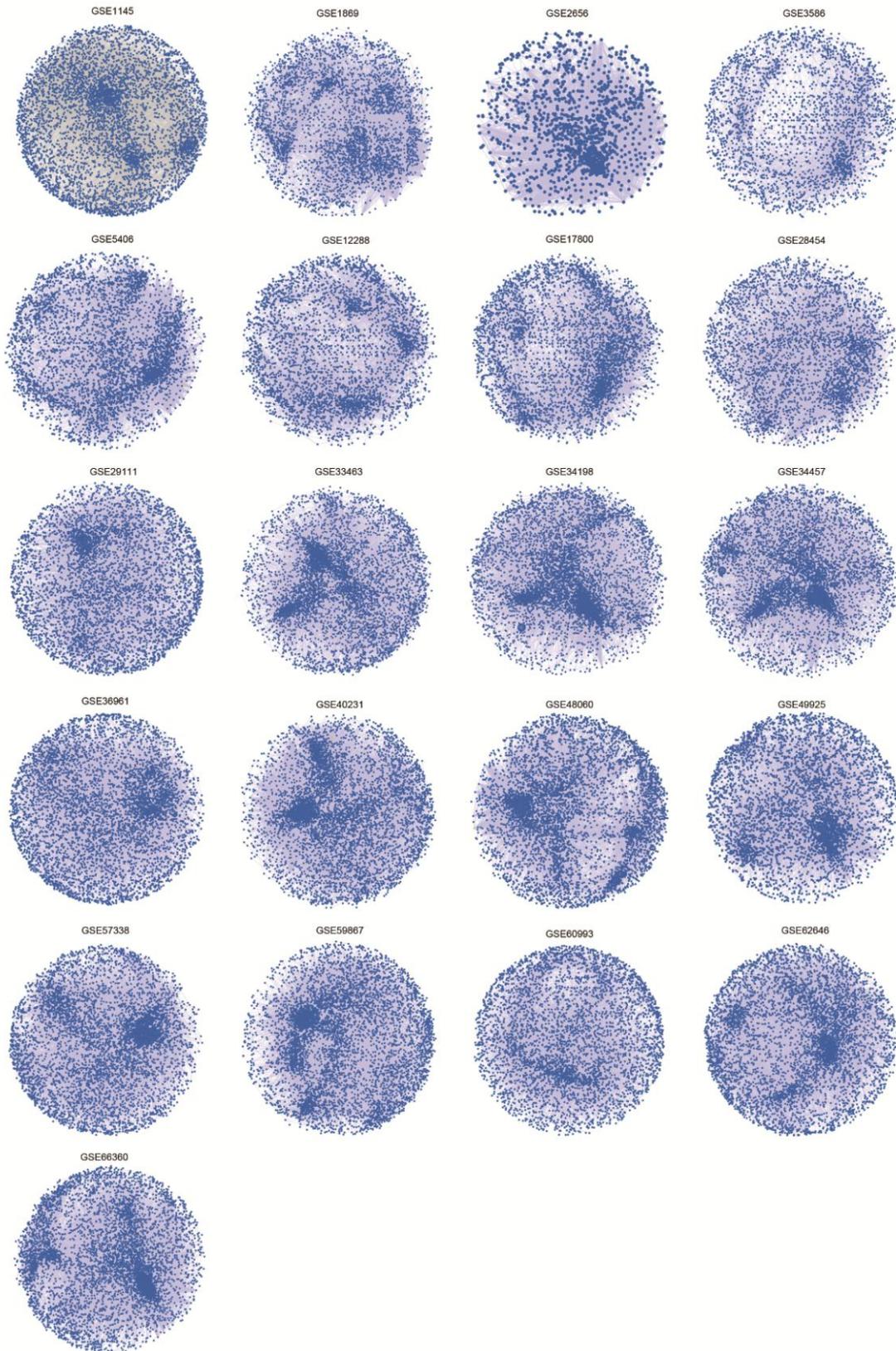


The global view of mRNA related ceRNA cross-talks across cardiovascular diseases

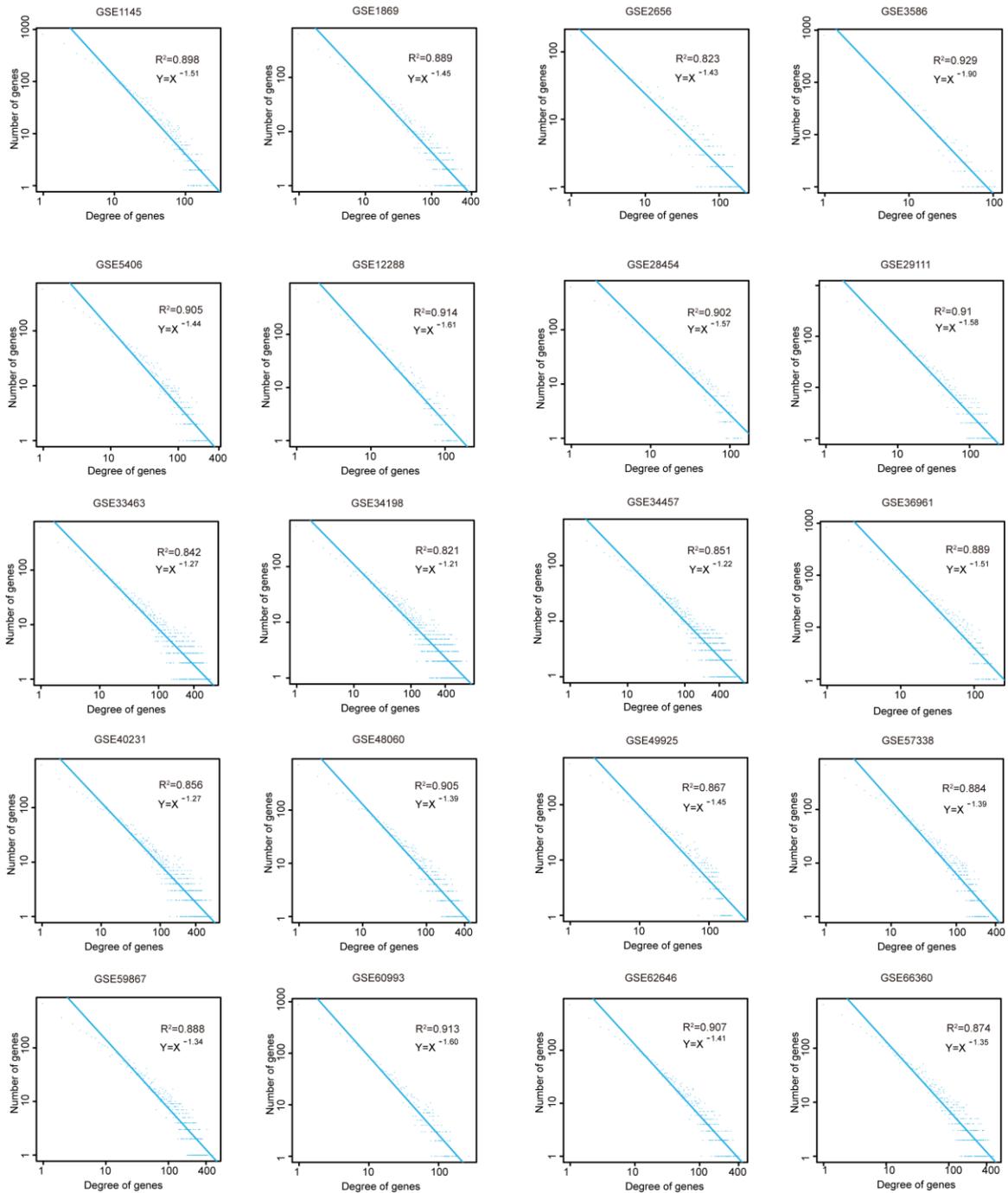
Chao Song^{1,†}, Jian Zhang^{2,†}, Hanping Qi^{1,†}, Chenchen Feng², Yunping Chen¹, Yonggang Cao¹,
Lina Ba¹, Bo Ai², Qiuyu Wang², Wei Huang¹, Chunquan Li^{2,*}, Hongli Sun^{1,*}

¹ Department of Pharmacology, Harbin Medical University-Daqing, Daqing, 163319, China

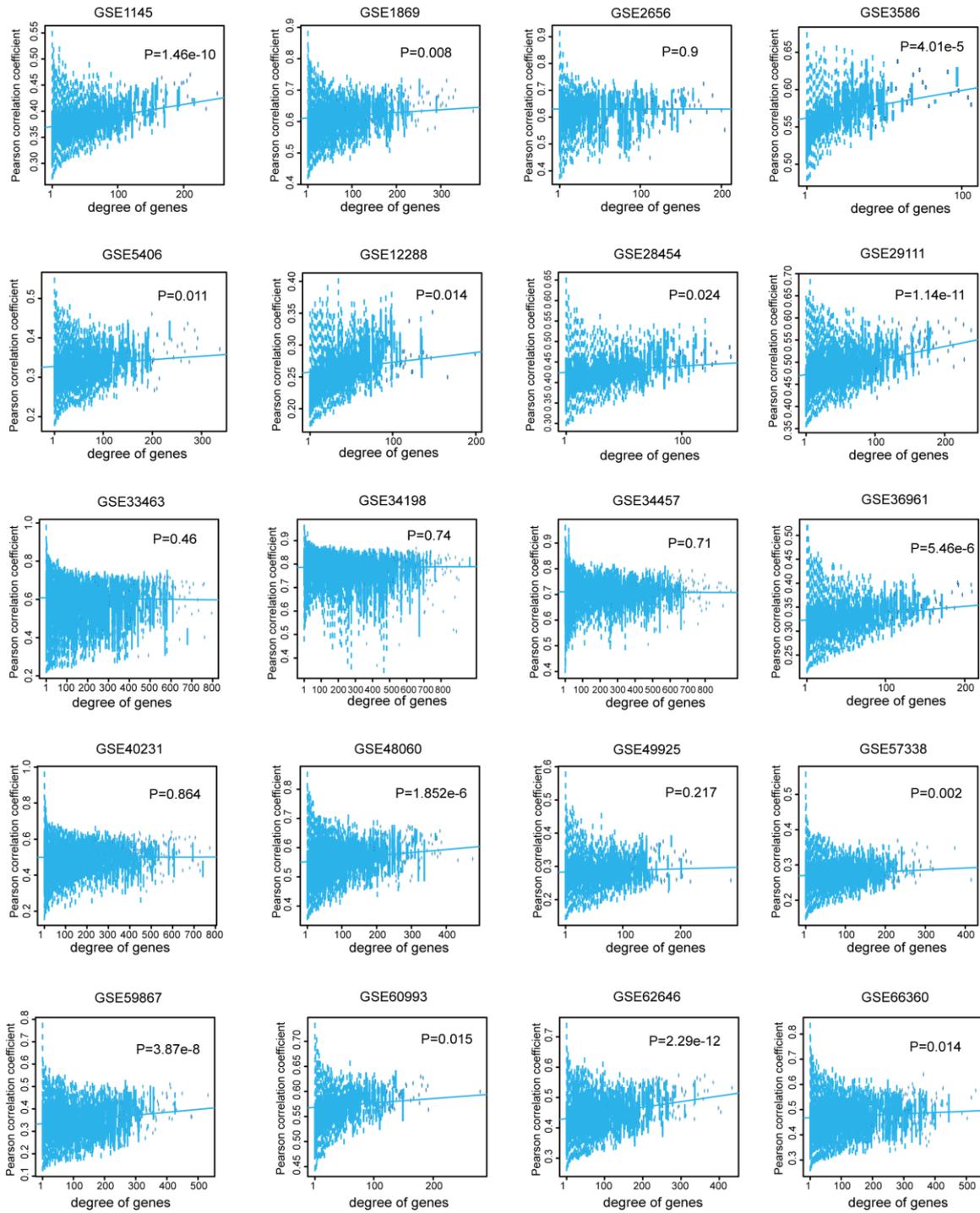
² Department of Medical Informatics, Harbin Medical University-Daqing, Daqing, 163319, China.



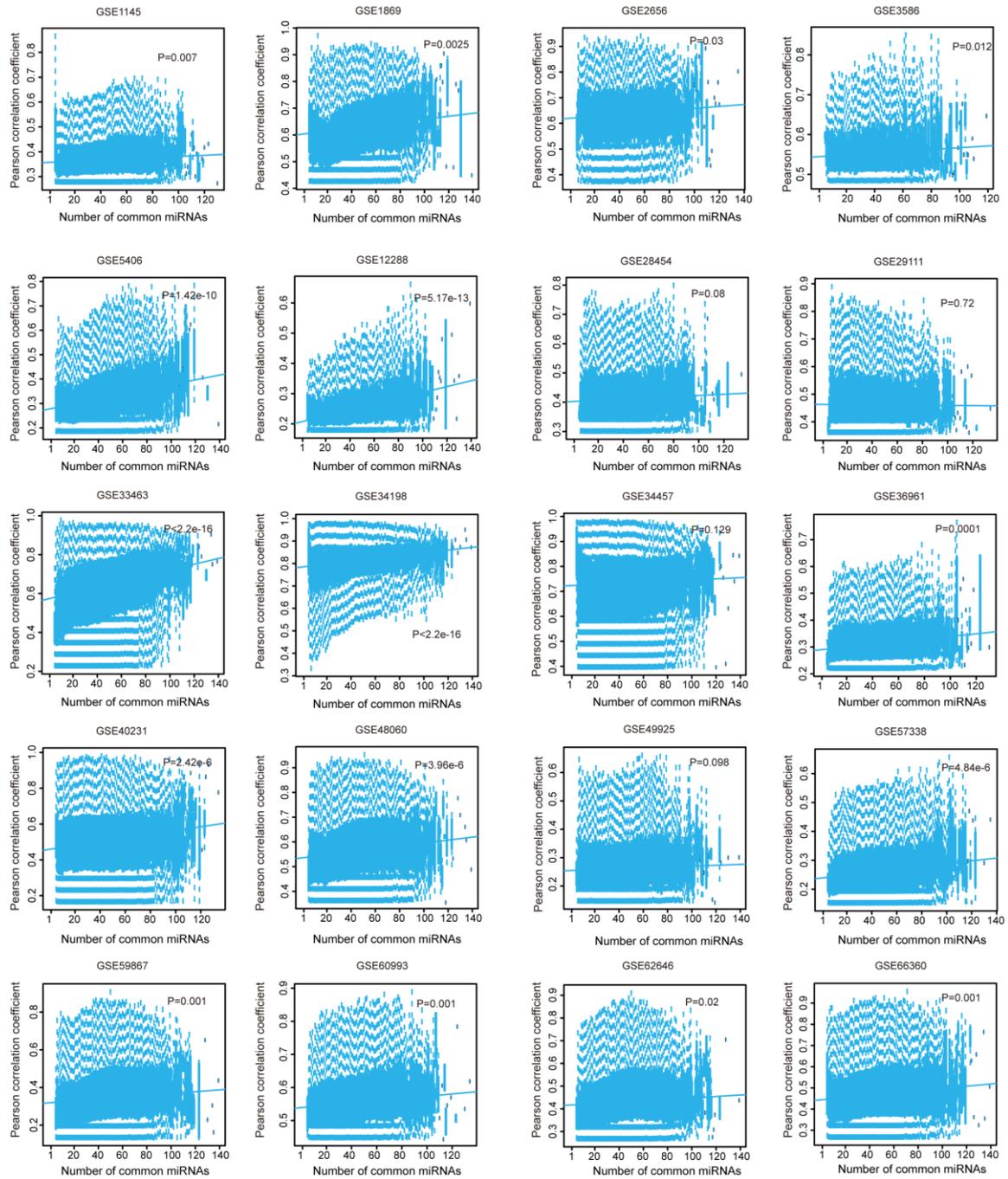
Supplementary Figure S1: The view of ceRNA networks. In our study, we performed 21 ceRNA networks from 8 CVDs and networks were visualized by Cytoscape.



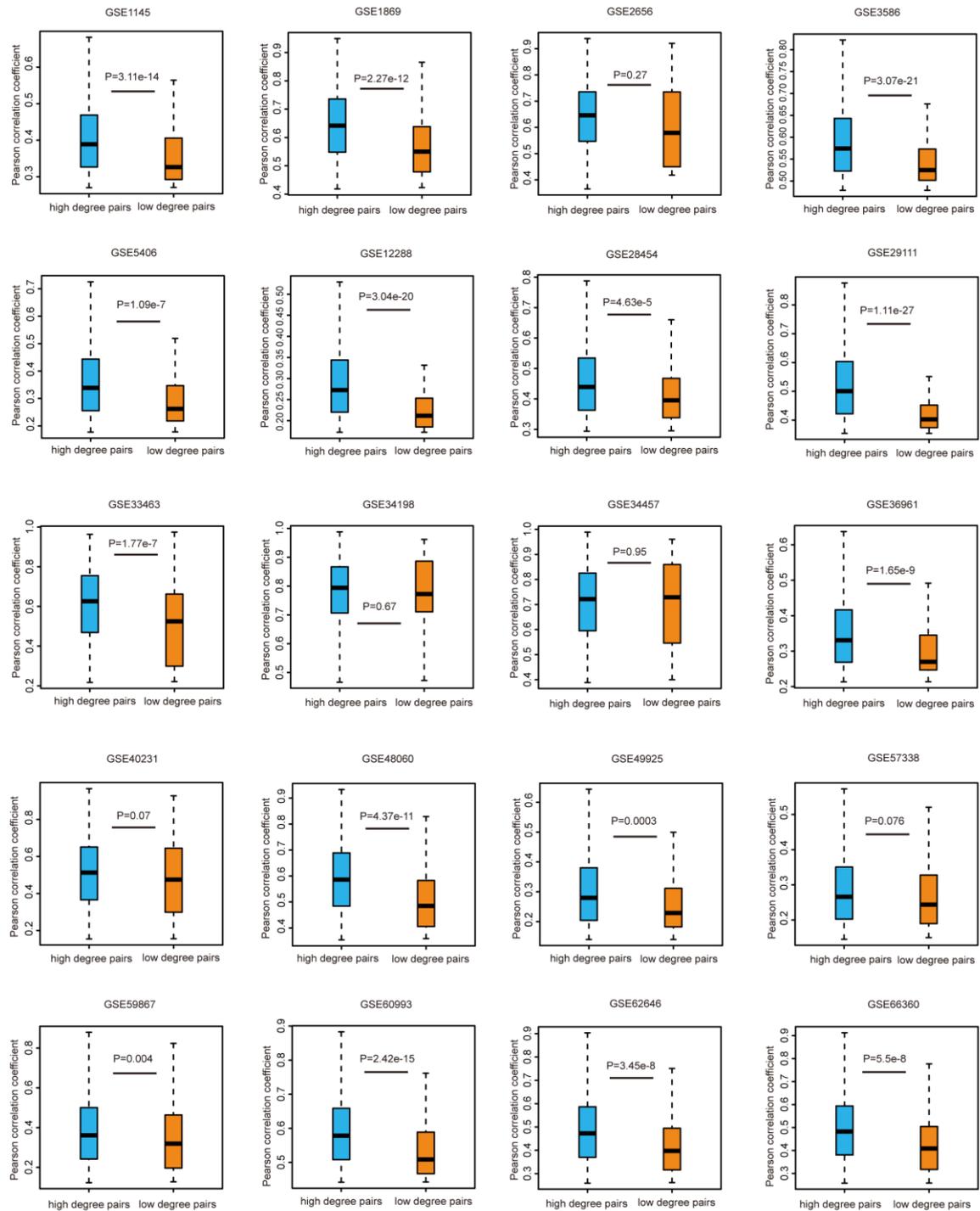
Supplementary Figure S2: Degree distributions of ceRNA networks. All these ceRNAs were followed power-law distributions, indicating that these ceRNA networks were scale-free.



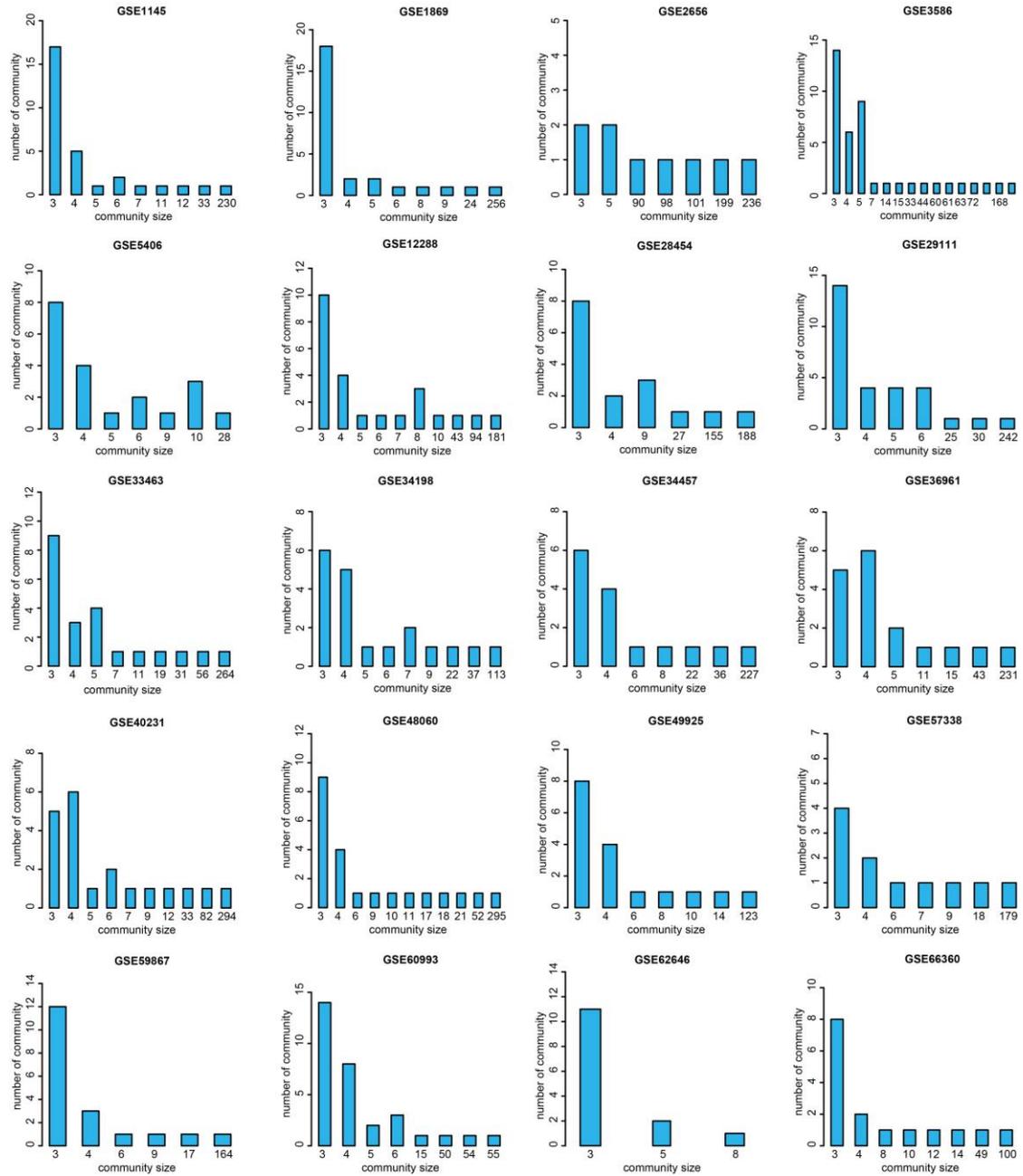
Supplementary Figure S3: ceRNAs with high degree were strongly co-expressed than others.



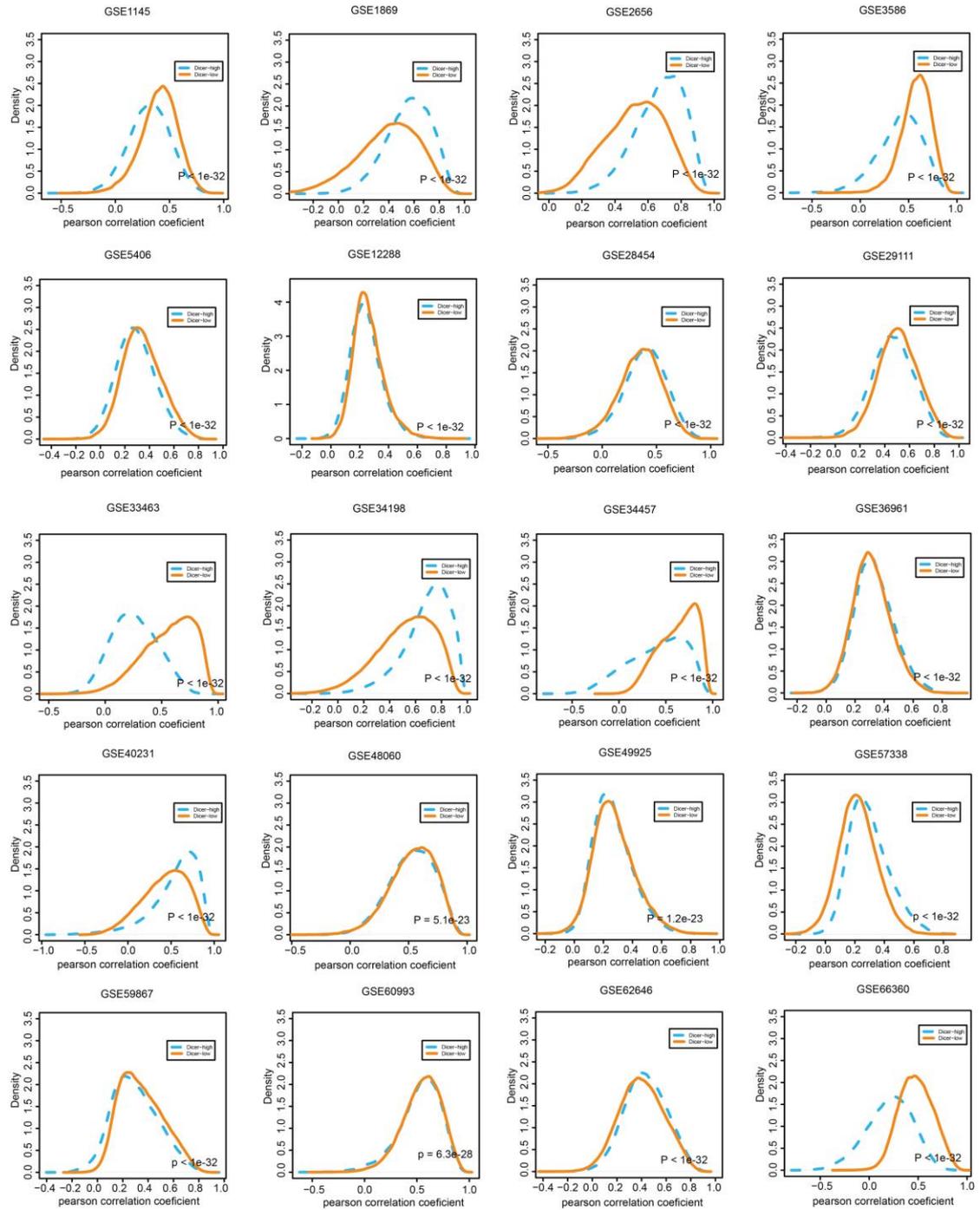
Supplementary Figure S4: ceRNA pairs shared more miRNAs were strongly co-expressed than others.



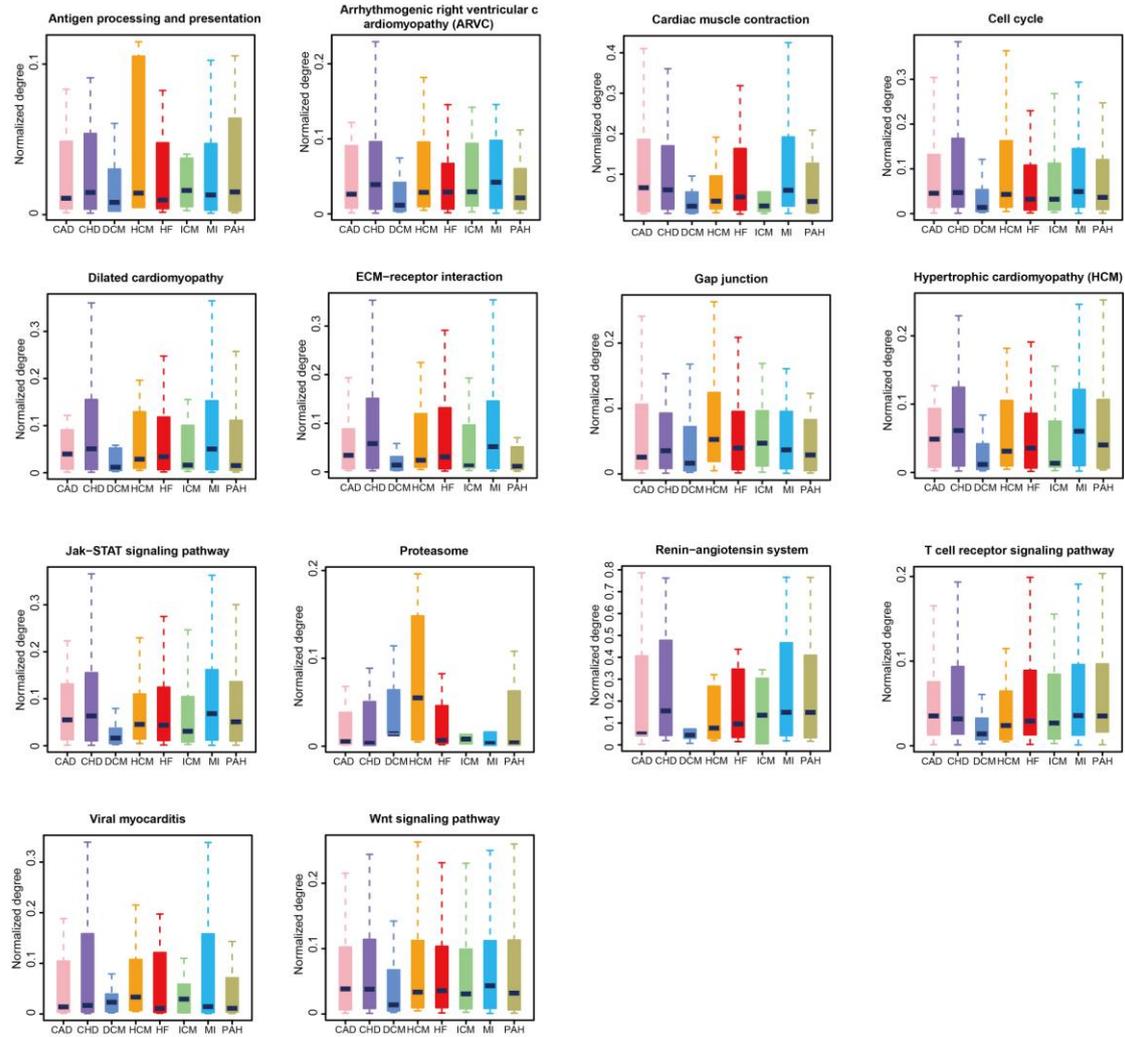
Supplementary Figure S5: ceRNA pairs with high degree were strongly co-expressed than others.



Supplementary Figure S6: ceRNAs were likely to exert functions in small communities.



Supplementary Figure S7: ceRNAs were likely to co-express in Dicer-low groups.



Supplementary Figure S8: Normalized degree of ceRNAs mapped in each CVD related pathways.

Supplementary Table S1

GSE	p-value	FDR	GSE	p-value	FDR
GSE1145	0.00999881	0.04279533	GSE36961	0.01	0.041233
GSE12288	0.00999893	0.05070619	GSE40231	0.009998	0.012222
GSE17800	0.009999983	0.06984682	GSE48060	0.01	0.022985
GSE1869	0.009998259	0.02478318	GSE49925	0.01	0.019608
GSE2656	0.009997529	0.01210045	GSE5406	0.01	0.02285
GSE28454	0.009999107	0.03521767	GSE57338	0.009998	0.022185
GSE29111	0.009999147	0.08085013	GSE59867	0.009999	0.014418
GSE33463	0.009997801	0.0136186	GSE60993	0.009996	0.07749
GSE34198	0.009990152	0.01001249	GSE62646	0.01	0.023343
GSE34457	0.009998558	0.01073682	GSE66360	0.01	0.017437
GSE3586	0.009998676	0.1658121			

Supplementary Table S2

Disease	Disease name	GSE number	Platform	Samples	Number of edges	Number of nodes
CAD	Coronary artery disease	GSE40231	GPL570	278	236986	6120
		GSE12288	GPL96	222	25491	4053
HCM	Hypertrophic cardiomyopathy	GSE36961	GPL15389	145	50302	5432
HF	Heart failure	GSE1145	GPL570	90	52279	5681
		GSE2656	GPL2041	49	17940	1192
		GSE5406	GPL96	210	57256	4474
		GSE57338	GPL11532	313	95542	5675
DCM	Dilated cardiomyopathy	GSE3586	GPL3050	28	8761	3061
		GSE17800	GPL570	48	40547	5061
MI	Myocardial infarction	GSE48060	GPL570	52	101896	5832
		GSE60993	GPL6884	33	32806	4892
		GSE62646	GPL6244	98	91534	5595
		GSE66360	GPL570	99	134936	5991
		GSE28454	GPL6883	76	27271	3780
		GSE29111	GPL570	52	40189	5173
		GSE34198	GPL6102	97	356446	6033
		GSE59867	GPL6244	436	136969	5755
PAH	Pulmonary hypertension	GSE49925	GPL10558	338	52116	4115
		GSE33463	GPL6947	140	236397	6026
ICM	Ischemic cardiomyopathy	GSE1869	GPL96	37	57922	4330
CHD	Congenital Heart Disease	GSE34457	GPL6102	43	332679	6033

Supplementary Table S3

pathwayId	pathwayName	annMoleculeRatio	annBgRatio	pvalue
path:04110_8	Cell cycle	5/688	28/21796	0.001661
path:04920_4	Adipocytokine signaling pathway	4/688	18/21796	0.002115
path:04010_18	MAPK signaling pathway	5/688	30/21796	0.002286
path:00600_2	Sphingolipid metabolism	5/688	31/21796	0.002656
path:04720_4	Long-term potentiation	7/688	60/21796	0.00274
path:04060_54	Cytokine-cytokine receptor interaction	2/688	3/21796	0.002922
path:04140_2	Regulation of autophagy	2/688	3/21796	0.002922
path:04920_7	Adipocytokine signaling pathway	5/688	32/21796	0.003067
path:04062_4	Chemokine signaling pathway	5/688	33/21796	0.003522
path:04010_12	MAPK signaling pathway	5/688	34/21796	0.004024
path:04010_13	MAPK signaling pathway	5/688	34/21796	0.004024

path:04920_3	Adipocytokine signaling pathway	5/688	34/21796	0.004024
path:04150_2	mTOR signaling pathway	5/688	35/21796	0.004575
path:04141_21	Protein processing in endoplasmic reticulum	4/688	22/21796	0.004575
path:04622_1	RIG-I-like receptor signaling pathway	4/688	23/21796	0.005402
path:04622_6	RIG-I-like receptor signaling pathway	3/688	12/21796	0.005566
path:00970_1	Aminoacyl-tRNA biosynthesis	2/688	4/21796	0.005722
path:04010_1	MAPK signaling pathway	5/688	37/21796	0.005834
path:04010_4	MAPK signaling pathway	5/688	38/21796	0.006547
path:04720_5	Long-term potentiation	6/688	54/21796	0.006905
path:04270_6	Vascular smooth muscle contraction	3/688	13/21796	0.007068
path:04620_5	Toll-like receptor signaling pathway	3/688	13/21796	0.007068
path:05145_12	Toxoplasmosis	3/688	13/21796	0.007068
path:04350_6	TGF-beta signaling pathway	4/688	25/21796	0.007343
path:04720_3	Long-term potentiation	6/688	56/21796	0.008234
path:04350_1	TGF-beta signaling pathway	4/688	26/21796	0.008465
path:04670_18	Leukocyte transendothelial migration	4/688	26/21796	0.008465
path:04670_20	Leukocyte transendothelial migration	4/688	26/21796	0.008465
path:04141_16	Protein processing in endoplasmic reticulum	3/688	14/21796	0.008787
path:04141_23	Protein processing in endoplasmic reticulum	3/688	14/21796	0.008787
path:05215_5	Prostate cancer	5/688	41/21796	0.009048
path:05210_4	Colorectal cancer	2/688	5/21796	0.009338

Supplementary Table S4

pathwayId	pathwayName	annMoleculeRatio	annBgRatio	pvalue
path:04350_8	TGF-beta signaling pathway	6/42	27/26232	3.35E-12
path:04110_16	Cell cycle	6/42	47/26232	1.19E-10
path:04350_1	TGF-beta signaling pathway	5/42	25/26232	4.27E-10
path:04110_11	Cell cycle	5/42	46/26232	1.07E-08
path:04110_15	Cell cycle	5/42	47/26232	1.20E-08
path:04110_12	Cell cycle	5/42	51/26232	1.83E-08
path:04110_3	Cell cycle	5/42	55/26232	2.70E-08
path:04350_6	TGF-beta signaling pathway	4/42	25/26232	7.01E-08
path:04010_3	MAPK signaling pathway	5/42	69/26232	8.57E-08
path:04114_8	Oocyte meiosis	4/42	28/26232	1.13E-07
path:04110_14	Cell cycle	4/42	30/26232	1.51E-07
path:04722_5	Neurotrophin signaling pathway	4/42	31/26232	1.73E-07
path:04914_4	Progesterone-mediated oocyte maturation	3/42	10/26232	4.54E-07
path:04722_4	Neurotrophin signaling pathway	4/42	42/26232	6.08E-07
path:04010_24	MAPK signaling pathway	4/42	47/26232	9.63E-07
path:04144_9	Endocytosis	3/42	15/26232	1.71E-06
path:04350_4	TGF-beta signaling pathway	3/42	15/26232	1.71E-06

path:04722_8	Neurotrophin signaling pathway	3/42	16/26232	2.11E-06
path:04010_22	MAPK signaling pathway	4/42	63/26232	3.16E-06
path:04010_23	MAPK signaling pathway	4/42	67/26232	4.04E-06
path:04350_5	TGF-beta signaling pathway	3/42	21/26232	4.97E-06
path:04350_7	TGF-beta signaling pathway	3/42	22/26232	5.75E-06
path:00512_1	Mucin type O-Glycan biosynthesis	3/42	26/26232	9.67E-06
path:04144_2	Endocytosis	3/42	37/26232	2.85E-05
path:04110_1	Cell cycle	3/42	40/26232	3.62E-05
path:04010_11	MAPK signaling pathway	3/42	56/26232	9.97E-05
path:04010_10	MAPK signaling pathway	3/42	57/26232	0.000105
path:04914_2	Progesterone-mediated oocyte maturation	2/42	10/26232	0.000112
path:04720_2	Long-term potentiation	3/42	60/26232	0.000123
path:04720_4	Long-term potentiation	3/42	60/26232	0.000123
path:05134_9	Legionellosis	2/42	11/26232	0.000136
path:04722_3	Neurotrophin signaling pathway	3/42	69/26232	0.000186
path:04914_7	Progesterone-mediated oocyte maturation	2/42	13/26232	0.000193
path:05145_11	Toxoplasmosis	2/42	13/26232	0.000193
path:04114_1	Oocyte meiosis	2/42	14/26232	0.000225
path:04114_2	Oocyte meiosis	2/42	14/26232	0.000225
path:04141_16	Protein processing in endoplasmic reticulum	2/42	14/26232	0.000225
path:04144_10	Endocytosis	2/42	14/26232	0.000225
path:04110_10	Cell cycle	2/42	16/26232	0.000296
path:04012_12	ErbB signaling pathway	2/42	17/26232	0.000335
path:04064_4	NF-kappa B signaling pathway	2/42	18/26232	0.000377
path:04110_4	Cell cycle	2/42	19/26232	0.000421
path:05164_15	Influenza A	2/42	19/26232	0.000421
path:04914_6	Progesterone-mediated oocyte maturation	2/42	21/26232	0.000515
path:04010_17	MAPK signaling pathway	2/42	22/26232	0.000566
path:04141_21	Protein processing in endoplasmic reticulum	2/42	22/26232	0.000566
path:04010_19	MAPK signaling pathway	2/42	23/26232	0.00062
path:04150_5	mTOR signaling pathway	2/42	23/26232	0.00062
path:04150_3	mTOR signaling pathway	2/42	28/26232	0.000921
path:04210_7	Apoptosis	2/42	28/26232	0.000921
path:04150_8	mTOR signaling pathway	2/42	30/26232	0.001058
path:04012_3	ErbB signaling pathway	2/42	32/26232	0.001204
path:04012_4	ErbB signaling pathway	2/42	32/26232	0.001204
path:04010_20	MAPK signaling pathway	2/42	33/26232	0.00128
path:04010_1	MAPK signaling pathway	2/42	37/26232	0.001609

path:04910_2	Insulin signaling pathway	2/42	39/26232	0.001786
path:04713_11	Circadian entrainment	2/42	42/26232	0.002069
path:04012_1	ErbB signaling pathway	2/42	43/26232	0.002168
path:04010_9	MAPK signaling pathway	2/42	44/26232	0.002269
path:04012_11	ErbB signaling pathway	2/42	45/26232	0.002372
path:04012_7	ErbB signaling pathway	2/42	47/26232	0.002585
path:04713_13	Circadian entrainment	2/42	47/26232	0.002585
path:04713_14	Circadian entrainment	2/42	49/26232	0.002806
path:04713_3	Circadian entrainment	2/42	50/26232	0.00292
path:04672_12	Intestinal immune network for IgA production	1/42	2/26232	0.0032
path:04380_3	Osteoclast differentiation	2/42	53/26232	0.003275
path:04010_16	MAPK signaling pathway	2/42	54/26232	0.003397
path:04713_9	Circadian entrainment	2/42	55/26232	0.003522
path:04010_15	MAPK signaling pathway	2/42	59/26232	0.004041
path:04010_2	MAPK signaling pathway	2/42	61/26232	0.004314
path:04510_12	Focal adhesion	2/42	63/26232	0.004594
path:04910_7	Insulin signaling pathway	2/42	64/26232	0.004738
path:04150_4	mTOR signaling pathway	1/42	3/26232	0.004796
path:04151_5	PI3K-Akt signaling pathway	2/42	71/26232	0.005799
path:04010_14	MAPK signaling pathway	1/42	4/26232	0.006389
path:04380_14	Osteoclast differentiation	1/42	4/26232	0.006389
path:05142_7	Chagas disease (American trypanosomiasis)	1/42	4/26232	0.006389
path:05323_5	Rheumatoid arthritis	1/42	4/26232	0.006389
path:04510_5	Focal adhesion	2/42	75/26232	0.006449
path:04060_23	Cytokine-cytokine receptor interaction	1/42	5/26232	0.007981
path:04145_3	Phagosome	1/42	5/26232	0.007981
path:04612_6	Antigen processing and presentation	1/42	5/26232	0.007981
path:04726_4	Serotonergic synapse	1/42	5/26232	0.007981
path:05210_4	Colorectal cancer	1/42	5/26232	0.007981
path:05220_5	Chronic myeloid leukemia	1/42	5/26232	0.007981
path:04320_6	Dorso-ventral axis formation	1/42	6/26232	0.009569
path:04350_2	TGF-beta signaling pathway	1/42	6/26232	0.009569
path:04350_3	TGF-beta signaling pathway	1/42	6/26232	0.009569
path:05161_25	Hepatitis B	1/42	6/26232	0.009569
path:05169_5	Epstein-Barr virus infection	1/42	6/26232	0.009569

Supplementary Table S5

pathwayId	pathwayName	annMoleculeRatio	annBgRatio	pvalue
path:04612_2	Antigen processing and presentation	1/38	8/26232	0.011532
path:04141_8	Protein processing in endoplasmic reticulum	1/38	12/26232	0.017249

path:04722_8	Neurotrophin signaling pathway	1/38	16/26232	0.022934
path:04916_6	Melanogenesis	1/38	18/26232	0.025765
path:04962_2	Vasopressin-regulated water reabsorption	1/38	20/26232	0.028587
path:05215_4	Prostate cancer	1/38	21/26232	0.029995
path:04722_5	Neurotrophin signaling pathway	1/38	31/26232	0.043969
path:04630_1	Jak-STAT signaling pathway	1/38	38/26232	0.053634
path:05215_5	Prostate cancer	1/38	41/26232	0.057747
path:04010_9	MAPK signaling pathway	1/38	43/26232	0.060479
path:04722_4	Neurotrophin signaling pathway	1/38	43/26232	0.060479
path:05215_10	Prostate cancer	1/38	44/26232	0.061843
path:04010_11	MAPK signaling pathway	1/38	55/26232	0.076712
path:04010_10	MAPK signaling pathway	1/38	56/26232	0.078052
path:04010_22	MAPK signaling pathway	1/38	63/26232	0.087381
path:04630_2	Jak-STAT signaling pathway	1/38	87/26232	0.118674

Supplementary Table legends:

Supplementary Table S1: Comparison and analysis of p-values and FDR that calculated from Pearson correlation coefficients. We calculated p-values and corresponding FDR values for candidate ceRNA interactions in each gene expression profile. In each gene expression profile, we listed the maximum p-value and its adjusted FDR value in the table.

Supplementary Table S2: The summary of data in this study. In our study, we downloaded 21 gene expression profiles encompassed 8 CVDs. We listed the disease name, GSE number, platform, samples, number of edges and number of nodes in each network.

Supplementary Table S3: Subpathway enrichment analysis of ceRNAs in common core ceRNA network. In total, 32 subpathways were enriched by mapping the ceRNAs in common core ceRNA network into enrichment program.

Supplementary Table S4: Subpathway enrichment analysis of common hub CDC40. Some CVD related pathways were enriched, indicating that CDC40 and its interacted partners exerted similar functions in multi-CVDs.

Supplementary Table S5: Subpathway enrichment analysis of differential hub BCL11A. Different subpathways were enriched in different disease indicated that the potential different roles of BCL11A in CVDs.

Supplementary Table S6: List of common ceRNA modules in our study. In total, we identified 131 common modules in this study.