

Table SI. Overlap between GeneCards disease-associated genes and the 100 predicted gomisin A targets.

Disease	Disease genes, n	Overlap, n	Overlapping GA target symbols
Acute liver injury	3,656	71	ATR, ALOX5, GSK3B, PRKCB, JAK3, JAK1, HMGR, EGFR, ERBB2, THRA, JAK2, F10, MTOR, PIK3CA, KCNH2, TYRO3, MAPK8, ABCB1, CHEK1, MAPK14, PRKCA, PRKDC, NQO1, MAPK11, AXL, MDM2, MERTK, LRRK2, NTRK1, IGF1R, ABCC9, MMP13, MMP2, CDK2, MET, TNF, F2, PARP1, ADORA2A, CDK1, ROCK1, ADAM17, MMP14, MAP3K20, MMP7, TGFB2, TGFB1, ALOX5AP, ADAM10, TACR1, HDAC4, KCNA5, PIK3CD, PIK3CB, PIK3CG, PDE5A, AR, FLT3, PIM1, KDR, GCK, PIM2, FKBP1A, STAT3, GSK3A, PDE4D, MAP2K1, DYRK1A, IL6ST, MAPK10, SRC
Hepatic fibrosis	1,828	45	ALOX5, GSK3B, JAK3, JAK1, HMGR, EGFR, ERBB2, JAK2, MTOR, PIK3CA, MAPK8, ABCB1, MAPK14, PRKCA, PRKDC, NQO1, AXL, MDM2, NTRK1, IGF1R, MMP13, MMP2, CDK2, MET, TNF, F2, PARP1, ADAM17, MMP14, MAP3K20, MMP7, TGFB2, TGFB1, ADAM10, PIK3CD, PIK3CB, PIK3CG, AR, FLT3, KDR, GCK, STAT3, MAP2K1, IL6ST, SRC
Cholestasis	189	1	ABCB1
Liver regeneration	907	35	GSK3B, JAK1, HMGR, EGFR, ERBB2, JAK2, MTOR, PIK3CA, MAPK8, ABCB1, MAPK14, AXL, MDM2, NTRK1, IGF1R, MMP2, CDK2, MET, TNF, F2, CDK1, MAP3K20, MMP7, TGFB2, TGFB1, PIK3CD, PIK3CG, AR, FLT3, KDR, GCK, STAT3, MAP2K1, IL6ST, SRC
Hepatitis C	2,486	61	ATR, ALOX5, GSK3B, PRKCB, JAK3, JAK1, HMGR, EGFR, ERBB2, THRB, JAK2, F10, MTOR, PIK3CA, KCNH2, MAPK8, ABCB1, CHEK1, MAPK14, PRKCA, PRKDC, NQO1, MAPK11, AXL, MDM2, MERTK, NTRK1, IGF1R, ABCC9, MMP13, MMP2, CDK2, MET, TNF, F2, PARP1, ROCK2, CDK1, ROCK1, ADAM17, MMP14, MAP3K20, MMP7, TGFB2, TGFB1, ADAM10, TACR1, KCNA5, PIK3CD, PIK3CB, PIK3CG, AR, FLT3, PIM1, KDR, GCK, STAT3, MAP2K1, IL6ST, MAPK10, SRC
Colorectal cancer	3,517	62	ATR, ALOX5, GSK3B, PRKCB, JAK3, JAK1, HMGR, EGFR, ERBB2, THRB, JAK2, MTOR, PIK3CA, KCNH2, TYRO3, MAPK8, ABCB1, CHEK1, MAPK14, PRKCA, PRKDC, NQO1, NQO2, AXL, MDM2, LRRK2, NTRK1, IGF1R, MMP13, MMP2, CDK2, MET, TNF, F2, PARP1, ROCK2, CDK1, ROCK1, ADAM17, MMP14, MAP3K20, MMP7, TGFB2, TGFB1, ADAM10, HDAC4, PIK3CD, PIK3CB, PIK3CG, AR, FLT3, PIM1, KDR, PIM2, STAT3, AKR1C3, GSK3A, MAP2K1, IL6ST, TNK2, MAPK10, SRC
Ovarian cancer	3,155	63	ATR, ALOX5, GSK3B, PRKCB, JAK3, JAK1, HMGR, EGFR, ERBB2, THRB, JAK2, MTOR, PIK3CA, KCNH2, TYRO3, MAPK8, ABCB1, CHEK1, MAPK14, PRKCA, PRKDC, NQO1, NQO2, AXL, MDM2, LRRK2, NTRK1, IGF1R, MMP13, MMP2, CDK2, MET, TNF, F2, PARP1, ROCK2, CDK1, ROCK1, ADAM17, MMP14, MAP3K20, MMP7, TGFB2, TGFB1, ADAM10, HDAC4, PIK3CD, PIK3CB, PIK3CG, AR, FLT3, PIM1, KDR, PIM2, FKBP1A, STAT3, AKR1C3, GSK3A, MAP2K1, IL6ST, TNK2, MAPK10, SRC
Prostate cancer	5,292	74	ATR, ALOX5, GSK3B, PRKCB, CFD, JAK3, JAK1, HMGR, EGFR, ERBB2, THRA, THRB, JAK2, F10, MTOR, PIK3CA, KCNH2, TYRO3, MAPK8, ABCB1, CHEK1, MAPK14, PRKCA, PRKDC, NQO1, NQO2, MAPK11, AXL, MDM2, MERTK, LRRK2, NTRK1, IGF1R, MMP13, MMP2, CDK2, MET, TNF, F2, PARP1, ADORA2A, ROCK2, CDK1, ROCK1, ADAM17, MMP14, MAP3K20, MMP7, TGFB2, TGFB1, ADAM10, TACR1, HDAC4, PIK3CD, PIK3CB, PIK3CG, PDE5A, AR, FLT3, PIM1, KDR, GCK, PIM2, FKBP1A, STAT3, AKR1C3, GSK3A, PDE4D, MAP2K1, DYRK1A, IL6ST, TNK2, MAPK10, SRC

Disease	Disease genes, n	Overlap, n	Overlapping GA target symbols
Breast cancer	4,188	67	ATR, ALOX5, GSK3B, PRKCB, JAK3, JAK1, HMGCR, EGFR, ERBB2, THRA, THRB, JAK2, MTOR, PIK3CA, KCNH2, TYRO3, MAPK8, ABCB1, CHEK1, MAPK14, PRKCA, PRKDC, NQO1, NQO2, MAPK11, AXL, MDM2, LRRK2, NTRK1, IGF1R, MMP13, MMP2, CDK2, MET, TNF, F2, PARP1, ROCK2, CDK1, ROCK1, ADAM17, MMP14, MAP3K20, MMP7, TGFBR2, TGFBR1, ADAM10, TACR1, HDAC4, PIK3CD, PIK3CB, PIK3CG, AR, FLT3, PIM1, KDR, PIM2, FKBP1A, STAT3, AKR1C3, GSK3A, MAP2K1, DYRK1A, IL6ST, TNK2, MAPK10, SRC
Retinoblastoma	140	4	MDM2, CDK2, CDK1, MAP2K1
Metastatic melanoma	548	32	ATR, GSK3B, JAK1, EGFR, ERBB2, JAK2, MTOR, PIK3CA, ABCB1, CHEK1, MAPK14, PRKCA, PRKDC, AXL, MDM2, NTRK1, IGF1R, MMP2, CDK2, MET, TNF, PARP1, MMP14, ADAM10, PIK3CD, PIK3CB, PIK3CG, AR, KDR, STAT3, MAP2K1, SRC

Disease-associated gene lists were compiled from GeneCards using a relevance-score cutoff of ≥ 10 and intersected with the 100 predicted GA targets. GA, gomisin A.

Table SII. Target genes of gomisins A.

No.	Name	Gene symbol
1	Serine-protein kinase ATR	ATR
2	Arachidonate 5-lipoxygenase	ALOX5
3	Glycogen synthase kinase-3 β	GSK3B
4	Protein kinase C β	PRKCB
5	Complement factor D	CFD
6	Phosphodiesterase 10A	PDE10A
7	Tyrosine-protein kinase JAK3	JAK3
8	Tyrosine-protein kinase JAK1	JAK1
9	HMG-CoA reductase (by homology)	HMGCR
10	Phosphodiesterase 2A	PDE2A
11	Epidermal growth factor receptor erbB1	EGFR
12	Receptor protein-tyrosine kinase erbB-2	ERBB2
13	Thyroid hormone receptor α	THRA
14	Thyroid hormone receptor β -1	THRB
15	Cyclin-dependent kinase 4/cyclin D1	CCND1, CDK4
16	Cyclin-dependent kinase 2/cyclin E	CCNE2, CDK2, CCNE1
17	Tyrosine-protein kinase JAK2	JAK2
18	γ -secretase	PSEN2, PSENEN, NCSTN, APH1A, PSEN1, APH1B
19	Thrombin and coagulation factor X	F10
20	Serine/threonine-protein kinase mTOR	MTOR
21	CDK2/cyclin A	CCNA2, CDK2
22	PI3-kinase p110- α subunit	PIK3CA
23	HERG	KCNH2
24	Phosphodiesterase 7A	PDE7A
25	Leukotriene B4 receptor 1	LTB4R
26	Neuropeptide Y receptor type 5	NPY5R
27	Tyrosine-protein kinase receptor TYRO3	TYRO3
28	LIM domain kinase 2	LIMK2
29	c-Jun N-terminal kinase 1	MAPK8

30	P-glycoprotein 1	ABCB1
31	Serine/threonine-protein kinase Chk1	CHEK1
32	MAP kinase p38 α	MAPK14
33	Protein kinase C α	PRKCA
34	DNA-dependent protein kinase	PRKDC
35	Quinone reductase 1	NQO1
36	Quinone reductase 2	NQO2
37	MAP kinase p38 β	MAPK11
38	Tyrosine-protein kinase receptor UFO	AXL
39	p53-binding protein Mdm-2	MDM2
40	Proto-oncogene tyrosine-protein kinase MER	MERTK
41	Leucine-rich repeat serine/threonine-protein kinase 2	LRRK2
42	GABA-A receptor; α -3/ β -3/ γ -2	GABRB3, GABRA3, GABRG2
43	GABA-A receptor; α -1/ β -3/ γ -2	GABRB3, GABRG2, GABRA1
44	GABA-A receptor; α -5/ β -3/ γ -2	GABRB3, GABRG2, GABRA5
45	GABA-A receptor; α -2/ β -3/ γ -2	GABRA2, GABRB3, GABRG2
46	Nerve growth factor receptor Trk-A	NTRK1
47	Insulin-like growth factor I receptor	IGF1R
48	Sulfonylurea receptor 2	ABCC9
49	Nociceptin receptor	OPRL1
50	dUTP pyrophosphatase	DUT
51	Matrix metalloproteinase 13	MMP13
52	Matrix metalloproteinase 2	MMP2
53	Cyclin-dependent kinase 2	CDK2
54	Probable G-protein coupled receptor 88	GPR88
55	Hepatocyte growth factor receptor	MET
56	TNF- α	TNF
57	Thrombin	F2
58	Poly (ADP-ribose) polymerase-1	PARP1
59	Adenosine A2a receptor	ADORA2A

60	Adenosine A3 receptor	ADORA3
61	Rho-associated protein kinase 2	ROCK2
62	Cyclin-dependent kinase 1	CDK1
63	Rho-associated protein kinase 1	ROCK1
64	ADAM17	ADAM17
65	Matrix metalloproteinase 14	MMP14
66	Mixed lineage kinase 7	MAP3K20
67	Matrix metalloproteinase 7	MMP7
68	TGF- β receptor type II	TGFBR2
69	TGF- β receptor type I	TGFBR1
70	5-lipoxygenase activating protein	ALOX5AP
71	A disintegrin and metalloproteinase domain-containing protein 10	ADAM10
72	Neurokinin 1 receptor	TACR1
73	Histone deacetylase 4	HDAC4
74	P2X purinoceptor 3	P2RX3
75	Voltage-gated potassium channel subunit Kv1.5	KCNA5
76	PI3-kinase p110- δ subunit	PIK3CD
77	PI3-kinase p110- β subunit	PIK3CB
78	PI3-kinase p110- γ subunit	PIK3CG
79	Phosphodiesterase 5A	PDE5A
80	Androgen receptor	AR
81	Tyrosine-protein kinase receptor FLT3	FLT3
82	Serine/threonine-protein kinase PIM1	PIM1
83	Vascular endothelial growth factor receptor 2	KDR
84	Hexokinase type IV	GCK
85	Serine/threonine-protein kinase PIM2	PIM2
86	FK506-binding protein 1A	FKBP1A
87	Signal transducer and activator of transcription 3	STAT3
88	Aldo-keto-reductase family 1 member C3	AKR1C3

89	Glycogen synthase kinase-3 α	GSK3A
90	Orexin receptor 2	HCRTR2
91	Phosphodiesterase 4D	PDE4D
92	Dual specificity mitogen-activated protein kinase kinase 1	MAP2K1
93	Cyclin-dependent kinase 5/CDK5 activator 1	CDK5R1, CDK5
94	Cyclin-dependent kinase 2/cyclin A	CDK2, CCNA1, CCNA2
95	Dual-specificity tyrosine-phosphorylation regulated kinase 1A	DYRK1A
96	IL-6 receptor subunit β	IL6ST
97	Tyrosine kinase non-receptor protein 2	TNK2
98	c-Jun N-terminal kinase 3	MAPK10
99	Tyrosine-protein kinase SRC	SRC
100	Probable G-protein coupled receptor 139	GPR139

Table SIII. Kyoto Encyclopedia of Genes and Genomes analysis.

ID	Description	FDR-adjusted P-value
hsa05200	Pathways in cancer	<0.000000001
hsa01521	EGFR tyrosine kinase inhibitor resistance	<0.000000001
hsa04151	PI3K-Akt signaling pathway	<0.000000001
hsa05205	Proteoglycans in cancer	<0.000000001
hsa05161	Hepatitis B	<0.000000001
hsa01522	Endocrine resistance	<0.000000001
hsa05212	Pancreatic cancer	<0.000000001
hsa04068	FoxO signaling pathway	<0.000000001
hsa05215	Prostate cancer	<0.000000001
hsa04917	Prolactin signaling pathway	<0.000000001
hsa05230	Central carbon metabolism in cancer	<0.000000001
hsa05226	Gastric cancer	0.000000001
hsa05167	Kaposi sarcoma-associated herpesvirus infection	0.000000001
hsa04926	Relaxin signaling pathway	0.000000005
hsa04933	AGE-RAGE signaling pathway in diabetic complications	0.000000012
hsa04010	MAPK signaling pathway	0.000000012
hsa04550	Signaling pathways regulating pluripotency of stem cells	0.000000015
hsa04659	Th17 cell differentiation	0.000000021
hsa05225	Hepatocellular carcinoma	0.000000075
hsa04012	ErbB signaling pathway	0.000000077
hsa05210	Colorectal cancer	0.000000084
hsa05163	Human cytomegalovirus infection	0.000000087
hsa05235	PD-L1 expression and PD-1 checkpoint pathway in cancer	0.000000111
hsa04510	Focal adhesion	0.000000411
hsa04218	Cellular senescence	0.000000582
hsa05223	Non-small cell lung cancer	0.000000587
hsa05166	Human T-cell leukemia virus 1 infection	0.000000999
hsa04935	Growth hormone synthesis, secretion and action	0.0000001222
hsa05171	Coronavirus disease - COVID-19	0.0000001840
hsa05418	Fluid shear stress and atherosclerosis	0.0000003748
hsa04380	Osteoclast differentiation	0.0000003957
hsa05169	Epstein-Barr virus infection	0.0000005256
hsa05203	Viral carcinogenesis	0.0000005710
hsa05415	Diabetic cardiomyopathy	0.0000005710
hsa05160	Hepatitis C	0.0000009392
hsa04066	HIF-1 signaling pathway	0.0000009395
hsa04664	Fc ϵ RI signaling pathway	0.0000010132
hsa05145	Toxoplasmosis	0.0000010630
hsa04914	Progesterone-mediated oocyte maturation	0.0000010630
hsa05120	Epithelial cell signaling in <i>Helicobacter pylori</i> infection	0.0000012016
hsa05218	Melanoma	0.0000014177
hsa04630	JAK-STAT signaling pathway	0.0000014255
hsa05219	Bladder cancer	0.0000015862
hsa04668	TNF signaling pathway	0.0000017023
hsa05214	Glioma	0.0000018006
hsa04014	Ras signaling pathway	0.0000019906
hsa05131	Shigellosis	0.0000028922
hsa04930	Type II diabetes mellitus	0.0000031757
hsa04062	Chemokine signaling pathway	0.0000040348
hsa05135	<i>Yersinia</i> infection	0.0000045904
hsa05162	Measles	0.0000048160
hsa04520	Adherens junction	0.0000058954
hsa04912	GnRH signaling pathway	0.0000058954

hsa05224	Breast cancer	0.0000072963
hsa04015	Rap1 signaling pathway	0.0000080832
hsa05207	Chemical carcinogenesis - receptor activation	0.0000089628
hsa05417	Lipid and atherosclerosis	0.0000092735
hsa05213	Endometrial cancer	0.0000099166
hsa05142	Chagas disease	0.0000106570
hsa04370	VEGF signaling pathway	0.0000107784
hsa04625	C-type lectin receptor signaling pathway	0.0000119064
hsa05208	Chemical carcinogenesis - reactive oxygen species	0.0000129148
hsa04620	Toll-like receptor signaling pathway	0.0000147616
hsa04931	Insulin resistance	0.0000147616
hsa05206	MicroRNAs in cancer	0.0000180428
hsa05221	Acute myeloid leukemia	0.0000199749
hsa04722	Neurotrophin signaling pathway	0.0000255648
hsa04660	T cell receptor signaling pathway	0.0000280813
hsa04919	Thyroid hormone signaling pathway	0.0000280813
hsa05165	Human papillomavirus infection	0.0000302615
hsa05220	Chronic myeloid leukemia	0.0000366262
hsa04210	Apoptosis	0.0000518375
hsa04910	Insulin signaling pathway	0.0000562578
hsa05170	Human immunodeficiency virus 1 infection	0.0000767149
hsa04072	Phospholipase D signaling pathway	0.0000862812
hsa04148	Efferocytosis	0.0001112501
hsa04150	mTOR signaling pathway	0.0001193494
hsa05231	Choline metabolism in cancer	0.0001222719
hsa04750	Inflammatory mediator regulation of TRP channels	0.0001222719
hsa04217	Necroptosis	0.0001235714
hsa04071	Sphingolipid signaling pathway	0.0003256110
hsa04611	Platelet activation	0.0003643618
hsa04920	Adipocytokine signaling pathway	0.0003854532
hsa04915	Estrogen signaling pathway	0.0005933024
hsa04114	Oocyte meiosis	0.0005933024
hsa05010	Alzheimer disease	0.0005952079
hsa04932	Non-alcoholic fatty liver disease	0.0010294790
hsa04658	Th1 and Th2 cell differentiation	0.0010849448
hsa04657	IL-17 signaling pathway	0.0012228369
hsa05132	Salmonella infection	0.0014089345
hsa04140	Autophagy - animal	0.0014302171
hsa05164	Influenza A	0.0015462510
hsa05152	Tuberculosis	0.0018896390
hsa04725	Cholinergic synapse	0.0024708245
hsa04613	Neutrophil extracellular trap formation	0.0025056267
hsa05202	Transcriptional misregulation in cancer	0.0025628385
hsa04152	AMPK signaling pathway	0.0030610563
hsa04213	Longevity regulating pathway - multiple species	0.0035460795
hsa05211	Renal cell carcinoma	0.0049926978
hsa04810	Regulation of actin cytoskeleton	0.0054235684
hsa01524	Platinum drug resistance	0.0060534811
hsa05140	Leishmaniasis	0.0065126942
hsa05100	Bacterial invasion of epithelial cells	0.0067498990
hsa04144	Endocytosis	0.0079304542
hsa04211	Longevity regulating pathway	0.0100016558
hsa04662	B cell receptor signaling pathway	0.0103071148
hsa04540	Gap junction	0.0106179745
hsa05020	Prion disease	0.0118250602

hsa04360	Axon guidance	0.0128930242
hsa05130	Pathogenic <i>Escherichia coli</i> infection	0.0179017013
hsa04928	Parathyroid hormone synthesis, secretion and action	0.0192919796
hsa04670	Leukocyte transendothelial migration	0.0197364604
hsa04650	Natural killer cell mediated cytotoxicity	0.0265558640
hsa05022	Pathways of neurodegeneration - multiple diseases	0.0312038048
hsa04371	Apelin signaling pathway	0.0321085519
hsa04936	Alcoholic liver disease	0.0344878297
hsa05017	Spinocerebellar ataxia	0.0344878297
hsa04020	Calcium signaling pathway	0.0368043196
hsa04921	Oxytocin signaling pathway	0.0408276660
hsa04929	GnRH secretion	0.0413212722
hsa04934	Cushing syndrome	0.0414921727
hsa05168	Herpes simplex virus 1 infection	0.0431546424
hsa04110	Cell cycle	0.0435186976
hsa04622	RIG-I-like receptor signaling pathway	0.0496857755
hsa00562	Inositol phosphate metabolism	0.0509272245
hsa04115	p53 signaling pathway	0.0534436230
hsa05133	Pertussis	0.0572999379
hsa04621	NOD-like receptor signaling pathway	0.0672748422
hsa05222	Small cell lung cancer	0.0779351146
hsa04666	Fc γ R-mediated phagocytosis	0.0852671955
hsa05146	Amoebiasis	0.0928015854

AGE-RAGE, advanced glycation end-products-receptor for AGE system; AMPK, AMP-activated protein kinase; COVID-19, coronavirus disease 2019; GnRH, gonadotropin-releasing hormone; HIF-1, hypoxia-inducible factor-1; JAK, Janus kinase; NOD, nucleotide-binding oligomerization domain; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; Th1, T helper 1; Rap1, Ras-related protein 1; Fc epsilon RI (Fc ϵ RI), high-affinity immunoglobulin E receptor I; RIG-I, retinoic acid-inducible gene I; TRP, transient receptor potential.