PRDM1/BLIMP1 is commonly inactivated in anaplastic large T-cell lymphoma.

Supplemental Materials

Supplementary Figure 1. Frequency of DNA gains (up) and losses (down) observed in seven ALCL cell lines [five derived from ALK(+), one from ALK(-) and one from cutaneous ALCL]. Red (up) represents gains and blue (down) represents losses. X-axis, chromosome localization and physical mapping; Y-axis, proportion of cases showing the aberrations.

Supplementary Figure 2. Validation of BLIMP1 deletion. FISH analysis has been performed for *PRDM1* gene deletion on all ALCL cell lines and three clinical specimens previously analyzed through the Affymetrix SNP6.0 platforms. Karpas299, SUDHL1 and ALK(-) clinical specimen 2475/05 pictures are reported as example. Orange: *PRDM1* gene locus (134 E15); Green: Cep 6 (RP11-164C22).

Figure S3. *PRDM1* is a tumor suppressor gene in other *in vitro* models of ALCL. (A) BLIMP1 protein level after infection with empty vector (pWPI) or vector for BLIMP1 re-expression (pWPI-HA-BLIMP1) in JB6 and SUDHL1 ALK(+) cell lines. (B) Growth curve after infection for JB6 and SUDHL1 cell lines, cells counted at day 2, 3, 4 after infection. (C) Percentage of GFP positive cells after infection at day 2, 3 and 4 in JB6 and SUDHL1 cell lines. (D) Percentage of dead cells after infection at day 2, 3 and 4 in JB6 and SUDHL1 cell lines.

Supplementary Figure 4. Kaplan-Meier graph showing OS in systemic ALCL according to the presence of *PRDM1* inactivation and/or *TP53* locus loss. X-axis, months; Y-axis, percentage of alive patients.

Supplementary Table 1. Primers used for DNA sequencing or real-time PCR.

Supplementary Table 2. Clinical characteristics of the ALCL series.

Supplementary Table 3. Significant regions affected by DNA gains and losses in ALCL, as estimated using the GISTIC algorithm.

Supplementary Table 4. Significant regions affected by DNA gains and losses in ALK-ALCL, as estimated using the GISTIC algorithm.

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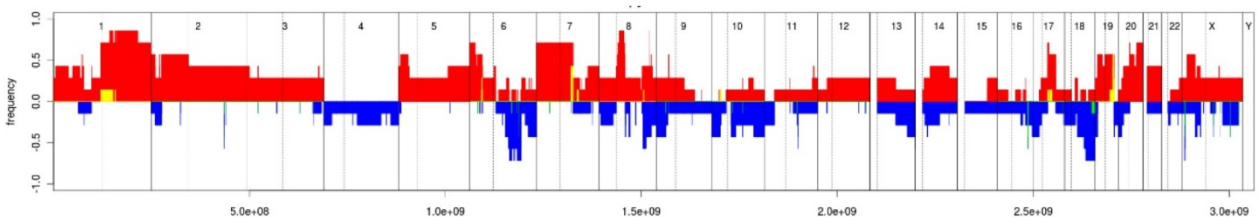

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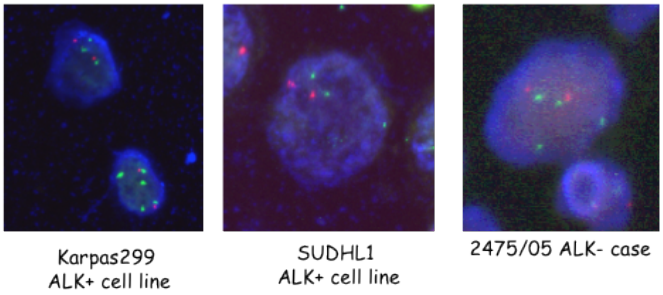

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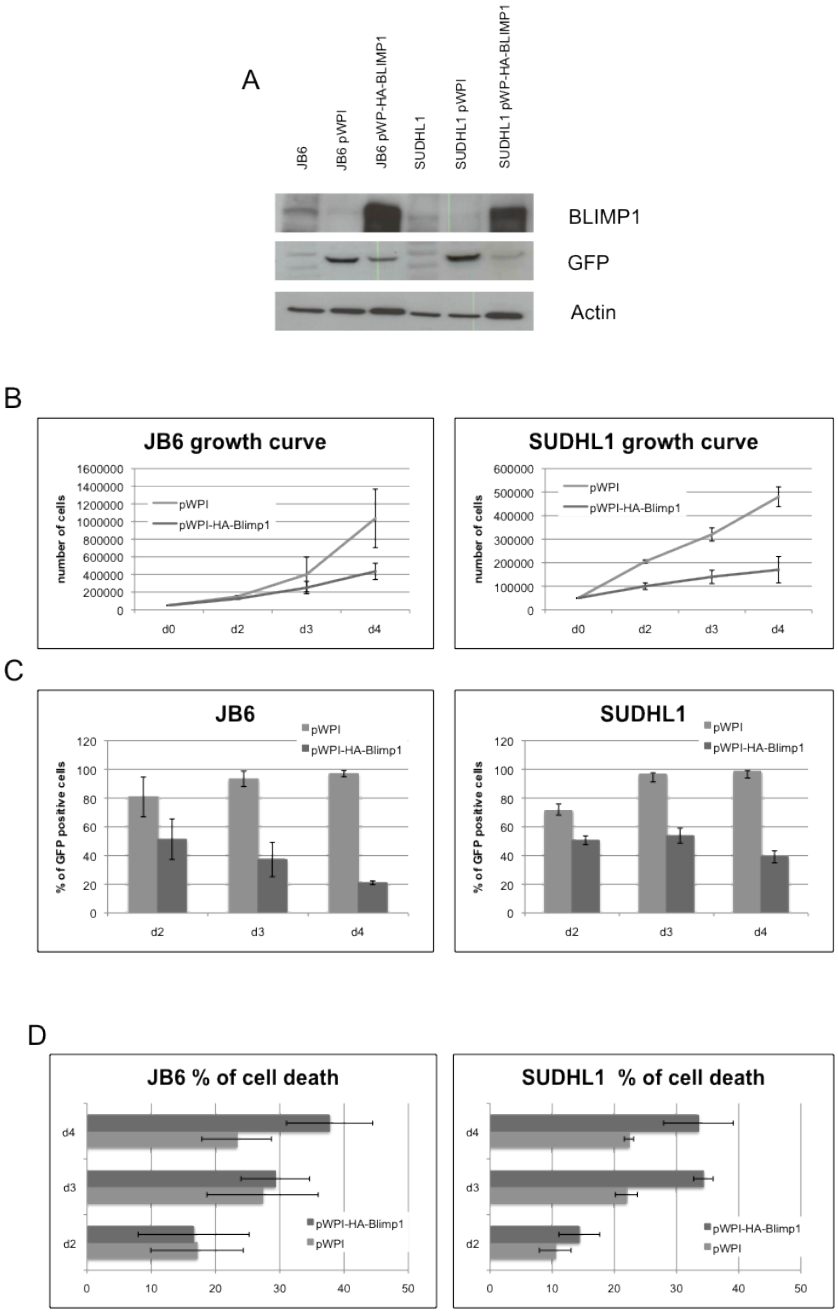

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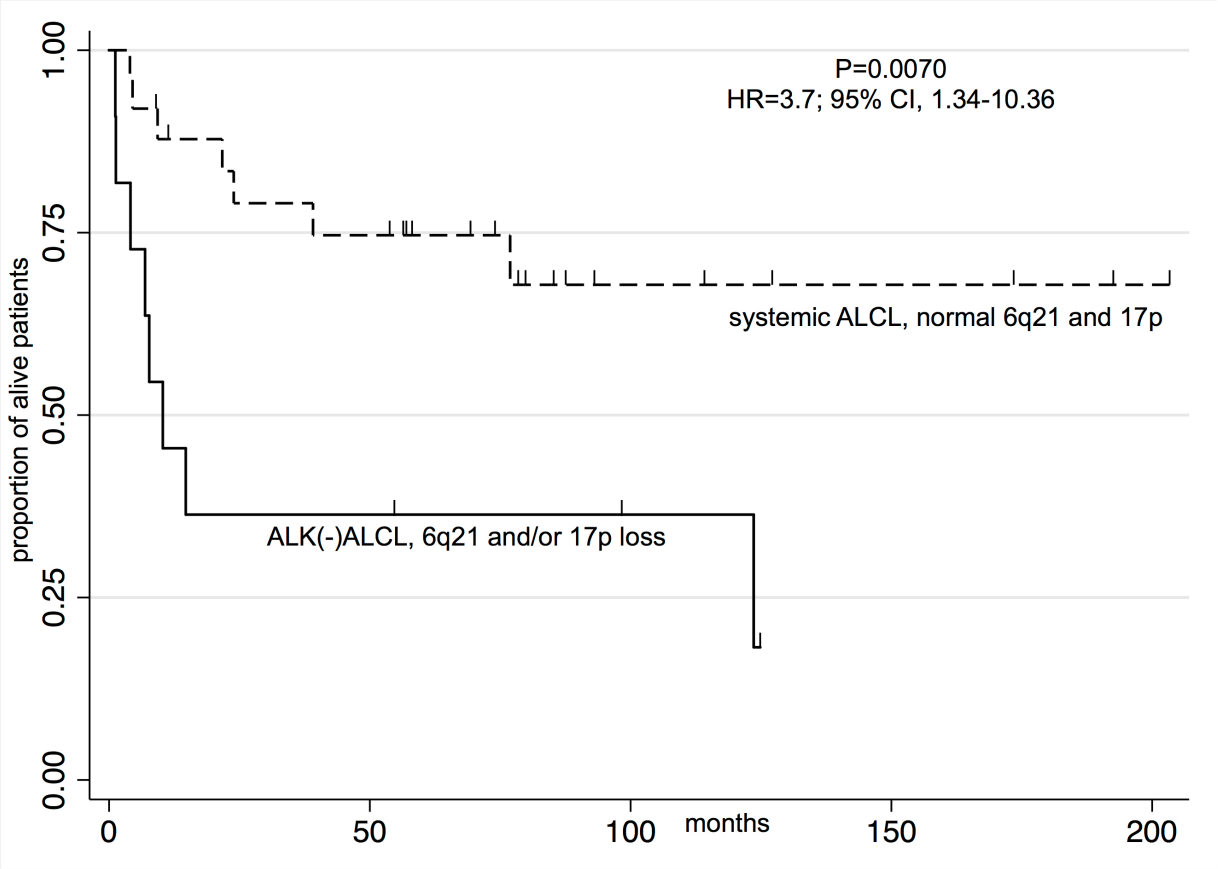

Supplementary Table 1. Primers used for DNA sequencing or real-time PCR.

Application	Target	Primer FW (5-'…-3')	Primer REV (5-'…-3')
Mutational analysis	PRDM1-ex1	TGACGCCAAACACATGTTAAA	GTTCCAGCTCACACTCGTCA
Mutational analysis	PRDM1-ex2[1]	TATACGGCTTCTTGGCTCTT	AGGAACAGTTGAAGGCTGG
Mutational analysis	PRDM1-ex3[1]	AGATGGTCTCCCCCTATGGT	AAGCAAGCAACAAACTGTTTC
Mutational analysis	PRDM1-ex4[1]	GCCCTGATTTCTGCTGATTC	GTCCCTAGCTTAAGCCACCT
Mutational analysis	PRDM1-ex1b	TAGATGTTCATCCCGTTCTGA	ACTTGAGAATGACCAAAATG
Mutational analysis	PRDM1-ex5[1]	TTGAGTGAGTGGCCCAGAG	AGGGAAGTCACTTGTCCAAA
Mutational analysis	PRDM1-ex6[1]	AAACTCCCTGCTAGCCTGTG	GCCATCTCAAGTCATCAGCA
Mutational analysis	PRDM1-ex7[1]	CACAAGGAGGCTTCTCACCT	GATTTCAGTAACTTTGGAGTT
Mutational analysis	TP53-ex4[2]	TCCTCTGACTGCTCTTTTCAC	TGAAGTCTCATGGAAGCCAG
Mutational analysis	TP53-ex5[2]	GTTTCTTTGCTGCCGTCTTC	AGCAATCAGTGAGGAATCAG
Mutational analysis	TP53-ex6[2]	TCTGATTCCTCACTGATTGCTC	CCACTGACAACCACCCTTAAC
Mutational analysis	TP53-ex7[2]	TCATCTTGGGCCTGTGTTATC	AGTGTGCAGGGTGGCAAG
Mutational analysis	TP53-ex8[2]	AGGACCTGATTTCCTTACTGCC	ATAACTGCACCCTTGGTCTCC
Methylation analyisis	PRDM1-meth	TTAGTAAATTTGGGGGAAAGTTTTG	TTAGTAAATTTGGGGGAAAGTTTTG
Real time PCR	PRDM1	ACATGACCGGCTACAAGACC	GGCATTCATGTGGCTTTTCT
Real time PCR	FGG	TGCATTAAGAGTGGAACTGGAA	TGTTAGGCGGTACTTGTCAG
Real time PCR	SERPINA3	GTTCAGAGAGATAGGTGAGC	CTGGTGAAGGCTTCCTCAAT
Real time PCR	SHIP1	CCCTGCAAGAAATCACCAGT	ATCCGGTTCTCGTGCTCAG
Real time PCR	PMAIP1	GAGATGCCTGGGAAGAAGG	TTCTGCCGGAAGTTCAGTTT
Real time PCR	GAPDH	CGACCACTTTGTCAAGCTCA	CCCTGTTGCTGTAGCCAAAT

1. Pasqualucci L, Compagno M, Houldsworth J, et al. Inactivation of the PRDM1/BLIMP1 gene in diffuse large B cell lymphoma. *J Exp Med*. 2006;203(2):311-317.
2. Rassidakis GZ, Thomaides A, Wang S, et al. p53 gene mutations are uncommon but p53 is commonly expressed in anaplastic large-cell lymphoma. *Leukemia*. 2005;19(9):1663-1669.

Supplementary Table 2. Clinical characteristics of the ALCL series [a].

	ALK-			**ALK+**		
	n	Valid	Percentage	n	Valid	Percentage
median age (range)	60 (13-83)	28		21.5 (8-68)	30	
Male/Female	17/11	28		16/14	30	
Stage						
I	3	14	21.4%	3	18	16.7%
II	6	14	42.8%	3	18	16.7%
III	1	14	7.2%	4	18	22.2%
IV	4	14	28.6%	8	18	44.4%
B symptoms						
Yes	6	9	66.7%	9	15	60%
No	3	9	33.3%	6	15	40%
Elevated LDH						
Yes	6	10	60%	10	18	55.6%
No	4	10	40%	8	18	44.4%
BM involvement						
Yes	0	13	0%	5	18	27.8%
No	13	13	100%	13	18	72.2%
Performance status						
0	3	8	37.5%	7	12	58.3%
1	4	8	50%	1	12	8.3%
2	1	8	12.5%	4	12	33.4%
Therapy						
CHOP regimen	7	13	53.8%	13	22	59.1%
no CHOP regimen	6	13	46.2%	9	22	40.9%

[a] LDH, lactate dehydrogenase; BM, bone marrow; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone.

Supplementary Table 3. Significant regions affected by DNA gains and losses in ALCL, as estimated using the GISTIC algorithm.

Lesions	Cytoband	Frequency	Start*	Size*	q-value	Residual q-value	Candidate gene
Gains							
	9p24.1	11%	5,51E+06	2,64E+06	0,23624	0,23624	*NCAM2*
	3p26.3	6%	1,67E+06	1,14E+05	0,23624	0,23624	
	15q11.2	7%	2,53E+07	3,74E+04	0,23624	0,23624	*IPW*
	20q11.22	6%	3,28E+07	2,69E+05	0,23624	0,23624	*ASIP, AHCY, ITCH, MIR644*
	11p13	5%	3,48E+07	6,87E+05	0,23624	0,23624	*APIP, PDHX, CD44*
	13q31.3	3%	8,90E+07	4,22E+06	0,23624	0,23624	*MIR17HG*
	15q25.2	3%	8,45E+07	2,85E+04	0,23624	0,23624	*ADAMTSL3*
Losses							
	17p13.1	25%	6094336	1,62E+06	0,081305	0,0099598	*TP53*
	6q21	17%	94817995	2,12E+07	4,68E-11	2,81E-10	*ATG5, PRDM1*
	13q32.3	16%	93231989	1,52E+07	0,0025428	0,011625	
	14q11.2	16%	22185014	1,29E+06	6,57E-08	1,88E-07	*TCRA, TRAC*
	16q23.2	16%	78750889	4,46E+03	1	0,1503	*WWOX*
	12q24.31	13%	121569998	5,68E+05	0,052865	0,08445	
	13q21.31	13%	62409809	3,97E+06	0,0092452	0,040311	
	13q31.1	13%	82365728	6,66E+06	0,052865	0,098264	*SLITRK1, SLITRK6*
	1p13.2	13%	108240651	1,09E+07	0,026836	0,014931	
	13q21.2	11%	60450644	2,02E+05	1	0,18826	*DIAPH3*
	12q12	9%	44431029	3,90E+05	0,57913	0,11838	*TMEM117*
	15q26.1	9%	89159161	4,58E+04	0,052865	0,08445	*AEN, ISG20*
	2q37.3	8%	240125114	1,50E+05	0,026836	0,041884	*HDAC4, MIR4269*
	18q22.1	5%	65059883	3,95E+05	0,0067821	0,013671	*DSEL*
	20q13.13	5%	48907930	7,76E+04	0,048594	0,069286	
	7q31.1	5%	110681611	8,13E+04	0,14064	0,18826	*IMMP2L*
	1q32.1	3%	198580256	3,31E+05	0,026836	0,041884	*PTPRC*
	14q23.1	3%	61926178	1,41E+03	1	0,18826	*PRKCH*
	1p31.3	3%	66726940	9,79E+04	0,081305	0,1503	*PDE4B*
	21q21.1	2%	22619036	3,63E+03	1	0,11838	*NCAM2*

* Numbering according to Genome Reference Consortium Human Build 37 (GRCh37) (hg19).

Supplementary Table 4. Significant regions affected by DNA gains and losses in ALK-ALCL, as estimated using the GISTIC algorithm.

Lesions	Cytoband	Frequency	Start*	Size*	q-value	Residual q-value	Candidate Gene
Gains							
	20q11.22	12%	3,28E+07	2,69E+05	0,22719	0,22719	*ASIP, AHCY, ITCH, MIR644*
	11p13	6%	3,48E+07	6,87E+05	0,22719	0,22719	*APIP, PDHX, CD44*
	13q31.3	6%	8,90E+07	4,22E+06	0,22719	0,22719	*MIR17HG*
Losses							
	17p13.1	42%	7,47E+06	1,06E+04	0,99208	0,1585	*TP53*
	14q11.2	39%	2,22E+07	1,29E+06	6,74E-06	3,35E-05	*TCRA, TRAC*
	6q21	33%	9,48E+07	1,86E+07	1,43E-08	8,94E-08	*ATG5, PRDM1*
	12q24.31	27%	1,22E+08	5,68E+05	0,021862	0,039734	
	1p13.2	24%	9,85E+07	2,19E+07	0,0095216	0,0063173	
	13q21.31	24%	6,24E+07	3,97E+06	0,003499	0,066829	
	13q21.33	24%	6,64E+07	7,05E+06	0,0010479	0,25555	*PCDH9, KHLH1*
	13q33.1	24%	9,32E+07	1,52E+07	0,003499	0,047195	*SLITRK1, SLITRK6*
	13q21.2	21%	6,05E+07	2,02E+05	0,99208	0,14511	*DIAPH3*
	13q31.1	21%	8,24E+07	6,59E+06	0,021862	0,091229	
	20p13	18%	7,35E+04	1,93E+03	0,1217	0,21329	
	20q13.13	18%	4,89E+07	4,00E+08	0,019672	0,039734	
	4q22.2	15%	9,40E+07	1,39E+04	1	0,21329	*GRID2*
	18q23	15%	6,51E+07	7,06E+07	0,021862	0,039734	
	21q21.1	6%	2,26E+07	3,63E+03	1	0,047195	*NCAM2*

* Numbering according to Genome Reference Consortium Human Build 37 (GRCh37) (hg19).