Title: Ursodeoxycholic acid (UDCA) mitigates the host inflammatory response during *Clostridioides difficile* infection by altering gut bile acids which attenuates NF-κB signaling via bile acid activated receptors

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Importance

The clinical utility of ursodiol for prevention of recurrent CDI is currently in Phase 4 clinical trials. However, the mechanism by which ursodiol exerts its impacts on *C. difficile* pathogenesis is poorly understood. Herein, we demonstrated that ursodiol pretreatment attenuates CDI pathogenesis early in the course of disease in mice, which coincides with alterations in the cecal and colonic inflammatory transcriptome, bile acid activated receptors nuclear farnesoid X receptor (FXR), and transmembrane G protein-coupled membrane receptor 5 (TGR5), which are able to modulate the innate immune response through signaling pathways such as NF-κB. Ursodiol attenuated an overly robust inflammatory response that is detrimental to the host during CDI, and thus remains a viable non-antibiotic treatment and/or prevention strategy against CDI. Likewise, modulation of the host innate immune response via bile acid activated receptors, FXR and TGR5, represents a new potential treatment strategy for patients with CDI.

Abstract

Clostridioides difficile infection (CDI) is associated with increasing morbidity and mortality posing an urgent threat to public health. Recurrence of CDI after successful treatment with antibiotics is high, thus necessitating discovery of novel therapeutics against this enteric pathogen. Administration of the secondary bile acid ursodeoxycholic acid (UDCA, ursodiol) inhibits the life cycle of various strains of *C. difficile in vitro*, suggesting the FDA approved formulation of UDCA, known as ursodiol, may be able to restore colonization resistance against *C. difficile in vivo*. However, the mechanism(s) by which ursodiol is able to restore colonization resistance against *C. difficile* remains unknown. Here, we confirmed that ursodiol inhibits *C. difficile* R20291 spore germination and outgrowth, growth, and toxin activity in a dose dependent manner *in vitro*. In a murine model of CDI, exogenous administration of ursodiol resulted in significant alterations in the bile acid metabolome with little to no changes in gut microbial community structure. Ursodiol pretreatment resulted in attenuation of CDI pathogenesis early in the course of disease, which coincided with alterations in the cecal and colonic inflammatory transcriptome, bile acid activated receptors nuclear farnesoid X receptor (FXR), and transmembrane G protein-coupled membrane receptor 5 (TGR5), which are able to modulate the innate immune response through signaling pathways such as NF-κB. Although ursodiol pretreatment did not result in a consistent decrease in the *C. difficile* life cycle *in vivo*, it was able to attenuate an overly robust inflammatory response that is detrimental to the host during CDI. Ursodiol remains a viable non-antibiotic treatment and/or prevention strategy against CDI. Likewise,

modulation of the host innate immune response via bile acid activated receptors, FXR and TGR5, represents a new potential treatment strategy for patients with CDI.

Abbreviations

αMCA – α-Muricholic acid; βMCA –β-Muricholic acid; ωMCA –ω-Muricholic acid; CA – Cholic acid; CDCA – Chenodeoxycholic acid; DCA – Deoxycholic acid; GCDCA – Glycochenodeoxycholic acid; GDCA – Glycodeoxycholic acid; GLCA – Glycolithocholic acid; GUDCA – Glycoursodeoxycholic acid; HCA – Hyodeoxycholic acid; iDCA – Isodeoxycholic acid; iLCA – Isolithocholic acid; LCA – Lithocholic acid; TCA – Taurocholic acid; TCDCA – Taurochenodeoxycholic acid; TDCA – Taurodeoxycholic acid; THCA – Taurohyodeoxycholic acid; TUDCA – Tauroursodeoxycholic acid; TβMCA– Tauro-β-muricholic acid; TωMCA –Tauro ω-muricholic acid; UDCA Ursodeoxycholic acid.

Introduction

Clostridioides difficile is a leading nosocomial enteric pathogen that causes significant human morbidity and mortality, resulting in 29,000 deaths per year and costing over $4.8 billion in healthcare expenses annually in the United States.[1-5] A major risk factor for *C. difficile* infection (CDI) is the use of antibiotics.[6,7] Antibiotics lead to significant and enduring shifts in the gut microbiota and metabolome[8-10], resulting in loss of colonization resistance against *C. difficile*. Although the exact mechanisms of colonization resistance against *C. difficile* remain unclear, there is increasing evidence that microbial derived secondary bile acids play an important role.[10-13]

Antibiotics, either vancomycin or fidaxomicin, are recommended for an initial episode of CDI.[14] Unfortunately antibiotic treatment can further disrupt the gut microbial

community and recurrence of CDI after cessation of antibiotics is high, occurring in 20-30% of patients.[3,15-18] Even fidaxomicin, a bactericidal antibiotic against *C. difficile,* alters the intestinal microbial community structure, just to a lesser extent than vancomycin.[19] Fecal microbiota transplantation (FMT) is a highly effective treatment for recurrent CDI, however the long-term ramifications of this conditionally FDA approved procedure are unknown.[20,21] A potential mechanism by which FMT leads to resolution of CDI in a mouse model[22,23] and in humans[13] is by restoring microbial derived secondary bile acids.

Secondary bile acids, such as deoxycholic acid (DCA), lithocholic acid (LCA) and ursodeoxycholic acid (UDCA, ursodiol), are produced as a collaborative effort by the host (production of primary bile acids) and the gut microbiota (biochemical modification of host primary bile acids into secondary bile acids).[24,25] Our group and others have demonstrated that numerous microbial derived secondary bile acids, including UDCA, are able to inhibit spore germination, growth, and toxin activity of various *C. difficile* strains *in vitro*.[26,27] We also know that secondary bile acids are associated with colonization resistance against *C. difficile* in mice and humans.[10,13,28] Furthermore, oral UDCA administration successfully prevented recurrence of *C. difficile* ileal pouchitis in a single patient,[29] suggesting that exogenous administration of the secondary bile acid UDCA may be able to restore colonization resistance against *C. difficile in vivo*.[29]

UDCA is available in an FDA approved formulation known as ursodiol.[30] Ursodiol is used to treat a variety of hepatic and biliary diseases due to its myriad of beneficial effects, including: anticholestatic, antifibrotic, antiproliferative, and anti-inflammatory properties.[31-40] Additionally, off-label use of ursodiol is currently in Phase 4 clinical trials

for the prevention of recurrent CDI.[41] It is well established that ursodiol alters the hepatic, biliary, and serum bile acid pools.[31,42] However, it remains unclear if and how exogenously administered ursodiol alters the indigenous gut microbial community structure and/or bile acid metabolome, which contributes to colonization resistance against *C. difficile*.

Based on our previous work with UDCA,[26] we hypothesized that ursodiol would *directly* inhibit different stages of the *C. difficile* life cycle*,* and ameliorate disease when administered to mice in a model of CDI. Due to their detergent like properties, bile acids can also directly alter the gut microbial composition, subsequently altering bile acid metabolism and host physiology.[43] Gastrointestinal crosstalk between bile acids and the gut microbiota is well recognized (reviewed in Wahlström et al.)[43], but the impact of ursodiol on these interactions remains unknown. Similarly, the central role bile acids play in regulation of the innate immune response is growing (reviewed in Fiorucci et al.).[44] Because of this, we also investigated the *indirect* effects or the extent to which the impact of ursodiol on CDI correlated with changes in the gut microbiota, bile acid metabolome, and the host inflammatory response.

Here we show that ursodiol is able to significantly decrease *C. difficile* spore germination, growth, and toxin activity in a dose-dependent manner *in vitro,* but not to the same level *in vivo*. In *C. difficile* infected mice, ursodiol pretreatment resulted in attenuation of CDI pathogenesis early in the course of disease, which coincided with alterations in gut bile acids, the host inflammatory transcriptome, and gene expression of bile acid activated receptors nuclear farnesoid X receptor (FXR) and transmembrane G protein-coupled membrane receptor 5 (TGR5), which are able to modulate the innate

immune response through signaling pathways such as NF-κB. Although ursodiol pretreatment did not restore colonization resistance against *C. difficile*, it attenuated an overly robust host inflammatory response that is detrimental to the host during CDI. Together, these results suggest that ursodiol remains a viable non-antibiotic treatment and/or prevention strategy against CDI by acting on the FXR-FGR axis via NF-kB signaling. Targeting the bile acid activated receptors, FXR and TGR5, represents a novel approach for the development of therapies for the prevention and treatment of CDI.

Materials and Methods

Spore preparation. *C. difficile* R20291 spores were prepared as described previously.[22,26,45] Briefly *C. difficile* R20291 were grown at 37°C anaerobically overnight in 2 ml Columbia broth and then added to 40 ml culture of Clospore media in which it was allowed to sporulate for 5–7 days. Spores were harvested by centrifugation, and subjected to 3–5 washes with sterile cold water to ensure spore purity. Spore stocks were stored at 4°C in sterile water until use.

***C. difficile in vitro* spore germination and outgrowth assay.** The spore germination and outgrowth assay performed was modified from Carlson et al., Theriot et al., and Thanissery et al.[22,26,46] Purified spores were enumerated and tested for purity before use. The spore stock was resuspended in ultrapure water to achieve an initial spore concentration of approximately 10^6 spores/ml. The spore suspension was subjected to heat treatment (65°C for 20 min) to eliminate any vegetative cells. The spores were then plated on both brain heart infusion (BHI) with 100 mg/liter L-cysteine, and BHI media supplemented with 0.1% TCA, and further incubated at 37°C for 24 hr. We observed a

lawn of *C. difficile* colonies on BHI media supplemented with 0.1% TCA, and no visible growth on BHI media alone, which indicates that the spore suspension was devoid of vegetative cells. Bile acid solutions containing four to five concentrations were used to study a dose response [Ursodiol U.S.P (0.0076, 0.076, 0.76, and 7.64 mM, Spectrum Chemical, CAS 128-13-2)]. Bile acids were dissolved in ethanol, passed into the anaerobic chamber (Coy labs), and added to BHI broth with 0.1% TCA. Chendeoxycholate (CDCA, Fisher Scientific, 50328656) at 0.04% is a known inhibitor of TCA mediated spore germination, and was used as a negative control. TCA at 0.1% made in water, and water and ethanol were used as positive controls. *C. difficile* R20291 spores were added to BHI broth supplemented with and without TCA 0.1% and bile acids at concentrations listed above, and allowed to incubate for 30 min at 37°C anaerobically. Bacterial enumeration of the samples was performed on both BHI agar (vegetative cells only) and BHI agar supplemented with 0.1% TCA (germinated spores and vegetative cells). Percent germination was calculated as [(CFUs on BHI supplemented with TCA + SBAs) / (CFUs on BHI supplemented with TCA alone)] × 100. All measurements were performed in triplicate for each isolate and expressed as percent germination.

***C. difficile in vitro* growth kinetics assay.** The growth kinetic assay was modified from Thanissery et al. and performed over a 24 hr period.[26] *C. difficile* R20291 was cultured overnight at 37°C in BHI plus 100 mg/liter L-cysteine broth in an anaerobic chamber. After 14 hr of growth, *C. difficile* R20291 was subcultured 1:10 and 1:5 into BHI plus 100 mg/liter L-cysteine and allowed to grow for 3 hr anaerobically at 37°C. The culture was then diluted in fresh BHI to a starting optical density at 600 nm (OD_{600}) of

0.01 within a conical tube at a final volume of 50 ml. Five concentrations of filter-sterilized ursodiol (0.0076, 0.076, 0.76, 3.82, 7.64 mM dissolved in ethanol) were added to each culture and anaerobically incubated for 72 hr at 37°C. The optical density was monitored every 4 hours for 12 hr and then once at 24 hr. Cultures were inverted prior to obtaining the optical density on a cell density meter (WPA Biowave). Due to optical density interference from gelatin formation at 7.64 mM ursodiol, this concentration was only assessed for viability.

To assess *C. difficile* R20291 viability, culture aliquots (100 μL) were taken at each time point and enumerated on TBHI plates to obtain total colony forming units (CFU)/mL, which represents total vegetative cells and spores of *C. difficile* R20291. At each time point, a second culture aliquot (100 μL) was heat-treated at 65°C for 20 min in order to eliminate all vegetative cells. This heat-treated culture aliquot was then enumerated on TBHI plates to obtain total CFU/ml, which represents total spores only.

***C. difficile in vitro* Vero cell cytotoxicity assay.** This protocol is modified from Winston et al.[47] Vero cells were grown and maintained in DMEM media (Gibco Laboratories, 11965-092) with 10% fetal bovine serum (Gibco Laboratories, 16140-071) and 1% Penicillin streptomycin solution (Gibco Laboratories, 15070-063). Cells were incubated with 0.25% trypsin (Gibco Laboratories, 25200-056) washed with 1X DMEM media and harvested by centrifugation 1,000 RPM for 5 min. Cells were plated at 1×10^4 cells per well in a 96-well flat bottom microtiter plate (Corning, 3596) and incubated overnight at 37°C / 5% CO_2. Culture supernatants from the anaerobic growth assay were defrosted on ice and three 200 μL aliquots from each treatment and time point were then centrifuged at 1,750 RPM for 5 min to pellet vegetative *C. difficile*.

Supernatants were collected from each sample and 10-fold dilutions, to a maximum of 10^{-6}, were performed. Sample dilutions were incubated 1:1 with PBS (for all dilutions) or antitoxin (performed for 10^{-1} and 10^{-4} dilutions only, TechLabs, T5000) for 40 min at room temperature. Following incubation, these admixtures were added to the Vero cells and plates were incubated overnight at 37°C / 5% CO_2. Vero cells were viewed under 200X magnification for rounding after overnight incubation. The cytotoxic titer was defined as the reciprocal of the highest dilution that produced rounding in 80% of Vero cells for each sample. Vero cells treated with purified *C. difficile* toxins (A and B) and antitoxin (List Biological Labs, 152C and 155C; TechLabs, T5000) were used as controls.

Ethics statement. The Institutional Animal Care and Use Committee (IACUC) at North Carolina State University College of Veterinary Medicine (NCSU) approved this study. The NCSU Animal Care and Use policy applies standards and guidelines set forth in the Animal Welfare Act and Health Research Extension Act of 1985. Laboratory animal facilities at NCSU adhere to guidelines set forth in the Guide for the Care and Use of Laboratory Animals. The animals' health statuses were assessed daily, and moribund animals were humanely euthanized by CO_2 asphyxiation followed by secondary measures (cervical dislocation). Trained animal technicians or a veterinarian performed animal husbandry in an AAALAC-accredited facility during this study.

Animals and housing. C57BL/6J mice (females and males) were purchased from Jackson Laboratories (Bar Harbor, ME) and quarantined for 1 week prior to starting the antibiotic water administration to adapt to the new facilities and avoid stress-associated responses. Following quarantine, the mice were housed with autoclaved food, bedding,

and water. Cage changes were performed weekly by laboratory staff in a laminar flow hood. Mice had a 12 hr cycle of light and darkness.

Ursodiol dosing experiment and sample collection. Groups of 5 week old C57BL/6J mice (male and female) were treated with ursodiol at three doses (50, 150, and 450 mg/kg dissolved in corn oil; Ursodiol U.S.P., Spectrum Chemical, CAS 128-13-2) given daily via oral gavage for 14 days. Concurrently mice were administered cefoperazone (0.5 mg/ml), a broad spectrum antibiotic, in their drinking *ad libitum* for 5 days. A control group of mice were only administered cefoperazone in their drinking water *ad libitum* for 5 days. Two independent experiments were performed, with a total of n = 8 mice/treatment group. Fecal pellets were collected twice daily, flash-frozen and stored at -80°C until further analysis.

Murine model of *C. difficile* infection and sample collection. Groups of 5 week old C57BL/6J mice (male and female, n = 12 mice/treatment group) were given cefoperazone (0.5 mg/ml), in their drinking *ad libitum* for 5 days followed by a 2-day wash out with regular drinking water *ad libitum* (Fig. 3A). A group of cefoperazone treated mice were pretreated with ursodiol (450 mg/kg dissolved in corn oil; Ursodiol U.S.P., Spectrum Chemical, CAS 128-13-2) daily via oral gavage. Mice were then challenged with 10^5 spores of *C. difficile* R20291 via oral gavage at Day 0 (*C. diff* + U450). Mice were monitored for weight loss and clinical signs of CDI (lethargy, inappetence, diarrhea, and hunched posture) for 7 days post challenge. Fecal pellets were collected daily for *C. difficile* enumeration. Controls for this experiment included cefoperazone treated mice, no ursodiol, challenged with *C. diff* (*C. diff* only), and cefoperazone treated mice pretreated with the corn oil vehicle (equivalent volume, 75

μl) daily via oral gavage and then challenged with 10^5 spores of *C. difficile* R20291 via oral gavage at Day 0 (*C. diff* + corn oil). Uninfected controls included cefoperazone treated mice with (Cef only), and with pretreatment of ursodiol (450 mg/kg dissolved in corn oil; Cef + U450). Animals were euthanized after losing 20% of initial baseline weight or after developing any serve clinical signs noted above.

Necropsy was performed on days 2, 4, and 7 post challenge. Contents and tissue from the cecum and colon were collected immediately at necropsy, flash frozen in liquid nitrogen, and stored at -80°C until further analysis. To prevent RNA degradation, snips of cecal and colonic tissue were also stored in RNA-Later at 80°C until further analysis. Cecum and colon were prepared for histology by placing intact tissue into histology cassettes and stored in 10% neutral buffered formalin at a ratio of 1:10 tissue:fixative at room temperature for 72 hr then transferred to room temperature 70% ethyl alcohol. Tissues were processed, paraffin embedded, sectioned at 4 μm thick, and stained by routine hematoxlyin and eosin for histopathological examination (LCCC Animal Histopathology Core Facility at the University of North Carolina at Chapel Hill). Histolopathologic evaluation was conducted by a board-certified veterinary pathologist (S. Montgomery) in an *a priori* blinded manner in which individuals within groups were masked at time of scoring. For tissue scoring, a 0-4 numerical scoring system was employed to separately assess edema, inflammatory cell infiltration, and epithelial cell damage in the cecum and colon based upon a previously published scoring scheme.[48]

Bile acid quantitation by UPLC-MS/MS of murine cecal and fecal content. Targeted analysis of bile acids on fecal pellets (n = 3 mice/treatment group were selected) were performed with an ACQUITY ultraperformance liquid-chromatography system using a

C8 BEH column (2.1 × 100 mm, 1.7 µm) coupled with a Xevo TQ-S triplequadrupole mass spectrometer equipped with an electrospray ionization (ESI) source operating in negative ionization mode (All Waters, Milford, MA) as previously described.[49] The sample was thawed on ice and 25 mg was added to 1 mL of pre-cooled methanol containing 0.5 µM stable-isotope-labeled bile acids as internal standards (IS), followed by homogenization (Precellys, Bertin Technologies, Rockville, MD) with 1.0 mm diameter zirconia/silica beads (BioSpec, Bartlesville, OK) and centrifugation (Eppendorf, Hamburg, Germany) at 13 200g, 4 °C, and 20 min. 200 µl of the supernatant was transferred to an autosampler vial. Following centrifugation, the supernatant was transferred to an autosampler vial for quantitation. Bile acids were detected by either multiple reaction monitoring (MRM) (for conjugated bile acid) or selected ion monitoring (SIM) (for non-conjugated bile acid). MS methods were developed by infusing individual bile acid standards. Calibration curves were used to quantify the biological concentration of bile acids. Bile acid quantitation was performed at Penn State University.

Heatmaps and box and whisker plots of bile acid concentrations, and nonmetric multidimensional scaling (NMDS) depicting the dissimilarity indices via Horn distances between bile acid profiles were generated using R packages (http://www.R-project.org).

Illumina MiSeq sequencing of bacterial communities. Microbial DNA was extracted from murine feces (n = 3 mice/treatment group were selected) using the PowerSoil-htp 96-well soil DNA isolation kit (Mo Bio Laboratories, Inc.). The V4 region of the 16S rRNA gene was amplified from each sample using a dual-indexing sequencing strategy.[50] Each 20 µl PCR mixture contained 2 µl of 10× Accuprime PCR buffer II (Life

Technologies), 0.15 µl of Accuprime high-fidelity Taq (catalog no. 12346094) high-fidelity DNA polymerase (Life Technologies), 2 µl of a 4.0 µM primer set, 1 µl DNA, and 11.85 µl sterile double-distilled water (ddH_2O) (free of DNA, RNase, and DNase contamination). The template DNA concentration was 1 to 10 ng/µl for a high bacterial DNA/host DNA ratio. PCR was performed under the following conditions: 2 min at 95°C, followed by 30 cycles of 95°C for 20 sec, 55°C for 15 sec, and 72°C for 5 min, followed by 72°C for 10 min. Each 20 µl PCR mixture contained 2 µl of 10× Accuprime PCR buffer II (Life Technologies), 0.15 µl of Accuprime high-fidelity Taq (catalog no. 12346094) high-fidelity DNA polymerase (Life Technologies), 2 µl of 4.0 µM primer set, 1 µl DNA, and 11.85 µl sterile ddH_2O (free of DNA, RNase, and DNase contamination). The template DNA concentration was 1 to 10 ng/µl for a high bacterial DNA/host DNA ratio. PCR was performed under the following conditions: 2 min at 95°C, followed by 20 cycles of 95°C for 20 sec, 60°C for 15 sec, and 72°C for 5 min (with a 0.3°C increase of the 60°C annealing temperature each cycle), followed by 20 cycles of 95°C for 20 sec, 55°C for 15 sec, and 72°C for 5 min, followed by 72°C for 10 min. Libraries were normalized using a Life Technologies SequalPrep normalization plate kit (catalog no. A10510-01) following the manufacturer's protocol. The concentration of the pooled samples was determined using the Kapa Biosystems library quantification kit for Illumina platforms (KapaBiosystems KK4854). The sizes of the amplicons in the library were determined using the Agilent Bioanalyzer high-sensitivity DNA analysis kit (catalog no. 5067-4626). The final library consisted of equal molar amounts from each of the plates, normalized to the pooled plate at the lowest concentration.

Sequencing was done on the Illumina MiSeq platform, using a MiSeq reagent kit V2 with 500 cycles (catalog no. MS-102-2003) according to the manufacturer's instructions, with modifications.[50] Libraries were prepared according to Illumina's protocol for preparing libraries for sequencing on the MiSeq (part 15039740 Rev. D) for 2 or 4 nM libraries. The final load concentration was 4 pM (but it can be up to 8 pM) with a 10% PhiX spike to add diversity. Sequencing reagents were prepared according to Illumina's protocol for 16S sequencing with the Illumina MiSeq personal sequencer.[50] (Updated versions of this protocol can be found at http://www.mothur.org/wiki/MiSeq_SOP.) Custom read 1, read 2, and index primers were added to the reagent cartridge, and FASTQ files were generated for paired-end reads.

Microbiome analysis. Analysis of the V4 region of the 16S rRNA gene was done using mothur (version 1.40.1).[50,51] Briefly, the standard operating procedure (SOP) at http://www.mothur.org/wiki/MiSeq_SOP was followed to process the MiSeq data. The paired-end reads were assembled into contigs and then aligned to the SILVA 16S rRNA sequence database (release 132)[52,53] and were classified to the mothur-adapted RDP training set v16[54] using the Wang method and an 80% bootstrap minimum to the family taxonomic level. All samples with <500 sequences were removed. Chimeric sequences were removed using UCHIME.[55] Sequences were clustered into operational taxonomic units (OTU) using a 3% species-level definition. The OTU data were then filtered to include only those OTU that made up 1% or more of the total sequences. The percentage of relative abundance of bacterial phyla and family members in each sample was calculated. A cutoff of 0.03 (97%) was used to define operational taxonomic units

(OTU) and Yue and Clayton dissimilarity metric (θYC) was utilized to assess beta diversity. Standard packages in R were used to create NMDS ordination on serial fecal samples.

mRNA isolation and gene expression analysis. RNA extraction was performed on cecal and colonic tissue using Zymo Research RNA extraction kit (Irvine, CA). After RNA extraction, samples were quantified using an Invitrogen Qubit (Thermo Fisher Scientific) and run on an Agilent Bioanalyzer NanoChip (Santa Clara, CA) to assess quality of RNA. RNA extraction, quantification, and purity assessment were performed at the Microbiome Shared Resource Lab, Duke University, Durham, NC.

The nCounter Mouse Inflammation v2 gene expression panel and custom code set was purchased from NanoString Technologies (Seattle, WA) and consists of 254 inflammation-related mouse genes including six internal reference genes (see Table S1) and 10 custom genes of interest (see Table S2). The nCounter assay was performed using 100 ng of total RNA. Hybridization reactions were performed according to the manufacturer's instructions with 5 µl diluted sample preparation reaction and samples were hybridized overnight. Hybridized reactions were purified using the nCounter Prep Station (NanoString Technologies) and data collection was performed on the nCounter Digital Analyzer (NanoString Technologies) following the manufacturer's instructions to count targets. Nanostring nCounter Max platform was utilized at UNC Translational Genomics Laboratory to perform these assays.

The raw data was normalized to six internal reference genes within each tissue type with the lowest coefficient of variation using nSolver software following the manufacturer’s instructions (Nanostring Technologies). Using the nSolver Advanced

analysis software, after pre-processing and normalization counts were log_2 transformed and z-scores were calculated (Nanostring Technologies).

To identify highly significant genes and molecular pathways, the gene set was subsequently uploaded to Ingenuity Pathway Analysis (IPA) database (Qiagen, Redwood City, CA) and analyzed in the context of known biological response and regulatory networks. IPA was also used to assess gene expression fold changes comparing ursodiol pretreated CDI mice to untreated CDI mice.

Statistical analysis. Statistical tests were performed using Prism version 7.0b for Mac OS X (GraphPad Software, La Jolla California USA) or using R packages (http://www.R-project.org). Statistical significance was set at a p value of < 0.05 for all analyses (*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$). For *in vitro* experiments, significance between treatments in spore germination was calculated by Student's parametric t-test with Welch's correction. Two-way analysis of variance (ANOVA) test followed by Dunnett's multiple comparisons *post hoc* test was used to calculate significance between treatments for the anaerobic growth assay and toxin activity assay.

For the *in vivo* experiments, a two-way ANOVA followed by Tukey's multiple comparisons post hoc test was used to calculate significance between treatment groups in bile acid profiles, individual bile acids, *C. difficile* load (CFU/g) cecal content, and total histologic score. A two-way ANOVA followed by Sidak's multiple comparisons *post hoc* test was used to calculate significance between treatment groups in baseline weight loss. A Student's t-test corrected for multiple comparisons using the Holm-Sidak method was used to calculate significance between treatment groups in cecal content toxin

activity and edema score. Analysis of molecular variance (AMOVA) was used to detect significant microbial community clustering of treatment groups in NMDS plots.[56] nSolver software and IPA were used to calculate significance in gene expression fold change comparing mice pretreated with ursodiol to untreated mice.

Availability of data and material. Raw 16S sequences have been deposited in the Sequence Read Archive (SRA) with SRA accession number: SUB6809988. All other data including bile acid metabolomics and Nanostrings expression data is provided in Tables S3-S7 in the supplemental material.

Results

Ursodiol directly inhibits different stages of the *C. difficile* life cycle *in vitro*.

To determine the direct effects of ursodiol on the life cycle of clinically relevant *C. difficile* strain R20291, *in vitro* assays to assess spore germination and outgrowth, growth, and toxin activity were performed (Fig. 1). Taurocholic acid (TCA) mediated spore germination and outgrowth of *C. difficile* was significantly inhibited by ursodiol in a dose dependent manner (Fig. 1A, blue bars). No significant difference was observed between positive controls, sterile ethanol, and water supplemented with 0.1% TCA (Fig. 1A, ethanol represented as solid grey bar). As expected, the negative control, 0.04% chenodeoxycholic acid (CDCA) supplemented with 0.1% TCA resulted in significant inhibition of spore germination and outgrowth (Fig. 1A, red bar). CDCA is a known inhibitor of spore germination.[57]

C. difficile growth decreased when exposed to ursodiol at 8, 12 and 24 hr in a dose dependent manner compared to the ethanol control (Fig. 1B, blue lines). For the ursodiol 3.82 mM concentration, a significantly lower optical density (OD) compared to

the ethanol control was observed at time points 8, 12, and 24 hr ($p = 0.0316$, $p = 0.0001$, $p = 0.0001$, respectively). For the ursodiol 0.76 mM treatment, a significantly lower OD compared to ethanol control was observed at time points 12 and 24 hr ($p = 0.0001$ for both time points), and for the ursodiol 0.076 mM treatment at time point 24 hr ($p = 0.0208$). No significant difference in OD between the ethanol control and treatments was noted at time point 0 or 4 hr. The highest concentration of ursodiol (7.64 mM) interfered with OD measurement and was not included in the analysis.

Since OD measurements do not capture viability and spore formation of *C. difficile*, we also did differential plating to evaluate the colony forming units (CFU)/ml at each time point (Fig. S1). At 24 hr ursodiol inhibited *C. difficile* total vegetative cells and spores compared to the ethanol control. The highest concentration of ursodiol (7.64 mM) had a significant and immediate inhibitory effect on *C. difficile* viability compared to ethanol at time 0 hr. Ursodiol treatment also significantly decreased *C. difficile* spores.

Toxin activity was not detected until eight hours of *C. difficile* growth (Fig. 1C). Higher concentrations of ursodiol resulted in significant decreases in *C. difficile* toxin activity compared to the ethanol control at 8, 12, and 24 hr (Fig. 1C, blue bars). Using a Spearman's correlation (r) the CFU/ml and toxin activity at 8 and 12 hr were significantly correlated (8 hr, $r = 0.6399$, $p = 0.0042$; 12 hr, $r = 0.6981$, $p = 0.0013$), suggesting low toxin activity is due to decreased growth.

Ursodiol alters the fecal bile acid metabolome with minimal change to the microbiota.

Since the gut microbiota and bile acids mediate colonization resistance against *C. difficile*, we aimed to determine how different doses of ursodiol administration alone

impacts them in our antibiotic treated mouse model. C57BL/6J mice were administered three doses of ursodiol (50, 150, 450 mg/kg/day) via oral gavage for 14 days (Fig. 2A). Mice were also concurrently administered cefoperazone (in drinking water *ad libitum*) for 5 days, in order to mimic the CDI mouse model. Paired fecal samples were collected from the same mice serially over the 14 day period to evaluate how ursodiol affected the gut microbial community structure and bile acid metabolome.

The fecal microbial community structures of all treatment groups were significantly different from pretreatment at all time points, based on an analysis of molecular variance (AMOVA) performed for each day (Fig. 2B). There were no significant differences between the fecal microbial community structures based on ursodiol pretreatment. The shifts in the fecal microbiota seen in the NMDS were predominantly due to the cefoperazone treatment and experiment day, and not as a result of the ursodiol pretreatment.

Targeted bile acid analysis via UPLC-MS/MS detected 38 bile acids in the feces of mice. During the first 9 days of the experiment (Day -2 to Day 7), the fecal bile acid profiles of mice cluster based on the dose of ursodiol administered (Fig. 2C). Ursodiol dramatically alters the fecal bile acid metabolome compared to pretreatment as seen in Fig. 2D and Table S3. Bile acids that significantly changed over the course of the experiment in mice that received ursodiol compared to mice that only received cefoperazone included TβMCA, TCA, TUDCA, βMCA, and UDCA (Fig. S2, two-way ANOVA with Tukey's multiple comparisons *post hoc* preformed on each experiment day, p values ranged from $p < 0.0001$ to $p = 0.0012$).

Ursodiol attenuates disease in mice early during *C. difficile* infection.

Due to potent inhibitory effect of ursodiol on *C. difficile in vitro*, and increased gastrointestinal bile acids *in vivo*, we sought to determine the extent to which pretreatment with ursodiol influences the natural course of CDI in a reproducible mouse model. Since supra-physiologic UDCA intestinal concentrations were achieved in Fig. 2D when mice were dosed with 450 mg/kg/day of ursodiol, we selected this dose.[58] All C57BL/6J mice in each group received cefoperazone in their drinking water from Day -7 to Day -2 with a two day washout on normal drinking water. Control groups included two uninfected groups that received cefoperazone no ursodiol (Cef only), and cefoperazone with ursodiol (Cef + U450) (Fig. 3A). An additional control group received cefoperazone no ursodiol, with *C. difficile* challenge (*C. diff* only). Mice were orally gavaged with ursodiol (450 mg/kg in corn oil vehicle) daily for 7 days prior to challenge with *C. difficile* on Day 0, and throughout the infection (*C. diff* + U450) (Fig. 3A).

Two groups of mice (*C. diff* only and *C. diff* + U450) were challenged with 10^5 spores of *C. difficile* R20291 on Day 0 and within 24 hr were colonized with greater than 10^7 CFUs per gram of feces (data not shown). Mice challenged with *C. difficile* with and without ursodiol pretreatment lost a significant amount of their baseline weight by Day 2 post challenge (*C. diff* only, red circles and *C. diff* + U450, blue circles Fig. 3B). Additionally, there was no significant difference in weight loss between these groups over the course of the experiment (based on two-way ANOVA). However, mice pretreated with ursodiol (*C. diff* + U450) had a 24-36 hr delay in clinical signs (lethargy, inappetence, diarrhea, and hunched posture) related to CDI compared to untreated mice (*C. diff* only). Uninfected control mice (Cef only and Cef + U450) revealed no clinical signs of disease during the experiment and remained *C. difficile* free. The Cef

only group of mice displayed weight gain over the course of the experiment as expected (Fig. 3B, gray circles). The Cef + U450 group did have significant weight loss compared to Cef only mice at Day 5 and Day 6 of the experiment (two-way ANOVA with Sidak's multiple comparisons *post hoc* test; $p = 0.0013$, $p = 0.0001$ respectively; Fig. 3B, orange circles). However, no significant difference was noted between these groups by Day 7 (Fig. 3B). An additional control group of mice challenged with *C. difficile* and pretreated with the vehicle corn oil alone (*C. diff* + corn oil) displayed no significant difference in disease outcome compared to the *C. diff* only group (Fig. S3).

Mice pretreated with ursodiol (*C. diff* + U450) had equivalent total cecal bacterial loads of *C. difficile* (CFU/g cecal content) compared to untreated mice (*C. diff* only) (Fig. 3C). However, mice pretreated with ursodiol had a significant reduction in *C. difficile* spores within cecal content at Day 2 compared to untreated mice (log transferred CFU/g content, two-way ANOVA with Tukey's multiple comparisons *post hoc* test, $p < 0.0001$; Fig. 3C). Mice ceca remained persistently colonized with *C. difficile* throughout the 7 day experiment. At Day 4, *C. difficile* toxin activity within cecal content was significantly reduced in ursodiol pretreated compared to untreated mice (Student's t- test corrected with the Holm-Sidak method for multiple comparisons, $p = 0.014$; Fig. 3D).

Histopathologic evaluation of cecal and colonic tissue revealed no significant difference in total histologic score between ursodiol pretreated and untreated mice (Fig. S4). When assessing individual parameters, there was no significant difference between epithelial damage or inflammatory infiltrate between the treatment groups. At Day 2, mice pretreated with ursodiol had a significant reduction in edema score (scored 0-4) in both cecal and colonic tissue compared to untreated mice (Student's t- test corrected

with the Holm-Sidak method for multiple comparisons, p = 0.00025, p = 0.0049 respectively; Fig. 3E and F).

Ursodiol alters the host inflammatory transcriptome early during CDI.

Since there were minimal changes in the *C. difficile* life cycle early during infection to explain the decrease in edema, we wanted to examine the impact of ursodiol pretreatment on the host inflammatory response during CDI. We interrogated transcriptional changes related to the cecal and colonic inflammatory response at Day 2 post challenge using a murine specific panel of inflammatory markers (Nanostring nCounter) that included 264 transcripts. After processing the raw data, mRNA log2 normalized z-scores for 261 genes were obtained and genes significantly altered by ursodiol pretreatment compared to untreated mice with CDI were evaluated. Ursodiol mediated alterations in gene expression fold change were different between cecal and colonic tissue (Fig. 4 and Fig. S5). In cecal tissue, 173 genes had a significant expression fold change when comparing ursodiol pretreated mice to untreated mice, with increased expression in 74 genes and decreased expression in 99 genes (Fig. 4A and B, Table S4 and S5). In colonic tissue, 139 genes had a significant expression fold change when comparing ursodiol pretreated to untreated mice, with increased expression in 58 genes and decreased expression in 81 genes (Fig. S5A and B, Table S4 and S5).

Ingenuity Pathway Analysis (IPA) identified NF-κB signaling as an inflammatory canonical pathway in both cecum and colon significantly altered in ursodiol pretreated mice ($p < 0.0001$ for both tissues). Based on unsupervised clustering, genes involved with NF-κB signaling in ursodiol pretreated mice clustered distinctly and separately from

untreated mice in both cecal and colonic tissue (Fig. 4C and Fig. S5C). Differences in individual gene expression fold changes were noted in NF-κB signaling between the cecal and colonic tissue (Fig. 4D and Fig. S5D). In both tissues, components important for mediating the host inflammatory response to CDI, such as IL-1R1 and various TLRs, were significantly decreased in expression in the ursodiol pretreated mice compared to untreated mice at Day 2 (Fig. 4D and Fig. S5D, see Table S6 for p-values). Collectively, these results suggest that ursodiol pretreatment in CDI mice alters the inflammatory transcriptome in cecal and colonic tissue by impacting essential host inflammatory signaling pathways, such as NF-κB, early in the course of CDI.

Ursodiol induces bile acid transport and signaling via FXR/FGF15 pathway.

Since ursodiol treatment alters the bile acid metabolome in mice (Fig. 2D) and bile acids are known to modulate signaling via the nuclear bile acid receptor FXR and the plasma membrane receptor TGR5[59], we sought to define transcriptional changes in bile acid transport and signaling via the FXR/FGF15 pathway. We selected seven genes in the FXR/FGF15 pathway to interrogate within cecal and colonic tissue using a customized murine panel (Nanostring nCounter). Bile acids within the gastrointestinal tract are transported back to the liver via enterohepatic recirculation by several active transporters, ASBT on the apical surface, and OSTα/β on the basolateral surface of enterocytes (Fig. 5C)[59]. Cytoplasmic Ibabp helps to facilitate bile acid transport (Fig. 5C)[59]. Bile acids in ileal enterocytes and colonic L cells bind to FXR and activate the FXR-RXR heterodimer complex, resulting in transcription of target genes, such as FGF15/19. FGF15/19 is secreted into the portal vein and transported back to the liver,

where it inhibits expression of *CYP7A1* in hepatocytes to directly regulate bile acid synthesis.[59]

In cecal tissue, mRNA expression of the receptors FXR and TGR5, and the bile acid transporters ASBT and OSTα/β were significantly increased in ursodiol pretreated mice compared to untreated mice at Day 2 post challenge (Fig. 5A, Student's parametric t-test with Welch's correction, see Table S7 for p values). In colonic tissue, mRNA expression of the receptors FXR and TGR5, the signaling molecule FGF15, and the bile acid transporters ASBT and OSTα/β were significantly increased in ursodiol pretreated mice compared to untreated mice (Fig. 5B, Student's parametric t-test with Welch's correction, see Table S7 for p values). Collectively, these results demonstrate that pretreatment of ursodiol in mice with CDI increases the expression of the FXR/FGF15 pathway transcriptome in both cecal and colonic tissue.

Discussion

Ursodiol, the FDA approved commercial formulation of UDCA, is used to treat a variety of hepatic and biliary diseases including: cholesterol gallstones, primary biliary cirrhosis, primary sclerosing cirrrhosis, cholangitis, non-alcoholic fatty liver disease, chronic viral hepatitis C, and cholestasis of pregnancy.[31-40] However, limited evidence is available for use of ursodiol in CDI patients. To date, only a single case report demonstrating successful prevention of recurrent *C. difficile* ileal pouchitis with oral UDCA administration is available,[29] suggesting that exogenous administration of the secondary bile acid UDCA may be able to restore colonization resistance against *C. difficile in vivo*.[29] Although the mechanisms by which ursodiol exerts its impact on *C. difficile* are unknown, off-label use of ursodiol is currently in Phase 4 clinical trials for the prevention

of recurrent CDI.[41] In the present study, ursodiol pretreatment impacted the life cycle of *C. difficile in vivo*. Although, *C. difficile* bacterial load and toxin activity was not affected at day 2, pretreatment with ursodiol resulted in a 24-36 hr delay in the clinical course of CDI, suggesting attenuation of CDI pathogenesis early during infection. Although ursodiol pretreatment did not alter the gut microbiota composition, significant modifications in the bile acid metabolome were observed. Several key bile acid species were significantly increased following ursodiol administration, namely UDCA, TUDCA, and TβMCA. The tissue inflammatory transcriptome was altered, including gene expression of bile acid activated receptors nuclear farnesoid X receptor (FXR) and transmembrane G protein-coupled membrane receptor 5 (TGR5), which are able to modulate the innate immune response through signaling pathways such as nuclear factor *κ*-B (NF-κB). This is the first study to investigate the impact of innate immune response regulation by bile acid activated receptors, FXR and/or TGR5, during CDI.

Modulation of bile acid pools to restore colonization resistance against *C. difficile* is a rational therapeutic option, based on the importance bile acids play in the life cycle of *C. difficile.*[25,27] Traditional therapeutic approaches to CDI have focused on restoring bile acid pools by reestablishing the entire microbial community, such as with fecal microbiota transplantation.[13,28] Or supplementation of key commensals, such as *Clostridium scindens*, a bacterium capable of synthesizing microbial derived secondary bile acids, which when supplemented leads to partial restoration of colonization resistance against *C. difficile*.[11] In the present study, we deduced that direct supplementation of bile acids, such as UDCA or ursodiol which are known to inhibit the life cycle of *C. difficile,*[26] may be sufficient to restore colonization resistance against this

enteric pathogen by directly impacting *C. difficile,* but also by modulating the host inflammatory response.

The host innate immune response to CDI is an essential component of *C. difficile* pathogenesis.[1] The acute host innate immune response is initiated by *C. difficile* toxin-mediated damage to the intestinal epithelial cells, loss of the epithelial barrier, and subsequent translocation of luminal gut microbes.[1,60] *C. difficile* toxin A (TcdA) and toxin B (TcdB), directly disrupt the cytoskeleton of intestinal epithelial cells, resulting in disassociation of tight junctions and loss of epithelial integrity.[1,61] In response to toxin-mediated destruction, resident immune cells and intoxicated epithelial cells release pro-inflammatory cytokines and chemokines to recruited circulating innate immune cells and adaptive immune cells (reviewed in Abt et al.).[1] A prominent inflammatory pathway that is activated in intestinal epithelial cells by TcdA and TcdB is the NFκ-B signaling pathway through the phosphorylation of mitogen-activated protein kinase (MAPK), which leads to the transcription of pro-inflammatory cytokines, including IFN-γ, TNF-α, IL-6, and IL-1β.[62-65] In the present study, pretreatment with ursodiol resulted in alterations in the host intestinal inflammatory transcriptome. Genes involved with NF-κB signaling pathway in both cecum and colon, segregated based on ursodiol pretreatment. This is not surprising given the broad ursodiol mediated alterations in bile acid metabolome observed and the building evidence that bile acid activated receptors regulate the host innate immune response (recently reviewed in Fiorucci et al. 2018).[44] In particular, interactions between the gut microbiota and bile acids result in alterations in bile acid pools, which in turn modulate signaling via the FXR and TGR5, both of which can regulate the innate immune response.[44,59,66] Bile acid activation of TGR5

involves cAMP-protein kinase A (PKA)-mediated inhibition of NF-κB, and bile acid activation of FXR leads to FXR-nuclear receptor corepressor 1 (NCor1)-mediated repression of NF-κB responsive elements (NRE). Bile acid activation of both pathways blunt NF-κB gene transcription including pro-inflammatory cytokines IFN-γ, TNF-α, IL-6, and IL-1β.[67,68] Additionally, TGR5 directly regulates IL-10 expression by a cAMP/PKA/p CAMP-responsive element binding protein pathway, thus further attenuating the inflammatory response.[69]

Bile acids differ in their affinity and agonistic/antagonistic effects for FXR and TGR5.[44] We observed global alterations in bile acids that are both FXR and TGR5 agonists and antagonists, lending to the complexity of unravelling the cumulative effects on bile acid activated receptors and how this impacts the overall innate immune response during CDI. Based on FXR and TGR5 signaling transcriptomics, ursodiol pretreatment in the present study resulted in increased cecal and colonic expression of genes in these pathways during CDI. Collectively, this suggests that ursodiol induced alterations in the bile acid metabolome results in alterations of host inflammatory transcriptome, including alterations in NF-κB signaling pathway, likely via the bile acid activated receptors FXR and TGR5. Furthermore, this principle has also recently been demonstrated in recurrent CDI patients receiving FMTs, where effectiveness of FMT was associated with an upregulation of the FXR-FGF pathway.[70]

Whilst the present study demonstrated ursodiol-mediated attenuation of CDI early in the disease course, complete restoration of colonization resistance against this enteric pathogen was not achieved. Several limitations of the use of ursodiol pretreatment prior to CDI need to be considered. First, once daily dosing may be

sufficient to obtain supraphysiologic pulses of UDCA, but these concentrations may not be sustained in the gastrointestinal tract throughout the day. Consequently, *C. difficile in vivo* is exposed to a daily pulse of ursodiol that inhibits its life cycle, similar to our *in vitro* results, only during a limited window. Alterations in the dosing scheme such as dividing the dose over two or four administration times may ameliorate this potential limitation. Secondly, alterations in the inflammatory microenvironment during the initial phases of CDI were observed in this study, however these effects were not sustained throughout CDI. Potentially, longer pretreatment with ursodiol is needed to result in sustained alterations to the host innate immune response. Lastly, ursodiol may be more effective as a preventative for relapsing CDI, meaning that following successful treatment of CDI with antibiotic treatment ursodiol could be administered to prevent relapse of infection.

Regardless, our results highlight that ursodiol pretreatment was able to significantly alter the bile acid metabolome and host inflammatory transcriptome during CDI. Although ursodiol pretreatment did not result in colonization resistance against *C. difficile*, attenuated pathogenesis of *C. difficile* was noted early in the disease course. Collectively, we theorize that ursodiol induced alterations within the intestinal bile acid metabolome result in activation of bile acid receptors, such as FXR and TGR5, which are able to modulate the innate immune response through signaling pathways such as NF-κB, thus mitigating an overly robust host inflammatory response that can be detrimental to the host. Given these results and the effectiveness of ursodiol to inhibit the *C. difficile* life cycle, ursodiol remains a viable non-antibiotic treatment and/or prevention strategy against CDI. Moreover, targeting bile acid activated receptors, FXR

and TGR5, to attenuate an overly robust detrimental host immune response during CDI merits further consideration as a potential therapeutic intervention for CDI patients.

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Disclosure statement.

CMT is a scientific advisor to Locus Biosciences, a company engaged in the development of antimicrobial technologies. CMT is a consultant for Vedanta Biosciences and Summit Therapeutics.

Figure legends

Figure 1: Ursodiol inhibits different stages of the *C. difficile* life cycle. *In vitro* assay to assess if the addition of ursodiol (0.0076, 0.076, 0.76, and 7.64 mM) **(A)** inhibits *C. difficile* R20291 TCA-mediated spore germination and outgrowth compared to positive control, ethanol (gray bar) and negative control, 0.04% CDCA (red bar). The data presented represents triplicate experiments. Statistical significance between

treatment groups and the positive controls was determined by Student's parametric t-test with Welch's correction. **(B)** alters the growth kinetics of *C. difficile* over a 24 hr period. Growth curves were done in BHI media with ethanol (gray line) and addition of varying concentrations of ursodiol (blue lines). The data presented represents OD_{600} ± SEM from triplicate experiments. **(C)** Culture supernatants, taken throughout a 24 hr growth curve in 1B, were used for a Vero cell cytotoxicity assay and the data is expressed as $\log_{10}$ reciprocal dilution toxin per 100 μL of *C. difficile* culture supernatant. The data presented represents triplicate experiments. Statistical significance between treatment groups and the positive controls was determined by a two-way ANOVA with Dunnett's multiple comparisons (*, $p < 0.05$; ***, $p < 0.001$; ****, $p < 0.0001$).

Figure 2: Ursodiol does not alter the gut microbiota but does alter the bile acid metabolome. Groups of C57BL/6J mice (n=8 mice/treatment group) were **(A)** given cefoperazone in their drinking water ad libitum for 5 days alone and or with ursodiol at three doses (50, 150, and 450 mg/kg) given daily via oral gavage for 14 days. An n = 3 mice/treatment group were selected for further microbiome and bile acid metabolomic analysis. **(B)** NMDS ordination of the fecal microbial communities from mice treated and untreated with ursodiol was calculated from Yue and Clayton dissimilarity metric (θ_{YC}) on OTU at a 97% cutoff. **(C)** NMDS ordination illustrates dissimilarity indices via Horn distances between the bile acid profiles of fecal samples from treated and untreated mice. **(D)** A heatmap of bile acid concentrations present in nanomoles (nmol) per gram of feces, ranging from 0 to 38221.91 (nmol/g feces). Asterisks next to bile acids represent ones that were significantly altered during ursodiol treatment.

Figure 3: Ursodiol attenuates disease early during *C. difficile* infection. (A) Groups of C57BL/6J mice (n=12 mice/treatment group) were given cefoperazone in their drinking water *ad libitum* for 5 days alone and or with ursodiol at 450 mg/kg given daily via oral gavage for 14 days. Two groups of mice were then challenged with 10^5 spores of *C. difficile* via oral gavage at day 0. Mice were monitored for weight loss and clinical signs of CDI from day 0 to day 7. Necropsy was performed on days 2, 4, 7 (open circles). **(B)** Baseline weight loss of mice challenged with and without *C. difficile,* and pretreated with and without ursodiol. Significance was determined by a two-way ANOVA with Sidak's multiple comparisons *post hoc* test. **(C)** *C. difficile* bacterial load in the cecal content throughout CDI. Solid boxes represent total vegetative cells and spores and hashed boxes represent spores only. Significance was determined by a two-way ANOVA with Tukey's multiple comparisons *post hoc* test. **(D)** Vero cell cytotoxicity assay from cecal content throughout CDI. Significance was determined by a Student's t-test corrected with the Holm-Sidak method for multiple comparisons. **(E)** Histopathologic scoring of edema in the murine cecum and colon at day 2 post challenge. Significance was determined by a Student's t-test corrected with the Holm-Sidak method for multiple comparisons. Error bars represent the standard deviations from the mean. **(F)** Representative histomicrograph images of H&E stained cecum (upper) and colon (lower) for groups indicated, shown at 100X total magnification with 500 µm scalebar. For all graphs (*, $p \leq 0.05$; **, $p \leq 0.01$; ***, $p \leq 0.001$; ****, $p \leq 0.0001$).

Figure 4: Ursodiol alters the host inflammatory transcriptome of the cecum early during CDI. (A) Venn diagram depicting the mRNA expression fold change comparing the ursodiol pretreated compared to untreated mice in cecal tissue at day 2 post

challenge with *C. difficile,* from two independent experiments performed with a total of n=12 mice/treatment group**.** Of the 261 genes evaluated, a total of 173 cecal genes had significant gene expression fold changes (increased expression, red; decreased expression, green). **(B)** Volcano plots highlighting genes whose transcript levels changed by greater than 1-fold and met the significant threshold $p \leq 0.05$. Genes highlighted in red had increased transcript levels, while those highlighted in green had decreased levels. Blue points represent genes whose results were significant but did not met the specify fold change. Black points represent genes whose results failed to meet the significance threshold. **(C)** Cecal inflammatory transcriptome heatmap of calculated z-scores for log2 transformed count data of mRNA expression levels (y-axis) comparing ursodiol pretreated (blue) to untreated mice (red). Dendrograms represent unsupervised clustering. **(D)** mRNA expression fold differences in increased expression (red) and decreased expression (green) of genes involved with NF-kB signaling in cecal tissue comparing ursodiol pretreated to untreated mice.

Figure 5: Ursodiol alters the FXF-FGF15 transcriptome during CDI. Violin plots of **(A)** cecal and **(B)** colonic mRNA expression levels of normalized log2 counts of seven genes involved with the FXF-FGF15 pathway. Significance determined by a Student's parametric t-test with Welch's corrected (*, $p \leq 0.05$; **, $p \leq 0.01$; ***, $p \leq 0.001$; ****, $p \leq 0.0001$). **(C)** Schematic of seven genes within the FXF-FGF15 pathway. Bile acids modulate signaling via the nuclear bile acid receptor FXR (farnesoid X receptor) and plasma membrane receptor TGR5 (or G-protein coupled bile acid receptor Gpbar1). Bile acid within the gastrointestinal tract are transported back to the liver via enterohepatic recirculation by several active transporters, ASBT (apical sodium dependent bile acid

transporter) on the apical surface, and OSTα/β (organic solute transporters) on the basolateral surface of enterocytes. Cytoplasmic Ibabp (ileal bile acid-binding protein) helps to facilitate bile acid transport. Bile acids in ileal enterocytes and colonic L cells bind to FXR and activate the FXR-RXR heterodimer complex, resulting in transcription of target genes, such as FGF15/19. FGF 15/19 is secreted into the portal vein and transported back to the liver, where it inhibits expression of *CYP7A1* in hepatocytes to directly regulate bile acid synthesis.

Supplemental Figure 1: Effect of ursodiol on viability and spore formation of *C. difficile*. Culture aliquots (100 μL) of *C. difficile* R20291, grown in BHI media, were taken over a 24 hr period and enumerated on TBHI plates to obtain total CFU/ml of total vegetative cells and spores (solid bars) and spores only (hashed bars). The positive controls (EthOH, gray bars) represent *C. difficile* grown in BHI media with ethanol and the treatments groups (blue bars) represents *C. difficile* grown in BHI media with varying concentrations of ursodiol from lowest to highest concentration (left to right). The limit of detection for this assay is 10^2 CFU/ml. The data presented represents triplicate experiments. Significance was determined by Welch's t-test using log transformed CFU/ml.

Supplemental Figure 2: Ursodiol treatment alters the bile acid metabolome. Box and whisker plots of bile acids that were significantly altered over the course of ursodiol treatment compared to mice that only received cefoperazone (based on a Two-way ANOVA with Tukey's multiple comparisons post hoc test). An n=3 mice/treatment group were then selected for bile acid metabolomic analysis.

Supplemental Figure 3: No effect with corn oil vehicle alone on CDI in mice. (A) Baseline weight loss of cefoperazone treated mice challenged with *C. difficile* pretreated with (white, *C. diff* + corn oil) and without corn oil vehicle (red, *C. diff* only) (n=8 mice/treatment group). **(B)** *C. difficile* bacterial load in feces and **(C)** cecal content over the first 2 days post challenge. Solid boxes represent total vegetative cells and spores and hashed boxes represent spores only. Significance was determined by a two-way ANOVA test.

Supplemental Figure 4: Total histologic scores were not significantly different with ursodiol pretreatment. Histopathologic scoring of murine cecum and colon throughout CDI. Total histologic scores were calculated by adding all three scores from parameters assessed: epithelial damage, inflammation, and edema. Significance was determined by a two-way ANOVA with Sidak's multiple comparisons *post hoc* test. Error bars represent the standard deviations from the mean.

Supplemental Figure 5: Ursodiol alters the host inflammatory transcriptome of the colon early during CDI. (A) Venn diagram depicting the mRNA expression fold change comparing the ursodiol pretreated to untreated mice in colonic tissue at day 2 post challenge with *C. difficile,* from two independent experiments performed with a total of n=12 mice/treatment group**.** Of the 261 genes evaluated, a total of 139 colonic genes had significant gene expression fold changes (increased expression, red; decreased expression, green). **(B)** Volcano plots highlighting genes whose transcript levels changed by greater than 1-fold and met the significant threshold $p \leq 0.05$. Genes highlighted in red had increased transcript levels, while those highlighted in green had decreased levels. Blue points represent genes whose results were significant but did

not met the specify fold change. Black points represent genes whose results failed to meet the significance threshold. **(C)** Colonic inflammatory transcriptome heatmap of calculated z-scores for log2 transformed count data of mRNA expression levels (y-axis) comparing ursodiol pretreated (blue) to untreated mice (red). Dendrograms represent unsupervised clustering. **(D)** mRNA expression fold differences in increased expression (red) and decreased expression (green) of genes involved with NF-kB signaling in colonic tissue comparing ursodiol pretreated to untreated mice.

Supplemental Table 1: Nanostrings nCounter Mouse Inflammation V2 Panel Gene List (in word document)

Supplemental Table 2: Nanostrings nCounter Mouse Custom Code Set Gene List (in word document)

Supplemental Table 3: Targeted bile acid metabolomics data from mice treated with cefoperazone with and without different doses of ursodiol.

Supplemental Table 4: Nanostrings differential gene expression data from cecal and colonic tissue comparing ursodiol pretreated to untreated mice.

Supplemental Table 5: Nanostrings z-score data from the cecal and colonic tissue comparing ursodiol pretreated to untreated mice.

Supplemental Table 6: Cecal and Colonic Tissue mRNA Expression Fold Change for NF-kB Signaling

Supplemental Table 7: Cecal and Colonic Tissue mRNA Expression Fold Change for FXR-FGF15 Pathway

Continue Table S1: Nanostring nCounter SC Mouse Inflammation V2 Panel Gene List

Ccl2	NM_011333.3	AI323594, HC11, JE, MCAF, MCP-1, MCP1, SMC-CF, Scya2, Sigje	Extracellular Region,Cytoplasm,Cell Soma,Extracellular Space,Negative Regulation Of Angiogenesis,Response To Heat,Inflammatory Response,Immune Response,Angiogenesis,Positive Regulation Of T Cell Activation,Regulation Of Cell Shape,Cellular Homeostasis,Anti Apoptosis,Transforming Growth Factor Beta Receptor Signaling Pathway,Cytokine And Ch	TCTTCAGCACCTTTGAATGTGAAGTTGACCCGTAAATCTGAAGCTAATGCATCCACTACCTTTTCCACAACCACCTCAA GCACTTCTGTAGGAGTGACCA	chemokine (C-C motif) ligand 2
Ccl20	NM_016960.1	CKb4, LARC, MIP-3A, MIP-3[a], MIP3A, ST38, Scya20, exodus-1	Extracellular Region,Extracellular Space,Inflammatory Response,Immune Response,Chemokine Activity,Cytokine Activity	GCAGCAAGCAACTACGACTGTTGCCTCTCGTACATACAGACGCCTCTTCCTTCCACAGAGCTATTGTGGGTTTCACAAGA CAGATGGCCGATGAAGCTTGTG	chemokine (C-C motif) ligand 20
Ccl22	NM_009137.2	ABCD-1, DCBCK, MDC, Scya22	Extracellular Region,Extracellular Space,Inflammatory Response,Immune Response,Chemokine Activity,Cytokine Activity	CCAAGAATCAACTTCCACCCCTCTTCAACCACATGCTAGGGTCTTTTACTTTCTCTGCCCCACACCTTTGACTCCTTGCC TGTGTAGCTGATAGTCGAAG	chemokine (C-C motif) ligand 22
Ccl24	NM_019577.4	CKb-6, MPIF-2, Scya24	Extracellular Region,Extracellular Space,Inflammatory Response,Immune Response,Regulation Of Cell Shape,Positive Regulation Of Cell Migration,Positive Regulation Of Angiogenesis,Cytoskeleton Organization And Biogenesis,Chemokine Activity,Cytokine Activity	CTGGATGCCAAGAAAAACCAGCCTTCTAAAGGGGCCAAGGCAGTGAGAACCAAGTTTGCTGTCCAGAGACGCCGTG GCAATAGCACCGAGGTTTAGCCGC	chemokine (C-C motif) ligand 24
Ccl3	NM_011337.1	AI323804, G0S19-1, LD78alpha, MIP-1alpha, MIP1-(a), MIP1-alpha, Mip1a, Scya3	Extracellular Region,Cytoplasm,Cytosol,Extracellular Space,Soluble Fraction,Cell Activation,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Response To Toxin,Calcium Mediated Signaling,Behavior,Calcium Ion Transport,Leukocyte Chemotaxis,Cell Cell Signaling,Inflammatory Response,Immune Response,Regulation Of Cell Shape,	TCTGTCACCTGCTCAACATCATGAAGGTCTCCACCACTGCCCTTGCTGTTCTTCTGTACCATGACACTCTGCAACCA AGTCTTCTCAGCGCCATATGG	chemokine (C-C motif) ligand 3
Ccl4	NM_013652.1	AT744.1, Act-2, MIP-1B, Mip1b, Scya4	Extracellular Region,Extracellular Space,Soluble Fraction,Response To Toxin,Leukocyte Chemotaxis,Inflammatory Response,Immune Response,Chemokine Activity,Cytokine Activity	TTCTCAGCACCAATGGGCTCTGACCCTCCCACTTCCTGCTGTTTCTCTTACACCTCCCGGCAGCTTCACAGAAGCTTTG TGATGGATTACTATGAGACCA	chemokine (C-C motif) ligand 4
Ccl7	NM_013654.2	MCP-3, Scya7, fic, marc, mcp3	Extracellular Region,Extracellular Space,Inflammatory Response,Immune Response,Regulation Of Cell Shape,Positive Regulation Of Cell Migration,Cytoskeleton Organization And Biogenesis,Heparin Binding,Chemokine Activity,Cytokine Activity	ACAGAAGGATCACCAGTAGTCGGTGTCCCTGGGAAGCTGTTATCTTCAAGACAAAGAAGGGCATGGAAGTCTGTGCT GAAGCCCATCAGAAGTGGGTCGA	chemokine (C-C motif) ligand 7
Ccr1	NM_009912.4	Cmkbr1, Mip-1a-R	External Side Of Plasma Membrane,Membrane,Integral To Membrane,Plasma Membrane,Signal Transduction,Calcium Ion Transport,Myeloid Cell Differentiation,Leukocyte Chemotaxis,Cell Cell Signaling,Inflammatory Response,Immune Response,Exocytosis,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Act	CTTCTGATTCAGACCATAGGTGTCAACCAAGGAAGGTCTAAGAAGAGAATGAGGAGACAGTATATAGCTCTCCAAGA CTGATACTGACAGTTCTTACAGT	chemokine (C-C motif) receptor 1
Ccr2	NM_009915.2	Cc-ckr-2, Ccl2a, Ccr2b, Ckr2, Ckr2a, Ckr2b, Cmkbr2, mJe-r	Membrane,Cytosol,Perinuclear Region Of Cytoplasm,Integral To Membrane,Integral To Plasma Membrane,Cell Soma,Dendrite,Plasma Membrane,Signal Transduction,Regulation Of Cell Migration,Hemopoiesis,Negative Regulation Of Angiogenesis,Inflammatory Response,Immune Response,Angiogenesis,Positive Regulation Of T Cell Activation,Cellular Homeostasi	ATGAACTAACATAGACAGCTCAGGATTAACAGGGACTTGTGGTTTGTGGTCTGTGGGCTTATCCAAGCATGGTGATTT AGACTCTAAGGTCCGTCTGGAT	chemokine (C-C motif) receptor 2
Ccr3	NM_009914.4	CC-CKR3, CKR3, Cmkbr1l2, Cmkbr3	Membrane,Integral To Membrane,Endosome,Extracellular Space,Plasma Membrane,Signal Transduction,Positive Regulation Of Angiogenesis,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Activity	CTATATGTTCATTATTCTGGCACACAGACCCTAGAAATCTCAGGAGGTGCTCTCTGGATTGAAGTGTGCACTTATAGCA CCACCTCAGTGCTTATGACTC	chemokine (C-C motif) receptor 3
Ccr4	NM_009916.2	C-C CKR-4, CHEMR1, Cmkbr4, LESTR, Sdf1r	External Side Of Plasma Membrane,Membrane,Integral To Membane,Cell Soma,Plasma Membrane,Signal Transduction,Inflammatory Response,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Activity	GCTTGTAGAAGAAGCTCGTCGGTGCAGAGAAGGGTGAAATGCCCTTGTAATTCTAGCTACTCCGGGGATAAGGCCAA GAGATCTTAGATTCAAGGATGGC	chemokine (C-C motif) receptor 4
Ccr7	NM_007719.2	CD197, Cdw197, Cmkbr7, EBI1, Ebi1h	External Side Of Plasma Membrane,Membrane,Integral To Membane,Plasma Membrane,Signal Transduction,Activation Of Jnk Activity,Positive Regulation Of T Cell Proliferation,Inflammatory Response,Immune Response,Actin Cytoskeleton Organization And Biogenesis,G Protein Coupled Receptor Protein Signaling Pathway,Cell Maturation,G Protein Coupled	CCCAGATGGTTTTTGGGTTCCTAGTGCCTATGCTGGCTATGAGTTTCTGCTACCTCATTATCATCCGTACCTTGCTCCA GGCACGCAACTTTGAGCGGAA	chemokine (C-C motif) receptor 7
Cd163	NM_053094.2	CD163v2, CD163v3	Extracellular Region,Membrane,Integral To Membrane,Plasma Membrane,Inflammatory Response,Receptor Mediated Endocytosis	TCACGGCACTCTTGGTTTGTGGAGCCATTCTATTGGTCCTCCTCATTGTCTTCCTCCTGTGGACTCTGAAGCGACGACA GATTCAGCGACTTACAGTTTC	CD163 antigen
Cd4	NM_013488.2	L3T4, Ly-4	External Side Of Plasma Membrane,Cell Surface,Membrane,Endoplasmic Reticulum Membrane,Integral To Membrane,Lipid Raft,Endoplasmic Reticulum Lumen,Plasma Membrane,Cell Surface Receptor Linked Signal Transduction Go 0007166,T Cell Differentiation,Regulation Of T Cell Activation,Cytokine Production,Immune Response,Positive Regulation Of T Cel	AAGAGGTGTCCGTACAAAAGTCCACCAAAGACCTCAAGCTCCAGCTGAAGGAAACGCTCCCACTCACCCTCAAGATA CCCCAGGTCTCGCTTCAGTTTGC	CD4 antigen
Cd40	NM_011611.2	AI326936, Bp50, GP39, HIGM1, IGM, IMD3, T-BAM, TRAP, Tnfrsf5, p50	External Side Of Plasma Membrane,Cell Surface,Extracellular Region,Membrane,Integral To Membrane,Extracellular Space,Plasma Membrane,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Activation Of Nf Kappab Transcription Factor,Positive Regulation Of Map Kinase Activity,Defense Response To Virus,Inflammatory Response,B C	GCTGCCCAAACCCGGTTACCTGATTTTGATCCCTGGGACTTCATGGTAAAAGGAGAGAACCAAATCCAGAGGGTTG TCATTTGACCTCCATGTGTGCTC	CD40 antigen
Cd40lg	NM_011616.2	CD154, CD40-L, Cd40l, HIGM1, IGM, IMD3, Ly-62, Ly62, T-BAM, TRAP, Tnfsf5, gp39	External Side Of Plasma Membrane,Extracellular Region,Membrane,Integral To Membrane,Extracellular Space,Plasma Membrane,Signal Transduction,B Cell Differentiation,Inflammatory Response,Immune Response,Anti Apoptosis,Cytokine Activity	AGCAGTGGATCTGAGAGAATCTTACTCAAGGCGGCAAATACCCACAGTTCCTCCCAGCTTTGCGAGCAGCAGTCTGTT CACTTGGGCGGAGTGTTTGAAT	CD40 ligand
Cd55	NM_010016.2	Daf, Daf-GPI, Daf1, GPI-DAF	External Side Of Plasma Membrane,Cell Surface,Membrane,Anchored To Membrane,Lipid Raft,Apical Plasma Membrane,Plasma Membane,Innate Immune Response,Negative Regulation Of Catalytic Activity,Enzyme Inhibitor Activity	ACAGTTAAAGTTTCAGCAACCCAGCATGTACCTGTTACCAAGACAACAGTACGTCATCCAATAAGAACATCTACAGAC AAAGGAGAGCCTAACACAGGTG	CD55 antigen
Cd86	NM_019388.3	B7, B7-2, B7.2, B70, CLS1, Cd28l2, ETC-1, Ly-58, Ly58, MB7, MB7-2, TS/A-2	External Side Of Plasma Membrane,Membrane,Integral To Membrane,Plasma Membrane,Positive Regulation Of T Cell Proliferation,Defense Response To Virus,B Cell Activation,T Cell Activation,Receptor Binding,Receptor Activity	CAAAACATAAGCCTGAGTGAGCTGGTAGTATTTTGGCAGGACCAGCAAAAGTTGGTTCTGTACGAGCACTATTTGGG CACAGAGAAACTTGATAGTGTGA	CD86 antigen
Cdc42	NM_009861.1	AI747189, AU018915	Golgi Membrane,Membrane,Cytoplasm,Cytoskeleton,Cell Projection,Apical Part Of Cell,Secretory Granule,Plasma Membrane,Nervous System Development,Regulation Of Protein Kinase Activity,Regulation Of Mitosis,Regulation Of Protein Metabolic Process,Actin Cytoskeleton Organization And Biogenesis,Cell Cell Adhesion,Endosome Transport,Establishmen	TGATTGGTGGAGAGCCATACACTCTTGGACTTTTTGATACTGCAGGGCAAGAGGATTATGACAGACTACGACCGCTAA GTTATCCACAGACAGATGTTTT	cell division cycle 42
Cebpb	NM_009883.3	C/EBPbeta, CRP2, IL-6DBP, LAP, LIP, NF-IL6, NF-M, Nfl6	Cytoplasm,Nucleus,Nuclear Matrix,Nuclear Chromatin,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Negative Regulation Of Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent,Anti Apoptosis,Neuron Differentiation,Protein Homod	CGGGCACCGCGCGCACGCACCTGCACAGCGCACCGGGTTTCGGGACTTGATGCAATCCGGATCAAACGTGGCTGAG CGCGTGTGGACACGGGACTGACGC	CCAAT/enhancer binding protein (C/EBP), beta
Cfb	NM_008198.2	AI195813, AI255840, B, Bf, C2, Fb, H2-Bf	Extracellular Region,Extracellular Space,Proteolysis,Cell Proliferation Go 0008283,Innate Immune Response,Serine Type Peptidase Activity,Peptidase Activity,Serine Type Endopeptidase Activity	GGTGGGGCCTCTGGTGGACTCCGTGAACATCAATGCCTTAGCTTCCAAAAAGGACAATGAGCATCATGTGTTTAAAGT CAAGGATATGGAAGACCTGGAG	complement factor B
Cfd	NM_013459.1	Adn, DF	Extracellular Region,Extracellular Space,Proteolysis,Notch Signaling Pathway,Innate Immune Response,Serine Type Peptidase Activity,Endopeptidase Activity,Peptidase Activity,Serine Type Endopeptidase Activity	AGTGTCAATCATGAACCGGACAACCTGCAATCTGCGCACGTACCATGACGGGGTAGTCACCATTAACATGATGTGTG CAGAGAGCAACCGCAGGGACACT	complement factor D (adipsin)
Cfl1	NM_007687.5	AA959946, Cof	Membrane,Cytoplasm,Nucleus,Cytoskeleton,Lamellipodium,Cell Projection,Leading Edge,Cortical Actin Cytoskeleton,Plasma Membrane,Actin Filament Organization,Cytokinesis,Protein Import Into Nucleus,Regulation Of Cell Morphogenesis,Cytoskeleton Organization And Biogenesis,Protein Amino Acid Phosphorylation,Actin Binding	TGCTGCCAACTTCTAACCACAATAGTGACTCTGTGCTTGTCTGTTTAGTTCTGTGTGTAAATGAAATGTGGAAATGACC CTCCCTGCCCCAGCTGGCTGC	cofilin 1, non-muscle
Creb1	NM_133828.2	2310001E10Rik, 3526402H21Rik, AV083133, Creb, Creb-1	Chromatin,Nucleus,Nuclear Chromatin,Mitochondrion,Transcription Factor Complex,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Axonogenesis,Regulation Of Transcriptiondna Dependent,Transforming Growth Factor Beta Receptor Signaling Pathway,Protein Amino Acid Phosphorylation,Transcription Fro	CATGTCATACACACGGTGCCACTTTCCATTAAGTTGACTGTCAAGCCCAGGAAAGCACTGTTCGTCCGTGCCACCTTG CCTGAGACTGAATTTTCTTCAG	cAMP responsive element binding protein 1
Crp	NM_007768.4	AI255847	Extracellular Space,Protein Polymerization,Protein Homodimerization Activity,Low Density Lipoprotein Binding	TTGTATTTCCCAAGGAGTCAGATACTTCCTATGTGTCTCTGGAAGCAGAGTCAAAGAAGCCACTGAACACCTTTACTGT GTGTCTCCATTTCTACACTGC	C-reactive protein, pentraxin-related
Csf1	NM_001113530.1	C87615, Csfm, MCSF, op	Extracellular Region,Membrane,Perinuclear Region Of Cytoplasm,Integral To Membrane,Receptor Complex,Extracellular Space,Plasma Membrane,Positive Regulation Of Cell Proliferation,Positive Regulation Of Cellular Protein Metabolic Process,Inflammatory Response,Cell Proliferation Go 0008283,Positive Regulation Of Cell Migration,Innate Immune R	TCCAGCTGCTGGAGAAGATCAAGAACTTCTTTAATGAAACAAAGAATCTCCTTGAAAAGGACTGGAACATTTTTACCAA GAACTGCAACAACAGCTTTGC	colony stimulating factor 1 (macrophage)

Continue Table S1: Nanostring nCounter SC Mouse Inflammation V2 Panel Gene List

Csf2	NM_009969.4	Csfgm, GMCSF, Gm-CSf, MGI-IGM	Extracellular Region,Extracellular Space,Positive Regulation Of Cell Proliferation,Negative Regulation Of Apoptosis,Regulation Of Gene Expression,Immune Response,Regulation Of Cell Proliferation,Cytokine Activity,Growth Factor Activity	AAGTCGTCTCTAACGAGTTCTCCTTCAAGAAGCTAACATGTGTGCAGACCCGCCTGAAGATATTCGAGCAGGGTCTAC GGGGCAATTTCACCAAACTCAA	colony stimulating factor 2 (granulocyte-macrophage)
Csf3	NM_009971.1	Csfg, G-CSF, MGI-IG	Extracellular Region,Extracellular Space,Positive Regulation Of Cell Proliferation,Immune Response,Enzyme Binding,Cytokine Activity,Growth Factor Activity	TTGTTCTCCTGCTTAGAGCAGAGAGAGAAGGCTCTTGTGTCCTCCTGTGGAGGCCAGGGAAGGAGATGGGTAAATAC CAAGTATTGATTCCTGCTGCTGC	colony stimulating factor 3 (granulocyte)
Cxcl1	NM_008176.1	Fsp, Gro1, KC, Mgsa, N51, Scyb1, gro	Extracellular Region,Extracellular Space,Inflammatory Response,Immune Response,Acute Inflammatory Response,Chemokine Activity,Cytokine Activity,Growth Factor Activity	TGCTAGTAGAAGGGTGTTGTGCGAAAAGAAGTGCAGAGAGATAGAGTTTAGTATTATGTTTTGTATGTATTAGGGTGA GGACATGTGTGGGAGGCTGTGT	chemokine (C-X-C motif) ligand 1
Cxcl10	NM_021274.1	C7, CRG-2, INP10, IP-10, IP10, Ifi10, Scyb10, gIP-10, mob-1	External Side Of Plasma Membrane,Extracellular Region,Extracellular Space,Positive Regulation Of Cell Proliferation, Signal Transduction,Negative Regulation Of Angiogenesis,Defense Response To Virus,Inflammatory Response,Immune Response,Protein Secretion,Positive Regulation Of Cell Migration,Chemokine Activity,Cytokine Activity	AGGACGGTCCGCTGCAACTGCATCCATATCGATGACGGGCCAGTGAGAATGAGGGCCATAGGGAAGCTTGAAATCA TCCCTGCGAGCCTATCCTGCCCAC	chemokine (C-X-C motif) ligand 10
Cxcl2	NM_009140.2	CINC-2a, GROb, Gro2, MIP-2, MIP-2a, Mgsa-b, Mip2, Scyb, Scyb2	Extracellular Region,Extracellular Space,Leukocyte Chemotaxis,Inflammatory Response,Immune Response,Chemokine Activity,Cytokine Activity	GGTGGGGGTGGGGACAAATAGATGCAGTCGGATGGCTTTCATGGAAGGAGTGTGCATGTTCACATCATTTTTTTGTA AGCACCGAGGAGAGTAGAACAGC	chemokine (C-X-C motif) ligand 2
Cxcl3	NM_203320.2	Dcip1, Gm1960	Extracellular Region,Extracellular Space,Inflammatory Response,Immune Response,Chemokine Activity,Cytokine Activity	ACTCTCAAGGATGGTCAAGAAGTTTGCCTCAACCCCAAGGCCCAGGCTTCAGATAATCATCAAGAAGATACTGAAG AGCGGCAAGTCCAGCTGAGCCG	chemokine (C-X-C motif) ligand 3
Cxcl5	NM_009141.2	AMCF-II, ENA-78, GCP-2, LIX, Scyb5, Scyb6	Extracellular Region,Extracellular Space,Cytokine Production,Inflammatory Response,Chemokine Activity	CCCAGTGAAGATAAGAAGAAGGGCTGATTCTCTCCACCCACGGATTTTCTTTATGAACTCCCTGCTTTGATGAGAAA AGGGAACCATTGTCCCTGAAG	chemokine (C-X-C motif) ligand 5
Cxcl9	NM_008599.2	BB139920, CMK, Mig, MuMIG, Scyb9, crg-10	External Side Of Plasma Membraine,Extracellular Region,Extracellular Space,Defense Response To Virus,Cytokine Activity	TAGAACTCAGCTCTGCCATGAAGTCCGCTGTTCTTTTCCTCTTGGGCATCATCTTCCTGGAGCAGTGTGGAGTTCGAG GAACCCTAGTGATAAGGAATGC	chemokine (C-X-C motif) ligand 9
Cxcr1	NM_178241.4	Il8ra	Membrane, Integral To Membrane,Plasma Membrane, Signal Transduction,Cell Surface Receptor Linked Signal Transduction Go 0007166,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Activity	TCTCTTAGGAGCCCACTTGATTGAAGATACTTGCGAACGCCGCAATGACATTGACCAGGCCCTGTATATTACTGAGAT CCTGGCCTTTTCTCATAGTTGT	chemokine (C-X-C motif) receptor 1
Cxcr2	NM_009909.3	CD128, CDw128, Cmkar2, Gpcr16, IL-8Rh, IL-8rb, IL8RA, Il8rb, mIL-8RH	Cell Surface,Membrane, Integral To Membrane,Plasma Membrane,G Protein Signaling Coupled To Ip3 Second Messengerphospholipase C Activating,Positive Regulation Of Cell Proliferation,Signal Transduction,Cell Surface Receptor Linked Signal Transduction Go 0007166,Cytokine And Chemokine Mediated Signaling Pathway,G Protein Coupled Receptor Prote	CCTTGCCTGTCTGGGCTGCATCTAAAGTAAATGGATGGACTTTTGGCTCAACCCTGTGCAAGATATTCTCATACGTGAA GGAGGTTACCTTCTACAGCAG	chemokine (C-X-C motif) receptor 2
Cxcr4	NM_009911.3	CD184, Cmkar4, LESTR, PB-CKR, PBSF/SDF-1, Sdf1r	External Side Of Plasma Membrane, Cell Surface,Membrane,Cytoplasmic Vesicle,Integral To Membrane,Endosome,Cytoplasmic Membrane Bound Vesicle,Leading Edge,Growth Cone,Plasma Membrane,Nervous System Development,T Cell Proliferation, Signal Transduction,Regulation Of Cell Migration,Calcium Mediated Signaling,Brain Development,Organ Morphogenesi	GTTTCAATTCCAGCATATAATGGTGGGTCTCGTCCTGCCCGGCATCGTCATCCTCTCCTGTTACTGCATCATCATCTCTA AGCTGTCACACTCCAAGGGC	chemokine (C-X-C motif) receptor 4
Cysltr1	NM_021476.4	BB147369, CysLT1R, Cyslt1	Membrane, Integral To Membrane,Integral To Plasma Membrane,Plasma Membrane,Signal Transduction,Cell Surface Receptor Linked Signal Transduction Go 0007166,Calcium Ion Transport,Inflammatory Response,Positive Regulation Of Angiogenesis,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Activity	TGAAGATTTGGATCTTGCTTCAGGGAGCAAAAGGACCTTAAACTGTGAAGCTTGGAATCAGCAGCTTGAACGTACTCT GACACTACAACATAAGAACAGT	cysteinyl leukotriene receptor 1
Cysltr2	NM_001162412.1	2300001H05Rik, CYSLT2R, Cllt2, Cyslt2	Membrane, Integral To Membrane,Plasma Membrane,Signal Transduction, Positive Regulation Of Angiogenesis,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Activity	GGAAGGCGCTGACCACCATTGTCATTGCCATGATCACCTTCCTCCTCTGTTTTCTGCCATACCATGCACTGCGGACCCT CCACTTGGTCACATGGGATAA	cysteinyl leukotriene receptor 2
Daxx	NM_007829.3		Cytoplasm,Nucleus,Cytosol,Cell Cortex,Pml Body,Neuron Projection,Transcription Dna Dependent,Negative Regulation Of Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent,Androgen Receptor Signaling Pathway,Apoptosis Go,Protein Homodimerization Activity,Protein N Terminus Binding,Transcription Coactivator Activity,Transcripti	CTTCGGGAAAATCGAACCTTGGCCATGAACCGGCTGGATGAGGTCATCTCCAAGTATGCAATGATGCAAGACAAGAC TGAGGAGGGCGAGAGACAGAAGA	Fas death domain-associated protein
Ddit3	NM_007837.3	CHOP-10, CHOP10, chop, gadd153	Cytoplasm,Nucleus, Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Unfolded Protein Response,Regulation Of Transcriptiondna Dependent,Cell Cycle Arrest Go 0007050,Cell Cycle Go 0007049,Negative Regulation Of Transcription Factor Activity,Regul	CCTCAGATGAAATTGGGGGCACCTATATCTCATCCCCAGGAAACGAAGAGGAAGAATCAAAAACCTTCACTACTCTTG ACCCTGCGTCCCTAGCTTGGCT	DNA-damage inducible transcript 3
Elk1	NM_007922.4	Elk-1	Nucleus,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent,Sequence Specific Dna Binding,Transcription Factor Activity,Dna Binding	AGGGTCTCATCTTTGCCTAAACTTACCAGTTGGGATACACTTGCTGGCCATCAAGTCTCAAGGATCTACCTGGTTCTAC CTTGGGATTACAAGCATGTAC	ELK1, member of ETS oncogene family
Fasl	NM_010177.3	APT1LG1, CD178, CD95-L, CD95L, Fas-L, Faslg, Tnfsf6, gld	External Side Of Plasma Membrane,Extracellular Region,Membrane,Cytoplasmic Vesicle,Perinuclear Region Of Cytoplasm,Integral To Membrane,Lipid Raft,Cytoplasmic Membrane Bound Vesicle,Extracellular Space,Lysosome,Plasma Membrane,Positive Regulation Of Cell Proliferation, Signal Transduction,Induction Of Apoptosis By Extracellular Signals,Nega	CATTTAACAGGGAACCCCCACTCAAGGTCCATCCCTCTGGAATGGGAAGACACATATGGAACCGCTCTGATCTCTGGA GTGAAGTATAAGAAAGGTGGCC	Fas ligand (TNF superfamily, member 6)
Flt1	NM_010228.3	AI323757, Flt-1, VEGFR-1, VEGFR1, sFlt1	Golgi Apparatus,Membrane, Cytoplasm,Nucleus,Integral To Membrane, Integral To Plasma Membrane,Endosome,Plasma Membrane,Protein Amino Acid Autophosphorylation,Multicellular Organismal Development,Positive Regulation Of Map Kinase Activity,Angiogenesis,Embryonic Morphogenesis,Intracellular Receptor Mediated Signaling Pathway,Peptidyl Tyrosine	GAAAAGTCCGTGTCCTCGCTTCCAAGCCCACCTCTCTATCCGCTGGGCAGCAGACAAGTCCTCACTTGCACCGTGTAT GGCATCCCTCGGCCAACAATCA	FMS-like tyrosine kinase 1
Fos	NM_010234.2	D12Rfj1, c-fos, cFos	Nucleus,Membrane Fraction,Transcription Factor Complex,Positive Regulation Of Transcriptiondna Dependent,Nervous System Development,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Regulation Of Transcriptiondna Dependent,Cellular Response To Extracellular Stimulus,Transforming Growth Factor Beta Receptor Signaling Path	AGCTGGTGCATTACAGAGAGGAGAAACACGTCTTCCCTCGAAGGTTCCCGTCGACCTAGGGAGGACCTTACCTGTTC GTGAAACACACCAGCTGTGGGC	FBJ osteosarcoma oncogene
Fxyd2	NM_052823.2	Atp1g1	Membrane, Microsome,Integral To Membrane,Basolateral Plasma Membrane, Transport,Sodium Ion Transport,Potassium Ion Transport,Ion Transport,Regulation Of Cell Proliferation,Regulation Of Cell Growth,Ion Channel Activity	CTTCGTCGTGGGCCTCCTCATCATTCTCAGCAAAAGGTTCCGCTGTGGGGGCGGTAAGAAACATAGGCAGGTCAATG AAGATGAACTGTGACAGAAGAGC	FXYD domain-containing ion transport regulator 2
Gnaq	NM_008139.5	1110005L02Rik, 6230401I02Rik, AA408290, AW060788, Dsk1, Dsk10, Galphaq, Gq, Gql	Cytosol,Membrane Fraction,Protein Complex, Plasma Membrane,G Protein Signaling Coupled To Ip3 Second Messengerphospholipase C Activating,Glutamate Signaling Pathway,Signal Transduction,Phospholipase C Activation,Skeletal Development,Behavior,Protein Stabilization,Regulation Of Action Potential,G Protein Signaling Adenylate Cyclase Activatin	GAATTGGGCGCTTGAACCTAAGAAAGATTGTGGACTTATCAAAAGTCACCGCTCAGTGTTCCGTCAAGCATGTATTTA TGTGACGATCATACTAGGAGGG	guanine nucleotide binding protein, alpha q polypeptide
Gnas	NM_010309.3	5530400H20Rik, A930027G11Rik, C130027O20Rik, GPSA, GSP, Galphas, Gnas1, Gnasxl, Gsa, Nesp, Nespl, Oed-Sml, Oedsml, P1, P2, P3, PHP1A, PHP1B, POH	Extracellular Region,Intrinsic To Membrane,Membrane,Cytoplasm,Vesicle,Cytosol,Cytoplasmic Vesicle,Lipid Raft,Cell Projection,Ruffle,Endosome,Membrane Fraction,Plasma Membrane,Energy Reserve Metabolic Process,Signal Transduction,Skeletal Development,Behavior,Sensory Perception Of Chemical Stimulus,G Protein Signaling Adenylate Cyclase Activ	CAGTTCAGAGTGGACTACATTCTGAGCGTGATGAACGTGCCGAACTTTGACTTCCCACCTGAATTCTATGAGCATGCC AAGGCTCTGTGGGAGGATGAGG	GNAS (guanine nucleotide binding protein, alpha stimulating) complex locus
Gnb1	NM_008142.3	AA409223, C77571, Gnb-1	G Protein Signaling Coupled To Ip3 Second Messengerphospholipase C Activating,Signal Transduction,Sensory Perception Of Taste,Cell Proliferation Go 0008283,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Binding,Gtpase Activity,Gtpase Binding	CGCATACGCTCCTTCTGGGAATTATGTGGCCTGTGGTGGCCTGGATAACATCTGCTCCATTTACAACCTGAAAACTCG TGAAGGGAATGTGCGTGTGAGT	guanine nucleotide binding protein (G protein), beta 1
Gngt1	NM_010314.2	Gdy1, Gng1	Membrane, Plasma Membrane,Signal Transduction,Phototransduction,G Protein Coupled Receptor Protein Signaling Pathway,Protein Localization,Gtpase Activity	GAAGGAAGTGACACTGGAGAGAATGATGGTTTCCAAATGTTGTGAAGAAGTGAGAGATTATATTGAAGAAAGGTCTG GAGAAGACCTCTAGTGAAGGGG	guanine nucleotide binding protein (G protein), gamma transducing activity polypeptide 1
Gpr44	NM_009962.2	Cth2, Grp45, Ptgdr2	Membrane, Integral To Membrane,Integral To Plasma Membrane,Plasma Membrane,G Protein Signaling Adenylate Cyclase Inhibiting Pathway,Signal Transduction,Calcium Mediated Signaling,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Activity	GAAGCCGCTCTGTCCACTCTTGGAGGAGATGGTCCAGCTTCCAAACCACAGCAACTCTAGCCTCCGCTACATCGACCA CGTGTCGGTGCTGTTGCACGGG	G protein-coupled receptor 44
Grb2	NM_008163.3	AA408164, Ash	Golgi Apparatus,Membrane, Cytoplasm,Nucleus,Endosome,Protein Complex,Plasma Membrane, Vesicle Membrane,Positive Regulation Of Signal Transduction,Insulin Receptor Signaling Pathway,Regulation Of Mapkkk Cascade,Ras Protein Signal Transduction,Anatomical Structure Formation,Aging,Dna Damage Responsesignal Transduction,Protein Domain Specific B	AGGAGCTGGTAGAAGCAGAGAGTGTATTTCCCATCTTGAATGGGCGGAGGTCTCGAAGCCTCAGCTTTTACTTTGT GAGCTGCAACACTCGCTTCAGCT	growth factor receptor bound protein 2
H2-Ea-ps	NM_010381.2	AI323765, E-alpha-f, H-2Ea, H2-Ea, I-Ealpha, Ia-3, Ia3		ATCATGAAGGGTATTAAAAAACGCAATGTTGTAGAACGCCGACAAGGAGCCCTGTGAGATACCTGGAGGCAATGCCT TCAGTTAAAGTTCAGTGAAGAAA	histocompatibility 2, class II antigen E alpha, pseudogene

Continue Table S1: Nanostring nCounter SC Mouse Inflammation V2 Panel Gene List

H2-Eb1	NM_010382.2	H-2Eb, H2Eb, Ia-4, Ia4	External Side Of Plasma Membrane,Membane,Integral To Membrane,Lysosomal Membrane,Protein Tetramerization,Immune Response	AAACATGTCCTGCTTGGCCCACATCCCTCCAGAGACACTGCTCTTCCAGGACCTGGCTCCTCCTGATTCTCCACCCTG GAGATCTGTGCTCCTGATGGCT	histocompatibility 2, class II antigen E beta
Hc	NM_010406.1	C5, C5a, He	Extracellular Region,Extracellular Space,Soluble Fraction,Inflammatory Response,Positive Regulation Of Angiogenesis,Innate Immune Response	CTACACACTGAATTTGGTCGCTACTCCTCTTTTCGTGAAGCCGGGATTCCATTTTCCATCAAGGCACAGGTTAAAGAT TCACTCGAGCAGGCGGTAGGA	hemolytic complement
Hdac4	NM_207225.1	4932408F19Rik, AI047285	Sarcomere,Cytoplasm,Nucleus,Cytosol,Histone Deacetylase Complex,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Cell Proliferation,Chromatin Remodeling,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Skeletal Development,Negative Regulation Of Transcription Dna Depen	AGACGCTGAGTACTTGGCAGCCTTCAGAACGGTGGTTATGCCTATCGCAAATGAGTTTGCCCCAGATGTGGTACTGG TGTCATCGGGCTTCGATGCTGTG	histone deacetylase 4
Hif1a	NM_010431.2	AA959795, HIF1alpha, MOP1, bHLHe78	Cytoplasm,Nucleus,Transcription Factor Complex,Nucleolus,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Cell Proliferation,Negative Regulation Of Apoptosis,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Transcription Dna Dependent,Negative Regulation Of Growth,Epithelial T	ACCATGATATGTTTACTAAAGGACAAGTCACCACAGGACAGTACAGGATGCTTGCCAAAAGAGGTGGATATGTCTGG GTTGAAACTCAAGCAACTGTCAT	hypoxia inducible factor 1, alpha subunit
Hmgb1	NM_010439.3	DEF, HMG-1, Hmg1, SBP-1, amphoterin, p30	Cell Surface,Extracellular Region,Cytoplasm,Nucleus,Extracellular Space,Condensed Chromosome,Neuron Projection,Nucleolus,Soluble Fraction,Chromosome,Positive Regulation Of Cell Proliferation,Nervous System Development,Neurite Development,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Positive Regulation Of Caspase Act	GTGGGACTATTAGGATCAAGCAATCTGAACGTCTGTCCTTGAAGGACTGATAGAAAAGTACCTTCTAATCCTTACACG AGGACTCTCCTTTAACCGCCAT	high mobility group box 1
Hmgb2	NM_008252.3	C80539, HMG-2, Hmg2	Cytoplasm,Nucleus,Perinuclear Region Of Cytoplasm,Extracellular Space,Condensed Chromosome,Protein Complex,Nucleolus,Soluble Fraction,Chromosome,Positive Regulation Of Transcriptiondna Dependent,Nervous System Development,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Negative Regulation Of Transcription Dna Dependent	ATGTGTTGGGAAACTTGTGTAGATGTTGAAAGTAGTTATACCAGGCTGGGTGTGGTGGCAGGTACATGCAATCCCAG AGTGGAAGGTAGAGAGAGGGCAG	high mobility group box 2
Hmgn1	NM_008251.3	HMG-14, Hmg14	Chromatin,Cytoplasm,Nucleus,Establishment And Or Maintenance Of Chromatin Architecture,Chromatin Binding,Dna Binding	CCCTTGCCCTGTCAGAACTGTGATGTCTGTGGTCATGGCAGTCCATTTTCCTAACAGTTGTGATAATGTGCTGTGAAAG ATGGAAGTCCTGAGTCTGTTC	high mobility group nucleosomal binding domain 1
Hras1	NM_008284.2		Golgi Apparatus,Membrane,Microsome,Plasma Membrane,Soluble Fraction,Positive Regulation Of Cell Proliferation,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Ras Protein Signal Transduction,Negative Regulation Of Cell Proliferation,Cell Proliferation Go 0008283,Positive Regulation Of Epithelial Cell	CAAATGTTCAGCTTCCCTTGTCTGTGTGTATCTGGGGCTCCTGAGGTATCATCTGGAGCGTCAGTGACACCTTCGGAG CCTTGTTGGTCATGAACTTAAG	Harvey rat sarcoma virus oncogene
Hsh2d	NM_197944.1	ALX, Hsh2	Cytoplasm,Mitochondrion,Positive Regulation Of Signal Transduction,T Cell Activation,Sh3 Sh2 Adaptor Activity	CCACCTTTCGCCCCTGGGTACTGATAGAACTTTCTGTATCTTGGGTATTCCTCATCTCTCCTTTAGGTCCCCATCCTTGT CCTCACAGCCAGAGAACTGT	hematopoietic SH2 domain containing
Hspb1	NM_013560.2	27kDa, Hsp25	Cell Surface,Contractile Fiber,Cytoplasm,Insoluble Fraction,Proteasome Complex,Nucleus,Cytoskeleton,Plasma Membrane,Soluble Fraction,Negative Regulation Of Apoptosis,Response To Stress,Angiogenesis,Regulation Of I Kappab Kinase Nf Kappab Cascade,Ubiquitin Binding,Protein Kinase Binding	AGGGCACACTTACCGTGGAGGCTCCGTTGCCCAAAGCAGTCACGCAGTCAGCGGAGATCACCATTCCGGTTACTTTC GAGGCCCGCGCCCAAATTGGGGG	heat shock protein 1
Hspb2	NM_024441.3	27kDa, 2810021G24Rik, HSP27, MKBP	Cytoplasm,Nucleus,Soluble Fraction,Response To Heat,Response To Stress	CTGTCTACCTCCCGTGGTGATTCCATAAATCCACCACACCCAGAGGGAGCAGCATCCCTGGGAGATGGCATCGGTG CATGGTCCACAGTGTATGGTTTG	heat shock protein 2
Ifi27l2a	NM_029803.1	2310061N23Rik, Ifi27, Isg12, Isg12(b1)	Response To Virus,Aging	CTGGGGCAGCTGTTGGAGCCTTGCTCTGAGCTTAGGAGATGACACTTCTATCAGCTCAACTCAAAGCCTGTACAGACT ACGCAGGAGATGAAGTTCCAAA	interferon, alpha-inducible protein 27 like 2A
Ifi44	NM_133871.2	A430056A10Rik, AW261460, MTAP44, p44	Cytoplasm	CTGACAGATACCAGTTCGATTCCATGAAACCAATCACATCAAACCATCCGAACTATACCCATGACCCACTGCTGAAGG ACAGAATTCACTGTGTGGTTTT	interferon-induced protein 44
Ifit1	NM_008331.2	ISG56, Ifi56, P56	Cytoplasm,Response To Virus	AACAGGGCCTTGCAGGCATCACCTTCCTCTGGCTACTTACATTATCAAAAAGGGCTCTGCTACAAGCAACAAATCTCC CAACTGAGGAGATCCCGAAACA	interferon-induced protein with tetratricopeptide repeats 1
Ifit2	NM_008332.2	AV302338, Ifi54, P54	Response To Virus	ACAACGAGTAAGGAGTCACTGGAGAGGCAATCTGCGACAGCTAAAATGCCATTTCACCTGGAACCTGATAGCAGAAGA TGAGTCCTTGGATGAGTTTGAGG	interferon-induced protein with tetratricopeptide repeats 2
Ifnb1	NM_010510.1	IFN-beta, IFNB, Ifb	Extracellular Region,Extracellular Space,Response To Virus,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Defense Response,Defense Response To Virus,Defense Response To Bacterium,Humoral Immune Response,Caspase Activation,Hematopoietin Interferon Classd200 Domain Cytokine Receptor Binding,Transcription Corepressor Act	GATGAACTCCACCAGCAGACAGTGTTTCTGAAGACAGTACTAGAGGAAAAGCAAGAGGAAAGATTGACGTGGGAGA TGTCCTCAACTGCTCTCCACTTGA	interferon beta 1, fibroblast
Ifng	NM_008337.1	IFN-g, Ifg	External Side Of Plasma Membrane,Extracellular Region,Extracellular Space,Response To Virus,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Regulation Of Growth,Positive Regulation Of T Cell Proliferation,Defense Response To Virus,Immune Response,Unfolded Protein Respon	CTAGCTCTGAGACAATGAACGCTACACACTGCATCTTGGCTTTGCAGCTCTTCCTCATGGCTGTTTCTGGCTGTTACTG CCACGGCACAGTCATTGAAAG	interferon gamma
Iigp1	NM_021792.3	2900074L10Rik, AI046432, AW111922, Ifgga1, Iigp, Irga6	Golgi Apparatus,Membrane,Cytoplasm,Endoplasmic Reticulum Membrane,Endoplasmic Reticulum,Nucleus,Cytokine And Chemokine Mediated Signaling Pathway,Innate Immune Response,Hydrolase Activity Acting On Acid Anhydrides,Gtp Binding,Nucleotide Binding,Identical Protein Binding,Gtpase Activity	GGCAAAAAGGGGATGTCTTCGAGGTTAAAAGAGTTGGCCCAGTGGTTAAGAATACTGGCTACTCTTGCAAAGGACCA GGATTTAACTGCCAGAACCCACA	interferon inducible GTPase 1
Il10	NM_010548.1	CSIF, Il-10	Extracellular Region,Extracellular Space,Positive Regulation Of Transcriptiondna Dependent,Negative Regulation Of Apoptosis,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Inflammatory Response,Regulation Of Gene Expression,Positive Regulation Of Cytokine Secretion,Immune Response,Positive Regulation Of Transcription F	GGGCCCTTTGCTATGGTGTCCTTTCAATTGTCTCATCCCTGAGTTCAGAGCTCCTAAGAGAGTTGTGAAGAAACTCAT GGGTCTTGGGAAGAGAAACCA	interleukin 10
Il10rb	NM_008349.5	6620401D04Rik, AI528744, CRF2-4, Crfb4, D16H21S58, D21S58h, IL-10R2, Il10r2	Receptor Activity	CTTTACACCTGCGTTTCTCAGCCCCACAAATTGAGAATGAGCCTGAGACGTGGACCTTGAAGAACATTTATGACTCAT GGGCTTACAGAGTGCAATACTG	interleukin 10 receptor, beta
Il11	NM_008350.2	IL-11	Extracellular Region,Cytoplasm,Extracellular Space,Positive Regulation Of Cell Proliferation,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Positive Regulation Of Mapkkk Cascade,Positive Regulation Of Peptidyl Tyrosine Phosphorylation,Cytokine Activity,Growth Factor Activity	GCGCTGGGACATTGGGATCTTTGCAGCTTCCTGGTGTGCTGACAAGGCTTCGAGTAGACTTGATGTCCTACCTCCGG CATGTACAATGGCTGCGCCGTGC	interleukin 11
Il12a	NM_008351.1	IL-12p35, Il-12a, Lil2a, p35	Extracellular Region,Cytoplasm,Extracellular Space,Positive Regulation Of T Cell Proliferation,Immune Response,Positive Regulation Of Cell Adhesion,Cell Cycle Arrest Go 0007050,Cell Migration,Protein Heterodimerization Activity,Cytokine Activity,Growth Factor Activity	TCATGAAGACATCACACGGGACCAAACCAGCACATTGAAGACCTGTTTACCACTGGAACTACACAAGAACGAGAGTT GCCTGGCTACTAGAGAGACTTCT	interleukin 12a
Il12b	NM_008352.1	Il-12b, Il-12p40, Il12p40, p40	Extracellular Region,Membrane,Cytoplasm,Extracellular Space,Cell Surface Receptor Linked Signal Transduction Go 0007166,Positive Regulation Of T Cell Proliferation,Defense Response To Virus,Cytokine And Chemokine Mediated Signaling Pathway,Positive Regulation Of Cell Adhesion,Cell Cycle Arrest Go 0007050,Cell Migration,Hematopoietin Interf	TCGTAGAGAAGACATCTACCGAAGTCCAATGCAAAGGCGGGAATGTCTGCGTGCAAGCTCAGGATCGCTATTACAAT TCCTCGTGCAGCAAGTGGGCATG	interleukin 12b
Il13	NM_008355.2	Il-13	External Side Of Plasma Membrane,Extracellular Region,Cytoplasm,Extracellular Space,Immune Response,Positive Regulation Of Protein Secretion,Hematopoietin Interferon Classd200 Domain Cytokine Receptor Binding,Cytokine Activity	AGCTACACAAAGCAACTGTTTCGCCACGGCCCCTTCTAATGAGGAGAGACCATCCCTGGGCATCTCAGCTGTGGACT CATTTTCCTTTCTCACATCAGAC	interleukin 13
Il15	NM_008357.1	AI503618, IL-15	Extracellular Region,Cytoplasm,Extracellular Space,Positive Regulation Of Cell Proliferation,Positive Regulation Of Immune Response,Positive Regulation Of T Cell Proliferation,Immune Response,Hematopoietin Interferon Classd200 Domain Cytokine Receptor Binding,Cytokine Activity	GTGTTTGGAAGGCTGAGTTCCACATCTAACAGCTCAGAGAGGTCAGGAAAGAATCCACCTTGACACATGGCCCTCTG GCTCTTCAAAGCACTGCCTCTTC	interleukin 15
Il17a	NM_010552.3	Ctla-8, Ctla8, IL-17, IL-17A, Il17	External Side Of Plasma Membrane,Extracellular Region,Extracellular Space,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Inflammatory Response,Cytokine Activity	ACCTCAAAGTCTTTAACTCCCTTGGCGCAAAAGTGAGCTCCAGAAGGCCCTCAGACTACCTCAACCGTTCCACGTCAC CCTGGACTCTCCACCGCAATGA	interleukin 17A
Il18	NM_008360.1	Igif, Il-18	Extracellular Region,Cytoplasm,Extracellular Space,Apical Plasma Membrane,Regulation Of Cell Adhesion,Inflammatory Response,Immune Response,Angiogenesis,Mapkkk Cascade Go 0000165,Interferon Gamma Biosynthetic Process,Response To Hypoxia,Cytokine Activity	CCAGCATCAGGACAAAGAAAGCCGCCTCAAACCTTCCAAATCACTTCCTCTTGGCCCAGGAACAATGGCTGCCATGTC AGAAGACTCTTGCGTCAACTTC	interleukin 18
Il18rap	NM_010553.2	AcPL, IL-18R-beta, IL-18RAcP, IL-18Rbeta, IL-1RAcPL	Intrinsic To Membrane,Membrane,Integral To Membrane,Signal Transduction,Cytokine And Chemokine Mediated Signaling Pathway,Innate Immune Response,Receptor Activity,Transmembrane Receptor Activity	CTTGAAGTCGGTCCACGCCAGTTCCAGGTTCTGGACCCAAATTCGTTACCACATGCCTGTGAAGAACTCCAACAGGTT TATGTTCAACGGGCTCAGAATT	interleukin 18 receptor accessory protein
Il1b	NM_008361.3	IL-1beta, Il-1b	Extracellular Region,Vesicle,Secretory Granule,Extracellular Space,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Activation Of Mapk Activity,Activation Of Nf Kappab Transcription Factor,Positive Regulation Of I Kappab Kinase Nf Kappab Cascade,Positive Regulation Of T Cell Proliferation,Inflammatory Response,Response	GTTGATTCAAGGGGACATTAGGCAGCACTCTCTAGAACAGAACCTAGCTGTCAACGTGTGGGGGATGAATTGGTCAT AGCCCGCACTGAGGTCTTTCATT	interleukin 1 beta

Continue Table S1: Nanostring nCounter SC Mouse Inflammation V2 Panel Gene List

Il1r1	NM_001123382.1	CD121a, CD121b, IL-IR, Il1r-1	Cell Surface,Extracellular Region,Intrinsic To Membrane,Membrane,Integral To Membrane, Protein Complex, Plasma Membrane,Signal Transduction,Cytokine And Chemokine Mediated Signaling Pathway,Innate Immune Response,Receptor Activity,Transmembrane Receptor Activity	CTTCTTCGGAGTAAAAGATAAACTGTTGGTGAGGAATGTGGCTGAAGAGCACAGAGGGGACTATATATGCCGTATGTCCTATACGTTCCGGGGGGAAGCAA	interleukin 1 receptor, type I
Il1rn	NM_031167.4	F630041P17Rik, IL-1ra	Extracellular Region, Cytoplasm, Vesicle, Nucleus, Extracellular Space, Centrosome, Negative Regulation Of Apoptosis, Lipid Metabolic Process, Positive Regulation Of Jnk Activity, Receptor Activity	ACACTGAAAATGTCCACTTTGTTAGTTTGTGAACATGAGCCCAGGCCTAAGGTGCTGGGAAACAGAAAGGGGCGGGAGATTTTTCTTTATTCTATGGCTAG	interleukin 1 receptor antagonist
Il2	NM_008366.3	Il-2	Extracellular Region ,Extracellular Space,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Positive Regulation Of T Cell Proliferation,Immune Response,G Protein Coupled Receptor Protein Signaling Pathway,Positive Regulation Of Protein Amino Acid Phosphorylation,Carbohydrate Binding,Cytokine Activity,Growth Factor Activit	TCTTCAGTGCCTAGAAGATGAACTTGGACCTCTGCGGCATGTTCTGGATTTGACTCAAAGCAAAAGCTTTCAATTGGAAGATGCTGAAGAATTTCATCAGC	interleukin 2
Il21	NM_021782.2		Extracellular Region ,Extracellular Space,Positive Regulation Of T Cell Proliferation,Immune Response,Cell Maturation,Hematopoietin Interferon Classd200 Domain Cytokine Receptor Binding,Cytokine Activity	ATGGCCTGGGGGATGGTTTTGATCTAAGGAAAAAGGTGTCTGTACCTCACAGTGCCTTTAAAACAAGCAGAGATCCCGTGTACCGCCTAAGATAGCACA	interleukin 21
Il22ra2	NM_178258.5	CRF2-10, CRF2-s1, CRF2X, Il-22bp	Extracellular Region, Cytosol,Cytokine And Chemokine Mediated Signaling Pathway,Receptor Activity	TAAGCATTGCCTTCTAGGTCTCCTCATCATACTCTTGAGCAGTGCAACAGAAATACAACCAGCTCGTGTATCTCTGACGCCCCAGAAGGTCCGATTTCAG	interleukin 22 receptor, alpha 2
Il23a	NM_031252.1	IL-23, p19	Extracellular Region ,Extracellular Space,Response To Virus,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,T Cell Proliferation,Positive Regulation Of T Cell Proliferation,Inflammatory Response,Immune Response,Innate Immune Response,Tissue Remodeling,Cytokine Activity	CAAGGACAACAGCCAGTTCTGCTTGCAAAGGATCCGCCAAGGTCTGGCTTTTTATAAGCACCTGCTTGACTCTGACATCTTCAAAGGGGAGCCTGCTCTA	interleukin 23, alpha subunit p19
Il23r	NM_144548.1	IL-23R	Membrane, Integral To Membrane, Integral To Plasma Membrane, Plasma Membrane, Jak Stat Cascade, Inflammatory Response, Cytokine And Chemokine Mediated Signaling Pathway, Innate Immune Response, Receptor Activity	AAGTATTTGGTATGGGTCCAAGCTGTCAATTCCCTAGGCATGGAGAACTCACAACAACTACACGTCCATCTGGATGATATAGTGATACCTTCTGCGTCCA	interleukin 23 receptor
Il3	NM_010556.4	BPA, Csfmu, HCGF, Il-3, MCGF, PSF	Extracellular Region ,Extracellular Space,Positive Regulation Of Cell Proliferation, Negative Regulation Of Apoptosis, Hemopoiesis, Regulation Of Gene Expression, Immune Response,Cytokine And Chemokine Mediated Signaling Pathway,Response To Hormone Stimulus,Positive Regulation Of Protein Amino Acid Phosphorylation,Regulation Of Apoptosis,Respon	TGCAGCTCTATTGTCAAGGAGATTATAGGGAAGCTCCAGAACCTGAACTCAAAACTGATGATGAAGGACCCTCTCTGAGGAATAAGAGCTTTCGGAGAG	interleukin 3
Il4	NM_021283.1	BSF-1, Il-4	External Side Of Plasma Membrane, Extracellular Region, Extracellular Space, Positive Regulation Of Transcriptiondna Dependent, Positive Regulation Of Cell Proliferation, Negative Regulation Of Apoptosis, Positive Regulation Of Transcription From Rna Polymerase Ii Promoter, Negative Regulation Of Transcription Dna Dependent, Regulation Of Phosphor	TGCTTGAAGAAGAACTCTAGTGTTCTCATGGAGCTGCAGAGACTCTTTCGGGCTTTTCGATGCCTGGATTCATCGATAAGCTGCACCATGAATGAGTCCA	interleukin 4
Il5	NM_010558.1	Il-5	Extracellular Region ,Extracellular Space,Soluble Fraction, Positive Regulation Of Transcriptiondna Dependent, Positive Regulation Of Cell Proliferation, Immune Response, Positive Regulation Of Transcription Factor Activity, Cytokine And Chemokine Mediated Signaling Pathway, Positive Regulation Of Peptidyl Tyrosine Phosphorylation, Cytokine Activi	CAATGAGACGATGAGGCTTCCTGTCCCTACTCATAAAAATCACCAGCTATGCATTGGAGAAATCTTTCAGGGGCTAGACATACTGAAGAATCAAACTGTC	interleukin 5
Il6	NM_031168.1	Il-6	External Side Of Plasma Membrane, Extracellular Region, Extracellular Space, Positive Regulation Of Translation, Positive Regulation Of Transcriptiondna Dependent, Positive Regulation Of Cell Proliferation, Negative Regulation Of Apoptosis, Neurite Development, Positive Regulation Of Transcription From Rna Polymerase Ii Promoter, Positive Regulatio	CTCTCTGCAAGAGACTTCCATCCAGTTGCCTTCTTGGGACTGATGCTGGTGACAACCACGGCCTTCCCTACTTCACAAGTCCGGAGAGGAGACTTCACAG	interleukin 6
Il6ra	NM_010559.2	CD126, IL-6R, Il6r	Cell Surface,Extracellular Region,Membrane, Integral To Membrane,Extracellular Space,Apical Plasma Membrane, Positive Regulation Of Cell Proliferation,Cytokine And Chemokine Mediated Signaling Pathway, Positive Regulation Of Mapkkk Cascade,Positive Regulation Of Peptidyl Tyrosine Phosphorylation,Protein Homodimerization Activity,Receptor Acti	CACCTCACTGCCACCTTGGCCTTCCTTGCTTTACGTTTGACTGAGTGGCCTCAGATGCTTTCCCCTGGGGCTTTGAGGAATCCAGTGATGTTGGTCA	interleukin 6 receptor, alpha
Il7	NM_008371.2	A630026I06Rik, Il-7, hlb368	Extracellular Region, Extracellular Space,Negative Regulation Of Apoptosis,Regulation Of Gene Expression, Immune Response,Anti Apoptosis,Negative Regulation Of Catalytic Activity,Hematopoietin Interferon Classd200 Domain Cytokine Receptor Binding,Cytokine Activity,Growth Factor Activity	AAACATTCATTGGTGAACCACTGGGGGAGTGGAACTGTCCTGTTTAGACTGGAGATACTGGAGGGCTCACGGTGATGGATAATGCTCTTGAAAACAAGA	interleukin 7
Il9	NM_008373.1	Il-9, P40	Extracellular Region, Extracellular Space,Soluble Fraction, Immune Response,Hematopoietin Interferon Classd200 Domain Cytokine Receptor Binding,Cytokine Activity,Growth Factor Activity	TCTGTTTTGCTCTTCAGTTCTGTGCTGGGCCAGAGATGCAGCACCACATGGGGCATCAGAGACACCAATTACCTTATTGAAAATCTGAAGGATGATCCAC	interleukin 9
Irf1	NM_008390.1	AU020929, Irf-1	Nucleus,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,I Kappab Kinase Nf Kappab Cascade,Regulation Of Gene Expression,Regulation Of Transcriptiondna Dependent,Sequence Specific Dna Binding,Transcription Factor Activity,Dna Binding	TGTTCCGGAGCTGGGCCATTCACACAGGCCGATACAAAGCAGGAGAAAAAGAGCCAGATCCCAAGACATGGAAGGCAAACTTCCGTTGTGCCATGAACTC	interferon regulatory factor 1
Irf3	NM_016849.3	C920001K05Rik, IRF-3	Cytoplasm,Nucleus,Response To Virus,Transcription Dna Dependent,Positive Regulation Of I Kappab Kinase Nf Kappab Cascade,Positive Regulation Of Cytokine Secretion,Response To Bacterium,Regulation Of Transcriptiondna Dependent,Negative Regulation Of Transcription From Rna Polymerase Ii Promoter,Protein Homodimerization Activity,Identical Pr	GCTGCTACCAATAAAGCAGTTTATGCCGCCATCACATCTGCTGTCGACTGCGTCTAGGCTGGTGGTTATTCTACAAGGCTCAGTCTTCCCATCTGCAGCT	interferon regulatory factor 3
Irf5	NM_012057.3	AW491843, mirf5	Nucleus,Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent,Transcription Factor Activity,Dna Binding	CCTTTAGTACCACGGAGTCCAATTACCCCAGGGTAGCCAACTTTTAAGGTTGCCCCAATTCTTCTAGCAAAACCTGCCAAGGAGTGTTGTGGGGCTTTC	interferon regulatory factor 5
Irf7	NM_016850.2		Cytoplasm,Nucleus,Response To Virus,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent,Transcription Factor Activity,Dna Binding	CGCTGTGCACTCCACAGCACAGGGCGTTTTATCTTGCGCCAAGACAATTCAGGGGATCCAGTTGATCCGCATAAGGTGTACGAACTTAGCCGGGAGCTTG	interferon regulatory factor 7
Itgb2	NM_008404.4	2E6, AI528527, Cd18, LAD, LCAMB, Lfa1, MF17	Cell Surface,Membrane, Integral To Membrane, Lipid Raft,Membrane Fraction,Integrin Complex,Regulation Of Peptidyl Tyrosine Phosphorylation,Activation Of Nf Kappab Transcription Factor,Multicellular Organismal Development,Cell Cell Adhesion,Cell Matrix Adhesion, Positive Regulation Of Angiogenesis,Endothelial Cell Migration,Protein Complex Bin	GCTCGGTTTCTTTCCGCCATTATATCAAGTCTGCCAGGGTTTCCAGGGACTTGTCTTCCGACCTGCACAATCTTGCCGCAGAGCCCTAAGAATTGTCCCG	integrin beta 2
Jun	NM_010591.2	AP-1, Junc, c-jun	Nucleus,Cytosol,Nuclear Chromatin,Transcription Factor Complex,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Cell Proliferation,Negative Regulation Of Apoptosis,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Negative Regulation Of Transcription Dna Dependent,Negat	CGCGACCAGAACGATGGACTTTTCGTTAACATTGACCAAGAACTGCATGGACCTAACATTCGATCTCATTCAGTATTAAAGGGGGGTGGGAGGGGTTACA	jun proto-oncogene
Keap1	NM_016679.4	INRF2, mKIAA0132	Cytoplasm,Endoplasmic Reticulum,Nucleus,Focal Adhesion,Centrosome,Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent	TCTATTGTCTCTGCTTGCCATTGTACATTCTGCTCAGACAGGGCATCTTGCTTCTTGTGGGACACACAGTTGTCTGTCAGTTTCAGGCATTAGAAGCCA	kelch-like ECH-associated protein 1
Kng1	NM_023125.3	Kng	Extracellular Region, Microsome, Extracellular Space,Blood Coagulation,Inflammatory Response,Negative Regulation Of Cell Adhesion,Negative Regulation Of Map Kinase Activity,Positive Regulation Of Mapkkk Cascade,Protease Inhibitor Activity,Receptor Binding	ACTTGATGATTTTACAGTGGTCTCCTTTCAGCCATCCCTGACATGAGGCGAATTGGAGCTGTCTCTAAAGCTTGAGTTTGGCCACAGACGCTTATAGTCT	kininogen 1
Limk1	NM_010717.2		Golgi Apparatus,Cytoplasm,Nucleus,Perinuclear Region Of Cytoplasm,Focal Adhesion,Neuron Projection,Protein Amino Acid Phosphorylation,Phosphorylation,Nucleotide Binding,Zinc Ion Binding,Protein Kinase Activity,Kinase Activity,Protein Serine Threonine Kinase Activity,Protein Heterodimerization Activity,Transferase Activity,Transferring Phos	CCACAACTGTCTGGTCCGTGAGAATAGGAACGTGGTGGTGGCCGACTTTGGGCTGGCTCGACTCATGATCGATGAAAAGAATCAGTCTGAAGACTTACGC	LIM-domain containing, protein kinase
Lta	NM_010735.1	LT, LT-[a], LT-alpha, LT[a], LTalpha, Ltx, TNF-beta, TNFSF1, Tnfb, Tnfsf1b, hlb382	Extracellular Region, Membrane, Extracellular Space,Positive Regulation Of Cell Proliferation,Inflammatory Response,Immune Response,Cell Proliferation Go 0008283,Humoral Immune Response,Cytokine Activity	AAGAGGGAAAAATAGAAAGCCGTCAGATGACAACTAGGTCCCAGACACAAAGGTGTCTCACCTCAGACAGGACCCATCTAAGAGAGAGATGGCGAGAGA	lymphotoxin A
Ltb	NM_008518.2	AI662801, LTbeta, Tnfc, Tnfsf3, p33	Membrane, Integral To Membrane, Extracellular Space, Plasma Membrane, Immune Response, Cytokine Activity	ATCAGGGACGTCGGGTTGAGAAGATCATTGGCTCAGGAGCACAGGCTCAGAAAAGACTGGATGACAGCAAACCGTCGTGCATCTTGCCCTCACCCTCTAG	lymphotoxin B
Ltb4r1	NM_008519.2	BLT1, BLTR, Ltb4r, mBLTR	Membrane, Integral To Membrane, Plasma Membrane, Signal Transduction, G Protein Coupled Receptor Protein Signaling Pathway, G Protein Coupled Receptor Activity, Receptor Activity	AAACCCTGTCCTTTTGATGGCTGCAAACACTACATCTCCTGCAGCACCTTCTTCTCCTGGTGGCATGTCCCTGTCTCTGTTGCCCATTGTTCTACTGTCT	leukotriene B4 receptor 1
Ltb4r2	NM_020490.2	5830462O07Rik, BLT2, LTB4-R 2, LTB4-R-2, LTB4-R2	Membrane, Integral To Membrane, Membrane Fraction, Plasma Membrane, Signal Transduction, G Protein Coupled Receptor Protein Signaling Pathway, G Protein Coupled Receptor Activity, Receptor Activity	GCACACGGGTGGGTCGTCTGGTGAGCGCATCGTGCTGGCCTTTGGCTTGCTCTGGGCTCCCTACCACGCGGTCAATCTCCTACAGCGGTGGCGCGCT	leukotriene B4 receptor 2
Ly96	NM_016923.1	ESOP-1, MD-2, MD2	Extracellular Region, Inflammatory Response, Innate Immune Response	GAGCTCTGAAGGAGAGACTGTGAATACATCAATACCATTCTCTTTCGAGGGAATACTATTTCCTAAGGGCCATTACAGATGTGTTGCAGAAGCTATTGC	lymphocyte antigen 96

Continue Table S1: Nanostring nCounter SC Mouse Inflammation V2 Panel Gene List

Maff	NM_010755.3		Nucleus,Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent,Sequence Specific Dna Binding,Transcription Factor Activity,Dna Binding	TGGGGAGGGGCAACTTTGCTAAGTTGGGGGTGGGGGGAGGCGTTAGGGTTCTAAGTTTCCCTGGGCTGAAAGTCCG GCTCAAATTGAAAATGAGGTCGTG	v-maf musculoaponeurotic fibrosarcoma oncogene family, protein F (avian)
Mafg	XM_001002362.1	AA545192, C630022N07Rik	Nucleus,Regulation Of Cellular Ph,Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent,Regulation Of Cell Proliferation,Sequence Specific Dna Binding,Transcription Factor Activity,Dna Binding	AAGAATGTCCTTGGCAAGGCTTTAGAAAGCTGAAAATGAGGTTGAGCCCGGAGGGGCGGCTGACTGTAGGAGGGAC CTGTTTTGCTTTTGTTCCCTGGCC	v-maf musculoaponeurotic fibrosarcoma oncogene family, protein G (avian)
Mafk	NM_010757.2	AW061068, NF-E2, Nfe2u	Nucleus,Nervous System Development,Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent,Sequence Specific Dna Binding,Transcription Factor Activity,Dna Binding	GGGTAGACACCATTCTGCCTGTCCCTTTCTGGGCTTGGGCCTTCTTTGTCCTTATCAAAGGGCGCTACAACCTGCTTTAG CTCTTAGAGCCAGGCTCATGT	v-maf musculoaponeurotic fibrosarcoma oncogene family, protein K (avian)
Map2k1	NM_008927.3	MAPKK1, MEKK1, Mek1, Prkmk1	Golgi Apparatus, Cytoplasm, Nucleus,Cytosol,Cytoskeleton,Perinuclear Region Of Cytoplasm,Cell Cortex,Microtubule,Dendrite,Plasma Membrane,Soluble Fraction,Positive Regulation Of Cell Differentiation,Activation Of Mapk Activity,Response To Oxidative Stress,Keratinocyte Differentiation,Negative Regulation Of Cell Proliferation,Cell Proliferati	CTTTGTGCTTGGGCTATTTGTCTGTTCATCAAACACATGCCAGGCTGAACTACAGTGAAACCCTAGTGACCTGGGTG GTCGTTCTTACTGATGTTTGCA	mitogen-activated protein kinase kinase 1
Map2k4	NM_009157.4	JNKK1, MEK4, MKK4, PRKMK4, Sek1, Serk1	Cytoplasm,Nucleus,Cytosol,Activation Of Jnk Activity,Jnk Cascade,Response To Stress,Mapkkk Cascade Go 0000165,Protein Amino Acid Phosphorylation,Phosphorylation,Positive Regulation Of Protein Amino Acid Phosphorylation,Apoptosis Go,Nucleotide Binding,Protein Kinase Activity,Kinase Activity,Protein Serine Threonine Kinase Activity,Protein T	CTCGCCCAGACACCATGTGCAATAAGACTGGTGTTCGTTTCCATCATGTCTGTATACTTCTGTCATCTAGACTGTGCAT CCCTGTAATACCTGACTGATC	mitogen-activated protein kinase kinase 4
Map2k6	NM_011943.2	MEK6, MKK6, Prkmk6, SAPKK3	Cytoplasm,Nucleus,Cytoskeleton,Transcription Dna Dependent,Activation Of Mapk Activity,Response To Stress,Regulation Of Transcriptiondna Dependent,Mapkkk Cascade Go 0000165,Protein Amino Acid Phosphorylation,Phosphorylation,Apoptosis Go,Nucleotide Binding,Protein Kinase Activity,Kinase Activity,Protein Serine Threonine Kinase Activity,Prot	GGGCCTTAAGATTCCAAAAGAAGCGTTTGAACAGCCTCAGACCAGTTCCACGCCGCCTCGGGATTTAGACTCCAAGG CTTGCATATCTATTGGAAACCAG	mitogen-activated protein kinase kinase 6
Map3k1	NM_011945.2	MAPKKK1, MEKK1, Mekk	Cytoplasm,Cytoskeleton,Membrane Fraction,Protein Polyubiquitination,Protein Oligomerization,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Activation Of Jnk Activity,Regulation Of Cell Migration,Protein Amino Acid Autophosphorylation,Jnk Cascade,Positive Regulation Of Map Kinase Activity,Apoptotic Mitochondrial Change	CAGCAGATTCCTTCCGCTTACAAAGATTTGGCCGAGCCATGGATTCAGGTGTTTGGAATGGAACTCGTTGGCTGCTTA TTCTCTAGAAACTGGAACGTAA	mitogen-activated protein kinase kinase 1
Map3k5	NM_008580.4	7420452D20Rik, ASK, ASK1, MAPKKK5, Mekk5	Cytoplasm,Endoplasmic Reticulum,Activation Of Mapk Activity,Jnk Cascade,Positive Regulation Of Caspase Activity,Response To Stress,Mapkkk Cascade Go 0000165,Protein Amino Acid Phosphorylation,Innate Immune Response,Phosphorylation,Apoptosis Go,Caspase Activation,Nucleotide Binding,Protein Homodimerization Activity,Protein Kinase Activity,K	CATCATCCTCTACTGCGATACTAATTCCGATTCACTCCAGTCCCTGAAGGAAATTATTTGCCAGAAGAATACTGTGTGC ACCGGGAACTACACCTTCATC	mitogen-activated protein kinase kinase 5
Map3k7	NM_172688.2	B430101B05, C87327, Tak1	Membrane,Cytoplasm,Plasma Membrane,Soluble Fraction,Negative Regulation Of Apoptosis,Signal Transduction,Transcription Dna Dependent,Activation Of Mapk Activity,Jnk Cascade,Positive Regulation Of I Kappab Kinase Nf Kappab Cascade,Response To Stress,Angiogenesis,Regulation Of Transcriptiondna Dependent,Transforming Growth Factor Beta Recept	CAATACTAACTGTAGTCCCACCTGTTACTATTAAAGGTGAGTGGTGGCAGCTGTGCTTAAGGAGAGCAAGTTTACTGA CTTTCGTGAGGTTGAGCATCGT	mitogen-activated protein kinase kinase kinase 7
Map3k9	NM_177395.4	E130314H24Rik, Mlk1, Prke1	Transcription Dna Dependent,Protein Amino Acid Autophosphorylation,Response To Stress,Regulation Of Transcriptiondna Dependent,Protein Amino Acid Phosphorylation,Phosphorylation,Apoptosis Go,Nucleotide Binding,Protein Kinase Activity,Kinase Activity,Protein Serine Threonine Kinase Activity,Protein Tyrosine Kinase Activity,Transferase Activ	AATGCCCTTCTAGGCAACAGGTGCCTTAGGTGTGCTGCATCCTCACTTGTAGGCTGGAGGCCTGGGAAGCAAATTCTT TGCATCTCTGTTTTCATAGGC	mitogen-activated protein kinase kinase kinase 9
Mapk14	NM_011951.2	CSBP2, Crk1, Csbp1, Mxi2, PRKM14, PRKM15, p38, p38-alpha, p38MAPK, p38a, p38alpha	Spindle Pole,Cytoplasm,Cytosolic Part,Nucleus,Cytosol,Mitochondrion,Soluble Fraction,Glucose Metabolic Process,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Protein Amino Acid Autophosphorylation,Fatty Acid Oxidation,Response To Stress,Angiogenesis,Protein Kinase Cascade,Regulation Of Tran	GAAGACCTTCTCATGGGAACTCTCCAAATACCATTCAAGTGCCTCTTGTTGAAAGATTCCTTCATGGTGGAAGGGGGT GCATGTATGTGTTAGTGTTTGT	mitogen-activated protein kinase 14
Mapk3	NM_011952.2	Erk-1, Erk1, Ert2, Esrk1, Mnk1, Mtap2k, Prkm3, p44, p44erk1, p44mapk	Nucleoplasm,Cytoplasm,Insoluble Fraction,Nucleus,Cytosol,Protein Complex,Soluble Fraction,Positive Regulation Of Translation,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Transcription Dna Dependent,Response To Toxin,Organ Morphogenesis,Regulation Of Transcription Factor Activity,Protein Complex A	ACCTTAATTGCATCATTAACATGAAGGCCGGAAACTACCTGCAGTCTCTGCCCTCGAAACCAAGGTGGCTTGGGCCA AGCTCTTTCCTAAATCTGACTC	mitogen-activated protein kinase 3
Mapk8	NM_016700.3	AI849689, JNK, JNK1, Prkm8, SAPK1	Cytoplasm,Vesicle,Nucleus,Cytosol,Mitochondrion,Negative Regulation Of Apoptosis,Neurite Development,Signal Transduction,Response To Heat,Jnk Cascade,Inflammatory Response,Regulation Of Transcriptiondna Dependent,Response To Uv,Positive Regulation Of Cell Migration,Mapkkk Cascade Go 0000165,Protein Amino Acid Phosphorylation,Phosphorylatio	GAAAACAGGCCTAAATACGCTGGATATAGCTTTGAGAAACTGTTCCCCGATGTGCTTTTCCCAGCTGACTCAGAGCAT AACAAACTTAAAGCCAGTCAGG	mitogen-activated protein kinase 8
Mapkapk2	NM_008551.1	AA960234, MAPKAP-K2, MK-2, MK2, Rps6kc1	Cytoplasm,Nucleus,Inflammatory Response,Response To Stress,Protein Amino Acid Phosphorylation,Phosphorylation,Response To Dna Damage Stimulus,Nucleotide Binding,Protein Kinase Activity,Kinase Activity,Protein Serine Threonine Kinase Activity,Transferase Activity,Transferase Activity Transferring Phosphorus Containing Groups,Atp Binding	GTAGCCTCTGCTTGCCCTTCTTGCCACGATTAACCCACTCTTGTCGAGTTCTCTGAAATTTTAGCCATTTCTCAATGGG CTGTCCACTCCCACGGTGAG	MAP kinase-activated protein kinase 2
Mapkapk5	XM_990515.1	MK5, PRAK	Cytoplasm,Nucleus,Protein Amino Acid Autophosphorylation,Regulation Of Translation,Ras Protein Signal Transduction,Response To Stress,Protein Amino Acid Phosphorylation,Phosphorylation,Nucleotide Binding,Protein Kinase Activity,Kinase Activity,Protein Serine Threonine Kinase Activity,Transferase Activity Transferring Phosphorus Containing	GGCTGCAGCAGGCAGCAACATCTCCGACCCCGCTAAGCTGACAGGACGACGACGCGATCCGGCCAGGCCTCGCGCCGT CTTACGTCATTCACCCAGCGCCAC	MAP kinase-activated protein kinase 5
Masp1	NM_008555.2	AW048060, CCPII, Craf, Masp1/3	Extracellular Region,Extracellular Space,Proteolysis,Innate Immune Response,Serine Type Peptidase Activity,Protein Homodimerization Activity,Calcium Ion Binding,Peptidase Activity,Serine Type Endopeptidase Activity	CCCGGCAGGGGTTTCGAATCAAGCTTTACTTCATGCACTTCAACTTGGAATCCTCCTATCTTTGTGAATACGACTATGTG AAGGTAGAAACAGAAGACCAG	mannan-binding lectin serine peptidase 1
Masp2	NM_010767.3	MASP-2, MAp19	Extracellular Region,Proteolysis,Innate Immune Response,Serine Type Peptidase Activity,Calcium Ion Binding,Peptidase Activity,Serine Type Endopeptidase Activity	TCACTGGGTCCCAGCCTAAAGGTCACCTTCCACTCCGACTACTCCAATGAGAAGCCGTTCACAGGGTTTGAGGCCTTC TATGCAGCGGAGGATGTGGATG	mannan-binding lectin serine peptidase 2
Max	NM_008558.1	AA960152, AI875693, bHLHd4, bHLHd5, bHLHd6, bHLHd7, bHLHd8	Cytoplasm,Nucleus,Dendrite,Pml Body,Regulation Of Transcriptiondna Dependent,Protein Complex Assembly,Protein Homodimerization Activity,Protein Complex Binding,Sequence Specific Dna Binding,Transcription Factor Activity,Protein Heterodimerization Activity,Dna Binding	CCGGCCGCCGCTGCAGTGGCCGCTCCCTGGGCCGTAGGAAATGAGCGATAACGATGACATCGAGGTGGAGAGCGA CGAAGAGCAACGCAAGGTTTCAATCT	Max protein
Mbl2	NM_010776.1	L-MBP, MBL, MBL-C, MBP-C	Extracellular Region,Extracellular Space,Collagen,Protein Oligomerization,Innate Immune Response,Sugar Binding,Receptor Binding	CCCTGAGAAACTGGGTGCTCTTCTCTGAGTGAAAAAGTTGGAAAGAAGTATTTTGTGAGCAGTGTTAAAAAGATGA GCCTTGACAGAGTGAAGGCCCT	mannose-binding lectin (protein C) 2
Mef2a	XM_976032.1	A430079H05Rik	Nucleus,Nuclear Chromatin,Positive Regulation Of Transcriptiondna Dependent,Nervous System Development,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Multicellular Organismal Development,Regulation Of Transcription From Rna Polymerase Ii Promoter,Regulation Of Transcriptiondna Dependent,Neg	AAGTATCATTCAATGGCTCTTACAGAACCTGTGTATTCGACCTGTGCTCTCTAACACATTTTACAAAAACAAAGCAAAC AAACAAAGAGCTCATGGAAAG	myocyte enhancer factor 2A
Mef2b	NM_001045484.1	AI451606	Nucleus,Regulation Of Transcriptiondna Dependent,Transcription Factor Activity	GACAGCTGGCCACGGTAGCGCTCCAAGAGGTTCCTCCAGCCTCCACAGAGTTCCCGAAGTCTCAGGTTCCCTATACC ACCAGGACGGACGACGACGAGGCCA	myocyte enhancer factor 2B
Mef2c_Mm	NM_025282.2			AATAATCGTAAGCCAGATCTCCGCGTTCTTATCCCACCTGGCAGCAAGAACACGATGCCATCAGTGAATCAAGGGATA AATAACTCCCAGTCGGCTCAGT	myocyte enhancer factor 2C
Mef2d	NM_133665.3	C80750	Nucleus,Positive Regulation Of Transcriptiondna Dependent,Nervous System Development,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Multicellular Organismal Development,Regulation Of Transcriptiondna Dependent,Transcription From Rna Polymerase Ii Promoter,Apoptosis Go,Protein Homodimerizati	TCAGCTGTGAAGAGGATGCGGCTGGATACTTGGACATTAAAGTGATGGTTCCCACTCCCTCCTTTCAGCCTCCCTGAT GAAGAGTTGACAATCTCACCGC	myocyte enhancer factor 2D
Mknk1	NM_021461.4	2410048M24Rik, Mnk1	Regulation Of Translation,Response To Stress,Protein Kinase Cascade,Protein Amino Acid Phosphorylation,Phosphorylation,Nucleotide Binding,Protein Kinase Activity,Kinase Activity,Protein Serine Threonine Kinase Activity,Transferase Activity Transferring Phosphorus Containing Groups,Atp Binding	AAGGCATTGCTCACCGTGATCTGAAGCCAGAAAACATACTGTGTGAATCTCCAGAAAAGGTGTCTCCGGTGAAAATTT GTGACTTTGACTTGGGCAGTGG	MAP kinase-interacting serine/threonine kinase 1
Mmp3	NM_010809.1	SLN-1, SLN1, STR-1, Stmy1, Str1	Proteinaceous Extracellular Matrix,Extracellular Region,Nucleus,Dendrite,Extracellular Space,Extracellular Matrix,Protein Complex,Regulation Of Cell Migration,Proteolysis,Zinc Ion Binding,Calcium Ion Binding,Metallopeptidase Activity,Protein Complex Binding,Peptidase Activity,Metalloendopeptidase Activity	TCTTTGTGAAAGGAAGTGCTTTGTTCAGCATGTGCTATGGCAGAACCAAACAGGAGCTATGGATGACACCAGTCAAC GTCAAGTTGTCAAAGGATGTTCA	matrix metallopeptidase 3
Mmp9	NM_013599.2	AW743869, B/MMP9, Clg4b, MMP-9, pro-MMP-9	Proteinaceous Extracellular Matrix,Extracellular Region,Extracellular Space,Extracellular Matrix,Protein Complex,Skeletal Development,Embryo Implantation,Proteolysis,Response To Oxidative Stress,Positive Regulation Of Angiogenesis,Tissue Remodeling,Response To Drug,Zinc Ion Binding,Metallopeptidase Activity,Protein Complex Binding,Peptidas	CCTCTACAGAGTCTTTGAGTCCGGCAGACAATCCTTGCAATGTGGATGTTTTTGATGCTATTGCTGAGATCCAGGGCG CTCTGCATTTCTTCAAGGACGG	matrix metallopeptidase 9

Continue Table S1: Nanostring nCounter SC Mouse Inflammation V2 Panel Gene List

Mrc1	NM_008625.1	AW259686, CD206, MR	Cell Surface,Membrane,Integral To Membrane,Endosome,Plasma Membrane,Receptor Mediated Endocytosis,Sugar Binding,Receptor Activity,Transmembrane Receptor Activity	GTTCCGAAATGTTGAAGGGAAGTGGCTTTGGTTGAACGACAATCCTGTCTCCTTTGTCAACTGGAAAACAGGCGATCC CTCTGGTGAACGGAATGATTGT	mannose receptor, C type 1
Mx2	NM_013606.1	AI528743, Mx-2	Cytoplasm,Cytosol,Response To Virus,Innate Immune Response,Gtp Binding,Nucleotide Binding,Gtpase Activity	TGTCCTTCCCTGTGTTTCCTGGATTGTGATTCAGGGACAGAAGGGCTCCTGCCTTTCCTGGTAGCTATACCACCAGCCT TTATGCTCTGATAAGTGCTAG	myxovirus (influenza virus) resistance 2
Myc	NM_010849.4	AU016757, Myc2, Niard, Nird, bHLHe39	Nucleoplasm,Axon,Cytoplasm,Nucleus,Spindle,Nuclear Body,Protein Complex,Nucleolus,Glucose Metabolic Process,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Cell Proliferation,Chromatin Remodeling,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Positive Regulation Of	CCCTCAACGTGAACTTCACCAACAGGAACTATGACCTCGACTACGACTCCGTACAGCCCTATTTCATCTGCGACGAGG AAGAGAATTTCTATCACCAGCA	myelocytomatosis oncogene
Myd88	NM_010851.2	0 Cascade,Inflammato	Cytoplasm,Cytosol,Protein Complex,Plasma Membrane,Response To Virus,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Cell Surface Receptor Linked Signal Transduction Go 0007166,Activation Of Nf Kappab Transcription Factor,Jnk Cascade,Positive Regulation Of I Kappab Kinase Nf Kappab	GCTGCAGGCTCAGCTGTTTTCTCCCCAGCAGCGAGGTTTGCATCTTCTTATTCCTTTCACGTTCTCTACCATAGAGGCA ATGTCATGGTCCCTCTCAGGG	myeloid differentiation primary response gene 88
Myl2	NM_010861.3	MLC-2, MLC-2v, Mlc2v, Mylpc	Myofibril,Cytoskeleton,Myosin Complex,Heart Development,Calcium Ion Binding	TGCTGCCCTAGGACGAGTGAACGTGAAAAATGAAGAGATCGATGAAATGATCAAAGAGGCTCCAGGTCCAATTAACT TCACCGTGTTCCTCACGATGTTT	myosin, light polypeptide 2, regulatory, cardiac, slow
Nfatc3	NM_010901.2	C80703, D8Ertd281e, NFAT4, NFATx	Cytoplasm,Nucleus,Cytosol,Plasma Membrane,Nucleolus,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Regulation Of Transcriptiondna Dependent,Heart Development,Cellular Respiration,Transcription Factor Activity,Chromatin Binding,Dna Binding	GGGCTCACATTGTCCTTGAAGTTCCTCCCTATCATAACCCAGCAGTTACATCTGCCGTGCAGGTGCACTTTTATCTTTG CAATGGCAAGAGGAAAAAAAG	nuclear factor of activated T cells, cytoplasmic, calcineurin dependent 3
Nfe2l2	NM_010902.3	AI194320, Nrf2	Chromatin,Cytoplasm,Nucleus,Centrosome,Plasma Membrane,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Unfolded Protein Response,Regulation Of Transcriptiondna Dependent,Protein Domain Specific Binding,Sequence Specific Dna Binding,Transcript	CCAAGGAGCAATTCAATGAAGCTCAGCTCGCATTGATCCGAGATATACGCAGGAGAGGTAAGAATAAAGTCGCCGCC CAGAACTGTAGGAAAAGGAAGCT	nuclear factor, erythroid derived 2, like 2
Nfkb1	NM_008689.2	NF-KB1, NF-kappaB, NF-kappaB1, p105, p50, p50/p105	Cytoplasm,Nucleus,Cytosol,Mitochondrion,Protein Complex,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Transcription Dna Dependent,Negative Regulation Of Transcription Dna Dependent,Response To Oxidative Stress,Regulation Of Transcriptiondna Depende	GTCTTACACTTAGCCATCATCCACCTCCACGCTCAGCTTGTGAGGGATCTGCTGGAAGTCACATCTGGTTTGATCTCTG ATGACATCATCAACATGAGAA	nuclear factor of kappa light polypeptide gene enhancer in B cells 1, p105
Nlrp3	NM_145827.3	AGTAVPRL, AI/AVP, Cias1, FCAS, FCU, MWS, Mmig1, NALP3, Pypaf1	Cytoplasm,Positive Regulation Of Caspase Activity,Defense Response To Virus,Interleukin 1 Secretion,Inflammatory Response,Apoptosis Go,Caspase Activation,Nucleotide Binding,Atp Binding	TTGTCAGGATCTCGCATTGGTTCTGAGCTCCAACCATTCTCTGACCAGACTGTACATTGGAGAAAATGCCTTGGGAGA CTCAGGAGTCCAAGTTTTGTGT	NLR family, pyrin domain containing 3
Nod1	NM_172729.2	C230079P11, Card4, F830007N14Rik, Nlrc1	Membrane,Cytoplasm,Basolateral Plasma Membrane,Plasma Membrane,Interleukin 8 Biosynthetic Process,Defense Response,Activation Of Nf Kappab Transcription Factor,Positive Regulation Of I Kappab Kinase Nf Kappab Cascade,Defense Response To Bacterium,Regulation Of Apoptosis,Apoptosis Go,Caspase Activation,Nucleotide Binding,Protein Homodimeriz	TGGATCATCTTCGGTTGTTTCCAGCACTTCCAGACGGTCTTCGAGGGCTCCTCTTCACAGTTGCCGGACTGTGCTGTG ACCCTGACCGATGTCTTTCTGC	nucleotide-binding oligomerization domain containing 1
Nod2	NM_145857.2	ACUG, BLAU, CD, Card15, F830032C23Rik, IBD1, Nlrc2	Cell Surface,Cytoplasm,Vesicle,Cytosol,Plasma Membrane,Protein Oligomerization,Positive Regulation Of Cell Proliferation,Signal Transduction,Defense Response,Activation Of Nf Kappab Transcription Factor,Positive Regulation Of I Kappab Kinase Nf Kappab Cascade,Inflammatory Response,Activation Of Immune Response,Defense Response To Bacterium	CTGTGACGAAGGGGTATATTCTCTCGCAGAAGGACTCAAGAGAAATTCAACTTTGAAATTCTTGAAACTGTCCAACAA TGGCATCACCTACCGGGGTGCA	nucleotide-binding oligomerization domain containing 2
Nos2	NM_010927.3	NOS-II, Nos-2, Nos2a, i-NOS, iNOS	Cytoplasm,Nucleus,Cytosol,Perinuclear Region Of Cytoplasm,Extracellular Space,Cortical Cytoskeleton,Peroxisome,Vesicle Membrane,Signal Transduction,Superoxide Metabolic Process,Regulation Of Phosphorylation,Inflammatory Response,Regulation Of Heart Contraction,Protein Kinase Cascade,Regulation Of Catalytic Activity,Defense Response To Bact	CCCCCCTCCTCCACCCTACCAAGTAGTATTGTACTATTGTGGACTACTAAATCTCTCTCCTCTCCCCCTCCCTCTCTC CCTTTCCTCCCTTCTTCTCC	nitric oxide synthase 2, inducible
Nox1	NM_172203.1	GP91-2, MOX1, NOH-1, NOH1, NOX1a, NOX1alpha, Nox-1	Cell Junction,Membrane,Cytoplasm,Early Endosome,Integral To Membrane,Cell Projection,Endosome,Plasma Membrane,Positive Regulation Of Cell Proliferation,Signal Transduction,Superoxide Metabolic Process,Response To Stress,Angiogenesis,Transport,Cell Migration,Electron Carrier Activity,Oxidoreductase Activity	CTCCAAACATGACAGTGATGTATGCAGCATTTACCAGTATTGCTGGCCTTACTGGAGTGATTGCCACTGTAGCTTTGGT TCTCATGGTAACGTCAGCTAT	NADPH oxidase 1
Nr3c1	NM_008173.3	GR, Gr-1, Grl1	Membrane,Cytoplasm,Nucleus,Cytosol,Protein Complex,Chromatin Remodeling,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent,Anti Apoptosis,Regulation Of Cell Proliferation,Protein Homodimerization Activity,Hormone Binding,Protein Complex Binding,Transcrip	ACCAGGATTCAGAAACTTACACCTGGATGACCAAATGACCCTTCTACAGTACTCATGGATGTTTCTCATGGCATTTGCC CTGGGTTGGAGATCATACAGA	nuclear receptor subfamily 3, group C, member 1
Oas1a	NM_145211.2	L3		TCTGCATCAGGAGGTGGAGTTTGATGTGCTGCCAGCCTTTGATGTCCTGGGTCATGTTAATACTTCCAGCAAGCCTGA TCCCAGAATCTATGCCATCCTC	2'-5' oligoadenylate synthetase 1A
Oas2	NM_145227.2	Oasl11	Cytoplasm,Rna Catabolic Process,Zinc Ion Binding	CTGTGCAACTTTTAAGCAGAGCCGTGCAACATCCCAGGAGTTGACTTCTATGTAAACACCTTCATCCATTTCTGATGT ATGCTTTGAGGTGGCTCAGGC	2'-5' oligoadenylate synthetase 2
Oasl1	NM_145209.2	7530414C13Rik, oasl9		GGGGGCACTCGGATTTAACCTTCTGGGTGAACCCTTATGAACCCATAAAGAAACTGAAAGAGAAAATCCAACTGAGC CAGGGCTACTTGGGCCTGCAGCG	2'-5' oligoadenylate synthetase-like 1
Pdgfa	NM_008808.3		Cell Surface,Extracellular Region,Membrane,Extracellular Space,Microvillus,Positive Regulation Of Cell Proliferation,Regulation Of Peptidyl Tyrosine Phosphorylation,Multicellular Organismal Development,Organ Morphogenesis,Positive Regulation Of Map Kinase Activity,Angiogenesis,Actin Cytoskeleton Organization And Biogenesis,Positive Regulat	TGTGCGTGGCGTGTGACATTCCTGAACATACTATGTATGGTGCTTCATTGCCAATGTGCGTGCGGTCTTTGTTCTCCTC CGTGAAAAACTGTGTCCGAGG	platelet derived growth factor, alpha
Pik3c2g	NM_011084.2	C80387, PI3K-C2-gamma	Golgi Apparatus,Membrane,Nuclear Envelope,Plasma Membrane,Phosphoinositide Mediated Signaling,Phosphorylation,Nucleotide Binding,Phosphotransferase Activity Alcohol Group As Acceptor,Kinase Activity,Phosphoinositide Binding,Transferase Activity Transferring Phosphorus Containing Groups,Atp Binding	CTCACTTTGAAGACAAGTCTCTGCGCCCGGCTGTGTCTTTAAGGAGTTCATCGGTTGTGTTTACTGAACTTGAAGGACA CCTCTAAATGTAGACAGCGTCA	phosphatidylinositol 3-kinase, C2 domain containing, gamma polypeptide
Pla2g4a	NM_008869.2	Pla2g4, cPLA2, cPLA2alpha	Golgi Apparatus,Cytoplasm,Endoplasmic Reticulum,Nucleus,Cytosol,Cytoplasmic Vesicle,Perinuclear Region Of Cytoplasm,Membrane Fraction,Lipid Catabolic Process,Positive Regulation Of Cell Proliferation,Response To Organic Substance,Regulation Of Cell Proliferation,Calcium Ion Binding,Phospholipase A2 Activity,Phospholipase Activity	TACCAAAGCGACAACCAAGCAAGTTGGGTCCATCGGATGCTAATGGCCTTGGTGAGCGACTCGGCTTTATTCAATACC CGAGAAGGACGTGCCGGAAAGG	phospholipase A2, group IVA (cytosolic, calcium-dependent)
Plcb1	NM_019677.1	3110043I21Rik, AI132408, Plcb, mKIAA0581	Cytoplasm,Nucleus,Cytosol,Membrane Fraction,Nuclear Chromatin,Nuclear Speck,Lipid Catabolic Process,Positive Regulation Of Transcriptiondna Dependent,Insulin Receptor Signaling Pathway,Glutamate Signaling Pathway,G2 M Transition Of Mitotic Cell Cycle,Signal Transduction,Negative Regulation Of Transcription Dna Dependent,Regulation Of G Pro	CCAGAAGGGCGCATTCCTCTTAAAAACATCTATCGATTGTTCTCAGCAGACCGGAAGCGCGTTGAAACTGCACTAGAG GCTTGTAGTCTTCCATCTTCGA	phospholipase C, beta 1
Ppp1r12b	NM_001081307.1	1810037O03Rik, 9530009M10Rik, AI132431, Mypt2	Cytoplasm,Actin Cytoskeleton,Plasma Membrane	CACCGGCATTAACTTCTGGACAAATGACGAAGATGAAACAGATGTCTCTGAAGAGGTCAAAGAAGCTTTGCATGAAA GACTTTCTAGGTTGGAGTCAGGA	protein phosphatase 1, regulatory (inhibitor) subunit 12B
Prkca	NM_011101.3	AI875142, Pkca	Membrane,Cytoplasm,Endoplasmic Reticulum,Nucleus,Cytosol,Perinuclear Region Of Cytoplasm,Lipid Raft,Cell Soma,Dendrite,Membrane Fraction,Mitochondrion,Protein Complex,Plasma Membrane,Regulation Of Muscle Contraction,Protein Amino Acid Autophosphorylation,Regulation Of Peptidyl Tyrosine Phosphorylation,Angiogenesis,Negative Regulation Of Ce	TGGCTCAGCATTCGTGTGGTCAGGTGTCAGTCAATGAACAGAAGACACACCAGGTTGTTAAACAGCCTTACTGTGACC CTCCTCAGAAGCCCACAAGTTC	protein kinase C, alpha
Prkcb	NM_008855.2	A130082F03Rik, PKC-Beta, Pkcb, Prkcb1, Prkcb2	Membrane,Cytoplasm,Insoluble Fraction,Nucleus,Cytosol,Membrane Fraction,Centrosome,Plasma Membrane,Soluble Fraction,Transcription Dna Dependent,Regulation Of Growth,Calcium Ion Transport,Activation Of Nf Kappab Transcription Factor,Positive Regulation Of I Kappab Kinase Nf Kappab Cascade,Regulation Of Transcription From Rna Polymerase Ii P	TTACGATTTTAGCTGCCAAAAGAGACCAGAGCAATCCTGCTCCTCACTCTGCTATTAGGGCACCTGACATCTGAAGAG TAGAAGTTATTTTCTGCTTGGT	protein kinase C, beta
Ptger1	NM_013641.2	42kDa, EP1, Ptgerep1	Membrane,Integral To Membrane,Plasma Membrane,Signal Transduction,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Activity	TTGGCCTGGCCGCGCTCCTTGCGGCATTAGTGTGCAATACGCTCAGCGGCCTGGCGCTCCTCCGTGCCGCGTGGAGA CGGCGTCGCTCTCGACGATTCCG	prostaglandin E receptor 1 (subtype EP1)
Ptger2	NM_008964.4	EP2, Ptgerep2	Membrane,Integral To Membrane,Plasma Membrane,Signal Transduction,G Protein Coupled Receptor Protein Signaling Pathway,Regulation Of Cell Proliferation,G Protein Coupled Receptor Activity,Receptor Activity	TGTAAGGGGCTGGAATATAAACAGAATAACCTTGCCCTGAGAAGCAGATGAAACAGACTTTATGAGGTAGTTTGGGC TGCAGATGTGATGACAGAGCCCT	prostaglandin E receptor 2 (subtype EP2)

Continue Table S1: Nanostring nCounter SC Mouse Inflammation V2 Panel Gene List

Ptger3	NM_011196.2	EP3, Pgerep3, Ptgerep3	Plasma Membrane,G Protein Signaling Coupled To Ip3 Second Messengerphospholipase C Activating,G Protein Signaling Coupled To Camp Nucleotide Second Messenger,Receptor Activity	TCTAATAAGCCATGAGCCAAACAAGACAAAAAAGTCTACATGAGAGGGCAAGAGAGATTGTGCAAAGGGTATTTGTG CCAAGAAGGTATACAGTACCACA	prostaglandin E receptor 3 (subtype EP3)
Ptger4	NM_008965.1	EP4, Ptgerep4	Membrane,Integral To Membrane,Plasma Membrane,Signal Transduction,Jnk Cascade,Positive Regulation Of Cytokine Secretion,G Protein Signaling Coupled To Camp Nucleotide Second Messenger,G Protein Signaling Adenylate Cyclase Activating Pathway,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Ac	GGTGGCCATCGTAGTATTGTGCAAGTCGCGCAAGGAGCAGAAAGAGACGACCTTTTACACTCTAGTATGTGGGCTGG CTGTCACTGACCTTCTGGGCACCC	prostaglandin E receptor 4 (subtype EP4)
Ptgfr	NM_008966.3	AI957154, PGF, fp	Membrane,Cytoplasm,Integral To Membrane,Plasma Membrane,Negative Regulation Of Apoptosis,Signal Transduction,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Activity	TGGGTCTATATTCTGCTACGGAAGGCTGTCCTTAGGAACCTGTATAAACTTGCCAGTCGTTGCTGTGGAGTTAACATC ATCAGCTTGCATATCTGGGAAC	prostaglandin F receptor
Ptgir	NM_008967.3	IP, PGI2	Membrane,Integral To Membrane,Plasma Membrane,Signal Transduction,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Activity	GGTTCTATGGCTCTCAAGAAGGATTCTCTCAAAATAACCAGGGCCTGGGCAGGCTGCTCTGGCCCCTGGGCTCCTCC ATCCATCTCTCTGTCTAAATATT	prostaglandin I receptor (IP)
Ptgs1	NM_008969.3	COX1, Cox-1, Cox-3, PGHS-1, PHS 1, Pghs1	Cytoplasmic Part,Golgi Apparatus,Membrane,Cytoplasm,Endoplasmic Reticulum,Nucleus,Microsome,Nuclear Envelope,Plasma Membrane,Fatty Acid Biosynthetic Process,Lipid Biosynthetic Process,Response To Oxidative Stress,Keratinocyte Differentiation,Regulation Of Blood Pressure,Regulation Of Cell Proliferation,Lipid Binding,Oxidoreductase Activity	TTTAGAGTTCTACCCGGGGTTGCTGCTGGAGAAGTGCCAGCCCAACTCCATCTTTGGAGAAAGTATGATAGAGATGG GGGCTCCCTTTTCCCTCAAGGGC	prostaglandin-endoperoxide synthase 1
Ptgs2	NM_011198.3	COX2, Cox-2, PGHS-2, PHS-2, Pghs2, TIS10	Membrane,Cytoplasm,Endoplasmic Reticulum,Nucleus,Protein Complex,Neuron Projection,Positive Regulation Of Cell Proliferation,Negative Regulation Of Cell Cycle,Fatty Acid Biosynthetic Process,Lipid Biosynthetic Process,Inflammatory Response,Angiogenesis,Embryo Implantation,Response To Oxidative Stress,Keratinocyte Differentiation,Negative R	CCATCAGTTTTTCAAGACAGATCATAAGCGAGGACCTGGGTTCACCCGAGGACTGGGCCATGGAGTGGACTTAAATC ACATTTATGGTGAAACTCTGGAC	prostaglandin-endoperoxide synthase 2
Ptk2	NM_007982.2	FAK, FRNK, Fadk, mKIAA4203, p125FAK	Cell Junction,Membrane,Cytoplasm,Nucleus,Intercalated Disc,Cytosol,Cytoskeleton,Lamellipodium,Nuclear Body,Basolateral Plasma Membrane,Focal Adhesion,Apical Plasma Membrane,Plasma Membrane,Nucleolus,Positive Regulation Of Cell Proliferation,Negative Regulation Of Apoptosis,Protein Amino Acid Autophosphorylation,Microtubule Cytoskeleton Org	TGTACAGATTTGACAAAGAGTGCTTCAAGTGTGCCCTTGGGTCAAGTTGGATCATTTCTGTGGAATTGGCAATCGGCC CAGAAGAAGGGATCAGTTACCT	PTK2 protein tyrosine kinase 2
Rac1	NM_009007.2	AL023026, D5Ertd559e	Extrinsic To Plasma Membrane,Golgi Membrane,Membrane,Cytoplasm,Lamellipodium,Cytoplasmic Vesicle,Cell Projection,Cytoplasmic Membrane Bound Vesicle,Membrane Fraction,Plasma Membrane,Actin Filament Organization,Axon Guidance,Regulation Of Cell Migration,Intercellular Junction Assembly And Maintenance,Actin Cytoskeleton Organization And Biog	GCCAAAATACCTTCTGAACTAAGTTGCGTTGTGCTGAGAACACCTAAGCACTAAACTCTCTTGAGAGACTTCTGTTGCT AAGAAGACCGCAGCTTCTGGA	RAS-related C3 botulinum substrate 1
Raf1	NM_029780.3	6430402F14Rik, AA990557, BB129353, Craf1, D830050J10Rik, Raf-1, c-Raf, v-Raf	Membrane,Cytoplasm,Insoluble Fraction,Nucleus,Cytosol,Mitochondrion,Plasma Membrane,Negative Regulation Of Apoptosis,Signal Transduction,Protein Kinase Cascade,Negative Regulation Of Cell Proliferation,Mapkkk Cascade Go 0000165,Cytoskeleton Organization And Biogenesis,Protein Amino Acid Phosphorylation,Phosphorylation,Apoptosis Go,Response	CCTCAGATGATGGCAAGCTCACGGATCTTCTAAGACAAGCAATACTATCCGGGTTTTCTTGCCGAATAAGCAAAGGA CTGTGGTCAATGTGCGGAATGG	v-raf-leukemia viral oncogene 1
Rapgef2	NM_001099624.2	5830453M24Rik, CNRasGEF, Pdzgef1, RA-GEF-1, mKIAA0313, nRapGEP	Membrane,Plasma Membrane,Signal Transduction,Regulation Of Catalytic Activity,Regulation Of Small Gtpase Mediated Signal Transduction,Small Gtpase Mediated Signal Transduction,Protein Kinase Binding,Guanyl Nucleotide Exchange Factor Activity	TTATAACTGGATAGCATTGCAGTGAGGCAGCTTGGGGTGTTGGAGCGAATGCCAGCTGTTTGTACTGCTCTTTCAAGA CAGCCTCCCCTTGTTGGATTGG	Rap guanine nucleotide exchange factor (GEF) 2
Rela	NM_009045.4	p65	Cytoplasm,Nucleus,Cytosol,Transcription Factor Complex,Protein Complex,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Cell Proliferation,Negative Regulation Of Apoptosis,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Negative Regulation Of Transcription Dna Dependе	GAGGCTGACCTCTGCCCAGACCGCAGTATCCATAGCTTCCAGAACCTGGGGATCCAGTGTGTGAAGAAGCGAGACCT GGAGCAAGCCATTAGCCAGCGAA	v-rel reticuloendotheliosis viral oncogene homolog A (avian)
Relb	NM_009046.2	shep	Cytoplasm,Nucleus,Cytosol,Cytoskeleton,Transcription Dna Dependent,Regulation Of Transcriptiondna Dependent,Transcription Factor Activity,Dna Binding	TTCTCTTTGAGCCCATTTTACAGAATGCTGAGTCCGAAGAGGAAAAGGGGCTCCTGCAGATGGACCCCTTCTCAGGAC AGATTCTCAGAGATTGTACATA	avian reticuloendotheliosis viral (v-rel) oncogene related B
Retnla	NM_020509.3	1810019L16Rik, Fizz-1, Fizz1, HIMF, RELM-alpha, RELMa, RELMalpha, Xcp2	Extracellular Region,Hormone Activity	GAATACTGATGAGACCATAGAGATTATCGTGGAGAATAAGGTCAAGGAACTTCTTGCCAATCCAGCTAACTATCCCTC CACTGTAACGAAGACTCTCTCT	resistin like alpha
Ripk1	NM_009068.3	D330015H01Rik, RIP, Rinp, Rip1	Membrane,Cytoplasm,Lipid Raft,Receptor Complex,Mitochondrion,Protein Complex,Plasma Membrane,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Protein Amino Acid Autophosphorylation,Activation Of Nf Kappab Transcription Factor,Protein Amino Acid Phosphorylation,Phosphorylation,Apoptosis Go,Nucleotide	GCTTTGGCCTTGTTGGCCATTCTGGCACTCATTGGCACTTCATCCTCCTTTGTTGGGCTATCCTGTACTCAGTAGGATA TTTGGGAACATTCCTGGCCTC	receptor (TNFRSF)-interacting serine-threonine kinase 1
Ripk2	NM_138952.3	2210420D18Rik, CARD3, CARDIAK, CCK, D4Bwg0615e, RICK, RIP2	Cytoplasm,T Cell Proliferation,I Kappab Kinase Nf Kappab Cascade,Activation Of Nf Kappab Transcription Factor,Positive Regulation Of I Kappab Kinase Nf Kappab Cascade,Protein Amino Acid Phosphorylation,Innate Immune Response,Phosphorylation,Regulation Of Apoptosis,Apoptosis Go,Nucleotide Binding,Protein Homodimerization Activity,Non Membra	CCAGGGACATCGACCTGACACCAGTGAGGAGAATTTGCCATTTGATATACCTCATCGAGGTCTCATGATCTCTCTAAT ACAGAGTGGATGGGCGCAAAAC	receptor (TNFRSF)-interacting serine-threonine kinase 2
Rock2	NM_009072.2	B230113H15Rik, ROKalpha, Rho-kinase, Rock-II, Rock2m, mKIAA0619	Membrane,Cytoplasm,Nucleus,Cytoskeleton,Centrosome,Plasma Membrane,Cytokinesis,Signal Transduction,Negative Regulation Of Angiogenesis,Actin Cytoskeleton Organization And Biogenesis,Protein Amino Acid Phosphorylation,Phosphorylation,Rho Protein Signal Transduction,Nucleotide Binding,Phospholipid Binding,Protein Kinase Activity,Kinase Activ	ATCACATTTCAGCTTCAACAGAGGGTTTCACCAGCACATTAGCCAGAAGAAATTTGGGAGTGAATCCCACTACAGCGAT GCTGACTGCATCTTTAAGAAGT	Rho-associated coiled-coil containing protein kinase 2
Rps6ka5	NM_153587.2	3110005L17Rik, 6330404E13Rik, AI854034, MSK1, MSPK1, RLPK	Cytoplasm,Nucleus,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Negative Regulation Of Transcription Dna Dependent,Activation Of Nf Kappab Transcription Factor,Inflammatory Response,Response To Stress,Protein Kinase Cascade,Regulation Of Transcriptiondna Dependent,Protein Amino Acid Phosphorylation,Phosphorylation,Nu	TCCCTCAGCATGTGCCTGAGGTATGTTCTGCGCTTTAAAAGATGTGTCTCGCTGTTCTCATTGGAATCTGCCTCGTGAC GAATATTTTCCGGGGAAGCCT	ribosomal protein S6 kinase, polypeptide 5
Shc1	NM_011368.4	Shc, ShcA, p66, p66shc	Cytoplasm,Nucleus,Mitochondrion,Plasma Membrane,Insulin Receptor Signaling Pathway,Neurite Development,Regulation Of Growth,Activation Of Mapk Activity,Angiogenesis,Aging,Actin Cytoskeleton Organization And Biogenesis,Cell Cell Adhesion,Heart Development,Mapkkk Cascade Go 0000165,Neuron Differentiation,Protein Complex Binding,Insulin Like	AACGACAAAGTCATGGGACCTGGGGTTTCCTACTTGGTTCGGTACATGGGCTGTGTGGAGGTCTTACAGTCAATGCG AGCCCTTGACTTCAATACCCGGA	src homology 2 domain-containing transforming protein C1
Smad7	NM_001042660.1	Madh7	Cytoplasm,Nucleus,Centrosome,Transcription Factor Complex,Protein Complex,Plasma Membrane,Nucleolus,Regulation Of Transforming Growth Factor Beta Receptor Signaling Pathway,Transcription Dna Dependent,Protein Stabilization,Regulation Of Transcriptiondna Dependent,Negative Regulation Of Transcription From Rna Polymerase Ii Promoter,Transfor	CAGCCTGCTAGAAGGCTGAACCAGAACCAATTGTTTTCATCCCTGTCTTACTGCCGCCTGTCACCCGCTGCCATTGTC GAGTCTGTCTTTTTTGGCCATC	SMAD family member 7
Stat1	NM_009283.3	2010005J02Rik, AA408197	Axon,Cytoplasm,Nucleus,Dendrite,Nucleolus,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Cell Proliferation,Jak Stat Cascade,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Response To Nutrient,Transcription Dna Dependent,Negative Regulation Of Angiogenesis,Response To Bacterium,Cytokine And C	ACGCTGGGAACAGAACTAATGAGGGGCCTCTCATTGTCACCGAAGAACTTCACTCTCTTAGCTTTGAAACCCAGTTGT GCCAGCCAGGCTTGGTGATTGA	signal transducer and activator of transcription 1
Stat2	NM_019963.1	1600010G07Rik, AW496480	Cytoplasm,Nucleus,Plasma Membrane	TCAGTGAAACTCTGAAGGGGCATTACTTGTTCTTGGGTGGAGCACCAGGATGACGATAAAGTCGAAATCTACTCA GTGCAGCCCTACACCAAGGAAGT	signal transducer and activator of transcription 2
Stat3	NM_213659.2	1110034C02Rik, AW109958, Aprf	Cytoplasm,Nucleus,Plasma Membrane,Positive Regulation Of Transcriptiondna Dependent,Jak Stat Cascade,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Transcription Dna Dependent,Sexual Reproduction,Protein Import Into Nucleus,Regulation Of Transcriptiondna Dependent,Intracellular Receptor Mediated Si	GGGGTCACTTTCACTTGGGTGGAAAAGGACATCAGTGGCAAGACCCAGATCCAGTCTGTAGAGCCATACACCAAGCA GCAGCTGAACAACATGTCATTTG	signal transducer and activator of transcription 3
Tbxa2r	NM_001277265.1	TP, TXA2-R	Membrane,Integral To Membrane,Plasma Membrane,Signal Transduction,Inflammatory Response,Second Messenger Mediated Signaling,Positive Regulation Of Angiogenesis,G Protein Coupled Receptor Protein Signaling Pathway,G Protein Coupled Receptor Activity,Receptor Activity	GCTCCTCCTTCCTCGCTCTGCTGTGCGGCCTTGTTCTCACCGACTTCCTGGGGCTGCTAGTCACCGGCGCCATCGTGG CGTCGCAACACGCTGCCTTGTT	thromboxane A2 receptor
Tcf4	NM_013685.1	5730422P05Rik, ASP-I2, E2-2, E2.2, ITF-2, ITF-2b, ITF2, ME2, MITF-2A, MITF-2B, SEF-2, SEF2, SEF2-1, TFE, Tcf-4, bHLHb19	Nucleus,Transcription Factor Complex,Positive Regulation Of Transcriptiondna Dependent,Nervous System Development,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Transcription Dna Dependent,Transcription Initiation,Protein Dna Complex Assembly,Multicellular Organismal Development,Regulation Of Transcriptiondna Dependen	AATTACCGGATATTGAATAGGGGAAGCCCGGCTGCCCTCGTAACAAAACCAGCAAACGTCCTGATGGCAACGAAGTG ATGACATTAGCCATTCCTTAGGG	transcription factor 4

Continue Table S1: Nanostring nCounter SC Mouse Inflammation V2 Panel Gene List

Tgfb1	NM_011577.1	TGF-beta1, TGFbeta1, Tgfb, Tgfb-1	Proteinaceous Extracellular Matrix,Cell Surface,Axon,Extracellular Region,Cytoplasm,Nucleus,Cell Soma,Secretory Granule,Extracellular Space,Extracellular Matrix,Regulation Of Transforming Growth Factor Beta Receptor Signaling Pathway,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Cell Proliferation,Regulation Of D	GGAGTTGTACGGCAGTGGCTGAACCAAGGAGACGGAATACAGGGCTTTCGATTCAGCGCTCACTGCTCTTGTGACAG CAAAGATAACAAACTCCACGTGG	transforming growth factor, beta 1
Tgfb2	NM_009367.1	BB105277, Tgf-beta2, Tgfb-2	Cell Surface,Axon,Extracellular Region,Basement Membrane,Cytoplasm,Cell Soma,Secretory Granule,Extracellular Space,Trans Golgi Network,Extracellular Matrix,Axon Guidance,Positive Regulation Of Cell Proliferation,Negative Regulation Of Apoptosis,Hemopoiesis,Skeletal Development,Epithelial To Mesenchymal Transition,Growth,Intercellular Junct	CCCAAAGCCAGAGTGGCCGAGCAGCGGATTGAACTGTATCAGATCCTTAAATCCAAAGACTTAACATCTCCCACCCAG CGCTACATCGATAGCAAGGTTG	transforming growth factor, beta 2
Tgfb3	NM_009368.2	Tgfb-3	Cell Surface,Extracellular Region,Cytoplasm,Nucleus,Cell Soma,Secretory Granule,Extracellular Space,Extracellular Matrix,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Activation Of Mapk Activity,Organ Morphogenesis,Intercellular Junction Assembly And Maintenance,Posit	TCATGTAATTAGTTTCTGGGCCAGCAACTAGCTATCTCAGGTCCCTTAGAGATGCTGGACTCAAAAGCAGAGGTCAGA ATTGGTTCTCTCATGTATTCCC	transforming growth factor, beta 3
Tgfbr1	NM_009370.2	ALK5, AU017191, Alk-5, TbetaR-I, TbetaRI	Cell Junction,Tight Junction,Membrane,Integral To Membrane,Receptor Complex,Basolateral Plasma Membrane,Apical Plasma Membrane,Protein Complex,Plasma Membrane Part,Plasma Membrane,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Cell Proliferation,Negative Regulation Of Apoptosis,Signal Transduction,Skeletal Develop	TCAGAAGTAGTGGCCAGCTGTGTCTCTAGTAGGACAGTAAAGGCATGAAGCTCAGCCTGTAATCCTGCTACTACAGTA GTACTCCAGAAGTGCCTTGAGG	transforming growth factor, beta receptor I
Tlr1	NM_030682.1		Intrinsic To Membrane,Membrane,Cytoplasmic Vesicle,Integral To Membrane,Plasma Membrane,Signal Transduction,Defense Response,Inflammatory Response,Immune Response,Innate Immune Response,Receptor Activity,Transmembrane Receptor Activity,Protein Heterodimerization Activity	TCAGCACTACGATCGGTTTGGAACTGTCTAACATCAAGTGTGTCCTTGAAGACCAGGGCTGCTCTTATTTCTTACGTGC TTTGTCAAAGCTTGGAAAGAA	toll-like receptor 1
Tlr2	NM_011905.2	Ly105	External Side Of Plasma Membrane,Cell Surface,Intrinsic To Membrane,Membrane,Cytoplasm,Cytoplasmic Vesicle,Integral To Membrane,Plasma Membrane,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Activation Of Nf Kappab Transcription Factor,Inflammatory Response,Positive Regulation Of Cytokine Secretion	GCAGGCGGTCACTGGCAGGAGATGTGTCCGCAATCATAGTTTCTGATGGTGAAGGTTGGACGGCAGTCTCTGCGAC CTAGAAGTGGAAAAGATGTCGTTC	toll-like receptor 2
Tlr3	NM_126166.2	AI957183	Cell Surface,Membrane,Cytoplasm,Endoplasmic Reticulum,Integral To Membrane,Endosome,Response To Virus,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Defense Response,Activation Of Nf Kappab Transcription Factor,Positive Regulation Of I Kappab Kinase Nf Kappab Cascade,Defense Response To Virus,Infla	TTTCTCTGGGCTGAAGTGGACAAATCTCACCCAGCTCGATCTTTCCTACAACAACCTCCATGATGTCGGCAACGGTTCC TTCTCCTATCTCCCAAGCCTG	toll-like receptor 3
Tlr4	NM_021297.2	Lps, Ly87, Ran/M1, Rasl2-8	External Side Of Plasma Membrane,Cell Surface,Membrane,Cytoplasm,Perinuclear Region Of Cytoplasm,Integral To Membrane,Lipid Raft,Integral To Plasma Membrane,Plasma Membrane,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Activation Of Mapk Activity,Activation Of Nf Kappab Transcription Factor,Positi	AACGGCAACTTGGACCTGAGGAGAACAAAACTCTGGGGCCTAAACCCAGTCTGTTTGCAATTAATAAATGCTACAGCT CACCTGGGGCTCTGCTATGGAC	toll-like receptor 4
Tlr5	NM_016928.2		Membrane,Integral To Membrane,Membrane Fraction,Signal Transduction,Inflammatory Response,Innate Immune Response,Receptor Activity	CTGGGGACCCAGTATGCTAACTTGACCATTGGTCCAGGGGCTTTCAGAAACCTGCCCAATCTTAGGATCTTGGACTTG GGCCAAAGCCAGATCGAAGTCT	toll-like receptor 5
Tlr6	NM_011604.3		Intrinsic To Membrane,Membrane,Cytoplasmic Vesicle,Integral To Membrane,Plasma Membrane,Signal Transduction,Positive Regulation Of I Kappab Kinase Nf Kappab Cascade,Inflammatory Response,Immune Response,Defense Response To Bacterium,Positive Regulation Of Jnk Activity,Innate Immune Response,Receptor Activity,Transmembrane Receptor Activity	ACCTGGATGTCTCACACAATCGGTTGCAAAACATCTCTTGCTGCCCTATGGCGAGCCTGAGGCATCTAGACCTCTCAT TCAATGACTTTGATGTACTGCC	toll-like receptor 6
Tlr7	NM_133211.3		Membrane,Cytoplasm,Endoplasmic Reticulum,Cytoplasmic Vesicle,Integral To Membrane,Endosome,Lysosome,Plasma Membrane,Signal Transduction,Defense Response To Virus,Inflammatory Response,Response To Chemical Stimulus,Innate Immune Response,Drug Binding,Double Stranded Rna Binding,Receptor Activity,Single Stranded Rna Binding	TCTGCAGGAGCTCTGTCCTTGAGTGGCCTGCAAATCCACAGGCTCACCCATACTTCTGGCAGTGCCTGAAAAATGCCC TGACCACAGACAATCATGTGGC	toll-like receptor 7
Tlr8	NM_133212.2		Membrane,Integral To Membrane,Response To Virus,Signal Transduction,I Kappab Kinase Nf Kappab Cascade,Defense Response To Virus,Inflammatory Response,Innate Immune Response,Double Stranded Rna Binding,Receptor Activity,Dna Binding,Single Stranded Rna Binding	TCCATAAAGCGAACTATTCCAGAAGCTATCCTTGTGACGAGATAAGGCACAACTCCCTTGTGATTGCAGAATGCAACC ATCGTCAACTGCATGAAGTTCC	toll-like receptor 8
Tlr9	NM_031178.2		Membrane,Cytoplasm,Endoplasmic Reticulum,Cytoplasmic Vesicle,Integral To Membrane,Endosome,Basolateral Plasma Membrane,Apical Plasma Membrane,Lysosome,Plasma Membrane,Response To Virus,Positive Regulation Of Transcription From Rna Polymerase Ii Promoter,Signal Transduction,Activation Of Nf Kappab Transcription Factor,Positive Regulation Of	GGCCACAATTTCAGTTTTGTGACCCATCTGTCCATGCTACAGAGAGCCTTAGCCTGGCACACAATGACATTCATACCCGTG TGTCCTCACATCTCAACAGCA	toll-like receptor 9
Tnf	NM_013693.1	DIF, TNF-a, TNF-alpha, TNFSF2, TNFalpha, Tnfa, Tnfsf1a	External Side Of Plasma Membrane,Cell Surface,Extracellular Region,Membrane,Integral To Membrane,Lipid Raft,Integral To Plasma Membrane,Secretory Granule,Extracellular Space,Plasma Membrane,Response To Virus,Glucose Metabolic Process,Positive Regulation Of Transcriptiondna Dependent,Positive Regulation Of Cell Proliferation,Negative Regula	TTCCTGAGTTCTGCAAAGGGAGAGTGGTCAGGTTGCCTCTGTCTCAGAATGAGGCTGGATAAGATCTCAGGCCTTCCT ACCTTCAGACCTTTCCAGACTC	tumor necrosis factor
Tnfaip3	NM_009397.2	A20, Tnfip3	Cytoplasm,Nucleus,Centrosome,Proteolysis,Anti Apoptosis,Response To Wounding,Apoptosis Go,Kinase Binding,Zinc Ion Binding,Ligase Activity,Ubiquitin Binding,Cysteine Type Peptidase Activity,Peptidase Activity,Dna Binding,Ubiquitin Protein Ligase Activity	GGCTGAACAACTTCTTCCTCAGGCTTTGTATTTGAGCAATATGCGGAAAGCTGTGAAGATACGAGAGAGAACCCAG AAGACATTTTCAAACCTACCAAT	tumor necrosis factor, alpha-induced protein 3
Tnfsf14	NM_019418.2	HVEM-L, HVEML, LIGHT, LTg, Ly113	Extracellular Region,Membrane,Integral To Membrane,Extracellular Space,Plasma Membrane,Immune Response,Receptor Binding,Cytokine Activity	CAGGAAGAAAGAATCAAGCTGGGGTATTTATGCTTCTGATGCAAACACTGAGATTTCGGCTTTCTGGGTTTTGAGCTG GAGGCAAGAAACCTTCCCAGAG	tumor necrosis factor (ligand) superfamily, member 14
Tollip	NM_023764.3	4930403G24Rik, 4931428G15Rik	Cytoplasm,Perinuclear Region Of Cytoplasm,Nuclear Body,Signal Transduction,Inflammatory Response,Innate Immune Response,Phosphorylation,Kinase Binding	CTCAGCATCACTGTGGTACAGGCAAAATTGGCAAAGAATTATGGCATGACTCGTATGGACCCTTACTGCCGTCTGCGT CTGGCTATGCTGTTTATGAAA	toll interacting protein
Tradd	NM_001033161.2	9130005N23Rik, AA930854	Cytoplasm,Cytoskeleton,Lipid Raft,Receptor Complex,Protein Complex,Signal Transduction,Positive Regulation Of I Kappab Kinase Nf Kappab Cascade,Regulation Of Apoptosis,Apoptosis Go,Kinase Binding,Identical Protein Binding,Molecular Adaptor Activity,Protein Complex Binding	AGGTAGCTTCTGCAGGTTCGAAGTTCCCGGTTTCCTCTCCGACCGAGGAGAAACCACTGCCGGCCGCCTGCCAGACT TTTCTGTTCCACGGGCAGCTCGT	TNFRSF1A-associated via death domain
Traf2	NM_009422.2	AI325259	Cytoplasm,Cell Cortex,Lipid Raft,Protein Complex,Signal Transduction,Cellular Protein Complex Assembly,Activation Of Nf Kappab Transcription Factor,Regulation Of Jnk Cascade,Positive Regulation Of Transcription Factor Activity,Protein Catabolic Process,Anti Apoptosis,Protein Complex Assembly,Positive Regulation Of Jnk Activity,Regulation O	CAGAACTGTGCTGCCTGTGTCTATGAAGGCCTGTATGAAGAAGGCATTTCTATTTTAGAGAGTAGTTCGGCCTTTCCA GATAACGCTGCCGCAGAGAGG	TNF receptor-associated factor 2
Trem2	NM_031254.2	TREM-2, Trem2a, Trem2b, Trem2c	Extracellular Region,Membrane,Integral To Membrane,Plasma Membrane,Receptor Activity,Transmembrane Receptor Activity	GAATCAAGAGACCTCCTTCCCACCCACCTCCATTCTTCTCCTCCTGGCCTGCGGTTCTCCTGAGCAAGTTTCTTGCAGCC AGCATCCTCTGGGCTGTGGCC	triggering receptor expressed on myeloid cells 2
Tslp	NM_021367.1		Extracellular Region,Extracellular Space,Cytokine Activity	CTGTACTGTTAATGACCAGCTTCTGAGAAGTCTTTCTCACCTCCCCTGCACACACCTTACTCTAGGGCAAACCTAACTG TAGTAGGAAGAGAATTGAAAG	thymic stromal lymphopoietin
Twist2	NM_007855.2	Dermo1, bHLHa39	Cytoplasm,Nucleus,Transcription Factor Complex,Negative Regulation Of Apoptosis,Transcription Dna Dependent,Negative Regulation Of Transcription Dna Dependent,Multicellular Organismal Development,Regulation Of Transcription From Rna Polymerase Ii Promoter,Negative Regulation Of Dna Binding,Regulation Of Transcriptiondna Dependent,Negative	GTGACTGTTTCGAGGAAGCCTGGAATTCTTGCCGCATACTCCTGTTCTTTACGTCTCCATGGCCTGCTCAGCTAGCC GTGTTTTCTATTCCCTGTTCAG	twist basic helix-loop-helix transcription factor 2
Internal Reference Genes					
Citc	NM_001003908.1	3110065L21Rik, CHC, R74732	Membrane,Spindle,Cytoplasmic Vesicle,Clathrin Coated Vesicle,Membrane Fraction,Membrane Coat,Mitochondrion,Intracellular Protein Transport,Vesicle Mediated Transport,Mitosis,Receptor Mediated Endocytosis,Peptide Binding,Structural Molecule Activity,Protei	GAGTCTCAGCCAGTGAAAATGTTTGATCGTCATTCTAGCCTCGCAGGATGCCAGATCATCAATTACCGTACAGATGCA AAGCAGAAATGGTTGCTTCTCA	clathrin, heavy polypeptide (Hc)
Gapdh	NM_001001303.1	Gapd		AGGTTGTCTCCTGCCACTTCAACAGCAACTCCCACTCTTCCACCTTCGATGCCGGGGCTGGCATTGCTCTCAATGACA ACTTTGTCAAGCTCATTTCCTG	glyceraldehyde-3-phosphate dehydrogenase
Gusb	NM_010368.1	g, Gut, Gur, asd, adipose storage deficiency, Gus-r, Gus-s, Gus4, Gus-u, Gus	Endoplasmic Reticulum,Microsome,Lysosome,Soluble Fraction,Carbohydrate Metabolic Process,Sugar Binding,Cation Binding,Hydrolase Activity Acting On Glycosyl Bonds,Hydrolase Activity Hydrolyzing O Glycosyl Compounds	AATACGTGGTCGGAGAGCTCATCTGGAATTTCGCCGACTTCATGACGAACCAGTCACCGCTGAGAGTAATCGGAAAC AAGAAGGGGATCTTCACTCGCCA	glucuronidase, beta
Pgk1	NM_008828.2	Pgk-1	Cytoplasm,Cytosol,Soluble Fraction,Carbohydrate Metabolic Process,Phosphorylation,Nucleotide Binding,Kinase Activity,Adp Binding,Atp Binding	CCGGCATTCTGCACGCTTCAAAAGCGCACGTCTGCCGCGCTGTTCTCCTCTTCCTCATCTCCGGGCCTTTCGACCTCAC GGTGTTGCCAAAATGTCGCTT	phosphoglycerate kinase 1

Continue Table S1: Nanostring nCounter SC Mouse Inflammation V2 Panel Gene List

Tubb5	NM_011655.4	AA408537, AI961682, BI302022	CL4RIK, MObeta5	Cytoplasm,Cytoskeleton,Microtubule,Protein Complex,Microtubule Based Process,Protein Polymerization,Microtubule Based Movement,Gtp Binding,Nucleotide Binding,Protein Complex Binding,Structural Molecule Activity,Structural Constituent Of Cytoskeleton,Gtpas	ATTGGAACGTGTCTTCCCTGTATTGGTTCTCCTTTCTCGGAGAGATGGGGGTTGGGGGTGCGGCGAAGGTCTTGGTCTT GGTCTCTGAACACTCCCAATTCC
©2013 NanoString Technologies				Ltb, Tubb5	tubulin, beta 5 class I

Table S2: Nanostring nCounter SC Mouse Custom Code Set Gene List

CODESET DETAILS

	Customer Identifier	Accession	Position	Target Sequence	Tm CP	Tm RP	Flags	HUGO Gene
1	Ibabp	NM_008375.2	163-262	ATCACAGAGGTCCAGCAGGACGGACAGGACTTCACCTGGTCCCAGTCTTACTCTGGGGGCAACATTATGAGCAACAAGTTCACCATTGGCAAAGAATGTG	83	82		Fabp6
2	Fgf15	NM_008003.2	316-415	TCCGCTGGTCCCTATGTCTCCAACTGCTTCCTCCGAATCCGGAGCGACGGCTCTGTGGACTGCGAGGAGGACCAAAACGAACGAAATTTGTTGGAATTCC	83	82		Fgf15
3	TGR5	NM_174985.1	386-485	TCACCTGGGTCAGCTCCCTGTTCTTTGCCAGCCTGCCTGCTCTGGGCTGGAACCATTGGAGCCCTGATGCCAACTGCAGCTCCCAAGCTGTCTTCCCAGC	85	84		Gpbar1
4	MMP10	NM_019471.2	1051-1150	CAGACTTAGATGCTGCCTATGAGGCTCACAACACGGACAGTGTTCTGATTTTTAAAGGAAGTCAGTTCTGGGCAGTCCGAGGAAATGAAGTCCAAGCAGG	82	82		Mmp10
5	MMP-2	NM_008610.2	2377-2476	AGTTAACCAGCCTTCTCCTTCACCTGGTGACTTCAGATTTAAGAGGGTGGCTTCTTTTTGTGCCCAAAGAAAGGTGCTGACTGTACCCTCCCGGGTGCTG	81	82		Mmp2
6	MMP-7	NM_010810.4	351-450	CACCTACAGAATTGTATCCTATACTTCAGACTTACCTCGGATCGTAGTGGATCAAATCGTGAAAAAAGCTCTCAGAATGTGGAGTATGCAGATCCCACTG	78	82		Mmp7
7	FXR	NM_009108.2	1176-1275	CAGTTTCTATAAAAGTGTTGGAGAACTCAAAATGACTCAGGAGGAGTACGCTCTGCTCACAGCGATCGTCATCCTCTCTCCAGACAGACAATACATCAAG	79	83		Nr1h4
8	ASBT (Ibat)	NM_011388.2	661-760	CATTGTGCTCATAGCTGTGATTGGAGGAATACTGTACCAAAGTGCCTGGATCATTGAACCCAAACTGTGGATTATAGGAACAATATTCCCTATAGCTGGC	84	81		Slc10a2
9	OSTalpha	NM_145932.3	1213-1312	CCTCCCTACTCTTCTAAAATCAGGTCTCAAGTGATGAACTGCCACATGCTCATACTGGAGACCTTCCTGATGACAGTGCTGACACGAATGTACTATCGAA	83	85		Slc51a
10	OSTBeta	NM_178933.2	196-295	ATGACAAGCATGTTCCTCCTGAGAAGGAGCATCCTGGCAAACAGAAATCGAAAGAAGCAGCCACAAGACAAAGAAACACCAGAAGACCTGCATCTTGATG	79	78		Slc51b

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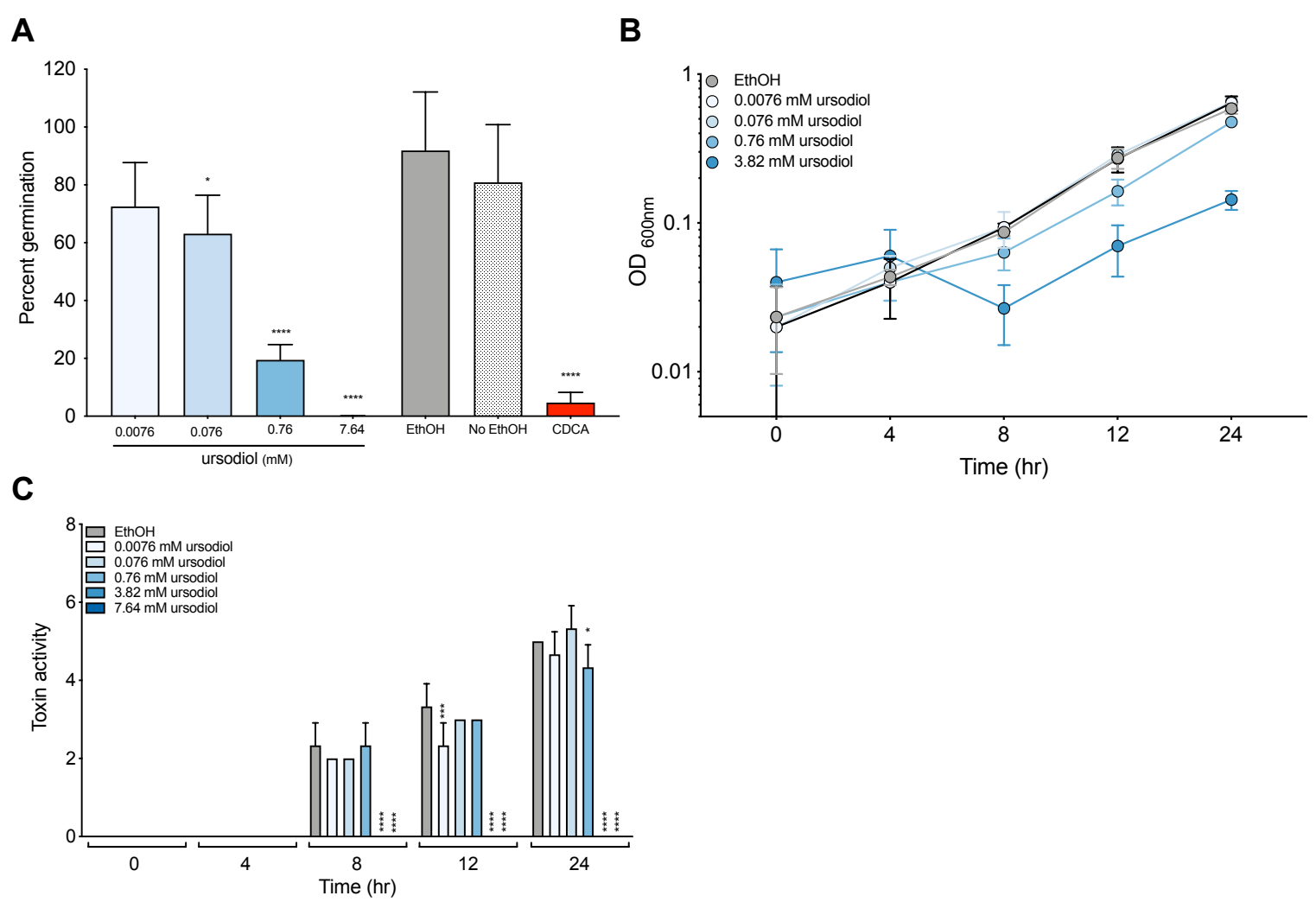
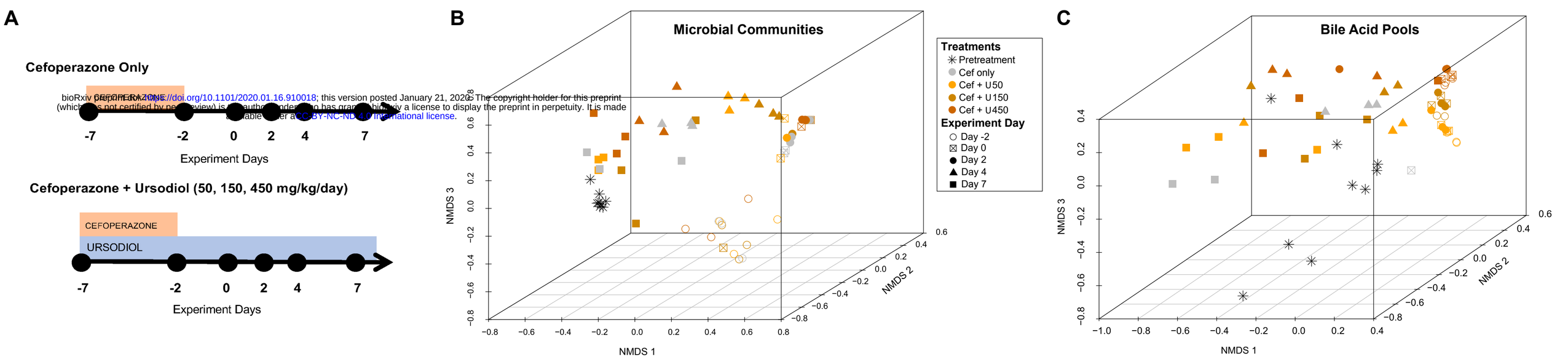
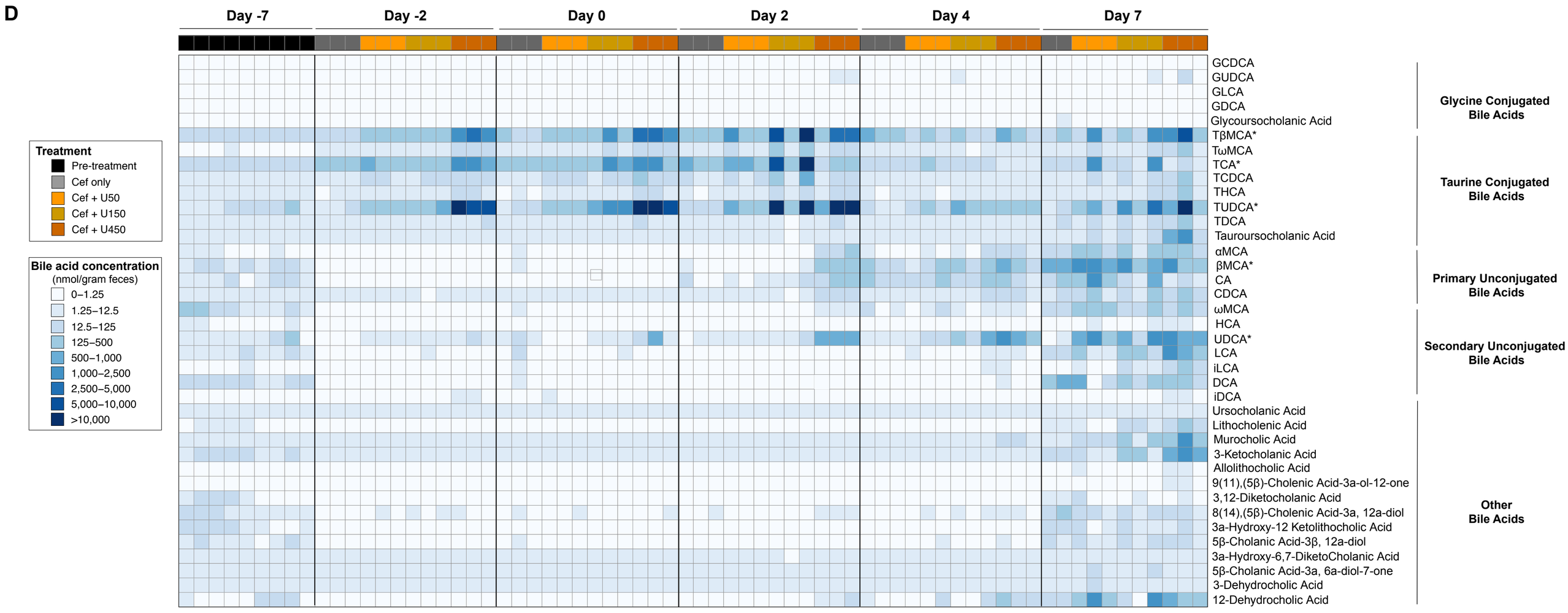
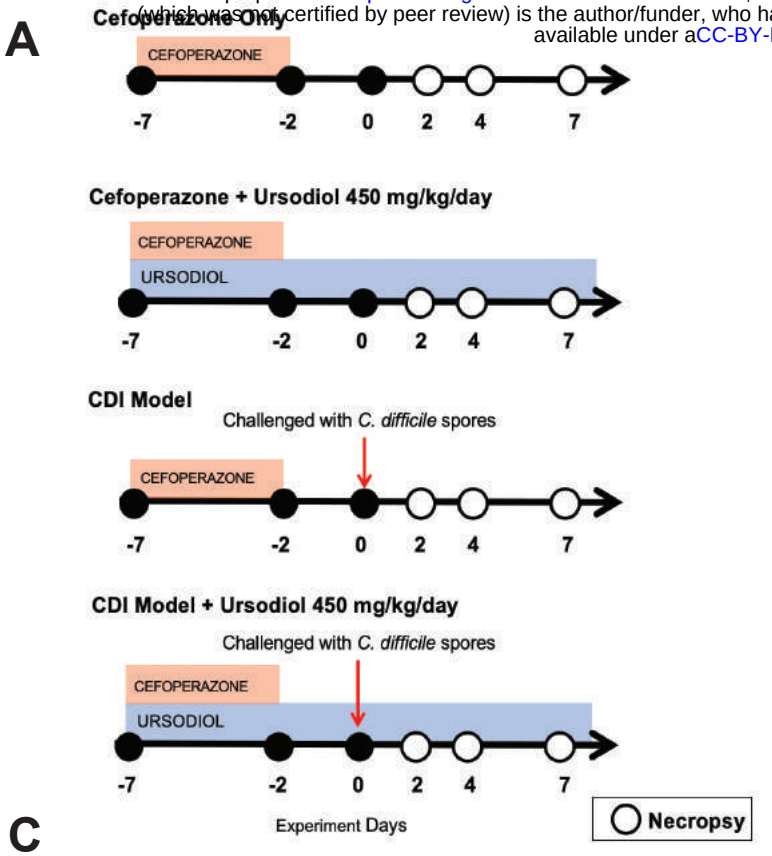
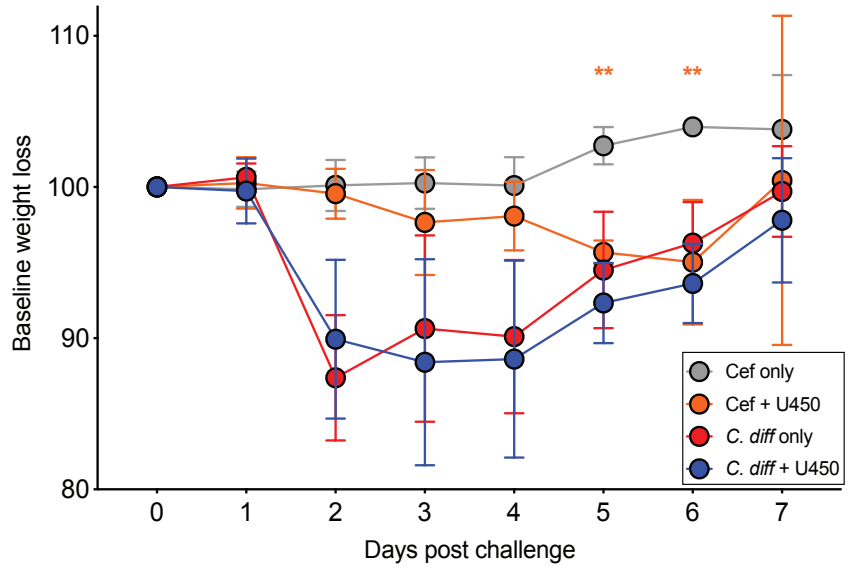
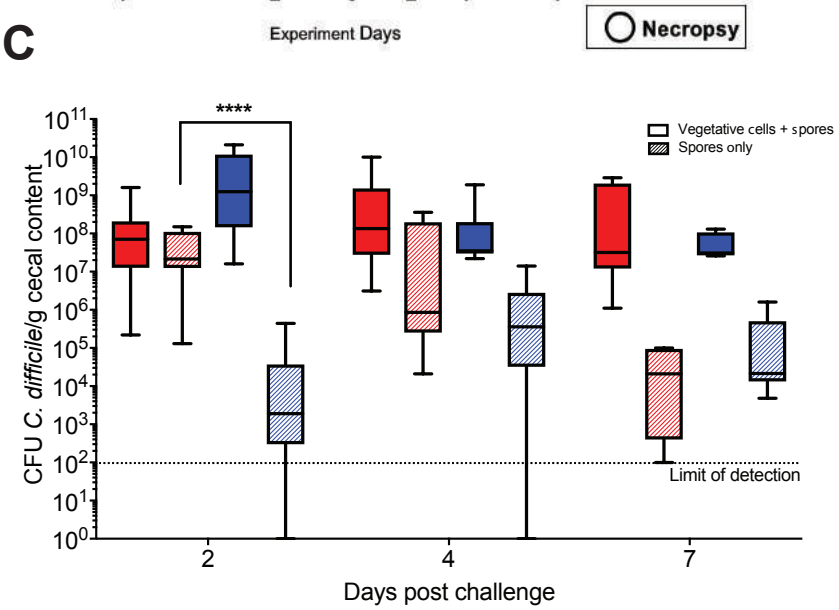

A
Percent germination
120
100
80
60
40
20
0
0.0076
0.076
0.76
7.64
EthOH
No EthOH
CDCA
ursodiol (mM)
B
OD 600nm
1
0.1
0.01
EthOH
0.0076 mM ursodiol
0.076 mM ursodiol
0.76 mM ursodiol
3.82 mM ursodiol
0
4
8
12
24
Time (hr)
C
Toxin activity
8
6
4
2
0
EthOH
0.0076 mM ursodiol
0.076 mM ursodiol
0.76 mM ursodiol
3.82 mM ursodiol
7.64 mM ursodiol
0
4
8
12
24
Time (hr)

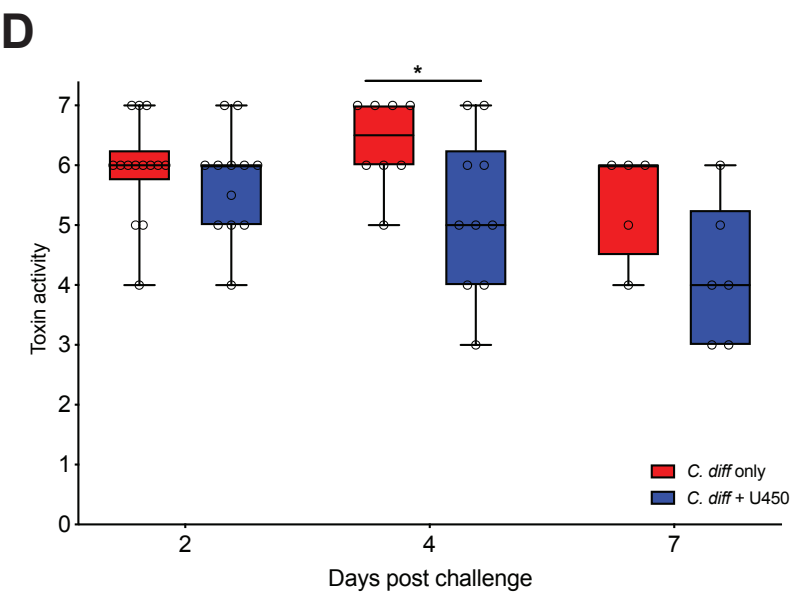


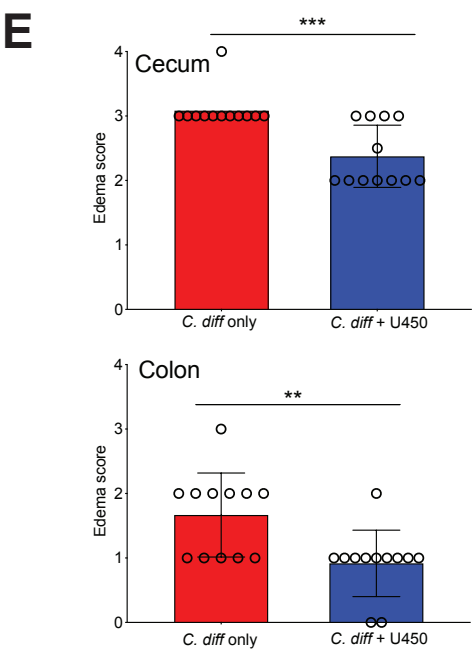


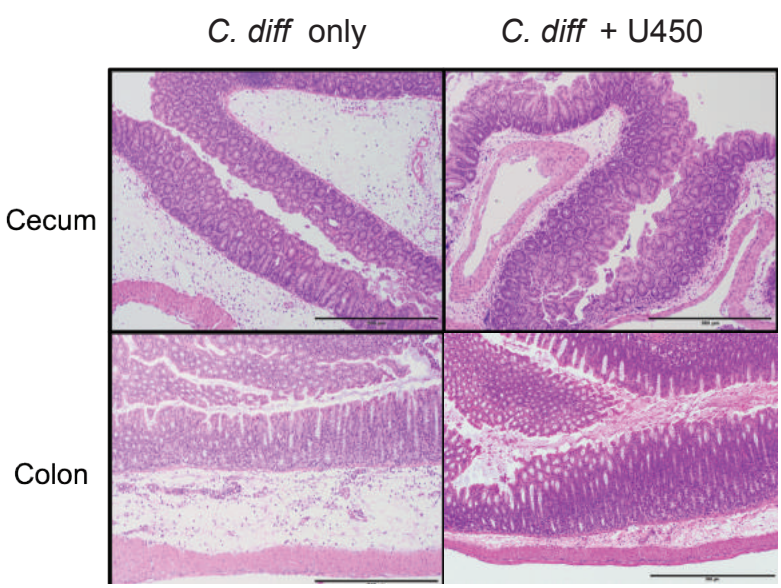


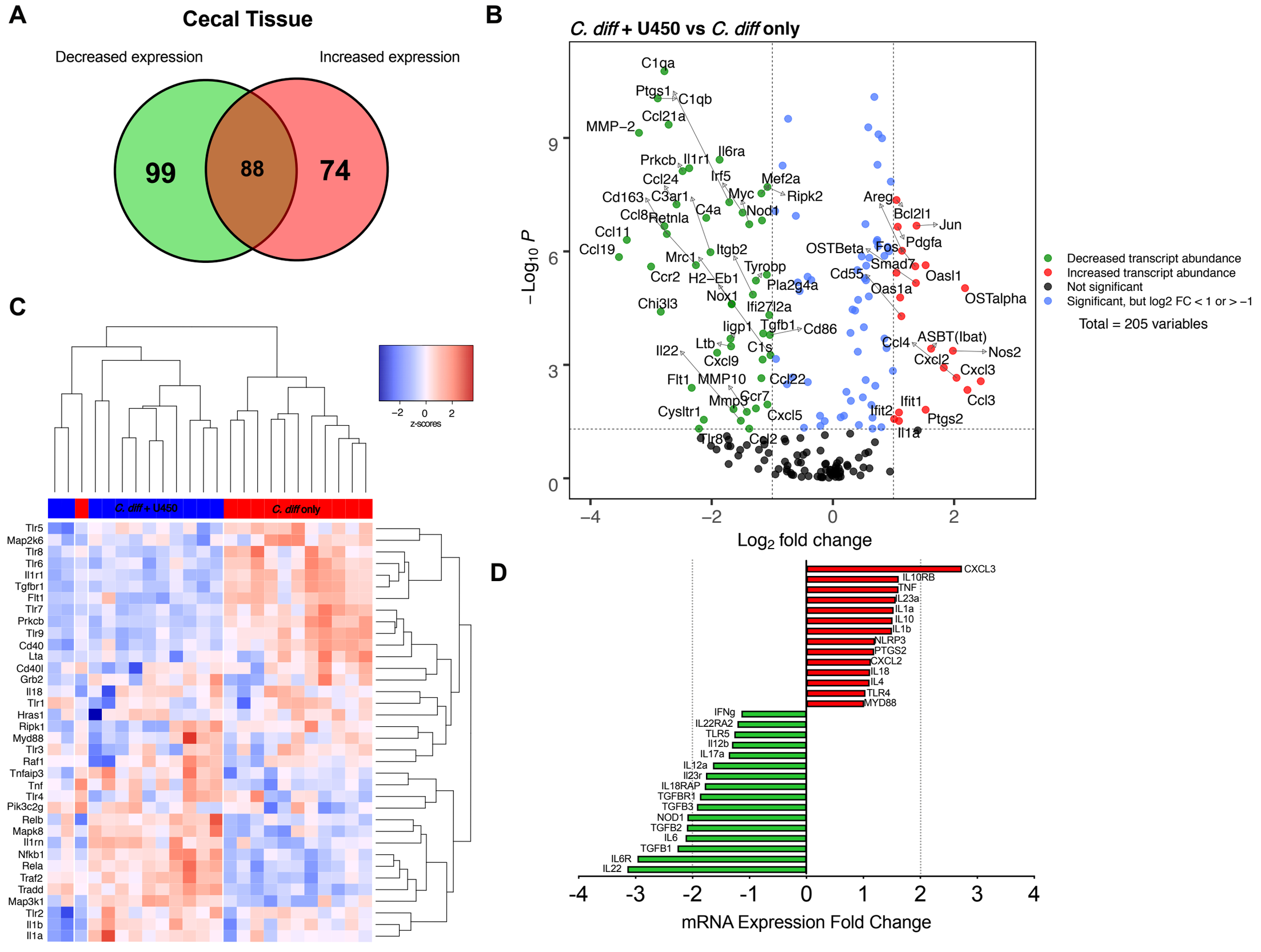











A
Cecal Tissue
Decreased expression
Increased expression
99
88
74
B
C. diff + U450 vs C. diff only
– Log10 P
Log2 fold change
Decreased transcript abundance
Increased transcript abundance
Not significant
Significant, but log2 FC < 1 or > –1
Total = 205 variables
C1qa
Ptgs1
C1qb
Ccl21a
MMP–2
Il6ra
Prkcb
Il1r1
Irf5
Ccl24
Mef2a
Cd163
C3ar1
Myc
Ripk2
Areg
C4a
Nod1
Ccl8
Retnla
Bcl2l1
Jun
Ccl11
Pdgfa
Ccl19
Itgb2
OSTBeta
Fos
Mrc1
Tyrobp
Smad7
Ccr2
H2–Eb1
Cd55
Oasl1
Pla2g4a
Oas1a
Nox1
OSTalpha
Chi3l3
Ifi27l2a
Iigp1
Tgfb1
Cd86
ASBT(Ibat)
Ltb
C1s
Ccl4
Nos2
Il22
Cxcl9
Cxcl2
Cxcl3
Flt1
MMP10
Ccl22
Ccr7
Ccl3
Mmp3
Ifit1
Cysltr1
Cxcl5
Ifit2
Ptgs2
Tlr8
Ccl2
Il1a
C
z-scores
C. diff + U450
C. diff only
Tlr5
Map2k6
Tlr8
Tlr6
Il1r1
Tgfbr1
Flt1
Tlr7
Prkcb
Tlr9
Cd40
Lta
Cd40l
Grb2
Il18
Tlr1
Hras1
Ripk1
Myd88
Tlr3
Raf1
Tnfaip3
Tnf
Tlr4
Pik3c2g
Relb
Mapk8
Il1rn
Nfkb1
Rela
Traf2
Tradd
Map3k1
Tlr2
Il1b
Il1a
D
CXCL3
IL10RB
TNF
IL23a
IL1a
IL10
IL1b
NLRP3
PTGS2
CXCL2
IL18
IL4
TLR4
MYD88
IFNg
IL22RA2
TLR5
Il12b
IL17a
IL12a
Il23r
IL18RAP
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TGFB3
NOD1
TGFB2
IL6
TGFB1
IL6R
IL22
mRNA Expression Fold Change