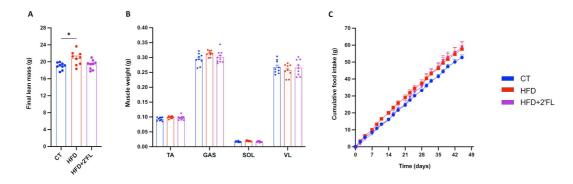
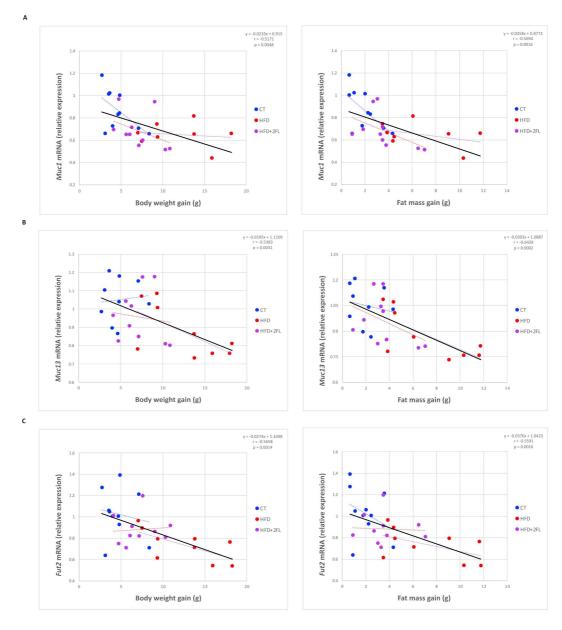
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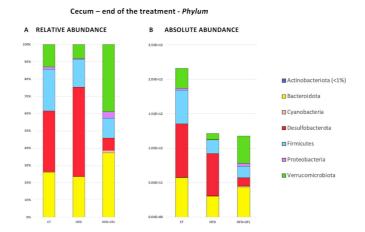


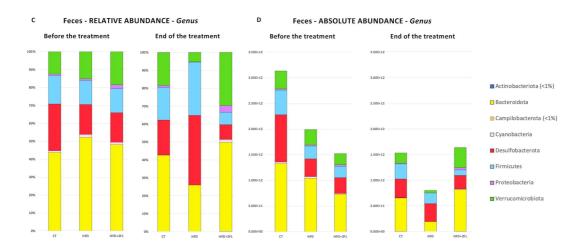
Supplemental Figure 1. (A) Final lean mass and (B) muscle weights (TA = tibialis anterior, VL = vastus lateralis, GAS = gastrocnemius, SOL = soleus). (C) Cumulative food intake. Data are means \pm s.e.m (n= 9-10/group). Data were analysed using one-way ANOVA for A and B and according to two-way ANOVA 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).

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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).

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		HFD v	vs CT		
		▲ UPREGULATED		1	DOWNREGULATED
nnotation	Enrichment	Term	Annotation		Term
Cluster	Score	Proteolysis	Cluster	Score	Carbon metabolism
		Protease	1	4.7	Biosynthesis of amino acids
1	9.4	Peptidase activity Hydrolase			2-Oxocarboxylic acid metabolism
		Hydrolase activity			Extracellular region Secreted
		Extracellular space	2	3.7	Extracellular space
2	5.8	Disulfide bond Extracellular region		5.7	Signal Disulfide bond
		Metallopeptidase activity			Glycoprotein
3	5.1	Aminopeptidase activity			Carbon metabolism
		Aminopeptidase Peptidase S1	-	3.3	Metabolic pathways Tricarboxylic acid cycle
	3.8	Peptidase S1, trypsin family, active site	4		Citrate cycle (TCA cycle)
		Protein digestion and absorption			Glyoxylate and dicarboxylate metabolism
		Serine-type peptidase activity Trypsin-like cysteine/serine peptidase domain			Mitochondrion Lipid metabolism
4		Activation peptide			Glyoxylate and dicarboxylate metabolism
		Charge relay system			Lipid metabolic process
		Serine-type endopeptidase activity Tryp_SPc			Lipid catabolic process Pancreatic secretion
		Serine protease	5	2.3	Hydrolase
		Peptidase S1A, chymotrypsin-type			Hydrolase activity NAD binding
		Zymogen Metalloprotease		1.9	Oxidoreductase activity
		Metallopeptidase activity	6		Oxidoreductase
5	3.5	Zinc ion binding Peptide catabolic process			Proton acceptor NAD
,	3.3	Metal ion binding			Mitochondrion
		Metal-binding			Calcium
		Zinc CUB 1	7	1.3	Metal ion binding Metal-binding
6	2.8	CUB 2			metal smalls
ь		CUB domain			
		CUB ZP	-		
7	2.6	Zymogen granule membrane			
· ′	2.0	Zona pellucida domain Cytoplasmic vesicle			
		HFD+2'FI			
		HPD+2 PI	LVS HFD		
		▲ UPREGULATED			DOWNREGULATED
	Enrichment Score	▲ UPREGULATED Term		Enrichment	TOWNREGULATED Term
nnotation Cluster	Enrichment Score	Term Extracellular space	Annotation Cluster		Term Protease
Cluster	Score	Term Extracellular space Extracellular region		Enrichment	Term Protease Proteolysis
		Term Extracellular space Extracellular region Secreted Signal		Enrichment	Term Protease Proteolysis Peptidase activity Aminopeptidase
	Score	Term Extracellular space Extracellular region Secreted Signal Disulfide bond		Enrichment	Term Protease Proteolysis Peptidase activity Aminopeptidase Aminopeptidase
Cluster	Score	Term Extracellular space Extracellular region Secreted Signal	Cluster	Enrichment Score	Term Protease Proteolysis Peptidase activity Aminopeptidase
Cluster 1	Score	Term Extracellular space Extracellular region Secreted Signal Disulfide bond Carbon metabolism Glycolysis / Gluconegenesis Biosynthesis of amino acids		Enrichment	Protesse Proteolyis Proteolyis Peptidase activity Aminopeptidase activity Hydrolase Metalloportease Metalloportease Metalloportease
Cluster	Score	Term Extracellular space Extracellular region Secreted Signal Disulfide bond Carbon metabolism Gkrolysis / Giuconeogenesis Biosynthesis of amino acids Canonical glycolysis	Cluster	Enrichment Score	Protease Proteolys Proteolys Proteolys Proteolys Proteolys Aminopeptidase activity Hydrolase Metalloprotease Metalloprotease Metalloprotease Metalloprotease Metalloprotease
Cluster 1	Score	Term Extracellular space Extracellular region Secreted Signal Disulfide bond Carbon metabolism Givolysis / Giuconeogenesis Biosynthesis of amino acids Canonical givolysis Giycolysis Giycolysis Giycolysis	Cluster	Enrichment Score	Protesse Proteolysis Proteolysis Proteolysis Poptidase activity Aminopeptidase activity Hydrolase Metalloprotesse Metalloprotesse Metalloprotesse Hydrolase activity Peptide catabolic process Hydrolase activity Zinc ion binding
Cluster 1	Score	Term Extracellular space Extracellular region Secreted Signal Disulfide bond Carbon metabolism Glycolysis / Gisconegenesis Biosynthesis of amino adds Canonical glycolysis Glycolysis Glycolytic process Hydroxylation	Cluster	Enrichment Score	Protease Proteolysis Proteolysis Poptidase activity Aminopeptidase activity Hydrolase Metallioprotease Metal
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1 2 3	4.8 4.8 3.4	Term Extracellular space Extracellular region Secreted Signal Disulfide bond Carbon metabolism Okvolysis / Gituconeogenesis Blosynthesis of amino adds Carnonical givolism Okvolysis / Gituconeogenesis Blosynthesis of amino adds Carnonical givolism Okvolysis Okvolysis Okvolysis Okvolysis Okvolysis Okvolysis Okvolysis Okvolysis Okvolysis Upidrostace NAD binding Proton sceptor NAD Lipid metabolism Lipid estabolism Lipid metabolism Lipid estabolism Upid estaboli	1 2 2 3	4.0 2.9 2.6	Protease Proteolysis Proteolysis Proteolysis Proteolysis Poptidase activity Aminopeptidase activity Hydrolase Metalloprotease Metalloprotease Metalloprotease Metalloprotease Metalloprotease Metalloprotease Hydrolase activity Poptide catabolic process Hydrolase activity Zinc ion binding Metal ion binding Metal ion binding Metal on binding Zincus Zincu
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1 2 2 3 4	4.8 3.4 2.3	Term Extracellular space Extracellular region Secreted Signal Disulfide bond Carbon metabolism Givolysis / Giluconeogenesis Biosynthesis of amino adds Caronical givolysis Giycolysis Jupid metabolic process Lipid metabolic process Lipid metabolic process Lipid metabolic process Lipid metabolic process Myelin sheath Catalytic activity Catolytic activity Ginase Tansiferase activity Transferase TAP-binding Nucleotide-binding Nucleoti	2 3 4	4.0 2.9 2.6 2.4	Protease Proteolysis Proteolysis Proteolysis Proteolysis Proteolysis Proteolysis Proteolysis Aminopeptidase activity Hydrolase Metallopoptidase activity Peptide catabolic process Hydrolase activity Zinc ion binding Metal ion binding Metal-binding Zinc CUB 1 CUB 2 CUB 4 CUB 3 Zinc CUB 3 Zinc CUB 4
1 2 2 3 4	4.8 3.4 2.3	Term Extracellular space Extracellular region Secreted Signal Disulfide bond Carbon metabolism Okvolysis / Gituconeogenesis Blosynthesis of amino adds Carnonical givolism Okvolysis / Gituconeogenesis Blosynthesis of amino adds Carnonical givolism Okvolysis Upidmotabolism Upidmotabolism Upid estabolism Upid estab	2 3 4	4.0 2.9 2.6 2.4	Protease Proteolysis Proteolysis Proteolysis Proteolysis Poptidase activity Aminoppidase activity Hydrolase Metalloprotease Metalloprotease Metalloprotease Metalloprotease Metalloprotease Hydrolase activity Poptide catabolic process Hydrolase activity Zinc ion binding Metal ion binding Metal on binding Metal binding Zinc CUB 2 CUB 4 CUB 2 CUB 4 CUB 2 CUB 4 CUB 5 CUB 5 CUB 5 CUB 6 CUB 6 CUB 6 CUB 6 CUB 7 CUB 6 CUB 7 CUB 6 CUB 7 C
1 2 3 4 4	4.8 3.4 2.3 2.2	Term Extracellular space Extracellular region Secreted Signal Disulfide bond Carbon metabolism Okvolysis of Giuconeogenesis Blosynthesis of amino adds Carnonical glycolist Giycolysis Giy	2 3 4	4.0 2.9 2.6 2.4	Protease Proteolysis Proteolysis Proteolysis Poptidase activity Aminopeptidase activity Hydrolase Metalloprotease Metallopeptidase activity Peptide catabolic process Hydrolase activity Zinc ion binding Metal ion binding Metal on binding Metal on binding Metal on binding Metal on binding Zinc CUB 20 CUB 20 CUB 40 CUB 20 CUB 40 CUB 20 CUB 40 CUB 20 CUB 50 CUB
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1 2 3 4 4	4.8 3.4 2.3 2.2	Term Extracellular space Extracellular region Secreted Signal Disulfide bond Carbon metabolism Glycolysis of Giuconeogenesis Blosynthesis of amino adds Carnonical glycolysis G	2 3 4	4.0 2.9 2.6 2.4	Protease Proteolysis Proteolysis Proteolysis Poptidase activity Aminopeptidase activity Hydrolase Metalloprotease Metallopeptidase activity Peptide catabolic process Hydrolase activity Zinc ion binding Metal ion binding Metal on binding Metal on binding Metal on binding Metal on binding Zinc CUB 20 CUB 20 CUB 40 CUB 20 CUB 40 CUB 20 CUB 40 CUB 20 CUB 50 CUB
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1 2 3 4 4 5 5 5 6 6 7 7	2.3 2.2 1.7 1.6	Term Extracellular space Extracellular region Secreted Signal Disulfide bond Carbon metabolism Glycolysis / Giuconeogenesis Blosynthesis of amino adds Cannolael glycolysis Gly	2 3 4	4.0 2.9 2.6 2.4	Protease Proteolysis Proteolysis Proteolysis Proteolysis Proteolysis Proteolysis Proteolysis Proteolysis Proteolysis Maninopeptidase activity Hydrolase Metalloprotease Metallopeptidase activity Peptide catabolic process Hydrolase activity Zinc ion binding Metal ion binding Metal binding Metal binding Zinc CUB 2 CUB 2 CUB 2 CUB 2 CUB 3 CUB 3 CUB 3 CUB 3 CUB 3 CUB 4 CUB 4 CUB 4 CUB 4 CUB 4 CUB 4 CUB 5 CUB 5 CUB 5 CUB 5 CUB 6 CUB 7 CUB 6 CUB 7
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Supplemental Figure 4. Functional annotation clustering performed with DAVID, showing annotation clustering, enrichment scores and terms significantly up/down-regulated by HFD and HFD+2'FL in mice. Only annotation clusters with enrichment scores ≥ 1.3 (corresponding to P-values <0.05) are shown. Terms that changed in an opposite way in HFD-fed mice compared to HFD+2'FL mice are highlighted in bold and red/blue.

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Functional Annotation Clustering

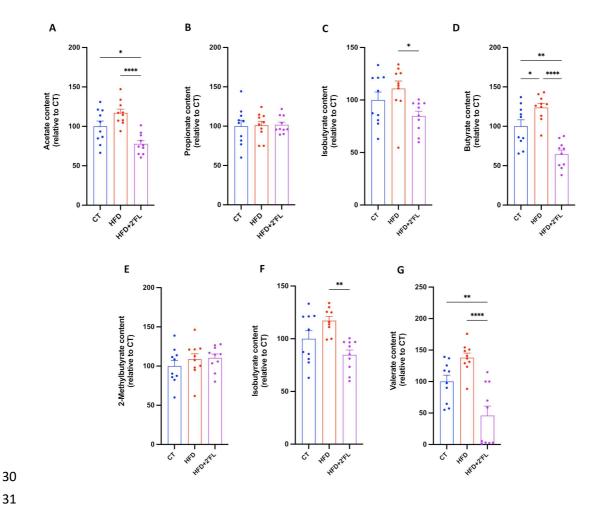
Obese vs Normal subjects						
▲ UPREGULATED						
Annotation	Enrichment	Term				
Cluster	Score	carboxypeptidase activity				
1	3.0	ACT_SITE:Proton donor/acceptor proteolysis Metalloprotease Carboxypeptidase Protease zinc ion binding				
		Metal-binding Zinc				
2	2.6	anchored component of membrane GPI-anchor 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				

Supplemental Figure 5. Functional annotation clustering performed with DAVID, showing annotation clustering, enrichment scores and terms significantly upregulated in obese human subjects compared to normal ones. Only annotation clusters with enrichment scores ≥ 1.3 (corresponding to P-values <0.05) are shown. Terms that are similar to those enriched in HFD-fed mice are in red and some of the terms related to metabolism are highlighted in light red.

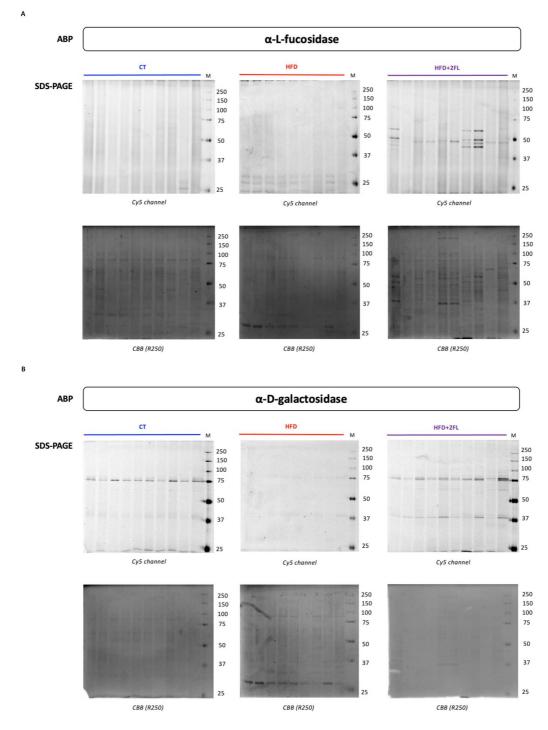
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Supplemental Figure 6. Short-chain fatty acids (SCFAs) content in the cecal content. (A) acetate, (B) propionate, (C) isobutyrate, (D) butyrate, (E) 2-methylbutyrate, (F) isovalerate, (G) valerate. Data are means±s.e.m (n= 11-12/group). Data were analysed 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

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