Supplementary Materials and Methods

Animals: The absence of *Helicobacter* species, including *H. bilis*, *H.* ganmani, *H.* hepaticus, *H.* rodentium and *H. typhlonius* was confirmed by PCR of fecal samples (IDEXX Laboratories, Columbia MO). Wild type (C57BL/6J), *Il10*$^{-/-}$, *Tnfr2*$^{-/-}$ and *Rag2*$^{-/-}$ mice were from The Jackson Laboratory (Bar Harbor, ME).

Chemicals, reagents and antibodies: Dextran Sodium Sulfate (36–50 KDa) was from MP Biomedicals (Burlingame, CA). AOM was from Wako (Richmond, VA). Recombinant murine IFN and TNF were from Peprotech (Rocky Hill, NJ). Rat anti–Ki-67 was from Dako. Rabbit antibodies for Cleaved Caspase-3, pH-H3, and phospho–histone H2AX were from Cell Signaling Technology (Beverly, MA). E-cadherin, MPO and 8-hydroxyguanosine antibodies were from Abcam (Cambridge, MA). Flow cytometry antibodies for CD16/32, TNF, Biotin-TNFR2, CD3, CD4, CD8 and were from BD Biosciences (San Jose, CA).

Colonoscopy. Mice were anesthetized with ketamine and xylazine. Distal colonoscopy was performed using a KARL STORZ Veterinary Endoscope (Karl Storz, Tuttlingen, Germany) to track the development of disease using a previously described scoring system [1].

Barrier Function Assay: Colonic *in vivo* permeability was measured using a previously described method [2]. Briefly, mice were anesthetized with ketamine and xylazine, and plasma fluorescence was measured at 30 min following intrarectal administration of 4 kDa FITC-dextran (Sigma-Aldrich, St Louis, MO); baseline plasma fluorescence was used as the blank.

Tissue harvesting and histology: Mice were euthanized as per institutional guidelines, colons were dissected free from the anus to distal to the cecum, emptied of fecal contents, weighed, opened longitudinally and fixed in 10% neutral buffered formalin followed by routine paraffin embedding. After paraffin embedding, 5µm longitudinal cross sections were cut and stained by H&E, or as noted. H&E sections were scored by a pathologist (MKW) in a blinded manner for colitis scores and tumor scores, as previously described [1]. Neoplastic lesions were classified as adenomas with low-grade or high-grade dysplasia, intramucosal carcinoma, or invasive carcinoma [3].

AOM/DSS tumor model: Adult 8 week-old mice received a single injection of AOM (12.5 mg/kg, i.p.); one week later, mice were given three rounds of DSS (3% w/v in drinking water) for 7 days with two week intervals of drinking water without DSS between each round, as indicated in Fig 2. Mice were euthanized 66 days following the start of the first round of DSS. Tumor progression scores indicate normal, 0; Low-grade dysplasia 1; High-grade dysplasia 2; Intramucosal adenocarcinoma 3; Invasive adenocarcinoma 4.

Immunohistochemistry. Paraffin-embedded colon sections were de-paraffinized, rehydrated, and pretreated with 3% hydrogen peroxide in methanol. Heat-induced antigen retrieval was performed in citrate buffer (10mM citrate, pH 6). After blocking with 10% normal goat serum, sections were incubated with primary antibody overnight at 4^oC. Rat antibodies were detected using biotinylated anti-rat secondary antibody (Vector Laboratories, Burlingame, CA), followed by streptavidin-labeled horseradish peroxidase (HRP, Life Technologies, Carlsbad, CA). Rabbit antibodies were detected using HRP-labeled anti-rabbit secondary antibody (Envision, Dako, Carpinteria, CA). DAB (Sigmafast, Sigma-Aldrich) was used to develop signal, and hematoxylin served as counterstain. TUNEL staining was performed using the peroxidase in situ cell death detection kit (ApopTag kit, EMD Millipore, Billerica, MA). Quantification of pH-H2AX and TUNEL was determined by the number of positive epithelial cells per mm in longitudinal colonic cross sections, and Ki67 was determined by counting the number of positive cells per hemicrypt (100 crypts/colon section) in ***Il10***$^{-/-}$ and ***Il10***$^{-/-}$*Tnfr2*$^{-/-}$ colonic sections

Cell based Caspase-3 activity assay: Caspase-3 activity for was measured using a previously described method [1]. Briefly, cells were treated for 1 h with a fluorescent caspase-3 substrate (Li-Cor Biosciences, Lincoln, NE) and in cell caspase-3 activity was determined by measuring resultant fluorescence (Odyssey System, Li-Cor Biosciences).

Cell based peroxidase induced DNA damage: For cell-based peroxide-induced DNA colonic epithelial damage assay, cells were stained for phospho–histone H2AX, and the relative expression was determined by quantitative in-cell Western analysis (Odyssey System, Li-Cor Biosciences), as we have previously published [1].

Generation of cDNA from RNA: Bio-Rad iScript kit was used to generate cDNA from isolated RNA (Bio-Rad Laboratories, Irvine, CA).

Real-time qPCR. Validated primer sets designed by Primer Bank (http://pga.mgh.harvard.edu/primerbank/) were used for real-time qPCR. Real-time qPCR was carried out with Maxima SYBR Green qPCR master mix (Thermo Scientific, Waltham, MA). Actin was the housekeeping gene used to normalize target gene expression.

Colon Explant Culture: Colon explant cultures were carried out according to a previously described procedure[1]. Culture supernatants were collected after 4 h. Cytokines were measured in colon explant culture supernatants for Th1, Th2, Th17 cytokines using ELISA array (SABiosciences, QIAGEN Inc., Valencia, CA). Protein concentration of culture supernatant was measured and used to calculate the cytokine concentration in pg/mg.

Flow Cytometry and Intracytoplasmic Cytokine Staining. For flow cytometry, whole colon was minced and digested with Collagenase, dispase II and DNAse (Sigma-Aldrich), and then stained with the indicated antibodies, as previously described[2]. Intracytoplasmic cytokine staining of colonic lymphocytes used a previously described protocol[2]. Basal apoptosis levels were measured using Annexin V Apoptosis Detection Kit (BD Pharmingen). Samples were analyzed using a Becton Dickinson LSRII (BD Biosciences) at the Children's Hospital Los Angeles Flow Core and data were analyzed using FlowJo software (Tree Star Inc., Ashland, OR).

RNA seq and data analysis: Total RNA from entire colons of 8 week-old male wildtype C57Bl/6 and *Tnfr2*$^{-/-}$ mice (n=3 each) was isolated using the PureLink RNA kit (Ambion, Life Technologies). RNA samples were submitted to the Genomic Services Lab at the HudsonAlpha Institute for Biotechnology (Huntsville, AL) for multiplex library preparation, mRNA enrichment, and sequencing. Sequencing was performed to an average depth of 50M paired-end 50bp reads per sample (HiSeq, Illumina, San Diego, CA). Data files containing raw reads were aligned to the mouse genome using Tophat2/Bowtie2 [4]. Alignments were assembled into transcript representations with Cufflinks, and statistical tests for differential expression were performed with Cuffdiff 2[4]. An adjusted P value < 0.05 (q<0.05) from the Cuffdiff 2 output was used as the cutoff for statistical significance. Human protein-protein interactions were downloaded from the Reactome Pathway Database (www.reactome.org, accessed 4/2014, Fig 5C) [5,6]. All first-order interactions were isolated for human homologs of mouse colonic TNFR2-regulated genes. IBD GWAS risk loci were color-coded using a previously published list [7]; CD8^{+} T cell-enriched TNFR2 genes were identified using transcriptomic data from the Immunological Genome Project (www.immgen.org, accessed 4/2014)[8]. Computational analysis, including the generation of a Simple Interaction File (.sif), was performed using custom-written scripts in Python and R. Cytoscape 3.1 was used to plot the interaction networks[9].

Statistics. All data are presented as mean ± SEM, except where noted. Non-parametric methods (Mann-Whitney test) were used for categorical data sets (i.e. colitis scores and tumor scores). Parametric methods (Student's t test or ANOVA) were used for data sets that were non-categorical. Kaplan-Meier survival curves were compared using the log-rank test. Statistical analyses were performed using GraphPad Prism (GraphPad Software Inc., La Jolla, CA), except where noted above for RNAseq analyses.

Supplementary Materials and Methods References:

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gene	locus	WT	TNFR2-/-	log2 (fold_change)	Adj P
-	chr6:69900419-69900996	5.33769	0.862105	-2.63028	0.0455429
-	chr6:68807182-68807725	3.89312	0.350133	-3.47495	0.0310573
-	chr3:137561868-137563224	0.62258	0.01928	-5.01306	0.0310573
-	chr16:88923896-88924263	11.4593	1.71299	-2.74193	0.0255982
-	chr1:80227749-80229510	0.498294	0.063094	-2.98141	0.0250892
-	chr12:115833948-115834439	5.59516	0.941933	-2.57048	0.0199398
-	chr4:128917306-128926558	4.14496	7.7973	0.911617	0.00718532
-	chr11:99649297-99650219	1.78096	0.131583	-3.75861	0.00431857
-	chr15:81228150-81230579	1.85623	0.174539	-3.41076	0.00413511
-	chr16:89084028-89084507	3.54076	0.174344	-4.34405	0.00398276
-	chr6:69544356-69544963	4.36455	18.757	2.10353	0.00135292
-	chr16:89063406-89063907	12.138	0.659544	-4.20192	1.27E-06
N21Rik,Krt81,Kr	chr15:101431013-101491512	22.938	3.59712	-2.67283	7.77E-08
A530098C11Rik	chr1:44009300-44020006	11.3308	3.02544	-1.90503	0.00709903
Acta1	chr8:123891766-123894736	1026.66	273.982	-1.9058	5.43E-06
Actc1	chr2:114047288-114052811	20.2002	4.1997	-2.26601	2.69E-08
Actn2	chr13:12269426-12340732	19.4028	8.23535	-1.23636	1.41E-05
Actn3	chr19:4861222-4877884	69.7975	6.15332	-3.50374	0
Adh1	chr3:138277302-138291345	660.596	1323.79	1.00284	0.00809442
Adipoq	chr16:23146535-23157968	3.62821	1.01269	-1.84106	0.0237237
Adssl1	chr12:112620046-112641355	25.2798	8.43315	-1.58384	5.35E-07
Ak1	chr2:32621757-32635698	50.7709	18.4997	-1.4565	9.56E-07
Ankrd23,Ankrd3	chr1:36530190-36547205	22.9532	6.55167	-1.80876	1.29E-05
Ano5	chr7:51511028-51598709	1.18909	0.380072	-1.64552	0.00820937
Arg1	chr10:24915206-24927470	19.3359	8.15126	-1.24619	0.00109602
Art1	chr7:102101741-102111152	9.51142	2.10557	-2.17545	0.0358011
Asb10	chr5:24532696-24540448	2.01921	0.439219	-2.20078	0.00515146
Atp1a2	chr1:172271708-172298064	17.393	9.64203	-0.851097	0.00212063
Atp2a1	chr7:126428434-126463073	183.156	43.311	-2.08026	1.83E-10
Btaf1	chr19:36925840-37014061	11.8062	5.08255	-1.21592	0.000169109
C3	chr17:57203972-57228136	20.2503	12.9262	-0.647643	0.0412956
Cacna1s	chr1:136052800-136119822	4.30512	1.15733	-1.89526	2.82E-06
Cacng1	chr11:107703217-107716476	21.8562	7.14067	-1.61391	6.04E-05
Calml3	chr13:3802892-3804318	25.9538	14.5552	-0.834405	0.04726
Camk2b	chr11:5969663-6065748	28.793	80.8781	1.49003	3.75E-10
Car3	chr3:14863537-14872373	465.31	129.17	-1.84893	4.25E-09
Casq1	chr1:172209893-172219895	56.7585	15.5167	-1.87102	1.15E-12
Ccdc109b	chr3:129914942-129970206	3.46658	1.01328	-1.77448	0.0362877
Cdsn	chr17:35543105-35557180	12.2021	5.90835	-1.0463	0.0336613
Chac1	chr2:119351241-119354327	2.97964	0.731071	-2.02705	0.0106098
Ckm	chr7:19410932-19422841	721.781	192.333	-1.90795	3.50E-07
Ckmt2	chr13:91853382-91876894	15.3666	5.08057	-1.59673	0.000311989
Cmya5	chr13:93040713-93144724	5.41929	1.97289	-1.45779	6.58E-07
Cnfn	chr7:25367615-25369724	77.3107	33.1397	-1.22211	0.00887198
Col9a1	chr1:24177609-24252738	0.0258778	0.22691	3.13233	0.0171697
Cox6a2	chr7:128173945-128206366	39.26	12.5762	-1.64236	0.000233727
Cox8b	chr7:140898941-140900446	98.4386	40.2187	-1.29136	0.00849591
Crct1	chr3:93014204-93015686	58.2449	23.1631	-1.3303	0.000163268
Cst6	chr19:5344704-5349574	35.2405	13.9259	-1.33946	1.17E-07
Ctgf	chr10:24595441-24598682	37.2639	22.9451	-0.69959	0.0239166
Cyp2d12	chr15:82555046-82559756	12.4793	26.619	1.09292	0.00200931
Ddit4l	chr3:137623671-137628332	5.81605	1.70009	-1.77443	0.000227166
Duox2	chr2:122279242-122298791	4.56678	8.0337	0.814888	0.0108848
Dupd1	chr14:21676571-21714576	1.6588	0.118556	-3.8065	0.000305999
Eef1a2	chr2:181146211-181157026	36.669	11.8558	-1.62897	5.13E-09

gene	locus	WT	TNFR2-/-	log2 (fold_change)	Adj P
Efna3	chr3:89302835-89322879	0.942056	3.36966	1.83872	0.00920654
Elovl4	chr9:83778691-83806305	27.4063	12.3533	-1.14961	0.000186097
Fabp4	chr3:10204342-10208576	128.586	69.0142	-0.897771	0.00146387
Fabp5	chr3:10012605-10016610	142.478	83.1034	-0.77776	0.0150444
Fgl2	chr5:21292960-21424677	35.8345	21.121	-0.762673	0.00602927
Fhl3	chr4:124700533-124708628	17.3701	8.53101	-1.02582	0.038402
Fitm1	chr14:55575673-55576952	11.7072	2.71814	-2.1067	0.00115478
Fos	chr12:85473900-85477270	35.6187	59.0477	0.729245	0.0107985
Fsd2	chr7:81534353-81566981	2.51508	0.512612	-2.29466	0.000347941
Gabrr2	chr4:33063111-33095865	1.33511	0.12866	-3.37532	0.00089139
Gadl1	chr9:115909454-116076176	0.576077	0.114222	-2.33442	0.0120494
Gbp1	chr3:142594846-142619176	0.281631	10.6871	5.24592	0
Gm10229	chr16:89015276-89015846	68.2913	4.77851	-3.83707	1.26E-11
Gm11559	chr11:99864475-99865571	2.91148	0.483039	-2.59154	0.0118839
Gm11562	chr11:99619597-99620404	12.3767	1.0899	-3.50537	2.34E-06
Gm11563	chr11:99657941-99658959	5.00477	0.474914	-3.39756	0.000219417
Gm11567	chr11:99879186-99880229	3.65561	0.242567	-3.91366	5.96E-05
Gm11568	chr11:99857916-99859060	1.61685	0.262336	-2.6237	0.0329983
Gm11570	chr11:99984702-99986593	0.502986	0.029653	-4.08426	0.00849588
Gm11595	chr11:99771713-99772913	1.81241	0.166468	-3.44459	0.00348309
Gm11937	chr11:99609793-99610189	19.0506	1.48169	-3.68452	4.91E-05
Gm11938	chr11:99602645-99603308	19.5271	1.57113	-3.6356	3.46E-07
Gm13177	chr4:144613659-144623602	22.7452	2.84583	-2.99864	5.59E-05
Gm14446	chr19:34592887-34601968	70.744	42.7764	-0.725792	0.0177925
Gm17821	chr12:67656741-67669271	4.08606	7.76544	0.926356	0.000137196
Gm5105	chr3:138048760-138081498	5.53513	1.11309	-2.31405	1.50E-06
Gna14	chr19:16435666-16610950	11.9394	20.736	0.796406	0.0266774
Gpd1	chr15:99717592-99725007	19.1847	9.39952	-1.02929	0.000292091
H19	chr7:142575528-142578146	41.4779	11.486	-1.85246	1.15E-12
Hao2	chr3:98871466-98893273	48.3753	86.1739	0.832981	0.00206188
Hfe2	chr3:96525165-96529216	12.1968	3.26424	-1.90168	4.16E-05
Hrc	chr7:45335268-45338972	9.39644	3.69219	-1.34764	0.000784797
Jph1	chr1:16994939-17097889	3.59512	1.39576	-1.36499	0.043939
Jsrp1	chr10:80808495-80813498	16.6339	5.65807	-1.55574	0.0207347
Kbtbd10	chr2:69670119-69684239	23.2539	7.69194	-1.59606	3.95E-08
Klhl31	chr9:77636731-77660122	2.68014	0.704296	-1.92805	5.40E-05
Klk10	chr7:43781053-43785410	24.2807	9.03705	-1.42589	6.31E-05
Krt13	chr11:100117595-100121495	128.28	59.2919	-1.11339	2.77E-05
Krt14	chr11:100203161-100207510	93.0381	45.8393	-1.02124	0.000182937
Krt15	chr11:100131758-100135949	25.1099	12.9003	-0.960851	0.00500319
Krt17	chr11:100256216-100260989	38.1574	17.2303	-1.14702	0.000101523
Krt25	chr11:99315843-99322941	10.7499	1.68773	-2.67117	3.57E-07
Krt26	chr11:99328483-99337965	0.396487	0.020879	-4.24718	0.00431857
Krt27	chr11:99345565-99351094	8.12312	0.965082	-3.07331	1.92E-06
Krt31	chr11:100046645-100050551	4.75308	0.709119	-2.74476	0.000265438
Krt33a	chr11:100011198-100016212	6.9101	0.823918	-3.06813	6.08E-06
Krt33b	chr11:100023633-100029868	9.25366	0.959201	-3.27012	6.14E-07
Krt34	chr11:100037350-100041554	10.7382	1.18957	-3.17424	9.73E-08
Krt35	chr11:100092191-100096224	0.993515	0.192689	-2.36627	0.0345519
Krt39	chr11:99514623-99521258	0.560247	0.040181	-3.80149	0.0212277
Krt5	chr15:101707069-101715501	59.2609	33.2914	-0.831932	0.0171697
Krt6a	chr15:101689911-101694390	34.5912	15.5146	-1.15678	4.64E-05
Krt6b	chr15:101676022-101680289	15.4897	7.98799	-0.955403	0.0120494
Krt71	chr15:101733948-101743097	14.4172	1.58227	-3.18773	5.55E-12
Krt86	chr15:101431013-101491512	10.4141	1.19505	-3.1234	1.29E-05

gene	locus	WT	TNFR2-/-	log2 (fold_change)	Adj P
Krtap1-3	chr11:99590460-99591339	4.05164	0.473569	-3.09686	0.00089139
Krtap1-4	chr11:99582548-99583677	3.37664	0.369144	-3.19333	0.00135292
Krtap1-5	chr11:99579976-99581016	21.9583	1.93945	-3.50105	1.40E-09
Krtap11-1	chr16:89570175-89571183	5.25532	0.649658	-3.01602	0.00200338
Krtap13-1	chr16:88728861-88729611	9.30868	0.666353	-3.80422	2.44E-06
Krtap14	chr16:88825290-88826145	18.8462	1.64959	-3.5141	6.33E-07
Krtap15	chr16:88829008-88829844	30.6764	2.83718	-3.4346	1.49E-09
Krtap16-1	chr16:88873664-88874269	25.7315	1.86191	-3.78868	5.35E-07
Krtap16-10b	chr16:88931803-88932264	34.4121	2.77599	-3.63184	4.03E-06
Krtap16-2	chr16:88868917-88869410	10.1058	1.28761	-2.97241	0.00261628
Krtap16-3	chr16:88962197-88981822	55.6081	3.75644	-3.88786	1.48E-06
Krtap16-4	chr16:88884785-88885089	31.1103	2.46176	-3.65963	0.000448136
Krtap16-5	chr16:88877512-88878038	31.8244	2.9375	-3.43747	7.76E-07
Krtap16-7	chr16:89403026-89403774	16.4001	1.98106	-3.04936	3.01E-06
Krtap16-8	chr16:89040926-89047899	19.1432	1.47129	-3.70168	0.0319524
Krtap16-8	chr16:89040926-89047899	21.4573	2.13572	-3.32867	3.31E-05
Krtap2-4	chr11:99614016-99614846	17.8348	1.60981	-3.46973	1.99E-07
Krtap22-2	chr16:89010379-89010759	61.4747	5.55908	-3.46707	7.14E-07
Krtap3-1	chr11:99566026-99566630	43.7644	4.71037	-3.21585	1.14E-09
Krtap3-2	chr11:99555822-99556853	11.2799	1.24545	-3.17902	3.23E-06
Krtap3-3	chr11:99550131-99550863	20.4513	2.07503	-3.30099	2.57E-07
Krtap4-1	chr11:99627228-99628239	9.67631	0.900547	-3.42558	2.40E-06
Krtap4-16	chr11:99850654-99851605	2.96777	0.713751	-2.05589	0.0348264
Krtap4-2	chr11:99634113-99635084	5.09036	0.42189	-3.59283	1.29E-05
Krtap4-6	chr11:99665042-99665960	7.85043	0.676577	-3.53645	2.38E-05
Krtap4-7	chr11:99643111-99644089	6.93128	0.548229	-3.66027	5.33E-06
Krtap5-1	chr7:142296376-142297069	1.97541	0.075278	-4.71378	0.00921907
Krtap5-5	chr7:142228794-142229971	1.40354	0.072081	-4.2833	0.00513224
Krtap6-1	chr16:89031698-89032292	23.9881	2.18791	-3.45469	2.71E-06
Krtap6-2	chr16:89419322-89420111	15.3314	1.89842	-3.01361	2.56E-06
Krtap7-1	chr16:89507702-89508323	61.6646	6.02257	-3.35599	1.28E-11
Krtap8-1	chr16:89487373-89487952	62.707	5.37746	-3.54363	4.11E-11
Krtap8-2	chr16:88895967-88896449	25.0741	2.96015	-3.08246	0.000149928
Krtap9-1	chr11:99873388-99874000	2.93878	0.218168	-3.75171	0.0019124
Krtap9-3	chr11:99597347-99598106	20.8753	1.90765	-3.45193	4.03E-07
Ky	chr9:102506137-102546239	4.12539	1.11047	-1.89336	6.08E-06
Lbx1	chr19:45232713-45235808	1.34027	0.256194	-2.38722	0.00783287
Ldb3	chr14:34526634-34588695	42.9426	17.4104	-1.30246	0.000251198
Lrrc15	chr16:30269301-30283254	1.16855	0.342837	-1.76912	0.0146999
Lrrc30	chr17:67630964-67632723	0.969811	0.13755	-2.81774	0.00892244
Ltf	chr9:111019291-111042766	5.60136	1.87672	-1.57756	0.00146387
Ly6d	chr15:74762055-74763567	65.1309	33.6943	-0.950835	0.0123799
Ly6g6c	chr17:35062545-35070048	32.3802	15.6088	-1.05275	0.012171
Mal	chr2:127633225-127656695	12.1092	6.53365	-0.890139	0.0177535
Mb	chr15:77015486-77057108	320.667	92.7827	-1.78915	1.01E-07
Mef2c	chr13:83504033-83667079	9.30064	4.70928	-0.981824	0.00405399
Miip	chr4:147860746-147868719	8.95524	3.49203	-1.35866	0.0238179
Mlf1	chr3:67374096-67400000	18.3635	4.40731	-2.05887	5.67E-06
Mstn	chr1:53061662-53068079	2.72847	0.890945	-1.61468	0.0470183
Mybpc1	chr10:88518278-88605179	34.4867	13.1925	-1.38632	0.000373
Mybpc2	chr7:44501698-44524669	48.8537	5.95129	-3.03719	0
Myf6	chr10:107492859-107494729	6.03631	1.54239	-1.9685	0.00508676
Myh1	chr11:67200093-67225805	147.604	44.616	-1.72609	5.48E-05
Myh2	chr11:67171026-67197517	7.64859	3.44067	-1.15251	0.000185448
Myh4	chr11:67238028-67260446	8.25773	0.620914	-3.73328	0

gene	locus	WT	TNFR2-/-	log2 (fold_change)	Adj P
Myh8	chr11:67277123-67308633	115.281	46.6084	-1.30649	0.000522751
Myl1	chr1:66924293-66945460	418.012	77.9928	-2.42213	0
Myl3	chr9:110763680-110769794	275.574	115.996	-1.24836	2.71E-06
Mylk2	chr2:152911351-152923065	6.10214	2.4857	-1.29567	0.00647093
Mylk4	chr13:32700826-32784031	6.33977	1.35512	-2.22601	1.62E-06
Mylpf	chr7:127211607-127214287	724.247	163.54	-2.14684	4.77E-13
Myo18b	chr5:112688874-112896391	3.22949	1.26267	-1.35483	0.000225585
Myod1	chr7:46376473-46379092	1.03446	0.201878	-2.35733	0.0339073
Myom2	chr8:15057642-15133422	16.2818	5.29587	-1.62032	8.95E-05
Myot	chr18:44334073-44355844	14.9377	5.56074	-1.42561	7.58E-05
Myoz1	chr14:20646937-20656615	63.6254	15.7957	-2.01007	7.95E-12
Myoz3	chr18:60573148-60591716	4.40677	1.37367	-1.68169	0.0019124
Mypn	chr10:63115794-63203952	2.92098	0.952372	-1.61685	0.000843286
Neb	chr2:52136603-52338798	14.3612	4.531	-1.66427	1.91E-06
Nlrp6	chr7:140920711-140929289	31.4519	51.9749	0.724667	0.0199874
Nr4a1	chr15:101254249-101274797	19.9203	7.47922	-1.41328	3.59E-06
Padi3	chr4:140785368-140810648	0.490051	0.095555	-2.35853	0.0455429
Pdk4	chr6:5483350-5496278	9.72671	2.83732	-1.77742	3.01E-07
Pfkm	chr15:98038743-98132514	53.2471	22.164	-1.26449	9.15E-07
Pgam2	chr11:5787963-5804820	101.923	30.8297	-1.72508	4.61E-05
Phkg1	chr5:129846989-129879083	4.67363	0.910646	-2.35958	0.00360299
Pkia	chr3:7366603-7445365	10.98	5.51814	-0.992622	0.0291995
Pla2g12a	chr3:129878621-129895821	10.8404	5.01344	-1.11255	0.0417252
Ppbp	chr5:90768517-90770060	23.9357	6.90384	-1.79369	1.29E-05
Ppp1r3a	chr6:14713821-14755274	1.63191	0.500822	-1.70419	0.00323354
Ppp1r3c	chr19:36731730-36736604	15.0891	7.3409	-1.03948	0.00136483
Prkag3	chr1:74738921-74748955	2.39464	0.686718	-1.80202	0.0113044
Prr9	chr3:92122203-92123947	6.51331	0.532655	-3.61212	1.95E-07
Psapl1	chr5:36017178-36398139	26.5408	13.5304	-0.972009	0.00783287
Psca	chr15:74714838-74717065	45.8833	14.8946	-1.62318	3.01E-06
Ptp4a3	chr15:73723144-73758766	21.2656	12.0562	-0.818739	0.0455429
Ptprr	chr10:116018362-116274933	8.51919	15.5292	0.866196	0.025175
Pvalb	chr15:78191117-78206351	141.822	21.8878	-2.69589	0
Pygm	chr19:6384428-6398459	107.824	31.2957	-1.78464	1.58E-11
Rab6b	chr9:103112073-103185270	3.77634	1.36788	-1.46505	0.000883689
Rarres1	chr3:67478885-67515523	23.2937	10.7593	-1.11435	0.00307416
Rpl3l	chr17:24727828-24736149	17.4549	4.56317	-1.93552	0.000140649
Rtn2	chr7:19282666-19296160	41.8777	18.2823	-1.19573	0.000405712
Ryr1	chr7:29003339-29125151	6.52168	1.54312	-2.07939	4.11E-11
S100a3	chr3:90600214-90602702	6.25594	1.33995	-2.22304	0.00839983
Saa1,Saa3	chr7:46711997-46743053	696.923	1402.52	1.00895	0.000254025
Saa2	chr7:46751832-46754314	46.5193	89.9619	0.951486	0.00206188
Scd3	chr19:44203191-44244267	20.4953	10.0611	-1.0265	0.000545779
Scn1b	chr7:31116523-31126945	20.0843	10.3668	-0.954098	0.0172084
Scn4a	chr11:106317546-106349461	1.37366	0.482064	-1.51073	0.0132089
Scn4b	chr9:45139041-45154061	1.52774	0.496177	-1.62248	0.031792
Serpina3j	chr12:104300715-104321456	17.5039	9.42055	-0.893796	0.0255982
Serpinf1	chr11:75410028-75422623	34.962	19.7283	-0.82552	0.0103384
Sim2	chr16:94085259-94127032	3.18008	1.00484	-1.6621	0.00487532
Slc20a1	chr2:129198772-129211617	52.1808	87.7445	0.749789	0.00660277
Slc25a4	chr8:46207340-46211009	356.431	198.071	-0.847603	0.00438501
Slc37a2	chr9:37225183-37255738	26.5171	75.0227	1.5004	7.00E-08
Slc38a3	chr9:107651154-107668968	1.25028	0.31098	-2.00735	0.0417252
Slc38a4	chr15:96994822-97055956	1.71098	0.448675	-1.93108	0.00381629
Sln	chr9:53850250-53853849	146.534	54.8915	-1.41658	2.82E-06

gene	locus	WT	TNFR2-/-	log2 (fold_change)	Adj P
Slpi	chr2:164354069-164356507	112.778	67.2185	-0.746558	0.0162615
Smtnl2	chr11:72388923-72411771	11.9626	3.28244	-1.86568	2.77E-06
Smyd1	chr6:71213939-71262281	6.90551	1.9436	-1.82902	0.00179486
Sprr1a	chr3:92483880-92485972	169.905	69.7195	-1.2851	2.40E-06
Sprr3	chr3:92456500-92458722	40.4301	16.1081	-1.32765	5.25E-05
Srl	chr16:4476265-4541829	12.1762	4.82447	-1.33562	1.41E-05
St3gal4	chr9:35046572-35175987	54.934	95.5484	0.798533	0.0310573
St8sia5	chr18:77185846-77255450	2.09293	6.05265	1.53204	0.00642593
Synpo2l	chr14:20658948-20668308	2.55221	0.793296	-1.68582	0.00375708
Sypl2	chr3:108212265-108226599	7.21149	1.69685	-2.08744	6.58E-07
Syt8,Tnni2	chr7:142434855-142444414	592.741	207.222	-1.51623	2.34E-06
Tat	chr8:109986063-109999804	5.5205	11.7475	1.08948	0.0130277
Tbx15	chr3:99253759-99354260	3.74846	1.55151	-1.27262	0.031792
Tcap	chr11:98383810-98384953	86.2479	32.7099	-1.39876	6.58E-07
Tchh	chr3:93442311-93449077	4.96052	0.739328	-2.7462	6.38E-08
Tchhl1	chr3:93468753-93471980	0.752094	0.061542	-3.61128	0.00524689
Tmem38a	chr8:72571212-72587286	33.5368	14.4231	-1.21737	0.000101787
Tmem41b	chr7:109972186-109986230	14.7794	8.76794	-0.753274	0.0243661
Tmod4	chr3:95124473-95129209	16.0244	5.02884	-1.67198	0.000500115
Tnfrsf1b	chr4:145212367-145246870	7.89982	1.06101	-2.89638	0
Tnnc2	chr2:164777161-164779734	837.557	291.08	-1.52477	5.35E-07
Tnnt3	chr7:142460847-142516017	677.388	212.902	-1.6698	0.000119894
Trdn	chr10:33083335-33478046	3.25336	0.689966	-2.23733	0.0123799
Trdn	chr10:33083335-33478046	12.6342	5.06271	-1.31936	0.00430626
Trim54	chr5:31116611-31137626	9.42906	2.81292	-1.74504	0.00122811
Trim63	chr4:134315119-134329629	2.91352	0.848967	-1.77898	0.0255982
Txlnb	chr10:17796218-17845754	3.90334	1.51275	-1.36753	0.0100553
Ubiad1	chr4:148434496-148444763	5.04125	9.8057	0.95984	0.0393959
Ucp3	chr7:100472990-100486432	1.58003	0.280035	-2.49627	0.00145637
Xirp2	chr2:67446001-67526618	2.6327	1.01333	-1.37743	0.000556385
Zfp534	chr4:147673502-147702553	0.0718613	0.640609	3.15616	0.00013417
Zmynd17	chr14:20482863-20496901	17.3346	2.89415	-2.58244	3.61E-10

NOTES:
**Two transcripts mapped to the Trdn gene locus.*
" - " indicates a previously unidentified transcript.

Supplementary Table 2. Immune cell-specific expression of TNFR2-regulated genes

Gene	Max_ Exprs	Median_ Exprs	Which_ Max	Fold_ Change	FClog	Cell Type
Car3	54.9659	35.98265	14	1.527567	0.611235	Blood Endothelium
Ctgf	917.779	155.2055	14	5.913315	2.563967	Blood Endothelium
Fabp4	1274.17	23.08425	14	55.19651	5.786505	Blood Endothelium
Fabp5	432.336	83.03575	14	5.206625	2.380348	Blood Endothelium
Klk10	92.5803	76.76105	14	1.206084	0.270331	Blood Endothelium
Mlf1	17.5898	13.06015	14	1.34683	0.429568	Blood Endothelium
Pdk4	479.213	29.59365	14	16.1931	4.017307	Blood Endothelium
Rarres1	52.1398	41.3356	14	1.261378	0.335	Blood Endothelium
Slc38a3	92.4815	49.4532	14	1.870081	0.903101	Blood Endothelium
St3gal4	611.279	255.8965	14	2.388774	1.256271	Blood Endothelium
A530098C11Rik	27.9519	20.21175	10	1.382953	0.467752	CD4 DC
Cacng1	81.2063	67.21555	10	1.208148	0.272797	CD4 DC
Cox6a2	211.782	150.8665	10	1.403771	0.489307	CD4 DC
Gm11563	337.698	256.599	10	1.316053	0.396218	CD4 DC
Hrc	74.0203	60.61635	10	1.221128	0.288214	CD4 DC
Ly6g6c	93.8809	59.9765	10	1.565295	0.646434	CD4 DC
Myf6	32.5893	28.79415	10	1.131803	0.178623	CD4 DC
Mylk2	76.0112	58.3924	10	1.301731	0.380431	CD4 DC
Pgam2	119.643	73.7381	10	1.62254	0.698254	CD4 DC
Prr9	25.3363	22.24675	10	1.138876	0.187611	CD4 DC
S100a3	41.3311	33.1688	10	1.246084	0.317401	CD4 DC
Saa1	12.7903	10.1412	10	1.261222	0.334822	CD4 DC
Acta1	200.916	150.6235	4	1.333895	0.415646	CD4 T
Actc1	192.921	159.1475	4	1.212215	0.277646	CD4 T
Adipoq	21.0798	17.7445	4	1.187962	0.248489	CD4 T
Ano5	25.7272	21.8656	4	1.176606	0.234632	CD4 T
Camk2b	116.101	80.28135	4	1.446176	0.532244	CD4 T
Cmya5	82.3801	64.7319	4	1.272635	0.347819	CD4 T
Cst6	41.9017	35.8033	4	1.170331	0.226916	CD4 T
Cyp2d12	19.4047	16.32815	4	1.18842	0.249045	CD4 T
Gabrr2	128.577	68.84555	4	1.867615	0.901197	CD4 T
Krt25	59.051	40.52325	5	1.457213	0.543212	CD4 T
Krt26	24.8054	22.24715	5	1.114992	0.157034	CD4 T
Krt27	109.312	63.0236	4	1.734461	0.794488	CD4 T
Krt31	76.3496	63.26845	4	1.206756	0.271134	CD4 T
Krt39	45.8357	32.0924	5	1.428242	0.51424	CD4 T
Krt86	43.9563	25.4467	5	1.727387	0.788591	CD4 T
Lrrc15	71.4131	44.26435	5	1.613332	0.690044	CD4 T
Myh4	39.3143	32.36985	4	1.214535	0.280403	CD4 T
Mylpf	79.8908	48.3563	4	1.652128	0.724326	CD4 T
Ppp1r3a	18.3939	13.20605	5	1.392839	0.478028	CD4 T
Rab6b	269.584	138.3965	4	1.947911	0.961927	CD4 T
Rpl3l	39.7774	33.6215	4	1.183094	0.242565	CD4 T
Scd3	49.1698	33.8439	5	1.452841	0.538877	CD4 T
Sln	52.7484	43.14145	5	1.222685	0.290053	CD4 T
Casq1	48.3378	42.83065	11	1.12858	0.174508	CD8 DC
Krt6a	76.4866	53.12225	11	1.439822	0.525891	CD8 DC
Saa2	13.9205	11.9507	11	1.164827	0.220116	CD8 DC
Scn4b	57.0591	38.16435	11	1.495089	0.580231	CD8 DC

Supplementary Table 2. Immune cell-specific expression of TNFR2-regulated genes

Gene	Max_ Exprs	Median_ Exprs	Which_ Max	Fold_ Change	FClog	Cell Type
Smyd1	48.9394	38.6965	11	1.264698	0.338793	CD8 DC
Sprr1a	87.862	67.57835	11	1.30015	0.378678	CD8 DC
Tnnt3	254.265	161.837	11	1.571118	0.651791	CD8 DC
Actn2	120.91	71.00925	2	1.702736	0.767855	CD8 T
Ankrd23	178.807	115.42	1	1.549186	0.63151	CD8 T
Arg1	56.233	38.8528	2	1.447335	0.533398	CD8 T
Art1	109.642	73.41755	2	1.493403	0.578604	CD8 T
Asb10	92.3681	69.80845	2	1.323165	0.403993	CD8 T
Cacna1s	66.5446	49.8867	2	1.333915	0.415666	CD8 T
Calml3	34.202	30.10705	2	1.136013	0.183979	CD8 T
Cdsn	150.982	93.75335	2	1.610417	0.687434	CD8 T
Chac1	165.262	120.4365	2	1.372192	0.456482	CD8 T
Ckm	121.306	74.9309	2	1.618905	0.695018	CD8 T
Ckmt2	41.6323	27.8768	2	1.493439	0.578638	CD8 T
Cnfn	219.882	141.123	2	1.558088	0.639776	CD8 T
Col9a1	109.604	85.7255	2	1.278546	0.354504	CD8 T
Cox8b	93.3048	65.34945	2	1.427782	0.513776	CD8 T
Ddit4l	86.6861	57.3527	2	1.511456	0.595939	CD8 T
Dupd1	192.122	137.35	2	1.398777	0.484166	CD8 T
Eef1a2	147.328	124.1055	2	1.187119	0.247465	CD8 T
Efna3	60.1566	40.5051	2	1.485161	0.570619	CD8 T
Fitm1	60.4819	48.8239	2	1.238777	0.308916	CD8 T
Gadl1	54.2578	42.0121	2	1.29148	0.369026	CD8 T
Gm10229	24.1568	18.31245	2	1.319146	0.399605	CD8 T
Gm11559	13.885	10.4313	2	1.33109	0.412608	CD8 T
Gm11567	22.7365	18.56565	1	1.224654	0.292374	CD8 T
Gm13177	40.1918	36.07565	1	1.114098	0.155876	CD8 T
Gm5105	97.3833	66.0552	2	1.474272	0.560002	CD8 T
Gpd1	79.0393	62.60185	2	1.262571	0.336365	CD8 T
H19	97.5551	80.9888	2	1.204551	0.268495	CD8 T
Hfe2	104.958	69.6826	2	1.50623	0.590942	CD8 T
Jsrp1	336.888	211.1755	2	1.595299	0.673827	CD8 T
Klhl31	78.7352	52.7957	2	1.491318	0.576588	CD8 T
Krt13	52.5097	37.7052	2	1.392638	0.47782	CD8 T
Krt14	61.7941	50.3034	2	1.228428	0.296813	CD8 T
Krt15	80.3277	61.4221	2	1.307798	0.38714	CD8 T
Krt17	56.81	41.79185	2	1.359356	0.442923	CD8 T
Krt33a	62.8482	43.8797	2	1.432284	0.518318	CD8 T
Krt33b	411.303	270.989	2	1.517785	0.601967	CD8 T
Krt34	80.1967	58.8778	2	1.362087	0.445819	CD8 T
Krt35	97.1659	65.07035	2	1.493244	0.57845	CD8 T
Krt5	45.2961	36.3504	2	1.246096	0.317416	CD8 T
Krt6b	13.573	10.2774	2	1.320665	0.401264	CD8 T
Krt71	74.7779	57.8991	2	1.291521	0.369071	CD8 T
Krtap14	44.1425	31.9071	2	1.38347	0.468291	CD8 T
Krtap15	14.3805	11.05145	2	1.301232	0.379878	CD8 T
Ky	64.6469	45.30215	2	1.427016	0.513002	CD8 T
Lbx1	204.383	127.4585	2	1.603526	0.681248	CD8 T
Ldb3	128.775	92.67065	2	1.389599	0.474668	CD8 T

Supplementary Table 2. Immune cell-specific expression of TNFR2-regulated genes

Gene	Max_ Exprs	Median_ Exprs	Which_ Max	Fold_ Change	FClog	Cell Type
Lrrc30	84.6899	68.6722	2	1.233249	0.302464	CD8 T
Mal	102.676	65.43275	2	1.569184	0.650014	CD8 T
Mb	118.952	85.6105	2	1.389456	0.47452	CD8 T
Miip	343.326	249.175	1	1.377851	0.46242	CD8 T
Mstn	34.6701	20.79805	2	1.666988	0.737244	CD8 T
Mybpc1	70.9431	46.49815	2	1.525719	0.609489	CD8 T
Mybpc2	74.8514	47.38915	2	1.579505	0.659473	CD8 T
Myh1	35.224	29.73765	2	1.184492	0.244268	CD8 T
Myh2	57.0271	41.2945	2	1.380985	0.465698	CD8 T
Myh8	63.9911	50.37515	2	1.270291	0.345159	CD8 T
Myl1	23.4096	19.26895	2	1.214887	0.280822	CD8 T
Myl3	80.846	65.91505	2	1.226518	0.294568	CD8 T
Mylk4	21.6585	18.97405	2	1.14148	0.190906	CD8 T
Myo18b	124.756	83.72225	2	1.490118	0.575426	CD8 T
Myod1	105.383	82.1732	2	1.28245	0.358902	CD8 T
Myom2	42.2199	32.2744	2	1.308154	0.387533	CD8 T
Myot	41.6755	35.0177	2	1.190127	0.251115	CD8 T
Myoz3	181.067	109.958	2	1.646692	0.719571	CD8 T
Mypn	35.0759	22.20735	2	1.579473	0.659443	CD8 T
Neb	70.3659	36.10315	2	1.949024	0.962752	CD8 T
Nlrp6	93.2744	73.65765	2	1.266323	0.340646	CD8 T
Padi3	121.42	80.9755	2	1.499466	0.584449	CD8 T
Prkag3	134.77	93.5242	2	1.441017	0.527088	CD8 T
Psapl1	114.883	85.66505	2	1.341072	0.423387	CD8 T
Psca	51.2223	39.52295	2	1.296014	0.374081	CD8 T
Ptprr	65.608	43.4942	2	1.508431	0.593049	CD8 T
Pvalb	54.5752	37.3585	2	1.460851	0.546809	CD8 T
Ryr1	82.6806	66.00785	2	1.252587	0.324911	CD8 T
Scn4a	77.7898	55.814	2	1.393733	0.478954	CD8 T
Sim2	58.3201	39.37015	2	1.481328	0.566891	CD8 T
Sprr3	29.9162	23.89235	1	1.252125	0.324378	CD8 T
St8sia5	37.3147	31.5128	2	1.184112	0.243806	CD8 T
Synpo2l	88.1433	64.2715	2	1.371421	0.455672	CD8 T
Sypl2	92.0231	68.28925	2	1.347549	0.430338	CD8 T
Syt8	111.134	88.7088	2	1.252796	0.325151	CD8 T
Tat	66.4435	40.42155	2	1.643764	0.717003	CD8 T
Tbx15	28.0711	20.7949	2	1.349903	0.432856	CD8 T
Tcap	85.5632	66.5705	2	1.285302	0.362107	CD8 T
Tchh	91.6129	47.8785	2	1.913445	0.936173	CD8 T
Tnnc2	106.815	70.76575	2	1.509417	0.593991	CD8 T
Trdn	82.1907	63.4863	2	1.294621	0.37253	CD8 T
Trim54	100.34	58.65395	2	1.710712	0.774597	CD8 T
Trim63	90.7309	58.603	2	1.54823	0.630619	CD8 T
Ucp3	71.2701	45.97475	2	1.550201	0.632455	CD8 T
Xirp2	29.9763	23.22585	2	1.290644	0.368091	CD8 T
Zmynd17	121.427	70.84985	2	1.713864	0.777253	CD8 T
Ankrd39	208.164	148.144	1	1.405146	0.49072	CD8 T
Nr4a1	7411.4	2226.59	9	3.328588	1.73491	DC
Slc20a1	1246.87	589.9215	9	2.11362	1.079716	DC

Supplementary Table 2. Immune cell-specific expression of TNFR2-regulated genes

Gene	Max_ Exprs	Median_ Exprs	Which_ Max	Fold_ Change	FClog	Cell Type
Tnni2	292.285	141.2025	9	2.06997	1.04961	DC
Actn3	98.2603	61.39435	12	1.600478	0.678503	Fibroblasts
Adh1	2351.42	57.21215	12	41.10001	5.361067	Fibroblasts
Ak1	262.727	72.6759	12	3.61505	1.854016	Fibroblasts
Atp1a2	1243.09	77.07815	12	16.12766	4.011465	Fibroblasts
C3	13097.5	108.6502	12	120.5474	6.913457	Fibroblasts
Elovl4	56.009	39.4477	12	1.419829	0.505717	Fibroblasts
Fos	6448.97	1657.16	12	3.89158	1.960356	Fibroblasts
Gna14	89.4295	44.8382	12	1.994494	0.996022	Fibroblasts
Pfkm	346.188	156.5525	12	2.211322	1.144909	Fibroblasts
Phkg1	43.9753	22.64475	12	1.941964	0.957517	Fibroblasts
Pkia	121.465	14.2564	12	8.520033	3.090859	Fibroblasts
Ppp1r3c	161.559	34.31755	12	4.707766	2.235043	Fibroblasts
Pygm	518.532	80.7812	12	6.418969	2.682342	Fibroblasts
Rtn2	165.427	55.0313	12	3.006053	1.58787	Fibroblasts
Serpinf1	1586.27	76.7605	12	20.66519	4.36913	Fibroblasts
Slc25a4	1006.33	621.7925	12	1.618434	0.694598	Fibroblasts
Saa3	36.9202	22.4639	12	1.643535	0.716802	Fibroblasts
Duox2	97.9309	35.36445	13	2.769191	1.469464	Lymphatic Endothelium
Jph1	59.13	41.82815	13	1.413641	0.499416	Lymphatic Endothelium
Scn1b	520.962	103.6755	13	5.024929	2.329103	Lymphatic Endothelium
Slc38a4	183	27.8189	13	6.578262	2.717706	Lymphatic Endothelium
Smtnl2	164.376	73.06495	13	2.249724	1.169748	Lymphatic Endothelium
Btaf1	865.266	494.341	8	1.750342	0.807637	Macrophage
Ccdc109b	150.146	41.41965	8	3.624994	1.857979	Macrophage
Fgl2	3917.63	119.926	8	32.66706	5.029765	Macrophage
Fsd2	55.52	36.95235	8	1.502475	0.587341	Macrophage
Gbp1	2932.83	38.8515	8	75.48821	6.238179	Macrophage
Kbtbd10	106.7	59.2326	8	1.801373	0.849097	Macrophage
Myoz1	51.8313	39.60695	8	1.308642	0.38807	Macrophage
Ppbp	30.6144	16.57345	8	1.847195	0.885336	Macrophage
Slc37a2	850.939	92.53055	8	9.196303	3.201054	Macrophage
Tmem41b	229.87	135.3335	8	1.698545	0.764299	Macrophage
Tnfrsf1b	1453.95	539.7885	8	2.693555	1.429512	Macrophage
Txlnb	70.4584	48.09125	8	1.465098	0.550997	Macrophage
Atp2a1	113.506	88.85965	7	1.277363	0.353168	Mature B
Crct1	46.8429	31.7126	7	1.477107	0.562774	Mature B
Hao2	25.5545	19.079	7	1.339405	0.421592	Mature B
Ly6d	4650.27	110.2315	7	42.1864	5.398706	Mature B
Mef2c	2073.18	272.5945	7	7.605363	2.927017	Mature B
Ptp4a3	1424.66	522.4705	7	2.726776	1.447196	Mature B
Tchhl1	115.644	87.16075	7	1.32679	0.40794	Mature B
Tmod4	50.3935	38.8674	7	1.296549	0.374677	Mature B
Ubiad1	64.2903	30.35845	7	2.117707	1.082503	Mature B
Adssl1	519.579	62.57405	6	8.303426	3.053707	Progenitor B
Fhl3	290.378	164.255	6	1.767849	0.821995	Progenitor B
Ltf	190.632	29.3154	6	6.502794	2.70106	Progenitor B
Pla2g12a	102.187	82.8843	6	1.232887	0.302041	Progenitor B
Slpi	97.3631	70.3139	6	1.384692	0.469565	Progenitor B

Supplementary Table 2. Immune cell-specific expression of TNFR2-regulated genes

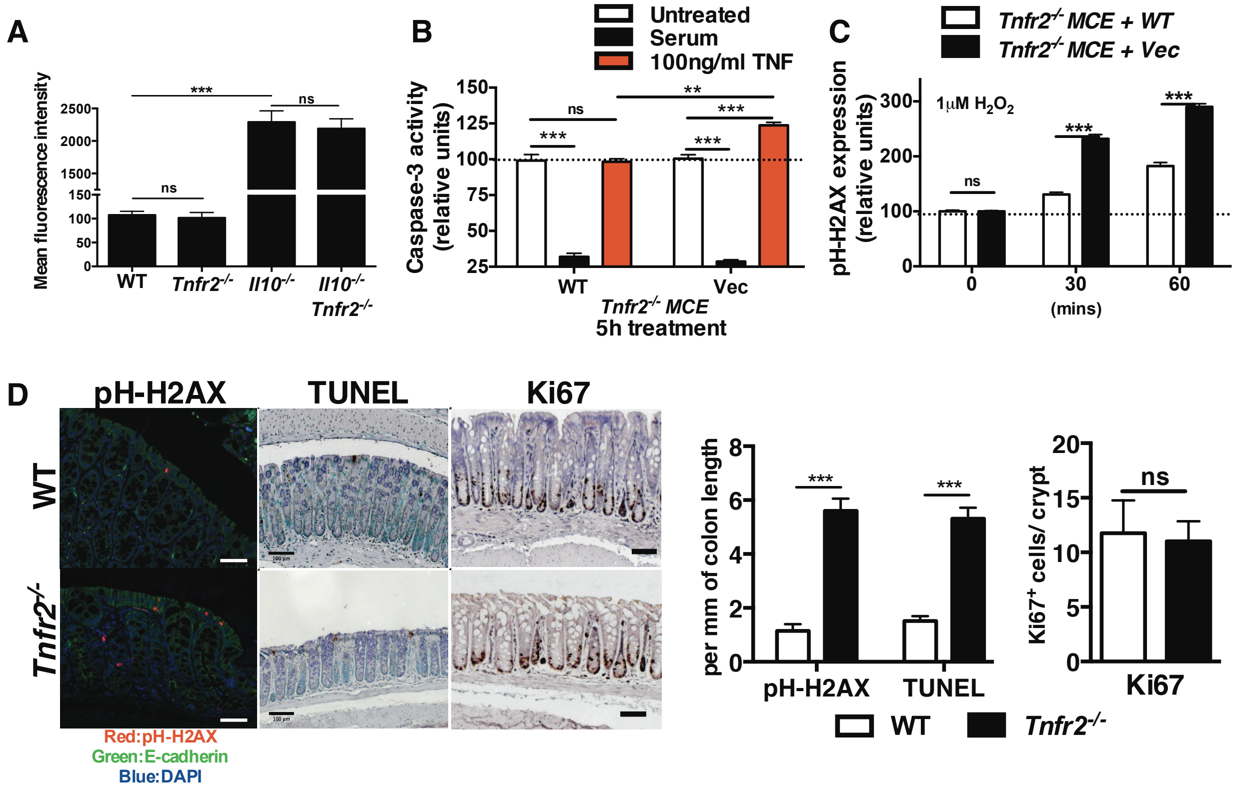
Gene	Max_ Exprs	Median_ Exprs	Which_ Max	Fold_ Change	FClog	Cell Type
Tmem38a	79.5859	46.5519	6	1.709617	0.773673	Progenitor B
Srl	96.7261	35.0546	3	2.759298	1.464301	Progenitor T

IBD Susceptibility Loci [1]	CD8$^+$ T cell activation [2,3]			CD8$^+$ T cell IBD signature [4]
ATP2A1	ACTN3	H19	PGAM2	ACTN2
CACNA1S	ADH1C	HAO2	PHKG1	CCDC109B
CDSN	ADSSL1	HRC	PKIA	H19
CST6	AK1	KRT27	PSCA	KRT71
EEF1A2	ARG1	KRT33A	PTP4A3	MSTN
FOS	ASB10	KRT35	PYGM	MYBPC2
H19	BTAF1	KRT5	S100A3	MYH8
MYLPF	CA3	KRT6A	SAA1	NEB
MYOZ3	CAMK2B	KRTAP8-1	SERPINF1	NR4A1
PPBP	CASQ1	LDB3	SLC20A1	PDK4
TCAP	CKMT2	LTF	SLC25A4	TCHHL1
TNNT3	CNFN	MAL	SLC37A2	TNFRSF1B
TRIM54	EEF1A2	MIIP	SLC38A4	
	EFNA3	MLF1	SMYD1	
	FABP5	MYH4	ST3GAL4	
	FGL2	MYL1	SYNPO2L	
	FOS	MYL3	TBX15	
	FSD2	MYLK4	TNFRSF1B	
	GABRR2	MYLPF	TNNC2	
	GADL1	MYOZ1	ZMYND17	
	GBP1	NR4A1		
	GNA14	PFKM		

Supplementary Table 3. TNFR2-regulated genes involved in CD8$^+$ T cells and IBD

1. Jostins L, Ripke S, Weersma RK, et al. Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature 2012;491:119-24.
2. Subramanian A, Tamayo P, Mootha VK, et al. Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. Proc Natl Acad Sci U S A 2005;102:15545-50.
3. Wang M, Windgassen D, Papoutsakis ET. Comparative analysis of transcriptional profiling of CD3+, CD4+ and CD8+ T cells identifies novel immune response players in T-cell activation. BMC Genomics 2008;9:225.
4. Lee JC, Lyons PA, McKinney EF, et al. Gene expression profiling of CD8+ T cells predicts prognosis in patients with Crohn disease and ulcerative colitis. J Clin Invest 2011;121:4170-9.

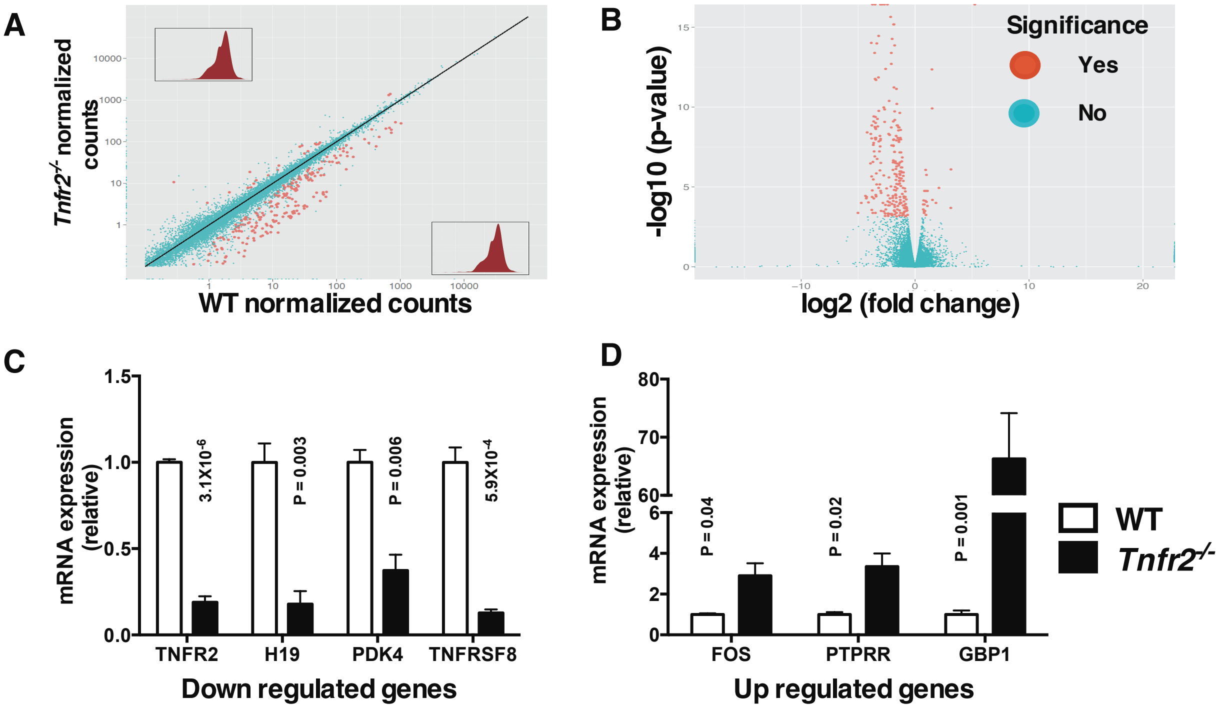
Supplementary figure 1



Supplemental figure 1:

(A) Barrier function assay showing mean plasma fluorescence following intra-rectal FITC-dextran administration of 16 week-old wildtype (WT), *Tnfr2*$^{-/-}$, *Il10*$^{-/-}$, and *Il10*$^{-/-}$*Tnfr2*$^{-/-}$ mice; ***P<0.001, ns not significant. (B) TNF-induced apoptosis in TNFR2$^{-/-}$ mouse colon epithelial cell lines stably transduced with wildtype TNFR2 (WT) add-back, or empty vector, measured by in-cell caspase-3 activity assay; ***P<0.001, ns not significant. (C) Hydrogen peroxide-induced DNA damage in *Tnfr2*$^{-/-}$ mouse colon epithelial cell lines stably transduced with wildtype TNFR2 (WT) add-back, or empty vector, measured by pH-H2AX expression by quantitative in-cell Western analysis; ***P<0.001, ns not significant. (D) Representative images and quantification of epithelial DNA-damage by phosphohistone-H2AX staining (red), apoptosis by TUNEL staining and proliferation by Ki67 staining in WT and *Tnfr2*$^{-/-}$colonic sections, as in Figure 1; n=5; ***P < 0.001, ns not significant; scale bars: 100µm.

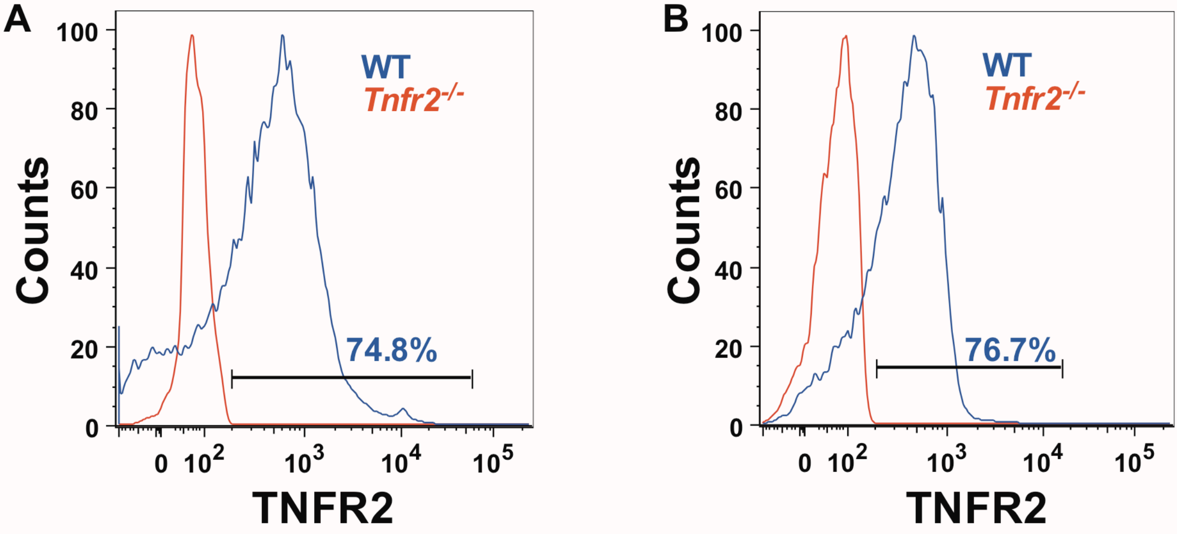
Supplementary figure 2



Supplemental figure 2:

(A) Scatter plot depicting RNAseq gene expression profiles of *Tnfr2*$^{-/-}$ (Y-axis) and WT (X-axis) colonic mRNA. Differentially expressed genes are represented by red dots. Inset histogram represents distribution of total read counts. (B) Volcano plot depicting relationship between p-value (Y-axis) and fold change (X-axis). Differentially expressed genes are represented by red dots. (C) qPCR validation of down-regulated genes of interest. (D) qPCR validation of up-regulated genes of interest.

Supplementary Figure 3



Supplemental figure 3:

(A) Representative histogram showing TNFR2 expression in CD3^{+}CD8^{+} T cells (%) from mesenteric lymph nodes of 8 week-old WT mice; *Tnfr2*$^{-/-}$ mice were used as negative control; n=5. (B) Representative histogram showing TNFR2 expression in naïve CD8^{+} T cells (CD44^{low}CD62^{+}CD8^{+}) (%) from the peripheral lymph nodes of 8 week-old WT mice; *Tnfr2*$^{-/-}$ mice were used as negative control: n=5.