

Supplement Table 1. Potential targets of GE.

Databases	Targets
SwissTargetPrediction	LGALS3, LGALS9, CA2, CA1, CA12, CA9, ADK, CA14, ADORA1, ADORA2A, ADORA3, HK2, HK1, ADA, GBA, FUCA1, OGA, SLC5A2, SLC29A1, TYR, CA7, CA13, ADORA2B, EIF4H, PABPC1, LGALS4, LGALS8, MMP2, EPHX2, CDK2, SLC5A1, CA4, CA5A, EDNRA, HSPA8, SLC5A4, MGAM, AKR1B1, HRAS, AKR1C3, DAO
TCMSP	CA2,BCL2,HMOX1,GAP43,PLB1,GCGR,GSTM1,GSTM2
Pharmmapper	CDK2,CTSV,NR1H2,CLC,CTSD,BCHE,PPIA,GSTP1,PDE4B,FKBP1A,MTAP,FAP,GBA1,CA1,TGFBR2,PNP, PGR,CA12,AURKA,IMPA,QPCT,CA2,TREM1,RTN4R, METAP1,HSPA8,NUDT9,FCAR,CTSB,CFD,HSP90AA1,AR,ICAM2,ANG,DDX6,AMY1,REN,CHEK1,PLA2G10,PDE4D,PIM1,F2,EPHB4,SORD,CCNA2,DHFR,F10, CSNK2A1,EGFR,PPARG,SRC,CMA1,PAH,MIF,SHBG, PNPO,CFB,BACE1,KDR,CRAT,MMP3,ALR,PDE3B,LGALS7,PDE5A,BAG1,BMP7,ISG20,LSS,MMP8,PYGL, BCAT2,CDA,FGFR1,ST14,C1R,MMP12,MTHFD1,IGLV2-8,PDPK1,PLAU,AZGP1,AMD1,AKT1,CES1,APCS, CSNK1G2,DAPK1,MAN1B1,RAB11A,DCK,GSK3B,CTNNA1,PTPN1,AHCY,MAPK14,HMGCR,HSD11B1,ESR1,CTSK,TYMP,HK1,REG1A,LCK,CBR1,DPP4,GPI, ALDOA,SHMT1,AKR1C3,ATOX1,ANXA5,CASP7,ESRRG,SOD2,PAK7,METAP2,TNK2,BST1,ADK,MAPK8, RNASE4,APAH,SYK,XIAP,CYP2C9,ACP3,AMY2A, MMP7,IMPDH2,RAC2,IGF1R,KIF11,ELANE,JAK3,LDHB,RHOA,PRKACA,NQO1,LGALS2,CPB1,CASP3,GALK1,ALDH2,ME2,GSR,OTC,ABO,ITK,RNASE3,NCS1, EPHX2,RHEB,GALE,B3GAT1,PCK1,PADI4,UCK2,CTSG,AKR1C2,ADH5,CDK5R1,HCK,RAB5A,TGM3,DHODH,MMP16,TYMS,MMP9,HSD17B1,BIRC7,MMP13,NMNAT1,JAK2,YARS1,PDHB,HRAS,GNPDA,HEXB,SULT2A1,APRT,PARP1,GCKR,NR3C2,CSK,ESR2, MAPK10,NOS2,HDAC8,UMPS,CTSS,MAPKAPK2,PPARA,PAK6,SERPINA1,C1S,HAGH,HEXB,AMY1A,SDS,LYZ,FDPS,SELP,ARHGAP1,ABO,IL2,SRM,DPEP1,SE1,NOS3,KYAT1,PLA2G2A,PGF,DTYMK,CCL5,INSR,NR1I2,SETD7,HINT1,MAPK1,ARSA,CTSF,TPI1,GART,F7,GSTA1,GSTA3,THRA,TPH1,FABP4,CD1A,ZAP

	70,PTK2,FABP6,GSTT2,TGM2,FNTA,MMP1,STAT1,F 11,ARG1,IMPDH,AGXT,BRAF,CLK1,IGF1,CHIT1,HP RT1,S100A9,LGALS3,PRKCQ,PRKACA,CAT,BHMT, PAPSS1,CD209,SULT1A3,MME,EIF4E,EPHA2,KIT,FE CH,RARA,MET,ABL1,HPN,ADAM33,PLEKHA4,SUL T2B1,NQO2,ACADM,NMNAT3,CTSL,ARG2,NR3C1, CDC42,RNASE2,PITPNA,CBS,CDK6,OAT,HPGDS,M TO1,BLVRB,GMPR2,TK1,KAT2B,GSTM2,PIK3R1,GS TZ1,AKT2,LTA4H,HADH,ALAD,HNMT,CASP1 ATPIA1
Batman	

Supplement Table 2. Relevant information about the core target of Geniposide in the treatment of RA.

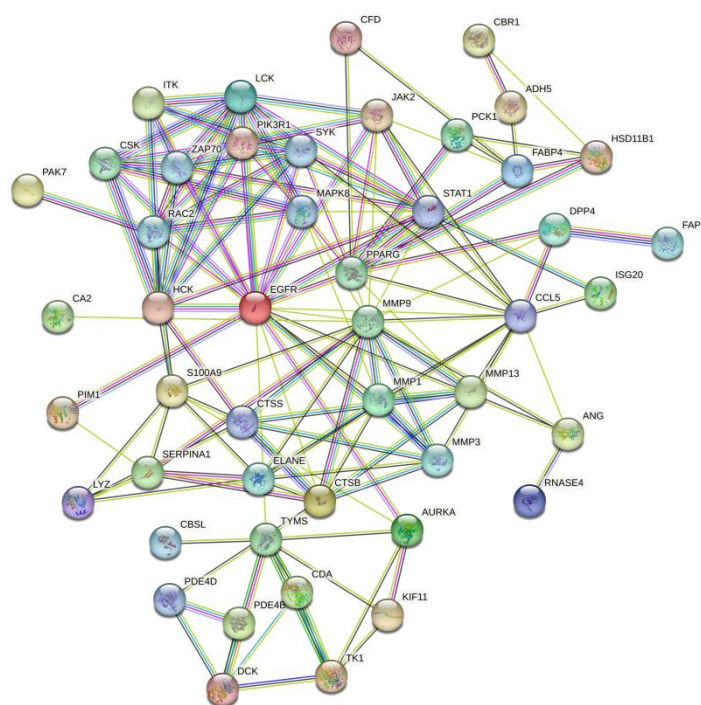
Uniprot ID	Gene name	Protein name	DC	BC	CC	NC
P00533	EGFR	Epidermal growth factor receptor	21	770.763	0.605	14.885
P14780	MMP9	Matrix metalloproteinase-9	17	345.117	0.548	11.266
P13501	CCL5	C-C motif chemokine 5	13	147.389	0.511	8.276
P37231	PPARG	Peroxisome proliferator-activated receptor gamma	13	442.807	0.511	8.168
P42224	STAT1	Signal transducer and activator of transcription 1-alpha/beta	12	71.940	0.489	8.239
P08631	HCK	Tyrosine-protein kinase HCK	11	45.583	0.451	7.680
P43405	SYK	Tyrosine-protein kinase SYK	10	42.626	0.474	7.278
P45983	MAPK8	Mitogen-activated protein kinase 8	9	43.238	0.479	5.011
P07858	CTSB	Cathepsin B	9	163.344	0.465	4.869
P15153	RAC2	Ras-related C3 botulinum toxin substrate 2	9	101.000	0.434	4.768
O60674	JAK2	Tyrosine-protein kinase JAK2	8	84.075	0.474	4.629
P04818	TYMS	Thymidylate synthase	7	306.522	0.438	4.417

Supplement Table 3. The list of genes contributing to the the 20 selected pathways.

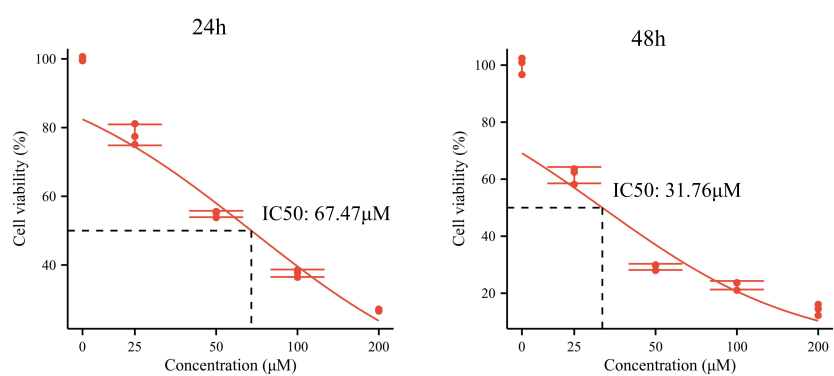
ID	Description	Gene
hsa05171	Coronavirus disease - COVID-19	CFD/EGFR/MMP3/MAPK8/SYK/MMP1/STAT1/PIK3R1
hsa05417	Lipid and atherosclerosis	PPARG/MMP3/MAPK8/MMP9/JAK2/CCL5/MMP1/PIK3R1
hsa04062	Chemokine signaling pathway	RAC2/ITK/HCK/JAK2/CCL5/STAT1/PIK3R1
hsa05167	Kaposi sarcoma-associated herpesvirus infection	MAPK8/SYK/HCK/JAK2/STAT1/PIK3R1
hsa04926	Relaxin signaling pathway	EGFR/MAPK8/MMP9/MMP13/MMP1/PIK3R1
hsa04380	Osteoclast differentiation	PPARG/LCK/MAPK8/SYK/STAT1/PIK3R1
hsa04657	IL-17 signaling pathway	MMP3/MAPK8/MMP9/MMP13/MMP1/S100A9
hsa05235	PD-L1 expression and PD-1 checkpoint pathway in cancer	EGFR/LCK/JAK2/ZAP70/STAT1/PIK3R1
hsa04024	cAMP signaling pathway	PDE4B/PDE4D/MAPK8/RAC2/PIK3R1
hsa05152	Tuberculosis	MAPK8/SYK/JAK2/CTSS/STAT1
hsa05161	Hepatitis B	MAPK8/MMP9/JAK2/STAT1/PIK3R1
hsa04630	JAK-STAT signaling pathway	PIM1/EGFR/JAK2/STAT1/PIK3R1
hsa05135	Yersinia infection	LCK/MAPK8/RAC2/ZAP70/PIK3R1
hsa04650	Natural killer cell mediated cytotoxicity	LCK/SYK/RAC2/ZAP70/PIK3R1
hsa04668	TNF signaling pathway	MMP3/MAPK8/MMP9/CCL5/PIK3R1
hsa04659	Th17 cell differentiation	LCK/MAPK8/JAK2/ZAP70/STAT1
hsa04660	T cell receptor signaling pathway	LCK/MAPK8/ITK/ZAP70/PIK3R1
hsa04933	AGE-RAGE signaling pathway in diabetic complications	PIM1/MAPK8/JAK2/STAT1/PIK3R1
hsa04658	Th1 and Th2 cell differentiation	LCK/MAPK8/JAK2/ZAP70/STAT1
hsa05212	Pancreatic cancer	EGFR/MAPK8/RAC2/STAT1/PIK3R1

Supplement Table 4. Primer sequences for all genes.

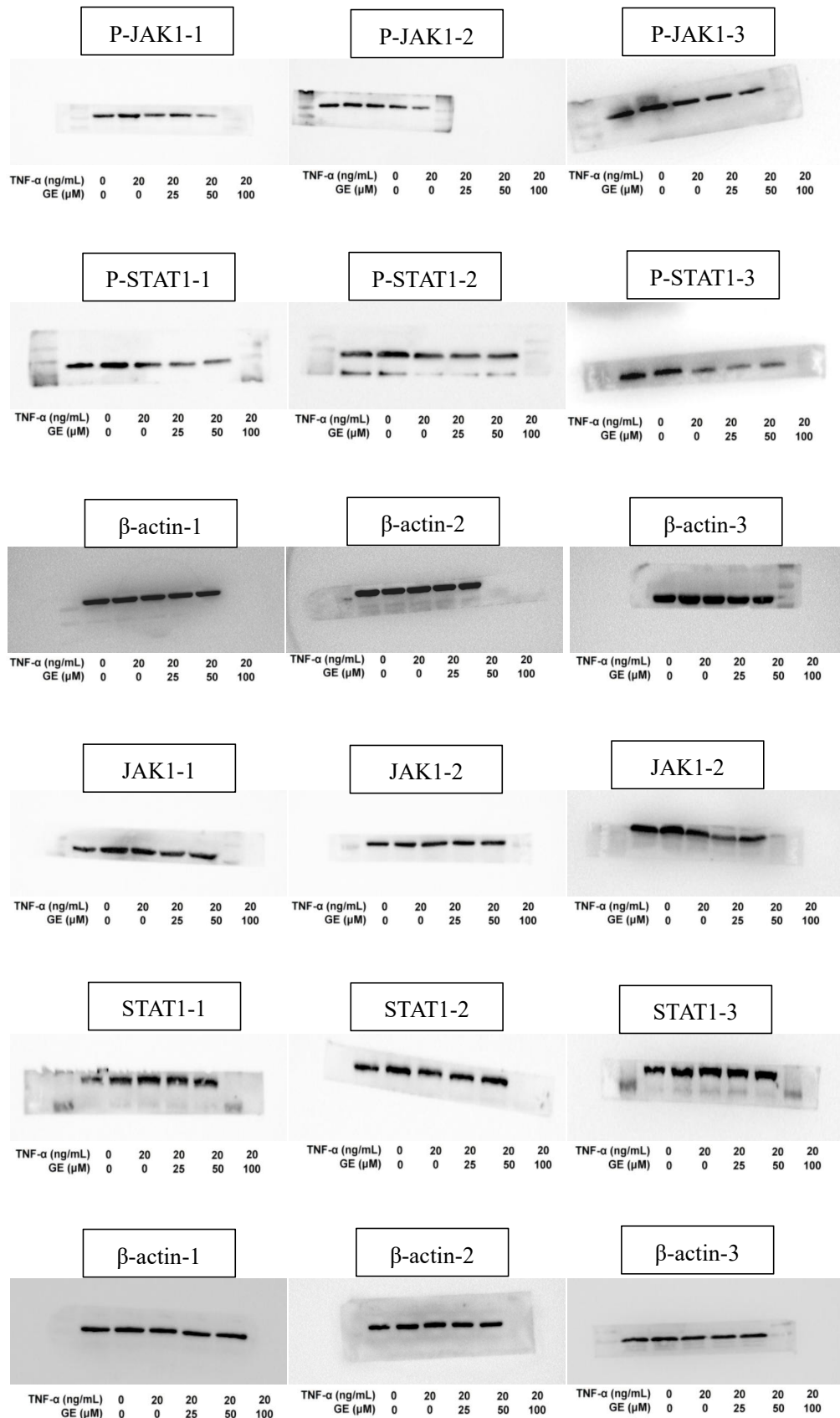
Gene Symbol	NCBI ID		Sequences (5'-3')
EGFR	1956	F	AGGCACGAGTAACAAGCTCAC
		R	ATGAGGACATAACCAGCCACC
MMP9	4318	F	TGTACCGCTATGGTTACACTCG
		R	GGCAGGGACAGTTGCTTCT
CCL5	6352	F	CCAGCAGTCGTCTTTGTCAC
		R	CTCTGGGTTGGCACACACTT
PPARG	5468	F	GGGATCAGCTCCGTGGATCT
		R	TGCACTTTGGTACTCTTGAAGTT
STAT1	6772	F	CAGCTTGACTCAAAATTCCTGGA
		R	TGAAGATTACGCTTGCTTTTCCT
HCK	3055	F	CCCTGTATGATTACGAGGCCA
		R	CACTCCCCGGATTCCCTCTAGG
SYK	6850	F	CATGGAAAAATCTCTCGGGAAGA
		R	GTCGATGCGATAGTGCAGCA
MAPK8	5599	F	TGTGTGGAATCAAGCACCTTC
		R	AGGCGTCATCATAAACTCGTTC
CTSB	1508	F	GAGCTGGTCAACTATGTCAACA
		R	GCTCATGTCCACGTTGTAGAAGT
RAC2	5880	F	CAACGCCTTTCCCGGAGAG
		R	TCCGTCTGTGGATAGGAGAGC
JAK2	3717	F	TCTGGGGAGTATGTTGCAGAA
		R	AGACATGGTTGGGTGGATACC
TYMS	7298	F	CTGCTGACAACCAAACGTGTG
		R	GCATCCCAGATTTTCACTCCCTT
β-Actin	60	F	ACCCAGAAGACTGTGGATGGC
		R	TCAGATCCACGACGGACACAT



Supplement Figure 1. The PPI network of 53 common targets.(Removing unconnected targets)



Supplement Figure 2. IC50 experiment of RA-FLS cells treated with GE for 24 and 48 hours..



Supplement Figure 3. The original immunoblot images of JAK/STAT signaling pathway. The experiment was independently repeated three times.