Table SI. Distribution of clinical, genetic and immune variables across LymphoMAP archetypes in the full DLBCL-2018 cohort.

Variable	Overall	LN	FMAC	TEX
Median age, years	62.00	63.00	60.00	66.00
Sex				
F	242 (43.1%)	78 (43.6%)	97 (42.7%)	67 (42.9%)
M	320 (56.9%)	101 (56.4%)	130 (57.3%)	89 (57.1%)
ECOG				
0	90 (16.0%)	33 (18.4%)	24 (10.6%)	33 (21.2%)
0.5	1 (0.2%)	0 (0%)	1 (0.4%)	0 (0%)
1	148 (26.3%)	52 (29.1%)	62 (27.3%)	34 (21.8%)
1.5	2 (0.4%)	0 (0%)	1 (0.4%)	1 (0.6%)
2	112 (19.9%)	32 (17.9%)	48 (21.1%)	32 (20.5%)
3	45 (8.0%)	21 (11.7%)	11 (4.8%)	13 (8.3%)
4	19 (3.4%)	5 (2.8%)	8 (3.5%)	6 (3.8%)
5	2 (0.4%)	0 (0%)	2 (0.9%)	0 (0%)
Missing	143 (25.4%)	36 (20.1%)	70 (30.8%)	37 (23.7%)
IPI group				
High	275 (48.9%)	84 (46.9%)	116 (51.1%)	75 (48.1%)
High-Intermediate	82 (14.6%)	32 (17.9%)	28 (12.3%)	22 (14.1%)
Low	112 (19.9%)	33 (18.4%)	53 (23.3%)	26 (16.7%)
Low-Intermediate	93 (16.5%)	30 (16.8%)	30 (13.2%)	33 (21.2%)
Cell-of-origin				
ABC	286 (50.9%)	82 (45.8%)	112 (49.3%)	92 (59.0%)
GCB	162 (28.8%)	59 (33.0%)	75 (33.0%)	28 (17.9%)
Missing	114 (20.3%)	38 (21.2%)	40 (17.6%)	36 (23.1%)
Genetic subtype				
BN2	98 (17.4%)	40 (22.3%)	36 (15.9%)	22 (14.1%)
EZB	68 (12.1%)	25 (14.0%)	33 (14.5%)	10 (6.4%)
MCD	68 (12.1%)	15 (8.4%)	33 (14.5%)	20 (12.8%)

N1	18 (3.2%)	4 (2.2%)	4 (1.8%)	10 (6.4%)
Other	310 (55.2%)	95 (53.1%)	121 (53.3%)	94 (60.3%)
Median immune evasion-associated index	-0.07	-0.35	0.40	-0.23
Treatment				
Ibrutinib monotherapy	9 (1.6%)	1 (0.6%)	7 (3.1%)	1 (0.6%)
Immunochemotherapy	234 (41.6%)	74 (41.3%)	90 (39.6%)	70 (44.9%)
Treatment not specified	319 (56.8%)	104 (58.1%)	130 (57.3%)	85 (54.5%)

Values are shown as counts (%), unless otherwise indicated. ABC, activated B-cell-like; GCB, germinal center B-cell-like; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; F, female; FMAC, fibroblast-macrophage-rich; IPI, International Prognostic Index; LN, lymph node-like; M, male; TEX, T cell-exhausted.

Table SII. Expression-level evidence for antigen-processing and immune evasion-associated genes in IEAI-high versus IEAI-low cases.

A, All cohorts				
Gene	n	Median difference (high - low)	P-value	Q-value
TAP1	376	-0.552	1.73×10^{-11}	1.38×10^{-10}
TAP2	376	-0.556	7.29×10^{-9}	2.92×10^{-8}
CIITA	376	-0.333	0.0002	0.0004
HLA-A	376	-0.219	0.0005	0.0010
HLA-C	376	-0.223	0.0034	0.0055
HLA-B	376	-0.231	0.0052	0.0070
CD58	376	0.136	0.0356	0.0407
B2M	376	0.115	0.7843	0.7843
B, Discovery (R-CHOP) cohort				
Gene	n	Median difference (high - low)	P-value	Q-value
TAP1	156	-0.746	1.63×10^{-7}	1.31×10^{-6}
TAP2	156	-0.452	0.0030	0.0122
HLA-A	156	-0.236	0.0661	0.1762
HLA-C	156	-0.062	0.1139	0.2278
HLA-B	156	-0.202	0.2187	0.3500
B2M	156	0.021	0.9139	0.9350
CIITA	156	-0.025	0.9280	0.9350
CD58	156	-0.031	0.9350	0.9350

Median differences are reported as high - low. For each gene listed, expression was compared between IEAI-high and IEAI-low cases within the corresponding analysis set; genes were not compared with one another. Q-values were calculated using the Benjamini-Hochberg procedure to adjust for multiple testing across the gene-level IEAI-high versus IEAI-low comparisons listed in each panel of this table (8 genes in panel A and 8 genes in panel B). IEAI, immune evasion-associated index; R-CHOP, rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisone.

Table SIII. Multivariate Cox regression analyses in the discovery cohort.

Predictor	HR	95% CI	P-value
LymphoMAP: FMAC vs. LN	0.903	0.498-1.637	0.7374
LymphoMAP: TEX vs. LN	0.612	0.318-1.180	0.1429
Genetic subtype: MCD vs. BN2	5.005	1.890-13.251	0.0012
Genetic subtype: N1 vs. BN2	6.057	1.594-23.018	0.0082
Genetic subtype: EZB vs. BN2	2.775	0.951-8.099	0.0619
Genetic subtype: Other vs. BN2	1.833	0.768-4.375	0.1724
Immune evasion-associated index (continuous)	1.077	0.863-1.345	0.5108
COO: ABC vs. GCB	2.649	1.296-5.411	0.0075
Age (per year)	1.025	1.008-1.043	0.0050
IPI: Low-Intermediate vs. Low	1.179	0.555-2.504	0.6684
IPI: High-Intermediate vs. Low	1.662	0.782-3.530	0.1865
IPI: High vs. Low	1.670	0.874-3.193	0.1206

HRs are from the discovery cohort multivariate model including LymphoMAP archetype, genetic subtype, IEAI, COO, age and IPI group. ABC, activated B-cell-like; COO, cell-of-origin; GCB, germinal center B-cell-like; FMAC, fibroblast-macrophage-rich; IPI, International Prognostic Index; LN, lymph node-like; TEX, T cell-exhausted.

Table SIV. External validation summary for overall survival.

Cohort	n	Events	HR per 1 SD	95% CI	P-value
GSE10846	233	60	1.27	0.98-1.65	0.0733
GSE31312	470	170	1.01	0.87-1.17	0.9302
GSE32918	249	137	1.17	0.99-1.38	0.0629
GSE87371	221	53	1.24	0.93-1.63	0.1385
Pooled random-effects meta-analysis	1,173	420	1.13	1.01-1.26	0.0328

Primary external validation treated RScore-Expr as a continuous predictor and reports hazard ratios per 1 standard deviation increase.

Table SV. External validation summary for PFS.

Cohort	n	Events	HR per 1 SD	95% CI	P-value
GSE31312	470	178	1.085	0.940-1.253	0.2664
GSE87371	221	71	1.267	0.997-1.610	0.0528
Pooled random-effects meta-analysis	691	249	1.137	0.989-1.307	0.0716

PFS validation was available in a subset of cohorts and is reported as HR per 1 SD increase. HR, hazard ratio; PFS, progression-free survival; SD, standard deviation.

Table SVI. Cohort-level mutation and homozygous deletion frequencies of selected antigen-presentation and immune evasion-associated genes.

A, Homozygous deletion frequency									
Gene	Total	ABC	GCB	Unclassified	MCD	BN2	N1	EZB	Other
B2M	0.043	0.048	0.057	0.009	0.000	0.031	0.000	0.048	0.058
CD58	0.043	0.076	0.013	0.000	0.157	0.031	0.000	0.000	0.032
TAP1	0.021	0.024	0.013	0.027	0.029	0.021	0.000	0.000	0.026
TAP2	0.021	0.024	0.013	0.027	0.029	0.021	0.000	0.000	0.026
HLA-B	0.018	0.021	0.013	0.018	0.043	0.031	0.000	0.016	0.010
HLA-C	0.018	0.024	0.006	0.018	0.043	0.042	0.000	0.000	0.010
CIITA	0.011	0.007	0.019	0.009	0.029	0.010	0.000	0.048	0.000
HLA-A	0.002	0.000	0.006	0.000	0.000	0.000	0.000	0.000	0.003
B, Mutation frequency									
Gene	Total	ABC	GCB	Unclassified	MCD	BN2	N1	EZB	Other
HLA-B	0.216	0.293	0.086	0.207	0.623	0.301	0.053	0.014	0.154
HLA-A	0.160	0.212	0.068	0.162	0.391	0.226	0.211	0.043	0.111
B2M	0.159	0.112	0.250	0.148	0.056	0.255	0.105	0.246	0.136
CD58	0.092	0.092	0.085	0.104	0.155	0.122	0.158	0.043	0.076
HLA-C	0.072	0.102	0.031	0.054	0.188	0.140	0.053	0.014	0.039
CIITA	0.054	0.034	0.098	0.043	0.042	0.061	0.000	0.130	0.041
TAP1	0.029	0.042	0.025	0.000	0.101	0.011	0.053	0.014	0.020
TAP2	0.013	0.014	0.000	0.027	0.014	0.054	0.000	0.000	0.003

Values were extracted from the public DLBCL-2018 Appendix S2 summary sheets (‘Tab S1 Mutation Freq Genes’ and ‘Tab S6 Hom Del Freq Genes’).ABC, activated B-cell-like; GCB, germinal center B-cell-like.

Table SVII. Correlation of IEAI with ESTIMATE-derived scores.

A, Full cohort			
Variable	n	Spearman ρ	P-value
Tumor purity	562	-0.142	0.0008
Stromal score	562	0.327	2.25×10^{-15}
Immune score	562	-0.141	0.0008
ESTIMATEScore	562	0.142	0.0008
B, Discovery cohort			
Variable	n	Spearman ρ	P-value
Tumor purity	234	-0.160	0.0144
Stromal score	234	0.370	6.80×10^{-9}
Immune score	234	-0.162	0.0131

Correlations are Spearman coefficients between the IEAI and ESTIMATE-derived variables in the full and discovery cohorts. IEAI, immune evasion-associated index.

Table SVIII. Minimal multivariate Cox models with and without tumor purity

A, Without purity			
Predictor	HR	95% CI	P-value
LymphoMAP: FMAC vs. LN	1.137	0.683-1.894	0.6205
LymphoMAP: TEX vs. LN	1.161	0.700-1.927	0.5622
immune evasion-associated index (continuous)	1.008	0.821-1.238	0.9362
Age (per year)	1.025	1.009-1.042	0.0021
IPI: Low-Intermediate vs. Low	1.340	0.678-2.648	0.4001
IPI: High-Intermediate vs. Low	2.256	1.208-4.216	0.0107
IPI: High vs. Low	2.389	1.345-4.243	0.0030
B, With purity			
Predictor	HR	95% CI	P-value
LymphoMAP: FMAC vs. LN	1.145	0.687-1.910	0.6030
LymphoMAP: TEX vs. LN	1.221	0.695-2.145	0.4872
immune evasion-associated index (continuous)	1.020	0.824-1.262	0.8546
Age (per year)	1.025	1.009-1.042	0.0020
IPI: Low-Intermediate vs. Low	1.350	0.682-2.672	0.3891
IPI: High-Intermediate vs. Low	2.248	1.202-4.204	0.0112
IPI: High vs. Low	2.373	1.334-4.221	0.0033
Tumor purity	1.289	0.368-4.512	0.6915

The minimal model includes LymphoMAP archetype, IEAI, age and IPI group. Tumor purity was added as a sensitivity-analysis covariate. FMAC, fibroblast-macrophage-rich; IPI, International Prognostic Index; LN, lymph node-like; TEX, T cell-exhausted.