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SUPPLEMENTAL DATA

Sabinene attenuates inflammation and oxidative stress in CFA-induced arthritis: *In vivo* and *in silico* evidence implicating TLR4/NLRP3/NF-κB signaling

Kanwal Asif[1], Ambreen Malik Uttra[1*], Arham Shabbir[2], Sumera Qasim[3], Saima Kalsoom[4], Abdulelah Alhazza[5], Hamoud Alotaibi[5], Mona Al Hamod[5], Saleh Alfuraih[6], Ali F. Almutairy[7], Raiyan Faisal Alharbi[8], Ashfaq Ahmad[8*]

[1]Department of Pharmacology, College of Pharmacy, University of Sargodha, Sargodha, Pakistan;

[2]Department of Pharmacology, Institute of Pharmacy, Faculty of Pharmaceutical and Allied Health Sciences, Lahore College for Women University, Lahore, Pakistan;

[3]Department of Pharmacology, College of Pharmacy, Jouf University, Sakaka, Saudi Arabia;

[4]Department of Chemistry, PMAS-Arid Agriculture University, Rawalpindi, Pakistan;

[5]Department of Pharmaceutics, Faculty of Pharmacy, Northern Border University, Rafha, Saudi Arabia;

[6]Department of Pharmacology and Toxicology, College of Pharmacy, Northern Border University, Rafha, Saudi Arabia;

[7]Department of Pharmacology and Toxicology, College of Pharmacy, Qassim University, Buraydah, Saudi Arabia;

[8]Department of Pharmacy Practice, College of Pharmacy, University of Hafr Al Batin, Hafr Al Batin, Saudi Arabia.

*Correspondence to **Ambreen Malik Uttra**: ambreen.malik@uos.edu.pk and **Ashfaq Ahmad:** ashfaqa@uhb.edu.sa

Table S1. Sabinene-associated targets predicted using SwissTargetPrediction

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability *	Known actives (3D/2D)
Cannabinoid receptor 2	CNR2	P34972	CHEMBL253	Family A G protein-coupled receptor	0.3483	3 / 3Â Â Â
Peroxisome proliferator-activated receptor alpha	PPARA	Q07869	CHEMBL239	Nuclear receptor	0.326091	2 / 4Â Â Â
Acetylcholinesterase	ACHE	P22303	CHEMBL220	Hydrolase	0.250637	8 / 1Â Â Â
Tyrosine-protein phosphatase non-receptor type 1	PTPN1	P18031	CHEMBL335	Phosphatase	0.150427	1 / 19Â Â Â
Sex hormone-binding globulin	SHBG	P04278	CHEMBL3305	Secreted protein	0.138467	1 / 27Â Â Â
Aromatase	CYP19A1	P11511	CHEMBL1978	Cytochrome P450	0.124841	12 / 177Â Â Â
Liver carboxylesterase 1	CES1	P23141	CHEMBL2265	Hydrolase	0.124033	0 / 3Â Â Â
Cocaine esterase	CES2	O00748	CHEMBL3180	Hydrolase	0.124033	0 / 4Â Â Â
Transcription factor p65	RELA	Q04206	CHEMBL5533	Transcription factor	0.117596	1 / 3Â Â Â
Sodium-dependent serotonin transporter	SLC6A4	P31645	CHEMBL228	Electrochemical transporter	0.116776	3 / 3Â Â Â
Receptor-interacting serine/threonine-protein kinase 1	RIPK1	Q13546	CHEMBL5464	Kinase	0.114937	1 / 0Â Â Â
Androgen receptor	AR	P10275	CHEMBL1871	Nuclear receptor	0.111867	2 / 28Â Â Â
Sodium-dependent noradrenaline transporter	SLC6A2	P23975	CHEMBL222	Electrochemical transporter	0.095203	3 / 3Â Â Â
UDP-glucuronosyltransferase 2B7	UGT2B7	P16662	CHEMBL4370	Transferase	0.093983	0 / 21Â Â Â
Cytochrome P450 1B1	CYP	Q16678	CHE	Cytochrome	0.0	4 /

	1B1		MBL 4878	P450	932 39	1Â Â Â
Glucocorticoid receptor	NR3 C1	P04150	CHE MBL 2034	Nuclear receptor	0.0 863 69	2 / 7Â Â Â
cGMP-dependent 3',5'-cyclic phosphodiesterase	PDE 2A	O00408	CHE MBL 2652	Phosphodies terase	0.0 780 69	1 / 0Â Â Â
Sodium-dependent dopamine transporter	SLC 6A3	Q01959	CHE MBL 238	Electrochem ical transporter	0.0 765 3	5 / 3Â Â Â
Monoglyceride lipase	MG LL	Q99685	CHE MBL 4191	Hydrolase	0.0 739 74	2 / 0Â Â Â
Oxysterols receptor LXR-alpha	NR1 H3	Q13133	CHE MBL 2808	Nuclear receptor	0.0 739 65	0 / 18Â Â Â
Amine oxidase [flavin-containing] B	MA OB	P27338	CHE MBL 2039	Oxidoreduct ase	0.0 707 13	16 / 0Â Â Â
Short transient receptor potential channel 6	TRP C6	Q9Y210	CHE MBL 24173 47	Voltage-gated ion channel	0.0 675 01	0 / 1Â Â Â
Prostaglandin G/H synthase 2	PTG S2	P35354	CHE MBL 230	Oxidoreduct ase	0.0 619 15	4 / 2Â Â Â
Adenosine receptor A3	AD OR A3	P0DMS8	CHE MBL 256	Family A G protein-coupled receptor	0.0 583 99	3 / 1Â Â Â
Indoleamine 2,3-dioxygenase 1	IDO 1	P14902	CHE MBL 4685	Oxidoreduct ase	0.0 581 55	10 / 0Â Â Â
Carbonic anhydrase 1	CA1	P00915	CHE MBL 261	Lyase	0.0 560 62	8 / 0Â Â Â
C-C chemokine receptor type 2	CCR 2	P41597	CHE MBL 4015	Family A G protein-coupled receptor	0.0 558 06	1 / 0Â Â Â
Gamma-aminobutyric acid receptor subunit alpha-6/beta-3	N/A	P28472 &Q1644 5	CHE MBL 38855 78	Ligand-gated ion channel	0.0 558 06	1 / 0Â Â Â
Gamma-aminobutyric acid receptor subunit beta-3	GA BRB 3	P28472	CHE MBL 1847	Ligand-gated ion channel	0.0 558 06	1 / 0Â Â Â
Gamma-aminobutyric acid receptor subunit rho-1	GA BRR	P24046	CHE MBL	Ligand-gated ion	0.0 558	1 / 0Â Â Â

	1		3561	channel	06	
Alpha-2C adrenergic receptor	ADRA2C	P18825	CHEMBL1916	Family A G protein-coupled receptor	0.055806	1 / 0Â Â Â
GABA-A receptor; alpha-6/beta-3/gamma-2	N/A	P18507 & P28472 &Q16445	CHEMBL2095190	Ligand-gated ion channel	0.055806	1 / 0Â Â Â
GABA-A receptor alpha-1/beta-3	N/A	P14867 &P28472	CHEMBL4106151	Ligand-gated ion channel	0.055806	1 / 0Â Â Â
GABA-A receptor; alpha-1/beta-3/gamma-2	N/A	P14867 &P18507&P28472	CHEMBL2094121	Ligand-gated ion channel	0.055806	3 / 0Â Â Â
GABA A receptor alpha-1/beta-1/gamma-2	N/A	P14867 &P18507&P18505	CHEMBL2111392	Ligand-gated ion channel	0.055806	1 / 0Â Â Â
Gamma-aminobutyric acid receptor subunit alpha-1/ beta-1	N/A	P14867 &P18505	CHEMBL3885570	Ligand-gated ion channel	0.055806	1 / 0Â Â Â
Cytochrome P450 2A6	CYP2A6	P11509	CHEMBL5282	Cytochrome P450	0.055806	5 / 0Â Â Â
Alpha-2A adrenergic receptor	ADRA2A	P08913	CHEMBL1867	Family A G protein-coupled receptor	0.055806	2 / 0Â Â Â
Cytochrome P450 1A2	CYP1A2	P05177	CHEMBL3356	Cytochrome P450	0.055806	4 / 0Â Â Â
Cytochrome P450 2C19	CYP2C19	P33261	CHEMBL3622	Cytochrome P450	0.054713	0 / 2Â Â Â
11-beta-hydroxysteroid dehydrogenase 1	HSD11B1	P28845	CHEMBL4235	Oxidoreductase	0.054713	0 / 7Â Â Â
Prostaglandin G/H synthase 1	PTGS1	P23219	CHEMBL221	Oxidoreductase	0.054713	0 / 2Â Â Â
Muscarinic acetylcholine receptor M2	CHRM2	P08172	CHEMBL211	Family A G protein-coupled receptor	0.054713	0 / 1Â Â Â
Estrogen receptor	ESR	P03372	CHE	Nuclear	0.0	0 /

	1		MBL 206	receptor	547 13	22Â Â Â
Palmitoleoyl-protein carboxylesterase NOTUM	NOTUM	Q6P988	CHEMBL 3714531	Hydrolase	0.0 542 89	12 / 0Â Â Â
Tryptophan 2,3-dioxygenase	TDO2	P48775	CHEMBL 2140	Oxidoreductase	0.0 542 89	1 / 0Â Â Â
Apelin receptor	APLNR	P35414	CHEMBL 1628481	Family A G protein-coupled receptor	0.0 540 4	4 / 0Â Â Â
Aryl hydrocarbon receptor	AHR	P35869	CHEMBL 3201	Transcription factor	0.0 506 66	9 / 0Â Â Â
Transient receptor potential cation channel subfamily V member 1	TRPV1	Q8NER1	CHEMBL 4794	Voltage-gated ion channel	0.0 501 2	0 / 3Â Â Â
Delta(24)-sterol reductase	DHCR24	Q15392	CHEMBL 2331059	Oxidoreductase	0.0 501 2	0 / 2Â Â Â
Nuclear receptor ROR-gamma	RORC	P51449	CHEMBL 1741186	Nuclear receptor	0.0 501 2	0 / 13Â Â Â
Alpha-crystallin B chain	CRYAB	P02511	CHEMBL 3621022	Unclassified protein	0.0 501 2	0 / 7Â Â Â
Alpha-crystallin A chain	CRYAA	P02489	CHEMBL 4296283	Unclassified protein	0.0 501 2	0 / 1Â Â Â
Amyloid-beta precursor protein	APP	P05067	CHEMBL 2487	Membrane receptor	0.0 486 56	1 / 1Â Â Â
Hypoxanthine-guanine phosphoribosyltransferase	HPRT1	P00492	CHEMBL 2360	Transferase	0.0 479 34	2 / 0Â Â Â
Glutamate NMDA receptor; GRIN1/GRIN2B	N/A	Q05586 &Q13224	CHEMBL 1907603	Ligand-gated ion channel	0.0 466 59	0 / 28Â Â Â
Glutamate NMDA receptor; GRIN1/GRIN2A	N/A	Q05586 &Q12879	CHEMBL 1907604	Ligand-gated ion channel	0.0 466 59	0 / 26Â Â Â
SUMO-activating enzyme	N/A	Q9UBE0	CHE	Aminoacyltr	0.0	0 /

		&Q9UBT2	MBL 2095174	ansferase	46164	1Â Â Â
Bile acid receptor	NR1H4	Q96RI1	CHEMBL2047	Nuclear receptor	0.046164	0 / 2Â Â Â
5'-nucleotidase	NT5E	P21589	CHEMBL5957	Phosphatase	0.046164	0 / 1Â Â Â
Aldo-keto reductase family 1 member B10	AKR1B10	O60218	CHEMBL5983	Oxidoreductase	0.046164	0 / 1Â Â Â
Prostaglandin E synthase	PTGES	O14684	CHEMBL5658	Isomerase	0.046164	0 / 7Â Â Â
Estrogen receptor beta	ESR2	Q92731	CHEMBL242	Nuclear receptor	0.045904	1 / 25Â Â Â
5-hydroxytryptamine receptor 6	HTR6	P50406	CHEMBL3371	Family A G protein-coupled receptor	0.044923	1 / 0Â Â Â
5-hydroxytryptamine receptor 2B	HTR2B	P41595	CHEMBL1833	Family A G protein-coupled receptor	0.044923	1 / 0Â Â Â
Acetyl-CoA acetyltransferase, mitochondrial	ACAT1	P24752	CHEMBL2616	Transferase	0.044923	1 / 0Â Â Â
Sigma non-opioid intracellular receptor 1	SIGMAR1	Q99720	CHEMBL287	Membrane receptor	0.044644	1 / 2Â Â Â
Transient receptor potential cation channel subfamily A member 1	TRPA1	O75762	CHEMBL6007	Voltage-gated ion channel	0.044109	17 / 2Â Â Â
Tissue factor	F3	P13726	CHEMBL4081	Surface antigen	0.042733	0 / 1Â Â Â
Progesterone receptor	PGR	P06401	CHEMBL208	Nuclear receptor	0.042431	1 / 6Â Â Â
Macrophage migration inhibitory factor	MIF	P14174	CHEMBL2085	Enzyme	0.042093	11 / 0Â Â Â
Dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex, mitochondrial	DLAT	P10515	CHEMBL4523180	Transferase	0.042007	0 / 1Â Â Â
Nuclear receptor subfamily 1 group I member 2	NR1I2	O75469	CHEMBL	Nuclear receptor	0.0420	0 / 3Â Â Â

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Carbonic anhydrase 9	CA9	Q16790	CHEMBL3594	Lyase	0.04131616	2 / 0Â Â Â
Fatty-acid amide hydrolase 1	FAAH	O00519	CHEMBL2243	Hydrolase	0.04118787	0 / 3Â Â Â
Cholinesterase	BCHE	P06276	CHEMBL1914	Hydrolase	0.04056363	1 / 1Â Â Â
Cholesterol 24-hydroxylase	CYP46A1	Q9Y6A2	CHEMBL4523510	Oxidoreductase	0.03974	0 / 1Â Â Â
NPC1-like intracellular cholesterol transporter 1	NPC1L1	Q9UHC9	CHEMBL2027	Other membrane protein	0.03974	0 / 5Â Â Â
Oxysterol-binding protein 2	OSBP2	Q969R2	CHEMBL5465343	Unclassified protein	0.03974	0 / 7Â Â Â
Sterol regulatory element-binding protein 2	SREBF2	Q12772	CHEMBL1795166	Transcription factor	0.03974	0 / 1Â Â Â
P2X purinoceptor 3	P2RX3	P56373	CHEMBL2998	Ligand-gated ion channel	0.03974	0 / 1Â Â Â
Oxysterols receptor LXR-beta	NR1H2	P55055	CHEMBL4093	Nuclear receptor	0.03974	0 / 6Â Â Â
3-oxo-5-alpha-steroid 4-dehydrogenase 2	SRD5A2	P31213	CHEMBL1856	Oxidoreductase	0.03974	0 / 1Â Â Â
M-phase inducer phosphatase 2	CDC25B	P30305	CHEMBL4804	Phosphatase	0.03974	0 / 7Â Â Â
M-phase inducer phosphatase 1	CDC25A	P30304	CHEMBL3775	Phosphatase	0.03974	0 / 7Â Â Â
Oxysterol-binding protein 1	OSBP	P22059	CHEMBL4523203	Unclassified protein	0.03974	0 / 11Â Â Â
3-oxo-5-alpha-steroid 4-dehydrogenase 1	SRD5A1	P18405	CHEMBL1787	Oxidoreductase	0.03974	0 / 1Â Â Â
Mineralocorticoid receptor	NR3C2	P08235	CHEMBL1994	Nuclear receptor	0.03974	0 / 3Â Â Â

Corticosteroid-binding globulin	SERPINA6	P08185	CHEMBL2421	Secreted protein	0.039744	0 / 9Â Â Â
Cathepsin D	CTSD	P07339	CHEMBL2581	Protease	0.039744	0 / 1Â Â Â
Integrin alpha-V/beta-3	N/A	P05106 &P06756	CHEMBL1907598	Membrane receptor	0.039744	0 / 1Â Â Â
Steroid 17-alpha-hydroxylase/17,20 lyase	CYP17A1	P05093	CHEMBL3522	Cytochrome P450	0.039744	0 / 13Â Â Â
3-hydroxy-3-methylglutaryl-coenzyme A reductase	HMGCR	P04035	CHEMBL402	Oxidoreductase	0.039744	0 / 3Â Â Â
Prothrombin	F2	P00734	CHEMBL204	Protease	0.039744	0 / 1Â Â Â
Carbonic anhydrase 2	CA2	P00918	CHEMBL205	Lyase	0.038885	4 / 0Â Â Â
Amine oxidase [flavin-containing] A	MAOA	P21397	CHEMBL1951	Oxidoreductase	0.037284	9 / 0Â Â Â
C-C chemokine receptor type 5	CCR5	P51681	CHEMBL274	Family A G protein-coupled receptor	0.037111	0 / 1Â Â Â
17-beta-hydroxysteroid dehydrogenase type 3	HSD17B3	P37058	CHEMBL4234	Oxidoreductase	0.037111	0 / 1Â Â Â
Ribosyldihydronicotinamide dehydrogenase [quinone]	NQO2	P16083	CHEMBL3959	Oxidoreductase	0.03711	2 / 0Â Â Â
Heat shock protein HSP 90-alpha	HSP90AA1	P07900	CHEMBL3880	Other cytosolic protein	0.036185	0 / 3Â Â Â

Sabinene-associated targets predicted through Super-PRED						
Target Name	ChEMBL-ID	UniProt ID	PDB Visualization	TTD ID	Probability	Model accuracy
Cannabinoid CB2 receptor	CHEMBL253	P34972	6KPF	Not Available	91.97%	97.25%
G-protein coupled receptor 55	CHEMBL1075322	Q9Y2T6	Not Available	T87670	90.90%	78.15%

Nuclear factor NF-kappa-B p105 subunit	CHEMBL 3251	P19838	1SVC	Not Available	89.71 %	96.09%
Cathepsin D	CHEMBL 2581	P07339	4OD9	T67102	81.75 %	98.95%
LSD1/CoREST complex	CHEMBL 3137262	O60341	5L3D	Not Available	81.14 %	97.09%
Mineralocorticoid receptor	CHEMBL 1994	P08235	4PF3	Not Available	80.71 %	100%
Cyclooxygenase-1	CHEMBL 221	P23219	6Y3C	Not Available	79.64 %	90.17%
Tyrosyl-DNA phosphodiesterase 1	CHEMBL 1075138	Q9NUW8	6N0D	Not Available	79.50 %	71.22%
Matrix metalloproteinase 14	CHEMBL 3869	P50281	3C7X	Not Available	79.33 %	93.10%
DNA-(apurinic or apyrimidinic site) lyase	CHEMBL 5619	P27695	6BOW	T13348	78.93 %	91.11%
Isocitrate dehydrogenase [NADP] cytoplasmic	CHEMBL 2007625	O75874	6BKX	T69563	78.06 %	99%
Transcription intermediary factor 1-alpha	CHEMBL 3108638	O15164	4YBM	Not Available	77.54 %	95.56%
NT-3 growth factor receptor	CHEMBL 5608	Q16288	6KZD	Not Available	76.22 %	95.89%
Voltage-gated N-type calcium channel alpha-1B subunit	CHEMBL 4478	Q00975	Not Available	T38338	75.33 %	97.14%
Lipoxin A4 receptor	CHEMBL 4227	P25090	6OMM	Not Available	74.93 %	100%
Ribosomal protein S6 kinase alpha 1	CHEMBL 2553	Q15418	2Z7Q	Not Available	73.32 %	85.11%
Indoleamine 2,3-dioxygenase	CHEMBL 4685	P14902	6.00E+43	T89697	72.17 %	96.38%
DCN1-like protein 1	CHEMBL 4105838	Q96GG9	6BG3	Not Available	71.65 %	95%
Aurora kinase B/Inner centromere protein	CHEMBL 3430907	Q96GD4	6YIH	T46781	71.60 %	97.50%
Lysosomal Pro-X carboxypeptidase	CHEMBL 2335	P42785	3N2Z	Not Available	71.49 %	100%
Protein kinase C delta	CHEMBL 2996	Q05655	1YRK	T44861	71.29 %	97.79%

Acetyl-CoA carboxylase 1	CHEMBL3351	Q13085	6G2H	Not Available	70.87%	93.04%
C5a anaphylatoxin chemotactic receptor	CHEMBL2373	P21730	6C1R	T15439	70.63%	92.62%
Formyl peptide receptor 1	CHEMBL3359	P21462	Not Available	T87831	70.61%	93.56%
Vitamin D receptor	CHEMBL1977	P11473	3B0T	T34234	70.13%	99.43%
Histone deacetylase 2	CHEMBL1937	Q92769	7KBG	T51191	69.87%	94.75%
ADAM10	CHEMBL5028	O14672	6BE6	T31902	69.73%	97.50%
Glycine receptor subunit alpha-1	CHEMBL5845	P23415	4X5T	T50269	69.49%	90.71%
PI3-kinase p110-delta subunit	CHEMBL3130	O00329	6PYR	T67849	68.81%	96.47%
11-beta-hydroxysteroid dehydrogenase 2	CHEMBL3746	P80365	Not Available	T43721	68.75%	94.78%
Vitamin K-dependent protein C	CHEMBL4444	P04070	6M3B	T24836	68.28%	93.89%
Kappa opioid receptor	CHEMBL237	P41145	4DJH	T60693	68.22%	98.10%
Monoamine oxidase A	CHEMBL1951	P21397	2Z5Y	Not Available	68.14%	91.49%
FML2_HUMAN	CHEMBL5646	Q6L5J4	Not Available	Not Available	68.03%	100%
Sodium/hydrogen exchanger 1	CHEMBL2781	P19634	7DSX	T82028	67.89%	90.24%
Integrin alpha-V/beta-3	CHEMBL1907598	P05106	6UJA	T67103	67.52%	95.71%
Dopamine transporter	CHEMBL238	Q01959	Not Available	Not Available	67.25%	95.88%
Cyclin-dependent kinase 5	CHEMBL4036	Q00535	4AU8	T20973	67.18%	79.09%
Cathepsin K	CHEMBL268	P43235	5Z5O	T11388	66.95%	96.85%
Adenosine A1 receptor	CHEMBL226	P30542	5N2S	T92072	66.04%	95.93%
Serotonin 7 (5-HT7) receptor	CHEMBL3155	P34969	Not Available	T79062	65.98%	90.71%
Transmembrane protease serine 6	CHEMBL1795139	Q8IU80	Not Available	Not Available	65.86%	98.33%
Serine/threonine-protein kinase MST2	CHEMBL4708	Q13188	6AO5	Not Available	65.63%	71.67%

Sodium channel protein type II alpha subunit	CHEMBL 4187	Q992 50	6J8E	Not Availab le	65.27 %	95.50%
Histone deacetylase 10	CHEMBL 5103	Q969 S8	Not Available	T94324	65.25 %	90.08%
T-cell protein-tyrosine phosphatase	CHEMBL 3807	P177 06	1L8K	Not Availab le	65.08 %	93%
Androgen Receptor	CHEMBL 1871	P102 75	3V49	T11211	64.93 %	96.43%
Melanocortin receptor 4	CHEMBL 259	P322 45	7AUE	T72458	64.93 %	95.38%
Tyrosine-protein kinase ITK/TSK	CHEMBL 2959	Q088 81	4HCU	T91761	64.68 %	95%
Dual specificity protein kinase CLK2	CHEMBL 4225	P497 60	6KHE	Not Availab le	64.34 %	80.96%
Coagulation factor VII/tissue factor	CHEMBL 2095194	P087 09	4YLQ	T72702	64.22 %	99.17%
Hypoxanthine-guanine phosphoribosyltransferase	CHEMBL 2360	P004 92	5HIA	Not Availab le	64.10 %	87.38%
dUTP pyrophosphatase	CHEMBL 5203	P333 16	3ARA	T39054	63.91 %	99.18%
Sphingosine 1-phosphate receptor Edg-5	CHEMBL 2955	O951 36	Not Available	T47888	63.73 %	92.86%
L-lactate dehydrogenase A chain	CHEMBL 4835	P003 38	5W8J	Not Availab le	63.56 %	95.34%
C-C chemokine receptor type 2	CHEMBL 4015	P415 97	5T1A	T89988	63.50 %	98.57%
Sodium channel protein type III alpha subunit	CHEMBL 5163	Q9N Y46	Not Available	T76937	63.21 %	96.90%
Sphingosine 1-phosphate receptor Edg-8	CHEMBL 2274	Q9H2 28	Not Available	T50089	63.13 %	100%
Glutamate NMDA receptor; GRIN1/GRIN2B	CHEMBL 1907603	Q055 86	5EWM	Not Availab le	63.02 %	95.89%
Voltage-gated T-type calcium channel alpha-1H subunit	CHEMBL 1859	O951 80	Not Available	T54644	63%	98.57%
DNA topoisomerase II alpha	CHEMBL 1806	P113 88	6ZY5	T17048	62.96 %	89%
Histone deacetylase 11	CHEMBL 3310	Q96D B2	Not Available	Not Availab le	62.89 %	88.56%
Coagulation factor XI	CHEMBL 2820	P039 51	6I58	T46040	62.71 %	95.29%
Egl nine homolog 1	CHEMBL 5697	Q9G ZT9	4BQY	Not Availab le	62.48 %	93.40%

Matrix metalloproteinase 8	CHEMBL 4588	P22894	1I76	Not Available	62.02 %	94.66%
Cytochrome P450 3A4	CHEMBL 340	P08684	5VCC	T37848	61.87 %	91.19%
Neurotensin receptor 2	CHEMBL 2514	O95665	Not Available	Not Available	61.86 %	100%
Protein tyrosine kinase 2 beta	CHEMBL 5469	Q14289	4EKU	T07087	61.73 %	91.03%
Gamma-secretase	CHEMBL 2094135	Q96BI3	6IYC	Not Available	61.65 %	98.05%
Signal transducer and activator of transcription 3	CHEMBL 4026	P40763	6QHD	T29130	61.63 %	82.69%
Kinesin-like protein 1	CHEMBL 4581	P52732	6TIW	T28484	61.50 %	93.18%
Proteasome component C5	CHEMBL 4208	P20618	6KWY	Not Available	61.47 %	90%
Tyrosine-protein kinase FER	CHEMBL 3982	P16591	6KC4	Not Available	61.26 %	78.11%
Nicotinamide phosphoribosyltransferase	CHEMBL 1744525	P43490	4LVF	T54582	61.18 %	96.25%
Matrix metalloproteinase 7	CHEMBL 4073	P09237	2Y6D	Not Available	61.10 %	97.56%
CaM kinase II delta	CHEMBL 2801	Q13557	2WEL	Not Available	60.91 %	84.49%
Nuclear receptor ROR-beta	CHEMBL 3091268	Q92753	Not Available	Not Available	60.58 %	95.50%
Protein kinase C theta	CHEMBL 3920	Q04759	5F9E	T23995	60.51 %	97.69%
Phosphodiesterase 3B	CHEMBL 290	Q13370	1SO2	Not Available	60.01 %	94%
Proteasome subunit beta type-9	CHEMBL 1944495	P28065	6E5B	Not Available	59.94 %	97.50%
Retinoid X receptor alpha	CHEMBL 2061	P19793	3DZY	T13726	59.80 %	91.67%
Relaxin receptor 1	CHEMBL 1293316	Q9HBX9	Not Available	T73696	59.69 %	82.50%
Dual specificity protein kinase CLK4	CHEMBL 4203	Q9HAZ1	6FYV	Not Available	59.60 %	94.45%
Bloom syndrome protein	CHEMBL	P541	4O3M	Not	59.56	70.06%

	1293237	32		Availab le	%	
Melanin-concentrating hormone receptor 1	CHEMBL 344	Q997 05	Not Available	T09572	59.28 %	92.50%
Dopamine D3 receptor	CHEMBL 234	P354 62	7CMV	Not Availab le	59.20 %	90.48%
PRMT5/MEP50 complex	CHEMBL 3137261	O147 44	6V0P	T82665	58.52 %	100%
Dual specificity mitogen-activated protein kinase kinase 2	CHEMBL 2964	P365 07	1S9I	Not Availab le	58.39 %	80%
Protein kinase C alpha	CHEMBL 299	P172 52	4RA4	T12808	58.01 %	98.03%
Casein kinase II alpha/beta	CHEMBL 3038477	P678 70	6TLS	T51565	57.93 %	99.23%
Heat shock protein HSP 90-alpha	CHEMBL 3880	P079 00	3Q6M	Not Availab le	57.92 %	96.21%
Nuclear receptor ROR-gamma	CHEMBL 1741186	P514 49	5NTW	Not Availab le	57.91 %	99.17%
Acyl coenzyme A:cholesterol acyltransferase 1	CHEMBL 2782	P356 10	6P2J	Not Availab le	57.69 %	91.65%
Toll-like receptor 4	CHEMBL 5255	O002 06	4G8A	T81443	57.65 %	92.50%
C-C chemokine receptor type 1	CHEMBL 2413	P322 46	Not Available	T16016	57.56 %	89.50%
Serine/threonine-protein kinase mTOR	CHEMBL 2842	P423 45	6BCX	T75243	57.36 %	92.78%
Proteasome Macropain subunit	CHEMBL 3492	P497 21	5LE5	Not Availab le	57.36 %	90.24%
Cysteinyl leukotriene receptor 2	CHEMBL 4330	Q9NS 75	Not Available	T74238	57.32 %	98%
Dual specificity phosphatase Cdc25C	CHEMBL 2378	P303 07	3OP3	Not Availab le	57.23 %	96.67%
PI3-kinase p110-gamma subunit	CHEMBL 3267	P487 36	1E8Y	T95913	57.13 %	95.71%
Stimulator of interferon genes protein	CHEMBL 4523377	Q86 WV6	6NT5	Not Availab le	57.09 %	95.48%
Retinoid X receptor beta	CHEMBL 1870	P287 02	7A78	T60077	56.93 %	95%
Beta-glucocerebrosidase	CHEMBL 2179	P040 62	6TN1	T84173	56.27 %	85.31%
Acyl-CoA desaturase	CHEMBL 5555	O007 67	4ZYO	T10897	56.14 %	97.50%

Palmitoleoyl-protein carboxylesterase NOTUM	CHEMBL 3714531	Q6P988	4WBH	Not Available	55.96 %	97.14%
Tissue-type plasminogen activator	CHEMBL 1873	P00750	1RTF	T45299	55.95 %	93.33%
Cyclin-dependent kinase 5/CDK5 activator 1	CHEMBL 1907600	Q00535	1UNL	T20973	55.79 %	93.03%
Acetyl-CoA carboxylase 2	CHEMBL 4829	O00763	3TDC	T08922	55.77 %	98%
Ribosomal protein S6 kinase alpha 6	CHEMBL 4924	Q9UK32	6G77	Not Available	55.69 %	80%
Neuronal acetylcholine receptor; alpha3/beta4	CHEMBL 1907594	P30926	6PV7	T73724	55.45 %	97.23%
Dual specificity protein phosphatase 3	CHEMBL 2635	P51452	3F81	Not Available	55.42 %	94%
Nitric-oxide synthase, endothelial	CHEMBL 4803	P29474	4D1P	T06046	55.38 %	86%
Aldo-keto-reductase family 1 member C3	CHEMBL 4681	P42330	1S1P	T60857	55.21 %	89.05%
Cystic fibrosis transmembrane conductance regulator	CHEMBL 4051	P13569	6MSM	T55654	54.97 %	95.71%
PI3-kinase p110-beta subunit	CHEMBL 3145	P42338	Not Available	T05031	54.97 %	98.75%
P2X purinoceptor 7	CHEMBL 4805	Q99572	Not Available	T63414	54.84 %	97.50%
Autotaxin	CHEMBL 3691	Q13822	4ZG6	Not Available	54.54 %	96.39%
Dihydrofolate reductase	CHEMBL 202	P00374	1KMV	T17345	54.51 %	89.92%
Tyrosine-protein kinase receptor TYRO3	CHEMBL 5314	Q06418	1RHF	Not Available	54.41 %	96%
Caspase-6	CHEMBL 3308	P55212	2WDP	Not Available	54.33 %	97.56%
Histone-lysine N-methyltransferase EZH2	CHEMBL 2189110	Q15910	5HYN	T25265	54.26 %	97.50%
Tissue factor pathway inhibitor	CHEMBL 3713062	P10646	5NMV	T78890	54.16 %	97.33%
AMP-activated protein kinase, alpha-1 subunit	CHEMBL 4045	Q13131	6C9H	Not Available	54.04 %	73.50%
Phosphodiesterase 7A	CHEMBL 3012	Q13946	1ZKL	T39523	54.02 %	99.29%
C-X-C chemokine receptor type 4	CHEMBL 2107	P61073	3ODU	T96079	53.88 %	93.10%
Fatty acid binding protein	CHEMBL	P15090	3P6D	Not	53.39	95.71%

adipocyte	2083	90		Availab le	%	
Isoprenylcysteine carboxyl methyltransferase	CHEMBL 4699	O607 25	Not Available	Not Availab le	53.26 %	100%
Histone deacetylase 4	CHEMBL 3524	P565 24	2VQM	T63816	52.93 %	92.97%
Non-receptor tyrosine-protein kinase TNK1	CHEMBL 5334	Q134 70	Not Available	Not Availab le	52.92 %	73.33%
P-glycoprotein 1	CHEMBL 4302	P081 83	7A69	T25258	52.80 %	92.98%
Tryptophan 2,3-dioxygenase	CHEMBL 2140	P487 75	6PYZ	Not Availab le	52.75 %	98.46%
Integrin alpha-4/beta-1	CHEMBL 1907599	P055 56	3V4V	T97587	52.61 %	92.86%
Caspase-8	CHEMBL 3776	Q147 90	4JJ7	T15700	52.60 %	97.06%
Histone acetyltransferase PCAF	CHEMBL 5500	Q928 31	1CM0	Not Availab le	52.34 %	91.96%
SUMO-activating enzyme	CHEMBL 2095174	Q9U BE0	6XOG	Not Availab le	52.14 %	79%
Multidrug resistance-associated protein 1	CHEMBL 3004	P335 27	4C3Z	T11288	52.08 %	96.37%
WD repeat-containing protein 5	CHEMBL 1075317	P619 64	2GNQ	Not Availab le	51.74 %	96.33%
Ghrelin receptor	CHEMBL 4616	Q928 47	6KO5	T59604	51.69 %	92%
ADAM17	CHEMBL 3706	P785 36	2I47	T82393	51.55 %	90.71%
Tyrosyl-DNA phosphodiesterase 2	CHEMBL 2169736	O955 51	5J3P	Not Availab le	51.52 %	98.46%
Carnitine palmitoyltransferase 2	CHEMBL 3238	P237 86	Not Available	Not Availab le	51.37 %	94.05%
Protein-arginine N-methyltransferase 1	CHEMBL 5524	Q998 73	6NT2	Not Availab le	51.20 %	96.67%
Protein kinase N2	CHEMBL 3032	Q165 13	4CRS	Not Availab le	51.17 %	78%
Histone-arginine methyltransferase CARM1	CHEMBL 5406	Q86X 55	6DVR	T12837	51.03 %	94.33%
Methionine aminopeptidase 2	CHEMBL 3922	P505 79	1B6A	T75596	51.02 %	97.28%

Hypoxia-inducible factor 1 alpha	CHEMBL 4261	Q16665	4H6J	Not Available	50.98 %	85.14%
Lymphocyte differentiation antigen CD38	CHEMBL 4660	P28907	3F6Y	T10877	50.62 %	95.27%
PI3-kinase p110-alpha/p85-alpha	CHEMBL 2111367	P27986	4JPS	T80276	50.58 %	94.33%
Muscarinic acetylcholine receptor M4	CHEMBL 1821	P08173	5DSG	T20709	50.40 %	94.08%
Aminopeptidase N	CHEMBL 1907	P15144	4FYT	T67272	50.25 %	93.31%
Free fatty acid receptor 2	CHEMBL 5493	O15552	Not Available	T28213	50.10 %	92.86%
IgG receptor FcRn large subunit p51	CHEMBL 5966	P55899	6FGB	Not Available	50.05 %	90.93%

Abbreviations: 2D, two-dimensional; 3D, three-dimensional; ChEMBL, ChEMBL database; ID, identifier; N/A, not available; PDB, Protein Data Bank; TTD, Therapeutic Target Database; UniProt, Universal Protein Resource.

Table S2. Shared targets of rheumatoid arthritis and sabinene

P10275	P28472	Q99873	P49760
O75874	Q15418	P08183	O00763
O00408	P31213	P17706	Q92769
P14867	Q99685	Q9GZT9	Q9H228
Q13085	Q05586	P50281	Q9NY46
P05177	P10515	O14672	P24752
Q92753	P28065	O60725	P25090
Q8IU80	P32246	P05106	Q13546
Q14289	Q9Y2T6	P51452	Q96GG9
P35610	P40763	P33527	P50406
P34972	P67870	Q92847	P19634
Q13822	Q14790	P00750	P27338
P21589	P55055	O60341	P28845
Q99705	P56373	P41597	P16591
P04070	P14867	P06401	Q13557
Q13133	P48775	P34969	P30307
O95665	P16083	P20618	P22894
P23786	Q00975	P27986	Q16790
Q99250	Q04759	Q13470	P52732
P30926	P07339	P05093	O14744
P18031	P16662	P00338	Q9HAZ1
P56524	P42345	Q13946	P35414
Q8NER1	O75762	Q9UK32	P36507
P11511	Q99572	Q08881	O75469
Q86X55	Q6P988	P35462	Q9Y210
O15164	P18825	P05067	Q05586
O00206	P04278	O00519	O14684
Q9UBE0	P13726	P09237	P14867
P30542	P06276	P07900	P42330
Q16665	Q13370	Q969R2	P02511
P10646	Q06418	P78536	P08684
O00329	P61964	P48736	Q6L5J4
Q13188	O95551	P30305	O00767
P31645	P05556	P41145	Q16513
Q16678	P11509	P28702	P23219
Q969S8	P08172	P27695	P00734
P61073	P11473	P15090	O00748
P41595	P32245	P15144	Q01959
P30304	P02489	P51449	P00915
P22059	P80365	P08709	O95180
P28907	P19838	P28472	Q9UHC9
P33261	Q07869	P14174	Q9UBE0
Q15392	Q9HBX9	Q86WV6	Q92831
P04035	P04062	P18507	P23141
P18405	Q15910	P51681	Q96BI3
P43235	P55899	Q99720	P50579

P03951	P37058	Q9Y6A2	Q96RI1
P55212	P49721	Q12772	P42338
P21397	Q96GD4	P22303	P23975
P18507	P00918	P08235	P0DMS8
P28472	P18505	Q12879	Q16445
P18507	P28472	Q16445	

Table S3. Top 50 hub targets, ranked by the Degree method within the CytoHubba plugin in Cytoscape

No	Target	STRING–CytoHubba score	No.	Target	STRING–CytoHubba score
1	TNF	168	26	AR	50
2	IL6	164	27	PIK3CG	50
3	STAT3	122	28	NOS3	48
4	IFNG	108	29	PIK3R1	48
5	PTGS2	102	30	CCR2	46
6	NFKB1	100	31	NR1H4	46
7	IL10	100	32	PTGS1	46
8	HIF1A	100	33	EZH2	46
9	HSP90AA1	100	34	MMP7	44
10	BCL2	98	35	HDAC2	44
11	ESR1	98	36	ABCB1	44
12	TLR4	98	37	ADAM17	42
13	CASP3	98	38	CYP3A4	42
14	MMP9	94	39	CD38	42
15	MTOR	88	40	PRKCD	40
16	CXCR4	84	41	ITGB3	40
17	IL1A	82	42	MAOA	38
18	ICAM1	78	43	CCR1	36
19	JAK2	76	44	CYP19A1	34
20	PPARA	70	45	HDAC4	34
21	VCAM1	66	46	FPR2	32
22	ITGB1	62	47	PLAT	32
23	PRKCA	54	48	MMP14	32
24	IDO1	54	49	ACACA	32

25	CASP8	52	50	CTSK	32

The reported values represent the STRING–Cytoscape-derived connectivity/ranking score used for hub-target prioritization, not simple node degree. In a simplified undirected network with 132 nodes, the maximum simple node degree is 131. **Abbreviations:** ABCB1, ATP-binding cassette subfamily B member 1; ACACA, acetyl-CoA carboxylase alpha; ADAM17, ADAM metallopeptidase domain 17; AR, androgen receptor; BCL2, B-cell lymphoma 2; CASP3, caspase 3; CASP8, caspase 8; CCR1, C-C chemokine receptor type 1; CCR2, C-C chemokine receptor type 2; CD38, cluster of differentiation 38; CTSK, cathepsin K; CXCR4, C-X-C chemokine receptor type 4; CYP3A4, cytochrome P450 3A4; CYP19A1, cytochrome P450 family 19 subfamily A member 1; ESR1, estrogen receptor 1; EZH2, enhancer of zeste homolog 2; FPR2, formyl peptide receptor 2; HDAC2, histone deacetylase 2; HDAC4, histone deacetylase 4; HIF1A, hypoxia-inducible factor 1-alpha; HSP90AA1, heat shock protein 90 alpha family class A member 1; ICAM1, intercellular adhesion molecule 1; IDO1, indoleamine 2,3-dioxygenase 1; IFNG, interferon gamma; IL1A, interleukin-1 alpha; IL6, interleukin-6; IL10, interleukin-10; ITGB1, integrin subunit beta 1; ITGB3, integrin subunit beta 3; JAK2, Janus kinase 2; MAOA, monoamine oxidase A; MMP7, matrix metalloproteinase 7; MMP9, matrix metalloproteinase 9; MMP14, matrix metalloproteinase 14; MTOR, mechanistic target of rapamycin kinase; NFKB1, nuclear factor kappa B subunit 1; NOS3, nitric oxide synthase 3; NR1H4, nuclear receptor subfamily 1 group H member 4; PIK3CG, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma; PIK3R1, phosphoinositide-3-kinase regulatory subunit 1; PLAT, plasminogen activator, tissue type; PPARA, peroxisome proliferator-activated receptor alpha; PRKCA, protein kinase C alpha; PRKCD, protein kinase C delta; PTGS1, prostaglandin-endoperoxide synthase 1; PTGS2, prostaglandin-endoperoxide synthase 2; STAT3, signal transducer and activator of transcription 3; STRING, Search Tool for the Retrieval of Interacting Genes/Proteins; TLR4, toll-like receptor 4; TNF, tumor necrosis factor; VCAM1, vascular cell adhesion molecule 1.

Graphical abstract

