Supplementary data

Role of microRNAs and microRNA machinery in the pathogenesis of diffuse large B-cell lymphoma

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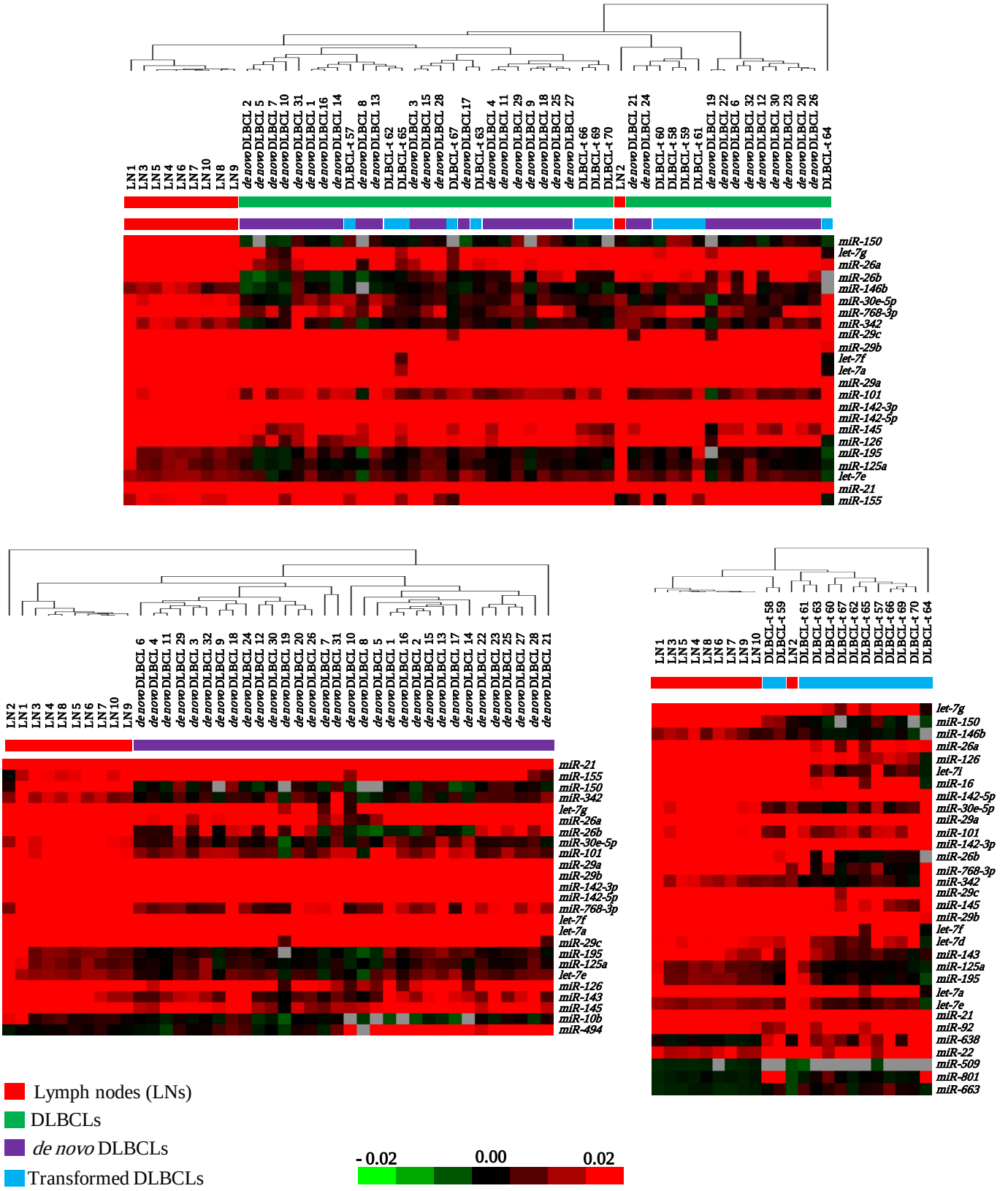

Figure S1. Supervised clustering of miRNA expression based on PAM analysis (cohort 1). The heat maps were generated using sets of miRNAs obtained by PAM analysis that could best distinguish different tumor groups from LNs. Median centered values for each miRNA are represented. The green and red colors indicate relatively low and high expression, respectively. Missing values are indicated in grey.

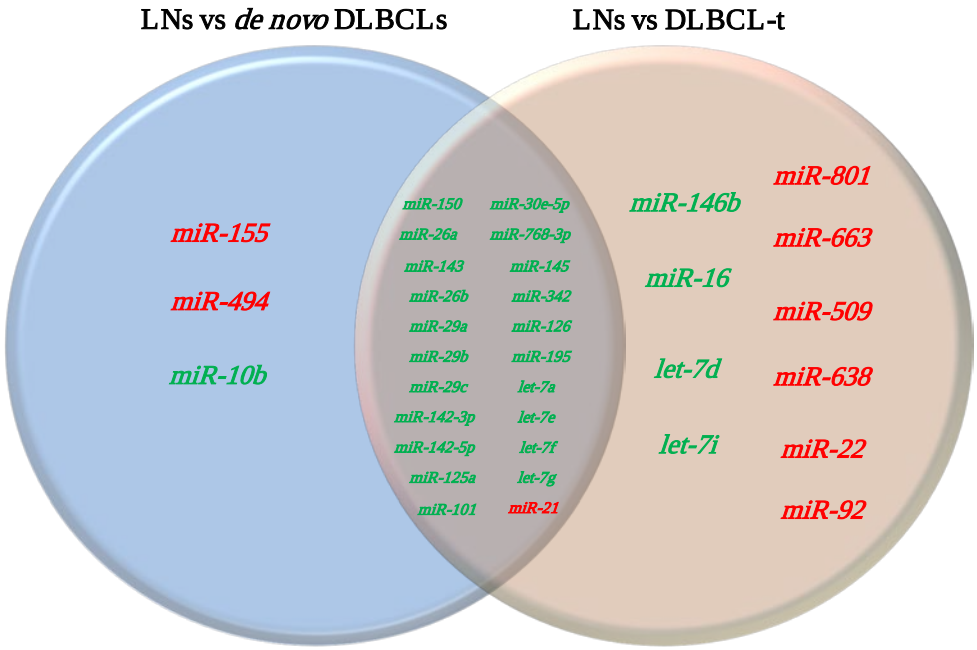

Figure S2. Deregulated miRNAs in *de novo* and transformed DLBCLs as compared to LNs. The Venn diagram shows miRNAs specifically or commonly deregulated in *de novo* and transformed DLBCL cases in comparison to LNs. Over-expressed or under-expressed miRNAs in tumors are labeled in red or green, respectively.

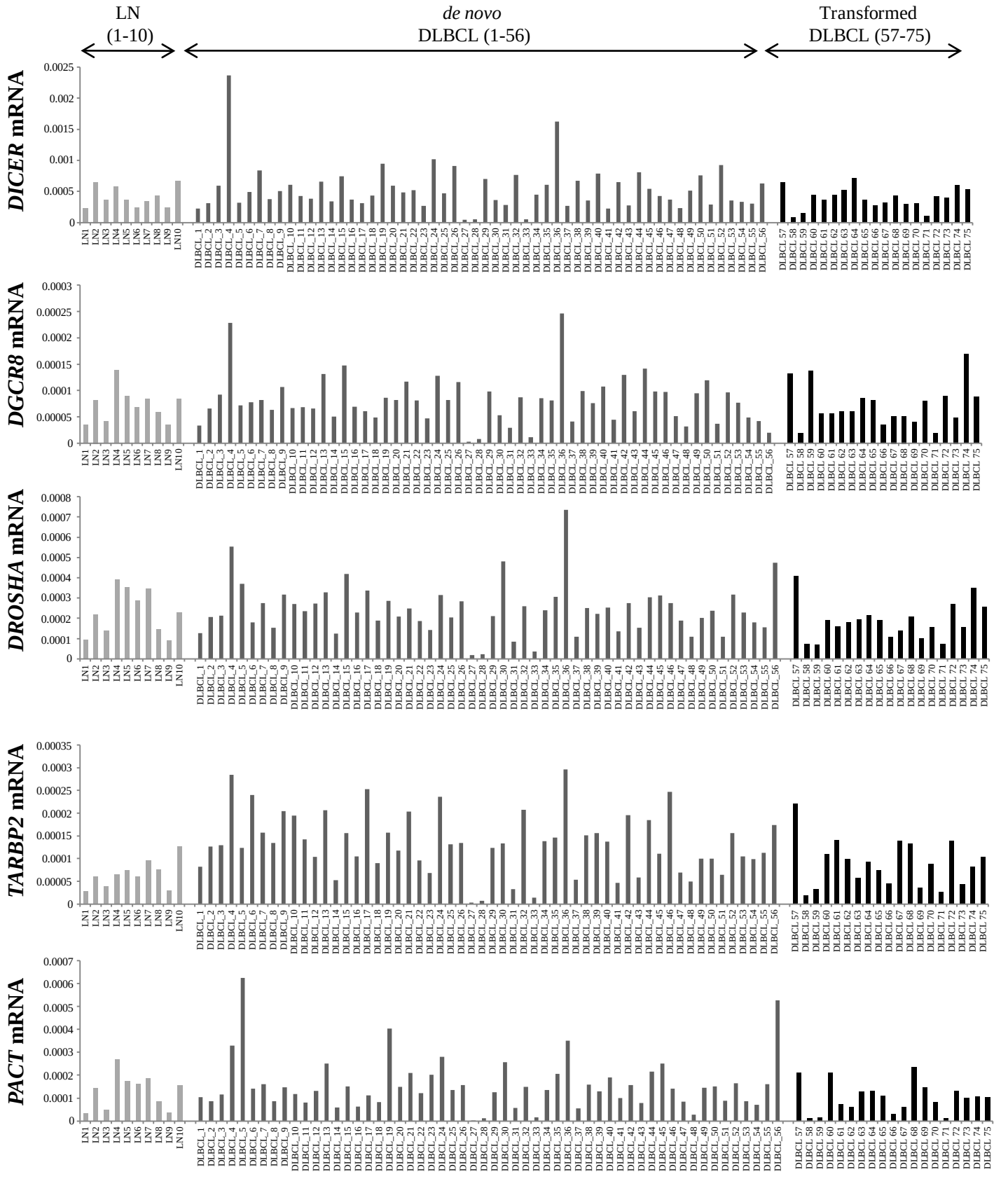

Figure S3. Gene expression levels of *DROSHA*, *DICER*, *TARBP2*, *DGCR8* and *PACT* in reactive lymph nodes and DLBCLs (cohort 1). The histograms illustrate the relative mRNA expression levels of each gene in 10 lymph nodes, 56 *de novo* DLBCLs and 19 transformed DLBCLs quantified using RT-qPCR.

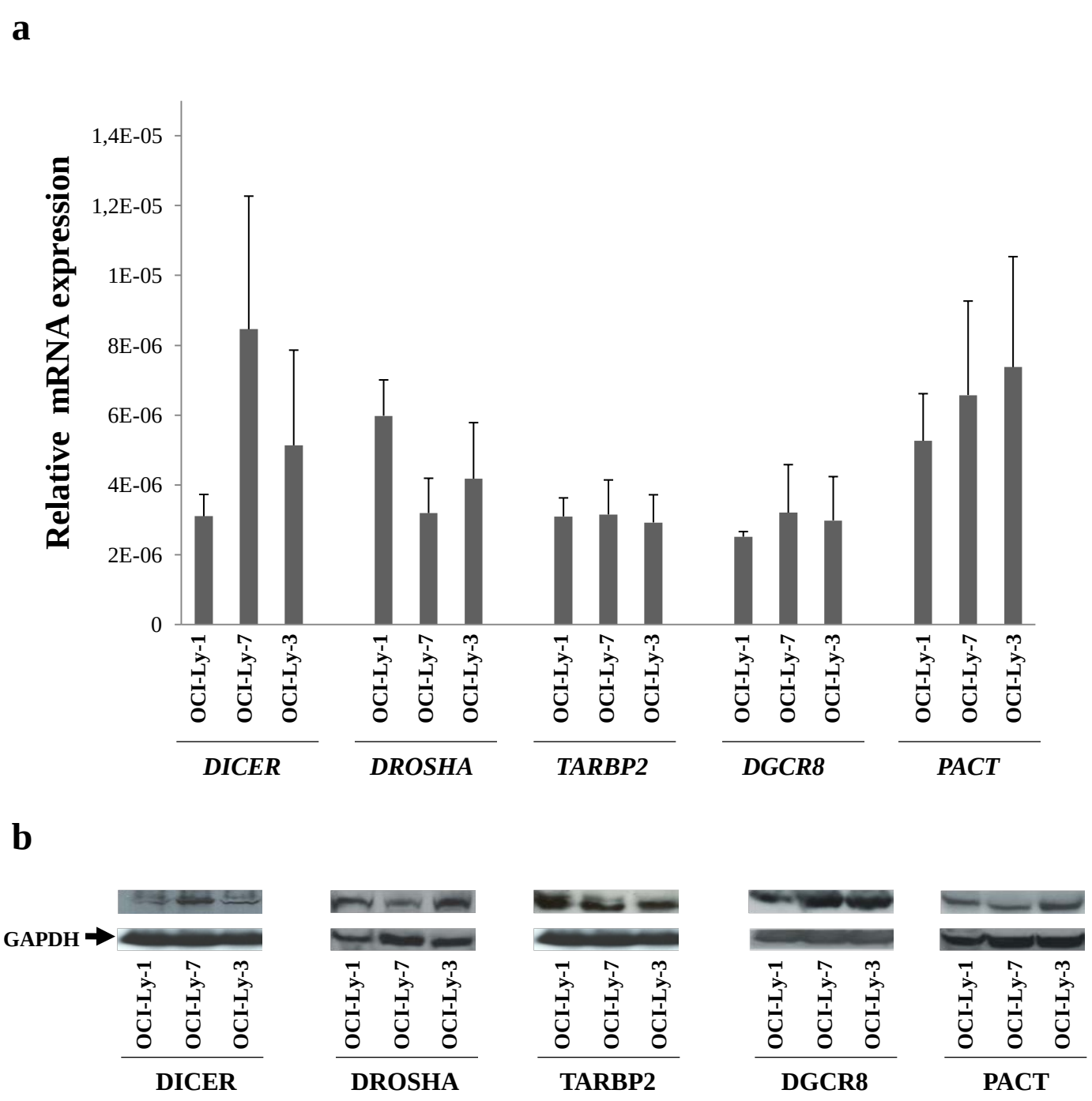

Figure S4. Expression levels of *DROSHA*, *DICER*, *TARBP2*, *DGCR8* and *PACT* in DLBCL cell lines. (**a**) The histogram illustrate the relative mRNA expression levels of each gene in three DLBCL cell lines including two GCB-type (OCI-Ly-1 and OCI-Ly-7) and one ABC-type (OCI-Ly-3) analyzed by RT-qPCR. (**b**) Representative Western blots showing protein expression levels of the five miRNA machinery factors analyzed in the three DLBCL cell lines.

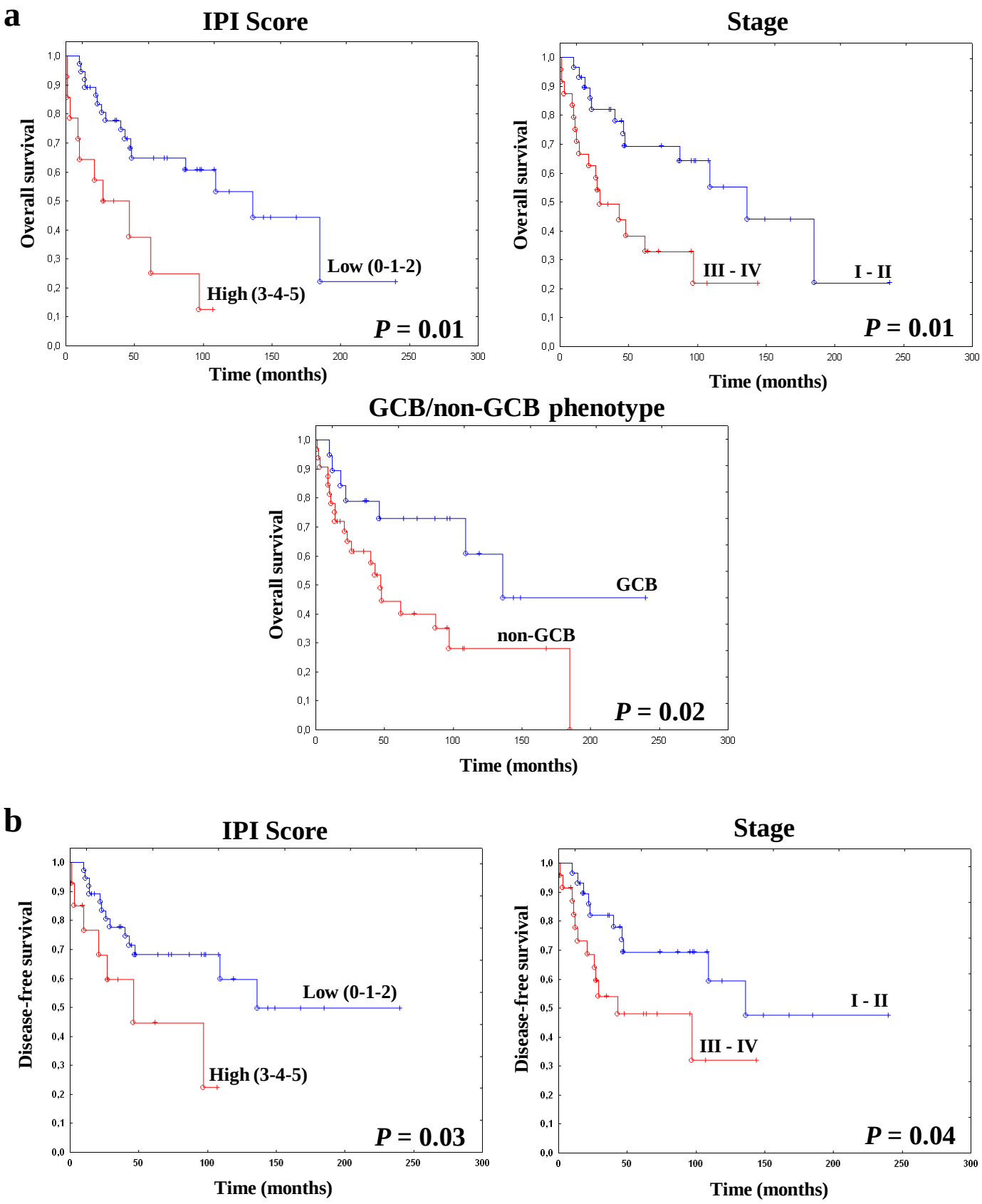

Figure S5. Association between clinical parameters and survival among *de novo* DLBCLs (cohort 1). (**a**) Kaplan-Meier plots display significant association between high IPI score, advance tumor stage and non-GCB phenotype with shorter overall survival in *de novo* DLBCL cases. (**b**) Kaplan-Meier plots display significant association between high IPI score and advance tumor stage with shorter disease-free survival in *de novo* DLBCL cases. Differences in survival between groups were calculated using log-rank test. *P*-values < 0.05 were considered significant.

Supplemental Table S1 Clinical and molecular features of the 75 DLBCL tumors studied in the cohort 1

Case	Sex -	DLBCL	IPI			Immunohistochemistry*				Treatment		Follow-up	
no.	Age	type	score	stage	GCB type#	CD10	BCL6	IRF4	BCL2	regime	outcome	time (months)	outcome
1	F-61	*de novo*	-	II	GCB	Pos.	Pos.	Neg.	Pos.	CHOP x6	CR	18	Dead - DOD
2	M-68	*de novo*	3	III	-	-	-	-	-	CHVmP-VB	CR	27	Dead - DOD
3	F-60	*de novo*	3	II	GCB	Pos.	Pos.	Pos.	Pos.	CHOP x 8	CR	46	Dead - DOD
4	F-69	*de novo*	1	I	non-GCB	Neg.	Neg.	Pos.	Neg.	R-CHOP x 4	CR	40	Dead - DOD
5	F-30	*de novo*	2	IV	non-GCB	Neg.	Neg.	Neg.	Neg.	VACOP-B	CR	14	Dead - DOD
6	F-67	*de novo*	3	III	non-GCB	Neg.	Pos.	Pos.	Pos.	CHOP x 6	CR	107	Alive
7	M-79	*de novo*	3	IV	non-GCB	Neg.	Neg.	Pos.	Pos.	CHOP x 6	no CR	21	Dead - DOD
8	F-90	*de novo*	1	I	non-GCB	Neg.	Neg.	Neg.	Neg.	-	CR	185	Dead
9	M-52	*de novo*	2	IV	non-GCB	Neg.	Neg.	Pos.	Pos.	CHOP x 6	no CR	43	Dead - DOD
10	F-67	*de novo*	-	IV	GCB	Pos.	Pos.	Neg.	Pos.	R-CHOP x 8	no CR	12	Dead - DOD
11	F-81	*de novo*	1	II	non-GCB	Neg.	Neg.	Pos.	Pos.	Palliative chemotherapy	no CR	14	Dead - DOD
12	M-77	*de novo*	1	II	GCB	Pos.	Pos.	Pos.	Neg.	R-CHOP x 4	CR	136	Dead - DOD
13	M-72	*de novo*	4	IV	non-GCB	Neg.	Neg.	Pos.	Pos.	CHOP	no CR	3	Dead - DOD
14	M-50	*de novo*	2	III	non-GCB	Neg.	Neg.	Pos.	Pos.	CHOP x 7	CR	26	Dead - DOD
15	F-79	*de novo*	4	IV	non-GCB	Neg.	Neg.	Pos.	Neg.	CHOP x 6	CR	62	Dead
16	M-42	*de novo*	0	I	GCB	Pos.	Neg.	Neg.	Pos.	R-CHOP x 3	CR	149	Alive
17	F-79	*de novo*	2	III	non-GCB	Neg.	Neg.	Neg.	Pos.	CHOP x 6	CR	48	Dead
18	M-78	*de novo*	4	IV	non-GCB	Neg.	Neg.	Neg.	Pos.	-	-	9	Dead
19	M-47	*de novo*	1	II	GCB	Pos.	Pos.	Pos.	Pos.	CHOP x 8	CR	109	Dead - DOD
20	F-71	*de novo*	3	III	non-GCB	Neg.	Neg.	Neg.	Pos.	CHOP x 8	CR	10	Dead - DOD
21	M-31	*de novo*	1	II	GCB	Pos.	Pos.	Pos.	Pos.	Other CT	CR	119	Alive
22	M-68	*de novo*	5	IV	non-GCB	Neg.	Pos.	Pos.	Neg.	CHOP x 9	CR	97	Dead - DOD
23	F-70	*de novo*	1	II	GCB	Pos.	Neg.	Pos.	Pos.	CHOP x 8	CR	240	Alive
24	F-49	*de novo*	0	I	GCB	Pos.	Pos.	Pos.	Neg.	CHOP x 3	CR	99	Alive
25	M-50	*de novo*	1	I	non-GCB	Neg.	Neg.	Neg.	Pos.	op	CR	47	Dead - DOD
26	M-64	*de novo*	1	II	GCB	Pos.	Neg.	Neg.	Pos.	CHOP x 6	CR	96	Alive
27	M-69	*de novo*	2	III	non-GCB	Neg.	Neg.	Neg.	Pos.	CHOP x 5	no CR	11	Dead - DOD
28	F-44	*de novo*	1	III	GCB	Pos.	Pos.	Pos.	Pos.	VACOP-B	CR	144	Alive
29	F-68	*de novo*	1	II	non-GCB	Neg.	Neg.	Neg.	Pos.	CHOP x6	CR	96	Alive
30	M-68	*de novo*	1	I	GCB	Pos.	Pos.	Neg.	Neg.	-	CR	98	Alive
31	M-25	*de novo*	2	III	-	-	Neg.	Neg.	Neg.	VACOP-B	CR	29	Dead - DOD
32	M-74	*de novo*	4	IV	non-GCB	Neg.	Neg.	Pos.	Pos.	CHOP x1	no CR	1	Dead - DOD
33	F-77	*de novo*	-	-	non-GCB	Neg.	Neg.	Pos.	Pos.	-	-	4	Dead
34	M-78	*de novo*	4	IV	non-GCB	Neg.	Pos.	Pos.	Pos.	no treatment	no CR	1	Dead
35	F-83	*de novo*	1	I	GCB	Pos.	Neg.	Neg.	Neg.	op	CR	22	Dead - DOD
36	M-65	*de novo*	1	I	non-GCB	Neg.	Pos.	Pos.	Neg.	-	-	16	Dead
37	F-78	*de novo*	1	I	non-GCB	Neg.	Neg.	Pos.	Neg.	-	-	87	Dead
38	M-66	*de novo*	-	-	non-GCB	Neg.	Neg.	Pos.	Neg.	-	-	9	Dead
39	F-79	*de novo*	1	II	GCB	Pos.	Pos.	Pos.	Pos.	R-CHOP-14 x 6	CR	36	Alive
40	F-80	*de novo*	3	IV	non-GCB	Neg.	Pos.	Pos.	Pos.	R-CHOP-14 x 6	CR	28	Alive
41	M-78	*de novo*	1	I	GCB	Pos.	Pos.	Neg.	Pos.	R-CHOP-21 x 6	CR	47	Alive
42	M-75	*de novo*	2	IV	non-GCB	Neg.	Neg.	Pos.	Pos.	CHOP x 8	CR	72	Alive
43	M-70	*de novo*	1	II	non-GCB	Neg.	Neg.	Pos.	Pos.	CHOP x 6	CR	108	Alive
44	M-72	*de novo*	4	III	non-GCB	Neg.	Neg.	Pos.	Neg.	R-CHOP 14 x 6	CR	35	Alive
45	F-73	*de novo*	1	II	GCB	Pos.	Pos.	Neg.	Pos.	R-CHOP-21 x 6	CR	10	Dead - DOD
46	F-69	*de novo*	3	IV	GCB	Pos.	-	-	Pos.	R-CHOP-14 x 6	CR	64	Alive
47	M-64	*de novo*	-	-	non-GCB	Neg.	Neg.	Neg.	Pos.	-	-	2	Dead
48	M-69	*de novo*	4	IV	non-GCB	Neg.	Pos.	Pos.	Pos.	R-CHOP-14 x 6	CR	28	Alive
49	F-63	*de novo*	1	I	GCB	Pos.	Pos.	Neg.	Neg.	CHOP x 4	CR	87	Alive
50	M-63	*de novo*	2	I	non-GCB	Neg.	Neg.	Neg.	Pos.	R-CHOP-14 x 6	CR	45	Alive
51	F-61	*de novo*	2	II	non-GCB	Neg.	Pos.	Pos.	Pos.	R-CHOP-14 x 6	CR	23	Dead - DOD
52	M-52	*de novo*	0	II	non-GCB	Neg.	Neg.	Neg.	Neg.	CHOP x 4 + RT	CR	168	Alive
53	F-52	*de novo*	1	III	non-GCB	Neg.	Pos.	Pos.	Neg.	R-CHOEP x 6	CR	96	Alive
54	M-49	*de novo*	0	II	GCB	Pos.	Pos.	Neg.	Pos.	R-CHOP-14 x 6	CR	37	Alive
55	M-48	*de novo*	1	II	non-GCB	Neg.	Pos.	Pos.	Pos.	R-CHOP-14 x 6	CR	18	Alive
56	M-17	*de novo*	0	I	GCB	Pos.	Pos.	Pos.	Neg.	R-CHOP-21 x 6	CR	74	Alive
57	M-49	Transformed	1	III	GCB	Pos.	Pos.	Neg.	Neg.	-	CR	-	-
58	F-68	Transformed	3	III	non-GCB	Neg.	Neg.	Neg.	Neg.	CHOP x 8	CR	-	-
59	F-74	Transformed	1	II	non-GCB	Neg.	Neg.	Neg.	Pos.	CHOP x 8	CR	-	-
60	F-47	Transformed	2	IV	GCB	Pos.	Pos.	Neg.	Pos.	CHOP x 6	no CR	-	-
61	M-76	Transformed	2	IV	GCB	Pos.	Neg.	Neg.	Pos.	CHOP x 5	no CR	-	-
62	M-66	Transformed	3	IV	GCB	Pos.	Neg.	Neg.	Pos.	CHOP x 9	no CR	-	-
63	F-33	Transformed	2	III	GCB	Pos.	Pos.	Neg.	Pos.	CHOP x 5	CR	-	-
64	F-68	Transformed	2	IV	non-GCB	Neg.	Neg.	Pos.	-	R-CHOP-14 x 6	CR	-	-
65	M-79	Transformed	5	IV	GCB	Pos.	Pos.	Neg.	-	CHOP x 1	no CR	-	-
66	F-63	Transformed	1	II	GCB	Pos.	Pos.	Neg.	-	R-CHOP x 6	CR	-	-
67	F-55	Transformed	2	III	-	-	-	-	-	R-CHOP-14 x 6	CR	-	-
68	M-53	Transformed	3	IV	GCB	Pos.	Pos.	Pos.	-	R-CHOP-14 x 6	CR	-	-
69	M-75	Transformed	2	III	GCB	Pos.	Pos.	Neg.	-	R-CHOP-14 x 6, R-ICE x 3	no CR	-	-
70	M-70	Transformed	3	III	GCB	Pos.	Pos.	Neg.	-	R-ICE x 6	CR	-	-
71	M-66	Transformed	1	II	GCB	Pos.	Pos.	Pos.	-	R-ICE x 5 + HDTC	CR	-	-
72	M-58	Transformed	1	I	GCB	Pos.	Pos.	Pos.	-	RT	no CR	-	-
73	F-83	Transformed	3	IV	GCB	Pos.	Pos.	Pos.	-	CVIP + RT	no CR	-	-
74	M-61	Transformed	1	II	-	-	-	-	-	R-CHOP-14 x 6	CR	-	-
75	F-63	Transformed	1	II	-	-	-	-	-	R-CHOP-21 x 6	CR	-	-

[#]GCB and non-GCB subtypes were classified based on the algorithm of Hans et al., 2004 (ref. 28);
*Immunohistochemistry results have been partly published in Berglund et al., 2005 (ref. 3);
F=female; M=male; GCB=Germinal center B-cell; Pos=positive; Neg=negative;
CHOP=Cyclophosphamide, Doxorubicin, Oncovin and Prednisone; R-CHOP=CHOP+Rituximab;
CHVmP-VB=Cyclophosphamide, Doxorubicin, Tenioposide, Prednisone, Vincristine and Bleomycin; CT=chemotherapy; op=operation;
VACOP-B=Etoposide, Doxorubicin, Cyclophosphamide, Vincristine, Prednisone and Bleomycin; RT=Radiotherapy; CHOEP=CHOP+Etoposide;
R-ICE=Rituximab, Ifosfamide, Carboplatin and Etoposide; HDCT=high dose chemotherapy followed by autologous stem cell transplantation;
CVIP=Cyclophosphamide, Oncovin, Idarubicin and Prednisone;
CR=complete response; no CR=no complete response; DOD=dead of disease

Supplemental Table S2 Clinical and molecular features of the 47 DLBCL tumors studied in the cohort 2

Case	Sex -	DLBCL	IPI			Immunohistochemistry*				Treatment		Follow-up	
no.	Age	type	score	stage	GCB type#	CD10	BCL6	IRF4	BCL2	regime	outcome	time (months)	outcome
1	M-57	*de novo*	0	II	non-GCB	Neg	pos	pos	neg	CHOP x 8	CR	5	Alive
2	M-84	*de novo*	2	III	non-GCB	neg	neg	pos	-	no treatment	-	5	Dead - DOD
3	M-84	*de novo*	2	III	non-GCB	neg	neg	pos	-	no treatment	-	5	Dead - DOD
4	M-48	*de novo*	1	I	GCB	Neg	w. pos	neg	-	CHOP-R x 6	CR	14	Alive
5	M-62	*de novo*	1	II	GCB	pos	neg	neg	neg	CHOP x 6	CR	51	Alive
6	M-79	*de novo*	3	II	GCB	neg	pos	neg	-	RT	-	3	Dead - DOD
7	M-60	*de novo*	2	I	non-GCB	neg	neg	pos	pos	CNOP-R x 6	-	5	Dead - DOD
8	F-62	*de novo*	3	II	GCB	pos	pos	pos	-	CHOP-R	no CR	41	Alive
9	F-77	*de novo*	3	I	non-GCB	neg	neg	neg	pos	CNOP x 6	no CR	34	Alive
10	M-61	*de novo*	1	I	non-GCB	neg	neg	pos		CHOP-R x 6 + MTX x 1 + RT	CR	29	Alive
11	M-74	*de novo*	1	I	GCB	neg	pos	neg	-	CHOP-R x 4 + IFRT	CR	36	Alive
12	F-59	*de novo*	0	I	GCB	neg	pos	neg	neg	CHOP-R x 4 + RT	CR	27	Alive
13	M-39	*de novo*	0	I	GCB	pos	neg	pos	pos	A-EPOCH-R x 4	no CR	15	Alive
14	M-63	*de novo*	1	I	non-GCB	neg	neg	pos	pos	CHOP-R	CR	14	Alive
15	-	*de novo*	-	-	GCB	pos	pos	pos	-	-	-	-	-
16	F-84	*de novo*	1	I	non-GCB	neg	pos	pos	-	PMitCEBO-R x 6	CR	24	Alive
17	F-81	*de novo*	2	II	-	-	-	-	-	PMitCEBO x 6	-	5	Dead
18	F-80	*de novo*	1	I	non-GCB	neg	pos	pos	-	CHOP-R x 6	-	16	Dead - DOD
19	M-44	*de novo*	1	I	non-GCB	neg	neg	neg	pos	CODOX-M / IVAC	CR	45	Alive
20	F-67	*de novo*	3	IV	GCB	pos	pos	neg	-	CHOP-R x 6	CR	46	Alive
21	F-62	*de novo*	4	III	GCB	pos	pos	neg	-	CODOX-M / IVAC	no CR	36	Alive
22	M-56	*de novo*	2	IV	GCB	neg	neg	neg	pos	CHOP-R x 8	CR	19	Alive
23	F-10	*de novo*	2	I	non-GCB	neg	neg	pos	-	CHOP-R x 6	CR	33	Alive
24	F-71	*de novo*	4	III	GCB	pos	pos	neg	neg	CHOP-R	no CR	7	Dead - DOD
25	F-64	*de novo*	2	III	GCB	pos	pos	pos	-	CHOP-R x 6	CR	21	Alive
26	M-38	*de novo*	1	I	GCB	pos	pos	neg	neg	CODOX-M + RT	no CR	11	Alive
27	M-48	*de novo*	4	IV	non-GCB	neg	neg	pos	-	CHOP-R-14 x 8	CR	21	Alive
28	M-83	*de novo*	-	-	-	-	-	-	-	-	-	-	-
29	M-62	*de novo*	1	II	GCB	pos	neg	neg	neg	CHOP x 6	CR	51	Alive
30	M-75	*de novo*	2	III	-	-	-	-	-	no treatment	-	2	Dead - DOD
31	M-66	*de novo*	3	II	GCB	pos	pos	neg	pos	CHOP x 8	-	43	Alive
32	M-75	*de novo*	4	III	non-GCB	neg	neg	pos	pos	no treatment	-	1	Dead - DOD
33	F-84	*de novo*	1	I	non-GCB	neg	pos	pos	neg	no treatment	-	60	Alive
34	M-65	*de novo*	1	I	non-GCB	neg	neg	pos	neg	CHOP-R x 4 IFRT	-	29	Alive
35	F-75	*de novo*	2	III	GCB	neg	pos	neg	pos	CHOP-R x 6	CR	27	Alive
36	M-58	*de novo*	1	III	non-GCB	neg	pos	pos	pos	CHOP-R x 6	CR	9	Alive
37	M-59	*de novo*	0	I	non-GCB	neg	pos	pos	pos	CHOP x 6	-	50	-
38	M-57	*de novo*	0	I	GCB	pos	pos	neg	neg	CHOP-R x 6	CR	34	Alive
39	M-54	Transformed	1	IV	non-GCB	neg	pos	pos	pos	CHOP	-	1	Dead - DOD
40	F-51	Transformed	1	II	GCB	Pos	neg	pos	neg	CHOP x 6	-	4	Alive
41	M-66	Transformed	3	IV	non-GCB	Neg	pos	pos	-	CHOP x 4	-	3	Dead - DOD
42	F-69	Transformed	2	III	GCB	neg	pos	neg	-	CHOP-R x 8	no CR	30	Alive
43	M-80	Transformed	-	-	non-GCB	neg	neg	pos	-	CHOP-R x 6	CR	-	-
44	F-91	Transformed	-	I	GCB	pos	pos	neg	-	RT	-	-	-
45	M-70	Transformed	3	III	GCB	pos	neg	neg	-	RT	no CR	-	Alive
46	M-71	Transformed	1	I	non-GCB	neg	pos	pos	-	CHOP-R x 6 + RT x 4 + adjuvant RT	CR	33	Alive
47	M-64	Transformed	-	-	GCB	pos	pos	neg	pos	CHOP-R	-	6	Dead - DOD

#GCB and non-GCB subtypes were classified based on the algorithm of Hans et al., 2004 (ref. 28);
*Immunohistochemistry results have been partly published in Lawrie et al., 2007 (ref. 13) and 2009 (ref. 14);
F=female; M=male; GCB=Germinal center B-cell; Pos=positive; Neg=negative;
CHOP=Cyclophosphamide, Doxorubicin, Oncovin and Prednisone; R=Rituximab;
RT=Radiotherapy; CNOP=Cyclophosphamide, Novantrone, Oncovin and Prednisone; MTX=Methotrexate;
IFRT=involved field RT; A-EPOCH=Doxorubicin, Etoposide, Prednisone, Oncovin and Cyclophosphamide;
PMitCEBO=Prednisolone, Mitoxantrone, Cyclophosphamide, Etoposide, Bleomycin and Oncovin;
CODOX-M / IVAC=Cyclophosphamide, Oncovin and Doxorubicin - Methotrexate / Isosfamide, Etoposide and high dose of Cytarubine;
CR=complete response; no CR=no complete response; DOD=dead of disease

Supplemental Table S3 Array-based SAM results for deregulated miRNAs in DLBCLs as compared to lymph nodes (LNs)

miRNA	Score (d)	*q* -value (%)
All DLBCLs vs. LNs		
Over-expressed miRNAs in all DLBCLs		
miR-21	3.83	0
miR-494	1.95	9.42
miR-155	1.94	9.42
miR-34a	1.89	9.42
miR-638	1.77	16.14
miR-20a	1.61	16.14
miR-19b	1.55	17.26
miR-19a	1.49	17.26
miR-22	1.48	17.26
miR-663	1.47	17.26
miR-106a	1.46	17.26
miR-92	1.45	17.26
miR-324-3p	1.43	17.26
miR-801	1.36	17.26
Under-expressed miRNAs in all DLBCLs		
miR-150	- 10.16	0
let-7g	- 9.04	0
miR-26a	- 7.56	0
miR-26b	- 5.39	0
miR-30e-5p	- 5.12	0
miR-145	- 4.46	0
miR-29c	- 4.37	0
miR-126	- 4.30	0
miR-101	- 3.93	0
miR-29a	- 3.82	0
miR-125a	- 3.51	0
miR-195	- 3.33	0
let-7f	- 3.12	0
miR-143	- 3.06	0
miR-142-3p	- 2.87	0
miR-768-3p	- 2.87	0
*miR-126**	- 2.84	0
miR-342	- 2.82	0
let-7a	- 2.78	0
miR-10b	- 2.74	0
let-7e	- 2.71	0
miR-29b	- 2.68	0
miR-142-5p	- 2.66	0
miR-146b	- 2.62	0

miR-497	- 2.23	0
miR-10a	- 1.99	2.42
miR-30a-5p	- 1.98	2.42
let-7d	- 1.94	2.42
let-7c	- 1.70	6.56
miR-374	- 1.70	6.56
miR-23b	- 1.52	10.27
miR-223	- 1.49	10.27
miR-23a	- 1.30	16.14
let-7i	- 1.24	16.14
miR-186	- 1.24	16.14
*miR-199a**	- 1.21	16.14
miR-199a	- 1.20	16.14
miR-125b	- 1.17	16.14
miR-130a	- 1.11	19.16
miR-191	- 1.11	19.16
miR-99a	- 1.10	19.16

De novo **DLBCLs vs. LNs**

Over-expressed miRNAs in de novo DLBCLs		
miR-21	3.46	0
miR-155	2.56	1.75
miR-494	2.23	4.40
miR-34a	2.17	4.40
miR-22	1.80	9.23
miR-324-3p	1.73	9.23
miR-20a	1.68	9.23
miR-19b	1.65	9.23
miR-638	1.63	9.23
miR-19a	1.62	9.23
miR-663	1.50	13.81
miR-106a	1.50	13.81
miR-92	1.48	13.81
miR-146a	1.41	13.81
miR-574	1.38	13.81
Under-expressed miRNAs in de novo DLBCLs		
miR-150	- 9.36	0
let-7g	- 8.71	0
miR-26a	- 7.16	0
miR-30e-5p	- 5.82	0
miR-26b	- 5.43	0
miR-126	- 4.87	0
miR-145	- 4.71	0
miR-101	- 3.98	0
miR-29c	- 3.72	0
miR-29a	- 3.59	0
miR-195	- 3.47	0

*miR-126**	- 3.44	0
miR-125a	- 3.33	0
miR-342	- 3.29	0
miR-10b	- 3.11	0
miR-768-3p	- 3.07	0
miR-143	- 2.99	0
miR-142-3p	- 2.75	0
let-7e	- 2.69	0
let-7f	- 2.65	0
let-7c	- 2.62	0
let-7a	- 2.45	0
miR-146b	- 2.37	0
*miR-199a**	- 2.14	0
miR-142-5p	- 2.06	2.09
miR-30a-5p	- 2.01	2.09
miR-125b	- 1.99	2.09
miR-29b	- 1.93	2.09
miR-10a	- 1.93	2.09
miR-23b	- 1.80	3.29
let-7d	- 1.76	3.29
miR-100	- 1.69	4.65
miR-223	- 1.68	4.65
miR-374	- 1.53	5.71
miR-497	- 1.46	8.14
miR-140	- 1.41	8.14
miR-199a	- 1.33	10.58
miR-23a	- 1.15	14.10
miR-186	- 1.13	14.10
miR-191	- 1.12	14.10
miR-130a	- 0.98	18.40

Transformed DLBCLs vs. LNs

Over-expressed miRNAs in transformed DLBCLs		
miR-21	4.55	0
miR-509	3.46	0
miR-638	3.17	0
miR-663	3.09	0
miR-370	2.30	1.69
miR-422b	2.00	7.73
miR-801	1.99	7.73
miR-630	1.77	17.25
Under-expressed miRNAs in transformed DLBCLs		
let-7g	- 7.54	0
miR-26a	- 7.07	0
miR-150	- 6.71	0
miR-26b	- 5.90	0
miR-30e-5p	- 4.56	0

miR-101	- 4.33	0
miR-29a	- 4.15	0
miR-142-5p	- 4.15	0
miR-29b	- 4.07	0
let-7f	- 3.64	0
miR-125a	- 3.50	0
miR-146b	- 3.49	0
miR-186	- 3.27	0
miR-29c	- 3.11	0
miR-145	- 3.05	0
miR-195	- 3.03	0
miR-374	- 3.02	0
miR-126	- 2.89	0
miR-768-3p	- 2.61	0
miR-497	- 2.61	0
let-7i	- 2.58	0
miR-143	- 2.49	0
miR-342	- 2.36	0
miR-30b	- 2.32	0
miR-142-3p	- 2.29	0
let-7d	- 2.21	0
miR-365	- 2.07	0
miR-130a	- 2.05	0
miR-16	- 2.05	0
let-7a	- 2.03	0
let-7e	- 1.95	0
*miR-126**	- 1.88	1.79
miR-146a	- 1.71	1.79
miR-27b	- 1.66	1.79
miR-30c	- 1.64	3.00
miR-23a	- 1.63	3.00
miR-98	- 1.60	3.00
miR-107	- 1.59	3.00
miR-100	- 1.48	5.48
miR-191	- 1.44	5.48
miR-148b	- 1.42	5.48
miR-10b	- 1.41	5.48
miR-223	- 1.32	7.73
miR-221	- 1.25	10.10
miR-7	- 1.19	14.31
miR-23b	- 1.17	14.31
miR-199a	- 1.14	14.31
miR-30a-5p	- 1.11	17.25
miR-10a	- 1.02	17.25

Only miRNAs with FDR < 20% are listed

Supplemental Table S4 Validation of differentially expressed miRNAs in DLBCLs vs. LNs by RT-qPCR

miRNA	DLBCLs (n=75) vs. LNs (n=6)	*P*- value
miR-150	Underexpressed in DLBCLs	0.01
miR-29b	Underexpressed in DLBCLs	0.03
miR-29a	Underexpressed in DLBCLs	< 0.001
miR-142-3p	Underexpressed in DLBCLs	0.03
miR-142-5p	Underexpressed in DLBCLs	< 0.01
miR-145	Underexpressed in DLBCLs	0.01
miR-143	Underexpressed in DLBCLs	< 0.01
miR-195	Underexpressed in DLBCLs	< 0.001
miR-497	Underexpressed in DLBCLs	< 0.001
miR-494	Overexpressed in DLBCLs	< 0.001
miR-638	Overexpressed in DLBCLs	< 0.01
miR-21	Overexpressed in DLBCLs	< 0.001
miR-155	Overexpressed in DLBCLs	< 0.001

P -values were determined by unpaired *t* -test

Supplemental Table S5 RT-qPCR analysis of differentially expressed miRNAs between *de novo* and transformed DLBCLs

miRNA	*de novo* (n=56) vs. transformed (n=19) DLBCLs	*P*- value
miR-103	Underexpressed in transformed DLBCLs	0.02
miR-107	Underexpressed in transformed DLBCLs	< 0.01
miR-146a	Underexpressed in transformed DLBCLs	< 0.001
miR-140	Overexpressed in transformed DLBCLs	0.03
let-7i	Underexpressed in transformed DLBCLs	< 0.01
miR-16	-	ns
miR-29b	-	ns
miR-155	Underexpressed in transformed DLBCLs	< 0.001
miR-142-5p	Underexpressed in transformed DLBCLs	0.04

P -values were determined by unpaired *t* -test

ns, not significant; -, no change

Supplemental Table S6 Array-based SAM results for association between miRNAs expression and clinical/molecular features of *de novo* DLBCLs

miRNA	Score (d)	*q-value* (%)
GCB (n = 11) vs. non-GCB (n = 17)		
Over-expressed miRNAs in non-GCB cases		
let-7g	2.02	0
miR-155	1.72	0
miR-29c	1.48	0
miR-146a	1.30	0
miR-451	1.30	0
miR-16	1.28	0
Positive (n = 10) vs. negative (n = 19) BCL6 expression		
Under-expressed miRNAs in BCL6 positive cases		
miR-142-3p	- 2.34	0
miR-29a	- 2.26	0
miR-142-5p	- 2.11	0
miR-101	- 1.73	0
Positive (n = 15) vs. negative (n = 14) IRF4 expression		
Under-expressed miRNAs in IRF4 positive cases		
miR-142-3p	- 2.60	0
miR-142-5p	- 2.57	0
miR-107	- 2.09	0
miR-29b	- 2.04	0
miR-425-5p	- 1.89	0
let-7g	- 1.76	17.33
miR-103	- 1.64	17.33
Stage I-II (n =15) vs. Stage III-IV (n = 17)		
Over-expressed miRNAs in stage III-IV DLBCLs		
miR-494	2.03	0

Only miRNAs with FDR < 20% are listed

Supplemental Table S7 Correlation between clinical and tumor characteristics and gene expression levels of *DROSHA* , *DICER* , *TARBP2* , *DGCR8* and *PACT* in *de novo* cases of the cohort 1

Parameter	No	*DROSHA*			*DICER*			*TARBP2*			*DGCR8*			*PACT*		
	Cases	high	low	*P*- value	high	low	*P*- value	high	low	*P*- value	high	low	*P*- value	high	low	*P*- value
Age																
> 68	26	15	11	0.28	11	15	0.28	15	11	0.28	13	15	1.00	13	15	1.00
≤ 68	30	13	17		17	13		13	17		15	15		15	15	
Gender																
Male	31	17	14	0.42	16	15	0.78	16	15	0.78	16	15	0.78	16	15	0.78
Female	25	11	14		12	13		12	13		12	13		12	13	
Disease stage																
I-II	29	14	15	0.67	15	14	1	14	15	0.67	14	15	0.67	15	14	1
III-IV	24	13	11		12	12		13	11		13	11		12	12	
IPI																
0-2	36	18	18	0.83	16	20	0.15	17	19	0.41	15	21	**0.01**	18	18	0.51
3-5	15	8	7		10	5		9	6		12	3		9	6	
GCB-phenotype																
GCB	20	11	9	0.86	10	10	0.69	10	10	0.69	9	11	0.33	11	9	0.86
non-GCB	34	17	17		18	16		18	16		19	15		17	17	
CD10																
Negative	35	18	17	0.77	18	17	1	18	17	0.77	19	16	0.38	17	18	0.77
Positive	17	8	9		9	8		8	9		7	10		9	8	
BCL2																
Negative	16	10	6	0.19	9	7	0.75	9	7	0.61	8	8	1	10	6	0.19
Positive	37	16	21		18	19		18	19		18	19		16	21	
BCL6																
Negative	29	15	14	0.52	15	14	1	15	14	0.43	15	14	0.66	15	14	0.66
Positive	24	15	9		12	12		15	9		11	13		11	13	
IRF4																
Negative	21	8	13	0.19	9	12	0.34	7	14	0.06	8	13	0.19	8	13	0.19
Positive	32	18	14		18	14		19	13		18	14		18	14	
Response to treatment																
CR	38	17	21	**0.04**	19	19	0.29	15	23	**0.02**	20	18	0.72	19	19	0.82
no CR	7	6	1		5	2		6	1		4	3		4	3	

CR, complete response; no CR, no complete response

P -values were determined by χ^2-test

Supplemental Table S8 Correlation between clinical and tumor characteristics and gene expression levels of *DROSHA* , *DICER* , *TARBP2* , *DGCR8* and *PACT* in *de novo* cases of the cohort 2

Parameter	No Cases	*DROSHA* high	*DROSHA* low	*DROSHA* *P*- value	*DICER* high	*DICER* low	*DICER* *P*- value	*TARBP2* high	*TARBP2* low	*TARBP2* *P*- value	*DGCR8* high	*DGCR8* low	*DGCR8* *P*- value	*PACT* high	*PACT* low	*PACT* *P*- value
Age																
> 63	18	10	8	0.62	11	7	0.25	8	10	0.41	10	8	0.41	11	7	0.25
≤ 63	19	9	10		8	11		11	8		8	11		8	11	
Gender																
Male	13	11	13	0.36	13	11	0.64	14	10	0.25	10	14	0.25	11	13	0.36
Female	24	8	5		6	7		5	8		8	5		8	5	
Disease stage																
I-II	24	14	10	0.16	10	14	0.16	14	10	0.35	10	14	0.64	11	13	0.81
III-IV	12	4	8		8	4		5	7		6	6		6	6	
IPI																
0-2	27	13	14	0.70	12	15	0.25	14	13	0.85	15	12	0.25	11	16	0.06
3-5	9	5	4		6	3		5	4		3	6		7	2	
GCB-phenotype																
GCB	18	8	10	0.62	9	9	0.86	5	13	**0.004**	8	10	0.62	9	9	0.86
non-GCB	17	9	8		9	8		13	4		9	8		8	9	
CD10																
Negative	23	12	11	0.55	12	11	1	14	9	0.12	13	10	0.19	11	12	1
Positive	12	5	7		6	6		4	8		4	8		6	6	
BCL2																
Negative	9	5	4	1	4	5	0.19	3	6	0.08	6	3	0.18	4	5	0.65
Positive	11	6	5		8	3		8	3		4	7		6	5	
BCL6																
Negative	15	8	7	0.63	8	7	0.85	10	5	0.12	6	9	0.38	5	10	0.12
Positive	20	9	11		10	10		8	12		11	9		12	8	
IRF4																
Negative	16	8	8	0.88	11	5	0.06	6	10	0.13	7	9	0.60	10	6	0.13
Positive	19	9	10		7	12		12	7		10	9		7	12	
Response to treatment																
CR	18	6	12	**0.03**	8	10	0.81	8	10	0.81	9	9	1	7	11	0.06
no CR	6	5	1		3	3		3	3		3	3		5	1	

CR, complete response; no CR, no complete response

P -values were determined by χ^2-test