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| Title | Microbiome and metabolome modifying effects of several cardiovascular disease interventions in apo-E ^{-/-} mice |
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ONLINE SUPPLEMENTAL MATERIAL

Supplementary Figure S1 – Phylum relative abundances of intervention and control groups. (i) *Phylum relative abundances, with inset plots representing phyla in which a significant difference between HFC and another group has been identified. * ($p < 0.05$) and ** ($p < 0.01$) represent significant differences recorded between HFC and one of the interventions, or NC. Plots depict individual replicates with mean and SEM, and dashed lines depict the HFC mean for use as comparison.*

Supplementary Figure S2 – Family relative abundances of intervention and control groups. *Column A inset plots represent families that contain species capable of converting choline into pro-atherogenic TMA. Column B represents families containing species known to produce SCFA, which interact with host cardiometabolic health. Column C represents families containing other species of interest for host metabolic and immunological health. * ($p < 0.05$) and ** ($p < 0.01$) represent significant differences recorded between HFC and one of the interventions, or NC. Plots depict individual replicates with mean and SEM, and dashed lines depict the HFC mean for use as comparison.*

Supplementary Figure S3 – Genus relative abundances of intervention and control groups. *Genus relative abundances, with inset plots representing genera in which a significant difference between HFC and another group has been identified. * ($p < 0.05$) and ** ($p < 0.01$) represent significant differences recorded between HFC and one of the interventions, or NC. Plots depict individual replicates with mean and SEM, and dashed lines depict the HFC mean for use as comparison.*

Supplementary Figure S4 – Faecal metabolome important features associated with each cardiovascular disease intervention. *The faecal metabolites found to be most important in explaining shifts in PLS-DA for each intervention (PSE [A], OBG [B], BSH [C] and STAT [D]) when compared to the HFC.*

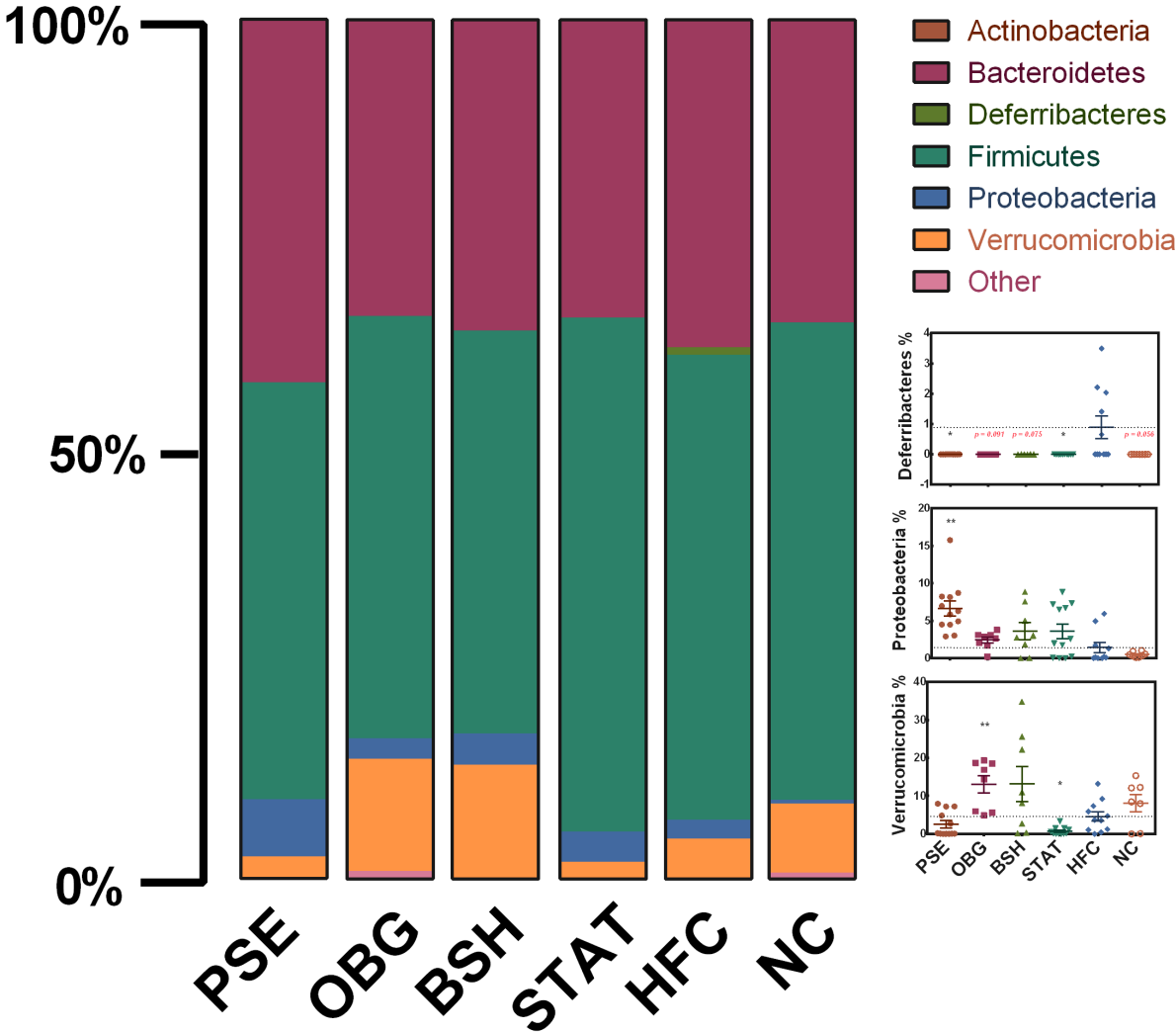
Supplementary Figure S5 – Serum metabolome important features associated with each cardiovascular disease intervention. *The serum metabolites found to be most important in explaining shifts in PLS-DA for each intervention (PSE [A], OBG [B], BSH [C] and STAT [D]) when compared to the HFC.*

Supplementary Figure S6 – Correlation heatmap containing physiological, microbiome and faecal metabolome data.

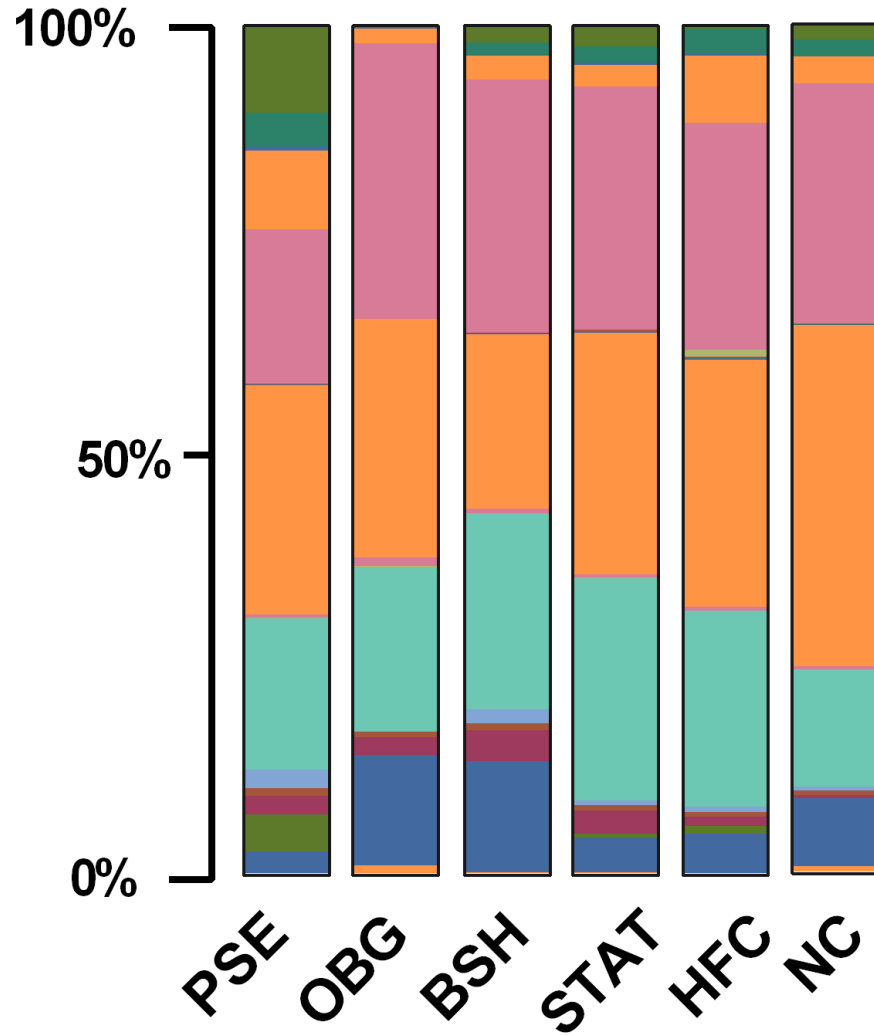
Supplementary Figure S7 – Correlation coefficient analysis plots of primary physiological outcomes with microbiome and faecal metabolome. *Several important metabolic markers are displayed with the microbial taxa and metabolites most correlated (Cholesterol [A], Plaque [B], TAG [C] and IAP [D]). * FDR adjusted $p < 0.05$.*

Supplementary Table S1 – Alpha diversity of intervention and control groups. *Means in a row with common superscripts do not differ ($P \geq 0.05$).*

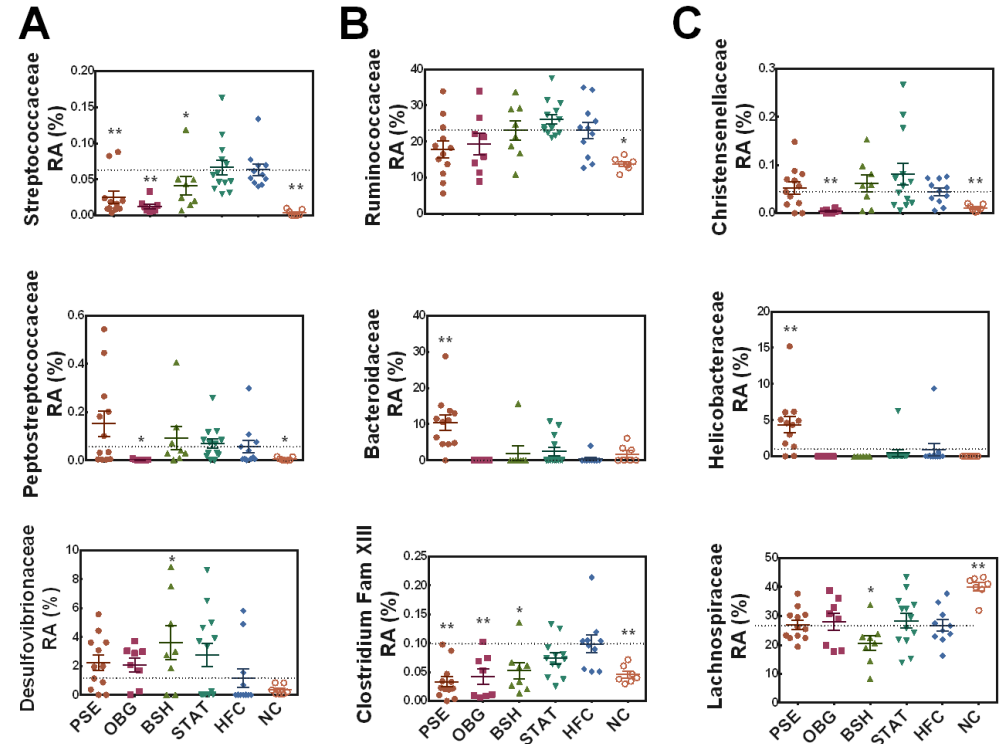
SUPPLEMENTARY FIGURE S1



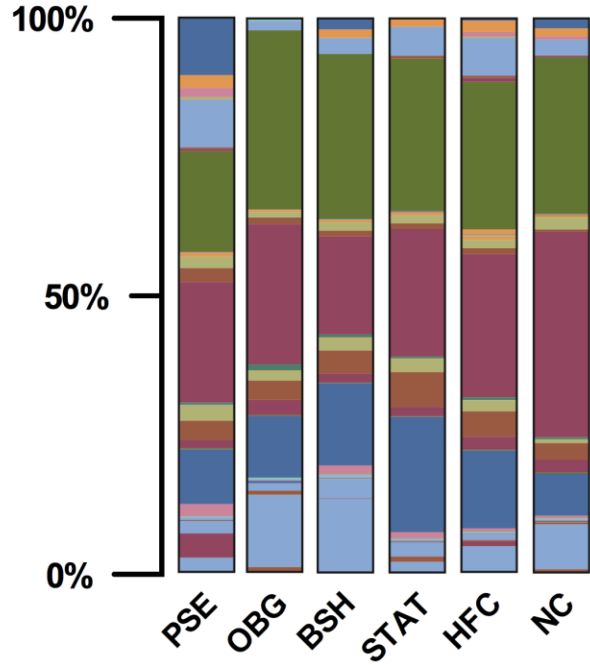
SUPPLEMENTARY FIGURE S2



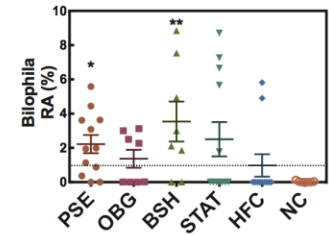
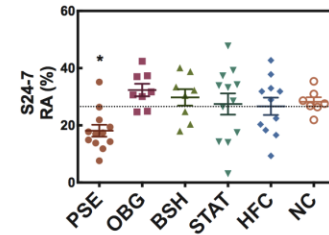
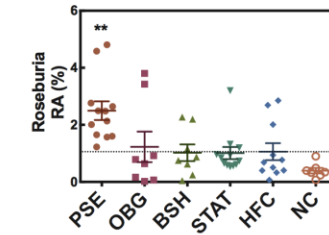
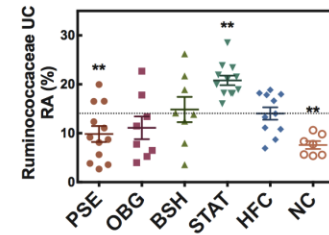
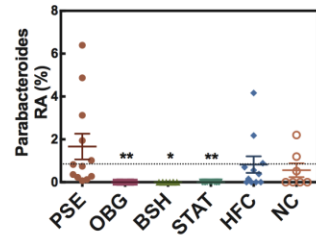
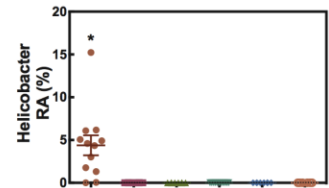
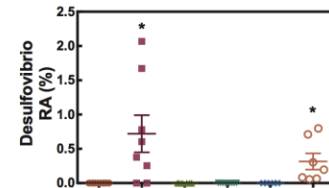
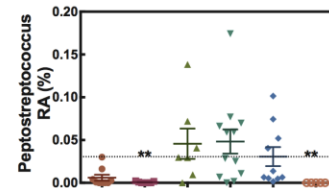
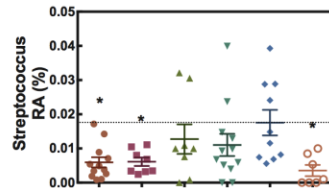
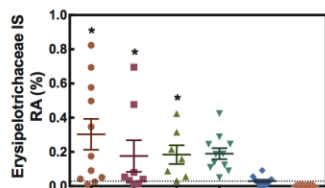
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- Coriobacteriaceae
- Bacteroidaceae
- Porphyromonadaceae
- Prevotellaceae
- Rikenellaceae
- S24-7
- Bacillaceae
- Lactobacillaceae
- Streptococcaceae
- Christensenellaceae
- Clostridiaceae
- Clostridium_Family_XIII_IS
- Lachnospiraceae
- Peptococcaceae
- Peptostreptococcaceae
- Ruminococcaceae
- Clostridiales_uncultured
- Erysipelotrichaceae
- Desulfovibrionaceae
- Helicobacteraceae
- Enterobacteriaceae
- Verrucomicrobiaceae
- Other



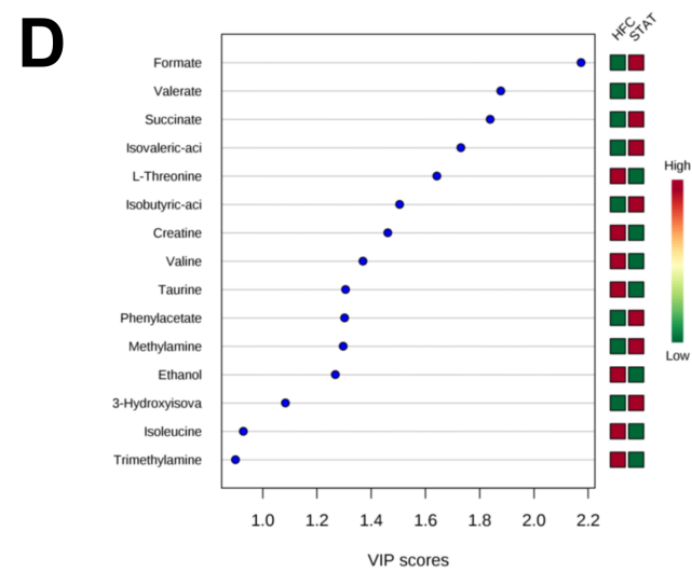
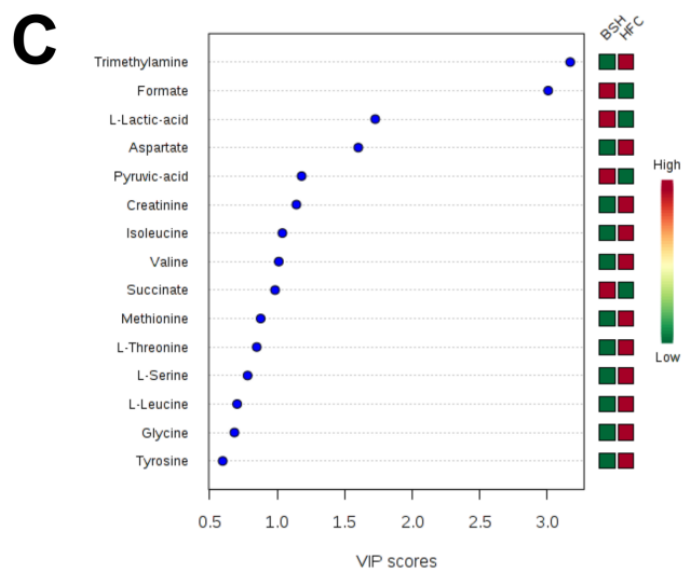
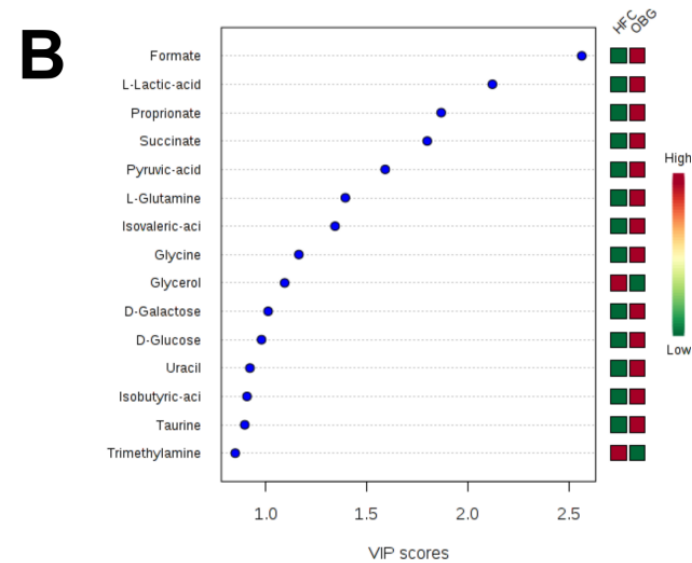
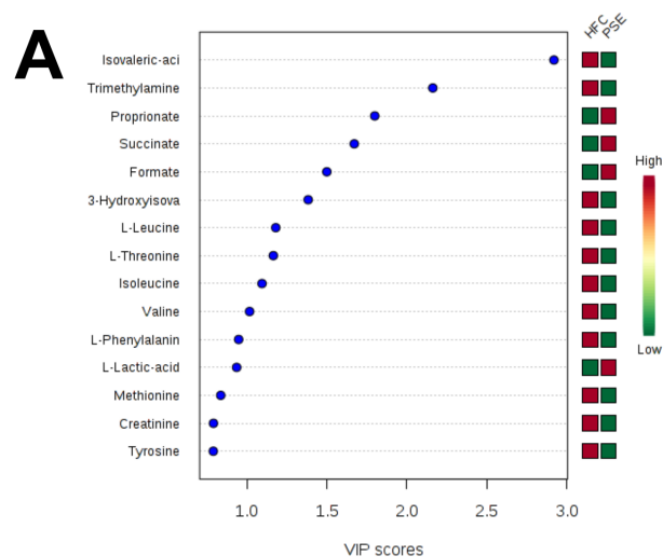
SUPPLEMENTARY FIGURE S3



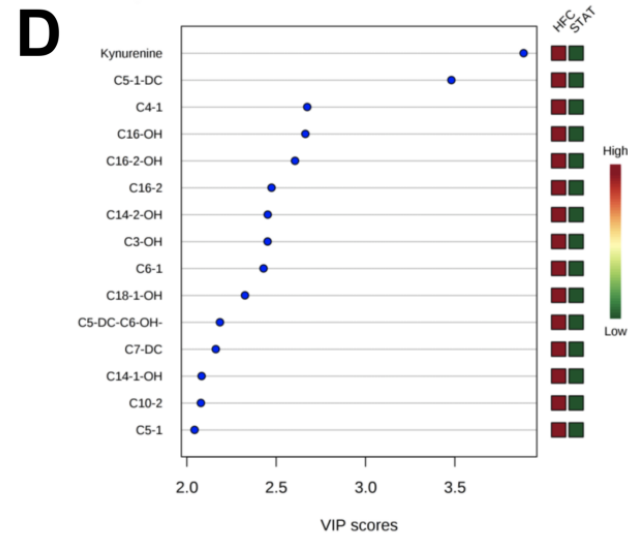
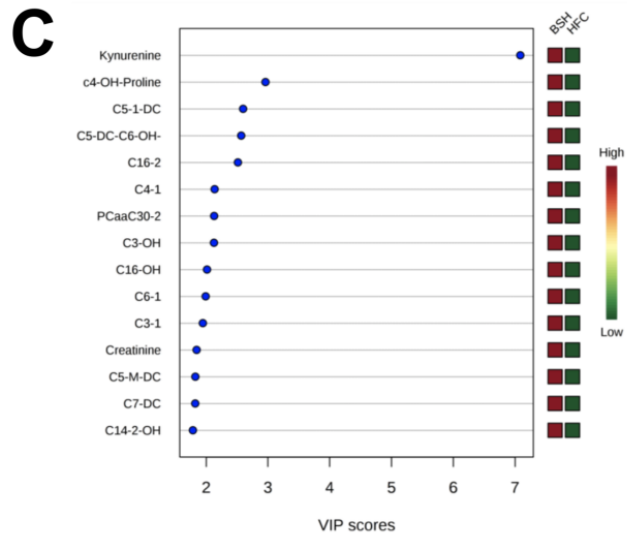
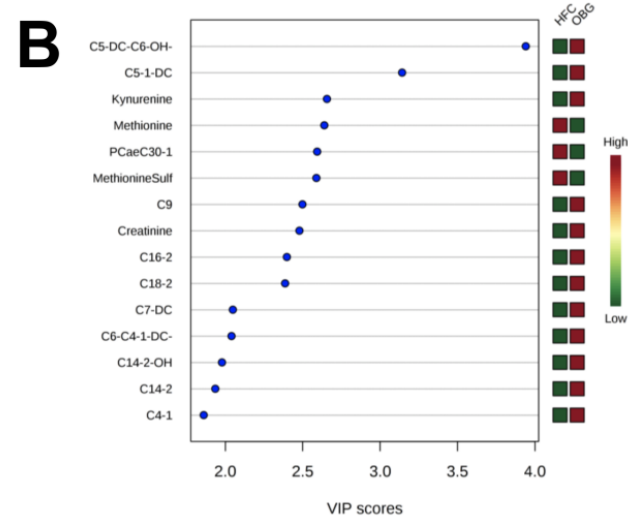
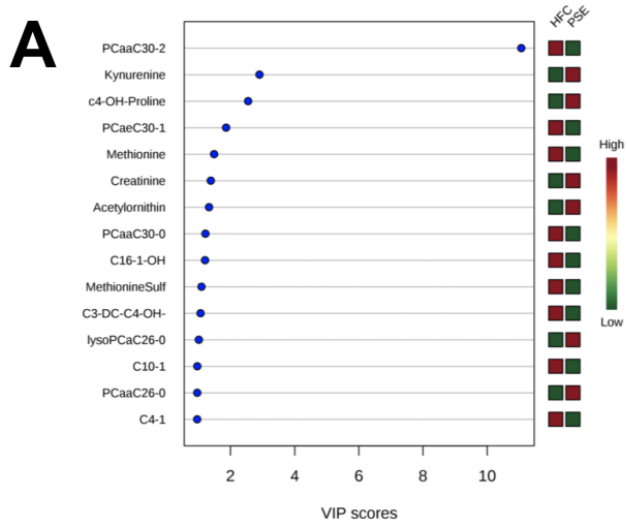
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- Coriobacteriaceae__Enterorhabdu
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- Porphyromonadaceae__Odoribacte
- Porphyromonadaceae__Parabacteroide
- Prevotellaceae__Prevotell
- Rikenellaceae__Alistpe
- Rikenellaceae__RC9_gut_grou
- Rikenellaceae__Rikenell
- S24-7__uncultured_bacteriu
- Deferribacteraceae__Mucispirillum__uncultured_bacteriu
- Bacillaceae__Anoxybacillu
- Staphylococcaceae__Staphylococcu
- Enterococcaceae__Enterococcu
- Lactobacillaceae__Lactobacillu
- Streptococcaceae__Lactococcu
- Streptococcaceae__Streptococcu
- Christensenellaceae__Christensenell
- Christensenellaceae__unculture
- Clostridiaceae__Candidatus__Arthromitu
- Clostridiaceae__Clostridiu
- Family_XII_Incertae_Sedis__Anaerovorax
- Family_XII_Incertae_Sedis__Incertae_Sedis
- Family_XII_Incertae_Sedis__unculture
- Lachnospiraceae__Anaerostipe
- Lachnospiraceae__Coproccocu
- Lachnospiraceae__Incertae_Sedi
- Lachnospiraceae__Marvinbryant
- Lachnospiraceae__Rosebur
- Lachnospiraceae__unculture
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- Peptococcaceae__unculture
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- Peptostreptococcaceae__unculture
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- Ruminococcaceae__Hydrogenoanaerobacteriu
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- Erysipelotrichaceae__Turicibacte
- Erysipelotrichaceae__unculture
- Rhizobiaceae__Rhizobiu
- Rhodospirillaceae__Thalassospir
- Burkholderiaceae__Ralstoni
- Helicobacteraceae__Helicobacte
- Desulfovibrionaceae__Desulfovibri
- Comamonadaceae__Delli
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- Enterobacteriaceae__Enterobacte
- Desulfovibrionaceae__Bilophi
- Akkerman
- Coriobacteriaceae__Adlercreutz
- Prevotellaceae__unculture
- Mycoplasmataceae__Ureaplasma
- Lachnospiraceae__Blaut
- Ruminococcaceae__Anaeroflu
- Ruminococcaceae__Flavonifab
- Pasteurellaceae__Pasteurell
- Coriobacteriaceae__Adlercreutz
- Lachnospiraceae__Anaeroporobacte
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- Aerococcaceae__Aerococcu
- Moraxellaceae__Acinetobacte
- Prevotellaceae__unculture
- Lachnospiraceae__Acellibaculu
- Clostridium__uncultured__uncultured_Clostridiales_bacteriu
- Clostridium__uncultured__uncultured_rumen_bacteriu
- mibochondria__tidispermu
- Anaeroplasmataceae__Anaeroplasm
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SUPPLEMENTARY FIGURE S4



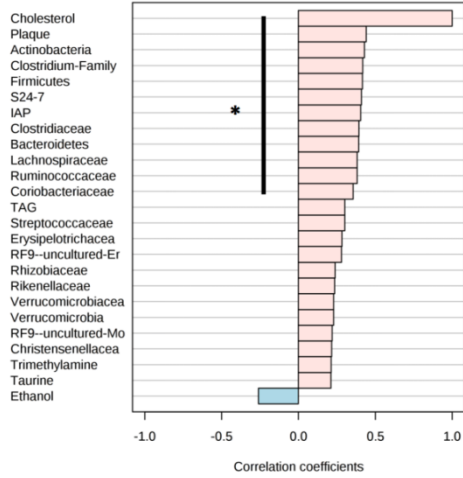
SUPPLEMENTARY FIGURE S5



SUPPLEMENTARY FIGURE S7

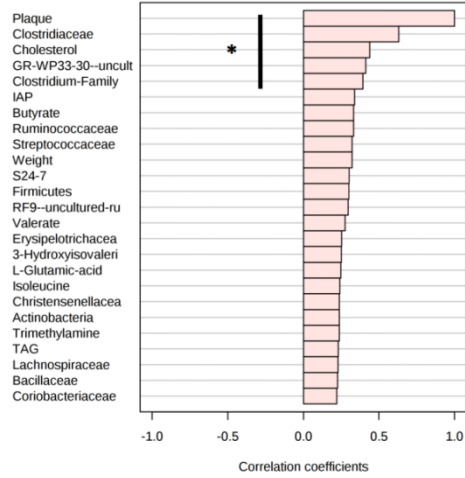
A

Top 25 compounds correlated with the Cholesterol



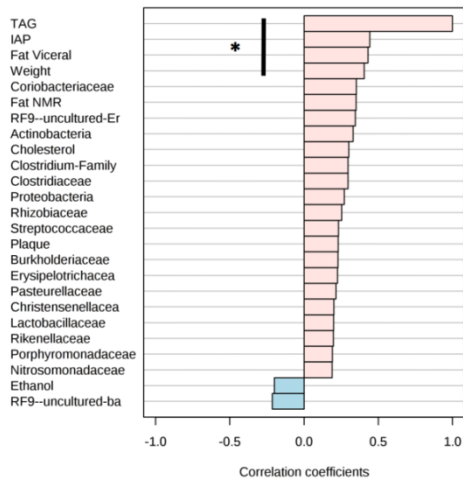
B

Top 25 compounds correlated with the Plaque



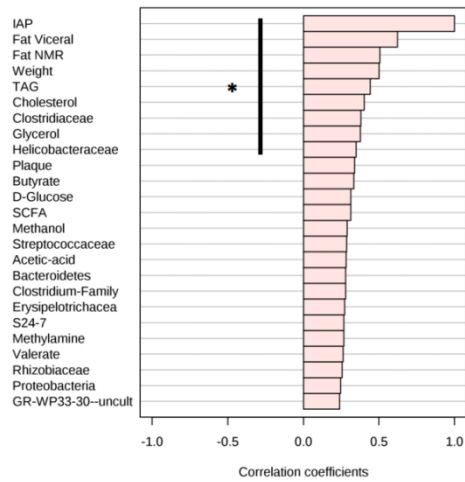
C

Top 25 compounds correlated with the TAG



D

Top 25 compounds correlated with the IAP



SUPPLEMENTARY TABLE S1

| | PSE | OBG | BSH | STAT | HFC | NC |
|-------------------------|----------------------|----------------------|---------------------|----------------------|----------------------|---------------------|
| Chao1 | 276.75 ^{bc} | 299.85 ^{bc} | 266.90 ^c | 290.15 ^{bc} | 315.39 ^{bc} | 443.73 ^a |
| Simpsons | 0.95 ^{ab} | 0.95 ^{ab} | 0.93 ^b | 0.95 ^{ab} | 0.96 ^{ab} | 0.97 ^a |
| Shannon | 5.30 ^{bc} | 5.39 ^{bc} | 5.09 ^c | 5.31 ^{bc} | 5.62 ^{bc} | 6.13 ^a |
| PD Whole Tree | 13.96 ^d | 15.85 ^{bc} | 13.85 ^d | 14.53 ^{cd} | 16.39 ^b | 22.45 ^a |
| Observed Species | 230.33 ^{cd} | 259.88 ^{bc} | 218.50 ^d | 238.08 ^{cd} | 271.64 ^b | 397.14 ^a |