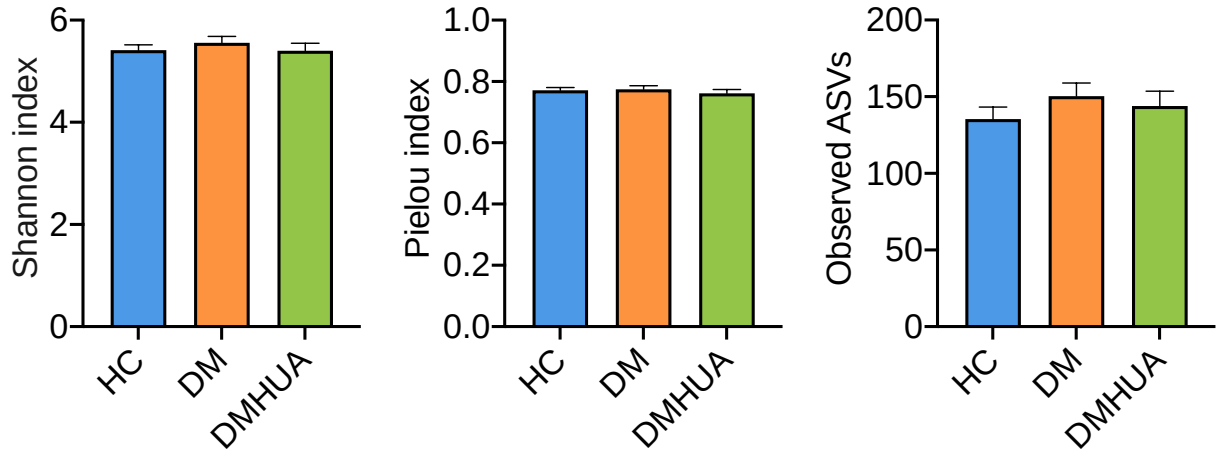
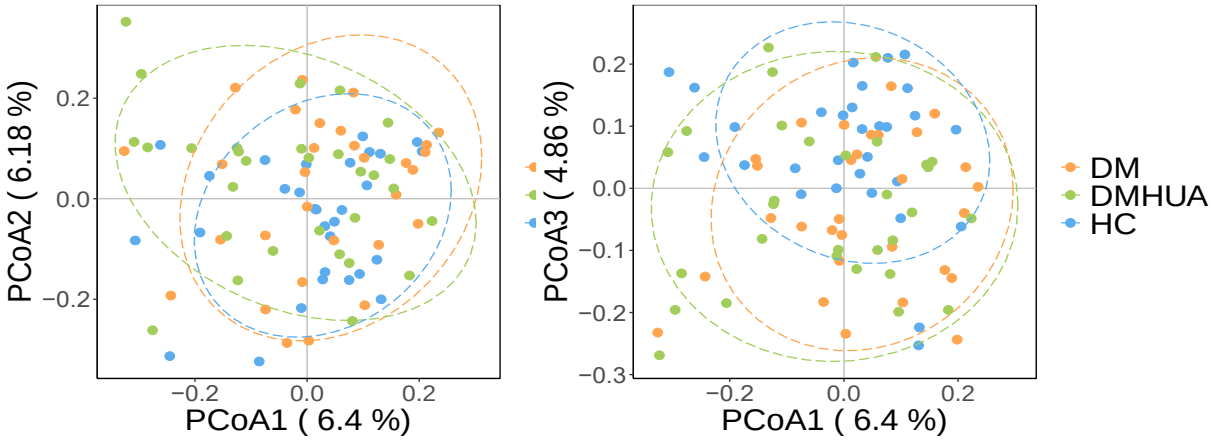
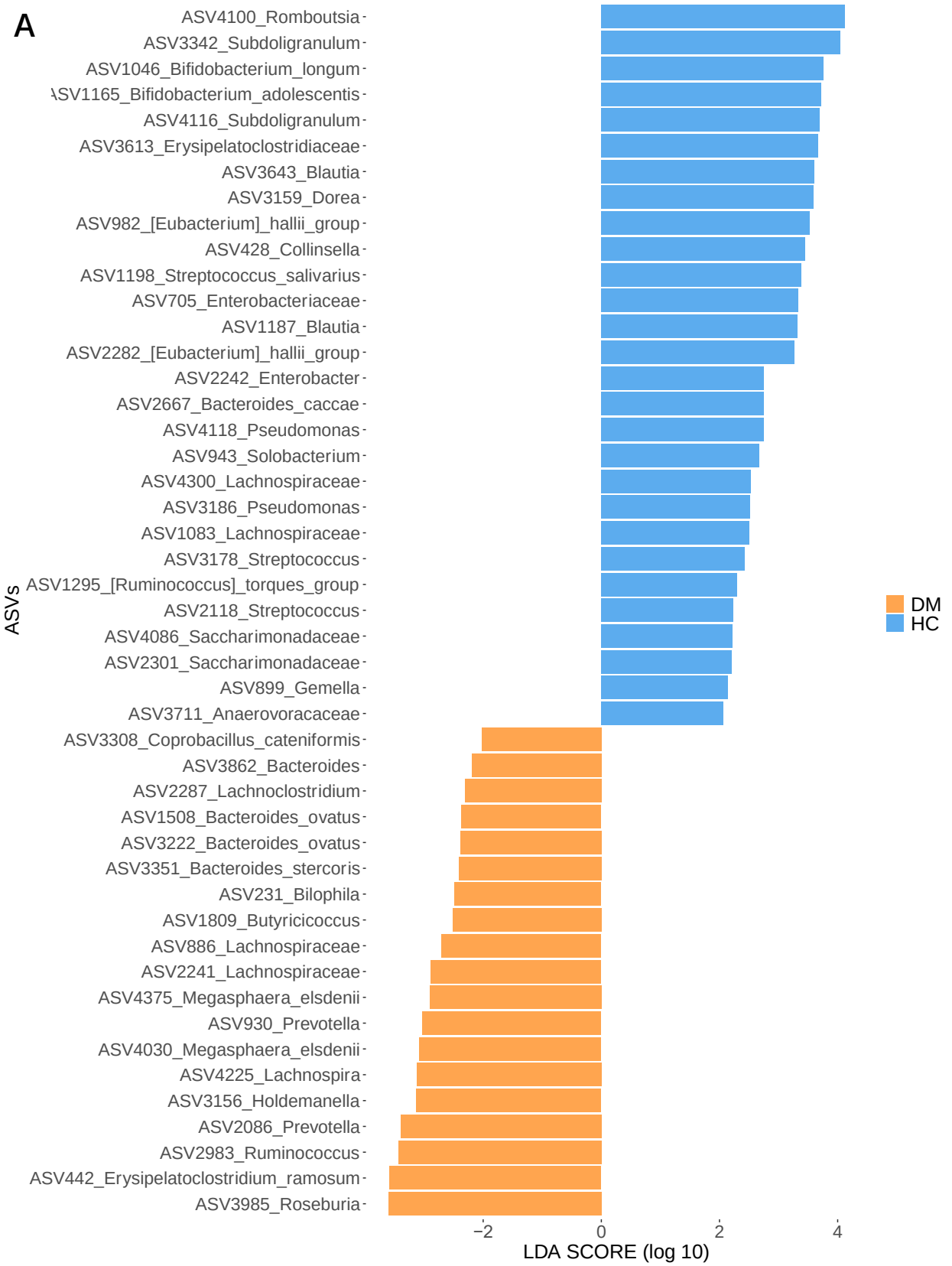


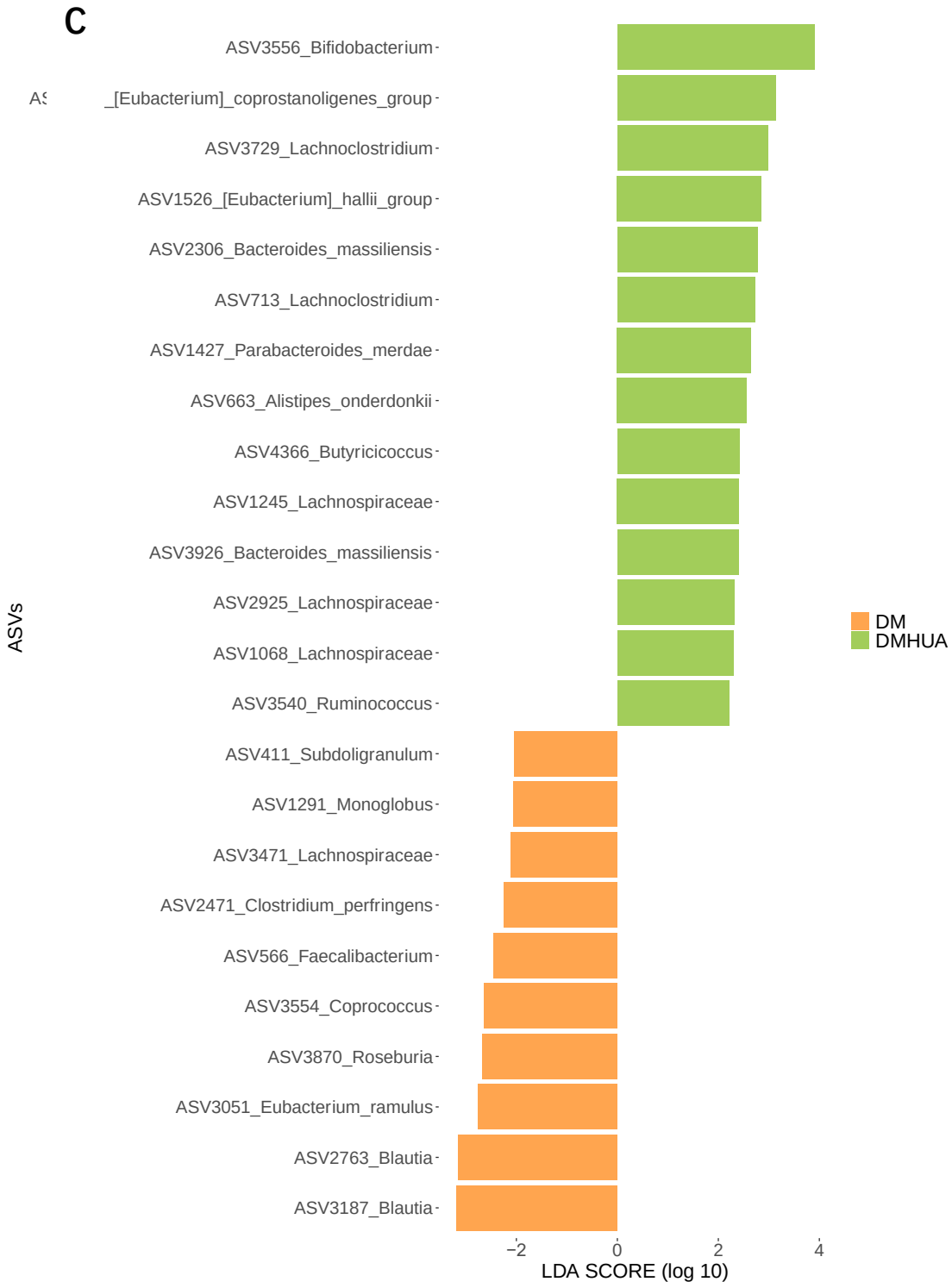
Supplementary Figure 1 Comparison of α-diversity. A: Richness; B: Evenness; C: Diversity among healthy subjects, T2DM, T2DM and HUA groups. Comparisons were performed using the Kruskal-Wallis test with Dunn's post-hoc analysis, for significant differences, the P-value was controlled at 0.05.



Supplementary Figure 2 Comparison of the gut microbiota among healthy subjects, T2DM, T2DM and HUA groups. Principle coordinates performed based on Bray-Burtis distance.

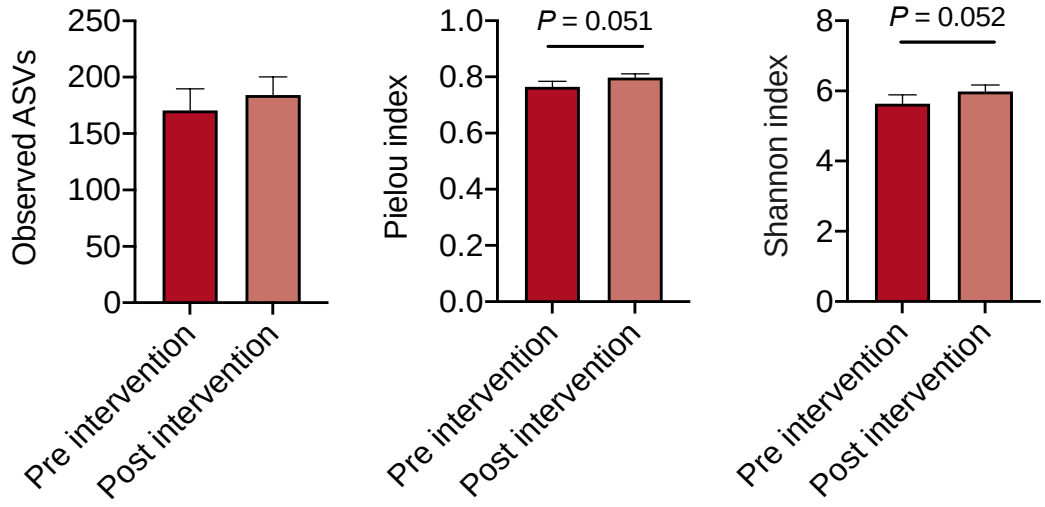

A
ASV4100_Romboutsia
ASV3342_Subdoligranulum
ASV1046_Bifidobacterium_longum
ASV1165_Bifidobacterium_adolescentis
ASV4116_Subdoligranulum
ASV3613_Erysipelatoclostridiaceae
ASV3643_Blautia
ASV3159_Dorea
ASV982_[Eubacterium]_hallii_group
ASV428_Collinsella
ASV1198_Streptococcus_salivarius
ASV705_Enterobacteriaceae
ASV1187_Blautia
ASV2282_[Eubacterium]_hallii_group
ASV2242_Enterobacter
ASV2667_Bacteroides_caccae
ASV4118_Pseudomonas
ASV943_Solobacterium
ASV4300_Lachnospiraceae
ASV3186_Pseudomonas
ASV1083_Lachnospiraceae
ASV3178_Streptococcus
ASV1295_[Ruminococcus]_torques_group
ASV2118_Streptococcus
ASV4086_Saccharimonadaceae
ASV2301_Saccharimonadaceae
ASV899_Gemella
ASV3711_Anaerovoracaceae
ASV3308_Coprobacillus_cateniformis
ASV3862_Bacteroides
ASV2287_Lachnoclostridium
ASV1508_Bacteroides_ovatus
ASV3222_Bacteroides_ovatus
ASV3351_Bacteroides_stercoris
ASV231_Bilophila
ASV1809_Butyricicoccus
ASV886_Lachnospiraceae
ASV2241_Lachnospiraceae
ASV4375_Megasphaera_elsdenii
ASV930_Prevotella
ASV4030_Megasphaera_elsdenii
ASV4225_Lachnospira
ASV3156_Holdemanella
ASV2086_Prevotella
ASV2983_Ruminococcus
ASV442_Erysipelatoclostridium_ramosum
ASV3985_Roseburia
ASVs
−2
0
2
4
LDA SCORE (log 10)
DM
HC


B
ASV4100_Romboutsia
ASV3159_Dorea
ASV3643_Blautia
ASV3613_Erysipelatoclostridiaceae
ASV4116_Subdoligranulum
ASV935_Anaerostipes
ASV1187_Blautia
ASV887_Blautia
ASV884_Anaerostipes
ASV1198_Streptococcus_salivarius
ASV1526_[Eubacterium]_hallii_group
ASV705_Enterobacteriaceae
ASV2282_[Eubacterium]_hallii_group
ASV3553_Klebsiella
ASV2109_Anaerostipes
ASV4446_Clostridium_sensu_stricto_1
ASV3303_Clostridium_sensu_stricto_1
ASV3941_Klebsiella
ASV3554_Coprococcus
ASV2667_Bacteroides_caccae
ASV1469_Turicibacter
ASV4118_Pseudomonas
ASV4315_Lactococcus_lactis
ASV3299_Blautia
ASV3186_Pseudomonas
ASV507_Lachnospiraceae
ASV3270_Anaerovoracaceae
ASV4086_Saccharimonadaceae
ASV1420_Leuconostoc_lactis
ASV1168_Phocea
ASV2269_Bacteroides_clarus
ASV1079_Agathobacter
ASV1286_Christensenellaceae
ASV3088_Alistipes
ASV1291_Monoglobus
ASV2236_[Clostridium]_innocuum_group
ASV4002_Prevotella
ASV231_Bilophila
ASV663_Alistipes_onderdonkii
ASV2287_Lachnoclostridium
ASV1575_[Eubacterium]_ventriosum_group
ASV120_Phascolarctobacterium_faecium
ASV1728_Dorea
ASV886_Lachnospiraceae
ASV1506_Tyzzerella
ASV2938_Lachnospiraceae
ASV3777_Bacteroides
ASV713_Lachnoclostridium
ASV4030_Megasphaera_elsdenii
ASV3351_Bacteroides_stercoris
ASVs
−2
0
2
4
LDA SCORE (log 10)
DMHUA
HC

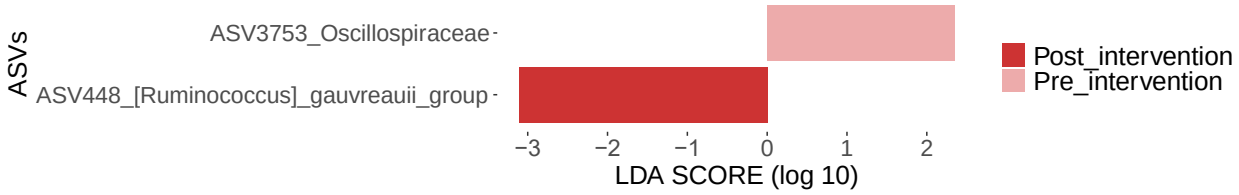


Supplementary Figure 3 Identification of major amplicon sequence variants contributing to the differences in the gut microbiota of patients with T2DM and HUA with other cohorts using LEfSe. (A) ASVs contributing to the differences between healthy subject and patients with T2DM. (B) ASVs contributing to the differences

between healthy subject and patients with T2DM and HUA. (C)ASVs contributing to the differences between T2DM with or without HUA.



Supplementary Figure 4 Comparison of α-diversity. A; Richness; B: Evenness; C: Diversity between patients before and after empagliflozin treatment. Comparisons were performed using the Kruskal-Wallis test, for significant differences, the P-value was controlled at 0.05.



Supplementary Figure 5 Identification of major amplicon sequence variants (ASVs) contributing to the differences in the gut microbiota of patients with T2DM and HUA before and after empagliflozin treatment using LEfSe.