

Table S1 Reverse MR results between gut microbiota and HF

id.exp osure	id.ou tcom e	outcome	method	nsnp	b	se	pval	lo_ci	up_ci	or	or_lci95	or_uci95	id
C1rR Hp	VQB uP7	LACTOSECAT.PWY ..lactose.and.galactose .degradation.I	IVW	8	0.347	0.301	0.249	-0.243	0.938	1.415	0.784	2.554	GCST 90027 488
C1rR Hp	QSg0 gn	PPGPPMET.PWY..pp Gpp.biosynthesis	IVW	8	-0.169	0.131	0.197	-0.425	0.087	0.845	0.654	1.091	GCST 90027 512
C1rR Hp	tMU XVh	PWY0.1241..ADP.L. glycero..beta..D.mann o.heptose.biosynthesis	IVW	8	0.065	0.156	0.675	-0.24	0.371	1.068	0.787	1.449	GCST 90027 515
C1rR Hp	WIB bey	PWY.5918..superpath ay.of.heme.biosynthes is.from.glutamate	IVW	8	0.366	0.234	0.117	-0.092	0.824	1.442	0.912	2.28	GCST 90027 562
C1rR Hp	FUIK WT	k__Bacteria.p__Bacte roidetes.c__Bacteroidi a.o__Bacteroidales.f_ _Prevotellaceae.g__Pr evotella	IVW	8	-0.114	0.13	0.379	-0.369	0.14	0.892	0.691	1.151	GCST 90027 700
C1rR Hp	MtFZ Bz	k__Bacteria.p__Firmi cutes.c__Clostridia.o_ _Clostridiales.f__Lac hnospiraceae.g__Lach nospiraceae_noname	IVW	8	0.182	0.124	0.141	-0.06	0.424	1.199	0.941	1.528	GCST 90027 712

C1rR Hp	jQH BxH	k__Bacteria.p__Bacteroidetes.c__Bacteroidia.o__Bacteroidales.f__Prevotellaceae.g__Prevotella.s__Prevotella_copri	IVW	8	-0.134	0.148	0.367	-0.424	0.157	0.875	0.654	1.17	GCST 90027 774
C1rR Hp	nZz2 lt	k__Bacteria.p__Bacteroidetes.c__Bacteroidia.o__Bacteroidales.f__Rikenellaceae.g__Alistipes.s__Alistipes_putredinis	IVW	8	-0.058	0.116	0.616	-0.285	0.169	0.943	0.752	1.184	GCST 90027 778
C1rR Hp	GL2o hD	k__Bacteria.p__Firmicutes.c__Clostridia.o__Clostridiales.f__Ruminococcaceae.g__Ruminococcus.s__Ruminococcus_callidus	IVW	8	0.005	0.312	0.986	-0.607	0.618	1.005	0.545	1.855	GCST 90027 800

Table S2: Mendelian analyses results between gut microbiota and heart failure with Finnngen database.

id.exposure	name	outcome	method	nsnp	b	se	pval	or	or_lci95	or_uci95
GCST90027475	GLYCOCAT.PWY.. glycogen.degradatio n.I..bacterial.	Heart Failure	IVW	11	-0.084	0.027	0.002	0.920	0.873	0.969
GCST90027561	PWY.5913..TCA.cy cle.VI..obligate.auto trophs.	Heart Failure	IVW	9	0.057	0.026	0.030	1.059	1.006	1.115
GCST90027564	PWY.5941..glycoge n.degradation.II..euk aryotic.	Heart Failure	IVW	10	0.060	0.029	0.036	1.062	1.004	1.123
GCST90027568	PWY.6121..5.amino imidazole.ribonucle otide.biosynthesis.I	Heart Failure	IVW	10	0.078	0.035	0.024	1.081	1.010	1.157
GCST90027569	PWY.6123..inosine. 5..phosphate.biosynt hesis.I	Heart Failure	IVW	6	-0.123	0.042	0.004	0.885	0.814	0.961
GCST90027601	PWY.6892..thiazole. biosynthesis.I..E..col i.	Heart Failure	IVW	6	-0.089	0.035	0.010	0.914	0.854	0.979
GCST90027605	PWY.7003..glycerol .degradation.to.buta nol	Heart Failure	IVW	14	-0.064	0.026	0.013	0.938	0.891	0.986

GCST90027622	PWY.7328..superpathway.of.UDP.glucose.derived.O.antigen.building.blocks.biosynthesis	Heart Failure	IVW	8	-0.087	0.040	0.029	0.917	0.848	0.991
GCST90027657	k_Bacteria.p_Proteobacteria.c_Betaproteobacteria	Heart Failure	IVW	13	0.102	0.030	0.001	1.108	1.045	1.174
GCST90027680	k_Bacteria.p_Proteobacteria.c_Betaproteobacteria.o_Burkholderiales.f_Burkholderiales_noname	Heart Failure	IVW	12	-0.060	0.020	0.002	0.942	0.907	0.979
GCST90027700	k_Bacteria.p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Prevotellaceae.g_Prevotella	Heart Failure	IVW	7	0.091	0.040	0.024	1.096	1.012	1.186
GCST90027725	k_Bacteria.p_Proteobacteria.c_Betaproteobacteria.o_Burkholderiales.f_Burkholderiales_noname.g_Burkholderiales_noname	Heart Failure	IVW	12	-0.059	0.020	0.002	0.942	0.907	0.979

GCST90027733	k_Bacteria.p_Proteobacteria.c_Gammaproteobacteria.o_Pasteurellales.f_Pasteurellaceae.g_Haemophilus	Heart Failure	IVW	5	0.085	0.038	0.025	1.089	1.011	1.172
GCST90027743	k_Bacteria.p_Proteobacteria.c_Betaproteobacteria.o_Burkholderiales	Heart Failure	IVW	14	0.096	0.029	0.001	1.101	1.041	1.165
GCST90027754	k_Bacteria.p_Actinobacteria.c_Actinobacteria.o_Bifidobacteriales.f_Bifidobacteriaceae.g_Bifidobacterium.s_Bifidobacterium_adolescentis	Heart Failure	IVW	9	-0.083	0.038	0.028	0.920	0.855	0.991
GCST90027774	k_Bacteria.p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Prevotellaceae.g_Prevotella.s_Prevotella_copri	Heart Failure	IVW	13	0.064	0.026	0.014	1.066	1.013	1.122
GCST90027808	k_Bacteria.p_Firmicutes.c_Negativicutes.o_Selenomonadales	Heart Failure	IVW	10	-0.042	0.021	0.050	0.959	0.920	1.000

GCST90027809	.f_Veillonellaceae.g_Veillonella.s_Veillonella_unclassified_k_Bacteria.p_Proteobacteria.c_Betaproteobacteria.o_Burkholderiales.f_Burkholderiales_noname.g_Burkholderiales_noname.s_Burkholderiales_bacterium_1_1_47_k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Lachnospiraceae.g_Roseburia.s_Roseburia_hominis	Heart Failure	IVW	12	-0.060	0.020	0.002	0.942	0.907	0.979
GCST90027854	Clostridiales.f_Lachnospiraceae.g_Roseburia.s_Roseburia_hominis	Heart Failure	IVW	8	-0.104	0.046	0.023	0.901	0.824	0.986

Table S3: Mendelian analyses results between differentially expressed genes and heart failure.

id. exposure (Genes)	outcome	method	nsnp	b	se	pval	lo_ci	up_ci	or
eqtl-a-ENSG00000215252	heart failure	Inverse variance weighted	4	-0.249	0.120	0.037	-0.483	-0.015	0.780
eqtl-a-ENSG00000077232	heart failure	Inverse variance weighted	3	-0.234	0.098	0.017	-0.427	-0.042	0.791
eqtl-a-ENSG00000141401	heart failure	Inverse variance weighted	10	-0.149	0.069	0.030	-0.283	-0.014	0.862
eqtl-a-ENSG00000119397	heart failure	Inverse variance weighted	3	-0.234	0.096	0.015	-0.422	-0.045	0.792
eqtl-a-ENSG00000198756	heart failure	Inverse variance weighted	6	0.123	0.055	0.025	0.016	0.231	1.131
eqtl-a-ENSG00000001561	heart failure	Inverse variance weighted	4	-0.095	0.040	0.018	-0.174	-0.017	0.909
eqtl-a-ENSG00000171791	heart failure	Inverse variance weighted	5	0.594	0.301	0.048	0.004	1.183	1.811
eqtl-a-ENSG00000139182	heart failure	Inverse variance weighted	3	-0.144	0.069	0.037	-0.280	-0.009	0.865
eqtl-a-ENSG00000137959	heart failure	Inverse variance weighted	7	0.242	0.106	0.023	0.033	0.450	1.273
eqtl-a-ENSG00000187608	heart failure	Inverse variance weighted	5	0.238	0.116	0.040	0.011	0.466	1.269

Figure S1 Sensitivity analysis of LOO plots in the MR analysis between gut microbiota and HF

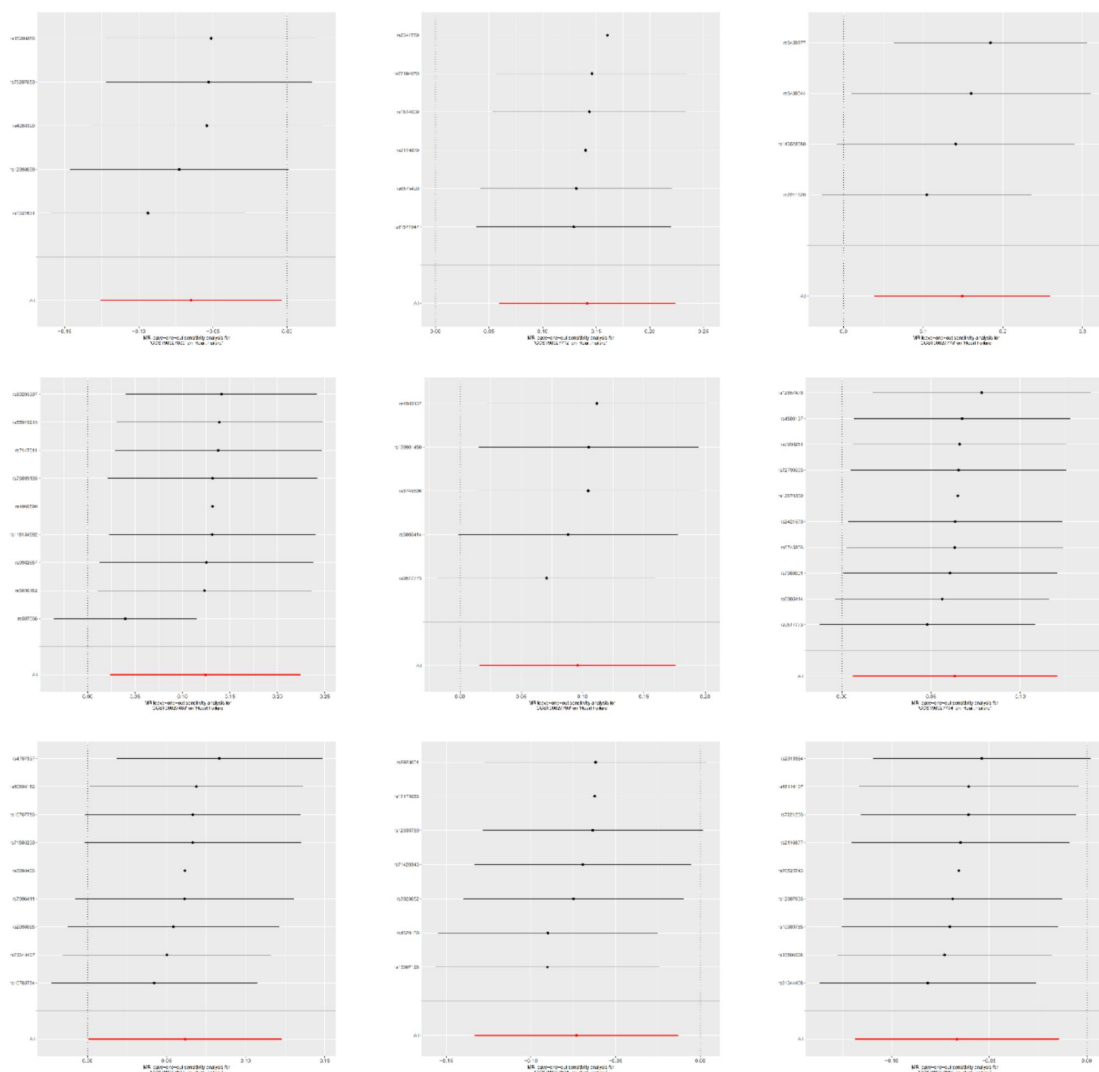


Figure S2 Sensitivity analysis of scatter plots in the MR analysis between plasma metabolites and HF

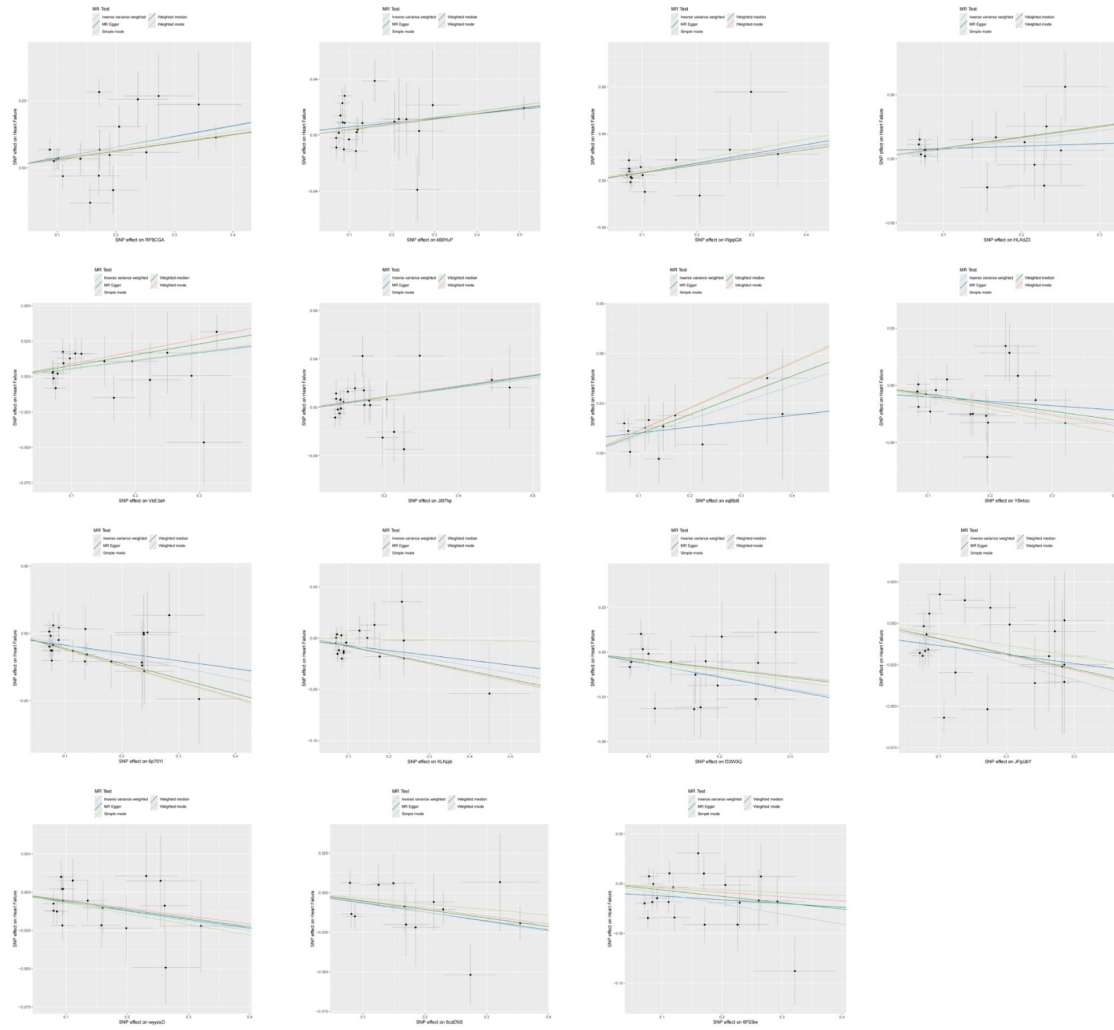


Figure S4: GO enrichment results.

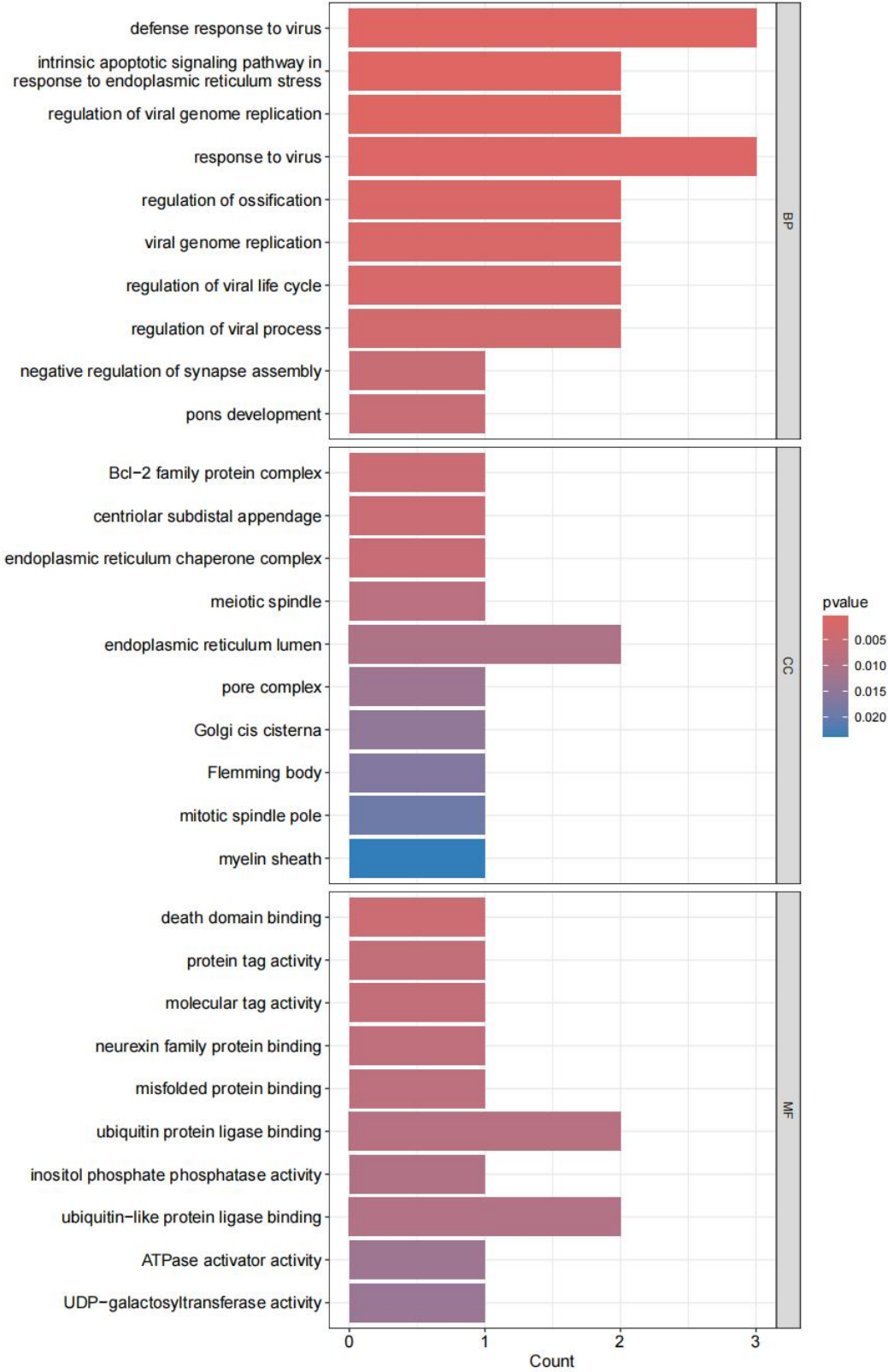


Figure S5: KEGG enrichment results

