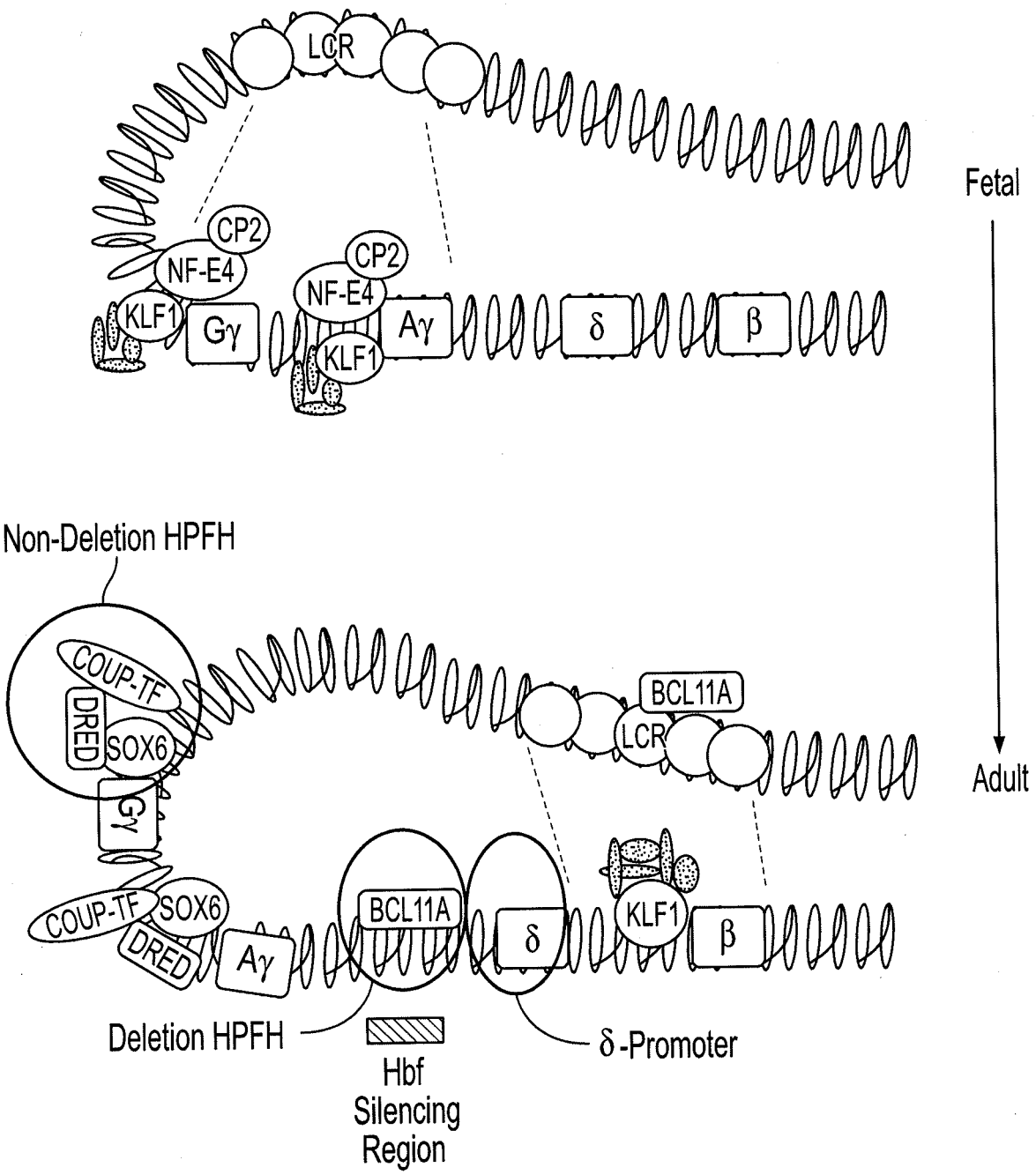

LCR
CP2
NF-E4
KLF1
Gγ
CP2
NF-E4
KLF1
Aγ
δ
β
Fetal
Non-Deletion HPFH
COUP-TF
DRED
SOX6
Gγ
BCL11A
LCR
Adult
COUP-TF
SOX6
DRED
Aγ
BCL11A
δ
KLF1
β
Deletion HPFH
Hbf
Silencing
Region
δ-Promoter

FIG. 1

"TALEN"
TAL Effector Nuclease
Two chains
5400 bp total CDS
5' overhang
Easy retargeting
Reasonably high specificity
Difficult vectorization/delivery
"ZFN"
Zinc Finger Nuclease
Two chains
2400 bp total CDS
5' overhang
Moderate retargeting
Reasonably high specificity
Moderate vectorization/delivery
"HE"
Homing Endonuclease
Single chain
800 bp CDS
3' overhang
Difficult retargeting
High specificity
Easiest vectorization/delivery

FIG. 2

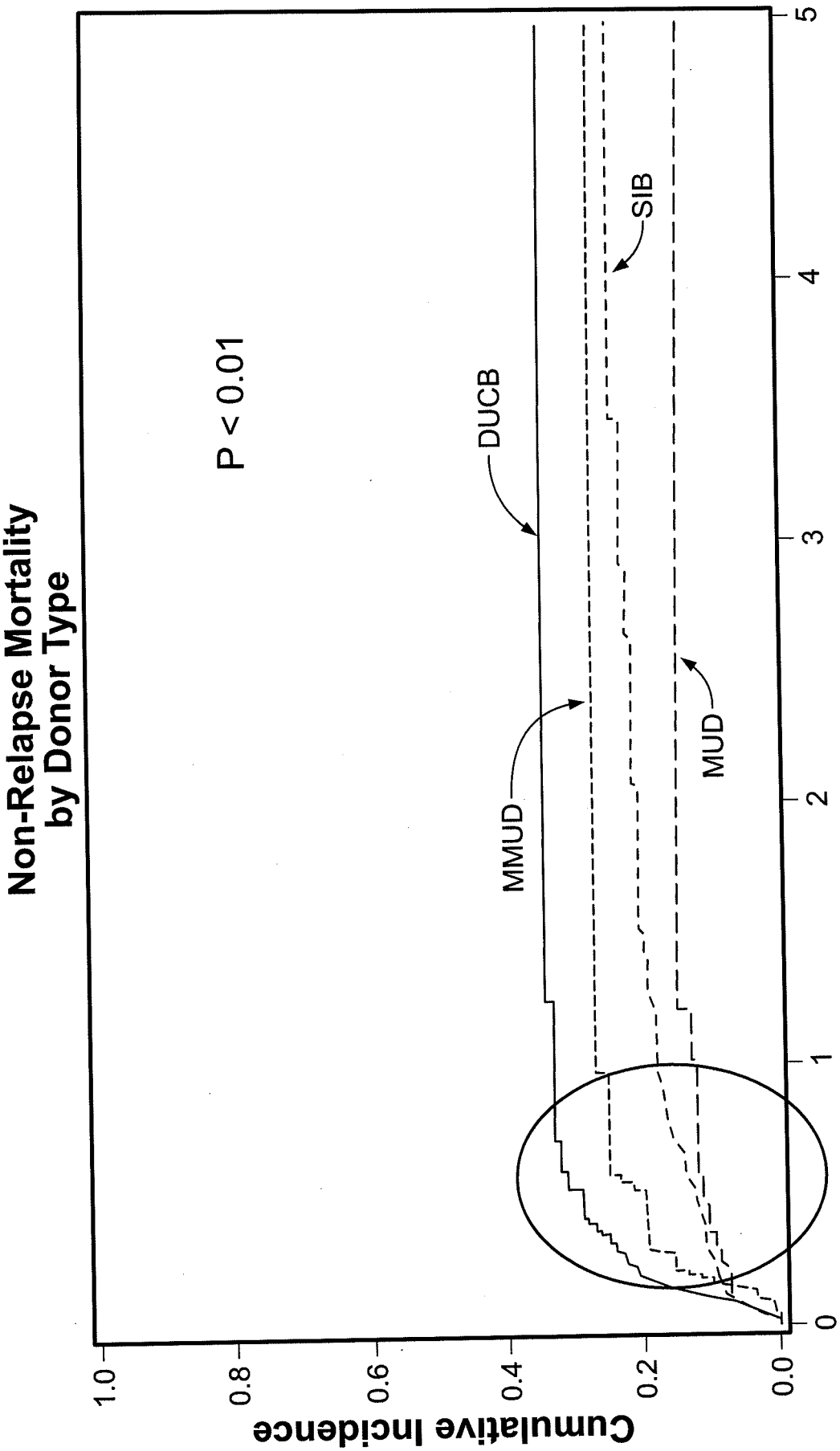

Non-Relapse Mortality
by Donor Type
P < 0.01
DUCB
SIB
MMUD
MUD
Cumulative Incidence
0.0
0.2
0.4
0.6
0.8
1.0
0
1
2
3
4
5
Years Post-Transplantation

FIG. 3

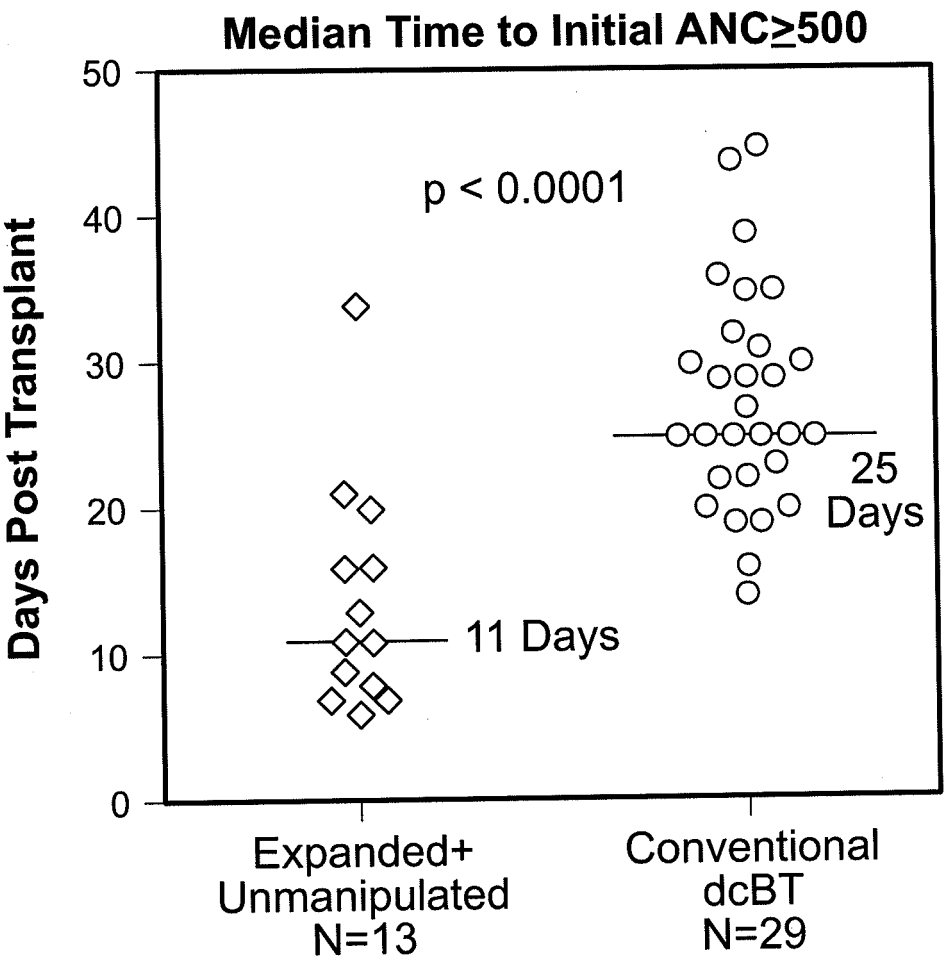

Median Time to Initial ANC≥500
Days Post Transplant
50
40
30
20
10
0
p < 0.0001
25
Days
11 Days
Expanded+
Unmanipulated
N=13
Conventional
dcBT
N=29

FIG. 4

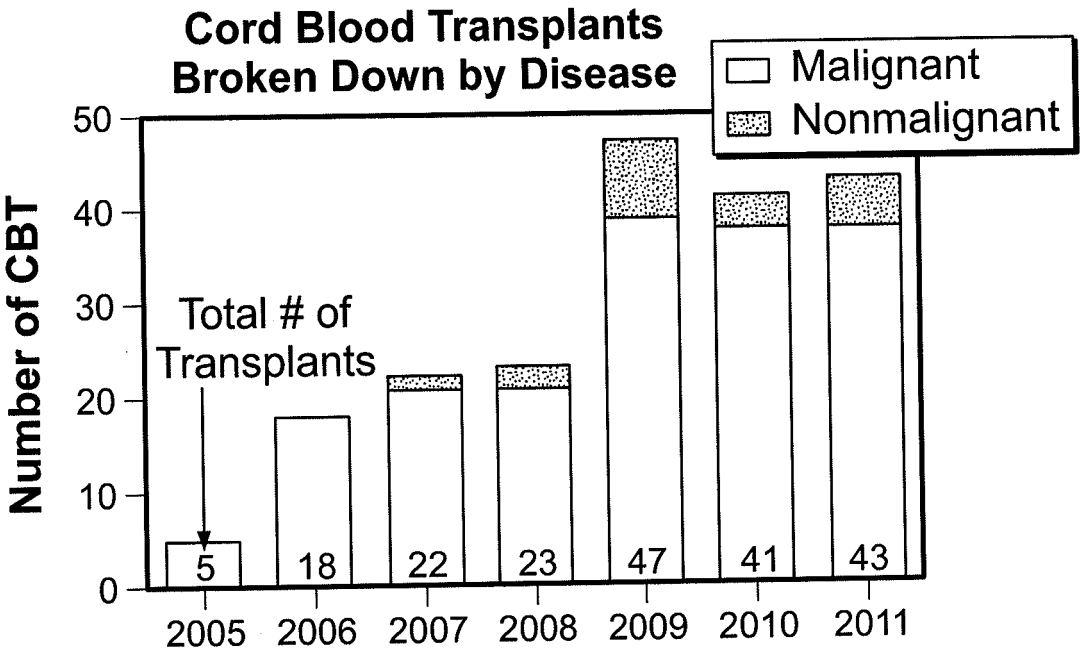

Cord Blood Transplants
Broken Down by Disease
Malignant
Nonmalignant
Number of CBT
50
40
30
20
10
0
Total # of
Transplants
5
18
22
23
47
41
43
2005
2006
2007
2008
2009
2010
2011

FIG. 5

(SEQ ID NO: 1)

Nucleotide Sequence of a Human Fetal Hemoglobin (HbF) Silencing Region

(chr11:5212342-5215944 in HG18)

```
   1 CCAGTGAGCAGGTTGGTTTAAGATAAGCAGGGTTTCATTAGTTTGTGAGA   50
  51 ATGAAAAATGAACCTTCATTCCACTATTCCCTTAACTTGCCCTGAGATTG  100
 101 GCTGTTCTGTCATGTGTGTCTTGACTCAGAAACCCTGTTCTCCTCTACAT  150
 151 ATCTCCCCACCGCATCTCTTTCAGCAGTTGTTTCTAAAAATATCCTCCTA  200
 201 GTTTCATTTTTGCAGAAGTGTTTTAGGCTAATATAGTGGAATGTATCTTA  250
 251 GAGTTTAACTTATTTGTTTCTGTCACTTTATACTAAGAAAACTTATCTAA  300
 301 AAGCAGATGTTTTAACAAGTTGACTCAATATAAAGTTCTTCTTTGCCTCT  350
 351 AGAGATTTTTGTCTCCAAGGGAATTTTGAGAGGTTGGAATGGACAAATCT  400
 401 ATTGCTGCAGTTTAAACTTGCTTGCTTCCTCCTTCTTTTGGTAAATTCTT  450
 451 CCTATAATAAAACTCtaatttttattatattgaaataaatatccattaa  500
 501 aagaatatttaaaaaatGAATAGTGTTTATTTACCAGTTATTGAAATAGG  550
 551 TTCTGGAAACATGAATTTTAAGGTTAACATTTTAATGACAGATAAAATCA  600
 601 AATATTATATACAAATATTTTGAATGTTTAAAATTATGGTATGACTAAAG  650
 651 AAAGAATGCAAAGTGAAAAGTAGATTTACCATATTCAGCCAGATTAAATT  700
 701 TAACGAAGTTCCTGGGAATATGCTAGTACAGAACATTTTTACAGATGTGT  750
 751 TCTTAAAAAAAAATGTGGAATTAGACCCAGGAATGAAGATCCCAGTAGTT  800
 801 TTTCACTCTTTTCTGAATTCAAATAATGCCACAATGGCAGACAAATACAC  850
 851 ACCCATGAGCATATCCAAaaggaaggattgaaggaaagaggaggaagaaa  900
 901 tggagaaaggaaggaaggaagaggggaagagagaggatggaagggatgga  950
 951 ggagaagaaggaaAAATAAATAATGgagaggagaggagaaaaaaggaggg 1000
1001 gagaggagaggagaagggatagggaagagaaagagaaagggaagggaaga 1050
1051 gaggaaagaagagaagaggagagaaaagaaacgaagagaggggaagggaa 1100
1101 ggaaaaaaaagaggaaaaaagagacaagagaagagaTaagactgacagtt 1150
1151 caaattttggtggtgatatggatcaatagaaactcaaactctgttggtga 1200
1201 cactgtacaatagtataacccctttggaaaacctttaatagtatccacaa 1250
1251 atgctggatgcttgataagtctattacctagcaattacattttagatat 1300
```

FIG. 6

1301 tcagaaacacatgcatgtgtgtatccaaagacatgtatagaaatgcttat 1350
1351 gacagcaataatcataaaaacctcaaaccggtagccacttaaatgcttac 1400
1401 caacagtagaattgataaattacggtatagtcaaagaatagaatattaca 1450
1451 cagaaatgaaaagaatcaactactgcttaacacgtagcgatacaaatgca 1500
1501 ttttacagcatttggttgattaaaagtaaccagaggtgagttcaaactat 1550
1551 atgactttatttgtatatagAAAGATGGATGATGTGCCTGAGATTCTGAT 1600
1601 CACAAGGGGAAATGTTATAAAATAGGGTAGAGAGGAGCCATGAATGACCT 1650
1651 TTAAACTTTGTTACAAGTTATTTTTCTGTAACCTggaagccaacgaaaga 1700
1701 tattgaataattcaagaaaggtggtggcatggtttgatttgtgtctttaa 1750
1751 aagattattctcacttagtgaagaaatgtattttagaagtagagaaaatg 1800
1801 ggagacaaatagctgggcttctgttgcagtaGGGAAGAAAGTGACAATGC 1850
1851 CATTTCTATTATCAGACTTGGACCATGACGGTGATGTCAGTCGTGAACAC 1900
1901 AAGAATAGGGCCACATTTGTGAGTTTAGTGGTACGATaaaatcagaaata 1950
1951 cagtcttggatacattgtattgtatgcactcttgtaaaatgcaaaaagat 2000
2001 gtacttagatatgtggatctggagctcagAAAGAATACAACCAGGTCAAG 2050
2051 AATACAGAATGGAACAGAACATACAAGAACAGATCATAATGTGCTGTGTG 2100
2101 AATCACTACCACTACCTGTTAAAAATGACAGATGATGTACTTCATcaata 2150
2151 tctccttaaaatcttagaatgtgtttgtgagggaggaattatgtttccaa 2200
2201 ttcatatataagaaaattgattctaaaaaaaatgttaggtaaattcttaa 2250
2251 ggccaTGAGGACTGTTATTTGATCTTTGTCTGTTAATTCCAAAGACTTGG 2300
2301 CTTTTCACTTTAATTCTGTTCTACCTGAAATGATTTTACACATTGGGAGA 2350
2351 TCTGGTTACATGTTTATTCTATATGGATTGCATTGAGAGGATTTGTATAA 2400
2401 CAGAATAAGGTCttttttttcttttctcttctgagatggagtttcatccct 2450
2451 attgcccaagctagagtgcaatggtgcaatctaggctcaccgcaacctct 2500
2501 gcctcctgggttcaagcaattctcctgcctcagccacctgaatagctggg 2550
2551 actgcaggcatgcaccacacgcccggctgattttgtatttttagtagaga 2600
2601 tggggtttcaccatgttggtcaggctggtcttgaactcctgacctcaagt 2650
2651 gatctgcctgccttggcctcccaaagtgctgggtttacaagcctgagcca 2700
2701 ccgcatccagccAGGATAAGGTCTAAAAGTGGAAAGAATAGCATCTACTC 2750

FIG. 6 (Cont.)

6

2751 TTGTTCAGGAAACAATGAGGACCTGACTGGGCAGTAAGAGTGGTGATTAA 2800
2801 TAGATAGGGACAAATTGAAGCAGAATCGAACTGTTGATTAgaggtaggga 2850
2851 aatgattttaatctgtgaccttggtgaatgggcaagtagctatctaatga 2900
2901 ctaaaatggaaaacactggaagagaaacagttttagtataacaagtgaaa 2950
2951 tacccatgctgagtctgaggtgcctataggacatctatataaataagccc 3000
3001 agtacattgtttgatatatgggtttggcactgaggttggaggtcagaggt 3050
3051 tagaaatcagagttgggaattgggattatacaggctgtatttaagagttt 3100
3101 agatataactgtgaatccaagagtgtgaTGAATACAAAGTTAAATGAAGG 3150
3151 ACCTTTAATGAACACCAACATTTAATGTGAAATCTCAAGGAAGTATGAAG 3200
3201 TAAGACATAGTCCCCAAAATCCCCGATGATTTTAGAACTCAGTATCGATT 3250
3251 TTAATTAGTGTAATGCCAATGTGGGTTAGAATGGAAGTCAACTTGCTGTT 3300
3301 GGTTTCAGAGCAGGTAGGAGATAAGGTTCTAGATTTTGACACAGTGAAAA 3350
3351 GCTGAAACAAAAAGGAAAAGGTAGGGTGAAAGATGGGAAATGTATGTAAG 3400
3401 GAGGATGAGCCACATGGTATGGGAGGTATACTAAGGACTCTAGGGTCAGA 3450
3451 GAAATATGGGTTATATCCTTCTACAAAATTCACATTCTTggctgggtgtg 3500
3501 gtggctcacgcctgtgatcccagcactttcagaggccgaggagggtggat 3550
3551 cacctgatgttaggagttcgagatcagcctgaccaacatggtgaaacccc 3600
3601 cta 3603

FIG. 6 (Cont.)

(SEQ ID NO: 2)

Nucleotide Sequence of a 350 bp Portion of a Human HbF Silencing Region (Including Sites for Bcl11a Occupancy)

1	AAAGATGGATGATGTGCCTGAGATTCTGATCACAAGGGGAAATGTTATAA	50
51	AATAGGGTAGAGAGGAGCCATGAATGACCTTTAAACTTTGTTACAAGTTA	100
101	TTTTTCTGTAACCTggaagccaacgaaagatattgaataattcaagaaag	150
151	gtggtggcatggtttgatttgtgtctttaaaagattattctcacttagtg	200
201	aagaaatgtattttagaagtagagaaaatgggagacaaatagctgggctt	250
251	ctgttgcagtaGGGAAGAAAGTGACAATGCCATTTCTATTATCAGACTTG	300
301	GACCATGACGGTGATGTCAGTCGTGAACACAAGAATAGGGCCACATTTGT	350

FIG. 7

(SEQ ID NO: 13)

Human b-globin Gene from 1 kb Upstream of the Cap Site through the PolyA Site

```
   1 GCAATGAAAATAAATGTTTTTTATTAGGCAGAATCCAGATGCTCAAGGCC  50
  51 CTTCATAATATCCCCCAGTTTAGTAGTTGGACTTAGGGAACAAAGGAACC 100
 101 TTTAATAGAAATTGGACAGCAAGAAAGCGAGCTTAGTGATACTTGTGGGC 150
 151 CAGGGCATTAGCCACACCAGCCACCACTTTCTGATAGGCAGCCTGCACTG 200
 201 GTGGGGTGAATTCTTTGCCAAAGTGATGGGCCAGCACACAGACCAGCACG 250
 251 TTGCCCAGGAGCTGTGGGAGGAAGATAAGAGGTATGAACATGATTAGCAA 300
 301 AAGGGCCTAGCTTGGACTCAGAATAATCCAGCCTTATCCCAACCATAAAA 350
 351 TAAAAGCAGAATGGTAGCTGGATTGTAGCTGCTATTAGCAATATGAAACC 400
 401 TCTTACATCAGTTACAATTTATATGCAGAAATATTTATATGCAGAGATAT 450
 451 TGCTATTGCCTTAACCCAGAAATTATCACTGTTATTCTTTAGAATGGTGC 500
 501 AAAGAGGCATGATACATTGTATCATTATTGCCCTGAAAGAAAGAGATTAG 550
 551 GGAAAGTATTAGAAATAAGATAAACAAAAAAGTATATTAAAAGAAGAAAG 600
 601 CATTTTTTAAAATTACAAATGCAAaattaccctgatttggtcaatatgtg 650
 651 tacacatattaaaacattacactttaacccataaatatgtataatgatta 700
 701 tgtatcaattaaaaataaaaGAAAATAAAGTAGGGAGATTATGAATATGC 750
 751 AAATAAGCACACATATATTCCAAATAGTAATGTACTAGGCAGACTGTGTA 800
 801 AAGTTTTTTTTTAAGTTACTTAATGTATCTCAGAGATATTTCCTTTTGTT 850
 851 ATACACAATGTTAAGGCATTAAGTATAATAGTAAAAATTGCGgagaagaa 900
 901 aaaaaaagaaagcaagaattaaacaaaagaaaacaattgttatgaacagc 950
 951 aaataaaagaaactaaaaCGATCCTGAGACTTCCACACTGATGCAATCAT 1000
1001 TCGTCTGTTTCCCATTCTAAACTGTACCCTGTTACTTATCCCCTTCCTAT 1050
1051 GACATGAACTTAACCATAGAAAAGAAGGGGAAAGAAAACATCAAGCGTCC 1100
1101 CATAGACTCACCCTGAAGTTCTCAGGATCCACGTGCAGCTTGTCACAGTG 1150
1151 CAGCTCACTCAGTGTGGCAAAGGTGCCCTTGAGGTTGTCCAGGTGAGCCA 1200
1201 GGCCATCACTAAAGGCACCGAGCACTTTCTTGCCATGAGCCTTCACCTTA 1250
1251 GGGTTGCCCATAACAGCATCAGGAGTGGACAGATCCCCAAAGGACTCAAA 1300
```

FIG. 8

1301	GAACCTCTGGGTCCAAGGGTAGACCACCAGCAGCCTAAGGGTGGGAAAAT	1350
1351	AGACCAATAGGCAGAGAGAGTCAGTGCCTATCAGAAACCCAAGAGTCTTC	1400
1401	TCTGTCTCCACATGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTA	1450
1451	ACCTTGATACCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTC	1500
1501	ACCTTGCCCCACAGGGCAGTAACGGCAGACTTCTCCTCAGGAGTCAGATG	1550
1551	CACCATGGTGTCTGTTTGAGGTTGCTAGTGAACACAGTTGTGTCAGAAGC	1600
1601	AAATGTAAGCAATAGATGGCTCTGCCCTGACTTTTATGCCCAGCCCTGGC	1650
1651	TCCTGCCCTCCCTGCTCCTGGGAGTAGATTGGCCAACCCTAGGGTGTGGC	1700
1701	TCCACAGGGTGAGGTCTAAGTGATGACAGCCGTACCTGTCCTTGGCTCTT	1750
1751	CTGGCACTGGCTTAGGAGTTGGACTTCAAACCCTCAGCCCTCCCTCTAAG	1800
1801	ATATATCTCTTGGCCCCATACCATCAGTACAAATTGCTACTAAAAACATC	1850
1851	CTCCTTTGCAAGTGTATTTACGTAATATTTGGAAtcacagcttggtaagc	1900
1901	atattgaagatcgttttcccaattttcttattacacaaataagaagttga	1950
1951	tgcactaaaagtggaagagttttgtctaCCATAATTCAGCTTTGGGATAT	2000
2001	GTAGATGGATCTCTTCCTGCGTCTCCAGAATATGCAAAATACTTACAGGA	2050
2051	CAGAATGGATGAAAACTCTACCTCGGTTCTAAGCATATCTTCTCCTTATT	2100
2101	TGGATTAAAACCTTCTGGTAAGAAAAGAAAAAatatatatatatatgtgt	2150
2151	gtatatatacacacatacatatacatatatatGCATTCATTTGTTGTTGT	2200
2201	TTTTCTTAATTTGCTCATGCATGCTAATAAATTATGTCTAAAAATAGAAT	2250
2251	AAATACAAATCAATGTGCTCTGTGCATTAGTTACTTATTAGGTTTTGGGA	2300
2301	AACAAGAGATAAAAAACTAGAGACCTCTTAATGCAGTCAAAAATACAAAT	2350
2351	AAATAAAAAGTCACTTACAACCCAAAGTGTGACTATCAATGGGGTAATCA	2400
2401	GTGGTGTCAAATAGGAGGTTAACTGGGGACATCTAACTGTTTCTGCCTGG	2450
2451	ACTAATCTGCAAGAGTGTCTGGGGGAACAAAAAGCCTCTGTGACTTAGAA	2500
2501	AGTAGGGGTAGGAGGGGAAAAGGTCTTCTACTTGGCTCAGATTATTTTTT	2550
2551	TCCTCTAGTCCACTAAGAATACTGCGTTTTAAAATCATTTCCTTGATTCA	2600
2601	AGTTCC	2606

FIG. 8 (Cont.)

(SEQ ID NO: 14)

606 bp Region of Human b-globin Spanning from the Promoter into Intron 2
(Mutations within this Region Result in Thalassemias and Sickle Cell Disease)

```
1   CACCCTGAAGTTCTCAGGATCCACGTGCAGCTTGTCACAGTGCAGCTCAC  50
51  TCAGTGTGGCAAAGGTGCCCTTGAGGTTGTCCAGGTGAGCCAGGCCATCA 100
101 CTAAAGGCACCGAGCACTTTCTTGCCATGAGCCTTCACCTTAGGGTTGCC 150
151 CATAACAGCATCAGGAGTGGACAGATCCCCAAAGGACTCAAAGAACCTCT 200
201 GGGTCCAAGGGTAGACCACCAGCAGCCTAAGGGTGGGAAAATAGACCAAT 250
251 AGGCAGAGAGAGTCAGTGCCTATCAGAAACCCAAGAGTCTTCTCTGTCTC 300
301 CACATGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGAT 350
351 ACCAACCTGCCCAGGGCCTCACCACCAACTTCATCCACGTTCACCTTGCC 400
401 CCACAGGGCAGTAACGGCAGACTTCTCCTCAGGAGTCAGATGCACCATGG 450
451 TGTCTGTTTGAGGTTGCTAGTGAACACAGTTGTGTCAGAAGCAAATGTAA 500
501 GCAATAGATGGCTCTGCCCTGACTTTTATGCCCAGCCCTGGCTCCTGCCC 550
551 TCCCTGCTCCTGGGAGTAGATTGGCCAACCCTAGGGTGTGGCTCCACAGG 600
601 GTGAGG                                            606
```

FIG. 9

(SEQ ID NO: 24)

Nucleotide Sequence of Human Bcl11a cDNA (CCDS1862.1)

1	ATGTCTCGCCGCAAGCAAGGCAAACCCCAGCACTTAAGCAAACGGGAATT	50
51	CTCGCCCGAGCCTCTTGAAGCCATTCTTACAGATGATGAACCAGACCACG	100
101	GCCCGTTGGGAGCTCCAGAAGGGGATCATGACCTCCTCACCTGTGGGCAG	150
151	TGCCAGATGAACTTCCCATTGGGGGACATTCTTATTTTTATCGAGCACAA	200
201	ACGGAAACAATGCAATGGCAGCCTCTGCTTAGAAAAAGCTGTGGATAAGC	250
251	CACCTTCCCCTTCACCAATCGAGATGAAAAAAGCATCCAATCCCGTGGAG	300
301	GTTGGCATCCAGGTCACGCCAGAGGATGACGATTGTTTATCAACGTCATC	350
351	TAGAGGAATTTGCCCCAAACAGGAACACATAGCAGATAAACTTCTGCACT	400
401	GGAGGGGCCTCTCCTCCCCTCGTTCTGCACATGGAGCTCTAATCCCCACG	450
451	CCTGGGATGAGTGCAGAATATGCCCCGCAGGGTATTTGTAAAGATGAGCC	500
501	CAGCAGCTACACATGTACAACTTGCAAACAGCCATTCACCAGTGCATGGT	550
551	TTCTCTTGCAACACGCACAGAACACTCATGGATTAAGAATCTACTTAGAA	600
601	AGCGAACACGGAAGTCCCCTGACCCCGCGGGTTGGTATCCCTTCAGGACT	650
651	AGGTGCAGAATGTCCTTCCCAGCCACCTCTCCATGGGATTCATATTGCAG	700
701	ACAATAACCCCTTTAACCTGCTAAGAATACCAGGATCAGTATCGAGAGAG	750
751	GCTTCCGGCCTGGCAGAAGGGCGCTTTCCACCCACTCCCCCCCTGTTTAG	800
801	TCCACCACCGAGACATCACTTGGACCCCCACCGCATAGAGCGCCTGGGGG	850
851	CGGAAGAGATGGCCCTGGCCACCCATCACCCGAGTGCCTTTGACAGGGTG	900
901	CTGCGGTTGAATCCAATGGCTATGGAGCCTCCCGCCATGGATTTCTCTAG	950
951	GAGACTTAGAGAGCTGGCAGGGAACACGTCTAGCCCACCGCTGTCCCCAG	1000
1001	GCCGGCCCAGCCCTATGCAAAGGTTACTGCAACCATTCCAGCCAGGTAGC	1050
1051	AAGCCGCCCTTCCTGGCGACGCCCCCCCTCCCTCCTCTGCAATCCGCCCC	1100
1101	TCCTCCCTCCCAGCCCCCGGTCAAGTCCAAGTCATGCGAGTTCTGCGGCA	1150
1151	AGACGTTCAAATTTCAGAGCAACCTGGTGGTGCACCGGCGCAGCCACACG	1200
1201	GGCGAGAAGCCCTACAAGTGCAACCTGTGCGACCACGCGTGCACCCAGGC	1250
1251	CAGCAAGCTGAAGCGCCACATGAAGACGCACATGCACAAATCGTCCCCCA	1300
1301	TGACGGTCAAGTCCGACGACGGTCTCTCCACCGCCAGCTCCCCGGAACCC	1350

FIG. 10

1351	GGCACCAGCGACTTGGTGGGCAGCGCCAGCAGCGCGCTCAAGTCCGTGGT	1400
1401	GGCCAAGTTCAAGAGCGAGAACGACCCCAACCTGATCCCGGAGAACGGGG	1450
1451	ACGAGGAGGAAGAGGAGGACGACGAGGAAGAGGAAGAAGAGGAGGAAGAG	1500
1501	GAGGAGGAGGAGCTGACGGAGAGCGAGAGGGTGGACTACGGCTTCGGGCT	1550
1551	GAGCCTGGAGGCGGCGCGCCACCACGAGAACAGCTCGCGGGGCGCGGTCG	1600
1601	TGGGCGTGGGCGACGAGAGCCGCGCCCTGCCCGACGTCATGCAGGGCATG	1650
1651	GTGCTCAGCTCCATGCAGCACTTCAGCGAGGCCTTCCACCAGGTCCTGGG	1700
1701	CGAGAAGCATAAGCGCGGCCACCTGGCCGAGGCCGAGGGCCACAGGGACA	1750
1751	CTTGCGACGAAGACTCGGTGGCCGGCGAGTCGGACCGCATAGACGATGGC	1800
1801	ACTGTTAATGGCCGCGGCTGCTCCCCGGGCGAGTCGGCCTCGGGGGGCCT	1850
1851	GTCCAAAAAGCTGCTGCTGGGCAGCCCCAGCTCGCTGAGCCCCTTCTCTA	1900
1901	AGCGCATCAAGCTCGAGAAGGAGTTCGACCTGCCCCCGGCCGCGATGCCC	1950
1951	AACACGGAGAACGTGTACTCGCAGTGGCTCGCCGGCTACGCGGCCTCCAG	2000
2001	GCAGCTCAAAGATCCCTTCCTTAGCTTCGGAGACTCCAGACAATCGCCTT	2050
2051	TTGCCTCCTCGTCGGAGCACTCCTCGGAGAACGGGAGTTTGCGCTTCTCC	2100
2101	ACACCGCCCGGGGAGCTGGACGGAGGGATCTCGGGGCGCAGCGGCACGGG	2150
2151	AAGTGGAGGGAGCACGCCCCATATTAGTGGTCCGGGCCCGGGCAGGCCCA	2200
2201	GCTCAAAAGAGGGCAGACGCAGCGACACTTGTGAGTACTGTGGGAAAGTC	2250
2251	TTCAAGAACTGTAGCAATCTCACTGTCCACAGGAGAAGCCACACGGGCGA	2300
2301	AAGGCCTTATAAATGCGAGCTGTGCAACTATGCCTGTGCCCAGAGTAGCA	2350
2351	AGCTCACCAGGCACATGAAAACGCATGGCCAGGTGGGGAAGGACGTTTAC	2400
2401	AAATGTGAAATTTGTAAGATGCCTTTTAGCGTGTACAGTACCCTGGAGAA	2450
2451	ACACATGAAAAAATGGCACAGTGATCGAGTGTTGAATAATGATATAAAAA	2500
2501	CTGAATAG	2508

FIG. 10 (Cont.)

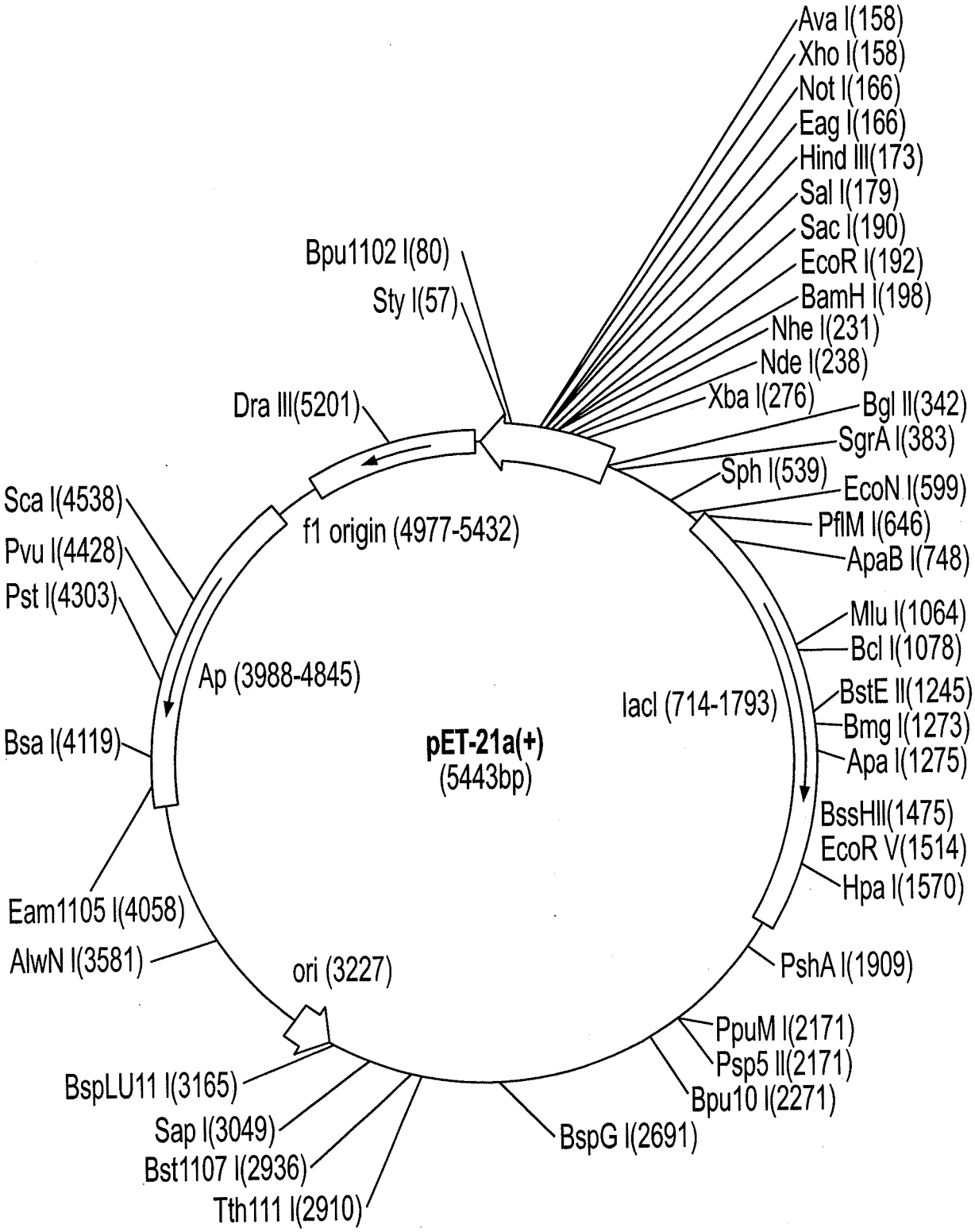

Ava I(158)
Xho I(158)
Not I(166)
Eag I(166)
Hind III(173)
Sal I(179)
Sac I(190)
EcoR I(192)
BamH I(198)
Nhe I(231)
Nde I(238)
Xba I(276)
Bgl II(342)
SgrA I(383)
Sph I(539)
EcoN I(599)
PflM I(646)
ApaB I(748)
Mlu I(1064)
Bcl I(1078)
BstE II(1245)
Bmg I(1273)
Apa I(1275)
BssHII(1475)
EcoR V(1514)
Hpa I(1570)
PshA I(1909)
PpuM I(2171)
Psp5 II(2171)
Bpu10 I(2271)
BspG I(2691)
Tth111 I(2910)
Bst1107 I(2936)
Sap I(3049)
BspLU11 I(3165)
ori (3227)
AlwN I(3581)
Eam1105 I(4058)
Bsa I(4119)
Pst I(4303)
Pvu I(4428)
Sca I(4538)
Dra III(5201)
Bpu1102 I(80)
Sty I(57)
f1 origin (4977-5432)
Ap (3988-4845)
lacI (714-1793)
pET-21a(+)
(5443bp)

FIG. 11

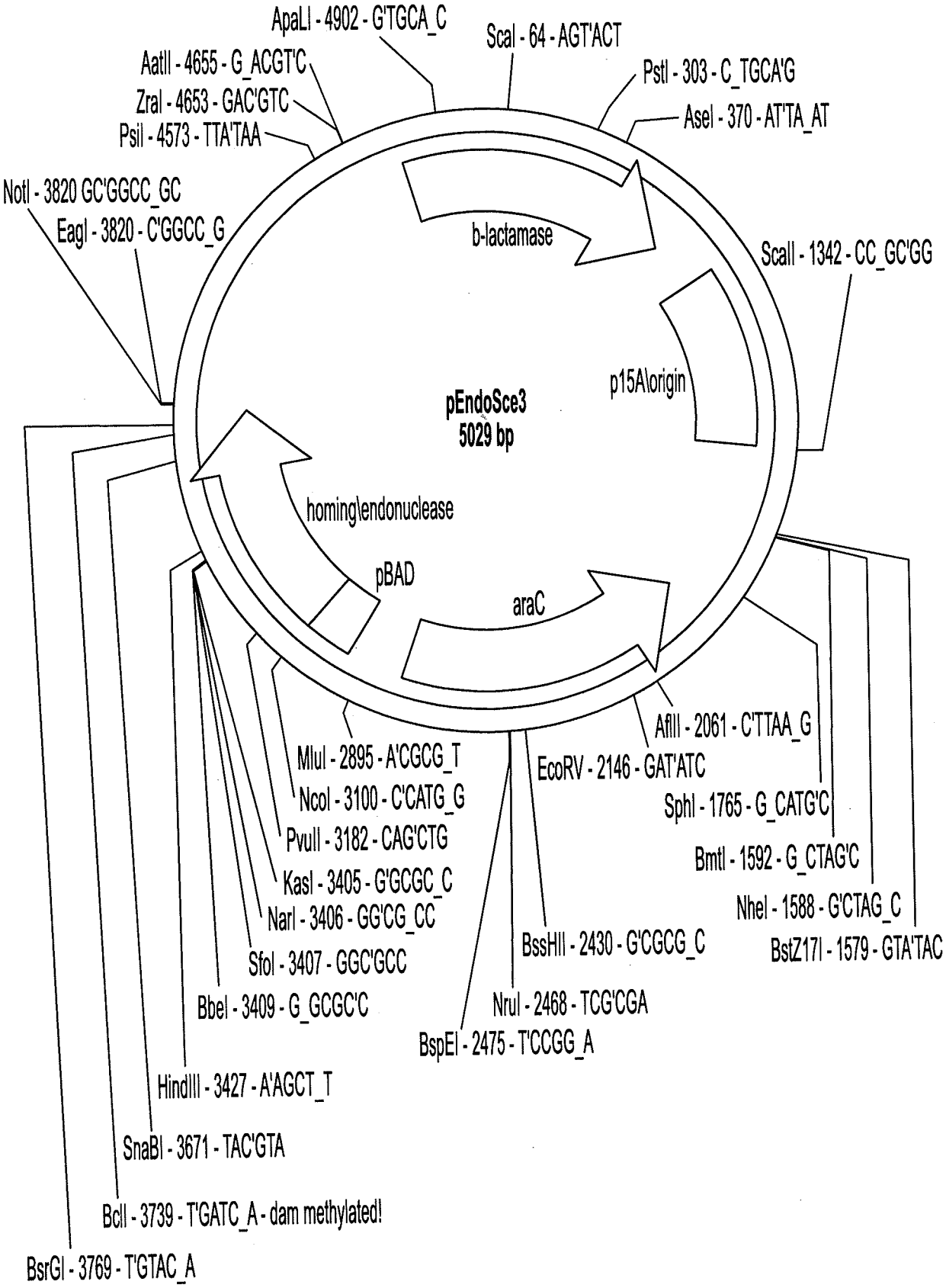

ApaLI - 4902 - G'TGCA_C
ScaI - 64 - AGT'ACT
AatII - 4655 - G_ACGT'C
PstI - 303 - C_TGCA'G
ZraI - 4653 - GAC'GTC
AseI - 370 - AT'TA_AT
PsiI - 4573 - TTA'TAA
NotI - 3820 GC'GGCC_GC
EagI - 3820 - C'GGCC_G
b-lactamase
ScaII - 1342 - CC_GC'GG
p15A\origin
pEndoSce3
5029 bp
homing\endonuclease
pBAD
araC
AflII - 2061 - C'TTAA_G
MluI - 2895 - A'CGCG_T
EcoRV - 2146 - GAT'ATC
NcoI - 3100 - C'CATG_G
SphI - 1765 - G_CATG'C
PvuII - 3182 - CAG'CTG
BmtI - 1592 - G_CTAG'C
KasI - 3405 - G'GCGC_C
NheI - 1588 - G'CTAG_C
NarI - 3406 - GG'CG_CC
BssHII - 2430 - G'CGCG_C
BstZ17I - 1579 - GTA'TAC
SfoI - 3407 - GGC'GCC
NruI - 2468 - TCG'CGA
BbeI - 3409 - G_GCGC'C
BspEI - 2475 - T'CCGG_A
HindIII - 3427 - A'AGCT_T
SnaBI - 3671 - TAC'GTA
BclI - 3739 - T'GATC_A - dam methylated!
BsrGI - 3769 - T'GTAC_A

FIG. 12

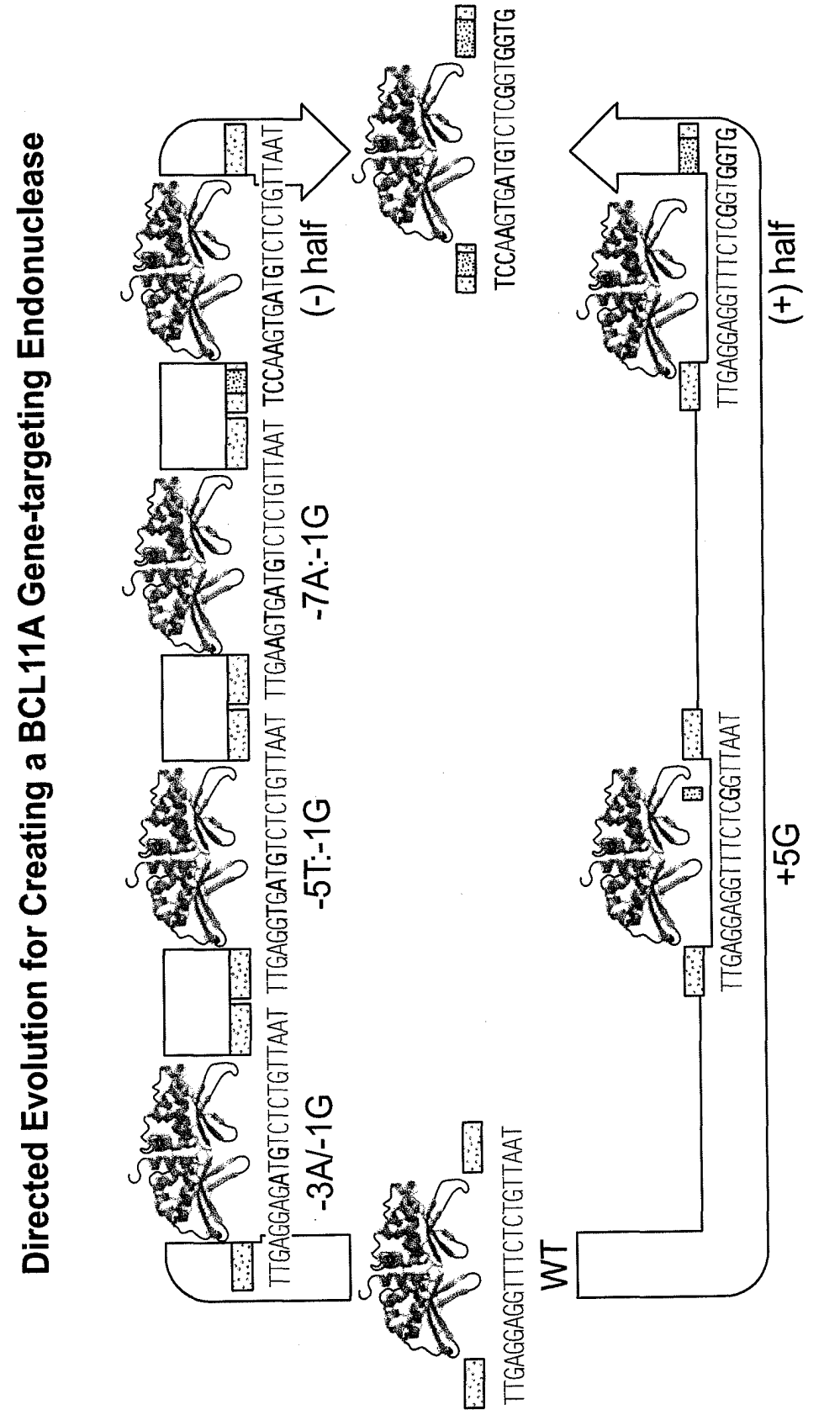

Directed Evolution for Creating a BCL11A Gene-targeting Endonuclease
TTGAGGAGATGTCTCTGTTAAT
-3A/-1G
TTGAGGAGGTTTCTCTGTTAAT
WT
TTGAGGAGATGTCTCTGTTAAT TTGAAGTGATGTCTCTGTTAAT TCCAAGTGATGTCTCTGTTAAT
-5T:-1G
-7A:-1G
(-) half
TCCAAGTGATGTCTCGGTGGTG
TTGAGGAGGTTTCTCGGTTAAT
+5G
TTGAGGAGGTTTCTCGGTGGTG
(+) half

FIG. 13

(SEQ ID NO: 28)

Nucleotide Sequence of I-HjeMI, Codon Optimized for Expression in E.coli

1	ATGGGATCCCACATGGACCTGACCTACGCTTACCTGGTTGGTCTGTTCGA	50
51	AGGTGACGGTTACTTCTCTATCACCAAAAAGGGTAAATACCTGACCTACG	100
101	AACTGGGTATCGAACTGTCTATCAAAGACGTTCAGCTGATCTACAAAATC	150
151	AAAGACATCCTGGGTGTTGGTAAAGTTTCTTTCCGTAAACGTAACGAAAT	200
201	CGAAATGGTTTCTCTGCGTATCCGTGACAAGAATCACCTGAAAAACTTCA	250
251	TCCTGCCGATCTTCGACAAATACCCGATGCTGTCTAACAAGCAGTACGAC	300
301	TACCTGCGTTTCAAAGACGCTCTCCTGTCTAACATTATCTACTCTGACGA	350
351	TCTGCCGGAATACGCTCGTTCTAACGAATCTATCAACTCTGTTGACTCTA	400
401	TTATCAACACCTCTTACTTCTCTGCTTGGCTGGTTGGTTTCATCGAAGCT	450
451	GAAGGTTGCTTCTCTACCTACAAACTGAACAAAGATGACGATTACCTGAT	500
501	CGCTTCTTTCGACATCGCTCAGAAAGACGGTGACATCCTGATCTCTGCTA	550
551	TCCACAAATACCTGTCTTTCACCACGAAAATCTACCTGGACAAAACCAAC	600
601	TGCTCTCGTCTGAAAGTGACCGGTGTACGTTCTGTTAAAAACGTGGTTAA	650
651	ATTCATCCAGGGTGCTCCGGTTAAACTGCTCGGTAACAAGAAACTGCAGT	700
701	ACAAACTGTGGATCAAACAGCTGCGTAAAATCTCTCGTTACTCTGAAAAA	750
751	ATCCAGCTGCCGTCTAACTAC	771

FIG. 14

(SEQ ID NO: 29)

Nucleotide Sequence of I-HjeMI, Codon Optimized for Expression in Mammals

1	ATGGGCAGCCACATGGACCTGACCTACGCCTATCTGGTCGGCCTGTTCGA	50
51	GGGCGACGGCTATTTTAGCATAACCAAGAAGGGCAAGTATCTGACGTATG	100
101	AACTGGGCATCGAGCTCTCCATCAAGGACGTGCAGCTCATCTACAAGATC	150
151	AAGGACATCCTCGGCGTGGGCAAAGTGTCTTTTAGGAAGAGGAACGAGAT	200
201	CGAGATGGTCAGCCTGCGAATCAGGGACAAAAACCACCTGAAGAACTTCA	250
251	TCCTGCCCATCTTCGACAAGTACCCCATGCTGAGCAACAAGCAGTACGAC	300
301	TATCTCCGATTCAAGGATGCCCTCCTGTCCAACATCATCTATAGCGACGA	350
351	CCTGCCCGAGTACGCCAGGAGCAACGAGTCAATCAATAGCGTGGACAGCA	400
401	TCATCAACACCTCATACTTCAGCGCCTGGCTGGTTGGCTTCATCGAGGCC	450
451	GAGGGCTGCTTCAGCACCTACAAGCTCAACAAGGACGACGATTATTTGAT	500
501	CGCGAGCTTCGATATAGCCCAGAAGGACGGCGACATTCTCATCTCCGCGA	550
551	TCCACAAATACCTGAGCTTCACGACCAAAATCTACCTGGACAAGACCAAC	600
601	TGTAGCAGGCTCAAGGTCACCGGCGTGAGGAGCGTCAAGAACGTGGTTAA	650
651	GTTCATCCAGGGTGCGCCGGTCAAGTTGCTGGGTAACAAGAAGCTGCAGT	700
701	ACAAACTTTGGATAAAGCAGCTGCGCAAGATCTCCCGATACAGCGAGAAA	750
751	ATCCAGCTGCCCAGTAACTAC	771

FIG. 15

(SEQ ID NO: 30)

Amino Acid Sequence of the Homing Endonuclease I-HjeMI

1	MGDLTYAYLVGLFEGDGYFSITKKGKYLTYELGIELSIKDVQLIYKIKDI	50
51	LGVGKVSFRKRNEIEMVSLRIRDKNHLKNFILPIFDKYPMLSNKQYDYLR	100
101	FKDALLSNIIYSDDLPEYARSNESINSVDSIINTSYFSAWLVGFIEAEGC	150
151	FSTYKLNKDDDYLIASFDIAQKDGDILISAIHKYLSFTTKIYLDKTNCSR	200
201	LKVTGVRSVKNVVKFIQGAPVKLLGNKKLQYKLWIKQLRKISRYSEKIQL	250
251	PSNY	254

FIG. 16

(SEQ ID NO: 31)

Nucleotide Sequence for a BCL11A Gene Targeting Nuclease Based on the Homing Endonuclease I-HjeMI

(Codon Optimized for Expression in E.coli and Obtained through Directed Evolution in IVC and in Bacteria)

1	ATGGGATCCCACATGGACCTGACCTACGCTTACCTGGTTGGTCTGTTCGA	50
51	AGGTGACGGTTACTTCACTATCGCTAAAGCGGGTAAGTACCTGAATTACG	100
101	AGCTGGGTATCACGCTGTCTATCAAAGACGCTCAGCTGATCTACAAAATC	150
151	AAAGACATCCTGGGTGTTGGTAATGTTTATTTCCGGAAATATAGGCAGCA	200
201	TGAAATGGTTTCTCTGCGGATCCAGGACAAGAATCACCTGAAAAACTTCA	250
251	TCCTGCCGATCTTCGACAAATACCCGATGCTGTCTAACAAGCAGTACGAC	300
301	TACCTGCGTTTCAAAGACGCTCTCCTGTCTAACATTATCTACTCTGACGA	350
351	TCTGCCGGAATACGCTCGTTCTAACGAATCTATCAACTCTGTTGACTCTA	400
401	TTATCAACACCTCTTACTTCTCTGCTTGGCTGGTTGGTTTCATCGAAGCT	450
451	GAAGGTTGCTTCACGACCTACAAAGCGAGTAAAGATAAGTACCTGACGGC	500
501	TGGGTTCAGTATCGCTCAGAAAGACGGTGACATCCTGATCTCTGCTATCC	550
551	ACAAATACCTGTCTTTCACCACGAAACCGTACAAGGACAAAACCAACTGC	600
601	TCTCATCTGAAGGTGACCGGTGTACGTTCTGTTAACAACGTGGTTAAATT	650
651	CATCCAGGGTGCTCCGGTTAAACTGCTCGGTAACAAGAAACTGCAGTACA	700
701	AACTGTGGATCAAACAGCTGCGTAAAATCTCTCGTTACTCTGAAAAAATC	750
751	CAGCTGCCGTCTAACTAC	768

FIG. 17

(SEQ ID NO: 32)

Nucleotide Sequence of a BCL11A Gene Targeting Nuclease Based on the Homing Endonuclease I-HjeMI

(Codon Optimized for Expression in Mammals and Obtained through Directed Evolution in IVC and in Bacteria)

```
  1 ATGGGCAGCCACATGGACCTGACCTACGCCTATCTGGTCGGCCTGTTCGA  50
 51 GGGCGACGGCTATTTTACaATAgCtAAGgccGGCAAGTATCTGAacTACG 100
101 AGCTGGGCATCacaCTCTCCATCAAGGACGctCAGCTCATCTACAAGATC 150
151 AAGGACATCCTCGGCGTGGGCAAcGTGtaCTTTAGGAAGtacAggcAaca 200
201 tGAGATGGTCAGCCTGCGAATCcaGGACAAAAACCACCTGAAGAACTTCA 250
251 TCCTGCCCATCTTCGACAAGTACCCCATGCTGAGCAACAAGCAGTACGAC 300
301 TACCTGCGATTCAAGGATGCCCTCCTGTCCAACATCATCTATAGCGACGA 350
351 CCTGCCCGAGTACGCCAGGAGCAACGAGTCAATCAATAGCGTGGACAGCA 400
401 TCATCAACACCTCATACTTCAGCGCCTGGCTGGTTGGCTTCATCGAGGCC 450
451 GAGGGCTGCTTCAcCACCTACAAGgcatcCAAGGACaAgTACCTGAcaGC 500
501 GgGCTTCtccATAGCCCAGAAGGACGGCGACATTCTCATCTCCGCGATCC 550
551 ACAAATACCTGAGCTTCACGACCAAAccCTACaaaGACAAGACCAACTGT 600
601 AGCcacCTCAAGGTCACCGGCGTGAGGAGCGTCAAtAACGTGGTTAAGTT 650
651 CATCCAGGGTGCGCCGGTCAAGCTGCTGGGTAACAAGAAGCTGCAGTACA 700
701 AACTTTGGATAAAGCAGCTGCGCAAGATCTCCCGATACAGCGAGAAAATC 750
751 CAGCTGCCCAGTAACTAC                                  768
```

FIG. 18

(SEQ ID NO: 33)

Amino Acid Sequence of a BCL11A Gene Targeting Nuclease Based on the Homing Endonuclease I-HjeMI

```
  1 MGSHMDLTYAYLVGLFEGDGYFTIAKAGKYLNYELGITLSIKDAQLIYKI  50
 51 KDILGVGNVYFRKYRQHEMVSLRIQDKNHLKNFILPIFDKYPMLSNKQYD 100
101 YLRFKDALLSNIIYSDDLPEYARSNESINSVDSIINTSYFSAWLVGFIEA 150
151 EGCFTTYKASKDKYLTAGFSIAQKDGDILISAIHKYLSFTTKPYKDKTNC 200
201 SHLKVTGVRSVNNVVKFIQGAPVKLLGNKKLQYKLWIKQLRKISRYSEKI 250
251 QLPSNY                                              256
```

FIG. 19

Distribution of Amino-acid Residues Different between the BCL11A Gene-targeting Endonuclease and its Parental LHE I-HjeMI

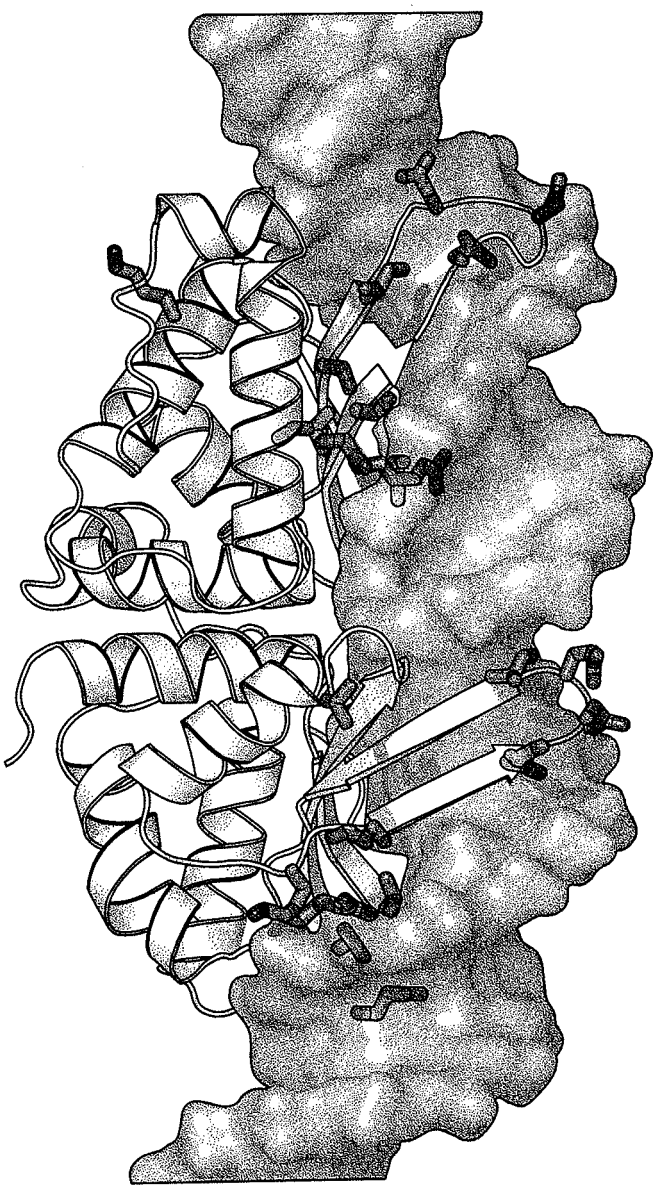


FIG. 20

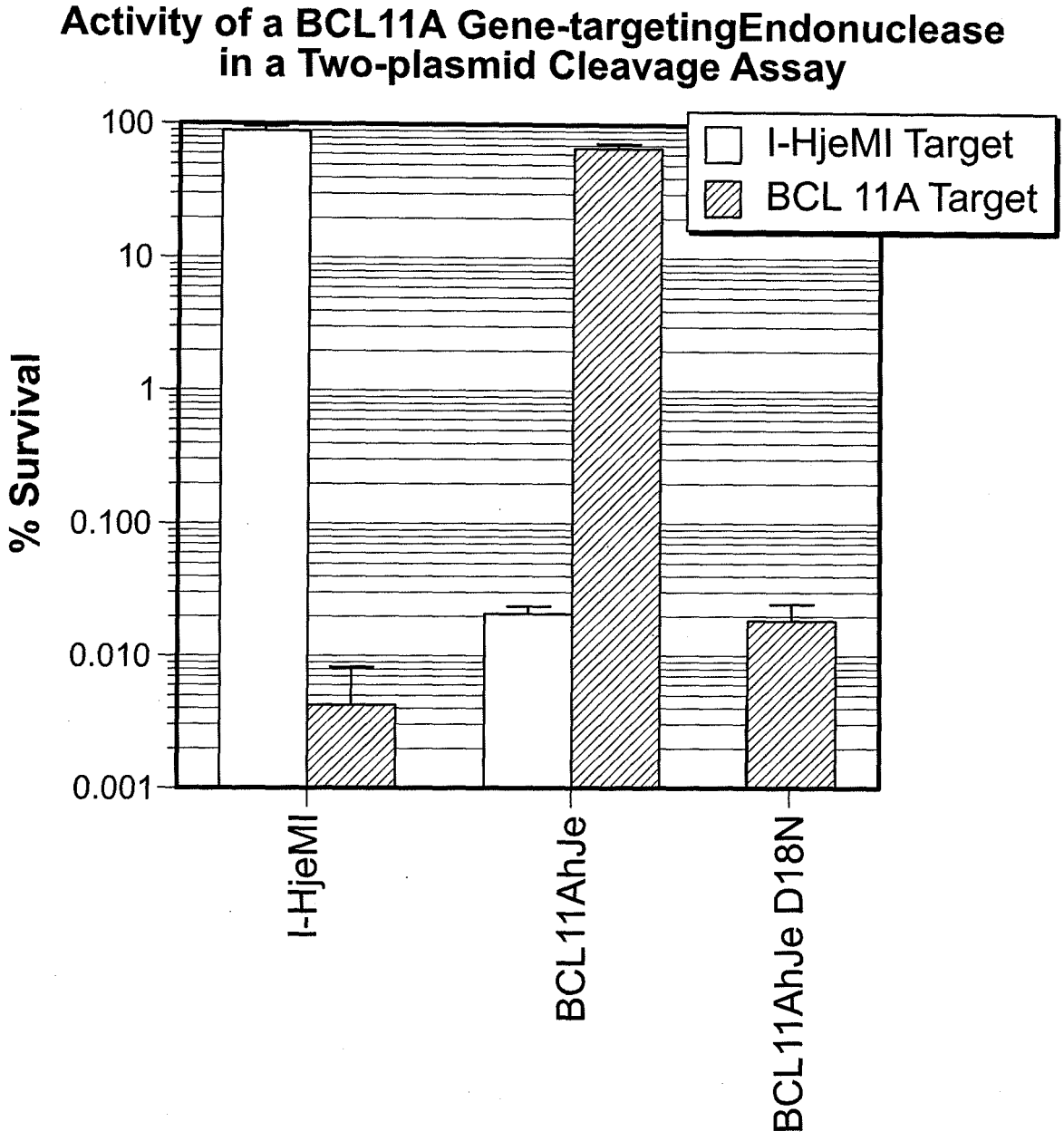

Activity of a BCL11A Gene-targetingEndonuclease in a Two-plasmid Cleavage Assay
% Survival
100
10
1
0.100
0.010
0.001
I-HjeMI Target
BCL 11A Target
I-HjeMI
BCL11AhJe
BCL11AhJe D18N

FIG. 21

(SEQ ID NO: 34)
Nucleotide Sequence of I-OnuI, Codon Optimized for Expression in *E. coli*
(parental enzyme for HEs targeting the HbF silencing)

```
   1 ATGTCCGCCTACATGTCCCGTCGCGAGTCCATTAACCCGTGGATTCTCAC  50
  51 CGGTTTCGCCGACGCGGAAGGCTCCTTTTTGCTGCGCATCCGCAACAACA 100
 101 ACAAGTCCAGCGTCGGCTACTCCACTGAGCTCGGCTTCCAAATTACACTT 150
 151 CATAACAAGGACAAGAGCATTCTTGAGAACATCCAGTCAACATGGAAGGT 200
 201 GGGCGTGATCGCCAACAGCGGTGACAACGCCGTGTCGCTGAAGGTCACGC 250
 251 GTTTTGAGGACCTGAAGGTCATTATCGACCATTTTGAAAAATACCCACTG 300
 301 ATTACGCAGAAGCTCGGTGACTACATGCTGTTTAAGCAGGCGTTTTGCGT 350
 351 CATGGAGAACAAGGAGCATTTGAAGATTAATGGTATCAAGGAGCTGGTGC 400
 401 GCATTAAGGCAAAGCTCAATTGGGGTCTGACGGATGAGCTGAAGAAGGCC 450
 451 TTTCCGGAGATCATCTCGAAGGAGCGCTCCCTCATCAACAAGAACATCCC 500
 501 TAATTTCAAGTGGCTGGCGGGTTTTACCTCGGGCGAGGGTTGCTTCTTTG 550
 551 TTAACCTGATCAAGTCAAAGTCGAAGCTAGGTGTCCAGGTGCAGCTGGTG 600
 601 TTCAGCATTACCCAACACATCAAGGATAAGAACCTCATGAACTCTCTGAT 650
 651 TACCTACTTGGGCTGCGGCTACATTAAGGAGAAAAACAAGAGTGAGTTCT 700
 701 CCTGGCTTGACTTCGTCGTCACGAAATTCTCCGACATCAACGACAAGATC 750
 751 ATTCCGGTCTTTCAGGAAAACACGCTCATCGGCGTGAAGCTCGAGGACTT 800
 801 CGAGGATTGGTGTAAGGTCGCTAAGCTGATCGAGGAGAAAAAGCACCTGA 850
 851 CAGAAAGTGGCCTGGACGAGATCAAGAAGATTAAGCTGAACATGAACAAG 900
 901 GGCAGAGTATTC                                       912
```

FIG. 22A

(SEQ ID NO: 15)

Amino Acid Sequence of I-OnuIhoming endonuclease.

SAYMSRRESI NPWILTGFAD AEGSFLLRIR NNNKSSVGYS TELGFQITLH NKDKSILENI 60
QSTWKVGVIA NSGDNAVSLK VTRFEDLKVI IDHFEKYPLI TQKLGDYMLF KQAFCVMENK 120
EHLKINGIKE LVRIKAKLNW GLTDELKKAF PEIISKERSL INKNIPNFKW LAGFTSGEGC 180
FFVNLIKSKS KLGVQVQLVF SITQHIKDKN LMNSLITYLG CGYIKEKNKS EFSWLDFVVT 240
KFSDINDKII PVFQENTLIG VKLEDFEDWC KVAKLIEEKK HLTESGLDEI KKIKLNMNKG 300
RVF 303

FIG. 22B

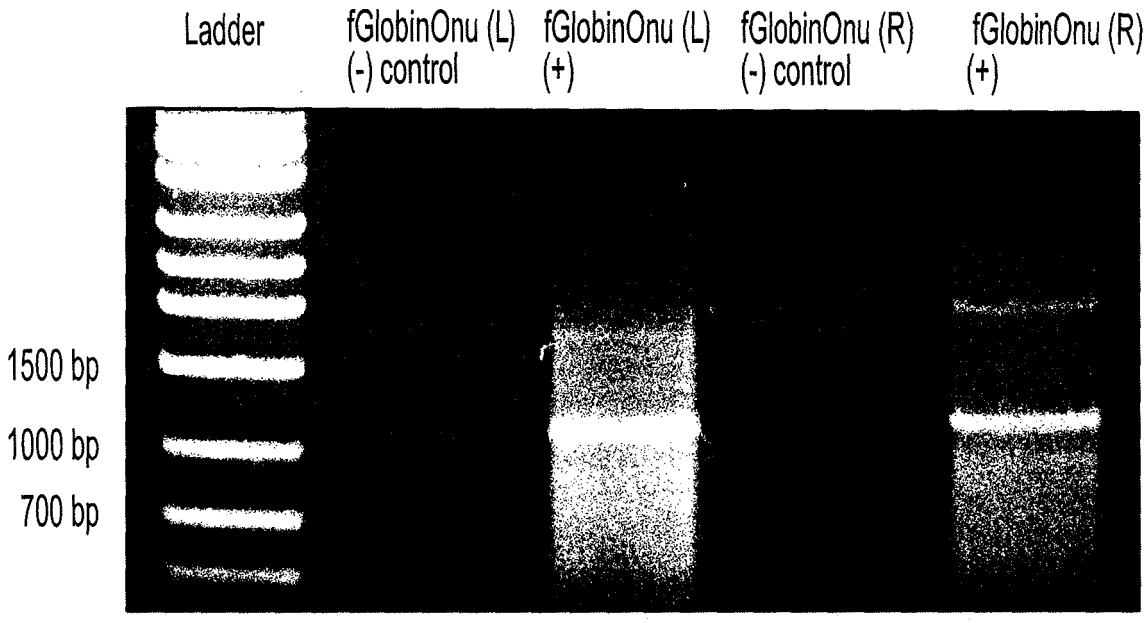

Ladder
fGlobinOnu (L) (-) control
fGlobinOnu (L) (+)
fGlobinOnu (R) (-) control
fGlobinOnu (R) (+)
1500 bp
1000 bp
700 bp

FIG. 23

(SEQ ID NO: 35)

Nucleotide Sequence of MegaTAL:5.5 RVD + Y2 I-AniI

1	gtggatctacgcacgctcggctacagtcagcagcagcaagagaagatcaa	50
51	accgaaggtgcgttcgacagtggcgcagcaccacgaggcactggtgggcc	100
101	atgggtttacacacgcgcacatcgttgcgctcagccaacacccggcagcg	150
151	ttagggaccgtcgctgtcacgtatcagcacataatcacggcgttgccaga	200
201	ggcgacacacgaagacatcgttggcgtcggcaaacagtggtccggcgcac	250
251	gcgccctggaggccttgctcacggatgcgggggagttgagaggtccgccg	300
301	ttacagttggacacaggccaacttgtgaagattgcaaaacgtggcggcgt	350
351	gaccgcaatggaggcagtgcatgcatcgcgcaatgcactgacgggtgccc	400
401	ccctgaacctgaccccggaccaagtggtggctatcgccagcaacaatggc	450
451	ggcaagcaagcgctcgaaacggtgcagcggctgttgccggtgctgtgcca	500
501	ggaccatggcctgactccggaccaagtggtggctatcgccagccacgatg	550
551	gcggcaagcaagcgctcgaaacggtgcagcggctgttgccggtgctgtgc	600
601	caggaccatggcctgaccccggaccaagtggtggctatcgccagcaacat	650
651	tggcggcaagcaagcgctcgaaacggtgcagcggctgttgccggtgctgt	700
701	gccaggaccatggcctgaccccggaccaagtggtggctatcgccagcaac	750
751	aatggcggcaagcaagcgctcgaaacggtgcagcggctgttgccggtgct	800
801	gtgccaggaccatggcctgactccggaccaagtggtggctatcgccagcc	850
851	acgatggcggcaagcaagcgctcgaaacggtgcagcggctgttgccggtg	900

FIG. 24

901 ctgtgccaggaccatggcctgaccccggaccaagtggtggctatcgccag 950
951 caacggtggcggcaagcaagcgctcgaaagcattgtggcccagctgagcc 1000
1001 ggcctgatccggcgttggccgcgttgaccaacgaccacctcgtcgccttg 1050
1051 gcctgcctcggcggacgtcctgccatggatgcagtgaaaaagggattgcc 1100
1101 gcacgcgccggaattgatcagaagagtcaatcgccgtattggcgaacgca 1150
1151 cgtcccatcgcgttgcgatatctagagtgggaggaagcgatcttacgtac 1200
1201 gcgtatttagttggtctctacgaaggggatggatactttagtatcaccaa 1250
1251 gaaaggcaagtacttgacttatgaattaggtattgagctgagcatcaaag 1300
1301 acgtccaattgatttacaagatcaagaaaatcctaggtattggcatcgta 1350
1351 agcttcaggaagagaaacgagattgaaatggttgcattgaggatccgtga 1400
1401 taagaatcatctaaaatctaagatattgcctatatttgagaagtatccaa 1450
1451 tgttttccaacaaacagtacgactatttaagattcaggaatgcattgtta 1500
1501 tctggcattatatacctagaagacttgcctgattacactagaagtgacga 1550
1551 accattgaattctatagaatccattatcaacacatcatacttctccgcct 1600
1601 ggctagttggatttatagaagctgagggctgtttcagtgtgtacaagctg 1650
1651 aacaaagacgatgactacttgattgcttcattcgacattgcccaaagaga 1700
1701 tggtgatatcttgatttcagcaattaggaagtacttaagtttcactacta 1750
1751 aggtttacctagacaagactaattgtagcaaattgaaggtcactagtgtt 1800
1801 agatccgtcgagaacatcattaagtttctgcagaatgctcctgtcaaatt 1850
1851 gttaggcaacaagaaactgcaatacaagttgtggttgaaacaactaagga 1900
1901 agatttctaggtattccgagaagatcaagattccatcaaactacgtcgac 1950
1951 cgagcatcttaccgccatttatacccatatttgttctgtttttcttga 1998

FIG. 24 (Cont.)

(SEQ ID NO: 36)

Amino Acid Sequence of MegaTAL:5.5 RVD + Y2 I-AniI

1	VDLRTLGYSQQQQEKIKPKVRSTVAQHHEALVGHGFTHAHIVALSQHPAA	50
51	LGTVAVTYQHIITALPEATHEDIVGVGKQWSGARALEALLTDAGELRGPP	100
101	LQLDTGQLVKIAKRGGVTAMEAVHASRNALTGAPLNLTPDQVVAIASNNG	150
151	GKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPVLC	200
201	QDHGLTPDQVVAIASNIGGKQALETVQRLLPVLCQDHGLTPDQVVAIASN	250
251	NGGKQALETVQRLLPVLCQDHGLTPDQVVAIASHDGGKQALETVQRLLPV	300
301	LCQDHGLTPDQVVAIASNGGGKQALESIVAQLSRPDPALAALTNDHLVAL	350
351	ACLGGRPAMDAVKKGLPHAPELIRRVNRRIGERTSHRVAISRVGGSDLTY	400
401	AYLVGLYEGDGYFSITKKGKYLTYELGIELSIKDVQLIYKIKKILGIGIV	450
451	SFRKRNEIEMVALRIRDKNHLKSKILPIFEKYPMFSNKQYDYLRFRNALL	500
501	SGIIYLEDLPDYTRSDEPLNSIESIINTSYFSAWLVGFIEAEGCFSVYKL	550
551	NKDDDYLIASFDIAQRDGDILISAIRKYLSFTTKVYLDKTNCSKLKVTSV	600
601	RSVENIIKFLQNAPVKLLGNKKLQYKLWLKQLRKISRYSEKIKIPSNYVD	650
651	RASYRHLYPYLFCFS	665

FIG. 25

(SEQ ID NO: 37)

Nucleotide Sequence of Cas9 Endonuclease

(from Mali *et al.*, *Science* (2013))

1	gccacc**ATG**GACAAGAAGTACTCC**ATTGGGCTCGATATCGGCACAAACAG**	50
51	**CGTCGGCTGGGCCGTCATT**ACGGACGAGTACAAGGTGCCGAGCAAAAAAT	100
101	TCAAAGTTCTGGGCAATACCGATCGCCACAGCATAAAGAAGAACCTCATT	150
151	GGCGCCCTCCTGTTCGACTCCGGGGAGACGGCCGAAGCCACGCGGCTCAA	200
201	AAGAACAGCACGGCGCAGATATACCCGCAGAAAGAATCGGATCTGCTACC	250
251	TGCAGGAGATCTTTAGTAATGAGATGGCTAAGGTGGATGACTCTTTCTTC	300
301	CATAGGCTGGAGGAGTCCTTTTTGGTGGAGGAGGATAAAAAGCACGAGCG	350
351	CCACCCAATCTTTGGCAATATCGTGGACGAGGTGGCGTACCATGAAAAGT	400
401	ACCCAACCATATATCATCTGAGGAAGAAGCTTGTAGACAGTACTGATAAG	450
451	GCTGACTTGCGGTTGATCTATCTCGCGCTGGCGCATATGATCAAATTTCG	500
501	GGGACACTTCCTCATCGAGGGGGACCTGAACCCAGACAACAGCGATGTCG	550
551	ACAAACTCTTTATCCAACTGGTTCAGACTTACAATCAGCTTTTCGAAGAG	600
601	AACCCGATCAACGCATCCGGAGTTGACGCCAAAGCAATCCTGAGCGCTAG	650
651	GCTGTCCAAATCCCGGCGGCTCGAAAACCTCATCGCACAGCTCCCTGGGG	700
701	AGAAGAAGAACGGCCTGTTTGGTAATCTTATCGCCCTGTCACTCGGGCTG	750
751	ACCCCCAACTTTAAATCTAACTTCGACCTGGCCGAAGATGCCAAGCTTCA	800
801	ACTGAGCAAAGACACCTACGATGATGATCTCGACAATCTGCTGGCCCAGA	850
851	TCGGCGACCAGTACGCAGACCTTTTTTTGGCGGCAAAGAACCTGTCAGAC	900
901	GCCATTCTGCTGAGTGATATTCTGCGAGTGAACACGGAGATCACCAAAGC	950
951	TCCGCTGAGCGCTAGTATGATCAAGCGCTATGATGAGCACCACCAAGACT	1000
1001	TGACTTTGCTGAAGGCCCTTGTCAGACAGCAACTGCCTGAGAAGTACAAG	1050
1051	GAAATTTTCTTCGATCAGTCTAAAAATGGCTACGCCGGATACATTGACGG	1100
1101	CGGAGCAAGCCAGGAGGAATTTTACAAATTTATTAAGCCCATCTTGGAAA	1150
1151	AAATGGACGGCACCGAGGAGCTGCTGGTAAAGCTTAACAGAGAAGATCTG	1200
1201	TTGCGCAAACAGCGCACTTTCGACAATGGAAGCATCCCCCACCAGATTCA	1250
1251	CCTGGGCGAACTGCACGCTATCCTCAGGCGGCAAGAGGATTTCTACCCCT	1300

FIG. 26

1301 TTTTGAAAGATAACAGGGAAAAGATTGAGAAAATCCTCACATTTCGGATA 1350
1351 CCCTACTATGTAGGCCCCCTCGCCCGGGGAAATTCCAGATTCGCGTGGAT 1400
1401 GACTCGCAAATCAGAAGAGACCATCACTCCCTGGAACTTCGAGGAAGTCG 1450
1451 TGGATAAGGGGGCCTCTGCCCAGTCCTTCATCGAAAGGATGACTAACTTT 1500
1501 GATAAAAATCTGCCTAACGAAAAGGTGCTTCCTAAACACTCTCTGCTGTA 1550
1551 CGAGTACTTCACAGTTTATAACGAGCTCACCAAGGTCAAATACGTCACAG 1600
1601 AAGGGATGAGAAAGCCAGCATTCCTGTCTGGAGAGCAGAAGAAAGCTATC 1650
1651 GTGGACCTCCTCTTCAAGACGAACCGGAAAGTTACCGTGAAACAGCTCAA 1700
1701 AGAAGACTATTTCAAAAAGATTGAATGTTTCGACTCTGTTGAAATCAGCG 1750
1751 GAGTGGAGGATCGCTTCAACGCATCCCTGGGAACGTATCACGATCTCCTG 1800
1801 AAAATCATTAAAGACAAGGACTTCCTGGACAATGAGGAGAACGAGGACAT 1850
1851 TCTTGAGGACATTGTCCTCACCCTTACGTTGTTTGAAGATAGGGAGATGA 1900
1901 TTGAAGAACGCTTGAAAACTTACGCTCATCTCTTCGACGACAAAGTCATG 1950
1951 AAACAGCTCAAGAGGCGCCGATATACAGGATGGGGGCGGCTGTCAAGAAA 2000
2001 ACTGATCAATGGGATCCGAGACAAGCAGAGTGGAAAGACAATCCTGGATT 2050
2051 TTCTTAAGTCCGATGGATTTGCCAACCGGAACTTCATGCAGTTGATCCAT 2100
2101 GATGACTCTCTCACCTTTAAGGAGGACATCCAGAAAGCACAAGTTTCTGG 2150
2151 CCAGGGGGACAGTCTTCACGAGCACATCGCTAATCTTGCAGGTAGCCCAG 2200
2201 CTATCAAAAAGGGAATACTGCAGACCGTTAAGGTCGTGGATGAACTCGTC 2250
2251 AAAGTAATGGGAAGGCATAAGCCCGAGAATATCGTTATCGAGATGGCCCG 2300
2301 AGAGAACCAAACTACCCAGAAGGGACAGAAGAACAGTAGGGAAAGGATGA 2350
2351 AGAGGATTGAAGAGGGTATAAAAGAACTGGGGTCCCAAATCCTTAAGGAA 2400
2401 CACCCAGTTGAAAACACCCAGCTTCAGAATGAGAAGCTCTACCTGTACTA 2450
2451 CCTGCAGAACGGCAGGGACATGTACGTGGATCAGGAACTGGACATCAATC 2500
2501 GGCTCTCC**GACTACGACGTGGATCATATCGTGCCCCAGTCTTTTCTCAAA** **2550**
2551 **GATGATTCTATTGATAATAAAGTGTTGACAAGATCCGATAAAAAT**AGAGG 2600
2601 GAAGAGTGATAACGTCCCCTCAGAAGAAGTTGTCAAGAAAATGAAAAATT 2650
2651 ATTGGCGGCAGCTGCTGAACGCCAAACTGATCACACAACGGAAGTTCGAT 2700
2701 AATCTGACTAAGGCTGAACGAGGTGGCCTGTCTGAGTTGGATAAAGCCGG 2750
2751 CTTCATCAAAAGGCAGCTTGTTGAGACACGCCAGATCACCAAGCACGTGG 2800
2801 CCCAAATTCTCGATTCACGCATGAACACCAAGTACGATGAAAATGACAAA 2850
2851 CTGATTCGAGAGGTGAAAGTTATTACTCTGAAGTCTAAGCTGGTCTCAGA 2900

FIG. 26 (Cont.)

2901	TTTCAGAAAGGACTTTCAGTTTTATAAGGTGAGAGAGATCAACAATTACC	2950
2951	ACCATGCGCATGATGCCTACCTGAATGCAGTGGTAGGCACTGCACTTATC	3000
3001	AAAAAATATCCCAAGCTTGAATCTGAATTTGTTTACGGAGACTATAAAGT	3050
3051	GTACGATGTTAGGAAAATGATCGCAAAGTCTGAGCAGGAAATAGGCAAGG	3100
3101	CCACCGCTAAGTACTTCTTTTACAGCAATATTATGAATTTTTTCAAGACC	3150
3151	GAGATTACACTGGCCAATGGAGAGATTCGGAAGCGACCACTTATCGAAAC	3200
3201	AAACGGAGAAACAGGAGAAATCGTGTGGGACAAGGGTAGGGATTTCGCGA	3250
3251	CAGTCCGGAAGGTCCTGTCCATGCCGCAGGTGAACATCGTTAAAAAGACC	3300
3301	GAAGTACAGACCGGAGGCTTCTCCAAGGAAAGTATCCTCCCGAAAAGGAA	3350
3351	CAGCGACAAGCTGATCGCACGCAAAAAAGATTGGGACCCCAAGAAATACG	3400
3401	GCGGATTCGATTCTCCTACAGTCGCTTACAGTGTACTGGTTGTGGCCAAA	3450
3451	GTGGAGAAAGGGAAGTCTAAAAAACTCAAAAGCGTCAAGGAACTGCTGGG	3500
3501	CATCACAATCATGGAGCGATCAAGCTTCGAAAAAAACCCCATCGACTTTC	3550
3551	TCGAGGCGAAAGGATATAAAGAGGTCAAAAAAGACCTCATCATTAAGCTT	3600
3601	CCCAAGTACTCTCTCTTTGAGCTTGAAAACGGCCGGAAACGAATGCTCGC	3650
3651	TAGTGCGGGCGAGCTGCAGAAAGGTAACGAGCTGGCACTGCCCTCTAAAT	3700
3701	ACGTTAATTTCTTGTATCTGGCCAGCCACTATGAAAAGCTCAAAGGGTCT	3750
3751	CCCGAAGATAATGAGCAGAAGCAGCTGTTCGTGGAACAACACAAACACTA	3800
3801	CCTTGATGAGATCATCGAGCAAATAAGCGAATTCTCCAAAAGAGTGATCC	3850
3851	TCGCCGACGCTAACCTCGATAAGGTGCTTTCTGCTTACAATAAGCACAGG	3900
3901	GATAAGCCCATCAGGGAGCAGGCAGAAAACATTATCCACTTGTTTACTCT	3950
3951	GACCAACTTGGGCGCGCCTGCAGCCTTCAAGTACTTCGACACCACCATAG	4000
4001	ACAGAAAGCGGTACACCTCTACAAAGGAGGTCCTGGACGCCACACTGATT	4050
4051	CATCAGTCAATTACGGGGCTCTATGAAACAAGAATCGACCTCTCTCAGCT	4100
4101	CGGTGGAGAC**AGCAGGGCTGACCCCAAGAAGAAGAGGAAGGTGTGA**	4046

FIG. 26 (Cont.)

(SEQ ID NO: 38)

Nucleotide Sequence of RNA Guide Strand for use with Cas9 Endonuclease (from Mali *et al.*, *Science* (2013))

```
   1 TGTACAAAAAAGCAGGCTTTAAAGGAACCAATTCAGTCGACTGGATCCGG  50
  51 TACCAAGGTCGGGCAGGAAGAGGGCCTATTTCCCATGATTCCTTCATATT 100
 101 TGCATATACGATACAAGGCTGTTAGAGAGATAATTAGAATTAATTTGACT 150
 151 GTAAACACAAAGATATTAGTACAAAATACGTGACGTAGAAAGTAATAATT 200
 201 TCTTGGGTAGTTTGCAGTTTTAAAATTATGTTTTAAAATGGACTATCATA 250
 251 TGCTTACCGTAACTTGAAAGTATTTCGATTTCTTGGCTTTATATATCTTG 300
 301 TGGAAAGGACGAAACACCGNNNNNNNNNNNNNNNNNNGTTTTAGAGCTA 350
 351 GAAATAGCAAGTTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGG 400
 401 CACCGAGTCGGTGCTTTTTTTCTAGACCCAGCTTTCTTGTACAAAGTTGG 450
 451 CATTA                                              455
```

FIG. 27

(SEQ ID NO: 62)

Nucleotide Sequence of a I-CpaMI homing endonuclease

(ORF, codon optimized for mammalian expression)

ATGAACACCA GCTCTAGCTT CAATCCCTGG TTCCTGACCG GCTTTAGCGA TGCAGAGTGC 60
TCTTTCAGCA TCCTGATACA GGCCAACAGC AAGTACTCCA CCGGTTGGAG GATCAAGCCC 120
GTGTTCGCCA TCGGCTTGCA CAAGAAGGAC CTGGAGCTTC TGAAGAGAAT CCAGAGCTAT 180
CTGGGCGTGG GCAAGATACA CATTCACGGC AAAGACAGCA TTCAGTTCAG GATTGACAGC 240
CCCAAGGAGC TGGAGGTGAT CATCAACCAC TTTGAGAACT ACCCCCTGGT AACCGCCAAG 300
TGGGCCGACT ACACCCTCTT TAAGAAGGCC CTGGACGTAA TTCTGTTGAA GGAGCACCTG 360
AGCCAGAAGG GCCTGCTTAA ACTGGTAGGC ATTAAGGCGA GCCTGAATCT CGGGTTGAAC 420
GGCAGCCTCA AGGAGGCGTT CCCGAACTGG GAAGAACTGC AGATCGACAG GCCGAGCTAC 480
GTGTTCAAGG GCATCCCCGA CCCCAACTGG ATCAGCGGCT TCGCGTCAGG CGATAGCAGC 540
TTTAATGTGA AAATCAGCAA CTCCCCCACG TCACTGCTCA ATAAAAGGGT GCAGCTGAGG 600
TTCGGCATCG GACTGAACAT CAGAGAGAAA GCCCTTATCC AATACCTGGT GGCCTACTTT 660
GACCTGTCAG ACAACCTGAA GAACATCTAC TTCGACCTGA ACAGCGCACG GTTCGAGGTG 720
GTGAAGTTCA GCGACATCAC CGACAAGATC ATCCCCTTCT TCGACAAGTA CAGCATACAA 780
GGCAAGAAGA GCCTGGACTA CATCAACTTC AAGGAAGTGG CCGACATTAT CAAGAGCAAG 840
AACCATCTTA CTAGCGAGGG CTTCCAGGAA ATCTTGGACA TCAAAGCCAG TATGAACAAG 900

FIG. 28

(SEQ ID NO: 63)

Amino Acid Sequence of I-CpaMI homing endonuclease

MNTSSSFNPW FLTGFSDAEC SFSILIQANS KYSTGWRIKP VFAIGLHKKD LELLKRIQSY 60
LGVGKIHIHG KDSIQFRIDS PKELEVIINH FENYPLVTAK WADYTLFKKA LDVILLKEHL 120
SQKGLLKLVG IKASLNLGLN GSLKEAFPNW EELQIDRPSY VFKGIPDPNW ISGFASGDSS 180
FNVKISNSPT SLLNKRVQLR FGIGLNIREK ALIQYLVAYF DLSDNLKNIY FDLNSARFEV 240
VKFSDITDKI IPFFDKYSIQ GKKSLDYINF KEVADIIKSK NHLTSEGFQE ILDIKASMNK 300

FIG. 29

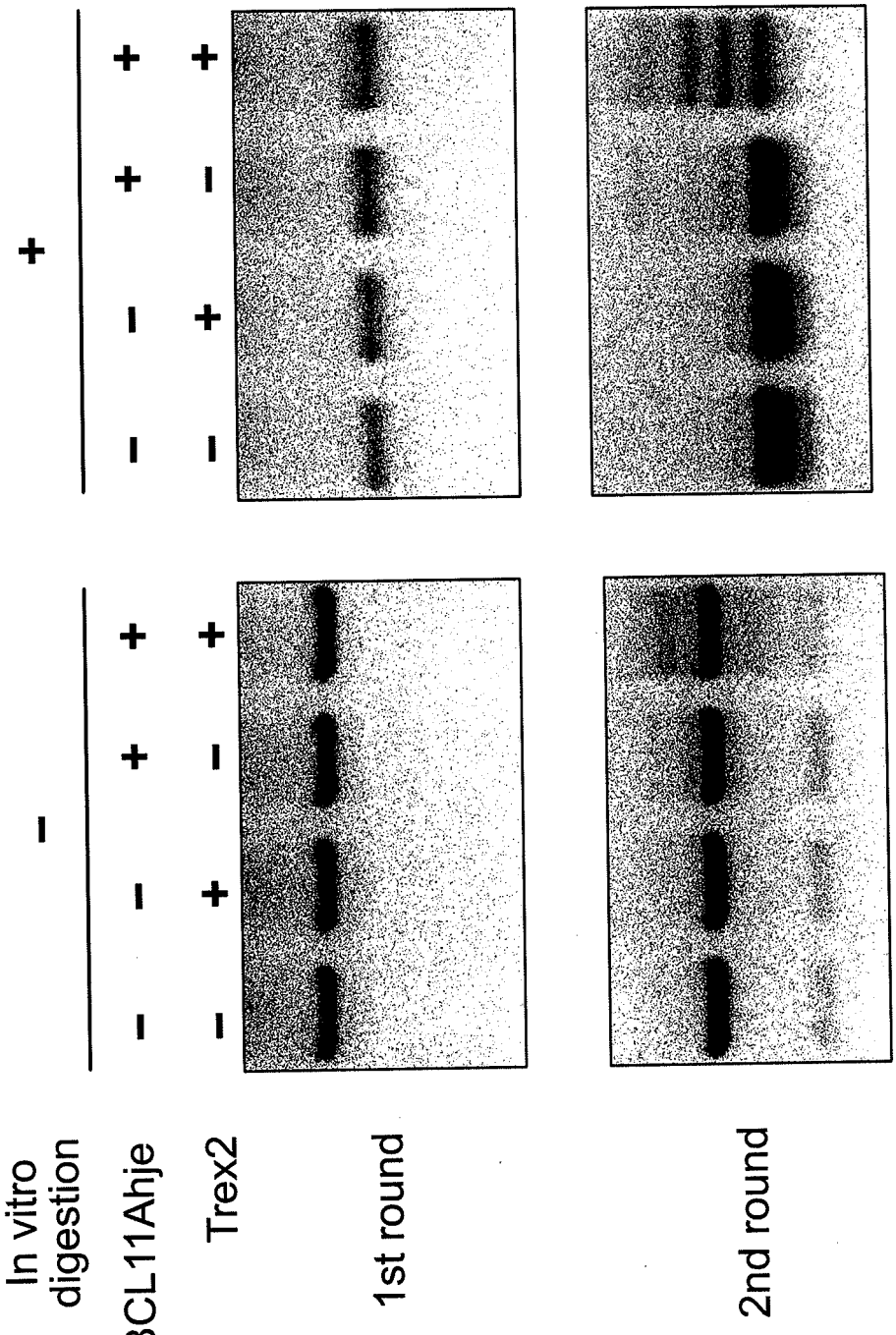


FIG. 30

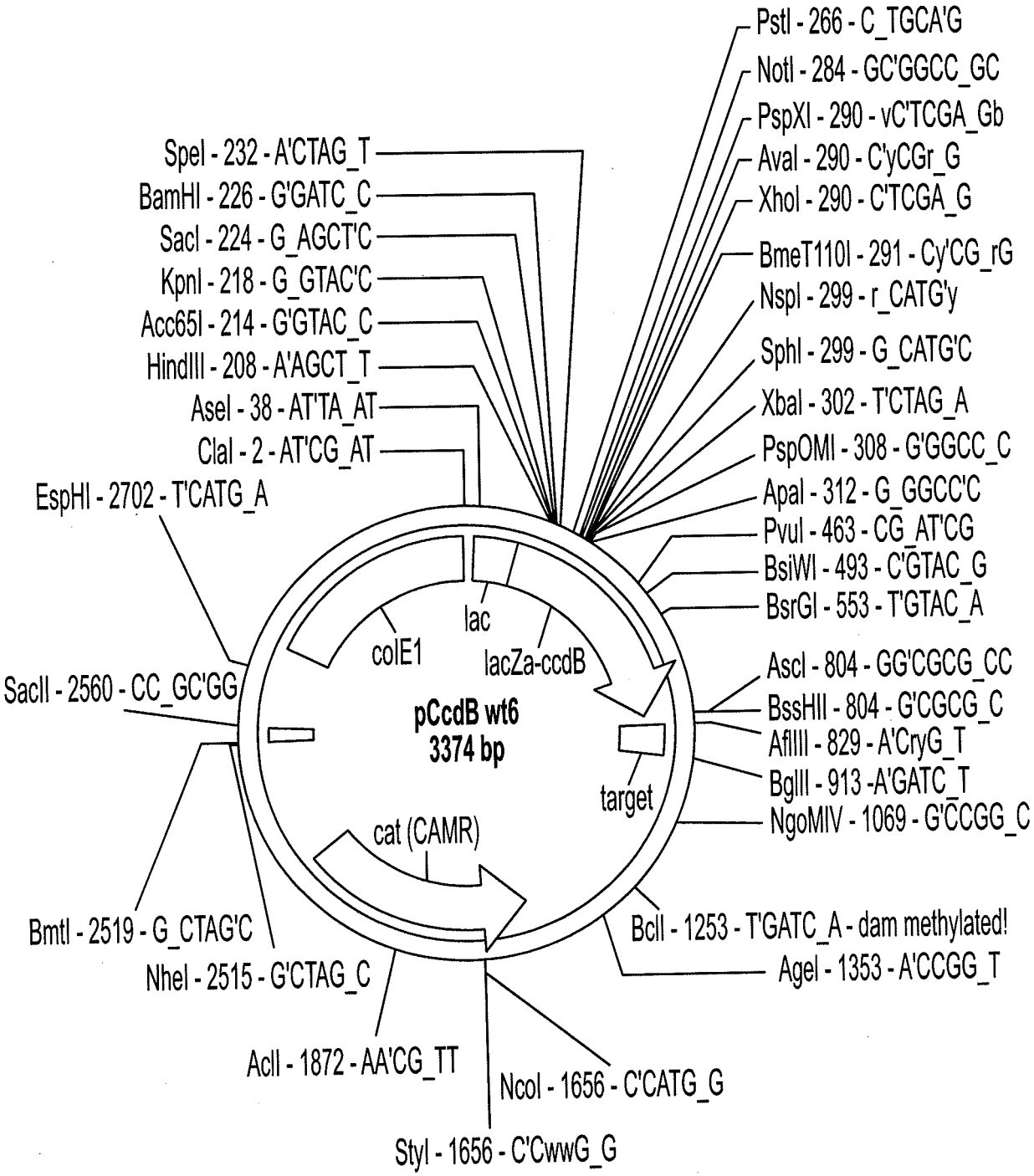

PstI - 266 - C_TGCA'G
NotI - 284 - GC'GGCC_GC
PspXI - 290 - vC'TCGA_Gb
AvaI - 290 - C'yCGr_G
XhoI - 290 - C'TCGA_G
BmeT110I - 291 - Cy'CG_rG
NspI - 299 - r_CATG'y
SphI - 299 - G_CATG'C
XbaI - 302 - T'CTAG_A
PspOMI - 308 - G'GGCC_C
ApaI - 312 - G_GGCC'C
PvuI - 463 - CG_AT'CG
BsiWI - 493 - C'GTAC_G
BsrGI - 553 - T'GTAC_A
AscI - 804 - GG'CGCG_CC
BssHII - 804 - G'CGCG_C
AflIII - 829 - A'CryG_T
BglII - 913 -A'GATC_T
NgoMIV - 1069 - G'CCGG_C
BclI - 1253 - T'GATC_A - dam methylated!
AgeI - 1353 - A'CCGG_T
NcoI - 1656 - C'CATG_G
StyI - 1656 - C'CwwG_G
AclI - 1872 - AA'CG_TT
NheI - 2515 - G'CTAG_C
BmtI - 2519 - G_CTAG'C
SacII - 2560 - CC_GC'GG
EspHI - 2702 - T'CATG_A
ClaI - 2 - AT'CG_AT
AseI - 38 - AT'TA_AT
HindIII - 208 - A'AGCT_T
Acc65I - 214 - G'GTAC_C
KpnI - 218 - G_GTAC'C
SacI - 224 - G_AGCT'C
BamHI - 226 - G'GATC_C
SpeI - 232 - A'CTAG_T
colE1
lac
lacZa-ccdB
pCcdB wt6
3374 bp
target
cat (CAMR)

FIG. 31

(SEQ ID NO: 64)

Nucleotide sequence of BCL11A gene targeting nuclease-encoding plasmid (pExodusBCL11Ahje)

GACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCCAGTAT
CTGCTCCCTGCTTGTGTGTTGGAGGTCGCTGAGTAGTGCGCGAGCAAAATTTAAGCTACAACAAGGCAAGGCTTGACCGA
CAATTGCATGAAGAATCTGCTTAGGGTTAGGCGTTTTGCGCTGCTTCGCGATGTACGGGCCAGATATACGCGTTGACATT
GATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA
CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGT
AACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGT
ATCATATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTA
TGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACC
AAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAG
GTCTATATAAGCAGAGCTCTCTGGCTAACTAGAGAACCCACTGCTTACTGGCTTATCGAAATTAATACGACTCACTATAG
GGAGACCCAAGCTGGCTAGCGTTTAAACTTAAGCTTGGTACCGAGCTCGGATCCACTAGTCCAGTGTGGTGGAATTCTGC
AGGTACGTTGACGCCGCCACCATGGGATATCCATACGATGTCCCAGATTATGCGCCACCTAAGAAGAAACGCAAAGTCCC
CGGGGGCAGCCACATGGACCTGACCTACGCCTATCTGGTCGGCCTGTTCGAGGGCGACGGCTATTTTAcaATAgCtAAGg
ccGGCAAGTATCTGAacTACGAGCTGGGCATCacaCTCTCCATCAAGGACGctCAGCTCATCTACAAGATCAAGGACATC
CTCGGCGTGGGCAAcGTGtaCTTTAGGAAGtacAggcAacatGAGATGGTCAGCCTGCGAATCcaGGACAAAAACCACCT
GAAGAACTTCATCCTGCCCATCTTCGACAAGTACCCCATGCTGAGCAACAAGCAGTACGACTACCTGCGATTCAAGGATG
CCCTCCTGTCCAACATCATCTATAGCGACGACCTGCCCGAGTACGCCAGGAGCAACGAGTCAATCAATAGCGTGGACAGC
ATCATCAACACCTCATACTTCAGCGCCTGGCTGGTTGGCTTCATCGAGGCCGAGGGCTGCTTCAcCACCTACAAGgcatc
CAAGGACaAgTACCTGAcaGCGgGCTTCtccATAGCCCAGAAGGACGGCGACATTCTCATCTCCGCGATCCACAAATACC
TGAGCTTCACGACCAAAccCTACaaaGACAAGACCAACTGTAGCcacCTCAAGGTCACCGGCGTGAGGAGCGTCAAtAAC
GTGGTTAAGTTCATCCAGGGTGCGCCGGTCAAGCTGCTGGGTAACAAGAAGCTGCAGTACAAACTTTGGATAAAGCAGCT
GCGCAAGATCTCCCGATACAGCGAGAAAATCCAGCTGCCCAGTAACTACTAATCTAGAGGGCCCGTTTAAACCCGCTGAT
CAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCC
ACTCCCACTGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGG
GGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGCTTCTG
AGGCGGAAAGAACCAGCTGGGGCTCTAGGGGGTATCCCCACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTG
GTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCAC
GTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACC
CCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAG
TCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATTTATA
AGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTAATTCTGTGGAA
TGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCCTATCAGGACATAGCGTTG
GCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCCGA
TTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGC
GACGCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGG
ACGCCGGCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTTTATTGCAGCTTAT
AATGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTC

FIG. 32

CAAACTCATCAATGTATCTTATCATGTCTGTATACCGTCGACCTCTAGCTAGAGCTTGGCGTAATCATGGTCATAGCTGT
TTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCC
TAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCA
TTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGC
GCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAAC
GCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAG
GCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACC
AGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTC
CCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGG
CTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGAC
ACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTG
AAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAA
AAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCA
GAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGG
ATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAG
TATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTT
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TCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTT
TGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCC
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CTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTT
TCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGA
ATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATG
TATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTC

FIG. 32 (Cont.)

(SEQ ID NO: 65)

Nucleotide sequence of TREX2-encoding plasmid (pExodus CMV.Trex2)

gacggatcgggagatctcccgatcccctatggtgcactctcagtacaatctgctctgatgccgcatagtt
aagccagtatctgctccctgcttgtgtgttggaggtcgctgagtagtgcgcgagcaaaatttaagctaca
acaaggcaaggcttgaccgacaattgcatgaagaatctgcttagggttaggcgttttgcgctgcttcgcg
atgtacgggccagatatacgcgttgacattgattattgactagttattaatagtaatcaattacggggtc
attagttcatagcccatatatggagttccgcgttacataacttacggtaaatggcccgcctggctgaccg
cccaacgacccccgcccattgacgtcaataatgacgtatgttcccatagtaacgccaatagggactttcc
attgacgtcaatgggtggagtatttacggtaaactgcccacttggcagtacatcaagtgtatcatatgcc
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tgggagtttgttttggcaccaaaatcaacgggactttccaaaatgtcgtaacaactccgccccattgacg
caaatgggcggtaggcgtgtacggtgggaggtctatataagcagagctctctggctaactagagaaccca
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cacctcgggctgagacctttgtattcctggacctagaagccactgggctcccaaacatggaccctgagat
tgcagagatatccctttttgctgttcaccgctcttccctggagaacccagaacgggatgattctggttcc
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ccagtgagattactggtttgagcagcgaaagcctgatgcactgcgggaaggctggtttcaatggcgctgt
ggtaaggacactgcagggcttcctaagccgccaggagggccccatctgccttgtggcccacaatggcttc
gattatgacttcccactgctgtgcacggagctacaacgtctgggtgcccatctgccccaagacactgtct
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caaaagctacagcctggccagtctcttccaccgctacttccaggctgaacccagtgctgcccattcagca
gaaggtgatgtgcacaccctgcttctgatcttcctgcatcgtgctcctgagctgctcgcctgggcagatg

FIG. 33

agcaggcccgcagctgggctcatattgagcccatgtacgtgccacctgatggtccaagcctcgaagcctg
aattctgcagatatccagcacagtggcggccgctcgagtctagagggcccgtttaaacccgctgatcagc
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gttacaaataaagcaatagcatcacaaatttcacaaataaagcatttttttcactgcattctagttgtgg
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cggtatcagctcactcaaaggcggtaatacggttatccacagaatcaggggataacgcaggaaagaacat
gtgagcaaaaggccagcaaaaggccaggaaccgtaaaaaggccgcgttgctggcgtttttccataggctc
cgccccctgacgagcatcacaaaaatcgacgctcaagtcagaggtggcgaaacccgacaggactataaa

FIG. 33 (Cont.)

gataccaggcgtttccccctggaagctccctcgtgcgctctcctgttccgaccctgccgcttaccggata
cctgtccgcctttctcccttcgggaagcgtggcgctttctcatagctcacgctgtaggtatctcagttcg
gtgtaggtcgttcgctccaagctgggctgtgtgcacgaacccccgttcagcccgaccgctgcgccttat
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caggattagcagagcgaggtatgtaggcggtgctacagagttcttgaagtggtggcctaactacggctac
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ccagtctattaattgttgccgggaagctagagtaagtagttcgccagttaatagtttgcgcaacgttgtt
gccattgctacaggcatcgtggtgtcacgctcgtcgtttggtatggcttcattcagctccggttcccaac
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ggcgaccgagttgctcttgcccggcgtcaatacgggataataccgcgccacatagcagaactttaaaagt
gctcatcattggaaaacgttcttcggggcgaaaactctcaaggatcttaccgctgttgagatccagttcg
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aaacaggaaggcaaaatgccgcaaaaaagggaataagggcgacacggaaatgttgaatactcatactctt
cctttttcaatattattgaagcatttatcagggttattgtctcatgagcggatacatatttgaatgtatt
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FIG. 33 (Cont.)

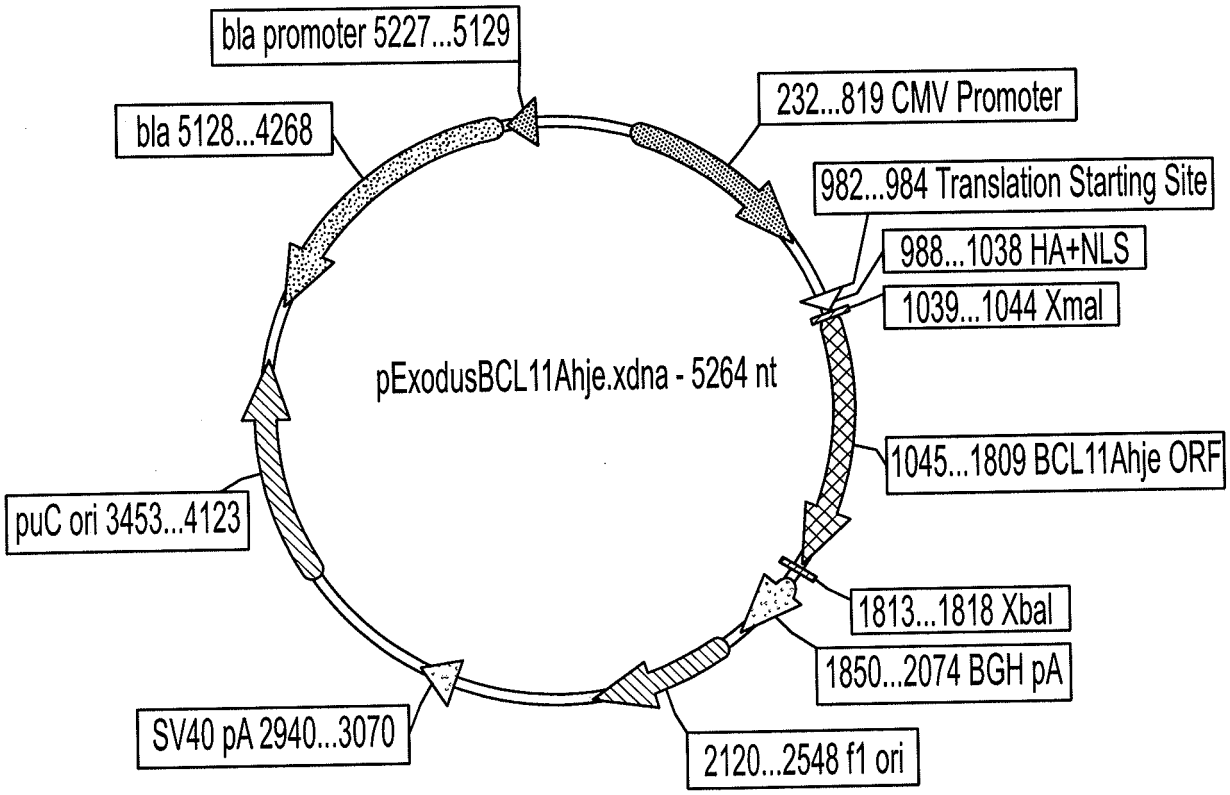

bla promoter 5227...5129
232...819 CMV Promoter
bla 5128...4268
982...984 Translation Starting Site
988...1038 HA+NLS
1039...1044 XmaI
pExodusBCL11Ahje.xdna - 5264 nt
1045...1809 BCL11Ahje ORF
puC ori 3453...4123
1813...1818 XbaI
1850...2074 BGH pA
SV40 pA 2940...3070
2120...2548 f1 ori

FIG. 34

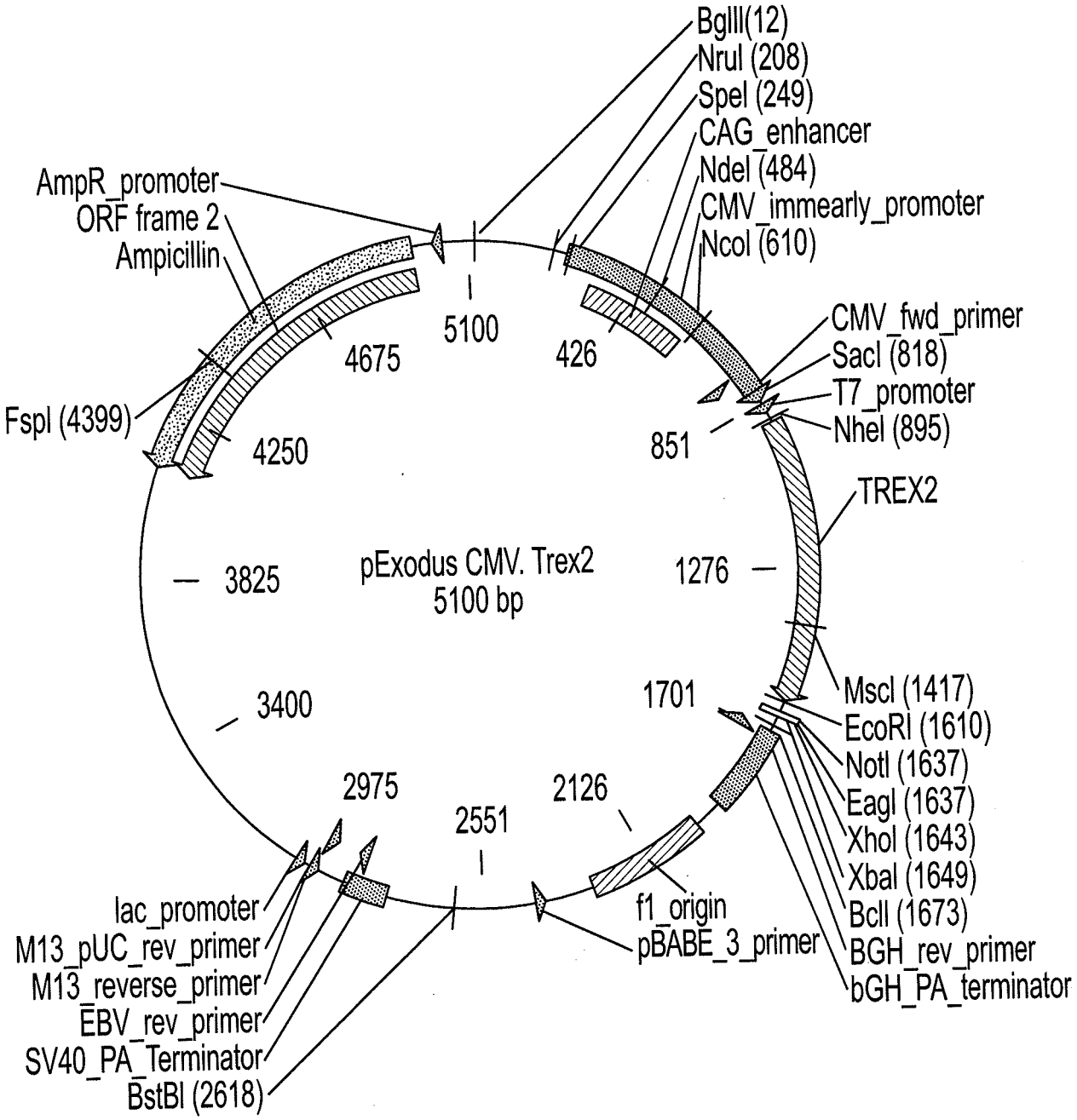

BglII(12)
NruI (208)
SpeI (249)
CAG_enhancer
NdeI (484)
CMV_immearly_promoter
NcoI (610)
CMV_fwd_primer
SacI (818)
T7_promoter
NheI (895)
TREX2
MscI (1417)
EcoRI (1610)
NotI (1637)
EagI (1637)
XhoI (1643)
XbaI (1649)
BclI (1673)
BGH_rev_primer
bGH_PA_terminator
f1_origin
pBABE_3_primer
lac_promoter
M13_pUC_rev_primer
M13_reverse_primer
EBV_rev_primer
SV40_PA_Terminator
BstBI (2618)
AmpR_promoter
ORF frame 2
Ampicillin
FspI (4399)
5100
426
851
1276
1701
2126
2551
2975
3400
3825
4250
4675
pExodus CMV. Trex2
5100 bp

FIG. 35