

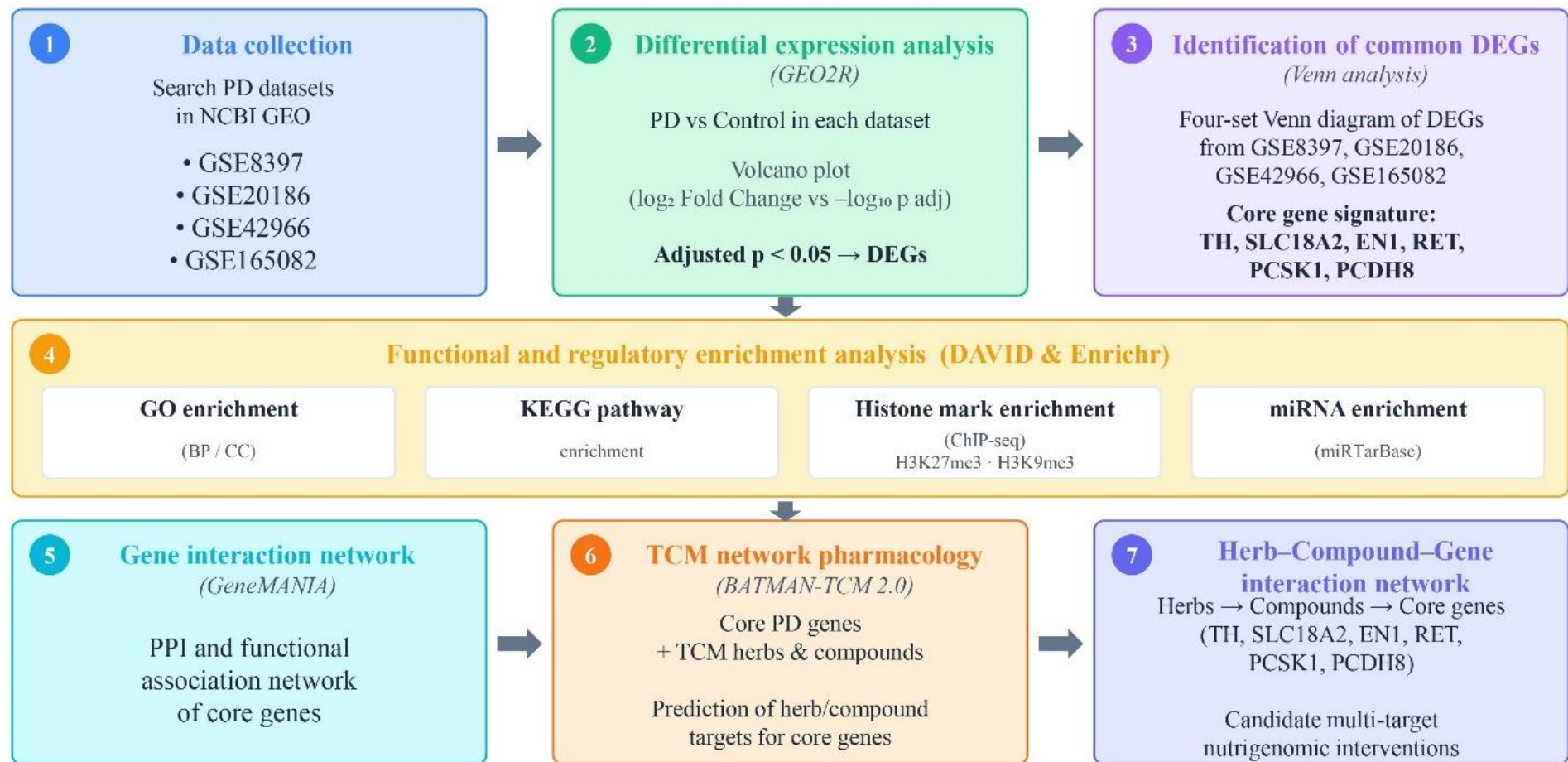


Figure S1 Schematic overview of the integrative systems-biology workflow for identifying core Parkinson's disease genes and predicting TCM interventions.

Table S4 Enriched TCM herbs targeting Parkinson's disease genes, ranked by enrichment ratio. Columns include Latin/English/Pinyin names, number of TCM ingredients, number of genes, and enrichment ratio.

Herb (Latin)	Herb (Pinyin)	#TCM ingredients	#Genes	Enrichment ratio
<i>Pinus koraiensis</i>	HAI SONG ZI	2	2	234.77
<i>Rauwolfia latifrons</i>	KUO YE LUO FU MU	2	2	171.32
<i>Alstonia yunnanensis</i>	DIAN JI GU CHANG SHAN	2	2	171.32
<i>Rauwolfia perakensis</i>	PI LI LUO FU MU	2	2	166.81
<i>Bos taurus domesticus, bubalus bubalis</i>	NIU NAO	2	2	124.29
<i>Lolium multiflorum</i>	DUO HUA HEI MAI CAO	3	2	121.90
<i>Lamium barbatum</i>	YE ZHI MA	3	2	121.90
<i>Tephrosia noctiflora</i>	YE HUA HUI MAO DOU	3	2	121.90
<i>Allium victorialis</i>	GE CONG	3	2	121.90
<i>Lawsonia alba</i>	BAI SAN MO HUA	1	2	117.38
<i>Pachyrrhizus erosus</i>	DOU SHU	1	2	115.25
<i>Cassytha filiformis</i>	WU YE TENG	2	2	113.19
None	JIN JI NA	2	2	105.64
<i>Viscum album</i>	LUAN YE HU JI SHENG	3	2	90.55
<i>Lawsonia inermis</i>	ZHI JIA HUA YE	1	2	89.28
<i>Homalium cochinchinensis</i>	TIAN LIAO MU	1	2	89.28
<i>Dalbergia spruceana</i>	QIAO HUANG TAN	1	2	88.04
<i>Dalbergia cochinchinensis</i>	JIAO ZHI HUANG TAN	1	2	88.04
<i>Uvaria angolensis</i>	GUAN ZI YU PAN	1	2	88.04
<i>Datura innoxia</i>	MAO MAN TUO LUO HUA	3	2	86.83
<i>Nelumbo nucifera</i>	LIAN ZI	2	2	82.32
None	LI CHUN HUA GUO SHI	1	3	52.53
<i>Pericarpium papaveris</i>	SU QIAO	1	3	41.89
None	YING SU NEN MIAO	1	3	35.48

None	BAI YING SU	1	3	35.48
<i>Papaver commutatum</i> [syn. <i>papaver rhoeas</i>]	LI CHUN HUA	1	3	31.38
<i>Adina pilulifera</i> [syn. <i>cephalanthus pilulifera</i>]	SHUI TUAN HUA	1	3	30.09
<i>Rhizoma corydalis</i>	YUAN HU	1	3	28.38
<i>Nodus nelumbinis rhizomatis</i>	OU JIE	5	3	22.97
<i>Papaver somniferum</i>	YING SU KE	3	3	21.66
<i>Folium pini</i>	SONG ZHEN	3	3	21.51
<i>Papaver somniferum</i>	YA PIAN	1	3	20.76
<i>Coptis chinensis</i>	HUANG LIAN	4	3	19.89
<i>Stephania tetrandra</i>	FANG JI	3	3	18.87
<i>Papaver somniferum</i>	YING SU	1	3	18.61
None	GUAN YE JIN SI TAO	3	3	18.46
<i>Uncaria rhynchophylla</i> [syn. <i>nauclea rhynchophylla</i>]	GOU TENG	4	3	17.87
<i>Bufo bufo gargarizans</i> , <i>bufo melanostictus</i>	CHAN SU	8	3	16.65
<i>Ilex chinensis</i> [syn. <i>ilex purpurea</i>]	SI JI QING	2	3	14.93
<i>Stephania cepharantha</i>	BAI YAO ZI	4	4	14.99
<i>Zanthoxylum bungeanum</i>	HUA JIAO	4	3	11.88
<i>Oroxylum indicum</i>	MU HU DIE	3	3	11.84
<i>Phellodendron amurense</i>	HUANG BAI	4	3	11.81
<i>Chelidonium majus</i>	BAI QU CAI	8	4	13.00
<i>Curcuma aromatica</i>	YU JIN	2	3	10.52
<i>Curcuma longa</i>	JIANG HUANG	3	3	10.39
<i>Achyranthes bidentata</i>	NIU XI	3	3	9.61
<i>Amomum villosum</i>	SHA REN	3	3	9.46
<i>Lycium chinense</i>	GOU QI ZI	7	3	8.05
<i>Ziziphus jujuba</i>	DA ZAO	5	3	7.49

*Enrichment ratios indicate predicted target engagement but do not predict directionality (activation vs. inhibition).

Table S5 Known and predicted compounds interacting with key Parkinson's disease genes (SLC18A2, TH, RET, PCSK1). Includes compound IDs, gene symbols, and confidence scores (e.g., known targets or predicted with scores like 0.99).

<i>PubChem_ID</i>	<i>TCM Ingredients</i>	<i>Enrichment Ratio</i>	<i>Associated Genes</i>
442195	Cephaeline	1584.67	SLC18A2 (0.89)
442166	Ankorine	1584.67	SLC18A2 (0.89)
3945	3945	1584.67	SLC18A2 (known target)
160597	Anonaine	1584.67	TH (known target)
5320759	[(1R,15S,17R,18R,19R,20S)-19-acetyloxy-18-hydroxy-6-methoxy-1,3,11,12,14,15,16,17,18,19,20,21-dodecahydroyohimban-17-yl] 3,4,5-trimethoxybenzoate	1056.44	SLC18A2 (0.89)
251566	RAUNESCINE	1056.44	SLC18A2 (0.89)
24848119	60747-11-7	1056.44	SLC18A2 (0.9)
12442718	474-48-6	1056.44	SLC18A2 (0.89)
11865425	CHEMBL1325269	1056.44	SLC18A2 (0.89)
247704	(S)-adrenaline	275.59	TH (known target), SLC18A2 (0.89)
1125	2-amino-6-(1,2-dihydroxypropyl)-5,6,7,8-tetrahydro-1H-pteridin-4-one	226.38	TH (0.99), SLC18A2 (0.92)
1738	Homovanillic acid	176.07	TH (0.96), SLC18A2 (0.92)
5770	reserpine	144.06	SLC18A2 (known target), RET (known target)
6758	rotenone	100.61	TH (known target), SLC18A2 (0.88)
6047	levodopa	83.40	TH (0.92), SLC18A2 (0.92)

243	benzoic acid	60.95	TH (0.94), SLC18A2 (0.86)
5288826	morphine	50.84	TH (known target), PCSK1 (known target), SLC18A2 (0.96)
439260	norepinephrine	34.45	TH (known target), SLC18A2 (known target)
5202	serotonin	32.84	TH (0.92), SLC18A2 (0.92)
5757	estradiol	26.97	TH (known target), SLC18A2 (0.88)
446220	cocaine	26.41	TH (known target), SLC18A2 (0.92)
681	dopamine	24.01	TH (known target), SLC18A2 (known target)
94340	gamma-Glutamyltyrosine	792.33	TH (0.84)
73804405	4,5-dihydroxy-N-(2-methylpropyl)dec-2-enamide	792.33	TH (0.84)
68309	N-Methyl-L-tyrosine	792.33	TH (0.89)
6442992	N-Methylhumantenirine	792.33	SLC18A2 (0.84)
5320135	[(1'R,2S,2'R,3'R,5'S,8'R,9'R,10'R,13'S)-2',10',13'-triacetyloxy-5'-[(3R)-3-(dimethylamino)-3-phenylpropanoyl]oxy-8',12',15',15'-tetramethylspiro[oxirane-2,4'-tricyclo[9.3.1.03,8]pentadec-11-ene]-9'-yl] pyridine-3-carboxylate	792.33	SLC18A2 (0.84)
5319245	[(1'R,2S,2'R,3'R,5'S,7'S,8'S,9'R,10'R,13'S)-2',7',9',10',13'-pentaacetyloxy-8',12',15',15'-tetramethylspiro[oxirane-2,4'-tricyclo[9.3.1.03,8]pentadec-11-ene]-5'-yl] (3R)-3-(dimethylamino)-3-phenylpropanoate	792.33	SLC18A2 (0.84)
5315214	[(2R,3R,6S,8R,13S,17R)-8-acetyloxy-11-ethyl-6,16,18-trimethoxy-13-(methoxymethyl)-11-azahexacyclo[7.7.2.12,5.01,10.03,8.013,17]nonadecan-4-yl] 4-methoxybenzoate	792.33	SLC18A2 (0.84)
44583832	11-Methoxyhumantenine	792.33	SLC18A2 (0.84)

20055981	<i>Foresaconitine</i>	792.33	SLC18A2 (0.84)
13891912	<i>6,7-seco-angustilobine B</i>	792.33	SLC18A2 (0.84)
133246	<i>(6R)-2-amino-6-[(1R,2S)-1,2-dihydroxypropyl]-6,7-dihydro-1H-pteridin-4-one</i>	792.33	TH (0.92)
1217	<i>31932-87-3</i>	792.33	TH (0.84)
11447544	<i>CHEMBL571317</i>	792.33	TH (0.84)
11382599	<i>Lochnericine</i>	792.33	SLC18A2 (0.84)
10729	<i>2-amino-1,8-dihydropteridine-4,7-dione</i>	792.33	TH (0.88)
101939158	<i>Foresaconitine</i>	792.33	SLC18A2 (0.84)
101670646	<i>7beta-Acetoxy-9-acetylspicataxine</i>	792.33	SLC18A2 (0.84)
101636548	<i>6,7-Seco-19,20-epoxyangustilobine B</i>	792.33	SLC18A2 (0.84)
101235457	<i>Leueantine B</i>	792.33	SLC18A2 (0.84)
69520	<i>3-Methylhistamine</i>	633.87	SLC18A2 (0.89)
25201573	<i>histaminium</i>	633.87	SLC18A2 (0.97)
1615	<i>MDMA</i>	633.87	SLC18A2 (known target)
12656	<i>N,N-Dimethylhistamine</i>	633.87	SLC18A2 (0.89)
95174	<i>2922-41-0</i>	452.76	TH (0.89)
8902	<i>DIPROPYLAMINE</i>	452.76	SLC18A2 (0.84)
8148	<i>DIBUTYLAMINE</i>	452.76	SLC18A2 (0.84)
8021	<i>DIETHYLAMINE</i>	452.76	SLC18A2 (0.84)
70134	<i>875-74-1</i>	452.76	TH (0.84)

*Enrichment ratios indicate predicted target engagement but do not predict directionality (activation vs. inhibition). Notably, some highly enriched compounds such as reserpine and rotenone are known VMAT2 inhibitors with parkinsonism-inducing potential.

Table S6 Detailed TCM-derived compound interactions with key Parkinson’s disease target genes. Columns include Entrez Gene ID, Gene Symbol (SLC18A2, TH, RET, PCSK1), and associated TCM ingredients by PubChem ID with interaction confidence (“known target” or predicted probability score in parentheses).

Entrez_Gene_ID	Gene_Symbol	Associated_TCM_ingredients(PubChem_ID)
6571	SLC18A2	24832061(known target) 5770(known target) 101616(known target) 896(known target) 3945(known target) 439302(known target) 1615(known target) 5826(known target) 681(known target) 439260(known target) 8550(known target) 774(known target) 6921840(0.97) 53486464(0.97) 25201573(0.97) 11993858(0.97) 32893(0.97) 5610(0.96) 289(0.96) 5288826(0.96) 1001(0.96) 980(0.96) 4253(0.96) 4723(0.94) 1727(0.94) 1738(0.92) 89594(0.92) 446220(0.92) 33032(0.92) 5202(0.92) 1125(0.92) 6047(0.92) 24848119(0.9) 78090(0.89) 184180(0.89) 5317104(0.89) 1001(0.89) 3085010(0.89) 65055(0.89) 247704(0.89) 4581(0.89) 442166(0.89) 10219(0.89) 5353923(0.89) 251566(0.89) 5315575(0.89) 5249538(0.89) 69520(0.89) 441411(0.89) 7381(0.89) 4102253(0.89) 11417103(0.89) 442195(0.89) 11503(0.89) 197857(0.89) 8168(0.89) 6041(0.89) 75539(0.89) 12442718(0.89) 5816(0.89) 5280954(0.89) 21680226(0.89) 265756(0.89) 12656(0.89) 4181541(0.89) 119633(0.89) 5317107(0.89) 11865425(0.89) 5320759(0.89) 54612858(0.89) 11865426(0.89) 165581(0.89) 547(0.88) 2215(0.88) 6758(0.88) 6169(0.88) 1045(0.88) 702(0.88) 2866(0.88) 5961(0.88) 2725(0.88) 187(0.88) 4873(0.88) 5203(0.88) 5757(0.88) 2726(0.88) 1123(0.88) 2519(0.88) 439280(0.88) 243(0.86) 155431(0.84) 5317208(0.84) 119026174(0.84) 13891912(0.84) 5319710(0.84) 44575155(0.84) 5477056(0.84) 44584610(0.84) 137628555(0.84) 100010168(0.84) 7681(0.84) 628879(0.84) 6919000(0.84) 25914(0.84) 442058(0.84) 101967169(0.84) 101733513(0.84) 394162(0.84) 91693(0.84) 8902(0.84) 11169934(0.84) 98104494(0.84) 134688048(0.84) 101235457(0.84) 101636548(0.84) 11953931(0.84) 5315214(0.84) 101939158(0.84) 442994(0.84) 5319245(0.84) 134714950(0.84) 164543(0.84) 110695(0.84) 54601825(0.84) 101277346(0.84) 5317192(0.84) 138857792(0.84) 5320135(0.84) 101733514(0.84) 499683(0.84) 4486617(0.84) 188298(0.84) 10604660(0.84) 6419932(0.84) 14584(0.84) 44418786(0.84) 7669(0.84) 101670646(0.84) 443356(0.84) 10629435(0.84) 27445(0.84)

		) 2724998(0.84) 1150(0.84) 20055981(0.84) 101699(0.84) 68315(0.84) 3083909(0.84) 64429 92(0.84) 44583832(0.84) 11035395(0.84) 5392245(0.84) 16316(0.84) 8021(0.84) 75818(0.84) 442246(0.84) 172448(0.84) 8148(0.84) 73255(0.84) 76908(0.84) 183141(0.84) 102595414(0. 84) 5319063(0.84) 71719400(0.84) 61211(0.84) 42636514(0.84) 21579239(0.84) 102469882(0.84) 11382599(0.84) 171175(0.84) 635745(0.84) 76751(0.84) 10075(0.84) 10451681(0.84) 4 42525(0.84) 134814708(0.84) 157672(0.84) 102004683(0.84) 288122(0.84) 5325719(0.84) 10 1707(0.84) 443417(0.84)
7054	TH	681(known target) 247704(known target) 446220(known target) 439260(known target) 2153(known target) 5757(known target) 160597(known target) 16078(known target) 19009(known target) 25201694(known target) 5288826(known target) 5785(known target) 5991(known target) 5994(known target) 6758(known target) 942(known target) 6057(known target) 6140(known target) 1125(0.99) 6925665(0.97) 71567(0.97) 1153(0.97) 71098(0.97) 1738(0.96) 6306(0.96) 999(0.94) 243(0.94) 65253(0.92) 133246(0.92) 5202(0.92) 6047(0.92) 4740700(0.89) 10394(0.89) 1268124(0.89) 23497(0.89) 107(0.89) 3032857(0.89) 95174(0.89) 44134983(0.89) 1859 15(0.89) 11830289(0.89) 736190(0.89) 18644925(0.89) 6951135(0.89) 18608559(0.89) 68309 (0.89) 92222(0.89) 5962(0.88) 6287(0.88) 6137(0.88) 6037(0.88) 10729(0.88) 11447544(0.84) 73804405(0.84) 1217(0.84) 94340(0.84) 70134(0.84) 111299(0.84)
5979	RET	2353(known target) 5281767(known target) 5770(known target) 5291(0.94) 10343085(0.84) 100171446(0.84)
5122	PCSK1	5288826(known target)

*This table shows predicted and known interactions between TCM compounds and core PD genes. Interaction confidence is indicated as “known target” or predicted probability score (in parentheses). Predictions are based on structural similarity and do not indicate the direction of effect (activation vs. inhibition).