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Supplementary Materials for

Landscapes of bacterial and metabolic signatures and their interaction in major depressive disorders

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Tables S1 to S6

Table S1. Detailed clinical characteristics of the recruited subjects.

	Discovery set			Validation set		
	HC	**MDD**	**p-value**	**HC**	**MDD**	**p-value**
Samples	118	118	-	37	38	-
Gender (male %)	43.22%	43.22%	1	35.14%	13.16%	0.026
Age	26.86±5.24	27.19±4.71	0.178	36.39±10.75	37.07±9.45	0.77
BMI	22.09±3.33	22.50±3.56	0.357	23.34±3.22	21.56±2.92	0.15
HAMD-17	-	22.03±5.08	-	-	22.63±3.43	-
QIDS-16		15.8±3.93	-		15.43±3.61	-
Medication	0	0	-	0	38	-

Abbreviations: HC, Healthy controls; MDD, major depressive disorder; BMI, Body Mass Index; HAMD, The Hamilton Depression Rating Scale; QIDS, Quick Inventory of Depressive Symptomatology. Analysis of Variance for continuous variables (Age and BMI);

Table S2. Differential bacteria species between MDD and HC groups.

Family	Genus	Species	HC		MDD		Fold change (MDD/HC)	Enrichment	LDA	p value	RF Importance
			mean	sem	mean	sem					
Lachnospiraceae	Blautia	Blautia_obeum	1.0E-02	1.1E-03	7.6E-03	9.0E-04	0.73	HC	3.14	3.4E-03	0.016754
Clostridiaceae	Clostridium	Clostridium_sp._CAG:217	2.7E-03	5.8E-04	1.2E-03	4.1E-04	0.44	HC	2.85	3.4E-03	0.020179
Bacteroidaceae	Bacteroides	Bacteroides_thetaiotaomicron	4.7E-03	5.3E-04	6.2E-03	6.3E-04	1.32	MDD	2.92	1.5E-02	0.022699
Bifidobacteriaceae	Bifidobacterium	Bifidobacterium_longum	5.8E-03	8.2E-04	9.9E-03	1.5E-03	1.70	MDD	3.30	3.2E-02	0.0251
Veillonellaceae	Veillonella	Veillonella_sp._CAG:933	1.2E-03	4.4E-04	1.5E-03	8.1E-04	1.24	MDD	2.57	1.5E-02	0.027337
Eubacteriaceae	Eubacterium	Eubacterium_sp._CAG:202	5.6E-03	1.6E-03	2.9E-03	1.0E-03	0.52	HC	3.04	1.5E-02	0.017609
Ruminococcaceae	Faecalibacterium	Faecalibacterium_sp._CAG:74	4.8E-03	1.3E-03	1.8E-03	4.1E-04	0.37	HC	3.17	2.3E-02	0.014343
Lachnospiraceae	Coprococcus	Coprococcus_eutactus	2.7E-03	4.8E-04	1.7E-03	3.1E-04	0.65	HC	2.66	4.9E-02	0.016643
Lachnospiraceae	Anaerostipes	Anaerostipes_hadrus	4.9E-03	7.4E-04	3.6E-03	6.5E-04	0.74	HC	2.82	1.8E-02	0.015131
unclassified_o__Bacteroidales	unclassified_o__Bacteroidales	unclassified_o__Bacteroidales	9.9E-03	7.8E-04	1.3E-02	8.7E-04	1.29	MDD	3.17	2.3E-02	0.010661
Bacteroidaceae	Bacteroides	Bacteroides_stercoris	6.5E-03	1.3E-03	1.5E-02	2.2E-03	2.26	MDD	3.61	1.5E-02	0.01889
Bacteroidaceae	Bacteroides	Bacteroides_stercoris_CAG:120	1.2E-03	2.7E-04	2.9E-03	4.7E-04	2.36	MDD	2.92	3.7E-02	0.020478
Bacteroidaceae	Bacteroides	unclassified_g__Bacteroides	4.1E-02	3.9E-03	5.5E-02	4.3E-03	1.35	MDD	3.86	1.1E-02	0.012472
Eggerthellaceae	Adlercreutzia	Adlercreutzia_equolifaciens	2.9E-03	5.6E-04	2.0E-03	4.0E-04	0.71	HC	2.68	3.1E-03	0.026401
unclassified_p__Firmicutes	unclassified_p__Firmicutes	Firmicutes_bacterium_CAG:227	1.5E-03	3.4E-04	6.5E-04	1.2E-04	0.43	HC	2.64	4.8E-04	0.032782
Bacteroidaceae	Bacteroides	Bacteroides_fragilis	7.0E-03	5.4E-04	9.4E-03	8.2E-04	1.35	MDD	3.12	1.5E-02	0.012717
unclassified_c__Bacilli	unclassified_c__Bacilli	unclassified_c__Bacilli	6.8E-04	6.5E-04	1.7E-05	4.5E-06	0.03	HC	2.62	1.4E-02	0.020248
Eubacteriaceae	Eubacterium	Eubacterium_sp._CAG:156	1.3E-03	4.0E-04	1.0E-03	4.5E-04	0.78	HC	2.54	1.7E-03	0.023715
Lachnospiraceae	Blautia	Blautia_sp._GD8	1.7E-03	2.1E-04	1.1E-03	9.7E-05	0.65	HC	2.52	6.9E-03	0.014202
Ruminococcaceae	Ruminococcus	Ruminococcus_sp._5_1_39BFAA	2.1E-03	3.9E-04	1.3E-03	1.2E-04	0.58	HC	2.62	5.2E-03	0.017367
Lachnospiraceae	Dorea	Dorea_sp._CAG:105	1.8E-03	4.4E-04	1.0E-03	2.7E-04	0.56	HC	2.65	1.8E-04	0.030339
Bifidobacteriaceae	Bifidobacterium	unclassified_g__Bifidobacterium	1.8E-03	2.4E-04	2.8E-03	4.0E-04	1.59	MDD	2.71	1.8E-02	0.026248
Eubacteriaceae	Eubacterium	[Eubacterium]_hallii	8.7E-03	1.1E-03	4.2E-03	5.5E-04	0.49	HC	3.34	8.8E-05	0.029314
Enterococcaceae	Enterococcus	Enterococcus_faecalis	1.8E-03	1.4E-03	3.4E-04	1.9E-05	0.19	HC	2.97	3.5E-02	0.013192
Acidaminococcaceae	Phascolarctobacterium	Phascolarctobacterium_sp._CAG:207	4.0E-03	6.6E-04	5.3E-03	6.6E-04	1.31	MDD	2.84	5.2E-03	0.026834
Eubacteriaceae	Eubacterium	Eubacterium_hallii_CAG:12	1.5E-03	2.1E-04	6.9E-04	1.0E-04	0.46	HC	2.60	1.5E-04	0.023777
Bacteroidaceae	Bacteroides	Bacteroides_massiliensis	3.6E-03	6.9E-04	7.1E-03	1.3E-03	1.95	MDD	3.28	1.5E-02	0.016174
Bacteroidaceae	Bacteroides	Bacteroides_dorei	6.9E-03	8.0E-04	1.1E-02	1.2E-03	1.56	MDD	3.25	6.0E-03	0.01422

Lachnospiraceae	Blautia	Blautia_wexlerae	8.6E-03	1.4E-03	5.4E-03	4.5E-04	0.62	HC	3.18	9.6E-03	0.013673
Ruminococcaceae	Faecalibacterium	Faecalibacterium_prausnitzii	5.4E-02	4.3E-03	4.1E-02	3.0E-03	0.76	HC	3.80	4.5E-02	0.017864
Ruminococcaceae	Subdoligranulum	Subdoligranulum_variabile	2.2E-02	2.3E-03	1.4E-02	1.6E-03	0.65	HC	3.54	8.5E-03	0.012576
Lachnospiraceae	Blautia	Blautia_sp._Marseille-P2398	2.0E-03	3.5E-04	1.2E-03	1.1E-04	0.58	HC	2.59	3.8E-03	0.017873
Oscillospiraceae	Oscillibacter	Oscillibacter_sp._ER4	4.1E-03	4.2E-04	3.0E-03	4.9E-04	0.74	HC	2.70	2.4E-02	0.02115
Enterobacteriaceae	Citrobacter	Citrobacter_freundii	1.2E-03	8.0E-04	1.4E-04	3.3E-05	0.12	HC	2.78	6.4E-03	0.018924
Bacteroidaceae	Bacteroides	Bacteroides_vulgatus	2.4E-02	2.9E-03	3.7E-02	3.7E-03	1.51	MDD	3.79	2.6E-03	0.018394
Enterobacteriaceae	Klebsiella	unclassified_g__Klebsiella	1.2E-03	4.5E-04	6.5E-04	2.3E-04	0.53	HC	2.58	7.0E-05	0.055891
Clostridiaceae	Clostridium	Clostridium_sp._CAG:510	8.8E-04	6.3E-04	1.8E-04	1.6E-05	0.21	HC	2.56	4.0E-03	0.025147
Clostridiaceae	Clostridium	Clostridium_sp._CAG:62	1.2E-03	3.3E-04	5.0E-04	1.1E-04	0.43	HC	2.54	1.8E-02	0.017738
Bacteroidaceae	Bacteroides	Bacteroides_ovatus	7.4E-03	9.5E-04	8.8E-03	9.3E-04	1.20	MDD	2.96	2.0E-02	0.01711
Eubacteriaceae	Eubacterium	Eubacterium_ventriosum	3.3E-03	3.7E-04	2.3E-03	3.2E-04	0.70	HC	2.69	4.1E-03	0.022971
Porphyromonadaceae	Parabacteroides	Parabacteroides_distasonis	2.8E-03	2.5E-04	3.7E-03	2.9E-04	1.33	MDD	2.65	4.9E-03	0.015958
Eubacteriaceae	Eubacterium	Eubacterium_sp._CAG:146	1.6E-03	1.9E-04	2.4E-03	4.9E-04	1.52	MDD	2.53	2.4E-03	0.04402
Enterobacteriaceae	Klebsiella	Klebsiella_pneumoniae	7.4E-03	2.8E-03	3.7E-03	1.3E-03	0.51	HC	3.37	1.9E-03	0.027132
Eubacteriaceae	Eubacterium	Eubacterium_sp._CAG:180	8.1E-03	1.9E-03	9.4E-03	2.7E-03	1.16	MDD	3.19	2.1E-02	0.021554
unclassified_p__Firmicutes	unclassified_p__Firmicutes	Firmicutes_bacterium_CAG:41	6.0E-03	9.5E-04	3.7E-03	4.9E-04	0.61	HC	3.02	1.4E-03	0.03475
Lachnospiraceae	Blautia	Blautia_sp._CAG:237	2.3E-03	1.2E-03	8.4E-04	1.5E-04	0.36	HC	2.93	1.2E-02	0.015097
Bacteroidaceae	Bacteroides	Bacteroides_eggerthii	2.5E-03	7.5E-04	3.1E-03	7.8E-04	1.26	MDD	2.68	1.0E-02	0.016354

Table S3. Differential gut virus between MDD and HC groups.

Family	Species	HC		MDD		Fold change (MDD/HC)	Enrichment	LDA	p value	RF Importance
		mean	sem	mean	sem					
Siphoviridae	Clostridium_phage_phi8074-B1	4.8E-04	2.5E-04	2.7E-04	1.2E-04	0.55	HC	2.92	6.9E-03	0.237184
Podoviridae	Escherichia_phage_ECBP5	2.3E-04	8.5E-05	3.4E-03	3.4E-03	14.40	MDD	3.41	1.8E-18	0.614219
Podoviridae	Klebsiella_phage_vB_KpnP_SU552A	1.1E-03	7.7E-04	4.7E-04	3.4E-04	0.44	HC	2.69	2.4E-04	0.148597

Table S4. Protozoa and fungi data in MDD and HC groups.

Classification	Family	Species	HC		MDD	
			mean	sem	mean	sem
Protozoa	f__Reticulomyxidae	s__Reticulomyxa_filosa	9.3E-03	2.6E-03	1.7E-02	5.9E-03
Protozoa	f__Thalassiosiraceae	s__Thalassiosira_oceanica	6.4E-03	2.4E-03	3.9E-03	6.8E-04
Protozoa	f__Sarcocystidae	s__Toxoplasma_gondii	4.2E-03	1.7E-03	1.8E-02	9.0E-03
Protozoa	f__Noelaerhabdaceae	s__Emiliania_huxleyi	6.3E-02	7.7E-03	3.9E-02	5.0E-03
Protozoa	f__Plasmodiidae	s__Plasmodium_yoelii	7.7E-03	2.3E-03	2.5E-03	7.1E-04
Protozoa	f__Ectocarpaceae	s__Ectocarpus_siliculosus	6.9E-03	1.5E-03	1.2E-02	4.3E-03
Protozoa	f__unclassified_d__Eukaryota	s__Blastocystis_sp._subtype_1	1.8E-02	5.2E-03	2.4E-02	7.5E-03
Protozoa	f__Phaeodactylaceae	s__Phaeodactylum_tricornutum	3.1E-03	9.2E-04	5.2E-03	2.6E-03
Protozoa	f__Eimeriidae	s__Eimeria_acervulina	2.2E-03	9.0E-04	2.6E-03	6.9E-04
Protozoa	f__Cyanidiaceae	s__Cyanidioschyzon_merolae	2.0E-02	3.6E-03	2.2E-02	3.7E-03
Protozoa	f__Trypanosomatidae	s__Angomonas_deanei	1.4E-03	3.6E-04	3.2E-03	1.2E-03
Protozoa	f__Saprolegniaceae	s__Aphanomyces_invadans	2.8E-02	4.5E-03	2.8E-02	3.2E-03
Protozoa	f__unclassified_o__Ichthyophonida	s__Sphaeroforma_arctica	5.5E-03	1.7E-03	3.6E-03	1.2E-03
Protozoa	f__Codonosigidae	s__Monosiga_brevicollis	2.3E-02	5.6E-03	2.2E-02	6.0E-03
Protozoa	f__Trypanosomatidae	s__Leishmania_major	3.1E-03	7.9E-04	6.1E-03	1.9E-03
Protozoa	f__unclassified_o__Hymenostomatida	s__Ichthyophthirius_multifiliis	4.2E-03	9.5E-04	5.7E-03	2.7E-03
Protozoa	f__Plasmodiidae	s__Plasmodium_falciparum	3.7E-03	1.9E-03	2.8E-03	1.4E-03
Protozoa	f__unclassified_o__Peronosporales	s__Phytophthora_parasitica	2.9E-03	6.5E-04	1.1E-03	2.4E-04
Protozoa	f__Chrysochromulinaceae	s__Chrysochromulina_sp._CCMP291	4.0E-02	7.2E-03	5.6E-02	9.9E-03
Protozoa	f__Plasmodiidae	s__Plasmodium_vivax	6.7E-03	9.9E-04	2.0E-02	6.8E-03
Protozoa	f__Perkinsidae	s__Perkinsus_marinus	5.8E-02	8.4E-03	6.8E-02	1.3E-02
Protozoa	f__Eimeriidae	s__Eimeria_brunetti	4.4E-03	7.6E-04	3.2E-03	6.9E-04
Protozoa	f__Trypanosomatidae	s__Strigomonas_culicis	6.1E-03	1.6E-03	3.6E-03	1.1E-03
Protozoa	f__Plasmodiidae	s__Plasmodium_chabaudi	4.5E-03	9.4E-04	8.7E-03	4.5E-03
Protozoa	f__unclassified_d__Eukaryota	s__Blastocystis_hominis	1.0E-02	3.0E-03	3.1E-03	6.1E-04
Protozoa	f__unclassified_o__Dictyosteliida	s__Acytostelium_subglobosum	7.1E-02	1.3E-02	6.4E-02	1.5E-02
Protozoa	f__Trichomonadidae	s__Trichomonas_vaginalis	2.9E-01	2.0E-02	2.8E-01	2.2E-02
Protozoa	f__unclassified_c__Ichthyosporea	s__Capsaspora_owczarzaki	4.9E-03	2.0E-03	2.2E-03	6.0E-04

Protozoa	f__unclassified_d__Eukaryota	s__Entamoeba_dispar	9.7E-02	1.6E-02	1.2E-01	2.2E-02
Protozoa	f__Parameciidae	s__Paramecium_tetraurelia	9.3E-03	3.4E-03	2.5E-03	1.0E-03
Protozoa	f__Monodopsidaceae	s__Nannochloropsis_gaditana	3.2E-02	4.3E-03	2.4E-02	5.0E-03
Protozoa	f__Apusomonadidae	s__Thecamonas_trahens	1.4E-03	2.4E-04	1.5E-03	6.0E-04
Protozoa	f__unclassified_d__Eukaryota	s__Entamoeba_invadens	1.5E-02	8.3E-03	1.9E-03	1.3E-03
Protozoa	f__unclassified_o__Dictyosteliida	s__Dictyostelium_purpureum	1.1E-02	2.4E-03	1.6E-02	3.9E-03
Protozoa	f__unclassified_d__Eukaryota	s__Blastocystis_sp._ST4	1.2E-02	4.7E-03	1.9E-02	7.3E-03
Protozoa	f__Vahlkampfiidae	s__Naegleria_gruberi	1.2E-02	4.6E-03	7.7E-03	4.0E-03
Fungi	f__Pseudeurotiaceae	s__Pseudogymnoascus_sp._VKM_F4515_(FW2607)	3.4E-03	1.3E-03	8.3E-03	6.2E-03
Fungi	f__Cucurbitariaceae	s__Pyrenochaeta_sp._DS3sAY3a	2.0E-03	6.8E-04	1.2E-03	4.5E-04
Fungi	f__Clavicipitaceae	s__Pochonia_chlamydosporia	9.7E-04	3.3E-04	1.4E-03	5.0E-04
Fungi	f__Enterocytozoonidae	s__Enterocytozoon_bieneusi	1.6E-01	1.6E-02	1.3E-01	1.5E-02
Fungi	f__Cystofilobasidiaceae	s__Xanthophyllomyces_dendrorhous	1.7E-03	5.5E-04	8.5E-04	2.8E-04
Fungi	f__Ophiostomataceae	s__Sporothrix_schenckii	1.7E-02	6.6E-03	1.0E-02	4.3E-03
Fungi	f__Debaryomycetaceae	s__Scheffersomyces_stipitis	6.2E-03	1.0E-03	6.6E-03	1.5E-03
Fungi	f__Plectosphaerellaceae	s__Verticillium_longisporum	4.6E-02	1.1E-02	5.0E-02	9.3E-03
Fungi	f__Metschnikowiaceae	s__Clavispora_lusitaniae	1.9E-02	5.4E-03	3.6E-02	7.7E-03
Fungi	f__unclassified_p__Cryptomycota	s__Rozella_allomycis	3.9E-03	6.2E-04	3.2E-03	5.2E-04
Fungi	f__Trichomonascaceae	s__Sugiyamaella_lignohabitans	1.1E-03	3.1E-04	3.2E-03	1.0E-03
Fungi	f__Mortierellaceae	s__Mortierella_verticillata	2.1E-03	7.5E-04	3.6E-03	1.9E-03
Fungi	f__Pseudeurotiaceae	s__Pseudogymnoascus_sp._VKM_F3808	3.0E-03	7.4E-04	6.4E-03	3.5E-03
Fungi	f__Saccharomycetaceae	s__Saccharomyces_cerevisiae	5.8E-02	1.6E-02	5.5E-02	1.4E-02
Fungi	f__Myxotrichaceae	s__Oidiodendron_maius	1.3E-03	3.9E-04	2.5E-03	1.0E-03
Fungi	f__Microascaceae	s__Scedosporium_apiospermum	3.6E-03	1.4E-03	2.5E-03	7.5E-04
Fungi	f__Corticiaceae	s__Cylindrobasidium_torrendii	7.2E-03	2.3E-03	6.6E-03	3.0E-03
Fungi	f__Rhizopodaceae	s__Rhizopus_microsporus	4.0E-02	1.2E-02	6.5E-02	1.4E-02
Fungi	f__Ustilaginaceae	s__Moesziomyces_antarcticus	2.4E-03	5.6E-04	2.2E-03	5.9E-04
Fungi	f__Herpotrichiellaceae	s__Exophiala_spinifera	1.8E-03	9.9E-04	1.9E-03	9.8E-04
Fungi	f__Pleosporaceae	s__Pyrenophora_triticirepentis	2.3E-02	5.3E-03	2.6E-02	5.9E-03
Fungi	f__Lasiosphaeriaceae	s__Podospora_anserina	8.5E-03	6.0E-03	2.3E-03	1.0E-03
Fungi	f__Aspergillaceae	s__Aspergillus_niger	7.7E-03	2.4E-03	5.2E-03	2.1E-03
Fungi	f__Phaffomycetaceae	s__Cyberlindnera_jadinii	1.2E-03	3.0E-04	3.9E-03	1.7E-03

Fungi	f__Mucoraceae	s__Mucor_ambiguus	6.7E-02	9.4E-03	5.1E-02	7.0E-03
Fungi	f__Cordycipitaceae	s__Beauveria_bassiana	2.6E-01	2.8E-02	2.4E-01	2.5E-02
Fungi	f__Ophiocordycipitaceae	s__Ophiocordyceps_sinensis	5.5E-03	1.0E-03	5.2E-03	1.0E-03
Fungi	f__Debaryomycetaceae	s__Candida_parapsilosis	9.7E-03	3.2E-03	1.0E-02	3.1E-03
Fungi	f__Nectriaceae	s__Neonectria_ditissima	1.5E-03	3.3E-04	1.1E-03	2.2E-04
Fungi	f__Pseudeurotiaceae	s__Pseudogymnoascus_sp._VKM_F4520_(FW2644)	1.1E-02	5.5E-03	2.4E-02	8.8E-03
Fungi	f__Glomeraceae	s__Rhizophagus_irregularis	1.1E-01	1.4E-02	1.2E-01	1.4E-02

Table S5. Differential fecal metabolites between MDD and HC groups.

Metabolite	HC		MDD		Fold change (MDD/HC)	Enrichment	LDA	p value	RF Importance
	mean	sem	mean	sem					
Pipecolic Acid	6.2E-02	5.0E-03	4.5E-02	4.7E-03	0.73	HC	3.86	3.0E-03	0.01555
Leucine	3.7E-03	1.2E-03	4.5E-03	2.2E-03	1.20	MDD	2.98	7.9E-03	0.01093
Phosphate	1.5E-03	1.2E-04	3.1E-03	9.0E-04	1.98	MDD	2.80	1.1E-03	0.011954
Erythronic Acid Lactone	1.6E-02	1.9E-03	1.6E-02	2.7E-03	1.00	HC	3.11	3.4E-02	0.0211
Triacetin	4.5E-02	5.9E-03	3.2E-02	5.6E-03	0.71	HC	3.75	2.2E-03	0.018814
L-Homoserine	4.6E-06	4.8E-07	3.1E-06	4.3E-07	0.66	HC	2.77	3.1E-04	0.008073
Ciliatine	4.5E-02	6.7E-03	6.6E-02	6.9E-03	1.46	MDD	3.97	2.2E-03	0.011026
Norvaline	6.1E-02	7.3E-03	3.7E-02	5.3E-03	0.60	HC	4.09	7.2E-03	0.013604
Thymine	2.8E-03	3.9E-04	1.4E-03	2.5E-04	0.52	HC	2.79	2.4E-02	0.011891
Z Hexose	1.2E-03	2.7E-04	4.5E-04	9.3E-05	0.38	HC	2.56	1.8E-03	0.011257
Ibuprofen	2.5E-03	3.2E-04	1.2E-03	1.9E-04	0.50	HC	2.79	4.3E-05	0.032763
N-Acetylornithine	1.1E-02	1.4E-03	6.1E-03	1.0E-03	0.55	HC	3.39	3.2E-03	0.014191
Proline	2.4E-03	7.8E-04	5.3E-04	6.4E-05	0.22	HC	2.92	8.5E-03	0.017995
Altrose	4.8E-02	5.3E-03	2.1E-02	2.6E-03	0.43	HC	4.11	2.7E-04	0.020618
Amidosulfonic acid	1.4E-02	1.7E-03	1.2E-02	1.8E-03	0.86	HC	3.16	2.3E-02	0.018271
Edetic Acid	1.9E-02	4.2E-03	7.8E-02	9.5E-03	4.15	MDD	4.47	9.3E-09	0.041858
2-Dodecyl-1,4-dihydroxy-Benzene	2.4E-02	2.7E-03	1.3E-02	1.9E-03	0.54	HC	3.73	4.6E-03	0.013259
Quinolinic Acid	7.2E-06	6.5E-07	5.6E-06	7.4E-07	0.77	HC	2.62	3.9E-03	0.014284
Beta-Mannosylglycerate	2.2E-03	2.7E-04	1.6E-03	2.2E-04	0.74	HC	2.54	1.9E-02	0.012635
Cystine	1.5E-03	7.3E-04	4.3E-04	6.9E-05	0.28	HC	2.71	1.8E-02	0.014571
O-Phosphoethanolamine	9.6E-06	1.2E-06	4.9E-06	6.9E-07	0.51	HC	2.55	8.4E-03	0.018688
Oxoproline	5.4E-03	1.7E-03	3.7E-03	1.5E-03	0.68	HC	3.03	1.5E-02	0.020699
Sebacic acid	4.8E-03	1.3E-03	6.6E-03	7.6E-04	1.38	MDD	3.02	7.0E-09	0.081039
Isocitric Acid	1.1E-02	1.9E-03	2.9E-02	3.4E-03	2.60	MDD	3.94	8.4E-05	0.01876
Palmitic Acid	4.6E-03	6.4E-04	1.4E-03	3.5E-04	0.31	HC	3.23	5.2E-06	0.030712
Glutathione	8.9E-06	1.0E-06	6.3E-06	7.8E-07	0.71	HC	2.60	2.6E-02	0.00937
D-Fructose	1.7E-03	1.6E-04	3.0E-03	3.0E-04	1.75	MDD	2.81	1.6E-02	0.018479
2-Piperidinobenzonitrile	4.6E-06	6.1E-07	3.0E-06	6.4E-07	0.66	HC	2.70	4.7E-04	0.019312

Alpha-D-Glucose	4.3E-02	7.4E-03	3.5E-02	7.4E-03	0.83	HC	3.72	2.6E-02	0.013225
Trans-4-Hydroxy-L-Proline	3.7E-03	8.1E-04	7.1E-03	9.4E-04	1.91	MDD	3.22	3.3E-03	0.014382
Gamma-Aminobutyric Acid	6.2E-02	8.3E-03	4.7E-02	7.1E-03	0.76	HC	3.94	4.6E-02	0.018114
Bisphenol A	4.0E-06	5.0E-07	1.8E-06	3.6E-07	0.45	HC	2.75	1.7E-05	0.022189
Inosine-5'-Monophosphate	6.1E-06	7.1E-07	4.2E-06	5.2E-07	0.69	HC	2.55	2.9E-02	0.009297
4-Methylbenzenesulfonamide	1.4E-02	4.3E-03	5.7E-02	7.1E-03	4.00	MDD	4.35	1.2E-07	0.048183
Trans-4-Hydroxyproline	5.5E-06	6.6E-07	3.4E-06	5.5E-07	0.61	HC	2.63	1.1E-03	0.014747
N-{2-hydroxyethyl}tetradecan-1-amine	4.9E-03	8.5E-04	1.0E-02	1.1E-03	2.09	MDD	3.42	1.2E-03	0.014475
Tryptophol	6.7E-06	8.8E-07	4.5E-06	7.7E-07	0.67	HC	2.55	1.8E-03	0.009616
Terephthalic Acid	4.4E-06	4.0E-07	3.3E-06	5.6E-07	0.75	HC	2.77	5.8E-03	0.020425
Homovanillic Acid	4.1E-06	6.1E-07	2.7E-06	5.9E-07	0.66	HC	2.51	2.0E-05	0.014791
Biphenyl	1.0E-03	2.5E-04	2.8E-03	4.1E-04	2.69	MDD	2.91	4.0E-06	0.020437
4-Methyl-5-Thiazoleethanol	6.6E-06	8.2E-07	3.6E-06	4.8E-07	0.54	HC	2.55	4.1E-03	0.007881
Itaconic Acid	9.4E-03	2.7E-03	3.6E-02	4.5E-03	3.86	MDD	4.15	2.7E-08	0.063836
Arbutin	3.5E-06	3.7E-07	2.5E-06	3.0E-07	0.72	HC	2.78	2.1E-02	0.00856
Adenosine-5-Monophosphate	1.8E-06	2.7E-07	1.0E-06	2.4E-07	0.57	HC	2.91	3.6E-03	0.009432
2-Indolecarboxylic acid	2.0E-04	4.8E-05	1.7E-03	2.5E-04	8.26	MDD	2.86	7.3E-11	0.064682
Hydrocinnamic Acid	6.4E-02	1.2E-02	2.7E-02	7.1E-03	0.42	HC	4.28	1.2E-03	0.022258
2,2'-Biphenyldiol	3.2E-06	3.5E-07	2.0E-06	3.0E-07	0.63	HC	2.93	7.0E-03	0.011075
1,3,5-Benzetriol	2.7E-06	4.0E-07	3.6E-06	5.3E-07	1.34	MDD	2.80	2.3E-02	0.017862
5,7-Dimethyl[1,2,4]triazolo[1,5-a] pyrimidin-2-ylamine	1.8E-06	3.5E-07	4.0E-06	1.1E-06	2.24	MDD	2.58	2.9E-03	0.015467
Benzylamine	1.9E-06	2.6E-07	2.6E-06	3.6E-07	1.35	MDD	2.57	3.8E-02	0.007361

Table S6. The influence of confounding factors on bacterial composition

		PCA model generated with MDD and HC samples			
Variables		PC1	PC2	r2	P-value
Dietary preference	High_fat	0.2465	-0.9691	0.0169	0.486
	High_salt	-0.9217	0.3879	0.0004	0.981
	High_fiber	-0.9127	-0.4087	0.0274	0.278
	High_protein	0.3996	-0.9167	0.0105	0.605
Smoking		-0.2157	-0.9765	0.0009	0.954