

Supplementary material and methods

Genotyping

Genomic DNA (gDNA) was isolated from whole blood cells using the QIAamp[®] DNA Blood Mini Kit (Qiagen, Courtaboeuf, France), according to the manufacturer's protocol. Each coding exon (including intron/exon boundaries of *IL-10RA* and *ILRB* and the untranslated 3'UTR region surrounding the first polyadenylation signal) was amplified from gDNA in a polymerase chain reaction (PCR) using intronic primer pairs. The PCR products were separated by 1% agarose gel electrophoresis, purified with the QIAquick[®] PCR Purification Kit (Qiagen) and sequenced using the BigDye[®] Terminator Cycle Sequencing Kit PE (Applied Biosystems, Courtaboeuf, France).

Histology and immunohistochemistry

Surgical biopsies from IL-10R-deficient patients were fixed in 10% neutral buffered formalin, embedded in paraffin and stained with hematoxylin-eosin. Five samples from DLBCLs with a GCB profile (defined by the Hans algorithm¹) from immunocompetent hosts were used as controls in CD3, CD8, granzyme B and cREL immunostaining. Commercially available antibodies and the biotinylated streptavidin horseradish peroxidase technique were used for all immunohistochemical staining.

Immunohistochemistry was performed automatically with a Menarini Diagnostics system or manually with a DAKO Real detection system (peroxidase/DAB+ rabbit/mouse (K5001)). The antibodies and dilutions used were anti-CD3 (polyclonal, rabbit anti-human, Dakocytomation, 1/200), anti-CD8 (C8/144B, mouse anti-human, 1/100), anti-CD10 (56C6, Novocastra-Leica Microsystem, mouse anti-human, 1/50), anti-CD20 (L26, Dakocytomation, mouse anti-human, 1/400), anti-CD30 (Ber-H2, Dakocytomation, mouse anti-human, 1/50), anti-BCL2 (124, Dakocytomation, mouse anti-human, 1/200), anti-BCL6 (PG-B6p, Dakocytomation, mouse anti-human, 1/25), anti-granzyme B (11F1, Novocastra-Leica Microsystem, mouse anti-human, 1/100), anti-Ki67 (MIB1, Dakocytomation, mouse anti-human, 1/100), anti-MUM1 (MUM1p, Dakocytomation, mouse anti-human, 1/50) and anti-cREL (polyclonal, rabbit anti-human, Cell Signaling 4727, 1/100). *In situ* hybridization of EBV RNA was performed using an EBER-1 probe (Dako).

PCR amplification of immunoglobulin rearrangements and sequence analysis

The immunoglobulin gene rearrangement analysis was performed on genomic DNA isolated from the patients' tumor samples. Amplification of immunoglobulin heavy chain, kappa and

lambda light chain variable region gene rearrangements (IGHV-D-J, IGKV-J and IGLV-J, respectively) was performed with consensus primers for the peptide leader or framework 1 regions and IGHJ genes, as previously described^{2,3,4}. The PCR products were subsequently analyzed via GeneScan profiling on an ABI 3730 DNA Analyzer (Applied Biosystems) for IGH rearrangements (using a fluorochrome-labeled IGHJ primer) or standard polyacrylamide gel electrophoresis (for IGK and IGL rearrangements), according to the Biomed 2 protocols (3). Clonal PCR products were purified and sequenced directly on both strands using an ABI 3730 DNA Analyzer (Applied Biosystems). Sequence analysis (including comparison with germline V, D and J genes and a mutational status assessment) was performed using the IMGT® databases and the IMGT/V-QUEST tool (<http://www.imgt.org>).

Genome-wide, array-based comparative genomic hybridization (aCGH)

Array-based comparative genomic hybridization was performed on gDNA from P1-LPD, P3-L1 and P4-L1 and L2 tumors. Tumor gDNA was isolated by standard proteinase K digestion and phenol-chloroform extraction. The aCGH control was gender-matched DNA from pooled human individuals (Promega) for samples P1-LPD and P3-L1 and matched genomic constitutional DNA for samples P4-L1 and L2. Tumor samples were analyzed using 244K microarrays (Agilent Technologies, Palo Alto, CA, USA). Microarray labeling and hybridization were performed according to the manufacturer's recommendations. Array slides were analyzed in an Agilent scanner (G2505C) running Feature Extraction software (v10.1.1.1). The data were then analyzed with CytoGenomics software (version 1.5.2.0, Agilent).

Karyotyping and fluorescence *in situ* hybridization analysis

Cytogenetic analysis was performed on metaphase spreads obtained from tumor biopsy cells cultured at 37°C for 72h. In each case, 20 RHG-banded metaphases were analyzed. Clonal chromosomal anomalies were described according to the International Nomenclature⁵. The BAC clone RP11-1118K19 (covering the *REL* locus) was selected with the UCSC human genome browser, build 37 (<http://genome.ucsc.edu/>). Purified bacterial artificial chromosome DNA was labeled by nick translation, according to standard procedures. The FISH analysis was performed using specific probes and a standard protocol⁶.

Gene expression profiling

Total RNA was extracted from biopsies of tumors P3-L1 and P4-L2 using an RNeasy Microarray Tissue Mini Kit®. In a microanalysis (Agilent Bioanalyzer, Pico kit), the RNA integrity number was always over 7. The RNAs were hybridized on human oligonucleotide microarrays (U133+2.0, Affymetrix, Santa Clara, CA) containing >47,000 transcripts and variants (including 38,500 well-characterized human genes). Preparation of cRNA from 200 ng of total RNA, hybridization, washing and detection were performed as recommended by the supplier. The results were read with an Affymetrix GeneArray scanner and quantification was performed with Affymetrix GCOS software. Additional microarray data were downloaded from the public Gene Expression Omnibus database (<http://www.ncbi.nlm.nih.gov/geo/>): B cell lymphoma samples were extracted from GSE12453 and ABC and GCB samples were extracted from GSE17372. Hybridization images were inspected for artifacts. Scaling factors (SFs), percentages of present calls (%P) and signal ratios of probe sets interrogating different segments (3'/M) of transcripts were broadly similar when comparing samples (mean SF = 1.22 [0.9–1.3]; mean %P=46.9 [45.4–47.6]; mean slope = 3.0 [2.9–3.6]). Expression data were analyzed using the robust multi-array average (RMA) method in R using Bioconductor software and associated packages⁷. After the RMA normalization procedure, data were log₂-transformed and adjusted using non-parametric Loess regression. Before analysis, genes with low or poorly measured expression were filtered out of the dataset, leaving 28,489 genes/expressed sequence tags. In order to compare the patients' lymphomas with other known B-cell lymphoma subtypes, we selected genes with the highest standard deviation across all samples (SD > 2) and thus the highest variability (as in conventional, unsupervised, hierarchical clustering). Selected gene values (n=4862) were submitted to the Cluster program for calculation of the Pearson correlation coefficient (as a similarity metric) and centroid linkage clustering. The results were visualized with TreeView software. For the hierarchical clustering of the patients' lymphomas with ABC- or GCB-DLBCL, a list of 227 genes used to discriminate between ABC- or GCB-DLBCL was extracted using the non-parametric LIMMA package available in R, which is specifically designed to allow the performance of statistical analyses on small batches of microarray data⁸. Differentially expressed genes were selected (on the basis of a p value <0.05 and a fold-change >2) and submitted to the Cluster program, allowing calculation of the Pearson correlation coefficient (as a similarity metric) and centroid linkage clustering. The comparison of peripheral blood and paired biopsies from P3-L1 and P4-L2 was performed in R, using an “M versus A” plot of probe-level linear model data (threshold: |M| >3).

Ontology and pathway analyses were performed using the aaf.handler and hgu133plus2.db packages and the Database for Annotation, Visualization and Integrated Discovery⁹.

Electrophoretic Mobility Shift Assay (EMSA) and supershift assays

NF- κ B DNA binding activity was analyzed by electrophoretic mobility shift assay (EMSA) using the HIV-LTR tandem κ B oligonucleotide as κ B probe as previously described¹⁰. For supershift assays, cell or tissue extracts were incubated with specific antibodies for 30 min on ice before incubation with the labeled probe.

Whole-exome sequencing

Agilent SureSelect libraries were prepared from 3 μ g of genomic DNA sheared with a Covaris S2 Ultrasonicator, as recommended by the manufacturer. Exome capture was performed with the 50 Mb SureSelect Human All Exon kit (Agilent Technologies) using a multiplex approach with molecular barcodes for traceable sample IDs. Sequencing was performed with the SOLiD5500 system (Life Technologies) with a pool of barcoded exome libraries. Paired-end reads (75 +35) were generated and mapped on a human reference genome (NCBI build37/hg19 version) using LifeScope software (LifeTechnologies). Single-nucleotide polymorphisms and indel calls were identified using GATK tools. An in-house software package (PolyWeb) was used to annotate and filter the variants. Exomes of P3-L1, P4-L1 and P4-L2 and constitutional DNA from P3 and P4 were sequenced. The coverage of exonic regions ranged from 77% to 97% (median: 89%). Known polymorphisms (from public databases such as dbSNP and 1000 Genome), synonymous mutations and variants present in paired normal DNA were subtracted. After visual inspection, variants present in <15% of the reads were excluded.

Supplementary data

Genotypes

Functional studies

The genetic diagnoses of P1 and P2 were made retrospectively (after the patients died) and a lack of material prevented us from performing functional tests. Flow cytometry investigations confirmed the absence of IL-10R2 expression on P3 and P4's PBMCs (data not shown). IL-

10R1 expression was very low for P3's PBMCs and was not detected in P4's cells (data not shown). Lipopolysaccharide-stimulated PBMCs from P3, P4 and P5 did not respond to IL-10 (even at supraphysiological concentrations). Signal transduction by the IL-10 receptor complex in response to IL-10 was abrogated in P3, P4 and P5's cells, as demonstrated by (i) the cells' inability to phosphorylate STAT3 in response to IL-10 and (ii) full activation of the Jak1/STAT3 signaling pathway following IL-6 stimulation (data not shown). A Western blot analysis of P5 cells showed that the IL-10R1 protein was shorter than in control subjects (data not shown).

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Supplementary Figure Legends

Supplementary Fig 1: EMSA and supershift assay

(a) Whole cell extracts isolated from P3L1 and P5L1 patients were analyzed for NF- κ B activity by EMSA.

(b) For supershift, whole cell extracts were either left untreated or incubated with the indicated antibodies for 30 min prior to incubation with the labeled probe. Complex I, RelA/p50; complex II, RelB/p50.

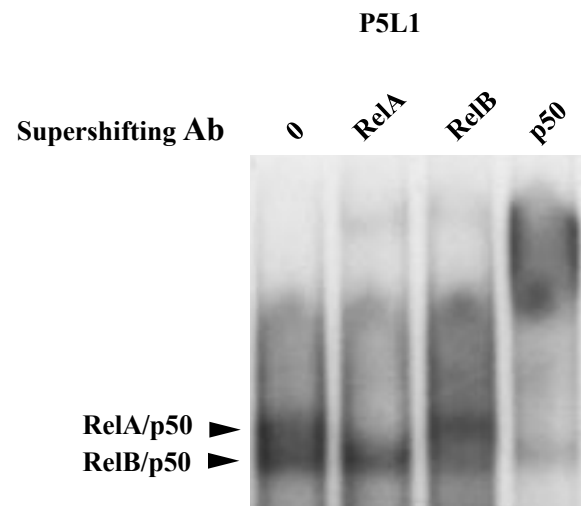
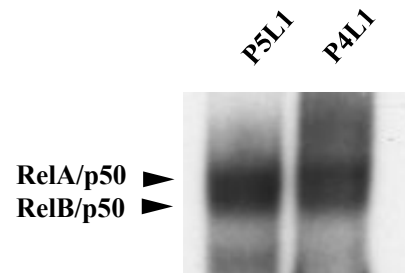
Supplementary Fig. 2: Heat map of the top 50 features for P3-L1, P4-L2 and P5-L1 versus GCB-DLBCL:

Even though GCB-DLBCL are the closest known malignant entities, this GSEA analysis clearly shows that P3-L1, P4-L2 and P5-L1 lymphomas all shared some of the distinct features from GCB-cell lymphoma. These distinct features revealed a strong transcriptional activity, notably with enhanced expression of the spliceosome pathway and ubiquitin-mediated proteolysis. These characteristics all attest to active cycling and a frozen GC-phenotype for the patients' lymphoma B-cells.

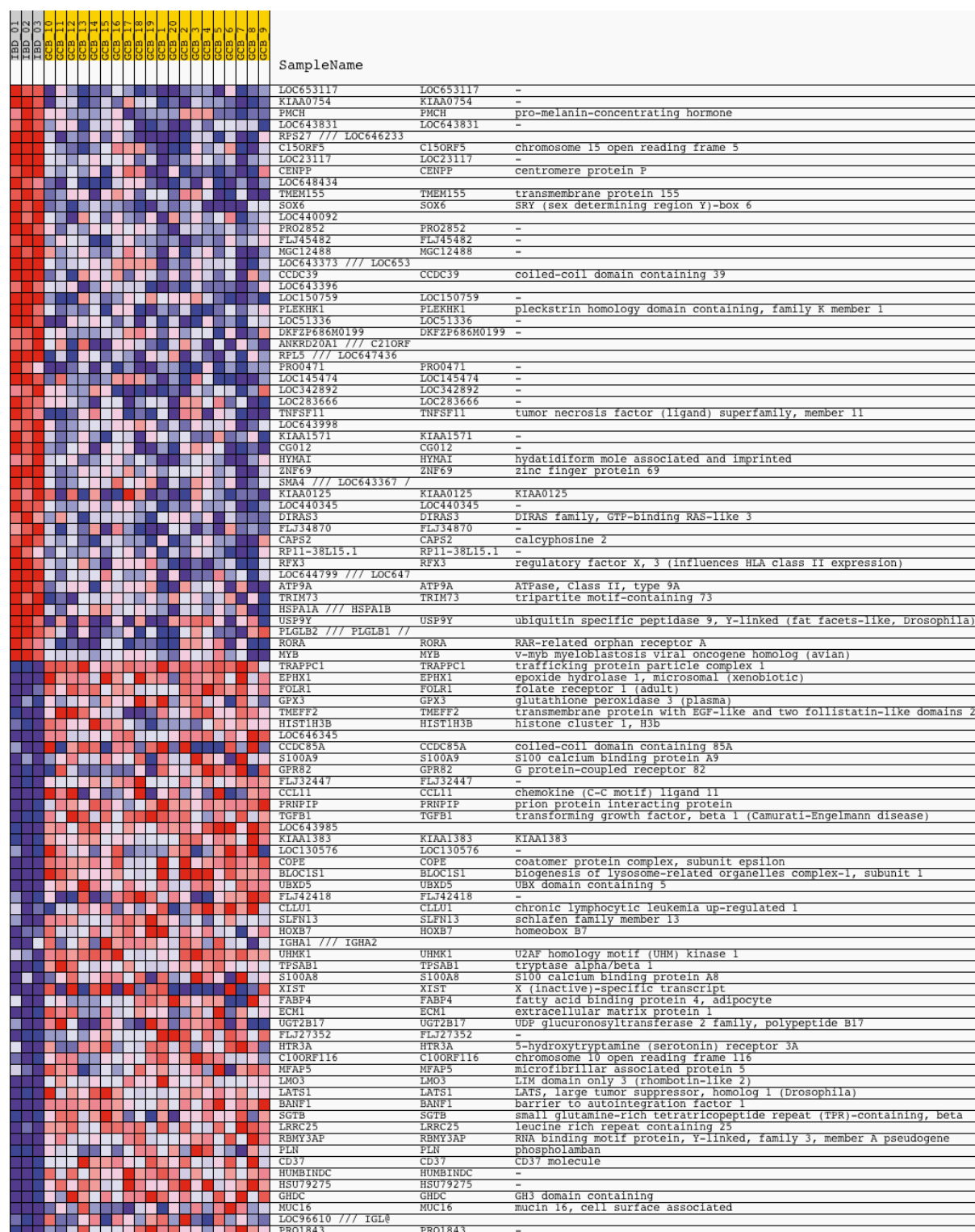
Supplementary Fig. 3: Heat map of the top 50 features for P3-L1, P4-L2 and P5-L1 versus non-malignant, reactive tonsils:

A GSEA comparison of P3-L1, P4-L2 and P5-L1 lymphomas with non-malignant reactive B-cells (from tonsils) confirmed the lymphomas' monoclonality and revealed the marked involvement of matrix remodeling and angiogenesis. All of these features were supportive of aggressive malignant behavior. Interestingly, this analysis revealed low levels of activation-induced cytidine deaminase and BACH2 and thus indicated the presence of another source of genomic instability.

Suppl. fig. 1



Suppl. fig 2



Suppl. fig 3

| EBD_01 | EBD_02 | EBD_03 | AMG_01 | AMG_02 | AMG_03 | SampleName |
|--------|--------|--------|--------|--------|--------|----------------------------------------------------------------------------------------------------------|
| | | | | | | C9ORF26 C9ORF26 chromosome 9 open reading frame 26 (NF-HEV) |
| | | | | | | CFH /// CFHR1 |
| | | | | | | COL3A1 COL3A1 collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant) |
| | | | | | | FAM70A FAM70A family with sequence similarity 70, member A |
| | | | | | | PMCH PMCH pro-melanin-concentrating hormone |
| | | | | | | LUM LUM lumican |
| | | | | | | MGP MGP matrix Gla protein |
| | | | | | | SPARCL1 SPARCL1 SPARC-like 1 (mast9, hev1n) |
| | | | | | | ELTD1 ELTD1 EGF, latrophilin and seven transmembrane domain containing 1 |
| | | | | | | COL5A2 COL5A2 collagen, type V, alpha 2 |
| | | | | | | AZM AZM alpha-2-macroglobulin |
| | | | | | | FSTL1 FSTL1 follistatin-like 1 |
| | | | | | | PLOD2 PLOD2 procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2 |
| | | | | | | COL1A2 COL1A2 collagen, type I, alpha 2 |
| | | | | | | TNC TNC tenascin C (hexabrachion) |
| | | | | | | THBS2 THBS2 thrombospondin 2 |
| | | | | | | ALDH1A1 ALDH1A1 aldehyde dehydrogenase 1 family, member A1 |
| | | | | | | TMEM155 TMEM155 transmembrane protein 155 |
| | | | | | | COL15A1 COL15A1 collagen, type XV, alpha 1 |
| | | | | | | IGFBP3 IGFBP3 insulin-like growth factor binding protein 3 |
| | | | | | | TDO2 TDO2 tryptophan 2,3-dioxygenase |
| | | | | | | CHI3L1 CHI3L1 chitinase 3-like 1 (cartilage glycoprotein-39) |
| | | | | | | RARRES1 RARRES1 retinoic acid receptor responder (tazarotene induced) 1 |
| | | | | | | COLEC12 COLEC12 collectin sub-family member 12 |
| | | | | | | ZC3H12C ZC3H12C zinc finger CCCH-type containing 12C |
| | | | | | | LOX LOX lysyl oxidase |
| | | | | | | ABI3BP ABI3BP ABI gene family, member 3 (NESH) binding protein |
| | | | | | | CHIT1 CHIT1 chitinase 1 (chitotriosidase) |
| | | | | | | LOC387763 LOC387763 - |
| | | | | | | TFPI TFPI tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor) |
| | | | | | | VEGFC VEGFC vascular endothelial growth factor C |
| | | | | | | TMEM47 TMEM47 transmembrane protein 47 |
| | | | | | | PDGFC PDGFC platelet derived growth factor C |
| | | | | | | PLEKHC1 PLEKHC1 pleckstrin homology domain containing, family C (with FERM domain) member 1 |
| | | | | | | HSD11B1 HSD11B1 hydroxysteroid (11-beta) dehydrogenase 1 |
| | | | | | | PLS3 PLS3 plastin 3 (T isoform) |
| | | | | | | CCL2 CCL2 chemokine (C-C motif) ligand 2 |
| | | | | | | CCL19 CCL19 chemokine (C-C motif) ligand 19 |
| | | | | | | LOXL1 LOXL1 lysyl oxidase-like 1 |
| | | | | | | SERPING1 SERPING1 serpin peptidase inhibitor, clade G (C1 inhibitor), member 1, (angioedema, hereditary) |
| | | | | | | ARHGAP29 ARHGAP29 Rho GTPase activating protein 29 |
| | | | | | | SEPT10 SEPT10 septin 10 |
| | | | | | | CYP11B1 CYP11B1 cytochrome P450, family 1, subfamily B, polypeptide 1 |
| | | | | | | LOC643424 |
| | | | | | | NRN1 NRN1 neuritin 1 |
| | | | | | | LOC653117 LOC653117 - |
| | | | | | | VNN1 VNN1 vanin 1 |
| | | | | | | SNAI2 SNAI2 snail homolog 2 (Drosophila) |
| | | | | | | HS3ST3A1 HS3ST3A1 heparan sulfate (glucosamine) 3-O-sulfotransferase 3A1 |
| | | | | | | COL4A1 COL4A1 collagen, type IV, alpha 1 |
| | | | | | | LOC96610 /// IGL@ |
| | | | | | | IGLC1 IGLC1 immunoglobulin lambda constant 1 (Mcg marker) |
| | | | | | | IGLV2-14 IGLV2-14 immunoglobulin lambda variable 2-14 |
| | | | | | | SCN3A SCN3A sodium channel, voltage-gated, type III, alpha |
| | | | | | | IGHA1 /// IGHD /// I |
| | | | | | | FLJ42418 FLJ42418 - |
| | | | | | | CCR6 CCR6 chemokine (C-C motif) receptor 6 |
| | | | | | | FCRL4 FCRL4 Fc receptor-like 4 |
| | | | | | | IGKC /// LOC642113 / |
| | | | | | | LOC651961 |
| | | | | | | C5ORF29 C5ORF29 chromosome 5 open reading frame 29 |
| | | | | | | SPRR3 SPRR3 small proline-rich protein 3 |
| | | | | | | LOC651629 LOC651629 - |
| | | | | | | LOC391427 |
| | | | | | | IGHA1 /// IGHG1 /// |
| | | | | | | MYRIP MYRIP myosin VIIA and Rab interacting protein |
| | | | | | | LOC652745 LOC652745 - |
| | | | | | | FLJ20366 FLJ20366 - |
| | | | | | | IGHA1 /// IGHA2 |
| | | | | | | NALP4 NALP4 NACHT, leucine rich repeat and PYD containing 4 |
| | | | | | | MGC24039 MGC24039 - |
| | | | | | | LOC642626 |
| | | | | | | IGHD IGHG1 immunoglobulin heavy constant delta |
| | | | | | | IGHV1-69 IGHV1-69 immunoglobulin heavy variable 1-69 |
| | | | | | | NYD-SP21 NYD-SP21 - |
| | | | | | | GPR82 GPR82 G protein-coupled receptor 82 |
| | | | | | | IL17A IL17A interleukin 17A |
| | | | | | | C16ORF74 C16ORF74 chromosome 16 open reading frame 74 |
| | | | | | | LOC201895 |
| | | | | | | IGLJ3 IGLJ3 immunoglobulin lambda joining 3 |
| | | | | | | IGHA1 /// LOC649805 |
| | | | | | | KLRC1 /// KLRC2 |
| | | | | | | DHRS9 DHRS9 dehydrogenase/reductase (SDR family) member 9 |
| | | | | | | GN7 GN7 guanine nucleotide binding protein (G protein), gamma 7 |
| | | | | | | PLAC8 PLAC8 placenta-specific 8 |
| | | | | | | FLJ38379 FLJ38379 - |
| | | | | | | PCDH9 PCDH9 protocadherin 9 |
| | | | | | | LOC283663 LOC283663 - |
| | | | | | | CLL01 CLL01 chronic lymphocytic leukemia up-regulated 1 |
| | | | | | | C20ORF133 C20ORF133 chromosome 20 open reading frame 133 |
| | | | | | | CD1C CD1C CD1c molecule |
| | | | | | | LOC96610 LOC96610 - |
| | | | | | | BACH2 BACH2 BTB and CNC homology 1, basic leucine zipper transcription factor 2 |
| | | | | | | C7ORF10 C7ORF10 chromosome 7 open reading frame 10 |
| | | | | | | FLJ22814 FLJ22814 - |
| | | | | | | IGHM /// LOC652494 / |
| | | | | | | IGHG1 IGHG1 immunoglobulin heavy constant gamma 1 (G1m marker) |
| | | | | | | AICDA AICDA activation-induced cytidine deaminase |
| | | | | | | IL26 IL26 interleukin 26 |
| | | | | | | KIAR0565 /// FLJ3649 |

Suppl. Table 1: IL10R deficient patients: clinical manifestations

| | P1 | P2 | P3* | P4 | P5 |
|--------------------------------|-----------------------------|-----------------------------|----------------------------------------|--------------------------------------------------------|------------------------------------------|
| gender | male | male | male | male | male |
| origin | sicilian | french | turkish | turkish | arabic |
| genotype | IL10-R2 Y59C/ Y59C | IL10-R2 W204C/F269fsX275 | IL10-R2 E141X/ E141X | IL10-R2 g.11930-17413/ g.11930-17413 | IL10-R1 c.368-10 C>G/ c.368-10 C>G |
| age at onset (weeks) | 2 | 2 | 12 | 2 | 9 |
| digestive manifestations | colitis, perianal abscesses | colitis, perianal abscesses | colitis, perianal abscesses | colitis | colitis, perianal abscesses |
| extra-digestive manifestations | recurrent skin folliculitis | recurrent skin folliculitis | recurrent skin folliculitis | recurrent skin folliculitis, syndactily, brachydactily | none |
| treatment | CS/AZA/Ciclo colectomy (4y) | CS/AZA | CS/AZA/ anti-TNF/MMF colectomy (3y) | CS/AZA/ciclo colectomy (3y) | none |

P denotes patient; CS: corticosteroids; AZA: azathioprine; ciclo: ciclosporin; anti TNF: anti tumor necrosis factor; MMF: mycophenolate mofetil, y: years; P3* was previously reported by Begue et al

Suppl. Table 2: Clonal IgH rearrangements and rate of somatic mutation in VH and VL regions in lymphoma samples

| | P3-L1 | P4-L1 | P4-L2 |
|--------------------------|---------------|---------------|--------------|
| Heavy chain mutation (%) | VH4-61 0.3 | VH3-7 6.2 | VH5-a 3.5 |
| Light chain mutation (%) | VL3-19 0 | VL3-10 3.3 | VK1-8 0.4 |

VH: variable region of heavy chain, VL: variable region of light chain (lambda) ; VK: variable region of light chain (kappa)

Suppl. Table 3: List of genes and associated pathways (established after GSEA analysis and DAVID Bioinformatics Resources 6.7, NIAID/NIH) enriched in P3-L1, P4-L2 ad P5-L1 lymphomas compared to GCB-DLBCL.

Up compared to GCB-DLBCL

| Term | p-value | Genes | Fold Enrichment |
|--------------------------------|-----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|
| Spliceosome | 2.2×10^{-12} | CHERP, TRA2B, U2AF2, TRA2A, SNRPB2, SR140, HSPA1A, HSPA1B, SFRS6, HNRNPA3, HNRNPM, SF3B1, SFRS7, SFRS4, TCERG1, HNRNPK, SFRS5, RBM8A, U2AF1, HSPA6, HNRNPC, ACIN1, RBM25, PRPF40A, DDX42, RBM22, SNRPA1, SNW1, SFRS1, DDX5, PRPF18, HNRNPA1, HNRNPU, AQR, SNRNP200, SYF2, SNRNP40, THOC4, PRPF38B, THOC1 | 2.6 |
| Ubiquitin mediated proteolysis | 2.0×10^{-11} | UBE2Z, XIAP, UBE3B, UBE3A, PPIL2, UBE2G2, PML, UBA6, CDC16, CUL2, UBE2D3, CUL5, FBXW7, WWP1, RCHY1, ITCH, NEDD4L, ANAPC1, ANAPC5, UBE4A, VHL, ANAPC4, BIRC6, HERC4, UBE2I, MID1, HERC1, UBE2B, CBLB, HUWE1, CUL4A, MDM2, PIAS2, SIAH1, SMURF2, PIAS1 | 2.7 |
| Pathways in cancer | 2.3×10^{-5} | FGFR1, E2F3, XIAP, PGF, STK36, STAT5B, PML, FASLG, NFKB2, PTEN, CTNNA1, ARNT, CUL2, CASP3, KRAS, SOS1, CASP8, PIK3CA, PIK3R5, AKT3, APC, AKT2, COL4A4, CTBP1, TCF7, PLD1, MSH3, VHL, TGFBR1, CYCS, SMAD4, RAF1, BRCA2, CDK6, SMAD2, STK4, CBLB, ETS1, VEGFA, MDM2, JAK1, PIAS2, MAPK8, PIAS1, IKBKB | 2.6 |
| Endocytosis/phagocytosis | 6.6×10^{-5} | CLTA, USP8, RAB5B, ARF6, EEA1, HSPA1A, HSPA1B, ZFYVE20, WWP1, PIKFYVE, HSPA6, ITCH, NEDD4L, VPS36, FLT1, TGFBR1, HLA-F, RAB11FIP4, RAB11FIP2, CBLB, RAB11FIP3, TFRC, AP2A1, RAB5A, MDM2, SMURF2, ARAP2, RAB11FIP1, PIP4K2B, RAF1, AKT2, INPP5D, PRKCE, RPS6KB1, PIK3R5, PLD1, PIK3CA, AKT3 | 1.8 |
| Apoptosis | 1.7×10^{-4} | CFLAR, XIAP, CYCS, PPP3R1, FASLG, PRKX, ATM, CAPN1, CASP10, CASP3, PRKAR2A, PRKAR1A, CASP8, PIK3CA, PIK3R5, IKBKB, IL1A, AKT3, AKT2, CASP3, CCND2, CYCS, CASP8, MDM2, SIAH1, CDK6, RCHY1, ATR, MDM4, PTEN, ATM | 1.9 |
| Neurotrophin signaling pathway | 1.9×10^{-4} | YWHAZ, ZNF274, FASLG, RAF1, LOC442113, KIDINS220, PTPN11, MAP3K5, YWHAH, KRAS, SOS1, PIK3CA, PIK3R5, MAPK8, IKBKB, MAP2K7, ARHGDI1, AKT3, CALM1, AKT2, MAP2K5 | 2.0 |
| GnRH signaling pathway | 2.3×10^{-4} | PLD1, ADCY7, GNRH1, RAF1, PRKX, PLCB4, KRAS, GNAQ, MAP3K2, SOS1, HBEGF, MAPK8, GNAS, MAP2K7, MAP2K6, CALM1 | 2.1 |
| MAPK signaling pathway | 2.6×10^{-4} | FGFR1, IL1R2, ZAK, PPP3R1, PPM1A, FASLG, HSPA1A, NFKB2, HSPA1B, PRKX, MAP3K7, MAP3K5, CASP3, KRAS, MAP3K2, SOS1, MAP3K8, DUSP16, HSPA6, RAPGEF2, MAP2K7, AKT3, MAP2K6, IL1A, MAP2K5, AKT2, TAOK1, TGFBR1, NF1, RAF1, CACNA2D3, STK4, FLNB, MAP4K4, DUSP4, MAPK8, IKBKB, MAP3K13 | 1.6 |
| Insulin signaling pathway | 9.4×10^{-4} | PHKB, PRKAG2, RHOQ, PDE3B, RPS6KB1, PRKX, PRKAR2A, PDPK1, KRAS, SOS1, PIK3CA, PRKAA1, PIK3R5, INPP5D, AKT3, AKT2, PTPRF, PRKAB2, RAF1, CBLB, PRKAR1A, MAPK8, IKBKB, EIF4E2, CALM1 | 1.8 |

| | | | |
|-----------------------------------|----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| Adherens junction | 1.6×10^{-3} | SYMPK, INADL, ZAK, MAGI1, CSNK2B, CASK, PRKCE, PTEN, CTNNA1, LIG1, PRKCQ, CTTN, KRAS, ASH1L, PPP2R2D, AKT2, AKT3, PPP2R2A, RAF1, FYN, SMAD4, PTPRF, CCND2, PPP1R12A, TCF7, MAP3K7, FLNB, FLT1, VEGFA, IQGAP1, COL6A1, ROCK1, PGF, FGFR1, TNC, PDPK1, XIAP, PIK3R5, MAPK8, COL4A4, SOS1, ARHGAP5, PIK3CA, TGFB1, SMAD2, ITGB8, ... | 2.1 |
| T cell receptor signaling pathway | 2.5×10^{-3} | CTLA4, PPP3R1, RAF1, MAP3K7, PRKCQ, CBLB, KRAS, FYN, SOS1, MAP3K8, NFAT5, PIK3CA, PIK3R5, IKBKB, MAP2K7, NFATC3, AKT3, LCP2, AKT2, DLG1, CARD11 | 1.8 |
| mTOR signaling pathway | 5.4×10^{-3} | RICTOR, AKT2, VEGFA, PRKAA1, PGF, PDPK1, RPS6KB1, EIF4E2, PIK3R5, PIK3CA, AKT3, AKT2, ... | 2.2 |
| Cell cycle | 3.1×10^{-2} | ANAPC1, E2F3, YWHAZ, ANAPC5, CDC14A, CDC14B, ANAPC4, SMAD4, PRKDC, CDK6, SMAD2, CDC16, ATR, ATM, SMC3, WEE1, YWHAH, CCND2, MDM2, STAG1 | 1.5 |
| Notch signalling pathway | 3.6×10^{-2} | NOTCH2, CTBP1, KAT2B, NUMB, ADAM17, SNW1, PSENEN, RBPJ, NUMBL | 2.0 |
| Long-term potentiation | 4.3×10^{-2} | RAF1, PPP1R12A, PLCB4, KRAS, PRKX /// PRKY, CALM1, GNAQ, ... | 1.7 |

Down compared to GCB-DLBCL

| Term | PValue | Genes | Fold Enrichment |
|-----------------------------------------|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| Calcium signaling pathway | 3.7×10^{-10} | CALML6, PLCD3, HTR6, CACNA1A, NOS1, ERBB3, SLC8A1, PLCE1, MYLK, GRIN2C, ADCY9, ATP2A1, CACNA1H, ITPKA, GRIN1, AVPR1A, PRKCG, ADCY8, ADRB3, ATP2B3, GRIN2D, PHKG1, TBXA2R, HTR4, HTR7, GRPR, AGTR1, AVPR1B, P2RX3, CACNA1F, CACNA1E, DRD5, SPHK2, CALML3, PLCB2, TACR1, GRM1, ADRA1D, EGFR, CCKAR, CACNA1G, GNAQ, ADRA1A, PDGFRA, ATP2B2, PLCB1, CAMK2G, CAMK2A, TACR2, ADCY1, PDE1C, GNAS, CALML5, CHRM5, P2RX2, PLCD4, NOS3, ATP2A1 /// LOC100294460, CAMK2D, ADCY4, PTGER1, MYLK2, CACNA1B, ATP2A2, PPP3CC, ... | 2.0 |
| Neuroactive ligand-receptor interaction | 1.2×10^{-8} | HTR6, UTS2R, RXFP2, TAAR8, LEPR, GRIK2, GABRG2, GRIN2C, GRIA3, PTGER4, VIPR1, CTSG, F2, PTH1R, GRIN1, AVPR1A, F2RL1, OPR1, CNR2, F2RL2, ADRB3, GRIN2D, THRB, GABRA3, AGTR2, GABRB2, GLRA2, OPRK1, TBXA2R, HTR4, HCRTR1, HTR7, GRPR, AGTR1, GABRR2, AVPR1B, GPR50, P2RX3, GABRD, GRM2, DRD5, ADRA2B, MC5R, MC2R, GRIA1, GABBR2, GPR35, SCTR, GRIN2B, TACR1, NPY2R, HTR1B, GRM1, ADRA1D, CCKAR, FSHR, GLP1R, OPRM1, ADRA1A, GNRHR, GHRHR, DRD2, PRLR, TACR2, SSTR5, DRD3, GABRA5, GRIK5, LPAR3, GABRQ, CHRM5, HTR1A, P2RX2, GHSR, MLNR, MTNR1A, P2RY4, HRH3, PTGER1, NPBWR1, GRIN3A, PLG, GABRG1, NR1D1 /// THRA, ... | 1.8 |
| Vascular smooth muscle contraction | 3.0×10^{-6} | CALML6, CYP4A11, LOC100129266, MYLK, MAP2K2, ADCY9, NPR1, AVPR1A, PRKCG, ADCY8, AGTR1, AVPR1B, CACNA1F, CALML3, PLCB2, ADRA1D, PRKG1, GNAQ, ADRA1A, PLCB1, MAPK3, KCNMA1, ADCY1, GNAS, JMJD7-PLA2G4B /// PLA2G4B, CALML5, PLA2G3, PLA2G2E, PLA2G2F, PLA2G12B, MRV1, ROCK1, ADCY4, MYLK2, ARHGEF12, ARHGEF11, ... | 2.0 |
| GnRH signaling pathway | 8.7×10^{-6} | CALML6, MAPK12, LOC100129266, SRC, KRAS, MMP2, MAP2K2, ELK1, ADCY9, ADCY8, CACNA1F, GNRH2, CDC42, CALML3, PLCB2, EGFR, GNAQ, MAPK11, GNRHR, PLCB1, MAPK3, CAMK2G, CAMK2A, ADCY1, GNAS, JMJD7-PLA2G4B /// PLA2G4B, CALML5, PLA2G3, PLA2G2E, PLA2G2F, PLA2G12B, GRB2, CAMK2D, ADCY4, SOS2, HBEGF, ... | 2.0 |

| | | | |
|----------------------------------|----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| Melanogenesis | 1.1×10^{-5} | CALML6, WNT9B, MITF, KRAS, EDN1, GNAI2, MAP2K2, ADCY9, GNAO1, FZD5, PRKCG, WNT11, ADCY8, WNT1, CREB3, CALML3, PLCB2, GNAQ, PLCB1, MAPK3, CAMK2G, CREB3L1, CAMK2A, ASIP, ADCY1, DCT, GNAS, CALML5, WNT6, WNT8A, WNT5B, CAMK2D, ADCY4, CREBBP, WNT7B, ... | 2.0 |
| Long-term potentiation | 1.1×10^{-4} | CALML6, RAPIA, RPS6KA2, KRAS, GRIN2C, MAP2K2, GRIN1, PRKCG, ADCY8, GRIN2D, GRIA1, CALML3, PLCB2, GRIN2B, GRM1, GNAQ, PLCB1, MAPK3, CAMK2G, CAMK2A, RAPGEF3, ADCY1, CALML5, RPS6KA6, CAMK2D, CREBBP, PPP3CC, ... | 2.1 |
| MAPK signaling pathway | 2.7×10^{-4} | CACNG5, MAP3K6, CACNG6, RAPIA, MAPK12, LOC100129266, RPS6KA2, CACNA1A, KRAS, PAK1, FGF22, LOC100288009, SRF, MAP2K2, TGFB1, ELK1, MAPT, RPS6KA4, FGF1, CACNA1H, PRKCG, NGF, CACNA2D1, NTRK2, TGFB2, FGFR2, CACNA1F, FGF6, CACNA1E, CDC42, PAK2, CACNB3, TGFB2, CACNB1, PTPRR, EGFR, FGF18, CACNA1G, MAPK11, PDGFRA, MAPK3, RASGRP2, FGF12, CACNB2, PPP5C, PDGFB, MAPK8IP3, JMJD7-PLA2G4B /// PLA2G4B, RPS6KA6, PLA2G3, FGF23, FGF16, FGF17, PLA2G2E, PLA2G2F, PLA2G12B, NFATC2, DUSP1, CACNA2D4, GRB2, ELK4, FGF10, HSPA1L, CACNG8, CACNA1B, DUSP8, SOS2, PPP3CC, IKBKG, CACNG4, ... | 1.5 |
| Axon guidance | 3.4×10^{-4} | CFL1, SLIT1, KRAS, PAK1, SRGAP1, GNAI2, SEMA3B, PAK4, SEMA4G, CDK5, L1CAM, EPHA1, NTN1, SEMA6C, EFNA2, CDC42, PAK2, EFNA3, NR1, EPHB2, MAPK3, SEMA3D, PLXNB1, SEMA6A, SEMA5B, DPYSL5, NFATC2, NGEF, ABLIM2, ROCK1, UNC5D, ARHGEF12, EPHA4, UNC5C, DCC, PPP3CC, ... | 1.7 |
| ErbB signaling pathway | 8.2×10^{-4} | CDKN1A, SRC, KRAS, GAB1, ERBB3, PAK1, MAP2K2, PAK4, ELK1, NRG1, PRKCG, SHC3, NRG2, PAK2, EGFR, TGFA, MAPK3, PIK3R1, CAMK2G, CAMK2A, AREG, CBL, EIF4EBP1, GRB2, CAMK2D, SOS2, HBEGF, ... | 1.8 |
| Oxidative phosphorylation | 4.2×10^{-3} | ATP6V0E1, NDUFA3, UQCRC1, NDUFB10, NDUFB9, NDUFS8, CYC1, ATP5O, ATP6V0D1, NDUFB1 | 3.1 |
| Long-term depression | 9.8×10^{-4} | LOC100129266, CACNA1A, KRAS, NOS1, GRIA3, PPP2R1A, GNAI2, MAP2K2, GNAO1, CRH, PRKCG, PRKG2, GRIA1, PLCB2, GRM1, PRKG1, GNAQ, PLCB1, MAPK3, GNAS, JMJD7-PLA2G4B /// PLA2G4B, PLA2G3, PLA2G2E, PLA2G2F, PLA2G12B, C7orf16, ... | 1.9 |
| Gap junction | 2×10^{-2} | SRC, KRAS, GNAI2, MAP2K2, ADCY9, PRKCG, ADCY8, PRKG2, TUBB1, PLCB2, GRM1, EGFR, PRKG1, GNAQ, PDGFRA, DRD2, PLCB1, MAPK3, ADCY1, PDGFB, GNAS, GJD2, GRB2, ADCY4, SOS2, GJD2, KRAS, GNAI2, PRKG2, | 1.5 |
| Regulation of actin cytoskeleton | 2.9×10^{-2} | CFL1, KRAS, PAK1, FGF22, MYLK, ARPC5, ITGA3, GRLF1, IGF2 /// INS-IGF2, MAP2K2, PAK4, ITGB4, FGF1, WAS, F2, WASL, ITGA2B, PIP5K1A, FGFR2, FGF6, CDC42, ARPC3, PAK2, EGFR, FGF18, PDGFRA, ARHGEF4, MAPK3, PIK3R1, FGF12, DIAPH1, PDGFB, ARPC4, GIT1, MYH14, ARPC5L, FGF23, CHRM5, FGF16, FGF17, MYL10, BCAR1, GSN, ROCK1, FGF10, MYLK2, ARHGEF12, SOS2, GNAS, ITGA8, ITGB6, IQGAP3, ... | 1.3 |
| Linoleic acid metabolism | 3.6×10^{-2} | LOC100129266, AKR1B10, CYP1A2, CYP2C19, JMJD7-PLA2G4B /// PLA2G4B, CYP2C8, CYP2C9, PLA2G3, PLA2G2E, PLA2G2F, PLA2G12B, | 2.0 |
| Arachidonic acid metabolism | 7.1×10^{-2} | CYP4A11, LOC100129266, GPX4, GPX2, CYP4F2, GPX5, CYP2C19, PTGES2, JMJD7-PLA2G4B /// PLA2G4B, CYP2C8, CYP2C9, PLA2G3, PLA2G2E, PLA2G2F, PLA2G12B, GGT7, GGT2, ... | 1.5 |
| ABC transporters | 7.8×10^{-2} | ABCB9, ABCA8, ABCD1, ABCG4, ABCB11, ABCC9, ABCA4, ABCA2, ABCC8, ABCC6, ABCA12, ABCC11, ABCG8, ABCB5, ... | 1.6 |

Suppl. Table 4: List of genes and associated pathways (established after GSEA analysis and DAVID Bioinformatics Resources 6.7, NIAID/NIH) enriched in P3-L1, P4-L2 and P5-L1 lymphomas compared to tonsils.

Up compared to Tonsil

| Term | p-value | Genes | Fold Enrichment |
|----------------------------------------|-----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|
| ECM-receptor interaction | 5.4×10^{-10} | TNC, COL3A1, DAG1, ITGB5, SDC4, SDC2, LAMB2, ITGAV, COL6A3, COL6A1, LAMB1, THBS2, FN1, SPP1, COL4A4, COL4A2, COL4A1, HSPG2, COL5A2, ITGA9, VWF, LAMA4, COL1A2, LAMC2, COL1A1, LAMC1 | 4.0 |
| Focal adhesion | 2.6×10^{-9} | CAV2, CAV1, TNC, COL3A1, ITGB5, PXN, DOCK1, LAMB2, PAK2, PAK3, ITGAV, COL6A3, RAC1, COL6A1, PDGFC, LAMB1, PIK3R3, THBS2, AKT3, SPP1, FN1, EGFR, COL4A4, COL4A2, FLT1, COL4A1, MET, ACTN1, COL5A2, FLNB, VEGFC, ITGA9, VWF, LAMA4, CCND1, COL1A2, PDGFRA, PDGFRB, LAMC2, LAMC1, COL1A1, MYLK, PARVA | 2.7 |
| Pathways in cancer | 7.5×10^{-6} | E2F1, MMP9, PPARG, MITF, GLI3, MMP2, TGFA, FAS, FGF2, AKT3, CSF2RA, EGFR, WNT10A, PLD1, HSP90AA1, CTBP2, RXRA, RUNX1T1, CDK6, MECOM, VEGFC, CCDC6, CCND1, PDGFRA, PDGFRB, LAMC2, LAMC1, EGLN3, KITLG, BCL2L1, TCF7L2, TCF7L1, ARNT, LAMB2, ITGAV, RAC1, LAMB1, PIK3R3, CSF1R, FN1, CEBPA, COL4A4, COL4A2, COL4A1, EPAS1, MET, FZD1, APPL1, FZD4, FZD7, LAMA4 | 1.9 |
| Complement and coagulation cascades | 1.8×10^{-5} | C7, A2M, C5AR1, CFB, C3, SERPING1, C1R, C1S, C1QC, C1QA, VWF, CD59, TFPI, CFH, C2, CFI, PROS1, PLAUI | 3.3 |
| Axon guidance | 2.0×10^{-5} | PLXNC1, NRP1, PLXNA1, EFNA1, GNAI1, L1CAM, LRRC4C, CXCL12, EPHB2, SEMA5A, UNC5B, PAK2, PAK3, SEMA3G, ROBO1, SEMA3F, RAC1, SEMA3C, SEMA3A, MET, SLIT2, EPHA3, SEMA4C, EFNA5, SRGAP1 | 2.5 |
| Cell adhesion molecules (CAMs) | 8.7×10^{-5} | GLG1, F11R, MPZL1, CADM1, PTPRF, CD8A, CD276, L1CAM, NEO1, CDH2, HLA-B, SDC4, SDC2, CDH5, VCAM1, ITGA9, CD80, CD34, ITGAV, PVRL2, CD58, PECAM1, SPN | 2.4 |
| Lysosome | 7.7×10^{-4} | SGSH, CTSL2, LIPA, GM2A, PSAP, HEXB, CD63, CTSL1, ASAH1, GNS, LAMP2, CTSK, CD68, NPC1, AP3M2, GNPTAB, IGF2R, CTSD, CTSC, CTSB, SCARB2, CD14 | 2.3 |
| Regulation of actin cytoskeleton | 1.5×10^{-3} | SSH1, DIAPH2, MRAS, DIAPH3, ITGB5, ABI2, IQGAP2, RDX, GNG12, PXN, DOCK1, PAK2, ITGAX, TIAM1, PAK3, ITGAV, RAC1, PDGFC, PIK3R3, FGF2, FN1, EGFR, ACTN1, NCKAP1, ITGA9, PDGFRA, PDGFRB, CYFIP1, WASL, CD14, MYLK | 1.8 |
| Adherens junction | 2.6×10^{-3} | EGFR, PTPRB, PTPRF, MET, ACTN1, SNAI2, TCF7L2, TCF7L1, TJP1, RAC1, PVRL2, SSX2IP, WASL, YES1, INSR | 2.4 |
| Cytokine-cytokine receptor interaction | 4.9×10^{-3} | TNFRSF21, IL1R1, ACVRL1, OSMR, IL18, KITLG, CD70, CX3CL1, TNFRSF4, CXCL12, TNFRSF1A, CCL21, TNFRSF18, PDGFC, FAS, IL13RA1, CSF2RA, CSF1R, EGFR, LTBR, FLT1, MET, LIFR, CCL19, CCL11, TNFRSF9, ACVR2A, VEGFC, TNFSF13B, CXCL16, PDGFRA, PDGFRB, IL3RA | 1.6 |

| | | | |
|-------------------------------|------------------------|------------------------------------------------------------------------------------------------------------------|-----|
| Gap junction | 9.8 x 10 ⁻³ | EGFR, GNAI1, GJA1, LPAR1, TJP1, PLCB4, GNAQ, ADCY9, PDGFRA, GUCY1A3, PDGFRB, GUCY1B3, PDGFC, HTR2B, PLCB1 | 2.1 |
| Ether lipid metabolism | 1.8 x 10 ⁻² | PLA2G4A, PLD1, ENPP2, PLA2G7, PPAP2A, PLA2G2D, AGPAT3, PPAP2B | 2.9 |
| PPAR signalling pathway | 1.9 x 10 ⁻² | ACOX2, ME1, LPL, CYP27A1, RXRA, SCD, PPARG, FABP3, SCD5, ACSL3, PLTP, NR1H3 | 2.2 |
| Tight junction | 6.4 x 10 ⁻² | F11R, MAGI2, MAGI1, MPDZ, GNAI1, MRAS, MPP5, ACTN1, CASK, AMOTL1, EPB41L3, TJP1, CTTN, PARD6G, RAB13, YES1, AKT3 | 1.6 |
| Hematopoietic cell lineage | 7.7 x 10 ⁻² | CD9, IL1R1, CD8A, TFRC, CD34, CD33, CD59, KITLG, CSF2RA, IL3RA, CD14, CSF1R | 1.8 |
| Glycosaminoglycan degradation | 8.0 x 10 ⁻² | SGSH, GNS, HYAL2, HS3ST3A1, HEXB | 3.0 |

Down compared to Tonsil

| Term | PValue | Genes | Fold Enrichment |
|----------------------------------------------|------------------------|-----------------------------------------------------------------------------------------------------------------------|------------------------|
| B cell receptor signaling pathway | 4,6 x 10 ⁻⁶ | PTPN6, MAPK1, CD19, VAV3, DAPP1, PLCG2, PPP3CC, PIK3AP1, PPP3CA, PRKCB, SYK, AFF3, AICDA, BACH2, BANK1, CD19, IGH@... | 3.9 |
| Hematopoietic cell lineage | 4.6 x 10 ⁻³ | CD38, CR1, CD37, IL9R, CD19, IL7, FCER2, MS4A1, CD1C | 3.1 |
| Calcium signaling pathway | 6.0 x 10 ⁻³ | TACR2, CAMK2G, TACR1, MYLK3, ITPR1, PRKCB, CD38, PDE1B, GRIN2C, PLCG2, PPP3CC, PLCD4, PPP3CA | 2.3 |
| Phosphatidylinositol signaling system | 6.2 x 10 ⁻³ | DGKD, PIK3C2B, PLCG2, SYNJ2, PLCD4, ITPR1, PRKCB | 3.2 |
| Long-term potentiation | 1.3 x 10 ⁻² | MAPK1, GRIA2, GRIN2C, CAMK2G, PPP3CC, PPP3CA, ITPR1, PRKCB | 3.1 |
| Inositol phosphate metabolism | 1.5 x 10 ⁻² | ISYNA1, PIK3C2B, PLCG2, SYNJ2, PLCD4 | 3.4 |
| Fc epsilon RI signaling pathway | 2.3 x 10 ⁻² | FCER1A, MAPK1, JMJD7-PLA2G4B, VAV3, PLCG2, PLA2G4B, PRKCB, SYK | 2.7 |
| Natural killer cell mediated cytotoxicity | 2.7 x 10 ⁻² | PTPN6, MAPK1, VAV3, PLCG2, PPP3CC, KIR2DS3, PPP3CA, NCR2, PRKCB, NCR3, SYK | 2.2 |
| VEGF signaling pathway | 6.2 x 10 ⁻² | MAPK1, JMJD7-PLA2G4B, PLCG2, PPP3CC, PPP3CA, PLA2G4B, PRKCB | 2.5 |
| GnRH signaling pathway | 7.4 x 10 ⁻² | MAPK1, JMJD7-PLA2G4B, MAP3K4, MAP3K1, CAMK2G, PLA2G4B, ITPR1, PRKCB | 2.2 |
| Intestinal immune network for IgA production | 7.2 x 10 ⁻² | TNFRSF13C, AICDA, MAP3K14, HLA-DOB, ICOSLG | 3.1 |

Suppl. Table 5: Cytogenetic characteristics of lymphomas in IL-10R deficient patients

| | | cytogenetic analysis |
|-----------|----|------------------------------------------------------------------------------------------------------------------------------|
| P1 | L1 | 45, X t(2;14)(q32;q34) |
| P2 | L1 | ND |
| P3 | L1 | 46,XY,del(1)(p3?p?),add(2)(p25)or dup(2)(p?p?),-5,add(5)(p14),del(9)(q22q32),del(13)(q14q31),add(14)(q32),+mar[15]/46,XY[1] |
| P4 | L1 | 54,XY,+X,+2,+8,+11,+12,+13,?del(18),+19,+20,+21,+22[cp5]/46,XY[7] |
| | L2 | 50,XY,+?add(1)(p?11),+2,add(3)(q27),add(6)(p11),+7,- 8,+12,del(15)(q?),+16[17] |
| | L3 | 46XY, del(1)(p32) or del(1)(p31p34) ,t(4;10)(q28;p14), t(5;14)(q23;q32);der(8)t(X;8)(?;p12),der(10)t(10;13)(p14;p14)/46XY[1] |
| | L4 | ND |
| P5 | L1 | ND |

Suppl. Table 6: Segments (regions) of tumor-acquired copy number alterations identified by array CGH in P3-L1, P4-L1, P4-L2 and P5-L1 lymphomas

| Patient ID | Chr | Cytoband | Start* | Stop* | Size | Aberration | First 10 gene names in segment |
|------------|-------|-----------------|-----------|-----------|-----------|----------------|-------------------------------------------------------------------------------------------------|
| P3-L1 | chr1 | p36.33 - p34.3 | 649718 | 38086410 | 37436692 | loss | LOC100133331, NCRNA00115, LOC643837, FAM41C, FLJ39609, SAMD11, NOC2L, KLHL17, PLEKHN1, C1orf170 |
| P3-L1 | chr2 | p16.3 - p12 | 48763856 | 77575248 | 28811392 | gain | STON1-GTF2A1L, STON1, GTF2A1L, LHCGR, FSHR, NRXN1, ASB3, LOC100302652, CHAC2, ERLEC1 |
| P3-L1 | chr9 | q21.33 - q31.1 | 86920129 | 107998204 | 21078075 | loss | SLC28A3, NTRK2, AGTPBP1, LOC389765, NAA35, GOLM1, C9orf153, ISCA1, ZCCHC6, GAS1 |
| P3-L1 | chr11 | q11 | 55368154 | 55450788 | 82634 | loss | OR4C11, OR4P4, OR4S2, OR4C6 |
| P3-L1 | chr12 | p13.33 - p13.32 | 361756 | 5393483 | 5031727 | gain | SLC6A13, KDM5A, CCDC77, B4GALNT3, NINJ2, WNK1, HSN2, RAD52, ERC1, LOC100292680 |
| P3-L1 | chr14 | q11.2 | 20198936 | 20420849 | 221913 | loss | OR4Q3, OR4M1, OR4N2, OR4K2, OR4K5, OR4K1 |
| P3-L1 | chr14 | q11.2 | 22578531 | 23001999 | 423468 | loss | |
| P3-L1 | chr15 | q11.1 - q11.2 | 20530575 | 22756564 | 2225989 | loss | GOLGA6L6, GOLGA8C, BCL8, POTE8, NF1P1, LOC646214, CXADRP2, LOC727924, OR4M2, OR4N4 |
| P3-L1 | chr15 | q14 | 34718131 | 34791250 | 73119 | gain | GOLGA8A |
| P3-L1 | chr16 | p11.2 | 32051472 | 33631581 | 1580109 | gain | HERC2P4, TP53TG3B, TP53TG3, SLC6A10P |
| P3-L1 | chr21 | q22.3 | 45642829 | 48090317 | 2447488 | loss | ICOSLG, DNMT3L, AIRE, PFKL, C21orf2, TRPM2, LRRC3, C21orf29, C21orf90, KRTAP10-1, ... |
| P4-L1 | chr2 | p25.3 - p11.2 | 30341 | 243041364 | 243011023 | gain | FAM110C, SH3YL1, ACP1, FAM150B, TMEM18, C2orf90, SNTG2, TPO, PXDN, MYT1L |
| P4-L1 | chr2 | p16.1 | 60932053 | 61204840 | 272787 | biallelic gain | PAPOLG, REL, PUS10 |
| P4-L1 | chr7 | q34 - q36.3 | 138738216 | 159118566 | 20380350 | gain | ZC3HAV1, TTC26, UBN2, C7orf55, LUC7L2, KLRG2, CLEC2L, HIPK2, TBXAS1, PARP12 |
| P4-L1 | chr8 | p23.3 - p12 | 229928 | 29493887 | 29263959 | loss | FBXO25, C8orf42, ERICH1, DLGAP2, CLN8, MIR596, ARHGEF10, KBTBD11, MYOM2, CSMD1 |
| P4-L1 | chr10 | q11.22 | 46951237 | 47148546 | 197309 | gain | SYT15, GPRIN2, PPYR1, LOC728643 |
| P4-L1 | chr11 | p15.5 - p11.12 | 192372 | 134802563 | 134610191 | gain | LOC653486, SCGB1C1, ODF3, BET1L, RIC8A, SIRT3, PSMD13, NLRP6, ATHL1, IFITM5 |
| P4-L1 | chr12 | p13.33 - q24.33 | 163593 | 133747307 | 133583714 | gain | IQSEC3, SLC6A12, SLC6A13, KDM5A, CCDC77, B4GALNT3, NINJ2, WNK1, HSN2, RAD52 |
| P4-L1 | chr13 | q11 - q34 | 19296527 | 115105806 | 95809279 | gain | LOC284232, LOC348021, DKFZp686A1627, TUBA3C, LOC100101938, TPTE2, MPHOSPH8, PSPC1, ZMYM5, ZMYM2 |
| P4-L1 | chr14 | q11.2 | 19434575 | 20420849 | 986274 | loss | POTEG, P704P, OR4Q3, OR4M1, OR4N2, OR4K2, OR4K5, OR4K1 |

| | | | | | | | |
|-------|-------|-----------------|-----------|-----------|-----------|------|--------------------------------------------------------------------------------------|
| P4-L1 | chr14 | q32.33 | 106072662 | 106209522 | 136860 | gain | |
| P4-L1 | chr14 | q32.33 | 106259868 | 106552084 | 292216 | loss | KIAA0125, ADAM6 |
| P4-L1 | chr15 | q11.1 - q11.2 | 20481702 | 22578630 | 2096928 | loss | GOLGA6L6, GOLGA8C, BCL8, POTE, NF1P1, LOC646214, CXADRP2, LOC727924, OR4M2, OR4N4 |
| P4-L1 | chr16 | p11.2 | 32051472 | 33625989 | 1574517 | gain | HERC2P4, TP53TG3B, TP53TG3, SLC6A10P |
| P4-L1 | chr17 | q21.31 | 44165726 | 44628150 | 462424 | gain | KIAA1267, LRRC37A, ARL17A, ARL17B, LRRC37A2 |
| P4-L1 | chr19 | p13.3 - p12 | 288700 | 59092570 | 58803870 | gain | PPAP2C, MIER2, THEG, C2CD4C, SHC2, ODF3L2, MADCAM1, C19orf20, CDC34, GZMM |
| P4-L1 | chr20 | p13 - p11.1 | 60747 | 62908674 | 62847927 | gain | DEFB125, DEFB126, DEFB127, DEFB128, DEFB129, DEFB132, C20orf96, ZCCHC3, SOX12, NRSN2 |
| P4-L1 | chr21 | q11.2 - q22.3 | 15398168 | 48090317 | 32692149 | gain | LIPI, RBM11, ABCC13, HSPA13, SAMSN1, NRIP1, USP25, C21orf34, MIR99A, MIRLET7C |
| P4-L1 | chr22 | q11.1 - q13.33 | 17065654 | 51219009 | 34153355 | gain | CCT8L2, psiTPTE22, XKR3, HSFYP1, GAB4, CECR7, IL17RA, CECR6, CECR5, CECR4 |
| P4-L1 | chrX | p22.33 - q26 | 2700316 | 154929279 | 152228963 | gain | XG, GYG2, ARSD, ARSE, ARSH, ARSF, MXRA5, PRKX, NLGN4X, VCX3A |
| P4-L1 | chrY | p11.31 - q11.23 | 2650450 | 28562852 | 25912402 | loss | SRY, RPS4Y1, ZFY, TGIF2LY, PCDH11Y, LOC100101121, TTTY23, TSPY2, TTTY1B, TTTY2B |
| P4-L2 | chr2 | p16.1 - p15 | 58948801 | 62938098 | 3989297 | gain | BCL11A, PAPOLG, REL, PUS10, PEX13, KIAA1841, C2orf74, AHSA2, USP34, SNORA70B |
| P4-L2 | chr14 | q11.2 | 22289891 | 23001999 | 712108 | loss | |
| P5-L1 | chr2 | p16.1 - p15 | 60541722 | 61940843 | 1399121 | gain | BCL11A, PAPOLG, REL, PUS10, PEX13, KIAA1841, C2orf74, AHSA2, USP34, SNORA70B |
| P5-L1 | chr3 | p14.1 | 66302508 | 67891719 | 1589211 | gain | SLC25A26, LRIG1, KBTBD8, SUCLG2 |
| P5-L1 | chr3 | q29 | 195482573 | 196302999 | 820426 | gain | MUC4, TNK2, SDHAP1, TFRC, ZDHHC19, OSTalpha, PCYT1A, TCTEX1D2, TM4SF19, UBXN7 |
| P5-L1 | chr7 | P22.3 - q36.3 | 45130 | 159118566 | 159073436 | gain | FAM20C, LOC442497, PDGFA, FLJ44511, PRKAR1B, HEATR2, SUN1, GET4, ADAP1, COX19 |
| P5-L1 | chr10 | p12.1 | 28220255 | 28264176 | 43921 | loss | ARMC4 |
| P5-L1 | chr10 | q11.22 | 46951237 | 48334466 | 1383229 | gain | SYT15, GPRIN2, PPYR1, LOC728643, ANXA8, ANXA8L1, FAM25B, FAM25C, FAM25G, LOC642826 |
| P5-L1 | chr11 | q13.1 - q25 | 64023191 | 134868407 | 70845216 | gain | PLCB3, BAD, GPR137, KCNK4, C11orf20, ESRRA, TRMT112, PRDX5, CCDC88B, RPS6KA4 |
| P5-L1 | chr12 | p13.33 - q24.33 | 163593 | 133747307 | 133583714 | gain | IQSEC3, SLC6A12, SLC6A13, KDM5A, CCDC77, B4GALNT3, NINJ2, WNK1, RAD52, ERC1 |
| P5-L1 | chr14 | q11.2 | 20198936 | 20420849 | 221913 | loss | OR4Q3, OR4M1, OR4N2, OR4K2, OR4K5, OR4K1 |
| P5-L1 | chr14 | q11.2 | 22378795 | 22976316 | 597521 | loss | |

| | | | | | | | |
|-------|-------|-----------------|----------|-----------|-----------|------|-----------------------------------------------------------------------------------------|
| P5-L1 | chr15 | q11.1 - q11.2 | 20481702 | 20870793 | 389091 | loss | GOLGA6L6, GOLGA8C |
| P5-L1 | chr15 | q11.2 | 21272376 | 22578630 | 1306254 | loss | LOC646214, CXADRP2, POTE, NF1P1, LOC727924, OR4M2, OR4N4, OR4N3P |
| P5-L1 | chr15 | q15.3 | 43888927 | 43995250 | 106323 | gain | CKMT1B, STRC, CATSPER2, CKMT1A |
| P5-L1 | chr16 | p11.2 | 29712047 | 31062281 | 1350234 | gain | C16orf54, ZG16, KIF22, MAZ, PRRT2, C16orf53, MVP, CDIPT, LOC440356, SEZ6L2 |
| P5-L1 | chr16 | p11.2 | 32051472 | 33625989 | 1574517 | gain | HERC2P4, TP53TG3B, TP53TG3, SLC6A10P |
| P5-L1 | chr17 | p11.2 | 19470255 | 19677849 | 207594 | gain | SLC47A1, ALDH3A2, SLC47A2, ALDH3A1, ULK2 |
| P5-L1 | chr17 | p11.2 - p11.1 | 20581394 | 22218445 | 1637051 | gain | CCDC144NL, USP22, DHRS7B, TMEM11, C17orf103, MAP2K3, KCNJ12, C17orf51, FAM27L, FLJ36000 |
| P5-L1 | chr17 | q11.1 - q11.2 | 25318639 | 27771401 | 2452762 | gain | WSB1, KSR1, LGALS9, NOS2, C17orf108, NLK, PYY2, PPY2, FLJ40504, TMEM97 |
| P5-L1 | chr17 | q11.2 | 27778485 | 30374632 | 2596147 | gain | TAOK1, ABHD15, TP53I13, GIT1, ANKRD13B, CORO6, SSH2, EFCAB5, CCDC55, MIR423 |
| P5-L1 | chr17 | q11.2 - q12 | 30426721 | 33921052 | 3494331 | loss | RHOT1, RHBDL3, C17orf75, ZNF207, PSMD11, CDK5R1, MYO1D, TMEM98, SPACA3, ASIC2 |
| P5-L1 | chr17 | q21.31 | 44165726 | 44628150 | 462424 | gain | KIAA1267, LRRC37A, ARL17A, ARL17B, LRRC37A2 |
| P5-L1 | chr17 | q22 | 54214083 | 56896140 | 2682057 | loss | ANKFN1, NOG, C17orf67, DGKE, MTRR2, TRIM25, COIL, SCPEP1, RNF126P1, AKAP1 |
| P5-L1 | chr17 | q23.2 - q24.1 | 59093083 | 62955304 | 3862221 | gain | BCAS3, TBX2, C17orf82, TBX4, NACA2, BRIP1, INTS2, MED13, TBC1D3P2, EFCAB3 |
| P5-L1 | chr21 | q21.3 - q22.11 | 15398168 | 48090317 | 32692149 | gain | AKAP8, AKAP8L, WIZ, RASAL3, PGLYRP2, CYP4F22, CYP4F8, CYP4F3, CYP4F12, ORIOH2 |
| P5-L1 | chr22 | q11.23 | 23745288 | 23979347 | 234059 | gain | IGLL1, C22orf43 |
| P5-L1 | chrX | p22.33 - q26 | 2724453 | 154929279 | 152204826 | gain | XG, GYG2, ARSD, ARSE, ARSH, ARSF, MXRA5, PRKX, NLGN4X, VCX3A |
| P5-L1 | chrY | p11.31 - q11.23 | 2650450 | 28536142 | 25885692 | loss | SRY, RPS4Y1, ZFY, TGIF2LY, PCDH11Y, LOC100101121, TTTY23, TSPY2, LOC100101116 |

* Numbering according to the human Genome hg 19 assembly
Segments highlighted in red represent 2p16 amplified region

Suppl. Table 7: List of NF- κ B pathways activated in P3-L1, P4-L2 and P5-L1 as compared to non malignant GC B-cells and GC-derived DLBCLs

P3-L1, P4-L2 and P5-L1 vs non malignant GC-B cells

| Pathways | p-Value | Genes |
|-------------------------------------------|----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cytosolic DNA-sensing pathway | 8.5×10^{-8} | POLR3G, IKBKE, TBK1, NFKBIB, NFKBIA, POLR1C, CASP1, CCL5, CCL4, CHUK, AIM2 |
| NOD-like receptor signaling pathway | 2.8×10^{-7} | HSP90AB1, NOD2, HSP90B1, CCL2, NFKBIB, NFKBIA, TNFAIP3, CASP1, BIRC3, CCL5, CHUK |
| Apoptosis | 8.8×10^{-7} | TRAF2, TNFRSF1A, CFLAR, IL1R1, TNFSF10, TNFRSF10B, CSF2RB, NFKBIA, FASLG, FADD, BIRC3, CHUK, ... |
| Cytokine-cytokine receptor interaction | 2.9×10^{-6} | IL1R1, CCL2, LTBR, CCR1, GDF5, FASLG, TNFSF14, TNFSF13, CCL5, CCL4, IL10, TNFRSF1A, TNFSF10, TNFRSF10B, TNFSF13B, IFNG, CSF2RB, IL2RG, CD27 |
| Toll-like receptor signaling pathway | 2.6×10^{-5} | IKBKE, TBK1, TLR2, NFKBIA, TLR3, FADD, TLR4, STAT1, CCL5, CCL4, CHUK |
| T cell receptor signaling pathway | 1.3×10^{-3} | BCL10, NRAS, NFKBIE, PAK4, NFKBIB, IFNG, NFKBIA, CHUK, IL10 |
| RIG-I-like receptor signaling pathway | 2.7×10^{-3} | TRAF2, IKBKE, TBK1, NFKBIB, NFKBIA, FADD, CHUK |
| Natural killer cell mediated cytotoxicity | 4.7×10^{-3} | ICAM1, NRAS, TNFSF10, TNFRSF10B, IFNG, FASLG, HLA-B, HLA-G, HCST |
| Allograft rejection | 5.3×10^{-3} | IFNG, FASLG, HLA-B, HLA-G, IL10 |
| Adipocytokine signaling pathway | 1.1×10^{-3} | TRAF2, TNFRSF1A, NFKBIE, NFKBIB, NFKBIA, CHUK |
| Chemokine signaling pathway | 1.1×10^{-3} | NRAS, CCL2, CCR1, NFKBIB, NFKBIA, STAT1, CCL5, GNG5, CCL4, CHUK |
| Pathways in cancer | 1.2×10^{-3} | HSP90AB1, TRAF1, TRAF2, PTGS2, MMP9, FASLG, NFKBIA, FADD, NFKB2, BIRC3, STAT1, NRAS, HSP90B1, CHUK, TRAF1, TRAF2, PTGS2, NFKBIA, BIRC3, CHUK, HSP90AB1, NRAS, HSP90B1, CREB1, NFKBIA, CHUK, |
| B cell receptor signaling pathway | 1.6×10^{-3} | BCL10, NRAS, NFKBIE, NFKBIB, NFKBIA, CHUK |

P3-L1, P4-L2 and P5-L1 vs GC-derived DLBCL cells

| Pathways | p-Value | Genes |
|--------------------------------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Toll-like receptor signaling pathway | 3.8×10^{-17} | IRAK1, TBK1, TLR1, TLR2, TLR3, NFKB1, TLR4, CD40, TLR6, STAT1, CCL5, CCL4, FOS, MYD88, JUN, TICAM1, CASP8, IL1B, TRAF6, IKBKB, CHUK, TRAF3, TNF, |
| NOD-like receptor signaling pathway | 1.7×10^{-13} | NFKBIB, NFKB1, BIRC3, CCL5, BIRC2, NOD2, HSP90B1, NOD1, ERBB2IP, CASP8, IL1B, TNFAIP3, TRAF6, IKBKB, CASP1, CHUK |
| Apoptosis/p53 signalling pathway | 3.4×10^{-11} | IRAK1, CFLAR, IL1R1, FASLG, NFKB1, BIRC3, BIRC2, TNFRSF10A, TNFRSF1A, MYD88, TNFRSF10B, CASP8, CSF2RB, IL1B, IKBKB, CHUK, TNFRSF10B, SERPINE1, CASP8, PMAIP1, GADD45B, CCNG2 |
| B cell receptor signaling pathway | 9.8×10^{-8} | BCL10, NRAS, FOS, NFKBIE, JUN, NFKBIB, RAF1, NFKB1, MALT1, IKBKB, VAV1, CHUK |

| | | |
|-----------------------------------------------|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| T cell receptor signaling pathway | 5.8 x 10 ⁻⁸ | BCL10, NFKBIE, NFKBIB, RAF1, NFKB1, MALT1, VAV1, IL10, FOS, NRAS, JUN, IKBKB, CHUK |
| Cytosolic DNA-sensing pathway | 6.5 x 10 ⁻⁶ | TBK1, NFKBIB, IL1B, NFKB1, CASP1, IKBKB, CCL5, CCL4, CHUK |
| Neurotrophin signaling pathway | 1.6 x 10 ⁻⁵ | IRAK1, NRAS, NFKBIE, MAP3K1, JUN, NFKBIB, YWHAB, RAF1, FASLG, NFKB1, TRAF6, IKBKB |
| Pathways in cancer | 2.7 x 10 ⁻⁵ | TRAF1, PTGS2, MMP9, STAT5A, FASLG, RAF1, NFKB1, BIRC3, STAT1, BIRC2, FOS, NRAS, HSP90B1, JUN, CASP8, TRAF6, IKBKB, CHUK, TRAF3, RAF1, NFKB1, IKBKB, STAT1, CHUK, NRAS, STAT5A, RAF1, NFKB1, IKBKB, CHUK, NRAS, HSP90B1, CREB1, RAF1, NFKB1, IKBKB, CHUK |
| RIG-I-like receptor signaling pathway | 4.5 x 10 ⁻⁵ | TBK1, MAP3K1, NFKBIB, CASP8, NFKB1, TRAF6, IKBKB, CHUK, TRAF3 |
| Cytokine-cytokine receptor interaction | 8.6 x 10 ⁻⁵ | IL1R1, LTBR, CCR1, FASLG, TNFSF14, CD40, CCL5, CCL4, IL10, TNFRSF10A, TNFRSF1A, TNFRSF10B, CSF2RB, IL1B, IFNGR1, CD27 |
| Small cell lung cancer | 1.5 x 10 ⁻⁴ | TRAF1, PTGS2, NFKB1, TRAF6, IKBKB, BIRC3, BIRC2, CHUK, TRAF3 |
| Natural killer cell mediated cytotoxicity | 1.6 x 10 ⁻⁴ | TNFRSF10A, NRAS, TNFRSF10B, RAF1, FASLG, HLA-B, NCR1, VAV1, HLA-G, IFNGR1, HCST |
| MAPK signaling pathway | 3.8 x 10 ⁻⁴ | IL1R1, RELB, FASLG, RAF1, NFKB1, FOS, NRAS, TNFRSF1A, MAP3K1, JUN, IL1B, GADD45B, IKBKB, TRAF6, CHUK |
| Allograft rejection | 4.9 x 10 ⁻⁴ | FASLG, HLA-B, CD40, HLA-G, IL10, HLA-F |
| Adipocytokine signaling pathway | 1.4 x 10 ⁻³ | TNFRSF1A, NFKBIE, NFKBIB, PRKAB2, NFKB1, IKBKB, CHUK |
| Chemokine signaling pathway | 2.3 x 10 ⁻³ | NRAS, CCR1, NFKBIB, RAF1, NFKB1, IKBKB, STAT1, CCL5, VAV1, CCL4, CHUK |

Suppl. Table 8: somatic mutations identified in whole exome sequencing in P3-L1, P4-L1 and P4-L2 lymphomas

| Sample ID | gene name | chr | Start^ | End | ref. N. | var. N | % | cov T | cov N | mut. type | mutation | Polyphen | Sift | cosmic all | Cosmic HP | CCDS ID |
|-----------|--------------|----------|-----------------|-----------------|----------|----------|-----------|-----------|------------|-----------------|---------------|-------------|-------------|-----------------|-----------------|---------|
| P3-L1 | KLHL17 | 1 | 896467 | 901595 | A | G | 40 | 2 | 3 | missense | R567G | 0.99 | 0 | 14/5089 | 0/462 | 30550.1 |
| P3-L1 | ZBTB8B | 1 | 32931170 | 32953961 | C | T | 31 | 11 | 24 | missense | P252L | 0.235 | 0.1 | 819605 | 0/462 | 44104.1 |
| P3-L1 | TRANK1 | 3 | 36868811 | 36987048 | G | A | 24 | 45 | 140 | missense | R947H | 0.008 | 0.05 | 58/4171 | 1/462 | 46789.2 |
| P3-L1 | MYD88 | 3 | 38180469 | 38185013 | C | G | 26 | 61 | 175 | missense | S219C | 0.98 | 0.01 | 236/5868 | 225/1683 | 2674.2 |
| P3-L1 | CCR1 | 3 | 46243700 | 46250387 | C | T | 30 | 27 | 82 | missense | T342I | 0,001 | 0.22 | 20/5640 | 0/462 | 2737.1 |
| P3-L1 | ZNF518B | 4 | 10441998 | 10459534 | A | C | 15 | 9 | 49 | missense | E644D | 0.86 | 0 | 37/4216 | 0/462 | 33960.1 |
| P3-L1 | TMCO6 | 5 | 140019512 | 140025493 | G | T | 15 | 9 | 50 | missense | R76L | 0.99 | 0 | 16/5089 | 0/462 | 4233.2 |
| P3-L1 | BNIP1 | 5 | 172571945 | 172591890 | G | A | 21 | 17 | 63 | missense | E200K | 0,205 | 0.12 | 15/5209 | 0/462 | 4385.1 |
| P3-L1 | TDRD6 | 6 | 46656112 | 46672556 | T | C | 23 | 10 | 33 | missense | S1722P | 0.002 | 0.22 | 80/4287 | 1/462 | 34470.1 |
| P3-L1 | OPRM1 | 6 | 154332131 | 154568501 | G | C | 21 | 28 | 107 | missense | E351D | 0,033 | 0.51 | 32/4212 | 1/462 | 55070.1 |
| P3-L1 | ZAN | 7 | 100331249 | 100395419 | C | A | 20 | 10 | 40 | missense | R2134S | 0 | 0.73 | 119/4283 | 0/462 | NA |
| P3-L1 | CNTNAP2 | 7 | 145813953 | 148118590 | AAG | CCT | 38 | 6 | 10 | missense | K441P | 0.637 | | 150/4238 | 2/462 | 5889.1 |
| P3-L1 | CNTNAP2 | 7 | 145813953 | 148118590 | A | C | 46 | 6 | 7 | missense | M442L | 0 | 0.35 | 150/4238 | 2/462 | 5889.1 |
| P3-L1 | NCOA2 | 8 | 71022497 | 71316540 | G | A | 18 | 21 | 95 | missense | G1306R | 0.798 | 0 | 54/4856 | 0/462 | 47872.1 |
| P3-L1 | VPS13B | 8 | 100025994 | 100890308 | G | A | 21 | 11 | 40 | missense | R2643Q | 0.99 | 0.01 | 156/4515 | 4/463 | 6280.1 |
| P3-L1 | GRHL2 | 8 | 102505160 | 102682454 | G | A | 24 | 13 | 40 | missense | R209H | 0.93 | 0 | 27/4238 | 0/462 | 34931.1 |
| P3-L1 | SOX5 | 12 | 23682940 | 24104466 | G | A | 17 | 6 | 29 | missense | A438T | 0,021 | 0.61 | 52/ 4782 | 1/462 | 44844.1 |
| P3-L1 | C12orf56 | 12 | 64661263 | 64784971 | T | G | 32 | 8 | 17 | missense | I85M | 0.99 | | 15/4216 | 0/462 | 44935.1 |
| P3-L1 | C12orf56 | 12 | 64661263 | 64784971 | G | T | 36 | 8 | 14 | missense | D86Y | 0.98 | 0.23 | 15/4216 | 0/462 | 44935.1 |
| P3-L1 | SALL1 | 16 | 51170386 | 51185778 | G | A | 21 | 15 | 56 | missense | G596R | 0.89 | 0.5 | 104/4239 | 0/462 | 10747.1 |
| P3-L1 | B3GNT9 | 16 | 67182508 | 67185617 | T | C | 45 | 9 | 11 | missense | F318S | 0.99 | 0 | 819757 | 1/462 | 45509.1 |
| P3-L1 | PRR11 | 17 | 57233601 | 57280424 | G | C | 31 | 5 | 11 | missense | R296P | 0.99 | 0 | 16/5240 | 0/462 | 11614.1 |
| P3-L1 | MBP | 18 | 74691283 | 74846139 | C | T | 26 | 16 | 46 | missense | A71V | 0.549 | 0.07 | 14/4652 | 1/462 | 42450.1 |
| P3-L1 | MORC2 | 22 | 31323096 | 31364784 | G | A | 16 | 32 | 164 | missense | R 91Q | 0.003 | 0.62 | 19/4238 | 0/462 | 33636.1 |
| P3-L1 | CPT1B | 22 | 51007790 | 51018399 | G | A | 28 | 20 | 50 | splice site | c.970+1 | na | na | 20/4263 | 0/462 | 14098.1 |
| P3-L1 | HPRT1 | X | 133594683 | 133655043 | AG | GA | 37 | 3 | 5 | splice site | c.385-1 | na | na | 11/5209 | 0/462 | 14641.1 |
| P4-L1 | SFPQ | 1 | 35642479 | 35659249 | T | C | 22 | 13 | 45 | missense | F300L | 0.86 | 0.02 | 22/4450 | 0/462 | 388.1 |
| P4-L1 | GTF2A1L | 2 | 48845437 | 48960787 | C | T | 40 | 37 | 127 | missense | L4F | 0 | 0.17 | 97/5023 | 0/514 | 46281.1 |
| P4-L1 | CCDC148 | 2 | 159027593 | 159313265 | A | G | 50 | 8 | 8 | missense | K415E | 0.065 | 0.11 | 23/4216 | 0/462 | 33304.1 |
| P4-L1 | LPHN3 | 4 | 62067476 | 62938684 | G | T | 17 | 10 | 47 | missense | A523S | 0.017 | 0.23 | 109/4653 | 5/462 | 54768.1 |
| P4-L1 | DDX60L | 4 | 169278386 | 169459437 | | | | 10 | 13 | splice site | c.3811-4 insC | na | na | 39/ 4216 | 2/462 | 47161.1 |
| P4-L1 | C7 | 5 | 40909854 | 40983541 | A | T | 28 | 8 | 21 | missense | L324F | 0.192 | 0.23 | UK | UK | 47201.1 |

| | | | | | | | | | | | | | | | | |
|-------|----------|----|-----------|-----------|---|---|----|----|-----|-------------|-----------|-------|------|-----------|-------|---------|
| P4-L1 | LIX1 | 5 | 96428074 | 96479076 | C | G | 31 | 11 | 24 | missense | D137E | 0.5 | 0.03 | 853085 | 0/462 | 4088.1 |
| P4-L1 | E2F3 | 6 | 20402637 | 20494445 | C | A | 40 | 2 | 3 | missense | P345H | 0.98 | 0 | 965518 | 0/462 | 4545.1 |
| P4-L1 | TRRAP | 7 | 98476056 | 98611366 | A | G | 33 | 8 | 17 | missense | M1711V | 0.024 | 0.17 | 143/ 5046 | 0/489 | 5659.1 |
| P4-L1 | CFTR | 7 | 117106338 | 117309219 | | | 22 | 11 | 35 | nonsense | G493X | na | na | 59/ 4662 | 0/462 | 5773.1 |
| P4-L1 | PBX3 | 9 | 128510124 | 128730156 | A | C | 40 | 4 | 6 | missense | I382L | 0.301 | 0.11 | 22/4238 | 1/462 | 6865.1 |
| P4-L1 | C9orf96 | 9 | 136243617 | 136271720 | C | A | 21 | 14 | 31 | splice site | c.870 +3 | na | na | 24/4469 | 0/489 | 35169.1 |
| P4-L1 | C9orf169 | 9 | 140119587 | 140121263 | A | G | 20 | 2 | 6 | missense | H125R | 0 | 0.04 | 2/4999 | 0/462 | 48064.1 |
| P4-L1 | TNKS1BP1 | 11 | 57067612 | 57092926 | C | T | 35 | 9 | 17 | missense | A286V | 0.127 | 0.04 | 59/4238 | 2/462 | 7951.1 |
| P4-L1 | NUBPL | 14 | 31959662 | 32330930 | A | C | 60 | 9 | 6 | missense | Q237H | 0.973 | 0 | 6/5209 | 0/462 | 41940.1 |
| P4-L1 | NUBPL | 14 | 31959662 | 32330930 | A | C | 56 | 9 | 6 | missense | N238H | 1 | 0 | 6/5209 | 0/462 | 41940.1 |
| P4-L1 | NFKBIA | 14 | 35871217 | 35874455 | C | T | 20 | 12 | 46 | nonsense | Q68X | na | na | 11/5083 | 0/462 | 9656.1 |
| P4-L1 | RCOR1 | 14 | 103059498 | 103197412 | G | A | 20 | 5 | 20 | splice site | c.651+1 | na | na | 16/5090 | 0/462 | 9974.2 |
| P4-L1 | NCOR1 | 17 | 15935218 | 16119510 | A | G | 20 | 18 | 55 | missense | T2366A | 0.031 | 0.17 | 95/4451 | 1/462 | 11175.1 |
| P4-L1 | DSC1 | 18 | 28709699 | 28743319 | C | A | 15 | 9 | 52 | nonsense | S142X | na | na | 51/4239 | 1/462 | 11895.1 |
| P4-L1 | ZNF557 | 19 | 7069971 | 7088479 | G | A | 19 | 8 | 34 | missense | A196T | 0 | 0.68 | 17/ 4238 | 0/462 | 42485.1 |
| P4-L1 | USP25 | 21 | 17102844 | 17252877 | C | T | 27 | 27 | 82 | splice site | c.123 +7 | na | na | 44/ 4789 | 0/462 | 33515.1 |
| | | | | | | | | | | | | | | | | |
| P4-L2 | FAM123C | 2 | 131513508 | 131526207 | G | A | 17 | 12 | 60 | missense | G580E | 0.2 | 0.25 | 69/4212 | 0/462 | 2164.1 |
| P4-L2 | FAM124B | 2 | 225243915 | 225267302 | C | A | 18 | 13 | 58 | missense | P317H | 0.637 | 0.03 | 16/4238 | 0/462 | 46527.1 |
| P4-L2 | PON2 | 7 | 95034675 | 95065010 | G | A | 43 | 3 | 4 | splice site | c.201 -5 | na | na | 11/5089 | 1/462 | 47644.1 |
| P4-L2 | STIP1 | 11 | 63953244 | 63972515 | A | C | 60 | 3 | 2 | missense | Y316C | 0.97 | 0 | 23/4238 | 0/462 | 8058.1 |
| P4-L2 | PAN3 | 13 | 28713143 | 28869975 | G | C | 23 | 19 | 73 | missense | D758H | 0,995 | 0,01 | 22/4216 | 0/462 | 9329.2 |
| P4-L2 | NUFIP1 | 13 | 45513884 | 45564118 | G | A | 20 | 21 | 78 | missense | E322K | 0.001 | 0.11 | 17/4238 | 0/462 | 9393.1 |
| P4-L2 | LAMA1 | 18 | 6942243 | 7118313 | A | T | 40 | 8 | 10 | missense | N1298Y | 1 | 0 | 168/4287 | 2/462 | 32787.1 |
| P4-L2 | ILF3 | 19 | 10765437 | 10803593 | G | A | 20 | 6 | 25 | splice site | c.1181 -1 | na | na | 27/4239 | 0/462 | 12246.1 |
| P4-L2 | MAP4K1 | 19 | 39078781 | 39109143 | A | G | 29 | 34 | 141 | missense | T505A | 0.984 | 0.04 | 40/5114 | 3/489 | 42564.1 |

^numbering according to Human Genome hg 19 assembly

Sample ID: identification of sample; Chr denotes chromosome; ref N.: reference nucleotide; var N.: variant nucleotide; %: fraction of sequence reads showing the variant nucleotide; Cov T coverage tumor; cov N coverage normal; mut type: mutation type; Cosmic: Cancer Gene census database, december 2012

(<http://www.sanger.ac.uk/genetics/CGP/Census>); cosmic all: frequency reported in all type of tumors; cosmic HP: frequency reported in hematopoietic tumors

In red, mutations affecting genes related to the NF-κB pathway.