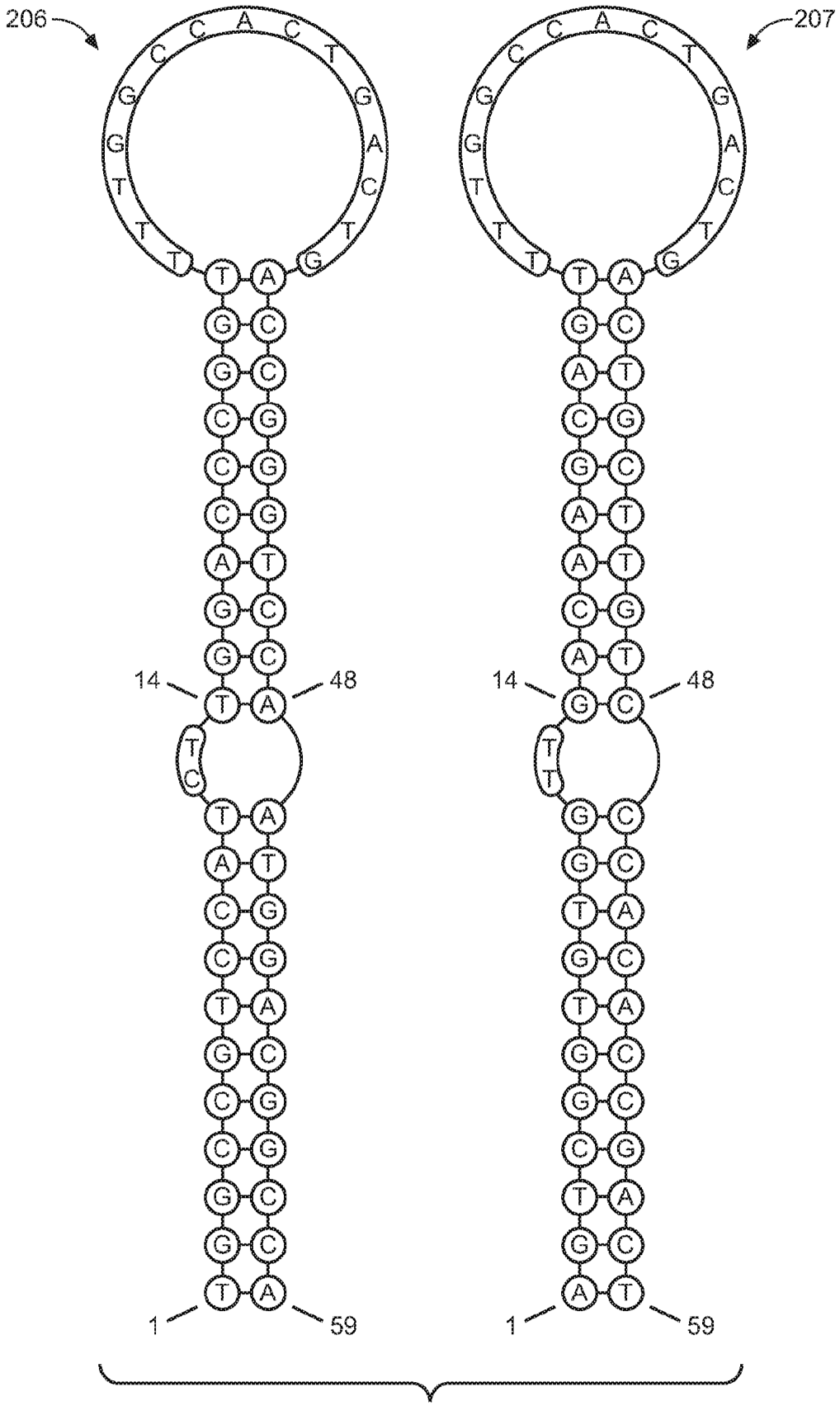


Fig. 1A

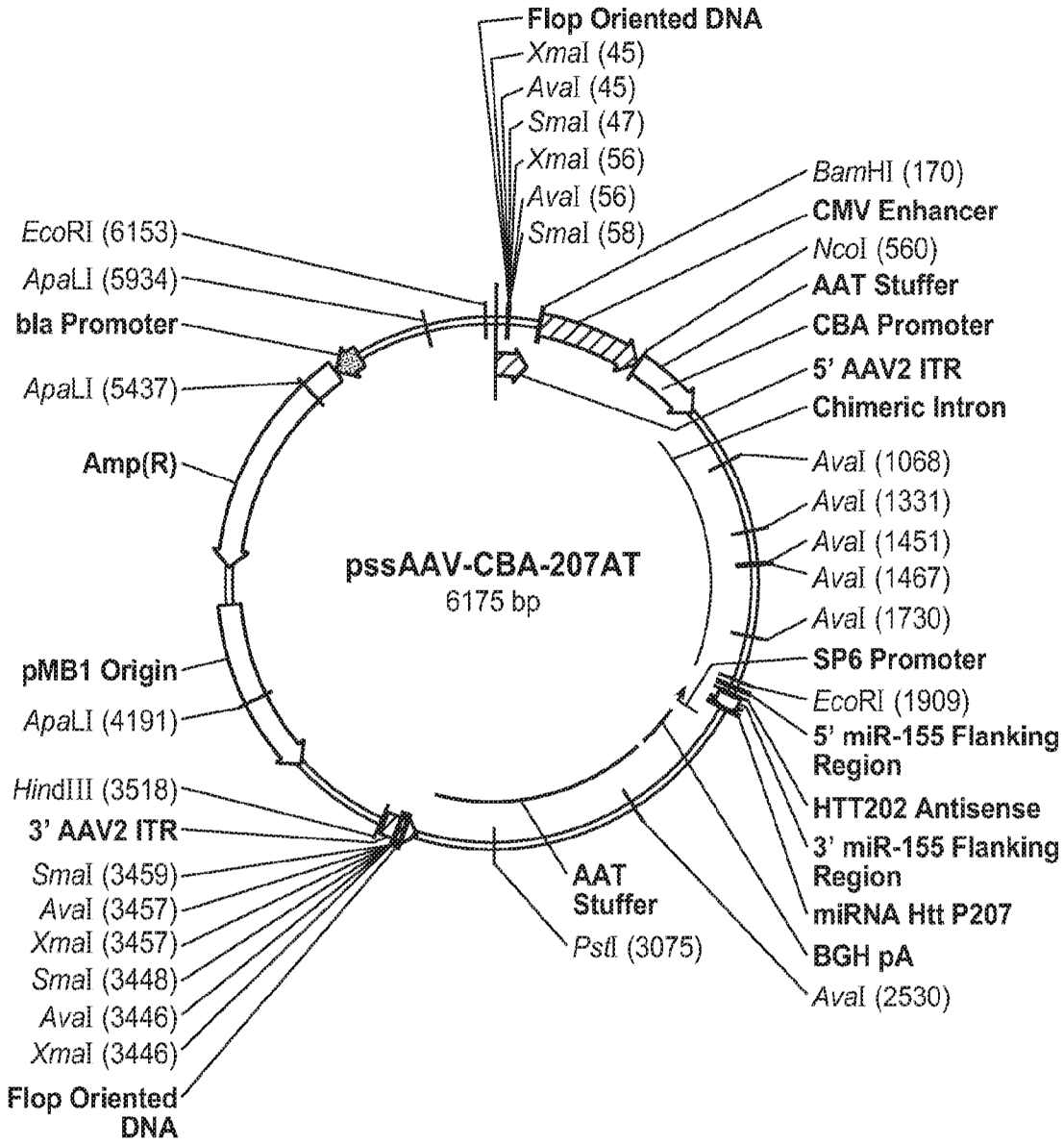

Flop Oriented DNA
XmaI (45)
AvaI (45)
SmaI (47)
XmaI (56)
AvaI (56)
SmaI (58)
BamHI (170)
CMV Enhancer
NcoI (560)
AAT Stuffer
CBA Promoter
5' AAV2 ITR
Chimeric Intron
AvaI (1068)
AvaI (1331)
AvaI (1451)
AvaI (1467)
AvaI (1730)
SP6 Promoter
EcoRI (1909)
5' miR-155 Flanking Region
HTT202 Antisense
3' miR-155 Flanking Region
miRNA Htt P207
BGH pA
AvaI (2530)
PstI (3075)
AAT Stuffer
pssAAV-CBA-207AT
6175 bp
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

Fig. 1B

Fig. 1C-1

Fig. 1C-2

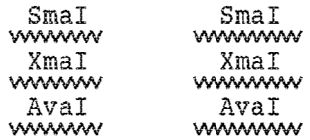
Fig. 1C-3

Fig. 1C-4

Fig. 1C

Fig. 1C-1

pssAAV-CBA-202AT




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      AACCGGTGAG GGAGAGACGC GCGAGCGAGC GAGTGACTCC GGCGGGCCCG TTTCGGGCCC GCAGCCCGCT GGAAACCAGC GGGCCGGAGT CACTCGCTCG

                                                                                                      BamHI
 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
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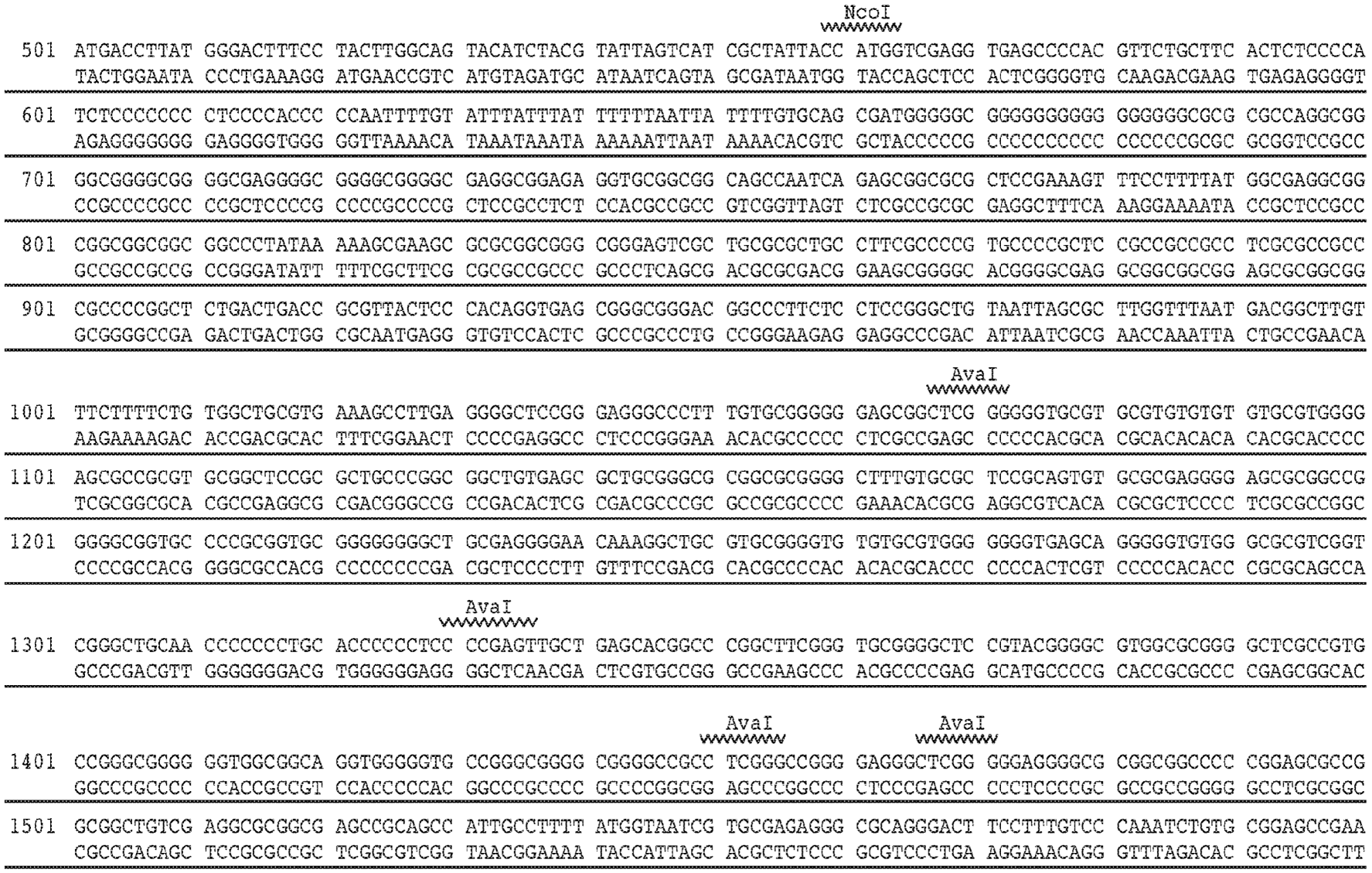

NcoI
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TACTGGAATA CCCTGAAAGG ATGAACCGTC ATGTAGATGC ATAATCAGTA GCGATAATGG TACCAGCTCC ACTCGGGGTG CAAGACGAAG TGAGAGGGGT
601 TCTCCCCCCC CTCCCCACCC CCAATTTTGT ATTTATTTAT TTTTTAATTA TTTTGTGCAG CGATGGGGGC GGGGGGGGGG GGGGGGCGCG CGCCAGGCGG
AGAGGGGGGG GAGGGGTGGG 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
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Fig. 1C-2

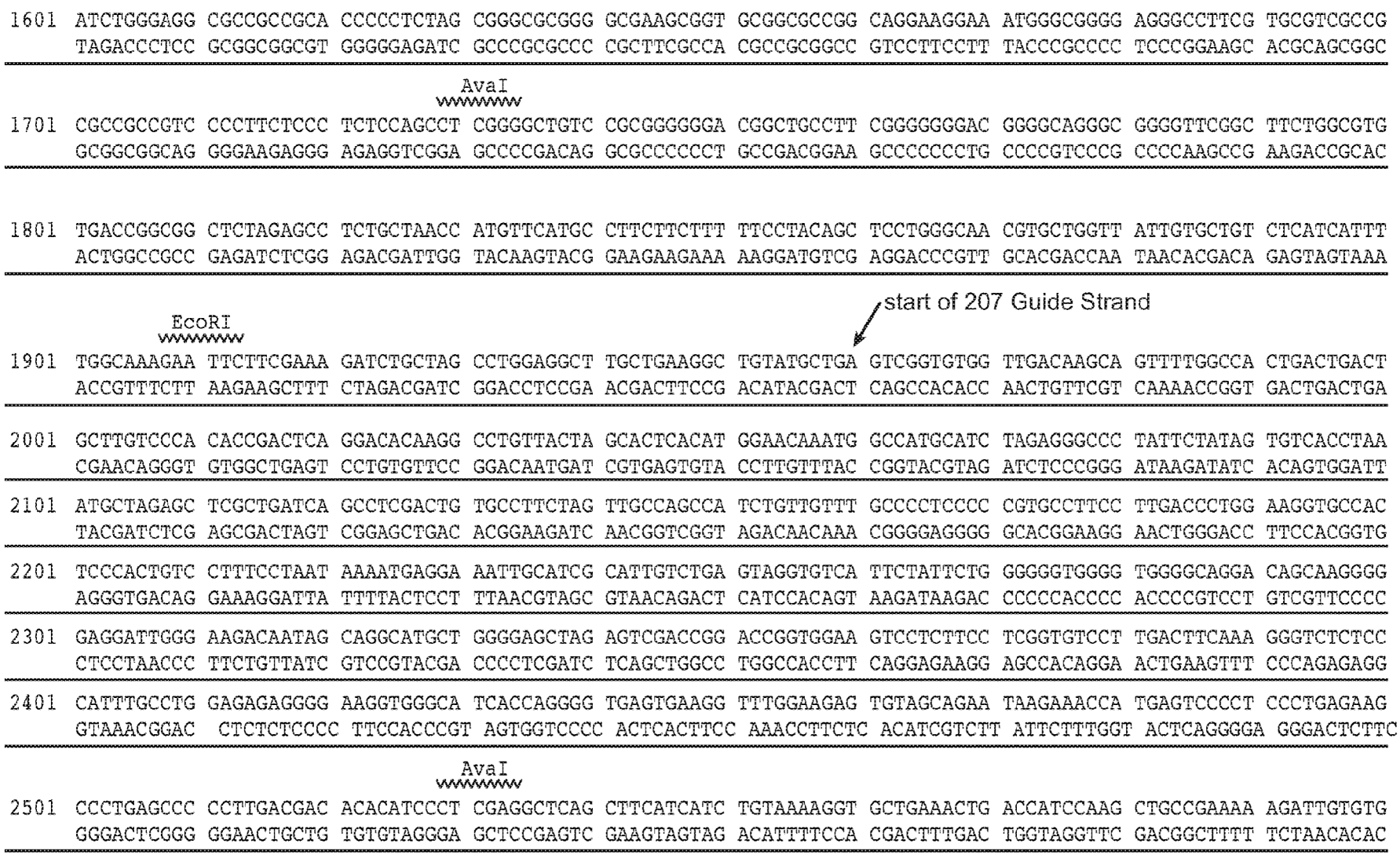


Fig. 1C-3

```
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
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
                                  XmaI        XmaI
                                  AvaI        AvaI
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

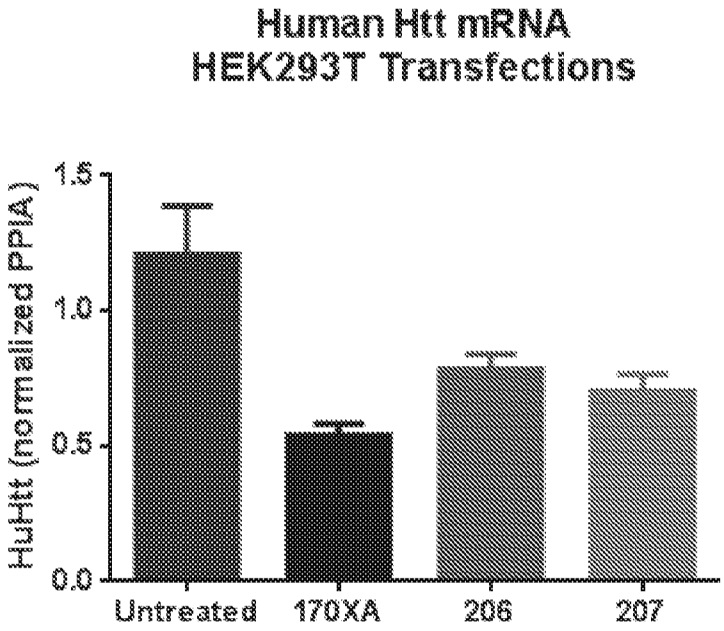

Human Htt mRNA
HEK293T Transfections
HuHtt (normalized PPIA)
1.5
1.0
0.5
0.0
Untreated
170XA
206
207

Fig. 3A

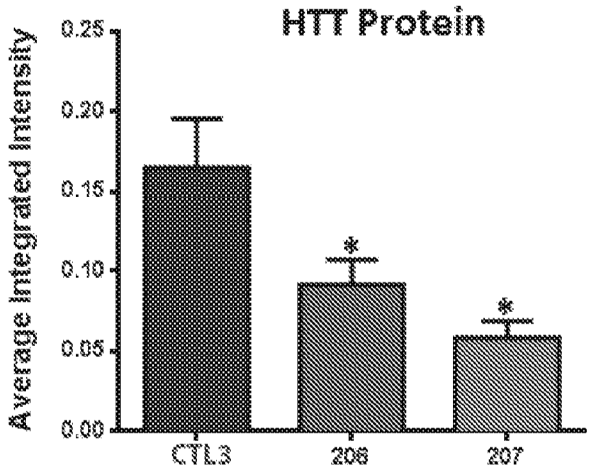

HTT Protein
Average Integrated Intensity
0.25
0.20
0.15
0.10
0.05
0.00
*
*
CTL3
206
207

Fig. 3B

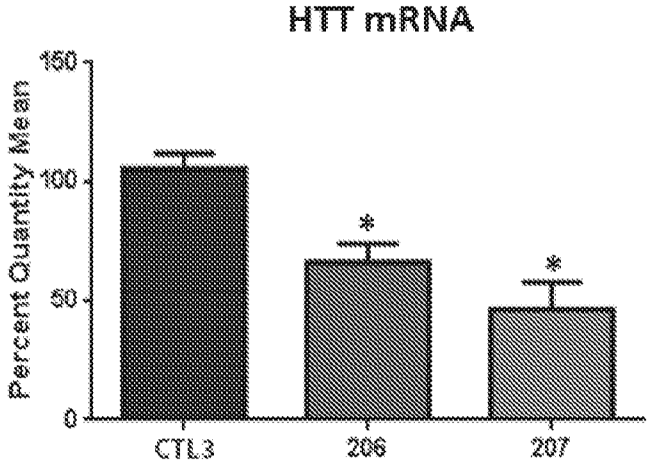

HTT mRNA
Percent Quantity Mean
150
100
50
0
*
*
CTL3
206
207

Fig. 4A

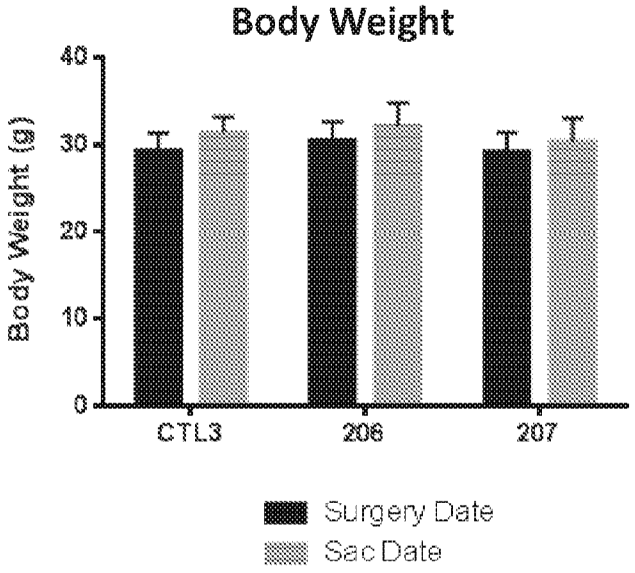
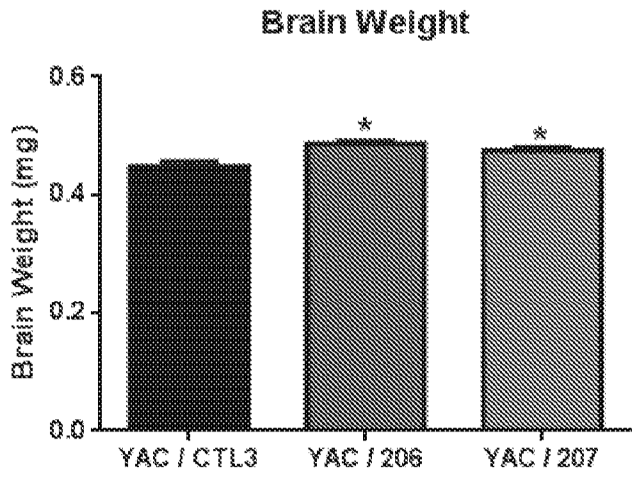


Fig. 4B



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

Fig. 5A

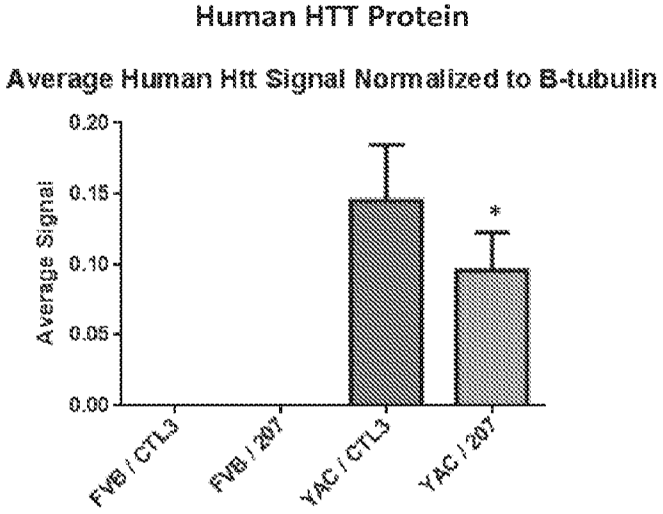

Human HTT Protein
Average Human Htt Signal Normalized to B-tubulin
Average Signal
0.20
0.15
0.10
0.05
0.00
*
FVB / CTL3
FVB / 207
YAC / CTL3
YAC / 207

Fig. 5B

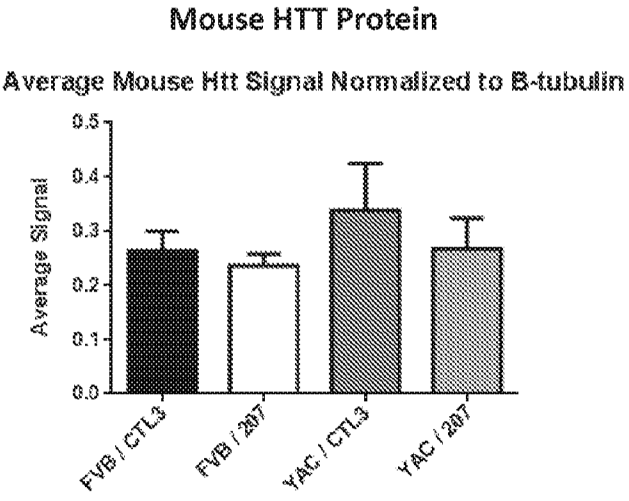

Mouse HTT Protein
Average Mouse Htt Signal Normalized to B-tubulin
Average Signal
0.5
0.4
0.3
0.2
0.1
0.0
FVB / CTL3
FVB / 207
YAC / CTL3
YAC / 207

Fig. 5C

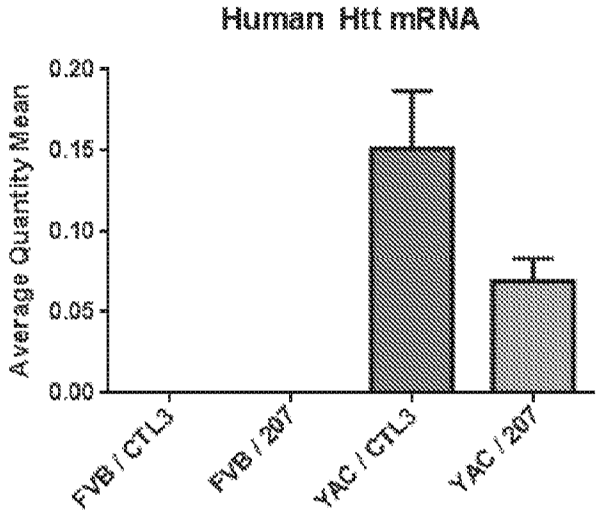

Human Htt mRNA
Average Quantity Mean
0.20
0.15
0.10
0.05
0.00
FVB / CTL3
FVB / 207
YAC / CTL3
YAC / 207

Fig. 5D

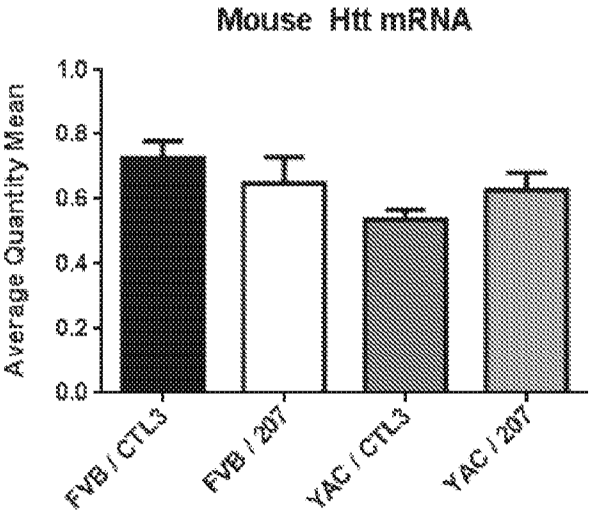

Mouse Htt mRNA
Average Quantity Mean
1.0
0.8
0.6
0.4
0.2
0.0
FVB / CTL3
FVB / 207
YAC / CTL3
YAC / 207

Fig. 6A

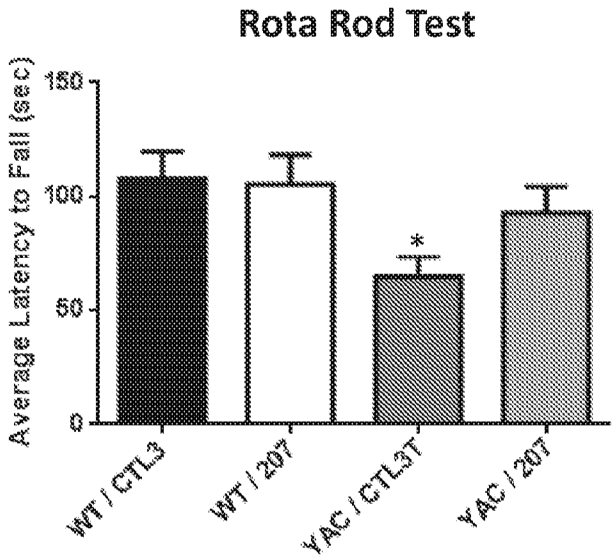

Rota Rod Test
Average Latency to Fall (sec)
150
100
50
0
*
WT / CTL3
WT / 207
YAC / CTL3T
YAC / 207

Fig. 6B

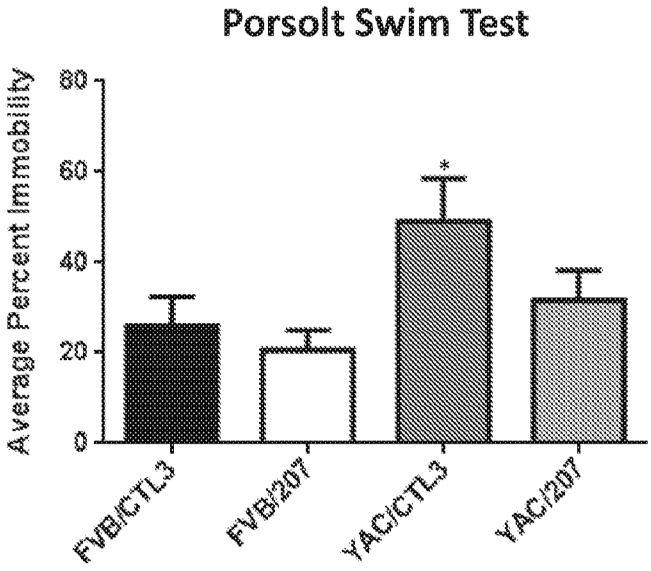

Porsolt Swim Test
Average Percent Immobility
80
60
40
20
0
*
FVB/CTL3
FVB/207
YAC/CTL3
YAC/207

Fig. 7A

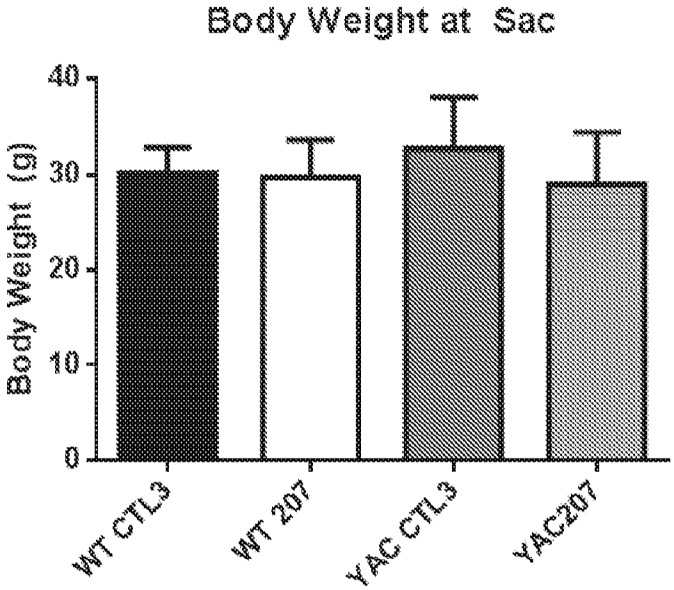
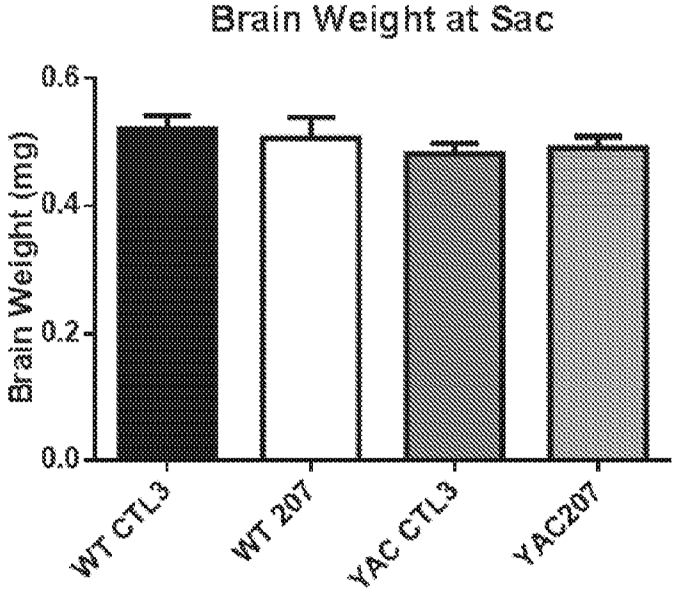

Body Weight at Sac
Body Weight (g)
40
30
20
10
0
WT CTL3
WT 207
YAC CTL3
YAC207

Fig. 7B


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

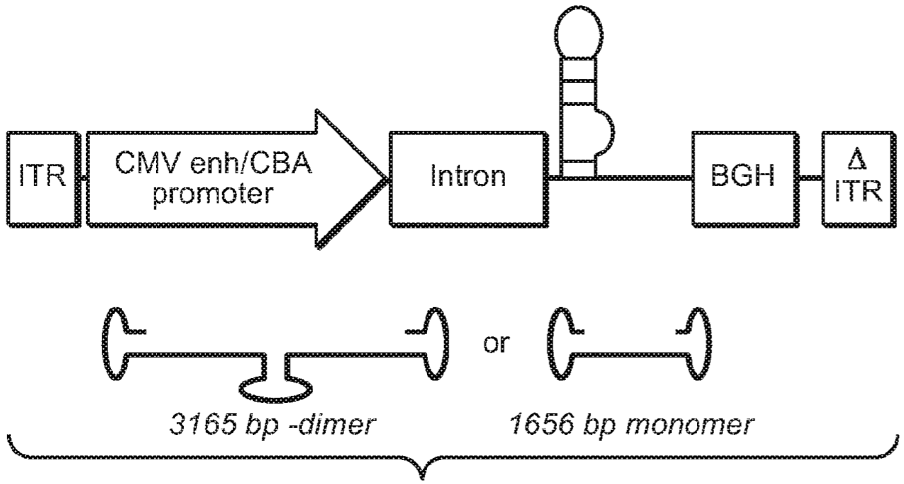

ITR
CMV enh/CBA promoter
Intron
BGH
Δ ITR
or
3165 bp -dimer
1656 bp monomer

Fig. 8

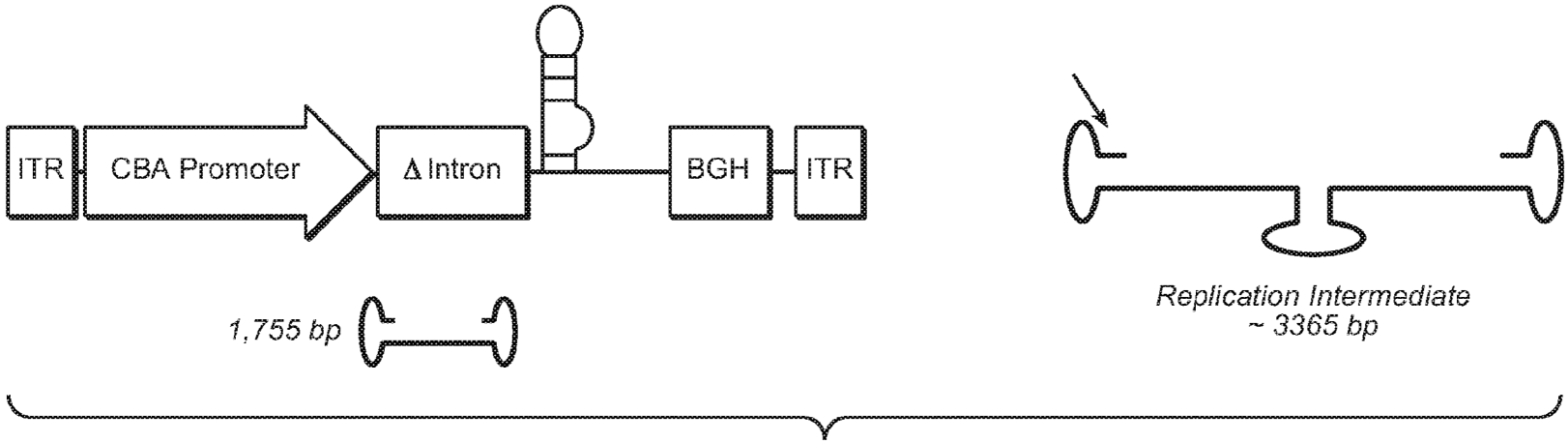

ITR
CBA Promoter
Δ Intron
BGH
ITR
1,755 bp
Replication Intermediate
~ 3365 bp

Fig. 9