

Supplementary Tables

Supplementary Table 1. Enriched signaling pathways for the differentially expressed genes in brain, lung and bone metastasis.

Tropism	Ingenuity Canonical Pathways	-log(p-value)	Ratio	Molecules
Brain metastasis	NF-κB Signaling	4.57	1.20E-01	RAC2,TLR10,TRAF3,IL36G,PRKCQ,MAPK8,TGFA,PIK3R5,TNFRSF1B,TNFSF13B,EGFR,PRKCB
	T Cell Receptor Signaling	4.56	1.43E-01	FYN,PTPN7,PRKCQ,CD3E,PAG1,MAPK8,PIK3R5,VAV1,CD8A,LCP2
	Natural Killer Cell Signaling	4.45	1.55E-01	FYN,RAC2,PRKCQ,KLRD1,PIK3R5,VAV1,HCST,LCP2,PRKCB
	Cdc42 Signaling	3.54	1.09E-01	WIPF1,MAPK14,null,CD3E,HLA-E,WAS,MAPK8,VAV1,HLA-F,null
	HER-2 Signaling in Breast Cancer	1.94	9.09E-02	RAC2,PRKCQ,FOXO1,PIK3R5,EGFR,PRKCB
	CD40 Signaling	1.82	9.80E-02	TRAF3,MAPK14,MAPK8,PIK3R5,JAK3
	mTOR Signaling	1.74	6.90E-02	RAC2,PRKCQ,PPP2R4,RHOT2,PIK3R5,PLD1,EIF4B,PRKCB
Lung metastasis	PI3K Signaling in B Lymphocytes	1.61	7.00E-02	CD81,FYN,RAC2,LYN,VAV1,IL4 (includes EG:16189),PRKCB
	Cdc42 Signaling	2.21	1.61E-01	VAV2,ACTR2,MYL6,MAPK9,LIMK2,FGD1,PARD6A,CLIP1,PRKCZ,ATF2,DIAPH1,PRKCI,MAPK14,WASL,PAK3,HLA-E,ARPC2,ARHGEF6,HLA-DRA,HLA-B,PPP1R12A,HLA-F,null
	LPS-stimulated MAPK Signaling	2.09	2.03E-01	RAC1,HRAS,MAPK9,IKBKE,NFKB2,PRKCZ,ATF2,PRKCI,MAPK14,MAP3K7 (includes EG:26409), PIK3CG,CREB1, MRAS, MAP2K3, PRKCH, PRKD3
	SAPK/JNK Signaling	1.96	1.80E-01	SH2D2A,MAP2K7,NFATC3,MAP3K13,RAC1,HRAS,MAPK9,CRK,MAPK8IP1,HNRNPK,GNG7,ATF2,SHC1 (includes EG:20416), LCK,GAB1,MAP3K7 (includes EG:26409), PIK3CG,MRAS
	CD27 Signaling in Lymphocytes	1.95	2.18E-01	BCL2L1,MAP2K7,SIVA1,MAP3K7 (includes EG:26409), MAP3K13,MAPK9,IKBKE,IKBKAP,MAP2K3,NFKB2,CD27,MAP2K5
	ATM Signaling	1.82	2.03E-01	SMC3,GADD45B,MAPK14,H2AFX,CREB1,MAPK9,MDM2,TP53BP1,TLK2,CDK1,RAD50,ATF2
	Calcium-induced T Lymphocyte Apoptosis	1.72	1.15E-01	TRD@,ITPR3,NR4A1,PRKCE,PLCG1,ATP2A2,PPP3CA
Bone metastasis	B Cell Activating Factor Signaling	1.62	2.05E-01	TRAF6,MAP2K7,MAPK14,NFATC3,MAPK9,IKBKE,IKBKAP,NFATC4,NFKB2
	HER-2 Signaling in Breast Cancer	1.38	1.77E-01	TSC1,CCNE2,HRAS,MDM2,ITGB8,PARD6A,ITGB7,PRKCZ,PRKCI,PIK3CG,MRAS,PRKCH,PRKD3,ITGB5
	EIF2 Signaling	23.5	2.64E-01	RPL24,EIF2S3,RPL22,RPL27A,MAPK1,null,null,RPS8,RPS6,RPL14,RPL26,RPS23,RPL37A,RPS11,RPL10A,RPS7,SHC1 (includes EG:20416),RPL6,RPS3A,null,PIK3C3,RPS9,SOS1,RPL35,RPLP2,EIF3A,RPL3,RPL17,null,null,RPS19,RPL23A,RPL9,RPLP0,null,RPL15,RPS4X,null,RPL5,null,RPS15,EIF2B1,null,RPS15A,RPL38 (includes EG:3355144),EIF3L,RPL13A,RPSA
	Regulation of eIF4 and p70S6K Signaling	6.62	1.45E-01	EIF2S3,MAPK1,null,RPS19,RPS6,RPS8,MAPK11,RPS23,RPS11,RPS7,SHC1 (includes EG:20416), RPS4X, RPS3A, null, PIK3C3, SOS1,RPS9,EIF2B1,RPS15,EIF3A,RPS15A,EIF3L,RPSA
	Breast Cancer Regulation by Stathmin1	3.98	1.11E-01	ARHGEF12,MAPK1,null,TUBA4A,TUBB,TUBA1B,CDK1,GNG7,SHC1 (includes EG:20416), GNG11, PIK3C3, CDKN1A, ITPR3, SOS1,PRKCE,TUBA1C,ARHGEF3,ARHGEF9,OPN1SW,CDK2,CAMK2B,CAMK2G
	mTOR Signaling	3.84	1.11E-01	MAPK1,DDIT4,null,RPS19,RPS6,RPS8,RPS23,RPS11,RPS7,RPS4X,RPS6KA6,RPS3A,null,PIK3C3,RPS9,RPS15,EIF3A,PRKCE,RPS15A,EIF3L,RPSA
	HGF Signaling	3.65	1.37E-01	CDKN2A,MAP3K9,null,MAPK1,PLCG1,ETS2,IL6,ELF4,PIK3C3,CDKN1A,SOS1,PRKCE,MAP3K8,CDK2
Bone metastasis	VEGF Signaling	2.66	1.21E-01	EIF2S3,SHC1 (includes EG:20416), MAPK1, PIK3C3, SOS1, EIF2B1,PLCG1,VCL,SFN,ACTG1,ACTN1
	GM-CSF Signaling	2.62	1.36E-01	SHC1 (includes EG:20416),MAPK1,PIM1 (includes EG:18712),PIK3C3,SOS1,CSF2,PPP3CA,CAMK2B,CAMK2G
	Gap Junction Signaling	2.5	9.88E-02	MAPK1,TUBA4A,PLCG1,TUBB,ACTG1,TUBA1B,PIK3C3,ITPR3,SOS1,PRKCE,TUBA1C,MAPK7,NPR2,OPN1SW,PPP3CA,HTR2A
	Estrogen-mediated S-phase Entry	2.33	1.85E-01	TFDP1,CDKN1A,ESR2,CDK1,CDK2
	EGF Signaling	2.26	1.46E-01	SHC1 (includes EG:20416), MAPK1, PIK3C3, SOS1, ITPR3, SRF, PLCG1

GNRH Signaling	2.23	9.85E-02	MAP3K9,null,MAPK1,MAPK11,DNM1,SOS1,ITPR3,PRKCE,MAP3K8,MAPK7,OPN1SW,CAMK2B,CAMK2G
JAK/Stat Signaling	1.87	1.14E-01	SHC1 (includes EG:20416), MAPK1, PIK3C3, CDKN1A, SOS1, STAT2,IL6,CCKBR
Growth Hormone Signaling	1.83	1.13E-01	RPS6KA6,MAPK1,PIK3C3,IGF1R,SRF,IGFBP3,PRKCE,PLCG1
PDGF Signaling	1.73	1.10E-01	SHC1 (includes EG:20416), MAPK1, PIK3C3, SOS1, SRF, PLCG1, INPPL1,PDGFB
Calcium-induced T Lymphocyte Apoptosis	1.72	1.15E-01	TRD@,ITPR3,NR4A1,PRKCE,PLCG1,ATP2A2,PPP3CA
Cell Cycle: G1/S Checkpoint Regulation	1.68	1.09E-01	CDKN2A,HDAC6,RPL5,TFDP1,CDKN1A,GNL3,CDK2
SAPK/JNK Signaling	1.5	9.00E-02	MINK1,SHC1 (includes EG:20416), MAP3K9, GNG11, TRD, null, PIK3C3,SOS1,GNG7
PTEN Signaling	1.43	8.06E-02	FGFR3,SHC1 (includes EG:20416), null, MAPK1, CDKN1A, SOS1, IGF1R,FGFR2,INPPL1,IGF2R
Telomerase Signaling	1.42	9.09E-02	HDAC6,TERF2,SHC1 (includes EG:20416), ELF4, MAPK1, PIK3C3,CDKN1A,SOS1,ETS2
Erythropoietin Signaling	1.41E+00	9.46E-02	SHC1 (includes EG:20416), NFKBIA, MAPK1, PIK3C3, SOS1, PRKCE,PLCG1
AMPK Signaling	1.35	7.86E-02	GYS1,MAPK1,SMARCA2,PIK3C3,STRADA,LIPE,AK4,CHRNE,PFKL,MAPK11,ADRA1D

Supplementary Table 2. Repositioned drug candidates for lung metastasis of breast cancer.

Tropism	Repositioned targets	Repositioned drugs	Clinical information	Indications
Lung metastasis	RAC1	Pravastatin	Approved	Cardiovascular Disease Hyperlipidemia
	RAF1	Sorafenib	Approved	Hepatocellular Carcinoma Renal Cell Carcinoma
	RAC1	Simvastatin	Approved	CHD Mortality and Cardiovascular Events Hyperlipidemia Adolescent Patients with Heterozygous Familial Hypercholesterolemia (HeFH)
	CDC25B	Double Oxidized Cysteine	No clinical information	
	CDC25B	Beta-Mercaptoethanol	No clinical information	
	CDC25B	Cysteine Sulfenic Acid	No clinical information	
	CDC25B	Cysteinesulfonic Acid	No clinical information	
	CDC25B	Methyl Mercury Ion	No clinical information	
	RAC1 CDC42	Guanosine-5'-Diphosphate	No clinical information	
Bone metastasis	IKBKB	Auranofin	Approved	rheumatoid arthritis
	CDC42	Guanosine-5'-Diphosphate	No clinical information	

Supplementary Table 3. Expression of p-RET and p-FYN in brain metastases tissues of breast cancer patient.

H score	Negative (0-9)	Low (10-100)	Medium (101-200)	High (201-300)
p-FYN	4 (14%)	12 (41%)	6 (21%)	7 (24%)
p-RET	6 (21%)	14 (48%)	5 (17%)	4 (14%)