Table SI. Short hairpin RNA lentiviral information.

Sequencing of IDH2 small interfering RNA design					
NO.	Accession	Target Seq	CDS	GC%	
Idh2-RNAi (122232-2)	NM_173011	GAAGAGTTCAAGCTGAAGAAA	75..1433	36.84%	
Idh2-RNAi (122233-2)	NM_173011	GCTCTACTTGAGCACCAAGAA	75..1433	42.11%	
Idh2-RNAi (122234-1)	NM_173011	CGTGGATGTTCAGCTCAAGTA	75..1433	42.11%	
Synthetic oligo information					
NO.	5’	STEM	Loop	STEM	3’
Idh2-RNAi (122232-2)-a	Ccgg	GAAGAGTTCAAGCTGAAGAAA	CTCGAG	TTTCTTCAGCTTGAACTCTTC	TTTTTg
Idh2-RNAi (122232-2)-b	aattcaaaaa	GAAGAGTTCAAGCTGAAGAAA	CTCGAG	TTTCTTCAGCTTGAACTCTTC	
Idh2-RNAi (122233-2)-a	Ccgg	GCTCTACTTGAGCACCAAGAA	CTCGAG	TTCTTGGTGCTCAAGTAGAGC	TTTTTg
Idh2-RNAi (122233-2)-b	aattcaaaaa	GCTCTACTTGAGCACCAAGAA	CTCGAG	TTCTTGGTGCTCAAGTAGAGC	
Idh2-RNAi (122234-1)-a	Ccgg	CGTGGATGTTCAGCTCAAGTA	CTCGAG	TACTTGAGCTGAACATCCACG	TTTTTg
Idh2-RNAi (122234-1)-b	aattcaaaaa	CGTGGATGTTCAGCTCAAGTA	CTCGAG	TACTTGAGCTGAACATCCACG	
GV112-NC-1	CCGG	TTCTCCGAACGTGTCACGT	TTCAAGAGA	ACGTGACACGTTCGGAGAA	TTTTTg
GV112-NC-2	AATTCAAAAA	TTCTCCGAACGTGTCACGT	TCTCTTGAA	ACGTGACACGTTCGGAGAA	

RNAi, RNA interference.

Table SII. IDH 2 plasmid information.

gen ID	269951
Gene name	IDH2
Genes full name	IDH2 ($NADP^+$), mitochondrial
alias	IDPm; Idh-2; E430004F23
Transcript no	NM_173011
CDS length	1359 bp
Sequencing primers	Forward CAG: 5'-CTCTGCTAACCATGTTCATG-3'
	Reverse BGH: 5'-CCAGGGTCAAGGAAGGCAC-3'

IDH2, isocitrate dehydrogenase 2.

Table SIII. Information about binding of the modified protein to the substrate.

Original docking score		
Mode	Affinity (kcal/mol)	Distance from best mode
1	-5.0	0.000
2	-5.0	20.188
3	-5.0	13.238
4	-4.9	16.982
5	-4.8	23.946
6	-4.7	12.986
7	-4.7	9.000
8	-4.7	13.687
9	-4.7	13.209
Average	-4.83	-
Modified_docking_score		
1	-5.0	0.000
2	-4.9	1.344
3	-4.8	1.322
4	-4.8	8.541
5	-4.6	6.279
6	-4.5	2.840
7	-4.5	12.551
8	-4.4	8.174
9	-4.3	7.990
Average	-4.64	-

Structure acquisition: the pdb structure file of P54071_Idh 2 protein was downloaded from the Uniprot database; the sdf structure file of Isocitric acid was downloaded from the PubChem database. Protein site mutation / modification: add lactfied chemical group to the amino acid residue 275 of Idh 2 protein.

Table SIV. Docking results of target protein.

Protein 1	Protein 2	Binding energy (kcal/mol)	Contact sites (protein 1)	Contact sites (protein 2)	Combination type
IDH2	P300	-190.18	LYS-275, LYS-48, LYS-280, THR-276, ASP-279, GLY-339, HIS-273, LYS-340	GLU-1499, LYS-1425, ARG-1477, CYS-1602, HIS-1480, ASP-1492	Salt bridge, hydrogen bond, hydrophobic interaction
	Sirt1	-200.85	LYS-275, ASP-279, LYS-282, ILE-283, TRP-284, TYR-247, SER-301, SER-300	LYS-320, ASN-479, HIS-483	Salt bridge, hydrogen bond, hydrophobic interaction
	Sirt2	-195.69	LYS-275, GLY-163, THR-165, SER-301, ARG-288, GLU-286	LYS-275, ASN-238, GLY-236	Hydrogen bond, hydrophobic interaction
	Sirt3	-289.40	LYS-275, ASP-292, ASP-271, LYS-275, ASP-279, ILE-283, LYS-299	HIS-138, ARG-334, GLN-323, ARG-326, GLU-133, GLU-306	Salt bridge, hydrogen bond, hydrophobic interaction
	Sirt4	-216.39	LYS-275, ASP-292, ASP-279, LYS-282, LYS-275, LYS-263, HIS-287, ARG-288, LYS-256	GLN-112, TRP-123, PRO-120, LYS-148, PRO-111, SER-115, SER-66, TRP-189	Salt bridge, hydrogen bond, hydrophobic interaction
	Sirt6	-251.55	LYS-275, GLY-163, THR-165, LYS-282, TYR-247, ASP-271, GLN-267, GLU-286	ARG-232, ASP-251, ARG-231, ARG-248, HIS-246, ARG-220	Salt bridge, hydrogen bond, hydrophobic interaction

IDH2 (ID: 4J8A), Sirt2 (ID: Q8VDQ8), Sirt3 (ID: Q8R104), Sirt4 (ID: Q8R216), Sirt 6 (ID: P59941) target proteins were obtained from the RCSB and UniProT databases (https://www.rcsb.org/, https://www.uniprot.org/), Sirt1, The P300 performs homology modeling using the Swiss-Model online server according to its amino acid sequence (https://swissmodel.expasy.org/, Homologous template:8han, 5btr). The HDOCK server predicts binding complexes between two molecules, such as protein and nucleic acid, by using a hybrid docking strategy. Using HDOCK software, each protein was set to rigid, the docking contact site was set to full surface, the resulting conformation was set to 100, and docking scores were calculated based on knowledge iterative scoring function ITScorePP. A more negative docking score implies a more likely binding model. This time, the conformation with the most negative energy was selected by using the scoring function and optimized by using the Minimization module in the MOE 2019.1 software platform to solve the possible contact with unreasonable spatial structure of rigid docking. The force field of energy minimization is Amber10: ETH, and the solvation model selects water molecules. The optimization method is divided into two steps: steepest descent (Steepest Descent) and conjugate gradient (Conjugate Gradient), and the maximum number of iterations is 5000. The optimization results were most followed by using Pymol2.1 software. IDH2, isocitrate dehydrogenase 2.