The class-specific BCR tonic signal modulates lymphomagenesis in a *c-myc* deregulation transgenic model



Supplementary Material

Supplemental Figure 1: Development and proliferation of B cell in a1KI c-myc3'RR

(A) Evaluation of B cells in spleen (n=5) and LNs (n=3) from 6 weeks old mice before any disease development. Percentage of B220⁺ cells from α 1KI *c-myc*3'RR (white bars) compared to α 1KI (black bars). (NS, not significant; *, p <0.05) (**B**) Splenocytes from the same α 1KI *c-myc*3'RR (white circles) and α 1KI/control mice (black circles) were stimulated *in vitro* with LPS or with anti-CD40 plus IL4 for 4 days. Absorbance in the MTS assay evaluates proliferation. Results from 5 independent experiments are shown. (NS, not significant; *, p <0.05, unpaired t-test).



Supplemental Figure 2: Clonality of lymphomas in α1KI *c-myc***3'RR mice** Southern blot analysis was used to check lymphoma clonality with a JH4 probe. Genomic DNA from hyperplasic spleens (S) and LNs were prepared and digested with EcoRI from different tumors (3 individual mice per group, each analyzed for spleen and LN).





Supplemental Figure 3: RNA profiling of type Ia and Ib double transgenic tumors vs "Burkitt-like" (BL) and anaplastic (ANA) tumors from single transgenic *c-myc* mice: The clustered genes shows the most significantly genes up-regulated (A) and down-regulated (B) in type Ia (n=4) and type Ib (n=4) from α 1KI *c-myc*3'RR tumors vs *c-myc*3'RR. Red represents up-regulation of gene expression, and green represents down regulation of gene expression.

Supplemental Table 1: RNA profiling of type Ia and Ib α1KI *c-myc*3'RR tumors compared to *c-myc*3'RR lymphomas. Data for the 213 most different genes were reported. The upregulated (A) and down-regulated (B) genes in type Ia and Ib *vs c-myc*3'RR were represented in two different sub-tables. Columns include gene names, gene descriptions, absolute fold-change (FC), signal ratio between double transgenic and single transgenic tumors and P-values.

Gene symbol	Gene name	Supplemental Table 1 (A) : Up-regulated genes	Absolute (FC)	Log(FC)	adjust n-Value
Ribosome biogenesis and protein synthesis	Gene name		Absolute (PC)	LUG(FC)	aujust p-value
Tbc1d2	TBC1 domain fa	amily, member 2	5,84	2,55	5,68E-02
Tbc1d2	TBC1 domain f	amily, member 2	4,77	2,25	5,89E-02
Rpl21	ribosomal prot	ein L21	3,97	1,99	1,02E-02
Rnu1b6	U1b6 small nu	clear RNA , small nuclear RNA	3,83	1,94	2,88E-02
Ankrd34a	ankyrin repeat	domain 34A	3,56	1,83	4,17E-05
ENSMUST00000117580	ubiquitin A-52 I	pyrophosphatase/phosphodiesterase 4 residue ribosomal protein fusion product 1 Gene	3,45	1,78	4,37E-02 8.11E-02
ENSMUST00000119783	GATA zinc finge	r domain containing 1 Gene	2,74	1,45	2,60E-02
Gm14052	similar to hete	rogeneous nuclear ribonucleoprotein A3	2,69	1,43	3,41E-02
Kpi17 Gm4510	similar to ribos	ilus ribosomai protein L17 nmal protein S19	2,52	1,33	5,41E-03 2,69E-03
Gm9179	similar to ribos	omal protein L32	2,44	1,29	6,07E-03
Gm8880	similar to ribos	omal protein L21	2,34	1,22	7,02E-03
Gm2334 Grmm	similar to Ubtf	protein (mphocyte met-ase 1)	2,32	1,22	9,32E-02
LOC637851	similar to hete	rogeneous nuclear ribonucleoprotein A3	2,24	1,17	3,02E-02
LOC674157	hypothetical L0	DC674157	2,24	1,16	2,56E-02
4930565014	tRNA-guanine	transglycosylase {Homo sapiens}	2,20	1,14	6,24E-03
Dtymk Broß	deoxythymidyl ribosomal RNA	ate kinase , transcript variant 2 processing 8 methyltransferase, homolog (veast)	2,18	1,12	8,42E-02 3,68E-02
Eif4a2	eukaryotic tran	slation initiation factor 4A2, transcript variant 1	2,05	1,04	4,81E-02
Eif2s1	eukaryotic tran	slation initiation factor 2, subunit 1 alpha	5,31	2,41	1,16E-02
Rg9mtd2	RNA (guanine-9	-) methyltransferase domain containing 2, full insert sequence	2,27	1,18	1,53E-02
Fosb	FBJ osteosarco	ma oncogene B	52,30	5,71	9,95E-05
Hist1h2bg	histone cluster	1, H2bg	8,29	3,05	2,77E-02
H3f3b	H3 histone, far	nily 3B	4,49	2,17	6,28E-02
Hist2h2bb	histone cluster	2, H2bb	4,01	2,00	8,17E-02
Hist1h1e	histone cluster	1. H1e	2.79	1,61	7.01E-02
Hist1h3f	histone cluster	1, H3f	2,72	1,44	9,72E-02
Gm12260	similar to histo	ne H3	2,28	1,19	2,25E-02
Kbtbd12 Sath2	kelch repeat ar	nd BTB (POZ) domain containing 12, transcript variant 1	2,27	1,18	3,21E-02
Tiparp	TCDD-inducible	e poly(ADP-ribose) polymerase	2,28	1,15	6.24E-03
Hist1h2aa	histone cluster	1, H2aa	2,18	1,13	2,40E-02
Atad2	ATPase family,	AAA domain containing 2	2,18	1,12	7,77E-02
Hist1h3d Kbtbd11	histone cluster	1, H3d d PTP (PO7) domain containing 11	2,11	1,08	2,34E-02
H3f3b	H3 histone, fan	nily 3B	2,15	1,10	2,45E-02
Highly expressed in immune system		· ·			
Gm8909	predicted gene	8909	11,46	3,52	2,25E-03
Kiral6 Cd69	Killer cell lectin	-like receptor, subfamily A, member 16	4,15	2,05	6,07E-03
Ccl25	chemokine (C-	C motif) ligand 25 (Ccl25), transcript variant 1	2,80	1,48	1,24E-02
LOC235882	similar to Ifi20	3 protein	2,38	1,25	6,30E-02
F630048H11Rik	NOD-derived C	D11c +ve dendritic cells cDNA, RIKEN full-length enriched library	2,26	1,18	8,93E-02
Kira22 Gm9442	similar to prot	-like receptor subfamily A, member 22 hymosin alnha	2,08	1,05	9,86E-02 5 16E-02
Intracellular signal transduction modulators and effe	ctors	in the second	2,00	2,00	5,102.02
Dusp6	dual specificity	phosphatase 6	3,96	1,98	5,65E-02
Ehd2	EH-domain cor	ntaining 2	3,13	1,65	7,77E-02
Dnahc8 Dnaib9	dynein, axonen Dnal (Hsn40) h	iai, heavy chain 8 iomolog, subfamily B, member 9	2,94	1,55	6,74E-02 8.31E-02
Ptk2	PTK2 protein t	vrosine kinase 2 , transcript variant 2	2,37	1,24	6,22E-02
Tram2	translocating c	hain-associating membrane protein 2, transcript variant 2	2,20	1,14	7,77E-02
Tmod4	tropomodulin 4	-	2,10	1,07	8,89E-02
Pkib	protein kinase	inhibitor beta, cAMP dependent, testis specific, transcript variant 2	2,09	1,05	8,41E-02
Metabolic enzyme-related proteins			_,	-/	
B3galtl	beta 1,3-galact	osyltransferase-like	2,47	1,31	7,16E-03
Linid metabolism	UDP-Gal:betaG	ICNAC beta 1,4-galactosyltransferase, polypeptide 3	3,96	1,98	7,48E-03
Lgr5	leucine rich rep	peat containing G protein coupled receptor 5	4,83	2,27	7,40E-02
LOC100046908	similar to cyclic	nucleotide gated channel beta 1	3,17	1,66	6,71E-02
ENSMUST00000101612	ATP-binding ca	ssette, sub-family B, member 4 Gene	3,02	1,59	1,95E-02
Hsd17b7	hvdroxysteroid	(17-beta) dehvdrogenase 7	2,66	1,41	2.41E-02
Cell cycle					
Rbl1	retinoblastoma	a-like 1 (p107) (Rbl1), transcript variant 2	2,10	1,07	5,65E-02
Cort Apitd1	cortistatin (Cort apontosis-indu	t) ring. TAF9-like domain 1	3,12	1,64	3,13E-02 4.05E-02
Apoptose	apoptosis indu	ang, n'n 5 me coman a	2,00	2,12	4,052.02
Ppp1r15a	protein phosph	atase 1, regulatory (inhibitor) subunit 15A	12,64	3,66	5,64E-03
Gas5	growth arrest s	pecific 5 (Gas5)	12,61	3,66	6,68E-03
Cell adhesion-related protein	b-cell transiona	uon gene 1, and promerative	3,24	2,35	1,300-02
Pvrl2	poliovirus recep	otor-related 2, transcript variant 2	4,35	2,12	7,18E-03
Pvrl2	poliovirus rece	otor-related 2 , transcript variant 1	9,45	3,24	4,81E-03
Dars2	aspartyl-tRNA	synthetase 2 (mitochondrial)	2.09	1.06	6.24E-03
SIc25a37	solute carrier f	amily 25, member 37, nuclear gene encoding mitochondrial protein	2,56	1,36	6,97E-02
Gm16399	similar to cytoc	hrome c oxidase, subunit Vic	2,32	1,21	5,64E-03
Mcart1	mitochondrial	carrier triple repeat 1, nuclear gene encoding mitochondrial protein	2,28	1,19	6,24E-03
Others (Table 1-suite)	mitochonunany	encoded NADH denydrogenase o Gene	2,22	1,15	8,702-02
4931429I11Rik	RIKEN cDNA 49	31429111 gene	31,75	4,99	9,95E-05
Gm1983	similar to CG15	5780-PA (LOC100038956)	4,19	2,07	2,69E-03
ENSMUS100000118228 C5300280218ik	RIKEN CDNA C	og 1 Gene	3,22	1,69	4,34E-02 3,21E-02
LOC100048452	hypothetical pr	otein LOC100048452	2,92	1,55	8,20E-02
Gm6323	predicted gene	e, EG622446 (EG622446)	2,92	1,54	4,81E-03
6230415J03Rik	11 days embry	o head cDNA, RIKEN full-length enriched library	2,70	1,43	1,24E-02
Gm12118	activated splee	in CLINA, RIKEN TUII-length enriched library 008 (LOC666269)	2,67	1,42	9,96E-02 6.68E-03
EG638052	predicted gene	, EG638052 (EG638052)	2,53	1,34	6,68E-03
Krtap8-2	keratin associa	ted protein 8-2 (Krtap8-2)	2,53	1,34	5,41E-03
Gm9456	hypothetical LC	0C669389 (LOC669389)	2,46	1,30	3,46E-02
Gm13154	predicted gene	036359 (LUC100039528) • 13154 (Gm13154)	2,40	1,26	4,28E-02 4.43E-02
Gm7721	predicted gene	EG665631	2,21	1,15	3,99E-02
D16Ertd472e	DNA segment,	Chr 16, ERATO Doi 472, expressed	2,18	1,12	1,33E-02
Gm3219	predicted pseu	dogene 3219	2,12	1,08	6,22E-02
Gm5196	predicted gene	EG382769	2,07	1,05	6,49E-02
C030048B08Rik	RIKEN cDNA CO	030048808 gene	2,03	1,02	1,69E-02
FC : Fold Change. Adujst p-Values were calculated us	ing Benjamani-H	oschberg method.			

Gene symbol	Supplemental Table1 (B) : Down-regulated genes	Absolute (EC)	Log(EC)	adjust n-Value
Ribosome biogenesis and protein synthesis	Gene hame	Absolute (FC)	LOG(FC)	adjust p-value
LOC100045542	similar to FERMRhoGEF (Arhgef) and pleckstrin domain protein 1	3,28	-1,71	3,90E-02
Rbm47	RNA binding motif protein 47 , transcript variant 1	5,43	-2,44	2,34E-02
Zc3h12d Tem2	zinc finger CCCH type containing 12D transelutaminase 2. C nolynentide	3,02	-1,59	6,14E-02 6,70E-02
Rps6ka1	ribosomal protein S6 kinase polypeptide 1	2,74	-1,45	8,48E-02
Anpep	alanyl (membrane) aminopeptidase	2,63	-1,40	9,57E-02
Acaala Pol21	acetyl-Coenzyme A acyltransferase 1A	2,18	-1,13	3,09E-02
Sympk	symplekin	2,22	-1,15	1,50E-02
Transcription factors and DNA-binding proteins				
Zbtb20 Din2c	zinc finger and BTB domain containing 20, transcript variant 1 DIP2 disco.interacting protein 2 homolog C	7,53	-2,91	8,70E-02 3.13E-02
Zfp760	zinc finger protein 760	2,29	-1,19	5,69E-02
Nfam1	Nfat activating molecule with ITAM motif 1	6,87	-2,78	3,58E-02
Nab2	Ngfi-A binding protein 2, transcript variant 1	6,21	-2,63	5,38E-02
Highly expressed in immune system	retinoic acid receptor, gamma, transcript variant 1	3,39	-1,04	2,502-02
ENSMUST00000103424	immunoglobulin heavy chain 5 (delta-like heavy chain)	25,76	-4,69	3,11E-04
Ncf1	neutrophil cytosolic factor 1	8,79	-3,14	3,01E-02
Csf2rb	colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	7,59	-2.92	4.57E-02
Sema7a	sema domain, immunoglobulin domain (Ig), and GPI membrane anchor 7A	6,38	-2,67	4,34E-02
Mpeg1	macrophage expressed gene 1	5,65	-2,50	6,63E-02
H2-DMB1 Lilrb3	nistocompatibility 2, class II, locus MD1 leukocyte immunozlobulin-like recentor, subfamily B (with TM and ITIM domains), member 3	5,21	-2,38	2,25E-02 4.79E-02
Cd300lf	CD300 antigen like family member F , transcript variant 2	4,17	-2,06	3,11E-02
LOC547349	similar to MHC class I antigen precursor	3,98	-1,99	2,06E-02
H2-19 C1ra	nistocompatibility 2, i region locus 9 complement component 1, r subcomponent A	3,62	-1,85	2,03E-02 2.34E-02
LOC675328	similar to MHC H2-TL-T10-b	3,48	-1,80	4,86E-03
Csf2rb2	colony stimulating factor 2 receptor, beta 2, low-affinity (granulocyte-macrophage)	3,42	-1,77	1,87E-02
Irgm2 Gm7229	immunity-related GTPase family M member 2 similar to II -1 recentor-associated kinase 2	3,23	-1,69	7,40E-02 4.05E-02
Sh2d3c	SH2 domain containing 3C	2,57	-1,36	9,18E-02
Csf2rb	colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	2,52	-1,33	6,88E-02
Spn Intracellular signal transduction modulators and eff	sialophorin (Spn), transcript variant 1	2,13	-1,09	9,47E-02
Tbkbp1	TBK1 binding protein 1	2,52	-1,33	3,09E-02
SIc7a7	solute carrier family 7 (cationic amino acid transporter, y+ system), member 7	9,19	-3,20	5,65E-02
SIC39a4 Hrk	solute carrier family 39 (zinc transporter), member 4 hemonoietic cell kinase (Hck), transcript variant 1	14,02	-3,81	6,01E-02 8,48E-02
Ggh	gamma-glutamyl hydrolase	10,03	-3,38	1,29E-02
Sirpa	signal-regulatory protein alpha, transcript variant 1	6,75	-2,76	4,30E-02
Lxn Raolgan	latexin (Lxn) Ban1 GTPsse-activating protein	6,44	-2,69	8,67E-02
Rassf4	Ras association (RalGDS/AF-6) domain family member 4	3.44	-2,18	3,59E-02 7.85E-02
Sla	src-like adaptor (Sla), transcript variant 1	3,33	-1,74	8,16E-02
H2afb3-ps	similar to vacuolar protein sorting 52	3,29	-1,72	8,41E-04
LOC100045542 Dusn16	similar to FERMRhoGEF (Arhget) and pleckstrin domain protein 1 dual specificity phosphatase 16. transcript variant 41	3,28	-1,71	3,90E-02 7.85E-02
Sic37a2	solute carrier family 37 (glycerol-3-phosphate transporter), member 2 , transcript variant 1	2,97	-1,57	6,07E-03
Ctsd	cathepsin D	2,91	-1,54	9,57E-02
Arhgap9 Gng12	Rho GTPase activating protein 9 guanine nucleotide binding protein gamma 12 transcript variant 2	2,82	-1,50	4,15E-02 5,57E-02
Eml2	echinoderm microtubule associated protein like 2 , transcript variant 1	2,82	-1,49	7,47E-02
Gpr18	G protein-coupled receptor 18	2,75	-1,46	9,55E-02
Ctsh Richard	cathepsin H	2,67	-1,42	6,30E-02
Gng12	guanine nucleotide binding protein, gamma 12, transcript variant 2	2,40	-1,27	7,09E-02
Exoc1	exocyst complex component 1	2,10	-1,07	2,59E-02
Metabolic enzyme-related proteins	neuropilin 2. transcript variant 1	10.96	-3.45	8 205-02
Gaa	glucosidase, alpha, acid, transcript variant 1	5,41	-2,44	6,68E-03
Nrp2	neuropilin 2 (Nrp2), transcript variant 5	4,93	-2,30	7,80E-02
B4galt6	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 6 palmitoul-protein thioacterate 2	4,73	-2,24	6,16E-02
Tcn2	transcobalamin 2, transcript variant 1	3,60	-1,85	6,96E-02
Col4a1	collagen, type IV, alpha 1	3,15	-1,66	6,22E-02
B4galt6	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 6	3,44	-1,78	7,80E-02
Anxa6	annexin A6 , transcript variant 1	3,19	-1,68	8,96E-03
Cyp4v3	cytochrome P450, family 4, subfamily v, polypeptide 3	3,91	-1,97	8,87E-02
Apobec3	apolipoprotein B, catalytic polypeptide 3, transcript variant 2	2,90	-1,54	7,51E-02
Cbr2	carbonyl reductase 2	2,33	-1,42	6,22E-02
Mthfd2l	methylenetetrahydrofolate dehydrogenase 2-like	2,32	-1,21	9,53E-02
Adcy7	adenylate cyclase 7 , transcript variant 3	2,21	-1,14	5,72E-02
Sepw1	selenoprotein W. muscle 1	2,21	-1,14	4.22E-02
Lipid metabolism				
Smpdl3a	sphingomyelin phosphodiesterase, acid-like 3A	6,97	-2,80	5,38E-02
Apoe St8sia6	apolipoprotein E ST8 aloha-N-acetyl-neuraminide aloha-2.8-sialyltransferase 6	9.65	-3,75	3,09E-02 3.26E-02
Plin3	perilipin 3	5,68	-2,51	8,02E-02
Abcb1b	ATP-binding cassette, sub-family B (MDR/TAP), member 1B	5,37	-2,43	5,17E-02
Sepl1	oxysterol binding protein-like 3, transcript variant 2 sphingosine phosphate lyase 1	2,76	-1,47	4,10E-02 9.12E-02
Abcg1	ATP-binding cassette, sub-family G , member 1	2,63	-1,39	7,77E-02
Cell cycle	B-cell loukemis/kumphema 2 related protein A1d	9.07	2.01	5 705 03
Bcl2a1c	B-cell leukemia/lymphoma 2 related protein A10 B-cell leukemia/lymphoma 2 related protein A10	5,31	-3,01	5,73E-02
Xaf1	XIAP associated factor 1	3,90	-1,96	6,84E-02
Cdk20	cyclin-dependent kinase 20	2,80	-1,49	8,15E-02
ceii aanesion-relatea protein (Table 2-suite) Nid1	nidogen 1	7,78	-2.96	5,62E-02
Rap1gap	Rap1 GTPase-activating protein	7,56	-2,92	3,49E-02
Rdx	radixin (Rdx), transcript variant 1	5,82	-2,54	9,57E-02
Kctd17	ref Mus musculus potassium channel tetramerisation domain containing 17	4.01	-2,46	3,08E-02 8,67E-02
ltgb1	ref Mus musculus integrin beta 1 (fibronectin receptor beta)	3,95	-1,98	5,07E-03
Thbs3	thrombospondin 3	2,26	-1,18	8,20E-02
Hba-a1	hemoglobin alpha, adult chain 1	8,06	-3.01	3,76E-02
Hbb-b1	hemoglobin, beta adult major chain	7,92	-2,99	3,09E-02
Hba-a2	hemoglobin alpha, adult chain 2	5,92	-2,57	3,22E-02
Mitochondrial -related protein	synuciem, aipria , transcript variant 1	3,37	-1,75	5,53E-02
Nmnat3	nicotinamide nucleotide adenylyltransferase 3	4,67	-2,22	3,09E-02
Alas2	aminolevulinic acid synthase 2, transcript variant 1	4,73	-2,24	7,85E-02
Others	isocnorismatase domain containing 2b	2,49	-1,32	3,91E-02
Trim12	tripartite motif-containing 12 (Trim12), mRNA [NM_023835]	29,52	-4,88	5,41E-03
BC018473	cDNA sequence BC018473	6,96	-2,80	3,01E-02
0610042G04Rik ENSMUST00000100423	KIKEN CDNA U610042G04 gene (0610042G04Rik), mRNA [XM_001472222] Putative uncharacterized protein/MCG123851	5,94	-2,57	2,40E-02
Trim12	tripartite motif-containing 12	4,34	-2,12	2,06E-02
ENSMUST00000101310	predicted gene 1070 Gene	3,50	-1,81	3,06E-02
Trim59	tripartite motif-containing 59 RKEN - DNA 2010016118 range	3,49	-1,80	3,11E-02
AA388235	expressed sequence AA388235	3,21 2,95	-1,68	6,51E-0Z 3,45E-03
LOC677216	similar to vacuolar protein sorting 52	2,62	-1,39	5,64E-03
A830007P12Rik	RIKEN cDNA A830007P12 gene	2,41	-1,27	8,71E-03
9530082P21Rik Gm4552	o day neonate lung CDNA, KIKEN tull-length enrichéd libráry similar to keratin associated protein 5-5	2,32	-1,21	6,49E-02 5.64E-03
9030607L17Rik	RIKEN cDNA 9030607L17 gene	2,07	-1,05	4,87E-02
Fam132a	family with sequence similarity 132, member A	2,00	-1,00	6,55E-02
FC : Fold Change. Adujst p-Values were calculated u	ising Benjamani-Hoschberg method.			

Supplemental Table 2

Top regulated network in up-regulated genes

1- Cell Cycle, Cancer, Gastrointestinal disease

Atad2, Btg1, Cort, Dnajb9, Eif2s1, Eif4a2, Gpdl1, H3f3b, Hist1h3b, Hist1h2aa, Gm12260, hist1h3f, Hist1h1e, hist2h2bb, hist1h2bg, Pkib, RPL21, Slc25a37, Tirap

2- Cellular development, Cellular growth and proliferation, Hepatic system, development and function *Abcb4, Atad2, Ehd2, Eif2s1, Gas5, Gzmm, Hist1h2ac, hist2h2be, Hsd17b7, Lgr5, Mt-nd6, Rpl17, Satb2, Tram2*

3- Cell death and survival, Cell morphology, Cellular assembly and organization *Ccl25, CD69, Dup6, Eif2s1, Fosb, Hla-b, Ppp1r15a, Ptk2, pvrl2, Rbl1, Trib1*

Top regulated network in down-regulated genes

1- Cellular Movement, Immune cell trafficking, Hematological System development and function *Abcb1b, anxa2, Anxa6, Bcl2a1, Col4a1, Csf2rb, Cybb, Fam132a, Hck, Igf1r, Itgb1, Lilrb3, ncf1, nid1, rap1gap, Sirpa, Snca, Spn, Tgm2, Zbtb20*

2- Cellular growth and proliferation, Lymphoid tissue structure and development, Organ morphology *Adcy7, Bcl2a1c, Cbr2, Cdk20, Cybb, exoc1, Gpr18, hba1/hba2, Hck, Nrp2, Osbpl3, Plin3, ppt2, Sgpl1, Sympk, x*

3- Cancer, Cell death and survival, Gastrointestinal disease abcb1b, abcg1, acaa1, anpep, c1r, Ctsh, Cybb, gaa, Manba, rassf4, Rbn47, rpl21, Sh2d3c, Slc7a7, thbs3

4- Development disorder, Hematological disease, Organ morphology *Abcg1, Alas2, ApoE, CD300lf, Ctsd, dusp16, Hba1/Hba2, Hbb, HLA-DMB, Ncf1, Ptprj, Rarg, Rps6Ka1, Sla*

5-Hematological disease, Infectious disease, RNA damage and repair

Apobec3b, B4galt6, Cyp4v2, Gng12, Irgm2, Mthfdl2l, plekho2, rdx, Sema7a, tcn2, tgm2

6- Cell death and survival, Cell morphology, Cellular function and maintenance *ggh, Kctd17, mpeg1, nab2, slc39a4, Snca, St8sia6, Tbkbp1*