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Supplementary Material

Table S1 Gene editing efficiency of different RNP delivery systems

Delivery system	Cell Type	Efficiency	Refs
CRISPR/Cas9$_{-3NLS}$/sgHMGA2@PDA	**MKN-45 cells**	**82%**	**This work**
Metal organic frameworks	MCF-7 cells	~60%	[1]
Graphene oxide	AGS cells	~39%	[2]
Black phosphorus nanosheets	MCF-7 cells	32.1%	[3]
Calcium phosphate	Protoplast cells	20%	[4]
Gold nanocluster	A375 cells	26.2%	[5]
DNA nanoclews	3T3-L1 cells	75%	[6]
Chitosan nanoparticles	U2OS cells	55.8%	[7]
Poly(β-amino ester) nanoparticles	HEK293T cells	77%	[8]
Lipid nanoparticles	HEK cells	70%	[9]
Lipid nanoparticles	Jurkat T cells	8%	[10]

Amino acid sequences of the CRISPR/Cas9：

10 20 30 40 50
MNFKILPIAI DLGVKNTGVF SAFYQKGTSL ERLDNKNGKV YELSKDSYTL
60 70 80 90 100
LMNNRTARRH QRRGIDRKQL VKRLFKLIWT EQLNLEWDKD TQQAISFLFN
110 120 130 140 150
RRGFSFITDG YSPEYLNIVP EQVKAILMDI FDDYNGEDDL DSYLKLATEQ
160 170 180 190 200
ESKISEIYNK LMQKILEFKL MKLCTDIKDD KVSTKTL**KE**I TSYEFELLAD
210 220 230 240 250
YLANYSESLK TQKFSYTDKQ GNL**KE**LSYYH HDKYNIQEFL KRHATINDRI
260 270 280 290 300
LDTLLTDDLD IWNFNFEKFD FDKNEEKLQN QEDKDHIQAH LHHFVFAVNK
310 320 330 340 350
IKSEMASGGR HRSQYFQEIT NVLDENNHQE GYLKNFCENL HNKKYSNLSV
360 370 380 390 400
KNLVNLIGNL SNLELKPLRK YFNDKIHAKA DHWDEQKFTE TYCHWILGEW
410 420 430 440 450
RVGVKDQDKK DGAKYSYKDL CNELKQKVTK AGLVDFLLEL DPCRTIPPYL
460 470 480 490 500
DNNNRKPPKC QSLILNPKFL DNQYPNWQQY LQELKKLQSI QNYLDSFETD
510 520 530 540 550
LKVLKSSKDQ PYFVEYKSSN QQIASGQRDY KDLDARILQF IFDRVKASDE
560 570 580 590 600
LLLNEIYFQA KKLKQKASSE LEKLESSKKL DEVIANSQLS QILKSQHTNG
610 620 630 640 650
IFEQGTFLHL VCKYYKQRQR ARDSRLYIMP EYRYDKKLHK YNNTGRFDDD
660 670 680 690 700
NQLLTYCNHK PRQKRYQLLN DLAGVLQVSP NFLKDKIGSD DDLFISKWLV
710 720 730 740 750
EHIRGFKKAC EDSLKIQKDN RGLLNHKINI ARNTKGKCE**K E**IFNLICKIE
760 770 780 790 800
GSEDKKGNYK HGLAYELGVL LFGEPNEASK PEFDRKIKKF NSIYSFAQIQ
810 820 830 840 850
QIAFAERKGN ANTCAVCSAD NAHRMQQIKI TEPVEDNKDK IILSAKAQRL
860 870 880 890 900
PAIPTRIVDG AVKKMATILA KNIVDDNWQN IKQVLSAKHQ LHIPIITESN
910 920 930 940 950
AFEFEPALAD VKGKSLKDRR KKALERISPE NIFKDKNNRI **KE**FAKGISAY
960 970 980 990 1000

SGANLTDGDF DGA**KE**ELDHI IPRSHKKYGT LNDEANLICV TRGDNKNKGN
1010 1020 1030 1040 1050
RIFCLRDLAD NYKLKQFETT DDLEIEKKIA DTIWDANKKD FKFGNYRSFI
1060 1070 1080 1090 1100
NLTPQEQKAF RHALFLADEN PIKQAVIRAI NNRNRTFVNG TQRYFAEVLA
1110 1120 1130 1140 1150
NNIYLRAK**KE** NLNTDKISFD YFGIPTIGNG RGIAEIRQLY EKVDSDIQAY
1160 1170 1180 1190 1200
AKGDKPQASY SHLIDAMLAF CIAADEHRND GSIGLEIDKN YSLYPLDKNT
1210 1220 1230 1240 1250
GEVFTKDIFS QIKITDNEFS DKKLVRKKAI EGFNTHRQMT RDGIYAENYL
1260 1270 1280 1290 1300
PILIH**KE**LNE VRKGYTWKNS EEIKIFKGKK YDIQQLNNLV YCLKFVDKPI
1310 1320 1330 1340 1350
SIDIQISTLE ELRNILTTNN IAATAEYYYI NLKTQKLHEY YIENYNTALG
1360 1370 1380 1390 1400
YKKYS**KE**MEF LRSLAYRSER VKIKSIDDVK QVLDKDSNFI IGKITLPFK**K**
1410 1420 1430 1440 1450
EWQRLYREWQ NTTIKDDYEF LKSFFNVKSI TKLHKKVRKD FSLPISTNEG
1460 1470 1480 1490 1500
KFLVKRKTWD NNFIYQILND SDSRADGTKP FIPAFDISKN EIVEAIIDSF
1510 1520 1530 1540 1550
TSKNIFWLPK NIELQKVDNK NIFAIDTSKW FEVETPSDLR DIGIATIQYK
1560 1570 1580 1590 1600
IDNNSRPKVR VKLDYVIDDD SKINYFMNHS LLKSRYPDKV LEILKQSTII
1610 1620 1621
EFESSGFNKT I**KE**MLGMKLA GIYNETSNN

Fig. S1. Amino acid sequences of the CRISPR/Cas9. The KE sequence has been highlighted in yellow.

The sequences are extracted from UniprotKB-A0Q5Y3 (CAS9_FRATN).

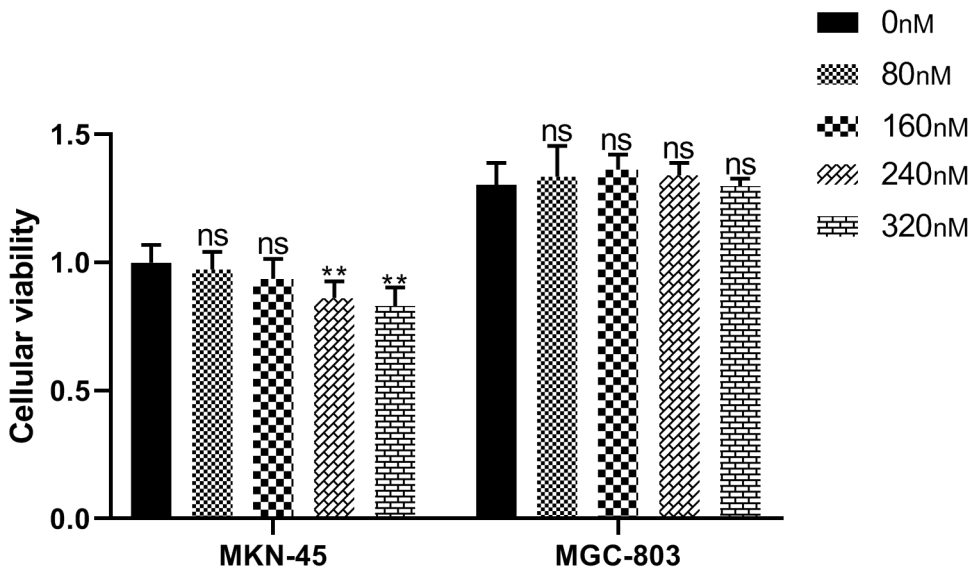

Fig. S2. Cell viability of MKN-45 and MGC-803 cells after incubating with CRISPR/Cas9-$_{3NLS}$@PDA (n=3)，ns: no significant differences; ** $P< 0.01$; **** $P< 0.001$, Student's t test. Error bars represent SD.

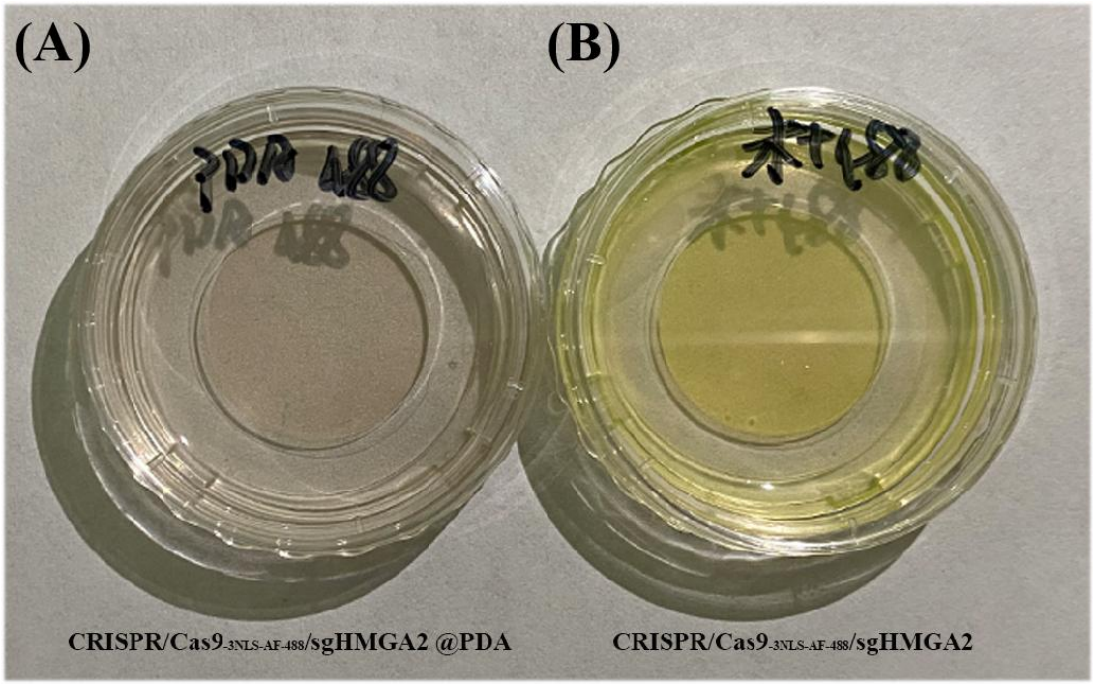

Fig. S3. (A) The color of CRISPR/Cas9-3NLS-AF-488/sgHMGA2@PDA solution. (B) The color of CRISPR/Cas9-3NLS-AF-488/sgHMGA2 solution

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