

Supplementary Table Legend

Table S1. Necropsy Information for Selected Tax+Hbz+ Cohort.

Characteristics of BRIGHT mice including; presence of Tax transgene (+ = mCherry-TET-TAX; +* = GZMB-TAX); presence of Hbz transgene; white blood cell count ($\times 10^3$ per ul); differential (SEG = % neutrophil, LYM = % lymphocyte, MON = % monocyte); red blood cell count ($\times 10^6$ per ul); hemoglobin (Hb; g/dL); hematocrit (Hct; %); Mean Corpuscular Volume (MCV; fL), Mean Corpuscular Hemoglobin (MCH; pg), Mean Corpuscular Hemoglobin Concentration (MCHC; g/dL), Platelets (PLAT; $\times 10^3$ per ul); Spleen weight (g); Enlarged Lymph Nodes; Presence of doxycycline in diet (DOX); Sex (SEX), Age at necropsy (AGE). Elevated values in red for WBC > 5k, SEG > 70%, LYM > 70% MON > 2%; SPLEEN > 0.2; NODE = Yes.

Supplementary Figure Legends

Figure S1. Biomarkers for Leukemia in BRIGHT mice.

A-C) Bulk RNAseq reads for 598 protein coding genes that, normalized to Actb, are expressed at >0.1% Actb and significantly upregulated in leukemia (>2 fold, $p < 0.05$) compared to remaining 4 mice. Using STRING (using MCL clustering with inflation parameter at 1.5), these 598 genes form 58 clusters, one of which included 13 genes associated with abnormal lymphocyte physiology (Mammalian Phenotype Ontology (monarch) enrichment). Reads for four genes (Tnfrsf8, Cd80, Cd69, and Syk) normalized to Actb shown for each sample. D) Reads obtained from scRNAseq that span slice junctions of the Tnfrsf8 gene normalized to Gapdh. Statistics (probability associated with 2-tailed, Type 2 Student's t-Test).

Figure S2. Biomarkers for Lymphoma in BRIGHT mice.

Bulk RNAseq reads for 85 protein coding genes that, normalized to Actb, are upregulated in lymphoma (>2 fold) compared to remaining 4 mice. Using STRING (using MCL clustering with inflation parameter at 1.5), these 85 genes form 5 clusters, one of which included 4 genes in the Tcstv family, two of which have been associated telomere length maintenance in mouse embryonic stem cells. Reads from scRNAseq for three genes (Cd59a, Prickle1, and Bambi) shown for each sample. Statistics (probability associated with 2-tailed, Type 2 Student's t-Test). T-SNE plots for scRNAseq data showing AF067061 (Tcstv2a) expression.

Figure S3. Biomarkers for Lymphoproliferative Disease in BRIGHT mice.

Bulk RNAseq reads for 240 protein coding genes that, normalized to Actb, were overexpressed in both leukemia and both lymphoma samples compared to the GZMB-TAX control splenocytes (>2 fold each), resulted in 22 clusters in STRING (using MCL clustering with inflation parameter at 1.5).

Figure S4. Expansion of Cd2+CD20+ Lymphocytes in BRIGHT mice.

T-SNE plots of scRNAseq data for each sample with Cd2+ T cells (Black), Cd19+Cd20+ B cells (Blue), and Cd2+Cd19+Cd20+ lymphocytes (Red)

Figure S5. DOX-Associated Genes in BRIGHT mice.

Bulk RNAseq reads for 16 protein coding genes that, normalized to Actb, are upregulated in DOX treated mice (>2 fold) compared DOX- mice. Using STRING (using MCL clustering with inflation parameter at 1.5), these 16 genes form 1 cluster of 14 genes which are all associated with protein and lipid metabolism especially abundant in pancreatic secretion (KEGG Pathways; Kanehisa, M., Sato, Y., Kawashima, M., Furumichi, M., and Tanabe, M.; KEGG as a reference resource for gene and protein annotation. Nucleic Acids Res. 44, D457-D462 (2016); Kanehisa, M. and Goto, S.; KEGG: Kyoto Encyclopedia of Genes and Genomes. Nucleic Acids Res. 28, 27-30 (2000)

Figure S6. Tax-Associated Genes in BRIGHT mice.

Bulk RNAseq reads for 104 protein coding genes that, normalized to Actb, are upregulated in DOX treated mice and GZMB-TAX (>3 fold) compared DOX- mice. Using STRING (using MCL clustering with inflation parameter at 2), these 104 genes form 12 clusters, the largest of which contains 23 genes associated with inflammatory response.

Figure S7. Elevated Expression of Ptch1, Kras, and Dnaja3 (Tid1) in Leukemia Samples

Bulk RNAseq reads normalized to Actb. P-values are two-tailed Student's t Test.

Table S1. Necropsy Information for selected TAX+HBZ+ Cohort

ID#	T	H	WBC	SEG	LYM	MON	RBC	HB	HCT	MCV	MCH	MCHC	PLAT	SPLEEN	NODE	DOX	SEX	AGE
294	+	+	27.5	10	86	2	6.8	9.7	32.1	47.2	14.3	30.2	608	.36	YES	YES	F	18
213	+	+	60.0	4	94	2	5.87	9.3	30.6	52.1	15.8	30.4	509	.69	YES	YES	F	24
239	+	+	46.1	23	57	20	3.34	5.3	15.0	44.8	15.9	35.3	575	.60	YES	YES	F	24
240	+	+	9.46	25	64	10	6.80	8.9	30.4	44.7	13.1	29.3	540	.78	YES	YES	F	24
272	+	+	4.04	14	82	4	4.26	5.5	19.0	44.6	12.9	28.9	178	.56	YES	NO	M	19
257	+	+	2.86	24	72	4	7.82	10.6	42.1	53.9	13.6	25.2	724	.30	YES	NO	F	24
296	+	+	1.66	39	61	0	7.84	10.0	39.1	49.9	12.8	25.6	945	.25	YES	YES	M	18
246	+	+	2.56	30	66	4	5.67	8.0	32.1	56.7	14.1	24.9	1306	.75	YES	YES	M	24
261	+	+	2.12	47	50	1	5.14	6.2	23.7	46.2	12.1	26.2	1105	.51		YES	M	24
244	+	+	5.44	60	35	4	5.58	7.5	25.7	46	13.4	29.2	797	.44	YES	YES	M	24
252	+	+	7.68	4	95	1	7.10	10.4	42.2	59.4	14.6	24.6	547	.20		YES	F	18
226	+	-	3.56	39	55	5	6.96	8.7	28.3	40.7	12.5	30.7	901	.17		YES	M	24
250	+	+	2.84	45	43	9	8.72	10.6	35.6	40.8	12.2	29.8	803	.39	YES	YES	M	24
235	+	+	3.02	49	47	4	8.66	11.1	37.8	43.7	12.8	29.4	826	.21		YES	M	20
291	+	+	21.6	38	59	3	6.61	9.9	29.5	44.6	15.0	33.6	991	.29		YES	M	21
221	+	+	3.60	45	44	7	7.41	10	40.5	54.7	13.5	24.7	832	.33		NO	M	18
286	+	+	3.58	25	71	2	8.56	11.1	45.3	52.9	13.0	24.5	986	.12		YES	M	18
LLTPD1	+	*	17.7	92	8	0	7.46	11.3	39.6	53.1	15.1	28.5	904	.21	YES	NO	M	6
LLT198	+	*	2.24	83	14	3	7.75	11.8	42.5	54.9	15.2	27.8	617	.28	YES	NO	F	24

Figure S1

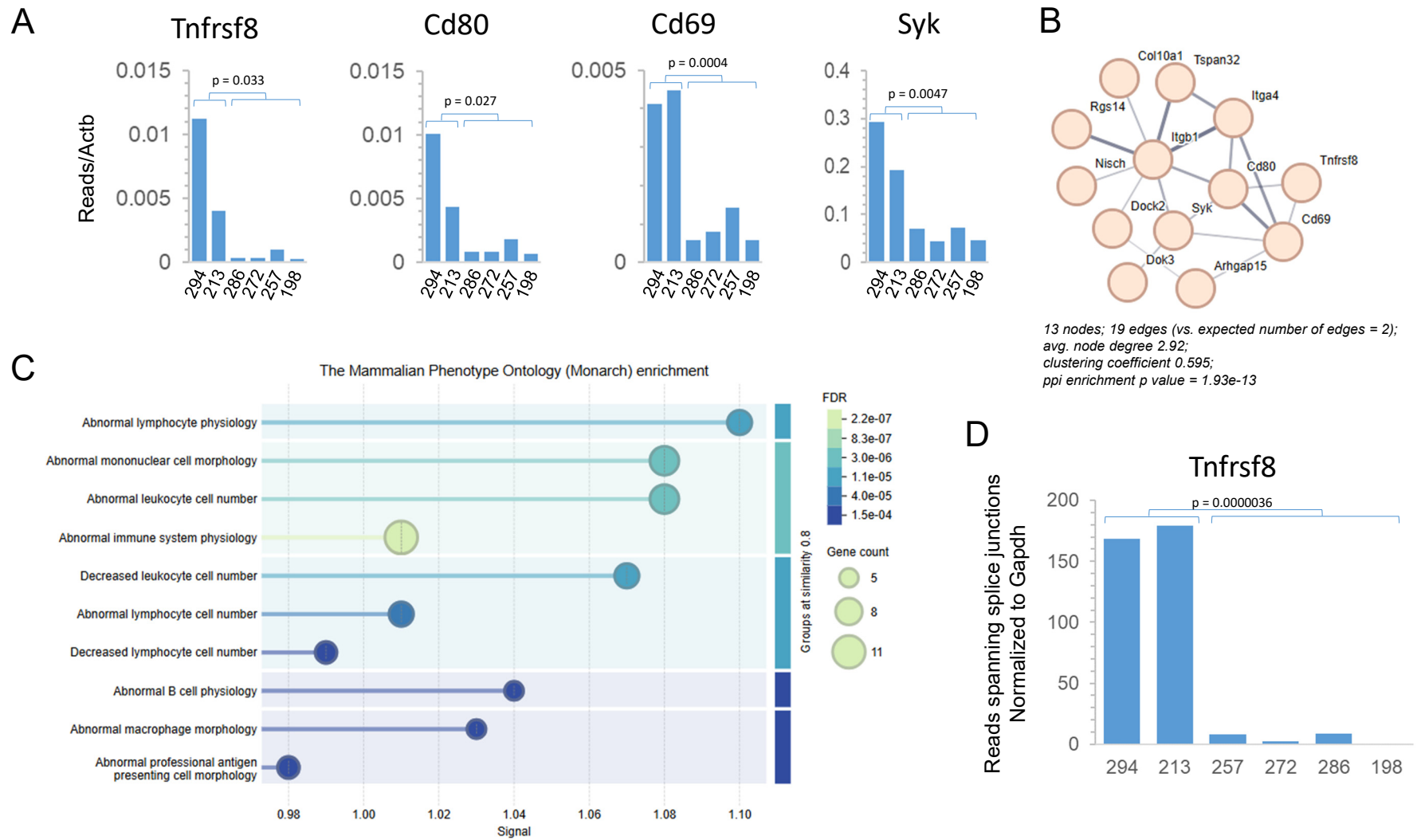


Figure S2

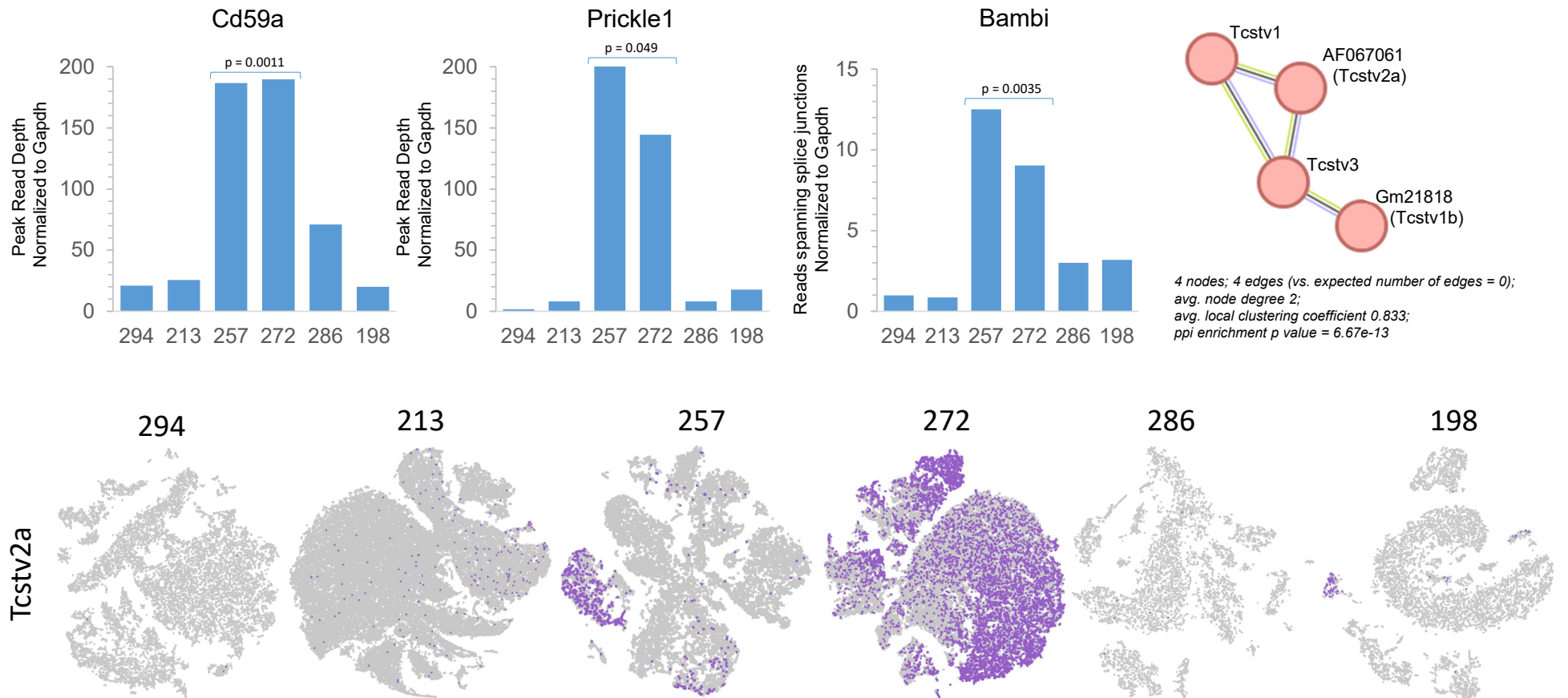
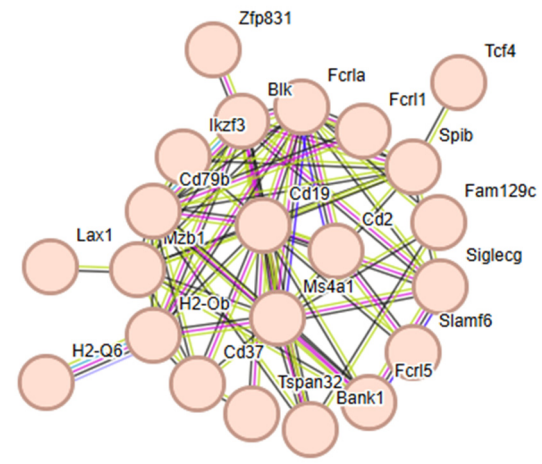
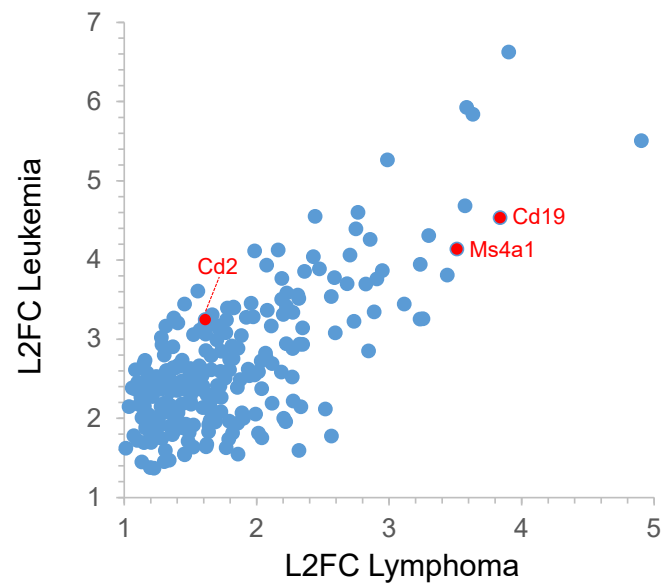


Figure S3

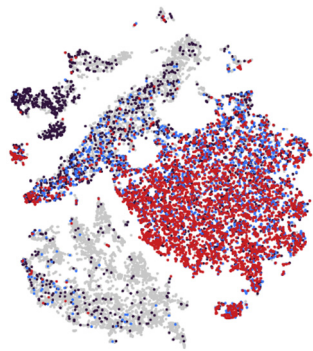


22 nodes; 63 edges (vs. expected number of edges = 1);
avg. node degree 5.73;
avg. local clustering coefficient 0.752;
ppi enrichment p value < 1.0e-16

Figure S4

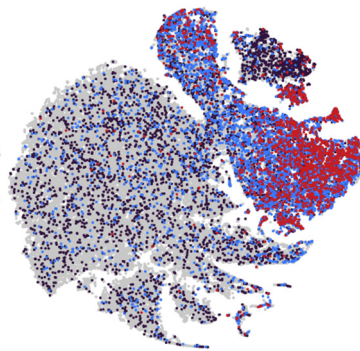
Leukemia

294



- ✓ Cd2+ (2901)
- ✓ Cd19+Cd20+ (2163)
- ✓ Cd2+Cd19+Cd20+ (3683)

213



- ✓ Cd2 (5821)
- ✓ Cd19+Cd20+ (4911)
- ✓ Cd2+Cd19+Cd20+ (1934)

Lymphoma

257



- ✓ Cd2+ (2159)
- ✓ CD19+CD20+ (2107)
- ✓ CD2+CD19+CD20+ (1855)

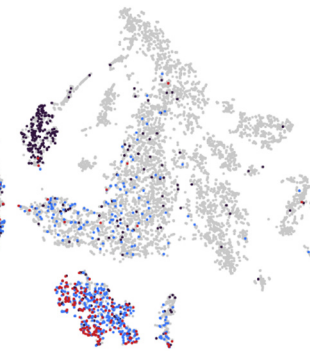
272



- ✓ Cd2+ (3302)
- ✓ Cd19+Cd20+ (4934)
- ✓ Cd2+Cd19+Cd20+ (1871)

Control

286



- ✓ Cd2+ (314)
- ✓ Cd19+Cd20+ (481)
- ✓ Cd2+Cd19+Cd20+ (169)

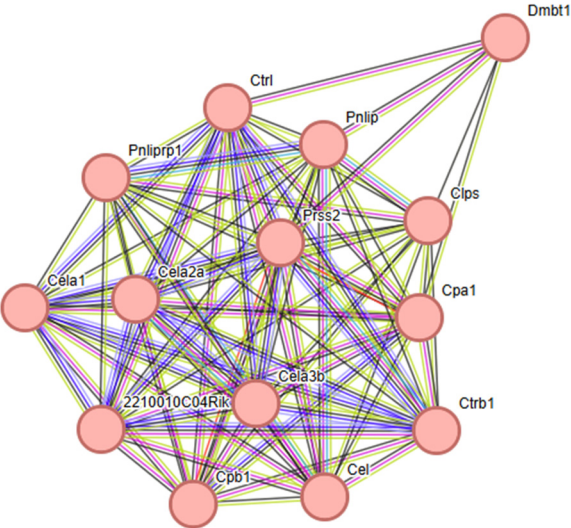
198



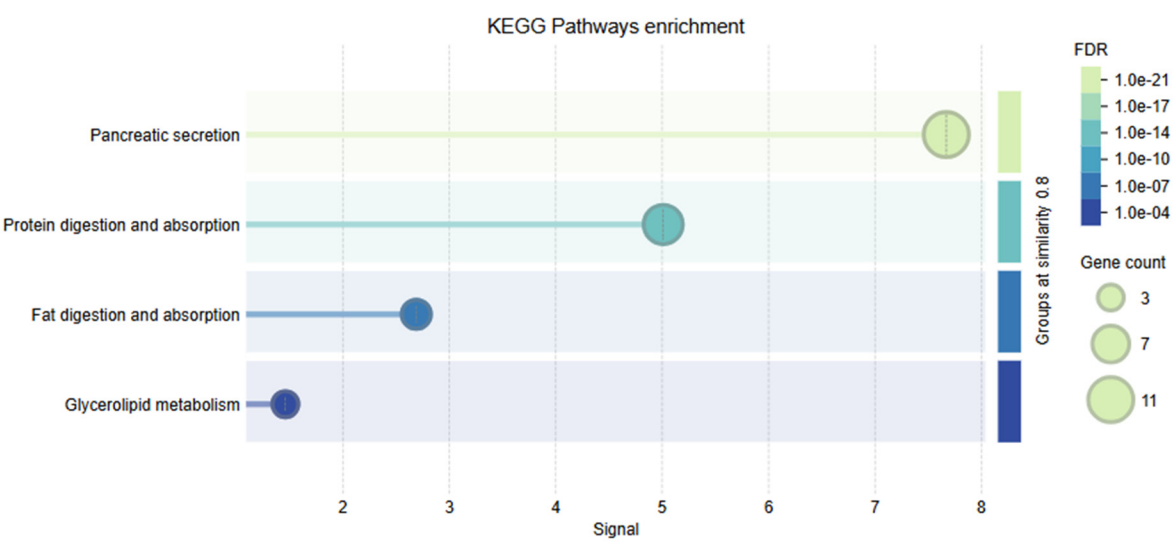
- ✓ Cd2+ (451)
- ✓ Cd19+Cd20+ (68)
- ✓ Cd2+Cd19+Cd20+ (84)

DOX Associated Genes

Figure S5

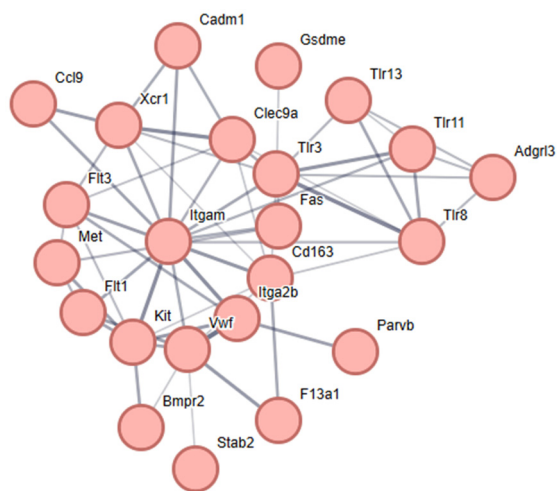


14 nodes; 83 edges (vs. expected number of edges = 0);
avg. node degree 11.9;
avg. local clustering coefficient 0.963;
ppi enrichment p value < 1.0e-16



TAX Associated Genes

Figure S6



23 nodes; 58 edges (vs. expected number of edges = 8);
avg. node degree 5.04;
avg. local clustering coefficient 0.684;
ppi enrichment p value < 1.0e-16

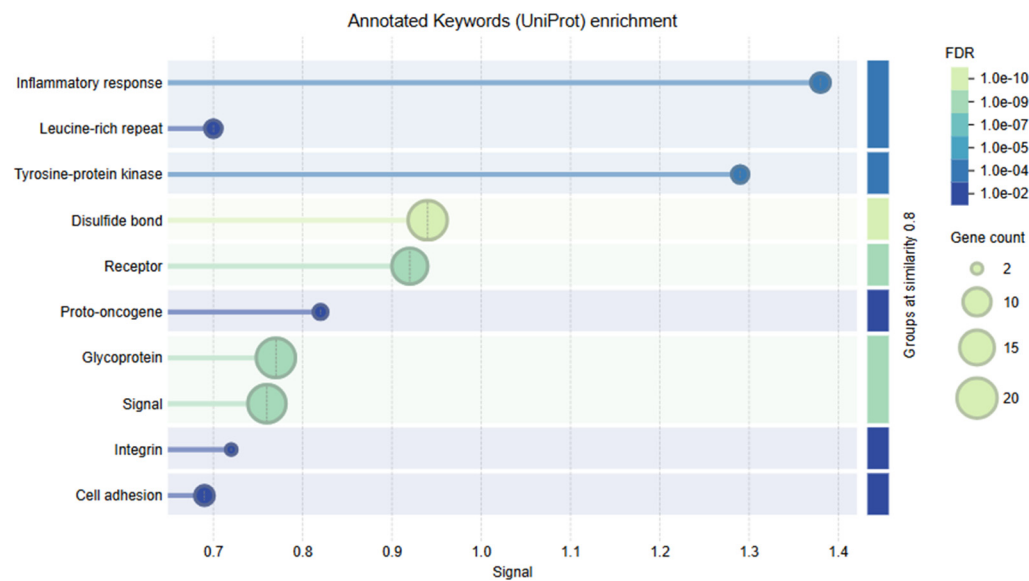


Figure S7

