

Supplementary Figures and Tables

Supplementary information, Figure S1. Identification of differential protein expressions from thioridazine and fluphenazine-treated GBM8401 cells *via* microwestern. GBM8401 cells were treated with various drugs for 24 h. Sample serials (each block from left to right): Lane M (Marker), Lane 1 (fluphenazine 20 μM) and Lane 2 (10 μM), Lane 3 (Control), Lane 4 (thioridazine 5 μM), Lane 5 (10 μM), and Lane 6 (15 μM). GAPDH and β-actin as internal control.



Supplementary information, Figure S2. GBM8401 cells were treated with thiostrepton, thioguanosine, parthenolide, and bepridil at concentrations ranging from 0.1 to 10 μ M, and the cell viability was determined using an MTT assay.



Supplementary information, Figure S3. Thioridazine decreased the expression of phospho-Raptor (Ser-792) in GBM cells. GBM8401 and U87MG cells were treated with thioridazine at 5, 10 and 15 μ M for 24 h. Phospho-Raptor (Ser-792) was detected by western blotting. GAPDH was used as an internal control.



Supplementary information, Figure S4. Fluphenazine increased the expression of phospho-epidermal growth factor receptor (p-EGFR) (Tyr-1068) in GBM cells. GBM8401 cells were treated with fluphenazine at 10 μ M for 24 h. Phospho-EGFR (Tyr-1068) was detected by western blotting. Tubulin was used as an internal control.

Supplementary information, Table S1. Two hundred fifteen drugs predicted by Cmap and the result of tested drugs in GBM8401. If the IC₅₀ value of the drug was less than 10 μ M, we defined the drug as an "effective" drug. ("v": effective in GBM cells. "x": ineffective in GBM cells. "ND": not determined.)

Drug name	Frequency	Result	Anti-psychotic agent
1,4-chrysenequinone	100%	ND	
0173570-0000	100%	ND	
Repaglinide	80%	Х	
Procaine	80%	Х	
Pargyline	80%	Х	
Luteolin	80%	V	
Gliclazide	80%	Х	
Chrysin	80%	Х	
Tyloxapol	60%	V	
Thiostrepton	60%	v	
Sulfamethoxypyridazine	60%	ND	
Skimmianine	60%	Х	
Ronidazole	60%	Х	
Phthalylsulfathiazole	60%	Х	
Pentoxyverine	60%	ND	
Omeprazole	60%	ND	
Nipecotic acid	60%	ND	
Meticrane	60%	Х	
Meropenem	60%	ND	
Medrysone	60%	Х	
Levamisole	60%	ND	
Ginkgolide A	60%	Х	
Dipyridamole	60%	Х	
Apigenin	60%	Х	
Prestwick-665	60%	Х	
Prestwick-559	60%	Х	
DL-thiorphan	60%	Х	
Zomepirac	40%	ND	
Vorinostat	40%	v	
Verteporfin	40%	v	
Triflusal	40%	Х	
Tridihexethyl	40%	ND	
Trichostatin A	40%	v	
Trazodone	40%	Х	
Thioguanosine	40%	V	
Terguride	40%	ND	
Sulfametoxydiazine	40%	X	

Sulconazole	40%	v	
Scopolamine N-oxide	40%	ND	
Riboflavin	40%	ND	
Resveratrol	40%	X	
Piperlongumine	40%	v	
Phenoxybenzamine	40%	v	
Morantel	40%	X	
Monobenzone	40%	ND	
Methazolamide	40%	ND	
Menadione	40%	ND	
Lysergol	40%	ND	
Ketanserin	40%	ND	
Imipenem	40%	ND	
Heliotrine	40%	ND	
Fipexide	40%	ND	
Eucatropine	40%	x	
Ellipticine	40%	v	
Diltiazem	40%	X	
Chlorzoxazone	40%	ND	
Carbachol	40%	ND	
Caffeic acid	40%	ND	
Bisacodyl	40%	ND	
Betaxolol	40%	ND	
Bepridil	40%	v	
Antimycin A	40%	v	
Alsternaullone	40%	ND	
Alpha-estradiol	40%	X	
Acepromazine	40%	x	0
Prestwick-682	40%	ND	
Prestwick-1084	40%	x	
PNU-0230031	40%	ND	
PHA-00851261E	40%	ND	
N-acetyl-L-leucine	40%	ND	
GW-8510	40%	v	
8-azaguanine	40%	v	
0297417-0002B	40%	ND	
Zimeldine	20%	X	
Yohimbic acid	20%	ND	
Velnacrine	20%	ND	
Valproic acid	20%	ND	
Ursodeoxycholic acid	20%	ND	
Trimetazidine	20%	ND	
Trifluridine	20%	ND	
Trifluoperazine	20%	v	0
Tretinoin	20%	ND	-
	2070		

Tolfenamic acid	20%	ND	
Tolbutamide	20%	ND	
Tobramycin	20%	ND	
Tinidazole	20%	ND	
Tiabendazole	20%	ND	
Thioridazine	20%	v	0
Thioperamide	20%	ND	
Thiamazole	20%	ND	
Thalidomide	20%	ND	
Tanespimycin	20%	v	
Talampicillin	20%	ND	
Sulfamethizole	20%	ND	
Streptozocin	20%	ND	
Streptomycin	20%	ND	
Spiradoline	20%	ND	
Solasodine	20%	ND	
Semustine	20%	Х	
Scriptaid	20%	ND	
Roxarsone	20%	ND	
Rottlerin	20%	ND	
Rimexolone	20%	ND	
Quinostatin	20%	ND	
Quinethazone	20%	ND	
Pyrvinium	20%	v	
Puromycin	20%	ND	
Pseudopelletierine	20%	ND	
Proxyphylline	20%	ND	
Propylthiouracil	20%	ND	
Propafenone	20%	v	
Prochlorperazine	20%	v	0
Piroxicam	20%	ND	
Piperidolate	20%	ND	
Piperacetazine	20%	ND	0
Pipenzolate bromide	20%	ND	
Phenacetin	20%	ND	
Parthenolide	20%	v	
Paroxetine	20%	ND	
Oxytetracycline	20%	ND	
Oxprenolol	20%	ND	
Novobiocin	20%	ND	
Norcyclobenzaprine	20%	v	
Nizatidine	20%	ND	
Nitrendipine	20%	ND	
Natamycin	20%	ND	

Metyrapone	20%	ND	
Methotrexate	20%	ND	
Mephenesin	20%	ND	
Mepenzolate bromide	20%	ND	
Lymecycline	20%	ND	
Loracarbef	20%	ND	
Lidoflazine	20%	ND	
Levonorgestrel	20%	X	
Karakoline	20%	ND	
Ifosfamide	20%	ND	
Hexestrol	20%	х	
Hexamethonium bromide	20%	ND	
Harmol	20%	ND	
Harmine	20%	ND	
Guanethidine	20%	ND	
Guaifenesin	20%	ND	
Glibenclamide	20%	ND	
Fusaric acid	20%	ND	
Fluspirilene	20%	Х	0
Fluorometholone	20%	ND	
Flunarizine	20%	ND	
Flumetasone	20%	ND	
Flecainide	20%	ND	
Flavoxate	20%	ND	
Famprofazone	20%	ND	
Etomidate	20%	ND	
Etofenamate	20%	ND	
Ethambutol	20%	ND	
Etanidazole	20%	ND	
Estriol	20%	Х	
Emetine	20%	v	
Ebselen	20%	ND	
Doxorubicin	20%	ND	
Dirithromycin	20%	ND	
Dioxybenzone	20%	ND	
Dinoprost	20%	ND	
Dimenhydrinate	20%	ND	
Dihydroergocristine	20%	ND	
Dicoumarol	20%	ND	
Dexpropranolol	20%	ND	
Dequalinium chloride	20%	ND	
Deptropine	20%	ND	
Daunorubicin	20%	v	
Dacarbazine	20%	ND	
Cycloserine	20%	V	
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Acebutolol 20% ND Y-27632 20% ND S-propranolol 20% ND Prestwick-860 20% ND Prestwick-685 20% v Prestwick-674 20% ND Prestwick-664 20% ND MS-275 20% ND LY-294002 20% ND H-7 20% ND CP-690334-01 20% ND CP-320650-01 20% ND 6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% V 0179445-0000 20% ND 0175029-0000 20% ND	Alfaxalone	20%	ND	
Y-27632 20% ND S-propranolol 20% ND Prestwick-860 20% ND Prestwick-685 20% V Prestwick-674 20% ND Prestwick-664 20% ND MS-275 20% ND LY-294002 20% ND H-7 20% ND CP-690334-01 20% ND CP-320650-01 20% ND 6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% ND 0179445-0000 20% ND 0175029-0000 20% ND	Acebutolol	20%	ND	
S-propranolol 20% ND Prestwick-860 20% ND Prestwick-685 20% v Prestwick-674 20% ND Prestwick-664 20% ND MS-275 20% ND LY-294002 20% ND H-7 20% ND CP-690334-01 20% ND CP-320650-01 20% ND 6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% V 0179445-0000 20% ND 0175029-0000 20% ND	Y-27632	20%	ND	
Prestwick-860 20% ND Prestwick-685 20% v Prestwick-674 20% ND Prestwick-664 20% ND MS-275 20% ND LY-294002 20% ND H-7 20% ND CP-690334-01 20% ND CP-320650-01 20% ND 6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% V 0179445-0000 20% ND 0175029-0000 20% ND	S-propranolol	20%	ND	
Prestwick-685 20% v Prestwick-674 20% ND Prestwick-664 20% ND MS-275 20% ND LY-294002 20% ND H-7 20% ND CP-690334-01 20% ND CP-320650-01 20% ND 6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% V 0179445-0000 20% ND 0175029-0000 20% ND	Prestwick-860	20%	ND	
Prestwick-674 20% ND Prestwick-664 20% ND MS-275 20% ND LY-294002 20% ND H-7 20% ND CP-690334-01 20% ND CP-320650-01 20% ND 6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% V 0179445-0000 20% ND 0175029-0000 20% ND	Prestwick-685	20%	v	
Prestwick-664 20% ND MS-275 20% ND LY-294002 20% ND H-7 20% ND CP-690334-01 20% ND CP-320650-01 20% ND 6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% V 0179445-0000 20% ND 0175029-0000 20% ND	Prestwick-674	20%	ND	
MS-275 20% ND LY-294002 20% ND H-7 20% ND CP-690334-01 20% ND CP-320650-01 20% ND 6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% V 0179445-0000 20% ND 0175029-0000 20% ND	Prestwick-664	20%	ND	
LY-29400220%NDH-720%NDCP-690334-0120%NDCP-320650-0120%ND6-bromoindirubin-3'-oxime20%ND570788520%ND4,5-dianilinophthalimide20%ND3-acetylcoumarin20%ND15-delta prostaglandin J220%V0179445-000020%ND0175029-000020%ND	MS-275	20%	ND	
H-720%NDCP-690334-0120%NDCP-320650-0120%ND6-bromoindirubin-3'-oxime20%ND570788520%ND4,5-dianilinophthalimide20%ND3-acetylcoumarin20%ND15-delta prostaglandin J220%V0179445-000020%ND0175029-000020%ND	LY-294002	20%	ND	
CP-690334-01 20% ND CP-320650-01 20% ND 6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% v 0179445-0000 20% ND 0175029-0000 20% ND	H-7	20%	ND	
CP-320650-01 20% ND 6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% V 0179445-0000 20% ND 0175029-0000 20% ND	CP-690334-01	20%	ND	
6-bromoindirubin-3'-oxime 20% ND 5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% v 0179445-0000 20% ND 0175029-0000 20% ND	CP-320650-01	20%	ND	
5707885 20% ND 4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% v 0179445-0000 20% ND 0175029-0000 20% ND	6-bromoindirubin-3'-oxime	20%	ND	
4,5-dianilinophthalimide 20% ND 3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% v 0179445-0000 20% ND 0175029-0000 20% ND	5707885	20%	ND	
3-acetylcoumarin 20% ND 15-delta prostaglandin J2 20% v 0179445-0000 20% ND 0175029-0000 20% ND	4,5-dianilinophthalimide	20%	ND	
15-delta prostaglandin J2 20% v 0179445-0000 20% ND 0175029-0000 20% ND	3-acetylcoumarin	20%	ND	
0179445-0000 20% ND 0175029-0000 20% ND	15-delta prostaglandin J2	20%	v	
0175029-0000 20% ND	0179445-0000	20%	ND	
	0175029-0000	20%	ND	

Supplementary information, Table S2. ConsensusPathDB analysis of common GBM differentially expressed probesets with at least 3 appearances from 5 GBM datasets.

pathway name	set	candidates	p-value	q-value	pathway
(up-regulated genes)	size	contained	-	-	source
interactions	66	7 (10.6%)	1.57E-08	2.17E-06	PID
Beta3 integrin cell surface interactions	44	5 (11.4%)	1.47E-06	8.55E-05	PID
Platelet aggregation inhibitor pathway, pharmacodynamics	49	5 (10.2%)	2.54E-06	8.55E-05	PharmGKB
Intrinsic prothrombin activation pathway	23	4 (17.4%)	3.10E-06	8.55E-05	PID
Intrinsic prothrombin activation pathway	23	4 (17.4%)	3.10E-06	8.55E-05	BioCarta
Complement and coagulation cascades	54	5 (9.3%)	4.14E-06	9.51E-05	Wikipathwa ys
Integrins in angiogenesis	65	5 (7.8%)	9.64E-06	0.00019	PID
Complement and coagulation cascades- <i>Homo sapiens</i> (human)	69	5 (7.2%)	1.40E-05	0.000241	KEGG
NCAM signaling for neurite out-growth	71	5 (7.0%)	1.61E-05	0.000247	Reactome
Muscle cell TarBase	354	9 (2.6%)	1.86E-05	0.000257	Wikipathwa ys
Extrinsic prothrombin activation pathway	13	3 (23.1%)	2.43E-05	0.00028	PID
Extrinsic prothrombin activation pathway	13	3 (23.1%)	2.43E-05	0.00028	BioCarta
Focal adhesion- <i>Homo sapiens</i> (human)	200	7 (3.5%)	2.93E-05	0.000311	KEGG
Epithelium TarBase	290	8 (2.8%)	3.56E-05	0.000351	Wikipathwa ys
ECM-receptor interaction- Homo sapiens (human)	85	5 (5.9%)	3.86E-05	0.000356	KEGG
PLK1 signaling events	44	4 (9.1%)	4.43E-05	0.000359	PID
NCAM1 interactions	44	4 (9.1%)	4.43E-05	0.000359	Reactome
Amoebiasis- <i>Homo sapiens</i> (human)	108	5 (4.7%)	0.000111	0.000853	KEGG
Focal adhesion	184	6 (3.3%)	0.000169	0.00123	Wikipathwa ys
Signaling by PDGF	125	5 (4.0%)	0.000233	0.00153	Reactome
Integrin	125	5 (4.0%)	0.000233	0.00153	INOH
Inflammatory response pathway	32	3 (9.4%)	0.000397	0.00238	Wikipathwa ys
Syndecan-4-mediated signaling	32	3 (9.4%)	0.000397	0.00238	PID

events					
Protein digestion and					
absorption-Homo sapiens	81	4 (4.9%)	0.00048	0.00276	KEGG
(human)					
Integrin cell surface	05	4 (4 70/)	0.000577	0.00219	Desetome
interactions	65	4 (4.7%)	0.000377	0.00518	Reactome
Diabetes pathways	39	3 (7.9%)	0.000662	0.00352	Reactome
APC/C-mediated degradation	10	2 (20,00/)	0.000000	0.00420	Wikipathwa
of cell cycle proteins	10	2 (20.0%)	0.000888	0.00438	ys
Regulation of insulin-like					•
growth factor (IGF) activity by	10	2(20,00)	0.000000	0.00429	Wikipathwa
insulin-like growth factor	10	2 (20.0%)	0.000888	0.00438	ys
binding proteins (IGFBPs)					
Regulators of bone	11	2(1920)	0.00109	0.00495	
mineralization	11	2(18.2%)	0.00108	0.00485	PID
Regulators of bone	11	2(19,20())	0.00109	0.00495	DieConto
mineralization	11	2(18.2%)	0.00108	0.00485	BioCarta
Syndecan-1-mediated signaling	45	2((70))	0.00100	0.00495	DID
events	45	3 (6.7%)	0.00109	0.00485	PID
Axon guidance	268	6 (2.3%)	0.0012	0.00518	Reactome
Regulation of insulin-like					
growth factor (IGF) activity by	10	$\mathbf{O}(1 \in 7)$	0.0012	0.005.40	DID
insulin-like growth factor	12	2 (16.7%)	0.0013	0.00542	PID
binding proteins (IGFBPs)					
GRB2 events in EGFR	14	2(14,20())	0.00179	0.00691	Desetares
signaling	14	2 (14.3%)	0.00178	0.00081	Reactome
Regulation of complement	14	2(14,20/)	0.00179	0.00691	Desetome
cascade	14	2 (14.3%)	0.00178	0.00081	Reactome
Nicotinate and nicotinamide	14	2(14,20())	0.00179	0.00691	CMDDD
metabolism	14	2 (14.3%)	0.00178	0.00081	SMPDB
SHC1 events in EGFR	15	2(12,20/)	0.00204	0.00762	Desetome
signaling	15	2(15.5%)	0.00204	0.00762	Reactome
Celecoxib pathway,	58	2(5,20/)	0.00227	0.00826	DhormCKB
pharmacodynamics	38	3 (3.270)	0.00227	0.00820	FliatiliOKD
Platelet activation, signaling	215	5(2.4%)	0.00261	0 00008	Paactoma
and aggregation	215	5 (2.470)	0.00201	0.00908	Reactonic
Regulation of insulin-like					
growth factor (IGF) activity by	17	2(11.8%)	0.00263	0.00008	Paactoma
insulin-like growth factor	17	2 (11.070)	0.00203	0.00708	Reactonic
binding proteins (IGFBPs)					
Lymphocyte TarBase	137	7 (1.6%)	0.00286	0 00062	Wikipathwa
	+37	7 (1.070)	0.00280	0.00702	ys
Nucleotide metabolism	10	2(10.5%)	0.00329	0.0106	Wikipathwa
	17	2 (10.370)	0.00327	0.0100	ys
Pathways in cancer-Homo	325	6 (1.8%)	0.00331	0.0106	KEGG
sapiens (human)	525	0 (1.070)	0.000001	0.0100	ML00
p53 signaling pathway-Homo	68	3(4.4%)	0.00358	0.0112	KEGG
sapiens (human)	00	5 (7.7/0)	0.000000	0.0112	ML00
Formation of fibrin clot	20	2 (10.0%)	0.00364	0.0112	Wikipathwa

(clotting cascade)					ys
GRB2 events in ERBB2 signaling	23	2 (8.7%)	0.00481	0.0141	Reactome
Nicotinate nicotinamide metabolism	23	2 (8.7%)	0.00481	0.0141	INOH
Complement cascade	78	3 (3.9%)	0.00489	0.0141	Reactome
Developmental Biology	363	6 (1.7%)	0.00545	0.0151	Reactome
SHC1 events in ERBB2 signaling	25	2 (8.0%)	0.00567	0.0151	Reactome
VEGFR3 signaling in lymphatic endothelium	25	2 (8.0%)	0.00567	0.0151	PID
Alpha9 beta1 integrin signaling events	25	2 (8.0%)	0.00567	0.0151	PID
Nicotinate and nicotinamide metabolism- <i>Homo sapiens</i> (human)	26	2 (7.7%)	0.00613	0.016	KEGG
Platelet degranulation	85	3 (3.6%)	0.00626	0.016	Reactome
Small cell lung cancer- <i>Homo</i> sapiens (human)	84	3 (3.6%)	0.00647	0.016	KEGG
Cdc20: phospho-APC/C mediated degradation of cyclin A	29	2 (7.4%)	0.0066	0.016	Reactome
APC/C: Cdc20 mediated degradation of mitotic proteins	29	2 (7.4%)	0.0066	0.016	Reactome
Activation of APC/C and APC/C: Cdc20 mediated degradation of mitotic proteins	30	2 (7.1%)	0.00708	0.0167	Reactome
Mitotic prometaphase	87	3 (3.4%)	0.00713	0.0167	PID
Response to elevated platelet cytosolic Ca ²⁺	90	3 (3.4%)	0.00736	0.0169	Reactome
Gap junction- <i>Homo sapiens</i> (human)	89	3 (3.4%)	0.00759	0.0172	KEGG
Mitotic prometaphase	95	3 (3.2%)	0.00908	0.0201	Reactome
Formation of fibrin clot (clotting cascade)	32	2 (6.2%)	0.00919	0.0201	Reactome
Cell surface interactions at the vascular wall	99	3 (3.1%)	0.00934	0.0201	Reactome

pathway name (down-regulated genes)	set size	candidates contained	p-value	q-value	pathway source
Transmission across chemical synapses	195	20 (10.3%)	4.66E-14	1.93E-11	Reactome
Neuronal system	288	23 (8.0%)	1.07E-13	2.22E-11	Reactome
GABAergic synapse- <i>Homo</i> sapiens (human)	89	14 (15.7%)	1.05E-12	1.45E-10	KEGG
Glutamatergic synapse-Homo sapiens (human)	126	13 (10.3%)	1.61E-09	1.67E-07	KEGG
Neurotransmitter release cycle	36	8 (22.2%)	5.20E-09	4.32E-07	Reactome

Morphine addiction-Homo	02	11	6/10E_00	1 19F-07	KEGG
sapiens (human)	92	(12.0%)	0.4912-09	4.4912-07	KLOU
Synaptic vesicle cycle-Homo	64	9 (14 1%)	3 89E-08	2 30E-06	KEGG
sapiens (human)	04) (14.170)	5.071 00	2.501 00	REGO
Neurotransmitter receptor					
binding and downstream	141	12 (8 5%)	6 29E-08	3 26F-06	Reactome
transmission in the	141	12 (0.570)	0.272 00	5.20E 00	Redetoine
postsynaptic cell					
Calcium regulation in the	149	12 (8 1%)	1 16F-07	5 35F-06	Wikipathwa
cardiac cell	147	12 (0.170)	1.10L-07	J.JJL-00	ys
Retrograde endocannabinoid					
signaling-Homo sapiens	102	10 (9.8%)	2.22E-07	9.22E-06	KEGG
(human)					
Glutamate neurotransmitter	16	5 (31.2%)	7.00F-07	2 64F-05	Reactome
release cycle	10	5 (51.270)	7.001 07	2.0112 03	Redetonie
GABA synthesis, release,	19	5 (26 3%)	1 81E-06	6 27E-05	Reactome
reuptake and degradation	17	5 (20.570)	1.012.00	0.2712 05	Redetoine
GABA receptor activation	55	7 (12.7%)	2.70E-06	8.63E-05	Reactome
Glutamate neurotransmitter	11	1 (36 104)	4 00E 06	0.000148	
release cycle	11	4 (30.4%)	4.99E-00	0.000146	ΓID
Serotonin neurotransmitter	10	1 (22 20/)	7 425 06	0.000102	Desetomo
release cycle	12	4 (33.3%)	7.42E-00	0.000193	Keactome
Dopamine neurotransmitter	10	1 (22 20/)	7 425 06	0.000103	Desetomo
release cycle	12	4 (33.3%)	7.42E-00	0.000195	Reactome
C protein signaling pathways	02	8 (8 7%)	0 12E 06	0.00021	Wikipathwa
O protein signaning pathways	92	8 (8.7%)	9.42E-00	0.00021	ys
Signaling pathway from G	26	5 (10.2%)	9.63E-06	0.00021	PID
protein families	20	5 (17.270)	7.03L-00	0.00021	TID
signaling pathway from G	26	5 (10.2%)	0.63E-06	0.00021	BioCarta
protein families	20	5 (17.270)	7.03L-00	0.00021	DioCarta
L1CAM interactions	97	8 (8.2%)	1.40E-05	0.000268	Reactome
Recycling pathway of L1	28	5 (17.9%)	1.41E-05	0.000268	Reactome
G alpha (z) signalling events	47	6 (12.8%)	1.42E-05	0.000268	Reactome
Endocrine and other factor-		/			
regulated calcium	10		101505	0.00000	WEGG
reabsorption- <i>Homo sapiens</i>	49	6 (12.2%)	1.81E-05	0.000327	KEGG
(human)					
	15		1.000.05	0.000222	Wikipathwa
Neurotransmitter release cycle	15	4 (26.7%)	1.99E-05	0.000333	VS
Gastric acid secretion-Homo	= 1			0.000000	
sapiens (human)	74	7 (9.5%)	2.01E-05	0.000333	KEGG
Endocytotic role of ndk				0 000 707	
phosphins and dynamin	17	4 (23.5%)	3.42E-05	0.000525	PID
Endocytotic role of ndk	15	1 (00 50)	0.405.05	0.000.505	
phosphins and dynamin	17	4 (23.5%)	3.42E-05	0.000525	B10Carta
Cholinergic synapse- <i>Homo</i>	1.1.5	0 /7 1>	2 007 07	0.000501	UDCC
sapiens (human)	112	8 (7.1%)	3.99E-05	0.000591	KEGG
Axon guidance	268	12 (4.5%)	4.89E-05	0.0007	Reactome
GPCR signaling-G alpha s	2.72	12 (4 4%)	6.07E-05	0.00084	INOH
		12 (1170)	5.07 <u>L</u> 05	5.00001	

Epac and ERK					
Gap junction-Homo sapiens	80	7(7.00%)	6 67E 05	0 000866	VECC
(human)	09	7 (7.9%)	0.07E-03	0.000800	KEUU
Myometrial relaxation and	155	9 (5.8%)	6 68E-05	0 000866	Wikipathwa
contraction pathways	155) (3.870)	0.001-05	0.000000	ys
Hemostasis	471	16 (3.4%)	7.31E-05	0.000919	Reactome
Endothelins	65	6 (9.4%)	8.47E-05	0.000978	PID
Activation of GABAB	40	5 (12.5%)	8.48E-05	0.000978	Reactome
GABA B recentor activation	40	5 (12 5%)	8 48F-05	0.000978	Reactome
GPCR signaling-G alpha s	10	5 (12.570)	0.101 05	0.000770	Redetoine
PKA and ERK	285	12 (4.2%)	9.50E-05	0.00107	INOH
Endocytosis-Homo sapiens	202	10 (5.0%)	0.0001	0.00107	KEGG
(human)	202	10 (3.070)	0.0001	0.00107	KL00
Beta-agonist/beta-blocker pathway, pharmacodynamics	66	6 (9.1%)	0.000101	0.00107	PharmGKB
Dopaminergic synapse-Homo	130	8 (6.2%)	0.000115	0.00109	KEGG
sapiens (human)	100	0 (0.270)	0.000110	0.00109	
Effects of Botulinum toxin	9	3 (33.3%)	0.000116	0.00109	PID
Dopamine neurotransmitter	9	3 (33.3%)	0.000116	0.00109	PID
Neurotransmitter release cycle	9	3 (33.3%)	0.000116	0.00109	PID
Serotonin neurotransmitter		5 (55.570)	0.000110	0.00102	
release cycle	9	3 (33.3%)	0.000116	0.00109	PID
GABA synthesis	2	2 (100.0%)	0.000129	0.00117	Reactome
Glutamate dependent acid	2	2	0.000129	0.00117	HumanCyc
Long_term_depression_Homo		(100.0%)			
sapiens (human)	70	6 (8.6%)	0.00014	0.00121	KEGG
Regulation of ck1/cdk5 by type	24	4 (16.7%)	0.000143	0.00121	PID
Regulation of ck1/cdk5 by type					
1 glutamate receptors	24	4 (16.7%)	0.000143	0.00121	BioCarta
Ion channels and their					
functional role in vascular	47	5 (10.6%)	0.000186	0.00151	BioCarta
endothelium					
Ion channels and their			0.00010.6	0 001 71	
functional role in vascular	47	5 (10.6%)	0.000186	0.00151	PID
endothelium	262	11 (4 00/)	0.000102	0.00151	NIOH
GPCK signaling-G alpha i	262	11 (4.2%)	0.000193	0.00151	INUH
GPCR signaling-pertussis toxin	262	11 (4.2%)	0.000193	0.00151	INOH
Interaction between L1 and	26	4 (15.4%)	0.000198	0.00152	Reactome
Ankyrins Coloium cionoliz a pathwar		. /			
Homo sapiens (human)	183	9 (5.0%)	0.000218	0.00157	KEGG
Acetylcholine neurotransmitter	11	3 (27 20/)	0.000224	0.00157	Paactomo
release cycle	11	5 (21.5%)	0.000224	0.00137	Neactonie

Acetylcholine neurotransmitter	11	3 (27 3%)	0.000224	0.00157	PID
release cycle	11	5 (27.570)	0.000224	0.00137	TID
Norepinephrine	11	3 (27.3%)	0.000224	0.00157	Reactome
neurotransmitter release cycle					
Norepinephrine	11	3 (27.3%)	0.000224	0.00157	PID
CPCP signaling shalars to yin	270	11(4 10/)	0.000251	0.00172	INOU
Selective constants revertable	270	11 (4.1%)	0.000231	0.00175	поп
selective serotonin reuptake	20	4(14.30)	0.000267	0 00191	DhormCVD
ninonol panway,	28	4 (14.3%)	0.000207	0.00181	FlialliUKD
CPCP signaling C alpha g	274	11(4.00%)	0.000285	0.00101	INOU
Alaring and agreetate	274	11 (4.0%)	0.000283	0.00191	INON Wilzingthyyg
matabalism	12	3 (25.0%)	0.000296	0.00195	wikipatiwa
Trafficking of AMPA					ys
receptors	30	4 (13.3%)	0.000351	0.00224	Reactome
Glutamate binding activation					
of AMPA receptors and	30	4 (13 3%)	0.000351	0 00224	Reactome
synaptic plasticity	50	+(15.570)	0.000331	0.00224	Redetoine
Effects of calcineurin in					
keratinocyte differentiation	13	3 (23.1%)	0.000381	0.00233	PID
Effects of calcineurin in					
keratinocyte differentiation	13	3 (23.1%)	0.000381	0.00233	BioCarta
Recycling pathway of L1	13	3 (23.1%)	0.000381	0.00233	PID
Opioid signalling	85	6 (7.1%)	0.000407	0.00245	Reactome
Alanine aspartate and	00	0 (/11/0)	0.000107	0.00210	Trouctonic
glutamate metabolism- <i>Homo</i>	32	4 (12.5%)	0.000452	0 00268	KEGG
saniens (human)	52	1 (12.570)	0.000102	0.00200	iiiiiii
Serotonergic synapse- <i>Homo</i>	100		0.000.455	0.00050	WEGG
sapiens (human)	122	7 (5.7%)	0.000477	0.00273	KEGG
S1P4 pathway	15	3 (21.4%)	0.000481	0.00273	PID
Retrograde neurotrophin			0.000.401	0.00050	2
signalling	14	3 (21.4%)	0.000481	0.00273	Reactome
G alpha (i) signalling events	206	9 (4.4%)	0.000566	0.00317	Reactome
Gamma-aminobutyric acid			0.000 70 6	0.00015	DID
receptor life cycle pathway	15	3 (20.0%)	0.000596	0.00317	PID
Gamma-aminobutyric acid	1.5		0.000506	0.00217	
receptor life cycle pathway	15	3 (20.0%)	0.000596	0.00317	BioCarta
GPCRs, class C metabotropic	15	2(20.00)	0.000506	0.00217	Wikipathwa
glutamate, pheromone	15	5 (20.0%)	0.000390	0.00517	ys
Class C/3 (Metabotropic					
glutamate/pheromone	15	3 (20.0%)	0.000596	0.00317	Reactome
receptors)					
Ion channel transport	61	5 (8.2%)	0.000634	0.00333	Reactome
Glutamate degradation III (via		2(50.0%)	0.000763	0 00306	HumanCyc
4-aminobutyrate)	-	2 (30.0%)	0.000703	0.00390	i i u i i all'e ye
Developmental biology	363	12 (3.3%)	0.000805	0.00413	Reactome
Internalization of ErbB1	39	4 (10.5%)	0.000881	0.00446	PID
Integration of energy	101	6 (6.0%)	0.000966	0.00483	Reactome

metabolism						
Melanogenesis-Homo sapiens	101	6 (5 0%)	0.00102	0.00407	VECC	
(human)	101	0 (3.9%)	0.00102	0.00497	KEUU	
Potassium channels	101	6 (5.9%)	0.00102	0.00497	Reactome	
Nicotine addiction-Homo	40	A(10.0%)	0.00107	0.00517	KEGG	
sapiens (human)	40	4 (10.070)	0.00107	0.00317	KEGO	
EGF-EGFR signaling pathway	141	7 (5.0%)	0.00113	0.00537	Wikipathwa ys	
Long-term potentiation- <i>Homo</i> sapiens (human)	70	5 (7.1%)	0.00119	0.00561	KEGG	
Nitric oxide signaling pathway	19	3 (15.8%)	0.00123	0.00566	PID	
Nitric oxide signaling pathway	19	3 (15.8%)	0.00123	0.00566	BioCarta	
Creatine-phosphate biosynthesis	5	2 (40.0%)	0.00126	0.00569	HumanCyc	
Transmembrane transport of small molecules	433	13 (3.0%)	0.00128	0.00569	Reactome	
Actions of nitric oxide in the heart	42	4 (9.5%)	0.00129	0.00569	BioCarta	
Actions of nitric oxide in the heart	42	4 (9.5%)	0.00129	0.00569	PID	
PAR1-mediated thrombin signaling events	44	4 (9.1%)	0.00154	0.00671	PID	
PLC beta mediated events	45	4 (8.9%)	0.00167	0.00723	Reactome	
G protein mediated events	46	4 (8.7%)	0.00182	0.00769	Reactome	
Proton pump inhibitor pathway, pharmacodynamics	46	4 (8.7%)	0.00182	0.00769	PharmGKB	
Regulation of insulin secretion	80	5 (6.3%)	0.00204	0.00856	Reactome	
How progesterone initiates the	23	3 (13.0%)	0.00217	0.00892	PID	
How progesterone initiates the	23	3 (13.0%)	0.00217	0.00892	BioCarta	
Cocaine addiction- <i>Homo</i>						
sapiens (human)	50	4 (8.0%)	0.00247	0.0101	KEGG	
Platelet homeostasis	85	5 (6.0%)	0.00267	0.0108	Reactome	
Alanine aspartate asparagine metabolism	25	3 (12.0%)	0.00277	0.0111	INOH	
Amyotrophic lateral sclerosis (ALS)- <i>Homo sapiens</i> (human)	53	4 (7.5%)	0.00306	0.0116	KEGG	
TSH	26	3 (11.5%)	0.00311	0.0116	NetPath	
Inhibition of insulin secretion			0.00011	0.0115	D	
by adrenaline/noradrenaline	26	3 (11.5%)	0.00311	0.0116	Reactome	
CXCR4-mediated signaling	89	5 (5.7%)	0.00312	0.0116	PID	
Salivary secretion-Homo	Salivary secretion-Homo					
sapiens (human)	89	5 (5.6%)	0.00344	0.0116	KEGG	
S1P5 pathway	8	2 (25.0%)	0.00346	0.0116	PID	
Axonal growth inhibition	8	2 (25.0%)	0.00346	0.0116	Reactome	
(KIIUA activation)						

Organic anion transporters	8	2 (25.0%)	0.00346	0.0116	Reactome
Creatine metabolism	8	2 (25.0%)	0.00346	0.0116	Reactome
Glutamate glutamine	27	2(11,10/)	0.00247	0.0116	INOU
metabolism	27	3 (11.1%)	0.00347	0.0110	INOH
Transcription factor creb and	27	2(11,10/)	0.00247	0.0116	DID
its extracellular signals	27	5(11.1%)	0.00347	0.0110	PID
Transcription factor creb and	27	2(11,10/)	0.00247	0.0116	DioConto
its extracellular signals	27	5(11.1%)	0.00347	0.0110	DioCarta
Activation of G protein gated	27	2(11,10/)	0.00247	0.0116	Desetance
potassium channels	27	5(11.1%)	0.00347	0.0110	Reactonie
G protein gated potassium	27	2(11,10/)	0.00247	0.0116	Basatama
channels	27	3 (11.170)	0.00347	0.0110	Reactonie
Inhibition of voltage gated					
Ca ²⁺ channels <i>via</i> G	27	3 (11.1%)	0.00347	0.0116	Reactome
beta/gamma subunits					
Basigin interactions	29	3 (11.1%)	0.00347	0.0116	Reactome
L1CAM interestions	27	2(11,10/)	0.00247	0.0116	Wikipathwa
LICAM interactions	27	3 (11.1%)	0.00347	0.0116	ys
T cell receptor signaling	55	4 (7 20()	0.00251	0.0116	
pathway	55	4 (7.3%)	0.00351	0.0116	PID
T cell receptor signaling	<i></i>	4 (7 20/)	0.00251	0.0116	Die Cente
pathway	55	4 (7.3%)	0.00351	0.0116	BioCarta
Antiarrhythmic pathway,	<i></i>	4 (7 20/)	0.00251	0.0116	Dia and CKD
pharmacodynamics	55	4 (7.3%)	0.00351	0.0116	PharmGKB
Arginine proline metabolism	56	4 (7.3%)	0.00351	0.0116	INOH
Tight junction- <i>Homo sapiens</i>	100		0.00201	0.0100	WEGG
(human)	132	6 (4.6%)	0.00381	0.0123	KEGG
Thrombin signaling and	20	2(10,70())	0.00205	0.0102	DID
protease-activated receptors	28	3 (10.7%)	0.00385	0.0123	PID
Thrombin signaling and	20	2(10.70())	0.00295	0.0102	Die Cente
protease-activated receptors	28	3 (10.7%)	0.00385	0.0125	BioCarta
GPCR Group I metabotropic	20	2(10.70())	0.00295	0.0122	INOU
glutamate receptor	28	3 (10.7%)	0.00385	0.0125	INOH
Nitric oxide stimulates	20	2(10.70())	0.00295	0.0122	Desetares
guanylate cyclase	28	5 (10.7%)	0.00385	0.0125	Reactome
G alpha (s) signalling events	132	6 (4.5%)	0.00396	0.0125	Reactome
p75NTR regulates	0		0.00441	0.0120	D (
axonogenesis	9	2 (22.2%)	0.00441	0.0139	Reactome
Fc gamma R-mediated					
phagocytosis-Homo sapiens	97	5 (5.3%)	0.00455	0.0141	KEGG
(human)					
Fmlp induced chemokine gene	20	2(10.00())	0.0047	0.0141	DID
expression in hmc-1 cells	30	3 (10.0%)	0.0047	0.0141	PID
Fmlp induced chemokine gene	20	2(10.00/)	0.0047	0.0141	PioConto
expression in hmc-1 cells	50	5 (10.0%)	0.0047	0.0141	BIOCarta
Role of mef2d in T-cell	20	3(10.00/)	0.0047	0.0141	DID
apoptosis	50	5 (10.0%)	0.0047	0.0141	LID
Role of mef2d in T-cell	20	3(10.0%)	0.0047	0.0141	BioConto
apoptosis	50	5 (10.0%)	0.0047	0.0141	DioCalita

Nongenotropic androgen signaling323 (9.7%)0.005160.0154PIDTaurine and hypotaurine metabolism-Homo sapiens (human)102 (20.0%)0.005470.0158KEGGRegulation of spermatogenesis by crem102 (20.0%)0.005470.0158PIDRegulation of spermatogenesis by crem102 (20.0%)0.005470.0158PIDRegulation of spermatogenesis by crem102 (20.0%)0.005470.0158PIDLysosome vesicle biogenesis102 (20.0%)0.005470.0158PIDHypothetical network for drug addiction323 (9.4%)0.005640.0158PIDBer signaling pathway323 (9.4%)0.005640.0158PIDSignaling pathway323 (9.4%)0.005640.0158ReactomeGnRH signaling pathway1015 (5.0%)0.005400.0164REGGPhospholipids as signalling intermediaries333 (9.1%)0.006160.0164PIDPhospholipids as signalling intermediaries333 (9.1%)0.006160.0164BioCartaBioactive peptide induced signaling pathway333 (9.1%)0.006160.0164PIDPhospholipids as signalling intermediaries333 (9.1%)0.006160.0164BioCartaBioactive peptide induced signaling pathway333 (9.1%)0.006160.0164PiDGlucaon signaling in metabolic regulation353 (8.6%)0.0072	G protein activation	30	3 (10.0%)	0.0047	0.0141	Reactome
signaling 32 $3(9.1\%)$ 0.0016 0.0134 110 Taurine and hypotaurine metabolism-Homo sapiens (human) 10 $2(20.0\%)$ 0.00547 0.0158 KEGGRegulation of spermatogenesis by crem 10 $2(20.0\%)$ 0.00547 0.0158 PIDRetrograde neurotrophin signalling 10 $2(20.0\%)$ 0.00547 0.0158 PIDLysosome vesicle biogenesis didiction 10 $2(20.0\%)$ 0.00547 0.0158 PIDHypothetical network for drug addiction 32 $3(9.4\%)$ 0.00564 0.0158 PIDBer signaling pathway 322 $3(9.4\%)$ 0.00564 0.0158 PIDSignaling by robo receptor 33 $3(9.4\%)$ 0.00564 0.0158 BioCartaBer signaling pathway 322 $3(9.4\%)$ 0.00564 0.0158 BioCartaBrancreatic secretion-Homo sapiens (human) 101 $5(5.0\%)$ 0.00589 0.0163 KEGGPhospholipids as signalling intermediaries 33 $3(9.1\%)$ 0.00616 0.0164 PiDPhospholipids as signalling intermediaries 33 $3(9.1\%)$ 0.00616 0.0164 PiDBioactive peptide induced signaling pathway 33 $3(9.1\%)$ 0.00616 0.0164 PiDPhospholipids as signalling intermediaries 33 $3(9.1\%)$ 0.00616 0.0164 PiDRegulation of Ras family activation 33 $3(9.1\%)$ 0.00616 0.0164 Reactome <td>Nongenotropic androgen</td> <td>32</td> <td>3 (9 7%)</td> <td>0.00516</td> <td>0.0154</td> <td>Ы</td>	Nongenotropic androgen	32	3 (9 7%)	0.00516	0.0154	Ы
Taurine and hypotaurine metabolism-Homo sapiens (human)102 (20.0%) 2 (20.0%) 0.00547 0.0158 KEGGRegulation of spermatogenesis by crem102 (20.0%) 0.00547 0.0158 PIDRegulation of spermatogenesis by crem102 (20.0%) 0.00547 0.0158 BioCartaRetrograde neurotrophin signalling102 (20.0%) 0.00547 0.0158 PIDLysosome vesicle biogenesis102 (20.0%) 0.00547 0.0158 PIDLysosome vesicle biogenesis102 (20.0%) 0.00547 0.0158 PIDSignalling pathway323 (9.4%) 0.00564 0.0158 BioCartaBer signaling pathway323 (9.4%) 0.00564 0.0158 BioCartaBer signaling pathway323 (9.4%) 0.00564 0.0158 ReactomeGnRH signaling pathway101 $5 (5.0\%)$ 0.00589 0.0163 KEGGPhospholipids as signalling intermediaries33 $3 (9.1\%)$ 0.00616 0.0164 PIDBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 PIDBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 PIDBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 PIDBioactive peptide induced signaling in metabolic regulation35 $3 (8.6\%)$ 0.00727 0.019 ReactomePost N	signaling	52	3 ().170)	0.00510	0.0134	
metabolism-Homo sapiens (human)10 $2 (20.0\%)$ 0.00547 0.0158 KEGGRegulation of spermatogenesis by crem10 $2 (20.0\%)$ 0.00547 0.0158 PIDRegulation of spermatogenesis by crem10 $2 (20.0\%)$ 0.00547 0.0158 PIDRetrograde neurotrophin signaling Lysosome vesicle biogenesis10 $2 (20.0\%)$ 0.00547 0.0158 PIDHypothetical network for drug addiction32 $3 (9.4\%)$ 0.00564 0.0158 PIDHypothetical network for drug addiction32 $3 (9.4\%)$ 0.00564 0.0158 PiDSignaling pathway32 $3 (9.4\%)$ 0.00564 0.0158 PiDSignaling pathway32 $3 (9.4\%)$ 0.00564 0.0158 ReactomeGnRH signaling pathway- Homo sapiens (human)101 $5 (5.0\%)$ 0.00589 0.0163 KEGGPhospholipids as signalling intermediaries33 $3 (9.1\%)$ 0.00616 0.0164 PiDBioactive petide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 PiDBioactive petide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 PiDPhospholipids as signalling intermediaries33 $3 (9.1\%)$ 0.00616 0.0164 PiDBioactive petide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 PiDRegulation of Ras family activation35 $3 (8.6\%)$ 0.00727 0.019	Taurine and hypotaurine					
(human)Image: Constraint of the second system and the second s	metabolism-Homo sapiens	10	2 (20.0%)	0.00547	0.0158	KEGG
Regulation of spermatogenesis by crem102 (20.0%)0.005470.0158PIDRegulation of spermatogenesis by crem102 (20.0%)0.005470.0158BioCartaRetrograde neurotrophin signalling102 (20.0%)0.005470.0158PIDLysosome vesicle biogenesis102 (20.0%)0.005470.0158PIDHypothetical network for drug addiction323 (9.4%)0.005640.0158BioCartaBer signaling pathway323 (9.4%)0.005640.0158BioCartaBer signaling pathway323 (9.4%)0.005640.0158ReactomeGnRH signaling pathway- Homo sapiens (human)1015 (5.0%)0.005890.0163KEGGPhacreatic secretion-Homo sapiens (human)333 (9.1%)0.006160.0164PIDPhospholipids as signalling intermediaries333 (9.1%)0.006160.0164PIDPhospholipids as signalling intermediaries333 (9.1%)0.006160.0164PIDBioactive peptide induced signaling pathway333 (9.1%)0.006160.0164ReactomeRegulation of Ras family activation333 (9.1%)0.006160.0164PIDBioactive peptide induced signaling pathway333 (9.1%)0.006160.0164ReactomeRegulation of Ras family activation353 (8.6%)0.007270.019ReactomeRegulation of Ras family activation353 (8.6	(human)					
by crem10 $2 (20.06)$ 0.00547 0.0150 110 Regulation of spermatogenesis by crem10 $2 (20.06)$ 0.00547 0.0158 BioCartaRetrograde neurotrophin signaling addiction10 $2 (20.06)$ 0.00547 0.0158 PIDLysosome vesicle biogenesis10 $2 (20.06)$ 0.00547 0.0158 PIDHypothetical network for drug addiction32 $3 (9.4%)$ 0.00564 0.0158 BioCartaBer signaling pathway32 $3 (9.4%)$ 0.00564 0.0158 BioCartaBer signaling pathway32 $3 (9.4%)$ 0.00564 0.0158 ReactomeGnRH signaling by robo receptor33 $3 (9.4%)$ 0.00564 0.0158 ReactomeGnRH signaling bribway- Homo sapiens (human)101 $5 (5.0%)$ 0.00589 0.0163 KEGGPhospholipids as signalling intermediaries33 $3 (9.1%)$ 0.00616 0.0164 BioCartaBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 BioCartaBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 BioCartaBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 ReactomeRegulation of Ras family activation33 $3 (9.1\%)$ 0.00616 0.0164 PIDGlucagon signaling in metabolic regulation35 $3 (8.6\%)$ 0.00727 0.019 Reactome <td>Regulation of spermatogenesis</td> <td>10</td> <td>2(20.0%)</td> <td>0.00547</td> <td>0.0158</td> <td>PID</td>	Regulation of spermatogenesis	10	2(20.0%)	0.00547	0.0158	PID
Regulation of spermatogenesis by crem102 (20.0%)0.005470.0158BioCartaRetrograde neurotrophin signalling102 (20.0%)0.005470.0158PIDLysosome vesicle biogenesis102 (20.0%)0.005470.0158PIDHypothetical network for drug addiction323 (9.4%)0.005640.0158PIDBer signaling pathway323 (9.4%)0.005640.0158BioCartaBer signaling pathway323 (9.4%)0.005640.0158ReactomeGnRH signaling pathway- Homo sapiens (human)1015 (5.0%)0.005890.0163KEGGPancreatic secretion-Homo sapiens (human)1015 (5.0%)0.005890.0164PIDPhospholipids as signalling intermediaries333 (9.1%)0.006160.0164PiDBioactive peptide induced signaling pathway333 (9.1%)0.006160.0164PiDBioactive peptide induced signaling pathway333 (9.1%)0.006160.0164ReactomeRegulation of Ras family activation333 (9.1%)0.006160.0164PiDReatome channels353 (8.6%)0.007270.019ReactomePost NMDA receptor activation events353 (8.6%)0.007270.019ReactomeInvardly rectifying K ⁺ channels353 (8.6%)0.007270.019ReactomePost NMDA receptor activation events353 (8.6%)0.007270.0	by crem	10	2 (20.070)	0.00547	0.0150	
by crem10 $2 (20.07)$ 0.00547 0.0156 $DioCata$ Retrograde neurotrophin10 $2 (20.0\%)$ 0.00547 0.0158 PIDLysosome vesicle biogenesis10 $2 (20.0\%)$ 0.00547 0.0158 PIDHypothetical network for drug addiction32 $3 (9.4\%)$ 0.00564 0.0158 PiDBer signaling pathway32 $3 (9.4\%)$ 0.00564 0.0158 PiDSignaling pathway32 $3 (9.4\%)$ 0.00564 0.0158 PiDSignaling pathway32 $3 (9.4\%)$ 0.00564 0.0158 ReactomeGnRH signaling pathway- Homo sapiens (human)101 $5 (5.0\%)$ 0.00589 0.0163 KEGGPhacreatic secretion-Homo sapiens (human)101 $5 (5.0\%)$ 0.00616 0.0164 PiDPhospholipids as signalling intermediaries33 $3 (9.1\%)$ 0.00616 0.0164 PiDPhospholipids as signalling intermediaries33 $3 (9.1\%)$ 0.00616 0.0164 PiDBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 ReactomeRegulation of Ras family activation33 $3 (9.1\%)$ 0.00616 0.0164 PiDRegulation of Ras family activation35 $3 (8.6\%)$ 0.00727 0.019 ReactomeRegulation of Ras family activation events35 $3 (8.6\%)$ 0.00727 0.019 ReactomePost NMDA receptor activation events35 $3 $	Regulation of spermatogenesis	10	2(20.0%)	0.00547	0.0158	BioCarta
Retrograde neurotrophin signalling102 (20.0%)0.005470.0158PIDLysosome vesicle biogenesis102 (20.0%)0.005470.0158Wikipathwa ysMypothetical network for drug addiction323 (9.4%)0.005640.0158BioCartaBer signaling pathway323 (9.4%)0.005640.0158BioCartaBer signaling pathway323 (9.4%)0.005640.0158ReactomeGnRH signaling pathway- Homo sapiens (human)1015 (5.0%)0.005890.0163KEGGPancreatic secretion-Homo sapiens (human)1015 (5.0%)0.006160.0164PiDPhospholipids as signalling intermediaries333 (9.1%)0.006160.0164PiDBioactive peptide induced signaling pathway333 (9.1%)0.006160.0164BioCartaBioactive peptide induced signaling pathway333 (9.1%)0.006160.0164BioCartaInwardly rectifying K [±] channels333 (9.1%)0.006160.0164PiDGlucagon signaling in metabolic regulation353 (8.6%)0.007270.019ReactomePost NMDA receptor activation events353 (8.6%)0.007270.019ReactomePost NMDA receptor activation events353 (8.6%)0.007270.019ReactomeFor the the in activation events353 (8.6%)0.007270.019ReactomeFor the the in activation events35	by crem	10	2 (20.070)	0.00547	0.0138	DioCarta
signalling10 $2 (20.0\%)$ 0.00547 0.0138 FIDLysosome vesicle biogenesis10 $2 (20.0\%)$ 0.00547 0.0158 PIDHypothetical network for drug addiction32 $3 (9.4\%)$ 0.00564 0.0158 BioCartaBcr signaling pathway32 $3 (9.4\%)$ 0.00564 0.0158 PIDSignaling pathway32 $3 (9.4\%)$ 0.00564 0.0158 PIDSignaling pathway-33 $3 (9.4\%)$ 0.00564 0.0158 ReactomeGnRH signaling pathway-101 $5 (5.0\%)$ 0.00589 0.0163 KEGGPancreatic secretion-Homo sapiens (human)101 $5 (5.0\%)$ 0.00516 0.0164 PIDPhospholipids as signalling intermediaries33 $3 (9.1\%)$ 0.00616 0.0164 PIDPhospholipids as signalling intermediaries33 $3 (9.1\%)$ 0.00616 0.0164 PIDBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 PIDRegulation of Ras family activation33 $3 (9.1\%)$ 0.00616 0.0164 ReactomeRegulation of Ras family activation35 $3 (8.6\%)$ 0.00727 0.019 ReactomePost NMDA receptor activation events35 $3 (8.6\%)$ 0.00727 0.019 ReactomeEndothelin35 $3 (8.6\%)$ 0.00727 0.019 ReactomeMathemaling addiction-Homo sapians109 $5 (4.6\%)$ 0.00727 0.01	Retrograde neurotrophin	10	2(20.0%)	0.00547	0.0158	
Lysosome vesicle biogenesis10 $2 (20.0\%)$ 0.00547 0.0158 PIDHypothetical network for drug addiction32 $3 (9.4\%)$ 0.00564 0.0158 Wikipathwa ysBer signaling pathway32 $3 (9.4\%)$ 0.00564 0.0158 BioCartaBer signaling pathway32 $3 (9.4\%)$ 0.00564 0.0158 PIDSignaling by robo receptor33 $3 (9.4\%)$ 0.00564 0.0158 ReactomeGnRH signaling pathway- Homo sapiens (human)101 $5 (5.0\%)$ 0.00589 0.0163 KEGGPancreatic sceretion-Homo sapiens (human)101 $5 (5.0\%)$ 0.00589 0.0164 PIDPhospholipids as signalling intermediaries33 $3 (9.1\%)$ 0.00616 0.0164 PIDPhospholipids as signalling intermediaries33 $3 (9.1\%)$ 0.00616 0.0164 PIDBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 PIDBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 PIDRegulation of Ras family activation33 $3 (9.1\%)$ 0.00616 0.0164 PIDGlucagon signaling in metabolic regulation35 $3 (8.6\%)$ 0.00727 0.019 ReactomePost NIDA receptor activation events35 $3 (8.6\%)$ 0.00727 0.019 Wikipathwa ysEndothelin35 $3 (8.6\%)$ 0.00727 0.019 ReactomeOha	signalling	10	2 (20.070)	0.00547	0.0138	1 ID
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Arginaling by 1000 receptor33 $3(9.4\%)$ 0.00304 0.0138 ReactonicGnRH signaling pathway- Homo sapiens (human)101 $5(5.0\%)$ 0.00589 0.0163 KEGGPancreatic secretion-Homo sapiens (human)101 $5(5.0\%)$ 0.00589 0.0163 KEGGPhospholipids as signalling intermediaries33 $3(9.1\%)$ 0.00616 0.0164 PIDPhospholipids as signalling intermediaries33 $3(9.1\%)$ 0.00616 0.0164 PiDBioactive peptide induced signaling pathway33 $3(9.1\%)$ 0.00616 0.0164 PiDBioactive peptide induced signaling pathway33 $3(9.1\%)$ 0.00616 0.0164 PiDBioactive peptide induced signaling pathway33 $3(9.1\%)$ 0.00616 0.0164 ReactomeRegulation of Ras family activation33 $3(9.1\%)$ 0.00616 0.0164 ReactomeRegulation of Ras family activation35 $3(8.6\%)$ 0.00727 0.019 ReactomePost NMDA receptor activation events35 $3(8.6\%)$ 0.00727 0.019 Wikipathwa ysPurine nucleotides nucleosides metabolism109 $5(4.6\%)$ 0.00786 0.0203 ReactomeGABA A receptor activation addiction-Homo sapiens (human)12 $2(16.7\%)$ 0.00828 0.0211 KEGGG13 signaling pathway37 $3(8.1\%)$ 0.00849 0.0215 Wikipathwa ys	Signaling by robo recentor	22	3(9.4%)	0.00564	0.0158	Desetome
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Homo sapiens (human)Image: transformation of the section of the sectin the section of	GnRH signaling pathway-	101	5 (5.0%)	0.00589	0.0163	KEGG
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saptens(human) 1 </td <td>Pancreatic secretion-Homo</td> <td>101</td> <td>5 (5.0%)</td> <td>0.00589</td> <td>0.0163</td> <td>KEGG</td>	Pancreatic secretion-Homo	101	5 (5.0%)	0.00589	0.0163	KEGG
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Phospholipids as signalling intermediaries33 $3 (9.1\%)$ 0.00616 0.0164 BioCartaBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 PIDBioactive peptide induced signaling pathway33 $3 (9.1\%)$ 0.00616 0.0164 BioCartaInwardly rectifying K ⁺ channels33 $3 (9.1\%)$ 0.00616 0.0164 ReactomeRegulation of Ras family activation33 $3 (9.1\%)$ 0.00616 0.0164 PIDGlucagon signaling in metabolic regulation35 $3 (8.6\%)$ 0.00727 0.019 ReactomePost NMDA receptor activation events35 $3 (8.6\%)$ 0.00727 0.019 ReactomeEndothelin35 $3 (8.6\%)$ 0.00727 0.019 Wikipathwa ysPurine nucleotides nucleosides metabolism109 $5 (4.6\%)$ 0.00778 0.0202 INOHIon transport by P-type ATPases36 $3 (8.3\%)$ 0.00786 0.0203 ReactomeGABA A receptor activation12 $2 (16.7\%)$ 0.00828 0.0211 KEGGGil3 signaling pathway37 $3 (8.1\%)$ 0.00849 0.0215 Wikipathwa ys	intermediaries		- (,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			
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signaling pathwaySo	Bioactive peptide induced	33	3 (9 1%)	0.00616	0.0164	PID
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signaling pathway355 (3.1%)0.000100.0101DiocatalInwardly rectifying K+ channels333 (9.1%)0.006160.0164ReactomeRegulation of Ras family activation333 (9.1%)0.006160.0164PIDGlucagon signaling in metabolic regulation353 (8.6%)0.007270.019ReactomePost NMDA receptor activation events353 (8.6%)0.007270.019ReactomeEndothelin353 (8.6%)0.007270.019Wikipathwa ysPurine nucleotides nucleosides metabolism1095 (4.6%)0.007780.0202INOHIon transport by P-type ATPases363 (8.3%)0.007860.0203ReactomeGABA A receptor activation122 (16.7%)0.008280.0211KEGGAmphetamine addiction-Homo sapiens (human)373 (8.1%)0.008490.0215Wikipathwa ys	Bioactive peptide induced	33	3 (9 1%)	0.00616	0.0164	BioCarta
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Post NMDA receptor activation events353 (8.6%)0.007270.019ReactomeEndothelin353 (8.6%)0.007270.019Wikipathwa ysPurine nucleotides nucleosides metabolism1095 (4.6%)0.007780.0202INOHIon transport by P-type ATPases363 (8.3%)0.007860.0203ReactomeGABA A receptor activation122 (16.7%)0.007910.0203ReactomeAmphetamine addiction-Homo sapiens (human)704 (5.7%)0.008280.0211KEGGG13 signaling pathway373 (8.1%)0.008490.0215Wikipathwa ys	metabolic regulation	55	5 (8.0%)	0.00727	0.019	Reactome
activation events353 (8.6%)0.007270.019ReactomeEndothelin353 (8.6%)0.007270.019Wikipathwa ysPurine nucleotides nucleosides metabolism1095 (4.6%)0.007780.0202INOHIon transport by P-type ATPases363 (8.3%)0.007860.0203ReactomeGABA A receptor activation122 (16.7%)0.007910.0203ReactomeAmphetamine addiction-Homo sapiens (human)704 (5.7%)0.008280.0211KEGGG13 signaling pathway373 (8.1%)0.008490.0215Wikipathwa ys	Post NMDA receptor	25	2(9,60/)	0.00727	0.010	Desetares
Endothelin 35 $3 (8.6\%)$ 0.00727 0.019 Wikipathwa ysPurine nucleotides nucleosides metabolism 109 $5 (4.6\%)$ 0.00778 0.0202 INOHIon transport by P-type ATPases 36 $3 (8.3\%)$ 0.00786 0.0203 ReactomeGABA A receptor activation 12 $2 (16.7\%)$ 0.00791 0.0203 ReactomeAmphetamine addiction-Homo sapiens (human) 70 $4 (5.7\%)$ 0.00828 0.0211 KEGGG13 signaling pathway 37 $3 (8.1\%)$ 0.00849 0.0215 Wikipathwa ys	activation events	35	3 (8.6%)	0.00727	0.019	Reactome
Endothelin353 (8.6%)0.007270.0191Purine nucleotides nucleosides metabolism1095 (4.6%)0.007780.0202INOHIon transport by P-type ATPases363 (8.3%)0.007860.0203ReactomeGABA A receptor activation122 (16.7%)0.007910.0203ReactomeAmphetamine addiction-Homo sapiens (human)704 (5.7%)0.008280.0211KEGGG13 signaling pathway373 (8.1%)0.008490.0215Wikipathwa vs		25	2 (9 (9))	0.00707	0.010	Wikipathwa
Purine nucleotides nucleosides metabolism1095 (4.6%)0.007780.0202INOHIon transport by P-type ATPases363 (8.3%)0.007860.0203ReactomeGABA A receptor activation122 (16.7%)0.007910.0203ReactomeAmphetamine addiction-Homo sapiens (human)704 (5.7%)0.008280.0211KEGGG13 signaling pathway373 (8.1%)0.008490.0215Wikipathwa vs	Endothelin	35	3 (8.6%)	0.00727	0.019	ys
metabolism 109 5 (4.6%) 0.007/8 0.0202 INOH Ion transport by P-type ATPases 36 3 (8.3%) 0.00786 0.0203 Reactome GABA A receptor activation 12 2 (16.7%) 0.00791 0.0203 Reactome Amphetamine addiction-Homo sapiens (human) 70 4 (5.7%) 0.00828 0.0211 KEGG G13 signaling pathway 37 3 (8.1%) 0.00849 0.0215 Wikipathwa	Purine nucleotides nucleosides	100		0.00770	0.0000	niou
Ion transport by P-type ATPases363 (8.3%)0.007860.0203ReactomeGABA A receptor activation122 (16.7%)0.007910.0203ReactomeAmphetamine addiction-Homo sapiens (human)704 (5.7%)0.008280.0211KEGGG13 signaling pathway373 (8.1%)0.008490.0215Wikipathwa vs	metabolism	109	5 (4.6%)	0.00778	0.0202	INOH
ATPases 36 3 (8.3%) 0.00786 0.0203 Reactome GABA A receptor activation 12 2 (16.7%) 0.00791 0.0203 Reactome Amphetamine addiction-Homo sapiens (human) 70 4 (5.7%) 0.00828 0.0211 KEGG G13 signaling pathway 37 3 (8.1%) 0.00849 0.0215 Wikipathwa	Ion transport by P-type					
GABA A receptor activation122 (16.7%)0.007910.0203ReactomeAmphetamine addiction-Homo sapiens (human)704 (5.7%)0.008280.0211KEGGG13 signaling pathway373 (8.1%)0.008490.0215Wikipathwa vs	ATPases	36	3 (8.3%)	0.00786	0.0203	Reactome
Amphetamine addiction-Homo sapiens (human)704 (5.7%)0.008280.0211KEGGG13 signaling pathway373 (8.1%)0.008490.0215Wikipathwa vs	GABA A receptor activation	12	2 (16 7%)	0.00791	0.0203	Reactome
rampletamine addretion-fromo 70 4 (5.7%) 0.00828 0.0211 KEGG sapiens (human) 37 3 (8.1%) 0.00849 0.0215 Wikipathwa	Amphetamine addiction_Homo	12	_ (10.770)	0.00771	0.0205	
Suprens (numar)Suprens (numar)WikipathwaG13 signaling pathway373 (8.1%)0.008490.0215	sanians (human)	70	4 (5.7%)	0.00828	0.0211	KEGG
G13 signaling pathway 37 3 (8.1%) 0.00849 0.0215 Wikipathwa	suprens (numan)					Wikinathwa
	G13 signaling pathway	37	3 (8.1%)	0.00849	0.0215	vs

CXCR3-mediated signaling	38	3 (7.9%)	0.00914	0.0221	PID
events			010071	010221	
Intracellular signalling through					
adenosine receptor A2a and	38	3 (7.9%)	0.00914	0.0221	SMPDB
adenosine		· · · ·			
Intracellular signalling through					
adenosine receptor A2b and	38	3 (7.9%)	0.00914	0.0221	SMPDB
adenosine					
Regulation of insulin secretion	20	2(7.0%)	0.00014	0.0221	Deastoma
by glucagon-like peptide-1	30	3(7.9%)	0.00914	0.0221	Reactome
Aspartate metabolism	13	2 (15.4%)	0.00928	0.0221	SMPDB
Adenylate cyclase inhibitory	12	2(15.40/)	0.00028	0.0221	Desetomo
pathway	15	2(13.4%)	0.00928	0.0221	Reactonie
Inhibition of adenylate cyclase	12	2(15,40())	0.00020	0.0221	Desetance
pathway	13	2(15.4%)	0.00928	0.0221	Reactome
Attenuation of GPCR signaling	13	2 (15.4%)	0.00928	0.0221	PID
Attenuation of GPCR signaling	13	2 (15.4%)	0.00928	0.0221	BioCarta
D-myo-inositol (1,4,5)-	12	2(15.40/)	0.00028	0.0221	HumonCuo
trisphosphate degradation	15	2(13.4%)	0.00928	0.0221	HumanCyc
Activation of NMDA receptor					
upon glutamate binding and	39	3 (7.7%)	0.00982	0.0233	Reactome
postsynaptic events					

A1	Bax antibody
A2	c-Myc (D84C12) XP® rabbit mAb
A3	c-Raf antibody
A4	FAK antibody
A5	FGF receptor 1 antibody
A6	GSK-3β (27C10) rabbit mAb
A7	HSP90 antibody
A8	Jak1 (6G4) rabbit mAb
A9	Jak2 (D2E12) XP® rabbit mAb
A10	mTOR (7C10) rabbit mAb
A11	p38α MAPK (7D6) rabbit mAb
A12	p70 S6 kinase (49D7) rabbit mAb
B1	PLCγ2 antibody
B2	Rb (D20) rabbit mAb
B3	SAPK/JNK (56G8) rabbit mAb
B4	Src (36D10) rabbit mAb
B5	Phospho-AMPKα (Thr172) (D79.5E) rabbit mAb
B6	Phospho-p38 MAPK (Thr180/Tyr182) (D3F9) XP™ rabbit mAb
B7	Phospho-PDGF receptor α (Tyr1018) antibody
B8	Phospho-PDGF receptor β (Tyr1009) (42F9) rabbit mAb
B9	Phospho-PLCγ1 (Tyr783) antibody
B10	Phospho-Raptor (Ser792) antibody
B11	Phospho-Rb (Ser780) (C84F6) rabbit mAb
B12	Phospho-SAPK/JNK (Thr183/Tyr185) (81E11) rabbit mAb
C1	Phospho-Src (Tyr527) antibody
C2	Phospho-Tuberin/TSC2 (Thr1462) (5B12) rabbit mAb
C3	Phospho-VEGF receptor 2 (Tyr1059) (D5A6) rabbit mAb

E1	Alpha-tubulin
E2	AMPKα1, rabbit monoclonal
E3	Cdk4
F4	Cyclin B1 (C-term), clone
Ľ4	Y106, rabbit monoclonal
F5	Cyclin D1, clone EP272Y,
LJ	rabbit monoclonal
E6	Cyclin E1, clone EP435E rabbit
	monoclonal
E7	Cyclin E2, clone EP454Y,
FO	rabbit monocional
E8	ErbB-2/HER-2
E9	Estrogen receptor α , clone E115
E10	Frizzled 5
E11	GRB2
E12	HDAC3, clone Y415, rabbit
	monoclonal; 100 μL
F1	HIF-1a
F2	MDM2
F3	NF- B p50, clone E381
F4	PI3 kinase, p110α rabbit
	monoclonal
F5	PI3 kinase, p85, N-SH2, clone
	UB93-3
F6	PTFN rabbit monoclonal
ľU	
	Phospho-erbB2 (Thr686), clone
F 7	7F8
E0	Phospho-GSK3
Гð	(Tyr279/Tyr216), clone 5G-2F
FO	Phospho-GSK3β (Ser9), clone
17	2D3
F10	Phospho-insulin receptor (Tyr
110	1150/1151), clone 10C3
F11	Phospho-Cdc25C (Ser216),
	clone E190, rabbit monoclonal
F1 3	Phospho-c-Jun (Ser63),clone
F12	Y172; 100 μL
G1	Phospho-c-Myc (Thr58/Ser62)
G2	Phospho-EGFR (Tyr1086)
C3	Phospho-estrogen receptor α
05	(Ser167)

Supplementary information, Table S3. Antibodies used in the microwestern assay.

C4	GAPDH
C5	Actin, near a.a. 50-70, clone C4
C6	APC, C-terminus, clone C-APC 28.9
C7	CrkL, clone 5-6; 100 μg
C8	p21/WAF1/Cip1, clone CP74
С9	β-Catenin, clone 2H4A7
C10	Phospho-ATM (Ser1981), clone 10H11.E12
C11	Phospho-acetyl CoA carboxylase (Ser79); 200 µg
C12	Phospho-JNK (Thr183/Tyr185, Thr221/Tyr223)
D1	Phospho-mTOR (Ser2481); 100 μL
D2	Phospho-STAT6 (Tyr641)
D3	Phospho-Akt1/PKBα (Ser473), clone 11E6
D4	Phospho-MKK4 (Ser257/Thr261)
D5	Phospho-PKCδ (Ser645)
D6	Bcl2, clone 100
D7	Cyclin A, clone BF 683
D8	EGFR, clone LA22
D9	p53, clone BP53-12
D10	PI3 Kinase, p85, N-SH3, clone AB6
D11	Acetyl CoA carboxylase 1, rabbit mAb
D12	Akt1/PKBα, clone AW24

G4	Phospho-FAK (Tyr861)
C5	Phospho-IRS1 (Ser307); 200
63	μL
C-6	Phospho-JAK1
90	(Tyr1022/Tyr1023)
G7	Phospho-JAK2 (Tyr1007/1008)
C8	Phospho-MAP kinase1/2
90	(Erk1/2)
	Phospho-MEK1
G9	(Ser218/222)/MEK2
	(Ser222/226)
G10	Phospho-Met (Tyr1003)
011	Phospho-p70 S6 kinase
GII	(Thr389), rabbit monoclonal
C12	Phospho-PAK1
GI2	(Ser199/Ser204)
Ц1	Phospho-PKA, RII (Ser96),
111	rabbit monoclonal
H2	Phospho-PKCε (Ser729)
Н3	Phospho-PKD (Ser916)
H4	Phospho-PPARγ (Ser82), clone
	AW504
H5	Phospho-PTEN (Ser385)
H6	Phospho-Src (Tyr416), clone
	9A6
H7	Phospho-c-Raf
	(Ser 538/1 yr 540)
H8	Phospho-Kai-1 (T_{vr}^{2} 40/ T_{vr}^{2} 41)
110	$\frac{(1y1340/1y1341)}{\text{Dhospho Src}(Tyr(19))}$
НУ	Phospho-Sic (191418)
H10	Phospho-STAT1 (Ser727)
H11	Phospho-STAT2 (Tyr689)
Ц12	Phospho-STAT5A/B
1112	(Tyr694/699), clone A11W

Supplementary information, Table S4. GBM differentially expressed probesets with at least 4 appearances from 5 GBM datasets.

probeset (up-regulated)	gene	times
211980_at	COL4A1	5
201761_at	MTHFD2	5
219918_s_at	ASPM	4
219410_at	TMEM45A	4
219148_at	PBK	4
218883_s_at	MLF1IP	4
218678_at	NES	4
218585_s_at	DTL	4
218039_at	NUSAP1	4
215076_s_at	COL3A1	4
211964_at	COL4A2	4
210809_s_at	POSTN	4
206157_at	PTX3	4
205347_s_at	TMSB15A	4
204915_s_at	SOX11	4
203820_s_at	IGF2BP3	4
203819_s_at	IGF2BP3	4
203548_s_at	LPL	4
203358_s_at	EZH2	4
203213_at	CDK1	4
202503_s_at	KIAA0101	4
202404_s_at	COL1A2	4
202403_s_at	COL1A2	4
202007_at	NID1	4
201984_s_at	EGFR	4
201983_s_at	EGFR	4
201664_at	SMC4	4
201617_x_at	CALD1	4
201292_at	TOP2A	4

probeset (down-regulated)	gene	times
221802_s_at	KIAA1598	5
213385_at	CHN2	5
212681_at	EPB41L3	5
209576_at	GNAI1	5
205814_at	GRM3	5
205637_s_at	SH3GL3	5
204681_s_at	RAPGEF5	5
204547_at	RAB40B	5
222005_s_at	GNG3	4
221916_at	NEFL	4
221805_at	NEFL	4
219685_at	TMEM35	4
219671_at	HPCAL4	4
219659_at	ATP8A2	4
219619_at	DIRAS2	4
219368_at	NAP1L2	4
218623_at	HMP19	4
214762_at	ATP6V1G2	4
214434_at	HSPA12A	4
214157_at	GNAS	4
214111_at	OPCML	4
214046_at	FUT9	4
213938_at	ERC2	4
213904_at		4
213558_at	PCLO	4
213486_at	COPG2IT1	4
213268_at	CAMTA1	4
213131_at	OLFM1	4
213122_at	TSPYL5	4
213106_at	ATP8A1	4
212624_s_at	CHN1	4
212473_s_at	MICAL2	4
212339_at	EPB41L1	4
211776_s_at	EPB41L3	4
	GABARAP	
211458_s_at	GABARAP	4
	L3	
211276_at	TCEAL2	4

20

210657_s_at	SEPT4	4
210404_x_at	CAMK2B	4
210222_s_at	RTN1	4
210016_at	MYT1L	4
209990_s_at	GABBR2	4
209956_s_at	CAMK2B	4
209839_at	DNM3	4
209755_at	NMNAT2	4
209685_s_at	PRKCB	4
209392_at	ENPP2	4
209242_at	PEG3	4
209072_at	MBP	4
207957_s_at	PRKCB	4
207093_s_at	OMG	4
207010_at	GABRB1	4
206710_s_at	EPB41L3	4
206385_s_at	ANK3	4
206349_at	LGI1	4
206196_s_at	RUNDC3A	4
205818_at	DBC1	4
205795_at	NRXN3	4
205751_at	SH3GL2	4
205737_at	KCNQ2	4
205591_at	OLFM1	4
205352_at	SERPINI1	4
205348_s_at	DYNC1I1	4
205278_at	GAD1	4
205110_s_at	FGF13	4
204995_at	CDK5R1	4
204953_at	SNAP91	4
204823_at	NAV3	4
204793_at	GPRASP1	4
204777_s_at	MAL	4
204743_at	TAGLN3	4
204720_s_at	DNAJC6	4
204684_at	NPTX1	4
204584_at	L1CAM	4
204466_s_at	SNCA	4
204465_s_at	INA	4
203999_at	SYT1	4
203798_s_at	VSNL1	4
203797_at	VSNL1	4
203607_at	INPP5F	4
203485_at	RTN1	4

203001_s_at	STMN2	4
203000_at	STMN2	4
202890_at	MAP7	4
202508_s_at	SNAP25	4
202507_s_at	SNAP25	4
202391_at	BASP1	4
202363_at	SPOCK1	4
202260_s_at	STXBP1	4

	Drug Name	Rank	Mean	Ν	Enrichment	Р
Wong et al. study	Trifluoperazine	1	-0.533	16	-0.579	0
	Prochlorperazine	2	-0.538	16	-0.577	0
	Thioridazine	3	-0.558	20	-0.534	0
	Chlorpromazine	17	-0.402	19	-0.393	0.00389
	Fluphenazine	21	-0.494	18	-0.392	0.00576
	Acepromazine	60	-0.59	4	-0.659	0.0306
	Promethazine	75	-0.582	4	-0.625	0.04884
	Perphenazine					
	Trifluoperazine	5	-0.342	16	-0.497	0.00028
y	Prochlorperazine	9	-0.329	16	-0.475	0.00082
tud	Thioridazine	13	-0.335	20	-0.401	0.00189
al. s	Chlorpromazine					
s et	Fluphenazine	43	-0.291	18	-0.266	0.04351
hats	Acepromazine					
S	Promethazine					
	Perphenazine	37	-0.453	5	-0.589	0.03446
	Trifluoperazine	47	-0.371	16	-0.417	0.00499
>	Prochlorperazine					
Suvà et al. study	Thioridazine	11	-0.407	20	-0.51	0
	Chlorpromazine					
	Fluphenazine					
	Acepromazine					
	Promethazine					
	Perphenazine					

Supplementary information, Table S5. Appearance of phenothiazines from the Cmap analysis of three anti-cancer stem cell signatures.

*(top) The dataset of different gene signatures of ESC and adult stem cells from Wong et al. (2008) [25] is available online (http://www.ncbi.nlm.nih.gov/geo/; [GEO Series accession number GSE10423]). Phenothiazine-like anti-psychotics appear frequently when the Cmap drug list is queried with differential ESC-like to adult stem-like cell gene signatures. There are a total of 77 potential drugs with negative enrichments and p < 0.05. Ranking refers to these 77 potential drugs.

(middle) Shats et al. (2011) [23] study used multiple cancer cell lines with differential stem-like cell characteristics, such as basal gene expression of breast cancer or

CD133-positive versus glioma cells, to query the Cmap database for drugs that reverse the CSC-associated signatures.

(bottom) Suvà et al. (2009) [24] found that EZH2 plays a crucial role in tissue-specific stem-like cell maintenance and is overexpressed in GBM. Treatment with DZNep strongly impairs GBM CSC self-renewal *in vitro* and tumor-initiating capacity *in vivo*. The expression signature was established using CSC enriched gliospheroids from primary GBM cell cultures, with or without DZNep treatment.

Supplementary information, Table S6. Up-regulated and down-regulated proteins in the microwestern assay.

Up-regulation

Protein	Samle	Fold change
p-AMPKa (Thr172) (D79.5E) rabbit mAb	Control	1.000
	Thioridazine 5 uM	1.287
	Thioridazine 10 uM	1.620
	Thioridazine 15 uM	3.403
PTEN	Control	1.000
	Thioridazine 5 uM	1.861
	Thioridazine 10 uM	6.263
	Thioridazine 15 uM	17.899
p-PAK1 (Ser199/Ser204)	Control	1.000
	Thioridazine 5 uM	1.075
	Thioridazine 10 uM	1.033
	Thioridazine 15 uM	3.823

Down-regulation

Protein	Samle	Fold change
Bax	Control	1.000
	Thioridazine 5 uM	0.869
	Thioridazine 10 uM	0.572
	Thioridazine 15 uM	0.682
c-Myc	Control	1.000
	Thioridazine 5 uM	0.978
	Thioridazine 10 uM	0.710
	Thioridazine 15 uM	0.464
GSK-3β	Control	1.000
	Thioridazine 5 uM	0.800
	Thioridazine 10 uM	0.505
	Thioridazine 15 uM	0.576
p38a MAPK	Control	1.000
	Thioridazine 5 uM	0.903
	Thioridazine 10 uM	0.598
	Thioridazine 15 uM	0.596
p70 S6 kinase	Control	1.000
	Thioridazine 5 uM	0.866

	Thioridazine 10 uM	0.496
	Thioridazine 15 uM	0.515
p-acetyl CoA carboxylase	Control	1.000
	Thioridazine 5 uM	0.598
	Thioridazine 10 uM	0.395
	Thioridazine 15 uM	0.414
p-JNK (Thr183/Tyr185, Thr221/Tyr223)	Control	1.000
	Thioridazine 5 uM	0.640
	Thioridazine 10 uM	0.244
	Thioridazine 15 uM	0.373
p-mTOR (Ser2481)	Control	1.000
	Thioridazine 5 uM	0.850
	Thioridazine 10 uM	0.409
	Thioridazine 15 uM	0.576
Akt1/PKBa	Control	1.000
	Thioridazine 5 uM	0.785
	Thioridazine 10 uM	0.471
	Thioridazine 15 uM	0.432
ΑΜΡΚα1	Control	1.000
	Thioridazine 5 uM	0.661
	Thioridazine 10 uM	0.512
	Thioridazine 15 uM	0.577
Cyclin B1	Control	1.000
	Thioridazine 5 uM	0.801
	Thioridazine 10 uM	0.440
	Thioridazine 15 uM	0.433
Cyclin E1	Control	1.000
	Thioridazine 5 uM	0.746
	Thioridazine 10 uM	0.452
	Thioridazine 15 uM	0.420
Cyclin E2	Control	1.000
-	Thioridazine 5 uM	0.724
	Thioridazine 10 uM	0.467
	Thioridazine 15 uM	0.216
GRB2	Control	1.000

	Thioridazine 5 uM	0.980
	Thioridazine 10 uM	0.691
	Thioridazine 15 uM	0.581
HDAC3	Control	1.000
	Thioridazine 5 uM	0.977
	Thioridazine 10 uM	0.673
	Thioridazine 15 uM	0.602
NF- B p50	Control	1.000
	Thioridazine 5 uM	0.835
	Thioridazine 10 uM	0.668
	Thioridazine 15 uM	0.639
p-p70 S6 kinase (Thr389)	Control	1.000
	Thioridazine 5 uM	0.865
	Thioridazine 10 uM	0.451
	Thioridazine 15 uM	0.462
p21/WAF1/Cip1	Control	1.000
	Thioridazine 5 uM	0.464
	Thioridazine 10 uM	0.205
	Thioridazine 15 uM	0.312
Bcl2	Control	1.000
	Thioridazine 5 uM	0.989
	Thioridazine 10 uM	0.661
	Thioridazine 15 uM	0.646
EGFR	Control	1.000
	Thioridazine 5 uM	0.905
	Thioridazine 10 uM	0.727
	Thioridazine 15 uM	0.730
Jak2	Control	1.000
	Thioridazine 5 uM	0.602
	Thioridazine 10 uM	0.241
	Thioridazine 15 uM	0.334
p-Tuberin/TSC2	Control	1.000
	Thioridazine 5 uM	0.680
	Thioridazine 10 uM	0.467
	Thioridazine 15 uM	0.574

p-STAT6	Control	1.000
	Thioridazine 5 uM	0.769
	Thioridazine 10 uM	0.649
	Thioridazine 15 uM	0.747
Cyclin D1	Control	1.000
	Thioridazine 5 uM	0.847
	Thioridazine 10 uM	0.693
	Thioridazine 15 uM	0.562
p-EGFR (Tyr1086)	Control	1.000
	Thioridazine 5 uM	0.670
	Thioridazine 10 uM	0.455
	Thioridazine 15 uM	0.554
p-estrogen receptor α (Ser167)	Control	1.000
	Thioridazine 5 uM	0.571
	Thioridazine 10 uM	0.422
	Thioridazine 15 uM	0.592
p-PDGF receptor α (Tyr1018)	Control	1.000
	Thioridazine 5 uM	0.914
	Thioridazine 10 uM	0.454
	Thioridazine 15 uM	0.539
p-Raptor (Ser792)	Control	1.000
	Thioridazine 5 uM	0.886
	Thioridazine 10 uM	0.600
	Thioridazine 15 uM	0.544
p-Met (Tyr1003)	Control	1.000
	Thioridazine 5 uM	0.744
	Thioridazine 10 uM	0.697
	Thioridazine 15 uM	0.630