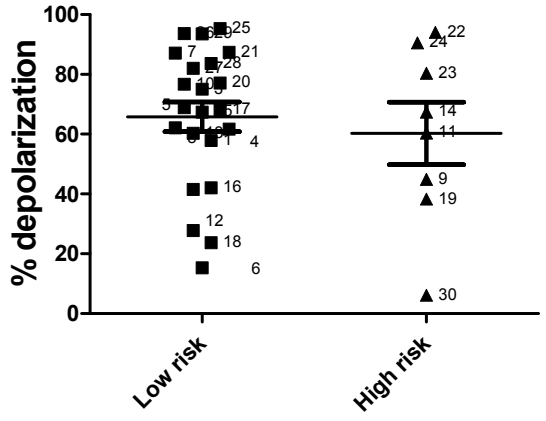
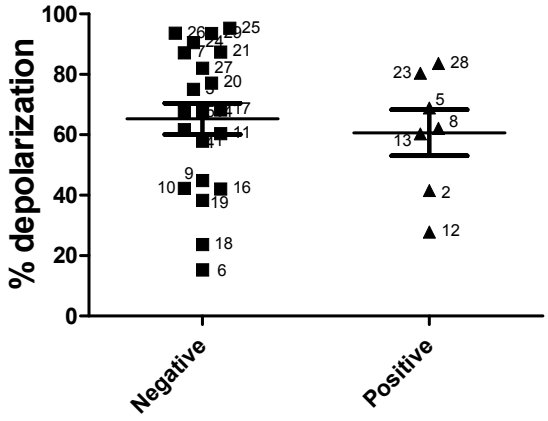
Supplemental Figure 1

A



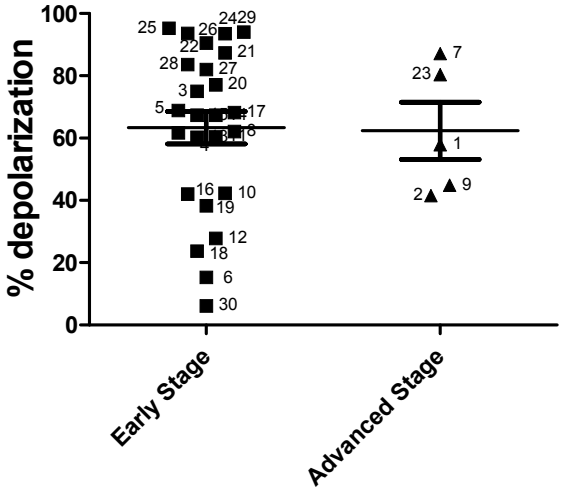
Mann Whitney test	
P value	0.7075

B



Mann Whitney test	
P value	0.5594

C



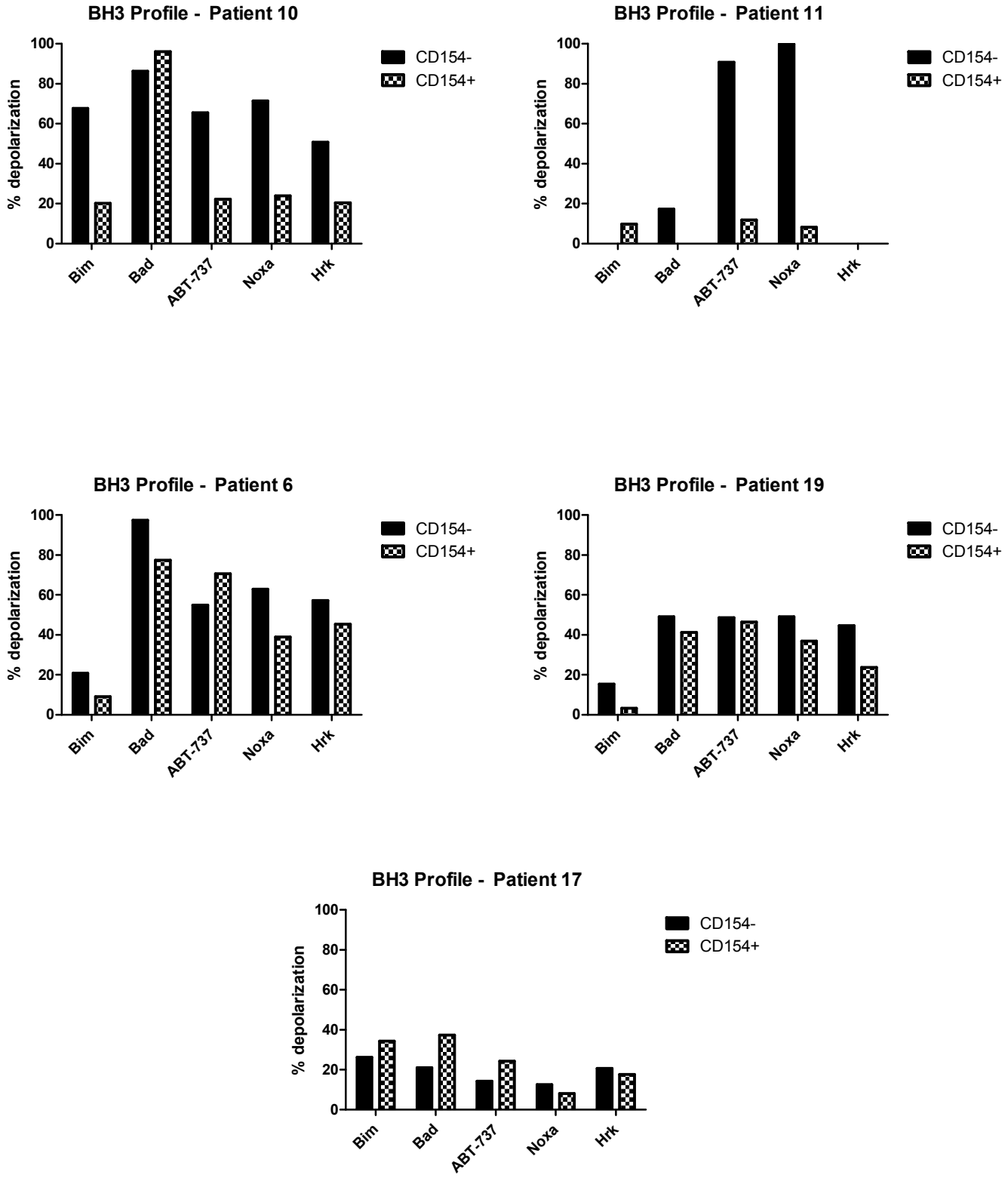
Mann Whitney test	
P value	0.6968

Clinical characteristics not associated with priming. Mitochondrial priming, as assessed by BH3 profiling with BIM BH3 peptide at 0.03 uM was not found to be different when comparing: (A) low risk [del(13p), trisomy 12, or normal) vs. high risk [del(17p), del(11q), complex] cytogenetics, (B) negative vs. positive ZAP-70 status (20% threshold for positive), or (C) early (Rai stages 0-2) vs. advanced (Rai stages 3 & 4) disease

Supplemental Figure 2

A

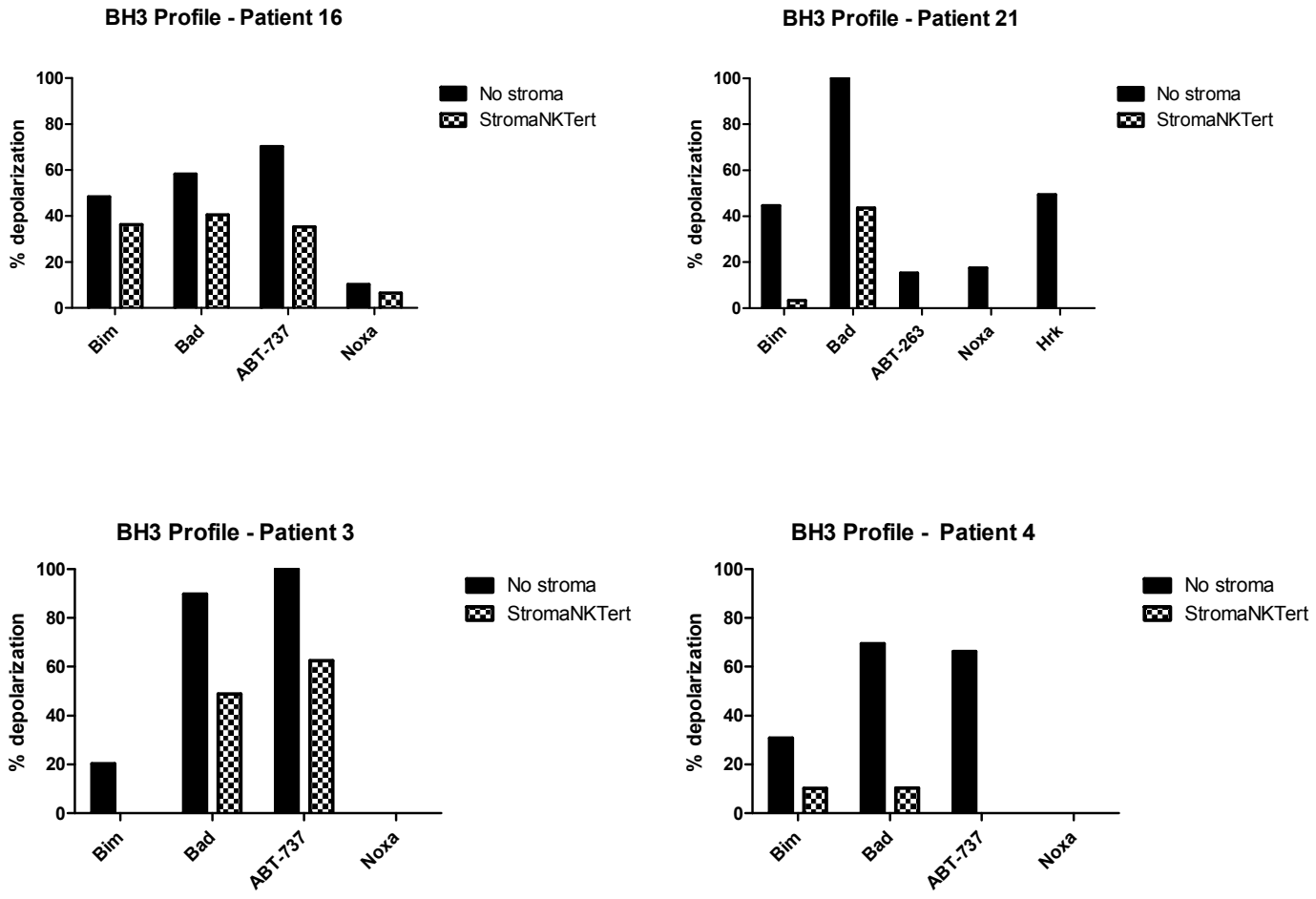
CD154+ L cell stroma



Supplemental Figure 2

B

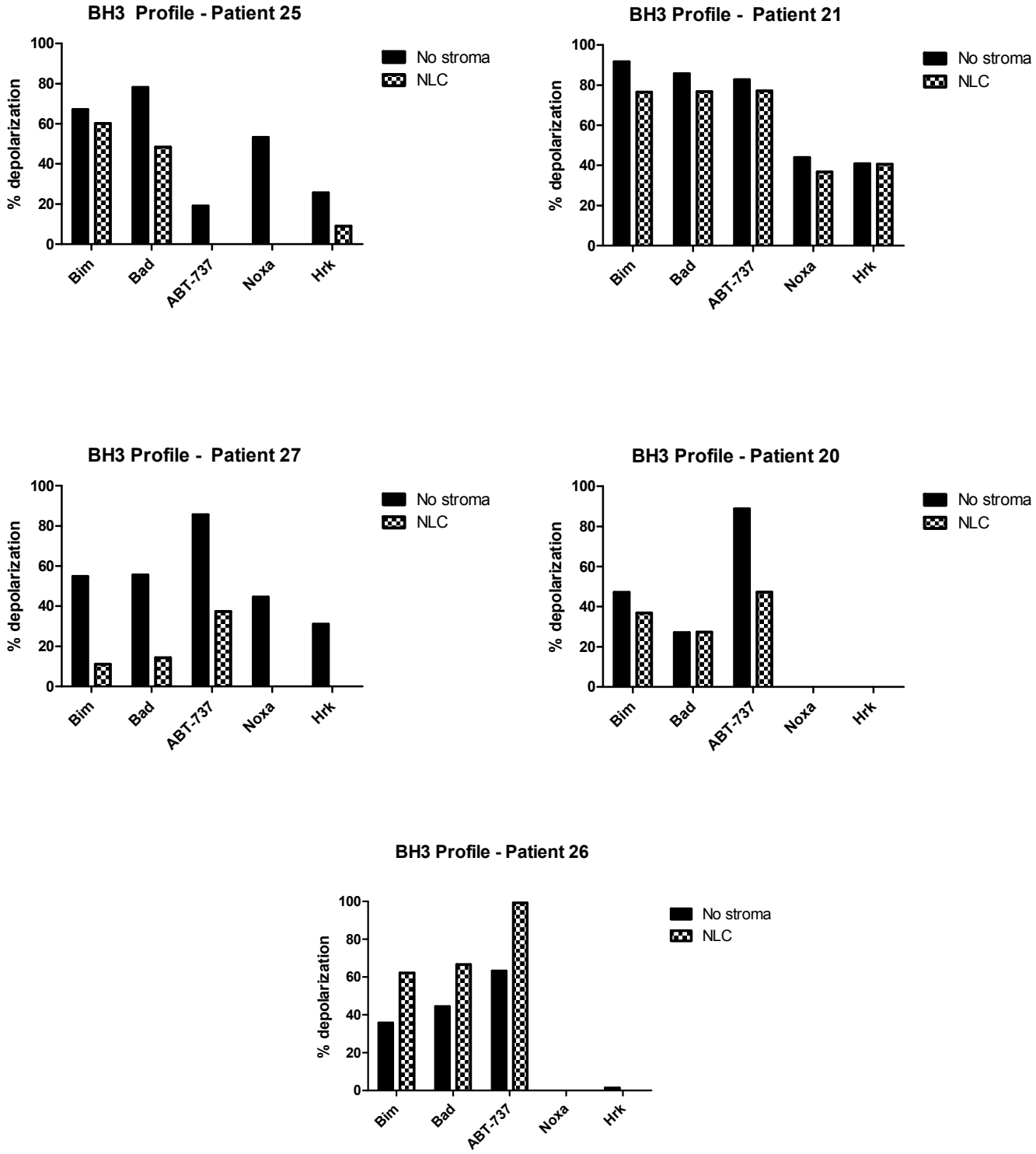
StromaNKTert stroma



Supplemental Figure 2

C

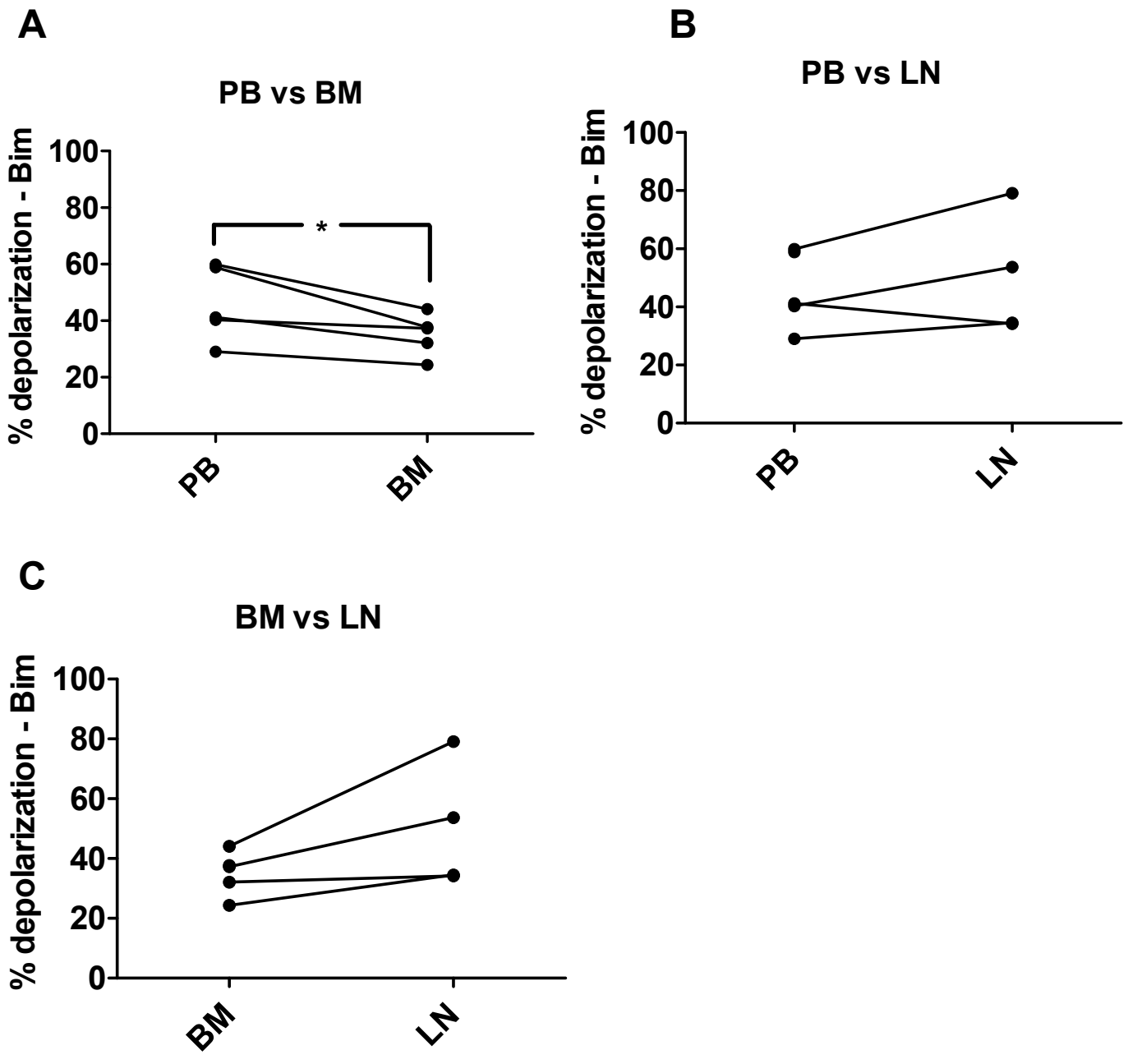
NLC stroma



Supplemental Figure 2

***In vitro,* BH3 profiling demonstrates that primary CLL cells co-cultured for 24 hrs. with a variety of stroma are less primed to undergo apoptosis.** (A-C) Complete BH3 profiling data from individual patients whose CLL cells were co-cultured with (A) CD154+ L cell (n=5), (B), StromaNKTert (n=4), or (C) primary human NLC (n=5) stroma demonstrate that CLL cells cultured in these simulated CLL stromal microenvironments consistently exhibit decreased mitochondrial priming compared to CLL cells cultured in the absence of stroma. Absent bars for a given peptide indicate no depolarization was observed.

Supplemental Figure 3



Pairwise comparison of priming of CLL cells obtained from peripheral blood, lymph node and bone marrow compartments. Comparison is made between samples obtained from different compartments from the same patients. A paired t-test provided the following two-tailed p values for each comparison: (A) 0.035; (B) 0.26; (C) 0.11.

Supplemental Table 1

No.	Sex	Age	Rai Stage	Treatment status	WBC (k/mm^3)	B_2M (mg/L)	IgG (mg/dL)	FISH cytogenetics	%VH Homology	%ZAP70	Therapy	Clinical Response	%BIM depol.	%BAD depol.	%NOXA depol.	%HRK depol.
1	F	68	3	Untreated	87.4	N/A	260	N/A	96	2.9	-	-	57.9	41.7	9.40	28.9
2	M	67	4	Untreated	254.4	9.1	1370	del 13q	90.4	27.3	LR	PD	41.5	24.1	17.0	10.9
3	F	70	1	Untreated	36.8	3.9	413	normal	N/A	1.34	chlor/ pred	PR	75	51.1	21.8	21.5
4	F	77	1	Untreated	72.3	3.1	1270	del 13q	N/A	3.13	-	-	61.7	39.6	28.6	33.3
5	M	70	1	Untreated	114.4	3.3	559	del 13q	98.6	65.2	-	-	68.9	44.6	24.9	21.7
6	M	73	2	Untreated	355.1	4.8	394	del 13q	85	0.7	-	-	15.3	29.2	22.7	7.47
7	F	67	4	s/p FR	101.5	2.3	543	del 13q	93.3	0.79	-	-	87.1	52.1	20.0	25.2
8	F	63	1	Untreated	207	3	991	del 13q	100	66.8	-	-	62.1	22.2	29.5	12.8
9	M	66	3	Untreated	247.1	3.1	687	del 17p and del 13q	93.3	2.7	-	-	44.9	17.9	28.8	22.4
10	M	64	2	s/p FR	86.6	2.3	293	del 13q	94.7	16.6	-	-	42.3	95.4	7.81	0
11	F	76	2	s/p F, FR	99.3	5.5	733	del 11q and trisomy 12	100	12.6	BR	-	60.4	48.7	23.6	36.8
12	M	66	1	Untreated	77.5	1.9	579	del 13q and trisomy 12	91.4	46.9	-	-	27.8	55.8	41.6	33.2
13	M	63	2	Untreated	203.3	N/A	N/A	del 13q	97.2	45.6	FR	PD	60.3	38.4	39.3	22.2
14	M	55	2	Untreated	465.1	3	317	del 11q and del 13q	100	10.8	FCR	PR	57.9	5.6	0	-
15	M	72	2	Untreated	165.7	3.6	2610	del 13q	90.6	6	-	-	67.4	54.0	11.2	14.2
16	F	66	1	Untreated	71.7	1.7	423	del 13q	94.2	1.3	-	-	42	32.1	24.4	25.3
17	M	62	1	Untreated	60.2	3.8	327	del 13q	97.2	8.9	R/pred	PR	68.2	51.2	19.7	23.8
18	M	56	0	Untreated	58.5	1.8	698	del 13q	93.3	2.9	-	-	23.7	54.2	24.6	25.3
19	F	79	2	Untreated	129.1	4	618	del 13q and del 17	95.4	0.6	-	-	38.3	52.9	32.2	25.6
20	F	65	2	Untreated	151.7	4.8	240	del 13q	89.1	0.3	-	-	77.1	62.5	28.5	39.6
21	F	54	2	Untreated	270.8	N/A	152	del 13q	93	0.5	-	-	87.4	56.1	37.9	37.9
22	M	68	2	R, O	16.1	4.5	807	del 11q	100	N/A	-	-	94	12.8	6.22	4.97
23	M	61	4	s/p FCR, CHOP-R	85.9	6.4	668	complex incl. del 17p	100	65.6	-	-	80.4	47.3	24.4	24.7
24	M	58	1	Untreated	53.3	2.7	851	del 17p	100	4.74	FCR	PR	90.5	16.1	28.0	0
25	F	66	1	Untreated	38.2	3.8	1180	del 6q	99.7	15.8	LR	CR	95.3	34.3	11.3	0.20
26	M	51	0	Untreated	81.4	4.6	805	del 13q	99.5	5.43	FCR	CR	93.6	55.7	33.4	25.6
27	F	58	1	Untreated	71.6	3.3	837	del 13q	96	0.28	-	-	82	23.5	37.5	20.1
28	F	77	1	Untreated	44.5	2.1	785	trisomy 12	100	51.8	FR	CR	83.6	61.1	0	15.4
29	M	56	2	Untreated	33.1	6.4	297	trisomy 12	100	3.06	FCR + PCI	-	93.5	47.4	0	36.5
30	F	53	0	Untreated	69.4	1.9	1270	del11q	N/A	N/A	FCR	PD	6.1	23.5	0	0

CLL patient characteristics. Clinical characteristics of the 30 CLL patients studied (determined at time of sampling). % mitochondrial depolarization at 1 hour as assessed by BH3 profiling reveals that primary CLL cells are mainly BCL-2 dependent, with some patient samples showing relatively more reliance on other anti-apoptotic proteins such as MCL-1 and BCL-XL, as indicated by relatively higher levels of depolarization by NOXA and HRK peptides, respectively.

Abbreviations:

- *Clinical Response:* PD = progressive disease, PR = partial response, CR = complete response

Therapy: FR = fludarabine/rituximab, FCR = fludarabine/cyclophosphamide/rituximab, R = rituximab, O = ofatumumab, CHOP-R = cyclophosphamide/ doxorubicin/vincristine/prednisone/rituximab, BR = bendamustine/rituximab, L = lenalidomide, PCI = PCI-32765,chlor = chlorambucil, pred = prednisone