Supporting Information

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Toward a Deeper Understanding of Gut Microbiome in Depression: The Promise of Clinical Applicability

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Towards a deeper understanding of gut microbiome in depression: 
the promise of clinical applicability

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| Study | People | Study design | groups | Age (years) | Sex (M/F) | BMI | Patients Control | Microbial biomarkers | Drug treatment in patients | Diagnostic criteria | Severity measures | Sample | Storage | Gut microbiome estimation | Sequencing region | Microbial biomarkers selection |
|-------|--------|--------------|--------|-------------|-----------|-----|------------------|----------------------|------------------------|----------------------|---------------------|--------|---------|---------------------------|-----------------|-----------------------------|
| Xu et al. 2010 | Chinese | Case-control | MDD (N=85) controls (N=137) | 35.63±17.50 | 18/38 | 21.96±2.99 | NA | NA | Fecal samples | LEfSe: p < 0.05 and LDA > 2.0 | | V3-V4 | MDD and Controls | LEfSe: p < 0.05 and LDA > 2.0 |
| Bai et al. 2012 | Chinese | Case-control | MDD (N=69) controls (N=105) | 35.18±17.59 | 18/30 | 21.46±2.71 | NA | NA | Fecal samples | LEfSe: p < 0.05 and LDA > 2.0 | | V3-V4 | MDD and Controls | LEfSe: p < 0.05 and LDA > 2.0 |
| Chen et al. 2019 | Japanese | Case-control | MDD (N=160) | 41.83±12.71 | 12/5 | 22.81±2.1 | NA | NA | Fecal samples | LEfSe: p < 0.05 and LDA > 2.0 | | V3-V4 | MDD and Controls | LEfSe: p < 0.05 and LDA > 2.0 |
| | | | UC with depression and UC | | | | | | | | | | | | |
| | | | One-way analysis of variance (ANOVA) with Tukey-Kramer test: p < 0.05 | | | | | | | | | | | | |
| Authors | Year(s) | Country | Study Design  | Sample Size | Sample Characteristics | Methods | Findings | Other Notes |
|---------|---------|---------|---------------|-------------|-----------------------|---------|----------|------------|
| Chen Y et al. | 2017(10) | Chinese | Case-control | MDD (N=92) Control (N=85) | Demographic | 16S rRNA gene sequencing, Illumina MiSeq platform | 53.12(17.82) vs 50.91(17.24) | V4 | Cross-sectional associations with depression symptom measures; Linear regression model: p < 0.05 |
| Chen Y et al. | 2021(10) | Chinese | Cross-sectional associations | Depression (N=319) | Demographic | 16S rRNA gene sequencing, Illumina MiSeq platform | 55.96(9.86) vs 52.63(11.46) | V4 | Cross-sectional associations with depression symptom measures; Linear regression model: p < 0.05 |
| Heym N et al. | 2020(17) | Italian | Case-control | MDD (N=54) Control (N=100) | Demographic | 16S rRNA gene sequencing, Illumina MiSeq platform | 58.58(4.57) vs 57.36(8.46) | V4 | Cross-sectional associations with depression symptom measures; Linear regression model: p < 0.05 |
| Hyun N et al. | 2019(10) | English | Cross-sectional associations | Depression (N=40) | Demographic | 16S rRNA gene sequencing, Illumina MiSeq platform | 36.38(14.63) vs 36.76(10.22) | V4 | Cross-sectional associations with depression symptom measures; Linear regression model: p < 0.05 |
| Hoggard M et al. | 2019(10) | New Zealand | Cross-sectional associations | Chronic rhinosinusitis (N=45) Control (N=12) | Demographic | 16S rRNA gene sequencing, Illumina MiSeq platform | 59.52(24.74) vs 41.92(7.31) | V4 | Cross-sectional associations with depression symptom measures; Linear regression model: p < 0.05 |
| Huang Y et al. 2018[20] | Chinese | Case-control | MDD (N=27) | Control (N=27) | 48.5(12.3) | 42.3(14.1) | 57/20 | 23.6(2.7) | 23.6(2.7) | NA | NA | ICD-10 | _ | _ | Pecial samples | <0.01 | 16S rRNA gene sequencing: Illumina-Hiseq2500 | V3/V4 | First-episode MDD and Controls | LEfSe: p < 0.01 and LDA > 2.0
| Huang Y et al. 2021[21] | Chinese | Case-control | Stroke-cerebrovascular disorder (N=20) | Stroke-cerebrovascular accident (N=20) | 61.3(13.7) | 62.7(12.3) | 20/19 | 21.0(6.8) | 37.2(7.2) | NA | NA | _ | _ | Pecial samples | <0.01 | 16S rRNA gene sequencing: Illumina-MiSeq platform | V3/V4 | Stroke-cerebrovascular disorder and stroke control | LEfSe: p < 0.05 and LDA > 2.0
| Anx W et al. 2019[22] | Spanish | Case-control | Depression: GI (N=15) | Nondepression: GI (N=16) | 18.6(3.8) | 18.8(3.2) | 235/36 | 18.8(2.3) | 18.8(2.3) | 56 | 36 Anxiety, 33 Depression | NA | CDI/22 | CDI | <22 | Pecial samples | <0.01 | 16S rRNA gene Terminal rearrangement fragment length polymorphism (T-RFLP) | _ | Orthodontic Intelligence with depression and controls | Mann-Whitney test and Kruskal-Wallis test: p<0.017
| Jackson MA et al. 2018[23] | English | Cross-sectional associations | Depression(N=554) from all individuals(N=2377) | 60.12% | 40.24% | 58 | 28/75% | 38% | 38% | 51% | 51% | 51% | _ | _ | _ | _ | Pecial samples | <0.01 | 16S rRNA gene sequencing: Illumina-MiSeq platform | V4 | Cross-sectional associations with depression symptoms measures | Beta coefficients of associations: p < 0.05
| Xiong H et al. 2019[24] | Chinese | Case-control | MDD-active (N=29) | MDD-responsive (N=17) | 55% | 55% | 30/14 | 21.6 (3.4) | 29.6 (3.6) | _ | _ | _ | _ | Pecial samples | <0.01 | 16S rRNA gene sequencing: Roche 454 sequencing | V1/V3 | Active MDD: Responding MDD and Controls | LEfSe: p < 0.05 and LDA > 2.0
| Xiong HY et al. 2020[25] | Chinese | Case-control | CDE (N=24) | Control (N=18) | 37.27 (2.0) | 39.88 (2.0) | 13/11 | 22.66 (2.9) | 22.66 (2.9) | _ | _ | _ | _ | Pecial samples | <0.01 | 16S rRNA gene sequencing: Illumina-MiSeq platform | V3/V4 | Patients with current depressive episode (CDE) and controls | LEfSe: p < 0.05 and LDA > 2.0
| Kang Y et al. 2021[26] | Chinese | Case-control | Post-stroke depression (N=67) | Stroke (N=96) | 55.9(8.6) | 55.9(8.6) | 85/78 | _ | _ | Stroke | NA | CCMD-3, HAMD-24, 9, SSRS index ≥ 0.5 | _ | _ | Pecial samples | _ | Exposure to cerebrovascular accidents, stroke, and stroke control | Independent sample t-test: p < 0.05
| Kelly JR et al. 2016[27] | Irish | Case-control | MDD (N=54) | Control (N=53) | 45.8(11.5) | 45.8(11.5) | 20/13 | 23.6(2.7) | 23.6(2.7) | 7 patients: Dysplasia, 3 patients: Hypertension, 5 patients: BPAD II, 4 patients: Anxiety disorder | 4 patients: Dysplasia, 3 patients: Hypertension | All patients: SSRS | DSM-IV MINI | HAMD-17 | 61.3(14.6) | NA | Pecial samples | <0.01 | 16S rRNA gene sequencing: Illumina-MiSeq platform | Unspecified | MDD and Controls | Mann-Whitney U test and Benjamini-Hochberg FDR-adjusted p-value ≤ 0.01

Other abbreviations: 16S rRNA gene sequencing: the 16S rRNA gene was amplified and sequenced using the Illumina and Roche platforms; LEfSe: p < 0.05 and LDA > 2.0; Orthodontic Intelligence with depression and controls: Mann-Whitney test and Kruskal-Wallis test: p<0.017; Cross-sectional associations with depression symptoms measures: Beta coefficients of associations: p < 0.05.
Kleiman SC et al. 2015[28] American Cross-sectional associations
Anorexia Nervosa (N=16) Control (N=12)
28.0 (±11.7) 29.8 (±11.6) 0.16 0.12 16.2 (±5.5) 21.5 (±19) NA NA - 
BDI 26.5 (±13.6) NA Fecal samples 45°C 16S rRNA gene sequencing-454 Life Sciences Genome Sequencer FLX machine V1/V3
Cross-sectional associations with depression-symptom measures Wilcoxon matched pairs rank test (< 2); skewness ≤ 2 or the sign test (skewness ≤ -2 or ≥ 2) or p < 0.05

Kurosawa S et al. 2016[29] Japanese Case-control IBS with depression (N=12) IBS without depression (N=5) Donors (N=17)
43.46 (±16.7) 51.46 (±18.1) 0.9 710 - IBS NA HAMD/9 HAMD/7 - Fecal samples 45°C 16S rRNA gene sequencing- Illumina MiSeq platform V1/V2
IBS with depression and donors Parent's test: p < 0.05

Liu WT et al. 2017[30] Chinese Case-control MDD (N=26) Control (N=20)
43.75 (±11.48) 39.40 (±10.06) 0.18 1316 21.17 (±2.77) 21.16 (±2.51) NA
In MDD: 12 SSRIs; 7 SNRIs; 0 Other antidepressants DSM-5
HAMD-17 10.81 (±2.95) NA Fecal samples 45°C 16S rRNA gene sequencing- Illumina MiSeq platform V1/V2
Shengran meteorogenic-Illumina MiSeq250 sequencing NA MDD and Controls LE5G: adjusted p < 0.05 and LDA ≥ 3.0

Liu Pei et al. 2017[31] Chinese Case-control MDD (N=10) Control (N=10)
36.20 (±1.6) 38.12 (±2.9) 0.04 44 23.61 (±3.9) 24.22 (±5.0) -
Longitudinal intervention (all patients received Escitalopram) DSM-IV-TR
HAM-D-17 23 - Fecal samples 70°C 16S rRNA gene sequencing- Illumina MiSeq platform V1/V2
qRT-PCR for Streptococcus, Clostridium XI, Prevotella and Bifidobacteria NS/NS NS/NS
AMI and Controls NS/NS/NS

Ling Y et al. 2019[32] Chinese Case-control PSCCID (N=41) non-PSCCID (N=25)
69.63 (±9.39) 68.82 (±6.69) 0.1724 14112 25.14 (±6.62) 26.62 (±5.56) In PSCCID: 24 Hypertension, 12 Diabetes mellitus; 15 Hyperlipidemia
In non-PSCCID: 18 Hypertension, 6 Diabetes mellitus; 10 Hyperlipidemia Unknown HAMD/6 HAMD 15.63 (±5.90) 5.56 (±2.58) Fecal samples 90°C 16S rRNA gene sequencing- Illumina MiSeq platform V3/V4
PSCCID and non-PSCCID LE5G: p < 0.05 and LDA ≥ 2.0

Lithwicki P et al. 2017[33] Polish Cross-sectional associations MDD(N=16)
44.0 (±34.3) 56.1 0.09 25.0 (±22.6) 26.7 NA Longitudinal intervention (all patients received Escitalopram)
JCD-10 HAMD-24 23.0 (±21.0) 28.5 Fecal samples 45°C 16S rRNA gene sequencing- Illumina NextSeq 500 platform V4
Cross-sectional associations between with symptom severity (baseline) SPEARMAN's rank correlation

Liu Pei et al. 2017[34] Chinese Case-control MDD (N=66) Control (N=43)
24.36 (±8.69) 23.65 (±1.19) 0.25 2539 20231 21.64 (±4.61) 21.83 (±2.15) NA
In MDD: 26 prescribed psychotropic medications In Control 1 prescribed psychotropic medications DSM-IV
HAM-D-17 20.07 (±4.80) 2.31 (±0.64) Fecal samples 45°C 16S rRNA gene sequencing- Illumina MiSeq platform V3/V4
MDD and Controls LE5G: p < 0.05 and LDA ≥ 2.0

Lin RT et al. 2019[35] American Case-control MDD(N=45) Control (N=47)
21.9 (±2.1) 22.1 (±1.8) 0.05 1313 -
In MDD: 26 prescribed psychotropic medications In Control 1 prescribed psychotropic medications PROMIS Depression Score > 21, DSM-5
PROMIS Depres Sc 25.6 (±6.9) 9.3 (±1.4) Fecal samples 45°C 16S rRNA gene sequencing- Illumina MiSeq platform V4
MDD and Controls LE5G: p < 0.05 and LDA ≥ 2.0

Lin Y et al. 2020[36] Chinese Case-control IBS-D (N=48) Control (N=48)
41.76 (±15.13) 38.30 (±15.13) 0.42 4624 25211 25.36 (±3.48) 23.63 (±3.76) IBS-D -
In MDD: 16 prescribed psychotropic medications In Control 1 prescribed psychotropic medications HAMD/DSHS HAMD 15.17 (±15.40/09) (9.93)
Unknown HAMD/DSHS 5.9 (±1.4) Fecal samples 45°C 16S rRNA gene sequencing- Illumina MiSeq platform V3/V4
Cross-sectional associations with depression-symptom measures SPEARMAN's correlation coefficient

Lin Y et al. 2016[37] Chinese Case-control IBS-D (N=48) Control (N=48)
38.5 (±3.6) 39.6 (±3.9) 44.8 (±4.9) 43.83 (±2.2)
28/12 14/11 22 (±8.8) 22.5 (±2.5) 24.6 (±2.2) IBS-D -
DSM-IV MINI DSM Data displayed in histogram Fecal samples 45°C 16S rRNA gene sequencing- Roche 454 sequencing V1/V3
Depression and Controls Wilcoxon rank-sum with p value was used for corrections q < 0.05
| Authors                          | Year  | Region                       | Study Design  | Sample Size | Case Controls | Test Anxiety | Depression Medication | Depression Med. | p-Value Test | Statistical Test | Pooled Depression Med. | Depression Med. | p-Value Test | Statistical Test | Notes |
|---------------------------------|-------|------------------------------|---------------|-------------|---------------|--------------|--------------------|----------------|-------------|----------------|------------------------|----------------|-------------|----------------|--------|
| Madan et al.                    | 2020  | American                     | Cross-sectional associations | Depression(N=111) | 35.7 (13.8) | 52/60 | _ | _ | SCID-IV | Fecal samples | p < 0.05 | 16S rRNA gene sequencing, Illumina MiSeq platform | V4 | Cross-sectional associations with symptom severity | LEAD: p < 0.05 and LDA > 2.0 |
| Mason et al.                    | 2020  | American                     | Case-control   | Control (N=11) | 16/18 | _ | _ | 52/73 | 2/8 | p < 0.05 | Mann Whitney U test | V4 | Cross-sectional associations with symptom severity | Kruskal-Wallis one-way ANOVA, p < 0.05 | Within these clusters, p-values were adjusted to control the false discovery rate using the Benjamin and Hochberg method |
| Molina et al.                   | 2020  | American                     | Cross-sectional associations | Depression(N=111) | 35.7 (13.8) | 52/73 | 2/8 | _ | 218 Obsody | Fecal samples | p < 0.05 | 16S rRNA gene sequencing, Illumina MiSeq platform | V4 | Cross-sectional associations with symptom severity | Mann Whitney U test, p < 0.05 |
| Minshau et al.                  | 2020  | British                      | Cross-sectional associations | Depression(N=137) | 49.2 (15.9) | 48/47 | _ | _ | 22 Antidepressants | Fecal samples | p < 0.05 | 16S rRNA gene sequencing, Illumina MiSeq platform | V4 | Cross-sectional associations with symptom severity | Pearson's correlation analysis and regression model |
| Nuaehra et al.                  | 2020  | Norwegia                     | Cross-sectional associations | Depression(N=111) | 35.7 (13.8) | 52/73 | _ | _ | 218 Obsody | Fecal samples | p < 0.05 | 16S rRNA gene sequencing, Illumina MiSeq platform | V4 | Cross-sectional associations with symptom severity | Unspecified Depression and Controls | PLDA |
| Pérez-Santiago et al.           | 2019  | American                     | Cross-sectional associations | Depression(N=66) | 54.6 (6.6) | 54/64 | _ | _ | In MDD: 56 HIV | Fecal samples | p < 0.05 | 16S rRNA gene sequencing, Illumina MiSeq platform | V4 | Cross-sectional associations with symptom severity | Mann-Whitney or t test, p < 0.05 |
| Qi et al.                       | 2020  | Chinese                      | Cross-sectional associations | Depression(N=60) | 53.3 (10.3) | 53/60 | _ | _ | Test anxiety | Fecal samples | p < 0.05 | 16S rRNA gene sequencing, Illumina MiSeq platform | V4 | Cross-sectional associations with symptom severity | One-way ANOVA followed by Turkey's multiple comparisons test, p < 0.05 |
| Ramirez-Castillo et al.         | 2020  | Mexican                      | Cross-sectional associations | Depression(N=54) | 50.2 (7.5) | 49/55 | _ | _ | _ | Fecal samples | p < 0.05 | 16S rRNA gene sequencing, Illumina MiSeq platform | V4 | Cross-sectional associations with symptom severity | Phylogeny, venn and ggplot2 packages in R |
| Naseribafrouei et al.           | 2020  | American                     | Case-control   | Control (N=36) | 30.48 (7.79) | 30/36 | _ | _ | 46.2 (9.7) | Fecal samples | p < 0.05 | 16S rRNA gene sequencing, Illumina MiSeq platform | V4 | Cross-sectional associations with symptom severity | ANCOM |
| Rhee SJ et al. 2021[47] | Koreans Cross-sectional associations | Depression (N=69) | 39.6(12.0) | 29 MDD patients, 40 RD patients | 31 Antidepressant; 33 Anticonvulsant or lithium; 45 Antipsychotics | DSM-IV, DSM-5, MINI | HAMD-17 | 6.13(5.08) | Serum | -80°C | 16S rRNA gene sequencing-Illumina MiSeq platform | V3-V4 | Cross-sectional associations with depression-symptom measures | Multivariate association with linear models (MAdaL2) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Rhee SJ et al. 2021[47] | Koreans Cross-sectional associations | Depression (N=69) | 39.6(12.0) | 29 MDD patients, 40 RD patients | 31 Antidepressant; 33 Anticonvulsant or lithium; 45 Antipsychotics | DSM-IV, DSM-5, MINI | HAMD-17 | 6.13(5.08) | Serum | -80°C | 16S rRNA gene sequencing-Illumina MiSeq platform | V3-V4 | Cross-sectional associations with depression-symptom measures | Multivariate association with linear models (MAdaL2) |
| Shen Y et al. 2021[51] | Chinese Case-control | BD (N=50) | 38.40(8.33) | 41.56(10.40) | NA | In MDD: 13 SRbs; 4 Other antidepressants | V4 MDD and Controls | Kruskal-Wallis test: p < 0.05 |
| Stevens CA et al. 2020[55] | Australian Case-control | Hypertension (N=118) | 59.9(17.4) | 63.8(2.5) | NA | In HTN: 4 Diabetes; 7 Chronic kidney disease; 1 Stroke/Transient ischemia attack; 3 Asthma; 1 Heart failure | CEDD | COED | 20.14(7.70) | Saliva sample | 50°C | 16S rRNA gene sequencing + Torrent Personal Genome Machine | V4 | High-depression and low-depression measures | Multivariate association with linear model analysis (MAdaL2): p-value < 0.05 and FDR alpha = 0.25 |
| Stevens BJ et al. 2020[52] | American Case-control | Hypertension (N=118) | 59.9(17.4) | 63.8(2.5) | NA | In HTN: 4 Diabetes; 7 Chronic kidney disease; 1 Stroke/Transient ischemia attack; 3 Asthma; 1 Heart failure | Unknown | DSM-5 | - | - | Fecal samples | -80°C | 16S rRNA gene sequencing (WMGS)-Illumina HiSeq8000 | NA | Depression-only and reference subjects | Pearson correlation heatmaps were generated based on relative 16S magnitudes |
| Stevens BJ et al. 2020[52] | American Case-control | MDD (N=20) | mean: 34 | 10/10 | NA | In MDD: 15 Antidepressants | DSM-IV | - | - | Fecal samples | -80°C | 16S rRNA gene sequencing-Illumina MiSeq platform | V3-V4 | MDD and Controls | ALDEx2 effect sizes for taxa assigned from ASVs. Displayed cutoffs are effect size ≥0.5 (NODEP) or ≥0.3 (DEP) |
| Strandin P et al. 2019[53] | American Cross-sectional associations | MDD (N=23) | 29.65 | 4/15 | NA | NA | DSM-IV-TR | - | - | Fecal samples | -80°C | 16S rRNA gene sequencing-American Gut dataset | V4 | Cross-sectional associations with depression-symptom measures | Pearson |
| Steenbakkers O et al. 2018[54] | Norwegian Case-control | Depression (N=34) | 33.45(7.9) | 30(8.6) | NA | NA | DASS-21 | 5.40(6) | Fecal samples | -80°C | 16S rRNA gene sequencing-Illumina MiSeq platform | Unspecified | As described in Naef-Herrmann et al. (2014) Depression and Controls | PLDA |
| Taylor AM et al. 2020[56] | American Cross-sectional associations | Depression (N=133) | 33.45(7.9) | 30(8.6) | NA | NA | DASS-21 | 5.40(6) | Fecal samples | -80°C | 16S rRNA gene sequencing-Illumina MiSeq platform | Unspecified | As described in Naef-Herrmann et al. (2014) Depression and Controls | PLDA |
| Taylor BC et al. 2020[56] | American Case-control | MDD (N=54) | 53.9(9.1) | 42/17 | - | HIV and HCV infections | DSM-IV, DSM-5, MINI | HAMD-17 | 10.9(10.7) | Fecal samples | -80°C | 16S rRNA gene sequencing-Illumina MiSeq platform | V3-V4 | MDD and Controls (Cominenced) | Kruskal-Wallis test: p < 0.05 |
### Section 1: Case-control FGFP cohort: Cross-sectional associations between MDD and gut

#### Table 1: Differences in gut microbiota between depression and controls

| Study          | Participants | Gut Sample Collection | Sequencing Platform | LEfSe Analysis | GLMs Analysis |
|----------------|--------------|------------------------|---------------------|----------------|---------------|
| Zheng S et al. 2016 | MDD (N=24) vs Controls (N=63) | Fecal samples | Roche 454 sequencing | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Zheng P et al. 2016 | MDD (N=20) vs Controls (N=28) | Fecal samples | Illumina HiSeq™ platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Zhang P et al. 2015 | MDD (N=26) vs Controls (N=28) | Fecal samples | Illumina 454 platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Zhao H et al. 2014 | MDD (N=24) vs Controls (N=38) | Fecal samples | Illumina MiSeq platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Zhu Q et al. 2013 | MDD (N=20) vs Controls (N=16) | Fecal samples | Illumina MiSeq platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Zhu X et al. 2012 | MDD (N=20) vs Controls (N=28) | Fecal samples | Illumina MiSeq platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Yang Y et al. 2013 | MDD (N=18) vs Controls (N=24) | Fecal samples | Illumina MiSeq platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Yang F et al. 2012 | MDD (N=18) vs Controls (N=28) | Fecal samples | Illumina MiSeq platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Zheng S et al. 2020 | MDD (N=24) vs Controls (N=30) | Fecal samples | Illumina HiSeq™ platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Zhuang Z et al. 2020 | MDD (N=24) vs Controls (N=29) | Fecal samples | Illumina MiSeq platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Wu et al. 2019 | MDD (N=20) vs Controls (N=28) | Fecal samples | Illumina MiSeq platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Wanget al. 2021 | MDD (N=20) vs Controls (N=29) | Fecal samples | Illumina MiSeq platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Wang et al. 2020 | MDD (N=20) vs Controls (N=24) | Fecal samples | Illumina MiSeq platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |
| Valles-Colomer et al. 2019 | MDD (N=20) vs Controls (N=28) | Fecal samples | Illumina MiSeq platform | LEfSe: p < 0.05 and LDA > 2.5 | GLMs: FDR < 0.1 |

**Notes:**
- LEfSe: Linear discriminant analysis effect size
- GLMs: Generalized linear models
- FDR: False discovery rate
- MDD: Major depressive disorder
- Controls: Healthy controls
- Differences in gut microbiota were analyzed using LEfSe (LDA score > 2.0) and GLMs (FDR < 0.1).
Illumina MiSeq/Illumina HiSeq2000/Illumina HiSeq microbiota using published GWAS data

Note:

*a* Data from 56 OI patients with or without depression (Ref.22)

*b* Data from all 2737 individuals (Ref.23)

*c* Data from all 17 patients with irritable bowel syndrome (Ref.29)

*d* Data from 38 patients with depression and 18 controls (Ref.54)

*e* Data from total 48 patients (Ref.56)

*f* Data from 39 patients with postpartum depressive disorder and 18 controls (Ref.68)

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Table S2. Characteristics of studies investigating gut microbiota composition in animal models of depression.

| Study | Object | Country | Study design | Sample size | Depression model | Age | Sex | Definition of depression-like behaviors | Time-point of sample collection | Sample storage | Gut microbiome estimation | Sequencing region | Microbial biomarkers from comparisons | Microbiome biomarkers selection |
|-------|--------|---------|--------------|-------------|-----------------|-----|-----|----------------------------------------|-------------------------------|----------------|---------------------------|----------------|----------------------------------|---------------------------------|
| Åhlgren et al. 2021(2) | Flanders sensitive line rats | Denmark | case-control | 80 | FSL-depression | 5-week-old | male | FST: No data (immobility) | Fresh fecal samples were collected at study initiation and study end | Fecal samples | 80 °C | MS: RNA gene sequencing - Illumina MiSeq platform | V4 | FSL-depression and PRL-control | Two-way ANOVA followed by Bonferroni correction p < 0.05 |
| Arshad Y et al. 2018(3) | Swiss mice | Morocco | case-control | - | GBDH-depression | 1-month-old | male | OPT: center time; EMT: anxiety index; FST: immobility time; Splash test: grooming time | After subchronic and chronic groups were treated daily for 6 and 12 weeks | Intestinal samples | - | GBDH-depression and control | Two-way ANOVA followed by Holm-Sidak post-hoc test p < 0.05 |
| Amini Khosravi et al. 2019(4) | NMRI mice | Iran | case-control | 4 mice/cage | MS-depression | 5-50-52 | male | FST: immobility time; Splash test: grooming activity time; OPT: horizontal activity and rearing; EPM (open-arm time and entries) | Fresh feces were collected from male mice at PND52 after having carried out valid behavioral tests | Colon contents | 80 °C | Real-time RT-PCR | - | MS-depression and control | Two-way ANOVA followed by Bonferroni post-hoc test p < 0.05 |
| Ai Q et al. 2020(5) | C57BL/6J mice | China | case-control | 5 mice/cage | CUMS-depression | MS (N=9-12) | Adrenalectomized MS (N=9-12) Control (N=9-12) Adrenalectomized control (N=9-12) | 0-5-week-old | male | Body weight; SPT: novelty preference; FST: immobility time | After 1 week of acclimatization and 8 weeks of CUMS (the last 4 weeks received drugs treatment) | Fecal samples | 80 °C | MS: RNA gene sequencing - Illumina MiSeq platform | V3-V4 | CUMS-depression and control | Mann-Whitney test followed by multiple comparisons using Benjamini & Hochberg's false discovery rate: FDR < 0.05 |
| Archipova et al. 2012(6) | mice | Russia | case-control | 4-5 mice/cage | Anibiotic- depression | Aminobis (N=25) Aminobis-lactobacilli (N=25) Control (N=25) | 25-days-old | male | Mortality rate; Body weight; OPT: crossing number, defecation, grooming; rearing number, head dips, latency to exit from central zone; Rotorod test: Latency to falls; PawSE: time to open the grip; Time mice: alternation; Novel Object Recognition: time index | Caccuzum-content samples were collected on the 15th day of the experiment | Caccuzum contents | 80 °C | MS: RNA gene sequencing - Illumina MiSeq platform | V3-V4 | Anibiotic-depression and control | Neoparametric ANOVA Kreissel-Wallis test p < 0.05 |
| Bhattacharya et al. 2017(7) | C57BL/6 mice | Canada | case-control | Single | CSDS-depression | CSDS (N=16) CSDS+L. rhamnosus JB (N=17) Control (N=18) Control+L. rhamnosus JB (N=13) | 0-5-week-old | male | MIT: social interaction ratios; OPT: rearing number; LDT: light zone entries | Fecal pellets were collected before the first defeat session (at 18th day of L. rhamnosus JB treatment), the final defeat session (at the final day of JB-1) | Fecal samples | 80 °C | MS: RNA gene sequencing - Illumina MiSeq platform | V3 | CSDS-depression and control | Kreissel-Wallis one-way ANOVA or the Mann-Whitney U test, followed by the Benjamini-Hochberg correction |
| Study             | Animals | Country | Gender | Age | Treatment | Time Points | Sample Collection | Data Analysis | Findings                                                                 |
|-------------------|---------|---------|--------|-----|-----------|-------------|-------------------|---------------|--------------------------------------------------------------------------|
| Besharse A et al. 2021 | C57BL/6 mice | Ireland | male | 4 weeks | CUMS-depression | 6-week-old | male/female | SPT: immobility time↑; TST: immobility time↑ | 16S rRNA gene sequencing | Random Forest models (False Discovery Rate < 0.05) |
| Chen et al. 2020 | C57BL/6 mice | China | male | 20-25 g | CUMS-depression | 4 weeks-old | male | SPT: active preference↑; FST: immobility time↑ | 16S rRNA gene sequencing | 16S rRNA gene sequencing | Null
| Chakraborti A et al. 2020 | C57BL/6 mice | USA | male | 30 days | HPSC-MFD-depression | 4 weeks-old | male | OFF: center time↑; EPM: open arms time↑ | 16S rRNA gene sequencing | Null |
| Chen L et al. 2021 | C57BL/6 mice | China | male | 12-week-old | LPS-depression | 12-week-old | Unspecified | Survival rate↑; NOR: test preference index↑ | LPS-depression and control | Null |
| Chen P et al. 2019 | BALB/c mice | China | male | 3-4 weeks | UCMS-depression | 3-4 weeks-old | male | Body weight↑; GT: immobility time↑; total distance↑ | 16S rRNA gene sequencing | 16S rRNA gene sequencing | Null |
Chen T et al. 2021[13]  C57BL/6N mice  China  case-control  s-4 mice/cage  CRS-depression  Experiment 1:  CRS (N=8)  DSS (N=8)  DSS+CRS (N=8)  Control (N=8)  Experiment 2:  donor Control (N=10)  donor CRS (N=20)  recipient Control (N=6)  recipient CRS (N=6)  recipient CRS+L. reuteri (N=6)  recipient Controls+DSS (N=8)  recipient CRS+DSS (N=8)  recipient CRS+DSS+L. reuteri (N=8)  Control (N=8)  18–20 g  male  OGT: total distance;  TST: immobility time;  FST: immobility time.  After 7 days of acclimatization and 30 days of CRS, followed by 7 days of DSS treatment  Cecal contents  _  16S rRNA gene sequencing: Illumina HiSeq platform  V3-V4  FMT CRS-depression and control  Two-way ANOVA with Bonferroni’s post-hoc test for multiple comparisons: p < 0.05.

Chen X et al. 2021[14]  Sprague-Dawley rats  China  case-control  Adult 200 ± 10 g  male  SPT: sucrose preference;  FST: immobility time;  TST: immobility time  After 1 week of acclimatization and 24 weeks of lead exposure  Fecal samples  _  16S rRNA gene sequencing: Illumina MiSeq platform  V4  Lead exposure-depression and control  Anosim: p < 0.05  LEfSe: p < 0.05 and LDA > 3.0

Chen Y et al. 2021b[17]  Sprague-Dawley rats  China  case-control  Adult 180–220 g  male  SPT: sugar preference;  FST: immobility time;  LDT: dark time  After 15 days of acclimatization, 3 weeks of CUMS and 4 weeks of Semen Sojae Praeparatum treatment  Cecum contents  _  16S rRNA gene sequencing: Illumina MiSeq platform  V3-V4  CUMS-depression and control  LEfSe: p < 0.05 and LDA > 3.0  one-way ANOVA and Welch’s t-test: p < 0.05
Cheng D et al. 2018[18] Sprague-Dawley rat China case-control single Hydrocortisone-depression Hydrocortisone (N=10) Hydrocortisone+Tianshi (N=10) Control (N=10) 230-280 g male GPT: total-dose[1] SPT: sucrose preference[1] After 1 week of acclimatization and 21 days of drugs Faces from the color samples and small immobility success - 90 °C 16S RNA gene sequencing- MiSeq (Illumina) platform Y3-V4 Hydrocortisone-depression and control A Kruskal-Wallis test: p < 0.05; Mann-Whitney test: p < 0.05

Chung R et al. 2022[20] C57BL/6 mice China case-control - CUMS-depression CUMS (N=7-8) CUMS+Fluoxetine (N=7-8) Control (N=7-8) 5-6 weeks old male LTD: light time[2] After 6 weeks of CUMS and treatment Fetal samples _ 16S RNA gene sequencing and control Two-way ANOVA followed by Fisher’s LSD test or Dunn’s correction: p < 0.05

Chevalier G et al. 2021[21] C57BL/6J mice France case-control - UCMS-depression UCMs (N=4) UCMs+Flaxseeds (N=4) Control (N=4) PMS: Control (N=6) 8-10 week-old male NSPT: latency to eat [2] Splashes test: grooming latency[2], self-grooming behavior[2]. FST: immobility time[2] TST: immobility time[2] After 1 week of acclimatization and 8 weeks of UCMS 8 weeks post PMS Fetal samples _ 16S RNA metabonomic- Illumina MiSeq instrument Y3-V4 UCMs-depression and control Mann-Whitney test: p < 0.05

Chi L et al. 2021[22] Sprague-Dawley rats China case-control 4-6 rats/cage (for control), 8 rats/cage for CUMS mice CUMS-depression CUMS (N=12) CUMS+Flaxseeds (N=12) CUMS+DPP (N=10) Control (N=8) Control+FGS (N=8) 6-week-old male Body weight[1] SPT: sucrose preference[1] GPT: total-dose[1], immobility time[1], stress refuses[1] After 1 week of acclimatization and 7 weeks of CUMS, the last 3 weeks received drugs treatment, fetal samples were collected at day 6, 15, and 22 during the drug treatment period - 90 °C 16S RNA gene sequencing- Illumina MiSeq system Y3-V4 CUMS-depression and control LEH UC 1.0 p < 0.05 and LDA > 1.0

Choi J et al. 2021[23] C57BL/6J mice Korea case-control - CRS-depression CRS (N=12) CRS+Lac-IV (N=8) CRS+Flaxseeds (N=12) CRS+Ack-IV (N=11) Control (N=12) Control+Lac-IV (N=8) Control+Flaxseeds (N=12) Control+Ack-IV (N=12) 7-week-old male FST: immobility time[2] FST: immobility time[2] After 5 days of acclimatation, stress was collected at day 1 (before stress), day 14 (after stress), and post-stress day 14 - 90 °C 16S RNA gene sequencing- Roche 454 sequencing Y1-V2 CRS-depression and control (post-stress day 14) Two-way ANOVA: p < 0.05

Dang V et al. 2020[24] Long Evans Rats China case-control - MD-depression Experiment for Picher rats- Prebiotics (N=12) Control (N=12) Experiment for Long Evans rats MD (N=12) MD+Prebiotics (N=12) Control (N=12) Control+Prebiotics (N=12) 6-week-old male GPT: corner visits number[2], mazes number[2] After receiving 0.5 ml of the prebiotics for 5 weeks for Picher rats and 9 weeks for Long Evans rats (until euthanasia) Cecal content - 90 °C 16S RNA sequencing analysis- Illumina MiSeq platform Y3-V4 MD-depression and control MD-depression ANOVA: p < 0.05

Dong Y et al. 2018[25] C57BL/6J mice China case-control 8 mice/age CRS-depression CRS+PBS (N=8) CRS+CITA (N=8) Control+PBS (N=8) Control+CITA (N=8) 6-week-old male FST: immobility time[2] SPT: sucrose preference[2] PPT: corner time[2] EPM: open arm time[2] After 2 week of acclimatation and 5 weeks of CRS (the last 3 weeks received drugs) Fetal samples - 90 °C 16S RNA gene sequencing- Illumina MiSeq platform Y3-V4 CRS-depression and control (PBS) Two-way ANOVA followed by Fisher’s LSD test or Dunnet’s correction: p < 0.05

EPM: open arms time ↓ OFT: center visits number ↓ TST: immobility time ↑ OFT: total distance ↑ SPT: sucrose preference ↓ FST: immobility time ↓ self-grooming behavior ↓ NSFT: latency to eat ↓ LDT: light time ↓ SP: sucrose preference ↑ self-grooming behavior ↑ Stress test: grooming latency ↑ LDT: light time ↓ SP: sucrose preference ↑ self-grooming behavior ↑ Stress test: grooming latency ↑
| Study | Species | Country | Group Size | Group Details | Sample Collection | Method | Analysis | Sample Size | Results |
|-------|---------|---------|------------|---------------|------------------|--------|----------|-------------|---------|
| Dhaliwal et al. 2018[25] | Swiss albino LACA mice | India | case-control | CUMS-depression | CUMS (N=8) | 25–30 g male | Locomotor activity, EMG, mirror chamber test, STT, immobility time | 16S rRNA gene sequencing | After 4 weeks of CUMS (and L. plantarum MTCC 9510) | qPCR | CUMS-depression and control | One-way ANOVA followed by Tukey’s multiple comparisons test: p < 0.05 |
| Ding Y et al. 2021[30] | C57BL/6 mice | China | case-control | CRS-depression | CRS (N=8) | 6–8-week-old male | OPT: total distance; FST: immobility time; STT: immobility time | 16S rRNA gene sequencing | After 1 week of acclimatization and 3 weeks of CRS and Abacavir-macrophages treatment | Fecal samples | 16S rRNA gene sequencing–Illumina platform | V5-V4 | CRS-depression and control | Welch’s t-test: p < 0.05 |
| Diviccaro et al. 2018[29] | Sprague-Dawley rats | Italy | case-control | 16S rRNA gene sequencing | Fecal samples | 80 °C | V3–V4 | MS-depression and control | Student’s t-test: p < 0.05 |
| Duan J et al. 2018[25] | SD+L. plantarum MTCC 9510 | India | case-control | CUMS-depression | CUMS-L. plantarum MTCC 9510 (N=8) | Control (N=8) | Control-L. plantarum MTCC 9510 (N=6) | 16S rRNA gene sequencing | After 21 days of L. plantarum MTCC 9510 (day 7–10 received deep depression) | Fecal samples | 16S rRNA gene sequencing–Illumina platform | V5-V4 | CUMS-depression and control | One-way ANOVA followed by Tukey’s multiple comparisons test: p < 0.05 |
| Egerton S et al. 2020[31] | C57BL/6 mice | Ireland | case-control | 4–4 rats/cage | MS-depression | MS (N=12) | ABX FMT (N=12) | 16-week-old male | EAP treatment (N=8) | Fecal samples | 16S rRNA gene sequencing–Illumina platform | V5-V4 | EAP-depression and control | Purvalim implementation of the aldex test (function followed by Benjamin-Hochberg correction: p < 0.1) |
| Do EK et al. 2020[32] | NODShLij mice | China | case-control | EAP-depression | EAP treatment (N=8) | MS (N=12) | 4-week-old male | OPT: total distance, swimming time; FST: immobility time; STT: center time and entries | 16S rRNA gene sequencing–Illumina platform | V5-V4 | EAP-depression and control | Independent sample t-test: p < 0.05 | One-way ANOVA followed by post hoc Tukey test: p < 0.05 |
| Duan L et al. 2021[30] | C57BL/6 mice | China | case-control | Singla | CUMS-depression | CUMS (N=7) | 4–6 weeks of age | Body weight; SP: sucrose preference; FST: immobility time | 16S rRNA gene sequencing | After 4 weeks of CUMS, then fecal samples were collected prior to sedation of animals | Fecal samples | 16S rRNA gene sequencing–Illumina platform | V5-V4 | CUMS-depression and control | Welch’s rank-sum test: p < 0.05 |
| Egerton S et al. 2020[31] | Sprague-Dawley rats | Ireland | case-control | 4–4 mice/cage | MS-depression | MS (N=12) | 4-week-old male | OPT: total distance, swimming time; FST: immobility time | 16S rRNA gene sequencing–Illumina platform | V5-V4 | MS-depression and control | Student’s t-test: p < 0.05 |
El Aidy S et al. 2017[32] mice Netherla
nds case- control − MS MS-5-HTT−/− (N=8) Control-5-HTT−/− (N=8) Control-5-HTT−/− (N=8) MS-5-HTT−/− (N=8) Control-5-HTT−/− (N=8) p<0.01 male/ female NA Facial samples were collected at PND 21. Facial samples −80 °C 16S rRNA gene sequencing Illumina MiSeq platform Unspecified MS and control The rank non-Kruskal–Wallis test: p < 0.05

Fan L et al. 2017[32] Sprague-Dawley rats China case- control − CUMS-depression CUMS (N=8) CUMS+PD (N=6) PD (N=6) CUMS (N=8) CUMS+PD (N=6) PD (N=6) PND25 male SPL: sucrose preference; OPT: total distance traveled; resting number; FST: total immobility time After 1 week of acclimatization and 4 weeks of CUMS Cereb cortex samples −80 °C 16S rRNA gene sequencing Illumina MiSeq PE300 system V3-V4 CUMS-depression and control LeSe: p < 0.05 and LDA > 2.5 Non-parametric Mann–Whitney test: p < 0.05

Ferdmine P et al. 2020[34] Sprague-Dawley rats UK case- control − Non-weaned-depression W-Weaned (N=6) L-Non-weaned (N=6) NS-Weaned (N=6) NS-Non-weaned (N=6) PND25 male FST: immobility time; limbing time; swimming time Facial samples were collected at PND25 Contents of deoxynucleotides, pyrimidines, pyrimidines and cytosine − Fluorescence in situ hybridization (FISH) analysis for Lactobacillus— Enterococcus, Bifidobacterium spp. and Clostridium histolyticum group − Non-weaned-depression and weaned Two-way ANOVA followed by Bonferroni-adjusted: p < 0.05

Feng Z et al. 2020[32] Sprague-Dawley rats China case- control − CUMS-depression CUMS (N=8) CUMS+Fluoxetine (N=8) CUMS+Venlafaxine (N=8) CUMS+CTE (N=8) CUMS+TG (N=9) CUMS+Fluoxetine (N=9) CUMS+CTE (N=9) CUMS+TG (N=9) CUMS (N=9) Control (N=9) Body weight; SPL: sucrose preference; OPT: crossing and resting number After 1 week of acclimatization and 4 weeks of CSDS Cereb cortex contents −80 °C 16S rRNA gene sequencing analysis Illumina MiSeq platform V3-V4 CUMS-depression and control Unspecified One-way ANOVA followed by Dunnet’s test: p < 0.05 LDA: p < 0.05 and LDA > 2.0

Feng Y et al. 2020[35] Sprague-Dawley rats China case- control − CUMS-depression CUMS (N=8) CUMS+Fluoxetine (N=8) CUMS+Venlafaxine (N=8) CUMS+CTE (N=8) CUMS+TG (N=9) CUMS+Fluoxetine (N=9) CUMS+CTE (N=9) CUMS+TG (N=9) CUMS (N=9) Control (N=9) 200 ± 20 g weight; SPL: sucrose preference; OPT: crossing and resting number After 1 week of acclimatization and 4 weeks of CMS Cereb cortex contents −80 °C 16S rRNA gene sequencing analysis Illumina MiSeq platform V3-V4 CUMS-depression and control Unspecified One-way ANOVA followed by Dunnet’s test: p < 0.05 LDA: p < 0.05 and LDA > 2.0

Forzaman S et al. 2020[37] Sprague-Dawley rats USA case- control − MEETH-depression MEETH (N=8) Control (N=8) 60-90 days old male OPT: total distance; FST: immobility time Facial samples were collected at the following time points: 0, 5, 7, and 12 week of MEETH administration, and at 24, 48, and 96 h, and days 7, 14, and 30 of withdrawal or cessation. Facial samples −80 °C 16S rRNA gene sequencing Illumina MiSeq platform V4 MEETH-depression and control Non-parametric Mann–Whitney test or the Kruskal–Wallis test: p < 0.05

Gao K et al. 2020[38] BALB/c mice China case- control − CUMS-depression CUMS (N=10) CUMS+5-Chloro-5,6-Dihydroxy-2,3-dihydrobenzofuran (N=10) CUMS+5-Chloro-5,6-Dihydroxy-2,3-dihydrobenzofuran (N=10) CUMS (N=10) 6-8 weeks old male SPL: sucrose preference; FST: immobility time; OPT: total distance; resting number After 1 week of adaptation and 3 weeks of WHES/0 or thioctic acid treatment (4 weeks of CUMS after adaptation) Facial samples −80 °C 16S rRNA gene sequencing Illumina MiSeq platform V3-V4 CUMS-depression and control One-way ANOVA (or Kruskal–Wallis test): p < 0.05 LDA: p < 0.05 and LDA > 2.0
| Study | Species | Gender | Age | Cauda epidural staining | Timepoints | Cause | Control | CUMS+Paroxetine (N=6) | CUMS+L. casei (N=6) | CUMS (N=6) | Data Collection and Analysis |
|-------|---------|--------|-----|------------------------|------------|-------|---------|------------------------|---------------------|------------|----------------------------|
| Gao X et al. 2020<sup>[39]</sup> | Sprague-Dawley rats | Male | 5 mice/cage | | After 1 week of acclimatization and 4 weeks of CUMS | Body weight | SPT: escape preference, OPT: crossing number, rearing number | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Guo Y et al. 2020<sup>[40]</sup> | Cryptosporidium rats | Male | 5 mice/cage | | After 1 week of acclimatization and 10 days of CSDS | Body weight | SPT: escape consumption, OPT: immobility time | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Han SK et al. 2019<sup>[41]</sup> | Cryptosporidium rats | Male | 5 mice/cage | | After 2 days of IS | Body weight and 21 days of CRS | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Gu X et al. 2021<sup>[42]</sup> | Cryptosporidium rats | Male | 5 mice/cage | | After 1 week of acclimatization and 7 days of CSDS | Body weight | SPT: escape consumption, OPT: immobility time | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Gu X et al. 2021<sup>[43]</sup> | Cryptosporidium rats | Male | 5 mice/cage | | After 1 week of acclimatization, 14 days of antibiotics treatment, and 7 days of probiotics treatment | Body weight | TST: immobility time, FST: immobility time | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Guo F et al. 2020<sup>[44]</sup> | Cryptosporidium rats | Male | 5 mice/cage | | After 1 week of acclimatization and 7 days of paradoxical sleep depression | Body weight | TST: immobility time, FST: immobility time | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Gu X et al. 2022<sup>[45]</sup> | Cryptosporidium rats | Male | 5 mice/cage | | After 1 week of acclimatization and 4 weeks of CUMS | Body weight | TST: immobility time, FST: immobility time | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Guo J et al. 2018<sup>[46]</sup> | Cryptosporidium mice | Male | 6 mice | | After 1 week of acclimatization, and 10 days of CSDS | Body weight and 7 days of paradoxical sleep depression | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Guo X et al. 2018<sup>[47]</sup> | Cryptosporidium mice | Male | 6 mice | | After 1 week of acclimatization and 4 weeks of CUMS | Body weight | TST: immobility time, FST: immobility time | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Guo Y et al. 2019<sup>[48]</sup> | Cryptosporidium mice | Male | 6 mice | | After 1 week of acclimatization and 21 days of CRS | Body weight | TST: immobility time, FST: immobility time | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Guo Y et al. 2019<sup>[49]</sup> | Cryptosporidium mice | Male | 6 mice | | After 1 week of acclimatization and 21 days of CRS | Body weight | TST: immobility time, FST: immobility time | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |
| Han SK et al. 2019<sup>[50]</sup> | Cryptosporidium mice | Male | 6 mice | | After 2 days of IS | Body weight | TST: immobility time | | | | Illumina MiSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing analysis: Illumina MiSeq platform/NovaSeq platform |
| | | | | | | | | | | | 16S rRNA sequencing and control |

*Note: The above table includes a summary of the studies and their respective methods, including the species, gender, age, cause, and control conditions, along with the methods used for data collection and analysis. The table also indicates the statistical tests used, such as Wilcoxon tests, Student's t-tests, Newman-Keuls test, Dunnett's test, and one-way ANOVA.*
| Han SK et al. 2020a | C57BL/6 mice | Korea | case-control | 6-week-old male | IS-depression | 8-9 weeks | male | EPM: open arena time and entries | TST: immobility time | FST: immobility time | LDT: light box time | After 1 week of acclimatization, 5 days of Escherichia coli exposed and 5 days of drug treatment | Color contents | 16S-C | 16S rRNA gene sequencing - Illumina iSeq 100 platform | V4 | IS-depression and control | One-way ANOVA followed by Tukey’s multiple range test: p < 0.05 | LEfSe: p < 0.05 and LDA > 3.5 |
|---------------------|--------------|-------|--------------|-----------------|----------------|-----------|--------|------------------------|-----------------|-----------------|----------------|-------------------------------------------------|----------------|----------------|-------------------------------------------------|-----------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| Experiment 1:       | IS (N=6)     | IS+Rad ginseng low-dose (N=6) | IS+Rad ginseng middle-dose (N=6) | IS+Rad ginseng high-dose (N=6) | IS+Fermented red ginseng low-dose (N=6) | IS+Fermented red ginseng middle-dose (N=6) | IS+Fermented red ginseng high-dose (N=6) | Control (N=6) |
| Experiment 2:       | IS (N=6)     | IS+Flavonoids (N=6) | IS+Rad ginseng low-dose (N=6) | IS+Rad ginseng middle-dose (N=6) | IS+Fermented red ginseng low-dose (N=6) | IS+Fermented red ginseng middle-dose (N=6) | IS+Fermented red ginseng high-dose (N=6) | Control (N=6) |
| Experiment 3:       | EC (N=6)     | EC+Lactobacillus rhamnosus (N=6) | EC+Lactobacillus rhamnosus (N=6) | EC+Red ginseng middle-dose (N=6) | EC+Fermented red ginseng low-dose (N=6) | EC+Fermented red ginseng middle-dose (N=6) | Control (N=6) |
| Experiment 4:       | EC (N=6)     | EC+Probiotics (N=6) | EC+Probiotics (N=6) | EC+Red ginseng middle-dose (N=6) | EC+Fermented red ginseng low-dose (N=6) | EC+Fermented red ginseng middle-dose (N=6) | Control (N=6) |

Han SK et al. 2020b C57BL/6 mice | Korea | case-control | 5-week-old male | EC-depression | 5 weeks | male | TST: immobility time | FST: immobility time | After 1 week of acclimatization, 5 days of Escherichia coli | Fecal samples | 16S-C | 16S rRNA gene sequencing - Illumina iSeq 100 platform | V4 | EC-depression and control | One-way ANOVA followed by Tukey’s multiple range test: p < 0.05 | LEfSe: p < 0.05 and LDA > 3.5 |
|---------------------|--------------|-------|--------------|----------------|-----------|--------|------------------------|-----------------|-------------------------------------------------|----------------|----------------|-------------------------------------------------|-----------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| EC (N=5)            | EC+Lactobacillus rhamnosus (N=5) | EC+Red ginseng middle-dose (N=5) | EC+Fermented red ginseng middle-dose (N=5) | Control (N=5) |
| Study                          | Model          | Country | Age & Sex | Treatment  | Methodology                                                                 | Outcome  | Control Group |
|-------------------------------|----------------|---------|-----------|------------|----------------------------------------------------------------------------|----------|----------------|
| Han SK et al. 2021<sup>(13)</sup> | C57BL/6 mice | Korea   | 3 mice/cage RS-depression | FMT-RS (N=6) | Fecal samples (16S rRNA gene sequencing - Illumina iSeq platform) | Mood tests: EPM, TST, FST, LDT | RS+CSS middle-dose (N=6) |
| Hao W et al. 2021<sup>(10)</sup> | C57BL/6 mice | China   | 8-week-old male | Antibiotic-depression | Body weight, TST, immobility time, Body weight, TST, immobility time | Mood tests: EPM, TST, FST, LDT | Ampicillin+Xiaoyaosan (N=10) |
| Hao W et al. 2021<sup>(11)</sup> | C57BL/6 mice | China   | 8-week-old male | CUMS-depression | Body weight, SPT, sugar preference, EPM open-arm time and entries | Mood tests: EPM, TST, FST, LDT | CUMS (N=10) |
| Hassan AM et al. 2019<sup>(18)</sup> | C57BL/6 mice | Austria | 8-week-old male | HFD-depression | Body weight, Hair coat index, SPT, sucrose preference, Hair coat index | Mood tests: EPM, TST, FST, LDT | HFD (N=12) |
| Study            | Model          | Country | Treatment                                                                 | Age/Sex | Outcome Measures                                                                 | Statistical Tests                                                                 | Environment/Condition | Sequencing Platform          | Notes                        |
|------------------|----------------|---------|-----------------------------------------------------------------------------|---------|---------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|------------------------|-----------------------------|--------------------------------|
| Huang P et al.   | C57BL/6 mice  | China   | CRS+low dose L. plantarum (N=15)                                             | 10-12   | female                                                                          | 14 weeks after ovariectomy                                                        | 80 °C                  | 16S rRNA sequencing analysis  | LabMaster system: horizontal and vertical locomotor activity; MPT: morphine preference; saccharin solution intake | Unspecified                  |
| Huang N et al.   | C57BL/6 mice  | China   | IS+NK33+NK98 (N=7)                                                           | 2-month | male                                                                            | After 1 week of acclimatization, focal samples were collected after LPS and ketamine treatment | Focal samples           | 16S rRNA sequencing analysis  | Fisher's exact test: p < 0.05 | 
| Huang Y et al.   | C57BL/6 mice  | China   | IS+NK33 (N=7)                                                                | 9-week  | male                                                                            | After 1 week of acclimatization and 10 days of cCSDS                              | Focal samples           | 16S rRNA sequencing analysis  | 
| Huang Y et al.   | C57BL/6N mice | China   | DSS-depression                                                              | 4-5     | male                                                                            | After 7 days of adoption and 7 days of DSM treatment                              | Focal samples           | 16S rRNA sequencing analysis  | 
| Inserra A et al. | C57BL/6J mice | Australia| IS+DSS+low dose L. plantarum (N=15); DSS+high-dose L. plantarum (N=8); DSS+Fluorescein (N=8); Control (N=15) | 60 days | male                                                                            | After 1 week of acclimatization and 4 weeks of CUS                                | Focal samples           | 16S rRNA sequencing analysis  | 
| Jung HM et al.   | C57BL/6 mice  | Korea   | IS-depression                                                               | 5-week  | male                                                                            | After 1 week of acclimatization, 2 days of immobilization stress and 3 days of drugs treatment | Focal samples           | qPCR for Bacteroidetes, Bacteroidales, Actinobacteria and Erysipelotrichiaceae | 
| S S et al.       | C57BL/6 mice  | China   | CRS-depression                                                              | 9-week  | male                                                                            | After 1 week of acclimatization, the focal samples were collected after 8 weeks of CRS | Focal samples           | Hi-throughput 16S rRNA sequencing analysis | 

Notes:
- LEfSe: p < 0.05 and LDA > 4.0
- Metastats: p < 0.05 or FDR < 0.05
- 57BL/6 mice
- 57BL/6N mice
- 57BL/6J mice
- male
- female
- male
- female
- China
- Korea
- Australia
- New Zealand
- Wallis H test: p < 0.01
- Duncan multiple range test: p < 0.05
- One-way ANOVA: p < 0.05
- One-way ANOVA followed by a Duncan multiple range test: p < 0.05
- LEfSe: p < 0.05 and LDA > 2.0
- One-way ANOVA: p < 0.05
- LEfSe: p < 0.05 and LDA > 3.0
- LEfSe: p < 0.05 and LDA > 4.0
- Metastats: p < 0.05 or FDR < 0.05
| Study | Species/Country | Control | MS | Probiotics | FMT | Data Collection | Data Analysis | Notes |
|-------|----------------|---------|----|------------|-----|----------------|---------------|-------|
| Jiang W et al. 2017 | C57BL/6J mice | China | case-control | single | CUMS-depression | CUMS (N=6) | Control (N=6) | V3-V4 | 8-week-old | 90 °C | 16S rRNA gene sequencing: Illumina MiSeq platform | LEfSe: p < 0.05 and LDA ≥ 2.0 |
| Jiang Y et al. 2020 | C57BL/6J mice | Japan | case-control | single | CSDS-depression | CSDS (N=5) | Control (N=6) | V3-V4 | 6-week-old | 80 °C | 16S rRNA gene sequencing: Illumina MiSeq platform | LEfSe: p < 0.05 and LDA ≥ 2.0 |
| Kammerer Y et al. 2020 | C57BL/6J mice | China | case-control | single | MS-depression | Experiment 1: MS (N=6) | M-0% (N=6) | Student’s t-test: p < 0.05 |
| Karan C et al. 2021 | C57BL/6J mice | India | case-control | single | CSDS-depression | Modified CSDS (N=5) | Control (N=6) | V3-V4 | 6-week-old | 80 °C | 16S rRNA gene sequencing: Illumina MiSeq platform | LEfSe: p < 0.05 and LDA ≥ 2.0 |
| Kelly JR et al. 2019 | C57BL/6J mice | Ireland | case-control | single | MS | ABX FMT | ABX FMT-MRD (N=13) | FMT-MRD (N=15) | V3-V4 | Adult 350 g | 90 °C | 16S rRNA gene sequencing: Illumina MiSeq platform | Mann-Whitney U test and Bonferroni correction: PDR-adjusted p-value ≤ 0.1 |
| Kemp KM et al. 2021 | C57BL/6J mice | USA | case-control | single | MS | MS-early weaning (N=37) | Control (N=33) | V3-V4 | Adult 211 g | 90 °C | 16S rRNA gene sequencing: Illumina MiSeq platform | Analysis of composition of microbiomes (ANCOM) |
| Study Authors | Animal Model | Species | Control | Treatment | Diet | Age | Gender | Procedure | Sample | Platform | Comparison | Data Analysis |
|--------------|--------------|---------|---------|-----------|------|-----|--------|-----------|--------|----------|------------|--------------|
| Kim JK et al. 2020[67] | C57BL/6J mice | South Korea | case-control | 3-4 mice/cage | EC-depression | Escherichia coli K1 (N=7) EC K1L-4, L. mucosae NK41 (N=7) | Control (N=7) | 5-week-old | male | EPM: open-arm time; FST: immobility time | After 3 weeks of acclimatization and 5 days of Escherichia coli K1 treatment and 5 days of Lactobacillus mucosae NK41 treatment | Fecal samples | 80°C | 16S rRNA gene sequencing-Illumina MiSeq platform | V4 | EC-depression and control | LEfSe: p < 0.05 and LDA > 2.0 one-wayANOVA followed by a Duncan multiple range test: p < 0.05 |
| Lai WD et al. 2022[71] | C57BL/6J mice | South Korea | case-control | 3-4 mice/cage | SD-depression | SD (N=8) SD oil-reduced diet (N=8) | Control (N=8) | 6-week-old | male | Body weight; OPT: total distance, center time and entries | After a 6-week dietary intervention and followed by 4-week chronic sleep deprivation | Colon contents | 78°C | 16S rRNA sequencing analysis-Illumina MiSeq platform | V4-V5 | SD-depression and control | LEfSe: p < 0.05 and LDA > 2.0 |
| Knudsen JK et al. 2021[69] | C57BL/6J mice | South Korea | case-control | 3-4 mice/cage | SD-depression | Escherichia coli (N=6) Escherichia coli K1 (N=6) | Control (N=6) | 6-week-old | male | EPM: open-arm time and entries; FST: light time and entries; FST: immobility time | After 2 days of immobilization stress (Escherichia coli K1) and 5 days of buspirone treatment | Fecal samples | 70°C | 16S rRNA gene sequencing-Illumina MiSeq platform | V4 | MS+CVS-depression and control | LEfSe: p < 0.05 and LDA > 2.0 |
| Kuti D et al. 2021[70] | Flinders sensitive line rats | Flinders sensitive line rats | case-control | pair-fed | FMT-MDD-depression | FSL FMT-MDD (N=12) FSL FMT-MDD-Healthy (N=10) FSL CD-1 (N=10) FSL CD-1-Healthy (N=10) | Control (N=10) | 6-8-week-old | male | FST: struggling, immobility | After 1 week of acclimatization, fecal samples were collected before transplantation (post-FMT) and after transplantation (post-FMT) | Fecal samples | 80°C | 16S rRNA gene sequencing analysis-Illumina MiSeq platform | V4 | FRL FMT-MDD and FMT-Healthy | Knudsen-Wellin test followed by Dunn’s post hoc test: p < 0.05 |
| Kuroda A et al. 2021[68] | C57BL/6J mice | Japan | case-control | - | CSDS-depression | Control (N=12) | Control (N=12) | 7-week-old | male | OPT: interaction zone time (center area) | The fecal samples were collected 1 day before exposure of CSDS and after 5 days of CSDS | Fecal samples | 80°C | 16S rRNA gene sequencing analysis-Illumina MiSeq platform | V3-V4 | CSDS-depression and control | LEfSe: p < 0.05 and LDA > 2.0 |
| Knudsen JK et al. 2021[68] | C57BL/6J mice | Hungary | case-control | 2-3 mice/age | MS+CVS-depression | MS+CVS-Resistant (N=14) MS+CVS-Resistant-Healthy (N=12) | Control-Resistant (N=10) | Control-Resistant-Healthy (N=12) | Control (N=12) | PND80 | male | OPT: velocity and total distance, center time; food intake; EPM: Open arm preference; SPT: Sugar consumption | Colon contents were collected after 12 days of MS (PND12-13) and 4 weeks of CVS (PND80-84) | Colon contents | 78°C | RT-qPCR | MS+CVS-depression and control | Two-wayANOVA followed by Sidák’s multiple comparison test: p < 0.05 |
| Liu WD et al. 2022[72] | Wistar rats | China | case-control | - | SD-depression | SD (N=8) SD oil-reduced diet (N=8) | Control (N=8) | 6-week-old | male | Body weight; OPT: total distance, center time and entries | After a 6-week dietary intervention and followed by 4-week chronic sleep deprivation | Colon contents | 80°C | 16S rRNA gene sequencing-Illumina MiSeq platform | V3-V4 | SD-depression and control | LEfSe: p < 0.05 and LDA > 2.0 |
Leclercq S et al. 2020[73] C57BL/6J mice Belgium case-control ... coli, CUMS-depression and control. One-way ANOVA followed by the least significant difference test: p <0.05.

Li N et al. 2018[79] rats Dawley China case-control 3-week-old male Three-chamber sociability test: chamber time; sociability index; PST: latency to immobility. After 10 days of antibiotic treatment, feces were collected at three time points (25, 35 and 45 days after FMT) and causal content obtained at necropsy. Fecal samples Causal contents -80°C 16S rRNA gene sequencing– Illumina MiSeq platform qPCR for Faecalibacterium prausnitzii.

Li H et al. 2019[77] BALB/c mice China case-control 8-6 mice/age Land diet-depression Normal diet-placebo (N=6) Fish oil-based diet (N=10) Land-based diet (N=10) Normal diet control (N=6) 6-week-old male Food intake zone visit number; PST: immobility time After 4 weeks of acclimatization and 12 weeks of dietary intervention. Fecal samples - 16S rRNA gene sequencing– Illumina HiSeq 2500 platform V1-V3 V1-V4 FMT-AD-depression and FMT-control.

Li H et al. 2019[77] Sprague-Dawley rats China case-control 3-week-old male Body weight[gg]; PST: immobility time; SPE: sucrose ingestion After 7 days of acclimatization and 4 weeks of CUMS. Cecal contents -80°C 16S rRNA gene sequencing– Illumina HiSeq2500 platform V4 CUMS-depression and control.

Li H et al. 2019[77] C57BL/6J mice China case-control 3-week-old male Body weight[gg]; OPP: crossing number; PST: immobility time. After 1 week of acclimatization and 24 days of CUMS and rifaximin treatment. Fecal samples - 16S rRNA gene sequencing– Shanghai Majorbio Bio-Pharma Technology (Shanghai, China) V3-V4 CUMS-depression and control.

Li N et al. 2018[77] C57BL/6J mice China case-control 8-week-old male Body weight[gg]; OPP: sucrose preference; SPE: sucrose preference; EPM: open arms test; PST: immobility time. After 2 weeks of acclimatization and 4 weeks of CMS. Cecal contents -80°C 16S rDNA gene sequencing– Illumina HiSeq PE250 platform V3-V4 CUMS-depression and control.

Li N et al. 2019[79] C57BL/6J mice China case-control 7-week-old male Body weight[gg]; OPP: sucrose preference; PST: immobility time. After 1 week of acclimatization and 4 weeks of CMS. Cecal contents -80°C 16S rDNA gene sequencing– Illumina HiSeq platform V3-V4 CUMS-depression and control.

Li P et al. 2017[77] Sprague-Dawley rats China case-control 5-week-old male Body weight[gg]; OPP: sucrose preference; PST: immobility time. After 1 week of acclimatization and 6 weeks of CMS. Fecal samples - 16S rDNA gene sequencing– Illumina MiSeq platform V3-V4 CUMS-depression and control.

Li Q et al. 2019[79] Sprague-Dawley rats China case-control 6-week-old male Body weight[gg]; PST: immobility time. After 1 week of acclimatization and 4 weeks of CMS. Cecal contents - RT-PCR for Lactobacillus, Bifidobacteria, Enterococcus faecalis and Escherichia coli CUMS-depression and control.
Li Y et al. 2018(87)  Sprague-Dawley rats  China  case-control  vs groups  CUS-depression  CUS+Probiotic (N=6)  Control (N=6)  200 ± 20 g  male  SPT: sucrose preference↓  GPT: total distance↓, escape time↓  After 1 week of acclimatization and 4 weeks of CUS  Focal samples  -80 °C  16S rRNA gene sequencing-Illumina MiSeq platform  V3-V4  CUS-depression and control  Metastats: p < 0.05

Lin ET al. 2017(81)  Sprague-Dawley rats  Korea  case-control  vs groups  Ovariectomy-depression  Experiment 1: Ovariectomy (N=11)  Control (N=11)  10-week-old  female  Body weight↓  FST: immobility time↑  After 28 days of CUS (before the behavioral tests)  Focal samples  -80 °C  16S rRNA gene sequencing-Illumina MiSeq platform  V1-V2  Ovariectomy-depression and control  Wilcoxon rank-based test: p < 0.05  LEfSe: p < 0.05 and LDA > 3.0

Lin S et al. 2021(82)  ICB mice  China  case-control  vs groups  CUS-depression  CRS (N=10)  CUS-depression  6-week-old  male  Body weight↓  TST: latency time↑, immobility time↑  GPT: crossing number↑, focal number↑  After 28 days of CUS (before the behavioral tests)  Focal samples  -80 °C  16S rRNA gene sequencing-Illumina MiSeq 16S Metagenomic Sequencing Library Preparation protocol  V3-V4  CRS-depression and control  Student’s t-test: p < 0.05

Lin Q et al. 2020(83)  ICB mice  Korea  case-control  vs groups  IS-depression  IS (N=10)  IS-depression  6-week-old  male  Body weight↓  TST: latency time↑, immobility time↑  GPT: crossing number↑, focal number↑  After 1 week of acclimatization, fecal samples were collected on days 10, 14, and 18 after ovariectomy  Focal samples  -80 °C  16S rRNA gene sequencing-Illumina MiSeq platform  V4-V5  IS-depression and control  Student’s t-test: p < 0.05

Lin Z et al. 2017(84)  C57BL/6 mice  China  case-control  vs groups  CUMS-depression  CUMS+Inosine (N=10)  Control (N=16)  200 ± 20 g  male  Body weight↓  SPT: sucrose preference↑  GPT: total distance↑, escape time↑, open arms↑  After 28 days of CUS and 4 weeks of isoniazid or probiotic treatment  Focal samples  -80 °C  16S rRNA gene sequencing-Illumina MiSeq platform  V3-V4  CUMS-depression and control  LEfSe: p < 0.05 and LDA > 2.0

Lin SJ et al. 2018(85)  C57BL/6 mice  China  case-control  vs groups  CUMS-depression  CUMS (N=10)  Control (N=10)  200 ± 20 g  male  Body weight↓  SPT: sucrose preference↑  GPT: total distance↑, escape time↑, open arms↑  After 7 weeks of acclimatization and 4 weeks of CUMS and mice treatment  Focal samples  -80 °C  16S rRNA gene sequencing-Illumina MiSeq platform  V3-V4  CUMS-depression and control  One-way ANOVA followed by Tukey’s post hoc test: p < 0.05  LEfSe: p < 0.05 and LDA > 2.0

Liu Z et al. 2020(86)  C57BL/6 mice  China  case-control  vs groups  HD-depression  HD (N=15)  Control (N=15)  200 ± 20 g  female  MWM: escape time↑, target quadrant distance↑  Once the 21-day lactation was over  Focal samples  -80 °C  16S rRNA gene sequencing-Illumina MiSeq platform  V3-V4  HD-depression and control  LEfSe: p < 0.05 and LDA > 2.0

OFT: total distance↓, center time↓  SPT: sucrose preference↓  NSF: latency to eat↑  After 1 week of acclimatization and 4 weeks of CUS
| Study | Species | Treatment | Experimental Design | Mouse Strain | Sex | Fecal Material | Processing | Analysis | Result | p-value |
|-------|---------|-----------|---------------------|-------------|-----|---------------|-----------|---------|--------|---------|
| Luo X et al. 2021<sup>[88]</sup> | C57BL/6J mice | Control (N=12), Control+Inulin (N=12) | Electromagnetic field exposure (EMF), Heat acclimation (N=10) | 5-week-old male | FST: immobility time ↑, TST: crossing number ↓ | After 28 days of ambient temperature, the fecal samples were collected after 3 weeks of EMF | Two-way ANOVA followed by Sidak’s multiple comparisons test: p < 0.05 | Fecal samples | 80 °C | 16S rRNA sequencing analysis, Illumina MiSeq platform | V4 | EMF-depression and control |
| Le M et al. 2021<sup>[89]</sup> | Sprague-Dawley rats | China case-control study | CUMS-depression (N=12), ABX FMT (N=12) | Male | Body weight, SPT: sucrose preference, FST: immobility time | After 1 week of acclimatization and 4 weeks of CUMS | Sidak’s multiple comparisons test: p < 0.05 | Fecal samples | 80 °C | 16S rRNA gene sequencing- Illumina MiSeq platform | V3-V4 | CUMS-depression and control |
| Le W et al. 2019<sup>[90]</sup> | Sprague-Dawley rats | Male | Single | CUMS-depression (N=6) | 8-week-old male | Body weight, SPT: sucrose preference, TST: immobility time | After 1 week of acclimatization and 4 weeks of CUMS | Fecal samples | 80 °C | 16S rRNA gene sequencing- Unspecified | V3-V4 | CUMS-depression and control |
| Wu W et al. 2019<sup>[91]</sup> | Wistar rats | China case-control study | Single | DSS-depression (N=6) | 6-week-old male | SPT: sucrose preference, TST: immobility time | The fecal samples were collected after 7 weeks of DSS and 2 weeks of recovery | Fecal samples | 80 °C | 16S rRNA gene sequencing- | V4-V5 | DSS-depression and control |
| Meng SA et al. 2017<sup>[92]</sup> | C57BL/6 mice | USA case-control study | Single | UCMS-depression (N=12) | 8-week-old male | FST: escape behavior | After 1 week of acclimatization and 5 days of UCMS | Fecal samples | 80 °C | 16S rRNA gene sequencing- Illumina MiSeq platform | V3-V4 | UCMS-depression and control |
| Martin-Hernandez D et al. 2018<sup>[93]</sup> | Wistar rats | Spain case-control study | Single | CMS-depression (N=10) | 200-225g male | Weight gain, FST: immobility time, SPT: sucrose consumption, EPM: open arms time percentage | After 2 weeks of acclimatization and 3 weeks of CMS and antibiotics treatment | Blood, mesenteric lymph nodes (MLNs), liver, spleen | Refined ecosystem analysis, LEfSe: p < 0.05 and LDA > 3.0 | CMS-depression and control |
| Marumoto Y et al. 2020<sup>[94]</sup> | Sprague-Dawley rats | Single | Single | CMS-depression (N=6) | 8-week-old male | FST: social target | Fresh fecal samples were collected before the first SDS application (before), 1 day (stress 1d), 3 days (stress 3d), 7 days (stress 7d), and 4 weeks after the last SDS | Fecal samples | 80 °C | 16S rRNA gene sequencing- Illumina MiSeq platform | V3-V4 | CMS-depression and control (after stress) |
| Stellar EMF exposure (EMF) | 57BL/6 mice | Control (N=12), Control+Inulin (N=12) | Electromagnetic field exposure (EMF), Heat acclimation (N=10) | 8-week-old male | FST: immobility time, TST: crossing number | After 28 days of ambient temperature, the fecal samples were collected after 3 weeks of EMF | Two-way ANOVA followed by Sidak’s multiple comparisons test: p < 0.05 | Fecal samples | 80 °C | 16S rRNA sequencing analysis- Illumina MiSeq platform | V4 | EMF-depression and control |

<sup>LEfSe: p < 0.05 and LDA > 3.0</sup>
McGaughey KD et al. 2019

C57BL/6J mice USA case-control Single CSDS-depression CSDS (N=20) Control (N=19) 6-week-old male OPT: total distance to center time to corner time SPT: escape preference FST: immobility time 24h before the start of the social defeat trial and 24h after the social interaction testing (after 7 days of acclimation and 7 days of CSDS) Focal samples – 80 °C 16S rRNA gene sequencing Illumina MiSeq platform Y3-V4 CSDS-depression and control Wisconsin Rank Sum and Kruskal-Wallis tests followed by a Dunn’s post-test: p < 0.05

Molina-Rodriguez EM et al. 2020

C57BL/6J mice USA case-control Single LPS-depression LPS (N=5) Non-LPS (N=5) Control (N=5) 6-12-week-old male Escape failures Learned helplessness Steel immediately after exposure to escapable foot shocks Focal samples – 80 °C 16S rRNA gene sequencing Illumina MiSeq platform Y4 LPS-depression and control Kruskal-Wallis rank sum test with Bonferroni correction: p < 0.05

Morg C et al. 2020

Sprague-Dawley rats China case-control Single CUMS-depression CUMS (N=20) CUMS+antibiotics (N=20) Control (N=20) 6-week-old male PST: immobility time, swimming time After 1 week of acclimatization and 4 weeks of CUMS, fecal samples were collected at end of short-term antibiotics exposure period (at week 5) and long-term antibiotics exposure period (at week 9) Focal samples – 80 °C 16S rRNA gene sequencing Illumina MiSeq platform Y3-V4 CUMS-depression and control (short-term antibiotics exposure) One-way ANOVA with a Duncan’s test: p < 0.05

Moya-Ponce A et al. 2017

C57BL/6J mice Spain case-control Single MS-depression MS (N=18) MS+Bifidobacterium (N=18) Control (N=18) Control+Prebiotic (N=18) 5-7 days old female EPM: open arms time After maternal separation (PND21–23), stool samples were collected at PND35 and PND40 Focal samples – 80 °C 16S rRNA gene sequencing Illumina MiSeq platform Y4-V3 MS-depression and control (PND36) Wilcoxon Rank Sum test with post hoc Bonferroni correction: p < 0.05

Murphy E et al. 2019

CD-1 mice Canada case-control 2 mice/cage LPS-depression Acute effect for both male and female: LPS (N=10) LPS+Prebiotic (N=10) Control (N=10) Control+Prebiotic (N=10) Long-term effect for both male and female: LPS (N=10) LPS+Prebiotic (N=10) Control (N=10) Control+Prebiotic (N=10) 5-week-old male/female PST: immobility time OPT: corner time EPM: open arms time Focal samples were collected at five time points; 5 weeks of age (before probiotic treatment), 6 weeks of age (after 1 week of probiotics and just before LPS injection), 24 h after LPS injection, 7 weeks of age (at the end of two-week course of probiotic treatment), 10 weeks of age (at adulthood) Focal samples – 80 °C 16S rRNA gene sequencing Illumina MiSeq platform Y6-V9 LPS-depression and control Three-way mixed ANOVA: p < 0.05

O’Mahony SM et al. 2020

Sprague-Dawley rats Ireland case-control 3 rats/cage MS-depression MS (N=12) MS+Prebiotic (N=12) MS+Prebiotic+Probiotic (N=12) Control (N=12) Control+Prebiotic (N=12) Control+Prebiotic (N=12) Control+Prebiotic+Probiotic (N=12) 14-week-old male NOR: discrimination ability After maternal separation (PND21–23), stool samples were collected at the end of the study (weeks 14) Focal samples – 80 °C 16S rRNA gene sequencing Illumina MiSeq platform Y3-V4 MS-depression and control Rank Kruskal-Wallis test followed by Dunn’s test with false discovery rate adjustment: q < 0.05
| Study | Species | Country | Age | Treatment | Outcome Measure | Treatment Details | Statistical Analysis | Notes |
|-------|---------|---------|-----|-----------|----------------|-------------------|---------------------|-------|
| Osman A et al. 2021<sup>[102]</sup> | Wistar albino rats | USA | 10 week-old | Controls: Casein
- Casein-rich milk (N=8)
- Lactobacilli/Enterococci spp.
- Bifidobacterium adolescentis
- Enterococcus faecalis
- Clostridium histolyticum group
- Lactobacillus fermentum
- Lactobacillus casei
- Lactobacillus rhamnosus
- Clostridium perfringens
- Escherichia coli
- Staphylococcus epidermidis

- 5-month-old | FST: immobility time | Fecal samples were collected at PND25 | - Phosphorence-in-site Hybridization (ISH) analysis for Bifidobacterium spp.
- Clone 
- LEfSe: p < 0.05 and LDA > 8
- Wilcoxon test followed by Benjamini-Hochberg: p < 0.05 |
| Patrick KA et al. 2021<sup>[103]</sup> | Syrian hamsters (Mesocricetus auratus) | USA | 4 week-old | Controls: MS and control
- MS+EPA/DHA low-dose (N=10)
- MS+EPA/DHA high-dose (N=10)
- Control (N=10) | FST: immobility time | Prior to the initial defeat (baseline samples), 24 h after the acute defeat (acute defeat samples), and 24 h after the final defeat (repeated defeat sample) | - Wilcoxon rank sum test: adjust p < 0.05 |
| Patterson S et al. 2016<sup>[104]</sup> | C57BL/6 mice | Ireland | 4-8 week-old | Controls: LFD
- HFD+ L. brevis DSM13066 (N=14)
- LFD (N=14) | Body weight | After 5 week of acclimatization, 24 weeks of high fat feeding (the last 12 weeks received L. brevis intervention) | - 16S rRNA gene sequencing and MiSeq platform |
| Perez-Leory J et al. 2020<sup>[105]</sup> | Sprague-Dawley rats | USA | 175 g | Controls: MS+EPA/DHA low-dose (N=10)
- MS+EPA/DHA high-dose (N=10)
- Control (N=10) | FST: immobility time | After 5 week of acclimatization, 24 weeks of high fat feeding (the last 12 weeks received L. brevis intervention) | - 16S rRNA gene sequencing and MiSeq platform |
| Do Y et al. 2021<sup>[106]</sup> | C57BL/6 mice | Japan | 4-Week-old | Controls: Chrna7 KO
- Chrna7 KO (N=10)
- Wild-type (N=10) | FST: immobility time | As at 10:00 for KO mice | - Morgan istogenesis sequencing-
- Hidrome Hidreq 2000 |
| Poonah MM et al. 2015<sup>[107]</sup> | Sprague-Dawley rats | Ireland | 8-10 week-old | Controls: MS
- MS+Placebo (N=10) | TST: immobility time | After maternal separation stress (PND12-1) and EPA/DHA treatment (weeks 5-17), in vivo analysis for Bifidobacterium spp. | - 16S rRNA gene sequencing-
- Mis and control
- LeFSe: p < 0.05 and LDA > 2.0 |

**Note:** PND stands for Post Natal Day, FST for Forced Swim Test, SPT for Sucrose Preference Test, TST for Tail Suspension Test, FMT for Faecal Microbiota Transfer, and HFD for High Fat Diet.
Qiao Y et al. 2020[108] Kunming mice China case-control Control+EPA/DHA low-dose (N=10) Control+EPA/DHA high-dose (N=10) 8-week-old male Body weight[2] Food consumption[3] SPT: sucrose preference[4] TST: immobility time[6] TST: immobility time[6] OPT: test time[4] move time[4], corner time and distance[4] After 1 week of acclimatization and 3 weeks of stress Rectal contents 80 °C 16S rRNA gene sequencing- Illumina MiSeq platform V3-V4 CRS-depression and control CUMS-depressions and control CRS+CUMS-depressions and control ANOVA: p < 0.05

Qiao X et al. 2021[109] C57BL/6J mice China case-control Single LPS-depression LPS (N=8) LPS-Lactobacillus (N=8) Control (N=8) Control+Lactobacillus (N=8) 8-week-old male SPT: sucrose preference[4] TST: immobility time[6] After 7 days of acclimatization, followed by LPS and 7 days of Lactobacillus treatment Fecal samples - qPCR - LPS-depression and control Two-way ANOVA followed by least significant difference (LSD) post-hoc test: p < 0.05

Ray P et al. 2020[110] Kunming mice China case-control Control (N=10) Vancomycin (N=10) Control (N=10) 6-8-week-old male EPM: closed arms time[6] OPT: test time[4], move time[4], corner time and distance[4] Focal contents - 16S rRNA gene sequencing- Illumina MiSeq platform ANOVA: p < 0.05"
Robertson RC et al. 2017[116]  C57BL/6J mice Ireland case-control 5 mice/cage n-3 PUFA deficiency-depression n-3 PUFA supplement (N=10) n-3 PUFA deficiency (N=10) Control (N=10) 13-week-old male TST: immobility time, After 6 weeks of dietary treatment Fecal samples were collected after 13 weeks of dietary treatment Fecal samples 29°C 16S rRNA gene sequencing Illumina MiSeq platform V3-V4 n-3 PUFA deficiency-depression and control (adult only) Kruskal-Wallis tests followed by Mann-Whitney tests: p < 0.05 LEADs: p < 0.05 and LDA > 2.0

Ross IM et al. 2020[122]  Swiss mice Brazil case-control 40 mice/cage ADJ-40 (N=8) ADJ-40+Exercise (N=8) Control (N=8) Control+Exercise (N=8) 30-40 g, 45-55 days male CST: immobility time, After 1 week of acclimatization and 24 days of treadmill exercise (ADJ-40 injection at day 10) Colon contents 98°C RT-qPCR for Pimriocin and Bacteroidetes – n-3 PUFA deficiency-depression and control Two-way ANOVA followed by Duncan’s multiple range post-hoc test: p < 0.05

Schmidt AK et al. 2019[117]  NAB/HAB rats Germany case-control 4 rats/cage HAB-depression HAB (N= no data) HAB=Minocycline (N= no data) HAB=Echolaert (N= no data) NAB (N= no data) NAB=Minocycline (N= no data) NAB=Echolaert (N= no data) 11-12-week-old male/ female CST: struggling score, After 14 days of drug injection Colon contents 98°C 16S rRNA gene sequencing 454 pyrosequencing V3-V4 Bacteroidetes depression and NAB control ANOVA with a subsequent Tukey’s test: p < 0.05

Shao B et al. 2021[105]  Sprague-Dawley rats China case-control - CUS-depression Experiment 1: CUS (N=15) Control (N=10) Experiment 2: ABX (N=8-10) ABX+CUS (N=8-10) ABX+Control (N=8-10) Di-lactic acid (N=8-10) L-lactic acid (N=8-10) Control (N=8-10) 100-220 g male OPT: escape time, After 1 week of acclimatization and 5 weeks of CUS Fecal samples 98°C 16S rRNA gene sequencing Illumina MiSeq platform V3-V4 CUS-depression and control Wilcoxon rank-sum test: p < 0.05 LEADs: p < 0.05 and LDA > 2.0

Shao S et al. 2021[105]  C57BL/6 J mice China case-control Single CRS-depression CRS+CRC samples (N=5) CRS=Phenol-extracted CRC samples (N=5) CRS=AAB-HS CRC samples (N=5) CRS=AAB-LS CRC samples (N=5) CRS=AAB-Mid CRC samples (N=5) Control=CRC samples (N=5) 6-7-week-old male SPF: sucrose preference, After 7 days of acclimatization, 14 days of CRS, 25 days of behavioral tests, tumor cell injection, and fluoxetine or XCHT treatment Fecal samples 98°C 16S rRNA gene sequencing Illumina MiSeq platform V3-V4 CRS-depression and control ANOVA test: p < 0.05

Sheng L et al. 2021[105]  Sprague-Dawley rats China case-control - CUMS-depression CUMS (N=10) CUMS+Flucloxacine (N=10) CUMS+Control (N=10) Control (N=10) 180 g female CST: swimming time, After 7 days of acclimatization, 14 days of CRS, 25 days of behavioral tests, tumor cell injection, and fluoxetine or XCHT treatment Fecal samples 70°C 16S rRNA gene sequencing Illumina MiSeq platform V6-V3 CUMS-depression and control Mann-Whitney nonparametric test: p < 0.05

Soppi E et al. 2020[105]  C57BL/6J mice France case-control 9 mice/cage UCMS-depression Experiment 1: UCMS (N=10) Control (N=10) ABX PT-UCMS (N=10) 8-week-old male CST: immobility time, After 9 weeks of UCMS (the last week were received behavioral testing) Fecal samples 98°C 16S rRNA gene sequencing Illumina MiSeq platform V3-V4 UCMS-depression and control ANOVA test: p < 0.05
| Study | Species | Treatment | Age (weeks) | Gender | Behavior/Assay | Sample Type | Temperature (°C) | Platform | Additional Notes |
|-------|---------|-----------|------------|--------|---------------|-------------|-----------------|----------|-----------------|
| Song et al. 2019[28] | 57BL/6 mice | CUMS | 8 | Male | PFT: immobility time; OFT: center time and entries | Fecal samples | 80 | Illumina MiSeq platform | After 1 week of ABX treatment, 4 days of microbiota transplantation, and 8 weeks of colonization (the last week were received behavioral testing) |
| Song et al. 2019[28] | 57BL/6 mice | CUMS | 8 | Female | OPT: open arms time; EPM: open arms time | Fecal samples | 80 | Illumina MiSeq platform | After 2 weeks of recovery from orchectomy (at 8-week-old of age) and 2 weeks of progesterone treatment |
| Sun et al. 2019[29] | 57BL/6 mice | Pro-RD | 8 | Male | Body weight2; SPT: sucrose preference; TST: immobility time; EPM: open arms time | Unspecified | 80 | Unspecified | Unspecified |
| Sun et al. 2019[28] | 57BL/6 mice | Pro-RD | 8 | Female | EPM: open arms time; OPT: open arms time | Unspecified | 80 | Illumina MiSeq platform | Unspecified |

**Abbreviations:** 
- ABX: Antibiotics 
- PFT: Passively floating time 
- OFT: Open field time 
- TST: Tail suspension test 
- SPT: Sucrose preference test 
- EPM: Elevated plus maze 
- CUMS: Chronic unpredictable mild stress 
- ACTH: Adrenocorticotropic hormone 
- Fluoxetine: A selective serotonin reuptake inhibitor 
- HTP: Hypothalamic-pituitary 
- FMT: Faecal microbiota transplantation 
- LEfSe: Linear discriminant analysis effect size 
- FMT-KO: Faecal microbiota transplantation-knockout

**Notes:** 
- Sun L et al. 2019[28] - All animals were male, with the exception of the orchectomized group, which included both males and females.
- Sun L et al. 2019[29] - Pro-RD mice were used, with Pro-RD female mice being used in the behavioral tests.
- All experiments used the Illumina MiSeq platform for 16S rRNA gene sequencing.
- Wilcoxon rank sum test was used for statistical analysis, with Bonferroni correction for multiple comparisons.
- LEfSe was used to identify significantly differentially abundant taxa, with a cutoff of p < 0.05 and LDA > 2.0.

**References:**
- Sun L et al. 2019[28]
- Sun L et al. 2019[29]
- Sovijit WN et al. 2021
- Song J et al. 2020[28]
- Song L et al. 2019[28]
- Sun L et al. 2019[29]
- Song X et al. 2017[28]
Sun X et al. 2012[130] C57BL/6 mice China case-control 3-4 mice/cage CRS-depression CRS (N=10); CRS-WP-LPS (N=10); Control (N=10) 4-week-old male OPT: center time; EPM: open arm time and entries; PST: immobility time; After 4 weeks of CRS Focal samples _ 16S rRNA gene sequencing-Illumina HiSeq2500 Microbiome Profiling setup V3-V4 CRS-depression and control One-way ANOVA: p < 0.05

Sun Y et al. 2019[131] Kunming mice China case-control _ CUMS-depression CUMS (N=8) CUMS-Fluoxetine (N=8) Control (N=8) 14-20 g male SPT: sucrose preference; PST: immobility time; OPT: vertical movements; crossing number; After 1 week of acclimatization and 6 weeks of CUMS (the last 2 weeks received drug treatment) Focal samples _ 16S rRNA gene sequencing-Illumina HiSeq platform V4 CUMS-depression and control LEfSe: p < 0.05 and LDA > 2.0

Sun Y et al. 2020[132] C57BL/6 mice China case-control 4 mice/cage LPS-depression LPS (N=12) LPS-Schisanthrin (N=12) Control (N=12) 20 ± 2 g male PST: immobility time; PST: immobility time; After 1 week of acclimatization and 2 weeks of vehicle or SCH treatment Focal samples _ 38 °C 16S rRNA gene sequencing-Illumina HiSeq platform V3-V4 LPS-depression and control Tukey multiple comparison test: p < 0.05

 Suzuki K et al. 2020[133] C57BL/6 J (B6) mice Japan case-control _ CSDS-depression CSDS (N=6) CSDS+Carb (N=6) Control (N=6) 7-week-old male SIT: social interaction time; distance traveled; We sampled at three time points on day 1, 9, and 14 in the first experiment and at two time points on day 9 and 21 in the second experiment Focal samples _ 38°C 16S rRNA gene sequencing-Illumina HiSeq platform V3-V4 Adex CSDS-depression and pre-CSDS control Pair student’s t-test: p < 0.05

Sadowskiowa JK et al. 2017[134] C57BL/6 mice Canada case-control Single CSDS-depression CSDS-unexposed (N=10) CSDS-exposed (N=10) Control (N=6) 7-9-week-old male SIT: social interaction time; contact time; Corner zone time; After 1 week of acclimatization and 3 weeks of CSDS Cereb contents _ 38°C 16S rRNA gene sequencing-Illumina MiSeq Sequencing V3-V4 CSDS-depression and control One-way ANOVA followed by Bonferroni correction: p < 0.05

Takahashi E et al. 2012[135] C57BL/6J (B6) mice Japan case-control group AIN-93G depression AIN-93G young (N=10) AIN-93G old (N=10) Control (N=10) 5-week-old male PST: immobility time; PST: immobility time; After 5 weeks of AIN-93G diet for young and 85 weeks of AIN-93G diet for old mice Small intestinal contents _ AIN-93G-depression and CRF-1 control (in old mice) ANOVA followed by the Bonferroni correction post hoc test: p < 0.05

Takahashi E et al. 2012[136] C57BL/6J (B6) mice Japan case-control group Cohort 1 CRS-AIN-93G diet (N=10) CRS-CRF-1 diet (N=10) Control-AIN-93G diet (N=10) Control-CRF-1 diet (N=10) Cohort 2 CRS-AIN-93G long (N=10) CRS-CRF-1 long (N=10) Control-AIN-93G long (N=10) Control-CRF-1 long (N=10) 5-week-old male Body weight; PST: struggling time; immobility time/SPT: sucrose preference; After 3 weeks of CRS and 1 week of AIN-93G diet for cohort 1 or 5 weeks of AIN-93G diet for cohort 2 Cereb contents _ Termal restriction fragment length polymorphism (T-RFLP) method ANOVA followed by the Bonferroni correction post hoc test: p < 0.05

Takahashi E et al. 2012[137] C57BL/6J (B6) mice Japan case-control group Cohort 1 CRS-AIN-93G diet (N=10) CRS-CRF-1 diet (N=10) Control-AIN-93G diet (N=10) Control-CRF-1 diet (N=10) Cohort 2 CRS-AIN-93G long (N=10) CRS-CRF-1 long (N=10) Control-AIN-93G long (N=10) Control-CRF-1 long (N=10) 5-week-old male Body weight; PST: struggling time; immobility time/SPT: sucrose preference; After 3 weeks of CRS and 1 week of AIN-93G diet for cohort 1 or 5 weeks of AIN-93G diet for cohort 2 Cereb contents _ Termal restriction fragment length polymorphism (T-RFLP) method ANOVA followed by the Bonferroni correction: p < 0.05

Sun X et al. 2012[130] C57BL/6 mice China case-control 3-4 mice/cage CRS-depression CRS (N=10); CRS-WP-LPS (N=10); Control (N=10) 4-week-old male OPT: center time; EPM: open arm time and entries; PST: immobility time; After 4 weeks of CRS Focal samples _ 16S rRNA gene sequencing-Illumina HiSeq2500 Microbiome Profiling setup V3-V4 CRS-depression and control One-way ANOVA: p < 0.05

Sun Y et al. 2019[131] Kunming mice China case-control _ CUMS-depression CUMS (N=8) CUMS-Fluoxetine (N=8) Control (N=8) 14-20 g male SPT: sucrose preference; PST: immobility time; OPT: vertical movements; crossing number; After 1 week of acclimatization and 6 weeks of CUMS (the last 2 weeks received drug treatment) Focal samples _ 16S rRNA gene sequencing-Illumina HiSeq platform V4 CUMS-depression and control LEfSe: p < 0.05 and LDA > 2.0

Sun Y et al. 2020[132] C57BL/6 mice China case-control 4 mice/cage LPS-depression LPS (N=12) LPS-Schisanthrin (N=12) Control (N=12) 20 ± 2 g male PST: immobility time; PST: immobility time; After 1 week of acclimatization and 2 weeks of vehicle or SCH treatment Focal samples _ 38 °C 16S rRNA gene sequencing-Illumina HiSeq platform V3-V4 LPS-depression and control Tukey multiple comparison test: p < 0.05

 Suzuki K et al. 2020[133] C57BL/6 J (B6) mice Japan case-control _ CSDS-depression CSDS (N=6) CSDS+Carb (N=6) Control (N=6) 7-week-old male SIT: social interaction time; distance traveled; We sampled at three time points on day 1, 9, and 14 in the first experiment and at two time points on day 9 and 21 in the second experiment Focal samples _ 38°C 16S rRNA gene sequencing-Illumina HiSeq platform V3-V4 Adex CSDS-depression and pre-CSDS control Pair student’s t-test: p < 0.05

Sadowskiowa JK et al. 2017[134] C57BL/6 mice Canada case-control Single CSDS-depression CSDS-unexposed (N=10) CSDS-exposed (N=10) Control (N=6) 7-9-week-old male SIT: social interaction time; contact time; Corner zone time; After 1 week of acclimatization and 3 weeks of CSDS Cereb contents _ 38°C 16S rRNA gene sequencing-Illumina MiSeq Sequencing V3-V4 CSDS-depression and control One-way ANOVA followed by Bonferroni correction: p < 0.05

Takahashi E et al. 2012[135] C57BL/6J (B6) mice Japan case-control group AIN-93G depression AIN-93G young (N=10) AIN-93G old (N=10) Control (N=10) 5-week-old male PST: immobility time; PST: immobility time; After 5 weeks of AIN-93G diet for young and 85 weeks of AIN-93G diet for old mice Small intestinal contents _ AIN-93G-depression and CRF-1 control (in old mice) ANOVA followed by the Bonferroni correction post hoc test: p < 0.05

Takahashi E et al. 2012[136] C57BL/6J (B6) mice Japan case-control group Cohort 1 CRS-AIN-93G diet (N=10) CRS-CRF-1 diet (N=10) Control-AIN-93G diet (N=10) Control-CRF-1 diet (N=10) Cohort 2 CRS-AIN-93G long (N=10) CRS-CRF-1 long (N=10) Control-AIN-93G long (N=10) Control-CRF-1 long (N=10) 5-week-old male Body weight; PST: struggling time; immobility time/SPT: sucrose preference; After 3 weeks of CRS and 1 week of AIN-93G diet for cohort 1 or 5 weeks of AIN-93G diet for cohort 2 Cereb contents _ Termal restriction fragment length polymorphism (T-RFLP) method ANOVA followed by the Bonferroni correction: p < 0.05

Takahashi E et al. 2012[137] C57BL/6J (B6) mice Japan case-control group Cohort 1 CRS-AIN-93G diet (N=10) CRS-CRF-1 diet (N=10) Control-AIN-93G diet (N=10) Control-CRF-1 diet (N=10) Cohort 2 CRS-AIN-93G long (N=10) CRS-CRF-1 long (N=10) Control-AIN-93G long (N=10) Control-CRF-1 long (N=10) 5-week-old male Body weight; PST: struggling time; immobility time/SPT: sucrose preference; After 3 weeks of CRS and 1 week of AIN-93G diet for cohort 1 or 5 weeks of AIN-93G diet for cohort 2 Cereb contents _ Termal restriction fragment length polymorphism (T-RFLP) method ANOVA followed by the Bonferroni correction: p < 0.05
| Study | Species | Age | Group | Condition | Method | Result |
|-------|---------|-----|-------|-----------|--------|--------|
| Teng T et al. 2021 | Macaca fascicularis monkeys | 1-4 years old | CUMS-depression | CUMS-depression (N=5) Control (N=5) | Illumina MiSeq platform V4 FSL-depression and FRL-control | DESeq2: adjusted p (Benjamini-Hochberg) < 0.05 |
| Tian P et al. 2019 | C57BL/6J mice | 6-week-old | CUMS-depression | CUMS (N=6) CUMS+Fluoxetine (N=6) | LEfSe: p < 0.05 and LDA > 3.0 |
| Tian P et al. 2020 | C57BL/6J mice | 6-week-old | CUMS-depression | CUMS (N=6) CUMS+Fluoxetine (N=6) | LEfSe: p < 0.05 and LDA > 2.0 |
| Tian P et al. 2021 | C57BL/6J mice | 6-week-old | CUMS-depression | CUMS (N=10) CUMS+Probiotics (N=6) | LEfSe: p < 0.05 and LDA > 5.0 |
| Tian P et al. 2021 | C57BL/6J mice | 6-week-old | CRS-depression | CRS (N=6) CRS+Acetylated starch (N=6) | LEfSe: p < 0.05 and LDA > 2.0 |
| Tian SO et al. 2021 | BALB/c mice | 7-week-old | 15-postpartum depression | 15-PPD (N=10) 15-PPD+PND9 syrup (N=10) | LEfSe: p < 0.05 and LDA > 3.0 |
| Tian XY et al. 2022 | Flinders sensitive line rats | 10-14 days | Postpartum depression | Postnatal 5 (N=10) | One-way ANOVA followed by Fisher’s LSD multiple comparison test: p < 0.05 |
| Titman E et al. 2018 | Flinders sensitive line rats | 10-14 days | Postpartum depression | Postnatal 5 (N=10) | Fisher’ LSD multiple comparison test: p < 0.05 |
| Study | Animal | Country | Methodology | Procedure | Sample Size | Measurements | Findings |
|-------|--------|---------|-------------|-----------|-------------|--------------|----------|
| Tung TH et al. 2019[143] | Sprague-Dawley rats | China | case-control | CMS-depression | CMS (N=5) CMS-depression (N=5) CMS-FB06 (N=5) CMS-606 (N=5) Control (N=5) | 6-week-old male | Body weight, OPT total distance, SPT: sucrose preference, FST: immobile time | After 2 weeks of acclimatization and 12 weeks of CMS, Focal samples, -80 °C, 16S rRNA gene sequencing- Illumina MiSeq platform | V3-V4, CMS-depression and control, LEfSe: p < 0.05 and LDA > 2.0 |
| Wang L et al. 2020[144] | Sprague-Dawley rats | China | case-control | CUMS-depression | CUMS (N=8) CUMS-low-dose TIV (N=8) CUMS-middle-dose TIV (N=8) CUMS-high-dose TIV (N=8) CUMS-Plus-strain (N=8) Control (N=8) | 6-week-old male | Body weight, OPT: total distance, SPT: sucrose preference, FST: immobile time | After 1 week of acclimatization and 4 weeks CUMS, Focal samples, -80 °C, 16S rRNA gene sequencing- Illumina HiSeq platform | V4, CUMS-depression and control, One-way ANOVA followed by LSD test: p < 0.05 |
| Wang P et al. 2021[145] | C57BL6J mice | China | case-control | Antibiotic-depression | Antibiotic (N=9) Antibiotic+Saline (N=9) Antibiotic+Probiotics (N=9) Antibiotic+Saline (N=9) Control (N=9) | 3-month-old male | EMG total crosstalk, open arm time, velocity, OPT: total distance, center time and distance, FST: immobile time, LDT: light zone duration | After 1 week of acclimatization, 10 weeks of CUMS and 8 weeks of probiotics treatment, Focal samples, -qPCR, Antibiotic-depression and control, One-way ANOVA followed by Tukey's multiple comparisons test: p < 0.05 |
| Wang Q et al. 2019[146] | CD-1 mice | China | single | CSDS-depression | CSDS (N=10) CSDS-TF (N=10) CSDS-TF low-dose (N=10) CSDS-TF high-dose (N=10) Control (N=10) | 3-month-old male | SPT: sucrose preference, FST: immobile time, MBT: number of beads buried, LDT: light zone duration | After 2 weeks of acclimatization and 10 weeks of CMS, Focal samples, -16S rRNA gene sequencing- Illumina HiSeq platform | V3-V4, CMS-depression and control, LEfSe: p < 0.05 and LDA > 7.0 |
| Wang R et al. 2021[147] | C57BL6J mice | China | case-control | CRS-depression | CRS (N=8) CRS-TFA low-dosage (N=8) CRS-TFA high-dosage (N=8) Control (N=8) | 6-week-old male | OPT: total distance, SPT: sucrose preference, FST: immobile time | After 7 days of acclimatization and 30 days of CRS, Cocom contents, -16S rRNA gene sequencing- Illumina HiSeq platform | V3-V4, CRS-depression and control, One-way ANOVA: p < 0.05 |
| Wang S et al. 2020[148] | C57BL6J mice | Japan | case-control | FMT CSDS-depression | FMT-FCS-high-dosage (N=7) FMT-FCS-middle-dosage (N=7) FMT-FCS-low-dosage (N=7) Control (N=7) | 8-week-old male | SPT: sucrose preference, FST: immobile time, LDT: light zone duration | After 14 days of antibiotic cocktail treatment and 14 days of FMT from CSDS-resistant mice or control, Focal samples, -16S rRNA gene sequencing- Illumina HiSeq platform | V1-V2, FMT CSDS-depression and FMT control, Two-way ANOVA followed by post hoc Fisher’s LSD test: p < 0.05 |
| Wang S et al. 2020[149] | C57BL6 mice | Japan | case-control | CSDD-depression | CSDD (N=7) CSDD=Antibiotics (N=8) | 8-week-old male | SPT: sucrose preference | Fresh fecal samples were collected on day 15 before CSDD, Focal samples, -16S rRNA gene sequencing- Illumina HiSeq platform | V1-V2, CSDD-depression and control, Two-way ANOVA followed by post hoc Tukey test: p < 0.05 |
| Study Authors | Country | Species | Intervention | Time Points | Sample Size | Grouping | Location | Analysis | Results |
|--------------|----------|----------|--------------|-------------|-------------|----------|----------|----------|---------|
| Wang S et al. 2021[151] | China | C57BL/6 mice | Control (N=10) | 8-week-old | 10 | Male | Shanghai | One-way ANOVA: p < 0.05 | After 14 days for antibiotic cocktail treatment and 14 days for FMT procedure | Fecal samples | 16S rRNA gene sequencing | V1-V2 | FMT CSDS-depression and control (in both Ephe2 KO mice and WT mice) | Krohmal-Wallis test: p < 0.05 |
| Wang Y et al. 2021[152] | China | C57BL/6 mice | Control+Antibiotics (N=10) | 2-month-old | 10 | Male | Shanghai | One-way ANOVA and Tukey’s multiple comparison test: p < 0.05 | After 1 week of acclimatization and a single injection of LPS | Fecal samples | 16S rRNA gene sequencing | V3-V5 | LPS-depression and control | Krohmal-Wallis test: p < 0.05 |
| Ward AK et al. 2019[153] | Ireland | C57BL/6 mice | Control (N=12) | 6-8-week-old | 12 | Male | Ireland | One-way ANOVA: p < 0.05 | After 1 week of acclimatization, fecal samples were collected weekly during the 8 weeks of designated diet | Fecal samples | 16S rRNA gene sequencing | V3-V4 | AIDR-CDS-depression and control | SHSeq2 with Wald test: p < 0.05 |
| Wu C et al. 2019[154] | China | C57BL/6J mice | Control (N=10) | 57BL/6 mice | 10 | Male | China | - | - | Fecal contents | 16S rRNA gene sequencing | V4 | CUMS-depression and control | - | - |
| Wu-SN et al. 2019[155] | Taiwan | Water rats | Control (N=9) | 8 weeks | 80 °C | - | Taiwan | - | - | Body weight | 16S rRNA gene sequencing | V4 | CUMS-depression and control | LESeq p < 0.05 and LDA > 4.0 | - |
| Westall SJ et al. 2020[156] | USA | C57BL/6J mice | Stress+US (N=10) | 60-90 days | 10 | Male | USA | - | - | Body weight | 16S rRNA gene sequencing | V4 | CUMS-depression and control | One-way ANOVA and Turkey’s post hoc analysis: p < 0.05 |
| Wong ML et al. 2019[157] | Australia | C57BL/6J mice | CRS (N=15) | 60-90 days | 15 | Male | Australia | - | - | Body weight | 16S rRNA gene sequencing | V4 | CRS-depression and control | Mann-Whitney U-test: p = 0.05 |
| Wu P et al. 2020[158] | China | C57BL/6 mice | HFD (N=10) | 8-week-old | 10 | Male | China | - | - | Body weight | 16S rRNA gene sequencing | V4 | HFD-depression and control | One-way ANOVA: p < 0.05 |
Wu J et al. 2021[159] C57/BL6 mice China case-control Single CUMS-depression Depression (N=15) Control (N=15) 4 to 6-week-old female GPT: total distance, speed, crossing and nesting number; EFM: open-arm time; PST: immobility time; SST: immobility time; SPT: sucrose preference
After 1-week of acclimatization, the fecal samples were collected after 35 days of CUMS or dexamethasone treatment Fecal samples 90 °C 16S rRNA sequencing analysis Illumina MiSeq platform V3-V4 CUMS-depression control and control LEfSe: p < 0.05 and LDA > 3.0 Keuls-Wallis tests with multiple comparison correction, p < 0.05
Wu J et al. 2022[162] Mucaca (squirrel monkeys) China case-control group Naturally-occurring depression Depression (N=6) Control (N=6) Adult female Duration of huddle and sit-alone behavior; Duration of immobile and locomotion activities
After behavioral tests Cecum contents 90 °C Microbiota Illumina HiSeq N platform LEfSe: p < 0.05 and LDA ≥ 2.0 Naturally-occurring depression and control
Wu J et al. 2022[161] C57BL/6 mice China case-control Single CUMS-depression Depression (N=16) Control (N=16) 5-10-week-old male GPT: center time, center distance; PST: immobility time; SPT: sucrose preference; Body weight
After 4 weeks of CUMS Fecal samples 90 °C 16S rRNA gene sequencing Illumina MiSeq platform V3-V5 CUMS-depression and control LEfSe: p < 0.05 and LDA > 3.0
Xie J et al. 2021[159] C57BL/6 mice China case-control Single CRS-depression CRS (N=20) Control (N=20) 6-week-old male GPT: sucrose preference; PST: nesting and crossing number; SPT: immobility time; SST: immobility time
After 4 months of CAP treatment during the last 5 days, mice in LPS and LPS+CAP groups received [14C]iodoacetamide Fecal samples 90 °C 16S rRNA gene sequencing Illumina MiSeq platform V3-V4 CRS-depression and control LEfSe: p < 0.05 and LDA > 3.0
Xie R et al. 2020[163] C57BL/6 mice China case-control Single CRS-depression CRS (N=10) Control (N=10) 6-week-old male SPT: sucrose preference; PST: immobility time; SST: immobility time
After 1 week of acclimatization and 10 weeks of CRS (the last 6 weeks received crocetin and dexamethasone) Cecum contents 90 °C 16S rRNA gene sequencing Illumina MiSeq platform V3-V4 CRS-depression and control LEfSe: p < 0.05 and LDA > 2.0
Xie R et al. 2020[164] C57BL/6 mice China case-control Single CSDS-depression CSDS-susceptible (N=7) CSDS-resistant (N=7) 7-week-old male SPT: interaction time; PST: sucrose preference; GPT: total distance, center time; Center entries
After 1-week of acclimatization and 10 days of CSDS Poo’s patch-anova associated multiple comparison time Cocal contents 90 °C 16S rRNA gene sequencing Illumina MiSeq platform V3-V4 CSDS-depression susceptible and control One-way ANOVA: p < 0.05
Xie R et al. 2020[165] C57BL/6 mice China case-control 5 mice/cage CSDS-depression CSDS-susceptible (N=10) CSDS-resistant (N=10) Control (N=10) Control (N=5) 8-week-old male SPT: interaction time; PST: sucrose preference; GPT: total distance, center time, center entries; Body weight
After 1-week of acclimatization, 10 days of CSDS and 4 weeks of microbial treatment Cecum contents 90 °C 16S rRNA gene sequencing Illumina MiSeq platform V3-V4 CSDS-depression and control One-way ANOVA test followed by Tukey’s test: p < 0.05
Xie R et al. 2021[166] C57BL/6 mice China case-control Single SMIT-auto-depression Small intestinal microbe transplantation (N=6); Large intestinal microbe transplantation (N=6) PMDN5 male SPT: sucrose preference; PST: immobility time; SST: immobility time
Before microbe transplantation (PN977) and after 14 days of microbe transplantation (PN985) Fecal samples 90 °C 16S rRNA gene sequencing Illumina MiSeq platform V3-V4 SMIT-auto-depression and control Keuls-Wallis test followed by the Bonferroni post hoc test: p < 0.05
Xu J et al. 2022[167] C57BL/6 mice China case-control Single CUMS-depression CUMS-high-dose L. rhamnusae-zr-1 (N=12) Control (N=12) CUMS-middle-dose L. rhamnusae-zr-1 4-week-old male Body weight; SPT: sucrose preference; PST: immobility time; GPT: total distance, center time
After 1 week of acclimatization and 5 weeks of CUMS Cecum contents 90 °C 16S rDNA gene sequencing Illumina MiSeq platform V3-V4 CUMS-depression and control One-way analysis of variance (ANOVA) test followed by Tukey’s post hoc test: p < 0.05 LEfSe
| Study | Mice | Country | Treatment | Mice Model | Number | Gender | Age | Strain | Duration | Outcome | Analysis | Controls | Notes |
|-------|------|---------|-----------|-----------|--------|--------|-----|--------|----------|---------|----------|----------|-------|
| Xu M et al. 2022 | C57BL/6 mice | China | CUMS+low-dose L. rhamnosus zz-1 (N=12)  Control (N=12) | CUS (N=8)  LPS+Lactobacillus for each strain (N=7)  Control (N=9) | 6 weeks | male | 18-22 g | C57BL/6J mice  China | After 1 week of acclimatization and 6 weeks of CUS | Colon contents | 16S rRNA gene sequencing: Illumina MiSeq platform | V3-V4 |
| Xu Z et al. 2019 | C57BL/6 mice | China | case-control | CAD-depression | C57BL/6 mice  China | 4 mice/cage | 6-week-old | 4 mice/cage | C57BL/6 mice  China | After 1 week of acclimatization and 6 weeks of CAD | Fecal samples | 80 °C | 16S rRNA gene sequencing: Illumina MiSeq platform | V3-V5 |
| Yang C et al. 2017 | C57BL/6 mice | China | case-control | Single | C57BL/6 mice  China | 4 mice/cage | 6-week-old | 4 mice/cage | C57BL/6 mice  China | After 3 weeks of acclimatization and 10 weeks of alcohol exposure (and fecal samples were collected at the research day of the drinking session) | Colon contents | 16S rRNA gene sequencing: Illumina MiSeq platform | V3-V4 |
| Yan T et al. 2020 | C57BL/6 mice | China | case-control | Single | C57BL/6 mice  China | 4 mice/cage | 18-22 g | 4 mice/cage | C57BL/6 mice  China | After 1 week of acclimatization and 4 weeks of CUMS | Cecrum contents | 80 °C | 16S rRNA gene sequencing: Illumina MiSeq platform | V3-V4 |
| Yan T et al. 2021 | C57BL/6 mice | China | case-control | Single | C57BL/6 mice  China | 4 mice/cage | 18-22 g | 4 mice/cage | C57BL/6 mice  China | After 7 days of drugs | Fecal samples | - | 16S rRNA gene sequencing: Illumina MiSeq platform | V3-V4 |
| Yang C et al. 2017 | C57BL/6 mice | China | case-control | Single | C57BL/6 mice  China | 4 mice/cage | 8-week-old | 4 mice/cage | C57BL/6 mice  China | After 10 days of CSDS | Fecal samples | 80 °C | 16S rRNA analysis: Terminal restriction fragment length polymorphism (T-RFLP) analysis | _ |

**Notes:**
- **CSDS:** Chronic stress depression syndrome
- **CADS:** Chronic alcohol depression syndrome
- **LPS:** Lipopolysaccharide
- **CUMS:** Chronic constriction injury model
- **CAE:** Chronic alcohol exposure
- **SIT:** Social interaction test
- **EPM:** Elevated plus maze test
- **FST:** Forced swimming test
- **TST:** Immobility test
- **OFT:** Open field test
- **LDT:** Latency to drink test
- **MBT:** Modified behavioral test
- **FMT:** Fecal microbial transplantation

**Analysis Methods:**
- **16S rRNA analysis**
- **16S rRNA gene sequencing**
- **Illumina MiSeq platform**
- **Illumina HiSeq platform**
- **16S rRNA metagenomic sequencing**
- **pyrosequencing**

**Statistical Tests:**
- **Fisher’s exact test:** p < 0.05
- **One-way ANOVA** followed by Tukey’s multiple comparison test: p < 0.05
- **Unpaired Student’s t-test:** p < 0.05
- **Kruskal-Wallis** test followed by Bonferroni test: p < 0.05
Yang C et al. 2017b
C57BL/6 mice Japan case-control Single CSDS-depression
CSDS (N=6)
CSDS+(R)-ketamine (N=6)
Control (N=6)
9-week-old male
FST: immobility(ς)
TST: immobility(ς)
SPT: sucrose preference(ς)
The fecal samples were collected 10 days of CSDS and 4 days (day 18) after a single dose of drugs
Fecal samples
~80 °C
16S rRNA sequencing analysis
Illumina MiSeq platform
V4
CSDS-depression and control
One-way ANOVA: p < 0.05

Yang C et al. 2019b
Sprague-Dawley rats China case-control Single SNI-depression
SNI anehdous susceptible (N=8)
SNI anehdous resistant (N=8)
Control (N=8)
2-month-old male
Body weight(ς)
MWT: withdrawal threshold(ς)
SPT: sucrose preference(ς)
TPT: tail flick latency(ς)
FST: immobile time(ς)
TST: immobile time(ς)
After 7 days of acclimation, than 21 days after spinal nerve injury (day 6)
After 7 days of acclimation, 14 days of antidepressants treatment and 14 days of focus transplantation
Fecal samples
~80 °C
16S rRNA gene sequencing
Illumina HiSeq platform
V3-V4
SNI-depression susceptible and control
One-way ANOVA followed by post-hoc Tukey’s test: p < 0.05

Yang J et al. 2021
C57BL/6 mice China case-control Single CVS-depression
CVS (N=8)
CVS+Antibiotic+CSGS (N=8)
CVS+CSGS (N=8)
CVS+Antibiotic (N=8)
Control (N=8)
7-week-old male
SPT: sucrose preference(ς)
FST: immobile time(ς)
OFT: center time(ς)
EPM: closed arms time(ς)
After 1 week of acclimation and 6 weeks of CVS along with diurethame
Fecal samples
~80 °C
16S rRNA gene sequencing
Illumina MiSeq platform
V3-V4
CRS-depression and control
One-way ANOVA followed by Dunnet’s multiple comparison test: p < 0.05

Yang Q et al. 2020
C57BL/6 mice China case-control Single MS-postpartum depression
MS (N=8)
MS-Lactobacillus casei (N=8)
MS-Parvovirus (N=8)
Control (N=8)
6~8 week-old male
OFT: total distance(ς), center time(ς)
TST: immobile time(ς)
FST: immobile time(ς)
After 1 week of acclimation and 6 weeks of CUMS (the last 4 weeks received drugs treatment)
Fecal samples
~80 °C
16S rRNA gene sequencing
Illumina MiSeq platform
V4-V5
CUMS-depression and control
LEfSe: p < 0.05 and LDA > 5.0

Yang R et al. 2020
Sprague-Dawley rats China case-control Single MPT SNL depression
MPT SNI anhedonic(resistant) (N=6)
MPT SNI anhedonic(susceptible) (N=6)
Control (N=6)
P2P rats
P2P peptide (N=6)
Female
EPM: open arm time and entries(ς)
FPT: immobile time(ς)
TST: immobile time(ς)
After 1 week of acclimatization, then 30 consecutive days of UCS
Fecal samples
~80 °C
16S rRNA gene sequencing
Sanger sequencing
Coral contents...
qPCR for Enzyme (Acetylcholinesterase, Butyrylcholinesterase, Lactobacillus, Escherichia coli...)
MS-postpartum depression and control
ANOVA: p<0.05

Yu B et al. 2019
Sprague-Dawley rats China case-control Single CUMS-depression
CUMS (N=8)
CUMS+Fluoxetine (N=8)
CUMS+Imipramine (N=8)
Control (N=8)
180~200g male
SPT: sucrose preference(ς)
FST: immobile time(ς)
After 2 weeks of CUMS (the last 2 weeks received drugs treatment)
Fecal samples
~80 °C
16S rRNA gene sequencing
Illumina MiSeq platform
V3-V4
CUMS-depression and control
Student’s t test: p < 0.05

Yu M et al. 2017
Wistar rats China case-control Single CVS-depression
CVS (N=8)
CVS+Antidepressant (N=8)
CVS+CSDS (N=8)
CVS+Anxiety-CGD (N=8)
CVS+Anxiety-CGES (N=8)
Control (N=8)
9-week-old male
Body weight(ς)
OFT: rearing and crossing numbers(ς)
SPT: sucrose preference(ς)
After 4 weeks of CVS
Fecal samples
~80 °C
16S rRNA gene sequencing
Illumina MiSeq platform
V4
CVS-depression and control
Student’s t test: p < 0.05

Yu M et al. 2020
Wistar rats China case-control Single CVS-depression
CVS (N=8)
CVS+(R)-ketamine (N=8)
CVS+Antidepressant (N=8)
CVS+CSDS (N=8)
CVS+Anxiety-CGD (N=8)
CVS+Anxiety-CGES (N=8)
Control (N=8)
200 ± 10g male
Body weight(ς)
OFT: rearing and crossing numbers(ς)
SPT: sucrose preference(ς)
After 28 days of CVS experiment
Fecal samples
~80 °C
16S rRNA gene sequencing
Illumina MiSeq platform
V3-V4
CVS-depression and control
One-way ANOVA: p < 0.05

| Year | Authors | Species | Sex | Age | Treatment 1 | Treatment 2 | Treatment 3 | Treatment 4 | Treatment 5 | Lethality | Post mortem | Organs | Pathological Observations | Comments |
|------|---------|---------|-----|-----|-------------|-------------|------------|------------|------------|-----------|-------------|--------|-------------------------|----------|
| 2021 | Yu et al. | 57BL/6 mice | Male | 8-12 weeks | CUMS | Imipramine | Control | Control | Control | 20% | 2 weeks | Brain, liver, kidney | Depressed behaviors, increased d-fosB mRNA in the prefrontal cortex | LEfSe: p < 0.05 and LDA > 2.0 |
| 2021 | Yun et al. | CR mice | Male | 8-12 weeks | CUMS | Fluoxetine | Control | Control | Control | 20% | 2 weeks | Brain, liver, kidney | Depressed behaviors, increased d-fosB mRNA in the prefrontal cortex | LEfSe: p < 0.05 and LDA > 2.0 |
| 2021 | Zhang J et al. | 57BL/6 mice | Male | 8-12 weeks | CUMS | Corticosterone | Control | Control | Control | 20% | 2 weeks | Brain, liver, kidney | Depressed behaviors, increased d-fosB mRNA in the prefrontal cortex | LEfSe: p < 0.05 and LDA > 2.0 |
| 2021 | Zhang Z et al. | 57BL/6 mice | Male | 8-12 weeks | CUMS | Fluoxetine | Control | Control | Control | 20% | 2 weeks | Brain, liver, kidney | Depressed behaviors, increased d-fosB mRNA in the prefrontal cortex | LEfSe: p < 0.05 and LDA > 2.0 |
| 2021 | Zhang X et al. | 57BL/6 mice | Male | 8-12 weeks | CUMS | Fluoxetine | Control | Control | Control | 20% | 2 weeks | Brain, liver, kidney | Depressed behaviors, increased d-fosB mRNA in the prefrontal cortex | LEfSe: p < 0.05 and LDA > 2.0 |

Reference: The table includes various studies on the effects of stress and its treatments on depressive-like behaviors and gut microbiota in mice. The studies used different models of stress (e.g., CUMS, LPS, and ECS) and treatments (e.g., antidepressants, corticosteroids, and probiotics). The data show that these interventions can alter gut microbiota, with significant changes observed using LEfSe and LDA analysis.

**Key Points:**
- Stress models: CUMS, LPS, and ECS
- Treatments: Antidepressants (imipramine, fluoxetine), Corticosteroids, Probiotics
- Gut microbiota analysis using LEfSe and LDA
- Depressed behaviors and d-fosB mRNA changes
- One-way ANOVA or Kruskal-Wallis H test with post-hoc Tukey's multiple comparison test or LSD test.
At weeks 15:
CUMS (N=6)
CUMS+Amitriptyline (N=6)
CUMS+Fluoxetine (N=7)
Control (N=12)

At weeks 15:
Shotgun metagenomic
Illumina HiSeq 4000 platform
NA

Zhong Y et al. 2021(198)
Sprague-Dawley rats  China  case-control  CUMS-depression  CUMS (N=9)
CUMS+Fluoxetine (N=9)
CUMS-low-dose jasmin tea (N=9)
CUMS-multiple-dose jasmin tea (N=9)
CUMS-high-dose jasmin tea (N=9)
Control (N=9)

4 weeks  male  Body weight,
SPT: sugar preference,
FST: immobility time,
GPT: time/space/maze running.

After 1 week of acclimatization, feces of rats in each group at day 29 were collected.
Fecal samples  80°C  16S rRNA gene sequencing-
Illumina MiSeq platform
V3-V4  CUMS-depression and control

Zhong Y et al. 2019(199)
C57BL/6 mice  China  case-control  NLRP-3 KO anti-depression  NLRP-3 KO (N=14)
Wild-type (N=14)
AXB FMT-NLRP-3 KO CUS (N=16)
AXB FMT-NLRP-3 KO Control (N=15)
AXB FMT-WT CUS (N=14)
AXB FMT-WT Control (N=15)

6-8 week-old  male  NLRP-3 KO,
FST: immobility time,
TST: immobility time,
GPT: total distance, center time, center
distance,
CUM,
SPT: sucrose preference,
FST: immobility time,
TST: immobility time.

Unspecified
Fecal samples  _  16S rRNA gene sequencing-
Illumina MiSeq platform
V6-V5  NLRP-3 KO anti-depression and wild-type
FMT-WT CUS and FMT-WT Control

Zhong Z et al. 2021(200)
C57BL/6 mice  China  case-control  Offspring of prenatal IS depression  Offspring of
Prenatal IS (N=12)
Control (N=12)

6-8 week-old  female  EPM: open arm time, closed arm time,
LEP: dark avoidance,
SPT: sucrose preference,
FST: immobility time.

Fecal samples were collected from F1 adult female mice at 6-8 weeks old.
Fecal samples  80°C  16S rRNA gene sequencing-
Illumina MiSeq platform
V3-V4  Prenatal IS depression and control

Zhong Z et al. 2020(201)
athymic nude mice (ND)-na  China  case-control  Offspring of prenatal IS- depression  Offspring of
Prenatal IS (N=12)
Control (N=12)

5 mice/cage  CRS-depression  CRS+BCG-CRC tumors (N=15)
CRS+Placebo-CRC tumors (N=15)
CRS+Xyloxaero-lesion CRC tumors (N=15)
CRS+Xyloxaero-high CRC tumors (N=15)
Treatment CRC tumors (N=15)
Control-CRC tumors (N=15)

6-7 week-old  male  APP: sucrose preference,
TST: immobility time.

After 7 days of acclimatization, 14 days of CRS.. 42 days of behavioral tests, tumour cell injection, and fluorescence imaging.
Fecal samples  _  16S rRNA gene sequencing-
Illumina MiSeq platform
V3-V4  CRS-depression and control

Zhong Z et al. 2017(202)
C57BL/6 mice  China  case-control  Single  CRS-depression  CRS (N=7)
CRS+Dipteria (N=7)
Control (N=7)

7-9 weeks  male  SPT: sucrose preference.

After 1 week of acclimatization and 10 days of CRS and
hypertension treatment
Fecal samples  Dry ice  Full-length 16S rRNA gene sequencing-
Illumina HiSeq platform
V3-V4  CUMS-depression and control

Zhao B et al. 2020(203)
C57BL/6 mice  China  case-control  DSS-depression  DSS (N=12)
DSS+Lecithin (N=12)
Control (N=12)

8-week-old  male  GPT: path length, dwell time,
EPM: open arm entries,
FST: immobility time,
TST: immobility time.

After 15 days of corresponding drug and 7 days of DSS treatment.
Fecal samples  80°C  16S rRNA gene sequencing-
Illumina MiSeq platform
V3-V4  DSS-depression and control

Zhao F et al. 2017(204)
Sprague-Dawley rats  China  case-control  single  CUMS-depression  Pregnant rat
CUMS (N=8)
CUMS+LBP (N=8)

200 ± 20 g  female  Pregnant rat
SPT: sucrose preference,
GPT: horizontal and vertical movements.

Fresh lice were collected from female rats at 31 days after
CUMS procedure, faces of
Fecal samples  80°C  16S rRNA gene sequencing-
Illumina MiSeq platform
V3-V4  Pregnant rat-CUMS-depressions and control

One-way ANOVA followed by Bonferroni’s multiple
comparison test: p < 0.05

LEfSe: p < 0.05 and LDA ≥ 2.0

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LEfSe: p < 0.05 and LDA ≥ 2.0
4 rats/cage

Offspring of prenatal/CUMS-depression

Control (N=8)

Offspring of Prenatal/CUMS (N=16)

Prenatal/CUMS+LBP (N=16)

Control (N=16)

PDN 20 female

male (1:1)

Offspring

Body weight

SPT: sucrose preference

GTP: horizontal and vertical movements

TST: immobility time↑

After 21 days of antibiotics administration and 13 days of FMT

Fecal samples

80°C

16S rRNA gene sequencing: ReSeq-454 sequencing

Morgan metagenomic-illumina HiSeq2500

V3-V4

Antibiotic-depression and control

One-way ANOVA or Wilcoxon rank sum test: p < 0.05

Zhu W et al. 2019[14]

C57BL/6J mice

China

case-control

AXB-OVA/Aic-depression

AXB-OVA-Aic (N=14)

AXB-OVA-Aic (N=14)

Control (N=16)

6-week-old

male

GTP: center time↓; center distance↓

SPT: open arms time and entries↓

TST: immobility time↑

After 1 week of acclimatization

11 weeks of clofazimine; sodium salicylate systemically

Fecal samples

80°C

16S rRNA gene sequencing: Illumina MiSeq platform

V3-V4

Anti-bacteria-depression and control

One-way ANOVA or Wilcoxon rank sum test: p < 0.05

Zhu Z et al. 2020[15]

BALB/c mice

China

case-control

10 mice/cage

Antibiotic-depression

Ceftazidime (N=20)

Control (N=20)

6-8-week-old

male

Body weight↓

GTP: center time↓; center distance↓

SPT: open arms time↑; peripheral distance↓

TST: activity phase↓; spinescence phase↑

After 1 week of acclimatization

11 weeks of clofazimine; sodium salicylate systemically

Fecal samples

80°C

16S rRNA gene sequencing: Illumina MiSeq platform

V3-V4

Anti-bacteria-depression and control

One-way ANOVA or Wilcoxon rank sum test: p < 0.05

Zhong P et al. 2016[16]

Kuming mice

China

case-control

5 mice/cage

GF FMT-depression

GF FMT-MED (N=8)

GF FMT-BIC (N=8)

GTP: proportion of center motion distance↑

SPT: duration of immobility↑

TST: duration of immobility↑

2 weeks post FMT

Fecal samples

80°C

16S rRNA gene sequencing: ReSeq-454 sequencing

Morgan metagenomic-illumina Hisseq2500

V3-V4

FMT-MED and FMT-BIC

Random Forests

Zhang P et al. 2020[17]

Macaca fascicularis monkeys

China

case-control

group

Naturally occurring depression

Depression (N=6)

Control (N=6)

Adult

female

Duration of huddles and shoal-alone behaviors

Duration of immobile and locomotion activities

After behavioral tests

Cecum samples

80°C

16S rRNA gene sequencing: Illumina MiSeq platform

Microbiome-illumina Hisseq X platform

V3-V4

Naturally occurring depression and control

LDA > 2.0, p < 0.05

Zhao H et al. 2022[18]

C57BL/6J mice

China

case-control

- Bcl-II KO-depression

Ddx12KO (N=5)

Ddx12KO×B. longum (N=5)

Ddx12KO×lactobacillus (N=5)

Ddx12KO×bacteroides (N=5)

MPT (N=5)

WT (N=5)

WT×fetal of Ddx1 KO mice (N=5)

Adult

20-25 g

male

SPT: sucrose preference↑

TST: immobility time↑

Fecal samples

80°C

16S rRNA gene sequencing

Unspecified

Ddx-KO-depression and wild-type

Zhu H et al. 2019[19]

Sprague-Dawley rats

China

case-control

- CRS-depression

CRS (N=5)

CRS×Salmonella (N=15)

CRS×Pseudomonas (N=15)

Control (N=15)

200 ± 20 g

male

Body weight↓

SPT: sugar preference↑

SPT: residence time↑; total distance↑

number of entries↑

After 7 days of acclimatization

21 days of CRS

Fecal samples

80°C

16S rRNA gene sequencing: Illumina MiSeq high-throughput sequencing platform

V3-V4

CRS-depression and control

Miniature: p < 0.05

LDA > 2.0

Zhu JY et al. 2017[20]

Sprague-Dawley rats

China

case-control

CUMS-depression

CUMS (N=12)

CUMS×Phasmeus (N=12)

CUMS-lower-dose BHT (N=12)

CUMS-middle-dose BHT (N=12)

CUMS-high-dose BHT (N=12)

Control (N=12)

250-250 g

male

SPT: sucrose preference↓

GTP: horizontal crossing↓; vertical stereotypy↓

After 5 days of acclimatization

10 consecutive days of CUMS

Rectum contents

Liquid nitrogen

16S rRNA sequencing: Shanghai Biotech Biotechnology Co., Ltd

Unspecified

CUMS-depression and control

One-way ANOVA or Kruskal-Wallis H test: p < 0.05

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| Study                   | Metric                  | Analysis                | Significance               |
|-------------------------|-------------------------|-------------------------|---------------------------|
| Bai S et al. 2021       | _                       | PCoA                    | Sig. difference           |
| Bai S et al. 2022       | _                       | OPLS-DA                 | Sig. difference           |
| Caso JR et al. 2021     | Bray–Curtis Jaccard     | PCoA, PERMANOVA         | No sig. difference        |
|                         | Unweighted UniFrac      |                         |                           |
| Chahwan B et al. 2019   | Weighted UniFrac        | PCoA, PERMANOVA         | No sig. difference        |
| Chen JJ et al. 2018     | UniFrac                 | PCoA, OPLS-DA          | Sig. difference           |
| Chen JJ et al. 2020     | _                       | OPLS-DA                 | Sig. difference           |
| Chen T et al. 2021      | Unweighted UniFrac      | PCoA, ANOSIM           | Sig. difference           |
| Chen YH et al. 2019     | Weighted UniFrac        |                         |                           |
|                         | Unweighted UniFrac      |                         |                           |
| Chung YE et al. 2019    | Weighted UniFrac        | PERMANOVA               | Sig. difference           |
|                         | Unweighted UniFrac      |                         | Sig. difference           |
| Ciocan D et al. 2021    | Weighted UniFrac        | ANOSIM                  | No sig. difference        |
|                         | Unweighted UniFrac      |                         | Sig. difference           |
| Dong Z et al. 2021      | Bray–Curtis             | PCA                     | No sig. difference        |
| Huang Y et al. 2018     | Weighted UniFrac        | PCoA                    | Sig. difference           |
|                         | Unweighted UniFrac      |                         | No sig. difference        |
| Huang Y et al. 2021     | Bray-Curtis             | PLS-DA, PCA, PCoA, NMDS | Sig. difference           |
| Jiang H et al. 2015     | Unweighted UniFrac      | PCoA                    | No sig. difference        |
| Jiang HY et al. 2020    | Bray-Curtis             | PCoA                    | Sig. difference           |
|                         | Weighted UniFrac        |                         | No sig. difference        |
|                         | Unweighted UniFrac      |                         | No sig. difference        |
| Kelly JR et al. 2016    | Bray-Curtis             | PCoA, Adonis PERMANOVA  | Sig. difference           |
|                         | Weighted UniFrac        |                         | Sig. difference           |
|                         | Unweighted UniFrac      |                         | Sig. difference           |
| Kleiman SC et al. 2015  | Weighted UniFrac        | _                       | No sig. difference        |
|                         | Unweighted UniFrac      |                         | Sig. difference           |
| Kurokawa S et al. 2018  | Weighted UniFrac        | PCoA                    | No sig. difference        |
|                         | Unweighted UniFrac      |                         | Sig. difference           |
| Lai WT et al. 2021      | Bray-Curtis             | PCoA, PERMANOVA         | Sig. difference           |
| Lin P et al. 2017       | Weighted UniFrac        | PCoA                    | Sig. difference           |
| Ling Y et al. 2020      | Bray-Curtis             | PCoA, ANOSIM           | No sig. difference        |
| Liśkiewicz P et al. 2021| Bray-Curtis             | PCoA, PERMANOVA        | _                         |
|                         | Unweighted UniFrac      |                         | No sig. difference        |
| Liu P et al. 2021       | Jaccard                 | PCoA                    | Sig. difference           |
| Liu RT et al. 2020      | Bray-Curtis             | PCoA, Adonis PERMANOVA  | Sig. difference           |
|                         | Weighted UniFrac        |                         | Sig. difference           |
|                         | Unweighted UniFrac      |                         | Sig. difference           |
| Liu T et al. 2020       | Bray-Curtis             | PCoA, ANOSIM           | No sig. difference        |
| Liu Y et al. 2016       | _                       | PCA                     | Sig. difference           |
| Madan A et al. 2020     | Jaccard similarity index| _                       | Sig. difference           |
| Mason BL et al. 2020    | Weighted UniFrac        | PERMANOVA               | No sig. difference        |
| Minichino A et al. 2021 | Weighted UniFrac        | PCoA                    | Sig. difference           |
|                         | Unweighted UniFrac      |                         | Sig. difference           |
| Naseribafrouei A et al. 2014 | _                       | PLS-DA                 | Sig. difference           |
| Pérez-Santiago J et al. 2021 | Weighted UniFrac      | PCoA, PERMANOVA        | Sig. difference           |
|                         | Unweighted UniFrac      |                         | Sig. difference           |
| Qin Q et al. 2021       | _                       | PCA, NMDS               | No sig. difference        |
| Study                      | Methodology | Analysis | Significance |
|----------------------------|-------------|----------|--------------|
| Rhee SJ et al. 2020        | Bray-Curtis | Weighted Unifrac | PCoA, PERMANOVA | Sig. difference |
|                            |             | Unweighted UniFrac |              | No sig. difference |
|                            |             | PCoA, PERMANOVA     |              | Sig. difference |
| Rhee SJ et al. 2021        | Bray-Curtis | Weighted Unifrac | PERMANOVA | No sig. difference |
|                            |             | Unweighted UniFrac |              | Sig. difference |
|                            |             | PCoA, PERMANOVA     |              | No sig. difference |
| Shen Y et al. 2021         | Binary jaccard algorithm | PCoA | Sig. difference |
| Simpson CA et al. 2020     | Weighted Unifrac | PCoA, PERMANOVA |              | No sig. difference |
|                            | Unweighted UniFrac |              |              | No sig. difference |
| Stevens BR et al. 2020     | Bray-Curtis (unfiltered data) | PERMANOVA | No sig. difference |
|                            | Bray-Curtis (filtered data) |              |              | Sig. difference |
| Stevens BR et al. 2021     | Bray-Curtis | PCoA | Sig. difference |
| Taylor AM et al. 2020      | Weighted UniFrac | _ | _ |
| Taylor BC et al. 2020      | Unweighted UniFrac | PCoA, PERMANOVA |              | Sig. difference |
| Wingfield B et al. 2021    | Bray-Curtis | _ | Sig. difference |
| Yang J et al. 2020         | Bray-Curtis | PCoA, PERMANOVA |              | Sig. difference |
| Yang Y et al. 2021         | Bray-Curtis | Weighted Unifrac | PCoA, NMDS, ADONIS | Sig. difference |
|                            |             | Unweighted UniFrac |              | Sig. difference |
|                            |             | PCoA, ANOSIM        |              | Sig. difference |
| Ye X et al. 2021           | Unweighted UniFrac | PCoA | Sig. difference |
| Zhang Q et al. 2021        | Bray-Curtis | Jaccard | PCoA, ANOSIM | Sig. difference |
|                            | Weighted Unifrac |              |              | Sig. difference |
|                            | Unweighted UniFrac |              |              | Sig. difference |
| Zhao H et al. 2021         | _ | PCoA | Sig. difference |
| Zheng P et al. 2016        | Bray-Curtis | Unweighted UniFrac | PCoA | Sig. difference |
| Zheng P et al. 2020        | _ | PLS-DA, PERMANOVA | Sig. difference |
| Zhou Y et al. 2020         | Weighted UniFrac | PCoA, Wilcoxon rank-sum test | Sig. difference |
| Zhu J et al. 2021          | Bary-Curtis | Jaccard | PCoA, PERMANOVA | No sig. difference |
|                            | Weighted Unifrac |              |              | Sig. difference |
|                            | Unweighted UniFrac |              |              | No sig. difference |
|                            |              |              |              | No sig. difference |
Table S4. Microbial β-diversity in animal models of depression.

| Study               | Metric                  | Analysis                      | Significance |
|---------------------|-------------------------|-------------------------------|--------------|
| Abildgaard A et al. 2021 | Bray-Curtis, Jaccard     | PCoA, PERMANOVA               | Sig. difference |
| An Q et al. 2020    | Unweighted UniFrac       | PCA, ANOSIM                   | Sig. difference |
| Arslanova A et al. 2021 | Weighted Unifrac, Unweighted UniFrac | PCoA                          |               |
| Bharwani A et al. 2017 | Bray-Curtis             | PCoA                          | Sig. difference |
| Bridgewater LC et al. 2017 | Bray-Curtis         | PCoA                          | Sig. difference |
| Burokas A et al. 2017 | Unweighted UniFrac       | PCoA                          | Sig. difference |
| Chakraborti A et al. 2021 | Weighted Unifrac, Unweighted UniFrac, Bray-Curtis | PCoA, PERMANOVA               | Sig. difference |
| Chen L et al. 2021   |                         | PCA                           | Sig. difference |
| Chen P et al. 2019   | Bray-Curtis, Jaccard     | PCoA, NMDS                     | Sig. difference |
| Chen T et al. 2021   | Unweighted UniFrac       | PCoA, ANOSIM                   | Sig. difference |
| Chen X et al. 2021   | Weighted UniFrac         | PCA                           | Sig. difference |
| Chen X et al. 2022   | Weighted UniFrac         | PCoA                          | Sig. difference |
| Chen Y et al. 2021b  | Weighted Unifrac, Bray-Curtis | PCoA, PERMANOVA               | Sig. difference |
| Cheng D et al. 2018  | Morisita-Horn dissimilarity | PCA                           | Sig. difference |
| Cheng R et al. 2021  | UniFrac                  | PCoA                          | Sig. difference |
| Chevalier G et al. 2020 | Bray-Curtis            | PCoA                          |               |
| Chi L et al. 2020    |                         | PLS-DA                        | Sig. difference |
| Daugé V et al. 2020  | Bray-Curtis             | MDS                           | Sig. difference |
| Deng Y et al. 2021   |                         | PCoA                          | Sig. difference |
| Ding Y et al. 2021   |                         | PCA, ANOSIM                    | Sig. difference |
| Diviccaro S et al. 2019 | Weighted Unifrac, Unweighted UniFrac, Bray-Curtis | PCoA, PEAMONVA               | Sig. difference |
| Donoso F et al. 2020 | Aitchison               | PCA, PERMANOVA                 | Sig. difference |
| Du HX et al. 2020    | Bray-Curtis             | NMDS                          | Sig. difference |
| Duan J et al. 2021   | Unweighted UniFrac       | PCoA, PLS-DA, ANOSIM          | Sig. difference |
| Egerton S et al. 2020 | Bray-Curtis             | PCoA, Adonis PERMANOVA        | Sig. difference |
| El Aidy S et al. 2017 | Weighted UniFrac        | PCoA, PEAMONVA                 | Sig. difference |
| Fan L et al. 2021    |                         | PCoA                          | Sig. difference |
| Feng Y et al. 2020   |                         | PLS-DA                        | Sig. difference |
| Feng Z et al. 2020   | UniFrac                  | PCA, NMDS                      | Sig. difference |
| Forouzan S et al. 2021 | Weighted UniFrac        | PCoA                          | Sig. difference |
| Gao K et al. 2022    | Bray–Curtis             | PCoA, PERMANOVA                | Sig. difference |
| Gao X et al. 2020    |                         | PLS-DA                        | Sig. difference |
| Gong X et al. 2021   | Weighted UniFrac         | PCoA                          | Sig. difference |
| Gu F et al. 2020     | Weighted UniFrac         | PCoA                          | Sig. difference |
| Gu X et al. 2022     | Weighted UniFrac         | PLS-DA, ANOSIM                 | Sig. difference |
| Guida F et al. 2018  | Bray-Curtis, Jaccard     | PEAMONVA                       | Sig. difference |
| Guo Y et al. 2018    |                         | NMDS                          | Sig. difference |
| Guo Y et al. 2019    |                         | PCA, Adonis                   | No sig. difference |
| Han SK et al. 2020a  | Jensen-Shannon           | PCoA                          | Sig. difference |
| Authors            | Methodology                        | Statistical Test | Result |
|--------------------|------------------------------------|------------------|--------|
| Han SK et al. 2020b | Jensen-Shannon PCoA                | Sig. difference  |        |
| Han SK et al. 2021  | Weighted UniFrac PCoA              | Sig. difference  |        |
| Hao W et al. 2021   | _                                  | PCA              | Sig. difference |
| Hao WZ et al. 2021  | Weighted UniFrac Unweighted UniFrac Bray-Curtis PCoA | Sig. difference |        |
| Hassan AM et al. 2019 | Weighted UniFrac                   | PCoA, Adonis     | Sig. difference |
| Huang F et al. 2021 | UniFrac PCA                        | Sig. difference  |        |
| Huang N et al. 2019 | Euclidean Bray-Curtis              | PCoA             | Sig. difference |
| Huang YJ et al. 2021 | Bray-Curtis                        | PCoA             | Sig. difference |
| Huang YY et al. 2022 | Bray–Curtis                        | PcoA             | Sig. difference |
| Inserra A et al. 2019 | Weighted UniFrac PERMANOVA         | Sig. difference  |        |
| Ji S et al. 2022    | Weighted UniFrac Unweighted UniFrac Bray-Curtis PCoA, PERMANOVA | No sig. difference |        |
| Jiang W et al. 2021 | _                                  | PCoA, Adonis     | Sig. difference |
| Jiang Y et al. 2020 | Unweighted UniFrac PCoA, ANOSIM    | Sig. difference  |        |
| Jianguo L et al. 2019 | Bray-Curtis                        | PERMANOVA        | Sig. difference |
| Kamimura Y et al. 2021 | Weighted UniFrac                  | PCoA             | Sig. difference |
| Kemp KM et al. 2021 | Aitchison PCA, Adonis PERMANOVA    | Sig. difference  |        |
| Kim JK et al. 2020  | Weighted UniFrac PcoA              | Sig. difference  |        |
| Kim JK et al. 2021  | Generalized UniFrac PcoA           | Sig. difference  |        |
| Knudsen JK et al. 2021 | _                                | PCA              | Sig. difference |
| Kosuge A et al. 2021 | Bray-Curtis                        | PCoA, Adonis PERMANOVA | Sig. difference |
| Lai WD et al. 2022  | _                                  | PCA, PcoA, NMDS  | Sig. difference |
| Leclercq S et al. 2020 | Bray-Curtis                        | PCoA             | Sig. difference |
| Lee HC et al. 2020  | Weighted UniFrac Unweighted UniFrac Bray-Curtis PCoA | Sig. difference |        |
| Li H et al. 2021    | Bray–Curtis                        | PCoA             | Sig. difference |
| Li N et al. 2018    | Weighted UniFrac Unweighted UniFrac Bray-Curtis PCoA, ANOSIM | Sig. difference |        |
| Li N et al. 2019    | Weighted UniFrac Unweighted UniFrac Bray-Curtis PCoA | Sig. difference |        |
| Li P et al. 2021    | Unweighted UniFrac PcoA            | Sig. difference  |        |
| Li Y et al. 2018    | Weighted UniFrac PcoA              | Sig. difference  |        |
| Lim EY et al. 2021  | Weighted UniFrac PcoA              | Sig. difference  |        |
| Lin S et al. 2021   | _                                  | PCA, NMDS        | Sig. difference |
| Liu QF et al. 2020  | Unweighted UniFrac PcoA            | Sig. difference  |        |
| Liu X et al. 2021a  | Bray-Curtis                        | PCoA, PLS-DA     | Sig. difference |
| Liu X et al. 2021b  | Bray-Curtis                        | PCoA, NMDS, Adonis, Permdisp | Sig. difference |
| Liu Z et al. 2020   | Unweighted UniFrac PcoA            | Sig. difference  |        |
| Luo X et al. 2021   | Bray-Curtis                        | NMDS, ANOSIM     | Sig. difference |
| Lv M et al. 2021    | Weighted UniFrac PcoA              | NMDS             | Sig. difference |
| Lv WJ et al. 2019   | Weighted UniFrac PCA, PcoA, PLS-DA | Sig. difference |        |
| Lv WJ et al. 2020   | Unweighted UniFrac PCA, PcoA, NMDS, PERMANOVA, ANOSIM | Sig. difference |        |
| Ma W et al. 2019    | Bray-Curtis                        | PCA              | Sig. difference |
| Authors                  | Methodology                      | Techniques          | Significance       |
|-------------------------|----------------------------------|---------------------|--------------------|
| Matsuda Y et al. 2020   | Bray-Curtis                      | PcoA                | Sig. difference    |
| McGaughey KD et al. 2019| Unweighted UniFrac               | PCoA, ANOSIM        | Sig. difference    |
| Meng C et al. 2022      |                                  | CPCoA, PcoA         | Sig. difference    |
| Moya-Pérez A et al. 2017| Bray-Curtis                      | PCoA, Permanova     | Sig. difference    |
| O'Mahony SM et al. 2020 | Bray-Curtis                      | PCoA, Adonis        | Sig. difference    |
| Partrick KA et al. 2021 | Unweighted UniFrac               | PCoA, PERMANOVA     | Sig. difference    |
| Patterson E et al. 2019 | Bray-Curtis                      | PCoA                | Sig. difference    |
| Pearson-Leary J et al. 2020 | Bray-Curtis                  | Weighted UniFrac    | Sig. difference    |
| Pu Y et al. 2021        |                                  | PCA, ANOSIM         | No sig. difference |
| Pusceddu MM et al. 2015 |                                  | RDA                 | Sig. difference    |
| Qiao Y et al. 2020      | Bray-Curtis                      | PcoA                | Sig. difference    |
| Qu W et al. 2019        | Bray-Curtis                      | PcoA                | Sig. difference    |
| Qu Y et al. 2017        | Bray-Curtis                      | PcoA                | Sig. difference    |
| Qu Y et al. 2020        | Weighted UniFrac                 | PcoA                | Sig. difference    |
| Rao J et al. 2021       | Bray-Curtis                      | PcoA                | Sig. difference    |
| Robertson RC et al. 2017| Unweighted UniFrac               | PcoA                | Sig. difference    |
| Schmidtner AK et al. 2019 | Bray-Curtis              | PcoA                | Sig. difference    |
| Shan B et al. 2021      | Bray-Curtis                      | PcoA                | Sig. difference    |
| Shao S et al. 2021      |                                  | PcoA                | No sig. difference |
| Sheng L et al. 2021     | Unweighted UniFrac               | PcoA                | Sig. difference    |
| Siopi E et al. 2020     | Bray-Curtis                      | PcoA                | Sig. difference    |
| Song J et al. 2019a     |                                  | PLS-DA              | Sig. difference    |
| Song J et al. 2019b     |                                  | PLS-DA              | Sig. difference    |
| Song X et al. 2021      | Bray-Curtis                      | PLS-DA, ANOSIM      | Sig. difference    |
| Sovijit WN et al. 2019  | Bray-Curtis                      | PCoA, PERMANOVA     | Sig. difference    |
| Sun L et al. 2019a      | Bray-Curtis                      | PcoA                | Sig. difference    |
| Sun L et al. 2019b      | Unweighted UniFrac               | PcoA                | Sig. difference    |
| Sun Y et al. 2019       | Unweighted UniFrac               | PCA, PCoA           | Sig. difference    |
| Sun Y et al. 2020       | Weighted UniFrac                 | PcoA                | Sig. difference    |
| Suzuki K et al. 2021    | Unweighted UniFrac               | PcoA, PERMANOVA     | Sig. difference    |
| Szyszkiowicz JK et al. 2017 |                                  | PCA                 | Sig. difference    |
| Teng T et al. 2021      | Bray-Curtis                      | PcoA, PLS-DA, sparse PLS-DA | Sig. difference    |
| Tian P et al. 2019a     |                                  | PcoA                | Sig. difference    |
| Tian P et al. 2019b     |                                  | PCA                 | Sig. difference    |
| Tian P et al. 2020      | Unweighted UniFrac               | PCA, PCoA, PERMANOVA| Sig. difference    |
| Tian P et al. 2021      | Aitchison                        | PCA, PERMANOVA      | Sig. difference    |
| Tian XY et al. 2021     |                                  | PCA, PCoA, ANOSIM, Adonis | Sig. difference    |
| Tillmann S et al. 2019  |                                  | PCA, PLS-DA         | Sig. difference    |
| Tung TH et al. 2019     | Bray-Curtis                      | NMDS                | Sig. difference    |
| Wang L et al. 2020      | Unweighted UniFrac               | PcoA                | Sig. difference    |
| Wang L et al. 2021      |                                  | PcoA                | Sig. difference    |
| Wang Q et al. 2019      | Unweighted UniFrac               | PcoA, PERMANOVA     | Sig. difference    |
| Wang R et al. 2021      | Bray-Curtis                      | PcoA                | Sig. difference    |
| Authors (Year) | Distance/Method | Analysis | Significance |
|---------------|-----------------|----------|--------------|
| Wang S et al. 2020a | Unweighted UniFrac | PCoA | Sig. difference |
| Wang S et al. 2020b | Unweighted UniFrac | PCoA | Sig. difference |
| Wang S et al. 2021 | - | PCA, ANOSIM | Sig. difference |
| Wang Y et al. 2021 | Weighted UniFrac, Jaccard | PCoA | Sig. difference |
| Warda AK et al. 2019 | Bray-Curtis | PCoA, PERMANOVA | Sig. difference |
| Wei LN et al. 2019 | Bray-Curtis | PCoA, NMDS | Sig. difference |
| Westfall S et al. 2021 | Weighted UniFrac | PCoA, PERMANOVA | Sig. difference |
| Wong ML et al. 2016 | Bray-Curtis | PERMANOVA | Sig. difference |
| Wu F et al. 2020 | Unweighted UniFrac | PCoA | Sig. difference |
| Wu J et al. 2021 | Unweighted UniFrac | PCoA | Sig. difference |
| Wu M et al. 2020 | - | PCoA | Sig. difference |
| Xia J et al. 2021 | Weighted UniFrac, Unweighted UniFrac | PCoA, OPLS-DA | Sig. difference |
| Xiao Q et al. 2020 | Unweighted UniFrac | PCoA, NMDS | Sig. difference |
| Xie R et al. 2020a | Weighted UniFrac, Unweighted UniFrac | PCoA | Sig. difference |
| Xie R et al. 2020b | - | PCA | Sig. difference |
| Xie Y et al. 2021 | Bray-Curtis | PCoA | Sig. difference |
| Xu M et al. 2022 | - | PCoA | Sig. difference |
| Xu Z et al. 2019 | Bray-Curtis, Euclidean | PCoA | Sig. difference |
| Xue M et al. 2021 | Unweighted UniFrac | PCoA, Adonis | Sig. difference |
| Yang C et al. 2017b | Bray-Curtis, Euclidean | PCoA | Not mention |
| Yang C et al. 2019 | - | PCoA | Sig. difference |
| Yang HL et al. 2021 | Unweighted UniFrac | PCoA | No sig. difference |
| Yang Q et al. 2020 | Bray-Curtis, Weighted UniFrac, Unweighted UniFrac | PCoA | Not mention |
| Yu M et al. 2017 | Bray-Curtis | PCoA | Sig. difference |
| Yu M et al. 2020 | - | PCoA | Sig. difference |
| Yu M et al. 2021 | Bray-Curtis | PCoA | Sig. difference |
| Yun SW et al. 2020 | Jansen-Shannon | PCoA | Sig. difference |
| Yun SW et al. 2021 | Bray-Curtis | PCoA | Sig. difference |
| Zhang F et al. 2020 | - | PCoA | Sig. difference |
| Zhang J et al. 2020 | Bray-Curtis | PCoA | Sig. difference |
| Zhang K et al. 2019 | - | PCoA | Sig. difference |
| Zhang L et al. 2021 | Bray-Curtis | PCoA, NMDS | Sig. difference |
| Zhang M et al. 2021 | Bray-Curtis | PCoA, PERMANOVA, ANOSIM | Sig. difference |
| Zhang W et al. 2021 | Weighted UniFrac, Unweighted UniFrac | PCoA | Sig. difference |
| Zhang Y et al. 2019 | Unweighted UniFrac | PCoA | Sig. difference |
| Zhang Y et al. 2021 | Bray-Curtis | PLS-DA | Sig. difference |
| Zhang Z et al. 2020 | - | PLS-DA | No sig. difference |
| Zhang Z et al. 2021 | Unweighted UniFrac | PCoA, NMDS, ANOSIM | Sig. difference |
| Zhang Z et al. 2022 | Unweighted UniFrac | PCoA, PERMANOVA, ANOSIM | No sig. difference |
| Zhao B et al. 2020 | Weighted UniFrac, Unweighted UniFrac | PCoA | Sig. difference |
| Authors          | Methodology             | Analysis Tools   | Results     |
|------------------|-------------------------|------------------|-------------|
| Zhao F et al. 2021 | Bray-Curtis             | PCoA             | Not mention |
| Zhao Z et al. 2020 | Weighted Unifrac        | PCA, PCoA, MDS   | Sig. difference |
| Zheng P et al. 2016 | Weighted Unifrac        | PCoA             | Sig. difference |
| Zheng P et al. 2020 | Weighted Unifrac        | PCoA             | Sig. difference |
| Zhou H et al. 2022 | Weighted Unifrac        | PCoA             | Sig. difference |
| Zhu HZ et al. 2019 | Weighted Unifrac        | PCA, PCoA, NMDS  | Sig. difference |
Table S5. Commensal microbiota alterations at Phylum, Class, Order, and Family levels in patients with depression.

| Microorganisms | Commensal microbiota | Gut microbiota |
|----------------|----------------------|----------------|
|                |                      | Total          | American | Chinese | MDD | Depression |
|                |                      | Total no. of frequency | No. of increased | No. of decreased | Total no. of frequency | No. of increased | No. of decreased | Total no. of frequency | No. of increased | No. of decreased | Total no. of frequency | No. of increased | No. of decreased |
| **Phylum**     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Actinobacteria | 11                   | 8                | 3        | 11         | 8    | 3             | 10         | 7           | 3             | 9    | 7           | 2             | 1           | 1             |
| Bacteroidetes  | 13                   | 7                | 6        | 13         | 7    | 6             | 12         | 6           | 6             | 13   | 7           | 6             |              |               |
| Firmicutes     | 13                   | 5                | 8        | 12         | 4    | 8             | 10         | 4           | 6             | 10   | 4           | 6             |              |               |
| Fusobacteria   | 3                    | 2                | 1        | 2          | 2    | 0             | 2          | 2           | 0             | 2    | 2           | 0             |              |               |
| Proteobacteria | 9                    | 7                | 2        | 8          | 6    | 2             | 8          | 6           | 2             | 6    | 4           | 2             | 2           | 0             |
| Saccharibacteria | 2              | 1                | 1        |            |      |                |            |              |                |      |              |                |              |               |
| **Phylum**     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| **Class**      |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Actinobacteria |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Bacteroidia    | 4                    | 2                | 2        | 4          | 2    | 2             | 3          | 1           | 2             | 4    | 2           | 2             |              |               |
| Bacilli        | 2                    | 2                | 0        | 2          | 2    | 0             | 2          | 0           | 2             | 2    | 0           | 2             |              |               |
| **Class**      |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Firmicutes     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Bacteroidia    | 2                    | 2                | 0        | 2          | 2    | 0             | 2          | 2           | 0             | 2    | 2           | 0             |              |               |
| **Order**      |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Actinobacteria |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Bacilli        | 2                    | 2                | 0        | 2          | 2    | 0             | 2          | 0           | 2             | 2    | 0           | 2             |              |               |
| Bacteroidia    | 3                    | 1                | 2        | 3          | 1    | 2             | 2          | 0           | 2             | 3    | 1           | 2             |              |               |
| **Order**      |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Firmicutes     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Bacteroidia    | 3                    | 3                | 0        | 3          | 3    | 0             | 2          | 2           | 0             | 2    | 2           | 0             |              |               |
| **Family**     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Actinomyctales | 2                    | 2                | 0        | 2          | 2    | 0             | 2          | 0           | 2             | 2    | 0           | 2             |              |               |
| Bifidobacteriales | 2           | 2                | 0        | 2          | 2    | 0             | 2          | 0           | 2             | 2    | 0           | 2             |              |               |
| **Family**     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| **Phylum**     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| **Class**      |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Bacteroidia    | 3                    | 1                | 2        | 3          | 1    | 2             | 2          | 0           | 2             | 3    | 1           | 2             |              |               |
| Bacilli        | 2                    | 2                | 0        | 2          | 2    | 0             | 2          | 0           | 2             | 2    | 0           | 2             |              |               |
| Bacteroidia    | 3                    | 3                | 0        | 3          | 3    | 0             | 2          | 2           | 0             | 2    | 2           | 0             |              |               |
| **Family**     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Actinobacteria |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Bacilli        | 2                    | 2                | 0        | 2          | 2    | 0             | 2          | 0           | 2             | 2    | 0           | 2             |              |               |
| Bacteroidia    | 3                    | 3                | 0        | 3          | 3    | 0             | 3          | 1           | 4             | 3    | 0           | 3             |              |               |
| **Family**     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| Bacteroidia    | 2                    | 2                | 0        | 2          | 2    | 0             | 2          | 0           | 2             | 2    | 0           | 2             |              |               |
| **Phylum**     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| **Class**      |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| **Order**      |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |
| **Family**     |                      |                  |          |            |      |              |          |            |                  |          |            |                  |          |            |

**Phylum**  **Class**  **Order**  **Family**
| Kingdom            | Phylum               | Class                           | Order                          | Family                           | Genus                        | Actinobacteria | Bifidobacteriales | Corynebacteriales | Micrococcaceae | Coriobacteriales |
|--------------------|----------------------|---------------------------------|--------------------------------|---------------------------------|------------------------------|----------------|-------------------|-------------------|----------------|------------------|
| Actinobacteria     | Actinomycetales      | Actinomycetales                 | 7 6 1 5 5 0                   | 4 4 0 4 4 0                     | 4 4 0 4 0 0                 |
|                    | Bifidobacteriales    | Bifidobacteriales               | 8 6 2 8 6 2                   | 7 6 1 7 6 1                     | 7 6 1 7 6 1 1              |
|                    | Corynebacteriales    | Corynebacteriales               | 2 1 1 2 1 1                   | 2 1 1 2 1 1                     | 2 1 1 2 1 1 1             |
|                    | Micrococcaceae       | Micrococcaceae                  | 3 1 2 2 1 1                   | 2 1 1 2 1 1                     | 2 1 1 2 1 1 1             |
| Coriobacteriales   | Coriobacteriales     | Coriobacteriales                | 9 5 4 9 5 4                   | 2 1 1 6 4 2                    | 7 4 3 2 1 1               |
| Bacteroidetes      | Bacteroidales        | Bacteroidales                   | 10 4 6 9 4 5                  | 9 4 5 9 4 5                    | 9 4 5 9 4 5 5             |
|                    | Bacteroidales        | Bacteroidales                   | 5 5 0 5 5 0                   | 5 5 0 5 5 0                    | 5 5 0 5 5 0 5             |
|                    | Prevotellales        | Prevotellales                    | 9 0 9 9 0 9                   | 8 0 8 8 0 8                    | 8 0 8 8 0 8 8           |
|                    | Rikenellales         | Rikenellales                     | 10 6 4 10 6 4 3 0 3 0 3 7 6 1 7 5 2 3 1 2 | 3 3 0 3 3 0                  |
|                    | Marinilabiales       | Marinilabiales                   | 2 1 1 2 1 1                   | 2 1 1 2 1 1                    | 2 1 1 2 1 1 1             |
|                    | Chitinophagales      | Chitinophagales                  | 2 0 2 2 0 2                   | 2 0 2 2 0 2                    | 2 0 2 2 0 2 2             |
|                    | Flavobacteriales     | Flavobacteriales                 | 3 1 2 2 1 1                   | 2 1 1 2 1 1                    | 2 1 1 2 1 1 1             |
|                    | Fusobacteriales      | Fusobacteriales                  | 3 2 1 2 2 0 2                | 2 2 0 2 2 0                    | 2 2 0 2 2 0 2             |
| Bacilli             | Lactobacillales      | Lactobacillales                  | 2 1 1 2 1 1                   | 2 1 1 2 1 1                    | 2 1 1 2 1 1 1             |
| Clostridia         | Clostridales         | Clostridales                     | 9 3 6 9 3 6                   | 9 3 6 9 3 6                    | 9 3 6 9 3 6 9             |
|                    |                     |                                 | 5 4 1 5 4 1                   | 4 4 0 4 3 1                    | 4 4 0 4 3 1 4             |
|                    |                     |                                 | 20 8 12 19 7 12 3 0 3 14 5 9 13 6 7 6 1 5 | 6 1 5 6                   |
|                    |                     |                                 | 4 3 1 4 3 1                   | 4 3 1 4 3 1                    | 4 3 1 4 3 1 4             |
|                    |                     |                                 | 6 1 5 6 1 5                   | 5 1 4 5 1 4                    | 5 1 4 5 1 4 5             |
|                    |                     |                                 | 15 6 9 15 6 9 4 1 3 10 5 5 11 4 7 4 2 2 | 2 1 2 2 1 2               |
|                    |                     |                                 | 2 0 2 2 0 2                   | 2 0 2 2 0 2                    | 2 0 2 2 0 2 2             |
|                    |                     |                                 | 8 5 3 8 5 3                   | 7 4 3 6 3 3 2 2 0 2           | 2 2 0 2 2 0 2             |
|                    |                     |                                 | 6 4 2 5 3 2                   | 5 3 2 5 3 2                    | 5 3 2 5 3 2 5             |
|                    |                     |                                 | 2 2 0 2 2 0                   | 2 2 0 2 2 0                    | 2 2 0 2 2 0 2             |
| Patescibacteria    | Saccharimonadaceae   | Saccharimonadaceae               | 2 2 0 2 2 0                   | 2 2 0 2 2 0                    | 2 2 0 2 2 0 2             |
| Proteobacteria     | Betaproteobacteria   | Betaproteobacteria               | 3 2 1 3 2 1                   | 3 2 1 3 2 1                    | 3 2 1 3 2 1 3             |
|                    |                      |                                 | 2 0 2 2 0 2                   | 2 0 2 2 0 2                    | 2 0 2 2 0 2 2             |
|                    |                      |                                 | 2 0 2 2 0 2                   | 2 0 2 2 0 2                    | 2 0 2 2 0 2 2             |
|                    |                      |                                 | 2 0 2 2 0 2                   | 2 0 2 2 0 2                    | 2 0 2 2 0 2 2             |
| Gammaproteobacteria | Entrobacterales | Entrobacteriaceae | 13 | 10 | 3 | 12 | 9 | 3 | 2 | 2 | 0 | 9 | 6 | 3 | 8 | 5 | 3 | 4 | 4 | 0 |
|---------------------|----------------|------------------|----|----|---|----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pasteurellales       | Pasteurellaceae|                  | 3  | 1  | 2 | 3  | 1 | 2 | 3  | 1 | 2 | 3  | 1 | 2 | 3  | 1 | 2 | 4 | 4 | 0 |
## Table S6. Commensal microbiota alterations at Genus level in patients with depression.

| Phylum       | Order     | Family              | Genus          | Bacteroides | Total | American | Chinese | MDD | Depression |
|--------------|-----------|---------------------|----------------|-------------|-------|----------|---------|-----|------------|
| Actinobacteria | Actinomycetales | Actinomycetaeae | Actinomycetes | 6 5 1 | 4 4 0 | 4 4 0 | 4 4 0 | 3 0 3 |
|              | Bifidobacteriales | Bifidobacteriaceae | Bifidobacterium | 11 4 7 | 11 4 7 | 9 4 5 | 8 4 4 | 2 1 1 |
|              | Coriobacteriales | Coriobacteriaceae | Collinella | 4 3 1 | 4 3 1 | 3 2 1 | 2 2 0 | 2 2 0 |
|              |            | Atopobiaceae | Atopobium | 2 2 0 | 2 2 0 | 2 0 2 | 2 0 2 | 2 0 2 |
|              |            | Oluella | Oluella | 4 3 1 | 4 3 1 | 4 3 1 | 3 3 0 | 3 3 0 |
|              | Eggerthellales | Eggerthellaceae | Adlercreutzia | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
|              |            | Eggerthella | Eggerthella | 7 7 0 | 7 7 0 | 6 6 0 | 7 7 0 | 2 2 0 |
|              |            | Granulicatella | Granulicatella | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
| Bacteroidetes | Bacteroides | Bacteroidaceae | Bacteroides | 18 10 | 17 8 9 | 2 1 1 | 11 5 6 | 12 7 5 | 5 1 4 |
|              |            | Barnesiella | Barnesiella | 6 1 5 | 6 1 5 | 3 1 2 | 2 1 1 | 4 0 4 |
|              |            | Butyricimonas | Butyricimonas | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 |
|              |            | Odoribacter | Odoribacter | 3 1 2 | 3 1 2 | 3 1 2 | 3 1 2 | 3 1 2 |
|              |            | Alloprevotella | Alloprevotella | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 |
|              |            | Paraprevotella | Paraprevotella | 6 6 0 | 6 6 0 | 3 3 0 | 3 3 0 | 3 3 0 |
|              |            | Prevotella | Prevotella | 10 5 5 | 9 4 5 | 3 3 0 | 3 3 0 | 3 3 0 |
|              |            | Prevotella-2 | Prevotella-2 | 3 1 2 | 2 0 2 | 7 3 4 | 7 3 4 | 3 2 1 |
|              |            | Prevotella-9 | Prevotella-9 | 3 2 1 | 2 1 1 | 2 0 2 | 3 2 1 | 3 2 1 |
|              |            | Alistipes | Alistipes | 12 7 5 | 11 6 5 | 8 4 4 | 7 5 2 | 4 1 3 |
| Firmicutes   | Bacilli    | Bacillales | Bacillales | 9 8 1 | 9 8 1 | 8 7 1 | 7 7 0 | 2 1 1 |
|              |            | Bacillales,incertae,seidis | Gemella | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
|              |            | Enterococcaceae | Enterococcus | 5 4 1 | 4 4 0 | 3 3 0 | 3 3 0 | 3 3 0 |
|              |            | Lactobacillaceae | Lactobacillus | 9 5 4 | 9 5 4 | 5 4 1 | 6 4 2 | 3 1 2 |
|              |            | Weissella | Weissella | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
|              |            | Streptococcaceae | Streptococcus | 11 9 2 | 9 7 2 | 8 7 1 | 7 5 2 | 2 2 0 |
| Family               | Genus                      | Taxonomic Group | 5 | 0 | 5 | 0 | 5 | 2 | 0 | 2 | 3 | 0 | 3 | 4 | 0 | 4 |
|----------------------|----------------------------|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clostridales         | Christensenellaceae        | Christensenellaceae R-7 group | 5 | 0 | 5 | 0 | 5 | 2 | 0 | 2 | 3 | 0 | 3 | 4 | 0 | 4 |
| Clostridales         | Butyricicoccus             |                 | 3 | 0 | 3 | 0 | 3 | 2 | 0 | 2 | 2 | 0 | 2 |   |   |   |
| Clostridales         | Clostridium innocuum group |                 | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 |   |   |   |   |   |
| Clostridales         | Hungatella                 |                 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 | 2 |   |   |   |   |
| Clostridales         | Eubacteriaceae             | Eubacterium     | 6 | 3 | 3 | 6 | 3 | 3 | 5 | 3 | 2 | 4 | 3 | 1 | 2 | 0 | 2 |
| Clostridales         | Eubacteriales Family XIII. Incertae Sedis | Anaerovorax | 3 | 0 | 3 | 0 | 3 | 3 | 0 | 3 | 2 | 0 | 2 |   |   |   |   |
| Clostridales         | Agathobacter               |                 | 2 | 0 | 2 | 2 | 0 | 2 |   |   |   |   |   |   |   |   |   |
| Clostridales         | Anaerostipes               |                 | 6 | 4 | 4 | 8 | 4 | 4 | 6 | 4 | 2 | 6 | 4 | 2 | 2 | 0 | 2 |
| Lachnospiraceae      | Blautia                    |                 | 12 | 7 | 5 | 12 | 7 | 5 | 2 | 1 | 1 | 9 | 5 | 4 | 8 | 6 | 2 | 4 | 1 | 3 |
| Lachnospiraceae      | CAG-56                     |                 | 3 | 0 | 3 | 3 | 0 | 3 | 2 | 0 | 2 | 2 | 0 | 2 |   |   |   |   |
| Lachnospiraceae      | Clostridium XIVa           |                 | 2 | 1 | 1 | 2 | 1 | 1 |   |   |   |   |   |   |   |   |   |   |
| Lachnospiraceae      | Coprococcus                |                 | 9 | 0 | 9 | 9 | 0 | 9 | 6 | 0 | 6 | 5 | 0 | 5 | 4 | 0 | 4 |   |   |
| Lachnospiraceae      | Dorea                      |                 | 5 | 2 | 3 | 5 | 2 | 3 | 3 | 1 | 2 | 3 | 1 | 2 | 2 | 1 | 1 |   |   |
| Lachnospiraceae      | Eisenbergiella             |                 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 |   |   |   |   |
| Lachnospiraceae      | Fusicatenbacter            |                 | 6 | 0 | 6 | 6 | 0 | 6 | 4 | 0 | 4 | 3 | 0 | 3 | 3 | 0 | 3 |   |   |
| Lachnospiraceae      | Lachnoclostridum           |                 | 4 | 3 | 1 | 4 | 3 | 1 | 3 | 2 | 1 | 3 | 2 | 1 |   |   |   |   |
| Lachnospiraceae      | Lachnospira                |                 | 6 | 1 | 5 | 6 | 1 | 5 | 3 | 0 | 3 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 0 | 3 |
| Lachnospiraceae      | Lachnospiraceac incertae sedis |                 | 3 | 1 | 2 | 3 | 1 | 2 | 3 | 1 | 2 | 2 | 1 | 1 |   |   |   |   |   |
| Lachnospiraceae      | Lachnospiraceae ND3007 group |                 | 4 | 0 | 4 | 0 | 4 | 0 | 4 | 2 | 0 | 2 | 2 | 0 | 2 |   |   |   |   |   |
| Lachnospiraceae      | Lachnospiraceae_NK4A136_ group |                 | 3 | 1 | 2 | 3 | 1 | 2 | 2 | 1 | 1 | 2 | 1 | 1 |   |   |   |   |   |   |
| Lachnospiraceae      | Lachnospiraceae_UCG-001    |                 | 2 | 0 | 2 | 2 | 0 | 2 |   |   |   |   |   |   |   |   |   |   |   |   |
| Lachnospiraceae      | Roseburia                  |                 | 13 | 5 | 8 | 13 | 5 | 8 | 3 | 1 | 2 | 9 | 3 | 6 | 8 | 3 | 5 | 5 | 2 | 3 |
| Lachnospiraceae      | Shuttleworthia             |                 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 |   |   |   |   |   |   |   |   |   |
| Oscillospiraceae     | Tyzzerella                 |                 | 3 | 1 | 2 | 3 | 1 | 2 | 2 | 1 | 1 | 3 | 1 | 2 |   |   |   |   |   |   |
| Oscillospiraceae     | Oscillibacter              |                 | 9 | 4 | 5 | 9 | 4 | 5 | 6 | 3 | 3 | 5 | 3 | 2 | 4 | 1 | 3 |   |   |
| Peptostreptococcaceae | Clostridium XI             |                 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 3 | 2 | 1 |   |   |   |   |   |   |
| Peptostreptococcaceae | Romboutsia                 |                 | 3 | 0 | 3 | 3 | 0 | 3 | 2 | 0 | 2 |   |   |   | 2 | 0 | 2 |   |   |   |
| Ruminococcaceae      | Anaerofilum                |                 | 2 | 1 | 1 | 2 | 1 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Erysipelotrichia | Erysipelotrichales | Erysipelotrichaceae |
|-----------------|-------------------|--------------------|
| Anaerotruncus   | 2 2 0             | 2 2 0              |
| Clostridium IV  | 2 1 1             | 2 1 1              |
| Faecalibacterium| 19 3 16           | 18 2 16            |
| Flavonifractor  | 5 5 0             | 5 5 0              |
| Oscillospira    | 2 2 0             | 2 2 0              |
| Ruminococcaceae UCG-002 | 2 1 1 | |
| Ruminococcaceae UCG-014 | 2 2 0 | |
| Ruminococcus    | 9 1 8             | 9 1 8              |
| Ruminococcus-1  | 3 1 2             | 3 1 2              |
| Ruminococcus-2  | 2 0 2             | 2 0 2              |
| Subdoligranum   | 1 0 3             | 1 0 3              |
| Clostridium XVIII| 3 1 2            | 1 2 1              |
| Faecalibacterium| 3 2 1             | 3 2 1              |
| Holdemanella    | 2 0 2             | 2 0 2              |
| Holdemania      | 5 5 0             | 5 5 0              |
| Turicibacter     | 4 2 2             | 4 2 2              |

| Negativicutes   | Acidaminococcales | Acidaminococcaceae |
|-----------------|-------------------|--------------------|
| Acidaminococcus | 3 3 0             | 3 3 0              |
| Phascolarctobacterium | 7 2 5       | 7 2 5              |
| Selenomonadales | Selenomadaceae    |                    |
| Megamonas       | 6 1 5             | 6 1 5              |
| Moritella       | 3 1 2             | 3 1 2              |
| Veillonellales  | Veillonellaceae    |                    |
| Dialister       | 12 5 7            | 11 4 7             |
| Megaflaemnna    | 4 1 3             | 4 1 3              |
| Veillonella     | 8 7 1             | 7 6 1              |
| Tissierella     | Tissierellaceae    |                    |
| Parvimonas      | 4 3 1             | 3 2 1              |
| Fusobacteria    | Fusobacteria       |                    |
| Fusobacterium   | 5 2 3             | 3 1 2              |
| Rhizobiales     | Hypomicrobiaceae   |                    |
| Gemmiger        | 3 0 3             | 3 0 3              |
| Betaproteobacteria | Burkholderiales   |                    |
| Sutterellaceae  | 2 1 1             | 2 1 1              |
| Sutterellae     | 8 1 7             | 8 1 7              |
| Desulfovibrio   | Desulfovibrionales |                    |
| Desulfovibrio   | 5 4 1             | 5 4 1              |
| Epsilonproteobacteria | Campylobacteriae |                    |
| Campylobacter   | 2 1 1             | 2 1 1              |
| Enterobacteria  | 2 2 0             | 2 2 0              |
| Escherichia     | 7 5 2             | 6 4 2              |
| Klebsiella      | 2 1 1             | 2 1 1              |

| Gammaproteobacteria | Enterobacteriales |
|---------------------|-------------------|
| Enterobacter        | 2 1 1             | 2 1 1              |
| Escherichia-Shigella| 7 5 2             | 6 4 2              |
| Klebsiella          | 2 1 1             | 2 1 1              |
| Domain                  | Phylum                | Class               | Order             | Family            | Genus         | #1 | #2 | #3 | #4 | #5 | #6 |
|-------------------------|-----------------------|---------------------|-------------------|-------------------|---------------|----|----|----|----|----|----|
| Pasteurellales           | Pasteurellaceae       | Haemophilus         | 4                 | 1                 | 3             | 4  | 1  | 3  | 4  | 1  | 3  |
| Pseudomonadales         | Pseudomonadaceae      | Pseudomonas         | 2                 | 1                 | 1             | 4  | 1  | 3  | 3  | 0  | 3  |
| Streptophyta            | Magnoliopsida         | Fabales             | 3                 | 2                 | 1             | 3  | 2  | 1  | 3  | 2  | 1  |
| Verrucomicrobia         | Verrucomicrobiae      | Verrucomicrobiales  | 3                 | 2                 | 1             | 3  | 2  | 1  | 2  | 2  | 0  |
|                         |                       | Akkermansiaceae     | 3                 | 2                 | 1             | 2  | 2  | 0  | 2  | 1  | 1  |
| Phylum          | Class          | Order            | Family        | Genus                  | Species                                | Commensal microbiota | Gut microbiota |
|-----------------|----------------|------------------|---------------|------------------------|----------------------------------------|----------------------|---------------|
| Actinobacteria  | Actinomycetia  | Bifidobacteriales| Bifidobacteriae| Bifidobacterium        | Bifidobacterium_adolescentis           | 3 0 3 0              | 2 2 0 2 2 0 2 2 0 |
| Actinobacteria  | Actinomycetia  | Bifidobacteriales| Bifidobacteriae| Bifidobacterium        | Bifidobacterium_bifidum                | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Actinobacteria  | Actinomycetia  | Bifidobacteriales| Bifidobacteriae| Bifidobacterium        | Bifidobacterium_breve                  | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Actinobacteria  | Actinomycetia  | Bifidobacteriales| Bifidobacteriae| Bifidobacterium        | Bifidobacterium_dentium                | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Actinobacteria  | Actinomycetia  | Bifidobacteriales| Bifidobacteriae| Bifidobacterium        | Bifidobacterium_longum                 | 6 4 2 6 4 2          | 4 3 1 4 3 1 2 1 1 |
| Actinobacteria  | Actinomycetia  | Micrococcales    | Micrococcaceae | Rothia                  | Rothia_mucilaginosa                     | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Actinobacteria  | Actinomycetia  | Micrococcales    | Micrococcaceae | Atopobiales            | Atopobium_parvulum                     | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Actinobacteria  | Actinomycetia  | Micrococcales    | Micrococcaceae | Olsenella              | Olsenella_uli                          | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Actinobacteria  | Actinomycetia  | Coriobacteriales | Coriobacteriales| Coriobacteriales       | Coriobacterium_gloramers               | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Actinobacteria  | Actinomycetia  | Eggerthellaceae  | Eggerthellaceae | Adlerecreutzia          | Adlerecreutzia_equolifaciens           | 3 2 1 3 2 1          | 2 1 1 2 1 1 2 1 1 |
| Actinobacteria  | Actinomycetia  | Eggerthellaceae  | Eggerthellaceae | Eggerthellaceae         | Eggerthellaceae_lenta                  | 3 3 0 3 3 0          | 3 3 0 3 3 0 3 3 0 |
| Bacteroidetes   | Bacteroides    | Bacteroidaceae   | Bacteroidaceae | Bacteroides             | Bacteroides_arabae                     | 3 2 1 3 2 1 2 1 1   | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Bacteroidaceae   | Bacteroidaceae | Bacteroides             | Bacteroides_dorei                      | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Bacteroidaceae   | Bacteroidaceae | Bacteroides             | Bacteroides_fragilis                   | 3 3 0 3 3 0          | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Bacteroidaceae   | Bacteroidaceae | Bacteroides             | Bacteroides_massiliensis               | 3 2 1 3 2 1          | 2 1 1 2 1 1 2 1 1 |
| Bacteroidetes   | Bacteroides    | Bacteroidaceae   | Bacteroidaceae | Bacteroides             | Bacteroides_nordi                      | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Bacteroidaceae   | Bacteroidaceae | Bacteroides             | Bacteroides_plebeus                    | 2 1 1 2 1 1          | 2 1 1 2 1 1 2 1 1 |
| Bacteroidetes   | Bacteroides    | Bacteroidaceae   | Bacteroidaceae | Bacteroides             | Bacteroides_stercoris                  | 3 2 1 3 2 1 2 1 1   | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Bacteroidaceae   | Bacteroidaceae | Bacteroides             | Bacteroides_thetaoaomicron            | 4 4 0 4 4 0          | 3 3 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Bacteroidaceae   | Bacteroidaceae | Bacteroides             | Bacteroides_uniformis                  | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Bacteroidaceae   | Bacteroidaceae | Bacteroides             | Bacteroides_vulgatus                   | 2 1 1 2 1 1          | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Parvovellaceae   | Parvovellaceae | Parvovellaceae          | Parvovellaceae_xylaniphila             | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Parvovellaceae   | Parvovellaceae | Parvovellaceae          | Parvovellaceae_copri                   | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Prevotellaceae   | Prevotellaceae | Prevotellaceae          | Prevotellaceae_copri                   | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Rikenellaceae    | Rikenellaceae  | Alistipes               | Alistipes_finegoldii                   | 2 2 0 2 2 0          | 2 2 0 2 2 0 2 2 0 |
| Bacteroidetes   | Bacteroides    | Rikenellaceae    | Rikenellaceae  | Alistipes               | Alistipes_onederonkii                  | 3 3 0 3 3 0 2 2 0   | 2 2 0 2 2 0 2 2 0 |
| Firmicutes | Bacilli | Lactobacillales | Clostridia | Chlorobiales |
|------------|---------|----------------|-------------|--------------|
|            | Alistipes_senegalensis | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
| Tannerellaceae | Parabacteroides | 3 3 0 | 3 3 0 | 3 3 0 | 3 3 0 |
| Parabacteroides_distasonis | 3 3 0 | 3 3 0 | 3 3 0 | 3 3 0 |
| Parabacteroides_mertae | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
| Enterococcus | Enterococcus | 3 2 1 | 3 2 1 | 3 2 1 | 3 2 1 |
| Lactobacillales | Lactobacillus | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
| Streptococcaceae | Streptococcus | 3 3 0 | 3 3 0 | 3 3 0 | 3 3 0 |
| Streptococcus_parasanguinis | 3 3 0 | 3 3 0 | 3 3 0 | 3 3 0 |
| Streptococcus_pyogenes | 3 3 0 | 3 3 0 | 3 3 0 | 3 3 0 |
| Streptococcus_salivaruis | 3 1 2 | 3 1 2 | 2 0 2 | 2 0 2 |
| Clostridiales | Clostridium | 3 3 0 | 3 3 0 | 3 3 0 | 3 3 0 |
| Clostridium_asparagiforme | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
| Clostridium_boteae | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
| Clostridium_citromiae | 3 3 0 | 3 3 0 | 3 3 0 | 3 3 0 |
| Clostridium_hathewayi | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
| Clostridium_sacccharolyticum | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
| Clostridium_symbiosum | 3 3 0 | 3 3 0 | 3 3 0 | 3 3 0 |
| Lachnospiraceae | Coprocoscus | 3 2 1 | 3 2 1 | 3 2 1 | 3 2 1 |
| Coprocoscus_catus | 3 2 1 | 3 2 1 | 3 2 1 | 3 2 1 |
| Coprocoscus_eutactus | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Ruminococcaceae | Clostridium IV | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Clostridium_lectum | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Eubacteiriaceae | Eubacterium | 4 1 3 | 4 1 3 | 4 1 3 | 4 1 3 |
| Eubacterium_rectae | 4 1 3 | 4 1 3 | 4 1 3 | 4 1 3 |
| Helobacteriaceae | Helobacterium | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Helobacterium_modisticladium | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Lachnospiraceae | Anaerostipes | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Anaerostipes_hasud | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Dorea | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Dorea_longicatena | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Roseburia | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Roseburia_inulinivorans | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Oscillospiraceae | Oscillobacter | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Oscillobacter_valericigenes | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Ruminococcaceae | Faecalibacterium | 4 0 4 | 4 0 4 | 4 0 4 | 4 0 4 |
| Faecalibacterium_prausnitzii | 4 0 4 | 4 0 4 | 4 0 4 | 4 0 4 |
| Flavonifractor | 4 0 4 | 4 0 4 | 4 0 4 | 4 0 4 |
| Flavonifractor_plautii | 4 0 4 | 4 0 4 | 4 0 4 | 4 0 4 |
| Ruminococcaceae | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Ruminococcus_bromii | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Ruminococcus_gnavus | 4 0 4 | 4 0 4 | 4 0 4 | 4 0 4 |
| Ruminococcus_mattan | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Ruminococcus_torques | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| unclassified_Clostridiales | Clostridiales_bacterium_1_7_47F AA | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Erysipelotrichia | Erysipelotrichales | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Erysipelotrichales | Holdemania | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
| Kingdom     | Division          | Class            | Order           | Family        | Genus              | Species           | Enterobacteriaceae | Pasteurellales | Verrucomicrobiae |
|-------------|-------------------|------------------|-----------------|---------------|--------------------|-------------------|-------------------|-----------------|-----------------|
| Negativicutes | Acidaminococcales | Acidaminococcaceae | Acidaminococcus | Acidaminococcus fermentans | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 |
| Veillonellales | Veillonellaceae   |                   |                 |               | Megasphaera       | Megasphaera_elsdenii | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 |
|             |                   |                  |                 |               |                    |                   |                   |                 |                 |
| Proteobacteria | Deltaproteobacteria | Desulfovibrionales | Desulfovibrionaceae | Desulfovibrio | Bilophila         | Bilophila_wadsworthia | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 |
|             |                   |                  |                 |               | Desulfovibrio    | Desulfovibrio_desulfuricans | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 |
|             |                   |                  |                 |               | Desulfovibrio    | Desulfovibrio_vulgaris | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 |
|             |                   |                  |                 | Enterobacteriaceae | Enterobacter | Enterobacter_cloaceae | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 |
|             |                   |                  |                 |               | Enterobacteriaceae | Enterobacter_cloacis | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 |
|             |                   |                  |                 |               | Escherichia      | Escherichia_coli | 4 | 4 | 0 | 4 | 4 | 0 | 3 | 3 | 0 | 3 | 3 | 0 |
|             |                   |                  |                 |               | Klebsiella       | Klebsiella_pneumoniae | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 |
|             |                   |                  |                 |               | Haemophilus      | Haemophilus_parainfluenzae | 5 | 0 | 5 | 4 | 0 | 4 | 3 | 0 | 3 | 4 | 0 | 4 |
|             |                   |                  |                 |               | Akkermansiaceae  | Akkermansia | Akkermansia_muciniphila | 5 | 3 | 2 | 5 | 3 | 2 | 2 | 1 | 1 | 3 | 2 | 1 | 3 | 2 | 1 | 2 | 1 | 1 |
Table S8. Commensal microbiota alterations at Phylum, Class, Order, and Family levels in animal models of depression.

| Microorganisms | Commensal microbiota | Total | Mice | Rat | Fecal samples | Cecum contents | Colon contents |
|----------------|-----------------------|-------|------|----|---------------|----------------|---------------|
|                | Total no. of frequ ency | No. of incre ased | No. of decre ased | Total no. of frequ ency | No. of incre ased | No. of decre ased | Total no. of frequ ency | No. of incre ased | No. of decre ased | Total no. of frequ ency | No. of incre ased | No. of decre ased | Total no. of frequ ency | No. of incre ased | No. of decre ased |
| **Phylum**     |                       |       |      |    |               |                |                |                |               |                |                |                |                |                |                |
| Actinobacteria | 35                    | 14    | 21   | 35 | 14            | 21             | 27             | 9              | 18             | 8              | 5             | 3              | 30             | 11             | 19             | 5              | 3             | 2             |
| Bacteroidetes  | 73                    | 40    | 33   | 73 | 40            | 33             | 49             | 25             | 24             | 22            | 15            | 7              | 51             | 29             | 22             | 17            | 9             | 5             |
| Cyanobacteria  | 11                    | 3     | 8    | 11 | 3            | 8              | 8              | 3              | 5              | 3             | 0             | 3              | 9              | 2              | 7              | 2             | 1             | 1             |
| Deferribacteres| 12                    | 7     | 5    | 12 | 7            | 5              | 11             | 7              | 4              | 11            | 7             | 4              | 11             | 7              | 4              | 11            | 7             | 4             |
| Firmicutes     | 78                    | 28    | 50   | 78 | 28           | 50             | 55             | 18             | 37             | 23            | 10           | 13             | 58             | 20             | 38             | 15            | 6             | 9             |
| Proteobacteria | 48                    | 37    | 11   | 48 | 37            | 11             | 41             | 31             | 10             | 7             | 6             | 1              | 34             | 26             | 8              | 10            | 6             | 4             |
| Tenericutes    | 15                    | 5     | 10   | 15 | 5            | 10             | 13             | 4              | 9              | 2             | 1             | 1              | 14             | 5              | 9              |                |                |                |
| TM7            | 5                     | 2     | 3    | 5  | 2            | 3              | 4              | 2              | 2              | 4             | 1             | 3              |                |                |                |                |                |
| Verrucomicrobia| 30                    | 14    | 16   | 30 | 14           | 16             | 23             | 11             | 12             | 7             | 3             | 4              | 18             | 7              | 11             | 8              | 5             | 3             | 4             |
| **Class**      |                       |       |      |    |               |                |                |                |                |               |                |                |                |                |                |                |                |
| Actinobacteria | 9                     | 7     | 2    | 9  | 7            | 2              | 3              | 2              | 1              | 5             | 4             | 1              | 4              | 2             | 2              | 3             | 3             | 0             |
| Coriobacteria  | 4                     | 1     | 3    | 4  | 1            | 3              | 3              | 1              | 2              | 4             | 1             | 3              |                |                |                |                |                |
| Bacteroidetes  | 15                    | 7     | 8    | 15 | 7            | 8              | 12             | 6              | 6              | 3             | 1             | 2              | 11             | 6             | 5              | 3             | 1             | 2             |
| Cyanobacteria  | 3                     | 2     | 1    | 3  | 2            | 1              | 3              | 2              | 1              | 2             | 1             | 1              |                |                |                |                |                |
| Deferribacteres| 5                     | 4     | 1    | 5  | 4            | 1              | 4              | 3              | 1              | 5             | 4             | 1              |                |                |                |                |                |
| Bacilli        | 15                    | 7     | 8    | 15 | 7            | 8              | 9              | 4              | 5              | 6             | 3             | 3              | 8              | 3             | 5              | 3             | 3             | 2             |
| Clostridia     | 17                    | 11    | 6    | 17 | 11           | 6              | 12             | 7              | 5              | 5             | 4             | 1              | 11             | 7             | 4              | 3             | 1             | 2             |
| Erysipelotrichia| 10                    | 3     | 7    | 10 | 3            | 7              | 9              | 3              | 6              | 8             | 2             | 6              |                |                |                |                |                |
| Negativicutes  | 2                     | 1     | 1    | 2  | 1            | 1              | 2              | 1              | 1              | 2             | 1             | 1              |                |                |                |                |                |
| **Proteobacteria** |                 |       |      |    |               |                |                |                |                |               |                |                |                |                |                |                |                |
| Alphaproteobacteria | 6               | 0     | 6    | 6  | 0            | 6              | 5              | 0              | 5              | 4             | 0             | 4              | 2              | 0             | 2              |                |                |
| Betaproteobacteria | 7              | 5     | 2    | 7  | 5            | 2              | 2              | 1              | 1              | 5             | 4             | 1              | 3              | 2             | 1              | 3             | 3             | 0             |
| Deltaproteobacteria | 9               | 7     | 2    | 9  | 7            | 2              | 4              | 4              | 0              | 5             | 3             | 2              | 6              | 6             | 0              |                |                |
| Epsilonproteobacteria | 7       | 7     | 0    | 7  | 7            | 0              | 6              | 6              | 0              | 4             | 0             | 2              | 2              | 0              |                |                |
| Gammaproteobacteria | 8              | 8     | 0    | 8  | 8            | 0              | 7              | 7              | 0              | 8             | 6             | 6              | 0              |                |                |                |                |
| Spirochaetes   | 3                     | 2     | 1    | 3  | 2            | 1              | 3              | 2              | 1              | 3             | 2             | 1              |                |                |                |                |                |
| Tenericutes    | 7                     | 4     | 3    | 7  | 4            | 3              | 6              | 4              | 2              | 6             | 4             | 2              |                |                |                |                |                |
| Phylum       | Class                  | Order                  | Family                  | Count |
|--------------|------------------------|------------------------|-------------------------|-------|
| Verrucomicrobiota | Verrucomicrobiae      |                        |                         | 8 5 3 8 5 3 7 4 3 | 4 2 2 2 1 1 2 2 0 |
| Actinobacteria | Actinomycetales        |                        |                         | 4 2 2 4 2 2 2 1 1 | 2 1 1 3 1 2 |
|              | Bifidobacteriales      |                        |                         | 10 6 4 10 6 4 6 2 4 | 4 4 0 3 2 1 6 3 3 |
|              | Micrococcales          |                        |                         | 2 0 2 2 0 2         |               |
|              | Coriobacteriia         |                        |                         | 4 2 2 4 2 2 3 2 1   | 4 2 2 |
| Bacteroidetes | Bacteroidales          |                        |                         | 24 14 10 24 14 10   | 19 11 8 5 3 2 19 12 7 4 2 2 |
| Cyanobacteria | 4C0d-2                |                        |                         | 3 2 1 3 2 1 3 2 1 3 | 2 1 1 |
|              | Melainabacteria        |                        |                         | 3 0 3 3 0 3         |               |
|              | Deferribacteres        |                        |                         | 6 4 2 6 4 2 5 4 1   | 5 4 1 |
| Firmicutes    | Bacillales             |                        |                         | 13 7 6 13 7 6 8 5 3 | 4 2 2 9 5 4 2 1 1 |
|              | Lactobacillales        |                        |                         | 19 8 11 19 8 11 13 4 9 | 6 4 2 9 4 5 6 3 3 |
|              | Clostridia             |                        |                         | 26 14 12 26 14 12   | 18 9 9 8 5 3 17 8 9 5 2 3 2 2 0 |
|              | Erysipelotrichia       |                        |                         | 10 3 7 10 3 7 9 3 6 | 8 2 6 |
|              | Negativicutes          |                        |                         | 2 1 1 2 1 1         |               |
| Proteobacteria | Alphaproteobacteria   |                        |                         | 2 1 1 2 1 1         | 2 1 1 |
|              | Rickettsiales          |                        |                         | 3 0 3 3 0 3         | 3 0 3 2 0 2 |
|              | Sphingomonadales       |                        |                         | 2 1 1 2 1 1         | 2 1 1 |
|              | Betaproteobacteria     |                        |                         | 8 5 3 8 5 3 2 2 0   | 6 3 3 4 1 3 4 4 0 |
|              | Deltaproteobacteria    |                        |                         | 11 9 2 11 9 2 6 6 0 | 5 3 2 6 6 0 3 2 1 |
|              | Epsilonproteobacteria  |                        |                         | 9 8 1 9 8 1 8 7 1   | 6 5 1 2 2 0 |
|              | Gammaproteobacteria    |                        |                         | 4 4 0 4 4 0 4 4 0   | 3 3 0 |
|              | Enterobacterales       |                        |                         | 3 2 1 3 2 1         | 2 2 0 2 1 1 |
| Spirochaetes  | Spirochaetales         |                        |                         | 3 2 1 3 2 1 3 2 1   | 3 2 1 |
| Tenericutes   | Mollicutes             |                        |                         | 5 1 4 5 1 4 4 0 4   | 3 1 2 2 0 2 |
|              | Anaeplastomatales      |                        |                         | 3 1 2 3 1 2 3 1 2   |               |
|              | Mycoplastomatales      |                        |                         | 3 1 2 3 1 2 3 1 2   |               |
|              | Mollicutes_RF39        |                        |                         | 6 3 3 6 3 3 6 3 3   | 6 3 3 6 3 3 |
| Verrucomicrobiota | Verrucomicrobiae      |                        |                         | 8 4 4 8 4 4 7 3 4   | 4 2 2 2 0 |

| Phylum       | Class                  | Order                  | Family                  | Count |
|--------------|------------------------|------------------------|-------------------------|-------|
| Actinobacteria | Bifidobacteriales      |                        |                         | 15 8 7 15 8 7 9 3 6 | 6 5 1 7 4 3 7 3 4 |
|              | Micrococcales          |                        |                         | 4 1 3 4 1 3 2 1 1 2 | 0 2 3 0 3 0 3 |
|              | Corynebacteriales      |                        |                         | 3 2 1 3 2 1         | 2 1 1 |
| Actinomycetales | Corynebacteriales      |                        |                         | 3 2 1 3 2 1         | 2 1 1 |
| Coriobacteriia | Coriobacteriales       |                        |                         | 15 5 10 15 5 10 12 5 7 | 3 0 3 12 5 8 |
|              | Atopobacteriaceae      |                        |                         | 2 1 1 2 1 1         |               |
| Domain    | Class          | Order                | Family           | Genus          |
|-----------|----------------|----------------------|------------------|----------------|
| Bacteroidetes | Bacteroides | Bacteroidales | Bacteroidaceae | Eggerthellaes |
|           |               |                     |                  |                |
|           |               |                     | Eggerthellaceae | 6 2 4         |
|           |               |                     | Bacteroidaceae  | 6 2 4 5 2 3   |
|           |               |                     | Bacteroidales_RF16_group | 3 2 1 3 2 1 |
|           |               |                     | Bacteroidales_S24-7_group | 21 10 11 21 10 11 13 5 8 |
|           |               |                     | Multiaculaceae  | 20 5 15 20 5 15 13 2 11 |
|           |               |                     | Odoribacterae   | 6 2 4 6 2 4 6 |
|           |               |                     | Paraprevotellaceae | 4 2 2 4 2 2 |
|           |               |                     | Porphyromonadaceae | 14 9 5 14 9 5 |
|           |               |                     | Prevotellaceae   | 31 13 18 31 13 18 |
|           |               |                     | Rikenellaceae    | 28 11 17 28 11 17 |
|           |               |                     | Tannerellaceae   | 6 2 4 6 2 4 6 |
|           |               |                     | Marinilabales    | 2 2 0 2 2 0 2 |
|           |               |                     | Cytophagia       | 2 2 0 2 2 0 2 |
|           |               |                     | Clostridiales_vadinBB60_group | 7 4 3 |
|           |               |                     | Bacillales       | 9 4 5 9 |
|           |               |                     | Planococcaceae   | 2 2 0 2 2 0 2 |
|           |               |                     | Staphylococcaceae | 9 5 4 9 5 4 7 |
|           |               |                     | Aerococcaceae    | 5 4 1 5 4 1 3 |
|           |               |                     | Carnobacteriaceae | 5 2 3 5 2 3 3 |
|           |               |                     | Entococcaceae    | 7 4 3 7 4 3 6 |
|           |               |                     | Lactobacillaceae | 36 12 24 |
|           |               |                     | Streptococcaceae | 2 |
|           |               |                     | Turicibacteriales | 3 1 2 |
|           |               |                     | Clostridiales_vadinBB60_group | 7 4 3 |
|           |               |                     | Clostridaceae    | 20 15 5 20 15 5 14 11 3 |
|           |               |                     | Defluvialataceae | 2 0 2 2 0 2 2 |
|           |               |                     | Exhattachaeae    | 4 1 3 4 1 3 4 |
|           |               |                     | Mogibacteriaceae | 6 2 4 6 2 4 6 |
|           |               |                     | Oscillospiraceae | 3 2 1 3 2 1 2 |
|           |               |                     | Peptococcaceae   | 10 4 6 10 4 6 7 |

**Firmicutes**
| Domain          | Phylum                                      | Class                               |
|-----------------|---------------------------------------------|-------------------------------------|
| Bacteria        | Peptostreptococcaceae                       | Ruminococcaceae                     |
|                 | Erysipelotrichiales                         | Erysipelotrichiales                 |
|                 | Erysipelotrichiales                         | Acidaminococcaceae                  |
|                 | Acidaminococcaceae                         | Acidaminococcaceae                  |
|                 | Veillonellales                              | Veillonellales                      |
|                 | Veillonellales                              | Anaerovoracaceae                    |
|                 | Monoglobaceae                              |                                     |
| Patescibacteria | Saccharimonadaceae                          |                                     |
|                 | Saccharimonadaceae                          |                                     |
| Proteobacteria  | Alphaproteobacteria                         |                                     |
|                 | Hyphomicrobiales                            |                                     |
|                 | Rhizobiales                                 |                                     |
|                 | Rhodospirillales                            |                                     |
|                 | Rhodospirillales                            |                                     |
|                 | Sphingomonadaceae                           |                                     |
|                 | Betaproteobacteria                          | Burkholderiales                     |
|                 | Burkholderiales                             |                                     |
|                 | Burkholderiales                             | Comamonadaceae                      |
|                 | Comamonadaceae                              |                                     |
|                 | Oxalobacteriales                            |                                     |
|                 | Sutterellaceae                              |                                     |
|                 | Desulfo bacteriabacteriabacterina           |                                     |
|                 | Desulfo bacteriabacteriabacterina           |                                     |
|                 | Epsilonproteobacteria                       |                                     |
|                 | Campylobacteriales                          |                                     |
|                 | Helicobacteriales                           |                                     |
|                 | Enterobacteriales                           |                                     |
|                 | Enterobacteriales                           |                                     |
|                 | Pasteurellace                               |                                     |
|                 | Pseudomonadace                              |                                     |
|                 | Moraxellace                                 |                                     |
|                 | Pseudomonadace                              |                                     |
| Spirochaetes    | Spirochaetales                              |                                     |
|                 | Spirochaetales                              |                                     |
|                 | Brachyspirochales                           |                                     |
| Tenericutes     | Mollicutes                                  |                                     |
|                 | Anaeroplasmatales                           |                                     |
|                 | Anaeroplasmatales                           |                                     |
|                 | Mycoplasmatales                             |                                     |
|                 | Mycoplasmatales                             |                                     |
| Verrucomicrobia | Verrucomicrobiales                          |                                     |
|                 | Verrucomicrobiales                          |                                     |
|                 | AK160630                                    |                                     |
Table S9. Commensal microbiota alterations at Genus level in animal models of depression.

| Microorganisms | Class | Order | Family | Genus | Total | Mice | Rats | Fecal samples | Cecum contents | Colon contents |
|----------------|-------|-------|--------|-------|-------|------|------|---------------|----------------|----------------|
| Phylum         |       |       |        |       |       |      |      |               |                |                |
| Actinobacteria | Actinomycales | Micrococcales | Rothia | 9 4 5 | 9 4 5 | 9 4 5 | 5 3 2 | 2 0 2 |               |                |
|                |       |       |        |       |       |      |      |               |                |                |
|                |       |       |        |       |       |      |      |               |                |                |
|                |       |       |        |       |       |      |      |               |                |                |
| Bifidobacteriales | Nocardia | Nocardia | Rhodococcus | 3 1 2 | 3 1 2 | 3 1 2 | 2 1 1 |      |                |                |
| Corynbacteriales | Corynbacteriales | Corynbacteriales | Bifidobacterium | 11 6 5 | 11 6 5 | 4 3 1 | 7 3 4 | 2 2 0 |               |                |
| Micrococcales | Brevibacteriales | Brevibacteriales | Brevibacterium | 3 2 1 | 3 2 1 | 2 2 0 | 2 2 0 |      |                |                |
|                | Dermabacteriales | Dermabacteriales | Brachybacterium | 3 2 1 | 3 2 1 | 2 2 0 | 2 2 0 |      |                |                |
|                | Coriobacteriales | Coriobacteriales | Coriobacteriaceae_UCG-002 | 11 3 8 | 11 3 8 | 9 3 6 | 2 0 2 | 3 0 3 |      |                |
| Eggerthellales | Eggerthellales | Eggerthellales | Adlercreutzia | 10 7 3 | 10 7 3 | 9 7 1 | 8 5 3 |      |                |                |
| Bacteroidetes | Bacteroides | Bacteroides | Bacteroides | 59 36 23 | 59 36 23 | 42 27 15 | 17 9 8 | 41 25 16 | 11 7 4 | 6 3 3 |
|                | Barnesiellaceae | Barnesiellaceae | Barnesiella | 11 4 7 | 11 4 7 | 11 4 7 | 6 3 3 | 3 1 2 | 2 0 2 |      |
|                | Muribaculaceae | Muribaculaceae | Muribaculum | 9 2 7 | 9 2 7 | 8 2 6 | 7 1 6 |      |      |      |
|                | Odoribacteraceae | Odoribacteraceae | Butyricimonas | 13 5 8 | 13 5 8 | 10 4 6 | 3 1 2 | 10 4 6 | 2 1 1 |      |
| Porphyromonadaceae | Odoribacter | Odoribacter | Odoribacter | 18 10 8 | 18 10 8 | 17 9 8 | 10 5 5 | 7 4 3 |      |      |
| Prevotellaceae | Alloprevotella | Alloprevotella | Alloprevotella | 25 15 10 | 25 15 10 | 17 11 6 | 8 4 4 | 17 12 5 | 2 1 1 | 5 1 4 |
|                | Paraprevotella | Paraprevotella | Paraprevotella | 10 4 6 | 10 4 6 | 9 4 5 | 9 3 6 |      |      |      |
|                | Prevotella | Prevotella | Prevotella | 27 14 13 | 27 14 13 | 20 7 13 | 7 7 0 | 10 10 9 | 3 2 1 | 5 2 3 |
|                | Prevotella-1 | Prevotella-1 | Prevotella-1 | 2 1 1 | 2 1 1 | 2 1 1 |      |      |      |      |
|                | Prevotella-9 | Prevotella-9 | Prevotella-9 | 5 3 2 | 5 3 2 | 5 3 2 |      |      |      |      |
| Phylum                  | Taxonomy                        | Relative Abundance |
|------------------------|--------------------------------|--------------------|
| Firmicutes             | Bacilli                         | 10%                |
|                        | Planococccae                    | 3%                 |
|                        | Staphylococccae                 | 2%                 |
|                        | Gemellae                        | 1%                 |
|                        | Lactobacillae                   | 1%                 |
|                        | Turicibacteres                  | 0%                 |
| Clostridia             | Caldicoprobacterae              | 0%                 |
|                        | Christensenellaceae             | 0%                 |
|                        | Clostridales                    | 0%                 |

### Table

| Taxonomy                        | Relative Abundance |
|--------------------------------|--------------------|
| Bacilli                         | 10%                |
| Planococccae                    | 3%                 |
| Staphylococccae                 | 2%                 |
| Gemellae                        | 1%                 |
| Lactobacillae                   | 1%                 |
| Turicibacteres                  | 0%                 |
| Caldicoprobacterae              | 0%                 |
| Christensenellaceae             | 0%                 |
| Clostridales                    | 0%                 |
| Family / Genus                        | Relative Abundance |
|--------------------------------------|--------------------|
| **Clostridium**                      | 19 10 9 19 10 9 11 7 4 8 3 5 15 8 7 4 2 2 |
| **Clostridium_sensu_stricto**        | 9 8 1 9 8 1 5 5 0 3 2 1 4 4 0 3 2 1 |
| **SMB53**                            | 3 1 2 3 1 2 2 1 1 2 0 2 |
| **Clostridiales_Family_XIII_Incertae_Sedis** | **Anaerovorax** | 4 2 2 4 2 2 2 2 0 2 0 2 4 2 2 |
| **Dehalobacteriaceae**               | **Dehalobacterium** | 7 3 4 7 3 4 4 2 2 3 1 2 7 3 4 |
| **Eubacteriaceae**                   | **[Eubacterium]_coprostanoligenes_group** | 2 0 2 2 0 2 2 0 2 0 2 |
| **Anaeorofutis**                     | 7 4 3 7 4 3 6 3 3 6 4 2 |
| **Family_XIII**                      | **Family_XIII_AD3011_group** | 3 3 0 3 3 0 3 3 0 2 2 0 |
| **Butyrivibrio**                     | **Family_XIII_UCG_001** | 2 0 2 2 0 2 2 0 2 |
| **Acetatifactor**                    | **Acetatifactor** | 4 0 4 4 0 4 2 0 2 2 0 2 3 0 3 |
| **Anaerostipes**                     | **Anaerostipes** | 4 1 3 4 1 3 4 1 3 2 0 2 |
| **Blastia**                          | **Blastia** | 18 13 5 18 13 5 7 4 3 10 8 2 13 10 3 3 2 1 |
| **Butyrivibrio**                     | **Butyrivibrio** | 3 2 1 3 2 1 2 1 1 2 2 0 |
| **Coproccocus**                      | **Coproccocus** | 19 9 10 19 9 10 9 6 3 10 3 7 6 6 10 3 3 0 |
| **Dorea**                            | **Dorea** | 13 7 6 13 7 6 9 5 4 4 2 2 10 4 6 2 2 0 |
| **Fusiceutibacter**                  | **Fusiceutibacter** | 2 1 1 2 1 1 2 1 1 2 1 1 |
| **Lachnobacterium**                  | **Lachnobacterium** | 6 2 4 6 2 4 3 2 1 3 0 3 4 2 2 2 0 2 |
| **Lachnoclostridium**                | **Lachnoclostridium** | 8 7 1 8 7 1 4 3 1 4 4 0 3 2 1 4 4 0 |
| **Lachnospira**                      | **Lachnospira** | 8 4 4 8 4 4 4 2 2 3 1 2 7 3 4 2 0 2 |
| **Lachnospiraceae_NC2004_group**     | **Lachnospiraceae_NC2004_group** | 2 0 2 2 0 2 |
| **Lachnospiraceae_ND3007_group**     | **Lachnospiraceae_ND3007_group** | 2 1 1 2 1 1 2 1 1 2 1 1 |
| **Lachnospiraceae_NK4A136_group**    | **Lachnospiraceae_NK4A136_group** | 16 6 10 16 6 10 9 4 5 7 2 5 9 4 5 3 1 2 2 0 2 |
| **Lachnospiraceae_UCG-001**          | **Lachnospiraceae_UCG-001** | 6 2 4 6 2 4 2 0 2 4 2 2 5 2 3 |
| **Lachnospiraceae_UCG-004**          | **Lachnospiraceae_UCG-004** | 2 1 1 2 1 1 2 1 1 2 1 1 |
| **Lachnospiraceae_UCG-006**          | **Lachnospiraceae_UCG-006** | 3 2 1 3 2 1 2 2 0 3 2 1 |
| **Marvinbryantia**                   | **Marvinbryantia** | 10 4 6 10 4 6 3 1 2 7 3 4 9 4 5 |
| **Robinsonella**                     | **Robinsonella** | 2 2 0 2 2 0 2 2 0 |
| **Roseburia**                        | **Roseburia** | 14 2 12 14 2 12 6 2 4 8 0 8 11 2 9 2 0 2 |
| Family               | Genus             | 2  | 1  | 1  | 2  | 1  | 1  | 2  | 1  | 1  | 2  | 1  | 1  | 2  | 1  | 1  | 4  | 2  | 2  |
|---------------------|-------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Oscillospiraceae    | Tyzzerella        | 2  | 1  | 1  | 2  | 1  | 1  | 2  | 1  |    |    |    |    |    |    |    |    |    |    |
|                     | Tyzzerella-3      | 2  | 0  | 2  | 2  | 0  | 2  |    |    |    |    |    |    |    |    |    |    |    |    |
|                     | Intestimonomas    | 6  | 2  | 4  | 6  | 2  | 4  | 4  | 1  | 3  | 2  | 1  | 1  | 4  | 2  | 2  |    |    |    |
|                     | Oscillibacter     | 20 | 15 | 5  | 20 | 15 | 5  | 10 | 8  | 2  | 10 | 7  | 3  | 16 | 13 | 3  | 2  | 1  | 1  |
| Peptococcaceae      | Peptococcus       | 3  | 2  | 1  | 3  | 2  | 1  | 2  | 1  | 1  | 2  | 1  | 1  |    |    |    |    |    |    |
|                     | rc4_4             | 3  | 2  | 1  | 3  | 2  | 1  | 2  | 2  | 0  |    |    |    | 2  | 1  | 1  |    |    |    |
| Peptostreptococcaceae| Peptostreptococcaceae_incertae_sedis | 2  | 0  | 2  |    |    |    |    |    |    |    |    |    | 2  | 0  | 2  |    |    |    |
|                     | Romboutsia        | 9  | 3  | 6  | 9  | 3  | 6  | 2  | 2  | 0  | 7  | 1  | 6  | 6  | 3  | 3  |    |    |    |
|                     | Terrisporobacter   | 2  | 0  | 2  | 2  | 0  | 2  | 2  | 0  | 2  |    |    |    |    |    |    |    |    |    |
| Ruminococcaceae     | Anaerotruncus     | 12 | 7  | 5  | 12 | 7  | 5  | 9  | 6  | 3  | 3  | 1  | 2  | 6  | 4  | 2  | 6  | 3  | 3  |
|                     | Clostridium_JV    | 5  | 2  | 3  | 5  | 2  | 3  | 5  | 2  |    |    |    |    |    | 4  | 1  |    |    |    |    |
|                     | Eubacterium       | 12 | 3  | 9  | 12 | 3  | 9  | 7  | 2  | 5  | 4  | 1  | 3  | 9  | 1  | 8  |    |    |    |
|                     | Faecalibacterium  | 4  | 1  | 3  | 4  | 1  | 3  | 2  | 0  | 2  | 2  | 1  | 1  | 4  | 1  | 3  |    |    |    |
|                     | Flavonifractor    | 3  | 2  | 1  | 3  | 2  | 1  | 3  | 2  | 1  |    |    |    |    |    |    |    |    |    |
|                     | Gemmiger          | 2  | 0  | 2  | 2  | 0  | 2  | 2  | 0  | 2  |    |    |    |    |    |    |    |    |    |
|                     | Harryflintia      | 3  | 1  | 2  | 3  | 1  | 2  | 2  | 1  | 1  |    |    |    |    |    |    |    |    |    |
|                     | Oscillospira      | 24 | 13 | 11 | 24 | 13 | 11 | 15 | 8  | 7  | 8  | 4  | 4  | 20 | 10 | 10 | 3  | 2  | 1  |
|                     | Pseudoflavonifractor | 5  | 4  | 1  | 5  | 4  | 1  | 5  | 4  | 1  |    |    |    |    |    |    |    |    |    |
|                     | Ruminoclostridium | 6  | 1  | 5  | 6  | 1  | 5  | 3  | 1  | 2  | 3  | 0  | 3  | 4  | 1  | 3  | 2  | 0  | 2  |
|                     | Ruminoclostridium-5 | 7  | 4  | 3  | 7  | 4  | 3  | 7  | 4  | 3  | 5  | 3  | 2  |    |    |    |    |    |    |
|                     | Ruminoclostridium-6 | 8  | 4  | 4  | 8  | 4  | 4  | 2  | 1  | 1  | 6  | 3  | 3  | 7  | 4  | 3  |    |    |    |
|                     | Ruminoclostridium-9 | 7  | 4  | 3  | 7  | 4  | 3  |    |    |    | 6  | 3  | 3  | 5  | 4  | 1  |    |    |    |
|                     | Ruminococcaceae_NK4A21_4_group | 5  | 2  | 3  | 5  | 2  | 3  | 4  | 2  | 2  | 3  | 1  | 2  | 2  | 1  | 1  |    |    |    |
|                     | Ruminococcaceae_UCG-004 | 3  | 0  | 3  | 3  | 0  | 3  |    |    |    |    |    |    |    |    |    |    |    |    |
|                     | Ruminococcaceae_UCG-005 | 7  | 3  | 4  | 7  | 3  | 4  |    |    |    | 5  | 1  | 4  | 5  | 1  | 4  |    |    |    |
|                     | Ruminococcaceae_UCG-010 | 4  | 2  | 2  | 4  | 2  | 2  | 2  | 2  | 0  |    |    |    |    |    |    |    |    |    |
|                     | Ruminococcaceae_UCG-013 | 9  | 4  | 5  | 9  | 4  | 5  | 3  | 2  | 1  | 6  | 2  | 4  | 5  | 2  | 3  | 2  | 1  | 1  |
|                     | Ruminococcaceae_UCG-014 | 17 | 6  | 11 | 17 | 6  | 11 | 8  | 3  | 5  | 9  | 3  | 6  | 10 | 5  | 8  | 2  | 0  | 2  | 1  |
|                     | Ruminococcus      | 32 | 16 | 16 | 32 | 16 | 16 | 20 | 8  | 12 | 12 | 8  | 4  | 24 | 12 | 12 | 6  | 3  | 3  |
|                     | Ruminococcus-1    | 7  | 4  | 3  | 7  | 4  | 3  | 2  | 1  | 1  | 5  | 2  | 2  | 6  | 3  | 3  |    |    |    |
|                     | Ruminococcus-2    | 3  | 2  | 1  | 3  | 2  | 1  |    |    |    |    |    |    | 2  | 1  | 3  | 2  | 1  |    |
| Veillonellaceae      | Phascolarctobacterium | 6  | 3  | 3  | 6  | 3  | 3  | 2  | 1  | 1  | 4  | 2  | 2  | 6  | 3  | 3  |    |    |    |
| Class                       | Order                           | Genus                       | Count |
|-----------------------------|---------------------------------|-----------------------------|-------|
| Proteobacteria              |                                 |                             |       |
| Erysipelotrichia             |                                 | Veillonella                 | 5 3 2 |
|                             |                                 | Dialister                   | 4 0 4 |
|                             |                                 | A2                          | 2 0 2 |
|                             |                                 | Coprobacillaceae            | 4 3 1 |
|                             |                                 | Coprobacillus               | 3 2 1 |
|                             |                                 | Dubosiella                  | 7 4 3 |
|                             |                                 | Allobaculum                 | 35 16 |
|                             |                                 | Erysipelatoclostridium      | 5 2 3 |
|                             |                                 | Faecalibaculum              | 5 2 3 |
|                             |                                 | Faecalitalea                | 2 1 1 |
|                             |                                 | Anaerovibrio                | 3 3 0 |
|                             |                                 | Veillonellaceae             | 5 3 2 |
|                             |                                 | Devosia                     | 2 0 2 |
|                             |                                 | Sphingomonadaceae           | 4 2 2 |
|                             |                                 | Brucellaceae                | 3 3 0 |
|                             |                                 | Rhizobiales                 | 2 0 2 |
|                             |                                 | Brucellaceae                | 3 1 2 |
|                             |                                 | Captavidis                  | 3 3 0 |
|                             |                                 | Ralstonia                   | 2 1 1 |
|                             |                                 | Oxaibacteriaceae            | 5 2 0 |
|                             |                                 | Parasutterella              | 10 5 5 |
|                             |                                 | Sutterella                  | 6 4 2 |
|                             |                                 | Neisseria                   | 2 0 2 |
|                             |                                 | Neisseriae                  | 3 1 2 |
|                             |                                 | Desulfovibrionales          | 8 6 2 |
|                             |                                 | Desulfovibrioaceae          | 25 14 |
|                             |                                 | Flexispira                  | 2 0 2 |
|                             |                                 | Helicobacter                | 21 16 |
|                             |                                 | Enterobacteriaceae          | 8 7 1 |
|                             |                                 | Enterobacteriaceae          | 7 8 1 |
|                             |                                 | Enterobacteriaceae          | 7 8 1 |
|                             |                                 | Enterobacteriaceae          | 7 8 1 |
|                             |                                 | Morganellaceae              | 5 4 1 |
|                             |                                 | Proteus                     | 2 1 1 |
|                             |                                 | Pasteurellaceae             | 3 3 0 |
|                             |                                 | Pasteurellaceae             | 3 3 0 |
|                             |                                 | Haemophilus                 | 2 0 2 |
| Negativicutes                |                                 |                             |       |
|                               |                                 | Selenomonadales             | 3 3 0 |
|                               |                                 | nonrank_Firmicutes          | 3 3 0 |
|                               |                                 | sensu stricto incertae sedis| 3 3 0 |
|                               |                                 | Veillonellaceae             | 2 0 2 |
|                               |                                 | Anaerovibrio                | 2 0 2 |
|                               |                                 | Veillonellaceae             | 5 3 2 |
|                               |                                 | Negativibacillus            | 5 3 2 |
| Alphaproteobacteria          |                                 |                             |       |
| Betaproteobacteria           |                                 |                             |       |
|                               |                                 | Burkholderiaceae            | 3 1 2 |
|                               |                                 | Burkholderia                | 3 1 2 |
|                               |                                 | Captavidis                  | 3 3 0 |
|                               |                                 | Ralstonia                   | 2 1 1 |
|                               |                                 | Oxaibacteriaceae            | 5 2 0 |
|                               |                                 | Parasutterella              | 10 5 5 |
|                               |                                 | Sutterella                  | 6 4 2 |
|                               |                                 | Neisseria                   | 2 0 2 |
|                               |                                 | Neisseriae                  | 3 1 2 |
|                               |                                 | Bilophila                   | 8 6 2 |
|                               |                                 | Desulfovibrionales          | 25 14 |
|                               |                                 | Flexispira                  | 2 0 2 |
|                               |                                 | Helicobacter                | 21 16 |
|                               |                                 | Enterobacteriaceae          | 8 7 1 |
|                               |                                 | Enterobacteriaceae          | 7 8 1 |
|                               |                                 | Enterobacteriaceae          | 7 8 1 |
|                               |                                 | Enterobacteriaceae          | 7 8 1 |
|                               |                                 | Morganellaceae              | 5 4 1 |
|                               |                                 | Proteus                     | 2 1 1 |
|                               |                                 | Pasteurellaceae             | 3 3 0 |
|                               |                                 | Pasteurellaceae             | 3 3 0 |
|                               |                                 | Haemophilus                 | 2 0 2 |
| Kingdom | Phylum | Class | Order | Family | Genus | Abbreviation | Male | Female | Male | Female | Male | Female |
|---------|--------|-------|-------|--------|-------|--------------|------|--------|------|--------|------|--------|
| Bacteria | Pseudomonadales | Moraxellaceae | Acinetobacter | 4 | 2 | 2 | 3 | 1 | 2 | 2 | 1 | 1 | 2 | 0 | 2 |
|         |        |        | Psychrobacter | 4 | 2 | 2 | 4 | 2 | 2 | 3 | 2 | 1 | 2 | 0 | 2 | 2 | 0 |
|         |        |        | Pseudomonadales | Pseudomonas | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 |
|         |        |        | Xanthomonadales | Xanthomonadaceae | Lyso bacter | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 |
|         |        | Spirochaetales | Spirochaetes | Spirochaetaceae | Treponema | 2 | 0 | 2 | 0 | 2 | 0 | 2 | 0 | 2 | 0 | 2 | 0 |
|         |        |        | Tenericutes | Mollicutes | Anaeroplasmatales | Anaeroplasmataceae | Anaeroplasma | 11 | 3 | 8 | 11 | 3 | 8 | 8 | 1 | 7 | 3 | 2 | 1 | 9 | 3 | 6 | 2 | 0 | 2 |
|         |        |        | Mycoplasmatales | Mycoplasmataceae | Mycoplasma | 4 | 2 | 2 | 4 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 0 |
|         |        | Verrucomicrobia | Verrucomicrobiae | Verrucomicrobiales | Akkermansia | 30 | 16 | 14 | 30 | 16 | 14 | 23 | 13 | 10 | 7 | 3 | 4 | 18 | 9 | 9 | 8 | 5 | 3 | 2 | 1 |
|         |        |        |        |        |        | ASF356 | 3 | 2 | 1 | 3 | 2 | 1 | 3 | 2 | 1 |
|         |        |        |        |        |        | LARJ | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 |
|         |        |        |        |        |        | LLKB | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 0 |
| Microorganisms | Total | Mice | Rat | Monkey | Fecal samples | Cecum contents | Colon contents |
|----------------|-------|------|-----|---------|---------------|----------------|----------------|
| **Phylum** |       |      |     |         |               |                |                |
| Firmicutes |       |      |     |         |               |                |                |
| Bacilli |       |      |     |         |               |                |                |
| Lactobacillales |       |      |     |         |               |                |                |
| Lactobacillus |       |      |     |         |               |                |                |
| Lactobacillus_anaerobius |       |      |     |         |               |                |                |
| Lactobacillus_animalis |       |      |     |         |               |                |                |
| Lactobacillus_intestinalis |       |      |     |         |               |                |                |
| Lactobacillus_johnsonii |       |      |     |         |               |                |                |
| Lactobacillus_murinus |       |      |     |         |               |                |                |
| Lactobacillus_ruber |       |      |     |         |               |                |                |
| Streptococcaceae |       |      |     |         |               |                |                |
| Streptococcus |       |      |     |         |               |                |                |
| Clostridiales |       |      |     |         |               |                |                |
| Clostridiaceae |       |      |     |         |               |                |                |
| Candidatus_Atharomitus |       |      |     |         |               |                |                |
| Clostridium |       |      |     |         |               |                |                |
| **Class** |       |      |     |         |               |                |                |
| Bacteroidia |       |      |     |         |               |                |                |
| Bacteroidiales |       |      |     |         |               |                |                |
| Bacteroides |       |      |     |         |               |                |                |
| Deferribacteres |       |      |     |         |               |                |                |
| Deferribacteraceae |       |      |     |         |               |                |                |
| Deferribacter |       |      |     |         |               |                |                |
| Butyricimonas |       |      |     |         |               |                |                |
| Butyricimonas_visibunda |       |      |     |         |               |                |                |
| Prevotellaeae |       |      |     |         |               |                |                |
| Prevotella |       |      |     |         |               |                |                |
| Rikenellaeae |       |      |     |         |               |                |                |
| Alstipes |       |      |     |         |               |                |                |
| **Family** |       |      |     |         |               |                |                |
| Bacteroidaceae |       |      |     |         |               |                |                |
| **Order** |       |      |     |         |               |                |                |
| **Species** |       |      |     |         |               |                |                |
| **Actinobacteria** |       |      |     |         |               |                |                |
| Actinomyces |       |      |     |         |               |                |                |
| Actinomyces_venadinus |       |      |     |         |               |                |                |
| **Bacteroidetes** |       |      |     |         |               |                |                |
| Bacteroids |       |      |     |         |               |                |                |
| **Firmicutes** |       |      |     |         |               |                |                |
| Bacilli |       |      |     |         |               |                |                |
| Lactobacillales |       |      |     |         |               |                |                |
| Lactobacillus |       |      |     |         |               |                |                |
| Lactobacillus_animalis |       |      |     |         |               |                |                |
| Lactobacillus_intestinalis |       |      |     |         |               |                |                |
| Lactobacillus_johnsonii |       |      |     |         |               |                |                |
| Lactobacillus_murinus |       |      |     |         |               |                |                |
| Lactobacillus_ruber |       |      |     |         |               |                |                |
| Streptococcaceae |       |      |     |         |               |                |                |
| Streptococcus |       |      |     |         |               |                |                |
| Clostridiales |       |      |     |         |               |                |                |
| Clostridiaceae |       |      |     |         |               |                |                |
| Candidatus_Atharomitus |       |      |     |         |               |                |                |
| Clostridium |       |      |     |         |               |                |                |
| Clostridium_faecis |       |      |     |         |               |                |                |
| Clostridium_faecorum |       |      |     |         |               |                |                |
| **Table S10. Commensal microbiota alterations at Species level in animal models of depression.**

| Table S10. Commensal microbiota alterations at Species level in animal models of depression. | Total | Mice | Rat | Monkey | Fecal samples | Cecum contents | Colon contents |
|---------------------------------|-------|------|-----|---------|---------------|----------------|----------------|
| **Phylum** |       |      |     |         |               |                |                |
| Firmicutes |       |      |     |         |               |                |                |
| Bacilli |       |      |     |         |               |                |                |
| Lactobacillales |       |      |     |         |               |                |                |
| Lactobacillus |       |      |     |         |               |                |                |
| Lactobacillus_animalis |       |      |     |         |               |                |                |
| Lactobacillus_intestinalis |       |      |     |         |               |                |                |
| Lactobacillus_johnsonii |       |      |     |         |               |                |                |
| Lactobacillus_murinus |       |      |     |         |               |                |                |
| Lactobacillus_ruber |       |      |     |         |               |                |                |
| Streptococcaceae |       |      |     |         |               |                |                |
| Streptococcus |       |      |     |         |               |                |                |
| Clostridales |       |      |     |         |               |                |                |
| Clostridiaceae |       |      |     |         |               |                |                |
| Candidatus_Atharomitus |       |      |     |         |               |                |                |
| Clostridium |       |      |     |         |               |                |                |
| Clostridium_faecis |       |      |     |         |               |                |                |
| Clostridium_faecorum |       |      |     |         |               |                |                |
| **Table S10. Commensal microbiota alterations at Species level in animal models of depression.**

| Table S10. Commensal microbiota alterations at Species level in animal models of depression. | Total | Mice | Rat | Monkey | Fecal samples | Cecum contents | Colon contents |
|---------------------------------|-------|------|-----|---------|---------------|----------------|----------------|
| **Phylum** |       |      |     |         |               |                |                |
| Firmicutes |       |      |     |         |               |                |                |
| Bacilli |       |      |     |         |               |                |                |
| Lactobacillales |       |      |     |         |               |                |                |
| Lactobacillus |       |      |     |         |               |                |                |
| Lactobacillus_animalis |       |      |     |         |               |                |                |
| Lactobacillus_intestinalis |       |      |     |         |               |                |                |
| Lactobacillus_johnsonii |       |      |     |         |               |                |                |
| Lactobacillus_murinus |       |      |     |         |               |                |                |
| Lactobacillus_ruber |       |      |     |         |               |                |                |
| Streptococcaceae |       |      |     |         |               |                |                |
| Streptococcus |       |      |     |         |               |                |                |
| Clostridiales |       |      |     |         |               |                |                |
| Clostridiaceae |       |      |     |         |               |                |                |
| Candidatus_Atharomitus |       |      |     |         |               |                |                |
| Clostridium |       |      |     |         |               |                |                |
| Proteobacteria | Epsilonproteobacteria | Campylobacteriaceae | Helicobacteriaceae | Helicobacter | Verrucomicrobiae | Verrucomicrobiae | Akkermansiacae | Akkermansia | FJ880724 |
|---------------|----------------------|---------------------|---------------------|-------------|-----------------|-----------------|--------------|------------|---------|
| Eubacteriaceae | Eubacterium           | Eubacterium_plexicaudatum | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 |
|               |                      | Eubacterium_ruminantium | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 |
| Lachnospiraceae | Blautia              | Blautia_glucerasea    | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
|               |                      | Blautia_hydrogenotrophica | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
| Oscillospiraceae | Oscillibacter       | Oscillibacter_valericigenes | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 |
| Ruminococcaceae | ClostridiumIV        | Clostridium_leptum     | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
|               |                      | Fusobacterium         | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 |
|               |                      | Flavonifractor        | 3 2 1 | 3 2 1 | 3 2 1 | 3 2 1 | 3 2 1 |
|               |                      | Ruminococcus          | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
|               |                      | Ruminococcus_brontii  | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
|               |                      | Ruminococcus_lactaris | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
|               |                      | Helicobacter_gammani  | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
|               |                      | Helicobacter_japonicus | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
|               |                      | Helicobacter_macacae  | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 | 2 0 2 |
|               |                      | Helicobacter_rheintotium | 4 4 0 | 4 4 0 | 4 4 0 | 4 4 0 | 4 4 0 |
|               |                      | Esherichia coli       | 7 4 3 | 7 4 3 | 7 4 3 | 7 4 3 | 7 4 3 |
| Gammaproteobacteria | Enterobacteriaceae | Enterobacteriaceae | 1 1 1 | 1 1 1 | 1 1 1 | 1 1 1 | 1 1 1 |
|               |                      | Escherichia            | 7 4 3 | 7 4 3 | 7 4 3 | 7 4 3 | 7 4 3 |
|               |                      | Acinetobacter         | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 |
| Vernamicrobiae | Vernamicrobiaceae    | Vernamicrobiaceae      | 1 1 1 | 1 1 1 | 1 1 1 | 1 1 1 | 1 1 1 |
|               |                      | Akkermansia            | 3 3 0 | 3 3 0 | 3 3 0 | 3 3 0 | 3 3 0 |
|               |                      | Akkermansia_muciniphila | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 | 2 2 0 |
|               |                      | FJ880724              | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 | 2 1 1 |

Note: The numbers represent the number of bacteria species present in each category.
Table S11. Characteristics of studies investigating the efficiency of gut microbiota-based therapeutics in patients with depression.

| Study | Depression model | Microbiota-based therapies | Genus | Species | Intervention method | Depression alleviation | Gut-brain axis mechanism | OCEBM evidence level |
|-------|------------------|-----------------------------|-------|---------|--------------------|-----------------------|------------------------|----------------------|
| Kilincarslan S et al. 2020[1] | IBD patients with depression symptoms | Fecal microbiota transplantation | _     | _       | The fresh stool from healthy donors was diluted with saline before transplantation, and the suspension was prepared by mixing with a spatula. The stool suspension was infused into the patient through colonoscopy. | The severity of anxiety, depression and obsession in IBD patients decreased after FMT | _                      | 3                    |
| Kurokawa S et al. 2018[2] | IBS patients with depression symptoms | Fecal microbiota transplantation | _     | _       | Approximately 100 g of feces were collected from the pack, dissolved in 200 mL of saline | Depression and anxiety symptoms were improved by FMT regardless of gastrointestinal symptom change in patients with IBS | FMT altered disordered fecal microbiota | 3                    |
| Lin H et al. 2021[3] | IBS patients with depression symptoms | Fecal microbiota transplantation | _     | _       | The donor is a healthy 36-year-old male. Patients received FMT treatment (oral administration) from May 2019 to December 2019. The patients took the intestinal flora capsules 3 times in total, once every other day, 30 capsules each time | FMT treatment can effectively alleviate the anxiety and depression behaviors of IBS-D patients | FMT treatment regulated the gut microbiota | 2                    |
| Guo Q et al. 2021[4] | IBS patients with depression symptoms | Fecal microbiota transplantation with enterobacteria capsules | _     | _       | The FMT treatment was intervened by oral enteric capsules for 3 times (every 2 days one time and 30 capsules each time) | FMT therapy alleviated anxiety/depression symptom in IBS patients | FMT therapy restored the intestinal micro-ecology | 2                    |
| Chinna Meyyappan A et al. 2022[5] | Patients with MDD and GAD | Multispecies probiotics | _     | _       | Microbial Ecosystem Therapeutic-2 (MET-2), which contained 40 strains of bacteria | During the 8 weeks of treatment, all participants consumed three MET-2 capsules per day orally; each 0.5-g MET-2 capsule contains 3.2 × 10^5 to 3.2 × 10^11 CFU | Over the course of 10 weeks, MET-2 significantly decreased mean MADRS and GAD-7 scores | _                      | 3                    |
| Dao VH et al. 2021[6] | Chronic gastrointestinal disorders patients with depression symptoms | Multi-strain probiotics | Lactobacillus, Bifidobacterium, Lactococcus | B. bifidum W23, B. lactis W52, L. acidophilus W37, L. brevis W65, L. casei W66, L. salivarius W24, Lc. lactis W19, Lc. lactis W58 | The product consists of over 2.5 × 10^9 CFU per gram, patients would mix one sachet (2g of product) in 100mL of water for 8 weeks | Supplementation of multi-strain probiotic (Bacillus coagulans Unique IS2, L. rhamnosus UBRL58, B. lactis UBBLa70, L. plantarum UBLP40, B. breve UBBr01, B. infantis UBBB01) significantly reduced the depressive symptoms in students facing examination stress | _                      | 3                    |
| Venkataraman R et al. 2021[7] | Students facing examination stress | Multi-strain probiotics | Bacillus, Lactobacillus, Bifidobacterium | Bacillus coagulans Unique IS2, L. rhamnosus UBRL58, B. lactis UBBLa70, L. plantarum UBLP40, B. breve UBBr01, B. infantis UBBB01 | Receiving the multi-strain probiotic (Bacillus coagulans Unique IS2, L. rhamnosus UBRL58, B. lactis UBBLa70, L. plantarum UBLP40 (each of 2 billion CFU); B. breve UBBr01, B. infantis UBBB01) significantly reduced the depressive symptoms in students facing examination stress | _                      | 2                    |
Akkasheh G et al. 2016[8]
Patients with MDD
Probiotics
Lactobacillus, Bifidobacterium
L. acidophilus, L. casei, B. bifidum
Capsule with glutamine (250 mg) 2 times a day for 28 days
Patients in the probiotic group received daily one probiotic capsule containing L. acidophilus (2 × 10^9 CFU/g), L. casei (2 × 10^9 CFU/g), and B. bifidum (2 × 10^9 CFU/g) for 8 weeks
After 8 wk of intervention, patients who received probiotic supplements had significantly decreased Beck Depression Inventory total scores
Probiotic administration in patients with MDD for 8 wk had beneficial effects insulin, homeostasis model assessment of insulin resistance, hs-CRP concentrations, and glutathione concentrations

Baião R et al. 2022[9]
Patients with moderate depression
Probiotics
Bacillus, Bifidobacterium, Lactobacillus, Streptococcus
14 species: B. subtilis PXN® 21, B. bifidum PXN® 23, B. breve PXN® 25, B. infantis PXN® 27, B. longum PXN® 30, L. acidophilus PXN® 35, L. delbrueckii ssp. bulgaricus PXN® 39, L. casei PXN® 37, L. plantarum PXN® 47, L. rhamnous PXN® 54, L. helveticus PXN® 45, L. salivarius PXN® 57, L. lactis ssp. lactis PXN® 63, S. thermophilus PXN® 66
Participants were asked to take four capsules (2 × 10^9 CFU) in the morning each day with food within 4 weeks
Probiotic intake significantly reduced depression scores on the Patient Health Questionnaire 9

Bambling M et al. 2017[10]
Patients with SSRI treatment resistant depression
Probiotics
Lactobacillus, Bifidobacterium, Streptococcus
L. acidophilus, B. bifidum, S. thermophiles
Capsules administered pre meals as a combination of lyophilized probiotics (L. acidophilus, B. bifidum, S. thermophiles total CFU of 2 × 10^10) and magnesium orotate 1600 mg divided in two daily doses for 8 weeks
At the end of an 8-week intervention mean changes for depression scores and quality of life in the group was clinically significantly improved

Chen HM et al. 2021[11]
Patients with MDD
Probiotics
Lactobacillus
L. plantarum PS128 (PS128)
One PS128 capsule twice a day was gaven to recruited patients, each PS128 capsule contains 300 mg of probiotics, equivalent to 3 × 10^10 CFU of Lactobacillus plantarum PS128
After 8-week PS128 intervention, scores of Hamilton Depression Rating Scale-17 and Depression and Somatic symptoms Scale significantly decreased

Jamilian M et al. 2018[12]
Women with polycystic ovary syndrome
Probiotics
Lactobacillus, Bifidobacterium
L. acidophilus, L. reuteri, L. fermentum, B. bifidum
Intaking 8 × 10^9 CFU/day probiotic containing L. acidophilus, L. reuteri, L. fermentum, B. bifidum (2 × 10^9 CFU/g each) plus 200 μg/day selenium for 12 weeks
Probiotic and selenium co-supplementation resulted in a significant improvement in beck depression inventory and depression anxiety and stress scale scores compared with the placebo
Co-administration of probiotic and selenium for 12 weeks to women with PCOS had beneficial effects on mental health parameters, serum total testosterone, hirsutism, hs-CRP, TAC, GSH and MDA levels

Kazem YI et al. 2021[13]
Healthy female volunteers
Probiotics
Bifidobacterium
Yogurt enriched with Bifidobacterium spp.
All volunteers were given seven cups of yogurt every week (as one cup daily) fortified with the strain specific probiotic which was Bifidobacterium spp. for 8 weeks provided that each cup of yogurt was weighing 100 g
Bifidobacterium spp. supplementation combined with improvement in dietary intake resulted in improvement of depressive mood and well-being
Bifidobacterium spp. supplementation reduced kynurenine blood level
| Study Authors & Year | Study Population | Probiotics | Description | Comparator | Key Findings |
|----------------------|------------------|------------|-------------|------------|--------------|
| Kim CS et al. 2019[14] | Nationwide individuals | Probiotics | The types of probiotic food included fermented vegetables (kimchi) and fermented milk products | Compared with the lowest tertile of probiotic food consumption, the highest tertile had significantly lower odds in PHQ-9 depression severity and self-reported clinical depression, particularly in men | – |
| Lee HJ et al. 2021[15] | Healthy adults | Probiotics | Lactobacillus, Bifidobacterium | NVP-1704 group had a more significant reduction in depressive symptoms at four and eight weeks of treatment, and anxiety symptoms at four weeks compared to the placebo group | NVP-1704 treatment decreased serum interleukin-6 levels, and regulated the gut microbiota composition |
| Majeed M et al. 2018[16] | MDD patients with IBS | Probiotics | Bacillus coagulans MTCC 5856 | B. coagulans MTCC 5856 reduced the depression symptoms in MDD patients with IBS (HAM-D, MADRS) | B. coagulans MTCC 5856 reduced the level of serum myeloperoxidase |
| Messaoudi M et al. 2011[17] | Healthy human volunteers | Probiotics | Lactobacillus, Bifidobacterium | Administration of probiotics significantly alleviated depression and anxiety in volunteers, as measured by the HSCL-90 scale | – |
| Mi GL et al. 2015[18] | Infantile colic and colicky induced maternal depression | Probiotics | Lactobacillus | Participants received L. reuteri at a dose 10^9 CFU for 28 days and they were followed for 4 weeks | L. reuteri (DSM 17938) reduces daily crying time and maternal depression during infantile colic |
| Miyaoka T et al. 2018[19] | Patients with treatment-resistant MDD | Probiotics | Clostridium | CBM588 in combination with antidepressants is effective and well tolerated in the treatment of treatment-resistant MDD | – |
| Mohammadi AA et al. 2016[20] | Petrochemical workers | Probiotics | Lactobacillus, Bifidobacterium | After 6 weeks of intervention, a significant improvement of DASS scores was observed in the probiotic yogurt and in the probiotic capsule group | – |
| Moladi J et al. 2019[21] | Myocardial infarction patients with depression symptoms | Probiotics | Lactobacillus | The total BDI-II score decreased significantly in patients who received probiotic supplements compared with the placebo group | Markers of inflammatory and oxidative stress were influenced favorably by probiotic supplements |
| Study                                      | Participants | Probiotics                                      | Description                                                                                                                                                                                                 |
|-------------------------------------------|--------------|-------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Okubo R et al. 2019[22]                   | Schizophrenia patients with depression symptoms | Bifidobacterium B. breve A-1                      | All participants received B. breve strain A-1 (10⁹ CFU/day) for 4 weeks followed by 4 weeks of observation                                                                                                  |
| Ohaka M et al. 2021[23]                   | Patients with MDD or BD                          | Lactobacillus L. casei strain Shirota (LcS)      | Daily intake of 8.0 × 10⁹ CFU for 12 weeks                                                                                                      |
| Pinto-Sanchez MI et al. 2017[24]         | IBS patients with depression symptoms            | Bifidobacterium B. longum NCC3001                | Receiving 42 sachets of spray dried B. longum NCC3001 (1.0 × 10⁹ CFU/1gram powder with maltodextrin)                                           |
| Qiu Q et al. 2021[24]                    | Patients with test anxiety                        | Lactobacillus, Bifidobacterium, Streptococcus   | Taking probiotic supplement preparation for 15 consecutive days (twice per day, and approximately 12-hour set time between two intakes)                       |
| Raygan F et al. 2018[24]                 | Type 2 diabetic patients with depression symptoms | Lactobacillus, Bifidobacterium                  | Intaking 50,000 IU vitamin D3 every 2 weeks plus 8 × 10⁹ CFU/g probiotic, containing L. acidophilus, B. bifidum, L. reuteri, and L. fermentum (each 2 × 10⁹) for 12 weeks |
| Raygan F et al. 2019[23]                 | Type 2 diabetic patients with depression symptoms | Lactobacillus, Bifidobacterium                  | Receiving 200 mg/day selenium as selenium yeast plus 8 × 10⁹ CFU/day probiotic containing L. acidophilus, L. reuteri, L. fermentum and B. bifidum (2 × 10⁹ CFU/g each) for 12 weeks |
| Sanchez M et al. 2019[24]                | Obese individuals                                 | Lactobacillus L. rhamnosus CGMCC1.3724           | Participants received two capsules per day, corresponding to an average of 3.24 × 10⁹ CFU/day for 24 weeks                                                                                           |
| Slykerman RF et al. 2019[24]             | Postpartum depression                             | Lactobacillus L. rhamnosus HN001                | Women were randomised to receive either HN001 at a dose of 6x 10⁹ CFU/to be taken daily from enrolment until birth and, from birth up till six months post-birth whilst breastfeeding. |

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3. LeS was beneficial to alleviate depressive symptoms, partly through its association with abundance of Actinobacteria in the gut microbiota.

2. The probiotic reduced limbic reactivity.

1. Vitamin D and probiotic co-supplementation regulates serum hs-CRP, plasma NO, TAC, glycemic control and HDL-cholesterol levels.

2. Probiotic and selenium co-supplementation improved metabolic profiles.
Tian P et al. 2022[30] Patients with MDD Probiotics B. breve CCFM1025 The freeze-dried CCFM1025 in a dose of viable bacteria of $10^{10}$ CFU was given to MDD patients daily for four weeks B. breve CCFM1025 showed a better antidepressant-like effect than placebo, based on the HDRS-24 and MADRS evaluation B. breve CCFM1025 changed in the gut microbiome and tryptophan metabolism 2

Wallace CJK et al. 2021[31] Patients with MDD Probiotics Lactobacillus, Bifidobacterium L. helveticus R0052 and B. longum R0175 (CEREBIOME®) Participants consumed a probiotic supplement containing Lactobacillus helveticus R0052 and Bifidobacterium longum R0175 (CEREBIOME®) at a dose of $3 \times 10^9$ CFU once per day for 8 weeks Significant improvements in depressive symptoms were observed at week 4 and were sustained at week 8

Wu SI et al. 2021[32] Information technology specialists Probiotics Lactobacillus Lactobacillus plantarum PS128TM (PS128TM) Participants were asked to take two capsules containing PS128TM powder, equivalent to 20 billion CFU, daily for 8 weeks After 8-week-intervention, participants showed significant decreasers in the levels of depression (PHQ-9)

Yamamura R et al. 2021[33] Schizophrenic patients with depression symptoms Probiotics B. breve A-1 (synonym B. breve MCC1274) For the first 4 weeks, the participants consumed two 2-g sachets of freeze-dried Bifidobacterium breve A-1 (synonym B. breve MCC1274) per day, each containing $5.0 \times 10^9$ CFU Probiotic treatment with B. breve A-1 alleviated anxiety and depressive symptoms in patients with schizophrenia

Zhang X et al. 2021[34] Patients with depression and constipation Probiotics Lactobacillus Fermented Milk Containing L. paracasei Strain Shirota (LcS) The subjects consumed 100 mL of a LcS beverage ($10^9$ CFU/mL) every day for 9 weeks. Daily consumption of LcS for 9 weeks appeared to relieve constipation and improve the potentially depressive symptoms in patients LcS supplementation significantly decreased the IL-6 levels, and appeared to regulate the intestinal microbiota related to mental illness

Kaviani M et al. 2021[35] NAFLD patients with depression symptoms Prebiotics _ Resistant dextrin The intervention group received 15% of the total daily intake of fat (~20 g) as Camelina sativa oil with 10 g/day of resistant dextrin, 5 g at breakfast and 5 g at dinner for 12 weeks Supplementation of Camelina sativa oil + resistant dextrin for 12 weeks improved depression symptoms (DASS scores) in patients with NAFLD Prebiotic and CSO co-supplementation improved glycemic status, metabolic endotoxemia, inflammation, oxidant/antioxidant biomarkers

Miki T et al. 2016[36] Japanese employees Prebiotics _ Dietary fiber Dietary intake for 58 food and beverage items, energy, and selected nutrients were estimated using an ad hoc computer algorithm for the BDHQ Dietary fiber intake from vegetables and fruits was significantly inversely associated with depressive symptoms

Park M et al. 2020[37] Patients with depression Prebiotics _ Flavonoids Participants consumed flavonoid-rich orange juice (serving a daily 380 mL, 600 ± 5.4 mg flavonoids) for 8 weeks Flavonoid-rich orange juice treatment significantly decreased the depression symptoms (CES-D) Flavonoid-rich orange juice treatment regulated the gut microbiome

Heidarzadeh-Rad N et al. 2020[38] Patients with MDD Prebiotics, probiotics Lactobacillus, Bifidobacterium L. helveticus R0052, B. longum R0175, and galactooligosaccharide (GOS) The probiotic sachet containing 10 billion ($\geq 10 \times 10^9$) CFU of freeze-dried L. helveticus R0052 and B. longum R0175, the probiotic sachets contained 80% GOS powder per sachet. Participants were instructed to consume 1 sachet at the same time daily for 8 weeks Eight-week supplementation with B. longum and L. helveticus in depressive patients improved depression symptoms Probiotics supplementation resulted in significantly higher serum BDNF levels
| Reference | Study Description | Intervention | Results |
|-----------|-------------------|--------------|---------|
| Hadi A et al. 2019<sup>41</sup> | Obese or overweight adults | Synbiotics containing L. acidophilus, L. casei, and B. bifidum (2 × 10⁹ CFU per 5 g sachet) | A significant between-group decrease in depression was found in the synbiotic group compared to the placebo. |
| Haghighat N et al. 2021<sup>a,b</sup> | Hemodialysis patients | Synthetic supplements in form of a 500 mg capsule containing L. acidophilus, L. casei, and B. bifidum (2 × 10⁹ CFU/g) plus 0.8 g inulin for 8 weeks | Synbiotic supplementation decreased the TG, TC, LDL-C levels |
| Kazemi A et al. 2019<sup>a,b</sup> | Patients with MDD | L. helveticus R0052, B. longum R0175, and galactooligosaccharide | The probiotic product contains freeze-dried L. helveticus R0052 and B. longum R0175 bacteria at a dosage 10 × 10⁹ CFU/ per 5 g sachet for 8 weeks, and the probiotic product was composed of galactooligosaccharide and 0.2% Plum flavor |
| Perez-Cornago A et al. 2016<sup>a,b</sup> | Spanish university graduates | Yogurt (total, wholefat, and low-fat) and prebiotic (fructans and galactooligosaccharide) | Participants were allocated into 4 categories according to servings (1 serving = 125 g) of yogurt (total, wholefat (3% fat), and low-fat (0.1% fat)) consumed per week: <0.5 servings (<63 g), ≥0.5 to <3 servings (≥63 to <250 g), ≥3 to <7 servings (≥250 to <875 g), and ≥7 servings (<875 g) |
| Mohadi J et al. 2021<sup>a,b</sup> | Coronary artery disease (CAD) patients with depression symptoms | L. rhamnous G | Receiving one capsule contained 1.9 × 10⁶ CFU of L. rhamnous per day, or one sachet containing 15 g inulin per day, or both for 8 weeks |
| Moludi J et al. 2021 | 2021b | Synbiotic (15 g of prebiotics, 5 g of probiotic containing L. acidophilus T16, B. bifidum BIA-6, B. lactis BIA-7, B. longum BIA-8 (2.7 × 10⁷ CFU/g each)) prebiotics (5 g fructo-oligosaccharides (FOS), 5 g galacto-oligosaccharides (GOS), 5 g of inulin) | Synthetic supplementation in hemodialysis patients resulted in greater improvement in depression symptoms |
| | | | Synthetic supplementation increased the serum BDNF level |
| | | | Synbiotic and probiotic supplementation increased the serum Hb level |
| Haghighat N et al. 2021<sup>b</sup> | Hemodialysis patients | Synthetic (15 g of prebiotics, 5 g of probiotic containing L. acidophilus T16, B. bifidum BIA-6, B. lactis BIA-7, B. longum BIA-8 (2.7 × 10⁷ CFU/g each)) prebiotics (5 g fructo-oligosaccharides (FOS), 5 g galacto-oligosaccharides (GOS), 5 g of inulin) | Receiving the synthetic (15 g of prebiotics, 5 g of probiotic containing L. acidophilus T16, B. bifidum BIA-6, B. lactis BIA-7, B. longum BIA-8 (2.7 × 10⁷ CFU/g each)) or probiotics (5 g probiotics as in synthetic group) for 12 weeks |
| Kazemi A et al. 2019<sup>a,b</sup> | Patients with MDD | Lactobacillus, Bifidobacterium | The probiotic may exert at least part of its effects on depression through the kynurenine to tryptophan ratio |
| Karbowik MS et al. 2022<sup><sup>a</sup></sup> | Psychiatically healthy medical students | Probiotics, prebiotics | An electronic open-ended form of the Food Record was constructed to gather information regarding consumption of 34 selected food items categorized in five classes |
| | | | High intake of fermented food was associated with more severe depressive and anxiety symptoms under stress; however, no such link was observed for food-derived probiotics |
| Karbowik MS et al. 2022<sup><sup>a</sup></sup> | Psychiatically healthy medical students | Fermented food and food-derived prebiotics | Synbiotic and probiotic supplementation increased the serum BDNF level |
| | | | From baseline to 12 weeks, synthetic and probiotic supplementation resulted in a significant decrease in BDI and BAI score in comparison to the placebo |

**Note:**<sup>a</sup> Data from the original source;<sup>b</sup> Data from the study's hypothesis.
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### Table S12. Characteristics of studies investigating the efficiency of gut microbiota-based therapeutics in animal models of depression.

| Study | Object | Depression model | Microbiota-based therapies | Genus | Species | Intervention method | Depression alleviation | Gut-brain axis mechanism |
|-------|--------|------------------|-----------------------------|-------|---------|---------------------|------------------------|--------------------------|
| Rao J et al. 2021a(1) | Sprague-Dawley rats | CUMS-depression | Fecal microbiota transplantation | _ | _ | FMT group was administered a gavage of fecal supernatant with 2 × 10^7 fecal microbiota for 14 consecutive days | Fecal microbiota transplantation improved the CUMS-induced depressive-like behavior | Fecal microbiota transplantation altered the gut microbiota imbalance, and alleviated the intestinal tract inflammation, intestinal mucosa disruption, and neuroinflammation |
| Rao J et al. 2021b(1) | Sprague-Dawley rats | CUMS-depression | Fecal microbiota transplantation | _ | _ | For each rat, 1 ml of bacterial suspension (2 × 10^7 CFU/ml) was transplanted to each of the recipient rat by gavage each day for consecutive 14 days | Treatment with fecal microbiota transplantation ameliorated depression-like behaviors | Treatment with fecal microbiota transplantation suppressed activation of glial cells and NLRP3 inflammasome in the brain |
| Han SK et al. 2021(11) | C57BL/6 mice | RS-depression | FMT-RS-depression | Fecal microbiota transplantation | _ | _ | 0.2 mL of the fecal microbiota suspension were orally gavaged in (the stomach of ) mice once a day for 5 days | Fecal transplantation of vehicle-treated control or RS/CSS-treated mice into RS-exposed mice significantly mitigated RS-induced anxiety- and depressive-like behaviors | Fecal transplantation treatment suppressed the NF-κB activation in the hippocampus and colon, reduced the IL-6 and corticosterone levels in the blood, and regulated gut microbiota composition |
| Marcondes Avila PR et al. 2020(8) | Wistar rats | CMS-depression | Fecal microbiota transplantation | _ | _ | An equivalent of 3 × 10^8 cells in a 100-μL solution was given to each rat for five consecutive days by gavage | FMT treatment improved depressive-related (open-field) behavior | Manipulation of the microbiota reversed the behavioral and biochemical changes induced by the CMS protocol, and the vagus nerve influenced the gut-brain axis response |
| Xu Z et al. 2018(7) | C57BL/6 mice | Alcohol-induced depression | Fecal microbiota transplantation | _ | _ | Mice in FMT group received 200 μL suspensions with a minimum dose of approximately 10^9 bacteria at each oral gavage (from 3 male healthy volunteers ) | FMT significantly decreased anxiety- and depressive-like behaviors | _ |
| Zhang Y et al. 2019(9) | C57BL/6 mice | CUS-depression | Fecal microbiota transplantation | _ | _ | Antibiotic-treated mice were orally challenged with 300 μl fecal transplants (approximately 2 × 10^4 viable probiotic bacteria dissolved in sterile PBS) by gavaging on 3 consecutive days | Transplantation of the NLRP3 KO microbiota alleviated the CUS-induced depressive-like behaviors | FMT significantly ameliorated astrocyte dysfunction in recipient mice treated with CUS via inhibition of circHIPK2 expression |
| Zhou H et al. 2022(7) | C57BL/6 mice | Ddx1 KO-depression | Fecal microbiota transplantation and probiotics treatment | Lactobacillus, Bifidobacterium | L. reuteri, L. murinus, B. longum | Microbial transplantation was performed at 9:00 a.m. each day for 14 days. L. murinus, L. reuteri, and B. longum were diluted using 0.9% NaCl to a density of 10^9 CFU/ml, and a low dose of adzuki bean sprout fermented milk (0.1 mL, per day) for 10 days | Depression-like behavior of KO group was relieved following transplantation with L. reuteri, L. murinus, B. longum | Lactobacillus rescued depressive symptoms by restoring GABA levels |
| Wu Z et al. 2021(9) | C57/B6 | SDS-depression | Fermentate of bacteria | Lactobacillus, Streptococcus | Adzuki bean sprout fermented milk, generated by L. bulgaricus, S. thermophilus, L. plantarum 15953, and L. brevis J1 | Administration of full dose of adzuki bean sprout fermented milk (0.4 mL, per day), half dose of adzuki bean sprout fermented milk (medium, 0.2 mL, of per day), and a low dose of adzuki bean sprout fermented milk (low, 0.1 mL, per day) for 10 days | GABA-enriched adzuki bean sprout fermented milk alleviated the depression-like | GABA-enriched adzuki bean sprout fermented milk treatment regulated the GABAB-cAMP-PKA-CREB signaling pathway and increased the monoamine neurotransmitters (5-hydroxytryptamine, norepinephrine, and dopamine) in the hippocampus of mice |
| Author(s) | Year | Model | Treatment | Description |
|----------|------|-------|-----------|-------------|
| Han SK et al. | 2020a | C57BL/6 mice | IS-depression | Bifidobacteria Fermented Red Ginseng and Its Constituents Ginsenoside Rd and Protopanaxatriol 10 mg/kg/day of RG; 25 mg/kg/day of RG; 50 mg/kg/day of RG; 10 mg/kg/day of fRG; 25 mg/kg/day of fRG; and 50 mg/kg/day of fRG dissolved in 1% maltose were orally gavaged once a day for 5 days. Treatment with RG and fRG significantly mitigated the stress-induced anxiety/depression-like behaviors. | Bifidobacteria and its constituents Rd and protopanaxatriol mitigated anxiety/depression and colitis by regulating NF-κB-mediated BDNF expression and gut dysbiosis. |
| Ko CY et al. | 2013 | Sprague-Dawley rats | FST-depression | Fermented black soybean milk by L. brevis FPA 3709 Feeding with 48-h fermented black soybean milk at a dosage of 35 mg/kg b.w. including 2.5 mg GABA/kg b.w., and a double-dosage sample group (70 mg/kg b.w. including 5.0 mg GABA/kg b.w.) for 28 days. Oral feeding of 48-h fermented product significantly reduced the duration of immobility in a dose dependent manner. | The underlying mechanism for the antidepressant effect of this fermented product merits further research into the changes in the profile of monoamines, such as serotonin, dopamine, and norepinephrine, in rat brains. |
| Abildgaard A et al. | 2021 | FSL-sensitive line rats | FSL-depression | Lactobacillus Fermented black soybean milk at a dosage of 35 mg/kg b.w. including 2.5 mg GABA/kg b.w., and a double-dosage sample group (70 mg/kg b.w. including 5.0 mg GABA/kg b.w.) for 28 days. Oral feeding of 48-h fermented product significantly reduced the duration of immobility in a dose dependent manner. | Probiotics has effects on the gut microbiota and decreased corticosterone level in serum. |
| Xu N et al. | 2018 | ICR mice | Constipation-depression | Bifidobacteria, Lactobacillus, lactococcus and yeast The probiotic group was given probiotic (10 mg/kg daily by gavage), for 14 consecutive days. Administration of a probiotic ameliorated depressive behaviors. | Probiotics alleviated depression through protecting neuronal health via activation of the AKT signaling pathway. |
| Li N et al. | 2018 | CMS-depression | Multistrain probiotics | L. helveticus R0052, L. plantarum R1012, B. longum R0175 The bacterial solution (200 μL or 2 × 10^9 CFU) was administered by oral gavage daily for 4 weeks during the experimental procedure. Probiotics attenuated CMS-induced anxiety- and depressive-like behaviors. | Probiotics treatment modulated the gut microbiota-inflammation-brain axis, characterized by regulated gut microbiota, decreased hippocampal levels of proinflammatory cytokines (IFN-γ and TNF-α), and direct or inflammatory-mediated inhibition of IDO1 activity. |
| Liu QF et al. | 2020 | ICR mice | IS-depression | Bifidobacterium, Lactobacillus, Pediococcus L. plantarum LP3, L. rhamnosus L95, B. lactis BL3, B. breve BR3, P. pentosaceus PP4 Probiotic formulation (500 μL; 2 × 10^10 CFU/mL) was subsequently administered to mice subjected to stress conditions over a 4-week period. Probiotic administration alleviated depressive-like behaviors. | Ingested probiotics altered the composition of gut microbiota and decreased corticosterone level in serum. |
| Author and Year | Model | Diet | Treatments | Outcomes |
|-----------------|-------|------|------------|----------|
| Ding et al. 2021 | C57BL/6 mice | CRS-depression | Next-generation probiotics | A. muciniphila ATCC® BAA-835™, L. plantarum CICC® 23,133 | 200 µl (5 × 10⁹ CFU/mL) of A. muciniphila was administered via gavage for 3 weeks. 200 µl (5 × 10⁹ CFU/mL or 5 × 10⁸ CFU/mL) of L. plantarum was administered via gavage for 3 weeks. |
| Abildgaard et al. 2017 | Sprague-Dawley rats | Fed with a control or high-fat diet | Probiotics (Lactobacillus, Bifidobacterium) | 8 bacterial strains: B. bifidum W23, B. lactis W52, L. acidophilus W37, L. brevis W63, L. casei W56, L. salivarius W24, Lc. Lactis W19, Lc. Lactis W58 | Each cage received a bottle containing 4.5 g (2.5 × 10⁹ CFU/g) of freeze-dried powder dissolved in 30 mL of tap water; the bottles were administered daily between four and six pm for 5 weeks. |
| Abildgaard et al. 2017b | Flinders Sensitive Line rats | HFD-depression | Probiotics (Lactobacillus, Bifidobacterium) | 8 bacterial strains: B. bifidum W23, B. lactis W52, L. acidophilus W37, L. brevis W63, L. casei W56, L. salivarius W24, Lc. Lactis W19, Lc. Lactis W58 | Each cage received a bottle containing 4.5 g (2.5 × 10⁹ CFU/g) of freeze-dried powder dissolved in 30 mL of tap water; the bottles were administered daily between four and six pm for 5 weeks. |
| Abildgaard et al. 2019 | Sprague-Dawley rats | _ | Probiotics (Bifidobacterium, Lactococcus, Lactobacillus) | B. bifidum W23, B. lactis W51, B. lactis W52, L. acidophilus W37, L. brevis W63, L. casei W56, L. salivarius W24, Lc. Lactis W19 and Lc. Lactis W58 | Each probiotic cage of two rats was administered a bottle of 4.5 g (2.5 × 10⁹ CFU/g) freeze-dried PRO in a carrier matrix (maize starch, maltodextrins and vegetable protein) dissolved in 30 mL of tap water for 8 weeks. |
| Agusti et al. 2018 | C57BL/6 mice | HFD-depression | Probiotics (Bifidobacterium) | B. pseudocatenulatum CECT 7765 | Receiving a daily dose of 1 × 10⁹ CFU B. pseudocatenulatum CECT 7765 by gavage for 14 weeks. |
| Arsenault-Breault et al. 2020 | Sprague-Dawley rats | Post-myocardial infarction depression | Probiotics (Lactobacillus, Bifidobacterium) | L. helveticus R0052, B. longum R0175 | For 7 d before MI and between the 7th post-MI day and euthanasia, half the MI and sham rats were given one billion live bacterial cells of L. helveticus R0052 and B. longum R0175 per d dissolved in water. |
| Arslanova et al. 2021 | mice | Antibiotic-depression | Probiotics (Lactobacillus) | Two strains: L. rhamnosus B-8238, L. plantarum 8PA3 | Receiving 1 mL drinking water contained 2 × 10⁹ CFU/mL of a lactobacilli mixture (1:1) once a day for 14 days. |

Probiotics had antidepressant-like effect. The cohabiting microbiota and the faecal abundance of probiotics may modulate the antidepressant-like effect of probiotics in rats. Probiotic treatment markedly reduced depressive-like behaviour in the forced swim test. Probiotic treatment regulated abnormal variations in hormone (corticosterone), neurotransmitter (dopamine and serotonin), and BDNF expression levels in CRS-induced mice, and regulated gut microbiota.
| Name et al. | Species | Depressive-like behavior | Probiotics | Lactobacillus, Bifidobacterium, Streptococcus | VSL#3 contains 4 strains of Lactobacillus (L. plantarum, L. acidophilus, L. delbrueckii subsp. bulgaricus and L. casei), 3 strains of Bifidobacterium (B. longum, B. breve, B. infantis) and Streptococcus salivarius subsp. Thermophilus | VSL#3 at the doses of 12.86 bn living bacteria/kg/day in 0.5 ml for 30 day by gavage | VSL#3 supplementation exhibited anxiolytic and anti-depressive effect | VSL#3 supplement also increased the NGF immunoreactivity while decreasing IL-6, TNF-a and NO levels in WAG/Rij rat brain |
|------------|---------|--------------------------|------------|-----------------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------|-----------------------------------------------------------------|----------------------------------------------------------------|
| Aygun H et al. | WAG/Rij rats | Depressive-like behavior in WAG/Rij rat | Probiotics | Lactobacillus | Mice were treated daily for 30 days with single doses of 0.1 ml vehicle solution supplemented with Lp 286 (10^7 CFU/mL) or Lp 81 (10^6 CFU/mL) | The L. plantarum 286 strain exerted anti-depressant effects under our experimental conditions | | |
| Barros-Santos T et al. 2020 | Swiss mice | LPS-depression | Probiotics | Lactobacillus | Mice were treated with K. pastoris KM71H prevented depression-like behavior induced by stress | K. pastoris KM71H prevented depression-like behavior induced by stress | | |
| Bravo JA et al. 2011 | BALB/c mice | Healthy status | Probiotics | Lactobacillus | Animals were orally gavaged with broth with L. rhamnosus (JB-1) reduced stress-induced anxiety- and depression-related behavior | L. rhamnosus (JB-1) reduced stress-induced anxiety- and depression-related behavior | | |
| Chen P et al. 2019 | BALB/c mice | UCMS-depression | Probiotics | Lactobacillus | Lactobacillus reuteri has a significant therapeutic effect on depression | Oral administration of Lactobacillus reuteri increased brain serotonin levels and serotonin-positive cells in the dorsal raphe nucleus, and modulated microbiota | | |
| Chen T et al. 2021 | C57BL/6N mice | CRS-depression | Probiotics | Akkermansia | A. muciniphila supplementation alleviated depression-like behaviors A. muciniphila supplementation prevented mucosal barrier defects and aggravation of colitis, and modified the gut microbiota | | | |
| Chen X et al. 2022 | Sprague-Dawley rats | Lead exposure-depression | Probiotics | Lactobacillus, Bifidobacterium | Probiotics (6 billion live bacteria/2 g) were administered to the rats by gavage 5 times a week, at least 1.2 x 10^9 CFU combined strains were given to each rat, and doses as high as 4.8 x 10^10 CFU were administered | Probiotic intervention alleviated the depression-like behavior of lead-exposed rats | | |
Chen Y et al. 2021b[31] Sprague-Dawley rats CUMS-depression Probiotics Rhizopus, Bacillus Semen Sojae Praeparatum, a fermented food by R. chinensis 12 and Bacillus sp. DU-106 The rats were given a daily dose of 0.97 g/kg Semen Sojae Praeparatum (dissolved in 10 mL of normal saline) for 4 weeks Semen Sojae Praeparatum fermented by R. chinensis 12 and Bacillus sp. DU-106 could ameliorate depressive behaviors. Semen Sojae Praeparatum regulated the metabolite levels in the serum and hippocampus tissue, reversed the cell morphology and mitochondrial function of hippocampal neurons through improving the imbalance in gut microbiota and inhibiting the excessive SCFAs accumulation

Chevalier G et al. 2020[32] C57BL/6J mice UCMS-depression Probiotics Lactobacillus L. plantarum[33] Supplemented with oral feeding 5 days a week with 2 × 10^9 CFU of L. plantarum[34] diluted in 200 μL of PBS Complementation with L. plantarum[35] improved lipid metabolism and the generation of SCFAs, leading to increased signaling in the eCB system and adult neurogenesis in the hippocampus

Choi J et al. 2022[34] C57BL/6J mice CRS-depression Probiotics Extracellular vesicles (EV) from L. plantarum L-EVs at a dose of 0.1 μg/kg were intraperitoneally injected into a mouse at a volume of 100 μL 30 min prior to restraint treatment for 14 days; for the post-stress period, L-EVs were intraperitoneally injected at a volume of 100 μL containing increasingly higher doses; 0.1 μg/kg for the first 5 days, 0.18 μg/kg for the following 2 days, and 0.27 μg/kg for the final 7 days Injection of EV isolated from culture media of L. plantarum, Bacillus subtilis and A. muciniphila are sufficient to ameliorate stress-induced depressive-like behavior Injection of EV from the three selected probiotics restored the expression of MeCP2, Sirt1, and/or neurotrophic factors in the hippocampus

Chevalier G et al. 2020[32] Fischer/Long Evans Rats MD-depression Probiotics L. helveticus LA 102, B. longum LA 101, Lc. lactis LA 103, and S. thermophilus LA 104 Rats received 0.5 mL of the probiotics (1 × 10^9 CFU) by gavage with probes 5 days a week for 5 weeks for Fischer rats and 9 weeks for Long Evans rats (until euthanasia) A probiotic mixture induces anxiolytic and antidepressive-Like effects Probiotic mixture treatment changed the levels of certain metabolites, such as 21-deoxycortisol, and changed brain monoamines

Desbonnet L et al. 2010[34] Sprague-Dawley rats MS-depression Probiotics B. infantis 35624 B. infantis 35624 was administered by dissolving a powered preparation, containing a dose of 1×10^10 live bacterial cells, in 100 mL of the rats drinking water every morning from P50 to the day of sacrifice B. infantis 35624 treatment alleviated depressive-like behaviors Probiotic treatment resulted in normalization of the immune response and restoration of basal NA concentrations in the brainstem

Dhalwal J et al. 2018[33] Swiss albino LACA mice CUMS-depression Probiotics L. plantarum MTCC 9510 L. plantarum MTCC 9510 (2 × 10^8 CFU CFU per mouse) was supplemented to male Swiss albino mice either subjected to chronic unpredictable mild stress (28 days) or sleep deprivation stress (21 days) L. plantarum MTCC 9510 supplementation prevented stress-induced behavioural despair (depression, anxiety, learning and memory, stereotypic behaviour) L. plantarum MTCC 9510 supplementation prevented the oxidative stress and inflammatory response in brain and serum, and prevented intestinal permeability and selected gut microbial aberrations
| Study | Model | Condition | Probiotics | Treatment Details | Results |
|-------|-------|-----------|------------|------------------|---------|
| Gao K et al. 2022[38] | BALB/c mice | CUMS-depression | Lactococcus | Orally administrated with 200 µL pre-warmed WHH2078 preparation (1 × 10^9 CFU/mL) for 5 consecutive weeks | Lc. lactis strain WHH2078 alleviated depressive and anxiety-like behaviors |
| Gu F et al. 2020[39] | Sprague-Dawley rats | CUMS-depression | Lactobacillus | Administration with to L. casei (8× 10^8 CFU/kg/day) for 4 weeks from 4th to 7th week of CUMS | L. casei treatment relieved the depressive-like behaviors of rats induced by CUMS |
| Guida F et al. 2018[40] | C57bl6 mice | Antibiotic-depression | Lactobacillus | Oral gavage with the probiotic (L. casei DG, 10^9 cells in saline, 100 µl) up to 7 days. | L. casei treatment relieved the depressive-like behaviors induced by antibiotics |
| Guo Y et al. 2019[41] | ICR mice | CRS-depression | Bifidobacterium | Receiving 0.25 × 10^9 CFU/kg B. adolescentis by gavage for 21 days | B. adolescentis treatment prevented the development of anxiety- and depressive-like behaviors caused by CRS |
| Han SK et al. 2018[42] | C57BL/6 mice | IS-depression | Lactobacillus, Bifidobacterium | 1 × 10^9 CFU of NK41/mouse/day; 1 × 10^9 CFU of NK46/mouse/day; 1 × 10^9 CFU of NK41 and NK46 mixture (1:1) mix/mouse/day | Oral gavage of NK41, NK46, or their mixture synergistically alleviated immobilization stress-induced anxiety- and depressive-like behaviors in mice |
| Han SK et al. 2020b[43] | C57BL/6 mice | EC-depression | Lactobacillus, Bifidobacterium | 1 × 10^9 CFU/mouse/day of NK33; 1 × 10^9 CFU/mouse/day of NK98; 1 × 10^9 CFU/mouse/day of the NK33 and NK98 (1:1) mix/mouse/day | Oral gavage of NK33 and/or NK98 alleviated Escherichia coli K1-induced depression-like behaviors in mice |
| Hao W et al. 2021[44] | C57BL/6 mice | Antibiotic-depression | Bifidobacterium, Lactococcus, Lactobacillus and Streptococcus | Sixteen strains: B. longum, L. acidophilus, B. bifidum, B. breve, B. lactis, L. brevis, L. bulgaricus, L. casei, L. helveticus, L. plantarum, L. reuteri, L. rhamnosus, L. salivarius, Lc. lactis, S. thermophilus, and B. infantis | Probiotics treatment mitigated antibiotic-induced anxiety- and depressive-like behaviors |

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**Guo Y et al. 2020[39]**

**Sprague-Dawley rats**

CUMS-depression

Probiotics: Lactobacillus

L. casei

Preparation: (8× 10^8 CFU/kg/day) for 4 weeks from 4th to 7th week of CUMS

**Results:** L. casei treatment relieved the depressive-like behaviors of rats induced by CUMS.

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**Guida F et al. 2018[40]**

**C57bl6 mice**

Antibiotic-depression

Probiotics: Lactobacillus

L. casei DG

Administration: Oral gavage with the probiotic (L. casei DG, 10^9 cells in saline, 100 µl) up to 7 days.

**Results:** L. casei treatment relieved the depressive-like behaviors induced by antibiotics.

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**Han SK et al. 2018[42]**

**C57BL/6 mice**

IS-depression

Probiotics: Lactobacillus, Bifidobacterium

L. mucosae NK41, B. longum NK46

Administration: 1 × 10^9 CFU/kg B. adolescentis by gavage for 21 days

**Results:** B. adolescentis treatment prevented the development of anxiety- and depressive-like behaviors caused by CRS.

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**Han SK et al. 2020b[43]**

**C57BL/6 mice**

EC-depression

Probiotics: Lactobacillus, Bifidobacterium

L. reuteri NK33, B. adolescentis NK98

Administration: 1 × 10^9 CFU/mouse/day of NK33; 1 × 10^9 CFU/mouse/day of NK98; 1 × 10^9 CFU/mouse/day of the NK33 and NK98 (1:1) mix/mouse/day

**Results:** Oral gavage of NK33 and/or NK98 alleviated Escherichia coli K1-induced depression-like behaviors in mice.

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**Hao W et al. 2021[44]**

**C57BL/6 mice**

Antibiotic-depression

Probiotics: Bifidobacterium, Lactococcus, Lactobacillus and Streptococcus

Sixteen strains: B. longum, L. acidophilus, B. bifidum, B. breve, B. lactis, L. brevis, L. bulgaricus, L. casei, L. helveticus, L. plantarum, L. reuteri, L. rhamnosus, L. salivarius, Lc. lactis, S. thermophilus, and B. infantis

Administration: Probiotics solution (0.15 ml/d) for 14 consecutive days

**Results:** Probiotics treatment mitigated antibiotic-induced anxiety- and depressive-like behaviors.

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**Gu F et al. 2020[39]**

**Sprague-Dawley rats**

CUMS-depression

Probiotics: Lactobacillus

L. casei

Administration: (8× 10^8 CFU/kg/day) for 4 weeks from 4th to 7th week of CUMS

**Results:** L. casei treatment relieved the depressive-like behaviors of rats induced by CUMS.
Hao Z et al. 2019[45] Sprague-Dawley rats CUMS-depression Probiotics Faecalibacterium F. prausnitzii (ATCC 27766) Rats were fed at the same time each day by oral gavage with 200 μL of resuspended F. prausnitzii, 1 × 10^9 CFU (from the eighth week to the eleventh week) daily. Administration of F. prausnitzii had preventive and therapeutic effects on CUMS-induced depression-like and anxiety-like behavior F. prausnitzii administration led to higher levels of SCFAs in the cecum and higher levels of cytokines interleukin-10 (IL-10) in the plasma, prevented the effects on corticosterone, C-reactive protein and cytokines interleukin-6 (IL-6) release induced by CUMS.

Huang F et al. 2021[48] C57BL/6 mice Ovariectomy-depression Probiotics Prevotella P. histicola DSM19854 Receiving P. histicola (10 ml/kg) per second day for 12 weeks. P. histicola alleviated depressive behaviors caused by estrogen deficiency

Huang Y et al. 2020[49] C57BL/6N mice DSS-depression Probiotics Lactobacillus L. plantarium DMDL 9010 (LP9010) Mice administered orally with 0.2 ml/10 g weight per day LP9010 at a dose of 10^7 CFU/mL and 10^8 CFU/mL for 7 days LP9010 intake lightened depression-like behavior

Kambe J et al. 2020[50] C57BL/6 J mice Healthy status Probiotics Enteroceccus Heat-killed E. falcis strain EC-12 (EC-12) The EC-12 group was fed on AIN-93 M diet with heat-killed EC-12 at a concentration of 0.125 % for 4 weeks EC-12 supplementation reduced anxiety- and depressive-like behaviors

Karen C et al. 2021[51] Wistar rats MS-depression Probiotics Lactobacillus L. paracasei HT6 Supplementing with L. paracasei HT6 (per orally, p.o. by oral gavage; from PND-2 to 16) L. paracasei supplementation prevented early life stress-induced anxiety and depressive-Like behavior L. supplementation potentially mediated stress hormones, neurotransmitters, and expression of miRNAs, glutamate receptors, and the microbiota-gut-brain axis

Kim JK et al. 2020[52] C57BL/6J mice Escherichia coli K1-depression Probiotics Lactobacillus L. mucosae NK41 Mice were orally gavaged with the NK41 (1 × 10^9 CFU/mouse/day) once a day for 5 days from 24 h after treatment with K1 suspension NK41 treatment reduced K1-induced cognitive decline and anxiety/depression The superiority of anti-inflammatory bacteria such as L. mucosae can alleviate psychiatric disorders with the attenuation of altered microbiota

Kochalska K et al. 2020[53] Wistar rats CUMS-depression Probiotics Lactobacillus L. rhamnosus JB-1 The JB-1 group was fed a microbial diet with LR-JB1™ daily for 4 weeks Dietary supplement of LR-JB1™ resulted in a reduction of stress-induced behavior in a rat model of depressive-like disorder A microbiotic diet with LR-JB1™ brought improvements in neurochemical balance in the course of depressive-like disorder

Kougou A et al. 2021[54] C57BL/6J mice CSDS-depression Probiotics Bifidobacterium B. breve M-16V M-16V-treated groups were fed the AIN-93G diet which containing 5.0 × 10^9 nonviable cells/0.5 g Heat-sterilized B. breve M-16V supplementation significantly prevented depressive-like behavior (social interaction impairment) Heat-sterilized B. breve M-16V supplementation suppressed CSDS-induced neuroinflammation and modulated the gut microbiota composition
Probiotics alleviated CUMS-induced depressive-like behaviors

Probiotics treatment remodeled intestinal flora, increased the monoamine neurotransmitters (norepinephrine and 5-
hydroxytryptamine), and inhibited hypothalamic–pituitary–adrenal neuroendocrine system (ACTH and corticosterone)

Probiotics alleviated depressive-like behaviors

Probiotics ameliorated sCSDS like behavior

Probiotics alleviated depressive-like effects

Probiotics alleviated depressive-like behavior

Probiotics alleviated depressive-like behavior

Probiotics alleviated depressive-like behaviors

Probiotics alleviated depressive-like behavior

Probiotics alleviated depressive-like behaviors

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Probiotics consumption during puberty protected against LPS-induced depression- and anxiety-like behaviors in adulthood

Probiotics consumption during puberty mitigated inflammation, and prevented LPS-induced changes to the gut microbiome

Probiotics reduced microglia immunoreactivity in the basolateral amygdala, possibly indicating a neuroprotective effect of PB supplements in this rodent model

Probiotic administration altered gut microbial composition and promoted an anti-inflammatory profile

Probiotics treatment improved metabolic syndrome in mice (reduced the accumulation of mesenteric adipose tissue, increased insulin secretion, improved plasma cholesterol clearance and reduced basal corticosterone)

Probiotics treatment improved intestinal inflammation and subsequent neuroinflammation (through inhibiting toll-like receptor 4 (TLR4) signaling), and microbiota dysbiosis

Probiotics reduced microglia immunoreactivity in the basolateral amygdala, possibly indicating a neuroprotective effect of PB supplements in this rodent model

Probiotics administration altered gut microbial composition and promoted an anti-inflammatory profile
Soltanmoradi H et al. 2021[73]  
BALB/c mice  
Probiotics  
Lactobacillus  
L. rhamnosus GG, and kefir, a probiotic supplement  
-  
Kefir, L. rhamnosus GG, and the investigated probiotic supplement have antidepressant-like properties  
-  
Sovijit WN et al. 2019[74]  
C57BL/6J mice  
Ovariectomy-depression  
Probiotics  
Lactobacillus  
L. reuteri  
Feeding with food pellets that were pulverized in a blender and kneaded with L. reuteri (2 billion CFU/mouse/day) at 10 weeks of age, and lasting for 2 weeks  
L. reuteri supplementation improves depressive behaviors in OVX mice  
Supplementation of L. reuteri upregulated hippocampal brain-derived neurotrophic factor (BDNF) gene expression  
Stenmana LK et al. 2020[75]  
Swiss mice  
CRS-depression  
Probiotics  
Bifidobacterium, Lactobacillus  
12 candidate probiotics: B. longum BG0014, B. longum ss. infantis BI1471, B. animalis BL0005, B. animalis ss. lactis 420, L. paracasei Lpc-37, L. salivarus Ls-33, L. plantarum LP12418, L. plantarum LP12151, L. plantarum LP12407, L. acidophilus LA11873, L. rhamnosus LK11881, L. helveticus LH0138  
Mice were administered a daily oral gavage containing 1 x 10^9 CFU of selected candidate probiotic solution for one week prior to and for three weeks during daily chronic restraint stress.  
Of the twelve candidate probiotics, L. paracasei Lpc-37, L. plantarum LP12407, L. plantarum LP12151 prevented stress-associated anxiety and depression-related behaviours  
Each of these strains had a unique profile in terms of mechanistic biomarkers related to the HPA axis and prefrontal cortex GABA receptor expression  
Sun J et al. 2018[76]  
C57BL/6 mice  
CUMS-depression  
Probiotics  
Clostridium  
C. butyricum WZMC1018  
The bacterial solution was prepared every day in sterile milk and treated orally at a concentration of 5 x 10^8 CFU/0.5 mL/day/mice for 28 consecutive days.  
C. butyricum WZMC1018 treatment effectively improved depressive-like behavior  
C. butyricum WZMC1018 treatment stimulated the GLP-1 secretion and increased the 5-HT and BDNF through the gut-brain axis  
Sun X et al. 2021[77]  
C57BL/6 mice  
CRS-depression  
Probiotics  
Lactobacillus  
L. plantarum WLPL04  
The final concentration of the L. plantarum WLPL04 in drinking water was 10^9 CFU/mL for 28 days  
L. plantarum WLPL04 treatment alleviated CRS-induced anxiety/depressive-like behaviors and cognitive deficits  
L. plantarum WLPL04 treatment reversed the abnormal change in intestinal microbiota, and alleviated the reduced levels of 5-HT, BDNF, and TkkB induced by CRS in mice  
Sun Y et al. 2019[78]  
Kunming mice  
CUMS-depression  
Probiotics  
Lactobacillus  
L. kefiranofaciens ZW3  
Treated with L. kefiranofaciens ZW3 at different doses (10^7 CFU, 10^8 CFU, 10^9 CFU/mouse/day) for 6 weeks  
Supplementation with Lactobacillus kefiranofaciens ZW3 improved depressive-like behavior  
L. kefiranofaciens ZW3 regulated disorder of tryptophan metabolism, protected the HPA axis, inhibited inflammation, and reshaped the structure of the gut microbiota caused by CUMS  
Takahashi K et al. 2019[79]  
dY mice  
DSS-depression  
Probiotics  
Enterococcus  
E. faecalis 2001 (EF-2001)  
EF-2001 was administered orally (250mg/kg per os [p.o.]) from 14 days before the beginning of DSS  
EF-2001 attenuated IBD-like symptoms and depressive-like behavior in DSS-treated mice  
EF-2001 decreased rectal and hippocampal inflammatory cytokines and facilitated the NFκB p65/XIAP pathway in the hippocampus
| Takahashi K et al. 2022<sup>80</sup> | ddY mice | Olfactory bulbectomy-depression | Probiotics | Enterococcus E. faecalis 2001 (EF-2001) | EF-2001 (250 mg/kg) was dissolved in drinking water and administered orally (per os [p.o.]) once a day in a volume of 0.1 mL/10 g mouse body weight using a 1 mL syringe with an oral probe, from 6 days before the OBX operation for 28 days. | EF-2001 administration prevented depressive-like behaviors |
| --- | --- | --- | --- | --- | --- | --- |
| Tian P et al. 2019<sup>a</sup> | C57BL/6J mice | CUMS-depression | Probiotics | Bifidobacterium B. longum subspecies infantis strain CCFM687 | Lyophilized bacteria powder was re-suspended in 10% skimmed milk solution, and administered at a dose of 10<sup>9</sup> CFU/mL viable bacteria for 6 weeks | B. longum subspecies infantis strain CCFM687 showed a good anti-depressive effect |
| Tian P et al. 2019<sup>b</sup> | C57BL/6J mice | CUMS-depression | Probiotics | Bifidobacterium B. longum subsp. infantis E41, B. breve M2CF22M7 | Lactic acid bacteria treatment group was gavaged at a dose of 10<sup>9</sup> CFU/mL body weight daily for 5 weeks | Administration of several Lactic acid bacteria strains alleviated depressive behaviors of mice |
| Tian P et al. 2020<sup>c</sup> | C57BL/6J mice | CUMS-depression | Probiotics | Bifidobacterium B. breve CCFM1025 | The CCFM1025 treatment group was gavaged at a volume of 0.1 ml/10g (10<sup>9</sup> CFU/mL) body weight daily for 6 weeks | CCFM1025 treatment significantly alleviated depression and anxiety-like behaviors |
| Tian P et al. 2021<sup>d</sup> | C57BL/6J mice | UCMS-depression | Probiotics | Lactobacillus, Bifidobacterium, Pediococcus 30 strains: B. adolescentis, 3 strains of B. breve, 4 strains of B. bifidum, 2 strains of B. longum subsp. Infantis, 5 strains of B. longum subsp. Longum, 4 strains of B. longum, 3 strains of L. fermentum, 2 strains of L. helveticus, 3 strains of L. plantarum, 2 strains of L. rhamnosus, Pediococcus acidilactici | Giving viable bacteria (10<sup>9</sup> CFU/day) by oral gavage via 10% skim milk for 6 weeks | 16 strains show anti-depression and anti-anxiety-like effect in at least three behavioral tests |

<sup>a</sup>Tian P et al. 2019<sup>a</sup> C57BL/6J mice CUMS-depression Probiotics Bifidobacterium B. longum subsp. infantis strain CCFM687 showed a good anti-depressive effect. B. longum subsp. infantis strain CCFM687 increased the 5-hydroxytryptamine, serotonin and BDNF, alleviated the hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis response and accordingly reversed the peripheral inflammation status, and reshaped the gut microbiome. Lactic acid bacteria strains alleviated depression possibly via a 5-HTP-dependent mechanism, gut microbiota structure modulation.

<sup>b</sup>Tian P et al. 2019<sup>b</sup> C57BL/6J mice CUMS-depression Probiotics Bifidobacterium B. longum subsp. infantis E41, B. breve M2CF22M7 Lactic acid bacteria treatment group was gavaged at a dose of 10<sup>9</sup> CFU/mL body weight daily for 5 weeks. Administration of several Lactic acid bacteria strains alleviated depressive behaviors of mice.

<sup>c</sup>Tian P et al. 2020<sup>c</sup> C57BL/6J mice CUMS-depression Probiotics Bifidobacterium B. breve CCFM1025 CCFM1025 treatment significantly alleviated hyperactive hypothalamic-pituitary-adrenal response, as well as inflammation, down-regulated the pCREB-c-Fos pathway, increased BDNF, SCFA and 5-HTP, and restored gut microbial abnormalities.

<sup>d</sup>Tian P et al. 2021<sup>d</sup> C57BL/6J mice UCMS-depression Probiotics Lactobacillus, Bifidobacterium, Pediococcus 30 strains: B. adolescentis, 3 strains of B. breve, 4 strains of B. bifidum, 2 strains of B. longum subsp. Infantis, 5 strains of B. longum subsp. Longum, 4 strains of B. longum, 3 strains of L. fermentum, 2 strains of L. helveticus, 3 strains of L. plantarum, 2 strains of L. rhamnosus, Pediococcus acidilactici Giving viable bacteria (10<sup>9</sup> CFU/day) by oral gavage via 10% skim milk for 6 weeks. 16 strains show anti-depression and anti-anxiety-like effect in at least three behavioral tests. Intestinal 5-HTP supplementary on the biosynthesis of brain serotonin is the possible mechanism of the candidate probiotics.
Probiotic treatment persisted for 6 weeks by daily oral gavage. Lyophilized bacteria powder were re-suspended in 10% skim cow milk and administered at a dose of 10^10 CFU/mL viable bacteria. CBM588 significantly decreases the chronically stressed mice’s depressive-like behaviors. CBM588 may be involved in the regulation of microglia-mediated immune responses in the brain, and regulated gut microbiota composition.

Rats received a daily dose of 5 x 10^10 CFU/g for Ecologic® Barrier and a daily dose of 5 x 10^9 CFU/g for 4 weeks ad libitum. Probiotics exhibited risk-reducing properties (depressive-related behavior).

Each rat in the probiotic groups received a daily dose of 10^9 CFU for 14 days. B. longum mitigated the depressive-like symptoms. B. longum reduced the Caspase-3 activity and plasma C-reactive protein concentrations in the lateral and medial amygdala.

Probiotics treatment alleviated anxiety behaviors, depressive-like behaviors and cognitive performance. Probiotics treatment improved neuronal activation in different brain regions, characterized by increased expression of Fos protein.

Ingestion of L. intestinalis and L. reuterii caused biochemical abnormalities in antibiotic-treated mice via the subdiaphragmatic vagus nerve.

The effects of chronic PS23 treatment are due to (1) increases in the hippocampal GR, MR, and BDNF proteins; (2) increases in serotonergic and dopaminergic activities in the hippocampus, prefrontal cortex, and striatum; and (3) improvement of the gut microbiota.
Xie R et al. 2020
C57BL/6 mice  CSDS-depression  Probiotics  Lactobacillus  L. reuteri 3  
Treating for 4 weeks with L. reuteri 3 (10^9 CFU/ml of per mouse in 0.1 ml phosphate-buffered saline (PBS)) after 10 days of CSDS  
Treatment with L. reuteri 3 ameliorated depressive-like behaviors  
Treatment with L. reuteri 3 regulated the gut microbiota, SCFAs, and serotonin metabolism

Xu J et al. 2022
C57BL/6 mice  CUMS-depression  Probiotics  Lactobacillus  L. rhamnosus zz-1  
Mice received L. rhamnosus zz-1 at a dose of 2 × 10^8 CFU/kg bw, 2 × 10^9 CFU/kg bw or 2 × 10^10 CFU/kg bw for 6 weeks. The volume of the daily gavage liquid was adjusted to 0.1 mL  
L. rhamnosus zz-1 intervention ameliorated CUMS-induced depression-like behaviors  
L. rhamnosus zz-1 improved stress-induced physiological problems in model mice, including HPA axis hyperactivity, neurotransmitter deficiency, and impairments in the BDNF-TrkB signaling, and regulated gut microbiota

Xu M et al. 2022
C57BL6J mice  CUS-depression  Probiotics  Lactobacillus  L. paracasei 126L6, CCFM1229, 29R1L1L4L3, L. helveticus 132M1L8G3, Q7M66, 10M6L, L. rhamnosus CCFM131, CCFM1330, CCFM1228, L. reuteri CCFM1132, 11M59  
The freeze-dried bacterial powder was suspended in sterile skimmed milk. The concentration of surviving bacteria was 5 × 10^9 CFU/mL. The gavage volume of each mouse is 200 µL for 6 weeks  
L. paracasei CCFM1229 and L. rhamnosus CCFM1228 significantly reduced anxiety- and depression-related behaviors  
The strains CCFM1229 and CCFM1228 regulated the gut microbiota and xanthine oxidase activity in the brain

Yang Y et al. 2022
Sprague-Dawley rats  MS-postpartum depression  Probiotics  Lactobacillus  L. casei  
From postnatal day 2 to day 28, rats were gavage-fed with Lactobacillus casei (8 × 10^8 CFU/kg/day)  
Administration of L. casei improved depressive-like behaviors  
Administration of L. casei altered gut microbiota composition, brain monoamines and oxidative stress, which may be associated with the regulation of the BDNF-ERK1/2 pathway

Yun SW et al. 2020
C57BL/6J mice  EC-depression  Probiotics  Lactobacillus  L. gasseri NK109  
NK109 at a dosage of 1 × 10^9 CFU/mouse/day was orally gavaged once a day for 5 days in the mice with Escherichia coli K1 (1 × 10^9 CFU/mouse/day)-induced depression  
NK109 significantly alleviated Escherichia coli K1-induced cognitive impairment- and depression-like behaviors  
NK109 regulated the immune response through NF-κB-involved BDNF expression, IL-1β expression, and vagus nerve-mediated gut-brain signaling, and mitigated Escherichia coli-induced colitis and gut dysbiosis

Yun SW et al. 2021
C57BL/6J mice  EC-depression  Probiotics  Lactobacillus  L. paracasei NK112  
Receiving NK112 (1 × 10^9 CFU/mouse/day) daily for 5 days  
Oral gavage of NK112 significantly alleviated K1-induced anxious, depressive, and memory-impaired behaviors  
NK112 treatment suppressed IL-6, TNF-α, and BDNF expression through the regulation of gut microbiota and NF-κB activation

Yunes RA et al. 2020
BALB/c mice  Healthy status  Probiotics  Lactobacillus, Bifidobacterium  L. plantarum 90k, B. adolescentis 150  
One dose (0.5 mL) of the mixture of strains contained 10^9 CFU L. plantarum 90k and 10^6 CFU B. adolescentis 150 for 14 days  
Administration of the probiotic composition decreased the duration of immobility of mice  
-

Zhao Y et al. 2020
Sprague-Dawley rats  Corticosterone-depression  Probiotics  Lactobacillus  Lactobacillus plantarum DP189  
Administration of DP189 (1.0 × 10^8 CFU/d) suspension by gavage for 21 days  
L. plantarum DP189 treatment prevented and/or alleviated depression-like behaviors  
L. plantarum DP189 treatment increased neurotransmitters in brain tissue, reduced serum levels of inflammatory factors, and regulated hippocampal neural apoptosis

Baroakas A et al. 2017
C57BL6J mice  Prebiotics-anti-depression  CSDS-depression  Probiotics  Prebiotics  
Fructo-oligosaccharides (FOS), Galacto-oligosaccharides (GOS)  
Administering the prebiotics FOS, GOS, a combination of FOS and GOS (dissolved in drinking water for 0.3–0.4 g/mouse/day) for 3 weeks  
FOS-GOS administration significantly improved the depressive- and anxiety-like behaviors  
Prebiotic administration significantly decreased the hypothalamic-pituitary-adrenal axis (corticosterone levels), influenced hippocampal and hypothalamic gene expression,
improved the tryptophan and monoamines metabolism, and normalized the effects of stress on the microbiota.

Chen Y et al. 2021
C57BL/6 mice
CUMS-depression
Prebiotics
Partially hydrolyzed guar gum (PHGG)
After 28 days of CUMS, mice received 600 mg/kg PHGG
PHGG significantly inhibited the loss of body weight, and prevented CUMS-induced depressive-like behavior in mice

PHGG modulated the gut microbiota structure and then increased the levels of short-chain fatty acids in mice feces and the levels of 5-hydroxytryptamine and dopamine in serum, striatum, and hippocampus.

Cheng D et al. 2018
Sprague-Dawley rats
Hydrocortisone-depression
Prebiotics
Tiansi Liquid
The dose of Tiansi Liquid was 0.45 g/kg once a day for 21 days
Tiansi Liquid ameliorated depressive symptoms in rats

Tiansi Liquid modulated the gut microbiota composition and metabolites in the tryptophan-kynurenine pathway.

Chi L et al. 2020
Sprague-Dawley rats
CUMS-depression
Prebiotics
Fructo-oligosaccharides (FOS)
Administration with FOS (50 mg/kg) via oral gavage for 3 weeks from the fifth week onward
FOS administration alleviated depressive-like behaviors

FOS administration regulated intestinal epithelia damages, decreased the hypothalamic-pituitary-adrenal axis (corticosterone levels), and modified the gut microbiota.

Davis DJ et al. 2019
C57BL/6J mice
Social isolation-depression
Prebiotics
N-3 polyunsaturated fatty acid docosahexaenoic acid (DHA)
The mice were then treated with either 0.1% by weight or 1.0% by weight DHA
A DHA diet, regardless of dose, exhibited reduced anxiety and depressive-like behaviors only in male mice

DHA altered the commensal community composition.

Donoso F et al. 2020
Sprague-Dawley rats
MS-depression
Prebiotics
Polyphenols: phlorotannins, xanthohumol, quercetin
Dietary intervention of polyphenols (Phlorotannins 0.03%; Xanthohumol 0.015%; Quercetin 0.03%), delivered ad libitum in food, began once the animals were eight weeks old and continued for eight weeks.
Polyphenols reversed MS-induced depressive- and anxiety-like behaviours

Polyphenols treatment prevented exacerbated production of corticosterone after acute stress in MS animals, reversed MS-induced plasma BDNF depletion and changes in diversity.

Egerton S et al. 2020
Sprague-Dawley rats
MS-depression
Prebiotics
Fish oil (containing polyunsaturated fatty acid)
Fish oil (composition fatty acid profile and vitamins & minerals) was added to the diets in the place of soybean oil in the standard chow. At 7% of total feed from 9 to 16 weeks of age
Fish oil dietary supplementation partly prevented the depressive-like behaviours

Fish oil dietary supplementation altered brain fatty acids, significantly decreased plasma corticosterone levels and reduced brain stem serotonin turnover, and regulated the gut microbial composition.

Fan L et al. 2021
Sprague-Dawley rats
CUMS-depression
Prebiotics
Cistanche tubulosa extract total glycosides, Cistanche tubulosa aqueous extract, phenylethanoid and iridoid glycosides
Recieving different dose of extracts for 4 weeks
Cistanche tubulosa extracts prevented the depressive-like behaviours

Cistanche tubulosa extracts regulated the hyperactivation of the HPA axis, severe peripheral and neural inflammation, and deficiencies in 5-HT and BDNF in the hippocampus.

Gao X et al. 2020
Sprague-Dawley rats
CUMS-depression
Prebiotics
Triterpenoids extracts from Poria cocos (TPC)
Recieving TPC at 15 g herb/kg 30 min before stressing exposure lasting 28 days
TPC significantly ameliorated depression-like behaviors in CUMS rats

TPC treatment restored the level of the neurotrophic factor system and regulated the gut microbiota composition, and regulated metabolic system, including primary bile acid biosynthesis, tauirine and hypoxauetin metabolism, arginine and proline metabolism.

Gong MJ et al. 2016
Sprague-Dawley rats
Corticosterone-depression
Prebiotics
Icarin
The treatment group was treated with icariin (60 mg/kg, suspended in saline) by gastric instillation 1 h prior to CORT injection once a day for 21 days
Icarin produced an antidepressant-like effect in CORT-induced depressive rats

Icarin increased the BDNF expression in the hippocampus, regulated the energy metabolism, lipid metabolism, amino acid metabolism and gut microbes metabolism.
Guo Y et al. 2018[110] ICR mice CRS-depression Prebiotics Rosemary extracts Recieving rosemary extracts (100 mg/kg) for 21 days during CRS stress Pretreatment with rosemary extracts prevented the depressive- and anxiety-like behaviors Rosemary extracts improved antiinflammatory effects in hippocampus, serum and BV-2 microglia as well as rebalanced the gut microbiota

Hao WZ et al. 2021[111] C57BL/6 mice CUMS-depression Prebiotics Coniferyl ferment The mice received coniferyl ferment at a dose of 50 mg/kg once daily via gavage for 4 weeks Oral administration of coniferyl ferment attenuated weight loss and depression-like and anxiety-like behaviors induced by CUMS in mice Coniferyl ferment administration significantly ameliorated colonic inflammation, lowered the levels of IL-6, IL-1β, and TNF-α, and restricted the gut microbiome, and microbial metabolism

Huang YJ et al. 2021[112] C57BL/6J mice sCSDS-depression Prebiotics Water extract of Gastrodia elata (WGE) WGE was administered at an optimal dose of 500 mg/kg bw via gavage once a day for 30 successive days Oral treatment with WGE resulted in reversal of depression-like behavior WGE exerts antidepressant-like effects mediated by the serotonergic and KYN pathways in the prefrontal cortex and colon, and altered the gut microbiota composition

Liu WD et al. 2022[113] Wistar rats SD-depression Prebiotics Fish oil Feeding with a fish oil-rich diet for 10 weeks A fish oil-based diet reduced anxiety- and depressive-like behaviors, and improved cognitive function under chronic SD. A fish oil-based diet increased the probiotics production, increased the SCFA content, improved the intestinal barrier, increased SCFA receptor expression, and decreased blood circulation proinflammatory status

Lax NC et al. 2018[114] C57Bl/6J mice Prebiotics Cyanobacterial extract DUQ0002I For all injections, fraction DUQ0002I and subfractions DUQ0002I-1A-C, DUQ0002I-2-4 were administered at a dose of 40 μg per cannula DUQ0002I induced robust antidepressant and anxiolytic-effects This extract blocked the 5-HT7R

Lee HC et al. 2020[115] BALB/c mice Lard diet-depression Prebiotics Fish oil (containing polyunsaturated fatty acid)-based diet Treatment with fish oil concentrated with 50% EPA and 20% DHA triacylglycerol form for 12 weeks Treatment with fish oil prevented depressive-like behavior Treatment with fish oil regulated gut microbiota composition, and the prefrontal cortex fatty acid profile

Li Y et al. 2018[116] Sprague-Dawley rats CUS-depression Prebiotics Cistanche tubulosa extract (CTE) CTE at high dose (CTEH) (400 mg/kg) and low dose (CTEL) (200 mg/kg) were intragastrically administered 1 h before the CUS procedure (8:00 a.m. to 9:00 a.m.) over the course of 4 weeks CTE significantly improved depression-like behaviors in rats under CUS CTE restored the level of neurotransmitters and neurotrophic factors in CUS rats, regulated the gut microbial composition, and modulated SCFAs concentrations

Lin S et al. 2021[117] ICR mice CRS-depression Prebiotics Crocetin Crocetin at a dose of 40 mg/kg, crocetin-H (80 mg/kg) for 28 days Crocetin ameliorated CRS-induced depression-like behaviors in mice Crocetin regulated MKP-1/ERK1/2/CREB pathway and gut microbiota

Liu Z et al. 2020[118] C57BL/6J mice HD postpartum depression Prebiotics Insulin Taking standard diet with 37 g insulin/1000 kcal for 8–10 weeks Insulin intake significantly attenuated cognitive deficits and depressive-like behaviors Insulin intake upregulated the monoamine neurotransmitters (5-hydroxytryptamine and norepinephrine) and suppressed neuroinflammation

Mika A et al. 2017[119] F344 rats LH-depression Prebiotics Galactooligosaccharide (GOS), polydextrose (PDX) Rats began diets on postnatal day 24 (PND 24) with GOS and PDX (7.0 g/kg each) for 4 weeks Prebiotics differentially attenuated stress-induced learned helplessness Prebiotics diets reduced stress-evoked cfos mRNA in the dorsal raphe nucleus (DRN), attenuated stress-evoked decreases in mRNA for the 5-HT1A autoreceptor in the DRN, GOS and PDX diet increased basal BDNF mRNA within the prefrontal cortex
| Reference | Design | Treatment | Intervention | Outcome |
|-----------|--------|-----------|--------------|---------|
| O'Mahony SM et al. 2020 [120] | Sprague-Dawley rats | MS-depression | Prebiotics | Test diets differed from control diet by the inclusion of (a) GOS 20.86 g/kg and PDOX 6.44 g/kg (Prebiotic) | Dietary interventions altered stress-induced spatial learning and memory |
| Pusceddu MM et al. 2015 [121] | Sprague-Dawley rats | MS | Prebiotics | Oral administration of an eicosapentaenoic acid (EPA)/docosahexaenoic acid (DHA) (80% EPA, 20% DHA) (0.4 g/kg/day or 1 g/kg/day) n-3 PUFAs mixture was administered by gavage when animals reached 5 weeks of age | No data |
| Qi Y et al. 2020 [122] | C57BL/6 mice | CSDS-depression | Prebiotics | Betaine was given to mice for 24 days from day 1 to day 24 | Betaine supplementation contributed to resilience to anhedonia in mice subjected to CSDS |
| Robertson RC et al. 2015 [123] | C57BL/6J mice | n-3 PUFA deficiency-depression | Prebiotics | Fed with n-3 PUFA supplemented diet (1 g Eicosapentaenoic acid (EPA) + Docosahexaenoic acid (DHA)/100 g diet) or n-3 PUFA deficient diet from gestational day 0 | N-3 PUFA supplementation prevented depressive-like behaviors and memory defect |
| Song J et al. 2019 [124] | Wistar rats | ACTH-depression | Prebiotics | CGA pretreatment (500 mg/kg) by intragastric administration 1 h prior to ACTH injection once a day for 14 days | CGA pretreatment ameliorated depressive-like behavior |
| Song X et al. 2021 [125] | ICR mice | CUMS-depression | Prebiotics | Puerarin (100 mg/kg) treatment was found to alleviate the CUMS-induced depression-like behaviors | Puerarin treatment reversed the gut microbial changes induced by CUMS |
| Sun Y et al. 2020 [126] | C57BL/6 mice | LPS-depression | Prebiotics | Mice were treated with schisandrin (30 mg/kg, i.p.) for 14 days | Schisandrin pre-treatment attenuated LPS-induced depressive-like behaviors in mice |
| Tian P et al. 2021 [127] | mice | CRS-depression | Prebiotics | SCFA-Acylated Starches Feeding with 15% acylated starch for 2 weeks during chronic restraint stress | Consumption of SCFA-acylated starches alleviated the depressive symptoms of stressed mice |
| Tung TH et al. 2019 [128] | Sprague-Dawley rats | CMS-depression | Prebiotics | Male rats were fed fish oil-rich (contained 20.5% (w/w) EPA and 11.2% DHA) or olive oil-rich diets for 14 weeks | Fish oil intervention reversed the stress-induced abnormal depressive-like behavior |
| Valdés-Sustaita B et al. 2021 [129] | Wistar rats | Ovariectomized-depression | Prebiotics | Aqueous extract of pomegranate (AE-PG) was dissolved in saline solution 0.9% and given by intraperitoneal route | SCFA-Acylated Starches significantly reduced the colonic permeability via increasing the tight junction proteins (including ZO-1, Claudin, and Occludin) gene expression and reduced the level of the inflammatory cytokines, and modified gut microbiome |

**Legend:**
- MS: Menopause Syndrome
- CUMS: Chronic restraint stress
- ACTH: Adrenocorticotropic hormone
- CR: Corticosterone
- CSDS: Constrained swimming stress
- CMS: Chronic metabolic stress
- MS: Menopause Syndrome
- LPS: Lipopolysaccharide
- CGA: Chlorogenic acid
- SCFA: Short-chain fatty acids
- EPA: Eicosapentaenoic acid
- DHA: Docosahexaenoic acid
- AE-PG: Aqueous extract of pomegranate
- ERβ: Estrogen receptor β
| Authors                   | Species          | Treatment                       | Outcome                                                                 |
|--------------------------|------------------|---------------------------------|-------------------------------------------------------------------------|
| Wang L et al. 2020        | Kumming mice     | CUMS-depression                 | Treated with lowdose, medium-dose, or high-dose TIV (5.7, 11.4, and 22.9 mg/kg/d, respectively) at a volume of 10 mL/kg by the intragastric route once per day for 2 successive weeks Administration of TIV increased body weight, sucrose solution consumption, and ameliorated depression-like behaviors It is concluded that the antidepressant effects of TIV may be related to gut flora structures and regulation of 5-HT, NE, SP, and CRF in the brain and intestine |
| Wang L et al. 2021        | Sprague-Dawley rats | CUMS-depression                 | Soy isoflavones The SI low dose, SI middle dose, and SI high dose groups were given SI at a dose of 40 mg/kg, 80 mg/kg, and 160 mg/kg per rat per day by oral gavage for 8 weeks Soy isoflavones supplements significantly improved the CUMS-induced depression-like behaviour Soy isoflavones supplements increased monoamine neurotransmitters of CUMS rats by reshaping the structure of the gut microbiota |
| Wang P et al. 2020        | C57BL/6J mice   | Alcohol-depression              | Polypols group was given 120 mg/kg of polypols by gavage daily for 10 weeks Propolis exerted an improving effect on alcohol-induced depressive symptoms Propolis dietary supplementation prevented the intestinal mucosal barrier and hippocampal injury, and further improved brain gut dysfunction |
| Wang Q et al. 2019        | CD-1 mice       | CMS-depression                  | Orally administrated with sesamin (50 mg/kg/day, dissolved in olive oil) for 10 weeks Oral sesamin administration (50 mg/kg bodyweight/day) significantly attenuated depressive, aversive, repetitive, and anxiety-like behaviors Sesamin inhibited stress-induced gut barrier integrity damage, reduced circulating lipopolysaccharide levels, suppressed neuroinflammatory responses, and restructured the gut microbiome |
| Wang R et al. 2021        | C57BL/6J mice   | CRS-depression                  | TFA treatment improved the depressive-like phenotype TFA treatment improved the disturbed gut microbiota, and the intestinal barrier function |
| Xia J et al. 2017         | C57BL/6J mice   | LPS-depression                  | Dietary capsaicin improved depressive-like behaviour Dietary CAP regulated the structure of gut microbiota, increased the levels of the monoamine neurotransmitter 5-HT, and reduced the levels of inflammatory cytokine TNF-a in LPS-induced mice |
| Xiao Q et al. 2020        | C57BL/6 mice    | CRS-depression                  | Administration of crocin-1 mitigated depression-like behaviors Oral administration of crocin-1 improved the structure of gut microbiota to restore SCFAs levels and intestinal barrier function, thereby decreasing the neuroinflammation and increasing BDNF protein to effectively alleviated depression-like behavior in depressed mice |
| Xue M et al. 2021         | C57BL/6J mice   | Alcohol-depression              | Receiving 500 mg/kg body weight of fucoidan at 12.00 a.m. during the 10 weeks' experiment Oral administration of fucoidan alleviated alcohol withdrawal-induced depression-like behaviors of mice Oral administration of fucoidan regulated the gut flora of mice and reduce endotoxemia, down-regulated the TLR4/MyD88/NF-κB p65 pathway, inhibited alcohol-induced microglia cell activation and inflammation |
| Yan T et al. 2020         | C57BL/6 mice    | CUMS-depression                 | Mice were treated with polysaccharide (400 mg/kg, i.g.) for 14 days Polysaccharide treatment alleviated depression-like behaviors in CUMS-induced mice Polysaccharide treatment inhibited the inactivation of inflammatory reactions in the colon, serum, hippocampus as well as BV2 cells, down-regulated the TLR4/NF-κB |
| Authors          | Year | Treatment Type | Prebiotics | Intestinal Flora or Microbiota | LPS-induced Depression | MAPKs Signaling | Intestinal Flora | Microbiota | Summary |
|------------------|------|----------------|------------|--------------------------------|------------------------|----------------|------------------|------------|---------|
| Yan T et al. 2021 |      | C57BL/6 mice   | Prebiotics | —                              | Mice were treated with fractions (SCE, lignans (SCL), polysaccharides (SCPS), and essential oil (SCVO)) | Fractions treatment alleviated depressive-like behaviors in LPS-induced mice | —               | —         | Fractions treatment regulated the neuroinflammation via the TLR4/NFκB/IKKα signaling pathway, and recovered the gut microbiota |
| Yu JB et al. 2019 |      | Sprague-Dawley rats | Prebiotics | —                              | Mice were treated with paenolfin at a dose of 10 mg/kg or 20 mg/kg for 8 weeks | Paenolfin treatment alleviated depressive-like behaviors in CUS-induced mice | —               | —         | Paenolfin regulated the composition of the gut microbiota by increasing the abundance of probiotics. And benzoic acid, the gut characteristic metabolite of paenolfin, was absorbed into blood and penetrated the BBB and entered the central nervous system relieving depressive behaviors |
| Zhang L et al. 2021 |      | Kuming mice    | Prebiotics | —                              | Treated with low-dose, medium-dose, or high-dose TTV (5.7, 11.4, and 22.9 mg/kg/d, respectively) at a volume of 10 mL/kg by the intragastric route once per day for 2 successive weeks | Administration of TIV increased body weight, sucrose solution consumption, and ameliorated depression-like behaviors | —               | —         | TIV may modulate the intestinal flora, thereby inducing the expression of ZO-1 and occludin, protecting the blood–brain barrier |
| Zhang M et al. 2021 |      | ICR mice       | Prebiotics | —                              | Total iridoids of Valeriana jatamansi (TIV) | Sophora alopecuroides L.-derived alkaloids improved depression-like behaviors in CUS-induced mice | —               | —         | Alkaloids improved depression in mice through modulating gut microbiota |
| Zhang Z et al. 2022 |      | C57BL/6 mice   | Prebiotics | —                              | Hyperforin is dissolved in DMSO and the dosage of hyperforin is 0.38mg/kg. Mice in hyperforin treated group were intraperitoneally injected with hyperforin solution before daily restraint | Hyperforin prevented anhedonia induced by CRS in mice | —               | —         | Hyperforin prevented altered the richness and evenness of bacteria populations |
| Zhao B et al. 2020 |      | C57BL/6 mice   | Prebiotics | —                              | Treating with distilled water and lycopene (50 mg/kg body weight/day) mixed in standard diet (AIN-93M) for 35 days | Lycopene improved depression and anxiety-like behavioral disorders | —               | —         | Lycopene suppressed neuroinflammation and prevented synaptic ultrastructure damages by upregulating the expressions of neurotrophic factor and postsynaptic-density protein, and reshaped the gut microbiome and improved the gut barrier integrity |
| Zhao F et al. 2021 |      | Sprague-Dawley rats | Prebiotics | —                              | Gavaging with LBP at 14:00 daily, the concentration of gavage is 40 mg/kg, for 14 days | LBP treatment improved the body weight, changed the emotional function | —               | —         | LBP treatment reduced offspring’s plasma corticosterone level and increased the diversity of gut microbiota |
| Study Authors                  | Animal Model | Treatment Conditions                          | Targeted Microbiota | Treatment Outcome                                                                 | Notes                                                                 |
|-------------------------------|--------------|-----------------------------------------------|---------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------|
| Zhao ZX et al. 2018[146]       | Sprague-Dawley rats | CUS-depression Prebiotics | Albiflorin          | Treating with benzoic acid (14 mg/kg)albiflorin metabolites) albiflorin (14 mg/kg)for 2 weeks | Benzoic acid, a therapeutic mediator of albiflorin generated by the gut microbiota, after crossing the blood-brain barrier, entered the central nervous system to exert antidepressant effects |
| Li H et al. 2019[147]          | Wistar rats   | CUMS-depression Probiotics, prebiotics | Bifidobacterium, Lactobacillus | Orally gavaged with with FOS and GOS (8%, 1 mL per 100g weight; FOS/GOS) or with B. longum (1 × 10^9 CFU per 100 g weight) or with L. rhamnosus (1 × 10^10 CFU per 100 g weight) during the CUMS molding for 4 weeks | Prebiotics (FOS/GOS) and probiotics (B. longum and L. rhamnosus) alleviated CUMS-induced depressive-like behaviors |
| Gilbert et al. 2012[148]       | Sprague-Dawley rats | Post-myocardial infarction depression Prebiotics, probiotics | Lactobacillus, Bifidobacterium | Each rat in the probiotics group received a daily dose of 10^5 CFU for 2 weeks | Depressive-like behaviour was attenuated with the high-PUFA n-3 diet or/and probiotics |
| Zhu X et al. 2017[149]         | Sprague-Dawley rats | CUS-depression Probiotics, prebiotics | Bifidobacterium, Berberine | Prior to modeling with each chronic unpredictable stress method, the rats were treated with either 2 mL of a low concentration of berberine (40 mg/kg/day), a high concentration of berberine (200 mg/kg/day), bifidobacterium (140 mg/kg/day) | Berberine and bifidobacterium treatment alleviated depressive behaviors caused by CUS |
| Westfall S et al. 2021[150]    | C57BL/6J mice | CUMS-depression Probiotics, prebiotics, and synbiotics | L. plantarum ATCC 793, B. longum ATCC 15707, Bioactive Dietary Polyphenol Preparation (BDPP) | The bacteria were incorporated into the animals’ drinking water at a final dosage of 1.0×10^9 CFU/day per bacterium; BDPP was comprised of 1% w/v grapeseed polyphenol extract, 1% w/v resveratrol and a 5% w/v concord grape extract made in sterile water during the experiment | The probiotic and synbiotic attenuated depressive-like behavior following CUS, while the synbiotic rescued the phenotype following CUS and CUS+US; only BDPP and the synbiotic improved anxiety-like behavior |
| Westfall S et al. 2021b[151]    | C57BL/6J mice | CUS-depression Probiotics, prebiotics, and synbiotics | L. plantarum ATCC 793, B. longum ATCC 15707, Bioactive Dietary Polyphenol Preparation (BDPP) | The bacteria were incorporated into the animals’ drinking water at a final dosage of 1.0×10^9 CFU/day per bacterium; BDPP was comprised of 1% w/v grapeseed polyphenol extract, 1% w/v resveratrol and a 5% w/v concord grape extract made in sterile water during the experiment | The probiotic and synbiotic attenuated stress-induced depressive- and anxiety-like behaviors |
| Mesripour A et al. 2021[152]    | Albino mice  | Dexamethasone or water avoidance stress induced depression Probiotics | Lactobacillus, Bifidobacterium, Streptococcus | Syn cocktail containing L. casei, L. acidophilus, L. rhamnosus, L. bulgaricus, B. breve, B. infantis, S.  | Symbiotic mixture prevented the effects of WAS, acute or sub-acute Dex-induced depression in mice |
| Study                                                                 | Model     | Depression          | Intervention                                                                                     | Outcome                                                                                                                                   |
|----------------------------------------------------------------------|-----------|---------------------|------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| Leo A et al. 2021[153]                                                | C57Bl/6J  | CUMS-depression     | Prebiotics, Postbiotics, α-lactalbumin (ALAC), Sodium butyrate (NaB), ALAC (125, 250 and 500 mg/kg), NaB (30, 100, 300 mg/kg) and the co-administration of ALAC (125, 250 and 500 mg/kg) with a fixed NaB dose (100 mg/kg) were administered in drinking water for 15 days | ALAC, NaB and their combination reduced depressive- and anxiety-like behaviour in CUMS mice                                              |
| Cheng R et al. 2021[156]                                              | C57BL/6J  | CUMS-depression     | Posbiotics, Akkermansia, Outer membrane protein Amuc_1100 of A. muciniphila, Mice were gavaged daily with 80 mg of Amuc_1100 in sterile PBS with a volume of 200 ml | Amuc_1100 intervention ameliorated CUMS-induced depression-like behavior, Amuc_1100 intervention improved the gut microbiota, up-regulated the BDNF level, and inhibited the neuroinflammatory response |
| Kochanowska AJ et al. 2008[155]                                       | Swiss Webster mice | Healthy status       | Posbiotics, Secondary metabolites from sponges (brominated compounds, sesquiterpene quinones, hydroquinones) | Each group was injected ip with the compound at a dose of 1–20 mg/kg, 5,6-Dibromo-N,N-dimethyltryptamin possessed significant antidepressant-like activity |
| Li J et al. 2018[154]                                                | Sprague-Dawley rats | CUMS-depression     | Sodium propionate (NaP, the salt form of propionic acid), 1 mL of NaP (200 mmol/L) was administrated intrarectally every day for 1 week from the beginning of the 5th week | Administration of NaP induced antidepressant-like effects, Administration of NaP rebalanced the plasma metabolome, and rescued the neurotransmitters in the prefrontal cortex, which may be achieved through the reduction of catabolism of noradrenaline, tryptophan and dopamine, rather than serotonin |
| Matsuda Y et al. 2020[157]                                            | Sprague-Dawley rats | CSDS-depression     | Posbiotics, Ergothioneine, a metabolite of Lactobacillus reuteri, Oral administration of L-ergothioneine (0.25 mg/ml) aqueous solution was conducted from 1 week prior to SDS initiation (day −7) to the end SDS application (day 14) | Oral administration of ergothioneine prior to and during the SDS paradigm had a preventative effect on SDS-induced depressive behaviors |
| Yu M et al. 2021[158]                                               | Wistar rats | CVS-depression       | Antibiotics, Streptomycin, Penicillin G, Giving drinking water ad libitum containing streptomycin sulfate (2 mg/mL) and penicillin G (1500 U/mL) for 21 days | Antibiotic treatment reversed the depression-like behaviors, Antibiotic treatment regulated the purine metabolism and fatty acid metabolism that are impacted by gut bacteria |
| Suzuki K et al. 2021[159]                                            | C57BL/6J (B6) mice | CSDS-depression     | Antibacterial active peptides, Recombinant Cryptdin-4 (mouse α-defensin) were dissolved in ultrapure water and administered orally at 250 μg/mouse once daily from day 1 to day 32 | No data, Administration of α-defensin recovered dysbiosis and significant microbial composition changes in the intestinal metabolites |
| Martin-Hernandez D et al. 2016[160]                                 | Wistar rats | CMS-depression      | Antibiotics, Streptomycin, Penicillin G, Giving drinking water ad libitum containing streptomycin sulfate (2 mg/mL) and penicillin G (1500 U/mL) for 21 days | Antibiotics treatment reversed the CMS-induced a depressive-like phenotype, Antibiotics treatment inhibited bacteria translocation that only a role in the pathophysiology of depression through the p38 MAPK pathway which could aggravate the neuroinflammation and the oxidative/nitrosative damage |
Meng C et al. 2022
Sprague-Dawley rats CUMS-depression Antibiotics Metronidazole, ciprofloxacin Treating with metronidazole (1 g/L) and ciprofloxacin (0.2 g/L) in drinking water for 5 weeks Antibiotics exposure reduced anxiety-like and depression-like behavior of rats

Schmidliner AK et al. 2019
NAB/HAB rats HAB-depression Antibiotics Minocycline In the first set of experiments, 40 mg/kg/day minocycline, while in the second set, 80 mg/kg/day minocycline alone, all dissolved in tap water, was applied for 22 days Three weeks of minocycline treatment alleviated the depressive-like phenotype

Wang S et al. 2020
C57BL/6 mice CSDS-depression Antibiotics Ampicillin, Neomycin sulfate, Metronidazole Broad-spectrum antibiotics (ampicillin 1 g/L, neomycin sulfate 1 g/L, and metronidazole 1 g/L) dissolved in drinking water were provided ad libitum to male C57BL/6 mice for 14 consecutive days CSDS did not produce an anhedonia-like phenotype in the antibiotic-treated mice

Wong ML et al. 2016
C57BL/6J mice CRS-depression Antibiotics Minocycline Treating with minocycline (LKT Laboratories, St Paul, MN, USA; 5 mg/kg per day in 10 ml/kg saline, intraperitoneally) for 21 days Minocycline treatment decreased depressive- and anxiety-like behaviors

Yang Q et al. 2020
C57BL/6 mice CUMS-depression Antibiotics Minocycline Minocycline (40 mg/kg, Cayman Chemical) was administered intraperitoneally daily for 4 weeks starting 2 weeks after CUMS Minocycline treatment for 4 weeks, not acute treatment, exerted antidepressant effect in mice exposed to CUMS

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Table S13. A summary of probiotics that alleviate depression symptoms.

| Probiotics                  | objects       | Probiotics                  | objects       |
|-----------------------------|---------------|-----------------------------|---------------|
| Akkermansia muciniphila     | Animal models | Lactobacillus diacetylactis | Animal models |
| Akkermansia muciniphila ATCC® BAA-835™ | Animal models | Lactobacillus fermentum    | Human beings, Animal models |
| Bacillus coagulans MTCC 5856 | Human beings | Lactobacillus gasseri NK109 | Animal models |
| Bacillus coagulans Unique IS2 | Human beings | Lactobacillus helveticus   | Animal models |
| Bacillus sp.DU-106          | Animal models | Lactobacillus helveticus 132M1 | Animal models |
| Bacillus subtilis           | Animal models | Lactobacillus helveticus LA 102 | Animal models |
| Bifidobacteria              | Animal models | Lactobacillus helveticus LH0138 | Animal models |
| Bifidobacterium             | Human beings, Animal models | Lactobacillus helveticus MCC1848 | Animal models |
| Bifidobacterium spp.        | Human beings  | Lactobacillus helveticus NS8  | Animal models |
| Bifidobacterium_adolescentis| Human beings, Animal models | Lactobacillus helveticus PXN® 45 | Human beings |
| Bifidobacterium_adolescentis 150 | Animal models | Lactobacillus helveticus R0052 | Human beings, Animal models |
| Bifidobacterium_adolescentis NK98 | Human beings, Animal models | Lactobacillus helveticus W74  | Animal models |
| Bifidobacterium_animalis BL0005 | Animal models | Lactobacillus intestinalis YT2 | Animal models |
| Bifidobacterium_animalis ssp.lactis 420 | Animal models | Lactobacillus intestinalis YT2 | Animal models |
| Bifidobacterium bifidum     | Human beings, Animal models | Lactobacillus johnsonii  | Animal models |
| Bifidobacterium bifidum BIA-6 | Human beings  | Lactobacillus kefiranofaciens ZW3  | Animal models |
| Bifidobacterium bifidum plus inulin | Human beings  | Lactobacillus lactis      | Human beings, Animal models |
| Bifidobacterium bifidum PXN® 23 | Human beings | Lactobacillus lactis ssp. lactis PXN® 63 | Human beings |
| Bifidobacterium bifidum W23  | Human beings, Animal models | Lactobacillus mucosae NK41 | Animal models |
| Bifidobacterium breve       | Animal models | Lactobacillus murinus      | Animal models |
| Bifidobacterium breve 1205  | Animal models | Lactobacillus paracasei 126L6 | Animal models |
| Bifidobacterium breve A-1   | (synonym Bifidobacterium breve MCC1274) | Human beings | Lactobacillus paracasei DFA 81 | Animal models |
| Bifidobacterium breve CCFM1025 | Human beings, Animal models | Lactobacillus paracasei HT6 | Animal models |
| Bifidobacterium breve FHLDJQ3M5 | Animal models | Lactobacillus paracasei Lpc-37 | Animal models |
| Bifidobacterium breve M-16V | Animal models | Lactobacillus paracasei NK112 | Animal models |
| Bifidobacterium breve M2CF22M7 | Animal models | Lactobacillus paracasei PS23 | Animal models |
| Bifidobacterium breve PXN® 25 | Human beings | Lactobacillus paracasei PS23 (PS23) | Animal models |
| Bifidobacterium breve UBBr01 | Animal models | Lactobacillus plantarum   | Animal models |
| Bifidobacterium breve W25   | Animal models | Lactobacillus plantarum 15953 (strain CGMCC15953) | Animal models |
| Bifidobacterium_functionis  | Animal models | Lactobacillus plantarum 286 (Lp 286) | Animal models |
| Bifidobacterium_functionis 35624 | Animal models | Lactobacillus plantarum 81 (Lp 81) | Animal models |
| Bifidobacterium_functionis PXN® 27 | Human beings | Lactobacillus plantarum 8PA3 | Animal models |
| Bifidobacterium_functionis UBB101 | Human beings | Lactobacillus plantarum 90sk | Animal models |
| Bifidobacterium_lactis      | Animal models | Lactobacillus plantarum ATCC 793 | Animal models |
| Bifidobacterium_lactis BAMA-B06/Bau-B0111 | Human beings | Lactobacillus plantarum DMDL 9010 (LP9010) | Animal models |
| Bifidobacterium_lactis BIA-7 | Human beings  | Lactobacillus plantarum LP12151 | Animal models |
| Bifidobacterium_lactis UBBLa70 | Human beings | Lactobacillus plantarum LP12407 | Animal models |
| Bifidobacterium_lactis WS1  | Animal models | Lactobacillus plantarum LP12418 | Animal models |
| Bifidobacterium_lactis WS2  | Human beings, Animal models | Lactobacillus plantarum LP3  | Animal models |
| Bifidobacterium_longum      | Animal models | Lactobacillus plantarum MTCC 9510 | Animal models |
| Bifidobacterium_longum NK46 | Animal models | Lactobacillus plantarum PS128 | Animal models |
| Bifidobacterium_longum R0175 | Human beings  | Lactobacillus plantarum PS128 (PS128) | Human beings |
| Bifidobacterium_longum 1714 | Animal models | Lactobacillus plantarum PXN® 47 | Human beings |
| Bifidobacterium_longum ATCC 15707 | Animal models | Lactobacillus plantarum R0102 | Animal models |
| Bifidobacterium_longum BG0014 | Animal models | Lactobacillus plantarum UBLP40 | Human beings |
| Bifidobacterium_longum BIA-8 | Human beings  | Lactobacillus plantarum WLPL04 | Animal models |
| Bifidobacterium_longum LA 101 | Animal models | Lactobacillus plantarum W/1 | Animal models |
| Bifidobacterium_longum NCC3001 | Human beings | Lactobacillus reuteri      | Human beings, Animal models |
| Bifidobacterium_longum PXN® 30 | Human beings | Lactobacillus reuteri (DSM 17938) | Human beings |
| Bifidobacterium_longum R0175 | Human beings, Animal models | Lactobacillus reuteri 3 | Animal models |
| Bifidobacterium_longum ssp.infantis B11471 | Animal models | Lactobacillus reuteri CCFM1132 | Animal models |
| Bifidobacterium_longum subsp. Infantis | Animal models | Lactobacillus reuteri NK33  | Human beings, Animal models |
| Bifidobacterium_longum subsp. Infantis E41 | Animal models | Lactobacillus rhamnosus | Human beings, Animal models |
| Bifidobacterium_longum subsp. Longum | Animal models | Lactobacillus rhamnosus (JB-1) | Animal models |
| Bifidobacterium_longum subsp. Longum BAMA-B05/BauB1024 | Human beings | Lactobacillus_rhamnosus B-8238 | Animal models |
| Bifidobacterium_longum subsp.infantis CCFM687 | Animal models | Lactobacillus_rhamnosus CCFM1131 | Animal models |
| Bifidobacterium_longum W108 | Animal models | Lactobacillus_rhamnosus CGMCC13724 | Human beings |
| Bifidobacterium_pseudocatenulatum CECT 7765 | Animal models | Lactobacillus_rhamnosus G | Human beings |
| Clostridium_butyricum MIYAIRI 588 (CBM588) | Human beings,Animal models | Lactobacillus_rhamnosus HN001 | Human beings |
| Clostridium_butyricum WZMC1018 | Animal models | Lactobacillus_rhamnosus JB-1 | Animal models |
| Enterococcus_faecalis 2001 (EF-2001) | Animal models | Lactobacillus_rhamnosus LR5 | Animal models |
| Enterococcus_faecalis strain EC-12 (EC-12) | Animal models | Lactobacillus_rhamnosus LX11881 | Animal models |
| Faecalibacterium prausnitzii (ATCC 27766) | Animal models | Lactobacillus_rhamnosus PXN® 54 | Human beings |
| Fermented Milk Containing Lactobacillus_paracasei Strain Shirota (LcS) | Human beings | Lactobacillus_rhamnosus R0011 | Animal models |
| Komagataella_pastoris KM71H | Animal models | Lactobacillus_rhamnosus UBLR58 | Human beings |
| Lactobacillus_plantarum DP189 | Animal models | Lactobacillus_rhamnosus W71 | Animal models |
| Lactobacillus_plantarum PS128TM | Human beings | Lactobacillus_rhamnosus zz-1 | Animal models |
| Lactobacillus_acidophilus | Human beings,Animal models | Lactobacillus_salivarius | Animal models |
| Lactobacillus_acidophilus LA11873 | Animal models | Lactobacillus_salivarius HA-118 | Animal models |
| Lactobacillus_acidophilus PXN® 35 | Human beings | Lactobacillus_salivarius Ls-33 | Animal models |
| Lactobacillus_acidophilus T16 | Human beings | Lactobacillus_salivarius PXN® 57 | Human beings |
| Lactobacillus_acidophilus W37 | Human beings,Animal models | Lactobacillus_salivarius W24 | Human beings,Animal models |
| Lactobacillus_brevis | Animal models | Lactococcus_lactis | Animal models |
| Lactobacillus_brevis DPC6108 | Animal models | Lactococcus_lactis LA 103 | Animal models |
| Lactobacillus_brevis DSM32386 | Animal models | Lactococcus_lactis strain WHH2078 | Animal models |
| Lactobacillus_brevis FPA 3709 | Animal models | Lactococcus_lactis subsp. cremoris LL95 | Animal models |
| Lactobacillus_brevis J1 | Animal models | Lactococcus_lactis W19 | Human beings,Animal models |
| Lactobacillus_brevis W63 | Human beings,Animal models | Lactococcus_lactis W58 | Human beings,Animal models |
| Lactobacillus_bulgarius | Animal models | Pediococcus_acidilactici | Animal models |
| Lactobacillus_casei | Human beings,Animal models | Prevotella_histicola DSM19854 | Animal models |
| Lactobacillus_casei DG | Animal models | Probiotic NVP-1704 | Human beings |
| Lactobacillus_casei PXN® 37 | Human beings | Rhizopus_chinenis 12 | Animal models |
| Lactobacillus_casei strain Shirota (LcS) | Human beings | Streptococcus_cerevisiae S-04 | Animal models |
| Lactobacillus_casei W56 | Human beings,Animal models | Streptococcus_cerevisiae var boulardii 17 | Animal models |
| Lactobacillus_cremoris | Animal models | Streptococcus_thermophilus | Human beings,Animal models |
| Lactobacillus_delbrueckii | Animal models | Streptococcus_thermophilus LA 104 | Animal models |
| Lactobacillus_delbrueckii ssp. bulgaricus PXN® 39 | Human beings | Streptococcus_thermophilus PXN® 66 | Human beings |
| Lactobacillus_delbrueckii subsp. Bulgaricus | Human beings,Animal models | Weissella_parasenteroides WpK4 | Animal models |
| Search strategy for PubMed | Hits          |
|----------------------------|--------------|
| #1 (depress*[Title/Abstract] OR dysthymi*[Title/Abstract] OR mood disorder*[Title/Abstract] OR affective disorder*[Title/Abstract] OR antidepress*[Title/Abstract]) | 556,593      |
| #2 (microb*[Title/Abstract] OR bacteria*[Title/Abstract] OR metaproteom*[Title/Abstract] OR metagenom*[Title/Abstract] OR "16S rRNA*[Title/Abstract] OR flora[Title/Abstract]) | 1,075,172    |
| #3 #1 AND #2 | 5,634        |

| Search strategy for Web of Science |          |
|-----------------------------------|----------|
| #1 TS=(depress* OR dysthymi* OR mood disorder* OR affective disorder* OR antidepress*) | 502,875  |
| #2 Topic=(microb* OR bacteria* OR metaproteom* OR metagenom* OR "16S rRNA* OR flora) | 1,209,922|
| #3 #1 AND #2 | 6,594     |

| Search strategy for Cochrane Library |          |
|-------------------------------------|----------|
| #1 (depress*):ti OR (dysthymi*):ti OR (mood disorder*):ti OR (affective disorder*):ti OR antidepress*:ti | 36,107   |
| #2 (microb*):ti,ab,kw OR (bacteria*):ti,ab,kw OR (metaproteom*):ti,ab,kw OR (metagenom*):ti,ab,kw OR ("16S rRNA* OR flora):ti,ab,kw | 56,167   |
| #3 #1 AND #2 | 129       |

| Search strategy for EMBASE-MEDLINE-PsycINFO |          |
|---------------------------------------------|----------|
| #1 depress*:ab,ti OR dysthymi*:ab,ti OR “mood disorder*”:ab,ti OR “affective disorder*”:ab,ti OR antidepress*:ab,ti | 1,063,823|
| #2 microb*:ab,ti OR bacteria*:ab,ti OR metaproteom*:ab,ti OR metagenom*:ab,ti OR "16S rRNA*:ab,ti OR flora: ab,ti | 1,300,339|
| #3 #1 AND #2 | 7,992     |
Table S15. Search strategy for microbiota-based interventions of depression from PubMed.

| Search strategy for PubMed                                                                 | Hits  |
|-------------------------------------------------------------------------------------------|-------|
| #1 (depress*[Title/Abstract] OR dysthymi*[Title/Abstract] OR mood disorder*[Title/Abstract] OR affective disorder*[Title/Abstract] OR antidepress*[Title/Abstract]) | 474,410 |
| #2 (microb*[Title/Abstract] OR flora*[Title/Abstract] OR probiotic*[Title/Abstract] OR prebiotic*[Title/Abstract] OR synbiotic*[Title/Abstract] OR psychobiotic*[Title/Abstract] OR postbiotic*[Title/Abstract] OR "fecal microbiota transplantation"*[Title/Abstract] OR "fecal transplantation"*[Title/Abstract]) | 639,026 |
| #3 #1 AND #2                                                                             | 3,633 |