

Supplementary Figure Legends

Supplementary Figure 1, Related to Figure 2. Cohort-dependent impacts on SCI-triggered dysbiosis.

16S sequencing results from an independent cohort of male mice. **A, B**, Pre-surgery to end point (14-dpi) changes in fecal microbiome 16S rRNA alpha diversity represented by Chao1 (**A**) and Shannon (**B**) diversity measures. **C**, Principal component analysis (PCA) plot representing changes in overall community structure of fecal microbiomes. **D**, Microbial composition barplot, order level, of fecal microbiomes at 14-dpi. Asterisks in (**A**) and (**B**) represent a significant decrease in alpha diversity from 0-dpi to 14-dpi in the sham group. Each circle represents the average of all mice in a group for all but **C**, where each circle represents an individual mouse. N=3-8. * $P < 0.05$. Data are shown as mean \pm SEM. Statistically significant differences were determined by repeated measures 2-way ANOVA with post-hoc Sidak's multiple comparison test to compare temporal changes within groups.

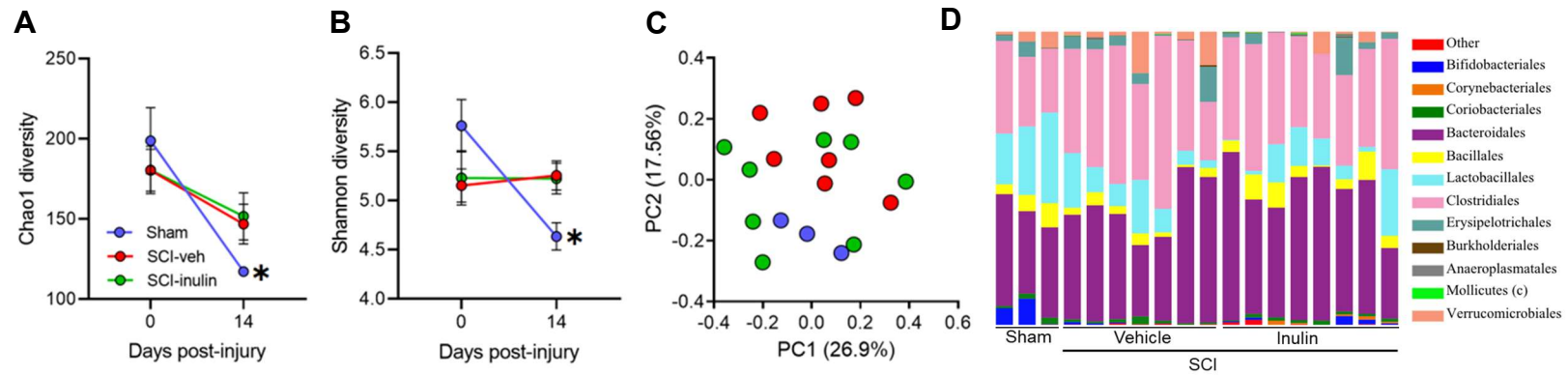
Supplementary Figure 2, Related to Figure 3. Injury and diet-associated microbes are not sufficient to trigger NBD.

A-C, Heatmap of cytokines present in proximal colon tissue lysate from male and female uninjured germ-free mice that were colonized with either sham-derived or SCI-veh-derived fecal microbiomes (**A**), as assessed by multiplexed ELISA, with significant increases in CXCL1 (**B**) and IL-12p70 (**C**). **D-G**, Heatmap of serum metabolic markers, as assessed by multiplexed ELISA (**D**), with significant decreases in C-peptide (**E**), TNF (**F**), and ghrelin (**G**). **H-M**, Heatmap of serum metabolic markers in male mice with laminectomy (Sham) or injury (SCI-veh), as assessed by multiplexed ELISA (**H**), with significant decreases in C-peptide (**I**), TNF (**J**), glucagon (**K**), GLP-1 (**L**), and leptin (**M**). Each data point represents one mouse. Squares represent ex-GF males, hexagons represent ex-GF females, and circles represent SPF males. N=19-21 (**A-C**), N=14-15 (**D-G**), N=11-14 (**H-M**). * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$. Data are shown as mean \pm SEM. Statistically significant differences were determined by two-tailed unpaired t-test.

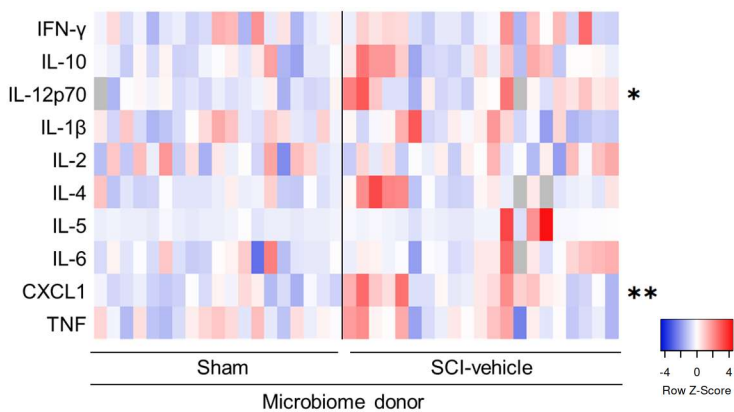
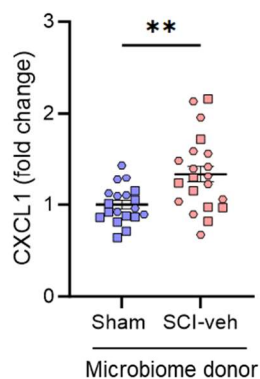
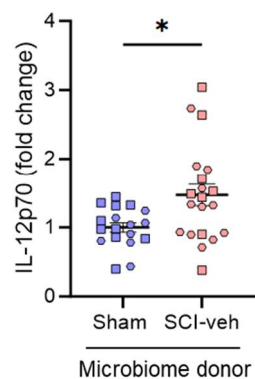
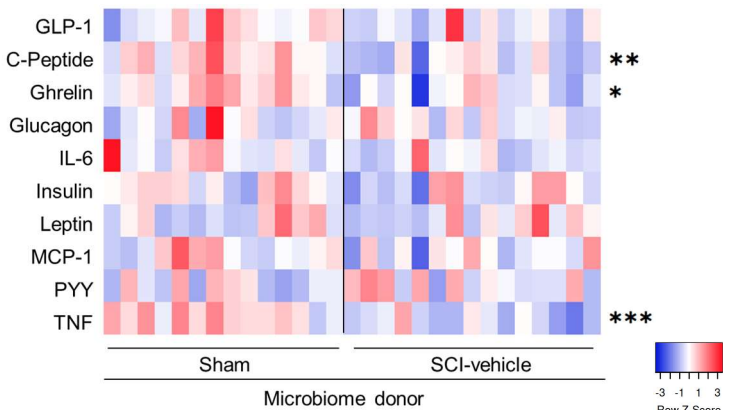
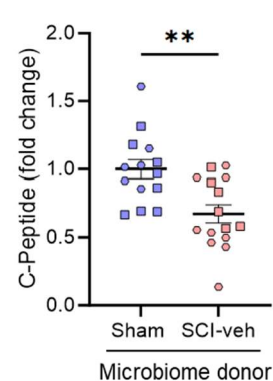
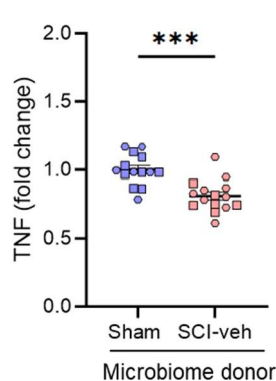
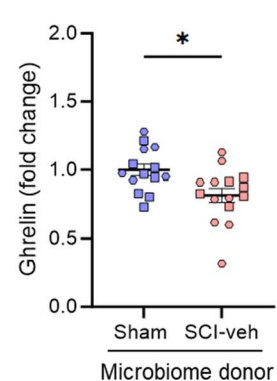
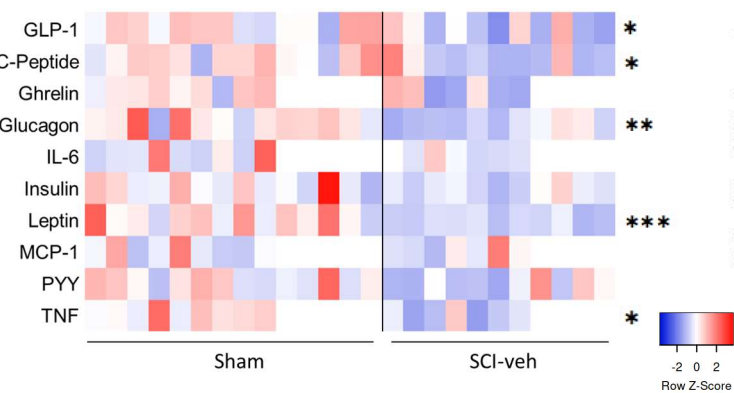
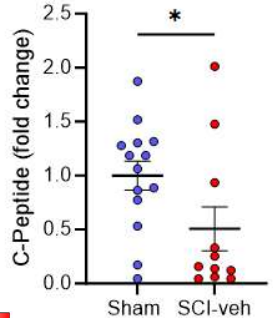
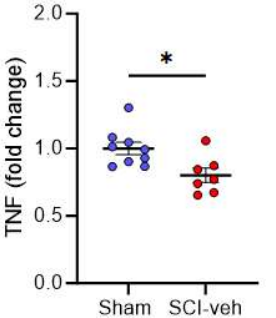
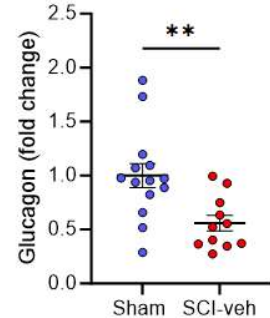
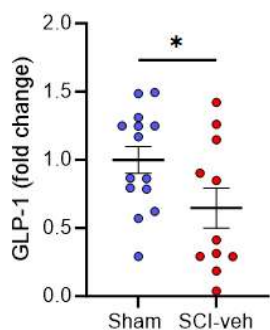
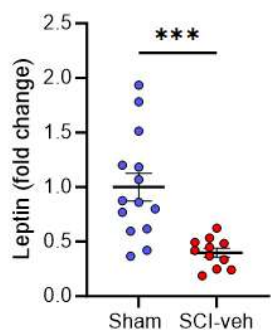
Supplementary Figure 3, Related to Figure 4. SCFA-induced IL-10 signaling is necessary for SCI recovery.

A, Heatmap of cytokines, assessed by multiplexed ELISA, in proximal colon tissue lysate from male wild-type mice with laminectomy (Sham), SCI with standard diet (SCI-vehicle), and SCI with inulin-supplemented diet (SCI-inulin). **B**, Concentration of colonic IL-1 β by ELISA. **C-E**, Endpoint quantification of indicated short-chain fatty-acids from fecal pellets of male IL10rb KO mice with SCI (SCI-veh) or inulin-supplemented diet (SCI-inulin). **F**, Quantification of colonic free fatty acid receptor 2 (FFAR2) levels, by western blot, in male IL10rb KO mice with SCI. **G**, Heatmap of cytokines, assessed by multiplexed ELISA, in serum from male wild type mice with SCI treated with either vehicle (SCI-veh), tripropionin (SCI-TRP), or tributyrin (SCI-TRB). **H**, Concentration of serum IL-6 by ELISA. **I-K**, Endpoint quantification of indicated short-chain fatty-acids from serum of male mice with SCI, treated with vehicle (Veh), tripropionin (TRP), or tributyrin (TRB). Each data point represents one mouse. N=11-17 (**A, B**), N=7-10 (**C-F**), N=11-13 (**G, H**), N=5-6 (**I-K**). * $P < 0.05$, ** $P < 0.01$. Data are shown as mean \pm SEM. Statistically significant differences were determined by ordinary one-way ANOVA with post-hoc Tukey's (**A, B**) or Dunnett's (**G, K**) multiple comparison test. Or by two-tailed unpaired t-test (**C-F**).

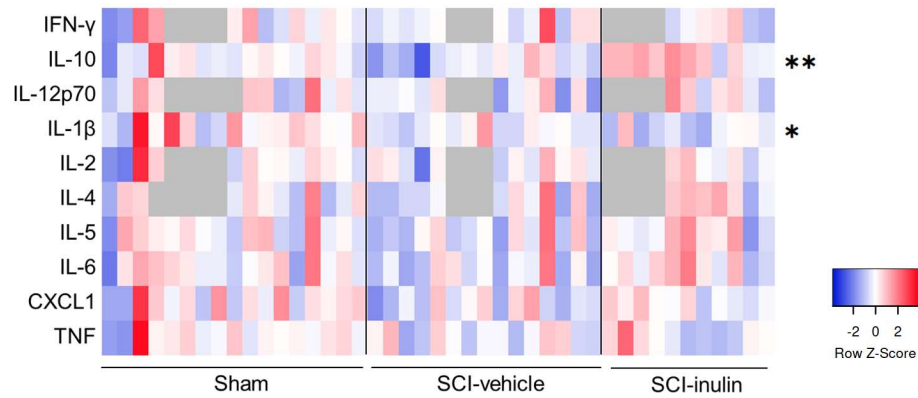
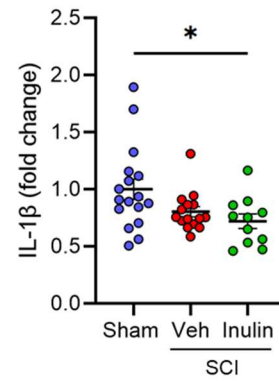
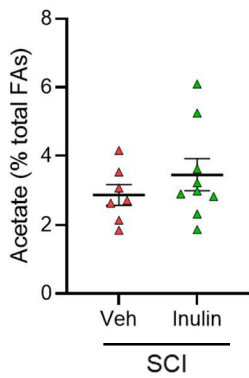
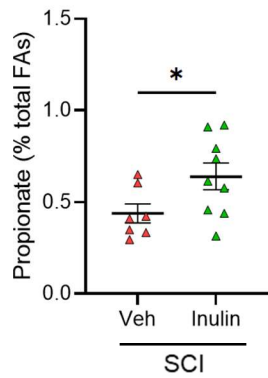
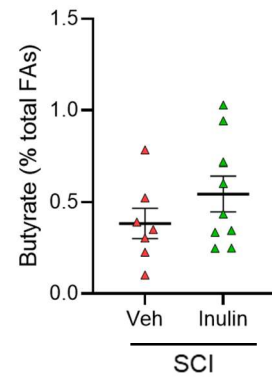
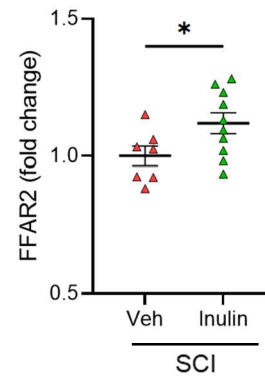
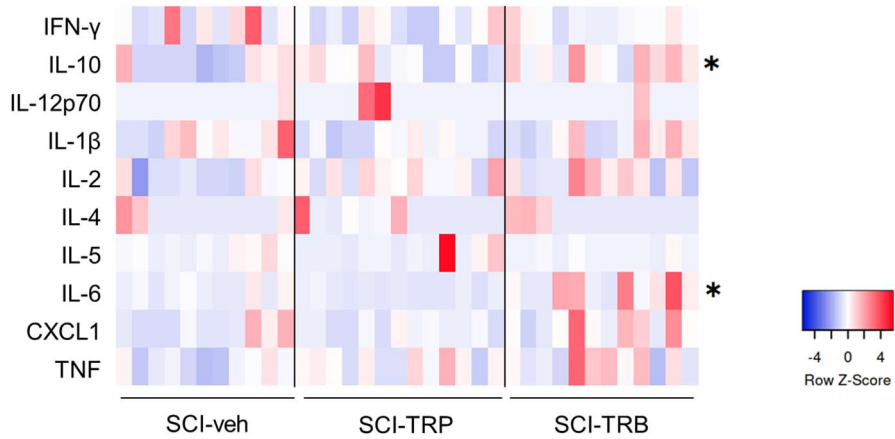
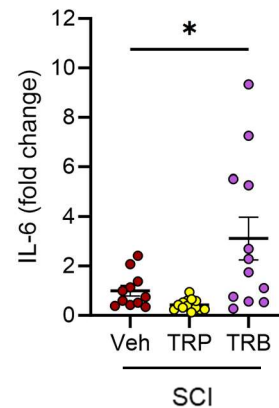
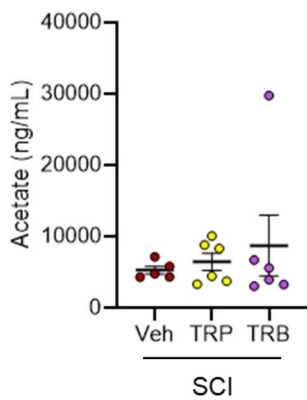
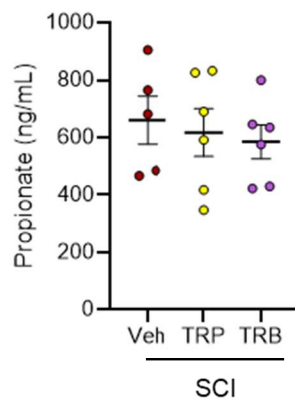
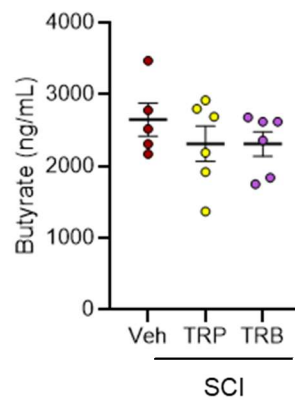
Supplementary Figure 1. Cohort-dependent impacts on SCI-triggered dysbiosis



Supplementary Figure 2. Injury and diet-associated microbes are not sufficient to trigger NBD

A**B****C****D****E****F****G****H****I****J****K****L****M**

Supplementary Figure 3. SCFA-induced IL-10 signaling is necessary for SCI recovery

A**B****C****D****E****F****G****H****I****J****K**

Supplementary Table 1. SCI-induced microbiome compositional differences. ASV-level taxonomic changes from stool microbiomes at 2 weeks post-SCI or sham, with 1% FDR

| Endpoint | | | |
|--|----------------|-------------------|---|
| Sham vs SCI-Vehicle | | | |
| ASV | Sham | SCI-Veh | Adjusted <i>p</i> value (1% FDR) |
| <i>Bacteroides sp12288 (thetaitotaomicron)</i> | 0.0448409 | 0.0186638 | 6.94559E-07 |
| <i>Bacteroidales sp12656</i> | 0.156247 | 0.0943178 | 1.16422E-30 |
| <i>Staphylococcus lentus</i> | 0.0334159 | 0.00351487 | 1.50293E-08 |
| <i>Lactobacillus johnsonii</i> | 0.0577711 | 0.0290364 | 5.24441E-08 |
| <i>Clostridium celatum</i> | 0.0875609 | 0 | 0 |
| <i>Lachnospiraceae sp33565</i> | 0.00720456 | 0.0506877 | 2.82898E-16 |
| <i>Turicibacter sanguinis</i> | 0.124592 | 0.0603193 | 8.76368E-33 |
| Sham vs SCI-Inulin | | | |
| ASV | Sham | SCI-Inulin | Adjusted <i>p</i> value (1% FDR) |
| <i>Bacteroides sp12288 (thetaitotaomicron)</i> | 0.0448409 | 0.0757577 | 5.81151E-08 |
| <i>Bacteroidales sp12550</i> | 0.138146 | 0.028615 | 0 |
| <i>Bacteroidales sp12656</i> | 0.156247 | 0.188446 | 1.62892E-08 |
| <i>Staphylococcus lentus</i> | 0.0334159 | 0.000353782 | 6.74178E-09 |
| <i>Clostridium celatum</i> | 0.0875609 | 0 | 0 |
| <i>Lachnospiraceae sp33565</i> | 0.00720456 | 0.040268 | 6.73239E-09 |
| <i>Turicibacter sanguinis</i> | 0.124592 | 0 | 0 |
| SCI-Vehicle vs SCI-Inulin | | | |
| ASV | SCI-Veh | SCI-Inulin | Adjusted <i>p</i> value (1% FDR) |
| <i>Bacteroides sp12288 (thetaitotaomicron)</i> | 0.0186638 | 0.0757577 | 1.15921E-15 |
| <i>Bacteroidales sp12550</i> | 0.135412 | 0.028615 | 0 |
| <i>Bacteroidales sp12656</i> | 0.0943178 | 0.188446 | 2.24226E-38 |
| <i>Lactobacillus johnsonii</i> | 0.0290364 | 0.061178 | 5.5047E-06 |
| <i>Turicibacter sanguinis</i> | 0.0603193 | 0 | 2.91586E-17 |
| Pre-SCI vs Post-SCI | | | |
| ASV | SCI-Pre | SCI-2wks | Adjusted <i>p</i> value (1% FDR) |
| <i>Bacteroidales sp12656</i> | 0.158599 | 0.0943178 | 2.06832E-30 |
| <i>Lactobacillus johnsonii</i> | 0.193283 | 0.0290364 | 0 |
| <i>Clostridium celatum</i> | 0.022866 | 0 | 2.92759E-05 |
| <i>Lachnospiraceae sp33565</i> | 0.0128364 | 0.0506877 | 6.26693E-12 |
| <i>Turicibacter sanguinis</i> | 0.00972012 | 0.0603193 | 7.71416E-20 |

Supplementary Table 2. LEfSE identified taxonomic changes from stool microbiomes at 2 weeks post-SCI or sham

| Bacterial taxa | Group | Effect size | p-value |
|---|--------------|--------------------|----------------|
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33760 | SCI.Inulin | 3.28014007 | 0.030197383 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f NA.g NA.s sp31072 | SCI.Inulin | 2.98922362 | 0.048484305 |
| k Bacteria.p Proteobacteria.c Gammaproteobacteria.o Pseudomonadales.f Moraxellaceae.g Acinetobacter.s radiorensistens | SCI.Inulin | 3.18049855 | 0.012764197 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp32706 | SCI.Inulin | 3.82883697 | 0.01334429 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp32638 | SCI.Inulin | 3.78461598 | 0.023383895 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33456 | SCI.Inulin | 3.17262743 | 0.027158625 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33694 | SCI.Inulin | 3.76036576 | 0.019757099 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Ruminococcaceae.g NA.s sp34867 | SCI.Inulin | 3.30028204 | 0.027323722 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Ruminococcaceae.g Anaerotruncus.s sp34475 | SCI.Inulin | 2.99522399 | 0.045806314 |
| k Bacteria.p Proteobacteria.c Gammaproteobacteria.o Pseudomonadales | SCI.Inulin | 3.25550068 | 0.016389554 |
| k Bacteria.p Proteobacteria.c Gammaproteobacteria.o Pseudomonadales.f Moraxellaceae.g Acinetobacter | SCI.Inulin | 3.22914314 | 0.016389554 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33417 | SCI.Inulin | 3.75893236 | 0.011625603 |
| k Bacteria.p Bacteroidetes.c Bacteroidia.o Bacteroidales.f Bacteroidaceae.g Bacteroides.s sp12288_thetaiotaomi cron | SCI.Inulin | 4.43785167 | 0.028207093 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33525 | SCI.Inulin | 3.26973262 | 0.048484305 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp32701 | SCI.Inulin | 3.96461728 | 0.015562692 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33616 sp33639 | SCI.Inulin | 3.42818688 | 0.029407217 |
| k Bacteria.p Firmicutes.c Bacilli.o Lactobacillales.f Enterococcaceae.g Enterococcus.s faecalis | SCI.Inulin | 3.05716304 | 0.024861262 |
| k Bacteria.p Proteobacteria.c Gammaproteobacteria.o Pseudomonadales.f Moraxellaceae.g Acinetobacter.s calc oaceticus radiorensistens variabilis | SCI.Inulin | 3.20043929 | 0.041388896 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Ruminococcaceae.g NA.s sp34731 | SCI.Inulin | 3.43239165 | 0.027158625 |
| k Bacteria.p Firmicutes.c Bacilli.o Lactobacillales.f Enterococcaceae | SCI.Inulin | 3.0725174 | 0.024861262 |
| k Bacteria.p Bacteroidetes.c Bacteroidia.o Bacteroidales.f Bacteroidaceae | SCI.Inulin | 4.41723887 | 0.028207093 |
| k Bacteria.p Bacteroidetes.c Bacteroidia.o Bacteroidales.f Bacteroidaceae.g Bacteroides | SCI.Inulin | 4.45069433 | 0.028207093 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp32758 | SCI.Inulin | 3.97272763 | 0.009403563 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp32623 | SCI.Inulin | 3.56178608 | 0.041041078 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f NA.g NA.s sp31116 | SCI.Inulin | 3.05573343 | 0.04376775 |
| k Bacteria.p Proteobacteria.c Gammaproteobacteria.o Pseudomonadales.f Moraxellaceae | SCI.Inulin | 3.23322001 | 0.016389554 |
| k Bacteria.p Firmicutes.c Bacilli.o Lactobacillales.f Enterococcaceae.g Enterococcus | SCI.Inulin | 3.06357795 | 0.024861262 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33721 | SCI.Inulin | 3.08898072 | 0.009139753 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Ruminococcaceae.g NA.s sp35841 | SCI | 3.08050444 | 0.030197383 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33658 | SCI | 3.42184273 | 0.023786517 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp32702 | SCI | 3.85317688 | 0.024861262 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g Lachnoclostridium.s sp32402 | SCI | 3.69380202 | 0.034609178 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33739 | SCI | 3.15551336 | 0.046329809 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae | SCI | 5.05697495 | 0.048668305 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33565 | SCI | 4.28952463 | 0.027158625 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp32872 | SCI | 3.09241069 | 0.028207093 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Ruminococcaceae.g Oscillibacter.s sp34648 | SCI | 3.04716797 | 0.028937471 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33718 | SCI | 3.35285573 | 0.023786517 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp32146 | SCI | 3.27855544 | 0.027158625 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Ruminococcaceae.g NA.s sp35077 | Sham | 3.08269556 | 0.027323722 |
| k Bacteria.p Firmicutes.c Bacilli.o Bacillales.f Staphylococcaceae.g Staphylococcus.s lentus | Sham | 4.22428258 | 0.015562692 |

| Supplementary Table 2 (continued) | | | |
|--|--------------|--------------------|----------------|
| Bacterial taxa | Group | Effect size | p-value |
| k Bacteria.p Firmicutes.c Erysipelotrichia.o Erysipelotrichales | Sham | 4.77308354 | 0.015562692 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Clostridiaceae | Sham | 4.65015938 | 0.025161049 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Clostridiaceae.g Clostridium.s celatum | Sham | 4.6301129 | 0.009139753 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Ruminococcaceae.g NA.s sp35361 | Sham | 3.59813998 | 0.019660049 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Ruminococcaceae.g NA.s sp35360 | Sham | 3.08921088 | 0.041041078 |
| k Bacteria.p Proteobacteria.c Betaproteobacteria.o Burkholderiales.f Alcaligenaceae | Sham | 3.43800153 | 0.011391522 |
| k Bacteria.p Firmicutes.c Bacilli.o Bacillales.f Staphylococcaceae.g Staphylococcus | Sham | 4.27885163 | 0.037902914 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33419 | Sham | 3.32307121 | 0.015562692 |
| k Bacteria.p Bacteroidetes.c Bacteroidia.o Bacteroidales.f NA.g NA.s sp12550 | Sham | 4.72904022 | 0.048484305 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Clostridiaceae.g Clostridium | Sham | 4.65240631 | 0.025161049 |
| k Bacteria.p Firmicutes.c Erysipelotrichia.o Erysipelotrichales.f Erysipelotrichaceae.g Turicibacter.s sanguinis | Sham | 4.7786212 | 0.012764197 |
| k Bacteria.p Firmicutes.c Bacilli.o Bacillales.f Staphylococcaceae.g Jeotgalicoccus | Sham | 3.42659395 | 0.013728404 |
| k Bacteria.p Firmicutes.c Bacilli.o Bacillales.f Staphylococcaceae | Sham | 4.30010345 | 0.037902914 |
| k Bacteria.p Firmicutes.c Erysipelotrichia | Sham | 4.76829196 | 0.015562692 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Lachnospiraceae.g NA.s sp33537 | Sham | 3.08288654 | 0.041388896 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f NA.g NA.s sp31125 | Sham | 3.07776853 | 0.041388896 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f NA.g NA.s sp31122 | Sham | 3.42566575 | 0.034411331 |
| k Bacteria.p Firmicutes.c Erysipelotrichia.o Erysipelotrichales.f Erysipelotrichaceae.g Turicibacter | Sham | 4.801587 | 0.012764197 |
| k Bacteria.p Firmicutes.c Erysipelotrichia.o Erysipelotrichales.f Erysipelotrichaceae | Sham | 4.77876752 | 0.015562692 |
| k Bacteria.p Firmicutes.c Clostridia.o Clostridiales.f Ruminococcaceae.g NA.s sp35498 | Sham | 3.08729405 | 0.041388896 |
| k Bacteria.p Proteobacteria.c Betaproteobacteria.o Burkholderiales | Sham | 3.41658553 | 0.011391522 |
| k Bacteria.p Proteobacteria.c Betaproteobacteria | Sham | 3.40401102 | 0.011391522 |
| k Bacteria.p Firmicutes.c Bacilli.o Bacillales | Sham | 4.30946747 | 0.037902914 |
| k Bacteria.p Proteobacteria.c Betaproteobacteria.o Burkholderiales.f Alcaligenaceae.g Parasutterella | Sham | 3.41352673 | 0.011391522 |
| k Bacteria.p Firmicutes.c Bacilli.o Bacillales.f Staphylococcaceae.g Jeotgalicoccus.s halophilus_halotolerans_nan haiensis | Sham | 3.4063761 | 0.013728404 |
| k Bacteria.p Proteobacteria.c Betaproteobacteria.o Burkholderiales.f Alcaligenaceae.g Parasutterella.s excremen tihominis | Sham | 3.42627509 | 0.011391522 |

Supplementary Table 3. Bacterial taxa significantly different following SCI in an independent cohort. With 1% FDR correction, alterations between Sham and SCI (a), sham and SCI-inulin (b), or SCI and SCI-inulin (c). Grey boxes indicate significant comparisons (1% FDR) between pre and post-SCI groups at 2wks post injury.

| ASV | Sham | SCI-Veh | SCI-Inulin | Sig comparisons by 1% FDR | Identified in independent cohort (Fig 2) |
|---|----------|----------|------------|---------------------------|--|
| <i>Akkermansia muciniphila</i> | 0.032851 | 0.04787 | 0.016194 | c | |
| <i>Alistipes sp14336</i> | 0.029102 | 0.067027 | 0.06584 | a, b | |
| <i>Allobaculum sp36555</i> | 0.000152 | 0.021406 | 0.006325 | a | |
| <i>Bacteroidales sp12473-sp12526-sp12633</i> | 0.074217 | 0.084304 | 0.042379 | b, c | |
| <i>Bacteroidales sp12610</i> | 0 | 0.030116 | 0.013937 | a | |
| <i>Bacteroidales sp12645</i> | 0 | 0.019732 | 0.058406 | b, c | |
| <i>Bacteroidales sp12656</i> | 0.105666 | 0.052678 | 0.156417 | a, b, c | Yes |
| <i>Bacteroidales sp12768</i> | 0.033087 | 0.05611 | 0.04598 | a | |
| <i>Bacteroides sp12288 (thetaitaomicron)</i> | 0.080995 | 0.071137 | 0.050251 | b, c | Yes |
| <i>Bifidobacterium choerinum-pseudolongum</i> | 0.049002 | 0.002335 | 0.007556 | a, b | |
| <i>Lachnoclostridium sp32402</i> | 0.021026 | 0.040619 | 0.01123 | c | |
| <i>Lachnospiraceae sp32778</i> | 0.009123 | 0.043795 | 0.014431 | a, c | |
| <i>Lactobacillus johnsonii</i> | 0.237838 | 0.079619 | 0.078155 | a, b | Yes |
| <i>Staphylococcus lentus</i> | 0.027879 | 0.005809 | 0.019373 | a | Yes |

Supplementary Table 4. Independent SCI-induced microbiome compositional differences. ASV-level taxonomic changes from stool microbiomes at 2 weeks post-SCI or sham, with 1% FDR, from independent cohort

| Endpoint | | | |
|--|----------------|-------------------|----------------------------------|
| Sham vs SCI-Vehicle | | | |
| ASV | Sham | SCI-Veh | Adjusted p value (1% FDR) |
| <i>Bifidobacterium choerinum-pseudolongum</i> | 0.0490019 | 0.00233502 | 1.38505E-15 |
| <i>Bacteroidales sp12610</i> | 0 | 0.0301156 | 2.27912E-07 |
| <i>Bacteroidales sp12656</i> | 0.105666 | 0.0526781 | 1.42237E-19 |
| <i>Bacteroidales sp12768</i> | 0.0330871 | 0.05611 | 7.46328E-05 |
| <i>Alistipes sp14336</i> | 0.0291018 | 0.0670273 | 7.71846E-11 |
| <i>Staphylococcus lentus</i> | 0.0278791 | 0.00580894 | 0.000146098 |
| <i>Lactobacillus johnsonii</i> | 0.237838 | 0.0796191 | 0 |
| <i>Lachnospiraceae sp32778</i> | 0.00912332 | 0.0437946 | 2.64513E-09 |
| <i>Allobaculum p36555</i> | 0.00015199 | 0.0214064 | 0.000254523 |
| Sham vs SCI-Inulin | | | |
| ASV | Sham | SCI-Inulin | Adjusted p value (1% FDR) |
| <i>Bifidobacterium choerinum-pseudolongum</i> | 0.0490019 | 0.00755608 | 4.74124E-08 |
| <i>Bacteroides sp12288 (thetaitotaomicron)</i> | 0.0809949 | 0.0502512 | 4.99359E-05 |
| <i>Bacteroidales sp12473-sp12526-sp12633</i> | 0.0742173 | 0.0423789 | 2.67067E-05 |
| <i>Bacteroidales sp12645</i> | 0 | 0.0584062 | 1.67097E-14 |
| <i>Bacteroidales sp12656</i> | 0.105666 | 0.156417 | 2.43458E-11 |
| <i>Alistipes sp14336</i> | 0.0291018 | 0.0658396 | 1.27625E-06 |
| <i>Lactobacillus johnsonii</i> | 0.237838 | 0.0781547 | 0 |
| SCI-Vehicle vs SCI-Inulin | | | |
| ASV | SCI-Veh | SCI-Inulin | Adjusted p value (1% FDR) |
| <i>Bacteroides sp12288 (thetaitotaomicron)</i> | 0.0711372 | 0.0502512 | 0.00013929 |
| <i>Bacteroidales sp12473-sp12526-sp12633</i> | 0.0843043 | 0.0423789 | 2.45024E-14 |
| <i>Bacteroidales sp12645</i> | 0.0197316 | 0.0584062 | 1.95902E-12 |
| <i>Bacteroidales sp12656</i> | 0.0526781 | 0.156417 | 0 |
| <i>Lachnoclostridium sp32402</i> | 0.040619 | 0.0112297 | 8.5429E-08 |
| <i>Lachnospiraceae sp32778</i> | 0.0437946 | 0.0144314 | 8.76893E-08 |
| <i>Akkermansia muciniphila</i> | 0.0478695 | 0.0161938 | 7.92208E-09 |
| Pre SCI vs Post SCI | | | |
| ASV | SCI-Pre | SCI-2wks | Adjusted p value (1% FDR) |
| <i>Other</i> | 0.0400304 | 0.00230997 | 3.01332E-20 |
| <i>Bifidobacterium choerinum-pseudolongum</i> | 0.0387627 | 0.00233502 | 5.35722E-19 |
| <i>Bacteroidales sp12473-sp12526-sp12633</i> | 0.0566063 | 0.0843043 | 1.20298E-11 |
| <i>Bacteroidales sp12768</i> | 0.0328508 | 0.05611 | 1.223E-08 |
| <i>Enterococcus faecalis</i> | 0.00133197 | 0.0180171 | 4.33168E-05 |
| <i>Lactobacillus johnsonii</i> | 0.130668 | 0.0796191 | 1.57727E-35 |
| <i>Lachnoclostridium sp32402</i> | 0.00983318 | 0.040619 | 4.98182E-14 |
| <i>Lachnospiraceae sp32778</i> | 0.00608032 | 0.0437946 | 3.05544E-20 |
| <i>Ruminococcaceae sp35297</i> | 0.0262177 | 0.0028927 | 1.11286E-08 |
| <i>Allobaculum sp36555</i> | 0.0653365 | 0.0214064 | 7.94526E-27 |

Supplementary Table 5. LEfSE identified taxonomic changes from stool microbiomes at 2 weeks post-SCI or sham, from independent cohort

| Bacterial taxa | Group | Effect size | p-value |
|--|--------------|--------------------|----------------|
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp33761 | SCI | 3.20746086 | 0.03938728 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Ruminococcaceae.g__Anaerotruncus.s__sp34475 | SCI | 3.14434302 | 0.01455464 |
| k_Bacteria.p__Bacteroidetes.c__Bacteroidia.o__Bacteroidales.f__NA.g__NA.s__sp12473_sp12526_sp12633 | SCI | 4.29010458 | 0.03319739 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp32862 | SCI | 3.49736231 | 0.03339209 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp32735 | SCI | 3.60307215 | 0.02671248 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp32721 | SCI | 3.47470577 | 0.02675007 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Ruminococcaceae.g__NA.s__sp33140 | SCI | 2.96559706 | 0.02508897 |
| k_Bacteria.p__Actinobacteria.c__Actinobacteria.o__Corynebacteriales.f__Corynebacteriaceae | SCI.Inulin | 3.5183703 | 0.01922687 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp33731 | SCI.Inulin | 3.21037177 | 0.01440632 |
| k_Bacteria.p__Actinobacteria.c__Actinobacteria.o__Corynebacteriales.f__Corynebacteriaceae.g__Corynebacterium | SCI.Inulin | 3.51837339 | 0.01922687 |
| k_Bacteria.p__Actinobacteria.c__Actinobacteria.o__Corynebacteriales | SCI.Inulin | 3.51837267 | 0.01922687 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp32635_sp32668 | SCI.Inulin | 3.09090389 | 0.01922687 |
| k_Bacteria.p__Actinobacteria.c__Actinobacteria.o__Corynebacteriales.f__Corynebacteriaceae.g__Corynebacterium.s__amycolatum | SCI.Inulin | 3.51837192 | 0.01922687 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp33432 | SCI.Inulin | 3.16044082 | 0.01835448 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__Acetatifactor | SCI.Inulin | 3.0869611 | 0.0469165 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp33421_sp33679 | SCI.Inulin | 3.69414989 | 0.00122429 |
| k_Bacteria.p__Firmicutes.c__Bacilli.o__Bacillales.f__Planococcaceae.g__Sporosarcina.s__luteola_pasteurii | Sham | 3.15351433 | 0.04203087 |
| k_Bacteria.p__Firmicutes.c__Bacilli.o__Lactobacillales.f__Lactobacillaceae.g__Lactobacillus | Sham | 4.94539917 | 0.04846866 |
| k_Bacteria.p__Firmicutes.c__Bacilli.o__Lactobacillales.f__Lactobacillaceae | Sham | 4.93387968 | 0.04846866 |

| Supplementary Table 5 (continued) | | | |
|--|--------------|--------------------|----------------|
| Bacterial taxa | Group | Effect size | p-value |
| k_Bacteria.p__Firmicutes.c__Bacilli.o__Bacillales.f__Staphylococcaceae.g__Staphylococcus.s__lentus | Sham | 4.0524116 4 | 0.0234515 3 |
| k_Bacteria.p__Firmicutes.c__Bacilli.o__Bacillales.f__Planococcaceae | Sham | 3.1353627 7 | 0.0420308 7 |
| k_Bacteria.p__Firmicutes.c__Erysipelotrichia.o__Erysipelotrichales.f__Erysipelotrichaceae.g__NA | Sham | 3.0456857 4 | 0.0094330 1 |
| k_Bacteria.p__Firmicutes.c__Erysipelotrichia.o__Erysipelotrichales.f__Erysipelotrichaceae.g__NA.s__sp36786 | Sham | 3.2849544 8 | 0.0010709 4 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp33694 | Sham | 3.5179440 8 | 0.0196145 7 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp33673 | Sham | 3.2005299 1 | 0.0242550 8 |
| k_Bacteria.p__Firmicutes.c__Bacilli.o__Bacillales.f__Staphylococcaceae.g__Staphylococcus | Sham | 4.2321641 6 | 0.0446212 7 |
| k_Bacteria.p__Actinobacteria | Sham | 4.407117 | 0.0277423 5 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp33636 | Sham | 3.4996426 9 | 0.0083140 5 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__Marvinbryantia.s__sp32979 | Sham | 3.5174996 7 | 0.0032249 9 |
| k_Bacteria.p__Firmicutes.c__Bacilli.o__Bacillales.f__Staphylococcaceae | Sham | 4.2207112 5 | 0.0446212 7 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__Blautia.s__sp32038 | Sham | 3.5580099 | 0.0259710 1 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp33374 | Sham | 3.3533870 6 | 0.0270878 6 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__NA.g__NA.s__sp31125 | Sham | 3.0240336 | 0.0050210 4 |
| k_Bacteria.p__Firmicutes.c__Bacilli.o__Bacillales.f__Planococcaceae.g__Sporosarcina | Sham | 3.1429381 3 | 0.0420308 7 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp32622 | Sham | 3.8416875 7 | 0.0378540 1 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__NA.s__sp32156 | Sham | 3.1342279 7 | 0.0394250 4 |
| k_Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Lachnospiraceae.g__Marvinbryantia | Sham | 3.6367098 1 | 0.0093402 |

Supplementary Table 6. Reagents & Resources.

| Antibodies used | | | | |
|--|----------------------|-------------|-----------------|-------------------|
| Primary antibodies for Western Blot | | | | |
| Antibody | Concentration | Host | Supplier | Cat Number |
| Neuronal nitric oxide synthase (nNOS) | 1:1000 | Rabbit | Cell Signaling | 4231S |
| Choline acetyltransferase (ChAT) | 1:1000 | Goat | Sigma | AB144P |
| Protein gene product 9.5 (PGP9.5) | 1:1000 | Rabbit | Millipore | AB1761-I |
| Free fatty acid receptor 2 (FFAR2 / GPR43) | 1:1000 | Rabbit | Thermo | PA5-111780 |
| Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) | 1:1000 | Rabbit | Cell Signaling | 5174S |
| β-Actin | 1:1000 | Rabbit | Cell Signaling | 8457S |
| Secondary antibodies for Western Blot | | | | |
| Antibody | Concentration | Host | Supplier | Cat Number |
| Anti-rabbit (HRP-linked) | 1:1000 | Goat | Cell Signaling | 7074S |
| Anti-goat (HRP-linked) | 1:1000 | Donkey | Thermo | A16005 |
| Primary antibodies for Immunohistochemistry | | | | |
| Antibody | Concentration | Host | Supplier | Cat Number |
| Neuronal nitric oxide synthase (nNOS) | 1:100 | Rabbit | Cell Signaling | 4231S |
| Anti-HuD + HuC antibody | 1:500 | Rabbit | Abcam | AB184267 |
| Protein gene product 9.5 (PGP9.5) | 1:200 | Mouse | Abcam | AB72911 |
| Secondary antibodies for Immunohistochemistry | | | | |
| Antibody | Concentration | Host | Supplier | Cat Number |
| Anti-mouse (Alexa Fluor™ 594) | 1:200 | Goat | Thermo | A-11005 |
| Anti-rabbit (Alexa Fluor™ 488) | 1:200 | Goat | Thermo | A-11008 |

| ATCC Strains and Growth Conditions | | | | |
|---|---------------------------|--------------------|-----------------------|--------------------|
| Bacterium | Medium | Environment | CFU per gavage | ATCC Number |
| <i>Lactobacillus johnsonii</i> | de Man-Rogosa-Sharpe | Aerobic | 10 ¹⁶ | 33200 |
| <i>Bacteroides thetaiotaomicron</i> | Brain-Heart Infusion | Anaerobic | 10 ¹⁴ | 29148 |
| <i>Clostridium celatum</i> | Chopped Meat Carbohydrate | Anaerobic | 10 ¹⁰ | 27791 |