Supplemental Material

Determination of gene and interval copy number by* FCGR *locus paralogue ratio test

In a paralogue ratio test (PRT), one pair of primers amplifies two regions of the genome in a single PCR reaction (Fig. S1A): typically one is a region to be tested for CNV, and the other is a reference locus. The two PCR products differ in size by a small number of nucleotides, and can be resolved by capillary electrophoresis (Fig. S1B). The relative intensity of the bands of product from the CNV locus versus the reference locus is proportional to the relative diploid gene copy numbers at the two genomic locations – for instance if the reference locus is invariant (two copies in the diploid genome) and there is twice as much of the CNV locus product, it can be extrapolated that there are four copies of the CNV region.

Two PRT assays were developed in this study. The first, PRT-3B/3A, amplified a region in both *FCGR3B* and *FCGR3A*, and the second, PRT-2C$^{3'}$/2A$^{3'}$, amplified a region in the 3' untranslated regions of both *FCGR2C* and *FCGR2A* (Fig. 1 and Fig. S1A). A third primer pair, PRT-3(A+B)/Chr18, was based on a published assay (1), and amplified a region of the same length in both *FCGR3A* and *FCGR3B,* and a third region of a slightly different length in Chromosome 18 (4149307-4149392, hg18, Fig. 1). By combining the three PRTs, no restriction digest was required to determine *FCGR3A* and *FCGR3B* relative CN, as previously required (1). At the start of this study, *FCGR2C* and *FCGR3B* were thought to be under copy number variation, and the copy number status of *FCGR2A* and *FCGR3A* was undetermined.

The integer diploid CN at each locus interrogated by a PRT assay can be determined from the relative amount of product amplified from each locus. To determine the CN at the amplified region in *FCGR3B*, for instance, the intensity of the signal of the *FCGR3B* product was first divided by that of *FCGR3A* (Fig. S1B). This value was consistent upon replication (Fig. S2A). The value was then related to the underlying gene CN. For instance, consider an individual in whom there is no

variation in the copy number at any of the amplified *FCGR* loci, i.e. two copies of each locus in a diploid individual. If the amount of product amplified from *FCGR3B* was divided by that from *FCGR3A*, the result would be 1. Similarly, *FCGR2C* 3'UTR / *FCGR2A* 3'UTR would be 1. In an individual, however, in which the *FCGR3B* diploid CN is 3 and *FCGR3A* remains invariant, *FCGR3B / FCGR3A* ~1.5. Similarly, if there is a single *FCGR3B* deletion (CN is 1) and *FCGR3A* remains invariant, *FCGR3B / FCGR3A* = 0.5 (Fig. S1B,C).

If two genes lie within the same CN variable region, PRT assays which compare them to loci outside this region should produce the same result. In the majority of individuals, when *FCGR3B / FCGR3A* ~1.5, *FCGR2C / FCGR2A* was also ~1.5 (Fig. S2C). Indeed *FCGR3B / FCGR3A* was consistently similar to *FCGR2C* 3'UTR / *FCGR2A* 3' UTR, and when the two PRT assays measuring these loci were plotted against each other, the points lay on the diagonal (Fig. S2C). This implied that the PRT amplification sites in *FCGR3B* and *FCGR2C* fall within the same CN variable region – designated CNR1 (Fig. 1 and Fig. S1D, blue).

The fact that *FCGR3B / FCGR3A* was similar to *FCGR2C* 3'UTR / *FCGR2A* 3' UTR in most individuals meant that the two PRT assays measuring these loci act as replicate assays for CN variation in CNR1. When plotted against each other, data clusters representing groups of individuals with the same underlying diploid CN variations in the *FCGR* locus could be distinguished. The largest of these groups (corresponding to *FCGR3B:FCGR3A* of 1:2, 2:2 or 3:2) were differentiated reliably using a clustering algorithm (Fig. S2B, Table S8), although the more diffuse or smaller clusters, such as *FCGR3B:FCGR3A* of 4:2, were unable to be clustered by the algorithm and had to be designated manually (Table S8).

Although many clusters could be explained by variation in the number of copies of CNR1 (Fig. S1C and Fig. S2C, blue), the cluster in which both *FCGR3B / FCGR3A* ~0.6 and *FCGR2C* 3'UTR /

FCGR2A 3' UTR ~0.6 could only be explained by three copies of *FCGR2A* 3'UTR and *FCGR3A*, with CNR1 invariant (Fig. S1C and Fig. S2C, red). This indicated a second CN variable region, CNR2 (Fig. 1 and Fig. S1D, red). Clusters which represented a single duplication in CNR1 and deletion in CNR2, or vice versa, were also observed (Fig. S1C and Fig. S2C, purple).

The cluster in which *FCGR3B / FCGR3A* = 2 could be explained in two ways: four copies of *FCGR3B* and invariant *FCGR3A*, or invariant *FCGR3B* and one copy of *FCGR3A*. These two possibilities could be distinguished by their total CN of *FCGR3.* A third assay, PRT-3(A+B)/Chr18, which compared the total *FCGR3* copy number to a region in chromosome 18, was therefore used to distinguish these two possibilities by manual calls, as well as improving the resolution of the other minor clusters (Fig. S1C and Fig. S2D). Manual calls were also required to distinguish these minor clusters. For instance, individuals with *FCGR3B: FCGR3A* CN of 2:3 were typically called as 1:2 by the clustering algorithm (Table S8). These calls were reliable: in replicate assays using all three PRTs on a set of Hong Kong Chinese samples, less than 3% of final CN designations made in one replicate changed in the second. Nearly all of the samples which failed in one replicate were able to receive a CN designation in the other (Table S8).

Not all potential combinations of relative *FCGR3B* and *FCGR3A* CN could be identified. Two combinations, *FCGR3B*:*FCGR3A* CN of 1:1 and 3:3, were indistinguishable from *FCGR3B*:*FCGR3A* CN of 2:2, despite the fact that they should be able to be discriminated on total *FCGR3* number. This was likely due to the variability in the PRT-3(A+B)/Chr18 assay and the fact that the 1:1 and 3:3 individuals were much rarer. Others, such as *FCGR3A* 0CN, may be too rare to be identified reliably. For a small percentage of individuals, no *FCGR* CN could be determined, reflecting either variability in the assay or very rare underlying CN combinations (Fig. S2F, Table S8).

In South East Asians a cluster in which *FCGR3B / FCGR3A* ~0.6 and *FCGR2C* 3'UTR / *FCGR2A* 3' UTR ~1.5 was identified (Fig. S1C and Fig. S2E, green). This represented three copies of *FCGR3A* and *FCGR2C* including the 3'UTR, with invariant *FCGR2A* 3'UTR and *FCGR3B*. This variation indicated the presence of a third CNV region, CNR3 (Fig. 1 and Fig. S1D, green) incorporating *FCGR3A* and *FCGR2C* 3'UTR. Individuals with a deletion in CNR3 were not identified, but may be rare.

CNR1 and CNR2 are comparable to two CNV regions previously identified using MLPA with multiple probes in each gene in the low affinity *FCGR* locus (2, 3). The most common CNV region, CNR1, included the PRT primer binding sites in the middle of *FCGR3B* and in the 3' UTR of *FCGR2C*. The MLPA studies supported a CNV region encompassing all of *FCGR2C* and *FCGR3B,* equivalent to CNR1. No CNV was reported in *FCGR2B.* The second region, CNR2, included the PRT primer sites in the 3'UTR of *FCGR2A* and the middle of *FCGR3A*. The MLPA studies report a CNV region encompassing *FCGR2C* and *FCGR3A*, as well as *HSP6* which lies between *FCGR2A* and *FCGR3A.* Combined with our findings, it suggested that the true extent of CNR2 runs from within the 3' end of *FCGR2A*, in which our PRT primer in falls closer to the end of *FCGR2A* than the last MLPA probe, through to the end of *FCGR2C* prior to the PRT 3'UTR binding site (Fig. 1). The final region, CNR3, was primarily observed in the Vietnamese and Chinese cohorts, and only individuals with a duplication in this interval were identified (Fig. S2E, Table S1). It incorporated *FCGR3A* and *FCGR2C* including the 3'UTR, but did not extend to the 3'UTR of *FCGR2A.* This region had not previously been identified.

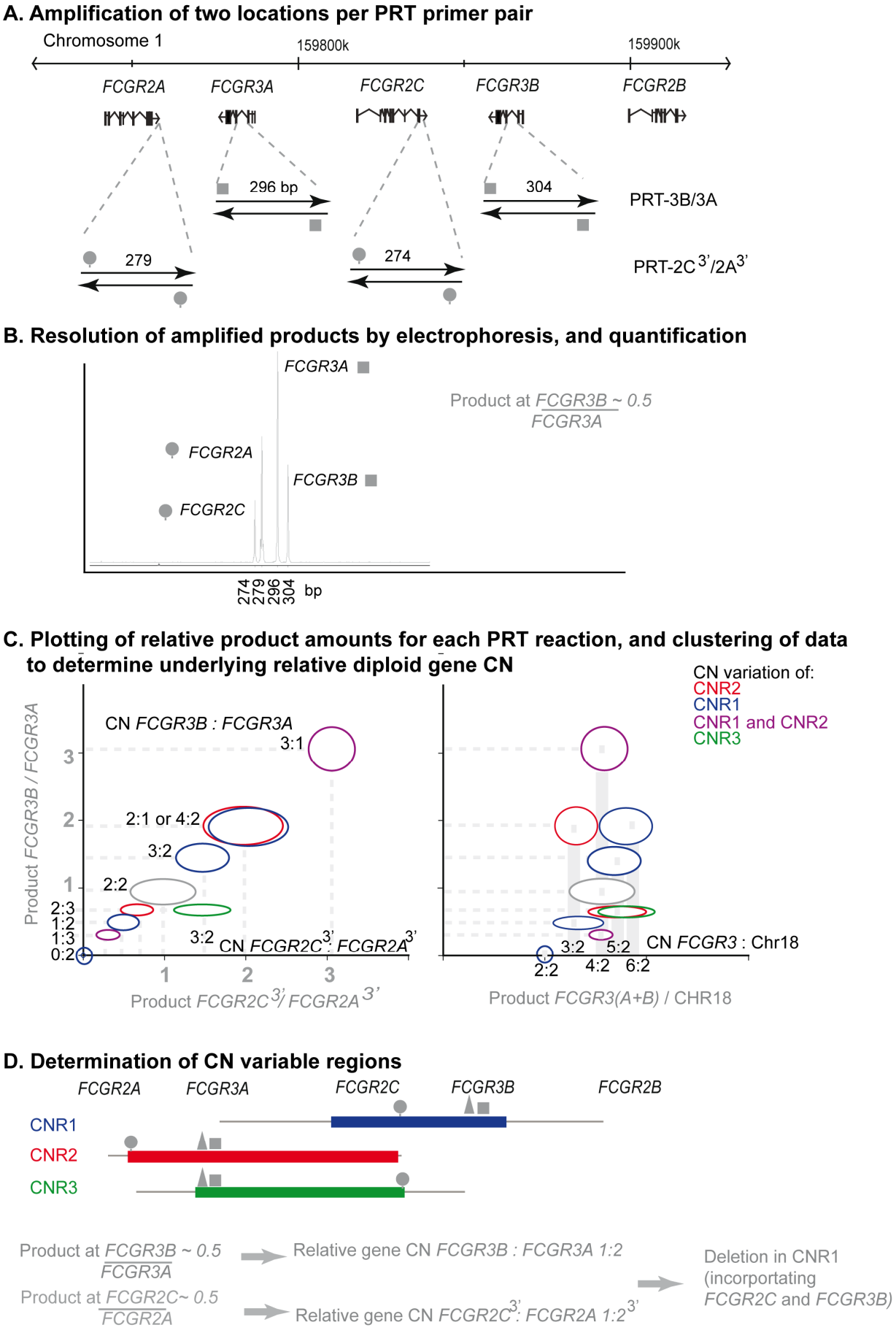

Figure S1: Diagram of *FCGR* paralogue ratio test assay

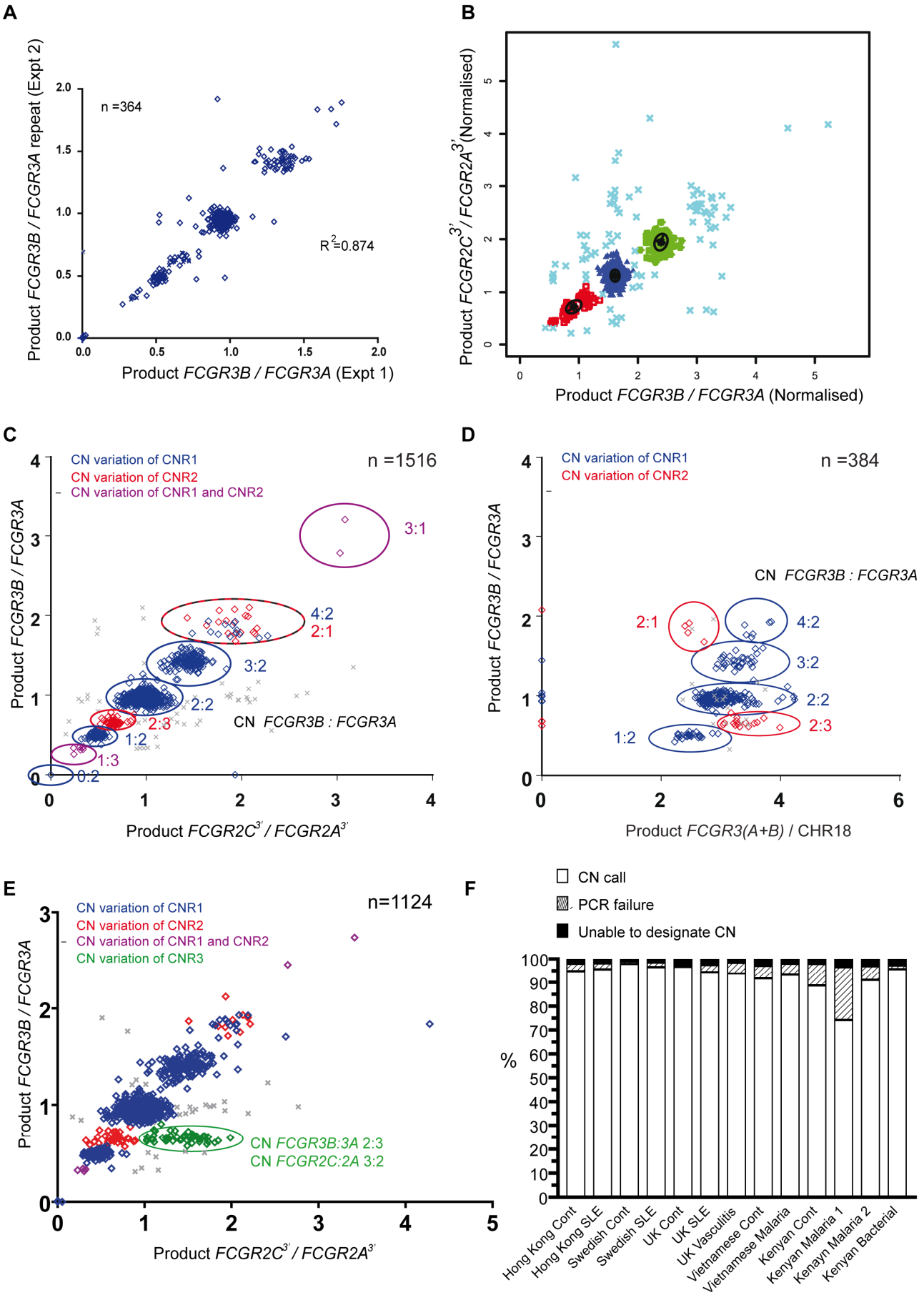

Figure S2: Replication and clustering of PRT assay results

A) The same genomic samples were amplified twice using paralogue ratio test PRT-3B/3A primers, and the relative amounts of product (*FCGR3B / FCGR3A*) for the replicated assays were plotted against each other. There was a strong correlation between the replicate experiments. R^2=0.8714. **B)** Relative product amounts of *FCGR3B / FCGR3A* (from PRT-3B/3A assay) and *FCGR2C 3'UTR / FCGR2A 3'UTR* (from PRT-2C$^{3'}$/2A$^{3'}$ assay) were plotted against each other to improve discrimination of CN ratio groups. After normalisation with controls, the data were clustered using a mclust algorithm with 95% confidence. Points which did not fall within a cluster were designated with an x. Clusters discriminated using the algorithm represent *FCGR3B:FCGR3A* copy number ratios of 3:2 (green), 2:2 (blue), and combined 1:3 + 1:2 + 2:3 (red). This cohort: UK Caucasian controls. **C)** Typically, values for *FCGR3B / FCGR3A* and *FCGR2C 3'UTR / FCGR2A 3' UTR* were the same. Clusters were distinguished, and relative copy number of genes was assigned in conjunction with **D)**, where clusters could be further discriminated by comparing *FCGR3B / FCGR3A* and *FCGR3* / Chr18. Clusters corresponding to *FCGR3B:FCGR3A* copy number ratios of 0:2, 1:3, 2:3, 2:1, and 4:2 were identified manually by researchers blinded to cohort. Variation in CNV regions producing the observed gene copy number could be inferred: blue, variation in CNR1; red, in CNR2; purple, in CNR1 and CNR2. This cohort: UK Caucasian controls. **E)** Duplication of the novel CNR3 interval (green) was identified where *FCGR3B / FCGR3A* and *FCGR2C 3'UTR / FCGR2A 3'UTR* differed, primarily in Asian cohorts. This cohort: Vietnamese controls. **F)** Percentages of each cohort in which copy number was able to be designated (white) or either a PCR failed (diagonal lines) or designation was not possible (black).

Table S1: Ethnic profiles of CN interval variation in control cohorts

CN region			UK Caucasian	Hong Kong Chinese	Vietnamese	Kenyan
CNR1	**CNR2**	**CNR3**				
0,1	2	2	103 (6.9) [a]	93 (9.4)	86 (9.7)	151 (18.1)
3,4	2	2	166 (11.2)	138 (13.9)	121 (13.6)	54 (6.4)
2	**1**	2	18 (1.2)	7 (0.7)	8 (0.9)	3 (0.3)
2	**3**	2	60 (4.0)	25 (2.5)	33 (3.7)	13 (1.5)
1	**3**	2	7 (0.47)	4 (0.4)	4 (0.4)	1 (0.1)
3	**1**	2	2 (0.13)	0 (0)	2 (0.2)	1 (0.1)
2	2	**3**	8 (0.54)	22 (2.2)	39 (4.4)	1 (0.1)
2	2	2	1120 (75.5)	700 (70.7)	592 (66.8)	609 (73.1)
	Total		**1484**	**989**	**885**	**833**

Abbreviations: CN, diploid copy number of region; CNR1, CN variable region including *FCGR2C* and *FCGR3B*; CNR2, CN variable region including *FCGR2A*$^{3'}$, *FCGR3A* and *FCGR2C* (not including 3' UTR); CNR3, CN variable region including *FCGR3A* and *FCGR2C* (including 3' UTR).
Bold: variation of CN in the interval.
[a]: counts (percentages).

Table S2: Association of *FCGR3A* CN with autoimmunity and infection

	Hong Kong Chinese		UK Caucasian		Swedish Caucasian	
FCGR3A	**Control** [a]	**SLE**	**Control**	**SLE**	**Control**	**SLE**
1	7 (0.7)	6 (0.7)	20 (1.3)	3 (1.4)	4 (1.4)	1 (0.4)
2	931 (94.1)	835 (94.9)	1389 (93.7)	198 (94.3)	260 (93.5)	231 (96.3)
3	51 (5.2)	39 (4.4)	75 (5.1)	9 (4.3)	13 (5.0)	8 (3.3)
TOTAL	**989**	**880**	**1484**	**210**	**277**	**240**
p 3 vs 1,2		0.51		0.74		0.39
OR		1.17		1.19		1.54
[95% CI]		[0.76-1.80]		[0.59-2.41]		[0.64-3.74}

	Vietnamese		Kenyan		Kenyan	
	Control	**Malaria**	**Control**	**Malaria**		**Sepsis**
1	10 (1.1)	6 (1.5)	4 (0.4)	6 (0.4)		1 (0.1)
2	799 (90.2)	351 (92.6)	814 (97.7)	1198 (97.9)		910 (96.5)
3	76 (8.5)	22 (5.8)	15 (1.8)	19 (1.5)		32 (3.3)
TOTAL	**885**	**379**	**833**	**1223**		**943**
p 3 vs 1,2		0.11		0.80		**0.039**
OR		0.66		0.86		1.92
[95% CI]		[0.40-1.072]		[0.43-1.70]		[1.03-3.56]

Abbreviations: CNV, copy number variation; 3 vs 12, comparison of three copies (diploid) of *FCGR3A* versus 1 or 2 by Fisher's exact test; OR, odds ratio; CI, confidence interval; p, significance level of Fisher's exact test;

[a] counts (percentages)

Table S3: *FCGR2B-I232T* and SLE

FCGR2B	**Hong Kong Chinese**			
I232T	**Control** [a]	**SLE**	**SLE+nephrits**	**SLE-nephritis**
TT	57 (5.6)	60 (7.3)	20 (6.3)	40 (8)
IT	404 (39.4)	284 (34.7)	117 (37.1)	167 (33.2)
II	565 (55.1)	475 (58)	179 (56.6)	296 (58.8)
Total	**1026**	**819**	**316**	**503**
T allele	0.252	0.247	0.248	0.246
I allele	0.748	0.753	0.752	0.754
p HW	0.382	0.160	0.989	0.066
p TT vs IT/II		0.13	0.58	0.07
OR		1.34	1.15	1.47
[95% CI]		[0.92-1.96]	[0.68-1.94]	[0.97-2.23]
p TT vs IT vs II		0.06	0.7	**0.03**

FCGR2B	**Swedish Caucasian**		**UK Caucasian**		**Combined Caucasian** [b]
I232T	**Control**	**SLE**	**Control**	**SLE**	
TT	11 (3.9)	23 (8.9)	11 (2.5)	12 (5.8)	
IT	49 (17.2)	60 (23.3)	81 (18.3)	41 (19.8)	
II	225	176 (67.7)	351 (79.2)	154 (74.4)	
Total	**285**	**259**	**443**	**207**	
T allele	0.125	0.206	0.116	0.157	
I allele	0.875	0.794	0.884	0.843	
p HW	**0.002**	**2.55×10^{-5}**	0.068	**0.001**	
p TT vs IT/II		**0.02**		**0.04**	**7×10^{-4}**
OR		2.45		2.42	2.62
[95% CI]		[1.17-5.13]		[1.05-5.57]	[1.52-4.52]
p TT vs IT vs II		**0.01**		0.08	**2×10^{-4}**

Abbreviations: SLE, systemic lupus erythematosus; p, significance of Fisher's exact test (TT vs II/IT) or chi squared test of independence (TT vs II vs IT); OR, odds ratio; CI, confidence interval; HW, p-value for the test of Hardy-Weinberg equilibrium;

[a] counts (percentages).

[b] Combined Caucasian cohort: sum of individuals from Swedish and UK cohorts

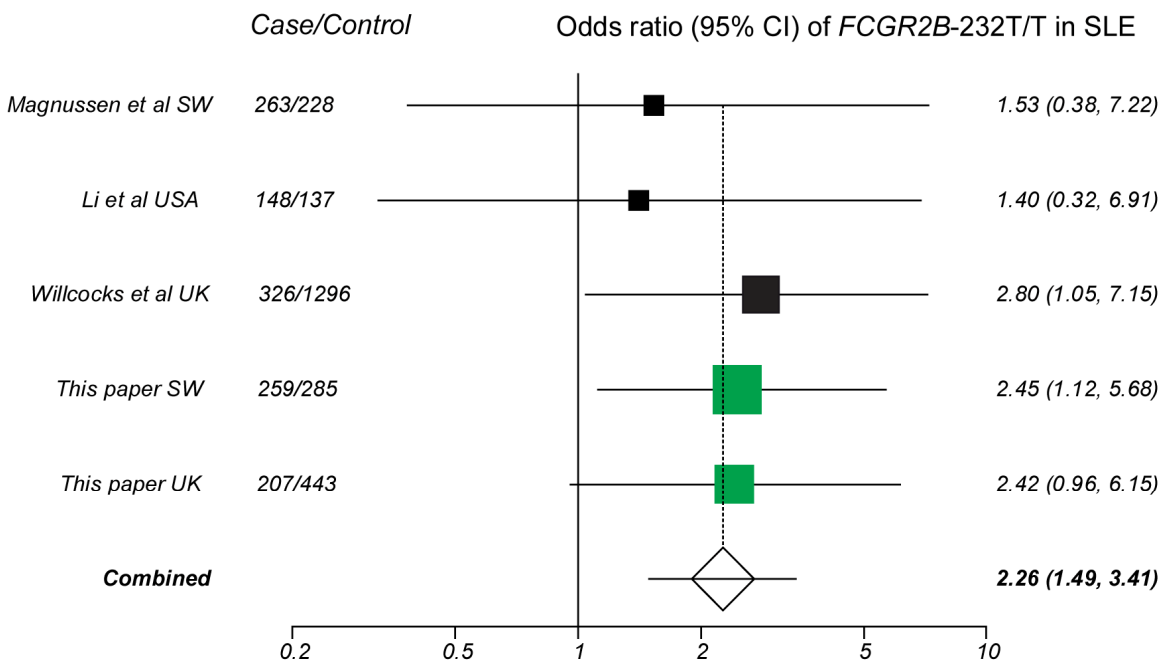

Figure S3: Meta-analysis of Caucasian *FCGR2B-I293T*
Meta-analysis (random effects model) of the association of homozygotes of the *FCGR2B* non-inhibitory allele (TT) versus the remainder (IT/II) between Caucasian systemic lupus erythematosus (SLE) cases and controls from the literature (4-6) and current cohorts in this study. Bars are proportional to study size. This study: green bars. SW, Swedish.

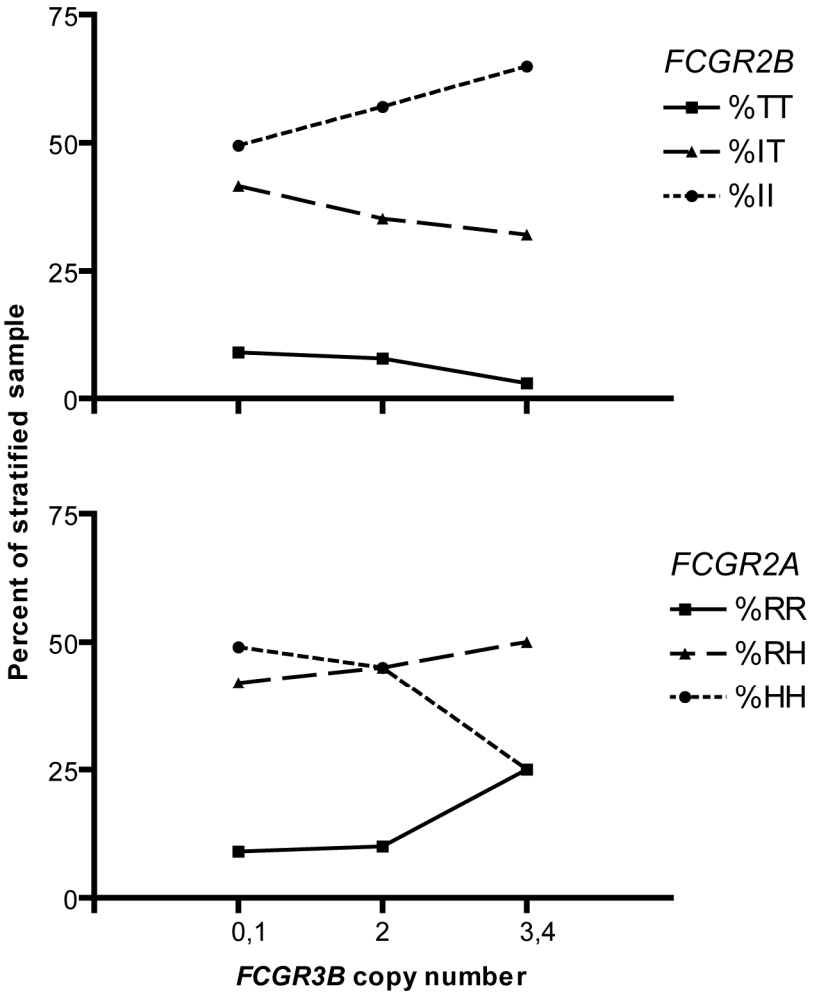

Figure S4: Distribution of *FCGR2A* and *FCGR2B* diplotypes over copy number groups
The percentage of *FCGR2A-R131H* and *FCGR2B-I232T* diplotypes in individuals stratified by *FCGR3B* copy number in a Hong Kong Chinese control population. This shows increased numbers of SLE risk genotype *FCGR2B-232T/T* individuals in the *FCGR3B* low copy number group, but increased SLE risk genotype *FCGR2A-131R/R* in the *FCGR3B* high copy number group.

Table S4: Linkage disequilibrium in the *FCGR* locus

FCGR		**Kenyan** [a,b]		**Hong Kong Chinese**		**Vietnamese**		**UK Caucasian**		**Swedish Caucasian**	
SNPxSNP		**n**	**P (cor)**	**n**	**P (cor)**	**n**	**P (cor)**	**n**	**P (cor)**	**n**	**P (cor)**
3A-VF	2A-RH	304	**< 0.0001**	292	**0.0131**	298	0.3080	315	**0.0004**	160	**<0.0001**
3A-VF	2B-IT	296	**< 0.0001**	318	**0.0025**	297	**0.0178**	335	0.9465	171	0.0584
2A-RH	2B-IT	295	**0.0072**	295	**0.0075**	302	**0.0003**	314	0.2412	160	**0.0291**
		r^2	**D'**	**r^2**	**D'**	**r^2**	**D'**	**r^2**	**D'**	**r^2**	**D'**
3A-VF	2A-RH	0.094	**0.421**	0.020	0.155	0.005	0.090	0.043	**0.278**	0.0967	**0.409**
3A-VF	2B-IT	0.049	**0.533**	0.031	**0.380**	0.021	0.295	0.00002	0.015	0.0139	**0.403**
2A-RH	2B-IT	0.020	0.248	0.020	**0.338**	0.039	**0.513**	0.0073	0.223	0.0268	**0.424**
SNPxCNV		**n**	**P (cov)**	**n**	**P (cov)**	**n**	**P (cov)**	**n**	**P (cov)**	**n**	**P (cov)**
3A-VF	3B CNV	307	0.767	319	0.288	302	0.311	340	0.967	174	**0.012**
2A-RH	3B CNV	306	0.183	296	**0.041**	307	0.265	317	0.412	163	0.450
2B-IT[c]	3B CNV	803	0.713	975	**0.020**	700	0.337	365	**0.026**	178	**0.023**
		r^2	**D'**	**r^2**	**D'**	**r^2**	**D'**	**r^2**	**D'**	**r^2**	**D'**
2B-IT[c]	3B HCN 0	0.000	0.100	0.002	0.096	0.002	0.113	0.002	0.083	0.007	0.158
	3B HCN 1	0.000	0.029	0.002	0.171	0.002	0.060	0.000	0.132	0.005	0.084
	3B HCN 2	0.005	0.231	0.007	**0.493**	0.000	0.023	0.003	**0.565**	0.000	0.019

Abbreviations: *FCGR*, Fc gamma receptor; 2A-RH, *FCGR2A-R131H*; 3A-VF, *FCGR3A-V176F*; 2B-IT, *FCGR2B-I232T*; 3B-CN, *FCGR3B* copy number; P(cor), p value associated with correlation of SNP genotypes; P(cov), p value determined by covariance of SNP and CNV genotypes; D' and r^2, LD measures derived from phased haplotypes;
3B HCN 0, LD measured between diallelic SNP and phased haplotype copy number of deletion vs duplication/normal; 3B HCN 2, LD measured between SNP and duplication vs deletion/normal.
[a] All individuals are from the control cohorts used in association studies
[b] *FCGR3A* CN=2 except where noted.
[c] All *FCGR3A* CN.
Bold: D' was considered appreciable if >0.25 and p values significant at 95% level

Table S5: *FCGR2A-R131H, FCGR3A-V176F*, and SLE

	Hong Kong Chinese				UK Caucasian				Swedish Caucasian			
	Control [a]		SLE		Control		SLE		Control		SLE	
FCGR2A-R131H												
R/R	34	(10.3)	45	(13.2)	101	(28.4)	47	(35.3)	52	(28.2)	77	(33.6)
R/H	152	(46.2)	156	(45.8)	177	(49.8)	60	(45.1)	86	(46.7)	103	(45.5)
H/H	143	(43.4)	139	(40.8)	77	(21.6)	26	(19.5)	46	(25)	47	(20.7)
Total	**329**		**340**		**355**		**133**		**184**		**227**	
HW	0.79		0.99		1.0		0.69		0.68		0.55	
p R/R vs. R/H+H/H			0.281				0.151				0.284	
Odds ratio [95% CI]			1.32 [0.82-2.13]				1.37 [0.90-2.10]				1.29 [0.84-1.96]	
					Caucasian combined[b]: p=0.065; OR=1.3 [0.98=1.75]							
FCGR3A-V176F												
F/F	133	(37.4)	133	(38.7)	166	(43.7)	78	(44.8)	86	(43.6)	112	(46.4)
F/V	166	(46.7)	161	(46.9)	178	(46.9)	83	(47.7)	86	(43.6)	99	(41)
V/V	56	(15.7)	49	(14.2)	35	(9.2)	13	(7.4)	25	(12.6)	30	(12.4)
Total	**355**		**343**		**379**		**174**		**197**		**241**	
HW	0.94		1.0		0.43		0.36		0.89		0.55	
FCGR3A-V176F*, *FCGR3A CN=2												
F/F	121	(37.9)	126	(40.9)	149	(43.8)	75	(48.3)	75	(43.3)	103	(46.7)
F/V	146	(45.7)	140	(45.4)	162	(47.6)	74	(47.7)	76	(43.3)	91	(41.7)
V/V	52	(16.3)	42	(13.6)	29	(8.5)	6	(3.8)	23	(13.2)	25	(11.4)
Total	**319**		**308**		**340**		**155**		**174**		**219**	
HW	0.78		0.95		0.26		0.06		0.83		0.79	
p F/F vs. V/F+V/V			0.46				0.38				0.54	
Odds ratio [95% CI]			1.13 [0.82-1.56]				1.20 [0.82-1.76]				1.15 [0.77-1.72]	

Abbreviations: SLE, systemic lupus erythematosus; CN, copy number; p, significance of Fisher's exact test; OR, odds ratio; CI, confidence interval; HW, p value for the test of Hardy-Weinberg equilibrium.

[a] counts (percentages)

[b] addition of Swedish and UK Caucasian cohorts

Bold: low affinity allele homozygote.

Table S6: *FCGR2A-R131H*, *FCGR3A-V176F* in Kenyan and Vietnamese control cohorts

	Kenyan[a]	**Vietnamese**		**Kenyan**	**Vietnamese**		**Kenyan**	**Vietnamese**
FCGR2A -R131H			***FCGR3A -V176F*** [b]			***FCGR2 B-I232T***		
R/R	114 (33.1)	37 (10.7)	**F/F**	157 (51.1)	102 (33.7)	**T/T**	28 (8.1)	18 (4.9)
R/H	169 (49.1)	133 (38.5)	V/F	125 (40.8)	150 (49.6)	I/T	159 (46.0)	152 (41.0)
H/H	61 (17.7)	175 (50.7	V/V	25 (8.1)	50 (16.5)	I/I	159(46.0)	201 (54.2)
Total	**344**	**345**	**Total**	**307**	**302**	**Total**	**346**	**371**

[a] counts (percentages)

[b] *FCGR3A* CN=2

Bold: low affinity or non-inhibitory allele homozygote.

Table S7: *FCGR* polymorphism diplotype combinations enriched

FCGR	[a,b]	Kenyan		Chinese		Vietnamese		UK Caucasian		Swedish Caucasian	
		O	O/E	O	O/E	O	O/E	O	O/E	O	O/E
3A-VF	**2A-RH**										
F/F	**R/R**	71	1.37	9	0.71	9	0.83	52	1.31	28	1.45
F/F	R/H	68	0.91	45	0.89	32	0.81	69	1.00	33	0.99
F/F	H/H	18	0.62	58	1.22	59	1.17	19	0.65	6	0.36
F/V	**R/R**	29	0.70	18	1.17	16	1.01	32	0.74	15	0.78
F/V	R/H	65	1.09	61	1.00	70	1.21	78	1.04	34	1.02
F/V	H/H	28	1.21	55	0.96	62	0.84	39	1.23	22	1.32
V/V	**R/R**	1	0.12	6	1.10	7	1.32	6	0.78	2	0.34
V/V	R/H	13	1.09	26	1.20	14	0.73	11	0.82	10	0.98
V/V	H/H	11	2.39	14	0.69	29	1.17	9	1.58	10	1.95
3A-VF	**2B-IT**										
F/F	**T/T**	16	1.32	11	1.48	8	1.38	3	1.15	7	1.67
F/F	I/T	81	1.21	50	1.08	45	1.12	27	0.97	14	1.15
F/F	I/I	56	0.77	59	0.88	48	0.89	118	1.01	53	0.92
F/V	**T/T**	5	0.52	7	0.78	6	0.70	3	1.06	3	0.72
F/V	I/T	46	0.86	58	1.04	61	1.03	30	0.99	10	0.82
F/V	I/I	68	1.18	81	1.00	79	0.99	125	0.99	61	1.06
V/V	**T/T**	2	1.03	1	0.31	2	0.70	0	0.00	0	0.00
V/V	I/T	4	0.38	13	0.66	14	0.71	6	1.11	4	1.07
V/V	I/I	18	1.56	38	1.32	34	1.28	23	1.02	19	1.07
2A-RH	**2B-IT**										
R/R	**T/T**	13	1.65	2	0.96	0	0.00	2	1.25	5	1.99
R/R	I/T	50	1.15	9	0.69	8	0.61	10	0.59	8	1.10
R/R	I/I	37	0.79	23	1.22	24	1.37	79	1.11	31	0.89
R/H	**T/T**	10	0.88	6	0.72	4	0.59	2	0.72	4	0.92
R/H	I/T	55	0.88	45	0.87	44	0.93	40	1.34	17	1.35
R/H	I/I	75	1.11	83	1.11	69	1.08	115	0.92	56	0.93
H/H	**T/T**	1	0.23	8	1.02	13	1.48	2	1.70	1	0.46
H/H	I/T	26	1.07	62	1.28	70	1.15	11	0.88	3	0.48
H/H	I/I	28	1.07	57	0.81	70	0.86	53	1.01	36	1.17
2A-RH	**3B-CN**										
R/R	01	12	0.60	3	0.84	3	0.78	7	1.01	4	1.22
R/R	2	80	1.06	23	0.87	19	0.83	67	0.92	34	0.91
R/R	34	10	1.52	8	1.96	11	1.76	17	1.53	7	1.64
R/H	01	34	1.18	14	0.99	13	0.93	12	1.00	5	0.88
R/H	2	106	0.98	105	1.00	85	1.02	131	1.03	67	1.03
R/H	34	7	0.74	16	0.99	22	0.97	16	0.82	6	0.81
H/H	01	13	1.16	16	1.20	20	1.11	4	0.79	2	0.71
H/H	2	42	1.00	103	1.05	111	1.04	57	1.06	33	1.02
H/H	34	2	0.54	8	0.52	23	0.79	6	0.73	4	1.08
2B-IT	**3B-CN**										
T/T	01	4	0.85	1	0.48	4	1.90	2	4.55	4	5.51
T/T	2	17	0.96	17	1.10	10	0.80	4	0.86	5	0.60
T/T	34	3	1.94	2	0.83	4	1.17	0	0.00	1	1.05
I/T	01	28	1.08	15	1.16	16	1.09	4	0.85	0	0.00
I/T	2	93	0.95	101	1.05	87	1.00	57	1.15	27	1.12
I/T	34	11	1.29	8	0.54	22	0.93	1	0.13	2	0.73
I/I	01	26	0.92	18	0.96	17	0.86	19	0.97	9	0.90
I/I	2	112	1.06	133	0.95	118	1.01	212	1.02	115	1.00
I/I	34	5	0.54	29	1.34	33	1.03	28	0.88	14	1.07

Abbreviations: *FCGR*, Fc gamma receptor; 2A-RH, *FCGR2A-R131H*; 3A-VF, *FCGR3A-V176F*; 2B-IT, *FCGR2B-I232T*; 3B-CN, *FCGR3B* copy number; O, observed number; O/E observed divided by expected (E calculated by probabilities of individual types multiplied).

[a] All individuals are from the control cohorts used in association studies

[b] *FCGR3A* CN=2.

Grey: increased observed over expected by >1.2x.

Bold: SLE risk genotypes.

Table S8: Concordance of calls in repeated assay of Hong Kong Chinese samples

Copy number designation [b]	By mclust clustering algorithm:			
FCGR3B: FCGR3A	Called [c]	Different call	Not clustered [d]	Total
1st replicate [a]				***364***
0 : 2			4 (100) [e]	*4*
1 : 1	47 (100)			*47*
1 : 3		2 (100)		*2*
2 : 2	211 (99.1)	1 (0.5)	1 (0.5)	*213*
2 : 1			2 (100)	*2*
2 : 3		8 (88.9)	1 (11.1)	*9*
2 : 3, 2C3 : 2A2			9 (100)	*9*
3 : 2	42 (97.7)		1 (2.3)	*43*
4 : 2			3 (100)	*3*
CN Undetermined [f]			12 (100)	*12 (3.3)*
PRT Fail [g]			20 (100)	*20 (5.5)*
2nd replicate				***364***
0 : 2			5 (100)	*5*
1 : 1	40 (97.6)		1 (2.4)	*41*
1 : 3		1 (100)		*1*
2 : 2	198 (94.3)	2 (1.0)	10 (4.8)	*210*
2 : 1			1 (100)	*2*
2 : 3		8 (100)		*8*
2 : 3, 2C3 : 2A2			8 (100)	*8*
3 : 2	46 (97.9)		1 (2.1)	*47*
4 : 2			3 (100)	*3*
CN Undetermined			13 (100)	*13 (3.6)*
PRT Fail			25 (100)	*25 (6.8)*

2nd replicate	**1st replicate**			
***FCGR3B: FCGR3A* CN**	Same CN	Different CN	CN Undetermined	PRT Fail
0 : 2	4 (100)			
1 : 2	37 (90.2)	2 (4.9)		2 (4.9)
1 : 3	1 (100)			
2 : 2	188 (89.5)	4 (1.9)	6 (2.9)	12 (4.7)
2 : 1	2 (100)			
2 : 3	7 (87.5)			1 (12.5)
2 : 3, 2C3 : 2A2	5 (62.5)	1 (12.5)	1 (12.5)	1 (12.5)
3 : 2	42 (89.4)	2 (4.3)	1 (2.1)	2 (4.3)
4 : 2	3 (100)			
CN Undetermined		11 (78.6)	2 (14.3)	1 (7.1)
PRT Fail		24 (96.0)		1 (4.0)

Abbreviations: CN, copy number; PRT, paralogue ratio test; 2C3:2A2, CN of $FCGR2C^{3'}$=3, $FCGR2A^{3'}$ =2.

[a] Full triple PRT assay of 364 Hong Kong Chinese case and control samples, repeated.

[b] Diploid CN assigned using both a clustering algorithm and manual calls on data from triple PRT.

[c] CN was able to be designated by clustering algorithm, and was unchanged by manual call.

[d] Unable to be assigned to a cluster by clustering algorithm.

[e] counts (percentages).

[f] CN unable to be determined by clustering algorithm or manual call.

[g] One or more of the paralogue ratio test products was not amplified.

References

1 Hollox, E.J., Detering, J.C. and Dehnugara, T. (2009) An integrated approach for measuring copy number variation at the FCGR3 (CD16) locus. *Hum. Mutat.*, **30**, 477-484.

2 Breunis, W.B., van Mirre, E., Bruin, M., Geissler, J., de Boer, M., Peters, M., Roos, D., de Haas, M., Koene, H.R. and Kuijpers, T.W. (2008) Copy number variation of the activating FCGR2C gene predisposes to idiopathic thrombocytopenic purpura. *Blood*, **111**, 1029-1038.

3 Breunis, W.B., van Mirre, E., Geissler, J., Laddach, N., Wolbink, G., van der Schoot, E., de Haas, M., de Boer, M., Roos, D. and Kuijpers, T.W. (2009) Copy number variation at the FCGR locus includes FCGR3A, FCGR2C and FCGR3B but not FCGR2A and FCGR2B. *Hum. Mutat.*, **30**, E640-E650.

4 Li, X., Wu, J., Carter, R.H., Edberg, J.C., Su, K., Cooper, G.S. and Kimberly, R.P. (2003) A novel polymorphism in the Fcgamma receptor IIB (CD32B) transmembrane region alters receptor signaling. *Arthritis Rheum.*, **48**, 3242-3252.

5 Magnusson, V., Zunec, R., Odeberg, J., Sturfelt, G., Truedsson, L., Gunnarsson, I. and Alarcon-Riquelme, M.E. (2004) Polymorphisms of the Fc gamma receptor type IIB gene are not associated with systemic lupus erythematosus in the Swedish population. *Arthritis Rheum.*, **50**, 1348-1350.

6 Willcocks, L.C., Carr, E.J., Niederer, H.A., Rayner, T.F., Williams, T.N., Yang, W., Scott, J.A.G., Urban, B.C., Peshu, N., Vyse, T.J. *et al.* (2010) A defunctioning polymorphism in FCGR2B is associated with protection against malaria but susceptibility to systemic lupus erythematosus. *Proc. Natl. Acad. Sci. U. S. A.*, **107**, 7881-7885.