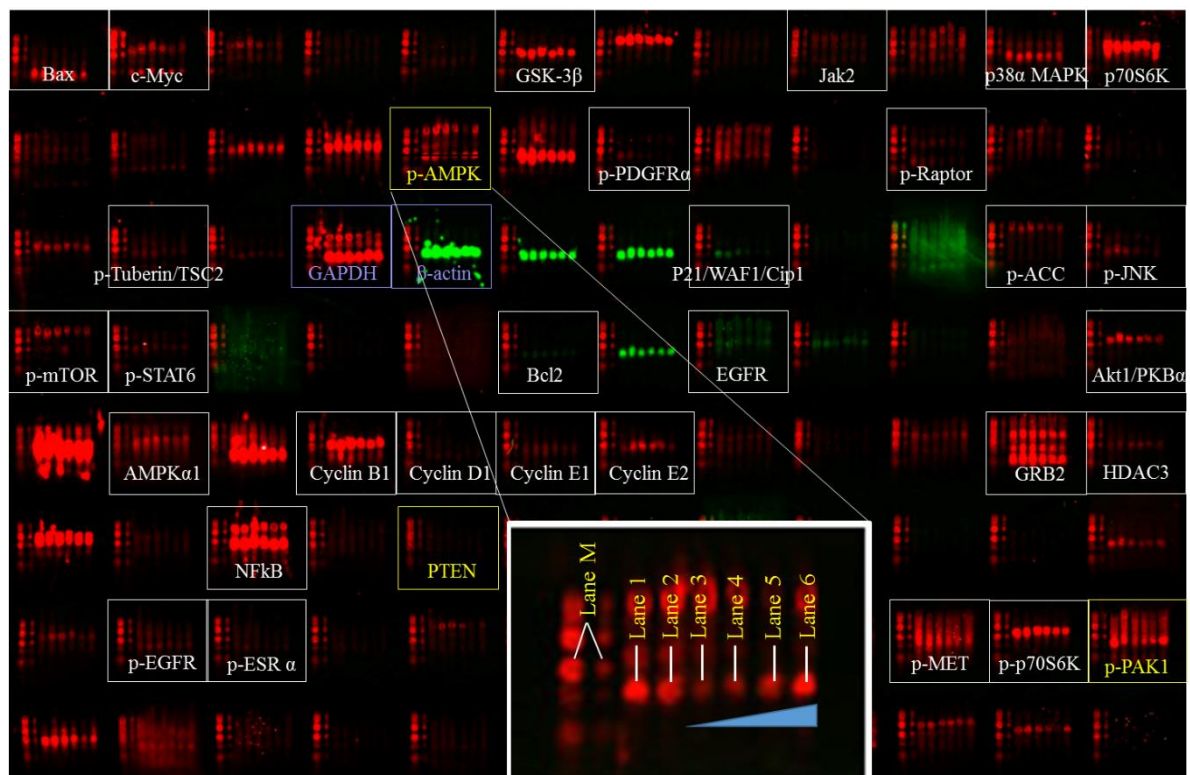
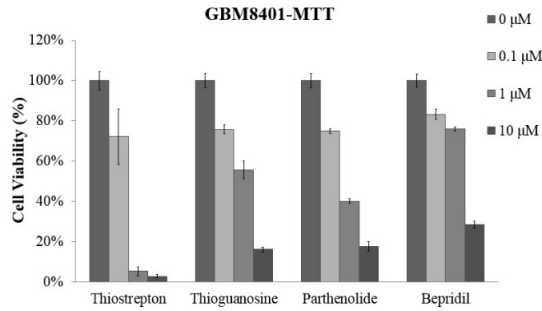


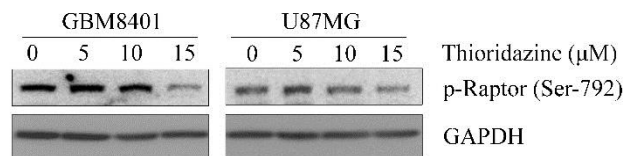
Supplementary Figures and Tables



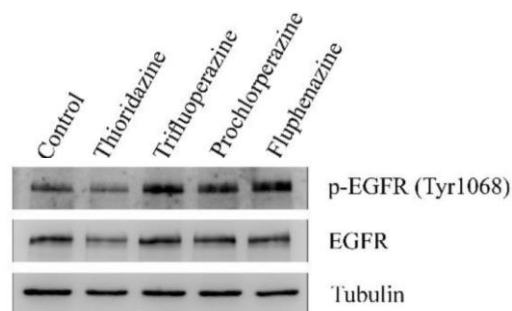
Supplementary information, Figure S1. Identification of differential protein expressions from thioridazine and fluphenazine-treated GBM8401 cells *via* microwestern. GBM8401 cells were treated with various drugs for 24 h. Sample serials (each block from left to right): Lane M (Marker), Lane 1 (fluphenazine 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 μM , 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 μM 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 μM 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% | x | |
| Procaine | 80% | x | |
| Pargyline | 80% | x | |
| Luteolin | 80% | v | |
| Gliclazide | 80% | x | |
| Chrysin | 80% | x | |
| Tyloxapol | 60% | v | |
| Thiostrepton | 60% | v | |
| Sulfamethoxypyridazine | 60% | ND | |
| Skimmianine | 60% | x | |
| Ronidazole | 60% | x | |
| Phthalylsulfathiazole | 60% | x | |
| Pentoxyverine | 60% | ND | |
| Omeprazole | 60% | ND | |
| Nipecotic acid | 60% | ND | |
| Meticrane | 60% | x | |
| Meropenem | 60% | ND | |
| Medrysone | 60% | x | |
| Levamisole | 60% | ND | |
| Ginkgolide A | 60% | x | |
| Dipyridamole | 60% | x | |
| Apigenin | 60% | x | |
| Prestwick-665 | 60% | x | |
| Prestwick-559 | 60% | x | |
| DL-thiorphan | 60% | x | |
| Zomepirac | 40% | ND | |
| Vorinostat | 40% | v | |
| Verteporfin | 40% | v | |
| Triflusal | 40% | x | |
| Tridihexethyl | 40% | ND | |
| Trichostatin A | 40% | v | |
| Trazodone | 40% | x | |
| 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 | |
| Ketanserine | 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 | |
| Bepidil | 40% | v | |
| Antimycin A | 40% | v | |
| Alsterpaullone | 40% | ND | |
| Alpha-estradiol | 40% | x | |
| Acepromazine | 40% | x | o |
| 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 | o |
| Tretinoin | 20% | ND | |

| | | | |
|---------------------|-----|----|---|
| Tolfenamic acid | 20% | ND | |
| Tolbutamide | 20% | ND | |
| Tobramycin | 20% | ND | |
| Tinidazole | 20% | ND | |
| Tiabendazole | 20% | ND | |
| Thioridazine | 20% | v | o |
| 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% | x | |
| 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 | o |
| Piroxicam | 20% | ND | |
| Piperidolate | 20% | ND | |
| Piperacetazine | 20% | ND | o |
| 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% | x | |
| 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% | x | o |
| 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% | x | |
| 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 | |

| | | | |
|-----------------------------|-----|----|---|
| Cromoglicic acid | 20% | ND | |
| Cortisone | 20% | ND | |
| Cloperastine | 20% | v | |
| Clomipramine | 20% | ND | |
| Cicloheximide | 20% | ND | |
| Chlorpromazine | 20% | v | o |
| Cefalonium | 20% | ND | |
| Cefalexin | 20% | ND | |
| Carbamazepine | 20% | ND | |
| Canrenoic acid | 20% | ND | |
| Canavanine | 20% | ND | |
| Camptothecin | 20% | v | |
| Bufexamac | 20% | ND | |
| Bromopride | 20% | ND | |
| Bephenium hydroxynaphthoate | 20% | ND | |
| Bemegrade | 20% | ND | |
| Atropine | 20% | ND | |
| Atovaquone | 20% | ND | |
| Arachidonic acid | 20% | ND | |
| Apramycin | 20% | ND | |
| Amylocaine | 20% | ND | |
| Amrinone | 20% | ND | |
| Amoxapine | 20% | x | |
| Amiodarone | 20% | v | |
| Alfaxalone | 20% | ND | |
| 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 | |
| 4,5-dianilinophthalimide | 20% | ND | |
| 3-acetylcoumarin | 20% | ND | |
| 15-delta prostaglandin J2 | 20% | v | |
| 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 (up-regulated genes) | set size | candidates contained | p-value | q-value | pathway source |
|--|----------|----------------------|----------|----------|----------------|
| Beta1 integrin cell surface 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 | Wikipathways |
| 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 | Wikipathways |
| 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 | Wikipathways |
| ECM-receptor interaction- <i>Homo sapiens</i> (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 | Wikipathways |
| 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 | Wikipathways |
| Syndecan-4-mediated signaling | 32 | 3 (9.4%) | 0.000397 | 0.00238 | PID |

| | | | | | |
|---|-----|-----------|----------|---------|--------------|
| events | | | | | |
| Protein digestion and absorption- <i>Homo sapiens</i> (human) | 81 | 4 (4.9%) | 0.00048 | 0.00276 | KEGG |
| Integrin cell surface interactions | 85 | 4 (4.7%) | 0.000577 | 0.00318 | Reactome |
| Diabetes pathways | 39 | 3 (7.9%) | 0.000662 | 0.00352 | Reactome |
| APC/C-mediated degradation of cell cycle proteins | 10 | 2 (20.0%) | 0.000888 | 0.00438 | Wikipathways |
| Regulation of insulin-like growth factor (IGF) activity by insulin-like growth factor binding proteins (IGFBPs) | 10 | 2 (20.0%) | 0.000888 | 0.00438 | Wikipathways |
| Regulators of bone mineralization | 11 | 2 (18.2%) | 0.00108 | 0.00485 | PID |
| Regulators of bone mineralization | 11 | 2 (18.2%) | 0.00108 | 0.00485 | BioCarta |
| Syndecan-1-mediated signaling 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 insulin-like growth factor binding proteins (IGFBPs) | 12 | 2 (16.7%) | 0.0013 | 0.00542 | PID |
| GRB2 events in EGFR signaling | 14 | 2 (14.3%) | 0.00178 | 0.00681 | Reactome |
| Regulation of complement cascade | 14 | 2 (14.3%) | 0.00178 | 0.00681 | Reactome |
| Nicotinate and nicotinamide metabolism | 14 | 2 (14.3%) | 0.00178 | 0.00681 | SMPDB |
| SHC1 events in EGFR signaling | 15 | 2 (13.3%) | 0.00204 | 0.00762 | Reactome |
| Celecoxib pathway, pharmacodynamics | 58 | 3 (5.2%) | 0.00227 | 0.00826 | PharmGKB |
| Platelet activation, signaling and aggregation | 215 | 5 (2.4%) | 0.00261 | 0.00908 | Reactome |
| Regulation of insulin-like growth factor (IGF) activity by insulin-like growth factor binding proteins (IGFBPs) | 17 | 2 (11.8%) | 0.00263 | 0.00908 | Reactome |
| Lymphocyte TarBase | 437 | 7 (1.6%) | 0.00286 | 0.00962 | Wikipathways |
| Nucleotide metabolism | 19 | 2 (10.5%) | 0.00329 | 0.0106 | Wikipathways |
| Pathways in cancer- <i>Homo sapiens</i> (human) | 325 | 6 (1.8%) | 0.00331 | 0.0106 | KEGG |
| p53 signaling pathway- <i>Homo sapiens</i> (human) | 68 | 3 (4.4%) | 0.00358 | 0.0112 | KEGG |
| Formation of fibrin clot | 20 | 2 (10.0%) | 0.00364 | 0.0112 | Wikipathways |

| | | | | | |
|---|-----|----------|---------|--------|----------|
| (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 sapiens</i> (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 sapiens</i> (human) | 89 | 14 (15.7%) | 1.05E-12 | 1.45E-10 | KEGG |
| Glutamatergic synapse- <i>Homo sapiens</i> (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- <i>Homo sapiens</i> (human) | 92 | 11 (12.0%) | 6.49E-09 | 4.49E-07 | KEGG |
| Synaptic vesicle cycle- <i>Homo sapiens</i> (human) | 64 | 9 (14.1%) | 3.89E-08 | 2.30E-06 | KEGG |
| Neurotransmitter receptor binding and downstream transmission in the postsynaptic cell | 141 | 12 (8.5%) | 6.29E-08 | 3.26E-06 | Reactome |
| Calcium regulation in the cardiac cell | 149 | 12 (8.1%) | 1.16E-07 | 5.35E-06 | Wikipathways |
| Retrograde endocannabinoid signaling- <i>Homo sapiens</i> (human) | 102 | 10 (9.8%) | 2.22E-07 | 9.22E-06 | KEGG |
| Glutamate neurotransmitter release cycle | 16 | 5 (31.2%) | 7.00E-07 | 2.64E-05 | Reactome |
| GABA synthesis, release, reuptake and degradation | 19 | 5 (26.3%) | 1.81E-06 | 6.27E-05 | Reactome |
| GABA receptor activation | 55 | 7 (12.7%) | 2.70E-06 | 8.63E-05 | Reactome |
| Glutamate neurotransmitter release cycle | 11 | 4 (36.4%) | 4.99E-06 | 0.000148 | PID |
| Serotonin neurotransmitter release cycle | 12 | 4 (33.3%) | 7.42E-06 | 0.000193 | Reactome |
| Dopamine neurotransmitter release cycle | 12 | 4 (33.3%) | 7.42E-06 | 0.000193 | Reactome |
| G protein signaling pathways | 92 | 8 (8.7%) | 9.42E-06 | 0.00021 | Wikipathways |
| Signaling pathway from G protein families | 26 | 5 (19.2%) | 9.63E-06 | 0.00021 | PID |
| signaling pathway from G protein families | 26 | 5 (19.2%) | 9.63E-06 | 0.00021 | BioCarta |
| 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 reabsorption- <i>Homo sapiens</i> (human) | 49 | 6 (12.2%) | 1.81E-05 | 0.000327 | KEGG |
| Neurotransmitter release cycle | 15 | 4 (26.7%) | 1.99E-05 | 0.000333 | Wikipathways |
| Gastric acid secretion- <i>Homo sapiens</i> (human) | 74 | 7 (9.5%) | 2.01E-05 | 0.000333 | KEGG |
| Endocytotic role of ndk phosphins and dynamin | 17 | 4 (23.5%) | 3.42E-05 | 0.000525 | PID |
| Endocytotic role of ndk phosphins and dynamin | 17 | 4 (23.5%) | 3.42E-05 | 0.000525 | BioCarta |
| Cholinergic synapse- <i>Homo sapiens</i> (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 | 272 | 12 (4.4%) | 6.07E-05 | 0.00084 | INOH |

| | | | | | |
|--|-----|------------|----------|----------|--------------|
| Epac and ERK | | | | | |
| Gap junction- <i>Homo sapiens</i> (human) | 89 | 7 (7.9%) | 6.67E-05 | 0.000866 | KEGG |
| Myometrial relaxation and contraction pathways | 155 | 9 (5.8%) | 6.68E-05 | 0.000866 | Wikipathways |
| 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 receptors | 40 | 5 (12.5%) | 8.48E-05 | 0.000978 | Reactome |
| GABA B receptor activation | 40 | 5 (12.5%) | 8.48E-05 | 0.000978 | Reactome |
| GPCR signaling-G alpha s PKA and ERK | 285 | 12 (4.2%) | 9.50E-05 | 0.00107 | INOH |
| Endocytosis- <i>Homo sapiens</i> (human) | 202 | 10 (5.0%) | 0.0001 | 0.00107 | KEGG |
| Beta-agonist/beta-blocker pathway, pharmacodynamics | 66 | 6 (9.1%) | 0.000101 | 0.00107 | PharmGKB |
| Dopaminergic synapse- <i>Homo sapiens</i> (human) | 130 | 8 (6.2%) | 0.000115 | 0.00109 | KEGG |
| Effects of Botulinum toxin | 9 | 3 (33.3%) | 0.000116 | 0.00109 | PID |
| Dopamine neurotransmitter release cycle | 9 | 3 (33.3%) | 0.000116 | 0.00109 | PID |
| Neurotransmitter release cycle | 9 | 3 (33.3%) | 0.000116 | 0.00109 | PID |
| Serotonin neurotransmitter 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 resistance | 2 | 2 (100.0%) | 0.000129 | 0.00117 | HumanCyc |
| Long-term depression- <i>Homo sapiens</i> (human) | 70 | 6 (8.6%) | 0.00014 | 0.00121 | KEGG |
| Regulation of ck1/cdk5 by type 1 glutamate receptors | 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 endothelium | 47 | 5 (10.6%) | 0.000186 | 0.00151 | BioCarta |
| Ion channels and their functional role in vascular endothelium | 47 | 5 (10.6%) | 0.000186 | 0.00151 | PID |
| GPCR signaling-G alpha i | 262 | 11 (4.2%) | 0.000193 | 0.00151 | INOH |
| GPCR signaling-pertussis toxin | 262 | 11 (4.2%) | 0.000193 | 0.00151 | INOH |
| Interaction between L1 and Ankyrins | 26 | 4 (15.4%) | 0.000198 | 0.00152 | Reactome |
| Calcium signaling pathway- <i>Homo sapiens</i> (human) | 183 | 9 (5.0%) | 0.000218 | 0.00157 | KEGG |
| Acetylcholine neurotransmitter release cycle | 11 | 3 (27.3%) | 0.000224 | 0.00157 | Reactome |

| | | | | | |
|--|-----|-----------|----------|---------|--------------|
| Acetylcholine neurotransmitter release cycle | 11 | 3 (27.3%) | 0.000224 | 0.00157 | PID |
| Norepinephrine neurotransmitter release cycle | 11 | 3 (27.3%) | 0.000224 | 0.00157 | Reactome |
| Norepinephrine neurotransmitter release cycle | 11 | 3 (27.3%) | 0.000224 | 0.00157 | PID |
| GPCR signaling-cholera toxin | 270 | 11 (4.1%) | 0.000251 | 0.00173 | INOH |
| Selective serotonin reuptake inhibitor pathway, pharmacodynamics | 28 | 4 (14.3%) | 0.000267 | 0.00181 | PharmGKB |
| GPCR signaling-G alpha q | 274 | 11 (4.0%) | 0.000285 | 0.00191 | INOH |
| Alanine and aspartate metabolism | 12 | 3 (25.0%) | 0.000296 | 0.00195 | Wikipathways |
| Trafficking of AMPA receptors | 30 | 4 (13.3%) | 0.000351 | 0.00224 | Reactome |
| Glutamate binding, activation of AMPA receptors and synaptic plasticity | 30 | 4 (13.3%) | 0.000351 | 0.00224 | Reactome |
| 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 glutamate metabolism- <i>Homo sapiens</i> (human) | 32 | 4 (12.5%) | 0.000452 | 0.00268 | KEGG |
| Serotonergic synapse- <i>Homo sapiens</i> (human) | 122 | 7 (5.7%) | 0.000477 | 0.00273 | KEGG |
| S1P4 pathway | 15 | 3 (21.4%) | 0.000481 | 0.00273 | PID |
| Retrograde neurotrophin 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 receptor life cycle pathway | 15 | 3 (20.0%) | 0.000596 | 0.00317 | PID |
| Gamma-aminobutyric acid receptor life cycle pathway | 15 | 3 (20.0%) | 0.000596 | 0.00317 | BioCarta |
| GPCRs, class C metabotropic glutamate, pheromone | 15 | 3 (20.0%) | 0.000596 | 0.00317 | Wikipathways |
| Class C/3 (Metabotropic glutamate/pheromone receptors) | 15 | 3 (20.0%) | 0.000596 | 0.00317 | Reactome |
| Ion channel transport | 61 | 5 (8.2%) | 0.000634 | 0.00333 | Reactome |
| Glutamate degradation III (<i>via</i> 4-aminobutyrate) | 4 | 2 (50.0%) | 0.000763 | 0.00396 | HumanCyc |
| 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 |

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|--|-----|-----------|---------|---------|--------------|
| metabolism | | | | | |
| Melanogenesis- <i>Homo sapiens</i> (human) | 101 | 6 (5.9%) | 0.00102 | 0.00497 | KEGG |
| Potassium channels | 101 | 6 (5.9%) | 0.00102 | 0.00497 | Reactome |
| Nicotine addiction- <i>Homo sapiens</i> (human) | 40 | 4 (10.0%) | 0.00107 | 0.00517 | KEGG |
| EGF-EGFR signaling pathway | 141 | 7 (5.0%) | 0.00113 | 0.00537 | Wikipathways |
| Long-term potentiation- <i>Homo sapiens</i> (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 oocyte maturation | 23 | 3 (13.0%) | 0.00217 | 0.00892 | PID |
| How progesterone initiates the oocyte maturation | 23 | 3 (13.0%) | 0.00217 | 0.00892 | BioCarta |
| Cocaine addiction- <i>Homo sapiens</i> (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 by adrenaline/noradrenaline | 26 | 3 (11.5%) | 0.00311 | 0.0116 | Reactome |
| CXCR4-mediated signaling events | 89 | 5 (5.7%) | 0.00312 | 0.0116 | PID |
| Salivary secretion- <i>Homo sapiens</i> (human) | 89 | 5 (5.6%) | 0.00344 | 0.0116 | KEGG |
| S1P5 pathway | 8 | 2 (25.0%) | 0.00346 | 0.0116 | PID |
| Axonal growth inhibition (RHOA activation) | 8 | 2 (25.0%) | 0.00346 | 0.0116 | Reactome |

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|--|-----|-----------|---------|--------|--------------|
| 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 metabolism | 27 | 3 (11.1%) | 0.00347 | 0.0116 | INOH |
| Transcription factor creb and its extracellular signals | 27 | 3 (11.1%) | 0.00347 | 0.0116 | PID |
| Transcription factor creb and its extracellular signals | 27 | 3 (11.1%) | 0.00347 | 0.0116 | BioCarta |
| Activation of G protein gated potassium channels | 27 | 3 (11.1%) | 0.00347 | 0.0116 | Reactome |
| G protein gated potassium channels | 27 | 3 (11.1%) | 0.00347 | 0.0116 | Reactome |
| Inhibition of voltage gated Ca ²⁺ channels <i>via</i> G beta/gamma subunits | 27 | 3 (11.1%) | 0.00347 | 0.0116 | Reactome |
| Basigin interactions | 29 | 3 (11.1%) | 0.00347 | 0.0116 | Reactome |
| L1CAM interactions | 27 | 3 (11.1%) | 0.00347 | 0.0116 | Wikipathways |
| T cell receptor signaling pathway | 55 | 4 (7.3%) | 0.00351 | 0.0116 | PID |
| T cell receptor signaling pathway | 55 | 4 (7.3%) | 0.00351 | 0.0116 | BioCarta |
| Antiarrhythmic pathway, 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> (human) | 132 | 6 (4.6%) | 0.00381 | 0.0123 | KEGG |
| Thrombin signaling and protease-activated receptors | 28 | 3 (10.7%) | 0.00385 | 0.0123 | PID |
| Thrombin signaling and protease-activated receptors | 28 | 3 (10.7%) | 0.00385 | 0.0123 | BioCarta |
| GPCR Group I metabotropic glutamate receptor | 28 | 3 (10.7%) | 0.00385 | 0.0123 | INOH |
| Nitric oxide stimulates guanylate cyclase | 28 | 3 (10.7%) | 0.00385 | 0.0123 | Reactome |
| G alpha (s) signalling events | 132 | 6 (4.5%) | 0.00396 | 0.0125 | Reactome |
| p75NTR regulates axonogenesis | 9 | 2 (22.2%) | 0.00441 | 0.0139 | Reactome |
| Fc gamma R-mediated phagocytosis- <i>Homo sapiens</i> (human) | 97 | 5 (5.3%) | 0.00455 | 0.0141 | KEGG |
| Fmlp induced chemokine gene expression in hmc-1 cells | 30 | 3 (10.0%) | 0.0047 | 0.0141 | PID |
| Fmlp induced chemokine gene expression in hmc-1 cells | 30 | 3 (10.0%) | 0.0047 | 0.0141 | BioCarta |
| Role of mef2d in T-cell apoptosis | 30 | 3 (10.0%) | 0.0047 | 0.0141 | PID |
| Role of mef2d in T-cell apoptosis | 30 | 3 (10.0%) | 0.0047 | 0.0141 | BioCarta |

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|---|-----|-----------|---------|--------|--------------|
| G protein activation | 30 | 3 (10.0%) | 0.0047 | 0.0141 | Reactome |
| Nongenotropic androgen signaling | 32 | 3 (9.7%) | 0.00516 | 0.0154 | PID |
| Taurine and hypotaurine metabolism- <i>Homo sapiens</i> (human) | 10 | 2 (20.0%) | 0.00547 | 0.0158 | KEGG |
| Regulation of spermatogenesis by crem | 10 | 2 (20.0%) | 0.00547 | 0.0158 | PID |
| Regulation of spermatogenesis by crem | 10 | 2 (20.0%) | 0.00547 | 0.0158 | BioCarta |
| Retrograde neurotrophin signalling | 10 | 2 (20.0%) | 0.00547 | 0.0158 | PID |
| Lysosome vesicle biogenesis | 10 | 2 (20.0%) | 0.00547 | 0.0158 | PID |
| Hypothetical network for drug addiction | 32 | 3 (9.4%) | 0.00564 | 0.0158 | Wikipathways |
| Bcr signaling pathway | 32 | 3 (9.4%) | 0.00564 | 0.0158 | BioCarta |
| Bcr signaling pathway | 32 | 3 (9.4%) | 0.00564 | 0.0158 | PID |
| Signaling by robo receptor | 33 | 3 (9.4%) | 0.00564 | 0.0158 | Reactome |
| GnRH signaling pathway- <i>Homo sapiens</i> (human) | 101 | 5 (5.0%) | 0.00589 | 0.0163 | KEGG |
| Pancreatic secretion- <i>Homo sapiens</i> (human) | 101 | 5 (5.0%) | 0.00589 | 0.0163 | KEGG |
| Phospholipids as signalling intermediaries | 33 | 3 (9.1%) | 0.00616 | 0.0164 | PID |
| Phospholipids as signalling intermediaries | 33 | 3 (9.1%) | 0.00616 | 0.0164 | BioCarta |
| Bioactive peptide induced signaling pathway | 33 | 3 (9.1%) | 0.00616 | 0.0164 | PID |
| Bioactive peptide induced signaling pathway | 33 | 3 (9.1%) | 0.00616 | 0.0164 | BioCarta |
| Inwardly rectifying K ⁺ channels | 33 | 3 (9.1%) | 0.00616 | 0.0164 | Reactome |
| Regulation of Ras family activation | 33 | 3 (9.1%) | 0.00616 | 0.0164 | PID |
| Glucagon signaling in metabolic regulation | 35 | 3 (8.6%) | 0.00727 | 0.019 | Reactome |
| Post NMDA receptor activation events | 35 | 3 (8.6%) | 0.00727 | 0.019 | Reactome |
| Endothelin | 35 | 3 (8.6%) | 0.00727 | 0.019 | Wikipathways |
| Purine nucleotides nucleosides metabolism | 109 | 5 (4.6%) | 0.00778 | 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- <i>Homo sapiens</i> (human) | 70 | 4 (5.7%) | 0.00828 | 0.0211 | KEGG |
| G13 signaling pathway | 37 | 3 (8.1%) | 0.00849 | 0.0215 | Wikipathways |

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|--|----|-----------|---------|--------|----------|
| CXCR3-mediated signaling events | 38 | 3 (7.9%) | 0.00914 | 0.0221 | PID |
| Intracellular signalling through adenosine receptor A2a and adenosine | 38 | 3 (7.9%) | 0.00914 | 0.0221 | SMPDB |
| Intracellular signalling through adenosine receptor A2b and adenosine | 38 | 3 (7.9%) | 0.00914 | 0.0221 | SMPDB |
| Regulation of insulin secretion by glucagon-like peptide-1 | 38 | 3 (7.9%) | 0.00914 | 0.0221 | Reactome |
| Aspartate metabolism | 13 | 2 (15.4%) | 0.00928 | 0.0221 | SMPDB |
| Adenylate cyclase inhibitory pathway | 13 | 2 (15.4%) | 0.00928 | 0.0221 | Reactome |
| Inhibition of adenylate cyclase 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)-trisphosphate degradation | 13 | 2 (15.4%) | 0.00928 | 0.0221 | HumanCyc |
| Activation of NMDA receptor upon glutamate binding and postsynaptic events | 39 | 3 (7.7%) | 0.00982 | 0.0233 | Reactome |

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

| | | | |
|------------|--|------------|--|
| A1 | Bax antibody | E1 | Alpha-tubulin |
| A2 | c-Myc (D84C12) XP® rabbit mAb | E2 | AMPK α 1, rabbit monoclonal |
| A3 | c-Raf antibody | E3 | Cdk4 |
| A4 | FAK antibody | E4 | Cyclin B1 (C-term), clone Y106, rabbit monoclonal |
| A5 | FGF receptor 1 antibody | E5 | Cyclin D1, clone EP272Y, rabbit monoclonal |
| A6 | GSK-3 β (27C10) rabbit mAb | E6 | Cyclin E1, clone EP435E rabbit monoclonal |
| A7 | HSP90 antibody | E7 | Cyclin E2, clone EP454Y, rabbit monoclonal |
| A8 | Jak1 (6G4) rabbit mAb | E8 | ErbB-2/HER-2 |
| A9 | Jak2 (D2E12) XP® rabbit mAb | E9 | Estrogen receptor α , clone E115 |
| A10 | mTOR (7C10) rabbit mAb | E10 | Frizzled 5 |
| A11 | p38 α MAPK (7D6) rabbit mAb | E11 | GRB2 |
| A12 | p70 S6 kinase (49D7) rabbit mAb | E12 | HDAC3, clone Y415, rabbit monoclonal; 100 μ L |
| B1 | PLC γ 2 antibody | F1 | HIF-1 α |
| B2 | Rb (D20) rabbit mAb | F2 | MDM2 |
| B3 | SAPK/JNK (56G8) rabbit mAb | F3 | NF- κ B p50, clone E381 |
| B4 | Src (36D10) rabbit mAb | F4 | PI3 kinase, p110 α rabbit monoclonal |
| B5 | Phospho-AMPK α (Thr172) (D79.5E) rabbit mAb | F5 | PI3 kinase, p85, N-SH2, clone UB93-3 |
| B6 | Phospho-p38 MAPK (Thr180/Tyr182) (D3F9) XP™ rabbit mAb | F6 | PTEN rabbit monoclonal |
| B7 | Phospho-PDGFR α (Tyr1018) antibody | F7 | Phospho-erbB2 (Thr686), clone 7F8 |
| B8 | Phospho-PDGFR β (Tyr1009) (42F9) rabbit mAb | F8 | Phospho-GSK3 (Tyr279/Tyr216), clone 5G-2F |
| B9 | Phospho-PLC γ 1 (Tyr783) antibody | F9 | Phospho-GSK3 β (Ser9), clone 2D3 |
| B10 | Phospho-Raptor (Ser792) antibody | F10 | Phospho-insulin receptor (Tyr 1150/1151), clone 10C3 |
| B11 | Phospho-Rb (Ser780) (C84F6) rabbit mAb | F11 | Phospho-Cdc25C (Ser216), clone E190, rabbit monoclonal |
| B12 | Phospho-SAPK/JNK (Thr183/Tyr185) (81E11) rabbit mAb | F12 | Phospho-c-Jun (Ser63), clone Y172; 100 μ L |
| C1 | Phospho-Src (Tyr527) antibody | G1 | Phospho-c-Myc (Thr58/Ser62) |
| C2 | Phospho-Tuberin/TSC2 (Thr1462) (5B12) rabbit mAb | G2 | Phospho-EGFR (Tyr1086) |
| C3 | Phospho-VEGF receptor 2 (Tyr1059) (D5A6) rabbit mAb | G3 | Phospho-estrogen receptor α (Ser167) |

| | | | |
|------------|---|------------|---|
| C4 | GAPDH | G4 | Phospho-FAK (Tyr861) |
| C5 | Actin, near a.a. 50-70, clone C4 | G5 | Phospho-IRS1 (Ser307); 200 μ L |
| C6 | APC, C-terminus, clone C-APC 28.9 | G6 | Phospho-JAK1 (Tyr1022/Tyr1023) |
| C7 | CrkL, clone 5-6; 100 μ g | G7 | Phospho-JAK2 (Tyr1007/1008) |
| C8 | p21/WAF1/Cip1, clone CP74 | G8 | Phospho-MAP kinase1/2 (Erk1/2) |
| C9 | β -Catenin, clone 2H4A7 | G9 | Phospho-MEK1 (Ser218/222)/MEK2 (Ser222/226) |
| C10 | Phospho-ATM (Ser1981), clone 10H11.E12 | G10 | Phospho-Met (Tyr1003) |
| C11 | Phospho-acetyl CoA carboxylase (Ser79); 200 μ g | G11 | Phospho-p70 S6 kinase (Thr389), rabbit monoclonal |
| C12 | Phospho-JNK (Thr183/Tyr185, Thr221/Tyr223) | G12 | Phospho-PAK1 (Ser199/Ser204) |
| D1 | Phospho-mTOR (Ser2481); 100 μ L | H1 | Phospho-PKA, RII (Ser96), rabbit monoclonal |
| D2 | Phospho-STAT6 (Tyr641) | H2 | Phospho-PKC ϵ (Ser729) |
| D3 | Phospho-Akt1/PKB α (Ser473), clone 11E6 | H3 | Phospho-PKD (Ser916) |
| D4 | Phospho-MKK4 (Ser257/Thr261) | H4 | Phospho-PPAR γ (Ser82), clone AW504 |
| D5 | Phospho-PKC δ (Ser645) | H5 | Phospho-PTEN (Ser385) |
| D6 | Bcl2, clone 100 | H6 | Phospho-Src (Tyr416), clone 9A6 |
| D7 | Cyclin A, clone BF 683 | H7 | Phospho-c-Raf (Ser338/Tyr340) |
| D8 | EGFR, clone LA22 | H8 | Phospho-Raf-1 (Tyr340/Tyr341) |
| D9 | p53, clone BP53-12 | H9 | Phospho-Src (Tyr418) |
| D10 | PI3 Kinase, p85, N-SH3, clone AB6 | H10 | Phospho-STAT1 (Ser727) |
| D11 | Acetyl CoA carboxylase 1, rabbit mAb | H11 | Phospho-STAT2 (Tyr689) |
| D12 | Akt1/PKB α , clone AW24 | H12 | Phospho-STAT5A/B (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 | probeset (down-regulated) | gene | times |
|----------------------------|----------|-------|------------------------------|------------------------------------|-------|
| 211980_at | COL4A1 | 5 | 221802_s_at | KIAA1598 | 5 |
| 201761_at | MTHFD2 | 5 | 213385_at | CHN2 | 5 |
| 219918_s_at | ASPM | 4 | 212681_at | EPB41L3 | 5 |
| 219410_at | TMEM45A | 4 | 209576_at | GNAI1 | 5 |
| 219148_at | PBK | 4 | 205814_at | GRM3 | 5 |
| 218883_s_at | MLF1IP | 4 | 205637_s_at | SH3GL3 | 5 |
| 218678_at | NES | 4 | 204681_s_at | RAPGEF5 | 5 |
| 218585_s_at | DTL | 4 | 204547_at | RAB40B | 5 |
| 218039_at | NUSAP1 | 4 | 222005_s_at | GNG3 | 4 |
| 215076_s_at | COL3A1 | 4 | 221916_at | NEFL | 4 |
| 211964_at | COL4A2 | 4 | 221805_at | NEFL | 4 |
| 210809_s_at | POSTN | 4 | 219685_at | TMEM35 | 4 |
| 206157_at | PTX3 | 4 | 219671_at | HPCAL4 | 4 |
| 205347_s_at | TMSB15A | 4 | 219659_at | ATP8A2 | 4 |
| 204915_s_at | SOX11 | 4 | 219619_at | DIRAS2 | 4 |
| 203820_s_at | IGF2BP3 | 4 | 219368_at | NAP1L2 | 4 |
| 203819_s_at | IGF2BP3 | 4 | 218623_at | HMP19 | 4 |
| 203548_s_at | LPL | 4 | 214762_at | ATP6V1G2 | 4 |
| 203358_s_at | EZH2 | 4 | 214434_at | HSPA12A | 4 |
| 203213_at | CDK1 | 4 | 214157_at | GNAS | 4 |
| 202503_s_at | KIAA0101 | 4 | 214111_at | OPCML | 4 |
| 202404_s_at | COL1A2 | 4 | 214046_at | FUT9 | 4 |
| 202403_s_at | COL1A2 | 4 | 213938_at | ERC2 | 4 |
| 202007_at | NID1 | 4 | 213904_at | --- | 4 |
| 201984_s_at | EGFR | 4 | 213558_at | PCLO | 4 |
| 201983_s_at | EGFR | 4 | 213486_at | COPG2IT1 | 4 |
| 201664_at | SMC4 | 4 | 213268_at | CAMTA1 | 4 |
| 201617_x_at | CALD1 | 4 | 213131_at | OLFM1 | 4 |
| 201292_at | TOP2A | 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 |
| | | | 211458_s_at | GABARAP L1 /// GABARAP L3 | 4 |
| | | | 211276_at | TCEAL2 | 4 |

| | | |
|-------------|----------|---|
| 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 | LG11 | 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 | DYNC111 | 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 |

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

| | Drug Name | Rank | Mean | N | Enrichment | P |
|--------------------|------------------|-------------|-------------|----------|-------------------|----------|
| 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 | -- | -- | -- | -- | -- |
| Shats et al. study | Trifluoperazine | 5 | -0.342 | 16 | -0.497 | 0.00028 |
| | Prochlorperazine | 9 | -0.329 | 16 | -0.475 | 0.00082 |
| | Thioridazine | 13 | -0.335 | 20 | -0.401 | 0.00189 |
| | Chlorpromazine | -- | -- | -- | -- | -- |
| | Fluphenazine | 43 | -0.291 | 18 | -0.266 | 0.04351 |
| | Acepromazine | -- | -- | -- | -- | -- |
| | Promethazine | -- | -- | -- | -- | -- |
| | Perphenazine | 37 | -0.453 | 5 | -0.589 | 0.03446 |
| Suvà et al. study | Trifluoperazine | 47 | -0.371 | 16 | -0.417 | 0.00499 |
| | Prochlorperazine | -- | -- | -- | -- | -- |
| | Thioridazine | 11 | -0.407 | 20 | -0.51 | 0 |
| | Chlorpromazine | -- | -- | -- | -- | -- |
| | Fluphenazine | -- | -- | -- | -- | -- |
| | Acepromazine | -- | -- | -- | -- | -- |
| | Promethazine | -- | -- | -- | -- | -- |
| | Perphenazine | -- | -- | -- | -- | -- |

*(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-AMPK α (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-3 β | Control | 1.000 |
| | Thioridazine 5 uM | 0.800 |
| | Thioridazine 10 uM | 0.505 |
| | Thioridazine 15 uM | 0.576 |
| p38 α 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/PKB α | Control | 1.000 |
| | Thioridazine 5 uM | 0.785 |
| | Thioridazine 10 uM | 0.471 |
| | Thioridazine 15 uM | 0.432 |
| | | |
| AMPK α 1 | 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 |