

Table S1. Supplementary materials. Distribution of variants and characteristics of skeletal and extra-skeletal features in probands

Patient №	Sex	Age y.o	SDS height	Nucleotide substitution	Amino Acid substitution	Family cases	Platyspondyly	Coxa vara	Myopia	Cleft palate	SNHL	Phenotype
1	f	5	-0,71	c.620G>T	p.Gly207Val	+	-	-	-	-	-	Mild SED
2	f	12	-3,7	c.654+4dupA		-	+	-	+	+	-	STL1
3	f	4	-4,65	c.709-1G>T		-	+	+	+	-	+	KD
4	f	13	-0,17	c.817-1G>A		-	-	-	-	-	-	SPPD
5	m	5	2,17	c.823C>T	p.Arg275Cys	-	+	-	-	-	-	KD
6	f	2	-3,47	c.905C>T	p.Ala302Val	-	-	+	+	+	+	SEDC/KD
7	f	2,5	-1,38	c.926G>T	p.Gly309Val	+	+	-	-	-	-	Mild SED
8	f	9	-3,42	c.970-8T>G		-	+	+	+	-	+	KD
9	m	13	-6,1	c.980G>T	p.Gly327Val	-	+	-	-	+	-	SEDC
10	f	4	-1,11	c.1023+1G>C		-	+	-	+	+	+	KD
11	f	8	-2,11	c.1043G>T	p.Gly348Val	-	-	-	-	-	-	Mild SED
12	f	4	-5,3	c.1068+1G>C		-	+	+	+	-	+	KD
13	f	5	-2,18	c.1069G>A	p.Gly357Ser	-	-	-	-	-	-	Mild SED
14	f	16	-1,08	c.1090G>T	p.Gly364Cys	+	+	+	-	-	-	SPPD
15	m	6	-5,51	c.1195G>A	p.Gly399Arg	-	+	+	-	+	-	SEDC
16	f	7	-1,36	c.1266+5G>C		-	+	+	+	-	-	KD
17	f	11 months	1,16	c.1348G>C	p.Gly450Arg	-	-	-	+	-	-	SEMD
18	m	8	-3,87	c.1421_1426del	p.Gly474_Pro475del	-	+	+	+	+	+	KD
19	m	14	-7,16	c.1484G>A	p.Gly495Glu	+	+	+	+	+	+	SEMD
20	f	7	-2,91	c.1510G>A	p.Gly504Ser	-	+	-	-	-	-	SEDC
21	f	17	-4,90	c.1510G>A	p.Gly504Ser	+	+	+	-	-	-	SEDC
22	f	2	-2,17	c.1636G>A	p.Gly546Ser	-	-	-	-	-	-	Mild SED
23	f	7	-4,80	c.1636G>A	p.Gly546Ser	-	+	+	-	-	-	SEMD
24	f	11	-4,40	c.1681G>A	p.Gly561Ser	-	+	+	-	-	-	SEDC
25	f	3	-2,93	c.1780G>A	p.Gly594Arg	-	-	-	+	-	-	SEDC
26	f	17	2,2	c.1833+1G>A		-	-	-	+	+	-	STL1
27	f	7	-9,70	c.2005G>A	p.Gly669Ser	-	+	-	+	-	-	SEDC
28	m	8	-2,21	c.2059G>A	p.Gly687Ser	-	-	+	-	-	-	Mild SED
29	m	8	-7,51	c.2095G>T	p.Gly699Cys	-	+	+	+	-	-	SEDC
30	m	10	0,96	c.2382delT	p.Gly795fs	+	-	-	+	-	-	STL1
31	f	6 months	-5,65	c.2600G>A	p.Gly867Asp	-	+	+	-	-	-	SEDC
32	m	6	-1,95	c.2600G>T	p.Gly867Val	-	+	-	-	-	-	Mild SED
33	f	12	-5,00	c.2609G>A	p.Gly870Glu	+	+	+	-	-	-	SEMD
34	m	9 months	-5,32	c.2617G>A	p.Gly873Arg	+	+	+	-	-	-	SEDC
35	m	6	-7,27	c.2671G>A	p.Gly891Ser	-	+	+	-	-	-	SEDC
36	m	2	-7,41	c.2671G>A	p.Gly891Ser	-	+	+	+	-	-	SEDC
37	f	9	-6,01	c.2671G>A	p.Gly891Ser	-	+	+	+	-	-	SEDC
38	f	12	-1,85	c.2710C>T	p.Arg904Cys	-	-	-	+	+	+	STL1
39	m	10	-1,51	c.2710C>T	p.Arg904Cys	-	-	-	+	-	+	STL1
40	m	6	0,24	c.2813dupC	p.Gly939Trpfs*5	+	-	-	+	+	-	STL1
41	m	11	-1,3	c.2833G>A	p.Gly945Ser	-	+	-	-	-	-	Mild SED
42	f	1 month	1,61	c.2839C>T	p.Gln947Ter	+	-	-	+	+	-	STL1

43	f	4	-8,00	c.2974A>G	p.Arg992Gly	-	+	-	+	-	-	SEDC
44	f	7	-8,73	c.3121G>A	p.Gly1041Ser	-	+	+	-	-	-	SEMD
45	f	1	-3,89	c.3346G>T	p.Gly1116Cys	-	+	+	-	-	-	SEDC
46	m	9	-0,57	c.3397C>T	p.Arg1133Cys	+	-	-	-	-	-	Mild SED
47	f	5	-4,2	c.3442_3444del TCT	p.Ser1148del	-	+	+	+	-	-	SEDC/KD
48	f	5	-5,29	c.3463G>C	p.Gly1155Arg	-	+	+	-	-	-	SEDC
49	f	14	-6,99	c.3464G>T	p.Gly1155Val	-	+	+	-	-	-	SEDC
50	f	9 months	-4,44	c.3464G>T	p.Gly1155Val	-	+	+	-	+	-	SEDC
51	f	11 months	-3,65	c. 3554G>A	p.Gly1185Glu	-	+	+	-	-	-	SEMD
52	m	3 months	-4,58	c.3589G>C	p.Gly1197Arg	-	-	-	-	+	-	SEDC
53	f	7	-7,8	c.3589G>A	p.Gly1197Ser	-	+	+	-	-	+	SEDC
54	f	4	-4,86	c.3627_3644del	p.Pro1211_Pro1216del	-	+	+	-	-	+	SEDC/KD
55	m	11	-3,15	c.3713A>G	p.Tyr1238Cys	-	+	-	+	-	+	STL1
56	m	8	-0,8	c.3897G>T	p.Trp1299Cys	-	+	+	-	-	-	Mild SED
57	f	8	-2,5	c.3950T>G	p.Met1317Arg	+	-	-	-	-	-	Mild SED
58	m	12	5,4	c.4074+1G>A		-	-	-	+	-	+	STL1
59	m	11	-1,8	c.4133T>A	p.Leu1378Gln	-	-	+	-	-	-	Mild SED
60	m	14	3,1	c.4317+1G>T		-	-	-	+	-	-	STL1

Table S2. Supplementary materials. Description of novel variants identified in the sample

Nº	Nucleotide substitution	Amino Acid substitution	Number of patients with novel confirmed mutation	Criteria for classifying pathogenic variants	Segregation analysis	Clinical significance ACMG Guidelines, 2015.	ClinVar ID	Phenotype
1	c.620G>T	p.Gly207Val	1	PM1, PM2, PM5, PP1, PP2, PP3, PP4	+	Likely pathogenic	SCV002029100	Mild SED
2	c.654+4dupA		1	PS2, PM2, PP4	de novo	Likely pathogenic	SCV002029089	STL1
3	c.817-1G>A		1	PVS1, PS2, PM2, PP3, PP4	de novo	Pathogenic	SCV002029107	SPPD
4	c.970-8T>G		1	PS2, PM2, PP4	de novo	Likely pathogenic	SCV002029110	KD
5	c.980G>T	p.Gly327Val	1	PS2, PM1, PM2, PM5, PP2, PP3, PP4	de novo	Pathogenic	SCV002029111	SEDC
6	c.1023+1G>C		1	PVS1, PS2, PM2, PP3, PP4	de novo	Pathogenic	SCV002029106	KD
7	c.1068+1G>C		1	PVS1, PS2, PM2, PP3, PP4	de novo	Pathogenic	SCV002029109	KD
8	c.1069G>A	p.Gly357Ser	1	PS2, PM1, PM2, PM5, PP2, PP3, PP4	de novo	Pathogenic	SCV002029112	Mild SED
9	c.1090G>T	p.Gly364Cys	1	PM1, PM2, PP1, PP2, PP4	+	Likely pathogenic	SCV002029113	SPPD
10	c.1195G>A	p.Gly399Arg	1	PS2, PM1, PM2, PM5, PP2, PP3, PP4	de novo	Pathogenic	SCV002029114	SEDC
11	c.1266+5G>C		1	PS2, PM2, PP3, PP4	de novo	Likely pathogenic	SCV002029115	KD
12	c.1348G>C	p.Gly450Arg	1	PS2, PM1, PM2, PM5, PP2, PP3, PP4	de novo	Pathogenic	SCV002029116	SEMD
13	c.1421_1426del	p.Gly474_Pro475del	1	PS2, PM1, PM2, PM4, PP3, PP4	de novo	Pathogenic	SCV002029090	KD
14	c.1780G>A	p.Gly594Arg	1	PS2, PM1, PM2, PM5, PP2, PP3, PP4	de novo	Pathogenic	SCV002029091	SEDC
15	c.2005G>A	p.Gly669Ser	1	PS2, PM1, PM2, PP2, PP3, PP4	de novo	Pathogenic	SCV002029105	SEDC
16	c.2095G>T	p.Gly699Cys	1	PS2, PM1, PM2, PP2, PP3, PP4	de novo	Pathogenic	SCV002029092	SEDC
17	c.2600G>T	p.Gly867Val	1	PS2, PM1, PM2, PM5, PP2, PP3, PP4	de novo	Pathogenic	SCV002029093	Mild SED
18	c.2671G>A	p.Gly891Ser	3	PS2, PM1, PM2, PM5, PP2, PP3, PP4	de novo	Pathogenic	SCV002029094	SEDC
19	c.3346G>T	p.Gly1116Cys	1	PS2, PM1, PM2, PP2, PP3, PP4	de novo	Pathogenic	SCV002029095	SEDC
20	c.3442_3444delTCT	p.Ser1148del	1	PS2, PM1, PM2, PM4, PP3	de novo	Pathogenic	SCV002029096	SEDC/KD

21	c.3463G>C	p.Gly1155Arg	1	PS2, PM1, PM2, PM5, PP2, PP3, PP4	de novo	Pathogenic	SCV002029097	SEDC
22	c.3554G>A	p.Gly1185Glu	1	PS2, PM1, PM2, PP2, PP3, PP4	de novo	Pathogenic	SCV002029098	SEMD
23	c.3589G>C	p.Gly1197Arg	1	PS2, PM1, PM2, PM5, PP2, PP3, PP4	de novo	Pathogenic	SCV002029099	SEDC
24	c.3897G>T	p.Trp1299Cys	1	PS2, PM2, PP3, PP4	de novo	Likely Pathogenic	SCV002029101	Mild SED
25	c.3950T>G	p.Met1317Arg	1	PM2, PP1, PP3, PP4	+	Uncertain Significance	SCV002029102	Mild SED
26	c.4074+1G>A		1	PVS1, PS2, PM2, PP3, PP4	de novo	Pathogenic	SCV002029108	STL1
27	c.4133T>A	p.Leu1378Gln	1	PS2, PM2, PP3, PP4	de novo	Likely Pathogenic	SCV002029103	Mild SED
28	c.4317+1G>T		1	PVS1, PS2, PM2, PP3, PP4	de novo	Pathogenic	SCV002029104	STL1