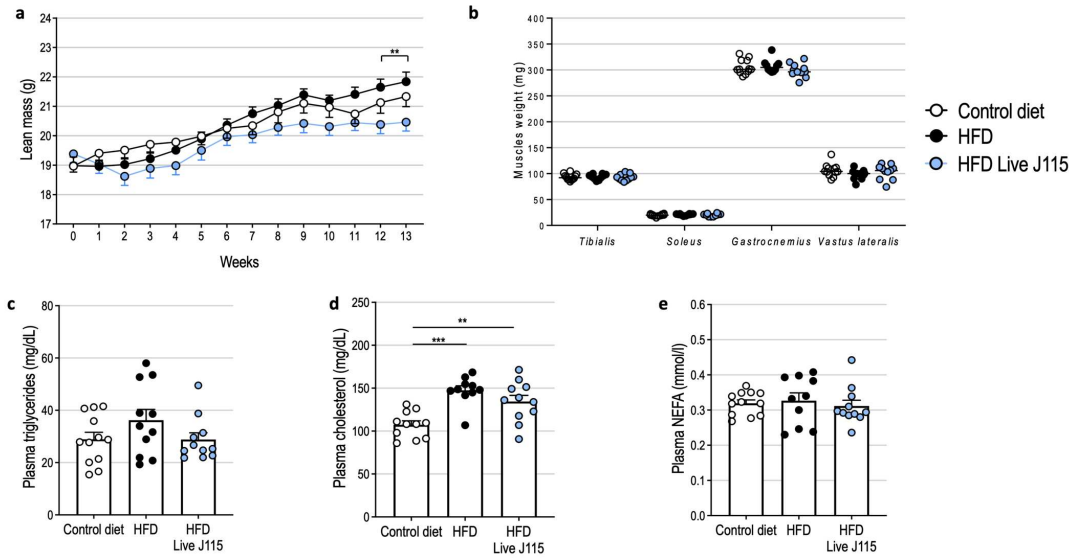
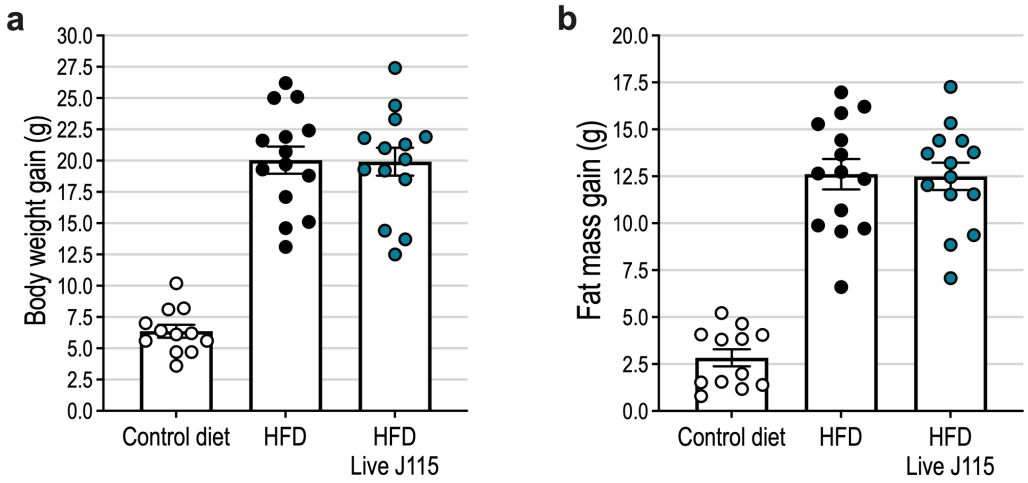
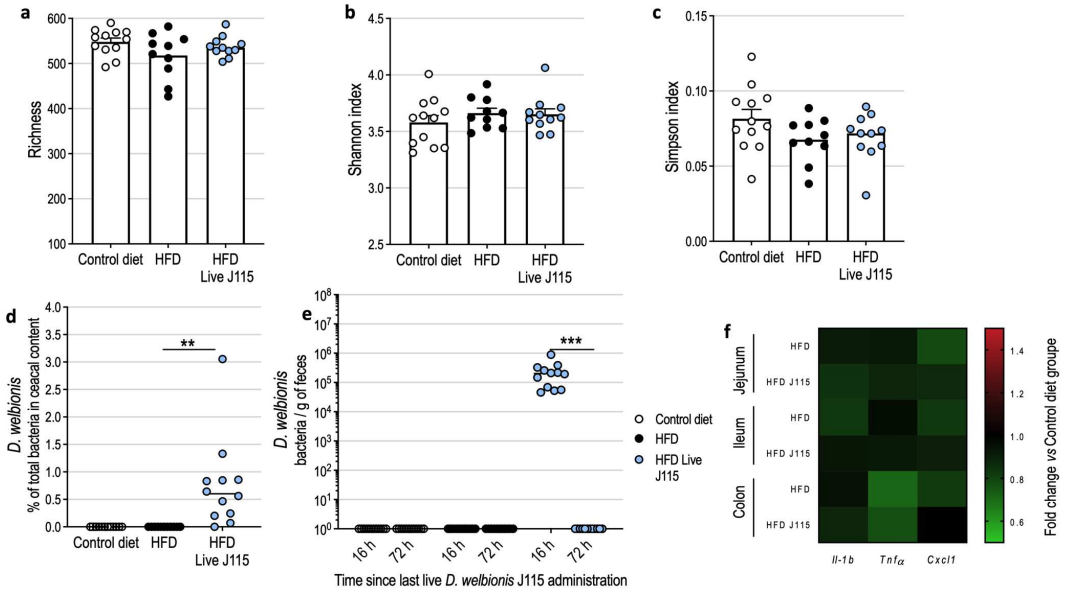


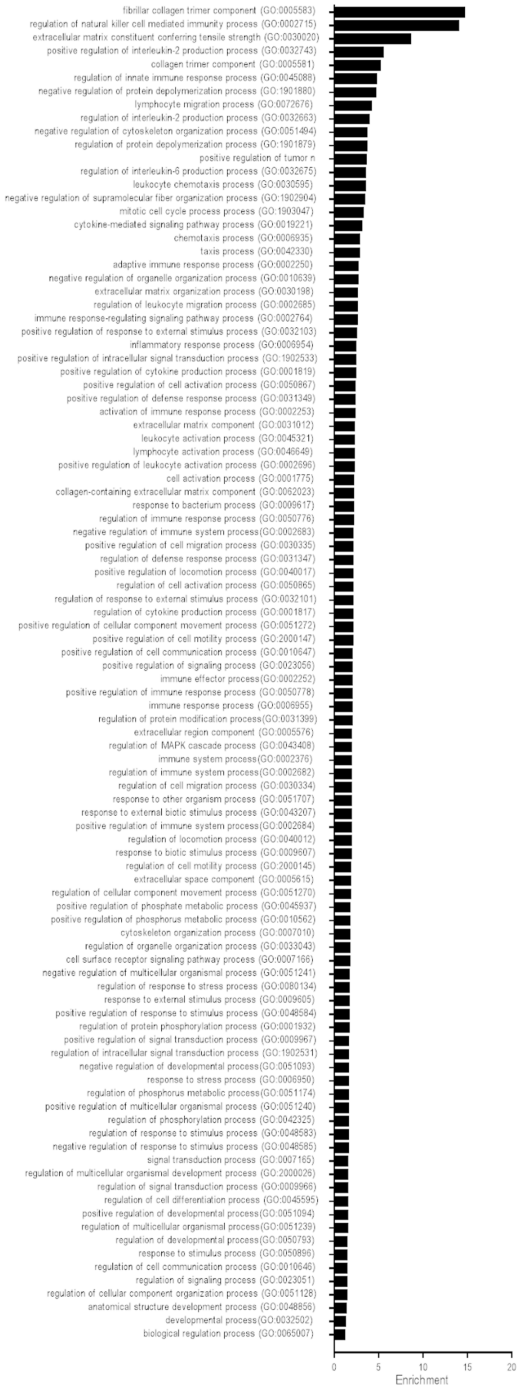
Supplementary Figure S1. Live *D. welbionis* J115^T has no impact on lean mass and plasma lipids levels. a, Lean mass evolution of mice treated during 13 weeks by daily oral gavage with live *D. welbionis* J115^T frozen in trehalose and fed a HFD (HFD J115) and mice fed a control diet or a HFD and treated by daily oral gavage with vehicle. **b**, *Tibialis*, *soleus*, *gastrocnemius* and *vastus lateralis* weight at the end of the 13-weeks period. **c**, Triglycerides, **d**, Total cholesterol and **e**, Non-esterified fatty acids (NEFA) levels in the plasma after a 6-hour fasting period. Number of mice per group: 10 to 12. Results are represented as dot-plots with mean for **b-e** and as bar-plots with mean ± SEM for **a.** Data were analysed using 2-way repeated measures ANOVA for **a** and one-way ANOVA followed by Tukey's post hoc test for **b-e**. * $q < 0.05$; ** $q < 0.01$; *** $q < 0.001$.



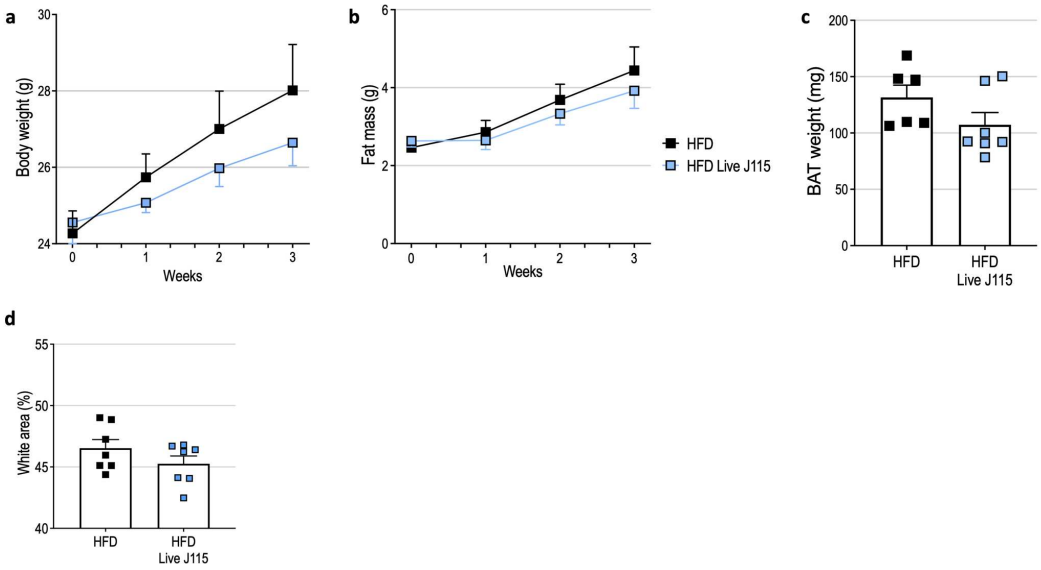
Supplementary Figure S2. Low dose of live *D. welbionis* J115^T did not impact on body weight gain and fat mass gain after 13 weeks of treatment (experiment 5). **a**, Body weight, **b**, fat mass of mice fed a HFD and treated during 13 weeks by daily oral gavage with 1.0 × 10^8 cells of live *D. welbionis* J115^T frozen in trehalose and mice fed a HFD and treated by daily oral gavage with vehicle (experiment 4). Number of mice per group: 12 to 14. Results are represented as dot-plots and bar-plots with mean +/- SEM.



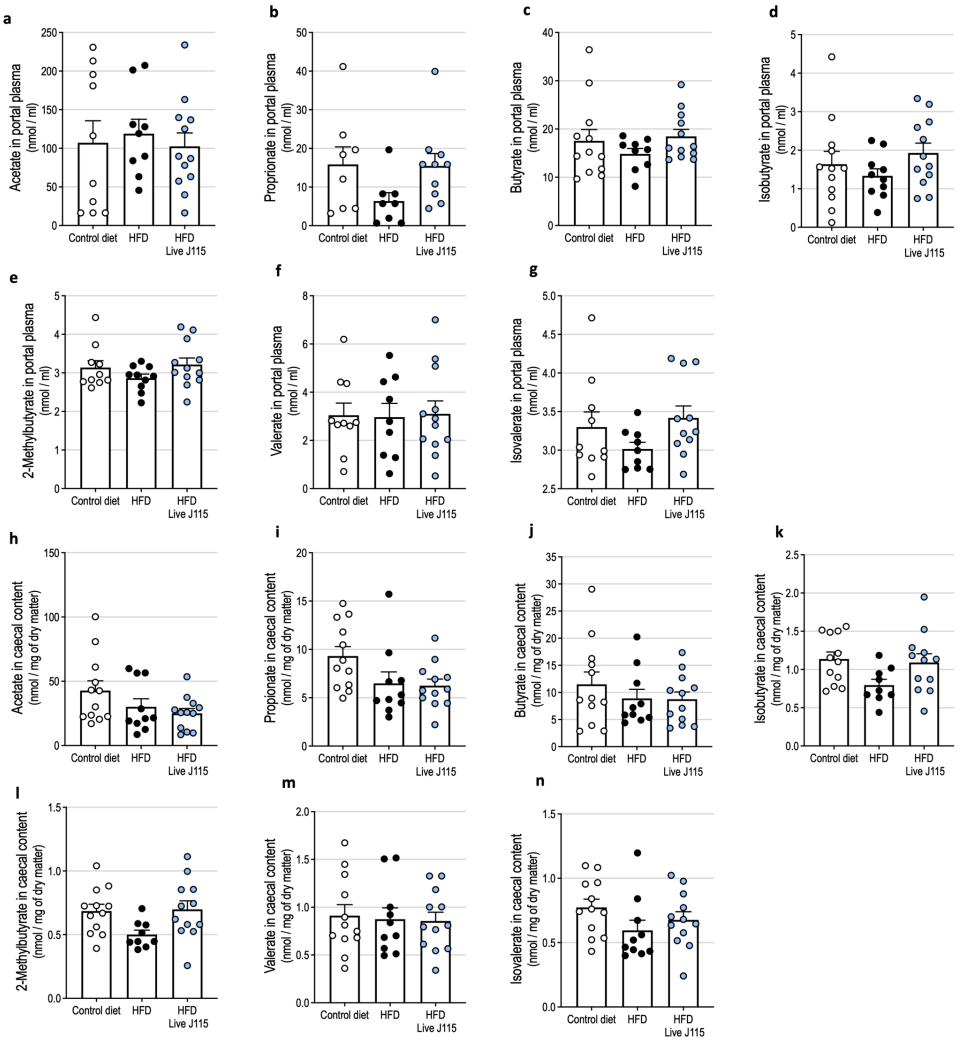
Supplementary Figure S3. **Live *D. welbionis* J115^T does not persist in the mouse gut and has little effect on intestinal microbiota and gut inflammation. a**, Richness of the caecal microbiota based on V3-V4 16S rRNA gene sequences analysis. **b**, Shannon index of the caecal microbiota. **c**, Simpson index of the caecal microbiota. **d**, *D. welbionis* relative abundance estimated by quantitative PCR in the caecal microbiota of mice treated during 13 weeks by daily oral gavage with live *D. welbionis* J115^T frozen in trehalose (HFD Live J115) and mice fed a control diet or a HFD and treated by daily oral gavage with vehicle. **e**, *D. welbionis* concentration estimated by quantitative PCR in the faeces of mice 16 and 72h after the last oral force feeding with live *D. welbionis* J115^T frozen in trehalose or with vehicle. **f**, Heatmap of the relative expression measured by qPCR of 3 inflammation markers (*Il-1b*, *Tnfα* and *Cxcl1*) in the jejunum, the ileum and the colon of the mice. Number of mice per group: 10 to 12. Results are represented as dot-plots with mean for **a-e** and as heatmap (mean of fold-change *vs* control diet group) for **f**. Data were analysed using one-way ANOVA followed by Tukey's post hoc test. ** q < 0.01; ***q < 0.001.



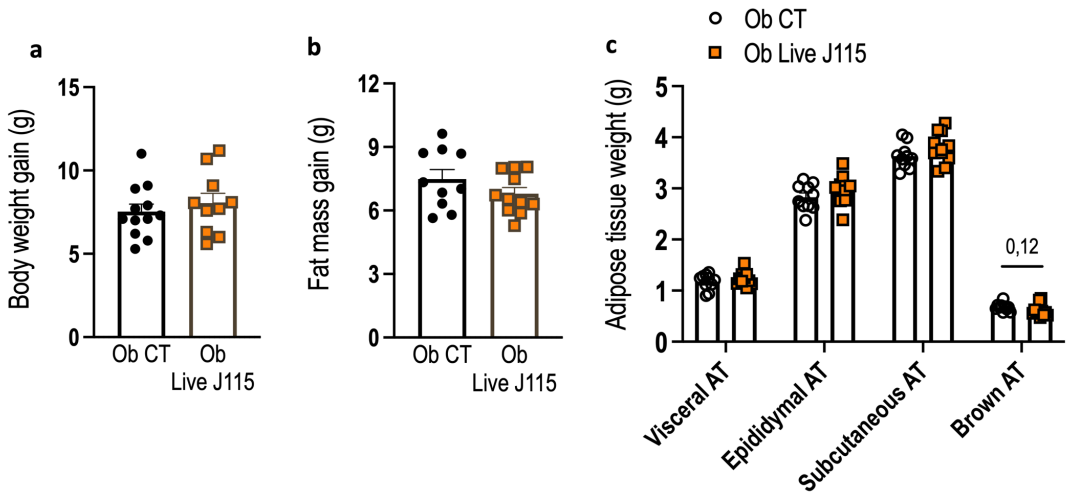
Supplementary Figure S4. Gene ontologies with an upregulated number of transcripts (RNAseq) in the interscapular brown adipose tissue of HFD-fed mice in comparison with HFD-fed mice supplemented with live *D. welbionis* J115^{T} frozen in trehalose during 13 weeks. False discovery rate (FDR) < 0.01.



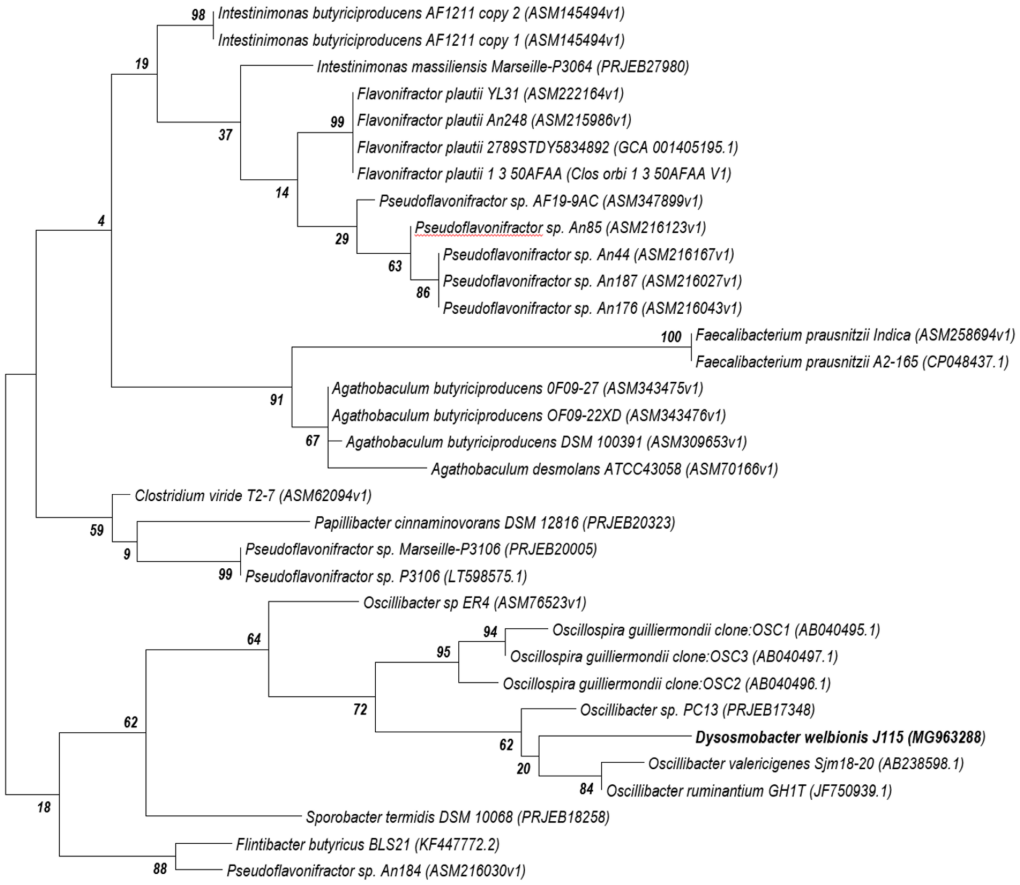
Supplementary Figure S5. Live *D. welbionis* J115^T impact on body weight, body composition and brown adipose tissue characteristics after 3 weeks of treatment (experiment 4). **a**, Body weight, **b**, fat mass, **c**, interscapular brown adipose tissue weight of mice fed a HFD and treated during 3 weeks by daily oral gavage with live *D. welbionis* J115^T frozen in trehalose (HFD Live J115) and mice fed a HFD and treated by daily oral gavage with vehicle (experiment 4). **d**, Percentage of white area on the slices, corresponding to lipid droplets, in the BAT. Number of mice per group: 7. Results are represented as bar-plots and dot-plots with mean ± SEM for **c-d.**



Supplementary Figure S6. Live *D. welbionis* J115^T does not affect short-chain fatty acids levels in portal blood and in caecal content 20 to 24 hours after last administration. **a**, Acetate, **b**, Propionate, **c**, Butyrate, **d**, Isobutyrate, **e**, 2-Methylbutyrate, **f**, Valerate, and **g**, Isovalerate concentrations in the portal plasma of mice treated during 13 weeks by daily oral gavage with live *D. welbionis* J115^T frozen in trehalose and fed a HFD (HFD Live J115) and mice fed a control diet. Last gavage was performed at 5 pm the day before the sacrifice. **h**, Acetate, **i**, Propionate, **j**, Butyrate, **k**, Isobutyrate, **l**, 2-Methylbutyrate, **m**, Valerate, and **n**, Isovalerate concentrations in the caecal content. Number of mice per group: 8 to 12. Results are represented as dot-plots with median. Data were analysed using one-way ANOVA followed by Tukey's post hoc test.



Supplementary Figure S7. Live *D. welbionis* J115^T did not impact on body weight gain and fat mass gain after 6 weeks of treatment in *ob/ob* mice (experiment 6). **a**, Body weight gain, **b**, fat mass gain, **c**, Visceral (mesenteric), epididymal, subcutaneous (inguinal) and brown adipose tissue (AT) weight of genetically obese *ob/ob* mice fed a CT diet and treated during 6 weeks by daily oral gavage with 1.0 × 10^9 cells of live *D. welbionis* J115^T frozen in trehalose (Ob Live J115) and mice fed a treated by daily oral gavage with vehicle (Ob CT) (experiment 6). Number of mice per group: Ob CT (n = 10) and Ob Live J115 (n = 11). Results are represented as dot-plots and bar-plots with mean +/- SEM.



Supplementary Figure S8. Phylogenetic tree based on 16S rRNA gene sequences, showing the connections between *D. welbionis* and related taxa used to design specific qPCR primers. Bootstrap values based on 1000 replicates are indicated on branch points. Bars, 0.02 substitutions per nucleotide position.