Supplemental Table S1. miR sequencing of double negative (DN) thymocytes.

DN thymocytes

miRNA	***Lin28b*/WT ratio**	**counts in WT DN cells**	**miRNA**	***Lin28b/WT ratio***	**counts in WT DN cells**
mmu-miR-449c	0.224	61	mmu-miR-139-5p	7.93	1117
mmu-miR-99a	0.247	1059	mmu-miR-542-5p	5.76	12
mmu-let-7i	0.251	55414	mmu-miR-598	4.77	12
mmu-miR-92b	0.264	258	mmu-miR-542-3p	4.46	332
mmu-let-7f	0.275	301860	mmu-miR-450b-3p	4.26	22
mmu-miR-98	0.312	3107	mmu-miR-223	3.98	3333
mmu-miR-20b	0.320	55202	mmu-miR-342-3p	3.95	10761
mmu-let-7g	0.321	89285	mmu-miR-338-3p	3.83	29
mmu-let-7d	0.324	21203	mmu-miR-139-3p	3.79	213
mmu-miR-126-3p	0.332	4850	mmu-miR-135a	3.64	7
mmu-miR-362-5p	0.338	611	mmu-miR-677	3.44	9
mmu-miR-128	0.360	18729	mmu-miR-195	3.39	37
mmu-miR-106a	0.361	12355	mmu-miR-196a	3.23	76
mmu-miR-196b	0.383	2179	mmu-miR-450b-5p	3.20	37
mmu-miR-671-3p	0.392	116	mmu-miR-669f	3.13	217
mmu-let-7b	0.393	158465	mmu-miR-365	3.08	18
mmu-miR-181b	0.397	92406	mmu-miR-450a-5p	3.02	114
mmu-miR-181d	0.398	15847	mmu-miR-504	2.99	14
mmu-miR-126-5p	0.407	221	mmu-miR-296-5p	2.93	109
mmu-miR-18b	0.432	1383	mmu-miR-99b	2.68	1529
mmu-miR-449a	0.438	195	mmu-miR-574-5p	2.67	62
mmu-miR-181a	0.441	352044	mmu-miR-150	2.62	34939
mmu-miR-224	0.468	35	mmu-miR-200b	2.60	308
mmu-miR-708	0.470	29	mmu-miR-342-5p	2.57	1164
mmu-miR-18a	0.474	16334	mmu-miR-130a	2.57	92

Counts refer to numbers of individual sequence tags for the specified miR.
miRs with at least 25 counts in one sample and a 2-fold or greater change are reported.
Ratios were calculated using percent of totals and counts are from the wild type tissue.

Supplemental Table S2. Mutation analysis in Lin28b mice.

Sample ID	**Diagnosis**	**Tissue**	**Notch1 HD**	**Notch1 JM**	**Notch1 PEST domain**	**Notch1 del mutation**	**Bcl11b del mutation**	**Idh1 exon 3**	**Idh2 exon 4**	**Fbxw7 exon 8**	**Fbxw7 exon 9**	**Pten RT-PCR**
6145	PTCL	LN	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6168	PTCL	LN	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6179	PTCL	Sp	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6180	PTCL	LN	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6207	PTCL	LN	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6208	PTCL	LN	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6214	PTCL	LN	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6216	PTCL	LN	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6219	PTCL	Sp	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6220	PTCL	Sp	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6222	PTCL	Thy	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6230	PTCL	LN	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6235	PTCL	Sp	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6239	pre-T LBL	Thy	GL	GL	GL	N	N	GL	GL	GL	GL	GL
6348	pre-T LBL	Thy	GL	GL	**66279C>CCTCC**	N	N	GL	GL	GL	GL	GL
6412	PTCL	LN	GL	GL	GL	N	N	GL	GL	GL	GL	GL
C3	PTCL	Sp	GL	GL	GL	N	N	GL	GL	GL	GL	GL

LN: lymph node, Sp: spleen, Thy: thymus

HD: heterodimerization domain, JM: juxtamembrane domain,

PEST: Proline/Glutmaic Acid/Serine/Threonine domain

GL, germline; N, negative

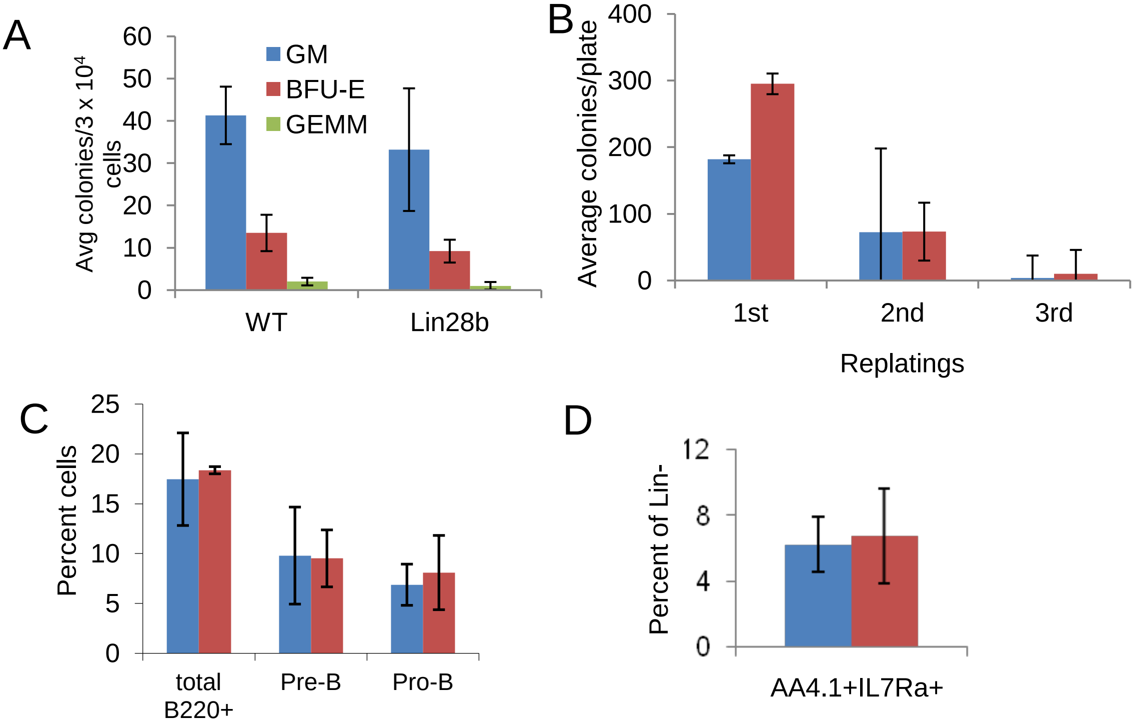
Supplemental Table S3. Upregulated genes in *Lin28b* PTCL

Gene Symbol	Average	SD
Ccl11	446.39	231.44
Ccl20	388.36	604.61
Ccl8	267.92	224.81
C4b	126.23	110.28
Ccl7	63.65	49.80
Il23r	54.53	82.22
Il7	32.66	38.22
Il1r1	32.39	17.69
Cxcl5	29.53	23.06
Cxcl1	28.08	14.92

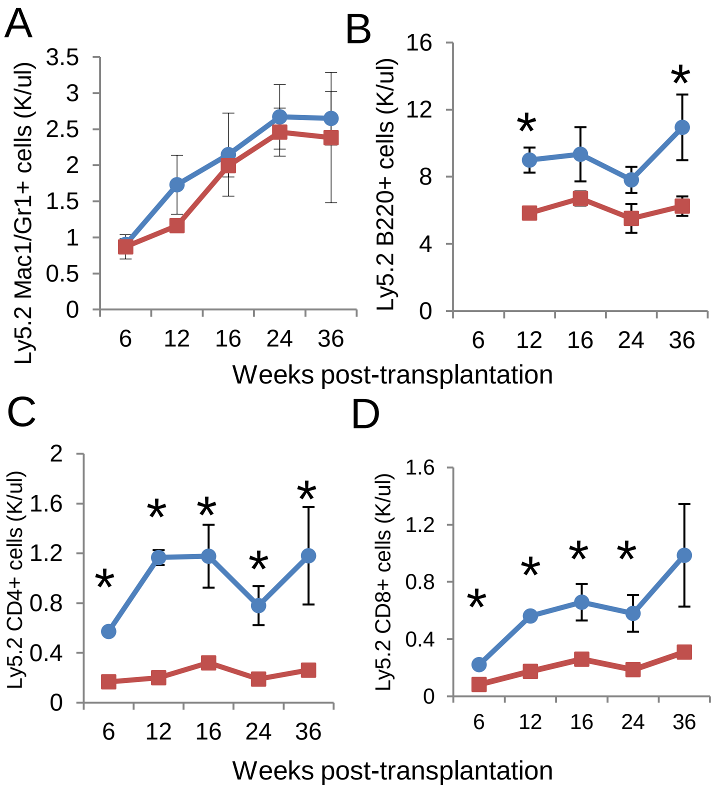
Acquired by PCR array assay (SA Bioscience) and compared with CD4+ WT splenocytes

Supplemental Table S4. Primer sequences.

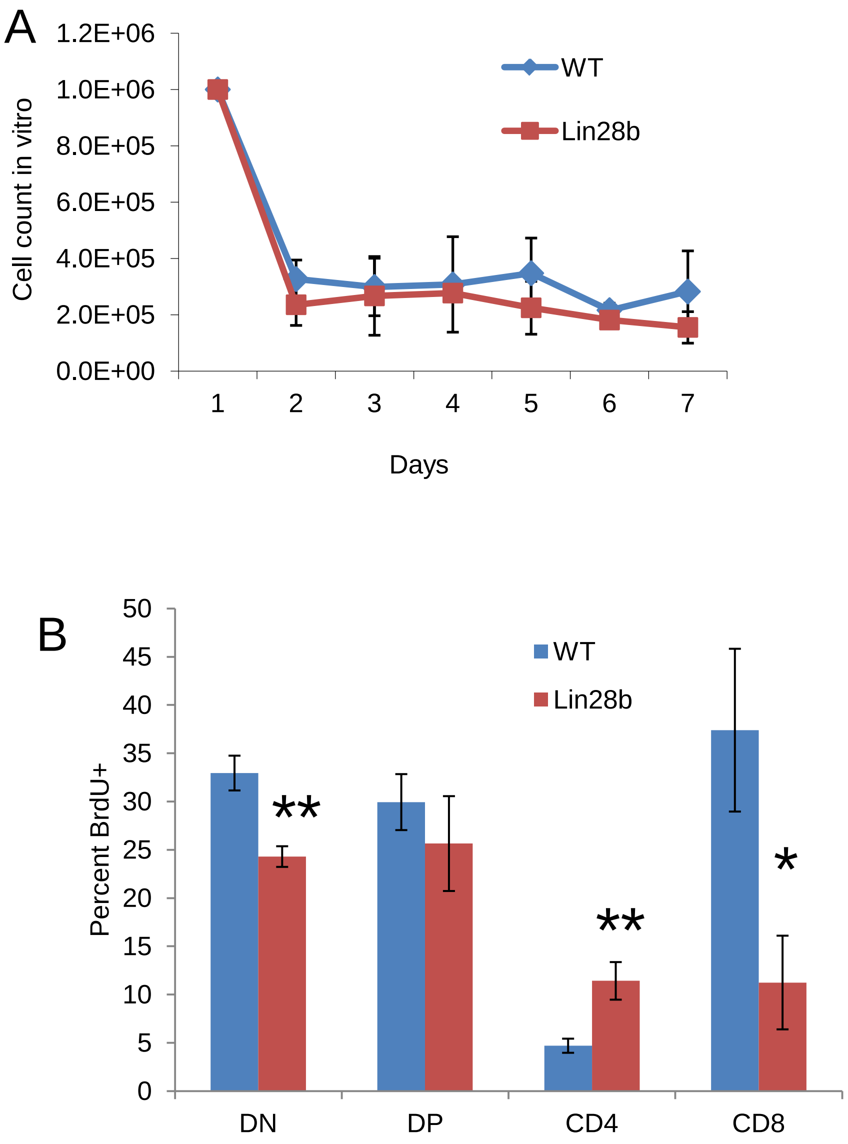
	Forward	Reverse
Lin28b transgene (Fig. 1)	5’-GGTTCAATTCGAAGTTCCTA-3’	5’- CATCCACTGGAATATCCAAGGG-3'
Transgenic *Lin28b* (Fig. 5)	5'-AGGCCTTGAGTCAATACGGGTAAC-3'	5'-TCACTGCATTCTAGTTGTGGTTTG-3'
Endogenous *Lin28b*	5'-AGGCCTTGAGTCAATACGGGTAAC-3'	5'-GTTCCTCAGCAGTAGTTAACATCC-3'
Lin28a	5'-GCATCTGTAAGTGGTTCAACGTG-3'	5'-ACTCCCAATACAGAACAACACCAC-3'
Actb	5’-GTGGGCCGCTCTAGGCACCAA-3	5’ CTCTTTGATGTCACGCACGATTTC-3’
Notch1 HD1	5'-GGCTGAGTTTCTTTAGAGTC-3'	5'-CCTCCCCTGAGGTTACACCT-3'
Notch1 HD2	5'-GAGTGTCCCATTGCGGGGCT-3'	5'-TGCAGAGGTCAGAAAGTGTT-3
Notch1 JM	5’-GTGCAGGAGAGAATTTAGCG-3’	5’-TACATGCAGAAGGGCTTAGG-3’
Notch1 PEST domain	5'-GCCTCTGGAATGTGGGTGAT-3'	5'-TACCAGGGCCTGCCCAACAC-3'
Notch1 PEST domain	5’-AAGGACCTCAAGGCACGGAG-3’	5’-GAGGTGTGGCTGTGATGGTG-3’
Notch1 5' deletion	5’-ATGGTGGAATGCCTACTTTGTA-3’	5’-CGTTTGGGTAGAAGAGATGCTTTAC-3’
Bcl11b internal deletion	5'-GGCTGAATTTACAGGATGAGG-3'	5'-ACTGGAGTTTCCGATGGCC-3'
IDH1 exon3	5'-GTCCAGCAAGCTCTGCGTGCAGG-3'	5'-ACCTCTCTTAAGGGTGTAGATGC-3'
IDH2 exon4	5'-TCCCTCCTCCGGGATGACTTCTGGGGC-3'	5'-TCAAGCCAAGGCTTCCTGTGGGGAGC-3'
FBXW7 exon8	5'-GTGATGGTGTCAGATAGCATTGG-3'	5'-CTGCACTATATCCTTAGTGTCC-3'
FBXW7 exon9	5'-TGGCCAGTTGATCTCCAAGTCTTCC-3'	5'-CAGCAACTTGACAGTAACTGAGG-3'
PTEN RT-PCR	5'-AGCTTCTGCCATCTCTCTCC-3'	5'-AATCTGACACAATGTCCTATTGCC-3'



Supplemental Figure S1. A) CFU assay after 10 days, n= 3 mice per genotype at 2-3 months of age and 2 plates/mouse with an initial plating of 3 x 10^4 bone marrow cells in M3434. **B)** CFC replating assay once a week in semi-solid culture. N= 3/group and 2 plates/mouse from initial cultures in A. **C)** Bone marrow B cell precursors: Pre-B (B220+CD43-) and Pro-B (B220+CD43+), n= 3. **D)** Common lymphoid progenitors in mice 2-3 months old, 3 mice/group. WT, blue; *Lin28b*, red in B, C, D.



Supplemental Figure S2. **Engraftment assays show cell autonomy of lymphopenic phenotype.** 1x10^6 donor BM cells (Ly5.2) were injected into lethally irradiated syngeneic recipient mice, and engraftment was quantified for **A)** Mac1$^+$/Gr1$^+$, **B)** B220$^+$, **C)** CD4$^+$ and **D)** CD8$^+$ in the peripheral blood at the indicated time points. WT, blue; *Lin28b*, red. *, $p < 0.05$.



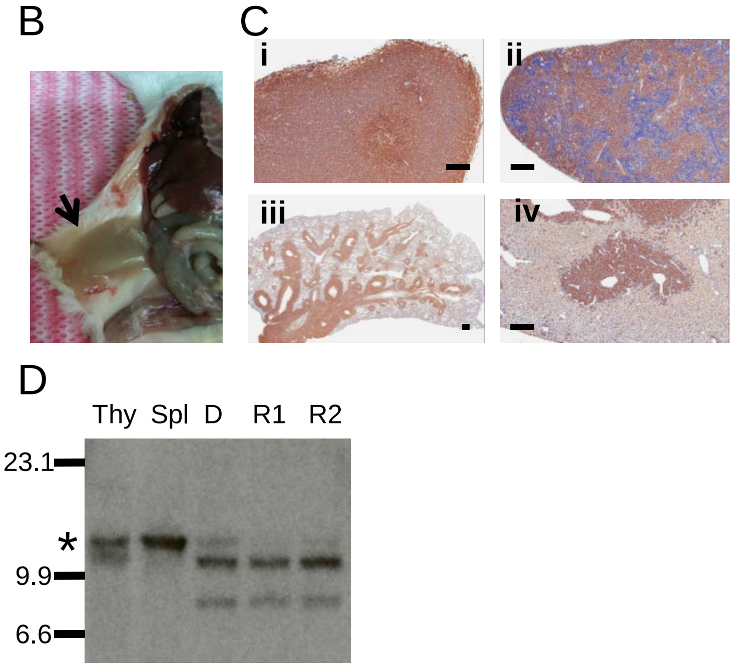
Supplemental Figure S3. **Proliferation studies of thymocytes.** **A)** 1×10^6 thymocytes plated in vitro at Day 1 and live cells counted on subsequent days by trypan blue exclusion. **B)** BrdU positivity reported for each thymocyte subset. *, $p< 0.05$ and **, $p< 0.01$.

A

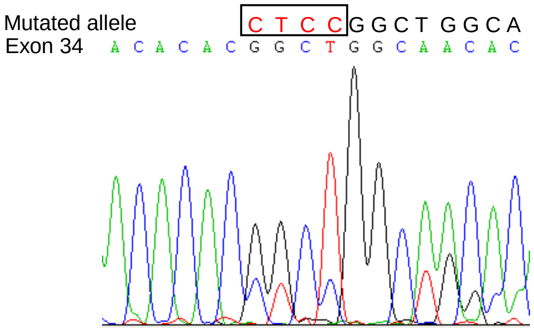
Summary of *Scid* mice injected for tumorigenicity assay

	Mice injected	Mice with tumor
WT thymocytes	3	0
Lin28b tumor cells	7	4*

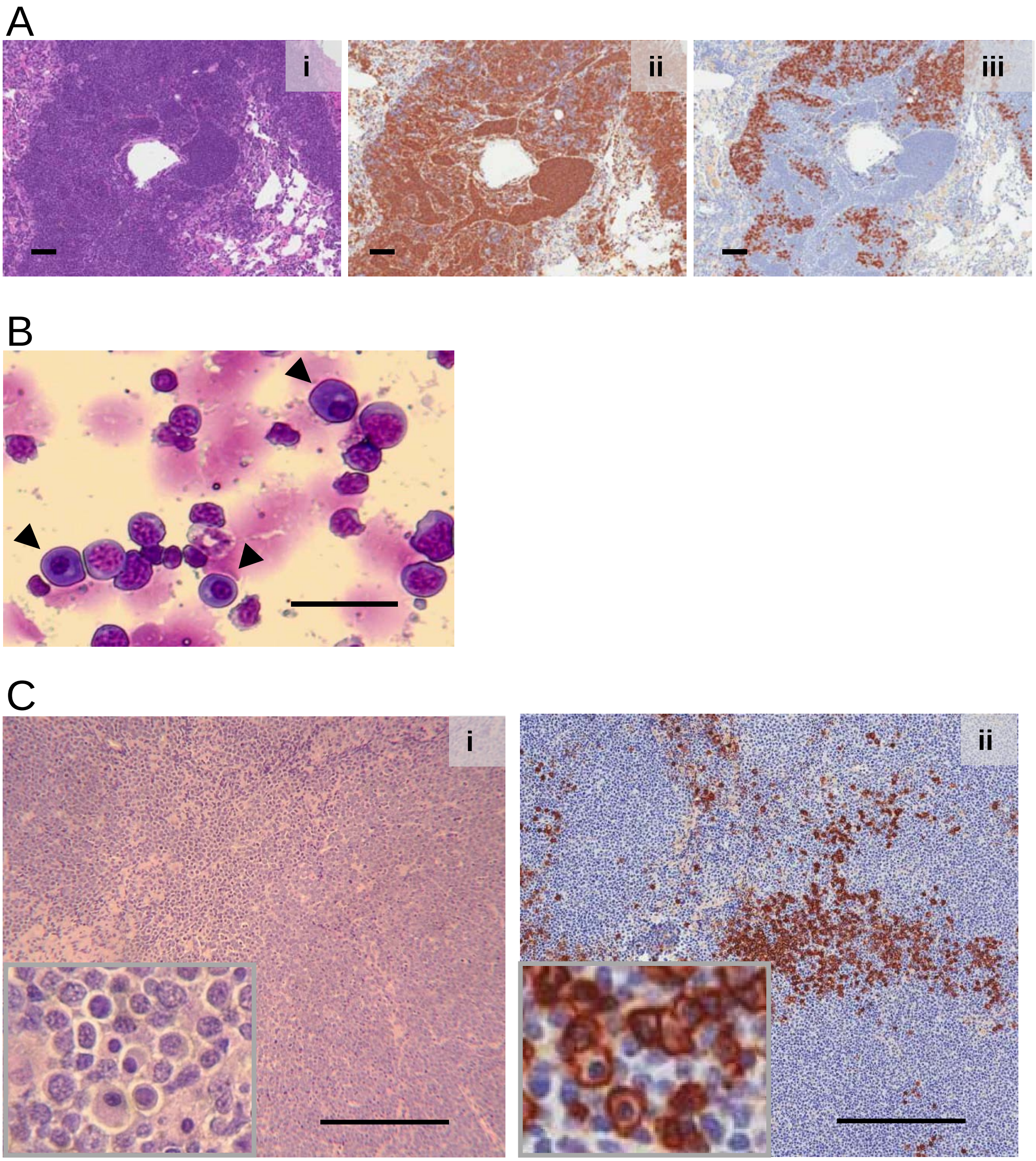
* one mouse found dead, decomposed



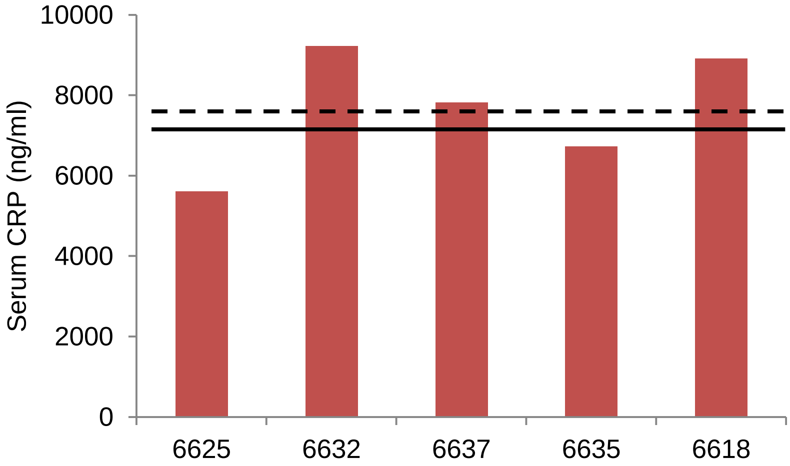
Supplemental Figure S4. ***Lin28b* tumor cells form subcutaneous tumors in *Scid* mice. A)** Summary of tumor growth in *Scid* mice. **B)** Subcutaneous tumor at injection site in *Scid* mouse recipient. **C)** CD3 staining of (i) subcutaneous tumor, (ii) spleen, (iii) lung, and (iv) liver. Scale bar = 400 µm. **D)** Southern blot reveals clonal *Tcrb* gene rearrangements. Thy, WT thymus; Spl, WT spleen; D, donor tumor 6266 from the lymph node; R1, recipient *Scid* C408; R2, recipient *Scid* C412. Samples digested with *Sst*I. * denotes germline band.



Supplemental Figure S5. ***Notch1* mutation found in a case of pre-T LBL in *Lin28b* mice.** Sequencing chromatogram of PCR product from mouse #6348. A 4 bp insertion (CTCC) within the Notch1 PEST domain leads to a frameshift, resulting in two superimposed sequences, one derived from the WT allele and one derived from the mutant allele.



Supplemental Figure S6. **Infiltration of PTCL tumor masses with B and plasma cells. A)** Lung histology for mouse 6297 shows a tumor mass of predominantly CD3+ T cells, along with a patchy infiltrate of B220+ B cells around the periphery of the tumor: i) H&E, ii) CD3 and iii) B220. Scale bar= 100µm. **B)** Plasma cells (black arrows) in a cytospin from the lymph node of mouse 6206 stained with May-Giemsa. Scale bar= 25µm. **C)** H&E (i) and CD138 (ii) stains are shown for 6206 lymph node. Scale bar= 250µm.



Supplemental Figure S7. C-reactive protein levels in 5-8 month old *Lin28b* mice. Solid line, mean (7160ng/ml) for age-matched WT serum samples, n=5. Dashed line, 1 standard deviation above the WT mean.