

Supplementary Materials

An integrated approach based on phytochemistry, network pharmacology and metabolomics reveals the mechanism of action of *Xanthium strumarium* L. for allergic rhinitis

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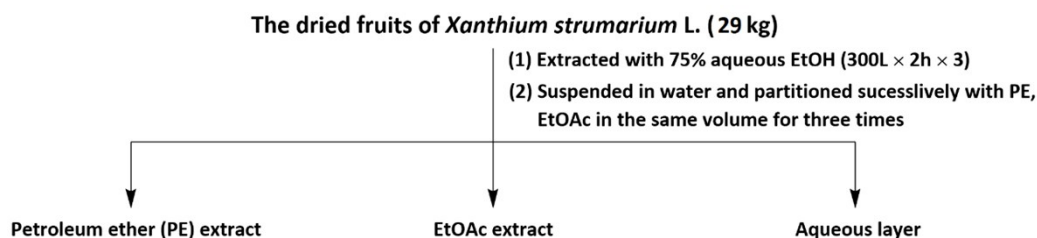
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¹ These authors contributed equally to this work.

General experimental procedures. Optical rotation were recorded on a Rudolph (Hackettstown, NJ) Autopol V automatic polarimeter. The NMR spectra were carried out on a Bruker (Billerica, MA) AM-600 spectrometer at 25°C referencing to the residuals of CD₃OD. Analytical HPLC were performed on a Waters e2695 system equipped with a 2998 PDA detector using a YMC Pack ODS-A (5μm, 4.6 × 250 mm, YMC). Preparative HPLC (LC-6AD) was performed on YMC Pack ODS-A (5μm, 10 × 250 mm, YMC) with SPD-20A. All reagents were HPLC or analytical grade and were purchased from Tianjin Damao Chemical Company. Column chromatography (CC) was done with Silica gel (100-200 mesh and 200-300 mesh, Qingdao Haiyang Chemical Co., LTD), Sephadex LH-20 (Pharmacia, Sweden), ODS-A-HG (50μm) (YMC Group, Japan), and Macroporous resin D101 (Chemical Plant of Nankai University, Tianjin, China).

Extraction and separation. The dried fruits of *Xanthium strumarium* L. (29 kg) were extracted with 75% aqueous EtOH (3 × 300 L, each 2 h) using reflux, and mixture was concentrated under reduced pressure to obtain the crude extract (2.8 kg). The extract was suspended in water and extracted with petroleum ether (PE, 60-90 °C) and EtOAc, as shown in Chart 1. Subsequently, the chromatographic separation techniques were applied to isolate the above three layers.



Identification. Finally, 119 compounds were isolated from *Xanthium strumarium*. The structures of these compounds were identified by spectroscopic methods and comparison with the reported data in reported data. All compounds were showed in Figure S1. Among them, Triterpenes and steroids **1–6**, others **3, 4, 9** and alkaloids **9** were isolated from PE extract, Anthraquinones **2, 5, 13, 19**, phenolic acids **16**, others **1, 2, 5, 7**, alkaloids **1**, and phenylpropanoids **24–27, 34, 42** were isolated from aqueous layer, while the remaining compounds were obtained from EtOAc extract.

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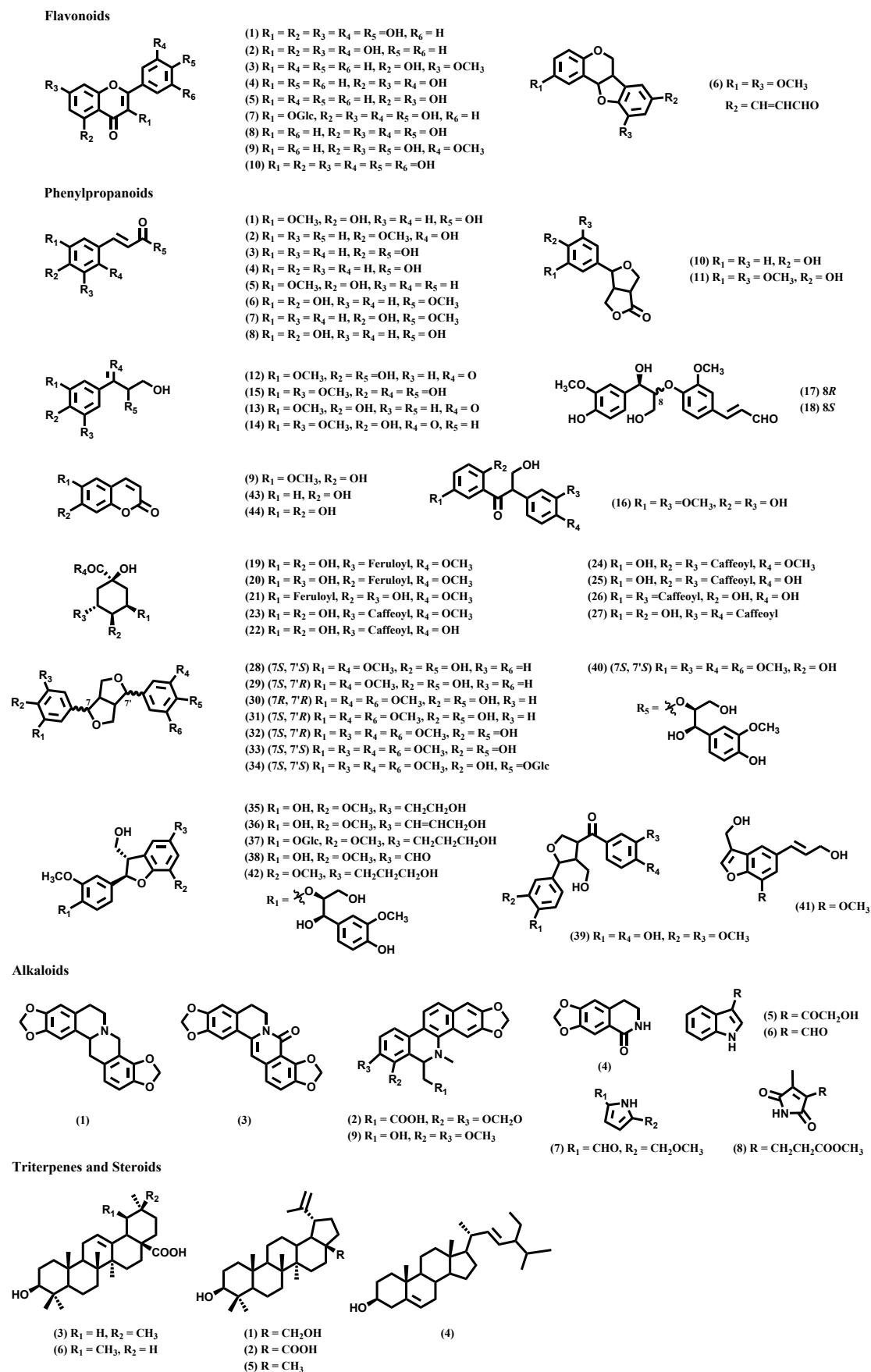


Figure S1. The structures of isolated compounds.

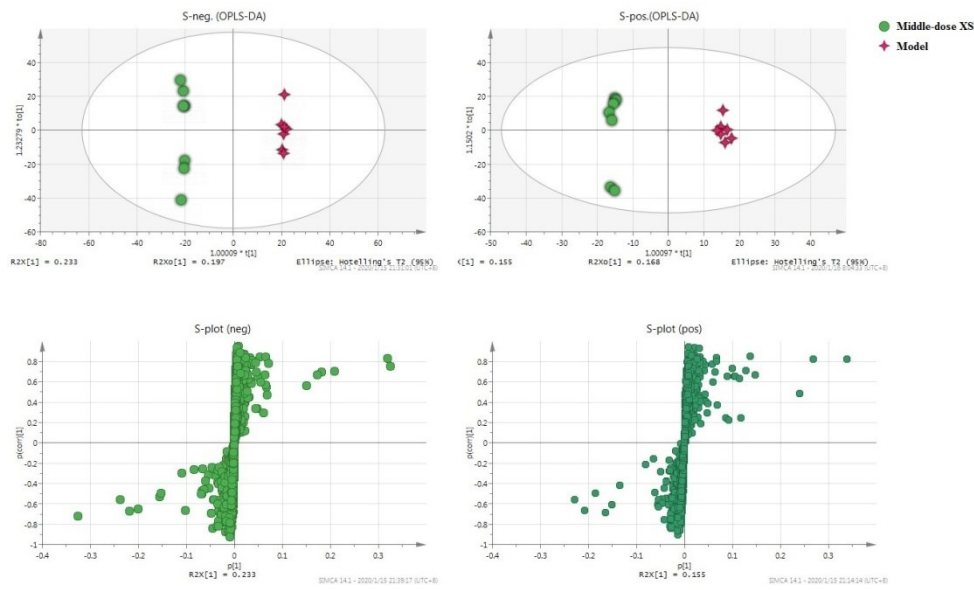


Figure S3. OPLS-DA and S-plot of OPLS-DA of middle-dose XS treatment groups compared with the model group.

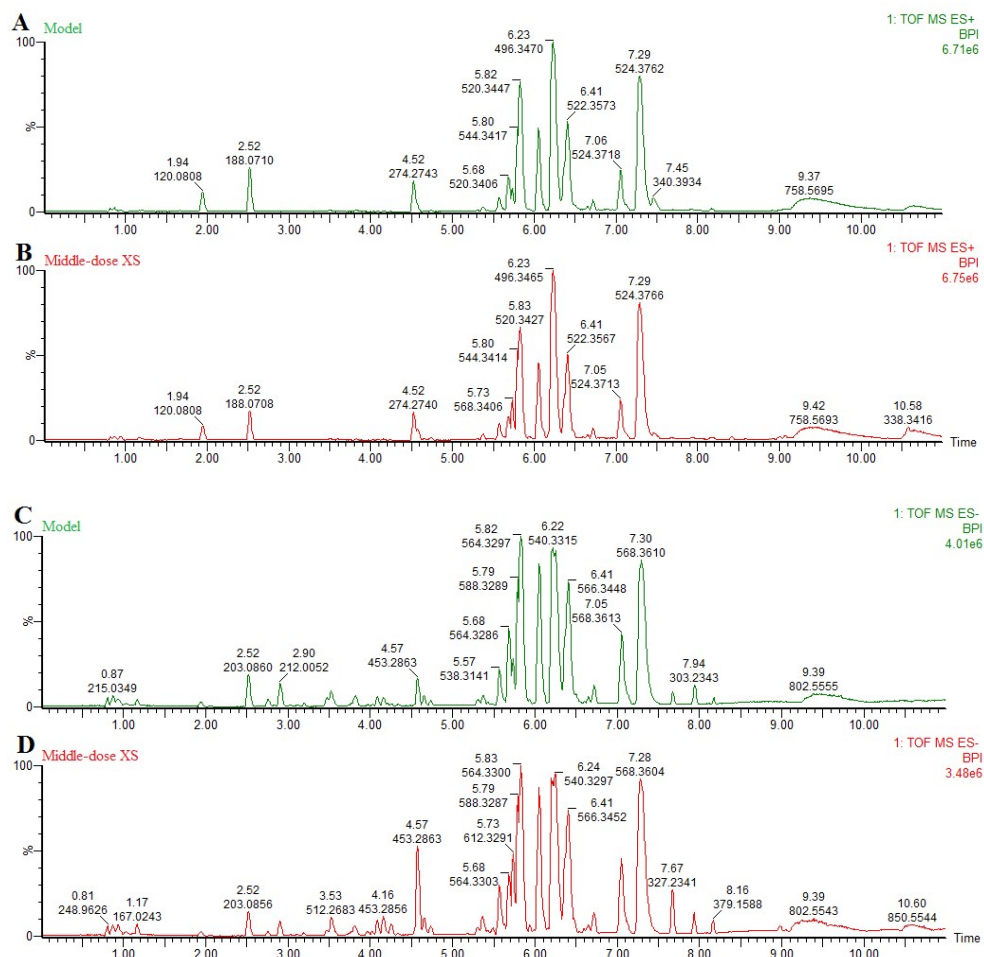


Figure S4. Base Peak Intensity (BPI) of Model and Middle-dose XS samples were measured in both positive and negative ion modes, respectively, (A): Model, ES+ ; (B): Middle-dose XS, ES+; (C) : Model, ES- ; (D) : Middle-dose XS, ES- .

Table S1. The chemical name of structures.

Antraquinones			
No.	Chemical Name	No.	Chemical Name
1	Chrysophanol	2	2-Hydroxy-1,7,8-trimethoxy-3-methyl-9,10-anthracenedione
3	Aurantioobtusin	4	1,3-Dihydroxy-2,7,8-trimethoxy-6-methyl-9,10-anthracenedione
5	Glucobtusifolin	6	Glucobtusin
7	Chrysoobtusin 2-glucoside	8	2-O- β -D-Glucopyranosyloxy-1,7,8-trimethoxy-3-methylanthraquinone
9	Obtusifolin	10	Chrysoobtusin
11	Obtusin	12	Parietin
13	2-methoxy-chrysophano-8-O- β -D-glucopyranoside	14	2-hydroxyemodin-1-methylether
15	8-Methoxylchrysophanol	17	Archin
18	Aloe emodin	19	Glucourantio-obtusin
20	Rhein		
Phenolic acids			
1	Galic acid	2	Gallincin
3	Cedar acid	4	Syringaldehyde
5	Vanillic acid	6	Methyl protocatechuate
7	Protocatechoic acid	8	Catechaldehyde
9	Lioxin	11	Anisic acid
12	<i>p</i> -Formylphenol	13	Piceol
14	Hydroxyhydroquinone	15	Catechol
16	Rhododin	17	Methyl 4-hydroxy-1,3-benzodioxole-5-acetate
18	(<i>E</i>)-3,3'-dimethoxy-4,4'-dihydroxystilbene	20	Ethyl gallate
Flavonoids			
1	Corvitin	2	Kaemferol
3	Tectochrysin	4	Apigenin
5	Crysin	6	Diospyrosin
7	Isoquercitrin	8	Flacitrin
9	Diosmetin	10	Myricetin
Phenylpropanoids			
1	Fumalic acid	2	3-(2-hydroxy-4-methoxyphenyl)prop-2-enal
3	Naringeninic acid	4	Isocinnamic acid
5	Ferulaldehyde	6	Methyl caffeate
7	Methyl <i>p</i> -coumarate	8	Caffeic acid
9	Buxuletin	10	Lyciumin
11	2-(3',5'-dimethoxy-4'-hydroxyphenyl)-3,7-dioxabicyclo[3.3.0]octan-6-one	12	(2 <i>R</i>)-2,3-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)propan-1-one
13	β -Hydroxypropiovanillone	14	β -Hydroxypropiosyringone
15	Syringylglycerol	16	Methoxyphenyl-1-propanone
17	(1 <i>R</i> ,2 <i>S</i>)-1-(3-Methoxy-4-hydroxyphenyl)-2- <i>O</i> -[2-methoxy-4-(3-oxo-1-propenyl)phenyl]glycerol	18	(1 <i>R</i> ,2 <i>R</i>)-1-(3-Methoxy-4-hydroxyphenyl)-2-[2-methoxy-4-[(<i>E</i>)-2-formylethenyl]phenoxy]-1,3-propanediol

19	Methyl 3- <i>O</i> -feruloylquininate	20	4- <i>O</i> -Feruloylquinic acid methyl ester
21	Methyl chlorogenate	22	Chlorogenic acid
23	Methyl 5- <i>O</i> -feruloylquininate	24	3,4-Di- <i>O</i> -caffeoylquinic acid methyl ester
25	3,4-Di- <i>O</i> -Caffeoylquinic acid	26	3,5-Dicaffeoylquinic acid
27	1,3-Dicaffeoylquinic acid	28	<i>d</i> -Pinoresinol
29	<i>epi</i> -Pinoresinol	30	(-)-Medioresinol
31	Asarinin B	32	(+)-Lirioresinol A
33	(+)-Syringaresinol	34	Eleutheroside E ₁
35	5-Benzofuranethanol	36	Dehydrodiconiferyl alcohol
37	Urolignoside	38	Ficusal
39	Valdinol D	40	Buddlenol C
41	Fructusol A	42	Xanthiumnolic C
43	Umbelliferone	44	Esculetin

Alkaloids

1	Stylopin	2	Spallidamine
3	8-Oxocoptisine	4	Noroxyhydrastinine
5	3-(Hydroxyacetyl)indole	6	β -Indolylaldehyde
7	5-(Methoxymethyl)-1 <i>H</i> -pyrrole-2-carbaldehyde	8	Methyl haematinimide
9	Bocconoline		

Triterpenes and Steroids

1	Betulin	2	Betulic acid
3	Caryophyllin	4	Stigmasterol
5	Lupeol	6	Malol

Other

1	β -D-galactopyranoside	2	Panaxcerol B
3	Linolic acid	4	Elaidinic acid
5	Geraniol glucoside	7	Xanthoside
8	Xanthiazone	9	11 α ,13-Dihydrotomentosin
10	Xanthinosin	11	(-)-Dihydroxanthatin
12	Sundiversifolide	13	Atractyligenin
14	2- <i>O</i> -(2- <i>O</i> -Isovaleryl- β -D-glucopyranosyl)attractyligenin		

Table S2. The score of molecular docking for compounds and 2D interaction diagrams.

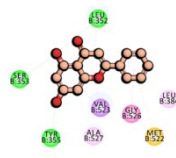
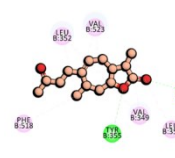
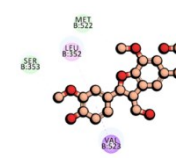
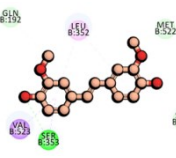
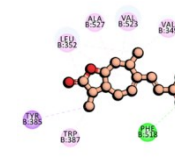
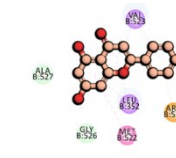
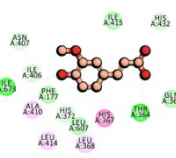
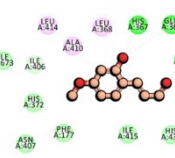
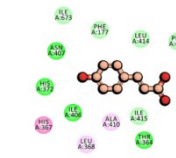
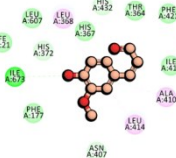
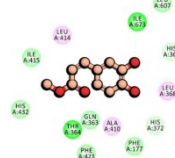
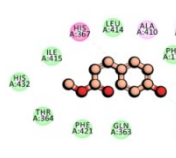
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<p>Flavonoids 5</p>  <p>LibDockScore: 102.5</p>	<p>Others 9</p>  <p>LibDockScore: 98.2</p>	<p>Phenylpropanoids 36</p>  <p>LibDockScore: 123.0</p>
<p>Phenolic acids 18</p>  <p>LibDockScore: 94.7</p>	<p>Others 11</p>  <p>LibDockScore: 93.9</p>	<p>Flavonoids 4</p>  <p>LibDockScore: 106.0</p>
ALOX5		
<p>Phenylpropanoids 1</p>  <p>LibDockScore: 99.3</p>	<p>Phenylpropanoids 2</p>  <p>LibDockScore: 92.0</p>	<p>Phenylpropanoids 3</p>  <p>LibDockScore: 86.7</p>
<p>Phenylpropanoids 5</p>  <p>LibDockScore: 92.6</p>	<p>Phenylpropanoids 6</p>  <p>LibDockScore: 98.4</p>	<p>Phenylpropanoids 7</p>  <p>LibDockScore: 91.3</p>

Table S3. The data of Elisa experiment.

IL-2						
pg/ml	Control	Model	Clarityne	Low	Middle	High
	576.3077	285.4615	514.6923	384.4615	445.0000	473.1538
	584.3846	265.6923	565.8462	422.2308	472.3846	489.1538
	481.9231	304.1538	463.3077	394.0769	508.0000	423.3077
	526.9231	232.9231	454.5385	432.0000	508.5385	483.0769
	464.7692	283.3846	421.9231	382.3077	409.9231	385.1538
	540.3077	230.4615	348.4615	271.6923	370.7692	415.6923
	484.0769	298.7692	388.7692	306.0000	451.0769	335.0000
AVE	522.6703	271.5495	451.0769	370.3956	452.2418	429.2198
STD	47.46421	29.86665	73.75927	59.54225	50.2767	56.95028
IL-4						
pg/ml	Control	Model	Clarityne	Low	Middle	High
	205.5272	254.8363	239.4181	245.3454	258.8727	258.8363
	230.3636	300.8727	231.0363	252.8000	276.0181	212.9454
	177.8363	250.4727	257.8181	263.8545	269.8181	244.9272
	194.4909	253.3454	244.0363	230.8000	233.9818	214.3272
	190.9272	307.6545	203.6181	284.2545	240.1636	252.2909
	208.1272	292.8000	225.5272	257.3272	234.8909	285.4545
	218.4000	348.6909	262.7090	281.74545	245.8727	284.2545
AVE	203.6675	286.9532	237.7376	259.4467	251.3740	250.4337
STD	17.63920	36.42303	20.11399	19.14959	16.99936	29.39310

Table S4. The targets of potential active ingredients from Swiss Target Prediction database.

Compound	Target	Swiss-Prot ID	Compound	Target	Swiss-Prot ID
Phenylpropanoids 1	CA2	P00918	Phenylpropanoids 2	CYP1B1	Q16678
Phenylpropanoids 1	CA7	P43166	Phenylpropanoids 2	ESR1	P03372
Phenylpropanoids 1	CA1	P00915	Phenylpropanoids 2	AKR1B1	P15121
Phenylpropanoids 1	CA6	P23280	Phenylpropanoids 2	ALOX5	P09917
Phenylpropanoids 1	CA12	O43570	Phenylpropanoids 2	CA2	P00918
Phenylpropanoids 1	CA14	Q9ULX7	Phenylpropanoids 2	CA1	P00915
Phenylpropanoids 1	CA9	Q16790	Phenylpropanoids 2	TLR4	O00206
Phenylpropanoids 1	CA5A	P35218	Phenylpropanoids 2	ESR2	Q92731
Phenylpropanoids 1	CA5B	Q9Y2D0	Phenylpropanoids 2	BACE1	P56817
Phenylpropanoids 1	MAOB	P27338	Phenylpropanoids 2	AHR	P35869
Phenylpropanoids 1	ALOX5	P09917	Phenylpropanoids 2	F3	P13726
Phenylpropanoids 1	MMP9	P14780	Phenylpropanoids 2	BCL2	P10415
Phenylpropanoids 1	MMP1	P03956	Phenylpropanoids 2	DAO	P14920
Phenylpropanoids 1	MMP2	P08253	Phenylpropanoids 2	MMP13	P45452
Phenylpropanoids 1	PTPN1	P18031	Phenylpropanoids 2	PIM1	P11309
Phenylpropanoids 3	AKR1B1	P15121	Phenylpropanoids 4	HCAR2	Q8TDS4
Phenylpropanoids 3	CA2	P00918	Phenylpropanoids 4	AKR1B1	P15121
Phenylpropanoids 3	CA7	P43166	Phenylpropanoids 4	TLR4	O00206
Phenylpropanoids 3	ESR2	Q92731	Phenylpropanoids 4	CA2	P00918
Phenylpropanoids 3	CA1	P00915	Phenylpropanoids 4	CA1	P00915
Phenylpropanoids 3	CA3	P07451	Phenylpropanoids 4	ESR2	Q92731
Phenylpropanoids 3	CA6	P23280	Phenylpropanoids 4	CA6	P23280
Phenylpropanoids 3	CA12	O43570	Phenylpropanoids 4	SLC16A1	P53985
Phenylpropanoids 3	CA14	Q9ULX7	Phenylpropanoids 4	CA7	P43166
Phenylpropanoids 3	CA9	Q16790	Phenylpropanoids 4	CA12	O43570
Phenylpropanoids 3	CA4	P22748	Phenylpropanoids 4	CA14	Q9ULX7
Phenylpropanoids 3	CA5B	Q9Y2D0	Phenylpropanoids 4	CA9	Q16790
Phenylpropanoids 3	CA5A	P35218	Phenylpropanoids 4	CA4	P22748
Phenylpropanoids 3	MIF	P14174	Phenylpropanoids 4	CA5B	Q9Y2D0
Phenylpropanoids 3	ALOX5	P09917	Phenylpropanoids 4	CA5A	P35218
Phenylpropanoids 5	APP	P05067	Phenylpropanoids 6	CA2	P00918
Phenylpropanoids 5	CA2	P00918	Phenylpropanoids 6	MMP2	P08253
Phenylpropanoids 5	CA1	P00915	Phenylpropanoids 6	CA7	P43166
Phenylpropanoids 5	CA9	Q16790	Phenylpropanoids 6	CA1	P00915
Phenylpropanoids 5	NFE2L2	Q16236	Phenylpropanoids 6	CA12	O43570
Phenylpropanoids 5	CA7	P43166	Phenylpropanoids 6	CA14	Q9ULX7
Phenylpropanoids 5	CA12	O43570	Phenylpropanoids 6	CA9	Q16790
Phenylpropanoids 5	CA14	Q9ULX7	Phenylpropanoids 6	CA6	P23280
Phenylpropanoids 5	ALOX5	P09917	Phenylpropanoids 6	CA5B	Q9Y2D0
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Phenylpropanoids 5	CA5A	P35218	Phenylpropanoids 6	MMP9	P14780

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Phenylpropanoids 5	CYP1B1	Q16678	Phenylpropanoids 6	AKR1B1	P15121
Phenylpropanoids 7	CA2	P00918	Phenylpropanoids 8	CA2	P00918
Phenylpropanoids 7	CA7	P43166	Phenylpropanoids 8	ALOX5	P09917
Phenylpropanoids 7	CA1	P00915	Phenylpropanoids 8	CA7	P43166
Phenylpropanoids 7	CA12	O43570	Phenylpropanoids 8	CA1	P00915
Phenylpropanoids 7	CA14	Q9ULX7	Phenylpropanoids 8	CA6	P23280
Phenylpropanoids 7	CA9	Q16790	Phenylpropanoids 8	MMP9	P14780
Phenylpropanoids 7	AKR1B1	P15121	Phenylpropanoids 8	CA12	O43570
Phenylpropanoids 7	ESR2	Q92731	Phenylpropanoids 8	MMP1	P03956
Phenylpropanoids 7	CA4	P22748	Phenylpropanoids 8	MMP2	P08253
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Phenylpropanoids 7	CA5A	P35218	Phenylpropanoids 8	CA14	Q9ULX7
Phenylpropanoids 7	CA6	P23280	Phenylpropanoids 8	CA9	Q16790
Phenylpropanoids 7	ALOX5	P09917	Phenylpropanoids 8	CA5B	Q9Y2D0
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Phenylpropanoids 9	CA13	Q8N1Q1	Phenylpropanoids 10	CA3	P07451
Phenylpropanoids 9	CA1	P00915	Phenylpropanoids 10	FFAR1	O14842
Phenylpropanoids 9	CA14	Q9ULX7	Phenylpropanoids 10	NR1H3	Q13133
Phenylpropanoids 9	CA4	P22748	Phenylpropanoids 10	NR1H2	P55055
Phenylpropanoids 9	EGFR	P00533	Phenylpropanoids 10	PIK3CD	O00329
Phenylpropanoids 9	CA5A	P35218	Phenylpropanoids 10	PRKDC	P78527
Phenylpropanoids 9	XDH	P47989	Phenylpropanoids 10	PIK3CB	P42338
Phenylpropanoids 9	CA6	P23280	Phenylpropanoids 10	HDAC8	Q98Y41
Phenylpropanoids 9	CA2	P00918	Phenylpropanoids 10	HDAC1	Q13547
Phenylpropanoids 9	SRD5A1	P18405	Phenylpropanoids 10	PIK3CG	P48736
Phenylpropanoids 9	CBR1	P16152	Phenylpropanoids 10	PIK3CA	P42336
Phenylpropanoids 9	CDK2	P24941	Phenylpropanoids 10	HTR2B	P41595
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Phenylpropanoids 28	ALOX5	P09917	Phenylpropanoids 29	MCL1	Q07820
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Phenylpropanoids 30	MCL1	Q07820	Phenylpropanoids 31	MCL1	Q07820
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Phenylpropanoids 30	SHBG	P04278	Phenylpropanoids 31	OPRM1	P35372
Phenylpropanoids 30	MMP1	P03956	Phenylpropanoids 31	SOAT1	P35610
Phenylpropanoids 30	MMP8	P22894	Phenylpropanoids 31	HIF1A	Q16665
Phenylpropanoids 30	CXCR2	P25025	Phenylpropanoids 31	SOAT2	O75908
Phenylpropanoids 30	CXCR1	P25024	Phenylpropanoids 31	PIK3CG	P48736
Phenylpropanoids 30	OPRM1	P35372	Phenylpropanoids 31	PIK3CA	P42336
Phenylpropanoids 30	SOAT1	P35610	Phenylpropanoids 31	CDK1	P06493
Phenylpropanoids 30	HIF1A	Q16665	Phenylpropanoids 31	CHEK1	O14757
Phenylpropanoids 30	SOAT2	O75908	Phenylpropanoids 31	WEE1	P30291
Phenylpropanoids 30	MMP7	P09237	Phenylpropanoids 31	SHBG	P04278
Phenylpropanoids 30	MAPK9	P45984	Phenylpropanoids 31	CXCR2	P25025
Phenylpropanoids 30	CDK1	P06493	Phenylpropanoids 31	CXCR1	P25024
Phenylpropanoids 32	ALOX5	P09917	Phenylpropanoids 33	ALOX5	P09917
Phenylpropanoids 32	MCL1	Q07820	Phenylpropanoids 33	PTAFR	P25105
Phenylpropanoids 32	PTAFR	P25105	Phenylpropanoids 33	MCL1	Q07820
Phenylpropanoids 32	SHBG	P04278	Phenylpropanoids 33	MAPK9	P45984
Phenylpropanoids 32	SOAT1	P35610	Phenylpropanoids 33	SHBG	P04278
Phenylpropanoids 32	HIF1A	Q16665	Phenylpropanoids 33	SLC5A2	P31639
Phenylpropanoids 32	SOAT2	O75908	Phenylpropanoids 33	SOAT1	P35610
Phenylpropanoids 32	CXCR2	P25025	Phenylpropanoids 33	HIF1A	Q16665
Phenylpropanoids 32	CXCR1	P25024	Phenylpropanoids 33	SOAT2	O75908
Phenylpropanoids 32	OPRM1	P35372	Phenylpropanoids 33	SLC6A2	P23975
Phenylpropanoids 32	MAPK9	P45984	Phenylpropanoids 33	SLC6A4	P31645
Phenylpropanoids 32	CDK1	P06493	Phenylpropanoids 33	PIK3CG	P48736
Phenylpropanoids 32	CHEK1	O14757	Phenylpropanoids 33	PIK3CA	P42336
Phenylpropanoids 32	WEE1	P30291	Phenylpropanoids 33	CNR2	P34972
Phenylpropanoids 32	MMP1	P03956	Phenylpropanoids 33	CNR1	P21554
Phenylpropanoids 32	ALOX5	P09917	Phenylpropanoids 33	ALOX5	P09917
Phenylpropanoids 32	MCL1	Q07820	Phenylpropanoids 33	PTAFR	P25105
Phenylpropanoids 32	PTAFR	P25105	Phenylpropanoids 33	MCL1	Q07820
Phenylpropanoids 32	SHBG	P04278	Phenylpropanoids 33	MAPK9	P45984
Phenylpropanoids 32	SOAT1	P35610	Phenylpropanoids 33	SHBG	P04278
Phenylpropanoids 32	HIF1A	Q16665	Phenylpropanoids 33	SLC5A2	P31639
Phenylpropanoids 32	SOAT2	O75908	Phenylpropanoids 33	SOAT1	P35610
Phenylpropanoids 32	CXCR2	P25025	Phenylpropanoids 33	HIF1A	Q16665
Phenylpropanoids 32	CXCR1	P25024	Phenylpropanoids 33	SOAT2	O75908
Phenylpropanoids 32	OPRM1	P35372	Phenylpropanoids 33	SLC6A2	P23975

Phenylpropanoids 32	MAPK9	P45984	Phenylpropanoids 33	SLC6A4	P31645
Phenylpropanoids 32	CDK1	P06493	Phenylpropanoids 33	PIK3CG	P48736
Phenylpropanoids 32	CHEK1	O14757	Phenylpropanoids 33	PIK3CA	P42336
Phenylpropanoids 32	WEE1	P30291	Phenylpropanoids 33	CNR2	P34972
Phenylpropanoids 32	MMP1	P03956	Phenylpropanoids 33	CNR1	P21554
Phenylpropanoids 43	CA12	O43570	Phenylpropanoids 44	XDH	P47989
Phenylpropanoids 43	CA9	Q16790	Phenylpropanoids 44	EGFR	P00533
Phenylpropanoids 43	CA7	P43166	Phenylpropanoids 44	CA12	O43570
Phenylpropanoids 43	EGFR	P00533	Phenylpropanoids 44	CA9	Q16790
Phenylpropanoids 43	XDH	P47989	Phenylpropanoids 44	AKR1B1	P15121
Phenylpropanoids 43	CA5A	P35218	Phenylpropanoids 44	CA7	P43166
Phenylpropanoids 43	CA1	P00915	Phenylpropanoids 44	CA13	Q8N1Q1
Phenylpropanoids 43	CA14	Q9ULX7	Phenylpropanoids 44	CA2	P00918
Phenylpropanoids 43	HSD17B3	P37058	Phenylpropanoids 44	CA1	P00915
Phenylpropanoids 43	CA2	P00918	Phenylpropanoids 44	CA14	Q9ULX7
Phenylpropanoids 43	CA3	P07451	Phenylpropanoids 44	SQLE	Q14534
Phenylpropanoids 43	AKR1B1	P15121	Phenylpropanoids 44	GPR35	Q9HC97
Phenylpropanoids 43	DAO	P14920	Phenylpropanoids 44	CCND1	P24385
Phenylpropanoids 43	ESR2	Q92731	Phenylpropanoids 44	FLT4	P35916
Phenylpropanoids 43	CA13	Q8N1Q1	Phenylpropanoids 44	INSR	P06213
Anthraquinones 1	ELANE	P08246	Anthraquinones 2	ELANE	P08246
Anthraquinones 1	ESR2	Q92731	Anthraquinones 2	LCK	P06239
Anthraquinones 1	CSNK2A1	P68400	Anthraquinones 2	EGFR	P00533
Anthraquinones 1	PTP4A3	O75365	Anthraquinones 2	PIM1	P11309
Anthraquinones 1	PIM1	P11309	Anthraquinones 2	DUSP3	P51452
Anthraquinones 1	ESR1	P03372	Anthraquinones 2	LIMK1	P53667
Anthraquinones 1	FTO	Q9C0B1	Anthraquinones 2	ESR2	Q92731
Anthraquinones 1	MCL1	Q07820	Anthraquinones 2	ESR1	P03372
Anthraquinones 1	BCL2	P10415	Anthraquinones 2	CSNK2A1	P68400
Anthraquinones 1	CYP19A1	P11511	Anthraquinones 2	CYP1B1	Q16678
Anthraquinones 1	FNTA	P49354	Anthraquinones 2	RET	P07949
Anthraquinones 1	EGFR	P00533	Anthraquinones 2	KDR	P35968
Anthraquinones 1	LCK	P06239	Anthraquinones 2	BCL2	P10415
Anthraquinones 1	CISD1	Q9NZ45	Anthraquinones 2	KCNA3	P22001
Anthraquinones 1	CA7	P43166	Anthraquinones 2	MCL1	Q07820
Anthraquinones 9	ELANE	P08246	Anthraquinones 12	ELANE	P08246
Anthraquinones 9	EGFR	P00533	Anthraquinones 12	LIMK1	P53667
Anthraquinones 9	LIMK1	P53667	Anthraquinones 12	PTP4A3	O75365
Anthraquinones 9	LCK	P06239	Anthraquinones 12	LCK	P06239
Anthraquinones 9	CSNK2A1	P68400	Anthraquinones 12	ESR1	P03372
Anthraquinones 9	DUSP3	P51452	Anthraquinones 12	ESR2	Q92731
Anthraquinones 9	PTP4A3	O75365	Anthraquinones 12	CSNK2A1	P68400
Anthraquinones 9	ESR2	Q92731	Anthraquinones 12	PIM1	P11309
Anthraquinones 9	PIM1	P11309	Anthraquinones 12	MCL1	Q07820

Anthraquinones 9	ESR1	P03372	Anthraquinones 12	EGFR	P00533
Anthraquinones 9	MCL1	Q07820	Anthraquinones 12	DUSP3	P51452
Anthraquinones 9	BCL2	P10415	Anthraquinones 12	BCL2	P10415
Anthraquinones 9	KCNA3	P22001	Anthraquinones 12	FTO	Q9C0B1
Anthraquinones 9	FTO	Q9C0B1	Anthraquinones 12	MMP3	P08254
Anthraquinones 9	MAOA	P21397	Anthraquinones 12	MMP1	P03956
Anthraquinones 15	ELANE	P08246	Phenolic acids 2	FUT7	Q11130
Anthraquinones 15	EGFR	P00533	Phenolic acids 2	CA2	P00918
Anthraquinones 15	LCK	P06239	Phenolic acids 2	CA7	P43166
Anthraquinones 15	DUSP3	P51452	Phenolic acids 2	CA1	P00915
Anthraquinones 15	ESR2	Q92731	Phenolic acids 2	CA12	O43570
Anthraquinones 15	PIM1	P11309	Phenolic acids 2	CA14	Q9ULX7
Anthraquinones 15	LIMK1	P53667	Phenolic acids 2	CA9	Q16790
Anthraquinones 15	CSNK2A1	P68400	Phenolic acids 2	CA3	P07451
Anthraquinones 15	BACE1	P56817	Phenolic acids 2	CA6	P23280
Anthraquinones 15	CYP19A1	P11511	Phenolic acids 2	CA4	P22748
Anthraquinones 15	ESR1	P03372	Phenolic acids 2	CA5B	Q9Y2D0
Anthraquinones 15	ADORA3	P0DMS8	Phenolic acids 2	CA5A	P35218
Anthraquinones 15	AKR1C3	P42330	Phenolic acids 2	CA13	Q8N1Q1
Anthraquinones 15	RET	P07949	Phenolic acids 2	SQLE	Q14534
Anthraquinones 15	KDR	P35968	Phenolic acids 2	SERPINE1	P05121
Phenolic acids 3	CA2	P00918	Phenolic acids 4	ERN1	O75460
Phenolic acids 3	CA7	P43166	Phenolic acids 4	CA2	P00918
Phenolic acids 3	CA1	P00915	Phenolic acids 4	CA7	P43166
Phenolic acids 3	CA3	P07451	Phenolic acids 4	CA3	P07451
Phenolic acids 3	CA6	P23280	Phenolic acids 4	CA6	P23280
Phenolic acids 3	CA12	O43570	Phenolic acids 4	CA14	Q9ULX7
Phenolic acids 3	CA14	Q9ULX7	Phenolic acids 4	CA5A	P35218
Phenolic acids 3	CA9	Q16790	Phenolic acids 4	CA1	P00915
Phenolic acids 3	CA5A	P35218	Phenolic acids 4	CA12	O43570
Phenolic acids 3	CA4	P22748	Phenolic acids 4	CA9	Q16790
Phenolic acids 3	FUT7	Q11130	Phenolic acids 4	ACHE	P22303
Phenolic acids 3	CA13	Q8N1Q1	Phenolic acids 4	TTR	P02766
Phenolic acids 3	CA5B	Q9Y2D0	Phenolic acids 4	CA4	P22748
Phenolic acids 3	TPMT	P51580	Phenolic acids 4	ERCC5	P28715
Phenolic acids 3	AKR1C3	P42330	Phenolic acids 4	FEN1	P39748
Phenolic acids 5	CA2	P00918	Phenolic acids 6	CA2	P00918
Phenolic acids 5	CA7	P43166	Phenolic acids 6	CA7	P43166
Phenolic acids 5	CA1	P00915	Phenolic acids 6	CA1	P00915
Phenolic acids 5	CA12	O43570	Phenolic acids 6	CA12	O43570
Phenolic acids 5	CA14	Q9ULX7	Phenolic acids 6	CA14	Q9ULX7
Phenolic acids 5	CA9	Q16790	Phenolic acids 6	CA9	Q16790
Phenolic acids 5	CA3	P07451	Phenolic acids 6	SQLE	Q14534
Phenolic acids 5	CA6	P23280	Phenolic acids 6	FUT7	Q11130

Phenolic acids 5	CA5A	P35218	Phenolic acids 6	CA13	Q8N1Q1
Phenolic acids 5	CA4	P22748	Phenolic acids 6	CA5B	Q9Y2D0
Phenolic acids 5	TPMT	P51580	Phenolic acids 6	SERPINE1	P05121
Phenolic acids 5	TTR	P02766	Phenolic acids 6	IGF1R	P08069
Phenolic acids 5	CA5B	Q9Y2D0	Phenolic acids 6	ALK	Q9UM73
Phenolic acids 5	CA13	Q8N1Q1	Phenolic acids 6	CA3	P07451
Phenolic acids 5	FUT7	Q11130	Phenolic acids 6	CA4	P22748
Phenolic acids 7	CA2	P00918	Phenolic acids 8	CA6	P23280
Phenolic acids 7	CA7	P43166	Phenolic acids 8	CA4	P22748
Phenolic acids 7	CA1	P00915	Phenolic acids 8	CA2	P00918
Phenolic acids 7	CA6	P23280	Phenolic acids 8	TYR	P14679
Phenolic acids 7	CA12	O43570	Phenolic acids 8	CA3	P07451
Phenolic acids 7	CA14	Q9ULX7	Phenolic acids 8	FUT7	Q11130
Phenolic acids 7	CA9	Q16790	Phenolic acids 8	CA5B	Q9Y2D0
Phenolic acids 7	CA4	P22748	Phenolic acids 8	CA5A	P35218
Phenolic acids 7	CA3	P07451	Phenolic acids 8	ERN1	O75460
Phenolic acids 7	CA5B	Q9Y2D0	Phenolic acids 8	CA7	P43166
Phenolic acids 7	CA5A	P35218	Phenolic acids 8	CA1	P00915
Phenolic acids 7	CA13	Q8N1Q1	Phenolic acids 8	CA12	O43570
Phenolic acids 7	FUT7	Q11130	Phenolic acids 8	CA14	Q9ULX7
Phenolic acids 7	SQLE	Q14534	Phenolic acids 8	CA9	Q16790
Phenolic acids 7	LDHA	P00338	Phenolic acids 8	COMT	P21964
Phenolic acids 9	ERN1	O75460	Phenolic acids 11	CA2	P00918
Phenolic acids 9	CA2	P00918	Phenolic acids 11	CA1	P00915
Phenolic acids 9	CA7	P43166	Phenolic acids 11	CA7	P43166
Phenolic acids 9	CA1	P00915	Phenolic acids 11	CA3	P07451
Phenolic acids 9	CA12	O43570	Phenolic acids 11	CA12	O43570
Phenolic acids 9	CA14	Q9ULX7	Phenolic acids 11	CA14	Q9ULX7
Phenolic acids 9	CA9	Q16790	Phenolic acids 11	CA9	Q16790
Phenolic acids 9	CA4	P22748	Phenolic acids 11	CA4	P22748
Phenolic acids 9	CA3	P07451	Phenolic acids 11	CA5A	P35218
Phenolic acids 9	CA6	P23280	Phenolic acids 11	CA5B	Q9Y2D0
Phenolic acids 9	CA5A	P35218	Phenolic acids 11	CA13	Q8N1Q1
Phenolic acids 9	CDC25B	P30305	Phenolic acids 11	MAOB	P27338
Phenolic acids 9	TTR	P02766	Phenolic acids 11	CHRNA7	P36544
Phenolic acids 9	NAT1	P18440	Phenolic acids 11	AHR	P35869
Phenolic acids 9	ALPG	P10696	Phenolic acids 11	TTR	P02766
Phenolic acids 12	ERN1	O75460	Phenolic acids 13	ALDH5A1	P51649
Phenolic acids 12	CA2	P00918	Phenolic acids 13	ABAT	P80404
Phenolic acids 12	CA7	P43166	Phenolic acids 13	ERN1	O75460
Phenolic acids 12	CA1	P00915	Phenolic acids 13	COMT	P21964
Phenolic acids 12	CA3	P07451	Phenolic acids 13	CA12	O43570
Phenolic acids 12	CA6	P23280	Phenolic acids 13	CA9	Q16790
Phenolic acids 12	CA12	O43570	Phenolic acids 13	SRD5A2	P31213

Phenolic acids 12	CA14	Q9ULX7	Phenolic acids 13	HSD17B1	P14061
Phenolic acids 12	CA9	Q16790	Phenolic acids 13	HTR6	P50406
Phenolic acids 12	CA4	P22748	Phenolic acids 13	ESRRG	P62508
Phenolic acids 12	CA5B	Q9Y2D0	Phenolic acids 13	DYRK1A	Q13627
Phenolic acids 12	CA5A	P35218	Phenolic acids 13	CLK1	P49759
Phenolic acids 12	CA13	Q8N1Q1	Phenolic acids 13	DYRK1B	Q9Y463
Phenolic acids 12	COMT	P21964	Phenolic acids 13	FASN	P49327
Phenolic acids 12	ACHE	P22303	Phenolic acids 13	CA7	P43166
Phenolic acids 14	FYN	P06241	Phenolic acids 15	CA2	P00918
Phenolic acids 14	EGFR	P00533	Phenolic acids 15	CA12	O43570
Phenolic acids 14	CA2	P00918	Phenolic acids 15	CA5B	Q9Y2D0
Phenolic acids 14	CA1	P00915	Phenolic acids 15	CA3	P07451
Phenolic acids 14	CA6	P23280	Phenolic acids 15	CA9	Q16790
Phenolic acids 14	NQO2	P16083	Phenolic acids 15	PTPN22	Q9Y2R2
Phenolic acids 14	CA12	O43570	Phenolic acids 15	CA4	P22748
Phenolic acids 14	CA4	P22748	Phenolic acids 15	EGFR	P00533
Phenolic acids 14	CA5B	Q9Y2D0	Phenolic acids 15	CA1	P00915
Phenolic acids 14	CA5A	P35218	Phenolic acids 15	FYN	P06241
Phenolic acids 14	CA3	P07451	Phenolic acids 15	CA6	P23280
Phenolic acids 14	CA9	Q16790	Phenolic acids 15	IDO1	P14902
Phenolic acids 14	MAOB	P27338	Phenolic acids 15	CA5A	P35218
Phenolic acids 14	LCK	P06239	Phenolic acids 15	HDAC6	Q9UBN7
Phenolic acids 14	TYR	P14679	Phenolic acids 15	HDAC8	Q9BY41
Phenolic acids 17	CDK5R1	Q15078	Phenolic acids 18	NQO2	P16083
Phenolic acids 17	CDK2	P24941	Phenolic acids 18	CYP1B1	Q16678
Phenolic acids 17	CDK9	P50750	Phenolic acids 18	CYP1A2	P05177
Phenolic acids 17	DYRK1A	Q13627	Phenolic acids 18	CYP1A1	P04798
Phenolic acids 17	ALPL	P05186	Phenolic acids 18	PTGS1	P23219
Phenolic acids 17	AOC3	Q16853	Phenolic acids 18	TUBB1	Q9H4B7
Phenolic acids 17	EGFR	P00533	Phenolic acids 18	ESR1	P03372
Phenolic acids 17	EGLN1	Q9GZT9	Phenolic acids 18	RELA	Q04206
Phenolic acids 17	RP56KA3	P51812	Phenolic acids 18	TUBB3	Q13509
Phenolic acids 17	ADORA2A	P29274	Phenolic acids 18	PTGS2	P35354
Phenolic acids 17	ADORA2B	P29275	Phenolic acids 18	APP	P05067
Phenolic acids 17	IDO1	P14902	Phenolic acids 18	AHR	P35869
Phenolic acids 17	F2	P00734	Phenolic acids 18	ABCB1	P08183
Phenolic acids 17	TERT	O14746	Phenolic acids 18	MAOA	P21397
Phenolic acids 17	GPR84	Q9NQ55	Phenolic acids 18	CA2	P00918
Flavonoid 3	ABCB1	P08183	Flavonoid 4	NOX4	Q9NPH5
Flavonoid 3	ABCG2	Q9UNQ0	Flavonoid 4	AKR1B1	P15121
Flavonoid 3	CYP1B1	Q16678	Flavonoid 4	CDK5R1	Q15078
Flavonoid 3	PTGS2	P35354	Flavonoid 4	XDH	P47989
Flavonoid 3	CYP19A1	P11511	Flavonoid 4	MAOA	P21397
Flavonoid 3	TNKS	O95271	Flavonoid 4	FLT3	P36888

Flavonoid 3	AKR1B1	P15121	Flavonoid 4	CYP19A1	P11511
Flavonoid 3	CA2	P00918	Flavonoid 4	ESR1	P03372
Flavonoid 3	CA1	P00915	Flavonoid 4	CCNB3	Q8WWL7
Flavonoid 3	CA12	O43570	Flavonoid 4	ACHE	P22303
Flavonoid 3	CA9	Q16790	Flavonoid 4	ADORA1	P30542
Flavonoid 3	FLT3	P36888	Flavonoid 4	PTGS2	P35354
Flavonoid 3	MAOA	P21397	Flavonoid 4	ESR2	Q92731
Flavonoid 3	ADORA1	P30542	Flavonoid 4	CDK6	Q00534
Flavonoid 3	ADORA3	P0DMS8	Flavonoid 4	ADORA2A	P29274
Flavonoid 5	AKR1B1	P15121	Flavonoid 6	CNR1	P21554
Flavonoid 5	CDK5R1	Q15078	Flavonoid 6	CNR2	P34972
Flavonoid 5	XDH	P47989	Flavonoid 6	OPRM1	P35372
Flavonoid 5	CYP19A1	P11511	Flavonoid 6	OPRD1	P41143
Flavonoid 5	CA2	P00918	Flavonoid 6	F10	P00742
Flavonoid 5	CCNB3	Q8WWL7	Flavonoid 6	SLC10A2	Q12908
Flavonoid 5	CA7	P43166	Flavonoid 6	ROCK2	O75116
Flavonoid 5	CDK6	Q00534	Flavonoid 6	BRD4	O60885
Flavonoid 5	CA1	P00915	Flavonoid 6	BRD3	Q15059
Flavonoid 5	CA12	O43570	Flavonoid 6	PTGDR2	Q9Y5Y4
Flavonoid 5	CA9	Q16790	Flavonoid 6	SYK	P43405
Flavonoid 5	CA4	P22748	Flavonoid 6	BRD2	P25440
Flavonoid 5	ABCB1	P08183	Flavonoid 6	DPP4	P27487
Flavonoid 5	CYP1B1	Q16678	Flavonoid 6	P2RY12	Q9H244
Flavonoid 5	ABCG2	Q9UNQ0	Flavonoid 6	PDE4B	Q07343
Alkaloids 1	DRD1	P21728	Alkaloids 2	CA2	P00918
Alkaloids 1	F3	P13726	Alkaloids 2	SLC22A12	Q96537
Alkaloids 1	DRD2	P14416	Alkaloids 2	CA1	P00915
Alkaloids 1	HTR1A	P08908	Alkaloids 2	AKR1B1	P15121
Alkaloids 1	CHRM4	P08173	Alkaloids 2	ADAMTS4	O75173
Alkaloids 1	HTR7	P34969	Alkaloids 2	BMP1	P13497
Alkaloids 1	SLC6A3	Q01959	Alkaloids 2	BCAT2	O15382
Alkaloids 1	ADRA1D	P25100	Alkaloids 2	PTGS2	P35354
Alkaloids 1	DRD3	P35462	Alkaloids 2	PDE4B	Q07343
Alkaloids 1	SIGMAR1	Q99720	Alkaloids 2	PTPN22	Q9Y2R2
Alkaloids 1	ADRA1A	P35348	Alkaloids 2	PYGL	P06737
Alkaloids 1	DRD4	P21917	Alkaloids 2	ACE	P12821
Alkaloids 1	ADRA1B	P35368	Alkaloids 2	MME	P08473
Alkaloids 1	DRD5	P21918	Alkaloids 2	PTGDR2	Q9Y5Y4
Alkaloids 1	ADRB2	P07550	Alkaloids 2	CA12	O43570
Alkaloids 3	GRK3	P35626	Alkaloids 4	SLC6A3	Q01959
Alkaloids 3	SAE1	Q9UBE0	Alkaloids 4	KIF11	P52732
Alkaloids 3	GRK2	P25098	Alkaloids 4	DHCR7	Q9UBM7
Alkaloids 3	CDC25A	P30304	Alkaloids 4	ACHE	P22303
Alkaloids 3	CDC25B	P30305	Alkaloids 4	ABCB1	P08183

Alkaloids 3	ABL1	P00519	Alkaloids 4	HTR2B	P41595
Alkaloids 3	CHEK2	O96017	Alkaloids 4	HTR2A	P28223
Alkaloids 3	PDE5A	O76074	Alkaloids 4	HTR2C	P28335
Alkaloids 3	CDK2	P24941	Alkaloids 4	NQO2	P16083
Alkaloids 3	CDK4	P11802	Alkaloids 4	CA2	P00918
Alkaloids 3	GRK5	P34947	Alkaloids 4	DRD2	P14416
Alkaloids 3	PARP1	P09874	Alkaloids 4	CA9	Q16790
Alkaloids 3	TTK	P33981	Alkaloids 4	CA1	P00915
Alkaloids 3	CSF1R	P07333	Alkaloids 4	CA14	Q9ULX7
Alkaloids 3	MAPK8	P45983	Alkaloids 4	DYRK1A	Q13627
Alkaloids 5	PIM1	P11309	Alkaloids 6	CYP2A6	P11509
Alkaloids 5	MPO	P05164	Alkaloids 6	IMPDH2	P12268
Alkaloids 5	ACPP	P15309	Alkaloids 6	PARP1	P09874
Alkaloids 5	CES1	P23141	Alkaloids 6	PIM3	Q86V86
Alkaloids 5	CES2	O00748	Alkaloids 6	ERN1	O75460
Alkaloids 5	NUDT1	P36639	Alkaloids 6	NOS2	P35228
Alkaloids 5	PIM3	Q86V86	Alkaloids 6	PIM1	P11309
Alkaloids 5	DAO	P14920	Alkaloids 6	PIM2	Q9P1W9
Alkaloids 5	CA6	P23280	Alkaloids 6	TPO	P07202
Alkaloids 5	CA14	Q9ULX7	Alkaloids 6	MALT1	Q9UDY8
Alkaloids 5	CA4	P22748	Alkaloids 6	CCR1	P32246
Alkaloids 5	CA13	Q8N1Q1	Alkaloids 6	MCL1	Q07820
Alkaloids 5	CA5B	Q9Y2D0	Alkaloids 6	KIF11	P52732
Alkaloids 5	CA5A	P35218	Alkaloids 6	CAPN1	P07384
Alkaloids 5	CDK5R1	Q15078	Alkaloids 6	ADH1B	P00325
Alkaloids 7	PPP5C	Q9BPW0	Alkaloids 8	PTPN1	P18031
Alkaloids 7	PPP1CA	P62136	Alkaloids 8	AKR1B1	P15121
Alkaloids 7	ELANE	P08246	Alkaloids 8	MALT1	Q9UDY8
Alkaloids 7	PPP1CC	P36873	Alkaloids 8	KDM5C	P41229
Alkaloids 7	PLAUR	Q03405	Alkaloids 8	KDM4B	O94953
Alkaloids 7	PPM1B	O75688	Alkaloids 8	KDM5B	Q9UGL1
Alkaloids 7	PSEN2	P49810	Alkaloids 8	KDM4A	O75164
Alkaloids 7	CHRM4	P08173	Alkaloids 8	AKR1A1	P14550
Alkaloids 7	CHRM2	P08172	Alkaloids 8	AKR1B10	O60218
Alkaloids 7	MAOB	P27338	Alkaloids 8	PTPRC	P08575
Alkaloids 7	AOC3	Q16853	Alkaloids 8	NAMPT	P43490
Alkaloids 7	MTNR1A	P48039	Alkaloids 8	CA2	P00918
Alkaloids 7	BCHE	P06276	Alkaloids 8	CA1	P00915
Alkaloids 7	PTGS2	P35354	Alkaloids 8	CA12	O43570
Alkaloids 7	PARP1	P09874	Alkaloids 8	CA9	Q16790
Alkaloids 9	ROCK2	O75116	Others 9	FNTA	P49354
Alkaloids 9	ROCK1	Q13464	Others 9	PTPN1	P18031
Alkaloids 9	SCN9A	Q15858	Others 9	HSD11B1	P28845
Alkaloids 9	ABCC9	O60706	Others 9	F2	P00734

Alkaloids 9	MKNK2	Q9HBH9	Others 9	PRSS1	P07477
Alkaloids 9	EPHB4	P54760	Others 9	CYP19A1	P11511
Alkaloids 9	ALOX5AP	P20292	Others 9	HMGCR	P04035
Alkaloids 9	CCNE2	O96020	Others 9	AR	P10275
Alkaloids 9	TK1	P04183	Others 9	PGR	P06401
Alkaloids 9	MTOR	P42345	Others 9	HSD17B2	P37059
Alkaloids 9	PIK3CA	P42336	Others 9	NR3C1	P04150
Alkaloids 9	AURKA	O14965	Others 9	CES2	O00748
Alkaloids 9	CDK2	P24941	Others 9	PTGES	O14684
Alkaloids 9	CFD	P00746	Others 9	PTGS2	P35354
Alkaloids 9	CHEK1	O14757	Others 9	NR3C2	P08235
Alkaloids 9	ROCK2	O75116	Others 9	FNTA	P49354
Alkaloids 9	ROCK1	Q13464	Others 9	PTPN1	P18031
Alkaloids 9	SCN9A	Q15858	Others 9	HSD11B1	P28845
Alkaloids 9	ABCC9	O60706	Others 9	F2	P00734
Alkaloids 9	MKNK2	Q9HBH9	Others 9	PRSS1	P07477
Others 10	PTGS2	P35354	Others 11	AR	P10275
Others 10	FNTA	P49354	Others 11	NR3C1	P04150
Others 10	CYP19A1	P11511	Others 11	CYP19A1	P11511
Others 10	PTPN1	P18031	Others 11	PGR	P06401
Others 10	F2	P00734	Others 11	HSD11B1	P28845
Others 10	PRSS1	P07477	Others 11	NR3C2	P08235
Others 10	HSD11B1	P28845	Others 11	PTGS2	P35354
Others 10	NOS2	P35228	Others 11	F2	P00734
Others 10	TERT	O14746	Others 11	HMGCR	P04035
Others 10	AR	P10275	Others 11	CYP17A1	P05093
Others 10	ACHE	P22303	Others 11	HSD17B2	P37059
Others 10	PGR	P06401	Others 11	MTNR1A	P48039
Others 10	CTRC	Q99895	Others 11	MTNR1B	P49286
Others 10	GSK3B	P49841	Others 11	PTPN1	P18031
Others 10	PARP1	P09874	Others 11	FNTA	P49354
Others 12	CYP19A1	P11511	Others 13	HSD11B1	P28845
Others 12	HMGCR	P04035	Others 13	SAE1	Q9UBE0
Others 12	PGR	P06401	Others 13	AKR1B10	O60218
Others 12	AR	P10275	Others 13	PTGS2	P35354
Others 12	CYP17A1	P05093	Others 13	PTPN1	P18031
Others 12	HSD17B2	P37059	Others 13	POLA1	P09884
Others 12	PTGES	O14684	Others 13	POLB	P06746
Others 12	FNTA	P49354	Others 13	TOP2A	P11388
Others 12	CTRC	Q99895	Others 13	CDC25C	P30307
Others 12	NR3C2	P08235	Others 13	IMPDH1	P20839
Others 12	GSK3B	P49841	Others 13	PTGES	O14684
Others 12	PTGS2	P35354	Others 13	PTGS1	P23219
Others 12	HSD11B1	P28845	Others 13	AMPD2	Q01433

Others 12	PTPN2	P17706	Others 13	NR1H4	Q96R11
Others 12	DRD2	P14416	Others 13	UGT2B7	P16662

Table S5. The targets of potential active ingredients from HIT database.

Compound	Target	Swiss-Prot ID	Compound	Target	Swiss-Prot ID
Phenylpropanoids 3	TYR	P14679	Flavonoid 4	IL4	P05112
Phenylpropanoids 3	Co-1	Q9ZP19	Flavonoid 4	ALG5	Q9Y673
Phenylpropanoids 3	NOS3	P29474	Flavonoid 4	CD40LG	P29965
Phenylpropanoids 3	CCL16	O15467	Flavonoid 4	RELA	Q04206
Phenylpropanoids 4	MGAM	O43451	Flavonoid 4	CFLAR	O15519
Phenylpropanoids 4	CYP73A5	P92994	Flavonoid 4	BCL2L1	Q07817
Phenylpropanoids 8	PTGS1	P23219	Flavonoid 4	MCL1	Q07820
Phenylpropanoids 8	PTGS2	P35354	Flavonoid 4	XIAP	P98170
Phenylpropanoids 8	SELP	P16109	Flavonoid 4	ALPI	P09923
Phenylpropanoids 8	ACHE	P22303	Flavonoid 4	PTGS2	P35354
Phenylpropanoids 8	GFAP	P14136	Flavonoid 4	NFKBIA	P25963
Phenylpropanoids 8	IGF2	P01344	Flavonoid 4	AKT1	P31749
Phenylpropanoids 8	RAC1	P63000	Flavonoid 4	BAD	Q92934
Phenylpropanoids 8	CYP1A1	P04798	Flavonoid 4	IGF1R	P08069
Phenylpropanoids 8	TNF	P01375	Flavonoid 4	CASP9	P55211
Phenylpropanoids 8	BTK	Q06187	Flavonoid 4	CYP19A1	P11511
Phenylpropanoids 8	PRKCB	P05771	Flavonoid 4	HIF1A	Q16665
Phenylpropanoids 44	CDK2	P24941	Flavonoid 4	GSK3B	P49841
Phenylpropanoids 44	CDK4	P11802	Flavonoid 4	VEGFA	P15692
Phenylpropanoids 44	RB1	P06400	Flavonoid 4	CCND1	P24385
Phenylpropanoids 44	CDKN1A	P38936	Flavonoid 4	EIF6	P56537
Phenylpropanoids 44	HERC5	Q9UII4	Flavonoid 4	NOS2	P35228
Phenylpropanoids 44	E2F1	Q01094	Flavonoid 4	TP53	P04637
Phenylpropanoids 44	MMP1	P03956	Flavonoid 4	CDKN2A	P42771
Phenylpropanoids 44	BCL2	P10415	Flavonoid 4	RUNX1T1	Q06455
Phenylpropanoids 44	CASP3	P42574	Flavonoid 4	HERC5	Q9UII4
Phenylpropanoids 44	MMP3	P08254	Flavonoid 4	CDK1	P06493
Anthraquinones 18	CCNA2	P20248	Flavonoid 4	CCNA2	P20248
Anthraquinones 18	CDK2	P24941	Flavonoid 4	CCNB1	P14635
Anthraquinones 18	PCNA	P12004	Flavonoid 4	CDKN1A	P38936
Anthraquinones 18	PRKCA	P17252	Flavonoid 4	BAX	Q07812
Anthraquinones 18	MYC	P01106	Flavonoid 4	CYCS	P99999
Anthraquinones 18	CCNB1	P14635	Flavonoid 4	AHSA1	O95433
Anthraquinones 18	CDK1	P06493	Flavonoid 4	MDM2	Q00987
Anthraquinones 18	IL1B	P01584	Flavonoid 4	BCL2	P10415
Anthraquinones 18	TNF	P01375	Flavonoid 4	PSME3	P61289
Anthraquinones 18	CASP3	P42574	Flavonoid 4	G6PC	P35575
Anthraquinones 18	TP53	P04637	Flavonoid 4	INS	P01308
Anthraquinones 18	CDKN1A	P38936	Flavonoid 4	APC	P25054

Anthraquinones 18	FASN	P49327	Flavonoid 4	HMOX1	P09601
Anthraquinones 18	BAX	Q07812	Flavonoid 4	ICAM1	P05362
Anthraquinones 18	PRKCD	Q05655	Flavonoid 4	MS4A2	Q01362
Anthraquinones 18	PRKCE	Q02156	Flavonoid 4	FCER2	P06734
Phenolic acids 5	TYRP1	P17643	Flavonoid 4	IL13	P35225
Phenolic acids 5	NOS3	P29474	Flavonoid 4	RB1	P06400
Phenolic acids 8	ODC1	P11926	Flavonoid 4	TRPM2	O94759
Phenolic acids 9	JUN	P05412	Flavonoid 4	ESR1	P03372
Phenolic acids 9	MAPK1	P28482	Flavonoid 4	ACACA	Q13085
Phenolic acids 9	MMP9	P14780	Flavonoid 4	AKR1C3	P42330
Phenolic acids 15	COMT	P21964	Flavonoid 4	CCND2	P30279
Phenolic acids 15	MYB	P10242	Flavonoid 4	CDK2	P24941
Flavonoid 5	IL4	P05112	Flavonoid 4	CDK4	P11802
Flavonoid 5	IL13	P35225	Flavonoid 4	CDK6	Q00534
Flavonoid 5	PTGS2	P35354	Flavonoid 4	EEF1E1	O43324
Flavonoid 5	CYP19A1	P11511	Flavonoid 4	ODC1	P11926
Flavonoid 5	TGFB1	P01137	Flavonoid 4	PSMD3	O43242
Flavonoid 5	CDKN1A	P38936	Flavonoid 4	CASP3	P42574
Flavonoid 5	MS4A2	Q01362	Flavonoid 4	SLC5A5	Q92911
Alkaloids 1	TNF	P01375	Flavonoid 4	PLAU	P00749
Alkaloids 1	IL1B	P01584	Flavonoid 4	SERPINE1	P05121
Alkaloids 1	IL6	P05231	Flavonoid 4	MMP9	P14780
Alkaloids 1	PTGS2	P35354	Flavonoid 4	FXYD2	P54710
Alkaloids 1	NOS2	P35228	Flavonoid 4	AAGAB	Q6PD74
Flavonoid 4	MMP1	P03956	Flavonoid 4	IKBK6	Q9Y6K9
Flavonoid 4	AR	P10275	Flavonoid 4	JUN	P05412
Flavonoid 4	IFNG	P01579	Flavonoid 4	FOS	P01100
Flavonoid 4	IL2	P60568	Flavonoid 4	TNF	P01375
Flavonoid 4	INSR	P06213			

Table S6. The genes from Drugbank, TTD, IPA databases.

Gene	Uniprot ID	Gene	Uniprot ID	Gene	Uniprot ID	Gene	Uniprot ID
HPGDS	O60760	CHRM2	P08172	FCER1G	P30273	TLR7	Q9NYK1
CYP1A2	P05177	IL3	P08700	FCER1A	P12319	TNF	P01375
HRH1	P35367	CYP2D6	P10635	CHRM5	P08912	PDE4B	Q07343
SLC18A2	Q05940	CHRM1	P11229	ADORA2A	P29274	HRH3	Q9Y5N1
TAAR1	Q96RJO	CHRM3	P20309	ADRA2C	P18825	HRH4	Q9H3N8
NTSR2	O95665	SLC6A2	P23975	ALOX5	P09917	ITGA5	P08648
HTR2A	P28223	SLC6A3	Q01959	BDKRB2	P30411	IL13	P35225
HTR2C	P28335	ADRA1A	P35348	PDE4A	P27815	PTGDR	Q13258
NR3C1	P04150	ADRA2A	P08913	CYSLTR1	Q9Y271	PTGDR2	Q9Y5Y4
KCNMA1	Q12791	SLC6A4	P31645	PLA2G1B	P04054	ESRRA	P11474
TLR8	Q9NR97	ADRB1	P08588	HTR2B	P41595	PDE3A	Q14432
TLR9	Q9NR96	ADRB2	P07550	IL10	P22301	PDE3B	Q13370

PDE4D	Q08499	ADRB3	P13945	LEP	P41159	PDE4C	Q08493
CCR3	P51677	ANXA1	P04083	LGALS9	O00182	PDE5A	O76074
ADORA1	P30542	CHRM4	P08173	MC2R	Q01718	PDE7A	Q13946
ADORA2B	P29275	CYSLTR2	Q9NS75	MS4A2	Q01362	PDE7B	Q9NP56
ADORA3	P0DMS8	FLG	P20930	OPRD1	P41143	PDE8A	O60658
ADRA1B	P35368	HAVCR2	Q8TDQ0	OPRK1	P41145	PDE8B	O95263
ADRA1D	P25100	HDAC2	Q92769	OPRM1	P35372	PGR	P06401
ADRA2B	P18089	HRH2	P25021	PDE11A	Q9HCR9	PTGDS	P41222
PTGS1	P23219	PTGS2	P35354	TRPV1	Q8NER1		

Table S7. Up-regulated genes.

Gene	Uniprot ID	Gene	Uniprot ID	Gene	Uniprot ID	Gene	Uniprot ID
ADAM19	Q9H013	CENPF	P49454	IDO1	P14902	NDFIP2	Q9NV92
AIM2	O14862	CEP55	Q53EZ4	IFNG	P01579	NKG7	Q16617
APOBEC3G	Q9HC16	CHEK1	O14757	IL18R1	Q13478	NUSAP1	Q9BXS6
ASF1B	Q9NVP2	CKS2	P33552	IL2RA	P01589	OIP5	O43482
ASPM	Q8IZT6	CST7	O76096	IL2RB	P14784	PCNA	P12004
AURKA	O14965	CTLA4	P16410	IL32	P24001	PDCD1	Q15116
AURKB	Q96GD4	CXCR3	P49682	IRF4	Q15306	PKMYT1	Q99640
BATF	Q16520	CXCR6	O00574	ITPKA	P23677	PLA2G16	P53816
BHLHE40	O14503	DEPDC1B	Q8WUY9	KIAA0101	Q15004	PLK4	O00444
BIRC5	O15392	DTL	Q9NZJ0	KIAA1324	Q6UXG2	PMAIP1	Q13794
BLM	P54132	DUSP5	Q16690	KIF14	Q15058	PMCH	P20382
BUB1	O43683	E2F2	Q14209	KIF15	Q9NS87	POLE2	P56282
C17orf53	Q8N3J3	EBI3	Q14213	KIF20A	O95235	POLQ	O75417
CCDC50	Q8IVM0	ECT2	Q9H8V3	KIF23	Q02241	PRC1	O43663
CCL1	P22362	ELOVL6	Q9HSJ4	KIF2C	Q99661	PRDM1	O75626
CCL17	Q92583	EXO1	Q9UQ84	KIFC1	Q9BW19	PRF1	P14222
CCL3L1	P16619	EZH2	Q15910	LAG3	P18627	PTTG1	O95997
CCNA2	P20248	FEN1	P39748	LAMP3	Q9UQV4	RACGAP1	Q9H0H5
CCNB1	P14635	FOXM1	Q08050	LAPTM4B	Q86VI4	RANBP1	P43487
CCNB2	O95067	GBP1	P32455	LMCD1	Q9NZU5	RBBP8	Q99708
CCNF	P41002	GBP4	Q96PP9	LMNB1	P20700	RDH10	Q8IZV5
CD38	P28907	GBP5	Q96PP8	MAD2L1	Q13257	RGS1	Q08116
CDC20	Q12834	GF11	Q99684	MAP1LC3A	Q9H492	SGPP2	Q8IWX5
CDC25A	P30304	GLDC	P23378	MCM10	Q7L590	SH2D2A	Q9NP31
CDCA3	Q99618	GMNN	O75496	MCM2	P49736	SLC27A2	O14975
CDCA5	Q96FF9	GNG4	P50150	MCM4	P33991	SLC35F2	Q8IXU6
CDCA7	Q9BWT1	GNLY	P22749	MCM5	P33992	SNX5	Q9Y5X3
CDCA8	Q53HL2	GZMA	P12544	MELK	Q14680	SOCS1	O15524
CDK6	Q00534	GZMB	P10144	MND1	Q9BWT6	SOCS2	O14508
CDKN3	Q16667	H2AFX	P16104	MTHFD1L	Q6UB35	SP140	Q13342
CDT1	Q9H211	HBG1	P69891	MYB	P10242	STAT1	P42224
CENPA	P49450	HELLS	Q9NRZ9	MYO1G	B011T2	STMN1	P16949

CENPE	Q02224	ICOS	Q9Y6W8	NCALD	P61601	TK1	P04183
TMEM173	Q86WV6	TOP2A	P11388	TYMS	P04818	ZBED2	Q9BTP6
TMEM97	Q5BJF2	TRIP13	Q15645	UBD	O15205	ZBTB32	Q9Y2Y4
TNFRSF18	Q9Y5U5	TROAP	Q12815	UBE2S	Q16763	ZWINT	O95229
TNFRSF4	P43489	TSPAN5	P62079	UBE2T	Q9NPD8		
TNFSF4	P23510	TTK	P33981	UHRF1	Q96T88		

Table S8. Down-regulated genes.

Gene	Uniprot ID	Gene	Uniprot ID	Gene	Uniprot ID	Gene	Uniprot ID
ABCA1	O95477	CSF1R	P07333	HNMT	P50135	PSAP	P07602
ADAMDEC1	O15204	CST3	P01034	IFI30	P13284	RAB32	Q13637
AIF1	P55008	EPB41L3	Q9Y2J2	LDLRAP1	Q55W96	RAB7B	Q96AH8
ALDH1A1	P00352	FAM46A	Q96IP4	LILRA5	A6NI73	RNASE1	P07998
ALDH2	P05091	FCGRT	P55899	LILRB2	Q8N423	S100A9	P06702
ALOX5	P09917	FCN1	O00602	MAFB	Q9Y5Q3	SLCO2B1	O94956
APOC1	P02654	FPR1	P21462	MERTK	Q12866	SNCA	P37840
APOE	P02649	FUCA1	P04066	MMP9	P14780	TGFBI	Q15582
C1orf162	Q8NEQ5	GAS7	O60861	MS4A6A	Q9H2W1	TMEM51	Q9NW97
CD14	P08571	GPR162	Q16538	MS4A7	Q9GZW8	TPM2	P07951
CDH23	Q9H251	GRN	P28799	NLRP3	Q96P20	VIPR1	P32241
CFD	P00746	GSN	P06396	NPC2	P61916	VSIG4	Q9Y279
CPVL	Q9H3G5	HAMP	P81172	NPL	Q9BXD5		

Table S9. Top 10 KEGG pathway.

Term	Count	P-value	Genes
Neuroactive ligand-receptor interaction	31	6.52E-19	OPRM1, ADORA3, ADORA2B, TRPV1, ADORA2A, DRD2, NR3C1, BDKRB2, ADORA1, HTR1A, HRH3, CNR1, CNR2, HRH4, ADRA2A, ADRA2C, LEP, ADRB2, CHRMS, CHRM4, CHRM3, CHRM2, HTR7, CHRM1, ADRA1B, ADRA1A, HTR2B, HTR2C, ADRA1D, HTR2A, OPRD1
Fc epsilon RI signaling pathway	13	1.69E-10	FCER1A, IL4, PIK3CG, IL3, TNF, IL13, BTK, AKT1, MAPK1, FYN, MS4A2, FCER1G, SYK
cGMP-PKG signaling pathway	16	6.30E-09	ADORA3, PDE3B, BDKRB2, ADORA1, AKT1, MAPK1, ADRB2, INS, PDE5A, ADRA2A, ADRA1B, ADRA1A, NOS3, ADRA2C, ADRA1D, OPRD1
Chagas disease	13	2.61E-08	PIK3CG, IRAK4, AKT1, MAPK1, IL6, TNF, JUN, IKBKG, IL1B, BDKRB2, IL10, TLR9, IL2

Calcium signaling pathway	16	3.47E-08	ADRB2, CHRM5, CHRM3, ADORA2B, ADORA2A, CHRM2, HTR7, CHRM1, ADRA1B, ADRA1A, NOS3, BDKRB2, HTR2B, HTR2C, ADRA1D, HTR2A
Progesterone-mediated oocyte maturation	12	3.94E-08	PIK3CG, CCNB1, PGR, AKT1, CDK1, MAPK1, CCNB2, INS, BUB1, PDE3B, CCNA2, CDK2
Measles	14	4.97E-08	IL4, PIK3CG, IL6, IL13, CDK6, CDK4, TLR7, CDK2, TLR9, AKT1, IRAK4, FYN, IL1B, IL2
Serotonergic synapse	13	5.47E-08	MAPK1, HTR1A, PTGS2, HTR7, MAOA, CYP2D6, SLC6A4, PTGS1, MAOB, ALOX5, HTR2B, HTR2C, HTR2A
Sphingolipid signaling pathway	13	1.31E-07	FCER1A, PIK3CG, TNF, ADORA3, BDKRB2, ADORA1, AKT1, MAPK1, FYN, MS4A2, FCER1G, NOS3, OPRD1
Hepatitis B	14	1.39E-07	PIK3CG, IL6, TNF, CYCS, BIRC5, CDK6, CDK4, CDK2, AKT1, MAPK1, CDKN1A, JUN, IKBKG, CCNA2

Table S10. Top 10 molecular function.

Term	Count	P-value	Genes
drug binding	13	9.66E-14	DRD2, SLC6A3, CYP2D6, TLR7, TLR8, CHRM3, CHRM2, CHRM1, CNR1, HTR2B, TOP2A, HTR2C, HTR2A
G-protein coupled acetylcholine receptor activity	7	5.48E-13	CHRM5, CHRM4, HRH3, CHRM3, CHRM2, CHRM1, HRH4
G-protein coupled adenosine receptor activity	5	9.47E-09	P2RY12, ADORA3, ADORA2B, ADORA2A, ADORA1
cyclin-dependent protein serine/threonine kinase activity	6	2.93E-06	CCNB1, CDK1, CCNB2, CDK6, CDK4, CDK2
cyclin binding	5	8.49E-06	CDK1, CDKN1A, CDK6, CDK4, CDK2

enzyme binding	12	1.45E-05	PGR, AKT1, CYP1A1, PTGS2, ADORA2A, FYN, JUN, ESR1, BIRC5, PTPN1, CYP1A2, TOP2A
neurotransmitter receptor activity	5	2.54E-05	HTR1A, HTR7, HTR2B, HTR2C, HTR2A
protein kinase activity	12	2.90E-05	PIK3CG, IRAK4, AKT1, CDK1, BUB1, AURKA, GRK2, CDK4, GRK3, CDK2, SYK, BTK
serotonin binding	4	3.39E-05	HTR1A, HTR2B, HTR2C, HTR2A
G-protein coupled serotonin receptor activity	5	3.44E-05	HTR1A, HTR7, HTR2B, HTR2C, HTR2A

Table S11. Top 10 cellular component.

Term	Count	P-value	Genes
integral component of plasma membrane	38	1.41E-14	OPRM1, TNF, ADORA2B, TRPV1, DRD2, SLC6A2, ADORA2A, SLC6A3, SLC6A4, BDKRB2, ADORA1, TLR7, HTR1A, HRH3, CNR1, CNR2, ADRA2A, FCER1G, MS4A2, ADRA2C, FCER1A, FLT4, P2RY12, CHRM5, ADRB2, CHRM4, CHRM3, CHRM2, HTR7, CHRM1, ADRA1B, ADRA1A, HTR2B, HTR2C, PTGDR2, ADRA1D, OPRD1, HTR2A
plasma membrane	55	3.28E-09	OPRM1, ADORA3, TRPV1, SLC6A2, SLC6A3, SLC6A4, ADORA1, TLR7, BTK, TLR9, AKT1, HTR1A, MS4A2, NOS3, SYK, PIK3CG, ESR1, CHRM5, ADRB2, CHRM4, CHRM3, CHRM2, HTR7, CHRM1, PTGDR2, TNF, ADORA2B, DRD2, ADORA2A, COMT, BDKRB2, IRAK4, HRH3, CNR1, HRH4, CNR2, ADRA2A, FCER1G, ADRA2C, FCER1A, FLT4, P2RY12, FYN, ITGA5, ADRA1B, ADRA1A, GRK5, PTPN1, GRK2, HTR2B, GRK3, HTR2C, ADRA1D, HTR2A, OPRD1
asymmetric synapse	5	9.62E-08	CHRM3, ADORA2A, CHRM2, CHRM1, ADORA1

spindle	9	8.56E-07	KIF23, AKT1, KIF11, NUSAP1, TTK, BIRC5, AURKA, NR3C1, KIF20A
midbody	9	1.39E-06	KIF23, CDK1, CDCA8, CENPE, BIRC5, AURKA, CEP55, ASPM, KIF20A
postsynaptic membrane	10	6.65E-06	CHRM5, CHRM4, CHRM3, ADORA2A, TRPV1, CHRM2, CHRM1, COMT, ADORA1, OPRD1
external side of plasma membrane	10	7.18E-06	IL4, FCER1A, P2RY12, IL6, TNF, TRPV1, ITGA5, FCER1G, MS4A2, IL13
dendrite	12	7.53E-06	HTR1A, CHRM3, ADORA2A, DRD2, TRPV1, CHRM2, HTR7, CHRM1, CNR2, HTR2B, HTR2C, HTR2A
cytosol	41	9.94E-06	KIF23, TRPV1, SLC6A4, PDE3B, AURKA, COMT, BTK, IRAK4, AKT1, AKR1C3, KIF2C, CDCA8, ALOX5AP, PDE4B, BUB1, IL1B, NOS3, HPGDS, SYK, PIK3CG, CDK1, KIF11, NAT1, CYCS, CENPE, BIRC5, CDK6, CDK4, CDK2, CCNB1, MAPK1, CDKN1A, CCNB2, FYN, JUN, IKBKG, PDE5A, ALOX5, PTPN1, GRK2, HTR2A
axon terminus	6	1.16E-05	CHRM3, DRD2, CHRM2, CHRM1, ADRA2C, OPRD1

Table S12. Top 10 molecular function.

Term	Count	P-value	Genes
adenylate cyclase-inhibiting G-protein coupled acetylcholine receptor signaling pathway	22	1.06E-15	IL4, CDK1, IL6, PTGS2, CYP1A1, ADORA2A, SLC6A2, DRD2, SLC6A3, SLC6A4, MAOB, COMT, CDK4, IL10, CCNB1, CDKN1A, FYN, JUN, ADRA1A, HTR2B, HTR2C, HTR2A
inflammatory response	7	5.65E-13	CHRM5, CHRM4, HRH3, CHRM3, CHRM2, CHRM1, HRH4
phospholipase C-activating G-protein coupled acetylcholine receptor signaling pathway	21	8.34E-13	PIK3CG, IL6, TNF, PTGS2, ADORA2A, PTGS1, IL13, BDKRB2, CCL16, TLR7, ADORA1, IL10, TLR8, TLR9, AKT1, CNR2, IKBKG, HRH4, IL1B, MS4A2, SYK

positive regulation of nitric oxide biosynthetic process	7	2.25E-12	CHRM5, CHRM4, HRH3, CHRM3, CHRM2, CHRM1, HRH4
cell-cell signaling	9	3.90E-10	OPRM1, AKT1, IL6, TNF, PTGS2, TRPV1, INS, ESR1, IL1B
positive regulation of cell proliferation	15	1.66E-09	IL3, ADORA2A, IL13, CCL16, ADORA1, IL10, PGR, ADRB2, INS, ADRA1B, ADRA1A, IL1B, ADRA2C, ADRA1D, IL2
adenylate cyclase-activating adrenergic receptor signaling pathway	19	2.04E-09	IL3, IL6, FLT4, TTK, BIRC5, CDK4, CDK2, LEP, AKR1C3, MAPK1, HTR1A, INS, CHRM1, ADRA2A, GRK5, HTR2B, ADRA1D, IL2, HTR2A
cyclooxygenase pathway	7	2.05E-09	ADRB2, DRD2, ADRA2A, ADRA1B, ADRA1A, ADRA2C, ADRA1D
synaptic transmission, cholinergic	6	3.10E-09	AKR1C3, PTGDS, PTGS2, PTGES, PTGS1, HPGDS
positive regulation of mast cell degranulation	8	4.51E-09	CHRM5, CHRM4, HRH3, CHRM3, ADORA2A, CHRM2, CHRM1, HRH4
