

## 1 **Supplementary material**

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### 3 **Supplementary methods**

#### 4 *Preparation of formalin-fixed, paraffin-embedded (FFPE) tissues*

5 Seven 10µm formalin-fixed, paraffin-embedded (FFPE) tissue slices were prepared for  
6 protein analysis, essentially as previously described<sup>1-3</sup>. In short, paraffin was removed with  
7 xylene followed by rehydration with decreasing levels of ethanol/water and dried. The tissue  
8 was dissolved in lysis buffer (5% SDS, 50 mM triethylammonium bicarbonate [TEAB], pH  
9 8.5) and further processed using S-Trap<sup>TM</sup> micro spin columns (Protifi, Farmingdale,  
10 Huntington, NY, USA) essentially as previously described<sup>1,2,4</sup>. A total of 74 samples (*i.e.*, 34  
11 nt-FL, 20 st-FL, and 20 tFL) were prepared and finally dissolved in 0.1% formic acid at a  
12 concentration of 0.5 µg/µL. One µg of each sample was injected in triplicate, except for one  
13 sample injected in duplicate due to limitations of sample amount.

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#### 15 *LFQ nLC-MS/MS and database searches*

16 Mass spectrometry was performed using an Orbitrap Fusion Tribrid mass spectrometer  
17 coupled to a Dionex Ultimate 3000 RSCL nano LC system (Thermo Fisher Scientific  
18 Instruments, Waltham, MA, USA) using the universal method with settings as previously  
19 described<sup>1,4</sup>. The 221 raw files were entered into MaxQuant version 1.6.6.0 (Max Planck  
20 Institute of Biochemistry, Martinsried, Germany: <https://maxquant.net/maxquant/>) for label-  
21 free quantification (LFQ) analysis<sup>5</sup> using the UniProt *Homo sapiens* filtered and reviewed  
22 database ([www.uniprot.org](http://www.uniprot.org), downloaded 19 March 2021). MaxQuant settings were as  
23 previously described<sup>6</sup>. Further processing was performed in Perseus version 1.6.14.0 (Max  
24 Planck Institute of Biochemistry, Martinsried, Germany: <https://maxquant.net/perseus/>) for

1 filtering and further statistical analysis<sup>7</sup>. The means of the Log<sub>2</sub> transformed LFQ values from  
2 each technical replicate were calculated for each protein in each sample. At least two unique  
3 peptides were required for identification. Proteins that were quantified in at least 70% of the  
4 samples in each group were included in the downstream analyses. The median technical  
5 coefficient of variation was calculated for each sample from proteins determined in triplicate.  
6 The mean value was 13.6% (Range 9.72%-20.3%). P-values were calculated by two-tailed t-  
7 test without further correction in order to not increase type 2 errors with the risk of  
8 overlooking putative predictive markers.

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#### 10 *Bioinformatic analysis*

11 Bioinformatic analysis was performed using both the STRING database (string-db.org) and  
12 with the use of QIAGEN IPA (QIAGEN Inc., <https://digitalinsights.qiagen.com/IPA>)<sup>8</sup>. For  
13 each protein, the corresponding UniProt ID were submitted to the software tools. When more  
14 than one UniProt protein ID were identified, only one representative, the first listed, was used  
15 in the analysis.

16 The STRING analyses were performed based on the set of significantly differentially  
17 expressed proteins ( $p < 0.05$ ) with at least 20% difference in fold change, and the  
18 corresponding calculated fold-changes. Analyses were performed with input of UniProt IDs.  
19 For the nt-FL vs st-FL analysis, one UniProt ID was not recognized in the Cytoscape  
20 STRING software, resulting in a total of 241 proteins in the analysis. In the st-FL vs tFL  
21 analysis, two UniProt IDs was not recognized in the STRING software, resulting in a total of  
22 798 proteins included in the analyses. The database was assessed using the StringApp  
23 (version 1.7.0) in Cytoscape (version 3.9.0)<sup>9-11</sup>. The minimum required interaction score was  
24 set to medium confidence, 0.4, with both functional and physical interactions included. For

1 enrichment analysis, enriched terms were filtered to include only terms from UniProt  
2 Keywords, Gene Ontology (GO) Biological Processes, GO cellular components, GO  
3 molecular functions, Kyoto Encyclopedia of Genes and Genomes Pathways, Reactome  
4 Pathways, and STRING clusters. The false discovery rate was set to 5%. The option to  
5 remove redundant terms was enabled, and the redundancy cut-off was set to 0.50.

6 The IPA analyses were performed with the combined set of identified proteins and the  
7 corresponding calculated fold-changes. IPA recognized 2657 of the 2665 protein uploaded.  
8 Analysis was performed with significantly differentially expressed proteins using  $p < 0.05$ .  
9 The IPA algorithms used are described by Krämer *et al.*<sup>8</sup> Here, z-scores  $\geq |2|$  are considered  
10 statistically significant, and a positive z-score indicates that the pathway is predicted to be  
11 activated, while a negative z-score indicates that the pathway is predicted to be inhibited.  
12 Missing z-scores indicate a pathway for which the z-score cannot be calculated.

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#### 14 *Immunohistochemical staining of selected proteins*

15 Selected proteins from the MS-based proteomics results were evaluated using  
16 immunohistochemistry, namely caspase 3 (CASP3), induced myeloid leukemia cell  
17 differentiation protein (MCL1), BCL-2-associated X protein (BAX), B-cell lymphoma-extra-  
18 large (BCL-xL), and BCL2-like 13 (BCL-rambo). One nt-FL sample was excluded from the  
19 analyses due to insufficient lymphoma material available (n=33). Staining was performed on  
20 4 $\mu$ m FFPE sections using the Ventana Benchmark Ultra automated staining system (Ventana  
21 Medical Systems, Oro Valley, Arizona). Slides were deparaffinized with EZ Prep (Ventana,  
22 950-102) followed by blocking of endogenous peroxidase activity using the OptiView DAB  
23 IHC Detection Kit (Ventana, 760-700)<sup>12-14</sup>. Heat induced epitope retrieval (HIER) was  
24 performed by heating slides to 100°C in ULTRA Cell Conditioning Solution 1 (CC1,  
25 Ventana, 950-224). After HIER, incubation with primary antibody was performed. For all

1 staining protocols see Supplemental Table S1. All antibodies were diluted in Tris-buffered  
2 antibody diluent (pH 7.2, 15mmol/L NaN<sub>3</sub> and stabilizing protein, Dako, Santa Clara,  
3 California), followed by incubation at 37°C. Visualization was performed using the OptiView  
4 DAB IHC Detection Kit with nuclear counterstaining by hematoxylin. Sections of appendix,  
5 tonsil, liver, and pancreas were included on all slides as positive and negative controls.

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### 7 **Digital image analysis**

8 Stained slides were scanned at a magnification of x20 using the Hamamatsu Nanozoomer  
9 2.0HT scanner (Hamamatsu, Shizouka, Japan). Expression levels of CASP3, MCL1, BAX,  
10 BCL-xL, and BCL-rambo were quantified using Visiopharm Integrator system 2020.01  
11 (Visiopharm A/S, Hoersholm, Denmark). As previously described<sup>12-14</sup>, areas for staining  
12 quantification were defined by manual outlining of regions of interest (ROI) on each digitized  
13 whole tissue section. Distinct areas of non-lymphoid tissue and technical artefacts were  
14 excluded. Analysis protocol packages (APPs) were designed to quantify the expression levels  
15 of each marker<sup>12-14</sup>. Staining quantification outputs were area fractions (AFs), defined as the  
16 stained area normalized to the total area within the ROI. Intrafollicular regions were manually  
17 outlined, guided by a consecutive parallel tissue section stained with PAX5 to identify B cell  
18 areas in the biopsy<sup>12-14</sup>. For the intrafollicular quantification, one sample was excluded from  
19 the cohort due to the inability to define follicles based on the consecutive PAX5 staining  
20 (n=52; nt-FL, n=32 and st-FL, n=20). Expression levels of CASP3, MCL1, BAX, and BCL-  
21 xL were based on all positive staining, while expression levels of BCL-rambo were based on  
22 strong-intensity staining.

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**Supplementary tables**

**Table S1:** Immunohistochemistry staining protocols

**Table S2:** 2665 identified proteins from MS-based proteomics analysis

**Table S3:** 795 identified proteins comparing st-FL and nt-FL samples

**Table S4:** significantly differentially expressed proteins, nt-FL and st-FL

**Table S5:** 800 significantly differentially expressed proteins comparing tFL and st-FL samples

**Table S6:** 63 significantly differentially expressed proteins comparing st-FL and nt-FL samples in high-risk group from *Analysis A*

**Table S7:** 68 significantly differentially expressed proteins comparing st-FL and nt-FL samples in high-risk group from *Analysis B*

**Table S8:** Complete STRING pathway analysis comparing nt-FL and st-FL samples

**Table S9:** IPA pathway analysis comparing nt-FL and st-FL samples

**Table S10:** IPA diseases and function pathway analysis comparing st-FL and tFL samples

**Table S11:** STRING pathway analysis comparing st-FL and tFL samples

**Table S12:** IPA pathway analysis comparing st-FL and tFL samples

**Table S13:** IPA diseases and function pathway analysis comparing st-FL and tFL samples



1 **Supplemental Table S1: immunohistochemistry staining protocols**

<b>Target protein</b>	<b>HIER incubation (min)</b>	<b>Primary antibody</b>	<b>Primary antibody dilution</b>	<b>Antibody incubation (min)</b>
<b>CASP3</b>	64	Polyclonal rabbit anti-human anti-CASP3 (HPA00264, Sigma-Aldrich, St. Louis, Missouri, USA)	1:750	32
<b>MCL1</b>	92	Polyclonal rabbit anti-human anti-MCL1 (HPA008455, Sigma-Aldrich)	1:300	32
<b>BCL-xL</b>	92	Monoclonal rabbit anti-human anti-BCL-xL (ab32370, Abcam, Cambridge, UK)	1:1000	32
<b>BCL-rambo</b>	64	Polyclonal rabbit anti-human anti-BCL-rambo (16612-1-AP, ProteinTech, Rosemont, Illinois, USA)	1:700	32
<b>BAX</b>	64	Monoclonal mouse anti-human anti-BAX (60267-1-Ig, ProteinTech)	1:2500	32

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**Supplementary Table S4: significantly differentially expressed proteins, nt-FL and st-FL**

<b>Fold change (st-FL/nt-FL)</b>	<b>p-value</b>	<b>Gene name</b>	<b>Protein name</b>
<b>Upregulated</b>			
2.5	0.038	<i>MPO</i>	Myeloperoxidase
2.1	0.025	<i>RNASE3</i>	Eosinophil cationic protein
2.0	0.014	<i>FABP3</i>	Fatty acid-binding protein, heart
1.9	0.003	<i>MPG</i>	DNA-3-methyladenine glycosylase
1.7	0.041	<i>NTPCR</i>	Cancer-related nucleoside-triphosphatase
1.6	0.010	<i>DBI</i>	Acyl-CoA-binding protein
1.6	0.010	<i>SNRPC</i>	U1 small nuclear ribonucleoprotein C
1.6	0.016	<i>HN1</i>	Hematological and neurological expressed 1 protein
1.5	0.010	<i>PAX5</i>	Paired box protein Pax-5
1.5	0.020	<i>MCL1</i>	Induced myeloid leukemia cell differentiation protein Mcl-1
1.5	0.031	<i>EXOSC6</i>	Exosome complex component MTR3
1.5	0.013	<i>SRSF3</i>	Serine/arginine-rich splicing factor 3
1.5	0.040	<i>RABIF</i>	Guanine nucleotide exchange factor MSS4
1.5	0.005	<i>CDC26</i>	Anaphase-promoting complex subunit CDC26
1.5	0.028	<i>LYZ</i>	Lysozyme C
1.5	0.003	<i>SARNP</i>	SAP domain-containing ribonucleoprotein
1.5	0.049	<i>TRMT61A</i>	tRNA (adenine(58)-N(1))-methyltransferase catalytic subunit TRMT61A
1.5	0.017	<i>CCAR1</i>	Cell division cycle and apoptosis regulator protein 1
1.5	0.009	<i>ALYREF</i>	THO complex subunit 4
1.5	0.014	<i>NUP35</i>	Nucleoporin NUP53
1.5	0.010	<i>PSME3</i>	Proteasome activator complex subunit 3
1.4	0.004	<i>ARL2</i>	ADP-ribosylation factor-like protein 2
1.4	0.019	<i>BAK1</i>	Bcl-2 homologous antagonist/killer
1.4	0.010	<i>LYPLAL1</i>	Lysophospholipase-like protein 1
1.4	0.010	<i>SRSF1</i>	Serine/arginine-rich splicing factor 1
1.4	0.002	<i>TRPT1</i>	tRNA 2-phosphotransferase 1
1.4	0.011	<i>SRA1</i>	Steroid receptor RNA activator 1
1.4	0.027	<i>PABPC4</i>	Polyadenylate-binding protein 4
1.4	0.014	<i>ISG20</i>	Interferon-stimulated gene 20 kDa protein
1.4	0.012	<i>CHERP</i>	Calcium homeostasis endoplasmic reticulum protein
1.4	0.007	<i>KPNA2</i>	Importin subunit alpha-1
1.4	0.001	<i>SRSF10</i>	Serine/arginine-rich splicing factor 10
1.4	0.007	<i>SAE1</i>	SUMO-activating enzyme subunit 1
1.4	0.025	<i>MMP9</i>	Matrix metalloproteinase-9
1.4	0.042	<i>SNRPB</i>	Small nuclear ribonucleoprotein-associated proteins B and B
1.4	0.006	<i>PLD3</i>	Phospholipase D3
1.4	0.012	<i>RMDN3</i>	Regulator of microtubule dynamics protein 3
1.4	0.007	<i>BAX</i>	Apoptosis regulator BAX
1.4	0.010	<i>NPEPL1</i>	Probable aminopeptidase NPEPL1
1.4	0.029	<i>NDUFS8</i>	NADH dehydrogenase [ubiquinone] iron-sulfur protein 8, mitochondrial
1.4	0.026	<i>CDK6</i>	Cyclin-dependent kinase 6
1.4	0.023	<i>BCS1L</i>	Mitochondrial chaperone BCS1
1.4	0.028	<i>SNRPG</i>	Small nuclear ribonucleoprotein G
1.4	0.024	<i>SRSF2</i>	Serine/arginine-rich splicing factor 2
1.4	0.045	<i>DR1</i>	Protein Dr1
1.4	0.044	<i>FUCA1</i>	Tissue alpha-L-fucosidase
1.4	0.025	<i>SEC23B</i>	Protein transport protein Sec23B
1.4	0.046	<i>ACOT7</i>	Cytosolic acyl coenzyme A thioester hydrolase
1.4	0.033	<i>CIRBP</i>	Cold-inducible RNA-binding protein
1.4	0.008	<i>MTMR14</i>	Myotubularin-related protein 14
1.4	0.019	<i>HTRA2</i>	Serine protease HTRA2, mitochondrial
1.4	0.036	<i>NDUFS3</i>	NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial
1.4	0.002	<i>TBC1D13</i>	TBC1 domain family member 13
1.4	0.044	<i>CSTF2</i>	Cleavage stimulation factor subunit 2
1.4	0.002	<i>SNRPD1</i>	Small nuclear ribonucleoprotein Sm D1
1.4	0.010	<i>NAA40</i>	N-alpha-acetyltransferase 40
1.4	0.043	<i>COX5A</i>	Cytochrome c oxidase subunit 5A, mitochondrial
1.4	0.005	<i>ATXN10</i>	Ataxin-10
1.3	0.015	<i>LEMD2</i>	LEM domain-containing protein 2
1.3	0.004	<i>FBXO22</i>	F-box only protein 22
1.3	0.006	<i>ARL1</i>	ADP-ribosylation factor-like protein 1



1.3	0.022	<i>TUBA1C</i>	Tubulin alpha-1C chain
1.3	0.019	<i>PMVK</i>	Phosphomevalonate kinase
1.3	0.042	<i>STX10</i>	Syntaxin-10
1.3	0.034	<i>NDUFA13</i>	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 13
1.3	0.031	<i>CPSF4</i>	Cleavage and polyadenylation specificity factor subunit 4
1.3	<0.001	<i>YBX3</i>	Y-box-binding protein 3
1.3	0.035	<i>SLC39A11</i>	Zinc transporter ZIP11
1.3	0.028	<i>CPSF6</i>	Cleavage and polyadenylation specificity factor subunit 6
1.3	0.019	<i>SRSF5</i>	Serine/arginine-rich splicing factor 5
1.3	0.033	<i>NUP43</i>	Nucleoporin Nup43
1.3	0.035	<i>TRA2A</i>	Transformer-2 protein homolog alpha
1.3	0.042	<i>POLR1C</i>	DNA-directed RNA polymerases I and III subunit RPAC1
1.3	0.001	<i>PRMT5</i>	Protein arginine N-methyltransferase 5
1.3	0.045	<i>BCL2L13</i>	Bcl-2-like protein 13
1.3	0.044	<i>CLNS1A</i>	Methylosome subunit pICln
1.3	0.048	<i>MRPS21</i>	28S ribosomal protein S21, mitochondrial
1.3	0.042	<i>HSPB1</i>	Heat shock protein beta-1
1.3	0.038	<i>EXOSC4</i>	Exosome complex component RRP41
1.3	0.038	<i>HNRNPA1</i>	Heterogeneous nuclear ribonucleoprotein A1
1.3	0.005	<i>MPST</i>	3-mercaptopyruvate sulfurtransferase
1.3	0.011	<i>UBE2K</i>	Ubiquitin-conjugating enzyme E2 K
1.3	0.013	<i>NIT1</i>	Nitrilase homolog 1
1.3	0.009	<i>RAB32</i>	Ras-related protein Rab-32
1.3	0.039	<i>GLMN</i>	Glomulin
1.3	0.039	<i>SCCPDH</i>	Saccharopine dehydrogenase-like oxidoreductase
1.3	0.008	<i>BID</i>	BH3-interacting domain death agonist
1.3	0.008	<i>TXN</i>	Thioredoxin
1.3	0.030	<i>MTCH2</i>	Mitochondrial carrier homolog 2
1.3	0.005	<i>WDR18</i>	WD repeat-containing protein 18
1.3	0.018	<i>SZRD1</i>	SUZ domain-containing protein 1
1.3	0.022	<i>TIGAR</i>	Fructose-2,6-bisphosphatase TIGAR
1.3	0.011	<i>CDK5</i>	Cyclin-dependent-like kinase 5
1.3	0.022	<i>ASPSCR1</i>	Tether containing UBX domain for GLUT4
1.3	0.024	<i>TBCA</i>	Tubulin-specific chaperone A
1.3	0.048	<i>CASP3</i>	Caspase-3
1.3	0.022	<i>SRSF11</i>	Serine/arginine-rich splicing factor 11
1.3	0.014	<i>PSMG2</i>	Proteasome assembly chaperone 2
1.3	0.019	<i>DCK</i>	Deoxycytidine kinase
1.3	0.021	<i>SF1</i>	Splicing factor 1
1.3	0.004	<i>CBFB</i>	Core-binding factor subunit beta
1.3	0.018	<i>HN1L</i>	Hematological and neurological expressed 1-like protein
1.3	0.036	<i>MRPS23</i>	28S ribosomal protein S23, mitochondrial
1.3	0.008	<i>TRA2B</i>	Transformer-2 protein homolog beta
1.3	0.006	<i>BCL2L1</i>	Bcl-2-like protein 1
1.3	0.015	<i>GID8</i>	Glucose-induced degradation protein 8 homolog
1.3	0.020	<i>PDCD5</i>	Programmed cell death protein 5
1.3	0.047	<i>ZC3H18</i>	Zinc finger CCCH domain-containing protein 18
1.3	0.043	<i>MRPL55</i>	39S ribosomal protein L55, mitochondrial
1.3	0.043	<i>APIP</i>	Methylthioribulose-1-phosphate dehydratase
1.2	0.001	<i>CCDC124</i>	Coiled-coil domain-containing protein 124
1.2	0.013	<i>TIPRL</i>	TIP41-like protein
1.2	0.038	<i>RNASEH2A</i>	Ribonuclease H2 subunit A
1.2	0.011	<i>WDR77</i>	Methylosome protein 50
1.2	0.048	<i>IFT27</i>	Intraflagellar transport protein 27 homolog
1.2	0.033	<i>BAG2</i>	BAG family molecular chaperone regulator 2
1.2	0.035	<i>PELP1</i>	Proline-, glutamic acid- and leucine-rich protein 1
1.2	0.024	<i>HSPA14</i>	Heat shock 70 kDa protein 14
1.2	0.023	<i>NUDT21</i>	Cleavage and polyadenylation specificity factor subunit 5
1.2	0.033	<i>ARL3</i>	ADP-ribosylation factor-like protein 3
1.2	0.041	<i>THOC6</i>	THO complex subunit 6 homolog
1.2	0.044	<i>PHYKPL</i>	5-phosphohydroxy-L-lysine phospho-lyase
1.2	0.031	<i>ADRM1</i>	Proteasomal ubiquitin receptor ADRM1
1.2	0.026	<i>MAT2B</i>	Methionine adenosyltransferase 2 subunit beta
1.2	0.045	<i>OVC42</i>	Ovarian cancer-associated gene 2 protein
1.2	0.043	<i>NUP214</i>	Nuclear pore complex protein Nup214
1.2	0.011	<i>UBAP2L</i>	Ubiquitin-associated protein 2-like
1.2	0.034	<i>KPNA3</i>	Importin subunit alpha-4

1.2	0.011	<i>PFDN2</i>	Prefoldin subunit 2
1.2	0.017	<i>PAAF1</i>	Proteasomal ATPase-associated factor 1
1.2	0.029	<i>COASY</i>	Bifunctional coenzyme A synthase
1.2	0.029	<i>PPAT</i>	Amidophosphoribosyltransferase
1.2	0.037	<i>SNAP29</i>	Synaptosomal-associated protein 29
1.2	0.017	<i>DTYMK</i>	Thymidylate kinase
1.2	0.011	<i>CHMP2A</i>	Charged multivesicular body protein 2a
1.2	0.039	<i>NECAP1</i>	Adaptin ear-binding coat-associated protein 1
1.2	0.002	<i>G3BP1</i>	Ras GTPase-activating protein-binding protein 1
1.2	0.041	<i>BTF3</i>	Transcription factor BTF3

### Downregulated

0.4	0.005	<i>IQGAP2</i>	Ras GTPase-activating-like protein IQGAP2
0.5	0.004	<i>UGGT1</i>	UDP-glucose:glycoprotein glucosyltransferase 1
0.5	0.001	<i>DOCK11</i>	Dedicator of cytokinesis protein 11
0.5	<0.001	<i>ACTB</i>	Actin, cytoplasmic 1
0.5	0.029	<i>AP2A2</i>	AP-2 complex subunit alpha-2
0.6	0.011	<i>AKAP13</i>	A-kinase anchor protein 13
0.6	<0.001	<i>MAP2K1</i>	Dual specificity mitogen-activated protein kinase kinase 1
0.6	0.040	<i>RBM25</i>	RNA-binding protein 25
0.6	0.018	<i>EHD3</i>	EH domain-containing protein 3
0.6	0.014	<i>STT3B</i>	Dolichyl-diphosphooligosaccharid-protein glycosyltransferase STT3B
0.6	0.027	<i>PLXNB2</i>	Plexin-B2
0.7	0.026	<i>CKAP5</i>	Cytoskeleton-associated protein 5
0.7	0.013	<i>FLNB</i>	Filamin-B
0.7	0.028	<i>KTN1</i>	Kinectin
0.7	0.039	<i>IGHG1</i>	Ig gamma-1 chain C region
0.7	0.005	<i>ADD1</i>	Alpha-adducin
0.7	0.025	<i>ACAP2</i>	Arf-GAP coiled-coil, ANK repeat and PH domain-containing protein 2
0.7	0.020	<i>NIPSNAP1</i>	Protein NipSnap homolog 1
0.7	0.043	<i>GLG1</i>	Golgi apparatus protein 1
0.7	0.048	<i>SBF1</i>	Myotubularin-related protein 5
0.7	0.009	<i>LMAN1</i>	Protein ERGIC-53
0.7	0.002	<i>SRP54</i>	Signal recognition particle 54 kDa protein
0.7	0.027	<i>ADD3</i>	Gamma-adducin
0.7	0.004	<i>HMHA1</i>	Minor histocompatibility protein HA-1
0.7	0.033	<i>SERPINC1</i>	Antithrombin-III
0.7	0.014	<i>SLCIA5</i>	Neutral amino acid transporter B(0)
0.7	0.016	<i>PALD1</i>	Paladin
0.7	0.010	<i>RPN2</i>	Dolichyl-diphosphooligosaccharide-protein glycosyltransferase 2
0.7	0.026	<i>PDIA4</i>	Protein disulfide-isomerase A4
0.7	0.047	<i>ATP2B1</i>	Plasma membrane calcium-transporting ATPase 1
0.7	0.009	<i>ABCE1</i>	ATP-binding cassette sub-family E member 1
0.7	0.046	<i>RPS6KA3</i>	Ribosomal protein S6 kinase alpha-3
0.7	0.005	<i>CD81</i>	CD81 antigen
0.7	0.011	<i>CTTN</i>	Src substrate cortactin
0.7	0.027	<i>PIK3AP1</i>	Phosphoinositide 3-kinase adapter protein 1
0.7	0.011	<i>PACSI</i>	Phosphofurin acidic cluster sorting protein 1
0.7	0.036	<i>OSBPL8</i>	Oxysterol-binding protein-related protein 8
0.7	0.016	<i>SEPT7</i>	Septin-7
0.7	0.005	<i>ELMO1</i>	Engulfment and cell motility protein 1
0.7	0.001	<i>GNPDA2</i>	Glucosamine-6-phosphate isomerase 2
0.7	0.002	<i>ECHDC1</i>	Ethylmalonyl-CoA decarboxylase
0.7	0.030	<i>ITGB1</i>	Integrin beta-1
0.7	0.046	<i>NT5C2</i>	Cytosolic purine 5-nucleotidase
0.7	0.003	<i>PDCD4</i>	Programmed cell death protein 4
0.7	0.012	<i>CD2AP</i>	CD2-associated protein
0.7	0.038	<i>HERC4</i>	Probable E3 ubiquitin-protein ligase HERC4
0.7	0.018	<i>ITGAL</i>	Integrin alpha-L
0.7	0.008	<i>GCLC</i>	Glutamate--cysteine ligase catalytic subunit
0.7	0.018	<i>TES</i>	Testin
0.7	0.014	<i>BRK1</i>	Protein BRICK1
0.7	0.049	<i>MAGED2</i>	Melanoma-associated antigen D2
0.7	0.023	<i>SLC48A1</i>	Heme transporter HRG1
0.7	0.025	<i>NCKAP1L</i>	Nck-associated protein 1-like
0.8	0.042	<i>AP1M1</i>	AP-1 complex subunit mu-1
0.8	0.012	<i>CDK5RAP3</i>	CDK5 regulatory subunit-associated protein 3

0.8	0.015	<i>PIK3R4</i>	Phosphoinositide 3-kinase regulatory subunit 4
0.8	0.020	<i>DCTN4</i>	Dynactin subunit 4
0.8	0.026	<i>SRPR</i>	Signal recognition particle receptor subunit alpha
0.8	0.043	<i>GGT5</i>	Gamma-glutamyltransferase 5
0.8	0.018	<i>DGKA</i>	Diacylglycerol kinase alpha
0.8	0.029	<i>ATP2A3</i>	Sarcoplasmic/endoplasmic reticulum calcium ATPase 3
0.8	0.038	<i>TRIM25</i>	E3 ubiquitin/ISG15 ligase TRIM25
0.8	0.032	<i>OAS2</i>	2-5-oligoadenylate synthase 2
0.8	0.026	<i>BCAP31</i>	B-cell receptor-associated protein 31
0.8	0.034	<i>PIP4K2A</i>	Phosphatidylinositol 5-phosphate 4-kinase type-2 alpha
0.8	0.013	<i>METAP2</i>	Methionine aminopeptidase 2
0.8	0.003	<i>HSPA1A</i>	Heat shock 70 kDa protein 1A
0.8	0.007	<i>MSN</i>	Moesin
0.8	0.035	<i>SRP72</i>	Signal recognition particle subunit SRP72
0.8	0.034	<i>VASP</i>	Vasodilator-stimulated phosphoprotein
0.8	0.040	<i>LANCL1</i>	LanC-like protein 1
0.8	0.038	<i>FKBP2</i>	Peptidyl-prolyl cis-trans isomerase FKBP2
0.8	0.001	<i>CCNY</i>	Cyclin-Y
0.8	0.011	<i>ABCF3</i>	ATP-binding cassette sub-family F member 3
0.8	0.002	<i>PDIA3</i>	Protein disulfide-isomerase A3
0.8	0.016	<i>LMAN2</i>	Vesicular integral-membrane protein VIP36
0.8	0.034	<i>SPG11</i>	Spatacsin
0.8	0.030	<i>CYB5B</i>	Cytochrome b5 type B
0.8	0.011	<i>DENND2D</i>	DENN domain-containing protein 2D
0.8	0.044	<i>DNAJB11</i>	DnaJ homolog subfamily B member 11
0.8	0.006	<i>NRAS</i>	GTPase NRas
0.8	0.005	<i>DRG2</i>	Developmentally-regulated GTP-binding protein 2
0.8	0.006	<i>TSG101</i>	Tumor susceptibility gene 101 protein
0.8	0.021	<i>KDSR</i>	3-ketodihydrospingosine reductase
0.8	0.006	<i>TMED10</i>	Transmembrane emp24 domain-containing protein 10
0.8	0.020	<i>RPN1</i>	Dolichyl-diphosphooligosaccharide-protein glycosyltransferase 1
0.8	0.007	<i>GEMIN5</i>	Gem-associated protein 5
0.8	0.031	<i>DSCR3</i>	Down syndrome critical region protein 3
0.8	0.003	<i>ADH5</i>	Alcohol dehydrogenase class-3
0.8	0.029	<i>NGLY1</i>	Peptide-N(4)-(N-acetyl-beta-glucosaminy)asparagine amidase
0.8	0.025	<i>SMYD5</i>	SET and MYND domain-containing protein 5
0.8	0.008	<i>EPN1</i>	Epsin-1
0.8	0.029	<i>PRKCSH</i>	Glucosidase 2 subunit beta
0.8	0.038	<i>TOR1A</i>	Torsin-1A
0.8	0.019	<i>CUL5</i>	Cullin-5
0.8	0.015	<i>SEPT6</i>	Septin-6
0.8	0.041	<i>GLTP</i>	Glycolipid transfer protein
0.8	0.011	<i>NCK1</i>	Cytoplasmic protein NCK1
0.8	0.023	<i>PPIB</i>	Peptidyl-prolyl cis-trans isomerase B
0.8	0.031	<i>TFAM</i>	Transcription factor A, mitochondrial
0.8	0.023	<i>PTPN11</i>	Tyrosine-protein phosphatase non-receptor type 11
0.8	0.028	<i>IQGAP1</i>	Ras GTPase-activating-like protein IQGAP1
0.8	0.020	<i>SEPT9</i>	Septin-9
0.8	0.046	<i>PAK2</i>	Serine/threonine-protein kinase PAK 2;PAK-2p27;PAK-2p34

1

2

1 **Supplementary figures**

2 **Figure S1: Unsupervised clustering based on all identified proteins**

3 (A) Principal component analysis based on all 2665 identified proteins comparing st-FL and  
4 nt-FL samples. Abbreviations: nt-FL, non-transforming FL; PC, principal component; st-FL,  
5 subsequently-transforming FL.

6

7 **Figure S2: Re-analysis of high-risk patients from *Analysis A* and *Analysis B***

8 (A) 3D PCA based on differentially expressed proteins at  $p < 0.05$  comparing nt-FL and st-FL  
9 from the high-risk group identified in *Analysis A*. (B) Hierarchical clustering with input of  
10 differentially expressed proteins at  $p < 0.05$  identified in the high-risk group in *Analysis A*. (C)  
11 3D PCA based on differentially expressed proteins at  $p < 0.01$  comparing nt-FL and st-FL  
12 from the high-risk group identified in *Analysis B*. (D) Hierarchical clustering based on  
13 differentially expressed proteins at  $p < 0.01$  identified in the high-risk group in *Analysis B*.  
14 Abbreviations: nt-FL, non-transforming samples; PC, principal component; st-FL,  
15 subsequently-transforming samples.

16

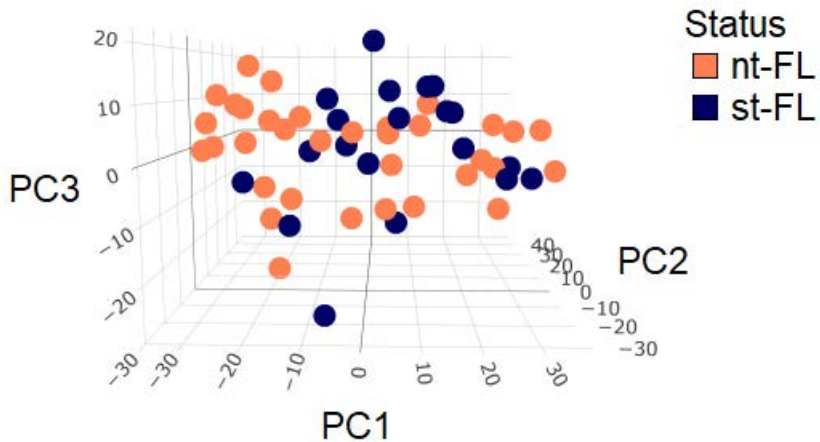
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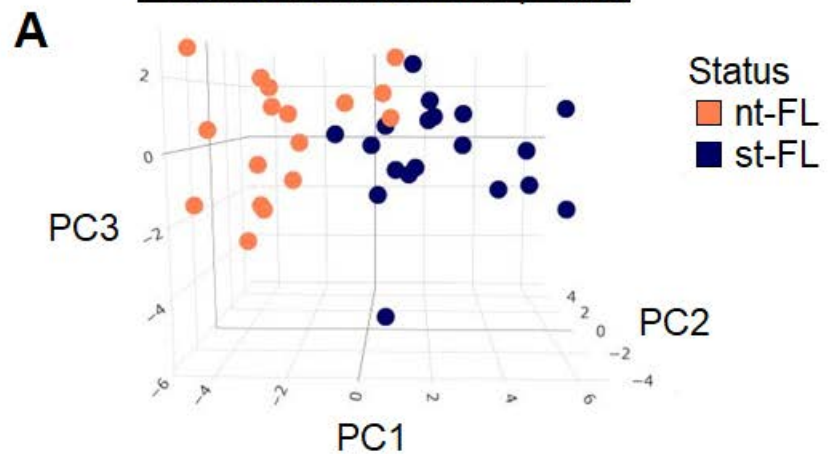
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# Figure S1

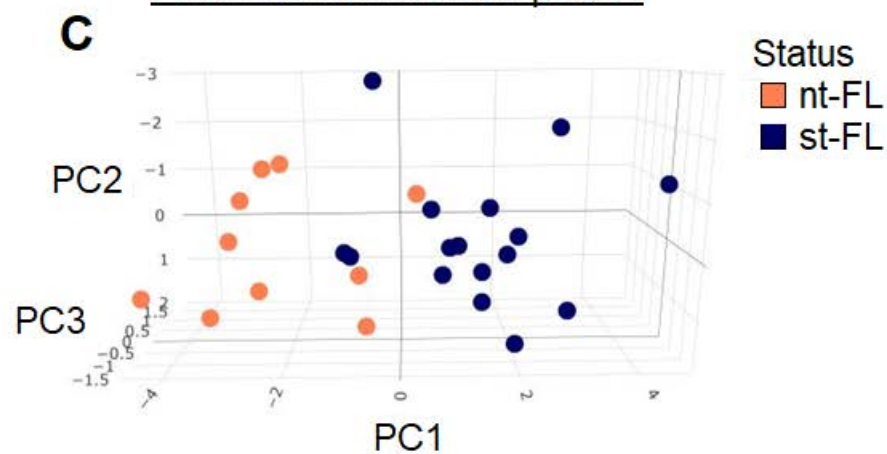


**Figure S2**

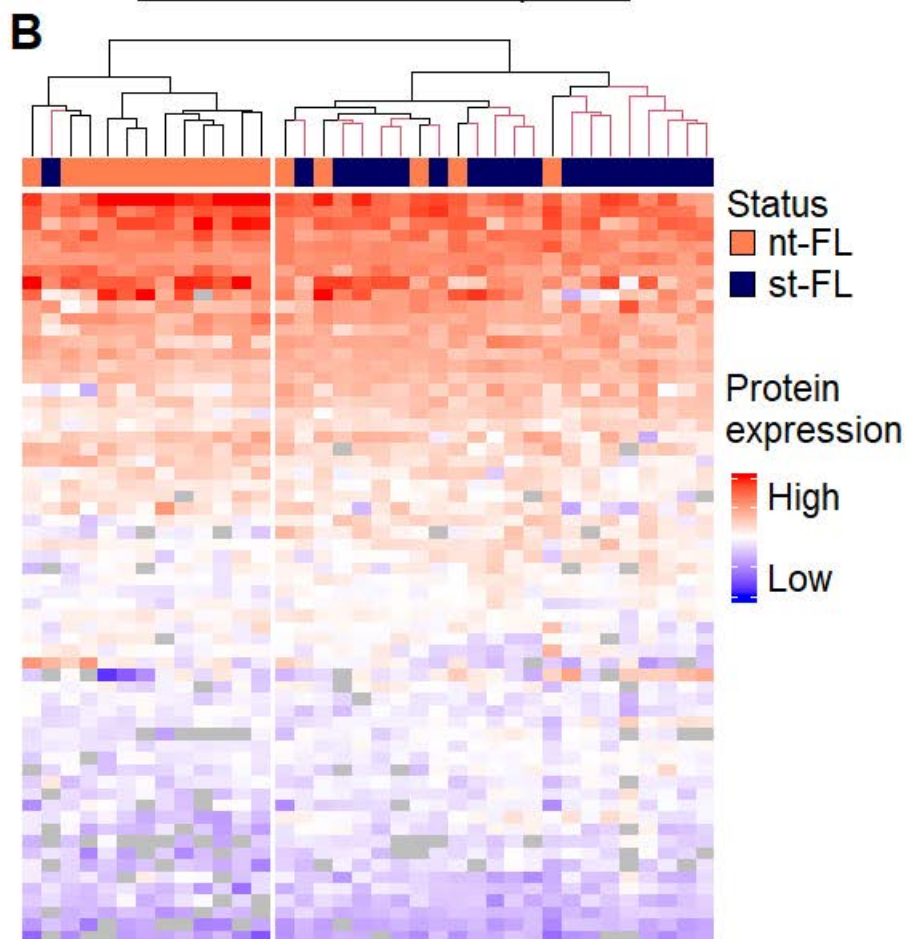
Proteins identified from  $p < 0.05$



Proteins identified from  $p < 0.01$



Proteins identified from  $p < 0.05$



Proteins identified from  $p < 0.01$

