Largest Copy Number Variation Regions in the Extended HLA Show Correlations with Ancestral HLA Haplotypes

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BACKGROUND

Besides being most gene-dense and polymorphic, the HLA region is also very rich in copy number variations (CNVs).

CNVs are equally important as SNPs in gene expression regulations and disease associations.

CNVs up to 368kb-long exist in the classical HLA region, but whether they map to particular haplotypes is unknown.

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A Study of CNVs As Trait-Associated Polymorphisms and As Expression Quantitative Trait Loci

Eric R. Gamazon[1], Dan L. Nicolae[1,2], Nancy J. Cox[1]*

Table 2. The observed overlap between the NHGRI SNPs and SNPs tagging CNVs ($r^2 \geq 0.80$).

SNPs tagging CNVs	*chromosome*	*position*	*NHGRI SNP*	*r^2 between SNPs*	*CNV (maximal r^2 with best tag SNP)*	*trait*
rs11576866	1	10337019	rs10492972	0.887	CNVR65.1(0.98)	Multiple sclerosis
rs12191877	6	31360904	rs10484554	1	CNVR2841.6(0.90)	Psoriasis, AIDS progression
rs1450111	3	157567524	rs3772255	0.948	CNVR1591.1(1)	Aging traits
rs2001114	6	167406568	rs2301436	0.814	CNVR3164.1(1)	Crohn's Disease
rs2410618	8	19897780	rs2083637	1	CNVR3814.1(0.998)	Waist circumference and related phenotypes, HDL cholesterol
rs36149991	6	32630367	rs3135388	1	CNVR2845.46(0.94)	Multiple sclerosis
rs6693105	1	150857287	rs4085613	1	CNVR358.1(0.956)	Psoriasis
rs7560547	2	203466161	rs6725887	1	CNVR1111.1(1)	Myocardial Infarction (early onset)
rs9635398	15	84147059	rs7176093	0.846	CNVR6495.1(1)	Aging traits
rs4882017	11	48526758	rs7395662	1	CNVR5165.1(1)	HDL cholesterol
rs4529687	1	87386671	rs7553864	1	CNVR240.1(0.99)	Smoking behavior
rs11249248	1	25625638	rs10903129	0.967	CNVR117.1(0.945)	Cholesterol, total
rs11209948	1	72584492	rs2568958	1	CNVR217.1(1)	Body mass index
rs9405040	6	32547371	rs2395185	1	CNVR2845.14(0.90)	Ulcerative colitis
rs1384601	12	33606133	rs9300212	0.99	CNVR5492.1(0.997)	Cognitive

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	A	B	C	D	E	F	G	H
1	*CNV*	*chr*	*start*	*end*	*length*	*number of eQTLs*	*best tagSNP*	*best r2*
2	CNVR2845.21	6	32519885	32887814	367929	425	rs9271720	1
3	CNVR2829.7	6	29761933	30031389	269456	324	rs3188482	0.96475
4	CNVR7114.2	17	41521114	42139954	618840	212	rs17651507	0.466607
5	CNVR6075.1	14	19870605	20327718	457113	202	rs10146419	0.98738
6	CNVR3898.4	8	58209490	58359267	149777	162	rs10504229	0.978912
7	CNVR3170.2	6	168076579	168341749	265170	154	rs637578	0.075667
8	CNVR6609.4	16	3815755	4260694	444939	126	rs13333551	0.050415
9	CNVR3936.3	8	75738134	76087773	349639	126	rs17292864	0.578093
10	CNVR7114.8	17	41568592	41626007	57415	106	rs2668628	0.365923
11	WTCCC1_56	4	135204855	135377711	172856	100	NA	0
12	CNVR8103.3	22	20783535	20935345	151810	92	rs5750449	0.017865
13	WTCCC1_91	6	162697695	162834267	136572	88	rs7758475	0.965544
14	CNVR6609.1	16	3815340	4105747	290407	86	rs13333551	0.06326
15	CNVR6072.4	14	19247050	19494593	247543	85	rs1632089	0.270602
16	CNVR7658.5	19	48239642	48492519	252877	75	rs1533709	0.021112
17	CNVR4713.1	10	46999208	47175011	175803	73	rs28580083	0.258429
18	CNVR4527.3	9	137287086	137450120	163034	72	rs2477078	0.033138
19	CNVR230.1	1	83370836	83727807	356971	69	rs6576760	0.054312
20	CNVR8103.16	22	20783598	20880884	97286	67	rs7286238	0.0283
21	CNVR1957.2	4	70052484	70328860	276376	66	rs12499133	0.9577
22	CNVR1120.1	2	205980337	206233532	253195	66	rs10207236	0.990362
23	CNVR5031.2	11	3382657	3631565	248908	65	rs10834648	1
24	CNVR7114.10	17	41626903	41724649	97746	63	rs17654016	0.301805
25	CNVR3428.1	7	64515314	64596817	81503	62	rs10215130	0.017223
26	CNVR7658.2	19	48000706	48238985	238279	59	rs4341855	0.177602
27	CNVR5432.2	12	11033424	11060725	27301	58	rs7138953	0.987586

CNVR2845.21

Tag SNPs: rs9271720

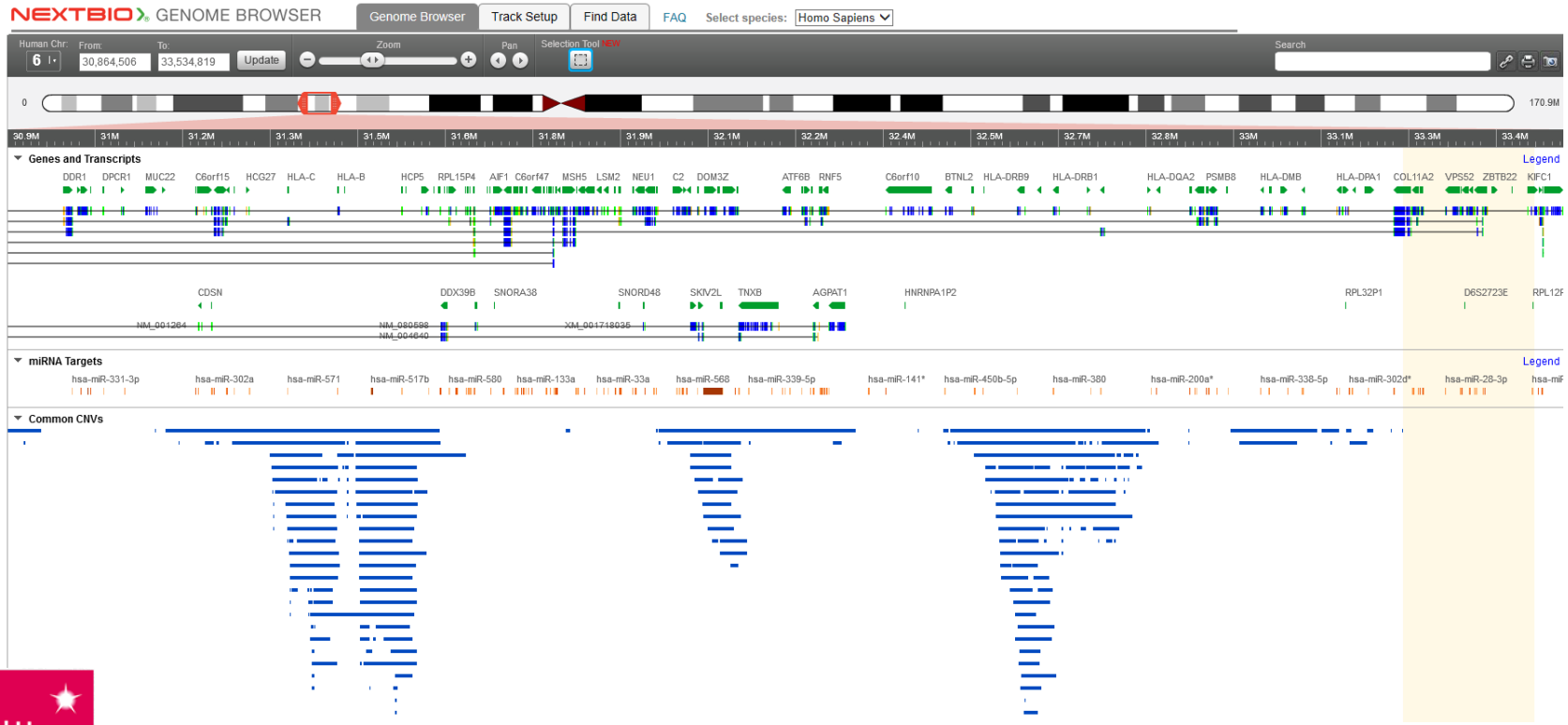
METHODS

We used the already available HapMap project data from HLA-typed participants to systematically survey the correlations among SNPs, CNVs, HLA types and gene expression.

We mapped proxy SNPs for CNVs to HLA haplotypes using existing information as well as our ImmunoChip data on 95 IHWG cell lines and published 1KG Project HLA types.

RESULTS

Most CNVs encompass multiple classical HLA genes: CNVR2841.6 (13kb - HLA-C and HLA-B); CNVR2829.7 (269kb - from ZFP57 to HLA-W including HLA-A); CNV2845.21 (368kb - from HLA-DRA to DQB1).



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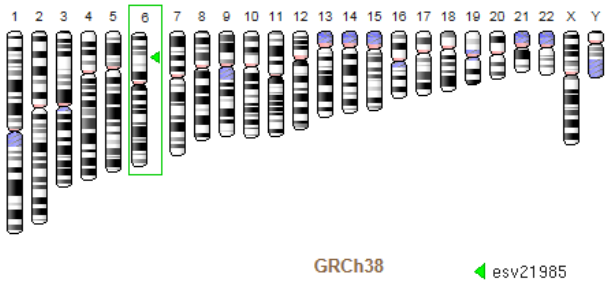
esv21985

Organism: Homo sapiens
Study: estd20 (Conrad et al. 2010) **Variant Calls:** 71
Variant Type: sequence alteration **Validation:** Not tested
Method Type: Oligo aCGH **Clinical Assertions:** No
Submitted on: NCBI36 (hg18) **Region Size:** 367,971
Publication(s): Conrad et al. 2010



Links to Other Resources
Overlapping Genes
Source: NCBI

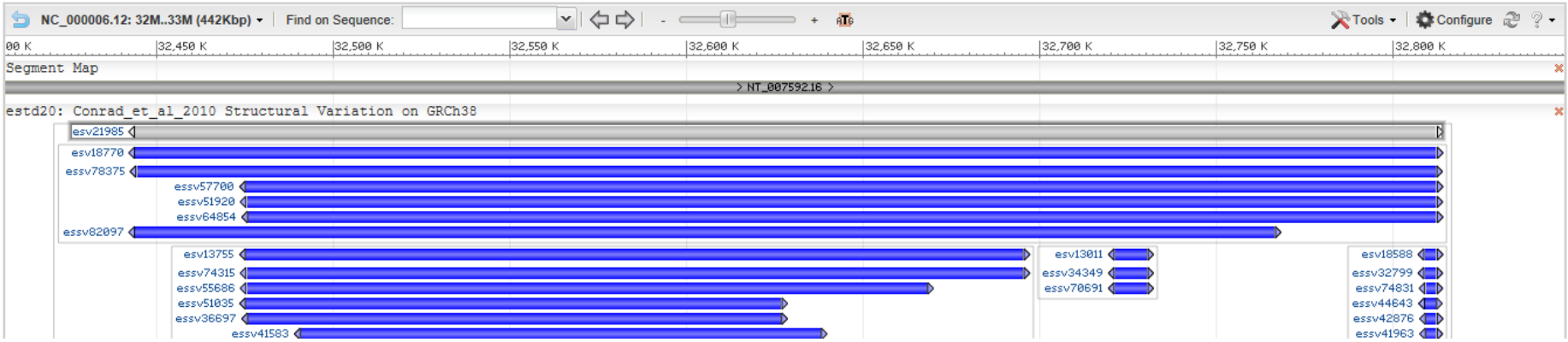
Genome View | Variant Region Details and Evidence | Validation Information | Clinical Assertions | Genotype Information

Genome View

Select assembly: GRCh38: Chr6

Overlapping variant regions from other studies: 5327 SVs from **47** studies. See in: genome view

Remapped (Score: Perfect): 32,444,130 - 32,812,100



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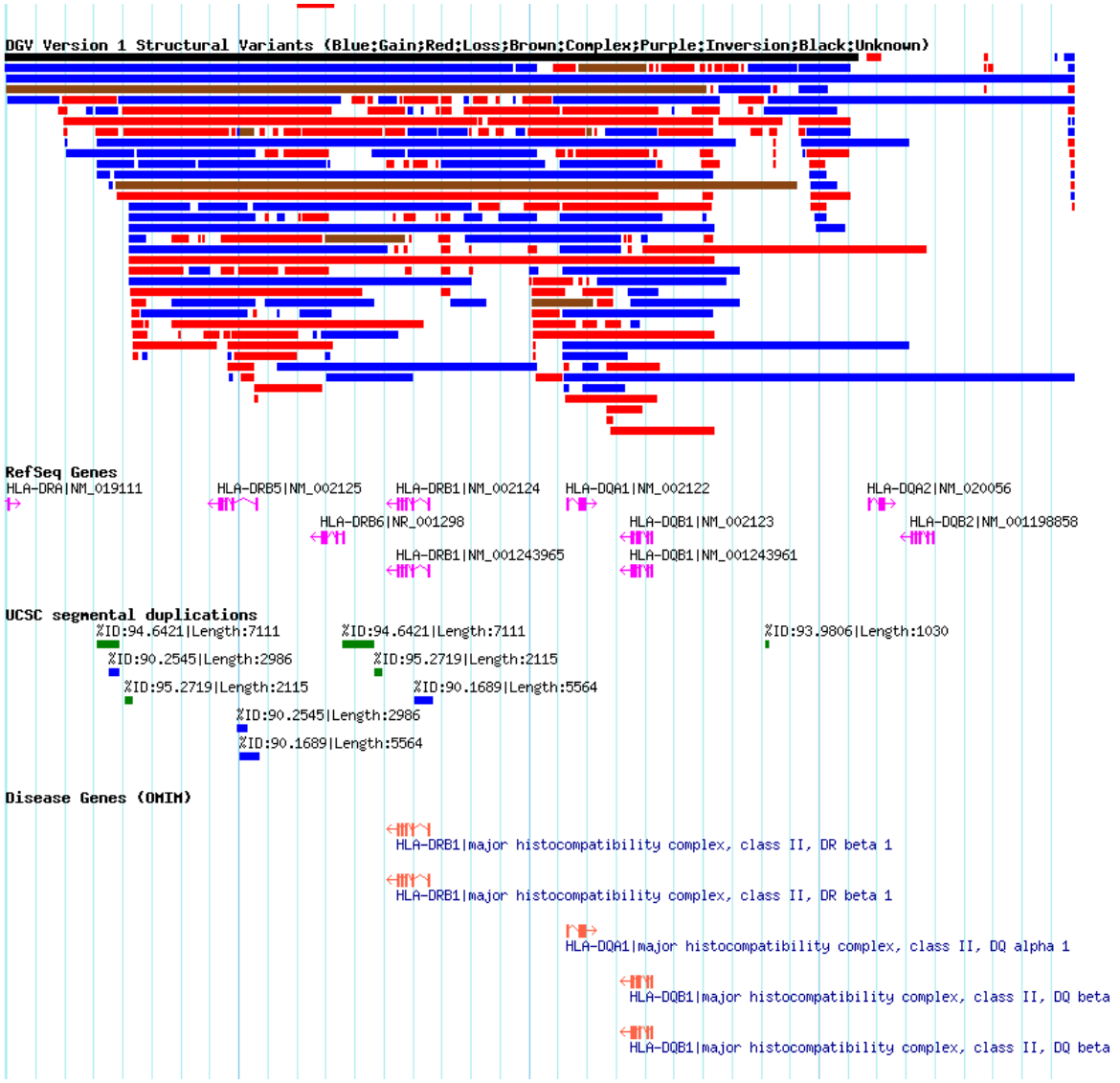
Database of Genomic Variants

A curated catalogue of human genomic structural variation

Variant Details

Variant: esv21985



RESULTS

HLA Typing from 1000 Genomes Whole Genome and Whole Exome Illumina Data

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In most studies, the CNV status was reported as gain or loss relative to the HapMap sample NA10851 (HLA-A*24:02/*01:01; B*40:01/*08:01; C*03:04/*07:01; DRB1*04:04/*07:01; DR53/DR53).

Those studies consistently reported a loss of large (>200kb, up to 337kb) CNV copies in samples that lacked a DR53 haplotype.

Suppl Tables 9 & 10 in:

Global variation in copy number in the human genome

Richard Redon[1], Shumpei Ishikawa[2,3], Karen R. Fitch[4], Lars Feuk[5,6], George H. Perry[7], T. Daniel Andrews[1], Heike Fiegler[1], Michael H. Shapero[4], Andrew R. Carson[5,6], Wenwei Chen[4], Eun Kyung Cho[7], Stephanie Dallaire[7], Jennifer L. Freeman[7], Juan R. González[8], Mónica Gratacós[8], Jing Huang[4], Dimitrios Kalaitzopoulos[1], Daisuke Komura[3], Jeffrey R. MacDonald[5], Christian R. Marshall[5,6], Rui Mei[4], Lyndal Montgomery[1], Kunihiro Nishimura[2], Kohji Okamura[3,6], Fan Shen[4], Martin J. Somerville[9], Joelle Tchinda[7], Armand Valsesia[1], Cara Woodwark[1], Fengtang Yang[1], Junjun Zhang[3], Tatiana Zerjal[1], Jane Zhang[4], Lluis Armengol[8], Donald F. Conrad[10], Xavier Estivill[8,11], Chris Tyler-Smith[1], Nigel P. Carter[1], Hiroyuki Aburatani[2,12], Charles Lee[7,13], Keith W. Jones[4], Stephen W. Scherer[5,6] & Matthew E. Hurles[1]

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RESULTS

Of the 50 HapMap subjects who had two copies of DR53 haplotypes, only three had loss or gain in the class II region, the rest did not vary from the reference sample suggesting stability of the CNV status in DR53 haplotypes.

Most samples that did not have two DR53 haplotypes show loss, and any sample with at least one DR15 haplotype shows gain compared to the reference sample NA10851.

RESULTS

For the largest CNVs in HLA class II region

HLA Class II Haplotypes		
Zero or one DR53	Two DR53	DR51-positive
Loss	Reference	Gain

RESULTS

Both class I and II CNVs are associated with increased expression of classical HLA genes. CNV2845.21 correlates with increased expression levels of HLA-DRA, DRB1, DQA1 and DQB1, but decreased expression of DQA2/DQB2.

Supplementary Table 3: List of CNV-associated eQTLs. This table displays all significantly associated CNV-gene pairs we identified with our FDR threshold (FDR≤10%).

Adj. P value	Spearman P val	Spearman Cor	Pop	CNV ID	CNV locus	CNV type	GENE name	GENElocus	GENEoverlap
0.000797967	1.65E-06	-0.5996951	CEU	CNVR2845.21	chr6:32519885-32887814	biallelic duplication	*HLA-DQB2*	chr6:32831853-32839308	FULL
0.001867884	4.43E-06	-0.5793454	CEU	CNVR2845.21	chr6:32519885-32887814	biallelic duplication	*HLA-DQA2*	chr6:32817141-32823199	FULL
0.009929516	3.99E-05	0.5285402	CEU	CNVR2845.21	chr6:32519885-32887814	biallelic duplication	*HLA-DRB5*	chr6:32593178-32606022	FULL
0.029962837	0.0001641	0.4908862	CEU	CNVR2845.21	chr6:32519885-32887814	biallelic duplication	*HLA-DQB1*	chr6:32735222-32754296	FULL
0.037437953	0.0002301	0.4811958	CEU	CNVR2845.21	chr6:32519885-32887814	biallelic duplication	*HLA-DQA1*	chr6:32713112-32719407	FULL
0.076264059	0.0007147	0.4464489	CEU	CNVR2845.21	chr6:32519885-32887814	biallelic duplication	*HLA-DRB1*	chr6:32654513-32665591	FULL
0.00107873	3.24E-06	0.530689	YRI	CNVR2845.21	chr6:32519885-32887814	biallelic duplication	*HLA-DRB5*	chr6:32593178-32606022	FULL

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Relating CNVs to transcriptome data at fine resolution: Assessment of the effect of variant size, type, and overlap with functional regions

Andreas Schlattl,[1] Simon Anders,[1] Sebastian M. Waszak,[1] Wolfgang Huber,[1,2] and Jan O. Korbel[1,2,3]

RESULTS

ImmunoChip data showed that rs9271720/rs9272143 (proxy for the largest CNV, CNV2845.21) split DR haplotypes in two groups confirming that the ancestral lineages DR51 and DR53 haplotypes had increased copy number.

IHWG	CELL LINE	ST	CEH	rs9272143	HLA-A 1	HLA-A 2	HLA-B 1	HLA-B 2
9001	SA	01	7.2	2	A*2402010	A*2402010	B*070201	B*070201
9002	MZ070782	01	65.1?	2	A*2402	A*2402	B*1402	B*1402
9003	KAS116	01	.	2	A*24:02:01	A*24:02:01	B*51:01	B*51:01
9004	JESTHOM	01	.	2	A*0201	A*0201	B*270502	B*270502
9005	HOM2	01	.	2	A*0301	A*0301	B*270502	B*270502
9006	WT100BIS	01	35.2	2	A*1101	A*1101	B*350101	B*350101
9016	RML REM	51		2	A*0204	A*0204	B*510101	B*510101
9019	DUCAF	52	18.2	2	A*3002	A*3002	B*1801	B*1801
9020	QBL	52	18.2	2	A*2601	A*2601	B*1801	B*1801
9022	COX	52	8.1	2	A*0101	A*0101	B*0801	B*0801
9039	JVM	52	18.3	2	A*0201	A*0201	B*1801	B*1801
9041	J0528239	52	35.5	2	A*0101	A*0101	B*3502	B*3502
9042	TISI	52	35.4	2	A*2402010	A*2402010	B*350801	B*350801
9043	BM21	52		2	A*0101	A*0101	B*4101	B*4101
9053	HQB	52	44.4	2	A*330301	A*330301	B*440301	B*440301
9054	EK EK(OH)	52	.	2	A*0201	A*0201	B*4402	B*4402
9055	HQ301	52	65.2	2	A*0301	A*0301	B*1402	B*1402
9056	KOSE	52	.	2	A*020101	A*020101	B*3503	B*3503
9058	QMW	52	.	2	A*0201	A*0201	B*4501	B*4501
9059	SLE005	52	60.3	2	A*0201	A*0201	B*4001	B*4001
9060	CB6B-CGE	52	62.3	2	A*0101	A*0101	B*1501	B*1501
9061	31227ABC	52	.	2	A*0201	A*0201	B*180101	B*180101
9062	WDV	52	.	2	A*02:01	A*02:01	B*38:01:01	B*38:01:01
9063	WT47	52	.	2	A*320101	A*320101	B*4402	B*4402
9064	AMALA	52	.	2	A*02:17:01	A*02:17:01	B*15:01:01:(	B*15:01:01:
9065	HHKB	52	.	2	A*0301	A*0301	B*0702	B*0702
9066	TAB089,TA	08	46.2	2	A*0207	A*0207	B*460101	B*460101
9079	LWAGS	01	65.1	2	A*3301	A*3301	B*1402	B*1402
9080	EHM	01	.	2	A*0301	A*0301	B*35:01	B*35:03
9088	PF04015	52	8.1	2	A*0101	A*0101	B*0801	B*0801
9097	EMJ	52	60.3	2	A*0201	A*0301	B*4001	B*4001
9099	LZL	52	.	2	A*021701	A*021701	B*1501	B*1501
9104	DHIF	52	.	2	A*3101	A*3101	B*38:01	B*38:01
9105	FPAF FPF F	52	35.5?	2	A*0101	A*0101	B*3502	B*3502
9157	HAU, ML	52	58.1	2	A*33	A*33	B*5801	B*58
9291	APD	52	.	2	A*01:01:01:(	A*01:01:01:(	B*40:01:01	B*40:01:01

IHWG	CELL LINE	ST	CEH	rs9272143	HLA-A 1	HLA-A 2	HLA-B 1	HLA-B 2
9008	DO208915	51	18.1	0	A*2501	A*2501	B*1801	B*1801
9009	KAS011	51		0	A*010101	A*010101	B*370101	B*370101
9010	AMAJ	51		0	A*68020101	A*6802010	B*530101	B*530101
9011	E4181324	51	52.1?	0	A*0101	A*0101	B*520101	B*520101
9012	WJR076	51		0	A*0201	A*0201	B*5701	B*5701
9014	MGAR	51		0	A*2601	A*2601	B*0801	B*0801
9015	WT24	51		0	A*02:01:01	A*02:01:01	B*27:05:02	B*27:05:02
9017	WT8	51		0	A*0301	A*0301	B*070201	B*070201
9021	RSH, RSH(	52	42.1	0	A*3001	A*6802010	B*4201	B*4201
9024	KT17	53	.	0	A*02:06	A*11:01	B*15:01:01:0	B*35:01:01
9026	YAR	53	38.1	0	A*2601	A*2601	B*380101	B*380101
9027	PF97387	53	44.2+4	0	A*2902	A*2902	B*440301	B*440301
9028	PE117	53	60.1+X	0	A*2402	A*2402	B*4001	B*4002
9029	WT51	53		0	A*2301	A*2301	B*1401	B*1401
9031	BOLETH B	53	62.1	0	A*020101	A*020101	B*1501	B*1501
9032	BSM	53	62.1	0	A*020101	A*020101	B*15010101	B*15010101
9033	BM14	53		0	A*0301	A*0301	B*0702	B*0702
9034	SAVC	53		0	A*0301	A*0301	B*070201	B*070201
9036	SPO010	52		0	A*0201	A*0201	B*4402	B*4402
9047	PLH	53	47.1	0	A*03010101	A*03010101	B*47010101	B*47010101
9048	LBUF	53	13.1	0	A*300101	A*300101	B*130201	B*130201
9049	IBW9	53		0	A*3301	A*3301	B*1402	B*1402
9050	MOU-MAN	53	44.3	0	A*2902	A*2902	B*440301	B*440301
9051	PITOUT	53	44.2	0	A*2902	A*2902	B*440301	B*440301
9052	DBB	53	57.1	0	A*02010101	A*02010101	B*570101	B*570101
9068	BM9	08	.	0	A*020101	A*020101	B*3501	B*3501
9069	MADURA	08	60.2?	0	A*0201	A*0201	B*4001	B*4001
9070	LUY	08	.	0	A*02:01	A*02:01	B*51:01	B*51:01
9071	OLGA	08	.	0	A*310102	A*310102	B*15010101	B*1520
9072	SPACHE(	08	.	0	A*3101	A*3101	B*15:01	B*15:01
9076	T7526	53	46.1	0	A*0206	A*0207	B*460101	B*460101
9081	EA	51	7.1	0	A*0301	A*0301	B*070201	B*070201
9084	CALOGER	51	.	0	A*0201	A*0201	B*4002	B*4002
9090	AWELLS	53	44.1	0	A*0201	A*0201	B*4402	B*4402
9092	BM92	53	51.1	0	A*2501	A*2501	B*510101	B*510101
9093	BER	53	13.1	0	A*0201	A*0201	B*1302	B*1302
9094	CF996	53	64.1	0	A*0201	A*0301	B*1401	B*1401
9098	MT14B	53	60.1	0	A*310102	A*310102	B*4001	B*4001
9101	SPL	08	.	0	A*310102	A*310102	B*15:01:01:0	B*15:01:01:(
9103	KT14, LKT1	53	.	0	A*24020101	A*2602	B*4006	B*510101

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DR01/DR52 vs DR08/DR51/DR53

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ARTICLES

Origins and functional impact of copy number variation in the human genome

Donald F. Conrad[1]*, Dalila Pinto[2]*, Richard Redon[1,3], Lars Feuk[2,4], Omer Gokcumen[5], Yujun Zhang[1], Jan Aerts[1], T. Daniel Andrews[1], Chris Barnes[1], Peter Campbell[1], Tomas Fitzgerald[1], Min Hu[1], Chun Hwa Ihm[5], Kati Kristiansson[1], Daniel G. MacArthur[1], Jeffrey R. MacDonald[2], Ifejinelo Onyiah[1], Andy Wing Chun Pang[2], Sam Robson[1], Kathy Stirrups[1], Armand Valsesia[1], Klaudia Walter[1], John Wei[2], Wellcome Trust Case Control Consortium†, Chris Tyler-Smith[1], Nigel P. Carter[1], Charles Lee[5], Stephen W. Scherer[2,6] & Matthew E. Hurles[1]

CNVR2845.21 and rs3129934

Table 2 | Trait-associated SNPs with possible causal CNVs

SNP	CNV	Location*	r^2†	Population‡	Data§	Reported gene	Trait	PMID
rs10492972	CNVR65.1	chr1: 10405137–10406094	0.92	CEU	Phased	*KIF1B*	Multiple sclerosis	18997785
rs11809207	CNVR118.1	chr1: 26332157–26337219	0.61	CEU	Phased	*CATSPER4*	Height	19343178
rs2815752	CNVR217.1	chr1: 72538870–72584557	0.96	CEU	Phased	*NEGR1*	Body mass index	19079261
rs7553864	CNVR240.1	chr1: 87385827–87386846	0.76	CEU	Intensities	*AK002179*	Smoking behaviour	19247474
rs4085613	CNVR358.1	chr1: 150822234–150856715	0.97	CEU	Phased	*LCE3D, LCE3A*	Psoriasis	19169255
rs11265260	CNVR381.1	chr1: 157915386–157916253	0.62	CHB+JPT	Phased	*CRP*	C-reactive protein	18439552
rs12029454	CNVR384.1	chr1: 160497369–160497846	0.57	CHB+JPT	Phased	*NOS1AP*	QT interval	19305408
rs6725887	CNVR1111.1	chr2: 203607766–203612122	1.00	CEU	Phased	*WDR12*	Myocardial infarction (early onset)	19198609
rs9311171	CNVR1355.1	chr3: 37953474–37961880	1.00	CHB+JPT	Phased	*CTDSPL*	Prostate cancer	17903305
rs3772255	CNVR1591.1	chr3: 157574746–157576258	0.90	CEU	Phased	*KCNAB1*	Ageing traits	17903295
rs9291683	CNVR1819.6	chr4: 9783252–9843664	0.51	YRI	Intensities	NR	Bone mineral density	17903296
rs9291683	CNVR1819.1	chr4: 9820419–9843664	0.51	YRI	Intensities	NR	Bone mineral density	17903296
rs401681	CNVR2293.1	chr5: 1386043–1386897	0.68	YRI	Intensities	*CLPTM1L*	Lung cancer	18978787
rs11747270	CNVR2646.1	chr5: 150157836–150161778	1.00	CEU	Phased	*IRGM*	Crohn's disease	18587394
rs11747270	CNVR2647_full	chr5: 150183562–150203623	1.00	CEU	Phased	*IRGM*	Crohn's disease	18587394
rs4704970	CNVR2659.1	chr5: 155409234–155427600	0.95	CEU	Phased	*SGCD*	Multiple sclerosis (age of onset)	19010793
rs12191877	CNVR2841.6	chr6: 31384505–31397416	0.79	CEU	Phased	*HLA-C*	Psoriasis	19169254
rs10484554	CNVR2841.6	chr6: 31384505–31397416	0.79	CEU	Phased	*HLA-C*	AIDS progression	19115949
rs3129934	CNVR2845.21	chr6: 32519885–32887814	0.87	CEU	Phased	*HLA-DRB1*	Multiple sclerosis	18941528
rs9277535	CNVR2846.3	chr6: 33156338–33162718	0.62	CEU	Intensities	*HLA-DPB1*	Hepatitis B	19349983
rs9277535	CNVR2846.5	chr6: 33159682–33163323	0.67	CEU	Intensities	*HLA-DPB1*	Hepatitis B	19349983
rs210138	CNVR2850.1	chr6: 33691917–33693857	0.55	CEU	Phased	*BAK1*	Testicular germ cell tumour	19483681
rs2301436	CNVR3164.1	chr6: 167408121–167409138	0.71	CEU	Intensities	*CCR6*	Crohn's disease	18587394
rs2705293	CNVR4074.1	chr8: 138980822–138981379	0.51	YRI	Intensities	*AK127771*	Neuroticism	18762592
rs1602565	CNVR5123.2	chr11: 29095953–29096982	0.64	CEU	Intensities	Intergenic	Schizophrenia	18677311
rs1602565	CNVR5123.1	chr11: 29096114–29096643	0.61	CEU	Intensities	Intergenic	Schizophrenia	18677311
rs7395662	CNVR5165.1	chr11: 48557432–48560877	1.00	CEU	Phased	*MADD, FOLH1*	HDL cholesterol	19060911
rs9300212	CNVR5492.1	chr12: 33606396–33608182	0.84	CEU	Phased	Intergenic	Cognitive test performance	17903297
rs1495377	CNVR5583.1	chr12:69818942-69819932	0.72	CEU	phased	NR	Type 2 diabetes	17554300
rs3118914	CNVR5871.1	chr13: 49967347–49973131	0.69	CEU	Phased	*DLEU7*	Height	19343178
rs763014	CNVR6576.1	chr16: 601068–603588	0.68	CEU	Intensities	*RAB40C*	Height	18391950
rs8049607	CNVR6636.1	chr16: 11591538–11592052	0.88	CHB+JPT	Phased	*LITAF*	QT interval	19305409
rs7188697	CNVR6746.1	chr16: 57231107–57233858	0.61	YRI	Phased	*NDRG4*	QT interval	19305409
rs1805007	CNVR6887.1	chr16: 88423599–88425903	0.87	CEU	Phased	*MC1R*	Skin sensitivity to sun	18488028

List of CNV correlations with trait-associated SNPs with $r^2 > 0.5$ (see main text for details). When a locus-trait association has been reported several times, only the results for the most recently published trait-associated SNPs are shown in this table. Some trait-associated SNPs are strongly correlated with more than one CNV in the same recombination hotspot interval. NR, no gene reported in original study; PMID, PubMed accession of the paper reporting the trait-associated SNP.

RESULTS

In the class I region, largest CNV gains (~324kb) were in samples positive for B*07:02; C*07:02. The largest CNV (402kb) in the extended HLA region was reported at the telomeric end (in a sample homozygous for B*07:02; C*07:02).

CONCLUSIONS

These results:

> Shed some light on the nature of variable DNA content in ancestral HLA class II haplotypes reported in the past

> Highlight the importance of taking into account the CNV status in disease association and transcriptomics studies

We are planning to examine the large CNV status of homozygous cell lines with specific qPCR analysis.

Liverpool Hope University EST. 1844

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