Supplementary tables

Table SI. Coverage and quality metrics of the whole-exome sequencing data for proband (IV-1), her mother (III-2), and her father (III-1).

Quality metrics	IV-1	III-2	III-1
Read Length	101	101	101
Number reads (M)	116.5	106.4	129.8
Number bases (G)	11.8	10.8	13.1
Mean coverage	118.2	111.6	132.9
Median coverage	110	104	124
PCR duplicates	19.74%	19.72%	19.70%
Unmapped	0.09%	0.09%	0.08%
Reads on-target	52.03%	53.78%	52.57%
Bases on-target	39.13%	40.40%	39.49%
Mean error rate	0.19%	0.20%	0.19%
1x target base coverage	98.80%	98.90%	98.80%
8x target base coverage	98.60%	98.60%	98.60%
10x target base coverage	98.50%	98.60%	98.50%
20x target base coverage	98.10%	97.90%	98.20%
40x target base coverage	95.00%	93.70%	96.20%
50x target base coverage	91.40%	89.30%	93.90%
100x target base coverage	58.10%	53.50%	67.20%
Targets	IDT	IDT	IDT

Table SII. Rare *de novo* heterozygous variants that were identified in the proband (IV-1) with MAF <1% sub-population.

Position	Gene	Variant	Intolerance	pLI	MAF gnomAD_All	CADD	SIFT	PPH	Effect score	ClinVar/ HGMD	Splicing dbscSNV11 /regSNP-intron Pathogenicity	OMIM	Dad	Mom
22:24581211_C>T	*SUSD2*	P311L	92.78%	0.00	0.0002	24.6	T	D	4	.	.	.	Ref	Ref
22:26995633_C>A	*CRYBB1*	V194F	61.60%	0.00	0	32	D	D	8	.	.	AD, AR: Cataract 17, multiple types,	Ref	Ref

pLI, loss-of-function intolerant probability score; CADD, combined annotation dependent depletion; SIFT, sorting intolerant from tolerant; PPH, PolyPhen; OMIM, online mendelian inheritance in man; SUSD2, Sushi domain containing 2; CRYBB1, crystallin beta B1; Ref, the individual does not harbor the variant.

Table SIII. Rare compound heterozygous variants that were identified in the proband (IV-1) with MAF <1% sub-population.

Position	Gene	Variant	Intolerance	pLI	MAF gnomAD_All	CADD	SIFT	PPH	Effect score	ClinVar/HGMD	Splicing dbscSNV11/regSNP-intron Pathogenicity	OMIM	Dad	Mom
1:39876890_A>G	*KIAA0754*	E318G	.	0.02	0	25.4	.	D	3	.	.	.	Ref	Het

1:39877829_T>C	*KIAA0754*	L631S	.	0.02	0.0027	22.6	.	D	5	.	.	.	Het	Ref
5:179315221_T>C	*TBC1D9B*	N379S	64.26%	0.00	$4.91x10^{-05}$	15.29	T	B	2	.	.	.	Het	Ref
5:179315315_G>C	*TBC1D9B*	c.1045-3C>G	64.26%	0.00	0	.	.	.	0	.	D	.	Ref	Het
9:2804375_T>C	*PUM3*	T635A	.		0.0003	9.21	T	B	0	.	.	.	Het	Ref
9:2837326_A>G	*PUM3*	F53S	.		0.0004	20.3	D	D	3	.	.		Ref	Het
15:42153959_G>A	*SPTBN5*	Q2571X	.	0.00	$1.28x10^{-05}$	37	.	.	1	.	.	.	Ref	Het
15:42177973_G>A	*SPTBN5*	R494W	.	0.00	0.0007	25.8	D	D	3	.	.	.	Het	Ref

pLI, loss-of-function intolerant probability score; CADD, combined annotation dependent depletion; SIFT sorting intolerant from tolerant; PPH, PolyPhen; OMIM online mendelian inheritance in man; KIAA0754, microtubule actin crosslinking factor 1; TBC1D9B, TBC1 domain family member 9B; PUM3, pumilio RNA binding family member 3; SPTBN5, spectrin beta, non-erythrocytic 5; Het, heterozygote; Ref, the individual does not harbor the variant.

Table SIV. Rare homozygous variants that were identified in the proband (IV-1) with MAF <1% sub-population.

Position	Gene	Variant	Intolerance	pLI	MAF gnomAD_All	CADD	SIFT	PPH	Effect score	ClinVar HGMD	Splicing dbscSNV11 regSNP-intron Pathogenic	OMIM	Dad	Mom

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11:75694549_A>C	*UVRAG*	Q273P	26.73%	0.86	0.0027	23.6	D	B	3	.	.	.	Het	Het
11:89028323_T>C	*TYR*	F460S	24.29%	0.00	0.0005	22.8	T	P	3	.	.	Albinism, oculocutaneous, type IA; Waardenburg syndrome/albinism, digenic; Albinism, oculocutaneous, type IB; [Skin/hair/eye pigmentation 3;	Het	Het

pLI, loss-of-function intolerant probability score; CADD, combined annotation dependent depletion; SIFT sorting intolerant from tolerant; PPH, PolyPhen; OMIM online mendelian inheritance in man; UVRAG, UV radiation resistance associated; TYR, tyrosinase; Het, heterozygote.

Table SV. Inherited rare heterozygous variants in congenital heart diseases genes that were identified in the proband (IV-1) with MAF <1% sub-population.

Position	Gene	Variant	Intolerance	pLI	MAF gnomAD_All	CADD	SIFT	PPH	Effect score	ClinVar HGMD	Splicing dbscSNV11/regSNP-intron Pathogenicity	OMIM	Dad	Mom

4:15518258_G>T	*CC2D2A*	W343L	92.94%	0.00	0	32	D	D	6	.	.	AR: Joubert syndrome 9; Meckel syndrome 6; COACH syndrome,	Het	Ref
4:167020555_G>A	*TLL1*	R928Q	12.35%	0.33	0.0006	21.9	T	P	1	.	.	AD: Atrial septal defect 6,	Het	Ref
12:114832632_C>A	*TBX5*	G193*	30.53%	0.99	0	40	.	.	Stop-gain	.	.	AD: Holt-Oram syndrome,	Ref	Het
20:45354670_T>C	*SLC2A10*	V332A	46.80%	0.01	$1.22x10^{-05}$	0.001	T	B	0	.	.	AR:Arterial tortuosity syndrome	Ref	Het

pLI, loss-of-function intolerant probability score; CADD, combined annotation dependent depletion; SIFT sorting intolerant from tolerant; PPH, PolyPhen; OMIM online mendelian inheritance in man; CC2D2A, coiled-coil and C2 domain containing 2A; TLL1, tolloid-like 1; TBX5, T-box transcription factor 5; SLC2A10, solute carrier family 2 member 10; Het, heterozygote; Ref, the individual does not harbor the variant; AD, autosomal dominate; AR, autosomal recessive.