

Table S3 Enrichment Analysis of Resveratrol-OA PPI Network

Category	Term	Description	Count	%	PValue	Genes
Biological processes	GO:0001501	skeletal system development	32	12.4031	7.28E-28	COL11A2, RARG, TFF3, MMP1, COL1A1
	GO:0043401	steroid hormone metabolic process	21	8.139535	1.33E-22	RARG, TFF3, AR, ERBB4
	GO:0030574	collagen catabolic process	20	7.751938	6.08E-20	MMP1, COL1A1, CNTF, AR, ERBB4
	GO:0006367	transcription initiation from promoter	24	9.302326	8.37E-17	RARG, TFF3, AR, ERBB4, CNTF
	GO:0030198	extracellular matrix organization	26	10.07752	2.32E-16	COL11A1, CNTF, AR, ERBB4, TFF3
	GO:0022617	extracellular matrix structural constituent	18	6.976744	1.09E-15	MMP1, COL1A1, CNTF, AR, ERBB4
	GO:0030199	collagen fibril organization	13	5.03876	3.01E-13	TGFB2, COL1A1, CNTF, AR, ERBB4
	GO:0045893	positive regulation of gene expression	35	13.56589	4.54E-13	SRC, NR1, MAP2K1, TAK1, AR, ERBB4
	GO:0043066	negative regulation of gene expression	32	12.4031	2.36E-12	GSK3B, RARG, TFF3, AR, ERBB4
	GO:0043627	response to estrogen stimulus	14	5.426357	1.30E-11	DTYMK, LRRK2, AR, ERBB4
	GO:0001503	ossification	15	5.813953	1.42E-11	SLC26A2, AR, ERBB4
	GO:0008284	positive regulation of transcription, promoter	31	12.0155	2.27E-11	RARG, ECER1, AR, ERBB4
	GO:0007179	transforming growth factor beta signaling pathway	15	5.813953	1.01E-10	SMAD2, TAK1, AR, ERBB4
	GO:0006954	inflammatory response	27	10.46512	1.34E-10	CRP, CXCL1, AR, ERBB4
	GO:0070374	positive regulation of gene expression	19	7.364341	1.70E-10	MAP2K1, TAK1, AR, ERBB4
	GO:0000187	activation of MAPK cascade	15	5.813953	7.99E-10	MAP2K1, AR, ERBB4
	GO:0010718	positive regulation of biological process	10	3.875969	1.01E-09	SMAD2, CNTF, AR, ERBB4
	GO:0008285	negative regulation of gene expression	26	10.07752	1.75E-09	RARG, CNTF, AR, ERBB4
	GO:0030335	positive regulation of transcription, promoter	18	6.976744	2.92E-09	TGFB1, SMC3, AR, ERBB4
	GO:0030522	intracellular receptor activity	10	3.875969	4.00E-09	AR, THREB1, AR, ERBB4
	GO:0030168	platelet activation	14	5.426357	1.98E-08	SYK, PDPK1, AR, ERBB4
	GO:0050728	negative regulation of gene expression	12	4.651163	2.79E-08	SMAD3, TAK1, AR, ERBB4
	GO:0014068	positive regulation of cell migration	11	4.263566	4.53E-08	TGFB2, EGR1, AR, ERBB4
	GO:0002062	chondrocyte differentiation	9	3.488372	1.01E-07	BMP2, CCN1, AR, ERBB4
	GO:0007165	signal transduction	43	16.66667	1.10E-07	ITK, CXCL1, AR, ERBB4
	GO:0048384	retinoic acid receptor signaling pathway	7	2.713178	1.80E-07	RXRB, RA, AR, ERBB4
	GO:0050900	leukocyte migration	13	5.03876	3.30E-07	MMP1, SFM1, AR, ERBB4
	GO:0042593	glucose homeostasis	12	4.651163	3.66E-07	IL6, RBP4, AR, ERBB4
	GO:0018105	peptidyl-serine phosphorylation	13	5.03876	4.30E-07	GSK3B, SMC3, AR, ERBB4
	GO:0030512	negative regulation of gene expression	10	3.875969	4.80E-07	SMAD2, AR, ERBB4
	GO:0007173	epidermal growth factor receptor signaling pathway	9	3.488372	1.86E-06	ADAM17, AR, ERBB4
	GO:0007169	transmembrane transport	11	4.263566	1.89E-06	ITK, ZAP70, AR, ERBB4
	GO:0001958	endochondral ossification	7	2.713178	2.02E-06	COL1A1, AR, ERBB4
	GO:0001666	response to hypoxia	14	5.426357	2.20E-06	TGFB2, SMC3, AR, ERBB4
	GO:0000165	MAPK cascade	17	6.589147	2.52E-06	MAP2K1, AR, ERBB4
	GO:0008202	steroid metabolic process	8	3.100775	3.38E-06	SULT2B1, AR, ERBB4
	GO:0007183	SMAD protein cascade	5	1.937984	3.41E-06	SMAD2, AR, ERBB4
	GO:0043410	positive regulation of gene expression	10	3.875969	3.63E-06	AR, IL6, BCL2L1, AR, ERBB4
	GO:0060395	SMAD protein signaling pathway	9	3.488372	4.10E-06	SMAD2, TAK1, AR, ERBB4
	GO:0048015	phosphatidylinositol metabolism	11	4.263566	4.68E-06	ERBB4, PIK3CA, AR, ERBB4
	GO:0051384	response to glucose stimulus	9	3.488372	5.88E-06	IL10, BCL2L1, AR, ERBB4
	GO:0010862	positive regulation of transcription, promoter	8	3.100775	7.24E-06	TGFB2, SMC3, AR, ERBB4
	GO:0032496	response to lipid stimulus	13	5.03876	7.57E-06	MAOB, TBL1XR1, AR, ERBB4
	GO:0030282	bone mineralization	7	2.713178	1.06E-05	BMP2, MNAT1, AR, ERBB4
	GO:0032869	cellular response to hormone stimulus	9	3.488372	2.10E-05	PDPK1, SMC3, AR, ERBB4
	GO:0014066	regulation of phosphoinositide cycle	9	3.488372	2.31E-05	ERBB4, LRRK2, AR, ERBB4

GO:0006955	immune response	20	7.751938	2.34E-05	IL10, IL1R
GO:0045780	positive regulation	5	1.937984	3.28E-05	SYK, CA2
GO:0010745	negative regulation	5	1.937984	3.28E-05	CRP, NR1
GO:0060389	pathway-restriction	5	1.937984	3.28E-05	TGFB2, B
GO:0003417	growth plate car	4	1.550388	3.34E-05	COMP, M
GO:0030593	neutrophil chem	8	3.100775	6.07E-05	TGFB2, C
GO:0010887	negative regulation	4	1.550388	6.61E-05	NR1H2, N
GO:0042110	T cell activation	7	2.713178	7.21E-05	FKBP1A, I
GO:0071560	cellular response	7	2.713178	9.16E-05	COL1A1, E
GO:0043552	positive regulation	6	2.325581	9.38E-05	TGFB1, E
GO:0000122	negative regulation	26	10.07752	9.86E-05	RARG, TF
GO:0032331	negative regulation	5	1.937984	1.04E-04	RARG, RA
GO:0030500	regulation of boi	5	1.937984	1.32E-04	ANKH, BC
GO:0001837	epithelial to mes	6	2.325581	1.48E-04	GSK3B, T
GO:0060021	palate development	8	3.100775	1.50E-04	SMAD2, T
GO:0048146	positive regulation	7	2.713178	1.59E-04	CCNA2, T
GO:0045416	positive regulation	4	1.550388	1.81E-04	APOA2, T
GO:0070723	response to chol	4	1.550388	1.81E-04	SMAD2, T
GO:0043065	positive regulation	15	5.813953	1.99E-04	RARG, TC
GO:0007184	SMAD protein i	4	1.550388	2.69E-04	TGFB2, T
GO:0050852	T cell receptor s	10	3.875969	4.25E-04	ITK, ZAP7
GO:0070371	ERK1 and ERK2	5	1.937984	4.28E-04	MAP2K1,
GO:0010575	positive regulation	5	1.937984	6.82E-04	IL1A, TGF
GO:0002224	toll-like receptor	5	1.937984	6.82E-04	CTSK, M
GO:0071347	cellular response	7	2.713178	7.11E-04	IL6, CXCL
GO:0048010	vascular endothel	7	2.713178	7.66E-04	HSP90AA
GO:2000352	negative regulation	5	1.937984	7.87E-04	IL10, ABL
GO:2001275	positive regulation	4	1.550388	8.74E-04	AKT2, NR
GO:0060391	positive regulation	4	1.550388	8.74E-04	SMAD4, T
GO:0006693	prostaglandin me	4	1.550388	8.74E-04	HPGDS, A
GO:0051092	positive regulation	9	3.488372	9.47E-04	AR, IL6, T
GO:0030217	T cell differentiat	5	1.937984	0.001028	ZAP70, LC
GO:0071732	cellular response	4	1.550388	0.0011	CCNA2, C
GO:0048701	embryonic crani	5	1.937984	0.001167	SMAD2, S
GO:0071392	cellular response	5	1.937984	0.001167	IL10, CCN
GO:0016477	cell migration	10	3.875969	0.00124	GSK3B, T
GO:0035556	intracellular sign	16	6.20155	0.001274	SMAD2, C
GO:0032909	regulation of tra	3	1.162791	0.00134	TGFB2, SI
GO:0071364	cellular response	5	1.937984	0.001482	COL1A1, I
GO:0043491	protein kinase B	5	1.937984	0.001482	TGFB1, IL
GO:0070373	negative regulation	6	2.325581	0.001815	PTPN1, SM
GO:0032722	positive regulation	4	1.550388	0.001988	IL6, ADA1
GO:0042523	positive regulation	4	1.550388	0.001988	ERBB4, K
GO:0060749	mammary gland	4	1.550388	0.001988	AR, ERBB
GO:0050714	positive regulation	5	1.937984	0.002059	IL1A, TGF
GO:0050679	positive regulation	6	2.325581	0.002111	IL6, TGFB
GO:0031622	positive regulation	3	1.162791	0.002212	IL1B, PTC
GO:1990314	cellular response	3	1.162791	0.002212	CCNA2, T

	GO:0010936	negative regulati	3	1.162791	0.002212	TGFB2, T
	GO:1905007	positive regulati	3	1.162791	0.002212	TGFB2, T
	GO:0060336	negative regulati	3	1.162791	0.002212	NR1H2, N
	GO:0006950	response to stres	6	2.325581	0.002272	HSP90AA
	GO:0001523	retinoid metabol	6	2.325581	0.002272	RBP4, TTI
	GO:2001240	negative regulati	5	1.937984	0.002281	IL1A, COI
	GO:0033189	response to vitar	4	1.550388	0.002359	ARG1, RA
	GO:0007597	blood coagulatio	4	1.550388	0.002359	F9, F10, F
	GO:0033280	response to vitar	4	1.550388	0.002359	TGFB1, B
	GO:0032720	negative regulati	5	1.937984	0.00252	IL10, GST
	GO:0001568	blood vessel dev	5	1.937984	0.00252	COL1A1, C
	GO:2001237	negative regulati	5	1.937984	0.00252	AR, SRC, C
	GO:0038128	ERBB2 signalin	5	1.937984	0.00252	HSP90AA
	GO:0032332	positive regulati	4	1.550388	0.00277	SMAD3, S
	GO:0045672	positive regulati	4	1.550388	0.00277	CA2, TNF
	GO:0043124	negative regulati	5	1.937984	0.003047	GSTP1, N
	GO:0038096	Fc-gamma recep	8	3.100775	0.003201	HSP90AA
	GO:0017015	regulation of tra	4	1.550388	0.003223	SMAD2, S
	GO:0061037	negative regulati	3	1.162791	0.003284	TGFB2, FI
	GO:0032964	collagen biosynt	3	1.162791	0.003284	COL1A1, C
	GO:0002740	negative regulati	3	1.162791	0.003284	IL10, APO
	GO:0007182	common-partner	3	1.162791	0.003284	SMAD2, T
	GO:0001957	intramembranou	3	1.162791	0.003284	COL1A1, I
	GO:0045599	negative regulati	5	1.937984	0.003645	IL6, TGFB
	GO:0042346	positive regulati	4	1.550388	0.003719	IL1B, PTC
	GO:0046427	positive regulati	4	1.550388	0.004258	IL10, IL6,
	GO:0045453	bone resorption	4	1.550388	0.004258	SRC, CTS
	GO:0071639	positive regulati	3	1.162791	0.004552	IL1A, IL1I
	GO:0032755	positive regulati	5	1.937984	0.004683	IL1A, IL6,
Cell Components						
	GO:0005576	extracellular reg	87	33.72093	4.29E-29	SERPINA1
	GO:0005615	extracellular spa	74	28.68217	1.01E-24	IL1RN, SE
	GO:0005578	proteinaceous ex	34	13.17829	9.49E-22	SERPINA1
	GO:0005829	cytosol	101	39.14729	2.64E-15	PNMT, HIF
	GO:0005788	endoplasmic reti	24	9.302326	3.61E-15	BCHE, SE
	GO:0031012	extracellular mat	26	10.07752	7.22E-13	AEBP1, H
	GO:0070062	extracellular exc	84	32.55814	6.79E-12	IL1RN, SE
	GO:0005581	collagen trimer	15	5.813953	3.88E-11	MMP1, C
	GO:0031093	platelet alpha gr	9	3.488372	9.36E-07	CFD, TGF
	GO:0031234	extrinsic compoi	9	3.488372	4.85E-06	ITK, ZAP70
	GO:0009986	cell surface	23	8.914729	8.88E-06	HSP90AA
	GO:0043235	receptor comple	11	4.263566	1.24E-05	RXRA, SM
	GO:0000790	nuclear chromat	12	4.651163	9.28E-05	SMAD2, A
	GO:0005737	cytoplasm	100	38.75969	3.23E-04	IL1RN, NI
	GO:0005654	nucleoplasm	61	23.64341	3.61E-04	RARG, TF
	GO:0005925	focal adhesion	16	6.20155	4.43E-04	MAP2K1,
	GO:0005594	collagen type IX	3	1.162791	5.84E-04	COL9A1, C
	GO:0045121	membrane raft	11	4.263566	6.88E-04	BACE1, D

	GO:0043234	protein complex	16	6.20155	7.59E-04	HSP90AA
	GO:0090575	RNA polymeras	5	1.937984	0.00113	SMAD4, F
	GO:0036021	endolysosome lu	3	1.162791	0.001158	CTSK, CT
	GO:0005796	Golgi lumen	7	2.713178	0.002341	ACAN, TC
	GO:0005911	cell-cell junctior	9	3.488372	0.003033	ITK, ZAP7
	GO:0005886	plasma membran	77	29.84496	0.004931	GSK3B, II
Molecular Function	GO:0003707	steroid hormone	24	9.302326	1.06E-27	RARG, TF
	GO:0005201	extracellular mat	17	6.589147	2.75E-15	COL11A1,
	GO:0004879	RNA polymeras	14	5.426357	2.85E-15	NR1H2, N
	GO:0008270	zinc ion binding	51	19.76744	1.76E-11	RARG, TF
	GO:0008144	drug binding	14	5.426357	1.08E-10	HSP90AB
	GO:0004713	protein tyrosine	17	6.589147	1.80E-10	MAP2K1,
	GO:0005125	cytokine activity	18	6.976744	1.54E-09	IL10, TGF
	GO:0004222	metalloendopept	15	5.813953	1.72E-09	MME, MN
	GO:0005496	steroid binding	9	3.488372	4.34E-09	AR, SULT
	GO:0005518	collagen binding	11	4.263566	2.09E-08	COMP, SM
	GO:0005524	ATP binding	52	20.15504	2.75E-08	GSK3B, I
	GO:0005515	protein binding	176	68.21705	6.78E-08	IL1RN, RC
	GO:0034713	type I transformi	6	2.325581	9.25E-08	SMAD2, F
	GO:0043565	sequence-specifi	27	10.46512	9.51E-08	RARG, TF
	GO:0004672	protein kinase ac	22	8.527132	1.42E-07	GSK3B, M
	GO:0004716	receptor signalin	6	2.325581	1.83E-07	SYK, ERB
	GO:0046332	SMAD binding	9	3.488372	2.30E-07	SMAD2, F
	GO:0003708	retinoic acid rece	5	1.937984	2.55E-07	RARG, R3
	GO:0008237	metallopeptidase	11	4.263566	3.94E-07	ADAMTS
	GO:0030020	extracellular mat	5	1.937984	7.57E-07	COL2A1, I
Signaling Pathway	hsa04151	PI3K-Akt signal	39	15.11628	2.72E-13	GSK3B, H
	hsa04068	FoxO signaling]	25	9.689922	3E-13	PIK3R1, E
	hsa04380	Osteoclast differ	22	8.527132	9.07E-11	TGFB2, M
	hsa05323	Rheumatoid arth	17	6.589147	2.63E-09	TGFB2, T
	hsa04350	TGF-beta signal	15	5.813953	8.57E-08	SMAD2, T
	hsa03320	PPAR signaling	13	5.03876	3.28E-07	PDPK1, M
	hsa04660	T cell receptor s	15	5.813953	7.97E-07	IL10, GSK
	hsa04620	Toll-like recepto	14	5.426357	8.99E-06	MAP2K1,
	hsa04010	MAPK signaling	22	8.527132	9.86E-06	TGFB2, M
	hsa04668	TNF signaling p	14	5.426357	9.98E-06	MAP2K1,
	hsa04064	NF-kappa B sign	12	4.651163	3.36E-05	ZAP70, C
	hsa04370	VEGF signaling	10	3.875969	5.15E-05	MAP2K1,
	hsa04066	HIF-1 signaling	12	4.651163	8.44E-05	IL6, MAP
	hsa04060	Cytokine-cytoki	18	6.976744	0.000561	IL10, TGF
	hsa04920	Adipocytokine s	9	3.488372	0.000808	RXRB, M
	hsa04150	mTOR signaling	8	3.100775	0.001238	PDPK1, A
	hsa04152	AMPK signaling	11	4.263566	0.002665	CCNA2, P
	hsa04062	Chemokine sign	13	5.03876	0.006948	GSK3B, I
	hsa04662	B cell receptor s	7	2.713178	0.013722	GSK3B, M
	hsa04640	Hematopoietic c	7	2.713178	0.038027	IL1A, IL6,

Fold Enrichment FDR

15.38125	1.66E-24
24.26089	1.51E-19
20.57843	4.62E-17
10.39752	4.77E-14
8.735334	1.06E-13
15.59628	4.15E-13
21.95033	9.81E-11
4.475309	1.29E-10
4.631278	5.98E-10
14.18329	2.95E-09
12.34706	2.95E-09
4.380645	4.30E-09
10.73657	1.65E-08
4.691231	2.03E-08
7.149535	2.28E-08
9.231446	7.92E-08
19.95484	9.40E-08
4.323549	1.53E-07
6.441944	2.46E-07
17.32921	3.26E-07
8.016641	1.41E-06
10.00268	1.87E-06
11.14401	2.79E-06
15.19638	6.04E-06
2.438925	6.43E-06
25.60871	1.00E-05
7.016908	1.79E-05
7.823879	1.94E-05
6.848502	2.23E-05
10.28922	2.43E-05
10.58319	8.63E-05
7.545425	8.63E-05
17.72911	9.02E-05
5.359964	9.63E-05
4.272774	1.09E-04
12.25135	1.32E-04
41.15686	1.32E-04
8.129751	1.38E-04
9.559013	1.53E-04
6.833592	1.72E-04
9.117828	2.13E-04
10.97516	2.58E-04
5.219895	2.65E-04
13.55755	3.68E-04
7.696868	6.55E-04
7.59819	7.11E-04

3.128313	7.12E-04
25.3273	9.36E-04
25.3273	9.36E-04
25.3273	9.36E-04
52.68078	9.41E-04
7.981937	0.001668
43.90065	0.001795
9.807593	0.001912
9.407283	0.002319
12.74535	0.002349
2.377952	0.002442
19.36794	0.002555
18.29194	0.00308
11.62076	0.003408
6.931682	0.003419
8.536238	0.003584
32.92549	0.003895
32.92549	0.003895
3.292549	0.00425
29.2671	0.005372
4.449391	0.008066
13.71895	0.008066
12.19463	0.011272
12.19463	0.011272
6.49235	0.011496
6.402179	0.012298
11.7591	0.012541
20.26184	0.013654
20.26184	0.013654
20.26184	0.013654
4.456081	0.01468
10.97516	0.015733
18.81457	0.016615
10.62113	0.017385
10.62113	0.017385
3.828545	0.018358
2.614431	0.018747
49.38824	0.019099
9.977421	0.020599
9.977421	0.020599
6.81217	0.024489
15.49435	0.0259
15.49435	0.0259
15.49435	0.0259
9.145969	0.026669
6.585098	0.027197
39.51059	0.027705
39.51059	0.027705

39.51059 0.027705
39.51059 0.027705
39.51059 0.027705
6.477146 0.028113
6.477146 0.028113
8.898781 0.028113
14.63355 0.028458
14.63355 0.028458
14.63355 0.028458
8.664603 0.029611
8.664603 0.029611
8.664603 0.029611
8.664603 0.029611
13.86336 0.031473
13.86336 0.031473
8.231373 0.03422
4.148093 0.034667
13.1702 0.034667
32.92549 0.034667
32.92549 0.034667
32.92549 0.034667
32.92549 0.034667
7.839402 0.037602
12.54304 0.037849
11.97291 0.041312
11.97291 0.041312
28.22185 0.043426
7.316776 0.044493

3.83181 1.15E-26
3.895603 1.35E-22
8.996109 8.48E-20
2.160471 1.77E-13
8.863813 1.94E-13
6.228626 3.23E-11
2.118991 2.60E-10
11.5615 1.30E-09
11.60354 2.79E-05
9.385214 1.30E-04
3.009117 2.16E-04
6.141855 2.78E-04
4.408943 0.001913
1.357919 0.006192
1.553714 0.006448
2.901709 0.007425
70.91051 0.00921
3.786483 0.010243

2.753806	0.01071
10.74402	0.014773
53.18288	0.014773
5.170558	0.028522
3.710433	0.035343
1.324948	0.053651

28.15064	6.01E-25
16.6663	5.39E-13
25.5441	5.39E-13
2.865634	2.51E-09
12.09984	1.23E-08
8.395805	1.71E-08
6.717766	1.22E-07
8.719225	1.22E-07
21.89494	2.74E-07
12.04222	1.19E-06
2.28469	1.42E-06
1.31594	3.21E-06
43.78988	3.86E-06
3.423726	3.86E-06
4.025254	5.38E-06
39.41089	6.49E-06
13.74799	7.68E-06
65.68482	8.06E-06
8.920161	1.18E-05
54.73735	2.15E-05

3.927404	2.28E-11
6.481796	2.28E-11
5.834606	2.58E-09
6.711605	4.62E-08
6.204004	1.03E-06
6.741067	3.12E-06
5.211364	6.99E-06
4.588622	6.03E-05
3.02108	6.32E-05
4.545738	6.32E-05
4.792059	0.000166
5.695479	0.000235
4.342803	0.00037
2.573513	0.002122
4.466883	0.00271
4.792059	0.003878
3.107046	0.007411
2.428234	0.018003
3.524594	0.03359
2.795367	0.082573