SUPPLEMENTARY METHODS

Copy number variations (CNVs) were called from exome data using the CoNIFER pipeline, described by Krumm and colleagues [5]. Exome reads were mapped to exons and 300 bp flanking sequence of the repeat-masked hg19 reference genome using mrsFAST. RPKM (mapped reads per kilobase per million reads) values were calculated for 194,075 exome capture targets and minimized systematic noise and bias by removing the first 30 SVD components. CNV calls were generated using the conifer-tools package, which implements DNACopy (REF Venkatraman 2007), with the following filtering criteria: CNVs of 3-5 probes average SVD-transformed signal >1; CNVs of 6 or greater probes, average signal > 0.5. CNVs more than 50% in repetitive or duplicated genomic space were removed. CNV calls were manually curated, and curated calls were compared to control CNV datasets to filter out common CNVs present in >1% of the general population. Control CNV datasets included (i) CNV calls from the Atherosclerosis Risk in Communities (ARIC) Study (n=11,305) analyzed using Affymetrix AFFY_6.0 SNP microarray and (ii) CNV calls from the NLHBI GO Exome Sequencing Project (ESP, n=2,972) from CoNIFER analysis of exome sequence data.

SNP array analysis: Copy number variants (CNVs) were called from the SNP microarray genotype data using the method described previously [2323]. Briefly, a Hidden Markov Model (HMM) integrating both B allele frequencies and intensity values (logR) was used to identify segments of individual chromosomes exhibiting a duplication or a deletion. All 311 samples were filtered by a maximal genome-wide logR standard deviation of 0.25. CNVs called by the HMM were then manually curated to remove known artifacts and large false positives (>100 probes and >1 Mb), followed by user-guided merging of calls within 1Mbp to correct for contiguous events broken up due to HMM overfragmentation. Samples with greater than 18 calls, 1 large false positive, or 1 artifact were removed from analysis following the merging step. After the final filtering, 483 calls remained from 161 samples. Quantitative PCR was performed for a subset of predicted CNVs that were <10 kb and for which available oligonucleotide and SNP array data had too few probes (<10) to reliably confirm the CNV.

SUPPLEMENTARY TABLE 1: Samples included in analysis

	Coriell ID			
Trio ID	**Proband**	**Father**	**Mother**	***Included in Ref X (Nat)?***
aa	ND27062	ND25915	ND25914	Y
ac	ND25793	ND26080	ND26079	Y
ad	ND26087	ND26085	ND26086	Y
af	ND24290	ND26361	ND24285	Y
ag	ND27949	ND26631	ND26629	Y
ah	ND26900	ND26899	ND26895	Y
ahc	EPGP015825	EPGP015827	EPGP015826	N
ahe	EPGP016251	EPGP016253	EPGP016252	N
ahf	ND36883	ND32228	ND32227	N
ahh	ND39531	ND40447	ND40448	N
ahi	ND40144	ND37824	ND37825	N
ahj	ND38557	ND39279	ND38556	N
ahk	ND37548	ND37646	ND37647	N
ahl	EPGP014670	ND39608	ND39416	N
ahm	ND37023	ND37022	ND37024	N
ahn	ND37134	ND37104	ND37100	N
aho	ND37815	ND37838	ND37734	N
ahp	ND37447	ND37449	ND37448	N
ahq	ND37431	ND37432	ND37433	N
ahr	ND37295	ND37243	ND37230	N
ahs	ND38114	ND38112	ND38113	N
aht	ND37900	ND38307	ND38308	N
ahu	ND37656	ND37853	ND37854	N
ahv	ND38771	ND37749	ND37748	N
ahw	ND38667	ND38697	ND38665	N
ahx	ND38644	ND39656	ND38264	N
ahy	ND37868	ND38255	ND38254	N
ahz	ND39665	ND37867	ND37866	N
ai	ND26970	ND26969	ND26971	Y
aia	ND38309	ND38085	ND38079	N
aib	ND39001	ND39000	ND38999	N
aic	ND38199	ND38194	ND38198	N
aid	ND38466	ND38464	ND38465	N
aie	ND38558	ND39337	ND38913	N
aif	ND38410	ND38411	ND38412	N
aig	ND38653	ND38654	ND38655	N
aih	ND38650	ND38651	ND38652	N
aii	ND38461	ND38462	ND38463	N
aij*	ND38912	ND38967	ND38966	N
aik	ND38835	ND38834	ND38837	N
ail	ND38947	ND38945	ND38946	N
aim	ND38768	ND38766	ND38767	N
ain	ND39695	ND39710	ND39693	N
aio	ND39662	ND39427	ND39426	N
aip	ND39284	ND39618	ND39617	N
aiq	ND39196	ND39456	ND39197	N
air	ND39395	ND39393	ND39394	N
ais	ND39474	ND39470	ND39473	N
ait	ND39708	ND39812	ND39709	N
aiu	ND39838	ND39834	ND39835	N
aiv	ND40021	ND40039	ND40038	N
aiw	ND37357	ND37963	ND37962	N
aix	ND37555	ND37553	ND37554	N
aiy	ND37816	ND37817	ND37882	N
aj	ND26974	ND26973	ND26972	Y
aja	ND37535	ND37424	ND37425	N
ajb	ND37855	ND37857	ND37856	N
ajc	ND38132	ND38131	ND38127	N
ajd	ND38656	ND38196	ND38197	N
aje	ND38344	ND38925	ND38346	N
ajf	ND38610	ND38588	ND38586	N
ajg	ND38706	ND38707	ND38708	N
ajh	ND39737	ND39736	ND39735	N
aji	ND37189	ND37188	ND37190	N
ajj	ND39606	ND39605	ND39604	N
ajk	ND37747	ND40236	ND37764	N
ajl	ND40148	ND40153	ND40154	N
ak	ND30086	ND27136	ND27135	Y
al	ND27253	ND27234	ND27233	Y
am	ND27474	ND27280	ND27281	Y
an	ND27732	ND27730	ND27731	Y
ao	ND29711	ND27972	ND27973	Y
ap	ND29304	ND27987	ND27986	N
aq	ND34430	ND28025	ND28024	Y
ar	ND27935	ND28028	ND28029	Y
as	ND30915	ND28222	ND28221	Y
at	ND28472	ND28470	ND28471	N
au	ND28478	ND28480	ND28479	Y
av	ND28661	ND28663	ND28660	Y
ax	ND28699	ND28701	ND28700	Y
ay	ND27841	ND28748	ND27840	Y
az	ND29844	ND28816	ND28815	Y
b	ND21451	ND21448	ND21012	Y
ba	ND31134	ND28820	ND28821	Y
bc	ND28982	ND28981	ND28983	Y
bcv	ND40745	ND38150	ND38149	N
bcw	ND40262	ND39396	ND39397	N
bcz	ND39270	ND39271	ND39269	N
bda	ND40292	ND40294	ND40295	N
bdb	ND40432	ND40300	ND40301	N
bde	ND40833	ND40830	ND40829	N
be	ND29057	ND29048	ND29046	Y
bf	ND29047	ND29056	ND29049	N
bg	ND29900	ND29093	ND29094	Y
bi	ND27521	ND29124	ND27520	Y
bj	ND29126	ND29128	ND29127	Y
bk	ND29199	ND29198	ND29197	Y
bl	ND29258	ND29255	ND29259	Y
bm	ND29267	ND29269	ND29268	Y
bn	ND33520	ND29320	ND33521	Y
bo	ND29319	ND29321	ND29322	Y
bp	ND33012	ND29324	ND33002	N
bq	ND29810	ND29348	ND29349	Y
br	ND29352	ND29353	ND29351	Y
bs	ND29366	ND29368	ND29367	Y
bt	ND29377	ND29375	ND29376	Y
bu	ND29378	ND29380	ND29379	Y
bv	ND29383	ND29382	ND29381	Y
bw	ND29514	ND29512	ND29513	Y
bx	ND28752	ND29782	ND29781	N
by	ND29866	ND29865	ND29867	Y
bz	ND29885	ND29882	ND29883	N
ca	ND29292	ND29888	ND29291	Y
cb	ND29975	ND29974	ND29973	N
cd	ND32722	ND30001	ND30000	Y
ce	ND32131	ND30050	ND29809	Y

	Coriell ID			
Trio ID	**Proband**	**Father**	**Mother**	***Included in Ref X (Nat)?***
cf	ND30071	ND30070	ND30069	Y
cg	ND30610	ND30127	ND30128	Y
ch	ND30474	ND30214	ND30213	Y
ci	ND30279	ND30274	ND30273	Y
cj	ND30280	ND30277	ND30276	Y
ck	ND30302	ND30304	ND30303	Y
cm	ND30377	ND30376	ND30375	Y
cn	ND30384	ND30382	ND30381	Y
co	ND29305	ND30418	ND29306	Y
cp	ND30431	ND30432	ND30433	Y
cq	ND31120	ND30435	ND30434	Y
cr	ND30441	ND30443	ND30442	Y
cs	ND30485	ND30486	ND30487	Y
ct	ND30552	ND30551	ND30565	Y
cu	ND30679	ND30673	ND30674	Y
cv	ND30439	ND30686	ND30440	Y
cx	ND30880	ND30856	ND30855	Y
cy	ND31770	ND30989	ND30993	Y
cz	ND30575	ND31078	ND30572	Y
d	ND24539	ND21692	ND21691	Y
da	ND31115	ND31114	ND31113	Y
db	ND31192	ND31191	ND31193	Y
dc	ND31228	ND31227	ND31226	Y
dd	ND31305	ND31301	ND31299	Y
de	ND31308	ND31306	ND31307	Y
df	ND31364	ND31366	ND31365	Y
dg	ND36211	ND31499	ND31474	Y
dh	ND31702	ND31605	ND31603	Y
di	ND31635	ND31637	ND31636	Y
dj	ND32121	ND31698	ND31699	Y
dk	ND30090	ND31772	ND30089	Y
dl	ND30831	ND31785	ND30832	Y
dm	ND30373	ND31818	ND31817	Y
dn	ND31821	ND31820	ND31819	Y
do	ND31831	ND31829	ND31830	Y
dq	ND31899	ND31909	ND31910	Y
dr	ND31241	ND31933	ND31240	Y
ds	ND31602	ND32000	ND31601	Y
dt	ND34170	ND32030	ND32028	Y
du	ND32641	ND32060	ND32061	Y
dv	ND32065	ND32063	ND32064	Y
dw	ND32132	ND32134	ND32133	Y
dy	ND30482	ND32385	ND30473	Y
dz	ND32398	ND32397	ND32396	Y
e	ND21751	ND21749	ND21750	Y
eb	ND32464	ND32618	ND32465	Y
ec	ND32241	ND32619	ND32240	Y
ed	ND33651	ND32640	ND32639	Y
ee	ND32757	ND32755	ND32756	Y
ef	ND32671	ND32843	ND32678	Y
eg	ND33197	ND33195	ND33196	Y
eh	ND33296	ND33298	ND33297	Y
ei	ND36496	ND33299	ND32621	N
ej	ND33342	ND33343	ND33341	Y
ek	ND35845	ND33454	ND33453	Y
el	ND33222	ND33461	ND33460	Y
ep	ND34128	ND33822	ND33820	Y
er	ND34077	ND33883	ND33891	Y
es	ND29429	ND33900	ND29428	Y
et	ND35575	ND33999	ND33998	Y
ev	ND34126	ND34125	ND34127	N
ew	ND34144	ND34143	ND34142	Y
ex	ND34274	ND34271	ND34272	Y
ey	ND34304	ND34320	ND34302	Y
ez	ND34338	ND34340	ND34339	Y
f	ND22993	ND22994	ND23034	Y
fa	ND34404	ND34402	ND34396	Y
fb	ND34548	ND34403	ND34399	Y
fc	ND34401	ND34407	ND34397	Y
fd	ND36066	ND34504	ND34505	Y
fe	ND34750	ND34753	ND34768	Y
ff	ND34116	ND34857	ND34441	Y
fg	ND34968	ND34946	ND34947	Y
fh	ND34962	ND34963	ND34969	Y
fi	ND35054	ND35052	ND35051	Y
fj	ND34680	ND35067	ND34679	Y
fl	ND35150	ND35148	ND35149	Y
fn	ND35197	ND35196	ND35198	Y
fo	ND35151	ND35222	ND35223	Y
fp	ND28895	ND35345	ND28973	Y
fr	ND35498	ND35496	ND35497	N
fs	ND35907	ND35908	ND35909	Y
fu	ND35951	ND36021	ND35980	Y
fv	ND36158	ND36156	ND36157	Y
fw	ND36206	ND36207	ND36208	Y
fx	ND36367	ND36368	ND36369	Y
fy	ND36387	ND36385	ND36386	Y
fz	ND35351	ND36497	ND35722	Y
g	ND23231	ND23233	ND23232	Y
ga	ND36561	ND36560	ND36563	Y
gb	ND30629	ND36648	ND30647	Y
gc	ND35929	ND36757	ND35930	Y
ge	ND36610	ND36789	ND36609	Y
gf	ND21693	ND21695	ND21694	N
gg	ND22752	ND22754	ND22753	Y
gh	ND29374	ND22981	ND22995	Y
gi	ND23319	ND23321	ND23320	Y
gj	ND24053	ND24055	ND24054	Y
gk	ND24070	ND24075	ND24069	Y
gl	ND23828	ND24283	ND23827	Y
gm	ND24447	ND24445	ND24446	Y
gn	ND24471	ND24472	ND25665	Y
go	ND24065	ND24563	ND24064	Y
gp	ND24646	ND24639	ND24641	Y
gq	ND24762	ND24764	ND24763	Y
gr	ND23543	ND25364	ND25363	Y
gs	ND25442	ND25441	ND25443	Y
gt	ND25544	ND25542	ND25543	Y
gu	ND24647	ND25597	ND24640	N
gv	ND23813	ND25797	ND25817	Y
gw	ND29554	ND25816	ND29555	Y
gx	ND28841	ND25937	ND26273	N
gy	ND26319	ND26320	ND26321	Y
gz	ND26363	ND26364	ND26362	N
h	ND23465	ND23489	ND23464	Y
ha	ND27753	ND26479	ND27754	Y

	Coriell ID			
Trio ID	**Proband**	**Father**	**Mother**	***Included in Ref X (Nat)?***
hc	ND25992	ND27008	ND27009	Y
hd	ND27109	ND27152	ND27153	Y
he	ND27155	ND27157	ND27156	Y
hf	ND28840	ND27269	ND27268	Y
hg	ND29877	ND27339	ND27340	N
hh	ND27345	ND27346	ND27344	Y
hi	ND27497	ND27500	ND27501	Y
hj	ND27594	ND27593	ND27597	Y
hk	ND27637	ND27638	ND27629	Y
hl	ND27682	ND27683	ND27154	Y
hm	ND28051	ND27711	ND27710	N
hn	ND27543	ND27974	ND27971	Y
hp	ND28181	ND28180	ND28192	Y
hq	ND28245	ND28254	ND28246	Y
hr	ND28509	ND28365	ND28364	Y
hs	ND28866	ND28398	ND28865	Y
ht	ND28633	ND28421	ND28422	Y
hu	ND28432	ND28424	ND28423	Y
hv	ND28881	ND28880	ND28879	Y
hw	ND28027	ND28922	ND28026	Y
hx	ND28949	ND28948	ND28950	Y
hy	ND28731	ND28971	ND28972	N
hz	ND29055	ND29053	ND29054	Y
ia	ND29058	ND29060	ND29059	Y
ic	ND29146	ND29147	ND29148	Y
id	ND31529	ND29323	ND31528	Y
ie	ND29394	ND29396	ND29395	Y
if	ND29446	ND29445	ND29447	Y
ig	ND29196	ND29460	ND29459	Y
ih	ND29528	ND29527	ND29529	Y
ii	ND29789	ND29788	ND29786	Y
ij	ND29838	ND29839	ND29837	Y
ik	ND29904	ND29903	ND29901	Y
il	ND29958	ND29957	ND29959	Y
im	ND28560	ND30006	ND28559	N
in	ND27952	ND30019	ND27953	Y
ip	ND28402	ND30130	ND28401	Y
iq	ND30133	ND30134	ND30132	Y
ir	ND30241	ND30242	ND30243	Y
is	ND30299	ND30297	ND30298	N
it	ND29864	ND30329	ND29863	Y
iu	ND33014	ND30333	ND30332	Y
iv	ND30383	ND30361	ND30362	Y
iw	ND30631	ND30374	ND30630	Y
ix	ND30378	ND30379	ND30380	Y
iy	ND30216	ND30558	ND30559	Y
iz	ND29125	ND30683	ND30682	Y
j	ND24005	ND24004	ND24003	Y
ja	ND30798	ND30799	ND30800	Y
jb	ND32224	ND30808	ND33927	Y
jc	ND36210	ND30809	ND30807	Y
jd	ND31159	ND30811	ND30810	Y
je	ND30052	ND30837	ND30074	Y
jf	ND30864	ND30849	ND30850	Y
jg	ND30965	ND30962	ND30953	Y
jh	ND31059	ND31061	ND31060	Y
ji	ND31063	ND31062	ND31076	Y
jj	ND31153	ND31155	ND31154	Y
jk	ND31244	ND31247	ND31246	Y
jl	ND32890	ND31464	ND32889	Y
jm	ND31574	ND31576	ND31575	Y
jn	ND31664	ND31665	ND31666	Y
jo	ND31533	ND31742	ND31534	Y
jp	ND31961	ND31746	ND31745	Y
jq	ND31867	ND31866	ND31864	Y
jr	ND32497	ND31912	ND31913	Y
js	ND30729	ND32117	ND32118	Y
jt	ND32265	ND32266	ND33882	Y
ju	ND32289	ND32288	ND32290	Y
jv	ND31650	ND32319	ND32317	Y
jw	ND24191	ND32352	ND24192	Y
jx	ND32562	ND32509	ND32500	Y
jy	ND32552	ND32555	ND32554	Y
jz	ND31894	ND32563	ND31895	Y
k	ND29556	ND24072	ND24071	Y
ka	ND32630	ND32629	ND32631	Y
kb	ND31959	ND32673	ND31958	Y
kc	ND33323	ND32699	ND32680	Y
kd	ND32727	ND32728	ND32726	Y
ke	ND32763	ND32734	ND32731	Y
kf	ND32802	ND32801	ND32803	Y
kg	ND32239	ND32842	ND32242	Y
kh	ND33064	ND33062	ND33063	Y
ki	ND34306	ND33169	ND32700	Y
kj	ND32879	ND33247	ND32878	Y
kk	ND32340	ND33279	ND32339	Y
kl	ND32670	ND33338	ND32647	Y
km	ND33346	ND33348	ND33347	Y
kn	ND33590	ND33588	ND33589	Y
ko	ND33706	ND33704	ND33705	Y
kp	ND35495	ND33770	ND33768	Y
kq	ND33762	ND34043	ND33761	Y
kr	ND34131	ND34133	ND34132	Y
ks	ND34164	ND34166	ND34165	Y
kt	ND34593	ND34314	ND34312	Y
ku	ND34816	ND34348	ND34346	Y
kv	ND34424	ND34368	ND34370	Y
kx	ND34500	ND34502	ND34501	Y
ky	ND35136	ND34900	ND35396	Y
kz	ND34528	ND35053	ND34503	Y
l	ND24104	ND24102	ND24103	Y
lb	ND35817	ND35844	ND35818	Y
lc	ND36163	ND36164	ND36162	Y
le	ND36440	ND36442	ND36443	Y
lf	ND35820	ND36607	ND35819	N
lg	ND36798	ND36799	ND36795	Y
n	ND24188	ND24190	ND24187	Y
o	ND24217	ND24216	ND24214	Y
p	ND24346	ND24344	ND24345	Y
r	ND24704	ND24703	ND24705	Y
s	ND24782	ND24781	ND25679	Y
t	ND24470	ND24961	ND24469	Y
u	ND25070	ND25069	ND25073	Y
v	ND25606	ND25607	ND25605	Y
w	ND25181	ND25622	ND25179	Y
x	ND25582	ND25623	ND25581	Y
y	ND25682	ND25681	ND25680	N
z	ND25839	ND25834	ND26772	Y

*did not pass QC, not included in analysis

Supplementary Table 2: Validated inherited CNVs in 43 individuals

		Predicted by CoNIFER			Breakpoints by chromosome array						
trio	**chr**	**start**	**stop**	**size (bp)**	**start**	**stop**	**size**	**event type**	**inheritance**	**validation platform**	**genes**
ac	chr23	74513306	74599033	85727	74505779	74606768	100989	duplication	mother	CGH	UPRT,ZDHHC1
ah	chr3	184953077	187387065	2433988	185131753	187214923	2083170	duplication	father	CGH, SNP	EHHADH,MAP
ai	chr7	16918133	17385775	467642	16918472	17407061	488589	duplication	mother	SNP	AGR3,AHR,LO
aq	chr3	45744929	45936446	191517	45671268	45871203	199935	deletion	mother	CGH, SNP	SACM1L,SLC6A
aq	chr10				15009109	15060883	51774	duplication	father	SNP	MEIG1
be	chr9	108151313	108301632	150319	108206884	108302402	95518	deletion	father	CGH	FSD1L
bs	chr16	2908023	3001208	93185	2928181	2998053	69872	deletion	father	CGH	FLYWCH2,FLY
bs	chr22	22300214	22599926	299712	22313954	22560977	247023	duplication	father	SNP	PPM1F,TOP3B
bs	chr7	110303109	111375223	1072114	110965837	111321438	355601	deletion	mother	CGH	IMMP2L
cr	chr9	132482874	132838741	355867	132507232	132783902	276670	duplication	mother	CGH	PRRX2,PTGES,
cz	chr7				7120557	7313294	192737	duplication	mother	SNP	C1GALT1
cz	chr21	40777771	40816128	38357	40776019	40809714	33695	duplication	father	CGH	LCA5L
db	chr5	110411643	110454818	43175	110416995	110446579	29584	duplication	mother	CGH	WDR36
dg	chr1	92224169	92327201	103032	91988685	92130915	142230	deletion	mother	CGH	LOC10028943
dz	chr1	169558089	169586652	28563	169574047	169580274	6227	deletion	mother	CGH	SELP
eb	chr17	3500211	3566189	65978	3492855	3560888	68033	deletion	father	CGH	TRPV1,SHPK,C
ff	chr9	213108	340321	127213	207735	361025	153290	duplication	father	CGH	C9ORF66,DOC
fh	chr7	17349559	17385775	36216	17040227	17436278	396051	duplication	mother	CGH, SNP	AHR
fp	chr21	33355838	33651376	295538	33632971	33645249	12278	duplication	mother	CGH	HUNK,NCRNA(
fu	chr22	22300214	22599271	299057	24346991	24395156	48165	deletion	mother	CGH	PPM1F,TOP3B
fw	chr14	61744090	62463260	719170	61607162	62476906	869744	duplication	mother	CGH	HIF1A,PRKCH,S
fy	chr1	162467654	162482613	14959	162411286	162486355	75069	duplication	father	CGH	UHMK1
fy	chrx	32456357	32662430	206073	32446527	32628462	181935	deletion	father	CGH	DMD
gc	chr21	35742765	35986745	243980	34641156	34835149	193993	duplication	father	CGH	FAM165B,KCN
gi	chr1	92327027	92613395	286368	92303122	92578324	275202	duplication	mother	CGH	TGFBR3,BRDT,
gk	chr1	206241532	206332103	90571	206311019	206331706	20687	deletion	father	CGH	CTSE
gk	chr17	72199794	72667797	468003	71841082	72718161	877079	duplication	father	CGH	BTBD17,C17OI
gk	chr19	40971516	41029546	58030	40969518	41038340	68822	duplication	mother	CGH	SPTBN4
gq	chr1	190066796	197522242	7455446	187227118	196024958	8797840	duplication	father	CGH, SNP	ASPM,B3GALT

		Predicted by CoNIFER			Breakpoints by chromosome array						
trio	**chr**	**start**	**stop**	**size (bp)**	**start**	**stop**	**size**	**event type**	**inheritance**	**validation platform**	**genes**
gy	chr21	15750519	15755509	4990	15748775	15754006	5231	duplication	mother	CGH	HSPA13
gz	chr10	54053561	55570426	1516865	54525678	54531534	5856	deletion	father	CGH, SNP	DKK1,MBL2,PC
hi	chr12	129180374	129373289	192915	129165912	129336953	171041	duplication	father	CGH, SNP	GLT1D1,SLC15
hl	chr2	110690664	110975365	284701	110883210	110983320	100110	deletion	mother	CGH, SNP	LIMS3-LOC440
hi	chr6				26411364	26467182	55818	deletion	mother	SNP	BTN3A1, BTN2
hn	chr1	225965514	226034633	69119	225993806	226028496	34690	deletion	father	CGH, SNP	SRP9,EPHX1
hs	chr17	10204182	10263505	59323	10207809	10254757	46948	deletion	mother	CGH, SNP	MYH13
hx	chr6	3123890	3129432	5542	3119466	3129905	10439	duplication	mother	CGH	BPHL
ih	chr19	45261980	45303707	41727	45284031	45296810	12779	duplication	father	CGH	BCL3,CBLC
ii	chr4	113360841	113502958	142117	113390782	113487520	96738	duplication	mother	CGH	ALPK1,NEURO
in	chr14	69922448	69969596	47148	69922607	69972990	50383	duplication	father	CGH	FLJ44817,SLC3
in	chr15	22835915	23205198	369283	22789022	23140114	351092	deletion	mother	CGH, SNP	TUBGCP5,CYFI
ip	chr17	41201137	41958957	757820	41215805	41952726	736921	duplication	father	CGH	ARL4D,BRCA1,
iq	chr10	14974852	15106501	131649	14987110	15027214	40104	deletion	mother	CGH, SNP	DCLRE1C,MEIG
ir	chr3	17333386	17665405	332019	17390957	17487701	96744	deletion	mother	CGH	TBC1D5
ir	chr3	53317449	53326857	9408	53317500	53329768	12268	deletion	mother	CGH	DCP1A
jp	chr2	32631566	33246273	614707	32832625	33320957	488332	duplication	father	SNP	BIRC6,LTBP1,T
ka	chr1	89270073	89301937	31864	89266173	89304701	38528	duplication	mother	CGH	PKN2
kb	chr4	47514520	47905340	390820	47585672	47896236	310564	duplication	father	CGH	ATP10D,CORIN
ks	chr15	85681027	86189185	508158	85815949	86140791	324842	duplication	mother	CGH, SNP	AKAP13
kx	chr12	76478346	76881398	403052	76683857	76982825	298968	duplication	father	SNP	BBS10,OSBPL8
t	chr23	69454504	69572506	118002	69438694	69582975	144281	duplication	mother	CGH	ARR3,AWAT1,I
v	chr9	4576000	4625566	49566	4588700	4606335	17635	deletion	father	CGH	SLC1A1,C9orf6
v	chr23	46322182	46457837	135655	46289765	46412525	122760	duplication	mother	CGH	KRBOX4 ZNF67

AVG	377073
MAX	8797840
MIN	5231

Supplementary Table 3: de novo CNVs in 43 individuals confirmed by chromosome microarray

Validated de novo CNVs

	Trio	hg19 breakpoints	size (bp)	CNV type	inheritance	validation pl	likely pathogenic?
	ad	chr1:145414781-145688220	273,439	duplication	de novo	pending	
	ig	chr1:91360000-91500000	140,000	duplication	de novo	CGH	
	iz	chr14:67191043-67775790	584,747	deletion	de novo	CGH	Y
*	fu	chr15:100595065-102413897	1,818,832	deletion	de novo	CGH	Y
	ag	chr15:20,538,067-32,549,762	12,011,695	duplication	de novo	CGH	Y
*	gq	chr15:20083496-28511775	8,428,279	duplication	de novo	CGH, SNP	Y
	eh	chr15:23632712-28616967	4,984,255	duplication	de novo	CGH	Y
*	fu	chr16:73989288-90294753	16,305,465	duplication	de novo	CGH	Y
	fx	chr2:159451725-166948342	7,496,617	duplication	de novo	CGH	Y
*	iq	chr2:166787061-167083214	296,153	deletion	de novo	CGH, SNP	Y
	aib	chr2:242109195-242263656	154,461	deletion	de novo	SNP	
	hj	chr5:7897177-11732384	3,835,207	deletion	de novo	CGH	Y
*	gc	chr7:100678748-101301362	622,614	deletion	de novo	CGH	Y
	ahp	chr7:120593357-120687047	93,690	duplication	de novo	SNP	
	cy	chr7:75157776-86595291	11,437,515	deletion	de novo	CGH	Y
	le	chr8:6320000-6480000	160,000	deletion	de novo	CGH	
	aia	chr9:1-8733843	8,733,843	deletion	de novo	SNP	Y

* present in one of the 43 validation samples

AVG	4,551,577
MAX	16,305,465
MIN	93,690

16 patients with de novo CNV(s) 4.75%

Predicted but not validated in 43 individuals

trio	predicted hg19 breakpoints	size (bp)	event type	inheritance	validation platform
ac	chr17:80011149-80038114	26965	duplication	de novo	CGH
be	chr12:104099409-104109666	10257	duplication	de novo	CGH
be	chr17:1494859-1543960	49101	duplication	de novo	CGH
bs	chr8:145641193-145656534	15341	deletion	de novo	CGH
aq	chr6:159004985-159050851	45866	deletion	de novo	CGH
aq	chr9:127176186-127230103	53917	duplication	de novo	CGH
gc	chr3:49322281-49348170	25889	duplication	de novo	CGH
fu	chr12:98909441-98987913	78472	duplication	de novo	CGH
fu	chr16:31392217-31419237	27020	deletion	de novo	CGH
gk	chr12:9020825-9075384	54559	duplication	de novo	CGH
hx	chr9:86582998-86587104	4106	deletion	de novo	CGH
ih	chr18:77090011-77134101	44090	deletion	de novo	CGH
be	chr3:113327265-113380272	53007	duplication	de novo	CGH
b	chr10:67748449-68040379	291930	deletion	de novo	CGH
gk	chr10:13803646-14572514	768868	deletion	de novo	CGH
ip	chr10:27399384-27409476	10092	duplication	de novo	CGH

Supplementary Table 4: All validated, inherited CNVs

trio	breakpoints	size (bp)	event type	inheritance	validation platform
ac	chrX:74505779-74606768	100989	duplication	mother	CGH
ah	chr3:185131753-187214923	2083170	duplication	father	CGH, SNP
ai	chr7:16918472-17407061	488589	duplication	mother	SNP
aq	chr10:15009109-15060883	51774	duplication	father	SNP
aq	chr3:45671268-45871203	199935	deletion	mother	CGH, SNP
be	chr9:108206884-108302402	95518	deletion	father	CGH
bs	chr16:2928181-2998053	69872	deletion	father	CGH
bs	chr22:22313954-22560977	247023	duplication	father	SNP
bs	chr7:110965837-111321438	355601	deletion	mother	CGH, SNP
cr	chr9:132507232-132783902	276670	duplication	mother	CGH
cz	chr21:40776019-40809714	33695	duplication	father	CGH
cz	chr7:7120557-7313294	192737	duplication	mother	SNP
db	chr5:110416995-110446579	29584	duplication	mother	CGH
dg	chr1:91988685-92130915	142230	deletion	mother	CGH
dj	chr1:206316872-206327339	10467	deletion	father	CGH
dl	chr17:10348288-10358006	9718	deletion	father	SNP
dz	chr1:169574047-169580274	6227	deletion	mother	CGH
eb	chr17:3492855-3560888	68033	deletion	father	CGH
ff	chr9:207735-361025	153290	duplication	father	CGH
fh	chr7:17040227-17436278	396051	duplication	mother	CGH, SNP
fp	chr21:33632971-33645249	12278	duplication	mother	CGH
fu	chr22:24346991-24395156	48165	deletion	mother	CGH
fw	chr14:61607162-62476906	869744	duplication	mother	CGH
fy	chr1:162411286-162486355	75069	duplication	father	CGH
fy	chrx:32446527-32628462	181935	deletion	father	CGH
gc	chr21:34641156-34835149	193993	duplication	father	CGH
gi	chr1:92303122-92578324	275202	duplication	mother	CGH
gk	chr1:206311019-206331706	20687	deletion	father	CGH
gk	chr17:71841082-72718161	877079	duplication	father	CGH
gk	chr19:40969518-41038340	68822	duplication	mother	CGH
gq	chr1:187227118-196024958	8797840	duplication	father	CGH, SNP
gs	chr9:201140-378149	177009	duplication	father	CGH
gs	chr3:182841152-182923907	82755	duplication	father	CGH
gx	chr22:22312863-22330179	17316	duplication	father	CGH
gy	chr21:15748775-15754006	5275	duplication	mother	CGH
gz	chr10:54525678-54531534	5856	deletion	father	SNP
ha	chr11:134152030-134194937	42907	deletion	mother	SNP

trio	breakpoints	size (bp)	event type	inheritance	validation platform
hi	chr12:129165912-129336953	171041	duplication	father	CGH, SNP
hi	chr6:26411364-26467182	55818	deletion	mother	SNP
hl	chr2:110828463-110973573	100110	deletion	mother	CGH, SNP
hl	chr8:68020804-68135095	114291	duplication	mother	CGH
hn	chr1:225993806-226028496	34690	deletion	father	CGH, SNP
hs	chr17:10207809-10254757	46948	deletion	mother	CGH, SNP
hx	chr6:3119466-3129905	10439	duplication	mother	CGH
ib	chr1:185106737-185137530	30793	duplication	unknown	CGH
ie	chr3:151514590-151538170	23580	deletion	mother	SNP
ih	chr19:45284031-45296810	12779	duplication	father	CGH
ii	chr4:113390782-113487520	96738	duplication	mother	CGH
in	chr14:69922607-69972990	50383	duplication	father	CGH
in	chr15:22764593-23173181	351092	deletion	mother	CGH, SNP
ip	chr17:41215805-41952726	736921	duplication	father	CGH
iq	chr10:14987110-15027214	40104	deletion	mother	CGH, SNP
ir	chr3:17390957-17487701	96744	deletion	mother	CGH
ir	chr3:53317500-53329768	12268	deletion	mother	CGH
iv	chr12:21578559-21629928	51369	duplication	father	SNP
jp	chr2:32832625-33320957	488332	duplication	father	SNP
js	chr17:402843-488260	85417	deletion	father	SNP
ju	chr8:15948235-16021468	73233	deletion	mother	SNP
jy	chr10:135256762-135353499	96737	deletion	mother	SNP
jy	chr4:71171720-71275301	103581	deletion	mother	SNP
jz	chr11:6740308-6805900	65592	deletion	mother	SNP
ka	chr1:89266173-89304701	38528	duplication	mother	CGH
kb	chr4:47585672-47896236	310564	duplication	father	CGH
ks	chr15:85815949-86140791	324842	duplication	mother	SNP
kx	chr12:76683857-76982825	298968	duplication	father	SNP
kz	chr6:137282117-137361670	79553	deletion	father	SNP
t	chrX:69438694-69582975	144281	duplication	mother	CGH
v	chrX:46289765-46412525	122760	duplication	mother	CGH
v	chr9:4588700-4606335	17635	deletion	father	CGH
	AVERAGE SIZE	**305061**			
	MAX	**8797840**			
	MIN	**5275**			

Supplementary Table 5: Genes in confirmed de novo CNVs

		540 genes	3 overlap	11 overlap	3 overlap	30 overlap	55 overlap	93 overlap	126 overlap	Genes that are enriched in patients with "epilepsy", "neuro" or "autism" phenotype on clinical CNV testing [3]						Enriched in expanded study of 29,085 cases vs 19,584 controls (p<0.05) [4]	
Del/dup	CNV interval	Gene within *de novo* CNV (this study)	Known EE gene	Gene has *de novo* variant in at least one Epi4K sample [1]	Gene has de novo variant in ID study [5,6]	Gene has de novo variant in ASD study [7-10]	RVIS <10th %ile [2]	RVIS <25th %ile [2]	Gene in epilepsy CNV [11-14]	DUP - epilepsy [3]	DEL - epilepsy [3]	DUP - neuro [3]	DEL - neuro [3]	DUP - autism [3]	DEL - autism [3]	DUP<10Mbp [4]	DEL<10Mbp [4]
dup	chr15:20083496-28511775	GABRB3	GABRB3	GABRB3		GABRB3		GABRB3		GABRB3		GABRB3	GABRB3	GABRB3		2.48E-13	1.09E-11
del	chr2:166787061-167083214	SCN1A	SCN1A	SCN1A		SCN1A	SCN1A	SCN1A			SCN1A						
dup	chr2:159451725-166948342	SCN2A	SCN2A	SCN2A	SCN2A	SCN2A	SCN2A	SCN2A									2.72E-02
del	chr9:1-8733843	GLIS3		GLIS3					GLIS3								1.17E-02
del	chr7:75157776-86595291	KIAA1324L		KIAA1324L					KIAA1324L								
dup	chr15:20083496-28511775	NIPA1		NIPA1					NIPA1		NIPA1		NIPA1		NIPA1		7.64E-11
dup	chr16:73989288-90294753	PLCG2		PLCG2		PLCG2		PLCG2									
del	chr9:1-8733843	RCL1		RCL1					RCL1								4.91E-03
del	chr9:1-8733843	RFX3		RFX3				RFX3	RFX3								7.11E-03
dup	chr16:73989288-90294753	SPG7		SPG7			SPG7	SPG7								5.15E-03	
del	chr7:75157776-86595291	YWHAG		YWHAG													2.72E-02
del	chr9:1-8733843	ERMP1			ERMP1		ERMP1	ERMP1	ERMP1								1.21E-02
dup	chr2:159451725-166948342	GRB14			GRB14												2.72E-02
del	chr15:100595065-102413897	ADAMTS17					ADAMTS17	ADAMTS17									
dup	chr16:73989288-90294753	ANKRD11					ANKRD11	ANKRD11				ANKRD11				2.02E-02	
dup	chr15:20538067-32549762	APBA2					APBA2	APBA2	APBA2							9.43E-04	
dup	chr2:159451725-166948342	BAZ2B					BAZ2B	BAZ2B									
dup	chr16:73989288-90294753	CBFA2T3					CBFA2T3	CBFA2T3									
del	chr7:75157776-86595291	CD36					CD36	CD36	CD36								
dup	chr16:73989288-90294753	CDH15					CDH15	CDH15									
dup	chr16:73989288-90294753	CDYL2					CDYL2	CDYL2									
dup	chr16:73989288-90294753	CMIP					CMIP	CMIP									
dup	chr16:73989288-90294753	CPNE7					CPNE7	CPNE7								1.75E-02	
del	chr5:7897177-11732384	CTNND2				CTNND2	CTNND2	CTNND2									
dup	chr15:20083496-28511775	CYFIP1					CYFIP1	CYFIP1	CYFIP1		CYFIP1		CYFIP1		CYFIP1		2.41E-10
del	chr9:1-8733843	DOCK8					DOCK8	DOCK8	DOCK8								1.57E-02
dup	chr2:159451725-166948342	DPP4				DPP4	DPP4	DPP4									
dup	chr2:159451725-166948342	FAP					FAP	FAP									
dup	chr2:159451725-166948342	FIGN					FIGN	FIGN									
dup	chr16:73989288-90294753	GLG1					GLG1	GLG1									
del	chr7:75157776-86595291	GRM3					GRM3	GRM3	GRM3								
del	chr2:242109195-242263656	HDLBP				HDLBP	HDLBP	HDLBP	HDLBP				HDLBP				2.47E-06
dup	chr15:20083496-28511775	HERC2					HERC2	HERC2								7.81E-08	2.57E-08
del	chr7:75157776-86595291	HIP1					HIP1	HIP1									9.72E-03
dup	chr16:73989288-90294753	JPH3					JPH3	JPH3				JPH3	JPH3			1.21E-02	9.72E-03
del	chr9:1-8733843	KANK1				KANK1	KANK1	KANK1	KANK1								
dup	chr16:73989288-90294753	KARS					KARS	KARS									
dup	chr16:73989288-90294753	KIAA0182					KIAA0182	KIAA0182					KIAA0182			4.55E-02	
del	chr9:1-8733843	KIAA1432				KIAA1432	KIAA1432	KIAA1432	KIAA1432								2.60E-02
dup	chr16:73989288-90294753	KLHL36					KLHL36	KLHL36									
del	chr15:100595065-102413897	LRRK1				LRRK1	LRRK1	LRRK1								3.05E-04	
del	chr7:75157776-86595291	MAGI2					MAGI2	MAGI2	MAGI2								
dup	chr16:73989288-90294753	MBTPS1					MBTPS1	MBTPS1									
dup	chr15:20083496-28511775	MKRN3					MKRN3	MKRN3		MKRN3		MKRN3	MKRN3	MKRN3		5.74E-14	2.69E-09
dup	chr16:73989288-90294753	MVD					MVD	MVD					MVD			9.72E-03	
dup	chr15:20538067-32549762	OTUD7A				OTUD7A	OTUD7A	OTUD7A	OTUD7A								
dup	chr2:159451725-166948342	PKP4				PKP4	PKP4	PKP4									
del	chr7:100678748-101301362	PLOD3				PLOD3	PLOD3	PLOD3									
del	chr7:75157776-86595291	POR					POR	POR									
del	chr9:1-8733843	PTPRD					PTPRD	PTPRD	PTPRD								
del	chr9:1-8733843	RANBP6					RANBP6	RANBP6	RANBP6								
dup	chr2:159451725-166948342	SCN3A					SCN3A	SCN3A									
del	chr5:7897177-11732384	SEMA5A					SEMA5A	SEMA5A									
dup	chr16:73989288-90294753	SLC38A8					SLC38A8	SLC38A8									
del	chr9:1-8733843	SMARCA2					SMARCA2	SMARCA2	SMARCA2								
dup	chr2:159451725-166948342	TANC1					TANC1	TANC1									
del	chr15:100595065-102413897	TARSL2					TARSL2	TARSL2					TARSL2				1.14E-02
dup	chr16:73989288-90294753	TCF25					TCF25	TCF25									
dup	chr15:20538067-32549762	TJP1					TJP1	TJP1	TJP1	TJP1						2.54E-04	7.72E-03
del	chr7:100678748-101301362	TRIM56					TRIM56	TRIM56									4.55E-02
del	chr9:1-8733843	VLDLR					VLDLR	VLDLR	VLDLR								4.91E-03
dup	chr16:73989288-90294753	WDR59					WDR59	WDR59									
dup	chr16:73989288-90294753	ZC3H18					ZC3H18	ZC3H18					ZC3H18			3.47E-03	4.55E-02
dup	chr16:73989288-90294753	ZCCHC14					ZCCHC14	ZCCHC14					ZCCHC14			1.63E-02	9.72E-03
dup	chr1:145414781-145688220	ANKRD34A						ANKRD34A				ANKRD34A	ANKRD34A			3.95E-07	8.65E-05
dup	chr1:145414781-145688220	ANKRD35				ANKRD35						ANKRD35	ANKRD35			3.95E-07	8.65E-05

		540 genes	3 overlap	11 overlap	3 overlap	30 overlap	55 overlap	93 overlap	126 overlap	Genes that are enriched in patients with "epilepsy", "neuro" or "autism" phenotype on clinical CNV testing [3]						Enriched in expanded study of 29,085 cases vs 19,584 controls (p<0.05) [4]	
Del/dup	**CNV interval**	**Gene within *de novo* CNV (this study)**	**Known EE gene**	**Gene has *de novo* variant in at least one Epi4K sample [1]**	**Gene has de novo variant in ID study [5,6]**	**Gene has de novo variant in ASD study [7-10]**	**RVIS <10th %ile [2]**	**RVIS <25th %ile [2]**	**Gene in epilepsy CNV [11-14]**	**DUP - epilepsy [3]**	**DEL - epilepsy [3]**	**DUP - neuro [3]**	**DEL - neuro [3]**	**DUP - autism [3]**	**DEL - autism [3]**	**DUP<10Mbp [4]**	**DEL<10Mbp [4]**
dup	chr1:145414781-145688220	GNRHR2										GNRHR2	GNRHR2			3.95E-07	8.65E-05
dup	chr1:145414781-145688220	HFE2										HFE2	HFE2			5.64E-07	8.65E-05
dup	chr1:145414781-145688220	ITGA10										ITGA10	ITGA10			3.95E-07	8.65E-05
dup	chr1:145414781-145688220	LIX1L										LIX1L	LIX1L			2.76E-07	8.65E-05
dup	chr1:145414781-145688220	NBPF10				NBPF10											
dup	chr1:145414781-145688220	NUDT17										NUDT17	NUDT17			1.02E-06	8.65E-05
dup	chr1:145414781-145688220	PEX11B										PEX11B	PEX11B			3.95E-07	8.65E-05
dup	chr1:145414781-145688220	PIAS3						PIAS3				PIAS3	PIAS3			1.02E-06	8.65E-05
dup	chr1:145414781-145688220	POLR3C										POLR3C	POLR3C			5.67E-06	7.67E-04
dup	chr1:145414781-145688220	POLR3GL										POLR3GL	POLR3GL			3.95E-07	8.65E-05
dup	chr1:145414781-145688220	RBM8A														3.95E-07	8.65E-05
dup	chr1:145414781-145688220	RNF115								RNF115		RNF115				2.99E-04	4.39E-02
dup	chr1:145414781-145688220	TXNIP										TXNIP	TXNIP			5.64E-07	8.65E-05
dup	chr1:91360000-91500000	ZNF644				ZNF644											
del	chr14:67191043-67775790	FAM71D															
del	chr14:67191043-67775790	GPHN															
del	chr14:67191043-67775790	MPP5															
del	chr15:100595065-102413897	ALDH1A3						ALDH1A3									
del	chr15:100595065-102413897	ASB7														4.91E-03	1.88E-02
del	chr15:100595065-102413897	CERS3															
del	chr15:100595065-102413897	CHSY1						CHSY1									
del	chr15:100595065-102413897	FLJ42289															1.88E-02
del	chr15:100595065-102413897	LINS														2.60E-02	1.88E-02
del	chr15:100595065-102413897	LOC100507472															
del	chr15:100595065-102413897	OR4F13P															
del	chr15:100595065-102413897	OR4F15															
del	chr15:100595065-102413897	OR4F6															
del	chr15:100595065-102413897	PCSK6															
del	chr15:100595065-102413897	SNRPA1															2.22E-03
del	chr15:100595065-102413897	TM2D3											TM2D3				3.29E-02
del	chr15:100595065-102413897	VIMP															
dup	chr15:20083496-28511775	ATP10A							ATP10A	ATP10A		ATP10A		ATP10A		6.06E-16	4.86E-05
dup	chr15:20083496-28511775	CHEK2P2															
dup	chr15:20083496-28511775	CXADRP2							CXADRP2								
dup	chr15:20083496-28511775	GABRA5															2.51E-05
dup	chr15:20083496-28511775	GABRG3								GABRG3		GABRG3	GABRG3	GABRG3		2.16E-16	1.43E-10
dup	chr15:20083496-28511775	GOLGA6L1							GOLGA6L1								
dup	chr15:20083496-28511775	GOLGA6L6							GOLGA6L6								
dup	chr15:20083496-28511775	GOLGA8C							GOLGA8C								
dup	chr15:20083496-28511775	GOLGA8DP							GOLGA8DP								
dup	chr15:20083496-28511775	GOLGA8E							GOLGA8E							4.48E-03	
dup	chr15:20083496-28511775	GOLGA8IP							GOLGA8IP								
dup	chr15:20083496-28511775	HERC2P2							HERC2P2								
dup	chr15:20083496-28511775	HERC2P3							HERC2P3								
dup	chr15:20083496-28511775	HERC2P7							HERC2P7								
dup	chr15:20083496-28511775	IPW								IPW		IPW	IPW	IPW		2.16E-16	5.12E-11
dup	chr15:20083496-28511775	LOC100128714															
dup	chr15:20083496-28511775	LOC283683							LOC283683								
dup	chr15:20083496-28511775	LOC348120							LOC348120								
dup	chr15:20083496-28511775	LOC503519															
dup	chr15:20083496-28511775	LOC646214							LOC646214								
dup	chr15:20083496-28511775	LOC653061															
dup	chr15:20083496-28511775	LOC727924							LOC727924								
dup	chr15:20083496-28511775	MAGEL2								MAGEL2		MAGEL2	MAGEL2	MAGEL2		5.74E-14	2.69E-09
dup	chr15:20083496-28511775	MIR4508															
dup	chr15:20083496-28511775	MIR4509-1							MIR4509-1								
dup	chr15:20083496-28511775	MIR4509-2							MIR4509-2								
dup	chr15:20083496-28511775	MIR4509-3							MIR4509-3								
dup	chr15:20083496-28511775	MIR4715															
dup	chr15:20083496-28511775	NBEAP1							NBEAP1								
dup	chr15:20083496-28511775	NDN														1.02E-15	1.43E-10
dup	chr15:20083496-28511775	NF1P2							NF1P2								
dup	chr15:20083496-28511775	NIPA2							NIPA2		NIPA2		NIPA2		NIPA2		7.64E-11
dup	chr15:20083496-28511775	NPAP1															
dup	chr15:20083496-28511775	OCA2								OCA2		OCA2		OCA2		1.24E-10	5.45E-07
dup	chr15:20083496-28511775	OR4M2							OR4M2								
dup	chr15:20083496-28511775	OR4N3P							OR4N3P								

		540 genes	3 overlap	11 overlap	3 overlap	30 overlap	55 overlap	93 overlap	126 overlap	Genes that are enriched in patients with "epilepsy", "neuro" or "autism" phenotype on clinical CNV testing [3]						Enriched in expanded study of 29,085 cases vs 19,584 controls (p<0.05) [4]	
Del/dup	**CNV Interval**	**Gene within *de novo* CNV (this study)**	**Known EE gene**	**Gene has *de novo* variant in at least one Epi4K sample [1]**	**Gene has de novo variant in ID study [5,6]**	**Gene has de novo variant in ASD study [7-10]**	**RVIS <10th %ile [2]**	**RVIS <25th %ile [2]**	**Gene in epilepsy CNV [11-14]**	**DUP - epilepsy [3]**	**DEL - epilepsy [3]**	**DUP - neuro [3]**	**DEL - neuro [3]**	**DUP - autism [3]**	**DEL - autism [3]**	**DUP<10Mbp [4]**	**DEL<10Mbp [4]**
dup	chr15:20083496-28511775	OR4N4							OR4N4								
dup	chr15:20083496-28511775	PAR-SN								PAR-SN		PAR-SN	PAR-SN	PAR-SN		6.31E-15	5.12E-11
dup	chr15:20083496-28511775	PAR1								PAR1		PAR1	PAR1	PAR1		2.16E-16	5.12E-11
dup	chr15:20083496-28511775	PAR4								PAR4		PAR4		PAR4			
dup	chr15:20083496-28511775	PAR5								PAR5		PAR5	PAR5	PAR5		6.31E-15	6.09E-10
dup	chr15:20083496-28511775	POTEB							POTEB								
dup	chr15:20083496-28511775	PWRN1														6.06E-16	1.68E-07
dup	chr15:20083496-28511775	PWRN2															
dup	chr15:20083496-28511775	REREP3							REREP3								
dup	chr15:20083496-28511775	SNORD107								SNORD107		SNORD107	SNORD107	SNORD107		6.31E-15	5.12E-11
dup	chr15:20083496-28511775	SNORD108								SNORD108		SNORD108	SNORD108	SNORD108		6.31E-15	6.09E-10
dup	chr15:20083496-28511775	SNORD109A								SNORD109A		SNORD109A	SNORD109A	SNORD109A		6.06E-16	8.57E-11
dup	chr15:20083496-28511775	SNORD109B								SNORD109B		SNORD109B	SNORD109B	SNORD109B		6.06E-16	8.57E-11
dup	chr15:20083496-28511775	SNORD115-1								SNORD115-1		SNORD115-1	SNORD115-1	SNORD115-1			9.49E-08
dup	chr15:20083496-28511775	SNORD115-10								SNORD115-10		SNORD115-1	SNORD115-1	SNORD115-10			1.27E-02
dup	chr15:20083496-28511775	SNORD115-11								SNORD115-11		SNORD115-1	SNORD115-1	SNORD115-11			1.29E-03
dup	chr15:20083496-28511775	SNORD115-12								SNORD115-12		SNORD115-12		SNORD115-12			
dup	chr15:20083496-28511775	SNORD115-13								SNORD115-13		SNORD115-13		SNORD115-13			
dup	chr15:20083496-28511775	SNORD115-14								SNORD115-14		SNORD115-14		SNORD115-14			
dup	chr15:20083496-28511775	SNORD115-15								SNORD115-15		SNORD115-1	SNORD115-1	SNORD115-15			1.27E-02
dup	chr15:20083496-28511775	SNORD115-16								SNORD115-16		SNORD115-16		SNORD115-16			
dup	chr15:20083496-28511775	SNORD115-17								SNORD115-17		SNORD115-17		SNORD115-17			
dup	chr15:20083496-28511775	SNORD115-18								SNORD115-18		SNORD115-18		SNORD115-18			
dup	chr15:20083496-28511775	SNORD115-19								SNORD115-19		SNORD115-19		SNORD115-19			
dup	chr15:20083496-28511775	SNORD115-2								SNORD115-2		SNORD115-2	SNORD115-2	SNORD115-2			
dup	chr15:20083496-28511775	SNORD115-20								SNORD115-20		SNORD115-20		SNORD115-20			
dup	chr15:20083496-28511775	SNORD115-21								SNORD115-21		SNORD115-21		SNORD115-21			
dup	chr15:20083496-28511775	SNORD115-22								SNORD115-22		SNORD115-22		SNORD115-22			
dup	chr15:20083496-28511775	SNORD115-23								SNORD115-23		SNORD115-23		SNORD115-23			
dup	chr15:20083496-28511775	SNORD115-24															
dup	chr15:20083496-28511775	SNORD115-25								SNORD115-25		SNORD115-25		SNORD115-25			
dup	chr15:20083496-28511775	SNORD115-26								SNORD115-26		SNORD115-26		SNORD115-26			
dup	chr15:20083496-28511775	SNORD115-27															
dup	chr15:20083496-28511775	SNORD115-28															
dup	chr15:20083496-28511775	SNORD115-29								SNORD115-29		SNORD115-2	SNORD115-2	SNORD115-29			1.29E-03
dup	chr15:20083496-28511775	SNORD115-3								SNORD115-3		SNORD115-3		SNORD115-3			
dup	chr15:20083496-28511775	SNORD115-30								SNORD115-30		SNORD115-30		SNORD115-30			3.43E-02
dup	chr15:20083496-28511775	SNORD115-31								SNORD115-31		SNORD115-31		SNORD115-31			2.36E-02
dup	chr15:20083496-28511775	SNORD115-32								SNORD115-32		SNORD115-32		SNORD115-32			1.00E-02
dup	chr15:20083496-28511775	SNORD115-33								SNORD115-33		SNORD115-33		SNORD115-33			1.00E-02
dup	chr15:20083496-28511775	SNORD115-34								SNORD115-34		SNORD115-34		SNORD115-34			1.00E-02
dup	chr15:20083496-28511775	SNORD115-35								SNORD115-35		SNORD115-35		SNORD115-35			6.20E-03
dup	chr15:20083496-28511775	SNORD115-36								SNORD115-3		SNORD115-3	SNORD115-3	SNORD115-36			1.29E-03
dup	chr15:20083496-28511775	SNORD115-37								SNORD115-37		SNORD115-37		SNORD115-37			1.27E-02
dup	chr15:20083496-28511775	SNORD115-38								SNORD115-38		SNORD115-38		SNORD115-38			1.27E-02
dup	chr15:20083496-28511775	SNORD115-39								SNORD115-39		SNORD115-3	SNORD115-3	SNORD115-39			7.83E-03
dup	chr15:20083496-28511775	SNORD115-4								SNORD115-4		SNORD115-4		SNORD115-4			
dup	chr15:20083496-28511775	SNORD115-40								SNORD115-40		SNORD115-4	SNORD115-4	SNORD115-40			7.83E-03
dup	chr15:20083496-28511775	SNORD115-41								SNORD115-41		SNORD115-4	SNORD115-4	SNORD115-41			7.83E-03
dup	chr15:20083496-28511775	SNORD115-42								SNORD115-42		SNORD115-4	SNORD115-4	SNORD115-42			1.27E-02
dup	chr15:20083496-28511775	SNORD115-43								SNORD115-43		SNORD115-4	SNORD115-4	SNORD115-43			1.29E-03
dup	chr15:20083496-28511775	SNORD115-44								SNORD115-44		SNORD115-4	SNORD115-4	SNORD115-44			4.86E-05
dup	chr15:20083496-28511775	SNORD115-45															
dup	chr15:20083496-28511775	SNORD115-47															
dup	chr15:20083496-28511775	SNORD115-48														6.06E-16	8.57E-11
dup	chr15:20083496-28511775	SNORD115-5								SNORD115-5		SNORD115-5		SNORD115-5			
dup	chr15:20083496-28511775	SNORD115-6								SNORD115-6		SNORD115-6		SNORD115-6			
dup	chr15:20083496-28511775	SNORD115-7								SNORD115-7		SNORD115-7		SNORD115-7			
dup	chr15:20083496-28511775	SNORD115-8								SNORD115-8		SNORD115-8		SNORD115-8			
dup	chr15:20083496-28511775	SNORD115-9								SNORD115-9		SNORD115-9		SNORD115-9			
dup	chr15:20083496-28511775	SNORD116-1								SNORD116-1		SNORD116-1	SNORD116-1	SNORD116-1		1.52E-08	1.48E-09
dup	chr15:20083496-28511775	SNORD116-10								SNORD116-10		SNORD116-1	SNORD116-1	SNORD116-10		2.84E-06	
dup	chr15:20083496-28511775	SNORD116-11								SNORD116-11		SNORD116-1	SNORD116-1	SNORD116-11		2.84E-06	
dup	chr15:20083496-28511775	SNORD116-12								SNORD116-12		SNORD116-1	SNORD116-1	SNORD116-12		2.84E-06	
dup	chr15:20083496-28511775	SNORD116-13								SNORD116-13		SNORD116-1	SNORD116-1	SNORD116-13		2.84E-06	
dup	chr15:20083496-28511775	SNORD116-14								SNORD116-14		SNORD116-1	SNORD116-1	SNORD116-14		1.52E-08	1.63E-06
dup	chr15:20083496-28511775	SNORD116-15								SNORD116-15		SNORD116-1	SNORD116-1	SNORD116-15		1.52E-08	1.63E-06

		540 genes	3 overlap	11 overlap	3 overlap	30 overlap	55 overlap	93 overlap	126 overlap	Genes that are enriched in patients with "epilepsy", "neuro" or "autism" phenotype on clinical CNV testing [3]						Enriched in expanded study of 29,085 cases vs 19,584 controls (p<0.05) [4]	
Del/dup	**CNV interval**	**Gene within *de novo* CNV (this study)**	**Known EE gene**	**Gene has *de novo* variant in at least one Epi4K sample [1]**	**Gene has de novo variant in ID study [5,6]**	**Gene has de novo variant in ASD study [7-10]**	**RVIS <10th %ile [2]**	**RVIS <25th %ile [2]**	**Gene in epilepsy CNV [11-14]**	**DUP - epilepsy [3]**	**DEL - epilepsy [3]**	**DUP - neuro [3]**	**DEL - neuro [3]**	**DUP - autism [3]**	**DEL - autism [3]**	**DUP<10Mbp [4]**	**DEL<10Mbp [4]**
dup	chr15:20083496-28511775	SNORD116-16								SNORD116-16		SNORD116-1	SNORD116-1	SNORD116-16		2.30E-10	2.26E-10
dup	chr15:20083496-28511775	SNORD116-17								SNORD116-17		SNORD116-1	SNORD116-1	SNORD116-17		9.37E-13	5.12E-11
dup	chr15:20083496-28511775	SNORD116-18								SNORD116-18		SNORD116-1	SNORD116-1	SNORD116-18		9.37E-13	5.12E-11
dup	chr15:20083496-28511775	SNORD116-19								SNORD116-19		SNORD116-1	SNORD116-1	SNORD116-19		9.37E-13	5.12E-11
dup	chr15:20083496-28511775	SNORD116-2								SNORD116-2		SNORD116-2	SNORD116-2	SNORD116-2		2.84E-06	
dup	chr15:20083496-28511775	SNORD116-20								SNORD116-20		SNORD116-20		SNORD116-20		9.37E-13	9.97E-09
dup	chr15:20083496-28511775	SNORD116-21								SNORD116-21		SNORD116-21		SNORD116-21		9.37E-13	5.43E-06
dup	chr15:20083496-28511775	SNORD116-22								SNORD116-22		SNORD116-2	SNORD116-2	SNORD116-22		9.37E-13	5.12E-11
dup	chr15:20083496-28511775	SNORD116-23								SNORD116-23		SNORD116-2	SNORD116-2	SNORD116-23		9.35E-14	5.12E-11
dup	chr15:20083496-28511775	SNORD116-24								SNORD116-24		SNORD116-2	SNORD116-2	SNORD116-24		2.16E-16	5.12E-11
dup	chr15:20083496-28511775	SNORD116-25								SNORD116-25		SNORD116-2	SNORD116-2	SNORD116-25		2.16E-16	5.12E-11
dup	chr15:20083496-28511775	SNORD116-26								SNORD116-26		SNORD116-2	SNORD116-2	SNORD116-26		2.16E-16	5.12E-11
dup	chr15:20083496-28511775	SNORD116-27								SNORD116-27		SNORD116-2	SNORD116-2	SNORD116-27		2.16E-16	5.12E-11
dup	chr15:20083496-28511775	SNORD116-28								SNORD116-28		SNORD116-2	SNORD116-2	SNORD116-28		2.16E-16	5.12E-11
dup	chr15:20083496-28511775	SNORD116-29								SNORD116-29		SNORD116-2	SNORD116-2	SNORD116-29		2.16E-16	5.12E-11
dup	chr15:20083496-28511775	SNORD116-3								SNORD116-3		SNORD116-3	SNORD116-3	SNORD116-3		2.84E-06	
dup	chr15:20083496-28511775	SNORD116-4								SNORD116-4		SNORD116-4	SNORD116-4	SNORD116-4		1.14E-06	
dup	chr15:20083496-28511775	SNORD116-5								SNORD116-5		SNORD116-5	SNORD116-5	SNORD116-5		2.84E-06	
dup	chr15:20083496-28511775	SNORD116-6								SNORD116-6		SNORD116-6	SNORD116-6	SNORD116-6		2.84E-06	
dup	chr15:20083496-28511775	SNORD116-7								SNORD116-7		SNORD116-7	SNORD116-7	SNORD116-7		2.84E-06	
dup	chr15:20083496-28511775	SNORD116-8								SNORD116-8		SNORD116-8	SNORD116-8	SNORD116-8		2.84E-06	
dup	chr15:20083496-28511775	SNORD116-9								SNORD116-9		SNORD116-9	SNORD116-9	SNORD116-9		2.84E-06	
dup	chr15:20083496-28511775	SNORD64								SNORD64		SNORD64	SNORD64	SNORD64		6.31E-15	9.99E-10
dup	chr15:20083496-28511775	SNRPN								SNRPN		SNRPN		SNRPN		6.31E-15	
dup	chr15:20083496-28511775	SNURF								SNURF		SNURF	SNURF	SNURF		6.31E-15	5.12E-11
dup	chr15:20083496-28511775	TUBGCP5				TUBGCP5		TUBGCP5	TUBGCP5		TUBGCP5		TUBGCP5				5.67E-10
dup	chr15:20083496-28511775	UBE3A						UBE3A	UBE3A	UBE3A		UBE3A	UBE3A	UBE3A		1.72E-14	8.57E-11
dup	chr15:20083496-28511775	WHAMMP3							WHAMMP3								
dup	chr15:20538067-32549762	ARHGAP11B															
dup	chr15:20538067-32549762	CHRFAM7A							CHRFAM7A								
dup	chr15:20538067-32549762	CHRNA7							CHRNA7		CHRNA7		CHRNA7		CHRNA7		
dup	chr15:20538067-32549762	DKFZP434L187							DKFZP434L187								
dup	chr15:20538067-32549762	FAM189A1							FAM189A1	FAM189A1						6.69E-05	
dup	chr15:20538067-32549762	FAN1							FAN1	FAN1	FAN1	FAN1	FAN1		FAN1	9.31E-03	4.60E-17
dup	chr15:20538067-32549762	GOLGA6L7P							GOLGA6L7P								
dup	chr15:20538067-32549762	GOLGA8F														2.78E-02	
dup	chr15:20538067-32549762	GOLGA8G														2.78E-02	
dup	chr15:20538067-32549762	HERC2P10															
dup	chr15:20538067-32549762	HERC2P9															
dup	chr15:20538067-32549762	KLF13							KLF13								2.54E-03
dup	chr15:20538067-32549762	LOC100288637							LOC100288637								
dup	chr15:20538067-32549762	LOC100289656							LOC100289656							1.45E-03	
dup	chr15:20538067-32549762	LOC283710							LOC283710								
dup	chr15:20538067-32549762	LOC646278							LOC646278								
dup	chr15:20538067-32549762	LOC653075							LOC653075								
dup	chr15:20538067-32549762	MIR211							MIR211	MIR211		MIR211	MIR211		MIR211	3.87E-03	2.68E-12
dup	chr15:20538067-32549762	MTMR10							MTMR10	MTMR10	MTMR10	MTMR10	MTMR10		MTMR10	7.12E-03	4.60E-17
dup	chr15:20538067-32549762	NDNL2							NDNL2	NDNL2						1.05E-04	1.21E-02
dup	chr15:20538067-32549762	TRPM1							TRPM1	TRPM1		TRPM1	TRPM1		TRPM1	4.10E-03	3.25E-11
dup	chr15:20538067-32549762	ULK4P1							ULK4P1								
dup	chr15:20538067-32549762	ULK4P2							ULK4P2								
dup	chr15:20538067-32549762	ULK4P3							ULK4P3								
dup	chr15:20538067-32549762	WHAMMP2							WHAMMP2								
dup	chr16:73989288-90294753	ACSF3						ACSF3									
dup	chr16:73989288-90294753	ADAD2															
dup	chr16:73989288-90294753	ADAMTS18															
dup	chr16:73989288-90294753	ADAT1															
dup	chr16:73989288-90294753	AFG3L1P															
dup	chr16:73989288-90294753	APRT											APRT				
dup	chr16:73989288-90294753	ATMIN						ATMIN									
dup	chr16:73989288-90294753	ATP2C2				ATP2C2											
dup	chr16:73989288-90294753	BANP						BANP				BANP	BANP				
dup	chr16:73989288-90294753	BCAR1															
dup	chr16:73989288-90294753	BCMO1															
dup	chr16:73989288-90294753	C16orf3															
dup	chr16:73989288-90294753	C16orf46															
dup	chr16:73989288-90294753	C16orf55											C16orf55				

		540 genes	3 overlap	11 overlap	3 overlap	30 overlap	55 overlap	93 overlap	126 overlap	Genes that are enriched in patients with "epilepsy", "neuro" or "autism" phenotype on clinical CNV testing [3]						Enriched in expanded study of 29,085 cases vs 19,584 controls (p<0.05) [4]	
Del/dup	**CNV Interval**	**Gene within *de novo* CNV (this study)**	**Known EE gene**	**Gene has *de novo* variant in at least one Epi4K sample [1]**	**Gene has de novo variant in ID study [5,6]**	**Gene has de novo variant in ASD study [7-10]**	**RVIS <10th %ile [2]**	**RVIS <25th %ile [2]**	**Gene in epilepsy CNV [11-14]**	**DUP - epilepsy [3]**	**DEL - epilepsy [3]**	**DUP - neuro [3]**	**DEL - neuro [3]**	**DUP - autism [3]**	**DEL - autism [3]**	**DUP<10Mbp [4]**	**DEL<10Mbp [4]**
dup	chr16:73989288-90294753	C16orf7											C16orf7			1.21E-02	
dup	chr16:73989288-90294753	C16orf74											C16orf74				
dup	chr16:73989288-90294753	C16orf95															
dup	chr16:73989288-90294753	CA5A															
dup	chr16:73989288-90294753	CDH13															
dup	chr16:73989288-90294753	CDK10											CDK10			2.60E-02	
dup	chr16:73989288-90294753	CDT1											CDT1				
dup	chr16:73989288-90294753	CENPBD1														1.21E-02	
dup	chr16:73989288-90294753	CENPN															
dup	chr16:73989288-90294753	CFDP1															
dup	chr16:73989288-90294753	CHMP1A											CHMP1A				
dup	chr16:73989288-90294753	CHST5				CHST5											
dup	chr16:73989288-90294753	CHST6						CHST6									
dup	chr16:73989288-90294753	CLEC18B															
dup	chr16:73989288-90294753	CLEC3A				CLEC3A											
dup	chr16:73989288-90294753	CMC2															
dup	chr16:73989288-90294753	CNTNAP4							CNTNAP4								
dup	chr16:73989288-90294753	COTL1															
dup	chr16:73989288-90294753	COX4I1											COX4I1			4.55E-02	
dup	chr16:73989288-90294753	CRISPLD2															
dup	chr16:73989288-90294753	CTRB1															
dup	chr16:73989288-90294753	CTRB2															
dup	chr16:73989288-90294753	CTU2											CTU2				
dup	chr16:73989288-90294753	CYBA											CYBA			5.81E-03	4.55E-02
dup	chr16:73989288-90294753	DBNDD1															
dup	chr16:73989288-90294753	DEF8														1.88E-02	
dup	chr16:73989288-90294753	DNAAF1															
dup	chr16:73989288-90294753	DPEP1						DPEP1									
dup	chr16:73989288-90294753	DYNLRB2				DYNLRB2											
dup	chr16:73989288-90294753	EMC8															
dup	chr16:73989288-90294753	FA2H															
dup	chr16:73989288-90294753	FAM92B															
dup	chr16:73989288-90294753	FANCA														1.24E-03	
dup	chr16:73989288-90294753	FBXO31						FBXO31					FBXO31				5.81E-03
dup	chr16:73989288-90294753	FLJ30679											FLJ30679				
dup	chr16:73989288-90294753	FOXC2											FOXC2				
dup	chr16:73989288-90294753	FOXF1											FOXF1				
dup	chr16:73989288-90294753	FOXF1-AS1															
dup	chr16:73989288-90294753	FOXL1											FOXL1				
dup	chr16:73989288-90294753	GABARAPL2															
dup	chr16:73989288-90294753	GALNS										GALNS	GALNS				
dup	chr16:73989288-90294753	GAN						GAN									
dup	chr16:73989288-90294753	GAS8															
dup	chr16:73989288-90294753	GCSH															
dup	chr16:73989288-90294753	GINS2						GINS2									
dup	chr16:73989288-90294753	HSBP1															
dup	chr16:73989288-90294753	HSD17B2															
dup	chr16:73989288-90294753	HSDL1						HSDL1									
dup	chr16:73989288-90294753	IL17C											IL17C			5.81E-03	4.55E-02
dup	chr16:73989288-90294753	IRF8											IRF8				
dup	chr16:73989288-90294753	KCNG4															
dup	chr16:73989288-90294753	KIAA0513						KIAA0513									
dup	chr16:73989288-90294753	KIAA1609															
dup	chr16:73989288-90294753	KLHDC4														3.83E-02	
dup	chr16:73989288-90294753	LDHD						LDHD									
dup	chr16:73989288-90294753	LINC00304															
dup	chr16:73989288-90294753	LINC00311															
dup	chr16:73989288-90294753	LOC100128881											LOC100128881			1.21E-02	
dup	chr16:73989288-90294753	LOC100129617															
dup	chr16:73989288-90294753	LOC100130015															
dup	chr16:73989288-90294753	LOC100287036															
dup	chr16:73989288-90294753	LOC146513															
dup	chr16:73989288-90294753	LOC283922															
dup	chr16:73989288-90294753	LOC400548											LOC400548				
dup	chr16:73989288-90294753	LOC400558															
dup	chr16:73989288-90294753	LOC727710															
dup	chr16:73989288-90294753	LOC732275											LOC732275				

		540 genes	3 overlap	11 overlap	3 overlap	30 overlap	55 overlap	93 overlap	126 overlap	Genes that are enriched in patients with "epilepsy", "neuro" or "autism" phenotype on clinical CNV testing [3]						Enriched in expanded study of 29,085 cases vs 19,584 controls (p<0.05) [4]	
Del/dup	**CNV Interval**	**Gene within *de novo* CNV (this study)**	**Known EE gene**	**Gene has *de novo* variant in at least one Epi4K sample [1]**	**Gene has de novo variant in ID study [5,6]**	**Gene has de novo variant in ASD study [7-10]**	**RVIS <10th %ile [2]**	**RVIS <25th %ile [2]**	**Gene in epilepsy CNV [11-14]**	**DUP - epilepsy [3]**	**DEL - epilepsy [3]**	**DUP - neuro [3]**	**DEL - neuro [3]**	**DUP - autism [3]**	**DEL - autism [3]**	**DUP<10Mbp [4]**	**DEL<10Mbp [4]**
dup	chr16:73989288-90294753	MAF															
dup	chr16:73989288-90294753	MAP1LC3B											MAP1LC3B			1.63E-02	5.81E-03
dup	chr16:73989288-90294753	MC1R									MC1R					7.72E-03	
dup	chr16:73989288-90294753	MGC23284											MGC23284			4.91E-03	
dup	chr16:73989288-90294753	MIR1910											MIR1910				
dup	chr16:73989288-90294753	MIR3182															
dup	chr16:73989288-90294753	MIR4719															
dup	chr16:73989288-90294753	MIR4720															
dup	chr16:73989288-90294753	MIR4722															
dup	chr16:73989288-90294753	MIR5093															
dup	chr16:73989288-90294753	MIR5189															
dup	chr16:73989288-90294753	MLKL				MLKL											
dup	chr16:73989288-90294753	MLYCD															
dup	chr16:73989288-90294753	MON1B						MON1B									
dup	chr16:73989288-90294753	MPHOSPH6															
dup	chr16:73989288-90294753	MTHFSD											MTHFSD				
dup	chr16:73989288-90294753	NECAB2														2.72E-02	
dup	chr16:73989288-90294753	NUDT7															
dup	chr16:73989288-90294753	OSGIN1														2.72E-02	
dup	chr16:73989288-90294753	PABPN1L										PABPN1L	PABPN1L				
dup	chr16:73989288-90294753	PIEZO1															
dup	chr16:73989288-90294753	PKD1L2															
dup	chr16:73989288-90294753	PRDM7															
dup	chr16:73989288-90294753	PSMD7															
dup	chr16:73989288-90294753	RFWD3				RFWD3		RFWD3									
dup	chr16:73989288-90294753	RNF166						RNF166					RNF166			4.91E-03	
dup	chr16:73989288-90294753	RPL13														7.79E-03	
dup	chr16:73989288-90294753	SDR42E1															
dup	chr16:73989288-90294753	SLC22A31															
dup	chr16:73989288-90294753	SLC7A5															
dup	chr16:73989288-90294753	SNAI3											SNAI3			4.91E-03	
dup	chr16:73989288-90294753	SNORD68														7.79E-03	
dup	chr16:73989288-90294753	SPATA2L											SPATA2L			2.60E-02	
dup	chr16:73989288-90294753	SPIRE2						SPIRE2								5.15E-03	
dup	chr16:73989288-90294753	SYCE1L															
dup	chr16:73989288-90294753	TAF1C															
dup	chr16:73989288-90294753	TERF2IP															
dup	chr16:73989288-90294753	TMEM170A															
dup	chr16:73989288-90294753	TMEM231															
dup	chr16:73989288-90294753	TRAPPC2L										TRAPPC2L	TRAPPC2L				
dup	chr16:73989288-90294753	TUBB3						TUBB3			TUBB3					7.72E-03	
dup	chr16:73989288-90294753	USP10															
dup	chr16:73989288-90294753	VAT1L															
dup	chr16:73989288-90294753	WFDC1															
dup	chr16:73989288-90294753	WWOX															
dup	chr16:73989288-90294753	ZDHHC7															
dup	chr16:73989288-90294753	ZFP1															
dup	chr16:73989288-90294753	ZFPM1															
dup	chr16:73989288-90294753	ZNF276														4.91E-03	
dup	chr16:73989288-90294753	ZNF469										ZNF469				1.21E-02	
dup	chr16:73989288-90294753	ZNF778										ZNF778					
dup	chr16:73989288-90294753	ZNRF1															
dup	chr2:159451725-166948342	CD302															
dup	chr2:159451725-166948342	COBLL1															
dup	chr2:159451725-166948342	CSRNP3															
dup	chr2:159451725-166948342	DAPL1															
dup	chr2:159451725-166948342	GALNT3															
dup	chr2:159451725-166948342	GCA															
dup	chr2:159451725-166948342	GCG															
dup	chr2:159451725-166948342	IFIH1				IFIH1											
dup	chr2:159451725-166948342	ITGB6						ITGB6									
dup	chr2:159451725-166948342	KCNH7															
dup	chr2:159451725-166948342	LOC100506124															
dup	chr2:159451725-166948342	LY75															
dup	chr2:159451725-166948342	LY75-CD302															
dup	chr2:159451725-166948342	MARCH7															
dup	chr2:159451725-166948342	MIR4785															

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Del/dup	**CNV interval**	**Gene within *de novo* CNV (this study)**	**Known EE gene**	**Gene has *de novo* variant in at least one Epi4K sample [1]**	**Gene has de novo variant in ID study [5,6]**	**Gene has de novo variant in ASD study [7-10]**	**RVIS <10th %ile [2]**	**RVIS <25th %ile [2]**	**Gene in epilepsy CNV [11-14]**	**DUP - epilepsy [3]**	**DEL - epilepsy [3]**	**DUP - neuro [3]**	**DEL - neuro [3]**	**DUP - autism [3]**	**DEL - autism [3]**	**DUP<10Mbp [4]**	**DEL<10Mbp [4]**
dup	chr2:159451725-166948342	PLA2R1															
dup	chr2:159451725-166948342	PSMD14															
dup	chr2:159451725-166948342	RBMS1															
dup	chr2:159451725-166948342	SLC38A11															2.72E-02
dup	chr2:159451725-166948342	SLC4A10						SLC4A10									
dup	chr2:159451725-166948342	SNORA70F															4.55E-02
dup	chr2:159451725-166948342	TANK															
dup	chr2:159451725-166948342	TBR1				TBR1											
dup	chr2:159451725-166948342	WDSUB1															
del	chr2:166787061-167083214	LOC100506134															
del	chr2:166787061-167083214	SCN9A															
del	chr2:166787061-167083214	TTC21B									TTC21B					2.72E-02	4.55E-02
del	chr2:242109195-242263656	ANO7							ANO7		ANO7		ANO7				8.41E-08
del	chr2:242109195-242263656	PPP1R7							PPP1R7		PPP1R7		PPP1R7				5.29E-09
del	chr2:242109195-242263656	SEPT2									SEPT2		SEPT2				
del	chr5:7897177-11732384	ANKRD33B															
del	chr5:7897177-11732384	CCT5															
del	chr5:7897177-11732384	CMBL															
del	chr5:7897177-11732384	DAP															
del	chr5:7897177-11732384	FAM173B															
del	chr5:7897177-11732384	LOC100505738															
del	chr5:7897177-11732384	LOC100505806															
del	chr5:7897177-11732384	LOC285692															
del	chr5:7897177-11732384	LOC729506															
del	chr5:7897177-11732384	MARCH6						MARCH6									
del	chr5:7897177-11732384	MIR4458															
del	chr5:7897177-11732384	MIR4636															
del	chr5:7897177-11732384	MTRR															
del	chr5:7897177-11732384	ROPN1L															
del	chr5:7897177-11732384	SNORD123															
del	chr5:7897177-11732384	TAS2R1															
del	chr7:100678748-101301362	AP1S1															
del	chr7:100678748-101301362	CLDN15															
del	chr7:100678748-101301362	EMID2															
del	chr7:100678748-101301362	FIS1															
del	chr7:100678748-101301362	MIR4653															
del	chr7:100678748-101301362	MOGAT3				MOGAT3											
del	chr7:100678748-101301362	MUC17				MUC17											4.55E-02
del	chr7:100678748-101301362	MYL10															4.55E-02
del	chr7:100678748-101301362	NAT16															
del	chr7:100678748-101301362	RABL5															
del	chr7:100678748-101301362	SERPINE1															
del	chr7:100678748-101301362	VGF															
del	chr7:100678748-101301362	ZNHIT1															
del	chr7:120593357-120687047	CPED1															
del	chr7:120593357-120687047	ING3															
del	chr7:75157776-86595291	CACNA2D1						CACNA2D1	CACNA2D1								
del	chr7:75157776-86595291	CCDC146							CCDC146								
del	chr7:75157776-86595291	CCL24														4.55E-02	2.72E-02
del	chr7:75157776-86595291	CCL26															2.72E-02
del	chr7:75157776-86595291	DTX2						DTX2									
del	chr7:75157776-86595291	DTX2P1-UPK3BP1-PMS2P11															
del	chr7:75157776-86595291	FDPSL2A															
del	chr7:75157776-86595291	FGL2							FGL2								
del	chr7:75157776-86595291	GNAI1							GNAI1								
del	chr7:75157776-86595291	GNAT3							GNAT3								
del	chr7:75157776-86595291	HGF							HGF								
del	chr7:75157776-86595291	HSPB1															2.72E-02
del	chr7:75157776-86595291	LOC100132832															
del	chr7:75157776-86595291	LOC100133091															
del	chr7:75157776-86595291	MAGI2-AS2															
del	chr7:75157776-86595291	MAGI2-AS3							MAGI2-AS3								
del	chr7:75157776-86595291	MDH2															
del	chr7:75157776-86595291	MIR4651															
del	chr7:75157776-86595291	MIR548AU															
del	chr7:75157776-86595291	MIR548M															
del	chr7:75157776-86595291	PCLO							PCLO								

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Del/dup	CNV interval	Gene within *de novo* CNV (this study)	Known EE gene	Gene has *de novo* variant in at least one Epi4K sample [1]	Gene has de novo variant in ID study [5,6]	Gene has de novo variant in ASD study [7-10]	RVIS <10th %ile [2]	RVIS <25th %ile [2]	Gene in epilepsy CNV [11-14]	DUP - epilepsy [3]	DEL - epilepsy [3]	DUP - neuro [3]	DEL - neuro [3]	DUP - autism [3]	DEL - autism [3]	DUP<10Mbp [4]	DEL<10Mbp [4]
del	chr7:75157776-86595291	PHTF2							PHTF2								
del	chr7:75157776-86595291	PION							PION								
del	chr7:75157776-86595291	POMZP3															
del	chr7:75157776-86595291	PTPN12						PTPN12	PTPN12								
del	chr7:75157776-86595291	RHBDD2						RHBDD2								4.55E-02	2.72E-02
del	chr7:75157776-86595291	RPL13AP17							RPL13AP17								
del	chr7:75157776-86595291	RSBN1L						RSBN1L	RSBN1L								
del	chr7:75157776-86595291	RSBN1L-AS1															
del	chr7:75157776-86595291	SEMA3A							SEMA3A								
del	chr7:75157776-86595291	SEMA3C						SEMA3C	SEMA3C								
del	chr7:75157776-86595291	SEMA3D							SEMA3D								
del	chr7:75157776-86595291	SEMA3E						SEMA3E	SEMA3E								
del	chr7:75157776-86595291	SNORA14A															2.72E-02
del	chr7:75157776-86595291	SRCRB4D															2.72E-02
del	chr7:75157776-86595291	SRRM3															2.72E-02
del	chr7:75157776-86595291	STYXL1															
del	chr7:75157776-86595291	TMEM120A															
del	chr7:75157776-86595291	TMEM60							TMEM60								
del	chr7:75157776-86595291	UPK3B															
del	chr7:75157776-86595291	ZP3															4.55E-02
del	chr8:6320000-6480000	ANGPT2											ANGPT2			2.92E-02	2.85E-04
del	chr8:6320000-6480000	MCPH1				MCPH1							MCPH1				4.22E-02
del	chr9:1-8733843	AK3							AK3								2.60E-02
del	chr9:1-8733843	C9orf123							C9orf123								
del	chr9:1-8733843	C9orf66							C9orf66								5.00E-03
del	chr9:1-8733843	CBWD1							CBWD1								
del	chr9:1-8733843	CD274							CD274								2.92E-02
del	chr9:1-8733843	CDC37L1							CDC37L1								2.60E-02
del	chr9:1-8733843	DDX11L5															
del	chr9:1-8733843	DMRT1							DMRT1								7.79E-03
del	chr9:1-8733843	DMRT2							DMRT2								1.97E-03
del	chr9:1-8733843	DMRT3							DMRT3								1.97E-03
del	chr9:1-8733843	FAM138C							FAM138C								
del	chr9:1-8733843	FLJ35024							FLJ35024								4.91E-03
del	chr9:1-8733843	FOXD4							FOXD4								
del	chr9:1-8733843	GLDC				GLDC		GLDC	GLDC								
del	chr9:1-8733843	GLIS3-AS1							GLIS3-AS1								
del	chr9:1-8733843	IL33							IL33								
del	chr9:1-8733843	INSL4							INSL4								1.88E-02
del	chr9:1-8733843	INSL6							INSL6								1.75E-02
del	chr9:1-8733843	JAK2							JAK2								
del	chr9:1-8733843	KCNV2						KCNV2	KCNV2								4.87E-02
del	chr9:1-8733843	KDM4C							KDM4C								
del	chr9:1-8733843	KIAA0020							KIAA0020								1.17E-02
del	chr9:1-8733843	KIAA2026							KIAA2026								
del	chr9:1-8733843	MIR101-2							MIR101-2								7.72E-03
del	chr9:1-8733843	MIR4665							MIR4665								
del	chr9:1-8733843	MLANA							MLANA								
del	chr9:1-8733843	PDCD1LG2							PDCD1LG2								1.88E-02
del	chr9:1-8733843	PLGRKT							PLGRKT								
del	chr9:1-8733843	PPAPDC2							PPAPDC2								7.72E-03
del	chr9:1-8733843	RLN1							RLN1								
del	chr9:1-8733843	RLN2							RLN2								
del	chr9:1-8733843	SLC1A1						SLC1A1	SLC1A1		SLC1A1		SLC1A1				7.11E-03
del	chr9:1-8733843	SPATA6L				SPATA6L			SPATA6L								
del	chr9:1-8733843	TPD52L3							TPD52L3								
del	chr9:1-8733843	UHRF2							UHRF2								
del	chr9:1-8733843	WASH1							WASH1								
del	chr17:34819500-36217700	ZNHIT3															
del	chr17:34819500-36217700	MYO19															
del	chr17:34819500-36217700	PIG2															
del	chr17:34819500-36217700	GGNBP2															
del	chr17:34819500-36217700	MRM1															
del	chr17:34819500-36217700	LHX1															
del	chr17:34819500-36217700	AATF															
del	chr17:34819500-36217700	ACACA															
del	chr17:34819500-36217700	TADA2A															

		540 genes	3 overlap	11 overlap	3 overlap	30 overlap	55 overlap	93 overlap	126 overlap	Genes that are enriched in patients with "epilepsy", "neuro" or "autism" phenotype on clinical CNV testing [3]						Enriched in expanded study of 29,085 cases vs 19,584 controls (p<0.05) [4]	
Del/dup	**CNV Interval**	**Gene within *de novo* CNV (this study)**	**Known EE gene**	**Gene has *de novo* variant in at least one Epi4K sample [1]**	**Gene has de novo variant in ID study [5,6]**	**Gene has de novo variant in ASD study [7-10]**	**RVIS <10th %ile [2]**	**RVIS <25th %ile [2]**	**Gene in epilepsy CNV [11-14]**	**DUP - epilepsy [3]**	**DEL - epilepsy [3]**	**DUP - neuro [3]**	**DEL - neuro [3]**	**DUP - autism [3]**	**DEL - autism [3]**	**DUP<10Mbp [4]**	**DEL<10Mbp [4]**
del	chr17:34819500-36217700	C17orf78															
del	chr17:34819500-36217700	DUSP14															
del	chr17:34819500-36217700	SYNRG															
del	chr17:34819500-36217700	DDX52															
del	chr17:34819500-36217700	HNF1B															

SUPPLEMENTARY TABLE 6: Genes in confirmed inherited CNVs

		211 genes	6 overlap	13 overlap	31 overlap	0 overlap	1 overlap	19 overlap	13 overlap	1 overlap	7 overlap	1 overlap	9 overlap	1 overlap	3 overlap	0 overlap	0 overlap
breakpoints	**CNV type**	**Genes**	**de novo Epi4k [1]**	**Intolerant (10%) [2]**	**Intolerant (25%) [2]**	**Known EE genes**	**de novo in ID trio [5-6]**	**de novo in ASD [7-10]**	**Epilepsy CNV Genes [11-14]**	**DUP genes - Epilepsy [3]**	**DEL genes - epilepsy [3]**	**DUP genes - Neuro [3]**	**DEL genes - Neuro [3]**	**DUP genes - autism [3]**	**DEL genes - autism [3]**	**Signature Under 10Mbp Dels p [4]**	**Signature Under 10Mbp Dups p [4]**
chr3:151514590-151538170	deletion	AADAC															
chr3:185131753-187214923	duplication	ADIPOQ															
chr3:185131753-187214923	duplication	ADIPOQ-AS1															
chr7:16918472-17407061	duplication	AGR3:AHR															
chr7:16918472-17407061	duplication	AHR															
chr3:185131753-187214923	duplication	AHSG															
chr15:85815949-86140791	duplication	AKAP13						AKAP13	AKAP13								
chr8:68020804-68135095	duplication	ARFGEF1	ARFGEF1	ARFGEF1	ARFGEF1												
chr17:41215805-41952726	duplication	ARL4D															
chrX:69438694-69582975	duplication	ARR3															
chr4:47585672-47896236	duplication	ATP10D						ATP10D									
chrX:69438694-69582975	duplication	AWAT1															
chr1:187227118-196024958	duplication	B3GALT2															
chr12:76683857-76982825	duplication	BBS10															
chr2:32832625-33320957	duplication	BIRC6		BIRC6	BIRC6			BIRC6									
chr19:40969518-41038340	duplication	BLVRB															
chr6:3119466-3129905	duplication	BPHL															
chr17:41215805-41952726	duplication	BRCA1															
chr1:92303122-92578324	duplication	BRDT															
chr17:71841082-72718161	duplication	BTBD17															
chr1:92303122-92578324	duplication	BTBD8															
chr6:26411364-26467182	deletion	BTN2A1															
chr6:26411364-26467182	deletion	BTN2A3P															
chr6:26411364-26467182	deletion	BTN3A3															
chr17:41215805-41952726	duplication	C17orf105															
chr17:71841082-72718161	duplication	C17orf77															
chr7:7120557-7313294	duplication	C1GALT1					C1GALT1										
chr3:185131753-187214923	duplication	C3orf65															
chr4:113390782-113487520	duplication	C4orf21															
chr9:207735-361025	duplication	C9orf66							C9orf66								
chr9:132507232-132783902	duplication	C9orf78						C9orf78									
chr4:71171720-71275301	deletion	CABS1															
chr19:45284031-45296810	duplication	CBLC															
chr17:71841082-72718161	duplication	CD300A															
chr17:71841082-72718161	duplication	CD300C															
chr17:71841082-72718161	duplication	CD300E															
chr17:71841082-72718161	duplication	CD300LB															
chr17:71841082-72718161	duplication	CD300LD															
chr17:71841082-72718161	duplication	CD300LF											CD300LF				
chr17:41215805-41952726	duplication	CD300LG															
chr1:91988685-92130915	deletion	CDC7						CDC7									
chr1:187227118-196024958	duplication	CDC73															
chr4:47585672-47896236	duplication	CORIN															
chr3:185131753-187214923	duplication	CRYGS															
chr8:68020804-68135095	duplication	CSPP1						CSPP1									
chr17:3492855-3560888	deletion	CTNS															
chr1:206316872-206327339	deletion	CTSE															

breakpoints	CNV type	Genes	de novo Epi4k [1]	Intolerant (10%) [2]	Intolerant (25%) [2]	Known EE genes	de novo in ID trio [5-6]	de novo in ASD [7-10]	Epilepsy CNV Genes [11-14]	DUP genes - Epilepsy [3]	DEL genes - epilepsy [3]	DUP genes - Neuro [3]	DEL genes - Neuro [3]	DUP genes - autism [3]	DEL genes - autism [3]	Signature Under 10Mbp Dels p [4]	Signature Under 10Mbp Dups p [4]
chr15:22764593-23173181	deletion	CYFIP1		CYFIP1	CYFIP1				CYFIP1		CYFIP1		CYFIP1		CYFIP1		
chr10:135256762-135353499	deletion	CYP2E1									CYP2E1		CYP2E1				
chr10:14987110-15027214	deletion	DCLRE1C						DCLRE1C	DCLRE1C								
chr3:53317500-53329768	deletion	DCP1A															
chr3:185131753-187214923	duplication	DGKG		DGKG	DGKG			DGKG									
chr17:41215805-41952726	duplication	DHX8		DHX8	DHX8												
chrx:32446527-32628462	deletion	DMD			DMD												
chr17:71841082-72718161	duplication	DNAI2															
chr3:185131753-187214923	duplication	DNAJB11															
chr9:207735-361025	duplication	DOCK8		DOCK8	DOCK8				DOCK8								
chr17:41215805-41952726	duplication	DUSP3						DUSP3									
chr3:185131753-187214923	duplication	EIF4A2															
chr1:225993806-226028496	deletion	EPHX1															
chr1:92303122-92578324	duplication	EPHX4			EPHX4												
chr17:41215805-41952726	duplication	ETV4															
chr3:185131753-187214923	duplication	ETV5															
chr1:187227118-196024958	duplication	FAM5C		FAM5C	FAM5C												
chr3:185131753-187214923	duplication	FETUB	FETUB														
chr14:61607162-62476906	duplication	FLJ22447															
chr16:2928181-2998053	deletion	FLYWCH1															
chr16:2928181-2998053	deletion	FLYWCH2									FLYWCH2		FLYWCH2				
chr9:132507232-132783902	duplication	FNBP1															
chr9:108206884-108302402	deletion	FSD1L															
chr11:134152030-134194937	deletion	GLB1L3	GLB1L3		GLB1L3												
chr1:187227118-196024958	duplication	GLRX2															
chr17:71841082-72718161	duplication	GPR142															
chr17:71841082-72718161	duplication	GPRC5C		GPRC5C	GPRC5C												
chr22:24346991-24395156	deletion	GSTT1															
chr22:24346991-24395156	deletion	GSTTP1															
chr22:24346991-24395156	deletion	GSTTP2															
chr11:6740308-6805900	deletion	GVINP1															
chr14:61607162-62476906	duplication	HIF1A															
chr14:61607162-62476906	duplication	HIF1A-AS2															
chr3:185131753-187214923	duplication	HRG	HRG														
chr1:91988685-92130915	deletion	HSP90B3P															
chr21:15748775-15754006	duplication	HSPA13															
chr21:34641156-34835149	duplication	IFNAR1															
chr21:34641156-34835149	duplication	IFNGR2															
chr3:185131753-187214923	duplication	IGF2BP2			IGF2BP2												
chr21:34641156-34835149	duplication	IL10RB															
chr6:137282117-137361670	deletion	IL20RA							IL20RA								
chr7:110965837-111321438	deletion	IMMP2L															
chr17:71841082-72718161	duplication	KIF19															
chrX:69438694-69582975	duplication	KIF4A			KIF4A			KIF4A									
chr3:185131753-187214923	duplication	KNG1															
chr3:182841152-182923907	duplication	LAMP3															
chr21:40776019-40809714	duplication	LCA5L															
chr3:45671268-45871203	deletion	LIMD1															
chr3:45671268-45871203	deletion	LIMD1-AS1															
chr2:110828463-110973573	deletion	LINC00116															
chr2:32832625-33320957	duplication	LINC00486															

breakpoints	CNV type	Genes	de novo Epi4k [1]	Intolerant (10%) [2]	Intolerant (25%) [2]	Known EE genes	de novo in ID trio [5-6]	de novo in ASD [7-10]	Epilepsy CNV Genes [11-14]	DUP genes - Epilepsy [3]	DEL genes - epilepsy [3]	DUP genes - Neuro [3]	DEL genes - Neuro [3]	DUP genes - autism [3]	DEL genes - autism [3]	Signature Under 10Mbp Dels p [4]	Signature Under 10Mbp Dups p [4]
chr3:185131753-187214923	duplication	LIPH															
chr17:41215805-41952726	duplication	LOC100130581															
chr7:7120557-7313294	duplication	LOC100131257															
chr2:32832625-33320957	duplication	LOC100271832															
chr3:185131753-187214923	duplication	LOC253573															
chr15:22764593-23173181	deletion	LOC283683							LOC283683								
chr3:185131753-187214923	duplication	LOC344887															
chr22:24346991-24395156	deletion	LOC391322															
chr1:187227118-196024958	duplication	LOC440704															
chr10:135256762-135353499	deletion	LOC619207									LOC619207		LOC619207				
chr2:32832625-33320957	duplication	LTBP1			LTBP1			LTBP1									
chr3:45671268-45871203	deletion	LZTFL1															
chr2:110828463-110973573	deletion	MALL															
chr3:185131753-187214923	duplication	MAP3K13															
chr3:185131753-187214923	duplication	MASP1			MASP1												
chr10:54525678-54531534	deletion	MBL2															
chr3:182841152-182923907	duplication	MCF2L2															
chr10:14987110-15027214	deletion	MEIG1							MEIG1								
chr17:41215805-41952726	duplication	MEOX1															
chr17:71841082-72718161	duplication	MGC16275															
chr3:185131753-187214923	duplication	MIR1248															
chr1:187227118-196024958	duplication	MIR1278															
chr17:41215805-41952726	duplication	MIR2117															
chr2:110828463-110973573	deletion	MIR4436B1															
chr2:110828463-110973573	deletion	MIR4436B2															
chr2:32832625-33320957	duplication	MIR4765															
chr21:33632971-33645249	duplication	MIS18A															
chr17:41215805-41952726	duplication	MPP3															
chr8:15948235-16021468	deletion	MSR1															
chr17:10207809-10254757	deletion	MYH13			MYH13												
chr17:10348288-10358006	deletion	MYH4															
chr17:41215805-41952726	duplication	NBR1															
chr17:41215805-41952726	duplication	NBR2															
chr4:113390782-113487520	duplication	NEUROG2															
chr4:47585672-47896236	duplication	NFXL1															
chr6:137282117-137361670	deletion	NHEG1							NHEG1								
chr15:22764593-23173181	deletion	NIPA1	NIPA1						NIPA1		NIPA1		NIPA1		NIPA1		
chr15:22764593-23173181	deletion	NIPA2							NIPA2		NIPA2		NIPA2		NIPA2		
chr2:110828463-110973573	deletion	NPHP1								NPHP1		NPHP1		NPHP1			
chr11:6740308-6805900	deletion	OR2AG2															
chr12:76683857-76982825	duplication	OSBPL8			OSBPL8												
chrX:69438694-69582975	duplication	P2RY4															
chrX:69438694-69582975	duplication	PDZD11															
chr1:89266173-89304701	duplication	PKN2		PKN2	PKN2												
chr14:69922607-69972990	duplication	PLEKHD1															
chr14:61607162-62476906	duplication	PRKCH			PRKCH												
chr4:71171720-71275301	deletion	PROL1															
chr9:132507232-132783902	duplication	PTGES						PTGES									
chr12:21578559-21629928	duplication	PYROXD1			PYROXD1												
chr17:71841082-72718161	duplication	RAB37											RAB37				
chrX:69438694-69582975	duplication	RAB41															

breakpoints	CNV type	Genes	de novo Epi4k [1]	Intolerant (10%) [2]	Intolerant (25%) [2]	Known EE genes	de novo in ID trio [5-6]	de novo in ASD [7-10]	Epilepsy CNV Genes [11-14]	DUP genes - Epilepsy [3]	DEL genes - epilepsy [3]	DUP genes - Neuro [3]	DEL genes - Neuro [3]	DUP genes - autism [3]	DEL genes - autism [3]	Signature Under 10Mbp Dels p [4]	Signature Under 10Mbp Dups p [4]
chr12:21578559-21629928	duplication	RECQL		RECQL	RECQL												
chr3:185131753-187214923	duplication	RFC4			RFC4												
chr1:187227118-196024958	duplication	RGS1															
chr1:187227118-196024958	duplication	RGS13															
chr1:187227118-196024958	duplication	RGS18															
chr1:187227118-196024958	duplication	RGS2						RGS2									
chr1:187227118-196024958	duplication	RGS21															
chr17:71841082-72718161	duplication	RPL38															
chr3:185131753-187214923	duplication	RPL39L															
chr3:185131753-187214923	duplication	RTP1	RTP1														
chr3:185131753-187214923	duplication	RTP4															
chr3:45671268-45871203	deletion	SACM1L															
chr1:169574047-169580274	deletion	SELP						SELP									
chr3:185131753-187214923	duplication	SENP2															
chr17:3492855-3560888	deletion	SHPK															
chr12:129165912-129336953	duplication	SLC15A4															
chr14:69922607-69972990	duplication	SLC39A9															
chr3:45671268-45871203	deletion	SLC6A20			SLC6A20												
chr4:71171720-71275301	deletion	SMR3A															
chr4:71171720-71275301	deletion	SMR3B															
chr14:61607162-62476906	duplication	SNAPC1															
chr3:185131753-187214923	duplication	SNORA4															
chr3:185131753-187214923	duplication	SNORA63															
chr3:185131753-187214923	duplication	SNORA81															
chr3:185131753-187214923	duplication	SNORD2															
chr17:41215805-41952726	duplication	SOST															
chr9:4588700-4606335	deletion	SPATA6L						SPATA6L	SPATA6L								
chr19:40969518-41038340	duplication	SPTBN4		SPTBN4	SPTBN4												
chr3:185131753-187214923	duplication	ST6GAL1			ST6GAL1												
chr1:185106737-185137530	duplication	SWT1															
chr14:61607162-62476906	duplication	SYT16						SYT16									
chr3:17390957-17487701	deletion	TBC1D5															
chr3:185131753-187214923	duplication	TBCCD1		TBCCD1	TBCCD1												
chr1:92303122-92578324	duplication	TGFBR3															
chr17:41215805-41952726	duplication	TMEM106A															
chr17:41215805-41952726	duplication	TMEM106A-AS1															
chr12:129165912-129336953	duplication	TMEM132C															
chr14:61607162-62476906	duplication	TMEM30B															
chr3:185131753-187214923	duplication	TMEM41A															
chr21:34641156-34835149	duplication	TMEM50B															
chr22:22313954-22560977	duplication	TOP3B			TOP3B												
chr9:132507232-132783902	duplication	TOR1A															
chr9:132507232-132783902	duplication	TOR1B			TOR1B												
chr3:185131753-187214923	duplication	TRA2B															
chr1:185106737-185137530	duplication	TRMT1L			TRMT1L												
chr1:187227118-196024958	duplication	TROVE2						TROVE2									
chr17:3492855-3560888	deletion	TRPV1															
chr2:32832625-33320957	duplication	TTC27															
chr17:71841082-72718161	duplication	TTYH2															
chr15:22764593-23173181	deletion	TUBGCP5			TUBGCP5			TUBGCP5	TUBGCP5		TUBGCP5		TUBGCP5				
chr1:187227118-196024958	duplication	UCHL5															

breakpoints	CNV type	Genes	de novo Epi4k [1]	Intolerant (10%) [2]	Intolerant (25%) [2]	Known EE genes	de novo in ID trio [5-6]	de novo in ASD [7-10]	Epilepsy CNV Genes [11-14]	DUP genes - Epilepsy [3]	DEL genes - epilepsy [3]	DUP genes - Neuro [3]	DEL genes - Neuro [3]	DUP genes - autism [3]	DEL genes - autism [3]	Signature Under 10Mbp Dels p [4]	Signature Under 10Mbp Dups p [4]
chr1:162411286-162486355	duplication	UHMK1															
chrX:74505779-74606768	duplication	UPRT															
chr9:132507232-132783902	duplication	USP20															
chr17:402843-488260	deletion	VPS53		VPS53	VPS53			VPS53									
chr5:110416995-110446579	duplication	WDR36															
chrX:74505779-74606768	duplication	ZDHHC15															
chrX:46289765-46412525	duplication	ZNF673															
chrX:46289765-46412525	duplication	ZNF674															
chrX:46289765-46412525	duplication	ZNF674-AS1															

SUPPLEMENTARY TABLE 7: Detailed phenotypes of patients with de novo CNVs

TRIO	CNV	Age at onset	First seizure type	Additional seizure types	EEG	MRI	DEV prior	DEV	OTHER
iq	2q24 deletion including *SCN1A*	< 1 yr	unk	GTC, atypical absence	background slowing and disorganization, bilateral independent sharp waves	subtle abnormality of R hippocampus with loss of internal architecture	normal	mild ID, FSIQ=60; working ~3 grade levels below expected; obsessive compulsive tendencies	
fx	2q24 duplication encompassing *SCN2A*	7 mo	IS	none	hypsarrhythmia, burst suppression type in sleep	normal	normal	developmental arrest with seizure onset; global delays at 12 mo; motor skills caught up by 2 yrs	
eh	15q11q13 dup, 5 Mb	2 wks	IS	multiple	initial EEG normal; repeat EEG, hypsarrhythmia; at 8 mo, diffuse slow background, frequent bilateral sharp epileptiform discharges; at 5 yrs, ESES during sleep	diffuse hypomyelination, brain atrophy at 7 mo	normal	significant delays; at 6 yrs, sits supported, has 2-3 words, follows simple commands, uses communication board	ex-35-week premature infant; spastic quadriplegia; hypogammaglobuinemia
gq	15q11q13 dup, 8.4 Mb	8 mo	convulsive	GTC, tonic, atonic	generalized slowing; frequent generalized slow spike wave discharges	generalized atrophy	mild delays by 3-4 mo	severe delays; at 21 yrs, no meaningful interactions	spastic quadriplegia
ag	47,XY psu dic(15;15)(q13;q13)	8 mo	IS	none reported	hypsarrythmia	normal	mild to moderate gross motor delay	at 8mo, not rolling or sitting; global delays	
fu	unbalanced translocation resulting in 15q26 deletion (1.8 Mb) and 16q22 duplication (16.3 Mb)	8 mo	IS	none reported	hypsarrythmia	dysgenesis of corpus callosum, mild prominence of extra-axial fluid	delayed	unk	multiple anomalies: hypospadias with chordee, esotropia, narrow airway, small jaw
hj	5p15 deletion	6 mo	Febrile seizure	focal, GTC, frequent status, atypical absence; refractory despite callosotomy, VNS placement	multifocal spike, polyspike and spike wave discharges	normal	unk	signficant delays; nonverbal at 13 yrs, in wheelchair	chronic esophagitis
cy	7q11 deletion	3 mo	IS	aytpical absence	hypsarrhythmia with superimposed multifocal independent spike/wave discharges	mild prominence of 3rd and 4th ventricles, mild thinning of corpus callosum	normal	severe delays, few words at 5 years, cognitive functioning at level of 1-2 yo	
iz	14q23 (GPHN) deletion	2.5 yrs (prior had one FS as a toddler)	febrile status epilepticus	refractory tonic seizures; drop seizures	generalized slowing with frequent runs of slow spike-wave discharges	normal	normal	mild language delay	microcephaly
aia	9pter deletion	5 mo	IS	none noted by 7 mo	disorganized background, multifocal spike discharges, modified hypsarrhythmia	normal	reported normal	hypotonic, head lag at 6 mo; not reaching, rolling, babbling at 7 mo;	small muscular VSD; undescended testes
ig	1p22 (ZNF644) duplication	2 yrs	absence	at 5 yrs, developed GTC, also myoclonic, drop attacks, tonic seizures	generalized abnormalities; focal sharps; paroxysmal fast bursts	evidence of callosotomy and resection	unk	mild to moderate intellectual disability, lives in a group home as an adult; behavioral outbursts	
le	8p23 deletion	3 yrs 10 mo	GTC at 3yr 10 mo then drop at 4 yrs	GTC, tonic, myoclonic, atypical absence, absence, atonic; all refractory	generalized slow spike wave discharges, polyspikes, bilateral independent spikes	normal	normal	regression following seizure onset, moderate developmental, behavioral, attention, speech delays with minimal verbal output	
gc	7q22 deletion	8 mo	IS, responded to ACTH	none	hypsarrythmia	normal	unk	IQ 80; language delay; ADHD; normal motor development	
ad	1q21 (TAR) duplication	8 mo	IS	none	hypsarrhythmia, multifocal spike, polyspike and spike wave discharges	normal	unk	unk	
ahp	7q31 duplication	7 mo	IS, responded to ACTH	none	hypsarrhthmia	normal	normal	mild speech delay at 12 mo, otherwise normal	
aib	2q37 deletion	5 mo	IS	tonic, clusters of spasms	hypsarrhythmia, multifocal spike, polyspike and spike wave discharges	normal	normal	crawled at 18 mo, walked at 2 1/2 yrs, nonverbal	autism spectrum disorder
bda	17q12 del	8 mo	IS	myoclonic, myoclonic status, generalized	Diffuse encephalopathy, slight response to pyridoxine	Cerebellar atrophy, cranial thickening	normal	Nonverbal, severe ID	Normal fasting glucose at 43 yrs