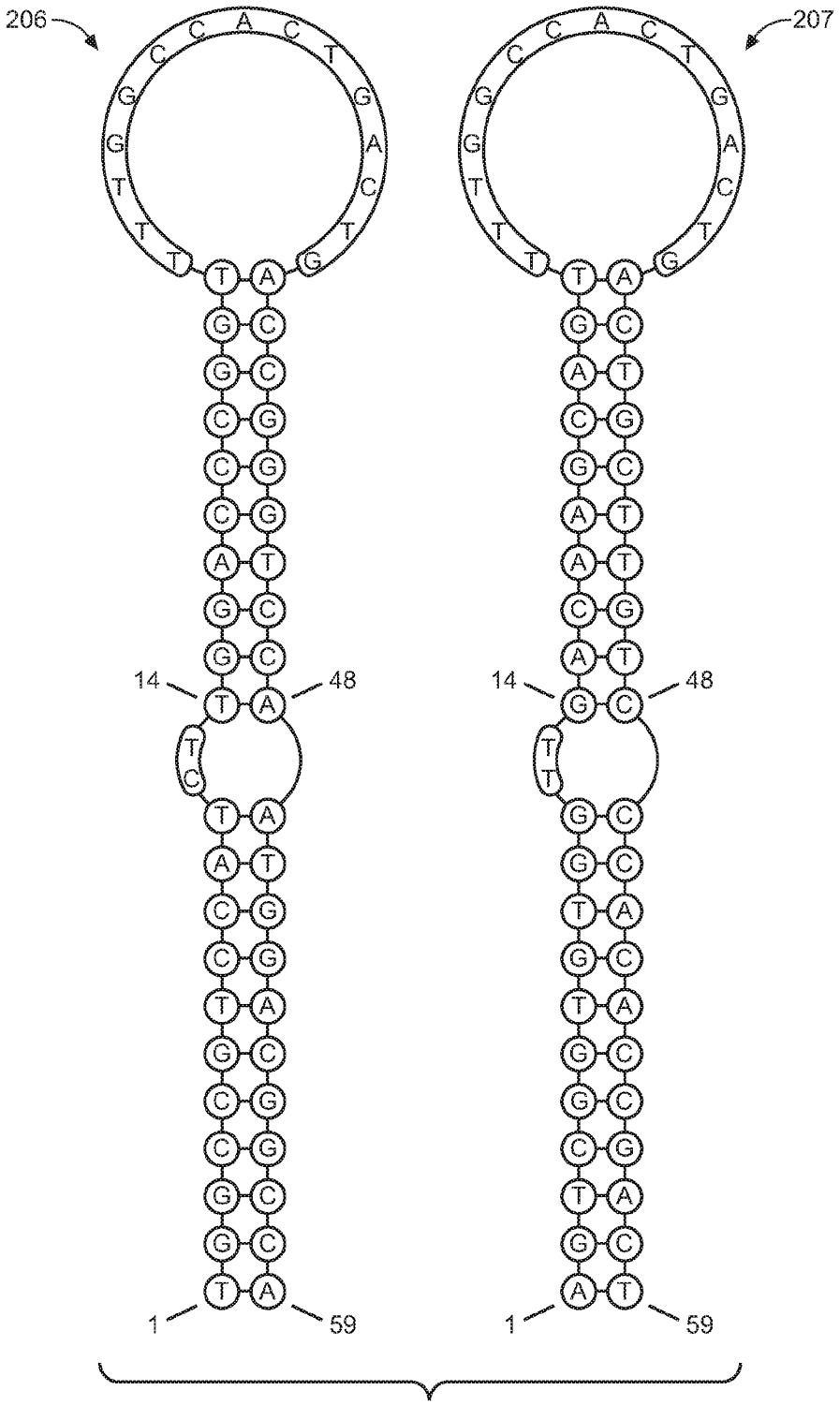


Fig. 1A

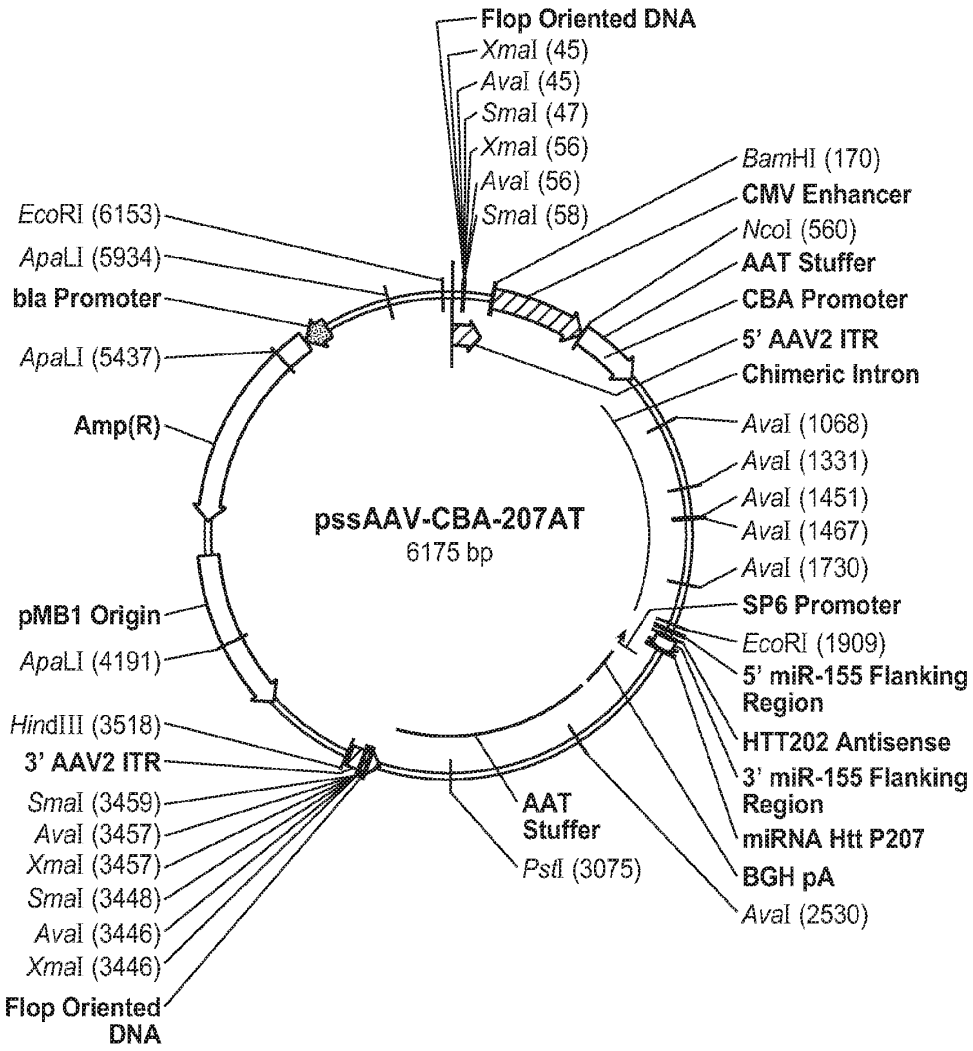

Flop Oriented DNA
XmaI (45)
AvaI (45)
SmaI (47)
XmaI (56)
AvaI (56)
SmaI (58)
BamHI (170)
CMV Enhancer
NcoI (560)
AAT Stuffer
CBA Promoter
5' AAV2 ITR
Chimeric Intron
AvaI (1068)
AvaI (1331)
AvaI (1451)
AvaI (1467)
AvaI (1730)
SP6 Promoter
EcoRI (1909)
5' miR-155 Flanking Region
HTT202 Antisense
3' miR-155 Flanking Region
miRNA Htt P207
BGH pA
AvaI (2530)
PstI (3075)
AAT Stuffer
EcoRI (6153)
ApaLI (5934)
bla Promoter
ApaLI (5437)
Amp(R)
pMB1 Origin
ApaLI (4191)
HindIII (3518)
3' AAV2 ITR
SmaI (3459)
AvaI (3457)
XmaI (3457)
SmaI (3448)
AvaI (3446)
XmaI (3446)
Flop Oriented DNA
pssAAV-CBA-207AT
6175 bp

Fig. 1B

Fig. 1C

Fig. 1C-1

Fig. 1C-2

Fig. 1C-3

Fig. 1C-4

Fig. 1C-1

psAAV-CBA-202AT

SmaI SmaI
XmaI XmaI
AvaI AvaI
BamHI

```
   1 TTGGCCACTC CCTCTCTGCG CGCTCGCTCG CTCACTGAGG CCGCCCGGGC AAAGCCCGGG CGTCGGGCGA CCTTTGGTCG CCCGGCCTCA GTGAGCGAGC
     AACCGGTGAG GGAGAGACGC GCGAGCGAGC GAGTGACTCC GGCGGGCCCG TTTCGGGCCC GCAGCCCGCT GGAAACCAGC GGGCCGGAGT CACTCGCTCG

 101 GAGCGCGCAG AGAGGGAGTG GCCAACTCCA TCACTAGGGG TTCCTCTATA TTACCCTGCT AGGCAATTGG ATCCCGGACC GTCGACATTG ATTATTGACT
     CTCGCGCGTC TCTCCCTCAC CGGTTGAGGT AGTGATCCCC AAGGAGATAT AATGGGACGA TCCGTTAACC TAGGGCCTGG CAGCTGTAAC TAATAACTGA

 201 AGTTATTAAT AGTAATCAAT TACGGGGTCA TTAGTTCATA GCCCATATAT GGAGTTCCGC GTTACATAAC TTACGGTAAA TGGCCCGCCT GGCTGACCGC
     TCAATAATTA TCATTAGTTA ATGCCCCAGT AATCAAGTAT CGGGTATATA CCTCAAGGCG CAATGTATTG AATGCCATTT ACCGGGCGGA CCGACTGGCG

 301 CCAACGACCC CCGCCCATTG ACGTCAATAA TGACGTATGT TCCCATAGTA ACGCCAATAG GGACTTTCCA TTGACGTCAA TGGGTGGAGT ATTTACGGTA
     GGTTGCTGGG GGCGGGTAAC TGCAGTTATT ACTGCATACA AGGGTATCAT TGCGGTTATC CCTGAAAGGT AACTGCAGTT ACCCACCTCA TAAATGCCAT

 401 AACTGCCCAC TTGGCAGTAC ATCAAGTGTA TCATATGCCA AGTACGCCCC CTATTGACGT CAATGACGGT AAATGGCCCG CCTGGCATTA TGCCCAGTAC
     TTGACGGGTG AACCGTCATG TAGTTCACAT AGTATACGGT TCATGCGGGG GATAACTGCA GTTACTGCCA TTTACCGGGC GGACCGTAAT ACGGGTCATG
```

```
                                                                       NcoI
 501 ATGACCTTAT GGGACTTTCC TACTTGGCAG TACATCTACG TATTAGTCAT CGCTATTACC ATGGTCGAGG TGAGCCCCAC GTTCTGCTTC ACTCTCCCCA
     TACTGGAATA CCCTGAAAGG ATGAACCGTC ATGTAGATGC ATAATCAGTA GCGATAATGG TACCAGCTCC ACTCGGGGTG CAAGACGAAG TGAGAGGGGT

 601 TCTCCCCCCC CTCCCCACCC CCAATTTTGT ATTTATTTAT TTTTTAATTA TTTTGTGCAG CGATGGGGGC GGGGGGGGGG GGGGGGCGCG CGCCAGGCGG
     AGAGGGGGGG GAGGGGTGGG GGTTAAAACA TAAATAAATA AAAAATTAAT AAAACACGTC GCTACCCCCG CCCCCCCCCC CCCCCCGCGC GCGGTCCGCC

 701 GGCGGGGCGG GGCGAGGGGC GGGGCGGGGC GAGGCGGAGA GGTGCGGCGG CAGCCAATCA GAGCGGCGCG CTCCGAAAGT TTCCTTTTAT GGCGAGGCGG
     CCGCCCCGCC CCGCTCCCCG CCCCGCCCCG CTCCGCCTCT CCACGCCGCC GTCGGTTAGT CTCGCCGCGC GAGGCTTTCA AAGGAAAATA CCGCTCCGCC

 801 CGGCGGCGGC GGCCCTATAA AAAGCGAAGC GCGCGGCGGG CGGGAGTCGC TGCGCGCTGC CTTCGCCCCG TGCCCCGCTC CGCCGCCGCC TCGCGCCGCC
     GCCGCCGCCG CCGGGATATT TTTCGCTTCG CGCGCCGCCC GCCCTCAGCG ACGCGCGACG GAAGCGGGGC ACGGGGCGAG GCGGCGGCGG AGCGCGGCGG

 901 CGCCCCGGCT CTGACTGACC GCGTTACTCC CACAGGTGAG CGGGCGGGAC GGCCCTTCTC CTCCGGGCTG TAATTAGCGC TTGGTTTAAT GACGGCTTGT
     GCGGGGCCGA GACTGACTGG CGCAATGAGG GTGTCCACTC GCCCGCCCTG CCGGGAAGAG GAGGCCCGAC ATTAATCGCG AACCAAATTA CTGCCGAACA

                                                                                AvaI
1001 TTCTTTTCTG TGGCTGCGTG AAAGCCTTGA GGGGCTCCGG GAGGGCCCTT TGTGCGGGGG GAGCGGCTCG GGGGGTGCGT GCGTGTGTGT GTGCGTGGGG
     AAGAAAAGAC ACCGACGCAC TTTCGGAACT CCCCGAGGCC CTCCCGGGAA ACACGCCCCC CTCGCCGAGC CCCCCACGCA CGCACACACA CACGCACCCC

1101 AGCGCCGCGT GCGGCTCCGC GCTGCCCGGC GGCTGTGAGC GCTGCGGGCG CGGCGCGGGG CTTTGTGCGC TCCGCAGTGT GCGCGAGGGG AGCGCGGCCG
     TCGCGGCGCA CGCCGAGGCG CGACGGGCCG CCGACACTCG CGACGCCCGC GCCGCGCCCC GAAACACGCG AGGCGTCACA CGCGCTCCCC TCGCGCCGGC

1201 GGGGCGGTGC CCCGCGGTGC GGGGGGGGCT GCGAGGGGAA CAAAGGCTGC GTGCGGGGTG TGTGCGTGGG GGGGTGAGCA GGGGGTGTGG GCGCGTCGGT
     CCCCGCCACG GGGCGCCACG CCCCCCCCGA CGCTCCCCTT GTTTCCGACG CACGCCCCAC ACACGCACCC CCCCACTCGT CCCCCACACC CGCGCAGCCA

                                  AvaI
1301 CGGGCTGCAA CCCCCCCTGC ACCCCCCTCC CCGAGTTGCT GAGCACGGCC CGGCTTCGGG TGCGGGGCTC CGTACGGGGC GTGGCGCGGG GCTCGCCGTG
     GCCCGACGTT GGGGGGGACG TGGGGGGAGG GGCTCAACGA CTCGTGCCGG GCCGAAGCCC ACGCCCCGAG GCATGCCCCG CACCGCGCCC CGAGCGGCAC

                                                            AvaI             AvaI
1401 CCGGGCGGGG GGTGGCGGCA GGTGGGGGTG CCGGGCGGGG CGGGGCCGCC TCGGGCCGGG GAGGGCTCGG GGGAGGGGCG CGGCGGCCCC CGGAGCGCCG
     GGCCCGCCCC CCACCGCCGT CCACCCCCAC GGCCCGCCCC GCCCCGGCGG AGCCCGGCCC CTCCCGAGCC CCCTCCCCGC GCCGCCGGGG GCCTCGCGGC

1501 GCGGCTGTCG AGGCGCGGCG AGCCGCAGCC ATTGCCTTTT ATGGTAATCG TGCGAGAGGG CGCAGGGACT TCCTTTGTCC CAAATCTGTG CGGAGCCGAA
     CGCCGACAGC TCCGCGCCGC TCGGCGTCGG TAACGGAAAA TACCATTAGC ACGCTCTCCC GCGTCCCTGA AGGAAACAGG GTTTAGACAC GCCTCGGCTT
```

Fig. 1C-2

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1601 ATCTGGGAGG CGCCGCCGCA CCCCCTCTAG CGGGCGCGGG GCGAAGCGGT GCGGCGCCGG CAGGAAGGAA ATGGGCGGGG AGGGCCTTCG TGCGTCGCCG
     TAGACCCTCC GCGGCGGCGT GGGGGAGATC GCCCGCGCCC CGCTTCGCCA CGCCGCGGCC GTCCTTCCTT TACCCGCCCC TCCCGGAAGC ACGCAGCGGC

                                AvaI
                               wwwwww
1701 CGCCGCCGTC CCCTTCTCCC TCTCCAGCCT CGGGGCTGTC CGCGGGGGGA CGGCTGCCTT CGGGGGGGAC GGGGCAGGGC GGGGTTCGGC TTCTGGCGTG
     GCGGCGGCAG GGGAAGAGGG AGAGGTCGGA GCGCCCCCCT GCCGACGGAA GCCCCCCCTG CCCCGTCCCG CCCCAAGCCG AAGACCGCAC

1801 TGACCGGCGG CTCTAGAGCC TCTGCTAACC ATGTTCATGC CTTCTTCTTT TTCCTACAGC TCCTGGGCAA CGTGCTGGTT ATTGTGCTGT CTCATCATTT
     ACTGGCCGCC GAGATCTCGG AGACGATTGG TACAAGTACG GAAGAAGAAA AAGGATGTCG AGGACCCGTT GCACGACCAA TAACACGACA GAGTAGTAAA

                                                                                  start of 207 Guide Strand
                          EcoRI                                                  /
                         wwwwwww                                                 /
1901 TGGCAAAGAA TTCTTCGAAA GATCTGCTAG CCTGGAGGCT TGCTGAAGGC TGTATGCTGA GTCGGTGTGG TTGACAAGCA GTTTTGGCCA CTGACTGACT
     ACCGTTTCTT AAGAAGCTTT CTAGACGATC GGACCTCCGA ACGACTTCCG ACATACGACT CAGCCACACC AACTGTTCGT CAAAACCGGT GACTGACTGA

2001 GCTTGTCCCA CACCGACTCA GGACACAAGG CCTGTTACTA GCACTCACAT GGAACAAATG GCCATGCATC TAGAGGGCCC TATTCTATAG TGTCACCTAA
     CGAACAGGGT GTGGCTGAGT CCTGTGTTCC GGACAATGAT CGTGAGTGTA CCTTGTTTAC CGGTACGTAG ATCTCCCGGG ATAAGATATC ACAGTGGATT

2101 ATGCTAGAGC TCGCTGATCA GCCTCGACTG TGCCTTCTAG TTGCCAGCCA TCTGTTGTTT GCCCCTCCCC CGTGCCTTCC TTGACCCTGG AAGGTGCCAC
     TACGATCTCG AGCGACTAGT CGGAGCTGAC ACGGAAGATC AACGGTCGGT AGACAACAAA CGGGGAGGGG GCACGGAAGG AACTGGCACC TTCCACGGTG

2201 TCCCACTGTC CTTTCCTAAT AAAATGAGGA AATTGCATCG CATTGTCTGA GTAGGTGTCA TTCTATTCTG GGGGGTGGGG TGGGGCAGGA CAGCAAGGGG
     AGGGTGACAG GAAAGGATTA TTTTACTCCT TTAACGTAGC GTAACAGACT CATCCACAGT AAGATAAGAC CCCCCACCCC ACCCCGTCCT GTCGTTCCCC

2301 GAGGATTGGG AAGACAATAG CAGGCATGCT GGGGAGCTAG AGTCGACCGG ACCGGTGGAA GTCCTCTTCC TCGGTGTCCT TGACTTCAAA GGGTCTCTCC
     CTCCTAACCC TTCTGTTATC GTCCGTACGA CCCCTCGATC TCAGCTGGCC TGGCCACCTT CAGGAGAAGG AGCCACAGGA ACTGAAGTTT CCCAGAGAGG

2401 CATTTGCCTG GAGAGAGGGG AAGGTGGGCA TCACCAGGGG TGAGTGAAGG TTTGGAAGAG TGTAGCAGAA TAAGAAACCA TGAGTCCCCT CCCTGAGAAG
     GTAAACGGAC CTCTCTCCCC TTCCACCCGT AGTGGTCCCC ACTCACTTCC AAACCTTCTC ACATCGTCTT ATTCTTTGGT ACTCAGGGGA GGGACTCTTC

                                AvaI
                               wwwwww
2501 CCCTGAGCCC CCTTGACGAC ACACATCCCT CGAGGCTCAG CTTCATCATC TGTAAAAGGT GCTGAAACTG ACCATCCAAG CTGCCGAAAA AGATTGTGTG
     GGGACTCGGG GGAACTGCTG TGTGTAGGGA GCTCCGAGTC GAAGTAGTAG ACATTTTCCA CGACTTTGAC TGGTAGGTTC GACGGCTTTT TCTAACACAC
```

Fig. 1C-3

```
2601  GGGATAATTC AAAACTAGAG GAAGATGCAG AATTTCTACA TCGTGGCGAT GTCAGGCTAA GAGATGCCAT CGTGGCTGTG CATTTTTATT GGAATCATAT
      CCCTATTAAG TTTTGATCTC CTTCTACGTC TTAAAGATGT AGCACCGCTA CAGTCCGATT CTCTACGGTA GCACCGACAC GTAAAAATAA CCTTAGTATA

2701  GTTTATTTGA GGGTGTCTTG GATATTACAA ATAAAATGTT GGAGCATCAG GCATATTTGG TACCTTCTGT CTAAGGCTCC CTGCCCCTTG TTAATTGGCA
      CAAATAAACT CCCACAGAAC CTATAATGTT TATTTTACAA CCTCGTAGTC CGTATAAACC ATGGAAGACA GATTCCGAGG GACGGGGAAC AATTAACCGT

2801  GCTCAGTTAT TCATCCAGGG CAAACATTCT GCTTACTATT CCTGAGAGCT TTCCTCATCC TCTAGATTGG CAGGGGAAAT GCAGATGCCT GAGCAGCCTC
      CGAGTCAATA AGTAGGTCCC GTTTGTAAGA CGAATGATAA GGACTCTCGA AAGGAGTAGG AGATCTAACC GTCCCCTTTA CGTCTACGGA CTCGTCGGAG

2901  CCCTCTGCCA TACCAACAGA GCTTCACCAT CGAGGCATGC AGAGTGGACA GGGGCCTCAG GGACCCCTGA TCCCAGCTTT CTCATTGGAC AGAAGGAGGA
      GGGAGACGGT ATGGTTGTCT CGAAGTGGTA GCTCCGTACG TCTCACCTGT CCCCGGAGTC CCTGGGGACT AGGGTCGAAA GAGTAACCTG TCTTCCTCCT

                                                                                PstI
                                                                                wwwwww
3001  GACTGGGGCT GGAGAGGGAC CTGGGCCCCC ACTAAGGCCA CAGCAGAGCC AGGACTTTAG CTGTGCTGAC TGCAGCCTGG CTTGCCTCCA CTGCCCTCCT
      CTGACCCCGA CCTCTCCCTG GACCCGGGGG TGATTCCGGT GTCGTCTCGG TCCTGAAATC GACACGACTG ACGTCGGACC GAACGGAGGT GACGGGAGGA

3101  TTGCCTCAAG AGCAAGGGAG CCTCAGAGTG GAGGAAGCAG CCCCTGGCCT TGCCTCCCAC CTCCCCTCCC CTATGCTGTT TTCCTGGGAC AGTGGGAGCT
      AACGGAGTTC TCGTTCCCTC GGAGTCTCAC CTCCTTCGTC GGGGACCGGA ACGGAGGGTG GAGGGGAGGG GATACGACAA AAGGACCCTG TCACCCTCGA

3201  GGCTTAGAAT GCCCTGGGGC CCCCAGGACC CTGGCATTTT AACCCCTCAG GGGCAGGAAG GCAGCCTGAG ATACAGAAGA GTCCATCACC TGCTGTATGC
      CCGAATCTTA CGGGACCCCG GGGGTCCTGG GACCGTAAAA TTGGGGAGTC CCCGTCCTTC CGTCGGACTC TATGTCTTCT CAGGTAGTGG ACGACATACG

3301  CACACACCAT CCCCACAGTT ACGTACTAGT TCGAAGCCAC GCGGACCGTT ATAGTTACGA GGAACCCCTA GTGATGGAGT TGGCCACTCC CTCTCTGCGC
      GTGTGTGGTA GGGGTGTCAA TGCATGATCA AGCTTCGGTG CGCCTGGCAA TATCAATGCT CCTTGGGGAT CACTACCTCA ACCGGTGAGG GAGAGACGCG

                                  SmaI                SmaI
                                  wwwwwww             wwwwwww
                                  XmaI                XmaI
                                  wwwwwww             wwwwwww
                                  AvaI                AvaI
                                  wwwwwww             wwwwwww
3401  GCTCGCTCGC TCACTGAGGC CGGGCGACCA AAGGTCGCCC GACGCCCGGG CTTTGCCCGG GCGGCCTCAG TGAGCGAGCG AGCGCGCAGA GAGGGAGTGG
      CGAGCGAGCG AGTGACTCCG GCCCGCTGGT TTCCAGCGGG CTGCGGGCCC GAAACGGGCC CGCCGGAGTC ACTCGCTCGC TCGCGCGTCT CTCCCTCACC

3501  CCAAAGATCT
      GGTTTCTAGA
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Fig. 1C-4

Fig. 2

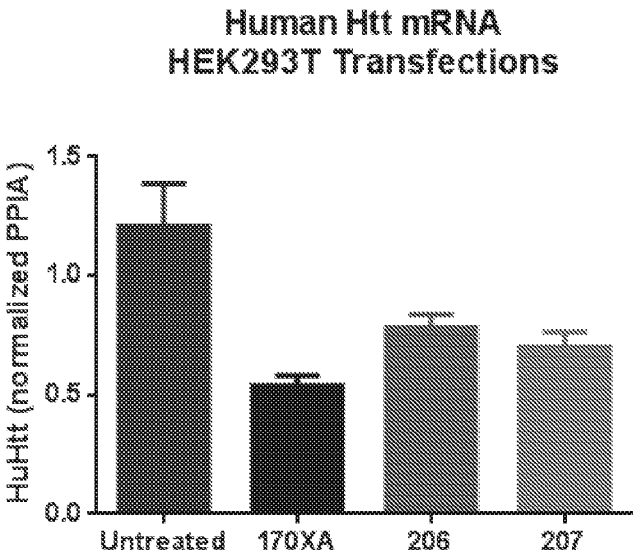

Human Htt mRNA
HEK293T Transfections
HuHtt (normalized PPIA)
1.5
1.0
0.5
0.0
Untreated
170XA
206
207

Fig. 3A

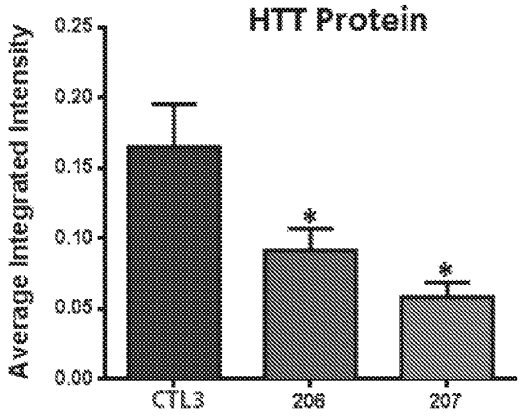

HTT Protein
Average Integrated Intensity
0.25
0.20
0.15
0.10
0.05
0.00
*
*
CTL3
206
207

Fig. 3B

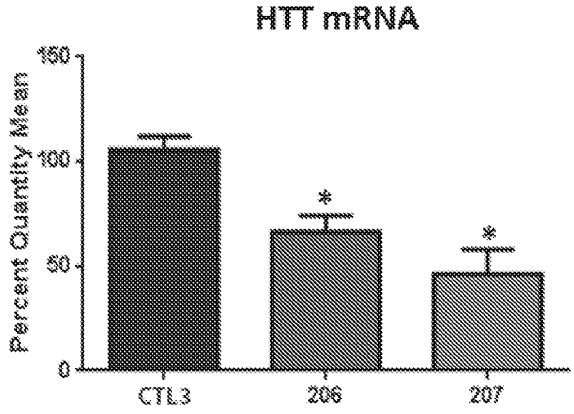

HTT mRNA
Percent Quantity Mean
150
100
50
0
*
*
CTL3
206
207

Fig. 4A

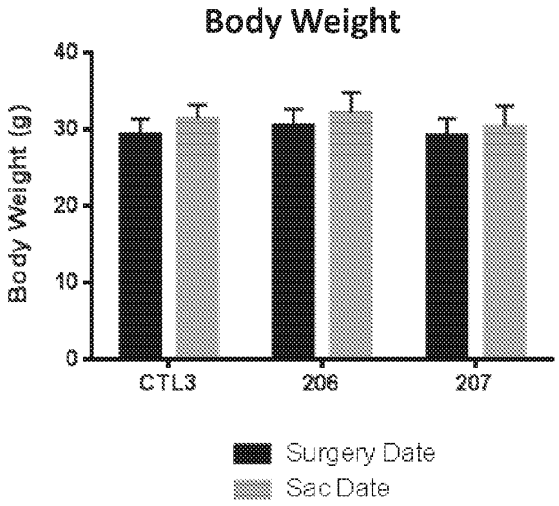
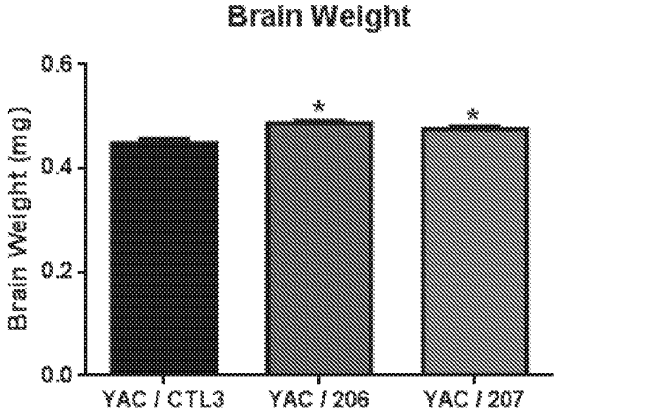


Fig. 4B



*Signficantly different from CTL3 by ANOVA, post hoc Tukey's Test

Fig. 5A

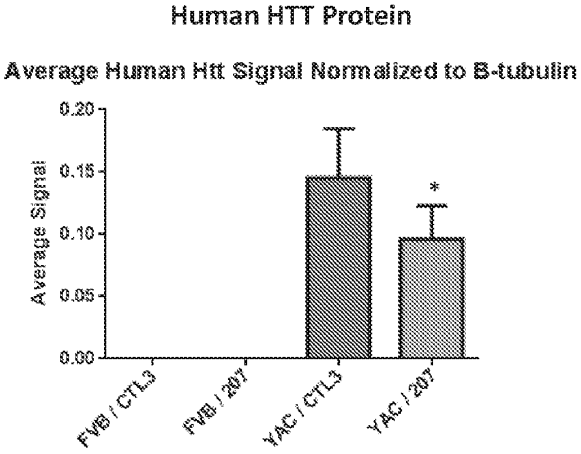

Human HTT Protein
Average Human Htt Signal Normalized to B-tubulin
Average Signal
0.20
0.15
0.10
0.05
0.00
*
FVB / CTL3
FVB / 207
YAC / CTL3
YAC / 207

Fig. 5B

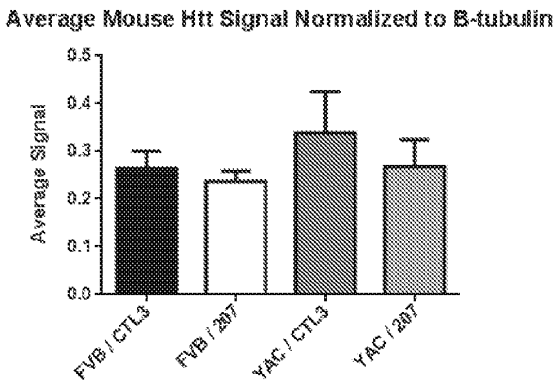

Mouse HTT Protein
Average Mouse Htt Signal Normalized to B-tubulin
Average Signal
0.5
0.4
0.3
0.2
0.1
0.0
FVB / CTL3
FVB / 207
YAC / CTL3
YAC / 207

Fig. 5C

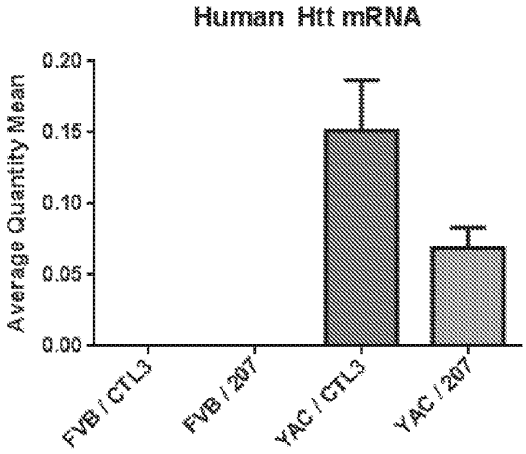

Human Htt mRNA
Average Quantity Mean
0.20
0.15
0.10
0.05
0.00
FVB / CTL3
FVB / 207
YAC / CTL3
YAC / 207

Fig. 5D

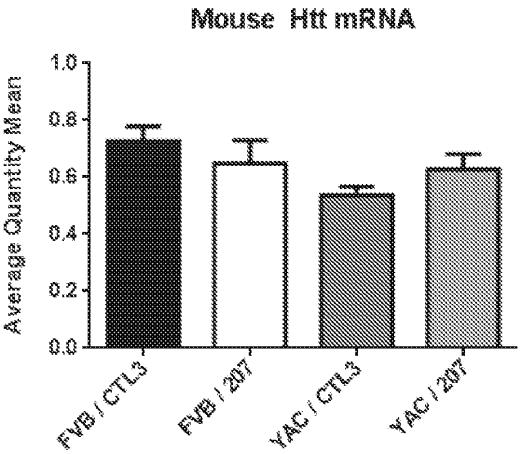

Mouse Htt mRNA
Average Quantity Mean
1.0
0.8
0.6
0.4
0.2
0.0
FVB / CTL3
FVB / 207
YAC / CTL3
YAC / 207

Fig. 6A

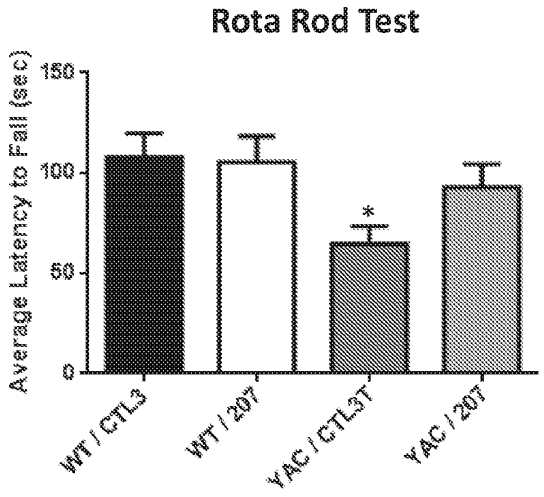

Rota Rod Test
Average Latency to Fall (sec)
150
100
50
0
*
WT / CTL3
WT / 207
YAC / CTL3
YAC / 207

Fig. 6B

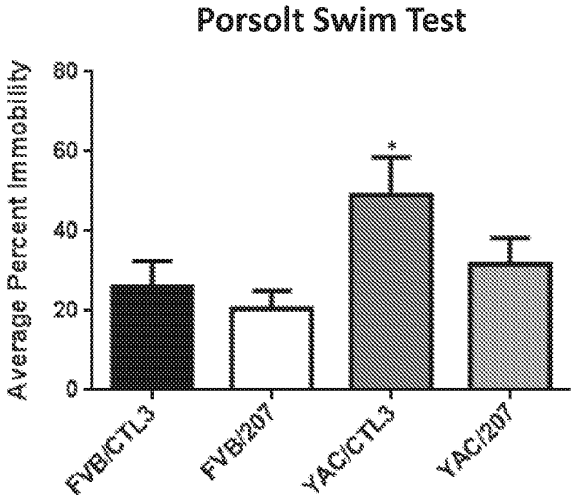

Porsolt Swim Test
Average Percent Immobility
80
60
40
20
0
*
FVB/CTL3
FVB/207
YAC/CTL3
YAC/207

Fig. 7A

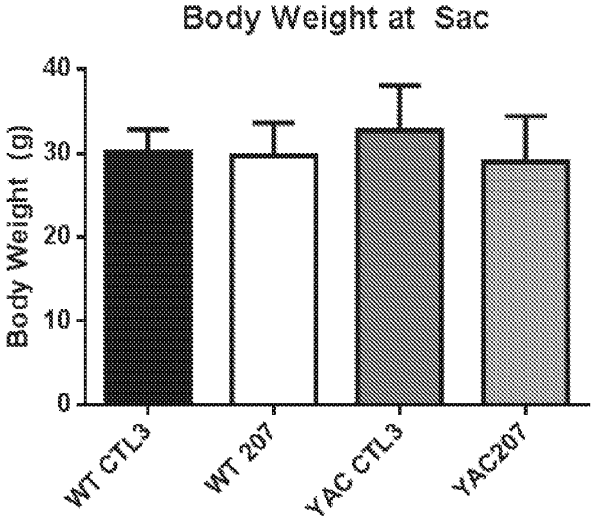
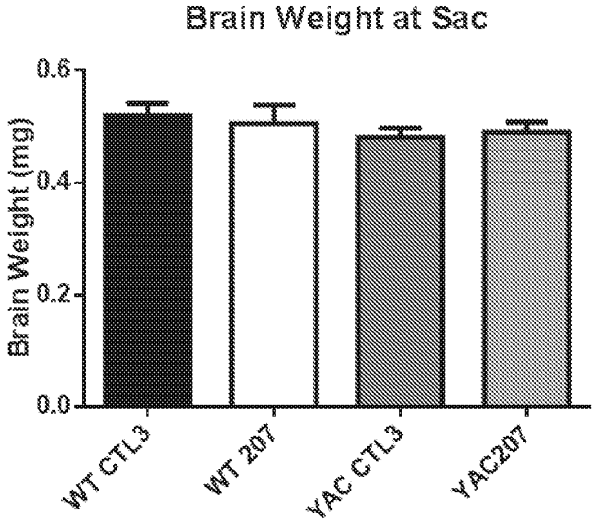

Body Weight at Sac
Body Weight (g)
40
30
20
10
0
WT CTL3
WT 207
YAC CTL3
YAC207

Fig. 7B


Brain Weight at Sac
Brain Weight (mg)
0.6
0.4
0.2
0.0
WT CTL3
WT 207
YAC CTL3
YAC207

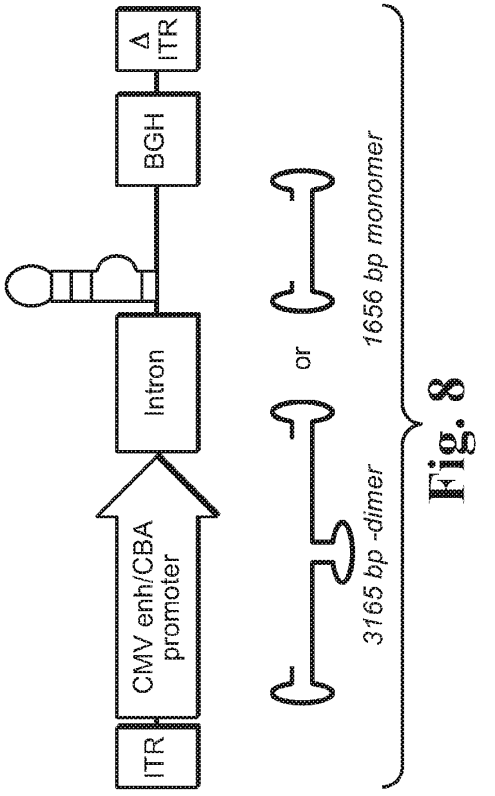

ITR
CMV enh/CBA promoter
Intron
BGH
Δ ITR
or
3165 bp -dimer
1656 bp monomer

Fig. 8

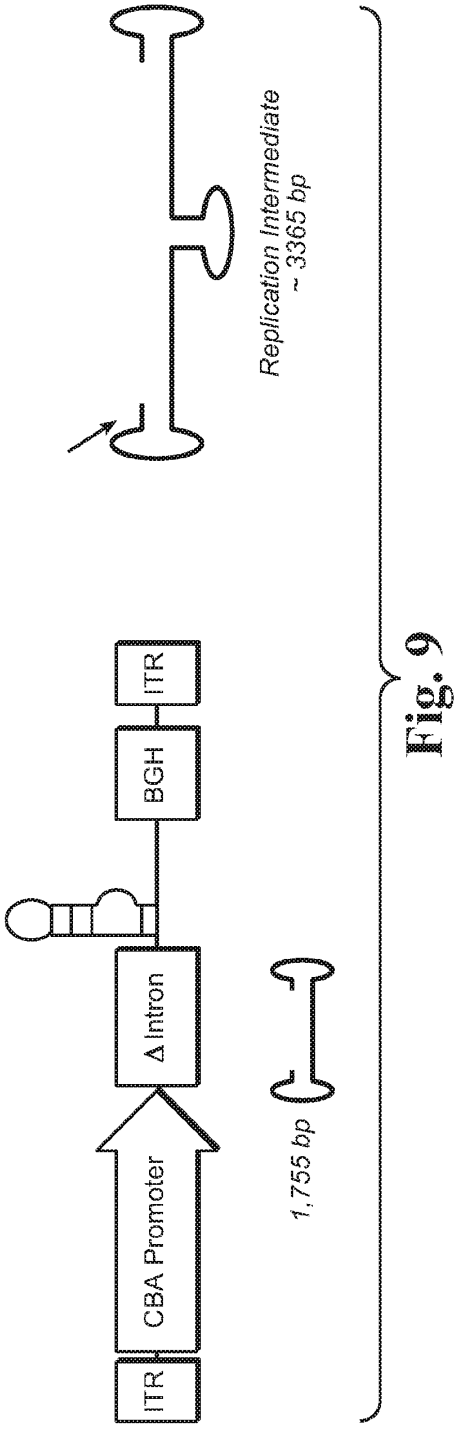

ITR
CBA Promoter
Δ Intron
BGH
ITR
1,755 bp
Replication Intermediate
~ 3365 bp

Fig. 9