

Number of interactions

INHIBITORY		ACTIVATING	
KIR	HLA	KIR	HLA
2DL1	C2	2DS1	C2
2DL2	C1	2DS2	C*16
2DL2	C2	2DS4	A*11
2DL3	C1	2DS4	C*01:02
3DL1	B-Bw4	2DS4	C*14:02
3DL1	A-Bw4	2DS4	C*16:01
3DL2	A*03	2DS4	C*02:02
3DL2	A*11	2DS4	C*05:01
		2DS4	C*04:01
		2DS5*003	C2
		2DS5*004	C2
		2DS5*005	C2
		2DS5*006	C2
		2DS5*007	C2
		2DS5*008	C2

Scoring matrix for counting number of interactions as previously described (21-23). HLA alleles were coded for their KIR ligand status (C1, C2, B-Bw4, A-Bw4) for those interactions involving only ligand status. For those with specific allotype designation, e.g. A*03, A*11, all alleles in those groups were counted. Homozygous interactions were counted twice.

Telomeric interactions

HLA	KIR3DL1 group			
	K015	K001	K005	K004
B*57:01	74.5	76.8	77.0	0
A*32:01	67.6	62.3	44.6	0
B*58:01	61.9	70.1	61.9	0
B*53:01	54.8	60.8	52.4	0
B*49:01	54.4	63.0	54.5	0
B*57:03	49.9	68.6	58.5	0
B*38:01	37.6	51.8	47.4	0
B*15:13	25.1	40.9	36.5	0
B*15:16	25.0	35.3	31.3	0
B*51:02	24.8	34.7	32.6	0
B*51:01	23.7	32.4	31.0	0
B*59:01	22.4	37.7	34.3	0
B*44:03	20.1	35.7	62.8	0
B*47:01	18.9	35.9	39.6	0
B*44:02	17.6	24.5	35.6	0
A*24:03	13.6	26.8	39.4	0
B*52:01	11.9	21.6	18.6	0
C*16:01	11.1	3.8	4.5	0
C*04:01	9.8	6.6	5.1	0
C*07:02	7.7	8.5	4.3	0
A*24:02	6.9	24.0	36.7	0
B*37:01	5.5	18.0	27.1	0
C*14:02	5.5	3.4	4.2	0
C*02:02	5.3	3.2	3.2	0
C*01:02	0.8	5.2	4.9	0
A*23:01	0.0	3.9	18.4	0
B*27:05	0.0	5.3	16.4	0
B*13:01	0.0	0.0	7.0	0

Cen and Tel interaction scores used the 'Telomeric Interactions' and 'Centromeric Interactions' scoring matrices. The results were summed for the composite interaction score. The centromeric interaction values were obtained from published binding studies where they were reported as absolute binding values. The values for low expressing alleles were multiplied by 0.5 to account for the expression level difference. Telomeric interaction scores were taken from Saunders et al along with allele assignment to one of four groups (K001, K004, K005, K015). These values were reported as percent of maximum and were normalized to the centromeric values so that the 100% score of Saunders was equivalent to the maximum centromeric value. KIR and/or HLA of the donor and/or recipient were given the value of the closest allele if they did not appear in the matrix. In homozygous individuals the interaction was counted twice, once for each of the homozygous alleles.

Example calculation.

Donor KIR: 2DL2*003|2DL3*002|2DL1*002|3DL1*001/009 (K001/K001)
Recipient HLA: A*01:01/03:01|B*07:02/44:03|C*07:02/16:01

Cen 19+7+12+0 = 38 Avg. = 38/4 = 9.5

Tel 35.7+35.7+8.5+8.5+3.8+3.8 = 98

Avg. = 98/6 = 16.33

Combined 38+98 = 136 Avg. = 136/10 = 13.6

Centromeric interactions

	Allotype	C1									C2								
		C*01:02	C*03:02	C*03:03	C*03:04	C*07:02	C*08:01	C*12:03	C*14:02	C*16:01	C*02:02	C*04:01	C*05:01	C*06:02	C*15:02	C*17:01	C*18:02		
2DL2/3	2*001	20	28	44	50	22	34	14	18	12	17	7	14	17	30	9	20		
	2*002	20	28	44	50	22	34	14	18	12	17	7	14	17	30	9	20		
	2*003	17	21	26	38	19	23	12	13	7	1	1	2	4	14	3	8		
	2*004	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	2*005	20	28	44	50	22	34	14	18	12	17	7	14	17	30	9	20		
	2*006	13	21	27	37	15	21	10	11	4	4	2	2	3	12	1	4		
	2*007	20	28	44	50	22	34	14	18	12	17	7	14	17	30	9	20		
	2*008	10	14	22	25	11	17	7	9	6	8.5	3.5	7	8.5	15	4.5	10		
	2*009	24	41	49	51	28	43	15	21	13	15	4	12	19	26	8	20		
	2*010	10	14	22	25	11	17	7	9	6	8.5	3.5	7	8.5	15	4.5	10		
	2*011	15	21	28	36	18	25	12	13	8	3	1	4	2	12	2	3		
	3*001	7	21	27	30	12	21	1	3	0	3	1	1	2	2	2	3		
	3*002	7	21	27	30	12	21	1	3	0	3	1	1	2	2	2	3		
	3*003	7	21	27	30	12	21	1	3	0	3	1	1	2	2	2	3		
	3*004	14	21	26	30	18	22	2	11	3	3	0	1	2	5	1	3		
	3*005	14	21	26	30	18	22	2	11	3	3	0	1	2	5	1	3		
	3*006	7	21	27	30	12	21	1	3	0	3	1	1	2	2	2	3		
	3*007	7	21	27	30	12	21	1	3	0	3	1	1	2	2	2	3		
3*008N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
3*009	3	21	24	28	12	23	0	1	0	0	0	0	2	1	1	2			
3*010	14	21	26	30	18	22	2	11	3	3	0	1	2	5	1	3			
3*011	8	22	27	32	14	21	2	2	2	2	0	1	2	4	1	1			
3*012	7	21	27	30	12	21	1	3	0	3	1	1	2	2	2	3			
3*013	6	21	27	30	10	21	2	3	0	3	0	0	0	1	1	2			
3*014	24	41	49	54	29	41	17	22	14	1	0	4	2	9	2	3			
3*015	12	22	26	32	21	21	2	5	3	3	2	2	2	5	1	4			
3*016	24	41	50	57	33	42	16	21	17	4	1	2	5	15	3	12			
3*017	24	41	49	54	29	41	17	22	14	1	0	4	2	9	2	3			
3*018	24	41	49	54	29	41	17	22	14	1	0	4	2	9	2	3			
2DL1	2DL1*022	34	35	54	57	27	44	24	22	18	0	0	0	0	0	0	0		
	*001										39	9	38	47	65	25	53		
	*002										39	9	38	47	65	25	53		
	*003										38	8	37	46	63	25	53		
	*004										15	3	15	18.5	25	10	21		
	*005										38	8	37	46	63	25	53		
	*006										19	4	18.5	23	31.5	12.5	26.5		
	*007										15.5	3.5	15	18.5	25.5	10	21.5		
	*008										8	2	7	9	13	5	11		
	*009										38	8	37	46	63	25	53		
	*010										30	6	30	37	50	20	42		
	*011										15	3	15	18.5	25	10	21		
	*012										36	8	35	44	59	23	50		
	*014										1	0	1	1	1	0	1		
	*020										50	11	48	61	77	33	66		
	*021										24	2	25	25	44	17	39		
	*023										46	9	45	58	74	31	67		
	*024										14.5	3	14.5	18	24.5	9.5	20.5		
*025										21	4	20	25	34	14	29			
*026										0	0	0	0	0	0	0			
*035										15	3	15	18.5	25	10	21			
*036										39	9	38	47	65	25	53			

Supplemental Figure1. Scoring matrices for calculating number of interactions (inset box) and interaction scores for centromeric and telomeric KIR.

Cen	Tel	Centromeric (Cen)							Telomeric (Tel)							N			
		3DL3	2DS2	2DL2	2DL3	2DLSB	2DS3/5	2DP1	2DL1	3DP1	2DL4	3DL1	3DS1	2DL5A	2DS3/5		2DS1	2DS4	3DL2
A/A	A/A	2			2			2	2	2	2	2					2	2	294
	DEL7	1			2			2	2	2	2	2					2	2	1
	DEL16	2			2			2	2	2	2	2					1	1	2
A/A	A/B	2			2			2	2	2	2	1	1	1	1	1	1	2	103
	DEL1	2			2			2	1	1	1	1	1	1	1	1	1	2	6
	DEL17	2			2			2	2	2	2	1	1	1	1	1	1	2	1
	DUP2	2			2			3	3	3	3	1	2	2	2	1	1	2	7
	DUP3	2			2			2	2	3	3	1	2	1	1	1	1	2	3
A/A	B/B	2			2			2	2	2	2		2	2	2	2		2	8
	DUP4	2			2			3	3	3	3		3	3	3	2		2	1
A/B01	A/A	2	1	1	1	1	1	2	2	2	2	2	2				2	2	56
	DEL8	2	1	1	1	1	1	2	2	2	2	2	2				2	2	2
A/B01	A/B	2	1	1	1	1	1	2	2	2	2	1	1	1	1	1	1	2	59
	DEL10	2	1	1	1	1	1	2	2	2	2	1	1	1	1	1	1	2	1
	DEL11	2	1	1	1	1	1	2	2	2	2	1	1	1	1	1	1	2	1
	DUP5	2	1	1	1	1	1	2	2	3	3	3	2	1			2	2	1
A/B01	B/B	2	1	1	1	1	1	2	2	2	2		2	2	2	2		2	9
A/B02	A/A	2	1	1	1			1	1	2	2	2	2				2	2	130
	DEL9	2	1	1	1			2	2	2	2	2	2				2	2	3
A/B02	A/B	2	1	1	1			1	1	2	2	1	1	1	1	1	1	2	65
	DEL2	2	1	1	1		1	1	1	1	1	1	1	1	1	1	1	2	1
	DEL3	2	1	1	1		1	1	1	1	1	1	1	1	1	1	1	2	1
	DEL4	2	1	1	1		1	1	1	1	1	1	1	1	1	1	1	2	10
	DUP6	2	1	1	1		1	1	1	3	3	2	1	1	1	1	2	2	1
	DUP7	2	1	1	1		1	2	2	3	3	2	1	1	1	1	2	2	9
	DUP8	2	1	1	1		1	1	1	3	3	1	2	1	1	1	1	2	1
	DUP9	2	1	1	1		1	2	2	3	3	1	2	2	2	1	1	2	2
A/B02	B/B	2	1	1	1			1	1	2	2		2	2	2	2		2	7
	DEL5	2	1	1	1		1	1	1	1	1		1	1	2	2		2	1
B01/B01	A/A	2	2	2				2	2	2	2	2	2				2	2	8
	DEL12	2	2	1				1	1	2	2	2	2				2	2	1
	DEL13	2	1	2				2	2	2	2	2	2				2	2	1
B01/B01	A/B	2	2	2				2	2	2	2	2	1	1	1	1	1	2	5
B01/B01	B/B	2	2	2				2	2	2	2	2	2	2	2	2		2	1
	DEL14	2	2	1				1	1	2	2	2	2	2	2	2		2	1
B01/B02	A/A	2	2	2				1	1	1	1	2	2	2			2	2	13
B01/B02	A/B	2	2	2				1	1	1	1	2	2	1	1	1	1	2	23
	DEL15	2	2	1				1	1	2	2	1	1	1	1	1	1	2	2
	DUP1	2	2	2				1	1	3	3	2	1	1	1	1	2	2	3
	DUP10	2	2	2				1	1	2	2	3	1	2	2	2	1	1	2
B01/B02	B/B	2	2	2				1	1	1	1	2	2	2	2	2		2	6
B02/B02	A/A	2	2	2						2	2	2					2	2	25
B02/B02	A/B	2	2	2						2	2	1	1	1	1	1	1	2	9
	DEL6	2	2	2		1		1	1	1	1	1	1	1	1	1	1	2	2
	DUP11	2	2	2				3	3	3	3	1	2	2	2	1	1	2	2
B02/B02	B/B	2	2	2						2	2		2	2	2	2		2	0

Supplemental Figure 2. This figure shows the genotypes of the cohort. Those that diverged from those predicted by the common structural types shown in Figure 2A are indicated as 'DEL' for deletion and 'DUP' for duplication. Gene presence is indicated by a shaded square and the number indicates the copy number of the gene. Black squares match the assigned genotype for the final analyses. Gray squares indicate genes with copy numbers different from expected. N are the number of observations of that genotype in the dataset. The individual genotypes are grouped with the genotype that they were assigned for the analyses.

CONTINUOUS

Factor	Level	Count	HRatio	HR Low	HR Up	Pvalue
Cen genotype v1	*overall	857	0.73	0.71	0.87	<0.001
Cen genotype v2	*overall	857	0.78	0.71	0.87	<0.001
B segment count	*overall	857	0.78	0.69	0.88	0.0001
Inhibitory interactions (D:R)	*overall	853	1.01	0.94	1.09	0.7607
Inhibitory interactions (D:D)	*overall	849	1.01	0.94	1.08	0.8315
Cen interaction score (D:R)	*overall	857	1	1	1	0.3275
Avg. Cen interaction score (D:R)	*overall	857	0.99	0.97	1.01	0.3667
Tel interaction score (D:R)	*overall	857	1	1	1	0.549
Avg. Tel interaction score (D:R)	*overall	857	0.99	0.98	1	0.1534
Total interaction score (D:R)	*overall	857	1	1	1	0.966
Avg. Total interaction score (D:R)	*overall	857	0.98	0.96	1	0.1104
Cen interaction score (D:D)	*overall	857	1	1	1.01	0.2091
Avg. Cen interaction score (D:D)	*overall	857	0.99	0.97	1.02	0.5206
Tel interaction score (D:D)	*overall	857	1	1	1	0.4636
Avg. Tel interaction score (D:D)	*overall	857	0.99	0.98	1	0.1146
Total interaction score (D:D)	*overall	857	1	1	1	0.923
Avg. Total interaction score (D:D)	*overall	857	0.98	0.96	1	0.1045

CATEGORICAL

Factor	Level	COUNT	HRatio	HR Low	HR Up	Pvalue
Cen genotype v1	*overall					0.0009
	A/A	408	1			
	A/B01	125	1	0.72	1.41	0.98
	A/B02	222	0.77	0.58	1.04	0.0891
	B01/B01	17	0.29	0.07	1.18	0.0832
	B01/B02	45	0.23	0.09	0.56	0.0012
	B02/B02	40	0.23	0.07	0.73	0.0122
Cen genotype v2	*overall					0.0003
	A/A	408	1			
	A/B01	125	1	0.72	1.41	0.9807
	A/B02	222	0.77	0.58	1.04	0.0892
	B01/Bx	62	0.24	0.11	0.52	0.0003
	B02/B02	40	0.23	0.07	0.73	0.0122
	Tel genotype	*overall				
A/A		516	1			
A/B		309	0.77	0.59	0.99	0.0448
B/B		32	0.7	0.34	1.42	0.3214
2DS4 expressed	*overall					0.7647
	expressed	521	1			
absent	336	1.04	0.81	1.34	0.7647	
3DL1 expressed	*overall					0.7134
	expressed	105	1			
	absent	752	0.93	0.65	1.34	0.7134
B segment count v1	*overall					0.0015
	0	284	1			
	1	292	1.01	0.77	1.33	0.9443
	2	195	0.53	0.37	0.77	0.0007
	3	71	0.55	0.33	0.93	0.0246
4	15	0	0	2.20E+247	0.9645	
B segment count v2	*overall					0.0001
	0	284	1			
	1	292	1.01	0.77	1.33	0.946
	2	195	0.53	0.37	0.77	0.0007
	< 3	86	0.46	0.27	0.77	0.0029
3DL1:Bw4(recipient)	*overall					0.6655
	none	418	1			
	weak	226	0.94	0.7	1.26	0.6587
	strong	213	1.09	0.82	1.46	0.5593
3DL1:Bw4(donor)	*overall					0.6584
	none	411	1			
	weak	238	0.96	0.72	1.28	0.7755
	strong	208	1.11	0.83	1.49	0.4778
Inhibitory interactions (D:R) donor KIR: recipient HLA	*overall					0.6154
	10	53	0.83	0.45	1.54	0.5551
	4	156	1			
	5	102	0.81	0.5	1.33	0.4089
	6	262	1.22	0.85	1.74	0.2816
	7	88	1.09	0.68	1.74	0.7163
	8	164	1.14	0.77	1.69	0.5194
	9	28	1.16	0.56	2.38	0.6946

CATEGORICAL (continued)

Factor	Level	COUNT	HRatio	HR Low	HR Up	Pvalue
Activating interactions (D:R) v1 donor KIR: recipient HLA	*overall					0.6701
	0	502	1			
	1	193	1.19	0.9	1.59	0.2243
	2	123	0.95	0.66	1.37	0.7938
	3	16	0.98	0.31	3.12	0.9787
4	20	0.72	0.26	1.95	0.5144	
Activating interactions (D:R) v2 donor KIR: recipient HLA	*overall					0.5442
	0	502	1			
1 or more	355	1.08	0.84	1.38	0.5442	
Inhibitory interactions (D:D) donor KIR: donor HLA	*overall					0.171
	10	46	0.59	0.28	1.26	0.173
	4	159	1			
	5	107	0.87	0.53	1.42	0.5783
	6	254	1.27	0.88	1.82	0.1987
	7	90	1.44	0.92	2.25	0.1078
	8	165	1.17	0.78	1.74	0.4481
	9	28	1.35	0.67	2.7	0.4008
	Activating interactions (D:D) v1 donor KIR: donor HLA	*overall				
0		491	1			
1		207	1.34	1.01	1.77	0.0415
2		125	0.93	0.65	1.35	0.7106
3		16	1.12	0.41	3.04	0.82
4	15	0.67	0.21	2.12	0.4934	
Activating interactions (D:D) v2 donor KIR: donor HLA	*overall					0.2554
	0	491	1			
1 or more	366	1.15	0.9	1.47	0.2554	
Cen interaction score (D:R) donor KIR: recipient HLA tertiles	*overall					0.4526
	0	271	1			
	1	296	0.83	0.61	1.12	0.2215
2	290	0.94	0.7	1.27	0.704	
Avg. Cen interaction score (D:R) donor KIR: recipient HLA tertiles	*overall					0.2547
	0	285	1			
	1	284	0.79	0.59	1.06	0.1098
2	288	0.85	0.63	1.14	0.2664	
Tel interaction score (D:R) donor KIR: recipient HLA tertiles	*overall					0.6839
	0	286	1			
	1	286	0.88	0.66	1.18	0.3912
2	285	0.96	0.71	1.29	0.7809	
Avg. TelInteraction score (D:R) donor KIR: recipient HLA tertiles	*overall					0.3365
	0	287	1			
	1	284	0.88	0.66	1.17	0.3809
2	286	0.8	0.59	1.08	0.1453	
Total interaction score (D:R) donor KIR: recipient HLA tertiles	*overall					0.5445
	0	287	1			
	1	284	0.85	0.63	1.16	0.3129
2	286	0.99	0.74	1.32	0.9209	
Avg. Total interaction score (D:R) donor KIR: recipient HLA tertiles	*overall					0.7497
	0	287	1			
	1	287	0.98	0.73	1.32	0.8835
2	283	0.9	0.67	1.2	0.4703	
Cen interaction score (D:D) donor KIR: donor HLA tertiles	*overall					0.5967
	0	281	1			
	1	293	0.87	0.65	1.18	0.3677
2	283	0.99	0.74	1.33	0.9537	
Avg. Cen interaction score (D:D) donor KIR: donor HLA tertiles	*overall					0.6677
	0	284	1			
	1	284	0.89	0.67	1.19	0.4311
2	289	0.89	0.66	1.2	0.4504	
Tel interaction score (D:D) donor KIR: donor HLA tertiles	*overall					0.7427
	0	277	1			
	1	297	0.9	0.67	1.21	0.4824
2	283	0.99	0.73	1.33	0.9371	
Avg. Tel interaction score (D:D) donor KIR: donor HLA tertiles	*overall					0.5458
	0	278	1			
	1	296	0.9	0.67	1.21	0.4949
2	283	0.85	0.63	1.14	0.2785	
Total interaction score (D:D) donor KIR: donor HLA tertiles	*overall					0.8315
	0	289	1			
	1	283	0.91	0.68	1.23	0.5438
2	285	0.96	0.71	1.29	0.7833	
Avg. Total interaction score (D:D) donor KIR: donor HLA tertiles	*overall					0.375
	0	289	1			
	1	287	0.81	0.6	1.09	0.1643
2	281	0.89	0.66	1.19	0.4318	

Supplemental Figure 4. Results of statistical analyses with the endpoint of relapse. Significant overall results are highlighted in gold. The telomeric, centromeric and total interaction scores were analyzed as both continuous variables and discretized into tertiles and analyzed as categorical variables.