Table S1. Detailed clinical phenotype and genetic variants in 42 patients.

Case number	Clinical phenotype										Main causes of death	Variant classification	Gene	Gene category	Chromosome	Position	Variant	Zygosity	Variant type	OMIM disease	Inheritance pattern	Reported previously	Confirmation by Sanger
	C	D	E	I	M	N	Rep	Res	U	Other													
P006	+	+	+					+	+		died at home	P	*NOTCH1*	Multiple	9	139399557	NM_017617:exon26:c.4587-1G>A	Het	splice_acceptor	Adams-Oliver syndrome 5, [MIM:616028]; Aortic valve disease 1, [MIM:109730]	AD	/	/
P051	+			+		+		+			give up treatment	P	*MAGEL2*	Multiple	15	23890978	NM_019066:exon1:c.1912C>T(p.Q638X)	Het	stop_gained	Schaaf-Yang syndrome, [MIM:615547]	AD/IM	PMID 27195816	Paternal
P076	+	+	+	+				+	+		infection	P	*CYBB*	Allergic/immunologic/infectious	X	37663371	NM_000397:exon9:c.1139G>A(p.W380X)	Hemi	stop_gained	Chronic granulomatous disease, X-linked, [MIM:306400]; Immunodeficiency 34, mycobacteriosis, X-linked, [MIM:300645]	XLR	PMID 9585602	De novo
P080	+		+					+	+		metabolic	P	*SLC25A20*	Metabolic/biochemical	3	48921485	NM_000387:exon3:c.270delC	Het	frameshift	Carnitine-acylcarnitine translocase deficiency, [MIM:212138]	AR	PMID 11592821	Maternal
P080	+		+					+	+		metabolic	P	*SLC25A20*	Metabolic/biochemical	3	48921567	NM_000387:exon3:c.199-10T>G	Het	intron	Carnitine-acylcarnitine translocase deficiency, [MIM:212138]	AR	PMID 24088670	Paternal
P081	+		+					+	+		metabolic	P	*SLC25A20*	Metabolic/biochemical	3	48921485	NM_000387:exon3:c.270delC	Het	frameshift	Carnitine-acylcarnitine translocase deficiency, [MIM:212138]	AR	PMID 11592821	Maternal
P081	+		+					+	+		metabolic	P	*SLC25A20*	Metabolic/biochemical	3	48921567	NM_000387:exon3:c.199-10T>G	Het	intron	Carnitine-acylcarnitine translocase deficiency, [MIM:212138]	AR	PMID 24088670	Paternal
P102	+	+		+	+		+	+	+	Retinopathy	give up treatment	P	*TCIRG1*	Skeletal	11	67817250	NM_006019:exon16:c.2008C>T(p.R670X)	Het	stop_gained	Osteopetrosis, autosomal recessive 1, [MIM:259700]	AR	PMID 11532986	Maternal
P102	+	+		+	+		+	+	+	Retinopathy	give up treatment	P	*TCIRG1*	Skeletal	11	67812518	NM_006019:exon10:c.1114C>T(p.Q372X)	Het	stop_gained	Osteopetrosis, autosomal recessive 1, [MIM:259700]	AR	PMID 11532986	Paternal
P105						+		+			give up treatment	P	*MTM1*	Neurologic	X	149828933	NM_000252:exon13:c.1446_1447delTG	Hemi	frameshift	Myotubular myopathy, X-linked, [MIM:310400]	XLR	/	Maternal
P118	+	+		+		+		+		Retinopathy	hematologic	P	*STXBP2*	Hematological	19	7705658	NM_006949:exon5:c.295_321del27	Het	inframe_deletion	Hemophagocytic lymphohistiocytosis, familial, 5, [MIM:613101]	AR	/	Paternal
P118	+	+		+		+		+		Retinopathy	hematologic	P	*STXBP2*	Hematological	19	7711208	NM_006949:exon16:c.1432delG	Het	frameshift	Hemophagocytic lymphohistiocytosis, familial, 5, [MIM:613101]	AR	/	Maternal
P119	+	+	+	+	+				+		hematologic	P	*STXBP2*	Hematological	19	7705658	NM_006949:exon5:c.295_321del27	Het	inframe_deletion	Hemophagocytic lymphohistiocytosis, familial, 5, [MIM:613101]	AR	/	Paternal
P119	+	+	+	+	+				+		hematologic	P	*STXBP2*	Hematological	19	7711208	NM_006949:exon16:c.1432delG	Het	frameshift	Hemophagocytic lymphohistiocytosis, familial, 5, [MIM:613101]	AR	/	Maternal
P123	+	+	+			+			+		metabolic	P	*CPT2*	Metabolic/biochemical	1	53676110	NM_000098:exon4:c.764A>G(p.D255G)	Het	missense	CPT II deficiency, infantile, [MIM:600649]; CPT II deficiency, lethal neonatal, [MIM:608836]; CPT II deficiency, myopathic, stress-induced, [MIM:255110]	AR	/	Paternal
P123	+	+	+			+			+		metabolic	P	*CPT2*	Metabolic/biochemical	1	53676379	NM_000098:exon4:c.1033G>A(p.G345R)	Het	missense	CPT II deficiency, infantile, [MIM:600649]; CPT II deficiency, lethal neonatal, [MIM:608836]; CPT II deficiency, myopathic, stress-induced, [MIM:255110]	AR	/	Maternal
P134	+		+			+		+			neuromuscular	P	*NFU1*	Metabolic/biochemical	2	69633155	NM_001002755:exon6:c.544C>T(p.R182W)	Het	missense	Multiple mitochondrial dysfunctions syndrome 1, [MIM:605711]	AR	PMID 25918518	Paternal
P134	+		+			+		+			neuromuscular	P	*NFU1*	Metabolic/biochemical	2	69642319	NM_001002755:exon5:c.482C>T(p.A161V)	Het	missense	Multiple mitochondrial dysfunctions syndrome 1, [MIM:605711]	AR	/	Maternal
P148	+	+	+					+	+	External ear malformation	give up treatment	P	*CHD7*	Multiple	8	61734709	NM_017780:exon11:c.2957+5G>A	Het	splice_region	CHARGE syndrome, [MIM:214800]; Hypogonadotropic hypogonadism 5 with or without anosmia, [MIM:612370]	AD	PMID 22461308	De novo
P153	+		+		+			+		epidermolysis bullosa	give up treatment	P	*ITGB4*	Dermatologic	17	73747118	NM_001005731:exon30:c.3719G>A(p.W1240X)	Het	stop_gained	Epidermolysis bullosa of hands and feet, [MIM:131800]; Epidermolysis bullosa, junctional, non-Herlitz type, [MIM:226650]; Epidermolysis bullosa, junctional, with pyloric atresia, [MIM:226730]	AR	PMID 18563182	Maternal
P153	+		+		+			+		epidermolysis bullosa	give up treatment	P	*ITGB4*	Dermatologic	17	73750839	NM_001005731:exon33:c.4291_4292delGT	Het	frameshift	Epidermolysis bullosa of hands and feet, [MIM:131800]; Epidermolysis bullosa, junctional, non-Herlitz type, [MIM:226650]; Epidermolysis bullosa, junctional, with pyloric atresia, [MIM:226730]	AR	/	Paternal
P164	+	+	+					+			cardiac	P	*OPLAH*	Metabolic/biochemical	8	145106241	NM_017570:exon28:c.3853C>T(p.Q1285X)	Het	stop_gained	5-oxoprolinase deficiency, [MIM:260005]	AR	/	Maternal
P164	+	+	+					+			cardiac	P	*OPLAH*	Metabolic/biochemical	8	145107351	NM_017570:exon23:c.3303+1G>C	Het	splice_donor	5-oxoprolinase deficiency, [MIM:260005]	AR	/	Paternal
P168	+		+			+		+	+	MODS	metabolic	P	*MUT*	Metabolic/biochemical	6	49425532	NM_000255:exon3:c.626dupC(p.K210X)	Het	frameshift	Methylmalonic aciduria, mut(0) type, [MIM:251000]	AR	PMID 26454439	Paternal
P168	+		+			+		+	+	MODS	metabolic	P	*MUT*	Metabolic/biochemical	6	49423917	NM_000255:exon4:c.787G>A(p.G263R)	Het	missense	Methylmalonic aciduria, mut(0) type, [MIM:251000]	AR	/	Maternal
P170	+	+	+	+		+		+	+		infection	P	*IL10RA*	Allergic/immunologic/infectious	11	117860269	NM_001558:exon3:c.301C>T(p.R101W)	Hom	missense	Inflammatory bowel disease 28, early onset, autosomal recessive, [MIM:613148]	AR	PMID 22476154	Paternal/ Maternal
P174	+			+		+		+			neuromuscular	P	*ACTA1*	Neurologic	1	229568080	NM_001100:exon4:c.553C>T(p.R185C)	Het	missense	Myopathy, actin, congenital, with cores, [MIM:161800]; Myopathy, actin, congenital, with excess of thin myofilaments, [MIM:161800]; Myopathy, congenital, with fiber-type disproportion 1, [MIM:255310]; Nemaline myopathy 3, autosomal dominant or recessive, [MIM:161800]	AD/AR	PMID 10508519	De novo
P182	+		+			+		+	+	MODS	metabolic	P	*MUT*	Metabolic/biochemical	6	49409682	NM_000255:exon10:c.1679G>A(p.C560Y)	Het	missense	Methylmalonic aciduria, mut(0) type, [MIM:251000]	AR	PMID 16435223	Maternal
P182	+		+			+		+	+	MODS	metabolic	P	*MUT*	Metabolic/biochemical	6	49425427	NM_000255:exon3:c.729insTT(p.D244Lfs*39)	Het	frameshift	Methylmalonic aciduria, mut(0) type, [MIM:251000]	AR	PMID 16281286	Paternal
P220	+				+	+					died at home	P	*FGFR2*	Skeletal	10	123276877	NM_000141:exon8:c.1040C>G(p.S347C)	Het	missense	Antley-Bixler syndrome without genital anomalies or disordered steroidogenesis, [MIM:207410]; Apert syndrome, [MIM:101200]; Beare-Stevenson cutis gyrata syndrome, [MIM:123790]; Bent bone dysplasia syndrome, [MIM:614592]; Craniofacial-skeletal-dermatologic dysplasia, [MIM:101600]; Craniosynostosis, nonspecific (3); Crouzon syndrome, [MIM:123500]; Jackson-Weiss syndrome, [MIM:123150]; LADD syndrome, [MIM:149730]; Pfeiffer syndrome, [MIM:101600]; Saethre-Chotzen syndrome, [MIM:101400]; Scaphocephaly and Axenfeld-Rieger anomaly (3); Scaphocephaly, maxillary retrusion, and mental retardation, [MIM:609579]	AD	PMID 7874170	De novo
P090	+					+		+			respiratory failure	LP	*PHOX2B*	Neurologic	4	41747992	NM_003924:exon3:c.756_776dup21(GCN)27	Het	inframe_insertion	Central hypoventilation syndrome, congenital, with or without Hirschsprung disease, [MIM:209880]; Neuroblastoma with Hirschsprung disease, [MIM:613013]	AD	/	/
P137	+		+	+		+		+	+	MODS	infection	LP	*SHOC2*	Multiple	10	112724120	NM_007373:exon2:c.4A>G(p.S2G)	Het	missense	Noonan-like syndrome with loose anagen hair, [MIM:607721]	AD	PMID 19684605	De novo
P085	+		+					+			give up treatment	VUS	*GDF1*	Cardiovascular	19	18980143	NM_001492:exon8:c.382A>C(p.T128P)	Het	missense	Double-outlet right ventricle, [MIM:217095]; Right atrial isomerism, [MIM:208530]; Tetralogy of Fallot, [MIM:187500]; Transposition of great arteries, dextro-looped 3, [MIM:613854]	AD/AR	/	/
P093	+	+	+	+	+	+		+			give up treatment	VUS	*ANKRD11*	Multiple	16	89348754	NM_013275:exon9:c.4196C>A(p.A1399E)	Het	missense	KBG syndrome, [MIM:148050]	AD	/	/
P096	+	+	+			+		+	+		give up treatment	VUS	*MYH9*	Multiple	22	36698664	NM_002473:exon20:c.2449G>T(p.A817S)	Het	missense	Deafness, autosomal dominant 17, [MIM:603622]; Epstein syndrome, [MIM:153650]; Fechtner syndrome, [MIM:153640]; Macrothrombocytopenia and progressive sensorineural deafness, [MIM:600208]; May-Hegglin anomaly, [MIM:155100]; Sebastian syndrome, [MIM:605249]	AD	/	/
P116		+	+					+		Meconium peritonitis	digestive tract perforation	VUS	*CHD7*	Multiple	8	61778137	NM_017780:exon38:c.8639C>T(p.P2880L)	Het	missense	CHARGE syndrome, [MIM:214800]; Hypogonadotropic hypogonadism 5 with or without anosmia, [MIM:612370]	AD	PMID 18834967	Maternal
P124	+					+		+		Pierre-Robin syndrome	give up treatment	VUS	*ASXL3*	Multiple	18	31318701	NM_030632:exon11:c.1333C>T(p.P445S)	Het	missense	Bainbridge-Ropers syndrome, [MIM:615485]	AD	/	/
P132	+	+	+				+	+			cardiac	VUS	*OCA2*	Dermatologic	15	28116337	NM_000275:exon21:c.2207C>T(p.S736L)	Hom	missense	Albinism, brown oculocutaneous, [MIM:203200]; Albinism, oculocutaneous, type II, [MIM:203200]	AR	PMID 9259203	Maternal
P133	+	+	+					+		Auricular malformation	give up treatment	VUS	*KDM6A*	Multiple	X	44969397	NM_021140:exon28:c.4079A>G(p.D1360G)	Het	missense	Kabuki syndrome 2, [MIM:300867]	XLD	/	/
P135	+			+				+			give up treatment	VUS	*ACY1*	Multiple	3	52022926	NM_000666:exon15:c.1063-1G>A	Hom	splice_acceptor	Aminoacylase 1 deficiency, [MIM:609924]	AR	PMID 26077850	/

P150	+	+	+				+			hematologic	VUS	*SERPINC1*	Hematological	1	173879975	NM_000488:exon4:c.679G>A(p.E227K)	Het	missense	Thrombophilia due to antithrombin III deficiency, [MIM:613118]	AD/AR	/	/
P155	+			+	+		+			hematologic	VUS	*SAMD9*	Multiple	7	92734381	NM_017654:exon3:c.1030C>T(p.R344X)	Het	stop_gained	MIRAGE syndrome, [MIM:617053]; Tumoral calcinosis, familial, normophosphatemic, [MIM:610455]	AD/AR	PMID 18094730	/
P160				+	+		+		MODS	give up treatment	VUS	*MTFMT*	Metabolic/biochemical	15	65316073	NM_139242:exon3:c.479T>C(p.I160T)	Het	missense	Combined oxidative phosphorylation deficiency 15, [MIM:614947]	AR	/	/
P160				+	+		+		MODS	give up treatment	VUS	*MTFMT*	Metabolic/biochemical	15	65295476	NM_139242:exon9:c.1094G>A(p.C365Y)	Het	missense	Combined oxidative phosphorylation deficiency 15, [MIM:614947]	AR	/	/
P161	+			+			+	+		give up treatment	VUS	*MEGF10*	Neurologic	5	126732263	NM_032446:exon7:c.452G>A(p.R151Q)	Het	missense	Myopathy, areflexia, respiratory distress, and dysphagia, early-onset, [MIM:614399]; Myopathy, areflexia, respiratory distress, and dysphagia, early-onset, mild variant, [MIM:614399]	AR	/	Maternal
P161	+			+			+	+		give up treatment	VUS	*MEGF10*	Neurologic	5	126758444	NM_032446:exon14:c.1673G>T(p.R558L)	Het	missense	Myopathy, areflexia, respiratory distress, and dysphagia, early-onset, [MIM:614399]; Myopathy, areflexia, respiratory distress, and dysphagia, early-onset, mild variant, [MIM:614399]	AR	/	Paternal
P169	+	+	+	+			+			infection	VUS	*ADAMTS13*	Hematological	9	136321241	NM_139025:exon26:c.3619G>A(p.G1207S)	Het	missense	Thrombotic thrombocytopenic purpura, familial, [MIM:274150]	AR	/	/
P169	+	+	+	+			+			infection	VUS	*ADAMTS13*	Hematological	9	136287573	NM_139025:exon1:c.10C>T(p.R4C)	Het	missense	Thrombotic thrombocytopenic purpura, familial, [MIM:274150]	AR	/	/
P179	+			+		+	+			infection	VUS	*CYBB*	Allergic/immunologic/infectious	X	37664401	NM_000397:exon10:c.1294A>C(p.T432P)	Hemi	missense	Chronic granulomatous disease, X-linked, [MIM:306400]; Immunodeficiency 34, mycobacteriosis, X-linked, [MIM:300645]	XLR	/	/
P185	+			+			+			respiratory failure	VUS	*F11*	Hematological	4	187209748_187209749	NM_000128.3: c.1858_1859delinsAG (p.E620R)	Het	missense	Factor XI deficiency, autosomal dominant, [MIM:612416]; Factor XI deficiency, autosomal recessive, [MIM:612416]	AD/AR	/	/
P185	+			+			+			respiratory failure	VUS	*VWF*	Hematological	12	6128145	NM_000552:exon28:c.4439C>T(p.P1480L)	Het	missense	von Willebrand disease, type 1, [MIM:193400]; von Willebrand disease, types 2A, 2B, 2M, and 2N, [MIM:613554]; von Willibrand disease, type 3, [MIM:277480]	AD/AR	/	/
P185	+			+			+			respiratory failure	VUS	*VWF*	Hematological	12	6161871	NM_000552:exon16:c.2024C>T(p.P675L)	Het	missense	von Willebrand disease, type 1, [MIM:193400]; von Willebrand disease, types 2A, 2B, 2M, and 2N, [MIM:613554]; von Willibrand disease, type 3, [MIM:277480]	AD/AR	/	/
P189		+	+			+		+		give up treatment	VUS	*MYO5B*	Digestive	18	47506849	NM_001080467:exon9:c.1021C>T(p.Q341X)	Het	stop_gained	Microvillus inclusion disease, [MIM:251850]	AR	PMID 21199752	/
P189		+	+			+		+		give up treatment	VUS	*MYO5B*	Digestive	18	47480726	NM_001080467:exon13:c.1625G>A(p.R542H)	Het	missense	Microvillus inclusion disease, [MIM:251850]	AR	/	/
P189		+	+			+		+		give up treatment	VUS	*MYO5B*	Digestive	18	47500877	NM_001080467:exon10:c.1165G>T(p.V389F)	Het	missense	Microvillus inclusion disease, [MIM:251850]	AR	/	/
P192	+			+			+			cardiac	VUS	*SCN5A*	Cardiovascular	3	38629052	NM_198056:exon15:c.2275A>T(p.I759F)	Het	missense	Atrial fibrillation, familial, 10, [MIM:614022]; Brugada syndrome 1, [MIM:601144]; Cardiomyopathy, dilated, 1E, [MIM:601154]; Heart block, nonprogressive, [MIM:113900]; Heart block, progressive, type IA, [MIM:113900]; Long QT syndrome-3, [MIM:603830]; Sick sinus syndrome 1, [MIM:608567]; Ventricular fibrillation, familial, 1, [MIM:603829]	AD/AR	PMID 19862833	/
P207	+			+			+			respiratory failure	VUS	*F12*	Hematological	5	176830291	NM_000505:exon12:c.1495C>G(p.L499V)	Het	missense	Angioedema, hereditary, type III, [MIM:610618]; Factor XII deficiency, [MIM:234000]	AD/AR	/	/
P219	+						+		MODS	cardiac	VUS	*CREBBP*	Multiple	16	3819324	NM_004380:exon15:c.2911A>G(p.R971G)	Het	missense	Rubinstein-Taybi syndrome 1, [MIM:180849]	AD	/	/
P221	+			+	+	+	+		MODS,hearing loss	died at home	VUS	*KAT6B*	Skeletal	10	76603163	NM_012330:exon3:c.548G>T(p.G183V)	Het	missense	Genitopatellar syndrome, [MIM:606170]; SBBYSS syndrome, [MIM:603736]	AD	/	/
P222	+			+			+			died at home	VUS	*EP300*	Multiple	22	41574181	NM_001429:exon31:c.6466C>T(p.P2156S)	Het	missense	Rubinstein-Taybi syndrome 2, [MIM:613684]	AD	/	/

Clinical phenotype, C: circulatory system, D: digestive system, E: endocrine system, I: immune system, M: motor system, N: nervous system, Rep: reproductive system, Res: respiratory system,U: urinary system. XLR: X-linked recessive, XLD: X-linked dominant.