A

Mutli-Lineage Chimerism

% Donor Chimerism
H2^k/H2^b x H2^d/H2^b

B cells   T cells   Granulocytes

Conditioning:	● PBS (n=5) ■ 4Ab (n=5)
Cell Dose:	30x10^6
Cell Type:	WBM

B

HSC Chimerism

% Donor Chimerism
H2^k/H2^b x H2^d/H2^b

Conditioning:	PBS 4Ab
Cell Dose:	30x10^6
Cell Type:	WBM

C

Granulocyte Chimerism

% Donor Chimerism
H2^k/H2^b x H2^d/H2^b

ns

**

Conditioning:	αKIT αCD47	αKIT αCD47 αCD40L	αKIT αCD47 αCD122	4Ab
Cell Dose:	30x10^6
Cell Type:	WBM

D

Granulocyte Chimerism

% Donor Chimerism
H2^k/H2^b x H2^d/H2^b

*

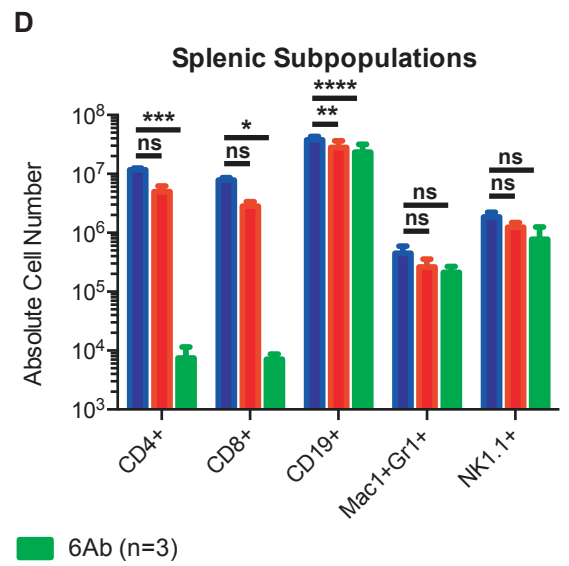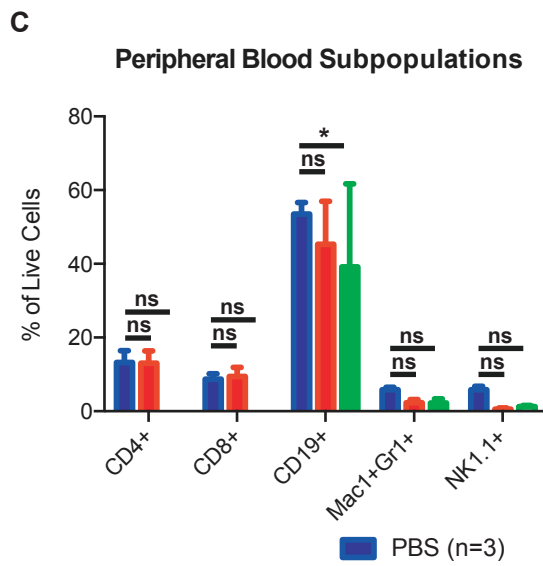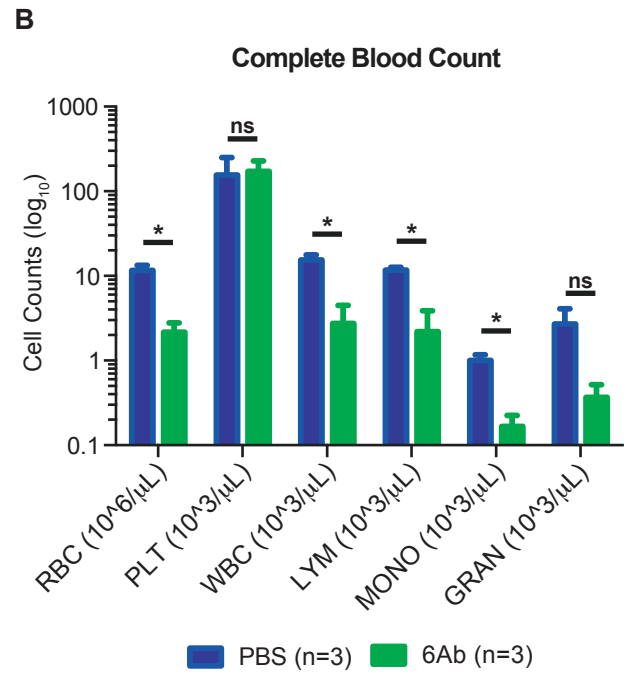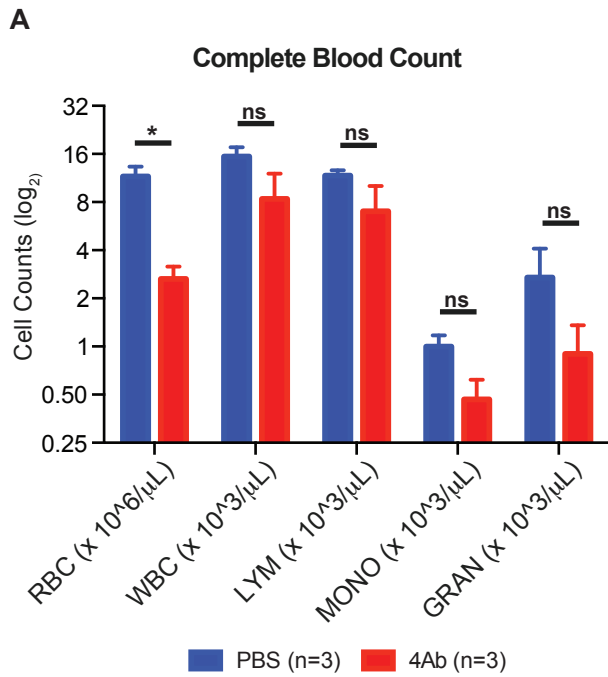| Antibodies witheld from 6Ab regimen: | αCD40L | αCD122 | αCD40L αCD122 | αCD4 | αCD8 | None Withheld |
| Cell Dose: | 9x10^3 |
| Cell Type: | LSK |

Figure S1, related to Figures 1 and 2: Peripheral blood and HSC chimerism following antibody conditioning

(a) Peripheral blood donor chimerism in the T cell, B cell, and granulocyte lineages 16 weeks following haploidentical WBM transplant (n=5). (b) Twenty-eight-week haploidentical donor chimerism in the long-term HSC compartment (Lin- KIT+ Sca1+ CD150+ CD34-) following PBS or Ab conditioning (n=5). (c) Donor granulocyte chimerism after haploidentical transplantation at 8-9 weeks following conditioning with permutations of 4Ab (pooled data from two replicate experiments, pooled n=7-9). (d) Donor granulocyte chimerism following exclusion of individual components of the 6Ab cocktail at 16 weeks in haploidentical transplantation (pooled data from two replicate experiments, pooled n=8-10). Data and error bars in (a-d) represent means ± SD; (a), (c), (d) one way ANOVA reveals *P≤0.05, **P≤0.01, ***P≤0.001, and ****P≤0.0001, (b) unpaired t-test reveals P≤0.01

A

Complete Blood Count

Cell Counts (log$_2$) vs RBC (x 10^6/µL), WBC (x 10^3/µL), LYM (x 10^3/µL), MONO (x 10^3/µL), GRAN (x 10^3/µL)

* ns ns ns ns

PBS (n=3)   4Ab (n=3)

B

Complete Blood Count

Cell Counts (log$_{10}$) vs RBC (10^6/µL), PLT (10^3/µL), WBC (10^3/µL), LYM (10^3/µL), MONO (10^3/µL), GRAN (10^3/µL)

ns * * * * ns

PBS (n=3)   6Ab (n=3)

C

Peripheral Blood Subpopulations

% of Live Cells vs CD4+, CD8+, CD19+, Mac1+Gr1+, NK1.1+

ns ns * ns ns

PBS (n=3)   4Ab (n=3)   6Ab (n=3)

D

Splenic Subpopulations

Absolute Cell Number vs CD4+, CD8+, CD19+, Mac1+Gr1+, NK1.1+

*** ns * ns **** ** ns ns ns ns

E

Overall Survival following Transplant

Percent survival vs Days

P=0.0001

WBM Only
4Ab + WBM
6Ab + LSK
WBM + Irradiation
LSK + Irradiation

Figure S2, related to Figures 1 and 2: Immunodepletion following antibody conditioning and survival following major mismatch transplant

(a-b) CBC following conditioning on Day 0 of the (a) 4Ab and (b) 6Ab conditioning protocol (n=3). (c-d) (c) Peripheral blood subpopulations and (d) splenic subpopulations from animals on Day 0 of the PBS, 4Ab, and 6Ab conditioning protocol (n=3). (e) Overall survival of animals transplanted with either LSK or WBM from fully MHC-mismatched donors using either antibody conditioning or irradiation (n=5). Data and error bars in (a-d) represent means ± SD; (a-b) multiple t-tests reveal *P≤0.05, (b-c) two way ANOVA was performed where *P≤0.05, **P≤0.01, ***P≤0.001 and ****P≤0.0001, (d) log-rank (Mantel-Cox) test yielded P = 0.0001.

Supplemental Table 1, related to Figures 1, 2, S1 and S2. All donor and recipient mice were female unless otherwise noted (*indicates male recipients were used, ** indicates male and female recipients were used).

Donor	Recipient	Mismatch	Conditioning Used	Cell Type	Cell Dose	Number Of Animals	Percentage of Animals Chimeric	Average Granulocyte Chimerism of Chimeric Animals	Timepoint (weeks)
A. Related to Figure 1C									
AKR/J x C57Bl/6 F1 (AB6F1)	Balb/c x C57Bl/6 F1 (CB6F1)	Haploidentical	anti-KIT anti-CD47 anti-CD40L	Whole Bone Marrow	30e6	10	90.00	79.39	14-16
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L	Whole Bone Marrow	3e6	10	30.00	32.20	14-16
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122	Whole Bone Marrow	30e6	5	100.00	76.88	14-16
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122	Whole Bone Marrow	3e6	10	90.00	27.38	14-16
B. Related to Figure 1D									
AB6F1	CB6F1	Haploidentical	Irradiation	Whole Bone Marrow	3e6	5	100.00	99.98	16
AB6F1	CB6F1	Haploidentical	Irradiation	Lin- KIT+ Sca-1+	9e3	5	100.00	99.96	16
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122	Whole Bone Marrow	3e6	5	80.00	19.05	16
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122	Lin- KIT+ Sca-1+	9e3	5	0.00	0.00	16
C. Related to Figure 1E, 2B									
AB6F1	CB6F1	Haploidentical	Irradiation	Lin- KIT+ Sca-1+	9e3	5	100.00	0.00	8
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122	Lin- KIT+ Sca-1+	9e3	10	10.00	1.56	8
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122 anti-CD4 anti-CD8	Lin- KIT+ Sca-1+	9e3	10	90.00	32.89	8
D. Related to Figure 1G									
DBA/1J	CB6F1	Full	Unconditioned	Whole Bone Marrow	3e6	5	0.00	0.00	8
DBA/1J	CB6F1	Full	anti-KIT anti-CD47 anti-CD40L anti-CD122 anti-CD4 anti-CD8	Whole Bone Marrow	3e6	5	40.00	3.65	8
DBA/1J	CB6F1	Full	anti-KIT anti-CD47 anti-CD40L anti-CD122 anti-CD4 anti-CD8	Lin- KIT+ Sca-1+	9e3	5	100.00	52.40	8
DBA/1J	CB6F1	Full	Irradiation	Whole Bone Marrow	3e6	5	100.00	98	8

DBA/1J	CB6F1	Full	Irradiation	Lin-KIT+Sca-1+	9e3	5	100.00	96.80	8

E. Related to Figure 2A, S1C

AB6F1	CB6F1*	Haploidentical	PBS	Whole Bone Marrow	30e6	2	0.00	0.00	8-9
AB6F1	CB6F1*	Haploidentical	anti-CD122	Whole Bone Marrow	30e6	3	0.00	0.00	8-9
AB6F1	CB6F1*	Haploidentical	anti-CD40L	Whole Bone Marrow	30e6	3	0.00	0.00	8-9
AB6F1	CB6F1*	Haploidentical	anti-KIT	Whole Bone Marrow	30e6	3	0.00	0.00	8-9
AB6F1	CB6F1*	Haploidentical	anti-CD47	Whole Bone Marrow	30e6	2	0.00	0.00	8-9
AB6F1	CB6F1**	Haploidentical	anti-KIT anti-CD47	Whole Bone Marrow	30e6	7	0.00	0.00	8-9
AB6F1	CB6F1**	Haploidentical	anti-KIT anti-CD47 anti-CD40L	Whole Bone Marrow	30e6	9	55.56	59.82	8-9
AB6F1	CB6F1**	Haploidentical	anti-KIT anti-CD47 anti-CD122	Whole Bone Marrow	30e6	9	11.11	63.40	8-9
AB6F1	CB6F1**	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122	Whole Bone Marrow	30e6	9	100.00	56.09	8-9

F. Related to Figure S1A-B

AB6F1	CB6F1*	Haploidentical	PBS	Whole Bone Marrow	30e6	5	0	0.00	16/28
AB6F1	CB6F1*	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122	Whole Bone Marrow	30e6	5	5	87.78	16/28

G. Related to Figure S1D

AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD122 anti-CD4 anti-CD8	Lin-KIT+Sca-1+	9e3	10	40.00	40.78	16
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD4 anti-CD8	Lin-KIT+Sca-1+	9e3	10	70.00	35.07	16
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD4 anti-CD8	Lin-KIT+Sca-1+	9e3	10	10.00	62.3	16
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122 anti-CD8	Lin-KIT+Sca-1+	9e3	8	62.50	18.16	16
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122 anti-CD4	Lin-KIT+Sca-1+	9e3	9	55.56	11.41	16
AB6F1	CB6F1	Haploidentical	anti-KIT anti-CD47 anti-CD40L anti-CD122 anti-CD4 anti-CD8	Lin-KIT+Sca-1+	9e3	9	88.89	36.84	16