X-exome Sequencing of 405 Unresolved Families Identifies Seven Novel Intellectual Disability Genes

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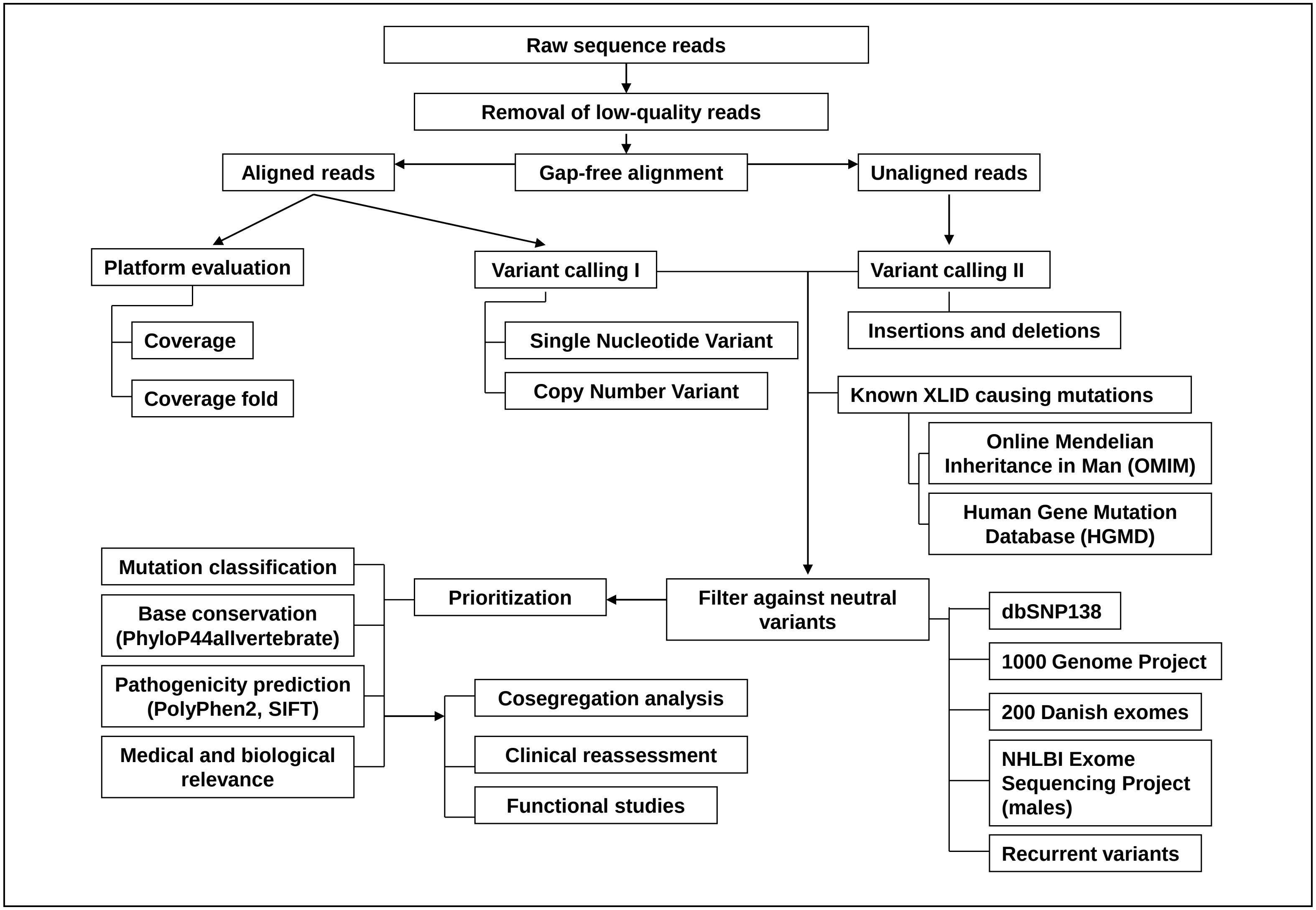
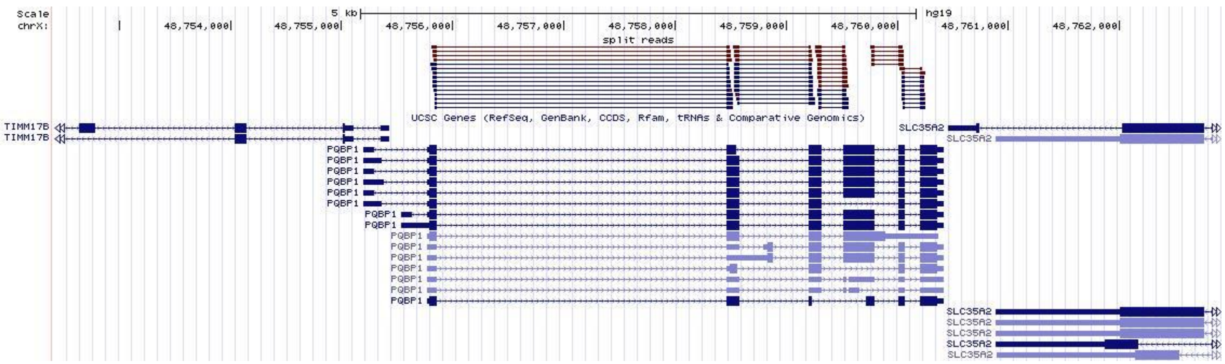
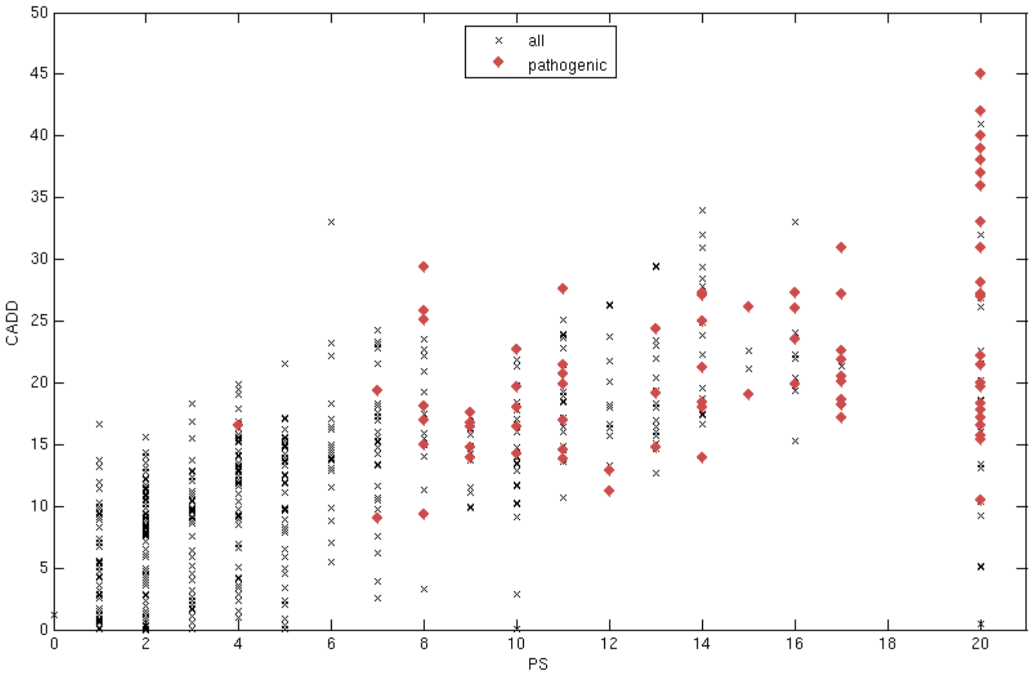


Supplementary Figure 1. NGS-based Variant Discovery Work-flow



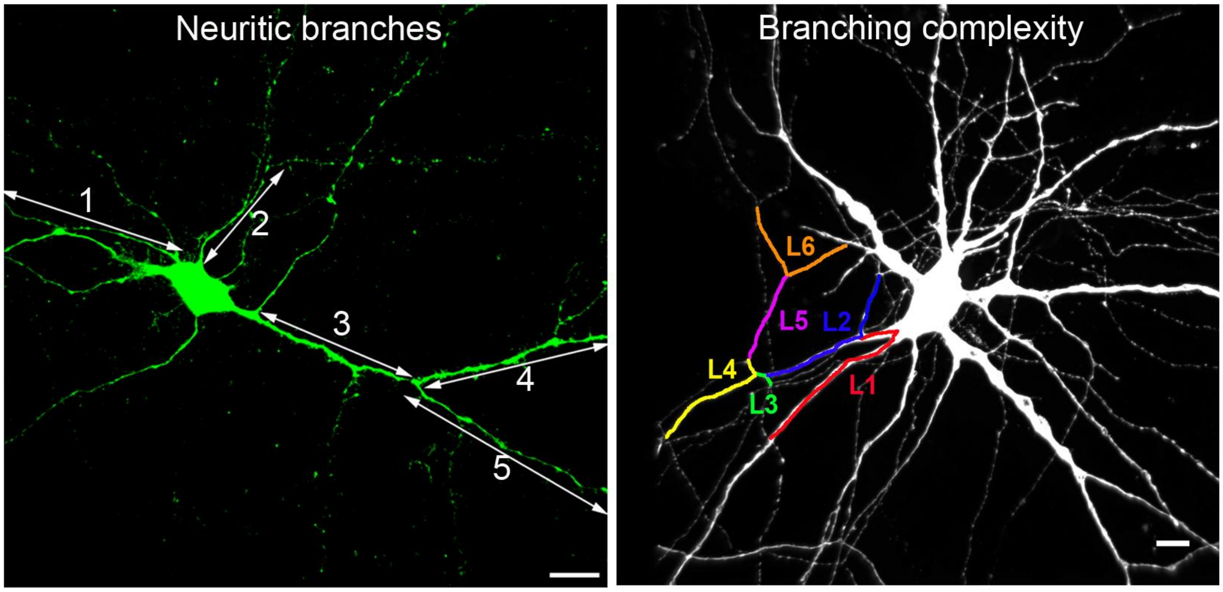
Supplementary Figure 2. Identification of a *PQBP1* Retrocopy

PQBP1 has been implicated in non-syndromic and different syndromic forms of XLID.[1-3] It usually exists as single copy gene in the human genome as indicated by our results and visualized in the UCSC GenomeBrowser (bottom track). However, in one of the index patients with non-syndromic ID, we identified the presence of a complete retrocopy of *PQBP1*, which was absent in his mother. Usually, retrocopies are not easy to discover based on reads covering a single exon since these reads will unambiguously map to exons of the original gene they are derived from. However, reads spanning exon boundaries are unique to the retrocopy and can be identified via a split read mapping approach (top track, colors reflect read orientation). Using this approach, split reads were recovered for all *PQBP1* exons of GenBank transcript NM_005710 and the results were validated by PCR amplifications using various *PQBP1* primer combinations and subsequent Sanger sequencing of the specific amplification products (data not shown). The clinical relevance of this finding could not be clarified because other family members were unavailable for testing.



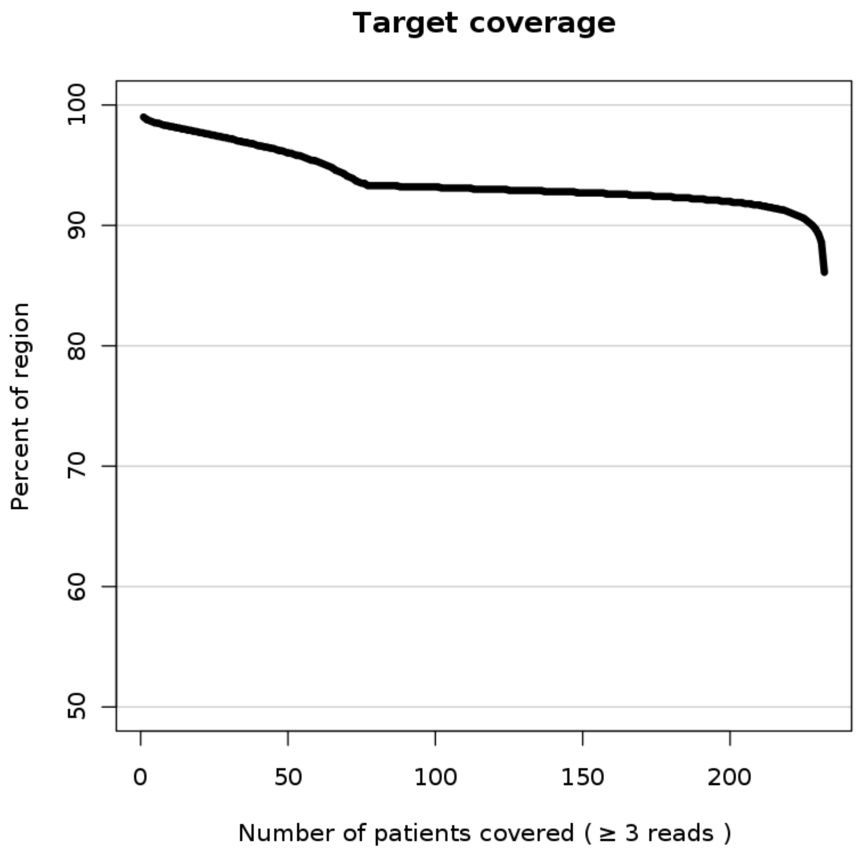
Supplementary Figure 3. Comparison of Prioritization (PS) and CADD Scores

Prioritization and CADD scores were used to rank all variants by their functional relevance. While CADD scores incorporate a large number of computational and experimental data, prioritization scores are more coarse grained but put special emphasis on already known XLID genes. However, not all highly scored variant are necessarily implicated in XLID as several of these have been excluded as likely XLID relevant by co-segregation analysis, e.g. *GUCY2F* with CADD 41 and PS: 20).



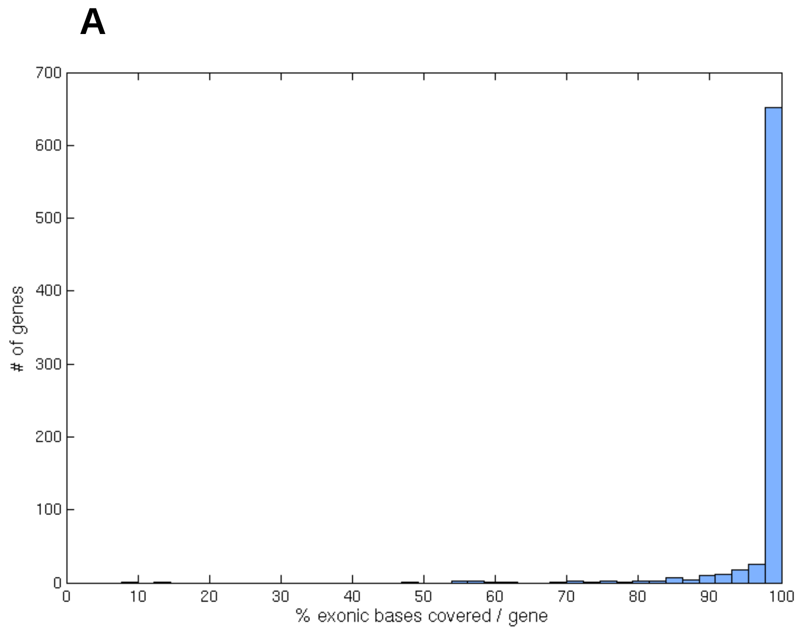
Supplementary Figure 4. Illustration of Neuritic Branches and Branching Complexity

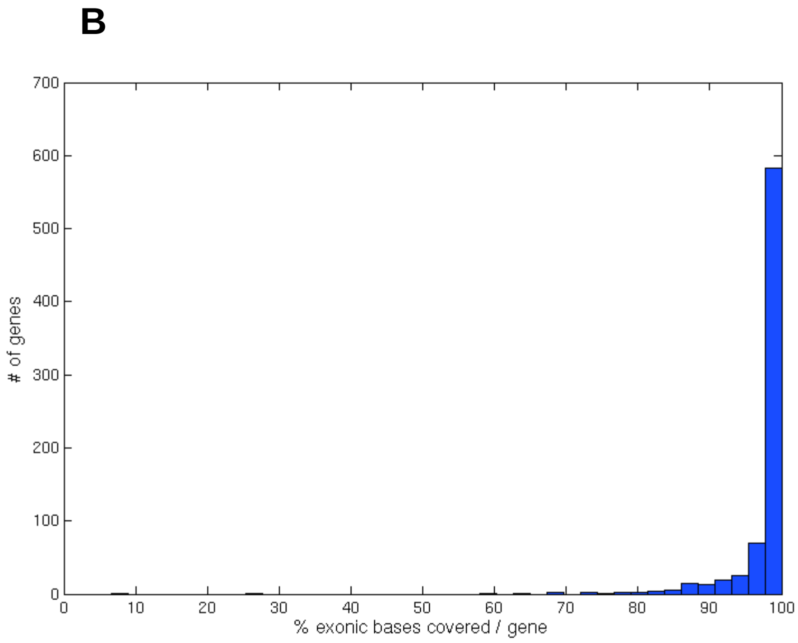
Both neuritic branches and branching complexity are exemplified from GFP-labeled mouse hippocampal neuron differentiated *in vitro* (18 DIV). Neuritic branches are shown as double-ended arrows on the neuron, with a single branch considered as the segment between two branching points of the dendrite. Neuritic branching complexity, i.e. the nomenclature used to classify the different levels (L) of branches is illustrated by artificial coloring of the neuron. A primary branch extends from the soma to the next branching point, a secondary branch extends from a primary branch to the next branching point, *et cetera*. The cell represented has primary branches with red color (L1), secondary branches with blue (L2), tertiary branches with green (L3) quaternary branch with yellow (L4), fifth level with pink and sixth level with orange. Scale bar represents 10 µm.

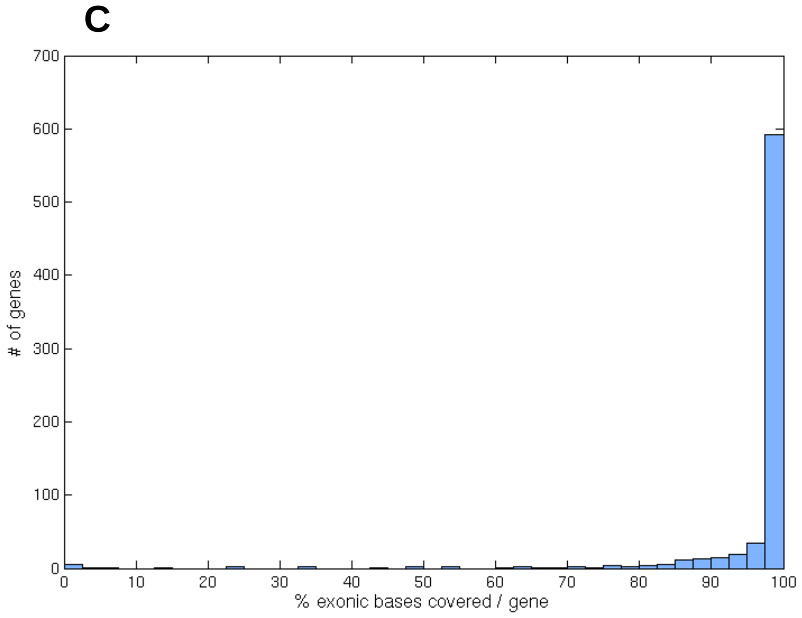


Supplementary Figure 5. Percentage of Covered (at Least Three Reads) Target Region against the Number of Probands Covered

Analysis of the coverage of the target regions reveals that the vast majority of targeted sequence is covered by at least three reads, the minimal number of reads required for calling variations. The drop at the far right can be attributed to uncovered regions private to individual probands. 92% of the target region is covered in 200 or more affected males.

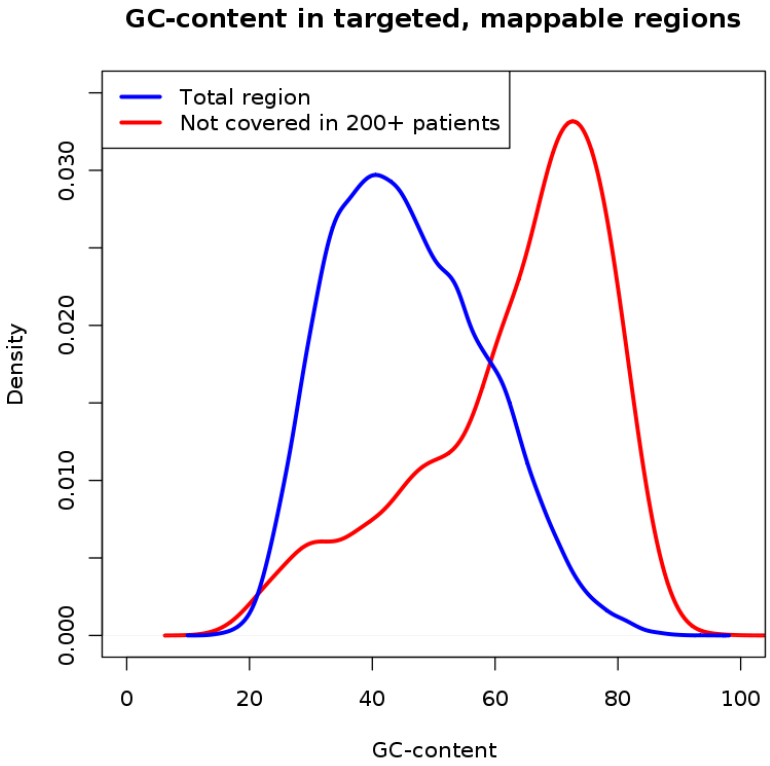






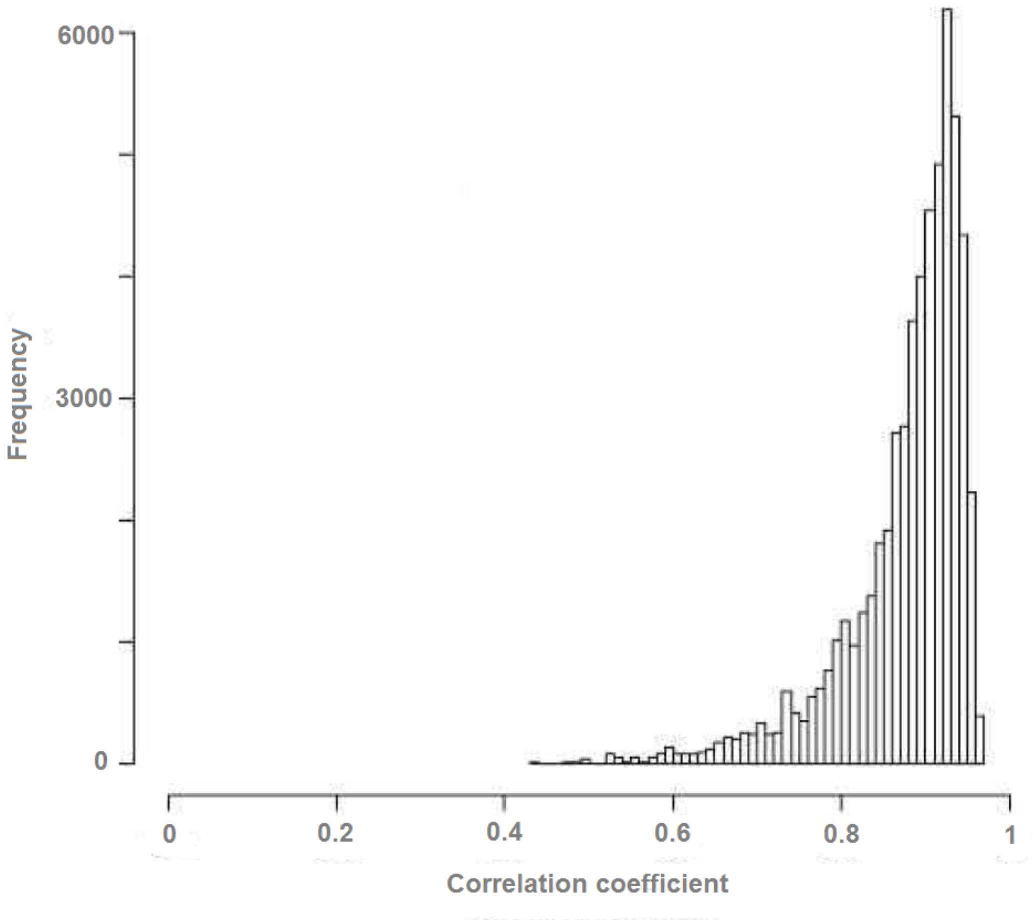
Supplementary Figure 6. Coverage of Targeted Regions of RefSeq Genes

The vast majority of targeted, coding regions of RefSeq genes is consistently (in >=90% of samples) covered by at least 3 non-redundant reads, independent of the enrichment technology applied. For the Agilent SureSelect platform coding sequences (A) are slightly better covered than entire exonic regions (B). The lower coverage of untranslated regions is likely due to differences in repeat- and/or GC-content. RainDance amplicons (C) were primarily designed for coding regions resulting in ~14% (~9% for Agilent SureSelect) of genes covered less than 95%.



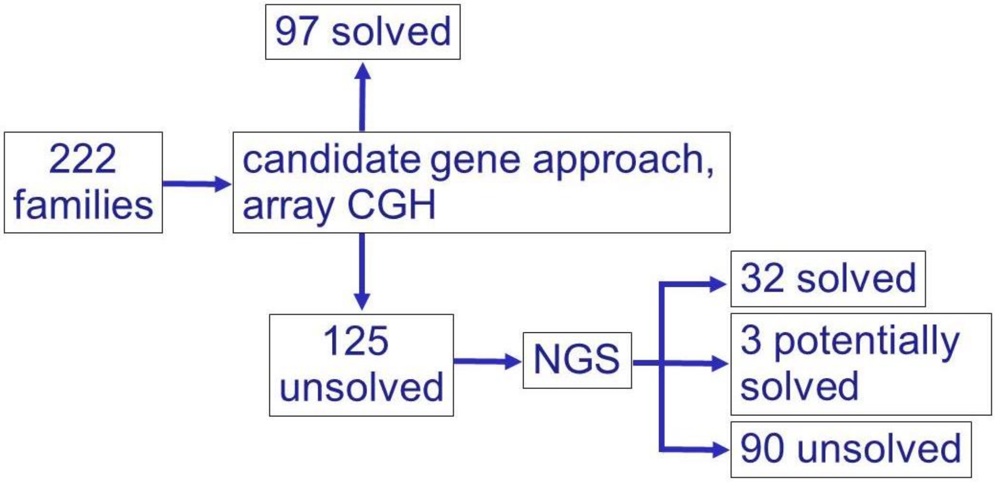
Supplementary Figure 7. GC-content in Targeted, Mappable regions

The targeted and mappable region has median GC-content of 45% (blue distribution) which closely matches the average GC content of the human genome. The small percent (1.8%) of this region not covered (<3 reads) in 200 or more affected males has a significantly higher median GC-content of 67% (red distribution). The difference is statistically significant (p-value < $2.2*10^{-16}$ using a Wilcoxon rank sum test).



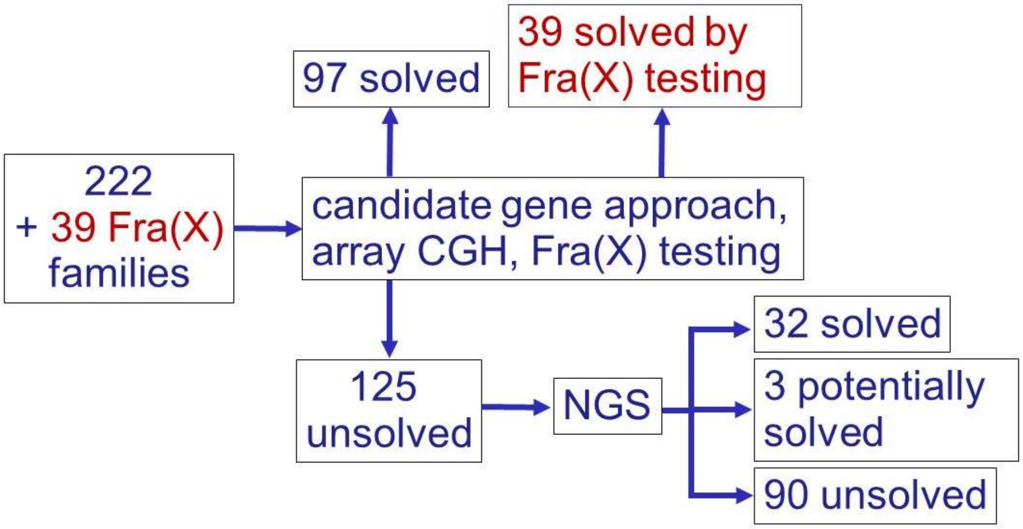
Supplementary Figure 8. Pair-wise Correlations of 248 Samples Based on Depth

Given that the same technology was used for all affected males analyzed from 248 families it is assumed that the samples will correlate in their patterns of positional depth. This is reflected in the high degree of pair-wise correlations (Pearson coefficient).



Supplementary Figure 9. Mutation Yield of NGS in Non Fra(X) XLID families

222 fragile X-negative families from the EUROMRX consortium with at least two affected in two generations and positive linkage to the X chromosome were previously screened in a subset of known XLID genes using Sanger sequencing and array CGH ([4] and unpublished results). The disease-causing DNA variant was found in 97 of these families. Index patients from the remaining 125 unsolved families were analyzed in this study. Combined, the gene defect could be identified in 58% of the 222 families.



Supplementary Figure 10. Mutation Yield of NGS in XLID families, Including Fra(X), which is Seen in 15% of XLID families

Combining NGS and Fra(X) screening allows a molecular diagnosis in 64% of all XLID families.

Supplementary Table 1. Non-recurrent Missense, Nonsense, Frameshift, Small Insertions and Deletions, and Splice Site Variants Identified in the Screen and Absent in Controls

Gene	Variant	Protein length	Genomic position (hg19)	PhyloP	PolyPhen2	SIFT	XLID gene*	In Tarpey et al. (number in list)[5]	PS	HGMD	C-Score
ABCD1	C>A, p.P480T	746	X:153002655-153002655	4.95	probably_damaging	DAMAGING	XLID	-	16		22.000
ABCD1	C>T, p.R191C	746	X:152991292-152991292	1.54	benign	DAMAGING	XLID	-	7		13.400
ACE2	T>C, p.D206G	806	X:15607546-15607546	4.13	benign	TOLERATED		-	5		12.610
ACE2	T>G, p.Q102P	806	X:15613008-15613008	3.06	benign	TOLERATED		-	4		8.974
ACRC	C>T, p.S242L	692	X:70823852-70823852	-0.14	possibly_damaging	TOLERATED		-	2		8.217
ACRC	G>A, p.D130N	692	X:70823515-70823515	1.23	benign	DAMAGING(Low_confidence)		-	3		9.902
ACRC	insATG, p.L135_E135insD	692	X:70823527-70823528	0.29	n/a	n/a		-	4		1.559
ACSL4	G>A, p.P375L	712	X:108917632-108917632	5.83	probably_damaging	DAMAGING	XLID	-	17	12525535	31.000
ACSL4	G>A, p.R654*	712	X:108902601-108902601	1.2	n/a	n/a	XLID	-	20		45.000
ACTRT1	C>T, p.G40R	377	X:127186068-127186068	3.11	probably_damaging	DAMAGING		-	12		18.030
ACTRT1	del1bp, p.S233TfsX52	377	X:127185488-127185488	-0.52	n/a	n/a		-	20		9.264
AFF2	G>A, p.A977T	1277	X:148048440-148048440	0.9	probably_damaging	TOLERATED	XLID	-	7		14.730
AFF2	G>A, p.V242M	1302	X:147743984-147743984	3.47	probably_damaging	TOLERATED	XLID	-	9		11.520
AIFM1	C>A, p.R463I	614	X:129267348-129267348	5.55	possibly_damaging	DAMAGING	XLID	-	14		24.900
AIFM1	G>A, p.A473V	614	X:129267318-129267318	2.56	possibly_damaging	TOLERATED	XLID	-	7		16.030
APEX2	C>T, p.R125W	519	X:55028815-55028815	2.95	probably_damaging	DAMAGING		-	11		24.000
APLN	T>C, p.M75V	78	X:128782614-128782614	2.48	probably_damaging	n/a		-	5		15.630
AR	C>T, p.P392S	921	X:66766162-66766162	1.06	benign	DAMAGING		-	4	10946887, 20305676	16.810
ARAF	G>C, p.Q208H	607	X:47426104-47426104	3.58	possibly_damaging	TOLERATED		-	5		15.000
ARHGAP4	G>A, p.A426V	947	X:153178912-153178912	0.79	benign	TOLERATED		-	2		8.363
ARHGAP4	G>C, p.R529G	947	X:153176601-153176601	1.98	probably_damaging	DAMAGING		-	10		17.100
ARHGEF6	A>G, p.I698T	777	X:135754221-135754221	4.39	possibly_damaging	DAMAGING	XLID	-	13		17.980
ARMCX5	C>T, p.A42V	559	X:101857194-101857194	0.83	probably_damaging	TOLERATED		-	4		16.380
ARMCX6	T>C, p.Q116R	301	X:100871264-100871264	0.62	benign	DAMAGING		-	4		4.227
ARR3	T>A, p.I363K	389	X:69501537-69501537	1.46	possibly_damaging	DAMAGING		-	7		15.290
ARSF	A>G, p.M258V	591	X:3002649-3002649	0.74	benign	TOLERATED		-	2		9.044

ARSF	G>A, p.V170I	591	X:3002385-3002385	-0.68	benign	TOLERATED		-	1		6.759
ARSF	del5bp, p.F283SfsX30	591	X:3007551-3007555	1.19	n/a	n/a		-	20		13.39
ARX	C>A, p.R536S	563	X:25022868-25022868	2.14	probably_damaging	DAMAGING	XLID	-	14		18.410
ASB9	G>T, p.H41N	253	X:15277041-15277041	2.86	probably_damaging	DAMAGING		-	11		14.530
ATP2B3	C>T, p.T407M	1174	X:152814194-152814194	5.43	possibly_damaging	DAMAGING		-	11		19.250
ATP2B3	G>A, p.E726K	1174	X:152821624-152821624	5.29	benign	TOLERATED		-	6		33.000
ATP2B3	T>C, p.V668A	1174	X:152818672-152818672	4.59	benign	TOLERATED		-	5		15.290
ATP7A	C>T, p.T680I	1501	X:77267038-77267038	-0.87	benign	TOLERATED	XLID	-	4		5.097
ATP7A	G>C, p.R648T	1501	X:77266746-77266746	0.3	benign	TOLERATED	XLID	-	5		8.042
ATP7A	del21997bp, p.M1*	1501	X:77223458-77245454	0.26	n/a	n/a	XLID	-	13		
ATRX	C>A, p.D1566Y	2493	X:76891409-76891409	5.44	probably_damaging	DAMAGING	XLID	-	17		17.130
ATRX	C>T, p.R2085H	2493	X:76829787-76829787	5.23	probably_damaging	DAMAGING	XLID	-	17	16813605	20.100
ATRX	G>A, p.R2085C	2493	X:76829788-76829788	5.23	probably_damaging	DAMAGING	XLID	-	17	12673795	18.620
ATRX	T>C, p.S742G	2493	X:76938524-76938524	1.08	benign	TOLERATED	XLID	-	5		3.424
ATXN3L	C>T, p.G257S	356	X:13337285-13337285	2.45	probably_damaging	TOLERATED		-	5		16.230
AWAT1	T>C, p.F10S	329	X:69454574-69454574	2.25	benign	DAMAGING		-	5		11.150
AWAT1	del926bp, p.G211*	329	X:69459585-69460510	0.48	n/a	n/a		-	10		
BCAP31	del3bp, p.S65del	314	X:152988709-152988711	0.05	n/a	n/a	XLID	-	4		12.85
BCOR	A>G, p.V714A	1722	X:39932458-39932458	4.52	possibly_damaging	DAMAGING	XLID	-	13		15.740
BCOR	C>G, p.L722F	1722	X:39932433-39932433	1.81	probably_damaging	TOLERATED	XLID	-	7		15.610
BCOR	C>T, p.A134T	1722	X:39934199-39934199	0.89	benign	TOLERATED	XLID	-	5		8.873
BCOR	C>T, p.V679I	1722	X:39932564-39932564	5.53	probably_damaging	DAMAGING	XLID	-	17		21.300
BCOR	G>A, p.P316S	1722	X:39933653-39933653	1.29	possibly_damaging	TOLERATED	XLID	-	6		12.860
BCORL1	C>T, p.R1149W	1712	X:129154963-129154963	0.91	probably_damaging	n/a		-	4		14.410
BCORL1	C>T, p.R250W	548	X:129168586-129168586	1.12	probably_damaging	n/a		-	4		19.430
BCORL1	G>A, p.A1080T	1712	X:129149986-129149986	0.7	probably_damaging	n/a		-	4		14.130
BEND2	C>A, p.M619I	800	X:18192274-18192274	-1.88	benign	TOLERATED		-	1		9.434
BEND2	C>T, p.R593H	800	X:18192353-18192353	-1.3	benign	TOLERATED		-	1		2.910
BMX	T>A, p.D292E	676	X:15544210-15544210	-0.09	benign	TOLERATED		-	1		0.787
BRWD3	C>T, p.A255T	1803	X:79999581-79999581	5.46	possibly_damaging	DAMAGING	XLID	-	14		32.000
BRWD3	dup1196bp, CDS		X:80064038-80065233	0.78	n/a	n/a	XLID	-	7		
BTK	T>C, p.K160R	660	X:100617590-100617590	4.46	probably_damaging	TOLERATED		-	7		24.300
CA5B	C>T, p.R290C	318	X:15800701-15800701	2.52	probably_damaging	DAMAGING		-	11		22.800
CACNA1F	C>T, p.R523H	1978	X:49082487-49082487	4.75	probably_damaging	TOLERATED		-	7		15.620

CACNA1F	T>C, acceptor		X:49063575-49063575	1.85	n/a	n/a		-	4		15.490
CCDC120	C>T, p.P584L	631	X:48925506-48925506	0.73	probably_damaging	TOLERATED		-	4		10.410
CCDC120	G>A, p.R71H	619	X:48921456-48921456	3.67	probably_damaging	DAMAGING		-	12		26.300
CCDC120	G>T, p.S424I	631	X:48925026-48925026	3.34	probably_damaging	TOLERATED		-	6		18.300
CCDC22	C>A, p.A120E	628	X:49098612-49098612	3.44	probably_damaging	TOLERATED		-	6		18.370
CCDC22	C>T, p.R490W	628	X:49105314-49105314	3.95	possibly_damaging	DAMAGING		-	9		17.250
CCDC22	G>A, p.E208K	628	X:49099836-49099836	3.61	probably_damaging	DAMAGING		-	12		23.700
CCDC22	T>C, p.V171A	628	X:49099627-49099627	2.56	benign	TOLERATED		-	3		3.208
CCNB3	C>T, p.R240W	1396	X:50051887-50051887	0.71	possibly_damaging	DAMAGING		-	7		9.709
CCNB3	G>A, p.M390I	1396	X:50052339-50052339	-2.73	benign	DAMAGING		-	3		2.047
CD40LG	G>A, p.R181Q	262	X:135741330-135741330	0.08	benign	TOLERATED		-	2		10.880
CDK16	del2bp, p.F322WfsX12	336	X:47085594-47085595	0.35	n/a	n/a		-	20		0.474
CDK16	del2bp, p.W326VfsX5	497	X:47086039-47086040	3.07	n/a	n/a		-	20		37
CDKL5	G>A, p.A491T	1031	X:18622515-18622515	2.98	possibly_damaging	TOLERATED	XLID	-	7		14.200
CENPI	A>G, p.E74G	757	X:100356280-100356280	2.31	possibly_damaging	TOLERATED		-	4		15.650
CENPI	T>C, p.F427L	757	X:100385054-100385054	2.87	probably_damaging	DAMAGING		-	11		23.600
CENPI	T>G, p.L66W	757	X:100356256-100356256	2.31	probably_damaging	DAMAGING		-	11		16.400
CHM	T>A, p.L241F	654	X:85213962-85213962	0.45	probably_damaging	TOLERATED		-	4		15.600
CHM	T>C, p.I263V	654	X:85213898-85213898	2.68	benign	TOLERATED		-	3		15.470
CLCN4	C>G, p.L221V	761	X:10174503-10174503	5.55	probably_damaging	TOLERATED		-	8		25.100
CLCN4	G>A, p.G731R	761	X:10188916-10188916	5.82	probably_damaging	TOLERATED		-	8		29.400
CLCN4	G>A, p.G78S	761	X:10155642-10155642	5.38	probably_damaging	DAMAGING		-	14		25.000
CLCN4	G>A, p.V536M	761	X:10181750-10181750	5.77	probably_damaging	DAMAGING		-	14		27.100
CLCN4	del13bp, p.D15SfsX18	761	X:10153111-10153123	2.78	n/a	n/a		-	20		36
CLCN5	G>T, donor		X:49832416-49832416	2.73	n/a	n/a		-	5		16.230
CNGA2	A>T, p.D347V	665	X:150912015-150912015	4.14	probably_damaging	DAMAGING		-	13		16.980
CNGA2	G>A, p.R195H	665	X:150911109-150911109	4.89	benign	TOLERATED		-	5		14.760
CNGA2	G>A, p.V151I	665	X:150909342-150909342	4.81	probably_damaging	TOLERATED		-	7		23.300
CNKSR2	del3bp, p.E886del	1035	X:21627678-21627680	1	n/a	n/a		-	4		12.83
CNKSR2	insA, p.D152RfsX8	899	X:21458832-21458833	2.81	n/a	n/a		-	20		19.66
COL4A5	C>A, p.P739H	1686	X:107846263-107846263	3.62	probably_damaging	n/a		-	6		14.520
COL4A6	G>A, p.A513V	1691	X:107431796-107431796	-0.08	benign	TOLERATED		-	1		13.680
COL4A6	G>A, p.P683L	1691	X:107423828-107423828	3.53	probably_damaging	DAMAGING		-	12		15.730
COL4A6	del1bp,	1691	X:107420086-107420086	0.6	n/a	n/a		-	20		32

	p.L891SfsX14										
CPXCR1	A>G, p.T29A	302	X:88008500-88008500	-1.04	benign	TOLERATED		-	1		11.900
CSTF2	A>C, p.D50A	578	X:100077251-100077251	4.33	probably_damaging	DAMAGING		-	13		22.000
CT47B1	C>A, p.A180S	300	X:120008987-120008987	-1.64	probably_damaging	TOLERATED		-	3		9.108
CT47B1	T>C, p.E239G	300	X:120008809-120008809	-0.36	benign	TOLERATED		-	1		5.447
CUL4B	del3bp, p.L767del	896	X:119666415-119666417	1.98	n/a	n/a	XLID	-	7		19.37
CUL4B	insGCA, p.S603_D604insA	896	X:119672558-119672559	2.88	n/a	n/a	XLID	-	8		14.99
CXCR3	C>G, p.V321L	416	X:70836502-70836502	2.18	possibly_damaging	TOLERATED		-	4		11.610
CXorf21	A>G, p.S146P	302	X:30578037-30578037	1.09	benign	TOLERATED		-	2		4.009
CXorf22	G>A, p.V890I	977	X:35993985-35993985	-0.04	benign	TOLERATED		-	1		1.725
CXorf22	G>C, p.D379H	977	X:35971797-35971797	3.74	possibly_damaging	TOLERATED		-	5		14.210
CXorf22	T>C, p.I972T	977	X:36007637-36007637	-0.25	benign	TOLERATED		-	1		4.367
CXorf27	G>A, p.V32M	118	X:37850186-37850186	-1.11	probably_damaging	DAMAGING		-	9		13.690
CXorf30	A>G, p.T545A	634	X:36397574-36397574	-0.37	benign	TOLERATED		-	1		0.562
CXorf30	C>T, p.R201C	634	X:36329023-36329023	-0.32	benign	TOLERATED		-	1		9.381
CXorf36	G>T, p.L305M	434	X:45013203-45013203	3.08	probably_damaging	DAMAGING		-	12		20.100
CXorf41	del15bp, p.D7_M11del	215	X:106456112-106456126	0.23	n/a	n/a		-	4		10.97
CXorf57	C>G, p.R661G	856	X:105905247-105905247	0.14	benign	TOLERATED		-	2		8.152
CXorf61	C>T, p.W19*	114	X:115593961-115593961	1.94	n/a	n/a		-	20		18.660
CXorf64	C>T, p.R201*	299	X:125955222-125955222	0.73	n/a	n/a		-	20		16.030
CXorf68	C>T, donor		X:154057809-154057809	2.49	n/a	n/a		-	5		8.883
CYLC1	A>T, p.D120V	652	X:83128075-83128075	0.37	possibly_damaging	DAMAGING		-	7		10.460
CYLC1	T>A, p.N439K	652	X:83129033-83129033	-0.61	benign	TOLERATED		-	1		0.015
CYSLTR1	C>T, p.A231T	338	X:77528553-77528553	4.65	probably_damaging	DAMAGING		-	13		14.640
DCAF8L2	C>T, p.T588M	632	X:27766775-27766775	1.62	possibly_damaging	DAMAGING		-	7		7.619
DDX26B	T>A, p.S529T	862	X:134707942-134707942	0.56	benign	TOLERATED		-	2		12.780
DDX3X	G>A, p.R110H	663	X:41201792-41201792	2.68	probably_damaging	TOLERATED		-	5		21.600
DDX3X	G>A, p.R351Q	663	X:41204459-41204459	4.25	probably_damaging	DAMAGING		-	13		20.400
DGAT2L6	G>A, p.R205H	338	X:69421881-69421881	3.03	benign	DAMAGING		-	6		14.530
DGKK	C>T, p.R1226H	1265	X:50113463-50113463	-1.21	benign	TOLERATED		-	1		0.016
DLG3	insC, p.T365HfsX13	818	X:69671817-69671818	1.11	n/a	n/a	XLID	-	20	15185169	22.2
DLG3	ins8bp, p.C181*	818	X:69669549-69669550	3.55	n/a	n/a	XLID	-	20		17.15
DMD	C>T, p.R1984Q	3563	X:32235151-32235151	3.62	probably_damaging	TOLERATED	XLID	-	9		15.850
DMD	C>T, p.R2068Q	3563	X:31986498-31986498	2.54	probably_damaging	TOLERATED	XLID	-	8		22.200

DMD	G>A, p.R2068W	3563	X:31986499-31986499	2.51	probably_damaging	DAMAGING	XLID	-	14		17.490
DMD	T>A, p.N986I	3563	X:32481662-32481662	4.44	probably_damaging	DAMAGING	XLID	-	16		22.300
DMD	T>C, p.E1286G	3563	X:32429876-32429876	3.75	probably_damaging	DAMAGING	XLID	-	15		21.100
DOCK11	A>G, p.H451R	2074	X:117707944-117707944	3.58	benign	TOLERATED		-	4		9.188
DUSP9	C>T, p.P152L	385	X:152914768-152914768	0.8	benign	TOLERATED		-	2		8.347
EFHC2	C>T, p.V566I	750	X:44088950-44088950	-0.78	benign	TOLERATED		-	1		3.208
EFHC2	G>A, p.P412L	750	X:44101412-44101412	2.65	benign	TOLERATED		-	3		9.792
EFHC2	G>T, p.R486S	750	X:44091891-44091891	2.52	probably_damaging	TOLERATED		-	5		14.990
EIF1AX	retrocopy		X:20148634-20150381	0	n/a	n/a		-	1		
EIF2S3	del4bp, p.I465SfsX4	473	X:24094874-24094877	3.42	n/a	n/a		-	20		37
ELF4	G>A, p.P496L	664	X:129201201-129201201	1.02	possibly_damaging	TOLERATED		-	3		11.230
ELK1	T>C, p.T108A	429	X:47498626-47498626	0.1	benign	TOLERATED		-	2	11186900	2.379
EMD	A>G, p.H166R	255	X:153609289-153609289	1.1	benign	DAMAGING		-	4		15.580
ERAS	G>T, p.G139V	234	X:48687949-48687949	0.4	possibly_damaging	DAMAGING		-	7		6.241
ESX1	G>A, p.R290C	407	X:103495262-103495262	0.87	benign	TOLERATED		-	2		7.829
F8	A>G, p.V1786A	2352	X:154134711-154134711	4.21	probably_damaging	DAMAGING		-	13		22.000
FAM104B	A>T, p.F33L	47	X:55185583-55185583	1.25	possibly_damaging	TOLERATED		-	3		13.740
FAM104B	retrocopy		X:55185559-55187628	0	n/a	n/a		-	1		
FAM122C	C>A, p.P68H	80	X:133955370-133955370	0.54	probably_damaging	DAMAGING(Low_confidence)		-	7		10.680
FAM123B	C>A, p.D233Y	1136	X:63412470-63412470	0.7	probably_damaging	DAMAGING		-	10		10.220
FAM123B	C>A, p.G62V	1136	X:63412982-63412982	2.86	probably_damaging	DAMAGING		-	11		17.150
FAM123B	G>C, p.Q461E	1136	X:63411786-63411786	5.08	probably_damaging	TOLERATED		-	8		17.500
FAM155B	C>T, p.R425C	473	X:68749653-68749653	-0.27	benign	DAMAGING		-	3		6.445
FAM47A	C>G, p.E520Q	792	X:34148838-34148838	0.59	benign	TOLERATED		-	2		5.921
FAM47A	C>T, p.R518H	792	X:34148843-34148843	-1.93	benign	TOLERATED		-	1		0.016
FAM47B	C>T, p.R219W	646	X:34961603-34961603	-2.08	probably_damaging	n/a		-	3		5.855
FAM47B	G>A, p.D484N	646	X:34962398-34962398	0.28	probably_damaging	n/a		-	4		12.450
FAM47C	G>A, p.D860N	1036	X:37029061-37029061	-0.25	possibly_damaging	TOLERATED		-	2		11.430
FAM47C	G>C, p.R415P	1036	X:37027727-37027727	-0.06	probably_damaging	TOLERATED		-	3		7.611
FAM47C	G>T, p.R458L	1036	X:37027856-37027856	-1.38	probably_damaging	TOLERATED		-	3		2.345
FAM58A	T>C, p.Y66C	248	X:152861558-152861558	4.23	probably_damaging	DAMAGING		-	13		18.300
FAM70A	G>A, p.T147I	350	X:119419535-119419535	1.43	benign	TOLERATED		-	2		7.118
FAM9B	G>C, p.L103V	187	X:8997434-8997434	0.43	possibly_damaging	TOLERATED		-	3		9.176
FANCB	C>T, p.R409Q	860	X:14871261-14871261	0.74	benign	TOLERATED	XLID	-	5		0.007

FANCB	G>A, p.A799V	860	X:14861873-14861873	0.05	benign	TOLERATED	XLID	-	5		0.035
FATE1	ins7bp, p.M38*	184	X:150885749-150885750	-0.69	n/a	n/a		-	20		10.98
FGD1	G>A, p.R263C	962	X:54496763-54496763	2.21	probably_damaging	TOLERATED	XLID	-	8		9.310
FGD1	G>C, p.P206R	962	X:54497058-54497058	0.56	benign	TOLERATED	XLID	-	5		11.950
FIGF	T>C, p.Q208R	355	X:15373290-15373290	1.89	benign	TOLERATED		-	2		12.200
FIGF	del3bp, p.E212_D213delinsE	355	X:15373275-15373277	1.66	n/a	n/a		-	4		11.97
FLNA	C>T, p.E1836K	2648	X:153582570-153582570	4.21	probably_damaging	DAMAGING	XLID	-	16		15.270
FLNA	G>A, p.P1751S	2648	X:153583046-153583046	0.24	benign	TOLERATED	XLID	-	5		5.856
FLNA	G>A, p.T1276I	2640	X:153588252-153588252	5.72	probably_damaging	DAMAGING(Low_confidence)	XLID	-	14		22.300
FLNA	G>T, p.A2544D	2648	X:153577855-153577855	-0.28	benign	TOLERATED	XLID	-	4		1.499
FLNA	T>G, p.I1844L	2648	X:153582546-153582546	4.77	probably_damaging	DAMAGING	XLID	-	16		24.100
FMR1	G>A, p.G540E	633	X:147026536-147026536	3.72	probably_damaging	TOLERATED	XLID	-	9		11.130
FOXP3	C>T, p.S219N	397	X:49111945-49111945	1.42	benign	TOLERATED		-	2		11.770
FOXP3	G>A, p.P24S	432	X:49114893-49114893	-0.03	benign	TOLERATED		-	1		8.316
FRMD7	del1bp, p.L713*	715	X:131211907-131211907	1.75	n/a	n/a		-	20		33
FRMPD4	G>A, p.R1189H	1323	X:12736511-12736511	0.4	benign	TOLERATED		-	2		4.772
FRMPD4	T>C, p.C553R	1323	X:12734235-12734235	2.17	possibly_damaging	TOLERATED		-	4		16.580
FRMPD4	T>C, p.I295T	1323	X:12712524-12712524	4.38	possibly_damaging	DAMAGING		-	10		16.670
FRMPD4	del1bp, p.C618VfsX8	1323	X:12734425-12734425	1.14	n/a	n/a		-	20		38
FTSJ1	G>A, p.G117R	328	X:48337492-48337492	2.67	probably_damaging	DAMAGING	XLID	-	14		18.390
GAB3	C>T, p.R462Q	587	X:153925446-153925446	0.62	benign	TOLERATED		-	2		7.989
GAB3	T>C, p.H197R	588	X:153941488-153941488	0.26	probably_damaging	TOLERATED		-	4		9.108
GABRA3	C>T, p.G47R	493	X:151532904-151532904	2.81	probably_damaging	TOLERATED		-	5		15.460
GABRE	G>A, p.R87C	507	X:151138672-151138672	0.85	probably_damaging	DAMAGING		-	10		18.410
GABRE	T>C, p.M1V	507	X:151143097-151143097	0.59	possibly_damaging	DAMAGING(Low_confidence)		-	5		2.319
GABRQ	G>C, p.E564D	633	X:151821537-151821537	-0.37	benign	TOLERATED		-	1		5.592
GDI1	del2bp, p.S396PfsX15	448	X:153670767-153670768	4.69	n/a	n/a	XLID	-	20	21836662, 22002931	27.0
GDPD2	C>A, p.R75S	540	X:69645626-69645626	0.89	benign	TOLERATED		-	2		10.460
GJB1	C>T, p.P174S[d]	284	X:70444077-70444077	5.65	probably_damaging	DAMAGING	XLID[c]	-	14	23707145	21.200
GLUD2	G>A, p.R460K	559	X:120182917-120182917	2.02	benign	TOLERATED		-	3		10.980
GNL3L	C>A, p.P44T	583	X:54566616-54566616	-0.26	benign	DAMAGING		-	3		1.769
GPKOW	G>A, p.R274C	477	X:48973477-48973477	2.22	probably_damaging	DAMAGING		-	11		18.520
GPKOW	T>C, p.I19V	477	X:48980018-48980018	-0.04	benign	TOLERATED		-	1		0.883

GPM6B	G>T, p.S77Y	306	X:13803879-13803879	5.53	probably_damaging	DAMAGING		-	14		28.400
GPR101	T>G, p.K271T	509	X:136113022-136113022	0.64	possibly_damaging	TOLERATED		-	3		1.572
GPR112	A>C, p.I2999L	3081	X:135494483-135494483	0	benign	TOLERATED		-	2		13.550
GPR112	A>G, p.H2937R	3081	X:135488006-135488006	0.42	benign	TOLERATED		-	2		2.732
GPR112	A>G, p.N2537S	3081	X:135453700-135453700	1	probably_damaging	TOLERATED		-	4		15.490
GPR112	C>T, p.P429S	3081	X:135427150-135427150	0.15	benign	TOLERATED		-	2		0.000
GPR112	G>A, p.R176H	3081	X:135405393-135405393	-0.93	benign	TOLERATED		-	1		2.512
GPR112	G>A, p.R3017Q	3081	X:135496331-135496331	-0.15	probably_damaging	TOLERATED		-	3		10.450
GPR112	insGG, p.A1156GfsX7	3081	X:135429330-135429331	1.12	n/a	n/a		-	20		21.6
GPR143	T>C, p.T166A	405	X:9716666-9716666	-0.5	benign	TOLERATED		-	1		5.082
GPR50	A>C, p.Q330P	618	X:150349044-150349044	-1.54	possibly_damaging	TOLERATED		-	2		9.876
GPRASP1	A>C, p.K674T	1396	X:101910862-101910862	-0.35	benign	TOLERATED		-	1		4.202
GRIA3	G>A, p.G721R	895	X:122598800-122598800	5.43	probably_damaging	DAMAGING	XLID	-	17		18.170
GRIA3	G>T, p.E224*	895	X:122460038-122460038	3.69	n/a	n/a	XLID	-	20		37.000
GSPT2	C>T, p.T94I	629	X:51487003-51487003	0.12	benign	TOLERATED		-	2		10.810
GUCY2F	G>A, p.R628*	1109	X:108652307-108652307	0.93	n/a	n/a		-	20		41.000
GUCY2F	T>G, p.K574Q	1109	X:108673607-108673607	1.04	probably_damaging	DAMAGING		-	10		16.070
GYG2	A>C, p.T377P	470	X:2793941-2793941	0.25	possibly_damaging	TOLERATED		-	3		8.646
HAUS7	G>A, p.P228L	237	X:152710206-152710206	0.22	benign	TOLERATED		-	2		8.776
HAUS7	G>C, p.H183D	428	X:152722039-152722039	-0.67	benign	TOLERATED		-	1		4.781
HCCS	C>G, p.S4C	269	X:11130191-11130191	1.98	probably_damaging	DAMAGING	XLID	-	13		12.720
HCFC1	C>T, p.S225N	2036	X:153228714-153228714	5.51	benign	DAMAGING	XLID	-	8	23000143, 23871722	25.800
HDAC8	A>G, p.X257Q	257	X:71694548-71694548	0.89	n/a	DAMAGING	XLID	-	4		2.354
HDHD1	G>A, p.R188W	209	X:6975813-6975813	-0.41	benign	DAMAGING		-	3		0.538
HDX	C>A, p.S61I	691	X:83724549-83724549	2.29	probably_damaging	DAMAGING(Low_confidence)		-	8		15.930
HDX	T>C, p.R119G	691	X:83724376-83724376	0.83	benign	TOLERATED		-	2		7.135
HS6ST2	G>A, p.S494L	646	X:131762708-131762708	5.83	probably_damaging	TOLERATED		-	8		15.540
HS6ST2	del1bp, p.V8AfsX27	606	X:132092608-132092608	0.85	n/a	n/a		-	20		22.6
HSD17B10	C>T, p.R116Q	262	X:53459205-53459205	1.09	possibly_damaging	TOLERATED	XLID	-	6		14.790
HTR2C	C>T, p.A7V	459	X:113961365-113961365	-0.22	benign	DAMAGING(Low_confidence)		-	2		10.880
HUWE1	C>T, p.R2040Q	4375	X:53600903-53600903	3.91	probably_damaging	n/a	XLID	-	9		16.210
HUWE1	T>C, p.K27R	4375	X:53675219-53675219	4.56	benign	n/a	XLID	-	8		14.970
IGSF1	A>G, p.F377L	1337	X:130416535-130416535	2.16	probably_damaging	DAMAGING		-	11		14.290

IGSF1	C>A, p.M335I	1337	X:130416659-130416659	0.26	benign	TOLERATED		-	2		6.078
IKBKG	G>A, p.G43R	488	X:153770605-153770605	0.4	possibly_damaging	DAMAGING(Low_confidence)	XLID	-	8		11.300
IL1RAPL1	A>G, p.I643V	697	X:29973773-29973773	1.22	benign	TOLERATED	XLID	-	5		7.894
IL1RAPL1	del75bp, p.A235Z[a]	697	X:29686547-29686621	1.73	n/a	n/a	XLID	-	13		
IL1RAPL2	A>G, p.K529R	687	X:105011179-105011179	4.37	benign	TOLERATED		-	5		13.710
IL1RAPL2	G>A, p.G651R	687	X:105011544-105011544	5.32	probably_damaging	DAMAGING(Low_confidence)		-	11		18.450
IQSEC2	G>A, p.A584V	950	X:53277996-53277996	4.06	probably_damaging	DAMAGING	XLID	-	16		19.410
IQSEC2	G>A, p.P1181S	1489	X:53264327-53264327	2.27	probably_damaging	TOLERATED	XLID	-	8		3.285
IQSEC2	T>C, p.K807E	950	X:53268458-53268458	4.58	probably_damaging	DAMAGING	XLID	-	16		27.300
IRS4	A>G, p.V400A	1258	X:107978376-107978376	1.26	benign	DAMAGING		-	4		1.034
ITGB1BP2	C>T, p.P78S	348	X:70522321-70522321	1.1	benign	TOLERATED		-	2		6.510
ITIH6	C>A, p.A1026S	1314	X:54783431-54783431	0.31	benign	TOLERATED		-	2		7.812
ITIH6	G>A, p.P1260S	1314	X:54776492-54776492	-0.03	benign	TOLERATED		-	1		1.224
ITIH6	G>T, p.P1307T	1314	X:54776351-54776351	0.65	probably_damaging	TOLERATED		-	4		13.360
ITIH6	G>T, p.P826T	1314	X:54784031-54784031	0.45	benign	DAMAGING		-	4		6.596
ITIH6	T>G, p.N90H	1314	X:54818459-54818459	0.11	benign	TOLERATED		-	2		11.050
KCND1	C>T, p.R471H	648	X:48823040-48823040	3.98	possibly_damaging	TOLERATED		-	5		17.030
KDM5C	del1bp, p.W534GfsX15	1561	X:53239743-53239743	-0.12	n/a	n/a	XLID	-	20		38
KDM6A	G>C, p.C960S	1402	X:44937691-44937691	5.41	probably_damaging	DAMAGING	XLID	-	14		23.800
KIAA1817	C>G, p.S445R	867	X:106845337-106845337	0.23	n/a	DAMAGING(Low_confidence)		-	3		12.410
KIAA1817	C>T, p.R398W	867	X:106845194-106845194	0.64	n/a	TOLERATED		-	2		9.353
KIAA1817	C>T, p.S850L	867	X:106846551-106846551	2.83	n/a	TOLERATED		-	3		12.800
KIAA1817	C>T, p.T354I	867	X:106845063-106845063	1.79	n/a	TOLERATED		-	2		9.496
KIAA1817	G>A, p.C390Y	867	X:106845171-106845171	4.53	n/a	DAMAGING(Low_confidence)		-	6		16.420
KIAA1817	G>C, p.Q544H	867	X:106845634-106845634	0.13	n/a	TOLERATED		-	2		2.911
KIAA1817	G>T, p.A48S	867	X:106844144-106844144	0.92	n/a	TOLERATED		-	2		13.150
KIF4A	C>T, p.A441V	680	X:69563608-69563608	4.93	benign	TOLERATED		p.A441V (850)	5		13.610
KLHL15	C>G, p.E518Q	605	X:24006301-24006301	5.63	benign	TOLERATED		-	6		13.060
KLHL15	C>T, p.V101I	605	X:24024510-24024510	3.73	possibly_damaging	TOLERATED		-	5		14.850
KLHL15	del1bp, p.Y394IfsX61	605	X:24006674-24006674	0.98	n/a	n/a		-	20		33
KLHL34	C>T, p.R303K	645	X:21674999-21674999	-0.84	benign	TOLERATED		-	1		0.003
KLHL4	A>G, p.T391A	721	X:86880643-86880643	0.8	benign	TOLERATED		-	2		10.980

KLHL4	G>A, p.R465H	721	X:86887279-86887279	2.94	probably_damaging	DAMAGING		-	11		21.500
KLHL4	G>T, p.K477N	721	X:86887316-86887316	0.03	possibly_damaging	TOLERATED		-	3		16.890
L1CAM	A>G, p.I1049T	1254	X:153130060-153130060	2.85	benign	TOLERATED	XLID	-	6		13.740
L1CAM	C>T, p.D202N	1254	X:153136335-153136335	5.12	probably_damaging	DAMAGING	XLID	-	17		22.600
L1CAM	T>C, acceptor		X:153128351-153128351	4.27	n/a	n/a	XLID	-	10		14.080
LAS1L	G>A, p.R415W	735	X:64743993-64743993	2.62	probably_damaging	DAMAGING		-	11		14.540
LAS1L	G>C, p.A269G	735	X:64749132-64749132	0.27	probably_damaging	DAMAGING		p.A269G (874)	10		18.020
LAS1L	del3bp, p.D597_E598delinsD	735	X:64738001-64738003	1.01	n/a	n/a		-	4		0.979
LRCH2	G>C, p.P150A	766	X:114422835-114422835	4.81	probably_damaging	DAMAGING		-	13		19.330
MAGEA1	C>T, p.V279I	310	X:152482176-152482176	0.9	possibly_damaging	TOLERATED		-	3		9.825
MAGEA1	G>A, p.S148F	310	X:152482568-152482568	-0.54	possibly_damaging	TOLERATED		-	2		9.906
MAGEA10	A>C, p.L16R	370	X:151304046-151304046	-1.73	possibly_damaging	TOLERATED		-	2		7.659
MAGEA10	G>T, p.F147L	370	X:151303652-151303652	-0.23	benign	TOLERATED		-	1		5.426
MAGEA11	T>G, p.Q4R	430	X:148794830-148794830	-0.17	possibly_damaging	DAMAGING		-	6		5.486
MAGEA5	C>T, p.W80*	125	X:151283773-151283773	-0.93	n/a	n/a		-	20		5.152
MAGEB2	C>A, p.R12S	320	X:30236731-30236731	0.25	probably_damaging	TOLERATED		-	4		14.090
MAGEB4	C>T, p.T246I	347	X:30260989-30260989	0.71	probably_damaging	DAMAGING		-	10		13.980
MAGEB6	C>T, p.A219V	408	X:26212619-26212619	-0.11	probably_damaging	DAMAGING		-	9		14.200
MAGEB6	G>A, p.E260K	408	X:26212741-26212741	-0.46	probably_damaging	TOLERATED		-	3		10.360
MAGEB6	G>C, p.V225L	408	X:26212636-26212636	-0.87	benign	TOLERATED		-	1		9.960
MAGEC1	C>T, p.P12S	1143	X:140993224-140993224	-0.54	benign	DAMAGING(Low_confidence)		-	2		3.778
MAGEC1	G>T, p.E587*	1143	X:140994949-140994949	-0.13	n/a	n/a		-	20		26.900
MAGEC3	C>T, p.P4S	644	X:140926111-140926111	-0.47	benign	DAMAGING(Low_confidence)		-	2		8.485
MAGEC3	del14157bp, p.S172Z	644	X:140969189-140983345	-0.06	n/a	n/a		-	9		
MAGEE2	A>G, p.M392T	524	X:75003712-75003712	1.38	possibly_damaging	DAMAGING		-	7		2.514
MAGEE2	C>T, p.V62I	524	X:75004703-75004703	0.6	benign	TOLERATED		-	2		7.609
MAGEE2	G>A, p.T262I	524	X:75004102-75004102	0.65	probably_damaging	DAMAGING		-	10		13.500
MAGEH1	A>C, p.N21T	220	X:55478869-55478869	0.03	benign	DAMAGING(Low_confidence)		p.N21T (986)	3		12.880
MAGIX	insT, p.G316RfsX20	335	X:49022676-49022677	0.65	n/a	n/a		-	20		15.55
MAGT1	C>G, p.R182P	368	X:77112936-77112936	0.65	benign	TOLERATED	XLID[c]	-	5		9.634
MAMLD1	A>C, p.D915A	999	X:149681090-149681090	0.08	benign	TOLERATED		-	2		0.958
MAMLD1	C>T, p.P835L	999	X:149680850-149680850	0.15	benign	TOLERATED		-	2		4.424

MAMLD1	C>T, p.P858L	999	X:149680919-149680919	1.58	probably_damaging	DAMAGING		-	10		11.760
MAP3K15	A>G, donor		X:19484782-19484782	0.72	n/a	n/a		-	4		4.237
MAP3K15	A>G, p.L304P	1314	X:19475115-19475115	4.49	n/a	DAMAGING		-	7		21.600
MAP3K15	A>T, p.Y645*	1314	X:19416475-19416475	-0.36	n/a	n/a		-	20		20.200
MAP3K15	C>A, acceptor		X:19433376-19433376	5.45	n/a	n/a		-	8	23352160	23.500
MAP3K15	G>A, p.P748L	1314	X:19410543-19410543	3.78	probably_damaging	DAMAGING		-	12		16.300
MAP7D2	C>T, p.G118D	187	X:20073950-20073950	4.52	probably_damaging	TOLERATED		-	7		22.800
MAP7D3	A>G, p.M559T	842	X:135310887-135310887	0.13	possibly_damaging	TOLERATED		-	3		10.840
MCF2	G>A, p.A893V	926	X:138667292-138667292	-0.09	benign	TOLERATED		-	1		11.420
MCF2	G>A, p.R364C	1002	X:138699761-138699761	1.12	probably_damaging	DAMAGING		-	10		18.080
MECP2	T>C, p.K256E[e]	487	X:153296513-153296513	4.2	probably_damaging	DAMAGING	XLID	-	16		20.400
MED12	A>G, p.Y166C	2178	X:70339964-70339964	4.33	probably_damaging	n/a	XLID	-	10	21836662	19.740
MED12	A>T, p.K956M	2178	X:70347203-70347203	4.61	probably_damaging	n/a	XLID	-	10		22.700
MED12	C>T, p.P739L	2178	X:70344986-70344986	5.61	probably_damaging	n/a	XLID	-	11		19.900
MED12	C>T, p.R1295C	2178	X:70349900-70349900	5.26	probably_damaging	n/a	XLID	-	11		21.500
MED12	G>A, p.V756I	2178	X:70345240-70345240	5.61	probably_damaging	n/a	XLID	-	11		25.100
MED12	insC, p.S1967QfsX84	2178	X:70357647-70357648	0.67	n/a	n/a	XLID	-	20		39
MID1IP1	G>C, p.D129H	184	X:38664584-38664584	2.23	possibly_damaging	TOLERATED		-	4		15.820
MID2	C>G, p.A280G	706	X:107147210-107147210	3.14	benign	TOLERATED	XLID	-	4		15.260
MPP1	C>T, p.G171D	220	X:154013220-154013220	-1.38	n/a	DAMAGING		-	3		0.602
MPP1	C>T, p.R67Q	467	X:154020463-154020463	0.93	possibly_damaging	TOLERATED		p.R67Q (1051)	3		10.370
MPP1	retrocopy		X:154006959-154012383	0	n/a	n/a		-	1		
MSL3	G>C, p.S365T	417	X:11783771-11783771	2.63	probably_damaging	TOLERATED		-	5		12.440
MTMR8	C>T, p.R267H	705	X:63564990-63564990	0.43	probably_damaging	DAMAGING		-	10		17.780
MTMR8	G>A, p.A249V	705	X:63565044-63565044	1.36	probably_damaging	DAMAGING		-	10		12.870
MTMR8	T>C, p.K522R	705	X:63490870-63490870	0.02	benign	TOLERATED		-	2		10.590
MXRA5	C>T, p.R1640H	2829	X:3238807-3238807	-0.01	benign	TOLERATED		-	1		1.530
NAP1L3	C>T, p.D98N	507	X:92928012-92928012	1.81	benign	DAMAGING		-	4		8.536
NHS	A>G, p.K1502R	1631	X:17750196-17750196	3.03	probably_damaging	DAMAGING	XLID	-	15		22.600
NHS	C>T, p.P886L	1631	X:17744946-17744946	2.61	benign	TOLERATED	XLID	-	6		8.809
NHS	C>T, p.R484W	1631	X:17743739-17743739	1.84	probably_damaging	DAMAGING	XLID	-	13		14.770
NHS	T>C, p.V500A	1631	X:17743788-17743788	0.6	benign	TOLERATED	XLID	-	5		2.020
NKAP	C>T, p.R361Q	416	X:119059349-119059349	4.11	probably_damaging	DAMAGING		-	13		29.500
NKRF	G>A, p.R14C	706	X:118726466-118726466	1.77	n/a	DAMAGING		-	4		15.330

NKRF	G>A, p.T178M	691	X:118724855-118724855	5.28	possibly_damaging	DAMAGING		-	11		13.660
NKRF	T>C, p.K50R	691	X:118725239-118725239	0.98	benign	TOLERATED		-	2		0.236
NLGN3	C>T, p.R162*	849	X:70368722-70368722	1.64	n/a	n/a	XLID	-	20		38.000
NLGN4X	C>T, p.V594I	817	X:5811529-5811529	5.03	probably_damaging	TOLERATED	XLID	-	11		13.790
NLGN4X	T>C, p.K321R	817	X:5821757-5821757	2.62	benign	TOLERATED	XLID	-	6		13.790
NONO	G>C, p.Q157H	472	X:70514199-70514199	1.37	probably_damaging	DAMAGING		-	10		14.740
NOX1	A>G, p.F529S	565	X:100099050-100099050	4.1	probably_damaging	DAMAGING		-	13		23.000
NOX1	A>G, p.S374P	516	X:100105153-100105153	0.14	possibly_damaging	TOLERATED		-	3		5.218
NOX1	G>A, p.R315C	516	X:100105330-100105330	-0.13	probably_damaging	DAMAGING		-	9		9.824
NR0B1	C>T, p.E310K	471	X:30326553-30326553	5.37	probably_damaging	DAMAGING		-	14		17.410
NRK	A>G, p.K1197E	1582	X:105179251-105179251	0.37	benign	DAMAGING		-	4		9.350
NRK	G>A, p.E369K	1582	X:105152738-105152738	1.25	probably_damaging	TOLERATED		-	4		17.880
NR_002784	C>A, p.R796L	833	X:27479027-27479027	-0.38	benign	TOLERATED		-	1		2.796
NR_002784	G>A, p.H472Y	833	X:27480000-27480000	0.13	probably_damaging	DAMAGING		-	10		2.913
NR_024062	G>A, p.R83Q	211	X:84189444-84189444	-1.77	n/a	n/a		-	0		1.216
NR_024062	G>A, p.W2*	211	X:84189201-84189201	0.57	n/a	n/a		-	20		5.029
NSDHL	A>G, p.N287S	374	X:152037398-152037398	2.57	benign	DAMAGING	XLID	-	8		14.020
NUP62CL	C>G, p.M72I	185	X:106397455-106397455	3.76	possibly_damaging	DAMAGING		p.M72I (1137)	9		16.320
NXF3	G>A, p.P387L	532	X:102334691-102334691	-0.9	benign	TOLERATED		-	1		7.059
NYX	G>A, p.G108S	482	X:41333028-41333028	3.98	probably_damaging	TOLERATED		-	6		23.200
OCRL	A>G, p.H51R	894	X:128678967-128678967	0.23	benign	TOLERATED	XLID	-	5		9.874
OCRL	C>T, p.T31I	894	X:128674773-128674773	1.1	benign	TOLERATED	XLID	-	5		14.260
ODZ1	A>C, p.F1113L	2726	X:123637516-123637516	0.99	benign	TOLERATED		-	2		11.730
ODZ1	A>G, p.Y914H	2726	X:123663745-123663745	4.61	probably_damaging	TOLERATED		-	7		23.100
ODZ1	T>C, p.M1696V	2726	X:123540215-123540215	1.98	benign	TOLERATED		-	2		4.259
ODZ1	insA, acceptor		X:123697624-123697625	1.69	n/a	n/a		-	4		16.66
OFD1	T>C, p.V539A	1013	X:13776529-13776529	3.74	possibly_damaging	DAMAGING	XLID	-	12		18.190
OPHN1	C>G, p.G529R	803	X:67316813-67316813	4.63	probably_damaging	DAMAGING	XLID	-	16		23.500
OPHN1	G>A, p.P619S	803	X:67283999-67283999	0.93	benign	TOLERATED	XLID	-	5		4.911
OPHN1	T>C, acceptor		X:67502961-67502961	2.15	n/a	n/a	XLID	-	8		18.060
OPHN1	del49301bp, p.D612X	803	X:67292994-67339174	0.23	n/a	n/a	XLID		13		
OPHN1	retrocopy		X:67268258-67518938	0	n/a	n/a	XLID	-	4		
OR13H1	G>A, p.R96Q	309	X:130678334-130678334	-0.56	benign	DAMAGING		-	3		4.583
P2RY4	C>G, p.W160S	366	X:69478996-69478996	5.18	probably_damaging	DAMAGING		-	14		18.770

PABPC5	T>C, p.F219S	383	X:90691232-90691232	3.69	probably_damaging	DAMAGING		-	12		16.610
PAGE2	C>G, p.L77V	112	X:55117800-55117800	0.84	probably_damaging	TOLERATED		-	4		10.390
PAGE2	del2394bp, p.M1Z	112	X:55115497-55117890	-0.28	n/a	n/a		-	9		
PAK3	A>G, p.N236S	545	X:110406896-110406896	2.15	benign	TOLERATED	XLID	-	6		9.836
PAK3	G>A, acceptor		X:110390964-110390964	5.56	n/a	n/a	XLID	-	11		16.860
PCDH19	C>T, p.A1040T	1101	X:99551460-99551460	1.32	benign	TOLERATED	XLID	-	5		7.868
PCYT1B	G>A, p.R20C	352	X:24690692-24690692	1.1	probably_damaging	TOLERATED		-	4		13.210
PDZD4	G>C, p.R538G	770	X:153069506-153069506	3.58	benign	TOLERATED		-	4		3.423
PDZD4	T>C, p.E595G	770	X:153069334-153069334	4.03	possibly_damaging	DAMAGING		-	10		16.030
PFKFB1	C>T, p.R269H	472	X:54978378-54978378	5.22	probably_damaging	DAMAGING		-	14		27.800
PHEX	A>G, p.Y327C	750	X:22117170-22117170	3.7	probably_damaging	DAMAGING		-	12		21.800
PHF6	C>A, p.T254K	313	X:133549074-133549074	5.22	probably_damaging	TOLERATED	XLID	-	11		27.600
PHKA1	C>G, p.E1122Q	1224	X:71802382-71802382	5.1	probably_damaging	DAMAGING		-	14		29.400
PHKA1	C>G, p.G1027A	1224	X:71813117-71813117	1.64	benign	TOLERATED		-	2		11.280
PHKA1	G>A, p.R14C	256	X:71813253-71813253	-1.46	n/a	DAMAGING(Low_confidence)		-	2		1.906
PHKA1	T>C, p.M502V	1152	X:71856192-71856192	4.45	benign	TOLERATED		-	5		11.880
PIGA	G>A, p.P22S	485	X:15349989-15349989	0.07	benign	TOLERATED	XLID	-	2		5.008
PIGA	insA, p.Y26LfsX4	485	X:15349976-15349977	-0.56	n/a	n/a	XLID	-	20		10.42
PLS3	T>C, p.M325T	631	X:114874802-114874802	2.74	possibly_damaging	TOLERATED		-	4		11.810
PLXNA3	A>G, p.D189G	1872	X:153689089-153689089	4.23	benign	TOLERATED		-	5		14.300
PLXNA3	A>G, p.H1288R	1872	X:153696467-153696467	4.2	benign	DAMAGING		-	7		13.330
PLXNA3	C>T, p.P906L	1872	X:153694531-153694531	5.47	possibly_damaging	TOLERATED		-	7		11.680
PLXNA3	C>T, p.T259M	1872	X:153689620-153689620	5.36	probably_damaging	DAMAGING		-	14		19.570
PLXNA3	G>A, p.D1639N	1872	X:153698439-153698439	5.35	probably_damaging	TOLERATED		-	8		22.700
PLXNA3	G>A, p.R613H	1872	X:153692754-153692754	0.19	benign	TOLERATED		-	2		0.026
PLXNA3	G>T, p.D1639Y	1872	X:153698439-153698439	5.35	probably_damaging	TOLERATED		-	8		19.300
PLXNB3	C>T, p.H1345Y	1910	X:153040436-153040436	3.59	benign	DAMAGING(Low_confidence)		-	5		12.500
PLXNB3	G>A, p.E1184K	1910	X:153039671-153039671	1.1	possibly_damaging	DAMAGING		-	7		16.960
PLXNB3	G>A, p.R1121Q	1910	X:153039396-153039396	1.53	possibly_damaging	TOLERATED		-	3		11.270
PLXNB3	G>A, p.R221H	1910	X:153032944-153032944	2.4	probably_damaging	DAMAGING		-	11		18.900
PLXNB3	G>A, p.R706Q	1910	X:153036319-153036319	1.09	benign	TOLERATED		-	2		9.096
PLXNB3	G>A, p.V624I	1910	X:153035876-153035876	-0.57	benign	TOLERATED		-	1		10.240
PNPLA4	A>G, p.C26R	254	X:7894085-7894085	0.42	benign	TOLERATED		-	2		0.004
POF1B	A>T, p.D348E	590	X:84563136-84563136	0.17	probably_damaging	TOLERATED		-	4		19.030

POF1B	C>T, p.C444Y	590	X:84560903-84560903	1.55	benign	TOLERATED		-	2		14.350
POF1B	T>A, p.M1L	590	X:84634459-84634459	2.5	possibly_damaging	DAMAGING(Low_confidence)		-	6		16.230
POLA1	C>G, p.L1261V	1463	X:24859831-24859831	0.97	benign	TOLERATED		-	2		0.328
PPEF1	G>A, p.A445T	626	X:18836179-18836179	2.19	probably_damaging	DAMAGING		-	11		14.900
PQBP1	G>A, p.A89T	266	X:48759292-48759292	4.87	probably_damaging	DAMAGING	XLID	-	16		33.000
PQBP1	del1bp, p.F240SfsX26	266	X:48760281-48760281	2.69	n/a	n/a	XLID	-	20		36
PQBP1	retrocopy		X:48755859-48760205	0	n/a	n/a	XLID	-	4		
PRKX	G>A, p.R87C	359	X:3592715-3592715	4.25	probably_damaging	DAMAGING		-	13		15.050
PTCHD1	C>T, p.A165V	889	X:23397850-23397850	2.66	benign	TOLERATED	XLID	-	6		7.092
RAB33A	G>A, p.S10N	238	X:129306065-129306065	-0.49	benign	TOLERATED		-	1		13.160
RAB40A	C>A, p.E169D	278	X:102755178-102755178	0.86	possibly_damaging	TOLERATED		-	3		18.300
RAB40A	T>C, p.N162S	278	X:102755200-102755200	2.58	possibly_damaging	DAMAGING		p.N162S (1337)	8		20.900
RBM10	A>T, p.D474V	931	X:47040786-47040786	2.15	possibly_damaging	TOLERATED	XLID	-	4		8.887
RBM10	del1292bp, p.I651*	931	X:47044423-47045714	1.2	n/a	n/a	XLID	-	10		
RBM3	G>A, p.R145H	158	X:48435434-48435434	2.09	possibly_damaging	n/a		-	4		14.420
RENBP	G>T, p.P184Q	428	X:153208443-153208443	0.84	probably_damaging	TOLERATED		-	4		3.563
RGAG1	T>C, p.S682P	1389	X:109695889-109695889	0.08	benign	TOLERATED		-	2		0.775
RGAG4	C>A, p.E154D	570	X:71350929-71350929	-0.33	possibly_damaging	TOLERATED		-	2		14.090
RGAG4	G>A, p.P442S	570	X:71350067-71350067	0.9	possibly_damaging	TOLERATED		-	3		9.578
RGAG4	del3bp, p.K390del	570	X:71350221-71350223	-0.43	n/a	n/a		-	3		3.973
RHOXF1	C>G, p.R106P	185	X:119249456-119249456	-2.96	possibly_damaging	TOLERATED		-	2		1.287
RHOXF1	C>G, p.S15T	185	X:119249729-119249729	-1.93	benign	TOLERATED		-	1		0.006
RHOXF2	G>T, p.E69*	289	X:119293046-119293046	0.05	n/a	n/a		-	20		15.550
RLIM	G>A, p.R387C	625	X:73811991-73811991	3.77	probably_damaging	DAMAGING		-	12		12.930
RLIM	G>A, p.R599C	625	X:73811355-73811355	5.43	probably_damaging	DAMAGING		-	14		18.000
RLIM	G>C, p.P587R	625	X:73811390-73811390	2.88	probably_damaging	DAMAGING		-	11		13.800
RLIM	T>C, p.I141V	625	X:73812729-73812729	4.64	probably_damaging	TOLERATED		-	7		17.600
RNF128	G>A, p.V53I	403	X:105937389-105937389	0.56	possibly_damaging	TOLERATED		-	3		8.999
RP2	G>A, p.D233N	351	X:46713505-46713505	5.51	benign	TOLERATED		-	6		17.090
RP2	G>A, p.D66N	351	X:46713004-46713004	5.5	benign	TOLERATED		-	6		13.960
RPA4	G>T, p.A190S	262	X:96139877-96139877	-0.49	benign	TOLERATED		-	1		3.617
RPGR	G>A, p.A707V	816	X:38134371-38134371	0.05	possibly_damaging	TOLERATED		-	3		10.480
RPGR	G>T, p.Q467K	1153	X:38156552-38156552	-1.07	benign	TOLERATED		-	1		5.437

RPL10	T>A, p.L194H	217	X:153629294-153629294	-0.91	n/a	DAMAGING(Low_confidence)	XLID	-	5		0.902
RPS6KA3	G>T, p.T276K	741	X:20204432-20204432	5.69	probably_damaging	DAMAGING	XLID	-	17		27.200
RPS6KA3	T>C, p.N544D	741	X:20183151-20183151	4.84	probably_damaging	DAMAGING	XLID	-	16		26.000
RRAGB	A>G, p.D339G	375	X:55783753-55783753	3.67	probably_damaging	TOLERATED		-	6		14.340
SAGE1	C>T, p.R228W	905	X:134988656-134988656	0.01	probably_damaging	DAMAGING		-	10		10.130
SATL1	T>C, p.D538G	633	X:84362362-84362362	2.17	probably_damaging	DAMAGING		-	11		10.690
SCML1	G>T, p.E127X[b]	209	X:17769973-17769973	0.26	n/a	n/a		-	20		26.100
SCML2	T>G, p.Q502P	701	X:18265954-18265954	3.27	possibly_damaging	TOLERATED		-	5		13.300
SERPINA7	G>T, p.T181N	416	X:105280508-105280508	1.47	probably_damaging	DAMAGING		-	10		11.670
SHROOM2	A>G, p.N1203S	1617	X:9905194-9905194	0.99	probably_damaging	TOLERATED		-	4		15.230
SHROOM2	G>A, p.R557H	1617	X:9863618-9863618	-1.01	benign	TOLERATED		-	1		9.736
SLC16A2	C>T, p.R371C	540	X:73745669-73745669	3.92	probably_damaging	DAMAGING	XLID	-	15	23568789	19.050
SLC16A2	G>T, p.V416F	540	X:73749123-73749123	4.09	benign	TOLERATED	XLID	-	8		16.990
SLC6A8	C>A, p.S197Y	277	X:152957720-152957720	0.09	n/a	n/a	XLID	-	4		2.907
SLC6A8	G>A, p.G466R	636	X:152959802-152959802	5.16	probably_damaging	DAMAGING	XLID	-	17	21140503	21.900
SLC6A8	G>A, p.V629I	636	X:152960646-152960646	1.16	benign	TOLERATED	XLID	-	5	22281021	7.919
SLC6A8	T>A, p.S524T	636	X:152960062-152960062	0.57	benign	TOLERATED	XLID	-	5		8.344
SLC6A8	T>C, p.L401P	636	X:152959420-152959420	4.3	probably_damaging	DAMAGING	XLID	-	16		19.860
SLC6A8	del2bp, donor		X:152957009-152957010	4.39	n/a	n/a	XLID	-	10		14.25
SLC6A8	del3bp, p.F408del	636	X:152959434-152959436	3.02	n/a	n/a	XLID	-	9	12210795	16.73
SLC7A3	A>G, p.F203S	620	X:70148405-70148405	4.11	possibly_damaging	DAMAGING		p.F203S (1539)	10		17.110
SLC7A3	C>T, p.A331T	620	X:70147700-70147700	1.52	benign	TOLERATED		-	2		10.890
SLC7A3	C>T, p.A58T	620	X:70149676-70149676	5.39	probably_damaging	DAMAGING		-	14		34.000
SLC7A3	G>A, p.P501S	620	X:70146496-70146496	2.47	benign	TOLERATED		-	3		0.022
SLC9A6	A>G, p.I57V	670	X:135067830-135067830	1.63	benign	TOLERATED	XLID	-	5		13.670
SLC9A6	del1bp, p.G494VfsX53	670	X:135106602-135106602	5.34	n/a	n/a	XLID	-	20		33
SLC9A7	C>T, p.A38T	727	X:46618353-46618353	-0.29	benign	TOLERATED		-	1		16.640
SLC9A7	G>A, p.L514F	726	X:46502744-46502744	3.97	probably_damaging	TOLERATED		-	6		22.200
SOWAHD	C>T, p.P233L	316	X:118893328-118893328	4.91	probably_damaging	DAMAGING		-	13		16.440
SPANXN3	G>A, p.T44I	142	X:142596939-142596939	-1.62	possibly_damaging	TOLERATED		-	2		10.160
SRPK3	A>T, p.K270M	568	X:153049241-153049241	2.73	probably_damaging	DAMAGING		-	11		23.900
SRPK3	C>T, p.R13C	634	X:153045720-153045720	0.03	benign	DAMAGING(Low_confidence)		-	3		10.500
SRPK3	C>T, p.T211M	534	X:153048457-153048457	4.16	probably_damaging	DAMAGING		-	13		16.960

SRPK3	G>A, p.D44N	634	X:153045813-153045813	-0.54	benign	TOLERATED		-	1		0.124
SRPK3	G>A, p.R13H	634	X:153045721-153045721	-3.12	benign	DAMAGING(Low_confidence)		-	2		0.006
SRPX	C>T, p.V159I	465	X:38031185-38031185	3.78	probably_damaging	TOLERATED		-	6		16.390
SSR4	G>A, p.A110T	185	X:153063213-153063213	2.15	possibly_damaging	TOLERATED		-	4		11.800
SSR4	G>A, p.E114K	185	X:153063225-153063225	3.13	possibly_damaging	TOLERATED		-	5		6.539
SSX1	del3bp, p.K150_E151delinsK	189	X:48123332-48123334	-0.12	n/a	n/a		-	3		2.653
SSX5	C>A, p.V192F	230	X:48049584-48049584	-1.02	possibly_damaging	TOLERATED		-	2		3.614
SSX5	C>T, p.D67N	230	X:48054284-48054284	-1.67	benign	TOLERATED		-	1		0.665
STAG2	C>G, p.A746G	1269	X:123200258-123200258	5.84	possibly_damaging	DAMAGING		-	11		16.030
STARD8	G>A, p.A793T	1024	X:67942306-67942306	3.21	possibly_damaging	DAMAGING		-	9		14.840
STARD8	del3bp, p.E437del	1024	X:67938302-67938304	0.9	n/a	n/a		-	4		12.15
TAF1	A>G, p.N493D	1894	X:70601649-70601649	4.41	probably_damaging	DAMAGING		-	13		19.160
TAF1	C>T, p.R1190C	1894	X:70617204-70617204	5.25	probably_damaging	DAMAGING		-	14		27.300
TAF7L	A>T, p.D66E	463	X:100547836-100547836	0.54	probably_damaging	TOLERATED		-	4		4.098
TAF9B	T>A, p.S152C	252	X:77392439-77392439	1.54	possibly_damaging	DAMAGING		-	7		18.120
TBC1D25	G>A, p.R649H	689	X:48419242-48419242	3.55	probably_damaging	DAMAGING		-	12		13.290
TBL1X	G>A, p.V222M	527	X:9660220-9660220	5.42	probably_damaging	DAMAGING		-	14		16.650
TCEAL2	G>A, p.E27K	228	X:101381881-101381881	-0.44	benign	TOLERATED		-	1		8.921
TCEAL5	C>T, p.G64E	207	X:102529301-102529301	0.11	possibly_damaging	TOLERATED		-	3		13.750
TEX11	G>A, p.R269W	941	X:69960634-69960634	1.71	probably_damaging	DAMAGING		-	10		10.280
TFDP3	A>C, p.S216A	406	X:132351642-132351642	1.11	benign	TOLERATED		-	2		0.025
THOC2	A>G, p.I800T	1594	X:122765621-122765621	4.95	possibly_damaging	DAMAGING		-	10		21.900
THOC2	A>G, p.L438P	1594	X:122799566-122799566	4.84	probably_damaging	DAMAGING		p.L359P (1657)	13		23.500
THOC2	A>G, p.S1012P	1594	X:122759786-122759786	4.81	possibly_damaging	DAMAGING		-	10		21.300
THOC2	G>A, p.L313F	1594	X:122802090-122802090	5.41	probably_damaging	DAMAGING		-	14		27.200
TIMM17B	A>G, p.I112T	223	X:48752326-48752326	4.25	probably_damaging	TOLERATED		-	7		15.210
TMSB15A	A>G, p.F13S	46	X:101770054-101770054	2.5	probably_damaging	TOLERATED		-	5		13.900
TRO	C>T, p.T1355M	1432	X:54957221-54957221	0.05	probably_damaging	n/a		-	4		12.850
TRO	G>A, p.V386I	707	X:54950121-54950121	1.64	probably_damaging	TOLERATED		-	4		13.000
TRO	T>G, p.N1296K	1432	X:54957045-54957045	0.37	probably_damaging	DAMAGING(Low_confidence)		-	7		17.250
TSPAN6	C>T, p.A87T	246	X:99890572-99890572	1.33	benign	TOLERATED		-	2		11.510
TXLNG	G>C, p.E423D	529	X:16859571-16859571	0.02	benign	TOLERATED		-	2		15.570
TXLNG	del12bp,	529	X:16859681-16859692	0.04	n/a	n/a		-	4		9.767

	p.I465_A469delinsA										
UBE2A	C>T, p.R7W	123	X:118708693-118708693	0.84	probably_damaging	DAMAGING	XLID	-	13	23685073	24.400
UBE2A	del2bp, p.I87MfsX14	153	X:118716567-118716568	3.18	n/a	n/a	XLID	-	20	23685073	33
UBQLN2	T>C, p.L253P	625	X:56591064-56591064	1.84	possibly_damaging	DAMAGING		-	7		3.878
UPF3B	del1bp, p.P437QfsX47	484	X:118968983-118968983	3.73	n/a	n/a	XLID	-	20		16.58
USP26	A>C, p.N695K	914	X:132160164-132160164	0.51	probably_damaging	DAMAGING		-	10		13.390
USP27X	T>C, p.Y381H	439	X:49646051-49646051	3.94	probably_damaging	DAMAGING		-	12		11.270
USP27X	del5bp, p.S342RfsX14	439	X:49645933-49645937	1.63	n/a	n/a		-	20		10.46
USP51	C>G, p.D296H	712	X:55514487-55514487	4.41	probably_damaging	DAMAGING		-	13		16.070
USP51	del3bp, p.G149_A150delinsG	712	X:55514925-55514927	-0.37	n/a	n/a		-	3		8.816
USP9X	A>C, p.T2018P	2555	X:41075872-41075872	4.52	benign	TOLERATED	XLID	-	5		14.760
USP9X	A>G, p.I2120M	2555	X:41077775-41077775	0.2	possibly_damaging	DAMAGING	XLID	-	7		18.370
UTP14A	G>A, p.R59Q	772	X:129042648-129042648	-0.74	benign	TOLERATED		-	1		9.158
VCX	G>A, p.E159K	207	X:7811911-7811911	-0.84	benign	TOLERATED		-	1		0.018
VSIG1	G>A, p.V183M	388	X:107316041-107316041	-1.39	probably_damaging	TOLERATED		-	3		10.480
VSIG4	C>T, p.D224N	400	X:65252334-65252334	-0.04	benign	TOLERATED		-	1		7.365
VSIG4	C>T, p.G215D	400	X:65252360-65252360	0.35	possibly_damaging	TOLERATED		-	3		1.144
VSIG4	T>A, p.T171S	228	X:65247333-65247333	0.19	possibly_damaging	TOLERATED		-	3		9.125
WDR13	G>A, p.R110H	486	X:48457787-48457787	3.54	probably_damaging	DAMAGING		-	12		26.400
WDR13	G>A, p.R187H	486	X:48458743-48458743	1.85	probably_damaging	TOLERATED		-	4		19.920
WDR45	C>T, p.R232H	361	X:48933234-48933234	4.94	probably_damaging	DAMAGING	XLID	-	13		23.400
WNK3	G>A, p.L1512F	1801	X:54263465-54263465	2.09	benign	TOLERATED		-	3		12.090
XG	G>A, p.G141R	196	X:2726228-2726228	1.1	probably_damaging	DAMAGING		-	10		9.110
XG	G>A, p.G152S	196	X:2726261-2726261	1.1	probably_damaging	TOLERATED		-	4		13.520
XIAP	A>T, p.T470S	498	X:123040945-123040945	1.91	benign	TOLERATED		-	2	21119115	13.070
YIPF6	G>A, p.R64H	237	X:67733173-67733173	4.44	probably_damaging	DAMAGING		-	13		29.400
ZC4H2	C>G, p.V63L	225	X:64141735-64141735	5.36	probably_damaging	DAMAGING	XLID	-	14	23623388	31.000
ZCCHC16	C>T, p.R26W	311	X:111698032-111698032	-0.12	probably_damaging	DAMAGING		-	9		9.933
ZCCHC5	G>A, p.R19W	476	X:77913863-77913863	0.63	benign	DAMAGING(Low_confidence)		-	3		9.699
ZDHHC9	A>G, p.C49R	365	X:128975777-128975777	3.07	benign	DAMAGING	XLID	-	9		17.560
ZDHHC9	G>A, p.R298*	365	X:128944967-128944967	1.3	n/a	n/a	XLID	-	20		38.000
ZIC3	C>T, p.A33V	468	X:136648948-136648948	1.65	benign	TOLERATED		-	2	23427188	12.270
ZMAT1	G>A, p.R107W	468	X:101139567-101139567	0.09	benign	TOLERATED		-	2		1.486

ZMAT1	T>A, p.E76V	468	X:101139659-101139659	0.46	benign	DAMAGING		-	4		12.190
ZMYM3	T>C, p.Q119R	496	X:70472750-70472750	0.41	possibly_damaging	TOLERATED	XLID[c]	-	6		11.580
ZNF182	G>A, p.A550V	640	X:47835837-47835837	0.46	probably_damaging	DAMAGING		-	10		16.390
ZNF630	G>A, p.A217V	658	X:47919181-47919181	-0.23	benign	DAMAGING		-	3		9.647
ZNF674	C>A, p.R142I	582	X:46360599-46360599	0.16	benign	TOLERATED	XLID[c]	-	5		4.579
ZNF711	A>G, p.K357R	762	X:84525114-84525114	2.36	benign	TOLERATED	XLID	-	6		14.970
ZNF711	C>T, p.A92V	762	X:84510460-84510460	1.63	possibly_damaging	TOLERATED	XLID	-	6		14.140
ZNF711	G>T, p.E622D	762	X:84526414-84526414	0.24	benign	TOLERATED	XLID	-	5		0.375
ZNF711	T>C, p.I244T	762	X:84519389-84519389	4.12	probably_damaging	TOLERATED	XLID	-	10		19.640
ZNF75D	T>G, p.K209N	416	X:134421690-134421690	0.18	benign	TOLERATED		-	2		9.034
ZNF81	G>A, p.G11R	662	X:47705697-47705697	0.13	benign	TOLERATED	XLID[c]	-	5		9.739
ZRSR2	C>T, p.A95V	483	X:15821891-15821891	3.2	possibly_damaging	TOLERATED		-	5		17.170
ZXDB	A>T, p.Q277L	804	X:57619311-57619311	0.73	benign	DAMAGING		-	4		6.906

*Established XLID gene prior to this study.

[a]Not confirmed by PCR, suggesting that this small deletion is a false positive,

[b]the *SCML1* truncating mutation has been found in the lymphoblastoid cell line of the index patient but not in his DNA isolated from blood nor in any other family member and was therefore very likely introduced by EBV transformation,

[c]implication of this gene in XLID considered uncertain,[6]

[d]clinical phenotype published in[7]

[e]the point mutation did not segregate with the phenotype and this family, previously described as a possible novel X-linked syndrome[8] turned out to carry a compound heterozygous mutation in *RAB3GAP1*.[9]

PS = Prioritization Score

Supplementary Table 2. Recurrent Coding and Splice Site Variants, and Synonymous Variants Identified in 248 Probands and Absent in Controls

Recurrence	Gene	Variant	Protein length	Genomic position (hg19)	PhyloP	XLID gene	In Tarpey et al. (number in list)[5]	HGMD	C-Score
1	ABCB7	G>A, p.N208N	754	X:74295431-74295431	0.6		-		7.322
1	ACE2	T>C, p.T434T	806	X:15593929-15593929	-0.34		-		9.413
1	ACTRT1	A>G, p.L219L	377	X:127185531-127185531	-0.57		-		0.430
1	AFF2	C>T, p.Y1146Y	1277	X:148059958-148059958	1.38	XLID	-		8.881
2	AGTR2	T>C, p.F150L	364	X:115303981-115303981	0.75	XLID[a]	-		2.908
1	AGTR2	T>C, p.Y108Y	364	X:115303857-115303857	0.05	XLID[a]	-		4.067
1	ALG13	C>A, p.P914P	955	X:111003104-111003104	-2.01	XLID	-		1.582
1	AMOT	C>T, p.S842S	1085	X:112022856-112022856	-0.77		-		7.488
1	ARHGAP4	C>T, p.S831S	947	X:153174911-153174911	-0.18		-		3.313
1	ARHGAP4	T>C, p.T274T	947	X:153184496-153184496	-0.46		-		5.620
1	ARMCX1	T>C, p.N269N	454	X:100808720-100808720	1.72		-		7.127
1	ARMCX2	A>G, p.I610I	633	X:100910745-100910745	-0.01		-		5.261
1	ARMCX5	A>G, p.Q395Q	559	X:101858254-101858254	0.2		-		0.013
1	ARMCX5	C>T, p.V564V	839	X:101971489-101971489	-0.32		-		0.016
1	ARSE	A>G, p.G368G	590	X:2861128-2861128	-3.98		-		2.032
2	ARSE	C>T, p.D509N	590	X:2853118-2853118	0.7		-		6.263
2	ASB12[b]	del1bp, p.L269CfsX18	319	X:63444725-63444725	3.29		-		34
1	ATP11C	T>C, p.A198A	1133	X:138884469-138884469	0.34		-		10.870
1	ATP7A	T>C, p.S1463S	1501	X:77301953-77301953	0.47	XLID	-		9.381
1	ATP7A	T>C, p.Y215Y	673	X:77244763-77244763	0.49	XLID	-		2.992
1	ATRX	C>T, p.K202K	2493	X:76940487-76940487	0.21	XLID	-		8.871
3	ATRX	C>T, p.R781Q	2493	X:76938406-76938406	2.74	XLID	-		13.710
1	ATRX	T>G, p.R1741R	2493	X:76875914-76875914	0.62	XLID	-		9.820

1	BCOR	G>A, p.N10N	1704	X:39937153-39937153	1.65	XLID	-		8.899
1	BMX	A>G, p.K200K	676	X:15540558-15540558	0.21		-		1.972
1	BMX	C>T, p.H650H	676	X:15568117-15568117	-1.37		-		9.695
1	BRS3	C>T, p.L365L	400	X:135574427-135574427	1.14		-		0.012
1	BRWD3	T>C, p.A255A	1803	X:79999579-79999579	1.25	XLID	-		10.390
2	CA5BP1	G>A, p.R70H	185	X:15720969-15720969	-0.97		-		2.231
1	CACNA1F	G>A, p.H551H	1978	X:49082402-49082402	2.19		-		8.968
1	CAPN6	T>G, p.T558T	642	X:110490665-110490665	-0.25		-		8.034
1	CASK	C>T, p.A809A	922	X:41390338-41390338	-3.5	XLID	-		4.313
1	CASK	T>G, p.T698T	898	X:41394201-41394201	0.85	XLID	-		7.726
1	CCDC120	C>T, p.S424S	631	X:48925027-48925027	1.95		-		7.811
1	CCDC160	C>T, p.S51S	326	X:133378983-133378983	-0.19		-		0.020
1	CCNB3	C>T, p.F927F	1396	X:50053950-50053950	-1.15		-		0.839
1	CDR1	C>T, p.L100L	263	X:139866232-139866232	1.3		p.L100L (269)		5.187
1	CFP	G>A, p.P29P	470	X:47489063-47489063	-1.61		-		2.889
1	CFP	T>C, p.P255P	470	X:47486541-47486541	1.82		-		6.457
1	CLCN4	C>T, p.S217S	761	X:10174493-10174493	-1.39		-		8.533
1	CTPS2	C>T, p.A162A	587	X:16711563-16711563	-1.74		-		2.466
1	CXCR3	C>T, p.V309V	416	X:70836536-70836536	0.42		-		0.064
1	CXorf36	G>A, p.D126D	434	X:45051116-45051116	0.68		-		9.702
1	CXorf38	A>G, p.D146D	320	X:40498294-40498294	0.35		-		9.322
1	CXorf40A	G>A, p.T70T	159	X:148627384-148627384	0.65		-		0.000
1	CXorf40A	T>A, p.P153P	159	X:148628490-148628490	-0.8		-		0.000
1	CXorf48	C>T, p.V39V	243	X:134303680-134303680	-1.05		-		3.080
1	CXorf56	C>T, p.A161A	174	X:118673729-118673729	-0.34		-		10.420
1	CXorf57	G>C, p.A567A	856	X:105882884-105882884	-0.01		-		1.234
1	CXorf64	C>T, p.L37L	299	X:125954730-125954730	0.52		-		3.482
1	CXorf65	G>A, p.I40I	184	X:70325980-70325980	-0.31		-		9.149
1	DCAF8L2	G>A, p.E133E	632	X:27765411-27765411	-1.46		-		0.385
1	DMD	A>G, p.T2318T	3563	X:31792296-31792296	1.06	XLID	-		9.066
2	DMD	T>A, p.K1800N	3563	X:32360370-32360370	2.19	XLID	-		15.660
1	DMD	T>G, p.T16T	3682	X:33038289-33038289	1.81	XLID	-		9.094

1	DOCK11	T>C, p.F1513F	2074	X:117783048-117783048	0.81		-		9.196
2	DYNLT3	G>A, p.A75V	117	X:37700331-37700331	3.02		-		19.720
1	DYNLT3	G>A, p.G77G	117	X:37700324-37700324	1.08		-		10.510
1	EDA2R	G>A, p.V300V	319	X:65819383-65819383	-0.33		-		0.010
2	EFNB1	G>A, p.R268Q	347	X:68060259-68060259	5.05		-		25.200
1	EGFL6	C>A, p.R363R	554	X:13636157-13636157	0.92		p.R363R (472)		8.547
1	EIF2S3	C>A, p.I207I	473	X:24080675-24080675	0.38		-		8.375
1	ESX1	C>T, p.P361P	407	X:103495047-103495047	-1.07		-		2.514
1	ESX1	T>G, p.P136P	407	X:103498933-103498933	-0.35		-		4.080
1	F8	C>T, p.S1114S	2352	X:154158723-154158723	-0.7		-		0.013
233	FAM104B	retrocopy		X:55171678-55187628	0		-		
1	FAM120C	G>A, p.D355D	1097	X:54177771-54177771	0.25		-		8.397
1	FAM122B	C>T, p.E235E	242	X:133905336-133905336	1.11		-		5.811
1	FAM123B	C>T, p.X1136*	1136	X:63409759-63409759	0.98		-		0.231
1	FAM127A	A>G, p.R39R	114	X:134166530-134166530	-0.14		-		7.238
1	FAM155B	G>A, p.A368A	473	X:68749484-68749484	1.54		-		3.765
1	FAM199X	C>T, p.S51S	389	X:103411619-103411619	-0.06		-		12.820
2	FAM47C	A>G, p.K805R	1036	X:37028897-37028897	1.6		-		12.610
3	FAM58A	insC, p.Q18AfsX39	248	X:152864477-152864478	1.03		-		12.39
1	FAM70A	G>A, p.P16P	242	X:119445117-119445117	0.19		-		7.947
1	FGD1	C>T, p.K722K	962	X:54475684-54475684	1.29	XLID	-		7.175
1	FLNA	C>T, p.P323P	2640	X:153595118-153595118	-0.35	XLID	-		10.120
1	FLNA	G>A, p.A1636A	2640	X:153585839-153585839	-1.47	XLID	-		9.559
1	FLNA	G>A, p.D1705D	2648	X:153583295-153583295	-1.31	XLID	-		2.884
1	FLNA	G>A, p.P1085P	2640	X:153588908-153588908	-0.85	XLID	-		6.603
1	FLNA	G>A, p.Y735Y	2640	X:153592465-153592465	0.07	XLID	-		9.596
1	FRMPD4	G>A, p.G1284G	1323	X:12736797-12736797	0.14		-		5.469
1	FRMPD4	G>A, p.P127P	1323	X:12632959-12632959	-1.67		-		0.751
1	GABRE	G>A, p.N134N	507	X:151131056-151131056	1.22		-		3.872
1	GLOD5	C>T, p.I41I	161	X:48624299-48624299	-1.08		-		9.113
1	GLRA4	G>A, p.S84S	343	X:102979487-102979487	0.04		-		5.316
1	GLUD2	G>A, p.K187K	559	X:120182099-120182099	0.08		-		5.424

1	GPKOW	C>T, p.A97A	477	X:48979012-48979012	0.95		-		2.502
1	GPM6B	G>A, p.A4A	306	X:13835012-13835012	3.87		-		10.610
1	GPR112	A>G, p.S2299S	3081	X:135438294-135438294	-0.75		-		0.011
1	GPR50	C>T, p.I124I	618	X:150348427-150348427	0.66		-		3.640
1	GYG2	C>T, p.H154H	470	X:2773171-2773171	-0.89		-		0.988
3	H2BFM	C>T, p.H48H	155	X:103294687-103294687	-0.36		-		1.860
1	HAUS7	C>T, p.K238K	428	X:152721744-152721744	0.09		-		3.639
1	HAUS7	C>T, p.L208L	237	X:152710265-152710265	-0.15		-		1.368
1	HCCS	C>T, p.N158N	269	X:11136693-11136693	-0.27	XLID	-		9.494
1	HCFC1	G>A, p.S1451S	2036	X:153219202-153219202	-1.64	XLID	-		0.577
1	HDAC6	C>T, p.R277R	1216	X:48672871-48672871	0.25		-		4.783
1	HEPH	A>G, p.P171P	1161	X:65393522-65393522	0		-		10.320
29	HS6ST2	A>G, p.V100V	606	X:132092331-132092331	1.92		-		0.000
1	HS6ST2	G>A, p.T25T	606	X:132092556-132092556	2.08		-		8.738
26	HS6ST2	G>C, p.G131G	606	X:132092240-132092240	-0.08		-		0.000
171	HS6ST2	insG, p.L107PfsX43	606	X:132092311-132092312	1.77		-		16.28
1	HUWE1	C>T, p.L3624L	4375	X:53573440-53573440	0.25	XLID	-		10.100
2	HUWE1	G>A, p.R4187C	4375	X:53562435-53562435	3.13	XLID	-	18252223, 23871722	13.980
1	HUWE1	G>A, p.T1509T	4375	X:53615429-53615429	-1.78	XLID	-		8.257
1	HUWE1	G>T, p.R1365R	4375	X:53617962-53617962	1.58	XLID	-		12.830
1	HUWE1	T>A, p.L3192L	4375	X:53576379-53576379	0.14	XLID	-		7.685
1	IDS	G>A, p.S386S	551	X:148568478-148568478	-1.79	XLID	-		11.450
1	IDS	G>C, p.P358P	551	X:148568562-148568562	-0.81	XLID	-		3.290
1	IGSF1	C>T, p.G250G	1337	X:130417156-130417156	0.52		-		9.406
2	IQSEC2	G>A, p.R1155W	1489	X:53265003-53265003	3.13	XLID	-		17.180
1	IRAK1	G>A, p.S137S	634	X:153284673-153284673	-0.5		-		9.252
1	ITGB1BP2	C>T, p.D327D	348	X:70524979-70524979	0.34		-		4.582
1	ITIH6	C>T, p.T405T	1314	X:54785292-54785292	-1.21		-		0.014
3	ITIH6	insA, donor		X:54786186-54786187	1.02		-		0.582
1	ITM2A	G>A, p.I63I	264	X:78618974-78618974	0.35		-		8.756
1	KIF4A	G>A, p.V492V	680	X:69572494-69572494	-0.67		-		0.265
1	KLHL4	A>G, p.E447E	721	X:86887226-86887226	0.76		-		7.864

1	L1CAM	G>A, p.P921P	1254	X:153130652-153130652	-3.57	XLID	-		3.923
1	L1CAM	G>A, p.R575R	1254	X:153133556-153133556	0.23	XLID	-		8.105
1	LAMP2	G>A, p.I143I	411	X:119582952-119582952	-0.08		-		4.018
1	LAS1L	G>C, p.P200P	248	X:64734720-64734720	0.1		-		3.293
1	LONRF3	C>T, p.F460F	760	X:118124488-118124488	0.09		-		6.688
1	LONRF3	C>T, p.P13P	719	X:118108782-118108782	1.7		-		4.439
1	LPAR4	A>C, p.A256A	371	X:78011134-78011134	1.97		-		3.378
1	LPAR4	C>T, p.H327H	371	X:78011347-78011347	-0.28		-		0.005
2	MAGEA1	del1bp, acceptor		X:152483225-152483225	0.85		-		3.895
1	MAGEA8	G>A, p.P220P	319	X:149013706-149013706	-0.15		-		2.182
1	MAGEB1	A>G, p.L120L	348	X:30268970-30268970	-1.93		-		3.369
1	MAGEB6	C>T, p.N298N	408	X:26212857-26212857	-0.81		-		2.204
1	MAGEC1	G>A, p.E955E	1143	X:140996055-140996055	-0.16		-		3.023
1	MAGEC3	G>C, p.G262G	644	X:140969459-140969459	0.17		-		1.419
1	MAGIX	G>A, p.G147G	335	X:49021362-49021362	-0.98		-		5.586
1	MAMLD1	C>T, p.D924D	999	X:149681118-149681118	0.22		-		0.015
1	MAMLD1	G>A, p.S37S	775	X:149631052-149631052	-1.61		-		1.519
1	MAMLD1	G>A, p.V859V	999	X:149680923-149680923	1.57		-		0.512
1	MAOB	G>A, p.N3N	521	X:43741537-43741537	2.47		-		11.810
2	MAP3K15	A>G, p.I387I	1314	X:19449561-19449561	0.45		-		10.790
1	MAP3K15	G>A, p.L837L	1314	X:19398318-19398318	1.08		-		9.656
1	MBTPS2	G>C, p.V325V	331	X:21887801-21887801	0.81		-		9.914
1	MCF2	C>T, p.G705G	926	X:138678870-138678870	-1.15		-		5.918
1	MECP2	G>A, p.P56P	487	X:153297867-153297867	-0.69	XLID	-		9.535
1	MED12	C>T, p.P712P	2178	X:70344906-70344906	-0.1	XLID	-		5.347
1	MID1	C>T, p.T5T	340	X:10443133-10443133	0	XLID	-		9.003
1	MID1IP1	G>T, p.S13S	184	X:38664238-38664238	0.5		-		8.973
1	MORC4	G>A, p.I816I	938	X:106185380-106185380	0.88		-		6.301
1	MPP1	C>T, p.S261S	467	X:154013327-154013327	-2		-		3.408
1	MPP1	G>A, p.V274V	467	X:154012346-154012346	-1.81		p.V274V (1052)		9.254
126	MSN	retrocopy		X:64955292-64956657	0		-		126
1	MTMR8	C>T, p.E547E	705	X:63488891-63488891	-0.01		-		4.976

2	MTMR8[b]	del1bp, p.L644CfsX18	694	X:63444725-63444725	3.29		-		34
1	MXRA5	A>G, p.C1972C	2829	X:3235806-3235806	-0.38		-		5.612
1	MXRA5	G>A, p.N137N	2829	X:3248357-3248357	3.06		-		4.278
1	MXRA5	G>A, p.P2662P	2829	X:3228258-3228258	-1.36		-		0.012
1	MXRA5	T>G, p.R1691R	2829	X:3238655-3238655	1.64		-		3.331
1	NAP1L3	A>G, p.P327P	507	X:92927323-92927323	0.05		-		5.416
2	NHS	T>C, p.H364H	1631	X:17742465-17742465	0.81	XLID	-		0.719
1	NKAP	A>G, p.H160H	416	X:119070633-119070633	0.41		-		7.409
1	NLGN4X	A>G, p.A442A	817	X:5821393-5821393	-1.3	XLID	-		1.376
1	NR0B1	C>T, p.A25A	471	X:30327406-30327406	-0.14		-		0.857
1	NRK	A>G, p.E721E	1582	X:105153796-105153796	0.69		-		0.070
1	NRK	T>C, p.H1396H	1583	X:105189992-105189992	1.94		-		6.695
1	NR_002784	C>T, p.S39S	833	X:27481297-27481297	-2.94		-		0.604
1	NR_002784	G>A, p.Y528Y	833	X:27479830-27479830	2.3		-		1.401
1	NR_002784	T>C, p.R459R	833	X:27480037-27480037	0.51		-		10.190
1	NR_002784	T>C, p.S601S	833	X:27479611-27479611	-0.58		-		13.010
1	NSDHL	C>A, p.I43I	374	X:152018829-152018829	-0.56	XLID	-		3.430
1	OCRL	C>T, p.Y805Y	902	X:128722936-128722936	-1.15	XLID	-		8.915
1	ODZ1	C>T, p.L1528L	2726	X:123554538-123554538	-0.24		-		7.050
1	ODZ1	G>A, p.S362S	2726	X:123805615-123805615	2.73		-		9.280
1	P2RY10	C>T, p.P278P	340	X:78216851-78216851	0.12		-		0.006
1	PAK3	T>A, p.I532I	545	X:110463636-110463636	0.85	XLID	-		8.011
1	PCYT1B	G>A, p.Y141Y	370	X:24608203-24608203	-0.27		-		7.413
1	PDZD4	C>T, p.E594E	770	X:153069336-153069336	0.07		-		4.427
1	PHEX	T>C, p.H487H	750	X:22186485-22186485	1.55		-		8.389
1	PHKA1	G>A, p.Y469Y	1152	X:71864264-71864264	-0.5		-		5.732
1	PHKA2	C>T, p.S846S	1236	X:18925195-18925195	-1.09		-		3.320
1	PHKA2	G>A, p.L159L	1236	X:18966922-18966922	-2.65		-		0.309
1	PJA1	G>A, p.A425A	644	X:68381807-68381807	0.94		-		2.970
1	PJA1	G>A, p.D362D	644	X:68381996-68381996	-4.26		-		2.260
1	PLS3	G>A, p.L532L	631	X:114881954-114881954	1.05		-		8.738

1	PLXNA3	C>T, p.N97N	1872	X:153688814-153688814	1		-		5.167
1	PLXNA3	C>T, p.S192S	1872	X:153689099-153689099	-0.63		-		4.001
1	PLXNA3	C>T, p.V171V	1872	X:153689036-153689036	-0.19		-		0.537
1	PLXNB3	G>A, p.Q429Q	1910	X:153034423-153034423	-0.05		-		3.306
1	PLXNB3	T>C, p.Y1827Y	1910	X:153043857-153043857	-0.27		-		0.405
2	PQBP1	C>T, p.R243W	266	X:48760290-48760290	2.25	XLID	-		20.900
1	PRRG3	G>A, p.E202E	232	X:150869415-150869415	-0.03		-		6.522
1	RAI2	C>T, p.Q5Q	531	X:17820116-17820116	0.78		-		10.770
1	RBM3	A>G, p.G126G	158	X:48434957-48434957	-0.19		-		15.940
3	RBMX	del3bp, p.Y187del	197	X:135954484-135954486	-0.32		-		5.139
3	RBMX	retrocopy		X:135958662-135960245	0		-		
1	RBMX2	G>A, p.T229T	323	X:129546540-129546540	-3.67		-		2.693
1	RBMX2	T>C, p.A213A	323	X:129546492-129546492	-0.87		-		6.129
1	RGAG4	G>C, p.R312R	570	X:71350455-71350455	-2.12		-		3.029
1	RP2	C>T, p.A250A	351	X:46713558-46713558	0.64		-		7.476
1	RPGR	C>T, p.E889E	1153	X:38145585-38145585	1.38		-		3.032
1	SAGE1	T>C, p.P406P	905	X:134990306-134990306	-0.16		-		2.209
1	SASH3	C>T, p.A377A	381	X:128927796-128927796	-2.12		-		1.897
1	SHROOM2	C>T, p.A286A	1617	X:9862806-9862806	-1.06		-		5.443
1	SHROOM2	C>T, p.L1330L	1617	X:9905574-9905574	2.51		-		9.212
1	SHROOM4	C>T, p.Q1128Q	1494	X:50350758-50350758	-2.15	XLID	-		0.007
1	SHROOM4	T>C, p.Q1130Q	1494	X:50350752-50350752	-0.53	XLID	-		0.007
2	SHROOM4	T>G, p.K1129Q	1494	X:50350757-50350757	0.04	XLID	-		0.039
1	SLC38A5	A>G, p.S178S	473	X:48321323-48321323	0.13		-		7.984
1	SLC6A8	C>G, p.L484L	636	X:152959858-152959858	0.45	XLID	-		7.346
1	SLC6A8	C>T, p.I211I	636	X:152956997-152956997	-0.27	XLID	-		8.701
1	SLC6A8	G>A, p.E148E	277	X:152957574-152957574	-0.74	XLID	-		3.802
1	SLC6A8	G>A, p.L472L	636	X:152959822-152959822	0.07	XLID	-		6.923
1	SLC9A7	C>T, p.A362A	726	X:46513102-46513102	-3.8		-		2.261
1	SLITRK2	C>T, p.D661D	846	X:144905926-144905926	-0.51		-		3.699
2	SLITRK4	A>G, p.P594P	838	X:142717143-142717143	-1.83		-		0.172
1	SMC1A	G>C, p.T1195T	1234	X:53407574-53407574	0.27	XLID	-		6.140

1	SMPX	C>T, p.E44E	89	X:21761868-21761868	4.65		-		11.680
1	SPANXN1	G>A, p.Q27Q	73	X:144337196-144337196	0.07		-		1.085
1	SPANXN2	G>A, p.D71D	181	X:142795465-142795465	-1.05		-		0.700
2	SPIN3	T>A, p.I229F	259	X:57020696-57020696	3.11		-		18.200
1	SRPX	A>G, p.F230F	465	X:38020271-38020271	0.83		-		9.198
1	SRPX	G>T, p.L224L	465	X:38020289-38020289	-0.72		-		4.796
1	STAG2	T>C, p.D409D	1269	X:123190008-123190008	0.69		-		10.550
1	STARD8	G>A, p.E342E	1024	X:67938022-67938022	0.08		-		0.013
1	STS	C>T, p.N400N	584	X:7243483-7243483	4.85		-		8.580
2	TAB3	G>A, p.P169L	713	X:30873276-30873276	5.3		-		13.680
1	TAF9B	G>T, p.S131S	252	X:77393258-77393258	0.8		-		7.359
2	TBC1D25	G>T, p.D522Y	689	X:48418860-48418860	0.63		-		9.135
1	TCEAL2	A>G, p.E109E	228	X:101382129-101382129	-0.04		-		2.006
1	TCEAL2	C>T, p.N173N	228	X:101382321-101382321	-1.09		-		10.830
1	TFE3	G>A, p.Y65Y	576	X:48898017-48898017	0.87		-		10.470
1	TGIF2LX	G>A, p.R227R	242	X:89177765-89177765	0.62		-		0.018
1	TIMM8A	A>G, p.D72D	98	X:100601565-100601565	2.82	XLID	-		8.598
4	TIMP1	G>A, p.L245L	262	X:47445366-47445366	-0.2		-		2.755
1	TKTL1	G>A, p.P75P	597	X:153533746-153533746	-2.33		-		0.157
1	TLR7	C>T, p.N1031N	1050	X:12906720-12906720	0.84		-		0.163
1	TLR7	T>C, p.N523N	1050	X:12905196-12905196	-0.08		-		0.005
1	TMEM164	A>G, p.K194K	298	X:109388100-109388100	3.16		-		10.710
1	TMLHE	G>A, p.L111L	422	X:154754144-154754144	0.27		-		0.077
1	TMLHE	G>A, p.Y73Y	422	X:154754256-154754256	0.45		-		7.832
1	TRO	C>A, p.R428R	707	X:54950929-54950929	-2.08		-		0.151
1	TRO	G>A, p.K143K	707	X:54949394-54949394	-0.72		-		0.032
1	TSPAN7	C>T, p.N177N	250	X:38535048-38535048	-0.47	XLID	-		6.668
1	UBA1	C>T, p.S414S	1059	X:47062350-47062350	-1.93		p.S414S (1700)		7.111
1	USP11	C>A, p.L874L	964	X:47106775-47106775	1.17		-		8.258
1	USP26	A>C, p.S633S	914	X:132160350-132160350	0.07		-		1.970
1	VCX	C>T, p.S198S	207	X:7812030-7812030	0.1		-		1.521
1	VCX3B	C>T, p.S168S	247	X:8434187-8434187	-2.34		-		0.829

1	VSIG4	C>T, p.A201A	400	X:65252401-65252401	-2.31		-		0.016
1	VSIG4	G>A, p.A331A	348	X:65241978-65241978	-1.53		-		4.620
1	VSIG4	G>A, p.L98L	322	X:65253434-65253434	0.63		-		0.411
1	WAS	C>T, p.P10P	503	X:48542272-48542272	-0.67		-		3.444
1	WAS	G>A, p.L95L	503	X:48543947-48543947	-0.08		-		8.605
2	WDR13	G>A, p.K294K	486	X:48460222-48460222	3.62		-		10.210
1	WDR45	C>A, p.V91V	179	X:48930216-48930216	0.38		-		5.166
1	WNK3	T>C, p.K1543K	1801	X:54259453-54259453	0.89		-		10.750
1	WWC3	T>C, p.A705A	1093	X:10096036-10096036	0.17		-		11.350
1	XG	C>T, p.P56P	181	X:2700147-2700147	-0.76		-		2.687
2	XPNPEP2	C>T, p.S412S	675	X:128889288-128889288	-1.34		p.S412S (1790)		8.606
1	XPNPEP2	G>A, p.L12L	675	X:128873225-128873225	0.02		-		7.968
1	ZC3H12B	C>G, p.S596S	837	X:64722366-64722366	1.61		-		4.127
1	ZFP92	C>T, p.C266C	417	X:152686633-152686633	1.35		-		0.973
1	ZMAT1	T>C, p.V342V	468	X:101138860-101138860	0.85		-		7.947
1	ZMYM3	A>G, p.T678T	1371	X:70467698-70467698	1.08	XLID	-		10.870
1	ZMYM3	G>T, p.L1180L	1371	X:70462827-70462827	-0.6	XLID	-		8.922
1	ZNF182	T>C, p.A238A	640	X:47836772-47836772	-0.25		-		7.519
1	ZNF280C	A>T, p.A549A	738	X:129349956-129349956	-0.27		-		6.738
1	ZNF41	A>G, p.Y719Y	780	X:47307012-47307012	0.37	XLID[a]	-		3.794
1	ZNF81	C>A, p.L513L	662	X:47775584-47775584	-0.43	XLID	-		3.864
1	ZXDB	C>G, p.R259R	804	X:57619258-57619258	1.43				0.579

[a] Implication of this gene in XLID was considered as uncertain.[6]

[b] *ASB12* and *MTMR8* deletions are identical variants and due to UCSC annotations have a different gene name, also present in four ‘normal’ males in the latest version of the Exome Variant Server with indels included.

Supplementary Table 3. Duplications and Deletions of >50 Kb Identified in the Screen

Position on chromosome X (Hg19)	Type	Predicted size
X:6452600-8095200	Duplication	~1,592,600bp
X:8497400-8591800	Duplication	~94,400bp
X:54029028-54265532	Deletion	~236,505bp
X:100523644-100852544	Duplication	~328,900bp
X:122695919-123236419	Duplication	~540,500bp
X:123034319-123236619	Duplication	~202,300bp
X:152710806-153609906	Duplication*	~889,100bp
X:153570406-153861106	Duplication*	~290,700bp
X:28960479-29301379	Duplication*	~340,900bp

*Only detected by using ExomeCopy.[10]

Supplementary Table 4. Predicted Cryptic Splice Sites

Gene	Variation	Genomic location (Hg19)	+/- Nucleotides from the Exon-Intron Boundary	PhyloP
FAM9B	A>C, donor	X:8996062-8996062	-55	-0.06
DIAPH2	G>T, donor	X:96139056-96139056	-2339	-0.44
STAG2	C>G, donor	X:123200258-123200258	28	5.84
FGF13	G>C, acceptor	X:137792940-137792940	-39	-0.48

Supplementary Table 5. Pathogenic Variants Identified in Established XLID Genes and in Novel Previously Published XLID Genes Identified Through this Screen

Family	Gene	Mutation	Genomic Location (Hg19)	PhyloP	PolyPhen2	SIFT	PS-Score	HGMD	C-Score	Total Number of Affected Males / Informative Unaffected MalesTested for Segregation / Obligate Carrier Females
AU33	ACSL4	G>A, p.R654*	X:108902601-108902601	1.2	N/A	N/A	20		45	7/5/10
MRX68[11] /D109	ACSL4	G>A, p.P375L[11]	X:108917632-108917632	5.83	probably_damaging	DAMAGING	17	12525535	31	1/0/3 this study 5/2/3[11]
T23	ARX	C>A, p.R536S	X:25022868-25022868	2.14	probably_damaging	DAMAGING	14		18	2/0/2
T48	ATRX	C>T, p.R2085H	X:76829787-76829787	5.23	probably_damaging	DAMAGING	17	16813605	20	3/0/1
AU12	ATRX	G>A, p.R2085C	X:76829788-76829788	5.23	probably_damaging	DAMAGING	17	12673795	19	3/0/3
D112	CUL4B	del3bp, p.L767del[12]	X:119666415-119666417	1.98	N/A	N/A	7		19	3/0/2
P142	CUL4B	insGCA, p.S603_D604insA[12]	X:119672558-119672559	2.88	N/A	N/A	8		15	2/0/2
D38	DLG3	ins8bp, p.C181*	X:69669549-69669550	3.55	N/A	N/A	20		17	3/1/2
P130	DLG3	insC, p.T365Hfs*13	X:69671817-69671818	1.11	N/A	N/A	20	15185169	22	2/0/2
D46	FTSJ1	G>A, p.G117R	X:48337492-48337492	2.67	probably_damaging	DAMAGING	14		18	3/0/2
D101	GDI1	del2bp, p.S396Pfs*15[13, 14]	X:153670767-153670768	4.69	N/A	N/A	20	21836662, 22002931	27	7/4/4
N21	GRIA3	G>T, p.E224X	X:122460038-122460038	3.69	N/A	N/A	20		37	5/7/4
P176	GRIA3	G>A, p.G721R	X:122598800-122598800	5.43	probably_damaging	DAMAGING	17		18	4/2/3
D144	HCFC1	C>T, p.S225N[15]	X:153228714-153228714	5.51	benign	DAMAGING	8	23000143, 23871722	26	4/0/2
T137	HUWE1	G>A, p.R4187C	X:53562435-53562435	3.13	probably_damaging	N/A	9	18252223, 23871722	14	2/0/2
D154	HUWE1	G>A, p.R4187C	X:53562435-53562435	3.13	probably_damaging	N/A	9	18252223, 23871722	14	3/2/7

N163	KDM5C	del1bp, p.W534Gfs*15	X:53239743-53239743	-0.12	N/A	N/A	20		38	3/0/1
AU30	L1CAM	C>T, p.D202N	X:153136335-153136335	5.12	probably_damaging	DAMAGING	17		23	5/0/3
T17	MED12	C>T, p.P739L	X:70344986-70344986	5.61	probably_damaging	N/A	11		20	5/3/4
P158	MED12	A>T, p.K956M	X:70347203-70347203	4.61	probably_damaging	N/A	10		23	2/4/2
D145	MED12	C>T, p.R1295C	X:70349900-70349900	5.26	probably_damaging	N/A	11		22	2/1/2
T7	MED12	insC, p.S1967Qfs*84[16]	X:70357647-70357648	0.67	N/A	N/A	20		39	9/5/9
T10	OPHN1	T>C, acceptor	X:67502961-67502961	2.15	N/A	N/A	8		18	2/0/6
MRX26[17] /D43[a]	OPHN1	del46181bp, p.D612*	X:67292994-67339174	0.23	N/A	N/A	13			1/0/2
D83	PHF6	C>A, p.T254K	X:133549074-133549074	5.22	probably_damaging	TOLERATED	11		28	5/0/4
P57	PQBP1	del1bp, p.F240Sfs*26	X:48760281-48760281	2.69	N/A	N/A	20		36	5/2/3
D24	RBM10	del1292bp, p.I651*[15]	X:47044423-47045714	1.2	N/A	N/A	10			2/0/4
L60	RPS6KA3	T>C, p.N544D	X:20183151-20183151	4.84	probably_damaging	DAMAGING	16		26	3/0/1
D64[a]	RPS6KA3	G>T, p.T276K	X:20204432-20204432	5.69	probably_damaging	DAMAGING	17		27	1/0/2
L107	SLC16A2	C>T, p.R371C[18]	X:73745669-73745669	3.92	probably_damaging	DAMAGING	15	23568789	19	2/1/1
P52	SLC16A2	G>T, p.V416F	X:73749123-73749123	4.09	benign	TOLERATED	8		17	2/2/2
D96	SLC6A8	del2bp, donor	X:152957009-152957010	4.39	N/A	N/A	10		14	2/0/2
AU36	SLC6A8	T>C, p.L401P	X:152959420-152959420	4.3	probably_damaging	DAMAGING	16		20	2/0/4
P86	SLC6A8	del3bp, p.F408del	X:152959434-152959436	3.02	N/A	N/A	9	12210795	17	2/1/1
D150	SLC6A8	G>A, p.G466R[19]	X:152959802-152959802	5.16	probably_damaging	DAMAGING	17	21140503	22	1/0/3
M2	SLC9A6	del1bp, p.G494Vfs*53	X:135106602-135106602	5.34	N/A	N/A	20		33	5/1/10
L67	UBE2A	C>T, p.R7W[20]	X:118708693-118708693	0.84	probably_damaging	DAMAGING	13	23685073	24	2/0/3
L95	UBE2A	del2bp, p.I87Mfs*14[20]	X:118716567-118716568	3.18	N/A	N/A	20	23685073	33	2/0/2
P4	UPF3B	del1bp, p.P437Qfs*47	X:118968983-118968983	3.73	N/A	N/A	20		17	3/2/2
D139	ZC4H2	C>G, p.V63L[21]	X:64141735-64141735	5.36	probably_damaging	DAMAGING	14		31	5/5/5

P148	ZDHHC9	G>A, p.R298*[22]	X:128944967-128944967	1.3	N/A	N/A	20		38	3/4/2
AU3	ZDHHC9	A>G, p.C49R	X:128975777-128975777	3.07	benign	DAMAGING	9		18	5/4/3
N10	ZNF711	T>C, p.I244T	X:84519389-84519389	4.12	probably_damaging	TOLERATED	10		20	6/4/4
P161	ATP7A	del21997bp	X:77223458-77245454	N/A	N/A	N/A	13			3/4/2
MRX75[19] /D13[a]	GDI1	dup290700bp	X:153570406-153861106	N/A	N/A	N/A	7			1/0/4
N14	IL1RAPL1	dup340900bp	X:28960479-29301379	N/A	N/A	N/A	7			3/1/1
AU29	MECP2	dup899100bp	X:152710806-153609906	N/A	N/A	N/A	7			2/0/1
P177	PHF8	del236505bp	X:54029028-54265532	N/A	N/A	N/A	13			2/1/2
Follow-up Study										
N141	AP1S2	G>A, p.R52*	X:15870494-15870494	0.72	N/A	N/A	20	17186471	38	2/1/1
D178	AP1S2	del2bp, p.K25Rfs*19	X:15870573-15870574	2.93	N/A	N/A	20		27	3/0/1
D137	ATRX	insT, p.I2402Nfs*49	X:76764103-76764104	3.18	N/A	N/A	20		40	2/2/2
D203	CUL4B	insA, p.G770Wfs*4[12]	X:119666408-119666409	2.98	N/A	N/A	20		31	3/0/3
D102	CUL4B	C>A, donor[12]	X:119672514-119672514	5.35	N/A	N/A	11		17	2/1/1
P194	CUL4B	G>A, p.R466*[12]	X:119675504-119675504	1.41	N/A	N/A	20		38	2/0/2
N146	CUL4B	del5bp, p.I318Kfs*2[12]	X:119678462-119678466	2.85	N/A	N/A	20	17236139	33	2/0/1
T131	CUL4B	del1bp, p.A252Dfs*17[12]	X:119681012-119681012	3.21	N/A	N/A	20		36	2/0/2
D287	CUL4B	del2bp, p.S143Yfs*24[12]	X:119694066-119694067	1.79	N/A	N/A	20		21	2/0/3
N31	DLG3	del1bp, p.G31Afs*90	X:69665142-69665142	4.52	N/A	N/A	20		16	6/1/ 2
D172	DLG3	G>C, donor[18]	X:69665409-69665409	4.47	N/A	N/A	20		15	3/4/3
D301	DLG3	G>C, donor[18]	X:69670634-69670634	4.77	N/A	N/A	20		18	5/0/5
D176	FGD1	del3bp, p.E676del	X:54476722-54476724	3.7	N/A	N/A	9	20082460	15	2/0/3
AU55	FTSJ1	G>C, p.A26P	X:48336511-48336511	3.58	probably_damaging	DAMAGING	15		26	2/2/5

L1005	HUWE1	G>A, p.R4013W[23]	X:53564617-53564617	2.04	probably_damaging	DAMAGING	14	18252223, 23871722	14	2/1/1
D205[a]	HUWE1	C>T, p.R2981H	X:53578381-53578381	5.64	probably_damaging	DAMAGING	17	18252223, 23871722	21	1/0/?
D211[a]	KDM5C	G>A, p.Q970*	X:53225941-53225941	1.97	N/A	N/A	20		45	1/0/?
D130[a]	KDM5C	A>G, donor	X:53228157-53228157	3.65	N/A	N/A	9		16	1/0/1
N186	KIAA2022	insA, p.S1200Yfs*5[24]	X:73960794-73960795	0.02	N/A	N/A	20		37	2/0/4
L96[a]	NLGN3	C>T, p.R162*	X:70368722-70368722	1.64	N/A	N/A	20		38	1/0/?
T144	OPHN1	del4bp, p.L503Qfs*16	X:67331711-67331714	2.69	N/A	N/A	20		40	2/0/2
AU49	OPHN1	C>A, p.E135*	X:67454412-67454412	1.82	N/A	N/A	20		42	1/2/3
AU72 [a]	PQBP1	C>T, p.R196*	X:48760017-48760017	1.12	N/A	N/A	20	20950397	20	1/0/1
N188	RAB39B	insA, p.H123Sfs*4	X:154490364-154490365	2.78	N/A	N/A	20		18	2/0/1
D299	SLC16A2	insGCTGC, p.G334Pfs*11[18]	X:73744608-73744609	1.86	N/A	N/A	20		28	1/0/1
P195	ZC4H2	G>A, p.R190W[21]	X:64137701-64137701	1.80	N/A	N/A	10		21	2/1/2

[a] Confirmed in proband, additional family members were unavailable for testing;

[b] also previously discovered by droplet-based multiplex PCR followed by NGS;[13; 14]

[c] also previously discovered by candidate gene approach;[11]

Supplementary Table 6. Likely Pathogenic Variants Identified in Established XLID Genes with Studies Continuing

Family	Gene	Mutation	Genomic Location (Hg19)	Phylo P	PolyPhen2	SIFT	PS-Score	C-Score	Total Number of Affected Males / Informative Unaffected Males Tested for Segregation / Obligate Carrier Females
L48	ATRX	C>A, p.D1566Y	X:76891409-76891409	5.44	probably_damaging	DAMAGING	17	17	3/0/2
N83	IQSEC2	T>C, p.K807E	X:53268458-53268458	4.58	probably_damaging	DAMAGING	16	27	1/0/?
T149	NHS	C>T, p.R484W	X:17743739-17743739	1.84	probably_damaging	DAMAGING	13	15	2/0/1
AU14	OPHN1	C>G, p.G529R	X:67316813-67316813	4.63	probably_damaging	DAMAGING	16	24	4/0/3
Follow-up Study									
AU54	ATRX	del3bp, p.K956del	X:76937880-76937882	0.54	N/A	N/A	7	9	2/3/2
AU90	OPHN1	C>T, acceptor	X:67316872-67316872	4.63	N/A	N/A	10	16	1/0/1

Supplementary Table7. Clinical Information for Families with *CLCN4* Mutation

	T8 / MRX15	L19 / MRX49	N70	AU27	AU4
Affected individuals (n/sex)	3/M	5/M	2/M For index patient	4/M	7/M, 1/F
Hypotonia in infancy	Present (3/3)	Not known (5/5)	Not known (1/1)	Present (1/4) Not known 3/4	Not known 8/8
Intellectual disability	Present (3/3)	Present (5/5)	Present (1/1)	Present (4/4)	Present (8/8)
Borderline	-	1 (IQ 74)	-	-	-
Mild	-	3 (IQ 61,61,60)	-	1	4
Moderate	-	1 (IQ 37)	1	2	2
Severe	1	-	-	-	2
Profound	2	-	-	-	-
Not known	-	-	-	1	-
Epilepsy	0/3	0/5	1/1	1/4	8/8
Behavioural abnormalities	3/3	None reported	1/1 (anxiety)	1/4 (unspecified)	0/7 Males, affected female – trichotillomania
Psychiatric illness	0/3	0/5	0/1	1/4 (Bipolar disorder)	0/8
Head circumference centile	90th-95th (3/3)	97th (3/5) 50th, 75th-97th (2/5)	Not known	50th (1/4) Not known (3/4)	Normal (8/8)
Dysmorphic features	Absent	Absent	Absent	Absent	Present (4/4 assessed) Coarse facial features, broad nasal tip, flat midface, prominent ears
Brain MRI scan	Cortical atrophy (1/2 studied)	Not performed	Not performed	No abnormality (1 studied)	Not performed
Other	Scoliosis (3/3) Strabismus (2/3)	-	-	-	Progressive spasticity (2/8)
Obligate heterozygotes (n)	2	2	0	4	6
Intellectual disability	0/2	Vocational training (1/2) Mild ID (1/2)	Not applicable	0/4	0/6
Psychiatric illness	0/2	0/2	Not applicable	0/4	1/6 Psychotic episode

Supplementary Table 8. Summary of Clinical Information for Families per Gene

Gene	**Clinical Synopsis**			**Presence in Affected Males / All Affected Males with Clinical Features Available**
ACSL4	Neurologic	Central Nervous System	Mild to moderate intellectual disability	7/7
	Miscellaneous		Hypotonia, tremor, pectus excavatum, psychiatric co-morbidities - anxiety, pyschosis & schizophrenia, internalising behavioral problems together with severe social problems, thought problems and attention deficit, autisitic like features, borderline ID in female carriers	
AP1S2	Head and Neck	Face	Coarse facial features	2/5
			Long face	2/5
			Prominent forehead	0/5
			Prominent jaw	2/5
		Eyes	Deep-set eyes	0/5
		Nose	Large nose	2/5
		Mouth	Large mouth	2/5
			Full lips	2/5
	Skeletal	-	Joint contractures	0/4
		Spine	Scoliosis	0/4
	Muscle, Soft Tissue	-	Hypotonia	3/5
	Neurologic	Central Nervous System	Delayed psychomotor development	5/5
			Mental retardation, severe	5/5
			Seizures	3/4
			Choreoathetosis	0/3
			Spasticity	3/4
			Ataxic gait	3/3
			Hydrocephalus (in some patients)	0/2
			Enlarged ventricles (in some patients)	NK
			Dandy-Walker malformation (in some patients)	NK
			Iron deposition in the basal ganglia (in some pa-	NK

			tients)	
			Intracranial calcifications (in some patients)	NK
			Axonal dystrophy (in some patients)	NK
		Peripheral Nervous System	Hyperreflexia	1/4
		Behavioral Psychiatric Manifestations	Self-injurious behavior	2/5
	Miscellaneous	-	Onset in infancy	2/2
			Additional features are variably present	2/2
ATRX	Growth	Height	Short stature	3/7
		Weight	Obesity, mild (rare)	0/7
		Other	Growth retardation	2/4
	Head and Neck	Head	Microcephaly	6/7
			Dolichocephaly	0/4
		Face	Midface hypoplasia	4/7
			Bitemporal narrowing	0/7
			Small philtrum	3/7
			Micrognathia	2/7
			Coarse facial features	4/7
		Ears	Low-set ears	3/7
			Small ears	2/7
			Everted ears	0/7
			Posteriorly rotated ears	3/7
			Hyperfolded ears	0/7
			Sensorineural hearing impairment (less common)	0/4
		Eyes	Epicanthal folds	4/7
			Hypertelorism	0/7
			Upslanting palpebral fissures	1/7
			Exotropia (less common)	1/7
			Ptosis	0/7
			Optic atrophy	0/5
		Nose	Flat, broad nasal bridge	3/7
			Depressed nasal bridge	5/7
			Triangular nasal tip	2/5
			Anteverted nostrils	5/7
		Mouth	'Carp-like' mouth	0/7
			Open mouth	4/7
			Macrostomia	1/7

			Short, thin upper lip	5/7
			Inverted V-shaped upper lip	3/7
			Prominent lower lip	4/7
			High-arched palate	0/4
			Protruding tongue	0/7
			Drooling	2/7
		Teeth	Widely-spaced upper incisors	1/7
		Neck	Short neck (less common	0/7
	Abdomen	Gastrointestinal	Gastroesophageal reflux	2/7
			Vomiting	0/7
			Constipation	1/7
			Gut dysmotility	0/5
	Genitourinary	External Genitalia (Male)	Hypogonadism	0/7
			Small testes	0/7
			Hypoplastic scrotum	0/7
			Micropenis	0/7
			Hypospadias	0/7
		Internal Genitalia (Male)	Cryptorchidism	0/7
		Kidneys	Renal hypoplasia (less common)	0/2
		Bladder	Vesicoureteral reflux (less common)	0/4
	Skeletal	-	Delayed bone age	0/2
		Spine	Kyphoscoliosis (approximately 30%)	0/4
		Limbs	Genua valga	0/7
		Hands	Slender, tapering fingers	2/4
			Brachydactyly	1/7
			Clinodactyly of isolated digits	2/7
		Feet	Talipes equinovarus	1/7
			Talipes calcaneovalgus	0/7
			Pes planus	0/7
	Neurologic	Central Nervous System	Mental retardation, severe, profound	3 mild, 4 severe, profound
			Hypotonia, early	2/7
			Hypertonia of lower limbs, later	1/7
			Hyperreflexia	1/7
			Seizures (in 35%)	1/7

		Behavioral Psychiatric Manifestations	Paroxysmal bursts of laughter	0/7
			Repetitive, self-stimulatory behavior using upper limbs	0/7
			Fingers in mouth	0/7
			Hyperactivity	1/7
			Self-absorbed	0/7
	Hematology	-	Absence of Hb H inclusions in red blood cells	0/4
	Miscellaneous	-	Variable phenotype	Stiff fingers, braxism
CUL4B	Growth	Height	Short stature (5th percentile)	10/14
		Weight	Central obesity	6/15
			Birthweight (<10th percentile)	3/9
	Head and Neck	Head	Macrocephaly, relative	1/11
		Mouth	Prominent lower lip	11/14
			Macroglossia	0/13
	Chest	Breasts	Gynecomastia	2/13
	Genitourinary	External Genitalia (Male)	Hypospadias	0/12
			Small penis	0/12
		Internal Genitalia (Male)	Cryptorchidism	1/12
			Small testes	7/11
	Skeletal	-	Joint laxity	1/11
		Spine	Kyphosis	3/12
		Hands	Brachydactyly (in 1 family)	9/12
		Feet	Small feet	9/13
			Pes cavus	1/12
			Pes planus	1/12
			Wide sandal gap	1/12
	Skin, Nails, Hair	Skin	Striae	0/11
	Muscle, Soft Tissue	-	Wasted lower leg muscles	4/11
	Neurologic	Central Nervous System	Mental retardation	14/14
			Speech delay, severe	9/13

			Lack of speech development	2/13
			Tremor	5/13
			Decreased fine motor coordination	3/10
			Seizures (onset <2 years)	3/13
			Abnormal gait	5/12
			Ataxic gait	3/10
		Behavioral Psychiatric Manifestations	Aggressive outbursts	8/11
			Hyperactivity	1/12
			Mood swings	0/12
			Decreased attention span	2/12
	Voice	-	Impaired/absent speech	2/12
	Endocrine Features	-	Delayed puberty	1/11
			Hypogonadism	7/11
DLG3	Head and Neck	Eyes	Strabismus	4/13
			Upslanting palpebral fissures	3/13
		Mouth	High-arched palate	3/13
		Teeth	Molar hypoplasia	3/13
	Chest	External Features	Narrow thorax	3/13
	Genitourinary	Bladder	Enuresis	4/12
	Muscle, Soft Tissue	-	Hypotonia	5/8
	Neurologic	Central Nervous System	Delayed psychomotor development	12/12
			Mental retardation, mild to severe	13/13
			Delayed speech development	10/10
			Seizures	3/13
		Behavioral Psychiatric Manifestations	Behavioral problems	3/13
			Attention-deficit hyperactivity disorder	3/11
FTSJ1	**Nonspecific XLID**		Mild to moderate intellectual disability	4/4
GDI1	**Nonspecific XLID**		Moderate intellectual disability	11/11
GRIA3	Growth	Height	Short stature	0/2
		Other	Asthenic body habitus	NK

	Head and Neck	Head	Brachycephaly	0/1
			Macrocephaly	0/2
		Face	Dysmorphic features	2/2
		Eyes	Prominent supraorbital ridges	NK
			Deep-set eyes	1/1
	Muscle, Soft Tissue	-	Poor muscle bulk	NK
	Neurologic	Central Nervous System	Mental retardation, severe	3/3
			Seizures	0/1
			Myoclonic jerks	0/1
		Peripheral Nervous System	Hyporeflexia	0/2
		Behavioral Psychiatric Manifestations	Autistic features	1/1
			Aggression	0/1
			Self-injury	0/1
	Miscellaneous	-	Variable features	1/1
HUWE1	Head and Neck	Head	Macrocephaly	0/8
	Neurologic	Central Nervous System	Mental retardation	6/8 severe, 2/8 moderate
			Variable contractures	0/8
	Miscellaneous	-	Variable features	(2/4) facial dysmorphia : upslanting palpebral fissures, microstomia, long philtrum, Short stature (1/4), Short fingers (2/4)
KDM5C	Growth	Height	Short stature (less than 3rd percentile)	2/5
	Head and Neck	Head	Microcephaly	1/5
			Macrocephaly	0/5
		Face	Small forehead	0/5

			Prognathism	2/5
			Micrognathia	1/5
			Maxillary hypoplasia	0/5
			Facial hypotonia	0/2
			Flat philtrum	0/2
		Ears	Large ears	3/5
			Raised earlobes	0/2
		Eyes	Small eyelashes	0/2
			Small, deep-set eyes	0/2
			Upslanting palpebral fissures	3/5
			Strabismus	0/2
			Hypermetropia	0/2
			Myopia	0/2
		Mouth	Thin upper lip	0/2
			High narrow palate	0/2
			Scrotal tongue	0/2
		Teeth	Diastema	0/2
	Chest	External Features	Pectus excavatum	0/2
	Genitourinary	External Genitalia (Male)	Small penis	0/5
			Small testes	0/5
		Internal Genitalia (Male)	Cryptorchidism	0/5
	Skeletal	Hands	Short distal phalanges	0/5
			Thick distal phalanges	0/5
			Brachydactyly	0/5
			Large hands	0/5
		Feet	Small feet	0/5
			Talipes calcaneus	0/5
			Club feet	0/5
	Skin, Nails, Hair	Hair	Small eyelashes	0/2
			Abundant body hair	0/5
			Alopecia areata	0/5
	Muscle, Soft Tissue	-	Lower limb muscle hypotrophy	0/2
	Neurologic	Central Ner-	Mental retardation, severe	5/5

		vous System	Seizures	1/5
			Spastic paraplegia, slowly progressive	3/5
			Lower limb hypertonia	0/5
			Lower limb hyperreflexia	0/2
			Pyramidal syndrome of the lower limbs	0/2
			Extensor plantar responses	0/2
			Shuffling gait	0/2
		Behavioral Psychiatric Manifestations	Aggressive behavior	2/5
			Low frustration tolerance	0/2
			Restlessness	0/2
			Indolence	0/2
			Outbursts	0/2
			Autistic features (reported in 1 patient)	0/2
MED12	**Lujan-Fryns sndrome**			
	Growth	Height	Short stature	2/11
		Other	Marfanoid habitus	0/11
	Head and Neck	Head	Macrocephaly	0/11
		Face	Prominent forehead	10/11
			Long face	10/11
			Narrow face	10/11
			Flat malar area	11/11
			Retrognathia	3/11
			Short philtrum	8/11
			Deep philtrum	NK
		Ears	Large ears	5/11
			Abnormally folded helix	ND
		Nose	Long nose	NK
			High nasal bridge	9/11
			Narrow nasal bridge	NK
		Mouth	High-arched palate	1/11
			Thin upper lip	NK
			Open mouth	1/11
		Teeth	Double row of teeth	NK
			Crowded teeth	NK
	Cardiovascular	Heart	Atrial septal defect	NK
			Ventricular septal defect	NK
		Vascular	Ascending aortic aneurysm	NK

	Chest	External Features	Pectus excavatum	NK
	Genitourinary	Internal Genitalia (Male)	Borderline to large testes	NK
	Skeletal	-	Joint laxity	NK
			Joint contractures	NK
		Skull	Small mandible	NK
		Hands	Long fingers	NK
			Thin fingers	NK
			Broad thumbs	NK
	Neurologic	Central Nervous System	Mental retardation, severe to profound	11/11
			Hypotonia, generalized	NK
			Seizures	4/11
			Agenesis of the corpus callosum	NK
		Behavioral Psychiatric Manifestations	Aggressive behavior	2/11
			Autistic-like behavior	2/11
			Poor social interactions	1/11
			Hyperactivity	5/11
			Repetitive behavior	5/11
			Friendly personality	7/11
			Shyness	3/11
			Low frustration tolerance	NK
			Psychosis	1/11
	Voice	-	Hypernasal voice	NK
	Miscellaneous	Eyes	Strabismus	5/10
		Gastrointestinal	Constipation	1/11
		Central Nervous System	Cognitive impairment in female carriers	8/10
MED12	**Opitz-Kaveggia syndrome**			
	Growth	Height	Short stature	0/2
	Head and Neck	Head	Macrocephaly	0/2
			Large anterior fontanel	0/2
			Plagiocephaly	0/2
		Face	Prominent forehead	1/2
			Frontal hair upsweep	0/2

			Micrognathia	1/2
			Long philtrum	1/2
		Ears	Small ears	2/2
			Sensorineural hearing loss	0/2
		Eyes	Strabismus	0/2
			Hypertelorism	0/2
			Epicanthal folds	0/2
			Downward slanting palpebral fissures	0/2
			Medial eyebrow flare	0/2
		Nose	Prominent nose	0/2
		Mouth	Prominent lower lip	2/2
			Narrow palate	0/2
			Cleft lip	0/2
			Cleft palate	0/2
			Large mouth	0/2
		Teeth	Dental crowding	0/2
		Neck	Short neck	0/2
	Respiratory	Nasopharynx	Choanal atresia	0/2
	Abdomen	External Features	Umbilical hernia	0/2
		Gastrointestinal	Anal stenosis	0/2
			Imperforate anus	0/2
			Anteriorly placed anus	0/2
			Constipation	0/2
			Pyloric stenosis	0/2
			Malrotation	0/2
	Genitourinary	External Genitalia (Male)	Hypospadias	0/2
		Internal Genitalia (Male)	Cryptorchidism	0/2
			Inguinal hernia	0/2
	Skeletal	Skull	Delayed closure of anterior fontanel	0/2
		Spine	Lumbar hyperlordosis	0/2
		Limbs	Joint hyperlaxity (infancy)	0/2
			Joint contractures	0/2
		Hands	Broad thumbs	0/2
			Clinodactyly	0/2
			Camptodactyly	0/2

			Syndactyly	0/2
			Single transverse palmar crease	0/2
			Persistent fetal fingertip pads	0/2
		Feet	Broad halluces [EoM image]	0/2
	Skin, Nails, Hair	Skin	Facial wrinkling	0/2
			Sacral dimple	0/2
			Perianal skin tags	0/2
			Single transverse palmar crease	0/2
			Persistent fetal fingertip pads	0/2
		Hair	Frontal hair upsweep	0/2
			Fine hair	2/2
			Sparse hair	0/2
	Neurologic	Central Nervous System	Global developmental delay	2/2
			Mental retardation	2/2
			Neonatal hypotonia	0/2
			Seizures	1/2
			Hydrocephalus	0/2
			Agenesis of corpus callosum	1/2
			Heterotopia	0/2
		Behavioral Psychiatric Manifestations	Repetitive behavior	0/2
			Hyperactivity	0/2
			Friendly personality	0/2
	Voice	-	High-pitched voice	0/2
OPHN1	Head and Neck	Head	Macrocephaly	0/8
		Face	Prominent forehead	0/19
			Prominent supraorbital ridges	0/19
			Long face	0/19
			Short philtrum	1/19
			Upturned philtrum	2/19
			Marked infraorbital creases	0/19
			Prominent chin	1/19
		Ears	Large ears	2/19
		Eyes	Hypotelorism	1/19
			Deep-set eyes	0/19
			Strabismus	2/19
			Nystagmus	0/19
		Nose	Long, tubular nose	1/19

		Mouth	Thin upper lip	1/19
	Genitourinary	External Genitalia (Male)	Hypoplastic scrotum	0/19
			Microphallus	0/19
		Internal Genitalia (Male)	Cryptorchidism	0/19
	Neurologic	Central Nervous System	Psychomotor delay	3/19
			Mental retardation, moderate to severe (IQ 40 to 60)	19/19
			Mental retardation, mild, in most carrier females	1/1
			Hypotonia	1/17
			Speech delay	14/19
			Seizures	1/19
			Ataxic gait	1/19
			Spasticity	0/19
			Cerebellar signs	1/19
			Cerebellar hypoplasia	1/19
			Disorganization of the anterior cerebellar vermis	1/19
			Enlarged ventricles	1/18
			Enlarged cisterna magna	0/19
			Retrocerebellar cyst	0/19
			Decreased cerebral volume, especially of the frontal lobes	0/19
		Behavioral Psychiatric Manifestations	Hyperactivity	0/19
			Autistic features	2/17
	Miscellaneous	-	Contractures of elbows, knees and fingers	2
			Onset in infancy	
			Most carrier females have mild mental retardation and subtle facial changes	0/2
PQBP1	Growth	Height	Short stature	1/6
		Other	Lean body build	6/6
	Head and Neck	Head	Microcephaly	1/6
			Brachycephaly	1/6
		Face	Long, narrow face (post adolescence)	4/5
			Triangular face	1/6
			Malar hypoplasia	1/6

			Micrognathia	1/6
			Short philtrum (rare)	0/6
			Prognathism	0/6
		Ears	Protruding ears	6/6
			Cupped ears	0/6
			Large ears	5/6
			Dysplastic ears	0/6
			Hearing loss (rare)	0/6
		Eyes	Upslanting palpebral fissures	0/6
			Epicanthus	1/6
			Cataract	0/1
			Ocular colobomas (rare)	0/5
			Blindness (rare)	0/6
			Microphthalmia (rare)	0/6
			Coloboma, choroid (rare)	0/1
			Sparse lateral eyebrows	0/6
			Long, curved eyelashes	1/6
			Hypermetropia	3/4
			Strabismus	0/6
		Nose	Large, ridged nose	0/6
			Bulbous nose	1/6
			Broad nasal bridge	1/5
			Overhanging columella	0/6
		Mouth	Cleft palate	0/6
			High-arched palate	0/6
			Thin upper lip	1/6
			Small mouth (rare)	0/6
	Cardiovascular	Heart	Congenital heart defects	0/1
			Tetralogy of Fallot	0/6
			Atrial septal defect	0/6
			Ventricular septal defect	0/6
			Situs inversus (rare)	0/6
	Respiratory	Nasopharynx	Velar dysfunction	0/6
	Chest	External Features	Pectus excavatum (rare)	0/6
	Abdomen	Gastrointestinal	Poor feeding and sucking in infancy	1/6
			Anal atresia (rare)	0/6

	Genitourinary	External Genitalia (Male)	Small testes	0/4
			Phimosis	0/6
			Hypospadias (rare)	0/6
		Kidneys	Renal hypoplasia (rare)	0/1
			Renal malposition (rare)	0/1
	Skeletal	Spine	Scoliosis	0/6
			Terminal spine defects	0/1
		Hands	Clinodactyly of fifth digit (rare)	0/6
			Camptodactyly	0/6
			Ankylosis of the thumb metacarpophalangeal joint	NK
		Feet	Pes cavus	0/6
			Slender feet	0/6
	Skin, Nails, Hair	Hair	Central balding	0/6
			Sparse hair	1/6
	Muscle, Soft Tissue	-	Muscle atrophy affecting the upper back and neck muscles	1/6
	Neurologic	Central Nervous System	Mental retardation	6/6
			Hyperreflexia	0/6
			Spasticity	0/6
			Brain atrophy	0/6
			Seizures (rare)	0/6
		Behavioral Psychiatric Manifestations	Autistic features	0/6
			Anxiety	0/2
	Voice	-	Nasal voice	High pitched voice in 1
	Miscellaneous	-	Clinical variability	
			Features in typical patient include mental retardation, microcephaly, short stature, and lean body build	1/6
			Skewed X-inactivation in carriers	NK
RPS6KA3	Growth	Height	Normal birth length	1/1
			Short stature	4/4
		Weight	Normal birth weight	4/4
			Weight less than 3rd percentile	0/4

	Head and Neck	Head	Microcephaly	1 with hydrocephalus
		Face	Coarse facies	3/4
			Prominent brow	3/4
			Prominent chin	0/4
		Ears	Prominent ears	3/4
			Sensorineural hearing loss	3/4
		Eyes	Downslanting palpebral fissures	3/4
			Hypertelorism	4/4
			Heavy eyebrows	3/4
			Arched eyebrows	3/4
		Nose	Broad nose	3/4
			Thick alae nasi	3/4
			Anteverted nares	3/4
			Thick nasal septum	3/4
		Mouth	Large, open mouth	3/4
			Thick, everted lower lip	3/4
			Narrow palate	0/4
			High palate	1/4
		Teeth	Hypodontia	0/1
			Malocclusion	0/4
			Wide-spaced teeth	3/3
			Large medial incisors	0/4
	Cardiovascular	Heart	Mitral insufficiency	0/4
	Chest	External Features	Pectus excavatum	1/4
			Pectus carinatum	0/4
		Ribs, Sternum, Clavicles and Scapulae	Short bifid sternum	0/4
	Abdomen	Gastrointestinal	Rectal prolapse	0/4
	Genitourinary	External Genitalia (Male)	Inguinal hernia	0/4
		Internal Genitalia (Female)	Uterine prolapse	0/4
	Skeletal	-	Delayed bone age	0/1
		Skull	Thick calvarium	0/1

			Hypoplastic sinuses	0/1
			Hypoplastic mastoids	0/1
			Delayed closure of anterior fontanel	0/1
		Spine	Scoliosis	1/4 mild
			Kyphosis	0/4
			Lumbar gibbus deformity	0/4
		Pelvis	Coxa valga	0/1
			Narrow iliac wings	0/1
		Limbs	Forearm fullness	0/1
			Extensible joints	0/1
		Hands	Large, soft hands	3/4
			Tapering fingers	4/4
			Transverse palmar creases	0/4
			Hyperextensible fingers	0/4
			Short metacarpals	1/4
			'Drumstick' terminal phalanges	0/4
		Feet	Flat feet	1/4
	Skin, Nails, Hair	Skin	Loose skin	0/4
			Cutis marmorata	0/4
			Dependent acrocyanosis	0/4
			Transverse palmar creases	0/4
		Nails	Small fingernails	0/4
			Hyperconvex fingernails	0/4
		Hair	Straight, coarse hair	0/4
	Neurologic	Central Nervous System	Mental retardation	4/4
			Hypotonia	4/4
			Seizures	0/4
			Ventricular dilatation	1/4
	Miscellaneous	-	Myopia gravior both eyes, retinal pigment changes of the maculae	2/2
SLC16A2	Head and Neck	Head	Microcephaly	1/2
		Face	Elongated face	1/2
			Bitemporal narrowing	0/2
		Ears	Large ears	0/2
			'Simple' ears	1/2
			Pinna modeling anomalies	0/1
			Prominent antihelix	0/1

			Flattened antihelix	0/1
		Eyes	Nystagmus, rotary (in some patients)	0/2
			Disconjugate eye movements	0/2
	Chest	External Features	Pectus excavatum, broad, shallow	1/1
	Abdomen	Gastrointestinal	Poor feeding	1/2
	Skeletal	-	Joint contractures (small and large joints affected)	1/1
		Spine	Scoliosis	2/2
		Feet	Flat feet	0/1
			Lateral deviation of great toe	0/1
	Neurologic	Central Nervous System	Neonatal hypotonia	1/1
			Hypotonia, proximal, severe	1/1
			Inability to hold neck up ('limber neck') onset at 6 months	0/1
			Neck drop	0/1
			Delayed psychomotor development, severe	4/4
			Spastic paraplegia	3/3
			Spastic quadriplegia	1/3
			Ataxia	0/3
			Inability to walk	2/4
			Inability to stand	3/4
			Dystonic posturing of the hands	2/4
			Involuntary writhing movements	0/1
			Generalized muscle atrophy	2/2
			Dysarthria	3/4
			Drooling	2/4
			Mental retardation, severe	4/4
			Inability to communicate	2/4
			No gaze contact	0/1
			Lack of communication	1/1
			Clonus	0/1
			Hyperreflexia	3/3
			Extensor plantar responses	2/3
			Delayed myelination	0/1
			Leukodystrophy and white matter changes, which improve with age	0/1
		Behavioral Psy-	Irritability	0/1

		chiatric Manifestations		
	Laboratory Abnormalities	-	Decreased serum thyroxine (T4)	1/2
			Decreased serum free thyroxine	1/1
			Normal or mildly increased thyroid-stimulating hormone (TSH)	1/2
			Increased serum triiodothyronine (T3)	1/1
			Decreased serum rT3	0/1
	Miscellaneous	-	Onset at birth	1/1
			Heterozygous females have milder thyroid phenotype and no neurologic abnormalities	YES
			No peripheral signs of hypothyroidism	NK
SLC6A8	Growth	Height	Short stature	1/4
			Tall stature	0/4
		Weight	Low weight	0/4
		Other	Failure to thrive	0/4
	Head and Neck	Head	Decreased head circumference	0/4
			Microcephaly	1/4
		Face	Broad forehead	0/4
			Midface hypoplasia	0/4
			Long, thin face	0/4
			Prominent chin	0/4
			Myopathic facies	0/4
		Ears	Unfolded superior helices	0/4
		Eyes	Exotropia	0/4
			Hypermetropia	0/4
			Ptosis	0/4
	Abdomen	Gastrointestinal	Constipation	0/4
			Megacolon	0/4
			Ileus	0/4
			Poor feeding	0/4
			Vomiting	0/4
	Skeletal	Limbs	Hyperextensible joints	0/4
		Hands	Stub thumb	1/4 Short fingers
		Feet	Pes cavus (less common)	0/4

	Neurologic	Central Nervous System	Hypotonia, neonatal	0/4
			Developmental delay	4/4
			Motor delay	3/3
			Mental retardation	5/5
			Hypotonia	0/3
			Speech and language delay, severe	4/5
			Poor hand-eye coordination	0/3
			Spasticity	0/3
			Gait abnormalities	0/3
			Dystonia	0/3
			Seizures	1/3
			Decreased creatine signal seen on magnetic resonance spectroscopy	3/3
			Mild structural abnormalities seen MRI (in some patients)	0/1
			Delayed myelination	0/1
			Thin corpus callosum	0/1
		Behavioral Psychiatric Manifestations	Behavioral changes consistent with an autistic disorder	0/3
			Stereotypical motor behaviors	0/3
			Impaired social interaction	0/3
			Aggressive behavior	1/3
			Attention deficit hyperactivity disorder	0/3
	Laboratory Abnormalities	-	Impaired creatine uptake in fibroblasts	1/1
			Increased urinary creatine	1/1
			Increased plasma creatine	1/1
			Increased urinary creatine-to-creatinine ratio	1/1
	Miscellaneous	-	Onset in first months of life	1/1
			Carrier females may show neuropsychologic impairment	NK
UBE2A	Growth	Weight	Increased weight	1/5
	Head and Neck	Head	Large head	1/5
		Face	Midface hypoplasia	3/5
			Wide face	2/5
			Prominent supraorbital ridges	5/5
		Eyes	Synophrys	2/5
			Upslanting palpebral fissures	0/5

			Deep-set eyes	5/5
			Almond-shaped eyes	2/5
		Nose	Low nasal bridge	0/5
		Mouth	Large mouth	3/5
			Downturned corners of the mouth	0/5
			Thin lips	2/5
		Neck	Short, broad neck	2/5
	Chest	Breasts	Widely spaced nipples	2/4
	Genitourinary	External Genitalia (Male)	Small penis	1/2
	Skeletal	Feet	Flat feet	1/3
			Small feet	1/3
			Broad first toe	1/3
	Skin, Nails, Hair	Skin	Dry skin	2/5
			Hypopigmented spots (less common)	0/5
		Nails	Onychodystrophy	0/5
		Hair	Hirsutism, generalized	2/5
			Low posterior hairline	2/5
			Synophrys	2/5
			Hair whorls	1/2
	Muscle, Soft Tissue	-	Myxedematous appearance	0/5
	Neurologic	Central Nervous System	Intellectual disability	5/5
			Seizures	0/5
			Lack of speech or poor speech	5/5
			White matter hypodensities on brain imaging	0/1
		Behavioral Psychiatric Manifestations	Echolalia	1/4
			Aggression	3/5
ZC4H2	Growth	Height	Short stature	2/8
	Head and Neck	Face	Facial weakness	1/8
			Micrognathia	0/8
			Retrognathia	0/8
			Flat philtrum	1/8
			Long philtrum	0/8

		Ears	Low-set ears	0/8
		Eyes	Upslanting palpebral fissures	0/8
			Ptosis	7/8
			Oculomotor apraxia (in some patients)	6/8
		Nose	Upturned nares	0/8
		Mouth	Carp-shaped mouth	3/8
			High-arched palate	2/8
			Drooling	1/8
			Broad alveolar ridges	2/8
		Neck	Short neck	1/8
	Respiratory	-	Neonatal respiratory distress	0/8
			Apnea	0/8
	Chest	External Features	Narrow thorax	2/8
			Narrow shoulders	2/8
	Abdomen	Gastrointestinal	Poor feeding	1/8
	Skeletal	-	Arthrogryposis, congenital	6/8
			Joint contractures	6/8
		Spine	Kyphosis	1/8
			Scoliosis	1/8
			Lordosis	1/8
		Pelvis	Hip dislocation	0/8
		Hands	Proximally placed thumbs	0/8
			Camptodactyly	0/8
			Ulnar deviation of the fingers	0/8
		Feet	Proximally placed toes	0/8
			Club feet	6/8
			Equinovarus	6/8
	Skin, Nails, Hair	Hair	High anterior hairline	0/8
	Muscle, Soft Tissue	-	Muscle weakness, severe	8/8
			Fat pads on the hands and feet	0/8
	Neurologic	Central Nervous System	Delayed psychomotor development	8/8
			Hypotonia	2/8
			Mental retardation	8/8
			Speech delay / Absent speech	8/8
			Dystonia	0/8

			Spasticity	1/8
			Seizures	2/8
			Delayed myelination	0/8
			Gyral disorganization	0/8
			Cerebral atrophy	1/8
		Peripheral Nervous System	Areflexia	
ZDHHC9	Growth	Height	Marfanoid	0/7
	Head and Neck	Face	Relatively long	5/7
			Flat midface	5/7
			Thin lips	5/7
			Small mouth	5/7
		Eyes	Short palpebral fissures	5/7
		Nose	High nasal bridge	5/7
	Neurologic	Central Nervous System	Delayed psychomotor development	2/7
			Poor or no speech	2/7
			Seizures	1/7
			Sleep disturbance in early infancy	1/7
			Mental retardation (learning difficulties/ borderline abilities to severe)	7/7
		Behavioral Psychiatric Manifestations	Anxiety	2/7
			Aggression	1/7
			Depression	1/7
		Skeletal	Joint contractures	2/7
	Miscellaneous	-	Other variable clinical features	5/5

NK = Not Known

Supplementary Table 9. Accuracy of Exon Target Sequencing Assessed by Genotyping SNPs With The Affymetrix Genome-Wide Human SNP Array

Patient	1	2	3	4	5
Genotype accuracy	99.5% (1142/1148)	99.4% (973/979)	99.2% (1038/1046)	99.5% (1030/1035)	98.9% (930/940)
Variant accuracy	98.5% (303/308)	99.6% (230/236)	97.5 (276/283)	97.9 (235/240)	95.8% (230/240)
False positive rate	0.1% (1/840)	0% (0/743)	0.1% (1/763)	0% (0/795)	0% (0/700)

Five samples were genotyped on the Affymetrix Genome-Wide Human SNP Array 6.0 (Atlas, Berlin, Germany). We compared the genotype calls of approximately 1000 SNPs located in the sequenced intervals with those observed from NGS sequencing. The SNP-array observations used for the comparison were those that are reliable (reported confidence *P-value* less than 0.01) and well covered (3 reads at least) by NGS. Referring to the array as gold standard, the genotype accuracy is defined as: (Number of genotypes matching exactly between sequencing and array)/(number of compared positions). Here we compared the homozygous positions on the X chromosome reported in the SNP array. Because genotype accuracy tends to be dominated by the large number of homozygous reference calls, we also calculated the variant accuracy which is restricted to the variant positions called by the SNP array. Variant accuracy is defined as the proportion of positions called by sequencing as the same homozygous SNPs as in the array to the homozygous SNP calls in the array. A false-positive is defined when the resequencing calls a variant where the array calls a homozygous reference. The genotype accuracy and variant accuracy ranges between 98.9-99.5% and 95.8-99.6%, respectively.

Supplementary Table 10. The Cohort is Nearly Devoid of Common Gene Defects

Gene	**No. of mutations out of 115 found prior to NGS**	**No. of mutations out of 80 identified by NGS**
KDM5C	13	3
MECP2	10	1
IL1RAPL1	8	1
PQBP1	7	2
Total	**38**	**7**

Five commonly mutated XLID genes in the EUROMRX cohort and the number of mutations identified prior to NGS and in this study.

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