## Supplementary material

| Case ID | 39 | 40 | 41 | 35 | 36 | 37 | Mean |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Gene |  |  |  |  |  |  |  |
| FN1 |  |  |  |  |  |  |  |
| COL3A1 |  |  |  |  |  |  |  |
| IL22RA2 |  |  |  |  |  |  |  |
| SAA1 |  |  |  |  |  |  |  |
| CTCFL |  |  |  |  |  |  |  |
| HAMP |  |  |  |  |  |  |  |
| LRP1 |  |  |  |  |  |  |  |
| CD70 |  |  |  |  |  |  |  |
| TNFSF4 |  |  |  |  |  |  |  |
| SLC11A1 |  |  |  |  |  |  |  |
| IL26 |  |  |  |  |  |  |  |
| IL10 |  |  |  |  |  |  |  |
| CD247 |  |  |  |  |  |  |  |
| CD7 |  |  |  |  |  |  |  |
| C1QB |  |  |  |  |  |  |  |
| TPSAB1 |  |  |  |  |  |  |  |
| ITGA6 |  |  |  |  |  |  |  |
| KLRG1 |  |  |  |  |  |  |  |
| CD8B |  |  |  |  |  |  |  |
| CD3E |  |  |  |  |  |  |  |
| CXCL12 |  |  |  |  |  |  |  |
| ICOS |  |  |  |  |  |  |  |
| TXK |  |  |  |  |  |  |  |
| CD3D |  |  |  |  |  |  |  |
| ABCB1 |  |  |  |  |  |  |  |
| ITGB4 |  |  |  |  |  |  |  |
| CD40LG |  |  |  |  |  |  |  |
| PTGS2 |  |  |  |  |  |  |  |
| SIGLEC1 |  |  |  |  |  |  |  |
| MARCO |  |  |  |  |  |  |  |
| CD28 |  |  |  |  |  |  |  |
| CR2 |  |  |  |  |  |  |  |
| IL18R1 |  |  |  |  |  |  |  |
| GZMM |  |  |  |  |  |  |  |
| CCR7 |  |  |  |  |  |  |  |
| TXNIP |  |  |  |  |  |  |  |
| CD27 |  |  |  |  |  |  |  |
| STAT4 |  |  |  |  |  |  |  |
| CD3G |  |  |  |  |  |  |  |
| KLRB1 |  |  |  |  |  |  |  |
| CXCL14 |  |  |  |  |  |  |  |
| TCF7 |  |  |  |  |  |  |  |
| CDH1 |  |  |  |  |  |  |  |
| C7 |  |  |  |  |  |  |  |
| CCL21 |  |  |  |  |  |  |  |

Fold change

| $>1.2$ | $<-1.2$ |
| :--- | :--- |
| $>1.5$ | $<-1.5$ |
| $>2$ | $<-2$ |
| $>5$ | $<-5$ |
| $\leq 1.2 ; \geq-1.2$ |  |

high in FL3B

Supplementary Figure 1: Fold changes of differentially expressed genes between follicular FL3B and DLBCL component of the same patient, in 6 patients with both components available. Individual cases are indicated by the case ID. The fold changes of each individual case and of the geometric mean expression levels over all 6 cases are displayed in color codes as indicated in the legend.

Supplementary Table 1: Overview of regions covered by the AmpliSeq Panel

| gene | Ref-Seq | analyzed region* | gene | Ref-Seq | analyzed region* |
| :---: | :---: | :---: | :---: | :---: | :---: |
| ARID1A | NM 006015, <br> NM 139135 | CDS | MEF2B | NM_001145785 | CDS |
| CARD11 | NM_NM032415 | CDS | MYC | NM_002467 | CDS |
| CCND3 | $\begin{gathered} \text { NM_001287427, } \\ \text { NM_001760 } \end{gathered}$ | CDS | MYD88 | NM_001172567 | L265 |
| CD79B | NM_000626 | CDS | NOTCH1 | NM_017617 | E25-E34 |
| CREBBP | NM_004380 | CDS | NOTCH2 | NM_024408 | E32-E34 |
| CXCR4 | NM_002467 | CDS | PIK3CD | NM_001350234 | CDS |
| EP300 | NM_001429 | CDS | PIM1 | NM_001243186 | CDS |
| EZH2 | NM_001203247 | E4, E14, E16 | PRDM1 | NM 001198, NM_182907 | CDS |
| FADD | NM_003824 | CDS | PTEN | NM_001304717 | CDS |
| FASLG | NM_002015 | CDS | PTPRD | NM_002839 | E30-E35 |
| FOXO1 | NM_001349339 | CDS | RHOA | NM_001664 | CDS |
| GNA13 | NM_006572 | CDS | SF3B1 | NM_001005526, NM_012433 | E14-E18 |
| ID3 | NM_002167 | CDS | SOCS1 | NM_003745 | CDS |
| IRF4 | NM_001195286, NM_002460 | CDS | TBL1XR1 | NM_024665 | E9-E12 |
| IRF8 | NM_002163 | E1,E2, E7, E8 | TCF3 | NM_001136139, NM_003200 | CDS |
| KMT2C | NM_170606 | CDS | TNFAIP3 | NM_001270507, NM_001270508, NM_006290 | CDS |
| KMT2D | NM_003482 | CDS | TNFRSF14 | NM_001270949, <br> NM_001270950, <br> NM_001270951, <br> NM_003839 | CDS |
| MAP2K1 | NM_002755 | E1-E6 | TP53 | NM_000546, <br> NM 001126112, <br> NM_001126113, <br> NM_001126114, <br> NM_001126115, <br> NM_001126116, <br> NM_001126117, <br> NM_001126118 | CDS |

[^0]Supplemantary Table 2: List of potential protein changing variants identified by targeted resequencing.(see excel file)

In column B those variants common in all analyzed components and those only identified in single comments are visible. Column C-E shows the different components of each samples and if a variant was identified this specific component (yes: variant was identified, no: variant could be not identified, NA: the component was not present in that sample). Those, variants initially identified as discrepant between the components of that sample but with low frequency $(<10 \%)$ in the sequencing data are described as "low". The chromosomal position according the genome build hg19 is provided.

Supplementary Table 3: Clinical characteristics and treatment response in follicular lymphoma grade 3B (FL3B) with or without a diffuse large B-cell lymphoma (DLBCL) in comparison with patients with DLBCL without FL 3B

|  | FL3B alone |  | FL3B with DLBCL |  | $\begin{aligned} & \text { DLBCL, NOS } \\ & \text { alone } \end{aligned}$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Number of patients | 17 |  | 16 |  | 551 |  |
| Median age (range) | 51 years (29-72) |  | 57 years (29-76) |  | 62 years (18-80)* |  |
| Baseline characteristics | Number | Percent | Number | Percent | Number | Percent |
| Male sex | 13 | 76.5\% | 7 | 43.8\% | 309 | 56.1\% |
| Age $\geq 60$ years | 5 | 29.4\% | 6 | 37.5\% | $307 *$ | 55.7\% |
| ECOG performance status $>1$ | 1 | 5.9\% | 0 | 0.0\% | 56 | 10.2\% |
| Lactate dehydrogenase > ULN | 10 | 58.8\% | 7 | 43.8\% | 306 | 55.5\% |
| Ann Arbor stage III or IV | 11 | 64.7\% | 10 | 62.5\% | 316 | 57.4\% |
| Extranodal manifestations $>1$ | 2 | 11.8\% | 3 | 18.8\% | 180 | 32.7\% |
| Bone marrow infiltration | 1 | 5.9\% | 0 | 0.0\% | 39 | 7.1\% |
| B symptoms | 5 | 29.4\% | 1 | 6.3\% | 168 | 30.5\% |
| International Prognostic Index |  |  |  |  |  |  |
| Low | 9 | 53.0\% | 8 | 50.0\% | 200 | 36.4\% |
| Low-intermediate | 3 | 17.6\% | 3 | 18.8\% | 143 | 26.0\% |
| High-intermediate | 4 | 23.5\% | 5 | 31.2\% | 117 | 21.3\% |
| High | 1 | 5.9\% | 0 | 0.0\% | 90 | 16.3\% |
| Treatment response |  |  |  |  |  |  |
| Overall response | 16 | 94.1\% | 15 | 93.8\% | 461 | 83.7\% |
| Complete remission | 12 | 70.6\% | 10 | 62.5\% | 346 | 62.8\% |

Supplementary Table 4: Genetic variants in FL3B and FL3B+DLBCL

| Gene | FL3B+DLBCL (n=16) | FL3B (n=11) | p-value <br> (Fisher's exact test) |
| :--- | :--- | :--- | :--- |
| ARID1A | 1 | 1 | $>0.9999$ |
| CD79B | 1 | 0 | $>0.9999$ |
| CARD11 | 1 | 1 | $>0.9999$ |
| CREBBP | 6 | 0 | 0.0536 |
| FASLG | 0 | 1 | 0.4074 |
| FOXO1 | 2 | 0 | 0.4986 |
| GNA13 | 1 | 0 | $>0.9999$ |
| ID3 | 1 | 0 | $>0.9999$ |
| IRF8 | 1 | 0 | $>0.9999$ |
| KMT2C | 5 | 1 | 0.3497 |
| KMT2D | 6 | 2 | 0.4048 |
| MEF2B | 2 | 1 | $>0.9999$ |
| MYC | 3 | 0 | 0,2479 |
| MYD88 | 0 | 2 | 0.1567 |
| NOTCH1 | 2 | 0 | 0.4986 |
| NOTCH2 | 3 | 1 | 0.6239 |
| PIK3CD | 1 | 0 | $>0.9999$ |
| PIM1 | 2 | $>0.9999$ |  |
| PRDM1 | 1 | 0 | $>0.9999$ |
| PTEN | 2 | 0 | 0.4986 |
| SF3B1 | 1 | 0 | $>0.9999$ |
| SOCS1 | 3 | 0 | 0,2479 |
| TBL1XR1 | 1 | 1 | 0.9999 |
| TNFAIP3 | 2 | 0 | 0.4986 |
| TNFRSF14 | 2 | 3 | 0.6618 |
| TP53 | 3 |  |  |


[^0]:    *:coding and intron bondaries

