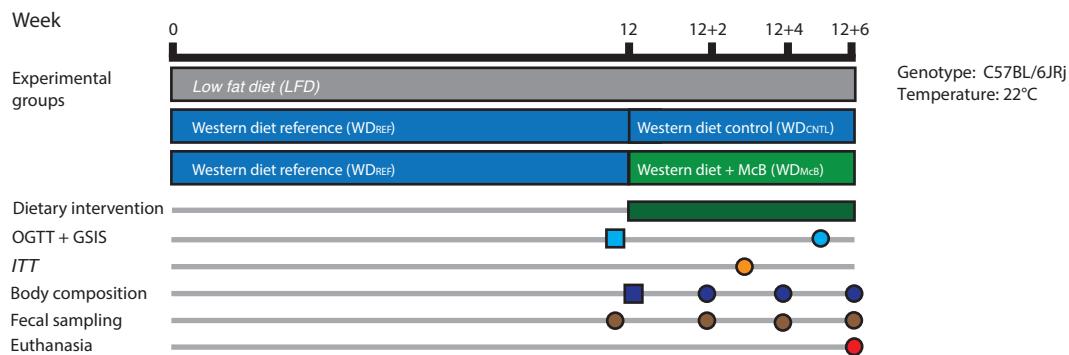
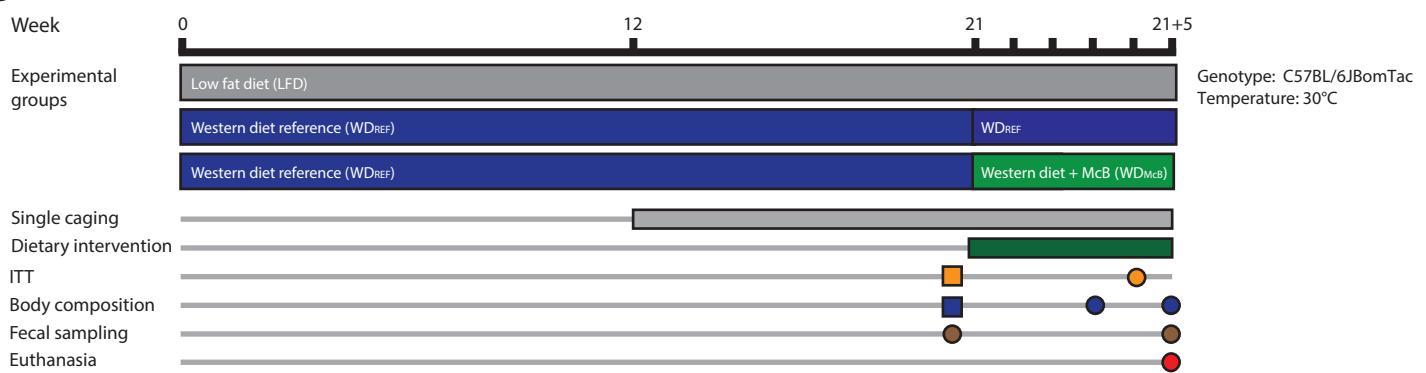


## Supplementary Figure 1

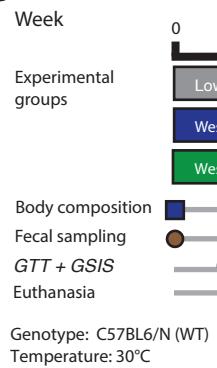
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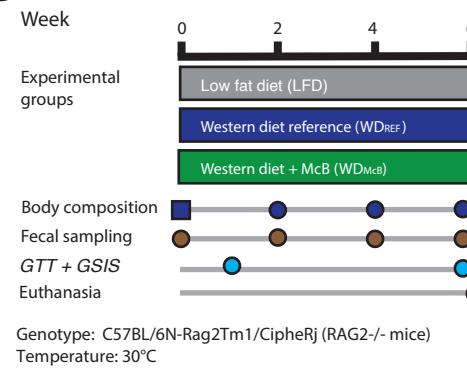
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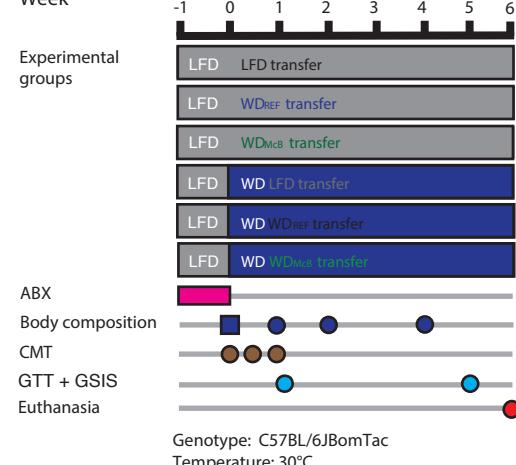
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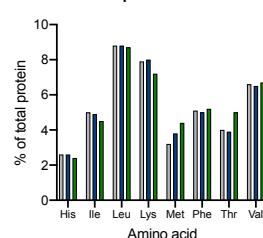
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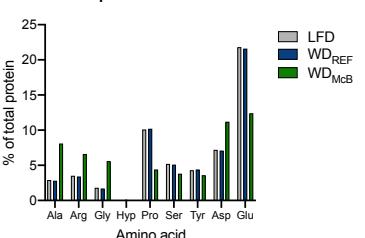
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F Indispensable AAs



Dispensable AAs

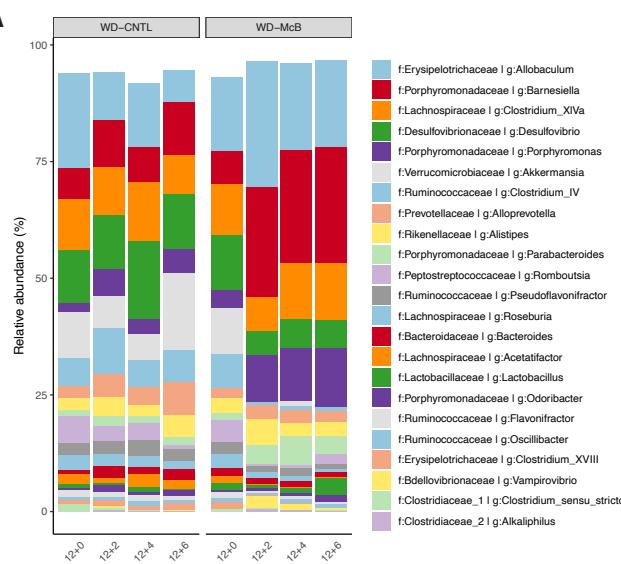


CMT from mice fed respective diets for 21+5 weeks (Panel B)

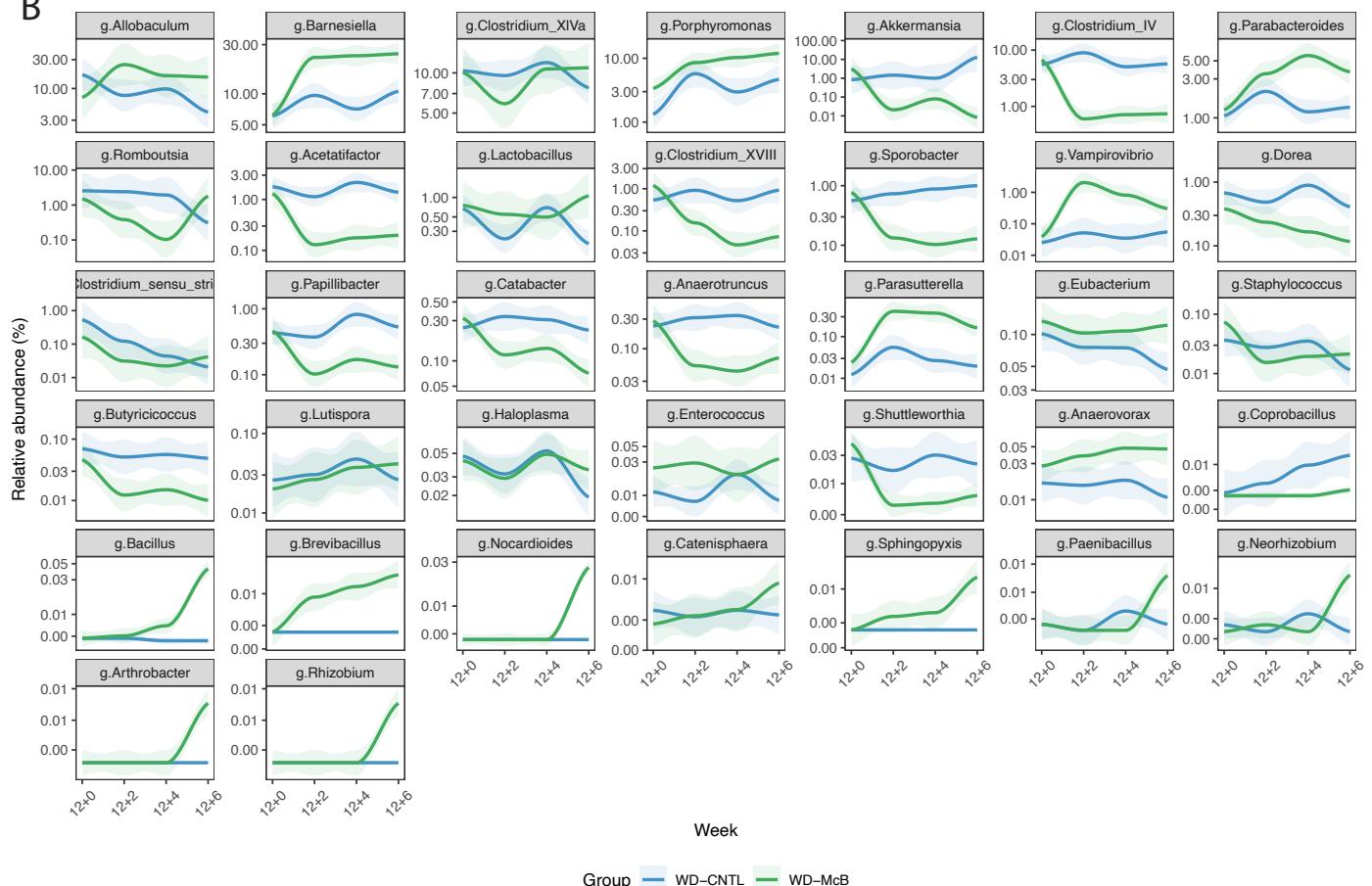
2 **Supplementary Figure 1: Experimental layouts and diet amino acid composition.** **A)** Study  
3 outline of two independent experiments with initial Western diet ( $WD_{REF}$ ) feeding for 12 weeks at  
4 22°C and oral glucose tolerance test (OGTT), glucose-stimulated insulin secretion (GSIS), and  
5 body composition by MR scan assessed after 11 weeks to stratify groups followed by dietary  
6 intervention for 6 weeks of feeding either WD including McB lysate ( $WD_{McB}$ ) or a matched WD  
7 control diet ( $WD_{CNTL}$ ). During the experimental period body composition, OGTT, GSIS, and fresh  
8 fecal sampling were carried out at the indicated intervals. An insulin tolerance test (ITT) was  
9 carried out in the first of two experiments at the indicated timepoint. The second experiment  
10 included a reference group fed low fat diet (LFD) fed mice. Groups or procedures featured uniquely  
11 in one experiment are italicized. **B)** Study outline with initial Western diet ( $WD_{REF}$ ) feeding for 21  
12 weeks at 30°C. Insulin tolerance test (ITT) and body composition by MR scan were assessed after  
13 20 weeks to stratify groups followed by dietary intervention for 5 weeks of feeding with either  
14  $WD_{REF}$  or WD including McB lysate ( $WD_{McB}$ ). A reference group fed low fat diet (LFD) was  
15 included throughout the experiment (week 0 to week 21+5). Body composition, ITT, and fresh fecal  
16 sampling were carried out at the indicated intervals. Mice were co-housed the first 12 weeks and  
17 then separated to individual cages. **C-D)** Study outline of ‘weight-matched’ WT mice and  $RAG2^{-/-}$   
18 mice fed experimental diets for 7 and 6 weeks, respectively, at 30°C. The two studies were run in  
19 parallel and followed the same scheme with the exception of OGTT + GSIS (italic letters), which  
20 was performed in  $RAG2^{-/-}$  only. Body composition, OGTT + GSIS, and fresh fecal sampling were  
21 carried out at the indicated intervals. **E)** Study outline of cecal microbiota transfer (CMT) studies at  
22 30°C. Mice were acclimatized on LFD and remained on this during 7 days of ABX treatment. Then,  
23 50% of the mice were shifted to  $WD_{REF}$ , while the other half remained on LFD for the following 5  
24 weeks of intervention. Body composition, CMT and OGTT + GSIS were carried out at the  
25 indicated time intervals. **F)** Relative distribution of indispensable amino acids (left panel) and  
26 dispensable amino acids (right panel) in the experimental diets.  
27  
28

## Supplementary Figure 2

A



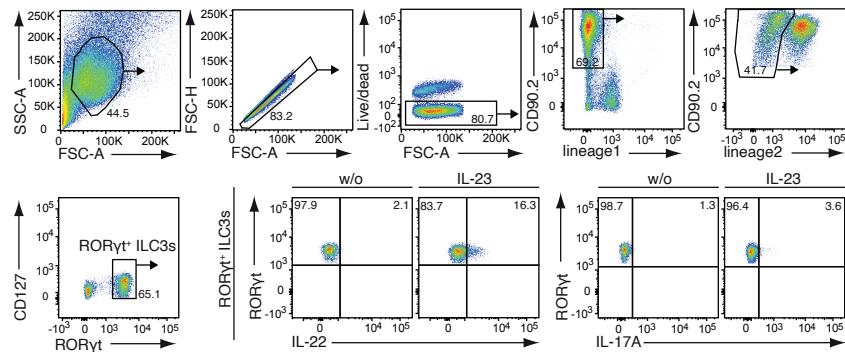
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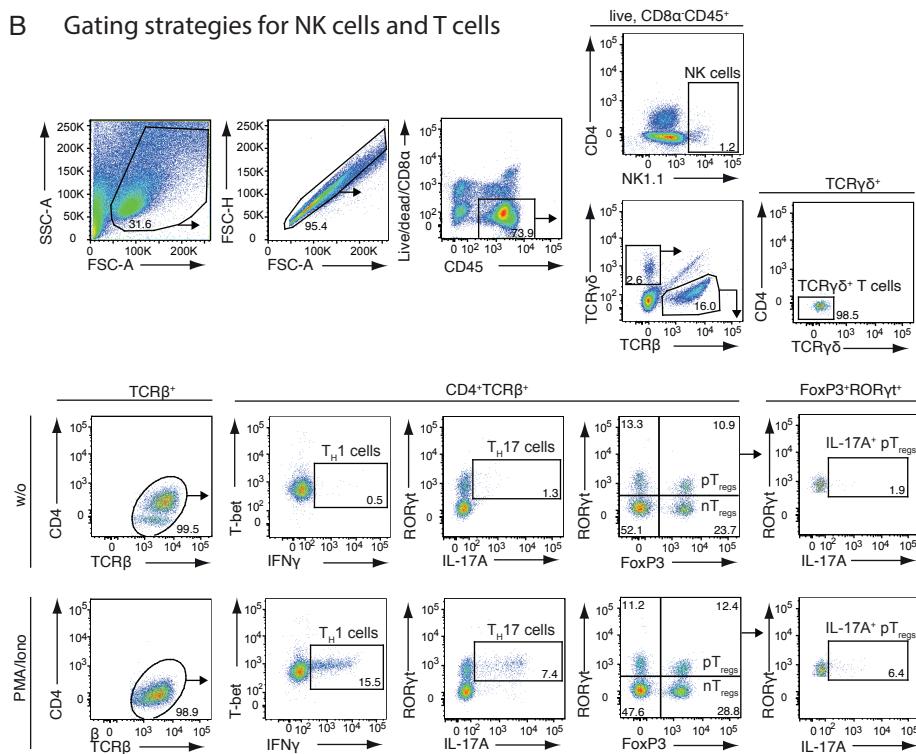
29 **Supplementary Figure 2: Gut microbiota abundance post dietary intervention. A)**  
30 Taxasummary of most abundant bacterial genera showing mean relative abundance in percentage of  
31 the indicated family and genera in each group at indicated time point. **B)** Deseq analysis of fecal  
32 bacterial genera abundances significantly regulated by McB intervention compared to the WD<sub>CNTL</sub>  
33 (p.adj. < 0.05). Relative abundance in % in each group and variation are shown for each regulated  
34 genus at the sampled time points. Fold-change and adjusted p values of individual are indicated in  
35 Supplementary Table 3.  
36  
37

## Supplementary Figure 3

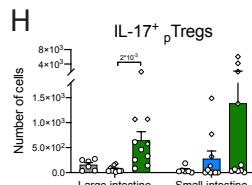
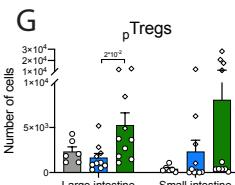
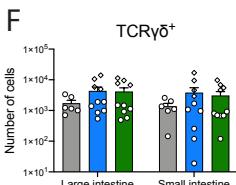
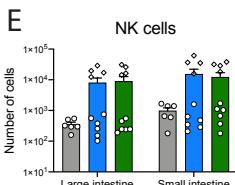
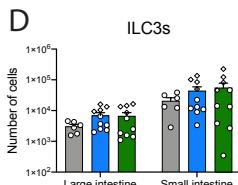
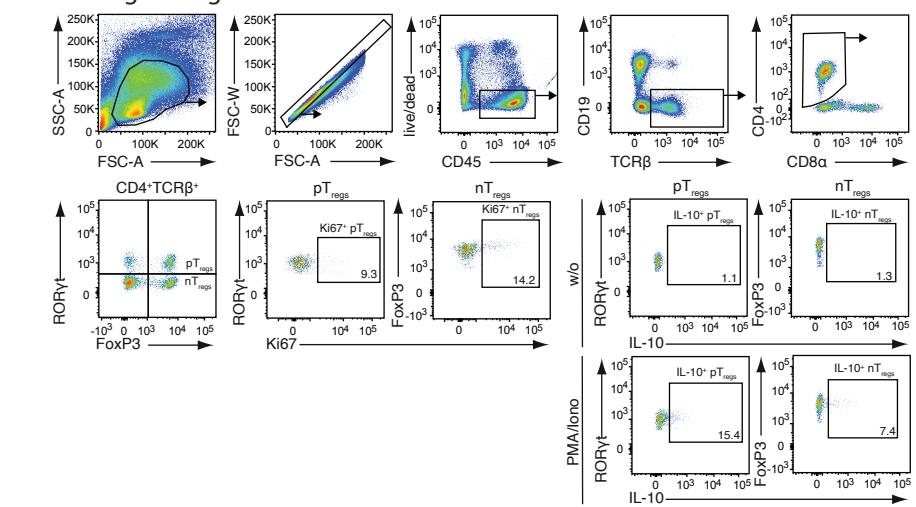
### A Gating strategies for ILC3s



### B Gating strategies for NK cells and T cells



### C Gating strategies for IL-10 and Ki67 in T cells

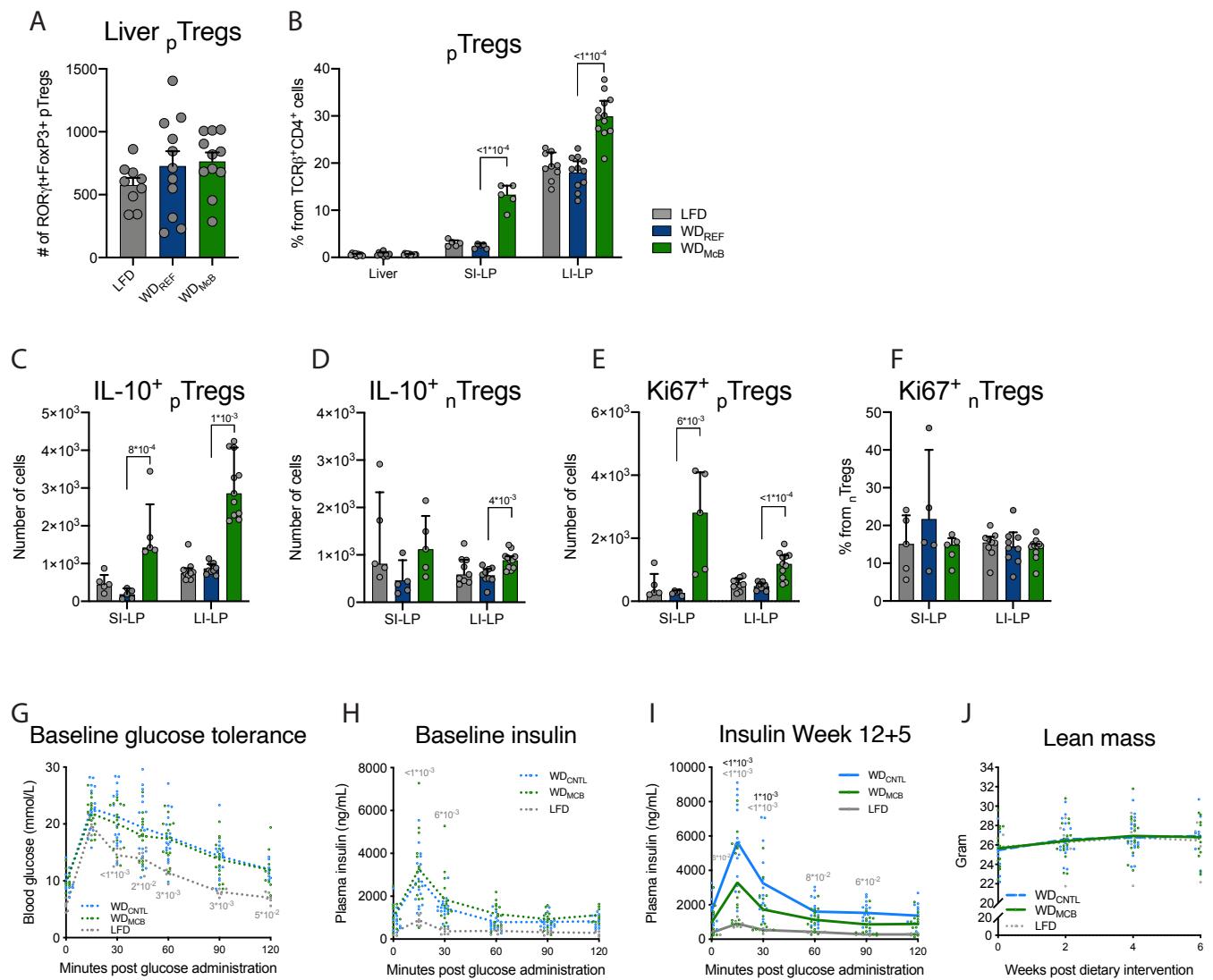


38 **Supplementary Figure 3: Gating strategies and immune cell distribution in small and large**  
39 **intestine.** **A)** Gating strategy for group 3 innate lymphoid cells (ILC3). Corresponds to  
40 Supplementary Figure 3D. Representative flow cytometry plots of *ex vivo* stimulated small intestine  
41 (SI) lamina propria (LP) cells. ILC3s were gated as single, live cells, lineage1<sup>+</sup>lineage2<sup>-</sup>  
42 CD90.2<sup>+</sup>CD127int<sup>+/−</sup>ROR $\gamma$ t<sup>+</sup> cells. Representative data of ROR $\gamma$ t<sup>+</sup> ILC3s after stimulation with or  
43 without (w/o) IL-23 are shown. Lineage1: CD11c, CD19, CD45R/B220, Ly-6G/Ly-6C (Gr-1), Ter119,  
44 NK1.1; Lineage2: CD3 $\epsilon$ , CD8 $\alpha$ , TCR $\beta$ , TCR $\gamma\delta$ . **B)** Gating strategy for NK cells and T cells.  
45 Corresponds to Supplementary Figure 3E-H; 4A-B; 5J. Representative flow cytometry plots of *ex*  
46 *vivo* stimulated colon lamina propria cells. NK cells were gated as single, live cells, CD8 $\alpha$ <sup>−</sup>  
47 CD45<sup>+</sup>NK1.1<sup>+</sup>; TCR $\gamma\delta$ <sup>+</sup> T cells were gated as single, live cells, CD8 $\alpha$ <sup>−</sup>CD45<sup>+</sup>TCR $\gamma\delta$ <sup>+</sup>CD4<sup>−</sup>; CD4<sup>+</sup> T<sub>H</sub>1  
48 cells were gated as single, live cells, CD8 $\alpha$ <sup>−</sup>CD45<sup>+</sup>TCR $\beta$ <sup>+</sup>CD4<sup>+</sup>T-bet<sup>+</sup>IFN $\gamma$ <sup>+</sup>; CD4<sup>+</sup> T<sub>H</sub>17 cells were  
49 gated as single, live cells, CD8 $\alpha$ <sup>−</sup>CD45<sup>+</sup>TCR $\beta$ <sup>+</sup>CD4<sup>+</sup>ROR $\gamma$ t<sup>+</sup>IL-17A<sup>+</sup>. Natural regulatory T cells (<sub>n</sub>T<sub>regs</sub>)  
50 were gated as single, live cells, CD8 $\alpha$ <sup>−</sup>CD45<sup>+</sup>TCR $\beta$ <sup>+</sup>CD4<sup>+</sup>FoxP3<sup>+</sup>ROR $\gamma$ t<sup>+</sup> and peripheral-induced  
51 regulatory T cells (<sub>p</sub>T<sub>regs</sub>) were gated as single, live cells, CD8 $\alpha$ <sup>−</sup>CD45<sup>+</sup>TCR $\beta$ <sup>+</sup>CD4<sup>+</sup>FoxP3<sup>+</sup>ROR $\gamma$ t<sup>+</sup>.  
52 Representative data of TCR $\beta$ <sup>+</sup>CD4<sup>+</sup> T cells after stimulation with or without (w/o) PMA and Ionomycin  
53 (PMA/Iono) are shown. **C)** Gating strategy for IL-10<sup>+</sup> and Ki67<sup>+</sup> <sub>n</sub>- and <sub>p</sub>T<sub>regs</sub>. Corresponds to  
54 Figure 2O-R and Supplementary Figure 4C-F. Representative flow cytometry plots of *ex vivo*  
55 stimulated colon lamina propria cells. Natural and peripheral-induced regulatory T cells (<sub>n</sub>T<sub>regs</sub> and <sub>p</sub>T<sub>regs</sub>,  
56 respectively) were gated as in (B), stained for Ki67 and IL-10; the latter with or without (w/o) PMA and  
57 Ionomycin (PMA/Iono). **D)** ILC3 cell number in large intestine (LI)-LP and SI-LP. **E)** NK1.1<sup>+</sup> NK  
58 cell number in LI-LP and SI-LP. **F)** TCR $\gamma\delta$ <sup>+</sup> T cell number in LI-LP and SI-LP. **G)** Amount of  
59 <sub>p</sub>T<sub>regs</sub> in LI-LP and SI-LP. **H)** Amount of IL17<sup>+</sup><sub>p</sub>T<sub>regs</sub> in LI-LP and SI-LP. **D-H)** Bars represent mean  
60  $\pm$  SEM and dots individual data points. All p-values < 1\*10<sup>-1</sup> between WD<sub>CNTL</sub> and indicated group  
61 are depicted. Dot shapes indicate individuals data points in Exp1 (squares) and Exp2 (circles). Grey  
62 bars: LFD-fed, n = 6; Blue bars: WD<sub>CNTL</sub>-fed, n= 10; and Green bars: WD<sub>McB</sub>-fed, n= 10. Statistical  
63 significant differences to WD<sub>CNTL</sub> by one-way ANOVA, adjusted for multiple comparisons by  
64 Dunnett's post hoc.

65

66

## Supplementary Figure 4

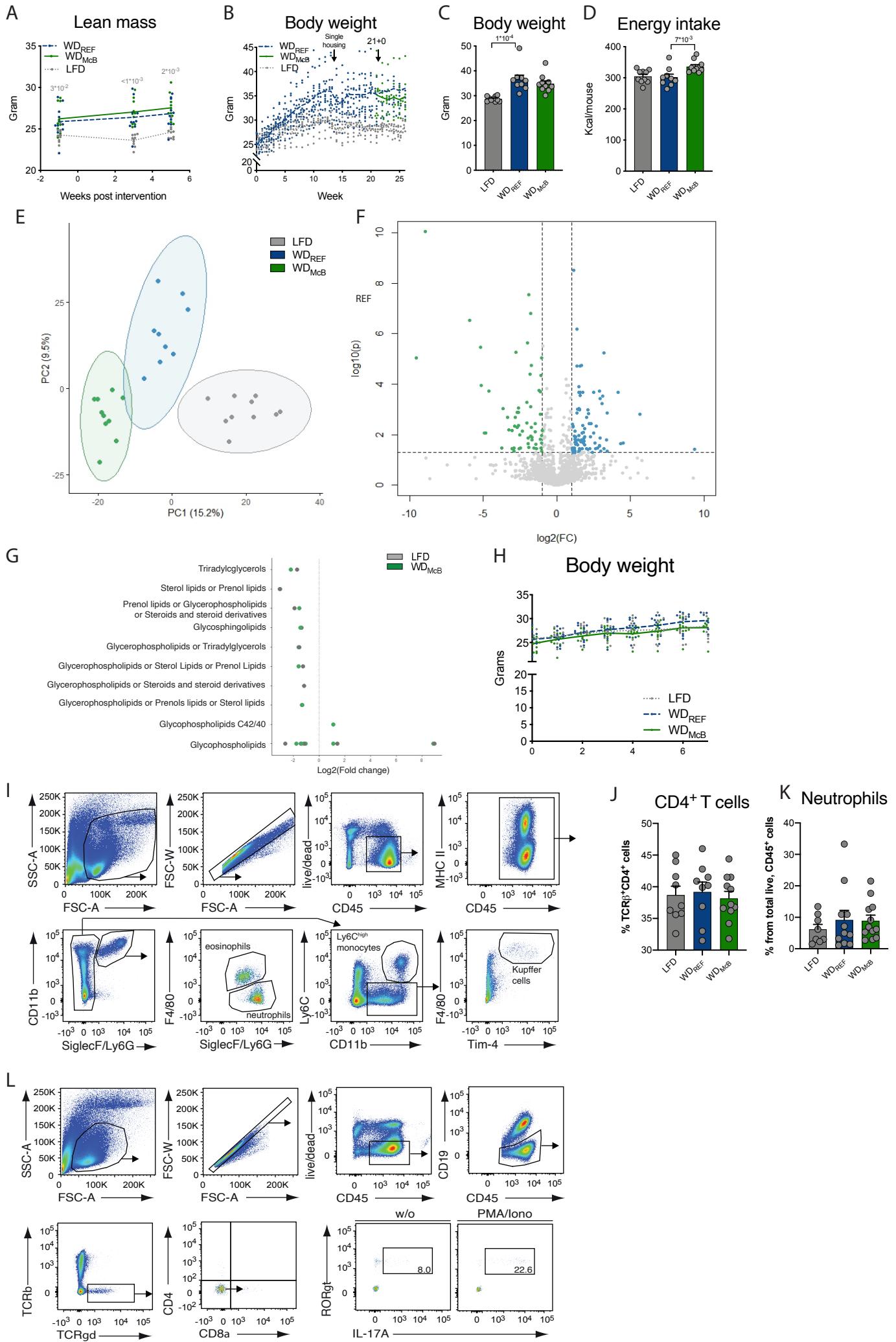


67 **Supplementary Figure 4: Immunometabolic response to experimental diet feeding. A-B)**  
68 Number of hepatic (A)  $pT_{reg}$ s and their relative distribution between liver, SI-LP and LI-LP (B).  
69 Statistical significant differences to WD<sub>REF</sub> by one-way ANOVA, adjusted for multiple comparisons  
70 by Dunnett's post hoc. In A, n = 9 (LFD) or 11 (WD<sub>REF</sub> and WD<sub>McB</sub>). In B, SI-LP n = 5 per group.  
71 Liver n = 9 (LFD and WD<sub>REF</sub>) or 11 (WD<sub>McB</sub>). LI-LP n = 9 (LFD), and 11 (WD<sub>REF</sub>) or 12 (WD<sub>McB</sub>).  
72 **C-F)** Amount of indicated cells in SI- and LI-LP from 'weight-matched' mice housed at  
73 thermoneutrality. Statistical significant differences to WD<sub>REF</sub> by one-way ANOVA, adjusted for  
74 multiple comparisons by Dunnett's post hoc, except for LI-LP in C and F where statistical  
75 differences were evaluated by Kruskal-Wallis test, adjusted with Dunn's post hoc. SI-LP n = 5 per  
76 group. LI-LP n = 9 (LFD and WD<sub>REF</sub>) or 11 (WD<sub>McB</sub>). **G-H)** Blood glucose and plasma insulin  
77 values, respectively, during oral glucose tolerance test (OGTT) before dietary intervention (week  
78 11). LFD n = 6, WD<sub>CNTL</sub> and WD<sub>McB</sub> n = 15 except in H at 60 min where WD<sub>CNTL</sub> and WD<sub>McB</sub> n =  
79 14 as well as 90 and 120 min where WD<sub>McB</sub> n = 12 due to insufficient sample material. **I)** Plasma  
80 insulin values from OGTT week 12+5. LFD n = 6, WD<sub>CNTL</sub> and WD<sub>McB</sub> n = 15. **J)** Lean mass in  
81 grams during the dietary intervention period as mean  $\pm$  SEM of two independent experiments. LFD  
82 n = 6, WD<sub>CNTL</sub> and WD<sub>McB</sub> n = 15. **A-F)** Bars represent mean  $\pm$  SEM and dots indicates individual  
83 data points. p-values <  $1 \times 10^{-1}$  between WD<sub>REF</sub> and indicated group are depicted. **G-J)** Lines  
84 represent mean and dots indicate individual data points from two independent experiments. p-values  
85 <  $1 \times 10^{-1}$  between WD<sub>CNTL</sub> and LFD (grey p-value), and WD<sub>CNTL</sub> and WD<sub>McB</sub> (black p-value) are  
86 depicted. Statistical significance compared to WD<sub>CNTL</sub> by two-way ANOVA-RM, adjusted for  
87 multiple comparisons by Dunnett post hoc except for H where mixed effect analysis and Dunnett's  
88 post hoc test were used.

89

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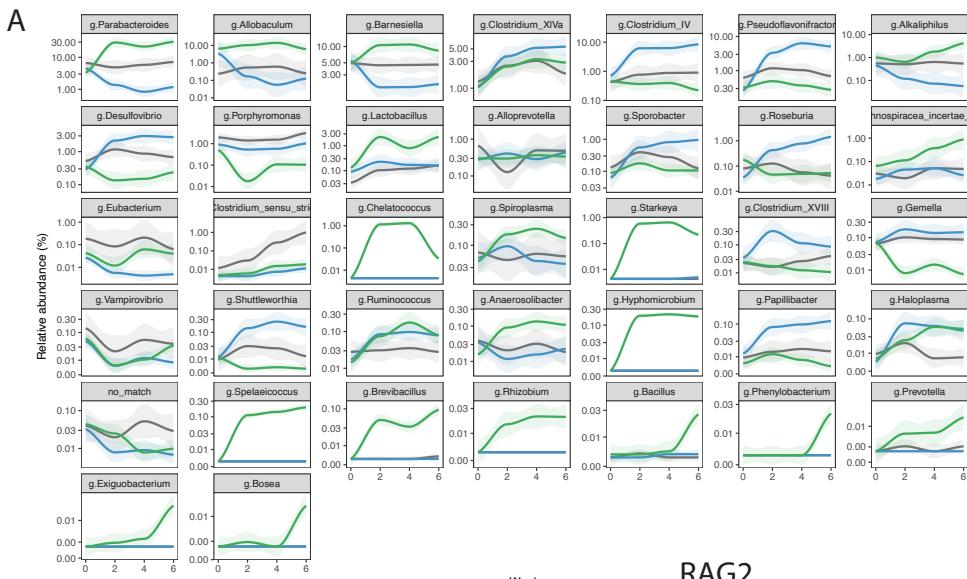
## Supplementary Figure 5



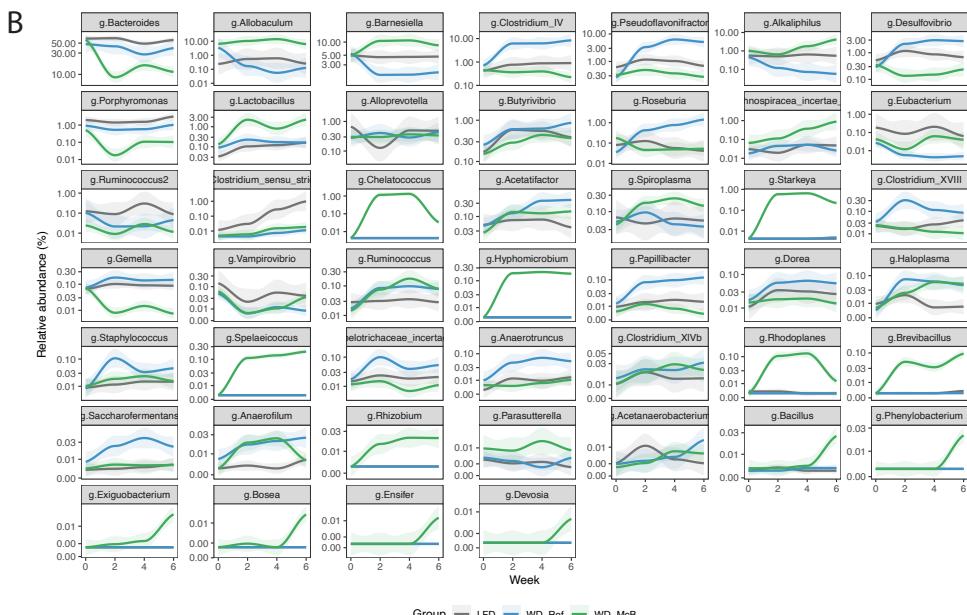
91 **Supplementary Figure 5: Altered hepatic lipidome profile in response to WD<sub>McB</sub> feeding.** **A)**  
92 Lean mass in grams during the dietary intervention period. Lines represent mean and dots indicate  
93 individual data points. Statistical significance compared to WD<sub>REF</sub> by two-way ANOVA-RM,  
94 adjusted for multiple comparisons by Dunnett post hoc. n = 10 per group. **B)** Body weight  
95 development; mice were fed either LFD or WD<sub>REF</sub> for the first 21 weeks, as indicated. WD<sub>REF</sub>-fed  
96 mice were subsequently stratified into experimental groups, fed indicated diets for additional 5  
97 weeks. n = 10 per group. **C)** Final body weight week 21+5. Bars represents mean ± SEM and dots  
98 indicate individual data points. Statistical significant differences to WD<sub>REF</sub> by one-way ANOVA,  
99 adjusted for multiple comparisons by Dunnett's post hoc. n = 10 (LFD and WD<sub>McB</sub>) or 9 (WD<sub>REF</sub>).  
100 **D)** Cumulative energy intake in kcal per mouse during dietary intervention (week 21+0 to 21+5).  
101 Bars represents mean ± SEM and dots indicate individual data points. Statistical significant  
102 differences to WD<sub>REF</sub> by one-way ANOVA, adjusted for multiple comparisons by Dunnett's post  
103 hoc. n = 10 (LFD and WD<sub>McB</sub>) or 9 (WD<sub>REF</sub>). **E)** Principle coordinate analysis (PCoA) of hepatic  
104 lipid species identified in positive ionization mode. **F)** As in (E) but depicted in a volcano plot with  
105 significantly regulated lipid species (FDR < 0.05) presented on a log2 scale in either green  
106 (WD<sub>McB</sub> > WD<sub>REF</sub>) or blue (WD<sub>McB</sub> < WD<sub>REF</sub>). **G)** Lipid pathways identified by fold-change  
107 analysis separating LFD (grey) and WD<sub>McB</sub> (green) groups from WD<sub>REF</sub> in positive ionization  
108 mode. **H)** Body weight development in ‘weight-matched’ WT mice fed the respective diets for 7  
109 weeks. Lines represent mean and dots indicate individual datapoints. n = 9 (LFD), 11 (WD<sub>REF</sub>) or  
110 12 (WD<sub>McB</sub>). **I)** Gating strategy of hepatic monocytes in mice from (H). Corresponds to Figure 5G,  
111 I-J; Supplementary Figure 5K. **J-K)** Amount of CD4<sup>+</sup> T cells and neutrophils in livers of ‘weight-  
112 matched’ WT mice fed the respective diets for 7 weeks. Bars represents mean ± SEM and dots  
113 indicate individual data points. Statistical significant differences to WD<sub>REF</sub> by one-way ANOVA,  
114 adjusted for multiple comparisons by Dunnett's post hoc. n = 9 (LFD and WD<sub>REF</sub>) or 11 (WD<sub>McB</sub>).  
115 **L)** Gating strategy of hepatic IL-17<sup>+</sup>  $\gamma\delta$ -T cells in mice from (H), gated as single live cells,  
116 CD45<sup>+</sup>CD19<sup>-</sup>TCR $\beta$ <sup>-</sup>CD4<sup>-</sup> CD8 $\alpha$ <sup>-</sup>TCR $\gamma\delta$ <sup>+</sup>ROR $\gamma\tau$ <sup>+</sup>IL-17A<sup>+</sup>. Corresponds to Figure 5K. Representative  
117 data of cells after stimulation with or without (w/o) PMA and Ionomycin (PMA/Iono) are shown.  
118  
119

## Supplementary Figure 6

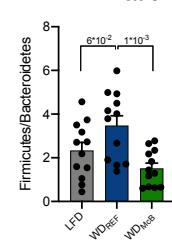
WT



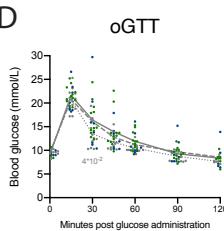
Week



F/B ratio



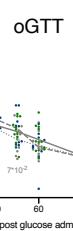
**D** Week 1



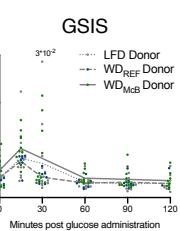
GSIS



**E** Week 5



GSIS



120 **Supplementary Figure 6: Immunometabolism and gut microbiota interactions. A-B)** ) Deseq  
121 analysis of fecal bacterial genera abundances significantly regulated by McB intervention compared  
122 to the WD<sub>REF</sub> ( $p.\text{adj.} < 0.05$ ) in either WT (A) and RAG2<sup>-/-</sup> (B) mice. Relative abundance in % in  
123 each group and variation are shown for each regulated genus at the sampled time points. **C)**  
124 Firmicutes/Bacteroidetes ratio of fecal bacteria sampled after 6 weeks of experimental treatment of  
125 RAG2<sup>-/-</sup> mice. Bars represents mean  $\pm$  SEM and dots indicate individual data points. Statistical  
126 significant differences to WD<sub>REF</sub> by Kruskal-Wallis, adjusted for multiple comparisons by Dunn's  
127 post hoc. n = 12 per group. **D-G)** Blood glucose and plasma insulin values, respectively, during oral  
128 glucose tolerance test (OGTT) either 1 or 5 weeks after first cecal microbiota transfer in LFD-fed  
129 recipient mice. Lines represent mean and dots indicate individual datapoints. Statistical significant  
130 differences to WD<sub>REF</sub> by mixed effect analysis and Dunnett's post hoc test. p-values  $< 1*10^{-1}$   
131 between WD<sub>REF</sub> and LFD (grey p-value), and WD<sub>REF</sub> and WD<sub>McB</sub> (black p-value) are depicted. **D-**  
132 **E)** n = 11 (LFD), 8 (WD<sub>REF</sub>) and 12 (WD<sub>McB</sub>), except for (E) time 0, where LFD = 8, WD<sub>REF</sub> = 6,  
133 and WD<sub>McB</sub> = 11, as well as time 60, 90 and 120 where WD<sub>McB</sub> = 11. **F)** n = 12 (LFD and WD<sub>McB</sub>)  
134 and 9 (WD<sub>REF</sub>), except for time 120 where WD<sub>McB</sub> = 11. **G)** n = 12 (LFD and WD<sub>McB</sub>) and 7  
135 (WD<sub>REF</sub>), except for time 0-60 WD<sub>McB</sub> = 11 and time 90-120 where LFD = 11 due to insufficient  
136 sample material.

137

138

139 **Supplementary Table 1: Experimental diet compositions**

		WD <sub>No Protein</sub>	WD <sub>REF</sub>	WD <sub>CNTL</sub>	WD <sub>McB</sub>	LFD
Corn starch	%	5,0000	5,0000	5,0000	5,0000	52,0000
Maltodextrin	%	10,0000	10,0000	10,0000	10,0000	-----
Sucrose	%	31,6300	31,6300	31,6300	31,6300	9,7270
Cellulose powder	%	5,0000	5,0000	5,0000	5,0000	5,0000
L-Cystine	%	0,3000	0,3000	0,3000	0,3000	0,3000
DL-Methionine	%	0,1600	0,1600	0,1600	0,1600	0,1600
Vitamin premix	%	1,0000	1,0000	1,0000	1,0000	1,0000
Mineral premix	%	6,0000	6,0000	6,0000	6,0000	3,5000
Choline chloride	%	0,2500	0,2500	0,2500	0,2500	0,2500
Vitamin K3	%	-----	-----	-----	-----	0,0005
Vitamin B12	%	-----	-----	-----	-----	0,0025
Butylated hydroxytoluene	%	0,0100	0,0100	0,0100	0,0100	0,0100
Cholesterol	%	0,1500	0,1500	0,1500	0,1500	-----
Na CMC	%	-----	-----	-----	-----	1,0000
Soybean oil	%	21,0000	21,0000	21,0000	21,0000	7,0000
Casein	%	-----	19,5000	16,5000	-----	20,0000
McB whole-cell lysate	%	-----	-----	-----	19,5000	-----
Macadamia oil	%	-----	-----	3,0000	-----	-----
Total	%	80,5	100,0	100,0	100,0	100,0

140

141 Supplementary Table 1: Composition of experimental diets used in the studies as % weight.  
 142 Experimental diets were based on lot-matched WDNo Protein, and subsequently added casein,  
 143 macadamia oil and McB whole-cell lysate as indicated.

144

145 **Supplementary Table 2: Primer sequences and annealing temperature for qPCR**

Target gene	Forward primer sequence	Reverse primer sequence	Annealing temp. (°C)
<i>Scdl</i>	ACA CCT GCC TCT TCG GGA TT	TGA TGC CCA GAG CGC TG	58
<i>Acaca</i>	TGC TGC CCC ATC CCC GGG	TCG AAC TCT CAC TGA CAC G	58
<i>Acox1</i>	GGG TCA TGG AAC	GAA TGA ACT CTT	58

	TCA TCT TCG A	GGG TCT TGG G	
<i>Pparg1</i>	GTG TGA CAG ACA AGA TTT GAA AG	GCT TGA TGT CAA AGG AAT GCG	60
<i>Pparg2</i>	ACA GCA AAT CTC TGT TTT ATG	TGC TGG AGA AAT CAA CTG TGG	60
<i>Ppara</i>	AGA GAG GAC AGA TGG GGC TC	CGT TTG TGG CTG GTC AAG TT	60

146

147 **Supplementary Table 3: Deseq analysis from 12+6 week experiments**

Related to Figure 1				
Genus	Fold change	Log2FC	p value	Adj p value
g:Chelatococcus	1573,07	10,62	4,43E-25	2,88E-23
g:Barnesiella	27,46	4,78	3,07E-20	6,65E-19
g:Parabacteroides	23,89	4,58	2,22E-20	6,65E-19
g:Vampirovibrio	1401,99	10,45	3,08E-18	5,01E-17
g:Anaerofilum	408,29	8,67	6,55E-18	8,52E-17
g:Parasutterella	109,80	6,78	8,74E-16	9,47E-15
g:Microvirga	268,76	8,07	1,35E-14	1,25E-13
g:Brevibacillus	88,56	6,47	9,74E-09	7,36E-08
g:Pseudoxanthomonas	84,23	6,40	1,02E-08	7,36E-08
g:Clostridium_IV	0,24	-2,06	5,16E-08	3,35E-07
g:Isoptericola	51,65	5,69	5,17E-07	3,05E-06
g:Eubacterium	7,88	2,98	3,56E-06	1,93E-05
g:Akkermansia	632,32	9,30	7,69E-06	3,84E-05
g:Clostridium_XIVa	2,64	1,40	2,23E-05	0,0001
g:Staphylococcus	7,28	2,86	0,0002	0,001
g:Papillibacter	0,25	-2,01	0,0002	0,001
g:Acetatifactor	0,44	-1,19	0,001	0,002
g:Lachnospiraceae_incertae_sedis	0,16	-2,61	0,001	0,002

<b>g:Odoribacter</b>	<b>8,16</b>	<b>3,03</b>	<b>0,001</b>	<b>0,002</b>
<b>g:Bacteroides</b>	<b>2,81</b>	<b>1,49</b>	<b>0,002</b>	<b>0,01</b>
<b>g:Alistipes</b>	<b>2,83</b>	<b>1,50</b>	<b>0,003</b>	<b>0,01</b>
<b>g:Porphyromonas</b>	<b>4,77</b>	<b>2,25</b>	<b>0,004</b>	<b>0,01</b>
<b>g:Haloplasma</b>	<b>5,41</b>	<b>2,44</b>	<b>0,01</b>	<b>0,02</b>
<b>g:Desulfovibrio</b>	<b>0,44</b>	<b>-1,17</b>	<b>0,01</b>	<b>0,03</b>
<b>g:Blautia</b>	<b>0,24</b>	<b>-2,05</b>	<b>0,01</b>	<b>0,03</b>
<b>g:Escherichia/Shigella</b>	<b>0,14</b>	<b>-2,88</b>	<b>0,01</b>	<b>0,04</b>
<b>g:Murimonas</b>	<b>0,34</b>	<b>-1,57</b>	<b>0,02</b>	<b>0,04</b>
<b>g:Anaerovorax</b>	<b>3,76</b>	<b>1,91</b>	<b>0,02</b>	<b>0,04</b>
<b>g:Shuttleworthia</b>	<b>0,27</b>	<b>-1,87</b>	<b>0,02</b>	<b>0,05</b>
<b>g:Alkaliphilus</b>	<b>0,15</b>	<b>-2,77</b>	<b>0,03</b>	<b>0,06</b>
<b>g:Dorea</b>	<b>0,41</b>	<b>-1,28</b>	<b>0,03</b>	<b>0,07</b>
<b>g:Allobaculum</b>	<b>2,17</b>	<b>1,12</b>	<b>0,04</b>	<b>0,07</b>
<b>g:Christensenella</b>	<b>8,11</b>	<b>3,02</b>	<b>0,04</b>	<b>0,07</b>
<b>g:Streptococcus</b>	<b>0,34</b>	<b>-1,57</b>	<b>0,03</b>	<b>0,07</b>
<b>g:Clostridium XVIII</b>	<b>0,39</b>	<b>-1,36</b>	<b>0,04</b>	<b>0,07</b>
<b>g:Clostridium III</b>	<b>2,16</b>	<b>1,11</b>	<b>0,04</b>	<b>0,07</b>
<b>g:Ruminococcus</b>	<b>0,42</b>	<b>-1,24</b>	<b>0,04</b>	<b>0,07</b>
<b>g:Pseudoflavonifractor</b>	<b>0,55</b>	<b>-0,86</b>	<b>0,05</b>	<b>0,08</b>
<b>g:Saccharofermentans</b>	<b>2,46</b>	<b>1,30</b>	<b>0,05</b>	<b>0,09</b>
<b>g:Lutispora</b>	<b>4,23</b>	<b>2,08</b>	<b>0,06</b>	<b>0,10</b>
<b>g:Butyrivibrio</b>	<b>1,75</b>	<b>0,81</b>	<b>0,08</b>	<b>0,12</b>
<b>g:Aestuariispira</b>	<b>3,27</b>	<b>1,71</b>	<b>0,09</b>	<b>0,15</b>
<b>g:Hydrogenoanaerobacterium</b>	<b>3,16</b>	<b>1,66</b>	<b>0,11</b>	<b>0,16</b>
<b>g:Anaerotruncus</b>	<b>0,55</b>	<b>-0,87</b>	<b>0,12</b>	<b>0,18</b>
<b>g:Enterorhabdus</b>	<b>0,46</b>	<b>-1,13</b>	<b>0,13</b>	<b>0,19</b>
<b>g:Flavonifractor</b>	<b>0,59</b>	<b>-0,76</b>	<b>0,14</b>	<b>0,19</b>
<b>g:Roseburia</b>	<b>0,54</b>	<b>-0,88</b>	<b>0,14</b>	<b>0,20</b>
<b>g:Sporobacter</b>	<b>1,95</b>	<b>0,96</b>	<b>0,15</b>	<b>0,21</b>
<b>g:Coprococcus</b>	<b>0,32</b>	<b>-1,62</b>	<b>0,17</b>	<b>0,22</b>
<b>g:Romboutsia</b>	<b>0,26</b>	<b>-1,95</b>	<b>0,26</b>	<b>0,34</b>
<b>g:Intestinimonas</b>	<b>0,59</b>	<b>-0,77</b>	<b>0,29</b>	<b>0,36</b>
<b>g:Butyricicoccus</b>	<b>0,34</b>	<b>-1,55</b>	<b>0,30</b>	<b>0,38</b>
<b>g:Marvinbryantia</b>	<b>1,69</b>	<b>0,75</b>	<b>0,35</b>	<b>0,44</b>
<b>g:Clostridium XIVb</b>	<b>0,78</b>	<b>-0,35</b>	<b>0,38</b>	<b>0,46</b>
<b>g:Clostridium sensu stricto</b>	<b>0,51</b>	<b>-0,97</b>	<b>0,50</b>	<b>0,59</b>
<b>g:Gracilibacter</b>	<b>1,44</b>	<b>0,53</b>	<b>0,52</b>	<b>0,60</b>
<b>g:Catabacter</b>	<b>1,22</b>	<b>0,29</b>	<b>0,56</b>	<b>0,64</b>
<b>g:Anaerosporobacter</b>	<b>0,69</b>	<b>-0,53</b>	<b>0,60</b>	<b>0,67</b>

g:Bilophila	0,79	-0,33	0,67	0,73
g:Enterococcus	1,46	0,54	0,67	0,73
g:Lactobacillus	1,17	0,23	0,73	0,78
g:Alloprevotella	1,17	0,23	0,75	0,79
g:Olsenella	1,13	0,17	0,84	0,86
g:Senegalimassilia	0,86	-0,21	0,85	0,86
g:Oscillibacter	1,01	0,01	0,99	0,99

**Related to Supplementary Figure 2**

Genus	Fold change	Log2FC	p value	Adj p value
g:Akkermansia	0,0007	-10,44	5,67E-35	4,08E-33
g:Bacillus	83,30	6,38	4,04E-15	1,45E-13
g:Acetatifactor	0,20	-2,30	9,26E-12	2,22E-10
g:Lactobacillus	32,59	5,03	1,43E-11	2,46E-10
g:Parasutterella	15,59	3,96	1,71E-11	2,46E-10
g:Clostridium_IV	0,17	-2,53	3,98E-11	4,78E-10
g:Nocardiooides	52,24	5,71	9,07E-11	9,33E-10
g:Clostridium_XVIII	0,09	-3,54	3,02E-09	2,72E-08
g:Clostridium_XIVa	2,25	1,17	1,36E-08	1,09E-07
g:Sporobacter	0,21	-2,22	1,77E-08	1,28E-07
g:Brevibacillus	22,94	4,52	6,24E-08	4,08E-07
g:Eubacterium	4,77	2,25	9,72E-08	5,83E-07
g:Parabacteroides	4,21	2,07	4,94E-07	2,74E-06
g:Porphyromonas	3,77	1,92	5,48E-07	2,82E-06
g:Barnesiella	3,31	1,73	1,09E-06	5,25E-06
g:Enterococcus	26,51	4,73	1,43E-06	6,42E-06
g:Sphingopyxis	21,41	4,42	1,72E-06	7,28E-06
g:Anaerovorax	5,93	2,57	2,10E-05	8,41E-05
g:Haloplasma	3,38	1,76	9,88E-05	0,0004
g:Arthrobacter	9,18	3,20	0,0003	0,001
g:Rhizobium	8,90	3,15	0,0003	0,001
g:Vampirovibrio	6,25	2,64	0,0003	0,001
g:Allobaculum	4,86	2,28	0,0004	0,001
g:Neorhizobium	8,18	3,03	0,001	0,002
g:Paenibacillus	7,85	2,97	0,001	0,002
g:Romboutsia	4,91	2,29	0,001	0,002
g:Clostridium_sensu_stricto	12,44	3,64	0,001	0,002
g:Anaerotruncus	0,48	-1,07	0,001	0,004
g:Butyricicoccus	0,22	-2,21	0,001	0,004
g:Staphylococcus	6,33	2,66	0,002	0,01

<b>g:Catenisphaera</b>	<b>7,26</b>	<b>2,86</b>	<b>0,002</b>	<b>0,01</b>
<b>g:Catabacter</b>	<b>0,47</b>	<b>-1,10</b>	<b>0,003</b>	<b>0,01</b>
<b>g:Papillibacter</b>	<b>0,43</b>	<b>-1,23</b>	<b>0,003</b>	<b>0,01</b>
<b>g:Coprobacillus</b>	<b>0,06</b>	<b>-4,00</b>	<b>0,01</b>	<b>0,01</b>
<b>g:Dorea</b>	<b>0,45</b>	<b>-1,16</b>	<b>0,01</b>	<b>0,02</b>
<b>g:Lutispora</b>	<b>2,96</b>	<b>1,56</b>	<b>0,02</b>	<b>0,04</b>
<b>g:Shuttleworthia</b>	<b>0,17</b>	<b>-2,54</b>	<b>0,02</b>	<b>0,04</b>
g:Alloprevotella	0,51	-0,98	0,03	0,05
g:Pseudoflavonifractor	0,63	-0,67	0,03	0,05
g:Hydrogenoanaerobacterium	2,49	1,32	0,03	0,06
g:Clostridium_XIVb	0,74	-0,44	0,08	0,14
g:Intestinimonas	1,79	0,84	0,08	0,14
g:Turicibacter	3,32	1,73	0,08	0,14
g:Prevotella	3,25	1,70	0,08	0,14
g:Erysipelotrichaceae_incertae_sedis	3,62	1,86	0,12	0,19
g:Roseburia	0,54	-0,88	0,14	0,21
g:Christensenella	2,02	1,01	0,18	0,27
g:Desulfovibrio	0,80	-0,33	0,23	0,34
g:Lachnospiracea_incertae_sedis	1,35	0,43	0,22	0,34
g:Murimonas	1,78	0,83	0,23	0,34
g:Anaeropsporobacter	0,59	-0,76	0,25	0,35
g:Odoribacter	1,55	0,63	0,31	0,42
g:Enterorhabdus	1,47	0,56	0,33	0,45
g:Blautia	0,61	-0,71	0,37	0,47
g:Butyrivibrio	0,70	-0,51	0,37	0,47
g:Oscillibacter	1,23	0,30	0,37	0,47
g:Streptococcus	0,69	-0,54	0,36	0,47
g:Olsenella	0,53	-0,91	0,46	0,58
g:Bilophila	1,15	0,20	0,53	0,64
g:Coprococcus	1,32	0,40	0,54	0,64
g:Aestuariispira	0,73	-0,46	0,57	0,67
g:Bacteroides	0,84	-0,26	0,58	0,67
g:Ruminococcus2	2,00	1,00	0,58	0,67
g:Saccharofermentans	1,16	0,22	0,64	0,72
g:Gracilibacter	0,88	-0,18	0,75	0,83
g:Alkaliphilus	0,84	-0,25	0,77	0,84
g:Alistipes	0,94	-0,09	0,85	0,89
g:Flavonifractor	1,04	0,06	0,86	0,89
g:Gemella	0,90	-0,15	0,88	0,89
g:Ruminococcus	1,05	0,07	0,87	0,89

g:Senegali massilia	0,90	-0,15	0,87	0,89
g:Clostridium III	1,01	0,01	0,96	0,96

148

149 Results from deseq analysis of bacterial genera of the two experiments presented in Figure 1 &  
 150 Supplementary Figure 2 featuring genus name, Fold change and Log2 fold change, comparing  
 151 WD<sub>McB</sub> to WD<sub>CNTL</sub>. Unadjusted p-values as well as p-values adjusted by Benjamini-Hochberg  
 152 method are reported and statistically significantly affected genera (Adj. p < 0.05) are marked in  
 153 bold.

154

155 **Supplementary Table 4: Lipid species altered by McB:**

Lipid	Adjusted p-value between WD <sub>REF</sub> and LFD	Adjusted p-value between WD <sub>REF</sub> and WD <sub>McB</sub>
<b>Upregulated by McB:</b>		
lysoPC 17:1	0,7072	0,0022
PC 33:1 B	0,5237	<0,0001
PC 33:5 D	0,0001	<0,0001
PC 38:4 C	<0,0001	<0,0001
PC 39:6	0,0021	<0,0001
PE 38:5	0,0004	0,0081
plasmenyl-PC 36:3	0,0002	0,0004
<b>Downregulated by McB:</b>		
lysoPC 16:1	0,9977	0,0023
lysoPC 18:1	0,4575	0,0065
lysoPC 20:1	0,0003	0,0001
lysoPC 20:2	0,0027	0,0028
lysoPC 20:3	0,0019	0,0005
lysoPC 20:4 A	0,9830	0,0018
PC 32:1	0,0004	0,0012
PC 33:5 C	0,0933	<0,0001
PC 34:3	0,4656	0,0001
PC 35:4	<0,0001	0,0003
PC 36:3 A	0,0003	0,0002
PC 36:3 B	<0,0001	<0,0001
PC 36:5 B	0,9151	<0,0001
PC 37:4 A	0,0009	0,0085
PC 38:4 A	0,0001	0,0004
PC 38:4 B	<0,0001	<0,0001
PC 38:5 A	0,2436	<0,0001
PC 38:6 B	0,0006	<0,0001
PC 39:7	0,0022	0,0033
PC 40:7 B	0,0006	0,0001

156

157 Reported p-values compared to the WD<sub>REF</sub> are obtained by mixed-effects analysis, adjusted for  
 158 multiple comparisons by Dunnett's post hoc.

159

160 **Supplementary Table 5: Deseq analysis from 21+5 week experiment**

161

Related to Figure 6				
Genus	Fold change	Log2FC	p value	Adj p value
g:Parasutterella	2066,66	11,013	1,4E-38	9,3E-37
g:Parabacteroides	94,91	6,568	7,6E-33	2,6E-31
g:Brevibacillus	138,42	7,113	9,1E-18	2,1E-16
g:Pseudoflavonifractor	0,09	-3,418	3,4E-14	5,9E-13
g:Odoribacter	19,74	4,303	1,9E-13	2,6E-12
g:Desulfovibrio	0,18	-2,501	4,8E-09	5,5E-08
g:Haloplasma	13,78	3,785	7,0E-09	6,9E-08
g:Dorea	0,11	-3,168	1,3E-08	9,9E-08
g:Flavonifractor	0,11	-3,153	1,3E-08	9,9E-08
g:Acetatifactor	0,16	-2,621	2,3E-07	1,6E-06
g:Rhodococcus	40,07	5,325	3,5E-07	2,2E-06
g:Romboutsia	0,04	-4,556	2,9E-06	1,7E-05
g:Alistipes	3,95	1,982	4,3E-06	2,3E-05
g:Porphyromonas	8,17	3,031	1,5E-05	7,4E-05
g:Shuttleworthia	0,09	-3,499	1,6E-05	7,4E-05
g:Allobaculum	2,74	1,454	1,0E-04	4,3E-04
g:Barnesiella	2,88	1,524	1,1E-04	4,7E-04
g:Anaerotruncus	0,24	-2,039	2,0E-04	7,5E-04
g:Akkermansia	8,07	3,013	3,5E-04	1,3E-03
g:Mucispirillum	0,14	-2,789	4,8E-04	1,7E-03
g:Cohnella	15,91	3,992	9,6E-04	3,1E-03
g:Clostridium IV	0,51	-0,966	1,2E-03	3,6E-03
g:Clostridium XIVa	0,54	-0,893	1,3E-03	3,8E-03
g:Eubacterium	4,77	2,253	1,6E-03	4,5E-03
g:Papillibacter	0,27	-1,874	2,1E-03	5,8E-03
g:Coprobacter	13,09	3,710	3,0E-03	7,8E-03
g:Oscillibacter	0,38	-1,415	3,2E-03	8,2E-03
g:Bifidobacterium	7,60	2,926	4,4E-03	1,1E-02
g:Sporobacter	0,39	-1,364	1,0E-02	2,5E-02
g:Clostridium XVIII	0,36	-1,481	1,2E-02	2,8E-02
g:Ruminococcus	0,44	-1,178	1,6E-02	3,6E-02

<b>g:Christensenella</b>	<b>4,25</b>	<b>2,086</b>	<b>2,3E-02</b>	<b>4,9E-02</b>
g:Clostridium XIVb	2,63	1,395	0,025	0,050
g:Hydrogenoanaerobacterium	0,25	-2,005	0,029	0,058
g:Streptococcus	0,38	-1,406	0,033	0,064
g:Butyrivibrio	1,64	0,715	0,041	0,077
g:Lactobacillus	2,02	1,018	0,046	0,083
g:Olsenella	2,39	1,260	0,069	0,123
g:Butyricicoccus	0,31	-1,678	0,079	0,137
g:Blautia	0,47	-1,096	0,113	0,182
g:Pedobacter	3,78	1,918	0,112	0,182
g:Roseburia	0,52	-0,954	0,111	0,182
g:Murimonas	0,28	-1,855	0,129	0,203
g:Fodinicurvata	3,54	1,822	0,140	0,214
g:Holdemania	1,96	0,970	0,150	0,225
g:Clostridium_III	1,42	0,506	0,184	0,264
g:Intestinimonas	0,54	-0,877	0,183	0,264
g:Anaerofilum	0,44	-1,168	0,191	0,269
g:Anaerosolibacter	0,32	-1,630	0,208	0,287
g:Coprococcus	2,06	1,042	0,242	0,327
g:Erysipelotrichaceae_incertae_sedis	0,44	-1,194	0,323	0,428
g:Bilophila	0,68	-0,546	0,329	0,428
g:Anaerovorax	1,79	0,843	0,352	0,449
g:Enterococcus	2,38	1,251	0,366	0,459
g:Staphylococcus	0,61	-0,707	0,379	0,468
g:Escherichia/Shigella	0,42	-1,250	0,411	0,498
g:Bacteroides	0,82	-0,293	0,420	0,500
g:Lachnospiracea_incertae_sedis	0,75	-0,408	0,469	0,548
g:Lutispora	1,83	0,871	0,493	0,567
g:Alkaliphilus	1,55	0,632	0,521	0,589
g:Clostridium_sensu_stricto	1,60	0,680	0,562	0,625
g:Enterorhabdus	1,27	0,346	0,573	0,625
no_match	2,30	1,202	0,579	0,625
g:Gracilibacter	1,23	0,304	0,591	0,627
g:Saccharofermentans	1,12	0,167	0,773	0,808
g:Anaerosporobacter	0,97	-0,047	0,938	0,952
g:Tissicrella	1,06	0,078	0,938	0,952
g:Spiroplasma	1,03	0,038	0,969	0,969

164 Results from deseq analysis of bacterial genera of the 21+5 week experiment featuring genus name,  
165 Log<sub>2</sub> fold change, comparing WD<sub>McB</sub> to WD<sub>REF</sub>. Unadjusted p-values as well as p-values adjusted  
166 by Benjamini-Hochberg method are reported and statistically significantly affected genera (Adj. p <  
167 0.05) are marked in bold.

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