

T-cell/histiocyte-rich large B-cell lymphoma shows transcriptional features suggestive of a tolerogenic host immune response

Peter Van Loo,^{1,2,3} Thomas Tousseyn,⁴ Vera Vanhentenrijk,⁴ Daan Dierickx,⁵ Agnieszka Malecka,⁶ Isabelle Vanden Bempt,⁴ Gregor Verhoef,⁵ Jan Delabie,⁶ Peter Marynen,^{1,2} Patrick Matthys,⁷ and Chris De Wolf-Peeters⁴

¹Department of Molecular and Developmental Genetics, VIB, Leuven, Belgium; ²Department of Human Genetics, K.U.Leuven, Leuven, Belgium; ³Bioinformatics Group, Department of Electrical Engineering, K.U.Leuven, Leuven, Belgium; ⁴Department of Pathology, University Hospitals K.U.Leuven, Leuven, Belgium; ⁵Department of Hematology, University Hospitals K.U.Leuven, Leuven, Belgium; ⁶Department of Pathology, The Norwegian Radium Hospital, University of Oslo, Oslo, Norway, and ⁷Department of Microbiology and Immunology, Rega Institute for Medical Research, K.U.Leuven, Leuven, Belgium

Citation: Van Loo P, Tousseyn T, Vanhentenrijk V, Dierickx D, Malecka A, Vanden Bempt I, Verhoef G, Delabie J, Marynen P, Matthys P, and De Wolf-Peeters C. T-cell/histiocyte-rich large B-cell lymphoma shows transcriptional features suggestive of a tolerogenic host immune response. *Haematologica*. 2010;95:440-448. doi:10.3324/haematol.2009.009647

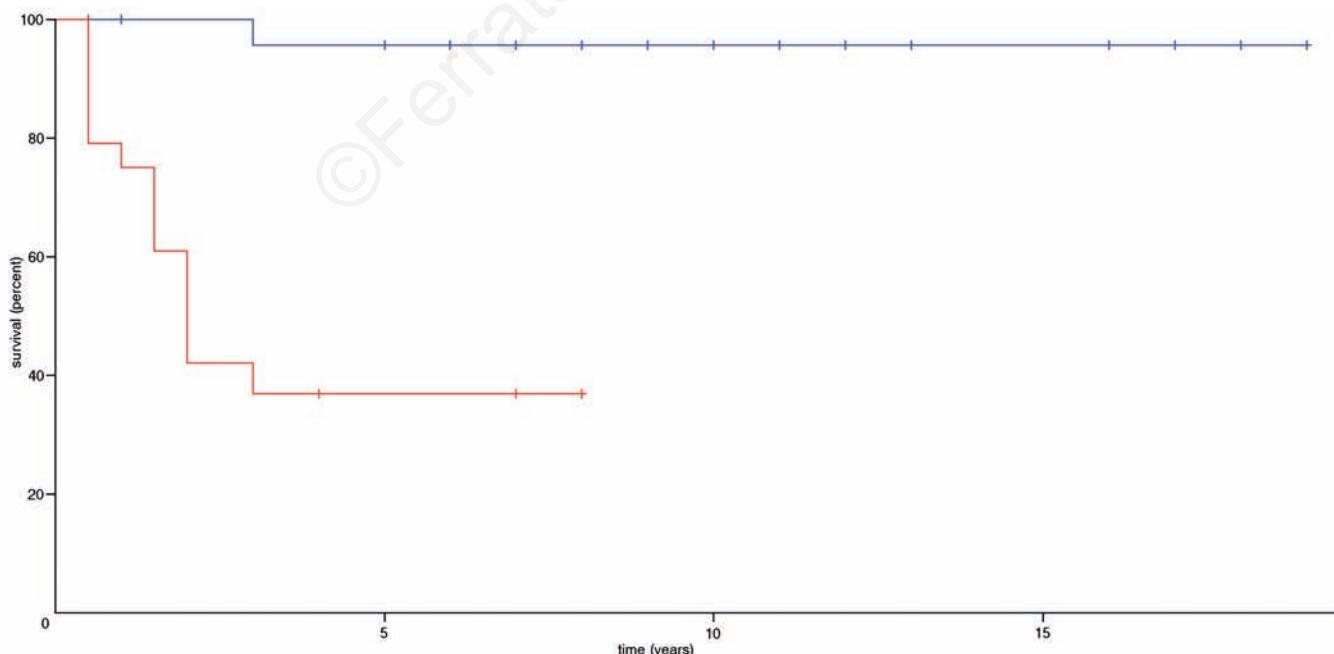
The Online Supplementary Tables S1-5 are in separate PDF files

Supplementary Design and Methods

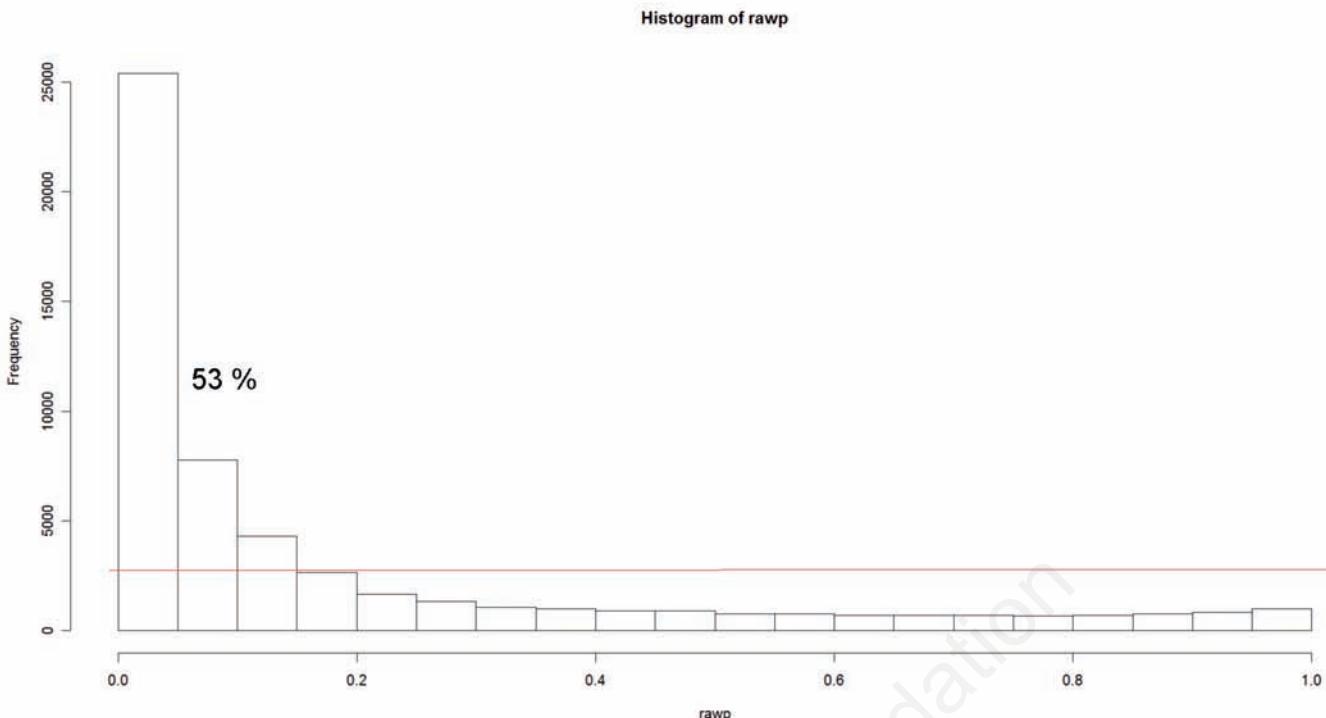
Validation of microarray results by real-time quantitative reverse transcriptase polymerase chain reaction

Ten genes measured by microarray gene expression profiling were validated by real-time quantitative reverse transcriptase polymerase chain reaction. These genes were selected for their involvement in interferon pathways, macrophage activation and innate immune responses. Five of these genes were in the T-cell/histiocyte-rich large B-cell lymphoma (THRLB-CL) signature (*Online Supplementary Table S1B*), while the other five genes were key genes in the selected pathways that were not differentially expressed according to our strict statistical criteria.

One microgram of total RNA was reverse transcribed using random primers and SuperScript II (Invitrogen, Merelbeke, Belgium), as recommended by the manufacturer. Relative quantification was subsequently performed using the comparative C_T method (see User Bulletin #2: Relative Quantitation of Gene Expression, Applied Biosystems). The real-time quantitative PCR reactions were performed using TaqMan gene expression assays (Applied Biosystems, Lennik, Belgium), with *GAPDH*, *RPLP0* and *PPIA* as housekeeping genes, and the mixture of RNA from five reactive lymph nodes as a calibrator sample.



Online Supplementary Figure S1. Kaplan-Meier estimates of overall survival. Red: THRLBCL; blue: NLPHEL. Survival was measured from the time of diagnosis to the time of disease-related death. Deaths from tumor-unrelated causes as well as patients lost to follow-up were considered as censoring events. Plus-signs indicate (one or more) censored observations. The survival difference between patients with THRLBCL and NLPHEL is statistically significant ($P=6.0 \times 10^{-6}$, log-rank test).



Online Supplementary Figure S2. The figure shows the (uncorrected) P value distribution of a t-test for genes differentially expressed between THRLBCL and NLPHL. Under the hypothesis that no genes are differentially regulated between the two lymphomas, these P values should be distributed uniformly between 0 and 1. Aiming to estimate the number of genes (or more correctly: microarray probe sets) differentially regulated, we inspected the deviation from this uniform distribution (indicated by the red line in the figure), and found that 53% of the probe sets differed in expression between THRLBCL and NLPHL, indicating that the expression profiles of the two lymphomas are extremely dissimilar. We, therefore, focused on highly significant differentially expressed genes for the construction of THRLBCL and NLPHL expression signatures. We used $P < 0.001$ after correction for multiple testing as an extremely stringent cut-off, and obtained 874 probe sets, corresponding to 527 unique genes.

Real-time quantitative polymerase chain reaction measurements of three selected genes from additional cases of T-cell/histiocyte-rich large B-cell lymphoma and nodular lymphocyte-predominant Hodgkin's lymphoma

To check the representativeness of the cases included in the microarray analysis we analyzed all other samples for their expression of three selected genes by quantitative RT-PCR. The three genes were selected as: (i) the two genes most significantly differentially expressed in our microarray experiment (*FCER1G* and *VSIG4*, both expressed at higher levels in THRLBCL) and (ii) the gene with the most significantly higher expression in NLPHL (*FCRL1*).

The real-time quantitative PCR reactions were performed at

the institution where the cases originated. For the cases from the University Hospitals of K.U.Leuven, SYBR green gene expression assays (Roche, Brussels, Belgium) were used, with *GAPDH* and *HPRT1* as housekeeping genes. As a reference sample, we used one THRLBCL sample, randomly chosen from the ten cases subjected to microarray expression profiling. For the cases from the Rikshospitalet-Radiumhospitalet HF Oslo, FastStart Universal SYBR Green Master (ROX) (Roche, Oslo, Norway) was used with GUS (β -glucuronidase) and *HPRT1* as housekeeping genes. A random THRLBCL sample was chosen as a reference. The real-time quantitative PCR reactions were performed on a 7900HT Fast Real-Time PCR System (Applied Biosystems, Stockholm, Sweden).

Supplementary References

- Monti S, Savage KJ, Kutok JL, Feuerhake F, Kurtin P, Mihm M, et al. Molecular profiling of diffuse large B-cell lymphoma identifies robust subtypes including one characterized by host inflammatory response. *Blood*. 2005;105(5):1851-61.
- Brune V, Tiacci E, Pfeil I, Doring C, Eckerle S, van Noesel CJ, et al. Origin and pathogenesis of nodular lymphocyte-predominant Hodgkin lymphoma as revealed by global gene expression analysis. *J Exp Med*. 2008;205(10):2251-68.
- Dave SS, Wright G, Tan B, Rosenwald A, Gascoyne RD, Chan WC, et al. Prediction of survival in follicular lymphoma based on molecular features of tumor-infiltrating immune cells. *N Engl J Med*. 2004;351(21):2159-69.

Supplementary Tables**Supplementary Table 1. Gene expression signatures of THRLBCL and NLPHL.****A. Signature of NLPHL**

HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
FCRL1	ENSG00000163534	Fc receptor-like 1	32.1	2.3E-12	1.1E-05
	ENSG00000167483	B-cell novel protein 1			
PAX5	ENSG00000196092	Paired box protein Pax-5 (B-cell-specific transcription factor) (BSAP).	8.3	4.9E-12	2.2E-05
BCL11A	ENSG00000119866	B-cell lymphoma/leukemia 11A (B-cell CLL/lymphoma 11A) (COUP-TF- interacting protein 1) (Ecotropic viral integration site 9 protein) (EVI-9).	12.0	1.1E-11	1.1E-05
BACH2	ENSG00000112182	Transcription regulator protein BACH2 (BTB and CNC homolog 2).	10.4	6.2E-11	3.2E-05
MEF2C	ENSG00000081189	Myocyte-specific enhancer factor 2C.	5.6	8.6E-11	3.2E-05
GNG7	ENSG00000176533	Guanine nucleotide-binding protein G(I)/G(S)/G(O) gamma-7 subunit precursor.	6.2	1.9E-10	2.2E-05
FGFR1OP	ENSG00000112486	C-C chemokine receptor type 6 (C-C CKR-6) (CC-CKR-6) (CCR-6) (LARC receptor) (GPR-CY4) (GPRCY4) (Chemokine receptor-like 3) (CKR-L3) (DRY6) (G-protein coupled receptor 29) (CD196 antigen).	23.4	2.1E-10	2.2E-05
MOBK1B	ENSG00000120162	Mps one binder kinase activator-like 2B (Mob1 homolog 2b) (Protein Mob3B).	11.0	2.2E-10	3.2E-05
FCER2	ENSG00000104921	Low affinity immunoglobulin epsilon Fc receptor (Lymphocyte IgE receptor) (Fc-epsilon-RII) (BLAST-2) (Immunoglobulin E-binding factor) (CD23 antigen) [Contains: Low affinity immunoglobulin epsilon Fc receptor membrane-bound form; Low affinity immunoglobul	14.0	2.3E-10	3.2E-05
MBD4	ENSG00000129071	Methyl-CpG-binding domain protein 4 (EC 3.2.2.-) (Methyl-CpG-binding protein MBD4) (Methyl-CpG-binding endonuclease 1) (Mismatch-specific DNA N-glycosylase).	1.9	7.5E-10	3.2E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
KLHL14	ENSG00000197705	Kelch-like protein 14.	11.8	8.7E-10	6.5E-05
KIAA1370	ENSG0000047346		2.1	9.3E-10	5.4E-05
CD37	ENSG00000104894	Leukocyte antigen CD37 (Tetraspanin-26) (Tspan-26).	3.2	1.0E-09	5.4E-05
UBTF	ENSG00000108312	Nucleolar transcription factor 1 (Upstream-binding factor 1) (UBF-1) (Autoantigen NOR-90).	1.8	1.1E-09	8.7E-05
FAM62B	ENSG00000117868	family with sequence similarity 62 (C2 domain containing) member B	1.9	1.2E-09	8.7E-05
SFPQ	ENSG00000116560	Splicing factor, proline- and glutamine-rich (Polypyrimidine tract- binding protein-associated splicing factor) (PTB-associated splicing factor) (PSF) (DNA-binding p52/p100 complex, 100 kDa subunit) (100-kDa DNA-pairing protein) (hPOMP100).	2.1	1.6E-09	9.7E-05
MKL2	ENSG00000186260	MKL/myocardin-like protein 2 (Myocardin-related transcription factor B) (MRTF-B) (Megakaryoblastic leukemia 2).	2.6	1.6E-09	6.5E-05
MS4A1	ENSG00000156738	B-lymphocyte antigen CD20 (B-lymphocyte surface antigen B1) (Leu-16) (Bp35).	5.5	1.7E-09	3.2E-05
ANP32B	ENSG00000136938	Acidic leucine-rich nuclear phosphoprotein 32 family member B (PHAPI2 protein) (Silver-stainable protein SSP29) (Acidic protein rich in leucines).	1.6	2.0E-09	4.3E-05
CD79A	ENSG00000105369	B-cell antigen receptor complex-associated protein alpha-chain precursor (Ig-alpha) (MB-1 membrane glycoprotein) (Surface IgM- associated protein) (Membrane-bound immunoglobulin-associated protein) (CD79a antigen).	12.4	2.2E-09	3.2E-05
CD22	ENSG0000012124	B-cell receptor CD22 precursor (Leu-14) (B-lymphocyte cell adhesion molecule) (BL-CAM) (Siglec-2).	15.0	2.4E-09	3.2E-05
PPP1CC	ENSG00000186298	Serine/threonine-protein phosphatase PP1-gamma catalytic subunit (EC 3.1.3.16) (PP-1G) (Protein phosphatase 1C catalytic subunit).	1.6	3.1E-09	9.7E-05
OXCT1	ENSG0000083720	Succinyl-CoA:3-ketoacid-coenzyme A transferase 1, mitochondrial precursor (EC 2.8.3.5) (Somatic-type succinyl CoA:3-oxoacid CoA- transferase) (Scot-S).	1.6	3.3E-09	9.7E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
PPAPDC1B	ENSG00000147535	HTPAP protein	2.0	3.9E-09	9.7E-05
CHMP7	ENSG00000147457	Protein CHMP7.	2.5	4.6E-09	6.5E-05
EEF2	ENSG00000167658	Elongation factor 2 (EF-2).	1.7	4.9E-09	9.7E-05
ALS2CR13	ENSG00000138439	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 13	4.3	6.0E-09	9.7E-05
SNORD50B	ENSG00000201865	U50 small nucleolar RNA	2.7	6.3E-09	1.5E-04
RABEP2	ENSG00000177548	Rab GTPase-binding effector protein 2 (Rabaptin-5beta).	2.6	6.4E-09	1.2E-04
SYTL1	ENSG00000142765	Synaptotagmin-like protein 1 (Exophilin-7) (JFC1 protein) (SB146).	3.9	7.1E-09	8.7E-05
C1orf109	ENSG00000116922		1.6	7.4E-09	8.7E-05
FBL	ENSG00000105202	Fibrillarin (34 kDa nucleolar scleroderma antigen).	2.2	8.0E-09	1.6E-04
RBM6	ENSG00000004534	RNA-binding protein 6 (RNA-binding motif protein 6) (RNA-binding protein DEF-3) (Lung cancer antigen NY-LU-12) (Protein G16).	1.6	8.1E-09	1.6E-04
ZNF395	ENSG00000186918	F-box only protein 16.	6.4	8.3E-09	1.8E-04
HOOK1	ENSG00000134709	Hook homolog 1 (h-hook1) (hHK1).	4.1	9.5E-09	1.3E-04
PNN	ENSG00000100941	Pinin (140 kDa nuclear and cell adhesion-related phosphoprotein) (Domain-rich serine protein) (DRS-protein) (DRSP) (Melanoma metastasis clone A protein) (Desmosome-associated protein) (SR-like protein) (Nuclear protein SDK3).	1.9	9.6E-09	1.8E-04
SMARCE1	ENSG00000073584	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily E member 1 (BRG1-associated factor 57).	1.4	9.7E-09	2.5E-04
ATP2A3	ENSG00000074370	Sarcoplasmic/endoplasmic reticulum calcium ATPase 3 (EC 3.6.3.8) (Calcium pump 3) (SERCA3) (SR Ca(2+)-ATPase 3).	2.4	9.7E-09	1.6E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
ABLIM1	ENSG00000099204	Actin-binding LIM protein 1 (Actin-binding LIM protein family member 1) (abLIM-1) (Actin-binding double-zinc-finger protein) (LIMAB1) (Limatin).	3.2	1.0E-08	1.1E-04
UBE2D2	ENSG00000131508	ubiquitin-conjugating enzyme E2D 2 isoform 2	1.4	1.0E-08	2.5E-04
C7orf30	ENSG00000156928		1.3	1.1E-08	9.7E-05
TBL1X	ENSG00000101849	F-box-like/WD repeat protein TBL1X (Transducin beta-like 1X protein) (Transducin-beta-like 1, X-linked) (SMAP55).	2.3	1.1E-08	1.5E-04
CRLF3	ENSG00000176390	cytokine receptor-like factor 3	1.6	1.1E-08	2.9E-04
	ENSG00000187904		2.6	1.3E-08	9.7E-05
OFD1	ENSG00000046651	Oral-facial-digital syndrome 1 protein (Protein 71-7A).	2.5	1.3E-08	9.7E-05
SLTM	ENSG00000137776	modulator of estrogen induced transcription isoform c	1.5	1.6E-08	2.7E-04
RNF44	ENSG00000146083	ring finger protein 44	1.6	1.6E-08	1.6E-04
RNPC1	ENSG00000132819	RNA-binding region-containing protein 1 (HSRNASEB) (ssDNA binding protein SEB4) (CLL-associated antigen KW-5).	2.1	1.6E-08	4.0E-04
SF3B1	ENSG00000115524	Splicing factor 3B subunit 1 (Spliceosome-associated protein 155) (SAP 155) (SF3b155) (Pre-mRNA-splicing factor SF3b 155 kDa subunit).	1.4	1.6E-08	4.1E-04
DDX17	ENSG00000100201	Probable ATP-dependent RNA helicase DDX17 (EC 3.6.1.-) (DEAD box protein 17) (RNA-dependent helicase p72) (DEAD box protein p72).	2.7	1.6E-08	1.5E-04
PABPN1	ENSG00000100836	Polyadenylate-binding protein 2 (Poly(A)-binding protein 2) (PolyA binding protein II) (PABII) (Polyadenylate-binding nuclear protein 1) (Nuclear poly(A)-binding protein 1).	1.3	1.7E-08	4.5E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
RBBP4	ENSG00000162521	Histone-binding protein RBBP4 (Retinoblastoma-binding protein 4) (RBBP-4) (Retinoblastoma-binding protein p48) (Chromatin assembly factor 1 subunit C) (CAF-1 subunit C) (Chromatin assembly factor I p48 subunit) (CAF-I 48 kDa subunit) (CAF-I p48).	1.4	1.8E-08	3.6E-04
	ENSG0000055163	cytoplasmic FMR1 interacting protein 2	2.2	1.8E-08	1.9E-04
C1orf165	ENSG00000162373		6.3	1.8E-08	1.6E-04
MALT1	ENSG00000172175	Mucosa-associated lymphoid tissue lymphoma translocation protein 1 (EC 3.4.22.-) (MALT lymphoma-associated translocation) (Paracaspase).	3.4	2.0E-08	5.4E-05
C11orf2	ENSG00000149823	Protein C11orf2 (Another new gene 2 protein).	2.0	2.1E-08	2.5E-04
PRKD2	ENSG00000105287	Serine/threonine-protein kinase D2 (EC 2.7.11.13) (nPKC-D2).	2.0	2.3E-08	4.0E-04
HNRPA1	ENSG00000135486	Heterogeneous nuclear ribonucleoprotein A1 (Helix-destabilizing protein) (Single-strand RNA-binding protein) (hnRNP core protein A1).	1.8	2.4E-08	2.9E-04
FOXP1	ENSG00000114861	Forkhead box protein P1.	3.7	2.7E-08	9.7E-05
CIRBP	ENSG00000099622	Cold-inducible RNA-binding protein (Glycine-rich RNA-binding protein CIRP) (A18 hnRNP).	2.0	2.7E-08	6.4E-04
CASP2	ENSG00000106144	Caspase-2 precursor (EC 3.4.22.-) (CASP-2) (ICH-1 protease) (ICH- 1L/1S) [Contains: Caspase-2 subunit p18; Caspase-2 subunit p13; Caspase-2 subunit p12].	1.8	2.7E-08	1.5E-04
	ENSG00000176718		3.0	2.8E-08	4.5E-04
QRSL1	ENSG00000130348	glutaminyl-tRNA synthase (glutamine-hydrolyzing)-like 1	3.7	2.9E-08	3.6E-04
LUC7L2	ENSG00000146963	Putative RNA-binding protein Luc7-like 2.	1.3	3.0E-08	6.4E-04
SH3YL1	ENSG00000035115	SH3 domain containing, Ysc84-like 1	4.2	3.1E-08	5.2E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
EIF3S6IP	ENSG00000100129	Eukaryotic translation initiation factor 3 subunit 6-interacting protein.	1.6	3.2E-08	1.6E-04
PLEKHF2	ENSG00000175895	phafin 2	2.0	3.4E-08	5.2E-04
C6orf111	ENSG00000132424	Splicing factor, arginine/serine-rich 130 (Serine-arginine-rich splicing regulatory protein 130) (SRrp130) (SR-rich protein) (SR-related protein).	2.0	3.5E-08	6.8E-04
TMSL8	ENSG00000158164	NB thymosin beta (Thymosin-like protein 8).	10.5	3.6E-08	6.3E-04
JMJD1C	ENSG00000171988	Probable JmjC domain-containing histone demethylation protein 2C (EC 1.14.11.-) (Jumonji domain-containing protein 1C) (Thyroid receptor-interacting protein 8) (TRIP-8).	1.9	3.8E-08	7.8E-04
ZNF512	ENSG00000198522	Zinc finger protein 512.	1.8	3.8E-08	4.5E-04
ADD3	ENSG00000148700	Gamma-adducin (Adducin-like protein 70).	2.2	3.9E-08	1.3E-04
RRS1	ENSG00000179041	Ribosome biogenesis regulatory protein homolog.	1.6	4.0E-08	8.3E-04
CD19	ENSG00000177455	B-lymphocyte antigen CD19 precursor (B-lymphocyte surface antigen B4) (Leu-12) (Differentiation antigen CD19).	18.1	4.1E-08	9.7E-05
CD180	ENSG00000134061	CD180 antigen precursor (Lymphocyte antigen 64) (Radioprotective 105 kDa protein).	4.9	4.2E-08	4.5E-04
RPL37	ENSG00000145592	60S ribosomal protein L37 (G1.16).	2.9	4.3E-08	2.7E-04
KIAA0892	ENSG00000129933		1.5	4.3E-08	1.8E-04
FOXO1A	ENSG00000150907	Forkhead box protein O1A (Forkhead in rhabdomyosarcoma).	2.5	4.3E-08	1.4E-04
DEF6	ENSG0000023892	differentially expressed in FDCP 6 homolog	1.7	4.5E-08	9.7E-05
GPR18	ENSG00000125245	Probable G-protein coupled receptor 18.	3.0	4.6E-08	3.6E-04
	ENSG00000182319		5.3	4.7E-08	2.6E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
PLAG1	ENSG00000181690	pleiomorphic adenoma gene 1	4.4	4.7E-08	3.2E-05
BANK1	ENSG00000153064	B-cell scaffold protein with ankyrin repeats 1	21.0	5.1E-08	5.4E-05
GNB2L1	ENSG00000204628	Guanine nucleotide-binding protein subunit beta 2-like 1 (Guanine nucleotide-binding protein subunit beta-like protein 12.3) (Receptor of activated protein kinase C 1) (RACK1) (Receptor for activated C kinase).	1.4	5.2E-08	8.7E-04
	ENSG00000112137	Phosphatase and actin regulator 1.	9.3	5.3E-08	6.8E-04
RPL38	ENSG00000172809	60S ribosomal protein L38.	1.4	5.6E-08	3.1E-04
	ENSG00000180632		1.7	5.7E-08	7.4E-04
TIAM2	ENSG00000146426	Putative RNA-binding protein 16 (RNA-binding motif protein 16).	1.5	6.2E-08	1.0E-03
RABGAP1L	ENSG00000152061	RAB GTPase activating protein 1-like isoform A	1.8	6.4E-08	6.1E-04
ZCCHC7	ENSG00000147905	Zinc finger CCHC domain-containing protein 7.	2.6	6.4E-08	3.1E-04
CD1C	ENSG00000158481	T-cell surface glycoprotein CD1c precursor (CD1c antigen).	13.4	6.4E-08	5.3E-04
	ENSG00000111913		2.7	6.5E-08	2.5E-04
FBXO21	ENSG00000135108	F-box only protein 21.	1.5	6.7E-08	8.0E-04
CNOT7	ENSG00000198791	CCR4-NOT transcription complex subunit 7 (CCR4-associated factor 1) (CAF1) (BTG1-binding factor 1).	1.5	6.9E-08	2.5E-04
FCRLM1	ENSG00000132185	Fc receptor-like and mucin-like 1 precursor (Fc receptor homolog expressed in B-cells) (Fc receptor related protein X) (FcRX) (Fc receptor-like protein).	11.8	7.0E-08	2.8E-04
ICAM3	ENSG0000076662	Intercellular adhesion molecule 3 precursor (ICAM-3) (ICAM-R) (CDw50) (CD50 antigen).	2.2	7.0E-08	3.0E-04
HP1BP3	ENSG00000127483	HP1-BP74	1.5	7.1E-08	9.4E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
	ENSG00000145868	F-box only protein 38 (Modulator of KLF7 activity homolog) (MoKA).	1.3	7.1E-08	9.7E-04
	ENSG00000175857		20.0	7.3E-08	1.6E-04
UBE2G2	ENSG00000184787	Ubiquitin-conjugating enzyme E2 G2 (EC 6.3.2.19) (Ubiquitin-protein ligase G2) (Ubiquitin carrier protein G2).	1.4	7.3E-08	1.6E-04
EEF1G	ENSG00000186676	Elongation factor 1-gamma (EF-1-gamma) (eEF-1B gamma).	1.5	7.7E-08	1.3E-04
RASGRP2	ENSG00000068831	RAS guanyl releasing protein 2 isoform 2	5.5	8.1E-08	7.8E-04
CD79B	ENSG0000007312	B-cell antigen receptor complex-associated protein beta-chain precursor (B-cell-specific glycoprotein B29) (Immunoglobulin- associated B29 protein) (IG-beta) (CD79b antigen).	7.2	8.4E-08	9.7E-05
REV1L	ENSG00000135945	DNA repair protein REV1 (EC 2.7.7.-) (Rev1-like terminal deoxycytidyl transferase) (Alpha integrin-binding protein 80) (AIBP80).	1.7	8.6E-08	8.2E-04
NAP1L1	ENSG00000187109	Nucleosome assembly protein 1-like 1 (NAP-1-related protein) (hNRP).	1.8	9.8E-08	9.1E-04
DGKA	ENSG00000065357	Diacylglycerol kinase alpha (EC 2.7.1.107) (Diglyceride kinase alpha) (DGK-alpha) (DAG kinase alpha) (80 kDa diacylglycerol kinase).	3.6	1.2E-07	5.3E-04
ZNF573	ENSG00000189144	zinc finger protein 573	2.2	1.3E-07	6.7E-04
SEPT1	ENSG00000180096	Septin-1 (LARP) (Serologically defined breast cancer antigen NY-BR- 24).	1.8	1.4E-07	9.7E-04
CD52	ENSG00000169442	CAMPATH-1 antigen precursor (Cambridge pathology 1 antigen) (Epididymal secretory protein E5) (CD52 antigen) (CDw52).	3.0	1.5E-07	9.7E-05
PIK3C2B	ENSG00000133056	Phosphatidylinositol-4-phosphate 3-kinase C2 domain-containing beta polypeptide (EC 2.7.1.154) (Phosphoinositide 3-Kinase-C2-beta) (PtdIns-3-kinase C2 beta) (PI3K-C2beta) (C2-PI3K).	4.6	1.5E-07	5.2E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
ZNF238	ENSG00000179456	Zinc finger protein 238 (Transcriptional repressor RP58) (58 kDa repressor protein) (Zinc finger protein C2H2-171) (Translin-associated zinc finger protein 1) (TAZ-1) (Zinc finger and BTB domain-containing protein 18).	2.5	1.6E-07	5.8E-04
POLR3E	ENSG00000058600	DNA-directed RNA polymerases III 80 kDa polypeptide (EC 2.7.7.6) (RNA polymerase III subunit 5) (RPC5).	1.9	1.6E-07	5.2E-04
MYCBP2	ENSG0000005810	Probable ubiquitin ligase protein MYCBP2 (EC 6.3.2.-) (Myc binding protein 2) (Protein associated with Myc) (Pam/highwire/rpm-1 protein).	1.9	1.7E-07	8.7E-04
VPREB3	ENSG00000128218	Pre-B lymphocyte protein 3 precursor (VpreB3 protein) (N27C7-2).	30.5	2.0E-07	2.9E-04
EIF4B	ENSG0000063046	Eukaryotic translation initiation factor 4B (eIF-4B).	1.8	2.1E-07	4.0E-04
YTHDC1	ENSG00000083896	YTH domain-containing protein 1 (Putative splicing factor YT521).	1.6	2.1E-07	3.6E-04
IL16	ENSG00000172349	Interleukin-16 precursor (IL-16) (Lymphocyte chemoattractant factor) (LCF).	3.1	2.2E-07	7.8E-04
EPHX2	ENSG00000120915	Epoxide hydrolase 2 (EC 3.3.2.3) (Soluble epoxide hydrolase) (SEH) (Epoxide hydratase) (Cytosolic epoxide hydrolase) (CEH).	5.8	2.4E-07	9.1E-04
PRKCB1	ENSG00000166501	Protein kinase C beta type (EC 2.7.11.13) (PKC-beta) (PKC-B).	2.1	2.5E-07	6.4E-04
SKIV2L2	ENSG00000039123	Superkiller viralicidic activity 2-like 2 (EC 3.6.1.-) (ATP-dependent helicase SKIV2L2).	1.5	2.7E-07	7.7E-04
	ENSG00000100796		1.4	2.8E-07	9.4E-04
EPB41	ENSG00000159023	Protein 4.1 (Band 4.1) (P4.1) (EPB4.1) (4.1R).	2.4	3.1E-07	4.7E-04
RALGPS2	ENSG00000116191	Ral GEF with PH domain and SH3 binding motif 2 isoform 1	7.5	3.4E-07	2.8E-04
CCDC57	ENSG00000176155	coiled-coil domain containing 57	1.7	3.5E-07	6.8E-04
	ENSG00000198146		1.9	3.5E-07	5.8E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
ABCB4	ENSG0000005471	Multidrug resistance protein 3 (EC 3.6.3.44) (P-glycoprotein 3).	12.8	3.5E-07	1.6E-04
IGHV@	ENSG0000130076	Ig alpha-1 chain C region.	33.2	4.0E-07	9.7E-05
SCN3A	ENSG0000153253	Sodium channel protein type 3 subunit alpha (Sodium channel protein type III subunit alpha) (Voltage-gated sodium channel subunit alpha Nav1.3) (Sodium channel protein, brain III subunit alpha) (Voltage- gated sodium channel subtype III).	9.4	7.0E-07	2.7E-04
TBC1D4	ENSG0000136111	TBC1 domain family member 4 (Akt substrate of 160 kDa) (AS160).	3.1	7.2E-07	8.9E-04
HNRPM	ENSG0000099783	Heterogeneous nuclear ribonucleoprotein M (hnRNP M).	1.4	1.7E-06	4.1E-04
RPL15	ENSG0000174748	60S ribosomal protein L15.	1.7	1.8E-06	7.8E-04
AFF3	ENSG0000144218	AF4/FMR2 family member 3 (Protein LAF-4) (Lymphoid nuclear protein related to AF4).	13.8	2.0E-06	5.4E-04
KIAA0125	ENSG0000184618		10.6	2.6E-06	1.5E-04
TCL1A	ENSG0000100721	T-cell leukemia/lymphoma protein 1A (P14 TCL1 protein) (TCL1 oncogene) (TCL-1 protein).	56.5	3.2E-06	9.1E-04

B. Signature of THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
FCER1G	ENSG0000158869	High affinity immunoglobulin epsilon receptor gamma-subunit precursor (FcεRI gamma) (IgE Fc receptor gamma-subunit) (Fc-epsilon RI-gamma).	9.7	5.1E-13	1.1E-05
VSIG4	ENSG0000155659	V-set and immunoglobulin domain-containing protein 4 precursor (Z39Ig protein).	569.0	6.9E-13	1.1E-05
PSTPIP2	ENSG0000152229	Proline-serine-threonine phosphatase-interacting protein 2.	27.4	1.0E-12	1.1E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
SLC31A2	ENSG00000136867	Probable low-affinity copper uptake protein 2 (hCTR2) (Copper transporter 2) (Solute carrier family 31 member 2).	5.8	1.1E-12	1.1E-05
GLUL	ENSG00000135821	Glutamine synthetase (EC 6.3.1.2) (Glutamate--ammonia ligase) (GS).	11.5	1.1E-12	1.1E-05
GALC	ENSG0000054983	Galactocerebrosidase precursor (EC 3.2.1.46) (GALCERase) (Galactosylceramidase) (Galactosylceramide beta-galactosidase) (Galactocerebroside beta-galactosidase).	3.6	1.4E-12	1.1E-05
FPRL1	ENSG00000171049	FMLP-related receptor I (FMLP-R-I) (Lipoxin A4 receptor) (LXA4 receptor) (Formyl peptide receptor-like 1) (RFP) (HM63).	48.8	2.0E-12	1.1E-05
MFSD1	ENSG00000118855	major facilitator superfamily domain containing 1	2.9	2.2E-12	1.1E-05
CMKLR1	ENSG00000174600	Chemokine receptor-like 1 (G-protein coupled receptor DEZ) (G-protein coupled receptor ChemR23).	7.1	2.8E-12	1.1E-05
NINJ1	ENSG00000131669	Ninjurin-1 (Nerve injury-induced protein 1).	5.7	4.6E-12	1.1E-05
CEPB	ENSG00000172216	CCAAT/enhancer-binding protein beta (C/EBP beta) (Nuclear factor NF- IL6) (Transcription factor 5).	4.5	5.0E-12	2.2E-05
BRI3	ENSG00000164713	Brain protein I3 (pRGR2).	3.3	8.2E-12	2.2E-05
SDCBP	ENSG00000137575	Syntenin-1 (Syndecan-binding protein 1) (Melanoma differentiation- associated protein 9) (MDA-9) (Scaffold protein Pbp1) (Pro-TGF-alpha cytoplasmic domain-interacting protein 18) (TACIP18).	2.3	8.5E-12	1.1E-05
NRP2	ENSG00000118257	Neuropilin-2 precursor (Vascular endothelial cell growth factor 165 receptor 2).	4.3	8.6E-12	2.2E-05
DMXL2	ENSG00000104093	Protein DmX-like 2 (Rabconnectin-3).	6.0	9.8E-12	2.2E-05
MPP1	ENSG00000130830	55 kDa erythrocyte membrane protein (p55) (Membrane protein, palmitoylated 1).	4.9	1.2E-11	2.2E-05
C3AR1	ENSG00000171860	C3a anaphylatoxin chemotactic receptor (C3a-R) (C3AR).	11.0	1.3E-11	2.2E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
IRAK3	ENSG0000090376	Interleukin-1 receptor-associated kinase 3 (EC 2.7.11.1) (IRAK-3) (IL-1 receptor-associated kinase M) (IRAK-M).	11.3	1.6E-11	1.1E-05
AGTRAP	ENSG0000177674	Type-1 angiotensin II receptor-associated protein (AT1 receptor-associated protein).	5.2	1.6E-11	2.2E-05
SIGLEC7	ENSG0000168995	Sialic acid-binding Ig-like lectin 7 precursor (Siglec-7) (QA79 membrane protein) (Adhesion inhibitory receptor molecule 1) (AIRM-1) (p75) (D-siglec) (CDw328 antigen).	6.5	1.7E-11	2.2E-05
S100A9	ENSG0000163220	Protein S100-A9 (S100 calcium-binding protein A9) (Calgranulin-B) (Migration inhibitory factor-related protein 14) (MRP-14) (P14) (Leukocyte L1 complex heavy chain) (Calprotectin L1H subunit).	35.5	1.7E-11	2.2E-05
SCARB2	ENSG0000138760	Lysosome membrane protein 2 (Lysosome membrane protein II) (LIMP II) (Scavenger receptor class B member 2) (85 kDa lysosomal membrane sialoglycoprotein) (LGP85) (CD36 antigen-like 2).	4.4	1.9E-11	2.2E-05
	ENSG0000180672		4.8	1.9E-11	2.2E-05
RNF130	ENSG0000113269	Goliath homolog precursor (RING finger protein 130).	4.4	1.9E-11	2.2E-05
PILRA	ENSG0000085514	Paired immunoglobulin-like type 2 receptor alpha precursor (Inhibitory receptor PILR-alpha) (Cell surface receptor FDF03).	15.2	2.0E-11	2.2E-05
RAB20	ENSG0000139832	Ras-related protein Rab-20.	4.3	2.0E-11	2.2E-05
TLR2	ENSG0000137462	Toll-like receptor 2 precursor (Toll/interleukin 1 receptor-like protein 4) (CD282 antigen).	11.6	2.2E-11	1.1E-05
CYBA	ENSG0000051523	Cytochrome b-245 light chain (p22 phagocyte B-cytochrome) (Neutrophil cytochrome b 22 kDa polypeptide) (p22-phox) (p22phox) (Cytochrome b(558) alpha chain) (Cytochrome b558 subunit alpha) (Superoxide- generating NADPH oxidase light chain subunit).	1.6	2.7E-11	2.2E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
CD63	ENSG00000135404	CD63 antigen (Melanoma-associated antigen ME491) (Lysosome-associated membrane glycoprotein 3) (LAMP-3) (Ocular melanoma-associated antigen) (OMA81H) (Granulophysin) (Tetraspanin-30) (Tspan-30).	2.6	2.8E-11	2.2E-05
HEXA	ENSG00000140488	Beta-hexosaminidase alpha chain precursor (EC 3.2.1.52) (N-acetyl- beta-glucosaminidase) (Beta-N-acetylhexosaminidase) (Hexosaminidase A).	2.2	2.9E-11	2.2E-05
SAT	ENSG00000130066	Diamine acetyltransferase 1 (EC 2.3.1.57) (Spermidine/spermine N(1)-acetyltransferase 1) (SSAT) (SSAT-1) (Putrescine acetyltransferase) (Polyamine N-acetyltransferase 1).	2.7	3.3E-11	2.2E-05
GSTO1	ENSG00000148834	Glutathione transferase omega-1 (EC 2.5.1.18) (GSTO 1-1).	2.3	3.5E-11	2.2E-05
TPD52L2	ENSG00000101150	Tumor protein D54 (hD54) (Tumor protein D52-like 2).	1.9	3.6E-11	2.2E-05
TLR1	ENSG00000174125	Toll-like receptor 1 precursor (Toll/interleukin-1 receptor-like protein) (TIL) (CD281 antigen).	3.1	4.4E-11	2.2E-05
CSF3R	ENSG00000119535	Granulocyte colony-stimulating factor receptor precursor (G-CSF-R) (CD114 antigen).	9.7	4.4E-11	2.2E-05
PNKD	ENSG00000127838	myofibrillogenesis regulator 1 isoform 2	6.3	4.6E-11	2.2E-05
	ENSG00000163694		5.4	5.8E-11	2.2E-05
SLC8A1	ENSG00000183023	Sodium/calcium exchanger 1 precursor (Na(+)/Ca(2+)-exchange protein 1).	12.9	6.1E-11	3.2E-05
CD33	ENSG00000105383	Myeloid cell surface antigen CD33 precursor (Siglec-3) (gp67).	21.4	6.7E-11	3.2E-05
TYROBP	ENSG00000011600	TYRO protein tyrosine kinase-binding protein precursor (DNAX- activation protein 12) (Killer-activating receptor-associated protein).	6.4	7.1E-11	2.2E-05
TSPAN4	ENSG00000177769	Tetraspanin-4 (Tspan-4) (Transmembrane 4 superfamily member 7) (Novel antigen 2) (NAG-2).	3.9	7.2E-11	2.2E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
KCNE3	ENSG00000175538	Potassium voltage-gated channel subfamily E member 3 (Minimum potassium ion channel-related peptide 2) (Potassium channel subunit beta MiRP2) (MinK-related peptide 2).	5.2	9.1E-11	3.2E-05
HTATIP2	ENSG00000109854	Oxidoreductase HTATIP2 (EC 1.1.1.-) (HIV-1 TAT-interactive protein 2) (30 kDa HIV-1 TAT-interacting protein).	1.9	1.0E-10	2.2E-05
LILRB1	ENSG00000104972	Leukocyte immunoglobulin-like receptor subfamily B member 1 precursor (Leukocyte immunoglobulin-like receptor 1) (LIR-1) (Immunoglobulin- like transcript 2) (ILT-2) (Monocyte/macrophage immunoglobulin-like receptor 7) (MIR-7) (CD85j antigen).	4.7	1.1E-10	2.2E-05
	ENSG00000074842	Uncharacterized protein C19orf10 precursor (Stromal cell-derived growth factor SF20) (Interleukin-25) (IL-25).			
CCR1	ENSG00000163823	C-C chemokine receptor type 1 (C-C CKR-1) (CC-CKR-1) (CCR-1) (CCR1) (Macrophage inflammatory protein 1-alpha receptor) (MIP-1alpha-R) (RANTES-R) (HM145) (LD78 receptor) (CD191 antigen).	10.4	1.2E-10	2.2E-05
MLSTD1	ENSG0000064763	male sterility domain containing 1	4.4	1.2E-10	3.2E-05
CREG1	ENSG00000143162	CREG1 protein precursor (Cellular repressor of E1A-stimulated genes 1).	3.6	1.3E-10	3.2E-05
ZNF438	ENSG00000183621	ZNF438 transcript variant 3	4.1	1.3E-10	3.2E-05
SERPINA1	ENSG00000197249	Alpha-1-antitrypsin precursor (Alpha-1 protease inhibitor) (Alpha-1- antiproteinase).	7.1	1.5E-10	3.2E-05
LAP3	ENSG0000002549	Cytosol aminopeptidase (EC 3.4.11.1) (Leucine aminopeptidase) (LAP) (Leucyl aminopeptidase) (Proline aminopeptidase) (EC 3.4.11.5) (Prolyl aminopeptidase) (Peptidase S).	2.7	1.5E-10	3.2E-05
MXD1	ENSG00000059728	MAD protein (MAX dimerizer) (MAX dimerization protein 1).	3.8	1.5E-10	3.2E-05
PYCARD	ENSG00000103490	Apoptosis-associated speck-like protein containing a CARD (hASC) (PYD and CARD domain containing protein) (Target of methylation-induced silencing 1) (Caspase recruitment domain protein 5).	2.4	1.5E-10	3.2E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
EPB41L3	ENSG0000082397	Band 4.1-like protein 3 (4.1B) (Differentially expressed in adenocarcinoma of the lung protein 1) (DAL-1).	5.0	1.6E-10	3.2E-05
STAT1	ENSG0000115415	Signal transducer and activator of transcription 1-alpha/beta (Transcription factor ISGF-3 components p91/p84).	1.6	1.6E-10	3.2E-05
ALDH1A1	ENSG0000165092	Retinal dehydrogenase 1 (EC 1.2.1.36) (RaLDH1) (RALDH 1) (Aldehyde dehydrogenase family 1 member A1) (Aldehyde dehydrogenase, cytosolic) (ALHDII) (ALDH-E1).	6.6	1.9E-10	3.2E-05
ARRB1	ENSG0000137486	Beta-arrestin-1 (Arrestin, beta 1).	9.2	2.0E-10	3.2E-05
ICAM1	ENSG0000090339	Intercellular adhesion molecule 1 precursor (ICAM-1) (Major group rhinovirus receptor) (CD54 antigen).	4.8	2.2E-10	3.2E-05
SLC7A7	ENSG0000155465	Y+L amino acid transporter 1 (y(+)-L-type amino acid transporter 1) (y+LAT-1) (Y+LAT1) (Monocyte amino acid permease 2) (MOP-2).	5.1	2.2E-10	3.2E-05
SNX10	ENSG0000086300	Sorting nexin-10.	9.3	2.2E-10	3.2E-05
MOSPD2	ENSG0000130150	Motile sperm domain-containing protein 2.	2.0	2.3E-10	3.2E-05
IDH1	ENSG0000138413	Isocitrate dehydrogenase [NADP] cytoplasmic (EC 1.1.1.42) (Cytosolic NADP-isocitrate dehydrogenase) (Oxalosuccinate decarboxylase) (IDH) (NADP(+)-specific ICDH) (IDP).	3.4	2.4E-10	3.2E-05
SECTM1	ENSG0000141574	Secreted and transmembrane protein 1 precursor (Protein K12).	9.8	2.4E-10	2.2E-05
FOSL2	ENSG0000075426	Fos-related antigen 2.	4.7	2.4E-10	2.2E-05
BST1	ENSG0000109743	ADP-ribosyl cyclase 2 precursor (EC 3.2.2.5) (Cyclic ADP-ribose hydrolase 2) (cADPr hydrolase 2) (Bone marrow stromal antigen 1) (BST- 1) (CD157 antigen).	6.0	2.7E-10	3.2E-05
GYG1	ENSG0000163754	Glycogenin-1 (EC 2.4.1.186).	2.3	2.7E-10	3.2E-05
MSRB2	ENSG0000148450	Methionine-R-sulfoxide reductase B2 (EC 1.8.4.-).	2.8	2.8E-10	3.2E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
CPNE8	ENSG00000139117	Copine-8 (Copine VIII).	3.5	2.8E-10	3.2E-05
	ENSG00000176778		1.9	3.2E-10	3.2E-05
PRDX1	ENSG00000117450	Peroxiredoxin-1 (EC 1.11.1.15) (Thioredoxin peroxidase 2) (Thioredoxin-dependent peroxide reductase 2) (Proliferation-associated protein PAG) (Natural killer cell-enhancing factor A) (NKEF-A).	2.3	3.8E-10	3.2E-05
C14orf58	ENSG00000119686	Feline leukemia virus subgroup C receptor-related protein 2 (Calcium- chelate transporter) (CCT).	5.2	3.9E-10	3.2E-05
NPL	ENSG00000135838	N-acetylneuraminate pyruvate lyase	4.2	4.0E-10	3.2E-05
CD14	ENSG00000170458	Monocyte differentiation antigen CD14 precursor (Myeloid cell-specific leucine-rich glycoprotein) [Contains: Monocyte differentiation antigen CD14, urinary form; Monocyte differentiation antigen CD14, membrane- bound form].	9.2	4.0E-10	2.2E-05
APOL6	ENSG00000170420	Apolipoprotein-L6 (Apolipoprotein L-VI) (ApoL-VI).	3.3	4.1E-10	2.2E-05
PLSCR1	ENSG00000188313	Phospholipid scramblase 1 (PL scramblase 1) (Ca(2+)-dependent phospholipid scramblase 1) (Erythrocyte phospholipid scramblase) (MmTRA1b).	2.5	4.3E-10	3.2E-05
RILP	ENSG00000167705	Rab-interacting lysosomal protein.	2.9	4.4E-10	3.2E-05
VAMP8	ENSG00000118640	Vesicle-associated membrane protein 8 (VAMP-8) (Endobrevin) (EDB).	1.8	4.5E-10	3.2E-05
S100A8	ENSG00000143546	Protein S100-A8 (S100 calcium-binding protein A8) (Calgranulin-A) (Migration inhibitory factor-related protein 8) (MRP-8) (Cystic fibrosis antigen) (CFAG) (P8) (Leukocyte L1 complex light chain) (Calprotectin L1L subunit) (Urinary stone protein band A).	40.4	4.6E-10	2.2E-05
PLXDC2	ENSG00000120594	Plexin domain-containing protein 2 precursor (Tumor endothelial marker 7-related protein).	15.9	4.6E-10	1.1E-05
RNF13	ENSG00000082996	RING finger protein 13.	2.5	4.7E-10	3.2E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
ACP2	ENSG00000134575	Lysosomal acid phosphatase precursor (EC 3.1.3.2) (LAP).	4.1	4.7E-10	4.3E-05
PLD3	ENSG00000105223	phospholipase D3 isoform 1	3.8	4.7E-10	3.2E-05
TIMP2	ENSG0000035862	Metalloproteinase inhibitor 2 precursor (TIMP-2) (Tissue inhibitor of metalloproteinases 2) (CSC-21K).	7.2	4.9E-10	5.4E-05
SGK3	ENSG00000104205	Serine/threonine-protein kinase Sgk3 (EC 2.7.11.1) (Serum/glucocorticoid-regulated kinase 3) (Serum/glucocorticoid- regulated kinase-like).	2.4	5.0E-10	5.4E-05
SIGLEC9	ENSG00000129450	Sialic acid-binding Ig-like lectin 9 precursor (Siglec-9) (Protein FOAP-9).	14.5	5.3E-10	1.1E-05
B4GALT5	ENSG00000158470	Beta-1,4-galactosyltransferase 5 (EC 2.4.1.-) (Beta-1,4-GalTase 5) (Beta4Gal-T5) (b4Gal-T5) (UDP-galactose:beta-N-acetylglucosamine beta- 1,4-galactosyltransferase 5) (UDP-Gal:beta-GlcNAc beta-1,4- galactosyltransferase 5) (Beta-1,4-GalT II).	4.4	5.3E-10	2.2E-05
SOD2	ENSG00000112096	Superoxide dismutase [Mn], mitochondrial precursor (EC 1.15.1.1).	5.7	5.4E-10	3.2E-05
FCGR3B	ENSG00000162747	Low affinity immunoglobulin gamma Fc region receptor III-B precursor (IgG Fc receptor III-1) (Fc-gamma RIII-beta) (Fc-gamma RIIIb) (FcRIIIb) (Fc-gamma RIII) (FcRIII) (FcR-10) (CD16b antigen).	25.7	5.5E-10	1.1E-05
LRRC25	ENSG00000175489	Leucine-rich repeat-containing protein 25 precursor (Monocyte and plasmacytoid-activated protein).	15.7	5.5E-10	5.4E-05
	ENSG00000052795	CDNA FLJ12906 fis, clone NT2RP2004373.	3.7	5.7E-10	5.4E-05
GNS	ENSG00000135677	N-acetylglucosamine-6-sulfatase precursor (EC 3.1.6.14) (G6S) (Glucosamine-6-sulfatase).	4.5	5.9E-10	3.2E-05
RNPEP	ENSG00000176393	Aminopeptidase B (EC 3.4.11.6) (Ap-B) (Arginyl aminopeptidase) (Arginine aminopeptidase).	2.0	6.0E-10	6.5E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
CXCL16	ENSG00000161921	Small inducible cytokine B16 precursor (Transmembrane chemokine CXCL16) (SR-PSOX) (Scavenger receptor for phosphatidylserine and oxidized low density lipoprotein).	7.9	6.2E-10	3.2E-05
ANKRD22	ENSG00000152766	Ankyrin repeat domain-containing protein 22.	17.4	6.3E-10	6.5E-05
IFI27	ENSG00000165949	Interferon-alpha-induced 11.5 kDa protein (p27) (ISG12(a) protein).	7.9	6.4E-10	3.2E-05
IFIT3	ENSG00000119917	Interferon-induced protein with tetratricopeptide repeats 3 (IFIT-3) (IFIT-4) (Interferon-induced 60 kDa protein) (IFI-60K) (ISG-60) (CIG49) (Retinoic acid-induced gene G protein) (RIG-G).	7.1	7.7E-10	5.4E-05
	ENSG00000135124	P2X purinoceptor 4 (ATP receptor) (P2X4) (Purinergic receptor).	2.5	7.7E-10	6.5E-05
MEGF9	ENSG00000106780	Multiple epidermal growth factor-like domains 9 precursor (EGF-like domain-containing protein 5) (Multiple EGF-like domain protein 5).	2.5	7.8E-10	6.5E-05
EFHD2	ENSG00000142634	EF-hand domain-containing protein 2 (Swiprosin-1).	3.1	8.0E-10	6.5E-05
C1orf85	ENSG00000198715	kidney predominant protein NCU-G1	3.2	8.5E-10	3.2E-05
LAMP2	ENSG0000005893	Lysosome-associated membrane glycoprotein 2 precursor (LAMP-2) (CD107b antigen).	3.8	8.6E-10	6.5E-05
CTSB	ENSG00000164733	Cathepsin B precursor (EC 3.4.22.1) (Cathepsin B1) (APP secretase) (APPS) [Contains: Cathepsin B light chain; Cathepsin B heavy chain].	6.1	8.6E-10	2.2E-05
DLL1	ENSG00000198719	Delta-like protein 1 precursor (Drosophila Delta homolog 1) (Delta1) (H-Delta-1).	5.1	8.7E-10	5.4E-05
C2	ENSG00000204364	Complement C2 precursor (EC 3.4.21.43) (C3/C5 convertase) [Contains: Complement C2b fragment; Complement C2a fragment].	10.9	8.8E-10	3.2E-05
HNMT	ENSG00000150540	Histamine N-methyltransferase (EC 2.1.1.8) (HMT).	6.8	1.0E-09	3.2E-05
AYTL1	ENSG00000087253		10.7	1.1E-09	8.7E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
SLC31A1	ENSG00000136868	High-affinity copper uptake protein 1 (hCTR1) (Copper transporter 1) (Solute carrier family 31 member 1).	8.6	1.1E-09	8.7E-05
CCL8	ENSG00000108700	Small inducible cytokine A8 precursor (CCL8) (Monocyte chemotactic protein 2) (MCP-2) (Monocyte chemoattractant protein 2) (HC14) [Contains: MCP-2(6-76)].	143.5	1.1E-09	6.5E-05
	ENSG00000121316		4.3	1.1E-09	6.5E-05
ASAHI	ENSG00000104763	Acid ceramidase precursor (EC 3.5.1.23) (Acylsphingosine deacylase) (N-acylsphingosine amidohydrolase) (AC) (Putative 32 kDa heart protein) (PHP32) [Contains: Acid ceramidase subunit alpha; Acid ceramidase subunit beta].	2.0	1.1E-09	3.2E-05
P4HA1	ENSG00000122884	Prolyl 4-hydroxylase alpha-1 subunit precursor (EC 1.14.11.2) (4-PH alpha-1) (Procollagen-proline,2-oxoglutarate-4-dioxygenase alpha-1 subunit).	2.8	1.2E-09	6.5E-05
PSAP	ENSG00000197746	Proactivator polypeptide precursor [Contains: Saposin A (Protein A); Saposin B-Val; Saposin B (Sphingolipid activator protein 1) (SAP-1) (Cerebroside sulfate activator) (CSAct) (Dispersin) (Sulfatide/GM1 activator); Saposin C (Co-beta-glucosidase)	2.2	1.2E-09	8.7E-05
IL18BP	ENSG00000137496	Interleukin-18-binding protein precursor (IL-18BP) (Tadekinig-alfa).	6.4	1.2E-09	3.2E-05
RGL1	ENSG00000143344	Ral guanine nucleotide dissociation stimulator-like 1 (RalGDS-like 1).	4.6	1.3E-09	8.7E-05
DNPEP	ENSG00000123992	Aspartyl aminopeptidase (EC 3.4.11.21).	1.6	1.3E-09	3.2E-05
STX12	ENSG00000117758	Syntaxin-12.	2.2	1.3E-09	5.4E-05
IFNGR2	ENSG00000159128	Interferon-gamma receptor beta chain precursor (Interferon-gamma receptor accessory factor 1) (AF-1) (Interferon-gamma transducer 1).	2.8	1.3E-09	3.2E-05
FPR1	ENSG00000171051	fMet-Leu-Phe receptor (fMLP receptor) (N-formyl peptide receptor) (FPR) (N-formylpeptide chemoattractant receptor).	6.7	1.4E-09	6.5E-05
DIRC2	ENSG00000138463	disrupted in renal carcinoma 2	3.3	1.4E-09	9.7E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
S100A11	ENSG00000163191	Protein S100-A11 (S100 calcium-binding protein A11) (Protein S100C) (Calgizzarin) (MLN 70).	3.1	1.4E-09	3.2E-05
LACTB	ENSG00000103642	Serine beta-lactamase-like protein LACTB.	3.2	1.4E-09	8.7E-05
TLR8	ENSG00000101916	Toll-like receptor 8 precursor.	11.5	1.4E-09	3.2E-05
ADIPOR1	ENSG00000159346	Adiponectin receptor protein 1 (Progesterin and adiponectin receptor family member I).	1.7	1.5E-09	4.3E-05
CPD	ENSG00000108582	Carboxypeptidase D precursor (EC 3.4.17.22) (Metallocarboxypeptidase D) (gp180).	2.8	1.6E-09	9.7E-05
CD80	ENSG00000121594	T-lymphocyte activation antigen CD80 precursor (Activation B7-1 antigen) (CTLA-4 counter-receptor B7.1) (B7) (BB1).	3.4	1.7E-09	8.7E-05
ALDH3B1	ENSG00000006534	Aldehyde dehydrogenase 3B1 (EC 1.2.1.5) (Aldehyde dehydrogenase 7).	6.1	1.7E-09	9.7E-05
LILRB2	ENSG00000131042	Leukocyte immunoglobulin-like receptor subfamily B member 2 precursor (Leukocyte immunoglobulin-like receptor 2) (LIR-2) (Immunoglobulin-like transcript 4) (ILT-4) (Monocyte/macrophage immunoglobulin-like receptor 10) (MIR-10) (CD85d antigen).	17.4	1.7E-09	3.2E-05
PQLC3	ENSG00000162976	PQ loop repeat-containing protein 3 precursor.	2.1	1.8E-09	6.5E-05
C1QB	ENSG00000173369	Complement C1q subcomponent subunit B precursor.	10.6	2.0E-09	2.2E-05
TNFSF13B	ENSG00000102524	Tumor necrosis factor ligand superfamily member 13B (TNF- and APOL-related leukocyte expressed ligand 1) (TALL-1) (B lymphocyte stimulator) (BLyS) (B cell-activating factor) (BAFF) (Dendritic cell-derived TNF-like molecule) (CD257 antigen)	3.9	2.0E-09	8.7E-05
HK3	ENSG00000160883	Hexokinase-3 (EC 2.7.1.1) (Hexokinase type III) (HK III).	14.7	2.1E-09	3.2E-05
CTSS	ENSG00000163131	Cathepsin S precursor (EC 3.4.22.27).	2.9	2.1E-09	9.7E-05
	ENSG00000122597	Putative S100 calcium-binding protein H_NH0456N16.1.	2.7	2.2E-09	3.2E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
NR1H3	ENSG0000025434	Oxysterols receptor LXR-alpha (Liver X receptor alpha) (Nuclear orphan receptor LXR-alpha).	3.7	2.2E-09	8.7E-05
SERPING1	ENSG0000149131	Plasma protease C1 inhibitor precursor (C1 Inh) (C1Inh).	5.7	2.2E-09	6.5E-05
	ENSG0000120306	putative nuclear protein ORF1-FL49	2.2	2.2E-09	5.4E-05
AKR1A1	ENSG0000117448	Alcohol dehydrogenase [NADP+] (EC 1.1.1.2) (Aldehyde reductase) (Aldo- keto reductase family 1 member A1).	2.3	2.3E-09	9.7E-05
KCNJ10	ENSG0000177807	ATP-sensitive inward rectifier potassium channel 10 (Potassium channel, inwardly rectifying subfamily J member 10) (Inward rectifier K(+) channel Kir1.2) (ATP-dependent inwardly rectifying potassium channel Kir4.1).	14.0	2.4E-09	9.7E-05
AP1S2	ENSG0000182287	AP-1 complex subunit sigma-2 (Adapter-related protein complex 1 sigma- 1B subunit) (Sigma-adaptin 1B) (Adaptor protein complex AP-1 sigma-1B subunit) (Golgi adaptor HA1/AP1 adaptin sigma-1B subunit)	2.3	2.4E-09	9.7E-05
PFKFB3	ENSG0000170525	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 (6PF-2-K/Fru- 2,6-P2ASE brain/placenta-type isozyme) (iPFK-2) (NY-REN-56 antigen) [Includes: 6-phosphofructo-2-kinase (EC 2.7.1.105); Fructose-2,6- bisphosphatase (EC 3.1.3.46)].	4.7	2.4E-09	9.7E-05
TLR4	ENSG0000136869	Toll-like receptor 4 precursor (hToll) (CD284 antigen).	4.0	2.5E-09	9.7E-05
MRAS	ENSG0000158186	Ras-related protein M-Ras (Ras-related protein R-Ras3).	3.1	2.5E-09	5.4E-05
CD86	ENSG0000114013	T-lymphocyte activation antigen CD86 precursor (Activation B7-2 antigen) (CTLA-4 counter-receptor B7.2) (B70) (FUN-1) (BU63).	3.8	2.5E-09	9.7E-05
DCTN4	ENSG0000132912	Dynactin subunit 4 (Dynactin subunit p62).	2.0	2.6E-09	9.7E-05
SCPEP1	ENSG0000121064	Retinoid-inducible serine carboxypeptidase precursor (EC 3.4.16.-) (Serine carboxypeptidase 1).	5.1	2.7E-09	9.7E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
ADM	ENSG00000148926	ADM precursor [Contains: Adrenomedullin (AM); Proadrenomedullin N-20 terminal peptide (ProAM-N20) (ProAM N-terminal 20 peptide) (PAMP)].	6.5	2.9E-09	9.7E-05
	ENSG00000134470	Interleukin-15 receptor alpha chain precursor (IL-15R-alpha) (IL- 15RA).	4.5	3.1E-09	6.5E-05
CD163	ENSG00000177575	Scavenger receptor cysteine-rich type 1 protein M130 precursor (CD163 antigen) (Hemoglobin scavenger receptor) [Contains: Soluble CD163 (sCD163)].	50.5	3.1E-09	2.2E-05
M6PR	ENSG0000003056	Cation-dependent mannose-6-phosphate receptor precursor (CD Man-6-P receptor) (CD-MPR) (46 kDa mannose 6-phosphate receptor) (MPR 46).	1.8	3.2E-09	8.7E-05
COMMD9	ENSG00000110442	COMM domain-containing protein 9.	1.6	3.4E-09	9.7E-05
YIF1B	ENSG00000167645	Yip1 interacting factor homolog B isoform 2	1.9	3.4E-09	9.7E-05
CD300LF	ENSG00000186074	NK inhibitory receptor precursor	5.1	3.5E-09	9.7E-05
INSIG2	ENSG00000125629	insulin induced protein 2	2.4	3.5E-09	3.2E-05
	ENSG00000137393	E3 ubiquitin ligase IBRDC2 (EC 6.3.2.-) (IBR domain-containing protein 2) (p53-inducible RING finger protein).	16.6	3.6E-09	9.7E-05
LILRB3	ENSG00000186152	Leukocyte immunoglobulin-like receptor subfamily B member 3 precursor (Leukocyte immunoglobulin-like receptor 3) (LIR-3) (Immunoglobulin- like transcript 5) (ILT-5) (Monocyte inhibitory receptor HL9) (CD85a antigen).	4.1	3.6E-09	9.7E-05
C1QA	ENSG00000173372	Complement C1q subcomponent subunit A precursor.	8.3	3.6E-09	2.2E-05
FAM20A	ENSG00000108950	Protein FAM20A precursor.	7.3	3.7E-09	9.7E-05
IL1RN	ENSG00000136689	Interleukin-1 receptor antagonist protein precursor (IL-1ra) (IRAP) (IL1 inhibitor) (IL-1RN) (ICIL-1RA).	67.7	3.7E-09	8.7E-05
GPD2	ENSG00000115159	Glycerol-3-phosphate dehydrogenase, mitochondrial precursor (EC 1.1.99.5) (GPD-M) (GPDH-M) (mtGPD).	4.5	3.9E-09	9.7E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
MGLL	ENSG0000074416	Monoglyceride lipase (EC 3.1.1.23) (MGL) (HU-K5) (Lysophospholipase homolog) (Lysophospholipase-like).	7.1	3.9E-09	9.7E-05
FTH1	ENSG0000167996	Ferritin heavy chain (EC 1.16.3.1) (Ferritin H subunit) (Proliferation-inducing gene 15 protein).	4.5	4.0E-09	9.7E-05
CTNNA1	ENSG0000044115	Alpha-1 catenin (Cadherin-associated protein) (Alpha E-catenin) (NY-REN-13 antigen).	2.0	4.1E-09	9.7E-05
CSTB	ENSG0000160213	Cystatin B (Liver thiol proteinase inhibitor) (CPI-B) (Stefin B).	2.4	4.2E-09	9.7E-05
TMBIM1	ENSG0000135926	Transmembrane BAX inhibitor motif-containing protein 1 (RECS1 protein homolog).	2.7	4.3E-09	1.1E-04
	ENSG0000101084	Uncharacterized protein C20orf24 (Rab5-interacting protein) (RIP5).	2.1	4.5E-09	9.7E-05
LTBR	ENSG0000111321	Tumor necrosis factor receptor superfamily member 3 precursor (Lymphotoxin-beta receptor) (Tumor necrosis factor receptor 2-related protein) (Tumor necrosis factor C receptor).	4.1	4.5E-09	9.7E-05
GZMA	ENSG0000145649	Granzyme A precursor (EC 3.4.21.78) (Cytotoxic T-lymphocyte proteinase 1) (Hanukkah factor) (H factor) (HF) (Granzyme-1) (CTL tryptase) (Fragmentin-1).	5.5	4.5E-09	6.5E-05
PTGER2	ENSG0000125384	Prostaglandin E2 receptor, EP2 subtype (Prostanoid EP2 receptor) (PGE receptor, EP2 subtype).	10.6	4.6E-09	1.3E-04
ZNF313	ENSG0000124226	Zinc finger protein 313 (RING finger protein 114).	2.0	4.7E-09	1.3E-04
PBEF1	ENSG0000105835	Nicotinamide phosphoribosyltransferase (EC 2.4.2.12) (NAmPRTase) (Nampt) (Pre-B cell-enhancing factor) (Pre-B-cell colony-enhancing factor 1) (Visfatin).	3.7	4.8E-09	6.5E-05
C1QC	ENSG0000159189	Complement C1q subcomponent subunit C precursor.	6.4	4.8E-09	3.2E-05
	ENSG0000166347	Cytochrome b5.	2.6	5.2E-09	1.3E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
NANS	ENSG00000095380	Sialic acid synthase (N-acetylneuraminate synthase) (EC 2.5.1.56) (N-acetylneuraminic acid synthase) (N-acetylneuraminate-9-phosphate synthase) (EC 2.5.1.57) (N-acetylneuraminic acid phosphate synthase).	2.3	5.3E-09	1.5E-04
MGAT1	ENSG0000131446	Alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase (EC 2.4.1.101) (N-glycosyl-oligosaccharide-glycoprotein N-acetylglucosaminyltransferase I) (GNT-I) (GlcNAc-T I).	2.2	5.3E-09	1.5E-04
FUCA2	ENSG0000001036	Plasma alpha-L-fucosidase precursor (EC 3.2.1.51) (Alpha-L-fucosidase 2) (Alpha-L-fucoside fucohydrolase 2).	2.3	5.4E-09	9.7E-05
DNASE1L1	ENSG0000013563	Deoxyribonuclease I-like 1 precursor (EC 3.1.21.-) (DNase I-like 1) (Muscle-specific DNase I-like) (DNase X) (XIB).	2.1	5.7E-09	1.2E-04
FER1L3	ENSG0000138119	Myoferlin (Fer-1-like protein 3).	13.8	5.7E-09	1.1E-04
BID	ENSG0000015475	BH3-interacting domain death agonist (BID) (p22 BID) [Contains: BH3- interacting domain death agonist p15 (p15 BID); BH3-interacting domain death agonist p13 (p13 BID); BH3-interacting domain death agonist p11 (p11 BID)].	2.5	6.0E-09	1.5E-04
PCBD1	ENSG0000166228	Pterin-4-alpha-carbinolamine dehydratase (EC 4.2.1.96) (PHS) (4-alpha- hydroxy-tetrahydropterin dehydratase) (Phenylalanine hydroxylase- stimulating protein) (Pterin carbinolamine dehydratase) (PCD)	2.3	6.0E-09	1.2E-04
ITFG1	ENSG0000129636	T-cell immunomodulatory protein precursor (Protein TIP).	1.9	6.0E-09	8.7E-05
TMEM135	ENSG0000166575		1.7	6.1E-09	9.7E-05
APOL3	ENSG0000128284	Apolipoprotein-L3 (Apolipoprotein L-III) (ApoL-III) (TNF-inducible protein CG12-1) (CG12_1).	3.8	6.1E-09	3.2E-05
PVRL2	ENSG0000130202	Poliovirus receptor-related protein 2 precursor (Herpes virus entry mediator B) (HveB) (Nectin-2) (CD112 antigen).	4.6	6.1E-09	1.5E-04
MS4A4A	ENSG0000110079	Membrane-spanning 4-domains subfamily A member 4A (Four-span transmembrane protein 1) (CD20 antigen-like 1).	11.9	6.2E-09	1.4E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
SLC38A6	ENSG00000139974	N system amino acid transporter NAT-1	3.9	6.3E-09	9.7E-05
H2AFY	ENSG00000113648	Core histone macro-H2A.1 (Histone macroH2A1) (mH2A1) (H2A.y) (H2A/y) (Medulloblastoma antigen MU-MB-50.205).	2.6	6.3E-09	6.5E-05
TNFAIP6	ENSG00000123610	Tumor necrosis factor-inducible protein TSG-6 precursor (TNF- stimulated gene 6 protein) (Hyaluronate-binding protein).	76.9	6.4E-09	9.7E-05
	ENSG00000188811		2.1	6.4E-09	9.7E-05
MITF	ENSG00000187098	Microphthalmia-associated transcription factor.	4.3	6.4E-09	1.6E-04
CXCL10	ENSG00000169245	Small inducible cytokine B10 precursor (CXCL10) (10 kDa interferon- gamma-induced protein) (Gamma-IP10) (IP-10) [Contains: CXCL10(1-73)].	7.7	6.6E-09	1.6E-04
IFNAR1	ENSG00000142166	Interferon-alpha/beta receptor alpha chain precursor (IFN-alpha-REC).	2.2	6.7E-09	9.7E-05
EXOC5	ENSG00000070367	Exocyst complex component 5 (Exocyst complex component Sec10) (hSec10).	1.6	6.9E-09	9.7E-05
DYNLT1	ENSG00000146425	Dynein light chain Tctex-type 1 (T-complex testis-specific protein 1 homolog (Protein CW-1).	2.1	7.0E-09	9.7E-05
SUCNR1	ENSG00000198829	Succinate receptor 1 (G-protein coupled receptor 91) (P2Y purinoceptor 1-like).	23.9	7.1E-09	1.6E-04
GPR137B	ENSG00000077585	Integral membrane protein GPR137B (Transmembrane 7 superfamily member 1).	3.1	7.2E-09	9.7E-05
RHEB	ENSG00000106615	GTP-binding protein Rheb (Ras homolog enriched in brain).	1.4	7.3E-09	1.6E-04
SLC17A5	ENSG00000119899	Sialin (Solute carrier family 17 member 5) (Sodium/sialic acid cotransporter) (AST) (Membrane glycoprotein HP59).	2.6	7.5E-09	9.7E-05
RAB1A	ENSG00000138069	Ras-related protein Rab-1A (YPT1-related protein).	1.9	7.5E-09	1.3E-04
VAMP5	ENSG00000168899	Vesicle-associated membrane protein 5 (VAMP-5) (Myobrevin).	4.7	7.6E-09	6.5E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
SLC1A3	ENSG0000079215	Excitatory amino acid transporter 1 (Sodium-dependent glutamate/aspartate transporter 1) (Glial glutamate transporter) (GLAST-1).	6.7	7.8E-09	1.4E-04
TFEC	ENSG0000105967	transcription factor EC isoform b	3.5	7.9E-09	1.2E-04
CLN3	ENSG0000188603	Protein CLN3 (Battenin) (Batten disease protein).	1.5	7.9E-09	9.7E-05
RAB18	ENSG0000099246	Ras-related protein Rab-18.	1.7	8.0E-09	1.6E-04
HCK	ENSG0000101336	Tyrosine-protein kinase HCK (EC 2.7.10.2) (p59-HCK/p60-HCK) (Hemopoietic cell kinase).	3.9	8.2E-09	1.6E-04
ABCA1	ENSG0000165029	ATP-binding cassette sub-family A member 1 (ATP-binding cassette transporter 1) (ATP-binding cassette 1) (ABC-1) (Cholesterol efflux regulatory protein).	3.9	8.4E-09	9.7E-05
RDX	ENSG0000137710	Radixin.	3.9	8.5E-09	3.2E-05
SLC39A11	ENSG0000133195	solute carrier family 39 (metal ion transporter), member 11	3.3	8.6E-09	9.7E-05
CYBB	ENSG0000165168	Cytochrome b-245 heavy chain (p22 phagocyte B-cytochrome) (Neutrophil cytochrome b 91 kDa polypeptide) (CGD91-phox) (gp91-phox) (gp91-1) (Heme-binding membrane glycoprotein gp91phox) (Cytochrome b(558) subunit beta) (Cytochrome b558 subunit beta)	2.8	8.8E-09	2.3E-04
RIN2	ENSG0000132669	Ras and Rab interactor 2 (Ras interaction/interference protein 2) (Ras inhibitor JC265) (Ras association domain family 4).	4.6	9.0E-09	2.3E-04
MT1L	ENSG0000169715	Metallothionein-1E (MT-1E) (Metallothionein-IE) (MT-IE).	22.4	9.9E-09	1.2E-04
GNG10	ENSG0000059769	Guanine nucleotide-binding protein G(I)/G(S)/G(O) gamma-10 subunit precursor.	1.9	1.0E-08	2.4E-04
IBRDC1	ENSG0000146373	IBR domain-containing protein 1.	4.8	1.0E-08	3.2E-05
	ENSG0000043822	phosphatidylinositol 4-kinase type II	3.2	1.1E-08	2.7E-04
UBADC1	ENSG0000130560	ubiquitin associated domain containing 1	1.5	1.1E-08	2.8E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
TNFAIP2	ENSG00000185215	Tumor necrosis factor, alpha-induced protein 2 (Primary response gene B94 protein).	5.3	1.2E-08	2.9E-04
DOCK4	ENSG00000128512	Dedicator of cytokinesis protein 4.	5.9	1.2E-08	2.9E-04
	ENSG00000204437		9.0	1.2E-08	1.5E-04
SH3GLB1	ENSG00000097033	SH3 domain GRB2-like protein B1 (EC 2.3.1.-) (Endophilin B1) (Bax- interacting factor 1) (Bif-1).	1.6	1.3E-08	2.8E-04
SLC15A3	ENSG00000110446	solute carrier family 15, member 3	3.6	1.3E-08	9.7E-05
SLC30A1	ENSG00000170385	Zinc transporter 1 (ZnT-1) (Solute carrier family 30 member 1).	10.1	1.3E-08	3.0E-04
TMED7	ENSG00000134970	Transmembrane emp24 domain-containing protein 7 precursor.	3.6	1.4E-08	1.9E-04
DUSP3	ENSG00000108861	Dual specificity protein phosphatase 3 (EC 3.1.3.48) (EC 3.1.3.16) (Dual specificity protein phosphatase VHR).	5.1	1.4E-08	1.2E-04
NCOA4	ENSG00000138293	Nuclear receptor coactivator 4 (NCoA-4) (70 kDa androgen receptor coactivator) (70 kDa AR-activator) (Ret-activating protein ELE1).	1.6	1.4E-08	2.9E-04
PICALM	ENSG00000073921	Phosphatidylinositol-binding clathrin assembly protein (Clathrin assembly lymphoid myeloid leukemia protein).	2.2	1.4E-08	3.2E-04
DYSF	ENSG00000135636	Dysferlin (Dystrophy-associated fer-1-like protein) (Fer-1-like protein 1).	5.0	1.4E-08	3.2E-05
SIRPB1	ENSG00000101307	Signal-regulatory protein beta-1 precursor (SIRP-beta-1) (CD172b antigen).	6.5	1.4E-08	1.3E-04
GLRX	ENSG00000173221	Glutaredoxin-1 (Thioltransferase-1) (TTase-1).	2.2	1.5E-08	2.3E-04
STOM	ENSG00000148175	Erythrocyte band 7 integral membrane protein (Stomatin) (Protein 7.2b).	2.4	1.5E-08	9.7E-05
HEXB	ENSG00000049860	Beta-hexosaminidase beta chain precursor (EC 3.2.1.52) (N-acetyl-beta-glucosaminidase) (Beta-N-acetylhexosaminidase) (Hexosaminidase B) (Cervical cancer proto-oncogene 7) (HCC-7)	2.7	1.5E-08	1.5E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
	ENSG00000122378	Protein C10orf58 precursor.	2.6	1.6E-08	3.6E-04
CHMP5	ENSG0000086065	Charged multivesicular body protein 5 (Chromatin-modifying protein 5) (Vacuolar protein sorting 60) (Vps60) (hVps60) (SNF7 domain-containing protein 2).	2.0	1.6E-08	4.2E-04
	ENSG0000168994	Uncharacterized protein C6orf145.	2.5	1.6E-08	4.1E-04
IFI6	ENSG0000126709	Interferon-induced protein 6-16 precursor (Ifi-6-16) (Interferon alpha-inducible protein 6).	4.7	1.7E-08	3.0E-04
CASP5	ENSG0000137757	Caspase-5 precursor (EC 3.4.22.-) (CASP-5) (ICH-3 protease) (TY protease) (ICE(rel)-III) [Contains: Caspase-5 subunit p20; Caspase-5 subunit p10].	20.0	1.7E-08	3.2E-05
SIRPA	ENSG0000198053	Tyrosine-protein phosphatase non-receptor type substrate 1 precursor (SHP substrate 1) (SHPS-1) (Inhibitory receptor SHPS-1) (Signal- regulatory protein alpha-1) (Sirp-alpha-1) (Sirp-alpha-2) (Sirp-alpha- 3) (MyD-1 antigen)	5.0	1.8E-08	3.6E-04
LGALS3	ENSG0000131981	Galectin-3 (Galactose-specific lectin 3) (Mac-2 antigen) (IgE-binding protein) (35 kDa lectin) (Carbohydrate-binding protein 35) (CBP 35) (Laminin-binding protein) (Lectin L-29) (L-31) (Galactoside-binding protein) (GALBP).	3.0	1.9E-08	9.7E-05
LRP1	ENSG0000123384	Low-density lipoprotein receptor-related protein 1 precursor (LRP) (Alpha-2-macroglobulin receptor) (A2MR) (Apolipoprotein E receptor) (APOER) (CD91 antigen).	6.3	1.9E-08	4.3E-04
C1orf38	ENSG0000130775	Induced by contact to basement membrane 1 protein (Protein ICB-1).	2.7	2.0E-08	9.7E-05
MOV10	ENSG0000155363	Putative helicase MOV-10 (EC 3.6.1.-) (Moloney leukemia virus 10 protein).	1.7	2.0E-08	4.7E-04
CD38	ENSG0000004468	ADP-ribosyl cyclase 1 (EC 3.2.2.5) (Cyclic ADP-ribose hydrolase 1) (cADPr hydrolase 1) (Lymphocyte differentiation antigen CD38) (T10) (Acute lymphoblastic leukemia cells antigen CD38).	5.4	2.0E-08	9.7E-05
CARD12	ENSG0000091106	Caspase recruitment domain-containing protein 12 (Ice protease- activating factor) (Ipaf) (CARD, LRR, and NACHT-containing protein) (Clan protein).	6.0	2.0E-08	2.8E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
TXN	ENSG00000136810	Thioredoxin (ATL-derived factor) (ADF) (Surface-associated sulphhydryl protein) (SASP).	3.2	2.1E-08	2.6E-04
PFKFB4	ENSG00000114268	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4 (6PF-2-K/Fru- 2,6-P2ASE testis-type isozyme) [Includes: 6-phosphofructo-2-kinase (EC 2.7.1.105); Fructose-2,6-biphosphatase (EC 3.1.3.46)].	6.0	2.1E-08	2.2E-05
CD74	ENSG0000019582	HLA class II histocompatibility antigen gamma chain (HLA-DR antigens- associated invariant chain) (Ia antigen-associated invariant chain) (II) (p33) (CD74 antigen).	2.8	2.2E-08	5.2E-04
GBP5	ENSG00000154451	Interferon-induced guanylate-binding protein 5 (GTP-binding protein 5) (Guanine nucleotide-binding protein 5) (GBP-TA antigen).	4.9	2.2E-08	1.2E-04
LGALS3BP	ENSG00000108679	Galectin-3-binding protein precursor (Lectin galactoside-binding soluble 3-binding protein) (Mac-2-binding protein) (Mac-2 BP) (MAC2BP) (Tumor-associated antigen 90K).	3.8	2.3E-08	1.2E-04
PTAFR	ENSG00000169403	Platelet-activating factor receptor (PAF-R).	6.2	2.3E-08	1.2E-04
NAGA	ENSG00000198951	Alpha-N-acetylgalactosaminidase precursor (EC 3.2.1.49) (Alpha- galactosidase B).	2.7	2.4E-08	5.2E-04
GZMH	ENSG00000100450	Granzyme H precursor (EC 3.4.21.-) (Cytotoxic T-lymphocyte proteinase) (Cathepsin G-like 2) (CTSGL2) (CCP-X) (Cytotoxic serine protease C) (CSP-C).	9.1	2.4E-08	6.1E-04
RNF149	ENSG00000163162	ring finger protein 149	1.6	2.4E-08	9.7E-05
DPYD	ENSG00000188641	Dihydropyrimidine dehydrogenase [NADP+] precursor (EC 1.3.1.2) (DPD) (DHPDHase) (Dihydouracil dehydrogenase) (Dihydrothymine dehydrogenase).	2.6	2.5E-08	4.5E-04
DHRS10	ENSG00000087076	Dehydrogenase/reductase SDR family member 10 (EC 1.1.--) (Retinal short-chain dehydrogenase/reductase retSDR3).	2.5	2.5E-08	5.8E-04
TNFSF10	ENSG00000121858	Tumor necrosis factor ligand superfamily member 10 (TNF-related apoptosis-inducing ligand) (TRAIL protein) (Apo-2 ligand) (Apo-2L) (CD253 antigen).	3.6	2.5E-08	3.0E-04
PDZD11	ENSG00000120509	PDZ domain-containing protein 11.	1.6	2.6E-08	3.0E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
GBP1	ENSG00000117228	Interferon-induced guanylate-binding protein 1 (GTP-binding protein 1) (Guanine nucleotide-binding protein 1) (HuGBP-1).	3.0	2.6E-08	6.1E-04
PPGB	ENSG0000064601	Lysosomal protective protein precursor (EC 3.4.16.5) (Cathepsin A) (Carboxypeptidase C) (Protective protein for beta-galactosidase) [Contains: Lysosomal protective protein 32 kDa chain; Lysosomal protective protein 20 kDa chain].	2.2	2.6E-08	4.5E-04
UBC	ENSG00000150991	Ubiquitin.	1.3	2.7E-08	4.5E-04
CD47	ENSG00000196776	Leukocyte surface antigen CD47 precursor (Integrin-associated protein) (IAP) (Antigenic surface determinant protein OA3) (MER6).	1.8	2.7E-08	9.7E-05
FGL2	ENSG00000127951	Fibroleukin precursor (Fibrinogen-like protein 2) (pT49).	6.0	2.7E-08	5.8E-04
RRAGD	ENSG0000025039	Ras-related GTP-binding protein D (Rag D).	3.3	2.7E-08	6.4E-04
NAGLU	ENSG00000108784	Alpha-N-acetylglucosaminidase precursor (EC 3.2.1.50) (N-acetyl-alpha-glucosaminidase) (NAG) [Contains: Alpha-N-acetylglucosaminidase 82 kDa form; Alpha-N-acetylglucosaminidase 77 kDa form].	2.5	2.8E-08	6.6E-04
SART2	ENSG00000111817	Squamous cell carcinoma antigen recognized by T-cells 2 precursor (SART-2).	2.9	2.9E-08	3.6E-04
AOAH	ENSG00000136250	Acyloxyacyl hydrolase precursor (EC 3.1.1.77) [Contains: Acyloxyacyl hydrolase small subunit; Acyloxyacyl hydrolase large subunit].	4.5	2.9E-08	2.1E-04
SLC35F5	ENSG00000115084	solute carrier family 35, member F5	1.8	2.9E-08	6.7E-04
PLEKHQ1	ENSG00000169094	PH domain-containing protein	2.1	3.0E-08	6.7E-04
CSF1R	ENSG00000182578	Macrophage colony-stimulating factor 1 receptor precursor (CSF-1-R) (EC 2.7.10.1) (Fms proto-oncogene) (c-fms) (CD115 antigen).	4.2	3.0E-08	6.4E-04
PLOD1	ENSG0000083444	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1 precursor (EC 1.14.11.4) (Lysyl hydroxylase 1) (LH1).	2.6	3.0E-08	3.1E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
CLEC12A	ENSG00000172322	myeloid inhibitory C-type lectin-like receptor isoform beta	22.7	3.1E-08	1.3E-04
	ENSG0000047621		1.9	3.1E-08	4.0E-04
CD300C	ENSG00000167850	CMRF35-A antigen precursor (CMRF-35) (CD300c antigen).	5.5	3.2E-08	6.3E-04
NPC2	ENSG00000119655	Epididymal secretory protein E1 precursor (Niemann-Pick disease type C2 protein) (hE1).	1.9	3.3E-08	7.4E-04
FZD1	ENSG00000157240	Frizzled-1 precursor (Fz-1) (hFz1) (FzE1).	5.0	3.3E-08	4.7E-04
ATP6V1B2	ENSG00000147416	Vacuolar ATP synthase subunit B, brain isoform (EC 3.6.3.14) (V-ATPase B2 subunit) (Vacuolar proton pump B isoform 2) (Endomembrane proton pump 58 kDa subunit) (HO57).	2.9	3.6E-08	2.5E-04
CD274	ENSG00000120217	Programmed cell death 1 ligand 1 precursor (Programmed death ligand 1) (PD-L1) (PDCD1 ligand 1) (B7 homolog 1) (B7-H1) (CD274 antigen).	6.6	3.7E-08	5.2E-04
FCGR1A	ENSG00000150337	High affinity immunoglobulin gamma Fc receptor I precursor (Fc-gamma RI) (FcRI) (IgG Fc receptor I) (CD64 antigen).	35.3	3.8E-08	9.7E-05
STARD3NL	ENSG0000010270	MLN64 N-terminal domain homolog (STARD3 N-terminal-like protein).	1.8	3.8E-08	4.7E-04
C10orf119	ENSG00000197771		1.5	3.8E-08	8.0E-04
C15orf24	ENSG00000134153	Uncharacterized protein C15orf24 precursor.	1.6	3.8E-08	7.4E-04
SDHB	ENSG00000117118	Succinate dehydrogenase [ubiquinone] iron-sulfur protein, mitochondrial precursor (EC 1.3.5.1) (Ip) (Iron-sulfur subunit of complex II).	2.1	3.8E-08	2.5E-04
P2RY6	ENSG00000171631	P2Y purinoceptor 6 (P2Y6).	6.6	3.9E-08	5.4E-05
IDO	ENSG00000131203	Indoleamine 2,3-dioxygenase (EC 1.13.11.42) (IDO) (Indoleamine-pyrrole 2,3-dioxygenase).	9.0	3.9E-08	1.6E-04
RAB7	ENSG0000075785	Ras-related protein Rab-7.	1.7	4.0E-08	6.8E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
SAMSN1	ENSG00000155307	SAM domain-containing protein SAMSN-1 (SAM domain, SH3 domain and nuclear localisation signals protein 1) (SH3-SAM adaptor protein) (Hematopoietic adaptor containing SH3 and SAM domains 1).	3.0	4.0E-08	2.8E-04
AP2S1	ENSG0000042753	AP-2 complex subunit sigma-1 (Adapter-related protein complex 2 sigma- 1 subunit) (Clathrin coat assembly protein AP17) (Clathrin coat- associated protein AP17) (Plasma membrane adaptor AP-2 17 kDa protein) (HA2 17 kDa subunit)	1.6	4.2E-08	1.1E-04
BATF2	ENSG00000168062	basic leucine zipper transcription factor, ATF-like 2	7.0	4.3E-08	5.7E-04
FUT4	ENSG00000196371	Alpha-(1,3)-fucosyltransferase (EC 2.4.1.-) (Galactoside 3-L- fucosyltransferase) (Fucosyltransferase 4) (FUCT-IV) (Fuc-TIV) (ELAM-1 ligand fucosyltransferase).	2.2	4.3E-08	4.3E-04
	ENSG00000157107	FCH domain only 2	3.9	4.5E-08	4.0E-04
CENPA	ENSG00000115163	Centromere protein A (CENP-A) (Centromere autoantigen A).	2.3	4.6E-08	9.7E-05
KMO	ENSG00000117009	Kynurenine 3-monoxygenase (EC 1.14.13.9) (Kynurenine 3-hydroxylase).	3.9	4.6E-08	8.0E-04
PIGT	ENSG00000124155	GPI transamidase component PIG-T precursor (Phosphatidylinositol- glycan biosynthesis, class T protein).	1.4	4.7E-08	4.5E-04
LGALS8	ENSG00000116977	Galectin-8 (Gal-8) (Prostate carcinoma tumor antigen 1) (PCTA-1) (Po66 carbohydrate-binding protein) (Po66-CBP).	1.9	5.1E-08	6.8E-04
CENTA2	ENSG00000184060	Centaurin-alpha 2.	5.6	5.2E-08	8.0E-04
	ENSG00000180263	FYVE, RhoGEF and PH domain-containing protein 6 (Zinc finger FYVE domain-containing protein 24).	3.6	5.3E-08	9.2E-04
PLXNC1	ENSG00000136040	Plexin-C1 precursor (Virus-encoded semaphorin protein receptor).	2.5	5.3E-08	9.2E-04
HSBP1	ENSG00000166530	Heat shock factor binding protein 1 (Nasopharyngeal carcinoma- associated antigen 13) (NPC-A-13).	1.7	5.3E-08	4.5E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
GRN	ENSG0000030582	Granulins precursor (Proepithelin) (PEPI) [Contains: Acrogranin; Paragranulin; Granulin-1 (Granulin G); Granulin-2 (Granulin F); Granulin-3 (Granulin B); Granulin-4 (Granulin A); Granulin-5 (Granulin C); Granulin-6 (Granulin D); Granulin-7 (Granulin E)].	3.1	5.4E-08	5.2E-04
SH3BP2	ENSG0000087266	SH3 domain-binding protein 2 (3BP-2).	2.2	5.4E-08	9.7E-04
FAM105A	ENSG0000145569		3.4	5.5E-08	7.4E-04
TMSB10	ENSG0000034510	Thymosin beta-10.	1.3	5.6E-08	9.2E-04
MKNK1	ENSG0000079277	MAP kinase-interacting serine/threonine-protein kinase 1 (EC 2.7.11.1) (MAP kinase signal-integrating kinase 1) (Mnk1).	1.9	5.6E-08	8.7E-04
DERA	ENSG0000023697	Putative deoxyribose-phosphate aldolase (EC 4.1.2.4) (Phosphodeoxyriboaldolase) (Deoxyriboaldolase) (DERA).	1.4	5.9E-08	8.6E-04
ARHGAP18	ENSG0000146376	Rho GTPase activating protein 18	2.0	6.0E-08	2.7E-04
CTSD	ENSG0000117984	Cathepsin D precursor (EC 3.4.23.5) [Contains: Cathepsin D light chain; Cathepsin D heavy chain].	3.4	6.4E-08	1.0E-03
ABHD5	ENSG0000011198	Abhydrolase domain-containing protein 5.	2.3	6.5E-08	9.5E-04
RAB31	ENSG0000168461	Ras-related protein Rab-31 (Rab-22B).	3.1	6.6E-08	1.0E-03
TMEM144	ENSG0000164124		5.8	6.8E-08	3.2E-05
DBNDD2	ENSG0000204070	Dysbindin domain-containing protein 2 (HSMNP1).	2.6	6.8E-08	5.7E-04
TBXAS1	ENSG0000059377	Thromboxane-A synthase (EC 5.3.99.5) (TXA synthase) (TXS) (Cytochrome P450 5A1).	4.5	6.8E-08	1.6E-04
	ENSG0000119321	Peptidyl-prolyl cis-trans isomerase (EC 5.2.1.8) (Fragment).	2.6	6.8E-08	9.7E-05
OSTM1	ENSG0000081087	Osteopetrosis-associated transmembrane protein 1 precursor.	2.2	6.9E-08	9.7E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
TSHZ3	ENSG00000121297	Teashirt homolog 3 (Zinc finger protein 537).	9.1	7.0E-08	2.5E-04
PDCD1LG2	ENSG00000197646	Programmed cell death 1 ligand 2 precursor (Programmed death ligand 2) (PD-L2) (PD-1-ligand 2) (PDCD1 ligand 2) (Butyrophilin B7-DC) (B7-DC) (CD273 antigen).	11.8	7.1E-08	1.2E-04
SFXN3	ENSG00000107819	Sideroflexin-3.	2.4	7.1E-08	3.8E-04
TK2	ENSG00000166548	Thymidine kinase 2, mitochondrial precursor (EC 2.7.1.21) (Mt-TK).	1.8	7.4E-08	2.3E-04
CCRL2	ENSG00000121797	C-C chemokine receptor-like 2 (Putative MCP-1 chemokine receptor) (Chemokine receptor CCR11) (Chemokine receptor X).	11.9	7.4E-08	7.4E-04
LOXL3	ENSG00000115318	Lysyl oxidase homolog 3 precursor (EC 1.4.3.-) (Lysyl oxidase-like protein 3).	2.2	7.6E-08	8.9E-04
RHOU	ENSG00000116574	ras homolog gene family, member U	7.2	7.6E-08	3.0E-04
PLAUR	ENSG0000011422	Urokinase plasminogen activator surface receptor precursor (uPAR) (U- PAR) (Monocyte activation antigen Mo3) (CD87 antigen).	10.0	7.8E-08	2.6E-04
	ENSG00000122694	Golgi-associated plant pathogenesis-related protein 1 (Golgi- associated PR-1 protein) (GAPR-1) (Glioma pathogenesis-related protein 2) (GliPR 2).	2.4	7.9E-08	6.8E-04
SEPX1	ENSG00000198736	Methionine-R-sulfoxide reductase (EC 1.8.4.-) (Selenoprotein X 1).	2.3	9.0E-08	3.6E-04
ACSL1	ENSG00000151726	Long-chain-fatty-acid--CoA ligase 1 (EC 6.2.1.3) (Long-chain acyl-CoA synthetase 1) (LACS 1) (Palmitoyl-CoA ligase 1) (Long-chain fatty acid CoA ligase 2) (Long-chain acyl-CoA synthetase 2) (LACS 2) (Acyl-CoA synthetase 1) (ACS1) (Palmitoyl-CoA ligase 2).	7.5	9.2E-08	9.7E-05
KCNMA1	ENSG00000156113	Calcium-activated potassium channel subunit alpha 1 (Calcium-activated potassium channel, subfamily M subunit alpha 1) (Maxi K channel) (MaxiK) (BK channel) (K(VCA)alpha) (BKCA alpha) (KCa1.1) (Slowpoke homolog) (Slo homolog) (Slo-alpha) (Slo1) (hSlo).	3.6	9.6E-08	1.5E-04
GCH1	ENSG00000131979	GTP cyclohydrolase I (EC 3.5.4.16) (GTP-CH-I).	4.8	9.7E-08	8.7E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
	ENSG0000023318	Thioredoxin domain-containing protein 4 precursor (Endoplasmic reticulum resident protein ERp44).	1.6	9.8E-08	9.2E-04
ATP6AP2	ENSG0000182220	Renin receptor precursor (Renin/prorenin receptor) (ATPase, H ⁺ - transporting, lysosomal accessory protein 2) (ATPase, H ⁺ -transporting, lysosomal-interacting protein 2) (Vacuolar ATP synthase membrane sector-associated protein M8-9) (V-ATPase M8.9 subunit)	1.4	1.0E-07	7.8E-04
HAVCR2	ENSG0000135077	Hepatitis A virus cellular receptor 2 precursor (HAVcr-2) (T cell immunoglobulin and mucin domain-containing protein 3) (TIMD-3) (T cell membrane protein 3) (TIM-3).	3.9	1.0E-07	9.7E-05
SFN	ENSG0000175793	14-3-3 protein sigma (Stratifin) (Epithelial cell marker protein 1).	2.2	1.1E-07	9.2E-04
MNDA	ENSG0000163563	Myeloid cell nuclear differentiation antigen.	3.8	1.1E-07	3.1E-04
CTBS	ENSG0000117151	Di-N-acetylchitobiase precursor (EC 3.2.1.-).	1.5	1.1E-07	8.0E-04
SLC39A8	ENSG0000138821	solute carrier family 39 (zinc transporter), member 8	23.3	1.1E-07	9.7E-05
PLEKHB2	ENSG0000115762	Pleckstrin homology domain-containing family B member 2 (Evectin-2).	1.8	1.2E-07	6.8E-04
YIPF1	ENSG0000058799	Protein YIPF1 (YIP1 family member 1).	1.6	1.3E-07	9.2E-04
ATP6V0B	ENSG0000117410	Vacuolar ATP synthase 21 kDa proteolipid subunit (EC 3.6.3.14) (HATPL).	2.1	1.3E-07	2.5E-04
ME1	ENSG0000065833	NADP-dependent malic enzyme (EC 1.1.1.40) (NADP-ME) (Malic enzyme 1).	11.7	1.3E-07	9.7E-04
	ENSG0000138600	Signal peptide peptidase-like 2A (EC 3.4.23.-) (Protein SPP-like 2A) (Protein SPPL2a) (Intramembrane protease 3) (IMP3) (Presenilin-like protein 2).	2.6	1.4E-07	9.7E-05
PDE4DIP	ENSG0000178104	phosphodiesterase 4D interacting protein isoform 3	32.0	1.4E-07	3.2E-05
SLC43A3	ENSG0000134802	solute carrier family 43, member 3	2.7	1.4E-07	2.8E-04
	ENSG0000153113	Calpastatin (Calpain inhibitor) (Sperm BS-17 component).	1.6	1.4E-07	1.2E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
CTSL	ENSG00000135047	Cathepsin L precursor (EC 3.4.22.15) (Major excreted protein) (MEP) [Contains: Cathepsin L heavy chain; Cathepsin L light chain].	5.1	1.4E-07	9.2E-04
IBRDC3	ENSG00000116514	IBR domain-containing protein 3.	3.4	1.5E-07	9.6E-04
GRIN3A	ENSG00000198785	Glutamate [NMDA] receptor subunit 3A precursor (N-methyl-D-aspartate receptor subtype NR3A) (NMDAR-L).	13.9	1.6E-07	9.7E-05
ATP6V0C	ENSG00000185883	Vacuolar ATP synthase 16 kDa proteolipid subunit (EC 3.6.3.14).	2.2	1.6E-07	9.7E-05
SPFH1	ENSG00000107566	SPFH domain-containing protein 1 precursor (Protein KE04).	2.1	1.6E-07	9.7E-05
NCF2	ENSG00000116701	Neutrophil cytosol factor 2 (NCF-2) (Neutrophil NADPH oxidase factor 2) (67 kDa neutrophil oxidase factor) (p67-phox) (NOXA2).	11.4	1.7E-07	1.4E-04
EMILIN2	ENSG00000132205	EMILIN-2 precursor (Elastin microfibril interface-located protein 2) (Elastin microfibril interfacser 2) (Protein FOAP-10).	6.7	1.7E-07	8.0E-04
RASSF4	ENSG00000107551	Ras association domain-containing protein 4.	3.7	1.8E-07	9.1E-04
ATP6V0A1	ENSG00000033627	Vacuolar proton translocating ATPase 116 kDa subunit a isoform 1 (V- ATPase 116-kDa isoform a1) (Clathrin-coated vesicle/synaptic vesicle proton pump 116 kDa subunit) (Vacuolar proton pump subunit 1) (Vacuolar adenosine triphosphatase subunit Ac116).	7.1	1.8E-07	6.8E-04
	ENSG00000178420		6.7	1.8E-07	5.8E-04
RAP2B	ENSG00000181467	Ras-related protein Rap-2b precursor.	2.7	1.9E-07	5.8E-04
PLOD3	ENSG00000106397	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 3 precursor (EC 1.14.11.4) (Lysyl hydroxylase 3) (LH3).	2.3	1.9E-07	7.6E-04
	ENSG00000105518		1.8	2.0E-07	8.6E-04
ACBD5	ENSG00000107897	acyl-Coenzyme A binding domain containing 5	1.7	2.2E-07	9.1E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
MCTP1	ENSG00000175471	multiple C2-domains with two transmembrane regions 1 isoform L	6.9	2.3E-07	1.4E-04
PDXK	ENSG00000160209		3.2	2.4E-07	3.1E-04
TMEM86A	ENSG00000151117	Transmembrane protein 86A.	5.7	2.4E-07	9.2E-04
RALB	ENSG00000144118	Ras-related protein Ral-B.	2.4	2.4E-07	9.7E-05
APOBEC3A	ENSG00000128383	Probable DNA dC->dU-editing enzyme APOBEC-3A (EC 3.5.4.-) (Phorbolin- 1).	27.0	2.6E-07	9.7E-05
CBARA1	ENSG00000107745	calcium binding atopy-related autoantigen 1	1.9	2.7E-07	4.3E-04
SPG21	ENSG00000090487	Maspardin (Spastic paraplegia 21 autosomal recessive Mast syndrome protein) (Acid cluster protein 33).	1.6	2.7E-07	9.7E-05
ATP6V0E	ENSG00000113732	Vacuolar ATP synthase subunit H (EC 3.6.3.14) (V-ATPase H subunit) (Vacuolar proton pump H subunit) (V-ATPase M9.2 subunit) (V-ATPase 9.2 kDa membrane accessory protein).	1.4	2.8E-07	9.2E-04
MSR1	ENSG00000038945	Macrophage scavenger receptor types I and II (Macrophage acetylated LDL receptor I and II) (Scavenger receptor class A member 1) (CD204 antigen).	38.3	2.9E-07	5.4E-05
C17orf58	ENSG00000186665		1.9	3.2E-07	7.1E-04
	ENSG00000162840	metallothionein 1H-like protein	16.2	3.3E-07	9.7E-05
MT1G	ENSG00000125144	Metallothionein-1G (MT-1G) (Metallothionein-IG) (MT-IG) (Metallothionein-1K) (MT-1K).	43.4	3.6E-07	9.7E-05
SQRDL	ENSG00000137767	Sulfide:quinone oxidoreductase, mitochondrial precursor (EC 1.---).	2.6	3.7E-07	8.7E-04
TP53INP2	ENSG00000078804	Tumor protein p53-inducible nuclear protein 2 (p53-inducible protein U) (PIG-U).	2.1	3.7E-07	8.0E-04
UBE2D4	ENSG00000078967	ubiquitin-conjugating enzyme E2D 4 (putative)	1.9	3.8E-07	8.2E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
NFE2L2	ENSG00000116044	Nuclear factor erythroid 2-related factor 2 (NF-E2-related factor 2) (NFE2-related factor 2) (Nuclear factor, erythroid derived 2, like 2) (HEBP1).	1.8	3.9E-07	8.3E-04
M6PRBP1	ENSG00000105355	Mannose-6-phosphate receptor-binding protein 1 (Cargo selection protein TIP47) (47 kDa mannose 6-phosphate receptor-binding protein) (47 kDa MPR-binding protein) (Placental protein 17) (PP17).	1.9	4.0E-07	9.1E-04
LIMK2	ENSG00000182541	LIM domain kinase 2 (EC 2.7.11.1) (LIMK-2).	4.3	4.0E-07	9.7E-05
	ENSG00000196814		2.7	4.3E-07	9.7E-05
SLAMF8	ENSG00000158714	SLAM family member 8 precursor (B-lymphocyte activator macrophage expressed) (BCM-like membrane protein).	6.2	4.8E-07	6.5E-04
ERO1L	ENSG00000197930	ERO1-like protein alpha precursor (EC 1.8.4.-) (ERO1-Lalpha) (Oxidoreductin-1-Lalpha) (Endoplasmic oxidoreductin-1-like protein) (ERO1-L).	2.4	4.8E-07	5.8E-04
GPR84	ENSG00000139572	Probable G-protein coupled receptor 84 (Inflammation-related G-protein coupled receptor EX33).	41.8	5.0E-07	9.7E-05
MT1M	ENSG00000205364	Metallothionein-1M (MT-1M) (Metallothionein-IM) (MT-IM).	247.2	5.1E-07	3.2E-05
NBN	ENSG00000104320	Nibrin (Nijmegen breakage syndrome protein 1) (Cell cycle regulatory protein p95).	1.7	5.6E-07	7.4E-04
DECR1	ENSG00000104325	2,4-dienoyl-CoA reductase, mitochondrial precursor (EC 1.3.1.34) (2,4- dienoyl-CoA reductase [NADPH]) (4-enoyl-CoA reductase [NADPH]).	1.4	5.8E-07	9.7E-04
PGD	ENSG00000142657	6-phosphogluconate dehydrogenase, decarboxylating (EC 1.1.1.44).	3.7	5.9E-07	1.7E-04
RNF135	ENSG00000181481	ring finger protein 135 isoform 2	1.9	6.2E-07	8.7E-04
	ENSG0000008382		2.7	6.9E-07	2.9E-04
VAT1	ENSG00000108828	Synaptic vesicle membrane protein VAT-1 homolog (EC 1.---).	2.9	7.2E-07	3.6E-04

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
SORT1	ENSG00000134243	Sortilin precursor (Neurotensin receptor 3) (NTR3) (NT3) (Glycoprotein 95) (Gp95) (100 kDa NT receptor).	7.5	7.5E-07	6.4E-04
TMEM51	ENSG00000171729	Transmembrane protein 51.	3.2	8.1E-07	1.5E-04
REEP4	ENSG00000168476	Receptor expression-enhancing protein 4.	2.6	8.2E-07	6.4E-04
BLVRB	ENSG00000090013	Flavin reductase (EC 1.5.1.30) (FR) (NADPH-dependent diaphorase) (NADPH-flavin reductase) (FLR) (Biliverdin reductase B) (EC 1.3.1.24) (BVR-B) (Biliverdin-IX beta-reductase) (Green heme-binding protein) (GHBP).	5.1	8.5E-07	6.4E-04
IFI35	ENSG00000068079	Interferon-induced 35 kDa protein (IFP 35).	2.4	1.1E-06	8.0E-04
MT1X	ENSG00000187193	Metallothionein-1X (MT-1X) (Metallothionein-IX) (MT-IX).	20.6	1.1E-06	1.6E-04
MT1F	ENSG00000198417	Metallothionein-1F (MT-1F) (Metallothionein-IF) (MT-IF).	17.9	1.5E-06	1.7E-04
PLEKHG3	ENSG00000126822	pleckstrin homology domain containing, family G, member 3	4.6	2.2E-06	8.0E-04
RAB39	ENSG00000179331	Ras-related protein Rab-39A (Rab-39).	3.5	2.3E-06	1.3E-04
	ENSG00000109756	Rap guanine nucleotide exchange factor 2 (Neural RAP guanine nucleotide exchange protein) (nRap GEP) (PDZ domain-containing guanine nucleotide exchange factor 1) (PDZ-GEF1) (RA-GEF).	2.8	3.6E-06	9.1E-04
METTL7B	ENSG00000170439		27.0	5.8E-06	5.8E-04

Supplementary Table 2. Results of real-time quantitative RT-PCR validation of the microarray gene expression data.

We performed real-time quantitative RT-PCR on 10 genes to validate the microarray gene expression data. Fold differences in gene expression for THRLBCL compared to NLPHL are shown, as measured by (i) microarray and (ii) quantitative RT-PCR, for 10 genes, selected for their involvement in interferon pathways, macrophage activation and innate immune responses. Expression values are averages of 10 NLPHL and 10 THRLBCL samples. The same cases were used for microarray and quantitative RT-PCR expression profiling. With the exception of the gene CD74 (differentially expressed according to the microarray data but showing no significant expression difference by real-time quantitative RT-PCR), the obtained expression fold differences for these genes correspond well to the microarray data.

Gene symbol	Description	Fold difference microarray	Fold difference quantitative RT-PCR (p-value ¹)
IFN- γ	Interferon gamma	4.7 ²	4.4 (p = 1.0 x 10 ⁻⁵)
STAT-1	Signal transducer and activator of transcription 1	1.6	2.9 (p = 4.4 x 10 ⁻⁹)
CD74	HLA class II histocompatibility antigen gamma chain	2.8	1.2 (p = 0.21)
CCL8 (MCP-2)	Monocyte chemotactic protein 2	143.5	84.8 (p = 3.9 x 10 ⁻⁹)
IDO	Indoleamine 2,3-dioxygenase	9.0	12.3 (p = 1.6 x 10 ⁻⁸)
IFN- α 1	Interferon alpha 1	1.0 ²	0.92 (p = 0.81)
IFN- α R2	Interferon alpha receptor 2	0.9 ²	1.3 (p = 5.3 x 10 ⁻³)
STAT-2	Signal transducer and activator of transcription 2	1.8 ²	1.3 (p = 0.11)
TLR8	Toll-like receptor 8	11.5	11.5 (p = 6.4 x 10 ⁻¹¹)
MyD88	Myeloid differentiation factor 88	1.8 ²	2.2 (p = 6.7 x 10 ⁻⁷)

¹ T-test, not corrected for multiple testing.

² Difference was not significant at p < 0.001 (after correction for multiple testing).

Supplementary Table 3. Results of quantitative RT-PCR measurements of additional THRLBCL and NLPHL samples based on core elements of the gene expression signatures.

Expression values of the three selected genes against each of the two calibrator samples are given, as measured by quantitative RT-PCR.

A. Lymphoma samples from the University Hospitals K.U.Leuven

diagnosis by morphology	FCER1G		VSIG4		FCRL1	
	NLPHL	THRLBCL	NLPHL	THRLBCL	NLPHL	THRLBCL
control NLPHL	1.00	0.093	1.00	0.0016	1.00	357
control THRLBCL	11	1.00	607	1.00	0.0028	1.00
NLPHL	1.63	0.099	0.0072	1.7E-05	4.15	6317
NLPHL	5.31	0.52	4.00	0.0071	0.33	22
NLPHL	1.52	0.17	13	0.027	1.75	10922
NLPHL	1.82	0.14	2.64	0.0048	2.49	129
NLPHL	1.61	0.14	11	0.018	6.57	699
NLPHL	0.92	0.073	0.010	0.00077	1.45	69
NLPHL	1.27	0.046	0.012	0.00050	2.27	1624
NLPHL	2.24	0.28	2.07	0.0036	2.65	21346
NLPHL	1.17	0.095	0.010	1.9E-05	5.27	17682
NLPHL	1.19	0.15	0.32	0.00071	2.25	7074
NLPHL	1.85	0.18	4.11	0.0063	0.47	30
NLPHL	0.93	0.034	0.0081	0.00015	1.35	2095
NLPHL	0.80	0.063	2.74	0.0040	2.65	105
NLPHL	1.43	0.14	1.37	0.0025	1.22	3857
NLPHL	1.47	0.14	0.013	2.7E-05	1.79	2086
NLPHL	4.13	0.18	2.52	0.0054	1.39	3140
NLPHL	1.13	0.10	1.28	0.0024	0.82	77
NLPHL	2.20	0.21	0.42	0.00096	0.41	51
NLPHL	2.65	0.25	0.50	0.00095	3.43	239
NLPHL	1.64	0.12	0.015	4.0E-05	16	978
NLPHL	3.05	0.25	1.11	0.0021	0.94	1100
NLPHL	0.80	0.073	1.55	0.0028	10	364
NLPHL	2.77	0.22	1.85	0.0038	6.04	207
NLPHL	3.10	0.28	10	0.016	1.37	108
NLPHL	0.56	0.043	0.010	1.6E-05	1.96	160

A tumor tolerogenic microenvironment in THRLBCL

diagnosis by morphology	FCER1G		VSIG4		FCRL1	
	NLPHL	THRLBCL	NLPHL	THRLBCL	NLPHL	THRLBCL
NLPHL	2.26	0.20	2.90	0.0050	2.17	324
NLPHL	2.39	0.25	7.86	0.016	2.25	139
NLPHL	2.38	0.23	62	0.069	1.09	133
NLPHL	0.63	0.061	0.33	0.00078	0.27	600
NLPHL	1.60	0.15	0.015	0.00075	4.26	212
NLPHL	1.65	0.14	0.013	2.0E-05	0.86	77
NLPHL	5.33	0.014	7.93	0.046	1.29	2571
NLPHL	2.81	0.24	3.58	0.0054	2.21	117
NLPHL	1.06	0.096	0.73	0.0012	1.40	61
NLPHL	1.92	0.28	1.39	0.0013	0.28	496
NLPHL	1.66	0.15	2.88	0.0047	1.59	5107
NLPHL	0.93	0.084	2.18	0.0035	0.69	70
THRLBCL	7.56	0.70	19	0.030	0.00035	0.020
THRLBCL	10	0.88	436	0.64	0.19	14
THRLBCL	21	1.77	1208	1.38	0.23	7.96
THRLBCL	6.66	0.60	278	0.45	0.11	2.86
THRLBCL	25	2.46	267	0.38	0.58	16
THRLBCL	8.11	0.73	373	0.58	0.052	5.21
THRLBCL	36	2.81	3595	3.85	0.00045	0.030
THRLBCL	12	1.12	514	0.75	0.12	407
THRLBCL	16	1.20	317	0.31	0.69	28
THRLBCL	6.39	0.53	526	0.90	0.028	83
THRLBCL	13	0.99	44	0.045	0.033	1.48
THRLBCL	17	1.55	1356	2.25	0.083	7.61
THRLBCL	12	0.92	713	0.80	0.00088	1.93
THRLBCL	8.48	1.04	698	0.74	0.0018	3.71
THRLBCL	5.62	0.56	152	0.26	0.13	13
THRLBCL	24	2.03	1457	1.98	0.023	0.011
THRLBCL	25	2.20	3692	5.63	0.034	3.26
THRLBCL	5.92	0.50	21	0.034	0.16	7.11

B. Lymphoma samples from the Rikshospitalet-Radiumhospitalet HF Oslo

diagnosis by morphology	FCER1G		VSIG4		FCRL1	
	NLPHL	THRLBCL	NLPHL	THRLBCL	NLPHL	THRLBCL
control NLPHL	1.00	0.23	1.00	0.19	1.00	36
control THRLBCL	4.29	1.00	5.25	1.00	0.028	1.00
NLPHL	13	2.97	0.27	0.052	0.24	8.41
NLPHL	0.66	0.15	0.098	0.019	0.041	1.45
NLPHL	2.89	0.67	0.81	0.15	1.54	55
NLPHL	5.55	1.30	0.29	0.054	0.27	9.62
NLPHL	8.61	2.01	0.26	0.050	0.24	8.36
NLPHL	2.89	0.67	0.65	0.12	1.86	66
NLPHL	11	2.50	1.82	0.35	2.58	92
NLPHL	1.44	0.34	0.11	0.021	0.18	6.37
NLPHL	5.10	1.19	0.40	0.077	0.62	22
THRLBCL	85	20	4.99	0.95	7.55	268
THRLBCL	77	18	256	49	0.0031	0.11
THRLBCL	7.05	1.64	1.37	0.26	0.0052	0.18
THRLBCL	27	6.40	149	28	0.0053	0.19
THRLBCL	149	35	198	38	0.014	0.48

Supplementary Table 4. Overlap of the NLPHL and THRLBCL gene expression signatures with signatures obtained in other studies.**A. Overlap of the NLPHL gene expression signature with the Monti et al. (1) B cell receptor/proliferation signature.**

HGNC ID	Ensembl gene ID	description	fold difference	p-value	corrected p-value
CD22	ENSG00000012124	B-cell receptor CD22 precursor (Leu-14) (B-lymphocyte cell adhesion molecule) (BL-CAM) (Siglec-2).	15.0	2.4E-09	3.2E-05
CD37	ENSG00000104894	Leukocyte antigen CD37 (Tetraspanin-26) (Tspan-26).	3.2	1.0E-09	5.4E-05
CD79A	ENSG00000105369	B-cell antigen receptor complex-associated protein alpha-chain precursor (Ig-alpha) (MB-1 membrane glycoprotein) (Surface IgM- associated protein) (Membrane-bound immunoglobulin-associated protein) (CD79a antigen).	12.4	2.2E-09	3.2E-05
BCL11A	ENSG00000119866	B-cell lymphoma/leukemia 11A (B-cell CLL/lymphoma 11A) (COUP-TF-interacting protein 1) (Ecotropic viral integration site 9 protein) (EVI-9).	12.0	1.1E-11	1.1E-05
FOXO1A	ENSG00000150907	Forkhead box protein O1A (Forkhead in rhabdomyosarcoma).	2.5	4.3E-08	1.4E-04
CD19	ENSG00000177455	B-lymphocyte antigen CD19 precursor (B-lymphocyte surface antigen B4) (Leu-12) (Differentiation antigen CD19).	18.1	4.1E-08	9.7E-05
PAX5	ENSG00000196092	Paired box protein Pax-5 (B-cell-specific transcription factor) (BSAP).	8.3	4.9E-12	2.2E-05

B. Overlap of the NLPHL gene expression signature with the Brune *et al.* (2) signature comparing microdissected NLPHL tumor cells to microdissected THRLBCL tumor cells.

HGNC ID	Ensembl gene ID	description	fold difference	p-value	corrected p-value
EEF2	ENSG00000167658	Elongation factor 2 (EF-2).	1.7	4.9E-09	9.7E-05
RPL15	ENSG00000174748	60S ribosomal protein L15.	1.7	1.8E-06	7.8E-04
EPB41	ENSG00000159023	Protein 4.1 (Band 4.1) (P4.1) (EPB4.1) (4.1R).	2.4	3.1E-07	4.7E-04

C. Overlap of the THRLBCL gene expression signature with Dave et al. (3), unfavorable immune response in follicular lymphoma.

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
ME1	ENSG00000065833	NADP-dependent malic enzyme (EC 1.1.1.40) (NADP-ME) (Malic enzyme 1).	11.7	1.3E-07	9.7E-04
DUSP3	ENSG00000108861	Dual specificity protein phosphatase 3 (EC 3.1.3.48) (EC 3.1.3.16) (Dual specificity protein phosphatase VHR).	5.1	1.4E-08	1.2E-04
SCARB2	ENSG00000138760	Lysosome membrane protein 2 (Lysosome membrane protein II) (LIMP II) (Scavenger receptor class B member 2) (85 kDa lysosomal membrane sialoglycoprotein) (LGP85) (CD36 antigen-like 2).	4.4	1.9E-11	2.2E-05
FCGR1A	ENSG00000150337	High affinity immunoglobulin gamma Fc receptor I precursor (Fc-gamma RI) (FcRI) (IgG Fc receptor I) (CD64 antigen).	35.3	3.8E-08	9.7E-05
	ENSG00000168994	Uncharacterized protein C6orf145.	2.5	1.6E-08	4.1E-04
C3AR1	ENSG00000171860	C3a anaphylatoxin chemotactic receptor (C3a-R) (C3AR).	11.0	1.3E-11	2.2E-05
C1QB	ENSG00000173369	Complement C1q subcomponent subunit B precursor.	10.6	2.0E-09	2.2E-05
C1QA	ENSG00000173372	Complement C1q subcomponent subunit A precursor.	8.3	3.6E-09	2.2E-05
MITF	ENSG00000187098	Microphthalmia-associated transcription factor.	4.3	6.4E-09	1.6E-04

D. Overlap of the THRLBCL gene expression signature with the Monti *et al.* (1) host inflammatory response in diffuse large B cell lymphoma signature.

HGNC ID	Ensembl gene ID	description	fold difference	p-value	corrected p-value
GRN	ENSG00000030582	Granulins precursor (Proepithelin) (PEPI) [Contains: Acrogranin; Paragranulin; Granulin-1 (Granulin G); Granulin-2 (Granulin F); Granulin-3 (Granulin B); Granulin-4 (Granulin A); Granulin-5 (Granulin C); Granulin-6 (Granulin D); Granulin-7 (Granulin E)].	3.1	5.4E-08	5.2E-04
STAT1	ENSG00000115415	Signal transducer and activator of transcription 1-alpha/beta (Transcription factor ISGF-3 components p91/p84).	1.6	1.6E-10	3.2E-05
GBP1	ENSG00000117228	Interferon-induced guanylate-binding protein 1 (GTP-binding protein 1) (Guanine nucleotide-binding protein 1) (HuGBP-1).	3.0	2.6E-08	6.1E-04
CTSD	ENSG00000117984	Cathepsin D precursor (EC 3.4.23.5) [Contains: Cathepsin D light chain; Cathepsin D heavy chain].	3.4	6.4E-08	1.0E-03
TNFSF10	ENSG00000121858	Tumor necrosis factor ligand superfamily member 10 (TNF-related apoptosis-inducing ligand) (TRAIL protein) (Apo-2 ligand) (Apo-2L) (CD253 antigen).	3.6	2.5E-08	3.0E-04
	ENSG00000134470	Interleukin-15 receptor alpha chain precursor (IL-15R-alpha) (IL- 15RA).	4.5	3.1E-09	6.5E-05
SERPING1	ENSG00000149131	Plasma protease C1 inhibitor precursor (C1 Inh) (C1Inh).	5.7	2.2E-09	6.5E-05
SLAMF8	ENSG00000158714	SLAM family member 8 precursor (B-lymphocyte activator macrophage expressed) (BCM-like membrane protein).	6.2	4.8E-07	6.5E-04
CTSB	ENSG00000164733	Cathepsin B precursor (EC 3.4.22.1) (Cathepsin B1) (APP secretase) (APPS) [Contains: Cathepsin B light chain; Cathepsin B heavy chain].	6.1	8.6E-10	2.2E-05

A tumor tolerogenic microenvironment in THRLBCL

HGNC ID	Ensembl gene ID	description	fold difference	p-value	corrected p-value
CD14	ENSG00000170458	Monocyte differentiation antigen CD14 precursor (Myeloid cell-specific leucine-rich glycoprotein) [Contains: Monocyte differentiation antigen CD14, urinary form; Monocyte differentiation antigen CD14, membrane-bound form].	9.2	4.0E-10	2.2E-05
C1QB	ENSG00000173369	Complement C1q subcomponent subunit B precursor.	10.6	2.0E-09	2.2E-05
CD163	ENSG00000177575	Scavenger receptor cysteine-rich type 1 protein M130 precursor (CD163 antigen) (Hemoglobin scavenger receptor) [Contains: Soluble CD163 (sCD163)].	50.5	3.1E-09	2.2E-05
CSF1R	ENSG00000182578	Macrophage colony-stimulating factor 1 receptor precursor (CSF-1-R) (EC 2.7.10.1) (Fms proto-oncogene) (c-fms) (CD115 antigen).	4.2	3.0E-08	6.4E-04
SIRPA	ENSG00000198053	Tyrosine-protein phosphatase non-receptor type substrate 1 precursor (SHP substrate 1) (SHPS-1) (Inhibitory receptor SHPS-1) (Signal-regulatory protein alpha-1) (Sirp-alpha-1) (Sirp-alpha-2) (Sirp-alpha-3) (MyD-1 antigen)	5.0	1.8E-08	3.6E-04

E. Overlap of the THRLBCL gene expression signature with the Brune et al. (2), genes up-regulated in microdissected NLPHL tumor cells compared with normal B cells and B-non Hodgkin lymphoma.

HGNC ID	Ensembl gene ID	description	fold difference	p-value	corrected p-value
NPL	ENSG00000135838	N-acetylneuraminate pyruvate lyase	4.2	4.0E-10	3.2E-05
SLC1A3	ENSG00000079215	Excitatory amino acid transporter 1 (Sodium-dependent glutamate/aspartate transporter 1) (Glial glutamate transporter) (GLAST-1).	6.7	7.8E-09	1.4E-04
CTSB	ENSG00000164733	Cathepsin B precursor (EC 3.4.22.1) (Cathepsin B1) (APP secretase) (APPS) [Contains: Cathepsin B light chain; Cathepsin B heavy chain].	6.1	8.6E-10	2.2E-05
SCARB2	ENSG00000138760	Lysosome membrane protein 2 (Lysosome membrane protein II) (LIMP II) (Scavenger receptor class B member 2) (85 kDa lysosomal membrane sialoglycoprotein) (LGP85) (CD36 antigen-like 2).	4.4	1.9E-11	2.2E-05
SERPING1	ENSG00000149131	Plasma protease C1 inhibitor precursor (C1 Inh) (C1Inh).	5.7	2.2E-09	6.5E-05
SLC31A1	ENSG00000136868	High-affinity copper uptake protein 1 (hCTR1) (Copper transporter 1) (Solute carrier family 31 member 1).	8.6	1.1E-09	8.7E-05
SCPEP1	ENSG00000121064	Retinoid-inducible serine carboxypeptidase precursor (EC 3.4.16.-) (Serine carboxypeptidase 1).	5.1	2.7E-09	9.7E-05
FPR1	ENSG00000171051	fMet-Leu-Phe receptor (fMLP receptor) (N-formyl peptide receptor) (FPR) (N-formylpeptide chemoattractant receptor).	6.7	1.4E-09	6.5E-05
PNKD	ENSG00000127838	myofibrillogenesis regulator 1 isoform 2	6.3	4.6E-11	2.2E-05

F. Overlap of the THRLBCL gene expression signature with Brune et al. (2), genes up-regulated in microdissected NLPHL tumor cells compared with classical Hodgkin lymphoma (and germinal centre B cells).

HGNC ID	Ensembl gene ID	Description	fold difference	p-value	corrected p-value
GBP1	ENSG00000117228	Interferon-induced guanylate-binding protein 1 (GTP-binding protein 1) (Guanine nucleotide-binding protein 1) (HuGBP-1).	3.0	2.6E-08	6.1E-04
STAT1	ENSG00000115415	Signal transducer and activator of transcription 1-alpha/beta (Transcription factor ISGF-3 components p91/p84).	1.6	1.6E-10	3.2E-05
SLC31A1	ENSG00000136868	High-affinity copper uptake protein 1 (hCTR1) (Copper transporter 1) (Solute carrier family 31 member 1).	8.6	1.1E-09	8.7E-05
BID	ENSG00000015475	BH3-interacting domain death agonist (BID) (p22 BID) [Contains: BH3-interacting domain death agonist p15 (p15 BID); BH3-interacting domain death agonist p13 (p13 BID); BH3-interacting domain death agonist p11 (p11 BID)].	2.5	6.0E-09	1.5E-04

Supplementary Table 5. Expression values of T cell genes.

Fold difference refers to average expression in THRLBCL compared to average expression in NLPHL. P-values are given before and after correction for multiple testing.

Affymetrix probe ID	HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
213539_at	CD3D	ENSG00000167286	T-cell surface glycoprotein CD3 delta chain precursor (T-cell receptor T3 delta chain).	0.76	0.016	1.00
205456_at	CD3E	ENSG00000198851	T-cell surface glycoprotein CD3 epsilon chain precursor (T-cell surface antigen T3/Leu-4 epsilon chain).	0.64	2.9E-04	0.65
206804_at	CD3G	ENSG00000160654	T-cell surface glycoprotein CD3 gamma chain precursor (T-cell receptor T3 gamma chain).	0.65	8.8E-04	0.92
203547_at	CD4	ENSG0000010610	T-cell surface glycoprotein CD4 precursor (T-cell surface antigen T4/Leu-3).	1.16	0.064	1.00
205758_at	CD8A	ENSG00000153563	T-cell surface glycoprotein CD8 alpha chain precursor (T-lymphocyte differentiation antigen T8/Leu-2) (CD8a antigen).	2.19	1.9E-03	0.99
215332_s_at	CD8B	ENSG00000172116	T-cell surface glycoprotein CD8 beta chain precursor (CD8b antigen).	1.21	0.44	1.00
206545_at	CD28	ENSG00000178562	T-cell-specific surface glycoprotein CD28 precursor (TP44).	0.54	1.1E-03	0.95
211856_x_at	CD28	ENSG00000178562	T-cell-specific surface glycoprotein CD28 precursor (TP44).	0.63	0.084	1.00
211861_x_at	CD28	ENSG00000178562	T-cell-specific surface glycoprotein CD28 precursor (TP44).	0.59	0.059	1.00
208850_s_at	THY1	ENSG00000154096	Thy-1 membrane glycoprotein precursor (Thy-1 antigen) (CD90 antigen) (CDw90).	0.51	0.015	1.00
208851_s_at	THY1	ENSG00000154096	Thy-1 membrane glycoprotein precursor (Thy-1 antigen) (CD90 antigen) (CDw90).	0.60	0.029	1.00

A tumor tolerogenic microenvironment in THRLBCL

Affymetrix probe ID	HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
213869_x_at	THY1	ENSG00000154096	Thy-1 membrane glycoprotein precursor (Thy-1 antigen) (CD90 antigen) (CDw90).	0.52	0.016	1.00
231794_at	CTLA4	ENSG00000163599	Cytotoxic T-lymphocyte protein 4 precursor (Cytotoxic T-lymphocyte- associated antigen 4) (CTLA-4) (CD152 antigen).	0.72	0.18	1.00
234362_s_at	CTLA4	ENSG00000163599	Cytotoxic T-lymphocyte protein 4 precursor (Cytotoxic T-lymphocyte- associated antigen 4) (CTLA-4) (CD152 antigen).	0.71	0.23	1.00
234895_at	CTLA4	ENSG00000163599	Cytotoxic T-lymphocyte protein 4 precursor (Cytotoxic T-lymphocyte- associated antigen 4) (CTLA-4) (CD152 antigen).	1.01	0.033	1.00
236341_at	CTLA4	ENSG00000163599	Cytotoxic T-lymphocyte protein 4 precursor (Cytotoxic T-lymphocyte- associated antigen 4) (CTLA-4) (CD152 antigen).	0.67	0.19	1.00
207892_at	CD40LG	ENSG00000102245	CD40 ligand (CD40-L) (Tumor necrosis factor ligand superfamily member 5) (TNF-related activation protein) (TRAP) (T cell antigen Gp39) (CD154 antigen) [Contains: CD40 ligand, membrane form; CD40 ligand, soluble form].	0.75	0.029	1.00
210439_at	ICOS	ENSG00000163600	Inducible T-cell co-stimulator precursor (Activation-inducible lymphocyte immunomediatory molecule) (CD278 antigen).	0.34	7.8E-04	0.90
207849_at	IL2	ENSG00000109471	Interleukin-2 precursor (IL-2) (T-cell growth factor) (TCGF) (Aldesleukin).	1.01	0.48	1.00
207538_at	IL4	ENSG00000113520	Interleukin-4 precursor (IL-4) (B-cell stimulatory factor 1) (BSF-1) (Lymphocyte stimulatory factor 1) (Binetrakin) (Pitrakinra).	1.01	0.073	1.00
207952_at	IL5	ENSG00000113525	Interleukin-5 precursor (IL-5) (T-cell replacing factor) (TRF) (Eosinophil differentiation factor) (B cell differentiation factor I).	1.02	0.046	1.00
207844_at	IL13	ENSG00000169194	Interleukin-13 precursor (IL-13).	1.01	0.81	1.00
208402_at	IL17A	ENSG00000112115	Interleukin-17A precursor (IL-17A) (IL-17) (Cytotoxic T-lymphocyte-associated antigen 8) (CTLA-8).	1.02	0.046	1.00

A tumor tolerogenic microenvironment in THRLBCL

Affymetrix probe ID	HGNC	Ensembl ID	description	fold difference	p-value	corrected p-value
216876_s_at	IL17A	ENSG00000112115	Interleukin-17A precursor (IL-17A) (IL-17) (Cytotoxic T-lymphocyte-associated antigen 8) (CTLA-8).	1.16	0.64	1.00
206341_at	IL2RA	ENSG00000134460	Interleukin-2 receptor alpha chain precursor (IL-2 receptor alpha subunit) (IL-2-RA) (IL2-RA) (p55) (TAC antigen) (CD25 antigen).	2.32	1.9E-03	0.99