Figure1

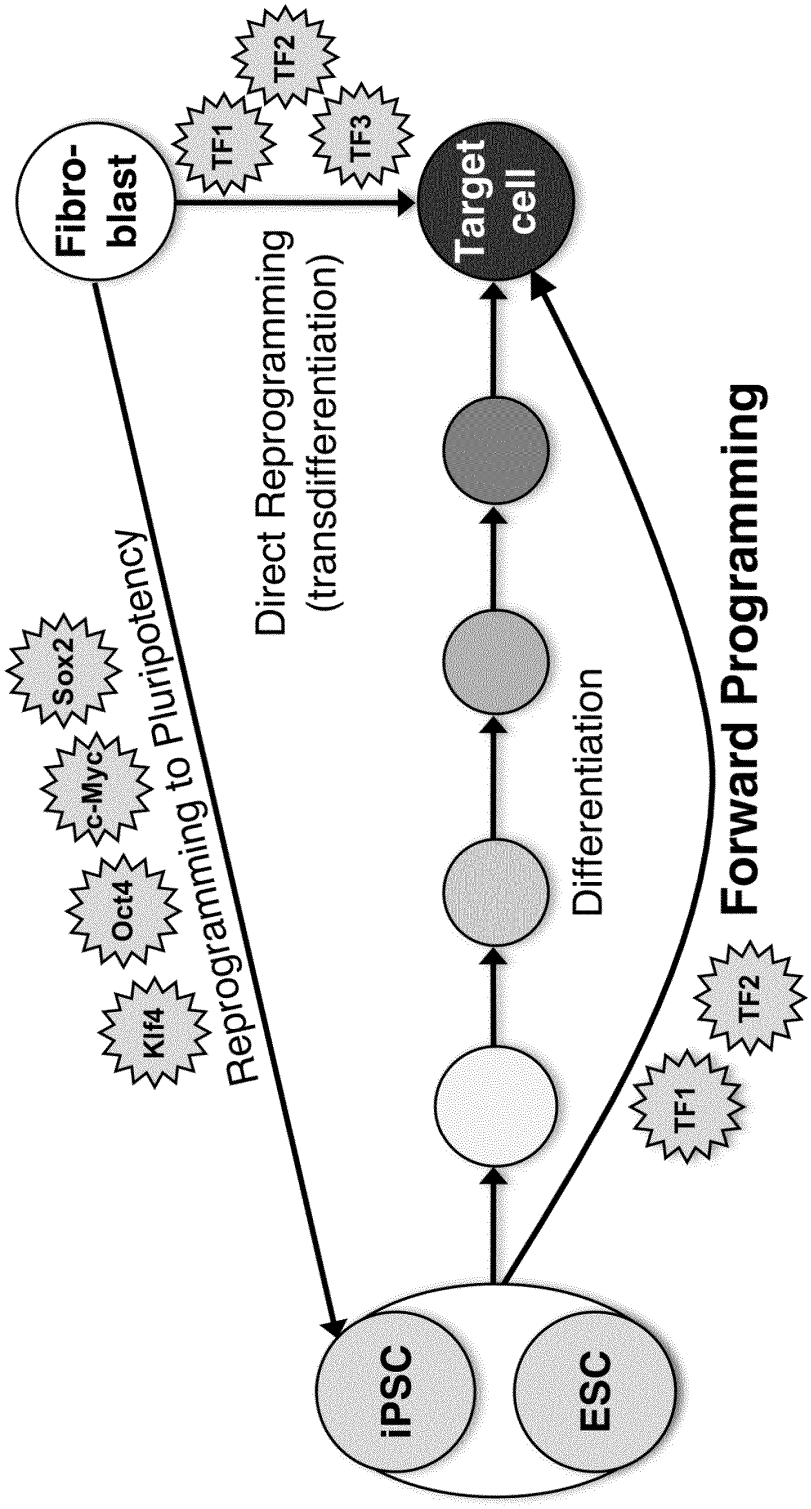

Fibro-blast
TF1
TF2
TF3
Target cell
Direct Reprogramming (transdifferentiation)
Sox2
c-Myc
Oct4
Klf4
Reprogramming to Pluripotency
Differentiation
Forward Programming
TF1
TF2
iPSC
ESC

Figure 2

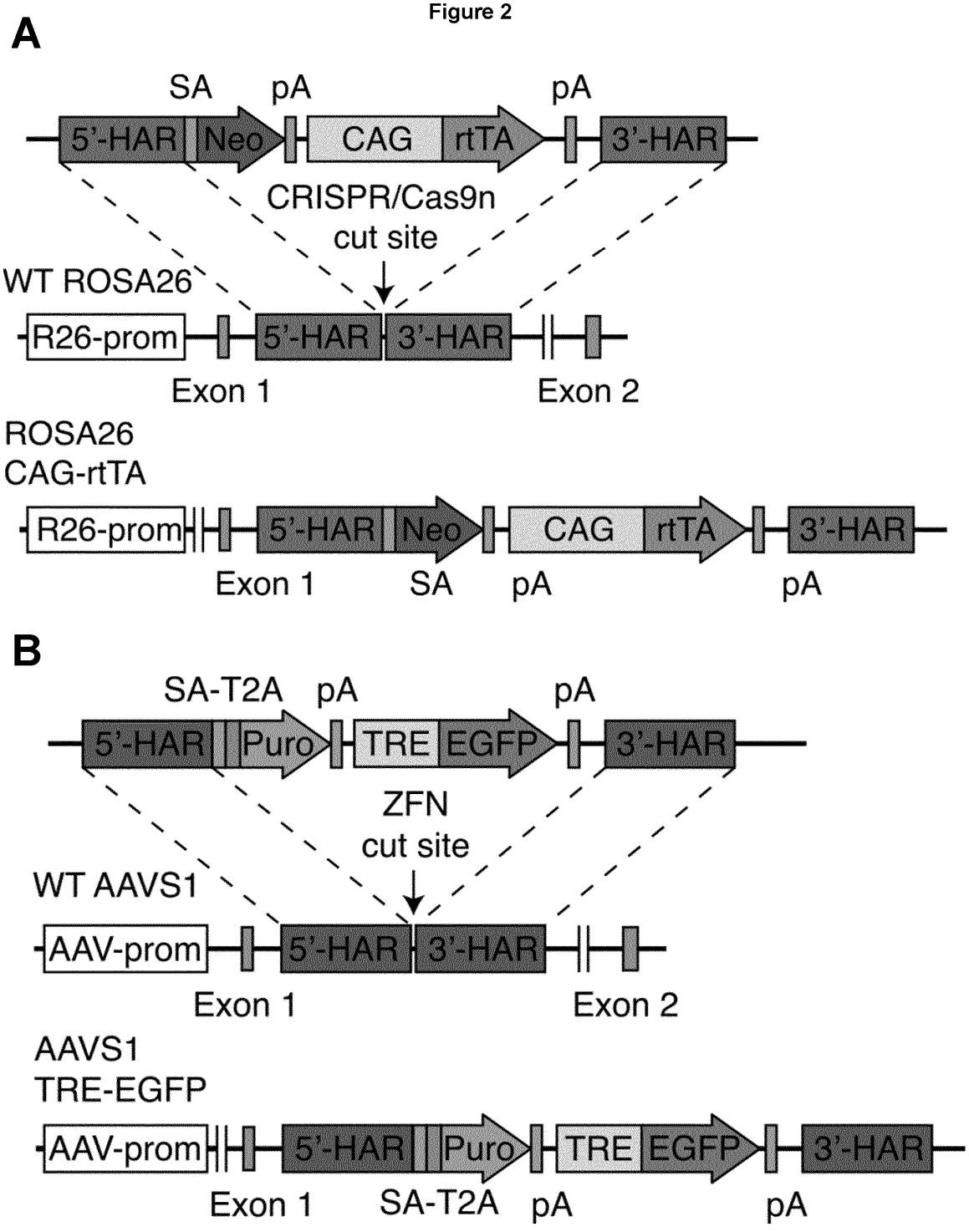

A
SA
pA
pA
5'-HAR
Neo
CAG
rtTA
3'-HAR
CRISPR/Cas9n
cut site
WT ROSA26
R26-prom
5'-HAR
3'-HAR
Exon 1
Exon 2
ROSA26
CAG-rtTA
R26-prom
5'-HAR
Neo
CAG
rtTA
3'-HAR
Exon 1
SA
pA
pA
B
SA-T2A
pA
pA
5'-HAR
Puro
TRE
EGFP
3'-HAR
ZFN
cut site
WT AAVS1
AAV-prom
5'-HAR
3'-HAR
Exon 1
Exon 2
AAVS1
TRE-EGFP
AAV-prom
5'-HAR
Puro
TRE
EGFP
3'-HAR
Exon 1
SA-T2A
pA
pA

Figure 3

Symbol	Gene Name	CDS [bp]	Source
CEBPB	CCAAT/enhancer binding protein beta	1281	Dharmacon, BC007538
IRF8	interferon regulatory factor 8	1038	GenScript, NM_002163
RUNX1	runt related transcription factor 1	1443	GenScript, NM_001754
SPI1	Spi-1 proto-oncogene	813	gift by Thomas Moreau

Figure 4

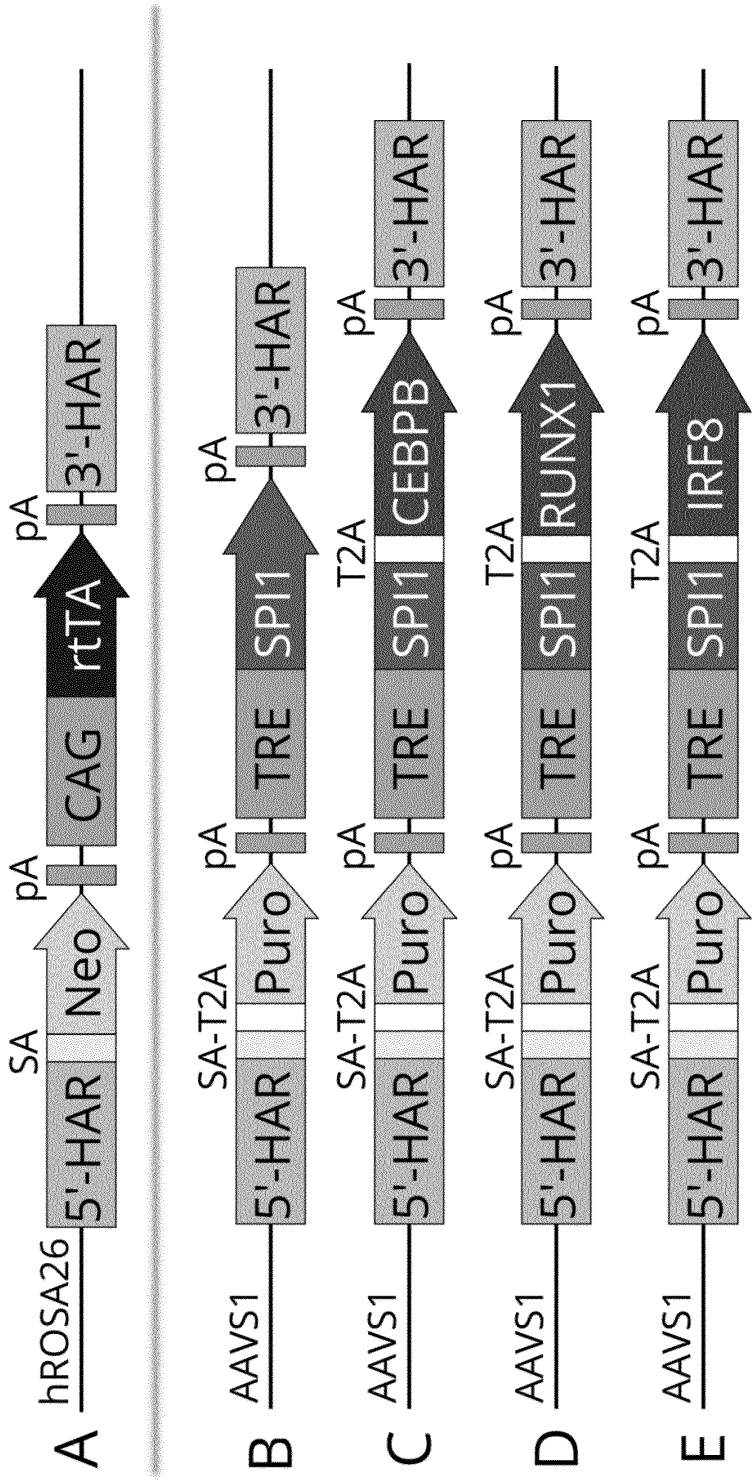

A
hROSA26
5'-HAR
SA
Neo
pA
CAG
rtTA
pA
3'-HAR
B
AAVS1
5'-HAR
SA-T2A
Puro
pA
TRE
SPI1
pA
3'-HAR
C
AAVS1
5'-HAR
SA-T2A
Puro
pA
TRE
SPI1
T2A
CEBPB
pA
3'-HAR
D
AAVS1
5'-HAR
SA-T2A
Puro
pA
TRE
SPI1
T2A
RUNX1
pA
3'-HAR
E
AAVS1
5'-HAR
SA-T2A
Puro
pA
TRE
SPI1
T2A
IRF8
pA
3'-HAR

Figure 5

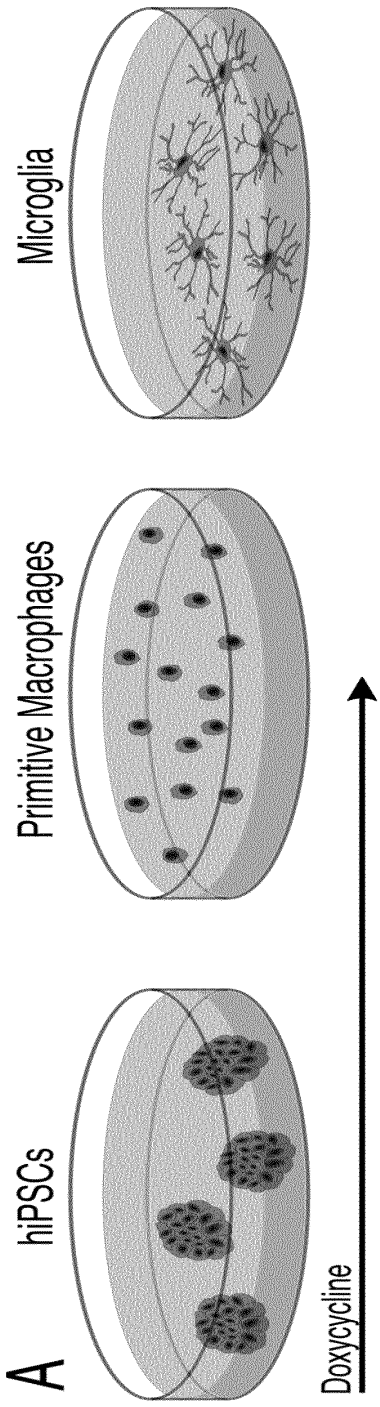


Figure 5 (cont.)

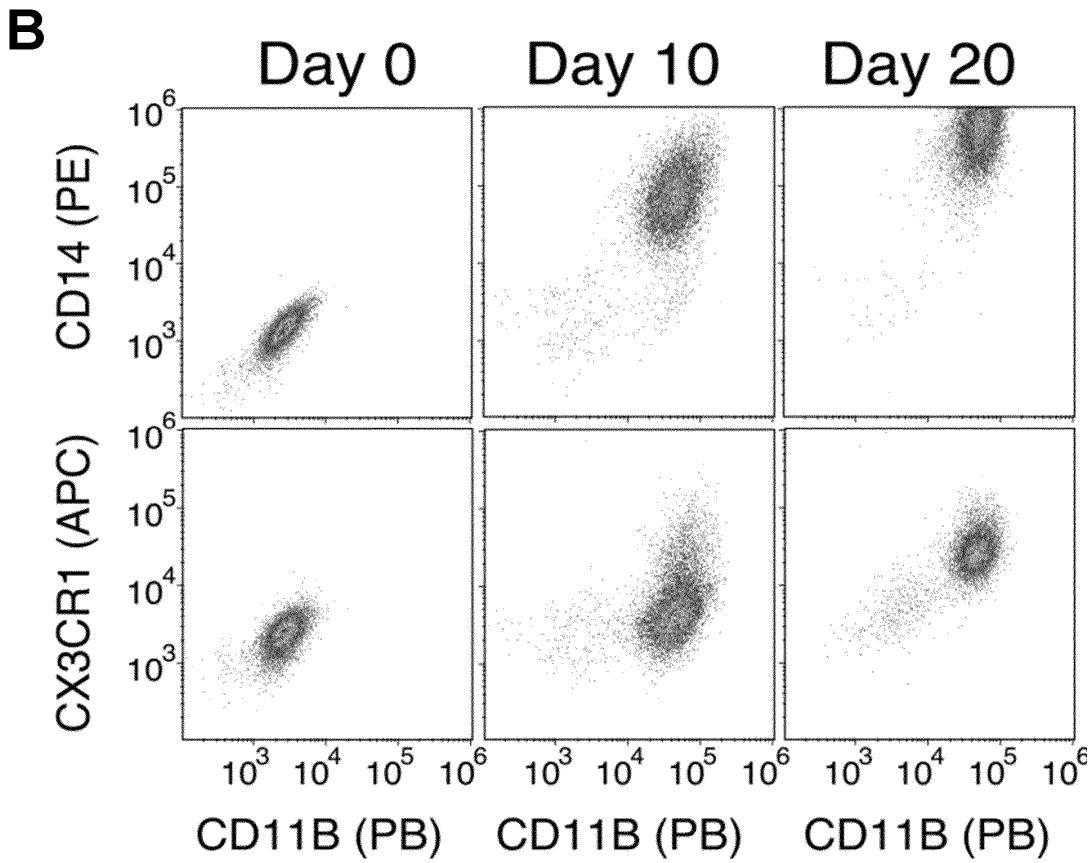


Figure 5 (cont.)

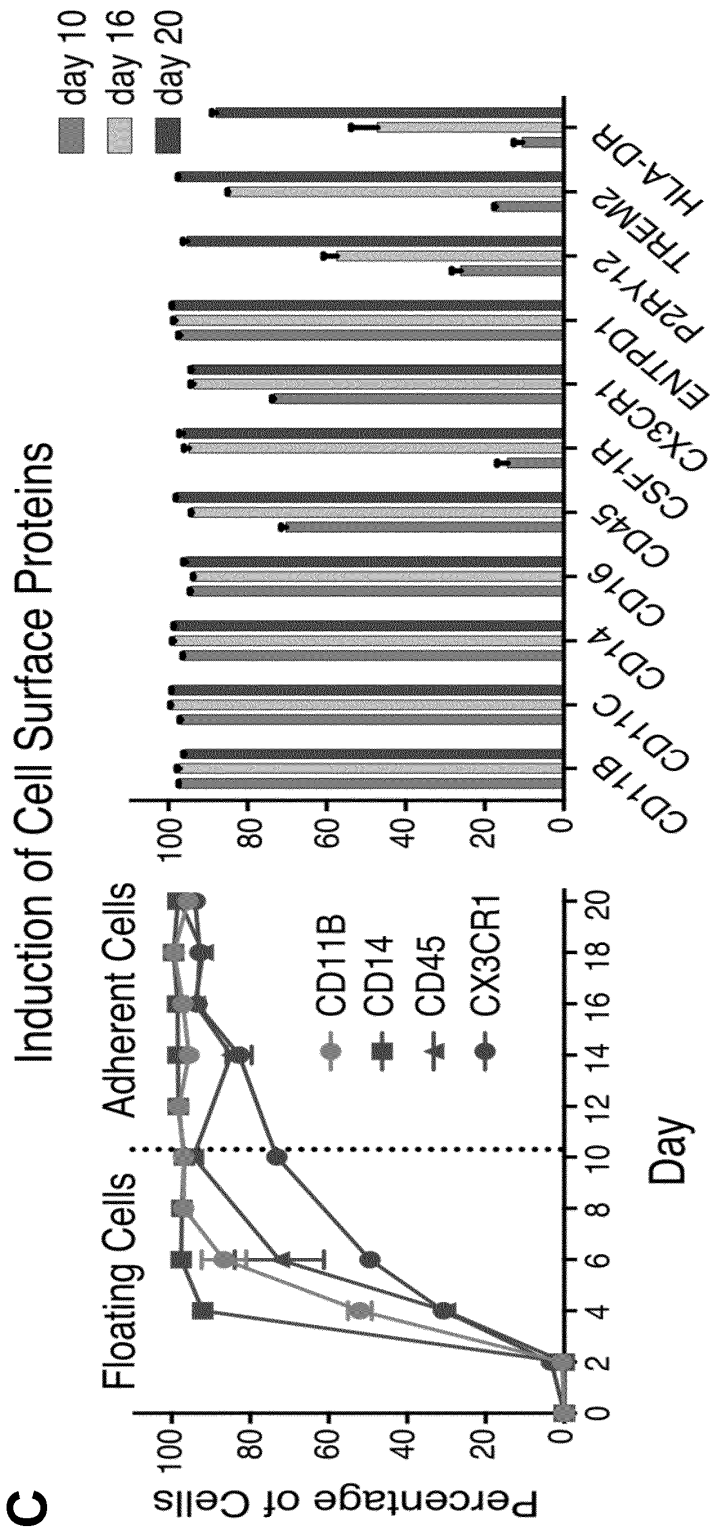


Figure 5 (cont.)

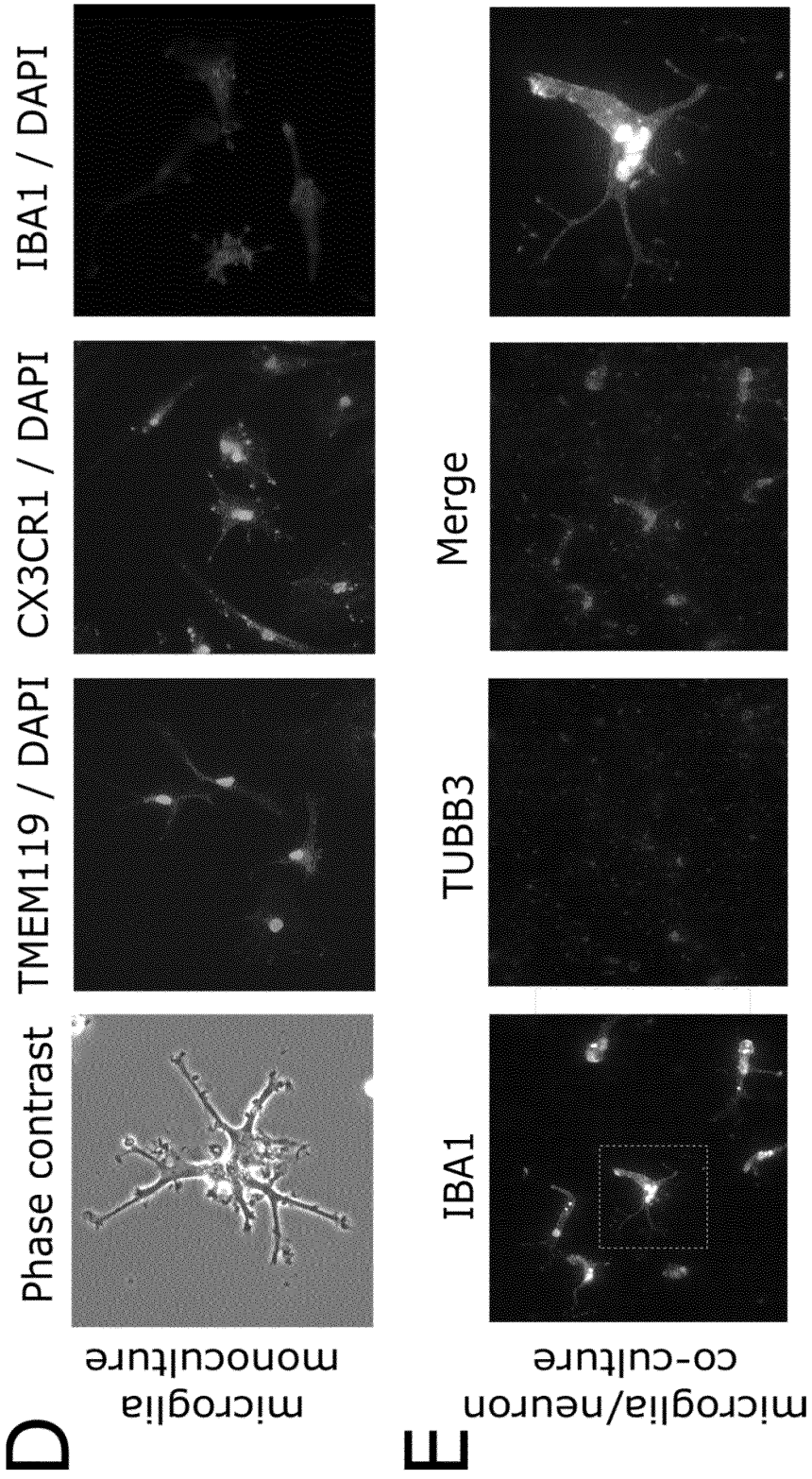


Figure 5 (cont.):

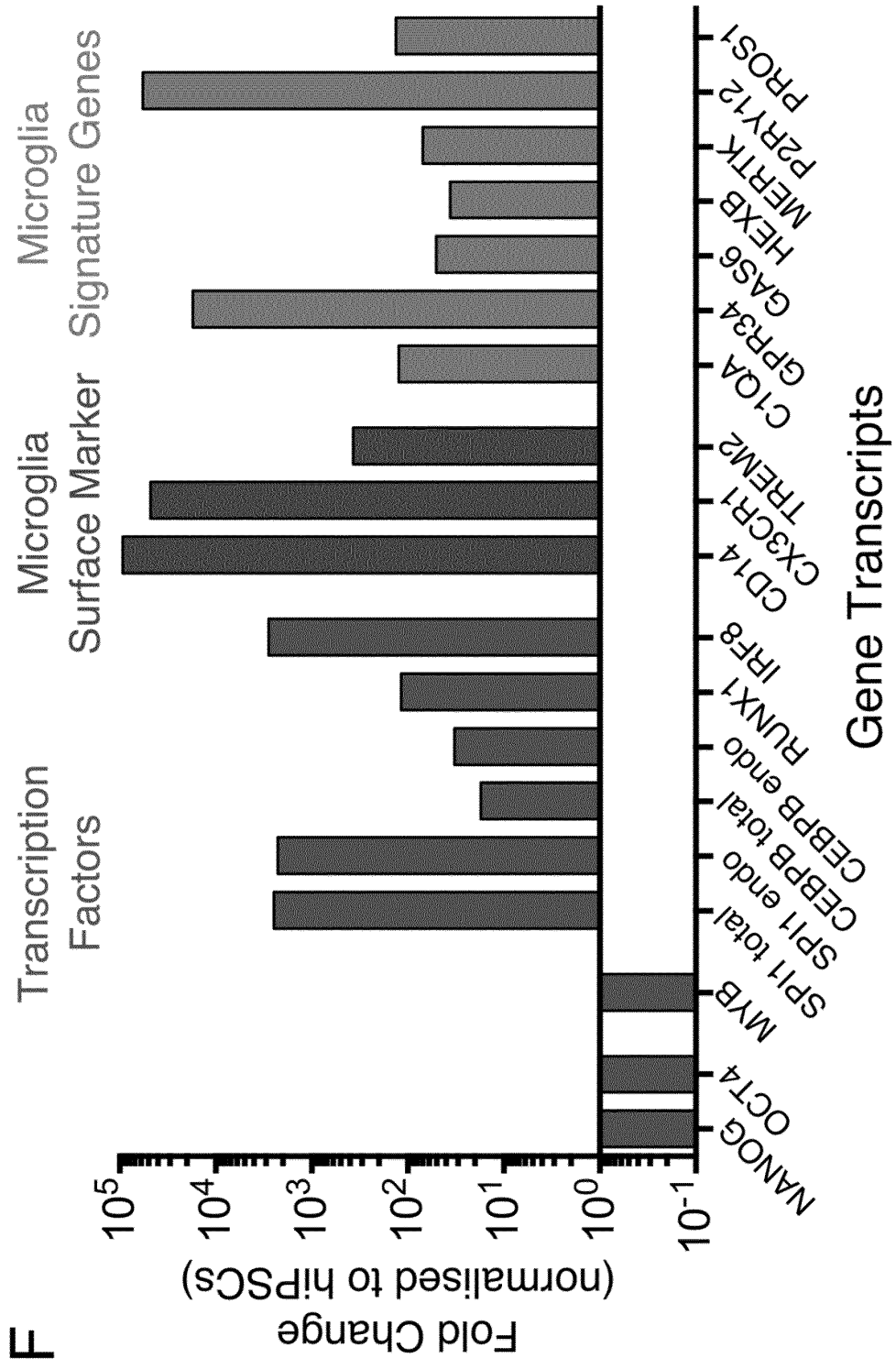


Figure 6:

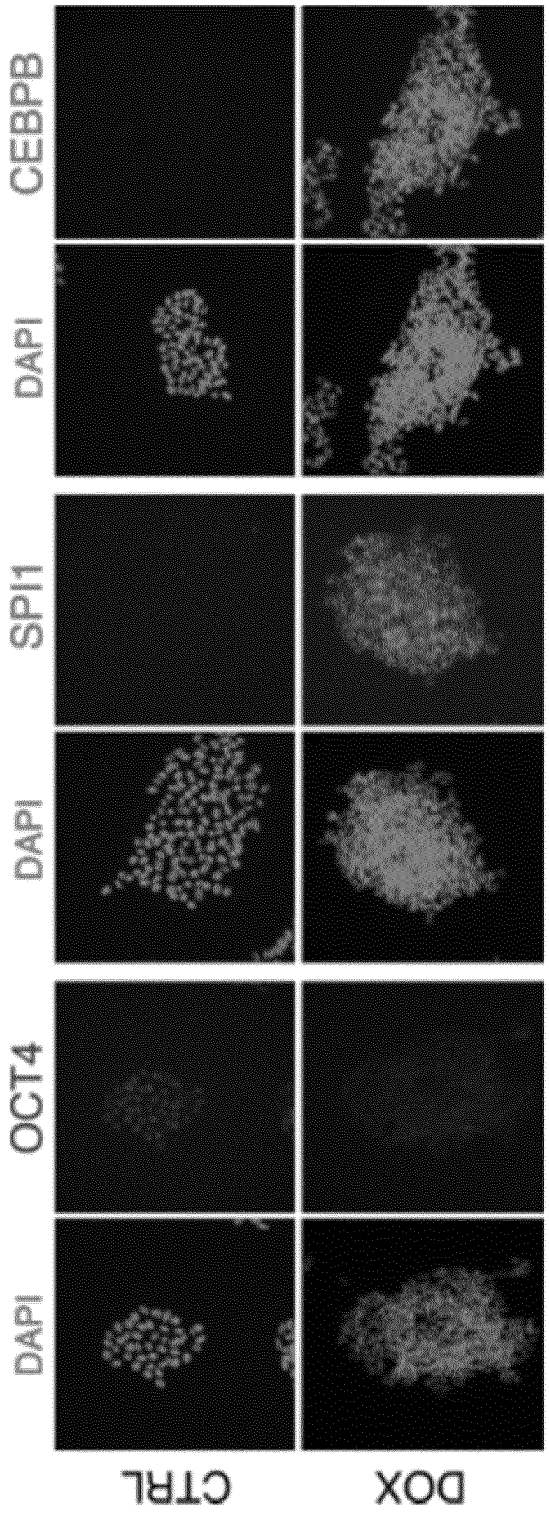


Figure 7

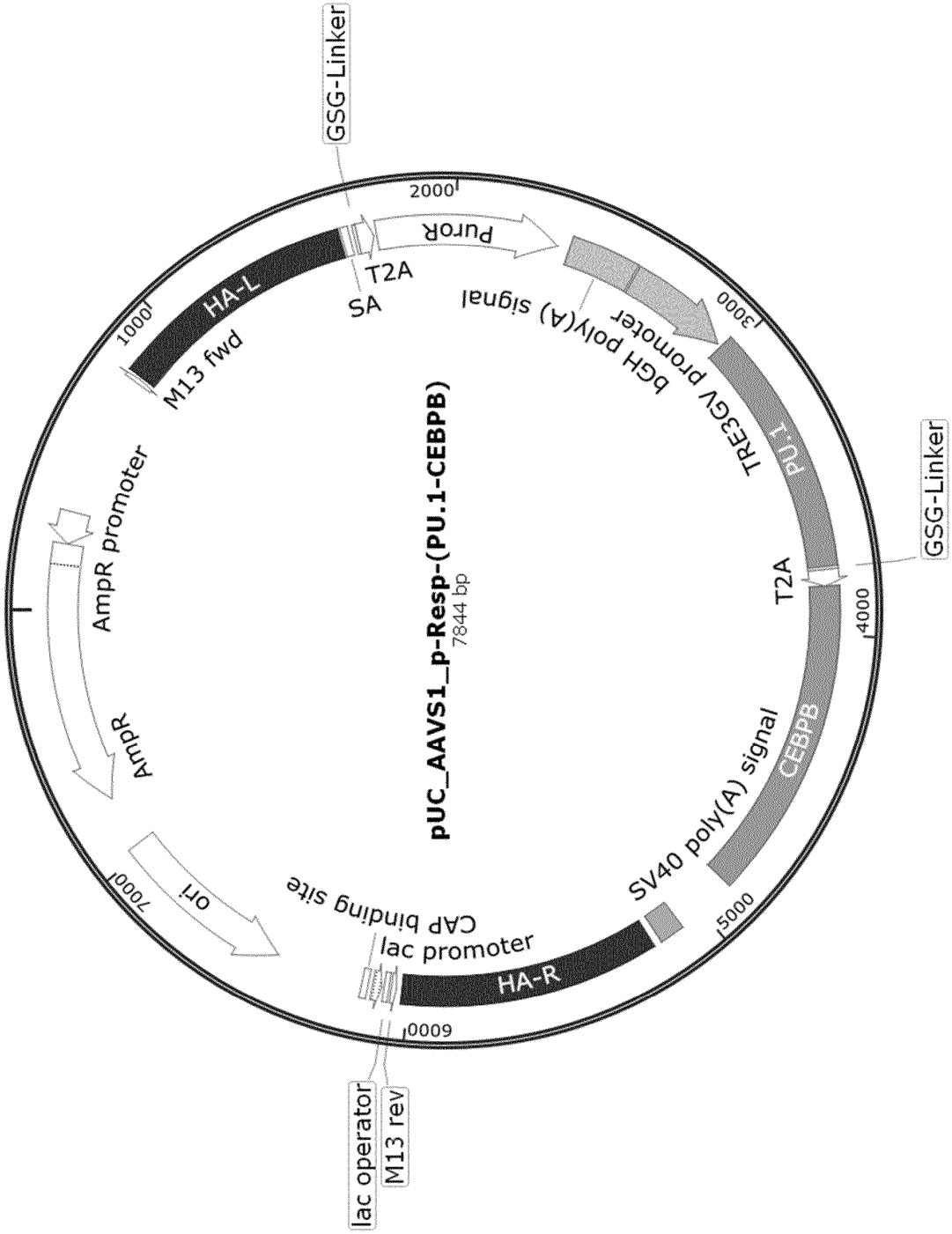

pUC_AAVS1_p-Resp-(PU.1-CEBPB)
7844 bp
GSG-Linker
2000
PuroR
T2A
SA
HA-L
1000
M13 fwd
bGH poly(A) signal
3000
TRE3GV promoter
PU.1
GSG-Linker
T2A
4000
CEBPB
SV40 poly(A) signal
5000
HA-R
6000
lac promoter
CAP binding site
ori
7000
AmpR
AmpR promoter
lac operator
M13 rev

Figure 8:

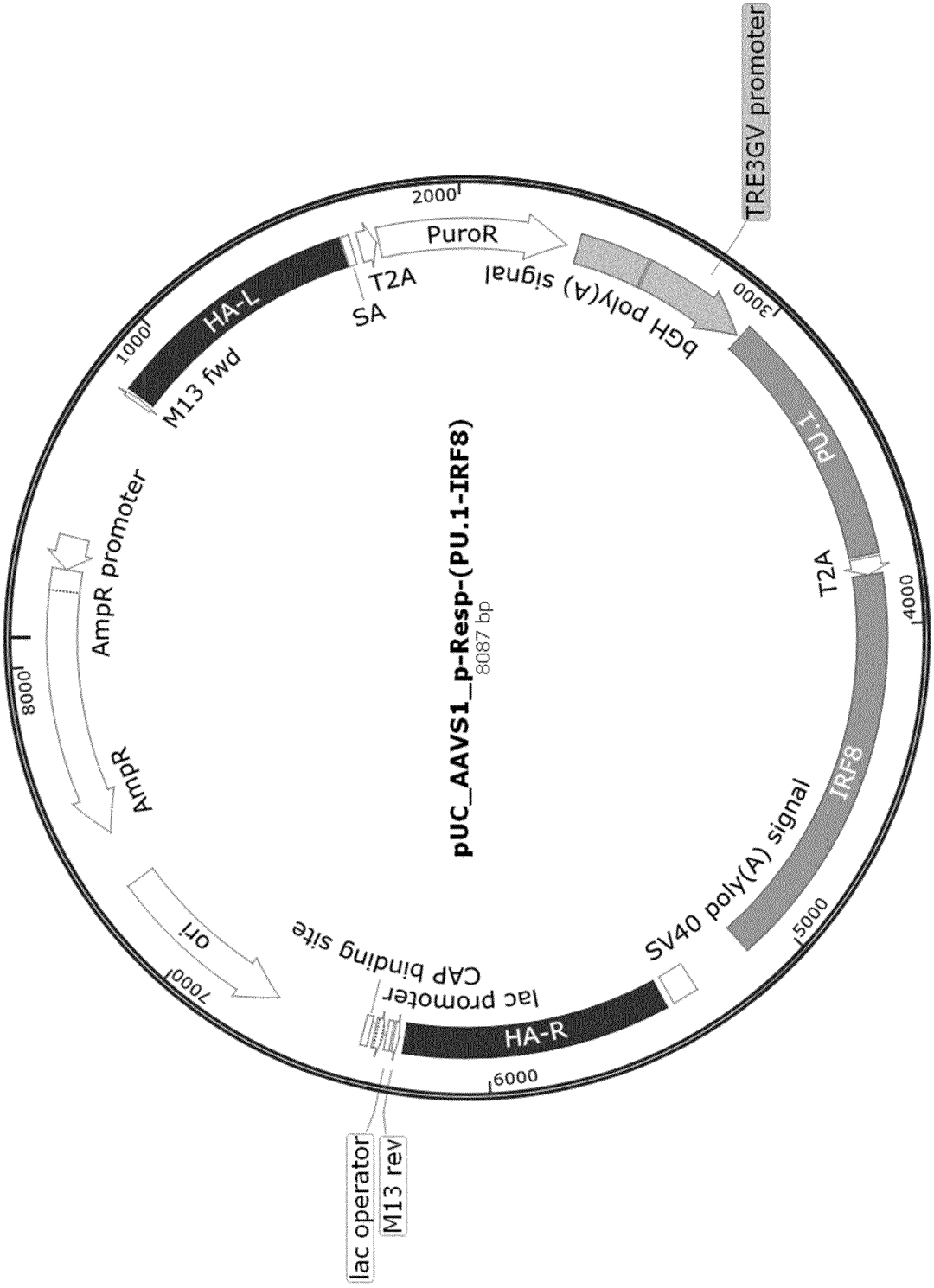

pUC_AAVS1_p-Resp-(PU.1-IRF8)
8087 bp
TRE3GV promoter
PuroR
T2A
SA
HA-L
M13 fwd
bGH poly(A) signal
PU.1
T2A
IRF8
SV40 poly(A) signal
HA-R
lac promoter
CAP binding site
ori
AmpR
AmpR promoter
lac operator
M13 rev
1000
2000
3000
4000
5000
6000
7000
8000

Figure 9:

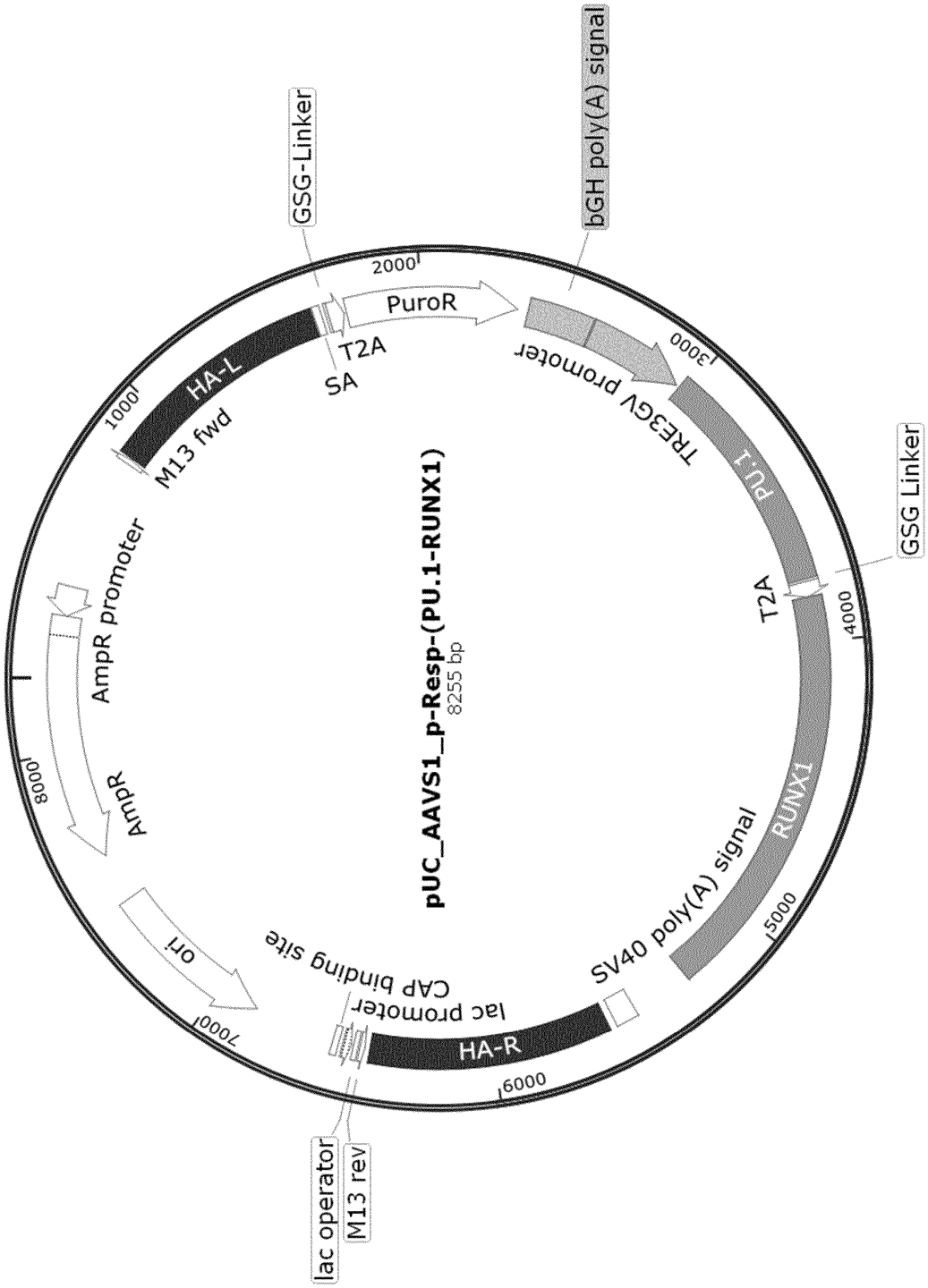

pUC_AAVS1_p-Resp-(PU.1-RUNX1)
8255 bp
GSG-Linker
bGH poly(A) signal
PuroR
T2A
SA
HA-L
M13 fwd
TRE3GV promoter
PU.1
GSG Linker
T2A
RUNX1
SV40 poly(A) signal
HA-R
lac promoter
CAP binding site
ori
AmpR
AmpR promoter
lac operator
M13 rev
1000
2000
3000
4000
5000
6000
7000
8000

Figure 10:

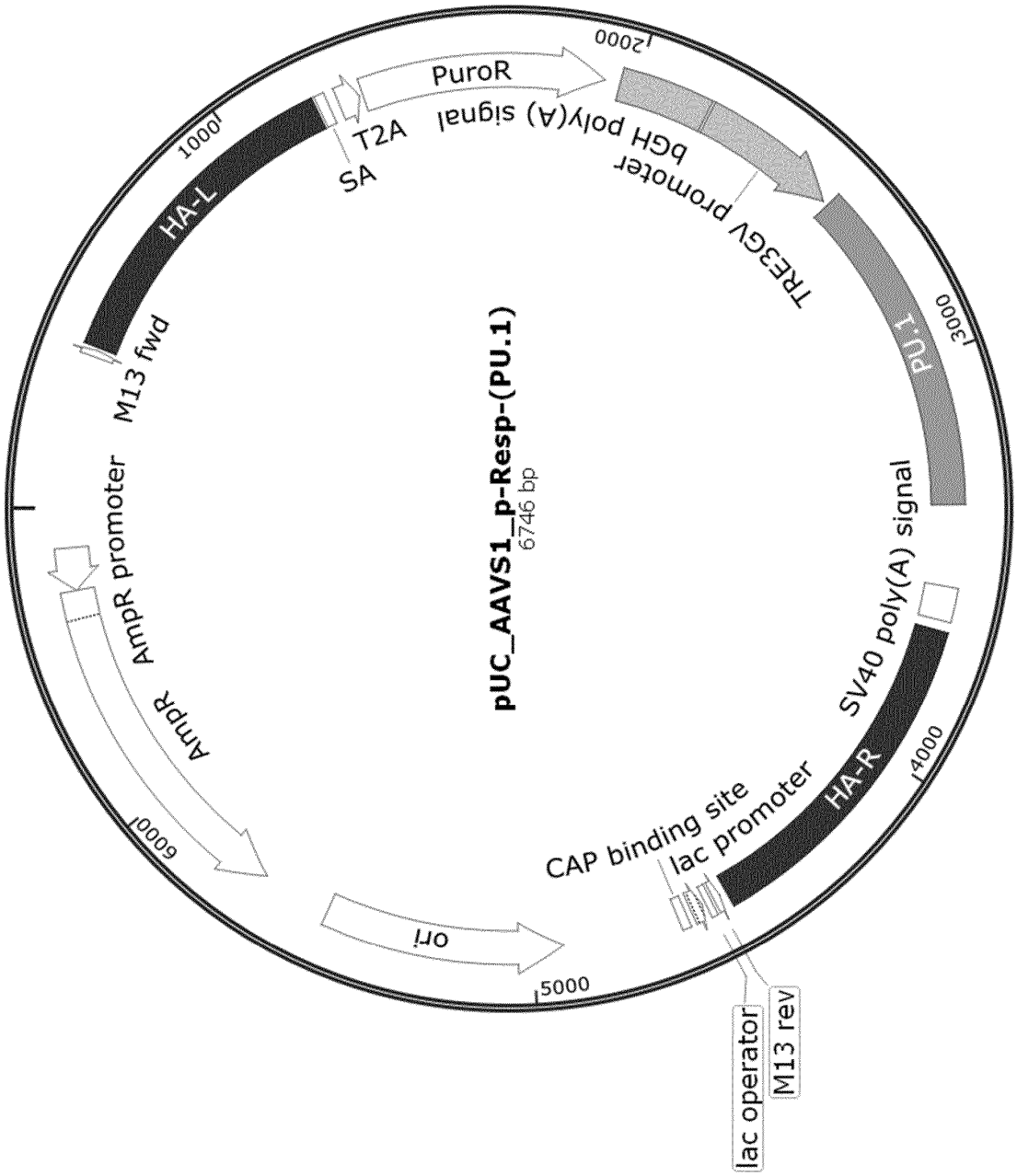

pUC_AAVS1_p-Resp-(PU.1)
6746 bp
1000
2000
3000
4000
5000
6000
HA-L
M13 fwd
SA
T2A
PuroR
bGH poly(A) signal
TRE3GV promoter
PU.1
SV40 poly(A) signal
HA-R
CAP binding site
lac promoter
lac operator
M13 rev
ori
AmpR
AmpR promoter

Figure 11:

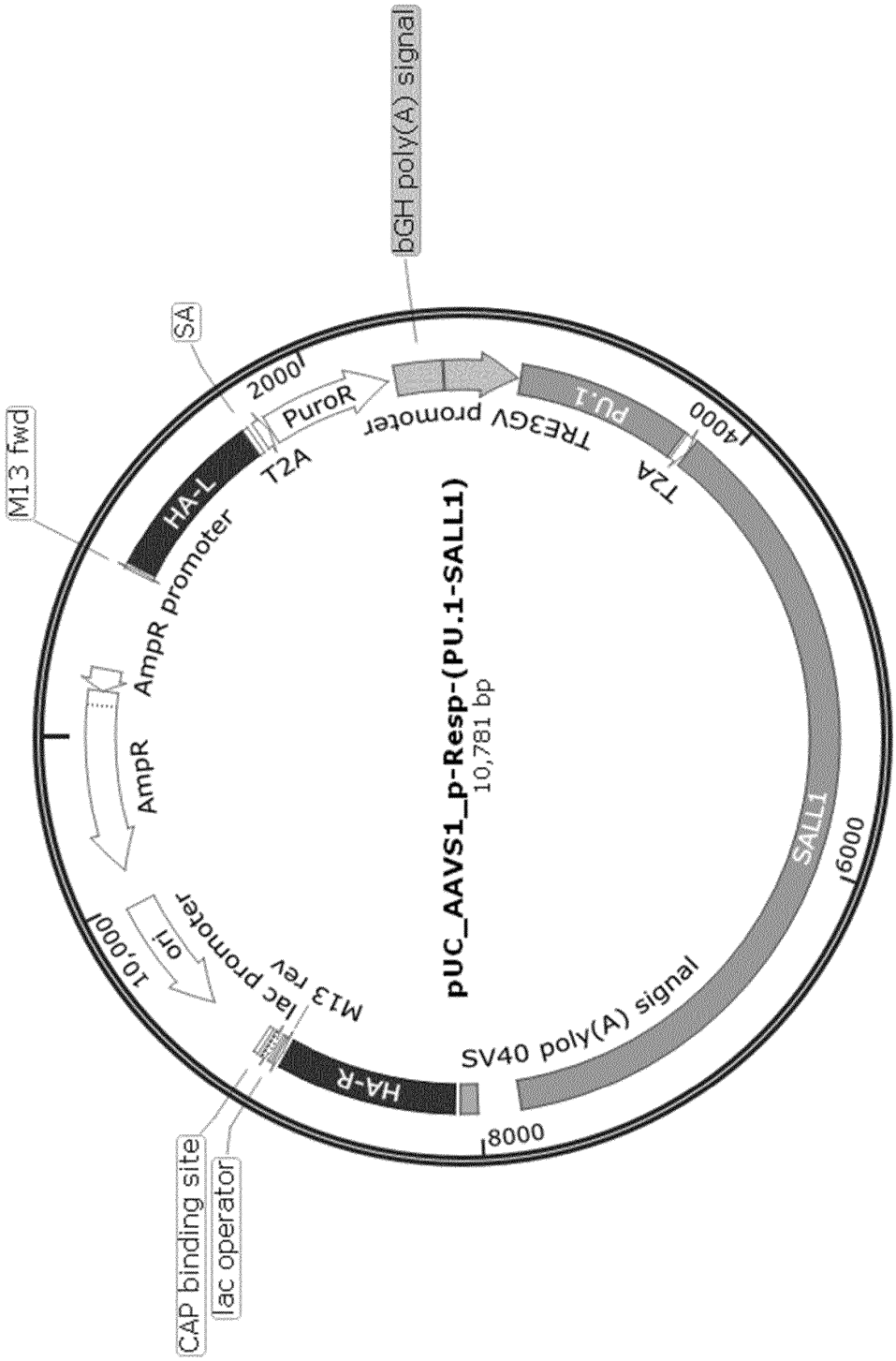

pUC_AAVS1_p-Resp-(PU.1-SALL1)
10,781 bp
bGH poly(A) signal
SA
2000
PuroR
T2A
HA-L
M13 fwd
AmpR promoter
AmpR
10,000
ori
lac promoter
M13 rev
HA-R
CAP binding site
lac operator
8000
SV40 poly(A) signal
SALL1
6000
PU.1
4000
T2A
TRE3GV promoter

Figure 12:

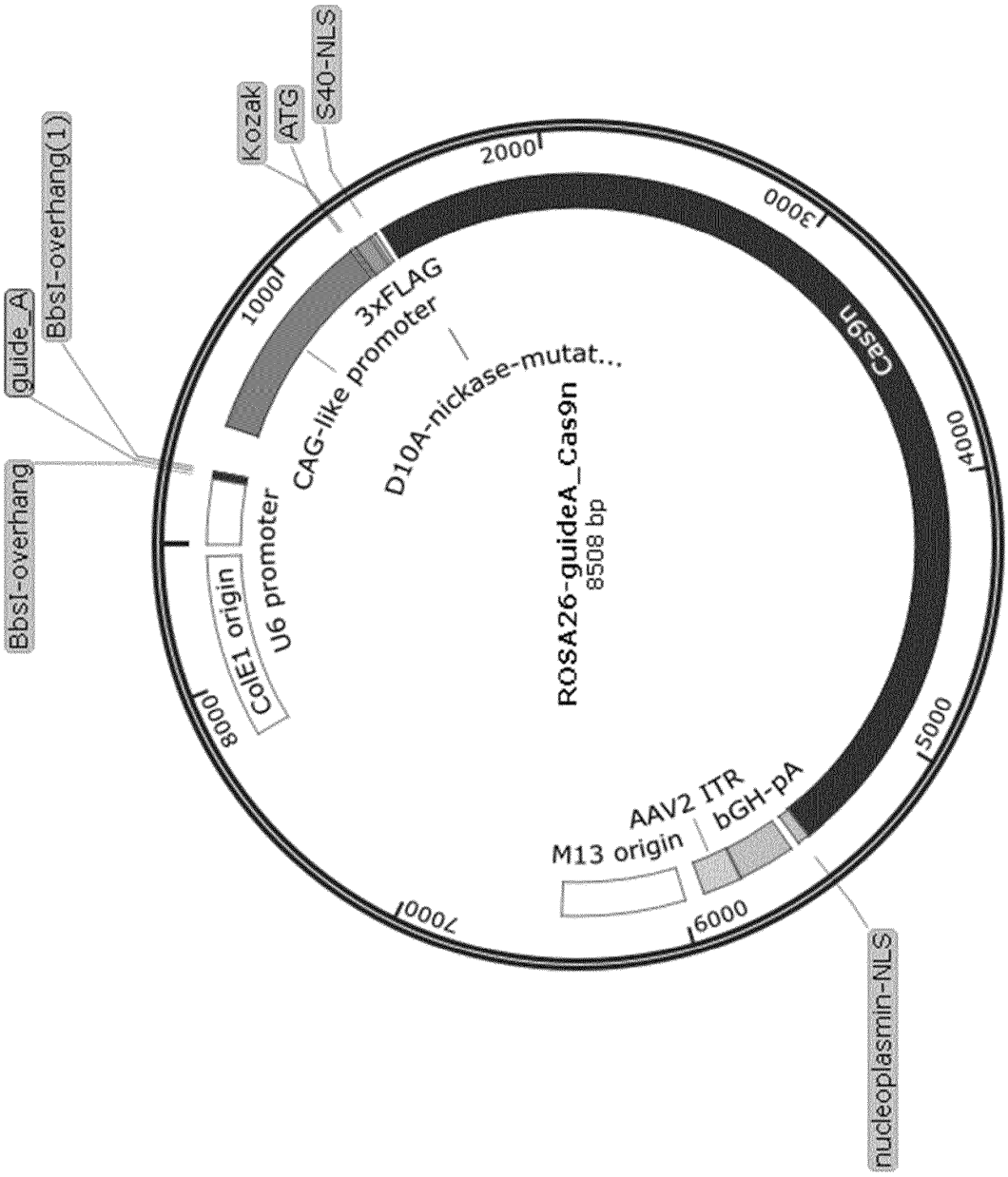

ROSA26-guideA_Cas9n
8508 bp
1000
2000
3000
4000
5000
6000
7000
8000
Kozak
ATG
S40-NLS
3xFLAG
CAG-like promoter
D10A-nickase-mutat...
Cas9n
nucleoplasmin-NLS
AAV2 ITR
bGH-pA
M13 origin
ColE1 origin
U6 promoter
BbsI-overhang
guide_A
BbsI-overhang(1)

Figure 13:

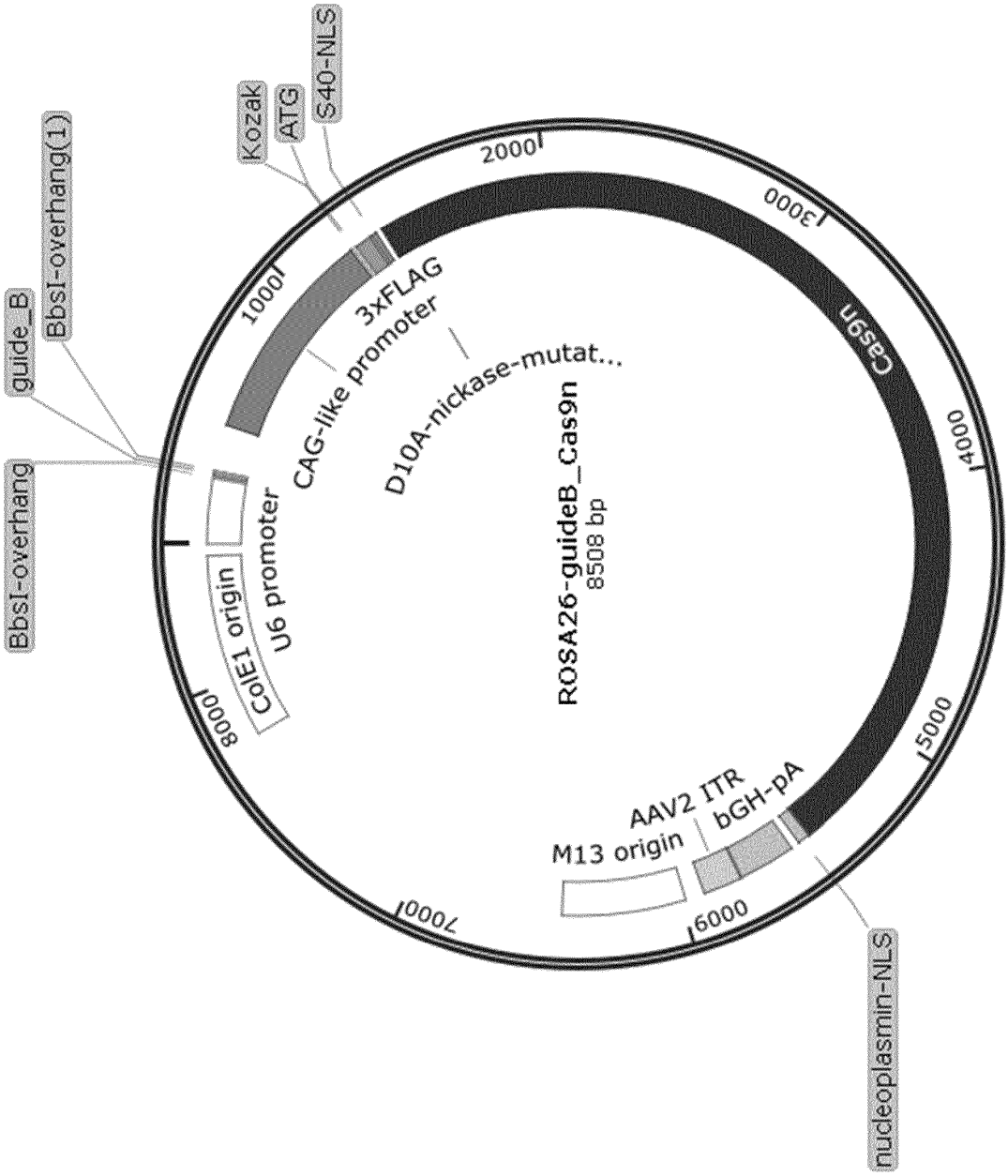

ROSA26-guideB_Cas9n
8508 bp
1000
2000
3000
4000
5000
6000
7000
8000
Kozak
ATG
S40-NLS
3xFLAG
CAG-like promoter
D10A-nickase-mutat...
Cas9n
nucleoplasmin-NLS
AAV2 ITR
bGH-pA
M13 origin
ColE1 origin
U6 promoter
BbsI-overhang
guide_B
BbsI-overhang(1)

Figure 14:

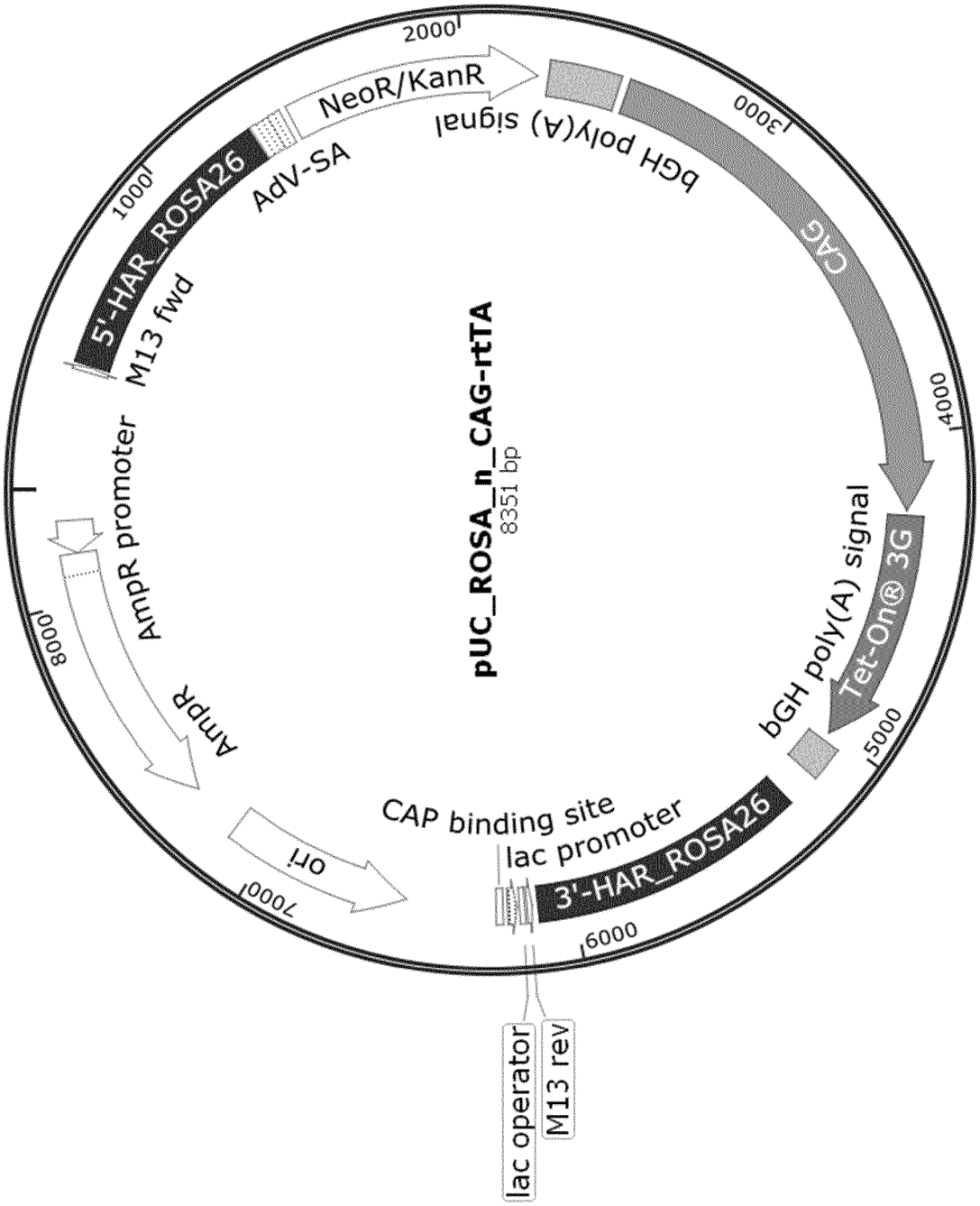

pUC_ROSA_n_CAG-rtTA
8351 bp
2000
3000
4000
5000
6000
7000
8000
1000
NeoR/KanR
AdV-SA
5'-HAR_ROSA26
M13 fwd
bGH poly(A) signal
CAG
Tet-On® 3G
bGH poly(A) signal
AmpR promoter
AmpR
ori
CAP binding site
lac promoter
3'-HAR_ROSA26
lac operator
M13 rev

Figure 15:

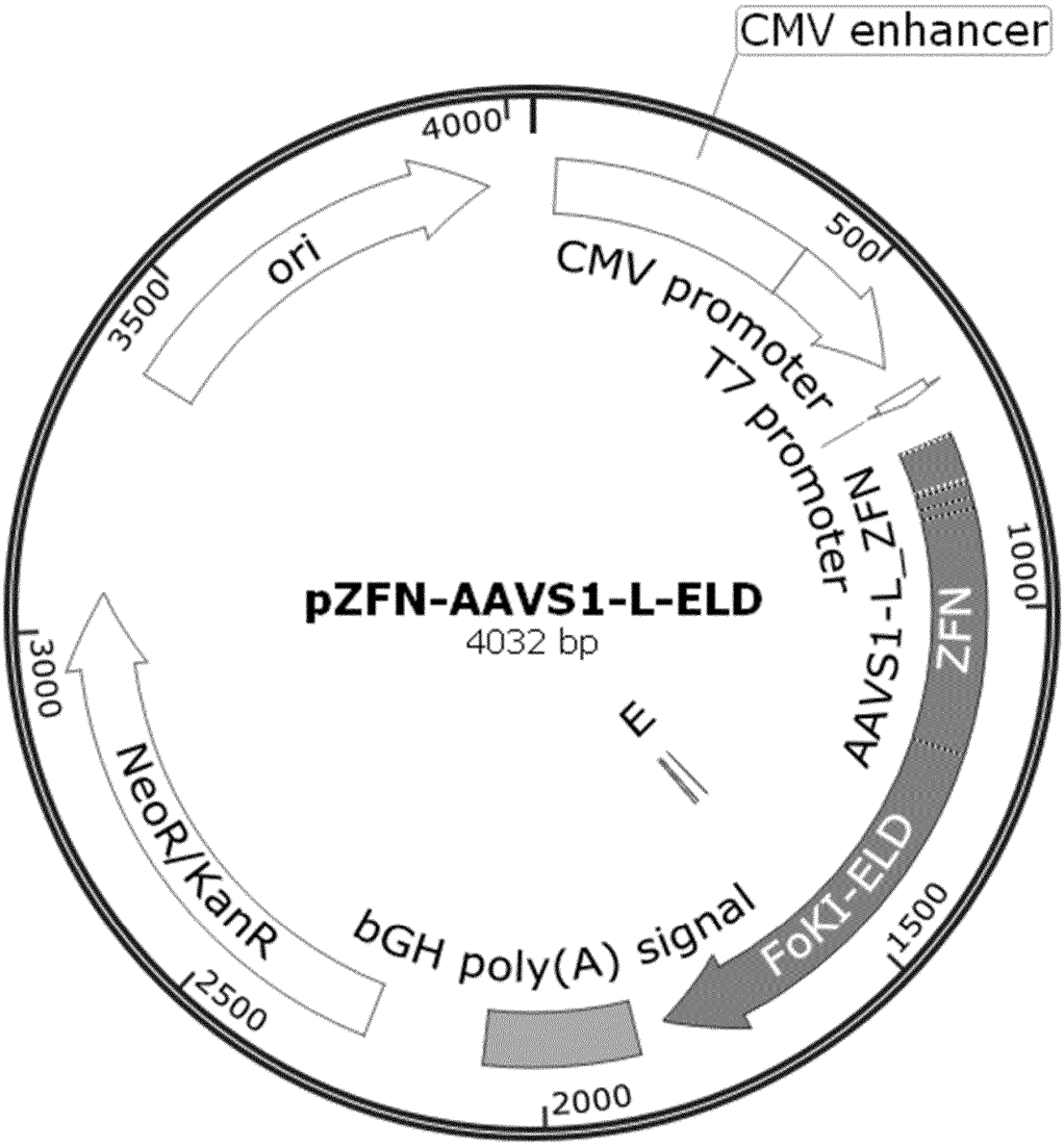
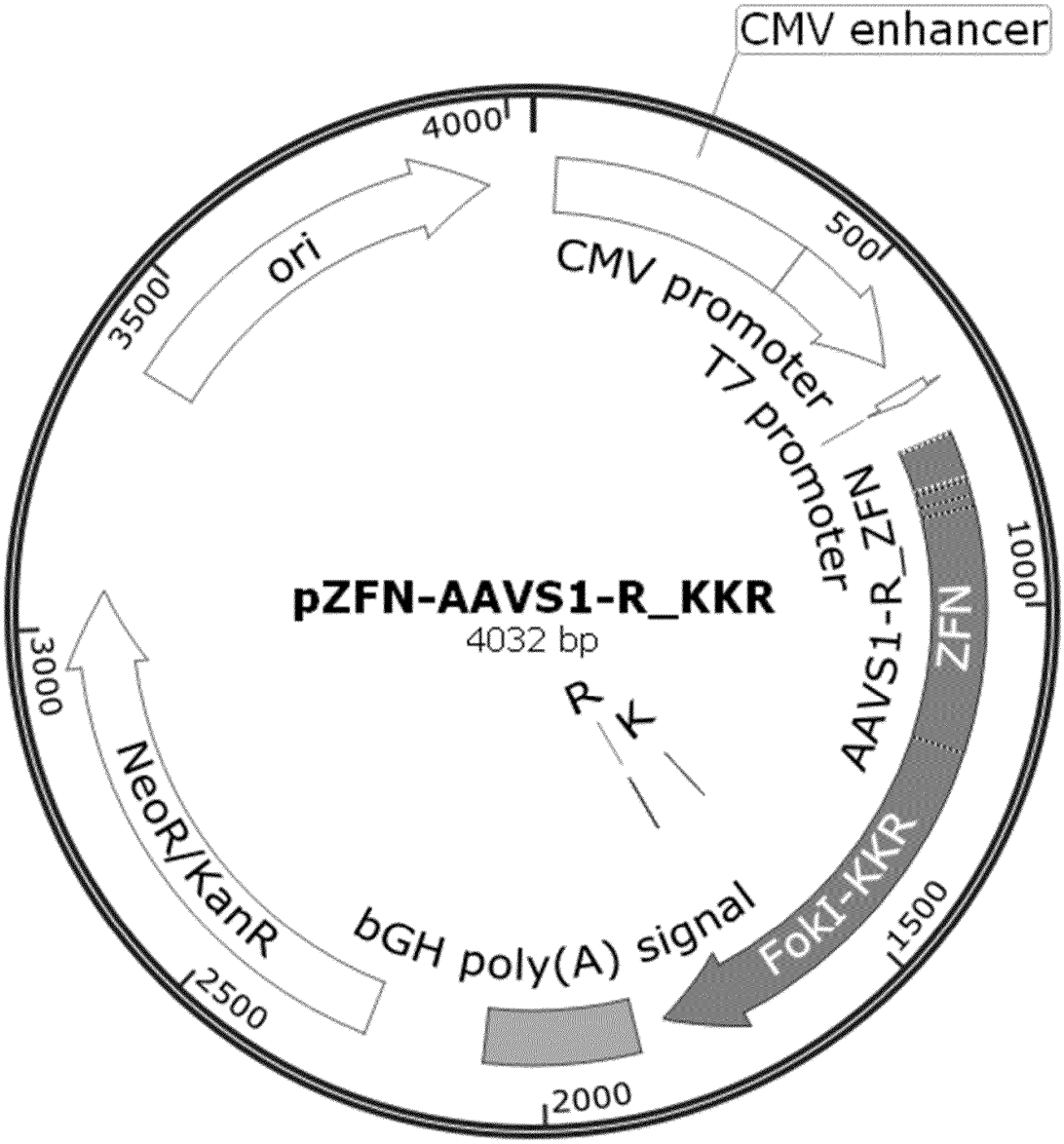

CMV enhancer
4000
500
1000
1500
2000
2500
3000
3500
ori
CMV promoter
T7 promoter
AAVS1-L_ZFN
ZFN
FoKI-ELD
bGH poly(A) signal
NeoR/KanR
pZFN-AAVS1-L-ELD
4032 bp

Figure 16:


CMV enhancer
4000
500
1000
1500
2000
2500
3000
3500
ori
CMV promoter
T7 promoter
AAVS1-R_ZFN
ZFN
FokI-KKR
pZFN-AAVS1-R_KKR
4032 bp
R
K
bGH poly(A) signal
NeoR/KanR