

Supplementary Table 1. Cell line and Reagents information

Name	Source (Vender)	Identifier
HDFn (Human Neonatal Dermal Fibroblast)	ATCC	PCS-201-010
DMEM, high glucose, HEPES	Thermo Fischer Scientific	12430-054
P/S	Thermo Fischer Scientific	15140-122
Primocin	Invivogen	ant-pm-2
Senescence β -Galactosidase Staining Kit	Cell Signaling	9860
4-Methylumbelliferyl α -L-fucopyranoside	Dextra	UM004
Passive Lysis Buffer	Promega	E194A
cOmplete™ Protease Inhibitor Cocktail	Roche	11697498001
Citrate Buffer 0.5M, pH 4.5, Sterile	bioWORLD	40320055-1
Hoechst 33342	Thermo Fischer Scientific	62249
CellTiter-Glo® 3D Cell Viability Assay	Promega	G9683
TrypLE™ Express Enzyme (1X), phenol red	Gibco™	12605028
PrimeScript™ 1st strand cDNA Synthesis Kit	Takara	6110A
SYBR® Green Realtime PCR Master Mix	TOYOBO	QPK-201
Cultrex Reduced Growth Factor Basement Membrane Extract	R&D systems	3533-010-02
Sodium carbonate	Sigma-Aldrich	1003571210
AllPrep DNA/RNA Mini Kit	Qiagen	80204

Supplementary Table 2. Drug information

Name	Source (Vendor)	Identifier	Primary target	Annotated mechanism/class
JQ1	Selleckchem	Cat# S7110	BET bromodomain proteins (BRD2/3/4)	BET bromodomain inhibitor
Ibrutinib	Selleckchem	Cat# S2680	BTk	BTk inhibitor
Cyclophosphamide	Selleckchem	Cat# S2057	DNA	DNA alkylating agent
Gefitinib	Selleckchem	Cat# S1025	EGFR	EGFR inhibitor
Genistein	Selleckchem	Cat# S1342	Protein tyrosine kinases (broad)	Broad-spectrum tyrosine kinase inhibitor / isoflavone
Vorinostat	Selleckchem	Cat# S1047	HDAC1/2/3/6	Histone deacetylase inhibitor
Adagrasib	Selleckchem	Cat# S8884	KRAS G12C	KRAS G12C inhibitor
Sotorasib	Selleckchem	Cat# S8830	KRAS G12C	KRAS G12C inhibitor
Nutlin-3	Selleckchem	Cat# S1061	MDM2	MDM2-p53 interaction inhibitor
Binimetinib	Selleckchem	Cat# S7007	MEK1/2	MEK1/2 inhibitor
Ulixertinib	Selleckchem	Cat# S7854	ERK1/2	ERK1/2 inhibitor
Tivantinib	Selleckchem	Cat# S2753	c-MET; microtubules	MET inhibitor; microtubule-disrupting activity
Savolitinib	Selleckchem	Cat# S7674	MET	Selective MET inhibitor
Tazemetostat	Selleckchem	Cat# S7128	EZH2	EZH2 methyltransferase inhibitor
Resveratrol	Selleckchem	Cat# S1396	SIRT1 / AMPK-associated signaling	Polyphenol; pleiotropic signaling modulator
Epacadostat	Selleckchem	Cat# S7910	IDO1	IDO1 inhibitor
APR-246	Selleckchem	Cat# S7724	Mutant p53 / cellular thiols	Mutant p53 reactivator / redox modulator
RO4929097	Selleckchem	Cat# S1575	γ -secretase / Notch	γ -secretase inhibitor; Notch pathway inhibitor
Crenigacestat	Selleckchem	Cat# S7169	γ -secretase / Notch	γ -secretase inhibitor; Notch pathway inhibitor
Fluorouracil	Selleckchem	Cat# S1209	Thymidylate synthase / RNA-DNA synthesis	Antimetabolite; fluoropyrimidine
Folinic acid	Selleckchem	Cat# S5790	Reduced folate pathway	Reduced folate rescue agent; 5-FU modulator
Raltitrexed	Selleckchem	Cat# S1192	Thymidylate synthase	Thymidylate synthase inhibitor
Niraparib	Selleckchem	Cat# S7625	PARP1/2	PARP inhibitor
Talazoparib	Selleckchem	Cat# S7048	PARP1/2	PARP inhibitor
Sorafenib	Selleckchem	Cat# S1040	RAF / VEGFR / PDGFR / FLT3 / KIT	Multikinase inhibitor
Vemurafenib	Selleckchem	Cat# S1267	BRAF V600	BRAF inhibitor
Dabrafenib	Selleckchem	Cat# S2807	BRAF	BRAF inhibitor
Vismodegib	Selleckchem	Cat# S1082	SMO	Hedgehog pathway inhibitor
Napabucasin	Selleckchem	Cat# S7977	STAT3 / cancer stemness	STAT3 inhibitor; cancer stemness inhibitor
Irinotecan HCl	Selleckchem	Cat# S2217	Topoisomerase I	Topoisomerase I inhibitor
Larotrectinib	Selleckchem	Cat# S7960	TRK (NTRK1/2/3)	TRK inhibitor
Regorafenib	Selleckchem	Cat# S1178	VEGFR / TIE2 / PDGFR / FGFR / RAF / KIT / RET	Multikinase inhibitor
Vandetanib	Selleckchem	Cat# S1046	VEGFR2 / EGFR / RET	Multikinase inhibitor
Lenvatinib	Selleckchem	Cat# S1164	VEGFR1/2/3 / FGFR1/2/3/4 / PDGFR α / RET / KIT	Multikinase inhibitor
OSI-930	Selleckchem	Cat# S1220	KIT / VEGFR2 (KDR) / PDGFR β	Multikinase inhibitor
LGK-974	Selleckchem	Cat# S7143	PORCN	Porcupine inhibitor; Wnt secretion inhibitor
Carboplatin	Adooq	Cat# A10182	DNA	Platinum-based DNA crosslinking agent
Oxaliplatin	Adooq	Cat# A10346	DNA	Platinum-based DNA crosslinking agent
KU-60019	Selleckchem	Cat# S1570	ATM	ATM inhibitor

Supplementary Table 3. Software and algorithms

Name	Source (Vendor)	Identifier
Gen5	Agilent	3.14
R	The R Foundation	4.3.0
ggplot2	Tidyverse team	4.0.0
GGally	Barret Schloerke	2.2.1
ggpubr	Alboukadel Kassambara	0.6.0

Supplementary Table 4. Drug class and qCAI value

Drug	Class	qCAI
Lenvatinib	Senolytic-like	5.3287
Dabrafenib	Pro-aging-like	8.5055
Regorafenib	Pro-aging-like	13.5501
Napabucasin	Cytotoxic	15.7322
Ulixertinib	Cytotoxic	26.2941
Oxaliplatin	Cytotoxic	46.2710
Binimetinib	Cytotoxic	56.9593
Sorafenib	Pro-aging-like	74.0922
OSI-930	Pro-aging-like	76.6148
Vandetanib	Pro-aging-like	78.9205
Gefitinib	Pro-aging-like	92.6806
Ibrutinib	Pro-aging-like	107.7591
Tazemetostat	Pro-aging-like	115.3752
JQ1	Cytotoxic	126.3965
APR-246	Pro-aging-like	147.9426
Cyclophosphamide	Pro-aging-like	148.8081
Fluorouracil	Pro-aging-like	150.9848
Tivantinib	Cytotoxic	157.5525
Resveratrol	Pro-aging-like	163.1568
Crenigacestat	Pro-aging-like	166.1072
Vorinostat	Cytotoxic	179.9378
RO4929097	Pro-aging-like	188.3859
Adagrasib	Pro-aging-like	191.4255
Larotrectinib	Pro-aging-like	193.1884
Vismodegib	Pro-aging-like	200.8738
Nutlin-3	Cytotoxic	210.0811
Folinic acid	Pro-aging-like	210.9772
Savolitinib	Pro-aging-like	214.7543
Genistein	Pro-aging-like	215.7366
Niraparib	Pro-aging-like	222.0918
LGK-974	Pro-aging-like	226.3963
Talazoparib	Cytotoxic	227.9284
Epacadostat	Pro-aging-like	236.5985
Raltitrexed	Pro-aging-like	248.0886
Vemurafenib	Pro-aging-like	266.0141
Carboplatin	Cytotoxic	278.2139
Irinotecan HCl	Cytotoxic	283.9452
Sotorasib	Pro-aging-like	330.6644
KU-60019	Anti-aging-like	814.6177