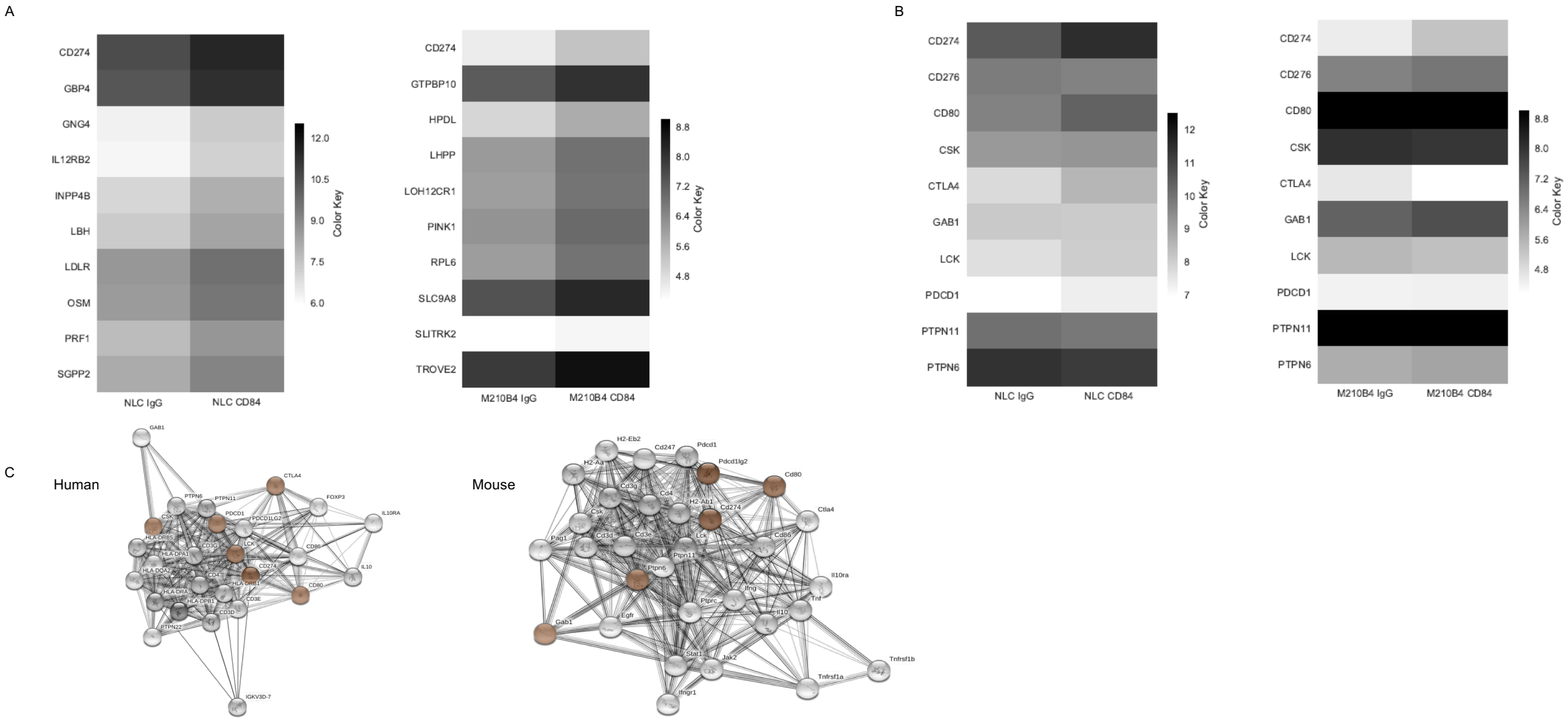

Fig S1- CD84 activation increases PD-L1

(A) Nurse like cells (NLC) or M210B4 cells were stimulated with anti-CD84 (5 mg/ml) or control IgG antibodies. Thereafter RNA was purified and analyzed by Affymetrix Human Gene 1.0 ST or Affymetrix Mouse Gene 2.0 ST, respectively. Thereafter, ten genes were selected based on high increase with anti-CD84 compared to control IgG and their intensities displayed by heatmaps.

(B) Nurse like cells (NLC) or M210B4 cells were stimulated with anti-CD84 (5 mg/ml) or control IgG antibodies. Thereafter RNA was purified and analyzed by Affymetrix Human Gene 1.0 ST or Affymetrix Mouse Gene 2.0 ST, respectively. Thereafter, ten genes found in both mouse and human were selected based on known interaction found between PD-L1 (CD274) and other proteins from the STRING database (C) Images from STRING database displaying proteins known to interact with PD-L1 (CD274), proteins found to increase in the Affymetrix chip (B) are marked in red.

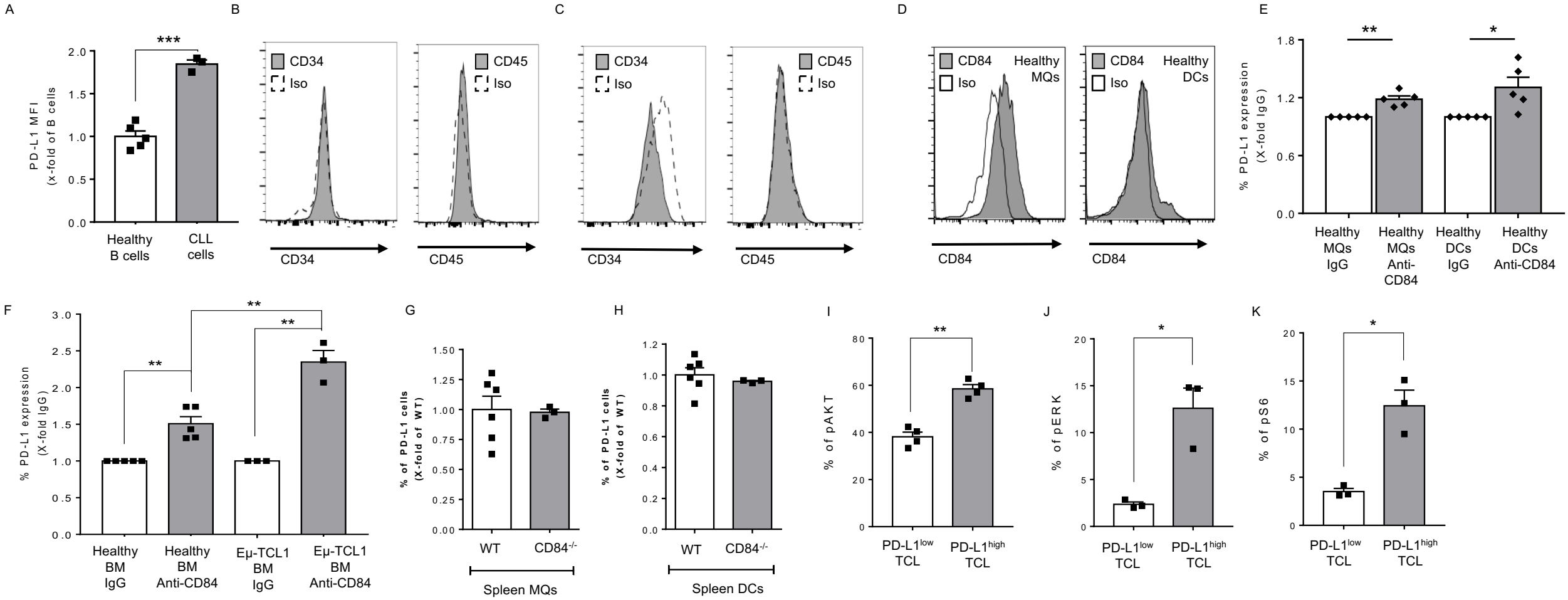

Fig S2- CD84 regulates PD-L1 expression on CLL cells and their microenvironment.
(A) CLL cells or healthy B cells were analyzed for PD-L1 expression by FACS analysis. Graph shows MFI levels of PD-L1 (n=3-5, Two tailed T-test, ***p<0,001). (B-C) Human (B) and mouse (C) adherent cells derived from bone marrow cultures stained for CD34 and CD45. Gray- staining compared to black dashed line. (D-E) Splenic MQs and DCs (D) from healthy animals were analyzed for CD84 cell surface expression, or (E) stimulated with anti-CD84 (5 mg/ml) or control IgG antibodies. PD-L1 cell surface expression was analyzed on the activated cells (n=5, Two tailed Paired T-test, *p<0.05, **p<0,01). (F) Bone marrow stromal cells were harvested from either healthy or *Eμ-TCL1* sick mice and cultured until confluent. The cells were then stimulated with anti-CD84 (4 mg/ml) for 48 hrs, and their PD-L1 expression was determined (n=3-5, One Way Anova with Holm corrected multiple comparisons, **p<0.01). (G-I) Purified splenocytes from *Eμ-TCL* mice, were gated for CD5 CD19 and PD-L1, and analyzed for pAkt (G), pS6 (H), and pERK (I) (n=3, Two tailed Paired T-test, *p<0.05, **p<0.01).

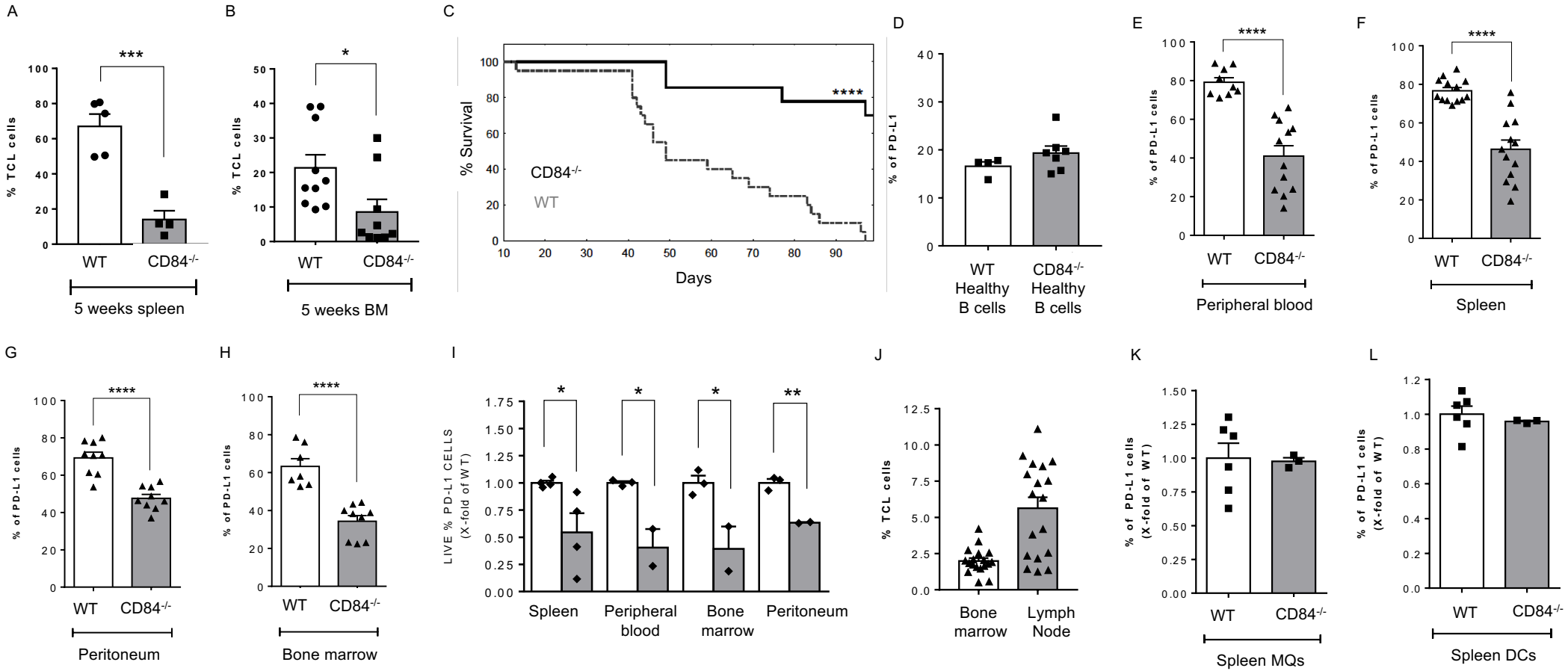

Fig S3- Decreased PD-L1 expression and elevated survival in the absence of CD84 in the tumor microenvironment.
Eμ-TCL1 splenocytes (4×10^7) were injected i.v. into the tail vein of C57BL/6 WT or *CD84*$^{-/-}$ mice. (A-B) After 5 weeks, the mice were sacrificed and the number of Eμ-TCL1 cells was determined in spleen (A) and BM (B) (n=4-10, Two tailed T-test, **p<0,01, *p<0,05). (C) Mice were monitored daily for survival. The figure displays the survival curves of *CD84*$^{-/-}$ mice compared to WT mice (n = 14-20, ****p<0.0001, Log-rank test). (D) Splenic B cells from healthy WT and *CD84*$^{-/-}$ mice were stained for PD-L1 expression (n=4-7, Two tailed T-test, p=0.2194). (E-I) Eμ-TCL1 splenocytes (4×10^7) were injected i.v. into the tail vein of C57BL/6 WT or *CD84*$^{-/-}$ mice. After 14-21 days, the mice were sacrificed and the percentage of PD-L1 positive cells was analyzed in WT and CD84-/- in peripheral blood (E), spleen (F), peritoneum (G), bone marrow (H) (n=7-11, Two tailed T-test, ****p<0,0001), and in the live Annexin-V and 7AAD negative population (I) (n=2-4, Two tailed T-test, **p<0,01, T-test, *p<0,05). (J) Percentage of Eμ-TCL1 cells in BM and spleen at 21 days after i.v. injection of Eμ-TCL1 splenocytes (n=17-18). (K-L) Expression of PD-L1 on splenic monocytes and DCs derived from healthy WT and *CD84*$^{-/-}$ mice (n=3-6).

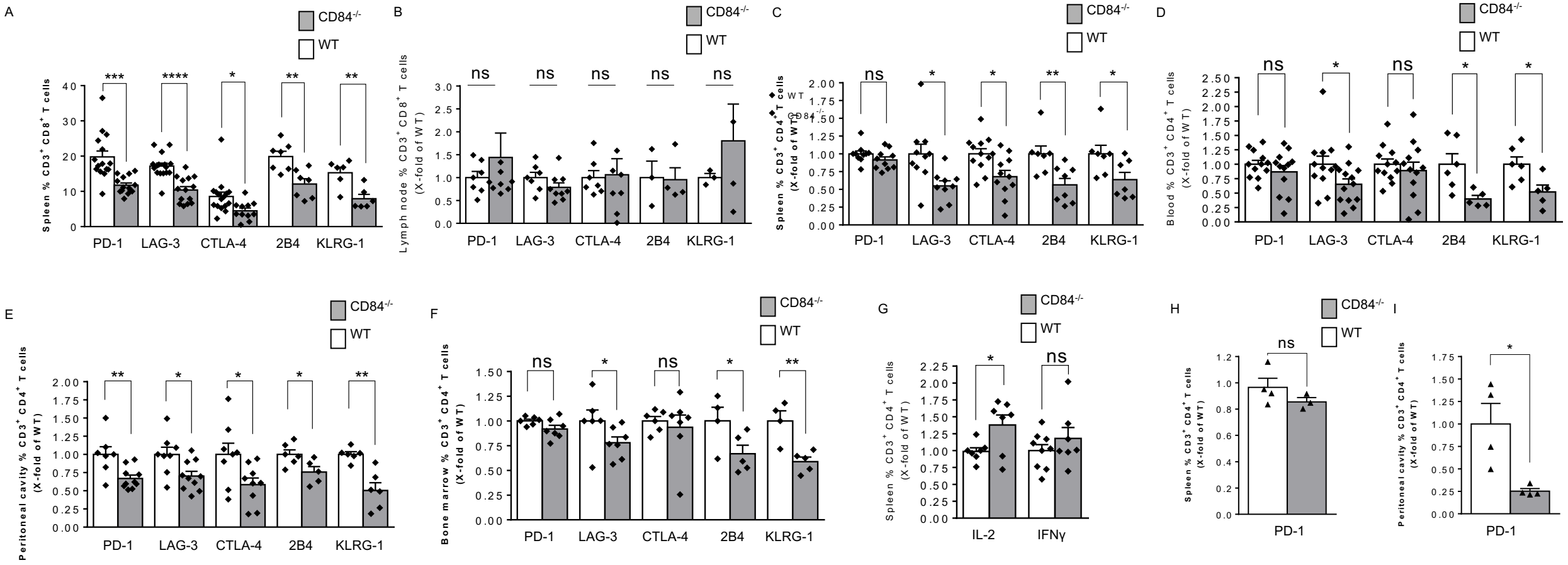

Fig S4-Reduction in exhausted T cell phenotype in the *CD84-/-* environment.
(A-F) Eμ-TCL1splenocytes (4×10^7) were injected i.v. into the tail vein of C57BL/6 WT or *CD84-/-* mice. After 14-21 days, the mice were sacrificed. (A-B) Percent of PD-1, Lag-3, CTLA-4, 2B4, and KLRG-1 positive CD8 T cells in (A) spleen (n=6-11, Two tailed T-test, ****p<0,0001, ***p<0,001, **p<0,01, *p<0,05) and (B) lymph node (n=3-9). (C-F) Expression of the exhaustion markers PD-1, Lag-3, CTLA-4, 2B4 and KLRG1 was determined on CD4 in (C) spleen (n=6-11, Two tailed T-test, ns = not significant ,*p<0,05, **p<0,01), (D) peripheral blood (n=5-11, Two tailed T-test, ns p =, *p<0,05, ns p =), (E) peritoneal cavity (n=6-10, Two tailed T-test, *p<0,05, **p<0,01) and (F) bone marrow (n=4-7, Two/One Tailed T-test, ns = not significant, *p<0,05, ns = not significant, **p<0,01). (G) Splenic cells were cultured for 24 hrs with anti-CD3, and in the last 2 hours of culture with brefeldin-A. CD4 T cells were then analyzed for IFNγ and IL-2 (n=7-8, Two tailed T-test, *p<0,05, ns = not significant). (H-I) BM cells (5×10^6) derived from 8-week-old *Eμ-TCL1* mice or negative control littermates (WT) were injected into lethally irradiated C57BL/6 (WT) or CD84-deficient (*CD84*$^{-/-}$) mice. After 6 months, mice were killed, and the expression of PD-1 was determined on CD4 T cells in the spleen (H) and peritoneum (I) (n=3-4, Two tailed T-test, *p<0,05, ns = not significant).

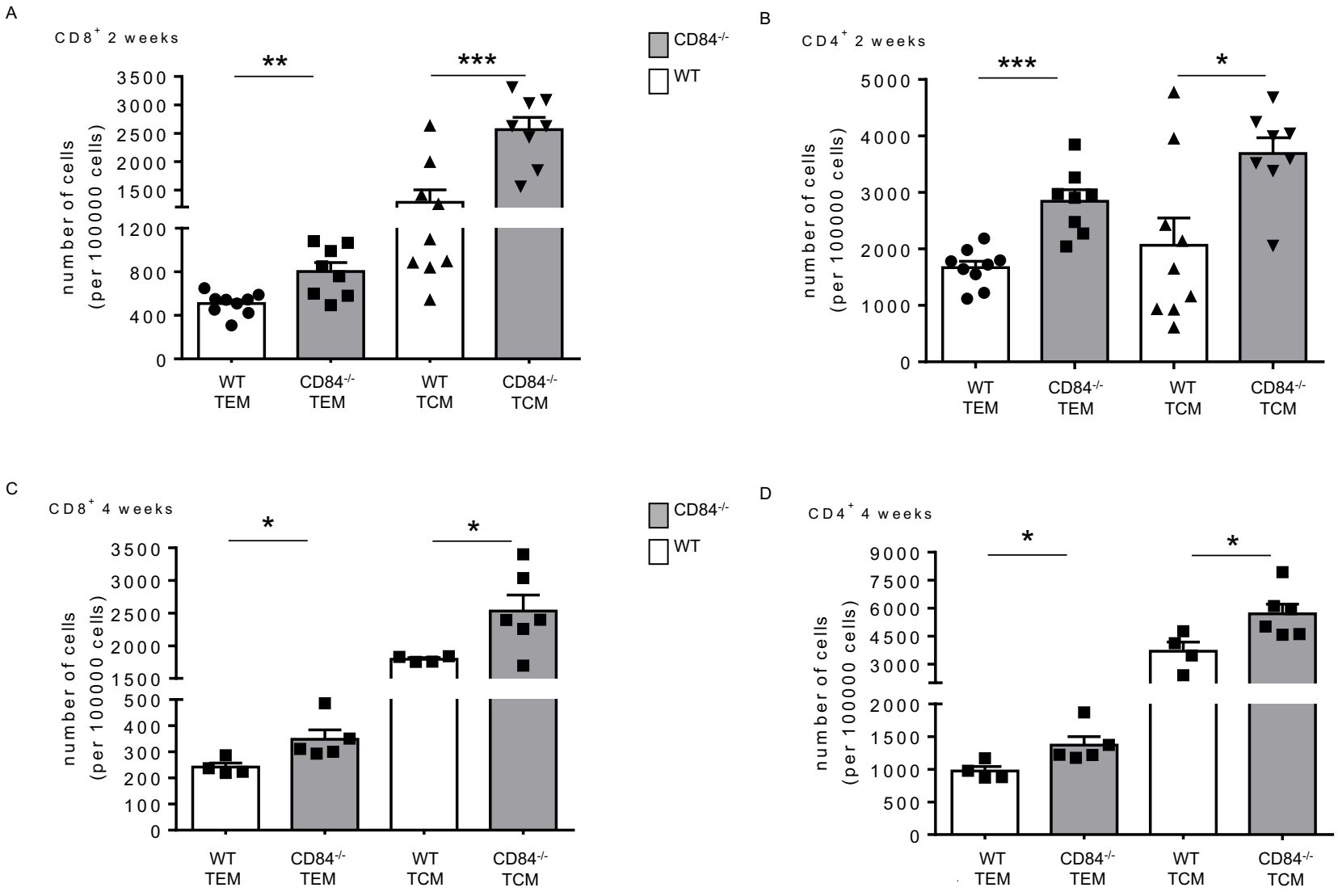

Fig S5- The TEM and TCM populations are increased in the CD84-/- environment.
Eμ-TCL1splenocytes (4 × 10^7) were injected i.v. into the tail vein of C57BL/6 WT or CD84-/- mice. After 14 (A-B), or 28 (C-D) days, the mice were sacrificed. Splenocytes were analyzed for CD8 (A,C), and CD4 (B,D). The number of TEM (CD44+, CD62L-) and TCM (CD44+, CD62L+) was determined by flow cytometry (n=4-9, Two tailed T-test, *p<0.05, **p<0.01, ***p<0.001).

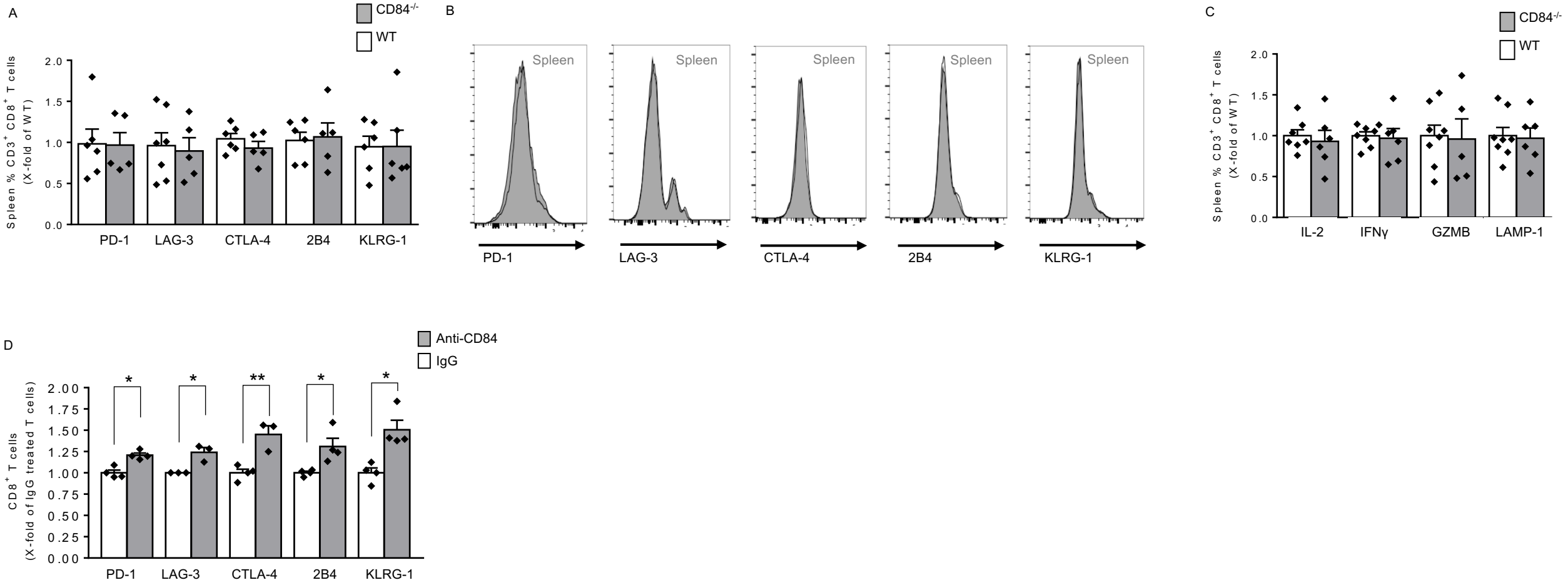

Fig S6-WT and *CD84-/-* CD8 T cells respond similarly to activation.
(A-C) Healthy CD84$^{-/-}$ and WT splenic cells were cultured for 24 hrs with anti-CD3 and in the last 2 hours of culture with brefeldin-A. CD8 T cells were stained for the (A-B) exhaustion markers: PD-1, Lag-3, CTLA-4, 2B4, KLRG-1, and (C) the cytokines/cytotoxic markers: IFN-g, IL-2, Granzyme B, and LAMP-1 (n=6-8). (D) Enriched splenic T cells from Eμ-TCL1 sick mice were stimulated with anti-CD84 antibody and stained for CD8 and PD-1, LAG-3, CTLA4, 2B4 and KLRG-1 (n=3-4, Two tailed Paired T-test, *p<0.05, **p<0.01).

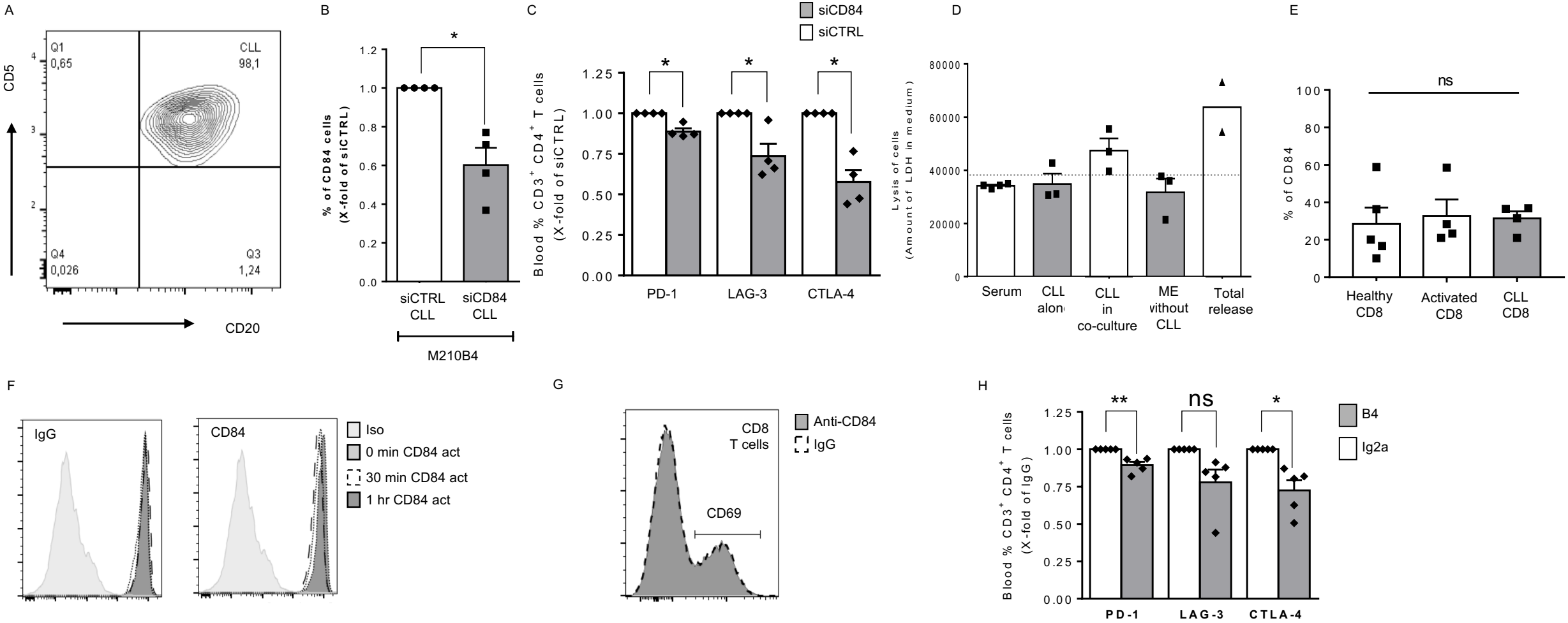

Fig S7- CD84 regulates PD-L1 and T cell function in human CLL patients.
(A) Lymphocytes from whole CLL blood samples were purified by Ficoll gradient, and CLL cells were then isolated using CD19 beads. (B) Purified CLL cells were treated with siCD84 or siCTRL and cultured for 24 hrs; a 48 hr co-culture was then established M210B4 cells. CD84 expression on M210B4 derived from the co-culture was analyzed by FACS analysis (n=4, Two tailed Paired T-test, p<0,05). (C) CD4 T cell expression of PD-1, Lag3 and CTLA-4 following co-culture with siCD84 treated CLL or siCTRL treated CLL (n=4 , Two tailed Paired T-test, *p<0,05). (D) Amount of lysed cells, measured by LDH release in medium in the different culture conditions (ME = microenvironment, medium was replaced for all conditions 24 hrs after treatment with siRNA). (E) CD84 expression was determined on healthy, healthy activated (CD3, CD28) and CLL derived purified human T cells (CD3 beads) (n=4-5, Two tailed T-test,, ns p = non significant). (F-G) Purified T cells were stimulated with anti-CD84 or a control antibody IkB (F) and CD69 (G) expression levels were determined (histograms representative of n=2-3 independent experiments). (H) Lymphocytes from whole CLL blood samples were purified by Ficoll gradient, and CLL cells were then isolated with CD19 beads and treated with the B4 antagonistic CD84 antibody or control IgG2a, and cultured for 24 hrs; a 48 hr co-culture was then established with the non-CLL population. Graph shows CD4 T cell expression of PD-1, Lag3 and CTLA-4, following co-culture with B4 treated or IgG2a treated CLLs (n=5, Two tailed Paired T-test, **p<0,01, *p<0,05, ^{ns} p = 0,06).

Patient	Age	Sex	Binet	WBC[a] K/ul	State of disease	previous therapy	IGHV[a, c]	CD38%[a,b]	ZAP70[c]	FISH[d]	Figure
1	74	F	Rai III	90	progressive	no	1.5y	1	0	ND	1A
2	68	M	A	24.9	stable	no	ND	0	ND	ND	1A
3	62	F	B	99	Progressive	no	U	83	ND	ND	1A
4	57	M	A	142	Progressive	ND	ND	ND	ND	ND	1B, 6D, 6F, 2C, 2D, 2E
5	84	M	A	35	Stable	ND	ND	8	ND	ND	1B, 6E, 6G, 6A, 2I, 6L, 6J
6	61	M	Rai II	173	Progressive	no	6m	11%	11%		1B
7	70	M	C	156	Progressive	COP-R	ND	78	ND	ND	1B
8	50	M	C	99	Progressive	FCR	ND	ND	ND	N/A	1C
9	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	1C
10	69	M	C	110	Stable	Chlorambucil + Rituximab	ND	ND	ND	13q- 65% 11q- 98%	1C, 1F, 6E, 6G, 6I
11	72	F	A	55.5	Indolent	No	ND	ND	ND	N/A	1C, 1D, 1G, 6A, 6B,
12	81	M	B	149.6	Chlorambucil + Rituximab	Progressive disease	ND	ND	ND	N/A	1C, 1F, 1G, 6F
13	82	M	A	30,5	Indolent course	No	ND	ND	ND	N/A	6B, 6C
14	85	M	A	27.4	Indolent course	No	ND	ND	ND	N/A	6B, 6C
15	64	F	C	150	Stable	no	M	4	negative	ND	6B, 6C
16	74	M	A	62	Stable	ND	ND	27	ND	ND	6D, 6F,
17	60	F	A	101.72	Progressive	no		8	ND	ND	6D, 6F
18	69	M	Rai 0	49.7	Stable	no	14m	5	ND	ND	6D, 6E, 6F, 6G, 6I
19	63	F	A	70	Progressive	ND	ND	27	ND	ND	6G
20	60	M	C	37.7	Progressive disease	FCR, BR, Ofatumumab Ibrutinib	ND	ND	ND	Trisomy 12 17q-	6I
21	79	M	A	27,8	Indolent course	No	ND	ND	ND	N/A	7A, 7B, 7C
22	51	M	C	80	Progressive	no	U	0	ND	ND	7A, 7B, 7C
23		M	A	200	Indolent course	No	ND	ND	ND	N/A	7A, 7B
24	68	F	C	80	progressive	ND	ND	ND	3	ND	7A, 7B, 7C, 6A, 2I
25	73	M	A	43.4	Indolent, without treatment	No	NA	NA	NA	NA	6A, 2I, 2C, 2D, 2E
26	84	M	A	62	progressive	NO	U	65	n/d	trisomy 12	6A, 2I
27	52	M	C	86	progressive	NO	M	0	n/d	normal	2C, 2D
28	80	M	A	20.6	Indolent, without treatment	No	NA	0%	NA	NA	S6E
29	59	M	B	217	progressive	NO	U	0	n/d	del13q	S6E
30	64	M	B	40	progressive	NO	N/D	10	pos	trisomy 12	S6E
31	65	M	B	249	progressive	NO	U	n/d	neg	del13q	S6E, 2F
32	66	M	A	20	progressive	NO	M				6G, 6H, 6K, 6L, S1A, 6J
33	-	-	-	-	-	-	-	-	-	-	6G, 6H
34	61	M	A	83.11	stable	no	N/D	negative	N/D	t12	6G, 6H, 6K, 6L
35	62	M	A	52.86	stable	No	N/D	negative	N/D	N/D	6G, 6H
36	69	M	A	16.94	stable	No	N/D	negative	N/D	N/D	6H, 6J
37	66	M	A	52.03	stable	No	N/D	negative	N/D	N/D	6K, 6L, 6J
38	67	M	A	61.36	stable	No	N/D	negative	23	N/D	S1A
39	73	M	A	24.85	stable	No	N/D	negative	N/D	N/D	S1A
40	69		B	126	progressive	NO	U	0	n/d	trisomy 12	2F

41	70	M	A	247	progressive	NO	n/d	n/d	n/d	del17p	2F
42	65	M	A	100	stable	NO	M	0	pos	del13q	2F
43	61	F	A	24.08	stable	No	N/D	negative	N/D	N/D	6M
44	69	M	A	26.46	stable	No	N/D	positive	9	N/D	6M
45	82	M	A	25.4	stable	No	N/D	negative	N/D	N/D	6M

Supplementary table 1-Patient data

[a] Lymphocyte count at bleeding, $x10^3/\mu L$
[b] mutation status: mutated (M), unmutated (U)
[c] N/D – not determined, + positive, - negative
[d] Flouresence in situ hibridisation; N/A, not available
FCR, Fludarabine, Cyclophosphamide, Rituximab; BR, Bendamusine, Riruximab.N

Supplementary table 2- List of antibodies used

Target	Species	Fluorophore	Company	Clone
CD5	Mouse	BV421	Biolegend	53-7.3
PD-L1	Human	PE/CY7	Biolegend	29E.2A3
PD-L1	Mouse	BV711	Biolegend	10F.9G2
B220/CD45R	Human/Mouse	FITC or APC	Biolegend	RA3-6B2
CD19	Mouse	FITC/PE	Biolegend	6D5
CD19	Human	APC-CY7	Biolegend	HIB19
CD20	Human	FITC	Biolegend	2H7
CD3	Mouse	APC-CY7	Biolegend	145-2C11
CD3	Human	Pacific blue	Biolegend	UCHT1
CD4	Mouse	FITC/PERCP	Biolegend	RMA4-5
CD4	Human	FITC	Biolegend	OKT4
CD8	Mouse	BV711	Biolegend	53-6.7
CD8	Human	APC-CY7	Biolegend	HIT8a
PD1	Mouse	PE/CY7	Biolegend	29F.1A12
PD1	Human	BV711	BD Bioscience	EH12.1
Lag-3	Mouse	PE	BD Bioscience	C9B7W
Lag-3	Human	APC	Biolegend	11C3C65
CTLA-4	Mouse	APC	Biolegend	UC10-4B9
CTLA-4	Human	PE-CY7	Biolegend	L3D10
2B4	Mouse	FITC	Biolegend	m2B4.(B6)45B.1
KLRG-1	Mouse	BV421/efluor405	Biolegend/eBioescience	2F1/KLRG1
LAMP-1	Mouse	PE	Biolegend	1D48
Granzyme B	Mouse/Human	APC	Biolegend	GB11
IL-2	Mouse	PE-CY7	Biolegend	JES6-5H4
IFNgamma	Mouse	Pacific blue	Biolegend	XMG1.2
IFNgamma	Human	PE-CY7	Biolegend	B27
pAKT	Mouse/Human	-	Cell signaling	D25E6
pS6	Mouse/Human	-	Cell signaling	D57.2.2E
pERK	Mouse/Human	-	Cell signaling	D13.14.4E
Actin	Mouse/Human	-	SCBT	H-6
IkB	Mouse/Human	-	BD bioscience	25/IKBa/MAD-3
pSTAT3	Mouse/Human	-	Cell signaling	D3A7

Isotype controls were used according to the data sheets.

Supplementary Table 3: Primer Sequences

Real-Time Primers

target	species	forward primer	reverse primer
Bcl2	human	GGATCAGGGAGTTGGAAG	GCACTGCCAAACGGAG
CD84	human	TTGTTCCGTTTGTTCAAGAG	CGGAATAAACTGTGTTCACTG
PSMB2	human	AGGTTGGCAGATTCAGGATG	AGAGGGCAGTGGAACTCCTT
PD-L1	human	TGGCATTTGCTGAACGCATTT	AGTGCAGCCAGGTCTAATTGT
Bcl2	mouse	GCTACCGTCGTGACTT	GCCGGTTCAGGTACTC
Rpl32	mouse	TTAAGCGAAACTGGCGGGAAAC	TTGTTGCTCCCATAACCGATG
CD84	mouse	ATATAGCTGGAGTCCCTTTGGAG	AAAGAGCACGGCCAATCCTC
PD-L1	mouse	GAGCTGATCATCCCAGAACTGC	GACCGTGGACACTACAATGAGGA

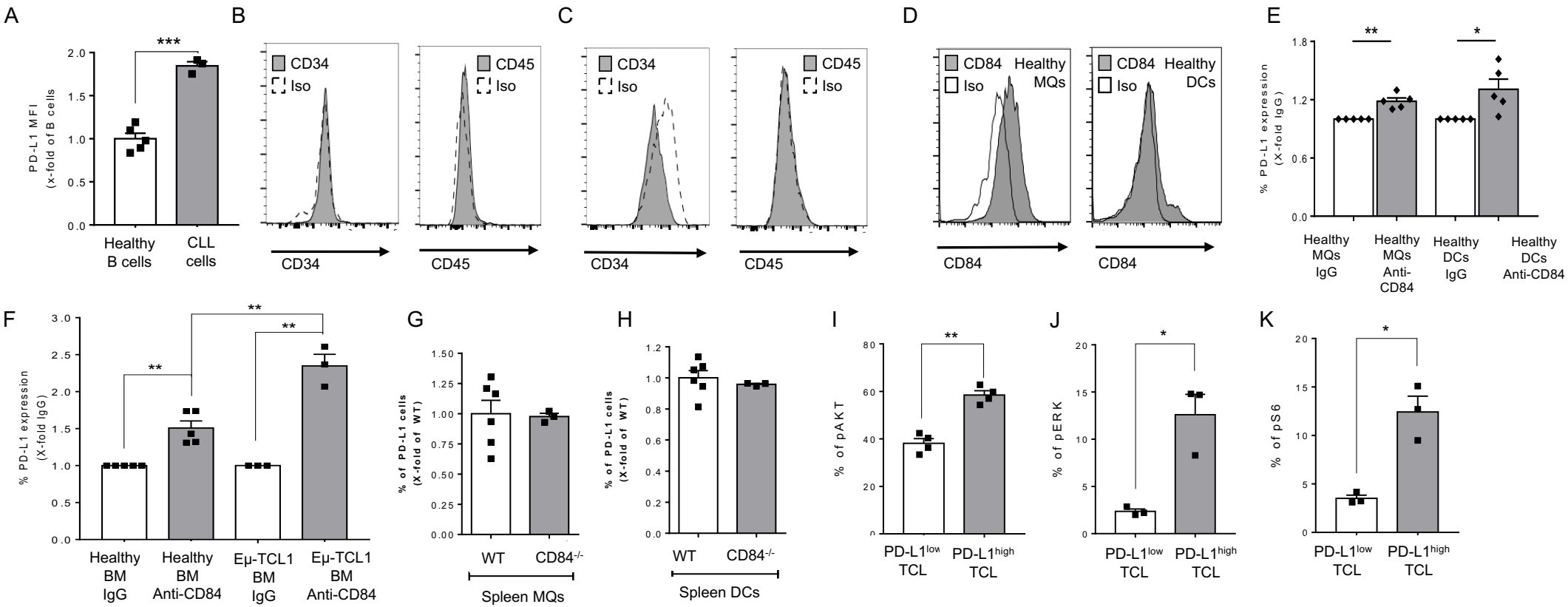

Fig S1- **CD84 regulates PD-L1 expression on CLL cells and their microenvironment. (A)** CLL cells or healthy B cells were analyzed for PDL1 expression by FACS analysis. Graph shows MFI levels of PD-L1 (n=3-5, ***p<0,001). **(B-C)** Human **(B)** and mouse **(C)** adherent cells derived from bone marrow cultures stained for CD34 and CD45. Gray- staining compared to black dashed line. **(D-E)** Splenic MQs and DCs (D) from healthy animals were analyzed for CD84 cell surface expression, or (E) stimulated with anti-CD84 (5 μg/ml) or control IgG antibodies. PD-L1 cell surface expression was analyzed on the activated cells (n=5, *p<0.05, **p<0,01). **(F)** Bone marrow stromal cells were harvested from either healthy or Eμ-TCL1 sick mice and cultured until confluent. The cells were then stimulated with anti-CD84 (4 μg/ml) for 48 hrs, and their PD-L1 expression was determined (n=3-5, **p<0.01). **(G-H)** Expression of PD-L1 on splenic monocytes and DCs derived from healthy wt and CD84-/- mice (n=3-6). **(I-K)** Purified splenocytes from Eμ-TCL mice, were gated for CD5 CD19 and PD-L1, and analyzed for pAkt (G), pS6 (H), and pERK (I) (n=3, *p<0.05, **p<0.01).

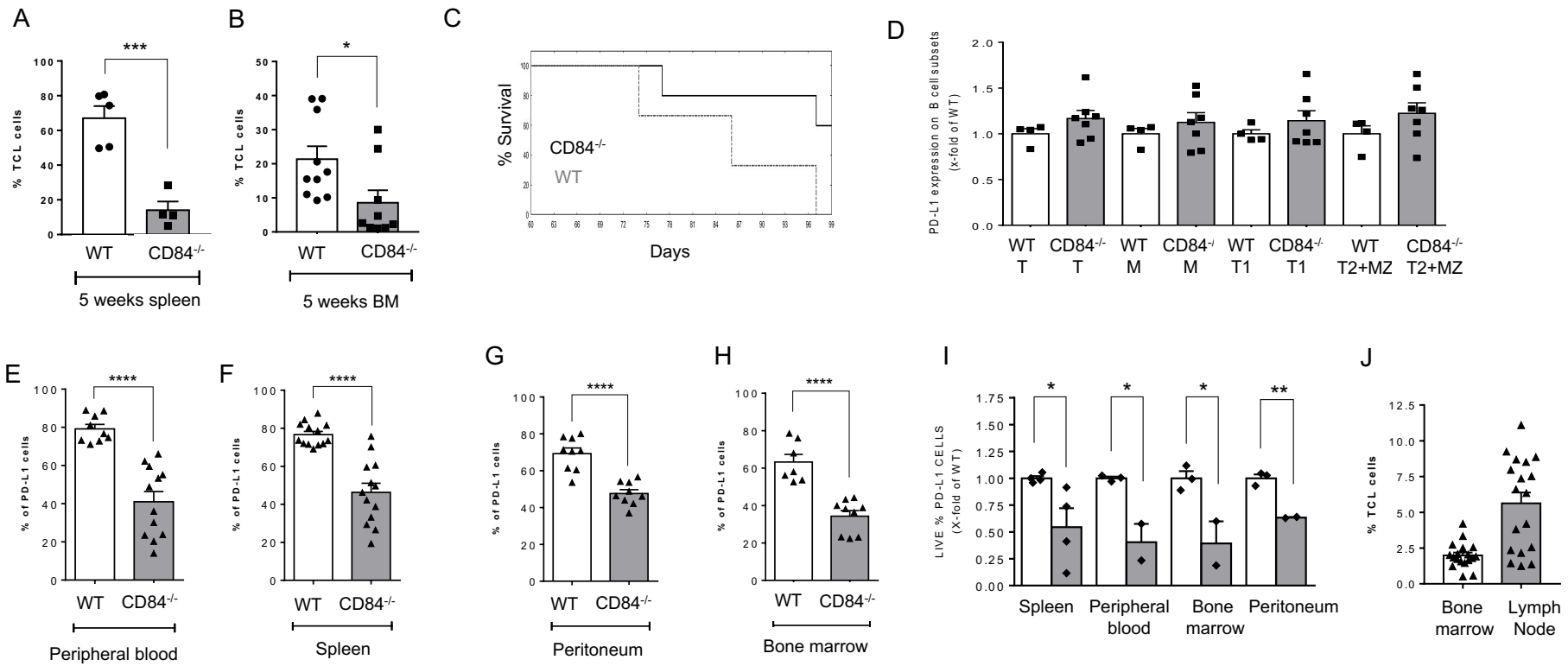

Fig S2- Decreased PD-L1 expression and elevated survival in the absence of CD84 in the tumor microenvironment.

Eμ-TCL1 splenocytes (4 × 10^7) were injected i.v. into the tail vein of C57BL/6 wt or CD84−/− mice. **(A-B)** After 5 weeks, the mice were sacrificed and the number of Eμ-TCL1 cells was determined in spleen (A) and BM (B) (n=4-10, **p<0,01, *p<0,05). **(C)** Mice were monitored daily for survival. The figure displays the survival curves of CD84$^{-/-}$ mice compared to WT mice (n = 3, 5, p<0.05, Log-rank test, Chi square 2.863 df:1, one-tailed Chi-square). **(D**) Splenic B cells from healthy WT and CD84$^{-/-}$ mice were stained for PD-L1 expression (T – total B cells, M – Mature B cells) (n=4-7, p=0.2194). **(E-I)** Eμ-TCL1 splenocytes (4 × 10^7) were injected i.v. into the tail vein of C57BL/6 wt or CD84−/− mice. After 14-21 days, the mice were sacrificed and the percentage of PD-L1 positive cells was analyzed in WT and CD84-/- in peripheral blood (E), spleen (F), peritoneum (G), bone marrow (H) (n=7-11, ****p<0,0001), and in the live Annexin-V and 7AAD negative population (I) (n=2-4, **p<0,01, *p<0,05). **(J)** Percentage of Eμ-TCL1 cells in BM and spleen at 21 days after i.v. injection of Eμ-TCL1 splenocytes (n=17-18).

Fig S3

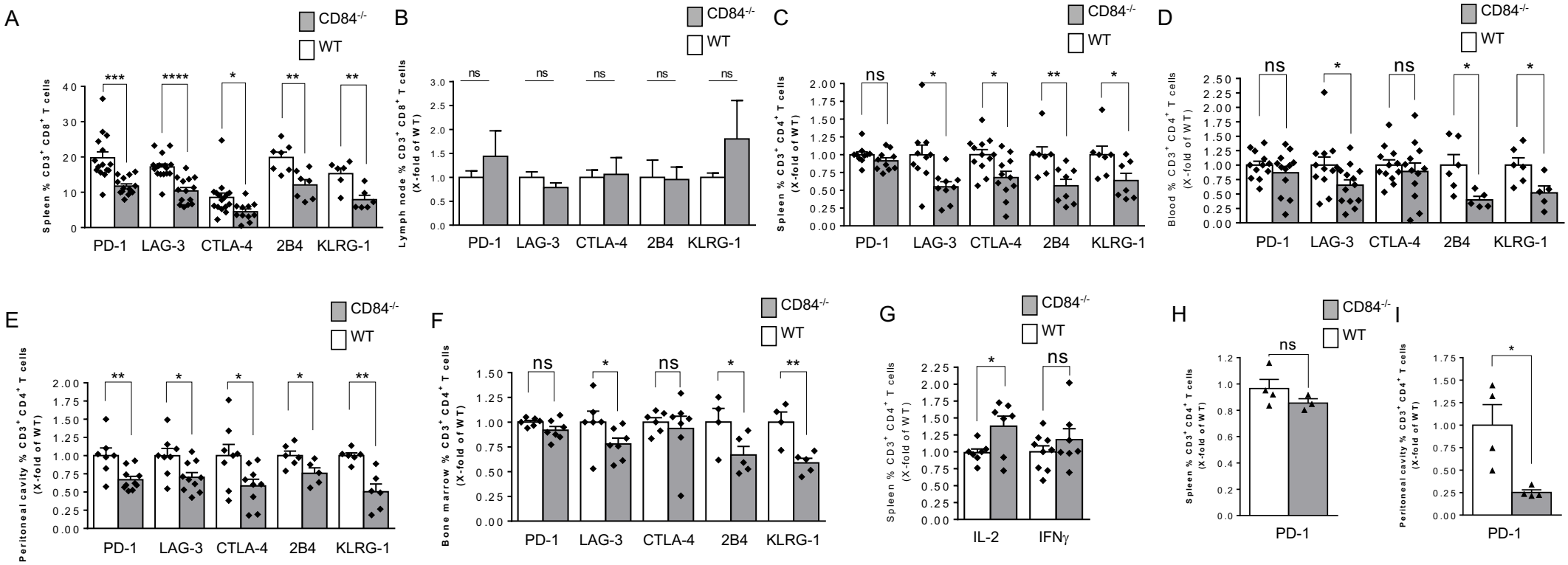

Fig S3-Reduction in exhausted T cell phenotype in the CD84-/- environment.
(A-F) Eμ-TCL1splenocytes (4×10^7) were injected i.v. into the tail vein of C57BL/6 wt or CD84-/- mice. After 14-21 days, the mice were sacrificed. (A-B) Percent of PD-1, Lag-3, CTLA-4, 2B4, and KLRG-1 positive CD8 T cells in (A)spleen (n=6-11, ****p<0,0001, ***p<0,001, **p<0,01, *p<0,05) and (B) lymph node (n=3-9). **(C-F)** Expression of the exhaustion markers PD-1, Lag-3, CTLA-4, 2B4 and KLRG1 was determined on CD4 in (C) spleen (n=6-11, ns = not significant ,*p<0,05, **p<0,01), (D) peripheral blood (n=5-11, ns p =, *p<0,05, ns p =), (E) peritoneal cavity (n=6-10, *p<0,05, **p<0,01) and (F) bone marrow (n=4-7, ns = not significant, *p<0,05, ns = not significant, **p<0,01). **(G)** Splenic cells were cultured for 24 hrs with anti-CD3, and in the last 2 hours of culture with brefeldin-A. CD4 T cells were then analyzed for IFN-γ and IL-2 (n=7-8, *p<0,05, ns = not significant). **(H-I)** BM cells (5×10^6) derived from 8-week-old Eμ-TCL1 mice or negative control littermates (wt) were injected into lethally irradiated C57BL/6 (wt) or CD84-deficient ($CD84^{-/-}$) mice. After 6 months, mice were killed, and the expression of PD-1 was determined on CD4 T cells in the spleen (H) and peritoneum (I) (n=3-4, *p<0,05, ns = not significant).

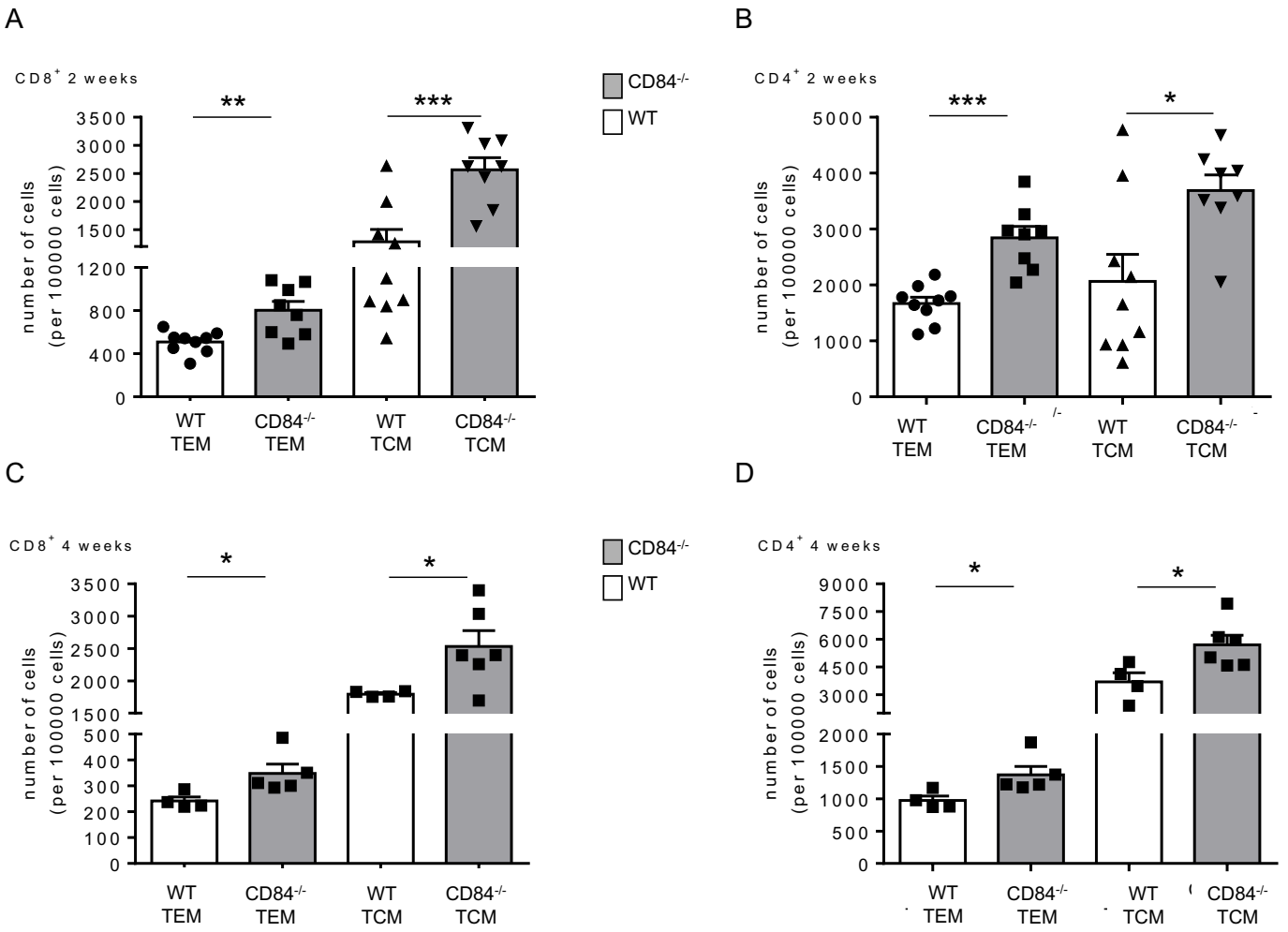

Fig S4- The TEM and TCM populations are increased in the CD84-/- environment.

Eμ-TCL1splenocytes (4 × 10^7) were injected i.v. into the tail vein of C57BL/6 wt or CD84-/- mice. After 14 (A-B), or 28 (C-D) days, the mice were sacrificed. Splenocytes were analyzed for CD8 (A,C), and CD4 (B,D). The number of TEM (CD44+, CD62L-) and TCM (CD44+, CD62L+) was determined by flow cytometry (n=4-9, *p<0.05, **p<0.01, ***p<0.001).

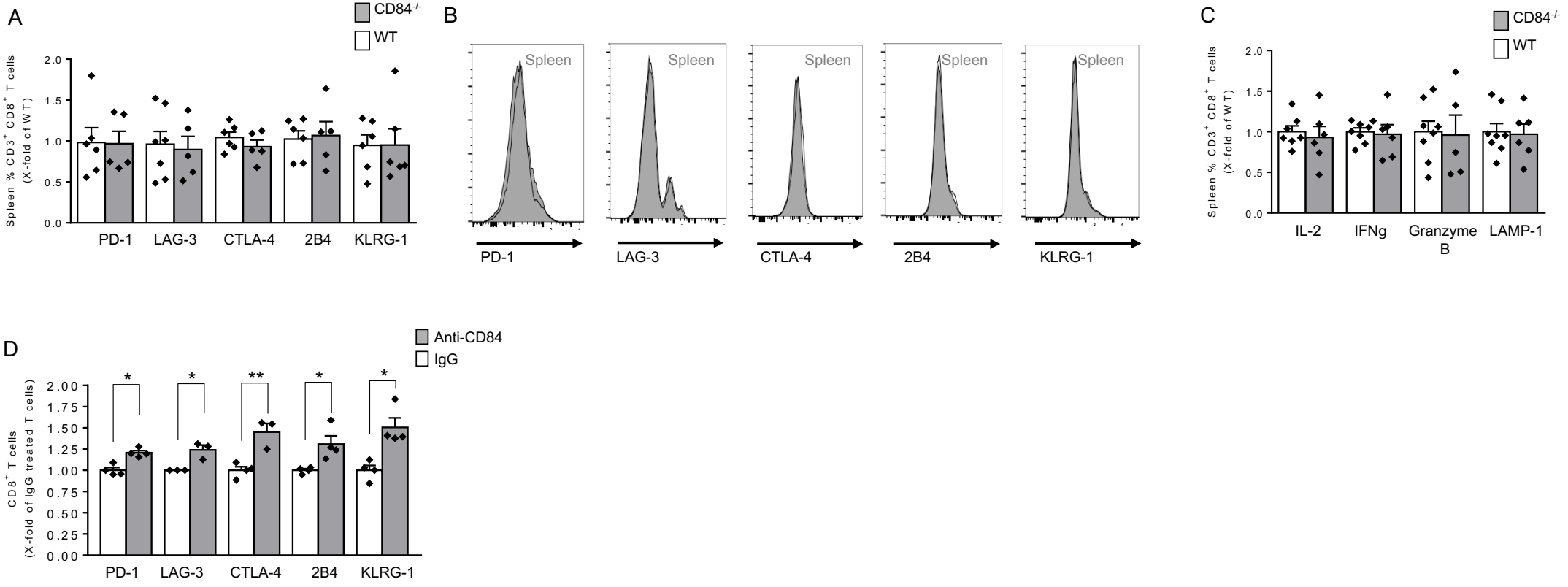

Fig S5-wt and CD84-/- CD8 T cells respond similarly to activation.
(A-C) Healthy CD84$^{-/-}$ and wt splenic cells were cultured for 24 hrs with anti-CD3 and in the last 2 hours of culture with brefeldin-A. CD8 T cells were stained for the (A-B) exhaustion markers: PD-1, Lag-3, CTLA-4, 2B4, KLRG-1, and (C) the cytokines/cytotoxic markers: IFN-γ, IL-2, Granzyme B, and LAMP-1 (n=6-8, ns p = not significant). **(D)** Enriched splenic T cells from Eμ-TCL1 sick mice were stimulated with anti-CD84 antibody and stained for CD8 and PD-1, LAG-3, CTLA4, 2B4 and KLRG-1 (n=3-4, *p<0.05, **p<0.01).

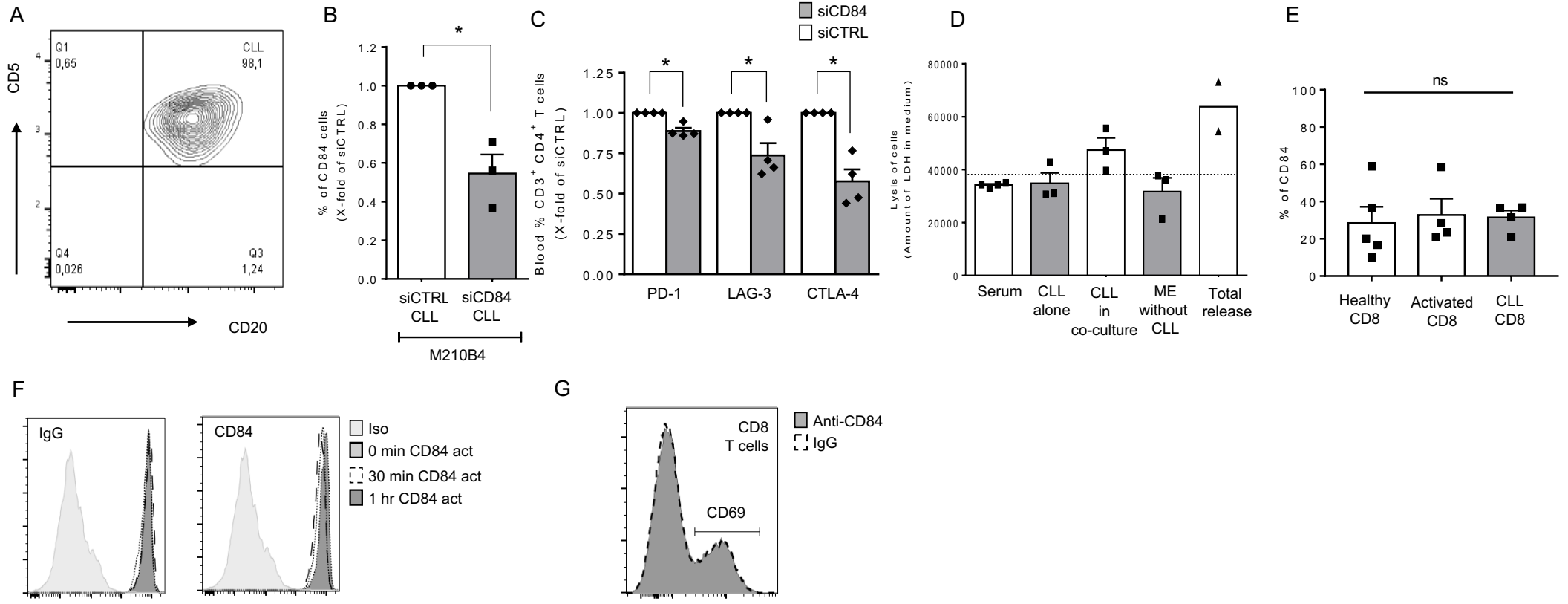

Fig S6- CD84 regulates PD-L1 and T cell function in human CLL patients. (A) Lymphocytes from whole CLL blood samples were purified by Ficoll gradient, and CLL cells were then isolated using CD19 beads. **(B)** Purified CLL cells were treated with siCD84 or siCTRL and cultured for 24 hrs; a 48 hr co-culture was then established M210B4 cells. CD84 expression on M210B4 derived from the co-culture was analyzed by FACS analysis (n=3, $p<0,05$). **(C)** CD4 T cell expression of PD-1, Lag3 and CTLA-4 following co-culture with siCD84 treated CLL or siCTRL treated CLL (n=4, *$p<0,05$). (**D)** Amount of lysed cells, measured by LDH release in medium in the different culture conditions (ME = microenvironment, medium was replaced for all conditions 24 hrs after treatment with siRNA). **(E)** CD84 expression was determined on healthy, healthy activated (CD3, CD28) and CLL derived purified human T cells (CD3 beads) (n=4-5, ns p = non significant). **(F-G)** Purified T cells were stimulated with anti-CD84 or a control antibody IκB (F) and CD69 (G) expression levels were determined (n=2-3).

A

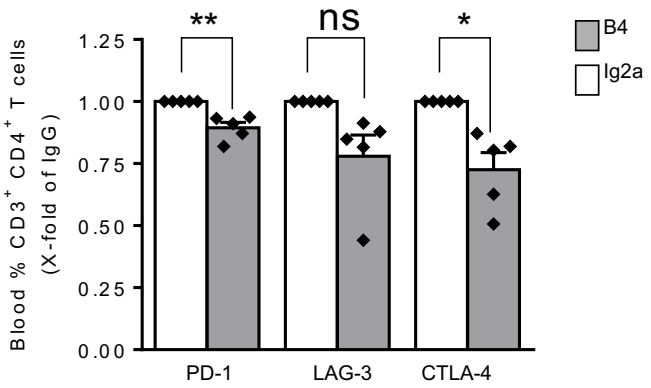

Fig S7- Blocking CD84 on CLL cells affects CD4 T cells to a lesser extent than CD8.
Lymphocytes from whole CLL blood samples were purified by Ficoll gradient, and CLL cells were then isolated with CD19 beads and treated with the B4 antagonistic CD84 antibody or control IgG2a, and cultured for 24 hrs; a 48 hr co-culture was then established with the non-CLL population. Graph shows CD4 T cell expression of PD-1, Lag3 and CTLA-4, following co-culture with B4 treated or IgG2a treated CLLs (n=5, **p<0,01, *p<0,05, ^{ns} p = 0,06).