Supplemental material

Supplemental methods

Glucose homeostasis.

At week 6, mice were fasted for 6 hours and insulin tolerance tests (ITT) were performed after intraperitoneal injections of insulin (0.75 UI/kg body weight). Glycæmia was measured with an Accu-Check glucometer (Bayer) before (0 min) and after (10, 20, 30, 60 min) insulin injection. At the end of week 7, mice were fasted overnight (12 h) and subjected to oral glucose tolerance test (OGTT, 1 g of glucose/kg body weight). Blood was collected before (0 min) and after (15, 30, 60, 90 and 120 min) glucose challenge for glycæmia determination. Blood samples (~30µL) were collected at each time point during OGTT for insulinaemia determination. The homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated based on the following formula: fasting insulinæmia (µUI/mL) x fasting glycæmia (mM)/22.5.

Analytical methods

Plasma insulin was assessed using an ultra-sensitive ELISA kit (Alpco, USA). *Liver triglyceride* (TG) was measured after chloroform-methanol extraction and enzymatic reactions with a commercial kit (Randox Laboratories, Crumlin, UK). *Chemokines and cytokines* were quantified in 25 µl of adipose tissue lysates (50 ug of protein in PBS containing 1% NP-40) using a Milliplex MAP kit (Millipore). *Plasma endotoxin (LPS)* concentration was determined using a kit based on a Limulus amebocyte extract (LAL kit endpoint-QCL1000, Lonza, USA). Samples were diluted in endotoxin-free water (Charles River, USA) and incubated at 70 °C for 15 minutes to overcome assay inhibition. Plasma bile acids were assessed using liquid chromatography coupled to tandem mass spectrometry as previously described [1].

Proanthocyanidins were quantified as previously reported by Fracassetti et al. [2] using acid catalysis in the presence of phloroglucinol. Briefly, 50 mg of camu camu extract was dissolved in 800 µL of phloroglucinol (50 mg mL^{-1}), added with ascorbic acid (10 mg mL^{-1}) and dissolved in methanol acidified with 0.1 N HCl. The reaction mix was vortexed and incubated at 50 °C for 20 min. The reaction tube was placed in ice and 1 mL 40 mM sodium acetate was added to stop the reaction. Sample was centrifuged, filtered with 0.22 µm PTFE filters, and injected in LC/MS. The identification and quantification of catechin, epicatechin and their derivatives was carried out in an Acquity H-Class Ultra-Performance LC system equipped with a quaternary pump (Waters, Milford, MA, USA), with Acquity PDA detector and TQD mass spectrometer equipped and with a Z-spray electrospray interface. Briefly, the column used Acquity UPLC HSS T3 (1.8 µm, 2.1x100mm, UPLC 12), operating at a flow rate of 0.4 mL min^{-1}; the injection volume was 2.5µl. The solvents were 0.1% acetic acid in water (A) and 100% acetonitrile (B) with a separation gradient starting with 5% B in A at 0 min, 21.5% at 5 min, 24% at 7 min, 37% at 7.8 min, 41% at 10 min, 90% at 10.2 min, 90% at 11.2 min, 5% at 11.3 min followed by washing and conditioning steps. The phenolic compounds were quantified at 280 nm with a calibration curve of catechin (0.5 to 100 mg L^{-1}). The MS/MS analyses were carried out in negative mode using electrospray source parameters as follows: electrospray capillary voltage was 0.8 kV, source temperature was 150 °C, desolvation temperature was 400 °C, cone and desolvation gas flows were 50 l/h and 800 l/h, respectively. Data were acquired through multiple reaction monitoring (MRM) using Waters Masslynx V4.1 software.

RNA extraction and qPCR analysis

Sections of the ileum (approximately 0.5 cm) were homogenized in 1 ml of TRIzol reagent (Thermo Fisher Scientific) using a power homogenizer (Polytron). Freeze-powdered liver, inguinal white adipose tissue, epididymal white adipose tissue and interscapular brown adipose tissue were homogenized in 1 ml of TRIzol reagent in a bead beater. Total RNA purification was performed using a RNeasy mini kit (Qiagen). Total RNA was used for cDNA synthesis with a reverse transcription PCR kit (Applied Biosystems). Real-time PCR was performed using SYBR Green Jump-Start Gene Expression Kit (Sigma) with 1:25 diluted cDNA or TaqMan gene expression master mix (Applied Biosystems) with 1:10 diluted cDNA. Gene expression was assessed by the $\Delta\Delta_{Ct}$ method and Actin was used as the reference gene. Primer sequences are available in supplemental table 2.

Western blotting

Western blots were carried out as previously described [3]. Briefly, protein lysates were loaded onto a 10% acrylamide gel, resolved in SDS-PAGE systems, and then transferred onto nitrocellulose membranes. Membranes were then blocked and probed with the appropriate antibodies. Antibodies were purchased from Cell Signaling (PPARɣ #2443, ACC #3662, FABP4 #2120, CD36 #14347, FAS #3189), Abcam (UCP1 #AB10983) and Millipore (Actin #MAB1501) and used according to instructions from manufacturers.

Assessment of interscapular temperature

Body temperature was measured using a Thermoscan® thermometer (PRO-1, Braun) as previously reported [4]. In sum, the interscapular area was shaved off one day prior to the test. Mice were immobilized in a 50 mL tube with a hole allowing direct aiming of the infra-red beam to the interscapular region. Temperature was assessed in triplicates.

Fæcal sample processing

Fæcal samples were freshly collected at baseline and week 8 and immediately stored at -80 °C. Bacterial genomic DNA was extracted from approximately 50 mg of fæcal material. Samples were resuspended in lysis buffer containing 20 mg/ml lysozyme and incubated for 30 minutes at 37°C. Further lysis was performed by adding 10% SDS and proteinase K to 350 µg/ml followed by incubation for 30 minutes at 60°C. Samples were homogenized using a bead beater and 0.1mm zirconium beads and then processed using a DNA extraction kit (DNeasy, Qiagen). DNA yield was assessed using a NanoDrop ND-1000 spectrophotometer (Thermo Scientific). Extracted DNA was stored at -20 ºC until further use. Each DNA sample was subsequently used for 16S amplification of the V3-V4 region using the primers 341F (5'-CCTACGGGNGGCWGCAG-3') and 805R (5'-GACTACHVGGGTATCTAATCC-3') adapted to incorporate the transposon-based Illumina Nextera adapters (Illumina, USA) and a sample barcode sequence allowing multiplexed paired-end sequencing. The amplification mix contained 1X Q5 buffer (NEB), 1X Q5 Enhancer (NEB), 200 µM dNTP (VWR International, Canada), 0.2 µM of forward and reverse primers (Integrated DNA Technologies, USA), 1 U of Q5 (NEB) and 1 µL of template DNA in a 50 µL reaction. Cycling condition was as follows: denaturation (30 s at 98°C), followed by a first set of 15 cycles (98°C for 10 s, 55°C for 30 s and 72°C for 30 s), then by a second step of 15 cycles (98°C for 10 s, 65°C for 30 s and 72°C for 30 s) and final elongation (2 min at 72°C).

Constructed 16S metagenomic libraries were purified using 35 µL of magnetic beads (AxyPrep Mag PCR Clean up kit; Axygen Biosciences, USA) per 50 µL PCR reaction. Library quality control was performed with a Bioanalyzer 2100 using DNA 7500 chips (Agilent Technologies, USA). An equimolar pool was obtained and checked for quality prior

to further processing. The pool was quantified using picogreen (Life Technologies, USA) and loaded on a MiSeq platform using 2 x 300 bp paired-end sequencing (Illumina, USA). High-throughput sequencing was performed at the IBIS (Institut de Biologie Intégrative et des Systèmes - Université Laval). All raw sequences were deposited in the public European Nucleotide Archive server under accession number PRJEB23031.

16S rRNA gene-based gut microbial analysis

Generated and demultiplexed sequences were analyzed using the QIIME software package (version 1.9.1). Paired-end sequences were merged with at least a 50-bp overlap. Resulting sequences containing ambiguous or low quality reads (Phred score ≤ 25) were removed from the dataset. Forward and reverse primers were trimmed from the filtered sequences; reads with at least one reverse primer mismatch or where the reverse primer was not found were discarded. Chimera checking and filtering was performed using UCHIME. OTU (Operational Taxonomic Units)-picking from post-filtering reads was performed using USEARCH 61 version 6.1.544 with an open-reference methodology, which consisted of clustering sequences *de novo* at 97% identity threshold if they did not hit the reference sequence collection. Representative OTU sequences were assigned taxonomy against the Greengenes reference database (August 2013 release) using the RDP-classifier. Singleton OTUs and OTUs with a number of sequences < 0.005% of total number of sequences were discarded at this step. A subsampling depth of 3159 reads (smallest amount of sequences originally found among our metagenomic samples) was chosen to rarefy the OTU tables used in the downstream analyses. In order to potentially detect *Oscillibacter* and *Barnesiella,* two physiologically important genera of the mouse intestine and which are not represented in the Greengenes database, OTUs assigned to the *Ruminococcaceae* and the *S24-7* families but unclassified at the genus

level against Greengenes were further investigated with the RDP classifier against the RDP database (version September 30, 2016) using a minimum bootstrap cutoff of 50%.

Bacterial quantification by qPCR

The presence of specific taxa in the fæces of HFHS-receiver and CC-receiver mice was assessed by qPCR as previously described [5]. Briefly, copy numbers of Firmicutes, Bacteroidetes, *Lactobacillus spp*., *Akkermansia muciniphila*, *Bifidobacterium spp*., *Barnesiella spp*., *Allobaculum spp*. and *Turicibacter spp*. per ng of fæcal DNA were calculated on the basis of the *Ct* values obtained using standard curves designed for each taxon. The number of copies of each taxon was then normalized by total bacteria (891F/1033R). Primers were *in silico* designed and tested by Primer-BLAST analysis and their sequences are available in supplemental table 2.

References

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