# Appetite Questionnaire

**"An exploratory study on the impact of a food-based restrictive diet and liquid exclusive enteral nutrition (milk-based diet) on healthy gut microbiota composition (bugs) and metabolic activity (chemical markers)"**

*Name of Researcher: Mr Vaios Svolos, PhD Student, University of Glasgow.*

Study Number: ***Exclusive Enteral Nutrition OR CD-TREAT***

Please answer the following questions by placing a vertical mark through the line for each question. Regard the end of each line as indicating the most extreme sensation you have ever felt and mark how you felt **DURING THE DAY.**

**Day 1** _____

1. How **hungry** did you feel (during the day)?

**I am not hungry** _____ **Never been hungrier**

2. How **satisfied** did you feel (during the day)?

**I am not satisfied at all** _____ **I cannot eat another bite**

3. How **full** did you feel (during the day)?

**Not at all full** _____ **Totally full**

4. How **much** did you think you **could eat** (during the day)?

**A lot** _____ **Nothing at all**

5. How strong was your **desire to eat** (during the day)?

**Not at all** _____ **Very**

# Symptoms Questionnaire

**"An exploratory study on the impact of a food-based restrictive diet and liquid exclusive enteral nutrition (milk-based diet) on healthy gut microbiota composition (bugs) and metabolic activity (chemical markers)"**

*Name of Researcher: Mr Vaios Svolos, PhD Student, University of Glasgow.*

Study Number: ***Exclusive Enteral Nutrition*** OR ***CD-TREAT***

*In the past **ONE week**, how often have you had difficulty with…*

| **Gastrointestinal Symptoms (*PROBLEMS WITH…*)** | **Never** | **Almost Never** | **Some-times** | **Often** | **Almost Always** |
|---|---|---|---|---|---|
| 1. Pain in your abdomen or stomach | 0 | 1 | 2 | 3 | 4 |
| 2. Diarrhoea | 0 | 1 | 2 | 3 | 4 |
| 3. Constipation | 0 | 1 | 2 | 3 | 4 |
| 4. Nausea | 0 | 1 | 2 | 3 | 4 |
| 5. Vomiting | 0 | 1 | 2 | 3 | 4 |
| 6. Discomfort in your abdomen or stomach | 0 | 1 | 2 | 3 | 4 |
| 7. Passing wind | 0 | 1 | 2 | 3 | 4 |
| 8. Bloating | 0 | 1 | 2 | 3 | 4 |

# Compliance Questionnaire

**"An exploratory study on the impact of a food-based restrictive diet and liquid exclusive enteral nutrition (milk-based diet) on healthy gut microbiota composition (bugs) and metabolic activity (chemical markers)"**

*Name of Researcher: Mr Vaios Svolos, PhD Student, University of Glasgow.*

***Exclusive Enteral Nutrition OR CD-TREAT***

| Questions | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 |
|---|---|---|---|---|---|---|---|
| Except for tea, coffee, 7up, water, Foxes glacier mints or chewing gum, did you need to eat other foods or have additional drinks while on EEN? | | | | | | | |
| What type of drinks did you have?<br>How often did you take these drinks? | | | | | | | |
| What kind of foods did you have?<br>How often did you take these foods? | | | | | | | |
| On a scale of 1-10 where 1 is very easy and 10 is almost impossible;<br>How difficult was it to stay on the liquid diet so far? | | | | | | | |

# Supplementary methods

## RCT in healthy volunteers

### *Acceptability of interventions*

Appetite, gastrointestinal symptoms and adherence to the experimental diets were assessed by self-reported questionnaire. This was compiled and checked for content validity by the research team and for readability by lay people. The questionnaire collected information from each participant on their appetite on days one and six of each intervention, using Visual Analogue Scales extracted from an existing questionnaire[1]. Gastrointestinal symptoms and the level of adherence to the diet were also assessed at the end of each intervention, using Likert scales from a validated questionnaire[2]. Additional meals outside the experimental diets were recorded.

### *Fecal sample collection*

The entire bowel movement was collected, stored immediately under anaerobic (Oxoid™ AnaeroGen™ Sachet) cold conditions, and processed within 60 minutes of defecation. The entire bowel movement was weighed, homogenized and stored appropriately for the downstream methods.

### *Untargeted fecal metabolomics*

#### *Extraction*

Freeze-dried fecal samples were extracted by chloroform/methanol/water at a volume ratio of 1:3:1. The extraction was carried out by mixing 800µl extraction mixture with 20mg freeze dried fecal sample. The supernatant was recovered to another vial and the extracts were stored at -80$^{o}$C until LC-MS analysis.

#### *Solvents and Chemicals*

HPLC-grade acetonitrile, chloroform and water were obtained from Fisher Scientific, UK. Ammonium carbonate and methanol were purchased from Sigma-Aldrich, UK. HPLC grade water was produced in house by a Direct-Q 3 Ultrapure water purification system (Millipore, Watford, UK). The metabolite standards were obtained from Sigma-Aldrich, UK and were prepared as previously described[3].

#### *HPLC conditions*

**Mobile phase and column:** The mobile phase solutions were freshly prepared and stored at room temperature for up to 48 hours as follows: Mobile phase A: (20mM Ammonium carbonate buffer, pH 9.2) was prepared by dissolving 1.92 g of ammonium carbonate in 800 ml of HPLC-grade water followed by adjustment to pH 9.2 with ammonia solution and then made up to 1L. Mobile phase B: HPLC-grade acetonitrile. The column used was a ZIC-pHILIC (L150 × I.D. 4.6 mm, 5µm, polymeric

bead support) column from Hichrom Ltd, Reading, UK. The column was attached to a ZIC®-pHILIC guard column.

**HPLC setup:** A gradient elution method (Table 1) was used as described previously[3]. The flow rate was set to 0.3 mL/min.

Table 1 Gradient elution programme applied for ZICpHILIC column in LC-MS analysis.

| Time (min) | Mobile phase A% | Mobile phase B % | Flow rate (ml/min) |
|---|---|---|---|
| 0 | 20 | 80 | 0.3 |
| 30 | 80 | 20 | 0.3 |
| 31 | 92 | 8 | 0.3 |
| 36 | 92 | 8 | 0.3 |
| 37 | 20 | 80 | 0.3 |
| 46 | 20 | 80 | 0.3 |

**Orbitrap Exactive Mass-Spectrometer setup:** Samples were analysed using an Accela HPLC system connected to an Orbitrap Exactive mass spectrometer (Thermo Fisher Scientific, Bremen, Germany). The quality of the data and identified metabolites were confirmed by standard mixtures introduced within the running sequence[4]. During the analysis, peak characteristics such as width and height were determined using relative standard deviation (RSD) values. The acceptable value of RSD was set not exceeding 20% for each standard and the retention time shift should not be more than 0.3 min between the initial and final sample in a sequence.

*Data extraction*

The raw files for the samples were extracted and processed using mzMatch/Peak ML: metabolomics data analysis[5]. IDEOM provided a free data extraction application that is able to identify spectrum peaks while considering noise sources in the LC/MS analysis. This macro-based spreadsheet was obtained from http://mzmatch.sourceforge.net/ideom.htm and the analysis depends on the LC/MS data extraction method[6]. The R package from http://www.r-project.org was pre-installed to create a readable environment for LC/MS processing[7]. The identified metabolites and quality of peaks were examined manually using different databases including HMDB (http://www.hmdb.ca/), KEGG (http://www.genome.jp/kegg/) and LIPID MAPS (http://www.lipidmaps.org/).

## Animal experiments

### *Gut histopathology*

Colonic and ileal specimens were fixed in 10% formalin until the tissue was paraffin-embedded, stained with hematoxylin and eosin and evaluated by two pathologists (RK and JS) in a blinded manner. Tissue sections (5µm) were stained with hematoxylin and eosin, imaged (EVOS FL Auto Cell Imaging System, Life Technologies), and evaluated by two pathologists (RK and JS) in a blinded manner.

The colon was assessed for leukocyte infiltration, mucosal damage, neutrophil infiltration, crypt abscesses or hyperplasia and goblet cell depletion. The ileum was assessed for leukocyte infiltration, villous fusion, shortening or hyperplasia, and mucosal necrosis, erosion and ulceration. Each parameter was scored from 0 to 3 (0=no; 1=mild; 2=moderate; 3=severe presence). The sum of the individual parameters generated an ileal (min-max score: 0-12) and colonic (min-max score: 0-15) inflammatory score[8].

***Expression of cytokines in ileum***

The expression of the following genes was quantified TNF-α (GenBank accession number Rn99999017_m1), Il-6 (GenBank accession number Rn01410330_m1), IL-10 (GenBank accession number Rn01483988_g1), IL-1b (GenBank accession number Rn00580432_m1), CXCL-1 (GenBank accession number Rn00578225_m1). Amplification reactions were analyzed by relative quantification using the comparative CT method and using the housekeeping genes GAPDH (GenBank accession number Rn01775763_g1) and RPLNO (GenBank accession number Rn03302271_gH) as endogenous controls. Data are displayed as fold change of gene expression against the average of B7-CONTROL samples.

## Bioinformatics

We retained the paired-end reads between 225bp and 275bp length, overlapped the reads and performed OTU clustering on dereplicated reads after removing singletons and using 98% similarity. Afterwards, we removed chimera based on both de-novo (utilizing the most abundant dereplicated reads) and reference-based approach (as mentioned in the link) finally generating OTU at 97% similarity with taxonomy assigned using functions given in Dada2 pipeline after filtering out OTU with mean proportional abundance<0.01%.

## Statistics

***Power calculation***

The power calculation for the RCT in health volunteers was revised after completion of the first 10 participants at which point we were already powered to detect significant changes for SCFA and bacterial load both during EEN and CD-TREAT (Table 1). However, we continued recruitment to our original target number of 25 participants to maximize statistical power for secondary outcomes of the study where higher inter-individual variation and potentially smaller effect size (i.e. 16S rRNA sequencing, metabolome) were expected.

Table 1. Fecal sample characteristics, metabolites and bacterial load before and after dietary EEN and CD-TREAT in the first 10 participants who completed the healthy volunteers RCT (n=40 fecal samples from 10 participants).

| | **Pre EEN** | **Post EEN** | **Pre CD-TREAT** | **Post CD-TREAT** |
|---|---|---|---|---|
| Bristol Stool Form Scale | 3.7, 1.6 | 1.6, 1.0[a**] | 3.0, 1.3 | 1.9, 0.9[a†] |
| Fecal pH | 7.0, 0.5 | 8.2, 0.2[a¥] | 7.0, 0.6 | 7.7, 0.4[a**,c**] |
| Acetate, µmol/g | 67.6, 11.9 | 48.6, 14.4[a*] | 76.9, 17.6 | 65.5, 19.8[a†,c**] |
| Propionate, µmol/g | 15.6, 5.4 | 9.9, 4.9[a**] | 15.8, 5.8 | 13.3, 9.2[a*] |
| Butyrate, µmol/g | 11.9, 5.0 | 6.3, 2.5[a**] | 14.1, 10.3 | 7.9, 5.4[a**] |
| Valerate, µmol/g | 2.2, 0.6 | 2.0, 0.8 | 2.4, 1.5 | 1.9, 1.1 |
| Iso-butyrate, µmol/g | 1.7, 0.8 | 2.4, 1.0[a*] | 2.0, 1.1 | 2.1, 1.0 |
| Iso-valerate, µmol/g | 1.8, 1.0 | 2.7, 1.1[a**] | 2.1, 1.4 | 2.3, 1.1 |
| Free sulfide, nmol/g | 5.1, 2.6 | 1.5, 1.6[a¥] | 4.2, 1.0 | 6.0, 4.7[c¥] |
| Total sulfide, nmol/g | 82.2, 62.9 | 250.4, 83.7[a¥] | 66.5, 30.6 | 141.4, 69.8[a**,c**] |
| Total bacteria | 11.3, 0.2 | 11.1, 0.2[a**] | 11.2, 0.2 | 11.0, 0.3[a*] |

Data are displayed with means and standard deviations. [a] significant difference between Pre EEN & Post EEN or Pre CD-TREAT & Post CD-TREAT; [b] significant difference between Pre EEN & Pre CD-TREAT; [c] significant difference between Post EEN & Post CD-TREAT; [†] $p<0.1$; [*] $p<0.05$; [**] $p<0.01$; [¥] $p<0.001$. p for Fisher pairwise comparisons following general linear model with Box-Cox transformation; Total bacteria, $\log_{10}$ 16S rRNA gene copy number/g stool.

## References


1. Flint A, Raben A, Blundell JE, et al. Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. Int J Obes Relat Metab Disord 2000;24:38-48.
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4. Zhang T, Watson DG, Wang L, et al. Application of Holistic Liquid Chromatography-High Resolution Mass Spectrometry Based Urinary Metabolomics for Prostate Cancer Detection and Biomarker Discovery. PLoS One 2013;8:e65880.
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8. Klopfleisch R. Multiparametric and semiquantitative scoring systems for the evaluation of mouse model histopathology--a systematic review. BMC Vet Res 2013;9:123.

**"An open label pilot study of the CD-TREAT diet as a novel therapy for active luminal Crohn's disease"**

Researcher – Vaios Svolos, University of Glasgow

***CD-TREAT diet Checklist***

| Study Number: | Date: |
|---|---|
| Please tick the choice that you/your child chose and how many quarters of the portion you/your child ate? | |
| **Breakfast:**<br>1 Multivitamin Tablet □ yes □ no | |
| 1 ½ cup (360ml) lactofree milk With ¾ cup (45g):<br>□ rice krispies □ corn flakes<br>□ honey hoops □ rice and corn flakes | |
| 1 cup (240ml) pure juice:<br>□ pineapple juice □ apple juice<br>□ apple & raspberry juice □ cranberry juice<br>□ cranberry & raspberry juice | |
| **Morning Snack:**<br>1 cup (240ml) pure juice:<br>□ pineapple juice □ apple juice<br>□ apple & raspberry juice □ cranberry juice<br>□ cranberry & raspberry juice | |
| **Lunch:**<br>**No**_____<br>Please write the meal number mentioned on your lunch pack | |
| **Afternoon snack**<br>1 cup (240ml) LactoFree Milk | |
| □ 1 peeled apple □ 1 peeled pear | |
| **Dinner:**<br>**No**_____<br>Please write the meal number mentioned on your dinner pack | |

Did you eat anything outside the CD-TREAT diet plan during the day? If yes, please write it below:

_____

_____

_____

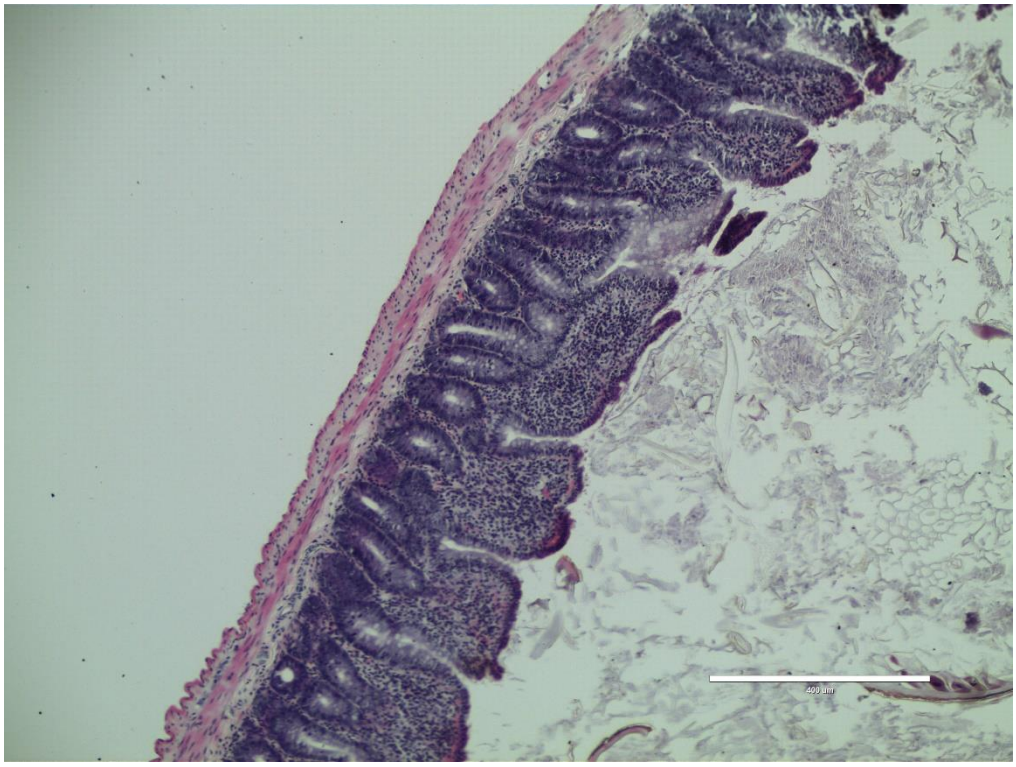
_____

_____

_____

_____

**HLA-B27 CONTROL Rat i**

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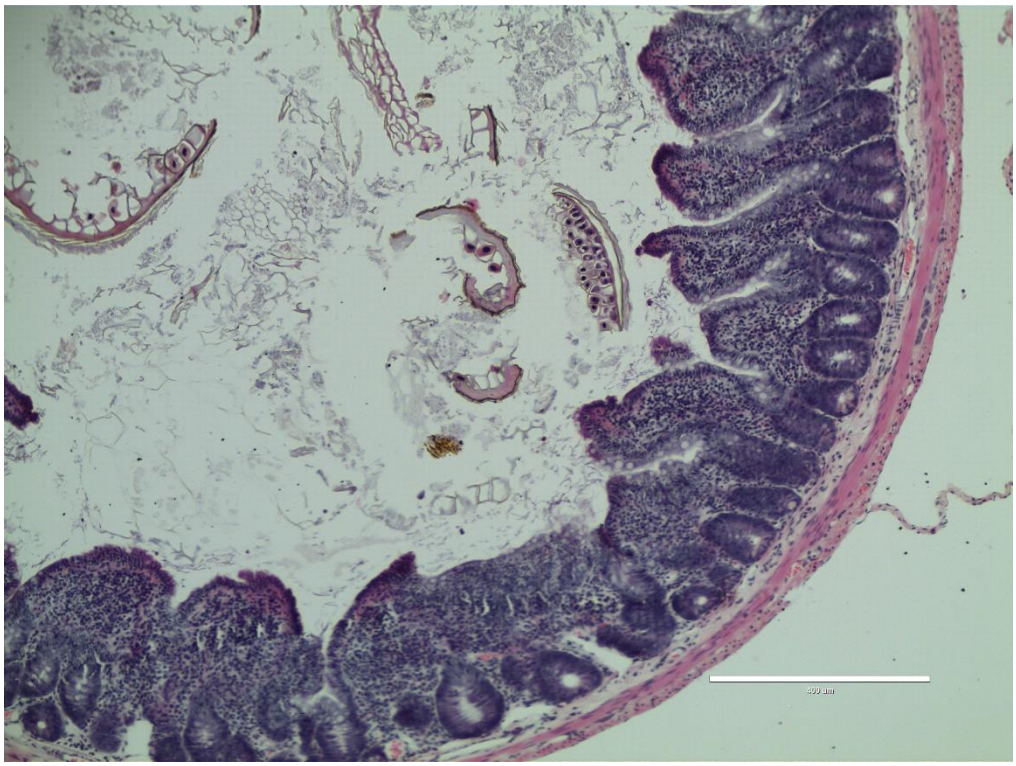

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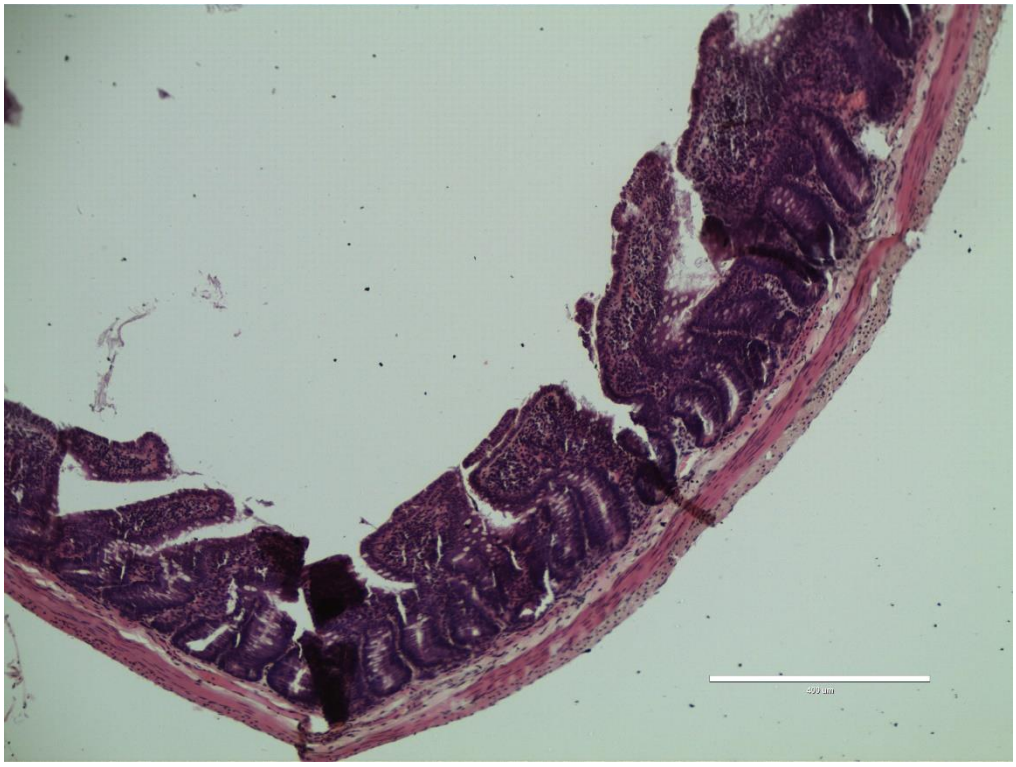

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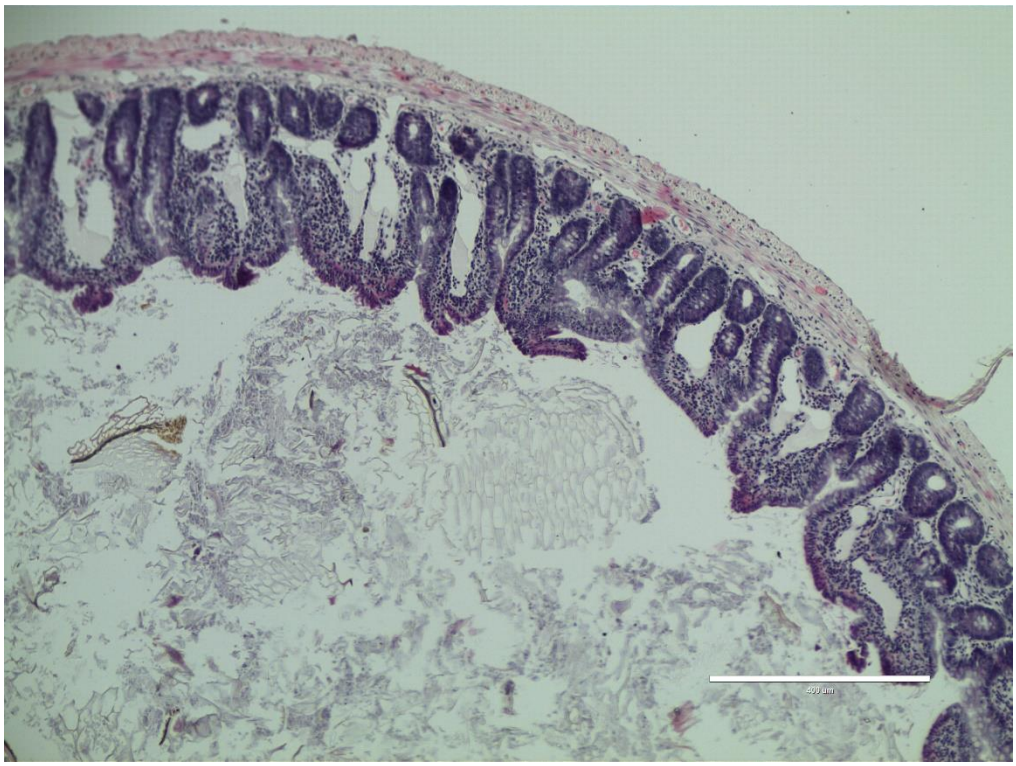

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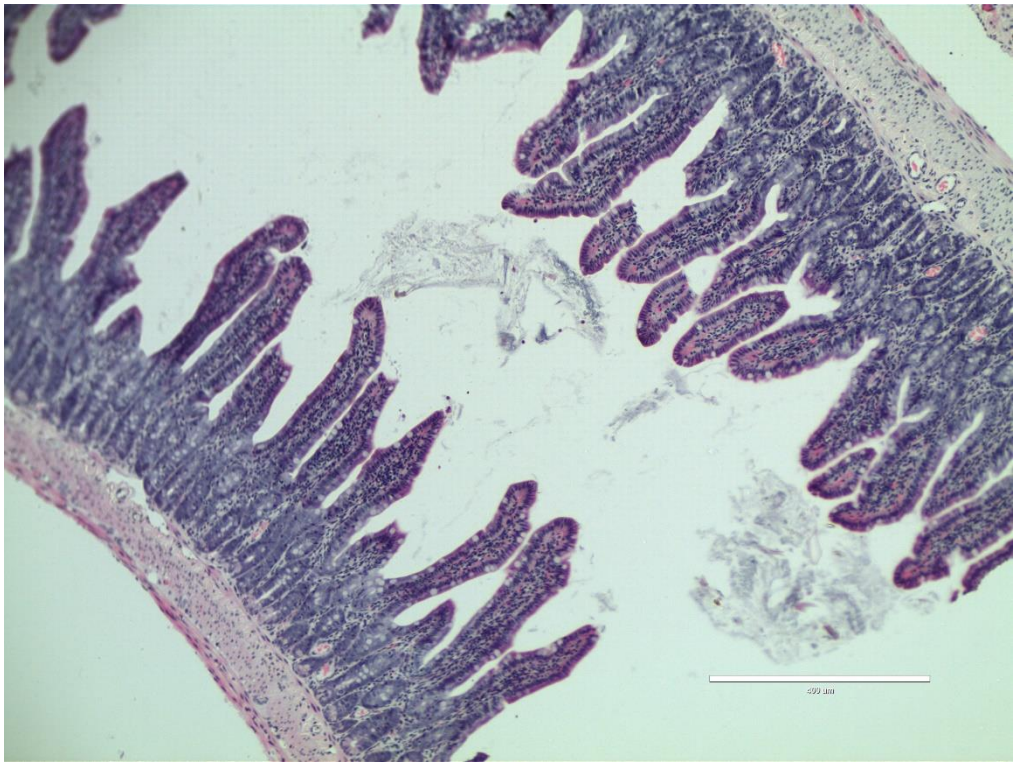

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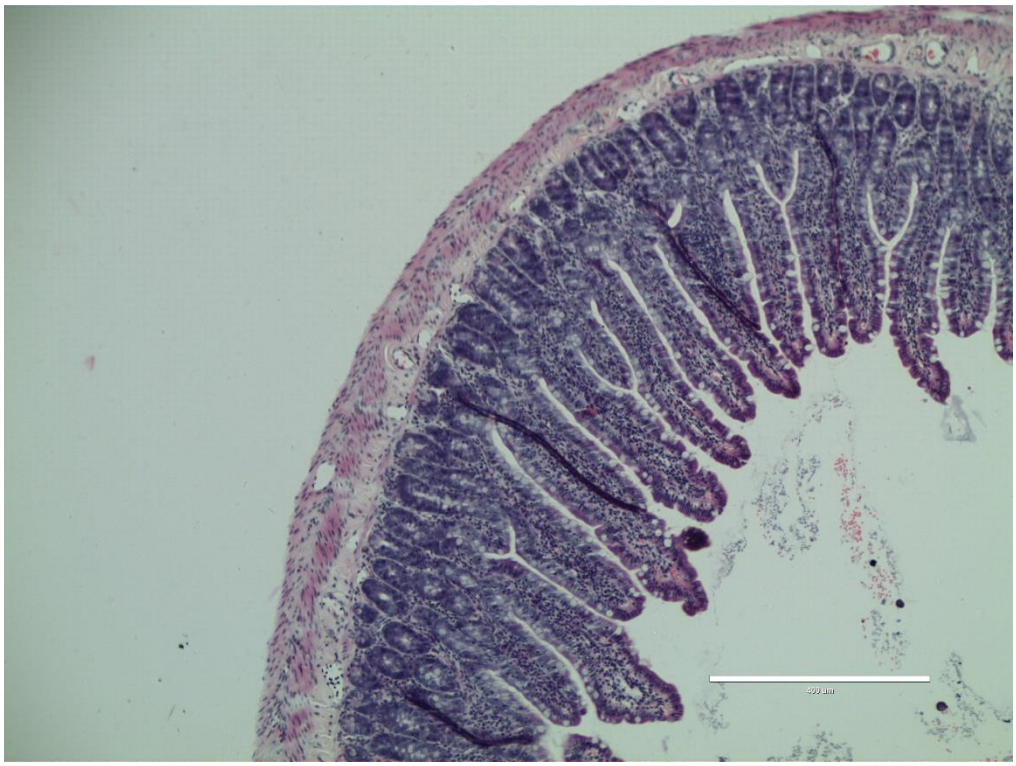

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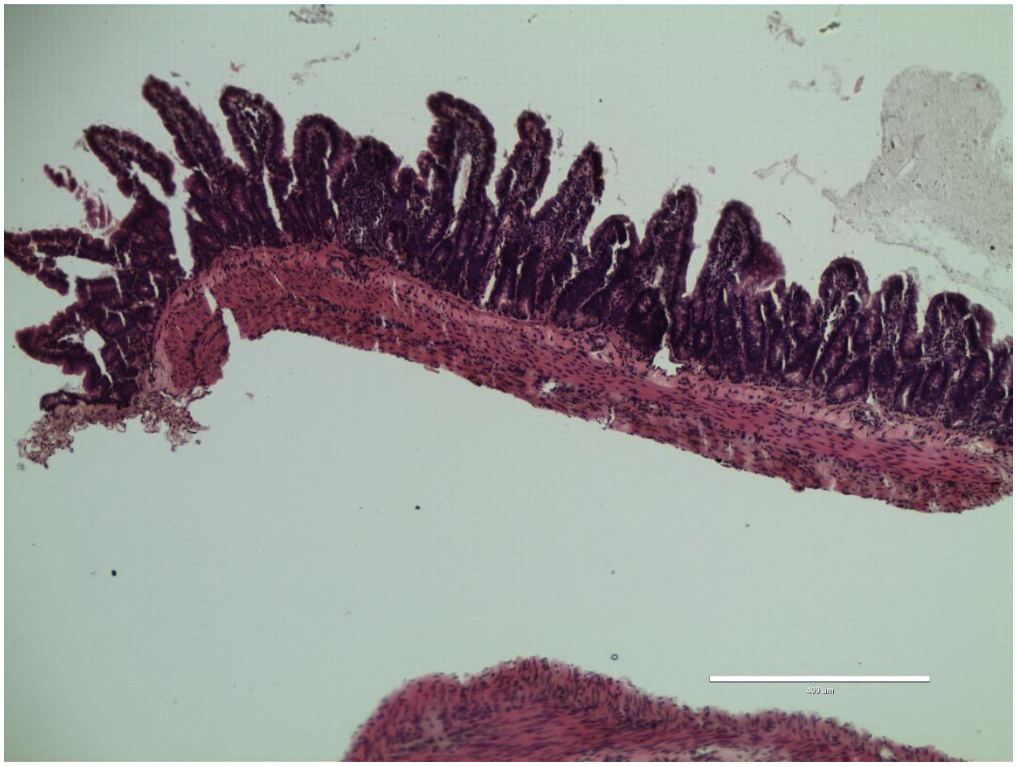


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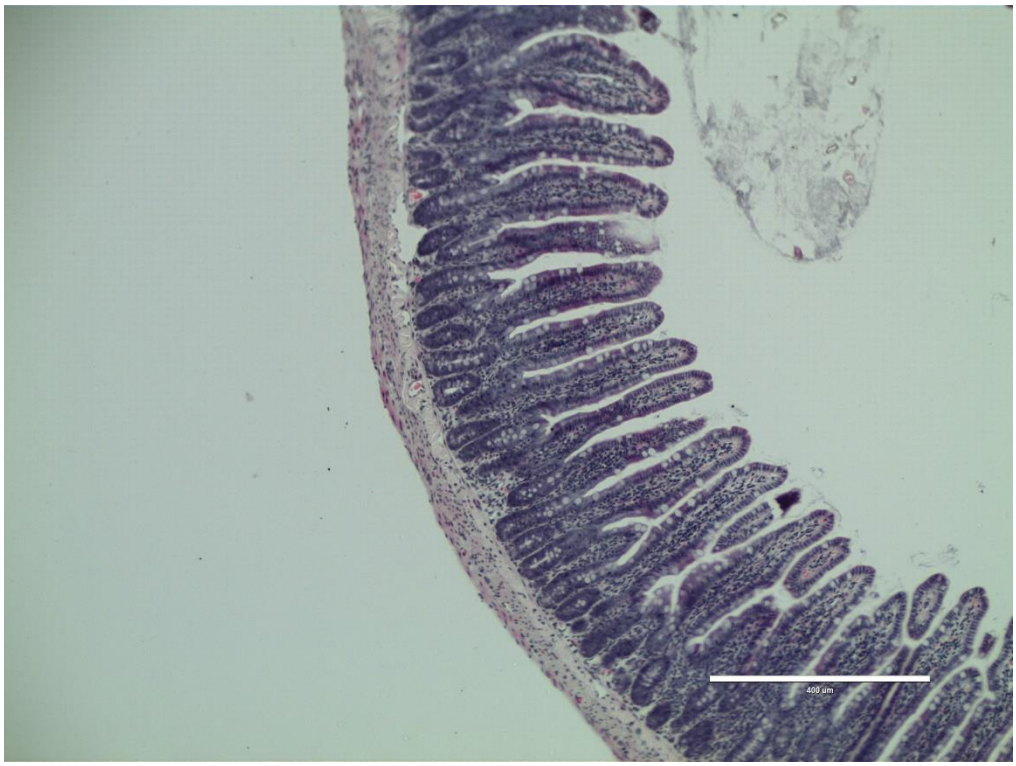
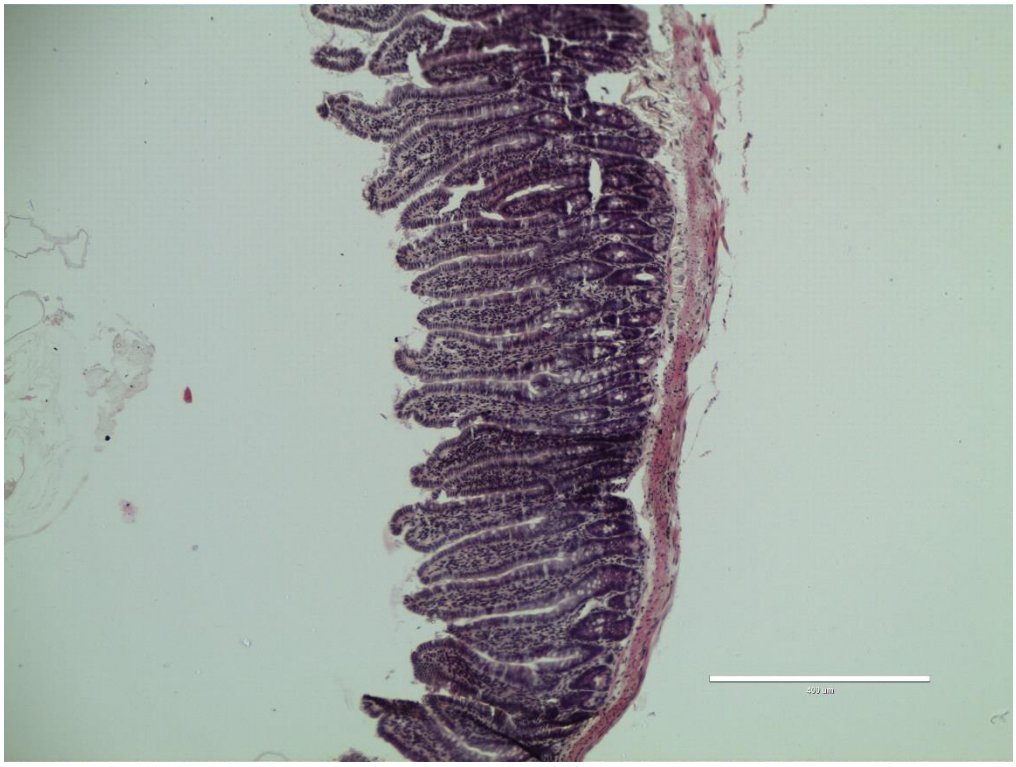


**HLA-B27 CD-TREAT Rat i**

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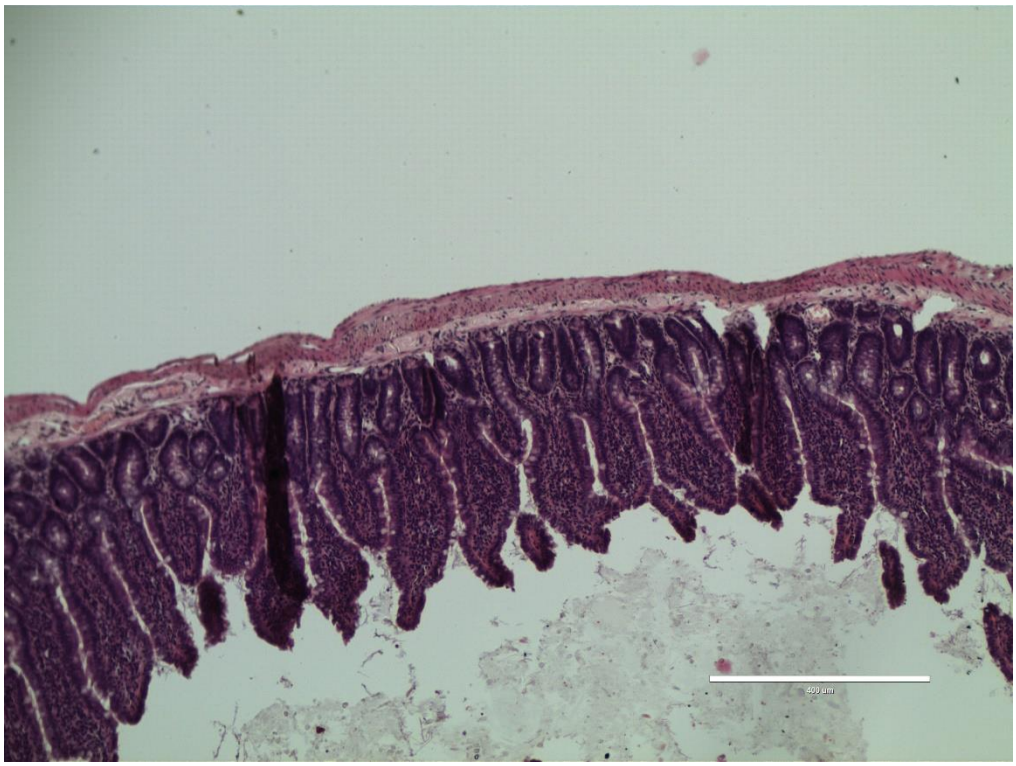

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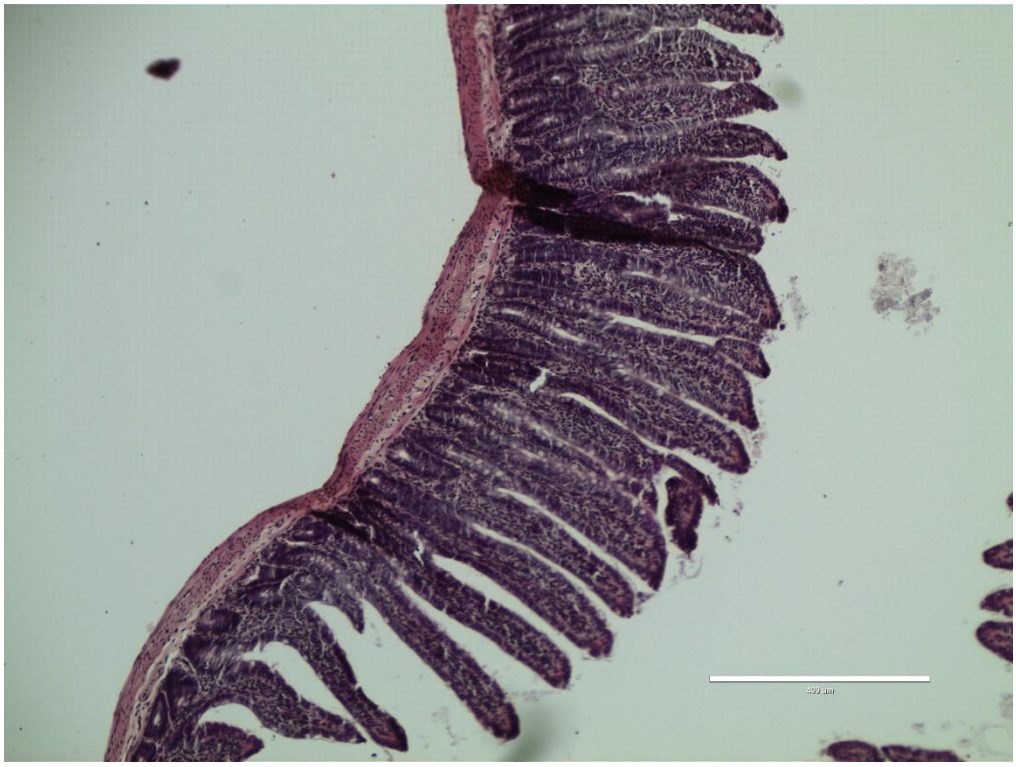

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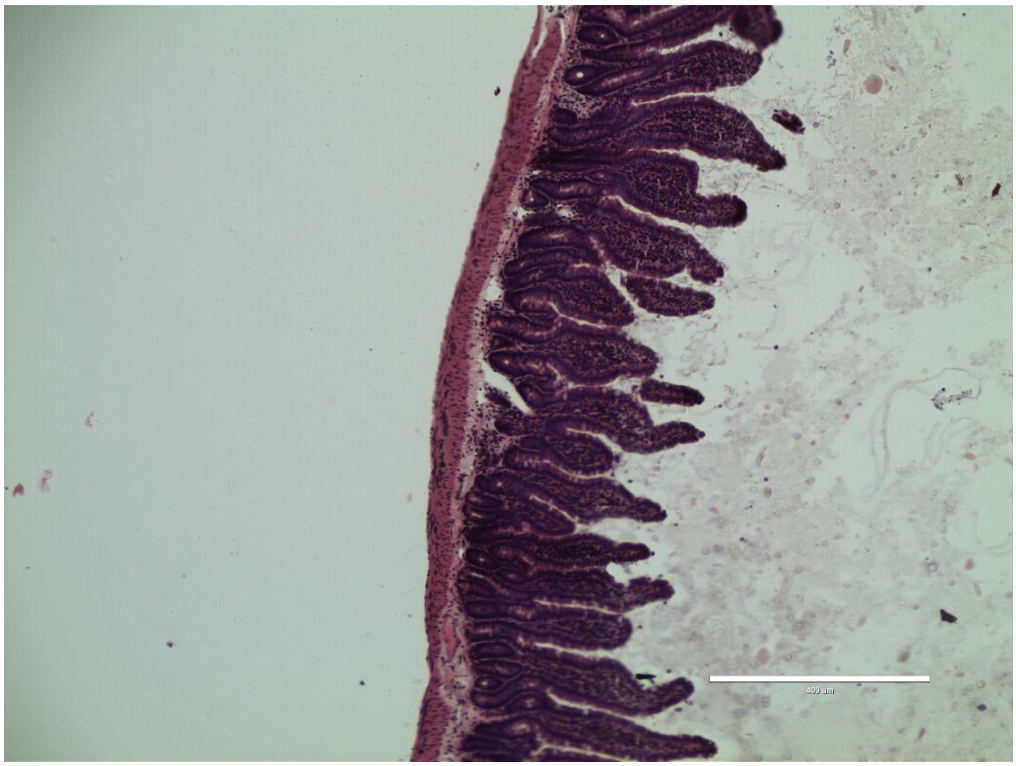

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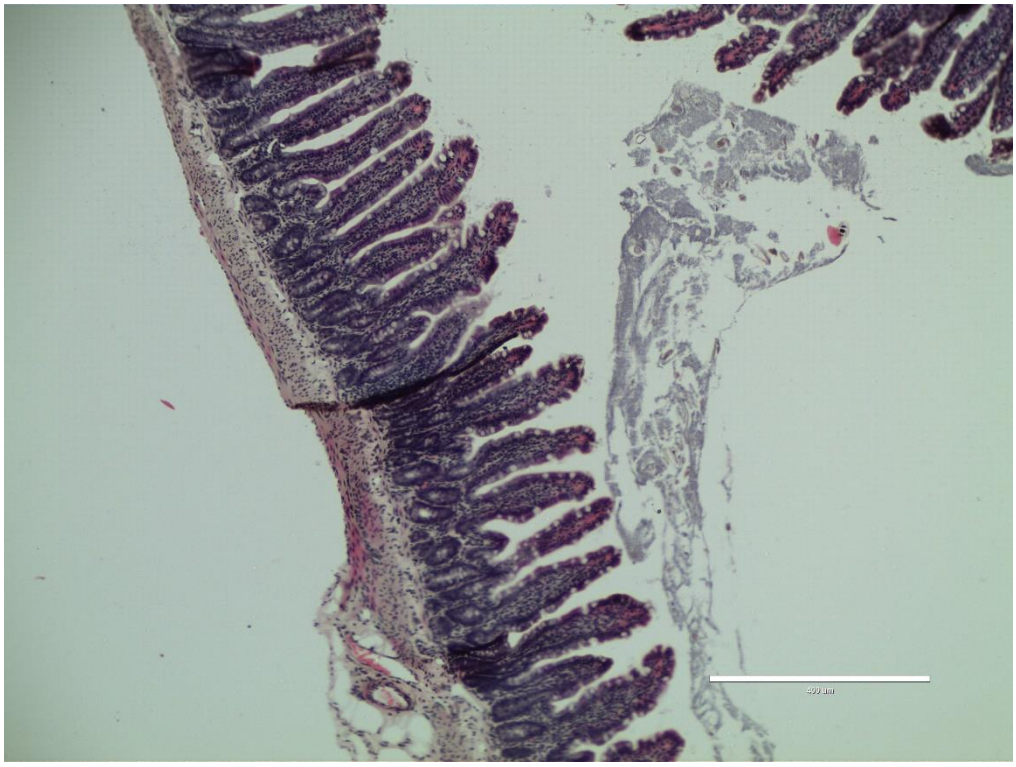

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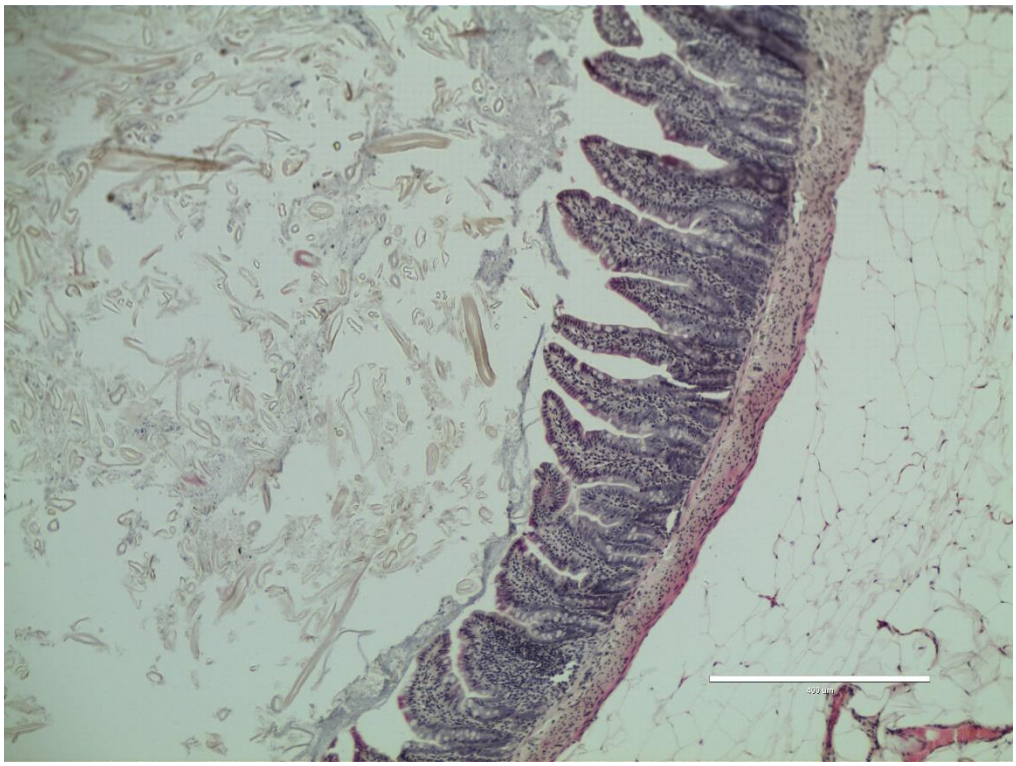

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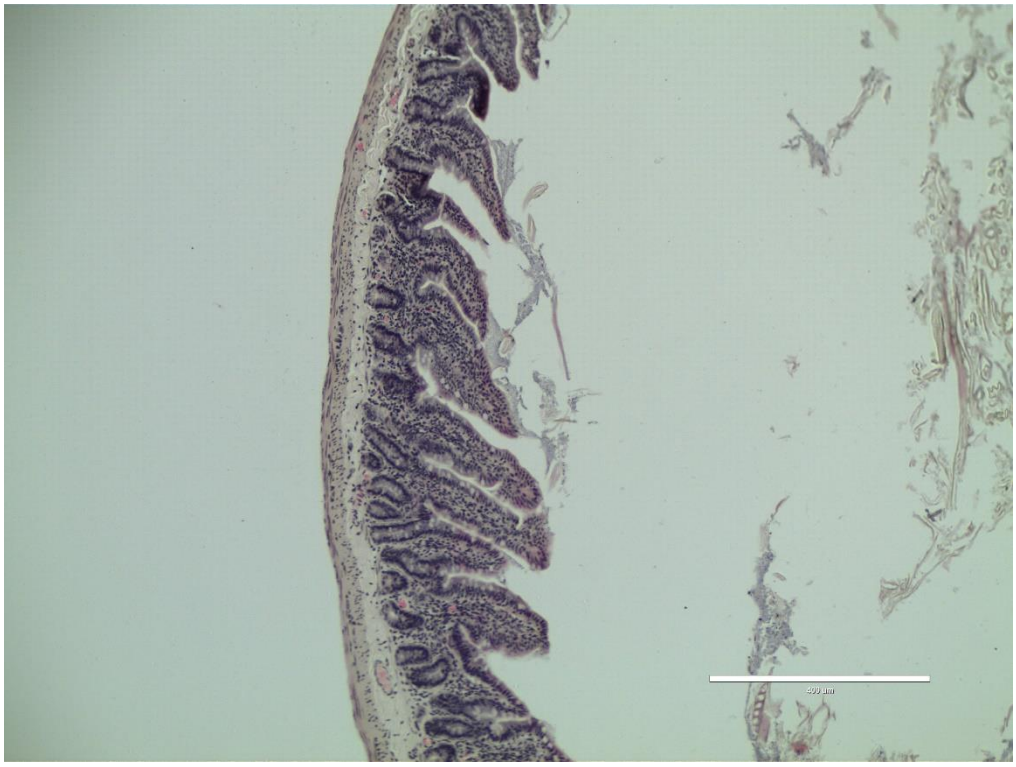

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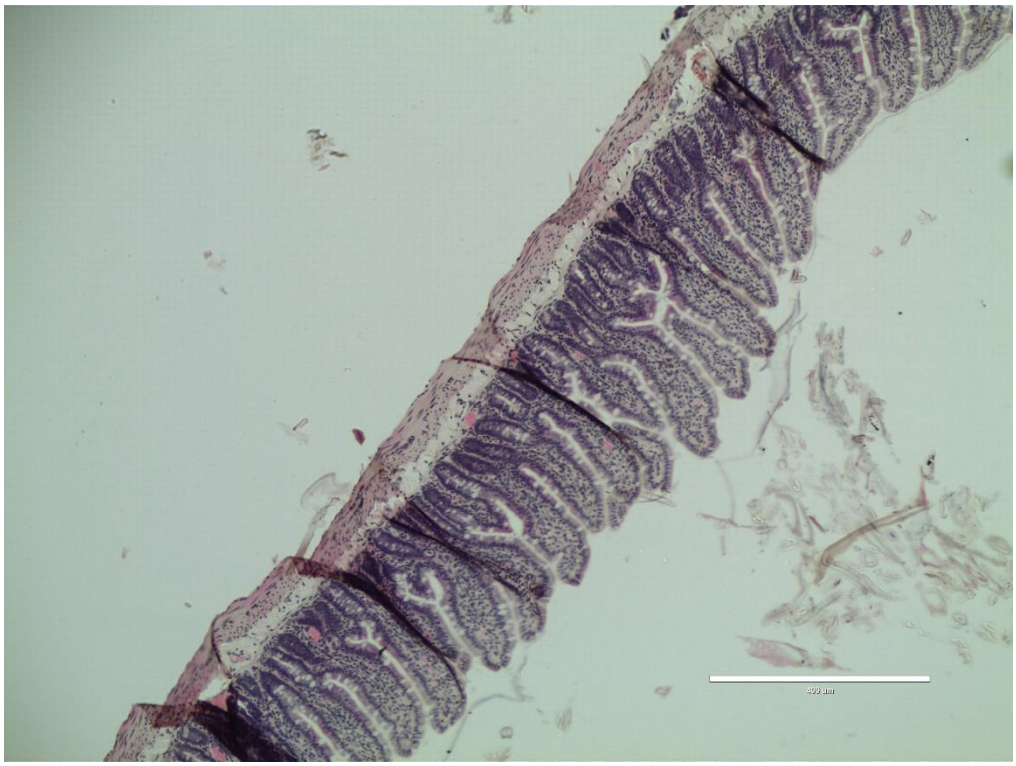

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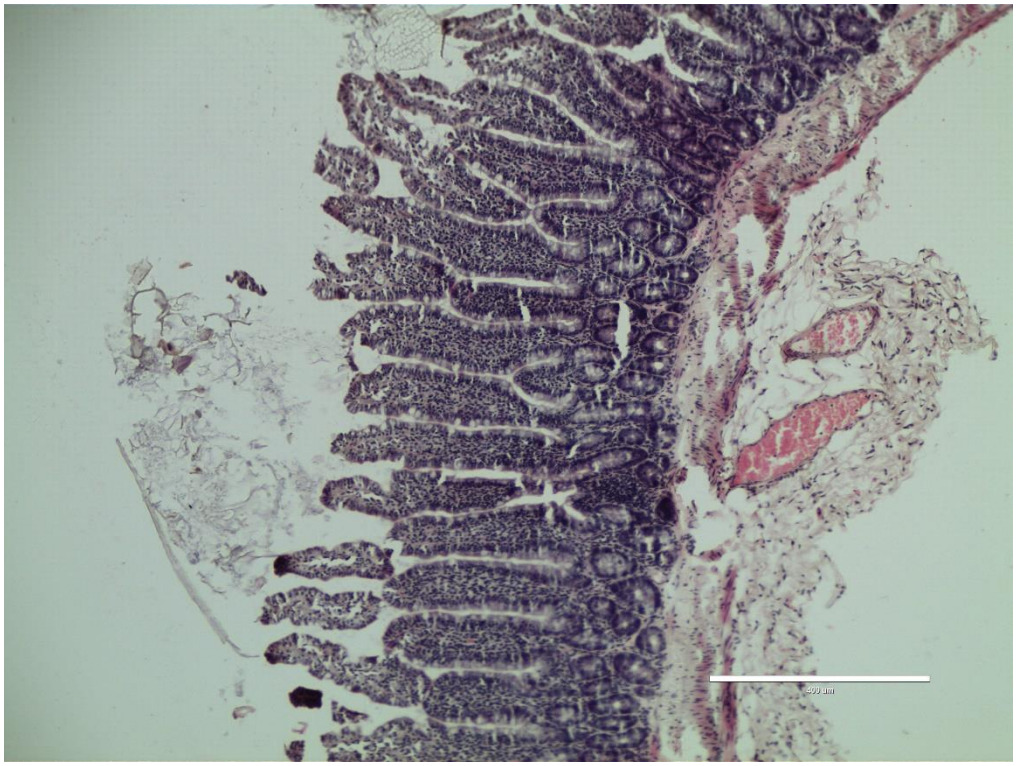

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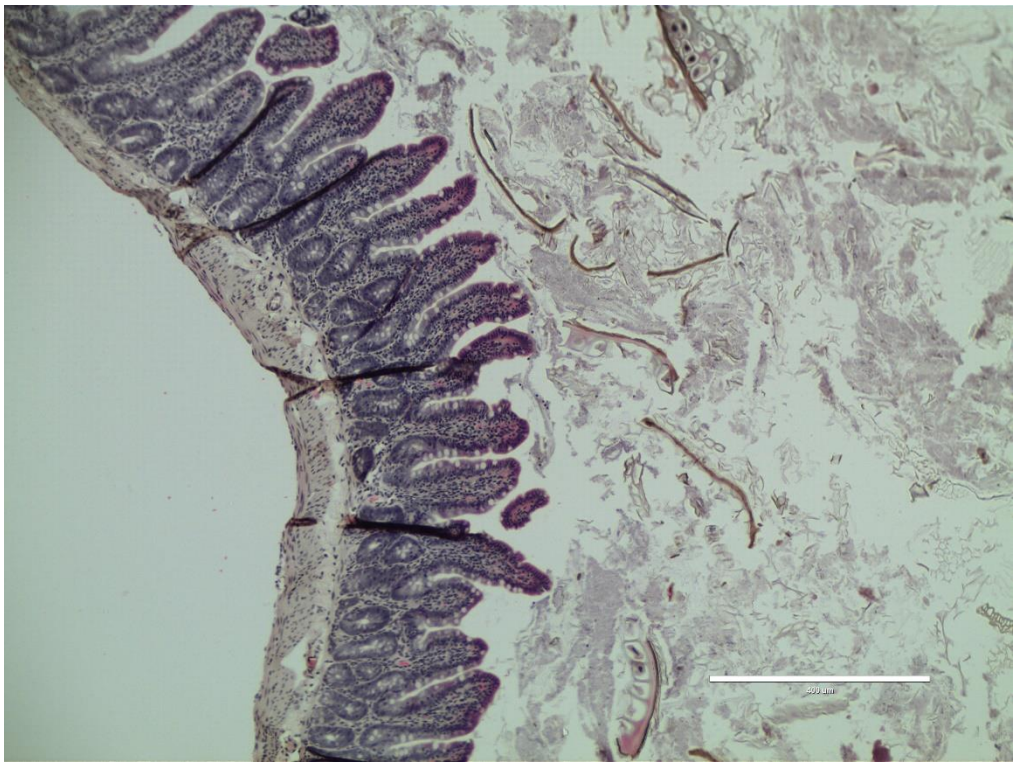

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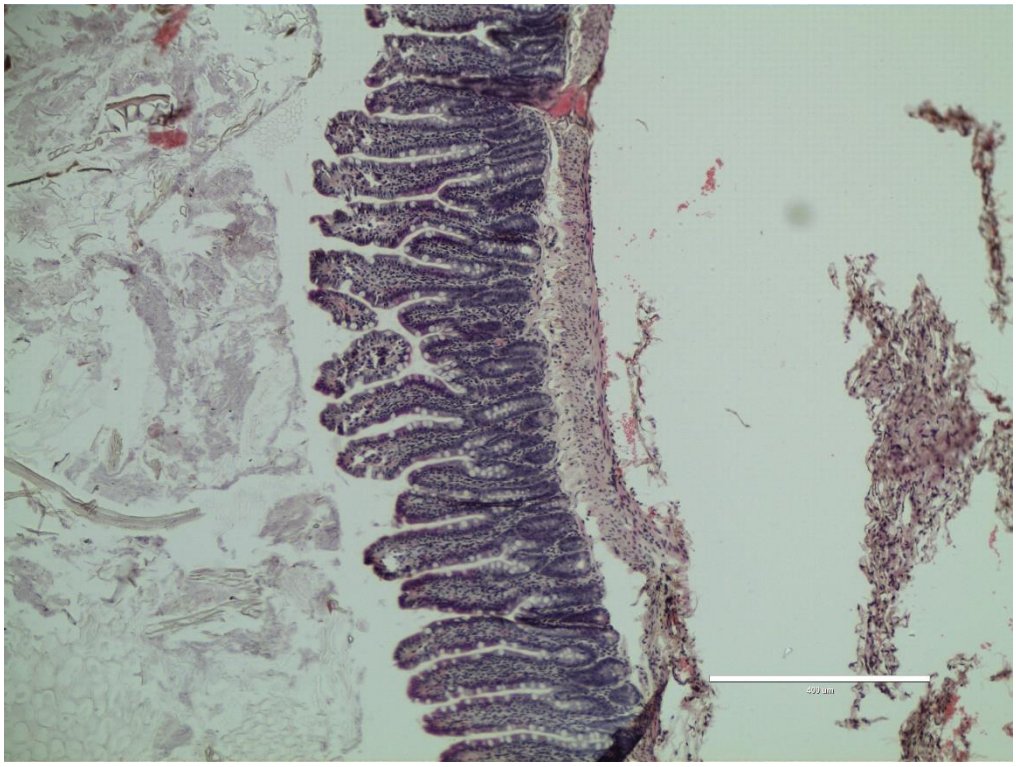

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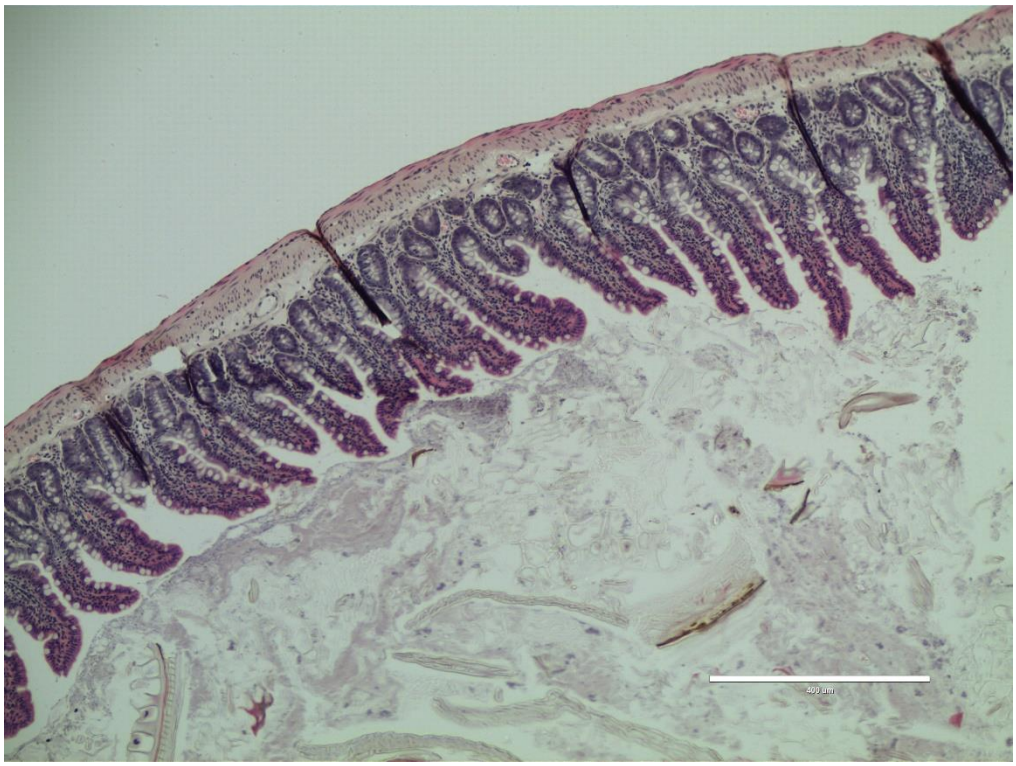
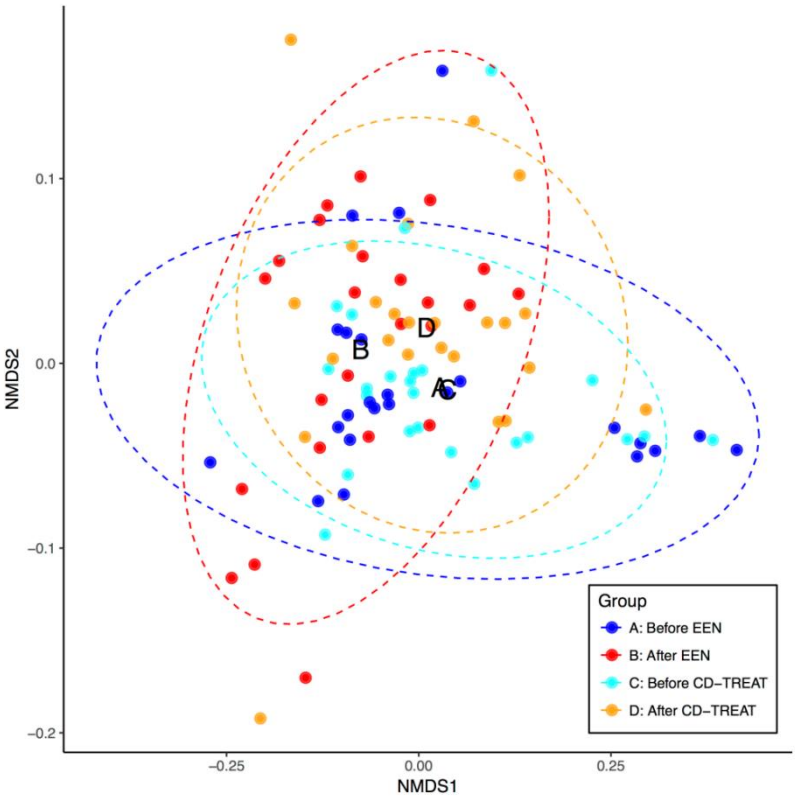


Figure S1. Example CD-TREAT meals prepared by the catering company

Figure S2. Non-metric multidimensional scaling (NMDS) using weighted UniFrac distances of the 3% operational taxonomic unit (OTU) community structures during dietary interventions on healthy human fecal microbiome (n=24).




Adonis for A-B: $R^2 = 0.11$, Adjusted $P$=.001

Adonis for C-D: $R^2 = 0.03$, Adjusted $P$=.031

Adonis for A-C: $R^2 = 0.008$, Adjusted $P$=.080

Figure S3. Scatterplot with genera changes before and after EEN and CD-TREAT diet in the crossover RCT in healthy volunteers (n=24).

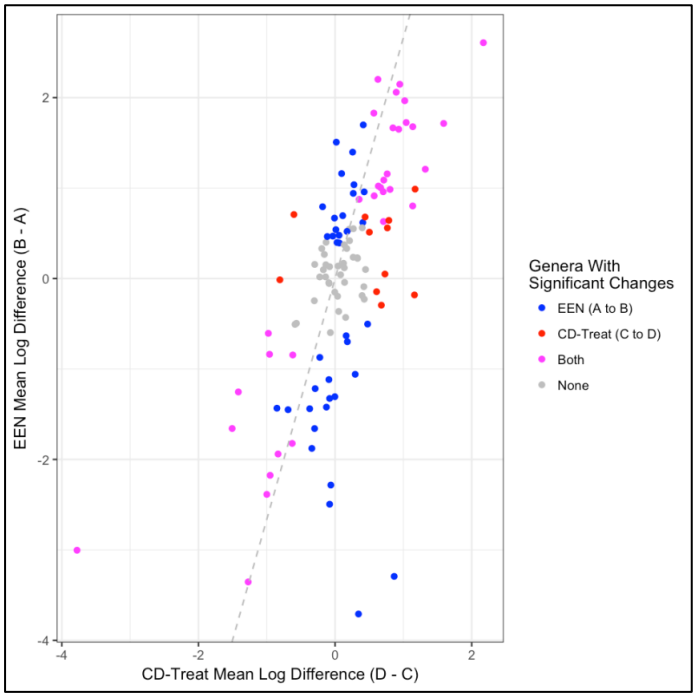


Figure S4. Representative hematoxylin and eosin stained sections of the colon of: i) EEN, ii) CD-TREAT, iii) CONTROL treated HLA-B27 rats and i) EEN, ii) CONTROL treated HLA-B7 rats. Colon tissue sections were visualized and digital images were captured using an EVOS FL Auto Cell Imaging System (Life Technologies) with a 10× objective (in all cases data of all studied animals were included, n=20).

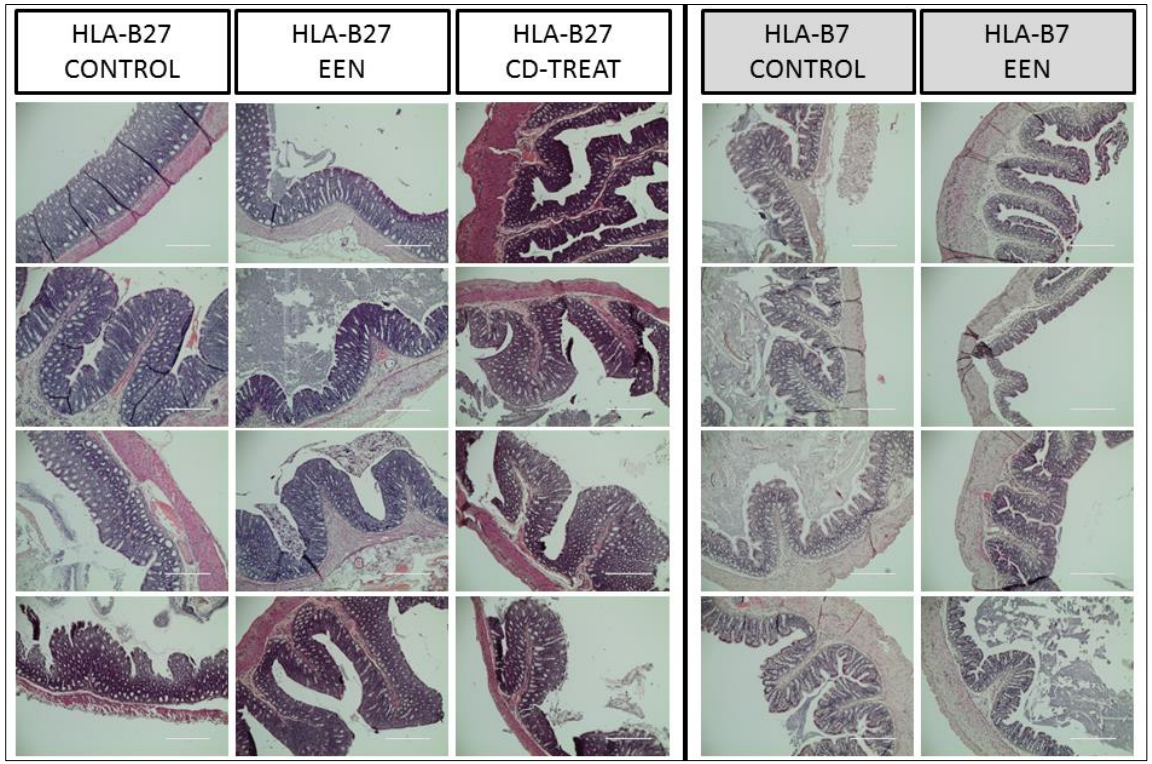


Figure S5. Non-metric multidimensional scaling (NMDS) using Bray-Curtis distances of the 3% OTU community structures of B27-CONTROL, B27-EEN, B27-CD-TREAT, B7-CONTROL and B7-EEN animals': (a) cecum tissue microbiome (n=19), (b) colon tissue microbiome (n=10) and (c) colon content microbiome at sacrifice (n=17).

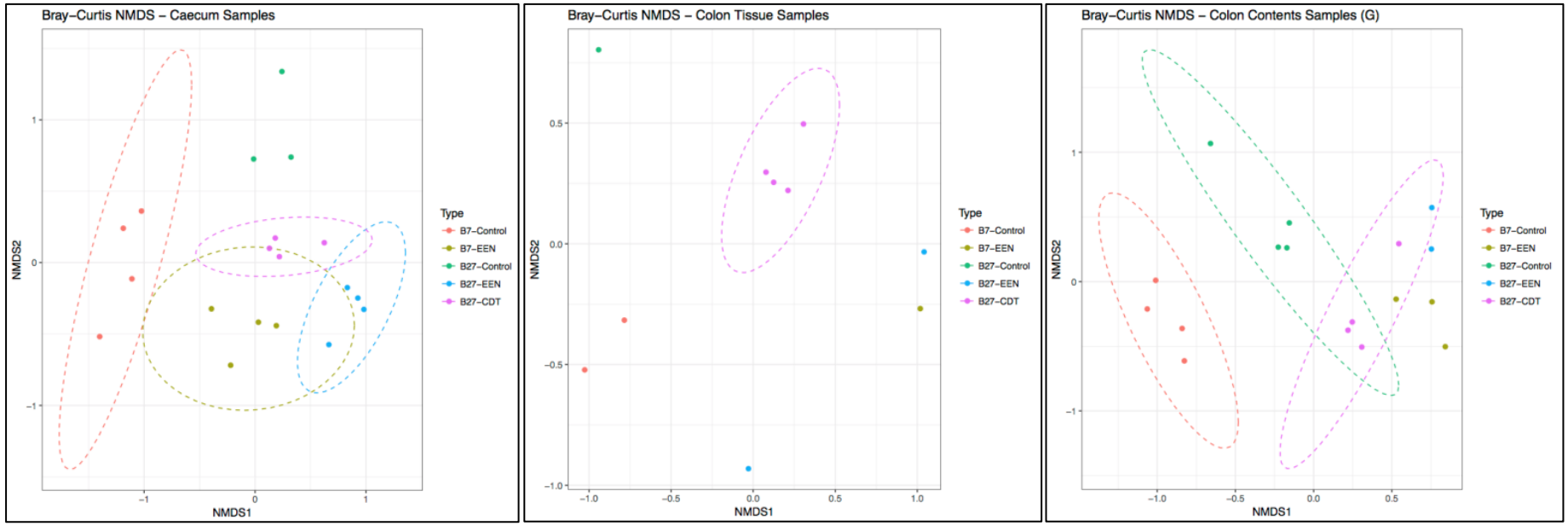
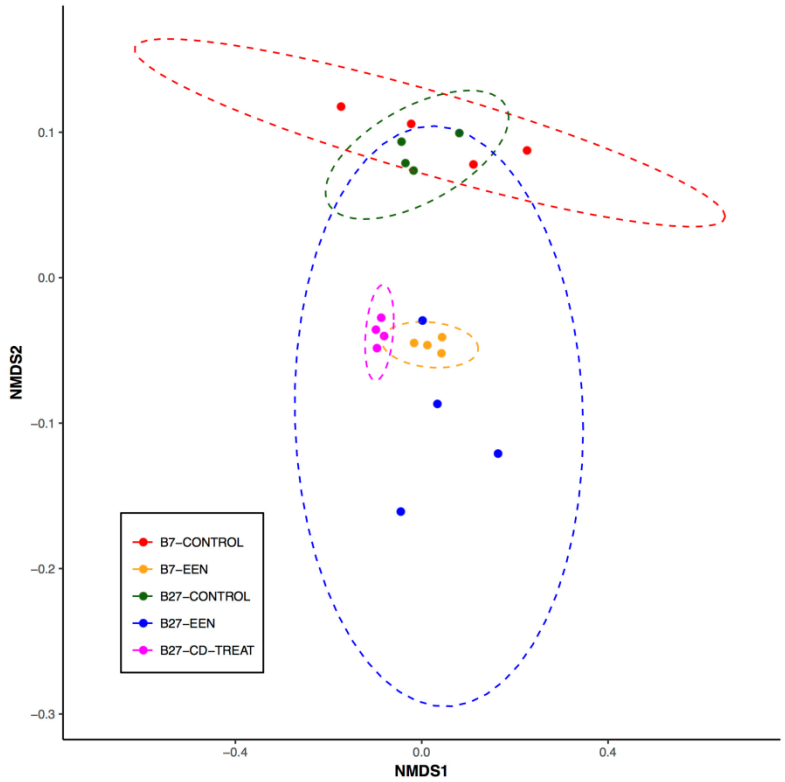


Figure S6. Non-metric multidimensional scaling (NMDS) using weighted Unifrac distances of the 3% operational taxonomic unit (OTU) community structures of the rat cecal luminal content microbiome at sacrifice (n=20).



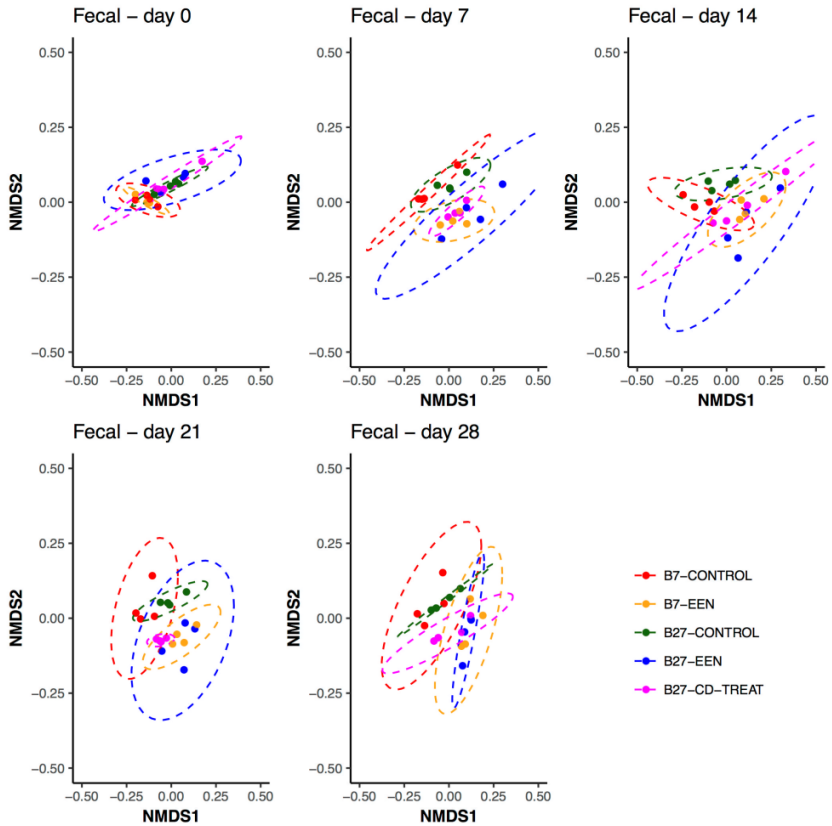

Adonis for B27-EEN-B27-CONTROL: $R^2 = 0.45$, Adjusted $P$=.038

Adonis for B27-CD-TREAT-B27-CONTROL: $R^2 = 0.79$, Adjusted $P$=.038

Adonis for B27-CONTROL-B7-CONTROL: $R^2 = 0.35$, Adjusted $P$=.094

Adonis for B7-EEN-B7-CONTROL: $R^2 = 0.63$, Adjusted $P$=.038

Figure S7. Non-metric multidimensional scaling (NMDS) using weighted Unifrac distances of the 3% operational taxonomic unit (OTU) community structures of the rat fecal microbiome during the course of dietary interventions (n=20).




| Time | Group 1 | Group 2 | $R^2$ | Adjusted *P* |
|---|---|---|---|---|
| Day 0 | B27-CONTROL | B7-CONTROL | 0.515736 | .315 |
| Day 7 | B27-EEN | B27-CONTROL | 0.389642 | .066 |
| Day 7 | B27-CD-TREAT | B27-CONTROL | 0.434009 | .066 |
| Day 7 | B27-CONTROL | B7-CONTROL | 0.445806 | .066 |
| Day 7 | B7-EEN | B7-CONTROL | 0.540451 | .066 |
| Day 14 | B27-EEN | B27-CONTROL | 0.416568 | .080 |
| Day 14 | B27-CD-TREAT | B27-CONTROL | 0.238897 | .148 |
| Day 14 | B27-CONTROL | B7-CONTROL | 0.330802 | .148 |
| Day 14 | B7-EEN | B7-CONTROL | 0.650334 | .080 |
| Day 21 | B27-EEN | B27-CONTROL | 0.440758 | .067 |
| Day 21 | B27-CD-TREAT | B27-CONTROL | 0.604733 | .039 |
| Day 21 | B27-CONTROL | B7-CONTROL | 0.562680 | .039 |
| Day 21 | B7-EEN | B7-CONTROL | 0.704100 | .039 |
| Day 28 | B27-EEN | B27-CONTROL | 0.584165 | .070 |
| Day 28 | B27-CD-TREAT | B27-CONTROL | 0.291496 | .188 |
| Day 28 | B27-CONTROL | B7-CONTROL | 0.230795 | .201 |
| Day 28 | B7-EEN | B7-CONTROL | 0.596205 | .070 |

Table S1: A day's menu of CD-TREAT diet for a boy with CD, 15 y, 48 kg and 170cm.

| |
|---|
| **Breakfast:** |
| 1 multivitamin tablet |
| Full fat milk (360ml) |
| Rice breakfast cereals (45g) |
| Apple juice (360ml) |
| **Morning snack:** |
| Pineapple juice (360ml) |
| 1 peeled apple |
| **Lunch:** |
| 1 sandwich with white bread (2 slices), cheddar (45g) and cream cheese (45g), lettuce (20g) and peeled cucumber (20g) |
| 1 bowl chicken and rice soup |
| **Afternoon snack:** |
| 1 rice pudding |
| **Dinner:** |
| 1 portion grilled salmon (180g) with mashed potatoes (260g) and cheese sauce |

All dairy products were lactose free; all cereal-based products were gluten free

Table S2. Body weight, fecal characteristics, metabolites and bacterial load before and after EEN and CD-TREAT in the crossover RCT in healthy volunteers (n=100 samples from 25 participants).

| | **Pre EEN** | **Post EEN$** | **ΔEEN** | **Pre CD-TREAT$** | **Post CD-TREAT$** | **ΔCD-TREAT$$** |
|---|---|---|---|---|---|---|
| Body weight (kg) | 66.0, 11.3 | 65.2, 10.5 | -0.7, 1.3 | 65.9, 11.2 | 65.5, 11.0 | -0.4, 0.8 |
| Fecal water (%) | 70.9, 5.3 | 67.1, 5.8$^{a**}$ | -3.8, 5.2 | 71.5, 5.1 | 70.0, 6.1$^{c*}$ | -1.5, 7.0 |
| Weight of bowel movement, g | 94.2, 54.5 | 63.2, 38.4$^{a*}$ | -31.0, 56.9 | 108.9, 60.8 | 74.9, 48.73$^{a*}$ | -34.1, 88.3 |
| Bristol Stool Form Scale | 3.8, 1.4 | 1.9, 1.3$^{a¥}$ | -1.9, 1.5 | 3.8, 1.6 | 2.1, 1.0$^{a¥}$ | -1.7, 1.7 |
| Fecal pH | 6.9, 0.5 | 8.2, 0.3$^{a¥}$ | 1.3, 0.5 | 6.8, 0.7 | 7.7, 0.5$^{a¥,c¥}$ | 0.9, 0.6$^{d**}$ |
| Ammonia, mg/g | 1.4, 1.0 | 1.7, 0.8 | 0.2, 1.2 | 1.6, 1.1 | 1.7, 1.0 | 0.0, 1.4 |
| Free sulfide, nmol/g | 7.6, 3.6 | 3.1, 4.2$^{a¥}$ | -4.5, 3.6 | 7.5, 4.3 | 8.8, 5.1$^{c¥}$ | 1.3, 4.5$^{d¥}$ |
| Total sulfide, nmol/g | 62.4, 43.8 | 195.4, 75.8$^{a¥}$ | 133.0, 80.5 | 49.8, 26.8 | 104.0, 56.4$^{a¥,c¥}$ | 54.3, 47.0$^{d¥}$ |
| Acetate, µmol/g | 79.1, 20.3 | 51.7, 15.5$^{a¥}$ | -27.4, 22.6 | 91.8, 25.4$^{b*}$ | 70.2, 17.3$^{a¥,c¥}$ | -21.6, 20.4 |
| Propionate, µmol/g | 18.5, 8.0 | 12.8, 6.2$^{a¥}$ | -5.7, 7.8 | 19.3, 8.0 | 14.2, 7.3$^{a¥}$ | -5.2, 7.9 |
| Butyrate, µmol/g | 15.0, 6.8 | 8.1, 4.4$^{a¥}$ | -7.0, 7.4 | 18.8, 10.6 | 8.6, 4.2$^{a¥}$ | -10.2, 8.5 |
| Valerate, µmol/g | 2.6, 1.8 | 2.5, 1.3 | -0.1, 1.5 | 2.7, 1.3 | 1.9, 0.8$^{a**,c*}$ | -0.7, 1.0 |
| Iso-butyrate, µmol/g | 1.9, 0.8 | 3.0, 1.3$^{a¥}$ | 1.1, 1.4 | 2.1, 1.1 | 2.1, 0.7$^{c**}$ | 0.1, 0.9$^{d*}$ |
| Iso-valerate, µmol/g | 2.0, 0.9 | 3.2, 1.5$^{a¥}$ | 1.2, 1.6 | 2.1, 1.3 | 2.3, 0.8$^{c**}$ | 0.2, 1.0$^{d*}$ |
| Total bacteria | 11.3, 0.2 | 11.0, 0.2$^{a¥}$ | -0.3, 0.3 | 11.3, 0.2 | 11.0, 0.3$^{a¥}$ | -0.3, 0.3 |

Data are displayed with means and standard deviations; [a] significant difference between Pre EEN and Post EEN or Pre CD-TREAT and Post CD-TREAT; [b] significant difference between Pre EEN with Pre CD-TREAT; [c] significant difference between Post EEN with Post CD-TREAT; [d] significant difference between ΔEEN and ΔCD-TREAT; * $P$<.05; ** $P$<.01; ¥ $P$<.001; $$P$ for Fisher pairwise comparisons following general linear model with Box-Cox transformation. $$$P$ for paired t-tests on log-transformed data; Total bacteria, $\log_{10}$ 16S rRNA gene copy number/g stool; Δ, difference Post-Pre dietary intervention

Table S3. EEN and CD-TREAT acceptability and gastrointestinal symptoms in healthy volunteers of the RCT (n=25).

| | **EEN** | **CD-TREAT** | ***P*** |
|---|---|---|---|
| **Acceptability** | | | |
| *Difficulty to stay on the diet (LS: 1-10)?* | | | |
| Day 1 | 4.1, 2.0 | 2.7, 1.9 | **.005** |
| Day 2 | 4.1, 1.7 | 3.0, 1.8 | **.004** |
| Day 3 | 4.4, 1.9 | 3.2, 1.8 | **.031** |
| Day 4 | 4.7, 2.0 | 3.1, 1.9 | **.011** |
| Day 5 | 4.6, 1.9 | 3.6, 2.0 | **.040** |
| Day 6 | 4.4, 1.7 | 3.2, 2.1 | **.015** |
| Day 7 | 4.2, 1.8 | 2.9, 2.0 | **.019** |
| *Hunger during the day (VAS: 0-100)?* | | | |
| Day 1 | 37.5, 23.7 | 30.8, 28.2 | .054 |
| Day 6 | 36.7, 26.9 | 27.8, 28.8 | **.023** |
| *Satisfaction during the day (VAS: 0-100)?* | | | |
| Day 1 | 49.3, 23.4 | 59.2, 29.0 | .504 |
| Day 6 | 53.0, 24.1 | 66.3, 27.4 | .236 |
| *Fullness during the day (VAS: 0-100)?* | | | |
| Day 1 | 57.2, 22.9 | 63.9, 28.3 | .716 |
| Day 6 | 63.4, 21.6 | 70.5, 24.5 | .470 |
| *Prospective food consumption during the day (VAS: 0-100)?* | | | |
| Day 1 | 42.3, 24.0 | 41.5, 24.7 | .950 |
| Day 6 | 43.8, 25.3 | 44.7, 23.7 | .493 |
| *Desire to eat during the day (VAS from 0-100)?* | | | |
| Day 1 | 57.6, 25.8 | 50.0, 29.6 | .242 |
| Day 6 | 57.8, 27.9 | 48.2, 27.0 | .436 |
| | | | |
| **Gastrointestinal side effects** | | | |
| *Self-reported symptoms (LS: 0-4)* | | | |
| Pain in abdomen | 0.8, 0.9 | 0.2, 0.5 | **.005** |
| Diarrhea | 0.5, 0.9 | 0.0, 0.2 | **.005** |
| Constipation | 1.8, 1.5 | 1.4, 1.4 | .102 |
| Nausea | 0.7, 1.0 | 0.4, 0.9 | .165 |
| Vomiting | 0.1, 0.3 | 0.0, 0.2 | .574 |
| Discomfort in abdomen | 0.9, 1.0 | 0.6, 0.8 | .313 |
| Passing wind | 0.6, 1.0 | 0.7, 1.0 | .424 |
| Not feeling hungry | 0.9, 1.3 | 1.4, 1.3 | **.020** |
| Bloating | 1.1, 1.2 | 0.6, 1.2 | .052 |

Data are displayed with means and standard deviations. ***P*** for paired t-tests on log-transformed data indicating significant differences between EEN and CD-TREAT diet. LS, Likert Scale; VAS, Visual Analogue Scale

Table S4: Number of genera which significantly (*P*<.05) changed during EEN or CD-TREAT in the crossover RCT in healthy volunteers (n=24)

| **Intervention** | **Overall** | **Decreased** | **Increased** |
|---|---|---|---|
| EEN | 58 | 24 | 34 |
| CD-TREAT | 38 | 12 | 26 |
| **Both interventions similar direction** | **28** | **9** | **19** |
| EEN only | 30 | 15 | 15 |
| CD-TREAT only | 10 | 3 | 7 |
| Both interventions opposite direction | 0 | 0 | 0 |
| 48.28% (28 out of 58) of EEN induced genera changes are replicated by CD-TREAT | | | |
| 37.5% (9 out of 24) of genera decreased during EEN were decreased during CD-TREAT | | | |
| 55.88% (19 out of 34) of genera increased during EEN were increased during CD-TREAT | | | |
| 73.68% (28 out of 38) of CD-TREAT induced genera changes were EEN-alike | | | |

Table S5: Mean difference of $log_{10}$ relative abundance for genera significantly (*P*<.05) and similarly changing during both EEN and CD-TREAT in the crossover RCT in healthy volunteers (n=24)

| Phylum | Class | Order | Family | Genus | EEN | Adjusted *P* | CDT | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|
| Increased during both dietary interventions | | | | | | | | |
| Actinobacteria | Actinobacteria | Actinomycetales | Actinomycetaceae | Actinomyces | 1.67 | 2.20E-05 | 0.85 | 2.67E-03 |
| | Coriobacteriia | Coriobacteriales | Coriobacteriaceae | Eggerthella | 2.06 | 1.96E-06 | 0.90 | 5.79E-04 |
| | | | | Senegalimassilia | 1.02 | 8.41E-03 | 0.63 | 1.47E-02 |
| Bacteroidetes | Bacteroidia | Bacteroidales | Porphyromonadaceae | Butyricimonas | 1.16 | 2.00E-02 | 0.76 | 1.44E-02 |
| | | | Prevotellaceae | Prevotella | 1.83 | 1.66E-06 | 0.57 | 2.98E-02 |
| | | | Rikenellaceae | Alistipes | 1.01 | 1.22E-02 | 0.67 | 2.42E-02 |
| Firmicutes | Clostridia | Clostridiales | Family_XIII | Family_XIII_AD3011_group | 0.99 | 1.83E-04 | 0.80 | 1.48E-04 |
| | | | Lachnospiraceae | Eisenbergiella | 2.61 | 4.91E-06 | 2.17 | 1.48E-04 |
| | | | | Hungatella | 1.72 | 3.30E-05 | 1.04 | 2.01E-03 |
| | | | | Lachnoclostridium | 2.20 | 5.28E-07 | 0.63 | 2.01E-03 |
| | | | | Tyzzerella_4 | 1.68 | 7.78E-05 | 1.14 | 1.47E-02 |
| | | | Ruminococcaceae | Anaerofilum | 1.65 | 5.01E-05 | 0.93 | 3.49E-03 |
| | | | | Anaerotruncus | 1.21 | 1.83E-04 | 1.32 | 2.08E-04 |
| | | | | Candidatus_Soleaferrea | 1.09 | 5.01E-05 | 0.71 | 1.36E-02 |
| | | | | Flavonifractor | 2.15 | 1.60E-05 | 0.95 | 2.67E-03 |
| | | | | Oscillibacter | 1.97 | 9.27E-04 | 1.02 | 6.10E-03 |
| | | | | Ruminiclostridium_5 | 0.96 | 1.52E-03 | 0.70 | 1.36E-02 |
| Proteobacteria | Deltaproteobacteria | Desulfovibrionales | Desulfovibrionaceae | Bilophila | 0.80 | 2.35E-02 | 1.14 | 2.44E-03 |
| | Gammaproteobacteria | Enterobacteriales | Enterobacteriaceae | Escherichia/Shigella | 1.71 | 1.18E-04 | 1.59 | 1.02E-03 |
| Decreased during both dietary interventions | | | | | | | | |
| Actinobacteria | Actinobacteria | Bifidobacteriales | Bifidobacteriaceae | Bifidobacterium | -1.66 | 4.53E-04 | -1.51 | 3.33E-04 |
| Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnospiraceae_FCS020_group | -0.85 | 2.85E-02 | -0.62 | 7.18E-04 |
| | | | | Lachnospiraceae_UCG-004 | -2.18 | 5.01E-05 | -0.95 | 1.14E-02 |
| | | | | Pseudobutyrivibrio | -3.35 | 1.66E-06 | -1.27 | 1.60E-03 |
| | | | Ruminococcaceae | Fecalibacterium | -1.82 | 6.50E-06 | -0.63 | 1.08E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Ruminiclostridium_6 | -1.25 | 4.43E-03 | -1.42 | 1.76E-02 |
| | | | | Ruminococcaceae_UCG-013 | -1.94 | 1.70E-04 | -0.83 | 1.13E-02 |
| | | | | Ruminococcus_1 | -3.00 | 8.09E-05 | -3.78 | 1.72E-05 |
| | Negativicutes | Selenomonadales | Veillonellaceae | Dialister | -2.39 | 1.83E-04 | -1.00 | 1.36E-02 |

Table S6: Mean difference of $log_{10}$ relative abundance for genera significantly (*P*<.05) changing during CD-TREAT only or EEN only in the crossover RCT in healthy volunteers (n=24)

| Phylum | Class | Order | Family | Genus | CDT/ EEN | Adjusted *P* |
|---|---|---|---|---|---|---|
| Increased during CD-TREAT | | | | | | |
| Proteobacteria | Deltaproteobacteria | Desulfovibrionales | Desulfovibrionaceae | Desulfovibrio | 0.77 | 4.03E-02 |
| Actinobacteria | Coriobacteriia | Coriobacteriales | Coriobacteriaceae | Gordonibacter | 0.50 | 2.40E-02 |
| Firmicutes | Bacilli | Lactobacillales | Streptococcaceae | Lactococcus | 1.16 | 1.36E-02 |
| | Negativicutes | Selenomonadales | Acidaminococcaceae | Phascolarctobacterium | 0.79 | 2.98E-02 |
| | Clostridia | Clostridiales | Ruminococcaceae | Ruminococcaceae_UCG-002 | 0.61 | 2.27E-02 |
| | | | | Ruminococcaceae_UCG-005 | 0.73 | 2.27E-02 |
| | | | | Ruminococcaceae_UCG-010 | 0.68 | 2.48E-02 |
| Decreased during CD-TREAT | | | | | | |
| Firmicutes | Bacilli | Lactobacillales | Lactobacillaceae | Lactobacillus | -0.96 | 3.85E-02 |
| | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -0.81 | 1.48E-04 |
| | | | Ruminococcaceae | Ruminiclostridium | -0.98 | 1.02E-03 |
| Increased during EEN | | | | | | |
| Firmicutes | Bacilli | Lactobacillales | Carnobacteriaceae | Granulicatella | 1.40 | 3.84E-06 |
| | Clostridia | Clostridiales | Lachnospiraceae | Blautia | 0.67 | 1.35E-02 |
| | | | | Dorea | 1.16 | 1.83E-04 |
| | | | | Howardella | 0.40 | 4.60E-02 |
| | | | | Lachnospiraceae_UCG-010 | 0.91 | 3.57E-02 |
| | | | Peptococcaceae | Peptococcus | 0.70 | 2.92E-02 |
| | | | Ruminococcaceae | Intestinimonas | 1.70 | 1.02E-06 |
| | | | | Ruminococcaceae_UCG-004 | 0.88 | 6.52E-03 |
| | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Catenibacterium | 0.46 | 2.46E-02 |
| | | | | Erysipelatoclostridium | 1.51 | 8.85E-05 |
| | | | | Fecalitalea | 1.04 | 9.50E-03 |
| | | | | Holdemanella | 0.79 | 1.02E-02 |
| | Negativicutes | Selenomonadales | Veillonellaceae | Megamonas | 0.48 | 1.04E-02 |
| Fusobacteria | Fusobacteriia | Fusobacteriales | Fusobacteriaceae | Fusobacterium | 0.96 | 2.73E-04 |
| Synergistetes | Synergistia | Synergistales | Synergistaceae | Cloacibacillus | 0.39 | 1.01E-02 |
| Decreased during EEN | | | | | | |
| Bacteroidetes | Bacteroidia | Bacteroidales | Prevotellaceae | Prevotella_9 | -1.45 | 1.86E-02 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | [Eubacterium]_ventriosum_group | -2.28 | 1.96E-06 |
| | | | | Coprococcus_2 | -1.43 | 2.39E-02 |
| | | | | Incertae_Sedis | -1.88 | 3.17E-03 |
| | | | | Lachnospira | -3.71 | 1.17E-07 |
| | | | | Lachnospiraceae_ND3007_group | -1.44 | 1.34E-02 |
| | | | | Lachnospiraceae_UCG-001 | -2.50 | 7.78E-05 |
| | | | | Lachnospiraceae_UCG-005 | -1.66 | 1.42E-04 |
| | | | | Tyzzerella_3 | -1.22 | 2.85E-02 |
| | | | Peptostreptococcaceae | Terrisporobacter | -1.06 | 1.70E-02 |
| | | | Ruminococcaceae | Ruminococcaceae_UCG-003 | -1.12 | 2.39E-02 |
| | | | | Ruminococcus_2 | -3.29 | 6.55E-06 |
| | | | | Subdoligranulum | -1.31 | 2.54E-03 |
| | Negativicutes | Selenomonadales | Veillonellaceae | Veillonella | -1.33 | 4.71E-03 |
| Proteobacteria | Gammaproteobacteria | Pasteurellales | Pasteurellaceae | Haemophilus | -1.42 | 1.93E-03 |

Table S7: Number of 3% OTU which significantly (*P*<.05) changed during EEN & CD-TREAT in the crossover RCT in healthy volunteers (n=24)

| **Intervention** | **Overall** | **Decreased** | **Increased** |
|---|---|---|---|
| EEN | 109 | 35 | 74 |
| CD-TREAT | 64 | 14 | 50 |
| **Both interventions similar direction** | **47** | **11** | **36** |
| EEN only | 62 | 24 | 38 |
| CD-TREAT only | 17 | 3 | 14 |
| Both interventions opposite direction | 0 | 0 | 0 |
| 43.11% (47 out of 109) of EEN induced OTU changes were replicated by CD-TREAT | | | |
| 31.43% (11 out of 35) of OTU decreased during EEN were decreased during CD-TREAT | | | |
| 48.65% (36 out of 74) of OTU increased during EEN were increased during CD-TREAT | | | |
| 73.44% (47 out of 64) of CD-TREAT induced OTU changes were EEN-alike | | | |

Table S8: Mean difference of $log_{10}$ relative abundance for OTU significantly (*P*<.05) and similarly changing during both EEN and CD-TREAT in the crossover RCT in healthy volunteers (n=24)

| OTU | Phylum | Class | Order | Family | Genus | EEN | Adjusted *P* | CDT | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|---|
| Increased during both dietary interventions | | | | | | | | | |
| OTU_164 | Actinobacteria | Actinobacteria | Actinomycetales | Actinomycetaceae | Actinomyces | 1.71 | 1.05E-04 | 0.90 | 4.17E-03 |
| OTU_88 | | Coriobacteriia | Coriobacteriales | Coriobacteriaceae | Eggerthella | 2.07 | 4.46E-06 | 0.89 | 1.72E-03 |
| OTU_177 | Bacteroidetes | Bacteroidia | Bacteroidales | Porphyromonadaceae | Butyricimonas | 1.13 | 4.85E-02 | 0.80 | 3.86E-02 |
| OTU_303 | | | | Rikenellaceae | Alistipes | 1.37 | 2.43E-03 | 0.93 | 1.55E-02 |
| OTU_326 | | | | | Oscillibacter | 0.88 | 3.91E-02 | 1.05 | 2.62E-02 |
| OTU_242 | Firmicutes | Bacilli | Lactobacillales | Streptococcaceae | Streptococcus | 1.23 | 1.60E-04 | 0.81 | 2.62E-02 |
| OTU_111 | | Clostridia | Clostridiales | Family_XIII | Family_XIII_AD3011_group | 1.44 | 7.30E-03 | 0.70 | 4.84E-03 |
| OTU_17 | | | | Lachnospiraceae | Lachnoclostridium | 3.83 | 1.66E-06 | 2.33 | 2.21E-04 |
| OTU_21 | | | | | Lachnoclostridium | 2.30 | 2.11E-06 | 1.03 | 8.12E-04 |
| OTU_147 | | | | | Eisenbergiella | 2.79 | 4.16E-06 | 2.25 | 5.50E-04 |
| OTU_28 | | | | | Lachnoclostridium | 3.22 | 9.73E-06 | 0.80 | 4.42E-02 |
| OTU_528 | | | | | Hungatella | 1.69 | 8.06E-05 | 1.03 | 4.21E-03 |
| OTU_123 | | | | | Tyzzerella_4 | 1.65 | 2.18E-04 | 1.13 | 2.51E-02 |
| OTU_103 | | | | | Lachnoclostridium | 1.76 | 3.27E-04 | 1.16 | 2.58E-03 |
| OTU_304 | | | | | Lachnospiraceae_NK4A136_group | 1.68 | 8.01E-04 | 0.94 | 8.73E-04 |
| OTU_159 | | | | | Lachnoclostridium | 2.14 | 1.18E-03 | 0.77 | 2.00E-02 |
| OTU_320 | | | | | NA | 1.14 | 3.38E-03 | 0.58 | 4.97E-02 |
| OTU_191 | | | | | Lachnoclostridium | 1.32 | 1.83E-02 | 0.56 | 3.94E-02 |
| OTU_127 | | | | | Desulfovibrio | 0.88 | 4.32E-02 | 1.04 | 3.34E-02 |
| OTU_19 | | | | Ruminococcaceae | Anaerofilum | 2.38 | 2.11E-06 | 1.30 | 1.08E-03 |
| OTU_237 | | | | | Intestinimonas | 1.88 | 9.96E-06 | 0.88 | 1.28E-02 |
| OTU_300 | | | | | NA | 2.29 | 1.59E-05 | 1.04 | 4.21E-03 |
| OTU_90 | | | | | Flavonifractor | 2.29 | 3.50E-05 | 0.96 | 5.10E-03 |
| OTU_72 | | | | | Oscillibacter | 2.25 | 5.59E-04 | 1.16 | 7.41E-03 |
| OTU_83 | | | | | Anaerofilum | 1.38 | 1.49E-03 | 0.94 | 7.49E-03 |
| OTU_220 | | | | | Anaerotruncus | 1.29 | 3.94E-03 | 0.88 | 3.91E-02 |
| OTU_212 | | | | | Ruminiclostridium_5 | 1.76 | 5.10E-03 | 1.20 | 4.75E-03 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| OTU_149 | | | | | NA | 1.31 | 5.98E-03 | 0.81 | 6.99E-03 |
| OTU_415 | | | | | Anaerotruncus | 0.59 | 2.94E-02 | 1.89 | 8.73E-04 |
| OTU_204 | | | | | Klebsiella | 1.01 | 3.91E-02 | 0.99 | 4.71E-02 |
| OTU_315 | | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Erysipelatoclostridium | 1.37 | 4.26E-05 | 0.44 | 4.68E-02 |
| OTU_14 | | Negativicutes | Selenomonadales | Acidaminococcaceae | Phascolarctobacterium | 0.95 | 4.80E-02 | 0.89 | 1.18E-02 |
| OTU_100 | Proteobacteria | Deltaproteobacteria | Desulfovibrionales | Desulfovibrionaceae | Bilophila | 0.77 | 4.19E-02 | 1.13 | 4.75E-03 |
| OTU_34 | | | | | Blautia | 0.80 | 4.32E-02 | 0.55 | 1.51E-02 |
| OTU_89 | | Gammaproteobacteria | Enterobacteriales | Enterobacteriaceae | Escherichia/Shigella | 1.68 | 3.27E-04 | 1.58 | 2.45E-03 |
| OTU_13 | | | | | Alistipes | 1.17 | 3.91E-02 | 0.98 | 1.51E-02 |
| Decreased during both dietary interventions | | | | | | | | | |
| OTU_12 | Actinobacteria | Actinobacteria | Bifidobacteriales | Bifidobacteriaceae | Bifidobacterium | -1.80 | 5.77E-04 | -1.56 | 8.12E-04 |
| OTU_125 | Firmicutes | Clostridia | Clostridiales | Clostridiaceae_1 | Clostridium_sensu_stricto_1 | -1.27 | 3.21E-02 | -1.35 | 4.75E-03 |
| OTU_7 | | | | Lachnospiraceae | Pseudobutyrivibrio | -3.57 | 6.92E-07 | -1.29 | 2.83E-03 |
| OTU_112 | | | | | Incertae_Sedis | -3.27 | 3.20E-06 | -1.01 | 3.87E-02 |
| OTU_156 | | | | | Lachnospiraceae_UCG-004 | -2.23 | 6.89E-05 | -0.98 | 1.55E-02 |
| OTU_200 | | | | | Lachnospiraceae_FCS020_group | -0.82 | 4.32E-02 | -0.90 | 8.73E-04 |
| OTU_29 | | | | Ruminococcaceae | Subdoligranulum | -2.63 | 1.66E-06 | -0.53 | 4.42E-02 |
| OTU_26 | | | | | Fecalibacterium | -1.85 | 1.01E-05 | -0.62 | 1.51E-02 |
| OTU_182 | | | | | Ruminococcaceae_UCG-013 | -2.02 | 8.01E-04 | -0.73 | 3.91E-02 |
| OTU_65 | | | | | Ruminococcus_1 | -2.19 | 1.75E-03 | -2.37 | 2.90E-03 |
| OTU_186 | | | | | Ruminiclostridium_6 | -1.20 | 1.08E-02 | -1.33 | 3.95E-02 |

Table S9: Mean difference of $log_{10}$ relative abundance for OTU significantly (*P*<.05) changing during CD-TREAT only or EEN only in the crossover RCT in healthy volunteers (n=24)

| OTU | Phylum | Class | Order | Family | Genus | CDT/ EEN | Adjusted *P* |
|---|---|---|---|---|---|---|---|
| Increased during CD-TREAT only | | | | | | | |
| OTU_270 | Actinobacteria | Coriobacteriia | Coriobacteriales | Coriobacteriaceae | Senegalimassilia | 0.70 | 1.12E-02 |
| OTU_316 | | | | | Gordonibacter | 0.52 | 1.55E-02 |
| OTU_40 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidaceae | Bacteroides | 1.61 | 2.62E-02 |
| OTU_382 | Firmicutes | Bacilli | Lactobacillales | Streptococcaceae | Lactococcus | 1.17 | 2.18E-02 |
| OTU_376 | | Clostridia | Clostridiales | Christensenellaceae | Christensenellaceae_R-7_group | 0.90 | 1.55E-02 |
| OTU_277 | | | | Family_XIII | Family_XIII_AD3011_group | 0.65 | 1.18E-02 |
| OTU_468 | | | | | Family_XIII_AD3011_group | 0.51 | 4.97E-02 |
| OTU_190 | | | | Lachnospiraceae | NA | 1.03 | 6.48E-03 |
| OTU_278 | | | | | Blautia | 0.99 | 9.40E-03 |
| OTU_271 | | | | Ruminococcaceae | Ruminiclostridium_5 | 1.66 | 2.73E-03 |
| OTU_359 | | | | | Ruminiclostridium_5 | 0.70 | 3.95E-02 |
| OTU_361 | | | | | Ruminiclostridium_5 | 1.25 | 1.18E-02 |
| OTU_44 | | | | | Ruminococcaceae_UCG-005 | 0.98 | 3.50E-03 |
| OTU_46 | | | | | Ruminococcaceae_UCG-002 | 0.76 | 1.51E-02 |
| Decreased during CD-TREAT only | | | | | | | |
| OTU_11 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -0.85 | 6.64E-04 |
| OTU_192 | | | | Ruminococcaceae | Ruminiclostridium | -1.24 | 4.98E-03 |
| OTU_119 | | | | | Ruminococcus_1 | -1.42 | 3.94E-02 |
| Increased during EEN only | | | | | | | |
| OTU_113 | Actinobacteria | Coriobacteriia | Coriobacteriales | Coriobacteriaceae | NA | 0.45 | 4.80E-02 |
| OTU_285 | | | | | Slackia | 0.48 | 2.66E-02 |
| OTU_293 | | | | | Collinsella | 0.79 | 4.19E-02 |
| OTU_64 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidaceae | Bacteroides | 0.45 | 2.69E-02 |
| OTU_193 | | | | Porphyromonadaceae | Parabacteroides | 0.94 | 3.91E-02 |
| OTU_938 | | | | | Barnesiella | 0.78 | 2.61E-02 |
| OTU_201 | Cyanobacteria | Melainabacteria | Gastranaerophilales | NA | NA | 0.93 | 4.02E-02 |
| OTU_233 | | | | NA | NA | 0.41 | 2.19E-02 |
| OTU_426 | Firmicutes | Bacilli | Lactobacillales | Carnobacteriaceae | Granulicatella | 1.36 | 7.67E-06 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| OTU_10 | | Clostridia | Clostridiales | Lachnospiraceae | Lachnoclostridium | 1.78 | 1.70E-02 |
| OTU_138 | | | | | NA | 1.33 | 2.31E-03 |
| OTU_143 | | | | | Lachnospiraceae_UCG-010 | 1.17 | 4.85E-02 |
| OTU_153 | | | | | Blautia | 0.95 | 4.80E-02 |
| OTU_243 | | | | | NA | 2.38 | 2.60E-05 |
| OTU_301 | | | | | Blautia | 0.76 | 2.71E-02 |
| OTU_307 | | | | | Lachnospiraceae_UCG-010 | 0.80 | 3.17E-02 |
| OTU_4 | | | | | NA | 1.67 | 1.94E-02 |
| OTU_422 | | | | | NA | 0.98 | 1.86E-02 |
| OTU_54 | | | | | Dorea | 1.56 | 2.63E-05 |
| OTU_68 | | | | | Lachnoclostridium | 1.64 | 4.60E-03 |
| OTU_74 | | | | | NA | 0.97 | 1.08E-02 |
| OTU_137 | | | | Ruminococcaceae | Ruminococcaceae_UCG-005 | 1.10 | 4.30E-02 |
| OTU_148 | | | | | Ruminiclostridium_5 | 0.61 | 3.37E-02 |
| OTU_172 | | | | | Ruminococcaceae_UCG-004 | 0.90 | 5.92E-03 |
| OTU_187 | | | | | Ruminiclostridium_9 | 1.13 | 1.47E-02 |
| OTU_289 | | | | | Ruminiclostridium_5 | 1.00 | 4.99E-04 |
| OTU_290 | | | | | NA | 0.84 | 4.19E-02 |
| OTU_319 | | | | | Ruminiclostridium_5 | 0.80 | 3.67E-02 |
| OTU_104 | | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Holdemanella | 0.76 | 2.42E-02 |
| OTU_203 | | | | | Fecalitalea | 0.84 | 4.02E-02 |
| OTU_234 | | | | | NA | 1.07 | 1.70E-03 |
| OTU_279 | | | | | Erysipelatoclostridium | 0.89 | 4.02E-02 |
| OTU_302 | | | | | Incertae_Sedis | 1.75 | 6.36E-06 |
| OTU_32 | | Negativicutes | Selenomonadales | Acidaminococcaceae | Phascolarctobacterium | 0.46 | 3.37E-02 |
| OTU_50 | | | | Veillonellaceae | Megamonas | 0.45 | 2.69E-02 |
| OTU_61 | | | | | Veillonella | 0.50 | 2.11E-02 |
| OTU_197 | Synergistetes | Synergistia | Synergistales | Synergistaceae | Cloacibacillus | 0.36 | 2.94E-02 |
| OTU_296 | NA | NA | NA | NA | NA | 0.54 | 1.70E-02 |
| Decreased during EEN only | | | | | | | |
| OTU_1 | Bacteroidetes | Bacteroidia | Bacteroidales | Prevotellaceae | Prevotella_9 | -1.49 | 2.69E-02 |
| OTU_9 | | | | Bacteroidaceae | Bacteroides | -1.67 | 8.92E-03 |
| OTU_175 | | | | Rikenellaceae | Alistipes | -1.16 | 3.38E-03 |
| OTU_42 | Firmicutes | Clostridia | Clostridiales | Christensenellaceae | Christensenellaceae_R-7_group | -1.46 | 2.37E-02 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| OTU_105 | | | | Lachnospiraceae | Lachnospira | -2.60 | 9.86E-05 |
| OTU_178 | | | | | Incertae_Sedis | -2.51 | 2.65E-04 |
| OTU_194 | | | | | Lachnoclostridium | -0.77 | 2.16E-02 |
| OTU_207 | | | | | Lachnospiraceae_UCG-001 | -1.98 | 4.98E-03 |
| OTU_211 | | | | | Marvinbryantia | -0.73 | 4.04E-02 |
| OTU_35 | | | | | [Eubacterium]_ventriosum_group | -2.35 | 4.46E-06 |
| OTU_73 | | | | | Lachnospiraceae_NK4A136_group | -1.21 | 1.68E-02 |
| OTU_86 | | | | | Lachnospiraceae_ND3007_group | -1.47 | 2.13E-02 |
| OTU_912 | | | | | Lachnospiraceae_UCG-005 | -1.30 | 3.98E-03 |
| OTU_97 | | | | | Lachnospira | -3.07 | 3.38E-06 |
| OTU_210 | | | | Peptostreptococcaceae | Terrisporobacter | -1.09 | 2.34E-02 |
| OTU_107 | | | | Ruminococcaceae | Ruminococcaceae_NK4A214_group | -1.18 | 7.09E-03 |
| OTU_23 | | | | | Ruminococcus_2 | -3.34 | 1.01E-05 |
| OTU_244 | | | | | Ruminiclostridium_9 | -1.31 | 1.06E-02 |
| OTU_250 | | | | | Fecalibacterium | -1.14 | 2.69E-02 |
| OTU_309 | | | | | Ruminococcaceae_UCG-003 | -1.11 | 9.24E-03 |
| OTU_313 | | | | | Ruminiclostridium_9 | -0.89 | 2.69E-02 |
| OTU_259 | | Negativicutes | Selenomonadales | Veillonellaceae | Veillonella | -1.60 | 4.46E-04 |
| OTU_66 | | | | | Dialister | -2.71 | 1.03E-03 |
| OTU_184 | Proteobacteria | Gammaproteobacteria | Pasteurellales | Pasteurellaceae | Haemophilus | -1.45 | 3.11E-03 |

**Table S10:** Number of fecal metabolites which significantly (*P*<.05) changed during EEN & CD-TREAT in the crossover RCT in healthy volunteers (n=24)

| **Intervention** | **Overall** | **Decreased** | **Increased** |
|---|---|---|---|
| EEN | 675 | 354 | 321 |
| CD-TREAT | 573 | 290 | 283 |
| **Both interventions similar direction** | **294** | **148** | **146** |
| EEN only | 313 | 177 | 136 |
| CD-TREAT only | 211 | 103 | 108 |
| Both interventions opposite direction | 68 | EEN: 29; CD-TREAT: 39 | EEN: 39; CD-TREAT: 29 |
| 43.56% (294 out of 675) of EEN induced metabolite changes are replicated by CD-TREAT | | | |
| 41.81% (148 out of 354) of metabolites decreased during EEN were decreased during CD-TREAT | | | |
| 45.48% (146 out of 321) of metabolites increased during EEN were increased during CD-TREAT | | | |
| 51.31% (294 out of 573) of CD-TREAT induced metabolite changes are EEN-alike | | | |

Table S11. Baseline measurements and weekly changes (%) of fecal water content, body weight and fecal metabolites during the 4 weeks of the dietary interventions in the animal experiment (in all cases data from all studied animals were included, n=20)

| | **B27 CONTROL** | **B27 EEN** | **B27 CD-TREAT** | **B7 CONTROL** | **B7 EEN** |
|---|---|---|---|---|---|
| **Body wt(g)** | | | | | |
| Baseline | 282.8, 80.6 | 261.5, 83.1 | 298.8, 75.3 | 295.3, 112.6 | 288.5, 89.0 |
| $D_1$-$D_7$ | 0.9, 1.0 | 8.2, 4.4$^{b**,c*}$ | 12.9, 0.8$^{b¥}$ | 1.4, 1.5 | 6.4, 3.6$^{d*}$ |
| $D_1$-$D_{14}$ | 0.8, 2.5 | 8.6, 2.5$^{b**,c*}$ | 12.9, 2.0$^{b¥}$ | 0.2, 3.4 | 8.5, 4.2$^{d**}$ |
| $D_1$-$D_{21}$ | 1.4, 1.8 | 10.2, 4.0$^{b**,c†}$ | 15.9, 1.9$^{b¥}$ | -0.6, 4.2 | 11.1, 5.8$^{d**}$ |
| $D_1$-$D_{28}$ | -1.7, 1.4 | 9.3, 3.1$^{b¥}$ | 14.6, 4.0$^{b¥}$ | 1.2, 4.1 | 13.2, 5.8$^{d¥}$ |
| **Fecal water%** | | | | | |
| Baseline | 80.0, 1.7 | 79.7, 4.1 | 77.3, 3.4 | 64.3, 3.2$^{a**}$ | 59.9, 3.6 |
| $D_1$-$D_7$ | 2.0, 2.4 | 1.8, 4.5 | 6.5, 7.7 | 5.7, 9.3 | 20.3, 6.6$^{d**}$ |
| $D_1$-$D_{14}$ | -5.2, 2.6 | -4.1, 7.4 | 3.2, 6.2$^{b†}$ | -4.3, 9.3 | 11.6, 6.9$^{d**}$ |
| $D_1$-$D_{21}$ | -3.2, 6.0 | -3.0, 7.8 | 3.0, 4.3 | 4.0, 15.1 | 25.4, 10.1$^{d**}$ |
| $D_1$-$D_{28}$ | -9.6, 6.0 | -1.4, 6.8 | -2.8, 7.7 | 1.2, 14.1 | 14.1, 7.2$^{d*}$ |
| **Acetate, µmol/g** | | | | | |
| Baseline | 78.2, 24.2 | 98.1, 17.3 | 135.6, 24.2 | 86.5, 5.8 | 86.1, 7.4 |
| $D_1$-$D_7$ | 20.1, 44.5 | -37.5, 2.7$^{b**}$ | -47.4, 10.9$^{b¥}$ | -2.7, `28.5 | -51.0, 11.1$^{d**}$ |
| $D_1$-$D_{14}$ | 38.1, 44.0 | -23.9, 13.4$^{b**}$ | -32.4, 21.6$^{b**}$ | -14.8, 7.0 | -58.0, 2.9$^{d¥}$ |
| $D_1$-$D_{21}$ | 40.8, 65.5 | -37.3, 10.7$^{b**}$ | -29.5, 19.1$^{b**}$ | -5.7, 7.4 | -55.2, 10.5$^{d¥}$ |
| $D_1$-$D_{28}$ | 60.4, 55.2 | -46.8, 27.3$^{b¥}$ | -30.0, 20.0$^{b**}$ | -10.6, 12.2 | -61.2, 9.0$^{d**}$ |
| **Propionate, µmol/g** | | | | | |
| Baseline | 14.1, 3.6 | 17.0, 2.7 | 22.8, 5.4 | 12.8, 1.0 | 12.0, 3.3 |
| $D_1$-$D_7$ | -5.9, 31.2 | -41.1, 8.0$^{b†}$ | -24.2, 17.0 | 1.0, 55.0 | -31.2, 15.6 |
| $D_1$-$D_{14}$ | 8.5, 19.2 | -27.8, 19.8$^{b†}$ | -26.2, 30.5$^{b†}$ | -17.4, 34.6 | -45.9, 11.2 |
| $D_1$-$D_{21}$ | 17.8, 52.3 | -29.7, 18.0 | -18.1, 28.1 | 0.3, 45.4 | -20.2, 39.7 |
| $D_1$-$D_{28}$ | 46.0, 54.9 | -41.5, 25.3$^{b**}$ | -32.1, 29.7$^{b*}$ | -17.9, 12.1 | -48.7, 15.8$^{d†}$ |
| **Butyrate, µmol/g** | | | | | |
| Baseline | 5.2, 1.4 | 8.4, 5.1 | 5.3, 1.8 | 12.3, 5.3$^{a†}$ | 11.8, 4.3 |
| $D_1$-$D_7$ | -7.9, 67.3 | -23.6, 45.3 | -6.5, 26.8 | 48.5, 38.4 | -71.8, 5.17$^{d¥}$ |
| $D_1$-$D_{14}$ | -22.9, 31.5 | -20.6, 32.9 | 10.8, 45.8 | -13.8, 37.9 | -82.2, 3.7$^{d¥}$ |
| $D_1$-$D_{21}$ | 14.9, 105.7 | -33.8, 34.5 | 14.9, 50.9 | 21.8, 15.1 | -68.8, 15.1$^{d**}$ |
| $D_1$-$D_{28}$ | 4.2, 73.2 | -54.7, 25.5 | -9.4, 47.0 | 5.3, 55.9 | -80.2, 8.5$^{d**}$ |

| | | | | | |
|---|---|---|---|---|---|
| **Valerate, µmol/g** | | | | | |
| Baseline | 0.4, 0.1 | 0.6, 0.3 | 0.7, 0.2 | 0.6, 0.2 | 0.7, 0.2 |
| $D_1$-$D_7$ | -27.1, 23.5 | 136.8, 126.7[b¥,c†] | 40.7, 40.5[b**] | 24.6, 21.2 | 9.6, 29.6 |
| $D_1$-$D_{14}$ | 11.2, 46.5 | 245.0, 255.0[b**,c†] | 48.5, 44.5 | -1.4, 33.2 | -16.1, 20.8 |
| $D_1$-$D_{21}$ | 10.9, 83.0 | 165.8, 147.0[b*] | 44.2, 45.3 | -0.6, 14.9 | 23.4, 35.8 |
| $D_1$-$D_{28}$ | 84.0, 146.2 | 127.9, 176.9 | 26.4, 19.0 | 3.4, 47.2 | -14.7, 30.5 |
| **Iso-butyrate, µmol/g** | | | | | |
| Baseline | 0.3, 0.1 | 0.4, 0.1 | 0.4, 0.1 | 0.6, 0.3 | 0.6, 0.2 |
| $D_1$-$D_7$ | -9.8, 43.3 | 324.6, 166.4[b¥] | 209.1, 140.3[b**] | 30.8, 60.0 | 105.6, 46.3 |
| $D_1$-$D_{14}$ | -14.4, 14.8 | 487.0, 227.0[b¥,c*] | 201.1, 120.2[b**] | 8.3, 53.4 | 97.8, 39.6[d*] |
| $D_1$-$D_{21}$ | -23.3, 42.2 | 411.5, 167.0[b¥,c†] | 198.1, 102.3[b¥] | 5.5, 43.9 | 134.0, 54.6[d**] |
| $D_1$-$D_{28}$ | 91.4, 171.7 | 350.0, 245.0[b*] | 196.4, 28.7 | 36.9, 123.7 | 94.5, 54.7 |
| **Iso-valerate, µmol/g** | | | | | |
| Baseline | 0.2, 0.1 | 0.2, 0.1 | 0.2, 0.1 | 0.5, 0.3[a*] | 0.4, 0.1 |
| $D_1$-$D_7$ | -10.0, 35.3 | 470.6, 107.0[b¥,c**] | 182.5, 97.8[b**] | 39.7, 84.3 | 93.1, 37.2[d†] |
| $D_1$-$D_{14}$ | -13.2, 21.6 | 753.0, 477.0[b¥,c**] | 162.9, 95.8[b**] | 24.5, 66.3 | 108.6, 51.4[d†] |
| $D_1$-$D_{21}$ | -11.1, 47.3 | 567.0, 355.0[b¥,c**] | 137.8, 70.3[b**] | 26.5, 64.8 | 137.3, 67.3[d*] |
| $D_1$-$D_{28}$ | 109.3, 173.4 | 447.0, 497.0[b†] | 156.0, 35.5 | 60.3, 130.9 | 93.4, 49.6 |

Data are displayed with means and standard deviations. [a] significant difference between B27-CONTROL & B7-CONTROL; [b] significant difference between B27-CONTROL & B27-EEN or B27-CONTROL & B27-CD-TREAT; [c] significant difference between B27-EEN & B27-CD-TREAT; [d] significant difference between B7-CONTROL & B7-EEN; [†] $P<.1$; [*] $P<.05$; [**] $P<.01$; [¥] $P<.001$. $P$ for Fisher pairwise comparisons following general linear model with Box-Cox transformation; $D_1$: Baseline; $D_7$: 7 days on dietary intervention; $D_{14}$: 14 days on dietary intervention; $D_{21}$: 21 days on dietary intervention; $D_{28}$: days on dietary intervention

Table S12: Histopathology scores and relative expression of cytokines in gut tissues from rats treated with EEN, CD-TREAT or standard chow (in all cases data from all studied animals were included, n=20)

| | **B27 CONTROL** | **B27 EEN** | **B27 CD-TREAT** | **B7 CONTROL** | **B7 EEN** |
|---|---|---|---|---|---|
| Ileum histopathology | 3.75, 0.87 | 2.50, 0.58[b*] | 2.75, 0.87[b*] | 1.50, 0.41[a¥] | 1.13, 0.63 |
| Colon histopathology | 5.13, 1.40 | 5.38, 0.63 | 4.63, 1.11 | 1.00, 0.00[a¥] | 1.13, 0.25 |
| Colon I | 1.63, 0.48 | 1.88, 0.25 | 1.75, 0.29 | 0.50, 0.00[a¥] | 0.63, 0.48 |
| Colon M | 0.00, 0.00 | 0.00, 0.00 | 0.00, 0.00 | 0.00, 0.00 | 0.00, 0.00 |
| Colon N/AB | 0.88, 0.25 | 1.00, 0.00 | 0.88, 0.25 | 0.50, 0.00 [a**] | 0.50, 0.00 |
| Colon H | 1.38, 0.48 | 1.25, 0.29 | 1.00, 0.41[b†] | 0.00, 0.00[a¥] | 0.00, 0.00 |
| Colon G | 1.25, 0.29 | 1.25, 0.29 | 1.00, 0.41 | 0.00, 0.00[a¥] | 0.00, 0.00 |
| Ileum I | 2.00, 0.00 | 1.75, 0.29 | 1.75, 0.50 | 1.38, 0.25 [a**] | 1.00, 0.41 |
| Ileum V | 0.50, 0.41 | 0.25, 0.29 | 0.00, 0.00[b**,c†] | 0.00, 0.00 [a**] | 0.00, 0.00 |
| Ileum H | 1.25, 0.50 | 0.50, 0.00 | 1.00, 0.41 | 0.13, 0.25[a**] | 0.13, 0.25 |
| Ileum N | 0.00, 0.00 | 0.00, 0.00 | 0.00, 0.00 | 0.00, 0.00 | 0.00, 0.00 |
| Ileal TNF-α | 2.02, 0.96 | 1.67, 1.32 | 1.15, 0.64 | 1.39, 0.98 | 1.33, 0.77 |
| Ileal IL-6 | 3.44, 3.02 | 1.89, 1.07 | 0.72, 0.38[b*] | 1.28, 0.96 | 4.12, 3.04[d*] |
| Ileal IL-10 | 3.24, 1.89 | 1.21, 0.53 | 1.08, 0.83 | 1.57, 1.50 | 2.23, 2.11 |
| Ileal IL-1b | 0.76, 0.34 | 0.92, 0.19 | 0.64, 0.19 | 1.16, 0.68 | 1.23, 0.20 |
| Ileal CXCL-1 | 2.47, 1.73 | 2.60, 2.31 | 0.87, 0.55[b†,c†] | 1.45, 1.22 | 1.43, 0.43 |

Data are displayed with means and standard deviations. [a] significant difference between B27-CONTROL & B7-CONTROL; [b] significant difference between B27-CONTROL & B27-EEN or B27-CONTROL & B27-CD-TREAT; [c] significant difference between B27-EEN & B27-CD-TREAT; [d] significant difference between B7-CONTROL & B7-EEN; [†] $P<.1$; [*] $P<.05$; [**] $P<.01$; [¥] $P<.001$. $P$ for Fisher pairwise comparisons following general linear model with Box-Cox transformation. I: Infiltration with leukocytes in the lamina propria and tela submucosa; M: Mucosal defects and fibrose; N/AB: Neutrophile infiltration and crypt abscessation; H: Hyperplasia; G: Goblet cell depletion; V: Villi fusion and shortening; N: Mucosal necrosis, erosion and ulceration

Table S13. Weight of cecal and colonic luminal contents, cecal SCFA at sacrifice and fecal and cecal luminal total bacterial load during the 4 weeks of intervention in the animal experiment in all cases data from all studied animals were included, n=20)

| | **B27 CONTROL** | **B27 EEN** | **B27 CD-TREAT** | **B7 CONTROL** | **B7 EEN** |
|---|---|---|---|---|---|
| **Weight, g** | | | | | |
| Cecum content | 3.9, 1.3 | 1.0, 0.3$^{b¥,c¥}$ | 2.3, 0.6$^{b*}$ | 3.1, 0.8 | 1.3, 0.2$^{d**}$ |
| Colon content | 0.8, 0.5 | 0.1, 0.1$^{b**,c*}$ | 0.5, 0.2 | 1.2, 0.4 | 0.2, 0.2$^{d**}$ |
| **SCFA total µmol in cecum** | | | | | |
| Acetate | 413.0, 213.0 | 53.6, 6.9$^{b¥,c¥}$ | 229.9, 100.9$^{b†}$ | 269.5, 122.9 | 66.4, 17.0$^{d¥}$ |
| Propionate | 64.9, 33.3 | 11.8, 3.3$^{b¥,c¥}$ | 56.2, 22.7 | 39.6, 9.3 | 16.0, 3.6$^{d**}$ |
| Butyrate | 17.1, 8.7 | 4.4, 0.9$^{b¥,c¥}$ | 22.8, 8.9 | 106.6, 56.7$^{a**}$ | 4.9, 1.4$^{d¥}$ |
| Valerate | 1.3, 0.8 | 1.3, 0.1$^{c*}$ | 3.6, 1.7$^{b**}$ | 2.5, 0.9$^{a*}$ | 1.2, 0.1$^{d*}$ |
| Iso-butyrate | 0.7, 0.3 | 1.3, 0.2$^{b*, c*}$ | 2.9, 1.6$^{b¥}$ | 1.5, 0.5$^{a*}$ | 1.1, 0.2 |
| Iso-valerate | 0.4, 0.2 | 0.8, 0.2$^{b†,c†}$ | 1.8, 1.1$^{b**}$ | 1.0, 0.4$^{a*}$ | 0.8, 0.2 |
| **SCFA µmol/g cecum content** | | | | | |
| Acetate | 100.9, 19.1 | 49.0, 5.6$^{b¥,c¥}$ | 98.6, 23.5 | 84.2, 20.2 | 52.7, 9.2$^{d**}$ |
| Propionate | 15.9, 2.9 | 10.6, 1.82$^{b**,c¥}$ | 24.2, 6.0$^{b*}$ | 12.9, 1.0 | 12.6, 1.1 |
| Butyrate | 4.3, 1.4 | 4.1, 0.8$^{c**}$ | 9.9, 3.0$^{b**}$ | 32.8, 11.3$^{a¥}$ | 4.0, 1.4$^{d¥}$ |
| Valerate | 0.3, 0.1 | 1.2, 0.2$^{b¥}$ | 1.5, 0.5$^{b¥}$ | 0.8, 0.1$^{a¥}$ | 1.0, 0.2 |
| Iso-butyrate | 0.2, 0.0 | 1.2, 0.1$^{b¥}$ | 1.2, 0.4$^{b¥}$ | 0.5, 0.1$^{a¥}$ | 0.9, 0.2$^{d*}$ |
| Iso-valerate | 0.1, 0.0 | 0.7, 0.1$^{b¥}$ | 0.8, 0.3$^{b¥}$ | 0.3, 0.1$^{a¥}$ | 0.6, 0.1$^{d*}$ |
| **Total bacteria** | | | | | |
| /g cecum content | 10.7, 0.2 | 11.1, 0.2$^{b**}$ | 11.2, 0.0$^{b**}$ | 11.2, 0.1$^{a**}$ | 11.2, 0.2 |
| /total cecum content | 11.2, 0.3 | 11.1, 0.4$^{c*}$ | 11.5, 0.1$^{b†}$ | 11.7, 0.2$^{a**}$ | 11.3, 0.2$^{d*}$ |
| /g feces Baseline | 10.9, 0.3 | 11.0, 0.15 | 10.5, 0.2 | 11.1, 0.2 | 11.1, 0.2 |
| /g feces $D_1$-$D_7$% | -8.3, 48.0 | 109.5, 80.1$^{b*}$ | 134.6, 117.8$^{b*}$ | 67.6, 114.9 | -11.8, 25.5 |
| /g feces $D_1$-$D_{14}$% | -18.4, 38.6 | 76.2, 37.6$^{b*}$ | 168.1, 174.8$^{b*}$ | 40.4, 67.5 | -8.6, 14.17 |
| /g feces $D_1$-$D_{21}$% | -16.7, 40.6 | 171.4, 68.7$^{b**,c†}$ | 607.0, 468$^{b¥}$ | 10.4, 61.1 | 32.1, 116.9 |
| /g feces $D_1$-$D_{28}$% | 10.3, 63.8 | 73.7, 76.9$^{b†,c**}$ | 379.0, 265.0$^{b¥}$ | 30.3, 14.9 | -21.2, 24.8 |

Data are displayed with means and standard deviations. [a] significant difference between B27-CONTROL & B7-CONTROL; [b] significant difference between B27-CONTROL & B27-EEN or B27-CONTROL & B27-CD-TREAT; [c] significant difference between B27-EEN & B27-CD-TREAT; [d], significant difference between B7-CONTROL & B7-EEN; [†] $P$<.1; [*] $P$<.05; [**] $P$<.01; [¥] $P$<.001. $P$ for Fisher pairwise comparisons following general linear model with Box-Cox transformation

Table S14: Relative abundance (ln) of genera, in feces, which significantly (*P*<.10) differed between B27-CONTROL and B7-CONTROL at intervention initiation (in all cases data from all studied animals were included, n=8)

| Phylum | Class | Order | Family | Genus | B7 CONTROL | B27 CONTROL | Adjusted *P* |
|---|---|---|---|---|---|---|---|
| Significantly higher than B7-CONTROL group | | | | | | | |
| Firmicutes | Bacilli | Lactobacillales | Streptococcaceae | Streptococcus | -6.58 | -5.58 | 5.54E-02 |
| | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -9.70 | -5.54 | 3.12E-04 |
| | | | | Blautia | -6.10 | -1.36 | 3.37E-02 |
| | | | | Coprococcus_3 | -9.70 | -7.04 | 1.73E-03 |
| | | | | Eisenbergiella | -9.25 | -6.91 | 1.47E-02 |
| | | | | Fusicatenibacter | -9.60 | -2.46 | 2.74E-04 |
| | | | | Lachnoclostridium | -5.19 | -3.83 | 8.94E-02 |
| | | | Ruminococcaceae | Flavonifractor | -9.32 | -6.43 | 1.68E-02 |
| | | | | Oscillospira | -9.87 | -5.44 | 8.55E-04 |
| | | | | Ruminococcaceae_UCG-008 | -9.70 | -3.79 | 2.74E-04 |
| | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Erysipelatoclostridium | -9.87 | -7.44 | 3.37E-02 |
| | Negativicutes | Selenomonadales | Acidaminococcaceae | Phascolarctobacterium | -7.13 | -3.50 | 9.83E-02 |
| Significantly lower than B7-CONTROL group | | | | | | | |
| Actinobacteria | Actinobacteria | Corynebacteriales | Corynebacteriaceae | Corynebacterium_1 | -8.39 | -9.69 | 1.47E-02 |
| Bacteroidetes | Bacteroidia | Bacteroidales | Porphyromonadaceae | Odoribacter | -6.99 | -9.59 | 1.83E-03 |
| | | | Prevotellaceae | Prevotellaceae_Ga6A1_group | -3.90 | -8.55 | 7.03E-02 |
| | | | | Prevotellaceae_NK3B31_group | -2.30 | -4.00 | 3.52E-02 |
| | | | Rikenellaceae | Alistipes | -4.82 | -7.50 | 7.26E-03 |
| Firmicutes | Bacilli | Bacillales | Staphylococcaceae | Jeotgalicoccus | -7.65 | -9.59 | 3.67E-02 |
| | Clostridia | Clostridiales | Defluviitaleaceae | Defluviitaleaceae_UCG-011 | -7.81 | -9.87 | 1.28E-02 |
| | | | Family_XIII | Anaerovorax | -7.93 | -9.87 | 1.28E-02 |
| | | | Lachnospiraceae | [Eubacterium]_ventriosum_group | -7.10 | -8.28 | 3.67E-02 |
| | | | | Acetatifactor | -6.29 | -9.87 | 8.52E-03 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | Lachnospiraceae_NK4A136_group | -2.74 | -7.28 | 2.49E-02 |
| | | | | Lachnospiraceae_UCG-001 | -4.01 | -9.07 | 4.99E-03 |
| | | | | Lachnospiraceae_UCG-006 | -6.42 | -9.87 | 5.47E-03 |
| | | | Peptococcaceae | Peptococcus | -7.42 | -9.87 | 1.20E-02 |
| | | | Peptostreptococcaceae | Romboutsia | -4.47 | -8.28 | 8.44E-02 |
| | | | Ruminococcaceae | Anaerofilum | -7.78 | -8.76 | 7.87E-02 |
| | | | | Anaerotruncus | -5.75 | -7.62 | 1.47E-02 |
| | | | | Butyricicoccus | -6.29 | -9.87 | 1.28E-02 |
| | | | | Oscillibacter | -4.41 | -6.05 | 5.84E-02 |
| | | | | Ruminiclostridium_5 | -5.35 | -7.20 | 3.37E-02 |
| | | | | Ruminiclostridium_6 | -5.24 | -9.69 | 2.02E-03 |
| | | | | Ruminococcaceae_NK4A214_group | -5.24 | -9.00 | 7.85E-03 |
| | | | | Ruminococcaceae_UCG-002 | -7.46 | -9.59 | 5.13E-02 |
| | | | | Ruminococcaceae_UCG-003 | -5.84 | -8.21 | 9.83E-02 |
| | | | | Ruminococcaceae_UCG-009 | -7.24 | -9.14 | 3.67E-02 |
| | | | | Ruminococcaceae_UCG-010 | -6.71 | -9.46 | 3.82E-02 |
| | | | | Ruminococcus_1 | -3.88 | -8.31 | 3.37E-02 |
| | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Turicibacter | -3.61 | -9.87 | 1.68E-02 |
| Proteobacteria | Alphaproteobacteria | Rhodospirillales | Rhodospirillaceae | Thalassospira | -7.51 | -9.87 | 5.54E-02 |
| | Epsilonproteobacteria | Campylobacterales | Helicobacteraceae | Helicobacter | -6.41 | -9.69 | 2.51E-02 |

TableS15: Relative abundance (ln) of genera, in cecal contents, which significantly (*P*<.10) differed between B27-CONTROL and B7-CONTROL at intervention initiation (in all cases data from all studied animals were included, n=8)

| Phylum | Class | Order | Family | Genus | B7 CONTROL | B27 CONTROL | Adjusted *P* |
|---|---|---|---|---|---|---|---|
| Significantly higher than B7-CONTROL group | | | | | | | |
| Firmicutes | Bacilli | Lactobacillales | Streptococcaceae | Streptococcus | -7.86 | -5.15 | 3.04E-02 |
| | Clostridia | Clostridiales | Clostridiaceae_1 | Candidatus_Arthromitus | -9.07 | -6.15 | 7.74E-02 |
| | | | Lachnospiraceae | Anaerostipes | -9.12 | -5.70 | 2.13E-03 |
| | | | | Blautia | -7.46 | -1.28 | 2.13E-02 |
| | | | | Fusicatenibacter | -9.20 | -4.20 | 5.85E-02 |
| | | | Ruminococcaceae | Flavonifractor | -9.47 | -7.05 | 7.12E-02 |
| | | | | Oscillospira | -9.47 | -5.62 | 1.87E-02 |
| | | | | Ruminococcaceae_UCG-008 | -8.18 | -4.44 | 5.17E-02 |
| Proteobacteria | Betaproteobacteria | Burkholderiales | Alcaligenaceae | Parasutterella | -6.75 | -4.61 | 4.99E-02 |
| Significantly lower than B7-CONTROL group | | | | | | | |
| Bacteroidetes | Bacteroidia | Bacteroidales | Prevotellaceae | Prevotellaceae_Ga6A1_group | -3.45 | -9.90 | 4.79E-03 |
| | Bacteroidia | Bacteroidales | Rikenellaceae | Alistipes | -5.88 | -7.91 | 3.31E-02 |
| Firmicutes | Bacilli | Bacillales | Staphylococcaceae | Jeotgalicoccus | -7.78 | -9.62 | 3.40E-02 |
| | Clostridia | Clostridiales | Family_XIII | Anaerovorax | -8.19 | -9.90 | 5.17E-02 |
| | | | Lachnospiraceae | Acetatifactor | -4.90 | -9.90 | 7.99E-03 |
| | | | | Lachnospiraceae_FCS020_group | -7.83 | -9.62 | 5.85E-02 |
| | | | | Lachnospiraceae_NK4A136_group | -1.57 | -8.46 | 4.79E-03 |
| | | | | Lachnospiraceae_UCG-001 | -3.28 | -9.90 | 2.19E-03 |
| | | | | Lachnospiraceae_UCG-006 | -5.26 | -9.90 | 7.99E-03 |
| | | | | Tyzzerella | -7.63 | -9.90 | 5.85E-02 |
| | | | Peptococcaceae | Peptococcus | -7.12 | -9.90 | 1.91E-02 |
| | | | Ruminococcaceae | Anaerotruncus | -5.55 | -8.28 | 3.16E-02 |
| | | | | Butyricicoccus | -5.81 | -9.90 | 4.99E-02 |
| | | | | Oscillibacter | -4.37 | -6.03 | 4.99E-02 |
| | | | | Ruminiclostridium_5 | -5.18 | -7.13 | 4.99E-02 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | Ruminococcaceae_UCG-003 | -4.90 | -9.28 | 2.13E-02 |
| | | | | Ruminococcaceae_UCG-005 | -4.61 | -9.62 | 3.23E-02 |
| | | | | Ruminococcaceae_UCG-009 | -6.58 | -9.22 | 1.87E-02 |
| | | | | Ruminococcaceae_UCG-010 | -7.02 | -9.73 | 1.43E-02 |
| | | | | Ruminococcus_1 | -4.29 | -8.11 | 4.99E-02 |
| | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Incertae_Sedis | -5.07 | -7.91 | 7.12E-02 |
| | | | | Turicibacter | -5.88 | -9.73 | 5.05E-02 |
| Proteobacteria | Epsilonproteobacteria | Campylobacterales | Helicobacteraceae | Helicobacter | -5.34 | -9.73 | 1.87E-02 |

Table S16: Relative abundance (ln) of 3% OTU, in feces, which significantly (*P*<.10) differed between B27-CONTROL and B7-CONTROL at intervention initiation (in all cases data from all studied animals were included, n=8)

| OTU | Phylum | Class | Order | Family | Genus | B7 CONTROL | B27 CONTROL | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|
| Significantly higher than B7-CONTROL group | | | | | | | | |
| OTU_129 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidaceae | Bacteroides | -7.68 | -5.95 | 7.67E-02 |
| OTU_62 | | | | | Bacteroides | -9.89 | -7.45 | 1.29E-02 |
| OTU_4 | | | | | Bacteroides | -9.02 | -4.27 | 1.23E-02 |
| OTU_522 | | | | Bacteroidales_S24-7_group | NA | -10.07 | -8.36 | 5.15E-02 |
| OTU_50 | Firmicutes | Bacilli | Lactobacillales | Streptococcaceae | Streptococcus | -6.92 | -5.83 | 8.54E-02 |
| OTU_419 | | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -10.07 | -8.00 | 2.17E-02 |
| OTU_14 | | | | | Anaerostipes | -9.89 | -5.73 | 9.40E-04 |
| OTU_784 | | | | | Blautia | -9.79 | -5.57 | 2.82E-02 |
| OTU_8 | | | | | Blautia | -6.71 | -1.70 | 5.08E-02 |
| OTU_3 | | | | | Blautia | -9.62 | -3.72 | 1.67E-02 |
| OTU_165 | | | | | Coprococcus_1 | -9.89 | -6.01 | 1.60E-02 |
| OTU_106 | | | | | Coprococcus_3 | -9.89 | -7.14 | 2.95E-03 |
| OTU_48 | | | | | Eisenbergiella | -9.44 | -7.02 | 1.67E-02 |
| OTU_19 | | | | | Fusicatenibacter | -9.79 | -2.56 | 7.22E-04 |
| OTU_617 | | | | | Incertae_Sedis | -9.72 | -7.92 | 2.34E-02 |
| OTU_277 | | | | | Lachnoclostridium | -8.72 | -5.39 | 1.67E-02 |
| OTU_35 | | | | | Lachnoclostridium | -9.79 | -5.57 | 1.61E-02 |
| OTU_65 | | | | | Lachnoclostridium | -9.49 | -4.81 | 1.67E-02 |
| OTU_46 | | | | | Marvinbryantia | -10.07 | -7.39 | 1.55E-02 |
| OTU_197 | | | | | NA | -9.89 | -8.28 | 2.07E-02 |
| OTU_126 | | | | | NA | -10.07 | -7.35 | 6.50E-03 |
| OTU_314 | | | | | NA | -9.62 | -6.27 | 4.14E-02 |
| OTU_271 | | | | | NA | -9.17 | -5.72 | 5.12E-02 |
| OTU_18 | | | | | NA | -7.91 | -4.01 | 1.79E-02 |
| OTU_30 | | | | | NA | -9.62 | -5.67 | 3.47E-03 |
| OTU_316 | | | | | Roseburia | -10.07 | -6.90 | 3.90E-03 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OTU_49 | | | | Ruminococcaceae | Flavonifractor | -9.52 | -6.53 | 1.74E-02 |
| OTU_156 | | | | | NA | -10.07 | -5.81 | 2.95E-03 |
| OTU_38 | | | | | Oscillibacter | -10.07 | -7.57 | 5.82E-02 |
| OTU_247 | | | | | Oscillospira | -10.07 | -6.96 | 3.53E-03 |
| OTU_369 | | | | | Ruminiclostridium_5 | -10.07 | -8.56 | 4.23E-02 |
| OTU_102 | | | | | Ruminococcaceae_UCG-008 | -9.89 | -3.89 | 7.22E-04 |
| OTU_176 | | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Erysipelatoclostridium | -10.07 | -7.54 | 3.38E-02 |
| OTU_215 | | | | | NA | -10.07 | -6.17 | 3.47E-03 |
| OTU_109 | Proteobacteria | Deltaproteobacteria | Desulfovibrionales | Desulfovibrionaceae | Desulfovibrio | -8.04 | -6.43 | 5.50E-02 |
| Significantly lower than B7-CONTROL group | | | | | | | | |
| OTU_31 | Actinobacteria | Actinobacteria | Corynebacteriales | Corynebacteriaceae | Corynebacterium_1 | -8.61 | -9.80 | 2.46E-02 |
| OTU_298 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidales_S24-7_group | NA | -6.54 | -9.97 | 3.47E-03 |
| OTU_193 | | | | | NA | -5.91 | -9.05 | 3.31E-02 |
| OTU_273 | | | | | NA | -6.43 | -9.35 | 1.79E-02 |
| OTU_145 | | | | | NA | -4.79 | -7.27 | 3.74E-02 |
| OTU_209 | | | | | NA | -7.14 | -9.31 | 7.79E-02 |
| OTU_346 | | | | | NA | -7.26 | -9.31 | 2.46E-02 |
| OTU_447 | | | | | NA | -7.54 | -9.28 | 4.90E-02 |
| OTU_240 | | | | | NA | -6.52 | -7.95 | 6.44E-02 |
| OTU_228 | | | | | NA | -5.95 | -6.86 | 5.82E-02 |
| OTU_357 | | | | NA | NA | -7.45 | -8.66 | 5.92E-02 |
| OTU_150 | | | | Porphyromonadaceae | Odoribacter | -7.18 | -9.70 | 3.47E-03 |
| OTU_10 | | | | Prevotellaceae | Prevotellaceae_Ga6A1_group | -4.09 | -8.66 | 7.95E-02 |
| OTU_11 | | | | | Prevotellaceae_NK3B31_group | -2.49 | -4.10 | 4.48E-02 |
| OTU_269 | | | | Rikenellaceae | Alistipes | -6.64 | -9.52 | 1.67E-02 |
| OTU_76 | | | | | Alistipes | -6.51 | -8.95 | 2.46E-02 |
| OTU_138 | | | | | Alistipes | -6.27 | -8.46 | 9.76E-02 |
| OTU_289 | | | | | Alistipes | -7.48 | -9.45 | 9.29E-02 |
| OTU_214 | | | | | Alistipes | -7.60 | -9.14 | 1.79E-02 |
| OTU_221 | Cyanobacteria | Melainabacteria | Gastranaerophilales | NA | NA | -7.16 | -9.08 | 4.23E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OTU_173 | Firmicutes | Bacilli | Bacillales | Staphylococcaceae | Jeotgalicoccus | -7.84 | -9.70 | 4.61E-02 |
| OTU_302 | Firmicutes | Clostridia | Clostridiales | Clostridiales_vadinBB60_group | NA | -7.67 | -9.97 | 3.09E-02 |
| OTU_536 | Firmicutes | Clostridia | Clostridiales | Clostridiales_vadinBB60_group | NA | -7.90 | -9.97 | 3.39E-02 |
| OTU_408 | Firmicutes | Clostridia | Clostridiales | Family_XIII | Anaerovorax | -8.13 | -9.97 | 1.67E-02 |
| OTU_362 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | [Eubacterium]_ventriosum_group | -7.51 | -8.38 | 6.69E-02 |
| OTU_184 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Acetatifactor | -7.53 | -9.97 | 5.45E-02 |
| OTU_347 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Acetatifactor | -8.49 | -9.97 | 4.66E-02 |
| OTU_83 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Coprococcus_1 | -8.02 | -9.97 | 2.17E-02 |
| OTU_125 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnoclostridium | -5.91 | -9.97 | 2.95E-03 |
| OTU_72 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnoclostridium | -7.85 | -9.97 | 1.62E-02 |
| OTU_23 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnospiraceae_NK4A136_group | -4.25 | -9.45 | 3.47E-03 |
| OTU_93 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnospiraceae_NK4A136_group | -5.15 | -9.03 | 7.89E-02 |
| OTU_61 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnospiraceae_NK4A136_group | -7.19 | -9.97 | 6.42E-02 |
| OTU_67 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnospiraceae_NK4A136_group | -7.49 | -9.97 | 1.06E-02 |
| OTU_398 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnospiraceae_NK4A136_group | -7.76 | -9.97 | 8.70E-02 |
| OTU_232 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnospiraceae_UCG-006 | -7.40 | -9.97 | 1.61E-02 |
| OTU_177 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -6.96 | -9.97 | 1.82E-02 |
| OTU_255 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -7.00 | -9.97 | 1.23E-02 |
| OTU_223 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -7.12 | -9.97 | 2.87E-02 |
| OTU_77 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -7.55 | -9.97 | 8.24E-02 |
| OTU_469 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -7.55 | -9.97 | 1.06E-02 |
| OTU_178 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -7.63 | -9.97 | 1.67E-02 |
| OTU_140 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -7.36 | -9.63 | 2.70E-02 |
| OTU_270 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -7.80 | -9.97 | 2.90E-02 |
| OTU_265 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -7.98 | -9.97 | 2.46E-02 |
| OTU_222 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -8.01 | -9.97 | 1.79E-02 |
| OTU_348 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -7.91 | -9.80 | 6.36E-02 |
| OTU_474 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -8.09 | -9.97 | 1.67E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OTU_239 | | | | | NA | -8.21 | -9.97 | 1.79E-02 |
| OTU_319 | | | | | NA | -8.25 | -9.97 | 6.52E-02 |
| OTU_457 | | | | | NA | -8.49 | -9.97 | 5.58E-02 |
| OTU_411 | | | | | NA | -8.25 | -9.70 | 6.52E-02 |
| OTU_220 | | | | | Roseburia | -6.77 | -9.97 | 1.62E-02 |
| OTU_86 | | | | | Roseburia | -7.32 | -9.97 | 8.78E-02 |
| OTU_258 | | | | Peptococcaceae | NA | -6.62 | -9.97 | 9.75E-02 |
| OTU_260 | | | | | Peptococcus | -7.61 | -9.97 | 1.60E-02 |
| OTU_63 | | | | Peptostreptococcaceae | Romboutsia | -4.66 | -8.38 | 9.50E-02 |
| OTU_503 | | | | Ruminococcaceae | [Eubacterium]_coprostanoligenes_group | -8.45 | -9.97 | 6.17E-02 |
| OTU_486 | | | | | Anaerotruncus | -7.70 | -9.70 | 5.68E-02 |
| OTU_353 | | | | | Anaerotruncus | -8.00 | -9.80 | 4.71E-02 |
| OTU_152 | | | | | Butyricicoccus | -6.48 | -9.97 | 1.61E-02 |
| OTU_69 | | | | | NA | -5.40 | -9.97 | 3.56E-03 |
| OTU_119 | | | | | NA | -6.44 | -9.97 | 2.34E-02 |
| OTU_236 | | | | | NA | -6.47 | -9.97 | 6.50E-03 |
| OTU_73 | | | | | NA | -5.48 | -8.73 | 5.31E-02 |
| OTU_426 | | | | | NA | -6.84 | -9.97 | 1.67E-02 |
| OTU_190 | | | | | NA | -7.21 | -9.97 | 1.67E-02 |
| OTU_578 | | | | | NA | -8.14 | -9.97 | 1.67E-02 |
| OTU_139 | | | | | Oscillibacter | -5.08 | -9.17 | 6.02E-02 |
| OTU_201 | | | | | Oscillibacter | -7.38 | -9.97 | 4.85E-02 |
| OTU_318 | | | | | Oscillibacter | -7.78 | -9.97 | 2.93E-02 |
| OTU_276 | | | | | Oscillibacter | -7.48 | -9.63 | 2.46E-02 |
| OTU_310 | | | | | Ruminiclostridium_5 | -7.88 | -9.97 | 2.46E-02 |
| OTU_480 | | | | | Ruminiclostridium_5 | -7.90 | -9.80 | 4.69E-02 |
| OTU_442 | | | | | Ruminiclostridium_5 | -8.35 | -9.97 | 2.90E-02 |
| OTU_127 | | | | | Ruminiclostridium_6 | -5.94 | -9.97 | 8.61E-03 |
| OTU_429 | | | | | Ruminiclostridium_9 | -7.26 | -9.63 | 1.79E-02 |
| OTU_300 | | | | | Ruminiclostridium_9 | -5.97 | -8.26 | 7.87E-02 |
| OTU_103 | | | | | Ruminiclostridium_9 | -5.64 | -7.88 | 3.47E-03 |
| OTU_430 | | | | | Ruminiclostridium_9 | -7.74 | -9.97 | 1.23E-02 |
| OTU_114 | | | | | Ruminiclostridium_9 | -6.67 | -8.78 | 1.62E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OTU_110 | | | | | Ruminococcaceae_NK4A214_group | -5.64 | -9.97 | 1.86E-03 |
| OTU_421 | | | | | Ruminococcaceae_UCG-002 | -7.65 | -9.97 | 1.61E-02 |
| OTU_290 | | | | | Ruminococcaceae_UCG-009 | -7.68 | -9.97 | 2.49E-02 |
| OTU_414 | | | | | Ruminococcaceae_UCG-010 | -7.47 | -9.97 | 1.28E-02 |
| OTU_282 | | | | | Ruminococcaceae_UCG-013 | -6.73 | -9.29 | 2.46E-02 |
| OTU_388 | | | | | Ruminococcaceae_UCG-013 | -7.69 | -9.97 | 8.75E-02 |
| OTU_121 | | | | | Ruminococcaceae_UCG-014 | -7.27 | -9.97 | 1.23E-02 |
| OTU_387 | | | | | Ruminococcaceae_UCG-014 | -7.33 | -9.97 | 2.17E-02 |
| OTU_562 | | | | | Ruminococcaceae_UCG-014 | -7.72 | -9.97 | 1.23E-02 |
| OTU_259 | | | | | Ruminococcaceae_UCG-014 | -8.05 | -9.97 | 1.67E-02 |
| OTU_130 | | | | | Ruminococcus_1 | -4.70 | -9.80 | 1.23E-03 |
| OTU_34 | | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Turicibacter | -3.81 | -9.97 | 2.07E-02 |
| OTU_1 | Proteobacteria | Epsilonproteobacteria | Campylobacterales | Helicobacteraceae | Helicobacter | -6.60 | -9.80 | 2.70E-02 |

Table S17: Relative abundance (ln) of 3% OTU, in cecal contents, which significantly (*P*<.10) differed between B27-CONTROL and B7-CONTROL at intervention initiation (in all cases data from all studied animals were included, n=8)

| OTU | Phylum | Class | Order | Family | Genus | B7 CONTROL | B27 CONTROL | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|
| Significantly higher than B7-CONTROL group | | | | | | | | |
| OTU_133 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidaceae | Bacteroides | -8.92 | -7.37 | 5.32E-02 |
| OTU_129 | | | | | Bacteroides | -8.57 | -6.27 | 4.62E-02 |
| OTU_4 | | | | | Bacteroides | -8.65 | -4.89 | 1.29E-02 |
| OTU_60 | Firmicutes | Bacilli | Lactobacillales | Lactobacillaceae | Lactobacillus | -7.09 | -3.13 | 1.14E-02 |
| OTU_50 | | | | Streptococcaceae | Streptococcus | -8.40 | -5.33 | 2.90E-02 |
| OTU_142 | | Clostridia | Clostridiales | Clostridiaceae_1 | Candidatus_Arthromitus | -9.28 | -6.23 | 8.69E-02 |
| OTU_14 | | | | Lachnospiraceae | Anaerostipes | -9.34 | -5.89 | 2.69E-03 |
| OTU_784 | | | | | Blautia | -9.69 | -5.65 | 1.79E-02 |
| OTU_8 | | | | | Blautia | -8.08 | -2.23 | 1.14E-02 |
| OTU_3 | | | | | Blautia | -9.24 | -2.40 | 6.58E-03 |
| OTU_165 | | | | | Coprococcus_1 | -9.69 | -6.61 | 5.70E-02 |
| OTU_19 | | | | | Fusicatenibacter | -9.41 | -4.29 | 7.47E-02 |
| OTU_65 | | | | | Lachnoclostridium | -9.34 | -4.34 | 1.14E-02 |
| OTU_51 | | | | | NA | -9.51 | -7.20 | 2.76E-02 |
| OTU_126 | | | | | NA | -9.41 | -6.84 | 1.26E-02 |
| OTU_30 | | | | | NA | -9.28 | -5.33 | 1.42E-03 |
| OTU_271 | | | | | NA | -9.69 | -5.26 | 1.52E-02 |
| OTU_49 | | | | Ruminococcaceae | Flavonifractor | -9.69 | -7.14 | 7.94E-02 |
| OTU_156 | | | | | NA | -9.69 | -5.89 | 1.96E-02 |
| OTU_38 | | | | | Oscillibacter | -9.20 | -6.99 | 2.08E-02 |
| OTU_71 | | | | | Oscillibacter | -9.69 | -7.08 | 8.69E-02 |
| OTU_247 | | | | | Oscillospira | -9.69 | -7.48 | 8.13E-02 |
| OTU_102 | | | | | Ruminococcaceae_UCG-008 | -8.39 | -4.52 | 7.17E-02 |
| OTU_215 | | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | NA | -8.83 | -6.72 | 8.69E-02 |
| OTU_33 | Proteob | Betaproteobacteri | Burkholderiale | Alcaligenaceae | Parasutterella | -6.96 | -4.69 | 6.25E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | acteria | a | s | | | | | |
| Significantly lower than B7-CONTROL group | | | | | | | | |
| OTU_235 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidales_S24-7_group | NA | -5.91 | -9.16 | 2.33E-02 |
| OTU_298 | | | | | NA | -7.20 | -9.99 | 2.33E-02 |
| OTU_145 | | | | | NA | -5.94 | -8.48 | 9.61E-02 |
| OTU_273 | | | | | NA | -7.40 | -9.36 | 7.45E-02 |
| OTU_193 | | | | | NA | -7.88 | -9.64 | 1.96E-02 |
| OTU_10 | | | | Prevotellaceae | Prevotellaceae_Ga6A1_group | -3.67 | -9.99 | 1.14E-02 |
| OTU_138 | | | | Rikenellaceae | Alistipes | -7.14 | -8.92 | 7.17E-02 |
| OTU_173 | Firmicutes | Bacilli | Bacillales | Staphylococcaceae | Jeotgalicoccus | -8.00 | -9.71 | 6.38E-02 |
| OTU_302 | | Clostridia | Clostridiales | Clostridiales_vadinBB60_group | NA | -7.19 | -9.99 | 7.17E-02 |
| OTU_641 | | | | | NA | -7.88 | -9.81 | 1.52E-02 |
| OTU_408 | | | | Family_XIII | Anaerovorax | -8.40 | -9.99 | 8.13E-02 |
| OTU_267 | | | | Lachnospiraceae | Acetatifactor | -6.32 | -9.99 | 1.19E-02 |
| OTU_83 | | | | | Coprococcus_1 | -6.94 | -9.99 | 1.79E-02 |
| OTU_291 | | | | | Incertae_Sedis | -5.89 | -8.49 | 8.69E-02 |
| OTU_125 | | | | | Lachnoclostridium | -5.29 | -9.99 | 6.74E-03 |
| OTU_72 | | | | | Lachnoclostridium | -6.57 | -9.99 | 6.38E-02 |
| OTU_23 | | | | | Lachnospiraceae_NK4A136_group | -3.74 | -9.71 | 1.79E-02 |
| OTU_12 | | | | | Lachnospiraceae_NK4A136_group | -4.35 | -9.99 | 7.47E-02 |
| OTU_93 | | | | | Lachnospiraceae_NK4A136_group | -5.32 | -9.99 | 8.69E-02 |
| OTU_111 | | | | | Lachnospiraceae_UCG-001 | -5.66 | -9.99 | 2.08E-02 |
| OTU_94 | | | | | Lachnospiraceae_UCG-001 | -5.83 | -9.99 | 9.75E-02 |
| OTU_232 | | | | | Lachnospiraceae_UCG-006 | -6.53 | -9.99 | 1.73E-02 |
| OTU_16 | | | | | NA | -4.88 | -9.99 | 6.38E-02 |
| OTU_177 | | | | | NA | -5.81 | -9.99 | 1.14E-02 |
| OTU_255 | | | | | NA | -6.30 | -9.99 | 1.52E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OTU_140 | | | | | NA | -6.60 | -9.54 | 6.38E-02 |
| OTU_202 | | | | | NA | -6.69 | -9.58 | 5.17E-02 |
| OTU_222 | | | | | NA | -7.30 | -9.99 | 4.38E-02 |
| OTU_178 | | | | | NA | -7.33 | -9.99 | 7.21E-02 |
| OTU_239 | | | | | NA | -7.42 | -9.99 | 7.17E-02 |
| OTU_270 | | | | | NA | -7.42 | -9.99 | 8.32E-02 |
| OTU_266 | | | | | Tyzzerella | -7.85 | -9.99 | 8.69E-02 |
| OTU_260 | | | | Peptococcaceae | Peptococcus | -7.34 | -9.99 | 2.26E-02 |
| OTU_315 | | | | Ruminococcaceae | Anaerotruncus | -7.60 | -9.99 | 8.69E-02 |
| OTU_299 | | | | | Anaerotruncus | -7.70 | -9.99 | 5.70E-02 |
| OTU_486 | | | | | Anaerotruncus | -7.91 | -9.99 | 7.21E-02 |
| OTU_152 | | | | | Butyricicoccus | -6.02 | -9.99 | 6.38E-02 |
| OTU_69 | | | | | NA | -5.18 | -9.99 | 1.79E-02 |
| OTU_73 | | | | | NA | -4.33 | -9.07 | 1.51E-03 |
| OTU_236 | | | | | NA | -5.92 | -9.99 | 5.70E-02 |
| OTU_426 | | | | | NA | -6.05 | -9.99 | 1.14E-02 |
| OTU_119 | | | | | NA | -6.22 | -9.99 | 1.79E-02 |
| OTU_190 | | | | | NA | -7.14 | -9.99 | 2.75E-02 |
| OTU_139 | | | | | Oscillibacter | -5.36 | -9.99 | 1.26E-02 |
| OTU_276 | | | | | Oscillibacter | -7.24 | -9.71 | 5.90E-02 |
| OTU_736 | | | | | Oscillibacter | -7.52 | -9.81 | 5.92E-02 |
| OTU_393 | | | | | Oscillibacter | -7.86 | -9.81 | 8.69E-02 |
| OTU_340 | | | | | Ruminiclostridium_5 | -7.16 | -9.99 | 1.79E-02 |
| OTU_310 | | | | | Ruminiclostridium_5 | -7.95 | -9.99 | 6.38E-02 |
| OTU_103 | | | | | Ruminiclostridium_9 | -5.78 | -8.26 | 3.75E-02 |
| OTU_114 | | | | | Ruminiclostridium_9 | -6.81 | -8.99 | 7.94E-02 |
| OTU_429 | | | | | Ruminiclostridium_9 | -7.50 | -8.95 | 2.18E-02 |
| OTU_110 | | | | | Ruminococcaceae_NK4A214_group | -6.32 | -9.99 | 4.38E-02 |
| OTU_57 | | | | | Ruminococcaceae_UCG-003 | -5.12 | -9.36 | 2.76E-02 |
| OTU_27 | | | | | Ruminococcaceae_UCG-005 | -5.01 | -9.99 | 4.55E-02 |
| OTU_290 | | | | | Ruminococcaceae_UCG | -6.94 | -9.99 | 1.79E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | -009 | | | |
| OTU_34 | | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Turicibacter | -6.10 | -9.81 | 7.24E-02 |
| OTU_1 | Proteobacteria | Epsilonproteobacteria | Campylobacterales | Helicobacteraceae | Helicobacter | -5.55 | -9.81 | 1.98E-02 |

Table S18: Number of genera in cecal contents, collected at sacrifice, which significantly (*P*<.10) differed in relative abundance between B27-CONTROL group with B27-EEN and B27-CD-TREAT groups (in all cases data from all studied animals were included, n=12).

| **Intervention** | **Number of genera** |
|---|---|
| EEN | 27 |
| CD-TREAT | 25 |
| **Both interventions similar direction** | **13** |
| EEN only | 13 |
| CD-TREAT only | 11 |
| Both interventions opposite direction | 1 |
| 48.15% (13 out of 27) of EEN induced genera changes were replicated by CD-TREAT | |
| 52% (13 out of 25) of CD-TREAT induced genera changes were EEN-alike | |

Table S19: Relative abundance (ln) of genera in cecal contents, collected at sacrifice, which differed (*P*<.10) similarly for B27-EEN and B27-CD-TREAT when compared with the B27-CONTROL group (in all cases data from all studied animals were included, n=12)

| Phylum | Class | Order | Family | Genus | B27 CONTROL | B27 EEN | Adjusted *P* | B27 CD-TREAT | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|---|
| Significantly higher than B27-CONTROL group for both dietary interventions | | | | | | | | | |
| Actinobacteria | Coriobacteriia | Coriobacteriales | Coriobacteriaceae | Senegalimassilia | -9.28 | -6.94 | 0.026 | -7.99 | 0.055 |
| Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidaceae | Bacteroides | -3.02 | -1.40 | 0.040 | -1.16 | 0.042 |
| | | | Porphyromonadaceae | Butyricimonas | -8.56 | -4.04 | 0.001 | -4.99 | 0.004 |
| | | | Rikenellaceae | Alistipes | -7.91 | -4.65 | 0.013 | -4.93 | 0.015 |
| Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Hungatella | -9.55 | -5.40 | 0.013 | -7.42 | 0.042 |
| | | | Ruminococcaceae | Oscillibacter | -6.03 | -4.57 | 0.026 | -3.95 | 0.015 |
| | | | | Anaerotruncus | -8.28 | -5.55 | 0.026 | -5.94 | 0.042 |
| | | | | [Eubacterium]_coprostanoligenes_group | -7.45 | -4.18 | 0.017 | -6.01 | 0.092 |
| | | | | Ruminococcaceae_UCG-014 | -7.21 | -3.83 | 0.033 | -4.07 | 0.066 |
| Proteobacteria | Alphaproteobacteria | Rhodospirillales | Rhodospirillaceae | Thalassospira | -8.50 | -6.07 | 0.026 | -6.37 | 0.042 |
| Significantly lower than B27-CONTROL group for both dietary interventions | | | | | | | | | |
| Actinobacteria | Actinobacteria | Bifidobacteriales | Bifidobacteriaceae | Bifidobacterium | -5.13 | -7.16 | 0.033 | -8.55 | 0.004 |
| Firmicutes | Bacilli | Lactobacillales | Lactobacillaceae | Lactobacillus | -2.98 | -6.36 | 0.013 | -5.76 | 0.015 |
| | Clostridia | Clostridiales | Clostridiaceae_1 | Candidatus_Arthromitus | -6.15 | -9.79 | 0.014 | -8.38 | 0.046 |

Table S20: Relative abundance (ln) of genera in cecal contents, collected at sacrifice, which differed (*P*<.10) between B27-CONTROL with B27-EEN or B27-CD-TREAT group only (in all cases data from all studied animals were included, n=12)

| Phylum | Class | Order | Family | Genus | B27-EEN/ B27-CDTREAT | B27 CONTROL | Adjusted *P* |
|---|---|---|---|---|---|---|---|
| Significantly higher for B27-EEN than B27-CONTROL group | | | | | | | |
| Actinobacteria | Actinobacteria | Actinomycetales | Actinomycetaceae | Actinomyces | -7.71 | -9.73 | 8.00E-02 |
| Firmicutes | Clostridia | Clostridiales | Family_XIII | [Eubacterium]_nodatum_group | -5.31 | -8.08 | 3.16E-02 |
| | | | | Family_XIII_AD3011_group | -7.16 | -9.03 | 3.16E-02 |
| | | | Lachnospiraceae | [Ruminococcus]_gauvreauii_group | -3.50 | -8.07 | 8.00E-02 |
| | | | Ruminococcaceae | Anaerofilum | -5.51 | -7.85 | 8.00E-02 |
| | | | | Ruminiclostridium_5 | -5.40 | -7.13 | 1.38E-02 |
| | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Erysipelatoclostridium | -6.38 | -9.05 | 9.09E-02 |
| | | | | Holdemania | -7.41 | -9.45 | 2.60E-02 |
| Significantly lower for B27-EEN than B27-CONTROL group | | | | | | | |
| Bacteroidetes | Bacteroidia | Bacteroidales | Prevotellaceae | Prevotella_9 | -9.09 | -2.44 | 1.85E-02 |
| | | | | Prevotellaceae_UCG-001 | -9.38 | -2.50 | 1.16E-03 |
| Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -9.51 | -5.70 | 1.23E-03 |
| | | | | Fusicatenibacter | -9.17 | -4.20 | 6.28E-02 |
| | | | Ruminococcaceae | Ruminococcaceae_UCG-008 | -6.78 | -4.44 | 2.70E-03 |
| | Negativicutes | Selenomonadales | Acidaminococcaceae | Phascolarctobacterium | -5.31 | -3.46 | 8.00E-02 |
| Significantly higher for B27-CD-TREAT than B27-CONTROL group | | | | | | | |
| Firmicutes | Bacilli | Lactobacillales | Leuconostocaceae | Leuconostoc | -6.18 | -9.90 | 9.26E-03 |
| | | | Streptococcaceae | Lactococcus | -7.58 | -9.90 | 3.37E-02 |
| | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -4.10 | -5.70 | 1.48E-02 |
| | | | | Lachnospiraceae_NK4A136_group | -4.85 | -8.46 | 6.77E-02 |
| | | | | Lachnospiraceae_UCG-010 | -6.13 | -8.59 | 8.96E-02 |
| | | | | Marvinbryantia | -4.69 | -7.78 | 1.48E-02 |
| | | | | Tyzzerella | -7.43 | -9.90 | 3.27E-02 |
| | | | Ruminococcaceae | Intestinimonas | -7.03 | -9.73 | 4.23E-03 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | Ruminococcaceae_NK4A214_group | -5.07 | -8.40 | 2.55E-02 |
| | | | | Ruminococcaceae_UCG-009 | -7.07 | -9.22 | 6.56E-02 |
| Proteobacteria | Betaproteobacteria | Burkholderiales | Alcaligenaceae | Parasutterella | -3.82 | -4.61 | 9.22E-02 |
| Significantly lower for B27-CD-TREAT than B27-CONTROL group | | | | | | | |
| Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Blautia | -2.42 | -1.28 | 1.48E-02 |

Table S21: Number of genera in fecal samples (collected four weeks post treatment initiation) which significantly (*P*<.10) differed in relative abundance between B27-CONTROL group with B27-EEN and B27-CD-TREAT groups (in all cases data from all studied animals were included, n=12)

| | Number of genera |
|---|---|
| EEN | 17 |
| CD-TREAT | 12 |
| **Both interventions similar direction** | **5** |
| EEN only | 12 |
| CD-TREAT only | 7 |
| Both interventions opposite direction | 0 |
| 29.41% (5 out of 17) of EEN induced genera changes were replicated by CD-TREAT | |
| 41.17% (5 out of 12) of CD-TREAT induced genera changes were EEN-alike | |

Table S22: Relative abundance (ln) of genera in feces, collected four weeks post treatment initiation, which differed (*P*<.10) similarly for B27-EEN and B27-CD-TREAT when compared with the B27-CONTROL group (in all cases data from all studied animals were included, n=12)

| Phylum | Class | Order | Family | Genus | B27 CONTROL | B27 EEN | Adjusted *P* | B27 CD-TREAT | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|---|
| Significantly higher than B27-CONTROL group for both dietary interventions | | | | | | | | | |
| Actinobacteria | Coriobacteriia | Coriobacteriales | Coriobacteriaceae | Senegalimassilia | -9.41 | -7.27 | 8.27E-02 | -7.12 | 9.17E-02 |
| Bacteroidetes | Bacteroidia | Bacteroidales | Porphyromonadaceae | Butyricimonas | -9.31 | -4.34 | 9.34E-03 | -5.86 | 9.20E-02 |
| Firmicutes | Clostridia | Clostridiales | Ruminococcaceae | Anaerofilum | -8.37 | -5.31 | 7.08E-02 | -5.49 | 1.94E-02 |
| Significantly lower than B27-CONTROL group for both dietary interventions | | | | | | | | | |
| Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Fusicatenibacter | -4.12 | -9.89 | 5.42E-02 | -8.58 | 9.20E-02 |
| Actinobacteria | Actinobacteria | Bifidobacteriales | Bifidobacteriaceae | Bifidobacterium | -5.11 | -8.04 | 9.88E-02 | -8.23 | 5.81E-02 |

Table S23: Relative abundance (ln) of genera in feces, collected four weeks post treatment initiation, which differed (*P*<.10) between B27-CONTROL with B27-EEN or B27-CD-TREAT group only (in all cases data from all studied animals were included, n=12)

| Phylum | Class | Order | Family | Genus | B27-EEN/ B27-CDTREAT | B27 CONTROL | Adjusted *P* |
|---|---|---|---|---|---|---|---|
| Significantly higher for B27-EEN than B27-CONTROL group | | | | | | | |
| Bacteroidetes | Bacteroidia | Bacteroidales | Rikenellaceae | Alistipes | -4.59 | -7.98 | 8.27E-02 |
| Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | [Ruminococcus]_gauvreauii_group | -3.40 | -8.27 | 9.88E-02 |
| | | | | Hungatella | -5.11 | -9.58 | 8.27E-02 |
| | | | Ruminococcaceae | [Eubacterium]_coprostanoligenes_group | -4.30 | -8.03 | 9.40E-02 |
| | | | | Ruminiclostridium_5 | -5.41 | -6.95 | 8.27E-02 |
| | | | | Ruminococcaceae_UCG-014 | -3.36 | -6.54 | 8.27E-02 |
| Significantly lower for B27-EEN than B27-CONTROL group | | | | | | | |
| Bacteroidetes | Bacteroidia | Bacteroidales | Prevotellaceae | Prevotella_9 | -8.44 | -2.02 | 3.29E-02 |
| | | | | Prevotellaceae_UCG-001 | -9.89 | -2.79 | 9.34E-03 |
| Firmicutes | Bacilli | Lactobacillales | Lactobacillaceae | Lactobacillus | -6.68 | -3.74 | 8.27E-02 |
| | Clostridia | Clostridiales | Clostridiaceae_1 | Candidatus_Arthromitus | -10.06 | -7.24 | 8.27E-02 |
| | | | Lachnospiraceae | Anaerostipes | -9.05 | -5.38 | 8.27E-02 |
| | | | Ruminococcaceae | Ruminococcaceae_UCG-008 | -6.39 | -4.36 | 6.65E-02 |
| Significantly higher for B27-CD-TREAT than B27-CONTROL group | | | | | | | |
| Firmicutes | Bacilli | Lactobacillales | Leuconostocaceae | Leuconostoc | -4.36 | -9.93 | 7.58E-03 |
| | | | Streptococcaceae | Lactococcus | -6.94 | -9.93 | 3.90E-02 |
| | Clostridia | Clostridiales | Lachnospiraceae | Marvinbryantia | -4.24 | -7.23 | 5.67E-02 |
| | | | Ruminococcaceae | Oscillibacter | -4.01 | -5.69 | 6.72E-02 |
| | | | | Ruminiclostridium_9 | -3.47 | -6.13 | 9.20E-02 |
| | | | | Ruminococcaceae_UCG-010 | -8.06 | -9.93 | 9.20E-02 |
| Proteobacteria | Betaproteobacteria | Burkholderiales | Alcaligenaceae | Parasutterella | -3.75 | -4.42 | 6.72E-02 |

Table S24: Number of genera in fecal samples (collected one week post treatment initiation) which significantly (*P*<.10) differed in relative abundance between B27-CONTROL group with B27-EEN and B27-CD-TREAT groups (in all cases data from all studied animals were included, n=12).

| | Number of genera |
|---|---|
| EEN | 24 |
| CD-TREAT | 32 |
| **Both interventions similar direction** | **16** |
| EEN only | 8 |
| CD-TREAT only | 16 |
| Both interventions opposite direction | 0 |
| 66.67% (16 out of 24) of EEN induced genera changes were replicated by CD-TREAT | |
| 50% (16 out of 32) of CD-TREAT induced genera changes were EEN-alike | |

Table S25: Relative abundance (ln) of genera in feces, collected one week post treatment initiation, which differed (*P*<.10) similarly for B27-EEN and B27-CD-TREAT when compared with the B27-CONTROL group (in all cases data from all studied animals were included, n=12)

| Phylum | Class | Order | Family | Genus | B27 CONTROL | B27 EEN | Adjusted *P* | B27 CD-TREAT | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|---|
| Significantly higher than B27-CONTROL group for both dietary interventions | | | | | | | | | |
| Bacteroidetes | Bacteroidia | Bacteroidales | Rikenellaceae | Alistipes | -8.12 | -4.03 | 1.91E-02 | -5.27 | 7.00E-04 |
| Firmicutes | Clostridia | Clostridiales | Family_XIII | Family_XIII_AD3011_group | -9.50 | -7.11 | 1.11E-02 | -7.39 | 1.76E-02 |
| | | | Lachnospiraceae | Eisenbergiella | -6.96 | -3.51 | 6.97E-03 | -4.97 | 1.90E-02 |
| | | | | Hungatella | -9.68 | -5.48 | 3.66E-02 | -6.35 | 2.79E-03 |
| | | | Ruminococcaceae | [Eubacterium]_coprostanoligenes_group | -7.68 | -3.80 | 6.97E-02 | -4.52 | 9.58E-02 |
| | | | | Anaerofilum | -8.75 | -3.82 | 9.92E-03 | -5.03 | 1.90E-02 |
| | | | | Anaerotruncus | -7.84 | -6.03 | 1.11E-02 | -6.38 | 1.90E-02 |
| | | | | Intestinimonas | -9.68 | -8.42 | 4.76E-02 | -6.97 | 3.41E-03 |
| | | | | Oscillibacter | -6.24 | -4.04 | 8.92E-02 | -3.91 | 1.90E-02 |
| | | | | Ruminiclostridium_5 | -7.87 | -5.77 | 4.76E-02 | -5.41 | 5.27E-02 |
| | | | | Ruminiclostridium_9 | -6.19 | -4.24 | 6.08E-02 | -4.33 | 3.04E-02 |
| | | | | Ruminococcaceae_UCG-014 | -6.81 | -3.40 | 1.91E-02 | -3.20 | 1.06E-02 |
| | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Allobaculum | -7.86 | -4.36 | 5.10E-03 | -5.50 | 2.30E-02 |
| | | | | Holdemania | -9.23 | -7.34 | 7.34E-03 | -7.50 | 8.11E-02 |
| Significantly lower than B27-CONTROL group for both dietary interventions | | | | | | | | | |
| Bacteroidetes | Bacteroidia | Bacteroidales | Prevotellaceae | Prevotella_9 | -1.90 | -9.21 | 5.68E-03 | -7.38 | 2.38E-02 |
| Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Fusicatenibacter | -2.42 | -9.04 | 5.10E-03 | -6.49 | 2.91E-03 |

Table S26: Relative abundance (ln) of genera in feces, collected one week post treatment initiation, which differed (*P*<.10) between B27-CONTROL with B27-EEN or B27-CD-TREAT group only (in all cases data from all studied animals were included, n=12)

| Phylum | Class | Order | Family | Genus | B27-EEN/ B27-CDTREAT | B27 CONTROL | Adjusted *P* |
|---|---|---|---|---|---|---|---|
| Significantly higher for B27-EEN than B27-CONTROL group | | | | | | | |
| Actinobacteria | Actinobacteria | Actinomycetales | Actinomycetaceae | Actinomyces | -7.59 | -9.68 | 4.65E-02 |
| | Coriobacteriia | Coriobacteriales | Coriobacteriaceae | Collinsella | -7.50 | -9.16 | 8.61E-02 |
| Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Coprococcus_1 | -5.49 | -6.26 | 1.72E-02 |
| | | | | Lachnospiraceae_FCS020_group | -8.55 | -9.68 | 5.95E-02 |
| | | | Ruminococcaceae | Candidatus_Soleaferrea | -7.63 | -9.00 | 8.92E-02 |
| Significantly lower for B27-EEN than B27-CONTROL group | | | | | | | |
| Bacteroidetes | Bacteroidia | Bacteroidales | Prevotellaceae | Prevotellaceae_NK3B31_group | -9.14 | -4.81 | 3.66E-02 |
| | | | | Prevotellaceae_UCG-001 | -9.31 | -3.28 | 6.80E-03 |
| Firmicutes | Bacilli | Lactobacillales | Lactobacillaceae | Lactobacillus | -6.77 | -3.56 | 5.68E-03 |
| Significantly higher for B27-CD-TREAT than B27-CONTROL group | | | | | | | |
| Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidaceae | Bacteroides | -1.37 | -2.77 | 7.10E-02 |
| | | | Porphyromonadaceae | Butyricimonas | -6.11 | -9.23 | 1.06E-02 |
| Firmicutes | Bacilli | Lactobacillales | Leuconostocaceae | Leuconostoc | -6.60 | -9.68 | 9.83E-02 |
| | | | Streptococcaceae | Lactococcus | -6.56 | -9.68 | 2.79E-03 |
| | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -3.02 | -5.26 | 2.05E-02 |
| | | | | Coprococcus_3 | -5.19 | -7.32 | 6.18E-02 |
| | | | | Lachnospiraceae_UCG-004 | -5.15 | -8.48 | 1.90E-02 |
| | | | | Marvinbryantia | -3.91 | -8.34 | 3.25E-03 |
| | | | | Tyzzerella | -6.32 | -9.68 | 1.06E-02 |
| | | | Ruminococcaceae | Ruminococcaceae_NK4A214_group | -4.75 | -8.25 | 1.76E-02 |
| | | | | Ruminococcaceae_UCG-009 | -7.14 | -9.40 | 9.82E-02 |
| | | | | Ruminococcus_2 | -3.74 | -8.26 | 7.71E-02 |
| Proteobacteria | Betaproteobacteria | Burkholderiales | Alcaligenaceae | Parasutterella | -3.57 | -4.52 | 1.66E-02 |

| Significantly lower for B27-CD-TREAT than B27-CONTROL group | | | | | | | |
|---|---|---|---|---|---|---|---|
| Actinobacteria | Actinobacteria | Bifidobacteriales | Bifidobacteriaceae | Bifidobacterium | -7.93 | -4.56 | 2.01E-02 |
| Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnospiraceae_UCG-005 | -7.52 | -4.54 | 7.03E-02 |
| | | | Ruminococcaceae | Ruminococcaceae_UCG-008 | -4.77 | -4.09 | 6.18E-02 |

Table S27: Number of 3% OTU in cecal content samples (collected at sacrifice) which significantly (*P*<.10) differed in relative abundance between B27-CONTROL group with B27-EEN and B27-CD-TREAT groups (in all cases data from all studied animals were included, n=12).

| | Number of 3% OTU |
|---|---|
| EEN | 31 |
| CD-TREAT | 43 |
| **Both interventions similar direction** | **16** |
| EEN only | 14 |
| CD-TREAT only | 26 |
| Both interventions opposite direction | 1 |
| 51.61% (16 out of 31) of EEN induced OTU changes were replicated by CD-TREAT | |
| 37.21% (16 out of 43) of CD-TREAT induced OTU changes were EEN-alike | |

Table S28: Relative abundance (ln) of 3% OTU genera in cecal contents, collected at sacrifice, which differed (*P*<.10) similarly for B27-EEN and B27-CD-TREAT when compared with the B27-CONTROL group (in all cases data from all studied animals were included, n=12)

| OTU | Phylum | Class | Order | Family | Genus | B27 CONTROL | B27 EEN | Adjusted *P* | B27 CD-TREAT | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| Significantly higher than B27-CONTROL group for both dietary interventions | | | | | | | | | | |
| OTU_52 | Bacteroidetes | Bacteroidia | Bacteroidales | Porphyromonadaceae | Butyricimonas | -8.64 | -4.19 | 1.26E-02 | -5.29 | 6.32E-03 |
| OTU_76 | | | | Rikenellaceae | Alistipes | -9.36 | -5.04 | 2.23E-02 | -5.78 | 1.47E-02 |
| OTU_88 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Hungatella | -9.64 | -5.54 | 2.61E-02 | -7.72 | 8.33E-02 |
| OTU_168 | | | | | Lachnoclostridium | -9.24 | -5.39 | 1.26E-02 | -6.88 | 8.18E-02 |
| OTU_51 | | | | | NA | -7.20 | -4.31 | 1.26E-02 | -5.13 | 1.23E-02 |
| OTU_136 | | | | Peptococcaceae | NA | -7.64 | -5.24 | 6.96E-02 | -5.74 | 8.18E-02 |
| OTU_42 | | | | Ruminococcaceae | [Eubacterium]_coprostanoligenes_group | -9.09 | -4.32 | 2.61E-02 | -6.31 | 5.79E-02 |
| OTU_56 | | | | | Ruminococcaceae_UCG-014 | -9.24 | -5.12 | 1.56E-02 | -5.55 | 6.32E-03 |
| OTU_91 | Proteobacteria | Alphaproteobacteria | Rhodospirillales | Rhodospirillaceae | Thalassospira | -8.59 | -6.21 | 6.32E-02 | -6.76 | 7.17E-02 |
| Significantly lower than B27-CONTROL group for both dietary interventions | | | | | | | | | | |
| OTU_39 | Actinobacteria | Actinobacteria | Bifidobacteriales | Bifidobacteriaceae | Bifidobacterium | -5.22 | -7.30 | 6.96E-02 | -8.85 | 6.07E-03 |
| OTU_228 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidales_S24-7_group | NA | -7.10 | -9.93 | 6.32E-02 | -8.68 | 8.02E-02 |
| OTU_60 | Firmicutes | Bacilli | Lactobacillales | Lactobacillaceae | Lactobacillus | -3.13 | -6.59 | 2.61E-02 | -6.61 | 1.45E-02 |
| OTU_142 | | Clostridia | Clostridiales | Clostridiaceae_1 | Candidatus_Arthromitus | -6.23 | -9.93 | 2.61E-02 | -8.68 | 6.26E-02 |
| OTU_3 | | | | Lachnospiraceae | Blautia | -2.40 | -7.66 | 7.21E-02 | -4.55 | 6.26E-02 |
| OTU_784 | | | | | Blautia | -5.65 | -9.31 | 6.32E-02 | -7.99 | 4.36E-02 |
| OTU_316 | | | | | Roseburia | -7.19 | -9.93 | 6.32E-02 | -9.25 | 2.84E-02 |

Table S29: Relative abundance (ln) of 3% OTU in cecal contents, collected at sacrifice, which differed (*P*<.10) between B27-CONTROL with B27-EEN or B27-CD-TREAT group only (in all cases data from all studied animals were included, n=12)

| OTU | Phylum | Class | Order | Family | Genus | B27-EEN/ B27-CDTREAT | B27 CONTROL | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|
| Significantly higher for B27-EEN than B27-CONTROL group | | | | | | | | |
| OTU_378 | Actinobacteria | Coriobacteriia | Coriobacteriales | Coriobacteriaceae | Senegalimassilia | -7.08 | -9.36 | 6.05E-02 |
| OTU_214 | Bacteroidetes | Bacteroidia | Bacteroidales | Rikenellaceae | Alistipes | -6.95 | -9.09 | 3.97E-02 |
| OTU_397 | Firmicutes | Clostridia | Clostridiales | Christensenellaceae | NA | -7.93 | -9.99 | 6.96E-02 |
| OTU_99 | | | | Family_XIII | [Eubacterium]_nodatum_group | -5.46 | -8.17 | 6.96E-02 |
| OTU_418 | | | | | Family_XIII_AD3011_group | -7.99 | -9.36 | 7.28E-02 |
| OTU_227 | | | | Ruminococcaceae | Anaerotruncus | -6.94 | -9.10 | 2.61E-02 |
| OTU_463 | | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Holdemania | -7.55 | -9.54 | 6.32E-02 |
| Significantly lower for B27-EEN than B27-CONTROL group | | | | | | | | |
| OTU_183 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidales_S24-7_group | NA | -9.76 | -5.80 | 2.61E-02 |
| OTU_167 | | | | | NA | -9.93 | -7.09 | 6.96E-02 |
| OTU_37 | | | | Prevotellaceae | Alloprevotella | -9.93 | -4.35 | 2.61E-02 |
| OTU_5 | | | | | Prevotella_9 | -9.24 | -2.52 | 3.97E-02 |
| OTU_26 | | | | | Prevotellaceae_UCG-001 | -9.93 | -3.87 | 2.42E-02 |
| OTU_14 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -9.93 | -5.89 | 2.61E-02 |
| OTU_165 | | | | | Coprococcus_1 | -7.48 | -6.61 | 4.05E-02 |
| OTU_102 | | | | Ruminococcaceae | Ruminococcaceae_UCG-008 | -6.93 | -4.52 | 1.26E-02 |
| Significantly higher for B27-CD-TREAT than B27-CONTROL group | | | | | | | | |
| OTU_145 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidales_S24-7_group | NA | -5.70 | -8.48 | 9.64E-02 |
| OTU_170 | | | | | NA | -5.83 | -8.69 | 2.79E-02 |
| OTU_240 | | | | | NA | -6.04 | -8.25 | 3.64E-02 |
| OTU_70 | | | | | NA | -3.65 | -7.66 | 7.17E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OTU_36 | | | | Prevotellaceae | NA | -3.66 | -4.51 | 4.54E-02 |
| OTU_269 | | | | Rikenellaceae | Alistipes | -6.71 | -9.64 | 4.69E-02 |
| OTU_54 | Cyanobacteria | Melainabacteria | Gastranaerophilales | NA | NA | -4.67 | -9.10 | 6.07E-03 |
| OTU_116 | Firmicutes | Bacilli | Lactobacillales | Leuconostocaceae | Leuconostoc | -6.55 | -9.99 | 1.60E-02 |
| OTU_243 | | | | Streptococcaceae | Lactococcus | -7.88 | -9.99 | 6.56E-02 |
| OTU_14 | | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -4.40 | -5.89 | 3.82E-02 |
| OTU_84 | | | | | Lachnospiraceae_NK4A136_group | -5.32 | -9.99 | 8.18E-02 |
| OTU_144 | | | | | Marvinbryantia | -6.92 | -9.99 | 3.82E-02 |
| OTU_46 | | | | | Marvinbryantia | -5.54 | -7.94 | 8.18E-02 |
| OTU_539 | | | | | Marvinbryantia | -7.95 | -9.71 | 3.82E-02 |
| OTU_229 | | | | | NA | -8.10 | -9.99 | 9.84E-02 |
| OTU_30 | | | | | NA | -3.98 | -5.33 | 3.07E-02 |
| OTU_266 | | | | | Tyzzerella | -7.83 | -9.99 | 9.30E-02 |
| OTU_174 | | | | Ruminococcaceae | Anaerofilum | -8.40 | -9.81 | 4.36E-02 |
| OTU_353 | | | | | Anaerotruncus | -8.01 | -9.99 | 7.54E-02 |
| OTU_343 | | | | | Intestinimonas | -7.51 | -9.99 | 4.34E-02 |
| OTU_73 | | | | | NA | -5.67 | -9.07 | 4.36E-02 |
| OTU_306 | | | | | Oscillibacter | -6.30 | -8.82 | 2.56E-02 |
| OTU_103 | | | | | Ruminiclostridium_9 | -5.94 | -8.26 | 6.56E-02 |
| OTU_114 | | | | | Ruminiclostridium_9 | -4.63 | -8.99 | 6.07E-03 |
| OTU_429 | | | | | Ruminiclostridium_9 | -6.47 | -8.95 | 6.32E-03 |
| OTU_137 | | | | | Ruminococcaceae_NK4A214_group | -5.38 | -8.49 | 4.36E-02 |
| OTU_41 | Verrucomicrobia | Opitutae | Opitutae_vadinHA64 | NA | NA | -2.71 | -9.81 | 1.43E-02 |

Table S30: Number of 3% OTU in fecal samples (collected four weeks post treatment initiation) which significantly (*P*<.10) differed in relative abundance between B27-CONTROL group with B27-EEN and B27-CD-TREAT groups (in all cases data from all studied animals were included, n=12).

| | Number of 3% OTU |
|---|---|
| EEN | 22 |
| CD-TREAT | 15 |
| **Both interventions similar direction** | **4** |
| EEN only | 18 |
| CD-TREAT only | 11 |
| Both interventions opposite direction | 0 |
| 18.18% (4 out of 22) of EEN induced OTU changes were replicated by CD-TREAT | |
| 26.67% (4 out of 15) of CD-TREAT induced OTU changes were EEN-alike | |

Table S31: Relative abundance (ln) of 3% OTU genera in feces, collected four weeks post treatment initiation, which differed (*P*<.10) similarly for B27-EEN and B27-CD-TREAT when compared with the B27-CONTROL group (in all cases data from all studied animals were included, n=12)

| OTU | Phylum | Class | Order | Family | Genus | B27 CONTROL | B27 EEN | Adjusted *P* | B27 CD-TREAT | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| Significantly higher than B27-CONTROL group for both dietary interventions | | | | | | | | | | |
| OTU_52 | Bacteroidetes | Bacteroidia | Bacteroidales | Porphyromonadaceae | Butyricimonas | -9.39 | -4.50 | 2.27E-02 | -5.76 | 3.85E-02 |
| OTU_51 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | NA | -7.26 | -4.07 | 2.27E-02 | -4.99 | 3.85E-02 |
| Significantly lower than B27-CONTROL group for both dietary interventions | | | | | | | | | | |
| OTU_784 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Blautia | -5.59 | -9.65 | 3.48E-02 | -7.95 | 7.53E-02 |
| OTU_316 | | | | | Roseburia | -7.08 | -9.88 | 3.48E-02 | -9.12 | 8.96E-02 |

Table S32: Relative abundance (ln) of 3% OTU in feces, collected four weeks post treatment initiation, which differed (*P*<.10) between B27-CONTROL with B27-EEN or B27-CD-TREAT group only (in all cases data from all studied animals were included, n=12)

| OTU | Phylum | Class | Order | Family | Genus | B27-EEN/ B27-CDTREAT | B27 CONTROL | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|
| Significantly higher for B27-EEN than B27-CONTROL group | | | | | | | | |
| OTU_76 | Bacteroidetes | Bacteroidia | Bacteroidales | Rikenellaceae | Alistipes | -4.85 | -8.77 | 3.48E-02 |
| OTU_75 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Lachnoclostridium | -4.62 | -7.79 | 6.59E-02 |
| OTU_168 | | | | | Lachnoclostridium | -5.22 | -9.44 | 3.48E-02 |
| OTU_42 | | | | Ruminococcaceae | [Eubacterium]_coprostanoligenes_group | -4.47 | -8.95 | 5.31E-02 |
| OTU_108 | | | | | Ruminiclostridium_5 | -5.90 | -8.54 | 5.31E-02 |
| OTU_56 | | | | | Ruminococcaceae_UCG-014 | -4.62 | -8.60 | 3.48E-02 |
| Significantly lower for B27-EEN than B27-CONTROL group | | | | | | | | |
| OTU_183 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidales_S24-7_group | NA | -10.05 | -5.84 | 3.48E-02 |
| OTU_167 | | | | | NA | -10.23 | -6.96 | 4.37E-02 |
| OTU_37 | | | | Prevotellaceae | Alloprevotella | -10.05 | -4.36 | 3.48E-02 |
| OTU_36 | | | | | NA | -9.46 | -4.62 | 5.31E-02 |
| OTU_5 | | | | | Prevotella_9 | -8.88 | -2.11 | 3.48E-02 |
| OTU_26 | | | | | Prevotellaceae_UCG-001 | -10.23 | -3.91 | 2.04E-02 |
| OTU_66 | Firmicutes | Bacilli | Lactobacillales | Lactobacillaceae | Lactobacillus | -9.33 | -5.09 | 9.93E-02 |
| OTU_64 | | | | | Lactobacillus | -9.50 | -5.65 | 7.17E-02 |
| OTU_14 | | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -9.57 | -5.58 | 4.78E-02 |
| OTU_3 | | | | | Blautia | -8.03 | -2.39 | 5.31E-02 |
| OTU_19 | | | | | Fusicatenibacter | -10.05 | -4.21 | 4.77E-02 |
| OTU_102 | | | | Ruminococcaceae | Ruminococcaceae_UCG-008 | -6.56 | -4.45 | 4.77E-02 |
| Significantly higher for B27-CD-TREAT than B27-CONTROL group | | | | | | | | |
| OTU_149 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidaceae | Bacteroides | -6.35 | -9.84 | 8.96E-02 |
| OTU_54 | Cyanobacteria | Melainabacteria | Gastranaerophilales | NA | NA | -5.46 | -10.02 | 2.33E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OTU_116 | Firmicutes | Bacilli | Lactobacillales | Leuconostocaceae | Leuconostoc | -4.67 | -10.02 | 2.33E-02 |
| OTU_243 | | | | Streptococcaceae | Lactococcus | -7.21 | -10.02 | 6.22E-02 |
| OTU_397 | | Clostridia | Clostridiales | Christensenellaceae | NA | -7.71 | -10.02 | 8.96E-02 |
| OTU_539 | | | | Lachnospiraceae | Marvinbryantia | -7.18 | -9.57 | 7.53E-02 |
| OTU_144 | | | | | Marvinbryantia | -6.69 | -10.02 | 4.97E-02 |
| OTU_73 | | | | Ruminococcaceae | NA | -5.62 | -9.74 | 3.85E-02 |
| OTU_114 | | | | | Ruminiclostridium_9 | -4.33 | -9.39 | 3.85E-02 |
| Significantly lower for B27-CD-TREAT than B27-CONTROL group | | | | | | | | |
| OTU_39 | Actinobacteria | Actinobacteria | Bifidobacteriales | Bifidobacteriaceae | Bifidobacterium | -8.50 | -5.20 | 7.03E-02 |
| OTU_228 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidales_S24-7_group | NA | -8.95 | -7.08 | 7.53E-02 |

Table S33: Number of 3% OTU in fecal samples (collected one week post treatment initiation) which significantly (*P*<.10) differed in relative abundance between B27-CONTROL group with B27-EEN and B27-CD-TREAT groups (in all cases data from all studied animals were included, n=12).

| | Number of 3% OUT |
|---|---|
| EEN | 36 |
| CD-TREAT | 38 |
| **Both interventions similar direction** | **11** |
| EEN only | 25 |
| CD-TREAT only | 27 |
| Both interventions opposite direction | 0 |
| 30.56% (11 out of 36) of EEN induced OTU changes were replicated by CD-TREAT | |
| 28.95% (11 out of 38) of CD-TREAT induced OTU changes were EEN-alike | |

Table S34: Relative abundance (ln) of 3% OTU in feces, collected one week week post treatment initiation, which differed (*P*<.10) similarly for B27-EEN and B27-CD-TREAT when compared with the B27-CONTROL group (in all cases data from all studied animals were included, n=12).

| OTU | Phylum | Class | Order | Family | Genus | B27 CONTROL | B27 EEN | Adjusted *P* | B27 CD-TREAT | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| Significantly higher than B27-CONTROL group for both dietary interventions | | | | | | | | | | |
| OTU_76 | Bacteroidetes | Bacteroidia | Bacteroidales | Rikenellaceae | Alistipes | -9.34 | -4.49 | 4.29E-02 | -5.75 | 1.63E-03 |
| OTU_48 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Eisenbergiella | -7.07 | -3.72 | 1.74E-02 | -5.19 | 5.67E-02 |
| OTU_88 | | | | | Hungatella | -9.79 | -5.69 | 6.73E-02 | -6.57 | 5.83E-03 |
| OTU_168 | | | | | Lachnoclostridium | -9.21 | -6.10 | 1.74E-02 | -5.92 | 7.20E-03 |
| OTU_51 | | | | | NA | -7.68 | -4.44 | 2.84E-02 | -4.66 | 3.86E-02 |
| OTU_136 | | | | Peptococcaceae | NA | -7.98 | -5.10 | 2.74E-02 | -5.50 | 3.23E-03 |
| OTU_38 | | | | Ruminococcaceae | Oscillibacter | -7.67 | -4.39 | 7.27E-02 | -5.31 | 2.07E-02 |
| OTU_101 | | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Allobaculum | -9.17 | -4.70 | 1.19E-02 | -6.16 | 1.87E-02 |
| Significantly lower than B27-CONTROL group for both dietary interventions | | | | | | | | | | |
| OTU_5 | Bacteroidetes | Bacteroidia | Bacteroidales | Prevotellaceae | Prevotella_9 | -2.01 | -9.51 | 1.74E-02 | -7.66 | 5.67E-02 |
| OTU_19 | Firmicutes | Clostridia | Clostridiales | Lachnospiraceae | Fusicatenibacter | -2.53 | -9.24 | 1.19E-02 | -6.71 | 5.83E-03 |
| OTU_316 | | | | | Roseburia | -6.80 | -9.86 | 2.74E-02 | -9.65 | 7.16E-02 |

Table S35: Relative abundance (ln) of 3% OTU in feces, collected one week post treatment initiation, which differed (*P*<.10) between B27-CONTROL with B27-EEN or B27-CD-TREAT group only (in all cases data from all studied animals were included, n=12)

| OTU | Phylum | Class | Order | Family | Genus | B27-EEN/ B27-CDTREAT | B27 CONTROL | Adjusted *P* |
|---|---|---|---|---|---|---|---|---|
| Significantly higher for B27-EEN than B27-CONTROL group | | | | | | | | |
| OTU_337 | Firmicutes | Bacilli | Lactobacillales | Streptococcaceae | Streptococcus | -7.28 | -8.62 | 4.46E-02 |
| OTU_397 | | Clostridia | Clostridiales | Christensenellaceae | NA | -7.53 | -9.79 | 3.14E-02 |
| OTU_418 | | | | Family_XIII | Family_XIII_AD3011_group | -7.68 | -9.79 | 2.84E-02 |
| OTU_75 | | | | Lachnospiraceae | Lachnoclostridium | -5.08 | -8.05 | 6.73E-02 |
| OTU_197 | | | | | NA | -5.68 | -8.14 | 7.54E-02 |
| OTU_159 | | | | | NA | -5.23 | -8.28 | 9.59E-02 |
| OTU_42 | | | | Ruminococcaceae | [Eubacterium]_coprostanoligenes_group | -4.01 | -8.10 | 6.73E-02 |
| OTU_43 | | | | | Anaerofilum | -4.16 | -9.09 | 1.74E-02 |
| OTU_227 | | | | | Anaerotruncus | -6.74 | -8.81 | 8.87E-02 |
| OTU_108 | | | | | Ruminiclostridium_5 | -6.56 | -9.51 | 1.74E-02 |
| OTU_300 | | | | | Ruminiclostridium_9 | -5.55 | -7.94 | 7.54E-02 |
| OTU_124 | | | | | Ruminococcaceae_UCG-014 | -4.75 | -8.42 | 2.74E-02 |
| OTU_463 | | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | Holdemania | -7.54 | -9.34 | 1.74E-02 |
| OTU_109 | Proteobacteria | Deltaproteobacteria | Desulfovibrionales | Desulfovibrionaceae | Desulfovibrio | -5.66 | -7.00 | 3.12E-02 |
| Significantly lower for B27-EEN than B27-CONTROL group | | | | | | | | |
| OTU_228 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidales_S24-7_group | NA | -9.69 | -6.60 | 7.05E-02 |
| OTU_37 | | | | Prevotellaceae | Alloprevotella | -9.11 | -4.15 | 7.05E-02 |
| OTU_36 | | | | | NA | -9.29 | -4.28 | 5.17E-02 |
| OTU_11 | | | | | Prevotellaceae_NK3B31_group | -9.34 | -4.92 | 6.11E-02 |
| OTU_26 | | | | | Prevotellaceae_UCG-001 | -9.51 | -4.09 | 3.02E-02 |
| OTU_66 | Firmicutes | Bacilli | Lactobacillales | Lactobacillaceae | Lactobacillus | -9.86 | -5.15 | 1.74E-02 |
| OTU_64 | | | | | Lactobacillus | -9.59 | -5.45 | 1.74E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OTU_98 | | | | | Lactobacillus | -9.86 | -6.65 | 2.84E-02 |
| OTU_60 | | | | | Lactobacillus | -7.00 | -4.55 | 8.87E-02 |
| OTU_784 | | Clostridia | Clostridiales | Lachnospiraceae | Blautia | -9.17 | -5.57 | 1.74E-02 |
| OTU_215 | | Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae | NA | -7.23 | -6.02 | 6.73E-02 |
| Significantly higher for B27-CD-TREAT than B27-CONTROL group | | | | | | | | |
| OTU_263 | Actinobacteria | Coriobacteriia | Coriobacteriales | Coriobacteriaceae | NA | -7.33 | -9.61 | 1.22E-02 |
| OTU_133 | Bacteroidetes | Bacteroidia | Bacteroidales | Bacteroidaceae | Bacteroides | -5.47 | -7.76 | 7.47E-02 |
| OTU_240 | | | | Bacteroidales_S24-7_group | NA | -6.41 | -8.24 | 5.53E-02 |
| OTU_170 | | | | | NA | -6.19 | -8.20 | 1.87E-02 |
| OTU_648 | | | | | NA | -7.42 | -9.61 | 8.61E-02 |
| OTU_52 | | | | Porphyromonadaceae | Butyricimonas | -6.33 | -9.34 | 2.40E-02 |
| OTU_243 | Firmicutes | Bacilli | Lactobacillales | Streptococcaceae | Lactococcus | -6.79 | -9.79 | 5.83E-03 |
| OTU_14 | | Clostridia | Clostridiales | Lachnospiraceae | Anaerostipes | -3.25 | -5.48 | 5.67E-02 |
| OTU_404 | | | | | Blautia | -7.31 | -8.54 | 7.53E-02 |
| OTU_172 | | | | | Blautia | -5.89 | -8.79 | 6.92E-02 |
| OTU_79 | | | | | Lachnospiraceae_UCG-004 | -5.37 | -8.76 | 5.67E-02 |
| OTU_46 | | | | | Marvinbryantia | -4.48 | -8.76 | 1.63E-03 |
| OTU_30 | | | | | NA | -3.74 | -5.54 | 4.87E-02 |
| OTU_266 | | | | | Tyzzerella | -6.54 | -9.79 | 2.40E-02 |
| OTU_174 | | | | Ruminococcaceae | Anaerofilum | -7.21 | -9.61 | 4.44E-02 |
| OTU_43 | | | | | Anaerofilum | -5.46 | -9.09 | 3.86E-02 |
| OTU_343 | | | | | Intestinimonas | -7.25 | -9.79 | 1.46E-02 |
| OTU_73 | | | | | NA | -7.19 | -9.61 | 4.44E-02 |
| OTU_306 | | | | | Oscillibacter | -6.83 | -9.27 | 8.50E-02 |
| OTU_103 | | | | | Ruminiclostridium_9 | -6.22 | -8.01 | 7.47E-02 |
| OTU_114 | | | | | Ruminiclostridium_9 | -5.46 | -9.06 | 7.41E-02 |
| OTU_137 | | | | | Ruminococcaceae_NK4A214_group | -4.97 | -8.36 | 4.44E-02 |
| OTU_115 | | | | | Ruminococcaceae_UCG-014 | -5.15 | -9.09 | 4.87E-02 |
| OTU_55 | | | | | Ruminococcaceae_UCG-014 | -3.95 | -7.93 | 6.92E-02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| OTU_33 | Proteobacteria | Betaproteobacteria | Burkholderiales | Alcaligenaceae | Parasutterella | -3.80 | -4.63 | 5.33E-02 |
| Significantly lower for B27-CD-TREAT than B27-CONTROL group | | | | | | | | |
| OTU_39 | Actinobacteria | Actinobacteria | Bifidobacteriales | Bifidobacteriaceae | Bifidobacterium | -8.15 | -4.67 | 4.87E-02 |
| OTU_102 | Firmicutes | Clostridia | Clostridiales | Ruminococcaceae | Ruminococcaceae_UCG-008 | -4.99 | -4.20 | 8.35E-02 |

Table S36. Age, anthropometry, disease activity, blood inflammatory markers, fecal calprotectin and disease characteristics of the patients with CD enrolled in the open label trial (n=5)

| | |
|---|---|
| Age, years | 13.3, 3.2 |
| Gender, n (%) males | 4/5, 80% |
| Weight, kg | 40.8, 13.4 |
| Weight z-score, SD | -0.89, 0.51 |
| Height z-score, SD | -0.67, 0.66 |
| BMI z-score, SD | -0.71, 0.58 |
| Disease duration, years | 1.8, 2.3 |
| wPCDAI | 30.5, 7.8 |
| Raised wPCDAI (>12.5), n (%) | 5/5 (100%) |
| Albumin, g/L | 37.8, 4.0 |
| Low albumin (<35 g/L), n (%) | 1/5 (20%) |
| C-reactive protein, mg/L | 5.2, 6.0 |
| Raised C-reactive protein (>10 mg/L), n (%) | 1/5 (20%) |
| Fecal calprotectin (mg/kg) | 1973, 957 |
| Raised fecal calprotectin (> 250 mg/kg), n (%) | 5/5 (100%) |
| | |
| Concurrent treatment | |
| Thiopurine monotherapy, n (%) | 3/5 (60%) |
| Anti-TNF/thiopurine combination, n (%) | 1/5 (20%) |
| | |
| Paris classification | |
| Patient 1 | A1a, L3, B1, G0 |
| Patient 2 | A1b, L2, B1, G0 |
| Patient 3 | A1b, L3 + L4a, B1, G0 |
| Patient 4 | A1b, L3 + L4a, B1, G0 |
| Patient 5 | A1b, L2 + L4a, B1, G0 |

Data are displayed with means and standard deviations, unless stated otherwise; BMI: Body mass index; wPCDAI: weighted pediatric Crohn's disease activity index; TNF: Tumor necrosis factor; Baseline diagnostic clinical phenotype was recorded using Paris criteria[1]

Table S37. Anthropometry, disease activity, inflammatory markers and fecal calprotectin levels of the patients who completed 8 week course of CD-TREAT (n=4).

| | Pre CD-TREAT | 4 weeks post CD-TREAT | 8 weeks post CD-TREAT |
|---|---|---|---|
| Weight, kg | 37.6, 13.1 | 38.5, 12.8 | 39.4, 13.2 |
| Weight z-score, SD | -1.05, 0.41 | -0.96, 0.20 | -0.86, 0.32 |
| Height z-score, SD | -0.82, 0.66 | -0.85, 0.72 | -0.83, 0.70 |
| BMI z-score, SD | -0.88, 0.52 | -0.71, 0.71 | -0.61, 0.96 |
| wPCDAI | 32.5, 7.4 | 11.3, 9.2[a*] | 7.5, 7.4[a**] |
| Albumin, g/L | 36.8, 3.8 | 38.3, 4.6 | 39.0, 4.8 |
| Abnormal albumin (<35 g/L) | 1/4, 25% | 0/4, 0% | 0/4, 0% |
| C-reactive protein, mg/L | 6.3, 6.4 | 4.3, 3.8 | 3.0, 2.5 |
| Abnormal C-reactive protein (>10 mg/L) | 1/4, 25% | 0/4, 0% | 0/4, 0% |
| Fecal calprotectin, mg/kg | 1960, 1104 | 981, 690[a**] | 1042, 776[a**] |
| Fecal calprotectin % change from baseline | - | -53.0, 14.9 | -55.4, 24.2 |
| Fecal calprotectin > 50% reduction | - | 3/4, 75% | 3/4, 75% |

Data are displayed with means and standard deviations; [a] significant difference between Pre CD-TREAT vs Post CD-TREAT (4 weeks) or Pre CD-TREAT vs Post CD-TREAT (8 weeks); [*] $P<.05$; [**] $P<.01$; [¥] $P<.001$. $P$ for Fisher pairwise comparisons following general linear model with Box-Cox transformation. BMI: Body mass index; wPCDAI: weighted pediatric Crohn's disease activity index

References

1. Levine A, Griffiths A, Markowitz J, et al. Pediatric modification of the Montreal classification for inflammatory bowel disease: the Paris classification. Inflamm Bowel Dis 2011;17:1314-21.