Supplementary Table 2

Summary of patients' variants: The table lists all variants that passed filters as described in Methods. Variant location, reference and variant alleles are reported from hg19 coordinates. Minor allele frequency is based on the overall allele frequency in the NHLBI Exome Variant Server (ESP 6500 release) (NHLBI GO exome variant server). Functional effect was assessed with PolyPhen2 prediction tool, which estimates the effect of missense variants (Adzhubei, 2010). A score of 0.00 is least likely to perturb protein function, while a score of 1.00 indicates a missense variant that is mostly likely to perturb protein function. Functional annotation of SNPs was assessed using SnpEff 2.0.5 (Cingolani, 2012) and validated manually. Protein function was summarized using information found in the UniProt database. Online Mendelian Inheritance of Man (OMIM) database was used to identify any known disease associations. Variants highlighted in yellow are pathogenic variants that we have determined cause short stature. These causal variants are also shown in Table 3.

Patient 01

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
KIAA1609	Compound	Chr 16: 84516214	G	A	0.003385	rs140439420	missense	T354M	1.000	probably damaging		
(TLDC1)	Heterozygous	Chr 16: 84520260	C	T	NA	NA	Nonsense	W312*	NA	NA	unknown	None
	Compound	Chr 19: 41114407	C	T	0.000922	NA	missense	R509C	1.000	probably damaging		Autosomal recessive cutis
LTBP4	Heterozygous	Chr 19: 41132912	C	T	0.000326	NA	missense	P1407S	1.000	probably damaging	regulating TGFB1	laxa, type IC
	Compound	Chr 2:179483341	C	T	NA	NA	missense	A14005T	0.989	probably damaging	component of striated	various muscular distrophies
TTN	Heterozygous	Chr 2: 179437928	T	C	0.00372	rs56201325	missense	T22670A	0.000	benign	muscle sarcomere	and cardiomyopathies
	Compound	Chr 11: 66243148	C	T	0.00362	rs145732233	missense	A307V	0.769	possibly damaging		
PELI3	Heterozygous	Chr 11: 66235631	C	T	0.000154	NA	missense	S11F	0.191	benign	E3 ubiquitin ligase	None
	de novo						Start codon					
ZBED4	heterozygous	Chr 22: 50277312	T	C	NA	NA	lost	M1T	0.842	possibly damaging	unknown	None
	Autosomal											Nocturnal frontal lobe epilepsy-5; Early infantile
KCNT1	recessive	Chr 9:138670668	G	A	0.002153	rs151272083	missense	R910Q	1.000	probably damaging	T-type potassium channel	epeliptic encephalopathy-14
												X-linked agammaglobulinemia-1;
BTK	X-linked recessive	Chr X: 100615717	C	A	0.001609	rs35877704	missense	E205D	0.084	benign	tyrosine kinase needed for B-cell development	Agammaglobulinemia and isolated hormone deficiency
GPKOW	X-linked recessive	Chr X: 48970674	C	T	NA	NA	missense	R439Q	0.604	possibly damaging	unknown	None
MAGEE2	X-linked recessive	Chr X: 75004476	G	C	NA	NA	missense	D137E	0.008	benign	unknown	None

Patient 02

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	AA change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
	Compound	Chr 5: 177035995 Chr	C	T	NA	rs28937869	missense	L41P	1	probably damaging		Progeroid Type of Ehlers
B4GALT7	Heterozygous	5: 177031251	T	C	0.000077	NA	missense	R270C	0.998	probably damaging	Proteoglycan Synthesis	Danlos Syndrome
	Compound	Chr 5: 90059282 Chr	A	G	NA	NA	missense	D4094G	0.166	benign	G-Protein coupled receptor	Familial febrile seizures type
GPR98	Heterozygous	5: 89969880	A	G	0.004988	rs72782753	missense	I1647V	0.001	benign	in the CNS	4, Usher's syndrome type 2C
	Compound	Chr 20: 25252069 Chr	G	A	NA	NA	missense	G159R	1.000	Probably damaging		
PYGB	Heterozygous	20: 25260969	G	A	NA	NA	missense	R387H	1.000	Probably damaging	Glycogen Phosphorylase	NA
	de novo										Disassembly of focal	
PPFIA1	heterozygous	Chr 11: 70218665	C	G	NA	NA	missense	Q1042E	0.009	benign	adhesions	NA
ACE2	X-Linked	Chr X: 15607532	C	T	NA	rs148771870	missense	G211R	0.551	Possibly Damaging	angiotensin I conversion	NA
BCORL1	X-Linked	Chr X: 129148489	G	A	NA	rs188957722	missense	A581T	0.056	benign	transcription co-repressor	NA
IL13RA2	X-Linked	Chr X: 114239813	C	G	NA	NA	missense	V355L	0.000	benign	Binds IL-13	NA
							codon	c.1182_1183				
VSIG1	X-Linked	Chr X: 107320521	G	GGAGCCA	0.003234	NA	insertion	insGAGCCA	NA	NA	NA	NA

Patient 03

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Predition	Function (UniProt)	Associated Diseases (OMIM)
	Compound	Chr 10: 56129008	C	T	NA	NA	missense	V116M	1.000	probably damaging	calcium-dependent cell-	Usher syndrome Type 1D/F; Autosomal recessive
PCDH15	Heterozygous	Chr 10: 55582676	T	C	NA	NA	missense	R1604G	0.129	benign	adhesion protein	deafness-23
IKZF4	*de novo* heterozygous	Chr 12: 56429081	C	T	NA	NA	missense	S575F	0.856	possibly damaging	Transcriptional repressor	None
PDXP	*de novo* heterozygous	Chr 22: 38061804	G	A	NA	NA	missense	A273T	0.099	benign	actin cytoskeleton reorganization	None
PHF16	X-linked recessive	Chr X: 46918243	T	C	NA	rs35292182	missense	F746L	0.000	benign	histone acetyltransferase	None

Patient 04

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
	Compound	Chr 3: 49742591	G	A	0.000308	NA	missense	V712M	0.776	possibly damaging		
RNF123	Heterozygous	Chr 3: 49739295	C	T	NA	NA	missense	R483W	1.000	probably damaging	E3 ubiquitin ligase	none
	Compound	Chr 2: 160194190	C	T	NA	NA	missense	E1850K	0.366	benign		
BAZ2B	Heterozygous	Chr 2: 160252332	C	T	0.000421	rs180681997	missense	R1008K	0.993	probably damaging	transcriptional regulation	none
		Chr 4: 8229688	C	T	NA	NA	missense	P756L	0.036	benign		
	Compound	Chr 4: 8230053	C	T	0.008002	rs116515695	missense	R878W	0.864	possibly damaging		
SH3TC1	Heterozygous	Chr 4: 8233750	A	G	0.007612	rs146877451	missense	M1000V	0.001	benign	unknown	none
	de novo											
LRRC6	heterozygous	Chr 8: 133645029	C	T	NA	NA	missense	A204T	0.000	benign	dynein arms in cilia	Primary ciliary dyskinesia-19
	de novo											
HSP90AB1	heterozygous	Chr 6: 44218299	G	C	NA	NA	missense	S307T	0.642	possibly damaging	unknown	none

Patient 05

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
	Compound	Chr 5: 75587140	G	A	0.002828	rs190593094	missense	R411H	0.973	probably damaging	secretion in neural and endocrine cells from	
SV2C	heterozygous	Chr 5: 75490776	G	T	NA	NA	missense	A205S	0.155	benign	secretory vescicles	none
	Compound	Chr 10: 99218996	C	T	0.003537	rs29001332	missense	R983H	0.006	benign	generation of iron sulfur	
MMS19	heterozygous	Chr 10: 99238117	G	A	0.002614	rs29001280	missense	R98H	1.000	probably damaging	proteins	none
	Compound	Chr 12: 10961777	C	T	0.002307	rs149844170	missense	V300M	0.677	possibly damaging		
TAS2R9	heterozygous	Chr 12: 10962022	C	T	0.009688	rs113883583	missense	G218E	0.996	possibly damaging	taste receptor	none

Patient 06

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
	Compound	Chr 11: 108128246	T	A	0.000462	rs34231402	missense	F763L	0.003	benign		
ATM	heterozygous	Chr 11: 108200949	T	C	NA	NA	missense	V2439A	0.196	benign	DNA damage response	Ataxia-telangiectasia
		Chr 14: 105415300	A	T	NA	NA	missense	F2163Y	0.995	probably damaging		
	Compound	Chr 14: 105415298	C	T	NA	NA	missense	G2164R	0.998	probably damaging		
AHNAK2	heterozygous	Chr 14: 105415294	A	G	0.004123	NA	missense	V2165A	0.997	probably damaging	unknown	none
	Compound	Chr 2: 141291667	C	T	NA	NA	missense	R2562H	0.017	benign	receptor-mediated	
LRP1B	heterozygous	Chr 2: 141816515;	A	T	0.000077	rs150873963	missense	S449T	0.000	benign	endocytosis	none
	Autosomal											
FAM129A	Recessive	Chr 1:184853890	T	C	0.004075	rs140191774	missense	K160E	0.997	probably damaging	regulation of translation	none

Patient 07

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
	Compound	Chr 13: 77742618	T	C	0.000461	rs141717634	missense	Y2020C	0.999	benign		
MYCBP2	Heterozygous	Chr 13: 77751957	T	C	0.001	rs144627155	missense	I1756V	0.000	benign	possible E3 ubiquitin ligase	None
	Compound	Chr 2: 141986957	C	A	NA	NA	missense	E215D	0.533	possibly damaging	receptor mediated	
LRP1B	Heterozygous	Chr 2: 141777554	C	T	0.0027	rs77234491	missense	R636Q	1.000	probably damaging	endocytosis	None
	Compound	Chr 16: 72154010	C	T	0.0014	rs72787072	missense	R791H	0.998	probably damaging	organization of cell	
PMFBP1	Heterozygous	Chr 16: 72164475	G	T	0.0005	rs140852275	missense	Q532K	0.008	benign	cytoskeleton	None
	Compound	Chr 17: 34192351	G	A	0.0018	rs141724302	missense					
C17ORF66	Heterozygous	Chr 17: 34191815	G	A	0.0005	rs116191233	nonsense	P63L	0.326	benign	unknown	None
	de novo											
*KLHL26**	heterozygous	Chr 19: 18778934	C	T	NA	NA	missense	R243C	0.018	benign	unknown	None
	de novo											
NUCB1	heterozygous	Chr 19: 49416343	G	A	NA	NA	missense	E186K	1.000	probably damaging	calcium binding in Golgi	None
	de novo										chromatin remodeling and	
SRCAP	heterozygous	Chr 16: 30748691	C	T	NA	NA	nonsense	R2444*	NA	NA	transcription coactivator	Floating Harbor Syndrome

*Sanger sequencing and genotyping primer design failed for this variant

Patient 08

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
	Compound	Chr 2: 179611372	T	C	NA	NA	missense	G5252E	1.000	probably damaging	component of striated	various muscular distrophies
TTN	Heterozygous	Chr 2: 179412337	G	A	NA	rs184078016	missense	T29698I	0.991	probably damaging	muscle sarcomere	and cardiomyopathies
	Compound	Chr 12: 48372421	G	T	NA	rs140740708	missense	P952T	0.000	benign		various skeletal and
COL2A1	Heterozygous	Chr 12: 48378858	C	T	NA	NA	missense	G585S	1.000	probably damaging	type II collagen	chondrodysplasias
	Compound	Chr 11: 22257752	G	T	0.000846	rs137854523	missense	G231V	0.997	probably damaging		Gnathodiaphyseal dysplasia; Miyoshi muscular dystrophy-3; Limb-girdle muscular
ANO5	Heterozygous	Chr 11: 22283684	G	A	0.000308	rs139618850	missense	R547Q	0.999	probably damaging	unknown	dystrophy type 2L
	Compound	Chr 19: 32845774	A	G	NA	NA	missense	N680D	0.000	benign		
ZNF507	Heterozygous	Chr 19:32845235	T	C	NA	NA	missense	L500P	1.000	probably damaging	unknown	none

Patient 09

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
		Chr 4: 88052985	C	T	0.000077	rs144598701	missense	P1041S	0.006	benign		
	Compound	Chr 4: 88035586	C	T	0.000622	NA	missense	A527V	0.000	benign		
AFF1	Heterozygous	Chr 4: 87968067	C	T	0.000077	rs150065985	missense	A120V	1.000	probably damaging	unknown	none
	Compound	Chr 10: 134622020	G	A	0.000154	NA	missense	R846W	0.000	benign		
C10orf93 (DK	Heterozygous	Chr 10: 134663840	G	A	NA	NA	missense	R115W	0.999	probably damaging	unknown	none
	Compound	Chr 19: 17648307	G	A	0.000077	NA	missense	A215T	1.000	probably damaging		
FAM129C	Heterozygous	Chr 19: 17660319	G	A	NA	NA	missense	W609*	NA	NA	unknown	none
	Compound	Chr 5: 192473	G	C	0.003112	rs151096925	missense	E274Q	0.100	benign		
LRRC14B	Heterozygous	Chr 5: 195192	C	A	0.00032	NA	missense	F423L	0.200	benign	unknown	none
		Chr 11: 1276084	T	A	NA	NA	missense	F5213Y	1.000	probably damaging		
	Compound	Chr 11: 1255461	G	T	NA	NA	missense	D802Y	1.000	probably damaging		
MUC5B	Heterozygous	Chr 11:1263730	G	A	NA	NA	missense	V1874M	0.964	probably damaging	mucin	none
	Compound	Chr 9: 33465808	G	C	NA	NA	missense	L818V	0.009	benign		
NOL6	Heterozygous	Chr 9: 33472070	G	C	NA	NA	missense	R104G	0.802	possibly damaging		none
ABCA13	Autosomal Recessive	Chr 7: 48318458	A	G	NA	NA	missense	D2556G	0.399	benign	ATP-binding transporter	
OBSL1	Autosomal Recessive	Chr 2: 220431551	C	T	NA	NA	splice site donor	c.2134+1C>T	NA	NA	cellular scaffold protein	3M Syndrome
OBSL1	Autosomal Recessive	Chr 2: 220420990	C	T	0.009044	rs183329050	missense	R1454Q	1.000	probably damaging	cellular scaffold protein	3M Syndrome
PKD1L1	Autosomal Recessive	Chr 7: 47927741	G	A	NA	NA	missense	H895Y	0.993	probably damaging	unknown	none
ACOT9	X-linked recessive	Chr X: 23754116	T	C	NA	NA	missense	K13R	0.028	benign	lipid metabolism	X-linked mental retardation type 46
ARHGEF6	X-linked recessive	Chr X: 135829739	C	G	0.000284	rs149768069	missense	D88H	0.000	benign	Guanine nucleotide exchange factor	none
P2RY4	X-linked recessive	Chr X: 48547058	C	T	0.000095	NA	missense	L14F	0.004	benign	G-protein coupled receptor signaling	none
WAS	X-linked recessive	Chr X: 69479435	G	A	NA	NA	missense	P314L	0.241	benign	regulation of actin organization	Wiskott Aldrich Syndrome

Patient 10

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
	Compound	Chr 6: 32095465	G	A	0.001922	rs17201623	missense	P52S	.001	benign	transcription factor in	
ATF6B	Heterozygous	Chr 6: 32086893	C	G	NA	NA	missense	R331P	1.000	probably damaging	unfolded protein response	none
	Compound	Chr 3: 130300740	C	T	0.000925	NA	nonsense	R1295*	NA	NA		
COL6A6	Heterozygous	Chr 3: 130290069	C	T	0.00327	rs111457392	missense	R937W	1.000	probably damaging	collage type 6	none
	Compound	Chr 15: 43818706	G	T	NA	NA	missense	D1679Y	0.891	possibly damaging	crossbriding of microtubules and other	
MAP1A	Heterozygous	Chr 15: 43819273	C	T	NA	NA	missense	P1868S	0.996	probably damaging	cytoskeletal elements	none
	de novo											
*FCGR1B**	heterozygous	Chr 1: 120930090	T	C	NA	NA	missense	M171V	0.315	benign	bind immunoglobulins	none
	de novo										tyrosine kinase needed for	X-linked agammaglobulinemia-1; Agammaglobulinemia and
BTK	hemizygous	Chr X: 100608911	G	A	NA	NA	missense	P566L	1.000	probably damaging	B-cell development	isolated hormone deficiency

**Sanger sequencing and genotyping primer design failed for this variant*

Patient 11

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
FAM134A	de novo heterozygous	Chr 2: 220045422	G	T	NA	NA	missense	V196L	0.828	possibly damaging	unknown	none
CUL7	Autosomal recessive	Chr 6: 43013346	G	GATCT	NA	NA	frame shift	c.2837_2840 dupAGAT	NA	NA	cell scaffolding protein	3M Syndrome

Patient 12

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
	Compound	Chr 2: 215876783	T	C	0.001922	rs147218173	missense	N678S	0.000	benign	transporter involved in	Harequin Ichthyosis Type 4B; Congeintal Autosomal
ABCA12	Heterozygous	Chr 2: 215813807	T	C	0.001384	rs150196545	missense	I2307V	0.001	benign	lipid homeostasis	recessive ichthyosis type 4A
	Compound	Chr 17: 48703747	C	T	NA	NA	missense	R2257W	0.999	probably damaging		
CACNA1G	Heterozygous	Chr 17: 48650063	G	A	0.001741	NA	missense	G299S	0.001	benign	T-type calcium channel	none
	Compound	Chr 15: 28412850	T	C	NA	NA	missense	M3513V	0.000	benign		
HERC2	Heterozygous	Chr 15: 28456199	G	A	NA	NA	missense	R2340W	1.000	probably damaging	E3 ubiquitin ligase	none
	Compound	Chr 16: 820127	G	A	NA	NA	missense	A602V	0.900	possibly damaging		
MSLNL	Heterozygous	Chr 16: 820203	A	C	NA	NA	missense	W577G	1.000	probably damaging	cell adhesion	none
	Compound	Chr 3: 47038529	A	G	NA	NA	missense	D881G	1.000	probably damaging		
NBEAL2	Heterozygous	Chr 3: 47041758	C	T	NA	NA	missense	S1390L	1.000	probably damaging	synthesis of platelets	Gray platelet syndrome
	Compound	Chr 12: 123463739	G	A	0.000157	NA	missense	R240H	1.000	probably damaging		
OGFOD2	Heterozygous	Chr 12: 123461223	G	A	0.000388	NA	missense	R11Q	1.000	probably damaging	unknown	none
	Compound	Chr 7: 47880144	C	T	0.005459	rs116988549	missense	D1823N	0.279	benign		
PKD1L1	Heterozygous	Chr 7: 47968953	C	T	0.003767	rs145088541	missense	R303Q	0.003	benign	unknown	none
	Compound	Chr 16: 81957106	A	G	0.001738	rs142825971	missense	K775R	0.121	benign	production of intracellular intracellular messenger	Autoinflammation, antibody deficiency, and immune dysregulation syndrome; Familial cold autoinflammatory syndrome
PLCG2	Heterozygous	Chr 16: 81939089	T	C	0.003443	rs187956469	missense	Y482H	0.974	probably damaging	molecules	3
	de novo											
NEFM	heterozygous	Chr 8: 24771390	C	G	NA	NA	missense	S28R	0.984	probably damaging	unknown	none

Patient 13

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Prediction	Function (UniProt)	Associated Diseases (OMIM)
	Compound	Chr 3: 148917570	G	A	0.003229	rs35331711	missense	P477L	1.000	probably damaging		Cerebellar ataxia; Systemic
CP	Heterozygous	Chr 3: 148899824	G	C	0.004536	rs56033670	missense	T841R	0.985	probably damging	binds plasma copper	hemosiderosis
	Compound	Chr 14: 36192385	G	A	0.000077	NA	missense	S651L	1.000	probably damaging		
RALGAPA1	Heterozygous	Chr 14: 36194277	T	C	0.001	rs144614582	missense	K607E	0.144	benign	GTPase activator	none
	Compound	Chr 7: 76131649	C	T	0.000616	rs148587797	missense	A422V	0.002	benign		
AC005522.1	Heterozygous	Chr 7: 76126681	T	C	0.001462	rs150299899	missense	I346T	0.788	possibly damaging	regulates NOTCH signaling	none
	de novo										signaling adapter involved	
PIK3AP1	heterozygous	Chr 10: 98469324	C	T	NA	NA	missense	D144N	1.000	probably damaging	in B-cell development	none
											possible transcription	
SSX7	X-linked recessive	Chr X: 52681967	A	T	NA	NA	missense	I46N	0.999	probably damaging	modulator	none

Patient 14

Gene	Inheritance Pattern	Position (hg19)	Reference	Variant	Frequency (Exome Variant Server)	dbSNP ID (if available)	Functional Annotation (SnpEff)	Amino Acid change	PolyPhen2	Predictio	Function (UniProt)	Associated Diseases (OMIM)
	compound	Chr1: 177901629	G	C	0.002267	rs78192809	missense		0.838	possibly damaging		
AL359075.1	heterozygous	Chr1: 177917055	A	T	0.002074	NA	missense	P1003R	0.989	probably damaging	unknown	none
FAM111A	*de novo* heterozygous	Chr11: 58920847	G	A	NA	NA	missense	R569H	0.901	possibly damaging	unknown	Kenny-Caffey Syndrome
LRRC30	*de novo* heterozygous	Chr18: 7231180	C	A	NA	NA	missense	P15H	0.726	possibly damaging	unknown	none