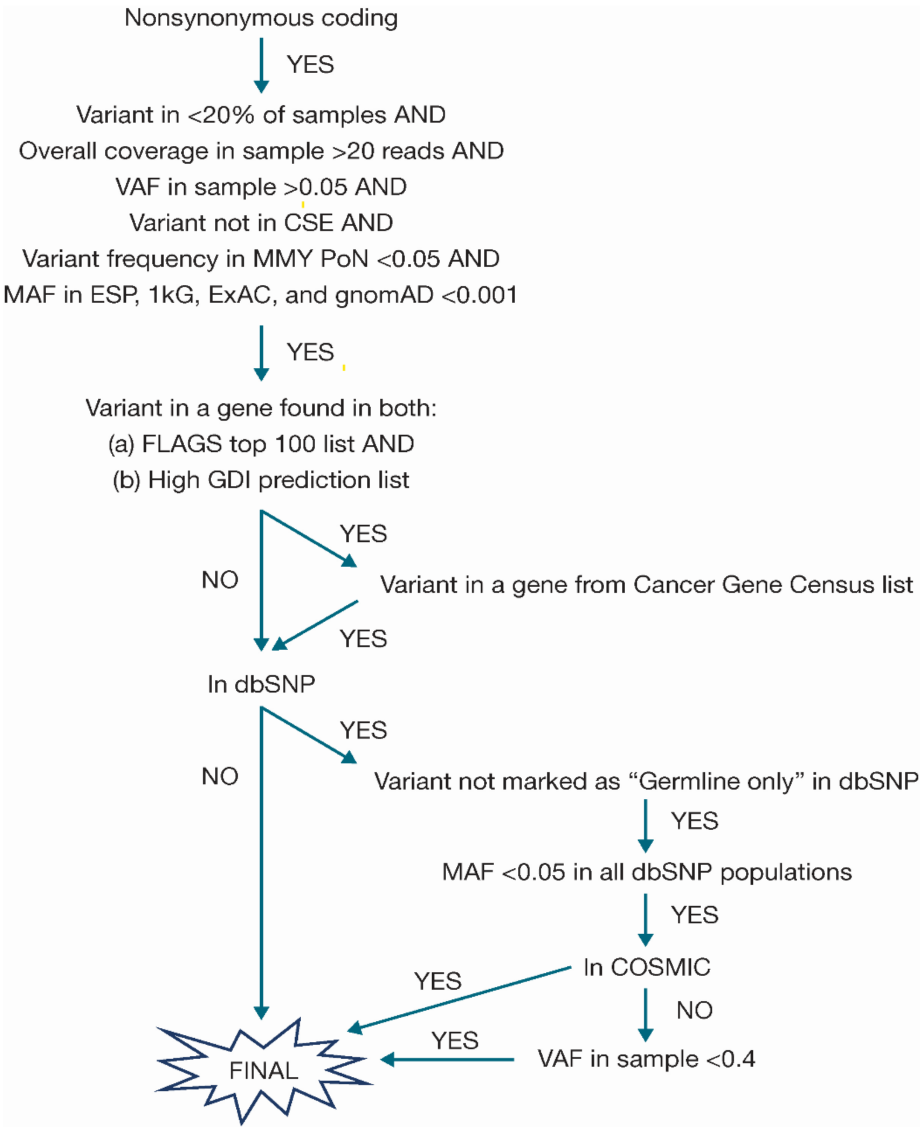
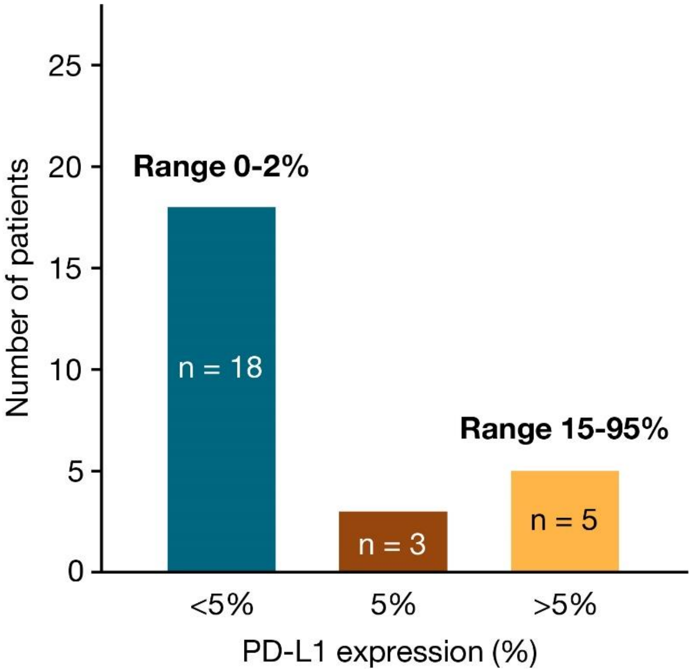
SUPPLEMENTARY MATERIALS

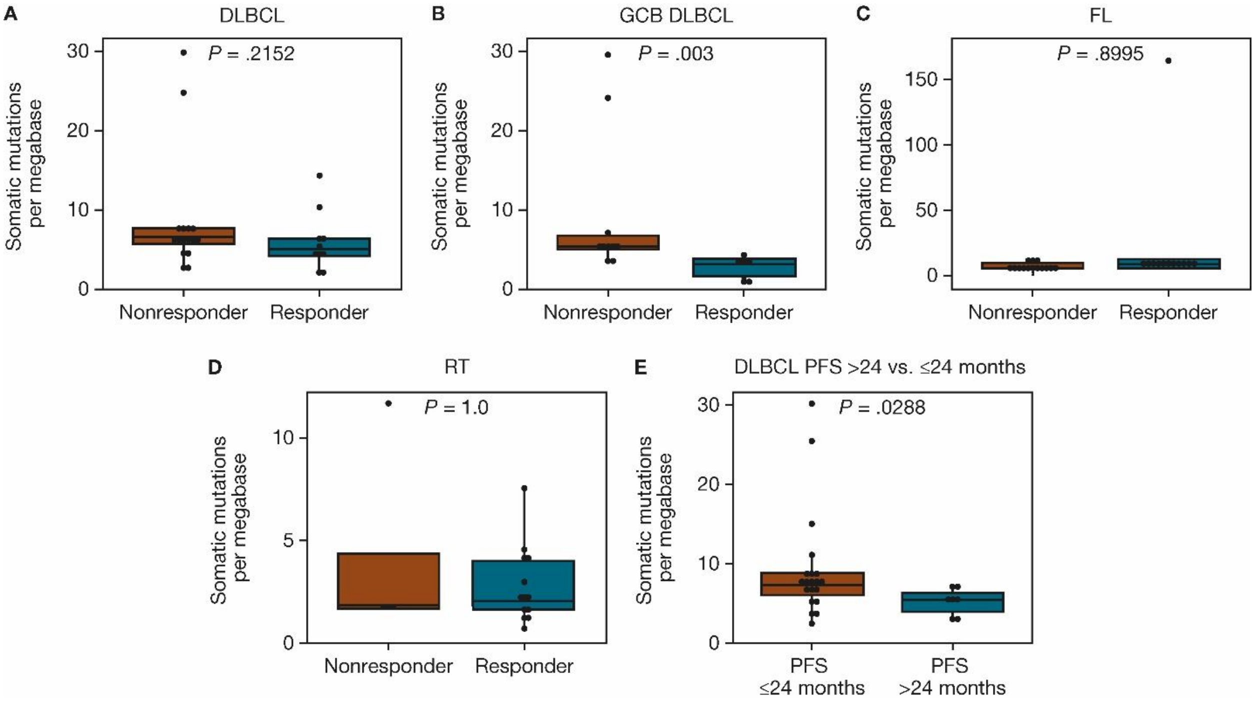
Supplementary Figure S1. Filtering criteria used to define likely somatic variants (in the absence of matched normal samples). COSMIC, Catalogue of Somatic Mutations in Cancer; CSE, context-specific errors; dbSNP, single nucleotide polymorphism; ESP, exome sequencing project; ExAC, exome aggregation consortium; FLAGS, frequently mutated genes in public exomes (Shyr C, et al. *BMC Med Genomics*. 2014;7:64); GDI, gene damage index (Itan Y, et al. *Proc Natl Acad Sci U S A*. 2014;112:13615-13620); gnomAD, genome aggregation database; MAF, minor allele frequency; MMY PoN, in-house panel of normals (from the phase III multiple myeloma studies CASTOR and POLLUX [Mateos MV, et al. *Haematologica*. 2020:105:468-477]); VAF, variant allele frequency.



Supplementary Figure S2. PD-L1 expression in DLBCL. DLBCL, diffuse large B-cell lymphoma, PD-L1, programmed death ligand 1.



Supplementary Figure S3. TMB for responders versus nonresponders in DLBCL (**A**), GCB DLBCL (**B**), FL (**C**), and RT (**D**), plus patients with DLBCL with PFS >24 versus ≤24 months (**E**). Data are expressed as the number of mutations per megabase. DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; GCB, germinal center B-cell–like; PFS, progression-free survival; RT, Richter's transformation; TMB, tumor mutational burden.



Supplementary Table S1

Functional Groupings of Genes Utilized in Pathway/Gene Set-Level Mutation Analyses

Pathway	Gene
Apoptosis	*CDKN2A*
Apoptosis	*CDKN2B*
Apoptosis	*MDM2*
Apoptosis	*RIPK1*
Apoptosis	*TP53*
Apoptosis	*VRK2*
BCR signaling	*BCL10*
BCR signaling	*BLK*
BCR signaling	*BLNK*
BCR signaling	*BMX*
BCR signaling	*BTK*
BCR signaling	*CARD11*
BCR signaling	*CD79A*
BCR signaling	*CD79B*
BCR signaling	*CSK*
BCR signaling	*GRB2*
BCR signaling	*ITK*
BCR signaling	*LCK*
BCR signaling	*LYN*
BCR signaling	*PLCG2*
BCR signaling	*PRKCB*
BCR signaling	*SYK*
BCR signaling	*TEC*
BCR signaling	*TXK*
Canonical NFkB	*IKBKB*
Canonical NFkB	*IKBKG*
Canonical NFkB	*IRF4*
Canonical NFkB	*IRS2*
Canonical NFkB	*MALT1*
Canonical NFkB	*MAP3K7*
Canonical NFkB	*TAB2*
Canonical NFkB	*TAB3*
Canonical NFkB	*MYD88*
Canonical NFkB	*NFKB1*
Canonical NFkB	*NFKBIB*
Canonical NFkB	*REL*
Canonical NFkB	*TLR2*
Canonical NFkB	*TNF*
Canonical NFkB	*TNFRSF11A*
Canonical NFkB	*TNFRSF13B*
Canonical NFkB	*TNFRSF13C*
Canonical NFkB	*TNFSF13B*
Canonical NFkB	*TRAF1*
Canonical NFkB	*TRAF4*
Canonical NFkB	*TRAF5*
Canonical NFkB	*TRAF6*
DNA repair	*ATM*
DNA repair	*CHEK2*
EGFR signaling	*EGFR*
EGFR signaling	*ERBB2*
EGFR signaling	*ERBB4*
EGFR signaling	*RGS4*
Epigenetic modifiers	*CREBBP*
Epigenetic modifiers	*EP300*
Epigenetic modifiers	*EZH2*
Epigenetic modifiers	*MLL2*
Epigenetic modifiers	*PRDM1*
Epigenetic modifiers	*TPMT*
Epigenetic modifiers	*WHSC1*
JAK/STAT signaling	*JAK2*
JAK/STAT signaling	*JAK3*
JAK/STAT signaling	*SOCS1*
JAK/STAT signaling	*STAT3*
JAK/STAT signaling	*STAT6*
MAPK signaling	*MAPK3*
MAPK signaling	*MAPK1*
MTTP	*MTTP*
NFkB	*NFKBIA*
NFkB	*TNFAIP3*
Non-canonical NFkB	*BIRC2*
Non-canonical NFkB	*BIRC3*
Non-canonical NFkB	*CD40*
Non-canonical NFkB	*CYLD*
Non-canonical NFkB	*MAP3K14*
Non-canonical NFkB	*NFKB2*
Non-canonical NFkB	*RELB*
Non-canonical NFkB	*TRAF2*
Non-canonical NFkB	*TRAF3*
Other oncogenes	*BCL2*
Other oncogenes	*BCL6*
Other oncogenes	*MCL1*
Other oncogenes	*MET*
Other oncogenes	*MYC*
Other oncogenes	*PIM1*
Other oncogenes	*RET*
PI3K signaling	*AKT1*
PI3K signaling	*MTOR*
PI3K signaling	*PIK3R1*
PI3K signaling	*PI3KD*
PI3K signaling	*PTEN*
Proliferation	*BTG1*
Proliferation	*CCND3*
Proliferation	*CEBPA*
VEGFA	*VEGFA*
Wnt signaling	*NOTCH1*

Supplementary Table S2

PD-L1 Expression in DLBCL by IHC

	DLBCL				
		Patients with GEP subtyping and IHC data			
	All *N*=26	ABC *n*=3	GCB *n*=17	Unclassified *n*=4	Total *n*=24
Patients with PD-L1 in ≥5% of tumor cells, *n* (%)	8/26 (30.8)	1 (33.3)	4 (23.5)	1 (25.0)	6 (25.0)
Proportion responding (CR or PR)	5/8	0/1	3/4	0/1	3/6

Supplementary Table S3

Frequencies of Gene Mutations Reported to be Functionally Relevant in Pathogenesis of DLBCL[a]

Gene	**Responders (*n*=10)**	**Nonresponders (*n*=16)**	**Odds Ratio (95% CI)**	***P* Value**
TP53	0 (0.0%)	3 (18.8%)	0.000 (0.000–3.825)	.262
TNFRSF14	0 (0.0%)	3 (18.8%)	0.000 (0.000–3.825)	.262
CREBBP	1 (10.0%)	5 (31.2%)	0.257 (0.005–2.940)	.352
CARD11	1 (10.0%)	0 (0.0%)	Inf (0.041–Inf)	.385
KMT2D	2 (20.0%)	6 (37.5%)	0.430 (0.034–3.353)	.420
MYD88	0 (0.0%)	2 (12.5%)	0.000 (0.000–8.573)	.508
GNA13	0 (0.0%)	2 (12.5%)	0.000 (0.000–8.573)	.508
EZH2	1 (10.0%)	2 (12.5%)	0.785 (0.012–17.245)	1.000
CD79B	1 (10.0%)	2 (12.5%)	0.785 (0.012–17.245)	1.000
BTG1	1 (10.0%)	3 (18.8%)	0.494 (0.008–7.368)	1.000
MEF2B	2 (20.0%)	3 (18.8%)	1.080 (0.075–11.763)	1.000

[a] Gene mutations chosen for inclusion in the table were reported in the literature (Lohr JG, et al. *Proc Natl Acad Sci U S A*. 2012;109:3879-3884).

Supplementary Table S4

Frequent Differentially Mutated Genes between Responders and Nonresponders in Germinal Center B-Cell-Like Diffuse Large B-Cell Lymphoma

Gene	**Responders (*n*=6)**	**Nonresponders (*n*=10)**	**Odds Ratio (95% CI)**	***P* Value**
Mutations more frequent in responders				
AMPH	1/6 (16.7%)	0/10 (0.0%)	Inf (0.043–Inf)	.375
AXIN1	1/6 (16.7%)	0/10 (0.0%)	Inf (0.043–Inf)	.375
BRCA2	1/6 (16.7%)	0/10 (0.0%)	Inf (0.043–Inf)	.375
CAMTA1	1/6 (16.7%)	0/10 (0.0%)	Inf (0.043–Inf)	.375
CEBPA	1/6 (16.7%)	0/10 (0.0%)	Inf (0.043–Inf)	.375
CLTC	1/6 (16.7%)	0/10 (0.0%)	Inf (0.043–Inf)	.375
Mutations more frequent in nonresponders				
CSMD3	0/6 (0.0%)	5/10 (50.0%)	0.000 (0.000–1.503)	.093
BCL2	1/6 (16.7%)	6/10 (60.0%)	0.152 (0.002–2.144)	.145
KMT2D	1/6 (16.7%)	6/10 (60.0%)	0.152 (0.002–2.144)	.145
CREBBP	0/6 (0.0%)	4/10 (40.0%)	0.000 (0.000–2.314)	.234
EBF1	0/6 (0.0%)	4/10 (40.0%)	0.000 (0.000–2.314)	.234
SGK1	0/6 (0.0%)	4/10 (40.0%)	0.000 (0.000–2.314)	.234
BCL7A	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250
BTG1	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250
CHD8	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250
FOXO1	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250
GPR124	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250
HIST1H1E	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250
KIAA1109	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250
P2RY8	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250
SPTA1	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250
TNFRSF14	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250
ZNF608	0/6 (0.0%)	3/10 (30.0%)	0.000 (0.000–3.967)	.250

Supplementary Table S5

Differentially Expressed Genes Between Responders and Nonresponders with Diffuse Large B-Cell Lymphoma

Gene	Description	Log FC	Adjusted *P* Value
Genes upregulated in the responder group			
CPVL	Carboxypeptidase, vitellogenic-like	1.274	1.000
E2F3	E2F transcription factor 3	0.634	1.000
CD163	CD163 molecule	1.854	1.000
LGMN	Legumain	1.718	1.000
ARFGAP3	ADP-ribosylation factor GTPase activating protein 3	1.175	1.000
C1orf54	Chromosome 1 open reading frame 54	0.955	1.000
BRD7P3	Bromodomain containing 7 pseudogene 3	0.709	1.000
GPRIN3	GPRIN family member 3	1.345	1.000
LMBRD1	LMBR1 domain containing 1	1.050	1.000
GGTA1P	Glycoprotein, alpha-galactosyltransferase 1 pseudogene	0.877	1.000
ATE1	Arginyltransferase 1	0.705	1.000
ZNF432	Zinc finger protein 432	1.547	1.000
CRTAM	Cytotoxic and regulatory T cell molecule	1.604	1.000
METTL18	Methyltransferase like 18	0.734	1.000
C2orf74	Chromosome 2 open reading frame 74	1.345	1.000
CCL4	Chemokine (C-C motif) ligand 4	0.929	1.000
GIMAP1	GTPase, IMAP family member 1	0.772	1.000
BCL11B	B-cell CLL/lymphoma 11B (zinc finger protein)	0.970	1.000
STAT5A	Signal transducer and activator of transcription 5A	0.975	1.000
GPR19	G protein-coupled receptor 19	0.884	1.000
Genes downregulated in the responder group			
C10orf12	Chromosome 10 open reading frame 12	–0.883	1.000
SGCE	Sarcoglycan, epsilon	–1.597	1.000
ZDHHC23	Zinc finger, DHHC-type containing 23	–0.975	1.000
TPPP	Tubulin polymerization promoting protein	-0.771	1.000
TIGD1	Tigger transposable element derived 1	–1.357	1.000
C5orf66	Chromosome 5 open reading frame 66	–0.712	1.000
HIST1H2AL	Histone cluster 1, H2al	–0.891	1.000
PCGF1	Polycomb group ring finger 1	–0.675	1.000
ASPM	Abnormal spindle microtubule assembly	–1.135	1.000
KIF11	Kinesin family member 11	–1.390	1.000
LOC728613	Programmed cell death 6 pseudogene	–1.116	1.000
ZNF587	Zinc finger protein 587	–0.717	1.000
ARR3	Arrestin 3, retinal (X-arrestin)	–0.785	1.000
LEAP2	Liver expressed antimicrobial peptide 2	–0.581	1.000
LRRC1	Leucine rich repeat containing 1	–1.069	1.000
FAM58A	Family with sequence similarity 58, member A	–0.565	1.000
HMGCS1	3-hydroxy-3-methylglutaryl-CoA synthase 1 (soluble)	–0.668	1.000
SLC25A37	Solute carrier family 25 (mitochondrial iron transporter), member 37	–0.684	1.000
DNMBP	Dynamin binding protein	–0.925	1.000
HILPDA	Hypoxia inducible lipid droplet-associated	–0.631	1.000

Supplementary Table S6

Differentially Expressed Genes Between Responders and Nonresponders with Follicular Lymphoma

Gene	Description	Log FC	Adjusted *P* Value
Genes upregulated in the responder group			
CCL21	Chemokine (C-C motif) ligand 21	1.671	.6
TESPA1	Thymocyte expressed, positive selection associated 1	0.785	.6
CDCA7L	Cell division cycle associated 7-like	0.967	.6
PRPSAP1	Phosphoribosyl pyrophosphate synthetase-associated protein1	0.757	.6
LEPROTL1	Leptin receptor overlapping transcript-like 1	1.017	.6
LEF1	Lymphoid enhancer-binding factor 1	0.923	.6
MYB	V-myb avian myeloblastosis viral oncogene homolog	1.114	.6
DNAJC16	DnaJ (Hsp40) homolog, subfamily C, member 16	0.710	.6
SMAD1	SMAD family member 1	1.188	.6
SNRPB2	Small nuclear ribonucleoprotein polypeptide B	0.571	.6
LAMP3	Lysosomal-associated membrane protein 3	1.115	.6
C7orf55	Chromosome 7 open reading frame 55	0.561	.6
HIST1H2BH	Histone cluster 1, H2bh	0.642	.6
LINC00525	Long intergenic non-protein coding RNA 525	1.369	.6
NPY1R	Neuropeptide Y receptor Y1	1.422	.6
SLC25A25-AS1	SLC25A25 antisense RNA 1	0.621	.6
SLA	Src-like-adaptor	0.728	.6
SFT2D1	SFT2 domain containing 1	0.936	.6
ZMAT2	Zinc finger, matrin-type 2	0.715	.6
STARD7	StAR-related lipid transfer (START) domain containing 7	0.746	.6
Genes downregulated in the responder group			
IQCG	IQ motif containing G	–1.085	.6
BHLHE41	Basic helix-loop-helix family, member e41	–0.893	.6
FOSL1	FOS-like antigen 1	–1.258	.6
TEX41	Testis expressed 41 (non-protein coding)	–0.590	.6
ZYG11A	Zyg-11 family member A, cell cycle regulator	–0.956	.6
ZDHHC4	Zinc finger, DHHC-type containing 4	–0.842	.6
TEAD3	TEA domain family member 3	–0.965	.6
EFNA1	Ephrin-A1	–0.650	.6
FAT4	FAT atypical cadherin 4	–1.188	.6
SLC46A2	Solute carrier family 46, member 2	–0.478	.6
CASC15	Cancer susceptibility candidate 15 (non-protein coding)	–0.577	.6
BBS12	Bardet-Biedl syndrome 12	–0.592	.6
TIGD6	Tigger transposable element derived 6	–0.515	.6
MRAS	Muscle RAS oncogene homolog	–0.501	.6
PTH2R	Parathyroid hormone 2 receptor	–0.452	.6
LINC01607	Long intergenic non-protein coding RNA 1607	–0.631	.6
STEAP1	Six transmembrane epithelial antigen of the prostate 1	–0.873	.6
PDE8B	Phosphodiesterase 8B	–0.486	.6
FIBIN	Fin bud initiation factor homolog (zebrafish)	–0.585	.6
RHD	Rh blood group, D antigen	–0.722	.6

Supplementary Table S7

Differentially Expressed Genes Between Responders and Nonresponders with Richter's Transformation

Gene	Description	Log FC	Adjusted *P* Value
Genes upregulated in the responder group			
BTLA	B and T lymphocyte associated	2.137	.391
ANKRD44-IT1	ANKRD44 intronic transcript 1	2.041	.391
PVRIG	Poliovirus receptor related immunoglobulin domain containing	1.213	.391
FCER2	Fc fragment of IgE, low affinity II, receptor for (CD23)	2.190	.485
ARHGAP15	Rho GTPase activating protein 15	1.364	.569
CCND2	Cyclin D2	2.096	.603
FCMR	Fc fragment of IgM receptor	2.742	.653
FRG1EP	FSHD region gene 1 family member E, pseudogene	2.766	.761
CELF2-AS1	CELF2 antisense RNA 1	1.523	.788
SLAMF6	SLAM family member 6	1.574	.930
LCK	LCK proto-oncogene, Src family tyrosine kinase	0.961	.930
FMO4	Flavin containing monooxygenase 4	1.598	.930
PATL2	Protein associated with topoisomerase II homolog 2 (yeast)	1.688	.953
FRG1CP	FSHD region gene 1 family member C, pseudogene	2.041	.953
RAC2	Ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	1.133	.953
KLHL6	Kelch-like family member 6	1.249	1.000
CD48	CD48 molecule	1.695	1.000
FCRLA	Fc receptor-like A	1.997	1.000
AFF3	AF4/FMR2 family, member 3	1.487	1.000
Genes downregulated in the responder group			
CCDC17	Coiled-coil domain containing 17	–1.73	.391
SLC47A1	Solute carrier family 47 (multidrug and toxin extrusion), member 1	–2.03	.391
NEK2	NIMA-related kinase 2	–1.63	.391
RTTN	Rotatin	–1.24	.391
OGN	Osteoglycin	–1.23	.391
VGLL3	Vestigial-like family member 3	–1.49	.472
ZNF426	Zinc finger protein 426	–1.76	.569
CENPI	Centromere protein I	–1.32	.569
GS1-600G8.3	Unknown transcript	–1.46	.569
MYO5C	Myosin VC	–1.87	.650
DEPDC1	DEP domain containing 1	–1.19	.650
LRP11	Low density lipoprotein receptor-related protein 11	–1.12	.788
GLDC	Glycine dehydrogenase (decarboxylating)	–1.95	.788
STEAP1	Six transmembrane epithelial antigen of the prostate 1	–2.22	.930
ILDR2	Immunoglobulin-like domain containing receptor 2	–1.34	.930
MLLT3	Myeloid/lymphoid or mixed-lineage leukemia; translocated to3'	–1.61	.930
UBAC1	UBA domain containing 1	–1.00	.930
NEDD4L	Neural precursor cell expressed, developmentally down-Regulated 4-like, E3 ubiquitin protein ligase	–1.14	.930
RHOBTB1	Rho-related BTB domain containing 1	–1.23	.930
TTC25	Tetratricopeptide repeat domain 25	–1.34	.953

Supplementary Table S8

Most Enriched Pathways in Responders and Nonresponders to Ibrutinib plus Nivolumab with Diffuse Large B-cell Lymphoma

Pathway Name	NES	FDR *P* Value	FWER *P* Value
Responders			
IL-12_2 pathway[a]	2.38	.000	.000
Immunoregulatory interactions between a lymphoid and a non-lymphoid cell[b]	2.31	.000	.000
T-cell receptor signalling pathway[c]	2.19	.000	.000
TCR signalling[b]	2.16	.000	.001
Lysosome[c]	2.15	.000	.001
Chemokine signalling pathway[c]	2.12	.000	.002
Chemokine receptors bind chemokines[b]	2.10	.001	.005
T-cell signal transduction[e]	2.09	.001	.007
CD8 TCR pathway[a]	2.08	.001	.008
IL-12/STAT4 pathway[a]	2.08	.001	.009
N glycan biosynthesis[c]	2.08	.001	.009
NO2/IL-12 pathway[d]	2.08	.001	.009
IL-12 pathway[d]	2.07	.001	.010
TCR pathway[a]	2.05	.001	.020
Generation of second messenger molecules[b]	2.04	.001	.023
IL-27 pathway[a]	2.02	.002	.028
Asparagine N-linked glycosylation[b]	2.02	.002	.030
Interferon gamma signaling[b]	2.00	.003	.051
Cytokine-cytokine receptor interaction[c]	1.98	.004	.075
FCER1 pathway[a]	1.94	.007	.134
Nonresponders			
Peptide chain elongation[b]	–2.46	.000	.000
Ribosome[c]	–2.36	.000	.000
Cell-cycle mitotic[b]	–2.33	.000	.000
G2/M checkpoints[b]	–2.31	.000	.000
Cell cycle[b]	–2.30	.000	.000
Activation of ATR in response to replication stress[b]	–2.24	.000	.000
E2F-mediated regulation of DNA replication[b]	–2.24	.000	.000
Nonsense-mediated decay enhanced by the exon junction complex[b]	–2.21	.000	.002
DNA replication[b]	–2.21	.000	.002
G1/S transition[b]	–2.21	.000	.002
MYC active pathway[a]	–2.21	.000	.002
Influenza viral RNA transcription and replication[b]	–2.19	.000	.005
3UTR-mediated translational regulation[b]	–2.14	.001	.008
Influenza life cycle[b]	–2.12	.001	.010
Activation of the pre-replicative complex[b]	–2.12	.001	.010
Mitotic M_M/G1 phases[b]	–2.12	.001	.010
Glycolysis[b]	–2.12	.001	.010
Mitotic G1_G1_S phases[b]	–2.07	.001	.025
DNA strand elongation[b]	–2.07	.002	.028
Cholesterol_biosynthesis[b]	–2.05	.002	.039

Databases: [a]PID; [b]REACTOME; [c]KEGG; [d]BIOCARTA; [e]ST.

Supplementary Table S9

Most Enriched Pathways in Responders and Nonresponders to Ibrutinib plus Nivolumab with Follicular Lymphoma

Pathway Name	**NES**	**FDR *P*-Value**	**FWER *P* Value**
Responders			
Metabolism of RNA[a]	3.35	.000	.000
Translation[a]	3.33	.000	.000
SRP-dependent cotranslational protein targeting to membrane[a]	3.24	.000	.000
Influenza life cycle[a]	3.24	.000	.000
3'UTR-mediated translational regulation[a]	3.19	.000	.000
Metabolism of mRNA[a]	3.18	.000	.000
Peptide chain elongation[a]	3.17	.000	.000
Processing of capped intron containing pre-mRNA[a]	3.08	.000	.000
mRNA processing[a]	3.05	.000	.000
Ribosome[b]	3.04	.000	.000
Influenza viral RNA transcription and replication[a]	3.03	.000	.000
Spliceosome[b]	3.00	.000	.000
Nonsense mediated decay enhanced by the exon junction complex[a]	2.99	.000	.000
Antiviral mechanism by IFN stimulated genes[a]	2.91	.000	.000
Signaling by the BCR[a]	2.90	.000	.000
Transcription[a]	2.89	.000	.000
mRNA splicing[a]	2.89	.000	.000
HIV infection[a]	2.88	.000	.000
BCR 5 pathway[c]	2.83	.000	.000
Host interactions of HIV factors[a]	2.82	.000	.000
Nonresponders			
Core matrisome[d]	–2.88	.000	.000
ECM glycoproteins[d]	–2.80	.000	.000
ECM organization[a]	–2.58	.000	.000
Neuroactive ligand-receptor interaction[b]	–2.56	.000	.000
Olfactory signaling pathway[a]	–2.49	.000	.000
ECM-receptor interaction[b]	–2.42	.000	.000
Integrin1 pathway[c]	–2.41	.000	.001
ECM regulators[d]	–2.39	.000	.001
Olfactory transduction[b]	–2.38	.000	.001
Collagen formation[a]	–2.38	.000	.001
Amine ligand-binding receptors[a]	–2.37	.000	.002
ECM affiliated[d]	–2.34	.000	.003
Potassium channels[a]	–2.33	.000	.003
Secreted factors[d]	–2.26	.000	.006
Proteoglycans[d]	–2.25	.000	.006
uPA-uPAR pathway[c]	–2.23	.000	.010
Regulation of IGF activity by IGFBPs[a]	–2.21	.000	.013
Syndecan 1 pathway[c]	–2.18	.001	.024
Collagens[d]	–2.17	.001	.026
Cell-cell junction organization[a]	–2.13	.001	.040

Databases: [a]REACTOME; [b]KEGG; [c]PID; [d]NABA; [e]BIOCARTA.

Supplementary Table S10

Most Enriched Pathways in Responders and Nonresponders to Ibrutinib plus Nivolumab with Richter's Transformation

Pathway Name	**NES**	**FDR *P* Value**	**FWER *P* Value**
Responders			
TCR signaling[a]	2.40	.000	.000
Generation of second messenger molecules[a]	2.36	.000	.000
Costimulation by the CD28 family[a]	2.35	.000	.000
Intestinal immune network for IgA production[b]	2.35	.000	.000
Interferon gamma signaling[a]	2.33	.000	.000
Graft versus host disease[b]	2.31	.000	.000
TCR pathway[c]	2.29	.000	.000
Type I diabetes mellitus[b]	2.24	.000	.000
Downstream TCR signaling[a]	2.21	.000	.000
Antigen processing and presentation[b]	2.18	.000	.003
Peptide chain elongation[a]	2.18	.000	.003
PD1 signaling[a]	2.18	.000	.003
CD8 TCR pathway[c]	2.17	.000	.004
Metabolism of mRNA[a]	2.16	.000	.004
Allograft rejection[b]	2.16	.000	.005
IL-12 pathway[d]	2.16	.000	.006
3'UTR mediated translational regulation[a]	2.13	.001	.008
Ribosome[b]	2.12	.001	.009
BCR5 pathway[c]	2.11	.001	.009
Metabolism of RNA[a]	2.10	.001	.010
Nonresponders			
Core matrisome[e]	–2.46	.000	.000
Basement membranes[e]	–2.39	.000	.000
Integrin1 pathway[c]	–2.33	.000	.000
ECM organization[a]	–2.30	.000	.000
Collagen formation[a]	–2.27	.000	.000
Proteoglycans[e]	–2.23	.000	.000
ECM glycoproteins[e]	–2.19	.000	.000
ECM receptor interaction[b]	–2.18	.000	.001
Collagens[e]	–2.15	.000	.004
NCAM1 interactions[a]	–2.09	.002	.019
Integrin3 pathway[c]	–2.01	.006	.076
Striated muscle contraction[a]	–1.84	.042	.450
Regulation of IGF activity by IGFBPs[a]	–1.81	.056	.575
NCAM signaling for neurite outgrowth[a]	–1.79	.067	.659
Integrin cell surface interactions[a]	–1.79	.063	.662
AMI pathway[d]	–1.77	.071	.727
Keratan sulfate biosynthesis[a]	–1.77	.074	.766
αvβ3 integrin pathway[c]	–1.76	.071	.771
Deposition of new CENP-A-containing nucleosomes at the centromere[a]	–1.76	.072	.791
Syndecan 1 pathway[c]	–1.75	.077	.832

Databases [a]REACTOME; [b]KEGG; [c]PID; [d]BIOCARTA; [e]NABA.