Supplemental Table 1: Characteristics of the *B*57*+ study population

Outcome measure	Controllers	Noncontrollers
Whole Genome Sequencing Single variant analysis	**N = 100** W=90, other=10	**N = 100** W=97, other=3
Single variant analysis (validation cohort)	**N = 297** W=136, B=139, other=22	**N = 213** W=115, B=91, other=7
Genotypic analysis	**N = 188** W=80, B=92, other=16	**N = 136** W=72, B=59, other=5
Longitudinal log_{10}VL	**N = 674** W=389, B=221, other=64	
Mean viral load (mVL)	**N = 674** W=389, B=221, other=64	
Longitudinal CD4 count	**N = 588** W=338, B=194, other=56	

W = Whites; B = Blacks; Other = Hispanic/Latino, Asian, mixed race, unknown race.

Supplemental Table 2: Pairwise LD analysis of KIR3DL1 amino acids 2,47 and 54

	Caucasians		African Americans	
	aa47	**aa54**	**aa47**	**aa54**
aa2				
r^2	0.92	0.99	0.69	0.74
D'	1.00	1.00	1.00	1.00
aa47				
r^2		0.93		0.93
D'		1.00		1.00

Supplemental Table 3: KIR3DL1 allele frequencies in controllers and noncontrollers[A]

	Whites		Blacks	
3DL1 allele	**CTR N (%)**	**NC N (%)**	**CTR N (%)**	**NC N (%)**
001	78 (15.4)	79 (20.0)	33 (11.3)	15 (8.5)
002	62 (12.3)	29 (7.4)	9 (3.1)	8 (4.5)
004	77 (15.2)	73 (18.5)	27 (9.2)	15 (8.5)
005	71 (14.1)	72 (18.3)	16 (5.1)	10 (5.7)
007	12 (2.4)	5 (1.3)	12 (4.1)	9 (5.1)
008	23 (4.6)	25 (6.3)	3 (1.0)	1 (0.6)
009	10 (2.0)	3 (0.8)	5 (1.7)	0 (0)
015/017	55 (10.9)	22 (5.6)	123 (42.0)	72 (40.9)
020	12 (2.4)	3 (0.8)	16 (5.5)	11 (6.2)
3DS1[B]	100 (19.8)	72 (18.3)	16 (5.5)	10 (5.7)

[A]The most common alleles are listed. [B]Individuals homozygous for *KIR3DS1* were excluded from the study and were therefore not included in the frequency calculation. Alleles with 47I are shown in red.

Supplemental Table 4: Effect of *KIR3DL1 I47V* on HIV control in *B*57+* individuals

3DL1 aa47	CTR N (%)	NC N (%)	OR adj.	*P* value
VV	91 (80.5)	48 (57.8)	0.2	$4x10^{-4}$
II	22 (19.5)	35 (42.2)		
IV	75 (77.3)	53 (60.2)	0.5	0.04
II	22 (22.7)	35 (39.8)		
VV	91 (54.8)	48 (47.5)	0.8	ns
IV	75 (45.2)	53 (52.5)		

Only individuals with 2 copies of KIR3DL1 were included in the analysis. Individuals with *3DL1/3DS1, 3DS1/3DS1, 3DL1*004* (1 or 2 copies), and *3DL1/-* were excluded.
CTR = controllers; NC = non-controllers; OR adj. = odds ratio adjusted by race; ns = not significant.

Supplemental Table 5: SPR-based equilibrium (K_D) values (μM) and standard errors for KIR3DL1-pHLA-B*57:01 interaction

Peptide	3DL1*001	3DL1*005	3DL1*015
IW9	16.7 ± 2.4	7.66 ± 0.8	21.3 ±3.1
KF11	34.6 ± 3.6	22.5 ± 2.1	49.3 ± 8.1
LF9	9.70 ± 0.4	4.29 ± 0.3	7.53 ± 1.2
QW9	21.8 ± 2.5	15.6 ± 1.2	25.8 ± 2.7

Supplemental Table 6: Relative effects of KIR3DL1 aa47, KIR3DS1 and KIR3DL1 expression level on HIV viremia[A].

Genotype	N	Effect (linear estimate)	SE	p value
B*57:01	398			
KIR3DL1 aa47 (per each additional aa47V)		-0.53	0.03	9×10^{-86}
KIR3DS1 (presence vs. absence)		-0.49	0.12	5×10^{-5}
KIR3DL1 expression level (h*/y vs. l/*x)[B]		-0.36	0.04	1×10^{-18}
B*57:03[C]	245			
KIR3DL1 aa47 (per each additional aa47V)		0.12	0.04	7×10^{-4}
KIR3DL1 expression level (h/*y vs. l/*x)[B]		0.25	0.05	6×10^{-7}

[A]Results are from a multivariate mixed linear effects model in individuals carrying one or more *HLA-B*57* alleles fitting the effect of the variable shown against longitudinal $\log_{10}$HIV VL. *HLA-A, -B* and *-C* alleles, and timing of viral load measurements were taken into account by being coded as random effects for all analyses.

[B]*KIR3DL1*h*/y* = individuals who carry a high expressing *KIR3DL1* allele (*KIR3DL1*h,* see Supplementary Figure 2) in the absence of a low expressing *KIR3DL1* allele (*KIR3DL1*l)*, i.e. *KIR3DL1*h/*h* or *KIR3DL1*h/*004*; abbreviated as *h/*y*, where **y* = **h* or **004*. *KIR3DL1*l/*y* = individuals with at least one copy of *KIR3DL1*l* (*KIR3DL1*l/*l*, *KIR3DL1*l/*h*, or *KIR3DL1*l/*004;* abbreviated as *l/*x*, where **x*= **l*, **h*, or **004* (1).

[C]Due to insufficient data, no results were generated for *KIR3DS1* (presence/absence).

1. Martin MP, Qi Y, Gao X, Yamada E, Martin JN, Pereyra F, Colombo S, Brown EE, Shupert WL, Phair J, et al. Innate partnership of HLA-B and KIR3DL1 subtypes against HIV-1. *Nat Genet.* 2007;39(6):733-40.

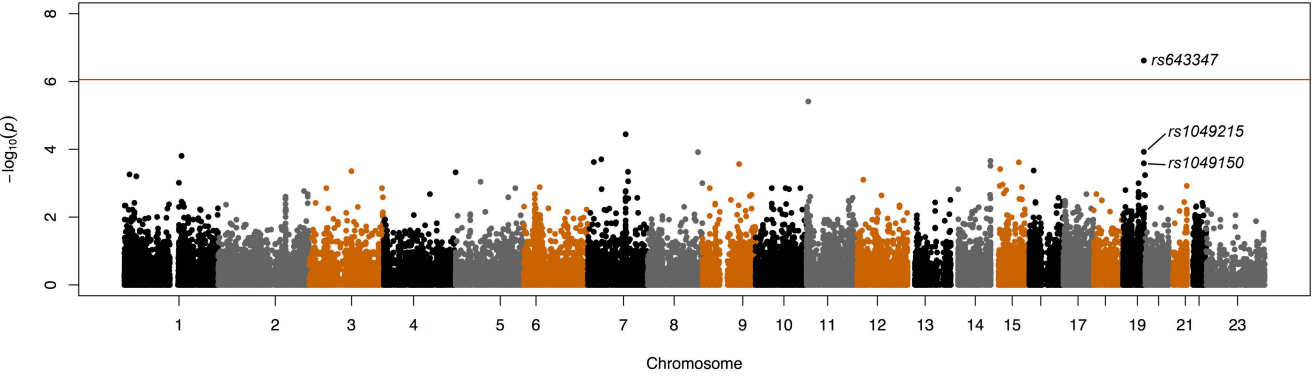
Supplemental Figure Legends

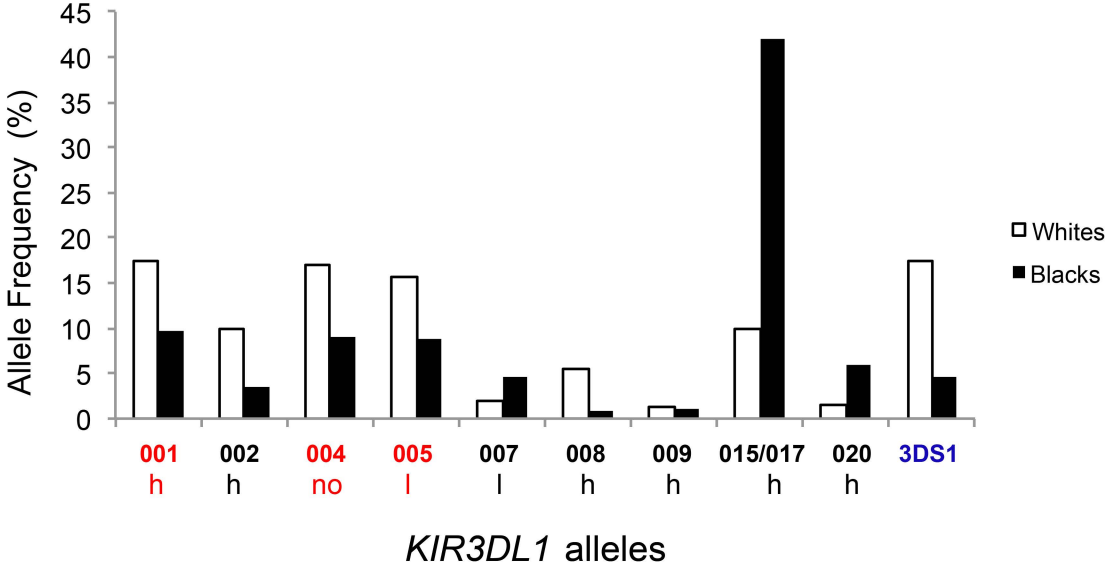
Supplemental Figure 1: Manhattan plot of whole genome sequencing data derived from 100 B*57+ HIV controllers and 100 B*57+ noncontrollers. p-values are shown for 56,808 data points for all functional variants that were tested in Table 1 (WGS analysis). A single SNP on chromosome 17 (rs643347) exceeded the threshold for statistical significance defined by $p < 8.8 \times 10^{-7}$ after correcting for multiple comparisons.

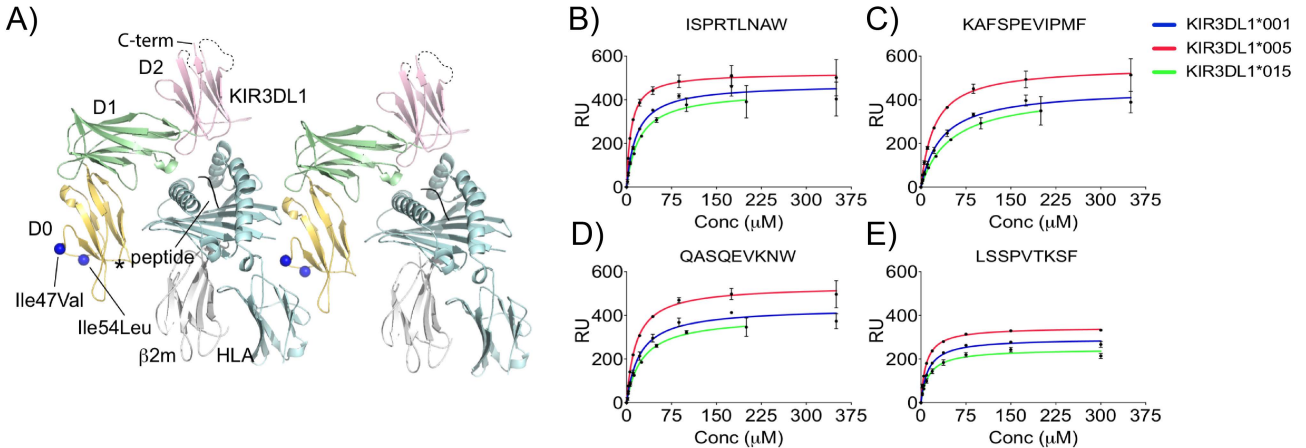
Supplemental Figure 2: Allele frequency of the most common *KIR3DL1* alleles in the *HLA-B*57* study cohort. The frequency of each variable is shown for Whites and Blacks. Individuals homozygous for *KIR3DS1* were excluded from the study and were therefore not included in the frequency calculation. Alleles with 47I are shown in red and those with 47V in black. h = high cell surface expression alleles; l = low cell surface expression alleles; no = no cell surface expression.

Supplemental Figure 3: KIR3DL1 polymorphism affects binding avidity: (a) Cartoon representation of the KIR3DL1*001-HLA-B*57:01-LF9 ternary complex. KIR3DL1*001 (D0 domain gold, D1 domain green, D2 domain pink), HLA-B*57:01 (blue), β2m (grey), the peptide (black). The polymorphisms that distinguish KIR3DL1*015 (Val47 and Leu54) are shown as blue spheres. The N-terminus of KIR3DL1 did not extend beyond residue 6 (shown as *) in available crystal structures. Accordingly, the Met2Val substitution at position 2 is not

shown. The C-terminus of KIR3DL1 is labeled. The polymorphisms at positions 47 and 54 are modelled as forming a clustering interface with the α2 and α3 domains of an adjoining pHLA molecule, as observed in the crystallographic arrangement of molecules of the KIR3DL1-B*57:01 complex (33). (b-e) SPR-based affinity measurements of the interaction between KIR3DL1*001 (blue line), KIR3DL1*005 (red line), KIR3DL1*015 (green line) and their HLA B*57:01 ligand in complex with the IW9 (ISPRTLNAW) peptide (b), the KF11 (KAFSPEVIPMF) peptide (c), the LF9 (LSSPVTKSF) peptide (d) and the QW9 (QASQEVKNW) peptide (e). All data are for experiments performed in duplicate, from two independent experiments. Data are shown as mean ± standard deviation.


rs643347
rs1049215
rs1049150
−log10(p)
0
2
4
6
8
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
17
19
21
23
Chromosome


45
40
35
30
25
20
15
10
5
0
Allele Frequency (%)
Whites
Blacks
001
h
002
h
004
no
005
l
007
l
008
h
009
h
015/017
h
020
h
3DS1
KIR3DL1 alleles


A)
C-term
D2
KIR3DL1
D1
D0
peptide
*
Ile47Val
Ile54Leu
β2m
HLA
B)
ISPRTLNAW
C)
KAFSPEVIPMF
D)
QASQEVKNW
E)
LSSPVTKSF
RU
Conc (μM)
0
75
150
225
300
375
200
400
600
KIR3DL1*001
KIR3DL1*005
KIR3DL1*015