FIG. 1

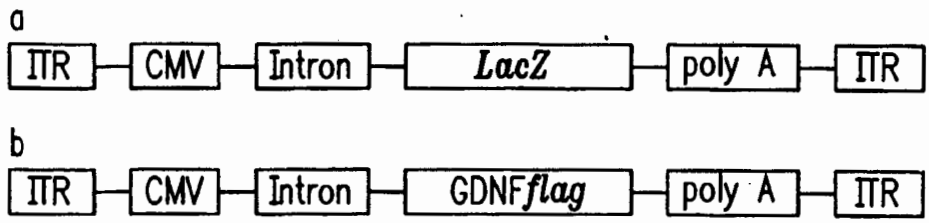

a
ITR
CMV
Intron
LacZ
poly A
ITR
b
ITR
CMV
Intron
GDNFflag
poly A
ITR

FIG.2

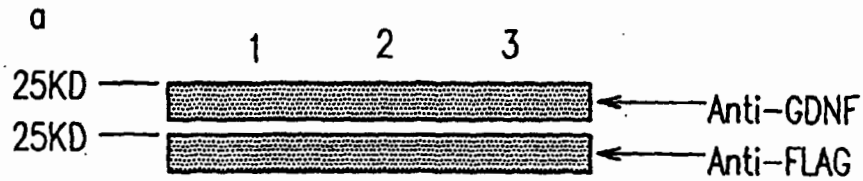

a
1
2
3
25KD
25KD
Anti-GDNF
Anti-FLAG

FIG.3

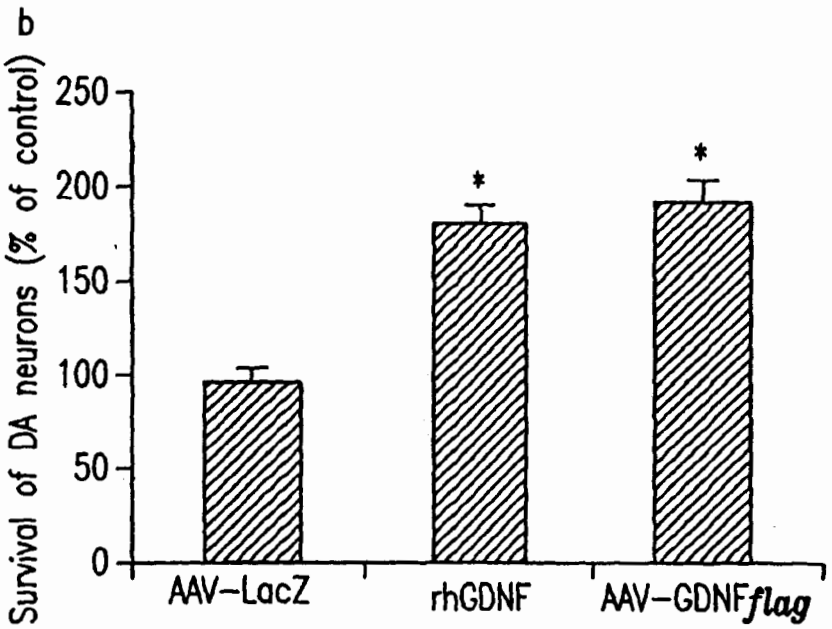

b
Survival of DA neurons (% of control)
250
200
150
100
50
0
*
*
AAV-LacZ
rhGDNF
AAV-GDNFflag

FIG. 4

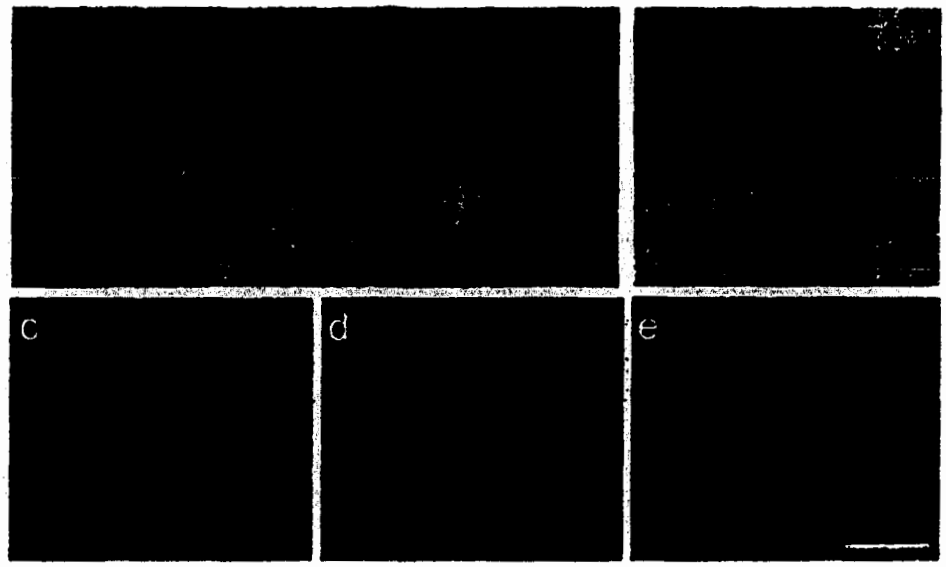


FIG. 5

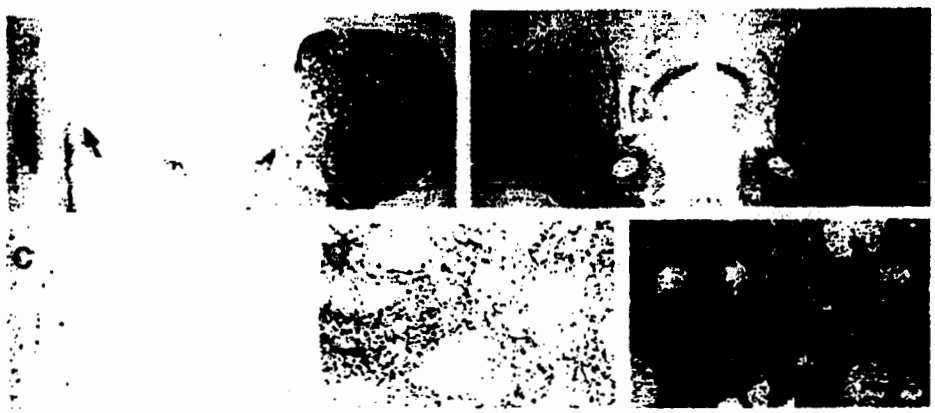


FIG. 6

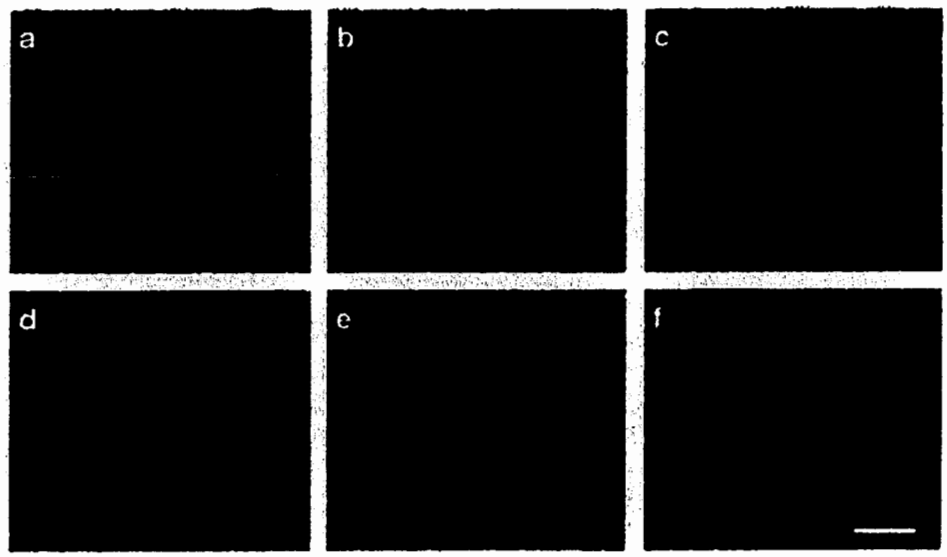


FIG. 7

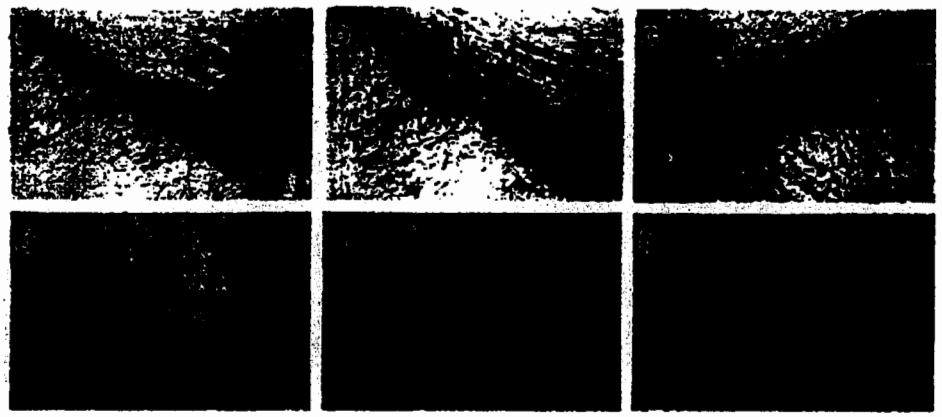


FIG.8

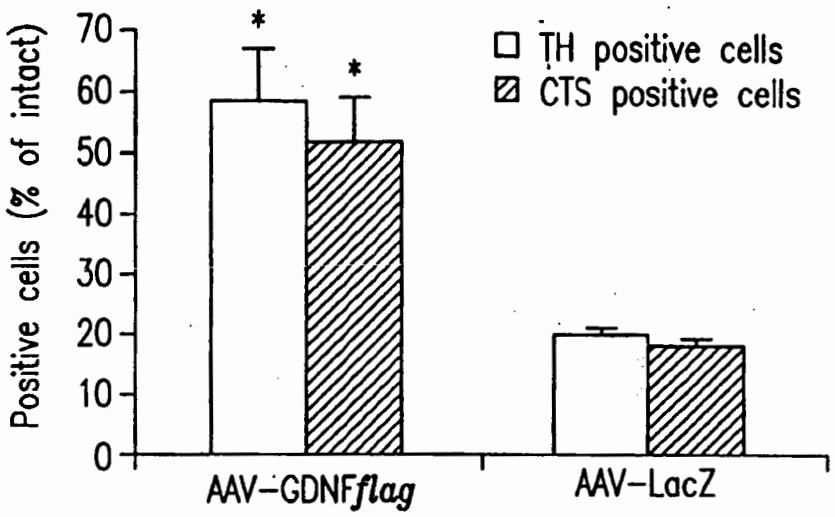

Positive cells (% of intact)
70
60
50
40
30
20
10
0
*
*
TH positive cells
CTS positive cells
AAV-GDNFflag
AAV-LacZ

FIG. 9

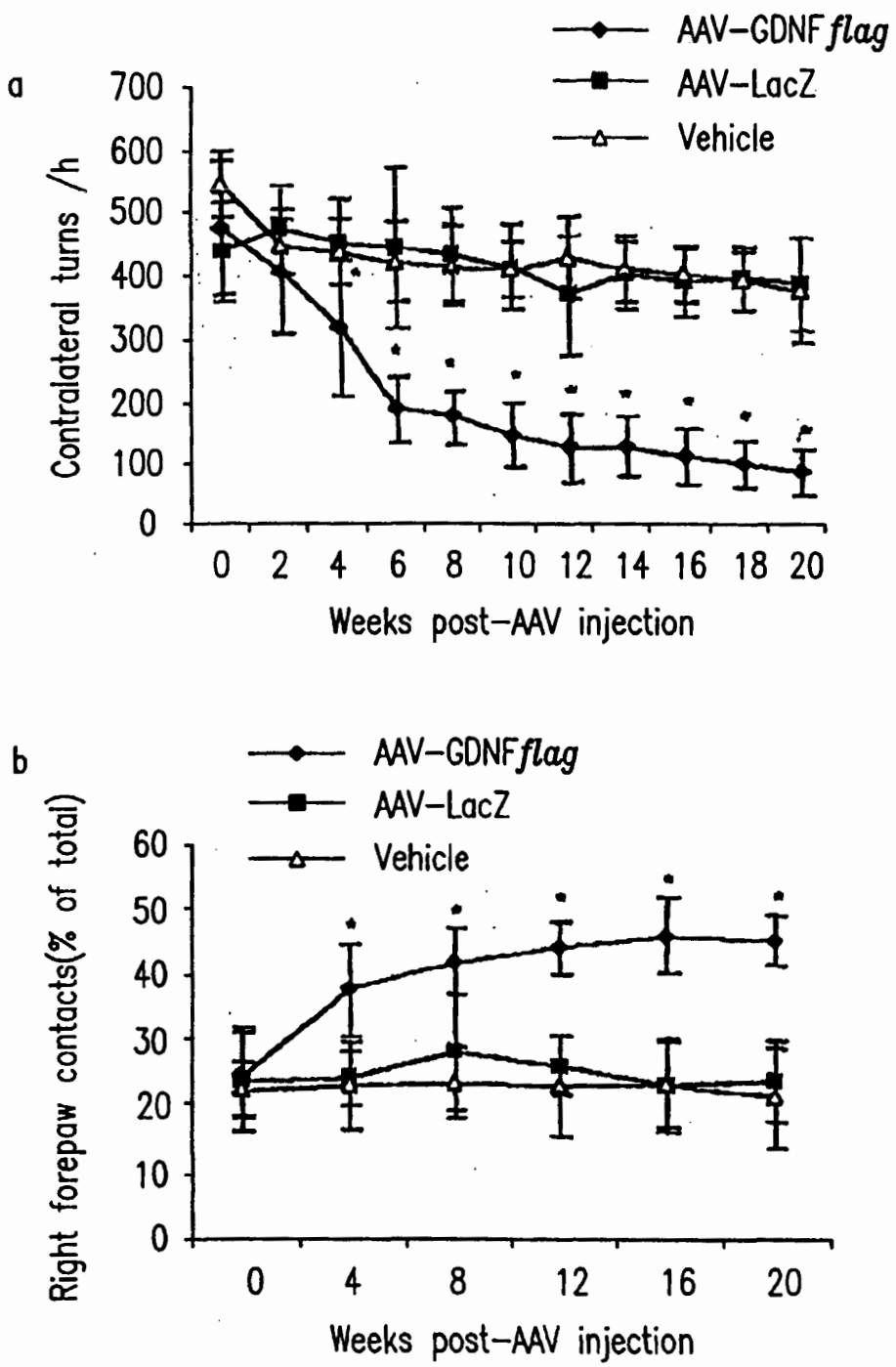
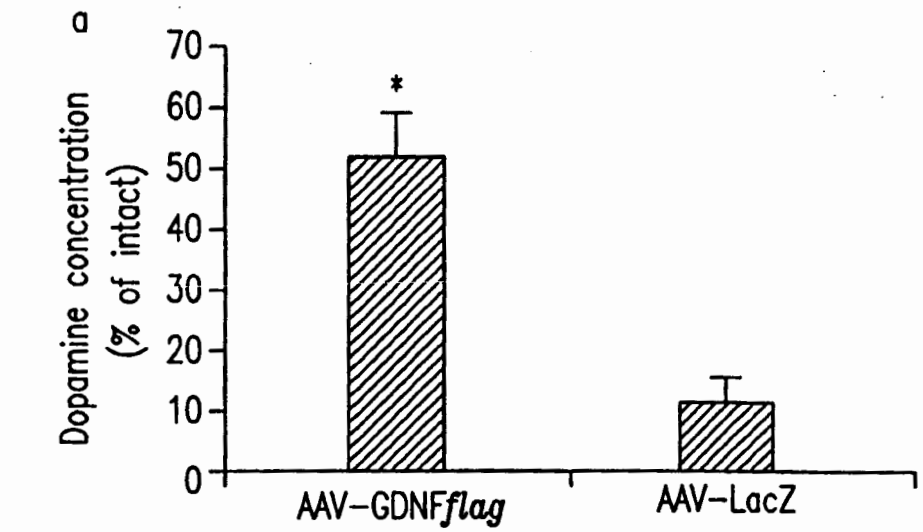

a
AAV-GDNF flag
AAV-LacZ
Vehicle
Contralateral turns /h
700
600
500
400
300
200
100
0
0 2 4 6 8 10 12 14 16 18 20
Weeks post-AAV injection
b
AAV-GDNF flag
AAV-LacZ
Vehicle
Right forepaw contacts(% of total)
60
50
40
30
20
10
0
0 4 8 12 16 20
Weeks post-AAV injection

FIG. 10


a
Dopamine concentration (% of intact)
70
60
50
40
30
20
10
0
*
AAV-GDNFflag
AAV-LacZ

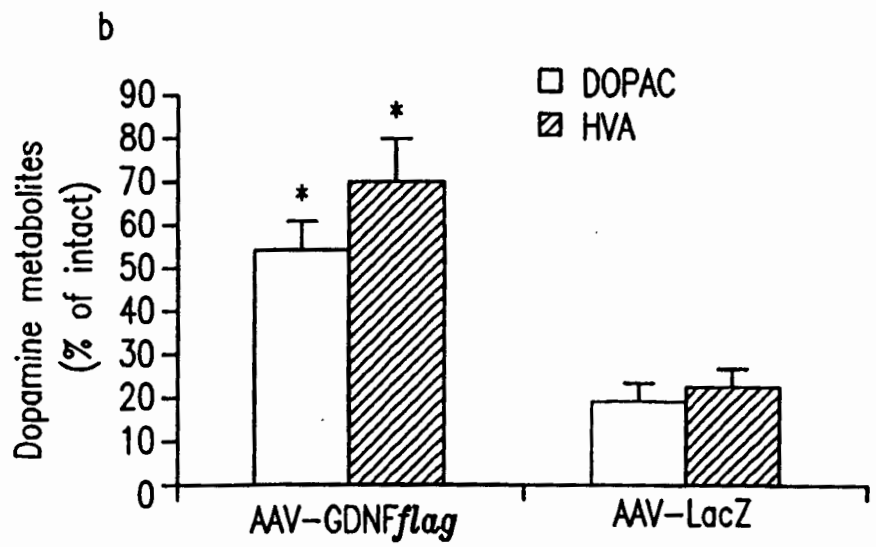

b
Dopamine metabolites (% of intact)
90
80
70
60
50
40
30
20
10
0
DOPAC
HVA
*
*
AAV-GDNFflag
AAV-LacZ

FIG. 11

```
atg aag tta tgg gat gtc gtg gct gtc tgc ctg gtg ctg ctc cac acc   48
Met Lys Leu Trp Asp Val Val Ala Val Cys Leu Val Leu Leu His Thr
  1               5                  10                  15

gcg tcc gcc ttc ccg ctg ccc gcc ggt aag agg cct ccc gag gcg ccc   96
Ala Ser Ala Phe Pro Leu Pro Ala Gly Lys Arg Pro Pro Glu Ala Pro
            20                  25                  30

gcc gaa gac cgc tcc ctc ggc cgc cgc cgc gcg ccc ttc gcg ctg agc  144
Ala Glu Asp Arg Ser Leu Gly Arg Arg Arg Ala Pro Phe Ala Leu Ser
        35                  40                  45

agt gac tca aat atg cca gag gat tat cct gat cag ttc gat gat gtc  192
Ser Asp Ser Asn Met Pro Glu Asp Tyr Pro Asp Gln Phe Asp Asp Val
    50                  55                  60

atg gat ttt att caa gcc acc att aaa aga ctg aaa agg tca cca gat  240
Met Asp Phe Ile Gln Ala Thr Ile Lys Arg Leu Lys Arg Ser Pro Asp
65                  70                  75                  80

aaa caa atg gca gtg ctt cct aga aga gag cgg aat cgg cag gct gca  288
Lys Gln Met Ala Val Leu Pro Arg Arg Glu Arg Asn Arg Gln Ala Ala
                85                  90                  95

gct gcc aac cca gag aat tcc aga gga aaa ggt cgg aga ggc cag agg  336
Ala Ala Asn Pro Glu Asn Ser Arg Gly Lys Gly Arg Arg Gly Gln Arg
            100                 105                 110

ggc aaa aac cgg ggt tgt gtc tta act gca ata cat tta aat gtc act  384
Gly Lys Asn Arg Gly Cys Val Leu Thr Ala Ile His Leu Asn Val Thr
        115                 120                 125

gac ttg ggt ctg ggc tat gaa acc aag gag gaa ctg att ttt agg tac  432
Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile Phe Arg Tyr
    130                 135                 140

tgc agc ggc tct tgc gat gca gct gag aca acg tac gac aaa ata ttg  480
Cys Ser Gly Ser Cys Asp Ala Ala Glu Thr Thr Tyr Asp Lys Ile Leu
145                 150                 155                 160

aaa aac tta tcc aga aat aga agg ctg gtg agt gac aaa gta ggg cag  528
Lys Asn Leu Ser Arg Asn Arg Arg Leu Val Ser Asp Lys Val Gly Gln
                165                 170                 175

gca tgt tgc aga ccc atc gcc ttt gat gat gac ctg tcg ttt tta gat  576
Ala Cys Cys Arg Pro Ile Ala Phe Asp Asp Asp Leu Ser Phe Leu Asp
            180                 185                 190

gat aac ctg gtt tac cat att cta aga aag cat tcc gct aaa agg tgt  624
Asp Asn Leu Val Tyr His Ile Leu Arg Lys His Ser Ala Lys Arg Cys
        195                 200                 205

gga tgt atc                                                     633
Gly Cys Ile
    210
```

FIG. 12

```
atg aag tta tgg gat gtc gtg gct gtc tgc ctg gtg ttg ctc cac acc   48
Met Lys Leu Trp Asp Val Val Ala Val Cys Leu Val Leu Leu His Thr
  1               5                  10                  15

gcg tct gcc ttc ccg ctg ccc gcc ggt aag agg ctt ctc gaa gcg ccc   96
Ala Ser Ala Phe Pro Leu Pro Ala Gly Lys Arg Leu Leu Glu Ala Pro
             20                  25                  30

gcc gaa gac cac tcc ctc ggc cac cgc cgc gtg ccc ttc gcg ctg acc   144
Ala Glu Asp His Ser Leu Gly His Arg Arg Val Pro Phe Ala Leu Thr
         35                  40                  45

agt gac tcc aat atg ccc gaa gat tat cct gac cag ttt gat gac gtc   192
Ser Asp Ser Asn Met Pro Glu Asp Tyr Pro Asp Gln Phe Asp Asp Val
     50                  55                  60

atg gat ttt att caa gcc acc atc aaa aga ctg aaa agg tca cca gat   240
Met Asp Phe Ile Gln Ala Thr Ile Lys Arg Leu Lys Arg Ser Pro Asp
 65                  70                  75                  80

aaa caa gcg gcg gca ctt cct cga aga gag agg aac cgg caa gct gca   288
Lys Gln Ala Ala Ala Leu Pro Arg Arg Glu Arg Asn Arg Gln Ala Ala
                 85                  90                  95

gct gcc agc cca gag aat tcc aga ggg aaa ggt cgc aga ggc cag agg   336
Ala Ala Ser Pro Glu Asn Ser Arg Gly Lys Gly Arg Arg Gly Gln Arg
            100                 105                 110

ggc aaa aat cgg ggg tgc gtc tta act gca ata cac tta aat gtc act   384
Gly Lys Asn Arg Gly Cys Val Leu Thr Ala Ile His Leu Asn Val Thr
        115                 120                 125

gac ttg ggt ttg ggc tac gaa acc aag gag gaa ctg atc ttt cga tat   432
Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile Phe Arg Tyr
    130                 135                 140

tgt agc ggt tcc tgt gaa gcg gcc gag aca atg tac gac aaa ata cta   480
Cys Ser Gly Ser Cys Glu Ala Ala Glu Thr Met Tyr Asp Lys Ile Leu
145                 150                 155                 160

aaa aat ctg tct cga agt aga agg cta aca agt gac aag gta ggc cag   528
Lys Asn Leu Ser Arg Ser Arg Arg Leu Thr Ser Asp Lys Val Gly Gln
                165                 170                 175

gca tgt tgc agg ccg gtc gcc ttc gac gac gac ctg tcg ttt tta gac   576
Ala Cys Cys Arg Pro Val Ala Phe Asp Asp Asp Leu Ser Phe Leu Asp
            180                 185                 190

gac agc ctg gtt tac cat atc cta aga aag cat tcc gct aaa cgg tgt   624
Asp Ser Leu Val Tyr His Ile Leu Arg Lys His Ser Ala Lys Arg Cys
        195                 200                 205

gga tgt atc                                                      633
Gly Cys Ile
    210
```

FIG. 13

```
atg gga ttc ggg cca ctt gga gtt aat gtc caa ctg ggg gtc tac gga   48
Met Gly Phe Gly Pro Leu Gly Val Asn Val Gln Leu Gly Val Tyr Gly
 1               5                  10                  15

gac cgg atc cga ggt gcc gcc gcc gga cgg gac tct aag atg aag tta   96
Asp Arg Ile Arg Gly Ala Ala Ala Gly Arg Asp Ser Lys Met Lys Leu
            20                  25                  30

tgg gat gtc gtg gct gtc tgc ctg gtg ttg ctc cac acc gcg tct gcc   144
Trp Asp Val Val Ala Val Cys Leu Val Leu Leu His Thr Ala Ser Ala
        35                  40                  45

ttc ccg ctg ccc gcc ggt aag agg ctt ctc gaa gcg ccc gct gaa gac   192
Phe Pro Leu Pro Ala Gly Lys Arg Leu Leu Glu Ala Pro Ala Glu Asp
    50                  55                  60

cac tcc ctc ggc cac cgc cgc gtg ccc ttc gcg ctg acc agt gac tcc   240
His Ser Leu Gly His Arg Arg Val Pro Phe Ala Leu Thr Ser Asp Ser
65                  70                  75                  80

aat atg cct gaa gat tat cct gac cag ttt gat gac gtc atg gat ttt   288
Asn Met Pro Glu Asp Tyr Pro Asp Gln Phe Asp Asp Val Met Asp Phe
                85                  90                  95

att caa gcc acc att aaa aga ctg aaa agg tca cca gat aaa caa gcg   336
Ile Gln Ala Thr Ile Lys Arg Leu Lys Arg Ser Pro Asp Lys Gln Ala
            100                 105                 110

gca gcg ctt cct cga aga gag agg aat cgg cag gct gca gct gcc agc   384
Ala Ala Leu Pro Arg Arg Glu Arg Asn Arg Gln Ala Ala Ala Ala Ser
        115                 120                 125

cca gag aat tcc aga ggg aaa ggt cgc aga ggc cag agg ggc aaa aat   432
Pro Glu Asn Ser Arg Gly Lys Gly Arg Arg Gly Gln Arg Gly Lys Asn
    130                 135                 140

cgg ggg tgc gtt tta act gcc ata cac tta aat gtc act gac ttg ggt   480
Arg Gly Cys Val Leu Thr Ala Ile His Leu Asn Val Thr Asp Leu Gly
145                 150                 155                 160

ttg ggc tat gaa acc aag gag gaa ctg atc ttt cga tat tgc agc ggt   528
Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile Phe Arg Tyr Cys Ser Gly
                165                 170                 175

tcc tgt gaa tcg gcc gag aca atg tat gac aaa ata cta aaa aac ctg   576
Ser Cys Glu Ser Ala Glu Thr Met Tyr Asp Lys Ile Leu Lys Asn Leu
            180                 185                 190

tct cgg agt aga agg cta aca agt gac aaa gta ggc cag gca tgt tgc   624
Ser Arg Ser Arg Arg Leu Thr Ser Asp Lys Val Gly Gln Ala Cys Cys
        195                 200                 205

agg ccg gtc gcc ttc gac gac gac ctg tcg ttt tta gat gac aac ctg   672
Arg Pro Val Ala Phe Asp Asp Asp Leu Ser Phe Leu Asp Asp Asn Leu
    210                 215                 220

gtt tac cat att cta aga aag cat tcc gct aaa cgg tgt gga tgt atc   720
Val Tyr His Ile Leu Arg Lys His Ser Ala Lys Arg Cys Gly Cys Ile
225                 230                 235                 240
```