

Supplementary Table

A proteotranscriptomic computational drug-repositioning method for Alzheimer's disease

Soo Youn Lee^{1#}, Min-Young Song^{1#}, Dain Kim¹, Chaewon Park¹, Da Kyeong Park¹, Dong Geun Kim^{1,2}, Jong Shin Yoo^{1,2*} and Young Hye Kim^{1*}

¹ Biomedical Omics Group, Korea Basic Science Institute, Cheongju, Chungbuk, 28119, Republic of Korea

² Graduated School of Analytical Science and Technology, Chungnam National University, Daejeon, 34134, Re-public of Korea

Equal contribution

*** Correspondence:**

Corresponding Author

E-mail: yhkim74@kbsi.re.kr (Kim YH), jongshin@kbsi.re.kr (Yoo JS).

Contents

Supplementary Table 1. Descriptions for symbols of the DRPS/C method.

Supplementary Table 2. Number of differential expressed genes per log2fold and nine cancer types.

Supplementary Table 3. Data description.

Supplementary Table 4. Anti-Alzheimer's disease drug candidates which were discovered by the DRPS/C method

Supplementary Table 1. Descriptions for symbols of the DRPS/C method.

Symbol	Description
PG	Pharmacogene set.
PGL	Pharmacogene list from DrugBank.
g_k	k^{th} gene
E_{kc}	mRNA expression value of k^{th} gene in c^{th} control sample.
E_{kj}	mRNA expression value of k^{th} gene in j^{th} drug treated sample.
E_{kn}	mRNA expression value of k^{th} gene in n^{th} normal sample.
E_{kd}	mRNA expression value of k^{th} gene in d^{th} disease sample.
E_{ic}	mRNA expression value of i^{th} pharmacogene (pg) in c^{th} control sample.
E_{ij}	mRNA expression value of i^{th} pharmacogene (pg) in j^{th} drug treated sample.
E_{in}	mRNA expression value of i^{th} pharmacogene (pg) in n^{th} normal sample.
E_{id}	mRNA expression value of i^{th} pharmacogene (pg) in d^{th} disease sample.
F_{drg_k}	Log_2 fold change value of k^{th} gene between drug treated and control expression value.
F_{dg_k}	Log_2 fold change value of k^{th} gene between disease and normal expression value.
F_{drpg_i}	Log_2 fold change value of i^{th} pharmacogene (pg) between drug treated and control expression value.
F_{dpg_i}	Log_2 fold change value of i^{th} pharmacogene (pg) between disease and normal expression value.
PS_{g_k}	Perturbation score of k^{th} gene.
PS_{pg_i}	Perturbation score of i^{th} pharmacogene.
$DRPS_{drug_j}$	Drug repositioning perturbation score of drug j

Supplementary Table 3. Data Description.

Data name	Data type	Data ID	Experiment technology type	No.Experiment data	Site
L1000	Drug-induced transcripomic Signature	GSE92742	Microarray (GPL20573)	7,519	https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE92742
cMAP	Drug-induced transcripomic Signature		Microarray	66,612	https://portals.broadinstitute.org/cmap/
TCGA	transcripomic Signature of personal cancer patients		RNA-seq	4,948	https://portal.gdc.cancer.gov/
	Clinical information of personal cancer patients				https://portal.gdc.cancer.gov/
Synapse	transcripomic Signature of AD patients	syn8690904	RNA-seq	159	https://www.synapse.org/#!Synapse:syn8690904
ArrayExpress	transcripomic Signature of AD patients	E-TABM-185	Microarray (HG-U133A)	108	https://www.ebi.ac.uk/arrayexpress/experiments/E-TABM-185/
PRIDE	Proteomic Signature of AD patients	PXD006122	LC-MS/MS	17	https://www.ebi.ac.uk/pride/archive/projects/PXD006122

Supplementary Table 4. Anti-Alzheimer's disease drug candidates which were discovered by the DRPS/C method

No.	Drug name	Pubchem CID	indication	ATC code	Target
1	Quinidine	441074	ventricular pre-excitation cardiac dysrhythmias	C01BA01, C01BA51, C01BA71	Sodium channel protein type 5 subunit alpha, UPotassium channel subfamily K member 1,6, UPotassium voltage-gated channel subfamily H member 2, UAlpha-1A,B,D adrenergic receptor
2	Tocainide	38945	ventricular arrhythmias	C01BB03	Sodium channel protein type 5 subunit alpha, cGMP-inhibited 3',5'-cyclic phosphodiesterase A, Prostaglandin G/H synthase 1, 2 and reductase 2
3	Milrinone	4197	congestive heart failure	C01CE02	cGMP-inhibited 3',5'-cyclic phosphodiesterase A
4	Indometacin	3715	rheumatoid arthritis ductus arteriosus	S01CC02, M01AB51, S01BC01, M02AA23, M01AB01, C01EB03	Prostaglandin G/H synthase 1, 2 and reductase 2, Phospholipase A2, membrane associated, Peroxisome proliferator-activated receptorn alphas, gamma, Lactoylglutathione lyase, Prostaglandin D2 receptor 2
5	Suloctidil	657255	vascular antispastic	C04AX19	-
6	Etilefrine	3306	cardiac stimulant antihypotensiv orthostatic hypotension of neurological, cardiovascular, endocrine or metabolic orig in	C01CA51, C01CA01	-
7	Mexiletine	4178	ventricular tachycardia, beats, fibrillation	C01BB02	Sodium channel protein type 5 subunit alpha, Aryl hydrocarbon receptor
8	Bupivacaine	2474	local or regional anesthesia obstetrical procedures	N01BB01, N01BB51	Sodium channel protein type 10 subunit alpha, Prostaglandin E2 receptor EP1 subtype
9	Selegiline	26757	initial treatment of Parkinson's disease palliative treatment of mild to moderate Alzheimer's disease depression	N04BD01	Amine oxidase [flavin-containing] A, B
10	Topiramate	5284627	tonic-clonic seizures seizures associated with Lennox-Gastaut syndrom migraine headach weight reduction in patients with obesity or diabetes	N03AX11	Gamma-aminobutyric acid receptor subunit alpha-1, GABA-A receptor (anion channel) (Protein Group), Sodium channel protein type 1 subunit alpha, Glutamate receptor ionotropic, kainate 1, Carbonic anhydrase 1, 2, 3, 4, Glutamate receptor 1
11	Iproniazid	C11777	depression	N06AF05	-
12	Sulfaguanidine	-	bacillary dysenteryenteric enteric infections	A07AB03	-
13	Streptomycin	19649	tuberculosis tularemia severe M. avium complex, brucellosis, and enterococcal endocarditis	J04AM01, J01GA01, A07AA54, A07AA04	30S ribosomal protein S12, 16S ribosomal RNA, Protein-arginine deiminase type-4
14	Orlistat	3034010	obesity	A08AB01	Pancreatic triacylglycerol lipase, Gastric triacylglycerol lipase, Fatty acid synthase
15	Riboflavin	C00255	aribo flavinosis	A11HA04, S01XA26	Riboflavin kinase, Riboflavin synthase, Flavin reductase (NADPH)
16	Cloperastine	2805		R05DB21	-
17	Antazoline	2200	allergic conjunctivitis.	R06AX05, R01AC04	Histamine H1 receptor
18	Ipratropium bromide	657308	Asthma Rhinorrhea bronchospasm sialorrhea	R03BB01, R01AX03, R03AL01, R03AL02	Muscarinic acetylcholine receptor M1, M2, M3

19	Mefloquine	C07633	malaria	P01BF02, P01BC02	Fe(II)-protoporphyrin IX, Hemoglobin subunit alpha, Adenosine receptor A2a
20	Dienestrol	667476	atrophic vaginitis kraurosis vulvae	G03CB01, G03CC02	Estrogen receptor alpha, Sex hormone-binding globulin
21	Latamoxef	C07231	bacterial infection	J01DD06	Penicillin-binding protein 1A, 1B, 3, D-alanyl-D-alanine carboxypeptidase DacB
22	Piperacillin	C14034	polymicrobial infections	J01CR50, J01CA12	Penicillin-binding protein 1b, 2a, 2b, 3
23	Vinblastine	13342	breast cancer testicular cancer lymphomas neuroblastoma mycosis fungoides histiocytosis Kaposi's sarcoma	L01CA01	Tubulin alpha-1A, beta, delta, gamma-1, epsilon chain Transcription factor AP-1
24	Paclitaxel	C07394	Kaposi's sarcoma cancer of the lung ovarian breast	L01CD01	Tubulin beta-1 chain, Apoptosis regulator Bcl-2, Microtubule-associated protein 2, 4, tau, Nuclear receptor subfamily 1 group 1 member 2
25	Sulindac	C01531	osteoarthritis rheumatoid arthritis ankylosing spondylitis acute painful shoulder acute gouty arthritis.	M01AB02	Prostaglandin G/H synthase 1, 2, Aldose reductase, Mitogen-activated protein kinase 3, Peroxisome proliferator-activated receptor delta Prostaglandin D2 receptor 2 Aldo-keto reductase family 1 member B10
26	Flufenamic acid	C13038	decrease pain and blood loss from menstrual periods.	M01AG03	Prostaglandin G/H synthase 1, 2, Aldo-keto reductase family 1 member C3, Androgen receptor, Peroxisome proliferator-activated receptor alpha, gamma
27	Torsemide	41781	edema associated with congestive heart failure, renal or hepatic diseases Hypertension	C03CA04, G01AE10	Solute carrier family 12 member 1, 2
28	Prestwick857	-	trypanocidal drug pentamidine(2+)	-	-
29	Triflusal	9458	Stroke myocardial infarction.	B01AC18	Prostaglandin G/H synthase 1, Nuclear factor NF-kappa-B p105 subunit, Nitric oxide synthase, inducible, cAMP and cAMP-inhibited cGMP 3',5'-cyclic phosphodiesterase 10A
30	Cortisone	C00762	allergic reaction arthritis	H02AB10, S01BA03	-
31	Fludrocortisone	31378	Addison's disease salt-losing androgenital syndrome	S02CA07, S01CA06, H02AA02, S03CA05	Mineralocorticoid receptor, Glucocorticoid receptor
32	Deferoxamine	C06940	aluminum toxicity anemia	V03AC01	Iron, Aluminum, Amyloid beta A4 protein