

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

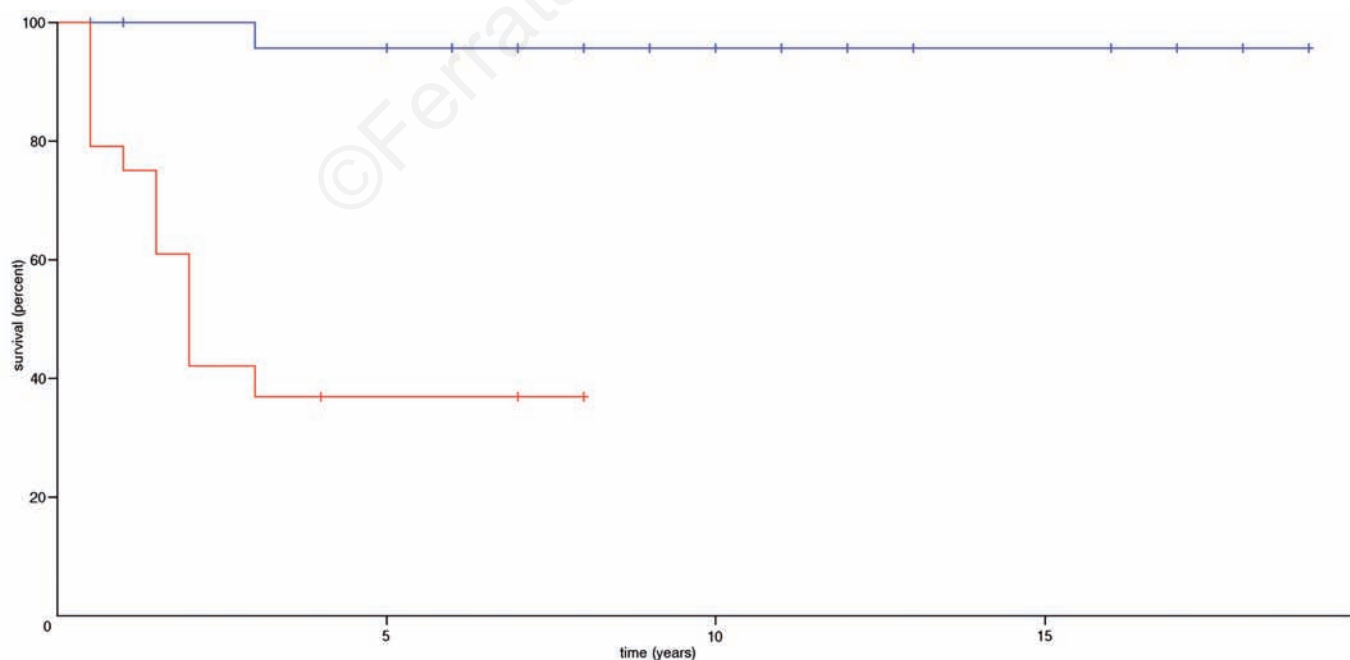
The Online Supplementary Tables S1-5 are in separate PDF files

Supplementary Design and Methods

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

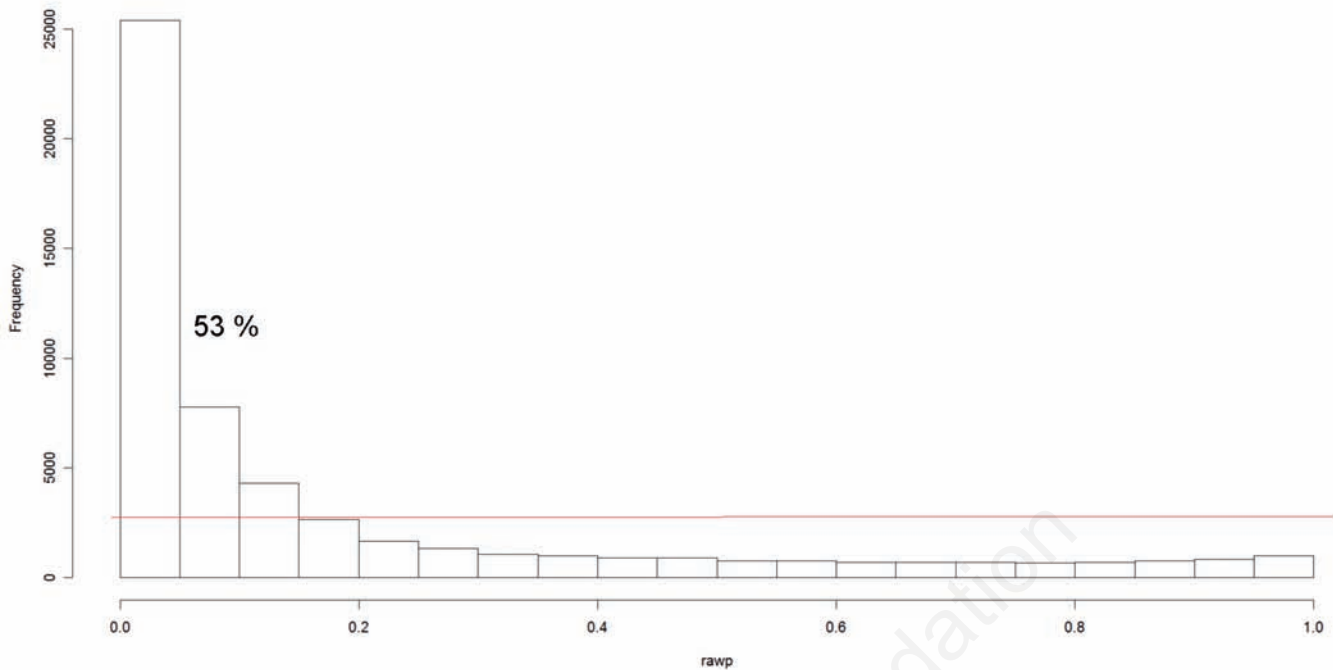
Ten genes measured by microarray gene expression profiling were validated by real-time quantitative reverse transcriptase polymerase chain reaction. These genes were selected for their involvement in interferon pathways, macrophage activation and innate immune responses. Five of these genes were in the T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL) 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: NLPHL. 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 NLPHL is statistically significant ($P=6.0 \times 10^{-6}$, log-rank test).

Histogram of rawp



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

1. 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.
2. 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.
3. 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	21.7	3.7E-12	1.1E-05
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
MOBK2B	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-R2) (BLAST-2) (Immunoglobulin E-binding factor) (CD23 antigen) [Contains: Low affinity immunoglobulin epsilon Fc receptor membrane-bound form; Low affinity immunoglobulin	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	ENSG00000047346		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	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
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	ENSG00000083720	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
	ENSG00000055163	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	ENSG00000023892	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	ENSG00000076662	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	ENSG00000007312	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	ENSG00000005810	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	ENSG00000063046	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	ENSG00000005471	Multidrug resistance protein 3 (EC 3.6.3.44) (P-glycoprotein 3).	12.8	3.5E-07	1.6E-04
IGHV@	ENSG00000130076	Ig alpha-1 chain C region.	33.2	4.0E-07	9.7E-05
SCN3A	ENSG00000153253	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	ENSG00000136111	TBC1 domain family member 4 (Akt substrate of 160 kDa) (AS160).	3.1	7.2E-07	8.9E-04
HNRPM	ENSG00000099783	Heterogeneous nuclear ribonucleoprotein M (hnRNP M).	1.4	1.7E-06	4.1E-04
RPL15	ENSG00000174748	60S ribosomal protein L15.	1.7	1.8E-06	7.8E-04
AFF3	ENSG00000144218	AF4/FMR2 family member 3 (Protein LAF-4) (Lymphoid nuclear protein related to AF4).	13.8	2.0E-06	5.4E-04
KIAA0125	ENSG00000184618		10.6	2.6E-06	1.5E-04
TCL1A	ENSG00000100721	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	ENSG00000158869	High affinity immunoglobulin epsilon receptor gamma-subunit precursor (FceRI gamma) (IgE Fc receptor gamma-subunit) (Fc-epsilon RI-gamma).	9.7	5.1E-13	1.1E-05
VSIG4	ENSG00000155659	V-set and immunoglobulin domain-containing protein 4 precursor (Z39Ig protein).	569.0	6.9E-13	1.1E-05
PSTPIP2	ENSG00000152229	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	ENSG00000054983	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
CEBPB	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	ENSG00000090376	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	ENSG00000177674	Type-1 angiotensin II receptor-associated protein (AT1 receptor- associated protein).	5.2	1.6E-11	2.2E-05
SIGLEC7	ENSG00000168995	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	ENSG00000163220	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	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
	ENSG00000180672		4.8	1.9E-11	2.2E-05
RNF130	ENSG00000113269	Goliath homolog precursor (RING finger protein 130).	4.4	1.9E-11	2.2E-05
PILRA	ENSG00000085514	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	ENSG00000139832	Ras-related protein Rab-20.	4.3	2.0E-11	2.2E-05
TLR2	ENSG00000137462	Toll-like receptor 2 precursor (Toll/interleukin 1 receptor-like protein 4) (CD282 antigen).	11.6	2.2E-11	1.1E-05
CYBA	ENSG00000051523	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).	1.7	1.1E-10	3.2E-05
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	ENSG00000064763	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	ENSG00000002549	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	ENSG00000082397	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	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
ALDH1A1	ENSG00000165092	Retinal dehydrogenase 1 (EC 1.2.1.36) (RaIDH1) (RALDH 1) (Aldehyde dehydrogenase family 1 member A1) (Aldehyde dehydrogenase, cytosolic) (ALHDII) (ALDH-E1).	6.6	1.9E-10	3.2E-05
ARRB1	ENSG00000137486	Beta-arrestin-1 (Arrestin, beta 1).	9.2	2.0E-10	3.2E-05
ICAM1	ENSG00000090339	Intercellular adhesion molecule 1 precursor (ICAM-1) (Major group rhinovirus receptor) (CD54 antigen).	4.8	2.2E-10	3.2E-05
SLC7A7	ENSG00000155465	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	ENSG00000086300	Sorting nexin-10.	9.3	2.2E-10	3.2E-05
MOSPD2	ENSG00000130150	Motile sperm domain-containing protein 2.	2.0	2.3E-10	3.2E-05
IDH1	ENSG00000138413	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	ENSG00000141574	Secreted and transmembrane protein 1 precursor (Protein K12).	9.8	2.4E-10	2.2E-05
FOSL2	ENSG00000075426	Fos-related antigen 2.	4.7	2.4E-10	2.2E-05
BST1	ENSG00000109743	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	ENSG00000163754	Glycogenin-1 (EC 2.4.1.186).	2.3	2.7E-10	3.2E-05
MSRB2	ENSG00000148450	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	ENSG00000035862	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	ENSG00000005893	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
ASAH1	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) (Calcizzarin) (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 adipoQ receptor family member I).	1.7	1.5E-09	4.3E-05
CPD	ENSG00000108582	Carboxypeptidase D precursor (EC 3.4.17.22) (Metalloprotease 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	ENSG00000025434	Oxysterols receptor LXR-alpha (Liver X receptor alpha) (Nuclear orphan receptor LXR-alpha).	3.7	2.2E-09	8.7E-05
SERPING1	ENSG00000149131	Plasma protease C1 inhibitor precursor (C1 Inh) (C1Inh).	5.7	2.2E-09	6.5E-05
	ENSG00000120306	putative nuclear protein ORF1-FL49	2.2	2.2E-09	5.4E-05
AKR1A1	ENSG00000117448	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	ENSG00000177807	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	ENSG00000182287	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	ENSG00000170525	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	ENSG00000136869	Toll-like receptor 4 precursor (hToll) (CD284 antigen).	4.0	2.5E-09	9.7E-05
MRAS	ENSG00000158186	Ras-related protein M-Ras (Ras-related protein R-Ras3).	3.1	2.5E-09	5.4E-05
CD86	ENSG00000114013	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	ENSG00000132912	Dynactin subunit 4 (Dynactin subunit p62).	2.0	2.6E-09	9.7E-05
SCPEP1	ENSG00000121064	Retinoid-inducible serine carboxypeptidase precursor (EC 3.4.16.-) (Serine carboxypeptidase 1).	5.1	2.7E-09	9.7E-05

