Supplementary Table 1. WES variants in CBA patients with known causative genes.

Family ID	Chromosome	Position	Reference	Mutant	Gene	Effect on protein	dbSNP	AA_Charge	AA_Pos	AF	consScoreGERP	In Homozygous Interval ?
760	23	107148774	G	A	MID2	missense		VAL/ILE	331/706	0.0014	5.35	
	23	53574861	G	A	HUWE1	missense		SER/LEU	3470/4375	0.0005	5.3	+
	23	20193290	T	C	RPS6KA3	missense		ILE/VAL	407/741	0.0005	5.14	
1074	14	68220462	C	T	ZFYVE26	missense		VAL/ILE	2384/2540	0.001	4.86	+
1091	9	135147123	TCTGACA	T	SETX	coding				0.0007	5.45	+
	23	105193709	A	G	NRK	missense		ASP/GLY	1499/1583	0.0007	5.41	
	23	102978859	G	A	GLRA4	missense		LEU/PHE	168/418	0.0007	5.11	+
	23	11157261	G	A	ARHGAP6	missense		PRO/SER	883/975	0.0007	4.77	
	2	215657132	C	A	BARD1	missense		VAL/LEU	85/778	0.0017	5.24	+
1092	10	81058854	G	A	ZMIZ1	missense		VAL/MET	572/1068	0.0005	5.17	
	5	14461395	C	T	TRIO	missense		THR/ILE	1824/3098	0.0005	5	
	9	37783990	T	G	EXOSC3	missense		ASP/ALA	132/165	0.0005	5.29	
	4	16504387	A	C	LDB2	missense		MET/ARG	334/374	0.0005	5.27	
	9	13121877	T	C	MPDZ	missense		ARG/GLY	1698/2042	0.0005	4.59	
1719	8	90937720	ATTTG	A	OSGIN2	frameshift				0.0016	5.44	
	4	25146422	A	G	SEPSECS	missense		TYR/HIS	334/502	0.0009	5.2	
	12	51584196	T	C	POU6F1	missense		GLU/GLY	247/302	0.0009	4.26	+
	4	22750572	A	G	GBA3	missense		GLU/GLY	399/470	0.0009	5.96	
	20	4768278	C	T	RASSF2	splice-5				0.0003	5.41	+
	4	169195105	C	T	DDX60	missense		VAL/MET	812/1713	0.0003	4.98	
	6	168910650	C	T	SMOC2	missense		SER/LEU	47/458	0.0005	4.82	+
	9	128246853	G	T	MAPKAP1	missense		ALA/GLU	359/523	0.0003	5.26	+
2029	2	231988281	T	C	HTR2B,PSMD1	missense		ILE/MET	66/482	0.001	-0.677	
	18	21131657	G	A	NPC1	missense		HIS/TYR	530/1279	0.001	5.58	
2088	17	73945964	CT	C	ACOX1	frameshift				0.0007	4.83	+
1898	15	43819181	C	T	MAP1A	missense	rs185524761	SER/LEU	1837/2804	0.0003	4.59	+
	20	49348331	G	A	PARD6B	missense		ARG/HIS	3/373	0.0005	4.28	
	15	43022061	A	G	CDAN1	missense	rs141931755	LEU/SER	762/1228	0.0003	5.49	+
	19	36558255	CCT	C	WDR62	frameshift				0.001	5.08	
	15	42459731	C	T	VPS39	missense		ARG/GLN	413/876	0.0003	6.04	+
1533	4	94137980	TAA	T	GRID2	frameshift				0.0007	4.43	
1373	7	87135241	G	A	ABCB1	missense		THR/MET	1203/1281	0.001	5.59	
	18	59780510	C	T	PIGN	missense		GLY/ARG	431/932	0.0007	5.16	+
	7	100371066	G	A	ZAN	missense		VAL/MET	1862/2722	0.0007	4.63	+
2477	15	68504102	CAG	C	CLN6	frameshift				0.0005	5.14	+
	7	98554070	G	A	TRRAP	missense		VAL/ILE	2024/3831	0.0014	4.29	+
	12	10124287	G	A	CLEC12A	splice-5				0.0016	4.07	+
	7	101267498	T	C	MYL10	missense		ASN/SER	42/227	0.0014	4.27	+
1679	18	19996290	C	T	CTAGE1	stop-gained		TRP/stop	495/746	0.0005	-1.23	
	11	66468197	G	A	SPTBN2	stop-gained		ARG/stop	1125/2391	0.0003	3.75	
	4	83774785	C	A	SEC31A	missense		VAL/LEU	659/1182	0.0003	5.04	
	19	4054825	C	G	ZBTB7A	missense	rs147200385	ALA/PRO	136/585	0.0003	4.9	
	23	70680560	A	G	TAF1	missense	rs147517498	ASN/SER	1789/1894	0.0007	4.9	+
	6	130413962	G	A	L3MBTL3	missense		GLY/SER	531/781	0.0003	5.42	
	3	16636084	G	A	DAZL	missense		PRO/SER	213/316	0.0005	6.02	
	6	129963054	T	C	ARHGAP18	missense		MET/VAL	75/664	0.0003	4.72	
	23	138827937	A	G	ATP11C	missense		PHE/LEU	973/1133	0.0003	5.97	
	7	155295771	C	T	CNPY1	missense		GLU/LYS	91/93	0.0003	4.46	

Causative candidates in red compared with other variants (in black) found in each family. Other variants passing criteria are listed for each family. Columns 1 Family number, 2 Chromosome number, 3 Position in hg19, 4 Reference base, 5 Mutant base, 6 Gene name, 7 Functional outcome predicted by Genome Variant Server (GVS), 8 dbSNP reference ID if exists, 9 Amino acid change, 10 Amino acid position, 11 Allele frequency (AF) with our in-house 4000 exome database, 12 GERP conservation score, 13 in homozygous interval within the exome sequence data.

Supplementary Table 2. Mutations in SNX14 identified in this study and method of mutation.

Family ID	Position (hg19)	Nucleotide Change	Deduced protein change	Effect on protein	Gene identification	Accession
1410	chr6:86277285 A>T	c.428T>A	p.Leu143*	stop-gained	WES	NM_153816.3
2935	chr6:82359586 A>AA	c.645dupA	p.Glu216Arg*fs**25	frameshift	Sanger	NM_153816.3
3423					Sanger	NM_153816.3
1902	chr6:86258072 CTCTTA>C	c.809_813delTAAGA	p.Ile270Arg*fs**17	frameshift	WES	NM_153816.3
3087	chr6: 86257219 C>T	c.912+5G>A	-	splice	Sanger	NM_153816.3
468	chr6:86253455 G>A	c.1132C>T	p.Arg378*	stop-gained	WES	NM_153816.3
525					WES	NM_153816.3
ABD					WES	NM_153816.3
2892					WES	NM_153816.3
1382	chr6:86253404 TC>T	c.1182delG	p.Lys395Arg*fs**22	frameshift	WES	NM_153816.3
1971	chr6:86216982 ACAATGTC>A	c.2764_2770delGACATTG	p.Asp922*	stop-gained	WES	NM_153816.3
HMF	chr6:86,217,761 AC>C	c. 2670delT	p.Cys890*	stop-gained	WES	NM_153816.3

Columns 1 Family number, 2 Position in hg19, 3 Nucleotide change in cDNA, 4 Protein change, 5 Functional outcome predicted by Genome Variant Server (GVS), 6 Gene identification method (Whole Exome Sequencing (WES) or Sanger sequencing), 7 RefSeq Accesion Number.

Supplementary Table 3. WES variants in SNX14 mutated families.

Family ID	Chromosome	Position	Reference	Mutant	Gene	Effect on protein	dbSNP	AA_Charge	AA_Pos	AF	consScoreGERP	In Homozygous Interval ?
468	6	86253455	G	A	SNX14	stop-gained		ARG/stop	378/947	0.0011	1.6	+
	10	11374574	CTCCAGTCTTCCTCTTCGGCATGCCCTGGAAGCTTCT	C	CELF2	splice-5	rs76081927	N/A		0.0073	4.06	
	6	86253404	TC	T	SNX14	frameshift		LYS/ARGfs*22	395/947	0.001	N/A	+
	19	33183410	T	G	NUDT19,LOC100288796	missense		CYS/GLY	182/376	0.0059	4.36	
	16	48121987	G	A	ABCC12	missense		SER/LEU	1162/1360	0.0027	4.68	
	14	23996935	C	T	ZFHX2	missense		VAL/MET	1027/2707	0.0022	4.33	
1382	13	96553101	T	C	UGGT2	missense	rs35060832	LYS/ARG	865/1517	0.0063	4.25	+
	7	2581807	A	C	BRAT1	missense		LEU/ARG	321/822	0.0057	4.96	
	6	87965700	A	G	ZNF292	missense		LYS/GLU	785/2724	0.001	5.41	+
	6	84567062	A	G	RIPPLY2	missense		ASP/GLY	114/129	0.001	5.17	+
	1	45190324	C	G	C1orf228	missense		ALA/GLY	345/441	0.0029	4.28	
	1	15429903	G	A	KAZ	missense		VAL/MET	610/776	0.0017	5.06	
1410	6	86277285	A	T	SNX14	stop-gained		LEU/stop	143/947	0.0003	N/A	+
	6	86258072	CTCTTA	C	SNX14	frameshift		ILE/ARGfs*17	270/947	0.0003	N/A	+
1902	9	90313595	C	T	DAPK1	missense		PRO/LEU	879/1431	0.0003	5.2	
	6	43607930	A	G	MAD2L1BP	missense		LYS/ARG	194/307	0.0003	5.73	+
	6	43607930	A	G	MAD2L1BP	missense		LYS/ARG	162/275	0.0003	5.73	+
1971	23	154010044	T	G	MPP1	missense		ASP/ALA	327/467	0.0006	5.39	+
	6	86216982	ACAATGTC	A	SNX14	frameshift		ASP/stop	922/947	0.0006	N/A	+
2892	1	20680261	GCTGGCCTCCGGAGC	G	VWA5B1	frameshift		ARG/PROfs*7	1053/1216	0.0005		+
	23	154059045	C	A	CXorf68	missense	rs184141613	LEU/PHE	29/100	0.0014		+
	6	86253455	G	A	SNX14	stop-gained		ARG/stop	378/947	0.0015	1.23	+

Mutations in SNX14 in red identified in this study compared with other variants found in each family. Other variants passing criteria are listed for each family. Columns 1 Family number, 2 Chromosome number, 3 Position in hg19, 4 Reference base, 5 Mutant base, 6 Gene name, 7 Functional outcome predicted by Genome Variant Server (GVS), 8 dbSNP reference ID if exists, 9 Amino acid change, 10 Amino acid position, 11 Allele frequency (AF) with our in-house 4000 exome database, 12 GERP conservation score, 13 in homozygous interval within the exome sequence data.

Supplementary Note

The two older affected members of family 1382 were subject to comprehensive analysis of lysosomal enzyme function, all of which were normal. These included the following: beta-galactosidase, beta-mannosidase, alpha-L-fucosidase, alpha-mannosidase, beta-glucuronidase, beta-hexosaminidase A, arylsulfatase A, galactocerebrosidase, sphingomyelinase, glucocerebrosidase, alpha-L-iduronidase, sialidase, arylsulfatase B, alpha-galactosidase, alpha-glucosaminidase, beta-hexosaminidase, and acid lipase. The glycosoaminoglycans were elevated in urine for age at 32 mg/mmol creatinine (reference for age is less than or equal to 10 mg/mmol creatinine), but two dimensional elecrophoretic separation of GAGs from urine shows a normal pattern. Very long chain fatty acids and phytanic acids were normal in plasma.