

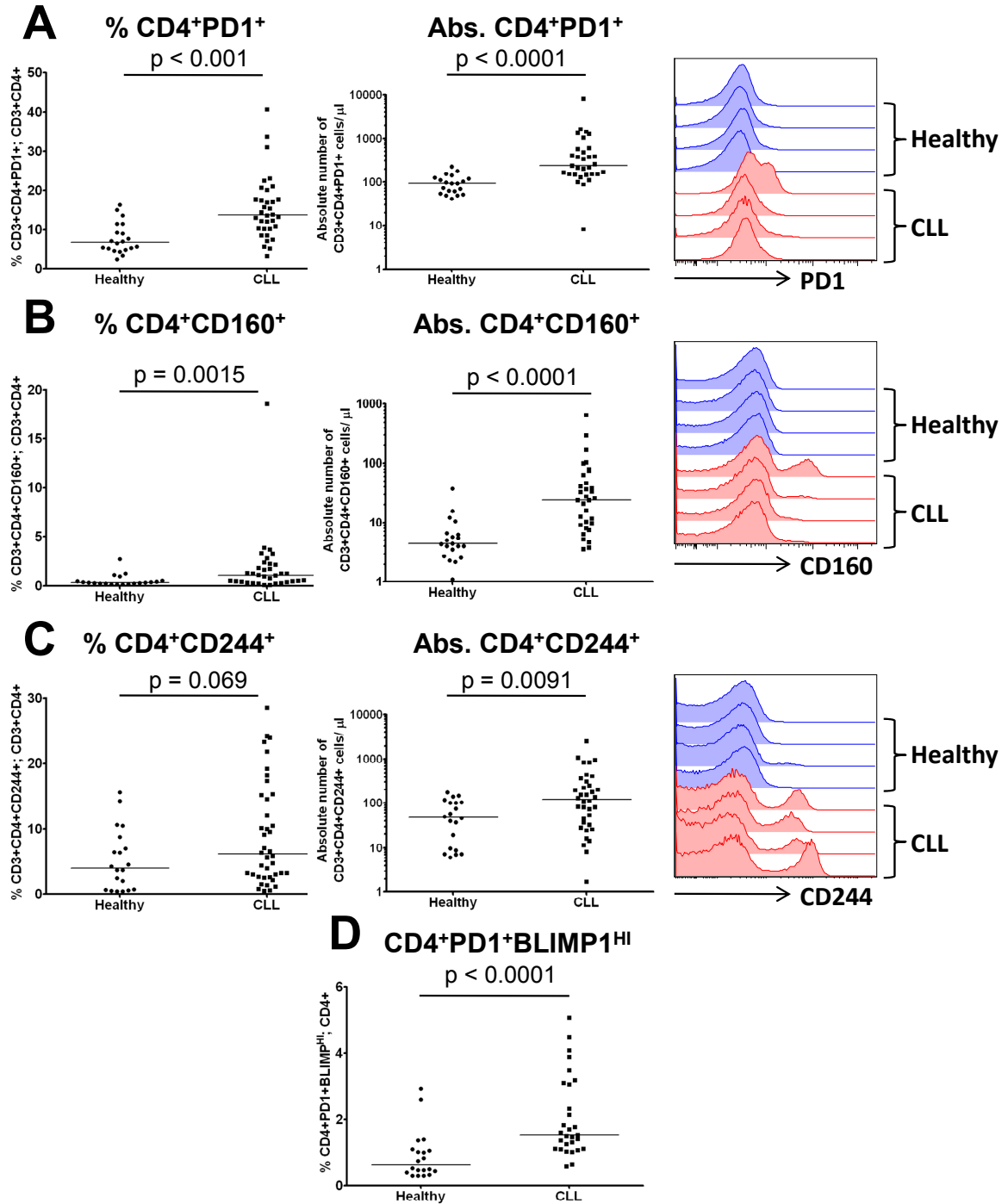
## Supplementary Data

**Supplementary Table 1. Comparison of the phenotypic and functional profile of CD8<sup>+</sup> T cells from CLL patients and healthy controls.**

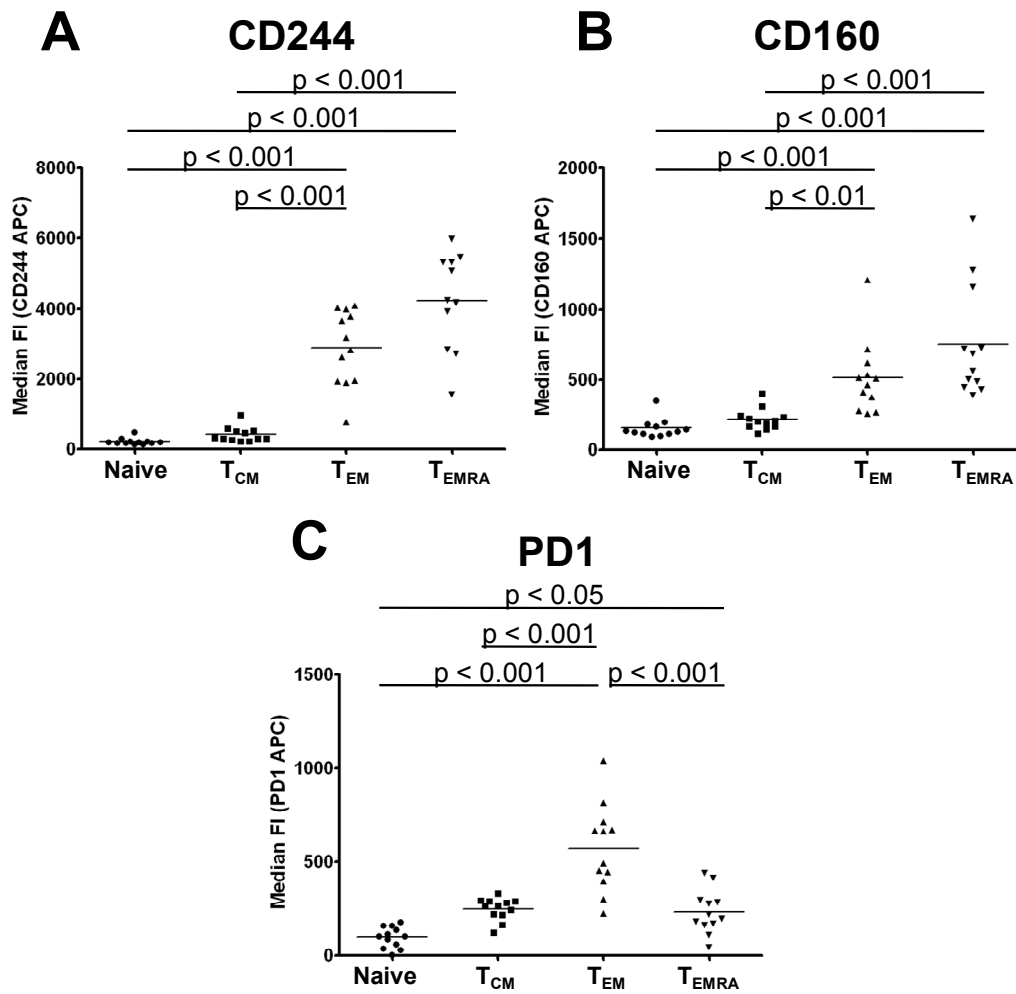
	<b>Healthy</b>	<b>CLL</b>	<b>p value</b>
	<b>Median/Mean(Range)</b>	<b>Median/Mean(Range)</b>	
<b>% CD8<sup>+</sup>CD244<sup>+</sup></b>	66.0% (21.8–85.9)	80.3% (33.7-97.3)	0.0014
<b>Abs. Nos. CD8<sup>+</sup>CD244<sup>+</sup></b>	329 cells/μl (55.9-1150)	826 cells/μl (20-23110)	0.0002
<b>% CD8<sup>+</sup>CD160<sup>+</sup></b>	13.4% (2.0-33.4)	29.3% (8.5-81.2)	0.0002
<b>Abs. Nos. CD8<sup>+</sup>CD160<sup>+</sup></b>	58.7 cells/μl (7.9-452)	295 cells/μl (7.6-13055)	<0.0001
<b>% CD8<sup>+</sup>PD1<sup>+</sup></b>	15.9%(9.8-38.5)	24.1% (4.9-58.6)	0.04
<b>Abs. Nos. CD8<sup>+</sup>PD1<sup>+</sup></b>	70.8 cells/μl (25.8-277)	210 cells/μl (8.8-6433)	<0.0001
<b>% CD8<sup>+</sup>CCR7<sup>-</sup></b>	68.6% (26.1-88.9)	77.9% (34.9-96.3)	0.0043
<b>Abs. Nos. CD8<sup>+</sup>CCR7<sup>-</sup></b>	348 cells/μl (79.8-1165)	884 cells/μl (19.5-24083)	<0.0001
<b>% CD8<sup>+</sup>PD1<sup>+</sup>BLIMP1<sup>HI</sup></b>	0.31%(0.11-1.33)	1.16%(0.36-3.9)	<0.0001
<b>% CD8<sup>+</sup>CD127<sup>+</sup></b>	75.3% (40.8-96.8)	60.5% (21.9-92.8)	0.079
<b>Proliferation Index</b>	1.58 (1.32-2.15)	1.24 (1.01-1.60)	<0.0001
<b>% CD8<sup>+</sup> Divided</b>	53.8 (31.0-70.3)	39.6% (4.8-66.5)	0.024
<b>% Specific lysis (30:1)</b>	55.5% (44.0-60.0)	14.0% (9.0-19.0)	<0.0001
<b>% CD8<sup>+</sup>IFNγ<sup>+</sup></b>	50.1% (20.8-81.1)	72.2% (43.2-97.6)	<0.0001
<b>% CD8<sup>+</sup>TNFα<sup>+</sup></b>	55.9% (28.8-88.9)	69.5% (52.6-92.9)	0.033
<b>% CD8<sup>+</sup>IL2<sup>+</sup></b>	33.6% (18.5-62.5)	38.7% (14.3-78.6)	0.29
<b>CD8<sup>+</sup>CCR7<sup>-</sup>TBET MFI</b>	4784 (1614-9252)	7416 (2272-13249)	0.0005

**Supplementary Table 2. Impact of CMV serostatus on the phenotypic and functional profile of CD8<sup>+</sup> T cells from CLL patients and healthy controls.**

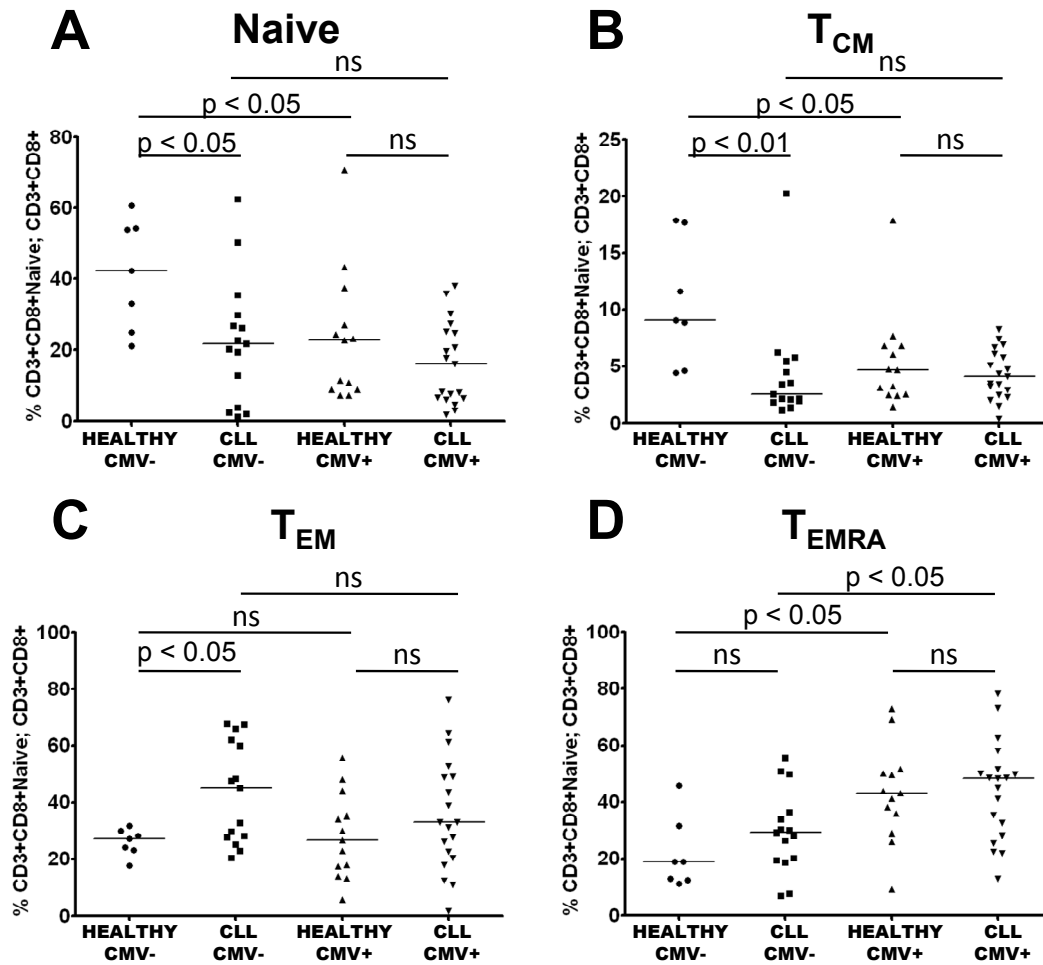
	<b>Healthy</b>	<b>CLL</b>	<b>p value</b>
	<b>Median/Mean(Range)</b>	<b>Median/Mean(Range)</b>	
<b>% CD8<sup>+</sup>CD244<sup>+</sup></b>			
- CMV-	41.0% (21.8-67.9)	68.8% (33.7-97.3)	0.0076
- CMV+	67.7% (29.2-85.9)	85.5% (61.3-94.5)	0.0051
<b>% CD8<sup>+</sup>CD160<sup>+</sup></b>			
- CMV-	10.6% (1.98-13.4)	18.4% (8.5-81.2)	0.0041
- CMV+	16.1% (4.3-33.4)	30.9% (9.2-49.2)	0.0019
<b>% CD8<sup>+</sup>PD1<sup>+</sup></b>			
- CMV-	17.0% (11.6-27.0)	33.8% (21.6-58.6)	0.0020
- CMV+	13.3% (9.8-38.5)	16.6% (4.9-46.7)	0.80
<b>% CD8<sup>+</sup>CCR7<sup>-</sup></b>			
- CMV-	40.1% (34.9-74.4)	76.7% (34.9-95.9)	0.014
- CMV+	73.2% (26.1-88.9)	87.0% (61.0-96.3)	0.047
<b>% CD8<sup>+</sup>IFN<math>\gamma</math><sup>+</sup></b>			
- CMV-	35.3% (20.8-59.1)	66.4% (43.2-97.6)	0.0012
- CMV+	53.2% (21.8-81.1)	82.7% (56.6-92.8)	0.0036
<b>CD8<sup>+</sup>CCR7<sup>-</sup>TBET MFI</b>			
- CMV-	3415 (1614-5542)	5710 (2272-8964)	0.0091
- CMV+	5032 (3399-9252)	9690 (4725-13249)	0.0003
<b>Proliferation Index</b>			
- CMV-	1.61 (1.32-1.99)	1.19 (1.01-1.60)	0.005
- CMV+	1.58 (1.38-2.15)	1.26 (1.07-1.57)	0.0008
<b>% Specific lysis (30:1)</b>			
- CMV-	56.0% (48.0-60.0)	14.0% (12.0-16.0)	0.012
- CMV+	55.0% (44.0-59.0)	15.0% (9.0-16.0)	0.0014
<b>% CD8<sup>+</sup>CD107a<sup>+</sup></b>			
- CMV-	2.9% (2.1-4.7)	15.7% (4.9-35.4)	0.0007
- CMV+	4.2% (2.3-12.2)	9.8% (4.3-37.8)	0.0026



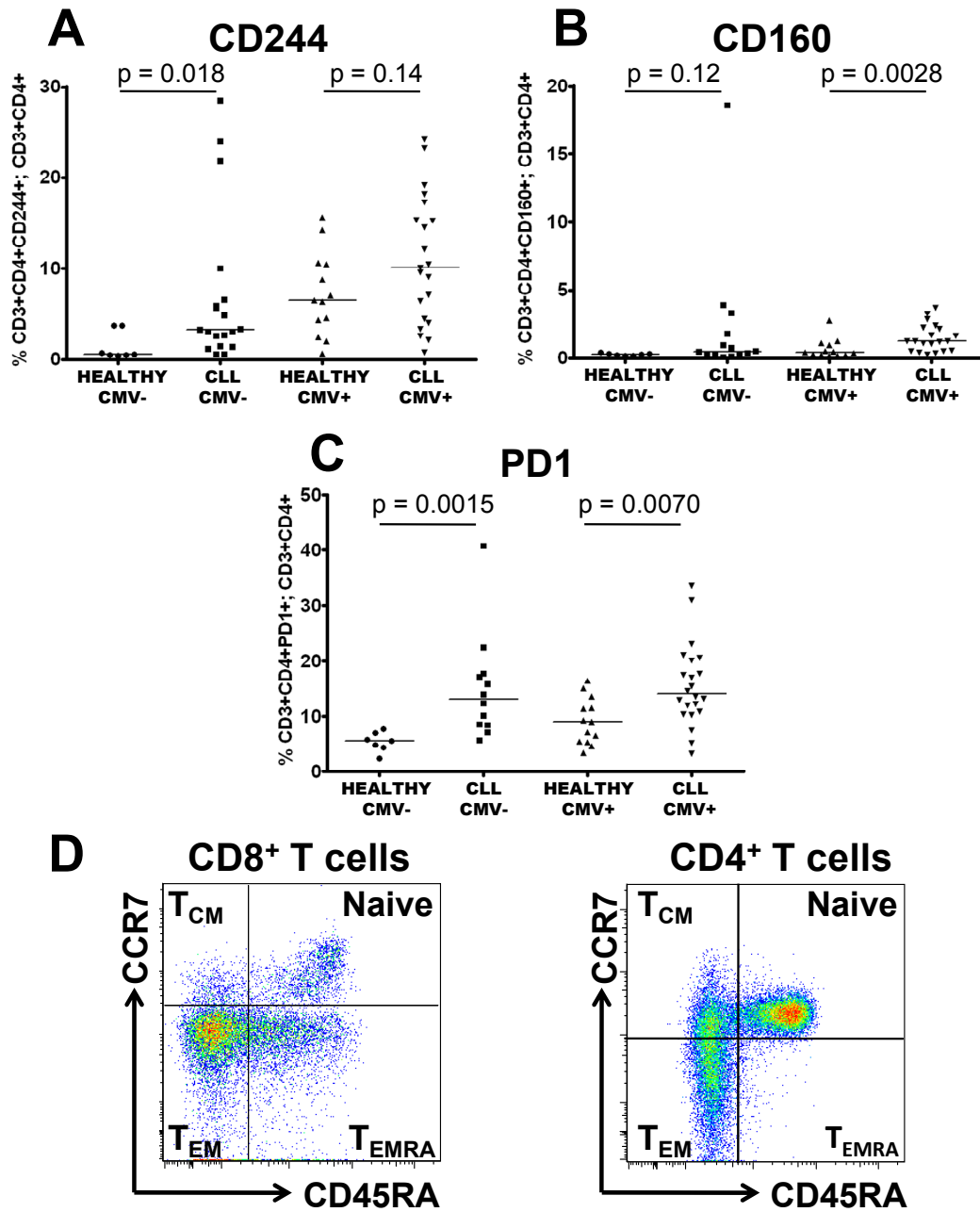
**Supplementary Figure 1. Expression of PD1, CD160 and CD244 on CD4<sup>+</sup> T cells from patients with CLL.** The expression PD1, CD160, and CD244 on CD4<sup>+</sup> T cells from patients with CLL and healthy age-matched controls was measured by flow cytometry. There was a significant increase in numbers of PD1<sup>+</sup> (A) and CD160<sup>+</sup> (B) and CD244<sup>+</sup> (C) CD3<sup>+</sup>CD4<sup>+</sup> T cells in CLL patients compared to healthy controls. (D) CD3<sup>+</sup>CD4<sup>+</sup>PD1<sup>+</sup>BLIMP1<sup>HI</sup> cells are expanded in CLL patients.



**Supplementary Figure 2. CD244, CD160, and PD1 are preferentially expressed on healthy CD3<sup>+</sup>CD8<sup>+</sup>CCR7<sup>-</sup> effector T cells.** The expression of CD244, CD160 and PD1 on CD8<sup>+</sup> T cells from healthy controls was assessed. Comparable to CD8<sup>+</sup> T cells from CLL patients, expression of CD244 (A) and CD160 (B) was increased on CCR7<sup>-</sup>CD45RA<sup>-</sup> T<sub>EM</sub> cells, and was highest on CCR7<sup>-</sup>CD45RA<sup>+</sup> T<sub>EMRA</sub> cells. (C) Expression of PD1 was highest on CCR7<sup>-</sup>CD45RA<sup>-</sup> T<sub>EM</sub> cells.



**Supplementary Figure 3. B-CLL skews the CD3<sup>+</sup>CD8<sup>+</sup> T cell repertoire towards a CCR7<sup>-</sup>CD45RA<sup>-</sup> effector memory phenotype, whereas the presence of CMV leads to an expansion of CCR7<sup>-</sup>CD45RA<sup>+</sup> T<sub>EMRA</sub> subtype.** B-CLL patients and healthy CMV+ individuals had a reduction in CCR7<sup>+</sup>CD45RA<sup>+</sup> naive (A) and CCR7<sup>+</sup>CD45RA<sup>-</sup> central memory T-cell (B) numbers when compared with healthy CMV- controls. (C) CCR7<sup>-</sup>CD45RA<sup>-</sup> effector memory T cells were only significantly expanded when comparing CMV- patients and controls. (D) In contrast CCR7<sup>-</sup>CD45RA<sup>+</sup> T<sub>EMRA</sub> cells were only significantly expanded in CMV+ patients and controls.



**Supplementary Figure 4. Increased expression of PD1, CD160 and CD244 on CD4<sup>+</sup> T cells from patients with CLL.** The proportion of CD4<sup>+</sup> T cells expressing PD1, CD160, and CD244 were measured by flow cytometry in patients with CLL and healthy controls matched for age and CMV serostatus. (A) There was a significant increase in the expression of CD244 when comparing CMV<sup>-</sup> patients and controls. (B) There was a significant increase in the expression of CD160 when comparing CMV<sup>+</sup> patients and controls. (C) In contrast, expression of PD1 was significantly increased when comparing both groups. (D) An equivalent to the CD8<sup>+</sup> T<sub>EMRA</sub> subset is not seen in the CD4<sup>+</sup> compartment.