

Supplementary Table 1. DNA sequences of expression constructs and CRISPR guides

DNA Name	DNA Sequence
Reporter constructs	
<i>IDH2-C-VN210</i>	<p>ATGGCCGGCTACCTGCGGGTCTGTCGCTCGCTCTGCAGAGCCTCAGGCTCGCGGCCGGCCTGGG CGCCGGCGGCCCTGACAGCCCCACCTCGCAAGAGCAGCCGCGGCCACTATGCCGACAAAAG GATCAAGGTGGCGAAGCCCGTGGTGGAGATGGATGGTATGAGATGACCCGTATTATCTGGCAGTT CATCAAGGAGAAGCTCATCCTGCCCCACGTGGACATCCAGCTAAAGTATTTTGACCTCGGGCTCCC AAACCGTGACCAGACTGATGACCAGGTACCATTGACTCTGCACTGGCCACCCAGAAGTACAGTGT GGCTGTCAAGTGTGCCACCATACCCCTGATGAGGCCCGTGTGGAAGAGTTCAAGCTGAAGAAGAT GTGGAAAAGTCCCAATGGAACATCCGGAACATCCTGGGGGGGACTGTCTTCCGGGAGCCCATCAT CTGCAAAAACATCCCACGCCCTAGTCCCTGGCTGGACCAAGCCCATCACCATTGGCAGGCACGCCA TGGCGACCAGTACAAGGCCACAGACTTTGTGGCAGACCCGGCCGGCATTTCAAAATGGTCTTCAC CCCAAAAGATGGCAGTGGTGTCAAGGAGTGGGAAGTGTACAACCTCCCCGAGGCCGGCGTGGGCA TGGGCATGTACAACACCGACGAGTCCATCTCAGGTTTTGCGCACAGCTGCTTCCAGTATGCCATCC AGAAGAAATGGCCGCTGTACATGAGCACCAAGAACCATACTGAAAGCCTACGATGGGCGTTTTCA AGGACATCTTCCAGGAGATCTTTGACAAGCACTATAAGACCGACTTCGACAAGAATAAGATCTGGTA TGAGCACCGGCTCATTGATGACATGGTGGCTCAGGTCCTCAAGTCTTCCGGGTGGCTTTGTGTGGGC CTGCAAGAACTATGACGGAGATGTGCAGTCAGACATCCTGGCCCAGGGCTTTGGCTCCCTTGGCCT GATGACGTCCTGCTGGTCTGCCCTGATGGGAAGACGATTGAGGCTGAGGCCGCTCATGGGACCCG TCACCCGCCACTATCGGGAGCACCAGAAGGGCCGGCCACCAGCACCAACCCCATCGCCAGCATC TTTGCCTGGACACGTGGCCTGGAGCACCGGGGGAAGCTGGATGGGAACCAAGACCTCATCAGGTT TGCCCAGATGCTGGAGAAGGTGTGCGTGGAGACGGTGGAGAGTGGAGCCATGACCAAGGACCTG GCGGGCTGCATTACGGCCTCAGCAATGTGAAGCTGAACGAGCACTTCTGAACACCACGGACTTC CTCGACACCATCAAGAGCAACCTGGACAGACCCTGGGCAGGCAGGGCGGAGGTGGGAGCGGTG GAGGGGGAAGTGTGAGCAAGGGCGAGGAGCTGTTACCGGGGTGGTGGCCATCCTGGTTCGAGCT GGACGGCGACGTAACGGCCACAAGTTGAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTAC GGCAAGCTGACCCTGAAGCTGATCTGCACCACCGGCAAGCTGCCCGTGCCTTGGCCACCCTCGT GACCACCCTGGGCTACGGCCTGCAGTCTTCCCGCTACCCCGACACATGAAGCAGCACGACT TCTTCAAGTCCGCCATGCCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACACGGCA ACTACAAGACCCGCGCGGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAG GGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACATAACAGCCA CAACGTCTATATCACCGCCGACAAGCAGAAGAACGGCATCAAGGCCAACTTCAAGATCCGCCACAA CATCGAGGACGGCGGCGTGCAGCTCGCCGACCCTACCCAGCAGAACAACCCCATCGGCAGCGCC CCCGTGTCTGCTGCCCGACAACCACTACCTGAGCTACCAGTCCAAGCTGAGCAAAGACTAG</p>
<i>IDH2-C-VC210</i>	<p>ATGGCCGGCTACCTGCGGGTCTGTCGCTCGCTCTGCAGAGCCTCAGGCTCGCGGCCGGCCTGGG CGCCGGCGGCCCTGACAGCCCCACCTCGCAAGAGCAGCCGCGGCCACTATGCCGACAAAAG GATCAAGGTGGCGAAGCCCGTGGTGGAGATGGATGGTATGAGATGACCCGTATTATCTGGCAGTT CATCAAGGAGAAGCTCATCCTGCCCCACGTGGACATCCAGCTAAAGTATTTTGACCTCGGGCTCCC AAACCGTGACCAGACTGATGACCAGGTACCATTGACTCTGCACTGGCCACCCAGAAGTACAGTGT GGCTGTCAAGTGTGCCACCATACCCCTGATGAGGCCCGTGTGGAAGAGTTCAAGCTGAAGAAGAT GTGGAAAAGTCCCAATGGAACATCCGGAACATCCTGGGGGGGACTGTCTTCCGGGAGCCCATCAT CTGCAAAAACATCCCACGCCCTAGTCCCTGGCTGGACCAAGCCCATCACCATTGGCAGGCACGCCA TGGCGACCAGTACAAGGCCACAGACTTTGTGGCAGACCCGGCCGGCATTTCAAAATGGTCTTCAC CCCAAAAGATGGCAGTGGTGTCAAGGAGTGGGAAGTGTACAACCTCCCCGAGGCCGGCGTGGGCA TGGGCATGTACAACACCGACGAGTCCATCTCAGGTTTTGCGCACAGCTGCTTCCAGTATGCCATCC AGAAGAAATGGCCGCTGTACATGAGCACCAAGAACCATACTGAAAGCCTACGATGGGCGTTTTCA AGGACATCTTCCAGGAGATCTTTGACAAGCACTATAAGACCGACTTCGACAAGAATAAGATCTGGTA TGAGCACCGGCTCATTGATGACATGGTGGCTCAGGTCCTCAAGTCTTCCGGGTGGCTTTGTGTGGGC CTGCAAGAACTATGACGGAGATGTGCAGTCAGACATCCTGGCCCAGGGCTTTGGCTCCCTTGGCCT GATGACGTCCTGCTGGTCTGCCCTGATGGGAAGACGATTGAGGCTGAGGCCGCTCATGGGACCCG TCACCCGCCACTATCGGGAGCACCAGAAGGGCCGGCCACCAGCACCAACCCCATCGCCAGCATC TTTGCCTGGACACGTGGCCTGGAGCACCGGGGGAAGCTGGATGGGAACCAAGACCTCATCAGGTT TGCCCAGATGCTGGAGAAGGTGTGCGTGGAGACGGTGGAGAGTGGAGCCATGACCAAGGACCTG GCGGGCTGCATTACGGCCTCAGCAATGTGAAGCTGAACGAGCACTTCTGAACACCACGGACTTC CTCGACACCATCAAGAGCAACCTGGACAGACCCTGGGCAGGCAGGGCGGAGGTGGGAGCGGTG GAGGGGGAAGTGAACCAACGAGAAGCGGATCACATGGTCTGCTGGAGTTCGTGACCGCCGCC GGGATCACTCTCGGCATGGACGAGCTGTACAAGTAG</p>

<p><i>UQCRB-C-VN210</i></p>	<p>ATGGCTGGTAAGCAGGCCGTTTCAGCATCAGGCAAGTGGCTGGATGGTATTTCGAAAAATGGTATTAC AATGCTGCAGATTCAATAAACTGGGGTTAATGCGAGATGATACAATATACGAGGATGAAGATGTAA AAGAAGCCATAAGAAGACTTCTGAGAACCCTTATAATGACAGGATGTTTTCGCATTAAGAGGGCCT GGACCTGAACTTGAAGCATCAGATCTTGCCTAAAGAGCAGTGGACCAAATGAAGAGGAAAAATTTCT TACCTTGAACCGTATCTGAAAGAGGTTATTGCGGAAAGAAAAGAAAAGAGAAGAATGGGCAAAGAAG GGCGGAGGTGGGAGCGGTGGAGGGGGAAAGTGTGACCAAGGGCGAGGAGCTGTTACCGGGGGTG GTGCCCATCTGGTCGAGCTGGACGGCGACGTAACGGCCACAAGTTCAGCGTGTCCGGCGGAGG GCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGCTGATCTGCACCACCGCCAAAGCTGCC GTGCCCTGGCCACCCTCGTGACCACCCTGGGCTACGGCCTGCAGTGTTCGCCCGCTACCCCGA CCACATGAAGCAGCAGACTTCTTCAAGTCCGCCATGCCCGAAGGCTACGTCCAGGAGCGCACCAT CTTCTTCAAGGACGACGGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGGCGACACCCTGG TGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCTGGGGCACAAGCTG GAGTACAATAACAAGCCACAACGCTATATCACCGCCGACAAGCAGAAGAACGGCATCAAGGCC AACTTCAAGATCCGCCACAACATCGAGGACGGCGGGCTGCAGCTCGCCGACCACTACCAGCAGAA CACCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCTACCAGTCCAAGC TGAGCAAAGACTAA</p>
<p><i>UQCRC1-C-VN210</i></p>	<p>ATGGCGGCGTCCGTGGTCTGTGCGGGCCGCTACCGCCGGGGCACAAGTGTATTGCGCGCCCGCC GCTCGCCGGCCCTGCTGCGGACGCCAGCCTTGGGAGTACGGCAGTGAGCAAGGGCGAGGAGCT GTTACCGGGGGTGGTCCCATCCTGGTTCGAGCTGGACGGCGACGTAACGGCCACAAGTTCAGCG TGTCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGCTGATCTGCACCACC GGCAAGCTGCCCGTCCCTGGCCACCCCTGACCCCTGGGCTACCGCTGCAGTGTCTTCCG CCGCTACCCCGACCACATGAAGCAGCAGACTTCTTCAAGTCCGCCATGCCCGAAGGCTACGTCCA GGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGAGG GGGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTG GGCACAAGCTGGAGTACAACATAACAGCCACAACGCTTATATCACCGCCGACAAGCAGAAGAAC GGCATCAAGGCCAACTTCAAGATCCGCCACAACATCGAGGACGGCGGGCTGCAGCTCGCCGACCA CTACCAGCAGAACACCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCT ACCAGTCCAAGCTGAGCAAAGACGGCGGAGGTGGGAGCGGTGGAGGGGGAAGTACGGCAACCTT CGCTCAGGGCTCCAGTTCTGTCGGGAGACGAGGTTAGCCTGCTGGACAACCGCCCTGCGTGTGG CCTCCGAGCAGTCTCTCAGCCACTTGCACGGTGGGAGTGTGGATTGATGTTGGCAGCCGTTTTG AGACTGAGAAGAATAATGGGGCAGGCTACTTTTTGGAGCATCTGGCTTTCAGGGAAACAAAGAATC GGCCTGGCAGTGGCCTGGAGAAGGAGGTGGAGGACATGGGGGGCCATCTTAATGCCTACAGCAC CGGGAGCACACAGCTTACTACATCAAGCGCTTCCAAGGATCTGCCGAAAGCTGTGGAGCTCT GGGTGACATTGTGCAGAACTGTAGTCTGGAAGACTCACAGATTGAGAAGGAACGTGATGTGATCCT GCGGGAGATGCAGGAGAATGATGCATCTATGCGAGATGTGGTCTTTAACTACCTGCATGCCACAGC ATTCCAGGGCACACCTCTAGCCAGGCTGTGGAGGGGGCCAGTGAGAATGTCAGGAAGCTGTCTC GTGCAGACTTGACCGAGTACCTCAGCACACATTACAAGGCCCCCTCGAATGGTGTGCCAGCAGCTG GAGGATGGAGCACCCAGCAACTGTTAGACCTCGCCCAAGAGCACCTCGGTGGCATCCCATGGACA TATGCAGAGGACGCTGTGCCACTTACTCCATGCCGCTTCACTGGCAGTGAGATCCGCCACCGT GATGATGCTTACCTTTTGGCCACGTGGCCATTGCAAGTAGAGGGTCTGGCTGGGCCAGCCCGGA CAATGTGGCCTTGAAGTGGCCAATGCCATCATCGGCCACTATGACTGCATATGGTGGTGGCGT GCACCTGTCCAGCCCACTGGCTTCCAGGTGCTGTGGCCAACAAGCTATGCCAGAGTTCCAGACCTT CAGCATCTGCTATGCAGAGACGGGCTTGTGGGTGCACACTTTGTCTGTGACCGAATGAAAATCGA TGACATGATGTTCTGCTGCAAGGGCAGTGGATGCGCCTGTGTACCAGTGCCACGGAGAGTGAGG TGGCCCGGGGCAAAAACATCCTCAGAAATGCCCTGGTATCTCATCTAGATGGCACTACTCCTGTGT GTGAGGACATCGGACGACGCTCTGACCTATGGCCGCGCATCCCCCTGGCTGAATGGGAAAGC CGGATTGCGGAGGTGGATGCCAGTGTGGTACGTGAGATCTGCTCCAAGTACATCTATGACCAAGTC CCAGCAGTGGCTGGATATGGCCCCATTGAGCAGCTCCAGACTACAACCGGATCCGTAGCGGCAT GTTCTGGCTGCGCTTCTAG</p>
<p><i>COX5B-N-VC210</i></p>	<p>ATGGCTTCAAGGTTACTTCGCGGAGCTGGAACGCTGGCCGCGCAGGCCCTGAGGGCTCGCGGCC CCAGTGGCGCGGCCGCGATGCGCTCCATGGCAGACCCCAACGAGAAGCGCGATCACATGGTCTCT GCTGGAGTTCGTGACCGCCGCGGGCGGAGGTGGGAGCGGTGGAGGGGGAAGTATGGCATCTGGA GGTGGTGTCCCACTGATGAAGAGCAGGCGACTGGGTTGGAGAGGGAGATCATGCTGGCTGCAAA GAAGGGACTGGACCCATACAATGTACTGGCCCCAAAGGGAGCTTCAGGCCACCAGGGAAGACCCTA ATTTAGTCCCCTCCATCTCCAACAAGAGAATAGTAGGCTGCATCTGTGAAGAGGACAATACCAGCGT CGTCTGGTTTTGGTGCACAAAGGCGAGGCCAGCGATGCCCCCGCTGTGGAGCCCATACAAGC TGGTGCCCGCAGCAGCTGGCACACTAG</p>
<p><i>COX5B-C-VC210</i></p>	<p>ATGGCTTCAAGGTTACTTCGCGGAGCTGGAACGCTGGCCGCGCAGGCCCTGAGGGCTCGCGGCC CCAGTGGCGCGGCCGCGATGCGCTCCATGGCAGTGGAGGTGGTGTTCCTCACTGATGAAGAGCAG GCGACTGGGTTGGAGAGGGGAGATCATGGCTGCAAAAGAAGGGACTGGACCCATACAATGTACT GGCCCCAAAGGGAGCTTCAGGCACCAGGGAAGACCCTAATTTAGTCCCCTCCATCTCCAACAAGAG AATAGTAGGCTGCATCTGTGAAGAGGACAATACCAGCGTCTGCTGGTTTTGGCTGCACAAAGGCCGA GGCCAGCGATGCCCCCGCTGTGGAGCCATTACAAGCTGGTGGCCAGCAGCTGGCACACGGC GGAGGTGGGAGCGGTGGAGGGGGAAGTGAACCCCAACGAGAAGCGCGATGATGTTCTGCTGG AGTTCGTGACCGCCGCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAG</p>
<p><i>COX7A2L-N-VC210</i></p>	<p>ATGGCTTCAAGGTTACTTCGCGGAGCTGGAACGCTGGCCGCGCAGGCCCTGAGGGCTCGCGGCC CCAGTGGCGCGGCCGCGATGCGCTCCATGGCAGACCCCAACGAGAAGCGCGATCACATGGTCTCT CTGGAGTTCGTGACCGCCGCGGGCGGAGGTGGGAGCGGTGGAGGGGGAAGTATGGCATCTGGA GGTGGTGTCCCACTGATGAAGAGCAGGCGACTGGGTTGGAGAGGGAGATCATGCTGGCTGCAAA GAAGGGACTGGACCCATACAATGTACTGGCCCCAAAGGGAGCTTCAGGCCACCAGGGAAGACCCTA ATTTAGTCCCCTCCATCTCCAACAAGAGAATAGTAGGCTGCATCTGTGAAGAGGACAATACCAGCGT CGTCTGGTTTTGGTGCACAAAGGCGAGGCCAGCGATGCCCCCGCTGTGGAGCCCATACAAGC TGGTGCCCGCAGCAGCTGGCACACTAG</p>

	AGTTCCAGAGCTACAAAAGTTTTCCAGAAAGCTGATGGTGTGCCCGTCTACCTGAAACGAGGCCTGCCTGACCAAATGCTTTACCGGACCACCATGGCGCTGACTGTGGGAGGGACCATCTACTGCCTGATCGCCCTCTACATGGCTTCGCAGCCCAAAAACAATAA
<i>UQCRB-C-LgBit</i>	ATGGCTGGTAAGCAGGCCGTTTCAGCATCAGGCAAGTGGCTGGATGGTATTGAAAAATGGTATTAC AATGCTGCAGGATTCAATAAACTGGGGTTAATGCGAGATGATACAATATACGAGGATGAAGATGTAA AAGAAGCCATAAGAAGACTTCTGAGAACCTTTATAATGACAGGATGTTTCGCATTAAGAGGGCACT GGACCTGAACTTGAAGCATCAGATCTTGCCTAAAGAGCAGTGGACCAAATGAAGAGGAAAAATTC TACCTTGAACCGTATCTGAAAGAGGTTATTTCGGGAAAGAAAAGAAAAGAGAAGAATGGGCAAAGAAG GGCGGAGGTGGGAGCGGTGGAGGGGGAAGTGTCTTACACTCGAAGATTTCTTGGGGACTGGG AACAGACAGCCGCTACAACCTGGACCAAGTCTTGAACAGGGAGGTGTGTCCAGTTTGTGCAGA ATCTCGCCGTGTCCGTAACCTCCGATCCAAAGGATTGTCCGGAGCGGTGAAAATGCCCTGAAGATCG ACATCCATGTCATCATCCCGTATGAAGGTCTGAGCGCCGACCAAATGGCCAGATCGAAGAGGTGT TTAAGTGGTGTACCCTGTGGATGATCATCACTTTAAGGTGATCCTGCCCTATGGCACACTGGTAAT CGACGGGTTACGCCGAACATGCTGAACTATTTCCGACGGCCGATGAAGGCATCGCCGTGTTCCG ACGGCAAAAAGATCACTGTAACAGGGACCCTGTGGAACGGCAACAAAATTATCGACGAGCGCCTGA TCACCCCGACGGTCCATGCTGTTCCGAGTAACCATCAACAGCTAA
<i>COX5B-N-SmBit</i>	ATGGCTCAAGGTTACTTCGCGGAGCTGGAACGCTGGCCGCGCAGGCCCTGAGGGCTCGCGGCC CCAGTGGCGCGGCCGCGATGCGCTCCATGGCAGTGACCGCTACCGGCTGTTCCAGGAGATTCTC GCGGAGGTGGGAGCGGTGGAGGGGGAAGTATGCGCATCTGGAGGTGGTGTCCCACTGATGAAG AGCAGGCGACTGGGTTGGAGAGGGAGATCATGCTGGTGCAAAGAAGGGACTGGACCCATACAAT GTACTGGCCCCAAAGGGAGCTTCAGGCACCAGGGAAGACCCTAATTTAGTCCCCTCCATCTCCAAC AAGAGAATAGTAGGCTGCATCTGTGAAGAGGACAATACCAGCGTCGTCTGGTTTTGGCTGCACAAA GCGGAGGCCAGCGATGCCCCCGCTGTGGAGCCCATTACAAGCTGGTGGCCAGCAGCTGGCAC ACTAG
<i>COX5B-C-SmBit</i>	ATGGCTCAAGGTTACTTCGCGGAGCTGGAACGCTGGCCGCGCAGGCCCTGAGGGCTCGCGGCC CCAGTGGCGCGGCCGCGATGCGCTCCATGGCAGTGGAGGTGGTGTCCCACTGATGAAGAGCAG GCGAGTGGTTGGAGAGGGGAGATCATGCTGGTGCAAAGAAGGGACTGGACCCATACAATGTACT GGCCCCAAAGGGAGCTTCAGGCACCAGGGAAGACCCTAATTTAGTCCCCTCCATCTCCAACAAGAG AATAGTAGGCTGCATCTGTGAAGAGGACAATACCAGCGTCGTCTGGTTTTGGCTGCACAAAGGCGA GGCCAGCGATGCCCCCGCTGTGGAGCCCATTACAAGCTGGTGGCCAGCAGCTGGCACACGGC GGAGGTGGGAGCGGTGGAGGGGGAAGTGTGACCGCTACCGGCTGTTTCGAGGAGATTCTCTAA

CRISPR sgRNAs	
<i>NTC_F</i>	caccgCTGAAGGTGTCTGGCAGAGC
<i>NTC_R</i>	aaacGCTCTGCCAGACACCTTCAGc
<i>SCAF1_F</i>	caccgGCAGAAGTTGGCAGGAGCAT
<i>SCAF1_R</i>	aaacATGCTCCTGCCAACTTCTGCc
<i>HIGD2A_F</i>	caccgACTTACCTATGGGTACCACC
<i>HIGD2A_R</i>	aaacGGTGGTACCCATAGGTAAGTc
<i>DHODH_F</i>	caccgATCTCCCGTGGCCATCAGGT
<i>DHODH_R</i>	aaacACCTGATGGCCACGGGAGATc
<i>FAR1_F</i>	caccgAGCACTAATCCTTTCCACTG
<i>FAR1_R</i>	aaacCAGTGGAAGGATTAGTGCTc
<i>AGPS_g1_F</i>	caccgCAATTTGACAGCTCATGTAG
<i>AGPS_g1_R</i>	aaacCTACATGAGCTGTCAAATTGc
<i>AGPS_g2_F</i>	caccgGTACCAATGAGTGCAAAGCG
<i>AGPS_g2_R</i>	aaacCGCTTTGCACTCATTGGTACc

Expression constructs	
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*FAR1 (CRISPR
resistant)*

atggttcaatcccagaatactatgaaggcaagaacgtcctcctcacaggagctaccggtttctaggaagggtcctctggaagggtgctgaggtc
ttgtcctaaggtaattcagtatatggttgaggcagaagctggacagacaccaagagcgagtggaagaagtccttagtggcaagcttttg
acagattgagagatgaaaatccagatttagagagaaaattatagcaatcaacagcgaactcaccacctaactggctctcagtgaagaaga
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caagaggaatcctctcgaacaggcctcagacggcccaatgtaaatctaacctccaatcatctttatacattactggattgctgtaagccataaggc
cccagcattcctgtatgatatctacctcaggatgactggaagaagcccaaggatgataaaacaataactcgtctcacaagcctatggtgtttctg
aatattcacaagtaattctgggttgaatactgagaatgtcaaatgttaaatcaactaaacctgaagataaaaagacctcaatattgatgt
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aaaaatctgaacaagttgcggaatatacgttatggtttaatactatcctgtgatcctcatctggcatttttattgcaagatcacaatggcaagaa
atatctggtactttggttagtctgtgtacaagttttgcatactccgagcatccagcactatgagatactga

Supplementary Table 2. Small molecule screening data

Category	Parameter	Description
Assay	Type of assay	Luminescent/fluorescent plate reader assay
	Target	NanoBit luminescence per cell
	Primary measurement	Luminescence
	Key reagents	NanoGlo Live Cell Assay System (Promega, N2012)
	Assay protocol	Cells resuspended in DMEM high glucose (HyClone) supplemented with 10% FBS, 1% P/S, and 1 mM pyruvate were seeded into 384-well plates (Corning, 3765) at a density of 1,000 cells/well in 30 μ l. Compounds dissolved in DMSO were pin replicated (33 nl) into 384-well plates containing seeded cells and incubated at 37°C with 5% CO ₂ for two days. On the day of analysis, 10 μ l of Hoescht solution dissolved in PBS was added to each well (5 μ g/ml final) and incubated at room temperature for 30 minutes. Hoescht imaging and cell counting was performed using the TTPLabTech Acumen eX3/HCl. Next, 20 μ l of NanoGlo solution was added to each well and incubated on a shaker for 10 minutes. A white plate seal (Sigma Aldrich, Z732117) was attached to the bottom of each plate and luminescence was measured twice/well using Perkin Elmer EnVision plate reader.
	Additional comments	
Library	Library size	4,703 compound wells
	Library composition	Known bioactive compounds
	Source	Various
	Additional comments	https://iccb.med.harvard.edu/compound-libraries
Screen	Format	384-well
	Concentration(s) tested	~10, 2, 0.4, 0.08 μ M
	Plate controls	Tunicamycin (15 nM), DMEM [0 mM glucose + 10 mM galactose + 1 mM glucosamine]
	Reagent/ compound dispensing system	Custom pin transfer workstation at ICCB-Longwood Screening Facility, Harvard Medical School
	Detection instrument and software	TTPLabTech Acumen eX3/HCl, Perkin Elmer EnVision plate reader
	Assay validation/QC	Z' factors for each assay plate
	Correction factors	
	Normalization	NanoBit luminescence was corrected by cell number (Hoescht)
	Additional comments	N/A
Post-HTS analysis	Hit criteria	z-score>1.98
	Hit rate	~2%
	Additional assay(s)	
	Confirmation of hit purity and structure	N/A
	Additional comments	N/A

Supplementary Figure 1. Gating strategy for flow cytometry (related to Fig. 4j).

DMSO

Brequinar (250 nM)

