Supplementary File 1

Patient Summaries: This file provides clinical descriptions for all patients in the cohort. The clinical descriptions are based on the patient's prior medical history and/or physical examination by a trained pediatric specialist physician.

Patient P01

This patient is currently a 19 year old male born of a normal pregnancy at 41 weeks gestation with a birth weight of 2892 grams. He was growing at a normal growth rate along the 5th percentile until age 8 when he had an abrupt fall of in both weight gain and linear growth. An extensive evaluation for failure to thrive did not reveal an etiology. Growth hormone stimulation testing revealed marked growth hormone deficiency with a peak response to arginine of 2.5 ng/ml and to insulin of 1.5 ng/ml. A brain MRI was normal and there was no evidence of other pituitary hormone deficiencies. The patient displayed a robust response to recombinant growth hormone therapy. The patient had significantly decreased bone density (-4.5 SD below mean) and delayed bone age. The patient has nondysmorphic facial features. The patient's past medical history is significant for anxiety, ADHD, and depression requiring medical treatment, as well as a history of recurrent febrile seizures as a young child. On exam, there was a mild pectus carinatum with slight asymmetry. Family history was notable for febrile seizures, which were present in several cousins as well as the patient's sister. At enrollment, the patient was age 15 years 9 months and had a height of -3.17 SD.

Patient P02

This patient has been previously reported as noted in the main text. The male patient is currently 10 years old and was born after a normal pregnancy at 40 weeks gestation with a birth weight of 2977 grams. The patient had a congenital unilateral ptosis that was surgically corrected. Throughout childhood, the patient exhibited slow growth in height and weight, remaining below the 5th percentile in both. At age 4, a random growth hormone (GH) level was 2.85 ng/mL, and a GH stimulation test at age 5 revealed a peak response to arginine of 8.96 ng/mL and a peak response to glucagon of 6.37 ng/mL. Based on this moderate response to GH stimulation, the patient was initiated on recombinant GH therapy from age 5.5 years to age 10 years. There was no convincing evidence of a significant change in growth velocity after initiation of GH. On physical exam, the patient has ulnar bowing of the forearms, varus bowing of the lower legs, bilateral elbow contractures with decreased supination, pes planus, and hyperextension of the fingers, knees, shoulders, and wrists. Skin was soft, hair was of normal texture and distribution, and there was one scar on the forehead. The facial appearance was nondysmorphic and the patient did not have progeroid features. Testing of the *SHOX* and *RMRP* genes were normal, as were molecular tests for procollagen type 1. At enrollment, the patient was age 7 years 5 months and had a height of -3.87 SD.

Patient P03

The patient is currently a 10 year old male born with a dizygotic twin sister. The twin pregnancy was complicated by an incompentent cervix, premature labor, and hypertension. The fetuses stopped growing at 33 weeks with marked intrauterine growth restriction, and the patient and his twin were delivered by C-section at 37 weeks gestation and each weighed 1928 grams. The twin sister is healthy and of normal stature.

The patient displayed poor weight gain throughout childhood despite normal feeding. The patient reached appropriate developmental milestones. Physical exam showed normal facial features. There was a slight pectus carinatum. Dermatological exam reveals vitiligo, but no other abnormalities. Hormone levels were normal, except for low IGF-1 on several occasions with a normal peak growth hormone response of 11.7 ng/ml to stimulation testing with arginine and gulcagon. The patient was initiated on GH therapy for idiopathic short stature starting at age 7.5 for about 2 years, but was discontinued due to side effects of recurrent headaches. There was a mild transient increase in his growth velocity after

initiation of GH but no marked catch up growth. At enrollment, the patient was age 9 years 4 months and had a height of -3.48 SD.

Patient P04

The patient is currently a 17 year old female who was born at 40 weeks gestation with a birth weight of 2013 g. There was slightly delayed developmental milestones as an infant, but the patient is now cognitively normal and socially adjusted. The patient had short stature throughout childhood and was started on growth hormone at age 6 years for idiopathic short stature. Growth hormone stimulation testing with insulin produced a peak GH of 11.8 ng/ml. She continued on growth hormone until age 15 with a mild initial increase in growth velocity but no marked catch up growth. Due to a relatively early puberty, the patient was treated with a histrelin implant at 11 years 11 months in order to delay epiphyseal fusion and allow for additional growth. The patient was noted to have a markedly decreased bone density (-5 SD) during this therapy and at pubertal suppression was discontinued at the age of 14 years 11 months. Medical history is also significant for diffuse mild hypotonia as infant and mild left sided hemiparesis as infant, both of which resolved. MRI and EEG of the brain were normal except for a small pituitary stalk with an otherwise normal pituitary gland. At enrollment, the patient was age 14 years 1 month and had a height of -3.69 SD.

Patient P05

The patient is currently an 18 year old female who was born of an uncomplicated pregnancy at 40 weeks gestation with a birth weight of 2211 grams. Medical history is significant for asthma. The patient has normal IGF-1 and IGFBP-3 levels. Bone age was consistent with chronological age. On exam, she had a mild thoracic scoliosis with no other significant dysmorphic features. Skeletal survey revealed a right sided hemivertabrae between T4/T6, with bifid spinous processes at C3 and T1. There are only 11 ribs on the right. Her X-rays were not consistent with any specific skeletal dysplasia. Genetic testing for Noonan's syndrome and Turner syndrome mosaicism was negative. The patient's father (5'1'') and brother (5'1'') both have short stature but do not have any known skeletal anomalies. The patient also has a step-brother (same mother) who is 6'2''. At enrollment, the patient was age 15 years 2 months and had a height of -3.15 SD.

Patient P06

The patient is currently a 12 year old female who was born of an uncomplicated pregnancy at 38 weeks gestation with a birth weight of 2400 grams. The patient reached appropriate developmental milestones. Facial appearance was nondysmorphic and the remainder of the physical exam was not remarkable. IGF-1 and IGFBP-3 levels were normal and a karyotype was normal. Bone age is about 1 year behind chronological age. The patient also has been diagnosed with anxiety disorder. The remainder of the medical history is unremarkable. At enrollment, the patient was age 9 years 1 months and had a height of -3.45 SD.

Patient P07

The patient is currently a 12 year old female and was twin A of a normal pregnancy at 39 weeks gestation. The patient was born at 2268 grams while her twin sister was born at 3827 grams. The patient had developmental delay most notable in her expressive language, while her twin sister did not demonstrate any delays. Medical history is notable for severe scoliosis, tethered cord, laryngomalacia, chronic constipation, and asymptomatic polycystic kidney disease. The patient has a history of hypothyroidism and relatively early puberty with breast development starting at age 9 years. She was started on pubertal suppression therapy with a histrelin implant in order to maximize growth potential. Growth hormone axis levels are normal. Physical exam reveals mildly dysmorphic facial appearance with a v-shaped nares, short philtrum, slightly beaked nose, and moderate scoliosis. Head circumference was normal. Prior genetic testing was all normal including a karyotype, FISH of 22q and 7q, fragile X

testing, and an extensive metabolic work up. At enrollment, the patient was age 9 years 3 months and had a height of -3.01 SD.

Patient P08

The patient is currently a 7 year old female who was born of an uncomplicated pregnancy at 39 weeks gestation with a birth weight of 2778 grams. She reached appropriate developmental milestones. The patient's medical history is significant for several episodes of pneumonia requiring hospitalization. She also has several severe food allergies, but is well-nourished. The patient has mild eczema. Her growth hormone and thyroid hormone axis levels are normal including a peak growth hormone of 11.0 ng/ml on stimulation testing with arginine and glucagon. Her bone age is slightly delayed (5 years at chronological age of 5 years 8 months by Gruelich and Pyle). Physical exam was unremarkable. The patient's parents and four sisters are all of normal stature. The patient has a paternal aunt and grandmother who have short stature at 4'10''. Karyotype and *SHOX* gene testing were normal. At enrollment, the patient was age 4 years 4 months and had a height of -3.90 SD.

Patient P09

The patient is currently a 14 year old male born of an uncomplicated pregnancy at 40 weeks gestation with a birth weight of 2268 grams. The patient reached appropriate developmental milestones. Medical history is unremarkable. Physical examination reveals an inverted triangular face with a normal head circumference. Facial appearance was otherwise nondysmorphic. Examination of the genitalia was normal with normal testicular size. The patient has gracile-appearing bones, but with normal limb length and a skeletal survey interpretation did not suggest any specific etiology. GH and thyroid hormone axes levels are normal. The patient was initiated on a trial of growth hormone at around age 12 but was withdrawn rapidly due to side effects. The parents are from the same town in India, and there is a distant relative with short stature. Fanconi's anemia chromosome breakage testing was negative. Russell-Silver Syndrome was suspected, but testing was negative. At enrollment, the patient was age 11 years 3 months and had a height of -3.18 SD.

Patient P10

The patient is currently an 11 year old female born of an uncomplicated pregnancy at 39 weeks gestation with a birth weight of 2778 grams. The patient reached appropriate developmental milestones. Her medical history is notable for mild chronic constipation and an episode of anemia. Physical examination is unremarkable. IGF-1 levels were mildly decreased (78 ng/mL; reference 88 to 474). GH stimulation testing was normal with a peak growth hormone level of 15.3 ng/ml after stimulation with arginine and glucagon. Thyroid function tests were normal. Bone age was markedly delayed (8-10/12 at chronological age of 11-7/12 by Greulich and Pyle). There is a family history of delayed puberty, but not short stature. At enrollment, the patient was age 11 years 8 months and had a height of -3.30 SD.

Patient P11

This patient has been previously reported as noted in the main text. The patient is currently a 21 year old male who was born without complications at 39 weeks gestation. The patient had a birth weight 1842 g (−3.7 SD) and length of 33 cm (−6.8 SD). He had difficulty feeding and subsequent poor growth, resulting in gastrostomy tube placement at age 17 months, which was removed at age 3 years. His head circumference was always large for his age (range +1.9 to +2.4 SD), but cognitive development was normal. The patient had an inverted triangular face with midface hypoplasia. Skeletal surveys revealed gracile-appearing bones. He was treated with growth hormone for a period of 5 years with a mild, transient increase in growth velocity. His history is also notable for significant scoliosis requiring surgical repair at age 14 years, delayed dentition, and tonsillectomy and tympanostomy tube placement as a

toddler for frequent otitis media. In addition, he had testicular maldescent and inguinal hernias requiring surgical repair. After his genetic diagnosis with 3M syndrome, evaluation revealed hypergonadotropic hypogonadism. Prior genetic testing of *PTPN11, SOS1, FGFR3, SHOX,* and molecular testing for Russell-Silver syndrome were negative. At enrollment, the patient was age 18 years 5 months and had a height of -4.07 SD.

Patient P12

The patient is currently an 11 year old female who was born of an uncomplicated pregnancy with a birth weight of 2637 grams. The patient reached appropriate developmental milestones. Medical history is significant for recurrent episodes of gastrointestinal pain, diarrhea, and vomiting throughout childhood and of unknown etiology. She had an extensive gastrointestinal work up including endoscopy and colonoscopy all of which were normal. She has had appropriate weight gain despite her abdominal complaints and her most recent BMI was at the 43rd percentile. Thyroid and growth hormone axes were normal including a normal response to growth hormone stimulation testing (peak growth hormone 11.2 ng/ml). Bone age was delayed (8-10/12 at chronological age of 10-9/12 by Greulich and Pyle). Physical exam is unremarkable. Facial appearance is non-dysmorphic. Karyotype and testing for *SHOX* were normal. Father was noted to have a delayed growth spurt, but currently measures 5'6''. At enrollment, the patient was age 8 years 8 months and had a height of -3.58 SD.

Patient P13

The patient is currently a 9 year old male born of an uncomplicated pregnancy at 40 weeks gestation and was appropriate for gestational age (3231 grams and 50.2 cm long). The patient reached appropriate developmental milestones. Medical history was unremarkable. IGF-1 and IGFBP-3 levels and thyroid hormone axis levels were normal. Bone age was mildly delayed (bone age was 7-0/12 months at age 8-3/12 by Gruelich and Pyle). Facial appearance was nondysmorphic. Skeletal survey was normal. At enrollment, the patient was age 7 years 7 months and had a height of -3.01 SD.

Patient P14

The patient is currently a 12 year old female born of an uncomplicated pregnancy at 40 weeks gestation with a birth weight of 3091 grams and length of 45.7 cm. She reached appropriate developmental milestones. The patient experienced failure to thrive in infancy requiring hospitalization at 6 months of age. Testing during the hospitalization revealed elevated liver enzymes which have self-resolved over time. Review of systems is notable for severe myopia but no other ophthalmological abnormalities. Facial appearance demonstrates a prominent forehead, a flat nasal bridge, and a curved and upturned nose. Skeletal survey was notable for bilateral coxa valga and mild medullary stenosis and cortical thickening of the long bones, particularly the femur. Head circumference at age 11-1/12 was 50.7 cm (6th percentile). Dental examination and history reveal soft enamel, five missing permanent teeth (all premolars), abnormal eruption pattern with delayed eruption of permanent teeth, and small permanent teeth. At enrollment, the patient was age 12 years and had a height of -5.99 SD.

GH, IGF-1, and IGF-BP3 levels, and GH stimulation tests were normal. She was started on GH at 3 ½ years of age and had a brisk response initially with a growth velocity of 7.5 cm/yr, 12.3 cm/yr, then 5.8 cm/yr at 6 month increments. Due to the slowing in her growth velocity, she was switched to IGF-1 at 5 ½ years of age. She experienced severe headaches, resulting in poor compliance and a poor growth response of 3 cm/y for 1 year. She was subsequently switched back to GH. Her GV then increased from the 25th to 95th percentile for her age until she was started on GnRH agonist therapy at 10 ½ years of age. In total, her height has increased from -5.99 SD to -3.38 SD. Her pubertal development started (Tanner II breasts) around 9 ½ years of age. This is likely familial as her mother also had early puberty. The patient had normal calcium and phosphate levels on three separate occasions including during infancy.

Family history was unremarkable, and the patient has three brothers, all of normal height. *SHOX* gene testing was normal and a chromosomal microarray revealed a 493 kb duplication on chromosome 4 also present in the mother.

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

Supplementary Table 3

Autosomal dominant variants in family P04: The table lists all variants that passed filters as described in Methods and demonstrated an autosomal dominant mode of inheritance. A sibling status of "Affected" indicates that the heterozygous variant is shared by the father, patient, and sibling. A sibling status of "Unaffected" indicates that the heterozygous variant is shared by the father and patient only. All other annotations are the same as Supplementary Table 2.

Patient 04 Dominant Analysis

Gene	Inheritance Pattern	Sibling Status	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)
CPXM2	Autosomal dominant	Unaffected	Chr 10: 125506395	C	T	NA	NA	missense	S719N	0.006	benign	unknown	none
MLL3	Autosomal dominant	Unaffected	Chr 7: 151878026	T	C	NA	NA	missense	R2307G	0.262	benign	unknown	none
RALGPS1	Autosomal dominant	Unaffected	Chr 9: 129812366	A	T	NA	NA	missense	L115F	1.000	probably damaging	guanine nucleotide exchange factor	none
PLEKHG1	Autosomal dominant	Unaffected	Chr 6: 151161760	C	T	NA	NA	missense	H1296Y	0.229	benign	unknown	none
HIST1H1A	Autosomal dominant	Unaffected	Chr 6: 26017679	T	TCC	NA	NA	frame shift	c.282_283insCC	NA	NA	histone protein	none
DBF4B	Autosomal dominant	Unaffected	Chr 17: 42828020	T	C	NA	NA	missense	M416T	0.000	benign	role in DNA replication and cell proliferation	none
BAIAP2L2	Autosomal dominant	Unaffected	Chr 22: 38484752	C	CA	NA	NA	splice site	c.1118+3_4insA	NA	NA	cell membrane formation	none
GTPBP1	Autosomal dominant	Unaffected	Chr 22: 39112035	G	A	NA	NA	missense	R143H	0.115	benign	mRNA degradation	none
ATP11B	Autosomal dominant	Unaffected	Chr 3: 182559873	C	G	NA	NA	missense	R223G	1.000	probably damaging	P-type ATPase ion transporter	none
GLS2	Autosomal dominant	Unaffected	Chr 12: 56868396	C	G	NA	NA	missense	V386L	0.994	probably damaging	unknown	none
THOC3	Autosomal dominant	Unaffected	Chr 5: 175395149	C	T	NA	NA	missense	M21I	0.001	benign	functions in mRNA transport	none
WNT9B	Autosomal dominant	Unaffected	Chr 17: 44952729	C	G	NA	NA	missense	I199M	0.689	possibly damaging	signaling molecule in tissue development	none
PDE3A	Autosomal dominant	Unaffected	Chr 12: 20766482	T	A	NA	NA	missense	S373T	0.671	possibly damaging	phosphodiesterase	none
OSMR	Autosomal dominant	Unaffected	Chr 5: 38876314	C	T	NA	NA	missense	R29C	0.876	possibly damaging	component of IL31 receptor, activates downstream STAT proteins	Primary localized cutaneous amyloidosis 1
KIAA0141	Autosomal dominant	Unaffected	Chr 5: 141314152	G	A	NA	NA	splice site	c.1149+1G>A	NA	NA	unknown	none
KAT6A (MYST	Autosomal dominant	Unaffected	Chr 8: 41800361	C	T	NA	NA	missense	E796K	0.181	benign	histone acetyltransferase	none

MYPN	Autosomal dominant	Unaffected	Chr 10: 69905256	G	A	NA	NA	missense	G368D	0.993	probably damaging	sarcomere component	Dilated cardiomyopathy 1KK, familial restrictive cardiomyopathy 4, familial hypertrophic cardiomyopathy 22
LMTK2	Autosomal dominant	Affected	Chr 7: 97822515	G	C	NA	NA	missense	S913T	0.094	benign	kinase	none
DTWD1	Autosomal dominant	Affected	Chr 15: 49917564	TCTA	T	NA	NA	codon deletion	c.201_203 delCTA	NA	NA	unknown	none
FUT2	Autosomal dominant	Affected	Chr 19: 49206910	C	T	NA	NA	missense	R233C	0.403	benign	fucosyltransferase	none
TTC31	Autosomal dominant	Affected	Chr 2: 74710253	A	T	NA	NA	missense	I11F	0.917	possibly damaging	unknown	none
DLL4	Autosomal dominant	Affected	Chr 15: 41227163	C	T	NA	NA	missense	T363I	0.001	benign	angiogenesis	none
WDR53	Autosomal dominant	Affected	Chr 3: 196288144	T	C	NA	NA	missense	Y68C	0.998	probably damaging	unknown	none
FLRT2	Autosomal dominant	Affected	Chr 14: 86087932	G	A	NA	NA	missense	G25E	0.965	probably damaging	cell adhesion and receptor signaling	none
NPR2	Autosomal dominant	Affected	Chr 9: 35800429	G	T	NA	NA	missense	E389D	0.000	benign	natriuretic peptide receptor	Maroteaux type acromesomelic dysplasia
CC2D1A	Autosomal dominant	Affected	Chr 19: 14037355	G	A	NA	NA	missense	D656N	0.120	benign	neuronal transcription factor	Autosomal recessive mental retardation 3
BAZ2B	Autosomal dominant	Affected	Chr 2: 160194190	C	T	NA	NA	missense	E1850K	0.366	benign	transcriptional regulation	none
RFC5	Autosomal dominant	Affected	Chr 12: 118469082	A	AGAT	NA	NA	codon insertion	c.959_960i nsGAT	NA	NA	DNA replication factor	none
LYPLA2	Autosomal dominant	Affected	Chr 1: 24121184	G	A	NA	NA	missense	V220M	0.795	possibly damaging	hydrolyze fatty acid moeities	none
SGTA	Autosomal dominant	Affected	Chr 19: 2767667	C	T	NA	NA	missense	E40K	0.998	probably damaging	protein chaperone	none
ZNF774	Autosomal dominant	Affected	Chr 15: 90903968	A	G	NA	NA	missense	Q302R	0.014	benign	possible role in transcription regulation	none
MUC16	Autosomal dominant	Affected	Chr 19: 9073879	C	T	NA	NA	missense	A4523T	0.001	benign	mucin	none
NR2F6	Autosomal dominant	Affected	Chr 19: 17356004	C	A	NA	NA	missense	G9V	0.082	benign	transcription repression	none
DHX33	Autosomal dominant	Affected	Chr 17: 5359481	T	C	NA	NA	missense	I291V	0.518	possibly damaging	transcription of rRNA	none
MUC16	Autosomal dominant	Affected	Chr 19: 9072538	C	A	NA	NA	missense	A4970S	0.087	benign	mucin	none

SERINC2	Autosomal dominant	Affected	Chr 1: 31906004	G	A	NA	NA	missense	V403I	0.002	benign	unknown	none
PAH	Autosomal dominant	Affected	Chr 12: 103249019	G	A	NA	rs62517205	missense	H201Y	0.943	possibly damaging	phenylalanine hydroxylase	phenylketonuria
MYH10	Autosomal dominant	Affected	Chr 17: 8424573	G	C	NA	NA	missense	T632S	0.001	benign	myosin heavy chain	none
AFAP1L1	Autosomal dominant	Affected	Chr 5: 148699238	G	A	NA	NA	missense	V525M	1.000	probably damaging	cell projection formation	none
PIGS	Autosomal dominant	Affected	Chr 17: 26881275	G	C	NA	NA	missense	T544S	0.000	benign	transfer of phosphatidylinositol-glycan membrane anchors	none
AP2A1	Autosomal dominant	Affected	Chr 19: 50298969	G	A	NA	NA	missense	R263Q	1.000	probably damaging	vescicle transport	none
FCGBP	Autosomal dominant	Affected	Chr 19: 40364055	G	A	NA	NA	missense	H4863Y	0.987	probably damaging	maintenance of mucosa	none
HTR6	Autosomal dominant	Affected	Chr 1: 20005569	G	A	NA	NA	missense	R344H	0.000	benign	serotonin receptor	none
KIR2DL1	Autosomal dominant	Affected	Chr 19: 55285012	T	G	NA	NA	missense	C100G	1.000	probably damaging	unknown	none
HS3ST3A1	Autosomal dominant	Affected	Chr 17: 13503872	T	C	NA	NA	missense	Y192C	1.000	probably damaging	heparan sulfate sulfotransferase	none
CERKL	Autosomal dominant	Affected	Chr 2: 182521519	G	A	NA	NA	missense	P72L	0.197	benign	regulation of apoptosis	none
RAI1	Autosomal dominant	Affected	Chr 17: 17698661	G	A	NA	NA	missense	G800E	0.22	benign	transcriptional regulator	Smith-magenis syndrome

Supplementary Table 4

Autosomal dominant variants in family P05: Annotation is the same as in Supplementary Table 3.

Patient 05 Dominant Analysis

Gene	Inheritance Pattern	Sibling Status	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)
C1orf141	Autosomal D	Unaffected	Chr1: 67559090	T	G	NA	NA	missense	K267N	0.046	benign	unknown	none
CELSR2	Autosomal D	Unaffected	Chr1: 109803819	T	C	NA	NA	missense	F1372L	0.998	probably damaging	receptor for cell/cell signaling in neural development	none
ILK	Autosomal D	Unaffected	Chr11: 6631060	A	G	NA	NA	missense	N321S	0.115	benign	regulates integrin-mediated signal transduction	
LAMB4	Autosomal D	Unaffected	Chr7: 107706230	C	T	NA	NA	missense	C938Y	1.000	probably damaging	laminin for extracellular interactions	none
GCC1	Autosomal D	Unaffected	Chr7: 127222636	T	C	NA	NA	missense	K587R	0.001	benign	involved in Golgi structure	none
SDS	Autosomal D	Unaffected	Chr12: 113836398	G	C	NA	NA	missense	A116G	0.004	benign	serine and threonine dehydratase	none
COX6B1	Autosomal D	Unaffected	Chr19: 36145529	G	A	NA	NA	missense	E55K	0.143	benign	cytochrome C oxidase subunit	cytochrome c oxidase deficiency
KCNJ14	Autosomal D	Unaffected	Chr19: 48967513	G	A	NA	NA	missense	D264N	0.996	probably damaging	potassium channel	none
NYNRIN	Autosomal D	Unaffected	Chr14: 24877504	G	A	NA	NA	missense	G210S	0.754	possibly damaging	unknown	none
IGF2R	Autosomal D	Unaffected	Chr6: 160489364	C	T	NA	NA	missense	P1400L	0.386	benign	receptor for IGF2 and other cell signaling ligands	
TTLL11	Autosomal D	Unaffected	Chr9: 124855120	C	G	NA	NA	missense	G193A	0.017	benign	modifies alpha tubulin	none
TMEM45B	Autosomal D	Unaffected	Chr11: 129728556	CTT	C	NA	NA	frame shift	NA	NA	NA	unknown	none
RELL1	Autosomal D	Unaffected	Chr4: 37640126	G	T	NA	NA	missense	A129E	1.000	probably damaging	unknown	none
BAG3	Autosomal D	Unaffected	Chr10: 121436295	CAGG	C	NA	NA	codon deletion	NA	NA	NA	regulates molecular chaperones and inhibit apoptosis	Dilated cardiomyopathy 1HH; Myofibrillar myopathy 6
WAC	Autosomal D	Unaffected	Chr10: 28878666	C	T	NA	NA	missense	P128L	0.000	benign	regulates transcription and RNA processing	none
ENAM	Autosomal D	Unaffected	Chr4: 71507984	A	T	NA	NA	missense	N281Y	0.967	probably damaging	formation of tooth enamel	Amelogenesis imperfecta type IB and IC
TRIM14	Autosomal D	Unaffected	Chr9: 100850210	A	T	NA	NA	missense	C291S	0.801	possibly damaging	unknown	none
CGB1	Autosomal D	Unaffected	Chr19: 49539490	C	A	NA	NA	missense	C27F	1.000	probably damaging	chorionic gonadotropin subunit	none

RBBP8	Autosomal D	Unaffected	Chr18: 20548820	GA	G	NA	NA	frame shift	NA	NA	NA	DNA repair pathways	Seckel syndrome 2; Jawad Syndrome
ZAN	Autosomal D	Unaffected	Chr7: 100389666	G	A	NA	NA	missense	P2536L	0.926	probably damaging	sperm protein for binding to egg	none
CCDC15	Autosomal D	Unaffected	Chr11: 124829751	C	T	NA	NA	missense	T123I	0.001	benign	unknown	none
SUPT5H	Autosomal D	Unaffected	Chr19: 39944011	C	T	NA	NA	missense	R31W	0.830	possibly damaging	regulates transcription and RNA processing	none
TMED6	Autosomal D	Unaffected	Chr16: 69383523	C	T	NA	NA	missense	R82Q	0.998	probably damaging	unknown	none
MOGAT2	Autosomal D	Unaffected	Chr11: 75428946	G	A	NA	NA	missense	A5T	0.999	probably damaging	fatty acid metabolism	none
GPR6	Autosomal D	Unaffected	Chr6: 110300437	C	T	NA	NA	missense	A41V	0.147	benign	G-protein coupled receptor	none
NLRP4	Autosomal D	Unaffected	Chr19: 56390314	G	T	NA	NA	missense	A951S	0.085	benign	regulates inflammatory pathways	none
KIAA1432	Autosomal D	Unaffected	Chr9: 5774209	C	G	NA	NA	missense	P1412R	0.077	benign	unknown	none
LRRC61	Autosomal D	Unaffected	Chr7: 150034315	C	T	NA	NA	missense	P122L	0.014	benign	unknown	none
NEMF	Autosomal dominant	Affected	Chr 14: 50253447	G	C	NA	NA	missense	Q973E	0.425	benign	nuclear export	none
PAX8	Autosomal dominant	Affected	Chr 2: 113977674	A	G	NA	NA	missense	L424S	0.992	probably damaging	thyroid transcription factor	Congenital hypothyroidism
MPP2	Autosomal dominant	Affected	Chr 17: 41960344	G	A	NA	NA	missense	T172I	0.173	benign	unknown	none
GTF3C2	Autosomal dominant	Affected	Chr 2: 27552024	T	C	NA	NA	missense	N668S	0.002	benign	transcription complex component	none
HECW2	Autosomal dominant	Affected	Chr 2: 197187284	C	A	NA	NA	missense	A268S	0.414	benign	E3 ubiquitin ligase	none
FAM83F	Autosomal dominant	Affected	Chr 22: 40417371	C	T	NA	NA	missense	T286M	0.950	possibly damaging	unknown	none
RNF40	Autosomal dominant	Affected	Chr 16: 30780841	C	T	NA	NA	nonsense	R836*	NA	NA	E3 ubiquitin ligase complex component	none
UGP2	Autosomal dominant	Affected	Chr 2: 64118276	A	C	NA	NA	missense	N481T	0.998	probably damaging	glucosyl donor	none
ZWILCH	Autosomal dominant	Affected	Chr 15: 66811324	C	T	NA	NA	missense	S143L	0.978	probably damaging	component of mitotic checkpoint	none
TTC3	Autosomal dominant	Affected	Chr 21: 38568067	T	A	NA	NA	missense	L1770H	0.681	possibly damaging	E3 ubiquitin ligase complex component	none
ZNF710	Autosomal dominant	Affected	Chr 15: 90622959	C	G	NA	NA	missense	F631L	0.038	benign	possible role in transcription regulation	none

A2ML1	Autosomal dominant	Affected	Chr 12: 8975800	G	C	NA	NA	missense	A29P	1.000	probably damaging	proteinase inhibitor	none
VPS13C	Autosomal dominant	Affected	Chr 15: 62253984	G	A	NA	NA	missense	R1238C	1.000	probably damaging	unknown	none
ELF5	Autosomal dominant	Affected	Chr 11: 34501833	G	A	NA	NA	missense	R244W	1.000	probably damaging	transcription factor in keratinocyte differentiation	none
IRF6	Autosomal dominant	Affected	Chr 1: 209961848	G	A	NA	NA	missense	R441C	0.134	benign	transcription factor in epidermal development	Popliteal pterygium syndrome 1; van der Woude syndrome
XPOT	Autosomal dominant	Affected	Chr 12: 64823883	A	G	NA	NA	missense	T598A	0.001	benign	nuclear export	none
DCTN2	Autosomal dominant	Affected	Chr 12: 57926769	T	C	NA	NA	missense	M258V	0.010	benign	chromosome alignment and microtubule alignment	none
LAMA1	Autosomal dominant	Affected	Chr 18: 7009319	C	T	NA	NA	missense	R1307Q	0.997	probably damaging	lamanin in extracellular matrix	none
COLQ	Autosomal dominant	Affected	Chr 3: 15498067	TG	T	NA	NA	frame shift	c.872_873insG	NA	NA	anchors acetylcholinesterase	Endplate acetylcholinesterase deficiency
ABHD15	Autosomal dominant	Affected	Chr 17: 27893425	T	C	NA	NA	missense	Y187C	0.004	benign	unknown	none
WDR6	Autosomal dominant	Affected	Chr 3: 49050602	T	G	NA	NA	missense	S545R	0.119	benign	cell growth suppression	none
LUZP2	Autosomal dominant	Affected	Chr 11: 24753719	T	C	NA	NA	missense	L79S	0.980	probably damaging	unknown	none
PLEC	Autosomal dominant	Affected	Chr 8: 144996248	G	A	NA	NA	missense	R2718W	0.740	possibly damaging	helps anchor various cytoskeletal elements	Epidermolysis bullosa simplex with pyloric atresia; Epidermolysis bullosa simplex, Ogna type; Muscular dystrophy with epidermolysis bullosa simplex; Limb-girdle muscular dystrophy
RIMS2	Autosomal dominant	Affected	Chr 8: 104897819	C	T	NA	NA	missense	S331L	0.000	benign	unknown	none
GAS6	Autosomal dominant	Affected	Chr 13: 114531579	A	G	NA	NA	missense	Y417H	0.130	benign	tyrosine kinase receptor ligand involved in various cell processes	none

POU6F2	Autosomal dominant	Affected	Chr 7: 39503980	G	C	NA	NA	missense	A591P	0.993	probably damaging	transcription factor involved in neuron differentiation	none
KRAS	Autosomal dominant	Affected	Chr 12: 25368389	A	AT	NA	NA	frame shift	NM_033360.2:c.556_557insT	NA	NA	GTPase	Cardiofaciocutaneous syndrome 2; Noonan syndrome 3
KIF14	Autosomal dominant	Affected	Chr 1: 200558395	T	TTTCCTG	NA	NA	codon change and codon insertion	c.3064_3065insTTCCTG	NA	NA	involved in cell division	none
UQCRC1	Autosomal dominant	Affected	Chr 3: 48638129	C	T	NA	NA	missense	V371I	0.001	benign	component of mitochondrial respiratory chain	none