

Table S3 Biological Processes of MBHD-VD PPI Network

Cluster	Term	Pathway	Count	%	Pvalue	
1	GO:0010628	positive regulation of gene expression	16	23.52941	8.88E-14	
	GO:0043066	negative regulation of apoptotic proce	19	27.94118	1.23E-13	
	GO:0045429	positive regulation of nitric oxide bios	9	13.23529	5.42E-12	
	GO:0050999	regulation of nitric-oxide synthase act	8	11.76471	7.23E-12	
	GO:0002576	platelet degranulation	11	16.17647	8.95E-12	
	GO:0048661	positive regulation of smooth muscle c	9	13.23529	9.06E-11	
	GO:0051092	positive regulation of NF-kappaB tran	11	16.17647	1.17E-10	
	GO:0006954	inflammatory response	15	22.05882	2.32E-10	
	GO:0030168	platelet activation	9	13.23529	1.76E-08	
	GO:0001525	angiogenesis	11	16.17647	1.79E-08	
	GO:0051000	positive regulation of nitric-oxide syn	6	8.823529	2.17E-08	
	GO:0014066	regulation of phosphatidylinositol 3-k	8	11.76471	2.47E-08	
	GO:0032355	response to estradiol	8	11.76471	7.25E-08	
	GO:0001666	response to hypoxia	9	13.23529	4.01E-07	
	GO:0048010	vascular endothelial growth factor rec	7	10.29412	4.08E-07	
	GO:1901215	negative regulation of neuron death	6	8.823529	5.13E-07	
	GO:0043536	positive regulation of blood vessel enc	5	7.352941	8.58E-07	
	GO:0043524	negative regulation of neuron apoptoti	8	11.76471	9.29E-07	
	GO:0035924	cellular response to vascular endothel	5	7.352941	1.94E-06	
	GO:0034097	response to cytokine	6	8.823529	1.95E-06	
	GO:0045766	positive regulation of angiogenesis	7	10.29412	6.43E-06	
	GO:0030949	positive regulation of vascular endoth	4	5.882353	3.28E-05	
	GO:0043123	positive regulation of I-kappaB kinase	7	10.29412	4.36E-05	
	GO:0042346	positive regulation of NF-kappaB imp	4	5.882353	7.67E-05	
	GO:0051402	neuron apoptotic process	4	5.882353	3.04E-04	
	GO:0010507	negative regulation of autophagy	4	5.882353	3.95E-04	
	GO:0006979	response to oxidative stress	5	7.352941	9.73E-04	
	GO:0030593	neutrophil chemotaxis	4	5.882353	0.002322	
	GO:0007179	transforming growth factor beta recep	4	5.882353	0.005919	
	GO:0043542	endothelial cell migration	3	4.411765	0.00594	
	GO:0045765	regulation of angiogenesis	3	4.411765	0.006768	
	2	GO:0045907	positive regulation of vasoconstrictor	6	20.68966	1.73E-09
		GO:0008284	positive regulation of cell proliferatio	9	31.03448	6.32E-07
GO:0008283		cell proliferation	8	27.58621	1.76E-06	
GO:0007268		chemical synaptic transmission	7	24.13793	2.32E-06	
GO:0007197		adenylate cyclase-inhibiting G-proteir	3	10.34483	5.60E-05	
GO:0007204		positive regulation of cytosolic calciu	5	17.24138	6.84E-05	
GO:0006939		smooth muscle contraction	3	10.34483	4.04E-04	
GO:0007186		G-protein coupled receptor signaling p	8	27.58621	5.41E-04	
GO:0051966		regulation of synaptic transmission, gl	3	10.34483	6.64E-04	
GO:0007611		learning or memory	3	10.34483	0.001631	
GO:0007271		synaptic transmission, cholinergic	3	10.34483	0.001722	

	GO:0010745 negative regulation of macrophage de	4	20	3.49E-07
	GO:0010875 positive regulation of cholesterol efflu	4	20	4.44E-07
	GO:0045861 negative regulation of proteolysis	4	20	1.61E-06
3	GO:0010887 negative regulation of cholesterol stor	3	15	1.81E-05
	GO:2000188 regulation of cholesterol homeostasis	3	15	4.35E-05
	GO:0042632 cholesterol homeostasis	4	20	4.90E-05
	GO:0042157 lipoprotein metabolic process	3	15	8.32E-04
	GO:0008203 cholesterol metabolic process	3	15	0.002643
	GO:0018108 peptidyl-tyrosine phosphorylation	7	0.163628	1.03E-07
	GO:0042127 regulation of cell proliferation	7	0.163628	3.16E-07
4	GO:0030168 platelet activation	5	0.116877	2.78E-05
	GO:0050900 leukocyte migration	4	0.093502	8.61E-04
	GO:0045909 positive regulation of vasodilation	3	0.070126	9.12E-04
	GO:0032229 negative regulation of synaptic transn	3	12	2.93E-05
	GO:0019433 triglyceride catabolic process	3	12	5.76E-04
	GO:0060079 excitatory postsynaptic potential	3	12	7.23E-04
	GO:0042157 lipoprotein metabolic process	3	12	0.001334
	GO:0001666 response to hypoxia	4	16	0.001825
	GO:0001523 retinoid metabolic process	3	12	0.003403
	GO:0042632 cholesterol homeostasis	3	12	0.003739
	GO:0050728 negative regulation of inflammatory r	3	12	0.00564
	GO:0033004 negative regulation of mast cell activa	2	8	0.005705
	GO:0007399 nervous system development	4	16	0.007666
	GO:0010886 positive regulation of cholesterol stor	2	8	0.009964
5	GO:0051001 negative regulation of nitric-oxide syn	2	8	0.011379
	GO:0051967 negative regulation of synaptic transn	2	8	0.012793
	GO:0042953 lipoprotein transport	2	8	0.021234
	GO:1904707 positive regulation of vascular smooth	2	8	0.021234
	GO:0030301 cholesterol transport	2	8	0.022635
	GO:0010744 positive regulation of macrophage der	2	8	0.022635
	GO:0042310 vasoconstriction	2	8	0.024033
	GO:0048169 regulation of long-term neuronal syna	2	8	0.025429
	GO:0001935 endothelial cell proliferation	2	8	0.025429
	GO:0045777 positive regulation of blood pressure	2	8	0.028216
	GO:0042127 regulation of cell proliferation	3	12	0.028424
	GO:0033344 cholesterol efflux	2	8	0.03515
	GO:0070328 triglyceride homeostasis	2	8	0.036531
6	GO:0055114 oxidation-reduction process	5	83.33333	7.43E-06
8	GO:0055114 oxidation-reduction process	5	1	1.53E-06
	GO:0009258 10-formyltetrahydrofolate catabolic p	2	0.4	4.76E-04
9	GO:0055114 oxidation-reduction process	6	85.71429	3.12E-07

10	GO:0043065 positive regulation of apoptotic process	5	0.270856	4.41E-05
	GO:0002576 platelet degranulation	4	0.216685	4.74E-05
	GO:0043547 positive regulation of GTPase activity	5	0.270856	5.06E-04
	GO:0000165 MAPK cascade	4	0.216685	7.44E-04
	GO:0070588 calcium ion transmembrane transport	3	0.162514	0.003138
	GO:0043524 negative regulation of neuron apoptotic process	3	0.162514	0.003844
	GO:0007268 chemical synaptic transmission	3	0.162514	0.012217
	GO:0048169 regulation of long-term neuronal synaptic transmission	2	0.108342	0.012792
	GO:0007597 blood coagulation, intrinsic pathway	2	0.108342	0.012792
	GO:2000463 positive regulation of excitatory postsynaptic potential	2	0.108342	0.014204
	GO:0035235 ionotropic glutamate receptor signaling pathway	2	0.108342	0.017022
	GO:0060079 excitatory postsynaptic potential	2	0.108342	0.019833
	GO:0001975 response to amphetamine	2	0.108342	0.021937
	GO:0045429 positive regulation of nitric oxide biosynthetic process	2	0.108342	0.03031
11	GO:0000165 MAPK cascade	3	0.303644	0.002351
	GO:0031293 membrane protein intracellular domain	2	0.202429	0.005349
	GO:0043066 negative regulation of apoptotic process	3	0.303644	0.006939
	GO:0008284 positive regulation of cell proliferation	3	0.303644	0.007269
	GO:0001755 neural crest cell migration	2	0.202429	0.013329
	GO:0097190 apoptotic signaling pathway	2	0.202429	0.020965
	GO:0033209 tumor necrosis factor-mediated signaling pathway	2	0.202429	0.034649
GO:0001934 positive regulation of protein phosphorylation	2	0.202429	0.037252	
14	GO:0055114 oxidation-reduction process	3	1.456311	0.001241
	GO:0016125 sterol metabolic process	2	0.970874	0.0025
	GO:0006695 cholesterol biosynthetic process	2	0.970874	0.004521

Genes	Fold Enrichment	Bonferroni
TGFB1, CSF2, STAT3, PIK3CD, NGF, MAPK14, T	15.08037719	1.43E-10
SRC, STAT3, IGF1, NGF, MT3, MMP9, EGFR, REL	10.31182935	1.97E-10
IL6, HSP90AA1, IL1B, AKT1, PTGS2, ESR1, TNF,	51.68536252	8.72E-09
HSP90AA1, NOS3, IL1B, AKT1, CALM3, CALM1,	75.98190045	1.16E-08
APP, TF, TGFB1, SERPINE1, CALM3, PLG, TIMP	26.37235865	1.44E-08
IL6, JUN, STAT1, AKT1, IGF1, PTGS2, TNF, FGF2	37.04117647	1.46E-07
AR, IL6, CD40, TGFB1, PLA2G1B, IL1B, CAT, TL	20.42370632	1.88E-07
CD40, TGFB1, CXCR4, PIK3CD, PTGS2, TNF, PIK	9.773397486	3.73E-07
IL6, CD40, PIK3CA, SRC, MAPK1, AKT1, F2, PIK	19.3258312	2.84E-05
JUN, FLT1, PIK3CA, NOS3, MMP2, SERPINE1, K	12.18095489	2.87E-05
AKT1, CALM3, APOE, CALM1, ESR1, CALM2	67.34759358	3.49E-05
PIK3CA, ERBB2, MAPK1, PIK3CD, AKT1, FGF2,	25.32730015	3.97E-05
CASP9, TGFB1, CASP8, CASP3, STAT3, CAT, PT	21.70911441	1.17E-04
TGFB1, CREB1, NOS2, CASP3, MMP2, CAT, CXC	12.92134063	6.46E-04
HSP90AA1, FLT1, PIK3CA, SRC, KDR, MAPK14,	24.00816993	6.57E-04
IL6, CREB1, STAT3, REL, AKT1, APOE	37.04117647	8.26E-04
TGFB1, AKT1, MAPK14, FGF2, VEGFA	64.98452012	0.001379722
JUN, PIK3CA, BDNF, BCL2, APOE, NGF, MT3, B	14.96613191	0.001494006
FLT1, KDR, AKT1, MAPK14, VEGFA	53.68286445	0.003111739
JUN, STAT1, BCL2, REL, TIMP1, BCL2L1	28.49321267	0.003139626
FLT1, NOS3, IL1B, SERPINE1, KDR, FGF2, VEGF	15.03120205	0.010292488
FLT1, IL1B, MT3, VEGFA	61.73529412	0.051377141
CD40, CASP8, TLR9, REL, TNF, RELA, TNFRSF1	10.73657289	0.067740884
IL1B, TLR9, PTGS2, TNF	47.03641457	0.116172164
APP, BCL2, GAPDH, BCL2L1	29.93226381	0.387130487
BCL2, AKT1, MT3, BCL2L1	27.4379085	0.470220002
APP, AKT1, APOE, PTGS2, EGFR	11.22459893	0.791336368
PLA2G1B, IL1B, PIK3CD, PIK3CG	14.96613191	0.976300721
JUN, TGFB1, CREB1, SRC	10.73657289	0.999929409
PIK3CA, STAT1, NOS3	25.54563895	0.999931703
IL6, ERBB2, FGF2	23.89753321	0.999982156
PTAFR, ADRA1D, AVP, HTR2A, ADRA1B, ADRA	108.5689655	1.07E-06
HCK, CHRM1, FLT4, CRH, ADRA1D, AVP, HTR2	11.18306941	3.92E-04
CHRM3, CHRM1, CDK5, NPY, CHRM5, ADRA1D	12.65649143	0.001090929
PRKCG, GRM5, CDK5, NPY, CRH, HTR2A, GRM	16.88850575	0.00143617
CHRM3, CHRM1, CHRM5	248.1576355	0.034135276
ADRA1D, FPR2, AVP, ADRA1B, ADRA1A	21.60576428	0.041532441
CHRM3, HTR2A, ADRA1A	96.50574713	0.221378982
CHRM3, CHRM1, PTAFR, ADRA1D, FPR2, ADRA	5.152698401	0.285183307
GRM5, LRRK2, GRM1	75.52623688	0.337480862
PRKCG, CRH, S100B	48.25287356	0.636524517
CHRM3, CHRM1, CHRM5	46.94874185	0.656587221

ABCA1, CETP, NR1H2, NR1H3	258.3384615	8.82E-05
ABCA1, LRP1, NR1H2, NR1H3	239.8857143	1.12E-04
CSTB, NR1H2, NR1H3, IDE	159.9238095	4.08E-04
ABCA1, NR1H2, NR1H3	419.8	0.004580295
NR1H2, NR1H3, SREBF2	279.8666667	0.010935573
ABCA1, CETP, NR1H2, NR1H3	52.475	0.012317064
ABCA1, CETP, LRP1	66.28421053	0.189939591
ABCA1, CETP, SREBF2	37.04117647	0.488048267
LYN, BCR, IL5, ERBB3, FYN, FGF1, MET	28.45412733	6.72E-05
JUND, ERBB3, PLAU, LCK, AGTR1, FYN, AGT	23.53233233	2.07E-04
LYN, SYK, VWF, LCK, FYN	27.04025765	0.018003253
LYN, MMP1, LCK, FYN	20.39101396	0.430699945
HMOX1, NOS1, AGT	64.33716475	0.449458741
CNR2, ADORA1, HTR1B	335.84	0.014006428
LPL, APOA1, APOB	80.6016	0.242357018
PPP3CA, ADORA1, SNCA	71.96571429	0.294476898
LPL, APOA1, APOB	53.02736842	0.474437682
F7, PRKCB, ADORA1, HSP90B1	15.62046512	0.585320852
LPL, APOA1, APOB	33.03344262	0.806608637
LPL, APOA1, APOB	31.485	0.835627575
CNR2, PRKCD, APOA1	25.50683544	0.934539495
CNR2, CNR1	335.84	0.936569822
CHRM2, GAL, ADORA1, APOB	9.361393728	0.975509457
LPL, APOB	191.9085714	0.991986348
CNR2, CNR1	167.92	0.995979258
ADORA1, HTR1B	149.2622222	0.997982729
PRKCB, APOB	89.55733333	0.999967853
ERN1, HTR1B	89.55733333	0.999967853
APOA1, APOB	83.96	0.999983876
LPL, APOB	83.96	0.999983876
HTR1A, HTR1B	79.02117647	0.999991913
SYP, SNCA	74.63111111	0.999995944
ERN1, APOA1	74.63111111	0.999995944
CNR1, ADORA1	67.168	0.99999898
BLK, FGR, YES1	10.89210811	0.99999908
APOA1, APOB	53.7344	0.99999968
LPL, APOA1	51.66769231	0.999999984
CBR1, ALDH1A3, ALDH1A2, CRYZ, CBR3	23.63738739	4.46E-04
ALDH1L1, AKR1B10, AKR1B15, AKR1A1, ALDH1L1, ALDH1L2	28.36486486	2.91E-05
ALDH1L1, ALDH1L2	3358.4	0.00901242
RDH8, MAOA, ALDH1A1, AKR1B1, AOX1, HSD1	24.31274131	1.28E-05

TOP2A, GRIN2A, PSEN1, CLU, GRIN1	21.52820513	0.012807144
SERPINA3, APOH, A2M, CLU	50.16280807	0.013736079
GRIN2A, DLG4, A2M, FGFR3, GRIN1	11.43090538	0.1373865
GRIN2A, DLG4, FGFR3, GRIN1	19.72049325	0.195408518
GRIN2A, PSEN1, GRIN1	32.56367162	0.60055057
HSP90AB1, PSEN1, GRIN1	29.35664336	0.675231951
GRIN2A, DLG4, GRIN1	16.14615385	0.972380656
DLG4, GRIN1	143.5213675	0.976700445
APOH, A2M	143.5213675	0.976700445
DLG4, GRIN1	129.1692308	0.984659708
GRIN2A, GRIN1	107.6410256	0.99335124
GRIN2A, GRIN1	92.26373626	0.997118882
GRIN2A, GRIN1	83.33498759	0.998461422
HSP90AB1, CLU	60.07871199	0.999875013
MAPK11, GDNF, ERBB4	32.04580153	0.313815614
NGFR, ADAM17	310.962963	0.57603884
NGFR, GDNF, ERBB4	18.45274725	0.671790067
ADAM17, GDNF, ERBB4	18.01716738	0.688801696
GDNF, ERBB4	124.3851852	0.883167254
NGFR, PRKCA	78.83568075	0.966296011
NGFR, ADAM17	47.43502825	0.996455097
ADAM17, ERBB4	44.07349081	0.997698566
CYP51A1, CYP46A1, LBR	28.36486486	0.013565319
CYP51A1, CYP46A1	533.0793651	0.027155612
CYP51A1, LBR	294.5964912	0.048621711