SUPPLEMENTARY INFORMATION

SUPPLEMENTARY METHODS

Sample Selection

For genome-wide genotyping, cases were defined as a child diagnosed with neuroblastoma or ganglioneuroblastoma and registered through the Children's Oncology Group (COG). The blood samples from the neuroblastoma cases were identified through the COG Neuroblastoma bio-repository for specimen collection at the time of diagnosis. The majority of specimens were annotated with clinical and genomic information that included: age at diagnosis, site of origin, disease stage by the International Neuroblastoma Staging System[26], INPC International Neuroblastoma Pathology Classification[27], *MYCN* oncogene copy number[28], DNA index (ploidy)[29], registration on clinical trial(s), event-free and overall survival, second malignancies, and any associated conditions (e.g. congenital abnormalities).

Eligibility criterion for genotyping was availability of 1.5 µg of high quality DNA from a tumor-free source such as peripheral blood or uninvolved (with tumor) bone marrow mononuclear cells. Because neuroblastoma in the United States is demographically a disease of Caucasians of European descent[32], we limited our initial analyses to this racial group to minimize phenotypic variability.

Additional criteria for incorporation into CNV analysis included standard deviation of Log-R-Ratio ≤ 0.35 and the ability to use a common reference set for copy number estimation. Given that neuroblastoma patients may have circulating tumor DNA/cells, we also carefully excluded any case in the discovery set with evidence in the blood/bone marrow of *MYCN* amplification and/or large-scale genomic alterations commonly detected in neuroblastoma primary tumors[5]; this assessment was based on DNA copy number generated from the SNP data. The exclusion criteria used in the replication sets was slightly different. Here, we excluded any case with evidence for large scale genomic alterations, but did not exclude a case if the only detectable tumor-like genomic alteration was amplification or low-level gain of *MYCN*.

Our starting point for the discovery case series and first replication case series were the exact discovery and replication set reported by Maris and colleagues[1]. These were all self-described Caucasian individuals, confirmed by SNP analysis of AIMs markers. After quality filtering described above, 846 (out of 1032) cases remained in the discovery case series, and 363 (out of 401) remained in the first replication case series. **Supplementary Table 1** details how we arrived at these numbers. To further address the possibility of population substructure captured by SNPs not in linkage disequilibrium (LD), we performed a multi-dimensional scaling (MDS) analysis of the discovery cases and controls along with a well-characterized set of Caucasian, African American, and Asian samples. **Supplementary Figure 1** plots the first two scaling dimensions and indicates that population substructure is not likely to have a significant impact on the findings of this CNV-based study.

For the second replication set used in this study, a starting set of 285 independent Caucasian cases were identified by assessing the first two components of an MDS analysis of all SNPs using ~20,000 individuals of multiple ethnicities that were accrued and genotyped at the Children's Hospital of Philadelphia (CHOP). Of these, 232 passed our quality control criteria and were utilized in the second replication set (**Supplementary Table 1**). **Supplementary Table 2** summarizes the clinical and biological co-variate data for each case series.

Control subjects were recruited from the Philadelphia region through the CHOP Health Care Network, including four primary care clinics and several group practices and outpatient practices that included well child visits. Eligibility criteria for control subjects were: 1) self-reported as Caucasian; 2) availability of 1.5 µg of high quality DNA from peripheral blood mononuclear cells; and 3) no serious underlying medical disorder, including cancer.

The controls in the discovery and first replication set used in this study represent a subset of those reported by Maris and colleagues[1]. Additional criteria for incorporation into CNV analysis included standard deviation of Log-R-Ratio ≤ 0.35 and the ability to use a common reference set for copy number estimation. **Supplemental Table 1** details how we arrived at our final discovery control set of 803 and initial replication set of 1139.

For the second replication set used in this study, a starting set of 2,267 independent Caucasian controls were identified by assessing the first two components of an MDS analysis of all SNPs using ~20,000 individuals of multiple ethnicities that were accrued and genotyped at CHOP. A total of 2,218 of these controls passed quality control and were used in this study (**Supplemental Table 1**). The median age of the control cohort at the time of sample collection was 10.0 years.

Genome-wide SNP Genotyping

Genotyping for both the discovery and replication phase was performed using the Illumina Infinium™ II HumanHap550 BeadChip according to methods detailed elsewhere[15,30], and summarized here. DNA samples were surveyed for quality both by optical density spectrophotometry and the pico-green assay. Samples judged to be of sufficient quality for genotyping were assayed on the Illumina Infinium™ II HumanHap550 BeadChip technology[15,30], (Illumina, San Diego) at the Center for Applied Genomics at the Children's Hospital of

Philadelphia. A total of 750 nanograms of germline genomic DNA was used to genotype each sample, according to the manufacturer's guidelines. On day one, genomic DNA was amplified 1000-1500-fold; and on day two, the amplified DNA was fragmented to ~300-600 basepairs (bp), precipitated and resuspended followed by hybridization onto a BeadChip. Single base extension (SBE) utilized a single probe sequence of approximately 50 bp long designed to hybridize immediately adjacent to the single nucleotide polymorphism (SNP) query site. Following targeted hybridization to the bead array, the arrayed SNP locus-specific primers (attached to beads) were extended with a single hapten-labeled dideoxynucleotide in the single base extension reaction. The haptens were subsequently detected by a multi-layer immunohistochemical sandwich assay. The Illumina BeadArray Reader scanned each BeadChip at two wavelengths and created an image file. As BeadChip images were collected, intensity values were determined for all instances of each bead type, and data files were created that summarized intensity values for each bead type. These files consisted of intensity data that was loaded directly into Illumina's genotype analysis software, BeadStudio. A bead pool manifest created from the Laboratory Information Management System (LIMS) database containing all the BeadChip data was loaded into BeadStudio along with the intensity data for the samples. Data was normalized within BeadStudio to minimize BeadChip to BeadChip variability. Once the normalization was complete, the clustering algorithm was run to evaluate cluster positions for each locus, assign individual genotypes, a B-Allele Frequency (BAF), and the Log-R-Ratio (LRR).

SUPPLEMENTARY TABLES

	Discovery Cases	Discovery Controls	Replication Set 1 Cases	Replication Set 1 Controls	Replication Set 2 Cases	Replication Set 2 Controls
Total considered	1,032	2,043	401	1,178	285	2,267
tumor DNA	112	0	12	0	10	0
common reference	0	1,130	0	0	0	0
SD LRR < 0.35	74	110	26	39	43	49
Total final set	**846**	**803**	**363**	**1,139**	**232**	**2,218**

Supplementary Table 1. Quality control of discovery and replication sets. List of total number of samples considered, total number excluded at each (successive) QC step, and the final number used in each phase of the GWAS. The starting point for the discovery and first replication set were the exact sample sets utilized by Maris and colleagues[7]. The starting point for the second replication set was an independent set of 285 Caucasian cases and 2,267 Caucasian controls as described in Detailed Methods.

Characteristic	Discovery Set *N*=846	Replication Set 1 *N*=363	Replication Set 2 *N*=232	Primary Tumor Set *N*=488
Sex				
Female	409 (49)	178 (49)	77 (45)	223 (46)
Male	432 (51)	185 (51)	95 (55)	265 (54)
Not Available	5	0	60	0
Age				
< 1 yr	325 (39)	128 (35)	68 (33)	153 (31)
≥ 1 yr	515 (61)	235 (65)	137 (67)	335 (69)
Not Available	6	0	27	0
INSS Stage				
Stage 1	192 (24)	58 (17)	29 (15)	54 (11)
Stage 2	124 (15)	43 (12)	22 (10)	46 (9)
Stage 3	140 (17)	59 (17)	33 (17)	86 (18)
Stage 4	304 (37)	165 (47)	98 (50)	259 (53)
Stage 4S	47 (6)	25 (7)	16 (8)	43 (9)
Not Available	39	13	35	0
MYCN				
Not Amplified	693 (86)	246 (79)	145 (79)	376 (77)
Amplified	112 (14)	63 (21)	38 (21)	109 (22)
Not available	41	54	49	0
Histology				
Favorable	392 (58)	151 (55)	91 (56)	196 (42)
Unfavorable	280 (42)	126 (45)	71	268 (58)
Not available	174	86	70	24
DNA index				
Hyperdiploid	539 (67)	190 (63)	92 (56)	305 (63)
Diploid	262 (33)	114 (37)	73 (44)	179 (37)
Not available	45	59	67	4
Risk				
Low	352 (44)	108 (32)	58 (30)	128 (26)
Intermediate	145 (18)	66 (20)	36 (19)	75 (15)
High	297 (37)	162 (48)	99 (51)	285 (58)
Not available	52	27	39	0

Supplementary Table 2. Neuroblastoma sample characteristics. Neuroblastoma patient and tumor characteristics for 846 cases used in the discovery set, 363 cases used in the replication set-1, 232 cases used in replication set-2, and 488 primary tumors after data quality control filtration and exclusion of outliers. 226 of the 488 tumors analyzed were matched to blood DNA from individuals in the CNV-based GWAS. Frequency within each clinical/biological subset is listed in parentheses.

SNP	Chr	Position	Gene(s)	Cases Loss	Cases No Loss	Ctrls Loss	Ctrls No Loss	Cases Loss %	Ctrls Loss %	*P*-value
rs11579261	1	147305744	*Putative NBPF*	128	718	42	761	15.1	5.2	2.38E-11
rs17162082	1	147306690	*Putative NBPF*	128	718	42	761	15.1	5.2	2.38E-11
rs17161949	1	147311729	*Putative NBPF*	128	718	42	761	15.1	5.2	2.38E-11
rs6673776	1	147327306	*Putative NBPF*	128	718	42	761	15.1	5.2	2.38E-11
rs17162074	1	147331145	*Putative NBPF*	128	718	42	761	15.1	5.2	2.38E-11
rs11587304	1	147414362	*Putative NBPF*	108	738	31	772	12.8	3.9	3.62E-11
rs3853524	1	147427061	*Putative NBPF*	103	743	29	774	12.2	3.6	7.83E-11
rs7782269	7	38285115	*TCRG*	267	579	123	680	31.6	15.3	5.31E-15
rs2240826	7	38285864	*TCRG*	268	578	123	680	31.7	15.3	3.52E-15
rs2240827	7	38285961	*TCRG*	268	578	123	680	31.7	15.3	3.52E-15
rs1546833	7	38290215	*TCRG*	269	577	123	680	31.8	15.3	2.33E-15
rs10155916	7	38292303	*TCRG*	271	575	123	680	32.0	15.3	1.02E-15
rs1860516	7	38292502	*TCRG*	271	575	123	680	32.0	15.3	1.02E-15
rs2240832	7	38295538	*TCRG*	292	554	127	676	34.5	15.8	1.52E-18
rs12154478	7	38296343	*TCRG*	301	545	128	675	35.6	15.9	4.60E-20
rs1860517	7	38297335	*TCRG*	301	545	126	677	35.6	15.7	1.34E-20
rs1860520	7	38297796	*TCRG*	301	545	126	677	35.6	15.7	1.34E-20
rs1860521	7	38298029	*TCRG*	302	544	126	677	35.7	15.7	8.35E-21
rs6462829	7	38298742	*TCRG*	308	538	128	675	36.4	15.9	1.72E-21
rs10441090	7	38301343	*TCRG*	303	543	130	673	35.8	16.2	6.18E-20
rs2191311	7	38302045	*TCRG*	302	544	130	673	35.7	16.2	9.78E-20
rs2248839	7	38307751	*TCRG*	284	562	115	688	33.6	14.3	4.09E-20
rs2736973	7	38308140	*TCRG*	281	565	114	689	33.2	14.2	5.86E-20
rs2240839	7	38308450	*TCRG*	260	586	107	696	30.7	13.3	1.16E-17
rs2392545	7	38309522	*TCRG*	249	597	106	697	29.4	13.2	5.60E-16
rs2392546	7	38309610	*TCRG*	246	600	105	698	29.1	13.1	1.13E-15
rs2736969	7	38310481	*TCRG*	228	618	74	729	27.0	9.2	3.13E-21
rs2736964	7	38311294	*TCRG*	221	625	69	734	26.1	8.6	2.27E-21
rs6953248	7	38322940	*TCRG*	214	632	61	742	25.3	7.6	6.76E-23
rs17171329	7	38323070	*TCRG*	215	631	61	742	25.4	7.6	3.95E-23
rs11769443	7	38323600	*TCRG*	208	638	59	744	24.6	7.3	2.96E-22
rs11980080	7	38323719	*TCRG*	208	638	59	744	24.6	7.3	2.96E-22
rs11765884	7	38323848	*TCRG*	204	642	55	748	24.1	6.8	7.43E-23
rs2534565	7	38324752	*TCRG*	187	659	22	781	22.1	2.7	6.84E-36
rs2240845	7	38324937	*TCRG*	188	658	22	781	22.2	2.7	3.45E-36
rs2534567	7	38325481	*TCRG*	184	662	22	781	21.7	2.7	5.31E-35
rs2534568	7	38326165	*TCRG*	183	663	22	781	21.6	2.7	1.05E-34
rs2240848	7	38327992	*TCRG*	185	661	23	780	21.9	2.9	1.27E-34
rs11975431	7	38328150	*TCRG*	189	657	23	780	22.3	2.9	8.43E-36
rs718880	7	38328524	*TCRG*	192	654	22	781	22.7	2.7	2.20E-37
rs2240849	7	38328597	*TCRG*	192	654	23	780	22.7	2.9	1.09E-36
rs17171331	7	38329482	*TCRG*	194	652	27	776	22.9	3.4	1.25E-34

rs11984094	7	38330091	*TCRG*	189	657	29	774	22.3	3.6	5.62E-32
rs2240850	7	38330273	*TCRG*	191	655	35	768	22.6	4.4	6.73E-29
rs2240851	7	38330454	*TCRG*	188	658	35	768	22.2	4.4	2.50E-28
rs17496969	7	38330814	*TCRG*	189	657	35	768	22.3	4.4	2.34E-28
rs2735179	7	38331130	*TCRG*	190	656	33	770	22.5	4.1	6.01E-30
rs10487742	7	38333037	*TCRG*	180	666	25	778	21.3	3.1	7.01E-32
rs2191312	7	38333784	*TCRG*	172	674	25	778	20.3	3.1	1.30E-29
rs6966279	7	38336073	*TCRG*	171	675	24	779	20.2	3.0	6.11E-30
rs2534575	7	38337999	*TCRG*	158	688	23	780	18.7	2.9	3.49E-27
rs2534578	7	38340056	*TCRG*	126	720	17	786	14.9	2.1	2.28E-22
rs2240853	7	38341222	*TCRG*	99	747	9	794	11.7	1.1	2.12E-20
rs733905	7	38346971	*TCRG*	73	773	4	799	8.6	0.5	1.90E-17
rs2213212	7	142086318	*TCRVB*	33	813	1	802	3.9	0.1	4.10E-09
rs2027801	7	142100266	*TCRVB*	38	808	1	802	4.5	0.1	1.45E-10
rs17251	7	142102868	*TCRVB*	39	807	1	802	4.6	0.1	7.42E-11
rs4726572	7	142104421	*TCRVB*	39	807	1	802	4.6	0.1	7.42E-11
rs6464528	7	142104463	*TCRVB*	39	807	1	802	4.6	0.1	7.42E-11
rs6959895	7	142114524	*TCRVB*	44	802	2	801	5.2	0.2	3.02E-11
rs1964986	7	142127214	*TCRVB*	40	806	2	801	4.7	0.2	4.09E-10
rs2855983	7	142178383	*TCRVB*	43	803	2	801	5.1	0.2	5.80E-11
rs2734222	7	142187838	*TCRVB*	41	805	2	801	4.8	0.2	2.14E-10
rs2734224	7	142188690	*TCRVB*	38	808	2	801	4.5	0.2	1.49E-09
rs2367486	7	142192134	*TCRVB*	35	811	2	801	4.1	0.2	1.03E-08
rs979027	14	21558349	*TCRA, TCRD*	44	802	5	798	5.2	0.6	1.35E-08
rs17113407	14	21558421	*TCRA, TCRD*	44	802	5	798	5.2	0.6	1.35E-08
rs7147975	14	21560562	*TCRA, TCRD*	44	802	5	798	5.2	0.6	1.35E-08
rs12888049	14	21564578	*TCRA, TCRD*	47	799	7	796	5.6	0.9	3.58E-08
rs8022710	14	21565869	*TCRA, TCRD*	52	794	10	793	6.1	1.2	7.86E-08
rs990962	14	21637401	*TCRA, TCRD*	103	743	38	765	12.2	4.7	5.09E-08
rs8022578	14	21640025	*TCRA, TCRD*	107	739	40	763	12.6	5.0	3.46E-08
rs6572261	14	21641738	*TCRA, TCRD*	108	738	40	763	12.8	5.0	2.30E-08
rs6572331	14	21784682	*TCRA, TCRD*	174	672	80	723	20.6	10.0	2.17E-09
rs4982590	14	21788239	*TCRA, TCRD*	174	672	79	724	20.6	9.8	1.32E-09
rs10148895	14	21792564	*TCRA, TCRD*	184	662	80	723	21.7	10.0	4.90E-11
rs7155927	14	21800821	*TCRA, TCRD*	196	650	80	723	23.2	10.0	3.83E-13
rs7141113	14	21805737	*TCRA, TCRD*	196	650	79	724	23.2	9.8	2.11E-13
rs6572349	14	21806088	*TCRA, TCRD*	196	650	79	724	23.2	9.8	2.11E-13
rs6572351	14	21806138	*TCRA, TCRD*	196	650	79	724	23.2	9.8	2.11E-13
rs12881142	14	21806360	*TCRA, TCRD*	196	650	79	724	23.2	9.8	2.11E-13
rs2331599	14	21806501	*TCRA, TCRD*	200	646	78	725	23.6	9.7	2.05E-14
rs9972232	14	21807431	*TCRA, TCRD*	210	636	84	719	24.8	10.5	1.58E-14

rs3811272	14	21811574	*TCRA, TCRD*	215	631	86	717	25.4	10.7	6.10E-15
rs741711	14	21923525	*TCRA, TCRD*	262	584	114	689	31.0	14.2	2.99E-16
rs3811250	14	21925810	*TCRA, TCRD*	259	587	113	690	30.6	14.1	6.13E-16
rs3811247	14	21928200	*TCRA, TCRD*	255	591	114	689	30.1	14.2	5.80E-15
rs3811244	14	21929322	*TCRA, TCRD*	255	591	115	688	30.1	14.3	9.99E-15
rs12891257	14	21931475	*TCRA, TCRD*	257	589	114	689	30.4	14.2	2.51E-15
rs10142552	14	21933475	*TCRA, TCRD*	256	590	114	689	30.3	14.2	3.82E-15
rs3811240	14	21937715	*TCRA, TCRD*	259	587	115	688	30.6	14.3	1.88E-15
rs1040303	14	21941618	*TCRA, TCRD*	265	581	119	684	31.3	14.8	1.38E-15
rs7150307	14	21943295	*TCRA, TCRD*	267	579	119	684	31.6	14.8	5.96E-16
rs11624054	14	21944336	*TCRA, TCRD*	268	578	119	684	31.7	14.8	3.90E-16
rs714795	14	21946458	*TCRA, TCRD*	263	583	117	686	31.1	14.6	1.06E-15
rs4982635	14	21949578	*TCRA, TCRD*	265	581	123	680	31.3	15.3	1.20E-14
rs760019	14	21953018	*TCRA, TCRD*	269	577	131	672	31.8	16.3	2.02E-13
rs3811236	14	21956159	*TCRA, TCRD*	298	548	161	642	35.2	20.0	5.33E-12
rs2301201	14	21957570	*TCRA, TCRD*	301	545	159	644	35.6	19.8	7.49E-13
rs6572449	14	21970760	*TCRA, TCRD*	330	516	192	611	39.0	23.9	4.45E-11
rs7142158	14	21972830	*TCRA, TCRD*	330	516	192	611	39.0	23.9	4.45E-11
rs2141988	14	21973302	*TCRA, TCRD*	330	516	192	611	39.0	23.9	4.45E-11
rs3811232	14	21973771	*TCRA, TCRD*	330	516	192	611	39.0	23.9	4.45E-11
rs8021297	14	21974905	*TCRA, TCRD*	330	516	192	611	39.0	23.9	4.45E-11
rs11623995	14	21975565	*TCRA, TCRD*	335	511	201	602	39.6	25.0	2.54E-10
rs11157596	14	21976908	*TCRA, TCRD*	334	512	204	599	39.5	25.4	1.03E-09
rs12147516	14	21985656	*TCRA, TCRD*	382	464	243	560	45.2	30.3	5.32E-10
rs10483273	14	21986886	*TCRA, TCRD*	379	467	238	565	44.8	29.6	2.48E-10
rs11848747	14	21991120	*TCRA, TCRD*	368	478	216	587	43.5	26.9	2.08E-12
rs2242545	14	21994034	*TCRA, TCRD*	371	475	226	577	43.9	28.1	3.36E-11
rs1882704	14	21995192	*TCRA, TCRD*	370	476	229	574	43.7	28.5	1.38E-10
rs17794083	14	21996759	*TCRA, TCRD*	370	476	227	576	43.7	28.3	6.74E-11
rs10162417	14	21999540	*TCRA, TCRD*	364	482	241	562	43.0	30.0	4.35E-08
rs10131293	14	21999998	*TCRA, TCRD*	364	482	239	564	43.0	29.8	2.36E-08
rs2733776	14	22000627	*TCRA, TCRD*	359	487	233	570	42.4	29.0	1.52E-08
rs10483275	14	22002896	*TCRA, TCRD*	341	505	215	588	40.3	26.8	6.75E-09
rs8020193	14	22009307	*TCRA, TCRD*	254	592	119	684	30.0	14.8	1.23E-13

rs10483277	14	22010682	*TCRA, TCRD*	241	605	114	689	28.5	14.2	1.61E-12
rs2293732	14	22011989	*TCRA, TCRD*	237	609	113	690	28.0	14.1	3.19E-12
rs1076861	14	22012459	*TCRA, TCRD*	221	625	102	701	26.1	12.7	5.88E-12
rs2254272	14	22012730	*TCRA, TCRD*	220	626	98	705	26.0	12.2	1.09E-12
rs7161733	14	22015032	*TCRA, TCRD*	217	629	92	711	25.7	11.5	9.16E-14
rs10132733	14	22016071	*TCRA, TCRD*	202	644	85	718	23.9	10.6	8.37E-13
rs227859	14	22018311	*TCRA, TCRD*	162	684	68	735	19.1	8.5	2.69E-10
rs762578	14	22020088	*TCRA, TCRD*	155	691	63	740	18.3	7.8	2.54E-10
rs3811222	14	22020854	*TCRA, TCRD*	151	695	62	741	17.8	7.7	7.09E-10
rs3811221	14	22022792	*TCRA, TCRD*	146	700	60	743	17.3	7.5	1.66E-09
rs227867	14	22023701	*TCRA, TCRD*	141	705	57	746	16.7	7.1	1.50E-09
rs996165	14	22024524	*TCRA, TCRD*	134	712	50	753	15.8	6.2	3.77E-10
rs3811215	14	22024617	*TCRA, TCRD*	127	719	47	756	15.0	5.9	1.07E-09
rs2128997	14	22030942	*TCRA, TCRD*	87	759	29	774	10.3	3.6	7.57E-08

Supplementary Table 3. Genome-wide significant SNPs with copy number changes from Discovery Phase. Genomic coordinates based on build 36.1 of human genome. Two-tailed *P*-value based on Fisher's exact test reported. Results based on 846 Caucasian Cases and 803 healthy Caucasian Controls.

SNP	Chr	Position	Genes	Cases Loss	Cases No Loss	Ctrls Loss	Ctrls No Loss	Cases Loss %	Ctrls Loss %	*P*-value
rs11579261	1	147305744	Putative NBPF	52	311	99	1040	14.3	8.7	2.58E-03
rs17162082	1	147306690	Putative NBPF	52	311	99	1040	14.3	8.7	2.58E-03
rs17161949	1	147311729	Putative NBPF	52	311	99	1040	14.3	8.7	2.58E-03
rs6673776	1	147327306	Putative NBPF	52	311	99	1040	14.3	8.7	2.58E-03
rs17162074	1	147331145	Putative NBPF	52	311	99	1040	14.3	8.7	2.58E-03
rs11587304	1	147414362	Putative NBPF	39	324	73	1066	10.7	6.4	8.15E-03
rs3853524	1	147427061	Putative NBPF	39	324	73	1066	10.7	6.4	8.15E-03
rs7782269	7	38285115	*TCRG*	103	260	91	1048	28.4	8.0	9.41E-21
rs2240826	7	38285864	*TCRG*	104	259	91	1048	28.7	8.0	2.08E-21
rs2240827	7	38285961	*TCRG*	104	259	91	1048	28.7	8.0	2.08E-21
rs1546833	7	38290215	*TCRG*	104	259	90	1049	28.7	7.9	1.30E-21
rs10155916	7	38292303	*TCRG*	108	255	92	1047	29.8	8.1	8.61E-23
rs1860516	7	38292502	*TCRG*	108	255	92	1047	29.8	8.1	8.61E-23
rs2240832	7	38295538	*TCRG*	109	254	99	1040	30.0	8.7	1.04E-21
rs12154478	7	38296343	*TCRG*	110	253	99	1040	30.3	8.7	4.06E-22
rs1860517	7	38297335	*TCRG*	110	253	102	1037	30.3	9.0	2.07E-21
rs1860520	7	38297796	*TCRG*	110	253	105	1034	30.3	9.2	1.01E-20
rs1860521	7	38298029	*TCRG*	110	253	106	1033	30.3	9.3	1.47E-20
rs6462829	7	38298742	*TCRG*	110	253	105	1034	30.3	9.2	1.01E-20
rs10441090	7	38301343	*TCRG*	107	256	105	1034	29.5	9.2	2.08E-19
rs2191311	7	38302045	*TCRG*	107	256	104	1035	29.5	9.1	9.21E-20
rs2248839	7	38307751	*TCRG*	95	268	100	1039	26.2	8.8	8.21E-16
rs2736973	7	38308140	*TCRG*	86	277	91	1048	23.7	8.0	4.81E-14
rs2240839	7	38308450	*TCRG*	86	277	88	1051	23.7	7.7	1.26E-14
rs2392545	7	38309522	*TCRG*	81	282	86	1053	22.3	7.6	2.87E-13
rs2392546	7	38309610	*TCRG*	81	282	86	1053	22.3	7.6	2.87E-13
rs2736969	7	38310481	*TCRG*	79	284	63	1076	21.8	5.5	1.81E-17
rs2736964	7	38311294	*TCRG*	73	290	60	1079	20.1	5.3	1.76E-15
rs6953248	7	38322940	*TCRG*	63	300	58	1081	17.4	5.1	4.27E-12
rs17171329	7	38323070	*TCRG*	63	300	58	1081	17.4	5.1	4.27E-12
rs11769443	7	38323600	*TCRG*	54	309	43	1096	14.9	3.8	5.77E-12
rs11980080	7	38323719	*TCRG*	54	309	43	1096	14.9	3.8	5.77E-12
rs11765884	7	38323848	*TCRG*	54	309	38	1101	14.9	3.3	2.49E-13
rs2534565	7	38324752	*TCRG*	54	309	29	1110	14.9	2.5	4.06E-16
rs2240845	7	38324937	*TCRG*	54	309	29	1110	14.9	2.5	4.06E-16
rs2534567	7	38325481	*TCRG*	54	309	28	1111	14.9	2.5	1.80E-16
rs2534568	7	38326165	*TCRG*	54	309	28	1111	14.9	2.5	1.80E-16
rs2240848	7	38327992	*TCRG*	54	309	29	1110	14.9	2.5	4.06E-16
rs11975431	7	38328150	*TCRG*	54	309	28	1111	14.9	2.5	1.80E-16
rs718880	7	38328524	*TCRG*	49	314	22	1117	13.5	1.9	2.85E-16
rs2240849	7	38328597	*TCRG*	49	314	22	1117	13.5	1.9	2.85E-16
rs17171331	7	38329482	*TCRG*	51	312	20	1119	14.0	1.8	3.98E-18
rs11984094	7	38330091	*TCRG*	47	316	19	1120	12.9	1.7	1.70E-16

rs2240850	7	38330273	*TCRG*	47	316	20	1119	12.9	1.8	4.47E-16
rs2240851	7	38330454	*TCRG*	47	316	20	1119	12.9	1.8	4.47E-16
rs17496969	7	38330814	*TCRG*	47	316	20	1119	12.9	1.8	4.47E-16
rs2735179	7	38331130	*TCRG*	47	316	17	1122	12.9	1.5	2.19E-17
rs10487742	7	38333037	*TCRG*	46	317	15	1124	12.7	1.3	8.29E-18
rs2191312	7	38333784	*TCRG*	43	320	14	1125	11.8	1.2	1.08E-16
rs6966279	7	38336073	*TCRG*	39	324	13	1126	10.7	1.1	4.65E-15
rs2534575	7	38337999	*TCRG*	31	332	12	1127	8.5	1.1	2.19E-11
rs2534578	7	38340056	*TCRG*	31	332	12	1127	8.5	1.1	2.19E-11
rs2240853	7	38341222	*TCRG*	31	332	9	1130	8.5	0.8	8.20E-13
rs733905	7	38346971	*TCRG*	21	342	2	1137	5.8	0.2	1.10E-11
rs2213212	7	142086318	*TCRVB*	16	347	0	1139	4.4	0.0	1.05E-10
rs2027801	7	142100266	*TCRVB*	14	349	0	1139	3.9	0.0	1.91E-09
rs17251	7	142102868	*TCRVB*	14	349	0	1139	3.9	0.0	1.91E-09
rs4726572	7	142104421	*TCRVB*	14	349	0	1139	3.9	0.0	1.91E-09
rs6464528	7	142104463	*TCRVB*	14	349	0	1139	3.9	0.0	1.91E-09
rs6959895	7	142114524	*TCRVB*	15	348	0	1139	4.1	0.0	4.48E-10
rs1964986	7	142127214	*TCRVB*	15	348	0	1139	4.1	0.0	4.48E-10
rs2855983	7	142178383	*TCRVB*	9	354	0	1139	2.5	0.0	2.61E-06
rs2734222	7	142187838	*TCRVB*	7	356	0	1139	1.9	0.0	4.61E-05
rs2734224	7	142188690	*TCRVB*	7	356	0	1139	1.9	0.0	4.61E-05
rs2367486	7	142192134	*TCRVB*	7	356	0	1139	1.9	0.0	4.61E-05
rs979027	14	21558349	*TCRA, TCRD*	8	355	4	1135	2.2	0.4	2.11E-03
rs17113407	14	21558421	*TCRA, TCRD*	8	355	4	1135	2.2	0.4	2.11E-03
rs7147975	14	21560562	*TCRA, TCRD*	8	355	5	1134	2.2	0.4	4.35E-03
rs12888049	14	21564578	*TCRA, TCRD*	10	353	17	1122	2.8	1.5	1.17E-01
rs8022710	14	21565869	*TCRA, TCRD*	13	350	22	1117	3.6	1.9	7.45E-02
rs990962	14	21637401	*TCRA, TCRD*	49	314	62	1077	13.5	5.4	1.52E-06
rs8022578	14	21640025	*TCRA, TCRD*	52	311	67	1072	14.3	5.9	1.04E-06
rs6572261	14	21641738	*TCRA, TCRD*	52	311	67	1072	14.3	5.9	1.04E-06
rs6572331	14	21784682	*TCRA, TCRD*	63	300	125	1014	17.4	11.0	1.91E-03
rs4982590	14	21788239	*TCRA, TCRD*	62	301	121	1018	17.1	10.6	1.65E-03
rs10148895	14	21792564	*TCRA, TCRD*	61	302	114	1025	16.8	10.0	6.87E-04
rs7155927	14	21800821	*TCRA, TCRD*	60	303	100	1039	16.5	8.8	8.00E-05
rs7141113	14	21805737	*TCRA, TCRD*	59	304	93	1046	16.3	8.2	2.25E-05
rs6572349	14	21806088	*TCRA, TCRD*	59	304	93	1046	16.3	8.2	2.25E-05
rs6572351	14	21806138	*TCRA, TCRD*	59	304	93	1046	16.3	8.2	2.25E-05
rs12881142	14	21806360	*TCRA, TCRD*	59	304	93	1046	16.3	8.2	2.25E-05
rs2331599	14	21806501	*TCRA, TCRD*	60	303	92	1047	16.5	8.1	9.10E-06
rs9972232	14	21807431	*TCRA, TCRD*	66	297	95	1044	18.2	8.3	5.06E-07
rs3811272	14	21811574	*TCRA,*	71	292	101	1038	19.6	8.9	1.28E-07

			TCRD							
rs741711	14	21923525	*TCRA, TCRD*	91	272	134	1005	25.1	11.8	3.61E-09
rs3811250	14	21925810	*TCRA, TCRD*	92	271	133	1006	25.3	11.7	1.30E-09
rs3811247	14	21928200	*TCRA, TCRD*	93	270	133	1006	25.6	11.7	7.36E-10
rs3811244	14	21929322	*TCRA, TCRD*	97	266	135	1004	26.7	11.9	1.14E-10
rs12891257	14	21931475	*TCRA, TCRD*	97	266	136	1003	26.7	11.9	1.27E-10
rs10142552	14	21933475	*TCRA, TCRD*	97	266	136	1003	26.7	11.9	1.27E-10
rs3811240	14	21937715	*TCRA, TCRD*	98	265	135	1004	27.0	11.9	4.12E-11
rs1040303	14	21941618	*TCRA, TCRD*	98	265	134	1005	27.0	11.8	3.54E-11
rs7150307	14	21943295	*TCRA, TCRD*	97	266	132	1007	26.7	11.6	3.06E-11
rs11624054	14	21944336	*TCRA, TCRD*	97	266	130	1009	26.7	11.4	2.26E-11
rs714795	14	21946458	*TCRA, TCRD*	98	265	131	1008	27.0	11.5	1.47E-11
rs4982635	14	21949578	*TCRA, TCRD*	99	264	138	1001	27.3	12.1	5.56E-11
rs760019	14	21953018	*TCRA, TCRD*	97	266	141	998	26.7	12.4	5.72E-10
rs3811236	14	21956159	*TCRA, TCRD*	101	262	154	985	27.8	13.5	1.76E-09
rs2301201	14	21957570	*TCRA, TCRD*	101	262	151	988	27.8	13.3	8.60E-10
rs6572449	14	21970760	*TCRA, TCRD*	101	262	160	979	27.8	14.0	7.22E-09
rs7142158	14	21972830	*TCRA, TCRD*	101	262	160	979	27.8	14.0	7.22E-09
rs2141988	14	21973302	*TCRA, TCRD*	101	262	158	981	27.8	13.9	4.07E-09
rs3811232	14	21973771	*TCRA, TCRD*	101	262	160	979	27.8	14.0	7.22E-09
rs8021297	14	21974905	*TCRA, TCRD*	101	262	162	977	27.8	14.2	1.28E-08
rs11623995	14	21975565	*TCRA, TCRD*	103	260	170	969	28.4	14.9	3.27E-08
rs11157596	14	21976908	*TCRA, TCRD*	104	259	177	962	28.7	15.5	7.69E-08
rs12147516	14	21985656	*TCRA, TCRD*	112	251	209	930	30.9	18.3	1.05E-06
rs10483273	14	21986886	*TCRA, TCRD*	111	252	209	930	30.6	18.3	1.53E-06
rs11848747	14	21991120	*TCRA, TCRD*	105	258	198	941	28.9	17.4	4.07E-06
rs2242545	14	21994034	*TCRA, TCRD*	105	258	206	933	28.9	18.1	1.52E-05
rs1882704	14	21995192	*TCRA, TCRD*	105	258	208	931	28.9	18.3	2.21E-05
rs17794083	14	21996759	*TCRA, TCRD*	105	258	218	921	28.9	19.1	1.29E-04
rs10162417	14	21999540	*TCRA, TCRD*	104	259	227	912	28.7	19.9	6.24E-04
rs10131293	14	21999998	*TCRA, TCRD*	104	259	225	914	28.7	19.8	4.64E-04
rs2733776	14	22000627	*TCRA, TCRD*	104	259	223	916	28.7	19.6	4.37E-04
rs10483275	14	22002896	*TCRA, TCRD*	97	266	209	930	26.7	18.3	7.46E-04
rs8020193	14	22009307	*TCRA, TCRD*	90	273	136	1003	24.8	11.9	1.15E-08

rs10483277	14	22010682	*TCRA, TCRD*	89	274	134	1005	24.5	11.8	1.46E-08
rs2293732	14	22011989	*TCRA, TCRD*	89	274	134	1005	24.5	11.8	1.46E-08
rs1076861	14	22012459	*TCRA, TCRD*	87	276	129	1010	24.0	11.3	1.50E-08
rs2254272	14	22012730	*TCRA, TCRD*	87	276	121	1018	24.0	10.6	1.05E-09
rs7161733	14	22015032	*TCRA, TCRD*	78	285	111	1028	21.5	9.7	3.05E-08
rs10132733	14	22016071	*TCRA, TCRD*	76	287	109	1030	20.9	9.6	6.63E-08
rs227859	14	22018311	*TCRA, TCRD*	74	289	101	1038	20.4	8.9	1.76E-08
rs762578	14	22020088	*TCRA, TCRD*	69	294	91	1048	19.0	8.0	2.47E-08
rs3811222	14	22020854	*TCRA, TCRD*	69	294	91	1048	19.0	8.0	2.47E-08
rs3811221	14	22022792	*TCRA, TCRD*	62	301	72	1067	17.1	6.3	4.73E-09
rs227867	14	22023701	*TCRA, TCRD*	57	306	60	1079	15.7	5.3	1.71E-09
rs996165	14	22024524	*TCRA, TCRD*	53	310	50	1089	14.6	4.4	5.48E-10
rs3811215	14	22024617	*TCRA, TCRD*	53	310	50	1089	14.6	4.4	5.48E-10
rs2128997	14	22030942	*TCRA, TCRD*	23	340	25	1114	6.3	2.2	2.55E-04

Supplementary Table 4. Replication Set-1 results for genome-wide significant SNPs with copy number changes in Discovery Phase. Genomic coordinates based on build 36.1 of human genome. Two-tailed *P*-value based on Fisher’s exact test reported. Results based on 363 Caucasian Cases and 1,139 healthy Caucasian Controls.

SNP	**Chr**	**Position**	**Genes**	**Cases Loss**	**Cases No Loss**	**Ctrls Loss**	**Ctrls No Loss**	**Cases Loss %**	**Ctrls Loss %**	***P*-value**
rs11579261	1	147305744	Putative NBPF	44	188	239	1979	19.0	10.8	4.93E-04
rs17162082	1	147306690	Putative NBPF	44	188	239	1979	19.0	10.8	4.93E-04
rs17161949	1	147311729	Putative NBPF	44	188	239	1979	19.0	10.8	4.93E-04
rs6673776	1	147327306	Putative NBPF	44	188	236	1982	19.0	10.6	4.52E-04
rs17162074	1	147331145	Putative NBPF	44	188	236	1982	19.0	10.6	4.52E-04
rs11587304	1	147414362	Putative NBPF	33	199	122	2096	14.2	5.5	5.50E-06
rs3853524	1	147427061	Putative NBPF	33	199	120	2098	14.2	5.4	2.59E-06
rs7782269	7	38285115	*TCRG*	69	163	155	2063	29.7	7.0	7.25E-22
rs2240826	7	38285864	*TCRG*	69	163	155	2063	29.7	7.0	7.25E-22
rs2240827	7	38285961	*TCRG*	69	163	155	2063	29.7	7.0	7.25E-22
rs1546833	7	38290215	*TCRG*	69	163	155	2063	29.7	7.0	7.25E-22
rs10155916	7	38292303	*TCRG*	70	162	153	2065	30.2	6.9	9.34E-23
rs1860516	7	38292502	*TCRG*	70	162	153	2065	30.2	6.9	9.34E-23
rs2240832	7	38295538	*TCRG*	72	160	159	2059	31.0	7.2	3.00E-23
rs12154478	7	38296343	*TCRG*	72	160	163	2055	31.0	7.3	9.76E-23
rs1860517	7	38297335	*TCRG*	72	160	162	2056	31.0	7.3	7.29E-23
rs1860520	7	38297796	*TCRG*	72	160	162	2056	31.0	7.3	7.29E-23
rs1860521	7	38298029	*TCRG*	72	160	162	2056	31.0	7.3	7.29E-23
rs6462829	7	38298742	*TCRG*	72	160	158	2060	31.0	7.1	2.22E-23
rs10441090	7	38301343	*TCRG*	72	160	160	2058	31.0	7.2	4.04E-23
rs2191311	7	38302045	*TCRG*	71	161	159	2059	30.6	7.2	1.29E-22
rs2248839	7	38307751	*TCRG*	64	168	131	2087	27.6	5.9	7.13E-22
rs2736973	7	38308140	*TCRG*	60	172	111	2107	25.9	5.0	3.66E-22
rs2240839	7	38308450	*TCRG*	54	178	107	2111	23.3	4.8	7.90E-19
rs2392545	7	38309522	*TCRG*	53	179	104	2114	22.8	4.7	1.28E-18
rs2392546	7	38309610	*TCRG*	50	182	104	2114	21.6	4.7	9.81E-17
rs2736969	7	38310481	*TCRG*	51	181	89	2129	22.0	4.0	1.37E-19
rs2736964	7	38311294	*TCRG*	48	184	82	2136	20.7	3.7	1.02E-18
rs6953248	7	38322940	*TCRG*	48	184	72	2146	20.7	3.2	1.83E-20
rs17171329	7	38323070	*TCRG*	48	184	72	2146	20.7	3.2	1.83E-20
rs11769443	7	38323600	*TCRG*	44	188	68	2150	19.0	3.1	2.15E-18
rs11980080	7	38323719	*TCRG*	44	188	66	2152	19.0	3.0	9.28E-19
rs11765884	7	38323848	*TCRG*	44	188	64	2154	19.0	2.9	3.91E-19
rs2534565	7	38324752	*TCRG*	40	192	40	2178	17.2	1.8	1.81E-21
rs2240845	7	38324937	*TCRG*	40	192	40	2178	17.2	1.8	1.81E-21
rs2534567	7	38325481	*TCRG*	40	192	40	2178	17.2	1.8	1.81E-21
rs2534568	7	38326165	*TCRG*	40	192	40	2178	17.2	1.8	1.81E-21
rs2240848	7	38327992	*TCRG*	39	193	37	2181	16.8	1.7	1.78E-21
rs11975431	7	38328150	*TCRG*	39	193	36	2182	16.8	1.6	9.41E-22
rs718880	7	38328524	*TCRG*	39	193	34	2184	16.8	1.5	2.52E-22
rs2240849	7	38328597	*TCRG*	39	193	35	2183	16.8	1.6	4.90E-22
rs17171331	7	38329482	*TCRG*	39	193	39	2179	16.8	1.8	6.12E-21

rs11984094	7	38330091	*TCRG*	40	192	38	2180	17.2	1.7	5.25E-22
rs2240850	7	38330273	*TCRG*	40	192	39	2179	17.2	1.8	9.80E-22
rs2240851	7	38330454	*TCRG*	39	193	39	2179	16.8	1.8	6.12E-21
rs17496969	7	38330814	*TCRG*	39	193	38	2180	16.8	1.7	3.32E-21
rs2735179	7	38331130	*TCRG*	38	194	37	2181	16.4	1.7	1.12E-20
rs10487742	7	38333037	*TCRG*	36	196	29	2189	15.5	1.3	2.36E-21
rs2191312	7	38333784	*TCRG*	34	198	29	2189	14.7	1.3	1.05E-19
rs6966279	7	38336073	*TCRG*	32	200	27	2191	13.8	1.2	1.14E-18
rs2534575	7	38337999	*TCRG*	30	202	24	2194	12.9	1.1	6.05E-18
rs2534578	7	38340056	*TCRG*	26	206	18	2200	11.2	0.8	1.42E-16
rs2240853	7	38341222	*TCRG*	20	212	14	2204	8.6	0.6	6.45E-13
rs733905	7	38346971	*TCRG*	18	214	9	2209	7.8	0.4	4.34E-13
rs2213212	7	142086318	*TCRVB*	9	223	4	2214	3.9	0.2	2.69E-07
rs2027801	7	142100266	*TCRVB*	9	223	4	2214	3.9	0.2	2.69E-07
rs17251	7	142102868	*TCRVB*	9	223	3	2215	3.9	0.1	9.03E-08
rs4726572	7	142104421	*TCRVB*	9	223	3	2215	3.9	0.1	9.03E-08
rs6464528	7	142104463	*TCRVB*	9	223	3	2215	3.9	0.1	9.03E-08
rs6959895	7	142114524	*TCRVB*	10	222	3	2215	4.3	0.1	1.07E-08
rs1964986	7	142127214	*TCRVB*	10	222	3	2215	4.3	0.1	1.07E-08
rs2855983	7	142178383	*TCRVB*	8	224	3	2215	3.4	0.1	7.40E-07
rs2734222	7	142187838	*TCRVB*	8	224	2	2216	3.4	0.1	2.20E-07
rs2734224	7	142188690	*TCRVB*	8	224	2	2216	3.4	0.1	2.20E-07
rs2367486	7	142192134	*TCRVB*	7	225	2	2216	3.0	0.1	1.91E-06
rs979027	14	21558349	*TCRA, TCRD*	10	222	8	2210	4.3	0.4	1.06E-06
rs17113407	14	21558421	*TCRA, TCRD*	10	222	8	2210	4.3	0.4	1.06E-06
rs7147975	14	21560562	*TCRA, TCRD*	10	222	9	2209	4.3	0.4	2.06E-06
rs12888049	14	21564578	*TCRA, TCRD*	11	221	14	2204	4.7	0.6	5.86E-06
rs8022710	14	21565869	*TCRA, TCRD*	12	220	22	2196	5.2	1.0	3.25E-05
rs990962	14	21637401	*TCRA, TCRD*	25	207	78	2140	10.8	3.5	5.03E-06
rs8022578	14	21640025	*TCRA, TCRD*	28	204	83	2135	12.1	3.7	5.49E-07
rs6572261	14	21641738	*TCRA, TCRD*	28	204	85	2133	12.1	3.8	8.18E-07
rs6572331	14	21784682	*TCRA, TCRD*	38	194	104	2114	16.4	4.7	5.99E-10
rs4982590	14	21788239	*TCRA, TCRD*	37	195	100	2118	15.9	4.5	7.85E-10
rs10148895	14	21792564	*TCRA, TCRD*	39	193	100	2118	16.8	4.5	7.05E-11
rs7155927	14	21800821	*TCRA, TCRD*	40	192	105	2113	17.2	4.7	6.93E-11
rs7141113	14	21805737	*TCRA, TCRD*	40	192	100	2118	17.2	4.5	2.04E-11
rs6572349	14	21806088	*TCRA, TCRD*	40	192	102	2116	17.2	4.6	3.36E-11
rs6572351	14	21806138	*TCRA, TCRD*	40	192	102	2116	17.2	4.6	3.36E-11
rs12881142	14	21806360	*TCRA, TCRD*	40	192	102	2116	17.2	4.6	3.36E-11
rs2331599	14	21806501	*TCRA, TCRD*	40	192	104	2114	17.2	4.7	5.46E-11
rs9972232	14	21807431	*TCRA, TCRD*	47	185	120	2098	20.3	5.4	4.63E-13

rs3811272	14	21811574	*TCRA, TCRD*	49	183	124	2094	21.1	5.6	9.98E-14
rs741711	14	21923525	*TCRA, TCRD*	52	180	178	2040	22.4	8.0	2.74E-10
rs3811250	14	21925810	*TCRA, TCRD*	52	180	176	2042	22.4	7.9	2.12E-10
rs3811247	14	21928200	*TCRA, TCRD*	52	180	172	2046	22.4	7.8	8.24E-11
rs3811244	14	21929322	*TCRA, TCRD*	53	179	176	2042	22.8	7.9	9.71E-11
rs12891257	14	21931475	*TCRA, TCRD*	54	178	169	2049	23.3	7.6	5.23E-12
rs10142552	14	21933475	*TCRA, TCRD*	54	178	169	2049	23.3	7.6	5.23E-12
rs3811240	14	21937715	*TCRA, TCRD*	55	177	171	2047	23.7	7.7	2.52E-12
rs1040303	14	21941618	*TCRA, TCRD*	57	175	170	2048	24.6	7.7	2.06E-13
rs7150307	14	21943295	*TCRA, TCRD*	57	175	167	2051	24.6	7.5	1.09E-13
rs11624054	14	21944336	*TCRA, TCRD*	57	175	165	2053	24.6	7.4	7.11E-14
rs714795	14	21946458	*TCRA, TCRD*	59	173	165	2053	25.4	7.4	6.28E-15
rs4982635	14	21949578	*TCRA, TCRD*	58	174	173	2045	25.0	7.8	1.19E-13
rs760019	14	21953018	*TCRA, TCRD*	61	171	179	2039	26.3	8.1	1.20E-14
rs3811236	14	21956159	*TCRA, TCRD*	63	169	212	2006	27.2	9.6	1.03E-12
rs2301201	14	21957570	*TCRA, TCRD*	64	168	213	2005	27.6	9.6	5.01E-13
rs6572449	14	21970760	*TCRA, TCRD*	69	163	266	1952	29.7	12.0	1.46E-11
rs7142158	14	21972830	*TCRA, TCRD*	69	163	268	1950	29.7	12.1	1.81E-11
rs2141988	14	21973302	*TCRA, TCRD*	69	163	269	1949	29.7	12.1	2.04E-11
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rs8021297	14	21974905	*TCRA, TCRD*	69	163	269	1949	29.7	12.1	2.04E-11
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rs12147516	14	21985656	*TCRA, TCRD*	79	153	321	1897	34.1	14.5	2.32E-12
rs10483273	14	21986886	*TCRA, TCRD*	78	154	318	1900	33.6	14.3	3.95E-12
rs11848747	14	21991120	*TCRA, TCRD*	70	162	285	1933	30.2	12.8	1.05E-10
rs2242545	14	21994034	*TCRA, TCRD*	68	164	282	1936	29.3	12.7	3.60E-10
rs1882704	14	21995192	*TCRA, TCRD*	68	164	282	1936	29.3	12.7	3.60E-10
rs17794083	14	21996759	*TCRA, TCRD*	68	164	282	1936	29.3	12.7	3.60E-10
rs10162417	14	21999540	*TCRA, TCRD*	68	164	286	1932	29.3	12.9	7.94E-10
rs10131293	14	21999998	*TCRA, TCRD*	68	164	285	1933	29.3	12.8	7.56E-10
rs2733776	14	22000627	*TCRA, TCRD*	68	164	279	1939	29.3	12.6	2.77E-10
rs10483275	14	22002896	*TCRA, TCRD*	62	170	263	1955	26.7	11.9	6.17E-09
rs8020193	14	22009307	*TCRA, TCRD*	54	178	171	2047	23.3	7.7	7.72E-12

rs10483277	14	22010682	*TCRA, TCRD*	51	181	154	2064	22.0	6.9	7.80E-12
rs2293732	14	22011989	*TCRA, TCRD*	51	181	152	2066	22.0	6.9	5.18E-12
rs1076861	14	22012459	*TCRA, TCRD*	50	182	135	2083	21.6	6.1	4.08E-13
rs2254272	14	22012730	*TCRA, TCRD*	49	183	132	2086	21.1	6.0	6.90E-13
rs7161733	14	22015032	*TCRA, TCRD*	45	187	115	2103	19.4	5.2	1.65E-12
rs10132733	14	22016071	*TCRA, TCRD*	43	189	109	2109	18.5	4.9	4.56E-12
rs227859	14	22018311	*TCRA, TCRD*	37	195	91	2127	15.9	4.1	8.93E-11
rs762578	14	22020088	*TCRA, TCRD*	31	201	77	2141	13.4	3.5	4.39E-09
rs3811222	14	22020854	*TCRA, TCRD*	31	201	72	2146	13.4	3.2	1.20E-09
rs3811221	14	22022792	*TCRA, TCRD*	27	205	62	2156	11.6	2.8	1.29E-08
rs227867	14	22023701	*TCRA, TCRD*	25	207	61	2157	10.8	2.8	1.20E-07
rs996165	14	22024524	*TCRA, TCRD*	24	208	55	2163	10.3	2.5	8.63E-08
rs3811215	14	22024617	*TCRA, TCRD*	22	210	52	2166	9.5	2.3	4.74E-07
rs2128997	14	22030942	*TCRA, TCRD*	17	215	31	2187	7.3	1.4	6.52E-07

Supplementary Table 5. Replication Set-2 results for genome-wide significant SNPs with copy number changes in Discovery Phase. Genomic coordinates based on build 36.1 of human genome. Two-tailed *P*-value based on Fisher’s exact test reported. Results based on 232 Caucasian Cases and 2,218 healthy Caucasian Controls.

Deletion	**Age at Diagnosis**	**INSS Stage**	***MYCN* Status**	**DNA Index**	**Shimada Histology**	**COG Risk Group**
All Annotated Cases (N=1,418)						
	(n=1407)	(n=1352)	(n=1292)	(n=1272)	(n=1111)	(n=1323)
1q21.1 (*NBPF*)	0.0565	0.8195	0.5368	0.2276	0.8682	0.3576
Annotated Blood Cases (N=1,229)						
	(n=1222)	(n=1179)	(n=1133)	(n=1130)	(n=964)	(n=1155)
TCRG	<0.0001	0.0220	0.0015	0.3744	<0.0001	<0.0001
TCRVB	0.0063	0.2432	0.3354	0.2568	<0.0001	0.0710
TCRA/D	<0.0001	0.0036	<0.0001	0.7073	<0.0001	<0.0001

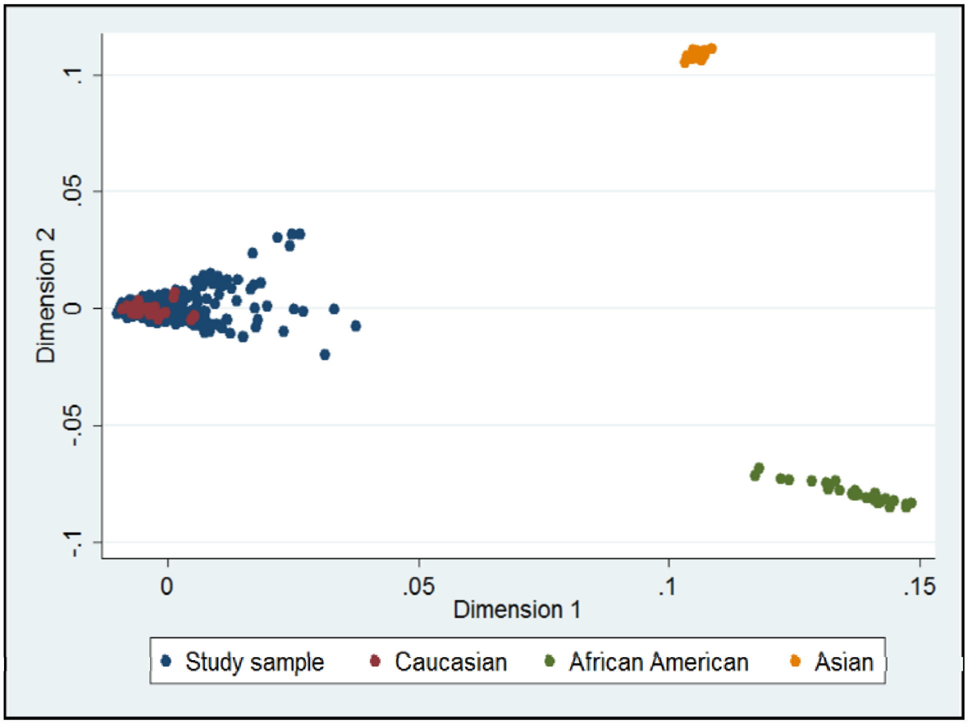
Supplementary Table 6. Association with clinical and biological co-variates.

Association with clinical and biological co-variates was assessed for each deletion associated with neuroblastoma using Fisher's exact Test. Two-sided p-values are listed. Annotated cases from the combined set of cases were divided into those with and without deletion and then into those with favorable vs. unfavorable assignment for the variable. Unfavorable was considered: Age ≥ 1 yr, INSS Stage = 4, *MYCN* status = Amplified, DNA index = diploid, Shimada Histology = unfavorable, Risk = high. TCR deletion associations were assessed using only blood cases given that deletions were significantly more common in peripheral blood than bone marrow (see text).

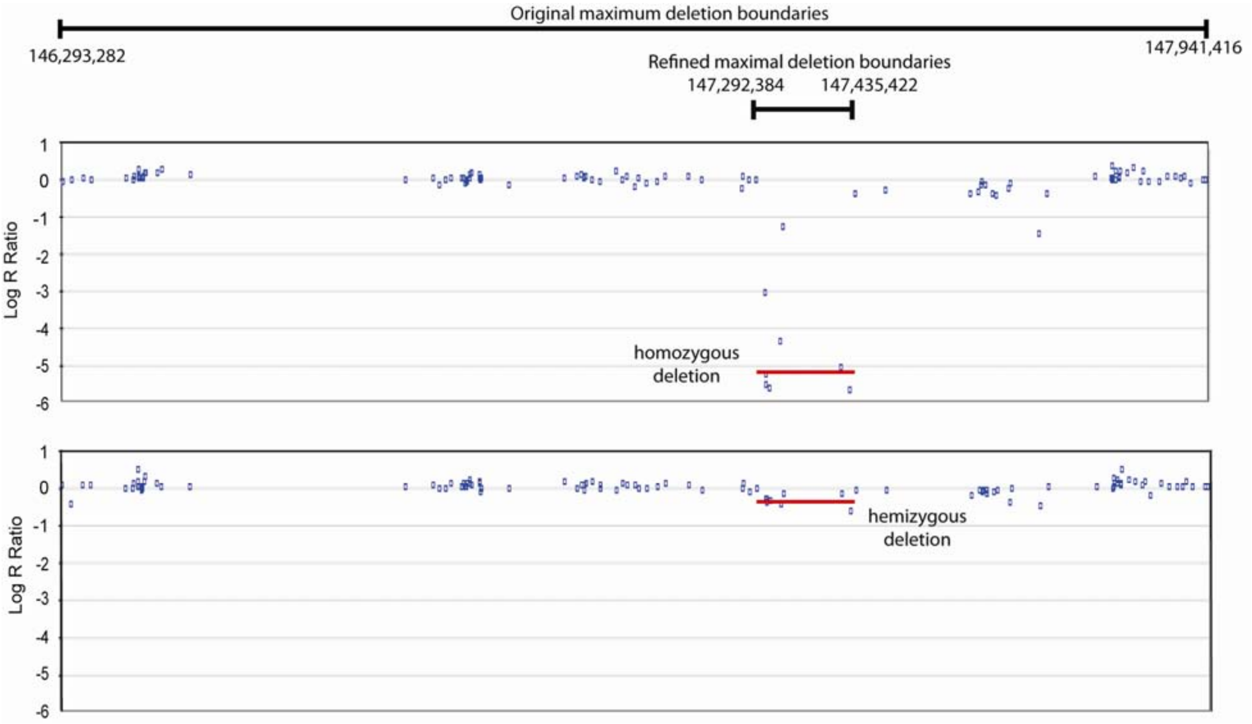
	rs9295536 genotype	**rs69393490 genotype**	**rs4712653 genotype**	***1q21.1* del**	***TCRG* del**	***TCRVB* del**	***TCRA/D* del**
***1q21.1* del**	0.244	0.915	0.948	0	0.3803	0.5893	0.3474
***TCRG* del**	0.388	0.587	0.343	-	0	< 0.0001	<0.0001
***TCRVB* del**	0.065	0.228	0.126	-	-	0	<0.0001
***TCRA/D* del**	0.319	0.337	0.534	-	-	-	0

Supplementary Table 7. Assessment of co-occurrence of predisposition loci. Interaction and co-occurrence of neuroblastoma susceptibility loci was assessed in 1,209 neuroblastoma cases common between this study and our previous SNP-based GWAS[7]. Previously identified SNPs on 6p22 associated with neuroblastoma were evaluated in a 2x3 contingency table analysis based on 1q21.1 and TCR deletion status (deletion yes/no) vs. genotype (AA, AB, BB). P-values are presented in columns 1-3; no significant interaction was detected. Co-occurrence of 1q21.1 deletion and TCR deletions was assessed using Fisher's exact test, two-sided p-values are listed in columns 4-7; a highly significant co-occurrence of TCR deletions was observed.

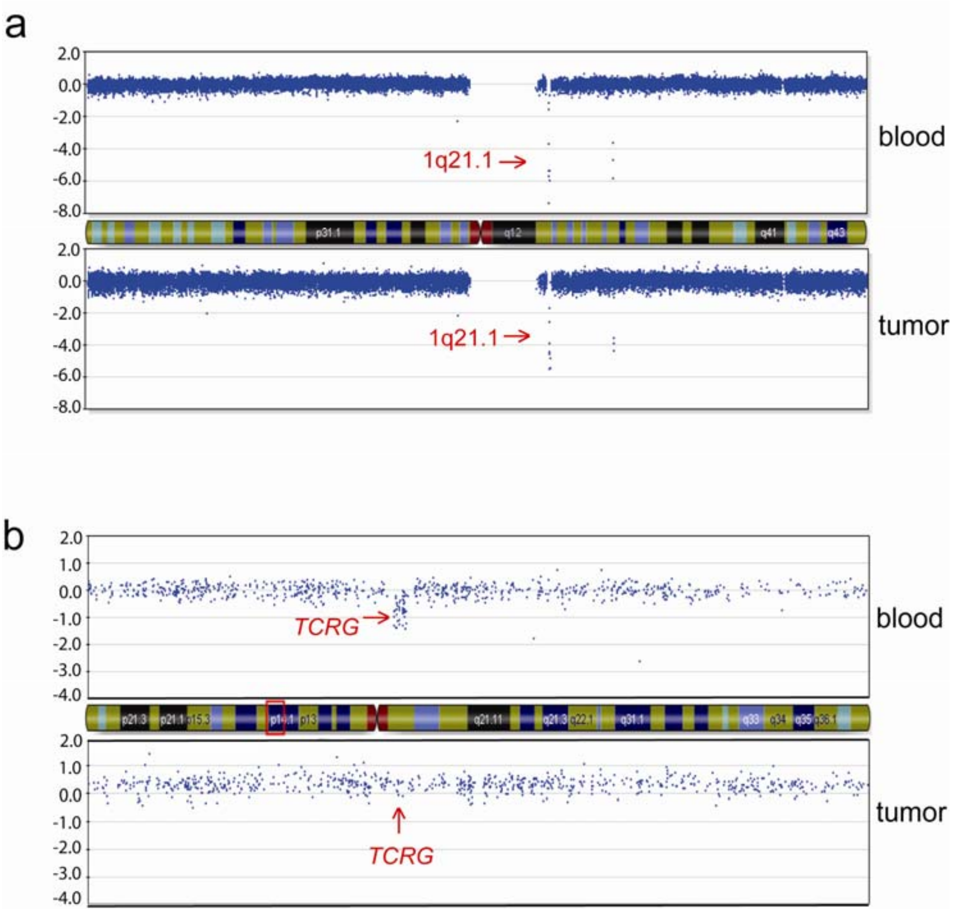
SUPPLEMENTARY FIGURES AND LEGENDS



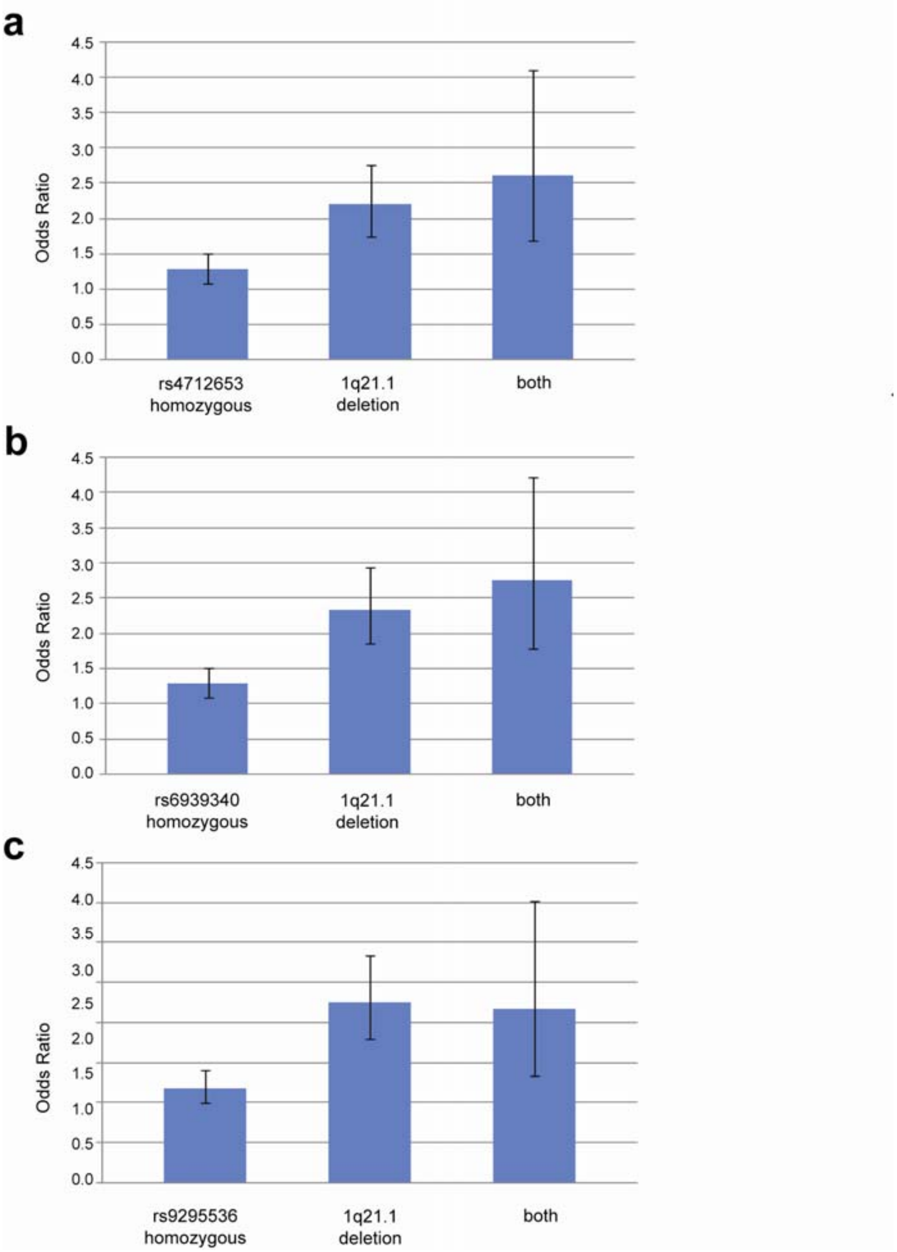
Supplementary Figure 1. 1q21.1 CNV remains significant after adjusting for potential population substructure. Plot of first two dimensions from multi-dimensional scaling (MDS) analysis of Caucasian cases (n=846) and controls (n=803) from discovery set (“Study sample”, blue) and independent sets of well-characterized Caucasian (red, n=27), African American (green. N=29) and Asian (orange, n=28) individuals, also genotyped on the Illumina HumanHap550 SNP array. 1q21.1 CNV remains significant (*P* < 0.0001) after adjusting for first three coordinates of MDS (C1-C3) in logistic regression analysis. CNV analyzed by copy number at representative SNP rs11579261.



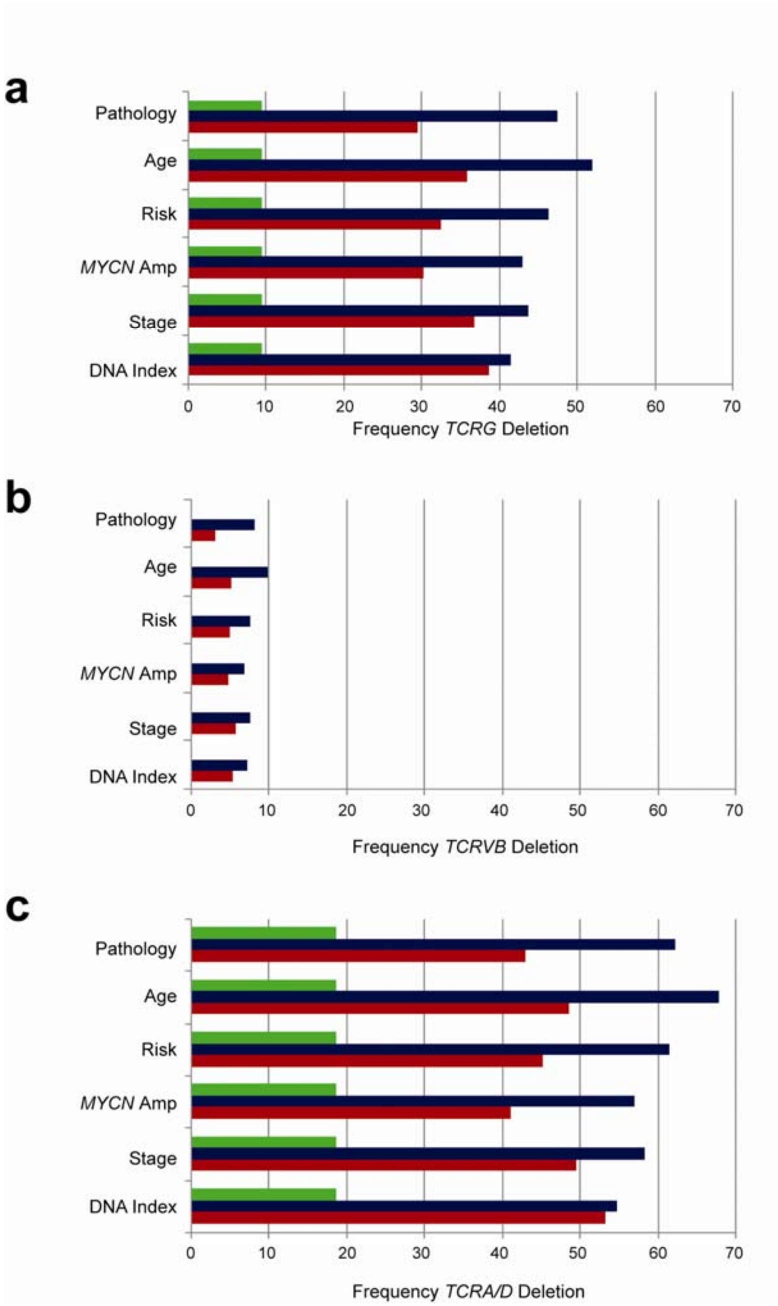
Supplementary Figure 2. Refinement of 1q21.1 maximal deletion boundaries. Original maximal boundaries based on 550K SNP data spanned over 1.6 megabases (146,293,282 - 147,941,416). Refined maximal deletion based on Illumina HumanHap610 SNP data is only 143,038 bp (147,292,384 - 147,435,422). The novel *NBPF* (partial) transcript identified in this study maps within the refined deletion boundaries (147,396,848 - 147,421,562). Shown are plots of the Log R Ratio signal intensity data for a homozygous deletion (top) and a hemizygous deletion (bottom) from two neuroblastoma cases. Red lines indicate the median Log R Ratio within the respective deletions. All genomic coordinates based on build 36 of the human genome.



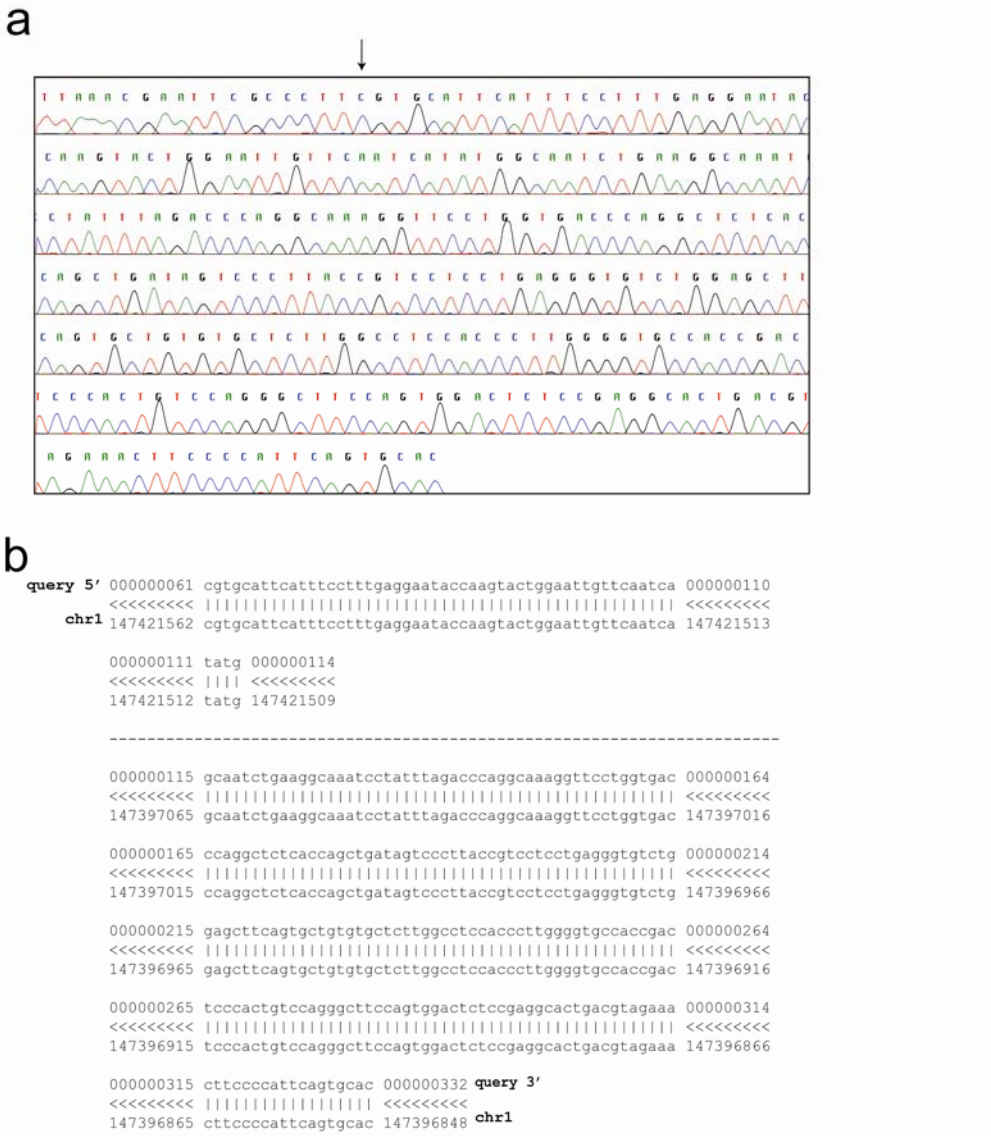
Supplementary Figure 3. Comparison of copy number in blood and matched tumor DNA. Matched tumor DNA on 226 cases was utilized to assess whether significant findings from the CNV-based GWAS were true germline deletions or somatically acquired rearrangements detected in the blood. 100% agreement was detected for the deletions at 1q21.1, consistent with germline alterations. 0% agreement was detected for the deletions within the T-cell receptor genes. Plots of Log R Ratio signal intensity data are shown. **a.** An example neuroblastoma case with homozygous deletion at 1q21.1 detected in the blood (top). This homozygous deletion was confirmed in matched tumor DNA from this patient (bottom). **b.** An example neuroblastoma case with detectable deletion within *TCRG* in the blood (top), but no evidence of deletion in the paired tumor DNA (bottom).



Supplementary Figure 4. Additive effect of combined 1q21.1 deletion and 6p22 risk alleles. Bar charts of the odds ratio for homozygosity (for risk allele) at each of the previously identified neuroblastoma-associated SNPs on 6p22[7], along with the odds ratio for 1q21.1 deletion identified in this study and the combination of homozygous SNP genotype and 1q21.1 deletion. 95% CI indicated by black bars. Only cases with both genotype and CNV data available were considered. (**a)** rs4712654 (1182 cases, 1940 controls) (**b)** rs6939340 (1206 cases, 1940 controls). (**c)** rs9295536 (1209 cases, 1940 controls).



Supplementary Figure 5. TCR deletions are more common in less aggressive phenotype. Bar chart of frequency of deletion is plotted for controls (green), cases in favorable subset (blue) and cases in unfavorable subset (red). Unfavorable was defined as Pathology = Unfavorable, Age ≥ 1-yr, Risk = High, *MYCN* Amp = yes, Stage = 4, DNA Index = diploid. **a.** *TCRG* **b**. *TCRVB* **c**. *TCRA*/*TCRD*. Frequencies are based on detection of deletion at any of the SNPs significantly associated with neuroblastoma.



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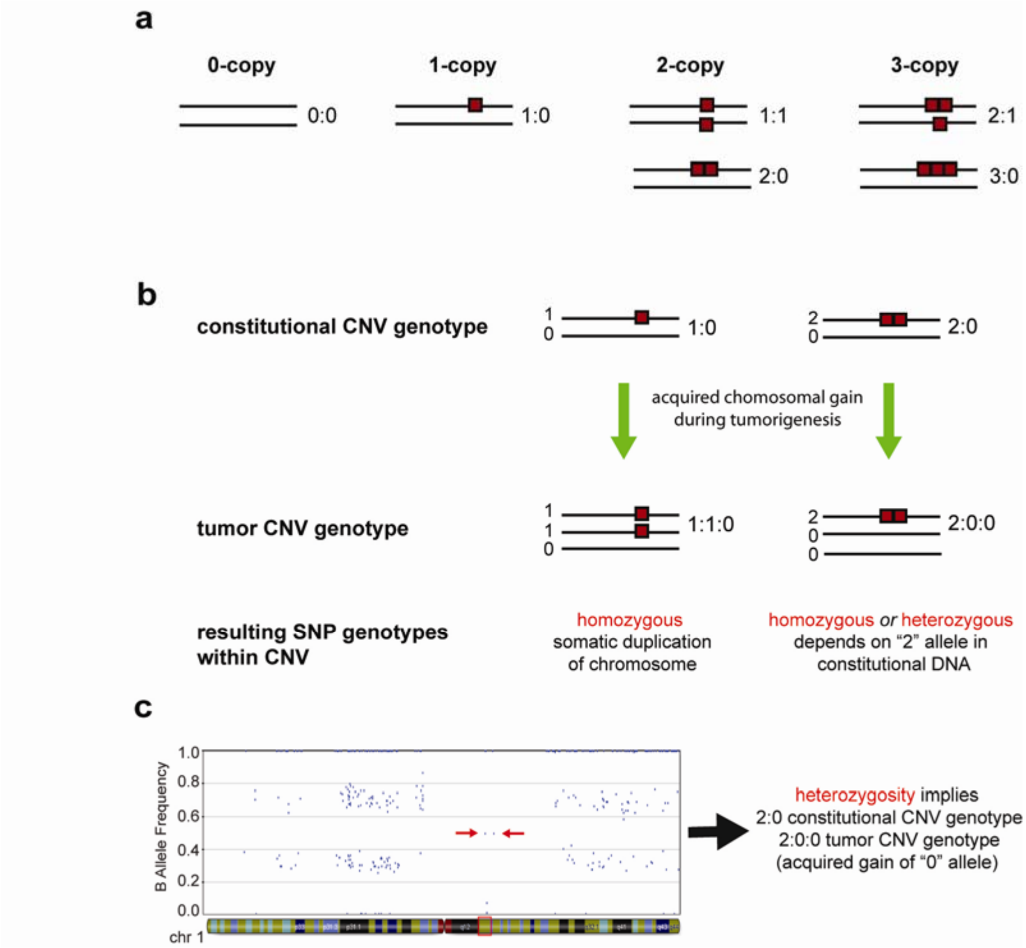
Supplementary Figure 6. Sequence of 1q21.1 transcript maps within CNV associated with neuroblastoma. **a.** Chromatogram of 271 bp sequence generated from cloned cDNA from fetal brain using primers designed against BQ431323 melanoma EST. Arrow indicates start of cloned sequence. **b.** Blat alignment of 271 bp 1q21.1 partial transcript maps uniquely within 1q21.1 CNV with 100% identity across entire sequence. The identical transcript was detected in the neuroblastoma cell line SKNAS (data not shown). Both cloned sequences indicate alternative splicing of the BQ431323 EST as exon 2 of the EST was not detected in fetal brain or SKNAS.



Supplementary Figure 7. Constitutional and tumor DNA 1q21.1 CNV genotypes. a. Possible constitutional 1q21.1 CNV genotypes for 0-, 1-, 2- and 3-copies. *Black lines*: copies of chromosome 1 in a diploid genome. *Red boxes*: copies of the DNA within the CNV. Only one possible CNV genotype exists for both 0- and 1-copy samples, however two possible underlying CNV genotypes exist for both 2- and 3-copy samples. **b.** Possible ways of obtaining 2-copies at 1q21.1 CNV in a tumor sample with somatically acquired gain of chromosome 1 (3 copies). Starting constitutional CNV genotype of 1:0 would result in homozygous SNPs in the tumor DNA, whereas a constitutional CNV genotype of 2:0 could present as homozygous or heterozygous SNPs in the tumor DNA. **c.** Neuroblastoma cell line with 2-copies at CNV and acquired gain of chromosome 1 (3-copy). Heterozygous SNPs are observed within the CNV (red arrows), consistent only with the 2:0 constitutional genotype.