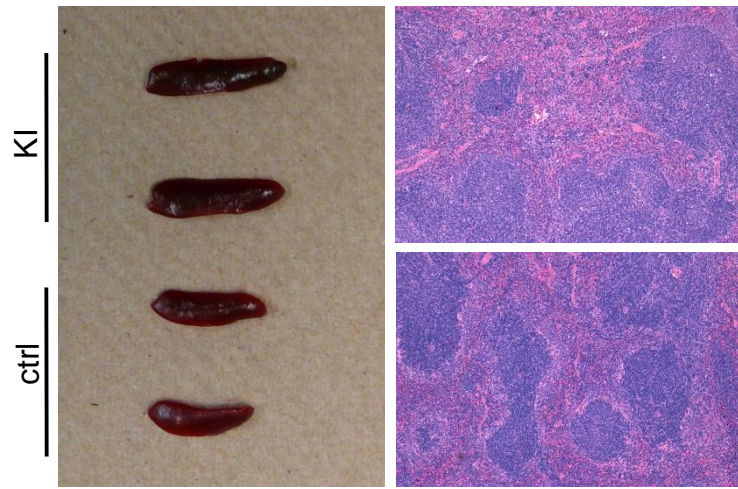
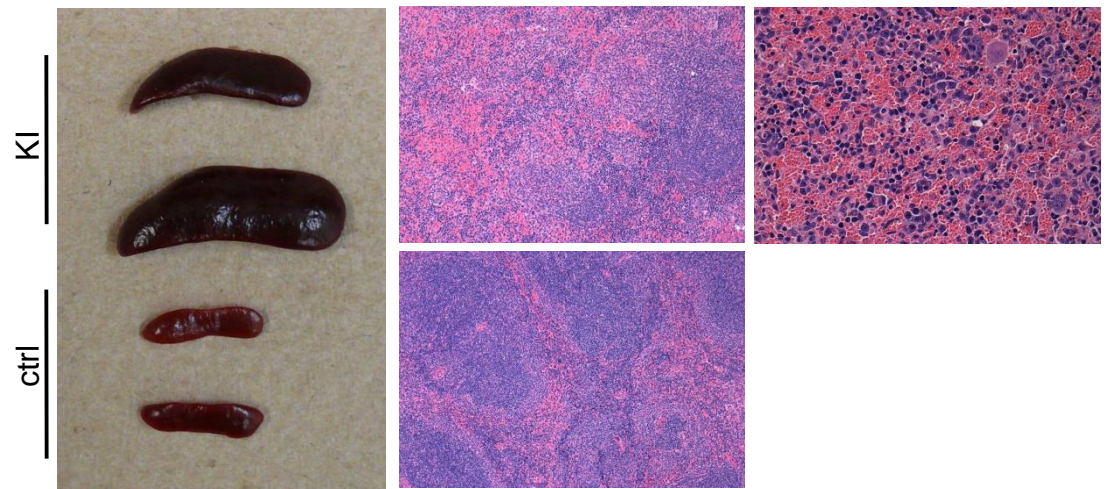


a young mice



50x

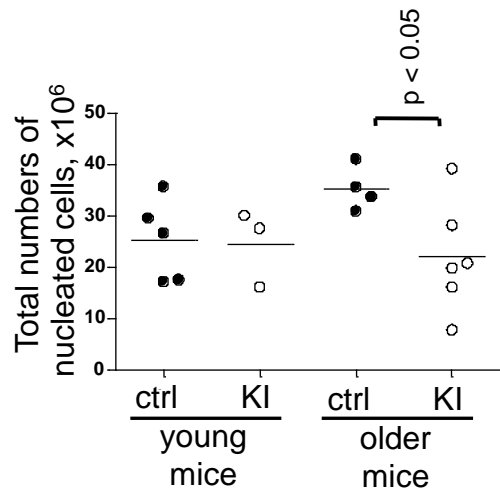
b older mice



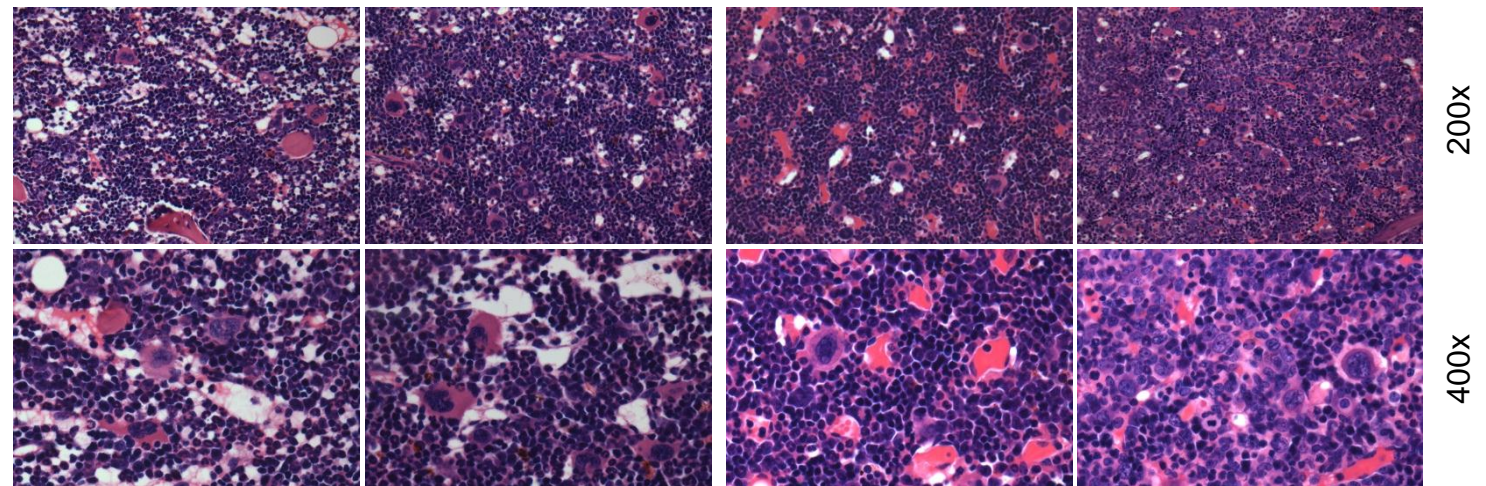
50x

200x

c bone marrow



d bone marrow



ctrl - 16 weeks

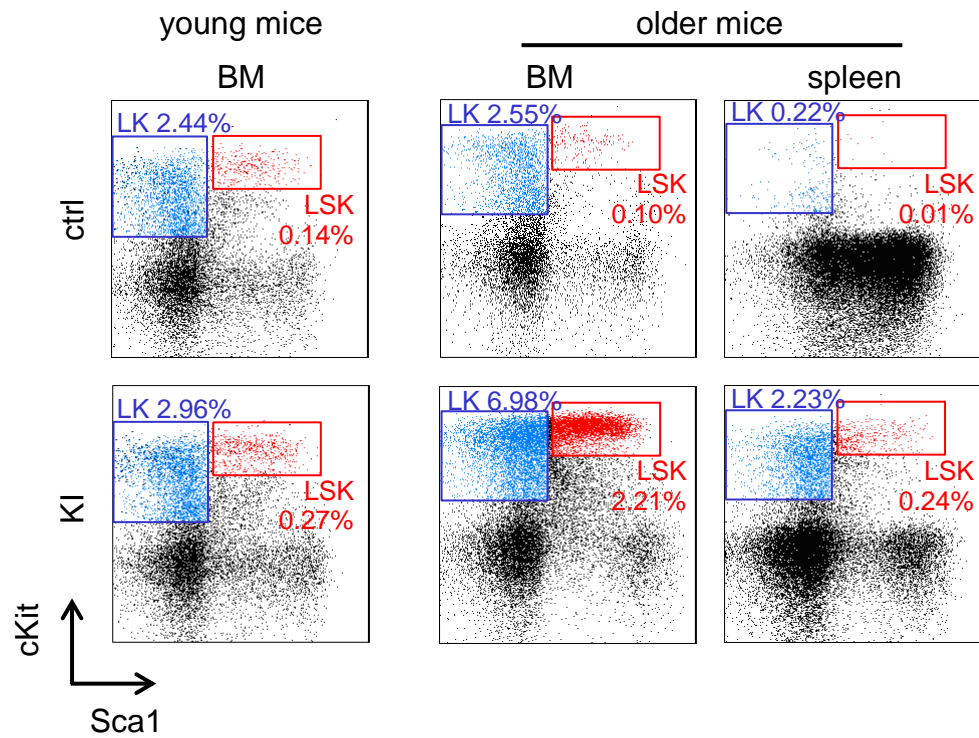
KI - 16 weeks

ctrl - 46 weeks

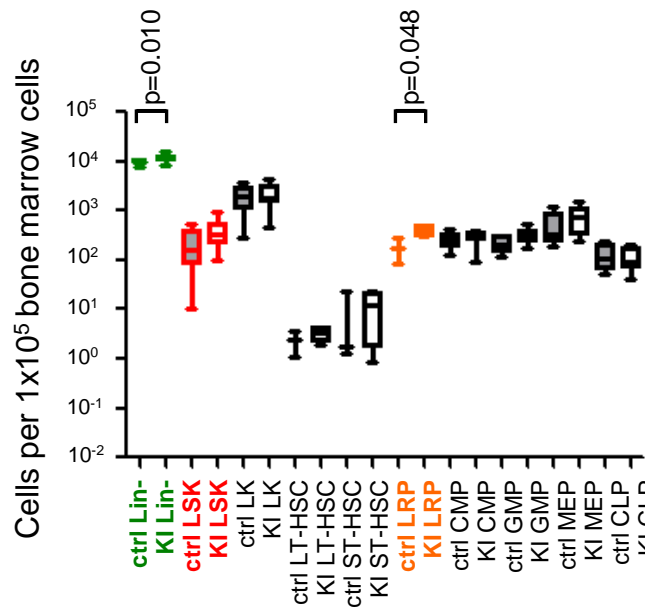
KI - 46 weeks

Figure 1 |

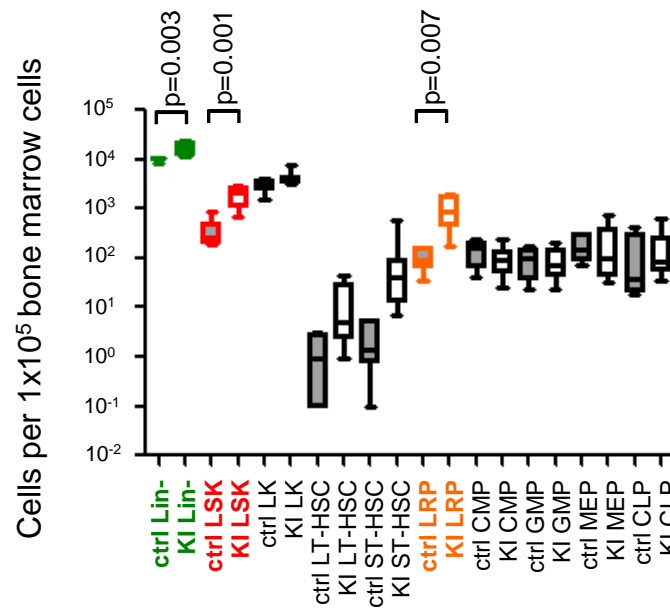
a Gated on live lineage-negative cells



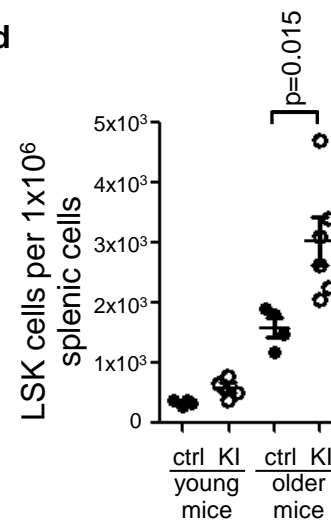
b young mice



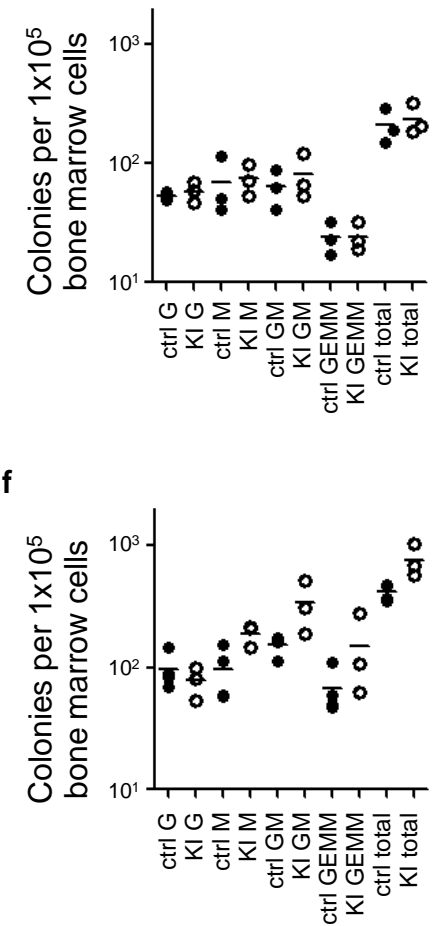
c older mice



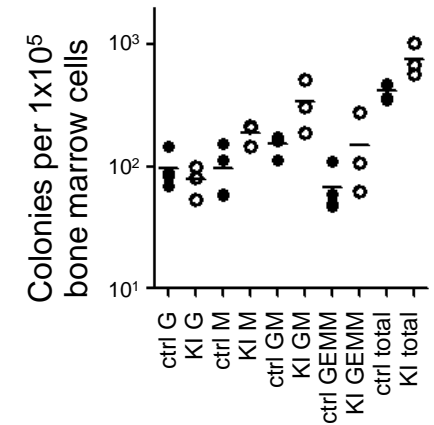
d



e



f



g

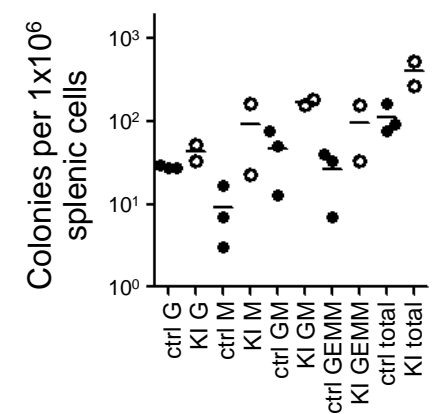


Figure 2

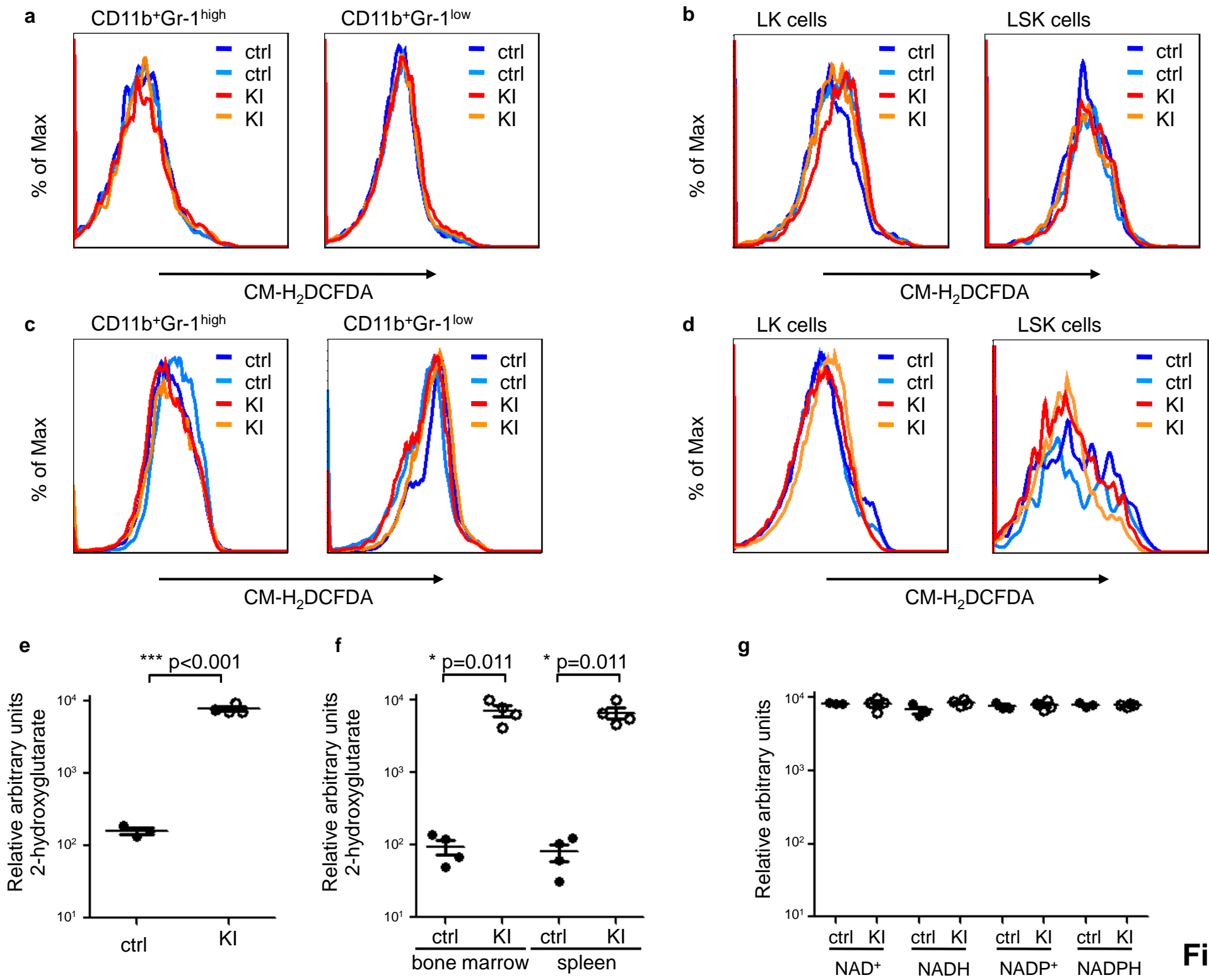


Figure 3

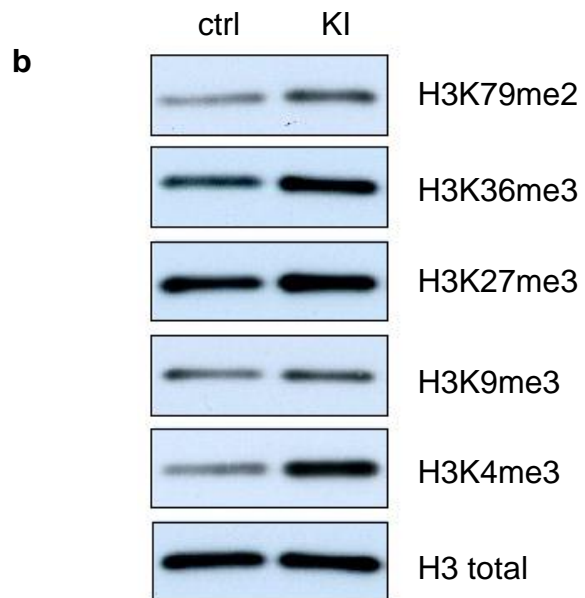
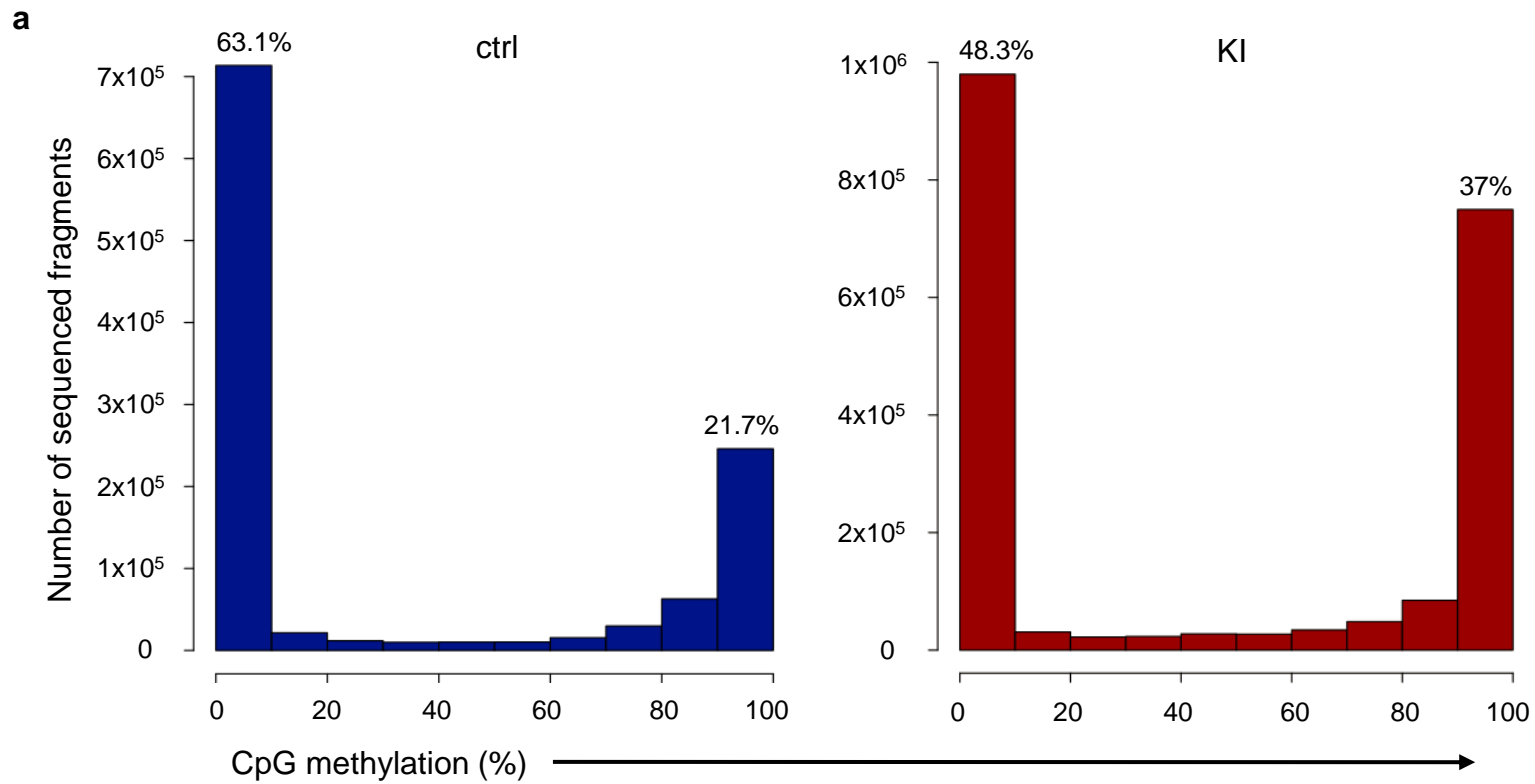
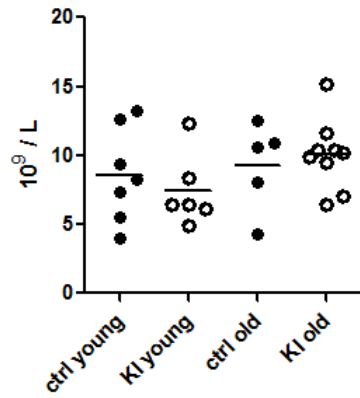
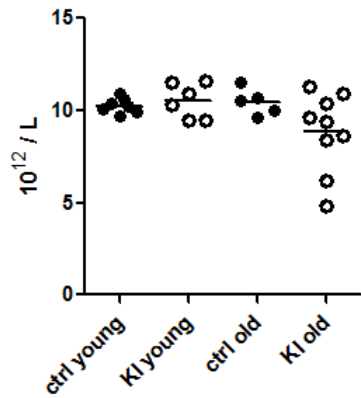
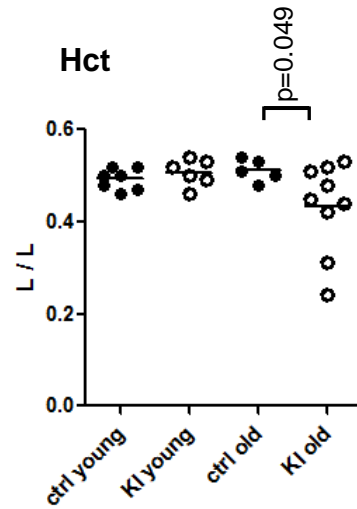
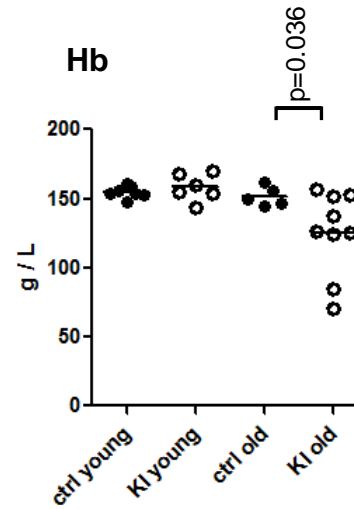
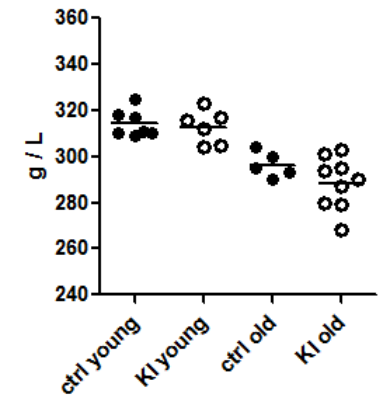
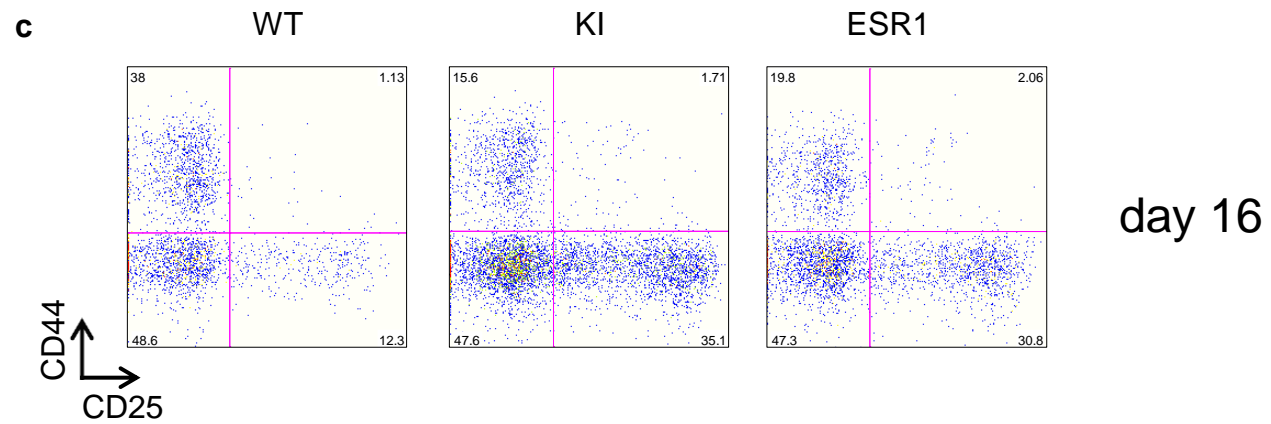
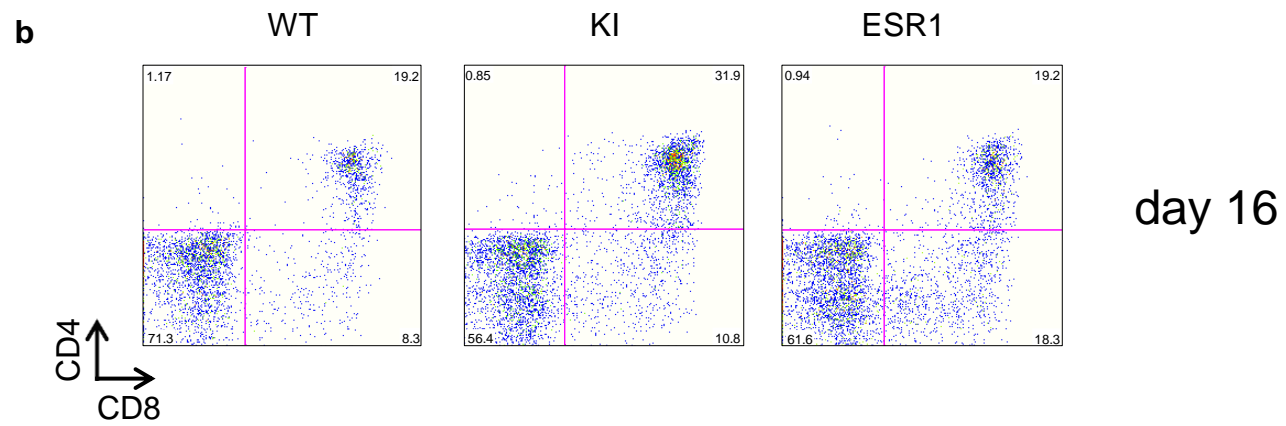
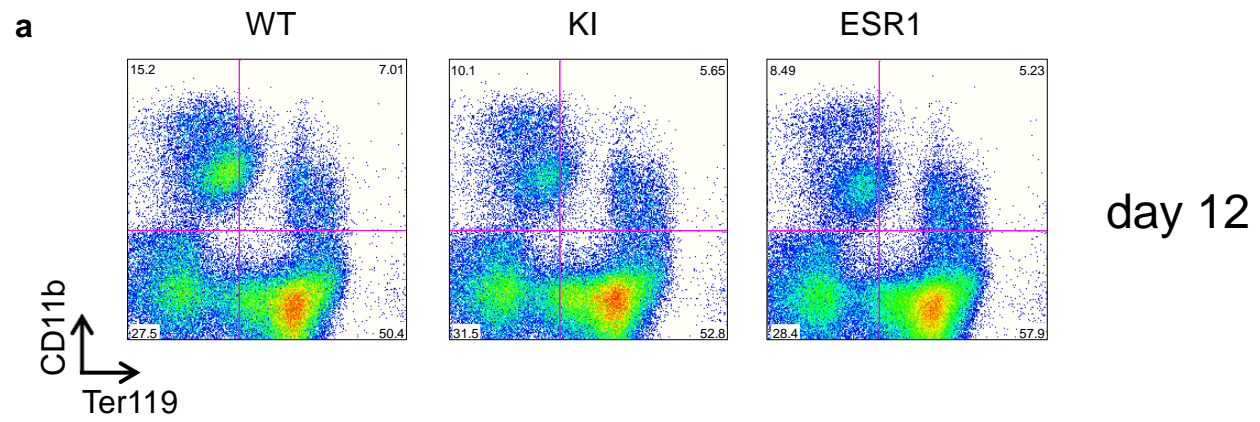
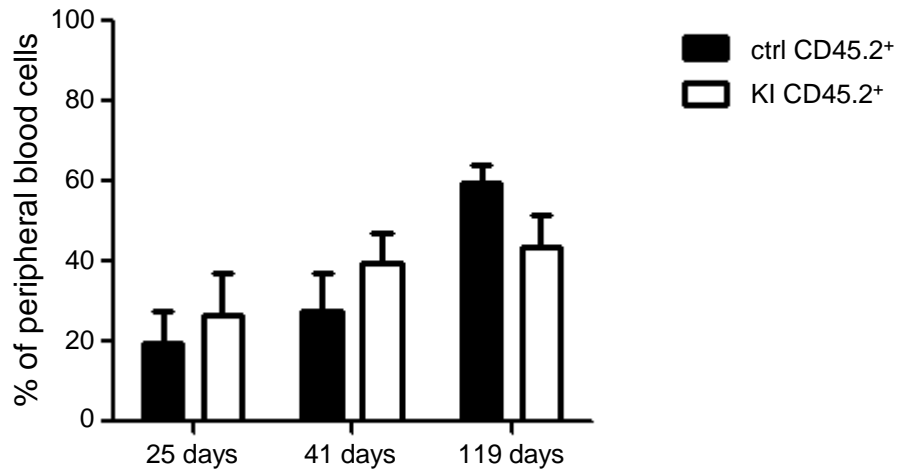
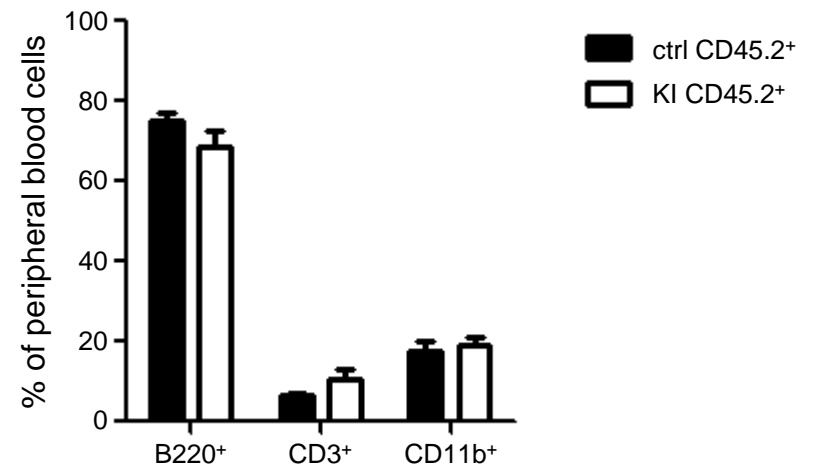


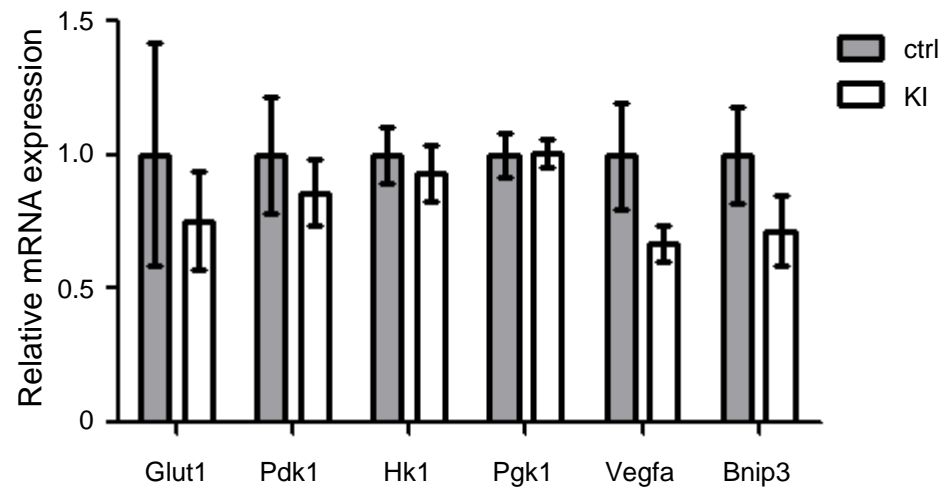
Figure 4

a **WBC****b** **RBC****c** **Hct****d** **Hb****e** **MCHC****f**

	Young mice (7-16 weeks)					Older mice (42-46 weeks)				
	WT Mean \pm SEM	N =	KI Mean \pm SEM	N =	p-value	WT Mean \pm SEM	N =	KI Mean \pm SEM	N =	p-value
WBC	8.600 \pm 1.295	7	7.400 \pm 1.076	6	0.4924	9.260 \pm 1.435	5	10.07 \pm 0.851	9	0.6458
RBC	10.26 \pm 0.156	7	10.55 \pm 0.383	6	0.5050	10.46 \pm 0.323	5	8.844 \pm 0.718	9	0.0674
Hct	0.493 \pm 0.009	7	0.507 \pm 0.012	6	0.3803	0.512 \pm 0.011	5	0.433 \pm 0.033	9	0.0491*
Hb	154.9 \pm 1.710	7	158.3 \pm 4.072	6	0.4612	151.6 \pm 3.311	5	125.3 \pm 10.13	9	0.0359*
MCHC	314.3 \pm 2.244	7	312.8 \pm 3.005	6	0.7075	296.4 \pm 2.502	5	286.3 \pm 4.308	9	0.1112



a**b**

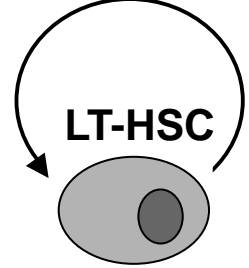




LysMCre-
R132H-IDH1-KI

- Elevated 2HG levels
- ↳ Changes in histone methylation
- ↳ Changes in DNA methylation

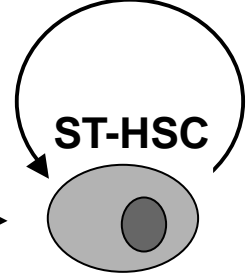
symmetric
cell division



CD150⁺
CD48⁻
LSK

asymmetric
cell division

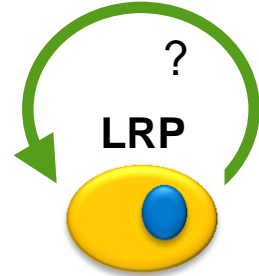
symmetric
cell division



CD150⁺
CD48⁺
LSK

asymmetric
cell division

symmetric
cell division

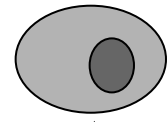
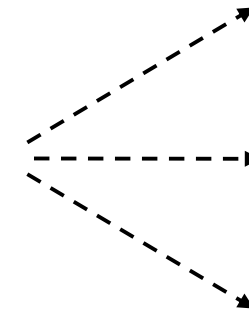


CD150⁻
CD48⁺
LSK

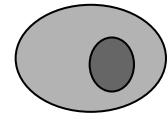


asymmetric
cell division

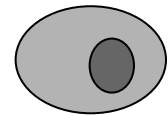
partial differentiation
block?



MEP



CMP



GMP

?

AML

second
tumorigenic
hit

	genotype				
	WT-	WT+	HET-	HET+ *	total
all	64 (23.0%)	77 (27.8%)	69 (24.8%)	68 (24.4%)	278
female	35	38	31	28	132
male	29	39	38	40	146

	Young mice (7-16 weeks)					Older mice (42-46 weeks)				
	WT Mean \pm SEM	N=	KI Mean \pm SEM	N=	p-value	WT Mean \pm SEM	N=	KI Mean \pm SEM	N=	p-value
Lin ⁻	9.85 \pm 0.23	14	11.26 \pm 0.44	14	0.0100*	10.12 \pm 0.437	6	17.19 \pm 1.612	8	0.0029**
LSK (Lin ⁻ Sca1 ⁺ cKit ⁺)	0.223 \pm 0.061	9	0.401 \pm 0.082	10	0.1003	0.360 \pm 0.102	6	1.946 \pm 0.311	8	0.0013**
LK (Lin ⁻ Sca1 ⁻ cKit ⁺)	1.987 \pm 0.366	9	2.167 \pm 0.364	10	0.7313	3.065 \pm 0.3535	6	4.329 \pm 0.529	5	0.0724
LT-HSC (CD150 ⁺ CD48 ⁻ LSK)	0.0023 \pm 0.0007	3	0.0032 \pm 0.0005	4	0.3694	0.0013 \pm 0.0006	6	0.0133 \pm 0.0061	8	0.0889
ST-HSC (CD150 ⁺ CD48 ⁺ LSK)	0.0090 \pm 0.0075	3	0.0117 \pm 0.0052	4	0.7911	0.0024 \pm 0.0009	6	0.1104 \pm 0.0719	8	0.1770
LRP (CD150 ⁻ CD48 ⁺ LSK)	0.1840 \pm 0.0594	3	0.3939 \pm 0.0450	4	0.0480*	0.1022 \pm 0.0194	6	0.9992 \pm 0.2358	8	0.0068**
CMP (CD34 ⁺ CD16/32 ^{med} LK)	0.2640 \pm 0.0480	5	0.2967 \pm 0.0429	6	0.6255	0.1417 \pm 0.0300	6	0.1009 \pm 0.0234	8	0.3090
GMP (CD34 ⁺ CD16/32 ^{high} LK)	0.2220 \pm 0.0381	5	0.3283 \pm 0.0488	6	0.1244	0.0973 \pm 0.0240	6	0.0967 \pm 0.0236	8	0.9864
MEP (CD34 ⁻ CD16/32 ^{low} LK)	0.5200 \pm 0.1820	5	0.7667 \pm 0.1880	6	0.3734	0.1790 \pm 0.0429	6	0.2104 \pm 0.0885	8	0.7566
CLP (Lin ⁻ Il7Ra ⁺ Sca1 ^{med} cKit ^{med})	0.1283 \pm 0.0308	6	0.1129 \pm 0.0238	7	0.7002	0.1263 \pm 0.0942	4	0.1695 \pm 0.0904	6	0.7504

	Forward oligonucleotide (5'→3')	Reverse oligonucleotide (5'→3')	Fragment length
Glut1	gtcaccatcttgagctgttc	cacctgccttctcgaagatg	139bp
Vegfa	catgcggatcaaacctcacca	ctggctttgttctgtctttcttg	101bp
Pgk1	ccttccttaaggtgctcaaca	gtcaacaggcaaggaatcttc	128bp
Hk1	ctgtctggacgacatcagaac	caggatgttacggacgatctc	127bp
Bnip3	cacagctactctcagcatgagaa	cagacgcctccaatgtagatc	145bp
Pdk1	ggaagatcgacagactctcaac	gaggcgtgatatgggcaatc	136bp
Hprt	ggtggagatgatctctcaactt	ccagcaagcttgcaaccttaac	142bp