M					
	c.7865G->A	~0.0003	Probably damaging	Damaging	Deleterious	VCK21
	p.R2622Q					
DNAH2	c.4648C->T	~0.000004	-	-	-	VCK1
	p.R1550Stop					
	c.6528G->C	~0.00003	Probably damaging	Damaging	Deleterious	VCK3, VCK16
	p.E2176D					
DNAH5	c.11476G->A	~0.00034	Probably damaging	Damaging	Deleterious	VCK2
	p.L3826F					
	c.9244G->T	~0.0006	Probably damaging	Damaging	Neutral	VCK20
	p.L3082I					
DNAH10	c.1716A->G	~0.000008	Probably damaging	Damaging	Deleterious	VCK19
	p.I572M					
DNAH11	c.8452T->C	Unknown	Probably damaging	Tolerated	Deleterious	VCK20
	p.Y2818H					
	c.7729G->A	Unknown		Damaging	Deleterious	VCK11

	p.D2577N		Probably damaging			
DZIP1	c.1033C->G	Unknown	Probably damaging	Damaging	Deleterious	VCK2
	p.D345H					
EFHC1	c.737A->G	~0.000008	Probably damaging	Damaging	Deleterious	VCK5
	p.Y246C					
EZR	c.146T->C	~0.00002	Probably damaging	Damaging	Deleterious	VCK10
	p.Y49C					
GLI1	c.3307delA	~0.000006	-	-	-	VCK6
	p.N1103T fsTer7					
GNAT2	c.633C->G	Unknown	Probably damaging	Damaging	Deleterious	VCK15
	p.W211C					
IFT57	c.1119C->A	~0.0001	Probably damaging	Damaging	Deleterious	VCK17
	p.L373F					
IFT88	c.884G->C	Unknown	Probably damaging	Damaging	Deleterious	VCK21
	p.G295A					
IFT172	c.3400G->A	~0.0002	Probably damaging	Damaging	Deleterious	VCK1
	p.R1134W					
IQCE	c.1045A->G	Unknown	Probably damaging	Damaging	Deleterious	VCK4
	p.K349E					
KIF19	c.2920C->T	~0.00008	-	-	-	VCK18
	p.R974Stop					
KLC3	c.509G->A	~0.00007	Probably damaging	Tolerated	Neutral	VCK2
	p.R170H					
MAK	c.10_11insATCG	Unknown	-	-	-	VCK21
	p.T5Rfs*21					
NEK8	c.1223_1223delA	Unknown	-	-	-	VCK1
	p.D408Afs*6					
NPHP4	c.3895C->T	~0.0001	Probably damaging	Tolerated	Deleterious	VCK11
	p.G1299S					
OFD1	c.974_975insT	Unknown	-	-	-	VCK14
	p.E326*					
PCDHB8	c.2203G->A	~0.00001	Probably damaging	Damaging	Deleterious	VCK18
	p.G735R					
PCM1	c.3841A->C	~0.000008	Probably damaging	Damaging	Neutral	VCK9
	p.K1281Q					
PGK2	c.509T->A	~0.0005	Probably damaging	Damaging	Deleterious	VCK4
	p.H170L					
PKD1	c.3994C->T	~0.0002	Probably damaging	Tolerated	Deleterious	VCK19
	p.D1332N					
PKD1L1	c.5125C->G	~0.0002	Probably damaging	Damaging	Deleterious	VCK17
	p.G1709R					
PKHD1L1	c.7204T->C	~0.001	Probably damaging	Damaging	Deleterious	VCK18
	p.W2402R					
POC1A	c.1085G->A	~0.0002	Probably damaging	Damaging	Deleterious	VCK13
	p.T362M					
RP1L1	c.3569G->A	~0.0001		Damaging	Neutral	VCK18

	p.T1190M		Probably damaging			
SCNN1A	c.745G->A	~0.0001	Probably damaging	Damaging	Deleterious	VCK15
	p.R249C					
	c.744C->A	~0.0001	Probably damaging	Tolerated	Neutral	
	p.Q248H					
SPEF2	c.1159C->G	~0.00003	Probably damaging	Damaging	Deleterious	VCK22
	p.R387G					
	c.887G->A	~0.00001	Probably damaging	Damaging	Deleterious	VCK20
	p.R296H					
SPTBN5	c.4243G->C	~0.00004	Probably damaging	Damaging	Deleterious	VCK16
	p.L1415V					
TCTEX1D4	c.601A->G	~0.0001	Probably damaging	Damaging	Deleterious	VCK20
	p.S201P					
TCTN3	c.978A->C	Unknown	-	-	-	VCK18
	p.Y326Stop					
TTBK2	c.3418G->A	~0.00006	Probably damaging	Tolerated	Neutral	VCK7
	p.P1140S					
TTLL3	c.766C->T	~0.0001	Probably damaging	Damaging	Deleterious	VCK16
	p.R256W					
TULP4	c.4012C->G	Unknown	Probably damaging	Damaging	Deleterious	VCK15
	p.R1338G					