Supplementary Information

Sec22b is a critical and non-redundant regulator of plasma cell maintenance.

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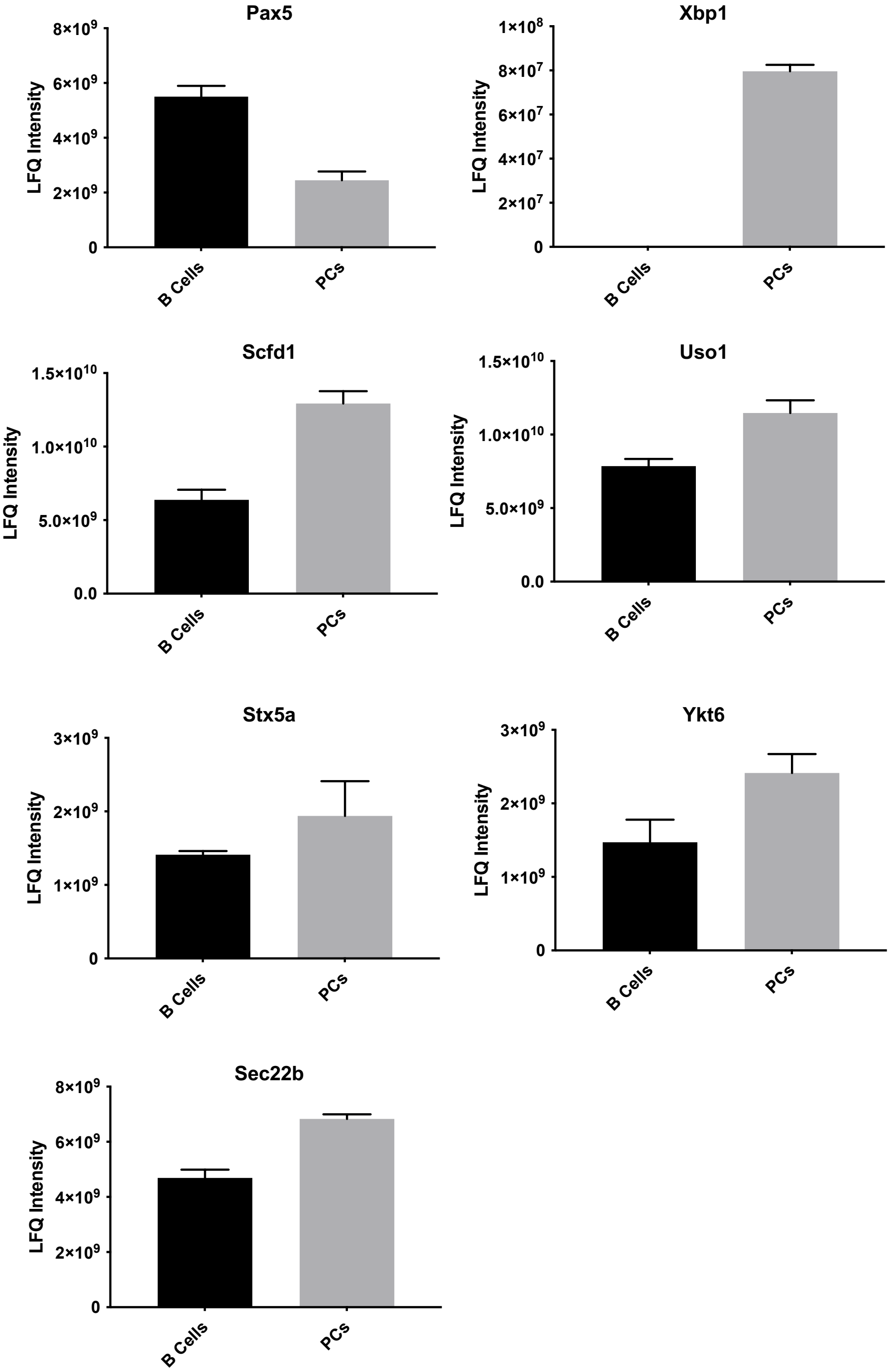
Supplementary methods for the proteomics studies and analyses:

To generate primary immune cells for proteomic studies, the spleens from healthy C57BL/6 mice, 8-10 weeks of age, were crushed through a 40 µM cell strainer into complete RPMI-1640 medium (50 µM β-mercaptoethanol, 10% endotoxin-free Foetal Calf Serum, 2mM Penicillin-Streptomycin and L-Glutamine). Red blood cells were removed by lysis and naive B cells purified using a mouse B cell isolation kit following the manufacturer's instructions (Miltenyi Biotec; catalogue number 130-090-862). To generate antibody secreting cells, B-cells were incubated with 10µg/ml lipopolysaccharide (Sigma) for 3 days. The differentiated cells were enriched using anti-CD138 antibodies coupled to PE and anti-PE magnetic beads (Miltenyi Biotec; catalogue number 130-048-801). This approach generated cells which were significantly enriched in markers of differentiation such as spliced Xbp1, MIST1 and intracellular IgM (~80% purity based on immunostaining).

For quantitative mass spectrometry analysis, purified cells from four biological repeats were lysed into FASP buffer and the protein concentrations determined using a BCA assay (Pierce). The protein concentration of the samples was normalised, digested using the FASP method (1) using trypsin and 100 µg was fractionated into 36 fractions by high pH reverse phase chromatography, pooled into 12 fractions and peptides were analysed using LC-MS/MS on an Orbitrap Elite (Thermo Fisher) hybrid mass spectrometer equipped with a nanospray source, coupled with an Ultimate RSLCnano LC System (Dionex). The system was controlled by Xcalibur 2.1 (Thermo Fisher). Peptides were desalted on-line using a micro-Precolumn cartridge (C18 Pepmap 100, LC Packings) and then separated using a 120 min RP gradient (4-32% acetonitrile/0.1% formic acid) on an Easy-Spray™ PepMap™ column (50 cm x 75 µm ID, PepMap C18, 2 µm particles (Thermo)). The instrument was operated with a cycle of one MS (in the Orbitrap) acquired at a resolution of 60,000 at m/z 400, with the top 20 most abundant multiply-charged (2+ and higher) ions in a given chromatographic window subjected to MS/MS fragmentation in the linear ion trap. An FTMS target values of 1e6 and an ion trap MSn target value of 1e4 was used and with the lock mass (445.120025) enabled. Maximum FTMS scan accumulation time of 200 ms and maximum ion trap MSn scan accumulation time of 50 ms were used. Dynamic exclusion was enabled with a repeat duration of 45s with an exclusion list of 500 and exclusion duration of 30s.

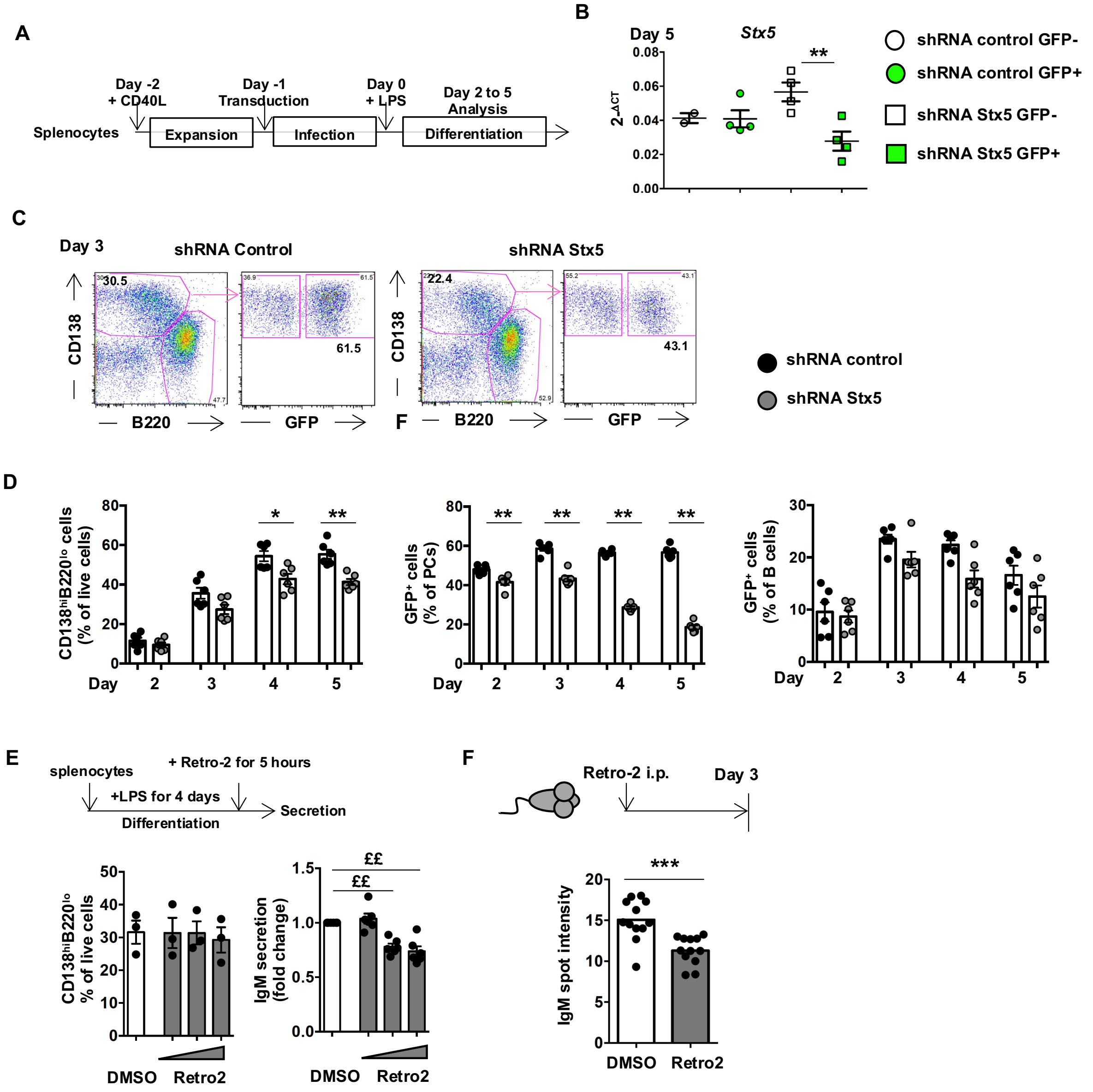
MS data was analysed using MaxQuant (2) version 1.5.8.3. Data was searched against mouse UniProt sequence databases (downloaded June 2015) using the following search parameters: trypsin with a maximum of 2 missed cleavages, 7 ppm for MS mass tolerance, 0.5 Da for MS/MS mass tolerance, with Acetyl (Protein N-term) and Oxidation (M) set as variable modifications and carbamidomethyl (C) as a fixed modification. A protein FDR of 0.01 and a peptide FDR of 0.01 were used for identification level cut offs. Label free quantification (LFQ) was performed using MaxQuant and data filtering and normalisation was performed using Perseus (3). Differential expression of RNA-Seq and proteomics data were computed separately using limma package in R and adjusted for multiple testing using Benjamini-Hochberg method. Genes or proteins with statistically significant differential expression (adjusted $p < 0.05$) in each study were marked with an asterisk. Raw p-values from these differential expression analyses were then combined using the adaptively weighted (AW) method provided in the MetaDE R package and then corrected for false discovery rate. Corrected AW p-values less than 0.05 indicated statistically significant differential expression across studies.

Supplementary figure 1: Raw Label-Free Quantification intensity values for the indicated proteins measured by LC-MS/MS analysis



To identify proteins that exhibit altered abundance when Naive B cells differentiate into PCs, we performed label-free mass spectrometry analysis of tryptic digests of proteins isolated from splenic B cells and *in vitro* differentiated PCs (CD138 enriched). Error bars show SEM for four biological repeats.

Supplementary figure 2: Stx5 controls plasma cell maintenance and antibody secretion



A) Schematic representation of the *in vitro* cell culture, transduction and differentiation assay.

B) Primary splenocytes were transduced with a vector encoding a control shRNA or with the vector encoding Stx5 specific shRNA together with a GFP reporter. Stx5 expression was quantified by qPCR in sorted GFP- and GFP+ cells from both experimental groups at day 5 after LPS stimulation. Data are representative of 2 independent experiments. Statistical analysis was performed with the Mann-Whitney non-parametric two-tailed unpaired test.

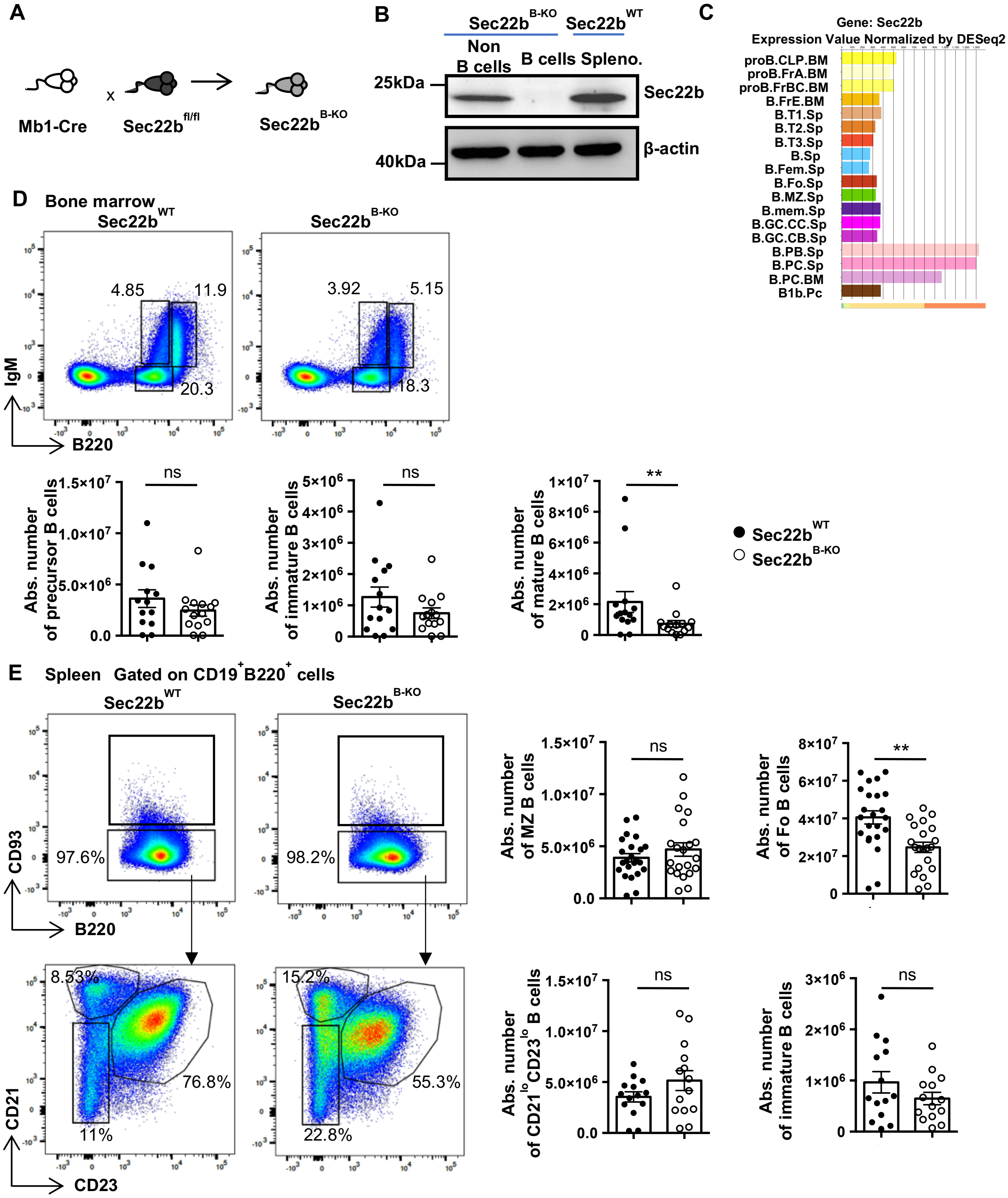
C-D) Representative dot plots showing the frequency of PCs (gated as CD138^{hi}CD19^{lo}) generated at day 3 (C) and the frequency of total PCs (D left), GFP^{+} PCs (D middle) and GFP+ B cells (D right) after transduction with a control vector or with a vector encoding for a Stx5 specific shRNA at day 2, 3, 4 and 5 after transduction. N= 6 independent experiments.

E) Schematic representation of the *in vitro* cell culture and treatment with Retro-2 (top), frequency of PCs (CD138$^+$B220^{low}) determined by flow cytometry (bottom left) and ELISA quantification of secreted IgM in the culture supernatant (bottom right, the fold change to DMSO is shown) after 5hours of incubation with increasing doses of Retro-2 (0.3, 3 and 30µM) of *in vitro* differentiated PCs. Two independent experiments were pooled for the ELISA (n=6) and one representative experiment is shown for the flow cytometry.

F) Schematic representation of the Retro-2 *in vivo* treatment (top), quantification of the intensity of IgM secretion by antibody forming cells (bottom) from the BM of mice injected with DMSO or with Retro-2 (80mg/kg) 3 days before. Two independent experiments were pooled, n=12 mice per group.

The p-values were determined with the two-tailed Mann-Whitney non-parametric test (*$p < 0.05$; **$p<0.01$; ***$p<0.001$), or with the 2way ANOVA with Sidak correction for multiple comparisons (**££** $p<0.01$).

Supplementary Figure 3: Characterization of the *Sec22b*$^{B\text{-}KO}$ mouse model



A) The Sec22b$^{B\text{-}KO}$ mouse model was generated by crossing mb1-Cre mice with Sec22b$^{fl/fl}$ mice, to obtain mice heterozygous for Cre recombinase and homozygous for Sec22b$^{fl/fl}$ (referred to as Sec22b$^{B\text{-}KO}$*)* to have a specific deletion of this SNARE protein in the B cell lineage.

B) Western blot analysis of Sec22b (top) and β-actin (bottom) from non-B cells or B cells isolated from Sec22b$^{B\text{-}KO}$ mice and total splenocytes from Sec22b^{WT} mice.

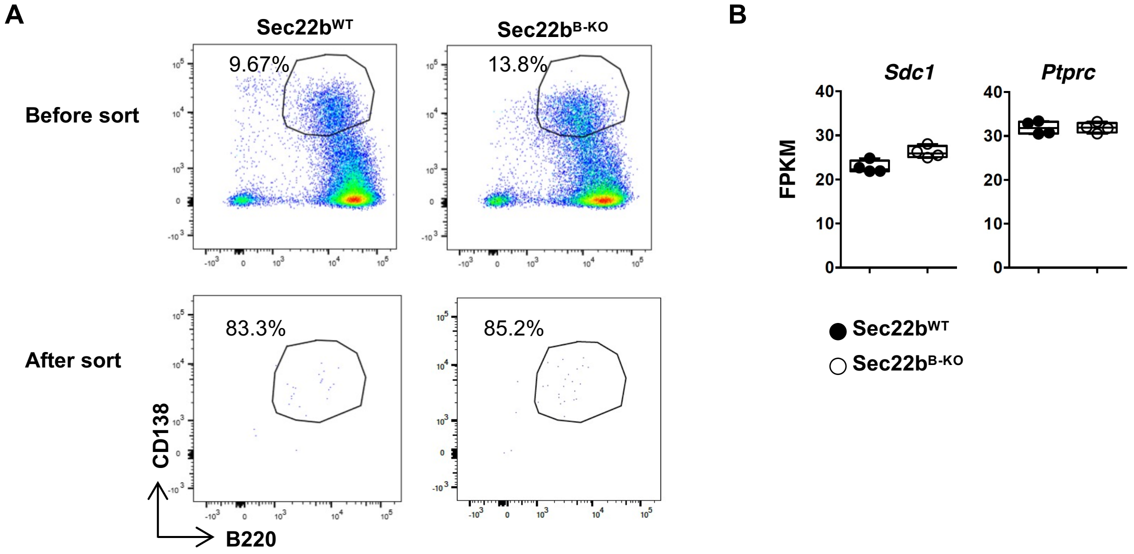
C) *Sec22b* expression across B cell differentiation determined through the Immgen Skyline website (http://rstats.immgen.org/Skyline/skyline.html). BM = Bone marrow, Sp = Spleen, Pc = Peritoneal cavity. CLP = common lymphoid progenitor, Fr = fraction, Fem = female, Fo = follicular, MZ = marginal zone, mem = memory, GC = germinal centre, CC = centrocyte, CB = centroblast, PB = plasmablast, PC= plasma cell.

D) Representative dot plots (top) and absolute number (bottom) of BM precursor B cells (B220^{low}IgM^{-}), immature B cells (B220^{low}IgM^{+}) and mature B cells (B220^{+}IgM^{+}) in Sec22b^{WT} and Sec22b$^{B\text{-}KO}$ mice.

E) Representative dot plots (left) and absolute number (right) of immature B cells (B220^{+}CD19^{+}CD93^{+}), follicular B cells (B220^{+}CD19^{+}CD93^{-}CD21^{+}CD23^{+}), marginal zone B cells (B220^{+}CD19^{+}CD93^{-}CD21^{-}CD23^{high}) and CD21^{-}CD23^{-} B cells (B220^{+}CD19^{+}CD93^{-}CD21^{-}CD23^{-}) in Sec22b^{WT} and Sec22b$^{B\text{-}KO}$ mice.

For flow cytometry experiment cells were first gated on their size and structure, their viability and doublets were excluded. n=13-23 mice from 4-5 independent experiments. The p-values were determined with the two-tailed Mann-Whitney non-parametric test. $**p < 0.01$. “ns” = non-significant *p*-value.

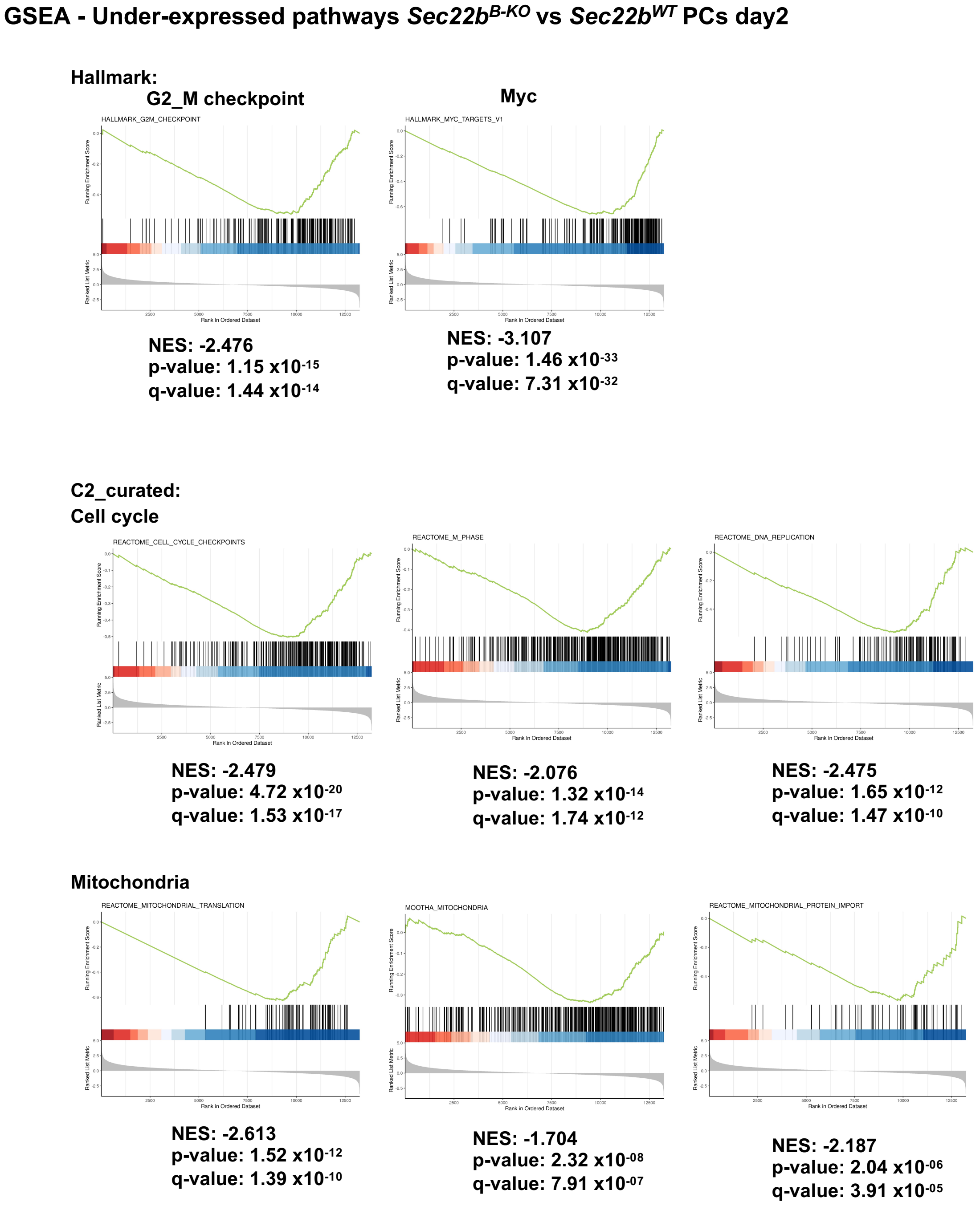
Supplementary Figure 4: Cell sorting purity for RNAseq analysis



A) Representative dot plots of *in vitro* generated PC (B220^{+}CD138^{+}) after 2 days of LPS stimulation, before (top) and after (bottom) cell sorting. Cells were first gated on their size and structure, then on their viability and doublets were excluded. Purity was above 80% for all samples used for RNAseq analysis.

B) Expression of *Sdc1*and *Ptprc* in fragments per kilobase of exon per million reads mapped (FPKM) determined by RNAseq in PC from Sec22b^{WT} and Sec22b$^{B\text{-}KO}$ mice

Supplementary Figure 5: Under-represented gene sets in Sec22b$^{B\text{-}KO}$ PCs



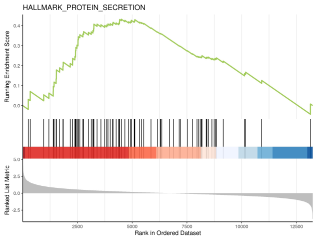
Gene set enrichment analyses were performed using the Hallmark and the C2_curated MSIgDB on RNAseq data obtained from *in vitro* generated Sec22b^{WT} and Sec22b$^{B\text{-}KO}$ PCs. NES, p-values and q-values for each selected gene set are shown.

Supplementary Figure 6: Over-represented gene sets in Sec22b$^{B\text{-}KO}$ PCs

GSEA - Over-expressed pathways *Sec22b*$^{B\text{-}KO}$ vs *Sec22b*^{WT} PCs day2

Hallmark:

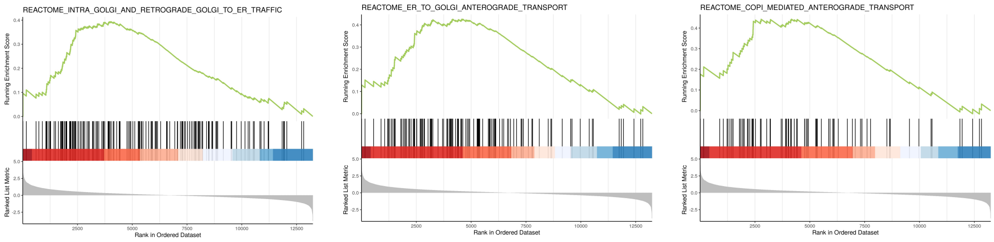
Hallmark_protein secretion



NES: 1.596
p-value: 0.0021
q-value: 0.0096

C2_curated:

ER-Golgi transport

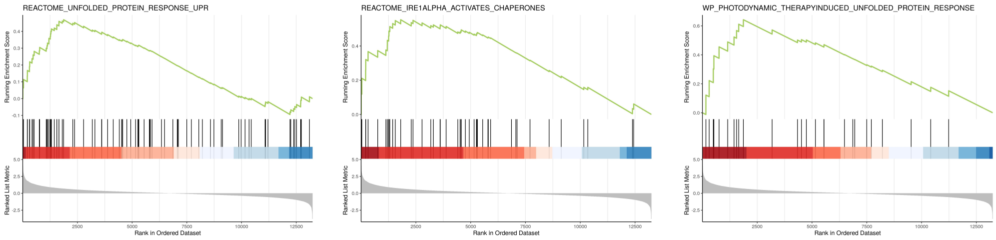


NES: 1.608
p-value: 0.00046
q-value: 0.0044

NES: 1.662
p-value: 0.00054
q-value: 0.0050

NES: 1.625
p-value: 0.0034
q-value: 0.022

UPR



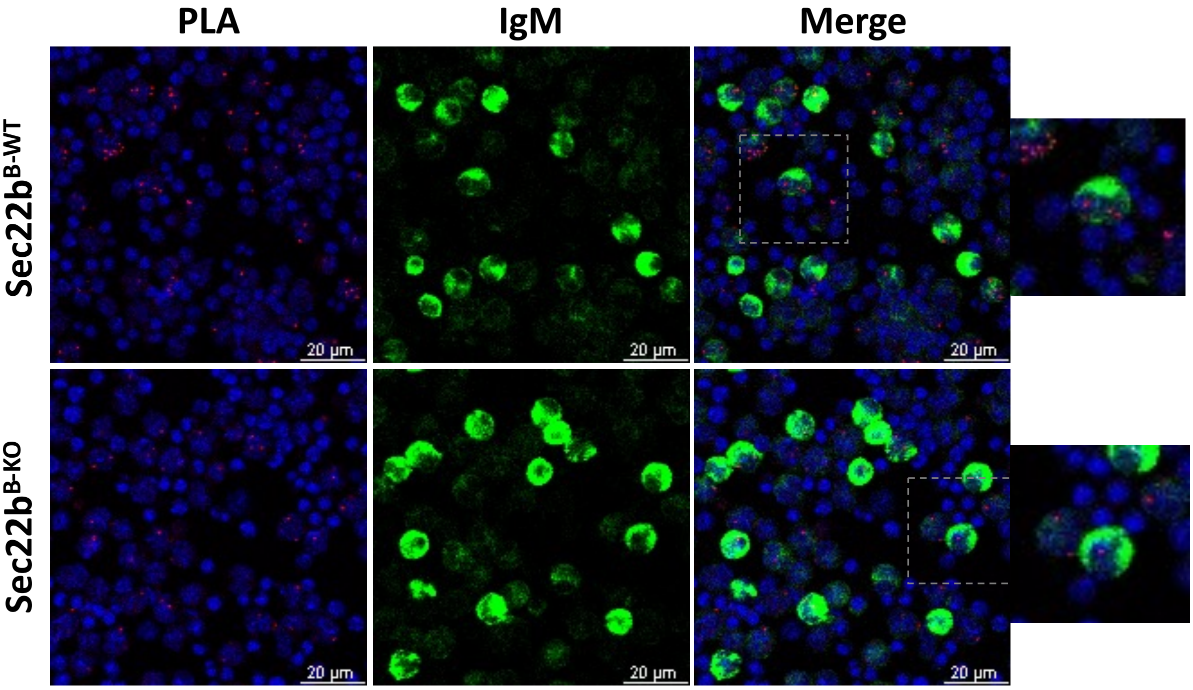
NES: 1.740
p-value: 0.00035
q-value: 0.0035

NES: 1.868
p-value: 0.00054
q-value: 0.0051

NES: 1.900
p-value: 0.00084
q-value: 0.0072

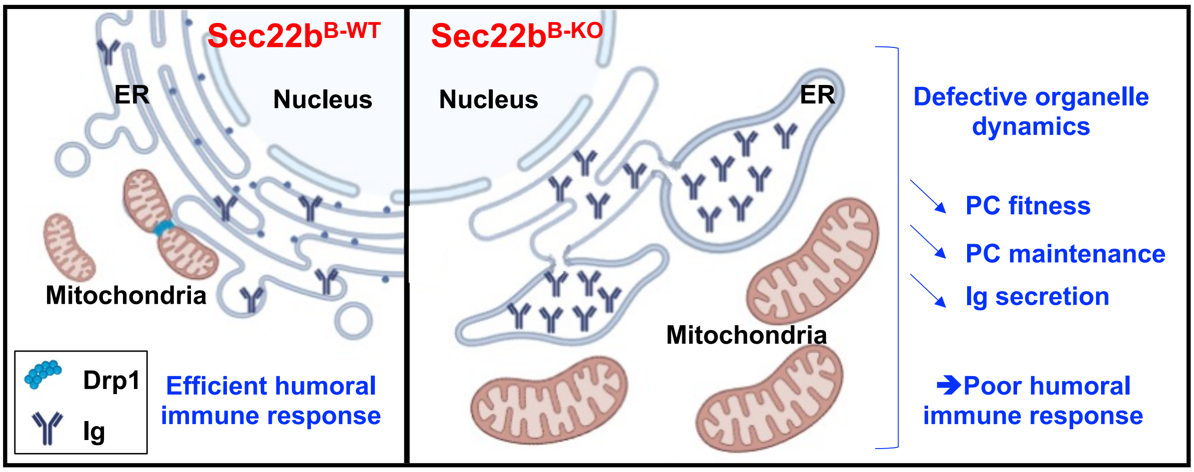
Gene set enrichment analyses were performed using the Hallmark and the C2_curated MSIgDB on RNAseq data obtained from *in vitro* generated Sec22b^{WT} and Sec22b$^{B\text{-}KO}$ PCs. NES, p-values and q-values for each selected gene set are shown.

Supplementary Figure 7: PLAssay on Sec22bWT and Sec22bB-KO PCs



PLA performed on splenocytes stimulated 2 days with LPS. Cells are stained with anti-IgM (green), PLA (red dot) and nuclei are counterstained with DAPI. Scale bar = 20µm

Supplementary Figure 8: Graphical abstract



Sec22b deficiency in plasma cells leads to disrupted ER architecture and altered mitochondrial morphology and function. Mechanistically this might be caused by a decreased expression of the Drp1 pro-fission molecule and by altered ER-mitochondria contact sites. These organelle defects translate into poor fitness of plasma cell, increased cell death and decreased immunoglobulin (Ig) secretion eventually causing a deficient humoral immune response.

Supplementary Table 1: 250 top down regulated genes in Sec22b$^{B\text{-}KO}$ PCs

Gene_Name	FPKM.WT	FPKM.KO	log2FC	pval	qval
Lss	8.56825401	2.87268283	-1.4610023	1.2401E-11	2.4849E-08
Hmgcs1	41.2146298	12.6431927	-1.5902623	2.8482E-11	4.4387E-08
Pcyt2	17.3690417	6.36857043	-1.3325615	4.7844E-11	6.1005E-08
Fads2	18.975706	4.07152798	-2.1062392	7.3186E-11	7.1963E-08
Cyp51	54.3406074	22.3476327	-1.1708981	1.7684E-10	1.2148E-07
Ldlr	8.6795728	2.45855603	-1.7101444	1.848E-10	1.2148E-07
Msmo1	17.6524776	7.96792128	-1.0359432	4.365E-10	1.776E-07
Acat2	20.2603535	6.05876713	-1.6241873	8.620E-10	2.4677E-07
Elovl6	6.36330644	2.17111917	-1.4369985	1.3888E-09	3.12E-07
Idi1	21.3717499	6.88668479	-1.5268591	1.4014E-09	3.12E-07
Sqle	31.146447	13.5704273	-1.0905489	2.4411E-09	4.4784E-07
Insig1	110.251597	47.5404861	-1.0995955	3.1548E-09	5.2677E-07
Dhcr24	28.7478759	10.3330917	-1.37764	3.6204E-09	5.7705E-07
Ldha	393.592265	110.980637	-1.7369734	4.7344E-09	6.9172E-07
Stard4	15.137827	6.81370915	-1.0386323	4.8045E-09	6.9472E-07
Fgfr1op	10.6784262	4.5618304	-1.1096151	5.5479E-09	7.6996E-07
Surf2	8.50161825	2.68843094	-1.5323306	5.5993E-09	7.6996E-07
Pgam1	65.6613951	22.2532633	-1.4543746	5.7267E-09	7.7984E-07
Echdc1	6.67061053	2.93570996	-1.0688897	6.3202E-09	8.1328E-07
Acsl3	16.7045304	7.92516022	-0.9659895	7.6698E-09	9.3545E-07
Apex1	74.6628606	20.6199279	-1.7413501	8.681E-09	1.0063E-06
Icam1	17.0459618	8.80207691	-0.8387712	8.6538E-09	1.0063E-06
Tspan15	1.49383694	0.56831499	-1.2785364	8.6057E-09	1.0063E-06
Dhcr7	10.0545011	5.24343935	-0.8279307	9.9074E-09	1.0689E-06
Flt3	5.55192425	2.21661128	-1.2069847	1.068E-08	1.1263E-06
Nsdhl	12.8649607	5.88050199	-1.0157331	1.1325E-08	1.1488E-06
Pfkl	25.384259	8.81633904	-1.4231302	1.4375E-08	1.3441E-06
Scd1	166.079584	41.6559021	-1.915811	1.5057E-08	1.3894E-06
Scarb1	5.03172711	1.96359529	-1.2493531	1.5385E-08	1.4012E-06
Ddx27	24.8941261	11.8483318	-0.9581696	1.7316E-08	1.4719E-06
Ppid	26.6879301	8.13557211	-1.6169173	1.8425E-08	1.5305E-06
Cdk5r1	2.41313742	0.59678053	-1.88986	1.9854E-08	1.6004E-06
Zbtb32	40.5827888	9.75916102	-1.9572858	2.0842E-08	1.6246E-06
Fkbp3	12.5446757	5.0815353	-1.1991922	2.3398E-08	1.7402E-06
Nat10	14.2840458	5.34668556	-1.3062485	2.3599E-08	1.7421E-06
Lmo2	40.6125984	18.1293906	-1.0471981	2.4732E-08	1.7881E-06
Mybl2	27.223812	10.9252737	-1.2175914	2.817E-08	1.9657E-06
Nop16	40.6356111	16.1184395	-1.2174837	2.9784E-08	2.0378E-06
Me2	14.3727844	7.51554974	-0.8264695	3.0655E-08	2.0771E-06
Scd2	164.307299	48.1071414	-1.6662771	3.1507E-08	2.1136E-06
Fus	25.2588217	11.6070257	-1.0150247	3.1906E-08	2.1168E-06
Ncl	203.823949	84.5942881	-1.1613783	3.3513E-08	2.1834E-06

Ppp5c	51.9729276	19.3188383	-1.3238802	3.3693E-08	2.1834E-06
Utp14b	2.739302	1.08058333	-1.2263403	3.385E-08	2.1834E-06
Fads1	16.4869904	8.97447958	-0.7637741	3.4572E-08	2.1855E-06
Pkm	399.846769	179.465117	-1.0529468	3.4523E-08	2.1855E-06
H4c9	38.700964	16.0462497	-1.159767	3.5035E-08	2.1938E-06
Prpf38b	16.258093	9.46884088	-0.666817	3.5443E-08	2.1996E-06
Inf2	15.493966	7.71312821	-0.8916687	3.7129E-08	2.2642E-06
Aprt	71.9016379	30.6749538	-1.1176302	3.7628E-08	2.2847E-06
Eno1	186.949881	57.476436	-1.6227098	3.8733E-08	2.3316E-06
Eno1b	4.77195102	1.35046988	-1.7096304	3.9072E-08	2.342E-06
Lonp1	32.4179483	17.0426778	-0.8191799	4.0741E-08	2.3909E-06
Aacs	13.4064779	7.4780055	-0.7286582	4.4211E-08	2.4985E-06
Grwd1	34.4037728	10.5583496	-1.5913526	4.4252E-08	2.4985E-06
Thop1	17.1790871	5.68553403	-1.4923155	4.4494E-08	2.4985E-06
Tpi1	200.078735	63.9924785	-1.5531212	4.4806E-08	2.5038E-06
Lipg	1.11282125	0.23394749	-2.1181924	4.6902E-08	2.5959E-06
Rpp40	1.7478984	0.66677602	-1.2753635	4.7439E-08	2.6093E-06
Znhit6	8.92700235	4.11670132	-0.9994352	4.7858E-08	2.6212E-06
Wdr4	8.16022015	2.66166574	-1.5006768	5.005E-08	2.6692E-06
Cnn3	20.3048434	10.1218672	-0.8891812	5.0405E-08	2.677E-06
Ftsj3	42.8574198	15.8569984	-1.32926	5.3539E-08	2.802E-06
Bri3bp	10.6187778	4.06748322	-1.2693983	5.482E-08	2.8278E-06
Mfsd2a	13.1107067	4.20057975	-1.5476844	5.5798E-08	2.8582E-06
Pdxk	4.49105218	1.47523748	-1.4961434	5.6151E-08	2.8639E-06
Rpf2	33.085641	11.9939701	-1.3517842	5.7114E-08	2.8746E-06
Pa2g4	157.989551	64.8145755	-1.1815235	5.8494E-08	2.9197E-06
Dctpp1	104.449569	41.5536628	-1.2216924	5.8752E-08	2.9222E-06
Sms	9.92595213	4.63665307	-0.9770364	5.967E-08	2.9573E-06
Mrpl42	19.0662535	8.79094583	-1.0058073	6.02E-08	2.9731E-06
Ranbp1	69.1663027	28.1863745	-1.1963613	6.1693E-08	3.0362E-06
Marcksl1	67.6115029	16.5464035	-1.9421071	6.2402E-08	3.0424E-06
Mif	444.464436	180.882376	-1.1984281	6.3179E-08	3.0663E-06
Gmip	8.99818043	4.87243959	-0.7683209	6.5782E-08	3.1598E-06
Rrp1b	12.4511431	3.98094015	-1.5597112	6.6686E-08	3.1745E-06
Slc20a1	8.91007222	4.51009675	-0.868933	6.7554E-08	3.2011E-06
Tkt	74.2154403	36.1727783	-0.9279239	7.1054E-08	3.3112E-06
Ydjc	2.45014308	0.75441484	-1.567073	7.1976E-08	3.325E-06
Gypc	24.3544816	5.114789	-2.1513416	7.4045E-08	3.4051E-06
Pmvk	23.4429288	12.4607926	-0.7994702	7.4342E-08	3.4076E-06
Traf4	18.0326208	8.87540096	-0.9110618	7.5373E-08	3.4341E-06
Shmt1	30.9301267	7.21985001	-2.018633	7.6658E-08	3.4684E-06
Wdr12	6.10414455	2.55028156	-1.1411704	7.7098E-08	3.4771E-06
Farsa	21.1588978	11.4584934	-0.7714129	7.8651E-08	3.5021E-06
Snrnp70	40.9377394	21.0592483	-0.8508479	8.0516E-08	3.5738E-06
1110038B12Rik	28.3962719	13.6917727	-0.9373481	8.2723E-08	3.6602E-06

Nbeal2	2.84961182	1.2279435	-1.0983979	8.4425E-08	3.7005E-06
Isyna1	75.4849984	30.5360452	-1.2085092	8.5468E-08	3.7315E-06
Nop56	69.6960607	25.0986184	-1.3767177	8.5665E-08	3.7315E-06
Epcam	13.5267062	6.45817477	-0.9461685	8.6845E-08	3.7396E-06
Gm17494	0.81248176	0.21012953	-1.8300529	8.9296E-08	3.7717E-06
Mtap	37.2196081	15.4490726	-1.1580458	8.9547E-08	3.7717E-06
Nsun5	6.28065341	2.78564997	-1.0540886	9.3574E-08	3.8946E-06
Pum3	14.4612984	6.43405529	-1.0614411	9.4464E-08	3.92E-06
Pgs1	9.90426581	5.79722283	-0.6578622	9.565E-08	3.9575E-06
Cacybp	82.1216986	30.058963	-1.3420252	1.0206E-07	4.1306E-06
Mvd	25.0809168	13.5491604	-0.7781807	1.0117E-07	4.1306E-06
Pus7	7.8476253	2.68193855	-1.4377053	1.0219E-07	4.1306E-06
Nudc	152.269089	63.8001613	-1.1534943	1.0279E-07	4.1428E-06
Gapdh	461.304721	240.23328	-0.8326048	1.0488E-07	4.1723E-06
Hmgn1	93.4987252	51.0894805	-0.7611395	1.048E-07	4.1723E-06
Sc5d	12.0999582	6.95568025	-0.684767	1.0656E-07	4.1984E-06
Ddx11	4.29229073	2.12125418	-0.8978846	1.1414E-07	4.4396E-06
Pnn	23.0757921	11.9046688	-0.846196	1.1442E-07	4.4396E-06
Crtc2	16.9579125	9.89598325	-0.6626003	1.1598E-07	4.4609E-06
Gart	57.972664	20.6816937	-1.3859317	1.1991E-07	4.558E-06
Atad3a	28.1887967	10.1383583	-1.3744741	1.2064E-07	4.5731E-06
Hsp90aa1	255.105755	89.7493845	-1.4181893	1.2211E-07	4.5919E-06
Snhg12	8.44866987	4.22167947	-0.8833022	1.2376E-07	4.6291E-06
Tagln2	139.55187	73.8092625	-0.8071984	1.2375E-07	4.6291E-06
Serbp1	41.4719696	20.2192668	-0.9270339	1.2535E-07	4.6519E-06
Slc29a1	10.8451604	4.61380416	-1.1208001	1.2534E-07	4.6519E-06
Wdr77	6.82500732	2.93431452	-1.1041624	1.2537E-07	4.6519E-06
Nsun2	58.2075831	23.40093	-1.2121876	1.3414E-07	4.938E-06
Mrto4	39.5360771	14.1046177	-1.3842843	1.3775E-07	5.0448E-06
Noc2l	54.9085113	22.3461613	-1.1979513	1.3751E-07	5.0448E-06
Cct8	156.429099	70.8344859	-1.0427393	1.394E-07	5.0637E-06
Fubp1	14.5763978	6.31556817	-1.101349	1.3946E-07	5.0637E-06
Pwp2	17.403609	7.11706501	-1.1798677	1.3953E-07	5.0637E-06
Carm1	21.1767643	10.6469565	-0.8860249	1.4498E-07	5.0759E-06
Dctd	5.06466071	1.30827224	-1.8220852	1.4324E-07	5.0759E-06
Fcer2a	4.94588061	0.73456418	-2.6976286	1.4348E-07	5.0759E-06
Gar1	41.9545035	17.6328305	-1.1457304	1.4474E-07	5.0759E-06
Gpn1	4.48627678	2.17971584	-0.9274573	1.4197E-07	5.0759E-06
Hsd17b7	5.32479599	1.89669135	-1.3976029	1.4406E-07	5.0759E-06
Pdcd5	19.7635177	11.0586376	-0.7230124	1.438E-07	5.0759E-06
Sema7a	25.2682779	12.7709944	-0.8749612	1.4858E-07	5.1583E-06
Ak2	87.5968588	41.6964534	-0.9638116	1.5025E-07	5.1905E-06
Dbi	63.3523148	31.5611039	-0.8936292	1.5424E-07	5.2786E-06
Fgd2	8.96809311	2.80076271	-1.5533949	1.5485E-07	5.2786E-06
Hspd1	280.824307	97.0305934	-1.4529475	1.5505E-07	5.2786E-06

Prag1	7.21418876	3.43495381	-0.9593574	1.5391E-07	5.2786E-06
Hirip3	31.7030198	14.7276123	-1.0076799	1.605E-07	5.3108E-06
Nasp	34.3617743	14.1421082	-1.1874818	1.5762E-07	5.3108E-06
Trap1	54.8779605	28.3681383	-0.8416449	1.6119E-07	5.3108E-06
Utp4	29.4714393	10.7522815	-1.3504047	1.5794E-07	5.3108E-06
3110082I17Rik	9.6509888	3.27484572	-1.4453386	1.6219E-07	5.3276E-06
Mat2a	51.7360175	19.6367395	-1.2907867	1.6639E-07	5.3772E-06
Wdr46	30.1119942	13.6781825	-1.0309348	1.6678E-07	5.3776E-06
Anp32a	73.6579402	33.7832778	-1.0216852	1.6783E-07	5.3872E-06
Grap	66.0028612	34.2189432	-0.8293041	1.7144E-07	5.4481E-06
Slc2a1	17.5323248	9.85000774	-0.7156347	1.7767E-07	5.6125E-06
Acy1	6.40415738	2.25328174	-1.4020424	1.7909E-07	5.6226E-06
Slc29a2	1.07433067	0.17848101	-2.4613394	1.7919E-07	5.6226E-06
Snhg3	13.3713253	3.80653698	-1.7136906	1.8027E-07	5.644E-06
A630001G21Rik	27.5241587	15.6243202	-0.701754	1.812E-07	5.6575E-06
Gemin6	27.4336311	13.3229124	-0.9302028	1.8151E-07	5.6575E-06
Pnpt1	20.4644811	8.72513327	-1.1207023	1.8715E-07	5.7693E-06
Fam111a	34.7621613	14.7941072	-1.1324791	1.8855E-07	5.7994E-06
Snrpa1	24.9647853	11.6509704	-0.9926056	1.9069E-07	5.8397E-06
Pgd	20.9643447	9.9754339	-0.9566437	1.9122E-07	5.8432E-06
Acaca	5.08754614	2.45588342	-0.9447636	1.9337E-07	5.896E-06
Fbl	37.5159634	14.8553059	-1.2331585	1.9535E-07	5.9308E-06
Set	174.478943	75.389788	-1.1075613	1.9672E-07	5.9465E-06
Fdft1	15.6190544	8.82099841	-0.7132296	1.9978E-07	6.0002E-06
Ppan	25.1963056	12.5514582	-0.8992079	2.1015E-07	6.2316E-06
Exosc1	11.2718921	5.32594244	-0.9673966	2.1384E-07	6.3131E-06
Lyar	68.499119	27.0162705	-1.2414494	2.215E-07	6.4229E-06
Sephs2	58.3709451	32.0605618	-0.7497708	2.2074E-07	6.4229E-06
Ddx55	4.69351957	2.4646651	-0.8150927	2.2668E-07	6.5286E-06
Dnajc2	29.2803674	14.9192668	-0.8673129	2.2968E-07	6.5478E-06
Dph2	7.05286765	3.63434931	-0.8418329	2.2913E-07	6.5478E-06
Nop2	52.5885297	20.3055697	-1.2622746	2.2884E-07	6.5478E-06
Uhrf1	75.7194421	35.5059418	-0.994123	2.2968E-07	6.5478E-06
Cluh	25.3568144	8.58660034	-1.4756737	2.351E-07	6.6887E-06
Ddx51	8.47567661	3.69402117	-1.0739422	2.3558E-07	6.6888E-06
Dkc1	39.8639743	14.4054823	-1.3735196	2.3687E-07	6.7118E-06
Cyth4	15.4093794	8.37167125	-0.7706545	2.3972E-07	6.7533E-06
Tfdp1	78.4400917	35.250557	-1.0554852	2.4103E-07	6.7613E-06
Prpf3	11.8770045	6.31080232	-0.8030732	2.4451E-07	6.8453E-06
Rrp12	19.9857853	7.5280107	-1.3074798	2.5147E-07	6.9568E-06
Setd6	7.59376952	2.63229132	-1.4140686	2.5144E-07	6.9568E-06
U2af1	52.6335964	27.1078286	-0.8538408	2.5132E-07	6.9568E-06
Ddx21	101.707977	45.9277155	-1.0458448	2.5357E-07	6.9653E-06
Dph5	3.27185564	1.51218776	-0.9893894	2.5426E-07	6.9653E-06
Ripk3	27.5796962	15.4859769	-0.7212982	2.5245E-07	6.9653E-06

Bzw2	24.2934115	10.0132953	-1.1776276	2.6184E-07	7.0683E-06
Gpatch4	24.1588158	10.0074096	-1.1673468	2.6191E-07	7.0683E-06
Polr3g	3.59767821	1.47671818	-1.1588163	2.6199E-07	7.0683E-06
Rsl1d1	104.282222	45.7529902	-1.0823063	2.6023E-07	7.0683E-06
Polr1b	13.9586963	5.32160318	-1.2849283	2.661E-07	7.1227E-06
Wdr18	16.6156591	8.48377892	-0.861252	2.6561E-07	7.1227E-06
Atic	27.831701	9.63385869	-1.4437515	2.6841E-07	7.1376E-06
Nhp2	133.783012	50.1121426	-1.3038279	2.8276E-07	7.3991E-06
Cd3eap	11.0155385	3.73219713	-1.4547488	2.8961E-07	7.4945E-06
Exosc2	22.9074875	9.79700992	-1.1144129	2.9198E-07	7.4988E-06
Shisa8	28.7109486	10.2772456	-1.3666173	2.9136E-07	7.4988E-06
Acly	62.6426972	36.7993259	-0.6581826	2.9694E-07	7.5622E-06
Chaf1b	9.77405337	4.40342274	-1.0399261	2.9872E-07	7.5622E-06
Phb2	86.2160716	42.4177006	-0.9084764	2.9679E-07	7.5622E-06
Tra2a	16.3512252	9.13556906	-0.7289314	2.985E-07	7.5622E-06
Ybx3	150.447731	64.2561079	-1.1313189	2.9923E-07	7.5622E-06
Snhg1	28.2846716	14.5070464	-0.8515614	3.0426E-07	7.6479E-06
Bop1	60.4070115	27.5585146	-1.024434	3.0643E-07	7.677E-06
Noc4l	32.7978959	13.7458394	-1.1449604	3.076E-07	7.677E-06
Tnfrsf22	1.66451967	0.63650961	-1.2771072	3.1222E-07	7.7371E-06
Tomm40	44.066503	19.233421	-1.0999855	3.1125E-07	7.7371E-06
Lactb2	6.02471241	2.92714593	-0.9238601	3.1585E-07	7.7739E-06
Sp110	18.2486258	9.12240564	-0.8904227	3.1514E-07	7.7739E-06
Ptpn6	61.2230187	25.0689157	-1.1788882	3.1875E-07	7.816E-06
Tardbp	43.2135414	22.1910373	-0.8582379	3.2934E-07	8.0065E-06
Uchl5	18.5742391	9.15139617	-0.90832	3.2937E-07	8.0065E-06
Nop10	70.8135977	29.4845157	-1.1487389	3.3141E-07	8.0134E-06
Pfas	14.9393854	6.29193403	-1.1521317	3.3157E-07	8.0134E-06
Rnps1	36.0336989	19.7844529	-0.7580303	3.3085E-07	8.0134E-06
Ddx39b	65.8868456	37.1617358	-0.7183831	3.3411E-07	8.0243E-06
Cdca7	28.7154846	8.86420421	-1.593075	3.3471E-07	8.0248E-06
Ppat	25.0878496	9.80951587	-1.2613522	3.3681E-07	8.0478E-06
Akap8	14.3351994	7.69481542	-0.786104	3.4231E-07	8.0631E-06
Dek	58.9413279	23.8490641	-1.1989629	3.4262E-07	8.0631E-06
Dhodh	4.0529472	1.91596783	-0.9649886	3.4012E-07	8.0631E-06
Otud6b	21.9949089	12.240962	-0.734482	3.3863E-07	8.0631E-06
Pdcd11	15.1730927	8.20718644	-0.7782819	3.3983E-07	8.0631E-06
Mybbp1a	112.341809	45.3315558	-1.2075281	3.4527E-07	8.1105E-06
Rbm19	12.3681261	5.75482361	-0.9998359	3.4579E-07	8.1105E-06
Lsm7	12.7719719	5.22323763	-1.1710838	3.4747E-07	8.1232E-06
Pif1	7.94548809	3.99930293	-0.8791316	3.4749E-07	8.1232E-06
Arglu1	15.6442207	7.37871689	-0.9687233	3.4907E-07	8.1464E-06
Mettl16	5.78411786	2.57338555	-1.060601	3.5388E-07	8.2328E-06
Slc6a6	8.21250997	4.53053398	-0.7436557	3.5588E-07	8.2497E-06
Igsf8	5.26673181	2.53394636	-0.9429703	3.5815E-07	8.2758E-06

Elac2	18.6556986	8.76591846	-0.9795827	3.6E-07	8.2763E-06
Npm1	641.680216	321.760204	-0.8850113	3.5959E-07	8.2763E-06
Rrp9	26.9895929	9.18592957	-1.4494495	3.5996E-07	8.2763E-06
Zfp608	1.71133655	0.82776843	-0.927823	3.6053E-07	8.2763E-06
Luc7l3	16.6864888	9.901422	-0.637643	3.6113E-07	8.2764E-06
Rrs1	42.0211858	18.4623088	-1.0771518	3.6311E-07	8.2947E-06
Tars2	8.74745541	4.93144657	-0.7171052	3.6254E-07	8.2947E-06
C1qbp	120.598641	50.2476547	-1.1640199	3.6629E-07	8.3268E-06
Nip7	24.5138904	11.0160419	-1.0354401	3.6711E-07	8.3319E-06
Tbrg4	36.8265773	18.7357568	-0.8677646	3.7077E-07	8.4013E-06
Dis3	13.3028362	5.80618046	-1.0952203	3.7159E-07	8.4062E-06
Lbhd1	3.90550219	1.87189609	-0.9453705	3.7824E-07	8.5292E-06
Agpat5	5.47982335	2.86237079	-0.8275443	3.8918E-07	8.72E-06
Fabp5	5.70244802	1.61362848	-1.7075375	3.8994E-07	8.723E-06
Amd1	23.1959124	10.989617	-0.9728992	3.9643E-07	8.8119E-06
Stip1	170.703396	75.2983801	-1.078698	4.0421E-07	8.9423E-06
Cd40	10.4896306	3.49203991	-1.4361713	4.0538E-07	8.954E-06
Cct6a	133.369771	58.8690206	-1.0694067	4.1025E-07	8.973E-06
Ebna1bp2	31.9362662	14.6199572	-1.0213358	4.1136E-07	8.973E-06
Eef1aknmt	3.8005288	1.74309112	-1.0168398	4.0951E-07	8.973E-06
Nop58	29.6806354	13.4691936	-1.0373355	4.1135E-07	8.973E-06
Tuba1b	207.392068	85.0044206	-1.1849099	4.1332E-07	9.0018E-06
Impdh2	90.7190753	46.4679314	-0.8541398	4.1653E-07	9.0437E-06
Nap1l1	113.513733	62.0763688	-0.7620347	4.193E-07	9.0758E-06
Kat2a	18.5453048	8.85440777	-0.9626712	4.2071E-07	9.0922E-06
2810004N23Rik	9.68216348	4.88400704	-0.8690086	4.2295E-07	9.0986E-06
Acsl4	17.1770638	10.8478202	-0.549714	4.2256E-07	9.0986E-06
Dnaja1	16.5014827	8.08866449	-0.9139051	4.2263E-07	9.0986E-06

Supplementary Table 2 : 250 top up regulated genes in Sec22b$^{B\text{-}KO}$ PCs

GEnE_NamE	FPKM.WT	FPKM.KO	log2FC	pval	qval
Rcn3	3.95244129	28.2256264	2.94541415	3.6538E-13	5.1248E-09
Aldh1l2	0.97068046	14.9693242	4.06771228	9.7284E-13	6.8225E-09
Anxa5	19.6312692	67.6798591	1.90267766	5.8389E-12	1.6379E-08
Ighv1-12	91.3141777	262.873354	1.63770725	3.6498E-12	1.6379E-08
KdElr3	2.89563443	32.0034861	3.58792461	5.6699E-12	1.6379E-08
Hapln4	0.35185669	3.1586156	3.26100562	7.1344E-12	1.6678E-08
Atf5	37.1824171	186.050449	2.43096651	2.3181E-11	4.0642E-08
Ighv1-74	158.191774	407.725183	1.48005927	4.2968E-11	6.0267E-08
Pck2	30.2316111	123.439586	2.13980755	6.8118E-11	7.1963E-08
Ptov1	0.83255733	5.15312938	2.72882675	6.7398E-11	7.1963E-08
VEgfa	16.4845734	44.916135	1.56414288	7.696E-11	7.1963E-08
Fcrla	30.0184528	70.5261476	1.34403108	1.1394E-10	9.7678E-08
Pycr1	13.500785	51.9078507	2.06442437	1.2535E-10	9.7678E-08
Tmc6	6.75469967	14.7802354	1.24056449	1.2089E-10	9.7678E-08
Hdac9	2.09836795	7.90746978	2.01222542	1.7737E-10	1.2148E-07
Ighv1-78	175.033675	523.163136	1.69867469	1.9054E-10	1.2148E-07
Dusp5	7.48036711	16.5835982	1.26197664	2.0654E-10	1.2596E-07
Rassf4	3.35563798	7.90633389	1.34615616	2.4681E-10	1.4424E-07
SElEnom	5.10934057	17.8335482	1.91632104	3.0367E-10	1.7037E-07
MagEd2	0.55352151	6.23833266	3.57222716	3.2248E-10	1.7397E-07
B3gnt9	5.26744261	21.6136886	2.14346305	4.5583E-10	1.776E-07
Cd28	1.30171125	7.0354162	2.53282616	3.6945E-10	1.776E-07
CEbpb	24.8524107	61.4684689	1.41125685	3.8996E-10	1.776E-07
Ighv8-8	296.018709	1102.1792	1.99658704	3.4409E-10	1.776E-07
MagEd1	7.11806636	24.2847606	1.86880346	4.4644E-10	1.776E-07
PlEkha1	2.15696285	5.23836059	1.39050571	4.1291E-10	1.776E-07
Plxna1	4.27809191	14.4071916	1.86793714	3.9552E-10	1.776E-07
Rrm2b	2.58130441	6.10816923	1.35127282	4.1430E-10	1.776E-07
Sft2d2	34.4282347	94.6883489	1.57779801	4.5466E-10	1.776E-07
Fam129a	4.81711927	18.273281	2.02779748	4.7637E-10	1.8059E-07
Fam114a1	0.76205666	5.12239184	2.85050222	5.3447E-10	1.9704E-07
Ighv3-8	77.7134879	326.521966	2.20463601	5.6191E-10	1.9704E-07
SEsn2	14.7650456	42.4472139	1.63728825	5.4822E-10	1.9704E-07
Evi2a	18.0110335	60.8388687	1.85330884	5.7990E-10	1.9839E-07
SEc23a	17.8776281	41.4506525	1.32789755	6.2665E-10	2.0297E-07
Tifa	2.09109694	5.69958631	1.55636589	6.2694E-10	2.0297E-07
Zfp9	1.32972835	4.3112639	1.79831354	6.3671E-10	2.0297E-07
Copz2	0.47058406	5.95454045	3.74816703	6.7108E-10	2.0462E-07
Ighv1-58	47.8972969	152.838548	1.77586681	6.6684E-10	2.0462E-07
Lasp1	6.64790742	11.9180495	0.95523756	6.8654E-10	2.0488E-07
Ikbip	1.87484725	4.98237371	1.52239466	8.4695E-10	2.4677E-07
CtsE	3.51488042	9.15376791	1.49343696	9.1224E-10	2.559E-07
Igkv12-98	107.721563	263.505214	1.40215105	9.3287E-10	2.5656E-07

Abr	2.51223188	5.24500495	1.17245331	1.0646E-09	2.6198E-07
BhlhE41	4.74207339	10.1582443	1.20860153	1.053E-09	2.6198E-07
Irgq	8.82528071	21.3618862	1.39116172	1.0566E-09	2.6198E-07
Slc3a2	111.000524	280.504692	1.44873381	1.0405E-09	2.6198E-07
Slc6a9	1.9816791	10.5969137	2.51914349	9.9537E-10	2.6198E-07
TmEm263	15.8314176	30.2251103	1.04471015	1.0584E-09	2.6198E-07
Chpf2	15.8208273	32.512173	1.15506603	1.0876E-09	2.6301E-07
Faah	3.57928509	7.79686525	1.23410039	1.1463E-09	2.725E-07
ArfgEf3	1.18740969	6.65536999	2.62340302	1.2781E-09	2.9879E-07
Dap	43.035225	111.589761	1.49780095	1.3962E-09	3.12E-07
MlEc	88.0293766	149.8739	0.88147187	1.5084E-09	3.2548E-07
Mxd4	8.35434174	25.9818553	1.7554385	1.4977E-09	3.2548E-07
Igkv16-104	680.272709	1459.30687	1.21156747	1.6217E-09	3.4463E-07
Chac1	29.129383	82.906231	1.62728404	1.6769E-09	3.4588E-07
S100a11	55.1503858	151.389057	1.57104305	1.6753E-09	3.4588E-07
Igkv4-50	141.049356	449.891241	1.77035923	1.7417E-09	3.5129E-07
TmEm26	1.1636833	3.8498455	1.84833775	1.7532E-09	3.5129E-07
Slc7a11	0.61297132	3.0328239	2.42421242	1.807E-09	3.5698E-07
LEprotl1	14.9103053	31.9438619	1.21314019	1.9815E-09	3.86E-07
RnasE6	6.56501051	16.2070318	1.40848039	2.0498E-09	3.9385E-07
Pi4k2b	8.53958866	15.5458883	0.97382013	2.2604E-09	4.2843E-07
Cth	7.15494982	33.6687109	2.35881238	2.358E-09	4.4098E-07
Trim35	19.016521	33.4483627	0.92676024	2.4585E-09	4.4784E-07
Vim	10.3259516	20.7216025	1.1177967	2.5649E-09	4.6123E-07
Ighv1-75	211.47111	524.66666	1.42540097	2.6451E-09	4.6962E-07
Pgghg	3.03465101	6.91086231	1.29198015	2.7368E-09	4.7984E-07
Igkv3-7	88.0774887	390.419959	2.23318595	3.0091E-09	5.2105E-07
Fut1	3.32197449	11.546848	1.90485349	3.1433E-09	5.2677E-07
Mvb12b	1.98977647	5.57786571	1.60793752	3.1426E-09	5.2677E-07
Igkv3-12	211.75589	469.149729	1.26373459	3.3043E-09	5.4524E-07
Rab3d	2.99415195	9.6165486	1.79447135	3.492E-09	5.6952E-07
Ighv5-6	222.340625	498.126916	1.27894106	3.547E-09	5.7185E-07
Dynlt3	13.0618782	23.145537	0.93705408	3.7139E-09	5.853E-07
Ighv1-72	356.730241	683.831458	1.05372924	3.8906E-09	6.0632E-07
MagEh1	2.21778289	10.4676177	2.36410193	3.9542E-09	6.0948E-07
Gpt2	6.76469786	16.8743894	1.43288768	4.2146E-09	6.4254E-07
Gpr107	3.26184279	5.67661715	0.91165444	4.4574E-09	6.7225E-07
Psd3	0.90277054	2.11359823	1.3441571	4.5302E-09	6.7596E-07
PdE4dip	4.33027968	8.79605459	1.13419308	4.6921E-09	6.9172E-07
Rap1gap2	2.37365066	7.12641108	1.68732496	4.8627E-09	6.9596E-07
Ighv9-3	845.080869	1823.04019	1.22378646	5.1931E-09	7.3574E-07
Sla	10.3130531	33.0893294	1.7887961	5.4657E-09	7.6662E-07
Arfgap1	13.6506179	23.2193189	0.88013341	5.9282E-09	7.922E-07
Ighv7-1	57.8715547	185.210762	1.78376919	5.9305E-09	7.922E-07
Atp1b1	2.2660117	9.54716438	2.17686473	5.9887E-09	7.9243E-07

Wipi1	3.7306877	10.6721124	1.61168347	6.1487E-09	8.06E-07
Ighv1-64	617.173425	1204.09356	1.07509134	6.2841E-09	8.1328E-07
Igkv2-109	287.82215	538.623955	1.01780736	6.6414E-09	8.4685E-07
Chst12	17.2410663	34.2471491	1.10523494	6.9979E-09	8.7636E-07
Rcn1	5.95526686	10.9502489	0.98721985	6.9631E-09	8.7636E-07
Cxcr4	34.2194442	71.7828985	1.17502586	7.275E-09	9.0301E-07
TcEal9	105.81069	187.609369	0.94026669	7.3757E-09	9.0746E-07
Tbc1d20	14.202912	22.7946966	0.79525867	7.8723E-09	9.5187E-07
Yipf3	26.4038598	51.001768	1.06570332	8.1676E-09	9.7914E-07
Ighv1-59	136.162105	282.814039	1.17170051	8.3655E-09	9.9436E-07
Hspa2	6.14059259	13.8861053	1.2802731	8.9608E-09	1.0262E-06
ManEa	37.8668744	73.2119093	1.06531703	8.9992E-09	1.0262E-06
SEc31a	38.1036651	66.136888	0.90935517	9.1265E-09	1.0323E-06
CrEb3	16.5128894	29.5790395	0.9496466	9.3113E-09	1.0365E-06
Jdp2	1.19205083	6.32176305	2.49753902	9.2812E-09	1.0365E-06
Coro2b	2.28618196	5.05399866	1.25600966	9.5561E-09	1.0554E-06
4933421O10Rik	2.28006423	5.15718667	1.28033209	9.8643E-09	1.0689E-06
Yipf6	7.95407591	12.6897598	0.7875543	9.8369E-09	1.0689E-06
Ighv4-1	99.3378797	302.735266	1.71218446	9.9876E-09	1.0694E-06
Soat2	0.75885652	4.18559775	2.59352619	1.0314E-08	1.0959E-06
Fam214a	9.33662461	21.2478234	1.30747877	1.1086E-08	1.1433E-06
Sar1a	61.5542207	95.0026689	0.7386418	1.1042E-08	1.1433E-06
Tlr4	2.18138918	4.80452863	1.2532204	1.1078E-08	1.1433E-06
Ighv5-12	83.3384642	165.019472	1.09839051	1.1459E-08	1.1488E-06
Raph1	0.36421368	1.1134717	1.70529336	1.1518E-08	1.1488E-06
Sh3bp5l	4.36236038	7.68444982	0.92495883	1.1222E-08	1.1488E-06
Trp53inp1	49.4207807	157.939944	1.79681397	1.1549E-08	1.1488E-06
Man1a	63.5384161	108.541952	0.88776836	1.212E-08	1.1972E-06
Dhrs7	9.05339474	23.5011877	1.48325556	1.2212E-08	1.1978E-06
Asns	67.3838875	158.609161	1.35761004	1.2423E-08	1.21E-06
Calu	89.7493436	142.866698	0.78412488	1.3481E-08	1.2951E-06
Pofut2	3.77669546	6.54083503	0.90289031	1.3421E-08	1.2951E-06
MEtrnl	2.07898767	5.48153633	1.5115834	1.3847E-08	1.3212E-06
Ighv6-6	494.366889	1029.03481	1.16762602	1.4143E-08	1.3313E-06
Nbas	22.376612	40.3065936	0.96697261	1.41E-08	1.3313E-06
March8	1.14904799	2.59744859	1.27977824	1.4717E-08	1.367E-06
Ttc39c	1.04253478	3.39717741	1.79315649	1.5201E-08	1.3935E-06
Golim4	3.32533095	5.96200264	0.95450019	1.5589E-08	1.4107E-06
Rhbdd1	4.06929643	8.09558848	1.10001075	1.5854E-08	1.4255E-06
Ighv1-20	31.0580896	86.6437394	1.60413591	1.6336E-08	1.4493E-06
Igkv1-122	105.305975	274.041408	1.48509659	1.6516E-08	1.4493E-06
Igkv8-30	806.690665	2738.69763	1.85815638	1.6636E-08	1.4493E-06
Il5ra	20.7553655	39.0275117	1.01678188	1.6576E-08	1.4493E-06
Mospd1	10.6793553	21.7265592	1.12801229	1.6431E-08	1.4493E-06
Ppp1r15a	15.8581232	27.9014134	0.93147207	1.6837E-08	1.4578E-06

Acbd3	11.6325609	18.0465504	0.74797655	1.7142E-08	1.4661E-06
Gm14137	0.90074637	4.01583048	2.25172185	1.7088E-08	1.4661E-06
Gm30211	12.2902208	24.1378561	1.08916142	1.7861E-08	1.5092E-06
Ctla4	13.9760963	38.1724462	1.57311333	1.8213E-08	1.5297E-06
IpcEf1	1.64955262	4.63477949	1.58437819	1.8441E-08	1.5305E-06
Slc7a3	17.9017152	43.2030852	1.38682823	1.9278E-08	1.5906E-06
Sqstm1	95.6690791	233.071757	1.39260349	1.9392E-08	1.5906E-06
Rgs12	0.34547675	0.92013488	1.52553039	1.9682E-08	1.5986E-06
TmEm167b	11.8839628	22.8986086	1.06340183	1.9717E-08	1.5986E-06
Igkv1-88	106.94773	307.237129	1.63506914	2.0161E-08	1.6159E-06
Ighv2-5	56.3886886	145.854396	1.47428516	2.0386E-08	1.6233E-06
Slc12a4	6.60095176	11.5270568	0.91251442	2.0485E-08	1.6233E-06
ErlEc1	24.5122791	45.4963191	1.00650571	2.0912E-08	1.6246E-06
Gadd45a	10.2008496	28.4897161	1.58648332	2.0965E-08	1.6246E-06
Tlr2	3.61433228	7.75343662	1.20865949	2.069E-08	1.6246E-06
Hmox1	13.6122844	24.6654684	0.9677937	2.1635E-08	1.6673E-06
Ddit3	6.14854641	17.8754547	1.62865743	2.2384E-08	1.7047E-06
Igkv1-133	81.010718	234.867302	1.65210838	2.2484E-08	1.7047E-06
Slc50a1	22.2875933	46.7446363	1.17191099	2.2465E-08	1.7047E-06
Slc26a2	3.47573678	5.813726	0.85498431	2.2926E-08	1.7288E-06
HErpud1	197.528765	357.204429	0.96986954	2.3247E-08	1.7402E-06
Ighv14-3	271.711793	695.678222	1.47525945	2.3449E-08	1.7402E-06
REEp6	0.46224492	2.50082952	2.52070194	2.3728E-08	1.7424E-06
Igkv5-45	78.6227622	221.9713	1.58989651	2.4123E-08	1.7614E-06
Unc13d	6.76383252	12.2349884	0.96284153	2.4237E-08	1.7614E-06
Ighv13-2	87.1523552	238.350201	1.54552775	2.5359E-08	1.8162E-06
St3gal1	13.8681071	22.7931321	0.83204387	2.538E-08	1.8162E-06
EthE1	10.5008401	19.2597169	0.98359719	2.6478E-08	1.8852E-06
Gfpt1	26.1110851	44.5335744	0.88472744	2.7662E-08	1.9399E-06
Inpp4b	2.12924116	4.45148634	1.18314577	2.7625E-08	1.9399E-06
REln	0.26533184	0.77656231	1.6720055	2.7612E-08	1.9399E-06
Il2ra	5.12527102	10.4770576	1.13580663	2.864E-08	1.9887E-06
Glipr2	27.8629379	50.970921	0.98469683	2.882E-08	1.9913E-06
Gpr180	15.8570288	27.2937074	0.89726059	2.9468E-08	2.0261E-06
Jchain	714.95209	1411.49132	1.09028911	2.998E-08	2.0413E-06
Ighv1-76	317.430465	612.753878	1.06069791	3.1154E-08	2.1008E-06
Snn	8.43828778	20.35443	1.3834221	3.1645E-08	2.1136E-06
Kcnk6	9.75839385	18.5056735	1.03935722	3.1996E-08	2.1168E-06
Cdkn1a	1.84936633	5.41871871	1.65105609	3.2588E-08	2.1359E-06
Slc7a7	5.86009167	13.7831684	1.35063664	3.2529E-08	2.1359E-06
Tvp23b	19.3302306	32.6427742	0.86499699	3.3936E-08	2.1834E-06
Gpx3	6.16358458	30.3180393	2.38096243	3.4574E-08	2.1855E-06
Trib2	8.63961301	15.8867067	0.99702627	3.4592E-08	2.1855E-06
GnE	14.0232896	27.4199704	1.08280767	3.4933E-08	2.1938E-06
PtprE	1.28405611	2.41783789	1.02138742	3.5308E-08	2.1996E-06

Bsdc1	6.21022664	10.3785412	0.85146346	3.6098E-08	2.2227E-06
Igkv15-103	400.681408	712.142057	0.93951616	3.6132E-08	2.2227E-06
Ighv8-12	303.281523	740.773658	1.39210929	3.683E-08	2.2558E-06
NdEl1	15.4372666	24.3417372	0.76852059	3.7821E-08	2.2866E-06
Inpp1	5.99734133	11.2262362	1.01543328	3.9591E-08	2.363E-06
Crlf2	16.2972407	38.3597722	1.33544547	3.9815E-08	2.3663E-06
Lipc	1.32408214	4.41486074	1.84464392	4.0313E-08	2.3858E-06
Mon2	9.23027003	15.2361839	0.83883763	4.0637E-08	2.3909E-06
Ttc39b	3.26640869	5.19248685	0.78041416	4.1332E-08	2.4155E-06
Cul7	1.00084922	3.35346293	1.83269295	4.2245E-08	2.4479E-06
Igkv4-74	48.8608106	119.216005	1.3949953	4.2169E-08	2.4479E-06
Mib2	5.1346544	14.1981036	1.58319683	4.2409E-08	2.4479E-06
Cog6	15.9612547	24.0849671	0.70686805	4.3689E-08	2.4985E-06
Ighv9-2	28.7142745	92.7714972	1.80983639	4.3613E-08	2.4985E-06
Trib3	5.85419084	21.1884096	1.96250387	4.4533E-08	2.4985E-06
Tspan13	77.8001979	131.917964	0.87743391	4.451E-08	2.4985E-06
SEl1l	74.0349733	141.875679	1.05635002	4.5223E-08	2.5171E-06
Slc1a4	7.04781183	11.4766503	0.81518158	4.701E-08	2.5959E-06
Atp9a	1.57194625	3.27298766	1.16168884	4.8779E-08	2.6212E-06
Pdxdc1	12.350447	19.4733908	0.77042941	4.8824E-08	2.6212E-06
SErpina3g	3.58522835	8.78025916	1.4277383	4.8962E-08	2.6212E-06
Slc35a2	7.31890771	11.5176053	0.7670044	4.8527E-08	2.6212E-06
Susd6	5.67195617	10.4634998	0.99234617	4.8388E-08	2.6212E-06
TmEm123	135.814148	242.749425	0.95188896	4.874E-08	2.6212E-06
NEo1	0.07054629	0.62612851	3.20581061	5.0577E-08	2.677E-06
Gabarap	91.102466	166.819847	0.98241311	5.1323E-08	2.7062E-06
Rab6a	29.6031566	43.8498005	0.67849197	5.3167E-08	2.793E-06
Prrc1	12.8510305	20.6633024	0.80155072	5.4544E-08	2.8278E-06
Rnf103	3.49859977	5.96573581	0.88511906	5.4837E-08	2.8278E-06
RnpEpl1	4.81889328	7.5543354	0.76074068	5.4383E-08	2.8278E-06
Endod1	6.15316971	10.1126632	0.83226657	5.5836E-08	2.8582E-06
Praf2	5.75380578	10.8659631	1.02993185	5.6876E-08	2.8746E-06
Spint2	7.34653617	12.2139734	0.84493543	5.7105E-08	2.8746E-06
Yif1a	21.6809215	38.5979021	0.94026825	5.718E-08	2.8746E-06
Lmo4	15.1512899	24.5464423	0.80920763	5.7623E-08	2.8865E-06
Dnajc1	3.60139592	5.54067935	0.7348424	6.2023E-08	3.0417E-06
Itpripl2	0.12803576	0.87919737	2.91518289	6.247E-08	3.0424E-06
Slc39a13	4.27827583	7.45111603	0.91148684	6.3512E-08	3.0718E-06
Pja2	7.85630026	13.6083297	0.90560669	6.4489E-08	3.1083E-06
Gm16350	23.5919258	55.308813	1.33667862	6.6362E-08	3.1745E-06
Prxl2c	6.00134439	10.7218524	0.94727964	6.6768E-08	3.1745E-06
Ighv5-15	25.9141269	93.8358001	1.95951179	6.9233E-08	3.2696E-06
Igkv8-21	253.683194	562.517456	1.25460324	7.0511E-08	3.3107E-06
Il3ra	2.82948133	7.56597796	1.52696051	7.0576E-08	3.3107E-06
Mthfr	5.233514	8.95630871	0.88638671	7.1059E-08	3.3112E-06

Igkv4-86	87.0225436	199.965094	1.30964676	7.1343E-08	3.3135E-06
Parp4	7.50761629	13.5623984	0.96836996	7.2066E-08	3.325E-06
CEbpg	12.43347	21.0710695	0.87044679	7.541E-08	3.4341E-06
Bckdha	9.20843982	20.0079007	1.22548147	7.6162E-08	3.4571E-06
DErl1	129.802242	211.170482	0.81522259	7.7354E-08	3.4774E-06
AU040320	8.82820863	15.8680335	0.96071512	7.7704E-08	3.4814E-06
Bmf	5.67799777	13.2170348	1.32586415	7.7938E-08	3.4814E-06
NfE2l1	34.552628	52.8959632	0.7293996	8.3007E-08	3.6612E-06
Cln8	1.85300726	3.56768818	1.05099426	8.3783E-08	3.6838E-06
HEatr5a	1.83001089	3.09829889	0.86998659	8.7052E-08	3.7396E-06
Mcrip1	21.7015057	41.1268732	1.0288351	8.7224E-08	3.7396E-06
Mknk1	15.440431	30.7643332	1.09712445	8.6447E-08	3.7396E-06
SErf2	14.1600435	23.0294803	0.8141757	8.7451E-08	3.7396E-06
Zfp260	8.1133273	15.370286	1.04214298	8.68E-08	3.7396E-06
SEcisbp2l	6.25666729	10.5971096	0.87534107	8.8421E-08	3.7696E-06
Aig1	0.94331833	2.25313561	1.35118953	8.8851E-08	3.7717E-06
Igkv5-43	770.267051	1568.91977	1.13458543	8.9395E-08	3.7717E-06
H6pd	6.36635909	10.2183714	0.79372077	9.0285E-08	3.7914E-06
Golga2	16.4318795	27.286247	0.84866278	9.2083E-08	3.8554E-06
Igkv4-58	88.4913289	188.755464	1.19631903	9.313E-08	3.8876E-06
Gpr155	2.52403384	4.25907048	0.86477407	9.7929E-08	4.0398E-06
Trib1	11.316922	21.1980173	1.02325024	9.9125E-08	4.0772E-06
Srgn	141.106116	248.672381	0.92835613	1.0119E-07	4.1306E-06
Yipf4	17.9864186	26.87745	0.69029546	1.0217E-07	4.1306E-06
Zfp324	4.62140848	7.11153232	0.73296432	1.0151E-07	4.1306E-06
BEt1l	4.86459743	8.43023078	0.89663215	1.0422E-07	4.1723E-06
Prkcz	0.73956701	1.61513008	1.23758219	1.0458E-07	4.1723E-06

Supplementary Table 3. List of antibodies used in flow cytometry, western blot and immunofluorescence

Antibody or Dye	Clone	Host/Isotype	Supplier
Flow cytometry			
Anti-CD138	281-2	Rat IgG2a, κ	BD Biosciences
Anti-CD45R/B220	RA3-6B2	Rat / IgG2a, kappa	BD Biosciences
Anti-CD19	1D3	Rat IgG2a, κ	BD Biosciences
Anti-CD21/35	7G6	Rat gG2b, κ	BD Biosciences
Anti-CD23	B3B4	Rat IgG2a, κ	BD Biosciences
Anti-CD93	AA4.1	Rat IgG2a, κ	BD Biosciences
Anti-IgM	II/41	Rat IgG2a, κ	eBioscience
Anti-Taci	8F10-3	Rat IgG2a, κ	eBioscience
V450-anti-cleaved caspase-3			BD Biosciences
Anti-KI67 Alexa fluor 700	B56	mouse IgG1	BD Biosciences
Dapi			
ER-Tracker Blue-White DPX			Invitrogen
MitoTracker Green FM			Invitrogen
MitoTracker Orange MTMRos			Invitrogen
Viability dye e506			Invitrogen
Aqua zombie			Biolegend
Immunofluorescence			
Anti-Calnexin		Rabbit IgG	Abcam
Anti-cytochrome c		Rabbit IgG	Thermofisher
Anti-Rabbit IgG Alexa fluor 555		Goat IgG	Thermofisher
Anti-mouse IgM Alexa fluor 647		Goat IgG	Thermofisher
Anti-mouse Irf4 Alexa fluor 488	IRF4.3E4	Rat IgG1	Biolegend
Hoescht33342			Thermofisher
Western blot			
Anti-sec22b		Rabbit IgG	Synaptic Systems
Anti-b actin		Rabbit IgG	Cell signaling
Anti-Xbp1		Rabbit IgG	Cell Signaling
Anti-IgM		Goat IgG	Southern Biotech
Anti-CD138		Rabbit IgG	Poteintech
Anti-Scfd1/rsly1		Rabbit IgG	Dr Jesse Hay, PMID: 14565970
Anti-Uso1/p115		Rabbit IgG	Dr Jesse Hay, PMID: 25406594
Anti-Stx5		Rabbit IgG	Synaptic Systems
Anti-Ykt6		Rabbit IgG	Dr Jesse Hay; PMID: 12589064
Anti- Rabbit HRP		Goat IgG	Jackson immuno research

ELISA			
Anti mouse Ig kappa HRP		Goat IgG	Southern Biotech
Anti mouse IgM HRP		Goat IgG	Southern Biotech
Anti mouse IgG1 HRP		Goat IgG	Southern Biotech
Anti mouse IgA HRP		Goat IgG	Southern Biotech
Anti mouse IgG3 HRP		Goat IgG	Southern Biotech

Supplementary Table 4: List of primers used for Biomark based qPCR

	Gene	Reference/ Primers
Taqman assays	*Gapdh*	Mm99999915_g1
	Actb	Mm01205647_g1
	Prdm1	Mm00476128_m1
	Xbp1	Mm00457357_m1
	Irf4	Mm00516431_m1
	Pax5	Mm00435501_m1
	Cd3e	Mm00599684_g1
	Bach2	Mm00464379_m1
	Cd93	Mm00440239_g1
	Hspa5	Mm00517691_m1
	Edem2	Mm00467468_m1
	Dnajb9	Mm01622956_s1
	Atg5	Mm01187303_m1
	Traf2	Mm00801978_m1
	Atg12	Mm00503201_m1
	Atg16L1	Mm00513085_m1
	Ddit3	Mm01135937_g1
	Becn1	Mm01265461_m1
	Herpud1	Mm01249592_m1
	Edem1	Mm00551797_m1
	Tnfrsf13b	Mm03047441_m1

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