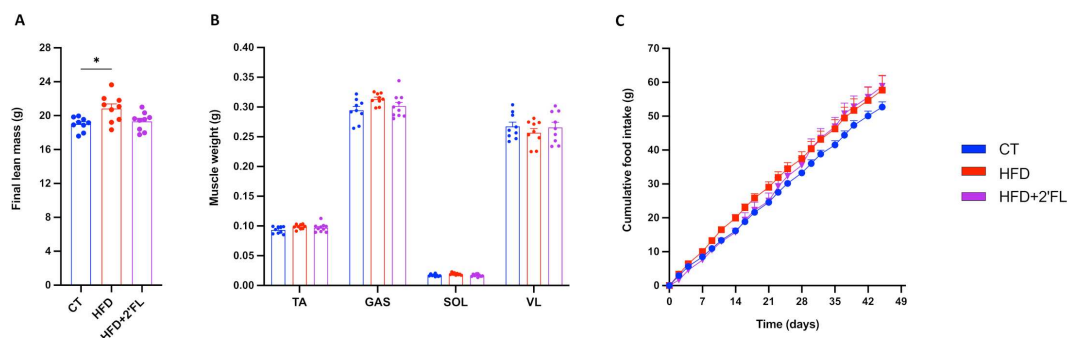
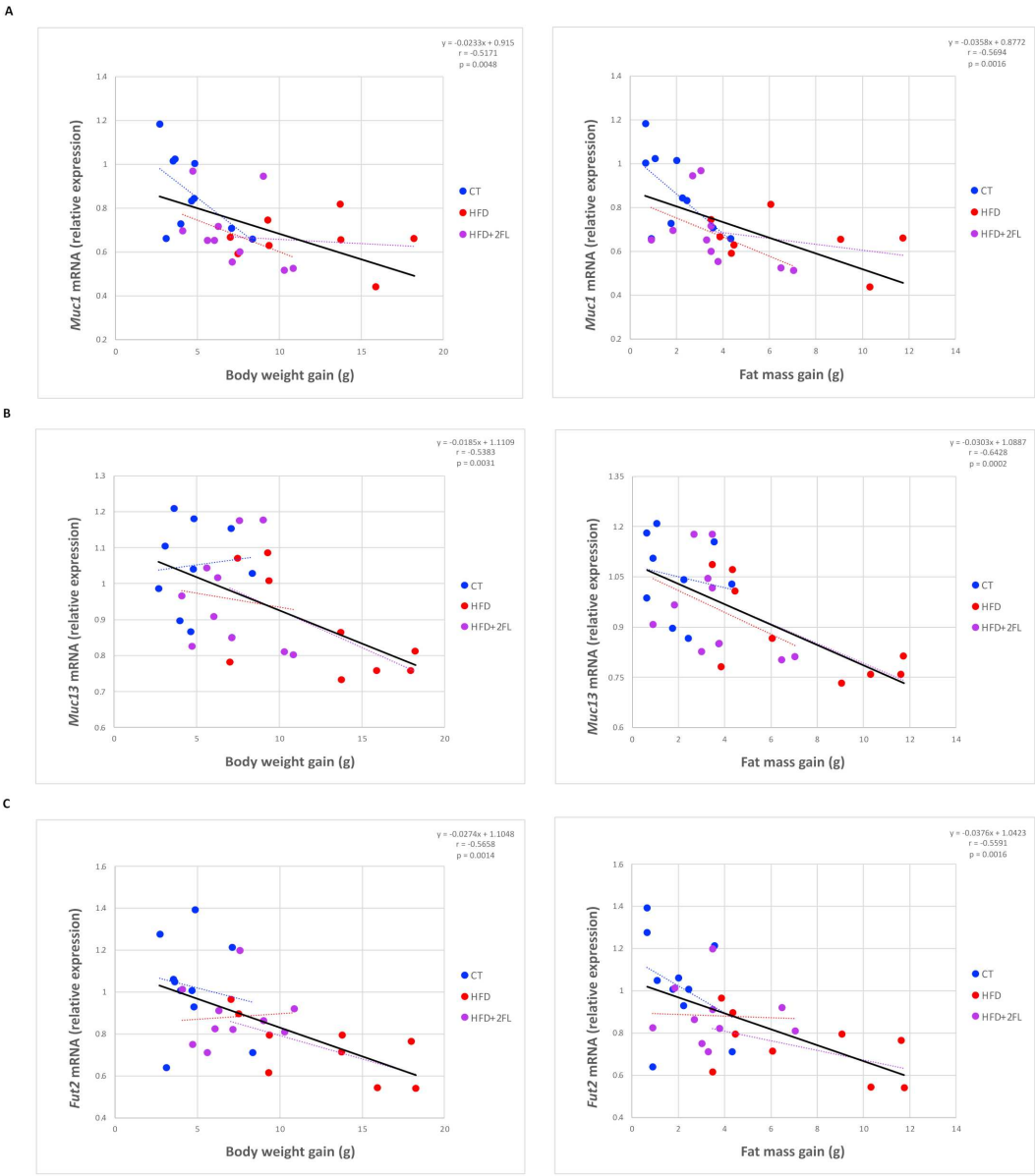
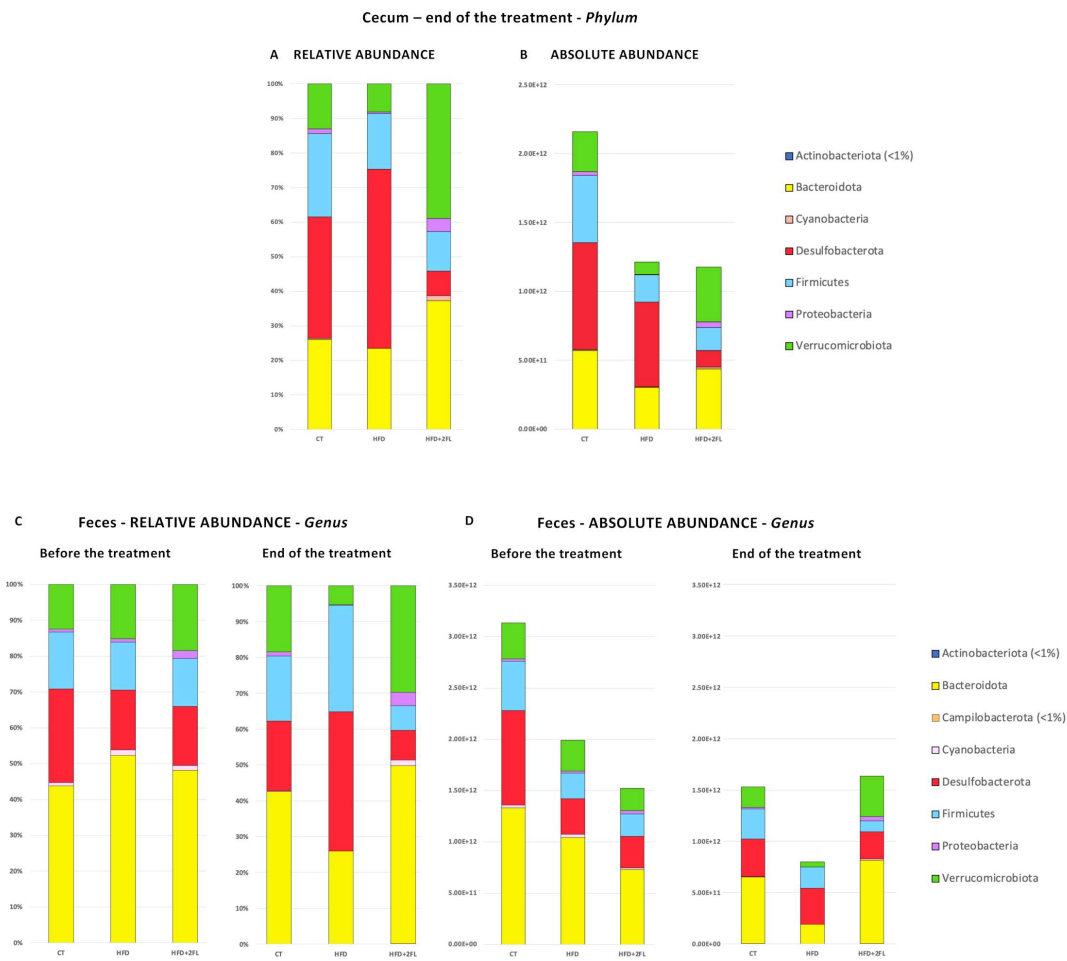




Supplemental Figure 1. (A) Final lean mass and (B) muscle weights (TA = tibialis anterior, VL = vastus lateralis, GAS = gastrocnemius, SOL = soleus). (C) Cumulative food intake. Data are means±s.e.m (n= 9-10/group). Data were analysed using one-way ANOVA for A and B and according to two-way ANOVA for C followed by Tukey post hoc test. *P < 0.05;



Supplemental Figure 2. Pearson correlation between mRNA colonic expression of (A) *Muc1*, (B) *Muc13* and (C) *Fut2* and body weight gain/fat mass gain (n=9-10/group).



Supplemental Figure 3. (A-D) Bar graphs showing grouped taxonomic profiles of the gut bacteria at a phylum level: (A,B) relative and absolute abundance in the cecum, before and at the end of the treatment; (C,D) relative and absolute abundance in the feces, at the end of the treatment. (n= 9-10/group).

Functional Annotation Clustering					
HFD vs CT					
▲ UPREGULATED			▼ DOWNREGULATED		
Annotation Cluster	Enrichment Score	Term	Annotation Cluster	Enrichment Score	Term
1	9.4	Proteolysis	1	4.7	Carbon metabolism
		Protease			Biosynthesis of amino acids
2	5.8	Peptidase activity	2	3.7	2-Oxocarboxylic acid metabolism
		Hydrolase			Extracellular region
3	5.1	Hydrolase activity	3	3.3	Secreted
		Extracellular space			Extracellular space
4	3.8	Disulfide bond	4	2.3	Signal
		Extracellular region			Disulfide bond
5	3.5	Metallopeptidase activity	5	2.3	Glycoprotein
		Aminopeptidase activity			Carbon metabolism
6	2.8	Aminopeptidase	6	1.9	Metabolic pathways
		Peptidase S1			Tricarboxylic acid cycle
7	2.6	Peptidase S1, trypsin family, active site	7	1.3	Citrate cycle (TCA cycle)
		Protein digestion and absorption			Glyoxylate and dicarboxylate metabolism
8	2.6	Serine-type peptidase activity	8	2.6	Mitochondrion
		Trypsin-like cysteine/serine peptidase domain			Lipid metabolism
9	1.3	Activation peptide	9	1.9	Glyoxylate and dicarboxylate metabolism
		Charge relay system			Lipid metabolic process
10	1.3	Serine-type endopeptidase activity	10	2.4	Lipid catabolic process
		Tryp_SPC			Pancreatic secretion
11	1.3	Serine protease	11	2.1	Serine-type peptidase activity
		Peptidase S1A, chymotrypsin-type			Tryp_SPC
12	1.3	Zymogen	12	1.9	Serine-type endopeptidase activity
		Metalloprotease			
13	1.3	Metallopeptidase activity	13	1.3	
		Zinc ion binding			
14	1.3	Peptide catabolic process	14	1.3	
		Metal ion binding			
15	1.3	Metal-binding	15	1.3	
		Zinc			
16	1.3	CUB 1	16	1.3	
		CUB 2			
17	1.3	CUB domain	17	1.3	
		CUB			
18	1.3	ZP	18	1.3	
		Zymogen granule membrane			
19	1.3	Zona pellucida domain	19	1.3	
		Cytoplasmic vesicle			
20	1.3		20	1.3	
HFD+2'FL vs HFD					
▲ UPREGULATED			▼ DOWNREGULATED		
Annotation Cluster	Enrichment Score	Term	Annotation Cluster	Enrichment Score	Term
1	4.8	Extracellular space	1	4.0	Protease
		Extracellular region			Proteolysis
2	3.4	Secreted	2	2.9	Peptidase activity
		Signal			Aminopeptidase
3	2.3	Disulfide bond	3	2.6	Aminopeptidase activity
		Carbon metabolism			Hydrolase
4	2.2	Glycolysis / Gluconeogenesis	4	2.4	Metalloprotease
		Biosynthesis of amino acids			Metallopeptidase activity
5	1.7	Canonical glycolysis	5	2.1	Peptide catabolic process
		Glycolysis			Hydrolase activity
6	1.7	Glycolytic process	6	1.9	Zinc ion binding
		Hydroxylation			Metal ion binding
7	1.6	Oxidoreductase activity	7	1.3	Metal-binding
		Oxidoreductase			Zinc
8	1.6	NAD binding	8	1.3	CUB 1
		Proton acceptor			CUB 2
9	1.6	NAD	9	1.3	CUB domain
		Lipid metabolic process			CUB
10	1.6	Lipid metabolism	10	1.3	ZP
		Lipid catabolic process			Zymogen granule membrane
11	1.6	Myelin sheath	11	1.3	Zona pellucida domain
		Catalytic activity			ZP
12	1.6	ADP binding	12	1.3	Cytoplasmic vesicle
		Membrane raft			Extracellular space
13	1.6	Nucleotide binding	13	1.3	Extracellular region
		Methylation			Secreted
14	1.6	ATP binding	14	1.3	Cadherin 4
		Phosphorylation			Cadherin 3
15	1.6	Kinase activity	15	1.3	Cadherin 1
		Kinase			Cadherin 2
16	1.6	Transferase activity	16	1.3	Cadherin
		Transferase			Calcium
17	1.6	ATP-binding	17	1.3	Cadherin conserved site
		Nucleotide-binding			Cadherin
18	1.6	Nucleus	18	1.3	Cadherin-like
		Cytosol			Homophilic cell adhesion
19	1.6	Acetylation	19	1.3	CA
		Cytoplasm			Cell adhesion
20	1.6	Glycolysis / Gluconeogenesis	20	1.3	Integral component of plasma membrane
		Glycyl lysine isopeptide (Lys-Gly)			Protein digestion and absorption
21	1.6	Isopeptide bond	21	1.3	Peptidase S1
		Ubi conjugation			Peptidase S1, trypsin family, active site
22	1.6	Antimicrobial	22	1.3	Peptidase S1A, chymotrypsin-type
		Inflammatory response			Trypsin-like cysteine/serine peptidase domain
23	1.3	Mitochondrion	23	1.3	Pancreatic secretion
		Transit peptide			Serine-type peptidase activity
24	1.3	Mitochondrial matrix	24	1.3	Serine protease
		Mitochondrial inner membrane			Tryp_SPC
25	1.3		25	1.3	Serine-type endopeptidase activity

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19 **Supplemental Figure 4.** Functional annotation clustering performed with DAVID, showing

20 annotation clustering, enrichment scores and terms significantly up/down-regulated by HFD

21 and HFD+2'FL in mice. Only annotation clusters with enrichment scores ≥ 1.3 (corresponding

22 to P-values <0.05) are shown. Terms that changed in an opposite way in HFD-fed mice

23 compared to HFD+2'FL mice are highlighted in bold and red/blue.

Functional Annotation Clustering		
Obese vs Normal subjects		
▲ UPREGULATED		
Annotation Cluster	Enrichment Score	Term
1	3.0	carboxypeptidase activity ACT_SITE:Proton donor/acceptor proteolysis Metalloprotease Carboxypeptidase Protease zinc ion binding Metal-binding Zinc
2	2.6	anchored component of membrane GPI-anchor LIPID:GPI-anchor amidated serine PROPEP:Removed in mature form Lipoprotein
3	2.6	DOMAIN:P-type 1 DOMAIN:P-type 2 alpha-1,4-glucosidase activity Starch and sucrose metabolism Glycoside hydrolase, family 31 P-type trefoil PD Galactose mutarotase-like domain Glycosidase Glycosyl hydrolase, family 13, all-beta hydrolase activity, hydrolyzing O-glycosyl compounds Galactose metabolism Glycoside hydrolase, superfamily Carbohydrate digestion and absorption Sulfation Metabolic pathways Signal-anchor carbohydrate binding apical plasma membrane Helical; Signal-anchor for type II membrane protein Lumenal Cytoplasmic integral component of membrane Repeat Helical Extracellular Transmembrane helix Transmembrane Disordered
4	2.5	proteolysis Activation peptide Protease Pancreatic secretion Protein digestion and absorption Zymogen
5	1.9	N-linked (GlcNAc...) asparagine Glycoprotein Cell membrane membrane plasma membrane Membrane

24

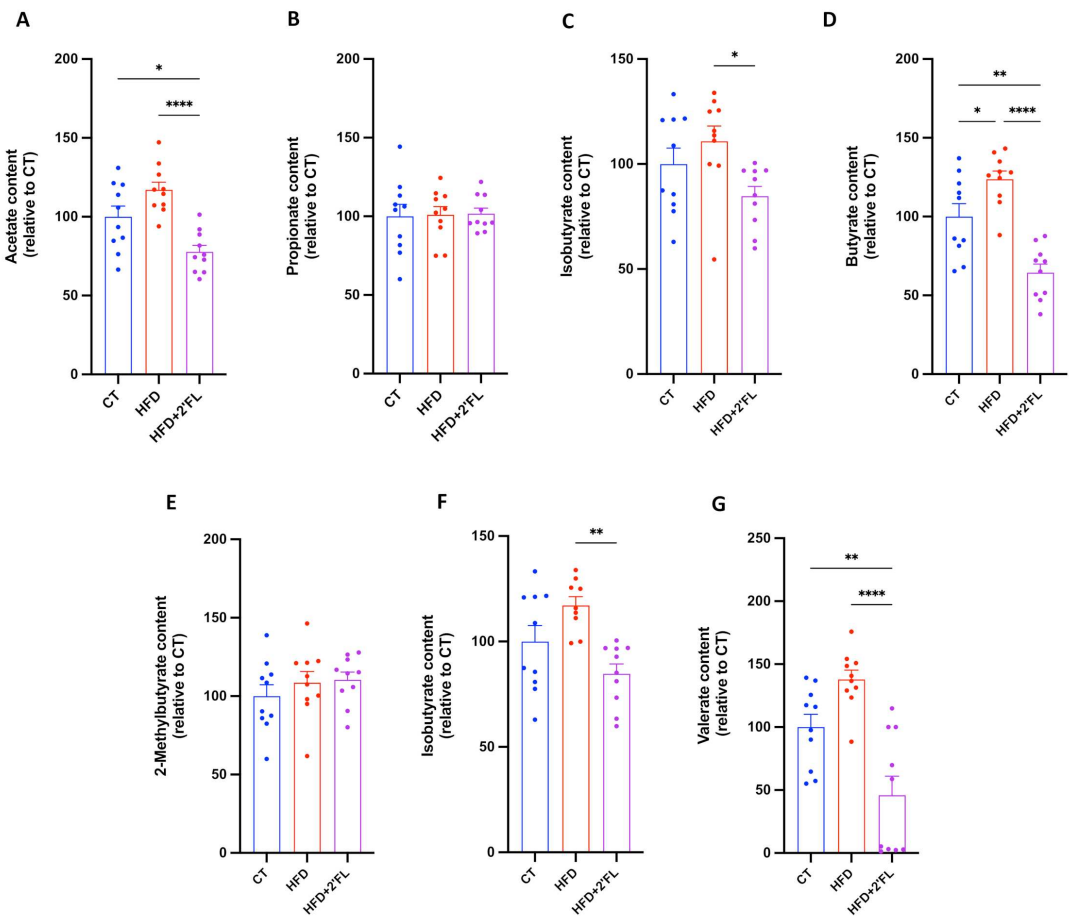
25 **Supplemental Figure 5.** Functional annotation clustering performed with DAVID, showing

26 annotation clustering, enrichment scores and terms significantly upregulated in obese human

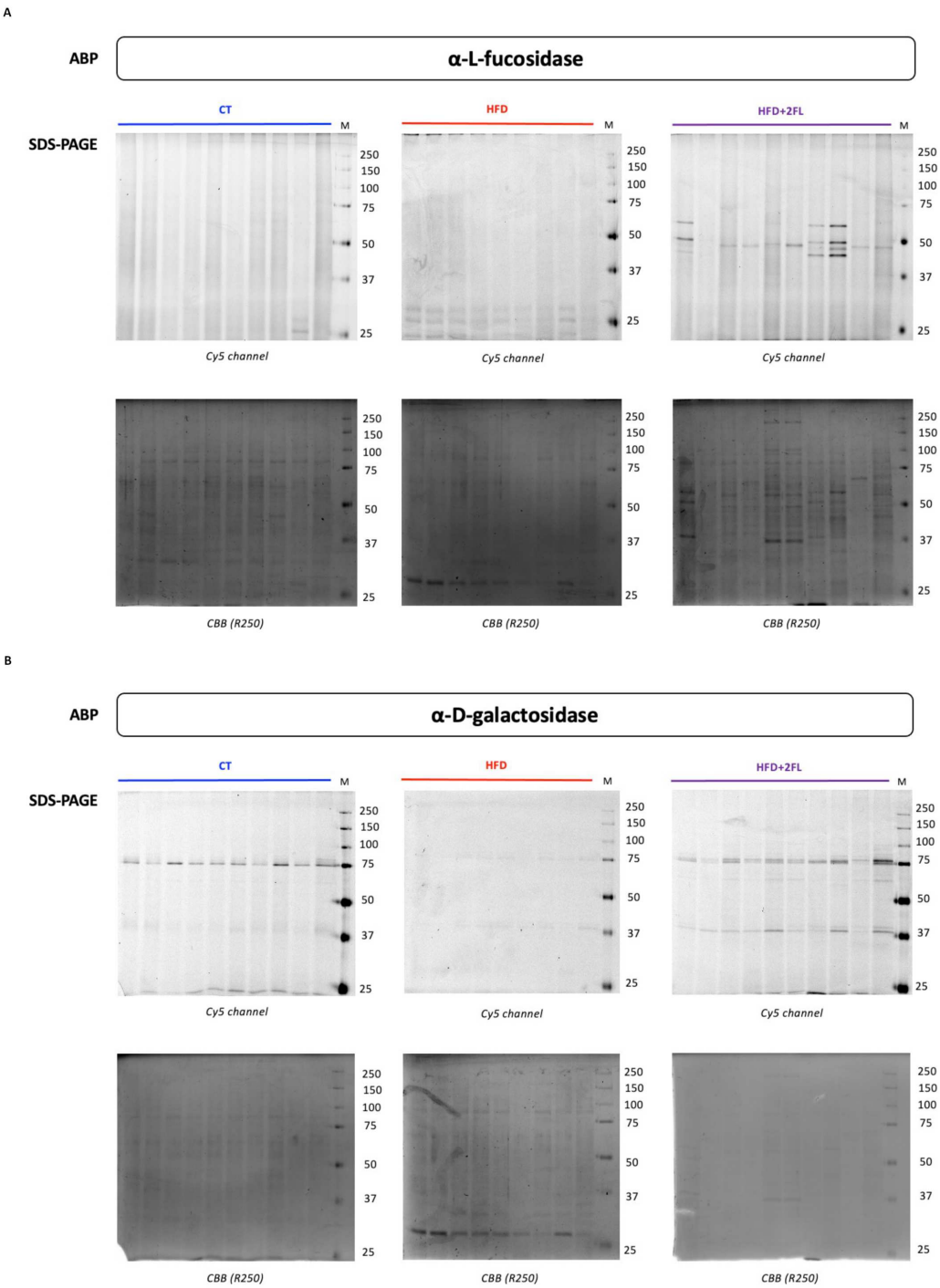
27 subjects compared to normal ones. Only annotation clusters with enrichment scores ≥ 1.3

28 (corresponding to P-values <0.05) are shown. Terms that are similar to those enriched in HFD-

29 fed mice are in red and some of the terms related to metabolism are highlighted in light red.



Supplemental Figure 6. Short-chain fatty acids (SCFAs) content in the cecal content. (A) acetate, (B) propionate, (C) isobutyrate, (D) butyrate, (E) 2-methylbutyrate, (F) isovalerate, (G) valerate. Data are means±s.e.m (n= 11-12/group). Data were analysed using one-way ANOVA followed by Tukey post hoc test. *P < 0.05; **P < 0.01; ***P < 0.001; ****P < 0.0001.



Supplemental Figure 7. In-gel fluorescent ABP labelling. (A) 1 μ M for alpha-L-fucosidase labeling (JJB38 1) and (B) 0.5 μ M for alpha-D-galactosidase (TB474) and their relative Coomassie Brilliant Blue (CBB) staining (n=9-10/group).