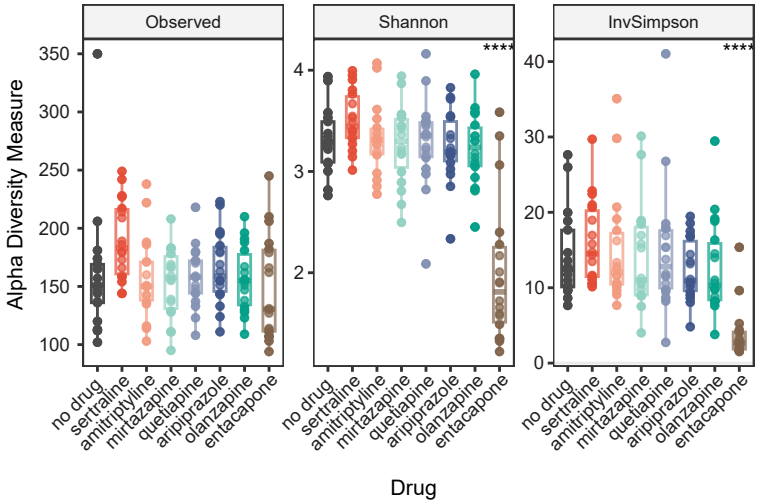
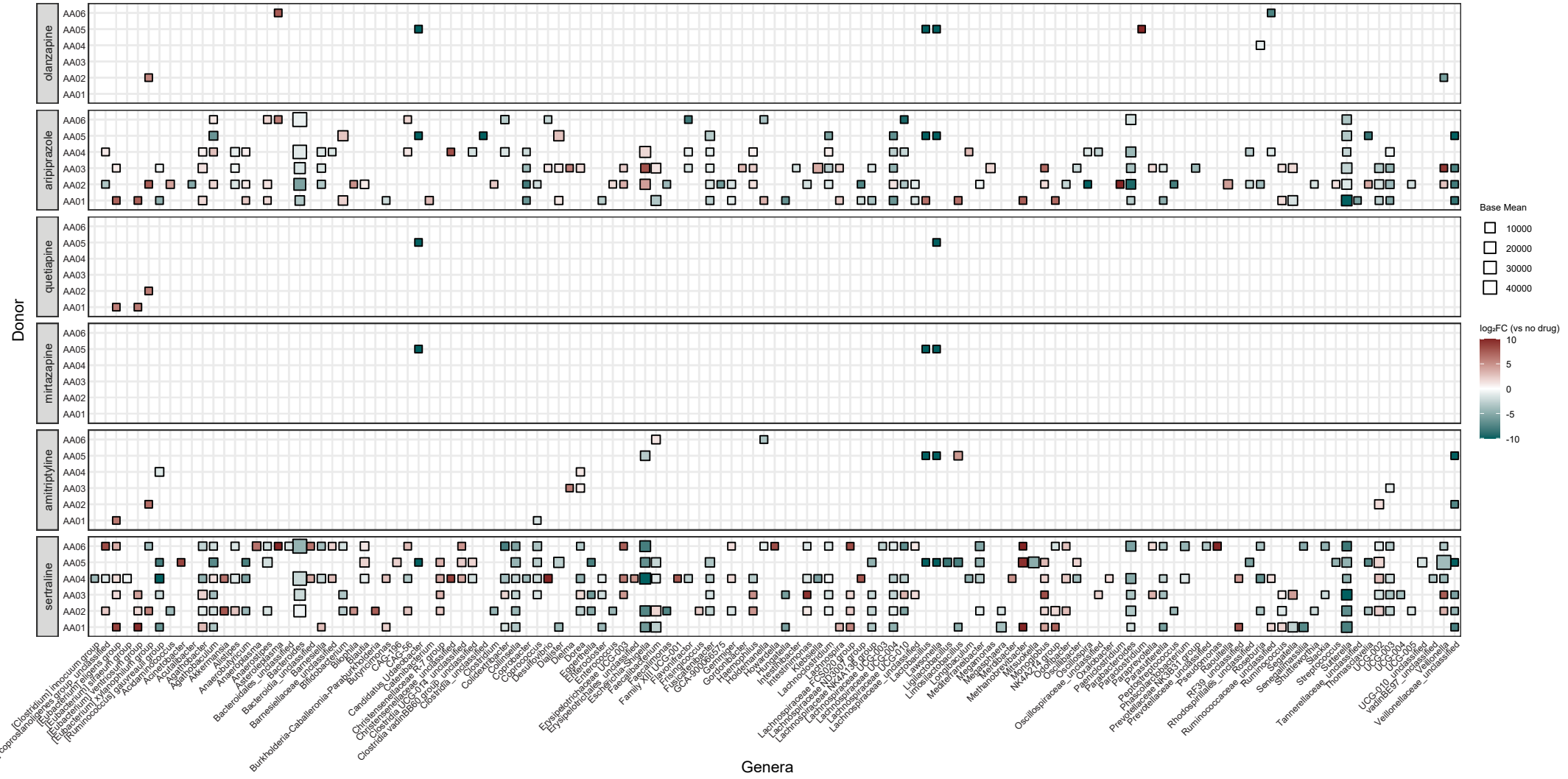
Psychotropic medications selectively reshape the human gut microbiota and alter neuroactive metabolite production

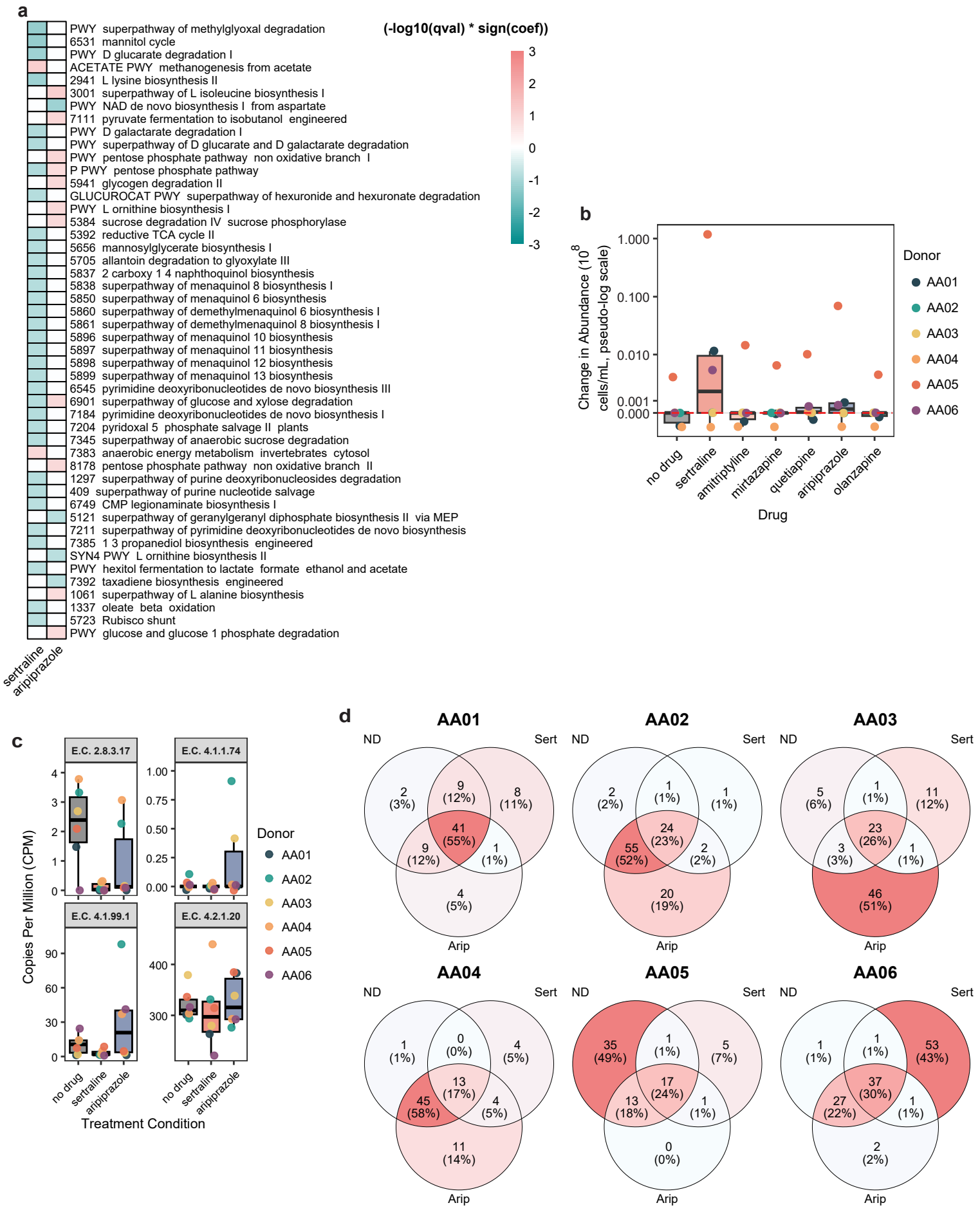
Supplementary Figure File



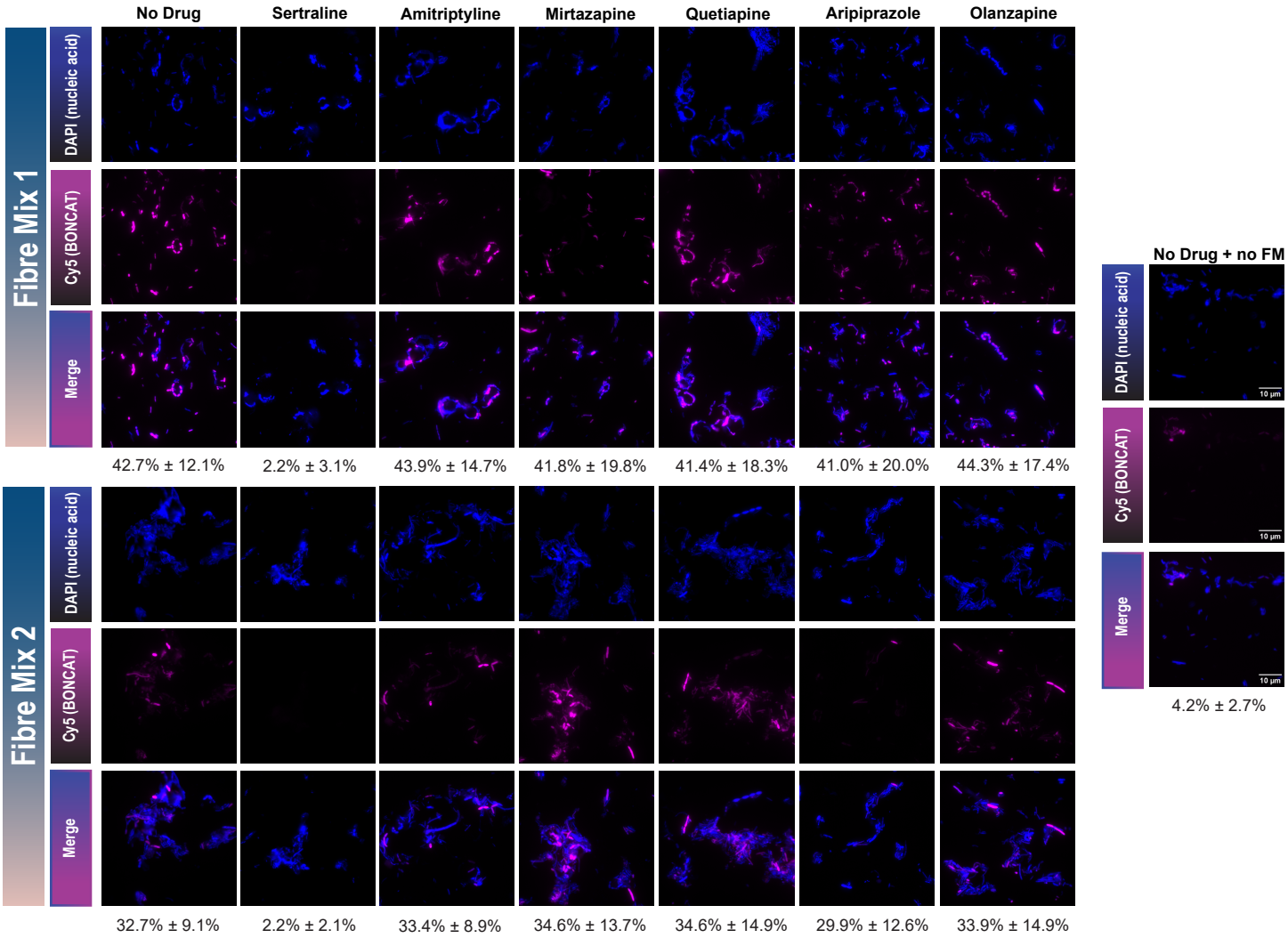
Supplementary Fig. 1: Amendment of faecal samples with psychotropic drugs influenced microbiome alpha diversity. Measures of alpha diversity (observed species, Shannon index and Inverse Simpson index) of faecal microbiome communities sampled 24 h post drug amendment and assessed by 16S rRNA gene amplicon sequencing (data in Supplementary Table 4). Boxes represent the median, first and third quartiles. Whiskers extend to the highest and lowest values that are within 1.5× the interquartile range (3 replicates per donor; n = 6) and significant differences calculated from unpaired two-sided t-test with 'no drug' used as the reference group. Only statistically significant differences are indicated with asterisks: ****$P < 0.0001$.



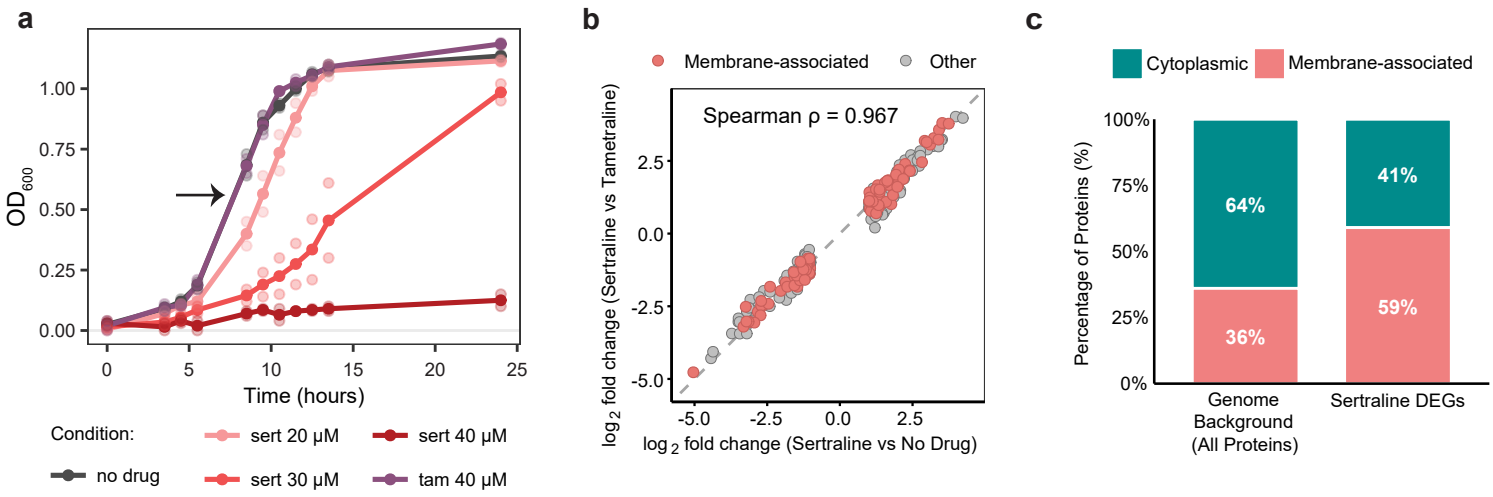
Supplementary Fig. 2: Psychotropic amendment of faecal samples drove shifts in microbial genera. DESeq2 differential abundance analysis of 16S rRNA gene amplicon sequencing of microbiome samples following 24 h incubation with drugs. Only statistically significant genera with **Padj* < 0.05 are displayed.



Supplementary Fig. 3: Sertraline and aripiprazole altered the functional potential and resistome of the gut microbiome within 24 hours of exposure. **a**, Heatmap of MaAsLin2 associations between unstratified pathway abundances (HUMAnN) and drug amendment. Only top 50 significant associations sorted by **Padj* are displayed. **b**, Net change in the absolute abundance of ASV_109_Methanobrevibacter_unclassified from 0 h to 24 h in faecal incubations of donors AA01 - AA06 (as assessed by 16S rRNA gene amplicon sequencing). **c**, Data show abundance of specified E.C. numbers related to microbial indole production. Box plots represent medians and interquartile ranges; coloured points indicate paired individual donors (n=6). Paired Wilcoxon tests against the no drug control with non-significant results hidden. **d**, Shared and unique antibiotic resistance ontology (ARO) terms by donor across the different treatment conditions as assessed by RGI using the CARD database. ND = no drug; Sert = sertraline; Arip = aripiprazole.



Supplementary Fig. 4: Bioorthogonal non-canonical amino acid tagging (BONCAT) activity visualised by fluorescence microscopy. Representative images from donor AA06 following incubation with fibre mixes and drugs, followed by BONCAT labelling. Indicated percentages represent the mean active cell fraction pooled across all 6 donors for each drug/fibre combination (± SD). The percentage for 'No Drug + no FM' was calculated from donor AA06 only. FM = Fibre Mix.



Supplementary Fig. 5: Sertraline inhibited growth of *Bacteroides ovatus* and enriched for membrane-associated proteins among differentially expressed genes. a, Growth of *B. ovatus* over time in the presence of increasing concentrations of sertraline (sert) and a fixed concentration of tametraline (tam). The arrow indicates the mid-exponential timepoint of sample collection for the transcriptomics experiment. **b**, Log_2 fold changes for genes differentially expressed in sertraline versus no drug ($|log_2FC| > 1$, adjusted $p < 0.05$) were compared with the corresponding log_2 fold changes for sertraline versus tametraline. Membrane-associated proteins, defined by PSORTb predictions as cytoplasmic membrane, outer membrane, periplasmic or extracellular, are highlighted in coral; other differentially expressed genes are shown in grey. The dashed line indicates $y = x$. Spearman's rank correlation ($\rho = 0.967$) indicates strong concordance between the two comparisons. **c**, Percentage of proteins predicted to be cytoplasmic or membrane-associated, using PSORTb, for the entire genome background of *B. ovatus* versus differentially expressed genes (DEGs) with sertraline treatment.