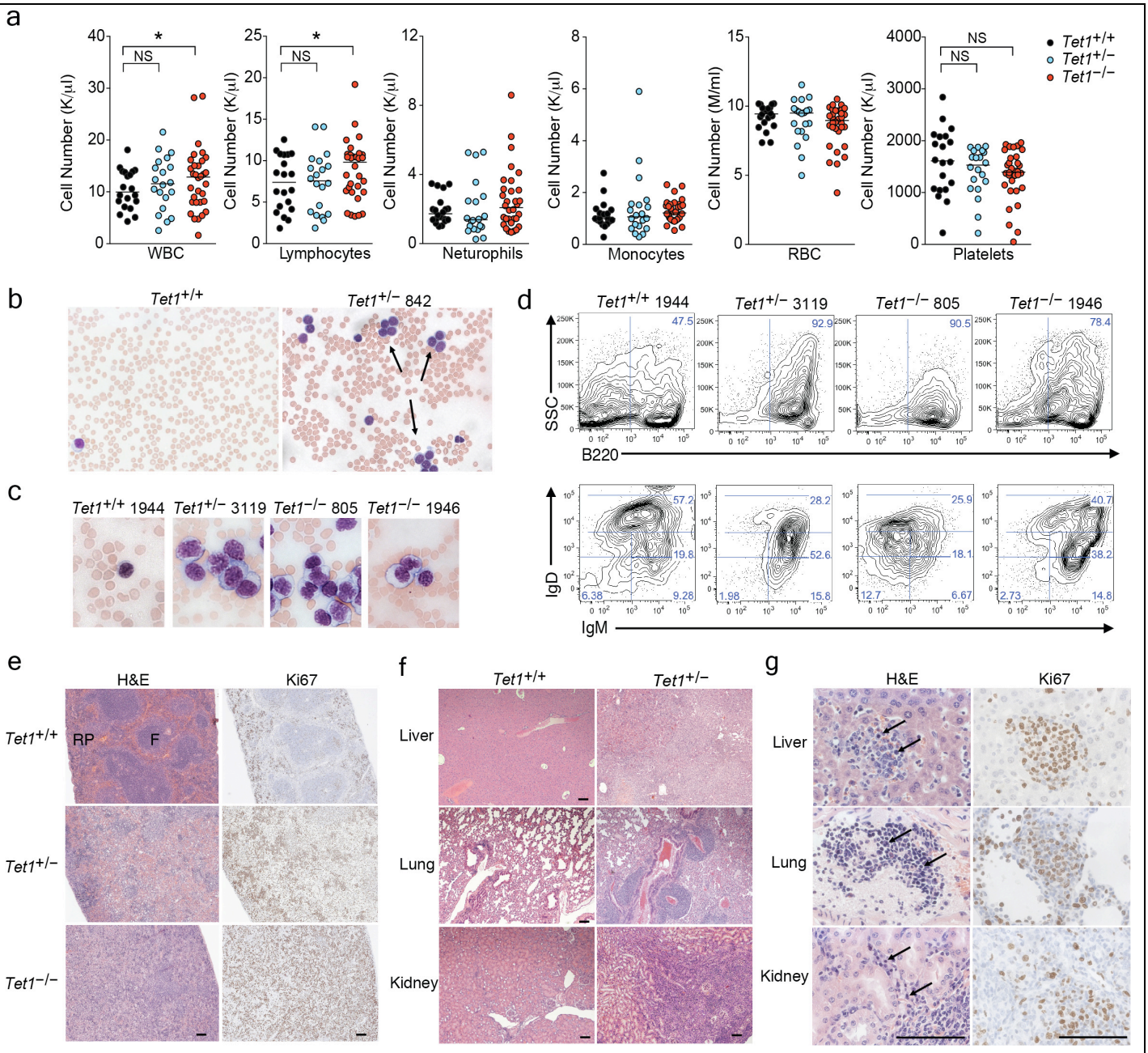
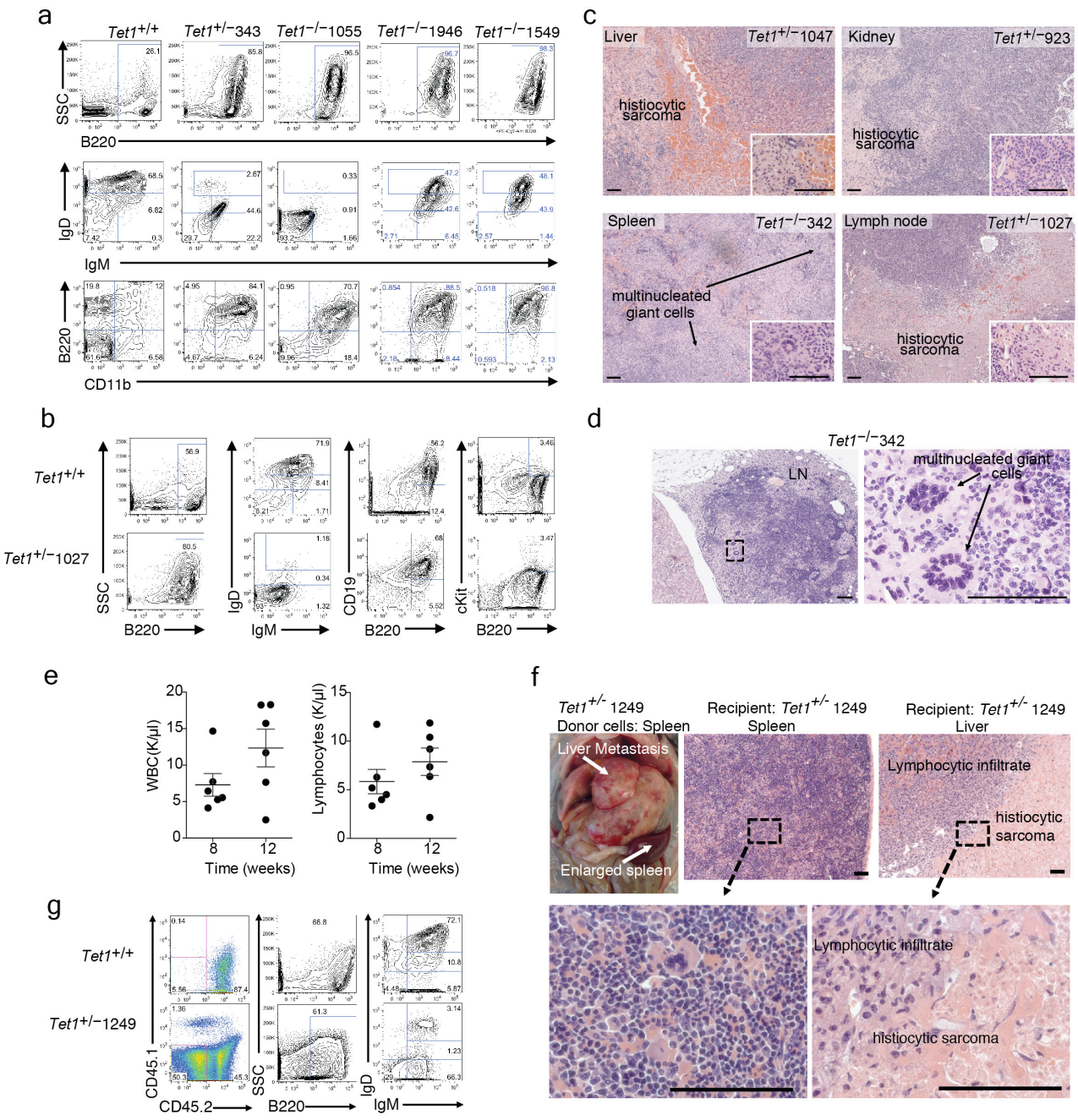


Supplementary Figure 1

Peripheral blood analysis and organ histology of sick Tet1-deficient mice.

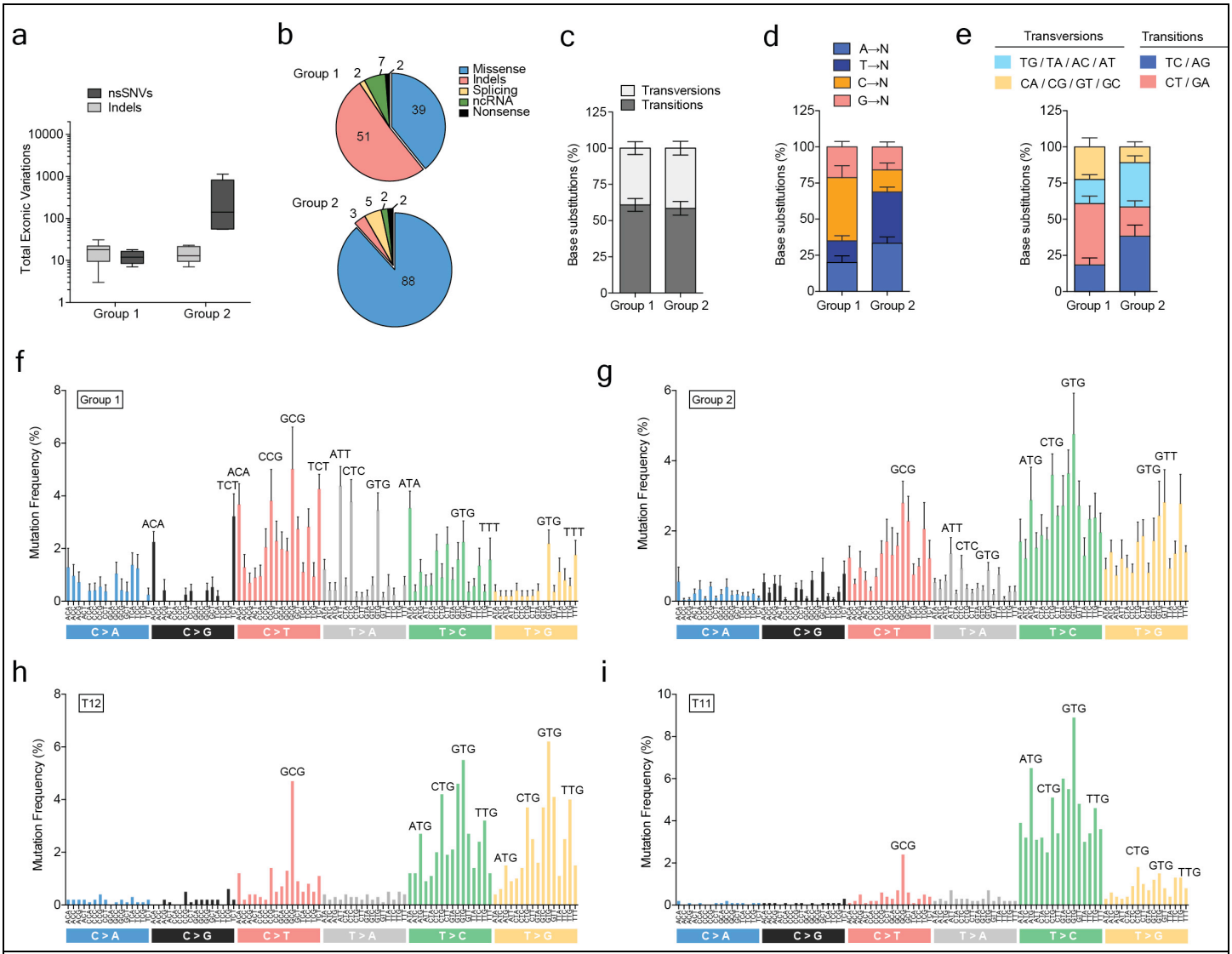
a) Hemavet quantification of whole blood cell numbers from *Tet1*$^{+/+}$, *Tet1*$^{+/-}$ and *Tet1*$^{-/-}$ mice aged 18-24 months. WBC = white blood cells, RBC = red blood cells, NS = not significant, * P = <0.05. Small horizontal lines indicate the mean; *Tet1*$^{+/+}$ (n = 20), *Tet1*$^{+/-}$ (n = 20) and *Tet1*$^{-/-}$ (n = 32). **b-c**) Peripheral blood smears stained with Wright-Giemsa and **d)** flow cytometric analysis of peripheral blood from sick Tet1-deficient mice compared to age-matched controls. Data are representative of 3 independent experiments, n = 8-10 mice per genotype. **e)** Histological analysis of spleens from sick *Tet1*$^{+/-}$ and *Tet1*$^{-/-}$ mice compared to *Tet1*$^{+/+}$ controls. Sections were stained with H&E and Ki67 as indicated. RP = Red pulp, F = Follicle. **f)** H&E staining of liver, lung and kidney sections from sick *Tet1*$^{+/-}$ compared to *Tet1*$^{+/+}$mice showing diffuse lymphocytic infiltration compared to age-matched *Tet1*$^{+/+}$ mice. **g)** H&E and Ki67 staining of hyperproliferative infiltrating cells in kidney, lung and liver of Tet1-deficient mice. Histology is representative of *Tet1*$^{-/-}$ *Tet1*$^{+/-}$ mice (n = 6-8 mice per genotype). Scale bar = 100μm in all panels.



Supplementary Figure 2

Tet1-deficient B cell lymphomas display both IgM$^-$ and IgM$^+$ phenotypes and are transplantable.

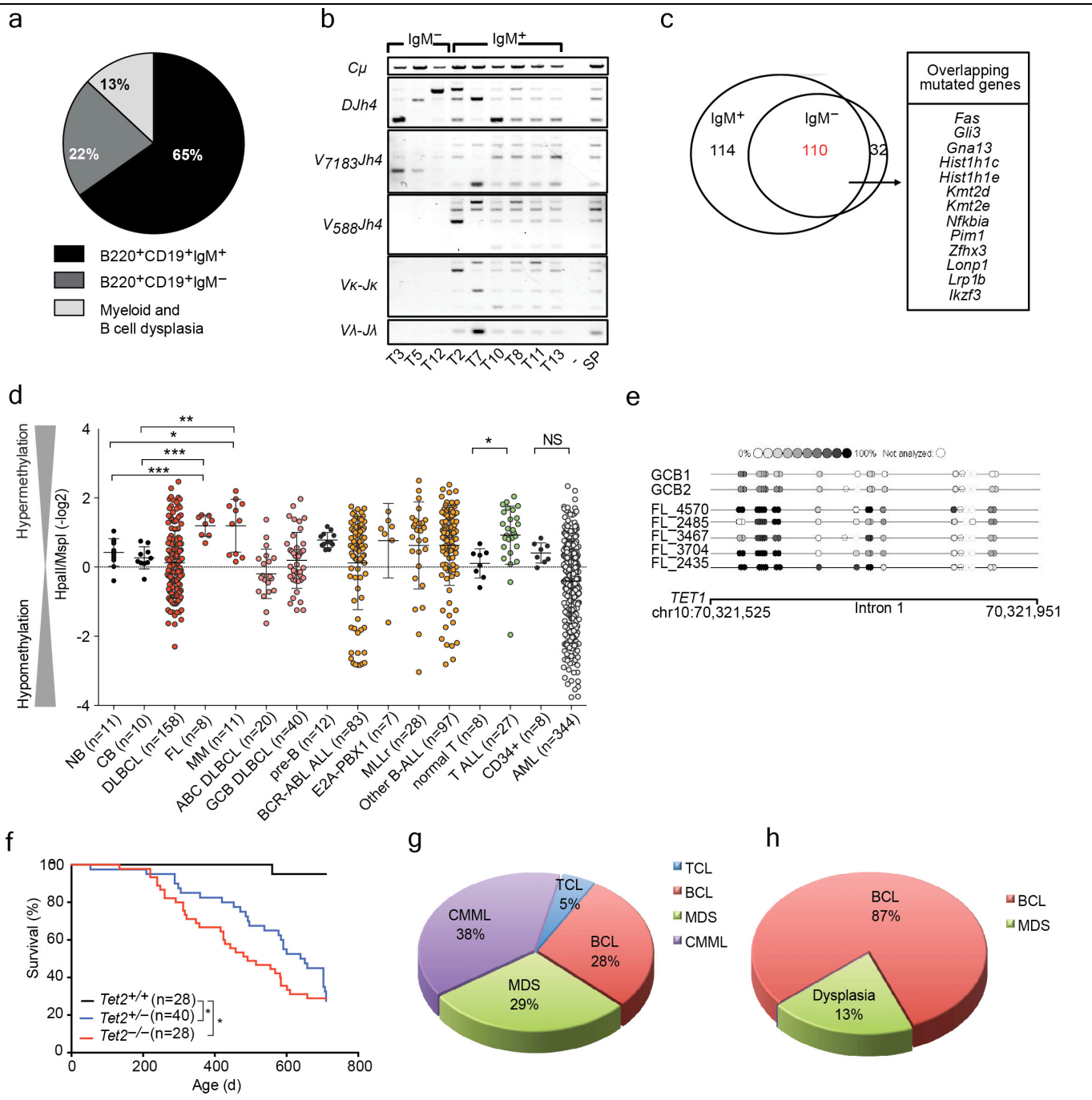
a-b) Additional examples of flow cytometric analysis of lymph nodes from sick *Tet1*$^{+/-}$ and *Tet1*$^{-/-}$ mice compared to *Tet1*$^{+/+}$controls, displaying IgM$^-$, IgM$^+$ and CD11b$^+$ staining patterns. **c-d)** H&E stained sections of liver, kidney, spleen and lymph nodes from sick *Tet1*$^{+/-}$ and *Tet1*$^{-/-}$ mice with multinucleated giant cells and histiocytic sarcoma. Scale bar = 100μm in all panels. **e)** Recipient mice 12 weeks post-transplant. Upper left panel; example of gross-anatomy of recipient mice with white patchy liver and enlarged spleen. Upper right and lower panels; H&E staining of recipient mouse tissue histological sections, with spleen and liver infiltration, and histiocytic sarcoma in the liver. Scale bar = 100μm in all panels. **f)** White blood cell (WBC) and lymphocyte cell counts in the peripheral blood of Tet1-deficient tumor recipient mice 8 and 12 weeks post-transplant. **g)** Representative flow cytometric analysis of spleen cells from recipient mice gated on CD45.2$^+$ donor cells co-stained for B cell (B220) and surface Ig (IgD and IgM) expression.



Supplementary Figure 3

Mutational analysis and base substitution frequency in Tet1-deficient lymphomas.

Exome sequencing data for thirteen Tet1-deficient tumors (T1-13) were divided into 2 groups; Group 1 = low mutation frequency (<50 total exonic variations), Group 2 = high mutation frequency (50-1200 total exonic variations). Low (Group1) and high-grade (Group 2) mutated tumors were compared for **a)** average number of indels and nsSNVs, **b)** mutation type and **c)** frequency of transversion or transition base substitutions**.** A, T, C or G base substitution frequencies were calculated **d)** overall and **e)** in the context of transversion or transition mutation. Average mutation frequency of base substitutions in **f)** low (Group1) and **g)** high-grade (Group 2) mutated Tet1-deficient tumors according to trinucleotide context with examples of individual high-grade mutated tumors; **h)** T12 and **i)** T11. Mean ± SEM (Group 1, n = 8; Group 2, n = 5).

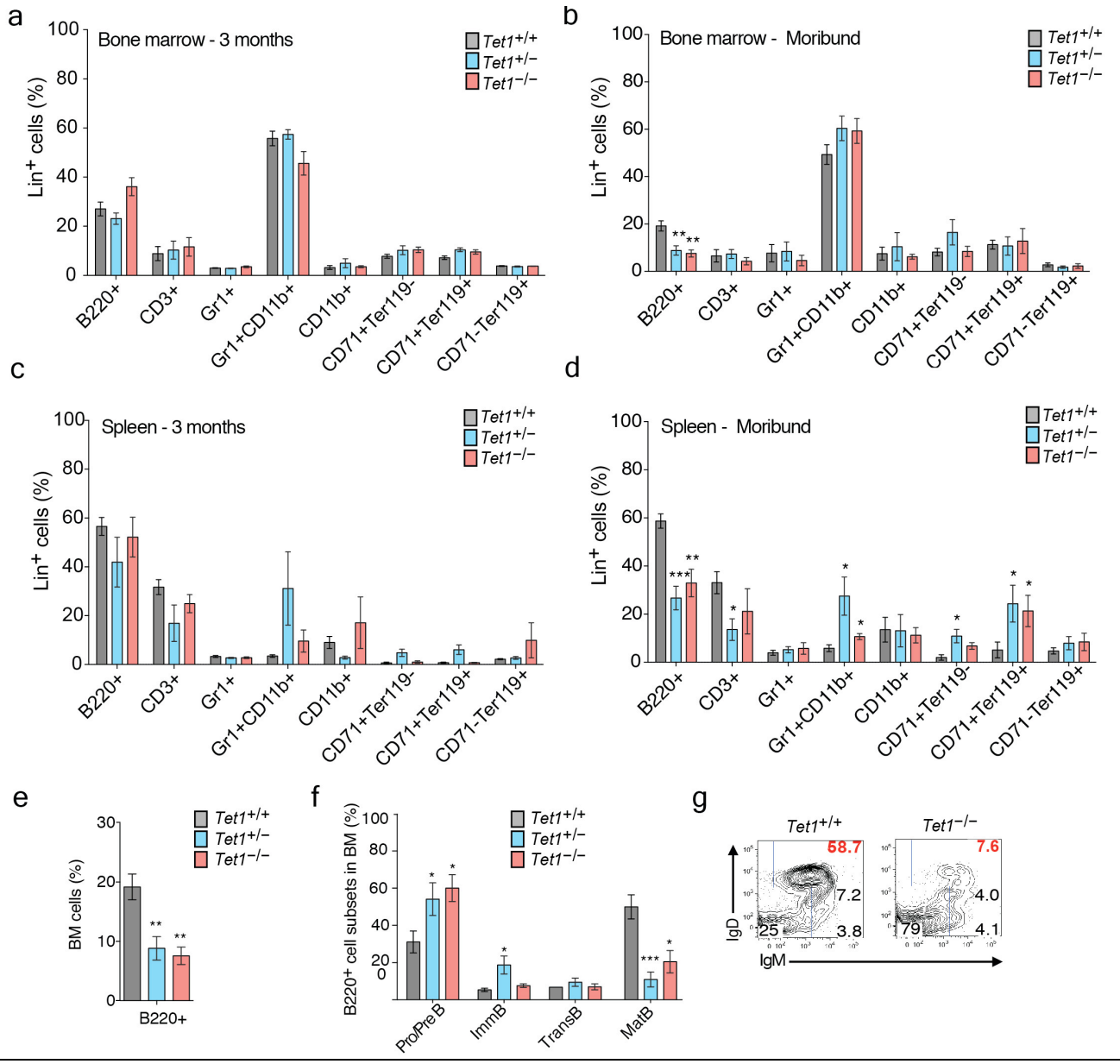


Supplementary Figure 4

Overlapping mutations in IgM$^+$ and IgM$^-$ Tet1-deficient tumors, hypermethylation of *TET1* in mature B cell lymphomas and contrasting disease spectra of Tet1- and Tet2-deficiency in mice.

a) Frequency of IgM$^+$ and IgM$^-$ lymphomas in Tet1-deficient mice. **b)** V(D)J-rearrangements in DNA of exome sequenced tumor samples. DNA isolated from total splenic cells (SP) was used as a control for the amplification of the constant heavy chain (Cμ), and for the rearrangements of D-J_H4, V_{7183}-J_H4 and V_{558}-J_H4, V_κ-J_κ and V_λ-J_λ. **c)** Venn Diagram of overlapping recurrently mutated genes in IgM$^+$ and IgM$^-$ tumors. **d)** HELP assay for methylation in patient samples are shown; human naïve B (NB), centroblast B (CB), diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL), multiple myeloma (MM), activated B-cell-like (ABC) and germinal center B-cell-like (GCB) DLBCL, precursor B (Pre-B), B-acute lymphoblastic leukemia (B-ALL) subtypes – BCR-ABL, E2A-PBX1, MLL-rearranged (MLLr)

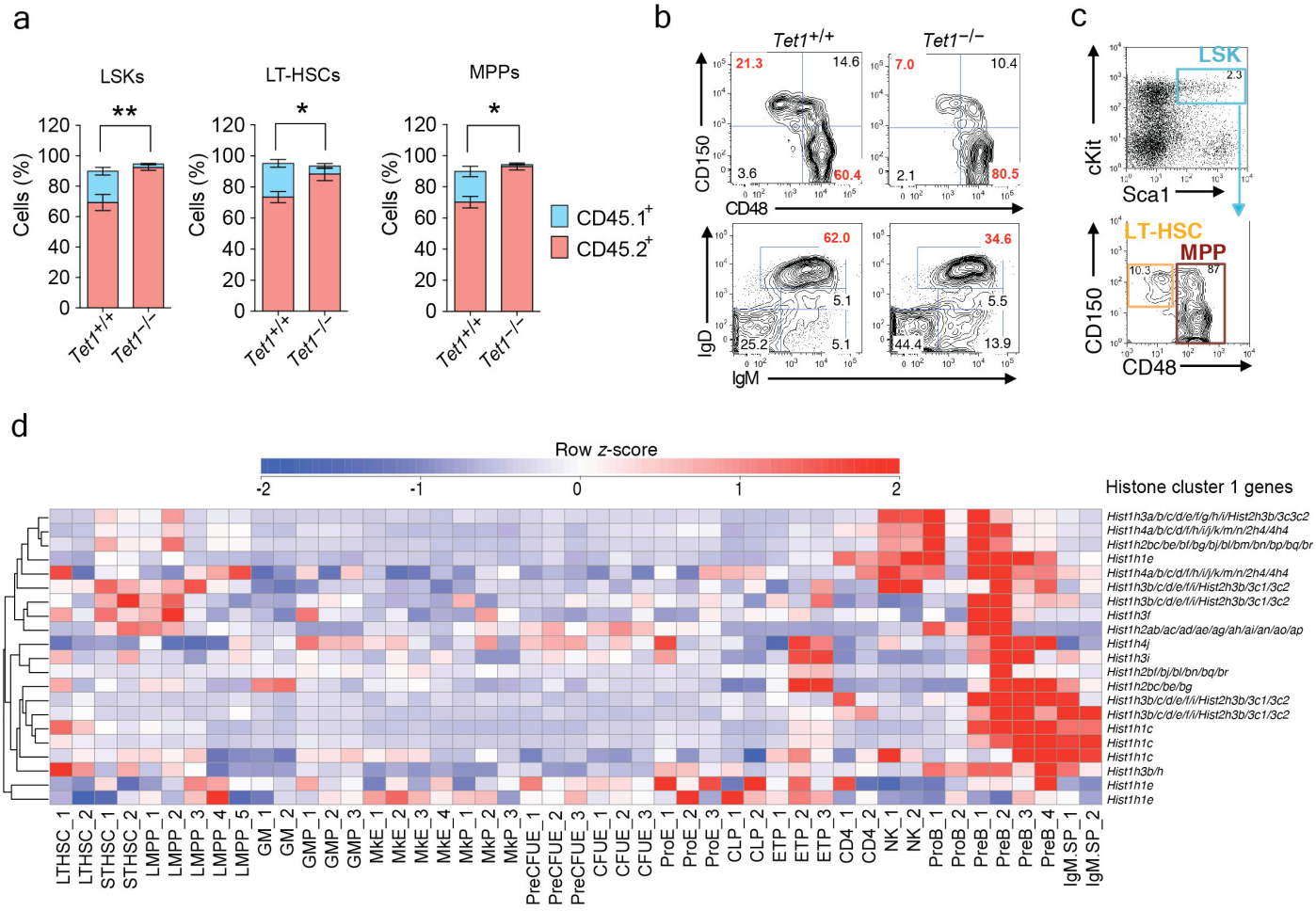
and other, normal T, T-acute lymphoblastic leukemia (T-ALL), $CD34^{+}$ progenitor cells and acute myeloid leukemia (AML). **e)** EpiGram of an amplicon targeting CpGs in the first intron of *TET1* used in Sequenom-Targeted Methylation Analysis by Sequenom MassARRAY. Two normal human germinal center B (GCB) samples are displayed compared to 5 FL patient samples. Circles depict increasing CpG methylation status from 0-100% as indicated. **f)** Kaplan-Meier survival curve of *Tet2*-deficient mice with heterozygous ($Tet2^{+/-}$) and homozygous ($Tet2^{-/-}$) deletion compared to wild-type mice ($Tet2^{+/+}$). * P = <0.0005. Frequency of diseases; acute myeloid leukemia (AML) and chronic myelomonocytic leukemia (CMML), myeloid dysplasia (MDS), B cell lymphoma (BCL) and T-cell lymphoma (TCL) observed in **g)** Tet2- and **h)** Tet1-deficient mice.



Supplementary Figure 5

Tet1-deficiency causes a decrease **in mature B cell frequency in the bone marrow and spleen.**

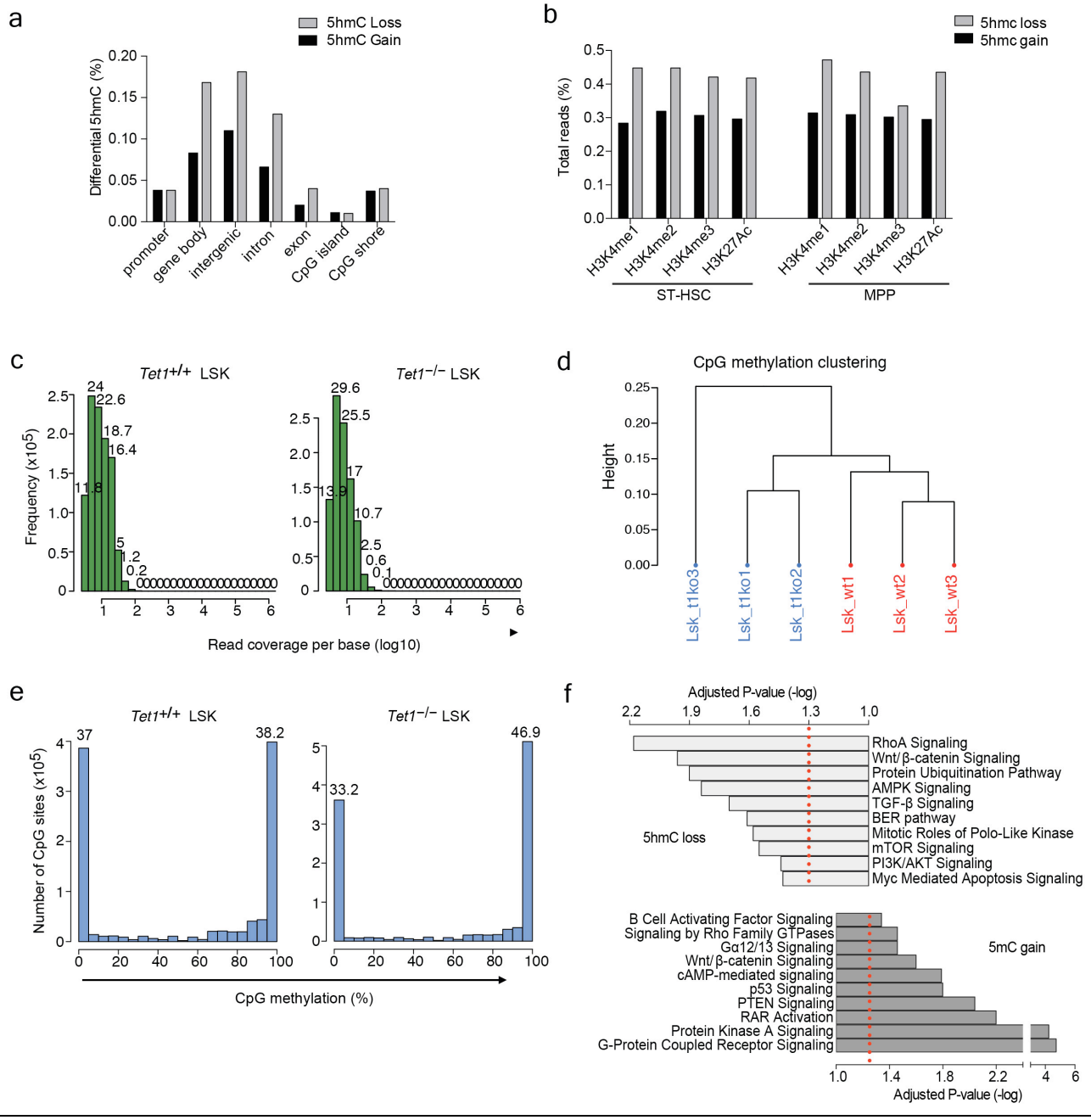
Summary of flow cytometric analysis of the frequency of lineage positive (% Lin^+) cells in the **a-b)** bone marrow and **c-d)** spleen of *Tet1*$^{+/+}$, *Tet1*$^{+/-}$ and *Tet1*$^{-/-}$ mice. B cell ($B220^+$), T cell ($CD3^+$), granulocyte ($Gr1^+$), neutrophil ($Gr1^+CD11b^+$), monocyte ($CD11b^+$), progenitor ($CD71^+Ter119^-$), precursor ($CD71^+Ter119^+$) and mature nucleated erythroid cell ($CD71^-Ter119^+$) frequencies are shown. **e-f)** Summary of flow cytometric analysis to assess the frequency of $B220^+$ B cell subsets in the bone marrow stained with IgM and IgD for progenitor and precursor B (Pro/PreB), immature (ImmB), transitional (TransB) and mature B cells (MatB). **g)** Representative flow cytometric analysis of the frequency of B cell subsets in the bone marrow of *Tet1*$^{+/+}$ and moribund *Tet1*$^{-/-}$ mice. All bar graphs display the mean ± SEM (3 months, n = 4 mice per genotype; Moribund, n = 6-8 mice per genotype); * P = <0.01, ** P = <0.001, *** = P <0.0001.



Supplementary Figure 6

Tet1-deficient HSCs display increased self-renewal *in vivo* with a BM mature B cell deficiency and histone cluster 1 gene expression in hematopoietic cell lineages.

a) Frequency of CD45.2$^+$ competitive donor cells in total LSKs, LT-HSCs and MPPs from the bone marrow of primary transplanted mice 20-weeks post-reconstitution (mean ± SEM, n = 6 mice per genotype); * P = <0.001, ** P = <0.0001) in all panels. **b)** Representative flow cytometry of CD45.2$^+$ cells from the bone marrow of primary transplanted mice. Upper panel; HSC subsets of CD45.2$^+$ LSK cells stained for LT-HSC, ST-HSC, MPP1 and MPP2 with CD150 and CD48 as previously described. Lower panel; CD45.2$^+$ B220$^+$ cells stained for B cell subsets with IgM and IgD. **c)** Sorting strategy for microarray and RNA-seq analysis of total LSK, LT-HSC and MPP populations. **d)** Heat map of Histone cluster 1 gene expression in hematopoietic stem, progenitor and mature cells[51].



Supplementary Figure 7

5hmC losses and 5mC gains in Tet1-deficient LSKs target genes involved in DNA repair, G-protein coupled receptor signaling and tumor suppressor pathways.

a) Percent of 5hmC losses and gains across genomic regions. **b)** Overlap of 5hmC losses and gains with enhancer histone marks in ST-HSCs and MPPs. **c)** Coverage per base and **d)** sample clustering of RRBS data from *Tet1*$^{+/+}$ and *Tet1*$^{-/-}$ LSKs. **e)** Representative frequency of CpG sites with 0-100 percent CpG methylation in *Tet1*$^{+/+}$ and *Tet1*$^{-/-}$ LSKs. **f)** Ingenuity Pathway Analysis (IPA) software was used to generate schematic representations of genes that lose 5hmC and gain 5mC in *Tet1*$^{-/-}$ LSK cells. Signaling pathways displayed include genes pathways involved in tumor suppression (TGF-β, WNT/β-Catenin, p53 and PTEN), DNA repair (BER) and B cell function (RhoA, G-protein coupled). Log adjusted *P*-value for significance is shown along the *x* axis. Red lines indicate threshold of significance (*P* = 0.05).

Supplementary Table 1. Summary of necropsy findings and immunophenotyping of hematopoietic organs in terminally diseased Tet1-deficient mice.

Mouse ID	Tet1 Genotype	Age (months)	Sex	Hematopoietic Disease Phenotype	Disease classification	Hematopoietic organs affected	Necropsy
1027	+/-	19	M	SSChi B220+ CD11b- Gr1- IgM- IgD- cKit-	B-ALL	Lymph nodes, Spleen, Peripheral blood	Lymphadenopathy
1249	+/-	19	M	SSChi B220+ CD11b+ Gr1+ CD71+ Ter119+ IgM+ IgDlo cKit-	B cell Lymphoma/Mixed Lineage	Lymph nodes, Spleen, Peripheral blood	Lymphadenopathy, Hepatomegaly, Splenomegaly
1148	+/-	20	F	SSChi B220+ CD11b+ Gr1+ IgM+ IgDlo cKit+	B cell Lymphoma/Mixed Lineage	Lymph nodes, Spleen, Peripheral blood	Lymphadenopathy, Splenomegaly
809	+/-	21	F	Erythroid, Monocyte, Immature B cell expansion	MDS, B cell dysplasia	Lymph nodes, Spleen, Peripheral blood	Lymphadenopathy
923	+/-	21	F	Erythroid, Monocyte, Immature B cell expansion	MDS, B cell dysplasia	Spleen, Bone marrow	Splenomegaly
1047	+/-	21	M	SSChi B220+ CD11b+ Gr1+ CD71- Ter119- IgM- IgD - cKit+	B cell Lymphoma/Mixed Lineage	Lymph nodes, Spleen, Bone marrow	Hepatomegaly, Splenomegaly
655	+/-	22	F	SSChi B220+ CD11b+ Gr1+ IgM+ IgDlo cKit-	B cell Lymphoma/Mixed Lineage	Lymph nodes, Spleen, Peripheral blood	Lymphadenopathy, Splenomegaly
668	+/-	22	F	B220+ IgM+ IgDlo Immature B cell expansion	B cell dysplasia	Spleen, Bone marrow	Hepatomegaly, Splenomegaly
343	+/-	27	M	SSChi B220+ CD11b+ Gr1+ IgM+ IgD- cKit+	B cell Lymphoma/Mixed Lineage	Lymph nodes, Spleen, Bone marrow, Peripheral Blood	Lymphadenopathy, Hepatomegaly, Splenomegaly
1142	+/-	27	M	SSChi B220+ CD11b+ Gr1- CD71-IgM+ IgD+ cKit+ CD43+	B cell Lymphoma/Mixed Lineage	Spleen, Peripheral blood	Hepatomegaly
3119	+/-	22	F	SSChi B220+ CD11b+ Gr1- CD71-IgM+ IgDlo cKit-	B cell Lymphoma/Mixed Lineage	Spleen, Peripheral blood	Normal sized organs
3112	+/-	27	M	SSChi B220+ CD11b+ Gr1- CD71+ IgM- IgD- cKit+ CD43+	B cell Lymphoma/Mixed Lineage	Spleen	Lymphadenopathy
1038	-/-	19	F	SSChi B220+ CD11b+ Gr1- IgM+ IgDlo	B cell Lymphoma/Mixed Lineage	Spleen, Peripheral blood	Hepatomegaly
1055	-/-	20	F	SSChi B220+ CD11b+ Gr1lo CD71- Ter119- IgM- IgD- cKit-	B cell Lymphoma/Mixed Lineage	Lymph nodes	Lymphadenopathy
1946	-/-	22	F	SSChi B220+ CD11b+ Gr1lo CD71+ IgM+ IgD+ cKit+ CD43+	B cell Lymphoma/Mixed Lineage	Lymph nodes, Peripheral blood	Lymphadenopathy
3113	-/-	22	M	SSChi B220+ CD11b+ Gr1- CD71+ IgM- IgD- cKit-	B cell Lymphoma/Mixed Lineage	Lymph nodes, Peripheral blood	Lymphadenopathy
732	-/-	22	F	SSChi B220+ CD11b+ Gr1+ CD71+ Ter119+ IgM+ IgDlo cKit+	B cell Lymphoma/Mixed Lineage	Spleen, Peripheral blood	Normal sized organs
1548	-/-	26	M	SSChi B220+ CD11b+ Gr1- CD71+ IgM- IgD- cKit+ CD43+	B cell Lymphoma/Mixed Lineage	Lymph nodes, Spleen, Peripheral blood	Lymphadenopathy
1549	-/-	26	F	SSChi B220+ CD11b+ Gr1- CD71- IgM+ IgD+ cKit+ CD43+	B cell Lymphoma/Mixed Lineage	Lymph nodes, Spleen, Peripheral blood	Lymphadenopathy, Hepatomegaly
330	-/-	26	F	Erythroid, Monocyte, Immature B cell expansion	MDS, B cell dysplasia	Spleen, Peripheral blood	Lymphadenopathy
805	-/-	30	F	SSChi B220+ CD11b+ Gr1- CD71- IgM+ IgD+ cKit-	B cell Lymphoma/Mixed Lineage	Spleen, Peripheral blood	Hepatomegaly

Supplementary Table 2. Summary of Tet1-deficient tumor samples selected for whole exome sequencing analysis.

Tumor Sample	Mouse ID	Age (months)	Genotype	Tumor source	Tumor Phenotype
T1	#655	22	*Tet1+/-*	SP	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{+}$ IgM^{+} IgD^{low} $cKit^{-}$
T2	#732	22	*Tet1-/-*	SP	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{+}$ $CD71^{+}$ $Ter119^{+}$ IgM^{+} IgD^{low} $cKit^{+}$
T3	#1027	19	*Tet1+/-*	LN	SSC^{high} $B220^{+}$ $CD11b^{-}$ $Gr1^{-}$ IgM^{-} IgD^{-} $cKit^{-}$
T4	#343	26	*Tet1+/-*	LN	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{+}$ IgM^{+} IgD^{-} $cKit^{+}$
T5	#1047	21	*Tet1+/-*	SP	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{+}$ $CD71^{-}$ $Ter119^{-}$ IgM^{-} IgD^{-} $cKit^{+}$
T6	#1249	21	*Tet1+/-*	SP	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{+}$ $CD71^{+}$ $Ter119^{+}$ IgM^{+} IgD^{low} $cKit^{-}$
T7	#805	30	*Tet1-/-*	PB	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{-}$ $CD71^{-}$ IgM^{+} IgD^{+} $cKit^{-}$
T8	#1142	27	*Tet1+/-*	SP	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{-}$ $CD71^{-}IgM^{+}$ IgD^{+} $cKit^{-}$ $CD43^{-}$
T9	#3112	27	*Tet1+/-*	SP	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{-}$ $CD71^{+}$ IgM^{+} IgD^{+} $cKit^{-}$ $CD43^{-}$
T10	#1549	26	*Tet1-/-*	LN	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{-}$ $CD71^{-}$ IgM^{+} IgD^{+} $cKit^{+}$ $CD43^{-}$
T11	#1946	22	*Tet1-/-*	LN	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{low}$ $CD71^{+}$ IgM^{+} IgD^{+} $cKit^{+}$ $CD43^{-}$
T12	#3113	22	*Tet1-/-*	LN	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{-}$ $CD71^{+}$ IgM^{-} IgD^{-} $cKit^{-}$ $CD43^{-}$
T13	#1548	26	*Tet1-/-*	LN	SSC^{high} $B220^{+}$ $CD11b^{+}$ $Gr1^{-}$ $CD71^{+}$ $IgM^{+/-}$ $IgD^{+/-}$ $cKit^{+/-}$ $CD43^{+/-}$

Supplementary Table 3. Overlapping somatic mutations in IgM+ and IgM- tumors from Tet1-deficient mice.

Tumor samples	Recurrently Mutated genes (≥2mutations/gene)
IgM+ and IgM -	*Abca1, Adam26a, Adamts5, Adamts20, Adcy2, Akap1, Ano5, Ar, Arcn1, Arhgap18, Bai1, Bnip3, Ccser1, Cdh7, Cdk5rap2, Cdv3, Cngb1, Cntn5, Cntnap5b, Cobll1, Csmd3, Cyp2c68, D630003M21Rik, Dcx, Ddx60, Dlc1, Dmd, Dnd1, Eif2ak3, Eif2b3, Fas, Gabra4, Gli3, Glis2, Gm382, Gm7173, Gm14124, Gna13, Golga4, Grik2, Gtf2a1, Hist1h1c, Hist1h1e, Il2, Kcnd2, Klf10, Klhl6, Kmt2d, Kmt2e, Lama1, Lama2, Lipn, Lonp1, Lphn3, Lrp1b, Lrrc4c, Map1a, Mmp16, Myo10, Neb, Nfkbia, Nisch, Nlgn1, Nr3c2, Nrip1, Nrk, Nrxn1, Pappa, Pappa2, Pars2, Pcdh7, Pcdh9, Pcdh11x, Pcdh17, Pgr, Pim1, Pip4k2b, Plcb1, Prpf40b, Rhag, Robo1, Robo2, Runx1t1, Scn3a, Scn7a, Scn9a, Setd5, Shroom4, Sirpb1a, Sis, Slc9a2, Slc39a6, Slco1b2, Snx19, Speer2, Taf15, Tlr4, Tpr, Tril, Trmt10a, Trpc4, Ugt2b37, Unc13c, Usp19, Utrn, Xirp2, Zcchc6, Zfhx3, Zfhx4, Zfp804a*
IgM+ only	*Adam29, Adam34, Alas1, Amer1, Arhgap20, Atp11b, Btaf1, Cadps, Ccdc71l, Cd79b, Cdh8, Cdh10, Cdk8, Cep350, Ces1e, Cfh, Chd1l, Chrna7, Chsy3, Cntln, Cntn6, Csmd1, Ctag2, Ctnna2, Dhx15, Dnah5, Dnah7b, Edc4, Efcab7, Epha3, Epha5, Ephb1, Fam135b, Fat1, Fbn2, Fign, Frmd4a, Gm4847, Gm5346, Gm13051, Gm13103, Gm13242, Gria1, Hist1h2bc, Hnrnpa2b1, Htr1a, Htr2c, Igf2r, Irx1, Jmjd4, Kcnh8, Kdm6b, Kitl, Klra10, Kmt2b, Lgals4,Lgals6, Lox, Lrrc16b, Magi1, Mettl25, Mpdz, Msantd4, Ndn, Ndst4, Nlrp4a, Notch2, Ntng1, Obscn, Parp14, Pcdh18, Pclo, Pde3b, Pkd1l2, Plcl2, Ppan, Ppargc1a, Ppfia2, Ptpn4, Ptprk, Pvrl3, Rasl2-9, Rnd3, Rnf20, Rnpc3, Scn1a, Sema3e, Sestd1, Slit2, Slitrk5, Smc2, Snx7, Sorcs1, Sorcs3, Sry, Tas2r123, Tas2r125, Tnc, Tram1l1, Trip12, Trps1, Try5, Tshz3, Ttn, Upf1, Ush2a, Wdr60, Xirp1, Xrn1, Yod1, Zcchc2, Zfp462, Zfp960, Zic1, Zim1*
IgM- only	*Apobec3, Aup1, Bend5, Bod1l, Brdt, Btla, Cd74, Cntn3, Flnc, Gcfc2, Gm13139,Gm13251, Gm13157, Gpr125, H2-Ab1, Herc1, Hist1h1d, Hmcn1, Ikzf3, Irx2, Jsrp1, Lrfn3, Lrfn5, Mcm2, Mroh2a, Mybl1, Nphp3, Pkhd1l1, Rims2, Scaf4, Smarca2, Tenm4, Zfp112*

Supplementary Table 4. Positively-enriched gene sets in *Tet1-/-* LSK, LT-HSC and MPP expression data by GSEA.

LSK microarray	SIZE	NES	NOM p-val	FDR q-val
MEISSNER_NPC_HCP_WITH_H3K4ME2_AND_H3K27ME3	274	1.86	0.00	0.23
LSK_CPG_PROMOTER_H3K27ME3_ONLY	656	1.84	0.00	0.00
MIKKELSEN_NPC_HCP_WITH_H3K27ME3	279	1.82	0.00	0.17
KEGG_AUTOIMMUNE_THYROID_DISEASE	23	1.81	0.00	0.15
SHIN_B_CELL_LYMPHOMA_CLUSTER_5	16	1.80	0.00	0.14
MIKKELSEN_MCV6_HCP_WITH_H3K27ME3	338	1.79	0.00	0.13
BENPORATH_PRC2_TARGETS	500	1.74	0.00	0.18
MIKKELSEN_MEF_HCP_WITH_H3K27ME3	473	1.72	0.00	0.19
MEISSNER_BRAIN_HCP_WITH_H3K27ME3	211	1.72	0.00	0.17
KEGG_NEUROACTIVE_LIGAND_RECEPTOR_INTERACTION	222	1.68	0.00	0.21
MIKKELSEN_MEF_HCP_WITH_H3_UNMETHYLATED	165	1.68	0.00	0.21
BIOCARTA_INFLAM_PATHWAY	25	1.67	0.01	0.21
MIKKELSEN_ES_HCP_WITH_H3_UNMETHYLATED	46	1.66	0.01	0.21
MIKKELSEN_IPS_WITH_HCP_H3K27ME3	80	1.64	0.00	0.22
LSK_BIVALENT	1318	1.12	0.07	0.04
LT-HSC RNA-seq	**SIZE**	**NES**	**NOM p-val**	**FDR q-val**
LSK_CPG_PROMOTER_H3K27ME3_ONLY	515	1.86	0.00	0.00
MEISSNER_NPC_HCP_WITH_H3K4ME2_AND_H3K27ME3	205	1.82	0.00	0.01
MIKKELSEN_MEF_HCP_WITH_H3K27ME3	324	1.81	0.00	0.01
MIKKELSEN_NPC_HCP_WITH_H3K27ME3	200	1.79	0.00	0.01
BENPORATH_PRC2_TARGETS	343	1.74	0.00	0.03
MIKKELSEN_MCV6_ICP_WITH_H3K27ME3	40	1.66	0.00	0.06
MEISSNER_NPC_HCP_WITH_H3K4ME3_AND_H3K27ME3	98	1.63	0.00	0.09
MIKKELSEN_ES_ICP_WITH_H3K4ME3_AND_H3K27ME3	84	1.63	0.00	0.09
MEISSNER_NPC_HCP_WITH_H3K27ME3	34	1.63	0.00	0.09
MIKKELSEN_NPC_HCP_WITH_H3K4ME3_AND_H3K27ME3	137	1.62	0.00	0.09
MIKKELSEN_MEF_ICP_WITH_H3K27ME3	108	1.61	0.00	0.09
MIKKELSEN_IPS_ICP_WITH_H3K4ME3_AND_H327ME3	74	1.58	0.00	0.11
MIKKELSEN_ES_HCP_WITH_H3K27ME3	18	1.54	0.02	0.15
LSK_BIVALENT	1396	1.37	0.00	0.00
LSK_CPG_PROMOTER_BIVALENT	450	1.09	0.16	0.07
MPP RNA-seq	**SIZE**	**NES**	**NOM p-val**	**FDR q-val**
BOYLAN_MULTIPLE_MYELOMA_PCA1_UP	78	2.01	0.00	0.00
PASQUALUCCI_LYMPHOMA_BY_GC_STAGE_UP	225	1.99	0.00	0.00
MORI_PLASMA_CELL_UP	45	1.89	0.00	0.00
PID_CD8TCRDOWNSTREAMPATHWAY	43	1.88	0.00	0.04
JAATINEN_HEMATOPOIETIC_STEM_CELL_DN	149	1.88	0.00	0.04
BIOCARTA_CTLA4_PATHWAY	15	1.87	0.00	0.04
MORI_PLASMA_CELL_UP	37	1.78	0.00	0.09
PID_CD8TCRPATHWAY	44	1.77	0.00	0.09
KEGG_PRIMARY_IMMUNODEFICIENCY	28	1.71	0.00	0.16
IVANOVA_HEMATOPOIESIS_MATURE_CELL	205	1.65	0.00	0.22
LSK_CPG_PROMOTER_H3K27ME3_ONLY	428	1.53	0.00	0.00
LSK_BIVALENT	1301	1.52	0.00	0.00
MEISSNER_NPC_HCP_WITH_H3K4ME2_AND_H3K27ME3	181	1.43	0.01	0.06
MIKKELSEN_MEF_HCP_WITH_H3K27ME3	285	1.41	0.00	0.07
LSK_CPG_PROMOTER_BIVALENT	428	1.35	0.00	0.00

SIZE: number of genes enriched in dataset
NES: normalized enrichment score
NOM p-val: nominal p-value
FDR q-val: False discovery rate q-value

Supplementary Table 5. Negatively-enriched gene sets in *Tet1-/-* LSK, and MPP expression data by GSEA.

LSK microarray	SIZE	NES	NOM p-val	FDR q-val
KEGG_DNA_REPLICATION	32	-1.745	0.00	0.01
KEGG_MISMATCH_REPAIR	22	-1.825	0.00	0.00
KEGG_RNA_POLYMERASE	25	-1.858	0.00	0.01
PID_HDAC_CLASSII_PATHWAY	31	-1.832	0.00	0.01
REACTOME_DNA_REPAIR	94	-1.639	0.01	0.01
REACTOME_MEIOTIC_SYNAPSIS	32	1.538	0.02	0.14
REACTOME_RNA_POL_I_RNA_POL_III_AND_MITOCHONDRIAL_TRANSCRIPTION	66	-1.498	0.01	0.03
REACTOME_RNA_POL_II_PRE_TRANSCRIPTION_EVENTS	55	-1.675	0.00	0.01
REACTOME_RNA_POL_II_TRANSCRIPTION	85	-1.862	0.00	0.01
REACTOME_RNA_POL_III_TRANSCRIPTION	30	-2.070	0.00	0.00
REACTOME_RNA_POL_III_TRANSCRIPTION_INITIATION_FROM_TYPE_2_PROMOTER	21	-1.785	0.01	0.01
REACTOME_S_PHASE	92	-1.697	0.00	0.01
REACTOME_SYNTHESIS_OF_DNA	77	-1.632	0.00	0.01
REACTOME_TRANSCRIPTION	136	-1.697	0.00	0.01
MPP RNA-seq	**SIZE**	**NES**	**NOM p-val**	**FDR q-val**
REACTOME_RNA_POL_I_PROMOTER_OPENING	44	-2.613186	0.00	0.00
REACTOME_RNA_POL_I_TRANSCRIPTION	66	-2.5215938	0.00	0.00
REACTOME_PACKAGING_OF_TELOMERE_ENDS	35	-2.4533944	0.00	0.00
REACTOME_DEPOSITION_OF_NEW_CENPA_CONTAINING_NUCLEOSOMES_AT_THE_CENTROMERE	46	-2.4302628	0.00	0.00
REACTOME_AMYLOIDS	51	-2.4286585	0.00	0.00
REACTOME_MEIOTIC_RECOMBINATION	66	-2.3482702	0.00	0.00
REACTOME_MEIOTIC_SYNAPSIS	51	-2.2943957	0.00	0.00
REACTOME_MEIOSIS	86	-2.221875	0.00	0.00
REACTOME_TELOMERE_MAINTENANCE	56	-2.1949067	0.00	0.00
REACTOME_RNA_POL_I_RNA_POL_III_AND_MITOCHONDRIAL_TRANSCRIPTION	98	-2.16059	0.00	0.00
REACTOME_CHROMOSOME_MAINTENANCE	87	-1.9773016	0.00	0.02
KEGG_SYSTEMIC_LUPUS_ERYTHEMATOSUS	81	-1.8950058	0.00	0.06
REACTOME_TRANSCRIPTION	167	-1.8681017	0.00	0.08
KEGG_DNA_REPLICATION	32	-1.8055322	0.01	0.14

SIZE: number of genes enriched in dataset
NES: normalized enrichment score
NOM p-val: nominal p-value
FDR q-val: False discovery rate q-value

Supplementary Table 6. Top 20 networks of genes identified by Ingenuity Pathway Analysis that lose 5hmC in gene bodies and promoters.

ID	Top Diseases and Functions	Molecules in Network
1	Hereditary Disorder, Ophthalmic Disease, Cancer	ADCK3, ATXN1L, CATSPER1, CCZ1/CCZ1B, COQ4, CPA2, CWC25, DDX41, ESYT1, EXOSC5, FYCO1, HNF4A, HPD, HUNK, ITIH3, MECR, MOCOS, MRPL4, MRPS12, MRPS28, PHPT1, PNPLA6, POLR3E, REXO2, SGCE, SPATA2, ST6GALNAC6, TM7SF2, TMEM8B, TOR2A, TXNDC12, UROS, WBSCR22, ZBTB37, ZNF644
2	Cellular Assembly and Organization, Cellular Movement, Nervous System Development and Function	ADAM9, AEBP1, AHSA1, AMPH, B3GNT2, BHMT, CTSA, DENND1A, DOK4, Dynamin, Endophilin, EPN1, ERK1/2, KARS, MGAT3, NAGLU, NECAP1, NEU1, PACSIN2, PACSIN3, PFN2, PIGF, PRR14, RTN4R, SARDH, SBSN, SH3GL2, SLC9A5, SNAP91, SYN2, TFEB, TMEFF2, TMEM55B, TRPM2, UCN3
3	Post-Translational Modification, Cell Death and Survival, Cellular Movement	ACTR5, AP2A1, ATAD3A, ATXN10, BAG6, CAD, Collagen type I, EEF2, GET4, HECTD3, KIFC2, PFK, PFKL, PHB2, PLOD2, Ppp2c, PPP2CB, PPP2R1A, PPP2R3C, PPP5C, PPP6R3, PRKAC, RAB18, RUVBL2, SHC1, SHCBP1, SLC1A2, SRGAP2, TAB2, TGFBI, TIP60, WRAP53, YEATS4, ZNF384, ZNHIT1
4	RNA Post-Transcriptional Modification, Cell Cycle, Nervous System Development and Function	APLF, CHERP, CPSF3, CPSF4, DHX37, EGR2, EXO1, F7, FARP2, FRYL, GADD45, GIGYF2, HEATR1, KHDRBS3, MAG, ME2, PAPOLA, PASK, RABGGTA, Rac, RECQL, Rho gdi, SART1, SF3B1, SIRT7, SOX8, SOX10, TBL3, TFIP11, U2AF2, UTP15, WDR46, ZCCHC3, ZNF574, ZSCAN12
5	Cell Signaling, Digestive System Development and Function, Cell Cycle	AGAP2, Akt, ARHGAP1, ARHGAP12, BNIPL, Caspase 3/7, CDH13, CHCHD2, CHRNA3, Ciap, CNKSR1, DAP3, DAPK3, Erm, Foxp2, GRB14, HIF3A, HOMER2, MAN1C1, MAN2A2, MAN2C1, Mannosidase Alpha, MAPKAPK3, MED25, Naip1 (includes others), NET1, PARG, PPT1, PTK6, PYCR1, RBM38, RhoGap, SEMA7A, STARD13, VARS
6	Cell Cycle, DNA Replication, Recombination, and Repair, Gene Expression	CHD2, COPS4, Coup-Tf, CYP4F8, EP400, ETV3, Gsk3, HDAC2, histone deacetylase, I kappa b kinase, IER5L, KLHL22, LGR6, MCM4, MCM10, NR2C1, NSFL1C, PEG10, POU5F1, RAD54B, REPIN1, SAE1, SALL1, Sf3a2, SMARCB1, SMARCC1, SOX2-OCT4-NANOG, SS18L1, TFCP2L1, TH2 Cytokine, TMED1, TRIM41, UBXN7, WWP2, ZMYM4
7	Neurological Disease, Ophthalmic Disease, Psychological Disorders	Alpha tubulin, BAZ2A, Beta Tubulin, Calmodulin, CETN3, DUB, Dynein, EML1, Gamma tubulin, Hdac, JRK, KCNN1, KCNQ5, LYPLA2, MRPS21, NDEL1, NEURL4, ONECUT2, PCGF3, PDCD6IP, POC5, PPL, SARS2, SCN2A, TSPAN2, TUBA1A, TUBA1B, TUBA1C, TUBGCP2, USP7, USP29, USP32, USP33, USP42, ZNF365
8	Behavior, Cardiac Enlargement, Cardiovascular Disease	2700097O09Rik, AGPAT6, ATF6, ATP6V1C2, CCDC25, CPLX1, DYRK1A, EXTL2, FMN2, Insulin, KCNA1, KCNIP4, KIAA0232, Klra4 (includes others), LSM1, LSM3, Mitochondrial complex 1, MTORC1, NDUFAF3, NDUFS6, NDUFV3, p70 S6k, Pcp4l1, PP1-C,PRPF40B, PSEN1, RBP3, RICTOR, RPL22, RPS6, snRNP, SUN5, TCR, TPPP, TSH
9	Cellular Assembly and Organization, Tissue Development, Carbohydrate Metabolism	AKR1B1, chemokine receptor, Cpla2, DUSP22, EIF4EBP2, EXOC4, Fc gamma receptor, FEM1A, Fgf, Fgfr, GALNT13, IDH1, Mapk, NCAN, NUP37, NUP85, PAX7, PEG3, PIAS4, PIGC, PIGH, PLA2, PLA2G6, PLA2G2F, PLAGL1, RGS13, SEH1L, SNX2, SNX4, Tenascin, TUBA8, tubulin (family), WASH1, ZHX1, ZMIZ2
10	Lipid Metabolism, Small Molecule Biochemistry, Carbohydrate Metabolism	AIF1L, BSG, CAV3, Caveolin, CLOCK, CTNNAL1, ELOVL2, ERN2, estrogen receptor, FASN, FNDC5, GCK, JPH2, KCTD9, MAPK12, MGP, Mmp, MVP, N-cor, NR1I2, PCBP1, PCCB, PCGF2, PHF19, PLEK2, PPARGC1A, Rar, Rnr, RRP36, Rxr, thymidine kinase,TMPRSS15, trypsin, USF2, ZNF335
11	Cell Morphology, Cellular Assembly and Organization, Tissue Development	Actin, ACTR2, Alpha Actinin, Alpha catenin, Arp2/3, ARPC1B, Cadherin, CCM2, CDH8, CDH11, F Actin, GAS8, GNA12, Ga12/13, IPP, JUP, Ktn1, MCF2L, NEUROG2, NEXN, NKX6-1, PARVG, PCSK2, Pde, PDE11A, PDYN, PITPNM1, PLS1, PTPRQ, RHOA, RPN2, SNX8, SNX33, Troponin t, VAPB
12	Lipid Metabolism, Nervous System Development and Function, Post-Translational Modification	AQP5, AQUAPORIN, BRE, CAPNS1, CASP8AP2, CD300LD, Cyb5r3, Filamin, FREM1, GFPT2, Ikk (family), Integrin, IRF, ITGAX, LDB2, LENG8, LTBR, MAP4K2, NFkB (complex), NOP14, NSMAF, PKP1, PLA2G2D, PYGO1, RNF25, SEC22B, SLC3A1, SMPD4, sphingomyelinase, ST8SIA1, Talin, Tnf receptor, TRAF, Trim30a/Trim30d, ZNF446
13	Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry	AAGAB, ABCD2, Adaptor protein 1, Angiotensin II receptor type 1, Ap1 gamma, AP1M1, Ap2 alpha, Arf, ARF3, ARFGEF1, BTG3, CLN3, ERK, FBXO46, GGA2, HMG CoA synthase, HMGCS2, LRP3, M6PR, NCF4, NPC1, NPC1L1, OSGEP, PDGFC, PIP5K1B, Secretase gamma, SIPA1, SLC25A11, SLC25A22, SRD5A1, Srebp, TMSB4, TRIB1, UNC45A, VASN

14	Behavior, Nervous System Development and Function, Cell Signaling	ADCY4, ADD1, AHCY, Ampa Receptor, Atrial Natriuretic Peptide, CA8, CaMKII, chymotrypsin, CORO1B, DTNB, GRIA4, inositol-trisphosphate 3-kinase, IPMK, ITPKA, ITPKC, ITPR, KCNC4, L-type Calcium Channel, MYOZ1, MYOZ3, NPR2, Pdgf Ab, PDLIM5, PEBP1, PER1, PER3, PHACTR3, PITPNB, Pkc(s), PMP22, PP1 protein complex group, REM1, SNTG1, STXBP3, TCAP
15	Cell Cycle, DNA Replication, Recombination, and Repair, Cellular Movement	ANAPC11, APC (complex), BRMS1, CCDC77, CCNB1, Cdc2, CDC20, Cdk, CNTROB, Cyclin B, DFFB, DLX5, DNM1L , Histone H1, KIF14, LATS2, MARS, MOB3B, MXD1, MYT1, Pka, Pka catalytic subunit, PPI, PPIG, PPP1R3A, RNA polymerase I, Sin3, SKP2, SNPH, TAF1B, TCHP, TNFRSF13B, Tnp2, UBE3D, UBTF
16	Developmental Disorder, Hereditary Disorder, Metabolic Disease	ARMC3, Calbindin, Cbp/p300, CCDC101, CCNK, CSRP2BP, ELL2, FLOT1, Gcn5l, GTF2B, HEXIM2, Holo RNA polymerase II, Igg3, IgG2b, Igh (family), KCNH6, LY86, MED20, mediator, MIR124, NECAB2, NR1D2, P-TEFb, POLR2K, PTK2B, PTOV1, REST, SCG3, SLC22A2, SLC22A12, SLC7A14, SPIB, TADA3, TCEA3, XKR4
17	DNA Replication, Recombination, and Repair, Energy Production, Nucleic Acid Metabolism	19S proteasome, 20s proteasome, 26s Proteasome, 3 beta HSD, ABHD4, APH1A, ATP5D, ATPase, CENPB, CSAD, Ctbp, FAM65A, GAS5, IGF1, KDM4A, MAP1LC3B, MHC CLASS I (family), MSH2, MUS81, OSBPL7, PSMA, PSMA7, PSMC, PSMC1, PSMC2, PSMC4, PSMD3, PSMD5, SEZ6L2, SRSF3, SYT10, TK1, TOR3A, TRA2B, Ubiquitin
18	DNA Replication, Recombination, and Repair, Cellular Compromise, Cell Morphology	ADCY, ADRB, APEX1, CAMSAP1, CD3, CD160, CDC40, Ck2, cytochrome C, FAM13B, FOXA2, HIST1H2BA, Histone h3, Histone h4, Ifn gamma, LRWD1, MAX, MPHOSPH9, NBN, PARP1, PCYT2, PLC, Proinsulin, PRPF19, PYGL, RAB17, SKIL, SMC3, STAG2, SYPL2, TRAF3IP1, TRIM29, YWHAG, ZBTB44, ZZEF1
19	Cellular Assembly and Organization, Cell Morphology, Cell-To-Cell Signaling and Interaction	C16orf45, C17orf96, CDC42BPB, CELA2A, CPNE1, elastase, ENO2, ETS, FERMT2, Fibrin, GM2A, GOLPH3, growth factor receptor, Integrin, MPZL2, MRPL36, MUC5B, MYL12A, MYO18A, PDGFB, PLXNA1, PMEPA1, PROZ, Ptk, PTK7, PTPRA, PXK, Ras, RNF111, RNF167, RRAS, Smad2/3, Sos, UBE2M, ZAP70
20	Embryonic Development, Organismal Development, Skeletal and Muscular System Development and Function	ACO2, Aconitase, APC, APC2, APC/APC2, AXIN1, Casein, CD34, CK1, CLASP1, CSNK1G1, CSNK1G3, Dishevelled, GCM2, Gli, Glycogen synthase, HCN4, Hedgehog, Importin beta, IPO8, ISCA1, MAPRE3, MCM3AP, MYBPH, Nes, NUP50, P38 MAPK, PITX2, SFRP1, SLC18A2, TCF, TNNT3, Wnt, WNT3, WNT7A

Supplementary Table 7. Disease categories of genes that lose 5hmC by Ingenuity Pathway Analysis.

Diseases or Functions and Categories	p-Value
Molecular Transport	1.67E-07-1.22E-02
Cancer	3.34E-07-1.27E-02
Cellular Growth and Proliferation	8.3E-06-1.19E-02
Cellular Assembly and Organization	1.68E-05-1.29E-02
Cellular Function and Maintenance	1.68E-05-1.06E-02
Small Molecule Biochemistry	2.32E-05-1.14E-02
Cell Death and Survival	7.77E-05-1.27E-02
Hematological System Development and Function	7.04E-04-1.17E-02
Hematopoiesis	7.04E-04-1.17E-02
DNA Replication, Recombination, and Repair	9.04E-04-1.26E-02
Nucleic Acid Metabolism	9.04E-04-8.58E-03
Lymphoid Tissue Structure and Development	1.67E-03-1.16E-02
Cell Cycle	2.06E-03-1.27E-02
Hematological Disease	2.15E-03-1.27E-02
Immunological Disease	2.15E-03-1.27E-02

Supplementary Table 8. Genes with gene body and promoter 5hmC loss and 5mC gain.

Overlapping Genes	Gene Symbol
127	*Adam2, Adamtsl5, Adra1d, Aebp1, Agpat6, Aldh1l2, Ankrd26, Aqp5, Armc3, Atg9b, C330005M16Rik, Camsap1, Catsper1, Ccdc92, Cd160, Cdh11, Cdh13, Cdk3-ps, Chchd2, Cplx1, Cpxm1, Cybasc3, D5Ertd579e, Dbx2, Efhd2, Eif3l, Engase, Exo1, Fam193b, Fhdc1, Gabrp, Gal3st1, Galnt13, Gdf1, Gm996, Gm10565, Gna12, Golph3, Gpsm2, H2-M10.2, Htr6, Inpp5f, Irf5, Irf8, Jph2, Kcna1, Kcnk10, Kcnn1, Kiss1r, Klhl1, Klhl25, Krt71, Krt83, Lgi2, Lgr6, Lhfpl4, Mamdc2, Man1c1, Meis3, Mmp16, Mogat2, Myo18a, Necab2, Neu1, Neurog2, Nexn, Ngef, Nos1, Npepl1, Npr2, Onecut2, Opalin, Pax7, Pex10, Phactr3, Pigf, Pitpnm1, Pkp1, Ptk2b, Ptprcap, Pycr1, Pygl, Qrfpr, Rab37, Rab44, Rabgap1, Rasef, Rem1, Rgs8, Rtn2, Scg3, Sebox, Shcbp1, Slc1a2, Slc4a11, Slc7a14, Slc22a12, Slc24a2, Slc35e4, Slc45a1, Snx8, Snx22, Sox8, Spire2, Srrm4, Srsf12, St8sia1, Sult2b1, Syn2, Sypl2, Tbccd1, Thbs4, Tk1, Tmem8b, Tmem51, Tmem198, Tnfrsf13b, Trim36, Tuba8, Usp33, Usp42, Vmn2r29, Wdr86, Wnk4, Zfp384, Zfp687, Zscan12*

Supplementary Table 9. Sequenom Epityper assay primers used for quantitative *TET1* DNA methylation assays.

Sequence Description	Sequence (5'-3')
MA_TET1h_1F	GGGTTATATAAGATTTATTTTAGGTTTGG
MA_TET1h_1R	CCTACACAAAAAAAACAAAAATTCC
MA_TET1h_11F	GAAATGTAATGAGGGATTGAATTTTT
MA_TET1h_11R	AAAATACCAAATCAAAAATAACACCA
MA_TET1h_13F	TGGTGTTATTTTTGATTTGGTATTTT
MA_TET1h_13R	CAATATCTCCCCAAAACAAACCT
MA_TET1h_17F	TTTTATTTTTTGAGGTTTGTTTTGG
MA_TET1h_17R	ATCCCCACAACTTTAAAACCC
MA_TET1h_21F	GTTGGTGTAGGTTTGGAGTTGG
MA_TET1h_21R	AACTCCCCAAAAAAACCAAAAAAC
MA_TET1h_22F	GTTGGTTTTTTGGTTTTTTTGG
MA_TET1h_22R	AACAAAACTACACCACTACCTCCAC
MA_TET1h_23F	TTATAAGAAGTGGTTTGGAAGGGAT
MA_TET1h_23R	cCACTCAAATCCAAAAAAAACCTAAA
MA_TET1h_25F	TTAGGTTTTTTTTGGATTTGAGTGT
MA_TET1h_25R	CCCAAAATTATAAACCTAAACTCCTC
MA_TET1h_26F	TTTTTTTGTAAAGATGAGGAGTTTAGG
MA_TET1h_26R	CAAAAAAAACATAACACACAACAAAA
MA_TET1h_31F	TTTTGTTGTGTGTTATGTTTTTTTTG
MA_TET1h_31R	AACAACACCTAACTCAATTTCCTCC
MA_TET1h_33F	TTTAGTTGTTGGAGGAAATTGAGTT
MA_TET1h_33R	CCAAAATCATACCACTACACTCTAACC
MA_TET1h_37F	GGTTTATTGTAATTTTTGTTTTTGGG
MA_TET1h_37R	AAACAACTATACTAACCCCTATACCATCA

Supplementary Table 10. NanoString nCounter Elements design details for mRNA expression quantitation

Gene name	Accession	Position	Target Sequence	NSID
Hprt	NM_013556.2	31-130	TGCTGAGGCGGCGAGGGAGAGCGTTGGGCTTACCTCACTGCTTTCCGGAGCGGTAGCACCTCCTCCGCCGGCTTCCTCCTCAGACCGCTTTTTGCCGCGA	NM_013556.2:30
Actin	NM_007393.1	816-915	CAGGTCATCACTATTGGCAACGAGCGGTTCCGATGCCCTGAGGCTCTTTTCCAGCCTTCCTTCTTGGGTATGGAATCCTGTGGCATCCATGAAACTACAT	NM_007393.1:815
Gapdh	NM_001001303.1	891-990	AGGTTGTCTCCTGCGACTTCAACAGCAACTCCCACTCTTCCACCTTCGATGCCGGGGCTGGCATTGCTCTCAATGACAACTTTGTCAAGCTCATTTCCTG	NM_001001303.1:890
Hist1h1a	NM_030609.2	353-452	GGCGCTGCTGGCTCTTTTAAGCTGAACAAGAAGGCTGAGTCCAAGGCCATCACCACCAAGGTGTCAGTGAAGGCGAAAGCATCCGGGGCTGCTAAGAAAC	NM_030609.2:352
Hist1h1b	NM_020034.1	543-642	AAAAGCAGCAAAGAGCCCGGCCAAGCCCAAGGCGGTGAAGTCTAAGGCATCCAAACCTAAGGTTACCAAGCCTAAGACCGCTAAGCCTAAGGCTGCCAAG	NM_020034.1:542
Hist1h1c	NM_015786.1	1006-1105	TCTTCGTTTGATTGGGCGCCATCCCGAAGTTTGAGCTTCCTGCCTGGAGAAACGCATCCGGGGCTTGTAGGTGGCTTCTATGCTCAGCCTCTTTTGTGGG	NM_015786.1:1005
Hist1h1d	NM_145713.3	2091-2190	GGAAGAACACAGGCTCCTAAAAGATGGTTTTTGACCTCCACAGGCCAGTGCTTGTGTAAGTCACCCTCTGCTCACATCTAGCCCAGATAAGGTAAAGCTA	NM_145713.3:2090
Hist1h1e	NM_015787.3	1017-1116	CTCCCGGCTGCCACGTCGATAACTTTTAAGGGAGATAGCAGAATGATTTAGAGATAGAATCTTAAGCATTGAGCGATTCAGTGCGTAAAGAGCAGGATCG	NM_015787.3:1016
Hist1h2ac	NM_178189.4	2414-2513	GGGGGCCAGGTGTTAAAACTTGACAGTATGTGAACAGCTGAAGTCTCAGCCGAGGCCAGCATGGCTTTTATTCAGGATCC	NM_178189.4:2413
Hist1h2ag	NM_178186.2	222-321	CGGGCAACGCGGCCCGCGACAACAAGAAGACGCGCATCATCCCGCGCCACCTGCAGCTGGCCATCCGCAACGACGAGGAGCTCAACAAGCTGCTGGGCCG	NM_178186.2:221
Hist1h2bb	NM_175664.2	39-138	TTGTGTGTCTTCTTTTGAACAGAATGCCAGAGCCTTCTAAGTCTGCACCAGCCCCTAAGAAGGGATCTAAGAAAGCCATCTCTAAGGCGCAGAAGAAGGA	NM_175664.2:38
Hist1h2bf	NM_178195.1	55-154	GTGACCAAGGCCCAGAAGAAGGACGGCAAGAAGCGCAAGCGCAGCCGCAAGGAGAGCTACTCGGTGTACGTGTACAAGGTGCTGAAGCAAGTGCACCCCG	NM_178195.1:54
Hist1h3b	NM_178203.1	122-221	GCTACCGTCCCGGCACCGTGGCGCTGCGCGAGATCCGGCGCTACCAGAAGTCGACCGAGCTGCTGATCCGCAAGCTGCCGTTCCAGCGCCTGGTGCGCGA	NM_178203.1:121
Hist1h3c	NM_175653.1	367-466	GCCAAGCGTGTCACCATCATGCCCAAGGACATCCAGCTCGCCCGCCGCATCCGCGGAGAGAGGGCATAATGGTTTTTATGCTATTTAAAAAAAGGCTCTT	NM_175653.1:366
Hist1h4f	NM_175655.1	36-135	CAAAGGCGGCGCTAAGCGCCACCGTAAGGTTCTTCGCGATAACATCCAGGGCATCACCAAGCCCGCCATCCGCCGCCTGGCCCGGCGCGGAGGAGTGAAG	NM_175655.1:35
Hist4h4	NM_175652.2	806-905	TTTCTCAGCTGTAGCTGTTTCTCTGCCTTAAGCACGTGGGTTTGGGGGAAGAGGAGCACTCGGATGTCTACCATTTAGTTCAGGCTGGTATAAGTCTTTC	NM_175652.2:805
Hmgn1	NM_008251.3	836-935	CCCTTGCCCTGTCAGAACTGTGATGTCTGTGGTCATGGCAGTCCATTTTCCTAACAGTTGTGATAATGTGCTGTGAAAGATGGAAGTCCTGAGTCTGTTC	NM_008251.3:835
Hmgb2	NM_008252.3	1668-1767	ATGTGTTGGGAAACTTGTGTAGATGTTGAAAGTAGTTATACCAGGCTGGGTGTGGTGGCAGGTACATGCAATCCCAGAGTGGAAGGTAGAGAGAGGGCAG	NM_008252.3:1667
Pcna	NM_011045.2	591-690	AGACCTTAGCCACATTGGAGATGCTGTTGTGATATCCTGTGCAAAGAATGGGGTGAAGTTTTCTGCAAGTGGAGAGCTTGGCAATGGGAACATTAAGTTG	NM_011045.2:590
Rad51	NM_011234.4	287-386	CAGCCTATTTCACGGTTAGAGCAGTGTGGCATAAATGCCAATGATGTGAAGAAATTAGAAGAAGCCGGTTACCATACAGTGGAGGCTGTTGCTTATGCAC	NM_011234.4:286
Ercc8	NM_028042.3	1895-1994	ACTCAAACTGAATGGCTTCATGTAATCGAGCCTCTTCTCCCTCATATTGAATGTTAGCCACTCATGCATCTTGCAGTGTGAACATCGTATCACATAGGCA	NM_028042.3:1894
Fen1	NM_001271614.1	1881-1980	TAGTACTGACCAGCTGATTTTTGTGGGCAGAAATTTGAACTTGCTGCCTGCTGAGTCCAGTAGTTGTGCAGGGAGTGAGATGGCAGTGTTTAAGTTTTGA	NM_001271614.1:1880
Lig1	NM_001083188.1	1457-1556	TACTATTTCTGGAGTCTTCACCAAATTCTGTGACATTGCCCGGCTCACTGGCAGTGCTTCCATGGCCAAGAAGATGGACATTATCAAGGGCCTTTTTGTT	NM_001083188.1:1456
Ercc2	NM_007949.4	1801-1900	TCTGCTCTCAGTGGCTCGGGGCAAAGTATCAGAAGGGATTGACTTTGTACACCACTACGGACGGGCTGTGATCATGTTTGGAGTTCCCTATGTCTATACC	NM_007949.4:1800
Alkbh3	NM_026944.1	1069-1168	CAGAAAGCGTGGTGTTTGCTTCTCAGGTTCTACTCCTCCTGAATGAGAGCTGCCAGCACGTCACCTTGTCAACATGTCTACTACAGGAACACTTACTTTG	NM_026944.1:1068
Ccnh	NM_023243.2	961-1060	GACTATGTGTCAAAGAAACCCAAACAGGAAGAGGAGGAATGGACTGATGACGACCTGGTAGATTCTCTCTAACCATAATAAATGACCGCAGCAGTACTTA	NM_023243.2:960
Polr2b	NM_153798.2	1091-1190	CGGTTCAAGAGGGGCAAAGCCTGGTGTTACTAAGGAGAAAAGAATTAAATATGCAAAAGAAGTCTTACAGAAAGAAATGCTCCCTCACGTTGGTGTCAGT	NM_153798.2:1090
Rfc2	NM_020022.2	979-1078	ATTTTCCGAGTCTGCAAAACCTTCCCGATGGCTGAATACTTGAAACTGGAGTTCATCAAGGAGATTGGATACACTCACATGAAAGTGGCGGAAGGAGTGA	NM_020022.2:978
Rpa1	NM_026653.2	931-1030	GCGCCCTGAAGATCGCTAACAAACAGTTCTCCGCTGTTAAAAATGACTATGAGATGACCTTCAATAATGAGACTTCTGTCCTTCCCTGTGAAGATGGCCA	NM_026653.2:930
Rpa2	NM_011284.3	501-600	TCCAGAACAAAAAGAGCTTGGTGGCCTTTAAGATCATTCCTCTGGAAGACATGAATGAGTTCACCGCACACATCCTGGAAGTGGTCAATTCACACATGAT	NM_011284.3:500
Rfc5	NM_028128.1	313-412	AATGCTTCTGACGACCGAGGGATCGATATTGTTCGGGGGCCAATCCTCAGCTTTGCCAGCACAAGGACAATCTTCAAGAAAGGGTTTAAGCTTGTGATCC	NM_028128.1:312
Pole	NM_011132.2	824-923	CTTTTCCTGTGGAAATCACCCGACGAGATGATCTTGTTGAACGACCTGACCCTGTGGTTTTGGCATTTGACATCGAGACGACCAAACTGCCTCTCAAATT	NM_011132.2:823
Ogg1	NM_010957.4	169-268	TCACTTGTGTGCGAGGCTTTAGGACTTGGGAAAGTCGAGTTCTGATTGGACAGTGCCGTAATGGGCTGGGGCTGCTAGCCGAATGTTATTCCGTTCCTGG	NM_010957.4:168
Ercc3	NM_133658.1	556-655	AAGGTCAAGCTGGTCCTCAAGCACAACAGGTACTTTGTTGAAAGTTCCCACCCTGATGTTATCCAGCATCTTCTTCAAGACCCAGTGATCCGGGAATGTC	NM_133658.1:555
Alkbh2	NM_175016.2	631-730	CACGTTTTCTGGTCTTACCCTGACACCAAAGCCCTGGGTTCCTGTTCTAGAGCGTGTTCGAGATCGAGTCTGCGAGGTGACAGGACAGACCTTCAACTTT	NM_175016.2:630
Atr	NM_019864.1	4393-4492	AGGAGTTGCTTTCTATTTATGACTGTAGAGAGATGCAGAGCAATGGCCCAGGTTACCAGTTGTGGAAAAGATTCCCTGAGCATGTCCGGGAAATATTAGA	NM_019864.1:4392
Polr2l	NM_025593.1	349-448	AAGTCCTGTTACCCTGGAAGGAACTGTTTAGTAAAGATGTTTGCAGAACCACCAACAGGTCTAACTTCCAAGGTGCTCCATGTCCATGTCTGTGCTGTCT	NM_025593.1:348
Palb2	NM_001081238.1	2571-2670	GCTGGTGCTAAGGAGCCATGTATCGTAACTGCTTGTGAAGATGTAGTTTCTCTTTGGAAACCCTTGAATTCTCTGCAGTGGGAGAAAGTTCATACCTGGC	NM_001081238.1:2570
Apex1	NM_009687.2	290-389	AAACCTCACCCAGTGGCAAATCTGCCACACTCAAGATATGCTCCTGGAATGTGGATGGGCTTCGAGCCTGGATTAAAAAGAAAGGTTTGGATTGGGTAAA	NM_009687.2:289
Nthl1	NM_008743.2	35-134	GCGGGGCTGCTCGGAGGAGTAGTTTACAGCCCAGGCATGAACTCAGGGGTGCGGATGGTGACTCGCAGTCGGAGCCGCGCGACTAGGATCGCGTCGGAAG	NM_008743.2:34
Rad21	NM_009009.4	1217-1316	GATTGTTGACAGTGTCAAAGAATTGGATAGTAAGACCATTAGAGCCCAGCTTAGCGATTATTCTGATATTGTTACGACTCTGGACCTGGCTCCGCCAACC	NM_009009.4:1216

Supplementary Table 11. Primers used for V(D)J rearrangement PCR analysis.

Primer	5' to 3' sequence
Cμ 5'	TGGCCATGGGCTGCCTAGCCCGGGACTT
Cμ 3'	GCCTGACTGAGCTCACACAAGGAGGA
Jh4	TCCCTCAAATGAGCCTCCAAAGTCC
Dh	TTCAAAGCACAATGCCTGGCT
Vh558	CGAGCTCTCCARCACAGCCTWCATGCARCTCARC
Vh7183	CGGTACCAAGAASAMCCTGTWCCTGCAAATGASC
Vκ	GGCTGCAGSTTCAGTGGCAGTGGRTCWGGRAC
Jκ	ATGCGACGTCAACTGATAATGAGCCCTCTCC
V1λ	GCCATTTCCCCAGGCTGTTGTGACTCAGG
Jλ	ACTCACCTAGGACAGTCAGCTTGGTTCC