Supplemental Material

IKKβ in intestinal epithelial cells regulates allergen-specific IgA and allergic inflammation at distant mucosal sites

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Running head: Intestinal epithelial cell ΙΚΚβ regulates allergy

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Supplemental Materials and Methods

Analysis of gut microbiota

The bacterial tag-encoded FLX amplicon pyrosequencing (bTEFAP) (Roche Titanium 454 FLX pyrosequencing platform) was used for detection and identification of the primary populations of microbes in fecal pellet samples. Briefly, freshly emitted fecal pellets samples were collected, snap frozen and stored at -80°C. Samples were collected twice a day from each individual mouse and pooled to minimize potential daily variation of the microbiota. Bacterial DNA was extracted by conventional methods (Qiagen, Valencia, CA), and 16S rRNA genes were amplified with the modified 16S Eubacterial primers 28F, 5'-GAG TTT GAT CNT GGC TCA G-3' and 519R, 5'-GTN TTA CNG CGG CKG CTG-3' for amplifying the 500 bp region of 16S rRNA genes. The primer sets used for FLX-Titanium amplicon pyrosequencing were designed with adding linker A and 8 base pair barcode sequence at the 5' end of forward primers as follow: 28F-A, 5'-CCA TCT CAT CCC TGC GTG TCT CCG ACT CAG-barcode-GAG TTT GAT CNT GGC TCA G-3'. The biotin and linker B sequence at the 5' end of reverse primer 519R-B: 5'-Biotin-CCT ATC CCC TGT GTG CCT TGG CAG TCT CAG GTN TTA CNG CGG CKG CTG-3'. HotStarTag Plus Master Mix Kit (QIAGEN, CA, USA) was used for PCR under the following conditions: 95 °C for 5 minutes followed by 35 cycles of 95 °C for 30 second; 54 °C for 40 second and 72 °C for 1 minute, a final elongation step at 72 °C for 10 minutes was also included. The PCR products were cleaned by using Diffinity Rapid Tip (Diffinity Genomics, Inc, West Henrietta, NY), and the small fragments were removed by using Agencourt Ampure Beads (Beckman Coulter, CA, USA).

Bacterial tag-encoded FLX-Titanium amplicon pyrosequencing (bTEFAP) was performed as described previously ¹. In preparation for FLX-Titanium sequencing (Roche, Nutley, New

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Jersey), DNA fragment sizes and concentration were accurately measured using DNA chips under a Bio-Rad Experion Automated Electrophoresis Station (Bio-Rad Laboratories, CA, USA) and a TBS-380 Fluorometer (Turner Biosystems, CA, USA). A sample of double-stranded DNA, 9.6 million molecules/ml, with an average size of 625 bp were combined with 9.6 million DNA capture beads, and then amplified by emulsion PCR. After bead recovery and bead enrichment, the bead attached DNAs were denatured with NaOH, and sequencing primers (Roche) were annealed. A four-region 454 sequencing run was performed on a GS PicoTiterPlate (PTP) using the Genome Sequencer FLX System (Roche). Forty tags were used on each quarter region of the PTP. All FLX procedures were performed using Genome Sequencer FLX System manufacturer's instructions (Roche). After denoising (USEARCH application) and chimera removal (UCHIIME in de novo mode), the sequences ware clustered into operational taxonomic units (OTU) clusters with 96.5% identity (3.5% divergence) using USEARCH and the seed sequence put into a FASTA formatted sequence file. The FASTA files were then queried against a database of high quality sequences derived from NCBI using a distributed .NET algorithm that utilizes BLASTN+ (KrakenBLAST www.krakenblast.com). For identification of segmented filamentous bacteria, blast search was performed with the fasta sequences against Candidatus Arthromitus (taxid:49082) genome sequences (Candidatus Arthromitus sp. SFB-mouse-Yit and Candidatus Arthromitus sp. SFB-mouse-Japan), using Megablast (optimized for highly similar sequences; \geq 95 %) and E-values below 1e-15.

Reference

1. Dowd SE, Wolcott RD, Sun Y, McKeehan T, Smith E, Rhoads D. Polymicrobial nature of chronic diabetic foot ulcer biofilm infections determined using bacterial tag encoded FLX amplicon pyrosequencing (bTEFAP). PLoS One 2008;3:e3326.

Supplemental Figure Legends

Figure S1. STAT3 responses in gut tissues of IKK $\beta^{\Delta IEC}$ after oral administration of cholera toxin. Control IKK β -competent C57BL/6 mice and IKK $\beta^{\Delta IEC}$ mice were orally administered cholera toxin (10 µg) by intragastric gavage. After 16 h, mice were euthanized and small intestines were collected. Tissue sections were labeled with anti-pSTAT3 Ab and counter-stained with hematoxylin and eosin (Original magnification: x40). The figure is representative of at least three independent experiments.

Figure S2. Cholera toxin does not induce fluid accumulation in the gut of IKKβ^{ΔIEC} mice. Control IKKβ-competent C57BL/6 mice and IKKβ^{ΔIEC} mice were orally administered cholera toxin (10 µg) by intragastric gavage. Mice were euthanized 10 or 16 hours later and intestinal fluid accumulation was evaluated by measuring the weight of intestine. The results are expressed as mean percentage of intestine weight over whole mouse body weight. (*,p < 0.05 compared to control C57BL/6 mice).

Figure S3. Oral cholera toxin treatment alters the distribution of bacteria families in the gut of IKK $\beta^{\Delta IEC}$ mice. Control IKK β -competent C57BL/6 mice and IKK $\beta^{\Delta IEC}$ mice were orally administered cholera toxin (10 µg) by intragastric gavage and fecal pellets were collected before (day 0) and 2 and 4 days later. The composition of the bacterial community was analyzed by pyrosequencing and heatmap of percentage of main bacteria family (at least 1 %) was generated.

The results are expressed as percentage of bacteria in individual samples with 3-4 mice per groups.

Figure S4. Oral cholera toxin treatment alters the distribution of bacteria genus in the gut of IKK β^{AIEC} mice. Control IKK β -competent C57BL/6 mice and IKK β^{AIEC} mice were orally administered cholera toxin (10 µg) by intragastric gavage and fecal pellets were collected before (day 0) and 2 and 4 days later. The composition of the bacterial community was analyzed by pyrosequencing and heatmap of percentage of main bacteria genus (at least 1 %) was generated. The results are expressed as percentage of bacteria in individual samples with 3-4 mice per groups.

Figure S5. Oral cholera toxin treatment alters the distribution of bacteria species in the gut of IKK $\beta^{\Delta IEC}$ mice. Control IKK β -competent C57BL/6 mice and IKK $\beta^{\Delta IEC}$ mice were orally administered cholera toxin (10 µg) by intragastric gavage and fecal pellets were collected before (day 0) and 2 and 4 days later. The composition of the bacterial community was analyzed by pyrosequencing and heatmap of percentage of the main bacteria species (at least 1 %) was generated. The results are expressed as percentage of bacteria in individual samples with 3-4 mice per groups.

Figure S6. IKKβ-deficiency in myeloid cells also alters innate and adaptive immune responses to ingested allergen. (A) STAT3 responses in gut tissues after oral administration of cholera toxin. Control IKKβ-competent C57BL/6 mice, IKK $\beta^{\Delta Mye}$ and IKK $\beta^{\Delta IEC}$ mice were orally administered cholera toxin (10 µg) by intragastric gavage. After 16 h, mice were euthanized and small intestines were collected, labeled with anti-pSTAT3 Ab and counterstained with hematoxylin and eosin (Original magnification: x40). The figure is representative of at least three independent experiments. (B-C) Serum antibody responses. Control C57BL/6 (open bars), IKK $\beta^{\Delta Mye}$ (grey bars) and IKK $\beta^{\Delta IEC}$ (solid bars) mice were orally sensitized on days 0 and 7 with of OVA (1 mg) and cholera toxin (10 µg). Blood was collected on day 14 and OVAspecific Ab responses were analyzed by ELISA. The results are expressed as the mean log₂ titers \pm one SD and are from three separate experiments and four mice / group. (*, p < 0.05).

Figure S7. Frequency of IgA secreting cells (ASC) in the lung and mesenteric lymph nodes of IKKβ^{ΔIEC} mice. Mice were sensitized on days 0 and 7 by oral administration of ovalbumin (OVA, 1 mg) and cholera toxin (10 µg). Nasal challenges were performed on days 15, 16, and 19 and lungs and mesenteric lymph nodes (MLN) were collected on day 20 and subjected to an IgAspecific ELISPOT assay. The results are expressed as mean number of ASC/10⁶ cells ± one SD and are from three experiments and four mice/group. (*,p < 0.05 compared to control C57BL/6 mice).

Figure S8. IKKβ-deficiency in intestinal epithelial cells alters serum and lung responses in mice sensitized by parenteral injection. Control C57BL/6 (open bars), and IKK β^{AIEC} (solid bars) mice were sensitized on days 0 and 7 by intraperitoneal injection of OVA (100 µg) and cholera toxin (1 µg). (A) Serum Ab responses. Blood was collected on day 14 and OVA-

specific Ab responses were analyzed by ELISA. The results are expressed as the mean \log_2 titers \pm one SD and are from three separate experiments and four mice / group. (*, p < 0.05). (B) Mucus secretion in the lungs after antigen challenge. Nasal challenges were performed on days 15, 16, and 19 and animals were euthanized on day 20. Lung sections were stained with PAS and counter stained with hematoxylin and eosin. Pictures are representative of three separate experiments and four mice / group. Original magnifications are indicated.

Figure S9. IKKβ-deficiency in intestinal epithelial cells alters immune cell recruitment and cytokine responses in the lungs of orally sensitized mice. Mice were sensitized on days 0 and 7 by oral administration of ovalbumin (OVA, 1 mg) and cholera toxin (10 µg). Nasal challenges were performed on days 15, 16, and 19. Flow cytometry analysis of the frequency of (A) $F4/80^+CD11c^+$ alveolar macrophages, $F4/80^+CD11c^-$ interstitial macrophages and $F4/80^-CD11^+$ dendritic cells and (B) CD103⁺ dendritic cells in the lungs after nasal antigen challenge of orally sensitized mice (C) Flow cytometry analysis of T cell subsets. Results are expressed as mean ± SD of three separate experiments, with 4 mice per group. (*, p < 0.05 compared to control C57BL/6 mice).

Figure S10. IKKβ-deficiency in intestinal epithelial cells alters airway cytokine responses to nasal antigen challenge of orally sensitized mice. Mice were sensitized on days 0 and 7 by oral administration of ovalbumin (OVA, 1 mg) and cholera toxin (10 µg). Nasal challenges were performed on days 15, 16, and 19. Bronchoalveolar lavage fluids (BAL) were collected on day 20 cytokine/chemokine responses were analyzed by conventional ELISA. Results are expressed as mean \pm SD of three separate experiments, with 4 mice per group. (*, p < 0.05 compared to control C57BL/6 mice).

Bonnegarde et al. Supplemental Materials Figure S1.



Cholera toxin

Bonnegarde et al. Supplemental Materials Figure S2.





Bonnegarde et al. Supplemental Materials Figure S3. Bonnegarde et al. Supplemental Materials Figure S4.



Bonnegarde et al. Supplemental Materials Figure S5.



Bonnegarde et al. Supplemental Materials New Figure S6.



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Bonnegarde et al. Supplemental Materials New Figure S9.



Bonnegarde et al. Supplemental Materials New Figure S10.



Table S1. Relative percentage of each Phylum

			C57BL/	6			ΙΚΚΌΔΙΕΟ						
	Day 0		Day 2		Day 4		Day 0		Day 2		Day 4		
Phylum	Mean	STD	Mean	STD	Mean	STD	Mean	STD	Mean	STD	Mean	STD	
Bacteroidetes	76.78	7.17	82.32	3.55	75.80	7.62	82.68	6.12	79.24	3.82	53.05	1.42	
Firmicutes	22.13	6.75	9.87	6.18	20.63	11.28	13.74	5.75	15.75	2.19	40.99	1.29	
Deferribacteres	0.30	0.25	0.05	0.02	0.30	0.27	0.03	0.02	0.06	0.10	1.02	0.29	
Proteobacteria	0.30	0.11	6.40	7.70	2.51	3.93	2.38	1.14	1.78	0.88	4.24	0.65	
Tenericutes	0.00	0.00	0.00	0.00	0.00	0.00	0.46	0.44	0.13	0.18	0.20	0.10	
Actinobacteria	0.10	0.04	0.08	0.08	0.04	0.05	0.10	0.07	0.42	0.37	0.04	0.04	
Verrucomicrobia	0.08	0.10	1.09	1.54	0.15	0.13	0.00	0.00	0.00	0.00	0.00	0.00	
Cyanobacteria	0.00	0.00	0.00	0.00	0.00	0.00	0.46	0.26	2.07	2.74	0.22	0.22	
TM7	0.32	0.17	0.18	0.30	0.57	0.13	0.06	0.01	0.00	0.00	0.24	0.15	
Spirochaetes	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.03	0.49	0.54	0.00	0.00	
Acidobacteria	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.07	0.05	0.09	0.01	0.01	
Chlorobi	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.03	0.00	0.00	
Chloroflexi	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	

Blue: IKK $\beta^{\Delta IEC}$ mice different than control C57B/L 6 group at day 0.

Red: Decreased percentage in IKK β^{AIEC} mice compared to same group at day 0. Green: Increased percentage in IKK β^{AIEC} mice compared to same group at day 0.

			C57BL	/6			ΙΚΚb ΔΙΕC								
	Day 0		Day 2		Day 4		_	Day 0		Day 2		Day 4			
Class	Mean	STD	Mean	STD	Mean	STD]	Mean	STD	Mean	STD	Mean	STD		
Bacteroidia	76.39	6.15	81.76	3.61	75.38	7.88		82.32	4.67	78.59	3.41	52.91	1.		
Clostridia	19.06	5.77	8.28	5.34	19.17	10.36		10.86	2.47	12.30	0.50	39.40) 1.		
Bacilli	3.04	2.19	0.75	0.54	1.10	1.12		2.68	3.18	2.69	0.93	1.49) 0.		
Erysipelotrichi	0.03	0.06	0.85	1.03	0.37	0.21		0.19	0.14	0.76	5 1.10	0.10) 0.		
Deferribacteres (class)	0.30	0.21	0.05	0.02	0.30	0.27		0.03	0.03	0.06	6 0.10	1.02	2 0.1		
Betaproteobacteria	0.04	0.02	0.19	0.16	0.06	0.06		0.59	0.42	0.63	0.87	0.32	2 0.		
Alphaproteobacteria	0.23	0.15	6.20	7.72	2.33	3.93		0.17	0.02	0.69	0.88	0.26	i 0.1		
Mollicutes	0.00	0.00	0.00	0.00	0.00	0.00		0.46	0.05	0.13	0.18	0.20) 0.		
Deltaproteobacteria	0.02	0.02	0.01	0.01	0.12	0.06		0.15	0.34	0.01	0.01	0.13	0.		
Actinobacteria (class)	0.10	0.04	0.08	0.08	0.04	0.05		0.10	0.09	0.42	0.37	0.04	0.0		
Verrucomicrobiae	0.08	0.13	1.09	1.54	0.15	0.13		0.00	0.00	0.00	0.00	0.00) 0.0		
Cyanobacteria (class)	0.00	0.00	0.00	0.00	0.00	0.00		0.04	0.03	0.18	0.26	0.18	3 0.2		
Chroococcales	0.00	0.00	0.00	0.00	0.00	0.00		0.42	0.22	1.88	3 2.48	0.04	0.0		
Epsilonproteobacteria	0.00	0.00	0.00	0.00	0.00	0.00		1.30	1.36	0.32	0.30	3.47	0.7		
TM7 (class)	0.32	0.16	0.18	0.30	0.57	0.13		0.06	0.01	0.00	0.00	0.24	0.1		
Spirochaetia	0.00	0.00	0.00	0.00	0.00	0.00		0.03	0.04	0.49	0.54	0.00) 0.0		
Flavobacteria	0.34	0.20	0.55	0.25	0.42	0.31		0.35	0.15	0.65	0.41	0.12	2 0.1		
Gammaproteobacteria	0.00	0.00	0.00	0.00	0.01	0.01		0.16	0.11	0.13	0.13	0.06	5 0.0		
Sphingobacteria	0.04	0.04	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00	0.00) 0.0		
Cytophagia	0.00	0.00	0.01	0.02	0.00	0.00		0.00	0.00	0.00	0.00	0.01	0.0		
Acidobacteria (class)	0.00	0.00	0.00	0.00	0.00	0.00		0.06	0.07	0.05	0.09	0.01	. 0.0		
Chlorobia	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.02	0.03	0.00) 0.0		
Anaerolineae	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.01	0.00	0.00	0.00) 0.0		

Table S2. Relative percentage of bacteria classes

Blue: IKK $\beta^{\Delta IEC}$ mice different than control C57B/L 6 group at day 0. Red: Decreased percentage in IKK $\beta^{\Delta IEC}$ mice compared to same group at day 0.

Green: Increased percentage in IKK $\beta^{\Delta IEC}$ mice compared to same group at day 0.

Table S3. Relative percentage of bacteria orders

			C57BL/	6				ΙΚΚβΔΙΕΟ							
	Day 0		Day 2		Day 4		1	Day 0		Day 2		Day 4			
Order	Mean	STD	Mean	STD	Mean	STD		Mean	STD	Mean	STD	Mean	STD		
Bacteroidales	76.16	7.09	81.59	3.69	75.27	7.84		82.31	6.10	78.54	3.44	52.90	1.47		
Clostridiales	19.06	7.46	8.28	5.34	19.17	10.36		10.86	4.44	12.30	0.50	39.40	1.76		
Lactobacillales	3.00	2.05	0.65	0.53	1.07	1.14		2.56	2.75	1.01	1.63	1.08	0.44		
Bacillales	0.04	0.04	0.10	0.09	0.03	0.04		0.13	0.09	1.68	1.33	0.41	0.41		
Erysipelotrichales	0.03	0.05	0.85	1.03	0.37	0.21		0.19	0.14	0.76	1.10	0.10	0.12		
Deferribacterales	0.30	0.25	0.05	0.02	0.30	0.27		0.03	0.02	0.06	0.10	1.02	0.29		
Burkholderiales	0.04	0.02	0.19	0.16	0.06	0.06		0.59	0.56	0.63	0.87	0.32	0.13		
Rhodospirillales	0.23	0.12	6.15	7.70	2.31	3.90		0.01	0.03	0.01	0.02	0.00	0.00		
Mycoplasmatales	0.00	0.00	0.00	0.00	0.00	0.00		0.14	0.12	0.10	0.18	0.12	0.11		
Desulfovibrionales	0.01	0.02	0.00	0.00	0.05	0.08		0.15	0.30	0.00	0.00	0.11	0.16		
Coriobacteriales	0.07	0.04	0.05	0.03	0.02	0.02		0.04	0.02	0.02	0.02	0.04	0.04		
Anaeroplasmatales	0.00	0.00	0.00	0.00	0.00	0.00		0.30	0.32	0.02	0.01	0.06	0.07		
Verrucomicrobiales	0.08	0.10	1.09	1.54	0.15	0.13		0.00	0.00	0.00	0.00	0.00	0.00		
Rickettsiales	0.00	0.00	0.00	0.00	0.00	0.00		0.01	0.01	0.04	0.06	0.24	0.29		
Actinomycetales	0.03	0.01	0.03	0.05	0.02	0.03		0.06	0.05	0.40	0.39	0.00	0.00		
Chroococcales	0.00	0.00	0.00	0.00	0.00	0.00		0.03	0.04	0.18	0.26	0.00	0.00		
Cyanobium (order)	0.00	0.00	0.00	0.00	0.00	0.00		0.42	0.26	1.88	2.48	0.04	0.04		
Caulobacterales	0.00	0.00	0.01	0.01	0.00	0.00		0.12	0.04	0.41	0.55	0.02	0.02		
Kiloniellales	0.00	0.00	0.01	0.02	0.00	0.00		0.01	0.02	0.13	0.20	0.00	0.00		
Rhizobiales	0.00	0.00	0.04	0.03	0.02	0.03		0.00	0.00	0.01	0.01	0.00	0.00		
Campylobacterales	0.00	0.00	0.00	0.00	0.00	0.00		1.30	1.22	0.32	0.30	3.47	0.76		
TM7 (order)	0.32	0.17	0.18	0.30	0.57	0.13		0.06	0.01	0.00	0.00	0.24	0.15		
Bacteroidia (order)	0.23	0.12	0.17	0.09	0.11	0.05		0.02	0.04	0.04	0.05	0.01	0.02		
Spirochaetales	0.00	0.00	0.00	0.00	0.00	0.00		0.03	0.03	0.49	0.54	0.00	0.00		
Flavobacteriales	0.34	0.17	0.55	0.25	0.42	0.31		0.35	0.14	0.65	0.41	0.12	0.11		
Pasteurellales	0.00	0.00	0.00	0.00	0.01	0.01		0.00	0.00	0.00	0.00	0.00	0.00		
Bdellovibrionales	0.01	0.02	0.00	0.00	0.05	0.06		0.00	0.00	0.00	0.00	0.00	0.00		
Pseudomonadales	0.00	0.00	0.00	0.00	0.00	0.00		0.04	0.04	0.00	0.00	0.01	0.01		
Acholeplasmatales	0.00	0.00	0.00	0.00	0.00	0.00		0.01	0.02	0.00	0.00	0.00	0.00		
Enterobacteriales	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.05	0.05	0.05	0.04		
Sphingobacteriales	0.04	0.03	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00	0.00	0.00		
Cytophagales	0.00	0.00	0.01	0.02	0.00	0.00		0.00	0.00	0.00	0.00	0.01	0.02		
Desulfuromonadales	0.00	0.00	0.01	0.01	0.02	0.00		0.00	0.01	0.01	0.01	0.01	0.02		
Mollicutes (order)	0.00	0.00	0.00	0.00	0.00	0.00		0.01	0.02	0.00	0.00	0.00	0.00		
Nostocales	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.01	0.00	0.00	0.18	0.20		
Kopriimonadales	0.00	0.00	0.00	0.00	0.00	0.00		0.02	0.03	0.09	0.08	0.00	0.00		
Methylococcales	0.00	0.00	0.00	0.00	0.00	0.00		0.12	0.13	0.08	0.09	0.00	0.00		
Acidobacteriales	0.00	0.00	0.00	0.00	0.00	0.00		0.06	0.07	0.05	0.09	0.01	0.01		
Thiotrichales	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.01	0.00	0.00	0.00	0.00		
Chlorobiales	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.02	0.03	0.00	0.00		
Anaerolineales	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.01	0.00	0.00	0.00	0.00		
Entomoplasmatales	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.01	0.00	0.00	0.01	0.02		

Blue: IKK $\beta^{\Delta IEC}$ mice different than control C57B/L 6 group at day 0.

Red: Decreased percentage in IKK $\beta^{\Delta IEC}$ mice compared to same group at day 0. Green: Increased percentage in IKK $\beta^{\Delta IEC}$ mice compared to same group at day 0.

Page **Sble Sol**. Relative percentage of bacteria families

			C57BL	/6	_				ΙΚΚβ	AIEC	_	
	Day 0		Day 2		Day 4		Day 0		Day 2		Day 4	
Family	Mean	STD										
Porphyromonadaceae	45.65	7.34	44.05	6.79	39.38	4.92	59.03	8.60	49.04	5.05	17.67	4.64
Broyotallacana	2.41	1.50	0.88	0.83	2.50	1.45	2.82	0.36	0.49	0.11	0.84	2.02
Streptococcaceae	2 99	2.07	0.46	9.08	0.71	0.63	2.42	2 51	0.77	1.30	0.92	0.32
Bacteroidaceae	14.96	3.88	20.39	7.87	16.65	5.79	18.65	2.82	25.08	3.81	27.60	3.95
Clostridiaceae	10.56	4.56	5.03	2.81	12.16	7.19	4.81	2.46	3.90	2.45	25.34	6.23
Bacillaceae	0.01	0.02	0.07	0.07	0.00	0.00	0.09	0.07	1.64	1.35	0.18	0.06
Eubacteriaceae	3.81	1.78	0.75	0.64	2.59	1.36	2.54	0.50	6.61	3.21	5.35	2.48
Erysipelotrichaceae	0.03	0.05	0.85	1.03	0.37	0.21	0.19	0.14	0.76	1.10	0.10	0.12
Clostridiaceae unclassified	0.25	0.14	0.07	0.10	0.05	0.03	0.14	0.11	0.31	0.23	0.20	0.13
Enterococcaceae	0.00	0.00	0.06	0.05	0.01	0.02	0.01	0.02	0.03	0.04	0.00	0.00
Rikenellaceae	4.03	1.42	1.72	0.55	2.75	0.81	2.15	0.44	1.24	0.51	6.68	4.33
Deferribacteraceae	0.30	0.25	0.05	0.02	0.30	0.27	0.03	0.02	0.06	0.10	1.02	0.29
Oscillospiraceae	0.04	0.02	0.19	0.10	0.05	0.05	0.59	0.56	0.03	0.87	0.52	0.15
Ruminococcaceae	0.78	0.72	0.39	0.50	0.98	0.40	0.10	0.13	0.30	0.23	1.07	0.07
Rhodospirillaceae	0.23	0.12	6.13	7.68	2.31	3.89	0.01	0.03	0.01	0.02	0.00	0.00
Mycoplasmataceae	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.12	0.10	0.18	0.12	0.11
Desulfovibrionaceae	0.01	0.02	0.00	0.00	0.05	0.08	0.15	0.30	0.00	0.00	0.11	0.16
Paenibacillaceae	0.01	0.01	0.03	0.05	0.03	0.04	0.01	0.02	0.03	0.03	0.02	0.00
Planococcaceae	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.18	0.32
Marinilabiaceae	0.02	0.02	0.01	0.01	0.00	0.00	0.05	0.03	0.01	0.02	0.03	0.03
Lactobacillaceae	0.02	0.03	0.14	0.14	0.34	0.53	0.25	0.25	0.22	0.35	0.68	0.16
Coriobacteriaceae	0.07	0.04	0.05	0.03	0.02	0.02	0.04	0.02	0.02	0.02	0.04	0.04
Anaeroplasmataceae	0.00	0.00	0.00	0.00	0.00	0.00	0.30	0.32	0.02	0.01	0.06	0.07
Pialattaiaaaaa	0.08	0.10	1.09	1.54	0.15	0.13	0.00	0.00	0.00	0.00	0.00	0.00
Nocardiaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.04	0.00	0.24	0.29
Chroococcaceae unclassified	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.04	0.20	0.19	0.00	0.00
Cyanobium (family)	0.00	0.00	0.00	0.00	0.00	0.00	0.42	0.26	1.88	2.48	0.04	0.04
Caulobacteraceae	0.00	0.00	0.01	0.01	0.00	0.00	0.12	0.04	0.41	0.55	0.02	0.02
Kiloniellaceae	0.00	0.00	0.01	0.02	0.00	0.00	0.01	0.02	0.13	0.20	0.00	0.00
Hyphomicrobiaceae	0.00	0.00	0.03	0.03	0.02	0.03	0.00	0.00	0.00	0.00	0.00	0.00
Helicobacteraceae	0.00	0.00	0.00	0.00	0.00	0.00	1.30	1.22	0.32	0.30	3.47	0.76
TM7 (family)	0.32	0.17	0.18	0.30	0.57	0.13	0.06	0.01	0.00	0.00	0.24	0.15
Peptococcaceae	0.14	0.06	0.05	0.05	0.08	0.05	0.06	0.05	0.26	0.40	0.12	0.08
Bacteroidia (family)	0.23	0.12	0.17	0.09	0.11	0.05	0.02	0.04	0.04	0.05	0.01	0.02
Spirochaetaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.03	0.49	0.54	0.00	0.00
Elavobacteriaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.05	0.00	0.00	0.02	0.04
Pasteurellaceae	0.04	0.17	0.55	0.23	0.42	0.01	0.33	0.14	0.03	0.41	0.12	0.11
Bacteriovoracaceae	0.00	0.02	0.00	0.00	0.01	0.06	0.00	0.00	0.00	0.00	0.00	0.00
Pseudomonadaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.04	0.00	0.00	0.01	0.01
Acholeplasmataceae	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.00
Enterobacteriaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.05	0.05	0.04
Streptomycetaceae	0.03	0.01	0.03	0.05	0.02	0.03	0.00	0.01	0.00	0.00	0.00	0.00
Chitinophagaceae	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Cytophagaceae	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02
Desulfuromonadaceae	0.00	0.00	0.01	0.01	0.02	0.00	0.00	0.01	0.01	0.01	0.00	0.00
Sphingobacteriaceae	0.03	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Acetobacteraceae	0.00	0.00	0.01	0.02	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Mollicutes (family)	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Nostocaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.00
Micromonosporaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.20	0.31	0.00	0.00
Kopriimonadaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.03	0.09	0.08	0.00	0.00
Methylococcaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.13	0.08	0.09	0.00	0.00
Acidobacteriaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.07	0.05	0.09	0.01	0.01
Staphylococcaceae	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Catabacteriaceae	0.01	0.01	0.03	0.06	0.00	0.00	0.01	0.03	0.00	0.00	0.00	0.00
Rhodobiaceae	0.00	0.00	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Micrococcaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.00
Geobacteraceae	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02
Chlorobiaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
Anaerolineaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.03	0.00	0.00
Spiroplasmataceae	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.01	0.02
Bradyrhizobiaceae	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00

Blue: IKK $\beta^{\Delta IEC}$ mice different than control C57B/L 6 group at day 0. Red: Decreased percentage in IKK $\beta^{\Delta IEC}$ mice compared to same group at day 0. Green: Increased percentage in IKK $\beta^{\Delta IEC}$ mice compared to same group at day 0.

Table S5. Relative percentage of bacteria genus

ΙΚΚβ ΔΙΕΟ

Day 4 Mean

0.01 5.35 0.00 0.37 0.20 0.27 0.42 0.00 6.66 1.02 0.32 0.48 0.01

0.56 3.14 0.00 3.80 2.20 1.30

 STD
 4.23

 0.86
 0.84

 0.86
 0.86

 0.86
 0.86

 0.87
 0.85

 1.09
 0.35

 6.21
 0.35

 7
 0.32

 9
 0.405

 9
 0.005

 9
 0.001

 0.13
 0.13

 0.14
 0.13

 0.15
 0.14

 0.16
 0.19

 0.17
 0.01

 0.18
 0.19

 0.19
 0.13

 0.10
 0.06

 0.00
 0.020

 0.00
 0.020

 0.00
 0.020

 0.01
 0.06

 0.00
 0.00

 0.00
 0.00

 0.00
 0.00

 0.00
 0.00

 0.00
 0.00

 0.00
 0.00

 0.00
 0.00

 0.00
 0.00

 0.00
 0.00

 0.00

 $\begin{array}{c} 0.360\\ 0.022\\ 0.002\\ 0.002\\ 0.000\\ 0.$

C57BL/6

Genus	Day 0 Mean	STD	Day 2 Mean	STD	Day 4 Mean	STD		Day 0 Mean	STD	Day 2 Mean	STD
Tannerella	38.30	6.26	34.95	6.05	31.87	5.45	1	49.83	6.84	38.63	2.31
Parabacteroides	0.24	0.11	2.91	1.78	0.24	0.82		4.20	1.62	7.32	3.14
Coprococcus	0.64	0.91	0.49	0.42	1.18	1.27		2.20	1.22	0.00	0.00
Prevotella	11.51	3.01	15.41	9.68	16.49	7.65		2.37	0.43	3.18	2.20
Bacteroides	14.52	3.03	20.01	8.12	16.33	5.89		18.45	2.89	24.66	3.69
Clostridium	10.51	2.19	5.02	2.82	12.14	7.20		4.75	1.22	3.79	2.35
Eubacterium	3.81	2.09	0.75	0.64	2.59	1.36		2.54	0.18	6.61	3.21
Eubacterium (Erysipelotric	0.03	0.06	0.01	0.02	0.00	0.00		0.00	0.00	0.00	0.00
Blautia	0.21	0.26	0.00	0.00	0.08	0.05		0.06	0.13	0.03	0.02
Porphyromonas	0.51	0.23	0.69	0.26	0.50	0.18		0.31	0.26	0.21	0.15
Roseburia	0.57	0.33	0.01	0.01	0.48	0.15		0.06	0.04	0.05	0.04
Alistipes	3.69	1.37	1.50	0.46	2.66	0.82		2.09	0.45	1.19	0.04
Mucispirillum	0.30	0.21	0.05	0.02	0.30	0.27		0.03	0.03	0.06	0.10
Oscillibacter	0.04	0.02	0.19	0.16	0.05	0.05		0.59	0.42	0.63	0.87
Clostridium (Erysipelotrich	0.00	0.00	0.70	1.12	0.02	0.02		0.00	0.01	0.46	0.80
Odoribacter Ruminococcue	0.66	0.25	0.53	0.16	0.53	0.19		1.28	0.86	0.96	0.25
Anaerostipes	0.50	0.62	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Turicibacter	0.01	0.01	0.13	0.23	0.34	0.21		0.15	0.14	0.00	0.00
Rhodospirillum	0.44	0.20	5.99	7.56	2.26	3.81		0.20	0.02	0.42	0.31
Lachnospira	0.03	0.04	0.03	0.04	0.03	0.02		0.02	0.03	0.02	0.04
Caminicella Streptococcus	0.02	0.01	0.00	0.00	0.01	0.02		0.00	0.00	0.01	0.01
Oscillospira	0.28	0.23	0.17	0.12	0.26	0.21		0.16	0.03	0.05	0.03
Hydrogenoanaerobacterium Conrobacillus	0.15	0.18	0.16	0.09	0.12	0.07		0.03	0.05	0.07	0.08
Anaerotruncus	0.00	0.00	0.00	0.00	0.00	0.00		0.05	0.01	0.29	0.01
Bryantella	0.07	0.10	0.03	0.01	0.13	0.05		0.12	0.10	0.23	0.04
Robinsoniella	0.00	0.00	0.00	0.00	0.00	0.00		0.14	0.06	0.10	0.18
Pseudobutyrivibrio	0.00	0.00	0.00	0.00	0.00	0.00		0.01	0.03	0.01	0.03
Bilophila Ethanoligeners	0.01	0.02	0.00	0.00	0.05	0.08		0.15	0.35	0.00	0.00
Brevibacillus	0.00	0.00	0.01	0.02	0.00	0.00		0.00	0.00	0.00	0.00
Filibacter	0.01	0.02	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Sporanaerobacter Oribacterium	0.10	0.13	0.06	0.08	0.02	0.04		0.00	0.00	0.00	0.00
Anaerophaga	0.02	0.03	0.01	0.01	0.00	0.00		0.05	0.04	0.01	0.02
Lactobacillus	0.02	0.04	0.14	0.14	0.34	0.53		0.25	0.23	0.22	0.35
Anaeroplasma	0.02	0.01	0.01	0.01	0.01	0.01		0.02	0.02	0.02	0.02
Bacillus	0.00	0.00	0.00	0.00	0.00	0.00		0.09	0.03	1.63	1.37
Arthromitus Enterorhabdus	0.00	0.00	0.01	0.01	0.00	0.00		0.01	0.02	0.08	0.14
Akkermansia	0.08	0.13	1.09	1.54	0.15	0.13		0.00	0.00	0.00	0.00
Haplosporidium	0.00	0.00	0.00	0.00	0.00	0.00		0.01	0.01	0.04	0.06
Gloeothece	0.00	0.00	0.00	0.00	0.00	0.00		0.04	0.05	0.20	0.19
Cyanobium	0.00	0.00	0.00	0.00	0.00	0.00		0.42	0.22	1.88	2.48
Brevundimonas Kiloniella	0.00	0.00	0.01	0.01	0.00	0.00		0.07	0.04	0.09	0.16
Maritalea	0.00	0.00	0.01	0.02	0.01	0.02		0.00	0.00	0.00	0.00
Helicobacter	0.00	0.00	0.00	0.00	0.00	0.00		1.30	1.36	0.32	0.30
Rhodocista	0.32	0.16	0.18	0.30	0.07	0.13		0.00	0.01	0.00	0.00
Sporobacter	0.02	0.03	0.01	0.01	0.00	0.00		0.00	0.00	0.00	0.00
Paludibacter Acetivibrio	0.01	0.01	0.00	0.00	0.00	0.00		0.02	0.01	0.01	0.03
Desulfitobacterium	0.10	0.04	0.05	0.05	0.06	0.04		0.06	0.05	0.24	0.37
Desulfotomaculum	0.05	0.04	0.00	0.00	0.02	0.03		0.00	0.00	0.02	0.04
Bacteroidales	0.01	0.01	0.13	0.14	0.05	0.08		0.00	0.00	0.00	0.00
Catonella	0.01	0.01	0.01	0.01	0.00	0.00		0.04	0.09	0.00	0.00
Treponema Gemella	0.00	0.00	0.00	0.00	0.00	0.00		0.03	0.04	0.49	0.54
Dysgonomonas	0.00	0.00	0.01	0.02	0.01	0.01		0.00	0.00	0.00	0.00
Gelidibacter	0.00	0.00	0.02	0.02	0.01	0.01		0.00	0.01	0.00	0.00
Butvricicoccus	0.00	0.00	0.00	0.00	0.01	0.01		0.00	0.00	0.00	0.00
Butyricimonas	0.00	0.00	0.00	0.00	0.00	0.00		0.02	0.01	0.00	0.00
Bacteriovorax	0.01	0.03	0.00	0.00	0.05	0.06		0.00	0.00	0.00	0.00
Acholeplasma	0.00	0.00	0.00	0.00	0.00	0.00		0.01	0.00	0.00	0.00
Escherichia	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.05	0.05
Streptomyces	0.00	0.00	0.02	0.02	0.02	0.02		0.01	0.01	0.01	0.02
Zhangella	0.00	0.00	0.02	0.02	0.01	0.01		0.00	0.00	0.00	0.00
Streptococcus (Erysipelotri Slackia	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Niastella	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Flexibacter	0.00	0.00	0.01	0.02	0.00	0.00		0.00	0.00	0.00	0.00
Desulfuromonas Pedobacter	0.00	0.00	0.01	0.01	0.02	0.00		0.00	0.01	0.01	0.01
Stella	0.00	0.00	0.00	0.00	0.01	0.01		0.00	0.00	0.00	0.00
Dorea	0.00	0.00	0.00	0.00	0.00	0.00		0.03	0.08	0.11	0.09
Rikenella	0.00	0.00	0.00	0.00	0.01	0.01		0.00	0.00	0.00	0.00
Flavobacterium	0.34	0.20	0.53	0.24	0.41	0.31		0.29	0.12	0.65	0.42
Salegentibacter Bacilloplasma	0.00	0.00	0.00	0.00	0.00	0.00		0.05	0.05	0.01	0.01
Acetanaerobacterium	0.00	0.00	0.00	0.00	0.00	0.00		0.01	0.02	0.00	0.00
Anacrofilum	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.12	0.07
Johnsonella	0.01	0.02	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Proteus	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Anabaena Actinoplanes	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.01	0.00	0.00
Caulobacter	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.01	0.20	0.31
Kopriimonas	0.00	0.00	0.00	0.00	0.00	0.00		0.02	0.03	0.09	0.08
Alkaliphilus	0.00	0.00	0.00	0.00	0.00	0.00		0.12	0.12	0.08	0.09
Paraprevotella	0.00	0.00	0.00	0.00	0.00	0.00		0.05	0.07	0.00	0.00
Acidobacterium Morvella	0.00	0.00	0.00	0.00	0.00	0.00		0.06	0.07	0.05	0.09
Halolactibacillus	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.01	0.00	0.00
Lysinibacillus	0.00	0.00	0.05	0.08	0.00	0.00		0.00	0.00	0.00	0.00
Staphylococcus Catabacter	0.01	0.03	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Roseomonas	0.00	0.00	0.03	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Roseospirillum	0.00	0.00	0.01	0.01	0.00	0.00		0.00	0.00	0.00	0.00
Aquisalibacillus	0.00	0.00	0.00	0.00	0.00	0.00		0.01	0.02	0.00	0.00
Rummeliibacillus	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Geobacter Lachnobacterium	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Francisella	0.00	0.00	0.00	0.00	0.02	0.00		0.00	0.00	0.00	0.00
Chlorobium	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.02	0.03
Spiroplasma	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.01	0.00	0.00
Nitrobacter	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.01	0.01

Blue: IKK $\beta^{\Delta IEC}$ mice different than control C57B/L 6 group at day 0. Red: Decreased percentage in IKK $\beta^{\Delta IEC}$

mice compared to same group at day 0. Green: Increased percentage in IKK $\beta^{\Delta IEC}$ mice compared to same group at day 0.

Page **Sole** Relative percentage of bacteria species

	-	C57BL	/6	-		-	D	κβ ΔΙ	EC						(57BL/6			_		IK	Κβ ΔΗ	C		
Species	Day 0 Mean STD	Day 2 Mean	STD	Day 4 Mean S	тр	Day 0 Mean	STD M	ay 2 Iean - S	TD D	Day 4 Mean S'	TD	Sn	recies	Day 0 Mean - S		ay 2 Iean S		Day 4 Mean ST		Day 0 Mean - S	TD M	ay 2 lean ST	D M	ay 4 Jean S	TD
Tannerella sp	38.25 5.13	34.92	6.09	31.84	5.43	49.79	7.76	38.59	2.35	13.27	4.22	Sp	orobacter sp	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Barnesiella intestinihominis	5.59 1.79	4.72	1.63	5.98	0.87	3.12	1.25	1.20	0.20	0.67	0.73	Pro	evotella dentalis	0.15	0.07	0.09	0.15	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00
Conrococcus sp	0.64 0.82	0.05	0.03	1.18	1.27	2.39	1.64	0.00	0.00	3.80	1.90	Bla	autia producta evotella dentasini	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.02	0.03	0.01
Candidatus Prevotella conceptionensis	10.01 3.49	13.06	9.09	14.58	7.27	0.18	0.14	0.06	0.04	0.03	0.06	Cle	ostridium proteolyticum	0.00	0.00	0.01	0.02	0.02	0.02	0.02	0.03	0.01	0.01	0.00	0.00
Parabacteroides sp	0.15 0.11	0.11	0.17	0.11	0.05	0.66	0.09	0.33	0.24	0.16	0.10	Tar	nnerella forsythia	0.05	0.04	0.03	0.06	0.03	0.04	0.04	0.03	0.04	0.04	0.01	0.01
Lactococcus lactis	2.90 2.03	0.00	0.40	0.59	0.54	2.18	2.56	0.77	1.30	0.31	0.35	Cle	ostridium populeti	0.03	0.03	0.00	0.00	0.04	0.03	0.02	0.02	0.00	0.00	0.00	0.00
Bacteroides acidifaciens	4.09 2.30	9.64	6.17	7.20	5.86	4.02	1.69	15.60	3.79	3.38	1.93	Cle	ostridium xylanolyticum	0.02	0.02	0.00	0.00	0.00	0.00	0.03	0.03	0.00	0.00	0.03	0.03
Bacteroides sp Prevotella sp	9.98 1.87 0.70 0.24	9.97	2.14	8.88	1.38	12.35	3.20	4.40	1.03	22.57	3.64	Ac	etivibrio sp	0.02	0.02	0.04	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Barnesiella viscericola	0.34 0.23	0.24	0.17	0.26	0.04	1.10	0.13	0.70	0.36	0.36	0.13	De	sulfotomaculum sp	0.10	0.05	0.05	0.05	0.06	0.04	0.06	0.05	0.24	0.37	0.12	0.08
Clostridium sp	3.03 1.74	2.21	1.11	2.42	0.72	2.34	0.87	2.26	1.31	14.37	5.31	Ro	seburia faecis	0.00	0.00	0.00	0.00	0.02	0.02	0.02	0.02	0.00	0.00	0.12	0.09
Europacialus naiophilus Eubacterium sp	2.35 1.52	0.02	0.03	0.00	0.00	0.00	0.00	6.55	3.24	2.04	0.01	Ph	aeospirillum sp	0.01	0.01	0.13	0.14	0.05	0.08	0.00	0.00	0.00	0.00	0.00	0.00
Eubacterium tortuosum	0.01 0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	Са	itonella sp	0.23	0.00	0.00	0.09	0.00	0.00	0.02	0.04	0.04	0.00	0.01	0.02
Butyrivibrio fibrisolvens	0.21 0.25	0.00	0.00	0.07	0.04	0.06	0.11	0.01	0.03	0.14	0.08	Tre	eponema sp	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.03	0.49	0.54	0.00	0.00
Porphyromonas sp	0.01 0.01	0.63	0.00	0.44	0.14	0.08	0.24	0.13	0.15	0.03	0.05	Ge	emella morbillorum	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.03	0.00	0.00	0.02	0.04
Roseburia intestinalis	0.06 0.05	0.00	0.00	0.01	0.01	0.00	0.01	0.00	0.00	0.03	0.04	Str	reptococcus constellatus	0.04	0.00	0.00	0.00	0.00	0.00	0.12	0.04	0.00	0.00	0.07	0.12
Clostridium nexile Enterococcus gallinarum	4.63 3.28	0.80	1.01	7.23	5.14	0.27	0.15	0.11	0.08	1.63	0.52	Ali	istipes finegoldii	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.04	0.00	0.00	0.01	0.02
Alistipes putredinis	2.53 1.17	1.14	0.54	2.17	0.79	1.03	0.18	0.91	0.61	1.11	0.15	La	ctobacillus sp	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.02
Mucispirillum schaedleri	0.30 0.25	0.05	0.02	0.30	0.27	0.03	0.02	0.06	0.10	1.02	0.29	La	ctobacillus murinus	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.00	0.00
Bacteroides sartorii	0.00 0.00	0.00	0.00	0.00	0.00	0.00	0.91	2.93	0.86	0.50	0.36	Pre	evotella albensis	0.03	0.02	0.02	0.02	0.04	0.04	0.03	0.03	0.00	0.00	0.00	0.00
Clostridium symbiosum	0.04 0.05	0.02	0.02	0.05	0.04	0.06	0.09	0.01	0.01	0.03	0.03	Ge	elidibacter sp	0.00	0.00	0.02	0.02	0.01	0.01	0.00	0.01	0.00	0.00	0.00	0.00
Clostridium indolis Restancidas chinchilles	1.18 1.22	0.44	0.63	0.86	0.50	0.18	0.15	0.14	0.24	0.64	0.23	Ha	iemophilus sp	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Alistipes onderdonkii	0.93 0.45	0.00	0.00	0.00	0.00	0.80	0.38	0.18	0.17	5.37	4.50	An	naerophaga thermohalophila	0.00	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Roseburia sp	0.51 0.39	0.01	0.01	0.44	0.14	0.04	0.03	0.05	0.04	0.26	0.14	Bu	ostridium ramosum	0.00	0.00	0.02	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Alistipes sp Clostridium hathewayi	0.10 0.07	0.26	0.12	0.11	0.08	0.00	0.00	0.01	0.02	0.02	0.02	Bu	ityricimonas synergistica	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.03	0.00	0.00	0.00	0.00
Eubacterium ramulus	0.24 0.46	0.00	0.00	0.16	0.15	0.64	0.33	0.01	0.03	2.77	2.06	Ba	acteriovorax sp	0.01	0.02	0.00	0.00	0.05	0.06	0.00	0.00	0.00	0.00	0.00	0.00
Parabacteroides merdae	0.00 0.00	0.00	0.00	0.00	0.00	0.26	0.11	0.32	0.15	0.16	0.17	Ac	choleplasma granularum	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.04	0.00	0.00	0.01	0.01
Eubacterium xylanophilum	0.04 0.02 0.24 0.19	0.19	0.16	0.05	0.05	0.59	0.56	0.03	0.87	0.32	0.13	Es	cherichia coli	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.04
Oscillibacter sp	0.74 0.54	0.38	0.39	0.63	0.24	0.10	0.11	0.07	0.11	0.28	0.03	Fa	ecalibacterium sp	0.00	0.00	0.02	0.02	0.02	0.02	0.01	0.02	0.01	0.02	0.00	0.00
Clostridium cocleatum	0.00 0.00	0.69	1.12	0.02	0.02	0.00	0.01	0.46	0.80	0.01	0.01	Pro	evotella loescheii	0.07	0.05	0.05	0.03	0.01	0.01	0.00	0.00	0.01	0.03	0.00	0.00
Odoribacter laneus	0.65 0.33	0.50	0.15	0.51	0.19	0.01	0.03	0.00	0.00	0.01	0.01	Zh	angella mobilis	0.00	0.00	0.02	0.02	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Ruminococcus sp	0.15 0.04	0.33	0.37	0.22	0.15	0.05	0.03	0.09	0.06	0.22	0.22	Str	ackia piriformis	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02
Clostridium leptum	0.01 0.01 0.03	0.01	0.01	0.09	0.01	0.00	0.01	0.56	0.34	0.01	0.01	Ni	astella sp	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Anaerostipes caccae	0.50 0.59	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	Fle	exibacter sp	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02
Clostridium bolteae	0.07 0.06	0.02	0.03	0.10	0.15	0.06	0.13	0.29	0.51	1.15	1.87	De	evotena buccae	0.00	0.01	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Clostridium lactatilermentans	0.38 0.53	0.00	0.00	0.03	0.02	0.00	0.00	0.03	0.05	0.39	0.55	Pe	dobacter sp	0.03	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Oscillibacter valericigenes	0.36 0.19	0.21	0.12	0.35	0.26	0.06	0.05	0.30	0.12	0.20	0.05	Ste	ella sp	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Furicibacter sp Pseudoflavonifractor canillosus	0.01 0.01	0.13	0.23	0.34	0.21	0.15	0.13	0.00	0.00	0.08	0.13	Do	orea sp	0.00	0.00	0.00	0.00	0.14	0.00	0.01	0.07	0.00	0.00	0.00	0.00
Rhodospirillum sp	0.23 0.11	5.99	7.56	2.26	3.81	0.01	0.03	0.01	0.02	0.00	0.00	Hy	/drogenophaga sp	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Eubacterium desmolans	0.07 0.11	0.00	0.00	0.08	0.12	0.03	0.06	0.02	0.02	0.03	0.05	Ril	kenella microfusus	0.34	0.14	0.22	0.09	0.09	0.05	0.06	0.07	0.05	0.02	0.01	0.01
Lachnospira pectinoschiza	0.03 0.04	0.00	0.00	0.03	0.04	0.02	0.03	0.03	0.09	0.22	0.20	Pro	evotella nigrescens	0.23	0.22	0.17	0.25	0.32	0.39	0.00	0.00	0.00	0.00	0.00	0.00
Clostridium orbiscindens	0.19 0.16	0.14	0.10	0.19	0.10	0.13	0.14	0.13	0.16	0.40	0.31	Po	rphyromonas catoniae	0.07	0.06	0.06	0.03	0.06	0.05	0.01	0.01	0.02	0.01	0.00	0.00
Caminicella sp Strentococcus inise	0.02 0.02	0.00	0.00	0.01	0.02	0.00	0.00	0.01	0.01	0.00	0.00	Sal	legentibacter sp	0.24	0.15	0.19	0.19	0.10	0.07	0.00	0.00	0.00	0.00	0.00	0.00
Clostridium phytofermentans	0.17 0.07	0.00	0.00	0.02	0.02	0.20	0.11	0.04	0.06	0.09	0.03	Par	rabacteroides johnsonii	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
Eubacterium fissicatena	0.01 0.01	0.01	0.01	0.02	0.03	0.00	0.01	0.02	0.04	0.01	0.01	Ru	iminococcus gauvreauii	0.01	0.02	0.00	0.00	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Alistipes indistinctus	0.10 0.11	0.04	0.48	0.08	0.19	0.01	0.01	0.42	0.04	0.36	0.32	Ba	cilloplasma sp	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00
Oscillospira sp	0.26 0.22	0.17	0.12	0.26	0.21	0.16	0.13	0.05	0.03	0.34	0.10	Ac	etanaerobacterium elongatum	0.02	0.02	0.01	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Hydrogenoanaerobacterium saccharovorans Streptococcus sp	0.15 0.14 0.00 0.01	0.16	0.09	0.11	0.06	0.03	0.04	0.04	0.05	0.07	0.08	An Eu	bacterium biforme	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.07	0.00	0.00
Coprobacillus sp	0.00 0.00	0.00	0.00	0.00	0.00	0.03	0.02	0.28	0.29	0.00	0.00	Ап	naerovorax sp	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Clostridium glycyrrhizinilyticum Anaerotruncus colihominis	0.00 0.00	0.02	0.02	0.01	0.01	0.00	0.00	0.00	0.00	0.18	0.19	Joi	hnsonella sp probacillus cateniformis	0.05	0.11	0.04	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.31	0.54
Eubacterium cylindroides	0.02 0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	La	ctobacillus intestinalis	0.01	0.01	0.03	0.05	0.06	0.09	0.00	0.00	0.00	0.00	0.00	0.00
Roseburia cecicola	0.00 0.00	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	Br	evibacillus parabrevis	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
Oscillospira guilliermondii	0.02 0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	Ba	icteroides oleiciplenus	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00
Bryantella formatexigens	0.07 0.09	0.03	0.01	0.13	0.05	0.12	0.09	0.23	0.04	0.02	0.02	Ru	iminococcus albus	0.02	0.04	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02
Eubacterium coprostanoligenes	0.00 0.00	0.00	0.00	0.00	0.00	0.14	0.12	0.10	0.18	0.12	0.11	En	abaena sp	0.02	0.02	0.00	0.00	0.00	0.00	0.02	0.02	0.00	0.00	0.00	0.00
Hydrogenoanaerobacterium sp	0.01 0.01	0.01	0.01	0.01	0.01	0.00	0.00	0.03	0.03	0.01	0.02	Ac	tinoplanes sp	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.20	0.31	0.00	0.00
Clostridium aminophilum Clostridium methylnentosum	0.07 0.05	0.06	0.11	0.34	0.35	0.02	0.02	0.07	0.08	0.40	0.35	Ca	ulobacter sp	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.05	0.32	0.40	0.00	0.00
Clostridium asparagiforme	0.03 0.02	0.12	0.12	0.01	0.02	0.02	0.03	0.00	0.00	0.03	0.06	Me	ethylobacter sp	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.03	0.09	0.08	0.00	0.00
Clostridium polysaccharolyticum	0.02 0.03	0.00	0.00	0.04	0.04	0.00	0.00	0.04	0.06	1.33	1.69	All	kaliphilus crotonatoxidans	0.03	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02	0.00	0.00
Ruminococcus gnavus Robinsoniella peoriensis	0.02 0.02 0.02 0.03 0.04	0.08	0.07	0.08	0.03	0.01	0.02	0.02	0.04	0.12	0.09	Par	raprevotella xylaniphila	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.07	0.00	0.00	0.00	0.00
Pseudobutyrivibrio ruminis	0.00 0.00	0.00	0.00	0.00	0.00	0.01	0.03	0.01	0.03	0.85	1.47	Ac	cidobacterium sp	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02	0.05	0.00	0.01	0.02
Eubacterium plexicaudatum Butyrivibrio en	0.04 0.07	0.01	0.01	0.26	0.20	0.19	0.38	0.00	0.00	0.15	0.13	Eu	bacterium hallii	0.00	0.00	0.03	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Bilophila sp	0.00 0.00	0.00	0.00	0.05	0.08	0.15	0.30	0.00	0.00	0.11	0.16	Cle	oryella sp ostridium xylanovorans	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
Clostridium herbivorans	0.12 0.11	0.10	0.10	0.10	0.14	0.26	0.24	0.06	0.10	0.30	0.36	An	naerotruncus sp	0.00	0.00	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Clostridium viride	0.00 0.00	0.01	0.20	0.00	0.13	0.00	0.00	0.01	0.00	0.00	0.03	Cle	ostridium subterminale	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.04
Brevibacillus sp	0.01 0.01	0.03	0.05	0.03	0.04	0.01	0.01	0.03	0.03	0.02	0.00	Fla	avobacterium columnare	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.03	0.00	0.00	0.00	0.00
Eubacterium eligens Filibacter limicola	0.00 0.00	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	De	sulfotomaculum ruminis	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Alistipes shahii	0.02 0.02	0.05	0.02	0.04	0.03	0.06	0.04	0.01	0.01	0.08	0.05	La	sinibacillus fusiformis	0.01	0.01	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01
Sporanaerobacter sp	0.10 0.11	0.06	0.08	0.02	0.04	0.00	0.00	0.00	0.00	0.00	0.00	Sta	aphylococcus saprophyticus	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Oribacterium sp	0.00 0.04 0.30 0.23	0.02	0.02	0.57	0.56	0.05	0.03	0.00	0.00	0.59	0.02	Ba	teteroides uniformis	0.00	0.00	0.02	0.04	0.00	0.00	0.00	0.00	0.01	0.02	0.00	0.00
Blautia hydrogenotrophica	0.12 0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.05	Ca	itonella morbi	0.01	0.01	0.03	0.06	0.00	0.00	0.01	0.03	0.00	0.00	0.00	0.00
Blautia coccoides Anaerophaga sp	0.02 0.02	0.01	0.02	0.00	0.00	0.06	0.07	0.15	0.15	0.07	0.10	All	kaliphilus peptidofermentans	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.02	0.00	0.00
Lactobacillus johnsonii	0.00 0.00	0.00	0.00	0.00	0.00	0.13	0.13	0.12	0.20	0.29	0.15	Ro	seomonas ludipueritiae	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Clostridium cellulovorans	0.02 0.02	0.11	0.11	0.02	0.03	0.00	0.00	0.00	0.00	0.00	0.00	Bu	ityrivibrio hungatei	0.00	0.00	0.00	0.00	0.02	0.03	0.00	0.00	0.00	0.00	0.01	0.02
Anaeroplasma sp	0.02 0.02 0.02	0.00	0.01	0.01	0.00	0.02	0.32	0.02	0.02	0.04	0.04	Cle	ostridium bovipellis	0.01	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Bacillus sp	0.00 0.00	0.00	0.00	0.00	0.00	0.08	0.06	1.63	1.37	0.18	0.06	En Ro	nerococcus casseliflavus ityricimonas virosa	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.00
Arthromitus sp actobacillus reuteri	0.00 0.00	0.01	0.01	0.00	0.00	0.01	0.02	0.08	0.14	0.26	0.29	Ar	throbacter sp	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.00
Enterorhabdus mucosicola	0.04 0.02	0.04	0.04	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	Es	cherichia sp	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.05	0.00	0.00
Eubacterium siraeum	0.00 0.00	0.00	0.00	0.01	0.01	0.04	0.05	0.01	0.02	0.07	0.07	Pre	evotella oulorum	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00
Haplosporidium sp	0.00 0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.04	0.06	0.24	0.29	Aq	uisalibacillus sp	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Rhodococcus sp	0.00 0.00	0.00	0.00	0.00	0.00	0.04	0.04	0.20	0.19	0.00	0.00	Pro R.	evotella oralis immeliibacillus stabekisii	0.03	0.06	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
Clostridium hveragerdense	0.00 0.00	0.00	0.00	0.00	0.00	0.03	0.04	0.18	0.26	0.00	0.00	An	aerostipes sp	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.04
Cyanobium sp	0.00 0.00	0.00	0.00	0.00	0.00	0.42	0.26	1.88	2.48	0.04	0.04	An	naerofilum pentosovorans	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00
Brevundimonas sp Prevotella oris	0.00 0.00	0.01	0.01	0.00	0.00	0.07	0.05	0.09	0.16	0.02	0.02	Ba	cillus megaterium	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02
Kiloniella laminariae	0.00 0.00	0.01	0.02	0.00	0.00	0.03	0.02	0.13	0.20	0.00	0.00	La	chnobacterium sp	0.00	0.00	0.00	0.00	0.02	0.03	0.00	0.00	0.00	0.00	0.00	0.00
Maritalea myrionectae Helicobacter apodemus	0.00 0.00	0.01	0.02	0.01	0.02	0.00	0.00	0.00	0.00	0.00	0.00	Fra Cla	ostridium saccharolyticum	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
Helicobacter ganmani	0.00 0.00	0.00	0.00	0.00	0.00	0.32	1.24	0.25	0.32	2.29	0.70	Or	ibacterium sinus	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02
Bacteroides cf forsythus	0.00 0.00	0.02	0.02	0.01	0.01	0.04	0.06	0.01	0.02	0.01	0.01	Cle	ostridium jejuense ostridium algidixylanolyticium	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02
Rhodocista sp	0.02 0.17	0.18	0.02	0.00	0.00	0.00	0.01	0.00	0.00	0.24	0.00	Ch	llorobium sp	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.03	0.00	0.00
Helicobacter hepaticus	0.00 0.00	0.00	0.00	0.00	0.00	0.12	0.13	0.03	0.04	0.08	0.14	Be	illinea sp iroplasma sp	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
Paludibacter propionicigenes	0.01 0.02	0.01	0.00	0.00	0.00	0.00	0.04	0.00	0.03	0.05	0.08	Nit	trobacter sp	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00
Eubacterium oxidoreducens	0.03 0.05	0.00	0.00	0.01	0.02	0.00	0.00	0.00	0.00	0.01	0.01														

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