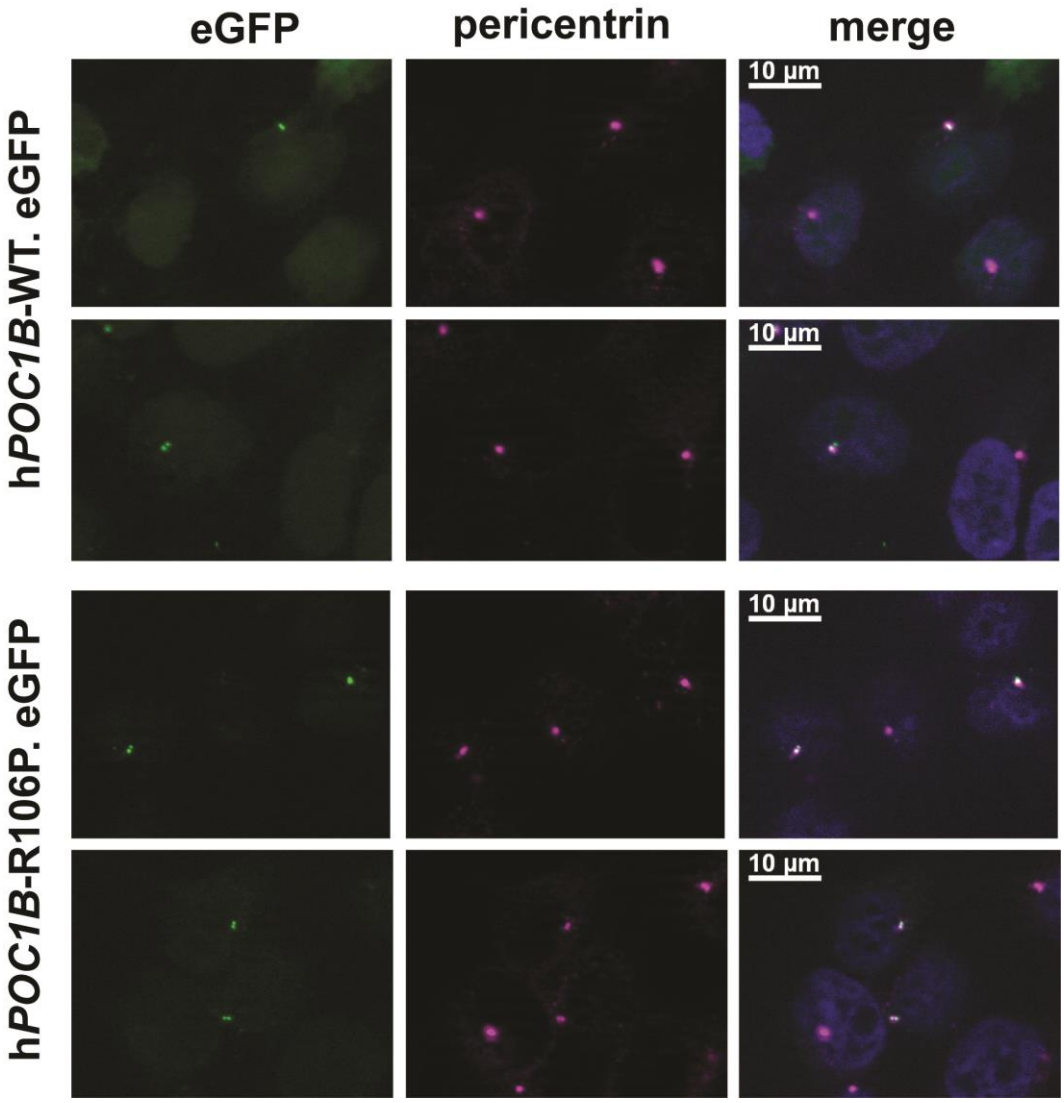
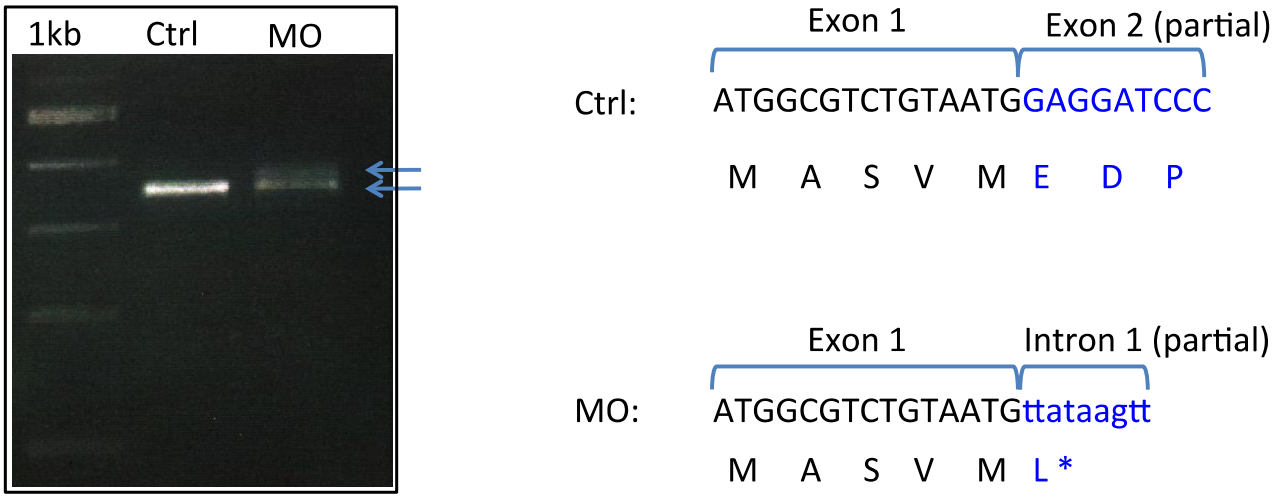


SUPP. FIGURE S1. Centrosomal localization of wild-type and mutant POC1B. HEK293T cells were transfected either with the h*POC1B*-WT.eGFP plasmid (containing wild-type *POC1B*) or with the h*POC1B*-R106P.eGFP (containing the mutation of the patient described herein, p.Arg106Pro). Immunofluorescence analysis reveals that mutant and wild-type POC1B both localize at the centrosome. The left panels show the localization of both h*POC1B*.eGFP fusion proteins (green). The middle panels show the localization of pericentrin, a centrosomal marker protein (magenta). The right panels show the merged images, DAPI was used to detect cell nuclei (blue). Scale bars = 10 µm.



SUPP. FIGURE S2. RT-PCR of cDNA from embryos injected with the *poc1b* splice blocking morpholino targeting the exon1/intron 1 boundary. 1 kB DNA ladder is in the left lane. In the control (center) lane, the normal transcript fragment size is approximately 360 bp. In the MO lane (right), the normal transcript is less abundant, and a slightly larger band is also observed (blue arrows). The larger band in the MO lane shown in A arises from a cryptic splice site in the first intron. Translation showing the early truncation resulting from this mis-splicing is shown to the right of the gel image.

SUPP. TABLE S1. Genes with two or more heterozygous rare variants from WES data of the index patient

Gene	Chr	Position (GRCh37)	RefSeq	Nucleotide alteration	Protein alteration	Variant name	Variant frequency	Sift	Polyphen	GERP	MutTast	Mendelian disease	ciliary/ centrosomal
HECTD3	1	45,475,886	NM_024602.5	c.610G>A	p.Val204Ile	rs41269097	0,0033	0.2	1	2.2	pat	unknown	no
		45,476,368		c.380C>G	p.Ala127Gly	-	0,0028	0.1	1	1.1	pol		
FAAH	1	46,874,246	NM_001441.2	c.1067C>T	p.Ala356Val	rs77101686	0,0016	na	3	5.4	pat	unknown	yes
		46,877,885		c.1427C>G	p.Ala476Gly	rs75429705	0,0015	0.76	1	4.7	pol		
LAMC1	1	183,079,729	NM_002293.3	c.961C>T	p.Pro321Ser	rs142614579	0,0005	na	3	4.9	pat	Dandy-Walker + occip. cephaloc. (ad)	no
		183,091,040		c.2173G>A	p.Ala725Thr	rs147401305	0,0005	0.79	1	1.5	pol		
DNAH14	1	225,268,346	NM_001373.1	c.3032G>T	p.Arg1011Leu	-	-	na	na	6.7	pol	unknown	likely (motile cilia)
		225,586,937		c.13514G>A	p.Arg4505Gln	rs45606432	0,0016	0.08	na	1.6	pol		
APOB	2	21,225,500	NM_000384.2	c.12794T>C	p.Val4265Ala	rs61743502	0,006	0,08	1	1.1	pol	hypobetalipo-protein. (ad)	no
		21,232,019		c.7721C>T	p.Ala2574Val	rs150843941	0,0003	0.02	2	5.2	pat		
OTOF	2	26,698,882	NM_194248.2	c.2891C>T	p.Ala964Glu	-	0,0001	0.52	1	5.4	pat	deafness (ar)	no
		26,700,288		c.2401_2402delinsTT	p.Glu801Leu	rs111033392	-	na	na	na	pat		
EVC2	4	5,633,668-5,633,676	NM_147127.4	c.1560_1562del	p.Glu520del	-	-	na	na	na	pol	Ellis-van Crefeld syndrome	yes
		5,667,334		c.913G>T	p.Ala305Ser	rs150367317	0,0005	na	3	5.3	pol		
		5,667,343		c.904T>A	p.Phe302Ile	rs138728350	0,0005	na	3	4.1	pol		
DNAH11	7	21,828,959	NM_003777.3	c.10046T>C	p.Val3349Ala	-	-	1	1	-7.6	pol	Kartagener syndrome (ar)	yes (motile cilia)
		21,847,518		c.10204C>G	p.Gln3402Glu	-	-	1	3	5.1	pol		
		21,940,816		c.13516G>A	p.Glu4506Lys	rs143362381	0,0022	1	1	0.5	pol		
C9orf174 (CCDC180)	9	100,092,918	NM_020893.2	c.2275G>C	p.Gly759Arg	rs79340881	0,0057	na	na	-0.7	pol	unknown	no
		100,133,973		c.4717G>A	p.Asp1573Asn	rs2306093	0,0057	na	na	5.3	pol		
ATN1	12	7,047,854	NM_001940.3	c.2728G>C	p.Ala910Pro	-	-	na	na	3.8	pat	DRPLA (ad)	no
		7,047,949		c.2823C>G	p.Asp941Glu	rs146691350	0,0023	na	na	0.4	pol		
SENP1	12	48,482,726	NM_001267594.1	c.238A>G	p.Ser80Gly	rs112688170	0,004	0.02	2	5.3	pol	unknown	no
		48,458,902		c.1221A>C	p.Gln407His	-	-	0.15	1	-2.2	pol		
TENC1	12	53,445,723	NM_015319.2	c.190G>A	p.Asp64Asn	-	-	na	na	5.4	pat	unknown	no
		53,453,014		c.1619G>A	p.Arg540Gln	rs186505042	0,004	na	na	4.6	pol		
NCOR2	12	124,815,439	NM_006312.5	c.6910A>G	p.Ser2304Gly	rs2228587	0,0067	na	na	4.7	pol	unknown	no

Gene	Chr	Position (GRCh37)	RefSeq	Nucleotide alteration	Protein alteration	Variant name	Variant frequency	Sift	Polyphen	GERP	MutTast	Mendelian disease	ciliary/ centrosomal
		124,957,669		c.420C>A	p.Ser140Arg	-	-	na	na	4.6	pat		
MYO5C	15	52,505,390	NM_018728.3	c.4136T>C	p.Ile1379Thr	-	-	0.01	3	5.4	pat	unknown	no
		52,539,165		c.1928C>T	p.Thr643Met	rs56250328	0,0008	0.05	3	4.4	pat		
NGRN	15	90,814,578	NM_001033088.1	c.434G>A	p.Gly145Glu	rs116320466	0,0009	0.18	na	2.7	pol	unknown	no
		90,814,944		c.800A>G	p.Asp267Gly	rs16944113	0,0095	0.76	na	-2.5	pol		
MSLN	16	815,549	NM_013404.4	c.727T>C	p.Ser243Pro	rs75279195	0,0058	0.13	3	1.9	pol	unknown	no
		815,565		c.743T>C	p.Leu248Pro	rs77260498	0,0058	0.02	3	3.4	pat		
FLII	17	18,148,496	NM_002018.3	c.3766C>T	p.Arg1256Cys	-	0,0001	0.03	1	4	pat	unknown	yes
		18,155,793		c.1091A>T	p.Glu364Val	rs61741784	0,0049	0.01	2	5.8	pat		
ZSWIM1	20	44,511,257	NM_080603.4	c.26G>A	p.Trp9*	rs35972756	0,0079	na	na	0.4	pat	unknown	no
		44,512,082		c.851G>A	p.Arg284His	rs45447691	0,0079	0.11	3	-1.7	pol		

SUPP. TABLE S2. Clinical features of affected persons from different branches of the family

Individual	Parental consanguinity	CNS	Renal	Lung, HEENT	Eye	Age at death
V:12 (index patient) born 2004	yes	MTS ataxia MR	PKD enlarged kidneys ROH ESRD	mild lung hypoplasia frequent pulmonary infections and otitis	LCA	survived and clinically improved after KTx current age: 9.5 years
IV:1 born 1971	yes	no MRI ataxia MR	PKD enlarged kidneys ESRD	ND	LCA	9 years
IV:6 born 1993	yes	no MRI ataxia MR	PKD enlarged kidneys ROH ESRD	lung hypoplasia	LCA	6 ½ years
V:1 born 2010	yes	ND	PKD enlarged kidneys ROH ESRD	severe lung hypoplasia	ND	1 day
V:2 born 2010	yes	ND	PKD enlarged kidneys ROH ESRD	severe lung hypoplasia	ND	2 days

MTS, molar tooth sign; MR, mental retardation/developmental delay; PKD, polycystic kidney disease; ROH, renal oligohydramnion; ESRD, endstage renal disease; LCA, Leber congenital amaurosis; KTx, kidney transplantation; ND, no data available.

SUPP. TABLE S3. Homozygous variants in candidate genes from WES data of the index patient contained in mapped chromosomal HBD regions

Gene	Chr	Position (GRCh37)	RefSeq	Nucleotide alteration	Protein alteration	Variant name	Variant frequency	Sift	Polyphen	GERP	MutTast	Mendelian disease	ciliary/ centrosomal	Mapped HBD regions (Mb)
NRXN1	2	50,573,999	NM_138735.2	c.89G>A	p.Arg30His	-	-	na	2	4.1	pat	unknown	no	
C2ORF42	2	70,406,718	NM_017880.1	c.880G>T	p.Ala294Ser	rs141350086	0,0015	na	1	3	pol	unknown	no	
TET3	2	74,274,537	NM_144993.1	c.1088_1093del	p.Ala367_Pro368del	-	-	na	na	na	na	unknown	no	65,93
SUCLG1	2	84,668,421	NM_003849.3	c.481C>T	p.Arg161Cys	rs141331864	0,0002	0.1	1	5.6	pat	MTDPS9 (ar)	no	
RETSAT	2	85,571,285	NM_017750.3	c.1370G>A	p.Arg457Gln	rs41289947	0,0017	0.23	1	na	pat	unknown	no	
ANKRD36	2	97,875,561	NM_001164315.1	c.3319G>C	p.Val1107Leu	-	0,0009	na	na	0.2	pol	unknown	no	
SLC40A1	2	190,428,384	NM_014585.5	c.1328C>T	p.Pro443Leu	rs45606432	0,0016	0.78	2	2.9	pol	HFE4 (ad)	no	
BOLL	2	198,631,285	NM_197970.2	c.559A>G	p.Ile187Val	rs61642236	0,0003	na	na	2.6	pol	unknown	no	
RNF25	2	219,530,673	NM_022453.2	c.539A>G	p.Gln180Arg	rs149561416	0,0018	0.52	1	-1.1	pol	unknown	no	
ABCB6	2	220,079,686	NM_005689.2	c.1273C>G	p.Leu425Val	rs111852229	0,0009	0.26	1	5	na	colob/ microphth (ad); Lan(-) blood-group (ar)	yes	56,62
GLB1L	2	220,103,915	NM_024506.3	c.961C>T	p.Arg321Cys	rs148493267	0,001	0.04	3	1.6	pol	unknown	no	
NCL	2	232,325,391	NM_005381.2	c.798_800del	p.Glu271del	-	-	na	na	na	na	unknown	no	
ALPI	2	233,323,405	NM_001631.3	c.1247C>T	p.Pro416Leu	-	0,0001	na	3	3.8	pat	unknown	no	
PPFIA2	12	81,661,833	NM_001220476.1	c.3326G>A	p.Arg1109His	rs61756413	0,0064	na	na	5.9	pat	unknown	no	
POC1B	12	89,885,848	NM_172240.2	c.317G>C	p.Arg106Pro	-	-	0.15	3	5.8	pat	LCA, JBTS with PKD, this study	yes	30,24
PAH	12	103,234,285	NM_000277.1	c.1208C>T	p.Ala403Val	rs5030857	0,0005	na	1	5.6	pat	PKU	no	
CCL15	17	34,324,806	NM_032965.4	c.339A>G	p.Ile113Met	rs147708747	0,0001	0.01	na	0.8	pol	unknown	no	
KRT34	17	39,535,305	NM_021013.3	c.1126C>T	p.Arg376Trp	rs61740668	0,0053	na	3	4	pat	unknown	no	7,27
GALK1	17	73,758,896	NM_000154.1	c.682C>T	p.Arg228Cys	-	-	na	3	5.3	pat	cataract (ar)	no	16,87

The extent of these regions is given in megabases, Mb. Chromosomal coordinates are given in GRCh37. Variant names and population allele frequencies are taken from dbSNP, the 1000 Genomes Project and the Exome Sequencing Project. Predictions of pathogenicity and evolutionary conservation (only available for SNPs) have been performed with SIFT (close to zero is most damaging), POLYPHEN2 (1=benign; 2=possibly damaging; 3=probably damaging), GERP++ (rejected substitution score; high numbers for high evolutionary conservation) and MutationTaster (pat=pathogenic, pol=polymorphism). The variants in *ABCB6* and *POC1B* (in bold) represented prime candidate variants because they were predicted as pathogenic by most programs and have documented ciliary/centrosomal expression. Assessment of deletions or insertions is out of scope for the methods of the prediction programs which require knowledge of the ancestral amino acids at that position (except MutationTaster). Due to ID-mapping problems between different databases, predictions were not available for some transcripts: na=not available. ar, autosomal recessive. MTDPS9, mitochondrial DNA depletion syndrome 9; HFE4, hemochromatosis type 4; PKU, phenylketonuria; Polyphen: 1=benign,2=possibly damaging, 3=probably damaging. na, not applicable.