

Supplemental Table SI. The drug library and drug concentrations

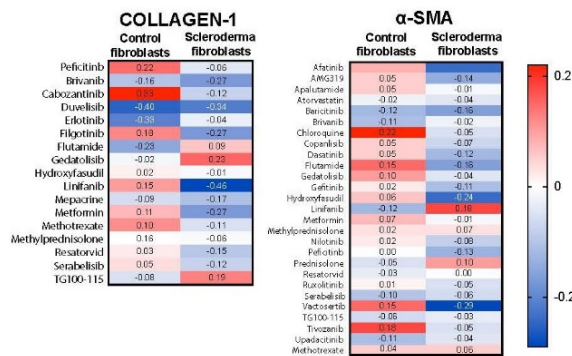
	Drug	Solvent	Concentrations (nM)	Approval status	Mechanism of action	Manufacturer	Cat.No
1	Tacrolimus	DMSO	1,10,100,1000,10000	Approved	Binds FKBP12, causes inhibition of calcineurin	Tocris Biosciences	3631
2	Decitabine	DMSO	1,10,100,1000,10000	Approved	Nucleoside analog DNA methyl transferase inhibitor	Selleck Chemicals	S1200
3	Everolimus	DMSO	0.01,0.1,1,10,100	Approved	Binds FKBP12, causes inhibition of mTORC1	Selleck Chemicals	S1120
4	Olaparib	DMSO	1,10,100,1000,10000	Approved	PARP inhibitor	Medchem Express	HY-10162
5	Sirolimus	DMSO	0.01,0.1,1,10,100	Approved	Binds FKBP12, causes inhibition of mTORC1	LC Laboratories	R-5000
6	Rucaparib	DMSO	1,10,100,1000,10000	Approved	PARP inhibitor	Axon Medchem	1529
7	Pirfenidone	DMSO	1,10,100,1000,10000	Approved	Antifibrotic and anti-inflammatory	ChemieTek	CT-PIRF
8	Acitretin	DMSO	1,10,100,1000,10000	Approved	Retinoid receptor agonist	Medchem Express	HY-B0107
9	Bexarotene	DMSO	1,10,100,1000,10000	Approved	Antineoplastic agent; retinoid specifically selective for retinoid X receptors	Selleck Chemicals	S2098
10	Hydroxyurea	DMSO	100,1000,10000,100000,1000000	Approved	Antineoplastic agent	Sigma-Aldrich	H8627
11	Bicalutamide	DMSO	1,10,100,1000,10000	Approved	Nonsteroidal antiandrogen	ChemieTek	CT-BIC
12	Azacitidine	DMSO	1,10,100,1000,10000	Approved	DNMT inhibitor	Medchem Express	HY-10586
13	Thalidomide	DMSO	1,10,100,1000,10000	Approved	Immunosuppressant	Medchem Express	HY-14658
14	Imiquimod	DMSO	0.25,2.5,25,250,2500	Approved	Immunomodulatory agent	Medchem Express	HY-B0180
15	Thioguanine	DMSO	1,10,100,1000,10000	Approved	Antimetabolite; Purine analog	Medchem Express	HY-13765
16	Mercaptopurine	DMSO	1,10,100,1000,10000	Approved	Antimetabolite	Medchem Express	HY-13677
17	Tretinoin	DMSO	1,10,100,1000,10000	Approved	Retinoic acid receptor agonist	Medchem Express	HY-14649
18	Fluorouracil	DMSO	1,10,100,1000,10000	Approved	Antimetabolite	Medchem Express	HY-90006
19	Dexamethasone	DMSO	1,10,100,1000,10000	Approved	Immunosuppressant	Selleck Chemicals	S1322
20	Auranofin	DMSO	0.25,2.5,25,250,2500	Approved	Antirheumatic agent	Medchem Express	HY-B1123
21	Allopurinol	DMSO	1,10,100,1000,10000	Approved	Xanthine oxidase inhibitor	Medchem Express	HY-B0219
22	Simvastatin	DMSO	1,10,100,1000,10000	Approved	HMG CoA reductase inhibitor	Medchem Express	HY-17502
23	Osimertinib	DMSO	0.25,2.5,25,250,2500	Approved	EGFR(L858R/T790M) inhibitor	Selleck Chemicals	S7297
24	Axitinib	DMSO	1,10,100,1000,10000	Approved	VEGFR, PDGFR, KIT inhibitor	LC Laboratories	A-1107

25	Nintedanib	DMSO	1,10,100,1000,10000	Approved	VEGFR, PDGFR, FGFR inhibitor	Selleck Chemicals	S1010-2
26	Enzalutamide	DMSO	1,10,100,1000,10000	Approved	AR antagonist	Medchem Express	HY-70002-2
27	Vandetanib	DMSO	0.1,1,10,100,1000	Approved	VEGFR,EGFR, RET inhibitor	LC Laboratories	V-9402
28	Ripasudil	DMSO	1,10,100,1000,10000	Approved	ROCK inhibitor	Selleck Chemicals	S7995
29	Lovastatin	DMSO	1,10,100,1000,10000	Approved	HMG-CoA reductase inhibitor	Selleck Chemicals	S2061
30	Apatinib	DMSO	1,10,100,1000,10000	Investigational (Ph 3)	VEGFR inhibitor	Selleck Chemicals	S2221
31	Pazopanib	DMSO	1,10,100,1000,10000	Approved	VEGFR, PDGFR, cKIT inhibitor	Selleck Chemicals	S3012
32	Vatalanib	DMSO	1,10,100,1000,10000	Investigational (Ph 2)	VEGFR-1 & -2 inhibitor	LC Laboratories	V-8303
33	Itraconazole	DMSO	0.5,5,50,500,5000	Approved	Antifungal, hedgehog signaling inhibitor	Selleck Chemicals	S2476
34	Idelalisib	DMSO	1,10,100,1000,10000	Approved	PI3K inhibitor, p110 δ -selective	ChemieTek	CT-CAL101-2
35	Nilutamide	DMSO	1,10,100,1000,10000	Approved	Nonsteroidal antiandrogen	Santa Cruz Biotechnology	sc-203644
36	Bosutinib	DMSO	1,10,100,1000,10000	Approved	Abl, Src inhibitor	LC Laboratories	B-1788
37	Lenvatinib	DMSO	0.25,2.5,25,250,2500	Approved	VEGFR inhibitor	Selleck Chemicals	S1164
38	Hydroxyfasudil	DMSO	1.9,19,190,1900,19000	Approved	ROCK, PKA, PKG, PRK inhibitor	Santa Cruz Biotechnology	sc-202176
39	Afatinib	DMSO	0.1,1,10,100,1000	Approved	EGFR inhibitor	Selleck Chemicals	S1011-3
40	Erlotinib	DMSO	1,10,100,1000,10000	Approved	EGFR inhibitor	Medchem Express	HY-50896
41	Flutamide	DMSO	1,10,100,1000,10000	Approved	Nonsteroidal antiandrogen	Tocris Biosciences	4094
42	Atorvastatin	DMSO	1,10,100,1000,10000	Approved	HMG CoA reductase inhibitor	Medchem Express	HY-17379
43	Nilotinib	DMSO	1,10,100,1000,10000	Approved	BCR/Abl inhibitor	LC Laboratories	N-8207
44	Dasatinib	DMSO	0.1,1,10,100,1000	Approved	BCR/Abl, Src, Kit, EphR... Inhibitor	LC Laboratories	D-3307
45	Gefitinib	DMSO	1,10,100,1000,10000	Approved	EGFR inhibitor	LC Laboratories	G-4408
46	Tivozanib	DMSO	1,10,100,1000,10000	Investigational (Ph 3)	VEGFR1, 2, 3, c-Kit, PDGFRB inhibitor	LC Laboratories	G-4408
47	Ruxolitinib	DMSO	1,10,100,1000,10000	Approved	JAK1&2 inhibitor	ChemieTek	CT-INCB-2
48	Tofacitinib	DMSO	0.5,5,50,500,5000	Approved	JAK3, JAK2(V617F) inhibitor	LC Laboratories	T-1377
49	Cabozantinib	DMSO	0.1,1,10,100,1000	Approved	VEGFR2, Met, FLT3, Tie2, Kit and Ret inhibitor	ChemieTek	CT-XL184
50	Linifanib	DMSO	0.1,1,10,100,1000	Investigational (Ph 3)	VEGFR, PDGFR, CSF-1R, FLT3 inhibitor	Selleck Chemicals	S1003
51	Taselisib	DMSO	0.1,1,10,100,1000	Investigational (Ph 3)	PI3K alpha, gamma selective inhibitor	Medchem Express	HY-13898

52	Brivanib	DMSO	0.1,1,10,100,1000	Investigational (Ph 3)	VEGFR inhibitor	Selleck Chemicals	S1084
53	Peficitinb	DMSO	0.25,2.5,25,250,2500	Investigational (Ph 3)	JAK3-selective inhibitor	Selleck Chemicals	S7650
54	Decernotinib	DMSO	1,10,100,1000,10000	Investigational (Ph 3)	JAK3 inhibitor	ChemieTek	CT-DECE
55	Duvelisib	DMSO	0.05,0.5,5,50,500	Approved	PI3K inhibitor	Selleck Chemicals	S7028
56	Upadacitinib	DMSO	1,10,100,1000,10000	Approved	JAK1-selective inhibitor	Medchem Express	HY-19569
57	Umbralisib	DMSO	0.25,2.5,25,250,2500	Approved	PI3Kdelta inhibitor	Medchem Express	HY-12279
58	Galunisertib	DMSO	0.1,1,10,100,1000	Investigational (Ph 3)	TGF-B/Smad inhibitor	Selleck Chemicals	S2230
59	Copanlisib	DMSO	0.1,1,10,100,1000	Approved	PI3K alpha, beta selective inhibitor	Selleck Chemicals	S2802-2
60	Gedatolisib	DMSO	0.1,1,10,100,1000	Investigational (Ph 2)	PI3K/mTOR inhibitor	Selleck Chemicals	S2628
61	Alpelisib	DMSO	0.25,2.5,25,250,2500	Approved	PI3Kalpha inhibitor	Selleck Chemicals	S2814
62	TG100-115	DMSO	1,10,100,1000,10000	Investigational (Ph 2)	PI3K gamma/delta inhibitor	Selleck Chemicals	S1352
63	Baricitinib	DMSO	0.25,2.5,25,250,2500	Approved	JAK inhibitor	Selleck Chemicals	S2851
64	Serabelisib	DMSO	1,10,100,1000,10000	Investigational (Ph 2)	PI3Kalpha selective inhibitor	Medchem Express	HY-12285
65	Filgotinib	DMSO	1,10,100,1000,10000	Approved	JAK1-selective inhibitor	Selleck Chemicals	S7605
66	AMG319	DMSO	0.1,1,10,100,1000	Investigational (Ph 2)	PI3Kdelta inhibitor	Selleck Chemicals	S7813
67	Apalutamide	DMSO	1,10,100,1000,10000	Approved	AR antagonist	Axon Medchem	1979
68	Vactosertib	DMSO	0.25,2.5,25,250,2500	Investigational (Ph 2)	TGF- β receptor ALK4/ALK5 inhibitor	Selleck Chemicals	S7530
69	Resatorvid	DMSO	1,10,100,1000,10000	Investigational (Ph 3)	TLR4 inhibitor	Medchem Express	HY-11109
70	Niraparib	DMSO	1,10,100,1000,10000	Approved	PARP inhibitor	Medchem Express	HY-10619
71	Talazoparib	DMSO	0.1,1,10,100,1000	Approved	PARP1/2 inhibitor	Medchem Express	HY-16106
72	Chloroquine	AQ	10,100,1000,10000,100000	Approved	Antimalaria agent; chemo/radio sensitizer	Sigma-Aldrich	C6628
73	Mepacrine	AQ	5,50,500,5000,50000	Approved	Unclear. PLA2 inhibitor. NF-kB inhibitor, p53 activator	Sigma-Aldrich	Q3251
74	Pravastatin	AQ	1,10,100,1000,10000	Approved	HMG CoA reductase inhibitor	Tocris Biosciences	2318
75	Metformin	AQ	10,100,1000,10000,100000	Approved	AMPK activator/mTOR/PI3K inhibitor	Tocris Biosciences	2864
76	Methylprednisolone	DMSO	1,10,100,1000,10000	Approved	Immunosuppressant	Santa Cruz Biotechnology	sc-205749
77	Prednisolone	DMSO	1,10,100,1000,10000	Approved	Immunosuppressant	Santa Cruz Biotechnology	sc-205815
78	Methotrexate	DMSO	0.5,5,50,500,5000	Approved	Antimetabolite; Anti-folate agent	Selleck Chemicals	S1210

Supplemental Figure S1. Spearman correlation analysis of drug effects on collagen-1 and α -SMA expression in fibroblasts from scleroderma patient 3 and control person 3. (A) Heatmaps showing Spearman correlation coefficients for selected drug hits based on collagen-1 and α -SMA mean intensity values across increasing drug concentrations. (B) Table listing drugs with negative Spearman correlations in both markers (collagen-1 and α -SMA).

(A) Spearman correlation



(B) Relevant drug hits from both markers

Control fibroblasts		
Drug	α -SMA p-value	Collagen-1 p-value
Erlotinib	1.67e-114	0.00
TG100-115	7.89 e-12	1.96e-22
Brivanib	1.99e-43	5.15e-92

Scleroderma fibroblasts		
Drug	α -SMA p-value	Collagen-1 p-value
Peficitinib	1.21e-114	1.18e-27
Methylprednisolone	2.01e-110	4.60e-3
Hydroxyfasudil	0.00	3.59e-2
Serabelisib	3.59e-23	5.73e-98
Brivanib	2.99e-3	0.00