

## Supplementary Information

# Genome Wide Copy Number Variation Study Associates Metabotropic Glutamate Receptor Gene Networks with Attention Deficit Hyperactivity Disorder

Josephine Elia, Joseph T. Glessner, Kai Wang, Nagahide Takahashi, Corina J. Shtir, Dexter Hadley, Patrick M.A. Sleiman, Haitao Zhang, Cecilia E. Kim, Reid Robison, Gholson J. Lyon, James H. Flory, Jonathan P. Bradfield, Marcin Imielinski, Cuiping Hou, Edward C. Frackelton, Rosetta M. Chiavacci, Takeshi Sakurai, Cara Rabin, Frank A. Middleton, Kelly A. Thomas, Maria Garris, Frank Mentch, Christine M. Freitag, Hans-Christoph Steinhausen, Alexandre A. Todorov, Andreas Reif, Aribert Rothenberger, Barbara Franke, Eric O. Mick, Herbert Roeyers, Jan Buitelaar, Klaus-Peter Lesch, Tobias Banaschewski, Richard P. Ebstein, Fernando Mulas, Robert D. Oades, Joseph Sergeant, Edmund Sonuga-Barke, Tobias J. Renner, Marcel Romanos, Jasmin Romanos, Andreas Warnke, Susanne Walitza, Jobst Meyer, Haukur Pálmason, Christiane Seitz, Sandra K. Loo, Susan L. Smalley, Joseph Biederman, Lindsey Kent, Philip Asherson, Richard J.L. Anney, J. William Gaynor, Philip Shaw, Marcella Devoto, Peter S. White, Struan F.A. Grant, Joseph D. Buxbaum, Judith L. Rapoport, Nigel M. Williams, Stanley F. Nelson, Stephen V. Faraone, Hakon Hakonarson

## Supplementary Note

### CNV Calls and Review of Significant Loci

No additional “CNV burden” was observed in cases vs. controls, rather the distribution of calls made was highly comparable (Supplementary Fig. 1). We established CNV call reliability in Illumina and Perlegen data by observing Mendelian patterns of inheritance. Trios were first verified by genotype inheritance and analyzed to establish the quality of CNV calls from both Illumina and Perlegen platforms based on observed inheritance. Based on all CNV calls called in trios from the Illumina CHOP data, 8,647 CNVs observed in offspring were inherited from a parent while 437 CNVs were putatively *de novo* which is a *de novo* rate of 4.811%. Based on all CNV calls called in trios from the Perlegen IMAGE data, 1,862 CNVs observed in offspring were inherited

from a parent while 505 CNVs were putatively *de novo* which is a *de novo* rate of 21.335%. 51 IMAGE cases, 22 deletion loci, and 5 duplication loci had multiple *de novo* events due to low data quality and were excluded as outliers; once excluded, 785 CNVs were inherited and 63 were *de novo* which lowered the observed *de novo* rate to an acceptable level of 7.429%. Based on CNVs observed in parents from Illumina CHOP data, 9,305 CNVs were passed to the child while 7,432 CNVs were not inherited resulting in a 55.595% inheritance rate. Based on all CNVs observed in parents from Perlegen IMAGE data, 2,114 CNVs were passed to the child while 3,789 CNVs were not inherited resulting in a 35.812% inheritance rate. We excluded 65 parent samples that were outliers with 20 or greater CNVs not inherited to offspring and filtering these samples out resulted in 1,204 CNVs were passed to the child while 1,221 were not inherited resulting in a 49.650% inheritance rate which established confidence in this CNV call set.

It is intractable to review all PennCNV calls and wasteful to exclude CNVs smaller than a size threshold. Instead, we statistically score the loci based on all CNVs detected and review these nominally associated CNVR loci for appropriate overlap, signal quality, and Mendelian inheritance. As in Table 1, all reported loci show at least one case with the CNV inherited from a parent, in cases where both parents were available.

In total, there are 3,506 cases and 13,327 controls, representing greater than a three-fold abundance of control samples to robustly define CNVs to be absent or at a lower frequency than case samples. Although the number of CNVs detected per sample was as high as 70, there are actually inferred normal diploid (CN=2) calls which make

every sample equivalent. These CNVs are very rare and thus the number of observed CNV calls will vary between samples.

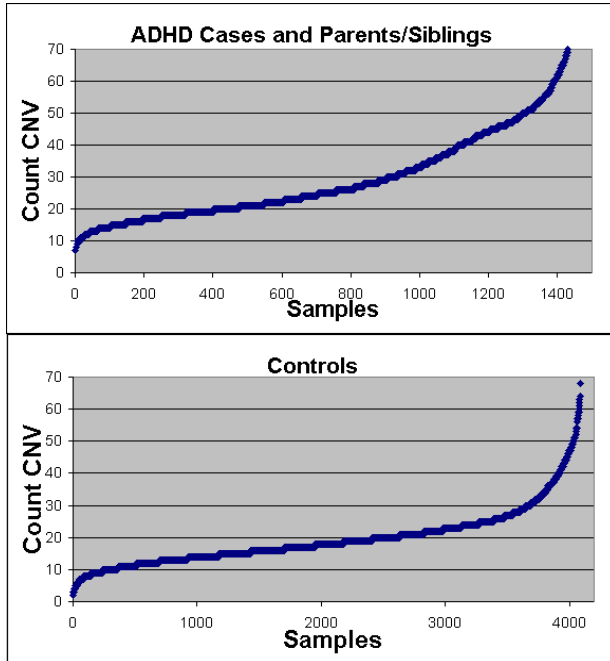
### **Analysis of Genotype Call Genome-Wide Association**

Full scale genotype genome-wide association was performed and the genomic inflation factor (GIF) was at an acceptable level (GIF=1.02409). We also checked pairwise population concordance to check for and filter out cryptic relatedness which could give rise to rare CNVs specific to ultra-stratified subpopulations of Europe. We performed Transmission Disequilibrium Test (TDT) statistic using Plink on 397 ADHD cases with both parents on the CHOP Illumina HumanHap550 genotype data (Supplementary Table 3). The top result with more than one significant SNP in a region was chr4p12  $P(\text{rs1018199})=2.71 \times 10^{-5}$  and  $P(\text{rs11724347})=6.19 \times 10^{-5}$  which impacts *TEC*. We also performed a case:control genotype genome-wide association on 735 cases and 2,298 controls using the same Illumina data set (Supplementary Table 4). The strongest signal was chr19p12  $P(\text{rs2081051})=4.60 \times 10^{-6}$  and  $P(\text{rs399686})=4.72 \times 10^{-6}$  residing between *ZNF66* and *ZNF85*. Lastly, 623 ADHD cases with both parents on the IMAGE Perlegen 600K data were analyzed with TDT statistic (Supplementary Table 5). The most significant signal was chr5q23.1  $P(\text{rs17144308})=9.70 \times 10^{-6}$  and  $P(\text{rs2043053})=3.36 \times 10^{-5}$  which is 237 kb from the closest proximal gene *DTWD2*. Taken together, SNPs residing around exon 4 of contactin 3 (*CNTN3*) appear to replicate most consistently between Illumina and Perlegen ADHD TDT statistics. SNP rs12488030 is common to both platforms  $P=2.51 \times 10^{-3}$  Illumina and  $P=4.97 \times 10^{-3}$  Perlegen. There are two supporting SNPs in close proximity also showing significance Illumina:  $P(\text{rs4073942})=2.78 \times 10^{-3}$

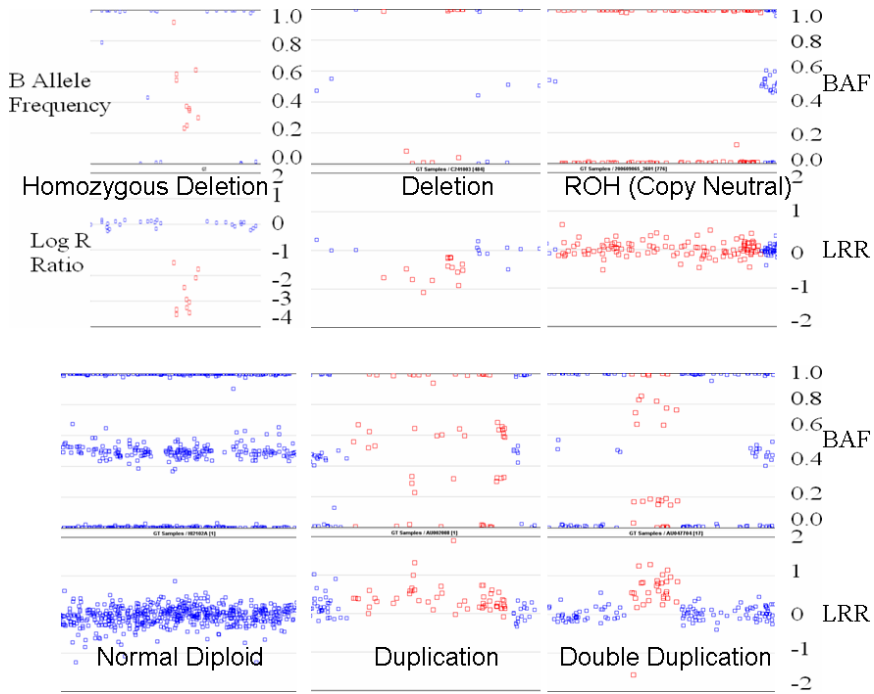
and  $P(\text{rs9869828})=8.61 \times 10^{-3}$  in addition Perlegen:  $P(\text{rs11915713})=1.86 \times 10^{-5}$  and  
 $P(\text{rs7372975})=7.59 \times 10^{-5}$

**Supplementary Figures:**

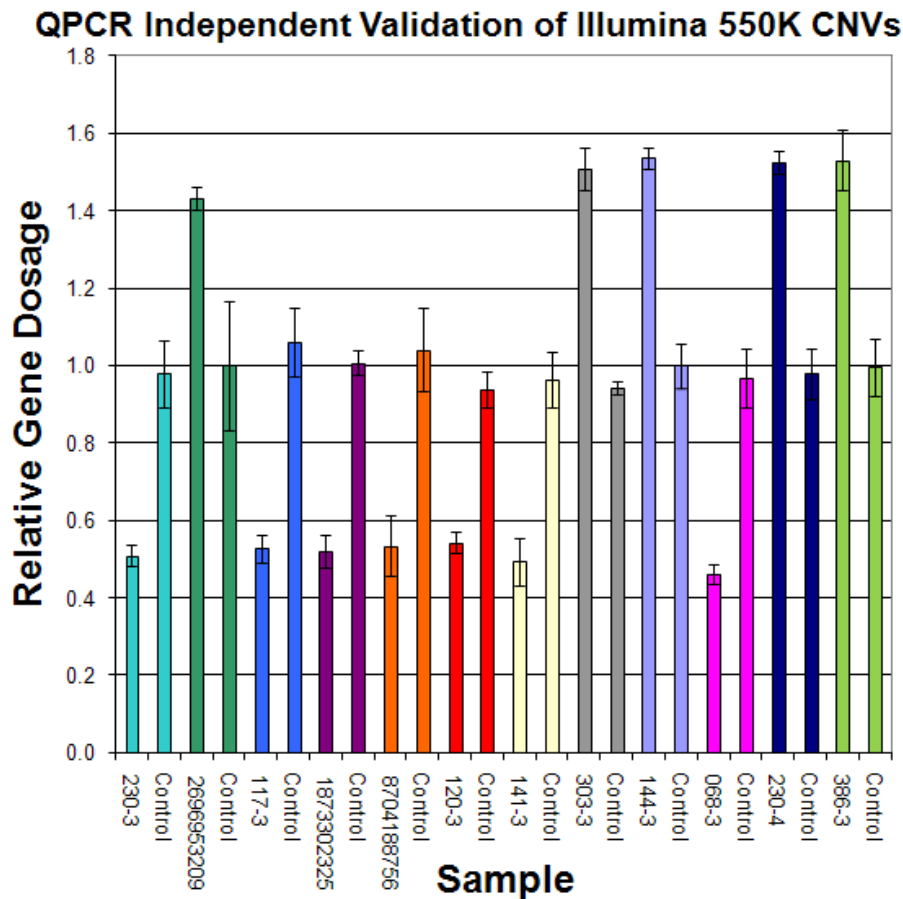
**Supplementary Figure 1.** Distribution of CNV calls per individual cases (top panel) vs controls (bottom panel).



**Supplementary Figure 2.** Examples of CNV observance based on B-allele frequency (BAF) and Log R Ratio (LRR).



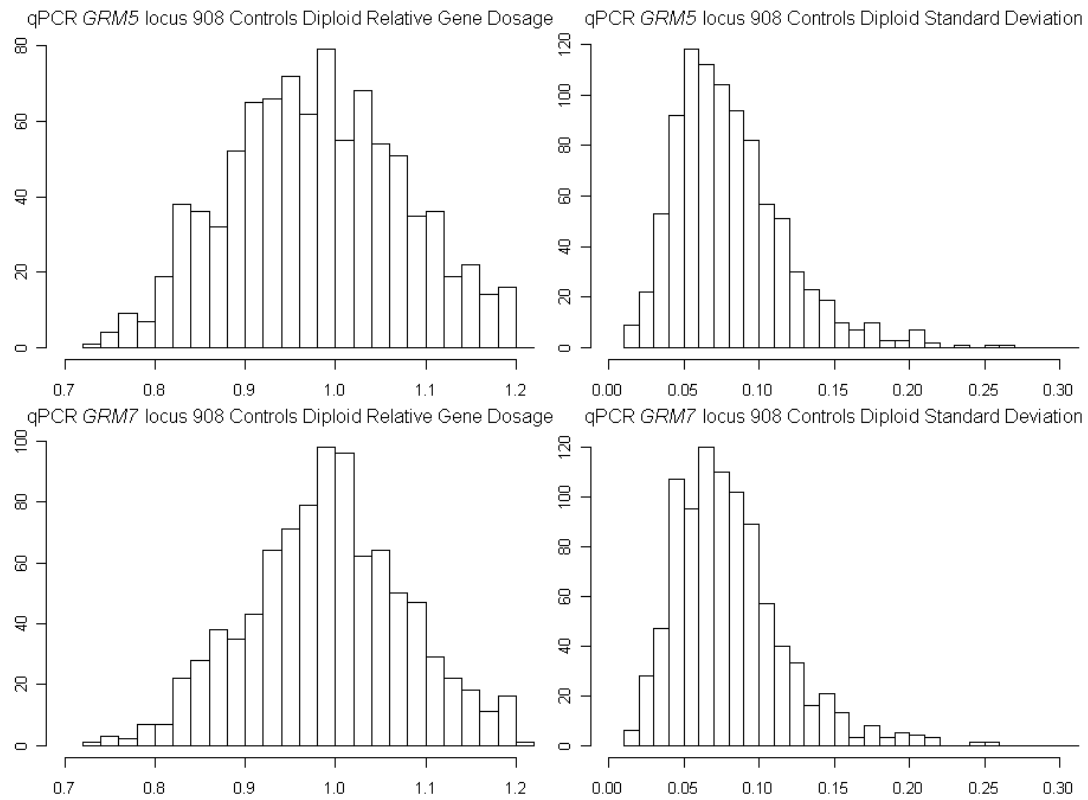
**Supplementary Figure 3.** Independent qPCR Validation of CHOP ADHD Case Discovery Cohort (Illumina Human Hap550).



- 11q14.3 GRM5 Del; ■ 7q36.2 DPP6 Dup; ■ 5q12.3 SGTB/NLN Del; ■ 1p32.3 USP24 Del;
- 7q31.33 GRM8 Del; ■ 19q13.11 SLC7A10 Del; ■ 3p26.3 CNTN4 Del; ■ 4q25 LARP7 Dup;
- 2p12 CTNNA2 Dup; ■ 3p26.1 GRM7 Del; ■ 1p31.1 NEGR1 Dup; ■ 6q24.3 GRM1 Dup

Fluorescent probe-based qPCR assays using Roche Universal probe were designed to validate every candidate CNV with a completely independent test (representative series shown for each locus in case and control pairs). Error bars denote the standard deviation of quadruplicate runs. Del, deletion; Dup, duplication.

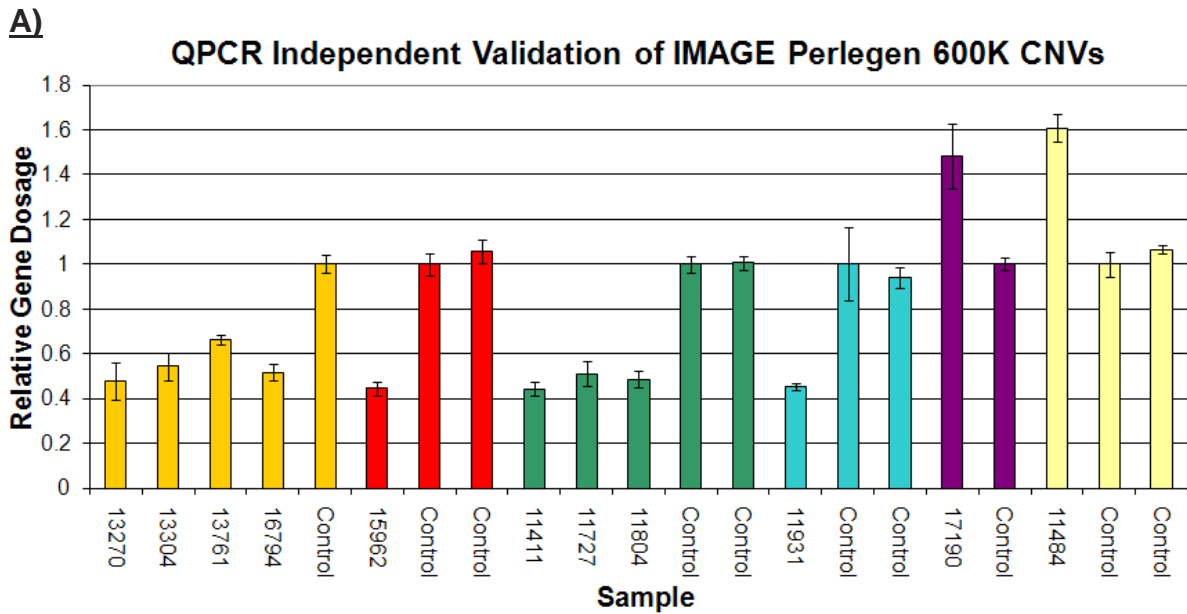
**Supplementary Figure 4.** Independent qPCR Validation of Controls Negative for CNVs



908 controls called for absence of CNV (diploid) by PennCNV in associated regions were screened by qPCR to limit the possibility of false negative calls. Controls were all confirmed to be diploid tightly distributed around one with low level of standard deviation.



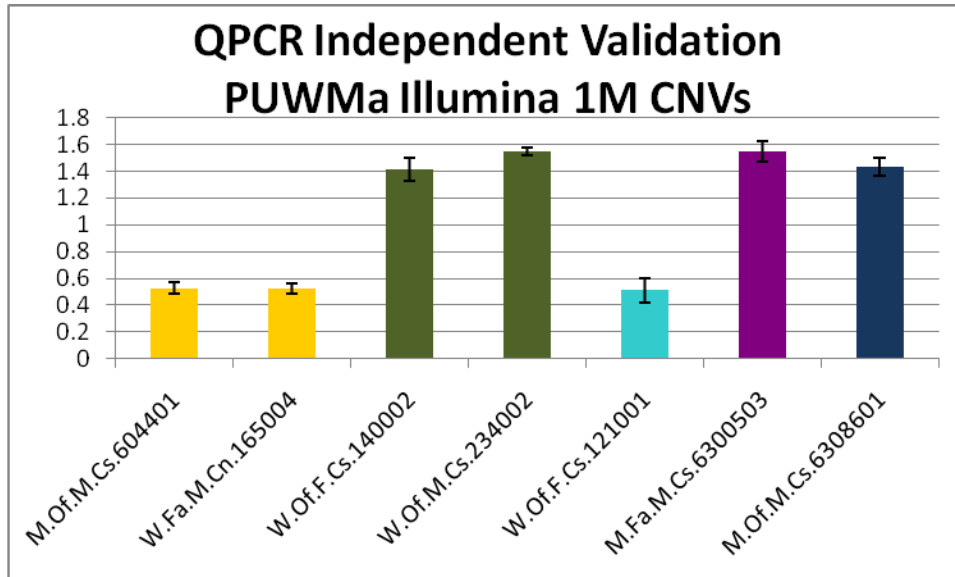
**Supplementary Figure 5.** Independent qPCR Validation of Replication Cohorts ADHD Cases A) IMAGE (Perlegen 600k) B) PUWMa (Illumina 1M) C) IMAGE II (Affymetrix 5.0)



■ 11q14.3 GRM5 Del; ■ 5q12.3 SGTB/NLN Del; ■ 1p32.3 USP24 Del; ■ 19q13.11 SLC7A10 Del; ■ 4q25 LARP7 Dup; ■ 2p12 CTNNA2 Dup. Samples in IMAGE/NIMH not available: 17580 (11q14.3), 1135 (7q36.2).

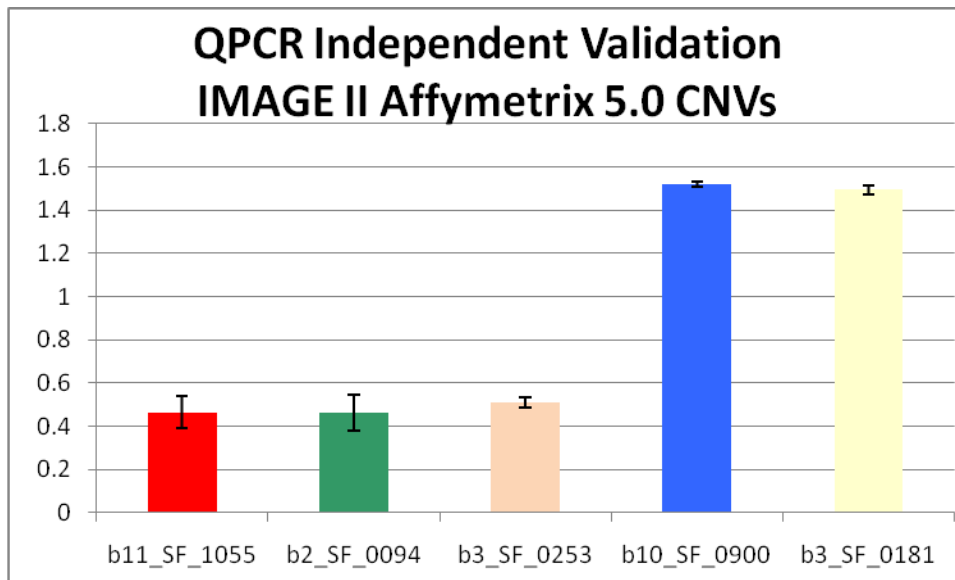
Fluorescent probe-based qPCR assays using Roche Universal probe were designed to validate every candidate CNV with a completely independent test (11 of the 14 IMAGE samples with replicating CNV calls for the loci reported were available for validation and all validated in comparison with control pairs; the other 3 loci were visually validated – see Supplementary Figures 6 and 7). Error bars denote the standard deviation of quadruplicate runs. Del: deletion; Dup: duplication.

**B)**



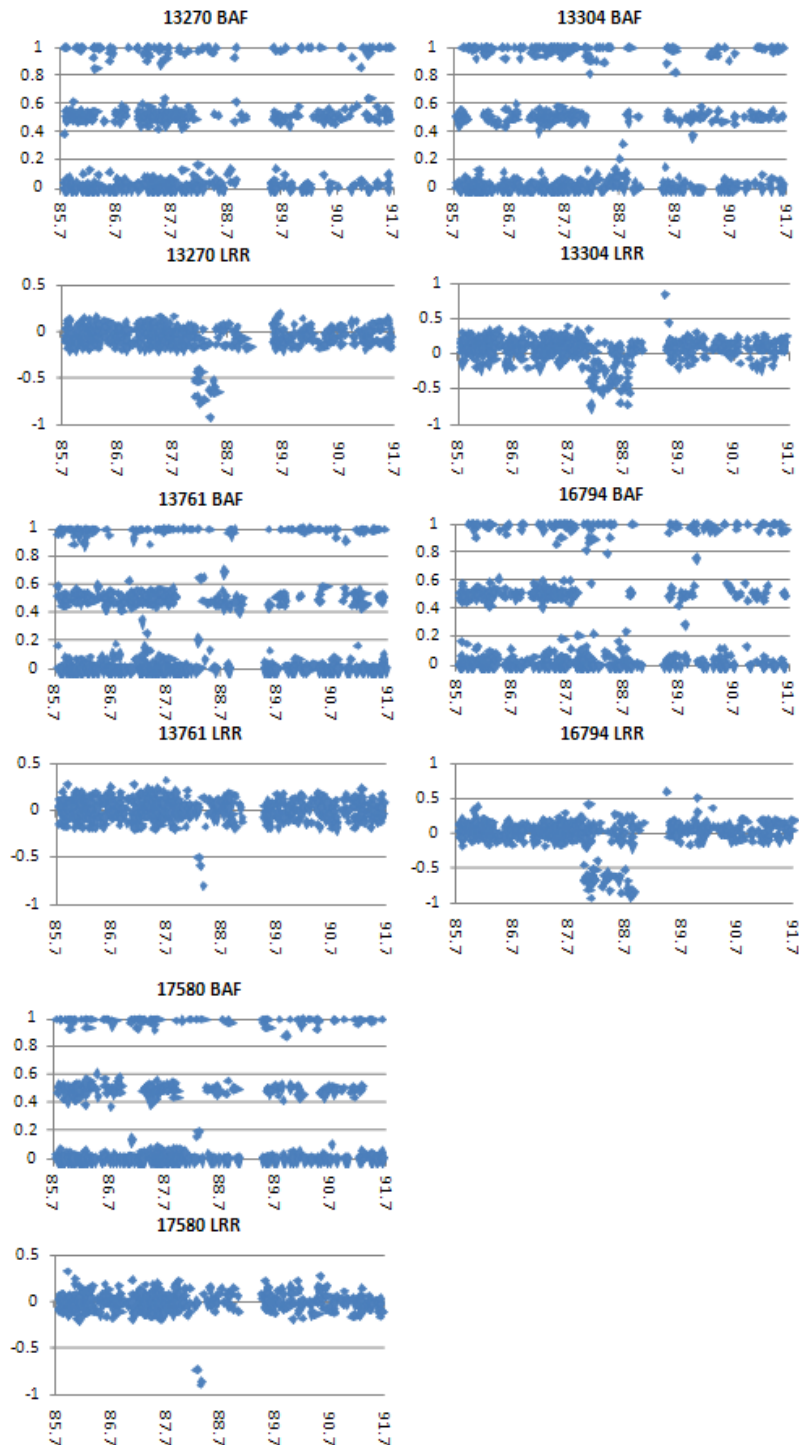
■ 11q14.3 GRM5 Del; ■ 7q36.2 DPP6 Dup; ■ 19q13.11 SLC7A10 Del; ■ 4q25 LARP7 Dup; ■ 1p31.1 NEGR1 Dup;

**C)**

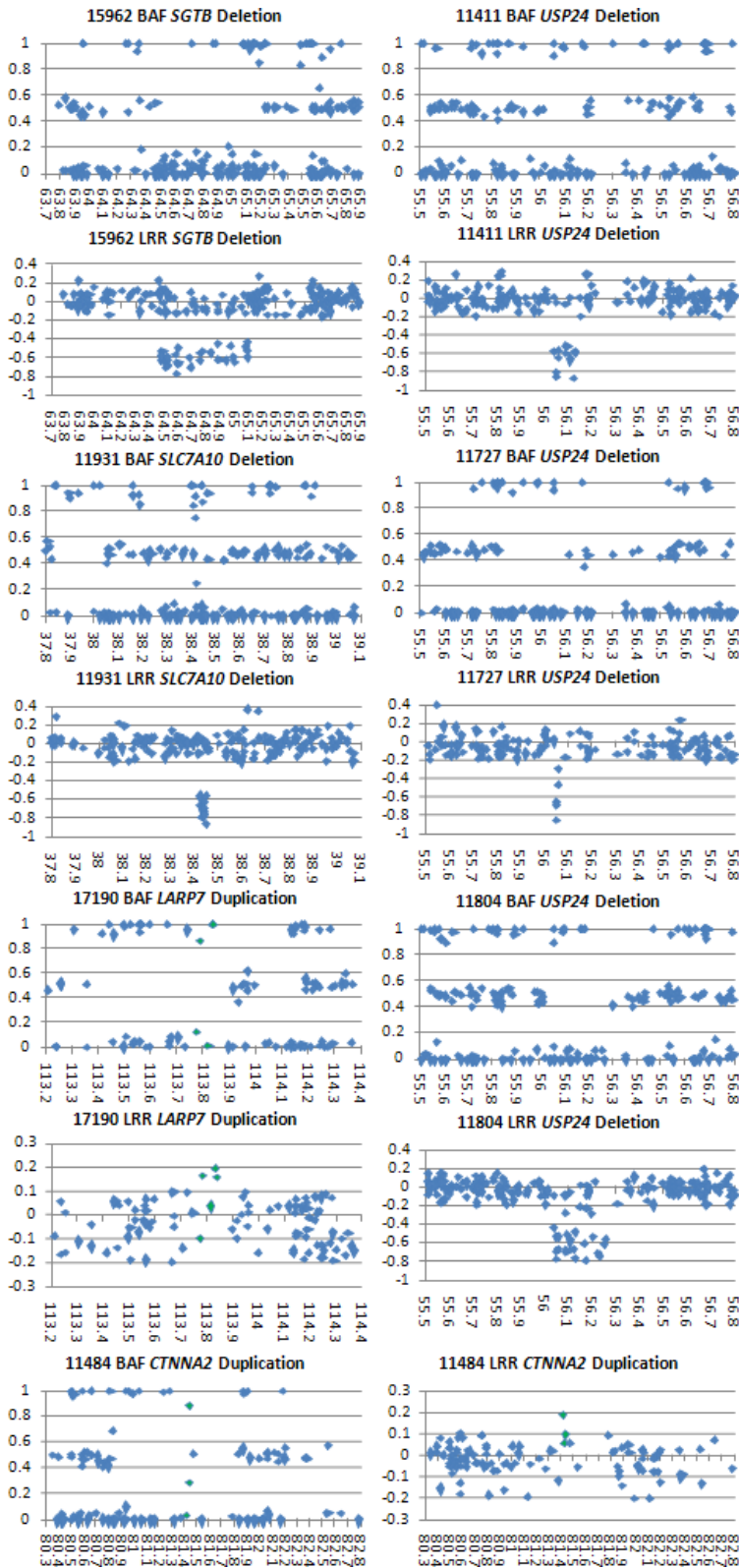


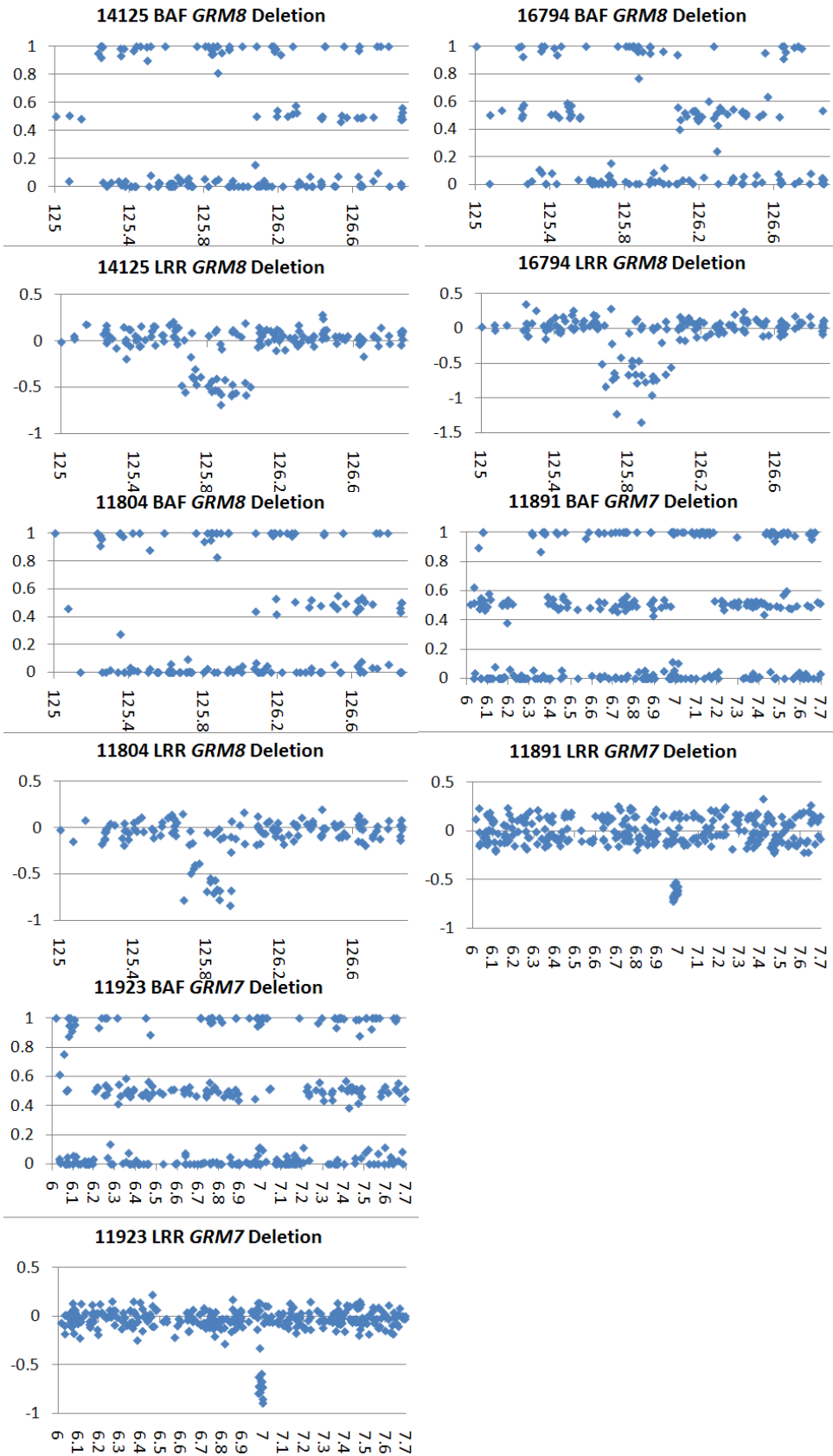
■ 5q12.3 SGTB/NLN Del; ■ 1p32.3 USP24 Del; ■ 3p26.3 CNTN4 Del; ■ 2p12 CTNNA2 Dup; ■ 6q24.3 GRM1 Dup

**Supplementary Figure 6.** Normalized SNP Level Perlegen 600K Data. The X axis shows base pair position in Megabases on chromosome 11. Raw SNP Level Data Showing GRM5 Deletion in five samples from IMAGE Perlegen 600K Data Normalized by Adapted PennCNV-Affy Protocol. Genotype data termed B-allele frequency (BAF) and intensity data termed Log R Ratio (LRR) plotted.

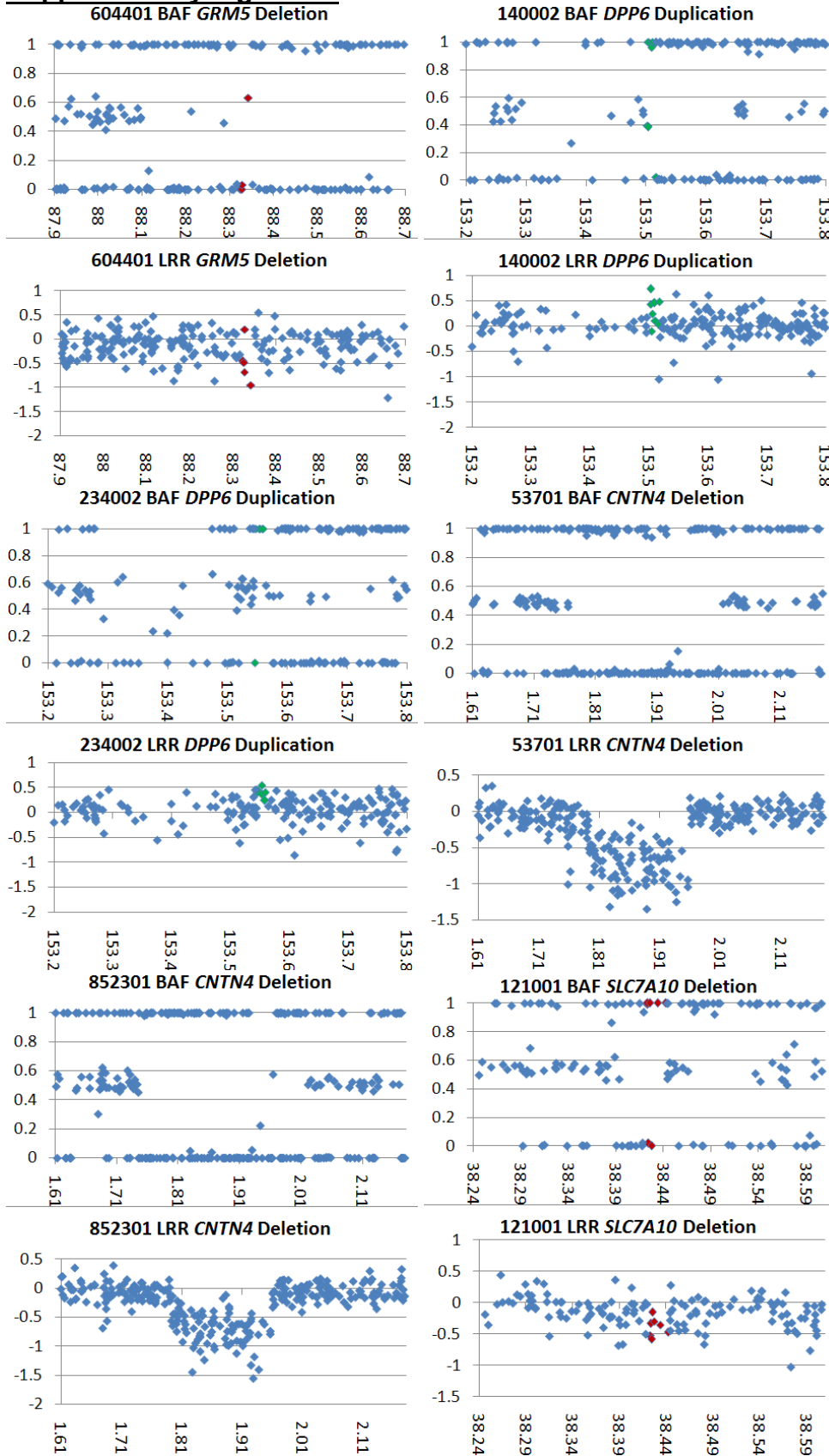


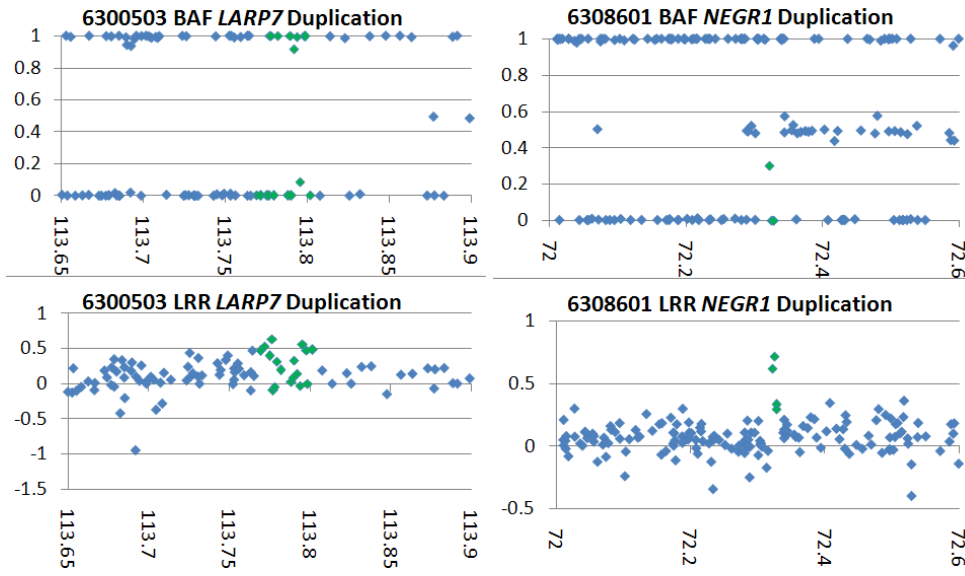
**Supplementary Figure 7A** Full SNP-Level Normalized Perlegen 600K Data.



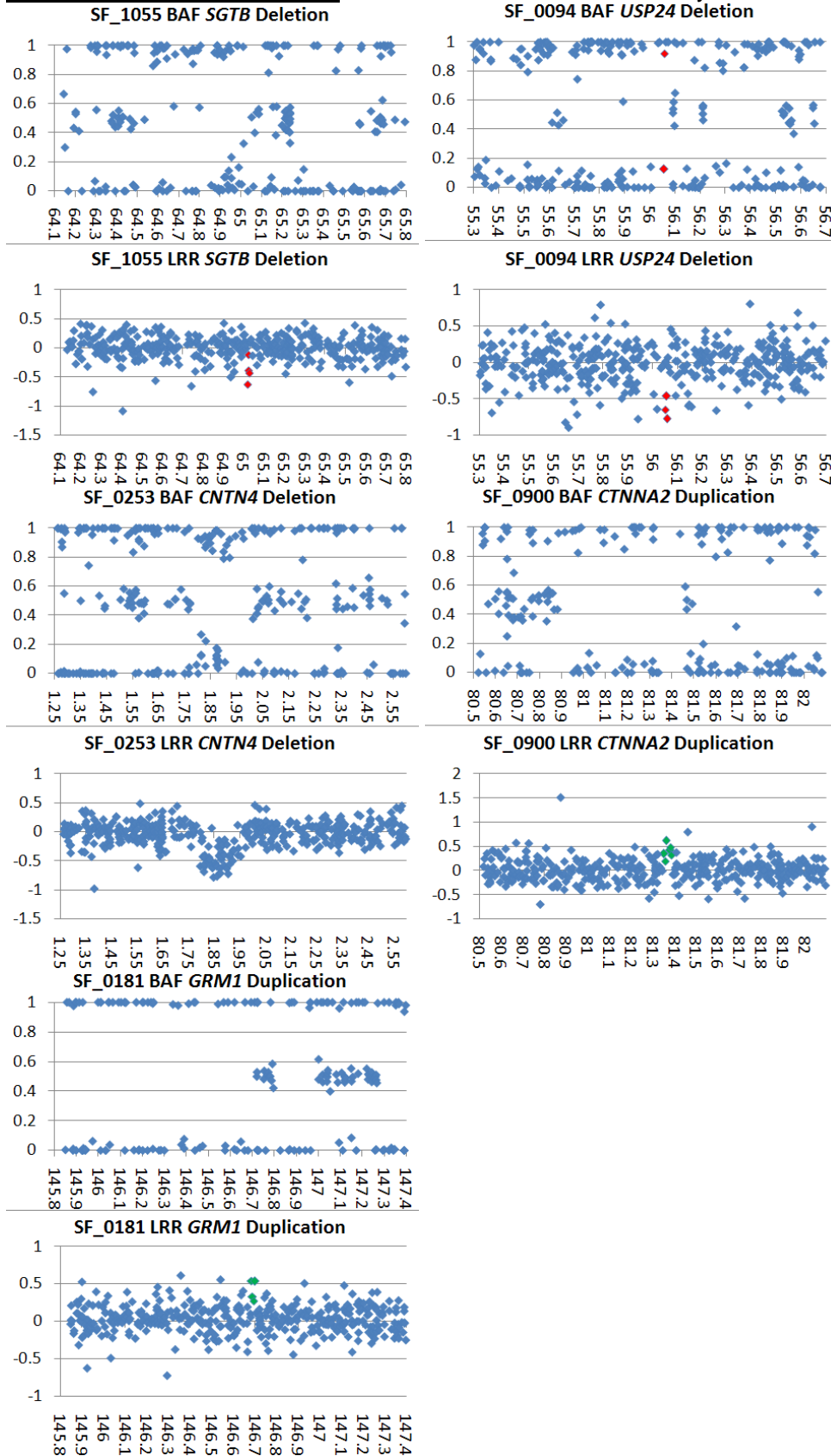


**Supplementary Figure 7B.** Full SNP-Level Normalized Illumina 1M PUWMA Data.





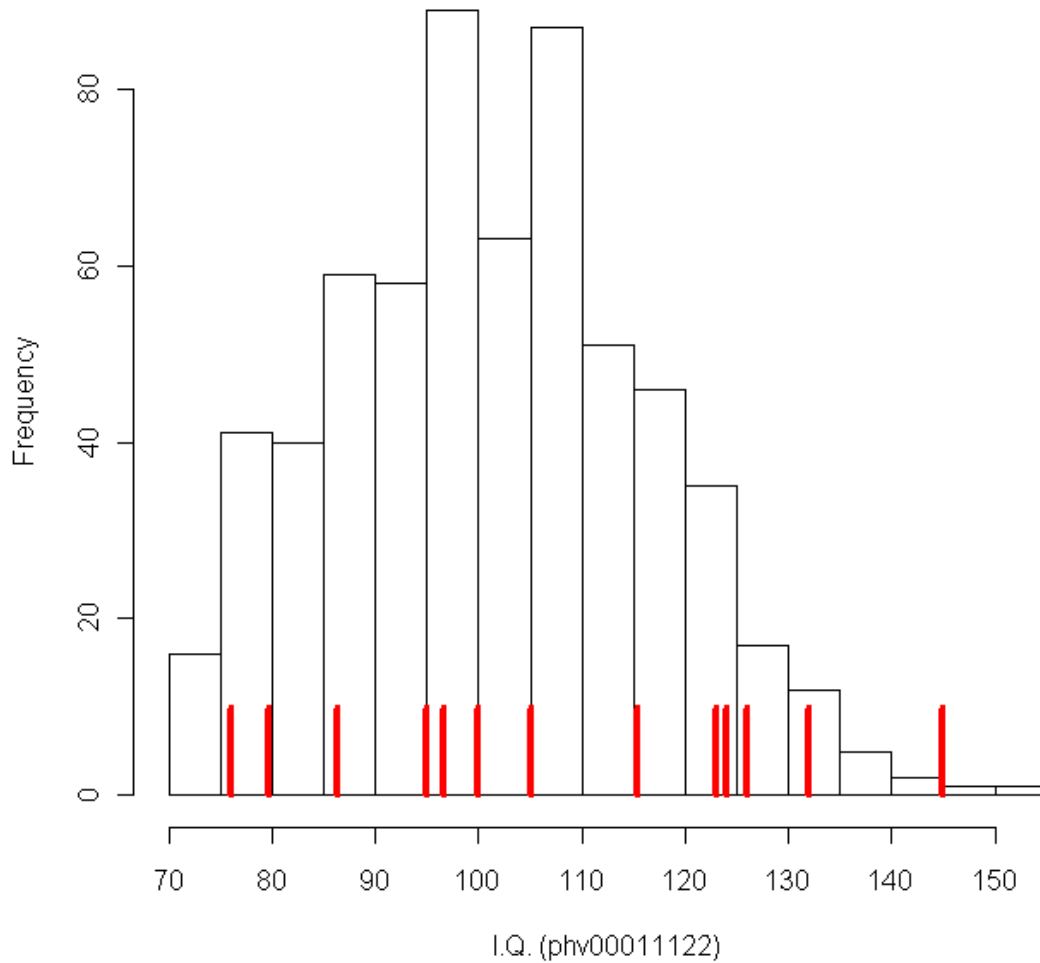
**Supplementary Figure 7C.** Full SNP-Level Normalized Affymetrix 5.0 IMAGE II Data.



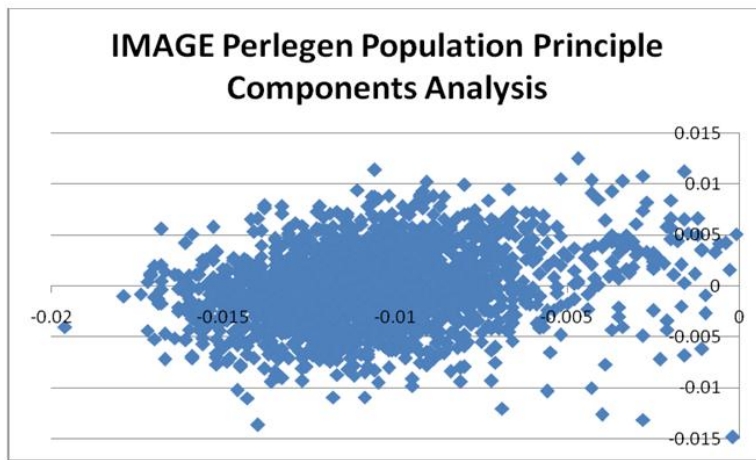
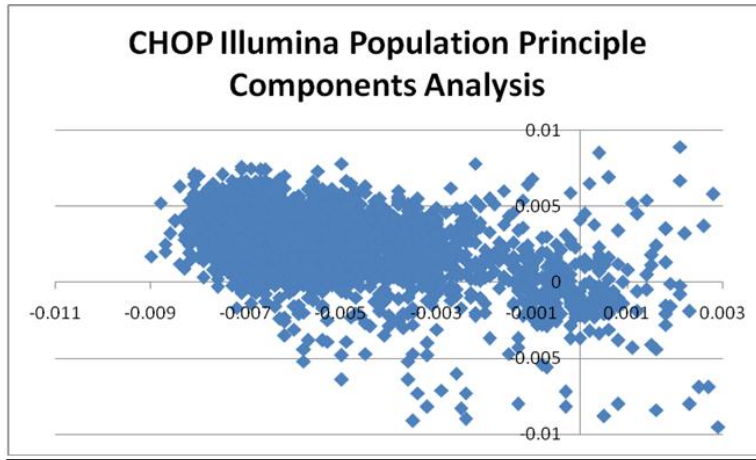


**Supplementary Figure 8.** Intelligence Quotient (IQ) ADHD Population Distribution. IQ measures in the ADHD subjects ranged from 70-155, with mean IQ of 103). ADHD subjects with GRM CNV (*GRM5*, *GRM7* and *GRM8* deletions *GRM1* duplication) are inserted in red color showing normal distribution across the ADHD cohort.

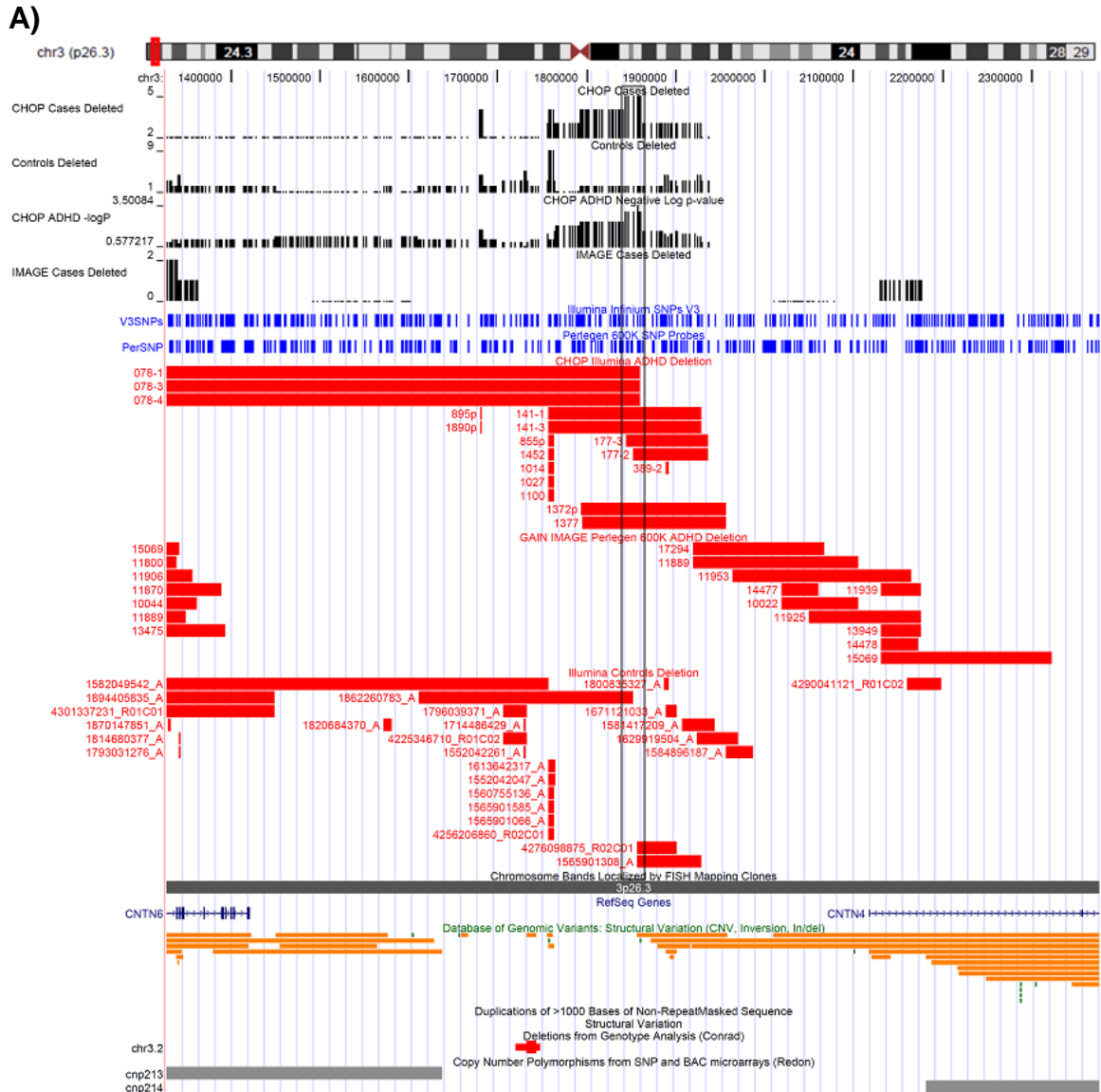
**Full Scale I.Q. (prorated) Red Lines: GRM CNV Subjects**



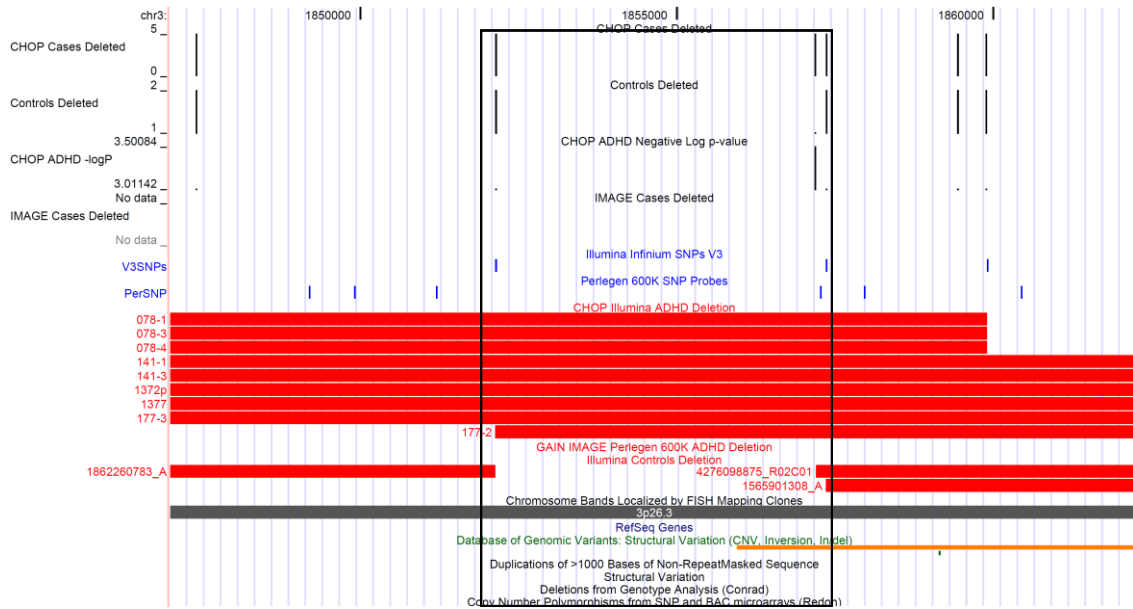
**Supplementary Figure 9.** Eigenstrat Principle Components Analysis. Cases and Controls were simultaneously analyzed to minimize population substructure in case control CNV association. Samples deviating from the Caucasian cluster shown were removed. The genomic inflation factor (GIF) within Plink was at an acceptable level (GIF=1.02409). We also checked pairwise population concordance to check for and filter out cryptic relatedness which could give rise to rare CNVs specific to ultra-stratified subpopulations of Europe.



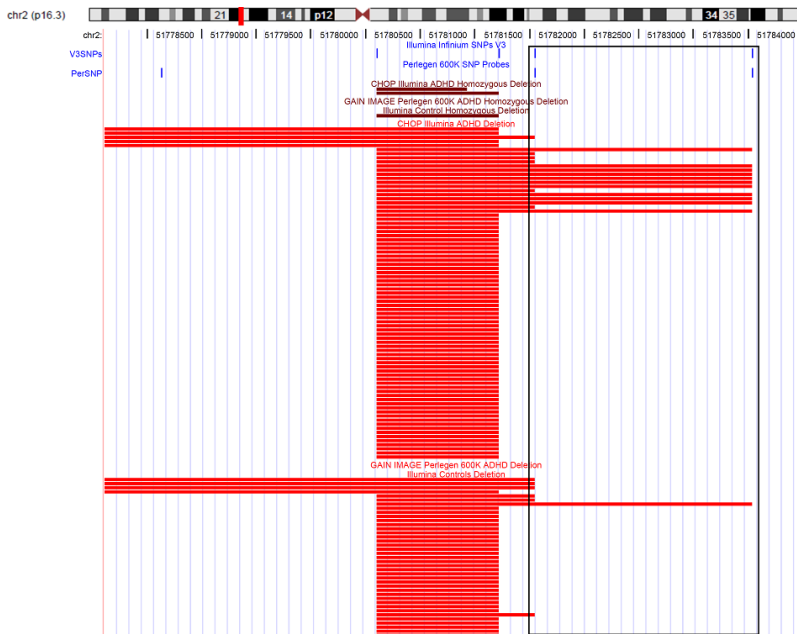
**Supplementary Figure 10.** Example of the SNP-based statistics applied and the resulting highest significance region Called. Examples from chr 3 are shown; A) 1,327,963-2,376,095 and B) 1,847,000-1,862,261. Complex CNV overlap is simplified by producing SNP-based statistics. As seen in plots for cases deleted and controls deleted, each SNP has a specific number of CNVs. The cases and controls are compared with a Fisher's exact test and the negative log p value is shown in the third plot. Regions of significance ranging within a power of ten are reported and the region of highest significance (local minimum p-value) within 1MB is reported. The IMAGE cases deleted plot shows only one case sample #11939 since the remaining red regions 3' are parents.



B)



**Supplementary Figure 11.** CNV peninsula false positive association example. An example from chr 2 is shown (location 51,777,616-51,784,033). All significant CNVRs are reviewed for CNV peninsulas indicating uncertainty in boundary truncation.



## **Supplementary Tables**

**Supplementary Table 1.** Clinical Demographics of Study Participants.

<b>ADHD Cohort</b>	<b>N</b>	<b>ADHD subjects Age range</b>	<b>Ancestry</b>	<b>ADHD ascertainment</b>
CHOP ADHD trios	349	6-18	European	K-SADS-IVR
CHOP ADHD cases	664	6-18	European	Clinical ADHD diagnosis & treatment with ADHD meds; K-SADS-IVR on majority
NIMH ADHD trios	128	6-12	European	DICA; Conners Scales
UTAH cases	90	19-60	European	WRAADDs, WURS, PRS, strict DSM-IV criteria, including age of onset before 7
IMAGE ADHD trios	642	6-17	European	PACS, Conners, SDQ, WISC
IMAGE II ADHD trios	787	5-14	European	K-SADS German version, Kinder-DIPS, Conners parent and teacher scales, WISC, K-ABC
PUWMA trios	864	6-18	European	K-SADS

PACS: Parental Account of Child Symptoms; Conners: Behavioral rating scales; SDQ: Strength and Difficulties Questionnaire; WISC: Wechsler Intelligence Scale for Children (WISC-IV); KSADS-IVR: Schedule for Affective Disorders and Schizophrenia for School-Age Children-IVR; DICA: Diagnostic Interview for Children and Adolescents; Kinder-DIPS: Diagnostic Interview for Psychiatric Disorders in Children, K-ABC: Kaufman-ABC intelligence scale. WRAADDs=Wender-Reimherr Adult Attention Deficit Disorder Scale; WURS=Wender Utah Rating Scale; PRS=Parent Rating Scale.

**Supplementary Table 2.** K-SADS ADHD Severity of of CHOP Study Participants in Inattentive, Impulsive, and Hyperactive Domains.

Diagnostic Criteria	Score 1	Score 2	Score 3	Score 4
Often Careless	7	40	372	81
Loses Things	18	126	277	79
Difficulty Finishing	16	90	311	83
Listening	10	22	320	148
Concentration*	2	25	337	135
Distracted	1	10	307	182
Organizing	19	79	304	98
Avoiding	19	55	278	148
Forgetful	19	75	290	116
Interrupts	28	73	305	94
Acts Before Thinking	28	112	283	77
Shifts Activities	72	134	247	47
Blurts†	135	82	232	48
Difficulty Waiting Turn	80	172	200	48
Hyperactive	53	127	227	93
Fidgeting	15	47	301	137
Difficulty Staying Seated	45	80	287	88
On the Go	49	89	255	107
Talks Excess	37	77	255	131
Difficulty Playing Quietly	98	120	233	49

\*Concentration 1 record missing †Blurts 3 records missing. Scores 1 and 2 means that symptoms are within the normal range while scores 3 and 4 are excessive.

**Supplementary Table 3.** Sample Cohorts (Cases and Controls) Used in the Study and Source of Sample DNA

Sample Source	Array Platform	Number	Case/Control	DNA Source
CHOP	Illumina 550k	1,013	Case	Blood/Cell line
NIMH	Illumina 550k	128	Case	Blood
Utah	Illumina 550k	90	Case	Blood
CHOP	Illumina 550k	4,105	Control	Blood
IMAGE	Perlegen 600k	624	Case	Blood /Cell line
Psoriasis	Perlegen 600K	1,600	Control	Blood /Cell line
Depression Control	Perlegen 600K	1,697	Control	Blood
PUWMa	Illumina 1M	864	Case	Blood
SAGE	Illumina 1M	2,211	Control	Blood
PUWMa Parents	Illumina 1M	1,258	Control	Blood
IMAGEII	Affymetrix 5.0	787	Case	Blood/Saliva
IMAGEII (nonGAIN)	Affymetrix 6.0	898	Control	Blood
AGRE Parents	Affymetrix 5.0	1,558	Control	Cell line

**Supplementary Table 4.** TDT Analysis of 397 ADHD Cases and Parents from CHOP genotyped on the Illumina HH550 chip.

CHR	SNP	BP	A1	A2	T	U	OR	CHISQ	P
18	rs8095193	58834095	1	2	167	92	1.815	21.72	3.16E-06
17	rs4357980	13498634	1	2	99	174	0.569	20.6	5.65E-06
18	rs8091710	72897492	1	2	29	73	0.3973	18.98	1.32E-05
14	rs899116	97495185	1	2	101	172	0.5872	18.47	1.73E-05
13	rs9595945	48099556	1	2	245	160	1.531	17.84	2.40E-05
4	rs1018199	47927632	1	2	35	80	0.4375	17.61	2.71E-05
1	rs3795324	157456184	2	1	91	157	0.5796	17.56	2.78E-05
3	rs6444186	188156541	1	2	81	36	2.25	17.31	3.18E-05
9	rs11144627	75654927	2	1	46	14	3.286	17.07	3.61E-05
8	rs1462011	108104653	1	2	199	125	1.592	16.9	3.94E-05
X	rs5991935	100480088	1	2	22	59	0.3729	16.9	3.94E-05
7	rs1013572	78350227	1	2	63	118	0.5339	16.71	4.35E-05
11	rs952619	20316347	1	2	108	177	0.6102	16.71	4.37E-05
4	rs7689018	85116479	1	2	41	87	0.4713	16.53	4.79E-05
18	rs1943825	69128567	2	1	97	162	0.5988	16.31	5.37E-05
4	rs4696821	8473961	1	2	210	135	1.556	16.3	5.39E-05
18	rs1943823	69131624	2	1	157	237	0.6624	16.24	5.57E-05
4	rs11724347	47923023	1	2	26	64	0.4062	16.04	6.19E-05
1	rs7530899	76950752	2	1	89	151	0.5894	16.02	6.28E-05
18	rs4890560	41457783	1	2	93	156	0.5962	15.94	6.54E-05
6	rs2677099	45527900	1	2	220	144	1.528	15.87	6.79E-05
12	rs11067228	113556980	2	1	231	153	1.51	15.84	6.88E-05
6	rs2790102	45540192	1	2	222	146	1.521	15.7	7.44E-05
1	rs4926757	48961624	1	2	192	122	1.574	15.61	7.80E-05
11	rs17147479	84055504	1	2	137	79	1.734	15.57	7.93E-05
17	rs9913261	12026365	2	1	89	150	0.5933	15.57	7.96E-05
9	rs7041883	135352660	1	2	17	49	0.3469	15.52	8.19E-05
12	rs7309946	103478293	2	1	119	188	0.633	15.51	8.22E-05
7	rs10226468	42907176	2	1	144	219	0.6575	15.5	8.27E-05
5	rs438418	2902436	2	1	78	36	2.167	15.47	8.37E-05
8	rs12682232	108078371	2	1	199	128	1.555	15.42	8.63E-05
X	rs5956634	123092612	2	1	59	110	0.5364	15.39	8.74E-05
7	rs7786719	42850356	1	2	133	205	0.6488	15.34	8.99E-05
6	rs910586	45518290	1	2	221	146	1.514	15.33	9.04E-05
6	rs9395010	44453984	1	2	152	91	1.67	15.31	9.11E-05
14	rs11844273	97489409	1	2	100	163	0.6135	15.09	1.02E-04
2	rs11904235	36288350	1	2	64	27	2.37	15.04	1.05E-04
11	rs487518	131283728	1	2	150	225	0.6667	15	1.08E-04
6	rs6920606	33105652	2	1	164	242	0.6777	14.99	1.08E-04
14	rs2014525	97491178	1	2	109	174	0.6264	14.93	1.12E-04
11	rs7948111	23403649	1	2	65	117	0.5556	14.86	1.16E-04
16	rs12598067	60940038	2	1	65	117	0.5556	14.86	1.16E-04
6	rs9472494	45559814	1	2	223	149	1.497	14.72	1.25E-04
7	rs533486	99085345	2	1	163	240	0.6792	14.71	1.25E-04
8	rs7835921	96345468	1	2	157	96	1.635	14.71	1.26E-04
4	rs827019	8460842	2	1	69	122	0.5656	14.71	1.26E-04

CHR:Chromosome number, SNP:SNP identifier, A1:Minor allele code, A2:Major allele code, T:Transmitted minor allele count, U:Untransmitted allele count, OR:TDT odds ratio, CHISQ:TDT chi-square statistic, P:TDT asymptotic p-value



**Supplementary Table 5.** Case:Control Analysis of 735 ADHD Cases and 2,298 Unrelated Controls from CHOP genotyped on the Illumina HH550 chip.

CHR	SNP	BP	A1	A2	F_A	F_U	OR	CHISQ	P
18	rs16943400	23086102	1	2	0.02778	0.08875	0.2934	57.53	3.33E-14
3	rs7649108	166136126	1	2	0.3156	0.2497	1.386	24.88	6.11E-07
6	rs9390261	145283744	1	2	0.02585	0.009072	2.899	24.54	7.29E-07
X	rs4609327	37790223	2	1	0.1441	0.08032	1.928	24.48	7.50E-07
X	rs5917547	37803525	2	1	0.1578	0.09074	1.878	24.22	8.59E-07
16	rs2278656	54885245	1	2	0.01443	0.04091	0.3432	22.04	2.67E-06
8	rs17834541	2674349	2	1	0.1083	0.1565	0.6545	21.01	4.56E-06
19	rs2081051	20866811	1	2	0.1382	0.1911	0.6786	21	4.60E-06
19	rs399686	20772798	1	2	0.143	0.1962	0.6833	20.95	4.72E-06
X	rs5917937	39750534	2	1	0.1195	0.06572	1.929	20.93	4.76E-06
19	rs10419820	20943636	2	1	0.1789	0.2357	0.7067	20.9	4.84E-06
X	rs10522011	32517409	1	2	0.05924	0.02509	2.447	19.48	1.02E-05
8	rs11203872	17531028	2	1	0.4342	0.37	1.306	19.34	1.09E-05
X	rs9633179	3535471	2	1	0.1089	0.05969	1.925	19.24	1.15E-05
4	rs10519629	143040375	2	1	0.1864	0.1398	1.409	18.81	1.44E-05
19	rs7253306	20951939	2	1	0.219	0.2759	0.736	18.77	1.48E-05
13	rs9569383	55299477	1	2	0.1415	0.1909	0.6984	18.64	1.58E-05
12	rs12229174	62532933	1	2	0.06054	0.03502	1.776	18.56	1.64E-05
19	rs6511169	20893589	1	2	0.1461	0.1961	0.7014	18.51	1.69E-05
11	rs10833476	21190445	1	2	0.1224	0.08502	1.502	18.48	1.72E-05
2	rs1821659	212064488	2	1	0.3109	0.2527	1.334	18.15	2.05E-05
X	rs2480443	53212284	2	1	0.06525	0.02994	2.262	18.1	2.09E-05
7	rs1486173	45965025	2	1	0.1131	0.07764	1.515	17.91	2.32E-05
15	rs4381545	93039961	2	1	0.2296	0.18	1.358	17.8	2.45E-05
7	rs10265665	96175055	1	2	0.0619	0.0365	1.742	17.79	2.46E-05
10	rs11593585	44391199	1	2	0.1286	0.09093	1.475	17.69	2.60E-05
X	rs4134188	17474194	1	2	0.1016	0.05571	1.917	17.62	2.69E-05
4	rs11131363	63013616	2	1	0.2643	0.212	1.335	17.6	2.72E-05
19	rs1469402	20738115	2	1	0.145	0.1934	0.7075	17.52	2.85E-05
11	rs12279152	133861485	1	2	0.02653	0.01139	2.365	17.43	2.98E-05
X	rs5957334	119125665	2	1	0.06667	0.03136	2.206	17.13	3.49E-05
X	rs6632558	36075450	2	1	0.0812	0.04176	2.028	16.94	3.85E-05
1	rs2057594	117348535	1	2	0.2483	0.1983	1.335	16.89	3.96E-05
8	rs17834523	2672777	1	2	0.09592	0.1367	0.6699	16.84	4.06E-05
7	rs10485959	78702412	2	1	0.3007	0.3595	0.7659	16.83	4.09E-05
X	rs5945330	152438289	2	1	0.08807	0.04698	1.959	16.63	4.55E-05
3	rs16854851	145238402	1	2	0.02381	0.009916	2.435	16.62	4.56E-05
8	rs2237826	17519195	2	1	0.4355	0.376	1.28	16.59	4.65E-05
X	rs16987407	35968032	2	1	0.1041	0.05857	1.868	16.5	4.87E-05
X	rs4089885	22878045	2	1	0.1193	0.07027	1.792	16.47	4.94E-05
1	rs2024766	181385290	2	1	0.5027	0.4424	1.274	16.45	4.99E-05
4	rs9312518	173526549	1	2	0.4639	0.4042	1.276	16.45	5.00E-05
4	rs9997484	173517324	2	1	0.4639	0.4042	1.276	16.45	5.00E-05
17	rs4338847	7870502	1	2	0.3102	0.3679	0.7725	16.35	5.28E-05
12	rs17497206	113000660	2	1	0.1537	0.2011	0.7219	16.33	5.32E-05

CHR:Chromosome, SNP:SNP ID, BP:Physical position (base-pair), A1:Minor allele name (based on whole sample), F\_A:Frequency of this allele in cases, F\_U:Frequency of this allele in controls, A2:Major allele name, OR:Estimated odds ratio (for A1, i.e. A2 is reference), CHISQ:Basic allelic test chi-square (1df), P:Asymptotic p-value for this test.

**Supplementary Table 6.** TDT Analysis of 623 ADHD Cases and Parents from IMAGE genotyped on the Perlegen platform.

CHR	SNP	BP	A1	A2	T	U	OR	CHISQ	P
12	rs3782309	26750663	1	2	172	99	1.737	19.66	9.23E-06
5	rs17144308	117965870	2	1	244	352	0.6932	19.57	9.70E-06
2	rs7609261	80530821	2	1	199	297	0.67	19.36	1.08E-05
3	rs1344870	21282405	2	1	16	52	0.3077	19.06	1.27E-05
18	rs7244637	17876224	1	2	134	215	0.6233	18.8	1.45E-05
1	rs3850879	48004718	1	2	226	143	1.58	18.67	1.56E-05
14	rs2295426	58446208	2	1	209	307	0.6808	18.61	1.60E-05
16	rs7204253	5576184	2	1	114	189	0.6032	18.56	1.64E-05
4	rs1378945	25382295	2	1	212	310	0.6839	18.4	1.79E-05
3	rs11915713	74568983	1	2	176	266	0.6617	18.33	1.86E-05
12	rs11830382	41718893	2	1	198	122	1.623	18.05	2.15E-05
12	rs4761641	93525817	2	1	137	215	0.6372	17.28	3.22E-05
5	rs2043053	117958083	2	1	126	201	0.6269	17.2	3.36E-05
18	rs12965880	22313077	1	2	235	333	0.7057	16.91	3.92E-05
9	rs17306197	97862011	1	2	162	96	1.688	16.88	3.97E-05
8	rs17668689	96254526	1	2	216	310	0.6968	16.8	4.16E-05
2	rs4852567	80556890	2	1	206	298	0.6913	16.79	4.17E-05
13	rs1002468	93085569	2	1	287	197	1.457	16.74	4.30E-05
1	rs10873925	77234323	2	1	305	212	1.439	16.73	4.31E-05
16	rs12596741	17345435	1	2	228	324	0.7037	16.7	4.39E-05
9	rs2991298	3284851	2	1	81	142	0.5704	16.69	4.41E-05
14	rs1427324	58434446	1	2	206	297	0.6936	16.46	4.96E-05
10	rs11258682	13951273	1	2	204	130	1.569	16.4	5.14E-05
4	rs10520276	175420068	2	1	216	140	1.543	16.22	5.63E-05
1	rs17375519	179499648	1	2	75	133	0.5639	16.17	5.78E-05
1	rs10800069	163296159	1	2	232	327	0.7095	16.14	5.87E-05
7	rs13340504	75277632	1	2	142	82	1.732	16.07	6.10E-05
2	rs6543239	104056246	2	1	251	349	0.7192	16.01	6.31E-05
2	rs4664452	162762970	1	2	30	6	5	16	6.33E-05
4	rs16889099	13341184	2	1	48	96	0.5	16	6.33E-05
5	rs12520147	2000122	1	2	158	237	0.6667	15.8	7.04E-05
11	rs10400283	23523711	1	2	222	314	0.707	15.79	7.07E-05
4	rs1378946	25382548	1	2	197	284	0.6937	15.74	7.28E-05
3	rs7372975	74602140	2	1	169	250	0.676	15.66	7.59E-05
17	rs11654470	74388926	2	1	82	141	0.5816	15.61	7.79E-05
3	rs9878591	121464488	1	2	107	173	0.6185	15.56	8.01E-05
12	rs1553953	28724544	1	2	76	133	0.5714	15.55	8.06E-05
11	rs7121790	45021541	1	2	171	252	0.6786	15.51	8.20E-05
12	rs1452231	83750252	2	1	223	314	0.7102	15.42	8.60E-05
7	rs194847	103560404	1	2	347	251	1.382	15.41	8.65E-05
2	rs11902138	80565100	1	2	173	254	0.6811	15.37	8.86E-05
16	rs12932714	80320240	1	2	150	226	0.6637	15.36	8.88E-05
1	rs1015144	200004976	2	1	204	291	0.701	15.29	9.22E-05
22	rs6009441	47873456	1	2	107	172	0.6221	15.14	9.97E-05
8	rs4734069	104169047	1	2	275	191	1.44	15.14	9.97E-05
20	rs2024946	61678306	2	1	112	61	1.836	15.03	1.06E-04

CHR:Chromosome number, SNP:SNP identifier, A1:Minor allele code, A2:Major allele code, T:Transmitted minor allele count, U:Untransmitted allele count, OR:TDT odds ratio, CHISQ:TDT chi-square statistic, P:TDT asymptotic p-value

**Supplementary Table 7.** SNP GWAS Significance of Top Ranked ADHD Associated SNPs Reported by Lesch and Zhou. A) ADHD TDT CHOP Illumina 550k data; B) ADHD Case:Control CHOP Illumina 550k data; C) ADHD IMAGE Perlegen 600k data.

A)

CHR	SNP	BP	A1	A2	T	U	OR	CHISQ	P
2	rs2241685	1896290	1	2	72	62	1.161	0.7463	0.3877
2	rs13395022	79793915	2	1	136	136	1	0	1
2	rs2587695	120038047	1	2	183	197	0.9289	0.5158	0.4726
2	rs2242073	208819551	2	1	108	106	1.019	0.01869	0.8913
2	rs1110998	217169458	1	2	175	159	1.101	0.7665	0.3813
3	rs10510238	2876647	2	1	84	93	0.9032	0.4576	0.4987
3	rs9879164	54040611	2	1	185	198	0.9343	0.4413	0.5065
3	rs2084358	57457928	2	1	182	198	0.9192	0.6737	0.4118
3	rs10490808	59939739	2	1	175	204	0.8578	2.219	0.1363
3	rs10510850	60542142	1	2	90	83	1.084	0.2832	0.5946
4	rs755403	6507714	2	1	195	180	1.083	0.6	0.4386
4	rs10516182	7143981	2	1	155	169	0.9172	0.6049	0.4367
4	rs7697323	7801488	1	2	180	222	0.8108	4.388	0.03619
5	rs173754	65102081	1	2	218	202	1.079	0.6095	0.435
5	rs258082	66166352	1	2	199	205	0.9707	0.08911	0.7653
6	rs160666	2719051	2	1	179	181	0.989	0.01111	0.9161
6	rs2842643	41758714	2	1	180	149	1.208	2.921	0.08744
6	rs3799977	44945334	2	1	209	183	1.142	1.724	0.1891
6	rs8180608	89064414	2	1	178	218	0.8165	4.04	0.04442
6	rs1358601	91532294	1	2	180	181	0.9945	0.00277	0.958
6	rs6921403	154156020	2	1	86	90	0.9556	0.09091	0.763
7	rs2237349	28536203	2	1	176	191	0.9215	0.6131	0.4336
7	rs2002865	154132035	2	1	134	157	0.8535	1.818	0.1776
8	rs6991017	5508780	2	1	127	126	1.008	0.003953	0.9499
8	rs2248529	14657354	1	2	188	190	0.9895	0.01058	0.9181
8	rs4961315	142110882	2	1	186	152	1.224	3.42	0.06441
9	rs2418326	114759028	1	2	141	142	0.993	0.003534	0.9526
9	rs2502731	128056111	2	1	170	178	0.9551	0.1839	0.668
14	rs10483393	31530235	1	2	146	137	1.066	0.2862	0.5927
15	rs2556560	42609135	2	1	169	171	0.9883	0.01176	0.9136
16	rs8060494	78808972	2	1	190	174	1.092	0.7033	0.4017
17	rs4790372	2701606	2	1	163	169	0.9645	0.1084	0.7419
17	rs12453316	69027654	1	2	177	179	0.9888	0.01124	0.9156
19	rs997669	34996323	2	1	201	183	1.098	0.8438	0.3583
20	rs1555322	33312595	1	2	94	79	1.19	1.301	0.2541

**B)**

CHR	SNP	BP	A1	F_A	F_U	A2	OR	CHISQ	P
2	rs2241685	1896290	1	0.09116	0.09283	2	0.9802	0.03733	0.8468
2	rs13395022	79793915	2	0.2088	0.2095	1	0.9961	0.002865	0.9573
2	rs2587695	120038047	1	0.4973	0.4922	2	1.021	0.1161	0.7333
2	rs2242073	208819551	2	0.1605	0.1568	1	1.029	0.1216	0.7273
2	rs1110998	217169458	1	0.3116	0.2928	2	1.093	1.886	0.1697
3	rs10510238	2876647	2	0.1293	0.1376	1	0.9304	0.6621	0.4158
3	rs9879164	54040611	2	0.4218	0.4359	1	0.9441	0.9084	0.3406
3	rs2084358	57457928	1	0.5184	0.4722	2	1.203	9.597	0.001949
3	rs10490808	59939739	2	0.4068	0.4266	1	0.9218	1.8	0.1797
3	rs10510850	60542142	1	0.1211	0.1116	2	1.097	1.001	0.3172
4	rs755403	6507714	2	0.3985	0.3973	1	1.005	0.007242	0.9322
4	rs10516182	7143981	2	0.2801	0.2954	1	0.9279	1.274	0.259
4	rs7697323	7801488	1	0.3782	0.38	2	0.9927	0.0142	0.9051
5	rs173754	65102081	1	0.4925	0.4915	2	1.004	0.004285	0.9478
5	rs258082	66166352	1	0.4619	0.4521	2	1.04	0.4342	0.5099
6	rs160666	2719051	2	0.2857	0.3025	1	0.9222	1.515	0.2183
6	rs2842643	41758714	2	0.2932	0.2909	1	1.011	0.02797	0.8672
6	rs3799977	44945334	2	0.4306	0.4076	1	1.099	2.452	0.1174
6	rs8180608	89064414	2	0.4101	0.4441	1	0.8703	5.265	0.02176
6	rs1358601	91532294	1	0.3852	0.3846	2	1.003	0.002076	0.9637
6	rs6921403	154156020	2	0.1373	0.1405	1	0.9736	0.09408	0.7591
7	rs2237349	28536203	2	0.4109	0.4082	1	1.011	0.03276	0.8564
7	rs2002865	154132035	2	0.2075	0.217	1	0.9445	0.6065	0.4361
8	rs6991017	5508780	2	0.1891	0.1873	1	1.012	0.02315	0.8791
8	rs2248529	14657354	1	0.3604	0.363	2	0.9888	0.03305	0.8557
8	rs4961315	142110882	2	0.2959	0.2995	1	0.983	0.06846	0.7936
9	rs2418326	114759028	1	0.2534	0.252	2	1.007	0.01179	0.9135
9	rs2502731	128056111	2	0.3626	0.3508	1	1.053	0.6767	0.4107
14	rs10483393	31530235	1	0.2272	0.2203	2	1.041	0.3146	0.5749
15	rs2556560	42609135	2	0.419	0.4215	1	0.9899	0.02811	0.8668
16	rs8060494	78808972	2	0.3215	0.3228	1	0.9943	0.008131	0.9282
17	rs4790372	2701606	2	0.3014	0.3112	1	0.9546	0.5122	0.4742
17	rs12453316	69027654	1	0.3612	0.3662	2	0.9788	0.1193	0.7298
19	rs997669	34996323	2	0.4023	0.3876	1	1.064	1.025	0.3114
20	rs1555322	33312595	1	0.1279	0.1277	2	1.002	0.0004034	0.984

C)

CHR	SNP	BP	A1	A2	T	U	OR	CHISQ	P
1	rs2281597	34132445	0	2	0	0	NA	NA	NA
1	rs642969	197590139	0	2	0	0	NA	NA	NA
2	rs2587695	120038287	1	2	320	294	1.088	1.101	0.2941
2	rs2242073	208702290	2	1	185	182	1.016	0.02452	0.8756
3	rs10510850	60542142	1	2	109	115	0.9478	0.1607	0.6885
3	rs17233461	125807474	2	1	305	322	0.9472	0.4609	0.4972
4	rs755403	6440543	2	1	296	278	1.065	0.5645	0.4525
4	rs3857174	7089831	2	1	202	217	0.9309	0.537	0.4637
4	rs7697323	7734317	1	2	269	278	0.9676	0.1481	0.7004
5	rs1457720	110998762	2	1	247	260	0.95	0.3333	0.5637
6	rs160666	2719051	2	1	248	262	0.9466	0.3843	0.5353
6	rs3799977	44945334	2	1	302	282	1.071	0.6849	0.4079
6	rs6921403	154105599	2	1	149	150	0.9933	0.003344	0.9539
8	rs6991017	5508780	2	1	193	191	1.01	0.01042	0.9187
9	rs2418326	116719295	1	2	236	210	1.124	1.516	0.2183
9	rs2416606	119862757	2	1	264	262	1.008	0.007605	0.9305
10	rs16928529	72652991	2	1	277	312	0.8878	2.08	0.1493
10	rs11594082	72969259	1	2	126	138	0.913	0.5455	0.4602
10	rs10786284	98125495	0	1	0	0	NA	NA	NA
10	rs515910	105956394	2	1	300	272	1.103	1.371	0.2417
11	rs3893215	17721406	0	2	0	0	NA	NA	NA
11	rs10830468	87604834	0	2	0	0	NA	NA	NA
12	rs4964805	102716954	0	2	0	0	NA	NA	NA
13	rs7995215	93206507	1	2	279	317	0.8801	2.423	0.1196
14	rs2239627	22705999	0	2	0	0	NA	NA	NA
14	rs10483286	24273582	0	2	0	0	NA	NA	NA
16	rs10514604	83003885	0	2	0	0	NA	NA	NA
17	rs2440129	6847295	0	2	0	0	NA	NA	NA

**Supplementary Table 8.** ADHD Genotype GWAS of Glutamatergic Genes. The most significant SNP genotype association in each of the eight GRM gene regions. A) ADHD TDT CHOP Illumina 550k B) ADHD Case:Control CHOP Illumina 550k C) ADHD IMAGE Perlegen 600k.

**A)**

CHR	SNP	BP	A1	A2	T	U	OR	CHISQ	P	Gene
11	rs4237549	88407924	2	1	31	61	0.5082	9.783	0.001762	GRM5
7	rs17864159	126444172	1	2	22	46	0.4783	8.471	0.003609	GRM8
6	rs3887555	34177040	1	2	208	161	1.292	5.986	0.01442	GRM4
7	rs6943762	86047914	2	1	69	99	0.697	5.357	0.02064	GRM3
3	rs7623055	7485891	1	2	151	193	0.7824	5.128	0.02354	GRM7
6	rs362839	146721428	2	1	125	161	0.7764	4.531	0.03328	GRM1
3	rs4687770	51730105	2	1	114	94	1.213	1.923	0.1655	GRM2
5	rs2078183	178357150	2	1	190	210	0.9048	1	0.3173	GRM6

**B)**

CHR	SNP	BP	A1	F_A	F_U	A2	OR	CHISQ	P	Gene
3	rs7623055	7485891	1	0.3582	0.4129	2	0.7936	15.48	8.35E-05	GRM7
11	rs1354411	88016449	2	0.03643	0.0566	1	0.6302	10.21	0.001396	GRM5
7	rs2283100	126643293	2	0.2281	0.193	1	1.235	9.527	0.002024	GRM8
6	rs1873250	34130718	2	0.2134	0.2455	1	0.8338	7.062	0.007873	GRM4
7	rs10952890	86193151	1	0.02753	0.03917	2	0.6945	4.782	0.02877	GRM3
5	rs2078183	178357150	2	0.4593	0.4897	1	0.8852	4.605	0.03189	GRM6
6	rs1983635	146707365	2	0.316	0.2917	1	1.122	3.515	0.06081	GRM1
3	rs4687592	51630896	1	0.03442	0.04041	2	0.8464	1.191	0.2752	GRM2

**C)**

CHR	SNP	BP	A1	A2	T	U	OR	CHISQ	P	Gene
6	rs12206652	34173960	2	1	265	216	1.227	4.992	0.02547	GRM4
11	rs160195	87932621	2	1	302	253	1.194	4.326	0.03753	GRM5
7	rs11563486	126621501	1	2	130	162	0.8025	3.507	0.06112	GRM8
3	rs11717471	7599469	2	1	238	280	0.85	3.405	0.06498	GRM7
6	rs2300620	146745874	2	1	160	133	1.203	2.488	0.1147	GRM1
7	rs1468413	86271589	1	2	190	162	1.173	2.227	0.1356	GRM3
5	rs7725272	178338994	2	1	289	261	1.107	1.425	0.2325	GRM6
3	rs6445959	51747387	2	1	169	153	1.105	0.795	0.3726	GRM2

**Supplementary Table 9.** ADHD CNV Family Based Transmission Disequilibrium and *de novo* Statistical Tests.

**A) Illumina CHOP Deletions Enriched for Inheritance**

CNVR	Count SNPs	P TDT Del	Inh Del	<i>de novo</i> Del	Par Del Not Inh	Gene	Distance
chr18:74258734-74260996	3	0.001953	<b>9</b>	0	0	<i>SALL3</i>	580267
chr7:120092385-120099982	3	0.001953	<b>9</b>	0	0	<i>KCND2</i>	0
chr4:92499956-92502794	8	0.001953	<b>9</b>	0	0	<i>KIAA1680</i>	0
chr11:69755529-69759313	12	0.007813	<b>7</b>	0	0	<i>FADD</i>	24395
chr4:42400885-42403451	15	0.007813	<b>7</b>	0	0	<i>ATP8A1</i>	47238
chr5:104463047-104518786	17	0.007813	<b>7</b>	0	0	<i>NR_000039</i>	0
chr13:69637654-69666685	18	0.015625	<b>6</b>	0	0	<i>NR_002717</i>	25969
chr3:195971510-195982215	5	0.03125	<b>5</b>	1	0	<i>FAM43A</i>	80455
chr19:44369918-44376749	3	0.03125	<b>5</b>	1	0	<i>LOC342897</i>	2695
chr1:2349841-2356176	4	0.03125	<b>5</b>	1	0	<i>PEX10</i>	15971
chr21:45777720-45782727	3	0.03125	<b>5</b>	0	0	<i>SLC19A1</i>	0
chr10:67748487-67785209	30	0.03125	<b>5</b>	0	0	<i>CTNNA3</i>	0

**B) Illumina CHOP Duplications Enriched for Inheritance**

CNVR	Count SNPs	P TDT Dup	Inh Dup	<i>de novo</i> Dup	Par Dup Not Inh	Gene	Distance
chr20:59015708-59022667	4	0.007813	<b>7</b>	0	0	<i>CDH4</i>	238287
chr12:72808323-72832667	5	0.015625	<b>6</b>	0	0	<i>BC061638</i>	0
chr6:73021641-73023171	3	0.03125	<b>5</b>	0	0	<i>RIMS1</i>	0
chr17:74089903-74106726	9	0.03125	<b>5</b>	0	0	<i>DNAHL1</i>	10904
chr1:9243828-9310031	22	0.03125	<b>5</b>	0	0	<i>H6PD,SPSB1</i>	0

**C) Illumina CHOP Deletions Enriched for *de novo***

CNVR	Count	Inh	<i>de</i>	Par Del	Gene	Distance
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	SNPs	Del	<i>nov</i> <b>Del</b>	Not Inh		
chr19:15992679-15997923	2	15	<b>6</b>	15	<i>LOC126536</i>	0
chr22:38384374-38403731	8	4	<b>4</b>	13	<i>CACNA1I</i>	0
chr17:71112486-71120734	4	12	<b>3</b>	16	<i>KIAA1783</i>	0
chr12:55902280-55923860	3	9	<b>3</b>	19	<i>NDUFA4L2,NXPH4,SHMT2,STAC3</i>	0
chr16:87694595-87778383	16	32	<b>2</b>	21	<i>AX748415,CDH15,LOC197322</i>	0
chr18:65358832-65367619	18	33	<b>2</b>	21	<i>DOK6</i>	0
chr17:74544687-74596676	20	5	<b>1</b>	8	<i>C1QTNF1,CTRP1,DKFZp434P174,FLJ21865</i>	0
chr20:35485009-35485260	2	14	<b>1</b>	9	<i>SRC</i>	17774
chr17:76554452-76570569	5	7	<b>1</b>	9	<i>AK127919,KIAA1303</i>	0
chr19:40353627-40354649	6	20	<b>1</b>	9	<i>FXVD5</i>	1002
chr1:6071709-6289806	34	2	<b>1</b>	9	<i>ACOT7,CHD5,GPR153,HES3,ICMT,KCNAB2,RNF207,RPL22</i>	0
chr21:44535630-44541978	5	10	<b>1</b>	10	<i>AIRE</i>	0
chr9:137731051-137745745	6	10	<b>1</b>	10	<i>KCNT1,SOHLH1</i>	0
chr19:14102205-14159442	7	14	<b>1</b>	11	<i>ASF1B,BX537706,LPHN1</i>	0
chr14:104256711-104750100	30	8	<b>1</b>	11	<i>ADSSL1,AHNAK2,BRF1,CDCA4,GPR132,JAG2,KIAA0284,NUDT14,PLD4,SIVA1</i>	0
chr11:68514489-68538799	8	13	<b>1</b>	12	<i>BC039516,MRGPRF</i>	0

#### D) Illumina CHOP Duplications Enriched for *de novo*

CNVR	Count SNPs	Inh Dup	<i>de novo</i> <b>Dup</b>	Par Dup Not Inh	Gene	Distance
chr19:59423491-59428132	12	74	<b>3</b>	38	<i>LILRB3,LIR-3</i>	0
chr5:180108611-180122934	13	17	<b>1</b>	11	<i>OR2Y1</i>	8947
chr9:138606913-138647195	17	10	<b>1</b>	10	<i>AF161442</i>	15688



chr16:87399730-87430019	22	7	1	7	APRT,CDT1,FLJ00319,GALNS	0
chr22:23994408-24235668	63	18	1	7	BC004918,BC037884,BC040576,BC047380,LOC91353,LRP5L	0
chr14:104225150-104339273	35	7	1	11	ADSS,ADSSL1,AKT1,AX721091,C14orf151,C14orf173,SIVA1	0
chr12:31248369-31298174	30	27	1	17	OVOS2	0
chr20:61642713-61668792	11	4	1	7	C20orf195,PRIC285,SRMS	0

#### E) Perlegen IMAGE Deletions Enriched for Inheritance

CNVR	Count SNPs	P TDT Del	Inh Del	<i>de novo</i> Del	Par Del Not Inh	Gene	Distance
chr7:19828746-19840916	7	0.041656	4	0	11	<i>MGC42090</i>	49005
chr2:180271795-180274556	5	0.003204	2	1	13	<i>ZNF533</i>	0
chr14:79919894-79924934	5	0.03125	1	0	7	<i>BC039670</i>	0

#### F) Perlegen IMAGE Duplications Enriched for Inheritance

CNVR	Count SNPs	P TDT Dup	Inh Dup	<i>de novo</i> Dup	Par Dup Not Inh	Gene	Distance
chr22:17361563-17369020	3	0.015625	6	0	0	<i>CR623368, KIAA1647</i>	0
chr15:30088094-30090949	3	0.03125	5	1	0	<i>CHRNA7</i>	19069
chr7:71664963-71712086	5	0.03125	5	0	0	<i>MGC87315</i>	0

#### G) Perlegen IMAGE Deletions Enriched for *de novo*

CNVR	Count SNPs	Inh Del	<i>de novo</i> Del	Par Del Not Inh	Gene	Distance
chr2:180271795-180274923	6	2	1	13	<i>ZNF533</i>	0
chr10:85445139-85446804	7	5	1	7	<i>GHITM</i>	442361

#### H) Perlegen IMAGE Duplications Enriched for *de novo*

CNVR	Count SNPs	Inh Dup	<i>de novo</i> Dup	Par Dup Not Inh	Gene	Distance
chr6:168234697-168295618	13	5	2	8	<i>FLJ00181</i>	9639

chr12:31276361-31285014	9	15	<b>1</b>	17	OVOS2	26006
chr10:47089854-47154881	31	11	<b>1</b>	17	AK057316	0
chr7:140018-162903	13	10	<b>1</b>	10	AL137655	23529
chr8:2437197-2492653	23	4	<b>1</b>	7	BC045738	0

**Supplementary Table 10.** ADHD CNV Family Based Transmission Disequilibrium and *de novo* Statistical Tests.

CNVR (hg18/B36/Mar2006)	Type	P TDT Del	P TDT Dup	Inh Del	<i>de novo</i> Del	Par Del Not Inh	Inh Dup	<i>de novo</i> Dup	Par Dup Not Inh
chr7:126441593-126621501	Del	1	1	0	0	0	0	0	0
chr11:88269449-88351661	Del	0.125	1	3	0	0	0	0	0
chr3:7183953-7197236	Del	0.25	1	2	0	0	0	0	0
chr6:146657076-146694047	Dup	1	1	0	0	0	0	0	0
chr7:153495598-153564827	Dup	0.205	1	4	0	6	0	0	0
chr5:65027976-65046520	Del	1	0.5	0	0	0	1	0	0
chr1:56053497-56064495	Del	1	1	0	0	0	0	0	0
chr1:72317292-72328395	Dup	1	1	0	0	0	0	0	0
chr19:38427720-38444834	Del	0.183	1	6	0	8	0	0	0
chr3:1844168-1859889	Del	0.063	1	4	0	0	0	0	0
chr2:81419297-81446082	Dup	1	0.5	0	0	0	1	0	0
chr4:113772340-113788584	Dup	0.375	1	2	0	1	0	0	0

**Supplementary Table 11.** Homozygous Deletion Analysis for CNVRs.

CNVR	P-value	OR	Cases Deletion	Control Deletion	Gene	Exon Distance
chr4:64398956-64398956	0.010184	8.066572	5	2	<i>SRD5A2L2</i>	427060
chr4:87198171-87198951	0.012506	3.695184	8	7	<i>MAPK10</i>	5492
chr1:109169467-109173397	0.013403	0	3	0	<i>AKNAD1</i>	0
chr22:21254995-21262241	0.013403	0	3	0	<i>DKFZp667J0810,abParts</i>	905
chr4:10007525-10009254	0.036934	1.320968	91	228	<i>KIAA1729</i>	41348
chr12:69160993-69162296*	0.041022	0.638139	26	128	<i>BC031864</i>	12619

\* significant control enrichment. Based on discovery cohort, subjects with a homozygous deletion detected included Cases: 711 and Controls: 2280.

**Supplementary Table 12.** Perlegen Data Reformatted File Samples to match Affymetrix Power Tools output format.

A) Genotype Calls File (0=AA,1=AB,2=BB,-1=NoCall).

probeset_id	10009	10010	10021	10022
SNP_rs10000023	1	1	2	1
SNP_rs10000030	1	0	0	1
SNP_rs10000037	0	0	1	1
SNP_rs10000068	2	2	2	2

B) Genotype Calls Confidence Scores (All set to 1).

probeset_id	10009	10010	10021	10022
SNP_rs10000023	1	1	1	1
SNP_rs10000030	1	1	1	1
SNP_rs10000037	1	1	1	1
SNP_rs10000068	1	1	1	1

C) Intensity Summary (-A=log<sub>10</sub>(X), -B=log<sub>10</sub>(Y) (X and Y value from dbGaP Single Sample Final Report files).

probeset_id	10009	10010	10021	10022
SNP_rs10000023-A	2.85	2.78	2.07	2.89
SNP_rs10000023-B	2.86	2.84	2.98	2.96
SNP_rs10000030-A	2.9	2.99	2.95	3.02
SNP_rs10000030-B	2.91	2.4	2.38	3.05

**Supplementary Table 13.** Sample exclusion based on quality control measures.

<b>Exclusion Criteria</b>	<b>CHOP</b>	<b>Control</b>
Call Rate < 98%	170	271
SD LRR > 0.35	73	124
Ethnicity non-Caucasian	71	48
GCWF >0.05	251	1040
Count CNVs > 70	197	237
Monozygotic Twin	31	38

Samples excluded based on Quality Control (QC) measures on our HumanHap550 GWAS data based on statistical distributions to exclude poor quality DNA samples and false positive CNVs.

**Supplementary Table 14.** Sample Source Contributions to Impacting CNV Loci.

CNVR	CHOP Cases	CHOP Controls	NIMH cases	Utah cases	IMAGE cases	Per Psoriasis Control	Per Depression Control	PUW Ma Cases	PUW Ma Parents	IMAGE II Cases	IMAGE II Controls	SAGE Illumina 1M Controls	AGRE Affy 5.0 Parents Controls	Type	Gene
chr11:88269449-88351661	4	0	0	0	5	0	0	1	1	0	0	0	0	Del	<i>GRM5</i>
chr7:126441593-126621501	3	0	0	0	3	0	0	2	0	0	0	0	0	Del	<i>GRM8</i>
chr3:7183953-7197236	4	0	0	0	2	0	0	0	0	0	0	0	0	Del	<i>GRM7</i>
chr6:146657076-146694047	5	2	1	1	0	0	0	0	0	1	0	0	0	Dup	<i>GRM1</i>
chr1:72317292-72328395	4	0	0	0	0	0	0	1	0	0	0	0	0	Dup	<i>NEGR1</i>
chr7:153495598-153564827	5	0	1	0	0	0	0	2	0	0	1	0	1	Dup	<i>DPP6</i>
chr5:65027976-65046520	4	0	0	0	1	0	0	0	0	1	1	0	0	Del	<i>SGTB/NLN</i>
chr1:56053497-56064495	2	0	0	0	3	0	0	0	0	1	0	0	2	Del	<i>USP24</i>
chr19:38427720-38444834	5	2	0	0	1	0	0	1	3	0	0	0	0	Del	<i>SLC7A10</i>
chr3:1844168-1859889	4	0	0	0	0	0	0	2	2 (inh)	1	1	4	1	Del	<i>CNTN4</i>
chr2:81419297-81446082	2	0	0	0	1	0	3	0	0	1	0	0	0	Dup	<i>CTNNA2</i>
chr4:113772340-113788584	2	0	0	0	1	0	0	1	1	0	0	1	1	Dup	<i>LARP7</i>

**Supplementary Table 15.** Boundaries of Individual CNVs in Table 1A and 1B.

CNVR	Gene	Type	Sample ID	Region Called in Sample	Exon Distance*	Sample Validation Run
chr11:88269449-88351661	<i>GRM5</i>	Del	230-3	chr11:88269449-88351661	5,858	Y
chr11:88269449-88351661	<i>GRM5</i>	Del	230-4	chr11:88269449-88351661	5,858	Y
chr11:88269449-88351661	<i>GRM5</i>	Del	230-5	chr11:88269449-88351661	5,858	Y
chr11:88269449-88351661	<i>GRM5</i>	Del	497	chr11:83876556-91038751	0	Y
chr11:88269449-88351661	<i>GRM5</i>	Del	16794	chr11:87996654-88837360	0	Y
chr11:88269449-88351661	<i>GRM5</i>	Del	13304	chr11:88109331-88827923	0	Y
chr11:88269449-88351661	<i>GRM5</i>	Del	13270	chr11:88115425-88481107	0	Y
chr11:88269449-88351661	<i>GRM5</i>	Del	13761	chr11:88305340-88385387	0	Y
chr11:88269449-88351661	<i>GRM5</i>	Del	17580	chr11:88305340-88385387	0	N^
chr11:88269449-88351661	<i>GRM5</i>	Del	M.Of.M.Cs.604401	chr11:88324615-88342595	14,924	Y
chr7:126441593-126621501	<i>GRM8</i>	Del	1953313026_A	chr7:126532786-126536202	0	Y
chr7:126441593-126621501	<i>GRM8</i>	Del	1965040688_A	chr7:126463602-126478050	54,536	Y
chr7:126441593-126621501	<i>GRM8</i>	Del	4011452014_A	chr7:126532786-126536202	0	Y
chr7:126441593-126621501	<i>GRM8</i>	Del	14125	chr7:125660695-126036276	0	N^
chr7:126441593-126621501	<i>GRM8</i>	Del	16794	chr7:125660695-126036276	0	N^
chr7:126441593-126621501	<i>GRM8</i>	Del	11804	chr7:125679479-125937528	0	N^
chr7:126441593-126621501	<i>GRM8</i>	Del	987314	chr7:126503602-126563602	0	Y
chr7:126441593-126621501	<i>GRM8</i>	Del	987124	chr7:126463602-126603602	0	Y
chr3:7183953-7197236	<i>GRM7</i>	Del	2023340146	chr3:7053179-7144453	18,686	Y
chr3:7183953-7197236	<i>GRM7</i>	Del	068-3	chr3:7183954-7197236	20,599	Y
chr3:7183953-7197236	<i>GRM7</i>	Del	068-4	chr3:7183954-7197236	20,599	Y
chr3:7183953-7197236	<i>GRM7</i>	Del	4079019863_A	chr3:7183954-7197236	20,599	Y
chr3:7183953-7197236	<i>GRM7</i>	Del	11891	chr3:6979874-7003319	101,280	Y
chr3:7183953-7197236	<i>GRM7</i>	Del	11923	chr3:6980446-7001696	101,852	Y
chr6:146657076-146694047	<i>GRM1</i>	Dup	388-3	chr6:146657077-146675511	0	Y
chr6:146657076-146694047	<i>GRM1</i>	Dup	387-3	chr6:146657077-146675511	0	Y
chr6:146657076-146694047	<i>GRM1</i>	Dup	386-3	chr6:146657077-146675511	0	Y
chr6:146657076-146694047	<i>GRM1</i>	Dup	4301337678_R02C01	chr6:146657077-146675511	0	Y
chr6:146657076-146694047	<i>GRM1</i>	Dup	4305910011_R01C02	chr6:146657077-146675511	0	Y
chr6:146657076-146694047	<i>GRM1</i>	Dup	1181	chr6:146657077-146694047	0	Y
chr6:146657076-146694047	<i>GRM1</i>	Dup	83158	chr6:146657077-146694047	0	Y
chr6:146657076-146694047	<i>GRM1</i>	Dup	b3_SF_0181	chr6:146685878-146701196	13,883	Y
chr1:72317292-72328395	<i>NEGR1</i>	Dup	230-3	chr1:72317292-72328395	10,621	Y
chr1:72317292-72328395	<i>NEGR1</i>	Dup	230-4	chr1:72317292-72328395	10,621	Y
chr1:72317292-72328395	<i>NEGR1</i>	Dup	230-5	chr1:72317292-72328395	10,621	Y
chr1:72317292-72328395	<i>NEGR1</i>	Dup	TD207.1	chr1:71648994-73025013	0	Y
chr1:72317292-72328395	<i>NEGR1</i>	Dup	M.Of.M.Cs.6308601	chr1:72322424-72328395	10,621	Y
chr7:153495598-153564827	<i>DPP6</i>	Dup	332-3	chr7:153495598-153578582	54,698	Y
chr7:153495598-153564827	<i>DPP6</i>	Dup	4079019863_A	chr7:153495598-153564827	68,453	Y

chr7:153495598-153564827	<i>DPP6</i>	Dup	4193372403_B	chr7:153495598-153554210	79,070	Y
chr7:153495598-153564827	<i>DPP6</i>	Dup	4243114113_R01C02	chr7:153495598-153577484	55,796	Y
chr7:153495598-153564827	<i>DPP6</i>	Dup	1135	chr7:153495598-153576455	56,825	N^
chr7:153495598-153564827	<i>DPP6</i>	Dup	8201671744	chr7:153118878-153338318	0	Y
chr7:153495598-153564827	<i>DPP6</i>	Dup	W.Of.F.Cs.140002	chr7:153502896-153517548	115,317	Y
chr7:153495598-153564827	<i>DPP6</i>	Dup	W.Of.M.Cs.234002	chr7:153545279-153559377	73,903	Y
chr5:65027976-65046520	<i>SGTB/NLN</i>	Del	067-3	chr5:65027976-65046520	0	Y
chr5:65027976-65046520	<i>SGTB/NLN</i>	Del	117-3	chr5:65027976-65046520	0	Y
chr5:65027976-65046520	<i>SGTB/NLN</i>	Del	152-3	chr5:65027976-65046520	0	Y
chr5:65027976-65046520	<i>SGTB/NLN</i>	Del	1670639198_A	chr5:65027976-65046520	0	Y
chr5:65027976-65046520	<i>SGTB/NLN</i>	Del	15962	chr5:64483534-65101307	0	Y
chr5:65027976-65046520	<i>SGTB/NLN</i>	Del	b11_SF_1055	chr5:65020291-65030503	3,236	Y
chr1:56053497-56064495	<i>USP24</i>	Del	4147907208_B	chr1:56053497-56064495	80,234	Y
chr1:56053497-56064495	<i>USP24</i>	Del	393-3	chr1:56053497-56064495	80,234	Y
chr1:56053497-56064495	<i>USP24</i>	Del	11411	chr1:56040939-56132401	67,676	Y
chr1:56053497-56064495	<i>USP24</i>	Del	11804	chr1:56040939-56263366	67,676	Y
chr1:56053497-56064495	<i>USP24</i>	Del	11727	chr1:56053497-56064840	80,234	Y
chr1:56053497-56064495	<i>USP24</i>	Del	b2_SF_0094	chr1:56051215-56057576	77,952	Y
chr19:38427720-38444834	<i>SLC7A10</i>	Del	120-3	chr19:38415546-38444834	6,998	Y
chr19:38427720-38444834	<i>SLC7A10</i>	Del	224-3	chr19:38415546-38444834	6,998	Y
chr19:38427720-38444834	<i>SLC7A10</i>	Del	305-3	chr19:38415545-38434210	6,997	Y
chr19:38427720-38444834	<i>SLC7A10</i>	Del	134-4	chr19:38418216-38444834	9,668	Y
chr19:38427720-38444834	<i>SLC7A10</i>	Del	168-3	chr19:38423641-38444834	15,093	Y
chr19:38427720-38444834	<i>SLC7A10</i>	Del	11931	chr19:38427721-38455315	19,173	Y
chr19:38427720-38444834	<i>SLC7A10</i>	Del	W.Of.F.Cs.121001	chr19:38423391-38442154	14,843	Y
chr3:1844168-1859889	<i>CNTN4</i>	Del	078-3	chr3:1273990-1859889	0	Y
chr3:1844168-1859889	<i>CNTN4</i>	Del	078-4	chr3:1273990-1859889	0	Y
chr3:1844168-1859889	<i>CNTN4</i>	Del	141-3	chr3:1756625-1928413	187,137	Y
chr3:1844168-1859889	<i>CNTN4</i>	Del	177-3	chr3:1844168-1936623	178,927	Y
chr3:1844168-1859889	<i>CNTN4</i>	Del	M.Of.F.Cs.53701	chr3:1793056-1956567	158,983	Y
chr3:1844168-1859889	<i>CNTN4</i>	Del	U.Of.F.Cs.852301	chr3:1835561-1852134	263,416	Y
chr3:1844168-1859889	<i>CNTN4</i>	Del	b3_SF_0253	chr3:1797102-1930071	185,479	Y
chr2:81419297-81446082	<i>CTNNA2</i>	Dup	134-4	chr2:81035643-81654296	0	Y
chr2:81419297-81446082	<i>CTNNA2</i>	Dup	144-3	chr2:81035643-81654296	0	Y
chr2:81419297-81446082	<i>CTNNA2</i>	Dup	11484	chr2:81419297-81446082	152,417	Y
chr2:81419297-81446082	<i>CTNNA2</i>	Dup	b10_SF_0900	chr2:81352586-81386102	85,706	Y
chr4:113772340-113788584	<i>LARP7</i>	Dup	303-3	chr4:113744172-113798058	0	Y
chr4:113772340-113788584	<i>LARP7</i>	Dup	314-3	chr4:113744172-113798058	0	Y
chr4:113772340-113788584	<i>LARP7</i>	Dup	17190	chr4:113772340-113788584	0	Y
chr4:113772340-113788584	<i>LARP7</i>	Dup	M.Fa.M.Cs.6300503	chr4:113769438-113801755	0	Y

\*exon distance of '0' indicates that exon is impacted by the CNV

^ sample not available for qPCR validation (sample visually validated in Bead Studio).

**Supplementary Table 16.** Frequency of CNVs in GRM Receptor Interacting Genes in ADHD Cases and Controls.

Gene	Del Counts (cases:controls)	Dup Counts (cases:controls)	ADHD Enrichment
<i>ACAT1</i>	0:0	1:0	Yes
<i>ACCN1</i>	0:0	3:1	Yes
<i>ACTR2</i>	1:0	0:1	Yes
<i>ADCY1</i>	0:0	1:1	Yes
<i>ADRBK1</i>	1:0	0:0	Yes
<i>ALDOA</i>	3:8	2:6	Yes
<i>APP</i>	0:0	8:2	Yes
<i>ARL15</i>	1:1	2:0	Yes
<i>ATXN7L3</i>	1:1	0:0	Yes
<i>BDKRB2</i>	1:1	0:0	Yes
<i>CA8</i>	0:0	1:0	Yes
<i>CACNA1B</i>	0:0	2:2	Yes
<i>CACYBP</i>	1:0	0:0	Yes
<i>CALM1</i>	1:2	0:0	Yes
<i>CHRM3</i>	0:0	2:1	Yes
<i>CIC</i>	1:1	0:0	Yes
<i>CNP</i>	1:2	0:0	Yes
<i>CRHR1</i>	1:0	0:0	Yes
<i>DISC1</i>	0:0	4:7	Yes
<i>DYNLL1</i>	0:0	1:0	Yes
<i>FPR1</i>	0:0	1:1	Yes
<i>GAPDH</i>	0:2	1:1	Yes
<i>GNA15</i>	1:1	1:0	Yes
<i>GNAI2</i>	2:4	0:0	Yes
<i>GNAO1</i>	0:0	1:1	Yes
<i>GNAQ</i>	1:0	0:0	Yes
<i>GRIK1</i>	0:0	8:2	Yes
<i>GRIK3</i>	1:0	0:0	Yes
<i>GRM1</i>	0:0	7:2	Yes
<i>GRM2</i>	1:0	1:0	Yes
<i>GRM3</i>	0:0	1:0	Yes
<i>GRM5</i>	4:0	3:2	Yes
<i>GRM6</i>	1:0	0:4	Yes
<i>GRM7</i>	4:0	0:0	Yes
<i>GRM8</i>	3:0	1:1	Yes
<i>GSN</i>	1:0	1:0	Yes
<i>HOMER1</i>	0:0	1:0	Yes
<i>HTR2A</i>	0:0	1:0	Yes
<i>MAPK1</i>	1:0	0:0	Yes
<i>MTHFD1</i>	1:1	0:0	Yes
<i>MX1</i>	0:0	7:2	Yes
<i>NARG1</i>	1:0	0:0	Yes
<i>NMI</i>	0:0	1:0	Yes
<i>PCBP3</i>	3:2	6:3	Yes
<i>PDE1C</i>	1:0	1:1	Yes



<i>PPP2R1A</i>	0:0	1:0	Yes
<i>PRPSAP1</i>	1:0	1:1	Yes
<i>PSMD11</i>	2:24	1:0	Yes
<i>PSMD13</i>	0:4	1:2	Yes
<i>PXN</i>	0:0	1:0	Yes
<i>QRICH2</i>	1:1	0:1	Yes
<i>RANBP1</i>	2:3	0:9	Yes
<i>RAP2A</i>	0:0	1:1	Yes
<i>RCC1</i>	0:0	1:0	Yes
<i>RGS12</i>	2:0	0:0	Yes
<i>RIF1</i>	0:0	1:0	Yes
<i>RUVBL2</i>	1:0	0:3	Yes
<i>RYR1</i>	1:2	1:1	Yes
<i>RYR2</i>	1:0	1:0	Yes
<i>SDC3</i>	1:0	0:1	Yes
<i>SELE</i>	1:0	0:0	Yes
<i>SERPINB9</i>	0:0	1:0	Yes
<i>SETD4</i>	2:0	8:3	Yes
<i>SHANK1</i>	0:0	1:0	Yes
<i>SORD</i>	0:0	1:0	Yes
<i>STRAP</i>	0:0	1:1	Yes
<i>TK1</i>	2:0	0:2	Yes
<i>TNIK</i>	1:0	0:0	Yes
<i>VHL</i>	0:0	1:0	Yes
<i>BTBD2</i>	0:7	1:15	No
<i>ECHS1</i>	0:1	1:22	No
<i>F2RL3</i>	1:16	0:0	No
<i>GNB2L1</i>	0:0	0:4	No
<i>HOMER3</i>	1:12	1:9	No
<i>ITGB7</i>	0:5	1:12	No
<i>KIAA1683</i>	3:18	0:3	No
<i>PDE6G</i>	3:26	1:12	No
<i>PLCB3</i>	0:5	0:2	No
<i>PYGM</i>	3:29	0:4	No
<i>RPLP2</i>	8:92	1:6	No
<i>SLC6A3</i>	0:0	0:11	No
<i>SRC</i>	1:19	0:2	No
<i>TBCA</i>	1:10	0:0	No
<i>TRAF2</i>	5:24	1:11	No
<i>40425</i>	0:0	0:0	NoSNPsOnGene
<i>ADRA2A</i>	0:0	0:0	NoSNPsOnGene
<i>ADRA2C</i>	1:1	0:1	NoSNPsOnGene
<i>C17orf44</i>	0:0	0:0	NoSNPsOnGene
<i>C7orf25</i>	0:0	0:0	NoSNPsOnGene
<i>F2RL2</i>	0:3	0:0	NoSNPsOnGene
<i>FKBP3</i>	0:0	0:0	NoSNPsOnGene
<i>FSCN1</i>	0:0	0:1	NoSNPsOnGene
<i>GRB7</i>	0:0	0:0	NoSNPsOnGene
<i>HSP90AB1</i>	1:0	0:0	NoSNPsOnGene
<i>IMPDH2</i>	0:0	0:0	NoSNPsOnGene
<i>LOC642393</i>	0:0	1:4	NoSNPsOnGene
<i>LOC653098</i>	0:0	0:0	NoSNPsOnGene
<i>MC4R</i>	0:0	0:0	NoSNPsOnGene
<i>MGC11082</i>	0:0	0:0	NoSNPsOnGene
<i>MRPS16</i>	0:0	0:0	NoSNPsOnGene
<i>NPY2R</i>	1:0	0:0	NoSNPsOnGene
<i>PAFAH1B3</i>	1:1	0:0	NoSNPsOnGene

<i>PCBP1</i>	0:0	0:0	NoSNPsOnGene
<i>PCMT1</i>	0:0	0:0	NoSNPsOnGene
<i>PHKG2</i>	0:0	0:0	NoSNPsOnGene
<i>PRLHR</i>	0:0	0:0	NoSNPsOnGene
<i>PSME1</i>	0:0	0:0	NoSNPsOnGene
<i>RAB2</i>	2:2	0:1	NoSNPsOnGene
<i>RGS2</i>	0:0	0:0	NoSNPsOnGene
<i>S100A6</i>	0:0	0:0	NoSNPsOnGene
<i>SET</i>	0:0	0:0	NoSNPsOnGene
<i>SF3B14</i>	0:0	0:0	NoSNPsOnGene
<i>TBXA2R</i>	10:44	0:10	NoSNPsOnGene
<i>TMEM4</i>	0:0	0:0	NoSNPsOnGene
<i>TPI1</i>	0:0	1:1	NoSNPsOnGene
<i>TRMT112</i>	0:1	0:2	NoSNPsOnGene
<i>TUBA1</i>	0:0	0:0	NoSNPsOnGene
<i>TUBA1A</i>	0:0	0:0	NoSNPsOnGene
<i>TUBA2</i>	0:1	0:0	NoSNPsOnGene
<i>TUBB</i>	0:0	0:0	NoSNPsOnGene
<i>TUBG1</i>	0:1	0:0	NoSNPsOnGene
<i>ACAT2</i>	0:0	0:0	
<i>ACCN2</i>	0:2	0:0	
<i>ACP1</i>	0:0	0:3	
<i>ACTB</i>	0:0	0:0	
<i>ADA</i>	0:0	0:0	
<i>ADD1</i>	0:0	0:0	
<i>ADD2</i>	0:0	0:0	
<i>ADORA1</i>	0:0	0:1	
<i>ADRA1B</i>	0:0	0:0	
<i>ADRB2</i>	0:0	0:0	
<i>ANXA2</i>	0:0	0:0	
<i>APTX</i>	0:0	0:0	
<i>AQP1</i>	0:0	0:1	
<i>ARHGAP24</i>	0:0	0:0	
<i>ARRB1</i>	0:0	0:0	
<i>ARRB2</i>	0:0	0:1	
<i>BDKRB1</i>	0:0	0:0	
<i>BTG2</i>	0:0	0:1	
<i>C1orf116</i>	0:0	0:1	
<i>CALB2</i>	0:0	0:0	
<i>CALM2</i>	0:0	0:0	
<i>CALM3</i>	0:0	0:0	
<i>CAMK1</i>	0:0	0:0	
<i>CAMK2B</i>	0:0	0:0	
<i>CAMK4</i>	0:0	0:0	
<i>CCNB1</i>	0:0	0:0	
<i>CDC42</i>	0:0	0:0	
<i>CENTG1</i>	0:1	0:0	
<i>CHGB</i>	0:0	0:0	
<i>CHP</i>	0:0	0:0	
<i>CHRM2</i>	0:0	0:0	
<i>CMPK</i>	0:0	0:0	
<i>CNR1</i>	0:0	3:8	
<i>COPB2</i>	0:0	0:0	
<i>CYCS</i>	0:0	0:0	
<i>DCN</i>	0:0	0:0	
<i>DHCR7</i>	0:0	0:1	
<i>DLST</i>	0:0	0:0	
<i>DRD2</i>	0:0	0:0	
<i>DRD3</i>	0:0	0:0	
<i>DSTN</i>	0:0	0:0	
<i>EGFR</i>	0:0	0:0	
<i>EIF3S3</i>	0:0	0:1	
<i>ERBB2</i>	0:0	0:0	

<i>F2R</i>	0:0	0:0	
<i>F3</i>	0:0	0:0	
<i>FURIN</i>	0:0	0:0	
<i>FYN</i>	0:0	0:0	
<i>GLP1R</i>	0:0	0:0	
<i>GLP2R</i>	0:0	0:0	
<i>GNAI1</i>	0:0	0:0	
<i>GNAI3</i>	0:0	0:0	
<i>GOT1</i>	0:0	0:0	
<i>GP1BA</i>	0:0	0:0	
<i>GPR26</i>	0:0	0:0	
<i>GRB2</i>	0:0	0:0	
<i>GRIA1</i>	0:0	0:0	
<i>GRM4</i>	0:0	0:0	
<i>HBXIP</i>	0:0	0:0	
<i>HD</i>	0:0	0:0	
<i>HNRPA3</i>	0:0	0:0	
<i>IL8RB</i>	0:0	0:0	
<i>IQGAP2</i>	0:0	0:0	
<i>ITGB1</i>	0:0	0:0	
<i>ITPR1</i>	0:0	0:0	
<i>KIAA0090</i>	0:1	0:0	
<i>LAMA4</i>	0:0	0:0	
<i>LRP2BP</i>	0:3	0:0	
<i>LRRC59</i>	0:0	0:0	
<i>LTA</i>	0:0	0:0	
<i>LYAR</i>	0:0	0:0	
<i>LYN</i>	1:3	0:0	
<i>MAP4</i>	0:0	0:0	
<i>MAPT</i>	0:0	0:0	
<i>MARK4</i>	0:0	0:0	
<i>MRPL14</i>	0:0	0:0	
<i>MTNR1A</i>	0:3	0:0	
<i>MTNR1B</i>	0:0	0:0	
<i>MYC</i>	0:1	0:0	
<i>MYO6</i>	0:0	0:0	
<i>NANS</i>	0:0	0:0	
<i>NCK1</i>	0:0	0:0	
<i>NFKBIA</i>	0:0	0:0	
<i>NUDC</i>	0:0	0:1	
<i>OPRD1</i>	3:13	0:0	
<i>PCDHA4</i>	0:0	0:0	
<i>PCID1</i>	0:0	0:0	
<i>PDCD5</i>	0:0	0:0	
<i>PDE1B</i>	0:0	0:0	
<i>PGM1</i>	0:0	0:0	
<i>PHKB</i>	0:0	0:0	
<i>PICK1</i>	0:3	0:1	
<i>PIK3CA</i>	0:0	0:0	
<i>PIK3R1</i>	0:0	0:0	
<i>PLA2G7</i>	0:0	0:0	
<i>PLCB1</i>	0:0	0:0	
<i>PLCG2</i>	0:0	0:0	
<i>PPIH</i>	0:0	0:0	
<i>PRDX1</i>	0:0	0:0	
<i>PRKCA</i>	0:0	0:0	
<i>PRMT1</i>	0:0	0:1	
<i>PSAT1</i>	0:0	0:0	
<i>PSEN1</i>	0:0	0:0	
<i>PSMA1</i>	0:0	0:1	
<i>PSMC1</i>	0:0	0:0	
<i>PSMD1</i>	0:0	0:0	
<i>PSMD6</i>	0:0	0:0	

<i>PTHR2</i>	0:0	0:0	
<i>PYGL</i>	0:0	0:0	
<i>RALA</i>	0:0	0:0	
<i>RCC2</i>	0:0	0:0	
<i>RHOA</i>	0:0	0:0	
<i>RPA2</i>	0:0	0:0	
<i>RPN2</i>	0:0	0:0	
<i>RPS14</i>	0:0	0:0	
<i>RRM1</i>	0:0	0:0	
<i>SACS</i>	0:0	0:1	
<i>SARS</i>	0:0	0:0	
<i>SCTR</i>	0:0	0:0	
<i>SHBG</i>	0:0	0:0	
<i>SIAH1</i>	0:0	0:0	
<i>SLC2A1</i>	0:0	0:0	
<i>SNCA</i>	0:0	0:0	
<i>SNRPB2</i>	0:0	0:0	
<i>SOCS6</i>	0:0	0:0	
<i>SOCS7</i>	0:0	0:0	
<i>STAU1</i>	0:0	0:0	
<i>STX12</i>	0:0	0:0	
<i>SYK</i>	0:0	0:0	
<i>TCP1</i>	0:0	0:0	
<i>TEAD3</i>	0:0	0:0	
<i>TFAM</i>	0:0	0:0	
<i>TGM2</i>	0:0	0:3	
<i>TJP1</i>	0:0	0:2	
<i>TLR10</i>	0:0	0:0	
<i>TUBA1B</i>	0:0	0:0	
<i>TXN</i>	0:0	0:0	
<i>TXNDC4</i>	0:2	0:1	
<i>TXNL2</i>	0:0	0:1	
<i>TYMS</i>	0:0	0:2	
<i>UBQLN4</i>	0:0	0:0	
<i>UCHL1</i>	0:0	0:0	
<i>VIPR1</i>	0:0	0:0	
<i>YWHAQ</i>	0:0	0:0	
<i>ZAP70</i>	0:0	0:0	

**Supplementary Table 17.** Gene clusters based on the network of interacting genes.

Cluster #	Genes
1	<i>SET, HNRPA3, RRM1, SORD, PSMC1, MTHFD1, CACYBP, PCBP1, TXNL2, 40425, SARS, PCID1, GSN, PSMD6, TBCA, MRPS16, RCC2, COPB2, RANBP1, PRMT1, ANXA2, FSCN1, RCC1, ACAT1, NUDC, EIF3S3, UCHL1, FKBP3, PDCD5, ACTR2, PSAT1, LYAR, PCBP3, SF3B14, LRRC59, ACP1, ACAT2, RUVBL2, GPR26, MAPK1, CYCS, MGC11082, STRAP, RAP2A, IMPDH2, ACTR2, PSMD1, SETD4, TRMT112, CMPK, MRPL14, SNRPB2, TEAD3, TMEM4, TFAM, DSTN, PRPSAP1, KIAA0090, PPIH, PSMA1, RPS14, DHCR7, PSMD13, TRAF2, TNIK, RPN2, TYMS, NCK1, NANS, NARG1, PPP2R1A, ECHS1, GOT1, PCMT1</i>
2	<i>GRB7, PYGL, CRHR1, PDE1C, CALM1, GLP1R, PYGM, PHKG2, PTHR2, PDE1B, GLP2R, ADD2, ADCY1, SCTR, PHKB, VIPR1, ADD1, PGM1, PGM1, IQGAP2</i>
3	<i>HBXIP, S100A6, TXN, SLC2A1, CAMK1, RAB2, PCDHA4, QRICH2, GAPDH, BTBD2, PAFAH1B3, SERPINB9, PSMD11, PRDX1, RPA2, CAMK2B, LAMA4, ARL15, TPI1, CAMK4, TK1, FYN, PGM1, ACTB, CHP</i>
4	<i>SLC6A3, UBQLN4, PRLHR, PICK1, CIC, APTX, ERBB2, ATXN7L3, ACCN2, AQP1, GRIA1, ACCN1, ECHS1, SACS, BTG2, LRP2BP, PRKCA</i>
5	<i>RALA, CDC42, DRD3, ITGB1, ITGB7, TLR10, HSP90AB1, TJP1, FURIN, VHL, MTNR1B, PSEN1, SHBG, DCN, F3, GRIK3, GP1BA, RHOA, SELE, DRD2, ARHGAP24, MTNR1A, FKBP3, ARRB2, GRM8</i>
6	<i>NPY2R, RGS12, GNAI3, ADRA2C, GNAI2, GNAO1, CACNA1B, GNAI1, GRM6, IL8RB, PLCB3</i>
7	<i>ADRA2A, PDE6G, SRC, MC4R, ARRB1, SNCA, RPLP2, FPR1, BDKRB2, ADRBK1, OPRD1</i>
8	<i>PLCB1, TXNDC4, ITPR1, CCNB1, LYN, CA8, PLCG2</i>
9	<i>F2RL3, HTR2A, ADRA1B, F2R, RGS2, HTR2A, GNAQ, F2RL2, CHRM3, PIK3CA, BDKRB2, TBXA2R, BDKRB1</i>
10	<i>GNB2L1, CNP, STAU1, CHGB, PSME1, SOCS7, DLST, ALDOA, SYK, SDC3, TUBB, TGM2, HD, MARK4, MAP4, MX1, TUBA1A, SOCS6, C7orf25, PLA2G7</i>
11	<i>HOMER1, STX12, CENTG1, RYR2, LOC653098, HOMER3, C1orf116, SHANK1, RYR1</i>
12	<i>CNR1, GNA15, CHRM2, ADRB2</i>
13	<i>DYNLL1, PIK3R1, NMI, TUBA2, PXN, TUBG1, NFKBIA, TUBA1B, YWHAQ</i>
14	<i>HRPT2, RIF1, GRM3</i>
15	<i>CALM3, GRM5, MYO6, KIAA1683, GRM7, LOC642393, C17orf44, CALM2</i>
16	<i>CALB2, TCP1, LTA, TUBA1, ZAP70</i>
17	<i>ADA, ADORA1</i>