nutrients

MDPI

Supplementary Material

Consumption of the total Western diet promotes colitis and inflammation-associated colorectal cancer in mice

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Supplementary Material

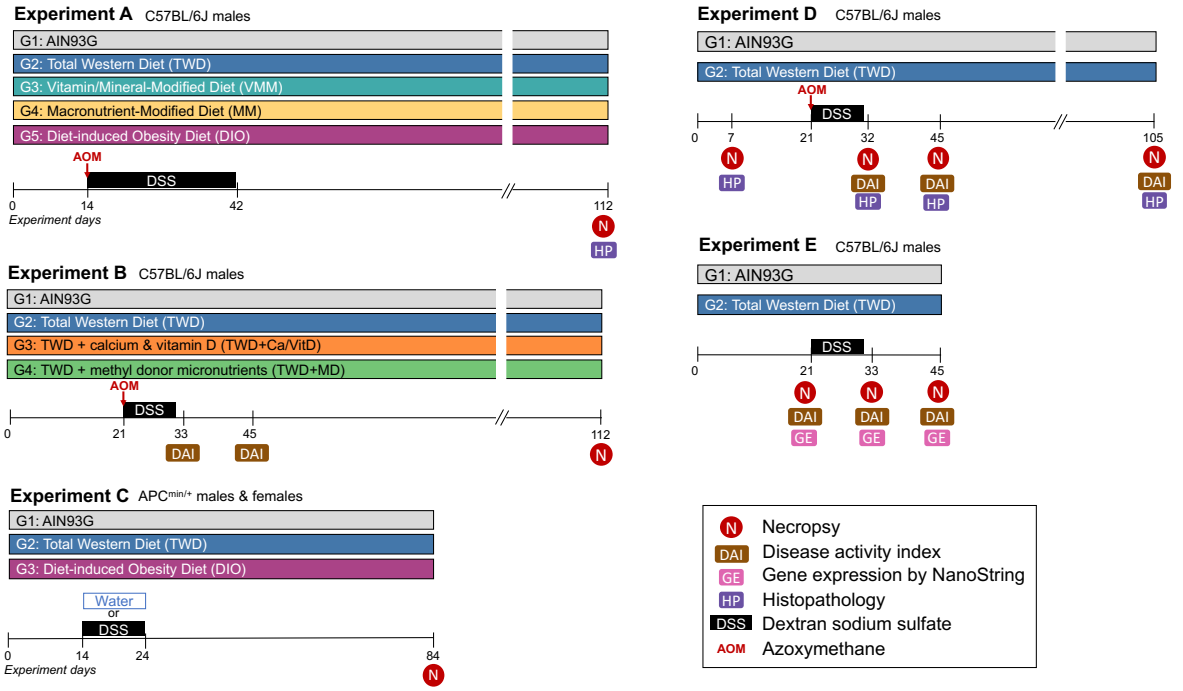


Figure S1. Design of animal model experiments. For each experiment described in the *Materials and Methods*, the test diet and duration of feeding is shown, along with the timing of exposure to the carcinogen azoxymethane (AOM) and/or 1% (w/v) dextran sodium sulfate (DSS) in drinking water as appropriate. Dates of necropsy are specified, along with dates for other endpoints including the colitis disease activity index (DAI), histopathology assessment of inflammation and mucosal injury, and gene expression profiling by the NanoString PanCancer Immune profile probe set. See Table S1 for composition of experimental diets.

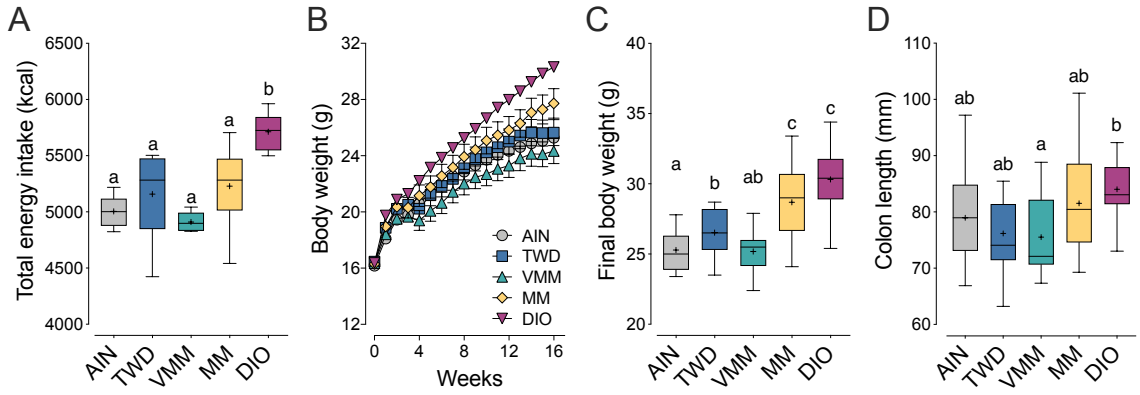


Figure S2. Impact of test diets on energy intake, body weight gain and colon length (Experiment A). C57BL/6J male mice were fed the standard AIN93G diet (AIN), the total Western diet (TWD), the vitamin- and mineral-modified diet (VMM), the macronutrient-modified diet (MM) or the 45% fat diet-induced obesity diet (DIO). (**A**) Total energy intake calculated based on the estimated food intake and the energy density of the test diets (see Table S1 for diet composition) (*n*=6 cages) (**B**) Body weight for each treatment group over the course of the study. (**C-D**) Final body weight (*n*=29 to 30) (C) and the colon length (n=19 to 20) determined at necropsy. Data are shown either as means ± SEM (B) or as Tukey box plots (box, 25th to 75th percentiles; whiskers, 1.5 IQR; +, mean) (A, C-D). Different letters indicate that diet treatment groups are significantly different (p<0.05) as determined by the appropriate linear mixed model or nonparametric test as outlined in the *Materials and Methods*.

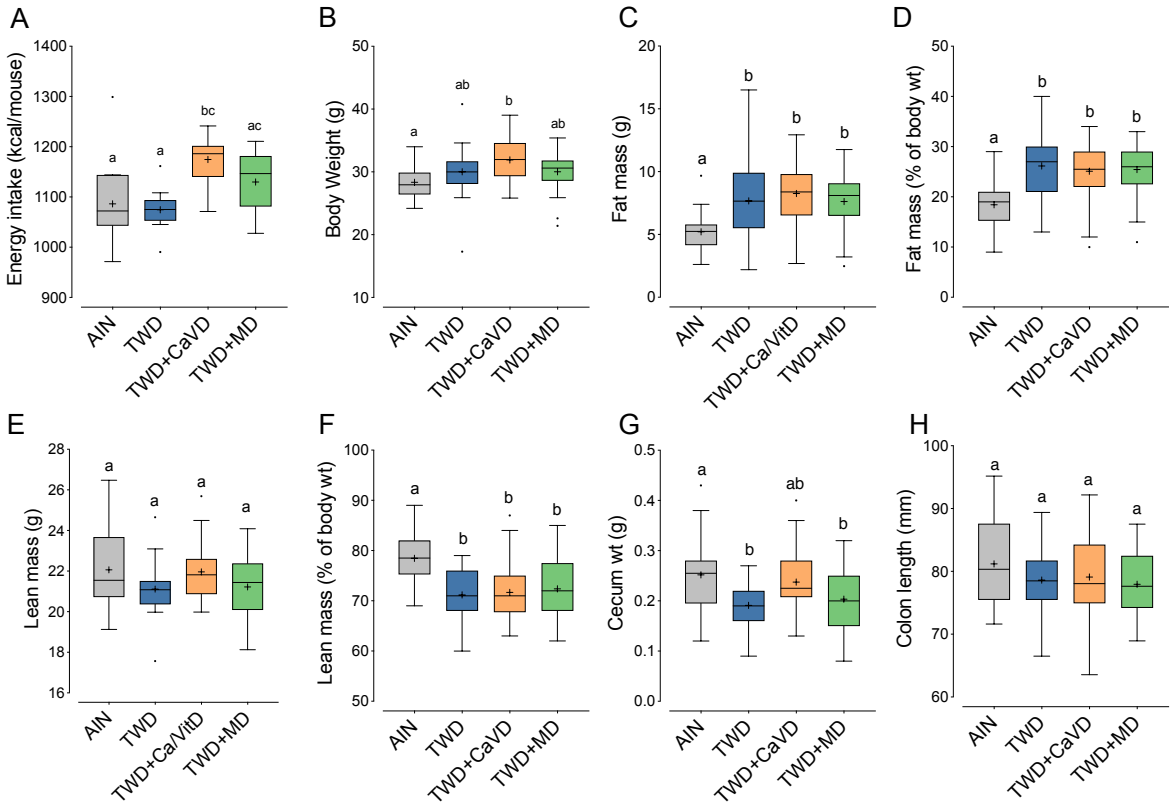
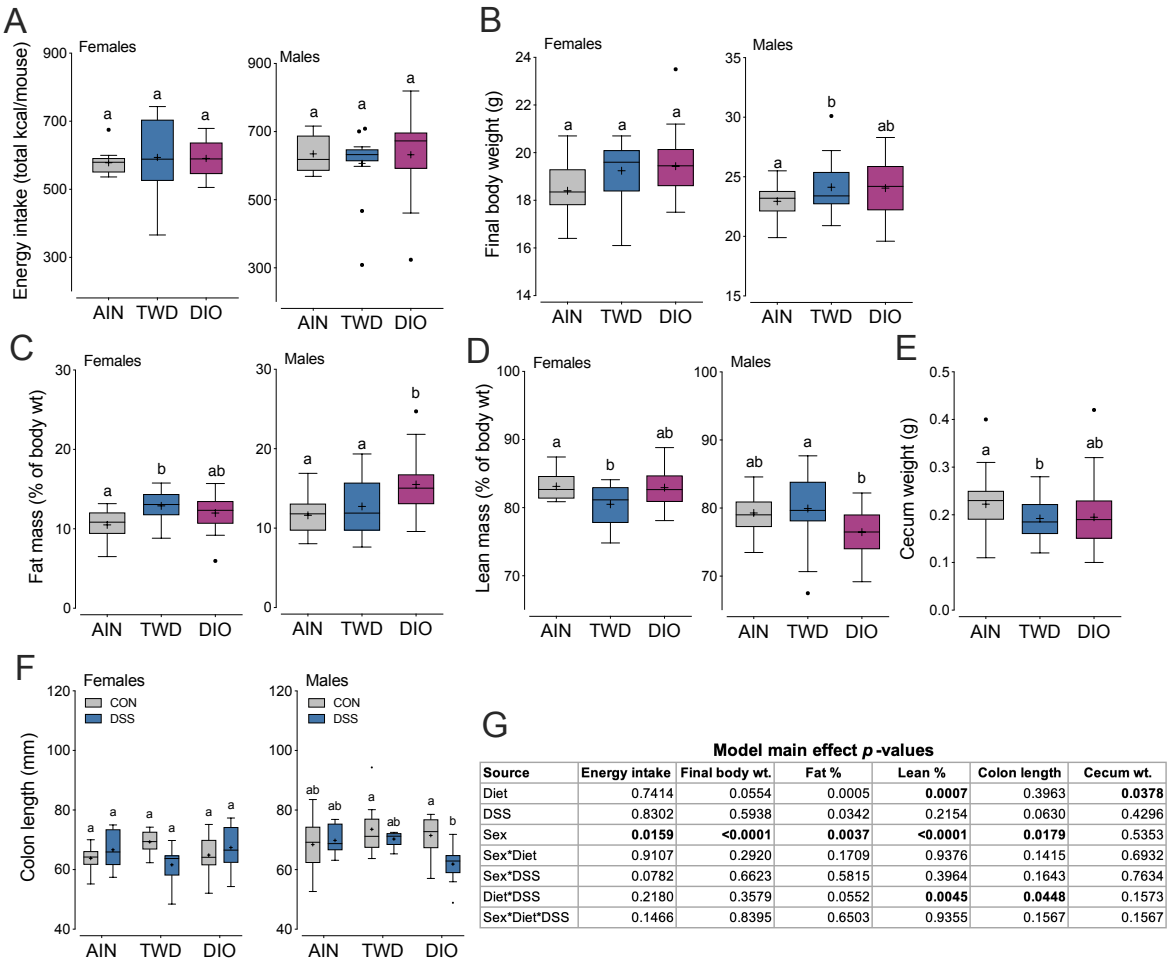


Figure S3. Impact of test diets on energy intake, body weight, body composition, cecum weight and colon length (Experiment B). Diet groups included the standard AIN93G diet (AIN), the total Western diet (TWD), the TWD with calcium and vitamin D restored to AIN amounts (TWD+Ca/VitD) or the TWD with methyl donor micronutrients B_2, B_6, B_{12}, folate and choline restored to AIN amounts (TWD+MD). (**A**) Total energy intake calculated based on the estimated food intake and the energy density of the test diets (see Table S1 for diet composition) (*n*=10-11 cages). (**B-H**) Body weight (B), fat mass (C), at mass as percent body weight (D), lean mass (E), lean mass as percent body weight (F), cecum weight (G) and colon length (H) determined at necropsy (*n*=29 to 32). All data are shown as Tukey box plots (box, 25th to 75th percentiles; whiskers, 1.5 IQR; +, mean). Different letters indicate that treatment groups are significantly different ($p<0.05$) as determined by the appropriate linear mixed model or nonparametric test as outlined in the *Materials and Methods*.



Model main effect *p*-values

Source	Energy intake	Final body wt.	Fat %	Lean %	Colon length	Cecum wt.
Diet	0.7414	0.0554	0.0005	**0.0007**	0.3963	**0.0378**
DSS	0.8302	0.5938	0.0342	0.2154	0.0630	0.4296
Sex	**0.0159**	**<0.0001**	**0.0037**	**<0.0001**	**0.0179**	0.5353
Sex*Diet	0.9107	0.2920	0.1709	0.9376	0.1415	0.6932
Sex*DSS	0.0782	0.6623	0.5815	0.3964	0.1643	0.7634
Diet*DSS	0.2180	0.3579	0.0552	**0.0045**	**0.0448**	0.1573
Sex*Diet*DSS	0.1466	0.8395	0.6503	0.9355	0.1567	0.1567

Figure S4. Effects of test diets, DSS treatment and sex on energy intake, body weight, body composition, colon length and cecum weight (Experiment C). APC$^{Min/+}$ female and male mice were fed a standard diet (AIN), the total Western diet (TWD) or the 45% fat diet-induced obesity diet (DIO) for 12 weeks. Half the mice were provided 1% DSS via drinking water for two weeks. Because sex was a significant factor in most endpoints (except cecum weight), the data were stratified by sex and males and females were analyzed separately. For all endpoints except colon length, data comparisons were made by diet group only as no main effect of or interaction with DSS was observed. (**A**) Total energy intake calculated based on the estimated food intake and the energy density of the test diets (see Supplementary Table 1 for diet composition) (*n*=12 to 17 cages per diet group per sex). (**B-F**) Data shown indicate final body weight by sex (*n*=29 to 32 per diet group per sex) (B), percentage fat mass by sex (*n*=29 to 32 per diet group per sex). (C), percentage lean mass by sex (*n*=29 to 32 per diet group per sex) (D), cecum weight (*n*=38 to 43 per diet group) (E), and colon length by sex and DSS treatment (*n*=9 to 12 per diet and DSS group per sex). Data are shown as Tukey box plots (box, 25th to 75th percentiles; whiskers, 1.5 IQR; +, mean). Different lowercase letters indicate that groups are significantly different (p<0.05) as determined by the appropriate linear mixed model or nonparametric test as outlined in the *Materials and Methods*. (**G**) Main effect *p*-values for diet, DSS treatment, sex and all possible interactions are shown.

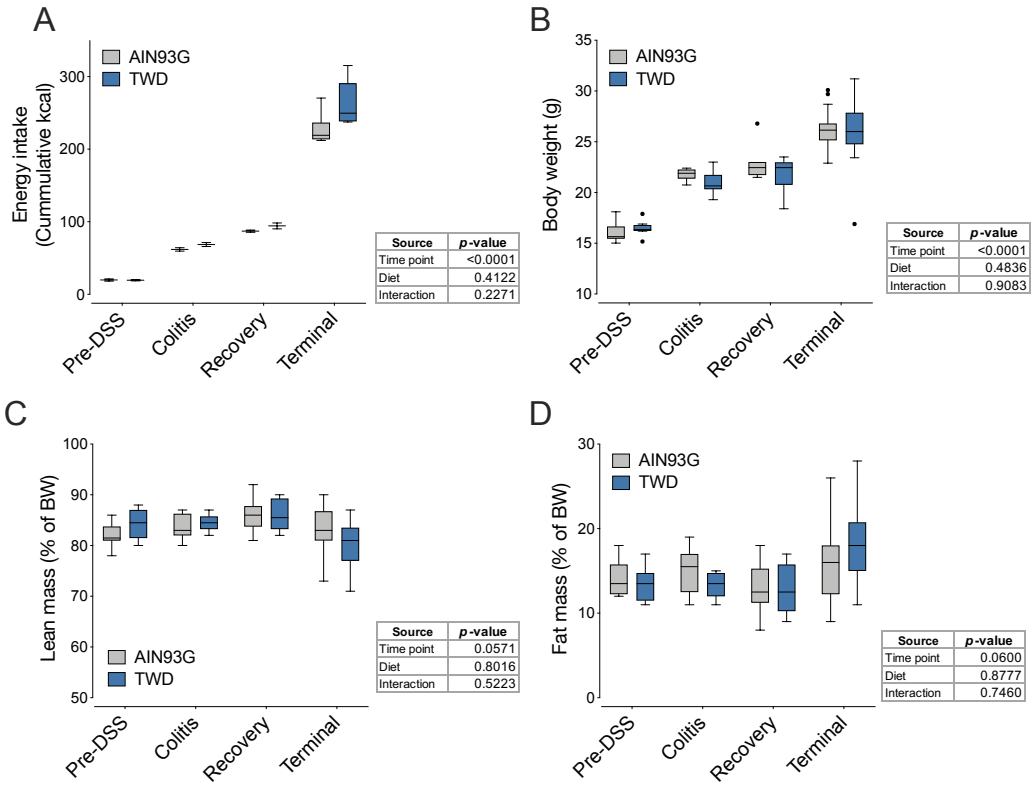


Figure S5. Comparison of AIN and TWD diets on energy intake, body weight and body composition over time (Experiment D). C57BL6/J male mice were fed AIN or TWD diets and provided DSS for 10 days to trigger colon inflammation. Measurements were made prior to DSS treatment (Pre-DSS), one days after completion of DSS (colitis), 14 days after completion of DSS (recovery) and at the study end (terminal). (**A**) Total energy intake calculated based on the estimated food intake and the energy density of the test diets (see Table S1 for diet composition) (*n*=2 cages for pre-DSS, colitis and recovery time points; *n*=6 for terminal time point). (**B-D**) Data are shown for final body weight (B), percentage lean mass (C) and percentage fat mass (D) (*n*=7 to 8 for pre-DSS, colitis and recovery time points; *n*=20 to 23 at terminal time point). Data are shown as Tukey box plots (box, 25th to 75th percentiles; whiskers, 1.5 IQR; +, mean). Main effect *p*-values for time point, diet and the interaction are indicated for each panel. No significant effects of diet were observed as determined by linear mixed model analyses for diet by time point with LS Means Student's *t*-test post-hoc test between AIN and TWD diet groups.

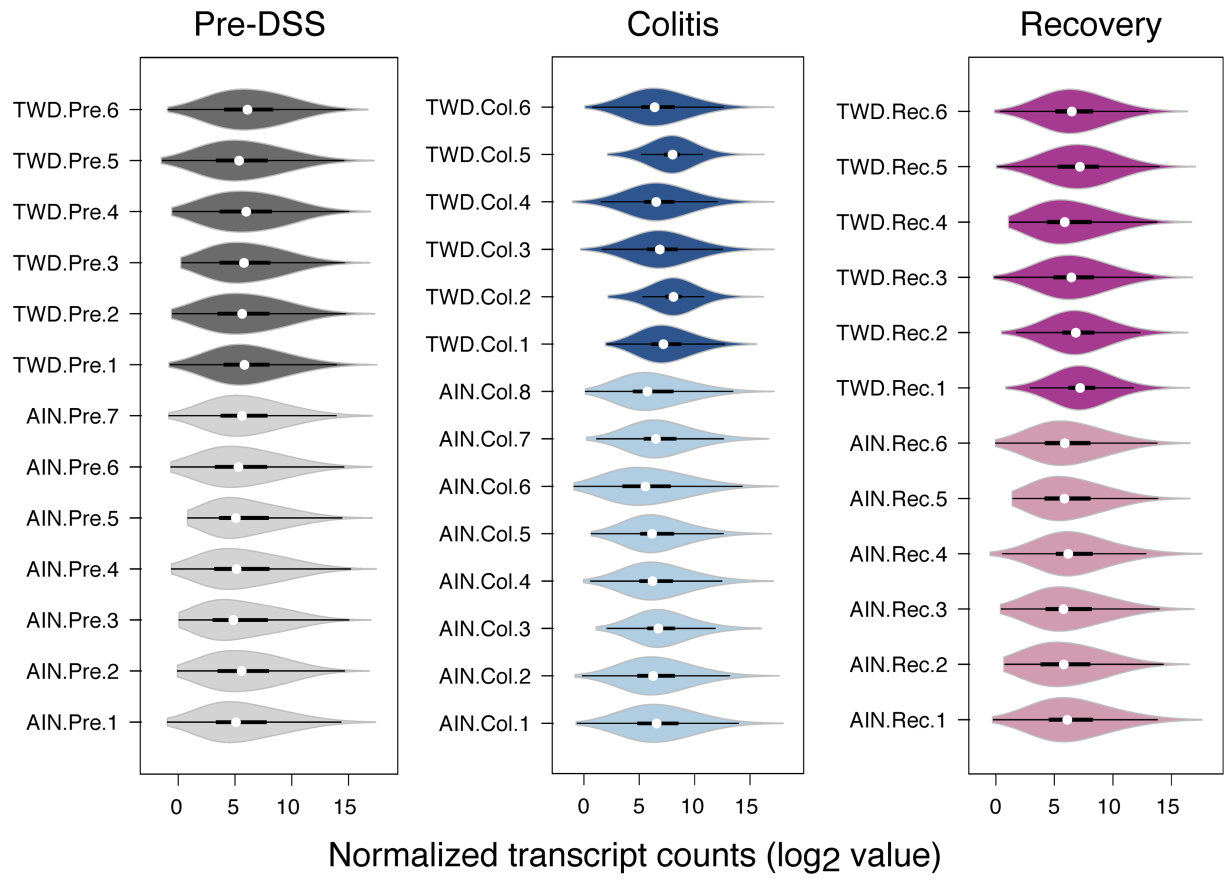


Figure S6. Violin plots depicting distribution of normalized expression of the NanoString PanCancer Immune gene panel for Experiment E. Samples are organized by diet group (AIN or TWD) and time point (pre-DSS, colitis or recovery). Shaded polygons represent density estimates of each dataset and extend to extreme values; within the violin polygons, the mean is indicated by a white circle, the 25th to 75th percentiles by a black box and whiskers extend 1.5 times the interquartile range.

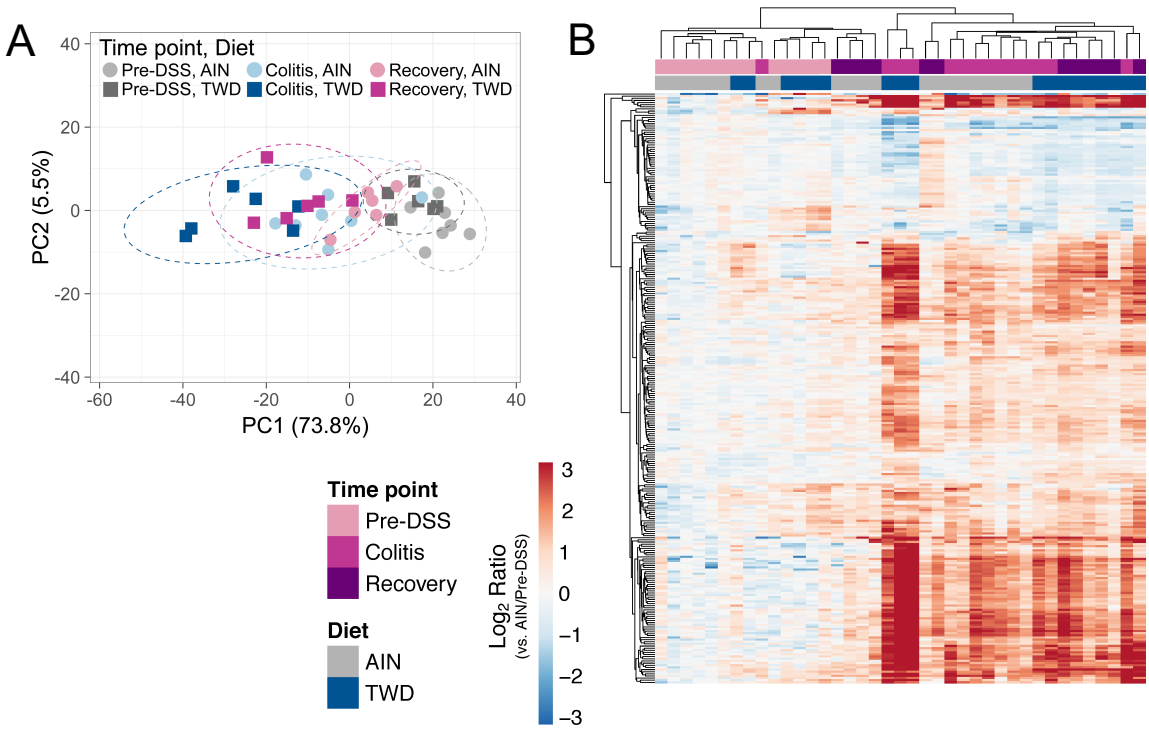


Figure S7. Principal components and hierarchical clustering analyses of all genes identified as differentially expressed for any of pairwise comparisons made, including by diet at each time point, by time point for AIN diet, and by time point for TWD diet. (**A**) Principal components analyses (PCA) of differentially expressed genes (BH q<0.05, $\log_2$ ratio >1 or <-1). PC1 and PC2 are shown with the 95% prediction ellipses for each diet and time point group. (**B**) Unsupervised, bidirectional hierarchical cluster analysis of colon transcriptome data using the Euclidean distance method with average linkage. For each time point, the heatmap shows all genes differentially expressed between TWD and AIN diet groups colored by the $\log_2$ ratio calculated with respect to AIN/Pre-DSS.

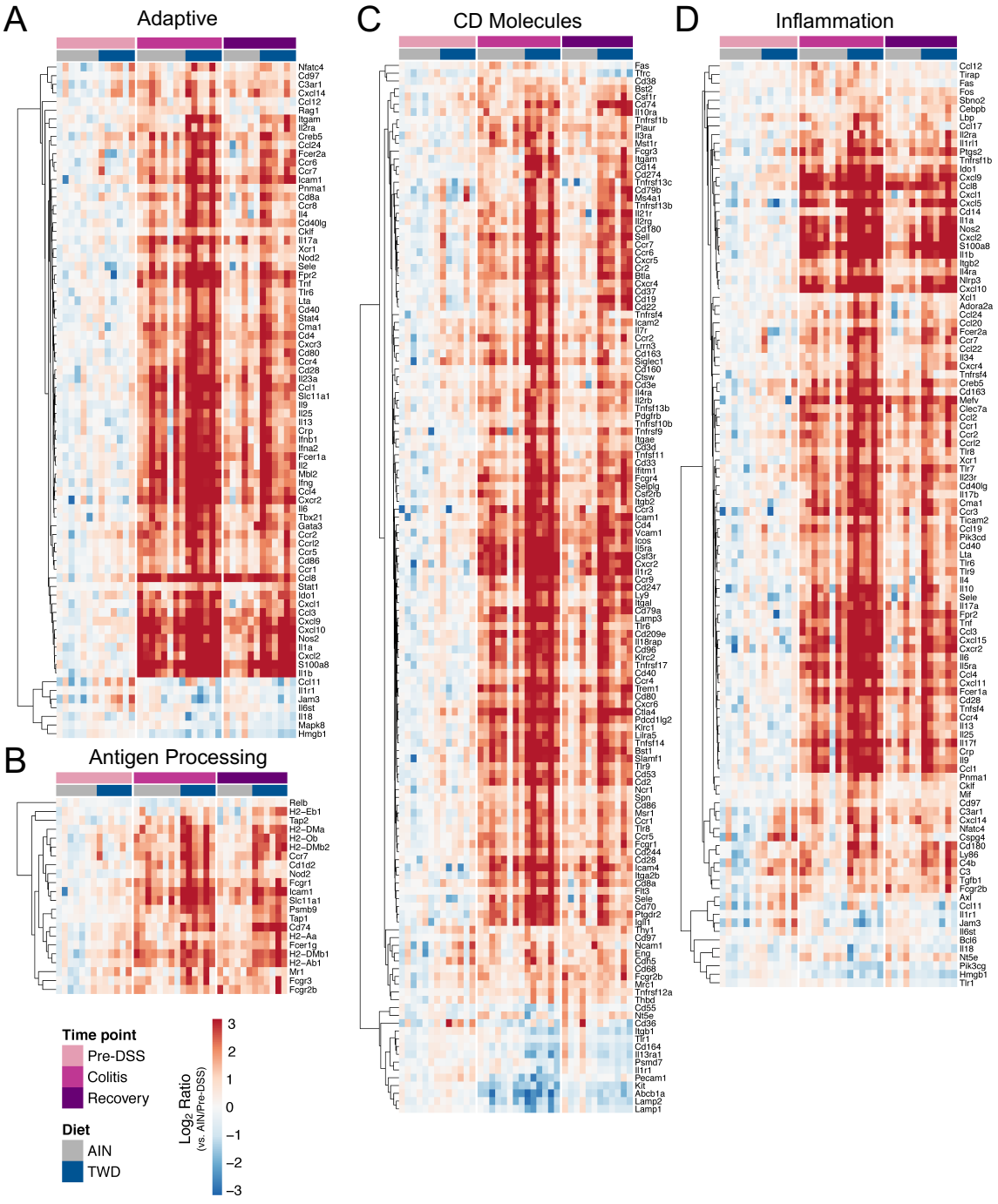


Figure S8. Time course of significant differentially expressed genes associated with adaptive immune response, antigen processing, CD molecules and inflammation in colon tissues of mice prior to, during and after DSS-induced gut injury. Gene expression data for adaptive (**A**), antigen processing (**B**), CD molecules (**C**) and inflammation (**D**) pathways were calculated as the $\log_2$ ratio of expression with respect to the AIN/Pre-DSS reference group. For each pathway of interest, a heatmap with unsupervised clustering (Euclidean distance method) by gene is shown for all genes identified as significantly differentially expressed (BH $q < 0.05$, $\log_2$ ratio >1 or < −1) at any one of the indicated time points. Note that some genes are associated with multiple immune response pathways, and thus, these genes appear in multiple panels.

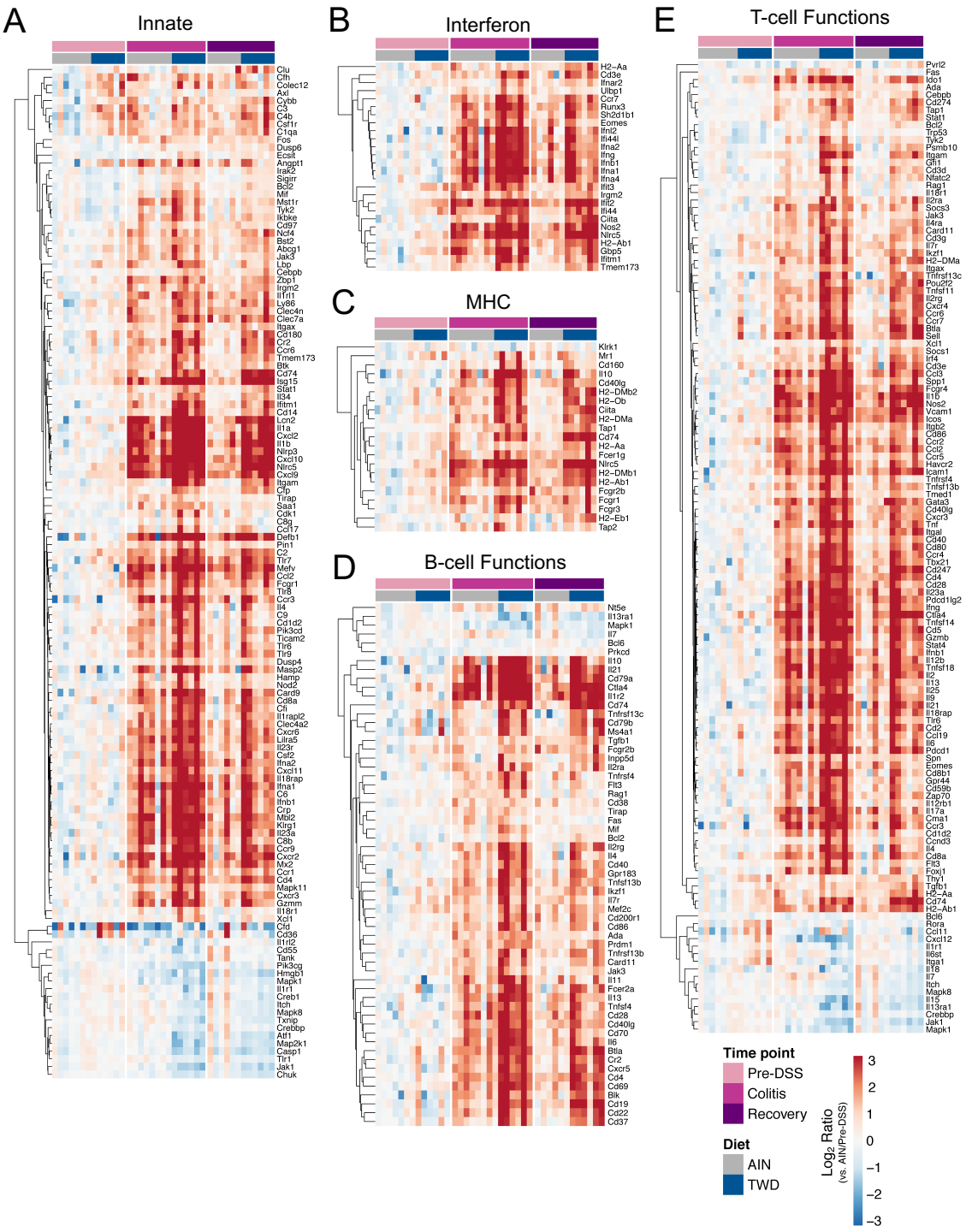


Figure S9. Time course of significant differentially expressed genes associated with innate immune response, interferon, MHC, B-cell functions, and T-cell functions in colon tissues of mice prior to, during and after DSS-induced gut injury. Gene expression data for innate (**A**), interferon (**B**), MHC (**C**), B-cell functions (**D**) and T-cell functions (**E**) pathways were calculated as the $\log_2$ ratio of expression with respect to the AIN/Pre-DSS reference group. For each pathway of interest, a heatmap with unsupervised clustering (Euclidean distance method) by gene is shown for all genes identified as significantly differentially expressed (BH $q < 0.05$, $\log_2$ ratio >1 or < −1) at any one of the indicated time points. Note that some genes are associated with multiple immune response pathways, and thus, these genes appear in multiple panels.

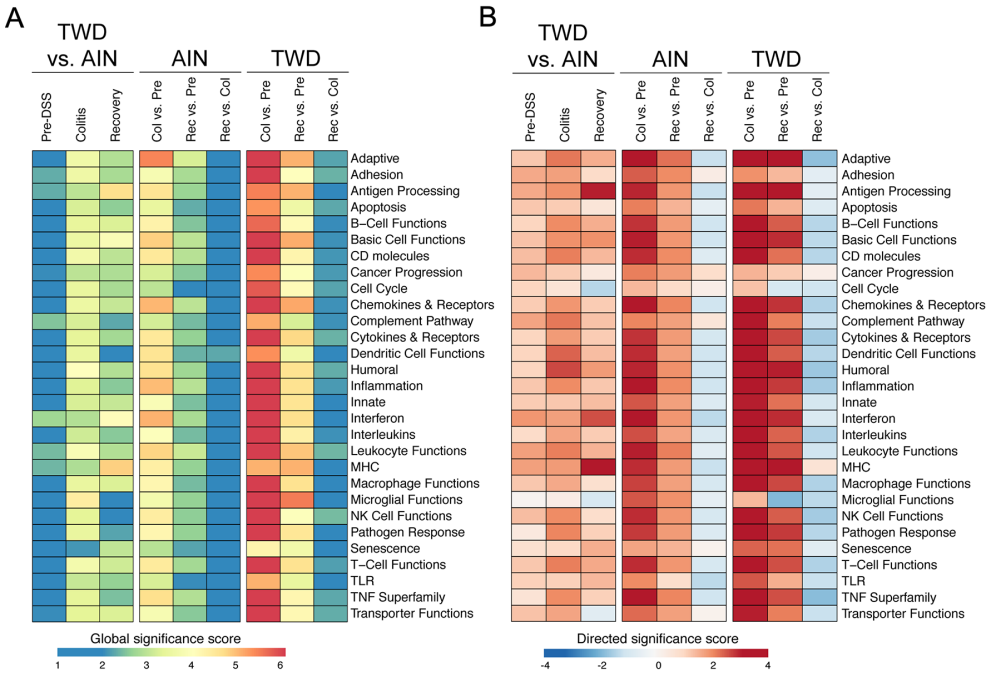


Figure S10. Global and directed significance scores for immune-related pathways over the course of onset of colitis and recovery from gut injury. Heatmaps depicting either global (**A**) or directed (**B**) significance scores for immune-related pathways included in the NanoString PanCancer Immune Profiling gene panel (see Materials and Methods for details on calculation of significance scores). Comparisons were made by diet at each time point, by time point for AIN diet, or by time point for TWD diet.

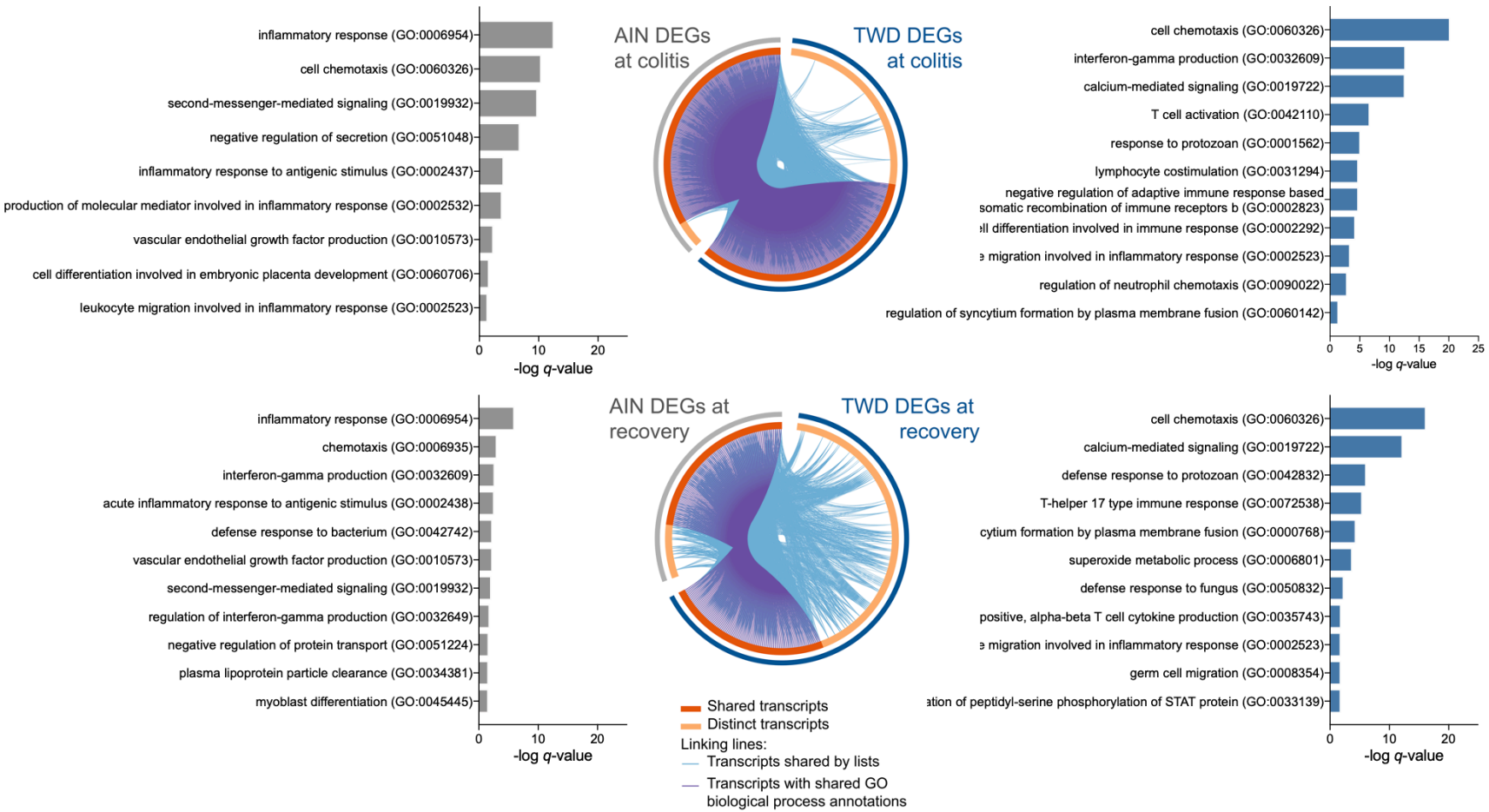


Figure S11. Circos plots and ontology terms for differentially expressed genes at colitis and recovery time points for AIN and TWD diets. Circos plots depict overlap of DEGs (purples lines) and overlap of shared ontology terms (blue lines). Bar charts depict significantly enriched (p<0.05, minimum overlap of 3, and enrichment >1.5) gene ontology biological process terms associated with genes differentially expressed in colon tissues of mice fed AIN or TWD at either the colitis or recovery time points compared to the pre-DSS time point. Redundant terms were clustered by similarity (kappa score >0.3), and up to 20 clustered terms are shown. Complete results from Metascape ontology analyses are provided in File S6.

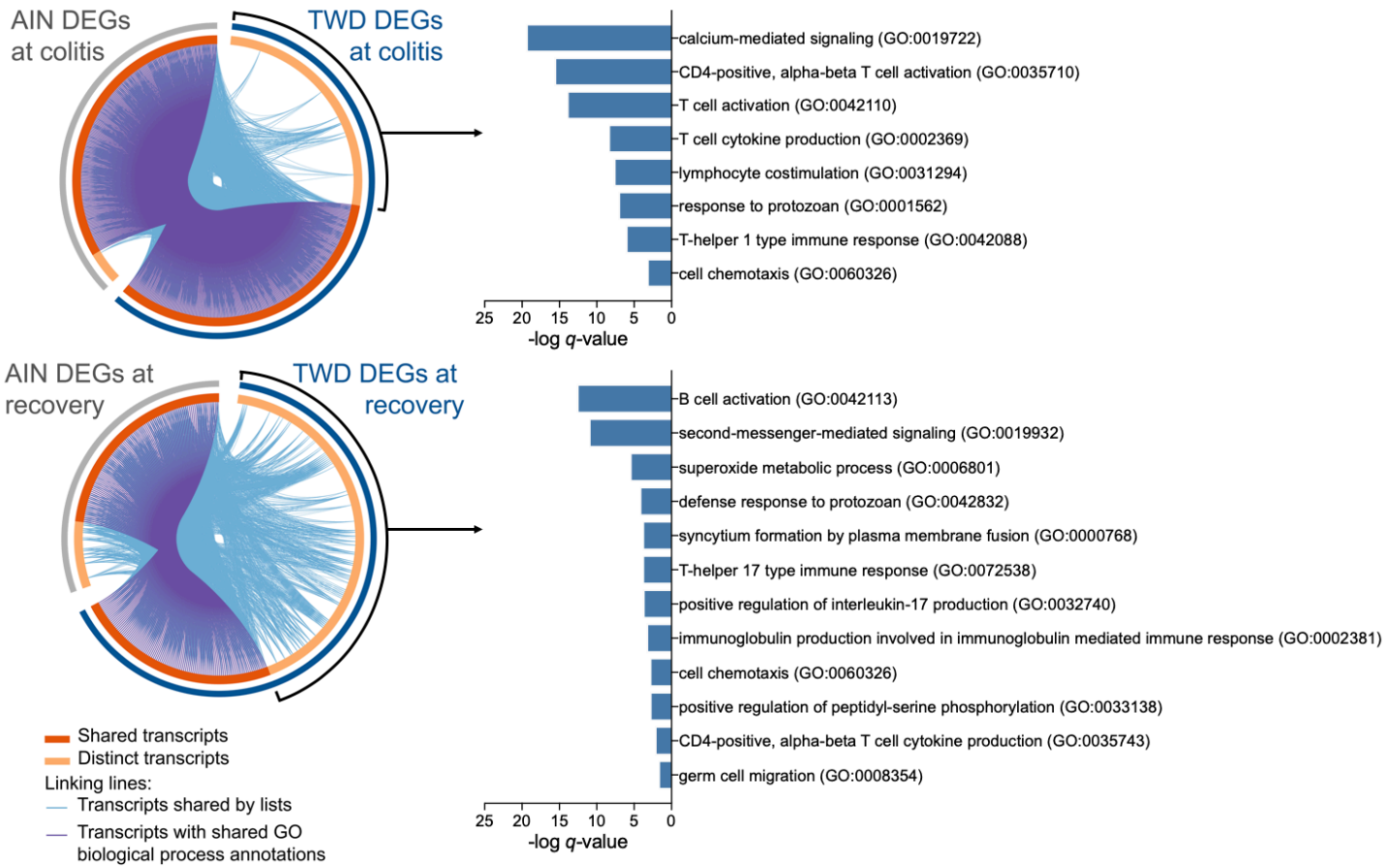


Figure S12. Circos plots and ontology terms for differentially expressed genes unique to TWD at colitis and recovery time point. Circos plots depict overlap of DEGs (purples lines) and overlap of shared ontology terms (blue lines). Bar charts depict significantly enriched (p<0.05, minimum overlap of 3, and enrichment >1.5) gene ontology biological process terms associated with DEGs unique to the TWD (as indicated by the black bracket) either the colitis or recovery time points compared to the pre-DSS time point. Redundant terms were clustered by similarity (kappa score >0.3), and up to 20 clustered terms are shown. Complete results from Metascape ontology analyses are provided in File S6.

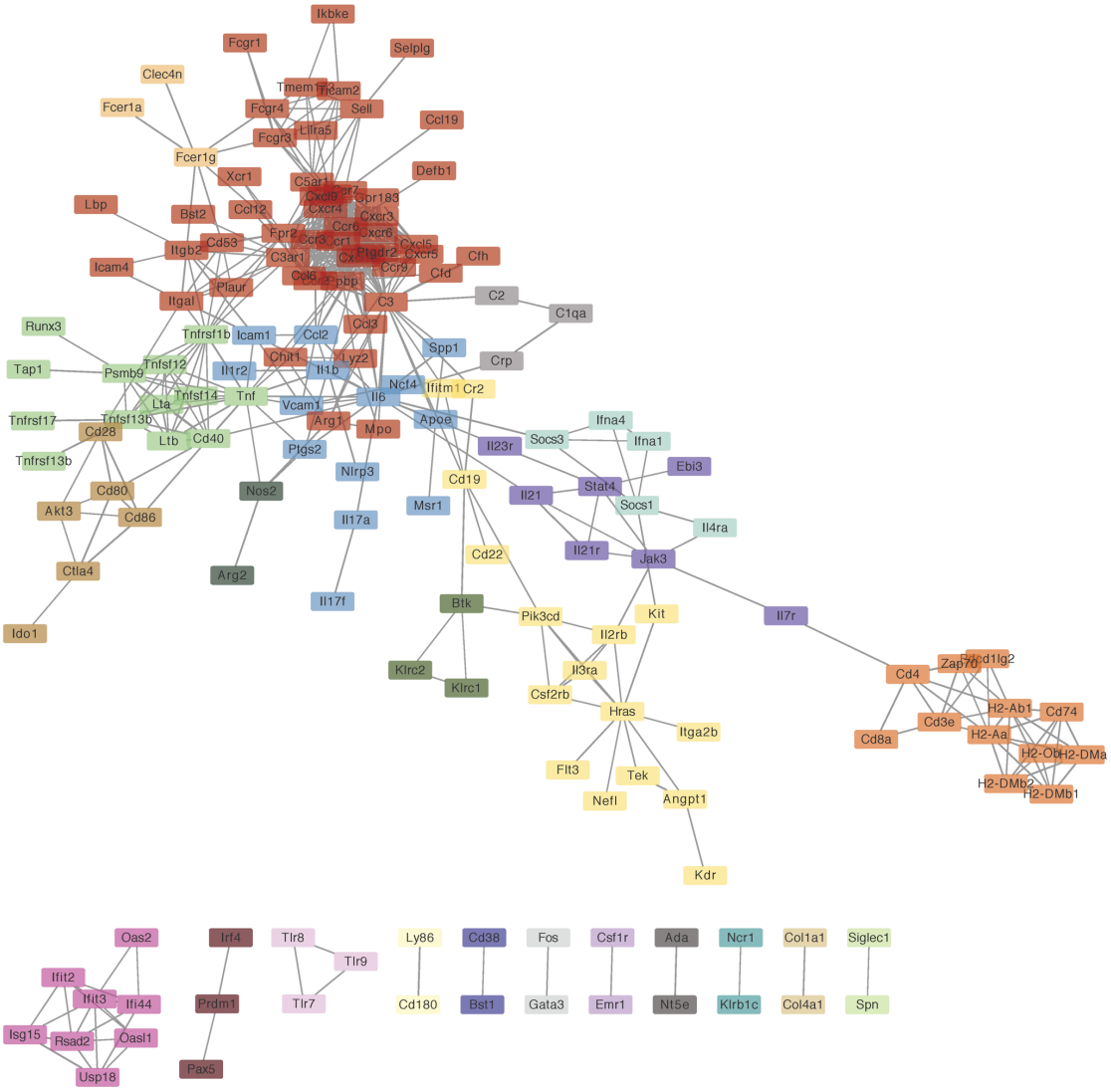


Figure S13. Network visualization of significant differentially expressed immune response genes at colitis as compared to pre-DSS time point in colon tissues of mice fed AIN. Network interactions were modeled using the STRING database (string-db.org) with a minimum required interaction score ≥0.9, and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape. See File S5 for protein-protein interactions and cluster predictions obtained from the STRING database.

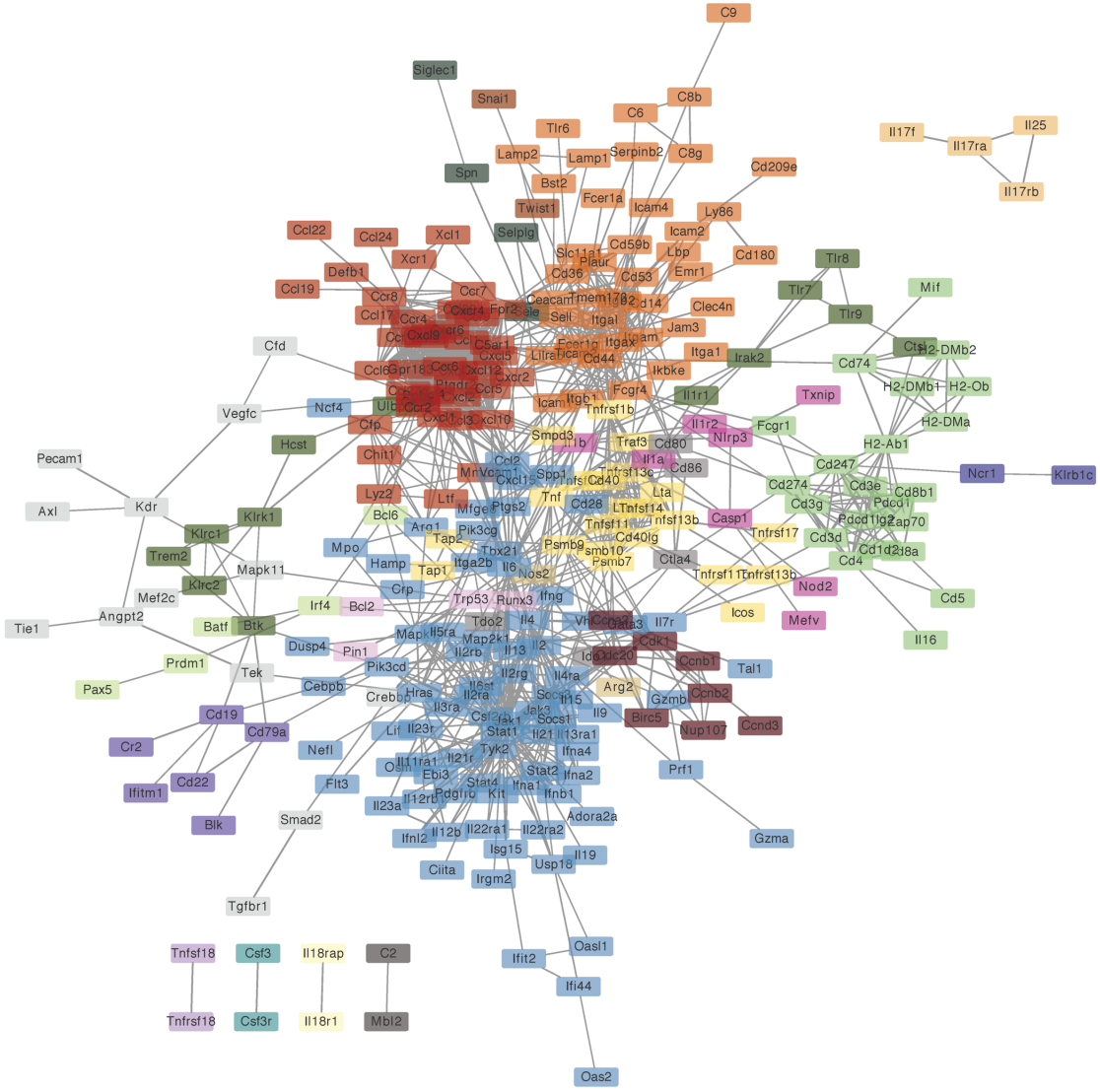


Figure S14. Network visualization of significant differentially expressed immune response genes at colitis as compared to pre-DSS time point in colon tissues of mice fed TWD. Network interactions were modeled using the STRING database (string-db.org) with a minimum required interaction score ≥0.9, and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape. See File S5 for protein-protein interactions and cluster predictions obtained from the STRING database.

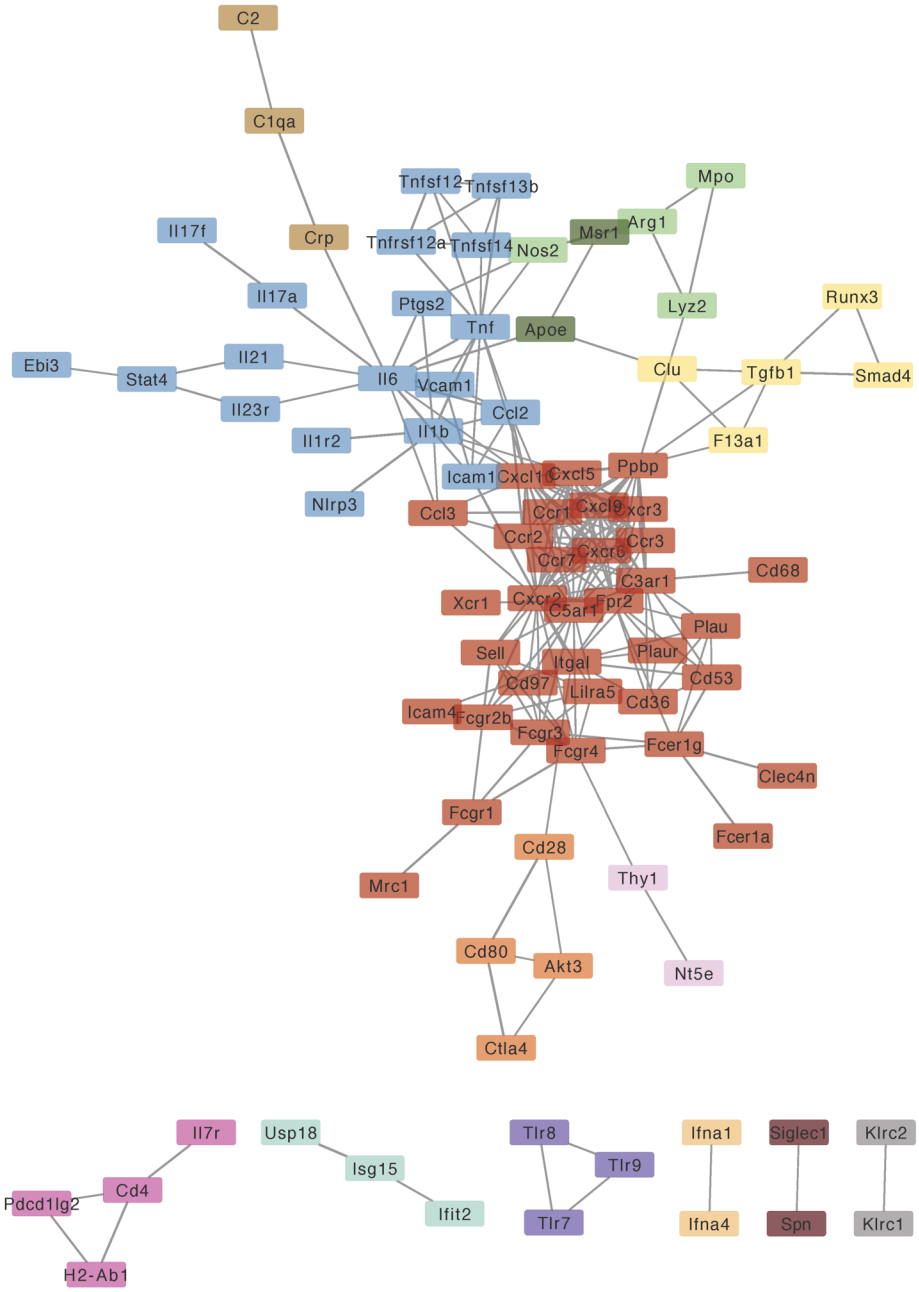


Figure S15. Network visualization of significant differentially expressed immune response genes at recovery as compared to pre-DSS time point in colon tissues of mice fed AIN. Network interactions were modeled using the STRING database (string-db.org) with a minimum required interaction score ≥0.9, and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape. See File S5 for protein-protein interactions and cluster predictions obtained from the STRING database.

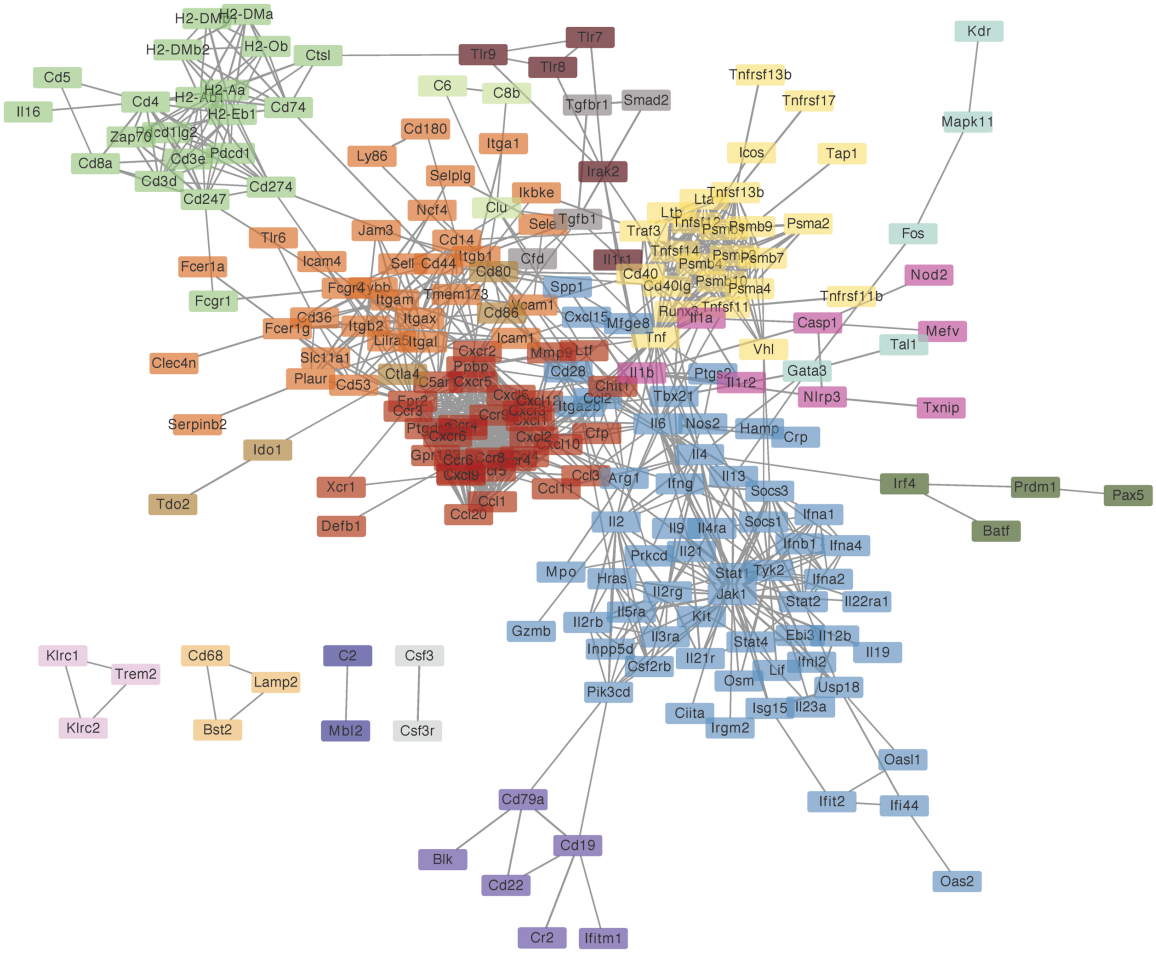
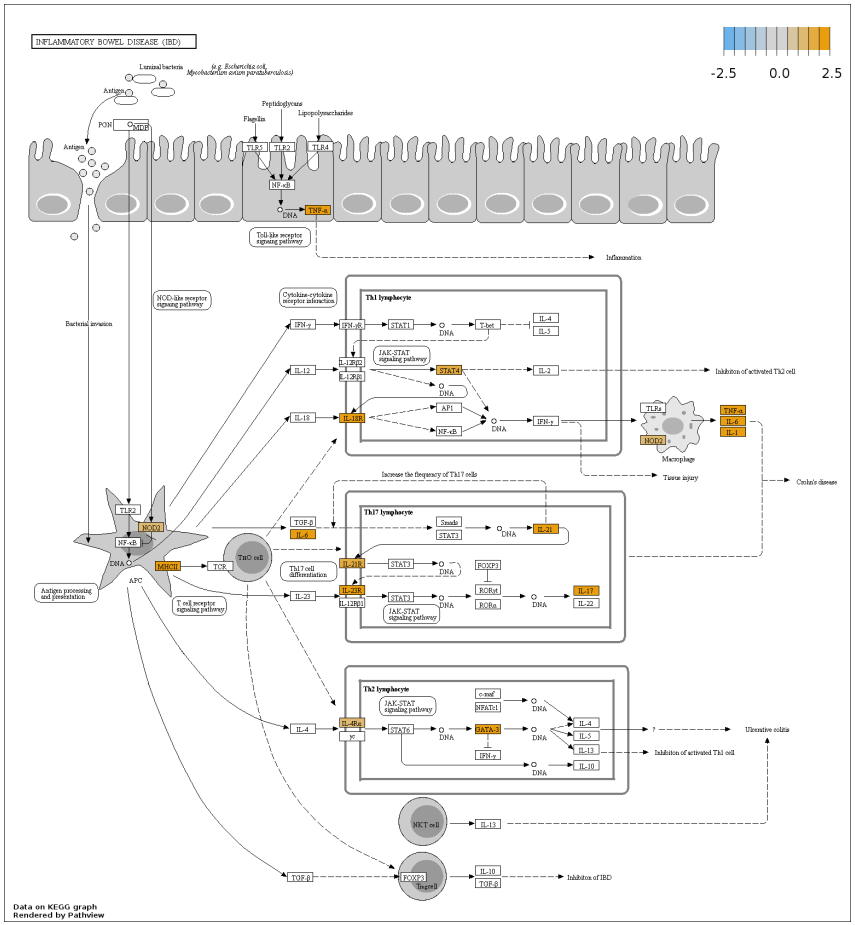


Figure S16. Network visualization of significant differentially expressed immune response genes at recovery as compared to pre-DSS time point in colon tissues of mice fed TWD. Network interactions were modeled using the STRING database (string-db.org) with a minimum required interaction score ≥0.9, and clusters were identified using the Markov Cluster (MCL) algorithm with inflation parameter of 1.5. The network was visualized in Cytoscape. See File S5 for protein-protein interactions and cluster predictions obtained from the STRING database.

AIN diet: Colitis vs Pre-DSS



TWD diet: Colitis vs Pre-DSS

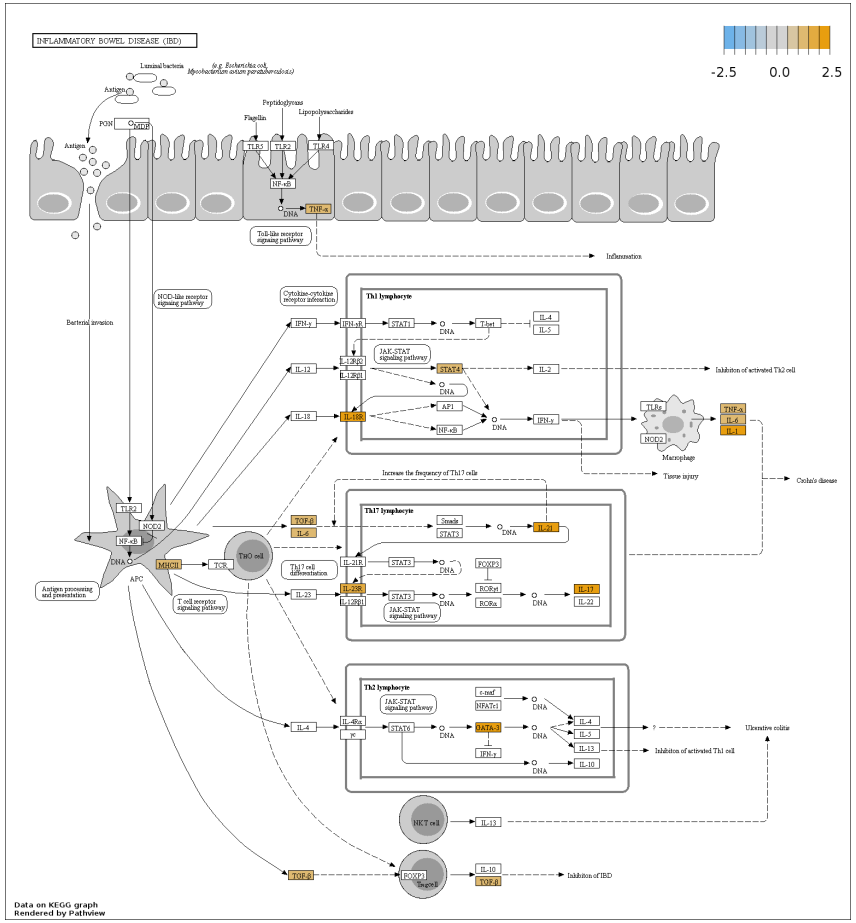
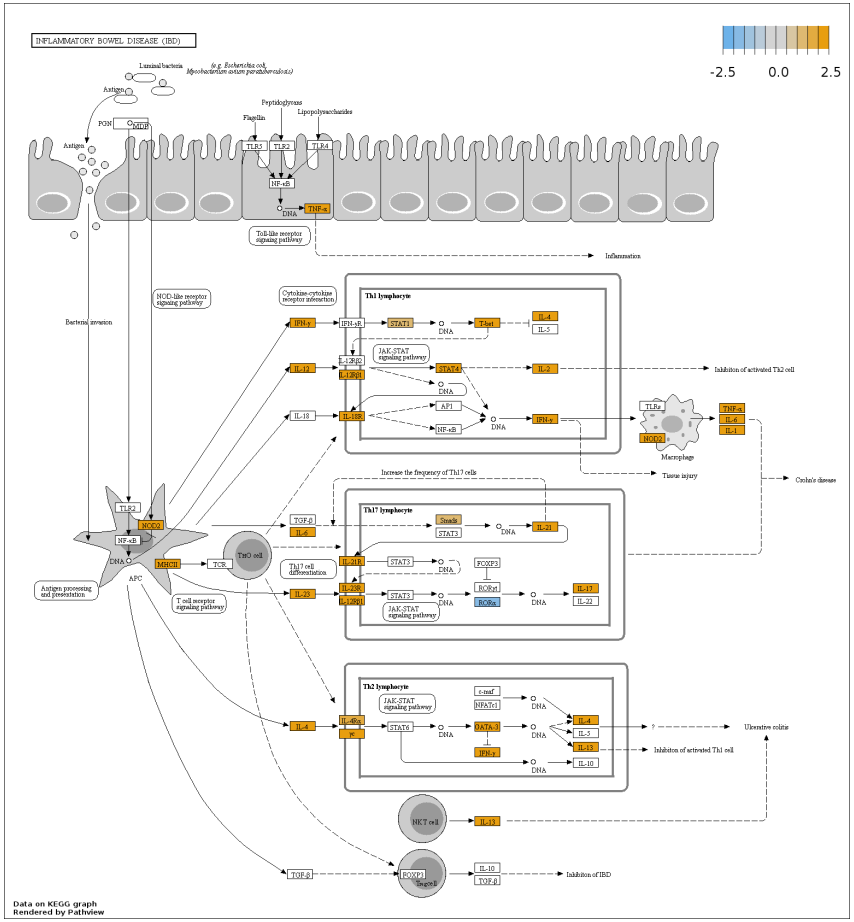


Figure S17. Changes in gene expression during colitis mapped to KEGG inflammatory bowel disease (mmu05321). For each experimental diet, genes induced or repressed during colitis as compared to the pre-DSS time point are colored according to their relative $\log_2$ ratio. Maps are provided for each diet, AIN (left) and TWD (right).

AIN diet: Recovery vs Pre-DSS



TWD diet: Recovery vs Pre-DSS

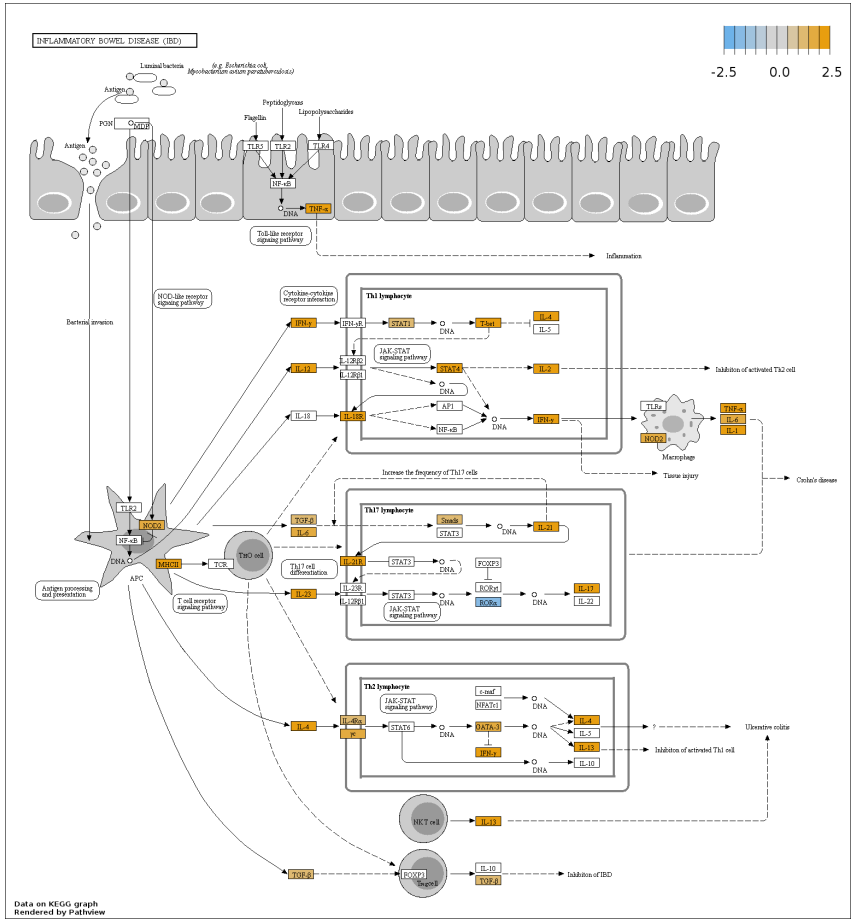


Figure S18. Changes in gene expression at recovery mapped to KEGG inflammatory bowel disease (mmu05321). For each experimental diet, genes induced or repressed at recovery as compared to the pre-DSS time point are colored according to their relative $\log_2$ ratio. Maps are provided for each diet, AIN (left) and TWD (right).

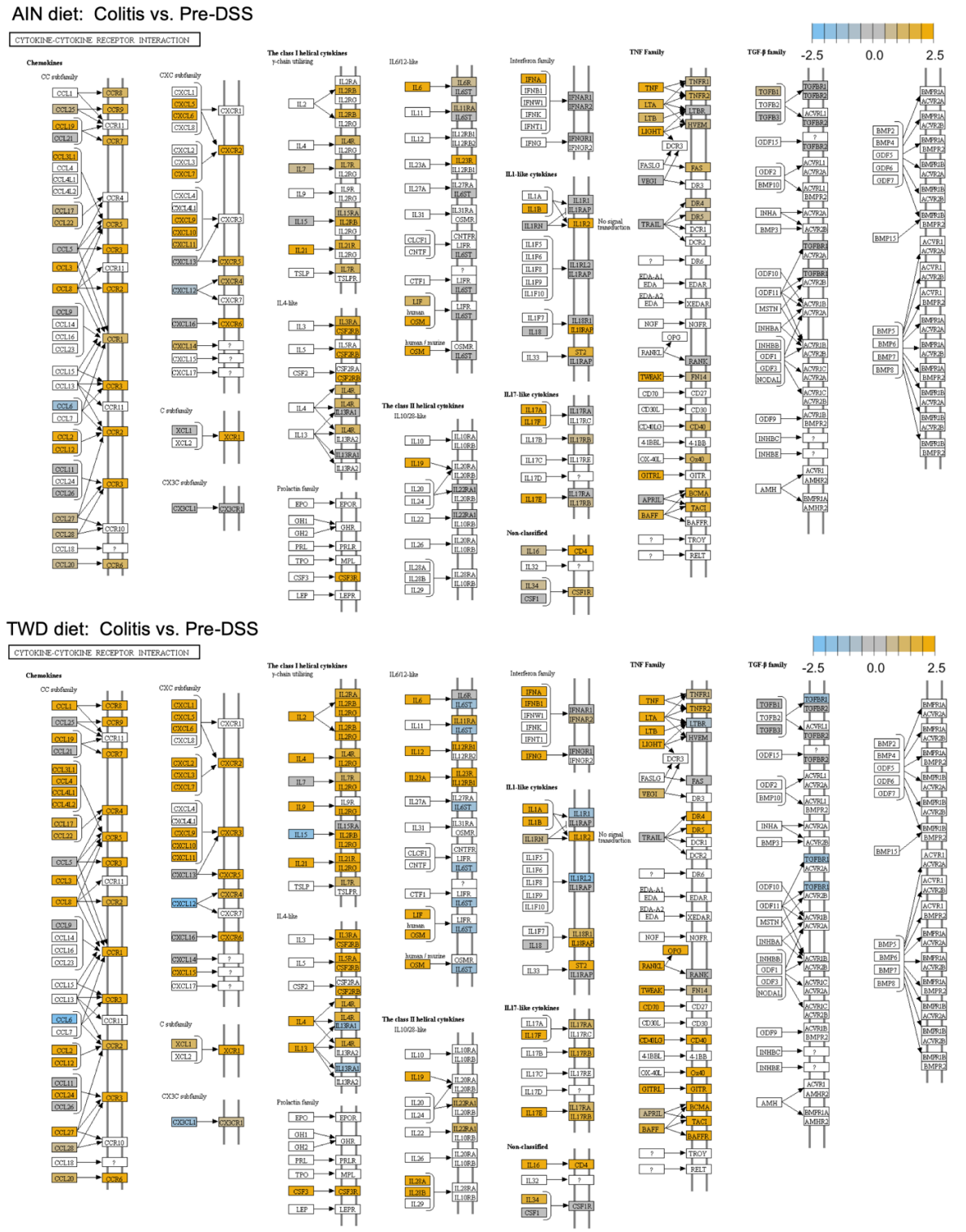


Figure S19. Changes in gene expression during colitis mapped to KEGG cytokine-cytokine receptor interaction pathway (mmu04060). For each experimental diet, genes induced or repressed during colitis as compared to the pre-DSS time point are colored according to their relative $\log_2$ ratio. Maps are provided for each diet, AIN (top) and TWD (bottom).

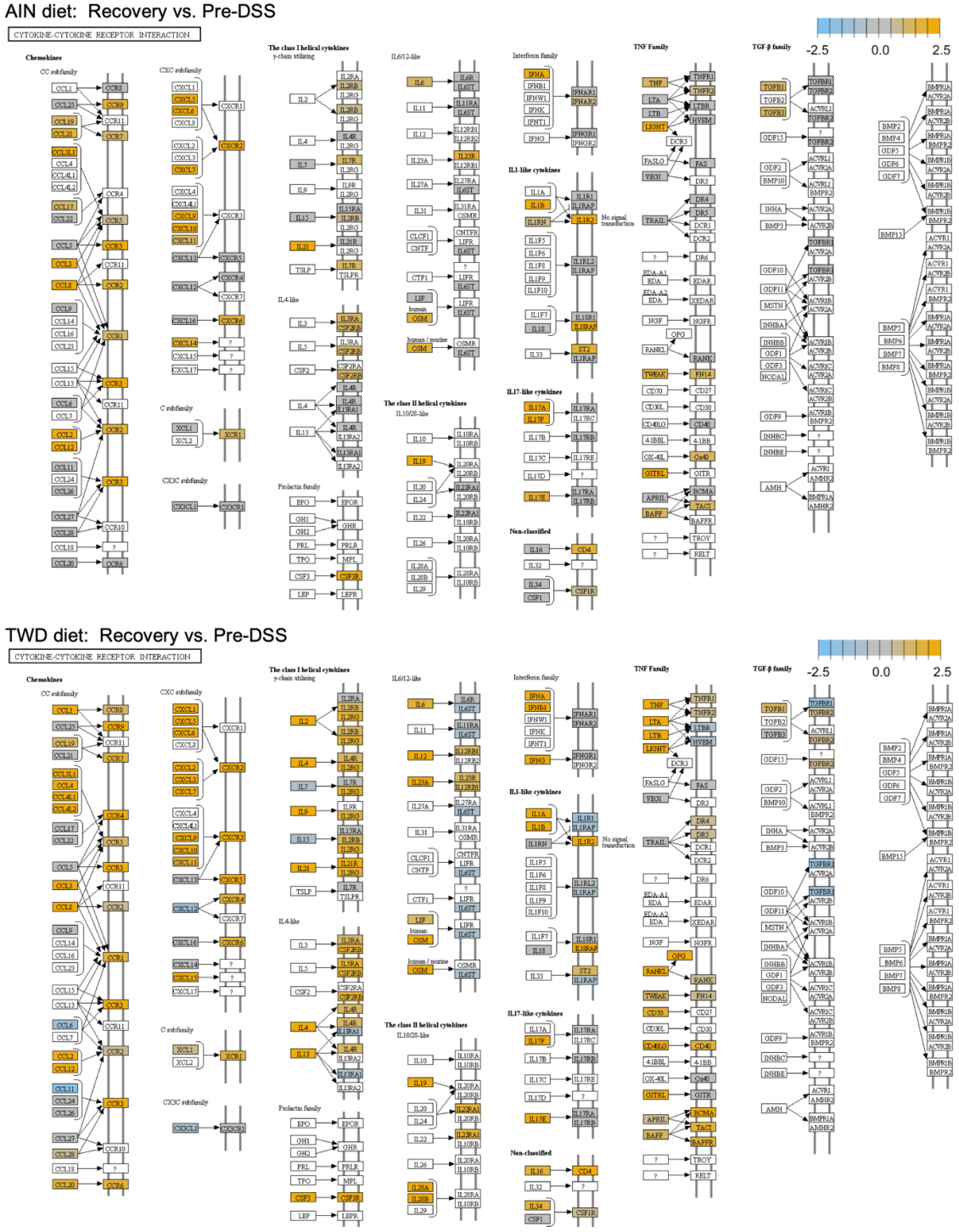


Figure S20. Changes in gene expression during recovery mapped to the KEGG cytokine-cytokine receptor interaction pathway (mmu04060). For each experimental diet, genes induced or repressed during recovery as compared to the pre-DSS time point are colored according to their relative $\log_2$ ratio. Maps are provided for each diet, AIN (top) and TWD (bottom).

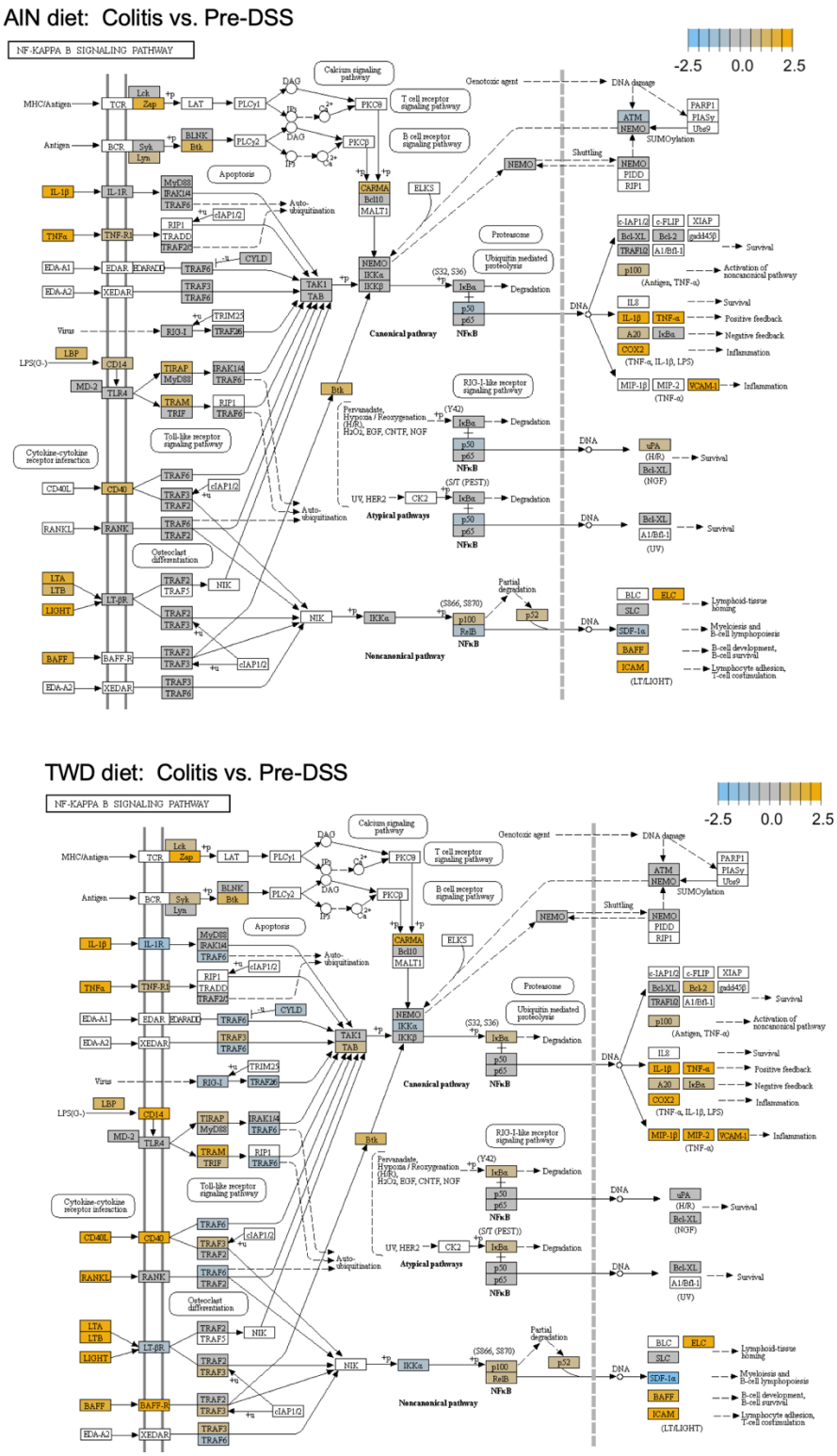


Figure S21. Changes in gene expression during colitis mapped to the KEGG NF-kappa B signaling pathway (mmu04151). For each experimental diet, genes induced or repressed during colitis as compared to the pre-DSS time point are colored according to their relative $\log_2$ ratio. Maps are provided for each diet, AIN (top) and TWD (bottom).

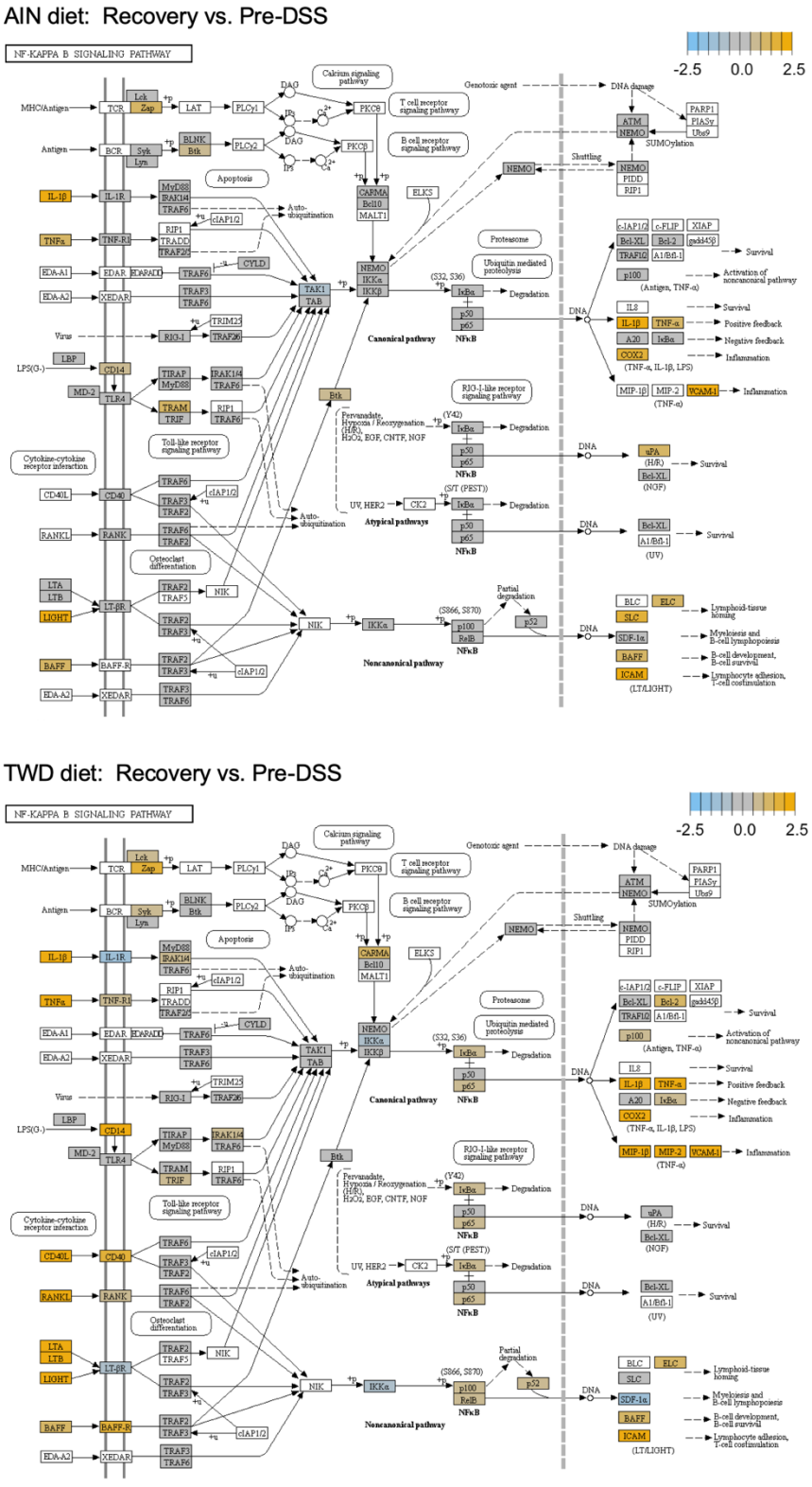


Figure S22. Changes in gene expression during recovery mapped to the KEGG NF-kappa B signaling pathway (mmu04151). For each experimental diet, genes induced or repressed during recovery as compared to the pre-DSS time point are colored according to their relative $\log_2$ ratio. Maps are provided for each diet, AIN (top) and TWD (bottom).

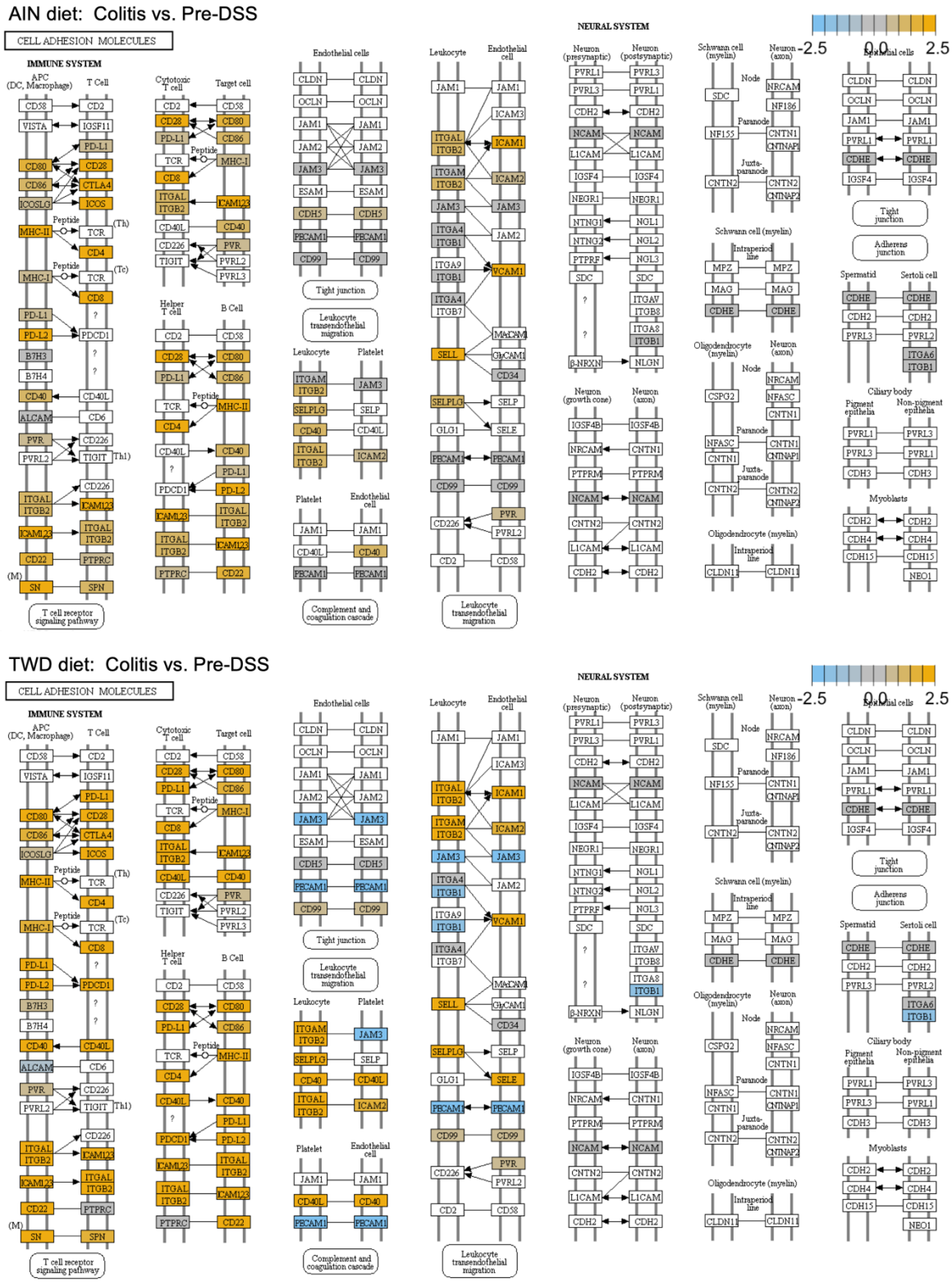


Figure S23. Changes in gene expression during colitis mapped to the KEGG cell adhesion pathway (mmu04514). For each experimental diet, genes induced or repressed during colitis as compared to the pre-DSS time point are colored according to their relative $\log_2$ ratio. Maps are provided for each diet, AIN (top) and TWD (bottom).

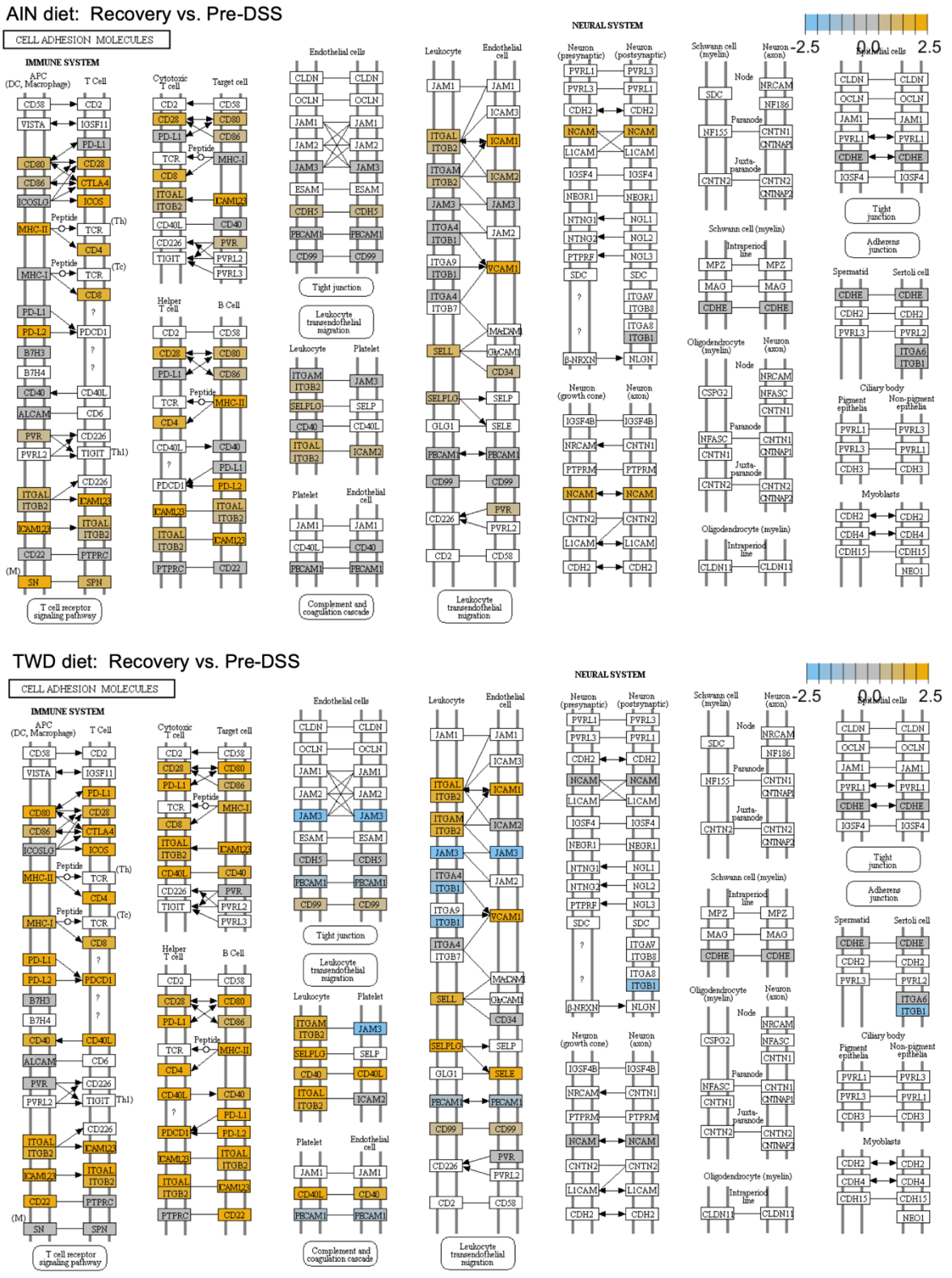


Figure S23. Changes in gene expression during recovery mapped to the KEGG cell adhesion pathway (mmu04514). For each experimental diet, genes induced or repressed during recovery as compared to the pre-DSS time point are colored according to their relative $\log_2$ ratio. Maps are provided for each diet, AIN (top) and TWD (bottom).

Table S1 Comparison of colitis-responsive genes across animal models and to human ulcerative colitis

Gene Symbol	AIN at colitis [b]	TWD at colitis [b]	Human UC [c]	Human UC [d]	3% DSS [e]	4% DSS [f]	PAC IL-10 k.o. [f]
Ada	1.27	1.49	1.66		*0.37*		
Bcl6	*-0.31*	-1.06	1.87		*0.47*		
Btk	1.13	1.34	1.78		*0.98*		
C3	1.31	*0.04*	2.50	2.80	2.46	1.51	1.93
C5ar1	1.37	2.66	1.31		1.56		
Casp1	*-0.18*	-1.17	1.90	1.46	*-0.19*	*0.94*	*0.41*
Ccl19	2.19	3.64	1.96		*0.06*		
Ccl2	2.67	3.25	1.51	1.94	2.95	2.46	2.48
Ccl20	*0.99*	1.35	2.94	2.59	*-0.58*	*-0.81*	*0.28*
Ccl3	3.33	5.05	2.09	*0.87*	4.55	-1.66	1.41
Ccl4		4.53	2.15	1.18	1.42	2.08	1.86
Ccr1	1.45	2.30	1.53		1.23		
Ccr2	2.06	1.57		*0.76*	*0.91*	1.39	2.22
Ccr7	1.92	2.59	1.60	2.11	1.68	1.53	*0.68*
Cd180	1.10	1.62	1.08		*0.30*		
Cd274	*0.94*	2.27	2.45		1.48		
Cd3d	*0.71*	2.68	1.28		1.32		
Cd4	2.16	3.13		1.51	*0.48*	1.50	*0.79*
Cd40	1.27	2.63	1.62		1.18		
Cd44		3.89	1.70	1.31	*0.22*	*0.63*	*0.25*
Cd69	2.01	2.98	1.19		*0.91*		
Cd79a		4.90	1.33		*0.23*		
Cd80	1.69	3.48	2.75	*0.79*	*-0.65*		
Cd86	1.28	1.96	1.55	1.47	*0.96*	*0.22*	1.09

Table S1 Comparison of colitis-responsive genes across animal models and to human ulcerative colitis

Gene Symbol	AIN at colitis [b]	TWD at colitis [b]	Human UC [c]	Human UC [d]	3% DSS [e]	4% DSS [f]	PAC IL-10 k.o. [f]
Cfi		4.49	3.26		*0.81*		
Cklf	*0.68*	1.48	1.41		*0.02*		
Clec7a	1.86	2.43	1.45		2.27		
Col3a1	*-0.16*	-1.62	1.27		*0.46*		
Cr2	1.88	2.34	2.16	2.96	*0.36*	1.44	*-0.14*
Csf3r	4.12	5.06	4.14		2.62		
Cxcl1		2.98	4.74	4.41	1.78	3.53	2.89
Cxcl10	4.00	5.74	2.70	2.55	2.88	3.11	4.22
Cxcl11	1.82	2.95	4.26		*0.21*		
Cxcl2		6.57	3.86	2.41	5.55	1.69	2.57
Cxcl5	4.13	5.48	6.28	1.32	4.31	3.70	5.20
Cxcl9	3.69	3.46	1.68	2.49	3.60	3.83	4.50
Cxcr2	3.36	5.22	5.55		1.71		
Cxcr4	1.07	1.95	1.16		*0.70*		
Defb1	3.44	5.44	-1.43	-2.42	1.54	*-0.20*	*-0.10*
Fcer1g	1.50	1.52	1.02		2.16		
Fpr2	3.18	5.05	2.27		3.18		
Gbp5	2.76	2.27	2.15		1.85		
Gpr183	1.29	2.68	1.28		*0.32*		
Icam1	2.37	3.09	1.03	1.94	1.76	2.53	2.22
Icam2	*0.85*	1.66	1.08		1.14		
Ido1	2.51	2.60	3.71		3.17		
Ifitm1	1.38	2.68	1.20		1.93		
Ikzf1	1.53	1.80	1.17		*-0.39*		
Il1b	4.61	6.09	2.57	2.79	3.81	3.36	3.46

Table S1 Comparison of colitis-responsive genes across animal models and to human ulcerative colitis

Gene Symbol	AIN at colitis [b]	TWD at colitis [b]	Human UC [c]	Human UC [d]	3% DSS [e]	4% DSS [f]	PAC IL-10 k.o. [f]
Il1r2	3.82	5.12	-1.45		2.49		
Il1rl1	1.70	2.45	1.01		2.38		
Il7r	1.13	1.03	1.37		*0.54*		
Itgam	*0.60*	3.16	1.35		1.43		
Itgb2	1.48	2.24	1.61		1.74		
Jak3	1.25	1.24	1.82		1.02		
Kdr	-1.07	-3.46	1.03		*0.44*		
Lamp3	2.77	4.23	1.86		*0.02*		
Lcn2	3.75	6.28	4.53	4.66	4.03	2.63	3.79
Ltb	1.14	2.57	1.38	2.39	*0.64*	1.17	*0.89*
Mapk1	*-0.44*	-1.27	1.03		*0.02*		
Mif	*0.63*	1.89	1.16		*-0.12*		
Mmp9		3.80	3.16	2.81	1.67	1.83	2.14
Ncf4	1.50	1.03	1.22		1.05		
Nod2	1.27	2.63	2.04	*0.68*	*0.35*	1.94	*0.84*
Nos2	3.28	4.64	5.37	3.80	2.16	5.29	5.24
Pax5	1.98	2.73	3.19		1.66		
Pdgfrb	*0.63*	1.81	1.59		*0.64*		
Pecam1	*-0.59*	-3.01	1.81		*0.90*		
Pik3cd	1.63	1.86	1.70		*0.24*		
Plaur	1.75	2.01	1.47		1.00		
Pou2af1	1.92	2.71			*0.25*		
Pou2f2	1.42	2.01	1.19		*0.37*		
Ppbp	2.59	4.88	2.24		1.27		
Psmb9	1.32	2.16	1.75		1.42		

Table S1 Comparison of colitis-responsive genes across animal models and to human ulcerative colitis

Gene Symbol	AIN at colitis [b]	TWD at colitis [b]	Human UC [c]	Human UC [d]	3% DSS [e]	4% DSS [f]	PAC IL-10 k.o. [f]
Ptgs2	2.21	4.02	1.27	1.27	*0.94*	*0.28*	*0.96*
Runx3	2.69	4.26	1.58		*0.59*		
S100a8	6.70	9.30	6.40	2.29	5.20	6.11	6.29
Saa1	1.15	2.02	6.14		*0.13*		
Sele		5.23	1.76	1.15	3.40	*0.31*	*0.17*
Sell	2.14	3.25	2.85		2.36		
Slc7a11	2.17	2.71	1.21		*0.34*		
Socs1	1.10	2.44	2.36		1.58		
Socs3	1.93	2.75	3.12		3.28		
Spp1	2.03	4.31	3.12		3.13		
Stat1	*0.82*	1.33	1.88	1.46	1.52	2.49	2.57
Tap1	1.07	1.76	1.44		*-0.42*		
Tap2	*0.94*	1.71	1.53		*0.58*		
Tdo2	*0.23*	2.62	2.88		*0.15*		
Tek	-1.18	-3.48	1.46		*0.51*		
Tlr8	1.27	2.09	1.65		*0.91*		
Tnf	2.32	3.69		1.39	1.70	2.68	2.85
Tnfrsf11b		3.52	1.03		*0.70*		
Tnfrsf1b	1.35	1.71	1.10		*0.53*		
Tnfsf13b	1.71	1.94	1.23		*0.64*		
Tpsab1		4.52	1.02		*0.20*		
Vcam1	2.44	3.01	1.73	2.44	1.13	1.02	1.27

[a] Numbers shown in gray italics did not meet the significance (FDR p-value <0.05) and/or the fold change (2-fold) criteria set for the present study. Cells with missing data indicate that the gene either was not detected or the data were not presented or made available with the cited paper.

Table S1 Comparison of colitis-responsive genes across animal models and to human ulcerative colitis

Gene Symbol	AIN at colitis [b]	TWD at colitis [b]	Human UC [c]	Human UC [d]	3% DSS [e]	4% DSS [f]	PAC IL-10 k.o. [f]

[b] Values shown are $\log_2$ ratios comparing the colitis vs. pre-DSS comparison for mice fed the AIN or the TWD diets [this study].

[c] Values shown are the $\log_2$ ratios for mRNA expression in colon tissues obtained from human ulcerative colitis patients (n=6) compared to healthy controls (n=5) as determined using the Affymetrix Human Genome U133 Plus 2.0 Array [2].

[d] Values are the $\log_2$ ratios for mRNA expression in colon tissues obtained from human ulcerative colitis patients (n=10) compared to healthy controls (n=15) as determined using RNAseq [3]. Note, the complete dataset was not available with this publication.

[e] Values are the $\log_2$ ratios of gene expression in colon mucosa of C57BL/6J mice following six days of exposure to 3% DSS as compared to day zero prior to DSS treatment as determined using the Affymetrix Mouse Genome 430 2.0 Array. Fold change values were calculated using the data set deposited at the Gene Expression Omnibus (accession GSE22307) using the GEO2R module with Benjamini & Hochberg method for false discovery rate correction [4].

[f] Values are the $\log_2$ ratios for gene expression in colon mucosa of BALB/c mice using either a 4% DSS treatment (5 days treatment, mucosa collection on day 8) compared to non-treated control or the PAC *Il10*$^{-/-}$ mouse model compared to wildtype control [3]. Note, the complete dataset was not available with this publication.

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