

NECo: A node embedding algorithm for multiplex heterogeneous networks: Supplementary Data

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Supplementary Table 1. Hypertension Disease Related Mammalian Phenotype Ontology Terms

TERM ID	TERM
MP:0000230	abnormal systemic arterial blood pressure
MP:0000231	hypertension
MP:0002842	increased systemic arterial blood pressure
MP:0003034	increased pulmonary vascular resistance
MP:0003328	portal hypertension
MP:0003349	abnormal circulating renin level
MP:0003352	increased circulating renin level
MP:0003547	abnormal pulmonary pressure
MP:0003548	pulmonary hypertension
MP:0003819	increased left ventricle diastolic pressure
MP:0003820	increased left ventricle systolic pressure
MP:0003823	increased left ventricle developed pressure
MP:0004012	increased pulmonary artery pressure
MP:0004118	abnormal baroreceptor morphology
MP:0004164	abnormal neurohypophysis morphology
MP:0004167	abnormal cingulate gyrus morphology
MP:0004184	abnormal baroreceptor physiology
MP:0004216	salt-resistant hypertension
MP:0004217	salt-sensitive hypertension
MP:0004875	increased mean systemic arterial blood pressure
MP:0004878	increased systemic vascular resistance
MP:0004879	decreased systemic vascular resistance
MP:0005522	increased circulating atrial natriuretic factor
MP:0005529	abnormal renal vascular resistance
MP:0005530	decreased renal vascular resistance
MP:0005531	increased renal vascular resistance
MP:0005532	abnormal vascular resistance
MP:0005611	decreased circulating antidiuretic hormone level
MP:0006143	increased systemic arterial diastolic blood pressure
MP:0006144	increased systemic arterial systolic blood pressure
MP:0006265	increased pulse pressure
MP:0006373	abnormal circulating angiotensinogen level
MP:0006375	increased circulating angiotensinogen level
MP:0008776	increased right ventricle peak pressure
MP:0008777	increased right ventricle diastolic pressure
MP:0010695	abnormal blood pressure regulation
MP:0010697	abnormal systemic arterial blood pressure regulation
MP:0010758	increased right ventricle systolic pressure
MP:0011022	abnormal circadian regulation of systemic arterial blood pressure
MP:0011312	abnormal kidney afferent arteriole morphology

MP:0012007	abnormal chloride level
MP:0012045	increased susceptibility to hypertension
MP:0012046	decreased susceptibility to hypertension

Supplementary Table 2. Hypertension Disease Related Disease Ontology Terms

TERM ID	TERM
DOID:1073	renal hypertension
DOID:10763	hypertension
DOID:10824	malignant hypertension
DOID:6432	pulmonary hypertension
DOID:9003234	Hypertensive Nephropathy
DOID:9006166	Pulmonary Hypertension, Hypoxia-Induced

Supplementary Table 3. Hypertension disease related genes having experimental annotations at Rat Genome Database. The genes having only expression based experimental evidence codes are excluded. IDA: Inferred from direct assay; IAGP: Inferred from association of genotype from phenotype; IMP: Inferred from mutant phenotype.

RGD ID	Gene Symbol	Disease Ontology Term	Evidence
2031	Ada	hypertension	IDA
2041	Add1	hypertension	IAGP
2041	Add1	hypertension	IDA
2042	Add2	hypertension	IDA
2043	Add3	hypertension	IDA
2048	Adora1	hypertension	IDA
2048	Adora1	hypertension	IMP
2057	Adra2b	hypertension	IMP
2059	Adrb1	renovascular hypertension	IDA
2059	Adrb1	renovascular hypertension	IMP
2069	Agt	hypertension	IDA
2069	Agt	hypertension	IMP
2069	Agt	pulmonary hypertension	IDA
2070	Agtr1a	Hypertensive Nephropathy	IMP
2070	Agtr1a	hypertension	IMP
2070	Agtr1a	renovascular hypertension	IMP
2072	Agtr2	hypertension	IMP
2072	Agtr2	renovascular hypertension	IDA
2072	Agtr2	renovascular hypertension	IMP
2081	Akt1	hypertension	IDA
2096	Alox5	hypertension	IDA
2096	Alox5	pulmonary hypertension	IDA
2096	Alox5	pulmonary hypertension	IMP
2097	Alox5ap	pulmonary hypertension	IMP
2147	Ar	hypertension	IDA
2147	Ar	hypertension	IMP
2150	Arg1	hypertension	IMP
2151	Arg2	hypertension	IMP
2167	Atp1a1	hypertension	IAGP
2186	Avpr2	hypertension	IDA
2200	Bcl2l1	pulmonary hypertension	IDA
2201	Bdkrb2	pulmonary hypertension	IDA
2232	C3	pre-eclampsia	IDA
2275	Casp3	hypertension	IDA
2279	Cat	Renoprival Hypertension	IMP
2369	Cnr1	hypertension	IMP
2379	Comt	hypertension	IDA
2453	Cyp11b1	hypertension	IAGP
2454	Cyp11b2	hypertension	IMP

2493	Ace	Hypertensive Nephrosclerosis	IMP
2493	Ace	hypertension	IDA
2493	Ace	hypertension	IMP
2493	Ace	renovascular hypertension	IDA
2503	Nqo1	hypertension	IDA
2521	Drd3	hypertension	IDA
2535	Ednra	hypertension	IDA
2535	Ednra	pulmonary hypertension	IDA
2535	Ednra	pulmonary hypertension	IMP
2536	Ednrb	hypertension	IMP
2536	Ednrb	pulmonary hypertension	IDA
2536	Ednrb	pulmonary hypertension	IMP
2582	Esr2	hypertension	IMP
2582	Esr2	pulmonary hypertension	IDA
2586	F2r	hypertension	IDA
2609	Fgf2	pulmonary hypertension	IMP
2624	Fn1	renovascular hypertension	IDA
2645	G6pd	Pulmonary Hypertension, Hypoxia-Induced	IMP
2692	Gja5	hypertension	IDA
2703	Glp1r	hypertension	IDA
2729	Gpx1	hypertension	IDA
2741	Nr3c1	hypertension	IMP
2802	Hmgb1	pulmonary hypertension	IMP
2803	Hmgcr	pulmonary hypertension	IMP
2806	Hmox1	hypertension	IDA
2806	Hmox1	pulmonary hypertension	IDA
2806	Hmox1	renal hypertension	IDA
2857	Icam1	pre-eclampsia	IMP
2858	Id1	pulmonary hypertension	IDA
2868	Igf1	hypertension	LAGP
2891	Il1b	hypertension	IDA
2901	Il6	eclampsia	IDA
2901	Il6	pulmonary hypertension	IDA
2916	Ins2	hypertension	IDA
2943	Jun	hypertension	IDA
2953	Kcna5	pulmonary hypertension	IDA
2960	Kcnj8	hypertension	IDA
2961	Kcnmb1	hypertension	IDA
3000	Lep	hypertension	IDA
3015	Lox	hypertension	IDA
3030	Smad1	pulmonary hypertension	IDA
3049	Mas1	hypertension	IMP
3098	Mme	hypertension	IMP

3100	Mmp7	hypertension	IMP
3130	Myc	pulmonary hypertension	IDA
3175	Klk1b3	hypertension	LAGP
3177	Ngfr	hypertension	LAGP
3184	Nos1	hypertension	IDA
3184	Nos1	hypertension	IMP
3185	Nos2	renal hypertension	IMP
3186	Nos3	hypertension	IDA
3186	Nos3	pulmonary hypertension	IDA
3186	Nos3	pulmonary hypertension	IMP
3186	Nos3	renal hypertension	IDA
3193	Nppa	pulmonary hypertension	IDA
3194	Nppb	hypertension	IDA
3195	Npr1	hypertension	LAGP
3197	Npy	hypertension	IMP
3198	Npy1r	hypertension	IMP
3238	Oxt	hypertension	IMP
3249	Serpine1	hypertension	IDA
3249	Serpine1	pulmonary hypertension	IDA
3326	Serpina1	pulmonary hypertension	IDA
3329	Pik3r1	hypertension	IMP
3346	Plcd1	hypertension	IDA
3369	Ppara	Hypertensive Nephropathy	IDA
3369	Ppara	hypertension	IMP
3371	Pparg	hypertension	IDA
3371	Pparg	hypertension	IMP
3395	Prkca	hypertension	LAGP
3396	Prkcb	hypertension	IDA
3438	Ptgis	pulmonary hypertension	IDA
3438	Ptgis	pulmonary hypertension	IMP
3439	Ptgs1	renovascular hypertension	IMP
3443	Ptk2	hypertension	LAGP
3454	Ptprj	hypertension	LAGP
3554	Ren	hypertension	IDA
3555	Resp18	hypertension	IMP
3645	Ccl2	hypertension	IDA
3714	Slc6a4	pulmonary hypertension	IDA
3714	Slc6a4	pulmonary hypertension	IMP
3720	Slc9a3	hypertension	IDA
3732	Sod2	hypertension	IDA
3733	Sod3	hypertension	IDA
3752	Spp1	renovascular hypertension	IDA
3807	Tac1	pulmonary hypertension	IMP

3810	Tacr3	hypertension	IDA
3811	Tacr1	pulmonary hypertension	IMP
3812	Tacr2	pulmonary hypertension	IMP
3826	Tbxas1	hypertension	IDA
3852	Tgfbr1	pulmonary hypertension	IMP
3876	Tnf	Hypertension, Pregnancy-Induced	IMP
3876	Tnf	hypertension	IAGP
3876	Tnf	hypertension	IMP
3903	Trh	hypertension	IDA
3904	Trhr	hypertension	IDA
3930	Uts2	hypertension	IDA
3932	Ucp2	hypertension	IDA
61276	Crhr1	hypertension	IDA
61925	Prkce	hypertension	IAGP
61927	Pecam1	pulmonary hypertension	IDA
62043	Xdh	hypertension	IDA
62086	Acsm3	hypertension	IAGP
67383	Prkcd	hypertension	IAGP
68371	Mtor	hypertension	IDA
68371	Mtor	pulmonary hypertension	IMP
68407	Lrp2	hypertension	IDA
68411	Sh2b3	hypertension	IMP
69305	Nr2f2	hypertension	IMP
70499	Birc5	pulmonary hypertension	IMP
71061	Kynu	hypertension	IAGP
619754	Smpd3	pulmonary hypertension	IMP
619790	Rag1	Hypertensive Nephropathy	IMP
619790	Rag1	hypertension	IMP
619796	Cysltr1	pulmonary hypertension	IMP
619806	Mtpn	hypertension	IDA
619830	Cd40	pulmonary hypertension	IMP
619866	Dynll1	hypertension	IMP
619993	Atp5f1a	pulmonary hypertension	IDA
620007	Cyp2j4	pre-eclampsia	IMP
620209	Cxcl10	renovascular hypertension	IDA
620217	Sle5a2	hypertension	IDA
620243	Gnai2	hypertension	IMP
620293	Ece1	hypertension	IDA
620293	Ece1	pulmonary hypertension	IMP
620322	Cldn16	hypertension	IDA
620349	Ptgs2	hypertension	IAGP
620349	Ptgs2	pulmonary hypertension	IMP
620396	Kl	hypertension	IDA

620401	Bdkrb1	hypertension	IMP
620446	Shc1	Hypertensive Nephropathy	IMP
620573	Cyba	hypertension	IDA
620573	Cyba	pulmonary hypertension	IDA
620600	Nox4	hypertension	IMP
620630	Hrh3	hypertension	IDA
620713	Fgfr1	pulmonary hypertension	IMP
620732	Ephx2	hypertension	IDA
620732	Ephx2	hypertension	IMP
620732	Ephx2	pulmonary hypertension	IMP
620795	Src	hypertension	IDA
620809	Slc12a2	hypertension	IDA
620948	Abat	hypertension	IDA
620995	Pde5a	pre-eclampsia	IMP
620995	Pde5a	pulmonary hypertension	IMP
621057	Tnc	pulmonary hypertension	IDA
621137	Rnpep	hypertension	IMP
621159	Il1rn	hypertension	IDA
621163	Mif	hypertension	IDA
621316	Mmp2	renal hypertension	IDA
621320	Mmp9	pulmonary hypertension	IDA
621320	Mmp9	renal hypertension	IDA
621376	Atp5pf	pulmonary hypertension	IMP
621503	Kcnq1	hypertension	LAGP
621506	Mapk8	hypertension	IDA
621528	Cxcr3	renovascular hypertension	IDA
621647	Vip	pulmonary hypertension	IDA
621862	Atf2	hypertension	IDA
621884	Uts2r	hypertension	IDA
631375	Egln1	hypertension	IMP
631401	Wnk4	hypertension	LAGP
708418	Cd40lg	pre-eclampsia	IMP
1306950	Nisch	hypertension	IMP
1307690	Nfatc2	pulmonary hypertension	IMP
1307917	Mmp1	pulmonary hypertension	IDA
1310046	Adamts16	hypertension	IMP
1310740	Lipg	hypertension	IDA
1559787	Srf	hypertension	IDA
1560646	Myo6	hypertension	IDA
1563603	Rad51	hypertension	IDA
1566119	H2ax	hypertension	IDA
1593188	Eng	pre-eclampsia	IDA

Supplementary Table 4. Mean AUC values with standard deviations are given for different combinations of multiplex and aggregated networks. The results are for 10 runs for each combination. PPI: protein-protein interaction, PWY: pathway, EXPR: co-expression, DO: Disease Ontology, MPO: Mammalian Phenotype Ontology, QP: Quantitative Phenotype Measurements

Rank	Networks Used		Mean AUC	Std. Dev.
	Gene	Phenotype		
1	Multiplex (PPI, PWY, EXPR)	Aggregated (MPO, QP)	94.97	0.24
2	Multiplex (PPI, PWY, EXPR)	Aggregated (MPO, DO)	94.92	0.25
3	Multiplex (PPI, PWY, EXPR)	Aggregated (MPO, DO, QP)	94.89	0.27
4	Multiplex (PPI, PWY, EXPR)	Multiplex (MPO, DO)	94.87	0.30
5	Multiplex (PPI, PWY, EXPR)	Multiplex (MPO, QP)	94.87	0.35
6	Multiplex (PPI, PWY, EXPR)	Multiplex (MPO, DO, QP)	94.85	0.29
7	Multiplex (PPI, PWY, EXPR)	Multiplex (DO, QP)	94.81	0.29
8	Multiplex (PPI, PWY, EXPR)	Aggregated (DO, QP)	94.52	0.12
9	Multiplex (PPI, EXPR)	Multiplex (MPO, DO, QP)	94.42	0.30
10	Multiplex (PPI, PWY)	Multiplex (MPO, DO, QP)	93.99	0.44
11	Aggregated (PPI, PWY, EXPR)	Multiplex (MPO, DO, QP)	93.51	0.39
12	Aggregated (PPI, PWY, EXPR)	Aggregated (MPO, DO, QP)	93.29	0.34
13	Multiplex (PWY, EXPR)	Multiplex (MPO, DO, QP)	92.69	0.38

Supplementary Table 5. Novel gene predictions of NECo sorted by prediction probability.

RGD ID	Symbol	Evidence
3277	Pdc	[2, 10, 26]
3548	Rcn2	[19]
619749	Gna11	[27]
621450	Kcnk6	[21, 28]
61835	Fkbp1b	[6, 22, 40]
62051	Pla2g5	[4, 23, 38]
61977	Ckmt2	-
620866	F2rl1	[20, 43]
3434	Ptger1	[1, 24, 32]
61935	Pla2g10	-
2051	Adora3	[11, 44]
620770	Gnaq	[39, 43]
1563131	Wnk3	[3, 12]
3026	Lyz2	[17, 29, 30, 37]
621767	Agxt2	[5, 13]
2603	Fga	[16, 31, 34, 35]
620287	Mybph	[8]
620598	Nox1	[9, 18, 25, 33, 41]
620020	Ptger2	[14, 36, 42]
619974	Asl	[7, 15]

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