



US008361708B2

(12) **United States Patent**  
Peiris et al.(10) **Patent No.:** US 8,361,708 B2  
(45) **Date of Patent:** \*Jan. 29, 2013(54) **HUMAN VIRUS CAUSING SEVERE ACUTE  
RESPIRATORY SYNDROME (SARS) AND  
USES THEREOF**(75) Inventors: **Joseph S. M. Peiris**, Hong Kong (CN);  
**Kwok Yung Yuen**, Hong Kong (CN); **Lit  
Man Poon**, Hong Kong (CN); **Yi Guan**,  
Hong Kong (CN); **Kwok Hung Chan**,  
Hong Kong (CN); **John M. Nicholls**,  
Hong Kong (CN); **Frederick C. Leung**,  
Hong Kong (CN)(73) Assignee: **Versitech Limited**, Hong Kong (CN)(\*) Notice: Subject to any disclaimer, the term of this  
patent is extended or adjusted under 35  
U.S.C. 154(b) by 368 days.This patent is subject to a terminal dis-  
claimer.(21) Appl. No.: **12/703,418**(22) Filed: **Feb. 10, 2010**(65) **Prior Publication Data**

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**Related U.S. Application Data**(60) Continuation of application No. 11/808,408, filed on  
Jun. 8, 2007, now Pat. No. 7,785,775, which is a  
division of application No. 10/808,121, filed on Mar.  
24, 2004, now Pat. No. 7,375,202.(60) Provisional application No. 60/457,031, filed on Mar.  
24, 2003, provisional application No. 60/457,730,  
filed on Mar. 26, 2003, provisional application No.  
60/459,931, filed on Apr. 2, 2003, provisional  
application No. 60/460,357, filed on Apr. 3, 2003,  
provisional application No. 60/461,265, filed on Apr.  
8, 2003, provisional application No. 60/462,805, filed  
on Apr. 14, 2003, provisional application No.  
60/464,886, filed on Apr. 23, 2003.(51) **Int. Cl.****C12Q 1/70** (2006.01)  
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**G01N 33/53** (2006.01)  
**C07H 21/04** (2006.01)  
**C07H 21/02** (2006.01)  
**A61K 39/395** (2006.01)  
**A61K 39/00** (2006.01)  
**A61K 39/42** (2006.01)(52) **U.S. Cl.** ..... **435/5**; 435/6.1; 435/6.11; 435/6.12;  
435/7.1; 536/24.3; 536/24.32; 536/24.33;  
536/23.72; 536/23.1; 424/130.1; 424/139.1;  
424/147.1(58) **Field of Classification Search** ..... None  
See application file for complete search history.(56) **References Cited**

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*Primary Examiner* — Louise Humphrey(74) *Attorney, Agent, or Firm* — Saliwanchik, Lloyd &  
Eisenschenk(57) **ABSTRACT**The present invention relates to an isolated novel virus caus-  
ing Severe Acute Respiratory Syndrome (SARS) in humans  
("hSARS virus"). The hSARS virus is identified to be mor-  
phologically and phylogenetically similar to known member  
of Coronaviridae. The present invention provides the com-  
plete genomic sequence of the hSARS virus. Furthermore,  
the invention provides the nucleic acids and peptides encoded  
by and/or derived from the hSARS virus and their use in  
diagnostic methods and therapeutic methods, including vac-  
cines. In addition, the invention provides chimeric or recom-  
binant viruses encoded by said nucleotide sequences and  
antibodies immunospecific to the polypeptides encoded by  
the nucleotide sequences.**3 Claims, 90 Drawing Sheets**

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a cag gac gct gta gct tca aaa atc tta gga ttg cct acg cag act gtt 49
  Gln Asp Ala Val Ala Ser Lys Ile Leu Gly Leu Pro Thr Gln Thr Val
  1           5           10           15
gat tca tca cag ggt tct gaa tat gac tat gtc ata ttc aca caa act 97
Asp Ser Ser Gln Gly Ser Glu Tyr Asp Tyr Val Ile Phe Thr Gln Thr
      20           25           30
act gaa aca gca cac tct tgt aat gtc aac cgc ttc aat gtg gct atc 145
Thr Glu Thr Ala His Ser Cys Asn Val Asn Arg Phe Asn Val Ala Ile
      35           40           45
aca agg gca aaa att ggc att ttg tgc ata atg tct gat aga gat ctt 193
Thr Arg Ala Lys Ile Gly Ile Leu Cys Ile Met Ser Asp Arg Asp Leu
      50           55           60
tat gac aaa ctg caa ttt aca agt cta gaa ata cca cgt cgc aat gtg 241
Tyr Asp Lys Leu Gln Phe Thr Ser Leu Glu Ile Pro Arg Arg Asn Val
      65           70           75           80
gct aca tta caa gca gaa aat gta act gga ctt ttt aag gac tgt agt 289
Ala Thr Leu Gln Ala Glu Asn Val Thr Gly Leu Phe Lys Asp Cys Ser
      85           90           95
aag atc att act ggt ctt cat cct aca cag gca cct aca cac ctc agc 337
Lys Ile Ile Thr Gly Leu His Pro Thr Gln Ala Pro Thr His Leu Ser
      100          105          110
gtt gat ata aaa ttc aag act gaa gga tta tgt gtt gac ata cca ggc 385
Val Asp Ile Lys Phe Lys Thr Glu Gly Leu Cys Val Asp Ile Pro Gly
      115          120          125
ata cca aag gac atg acc tac cgt aga ctc atc tct atg atg ggt ttc 433
Ile Pro Lys Asp Met Thr Tyr Arg Arg Leu Ile Ser Met Met Gly Phe
      130          135          140
aaa atg aat tac caa gtc aat ggt tac cct aat atg ttt atc acc cgc 481
Lys Met Asn Tyr Gln Val Asn Gly Tyr Pro Asn Met Phe Ile Thr Arg
      145          150          155          160
gaa gaa gct att cgt cac gtt cgt gcg tgg att ggc ttt gat gta gag 529
Glu Glu Ala Ile Arg His Val Arg Ala Trp Ile Gly Phe Asp Val Glu
      165          170          175
ggc tgt cat gca act aga gat gct gtg ggt act aac cta cct ctc cag 577
Gly Cys His Ala Thr Arg Asp Ala Val Gly Thr Asn Leu Pro Leu Gln
      180          185          190
cta gga ttt tct aca ggt gtt aac tta gta gct gta ccg act ggt tat 625
Leu Gly Phe Ser Thr Gly Val Asn Leu Val Ala Val Pro Thr Gly Tyr
      195          200          205
gtt gac act gaa aat aac cta 646
Val Asp Thr Glu Asn Asn Leu
      210          215

```

FIG. 1

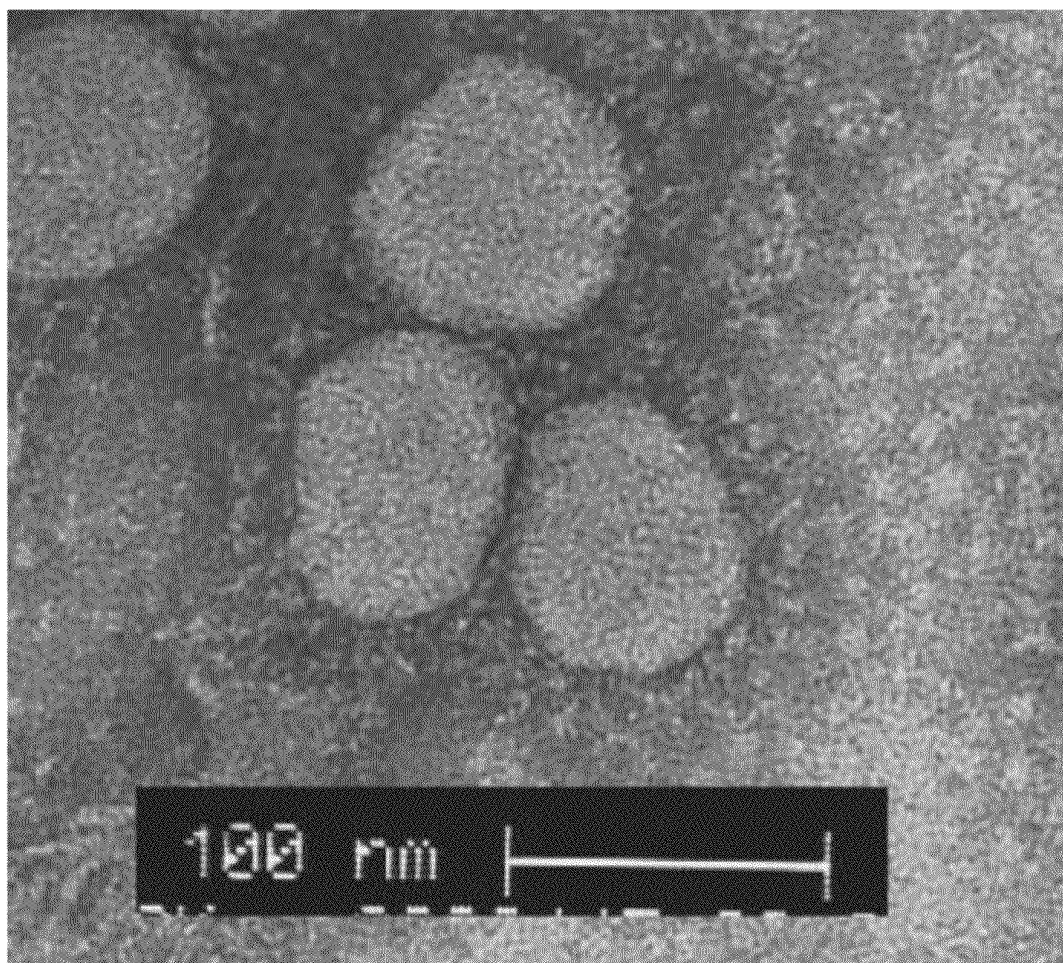


FIG. 2



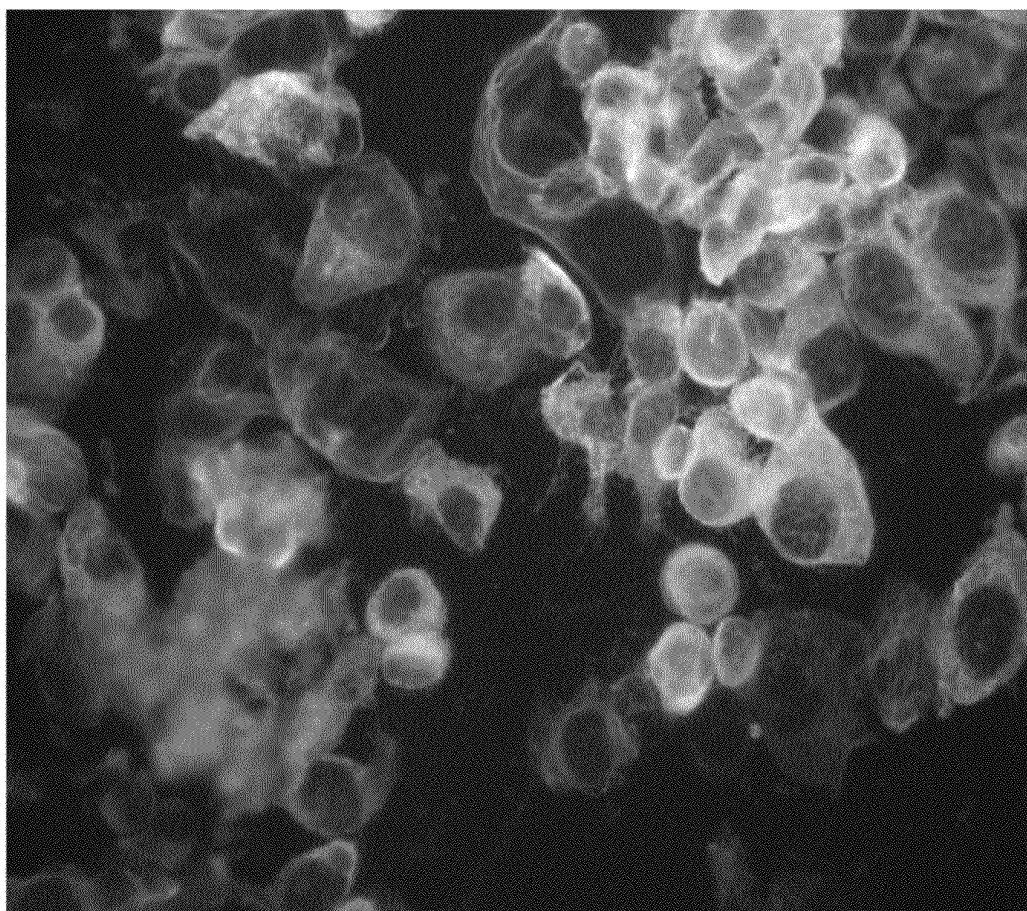
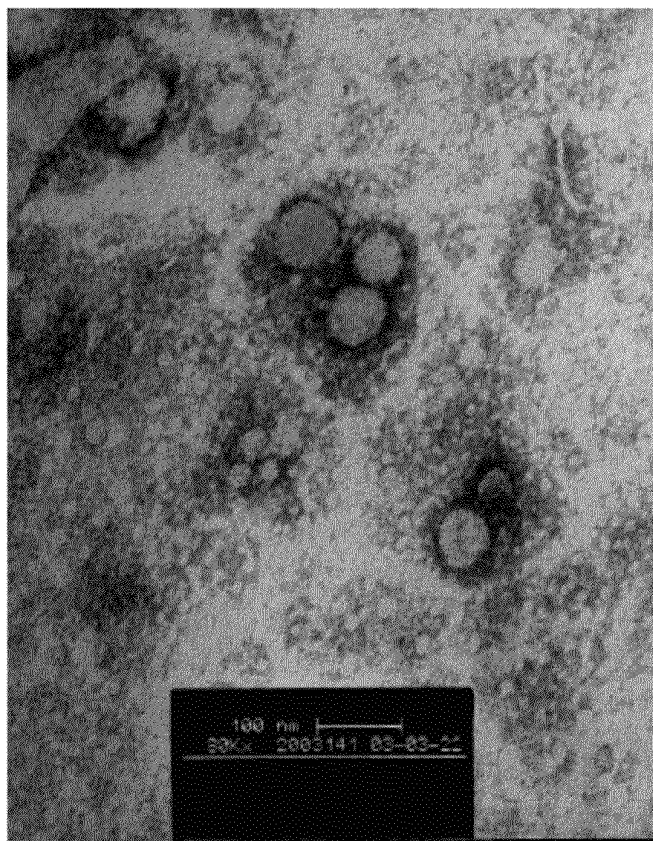
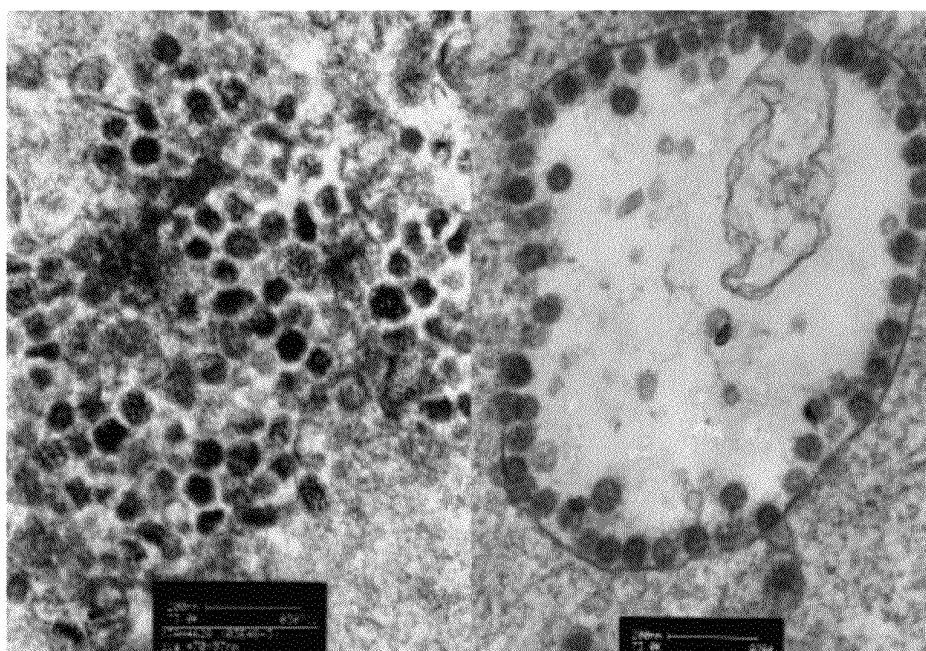


FIG. 3



**FIG. 4**



**FIG. 5A**

**FIG. 5B**

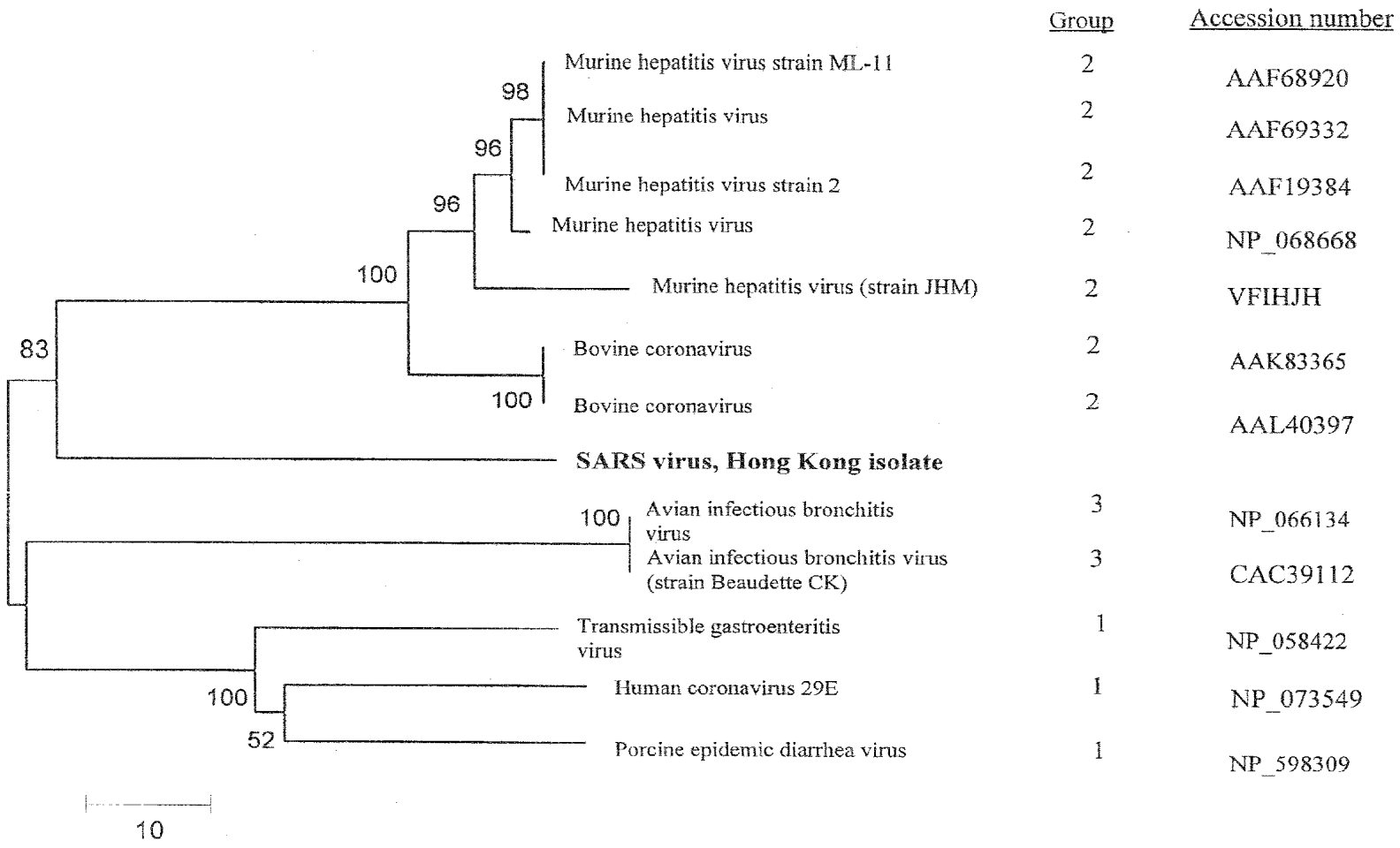


FIG. 6

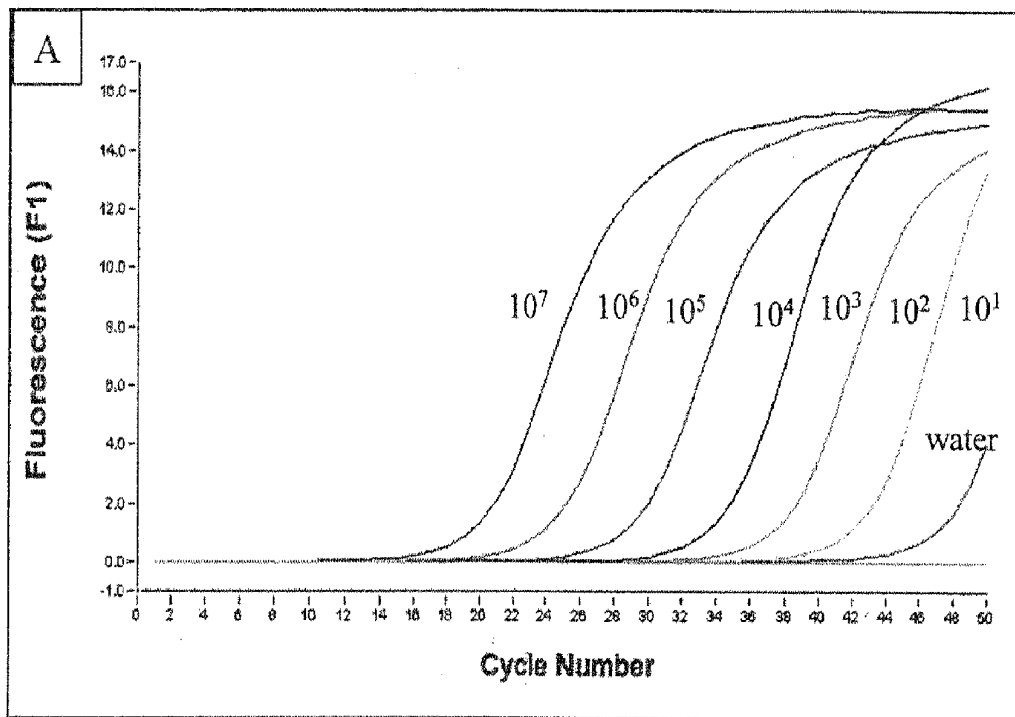


FIG. 7A

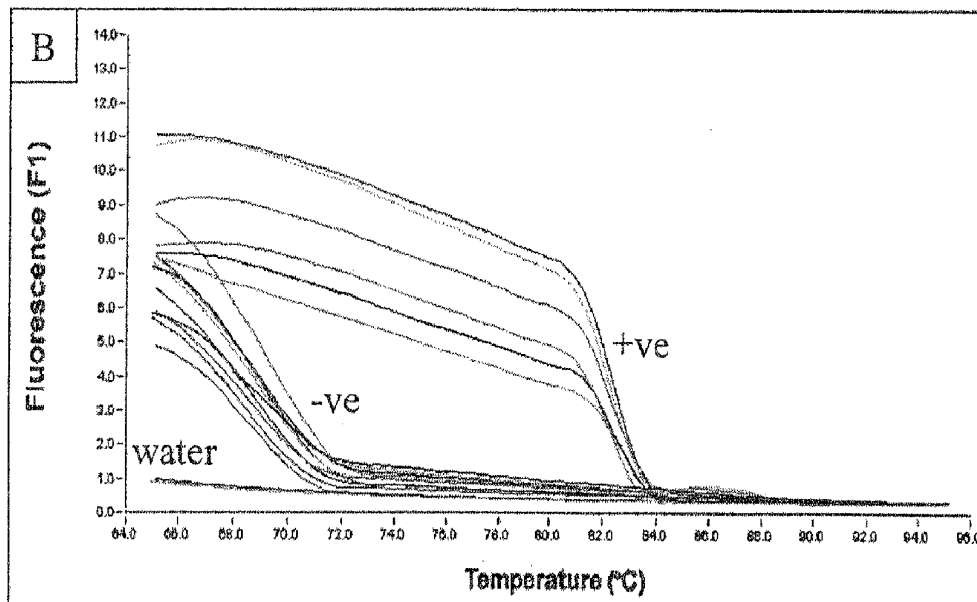


FIG. 7B

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t aaa tgt agt aga atc ata cct gcg cgt gcg cgc gta gag tgt ttt gat 49
  Lys Cys Ser Arg Ile Ile Pro Ala Arg Ala Arg Val Glu Cys Phe Asp
  1           5           10           15

aaa ttc aaa gtg aat tca aca cta gaa cag tat gtt ttc tgc act gta 97
Lys Phe Lys Val Asn Ser Thr Leu Glu Gln Tyr Val Phe Cys Thr Val
  20           25           30

aat gca ttg cca gaa aca act gct gac att gta gtc ttt gat gaa atc 145
Asn Ala Leu Pro Glu Thr Thr Ala Asp Ile Val Val Phe Asp Glu Ile
  35           40           45

tct atg gct act aat tat gac ttg agt gtt gtc aat gct aca ctt cgt 193
Ser Met Ala Thr Asn Tyr Asp Leu Ser Val Val Asn Ala Arg Leu Arg
  50           55           60

gca aaa cac tac gtc tat att ggc gat cct gct caa tta cca gcc ccc 241
Ala Lys His Tyr Val Tyr Ile Gly Asp Pro Ala Gln Leu Pro Ala Pro
  65           70           75           80

cgc aca ttg ctg act aaa ggc aca cta gaa cca gaa tat ttt aat tca 289
Arg Thr Leu Leu Thr Lys Gly Thr Leu Glu Pro Glu Tyr Phe Asn Ser
  85           90           95

gtg tgc aga ctt atg aaa aca ata ggt cca gac atg ttc ctt gga act 337
Val Cys Arg Leu Met Lys Thr Ile Gly Pro Asp Met Phe Leu Gly Thr
  100          105          110

tgt cgc cgt tgt cct gct gaa att gtt gac act gtg agt gct tta gtt 385
Cys Arg Arg Cys Pro Ala Glu Ile Val Asp Thr Val Ser Ala Leu Val
  115          120          125

tat gac aat aag cta aaa gca cac aag gag aag tca gct caa tgc ttc 433
Tyr Asp Asn Lys Leu Lys Ala His Lys Glu Lys Ser Ala Gln Cys Phe
  130          135          140

aaa atg ttc tac aaa ggt gtt att aca cat gal gtt tca tct gca atc 481
Lys Met Phe Tyr Lys Gly Val Ile Thr His Asp Val Ser Ser Ala Ile
  145          150          155          160

aac aga cct caa ata ggc gtt gta aga gaa ttt ctt aca cgc aat cct 529
Asn Arg Pro Gln Ile Gly Val Val Arg Glu Phe Leu Thr Arg Asn Pro
  165          170          175

gct tgg aga aaa gct gtt ttt atc tca cct tat aat tca cag aac gct 577
Ala Trp Arg Lys Ala Val Phe Ile Ser Pro Tyr Asn Ser Gln Asn Ala
  180          185          190

gta gct tca aaa atc tta gga ttg cct acg cag act gtt gat tca tca 625
Val Ala Ser Lys Ile Leu Gly Leu Pro Thr Gln Thr Val Asp Ser Ser
  195          200          205

cag ggt tct gaa tat gac tat gtc ata ttc aca caa act act gaa aca 673
Gln Gly Ser Glu Tyr Asp Tyr Val Ile Phe Thr Gln Thr Thr Glu Thr
  210          215          220

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FIG. 8



c aga acc atg cct aac atg ctt agg ata atg gcc tct ctt gtt ctt gct 49  
Arg Thr Met Pro Asn Met Leu Arg Ile Met Ala Ser Leu Val Leu Ala  
1 5 10 15  
  
cgc aaa cat aac act tgc tgt aac tta tca cac cgt ttc tac agg tta 97  
Arg Lys His Asn Thr Cys Cys Asn Leu Ser His Arg Phe Tyr Arg Leu  
20 25 30  
  
gct aac gag tgt gcg caa gta tta agt gag atg gtc atg tgt ggc ggc 145  
Ala Asn Glu Cys Ala Gln Val Leu Ser Glu Met Val Met Cys Gly Gly  
35 40 45  
  
tca cta tat gtt aaa cca ggt gga aca tca tcc ggt gat gct aca act 193  
Ser Leu Tyr Val Lys Pro Gly Gly Thr Ser Ser Gly Asp Ala Thr Thr  
50 55 60  
  
gct tat gct aat agt gtc ttt aac att tgt caa gct gtt aca gcc aat 241  
Ala Tyr Ala Asn Ser Val Phe Asn Ile Cys Gln Ala Val Thr Ala Asn  
65 70 75 80  
  
gta aat gca ctt ctt tca act gat ggt aat aag ata gct gac aag tat 289  
Val Asn Ala Leu Leu Ser Thr Asp Gly Asn Lys Ile Ala Asp Lys Tyr  
85 90 95  
  
gtc cgc aat cta caa cac agg ctc tat gag tgt ctc tat aga aat agg 337  
Val Arg Asn Leu Gln His Arg Leu Tyr Glu Cys Leu Tyr Arg Asn Arg  
100 105 110  
  
gat gtt gat cat gaa ttc gtg gat gag ttt tac gct tac ctg cgt aaa 385  
Asp Val Asp His Glu Phe Val Asp Glu Phe Tyr Ala Tyr Leu Arg Lys  
115 120 125  
  
cat ttc tcc atg atg att ctt tct gat gat gcc gtt gtg tgc tat aac 433  
His Phe Ser Met Met Ile Leu Ser Asp Asp Ala Val Val Cys Tyr Asn  
130 135 140  
  
agt aac tat gcg gct caa ggt tta gta gct agc att aag aac ttt aag 481  
Ser Asn Tyr Ala Ala Gln Gly Leu Val Ala Ser Ile Lys Asn Phe Lys  
145 150 155 160  
  
gca gtt ctt tat tat caa aat aat gtg ttc atg tct gag gca aaa tgt 529  
Ala Val Leu Tyr Tyr Gln Asn Asn Val Phe Met Ser Glu Ala Lys Cys  
165 170 175  
  
tgg act gag act gac ctt act aaa gga cct cac gaa ttt tgc tca cag 577  
Trp Thr Glu Thr Asp Leu Thr Lys Gly Pro His Glu Phe Cys Ser Gln  
180 185 190  
  
cat aca atg cta gtt aaa caa gga gat gat tac gtg tac ctg cct tac 625  
His Thr Met Leu Val Lys Gln Gly Asp Asp Tyr Val Tyr Leu Pro Tyr  
195 200 205  
  
cca gat cca tca aga ata tta ggc gca ggc tgt ttt gtc gat gat att 673  
Pro Asp Pro Ser Arg Ile Leu Gly Ala Gly Cys Phe Val Asp Asp Ile  
210 215 220  
  
gtc aaa cag atg gta cac tta tga ttg aaa ggt tcc gtg tca ctg gct 721  
Val Lys Gln Met Val His Leu  
225 230  
  
att gat gc 729

FIG. 9

1 atattagggt tttacctacc caggaaaagc caaccaacct cgatctcttg tagatctggt  
61 ctctaaacga actttaaaat ctgtgtagct gtogetcggc tgcattgcta gtgcacctac  
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481 cgttctgatg ccttaagcac caatcacggc cacaaggctg ttgagctggt tgcagaaatg  
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2761 gaagtccaag gttacaagaa tgtgagaatc acatttgagc ttgatgaacg tgttgacaaa  
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3001 ggtgaagaaa acttttctac acgtatgtat tgttctttt accctccaga tgaggaagaa  
3061 gaggacgatg cagagtgtga ggaagaagaa attgatgaaa cctgtgaaca tgagtacggt  
3121 acagaggatg attatcaagg tctcctctcg gaatttgggt cctcagctga acagttctga  
3181 cttgaggaag aagaagagga agactggctg gatgacta ctgagcaatc agagttagg  
3241 ccagaaccag aaactacacc tgaagaacca gttaatcagt ttactgggta tttaaaactt  
3301 actgacaatg ttgccattaa atgtgttgac atcgttaagg aggcacaaag tgctaactct

FIG. 10



3361 atgggtgattg taaatgctgc taacatacac ctgaaacatg gtggtggtgt agcagggtgca  
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 3661 ggtgctaaac cacttcagtc tttacaagtg tgcgtgcaga cggttcgtac acaggtttat  
 3721 attgcagtca atgacaaagc tctttatgag caggttgtca tggattatct tgataacctg  
 3781 aagcctagag tggaaagacc taacaagag gagccacca acacagaaga tccaaaact  
 3841 gaggagaaat ctgtogtaca gaagcctgtc gatgtgaagc caaaaattaa ggctgcatt  
 3901 gatgaggtta ccacaacact ggaagaaact aagtttctta ccaataagt actcttgttt  
 3961 gctgatataca atggtaagct ttaccatgat tctcagaaca tgccttagagg tgaagatatg  
 4021 tctttccttg agaaggatgc accttaccatg gtaggtgatg ttatcactag tggtgatatac  
 4081 acttgtgttg taataccctc caaaaaggct ggtggcacta ctgagatgct ctcaagagct  
 4141 ttgaagaaag tgcaggttga tgagtatata accacgtacc ctggacaagg atgtgctggt  
 4201 tatacacttg aggaagctaa gactgctctt aagaaatgca aatctgcatt ttatgtacta  
 4261 ccttcagaag cacctaagtc taaggaagag attctaggaa ctgtatcctg gaatttgaga  
 4321 gaaatgcttg ctcatgctga agagacaaga aaattaatgc ctatatgcat ggatgttga  
 4381 gccataatgg caaccatcca acgtaagtat aaaggaatta aaattcaaga gggcatcgtt  
 4441 gactatgggtg tccgattcct cttttatact agtaaagagc ctgtagcttc tattattacg  
 4501 aagctgaact ctctaaatga gccgcttgtc acaatgccaa ttggttatgt gacacatggt  
 4561 tttaatcttg aagaggtgc gcgctgtatg cgttctctta aagctcctgc cgtagtgtca  
 4621 gtatcatcac cagatgctgt tactacatat aatggatacc tcacttcgtc atcaaagaca  
 4681 tctgaggagc actttgtaga aacagttctt ttggctggct cttacagaga ttggctctat  
 4741 tcaggacagc gtacagagtt aggtgttga tttcttaagc gtggtgacaa aattgtgtac  
 4801 cacactctgg agagccccgt cgagtttcat cttgacggtg aggttcttct acttgacaaa  
 4861 ctaaagagtc tcttatccct gcgggaggtt aagactataa aagtgttcc aactgtggac  
 4921 aacactaatc tccacacaca gcttgtggat atgtctatga catatggaca gcagtttgg  
 4981 ccaacatact tggatggtgc tgatgttaca aaaattaaac ctcatgtaaa tcatgagggt  
 5041 aagactttct ttgtactacc tagtgatgac acactacgta gtgaagcttt cgagtactac  
 5101 catactcttg atgagagttt tcttggtagg tacatgtctg ctttaaacca cacaagaaa  
 5161 tggaaatttc ctcaagttgg tggtttaact tcaattaaat gggctgataa caattgttat  
 5221 ttgtctagtg ttttattagc acttcaacag cttgaagtca aattcaatgc accagcactt  
 5281 caagagctt attatagagc ccgtgctggt gatgctgcta acttttgtgc actcatactc  
 5341 gcttacagta ataaaaactgt tggcgagctt ggtgatgtca gagaaactat gacctctt  
 5401 ctacagcatg ctaatttggg atctgcaaaag cgagttctta atgtgggtg ataaacattgt  
 5461 ggtcagaaaa ctactacctt aacgggtgta gaagctgtga tgtatatgg tactctatct  
 5521 tatgataatc ttaagacagg tgttccatt ccatgtgtgt gtggctgtga tgetacacaa  
 5581 tatctagtac aacaagagtc ttcttttgtt atgatgtctg caccacctgc tgagtataaa  
 5641 ttacagcaag gtacattctt atgtgcgaat gagtacactg gtaactatca gtgtggctcat  
 5701 tacactcata taactgctaa ggagaccctc tatcgtattg acggagctca ccttacaag  
 5761 atgtcagagt acaaaggacc agtgactgat gtttctaca aggaaacatc ttacactaca  
 5821 accatcaagc ctgtgtcgtg taaactcgat ggagttactt acacagagat tgaacaaaa  
 5881 ttggatgggt attataaaaa ggataatgct tactatacag agcagcctat agaccttga  
 5941 ccaactcaac cattaccaa tgcgagtttt gataatttca aactcacatg ttctaacaca  
 6001 aaatttctg atgattttaa tcaaatgaca ggcttcacaa agccagcttc accagagcta  
 6061 tctgtcacat tcttcccaga cttgaatggc gatgtagtgg ctattgacta taacactat  
 6121 tcagcgagtt tcaagaaagg tgctaaatta ctgcataagc caattgtttg gcacattaac  
 6181 caggctacaa ccaagacaac gttcaaacca aacacttgggt gtttacgttg tcttggagt  
 6241 acaaagccag tagatacttc aaattcattt gaagttctgg cagtagaaga cacacaagga  
 6301 atggacaatc ttgcttgtga aagtcaacaa cccacctctg aagaagtagt ggaaaatct  
 6361 accatacaga aggaagtc atagagtgac gtgaaaacta ccgaagtgt agggatgtc  
 6421 atacttaaac catcagatga aggtgtttaa gtaacacaag agtttagtca tgaggactct  
 6481 atggctgctt atgtgaaaa cacaagcatt accattaaga aacctaatga gctttacta  
 6541 gccttaggtt taaaaacaat tgccactcat ggtattgctg caattaatag gtttcttgg  
 6601 agtaaaattt tggcttatgt caaaccttc ttaggacaag cagcaattac aacatcaaat  
 6661 tgcgctaaga gattagcaca acgtgtgttt aacaattata tgccttatgt gtttacatta

FIG. 10 Con't

6721 ttgttccaat tgtgtacttt tactaaaagt accaattcta gaattagage ttcactacct  
6781 acaactattg ctaaaaatag tgtaagagt gttgctaaat tatgtttggg tgccggcatt  
6841 aattatgtga agtcacccaa attttctaaa ttgttcacaa tcgctatgtg gctattgttg  
6901 ttaagtatth gcttaggttc tctaactctgt gtaactgctg cttttggtgt acttattatc  
6961 aattttggtg ctoccttctta ttgtaatggc gttagagaat tgtatcttaa ttcgtctaac  
7021 gttactacta tggatttctg tgaaggttct tttccttgca gcatttgttt aagtggatta  
7081 gactcccttg attcttatcc agctcttgaa accattcagg tgaagatttc atcgtacaag  
7141 ctagacttga caatttttagg tctggccgct gagtgggttt tggcatatat gttgttcaca  
7201 aaattctttt atttattagg tctttcagct ataatgcagg tgttctttgg ctattttgct  
7261 agtcatttca tcagcaattc ttggctcatg tggtttatca ttagtattgt acaaatggca  
7321 ccogtttctg caatggttag gatgtacatc tcttttgctt ctttctacta catatggaag  
7381 agctatgttc atatcatgga tggttgcacc tcttcgactt gcatgatgtg ctataagcgc  
7441 aatcgtgcca cacgcgttga gtgtacaact attgttaatg gcatgaagag atctttctat  
7501 gtctatgcaa atggaggcog tggcttctgc aagactcaca attggaattg tctcaattgt  
7561 gacacatttt gcactggtag tacattcatt agtgatgaag ttgctcgtga tttgtcactc  
7621 cagtttaaaa gaccaatcaa ccctactgac cagtcacgt atattgttga tagtggtgct  
7681 gtgaaaaatg gcgcgcttca cctctacttt gacaaggctg gtcaaaagac ctatgagaga  
7741 catocgctct cccattttgt caatttagac aatttgagag ctaacaacac taaaggttca  
7801 ctgocatta atgtcatagt ttttgatggc aagtcacaaat gogacgagtc tgccttaag  
7861 tctgcttctg tgtactacag tcagctgatg tgccaacctt ttctgttctg tgaccaagct  
7921 cttgtatcaa acgttggaga tagtactgaa gtttccgtta agatgtttga tgcctatgtc  
7981 gacacctttt cagcaacttt tagtgttcct atggaaaaac ttaaggcact tgttgctaca  
8041 gctcacagcg agttagcaaa ggggtgtagt tttagatggg tctttctac attcgtgtca  
8101 gctgcccagc aagggtgtgt tgataccgat gttgacacaa aggatgttat tgaatgtctc  
8161 aaactttcac atcaactctga cttagaagtg acaggtgaca gttgtaacaa tttcatgctc  
8221 acctataata aggttgaaaa catgacgccc agagatcttg gogcatgtat tgactgtaat  
8281 gcaaggcata tcaatgccc agtagcaaaa agtcacaatg tttcaactcat ctggaatgta  
8341 aaagactaca tgtctttatc tgaacagctg cgtaaacaaa ttogtactgc tgccaagaag  
8401 aacaacatac cttttacact aacttgtgct acaactagac aggttgtcaa tgcataact  
8461 actaaaatct cactcaaggg tggtaagatt gttagtactt gttttaaact tatgcttaag  
8521 gccacattat tgtgogttct tgcctgattg gtttgttata tcgttatgcc agtacatata  
8581 ttgtcaatcc atgatggtta cacaaatgaa atcattggtt acaaagccat tcaggatggt  
8641 gtcactcgtg acatcatttc tactgatgat tggtttgcaa ataaacatgc tggttttgac  
8701 gcatggttta gccagcgtgg tggttcatac aaaaatgaca aaagctgccc tgtagtactc  
8761 gctatcatta caagagagat tggtttcata gtgctggtt taccgggtac tgtgtgaga  
8821 gcaatcaatg gtgacttctt gcattttcta cctcgtggtt ttagtgtctg tggcaacatt  
8881 tgctacacac cttccaaact cattgagtat agtgattttg ctacctctgc tttgttctt  
8941 gctgctgagt gtacaatttt taaggatgct atgggcaaac ctgtgccata ttgttatgac  
9001 actaatttgc tagagggttc tttttcttat agtgagcttc gtccagacac tcgttatgtg  
9061 cttatggatg gttccatcat acagtttcct aacacttacc tggagggttc tgttagagta  
9121 gtaacaactt ttgatgctga gtaactgtaga catggtacat gcgaaaggtc agaagtaggt  
9181 atttgcctat ctaccagtgg tagatgggtt ctttaataatg agcattacag agctctatca  
9241 ggagtthctt gtgggtgttga tgcgatgaat ctcatagcta acatctttac tctcttctg  
9301 caacctgtgg gtgctttaga tgtgtctgct tcagtagtgg ctgggtggtat tattgccata  
9361 ttggtgactt gtgctgccta ctactttatg aaattcagac gtgtttttgg tgagtacaac  
9421 catgttgttg ctgctaatgc acttttgttt ttgatgtott tcaactatact ctgtctggtta  
9481 ccagcttaca gctttctgcc gggagctctac tcagcttttt acttgtactt gacattctat  
9541 ttcaccaatg atgtttcatt cttggctcac cttcaatggt ttgccatggt ttctctatt  
9601 gtgccttttt ggataacagc aatctatgta ttctgtattt ctctgaagca ctgccattgg  
9661 ttctttaaca actatcttag gaaaagagtc atgtttaatg gagttacatt tagtaacctc  
9721 gaggaggtct ctttgtgtac ctttttgcct aacaaggaaa tgtacctaaa attgogtagc  
9781 gagacactgt tgccacttac acagtataac aggtatcttg ctctatataa caagtacaag  
9841 tatttcagtg gagcctttaga tactaccage tctcgtgaag cagcttctct ccacttagca  
9901 aaggctctaa atgactttag caactcaggt gctgatgttc tctaccaacc accacagaca  
9961 tcaatcaact ctgctgttct gcagagtggg tttaggaaaa tggcattccc gtcaggcaaa  
10021 gttgaagggt gcatgttaca agtaacctgt ggaactacaa ctcttaattg attgtggttg

FIG. 10 Con't

10081 gatgacacag tatactgtcc aagacatgtc atttgcacag cagaagacat gcttaatcct  
10141 aactatgaag atctgctcat tcgcaaatcc aaccatagct ctcttgttca ggctggcaat  
10201 gttcaacttc gtgttattgg ccattctatg caaaattgtc tgcttaggct taaagttgat  
10261 accttaacc ctaagacacc caagtataaa tttgtccgta tccaacctgg tcaaacattt  
10321 tcagttctag catgctacaa tggttcacca tctgggtgtt atcagtgtag catgagacct  
10381 aatcatacca ttaaagggtc tttccttaat ggatcatgtg gtagtgttg ttttaacatt  
10441 gattatgatt gcgtgtcttt ctgctatatg catcatatgg agcttccaac aggagtacac  
10501 gctggtaoctg acttagaagg taaattctat ggtccatttg ttgacagaca aactgcacag  
10561 gctgcaggta cagacacaac cataacatta aatgttttgg catggctgta tgctgtgtt  
10621 atcaatgggtg ataggtggtt tcttaataga ttcaccacta ctttgaatga ctttaacctt  
10681 gtggcaatga agtacaacta tgaacctttg acacaagatc atgttgacat attgggacct  
10741 ctttctgctc aaacaggaat tgcogtctta gatatgtgtg ctgctttgaa agagctgtg  
10801 cagaatggta tgaatggctg tactatcctt ggtagcacta ttttagaaga tgagttaca  
10861 ccatttgatg ttgttagaca atgctctggt gttaccttc aaggttaagt caagaaatt  
10921 gtaagggca ctcactattg gatgctttta actttcttga catcactatt gattcttgtt  
10981 caagtacac agtggctact gttttcttt gtttacgaga atgctttctt gccatttact  
11041 cttggtatta tggcaattgc tgcctgtgct atgctgcttg ttaagcataa gcacgcattc  
11101 ttgtgcttgt ttctgttacc ttctcttgca acagttgctt actttaatat ggtctacatg  
11161 cctgctagct ggtgatgctg tatcatgaca tggcttgaat tggctgacac tagcttgcct  
11221 ggcttataggc ttaaggattg tgttatgtat gcttcagctt tagttttgct tattctcatg  
11281 acagctcgca ctgtttatga tgatgctgct agacgtgttt ggacactgat gaatgtcatt  
11341 acacttgttt acaaaglcta ctatggtaat gctttagalc aagctalttc catgtgggce  
11401 ttagttatct ctgtaacctc taactattct ggtgtcgtta cgactatcat gtttttagct  
11461 agagctatag tgtttgtgtg tgttgagtat taccattgtt tatttattac tggcaacacc  
11521 ttacagtgta tcatgcttgt ttattgtttc ttagctattt gttgctgctg ctactttggc  
11581 cttttctgct tactcaaccg ttaactcagg ctactcttg gtgtttatga ctacttggc  
11641 tctacacaag aatttaggta tatgaactcc caggggcttt tgccctctaa gagtagtatt  
11701 gatgctttca agcttaacat taagttggtt ggtattggag gtaaacatg tatcaaggct  
11761 gctactgtac agtctaaaat gctgacgta aagtgcacat ctgtggtaact gctctcggtt  
11821 cttcaacaac ttagagttaga gctcatctct aaattgtggg cacaatgtgt acaactccac  
11881 aatgatattc ttcttgcaaa agacacaact gaagctttcg agaagatggt ttctctttt  
11941 tctgttttgc tatccatgca ggtgctgta gacattaata ggtgtgcca ggaaatgctc  
12001 gataacctg ctactcttca ggcctatgct tcagaattta gttctttacc atcatatgcc  
12061 gcttatgcca ctgcccagga ggctatgag caggctgtag ctaatggtga ttctgaagtc  
12121 gttctcaaaa agttaaagaa atctttgaat gtggctaaat ctgagtttga ccgtgatgct  
12181 gccatgcaac gcaagttgga aaagatggca gatcaggcta tgacccaaat gtacaacag  
12241 gcaagatctg aggacaagag ggcaaaagta actagtgcta tgcaaacaaat gctcttcaact  
12301 atgcttagga agcttgataa tgatgcactt aacaacatta tcaacaatgc gcgtgatggt  
12361 tgtgttccac tcaacatcat accattgact acagcagcca aactcatggt tgttgcctc  
12421 gattatggta cctacaagaa cacttgtgat ggtaaacact ttacatagc atctgcactc  
12481 tgggaaatcc agcaagttgt tgatgoggat agcaagattg tcaacttag tgaaattaac  
12541 atggacaatt caccaaatth ggcttggcct ctattgttga cagctctaag agccaactca  
12601 gctgttaaac tacagaataa tgaactgagt ccagtagcac tacgacagat gtctgtgctg  
12661 gctggtacca cacaaacagc ttgtactgat gacaatgcac ttgctacta taacaattcg  
12721 aagggaggta ggtttgtgct ggcattacta tcagaccacc aagatctcaa atgggctaga  
12781 ttccctaaga gtgatggtag aggtacaatt tacacagaac tggaaaccac ttgtaggttt  
12841 gttacagaca caccaaaagg gctaaaagt aaactactgt acttcatcaa aggttaaac  
12901 aacctaaata gaggtatggt gctgggcagt ttagctgcta cagtaactct caggttga  
12961 aatgctacag aagtacotgc caattcaact gtgctttctc tctgtgcttt tgcaagtagc  
13021 cctgctaaag catataagga ttacctagca agtggaggac aaccaatcac caactgtgtg  
13081 aagatgttgt gtacacacac tggtagagga caggcaatta ctgtaacacc agaagctaac  
13141 atggaccaag agtcttttgg tggctgttca tgttgtctgt attgtagatg ccacattgac  
13201 catccaaatc ctaaaggatt ctgtgacttg aaaggtaagt acgtocaaat acctaccact  
13261 tgtgctaag acccagtggg ttttacactt agaaacacag tctgtaccgt ctgoggatg  
13321 tggaaagggt atggctgtag ttgtgaccaa ctccgcgaac ccttgatgca gtctgoggat  
13381 gcatcaacgt ttttaaacgg gtttgcgggt taagtgcagc ccgtcttaca ccgtgoggca

FIG. 10 Con't

13441 caggcactag tactgatgtc gtctacaggg cttttgatat ttacaacgaa aaaagtgotg  
13501 gttttgcaaa gttoctaaaa actaattgct gtcgottcca ggagaaggat gaggaaggca  
13561 atttattaga ctottacttt gtagttaaga ggcatactat gtctaactac caacatgaag  
13621 agactattta taacttgggt aaagattgct cagcgggtgc tgtccatgac tttttcaagt  
13681 ttagagtaga tggtgacatg gtaccacata taccacgtca gogtctaact aaatacacia  
13741 tggctgattt agtctatgct ctacgtcatt ttgatgaggg taattgtgat acattaaaag  
13801 aaatactcgt cacatacaat tgctgtgatg atgattatth caataagaag gattgggatg  
13861 acttcgtaga gaatcctgac atcttacgog tatatgctaa cttagggtgag cgtgtacgcc  
13921 aatcattatt aaagactgta caattctgog atgctatgog tgatgcaggo attgtaggog  
13981 tactgacatt agataatcag gatcttaatg ggaactggta cgattctoggt gatttcgtac  
14041 aagtagcacc aggctgogga gttcctattg tggattcata ttaactcattg ctgatgccca  
14101 tctcactttt gactagggca ttggctgctg agtcccataat ggatgctgat ctgcataaac  
14161 cacttattaa gtgggatttg ctgaaatatg attttacgga agagagactt tgtctcttcg  
14221 acogttatth taaatattgg gaccagacat accatcccaa ttgtattaac tgtttggatg  
14281 atagggtgat ctttcattgt gcaaacctta atgtgttatt ttctactgtg ttccacctta  
14341 caagttttgg accactagta agaaaaatat ttgtagatgg tgttcctttt gttgtttcaa  
14401 ctggatacca ttttcgtgag ttaggagctg tacataatca ggatgtaaac ttacatagct  
14461 cgcgtctcag tttcaaggaa ctttttagtgt atgctgctga tccagctatg catgcaagct  
14521 ctggcaattt attgctagat aaaogcacta catgcttttc agtagctgca ctaaacaaaca  
14581 atgttgcttt tcaaacgtc aaaccoggtta attttaataa agacttttat gactttgctg  
14641 tgtctaaagg tttctttaag gaaggaaagt ctgttgaact aaaacacttc tttttgctc  
14701 aggatggcaa cgtgctatc agtgattatg actattatcg ttataatctg ccaacaatgt  
14761 gtgatatcag acaactccta ttctgtagttg aagttgttga taaatacttc gattgttacg  
14821 atgggtggctg tattaatgcc aaccaagtaa tctgtaacaa tctggataaa tcagctgggt  
14881 tcccatttaa taaatggggg aaggctagac tttattatga ctcaatgag tatgaggatc  
14941 aagatgcact tttcgcgtat actaagcgtat atgtcatccc tactataact caaatgaatc  
15001 ttaagtatgc cattagtgca aagaatagag ctgcaccogt agctgggtgc tctatctgta  
15061 gtactatgac aaatagacag tttcatcaga aattattgaa gtcaatagcc gccactagag  
15121 gagctactgt ggttaattgga acaagcaagt tttacgggtg ctggcataat atgttaaaaa  
15181 ctgtttacag tgatgtagaa actccacacc ttatgggttg ggattatcca aaatgtgaca  
15241 gagccatgcc taacatgctt aggataattg cctctcttgt tcttgctcgc aaacataaca  
15301 cttgctgtaa cttatcacac ggtttctaca aggttagctaa cgagtgtgog caagtattaa  
15361 gttgagatgt catgtgtggc ggtcactat atgttaaac aggtggaaca tcatccgggtg  
15421 atgctacaac tgcttatgct aatagtgtct ttaacatttg tcaagctggt acagccaatg  
15481 taaatgcact tttttcaact gatggtaata agatagctga caagtatgct cgcaatctac  
15541 aacacaggct ctatgagtgt ctctatagaa atagggatgt tgatcatgaa ttctggtgatg  
15601 agttttacgc ttacctgctt aaacatttct ccatgatgat tctttctgat gatgocgttg  
15661 tgtgctataa cagtaactat gggctcaag gtttagtagc tagcattaag aactttaagg  
15721 cagttcttta ttatcaaaat aatgtgttca tgtctgaggc aaaatgttg actgagactg  
15781 accttactaa aggacctcac gaattttgct cacagcatab aatgctagtt aaacaaggag  
15841 atgattacgt gtacctgctt taccagatc catcaagaat attaggcgca ggctgttttg  
15901 tggatgatat tgtcaaaaa gatggtacac ttatgattga aaggttcgtg tcaactggcta  
15961 ttgatgctta cccacttaca aaacatccta atcaggagta tgotgatgct tttcacttgt  
16021 atttacaata cattagaaag ttacatgatg agcttactgg ccacatggtg gacatgtatt  
16081 ccgtaatgct aactaatgat aacacctcac ggtactggga acctgagttt tatgaggcta  
16141 tgtacacacc acatacagtc ttgcaggctg taggtgcttg tgtattgtgc aattcacaga  
16201 cttcacttcg ttgcgggtcc tgtattagga gaccattcct atgttgcaag tgotgctatg  
16261 accatgctat ttcaacatca cacaaattag tgttgtctgt taatccctat gtttgcaatg  
16321 ccccaggttg tgatgtcact gatgtgacac aactgtatct agggaggtatg agctattatt  
16381 gcaagtcaca taagcctccc attagtttct cattatgtgc taatggtcag gttttgggt  
16441 tatacaaaaa cacatgtgta ggcagtgaca atgtcactga cttcaatgog atagcaacat  
16501 gtgattggac taatgctggc gattacatac ttgccaacac ttgtactgag agactcaagc  
16561 ttttcgcagc agaaacgctc aaagccactg aggaacatt taagctgtca tatgggtattg  
16621 ccactgtacg cgaagtactc tctgacagag aattgcatct ttcattgggag gttggaaaac  
16681 ctgaccacc attgaaacaga aactatgtct ttactggtta ccgtgtaact aaaaaatgta  
16741 aagtacagat tggagagtac acctttgaaa aaggtgacta tgggtgatgct gttgtgtaca

FIG. 10 Con't

16801 gaggtactac gacatacaag ttgaatggtg gtgattactt tgtgttgaca tctcactctg  
16861 taatgccaact tagtgccaact actctagtgc cacaagagca ctatgtgaga attactggct  
16921 tgtacccaac aotcaacatc tcagatgagt tttctagcaa tgttgcaaat tatcaaaagg  
16981 toggcacgca aaagtactct acactccaag gaccacctgg tactggtaag agtcattttg  
17041 ccactggact tgcctctctat taccatctctg ctgcgcatagt gtatacggca tgcctctctg  
17101 cagctggttg tgcctctctat gaaaaggcat taaaatattt gcccatagat aaatgtagta  
17161 gaatcatacc tgcgctgtgc cgcgtagagt gttttgataa attcaaaagt aattcaaac  
17221 tagaacagta tgttttctgc actgtaaatg cattgccaga aacaactgct gacattgtag  
17281 tctttgatga aatctctatg gctactaatt atgacttgag tgttgtcaat gctagacttc  
17341 gtgcaaaaaca ctacgtctat attggcgatc ctgctcaatt accagcccc cgcacattgc  
17401 tgactaaagg cacactagaa ccagaatatt ttaattcagt gtgcgactt atgaaaacaa  
17461 taggtccaga catgttctctt ggaacttgc cgcgttctcc tgcctgaaat gttgacactg  
17521 tgagtgcctt agtttatgac aataagctaa aagcacacaa ggataagtca gctcaatgct  
17581 tcaaaatggt ctacaaagggt gttattacac atgatgttcc atctgcaatc aacagacctc  
17641 aaataggcgt tgtaagagaa tttcttacac gcaatcctgc ttggagaaaa getgttttta  
17701 tctcacctta taattcacag aacgctgtag cttcaaaaat cttaggattg cctaccgaga  
17761 ctgttgattc atcacagggt tctgaatag actatgtcat attcacacaa actactgaaa  
17821 cagcacaactc ttgtaatgct aaccgcttca atgtggetat cacaagggca aaaattggca  
17881 ttttgtgcat aatgtctgat agagatcttt atgacaaact gcaatttaca agtctagaaa  
17941 taccacgtcg caatgtggct acattacaag cagaaaatgt aactggactt ttaaggact  
18001 gtagtaagat cactactggt cttcatcota cacaggcacc tacacacctc agcgttgata  
18061 taaaattcaa gactgaagga ttatgtgttg acataccagg cataccaaag gacatgacct  
18121 accgtagact catctctatg atgggttcca aaatgaatta ccaagtcaat ggttacccta  
18181 atactgtttat caccocgcaa gaagctatc gtcacgttcc tgcgtggatt ggctttgatg  
18241 tagagggctg tcatgcaact agagatgctg tgggtactaa cctacctctc cagctaggat  
18301 tttctacagg tgtaactta gtagctgtac cgcactggta tgttgacact gaaaataaca  
18361 cagaattcac cagagttaat gcaaaacctc caccaggtga ccagtttaaa catcttatc  
18421 cactcatgta taaaggcttg ccttggatg tagtgctat taagatagta caaatgctca  
18481 gtgatacaact gaaaggattg tcagacagag tgcgttctgt cctttggcgc catggctttg  
18541 agcttacatc aatgaagtac tttgtcaaga ttggacctga aagaacgtgt tgcctgtgtg  
18601 acaaactgct aacttgcctt tctacttcat cagatactta tgcctgctgg aatcattctg  
18661 tgggttttga ctatgtctat aaccatctta tgattgatgt tcagcagtgg ggccttaacg  
18721 gtaacctca gagtaacct gagcaacatt gccaggtaca tggaaatgca atgtggcta  
18781 gttgtgatgc tatcatgact agatgtttag cagtcocatga gtgctttgtt aagcgcgttg  
18841 attggtctgt tgaataacct attataggag atgaaactgag ggttaattct gcttgcaaaa  
18901 aagtacaaca catggttgtg aagtctgcat tgcctgctga taagtttcca gttctctatg  
18961 acattggaaa tccaaaggct atcaagtgtg tgcctcagge tgaagttaga tggaaagtct  
19021 acgatgctca gccatgtagt gacaaagctt acaaaataga ggaactctc tattcttatg  
19081 ctacacatca cgataaattc actgatggtg tttgtttgtt ttggaattgt aacgttgatc  
19141 gttaccacgc caatgcaatt gtgtgtaggt ttgacacaag agtctgtca aacttgaact  
19201 taccaggctg tgatgggtgt agttgtatg tgaataagca tgcattccac actccagctt  
19261 tcgataaaaag tgcatttact aatttaaagc aattgccttt cttttactat tctgatagtc  
19321 cttgtgagtc tcatggcaaa caagtatgtt cggatattga ttatgttcca ctcaaatctg  
19381 ctacgtgtat tacacgatgc aatttaggtg gtgctgtttg cagacacctt gcaaatgagt  
19441 accgacagta cttggatgca tataatatga tgatttctgc tggatttagc ctatggattt  
19501 acaaaacaatt tgatacttat aacctgtgga atacatttac caggttacag agtttagaaa  
19561 atgtggctta taatgttgtt aataaaggac actttgatgg acacgocgce gaagcactg  
19621 tttccatcat taataatgct gtttacacaa aggtagatgg tattgatgtg gagatcttg  
19681 aaaataagac aacacttctt gttaatgttg catttgagct ttgggctaag cgtaacatta  
19741 aaccagtgcc agagattaag atactcaata atttgggtgt tgatatcctt gctaaactg  
19801 taactctggga ctacaaaaga gaagcccag cacatgtatc tacaatagggt gctctcacia  
19861 tgactgacat tgccaagaaa cctactgaga gtgctgttcc ttcacttact gctctgtttg  
19921 atggtagagt ggaaggacag gtagacctt ttgaaaocgc ccgtaaatgt gtttaataaa  
19981 cagaaggctt agtcaaagggt ctaacacctt caaagggacc agcacaagct agcgtcaatg  
20041 gagtacacatt aattggagaa tcagtaaaaa cacagtttaa ctactttaag aaagtagacg  
20101 gcattattca acagttgect gaaacctact ttactcagag cagagactta gaggatttta

FIG. 10 Con't

20161 agcccagatc acaaatggaa actgactttc tccagctcgc tatggatgaa ttcatacagc  
20221 gatataaget cgagggetat gccttcgaac acatcgttta tggagatttc agtcatggac  
20281 aacttggcgg ttttcattta atgataggct tagccaagcg ctcacaagat tcaccactta  
20341 aattagagga ttttatccct atggacagca cagtgaaaaa ttacttcata acagatgcgc  
20401 aaacaggttc atcaaatgt gtgtgtctcg tgattgatct tttacttgat gactttgtcg  
20461 agataataaa gtcacaagat ttgtcagtga tttcaaaagt ggtcaaggtt acaattgaot  
20521 atgctgaaat ttcattcoatg ctttgggtga aggatggaca tgttgaaacc ttcacoccaa  
20581 aactacaagc aagtcaagcg tggcaaccag gtgttcgat gcctaacttg tacaagatgc  
20641 aaagaatgct tcttgaaaag tgtgacctc agaattatgg tgaaaatget gttataccaa  
20701 aaggaataat gatgaatgtc gcaaagtata ctcaactgtg tcaatactta aatacactta  
20761 ctttagctgt acctacaac atgagagtta ttcactttgg tgcctggctct gataaaggag  
20821 ttgcaccagg tacagctgtg ctcagacaat ggttgccaac tggcacacta cttgtcgatt  
20881 cagatcttaa tgacttcgct tccgaocgag attctacttt aattggagac tgtgcaacag  
20941 tacatacggc taataaatgg gacottatta ttagcgatat gtatgacctt aggaccaaac  
21001 atgtgacaaa agagaatgac tctaaagaag ggttlllcac ttatctgtgt ggattataaa  
21061 agcaaaaact agcctgggtt ggttctatag ctgtaaagat aacagagcat tcttggaaatg  
21121 ctgaccttta caagcttatg ggccatttct catggtggac agcttttgtt acaaatgtaa  
21181 atgcatcctc atcgggaagca tttttaattg gggctaaact tcttggcaag ccgaaggaac  
21241 aaattgatgg ctataccatg catgctaact acattttctg gaggaacaca aatcctatcc  
21301 agttgtcttc ctattcactc tttgacatga gcaaatctcc tcttaaatga agaggaactg  
21361 ctgtaatgtc tcttaaggag aatcaaatca atgatatgat ttattctctt ctggaaaaag  
21421 gtaggcttat cattagagaa aacaacagag ttgtggtttc aagtgatatt cttgttaaca  
21481 actaaacgaa catgtttatt ttcttattat ttcttactct cactagtggg agtgacctg  
21541 acoggtgcac cacttttgat gatgttcaag ctcttaatta cactcaacat acttcatctc  
21601 tgaggggggt ttactatcct gatgaaattt ttagatcaga cactctttat ttaactcagg  
21661 atttatttct tccattttat tctaattgta cagggtttca tactattaat catacgtttg  
21721 gcaacctgt catacctttt aaggatggta tttattttgc tgcocagag aaatcaaatg  
21781 ttgtccgtgg ttgggttttt ggttctacca tgaacaacaa gtcacagtcg gtgattatta  
21841 ttaacaatcc tactaatggt ttatacggag catgtaacct tgaattgtgt gacaacctt  
21901 tctttgcctg ttctaaaccc atgggtacac agacacatac tatgatattc gataatgcat  
21961 ttaattgcac tttogagtac atatctgatg ctttttcgct tgatgtttca gaaaagtcag  
22021 gtaattttta acacttacga gagtttgtgt ttaaaaataa agatgggttt ctctatggtt  
22081 ataagggcta tcaacctata gatgtagtcc gtgatctacc ttctggtttt aacactttga  
22141 aacctatttt taagttgcct cttgggtatta acattacaaa ttttagagcc attcttacag  
22201 ctttttcacc tgcctcaagac atttggggca cgtcagctgc agcctatttt gttggctatt  
22261 taaagccaac tacatttatg ctcaagtatg atgaaaatgg tacaatcaca gatgctgttg  
22321 attgtttctc aaatccactt gctgaactca aatgctctgt taagagcttt gagattgaca  
22381 aaggaattta ccagacctct aatttcaggg ttgttccctc aggagatggt gtgagattcc  
22441 ctaatattac aaacttggtt ctttttggag aggtttttta tgctactaaa ttccctctg  
22501 totatgcatg ggagagaaaa aaaatttcta attgtgttgc tgattactct gtgctctaca  
22561 actcaacatt tttttcaacc ttttaagtgt atggcgtttc tgcocactaag ttgaatgate  
22621 tttgcttctc caatgtctat gcagattcct ttgtagtcaa gggagatgat gtaagacaaa  
22681 tagcgocagg acaaaactgtt gttattgctg attataatta taaattgcca gatgatttca  
22741 tgggttgtgt ctttgcttgg aatactagga acattgatgc tacttcaact ggtaattata  
22801 attataaata taggtatctt agacatggca agcttaggcc ctttgagaga gacatatcta  
22861 atgtgccttt ctccctgatg ggcaaacctt gcaccccacc tgcctttaat tgttattggc  
22921 cattaaatga ttatggtttt tacaccacta ctggcattgg ctaccaacct tacagagttg  
22981 tagtactttc ttttgaactt ttaaatgcac cggocacggt ttgtggacca aaattatcca  
23041 ctgaccttat taagaaccag tgtgtcaatt ttaattttta tggactcact ggtactggtg  
23101 tcttaactec ttcttcaag agatttcaac catttcaaca atttggcctg gatgtttctg  
23161 atttcaactga ttccgttcga gatcctaaaa catctgaaat attagacatt tcaacttget  
23221 cttttggggg tgtaagtgtg attacacctg gaacaaatgc ttcactctgaa gttgctgttc  
23281 tatatcaaga tgttaactgc actgatgttt ctacagcaat tcatgcagat caactcaac  
23341 cagcttggcg catatattct actggaaaca atgtattcca gactcaagca ggtctgctta  
23401 taggagctga gcatgtcgac acttcttatg agtggacat tctatttggg gctggcattt  
23461 gtgotagtta ccatacagtt tctttattac gtagtactag ccaaaaatct atttgggctt

FIG. 10 Con't

23521 ataactatgtc tttagggtgct gatagttcaa ttgcttactc taataacacc attgctatac  
 23581 ctactaaactt ttcaatttagc attactacag aagtaatgcc tgtttctatg gctaaaaact  
 23641 ccgtagattg taatatgtac atctgoggag attctactga atgtgcta atgtgctctc  
 23701 aatatggtag cttttgcaca caactaaatc gtgcaactctc aggtattgct gctgaacagg  
 23761 atcgcaacac acgtgaagtg ttogtcaag tcaaacaat gtacaaaaacc ccaactttga  
 23821 aatattttgg tggttttaat tttcacaaa tattacctga ccctctaaag ccaactaaga  
 23881 ggtcttttat tgaggacttg ctctttaata aggtgacact cgtgatgcl ggcttcatga  
 23941 agcaataatgg cgaatgccta ggtgatatta atgctagaga tctcatttgt ggcgagaagt  
 24001 tcaatggact tacagtgttg ccacctctgc tcaactgatga tatgattgct gctacactg  
 24061 ctgctctagt tagtggact gccactgctg gatggacatt tgggtctggc gctgctctc  
 24121 aaataccttt tgctatgcaa atggcatata ggttcaatgg cattggagtt acccaaatg  
 24181 ttctctatga gaacaaaaa caaatgcga accaatttaa caaggogatt agtcaaatc  
 24241 aagaatcact tacaacaaca tcaactgcat tgggcaagct gcaagacgtt gtaaacaga  
 24301 atgtcacaagc attaaacaca ctgttaaac aacttagctc taattttggg gcaatttcaa  
 24361 gtgtgctaaa tgatatcctt tggcagcttg ataaagtcca ggcgagggtg caaattgaca  
 24421 ggttaattac aggcagactt caaagccttc aaacctatgt aacacaaca ctaatcaggg  
 24481 ctgctgaaat cagggtctct gctaatcttg ctgctactaa aatgtctgag tgtgtcttg  
 24541 gacaatcaaa aagagttgac tttgtggaa agggctacca ccttatgtcc tcccaacag  
 24601 cagccccgca tgggtgtgtc ttctacatg tcaogtatgt gccatcccag gagaggact  
 24661 tcaccacagc gccagcaatt tgcctgaag gcaaaagcata ctccctctgt gaaggtgttt  
 24721 ttgtgtttaa tggcacttct tggtttatta cacagaggaa ctcttttct ccacaataa  
 24781 ttactacaga caatacattt gtctcaggaa attgtgatgt cgttatggc atcattaaca  
 24841 acacagttta tgatcctctg caacctgagc ttgactcatt caaagaagag ctggacaagt  
 24901 acttcaaaaa tcatacatca ccagatgttg atcttggoga catttcaggc attaacgctt  
 24961 ctgtcgtcaa cattcaaaaa gaaattgacc gctcaatga ggtcgtaaa aatttfaatg  
 25021 aatcactcat tgaccttcaa gaattgggaa aatatgagca atatattaaa tggccttggg  
 25081 atgtttggct cggcttcatt gctggactaa ttgccatcgt catggttaca atcttgcctt  
 25141 gttgcatgac tagttgttgc agttgcctca aggtgcatg ctcttgggt tcttctgca  
 25201 agtttgatga ggatgactct gagccagttc tcaaggggtg caaattacat tacacataa  
 25261 cgaacttatg gatttgttta tgagattttt tactcttggg tcaattactg cacagccagt  
 25321 aaaaattgac aatgcttctc ctgcaagtac tgttcatgct acagcaacga taccgtaca  
 25381 agctcactc cctttcggat ggttgttat tggcgttga tttcttctg ttttccagag  
 25441 cgtaaccaaa ataattgcgc tcaataaaag atggcagcta gcccttata agggcttcca  
 25501 tttcatttgc aatttactgc tgcattttgt taccatctat tcacatctt tgccttgcg  
 25561 tgcaaggtaag gagggcgaat tttgtacct ctatgccttg atatattttc tacaatgcat  
 25621 caagcagatg agaattatta tgagatgttg gcttgttgg aagtgcaaat ccaagaacc  
 25681 attactttat gatgccaact acttgttgg ctggcacaca cataactatg actactgat  
 25741 accatataac agtgtcacag atacaattgt cgttaactgaa ggtgacggca tttcaacacc  
 25801 aaaactcaaa gaagactacc aaattgggtg ttattctgag gataggcact cagggttaa  
 25861 agactatgtc gttgtacatg gctatttccac cgaagtttac taccagcttg agtctacaca  
 25921 aactactaca gacactggta ttgaaaatgc tacattcttc atctttaaca agcttgttaa  
 25981 agaccaccag aatgtgcaaa tacacacaat cgacggctct tcaggagttg ctaatccagc  
 26041 aatggatcca atttatgatg agccgacgac gactactagc gtgcctttgt aagcacaaga  
 26101 aagtgagtac gaacttatgt actcattcgt ttoggaagaa acaggtaact taatagttaa  
 26161 tagcgtactc cttttctctg ctctcgttgg attcttctga gtcacaactg ccatccttac  
 26221 tgcgcttcca ttgtgtcgt actgctgcaa tattgttaac gtgagtttag taaaaccaac  
 26281 ggtttacgtc tactcgcgtg ttaaaaactc gaactctct gaaggagttc ctgatctct  
 26341 ggtctaaacg aactaactat tattattatt ctgtttggaa cttaacatt gcttatcatg  
 26401 gcagacaacg gtactattac cgttgaggag cttaaacacac tctggaaca atggaacct  
 26461 gtaatagggt tccatttctc agcctggatt atgttactac aatttgcta ttctaatgg  
 26521 aacagggttt tgtaacataa aaagcttgtt ttctctggc tcttggggc agtaaacctt  
 26581 gcttgttttg tcttctctg tgtctacaga attaattggg tgactggcg gattgagatt  
 26641 gcaatggctt gtattgtagg ctgatgttg cttagctact tcttctctc ctccagctg  
 26701 tttgctctga ccgctcaat gtggtcattc aaccagaaa caaacattct tctcaatgtg  
 26761 cctctccggg ggacaattgt gaccagaccg ctcatggaaa gtgaacttgt cattgggtg  
 26821 gtgatcattc gtggtcactt gogaatggc ggacaactcc tagggcctg tgacattaag

FIG. 10 Con't

26881 gacctgccaa aagagatcac tgtggctaca tcacgaacgc tttcttatta caaattagga  
26941 gcgtcgcagc gtgtaggcac tgattcaggt tttgctgcat acaaccgcta ccgtattgga  
27001 aactataaat taaatacaga ccacgcgggt agcaacgaca atattgcttt gctagtaacag  
27061 taagtgacaa cagatgtttc atcttgttga cttccaggtt acaatagcag agatattgat  
27121 tatcattatg aggactttca ggattgctat ttggaatctt gacgttataa taagttcaat  
27181 agtgagacaa ttatttaagc ctctaactaa gaagaattat tcggagttag atgatgaaga  
27241 acctatggag tttagattatc cataaaacga acatgaaaat tattctcttc ctgacattga  
27301 ttgtattttac atcttgcgag ctatatcact atcaggagtg tgtttagaggt acgactgtac  
27361 tactaaaaga accttgccca tcaggaacat acgagggcaa ttcaccattt caccctcttg  
27421 ctgacaataa atttgcaacta acctgcaacta gcacacactt tgcttttget tggctgacg  
27481 gtactcgaca tacctatcag ctgcgtgcaa gatcagtttc accaaaactt ttcacagac  
27541 aagaggaggt tcaacaagag ctctactcgc cactttttct cattgttget gctctagtat  
27601 ttttaataact ttgcttcacc attaagagaa agacagaatg aatgagctca cttaattga  
27661 cttctatttg tgctttttg cctttctgtt attccttgtt ttaataatgc ttattatatt  
27721 ttggttttca ctogaaatcc aggatctaga agaacctgt accaaagtct aacgaacat  
27781 gaaactttctc attgttttga cttgtatttc tctatgcagt tgcatatgca ctgtagtaca  
27841 gcgctgtgca tctaataaac ctcatgtgct tgaagatcct tgtaaggtaac aacactaggg  
27901 gtaataactta tagcaactgct tggctttgtg ctctaggaaa ggttttacct tttcatagat  
27961 ggcacactat ggttcaaaca tgcacaccta atgttactat caactgtcaa gatccagctg  
28021 gtgggtgcgct tatagctagg tgttggtaacc ttcataagg tccacaaact gctgcattta  
28081 gagacgtact tgttgtttta aataaacgaa caaattaaaa tgtctgataa tggaccccaa  
28141 tcaaaccaac gtagtgcoccc ccgcattaca tttggtggac ccacagattc aactgacaat  
28201 aaccagaatg gaggacgcaa tggggcaagg ccaaacacgc gccgacccca aggtttacc  
28261 aataaactcg cgtcttgggt cacagetctc actcagcatg gcaaggagga acttagattc  
28321 cctcgaggcc agggcgttcc aatcaacacc aatagtggc cagatgacca aattggetac  
28381 taccgaagag ctacccgacg agttcgtggt ggtgacggca aaatgaaaga gctcagoccc  
28441 agatggtact tctattacct aggaactggc ccagaagctt cacttcccta cggcgtaac  
28501 aaagaaggca tcgtatgggt tgcaactgag ggagccttga atacacccaa agaccacatt  
28561 ggcacccgca atcctaataa caatgtgccc accgtgctac aacttctca aggaacaaca  
28621 ttgccaaaag gcttctacgc agaggggaagc agagggcgca gtcaagctc tttctgctcc  
28681 tcatcacgta gtcgcggtaa ttcaagaat tcaactctg gcagcagtag gggaaaltct  
28741 cctgctcgaa tggctagcgg aggtggtgaa actgcctcgc cgtattgct gctagacaga  
28801 ttgaaccagc ttgagagcaa agtttctggt aaaggccaac aacaacaagg ccaactgtc  
28861 actaagaat ctgctgctga ggcattctaaa aagcctcgc aaaaacgtac tgccacaaaa  
28921 cagtacaacg tcaactcaagc atttgggaga cgtggtccag acaaaacca aggaaatctc  
28981 ggggaccaag acctaatcag acaaggaact gattacaaac attggccgca aattgcacaa  
29041 tttgctccaa gtgcctctgc attctttgga atgtcaogca ttggcatgga agtcaacct  
29101 tcgggaacat ggctgaotta tcatggagcc attaaattgg atgacaaaga tccacaattc  
29161 aaagacaacg tcatactgct gaacaagcac attgacgcat acaaaacatt cccaccaaca  
29221 gagectaaaa aggacaaaaa gaaaaagact gatgaagctc agcctttgcc gcagagacaa  
29281 aagaagcagc ccactgtgac tcttcttctc gcggtgaca tggatgattt ctccagacaa  
29341 cttcaaaatt ccatgagtgg agcttctgct gattcaactc aggcataaac actcatgatg  
29401 accacacaag gcagatgggc tatgtaaacy ttttcgcaat tccgtttacg atacatagtc  
29461 tactcttgty cagaatgaat tctogtaact aaacagcaca agtaggttta gtaacttta  
29521 atctcacata gcaatcttta atcaatgtgt aacattaggg aggaactgaa agageccacca  
29581 cattttcact gaggccacgc ggagtacgat cgagggtaaca gtgaataatg ctagggagag  
29641 ctgcctatat ggaagagccc taatgtgtaa aattaatttt agtagtgcta tccccatgtg  
29701 attttaatag cttcttagga gaatgacaaa aaaaaaaaaa aa

FIG. 10 Con't



1 - ATATTAGGTTTTTACCTACCCAGGAAAAGCCAACCAACCTCGATCTCTTGTAGATCTGTT - 60  
- I L G F Y L P R K S Q P T S I S C R S V  
- Y \* V F T Y P G K A N Q P R S L V D L F  
- I R F L P T Q E K P T N L D L L \* I C S  
61 - CTCTAAACGAACCTTAAAATCTGTGTAGCTGTCGCTCGGCTGCATGCCTAGTGCACCTAC - 120  
- L \* T N F K I C V A V A R L H A \* C T Y  
- S K R T L K S V \* L S L G C M P S A P T  
- L N E L \* N L C S C R S A A C L V H L R  
121 - GCAGTATAAACATAATAAATTTTACTGTCGTTGACAAGAAACGAGTAACTCGTCCCTCT - 180  
- A V \* T I I N F T V V D K K R V T R P S  
- Q Y K Q \* \* I L L S L T R N E \* L V P L  
- S I N N K F Y C R \* Q E T S N S S L F  
181 - TCTGCAGACTGCTTACGGTTTCGTCGTTGTCAGTCGATCATCAGCATACCTAGGTTTC - 240  
- S A D C L R F R P C C S R S S A Y L G F  
- L Q T A Y G F V R V A V D H Q H T \* V S  
- C R L L T V S S V L Q S I I S I P R F R  
241 - GTCGGGTGTGACCGAAAGGTAAGATGGAGAGCCTTGTCTTGGTGTCAACGAGAAAACA - 300  
- V R V \* P K G K M E S L V L G V N E K T  
- S G C D R K V R W R A L F L V S T R K H  
- P G V T E R \* D G E P C S W C Q R E N T  
301 - CACGTCCAACCTCAGTTTGCCTGTCCTTCAGGTTAGAGACGTGCTAGTGCCTGGCTTCGGG - 360  
- H V Q L S L P V L Q V R D V L V R G F G  
- T S N S V C L S F R L E T C \* C V A S G  
- R P T Q F A C P S G \* R R A S A W L R G  
361 - GACTCTGTGGAAGAGGCCCTATCGGAGGCACGTGAACACCTCAAAAATGGCACTTGTGGT - 420  
- D S V E E A L S E A R E H L K N G T C G  
- T L W K R P Y R R H V N T S K M A L V V  
- L C G R G P I G G T \* T P Q K W H L W S  
421 - CTAGTAGAGCTGGAAAAGGGCTACTGCCCCAGCTTGAACAGCCCTATGTGTTTCATTAAA - 480  
- L V E L E K G V L P Q L E Q P Y V F I K  
- \* \* S W K K A Y C P S L N S P M C S L N  
- S R A G K R R T A P A \* T A L C V H \* T  
481 - CGTTCTGATGCCTTAAGCACCAATCACGGCCACAAGGTCGTTGAGCTGGTTGCAGAAATG - 540  
- R S D A L S T N H G H K V V E L V A E M  
- V L M P \* A P I T A T R S L S W L Q K W  
- F \* C L K H Q S R P Q G R \* A G C R N G  
541 - GACGGCATTTCAGTACGGTCGTACGGTATAAACTGGGAGTACTCGTCCACATGTGGGC - 600  
- D G I Q Y G R S G I T L G V L V P H V G  
- T A F S T V V A V \* H W E Y S C H M W A  
- R H S V R S \* R Y N T G S T R A T C G R  
601 - GAAACCCCAATTGCATACCGCAATGTTCTTCTTCGTAAGAACGTAATAAGGGAGCCGGT - 660  
- E T P I A Y R N V L L R K N G N K G A G  
- K P Q L H T A M F F F V R T V I R E P V  
- N P N C I P Q C S S S \* E R \* \* G S R W  
661 - GGTCATAGCTATGGCATCGATCTAAAGTCTTATGACTTAGGTGACGAGCTTGGCACTGAT - 720  
- G H S Y G I D L K S Y D L G D E L G T D  
- V I A M A S I \* S L M T \* V T S L A L I  
- S \* L W H R S K V L \* L R \* R A W H \* S  
721 - CCCATTGAAGATTATGAACAAAACCTGGAACACTAAGCATGGCAGTGGTGCACCTCCGTGAA - 780  
- P I E D Y E Q N W N T K H G S G A L R E  
- P L K I M N K T G T L S M A V V H S V N  
- H \* R L \* T K L E H \* A W Q W C T P \* T  
781 - CTCACTCGTGTGAGCTCAATGGAGGTGCAGTCACTCGCTATGTCGACAACAATTTCTGTGGC - 840  
- L T R E L N G G A V T R Y V D N N F C G  
- S L V S S M E V Q S L A M S T T I S V A  
- H S \* A Q W R C S H S L C R Q Q F L W P

FIG. 11

841 - CCAGATGGGTACCCCTCTTGATTGCATCAAAGATTTTCTCGCACGCGCGGGCAAGTCAATG - 900  
 - P D G Y P L D C I K D F L A R A G K S M  
 - Q M G T L L I A S K I F S H A R A S Q C  
 - R W V P S \* L H Q R F S R T R G Q V N V  
 901 - TGCACCTCTTTCCGAACAACTTGATTACATCGAGTCGAAGAGAG3TGTCTACTGCTGCCGT - 960  
 - C T L S E Q L D Y I E S K R G V Y C C R  
 - A L F P N N L I T S S R R E V S T A A V  
 - H S F R T T \* L H R V E E R C L L P \*  
 951 - GACCATGAGCATGAAATTGCOCTGGTTCAGTGCAGCGCTCTGATAAGAGCTACGAGCACCAG - 1020  
 - D H E H E I A W F T E R S D K S Y E H Q  
 - T M S M K L P G S L S A L I R A T S T R  
 - P \* A \* N C L V H \* A L \* \* E L R A P D  
 1021 - ACACCCTTCGAATTAAGAGTGCCAAGAAATTTGACACTTTCAAAGGGGAATGCCCAAAG - 1080  
 - T P F E I K S A K K F D T F K G E C P K  
 - H P S K L R V P R N L T L S K G N A Q S  
 - T L R N \* E C Q F I \* H F Q R G M P K V  
 1081 - TTTGTGTTTCCCTCTTAACCTCAAAGTCAAAGTCATTCAACCACGTGTGAAAAGAAAAG - 1140  
 - F V F P L N S K V K V I Q P R V E K K K  
 - L C F L L T Q K S K S F N H V L K R K R  
 - C V S S \* L K S Q S H S T T C \* K E K D  
 1141 - ACTGAGGGTTTCATGGGGGTATACGCTCTGTGTACCCTGTTGCATCTCCACAGGAGTGT - 1200  
 - T E G F M G R I R S V Y P V A S P Q E C  
 - L R V S W G V Y A L C T L L H L H R S V  
 - \* G F H G A Y T L C V P C C I S T G V \*  
 1201 - AACAAATGCACTTGTCTACCTTGATGAAATGTAATCATTCGCATGAAGTTTCATGGCAG - 1260  
 - N N M H L S T L M K C N H C D E V S W Q  
 - T I C T C L P \* \* N V I I A M K F H G R  
 - Q Y A L V Y L D E M \* S L R \* S F M A D  
 1261 - ACGTCCGACTTCTGAAAGCCACTGTGAACATGTGGCACTGAAAATTTAGTTATTGAA - 1320  
 - T C D F L K A T C E H C G T E N L V I E  
 - R A T F \* K P L V N I V A L K I \* L L K  
 - V R L S E S H L \* T L W H \* K F S Y \* R  
 1321 - GGACCTACTACATGTGGGTACCTACCTACTAATGCTGTAGTGAAAATGCCATGCTCTGCC - 1380  
 - G P T T C G Y L P T N A V V K M P C P A  
 - D L L H V G T Y L L M L \* \* K C H V L P  
 - T Y Y M W V P T Y \* C C S E N A M S C L  
 1381 - TGTCAGACCCAGAGATTGGACCTGAGCATAGTGTTCAGATTATCACAACCACTCAAAC - 1440  
 - C Q D P E I G P E H S V A D Y H N H S N  
 - V K T Q R L D L S I V L Q I I T T T Q T  
 - S R P R D W T \* A \* C C R L S Q P L K H  
 1441 - ATTGAAACTCGACTCCGCAAGGGAGGTAGGACTAGATGTTTGGAGGCTGTGTGTTTGCC - 1500  
 - I E T R L R K G G R T R C F G G C V F A  
 - L K L D S A R E V G L D V L E A V C L P  
 - \* N S T P Q G R \* D \* M F W R L C V C L  
 1501 - TATGTTGGCTGCTATAATAAGCGTGCCTACTGGGTTCCCTCGTGCCTAGTGTGATATTGSC - 1560  
 - Y V G C Y N K R A Y W V P R A S A D I G  
 - M L A A I I S V P T G F L V L V L I L A  
 - C W L L \* \* A C L L G S S C \* C \* Y W L  
 1561 - TCAGGCCATACTGGCATTACTGGTGACAATGTGGAGACCTTGAATGAGGATCTCCTTGAG - 1620  
 - S G H T G I T G D N V E T L N E D L L E  
 - Q A I L A L L V T M W R P \* M R I S L R  
 - R P Y W H Y W \* Q C G D L E \* G S P \* D  
 1621 - ATACTGAGTCGTGAACCTGTAAACATTAACATTGTGGCGATTTTCATTTGAATGAAGAG - 1680  
 - I L S R E R V N I N I V G D F H L N E E  
 - Y \* V V N V L T L T L L A I F I \* M K R  
 - T E S \* T C \* H \* H C W R F S F E \* R G

FIG. 11 Con't

1681 - GTTGCCATCATTTTTGGCATCTTTCTCTGCTTCTACAAGTGCCTTTATTGACACTATAAAG - 1740  
- V A I I L A S F S A S T S A F I D T I K  
- L P S F W H L S L L L Q V P L L T L \* R  
- C H H F G I F L C F Y K C L Y \* E Y K E  
1741 - AGTCTTGATTACAAGTCTTTCAAACCATTGTTGAGTCTTGC GGTAAC TATAAAGTTACC - 1800  
- S L D Y K S F K T I V E S C G N Y K V T  
- V L I T S L S K P L L S P A V T I K L P  
- S \* L Q V F Q N H C \* V L R \* L \* S Y Q  
1801 - AAGGGAAAGCCCGTAAAGGTGCTTGAACATTGGACAACAGAGATCAGTTTTAACACCA - 1860  
- K G K P V K G A W N I G Q Q R S V L T P  
- R E S P \* K V L G T L D N R D Q F \* H H  
- G K A R K R C L E H W T T E I S F N T T  
1861 - CTGTGTGGTTTTCCCTCACAGGCTGCTGGTGTATCAGATCAATTTTTGCGCGCACACTT - 1920  
- L C G F P S Q A A G V I R S I F A R T L  
- C V V F P H R L L V L S D Q F L R A H L  
- V W F S L T G C W C Y Q I N F C A H T \*  
1921 - GATGCAGCAAACCACTCAATTCCTGATTTGCAAAGAGCAGCTGTACCATACTTGATGGT - 1980  
- D A A N H S I P D L Q R A A V T I L D G  
- M Q Q T T Q F L I C K E Q L S P Y L M V  
- C S K P L N S \* F A K S S C H H T \* W Y  
1981 - ATTTCTGAACAGTCATTACGTCTTGTGCGACGCCATGGTTTATACTTCAGACCTGCTCACC - 2040  
- I S E Q S L R L V D A M V Y T S D L L T  
- F L N S H Y V L S T P W F I L Q T C S P  
- F \* T V I T S C R R H G L Y F R P A H Q  
2041 - AACAGTGTCAATTATTATGGCATATGTAACCTGGTGGTCTTGTACACAGACTTCTCAGTGG - 2100  
- N S V I I M A Y V T G G L V Q Q T S Q W  
- T V S L L W H M \* L V V L Y N R L L S G  
- Q C H Y Y G I C N W W S C T T D F S V V  
2101 - TTGTCTAATCTTTTGGGCACTACTGTTGAAAAACTCAGGCCTATCTTTGAATGGATTGAG - 2160  
- L S N L L G T T V E K L R P I F E W I E  
- C L I F W A L L L K N S G L S L N G L R  
- V \* S F G H Y C \* K T Q A Y L \* M D \* G  
2161 - GCGAAACTTAGTGCAGGAGTTGAATTTCTCAAGGATGCTTGGGAGATTCTCAAATTTCTC - 2220  
- A K L S A G V E F L K D A W E I L K F L  
- R N L V Q E L N F S R M L G R F S N F S  
- E T \* C R S \* I S Q G C L G D S Q I S H  
2221 - ATTACAGGTGTTTTTGACATCGTCAAGGGTCAAATACAGGTTGCTTCAGATAACATCAAG - 2280  
- I T G V F D I V K G Q I Q V A S D N I K  
- L Q V F L T S S R V K Y R L L Q I T S R  
- Y R C F \* H R Q G S N T G C F R \* H Q G  
2281 - GATTGTGTAATAATGCTTCATTGATGTTGTTAACAAGGCACCTCGAAATGTGCATTGATCAA - 2340  
- D C V K C F I D V V N K A L E M C I D Q  
- I V \* N A S L M L L T R H S K C A L I K  
- L C K M L H \* C C \* Q G T R N V H \* S S  
2341 - GTCACTATCGCTGGCGCAAAGTTGCGATCACTCAACTTAGGTGAAGTCTTCATCGCTCAA - 2400  
- V T I A G A K L R S L N L G E V F I A Q  
- S L S L A Q S C D H S T \* V K S S S L K  
- H Y R W R K V A I T Q L R \* S L H R S K  
2401 - AGCAAGGGACTTTACCGTCAGTGTATACGTGGCAAGGAGCAGCTGCAACTACTCATGCCT - 2460  
- S K G L Y R Q C I R G K E Q L Q L L M F  
- A R D F T V S V Y V A R S S C N Y S C L  
- Q G T L P S V Y T W Q G A A A T T H A S  
2461 - CTTAAGGCACCAAAAAGAAGTAACCTTTCTTGAAGGTGATTCCATGACACAGTACTTACC - 2520  
- L K A P K E V T F L E G D S H D T V L T  
- L R H Q K K \* P F L K V I H M T Q Y L P  
- \* G T K R S N L S \* R \* F T \* H S T Y L

FIG. 11 Con't

2521 - TCTGAGGAGGTTGTTCTCAAGAACGGTGAACCTCGAAGCACTCGAGACGCCCGTGGATAGC - 2580  
 - S E E V V L K N G E L E A L E T P V D S  
 - L R R L F S R T V N S K H S R R P L I A  
 - \* G G C S Q E R \* T R S T R D A R \* \* L  
 2581 - TTCACAAATGGAGCTATCGTGGGCACACCAGTCTGTGTAATGGCCCTCATGCTCTTAGAG - 2640  
 - F T N G A I V G T P V C V N G L M L L E  
 - S Q M E L S S A H Q S V \* M A S C S \* R  
 - H K W S Y R R H T S L C K W P H A L R D  
 2641 - ATTAAGGACAAAGAACAATACTGCGCATTGTCTCCTGGTTTACTGGCTACAAACAATGTC - 2700  
 - I K D K E Q Y C A L S P G L L A T N N V  
 - L R T K N N T A H C L L V Y W L Q T M S  
 - \* G Q R T I L R I V S W F T G Y K Q C L  
 2701 - TTTTCGCTTAAAAGGGGGTGCACCAATTAAGGTGTAACCTTTGGAGAAGATACTGTTTGG - 2760  
 - F R L K G G A P I K G V T F G E D T V W  
 - F A \* K G V H Q L K V \* P L E K I L F G  
 - S L K R G C T N \* R C N L W R R Y C L G  
 2761 - GAAGTCAAGGTTACAAGAATGTGAGAATCACATTTGAGCTTGATGAACGTTGTCACAAA - 2820  
 - E V Q G Y K N V R I T F E L D E R V D K  
 - K F K V T R M \* E S H L S L M N V L T K  
 - S S R L Q E C E N H I \* A \* \* T C \* Q S  
 2821 - GTGCTTAATGAAAAGTCTCTGTCTACACTGTTGAATCCGGTACCGAAGTTACTGAGTTT - 2880  
 - V L N E K C S V Y T V E S G T E V T E F  
 - C L M K S A L S T L L N P V P K L L S L  
 - A \* \* K V L C L H C \* I R Y R S Y \* V C  
 2881 - GCATGTGTTGTAGCAGAGGCTGTTGTAAGACTTTACAACCAGTTTCTGATCTCCTTACC - 2940  
 - A C V V A E A V V K T L Q P V S D L L T  
 - H V L \* Q R L L \* R L Y N Q F L I S L P  
 - M C C S R G C C E D F T T S F \* S P Y Q  
 2941 - AACATGGGTATTGATCTTGATGAGTGGAGTGTAGCTACATTCTACTTATTTGATGATGCT - 3000  
 - N M G I D L D E W S V A T F Y L F D D A  
 - T W V L I L M S G V \* L H S T Y L M M L  
 - H G A Y \* S \* \* V E C S Y I L L I \* \* C W  
 3001 - GGTGAAGAAAACCTTTTCATCAGTATGTATTGTTCCTTTACCCTCCAGATGAGGAAGAA - 3060  
 - G E E N F S R M Y C S F Y P P D E E E  
 - V K K T F H H V C I V P F T L Q M R K K  
 - \* R K L F I T Y V L F L L P S R \* G R R  
 3061 - GAGGACGATGCAGAGTGTGAGGAAGAAGAAATTGATGAAACCTGTGAACATGACTACGGT - 3120  
 - E D D A E C E E E E I D E T C E H E Y G  
 - R T M Q S V R K K L M K P V N M S T V  
 - G R C R V \* G R R N \* \* N L \* T \* V R Y  
 3121 - ACAGAGGATGATTATCAAGGCTCCCTCTGGAAATTTGGTGCCTCAGCTGAAACAGTTTCA - 3180  
 - T E D D Y Q G L P L E F G A S A E T V R  
 - Q R M I I K V S L W N L V P Q L K Q F E  
 - R G \* L S R S P S G I W C L S \* N S S S  
 3181 - GTTGAAGGAAGAAGAAGAGGAACTGGCTGGATGATACTACTGAGCAATCAGAGATTGAG - 3240  
 - V E E E E E E D W L D D T T E Q S E I E  
 - L R K K K R K T G W M I L L S N Q R I S  
 - \* G R R R G R L A G \* Y Y \* A I R D \* A  
 3241 - CCAGAACCAGAACCTACACCTGAAGAACCAGTTAATCAGTTTACTGGTTATTTAAAACCT - 3300  
 - P E P E P T P E E P V N Q F T G Y L K L  
 - Q N Q N L H L K N Q L I S L L V I \* N L  
 - R T R T Y T \* R T S \* S V Y W L F K T Y  
 3301 - ACTGACAATGTTGCCATTAATGTGTTGACATCGTTAAGGAGGCACAAAGTGCTAATCCT - 3360  
 - T D N V A I K C V D I V K E A Q S A N P  
 - L T M L P L N V L T S L R R H K V L I L  
 - \* Q C C H \* M C \* H R \* G G T K C \* S Y

FIG. 11 Con't

3361 - ATGGTGATTGTAAATGCTGCTAACATACACCTGAAACATGGTGGTGGTGTAGCAGGTGCA - 3420  
 - M V I V N A A N I H L K H G G G V A G A  
 - W \* L \* M L L T Y T \* N M V V V \* Q V H  
 - G D C K C C \* H T P E T W W W C S R C T  
 3421 - CTCAACAAGGCAACCAATGGTGCCATGCAAAAGGAGAGTGATGATTACATTAAGCTAAAT - 3480  
 - L N K A T N G A M Q K E S D D Y I K L N  
 - S T R Q P M V P C K R R V M I T L S \* M  
 - Q Q G N Q W C H A K G E \* \* L H \* A K W  
 3481 - GGCCCTCTTACAGTAGGAGGGTCTTGTGTTTCTGGACATAATCTTGCTAAGAAGTGT - 3540  
 - G P L T V G G S C L L S G H N L A K K C  
 - A L L Q \* E G L V C F L D I I L L R S V  
 - P S Y S R V L F A F W T \* S C \* E V S  
 3541 - CTGCATGTTGTTGGACCTAACCTAAATGCAGGIGAGGACATCCAGCTTCTTAAGGCAGCA - 3600  
 - L H V V G P N L N A G E D I Q L L K A A  
 - C M L L D L T \* M Q V R T S S F L R Q H  
 - A C C W T \* P K C R \* G H P A S \* G S I  
 3601 - TATGAAAATTTCAATTCACAGGACATCTTACTGACACCATTGTTGTCAGCAGGCATAETT - 3660  
 - Y E N F N S Q D I L L A P L L S A G I F  
 - M K I S I H R T S Y L H H C C Q Q A Y L  
 - \* K F Q F T G H L T C T I V V S R H I W  
 3661 - GGTGCTAAACCACTTCAGTCTTTACAAGTGTGCGTGCAGACGGTTCGTACACAGGTTTAT - 3720  
 - G A K P L Q S L Q V C V Q T V R T Q V Y  
 - V L N H F S L Y K C A C R R F V H R F I  
 - C \* T T S V F T S V R A D G S Y T G L Y  
 3721 - ATTGCAGTCAATGACAAAGCTCTTTATGAGCAGGTTGTCATGGATTATCTTGATAACCTG - 3780  
 - I A V N D K A L Y E Q V V M D Y L D N L  
 - L Q S M T K L F M S R L S W I I L I T \*  
 - C S Q \* Q S S L \* A G C H G L S \* \* P E  
 3781 - AAGCCTAGAGTGAAGCACCTAAACAAGAGGCCACCAACACAGAAGATTCACAAAACCT - 3840  
 - K P R V E A P K Q E E P P N T E D S K T  
 - S L E W K H L N K R S H Q T Q K I P K L  
 - A \* S G S T \* T R G A T K H R R F Q N \*  
 3841 - GAGGAGAAATCTGTCGTACAGAAGCCTGTCGATGTGAAGCCAAAATTAAGGCCTGCATT - 3900  
 - E E K S V V Q K P V D V K P K I K A C I  
 - R R N L S Y R S L S M \* S Q K L R P A L  
 - G E I C R T E A C R C E A K N \* G L H \*  
 3901 - GATGAGTTACCACAACACTGGAAGAACTAAGTTTCTTACCAATAAGTTACTCTTGTTT - 3960  
 - D E V T T T L E E T K F L T N K L L L F  
 - M R L P Q H W K K L S F L P I S Y S C L  
 - \* G Y H N T G R N \* V S Y Q \* V T L V C  
 3961 - GCTGATATCAATGGTAAGCTTTACCATGATTCTCAGAACATGCTTAGAGGTGAAGATATG - 4020  
 - A D I N G K L Y H D S Q N M L R G E D M  
 - L I S M V S F T M I L R T C L E V K I C  
 - \* Y Q W \* A L P \* F S E H A \* R \* R Y V  
 4021 - TCTTCTTGAGAAGGATGCACCTTACATGGTAGGTGATCTTATCACTAGTGGTGTATATC - 4080  
 - S F L E K D A P Y M V G D V I T S G D I  
 - L S L R R M H L T W \* V M L S L V V I S  
 - F P \* E G C T L H G R \* C Y H \* W \* Y H  
 4081 - ACTTGTGTTGTAATACCTCCAAAAGGCTGGTGGCACTACTGAGATGCTCTCAAGAGCT - 4140  
 - T C V V I P S K K A G G T T E M L S R A  
 - L V L \* Y P P K R L V A I L R C S Q E L  
 - L C C N T L Q K G W W H Y \* D A L K S F  
 4141 - TTGAAGAAAGTGCCAGTTGATGAGTATATAACCACGTACCCTGGACAAGGATGTGCTGGT - 4200  
 - L K K V P V D E Y I T T Y P G Q G C A G  
 - \* R K C Q L M S I \* P R T L D K D V L V  
 - E E S A S \* \* V Y N H V P W T R M C W L

FIG. 11 Con't

4201 - TATACACTTGAGGAAGCTAAGACTGCTCTTAAGAAATGCAAATCTGCATTTTATGTACTA - 4260  
 - Y T L E E A K T A L K K C K S A F Y V I  
 - I H L R K L R L L L R N A N L H F M Y Y  
 - Y T \* G S \* D C S \* E M Q I C I L C T T  
 4261 - CCTTCAGAAGCACCTAATGCTAAGGAAGATCTAGGAAGCTATCCTGGGATTTGAGA - 4320  
 - P S E A P N A K E E I L G T V S W N L R  
 - L Q K H L M L R K R F \* E L Y P G I \* E  
 - F R S T \* C \* G R D S R N C I L E F E R  
 4321 - GAAATGCTTGCTCATGCTGAAGAGACAAGAAAATTAATGCCTATATGCATGGATGTTAGA - 4380  
 - E M L A H A E E T R K L M P I C M D V R  
 - K C L L M L K R Q E N \* C L Y A W M L E  
 - N A C S C \* R D K K I N A Y M H G C \* S  
 4381 - GCCATAATGGCAACCATCCAACGTAAGTATAAAGGAATTAATAATCAAGAGGGCATCGTT - 4440  
 - A I M A T I Q R K Y K G I K I Q E G I V  
 - P \* W Q P S N V S I K E L K F K R A S L  
 - H N G N H P T \* V \* R N \* N S R G H R \*  
 4441 - GACTATGGTGTCCGATTCTTCTTTTATACTAGTAAAGAGCCCTGTAGCTTCTATTATTACG - 4500  
 - D Y G V R F F F Y T S K E P V A S I I T  
 - T M V S D S S F I L V K S L \* L L L L R  
 - L W C P I L L L Y \* \* R A C S F Y Y Y E  
 4501 - AAGCTGAACTCTCTAAATGAGCCGCTTGTCAATGCCAATGGTTATGTGACACATGGT - 4560  
 - K L N S L N E P L V T M P I G Y V T H G  
 - S \* T L \* M S R L S Q C Q L V M \* H M V  
 - A E L S K \* A A C H N A N W L C D T W F  
 4561 - TTTAATCTGAAGAGGCTGCGCGCTGTATGCGTCTCTTAAAGCTCCTGCGGTAGTGCA - 4620  
 - F N L E E A A R C M R S L K A P A V V S  
 - L I L K R L R A V C V L L K L L P \* C Q  
 - \* S \* R G C A L Y A F S \* S S C R S V S  
 4621 - GTATCATCACCAGATGCTGTTACTACATATAATGGATACCTCACTTCGTCATCAAAGACA - 4680  
 - V S S P D A V T T Y N G Y L T S S S K T  
 - Y H H Q M L L L H I M D T S L R H Q R H  
 - I I T R C C Y Y I \* W I P H F V I K D I  
 4681 - TCTGAGGACACTTTGTAGAAACAGTTTCTTTGGCTGGCTCTTACAGAGATTGGTCCCTAT - 4740  
 - S E E H F V E T V S L A G S Y R D W S Y  
 - L R S T L \* K Q F L W L A L T E I G P I  
 - \* G A L C R N S F F G W L L Q R L V L F  
 4741 - TCAGGACAGCGTACACAGTTAGCTCTTGAATTTCTTAAGCGTGGTGACAAAATTGTGTAC - 4800  
 - S G Q R T E L G V E F L K R G D K I V Y  
 - Q D S V Q S \* V L N F L S V V T K L C T  
 - R T A Y R V R C \* I S \* A W \* Q N C V P  
 4801 - CACACTCTGGAGAGCCCCGTCGAGTTTCATCTTGACGGTGAGGTTCTTCACTTGACAAA - 4860  
 - H T L E S P V E F H L D G E V L S L D K  
 - T L W R A P S S F I L T V R F F H L T N  
 - H S G E P R R V S S \* R \* G S F T \* Q T  
 4861 - CTAAGAGTCTCTTATCCCTGCGGGAGGTTAAGACTATAAAAAGTGTTCACAACCTGTGGAC - 4920  
 - L K S L L S L R E V K T I K V F T T V D  
 - \* R V S Y P C G R L R L \* K C S Q L W T  
 - K E S L I P A G G \* D Y K S V H N C G Q  
 4921 - AACACTAATCTCCACACAGCTTGTGGATATGTCTATGACATATGGACAGCAGTTTGGT - 4980  
 - N T N L H T Q L V D M S M T Y G Q Q F G  
 - T L I S T H S L W I C L \* H M D S S L V  
 - H \* S P H T A C G Y V Y D I W T A V W S  
 4981 - CCAACATACTTGGATGCTGCTGATGTTACAAAAATTAACCTCATGTAATCAIGAGGGT - 5040  
 - P T Y L D G A D V T K I K P H V N H E G  
 - Q H T W M V L M L Q K L N L M \* I M R V  
 - N I L G W C \* C Y K N \* T S C K S \* G \*

FIG. 11 Con't

5041 - AAGACTTTCTTTGTACTACCTAGTGATGACACACTACGTAGTGAAGCCTTCGAGTACTAC - 5100  
 - K T F F V L F S D D T L R S E A F E Y Y  
 - R L S L Y Y L V M T H Y V V K L S S T T  
 - D F L C T T \* \* \* H T T \* \* S F R V L P  
 5101 - CATACTCTTGATGAGAGTTTTCTTGGTAGGTACATGTCTGCTTTAAACCACACAAAGAAA - 5160  
 - H T L D E S F L G R Y M S A L N H T K K  
 - I L L M R V F L V G T C L L \* T T Q R N  
 - Y S \* \* E F S W \* V H V C F K P H K E M  
 5161 - TGGAAATTTCTCAAGTTGGTGGTTAACTTCAATTAATGGGCTGATAACAAATGTAT - 5220  
 - W K F P Q V G G L T S I K W A D N N C Y  
 - G N F S L K L V V \* L Q L N G L I T I V I  
 - E I S S S W F N F N \* M G \* \* Q L L F  
 5221 - TTGTCTAGTGTTTTATTAGCACTTCAACAGCTTGAAGTCAAATTCATGCACCAGCACTT - 5280  
 - L S S V L L A L Q Q L E V K F N A P A L  
 - C L V F Y \* H F N S L K S N S M H Q H F  
 - V \* C F I S T S T A \* S Q I Q C T S T S  
 5281 - CAAGAGGCTTATTATAGAGCCCGTGTGGTGTGCTGCTAACTTTTGTGCACTCATACTC - 5340  
 - Q E A Y Y R A R A G D A A N F C A L I L  
 - K R L I I E P V L V M L L T F V H S Y S  
 - R G L L \* S P C W \* C C \* L L C T H T R  
 5341 - GCTTACAGTAATAAAACTGTTGGCGAGCTTGGTGTGATGTGAGAGAACTATGACCCATCTT - 5400  
 - A Y S N K T V G E L G D V R E T M T H L  
 - L T V I K L L A S L V M S E K L \* P I F  
 - L Q \* \* N C W R A W \* C Q R N Y D P S S  
 5401 - CTACAGCATGCTAATTTGGAATCTGCAAAGCGAGTTCTTAATGTGGTGTGTAACATTGT - 5460  
 - L Q H A N L E S A K R V L N V V C K H C  
 - Y S M L I W N L Q S E F L M W C V N I V  
 - T A C \* F G I C K A S S \* C G V \* T L W  
 5461 - GGTCAGAAAATACTACTACCTAACGGGTGTAGAAGCTGTGATGTATATGGGTACTCTATCT - 5520  
 - G Q K T T T L T G V E A V M Y M G T L S  
 - V R K L L P \* R V \* K L \* C I W V L Y L  
 - S E N Y Y L N G C R S C D V Y G Y S I L  
 5521 - TATGATAATCTTAAGACAGGTGTTCCATTCCATGTGTGTGTGGTGTGATGCTACACAA - 5580  
 - Y D N L K T G V S I P C V C G R D A T Q  
 - M I I L R Q V F P F H V C V V V M L H N  
 - \* \* S \* D R C F H S M C V W S \* C Y T I  
 5581 - TATCTAGTACAACAAGAGTCTTCTTTTGTATGATGTCTGCACCACCTGCTGAGTATAA - 5640  
 - Y L V Q Q E S S F V M M S A P P A E Y K  
 - I \* Y N K S L L L L \* C L H H L L S I N  
 - S S T T R V F F C Y D V C T T C \* V \* I  
 5641 - TTACAGCAAGGTACATTCTTATGTGCGAATGAGTACACTGGTAACATCAGTGTGGTCAT - 5700  
 - L Q Q G T F L C A N E Y T G N Y Q C G H  
 - Y S K V H S Y V R M S T L V T I S V V I  
 - T A R Y I L M C E \* V H W \* L S V W S L  
 5701 - TACTTCATATAACTGCTAAGGAGACCCTCTATCGTATTGACGGAGCTCACCTTACAAAG - 5760  
 - Y T H I T A K E T L Y R I D G A H L T K  
 - T L I \* L L R R F S I V L T E L T L Q R  
 - H S Y N C \* G D P L S Y \* R S S P Y K D  
 5761 - ATGTCAGAGTACAAAGGACCAGTACTGATGTTTCTACAAGGAACATCTTACTACTACA - 5820  
 - M S E Y K G P V T D V F Y K E T S Y T T  
 - C Q S T K D Q \* L M F S T R K H L T L Q  
 - V R V Q R T S D \* C F L Q G N I L H Y N  
 5821 - ACCATCAAGCCTGTGTCGTATAAACTCGATGGAGTTACTTACACAGAGATTGAACCAAAA - 5880  
 - T I K P V S Y K L D G V T Y T E I E P K  
 - P S L C R I N S M E L L T Q R L N Q N  
 - H Q A C V V \* T R W S Y L H R D \* T K I

FIG. 11 Con't

5881 - TTGGATGGGTATTATAAAAAGGATAATGCTTACTATACAGAGCAGCCTATAGACCTTGTA - 5940  
 - L D G Y Y K K D N A Y Y T E Q P I D L V  
 - W M G I I K R I M L T I Q S S L \* T L Y  
 - G W V L \* K G \* C L L Y R A A Y R P C T  
 5941 - CCAACTCAACCATTACCAAATGCGAGTTTGTGATAATTCAAACTCACATGTTCTAACACA - 6000  
 - P T Q P L P N A S F D N F K L I C S N T  
 - Q L N H Y Q M R V L I I S N S H V L T Q  
 - N S T I T K C E F \* \* F Q T H M F \* H K  
 6001 - AAATTTGCTGATGATTTAAATCAAATGACAGGCTTCACAAAGCCAGCTTCACGAGAGCTA - 6060  
 - K F A D D L N Q M T G F T K P A S R E L  
 - N L L M I \* I K \* Q A S Q S Q L H E S Y  
 - I C \* \* F K S N D R L H K A S F T R A I  
 6061 - TCTGTCACATTCTTCCCAGACTTGAATGGCGATGTAGTGGCTATTGACTATAGACACTAT - 6120  
 - S V T F F P D L N G D V V A I D Y R H Y  
 - L S H S S Q T \* M A M \* W L L T I D T I  
 - C H I L P R L E W R C S G Y \* L \* T L F  
 6121 - TCAGCGAGTTTCAAGAAAGGTGCTAAATTAAGCCAAATGTTTGGCACATTAAC - 6180  
 - S A S F K K G A K L L H K P I V W H I N  
 - Q R V S R K V L N Y C I S Q L F G T L T  
 - S E F Q E R C \* I T A \* A N C L A H \* P  
 6181 - CAGGCTACAACCAAGACAACGTTCAAACCAAACACTTGGTGTTCGTTGCTTTGGAST - 6240  
 - Q A T T K T T F K P N T W C L R C L W S  
 - R L Q P R Q R S N Q T L G V V V F G V  
 - G Y N Q D N V Q T K H L V F T L S L E Y  
 6241 - ACAAAGCCACTAGATACTTCAAATTCATTTGAAGTCTGCGCACTAGAAGACACACAAGGA - 6300  
 - T K P V D T S N S F E V L A V E D T Q G  
 - Q S Q \* I L Q I H L K F W Q \* K T H K E  
 - K A S R Y F K F I \* S S G S R R H T R N  
 6301 - ATGGACAATCTTGTCTTGTGAAAGTCAACAACCCACCTCTGAAGAAGTAGTGAAAATCCT - 6360  
 - M D N L A C E S Q Q P I S E E V V E N P  
 - W T I L L V K V N N P P L K K \* W K I L  
 - G Q S C L \* K S T T H L \* R S S G K S Y  
 6361 - ACCATACAGAAGGAAGTCATAGAGTGTGACGTGAAAACCTACCGAAGTTGTAGGCAATGTC - 6420  
 - T I Q K E V I E C D V K T T E V V G N V  
 - P Y R R K S \* S V T \* K L P K L \* A M S  
 - H T E G S H R V \* R E N Y R S C R Q C H  
 6421 - ATACTTAAACCATCAGATGAAGGTGTTAAAGTAACACAAGAGTTAGTCATGAGGATCTT - 6480  
 - I L K P S D E G V K V T Q E L G H E D L  
 - Y L N H Q M K V L K \* H K S \* V M R I L  
 - T \* T I R \* R C \* S N T R V R S \* G S Y  
 6481 - ATGGCTGCTTATGTGGAACACAAGCATTACCATTAAGAAACCTAATGAGCTTTCACATA - 6540  
 - M A A Y V E N T S I T I K K P N E L S L  
 - W L L M W K T Q A L P L R N L M S F H \*  
 - G C L C G K H K H Y H \* E T \* \* A F T S  
 6541 - GCCTTAGGTTTAAAAACAATTGCCACTCATGGTATTGCTGCAATTAATAGTGTTCCTTGG - 6600  
 - A L G L K T I A T H G I A A I N S V P W  
 - P \* V \* K Q L P L M V L L Q L I V F L G  
 - L R F K N N C H S W Y C C N \* \* C S L E  
 6601 - AGTAAAAATTTGGCTTATGTCAAACCATTCTTAGGACAAGCAGCAATTACAACATCAAAT - 6660  
 - S K I L A Y V K P F L G Q A A I T T S N  
 - V K F W L M S N H S \* D K Q Q L Q H Q I  
 - \* N F G L C Q T I L R T S S N Y N I K L  
 6661 - TGCGCTAAGAGATTAGCACACGTTGTTTAAACAATTATATGCCTTATGTGTTTACATTA - 6720  
 - C A K R L A Q R V F N N Y M P Y V F T L  
 - A L R D \* H N V C L T I I C L M C L E Y  
 - R \* E I S T T C V \* Q L Y A L C V Y I I

FIG. 11 Con't



6721 - TTGTTCCAATTGTGTACTTTTACTAAAAGTACCAATTCTAGAATTAGAGCTTCACTACCT - 6780  
 - L F Q L C T F T K S T N S R I R A S L P  
 - C S N C V L L L K V P I L E L E L H Y L  
 - V P I V Y F Y \* K Y Q F \* N \* S F T T Y  
 6781 - ACAACTATTGCTAAAAATAGTGTAAAGAGTGTGCTAAATTATGTTGGATGCCGGCATT - 6840  
 - T T I A K N S V K S V A K L C L D A G I  
 - Q L L L K I V L R V L L N Y V W M P A L  
 - N Y C \* K \* C \* E C C \* I M F G C R H \*  
 6841 - AATTATGTGAAGTACCCCAAATTTCTAAATTGTTTCAATCGCTATGTGGCTATTTGTTG - 6900  
 - N Y V K S P K F S K L F T I A M W L L L  
 - I M \* S H P N F L N C S Q S L C G Y C C  
 - L C E V T Q I F \* I V H N R Y V A I V V  
 6901 - TTAAGTATTTGCTTAGGTTCTCTAATCTGTGTAAGTGTGCTTTTGGTGTACTCTTATCT - 6960  
 - L S I C L G S L I C V T A A F G V L L S  
 - \* V F A \* V L \* S V \* L L L L V Y S Y L  
 - K Y L L R F S N L C N C C F W C T L I \*  
 6961 - AATTTTGGTGTCTCTTATTGTAATGGCGTTAGAGAATTGTATCTTAATTCGCTAAC - 7020  
 - N F G A P S Y C N G V R E L Y L N S S N  
 - I L V L L L I V M A L E N C I L I R L T  
 - F W C S F L L \* W R \* R I V S \* F V \* R  
 7021 - GTTACTACTATGGATTTCTGTGAAGGTTCTTTTCCCTGCAGCATTGTTTAAAGTGGATTA - 7080  
 - V T T M D F C E G S F P C S I C L S G L  
 - L L L W I S V K V L F L A A F V \* V D \*  
 - Y Y Y G F L \* R F F S L Q H L F K W I R  
 7081 - GACTCCCTTGATTCTTATCCAGCTCTTGAACCATTTCAGGTGACGATTTTCATCGTACAAG - 7140  
 - D S L D S Y P A L E T I Q V T I S S Y K  
 - T P L I L I Q L L K P F R \* R F H R T S  
 - L P \* F L S S S \* N H S G D D F I V Q A  
 7141 - CTAGACTTGACAATTTTAGGTCTGGCCGCTGAGTGGGTTTGGCATATATGTTGTTTACA - 7200  
 - L D L T I L G L A A E W V L A Y M L F T  
 - \* T \* Q F \* V W P L S G F W H I C C S Q  
 - R L D N F R S G R \* V G F G I Y V V H K  
 7201 - AAATTTCTTTTATTATTAGGTCTTTTTCAGTATAATGCAGGTGTTCTTTGGCTATTTTGGCT - 7260  
 - K F F Y L L G L S A I M Q V F F G Y F A  
 - N S F I Y \* V F Q L \* C R C S L A I L L  
 - I L L F I R S F S Y N A G V L W L F C \*  
 7261 - AGTCATTTTCATCAGCAATTTCTGGCTCATCTGTTTATCATTAGTATTGTACAAATGGCA - 7320  
 - S H F I S N S W L M W F I I S I V Q M A  
 - V I S S A I L G S C G L S L V L Y K W H  
 - S F H Q Q F L A H V V Y H \* Y C T N G T  
 7321 - CCGTCTTCTGCAATGGTTAGGATGTACATCTTCTTTGCTTCTTTTCTACTACATATGGAAG - 7380  
 - P V S A M V R M Y I F F A S F Y Y I W K  
 - P F L Q W L G C T S S L L L S T T Y G R  
 - R F C N G \* D V H L L C F F L L H M E E  
 7381 - ACCTATGTTTCATATCATGGATGGTTGCACCTCTTCGACTTGCATGATGTGCTATAAGCGC - 7440  
 - S Y V H I M D G C T S S T C M M C Y K R  
 - A M F I S W M V A P L R L A \* C A I S A  
 - L C S Y H G W L H L F D L H D V L \* A Q  
 7441 - AATCGTGCCACACGCGTTGAGTGTACAATATTGTTAATGGCATGAAGAGATCTTTCTAT - 7500  
 - N R A T R V E C T T I V N G M K R S F Y  
 - I V P H A L S V Q L L L M A \* R D L S M  
 - S C H T R \* V Y N Y C \* W H E E I F L C  
 7501 - GTCTATGCAAAATGGAGGCCGTTGGCTTCTGCAAGACTACAATTTGGAATTTGTTCAATTGT - 7560  
 - V Y A N G G R G F C K T H N W N C L N C  
 - S M Q M E A V A S A R L T I G I V S I V  
 - L C K W R P W L L Q D S Q L E L S Q L \*

FIG. 11 Con't

7561 - GACACATTTTGCACCTGGTAGTACATTTCATTAGTGATGAAGTTGCTCGTGATTGTCACCTC - 7620  
 - D T F C T G S T F I S D E V A R D L S L  
 - T H F A L V V H S L V M K L L V I C H S  
 - H I L H W \* Y I H \* \* \* S C S \* F V T P  
 7621 - CAGTTTAAAAGACCAATCAACCCTACTGACCAGTCATCGTATATTGTTGATAGTGTGCT - 7680  
 - Q F K R P I N P T D Q S S Y I V D S V A  
 - S L K D Q S T L L T S H R I L L I V L L  
 - V \* K T N Q P Y \* P V I V Y C \* \* C C C C  
 7681 - GTGAAAAATGGCGCGCTTCACCTCTACTTTGACAAGGCTGGTCAAAAGACCTATGAGAGA - 7740  
 - V K N G A L H L Y F D K A G Q K T Y E R  
 - \* K M A R F T S T L T R L V K R P M R D  
 - E K W R A S P L L \* Q G W S K D L \* E T  
 7741 - CATCCGCTCTCCCATTTTGTCAATTTAGACAATTTGAGAGCTAACAACTAAAGGTTCA - 7800  
 - H P L S H F V N L D N L R A N N T K G S  
 - I R S P I L S I \* T I \* E L T T L K V H  
 - S A L P F C Q F R Q F E S \* Q H \* R F T  
 7801 - CTGCCTATTAATGTCATAGTTTTTGATGGCAAGTCCAAATGCGACGAGTCTGCTTCTAAG - 7860  
 - L P I N V I V F D G K S K C D E S A S K  
 - C L L M S \* F L M A S P N A T S L L L S  
 - A Y \* C H S F \* W Q V Q M R R V C F \* V  
 7861 - TCTGCTTCTGTGTACTACAGTCAGCTGATGTCCAACCTATTCTGTTGCTTGACCAAGCT - 7920  
 - S A S V Y Y S Q L M C Q P I L L L D Q A  
 - L L L C T T V S \* C A N L F C C L T K L  
 - C F C V L Q S A D V P T Y S V A \* P S S  
 7921 - CTTGTATCAAACGTTGGAGATAGTACTGAAGTTCCGTTAAGATGTTTGATGCTTATGTC - 7980  
 - L V S N V G D S T E V S V K M F D A Y V  
 - L Y Q T L E I V L K F P L R C L M L M S  
 - C I K R W R \* Y \* S F R \* D V \* C L C R  
 7981 - GACACCTTTTCAGCAACTTTTAGTGTTCCTATGGAAAAACTTAAGGCACTTGTGTGCTACA - 8040  
 - D T F S A T F S V P M E K L K A L V A T  
 - T P F Q Q L L V F L W K N L R H L L L Q  
 - H L F S N F \* C S Y G K T \* G T C C Y S  
 8041 - GCTCACAGCGAGTTAGCAAAGGGTGTAGCTTTAGATGGTGTCTTTCTACATTCGTGTCA - 8100  
 - A H S E L A K G V A L D G V L S T F V S  
 - L T A S \* Q R V \* L \* M V S F L H S C Q  
 - S Q R V S K G C S F R W C P F Y I R V S  
 8101 - GCTGCCCGACAAGGTGTTGTTGATACCGATGTTGACACAAAGGATGTTATTGAATGTCTC - 8160  
 - A A R Q G V V D T D V D T K D V I E C L  
 - L P D K V L L I P M L T Q R M L L N V S  
 - C P T R C C \* Y R C \* H K G C Y \* M S Q  
 8161 - AAACCTTTCACATCACTCTGACTTAGAAGTGACAGGTGACAGTTGTAACAATTTTCATGCTC - 8220  
 - K L S H H S D L E V T G D S C N N F M L  
 - N F H I T L T \* K \* Q V T V V T I S C S  
 - T F T S L \* L R S D R \* Q L \* Q F H A H  
 8221 - ACCTATAATAAGGTTGAAAACATGACGCCAGAGATCTTGGCGCATGTATTGACTGTAAT - 8280  
 - T Y N K V E N M T P R D L G A C I D C N  
 - P I I R L K T \* R P E I L A H V L T V M  
 - L \* \* G \* K H D A Q R S W R M Y \* L \* C  
 8281 - GCAAGGCATATCAATGCCCAAGTAGCAAAAAGTCACAATGTTTCACTCATCTGGAATGTA - 8340  
 - A R H I N A Q V A K S H N V S L I W N V  
 - Q G I S M P K \* Q K V T M F H S S G M \*  
 - K A Y Q C P S S K K S Q C F T H L E C K  
 8341 - AAAGACTACATGTCTTTATCTGAACAGCTGCGTAAACAAATTCGTACTGCTGCCAAGAAG - 8400  
 - K D Y M S L S E Q L R K Q I R T A A K K  
 - K T T C L Y L N S C V N K F V L L P R R  
 - R L H V F I \* T A A \* T N S Y C C Q E E

FIG. 11 Con't

8401 - AACACATACCTTTTACACTAACTTGTGCTACAACACTAGACAGGTTGTCAATGTCATAACT - 8460  
- N N I P F T L T C A T T R Q V V N V I T  
- T T Y L L H \* L V L Q L D R L S M S \* L  
- Q H T F Y T N L C Y N \* T G C Q C H N Y  
8461 - ACTAAAATCTCACTCAAGGGTGAAGATTGTTAGTACTTGTTTAAACTTATGCTTAAG - 8520  
- T K I S L K G G K I V S T C F K L M L K  
- L K S H S R V V R L L V L V L N L C L R  
- \* N L T Q G W \* D C \* Y L F \* T Y A \* G  
8521 - GCCACATTATTGTGCGTTCTTGTGTCATTGGTTTGTATATCGTTATGCCAGTACATACA - 8580  
- A T L L C V L A A L V C Y I V M P V H T  
- P H Y C A F L L E W F V I S L C Q Y I H  
- H I I V R S C C I G L L Y R Y A S T Y I  
8581 - TTGTCAATCCATGATGGTTACACAAATGAAATCATTGGTTACAAAGCCATTCCAGGATGGT - 8640  
- L S I H D G Y T N E I I G Y K A I Q D G  
- C Q S M M V T Q M K S L V T K P F R M V  
- V N P \* W L H K \* N H W L Q S H S G W C  
8641 - GTCACCTGACATCATTCTACTGATGATTGTTTTGCAAATAAACATGCTGGTTTTGAC - 8700  
- V T R D I I S T D D C F A N K H A G F D  
- S L V T S F L L M I V L Q I N M L V L T  
- H S \* H H F Y \* \* L F C K \* T C W F \* R  
8701 - GCATGGTTTAGCCAGCGTGGTTCATAAAAAATGACAAAAGCTGCCCTGTAGTAGCT - 8760  
- A W F S Q R G G S Y K N D K S C P V V A  
- H G L A S V V V H T K M T K A A L \* \* L  
- M V \* P A W W F I Q K \* Q K L P C S S C  
8761 - GCTATCATTACAAGAGATTGGTTTCATAGTGCCTGGCTACCGGGTACTGTGCTGAGA - 8820  
- A I I T R E I G F I V P G L P G T V L R  
- L S L Y Q E R L V S \* C L A Y R V L C \* E  
- Y H Y K R D W F H S A W L T G Y C A E S  
8821 - GCAATCAATGGTACTTCTTGCATTTCTACCTCGTGTITTTAGTGCCTGTGGCAACATT - 8880  
- A I N G D F L H F L P R V F S A V G N I  
- Q S M V T S C I F Y L V F L V L L A T F  
- N Q W \* L L A F S T S C F \* C C W Q H L  
8881 - TGCTACACACCTTCCAAACTCATTGAGTATAGTATTTTGTACCTCTGCTTGCCTTCTT - 8940  
- C Y T P S K L I E Y S D F A T S A C V L  
- A T H L P N S L S I V I L L P L L A F L  
- L H T F Q T H \* V \* \* F C Y L C L R S C  
8941 - GCTGCTGAGTGTACAATTTTAAAGGATGCTATGGGCAAACCTGTGCCATATTGTTATGAC - 9000  
- A A E C T I F K D A M G K P V P Y C Y D  
- L L S V Q F L R M L W A N L C H I V M T  
- C \* V Y N F \* G C Y G Q T C A I L L \* H  
9001 - ACTAATTTGCTAGAGGGTTCTATTTCTATAGTGAGCTTCGTCAGACACTCGTTATGTG - 9060  
- T N L L E G S I S Y S E L R P D T R Y V  
- L I C \* R V L F L I V S F V Q T L V M C  
- \* F A R G F Y F L \* \* A S S R H S L C A  
9061 - CTTATGGATGGTCCATCATAAGTTTCTAACAACCTTACCTGGAGGGTTCTGTTAGAGTA - 9120  
- L M D G S I I Q F P N T Y L E G S V R V  
- L W M V P S Y S F L T L T W R V L L E \*  
- Y G W F H H T V S \* H L P G G F C \* S S  
9121 - GTAACAACCTTTTGTGCTGAGTACTGTAGACATGGTACATGCGAAAGGTCAGAAGTAGGT - 9180  
- V T T F D A E Y C R H G T C E R S E V G  
- \* Q L L M L S T V D M V H A K G Q K \* V  
- N N F \* C \* V L \* T W Y M R K V R S R Y  
9181 - ATTTGCCTATCTACCAGTGGTAGATGGGTTCTTAATAATGAGCATTACAGAGCTCTATCA - 9240  
- I C L S T S G R W V L N N E H Y R A L S  
- F A Y L P V V D G F L I M S I T E L Y Q  
- L P I Y Q W \* M G S \* \* \* A L Q S S I R

FIG. 11 Con't

9241 - GGAGTTTTCTGTGGTGTTCATGCGATGAATCTCATAGCTAACATCTTTACTCCTCTTGTG - 9300  
- G V F C G V D A M N L I A N I F T P L V  
- E F S V V L M R \* I S \* L T S L L L L C  
- S F L W C \* C D E S H S \* H L Y S S C A  
9301 - CAACCTGTGGGTGCTTTAGATGTGTCTGCTTCAGTAGTGGCTGGTGGTATTATGCCATA - 9360  
- Q P V G A L D V S A S V V A G G I I A I  
- N L W V L \* M C L L Q \* W L V V L L P Y  
- T C G C F R C V C F S S G W W Y Y C H I  
9361 - TTGGTACTTGTGCTGCCTACTACTTTATGAAATTCAGACGTGTTTTGGTGAGTACAAC - 9420  
- L V T C A A Y Y F M K F R R V F G E Y N  
- W \* L V L P T T L \* N S D V F L V S T T  
- G D L C C L L L Y E I Q T C F W \* V Q P  
9421 - CATGTTGTTGCTGCTAATGCACTTTTGTGTTTTGATGTCTTTCACTATACTCTGTCTGGTA - 9480  
- H V V A A N A L L F L M S F T I L C L V  
- M L L L L M H F C F \* C L S L Y S V W Y  
- C C C C \* C T F C V F D V F H Y T L S G T  
9481 - CCAGCTTACAGCTTCTGCGGGAGTCTACTCAGTCTTTTACTTGTACTTGACATTCTAT - 9540  
- P A Y S F L P G V Y S V F Y L Y L T F Y  
- Q L T A F C R E S T Q S F T C T \* H S I  
- S L Q L S A G S L L S L L L V L D I L F  
9541 - TTCACCAATGATGTTTCATTCTTGGCTCACCTCAATGGTTGCCATGTTTTCTCCTATT - 9600  
- F T N D V S F L A H L Q W F A M F S P I  
- S P M M F H S W L T F N G L P C F L L L  
- H Q \* C F I L G S P S M V C H V F S Y C  
9601 - GTGCCTTTTTGGATAACAGCAATCTATGATATCTGATTTCTCTGAAGCACTGCCATTGG - 9660  
- V P F W I T A I Y V F C I S L K H C H W  
- C L F G \* Q Q S M Y S V F L \* S T A I G  
- A F L D N S N L C I L Y F S E A L F L V  
9661 - TTCTTTAAACAATCTTTAGGAAAAGATCATGTTTAAATGGAGTTACATTTAGTACCTTC - 9720  
- F F N N Y L R K R V M F N G V T F S T F  
- S L T I L G K E S C L M E L H L V P S  
- L \* Q L S \* E K S H V \* W S Y I \* Y L R  
9721 - GAGGAGGCTGCTTTGTGTACCTTTTGGCTCAACAAGGAAATGTACCTAAAATGCGTAGC - 9780  
- E E A A L C T F L I N K E M Y L K L R S  
- R R L L C V P F C S T R K C T \* N C V A  
- G G C F V Y L F A Q Q G N V P K I A \* R  
9781 - GAGACTGTTGCCACTTACACAGTATAACAGGTATCTTGTCTATATAACAAGTACAAG - 9840  
- E T L L P L T Q Y N R Y L A L Y N K Y K  
- R H C C H L H S I T G I L L Y I T S T S  
- D T V A T Y T V \* Q V S C S I \* Q V Q V  
9841 - TATTTAGTGGAGCCTTAGATACTACCAGCTATCGTGAAGCAGCTTGTGCTGCCACTTAGCA - 9900  
- Y F S G A L D T T S Y R E A A C C H L A  
- I S V E P \* I L P A I V K Q L A A T \* Q  
- F Q W S L R Y Y Q L S \* S S L L P L S K  
9901 - AAGGCTCTAAATGACTTTAGCAACTCAGGTGCTGATGTTCTCTACCAACCACCACAGACA - 9960  
- K A L N D F S N S G A D V L Y Q P P Q T  
- R L \* M T L A T Q V L M F S T N H H R H  
- G S K \* L \* Q L R C \* C S L P T T T D I  
9961 - TCAATCACTTCTGCTGTTCTGCAGAGTGGTTTTAGGAAAATGGCATTCCCGTCAGGCAAA - 10020  
- S I T S A V L Q S G F R K M A F P S G K  
- Q S L L L F C R V V L G K W H S R Q A K  
- N H F C C S A E W F \* E N G I P V R Q S  
10021 - GTTGAAGGGTGCATGGTACAAGTAACTGTGGAAGTACAAGTCTTAAATGGATTGTGGTTG - 10080  
- V E G C M V Q V T C G T T T L N G L W L  
- L K G A W Y K \* P V E L Q L L M D C G W  
- \* R V H G T S N L W N Y N S \* W I V V G

FIG. 11 Con't

10081 - GATGACACAGTATACTGTCCAAGACATGTCAATTTGCACAGCAGAAGACATGCTTAATCCT - 10140  
- D D T V Y C P R H V I C T A E D M L N P  
- M T Q Y T V Q D M S F A Q Q K T C L I L  
- \* H S I L S K T C H L H S R R H A \* S \*  
10141 - AACTATGAAGATCTGCTCATTCGCAAATCCAACCATAGCTTTCTTGTTCAGGCTGGCAAT - 10200  
- N Y E D L L I R K S N H S F L V Q A G N  
- T M K I C S F A N P T I A F L F R L A M  
- L \* R S A H S Q I Q P \* L S C S G W Q C  
10201 - GTTCAACTTCGTGTTATFGCCATTCTATGCAAAATGCTGCTTAGGCTTAAAGTTGAT - 10260  
- V Q L R V I G H S M Q N C L L R L K V D  
- F N F V L L A I L C K I V C L G L K L I  
- S T S C Y W P F Y A K L S A \* A \* S \* Y  
10261 - ACTTCTAACCTAAGACACCCCAAGTATAAATTTGTCCGTATCCAACCTGGTCAAACATT - 10320  
- T S N P K T P K Y K F V R I Q P G Q T F  
- L L T L R H P S I N L S V S N L V K H F  
- F \* P \* D T Q V \* I C P Y P T W S N I F  
10321 - TCAGTTCTAGCATGCTACAATGGTTCACCATCTGGTGTATATCAGTGTGCCATGAGACCT - 10380  
- S V L A C Y N G S P S G V Y Q C A M R P  
- Q F \* H A T M V H H L V F I S V P \* D L  
- S S S M L Q W F T I W C L S V C H E T \*  
10381 - AATCATACCATTAAGCTTCTTTCCTTAATGGATCATGTGGTAGTGTGGTTTTAACATT - 10440  
- N H T I K G S F L N G S C G S V G F N I  
- I I P L K V L S L M D H V V V L V L T L  
- S Y H \* R F F P \* W I M W \* C W F \* H \*  
10441 - GATTATGATTGCGTGTCTTTCTGCTATATGCATCATATGGAGCTTCCAACAGGAGTACAC - 10500  
- D Y D C V S F C Y M H H M E L P T G V H  
- I M I A C L S A I C I I W S F Q Q E Y T  
- L \* L R V F L L Y A S Y G A S N R S T R  
10501 - GCTGGTACTGACTTAGAAGCTAAATTCATGGTCCATTTGTTGACAGACAAACTGCACAG - 10560  
- A G T D L E G K E Y G P F V D R Q T A Q  
- L V L T \* K V N S M V H L L T D K L E R  
- W Y \* L R R \* I L W S I C \* Q T N C T G  
10561 - GCTGCAGGTACAGACACAACCATAACATTAATGTTTTGGCATGGCTGTATGCTGCTGTT - 10620  
- A A G T D T T I T L N V L A W L Y A A V  
- L Q V Q T Q P \* H \* M F W H G C M L L L  
- C R Y R H N H N I K C F G M A V C C C Y  
10621 - ATCAATGGTATAGGTGGTTTTCTTAATGATTCAACACTACTTTGAATGACTTTAACCTT - 10680  
- I N G D R W F L N R F T T T L N D F N L  
- S M V I G G F L I D S P L L \* M T L T L  
- Q W \* \* V V S \* \* I H H Y F E \* L \* P C  
10681 - GTGGCAATGAAGTACAACCTATGAACCTTTGACACAAGATCATGTTGACATATTGGGACCT - 10740  
- V A M K Y N Y E P L T Q D H V D I L G P  
- W Q \* S T T M N L \* H K I M L T Y W D L  
- G N E V Q L \* T F D T R S C \* H I G T S  
10741 - CTTTCTGCTCAAACAGGAATGCGCTCTTAGAATGTGTGCTGCTTTGAAAGAGCTGCTG - 10800  
- L S A Q T G I A V L D M C A A L K E L L  
- F L L K Q E L P S \* I C V L L \* K S C C  
- F C S N R N C R L R Y V C C F E R A A A  
10801 - CAGAATGGTATGAATGGTCTACTATCCTTGGTAGCACTATTTTAGAAGATGAGTTTACA - 10860  
- Q N G M N G R T I L G S T I L E D E F T  
- R M V \* M V V L S L V A L F \* K M S L H  
- E W Y E W S Y Y P W \* H Y F R R \* V Y T  
10861 - CCATTTGATGTTGTAGACAATGCTCTGGTGTACCTTCCAAGGTAAGTTCAAGAAAATT - 10920  
- P F D V V R Q C S G V T F Q G K E K K I  
- H L M L L D N A L V L P S K V S S R K L  
- I \* C C \* T M L W C Y L P R \* V Q E N C

FIG. 11 Con't

10921 - GTTAAGGGCACTCATCATTGGATGCTTTTAACTTICTTGACATCACTATTGATTCTTGT - 10980  
 - V K G T H H W M L L T F L T S L L I L V  
 - L R A L I I G C F \* L S \* H H Y \* F L F  
 - \* G H S S L D A F N F L D I T I D S C S  
 10981 - CAAAGTACACAGTGGTCACTGTTTCTTTGTTTACGAGAATGCTTCTTGCCATTACT - 11040  
 - Q S T Q W S L F F F V Y E N A F L P F T  
 - K V H S G H C F S L F T R M L S C H L L  
 - K Y T V V T V F L C L R E C F L A I Y S  
 11041 - CTGGTATTATGGCAATTGCTGCATGTGCTATGCTGCTGTTAAGCATAAGCACGCATTC - 11100  
 - L G I M A I A A C A M L L V K H K H A F  
 - L V L W Q L L H V L C C L L S I S T H S  
 - W Y Y G N C C M C Y A A C \* A \* A R I L  
 11101 - TTGTGCTTCTTTCTGTTACCTTCTTTCGCAACAGTTGCTTACTTTAATATGGTCTACATG - 11160  
 - L C L F L L P S L A T V A Y F N M V Y M  
 - C A C F C L L L Q Q L L T L I W S T C  
 - V L V S V T F S C N S C L L \* Y G L H A  
 11161 - CCTGCTAGCTGGGTGATGCGTATCATGACATGGCTTGAATTGGCTGACACTAGCTTGTCT - 11220  
 - P A S W V M R I M T W L E L A D T S L S  
 - L L A G \* C V S \* H G L N W L T L A C L  
 - C \* L G D A Y H D M A \* I G \* H \* L V W  
 11221 - GGTTATAGGCTTAAGGATTGTGTTATGTATGCTTCAGCTTTAGTTTTGCTTATTCTCATG - 11280  
 - G Y R L K D C V M Y A S A L V L L I L M  
 - V I G L R I V L C M L Q L \* F C L F S \*  
 - L \* A \* G L C Y V C F S F S F A Y S E D  
 11281 - ACAGCTCGCACTGTTTATGATGATGCTGCTAGACGTGTTGGACACTGATGAATGTCATT - 11340  
 - T A R T V Y D D A A R R V W T L M N V I  
 - Q L A L F M M M L L D V F G H \* \* M S L  
 - S S H C L \* \* C C \* T C L D T D E C H Y  
 11341 - ACACTGTTTACAAAGTCTACTATGGAATGCTTTAGATCAAGCTATTTCCATGTGGGCC - 11400  
 - T L V Y K V Y Y G N A L D Q A I S M W A  
 - H L F T K S T M V M L \* I K L F P C G P  
 - T C L Q S L L W \* C F R S S Y F H V G L  
 11401 - TTAGTATTCTGTAACCTCTAACTATTCTGGTGTGCTTACGACTATCATGTTTTAGCT - 11460  
 - L V E S V T S N Y S G V V T T I M F L A  
 - \* L F L \* P L T I L V S L R L S C F \* L  
 - S Y F C N L \* L F W C R Y D Y H V F S \*  
 11461 - AGAGCTATAGTGTGTTGTGTGTGATGATTACCCATTGTTATTTATTACTGGCAACACC - 11520  
 - R A I V F V C V E Y Y P L L F I T G N T  
 - E L \* C L C V L S I T H C Y L L L A T P  
 - S Y S V C V C \* V L P I V I Y Y W Q H L  
 11521 - TTACAGTGTATCATGCTTGTGTTATTGTTTCTTAGGCTATTGTTGCTGCTGCTACTTTGGC - 11580  
 - L Q C I M L V Y C F L G Y C C C C Y F G  
 - Y S V S C L F I V S \* A I V A A A T L A  
 - T V Y H A C L L F L R L L L L L L W P  
 11581 - CTTTCTGTTTACTCAACCGTTACTTCAGGCTTACTCTTGGTGTGTTATGACTACTTGGTC - 11640  
 - L F C L L N R Y F R L T L G V Y D Y L V  
 - F S V Y S T V T S G L L L V F M T T W S  
 - F L F T Q P L L Q A Y S W C L \* L L G L  
 11641 - TCTACACAAGAATTTAGGTATATGAACCTCCAGGGGCTTTTGCCTCCTAAGAGTAGTATT - 11700  
 - S T Q E F R Y M N S Q G L L P P K S S I  
 - L H K N L G I \* T P R G F C L L R V V L  
 - Y T R I \* V Y E L P G A F A S \* E \* Y \*  
 11701 - GATGCTTTCAGGCTTAACATTAAGTTGTTGGGTATTGGAGGTAAACCATGTATCAAGGTT - 11760  
 - D A F K L N I K L L G I G G K P C I K V  
 - M L S S L T L S C W V L E V N H V S R L  
 - C F Q A \* H \* V V G Y W R \* T M Y Q G C

FIG. 11 Con't

11761 - GCTACTGTACAGTCTAAAATGTCTGACGTAAAGTGCACATCTGTGGTACTGCTCTCGGTT - 11820  
 - A T V Q S K M S D V K C T S V V L L S V  
 - L L Y S L K C L T \* S A H L W Y C S R F  
 - Y C T V \* N V \* R K V H I C G T A L G S  
 11821 - CTTCAACAACCTTAGAGTAGAGTCATCTTCTAAATTGTGGGCACAATGTGTACAACCTCCAC - 11880  
 - L Q Q L R V E S S S K L W A Q C V Q L H  
 - F N N L E \* S H L L N C G H N V Y N S T  
 - S T T \* S R V I F \* I V G T M C T T P Q  
 11881 - AATGATATTCTTCTTGCAAAGACACAACCTGAAGCTTCGAGAAGATGGTTCTCTTTTG - 11940  
 - N D I L L A K D T T E A F E K M V S L L  
 - M I F F L Q K T Q L K L S R R W F L F C  
 - \* Y S S C K R H N \* S F R E D G F S F V  
 11941 - TCTGTTTTGCTATCCATGCAGGGTCTGTAGACATTAATAGGTTGTGCGAGGAAATGCTC - 12000  
 - S V L L S M Q G A V D I N R L C E E M L  
 - L F C Y P C R V L \* T L I G C A R K C S  
 - C F A I H A G C C R H \* \* V V R G N A R  
 12001 - GATAACCGTGCTACTCTTCAGGCTATTGCTTCAGAATTTAGTTCTTACCATCATATGCC - 12060  
 - D N R A T L Q A I A S E F S S L P S Y A  
 - I T V L L F R L L L Q N L V L Y H H M P  
 - \* P C Y S S G Y C F R I \* F F T I I C R  
 12061 - GCTTATGCCACTGCCCGAGGCTATGAGCAGGCTGTAGCTAATGGTGATTTCTGAAGTC - 12120  
 - A Y A T A Q R A Y E Q A V A N G D S E V  
 - L M P L P R R P M S R L \* L M V I L K S  
 - L C H C P G G L \* A G C S \* W \* F \* S R  
 12121 - GTTCTCAAAAAGTTAAAGAAATCTTGAATGTGGCTAAAATCTGAGTTTGACCGTGATGCT - 12180  
 - V L K K L K K S L N V A K S E F D R D A  
 - F S K S \* R N L \* M W L N L S L T V M L  
 - S Q K V K E I F E C G \* I \* V \* P \* C C  
 12181 - GCCATGCAACGCAAGTTGGAAAAGATGGCAGATCAGGCTATGACCCAAATGTACAAACAG - 12240  
 - A M Q R K L E K M A D Q A M T Q M Y K Q  
 - P C N A S W K R W Q I R L \* P K C T N R  
 - H A T Q V G K D G R S G Y D P N V Q T G  
 12241 - GCAAGATCTGAGGACAAGAGGGCAAAAGTAACTAGTGCTATGCAACAATGCTCTTCACT - 12300  
 - A R S E D K R A K V T S A M Q T M L F T  
 - Q D L R T R G Q K \* L V L C K Q C S S L  
 - K I \* G Q E G K S N \* C Y A N N A L H Y  
 12301 - ATGCTTAGGAAGCTTGATAATGATGCACTTAACAACATTATCAACAATGCGCGTGATGGT - 12360  
 - M L R K L D N D A L N N I I N N A R D G  
 - C L G S L I M M H L T T L S T M R V M V  
 - A \* E A \* \* \* C T \* Q H Y Q Q C A \* W L  
 12361 - TGTGTTCCACTCAACATCATACCATTGACTACAGCAGCCAAACTCATGGTTGTTGTCCT - 12420  
 - C V P L N I I P L T T A A K L M V V V P  
 - V F H S T S Y H \* L Q Q P N S W L L S L  
 - C S T Q H H T I D Y S S Q T H G C C P \*  
 12421 - GATTATGGTACCTACAAGAACACTTGTGATGGTAACACCTTTACATATGCATCTGCACTC - 12480  
 - D Y G T Y K N T C D G N T P F T Y A S A L  
 - I M V P T R T L V M V T P L H M H L H S  
 - L W Y L Q E H L \* W \* H L Y I C I C T L  
 12481 - TGGGAAATCCAGCAAGTTGTTGATGCGGATAGCAAGATTGTTCAACTTAGTGAATTAAC - 12540  
 - W E I Q Q V V D A D S K I V Q L S E I N  
 - G K S S K L L M R I A R L F N L V K L T  
 - G N P A S C \* C G \* Q D C S T \* \* N \* H  
 12541 - ATGGACAATTCACCAAATTTGGCTTGGCCTCTTATTGTTACAGCTCTAAGAGCCAACTCA - 12600  
 - M D N S P N L A W P L I V T A L R A N S  
 - W T I H Q I W L G L L L L Q L \* E P T Q  
 - G Q F T K F G L A S Y C Y S S K S Q L S

FIG. 11 Con't

12601 - GCTGTAAACTACAGAATAATGAAGTCCAGTCCAGTACACTACGACAGATGTCCTGTGCG - 12660  
 - A V K L Q N N E L S P V A L R Q M S C A  
 - L L N Y R I M N \* V Q \* H Y D R C P V R  
 - C \* T T E \* \* T E S S S T T T D V L C G  
 12661 - GCTGGTACCACACAAACAGCTTGTACTGATGACAATGCACCTGCCTACTATAACAATTCG - 12720  
 - A G T T Q T A C T D D N A L A Y Y N N S  
 - L V P H K Q L V L M T M H L P T I T I R  
 - W Y H T N S L Y \* \* Q C T C L L \* Q F E  
 12721 - AAGGGAGGTAGGTTGTGCTGGCATTACTATCAGACCACCAAGATCTCAAATGGGCTAGA - 12780  
 - K G G R F V L A L L S D H Q D L K W A R  
 - R E V G L C W H Y Y Q T T K I S N G L D  
 - G R \* V C A G I T I R P P R S Q M G \* I  
 12781 - TTCCCTAAGAGTGATGGTACAGGTACAATTTACACAGAAGTGAACCACCTTGTAGGTTT - 12840  
 - F P K S D G T G T I Y T E L E P P C R F  
 - S L R V M V Q V Q F T Q N W N H L V G L  
 - P \* E \* W Y R Y N L H R T G T T L \* V C  
 12841 - GTTACAGACACACAAAAGGGCCTAAAGTGAATACTTGTACTTCATCAAAGGCTTAAAC - 12900  
 - V T D T P K G P K V K Y L Y F L K G L N  
 - L Q T H Q K G L K \* N T C T S S K A \* T  
 - Y R H T K R A \* S E I L V L H Q R L K Q  
 12901 - AACCTAAATAGAGGTATGGTCTGGGAGTTTAGCTGCTACAGTACGTCCTCAGGCTGGA - 12960  
 - N L N R G M V L G S L A A T V R L Q A G  
 - T \* I E V W C W A V \* L L Q Y V F R L E  
 - P K \* R Y G A G Q F S C Y S T S S G W K  
 12961 - AATGTACAGAAGTACCTGCCAATTCAACTGTGCTTTCCTTCTGTGCTTTTGCAGTAGAC - 13020  
 - N A T E V P A N S T V L S F C A F A V D  
 - M L Q K Y L P I Q L C F P S V L L Q \* T  
 - C Y R S T C Q F N C A F L L C F C S R P  
 13021 - CCTGCTAAAGCATATAAGGATTACCTAGCAAGTGGAGGACAACCAATCACCAACTGTGTG - 13080  
 - P A K A Y K D Y L A S G G Q P I T N C V  
 - L L K H I R I T \* Q V E D N Q S P T V \*  
 - C \* S I \* G L P S K W R T T N H Q L C E  
 13081 - AAGATGTTGTGTACACACTGGTACAGGACAGGCAATTACTGTAACACCAGAAGCTAAC - 13140  
 - K M L C T H T G T G Q A I T V T P E A N  
 - R C C V H T L V Q D R Q L L \* H Q K L T  
 - D V V Y T H W Y R T G N Y C N T R S \* H  
 13141 - ATGGACCAAGAGTCCCTTTGGTGGTCTTCATGTTGTCTGTATTGTAGATGCCACATTGAC - 13200  
 - M D Q E S F G G A S C C L Y C R C H I D  
 - W T K S P L V V L H V V C I V D A T L T  
 - G P R V L W W C F M L S V L \* M P H \* P  
 13201 - CATCCAAATCCTAAAGGATTCTGTGACTTGAAAGGTAAGTACGTCCAAATACCTACCACT - 13260  
 - H P N P K G F C D L K G K Y V Q I P T T  
 - I Q I L K D S V T \* K V S T S K Y L P L  
 - S K S \* R I L \* L E R \* V R E N T Y H L  
 13261 - TGTGCTAATGACCCAGTGGGTTTACACTTAGAAACACAGTCTGTACCGTCTGCGGAATG - 13320  
 - C A N D P V G F T L R N T V C T V C G M  
 - V L M T Q W V L H L E T Q S V P S A E C  
 - C \* \* P S G F Y T \* K H S L Y R L R N V  
 13321 - TGGAAAGGTTATGGCTGTAGTTGTGACCAACTCCGGAACCCTTGATGCAGTCTGCGGAT - 13380  
 - W K G Y G C S C D Q L R E P L M Q S A D  
 - G K V M A V V V T N S A N P \* C S L R M  
 - E R L W L \* L \* P T P R T L D A V C G C  
 13381 - GCATCAACGTTTTTAAACGGGTTTGGGGTGTAAAGTGCAGCCCGTCTTACACCGTCCGGCA - 13440  
 - A S T F L N G F A V \* V Q P V L H R A A  
 - H Q R F \* T G L R C K C S P S Y T V R H  
 - I N V F K R V C G V S A A R L T P C G T

FIG. 11 Con't



13441 - CAGGCACTAGTACTGATGTCGTCTACAGGGCTTTTGATATTTACAACGAAAAAAGTGCTG - 13500  
 - Q A L V L M S S T G L L I F T T K K V L  
 - R H \* Y \* C R L Q G F \* Y L Q R K K C W  
 - G T S T D V V Y R A F D I Y N E K S A G  
 13501 - GTTTTGCAAAGTTCCATAAAACTAATTGCTGTCGCTTCCAGGAGAAGGATGAGGAAGGCA - 13560  
 - V L Q S S \* K L I A V A S R R R M R K A  
 - F C K V P K N \* L L S L P G E G \* G R Q  
 - F A K F L K T N C C R F Q E K D E E G N  
 13561 - ATTTATTAGACTCTTACTTGTAGTTAAGAGGCATACTATGTCTAACTACCAACATGAAG - 13620  
 - I Y \* T L T L \* L R G I L C L T T N M K  
 - F I R L L L C S \* E A Y Y V \* L P T \* R  
 - L L D S Y F V V K R H T M S N Y Q H E E  
 13621 - AGACTATTTATAACTTGGTTAAAGATTGTCCACCGGTTGCTGTCCATGACTTTTTCAAGT - 13680  
 - R L F I T W L K I V Q R L L S M T F S S  
 - D Y L \* L G \* R L S S G C C P \* L F Q V  
 - T I Y N L V K D C P A V A V H D F F K F  
 13681 - TTAGAGTAGATGGTGACATGGTACCACATATATCACGTCAGCGTCTAACTAAATACACAA - 13740  
 - L E \* M V T W Y H I Y H V S V \* L N T Q  
 - \* S R W \* H G T T Y I T S A S N \* I H N  
 - R V D G D M V P H I S R Q R L T K Y T M  
 13741 - TGGCTGATTTAGTCTATGCTCTACGTCATTTTGATGAGGGTAATTGTGATACATTAAG - 13800  
 - W L I \* S M L Y V I L M R V I V I E \* K  
 - G \* F S L C S T S F \* \* G \* L \* Y I K R  
 - A D L V Y A L R H F D E G N C D T L K E  
 13801 - AAATACTCGTCACATACAATTGCTGTGATGATGATTATTTCAATAAGAAGGATTGGTATG - 13860  
 - K Y S S H T I A V M M I I S I R R I G M  
 - N T R H I Q L L \* \* \* L F Q \* E G L V \*  
 - I L V T Y N C C D D D Y F N K K D W Y D  
 13861 - ACTTCGTAGAGAATCCTGACATCTTACCGGTATATGCTAACTTAGGTGAGCGGTACGCC - 13920  
 - T S \* R I L T S Y A Y M L T \* V S V Y A  
 - L R R E S \* H L T R I C \* L R \* A C T P  
 - F V E N P D I L R V Y A N L G E R V R Q  
 13921 - AATCATTATTAAGACTGTACAATTCTGCGATGCTATGCGTGATGAGGCAITGTAGGCG - 13980  
 - N H Y \* R L Y N S A M L C V M Q A L \* A  
 - I I I K D C T I L R C Y A \* C R H C R R  
 - S L L K T V Q F C D A M R D A G I V G V  
 13981 - TACTGACATTAGATAATCAGGATCTTAATGGGAAGGATGACGATTTCGGTGATTTCGTAC - 14040  
 - Y \* H \* I I R I L M G T G T I S V I S Y  
 - T D I R \* S G S \* W E L V R F R \* F R T  
 - L T L D N Q D L N G N W Y D F G D F V Q  
 14041 - AAGTAGCACCAGGCTGCGGAGTTCCTATTGTGGATTTCATTACTCATTGCTGATGCCCA - 14100  
 - K \* H Q A A E F L L W I H I T H C \* C P  
 - S S T R L R S S Y C G F I L L I A D A H  
 - V A P G C G V P I V D S Y Y S L L M P I  
 14101 - TCCTCACTTTGACTAGGGCATTGGCTGCTGAGTCCCATATGGATGCTGATCTCGCAAAC - 14160  
 - S S L \* L G H W L L S P I W M L I S Q N  
 - P H F D \* G I G C \* V P Y G C \* S R K T  
 - L T L T R A L A A E S H M D A D L A K P  
 14161 - CACTTATTAAGTGGGATTTGCTGAAATATGATTTTACGGAAGAGAGACTTTGTCTCTTCG - 14220  
 - H L L S G I C \* N M I L R K R D F V S S  
 - T Y \* V G F A E I \* F Y G R E T L S L R  
 - L I K W D L L K Y D F T E E R L C L F D  
 14221 - ACCGTTATTTTAAATATTGGGACCAGACATACCATCCCAATTGTATTAAGTGTGGATG - 14280  
 - T V I L N I G T R H T I P I V L T V W M  
 - P L F \* I L G P D I P S Q L Y \* L F G \*  
 - R Y F K Y W D Q T Y H P N C I N C L D D

FIG. 11 Con't

14281 - ATAGGTGTATCCTTCATTGTGCAAACTTTAATGTGTTATTTTCTACTGTGTTTCCACCTA - 14340  
 - I G V S F I V Q T L M C Y F L L C F H L  
 - \* V Y P S L C K L \* C V I F Y C V S T Y  
 - R C I L H C A N F N V L F S T V F P P T

14341 - CAAGTTTGGACCCTAGTAAGAAAAATATTGTAGATGGTGTTCCTTTTGTGTTCAA - 14400  
 - Q V L D H \* \* E K Y L \* M V F L L L F Q  
 - K F W T T S K K N I C R W C S F C C F N  
 - S F G P L V R K I F V D G V P F V V S T

14401 - CTGGATACCATTTTTCGTGAGTTAGGAGTCGTACATAATCAGGATGTAACCTACATAGCT - 14460  
 - L D T I F V S \* E S Y I I R M \* T Y I A  
 - W I P F S \* V R S R T \* S G C K L T \* L  
 - G Y H F R E L G V V H N Q D V N L H S S

14461 - CGCGTCTCAGTTTCAAGGAAGTTTACTGTGCTGCTGATCCAGCTATGCATGCAGCTT - 14520  
 - R V S V S R N F \* C M L L L I Q L C M Q L  
 - A S Q F Q G T F S V C C \* S S Y A C S F  
 - R L S F K E L L V Y A A D P A M H A A S

14521 - CTGGCAATTTATTGCTAGATAAACGCACTACATGCTTTTCAGTAGCTGCCTAACAAACA - 14580  
 - L A I Y C \* I N A L H A F Q \* L H \* Q T  
 - W Q F I A R \* T H Y M L F S S C T N K Q  
 - G N L L L D K R T T C F S V A A L T N N

14581 - ATGTTGCTTTTCAAAGTGTCAAACCCGGTAATTTTAAATAAGACTTTTATGACTTTGCTG - 14640  
 - M L L F K L S N P V I L I K T F M T L L  
 - C C F S N C Q T R \* F \* \* R L L \* L C C  
 - V A F Q T V K F G N F N K D F Y D F A V

14641 - TGTCTAAAGGTTTCTTTAAGGAAGGAGTTCGTGTAACATAAACTTCTTCTTTGCTC - 14700  
 - C L K V S L R K E V L L N \* N T S S L L  
 - V \* R F L \* G R K F C \* T K T L L L C S  
 - S K G F F K E G S S V E L K H F F F A Q

14701 - AGGATGGCAACGCTGCTATCAGTGATTATGACTATTATCGTTATAATCTGCCAACAAATGT - 14760  
 - R M A T L L S V I M T I I V E I C Q Q C  
 - G W Q R C Y Q \* L \* L L S L \* S A N N V  
 - D G N A A I S D Y D Y Y R Y N L P T M C

14761 - GTGATATCAGACAACCTCCTATTCCTAGTGAAGTTGTTGATAAATACTTTGATTGTTACC - 14820  
 - V I S D N S Y S \* L K L L I N T L I V T  
 - \* Y Q T T P I R S \* S C \* \* I L \* L L R  
 - D I R Q L L F V V E V V D K Y F D C Y D

14821 - ATGGTGGCTGTATTAATGCCAACCAAGTAATCGTTAACAACTGGATAAATCAGCTGGTT - 14880  
 - M V A V L M P T K \* S L T I W I N Q L V  
 - W W L Y \* C Q P S N R \* Q S G \* I S W F  
 - G G C I N A N Q V I V N N L D K S A G F

14881 - TCCCATTTAATAAATGGGGTAAGGCTAGACTTTATTATGACTCAATGAGTTATGAGGATC - 14940  
 - S H L I N G V R L D F I M T Q \* V M R I  
 - P I \* \* M G \* G \* T L L \* L N E L \* G S  
 - P F N K W G K A R L Y Y D S M S Y E D Q

14941 - AAGATGCACTTTTCGCGTATACTAAGCGTAATGTATCCCTACTATAACTCAAATGAATC - 15000  
 - K M H F S R I L S V M S S L L \* L K \* I  
 - R C T F R V Y \* A \* C H P Y Y N S N E S  
 - D A L F A Y T K R N V I P T I T Q M N L

15001 - TTAAGTATGCCATTAGTGCAAAGAAAGAGCTCGCACCGTAGCTGGTGTCTCTATCTGTA - 15060  
 - L S M P L V Q R I E L A P \* I V S L S V  
 - \* V C H \* C K E \* S S H R S W C L Y L \*  
 - K Y A I S A K N R A R T V A G V S I C S

15061 - GTACTATGACAAATAGACAGTTTCATCAGAAATTTATGAAGTCAATAGCCGCCACTAGAG - 15120  
 - V L \* Q I D S F E R N Y \* S Q \* P P L E  
 - Y Y D K \* T V S S E I I E V N S R H \* R  
 - T M T N R Q F E Q K L L K S I A A T R G

FIG. 11 Con't

15121 - GAGCTACTGTGGTAATGGAACAAGCAAGTTTTACGGTGGCTGGCATAATATGTTAAAAA - 15180  
 - E L L W \* L E Q A S F T V A G I I C \* K  
 - S Y C G N W N K Q V L R W L A \* Y V K N  
 - A T V V I G T S K F Y G G W H N M L K T  
 15181 - CTGTTTACAGTGATGTAGAAACTCCACACCTTATGGGTTGGGATTATCCAAAATGTGACA - 15240  
 - L F T V M \* K L H T L W V G I I Q N V T  
 - C L Q \* C R N S T P Y G L G L S K M \* Q  
 - V Y S D V E T P H L M G W D Y P K C D R  
 15241 - GAGCCATGCCTAACATGCTTAGGATAATGGCCTCTCTTGTCTTGCTCGCAAACATAACA - 15300  
 - E P C L T C L G \* W P L L F L L A N I T  
 - S H A \* H A \* D N G L S C S C S Q T \* H  
 - A M P N M L R I M A S L V L A R K E N T  
 15301 - CTTGCTGTAACCTTATCACACCGTTTCTACAGGTTAGCTAACGAGTGTGCGCAAGTATTAA - 15360  
 - L A V T Y H T V S T G \* L T S V R K Y \*  
 - L L \* L I T P F L Q V S \* R V C A S I K  
 - C C N L S H R F Y R L A N E C A Q V L S  
 15361 - GTGATGGTTCATGTGTGGCGGCTCACTATATGTTAAACCAGGTGGAACATCATCCGGTG - 15420  
 - V R W S C V A A H Y M L N Q V E R H P V  
 - \* D G H V W R L T I C \* T R W N I I R \*  
 - E M V M C G G S L Y V K P G G T S S G D  
 15421 - ATGCTACAACCTGCTTATGCTAATAGTGTCTTTAACATTTGTCAAGCTGTTACAGCCAATG - 15480  
 - M L Q L L M L I V S L T F V K L L Q P M  
 - C Y N C L C \* \* C L \* H L S S C Y S Q C  
 - A T T A Y A N S V F N I C Q A V T A N V  
 15481 - TAAATGCACTTCTTTCAACTGATCGTAATAAGATAGCTGACAAGTATGTCCGCAATCTAC - 15540  
 - \* M H F F Q L M V I R \* L T S M S A I Y  
 - K C T S F N \* W \* \* D S \* Q V C P Q S T  
 - N A L L S T D G N K I A D K Y V R N L Q  
 15541 - AACACAGSCTCTATGAGTGTCTCTATAGAAATAGGGATGTTGATCATGAATTCGTGGATG - 15600  
 - N T G S M S V S I E I G M L I M N S W M  
 - T Q A L \* V S L \* K \* G C \* S \* I R G \*  
 - H R L Y E C L Y R N R D V D H E F V D E  
 15601 - AGTTTTACGCTTACCTGCGTAAACATTTCTCCAPGATGATTTCTTTCTGATGATGCCGTTG - 15660  
 - S F T L T C V N I S P \* \* F F L M M P L  
 - V L R L P A \* T F L H D D S F \* \* C R C  
 - F Y A Y L R K H F S M M I L S D D A V V  
 15661 - TGTGCTATAACAGTAACTATGCGGCTCAAGGTTTGTAGTACGATTAAGAACITTAAGG - 15720  
 - C A I T V T M R L K V \* \* L A L R T L R  
 - V L \* Q \* L C G S R F S S \* H \* E L \* G  
 - C Y N S N Y A A Q G L V A S I K N F K A  
 15721 - CAGTCTTTTATTATCAAAAIAATGTGTTTCATGTCTGAGGCAAAATGTTGGACTGAGACTG - 15780  
 - Q F F I I K I M C S C L R Q N V G L R L  
 - S S L L S K \* C V H V \* G K M L D \* D \*  
 - V L Y Y Q N N V F M S E A K C W T E T D  
 15781 - ACCTTACTAAAGGACCTCACGAATTTGCTCACAGCATAACATGCTAGTTAAACAAGGAG - 15840  
 - T L L K D L T N F A H S I Q C \* L N K E  
 - P Y \* R T S R I L L T A Y N A S \* T R R  
 - L T K G P H E F C S Q H T M L V X Q G D  
 15841 - ATGATTACGTGTACCTGCCTTACCCAGATCCATCAAGAATATTAGGCGCAGGCTGTTTTG - 15900  
 - M I T C T C L T Q I H Q E Y \* A Q A V L  
 - \* L R V P A L P R S I K N I R R R L F C  
 - D Y V Y L P Y P D P S R I L G A G C F V  
 15901 - TCGATGATATTGTCAAACAGATGCTACACTTATGATTGAAAGGTTTCGTGCTCACTGGCTA - 15960  
 - S M I L S K Q M V H L \* L K G S C H W L  
 - R \* Y C Q N R W Y T Y D \* K V R V T G Y  
 - D D I V K T D G T L M I E R F V S L A I

FIG. 11 Con't

15961 - TTGATGCTTACCCACTTACAAAACATCCTAATCAGGAGTATGCTGATGCTTTCACTTGT - 16020  
 - L M L T H L Q N I L I R S M L M S F T C  
 - \* C L P T Y K T S \* S G V C \* C L S L V  
 - D A Y P L T K H P N Q E Y A D V F H L Y  
 16021 - ATTTACAATACATTAGAAAGTTACATGATGAGCTTACTGGCCACATGTTGGACATGTATT - 16080  
 - I Y N T L E S Y M M S L L A T C W T C I  
 - F T I H \* K V T \* \* A Y W P H V G H V F  
 - L Q Y I R K L H D E L T G H M L D M Y S  
 16081 - CCGTAATGCTAACTAATGATAACACCTCACGGTACTGGGAACCTGAGTTTATGAGGCTA - 16140  
 - P \* C \* L M I T P H G T G N L S F M R L  
 - R N A N \* \* \* H L T V L G T \* V L \* G Y  
 - V M L T N D N T S R Y W E P E F Y E A M  
 16141 - TGTCACACCACATACAGTCTTGCAGGCTGTAGGTGCTTGTGATTGTGCAATTCACAGA - 16200  
 - C T H H I Q S C R L \* V L V Y C A I H R  
 - V H T T Y S L A G C R C L C I V Q F T D  
 - Y T P H T V L Q A V G A C V L C N S Q T  
 16201 - CTTCACTTCGTTGCGGTGCCTGTATTAGGAGACCATTCCCTATGTTGCAAGTGCTGCTATG - 16260  
 - L H F V A V P V L G D H S Y V A S A A M  
 - F T S L R C L Y \* E T I P M L Q V L L \*  
 - S L R C G A C I R R P F L C C K C C Y D  
 16261 - ACCATGTCATTCAACATCACACAAATAGTGTGTCTGTTAATCCCTATGTTTGAATG - 16320  
 - T M S F Q H H T N \* C C L L I P M F A M  
 - P C H F N I T Q I S V V C \* S L C L Q C  
 - H V I S T S H K L V L S V N P Y V C N A  
 16321 - CCCCAGGTTGTGATGTCACTGATGTGACACAACCTGATCTAGGAGGTATGAGCTATTATT - 16380  
 - P Q V V M S L M \* H N C I \* E V \* A I I  
 - P R L \* C H \* C D T T V S R R Y E L L L  
 - P G C D V T D V T Q L Y L G G M S Y Y C  
 16381 - GCAAGTCACATAAGCCTCCCATTAGTTTCCATTATGTGCTAATGGTCAGGTTTTGGTT - 16440  
 - A S H I S L P L V F H Y V L M V R F L V  
 - Q V T \* A S H \* F S I M C \* W S G F W F  
 - K S H K P P I S F P L C A N G Q V F G L  
 16441 - TATACAAAACACATGTGTAGGCAGTGACAATGTCACTGACTTCAATGCGATAGCAACAT - 16500  
 - Y T K T H V \* A V T M S L T S M R \* Q H  
 - I Q K H M C R Q \* Q C H \* L Q C D S N M  
 - Y K N T C V G S D N V T D F N A I A T C  
 16501 - GTGATTGGACTAATGCTGGCGATTACATACTTGCCAACACTGTACTGAGAGACTCAAGC - 16560  
 - V I G L M L A I T Y L P T L V L R D S S  
 - \* L D \* C W R L H T C Q H L Y \* E T Q A  
 - D W T N A G D Y I L A N T C T E R L K L  
 16561 - TTTTCGCAGCAGAAACCGCTCAAAGCCACTGAGGAAACATTTAAGCTGTCATATGGTATTG - 16620  
 - F S Q Q K R S K P L R K H L S C H M V L  
 - F R S R N A Q S H \* G N I \* A V I W Y C  
 - F A A E T L K A T E E T F K L S Y G I A  
 16621 - CCACTGTACGCGAAGTACTCTCTGACAGAGAATTGCATCTTTCATGGGAGGTTGAAAAC - 16680  
 - P L Y A K Y S L T E N C I F H G R L E N  
 - H C T R S T L \* Q R I A S F M G G W K T  
 - T V R E V L S D R E L H L S W E V G K P  
 16681 - CTAGACCACCATTGAACAGAAACTATGTCTTACTGGTTACCGTGTAACTAAAANTAGTA - 16740  
 - L D H H \* T E T M S L L V T V \* L K I V  
 - \* T T I E Q K L C L Y W L P C N \* K \* \*  
 - R P P L N R N Y V F T G Y R V T K N S K  
 16741 - AAGTACAGATTGGAGAGTACACCTTGAAAAGGTGACTATGGTGTGCTGTTGTGTACA - 16800  
 - K Y R L E S T P L K K V T M V M L L C T  
 - S T D W R V H L \* K R \* L W \* C C C V Q  
 - V Q I G E Y T F E K G D Y G D A V V Y R

FIG. 11 Con't

16801 - GAGGTACTACGACATACAAGTTGAATGTTGGTGATTACTTTGTGTTGACATCTCACACTG - 16860  
 - E V L R H T S \* M L V I T L C \* H L T L  
 - R Y Y D I Q V E C W \* L L C V D I S H C  
 - G T T T Y K L N V G D Y F V L T S H T V  
 16861 - TAATGCCACTTAGTGACCTACTCTAGTGCCACAAGGACTATGTGAGAAATTACTGGCT - 16920  
 - \* C H L V H L L \* C H K S T M \* E L L A  
 - N A T \* C T Y S S A T R A L C E N Y W L  
 - M P L S A P T L V P Q E H Y V R I T G L  
 16921 - TGTACCCAACACTCAACATCTCAGATGAGTTTTCTAGCAATGTTGCAATTATCAAAAAGG - 16980  
 - C T Q H S T S Q M S F L A M L Q I I K R  
 - V P N T Q H L R \* V F \* Q C C K L S K G  
 - Y P T L N I S D E F S S N V A N Y Q K V  
 16981 - TCGGCATGCAAAAGTACTCTACACTCCAAGGACCACCTGGTACTGGTAAGAGTCATTTTG - 17040  
 - S A C K S T L H S K D H L V L V R V I L  
 - R H A K V L Y T P R T T W Y W \* E S F C  
 - G M Q K Y S T L Q G P P G T G K S H F A  
 17041 - CCATCGGACTTGCTCTATTACCCATCTGCTCGCATAGTGATATACGGCATGCTCTCATG - 17100  
 - P S D L L S I T H L L A \* C I R H A L M  
 - H R T C S L L P I C S H S V Y G M L S C  
 - I G L A L Y Y P S A R I V Y T A C S H A  
 17101 - CAGCTGTGATGCCCTATGTGAAAAGGCATTAATAATTTGCCCATAGATAAATGTAGTA - 17160  
 - Q L L M P Y V K R H \* N I C P \* I N V V  
 - S C \* C P M \* K G I K I F A H R \* M \* \*  
 - A V D A L C E K A L K Y L P I D K C S R  
 17161 - GAATCATACCTGCGCGTGC GCGTAGAGTGTGATAAATTCAAAGTGAATTCAACAC - 17220  
 - E S Y L R V R A \* S V L I N S K \* I Q H  
 - N H T C A C A R R V F \* \* I Q S E F N T  
 - I I P A R A R V E C F D K F K V N S T L  
 17221 - TAGAACAGTATGTTTTCTGCACTGTAATGCATTGCCAGAAACAACCTGCTGACATTGTAG - 17280  
 - \* N S M F S A L \* M H C Q K Q L L T L \*  
 - R T V C F L H C K C I A R N N C \* H C S  
 - E Q Y V F E C T V N A L P E T T A D I V V  
 17281 - TCTTTGATGAAATCTCTATGGCTACTAATTAGACTTGAGTGTGTC AATGCTAGACTTC - 17340  
 - S L M K S L W L L I M T \* V L S M L D F  
 - L \* \* N L Y G Y \* L \* L E C C Q C \* T S  
 - F D E I S M A T N Y D L S V V N A R L R  
 17341 - GTGCAAAACACTACGTCTATATTGGCGATCCTGCTCAATTACCAGCCCCCGCACATTGC - 17400  
 - V Q N T T S I L A I L L N Y Q P P A H C  
 - C K T L R L Y W R S C S I T S P P H I A  
 - A K H Y V Y I G D P A Q L P A P R T L L  
 17401 - TGAATAAAGGCACACTAGAACAGAAATATTTTAATTCAGTGTGCAGACTTATGAAAACAA - 17460  
 - \* L K A H \* N Q N I L I Q C A D L \* K Q  
 - D \* R H T R T R I F \* F S V Q T Y E N N  
 - T K G T L E P E Y F N S V C R L M K T I  
 17461 - TAGGTCCAGACATGTTCCCTTGGAACTGTGCGCGTGTGCTGCTGAAATGTTGACACTG - 17520  
 - \* V Q T C S L E L V A V V L L K L L T L  
 - R S R H V P W N L S P L S C \* N C \* H C  
 - G P D M F L G T C R R C P A E I V D T V  
 17521 - TGAGTGCTTTAGTTTATGACAATAAGCTAAAAGCACACAAGGATAAGTCAGCTCAATGCT - 17580  
 - \* V L \* F M T I S \* K H T R I S Q L N A  
 - E C F S L \* Q \* A K S T Q G \* V S S M L  
 - S A L V Y D N K L K A H K D K S A Q C F  
 17581 - TCAAATGTTCTACAAAGGTGTTATTACACAIGATGTTTCATCTGCAATCAACAGACCTC - 17640  
 - S K C S T K V L L H M M F H L Q S T D L  
 - Q N V L Q R C Y Y T \* C F I C N Q Q T S  
 - K M F Y K G V I T H D V S S A I N R P Q

FIG. 11 Con't

17641 - AAATAGGCGTTGTAAGAGAATTTCTTACACGCAATCCTGCTTGGAGAAAAGCTGTTTTTA - 17700  
 - K \* A L \* E N F L H A I L L G E K L F L  
 - N R R C K R I S Y T Q S C L E K S C F Y  
 - I G V V R E F L T R N P A W R K A V F I  
 17701 - TCTCACCTTATAATTCACAGAACGCTGTAGCTTCAAAAATCTTAGGATTGCCTACGCAGA - 17760  
 - S H L I I H R T L \* L Q K S \* D C L R R  
 - L T L \* F T E R C S F K N L R I A Y A D  
 - S P Y N S Q N A V A S K I L G L P T Q T  
 17761 - CTGTTGATTTCATCACAGGGTTCGAATATGACTATGTCATATTCACACAACTACTGAAA - 17820  
 - L L I H H R V L N M T M S Y S H K L L K  
 - C \* F I T G F \* I \* L C H I H T N Y \* N  
 - V D S S Q G S E Y D Y V I F T Q T T E T  
 17821 - CAGCACACTCTTGTAAATGTCAACCGCTCAATGTGGCTATCACAAGGGCAAAAATGGCA - 17880  
 - Q H T L V M S T A S M W L S Q G Q K L A  
 - S T L L \* C Q P L Q C G Y H K G K N W H  
 - A H S C N V N R F N V A I T R A K I G I  
 17881 - TTTTGTGCATAATGTCTGATAGAGATCTTATGACAACTGCAATTTACAAGTCTAGAAA - 17940  
 - F C A \* C L I E I F M T N C N L Q V \* K  
 - F V H N V \* \* R S L \* Q T A I Y K S R N  
 - L C I M S D R D L Y D K L Q F T S L E I  
 17941 - TACCACGTCGCAATGTGGCTACATTACAAGCAGAAAATGTAAGTGGACTTTTTAAGGACT - 18000  
 - Y H V A M W L H Y K Q K M \* L D F L R T  
 - T T S Q C G Y I T S R K C N W T F \* G L  
 - P R R N V A T L Q A E N V T G L F K D C  
 18001 - GTAGTAAGATCATTACTGGTCTTCATCCTACACAGGCACCTACACACCTCAGCGTTGATA - 18060  
 - V V R S L L V F I L H R H L H T S A L I  
 - \* \* D H Y W S S S Y T G T Y T P Q R \* Y  
 - S K I I T G L H P T Q A P T H L S V D I  
 18061 - TAAATTCAGACTGAAGGATTATGTGTTGACATACCAGGCATACCAAAGGACATGACCT - 18120  
 - \* N S R L K D Y V L T Y Q A Y Q R T \* P  
 - K I Q D \* R I M C \* H T R H T K G H D L  
 - K F K T E G L C V D I P G I P K D M T Y  
 18121 - ACCGTAGACTCATCTCTATGATGGGTTTCAAAATGAATTACCAAGTCAATGGTTACCCTA - 18180  
 - T V D S S L \* W V S K \* I T K S M V T L  
 - P \* T H L Y D G F Q N E L P S Q W L P \*  
 - R R L I S M M G F K M N Y Q V N G Y P N  
 18181 - ATATGTTTATCACCCGCGAAGAAGCTATTCGTACGTTTCGTGCGTGGATTGGCTTTGATG - 18240  
 - I C L S P A K K L F V T F V R G L A L M  
 - Y V Y H P R R S Y S S R S C V D W L \* C  
 - M F I T R E E A I R H V R A W I G F D V  
 18241 - TAGAGGGCTGTCACTGCAACTAGAGATGCTGTGGGFACTAACCTACCTCTCCAGCTAGGAT - 18300  
 - \* R A V M Q L E M L W V L T Y L S S \* D  
 - R G L S C N \* R C C G Y \* P T S P A R I  
 - E G C H A T R D A V G T N L P L Q L G F  
 18301 - TTTCTACAGGTGTTAACTTAGTAGCTGTACCGACTGGTTATGTTGACACTGAAAATAACA - 18360  
 - F L Q V L T \* \* L Y R L V M L T L K I T  
 - F Y R C \* L S S C T D W L C \* H \* K \* H  
 - S T G V N L V A V P T G Y V D F E N N T  
 18361 - CAGAATTCACCAGAGTTAATGCAAAACCTCCACCAGGTGACCAGTTTAAACATCTTATAC - 18420  
 - Q N S P E L M Q N L H Q V T S L N I L Y  
 - R I H Q S \* C K T S T R \* P V \* T S Y T  
 - E F T R V N A K P P P G D Q F K H L I P  
 18421 - CACTCATGTATAAAGGCTTGCCCTGGAATGTAGTGCCTATTAAGATAGTACAAATGCTCA - 18480  
 - H S C I K A C P G M \* C V L R \* Y K C S  
 - T H V \* R L A L E C S A Y \* D S T N A Q  
 - L M Y K G L P W N V V R I K I V Q M L S

FIG. 11 Con't

18481 - GTGATACACTGAAAGGATTGTCAGACAGAGTCGTGTTGTCCTTTGGGCGCATGGCTTTG - 18540  
 - V I H \* K D C Q T E S C S S F G R M A L  
 - \* Y T E R I V R Q S R V R P L G A W L \*  
 - D T L K G L S D R V V F V L W A H G F E  
 18541 - AGCTTACATCAATGAAGTACTTTGTCAAGATTGGACCTGAAAGAACGTGTTGTGTGTGTG - 18600  
 - S L H Q \* S T L S R L D L K E R V V C V  
 - A Y I N E V L C Q D W T \* K N V L S V \*  
 - L T S M K Y F V K I G P E R T C C L C D  
 18601 - ACAAACGTCGCAACTTGCTTTTCTACTTCATCAGATACTTATGCCTGCTGGAATCATTCTG - 18660  
 - T N V Q L A F L L H Q I L M P A G I I L  
 - Q T C N L L F Y F I R Y L C L L E S F C  
 - K R A T C F S T S S D T Y A C W N H S V  
 18661 - TGGGTTTTGACTATGTCTATAACCCATTTATGATTGATGTTGAGCAGTGGGGCTTTACGG - 18720  
 - W V L T M S I T H L \* L M F S S G A L R  
 - G F \* L C L \* P I Y D \* C S A V G L Y G  
 - G F D Y V Y N P F M I D V Q Q W G F T G  
 18721 - GTAACCTTCAGAGTAACCATGACCAACATTGCCAGGTACATGGAAATGCACATGTGGCTA - 18780  
 - V T F R V T M T N I A R Y M E M H M W L  
 - \* P S E \* P \* P T L P G T W K C T C G \*  
 - N L Q S N H D Q H C Q V H G N A H V A S  
 18781 - GTTGTGATGCTATCATGACTAGATGTTTAGCAGTCCATGAGTGCCTTGTAAAGCGCGTTG - 18840  
 - V V M L S \* L D V \* Q S M S A L L S A L  
 - L \* C Y H D \* M F S S P \* V L C \* A R \*  
 - C D A I M T R C L A V H E C F V K R V D  
 18841 - ATTGGTCTGTTGAATACCCATTTATAGGAGATGAACTGAGGGTTAATTCTGCTTGCAGAA - 18900  
 - I G L L N T L L \* E M N \* G L I L L A E  
 - L V C \* I P Y Y R R \* T E G \* F C L Q K  
 - W S V E Y P I I G D E L R V N S A C R K  
 18901 - AAGTACAACACATGGTTGTAAGTCTGCATTGCTTGCTGATAAGTTCAGTCTTTCATG - 18960  
 - K Y N T W L \* S L H C L L I S F Q F F M  
 - S T T H G C E V C I A C \* \* V S S S S \*  
 - V Q H M V V K S A L L A D K F P V L H D  
 18961 - ACATTGGAATCCAAAGGCTATCAAGTGTGTGCCTCAGGCTGAAGTAGAATGGAAGTTCT - 19020  
 - T L E I Q R L S S V C L R L K \* N G S S  
 - H W K S K G Y Q V C A S G \* S R M E V L  
 - I G N P K A I K C V P Q A E V E W K F Y  
 19021 - ACGATGCTCAGCCATGTAGTGACAAAGCTTACAAAATAGAGGAACCTTCTATTCTTATG - 19080  
 - T M L S H V V T K L T K \* R N S S I L M  
 - R C S A M \* \* Q S L Q N R G T L L F L C  
 - D A Q P C S D K A Y K I E E L F Y S Y A  
 19081 - CTACACATCAGATAAATTCAGTATGGTGTGTTGTTGTTGGAATTGTAACGTTGATC - 19140  
 - L H I T I N S L M V F V C F G I V T L I  
 - Y T S R \* I H \* W C L F V L E L \* R \* S  
 - T H H D K F T D G V C L F W N C N V D R  
 19141 - GTTACCCAGCCAATGCAATTGTGTAGGTTTGACACAAGAGTCTTGTCAAACCTTGAAC - 19200  
 - V T Q P M Q L C V G L T Q E S C Q T \* T  
 - L P S Q C N C V \* V \* H K S L V K L E L  
 - Y P A N A I V C R F D T R V L S N L N L  
 19201 - TACCAGGCTGTGATGGTGGTAGTTGTATGTGAATAAGCATGCATTCCACACTCCAGCTT - 19260  
 - Y Q A V M V V V C M \* I S M H S T L Q L  
 - T R L \* W W \* F V C E \* A C I P H S S F  
 - P G C D G G S L Y V N K H A F H T P A F  
 19261 - TCGATAAAAGTCATTACTAATTTAAAGCAATGCCTTTCTTTTACTATTCTGATAGTC - 19320  
 - S I K V H L L I \* S N C L S F T I L I V  
 - R \* K C I Y \* F K A I A F L L L F \* \* S  
 - D K S A F T N L K Q L P F F Y Y S D S P

FIG. 11 Con't

19321 - CTTGTGAGTCTCATGGCAAACAAGTAGTGTGGGATATTGATTATGTTCCACTCAAATCTG - 19380  
 - L V S L M A N K \* C R I L I M F H S N L  
 - L \* V S W Q T S S V G Y \* L C S T Q I C  
 - C E S H G K Q V V S D I D Y V P L K S A  
 19381 - CTACGTGTATTACACGATGCAATTTAGGTGGTGGTGGTTTGCAGACACCATGCAAATGAGT - 19440  
 - L R V L H D A I \* V V L F A D T M Q M S  
 - Y V Y Y T M Q F R W C C L Q T P C K \* V  
 - T C I T R C N L G G A V C R H H A N E Y  
 19441 - ACCGACAGTACTTGGATGCATATAATATGATGATTTCTGCTGGATTTAGCCTATGGATTT - 19500  
 - T D S T W M H I I \* \* F L L D L A Y G F  
 - P T V L G C I \* Y D D F C W I \* P M D L  
 - R Q Y L D A Y N M M I S A G F S L W I Y  
 19501 - ACAAACAATTTGATACTTATAACCTGTGGAATACATTTACCAGGTTACAGAGTTTAGAAA - 19560  
 - T N N L I L I T C G I H L P G Y R V \* K  
 - Q T I \* Y L \* P V E Y I Y Q V T E F R K  
 - K Q F D T Y N L W N T F T R L Q S L E N  
 19561 - ATGTGGCTTATAATGTTGTTAATAAAGGACACTTTGATGGACACGCCGGCGAAGCACCTG - 19620  
 - M W L I M L L I K D T L M D T P A K H L  
 - C G L \* C C \* \* R T L \* W T R R R S T C  
 - V A Y N V V N K G H F D G E A G E A P V  
 19621 - TTTCCATCATTATAATGCTGTTTACACAAAGGTAGATGGTATTGATGTGGAGATCTTTG - 19680  
 - F P S L I M L F T Q R \* M V L M W R S L  
 - F H H \* \* C C L H K G R W Y \* C G D L \*  
 - S I I N N A V Y T K V D G I D V E I F E  
 19681 - AAAATAAGACAACACTTCCCTGTTAATGTTCCATTGAGCTTTGGGCTAAGCGTAACATTA - 19740  
 - K I R Q H F L L M L H L S F G L S V T L  
 - K \* D N T S C \* C C I \* A L G \* A \* H \*  
 - N K T T L P V N V A F E L W A K R N I K  
 19741 - AACCAGTGCCAGAGATTAAGATACTCAATAATTTGGGTGTTGATATCGCTGCTAATACTG - 19800  
 - N Q C Q R L R Y S I I W V L I S L L I L  
 - T S A R D \* D T Q \* F G C \* Y R C \* Y C  
 - P V P E I K I L N N L G V D I A A N T V  
 19801 - TAATCTGGGACTACAAAAGAGAAGCCCCAGCACATGTATCTACAATAGGTGTCTGCACAA - 19860  
 - \* S G T T K E K P Q H M Y L Q \* V S A Q  
 - N L G L Q K R S P S T C I Y N R C L H N  
 - I W D Y K R E A P A H V S T I G V C T M  
 19861 - TGACTGACATTGCCAAGAACCTACTGAGAGTGTCTTCTTCACTTACTGTCTTGTGTTG - 19920  
 - \* L T L P R N L L R V L V L H L L S C L  
 - D \* H C Q E T Y \* E C L F F T Y C L V \*  
 - T D I A K K P T E S A C S S L T V L F D  
 19921 - ATGGTAGAGTGAAGGACAGGTAGACCTTTTTAGAAAACGCCGTAATGGTGTTTTAATAA - 19980  
 - M V E W K D R \* T F L E T P V M V F \* \*  
 - W \* S G R T G R P F \* K R P \* W C F N N  
 - G R V E G Q V D L F R N A R N G V L I T  
 19981 - CAGAAGGTTCAAGTCAAAGGTCTAACACCTTCAAAGGGACCAGCACAGCTAGCGTCAATG - 20040  
 - Q K V Q S K V \* H L Q R D Q H K L A S M  
 - R R F S Q R S N T F K G T S T S \* R Q W  
 - E G S V K G L T P S K G P A Q A S V N G  
 20041 - GAGTCACATTAATGGAGAATCAGTAAAAACACAGTTTAACTACTTTAAGAAAGTAGACG - 20100  
 - E S H \* L E N Q \* K H S L T T L R K \* T  
 - S H I N W R I S K N T V \* L L \* E S R R  
 - V T L I G E S V K T Q F N Y F K K V D G  
 20101 - GCATTATTCAACAGTTGCCTGAAACCTACTTTACTCAGAGCAGAGACTTAGAGGATTTTA - 20160  
 - A L F N S C L K P T L L R A E T \* R I L  
 - H Y S T V A \* N L L Y S E Q R L R G F \*  
 - I I Q Q L P E T Y F T Q S R D L E D F K

FIG. 11 Con't



20161 - AGCCAGATCACAATGGAAACTGACTTTCTCGAGCTCGCTATGGATGAATTCATACAGC - 20220  
 - S P D H K W K L T F S S S L W M N S Y S  
 - A Q I T N G N \* L S R A R Y G \* I H T A  
 - P R S Q M E T D F L E L A M D E F I Q R  
 20221 - GATATAAGCTCGAGGGCTATGCCTTCGAACACATCGTTTATGGAGATTTTCAGTCATGGAC - 20280  
 - D I S S R A M P S N T S F M E I S V M D  
 - I \* A R G L C L R T H R L W R F Q S W T  
 - Y K L E G Y A F E H I V Y G D F S H G Q  
 20281 - AACTTGGCGGTCTTCATTTAATGATAGGCTTAGCCAAGCGCTCACAAGATTCACCACTTA - 20340  
 - N L A V F I \* \* \* A \* P S A H K I H H L  
 - T W R S S F N D R L S Q A L T R F T T \*  
 - L G G L H L M I G L A K R S Q D S P L K  
 20341 - AATTAGAGGATTTTATCCCTATGGACAGCACAGTGAATAACTTTCATAACAGATGCGC - 20400  
 - N \* R I L S L W T A Q \* K I T S \* Q M R  
 - I R G F Y P Y G Q H S E K L L H N R C A  
 - L E D F I P M D S T V K N Y F I T D A Q  
 20401 - AAACAGGTTTCATCAAAATGTGTGTGTTCTGTGATTGATCTTTTACTTGATGACTTTGTGCG - 20460  
 - K Q V H Q N V C V L \* L I F Y L M T L S  
 - N R F I K M C V F C D \* S F T \* \* L C R  
 - T G S S K C V C S V I D L L L D D F V E  
 20461 - AGATAATAAAGTCACAAGATTTGTGAGTATTTCAAAGTGGTCAAGGTTACAATTGACT - 20520  
 - R \* \* S H K I C Q \* F Q K W S R L Q L T  
 - D N K V T R F V S D F K S G Q G Y N \* L  
 - I I K S Q D L S V I S K V V K V T I D Y  
 20521 - ATGCTGAAATTTTCATTCATGCTTTGGTGTAAAGATGGACATGTTGAAACCTTCTACCCAA - 20580  
 - M L K F H S C F G V R M D M L K P S T Q  
 - C \* N F I H A L V \* G W T C \* N L L P K  
 - A E I S F M L W C K D G H V E T F Y P K  
 20581 - AACTACAAGCAAGTCAAGCGTGGCAACCAGGTGTTGCGATGCCCTAACTTGTACAAGATGC - 20640  
 - N Y K Q V K R G N Q V L R C L T C T R C  
 - T T S K S S V A T R C C D A \* L V Q D A  
 - L Q A S Q A W Q P G V A M P N L Y K M Q  
 20641 - AAAGAATGCTTCTTGAAGTGTGACCTTCAGAATTATGGTGAATACTGTTTATACCAA - 20700  
 - K E C F L K S V T F R I M V K M L L Y Q  
 - K N A S \* K V \* P S E L W \* K C C Y T K  
 - R M L L E K C D L Q N Y G E N A V I P K  
 20701 - AAGGAATAATGATGAATGTCGCAAAGTATACTCAACTGTGTCAATACTTAATACACTTA - 20760  
 - K E \* \* \* M S Q S I L N C V N T \* I H L  
 - R N N D E C R K V Y S T V S I L K Y T Y  
 - G I M M N V A K Y T Q L C Q Y L N T L T  
 20761 - CTTTAGCTGTACCCTACAACATGAGAGTTATTCACCTTGGTGTGGCTCTGATAAAGGAG - 20820  
 - L \* L Y P T T \* E L F T L V L A L I K E  
 - F S C T L Q H E S Y S L W C W L \* \* R S  
 - L A V P Y N M R V I H F G A G S D K G V  
 20821 - TTGCACCAGGTACAGCTGTGCTCAGACAATGGTTGCCAACTGGCACACTACTTGTGATT - 20880  
 - L H Q V Q L C S D N G C Q L A H Y L S I  
 - C T R Y S C A Q T M V A N W H T T C R F  
 - A P G T A V L R Q W L P T G T L L V D S  
 20881 - CAGATCTTAATGACTTCCTCTCGACGAGATTCCTACTTTAATTGGAGACTGTGCAACAG - 20940  
 - Q I L M T S S P T Q I L L \* L E T V Q Q  
 - R S \* \* L R L R R R F Y F N W R L C N S  
 - D L N D F V S D A D S T L I G D C A T V  
 20941 - TACATACGGCTAATAAATGGGACCTTATTATTAGCGATATGTATGACCCTAGGACCAAC - 21000  
 - Y I R L I N G T L L A I C M T L G P N  
 - T Y G \* \* M G P Y Y \* R Y V \* P \* D Q T  
 - H T A N K W D L I I S D M Y D P R T K H

FIG. 11 Con't

21001 - ATGTGACAAAAGAGAATGACTCTAAAGAAGGGTTTTTCACTTATCTGTGTGGATTATAA - 21060  
 - M \* Q K R M T L K K G F S L I C V D L \*  
 - C D K R E \* L \* R R V F H L S V W I Y K  
 - V T K E N D S K E G F F T Y L C G F I K  
 21061 - AGCAAAAACACTGCCCTGGGTGGTTCTATAGCTGTAAAGATAACAGAGCATTCTTGGGAATG - 21120  
 - S K N \* P W V V L \* L \* R \* Q S I L G M  
 - A K T S P G W F Y S C K D N R A F L E C  
 - Q K L A L G G S I A V K I T E H S W N A  
 21121 - CTGACCTTTACAAGCTTATGGGCCATTCTCATGGTGGACAGCTTTTGTACAAATGTAA - 21180  
 - L T F T S L W A I S H G G Q L L L Q M \*  
 - \* P L Q A Y G P F L M V D S F C Y K C K  
 - D L Y K L M G H F S W W T A F V T N V N  
 21181 - ATGCATCATCATCGGAAGCATTTTTAATGGGGCTAACTATCTGGCAAGCCGAAGGAAC - 21240  
 - M H H H R K H F \* L G L T I L A S R R N  
 - C I I I G S I F N W G \* L S W Q A E G T  
 - A S S S E A F L I G A N Y L G K P K E Q  
 21241 - AAATTGATGGCTATACCATGCATGCTAACTACATTTTCTGGAGGAACACAATCCTATCC - 21300  
 - K L M A I P C M L T T F S G G T Q I L S  
 - N \* W L Y H A C \* L H F L E E H K S Y P  
 - I D G Y T M H A N Y I F W R N T N P I Q  
 21301 - AGTTGTCTTCTATTCACTCTTTGACATGAGCAAATTCCTCTTAAATTAAGAGGAAGT - 21360  
 - S C L P I H S L T \* A N F L L N \* E E L  
 - V V F L F T L \* H E Q I S S \* I K R N C  
 - L S S Y S L F D M S K F P L K L R G T A  
 21361 - CTGTAATGTCTCTTAAGGAGAATCAAATCAATGATATGATTTATTCTCTCTGGAAAAAG - 21420  
 - L \* C L L R R I K S M I \* F I L F W K K  
 - C N V S \* G E S N Q \* Y D L F S S G K R  
 - V M S L K E N Q I N D M I Y S L L E K G  
 21421 - GTAGGCTTATCATTAGAGAAAACAACAGAGTTGTGGTTCAAGTGATATTCTTGTAAACA - 21480  
 - V G L S L E K T T E L W F Q V I F L L T  
 - \* A Y H \* R K Q Q S C G F K \* Y S C \* Q  
 - R L I I R E N N R V V V S S D I L V N N  
 21481 - ACTA AACGAACATGTTTATTTTCTTATTATTCTTACTCTCACTAGTGGTAGTGACCTTG - 21540  
 - T K R T C L F S Y Y F L L S L V V V T L  
 - L N E H V Y F L I I S Y S H \* W \* \* P \*  
 - \* T N M F I F L L F L T L T S G S D L D  
 21541 - ACCGGTGCACCCTTTGATGATGTTCAAGCTCCTAATTACACTCAACATACTTCATCTA - 21600  
 - T G A P L L M M F K L L I T L N I L H L  
 - P V H H F \* \* C S S S \* L E S T Y F I Y  
 - R C T T F D D V Q A P N Y T Q H T S S M  
 21601 - TGAGGGGGTTTACTATCCTGATGAAATTTTAGATCAGACACTCTTTATTAACTCAGG - 21660  
 - \* G G F T I L M K F L D Q T L F I \* L R  
 - E G G L L S \* \* N F \* I R H S L F N S G  
 - R G V Y Y P D E I F R S D T L Y L T Q D  
 21661 - ATTTATTTCTTCCATTTTATTCTAATGTTACAGGGTTTCATACTATTAATCATACGTTTG - 21720  
 - I Y F F H F I L M L Q G F I L L I I R L  
 - F I S S I L F \* C Y R V S Y Y \* S Y V W  
 - L F L P F Y S N V T G F H T I N H T F G  
 21721 - GCAACCCGTGCATACCTTTTAAGGATGGTATTATTGCTGCCACAGAGAAATCAAATG - 21780  
 - A T L S Y L I R M V F I L L P Q R N Q M  
 - Q P C H T F \* G W Y L F C C H R E I K C  
 - N P V I P F K D G I Y F A A T E K S N V  
 21781 - TTGTCCGTGGTGGTTEGTTCTACCATGAACAACAAGTCACAGTCGGGTGATTATTA - 21840  
 - L S V V G F L V I P \* T P S H S R \* L L  
 - C P W I G F W F Y H E Q Q V T V G D Y Y  
 - V R G W V F G S T M N N K S Q S V I I I

FIG. 11 Con't

21841 - TTAACAATTCTACTAATGTTGTTATACGAGCATGTAACCTTGAATTGTGTGACAACCCTT - 21900  
 - L T I L L M L L Y E H V T L N C V T T L  
 - \* Q F Y \* C C Y T S M \* L \* I V \* Q P F  
 - N N S T N V V I R A C N F E L C D N P F  
 21901 - TCTTTGCTGTTTCTAAACCCATGGGTACACAGACATACTATGATATTCGATAATGCAT - 21960  
 - S L L F L N P W V H R H I L \* Y S I M H  
 - L C C F \* T H G Y T D T Y Y D I R \* C I  
 - F A V S K P M G T Q T H T M I F D N A F  
 21961 - TTAATTGCACTTTTCGAGTACATATCTGATGCCTTTTCGCTGATGTTTCAGAAAAGTCAG - 22020  
 - L I A L S S T Y L M P F R L M F Q K S Q  
 - \* L H F R V H I \* C L F A \* C F R K V R  
 - N C T F E Y I S D A F S L D V S E K S G  
 22021 - GTAATTTTAAACACTTACGAGAGTTTGTGTTTTAAAAATAAAGATGGGTTTCTCTATGTTT - 22080  
 - V I L N T Y E S L C L K I K M G F S M F  
 - \* F \* T L T R V C V \* K \* R W V S L C L  
 - N F K H L R E F V F K N K D G F L Y V Y  
 22081 - ATAAGGCTATCAACCTATAGATGTAGTTCGTGATCTACCTTCTGGTTTAACTTTGA - 22140  
 - I R A I N L \* M \* F V I Y L L V L T L \*  
 - \* G L S T Y R C S S \* S T F W F \* H F E  
 - K G Y Q P I D V V R D L P S G F N T L K  
 22141 - AACCTATTTTTAAGTTGCCTCTTGGTATTAACATTACAAATTTTAGAGCCATTCTTACAG - 22200  
 - N L F L S C L L V L T L Q I L E P F L Q  
 - T Y F \* V A S W Y \* H Y K F \* S E S Y S  
 - P I F K L P L G I N I T N F R A I L T A  
 22201 - CCTTTTCACCTGCCTCAAGACATTTGGGGCACGTCAGCTGCAGCCTATTTTGTGGCTATT - 22260  
 - P F H L L K T F G A R Q L Q P I L L A I  
 - L F T C S R H L G H V S C S L F C W L F  
 - F S P A Q D I W G T S A A A Y F V G Y L  
 22261 - TAAAGCCAACCTACATTTATGCTCAAGTATGATGAAAATGGTACAATCACAGATGCTGTTG - 22320  
 - \* S Q L H L C S S M M K M V Q S Q M L L  
 - K A N Y I Y A Q V \* \* K W Y N H R C C \*  
 - K P T T F M L K Y D E N G T I T D A V D  
 22321 - ATTGTTCTCAAAATCCACTTGCTGAACCTCAAATGCTCTGTTAAGAGCTTTGAGATTGACA - 22380  
 - I V L K I H L N S N A L L R A L R L T  
 - L F S K S T C \* T Q M L C \* E L \* D \* Q  
 - C S Q N P L A E L K C S V K S F E I D K  
 22381 - AAGGAATTTACCAGACCTTAATTTAGGGTTGTTCCCTCAGGAGATGTTGTGAGATTCC - 22440  
 - K E F T R P L I S G L F P Q E M L \* D S  
 - R N L P D L \* F Q G C S L R R C C E I P  
 - G I Y Q T S N F R V V P S G D V V R F P  
 22441 - CTAATATTACAAACTTGTGTCCTTTTGGAGAGGTTTTTAATGCTACTAAATTCCTTCTG - 22500  
 - L I L Q T C V L L E R F L M L L N S L L  
 - \* Y Y K L V S F W R G F \* C Y \* I P F C  
 - N I T N L C P F G E V F N A T K F P S V  
 22501 - TCTATGCATGGGAGAGAAAAAATTTCTAATTGTGTGCTGATTACTCTGTGCTCTACA - 22560  
 - S M H G R E K K F L I V L L I T L C S T  
 - L C M G E K K N F \* L C C \* L L C A L Q  
 - Y A W E R K K I S N C V A D Y S V L Y N  
 22561 - ACTCAACATTTTTTTCAACCTTTAAGTGCATGGCGTTTCTGCCACTAAGTTGAATGATC - 22620  
 - T Q H F F Q P L S A M A F L P L S \* M I  
 - L N I F F N L \* V L W R F C H \* V E \* S  
 - S T F F S T F K C Y G V S A T K L N D L  
 22621 - TTTGCTTCTCCAATGTCTATGCAGATTCTTTTGTAGTCAAGGGAGATGATGTAAGACAAA - 22680  
 - F A S P M S M Q I L L \* S R E M M \* D K  
 - L L L Q C L C R F F C S Q G R \* C K T N  
 - C F S N V Y A D S F V V K G D D V R Q I

FIG. 11 Con't

22681 - TAGGCCAGGACAACTGGTGTATTGCTGATTATAATTATAAATTGCCAGATGATTCA - 22740  
 - \* R Q D K L V L L L I I I I N C Q M I S  
 - S A R T N W C Y C \* L \* L \* I A R \* F H  
 - A P G Q T G V I A D Y N Y K L P D D F M  
 22741 - TGGGTGTGCTCCTTGCTTGAATACTAGGAACATTGATGCTACTTCAACTGGTAATTATA - 22800  
 - W V V S L L G I L G T L M L L Q L V I I  
 - G L C P C L E Y \* E E \* C Y F N W \* L \*  
 - G C V L A W N T R N I D A T S T G N Y N  
 22801 - ATTATAAATATAGGTATCTTAGACATGGCAAGCTTAGGCCCTTGAGAGAGACATATCTA - 22860  
 - I I N I G I L D M A S L G P L R E T Y L  
 - L \* I \* V S \* T W Q A \* A L \* E R H I \*  
 - Y K Y R Y L R H G K L R P F E R D I S N  
 22861 - ATGTGCCTTTCTCCCTGATGGCAACCTTGACCCACCTGCTCTTAATTGTTATTGGC - 22920  
 - M C L S P L M A N L A P H L L L I V I G  
 - C A F L P \* W Q T L E P T C S \* L L L A  
 - V P F S P D G K P C T P P A L N C Y W P  
 22921 - CATTAATGATTATGGTTTTACACCCTACTGGCATTGGCTACCAACCTTACAGAGTIG - 22980  
 - H \* M I M V F T P L L A L A T N L T E L  
 - I K \* L W F L H H Y W H W L P T L Q S C  
 - L N D Y G F Y T T T G I G Y Q P Y R V V  
 22981 - TAGTACTTCTTTTGAACTTTTAAATGCACCGGCCCGGTTTTGGACCAAAATTATCCA - 23040  
 - \* Y F L L N F \* M H R P R F V D Q N Y P  
 - S T F F \* T F K C T G H G L W T K I I H  
 - V L S F E L L N A P A T V C G P K L S T  
 23041 - CTGACCTTATTAAGAACCAGTGTGTCAATTTAATTTAATGGACTCACTGGTACTGGTG - 23100  
 - L T L L R T S V S I L I L M D S L V L V  
 - \* P Y \* E P V C Q F \* F \* W T H W Y W C  
 - D L I K N Q C V N F N F N G L T G T G V  
 23101 - TGTTAACTCCTTCTCAAGAGATTTCAACCATTCAACAATTTGGCCGATGTTTCTG - 23160  
 - C \* L L L Q R D F N H F N N L A V M F L  
 - V N S F F K E I S T I S T I W P \* C F \*  
 - L T P S S K R F Q P F Q Q F G R D V S D  
 23161 - ATTECACTGATTCGGTTCGAGATCCTAAAACATCTGAAATATTAGACATTTACCTTGCT - 23220  
 - I S L I P F F E I L K H L K Y \* T F H L A  
 - F H \* F R S R S \* N I \* N I R H F T L L  
 - F T D S V R D P K T S E I L D I S P C S  
 23221 - CTTTTGGGGGTGAAGTGAATTACACCTGGAACAAATGCTTCATCTGAAGTTGCTGTT - 23280  
 - L L G V \* V \* L H L E Q M L H L K L L F  
 - F W G C K C N Y T W N K C F I \* S C C S  
 - F G G V S V I T P G T N A S S E V A V L  
 23281 - TATATCAAGATGTTAAGTCACTGATGTTTCTACAGCAATTCATGCAGATCAACTCACAC - 23340  
 - Y I K M L T A L M F L Q Q F M Q I N S H  
 - I S R C \* L H \* C F Y S N S C R S T H T  
 - Y Q D V N C T D V S T A I H A D Q L T P  
 23341 - CAGCTTGGCGCATATATTCTACTGGAAACATGTATTCCAGACTCAAGCAGGCTGTCTTA - 23400  
 - Q L G A Y I L L E T M Y S R L K Q A V L  
 - S L A H I F Y W K Q C I P D S S R L S Y  
 - A W R I Y S T G N N V F Q T Q A G C L I  
 23401 - TAGGAGCTGAGCATGTCGACACTTCTTATGAGTGGACATTCTTATTGGAGCTGGCATT - 23460  
 - \* E L S M S T L L M S A T F L E L E L A F  
 - R S \* A C R E F L \* V R H S Y W S W H L  
 - G A E H V D E S Y E C D I P I G A G I C  
 23461 - GTGCTASTTACCATACAGTTCTTTATTACCTAGTACTAGCCAAAATCTATTGTGGCTT - 23520  
 - V L V T I Q F L Y Y V V L A K N L L W L  
 - C \* L P Y S F F I T \* Y \* P K I Y C G L  
 - A S Y H T V S L L R S T S Q K S I V A Y

FIG. 11 Con't

23521 - ATACTATGTCTTTAGGTGCTGATAGTTCAATTGCTTACTCTAATAACACCATTGCTATAC - 23580  
- I L C L \* V L I V Q L L T L I T P L L Y  
- Y Y V F R C \* \* F N C L L \* \* H H C Y T  
- T M S L G A D S S I A Y S N N T I A I P  
23581 - CTACTAACTTTTCAATTAGCATTACTACAGAAGTAATGCCITGTTTCTATGGCTAAAACCT - 23640  
- L L T F Q L A L L Q K \* C L F L W L K P  
- Y \* L F N \* H Y Y R S N A C F Y G \* N L  
- T N F S I S I T T E V M P V S M A K T S  
23641 - CCGTAGATTGTAATATGTACATCTGCGGAGATTCTACTGAATGTGCTAATTTGCTTCTCC - 23700  
- P \* I V I C T S A E I L L N V L I C F S  
- R R L \* Y V H L R R F Y \* M C \* F A S P  
- V D C N M Y I C G D S T E C A N L L L Q  
23701 - AATATGGTAGCTTTTGACACAATAAATCGTGCACTCTCAGGTATTGCTGCTGAACAGG - 23760  
- N M V A F A H N \* I V H S Q V L L L N R  
- I W \* L L H T T K S C T L R Y C C \* T G  
- Y G S F C T Q L N R A L S G I A A E Q D  
23761 - ATCGCAACACACGTGAAGTGTTCGCTCAAGTCAAACAAATGTACAAAACCCCAACTTTGA - 23820  
- I A T H V K C S L K S N K C T K P Q L \*  
- S Q H T \* S V R S S Q T N V Q N P N F E  
- R N T R E V F A Q V K Q M Y K T P T L K  
23821 - AATATTTTGGTGGTTTAATTTTTCACAAATATTACCTGACCCTCTAAAGCCAACTAAGA - 23880  
- N I L V V L I F H K Y Y L T L \* S Q L R  
- I F W W F \* F F T N I T \* P S K A N \* E  
- Y F G G F N F S Q I L P D P L K P T K R  
23881 - GGTCTTTTATTGAGGACTTGCTCTTTAATAAGGTGACACTCGCTGAGGCTGGCTTCATGA - 23940  
- G L L L R T C S L I R \* H S L M L A S \*  
- V F Y \* G L A L \* \* G D T R \* C W L H E  
- S F I E D L L F N K V T L A D A G F M K  
23941 - AGCAATATGGCGAATGCCTAGGTGATATTAATCCTAGAGATCTCATTGTGCGCAGAAGT - 24000  
- S N M A N A \* V I L M L E I S F V R R S  
- A I W R M P R \* Y \* C \* R S H L C A E V  
- Q Y G E C L G D I N A R D L I C A Q K F  
24001 - TCAATGGACTTACAGTGTGCCACCTCTGCTCACTGATGATATGATTGCTGCCCTACTG - 24060  
- S M D L Q C C H L C S L M I \* L L P T L  
- Q W T Y S V A T S A H \* \* Y D C C L H C  
- N G L T V L P P L L T D D M I A A Y T A  
24061 - CTGCTCTAGTTAGTGGTACTGCCACTGCTGGATGGACATTTGGTGTGCGCGTCTCTTC - 24120  
- L L \* L V V L P L L D G H L V L A L L F  
- C S S \* W Y C H C W M D I W C W R C S S  
- A L V S G T A T A G W T F G A G A A L Q  
24121 - AAATACCTTTTGCATGCAAATGGCATATPAGGTTCATGGCATTGGAGTTACCCAAAATG - 24180  
- K Y L L L C K W H I G S M A L E L P K M  
- N T F C Y A N G I \* V Q W H W S Y P K C  
- I P F A M Q M A Y R F N G I G V T Q N V  
24181 - TTCTCTATGAGAACCAAAAACAATAATCGCCAACCAATTTAACAAGGCGATTAGTCAAATTC - 24240  
- F S M R T K N K S P T N L T R R L V K F  
- S L \* E P K T N R Q P I \* Q G D \* S N S  
- L Y E N Q K Q I A N Q F N K A I S Q I Q  
24241 - AAGAATCACTTACAACAACATCAACTGCATTGGGCAAGCTGCAAGACGTTGTTAACCAGA - 24300  
- K N H L Q Q H Q L H W A S C K T L L T R  
- R I T Y N N I N C I G Q A A R R C \* P E  
- E S L T T T S T A L G K L Q D V V N Q N  
24301 - ATGCTCAAGCATTAAACACACTTGTAAACAACCTAGCTCTAATTTTGGTGCATTTCAA - 24360  
- M L K H \* T H L L N N L A L I L V Q F Q  
- C S S I K H T C \* T T \* L \* F W C N F K  
- A Q A L N T L V K Q L S S N F G A I S S

FIG. 11 Con't

24361 - GTGTGCTAAATGATATCCTTTTCGCGACTTGATAAAGTCGAGGCGGAGGTACAAATTGACA - 24420  
 - V C \* M I S F R D L I K S R R R Y K L T  
 - C A K \* Y P F A T \* \* S R G G G T N \* Q  
 - V L N D I L S R L D K V E A E V Q I D R  
 24421 - GGTTAATTACAGGCAGACTTCAAAGCCTTCAAACCTATGTAACACAACAATAATCAGGG - 24480  
 - G \* L Q A D E K A F K P M \* H N N \* S G  
 - V N Y R Q T S K P S N L C N T T T N Q G  
 - L I T G R L Q T Y V T Q Q L I R A  
 24481 - CTGCTGAAATCAGGGCTTCTGCTAATCTTGCTGCTACTAAAATGTCTGAGTGTGTTCTTG - 24540  
 - L L K S G L L L I L L L L K C L S V F L  
 - C \* N Q G F C \* S C C Y \* N V \* V C S W  
 - A E I R A S A N L A A T K M S E C V L G  
 24541 - GACAATCAAAAAGAGTTGACTTTTGTGGAAAGGGCTACCACCTTATGTCCTTCCACAAG - 24600  
 - D N Q K E L T F V E R A T T L C P S H K  
 - T I K K S \* L L W K G L P P Y V L P T S  
 - Q S K R V D F C G K G Y H L M S F P Q A  
 24601 - CAGCCCCGCATGGTGTGCTTCTCTACATGTCACGTATGTGCCATCCCAGGAGAGGAAGT - 24660  
 - Q P R M V L S S Y M S R M C H P R R G T  
 - S P A W C C L P T C H V C A I P G E E L  
 - A P H G V V F L H V T Y V P S Q E R N F  
 24661 - TCACCACAGCGCCAGCAATTTGTCATGAAGGCAAAGCATACTTCCCTCGTGAAGGTGTTT - 24720  
 - S P Q R Q Q F V M K A K H T S L V K V F  
 - H H S A S N L S \* R Q S I L P S \* R C V F  
 - T T A P A I C H E G K A Y F P R E G V F  
 24721 - TTGTGTTAATGGCACTTCTTGGTTTATTACACAGAGGAAGTCTTTTCTCCACAAATAA - 24780  
 - L C L M A L L G L L H R G T S F L H K \*  
 - C V \* W H F L V Y Y T E E L L F S T N N  
 - V F N G T S W F I T Q R N F F S P Q I I  
 24781 - TTACTACAGACAATACATTTGTCTCAGGAAATTGTGATGTCGTTATTGGCATCATTAACA - 24840  
 - L L Q T I R L S Q E I V M S L L A S L T  
 - Y Y R Q Y I C L R K L \* C R Y W H H \* Q  
 - T T D N T F V S G N C D V V I G I N N  
 24841 - ACACAGTTTATGATCCTCTGCAACCTGAGCTCATTCAAAGAAGAGCTGGACAAGT - 24900  
 - T Q F M I L C N L S L T H S K K S W T S  
 - H S L \* S S A T \* A \* L I Q R R A G Q V  
 - T V Y D P L Q P E L D S F K E E L D K Y  
 24901 - ACTTCAAAAATCATACATCACCAGATGTTGATCTTGGCGACATTTCAGGCATTAACGCTT - 24960  
 - T S K I I H H Q M L I L A T F Q A L T L  
 - L Q K S Y I T R C \* S W R H F R H \* R F  
 - F K N H T S P D V D L G D I S G I N A S  
 24961 - CTGTCGTCACATTCAAAAAGAAATTGACCGCCTCAATGAGGTCGCTAAAAATTTAAATG - 25020  
 - L S S T F K K K L T A S M R S L K I \* M  
 - C R Q H S K R N \* P P Q \* G R \* K F K \*  
 - V V N I Q K E I D R L N E V A K N L N E  
 25021 - AATCACTCATTGACCTTCAAGAATTGGGAAAATATGAGCAATATATTAATGGCCTTGGT - 25080  
 - N H S L T F K N W E N M S N I L N G L G  
 - I T H \* P S R I G K I \* A I Y \* M A L V  
 - S L I D L Q E L G K Y E Q Y I K W P W Y  
 25081 - ATGTTGGCTCGGCTTCATTGCTGGACTAATTGCCATCGTCATGGTTACAATCTTGCTTT - 25140  
 - M F G S A S L L D \* L P S S W L Q S C F  
 - C L A R L H C W T N C H R H G Y N L A L  
 - V W L G F I A G L I A I V M V T I L L C  
 25141 - GTTGCATGACTAGTTGTTGTCAGTTGCCTCAAGGCTGCATGCTCTTGTGCTTCTGCTGCA - 25200  
 - V A \* L V V A V A S R V H A L V V L A A  
 - L H D \* L L Q L P Q G C M L L W F L L Q  
 - C M T S C C S C L K G A C S C G S C C K

FIG. 11 Con't

25201 - AGTTTGATGAGGATGACTCTGAGCCAGTTCTCAAGGGTGTCAAATTACATTACACATAAA - 25260  
 - S L M R M T L S Q F S R V S N Y I T H K  
 - V \* \* G \* L \* A S S Q G C Q I T L H I N  
 - F D E D D S E P V L K G V K L H Y T \* T  
 25261 - CGAAGTATGGATTTGTTTATGAGATTTTTTACTCTTGGATCAATTACTGCACAGCCAGT - 25320  
 - R T Y G F V Y E I F Y S W I N Y C T A S  
 - E L M D L F M R F F T L G S I T A Q P V  
 - N L W I C L \* D F L L L D Q L L H S Q \*  
 25321 - AAAAATGACAATGCTTCTCCTGCAAGTACTGTTTCATGCTACAGCACGATACCGCTACA - 25380  
 - K N \* Q C F S C K Y C S C Y S N D T A T  
 - K I D N A S P A S T V H A T A T I P L Q  
 - K L T M L L L Q V L F M L Q Q R Y R Y K  
 25381 - AGCCTCACTCCCTTTCCGATGGCTTGTATTGGCGTTGCATTTCTTGCCTGTTTTTCAGAG - 25440  
 - S L T P F R M A C Y W R C I S C C F S E  
 - A S L P F G W L V I G V A F L A V F Q S  
 - P H S L S D G L L L A L H F L L F F R A  
 25441 - CGCTACAAAATAAATGGCGTCAATAAAAGATGGCAGCTAGCCCTTTATAAGGGCTTCCA - 25500  
 - R Y Q N N C A Q \* K M A A S P L \* G L P  
 - A T K I I A L N K R W Q L A L Y K G F Q  
 - L P K \* L R S I K D G S \* P F I R A S S  
 25501 - GTTCATTTGCAATTTACTGCTGCTATTGTTACCATCTATTCACATCTTTTGCTTGTCGC - 25560  
 - V H L Q F T A A I C Y H L F T S F A C R  
 - F I C N L L L L F V T I Y S H L L L V A  
 - S F A I Y C C Y L L P S I H I F C L S L  
 25561 - TGCAGTAAGGAGGCGCAATTTTTGTACCTCTATGCCCTTGATATATTTTCTACAATGCAT - 25620  
 - C R \* G G A I F V P L C L D I F S T M H  
 - A G K E A Q F L Y L Y A L I Y F L Q C I  
 - Q V R R R N F C T S M P \* Y I F Y N A S  
 25621 - CAACGCATGTAGAATTATTATGAGATGTTGGCTTTGTTGGAGTGCAAATCCAAGAACCC - 25680  
 - Q R M \* N Y Y E M L A L L E V Q I Q E P  
 - N A C R I I M R C W L C W K C K S K N P  
 - T H V E L L \* D V G F V G S A N P R T H  
 25681 - ATTACTTTATGATGCCAAGTACTTTGTTTGGCTGGCACACACATAACTATGACTACTGTAT - 25740  
 - I T L \* C Q L L C L L A H T \* L \* L L Y  
 - L L Y D A N Y F V C W H T H N Y D Y C E  
 - Y F M M P T T L F A G T H I T M T T V Y  
 25741 - ACCATATAACAGTGTACAGATACAATTGTCGTTACTGAAGGTGACGGCATTTCACACC - 25800  
 - T I \* Q C H R Y N C R Y \* R \* R H F N T  
 - P Y N S V T D T I V V T E G D G I S T P  
 - H I T V S Q I Q L S L L K V T A F Q H Q  
 25801 - AAAACTCAAAGAAGACTACCAAATTTGGTGGTTATTCTGAGGATAGGCACTCAGGTGTTAA - 25860  
 - K T Q R R L P N W W L F \* G \* A L R C \*  
 - K L K E D Y Q I G G Y S E D R H S G V K  
 - N S K K T T K L V V I L R I G T Q V L K  
 25861 - AGACTATGTCGTTGTACATGGCTATTTACCGAAGTTTACTACCAGCTTGAGTCTACACA - 25920  
 - R L C R C T W L F H R S L L P A \* V Y T  
 - D Y V V V H G Y F T E V Y Y Q L E S T Q  
 - T M S L Y M A I S P K E T T S L S L H K  
 25921 - AATTACTACAGACACTGGTATTGAAAATGCTACATTCTTCATCTTTAACAAGCTTGTAA - 25980  
 - N Y Y R H W Y \* K C Y I L H L \* Q A C \*  
 - I T T D T G I E N A T F F I E N K L V K  
 - L L Q T I V L K M L H S S S L T S L L K  
 25981 - AGACCCACCGAATGTGCAATACACACAATCGACGGCTCTTCAGGAGTTGCTAATCCAGC - 26040  
 - R P T E C A N T H N R R L F R S C \* S S  
 - D P P N V Q I H T I D G S S G V A N P A  
 - T H R M C K Y T Q S T A L Q E L L I Q Q

FIG. 11 Con't

26041 - AATGGATCCAATTTATGATGAGCCGACGACGACTACTAGCGTGCCTTTGTAAGCACAAGA - 26100  
- N G S N L \* \* A D D D Y \* R A F V S T R  
- M D P I Y D E P T T T T S V P L \* A Q E  
- W I Q F M M S R R R L L A C L C K H K K  
26101 - AAGTGAGTACGAACCTTATGACTCATTTCGTTTCGGAGAAACAGGTACGTTAATAGTTAA - 26160  
- K \* V R T Y V L I R F G R N R Y V N S \*  
- S E Y E L M Y S F V S E E T G T L I V N  
- V S T N L C T H S F R K K Q V R \* \* L I  
26161 - TAGCGTACTTCTTTTCTTGCTTTTCGTTGCTTCTTGCTAGTCACACTAGCCATCCTTAC - 26220  
- \* R T S F S C F R G I L A S E T S H P Y  
- S V L L F L A F V V F L L V T L A I L T  
- A Y F F F L L S W Y S C \* S H \* P S L L  
26221 - TGCGCTTCGATTGTGTGCGTACTGCTGCAATATTGTTAACGTGAGTTTAGTAAACCAAC - 26280  
- C A S I V C V L L Q Y C \* R E F S K T N  
- A L R L C A Y C C N I V N V S L V K P T  
- R F D C V R T A A I L L T \* V \* \* N Q R  
26281 - GGTTCAGTCTACTCGCGTGTAAAAATCTGAACCTCTCTGAAGGAGTTCCTGATCTTCT - 26340  
- G L R L L A C \* K S E L F \* R S S \* S S  
- V Y V Y S R V K N L N S S E G V P D L L  
- F T S T R V L K I \* T L L K E F L I F W  
26341 - GGTCTAAACGAACATAACTATTATTATTCTGTTTGGAACTTTAACATTGCTTATCATG - 26400  
- S L N E L T I I I I L F G T L T L L I M  
- V \* T N \* L L L L F C L E L \* H C L S W  
- S K R T N Y Y Y Y S V W N F N I A Y H G  
26401 - GCAGACAACGGTACTATTACCGTTGAGGAGCTTAAACAACCTCTGGAACAATGGAACCTA - 26460  
- A D N G T I T V E E L K Q L L E Q W N L  
- Q T T V L L P L R S L N N S W N N G T \*  
- R Q R Y Y Y R \* G A \* T T P G T M E P S  
26461 - GTAATAGGTTTCCTATTCTAGCCTGGATTATGTTACTACAATTTGCCTATCTCAATCGG - 26520  
- V I G F L F L A W I M L L Q F A Y S N R  
- \* \* V S Y S \* P G L C Y Y N L P I L I G  
- N R P P I P S L D Y V T T I C L F \* S E  
26521 - AACAGGTTTTGTACATAATAAAGCTTGTTCCTCTGGCTTGTGCCCAGTAACACTT - 26580  
- N R F L Y I I K L V F L W L L W P V T L  
- T G F C T \* \* S L F S S G S C G Q \* H L  
- Q V F V H N K A C F P L A L V A S N T C  
26581 - GCTTGTTTTGTGCTTGTCTGTGTCTACAGAATTAATTGGGTGACTGGCGGGATTGCGATT - 26640  
- A C F V L A V V Y R I N W V T G G I A I  
- I V L C L L L S T E L I G \* L A G L R I  
- L F C A C C C L Q N \* L G D W R D C D C  
26641 - GCAATGGCTTGTATTGTAGGCTTGATGTGGCTTAGCTACTCGTTGCTTCTTCAGGCTG - 26700  
- A M A C I V G I M W L S Y F V A S F R L  
- Q W L V L \* A \* C G L A T S L L P S G C  
- N G L Y C R L D V A \* L L R C F L Q A V  
26701 - TTTGCTCGTACCCGCTCAATGTGGTCATTCAACCCAGAAACAACATTCCTCAATGTG - 26760  
- F A R T R S M W S F N P E T N I L L N V  
- L L V P A Q C G H S T Q K Q T F F S M C  
- C S Y P L N V V I Q P R N K H S S Q C A  
26761 - CCTCTCCGGGGACAATTTGTGACCAGCCGCTCATGGAAGTGAACCTGTCATTGGTGCT - 26820  
- P L R G T I V T R P L M E S E L V I G A  
- L S G G Q L \* P D R S W K V N L S L V L  
- S P G D N C D Q T A E G K \* T C H W C C  
26821 - GTGATCATTTCGTTGCTACTTGCGAATGGCCGACACTCCCTAGGGCGCTGTGACATTAAG - 26880  
- V I I R G H L R M A G H S L G R C D I K  
- \* S E V V T C E W P D T P \* G A V T L R  
- D H S W S L A N G R T L P R A L \* H \* G

FIG. 11 Con't



26881 - GACCTGCCAAAAGAGATCACTGTGGCTACATCAGAACGCTTTCTTATTACAAATTAGGA - 26940  
 - D L P K E I T V A T S R T L S Y Y K L G  
 - T C Q K R S L W L H H E R F L I T N \* E  
 - P A K R D H C G Y I T N A F L L Q I R S  
 26941 - GCGTGCAGCGTGTAGGCACCTGATTTCAGGTTTTGCTGCATACAACCGCTACCGTATTGGA - 27000  
 - A S Q R V G T D S G F A A Y N R Y R I G  
 - R R S V \* A L I Q V L L H T T A T V L E  
 - V A A C R H \* F R F C C I Q P L P Y W K  
 27001 - AACTATAAATTAATACAGACCACGCCGGTAGCAACGACAATATTGCTTTGCTAGTACAG - 27060  
 - N Y K L N T D H A G S N D N I A L L V Q  
 - T I N \* I Q T P V A T T I L L C \* Y S  
 - L \* I K Y R P R R \* Q R Q Y C F A S T V  
 27061 - TAAGTGACAACAGATGTTTCATCTTGTGACTTCCAGGTTACAATACCAGAGATATTGAT - 27120  
 - \* V T T D V S S C \* L P G Y N S R D I D  
 - K \* Q Q M F H L V D F Q V T I A E I L I  
 - S D N R C F I L L T S R L Q \* Q R Y \* L  
 27121 - TATCATTATGAGGACTTTTCAGGATTGCTATTGGAATCTTGACGTTATAATAAGTTCAAT - 27180  
 - Y H Y E D F Q D C Y L E S \* R Y N K F N  
 - I I M R T F R I A I W N L D V I I S I  
 - S L \* G L S G L L F G I L T L \* \* V Q \*  
 27181 - AGTGAGACAATTATTAAGCCTCTAACTAAGAAGAATTATTCGGAGTTAGATGATGAAGA - 27240  
 - S E T I I \* A S N \* E E L F G V R \* \* R  
 - V R Q L F K P L T K K N Y S E L D D E E  
 - \* D N Y L S L \* L R R I I R S \* M M K N  
 27241 - ACCTATGGAGTTAGATTATCCATAAAAACGAACAAGAAAATTATTCCTTCCCTGACATGA - 27300  
 - T Y G V R L S I K R T \* K L F S S \* H \*  
 - P M E L D Y F \* N E E E N Y S L P D I D  
 - L W S \* I I H K T N M K I I L F L T L I  
 27301 - TTGTATTACATCTGCGAGCTATATCACTATCAGGAGTGTGTTAGAGGTACCAGCTGTAC - 27360  
 - L Y L H L A S Y I T I R S V L E V R L Y  
 - C I Y I L R A I S L S G V C \* R Y D C T  
 - V F T S C E L Y H Y Q E C V R G T T V L  
 27361 - TACTAAAAGAACCCTGCCCATCAGGAACATACGAGGGCAATTCACCATTTACCCTCTG - 27420  
 - Y \* K N L A H Q E H T R A I H H F T L L  
 - T K R T L P I R N I R G Q F T I S P S C  
 - L K E P C P S G T Y E G N S P F H P L A  
 27421 - CTGACAATAAATTTGCACTAAGTTCAGTACACTAGCACACTTTGCTTTGCTTGGCTGACG - 27480  
 - L T I N L H \* L A L A H T L L L L V L T  
 - \* Q \* I C T N L H \* H T L C F C L C \* R  
 - D N K F A L T C T S T H F A F A C A D G  
 27481 - GTACTCGACATACCTATCAGCTGCGTGCAAGATCAGTTTCACCAAACTTTTCATCAGAC - 27540  
 - V L D I P I S C V Q D Q F H Q N F S S D  
 - Y S T Y L S A A C K I S F T K T F H Q T  
 - T R H T Y Q L R A R S V S P K L F I R Q  
 27541 - AAGAGGAGTTCAACAAGAGCTCTACTGCCCACTTTTTCTCATTGTTGCTGCTCTAGTAT - 27600  
 - K R R F N K S S T R H F F S L L L L \* Y  
 - R G G S T R A L L A T F S H C C C S S I  
 - E E V Q Q E L Y S P L F L I V A A L V F  
 27601 - TTTTAATACTTTGCTTCACCATTAAGAGAAAGACAGAATGAATGAGCTCACTTTAATTGA - 27660  
 - F \* Y F A S P L R E R Q N E \* A H F N \*  
 - F N T L L H H \* E K D R M N E L T L I D  
 - L I L C F T I K R K T E \* M S S L \* L T  
 27661 - CTTCTATTTGCTTTTTAGCCTTTGCTATTCTGTTTTATAATGCTTATTATATT - 27720  
 - L L F V L F S L S A I P C F N N A Y Y I  
 - F Y L C F L A F L L F L V L I M L I I F  
 - S I C A F \* P F C Y S L F \* \* C L L Y F

FIG. 11 Con't

27721 - TTGGTTTTCACTCGAAATCCAGGATCTAGAAGAACCTTGTACCAAAGTCTAAACGAACAT - 27730  
 - L V F T R N P G S R R T L Y Q S L N E H  
 - W F S L E I Q D L E E P C T K V \* T N M  
 - G F H S K S R I \* K N L V P K S K R T \*  
 27781 - GAACTTCTCATTGTTTGGACTTGATTTCTCTATGCAGTTGCATATGCAGTGTAGTACA - 27840  
 - E T S H C F D L Y F S M Q L H M H C S T  
 - K L L I V L T C I S L C S C I C T V V Q  
 - N F S L F \* L V F L Y A V A Y A L \* Y S  
 27841 - GCGCTGTGCATCTAATAAACCTCATGTGCTTGAAGATCCTTGTAAAGGTACAACACTAGGG - 27900  
 - A L C I \* \* T S C A \* R S L \* G T T L G  
 - R C A S N K P H V L E D P C K V Q H \* G  
 - A V H L I N L M C L K I L V R Y N T R G  
 27901 - GTAATACTTATAGCACTGCTTGGCTTTGTGCTTAGGAAAGGTTTACCTTTTCATAGAT - 27960  
 - V I L I A L L G F V L \* E R F Y L F I D  
 - \* Y L \* H C L A L C S R K G F T F S \* M  
 - N T Y S T A W L C A L G K V L P F H R W  
 27961 - GGCACACTATGGTTCAAACATGCACACCTAATGTTACTATCAACTGTCAAGATCCAGCTG - 28020  
 - G T L W F K H A E L M L L S T V K I Q L  
 - A H Y G S N M H T \* C Y Y Q L S R S S W  
 - H T M V Q T C T P N V T I N C Q D P A G  
 28021 - GTGGTGGCTTATAGCTAGGTGTTGGTACCTTCATGAAGTCCACAAACTGCTGCATTA - 28080  
 - V V R L \* L G V G T F M K V T K L L H L  
 - W C A Y S \* V L V P S \* R S P N C C I \*  
 - G A L I A R C W Y L H E G H Q T A A F R  
 28081 - GAGACGTACTTGTGTTTAAATAAACGAACAATTAATAATGTCTGATAATGGACCCCAA - 28140  
 - E T Y L L F \* I N E Q I K M S D N G P Q  
 - R R T C C F K \* T N K L K C L I M D P N  
 - D V L V V L N K R T N \* N V \* \* W T P I  
 28141 - TCAAACCAACGTAGTGCCCCCGCATTACATTTGGTGGACCCACAGATTCAACTGACAAT - 28200  
 - S N Q R S A P R I T F G G P T D S T D N  
 - Q T N V V P P A I H L V C P Q I Q L T I  
 - K P T \* C P P H Y I W W T H R F N \* Q \*  
 28201 - AACCAGAATGGAGGACGCAATGGGGCAAGGCCAAAACAGCGCCGACCCCAAGGTTTACCC - 28260  
 - N Q N G G R N G A R F K Q R R P Q G L P  
 - T R M E D A M G Q G Q N S A D P K V Y P  
 - P E W R T Q W G K A K T A P T P R F T Q  
 28261 - AATAACTGCGTCTTGGTTCACAGCTCTCACTCAGCATGGCAAGGAGGAAGTCTAGATTC - 28320  
 - N N T A S W F T A L T Q H G K E E L R F  
 - I I L R L G S Q L S L S M A R R N L D S  
 - \* Y C V L V H S S E S A W Q G G T \* I P  
 28321 - CCTCGAGGCCAGGGCGTTCCAATCAACACCAATAGTGGTCCAGATGACCAAATTTGGCTAC - 28380  
 - P R G Q G V P I N T N S G P D D Q I G Y  
 - L E A R A F Q S T P I V V Q M T K L A T  
 - S R P G R S N Q H Q \* W S R \* P N W L L  
 28381 - TACCGAAGAGCTACCCGACGAGTTCGTGGTGGTACGGCAAAATGAAAGAGCTCAGCCCC - 28440  
 - Y R R A T R R V R G G D G K M K E L S P  
 - T E E L P D E F V V V T A K \* K S S A P  
 - P K S Y P T S S W W \* R Q N E R A Q P Q  
 28441 - AGATGGTACTTCTATTACCTAGGAAGTGGCCAGAGCTTCACTTCCCTACGGCGCTAAC - 28500  
 - R W Y F Y Y L G T G P E A S L P Y G A N  
 - D G T S I T \* E L A Q K L H F P T A L T  
 - M V L L L P R N W P R S F T S L R R \* Q  
 28501 - AAAGAAGGCATCGTATGGGTTGCAACTGAGGGAGCCTTGAATACCCCAAAGACCACATT - 28560  
 - K E G I V W V A T E G A L N T P K D H I  
 - K K A S Y G L Q L R E P \* I H P K T T L  
 - R R H R M G C N \* G S L E Y T Q R P H W

FIG. 11 Con't

28561 - GGCACCCGCAATCCTAATAACAATGCTGCCACCGTGCTACAACITTCCTCAAGGAACAACA - 28620  
- G T R N P N N N A A T V L Q L P Q G T T  
- A P A I L I T M L P P C Y N F L K E Q H  
- H P Q S \* \* Q C C H R A T T S S R N N I  
28621 - TTGCCAAAAGGCTTCTACGCAGAGGGAAGCAGAGGCGGCACTCAAGCCTCTTCTCGCTCC - 28680  
- L P K G F Y A E G S R G G S Q A S S R S  
- C Q K A S T Q R E A E A A V K P L L A P  
- A K R L L R R G K Q R R Q S S L F S I L  
28681 - TCATCACGTAGTCGGGTAATCAAGAAATCAACTCCTGGCAGCAGTAGGGGAAATCT - 28740  
- S S R S R G N S R N S T P G S S R G N S  
- H H V V A V I Q E I Q L L A A V G E I L  
- I T \* S R \* F K K F N S W Q Q \* G K F S  
28741 - CCTGCTCGAATGGCTAGCGGAGGTGGTAAACTGCCCTGGCGTATTGCTGCTAGACAGA - 28800  
- P A R M A S G G G E T A L A L L L L D R  
- L L E W L A E V V K L P S R Y C C \* T D  
- C S N G \* R R W \* N C P R A I A A R Q I  
28801 - TTGAACCAGCTTGAGAGCAAAGTTTCTGGTAAAGGCCAACAACAAGGCCAAACTGTC - 28860  
- L N Q L E S K V S G K G Q Q Q Q G Q T V  
- \* T S L R A K F L V K A N N N K A K L S  
- E P A \* E Q S F W \* R F T T T R P N C H  
28861 - ACTAAGAAATCTGCTGCTGAGGCATCTAAAAGCCTGCCAAAAACGTACTGCCACAAA - 28920  
- T K K S A A E A S K K P R Q K R T A T K  
- L R N L L L R H L K S L A K N V L P Q N  
- \* E I C C \* G I \* K A S P K T Y C H K T  
28921 - CAGTACAACGTCACCTCAAGCATTTGGGAGACGTGGTCCACAACAACCAAGGAAATTC - 28980  
- Q Y N V T Q A F G R R G P E Q T Q G N F  
- S T T S L K H L G D V V Q N K P K E I S  
- V Q R H S S I W E T W S R T N P R K F R  
28981 - GGGGACCAAGACCTAATCAGACAAGGAAGTATTACAACATTGGCCGCAAATTCACAAA - 29040  
- G D Q D L I R Q G T D Y K H W P Q I A Q  
- G T K T \* S D K E L I T N I G R K L H N  
- G P R P N Q T R N \* L Q T L A A N C T I  
29041 - TTTGCTCCAAGTGCCTCTGCAATCTTTPGGAATGTCAGCATTGGCATGGAAGTCACACT - 29100  
- F A P S A S A F F G M S R I G M E V T P  
- L L Q V P L H S L E C H A L A W K S H L  
- C S K C L C I L W N V T H W H G S H T F  
29101 - TCGGGAACATGGCTGACTTATCATGGAGCCATTAAATGGATGACAAAGATCCACAATTC - 29160  
- S G T W L T Y H G A I K L D D K D P Q F  
- R E H G \* L I M E P L N W M T K I H N S  
- G N M A D L S W S H \* I G \* Q R S T I Q  
29161 - AAAGACAACGTCATACTGCTGAACAAGCACATTGACGCATACAAAACATTCCCACCAACA - 29220  
- K D N V I L L N K H I D A Y K T F P P T  
- K T T S Y C \* T S T L T H T K H S H Q Q  
- R Q R H T A E Q A H \* R I Q N I P T N R  
29221 - GAGCCTAAAAAGGACAAAAAGAAAGACTGATGAGCTCAGCCTTTGCCGAGAGACAA - 29280  
- E P K K D K K K K T D E A Q P L P Q R Q  
- S L K R T K R K R L M K L S L C R R D K  
- A \* K G Q K E K D \* \* S S A F A A E T K  
29281 - AAGAAGCAGCCACTGTGACTCTTCTCGCGGCTGACATGGATGATTTCTCCAGACAA - 29340  
- K K Q P T V T L L P A A D M D D F S R Q  
- R S S P L \* L F F L R L T W M I S F D N  
- E A A H C D S S S C G \* H G \* F L Q T T  
29341 - CTTCAAAATCCATGAGTGGAGCTTCTGCTGATCAACTCAGGCATAAACACTCATGATG - 29400  
- L Q N S M S G A S A D S T Q A \* T L M M  
- F K I P \* V E L L L I Q L R H K H S \* \*  
- S K F H E W S F C \* F N S G I N T H D D

FIG. 11 Con't

29401 - ACCACACAAGGCAGATGGGCTATGTAAACGTTTTTCGCAATTCGGTTTACGATACATAGTC - 29460  
- T T Q G R W A M \* T F S Q F R L R Y I V  
- P H K A D G L C K R F R N S V Y D T \* S  
- H T R Q M G Y V N V F A I P F T I H S L  
29461 - TACTCTTGTGCAGAATGAATTCTCGTAACTAAACAGCACAAGTAGGTTTGTAGTTAACTTTA - 29520  
- Y S C A E \* I L V T K Q H K \* V \* L T L  
- T L V Q N E F S \* L N S T S R F S \* L \*  
- L L C R M N S R N \* T A Q V G L V N F N  
29521 - ATCTCACATAGCAATCTTTAATCAATGTGTAACATTAGGGAGGACTTGAAAGAGCCACCA - 29580  
- I S H S N L \* S M C N I R E D L K E P P  
- S H I A I F N Q C V T L G R T \* K S H H  
- L T \* Q S L I N V \* H \* G G L E R A T T  
29581 - CATTTCATCGAGGCCACGCGGAGTACGATCGAGGGTACAGTGAATAATGCTAGGGAGAG - 29640  
- H F H R G H A E Y D R G Y S E \* C \* G E  
- I F I E A T R S T I E G T V N N A R E S  
- F S S R P R G V R S R V Q \* I M L G R A  
29641 - CTGCCTATATGGAAGAGCCCTAATGTGTAATAATTTTGTAGTAGTCTATCCCATGTG - 29700  
- L P I W K S P N V \* N \* F \* \* C Y P H V  
- C L Y G R A L M C K I N F S S A I P M \*  
- A Y M E E P \* C V K L I L V V L S P C D  
29701 - ATTTTAATAGCTTCTTAGGAGAATGACAAAAAAAAAAAAAAAAA - 29742  
- I L I A S \* E N D K K K K K X  
- F \* \* L L R R M T K K K K X  
- F N S F L G E \* Q K K K K X

FIG. 11 Con't

1 - TTTTTTTTTTTTTTGTCAATCTCCTAAGAAGCTATTAAAAATCACATGGGGATAGCACTA - 60  
- F F F F F V I L L R S Y \* N H M G I A L  
- F F F F L S F S \* E A I K I T W G \* H Y  
- F F F F C H S P K K L L K S H G D S T T  
61 - CTAAAATAATTTACACATTAGGGCTCTCCATATAGGCAGCTCTCCCTAGCATTATTC - 120  
- L K L I L H I R A L P Y R Q L S L A L F  
- \* N \* F Y T L G L F H I G S S P \* H Y S  
- K I N F T H \* G S S I \* A A L P S I I H  
121 - ACTGTACCCTCGATCGTACTCCGCGTGGCCTCGATGAAAATGTGGTGGCTCTTTCAAGTC - 180  
- T V P S I V L R V A S M K M W W L F Q V  
- L Y P R S Y S A W P R \* K C G G S F K S  
- C T L D R T P R G L D E N V V A L S S P  
181 - CTCCTAATGTTACACATTGATTAAGATTGCTATGTGAGATTAAGTTAACTAAACCTA - 240  
- L P N V T H \* L K I A M \* D \* S \* L N L  
- S L M L H I D \* R L L C E I K V N \* T Y  
- P \* C Y T L I K D C Y V R L K L T K P T  
241 - CTTGTGCTGTTAGTTACGAGAATTCATTCTGCACAAGAGTAGACTATGTATCGTAAACG - 300  
- L V L F S Y E N S F C T R V D Y V S \* T  
- L C C L V T R I H S A Q E \* T M Y R K R  
- C A V \* L R E F I L H K S R L C I V N G  
301 - GAATTGCGAAAACGTTTACATAGCCCATCTGCCTTGTGTGGTCATCATGAGTGTTTATGC - 360  
- E L R K R L H S P S A L C G H H E C L C  
- N C E N V Y I A H L P C V V I M S V Y A  
- I A K T F T \* P I C L V W S S \* V F M P  
361 - CTGAGTTGAATCAGCAGAAGCTCCACTCATGGAATTTTGAAGTTGTCTGGAGAAATCATC - 420  
- L S \* I S R S S T H G I L K L S G E I I  
- \* V E S A E A P L M E F \* S C L E K S S  
- E L N Q Q K L H S W N F E V V W R N H P  
421 - CATGTCAGCCGAGGAAGAAGAGTCACAGTGGGCTGCTTCTTTTGTCTCTGCGGCAAAGG - 480  
- H V S R A R K K S H S G L L L S L R Q R  
- M S A A G R R V T V G C F F C L C G K G  
- C Q P Q E E E S Q W A A S F V S A A K A  
481 - CTGAGCTTCATCAGTCTTTTTCTTTTGTCTTTTGTAGGCTCTGTTGGTGGGAATGTTTT - 540  
- L S F I S L F L F V L F R L C W W E C F  
- \* A S S V F F F L S F L G S V G G N V L  
- E L H Q S F S F C P F \* A L L V G M F C  
541 - GTATGCGTCAATGTGCTTGTTCAGCAGTATGACGTTGTCTTTGAATTGTGGATCTTTGTC - 600  
- V C V N V I V Q Q Y D V V F E L W I F V  
- Y A S M C L F S S M T L S L N C G S L S  
- M R Q C A C S A V \* R C L \* I V D L C H  
601 - ATCCAATTTAATGGCTCCATGATAAGTCAGCCATGTTCCCGAAGGTGTGACTTCCATGCC - 660  
- I Q F N G S M I S Q P C S R R C D F H A  
- S N L M A P \* \* V S H V P E G V T S M P  
- P I \* W L R D K S A M F P K V \* L P C Q  
661 - AATGCGTGACATTCCAAAGATGCAGAGGCACTTGGAGCAAATTTGCAATTTGCGGCCA - 720  
- N A \* H S K E C R G T W S K L C N L R P  
- M R D I P K N A E A L G A N C A I C G Q  
- C V T F Q R M Q R H L E Q I V Q F A A N  
721 - ATGTTTGAATCAGTTCCTTGTCTGATTAGGTCTTGGTCCCCGAAATTTCTTGGGTTTG - 780  
- M F V I S S L S D \* V L V P E I S L G L  
- C L \* S V P C L I R S W S P K F P W V C  
- V C N Q F L V \* L G L G P R N F L G F V  
781 - TTCTGGACCACGTCTCCCAAATGCTTGTGAGTACGTTGTACTGTTTTGTGGCAGTACGTTT - 840  
- F W T T S P K C L S D V V L F C G S T F  
- S G P R L P N A \* V T L Y C F V A V R F  
- L D H V S Q M L E \* R C T V L W Q Y V F

FIG. 12

841 - TTGGCCAGGCTTTTTAGATGCCTCAGCAGCAGATTCTTAGTGACAGETTGGCCTTGTG - 900  
- L A R L F R C L S S R F L S D S L A L L  
- W R G F L D A S A A D F L V T V W P C C  
- G E A F \* M P Q Q Q I S \* \* Q F G L V V  
901 - TTGTTGGCCTTTACCAGAACTTTGCTCTCAAGCTGGTTCAATCTGTCTAGCAGCAATAG - 960  
- L L A F T R N F A L K L V Q S V \* Q Q \*  
- C W P L P E T L L S S W F N L S S S N S  
- V G L Y Q K L C S Q A G S I C L A A I A  
961 - CGCGAGGGCAGTTTCACCACCTCCGCTAGCCATTCGAGCAGGAGAATTTCCCCTACTGCT - 1020  
- R E G S F T T S A S H S S R R I S P T A  
- A R A V S P P P L A I R A G E F P L L  
- R G Q F H H L R \* P F E Q E N F P Y C C  
1021 - GCCAGGAGTTGAATTTCTTGAATTACCGCGACTACGTGATGAGGAGCGAGAAGAGGCTTG - 1080  
- A R S \* I S \* I T A T T \* \* G A R R G L  
- P G V E F L E L P R L R D E E R E E A \*  
- Q E L N F L N Y R D Y V M R S E K R L D  
1081 - ACTGCCGCTCTGCTTCCCTCTGCGTAGAAGCCTTTTGGCAATGTGTTCCTTGAGGAAG - 1140  
- T A A S A S L C V E A F W Q C C S L R K  
- L P P L L P S A \* K P F G N V V P \* G S  
- C R L C F P L R R S L L A M L F L E E V  
1141 - TTGTAGCACGGTGGCAGCATTGTTATTAGGATTGCGGGTGCCAATGTGGTCTTTGGGTGT - 1200  
- L \* H G G S I V I R I A G A N V V F G C  
- C S T V A A L L L G L R V P M W S L G V  
- V A R W Q E C Y \* D C G C Q C G L W V Y  
1201 - ATTCAGGCTCCCTCAGTTGCAACCCATACGATGCCTTCTTTGTTAGCCCGTAGGGAAG - 1260  
- I Q G S L S C N P Y D A F F V S A V G K  
- F K A P S V A T H T M P S L L A P \* G S  
- S R L P Q L Q P I R C L L C \* R R R E V  
1261 - TGAAGCTTCTGGGCCAGTTCCCTAGGTAATAGAAGTACCATCTGGGGCTGAGCTCTTTCAT - 1320  
- \* S F W A S S \* V I E V P S G A E L F H  
- E A S G P V P R \* \* K Y H L G L S S F I  
- K L L G Q F L G K R S T I W G \* A L S F  
1321 - TTTGCCGTCACCACCAGCACTCGTGGGTAGCTCTTGGTACTAGCCAATTTGGTCAATC - 1380  
- F A V T T T N S S G S S S V V A N L V I  
- L P S P P R T R R V A L R \* \* P I W S S  
- C R H H H E L V G \* L F G S S Q F G H L  
1381 - TGGACCACTATTGGTGTGATTGGAACGCCCTGGCCTCGAGGGAATCTAAGTTCCTCCTT - 1440  
- W T T I G V D W N A L A S R E S K F L L  
- G P L L V L I G T P W P R G N L S S S L  
- D H Y W C \* L E R P G L E G I \* V P P C  
1441 - GCCATGCTGAGTGAGAGCTGTGAACCAAGACGCAGTATTATTGGGTAAACCTTGGGGTCG - 1500  
- A M L S E S C E P R R S I I G \* T L G S  
- P C \* V R A V N Q D A V L L G K P W G R  
- H A E \* E L \* T K T Q Y Y W V N L G V G  
1501 - GCGCTGTTTGGCCTTGCCCCATTGCGTCTCCATCTCGTTATTGTGAGTTGAATCTGT - 1560  
- A L F W P C P I A S S I L V I V S \* I C  
- R C F G L A P L R P P F W L L S V E S V  
- A V L A L P H C V L H S G Y C Q L N W  
1561 - GGGTCCACCAAATGTAATGCGGGGGGCACTACGTTGGTTTGGATTGGGGTCCATTATCAGA - 1620  
- G S T K C N A G G T T L V \* L G S I I R  
- G P P N V M R G A L R W F D W G P L S D  
- V H Q M \* C G G H Y V G L I G V H Y Q T  
1621 - CATTTTAATTTGTTGCTTTATTTAAAACAACAAGTACGTCTCTAAATGCAGCAGTTTGGT - 1680  
- H F N L F V Y L K Q Q V R L \* M Q Q F G  
- I L I C S F I \* N N K Y V S K C S S L V  
- F \* F V R L F K T T S T S L N A A V W \*

FIG. 12 Con't

1681 - GACCTTCATGAAGGTACCAACACCTAGCTATAAGCGCACCACCAGCTGGATCTTGACAGT - 1740  
- D L H E G T N T \* L \* A H H Q L D L D S  
- T F M K V P T P S Y K R T T S W I L T V  
- P S \* R Y Q H L A I S A P P A G S \* Q L  
1741 - TGATAGTAACATTAGGTGTGCATGTTTGAACCATAGTGTGCCATCTATGAAAAGGTA AAA - 1800  
- \* \* \* H \* V C M F E P \* C A I Y E K V K  
- D S N I R C A C C L N H S V P S M K R \* N  
- I V T L G V H V \* T I V C H L \* K G K T  
1801 - CCTTTCCTAGAGCACAAAGCCAAAGCAGTGCATATAAGTATTACCCCTAGTGTGTGACCTTA - 1860  
- P F L E H K A K Q C Y K Y Y P \* C C T L  
- L S \* S T K P S S A I S I T P S V V P Y  
- F P R A Q S Q A V L \* V L P L V L Y L T  
1861 - CAAGGATCTTCAAGCACATGAGGTTTATTAGATGCACACGCGTGTACTACAGTGCATATG - 1920  
- Q G S S S T \* G L L D A Q R C T T V H M  
- K D L Q A H E V Y \* M H S A V L Q C I C  
- R I F K H M R F I R C T A L Y Y S A Y A  
1921 - CAACTGCATAGAGAAATACAAGTCAAAACAATGAGAAGTTTCATGTTTCGTTTAGACTTTG - 1980  
- Q L H R E I Q V K T M R S F M F V \* T L  
- N C I E K Y K S K Q \* E V S C S F R L W  
- T A \* R N T S Q N N E K F H V R L D F G  
1981 - GTACAAGGTTCTTCTAGATCCTGGATTTTCGAGTGAAAACCAAAATATAATAAGCATTATT - 2040  
- V Q G S S R S W I S S E N Q N I I S I I  
- Y K R V L L D P G F R V K T K I \* \* A L L  
- T R F F \* I L D F E \* K P K Y N K H Y \*  
2041 - AAAACAAGGAATAGCAGAAAGGCTAAAAAGCACAAATAGAAGTCAATTAAGTCAGCTCA - 2100  
- K T R N S R K A K K H K \* K S I K V S S  
- K Q G I A E R L K S T N R S Q L K \* A H  
- N K E \* Q K G \* K A Q I E V N \* S E L I  
2101 - TTCATTCTCTCTTTCTCTTAATGGTGAAGCAAAGTATTA AAAAATACTAGAGCAGCAACAA - 2160  
- F I L S F S \* W \* S K V L K I L E Q Q Q  
- S F C L S L N G E A K Y \* K Y \* S S N N  
- H S V F L L M V K Q S I K N T R A A T M  
2161 - TGAGAAAAAGTGGCGAGTAGAGCTCTTGTGAACCTCCTCTTGTCTGATGAAAAGTTTTG - 2220  
- \* E K V A S R A L V E P P L V \* \* K V L  
- E K K W R V E L L L N L L L S D E K F W  
- R K S G E \* S S C \* T S S C L M K S F G  
2221 - GTGAAACTGATCTTGACGCAGCTGATAGGTATGTCGAGTACCGTCAGCACAAAGCAAAG - 2280  
- V K L I L H A A D R Y V E Y R Q H K Q K  
- \* N \* S C T Q L I G M S S T V S T S K S  
- E T D L A R S \* \* V C R V P S A Q A K A  
2281 - CAAAGTGTGTGCTAGTGCAAGTTAGTGCAAAATTTATTGTCAGCAAGAGGTTGAAATGGTG - 2340  
- Q S V C \* C K L V Q I Y C Q Q E G E M V  
- K V C A S A S \* C K F I V S K R V K W \*  
- K C V L V Q V S A N L L S A R G \* N G E  
2341 - AATTGCCCTCGTATGTTCTCTGATGGGCAAGGTTCTTTTAGTAGTACAGTCGTACCTCTAA - 2400  
- N C P R M F L M G K V L L V V Q S Y L \*  
- I A L V C S \* W A R F F \* \* Y S R T S N  
- L P S Y V P D G Q G S F S S T V V P L T  
2401 - CACACTCCTGATAGTGATATAGCTCGCAAGATGTAATAACAATCAATGTCAGGAAGAGAA - 2460  
- H T P D S D I A R K M \* I Q S M S G R E  
- T L L I V I \* L A R C K Y N Q C Q E E N  
- H S \* \* \* Y S S Q D V N T I N V R K R I  
2461 - TAATTTTCATGTTTCGTTTATGGATAATCTAACTCCATAGTTCCTTCATCATCTAACTCC - 2520  
- \* F S C S F Y G \* S N S I G S S S S N S  
- N F H V R F M D N L T P \* V L H H L T P  
- I F M F V L W I I \* L H R F F I I \* L R

FIG. 12 Con't

2521 - GAATAATTCTTCTTAGTTAGAGGCTTAAATAATTGTCTCACTATTGAACTTATTATAACG - 2580  
 - E \* F F L V R G L N N C L T I E L I I T  
 - N N S S \* L E A \* I I V S L L N L L \* R  
 - I I L L S \* R L K \* L S H Y \* T Y Y N V  
 2581 - TCAAGATTCCAAATAGCAATCCTGAAAGTCCATATAATGATAATCAATATCTCTGCTATT - 2640  
 - S R F Q I A I L K V L I M I I N I S A I  
 - Q D S K \* Q S \* K S S \* \* \* S I S L L L  
 - K I P N S N P E S P H N D N Q Y L C Y C  
 2641 - GTAACCTGGAAGTCAACAAGATGAAACATCTGTTGTCACTTACTGTACTAGCAAAGCAAT - 2700  
 - V T W K S T R \* N I C C H L L Y \* Q S N  
 - \* P G S Q Q D E T S V V T Y C T S K A I  
 - N L E V N K M K H L L S L T V L A K Q Y  
 2701 - ATTTGCGTGTGCTACCGGCGTGGTCTGTATTTAATTTATAGTTTCCAATACGGTAGCGGTT - 2760  
 - I V V A T G V V C I \* F I V S N T V A V  
 - L S L L P A W S V F N L \* F P I R \* R L  
 - C R C Y R R G L Y L I Y S F Q Y G S G C  
 2761 - GTATGCAGCAAACCTGAAATCAGTGCCTACAGCTGCGAGCCTCTAATTTGTAATAAGA - 2820  
 - V C S K T \* I S A Y T L R R S \* F V I R  
 - Y A A K P E S V P T R C D A P N L \* \* E  
 - M Q Q N L N Q C L H A A T L L I C N K K  
 2821 - AAGCGTTCGTGATGTAGCCACAGTGTCTCTTTTGGCAGGTCCTTAATGTCACAGGCCCC - 2880  
 - K R S \* C S H S D L F W Q V L N V T A P  
 - S V R E V A T V I S F G R S L M S Q R P  
 - A F V M \* P Q \* S L L A G P \* C H S A L  
 2881 - TAGGGAGTGTCCGGCCATTCGCAAGTGACCAGGAATGATCACAGCACCAATGACAAGTTC - 2940  
 - \* G V S G H S Q V T T N D H S T N D K F  
 - R E C P A I R K \* P R M I T A P M T S S  
 - G S V R P F A S D H E \* S Q H Q \* Q V H  
 2941 - ACTTTCATGAGCGGTCTGGTCAACAATTGCCCCGGAGAGGCACATTGAGAAGAATGTT - 3000  
 - T F H E R S G H N C P P E R H I E K N V  
 - L S M S G I V T I V P R R G T L R R M F  
 - F P \* A V W S Q L S P G E A H \* E E C L  
 3001 - TCTTCTGGGTTGAATGACCACATTGAGCGGGTACGAGCAAACAGCCTGAAGGAAGCAAC - 3060  
 - C F W V E \* P H \* A G T S K Q P E G S N  
 - V S G L N D H I E R V R A N S L K E A T  
 - F L G \* M T T L S G Y E Q T A \* R K Q R  
 3061 - GAAGTAGCTAAGCCACATCAAGCCTACAATACAAGCCATTGCAATCGCAATCCCGCCAGT - 3120  
 - E V A K P H Q A Y N T S H C N R N P A S  
 - K \* L S H I K P T I Q A I A I A I P P V  
 - S S \* A T S S L Q Y K P L Q S Q S R Q S  
 3121 - CACCCAATTAATCTGTAGACAACAGCAAGCACAAAACAAGCAAGTGTACTGGCCACAA - 3180  
 - H P I N S V D N S K H K T S K C Y W P Q  
 - T Q L I L \* T T A S T K Q A S V T G H K  
 - P N \* F C R Q Q Q A Q N K Q V L L A T R  
 3181 - GAGCCAGAGGAAAACAAGCTTTATTATGTACAAAAACCTGTCCGATTAGAATAGGCAAA - 3240  
 - E P E E N K L Y Y V Q K P V P I R I G K  
 - S Q R K T S F I M Y K N L F R L E \* A N  
 - A R G K Q A L L C T K T C S D \* N R Q I  
 3241 - TTGTAGTAACATAATCCAGGCTAGGAATAGGAAACCTATTACTAGGTTCCATTGTTCCAG - 3300  
 - L \* \* H N P G \* E \* E T Y Y \* V P L F Q  
 - C S N I I Q A R N R K P I T R F H C S R  
 - V V T \* S R L G I G N L L L G S I V P G  
 3301 - GAGTTGTTTAAAGCTCCTCAACGGTAATAGTACCGTGTCTGCCATGATAAGCAATGTTAA - 3360  
 - E L F K L L N G N S T V V C H D K Q C \*  
 - S C L S S S T V I V P L S A M I S N V K  
 - V V \* A P Q R \* \* Y R C L P \* \* A M L K

FIG. 12 Con't



3361 - AGTTCCAAACAGAAATAATAATAATAGTTAGTTTCGTTTACAGACCAGAAAGATCAGGAACCTCT - 3420  
 - S S K Q N N N N S \* F V \* T R R S G T P  
 - V P N R I I I I V S S F R P E D Q E L L  
 - F Q T E \* \* \* \* L V R L D Q K I R N S F  
 3421 - TCAGAAGAGTTTCAGATTTTAAACACGCGAGTAGACGTAACCGTTGGTTTTACTAAACTC - 3480  
 - S E E F R F L T R E \* T \* T V G F T K L  
 - Q K S S D F \* H A S R R K P L V L L N S  
 - R R V Q I F N T R V D V N R W F Y \* T H  
 3481 - ACGTTAACAATATTGCAGCAGTACGCACACAATCGAAGCGCAGTAAGGATGGCTAGTGTG - 3540  
 - T L T I L Q Q Y A H N R S A V R M A S V  
 - R \* Q Y C S S T H T I E A Q \* G W L V \*  
 - V N N I A A V R T Q S K R S K D G \* C D  
 3541 - ACTAGCAAGAATAACCACGAAAGCAAGAAAAGAAGTACGCTATTAACCTATTACGTACCT - 3600  
 - T S K N T T K A R K R S T I L T I N V P  
 - L A R I P R K Q E K E V R Y \* L I T Y L  
 - \* Q E Y H E S K K K K Y A I N Y \* R T C  
 3601 - GTTCTTCCGAAACGAATGAGTACATAAGTTTCGTACTCACTTCTGTGCTTACAAAGGC - 3660  
 - V S S E T N E Y I S S Y S L S C A Y K G  
 - F L P K R M S T \* V R T H F L V L T K A  
 - F F R N E \* V H K F V L T F L C L Q R H  
 3661 - ACGTAGTAGTCGTCGTCGGCTCATCAAATTGGATCCATTGCTGGATTAGCAACTCCT - 3720  
 - T L V V V V G S S \* I G S I A G L A T P  
 - R \* \* S S S A H H K L D P L I D \* Q L L  
 - A S S R R R L I I N W I H C W I S N \*  
 3721 - GAAGAGCCGTCGATTGTGTGATTTGCACATTCGGTGGGTCTTAAACAAGCTGTAAAG - 3780  
 - E E P S I V C I C T F G G S L T S L L K  
 - K S R R L C V F A H S V G L \* Q A C \* R  
 - R A V D C V Y L H I R W V F N K L V K D  
 3781 - ATGAAGAATGTAGCATTTCATACCAGTGTCTGTAGTAATTTGTGTAGACTCAAGCTGG - 3840  
 - M K N V A F S I P V S V V I C V D S S W  
 - \* R M \* H F Q Y Q C L \* \* F V \* T Q A G  
 - E E C S I F N T S V C S N L C R L K L V  
 3841 - TAGTAAACTTCGGTGAATAGCCATGTACAACGACATAGTCTTTAACACCTGAGTGCCTA - 3900  
 - \* \* T S V K \* P C T T T \* S L T P E C L  
 - S K L R \* N S H V Q R H S L \* H L S A Y  
 - V N F G E I A M Y N D I V F N T \* V P I  
 3901 - TCCTCAGAATAACCACCAATTTGGTAGTCTTCTTTGAGTTTTGGTGTGAAATGCCGTC - 3960  
 - S S E \* P P I W \* S S L S F G V E M P S  
 - P Q N N H Q F G S L L \* V L V L K C R H  
 - L R I T T N L V V F F E F W C \* N A V T  
 3961 - CCTTCAGTAACGACAATTGTATCTGTGACACTGTTATATGGTATACAGTAGTCATAGTTA - 4020  
 - P S V T T I V S V T L L Y G I Q \* S \* L  
 - L Q \* R Q L Y L \* H C Y M V Y S S H S Y  
 - F S N D N C I C D T V I W Y T V V I V M  
 4021 - TGTGTGTGCCAGCAAACAAGTAGTTGGCATCAIAAAGTAATGGGTTCTTGATTGTCAC - 4080  
 - C V C Q Q T K \* L A S \* S N G F L D L H  
 - V C A S K Q S S W H H K V M G S W I C T  
 - C V P A N K V V C I I K \* W V L G F A L  
 4081 - TTCCAACAAAGCCAACATCTCATAATAATTCTACATGCGTTGATGCATTGTAGAAAATAT - 4140  
 - F Q Q S Q H L I I I L H A L M H C R K Y  
 - S N K A N I S \* \* F Y M R \* C I V E N I  
 - P T K P T S H N N S T C V D A L \* K I Y  
 4141 - ATCAAGGCATAGAGGTACAAAATTGCGCCTCCTTACCTGCAGCGACAAGCAAAAGATGT - 4200  
 - I K A \* R Y K N C A S L P A A T S K R C  
 - S R H R G T K I A P P Y L Q R Q A K D V  
 - Q G I E V Q K L R L L T C S D K Q K M \*

FIG. 12 Con't

4201 - GAATAGATGGTAACAAATAGCAGCAGTAAATTCGAAATGAACTGGAAGCCCTTATAAAGG - 4260  
- E \* M V T N S S S K L Q M N W K P L \* R  
- N R W \* Q I A A V N C K \* T G S P Y K G  
- I D G N K \* Q Q \* I A N E L E A L I K G  
4261 - GCTAGCTGCCATCTTTTATTGAGCCCAATTATTTGGTAGCGCTCTGAAAAACAGCAAGA - 4320  
- A S C H L L L S A I I L V A L \* K T A R  
- L A A I F Y \* A Q L F W \* R S E K Q Q E  
- \* L P S F I E R N Y F G S A L K N S K K  
4321 - AATGCAACGCCAATAACAAGCCATCCGAAAGGGAGTGAGGCTTGTAGCGGTATCGTTGCT - 4380  
- N A T P I T S H P K G S E A C S G I V A  
- M Q R Q \* Q A I R K G V R L V A V S L L  
- C N A N N K P S E R E \* G L \* R Y R C C  
4381 - GTAGCATGAACAGTACTTGCAGGAGAAGCATTGTCAATTTTACTGGCTGTGCAGTAATT - 4440  
- V A \* T V L A G E A L S I F T G C A V I  
- \* H E Q Y L Q E R K H C Q F L L A V Q \* L  
- S M N S T C R R S I V N F Y W L C S N \*  
4441 - GATCCAAGAGTAAAAAATCTCATAAACAATCCATAAGTTCGTTTATGTGTAATGTAATT - 4500  
- D P R V K N L I N K S I S S F M C N V I  
- I Q E \* K I S \* T N P \* V R L C V M \* F  
- S K S K K S H K Q I H K F V Y V \* C N L  
4501 - TGACACCCTTGAGAACTGGCTCAGAGTCATCTCATCAAACCTGCAGCAAGAACCACAAG - 4560  
- \* H P \* E L A Q S H P H Q T C S K N H K  
- D T L E N W L R V I L I K L A A R T T R  
- T P L R T G S E S S S S N L Q Q E P Q E  
4561 - AGCATGCACCCTTGAGGCAACTGCAACAACCTAGTCATGCAACAAAGCAAGATTGTAACCA - 4620  
- S M H P \* G N C N N \* S C N K A R L \* P  
- A C T L E A T A T T S H A T K Q D C N H  
- H A P L R Q L Q Q L V M Q Q S K I V T M  
4621 - TGACGATGGCAATTAGTCCAGCAATGAAGCCGAGCCAAACATACCAAGGCCATTTAATAT - 4680  
- \* R W Q L V Q Q \* S R A K H T K A I \* Y  
- D D G N \* S S N E A E P N I P R P F N I  
- T M A I S P A M K P S Q T Y Q G H L I Y  
4681 - ATTGCTCATATTTTCCCAATTCCTGAAGGTCAATGAGTGATTCAATTTAAATTTTAGCGA - 4740  
- I A H I F P I L E G Q \* V I H L N F \* R  
- L L I F S Q F L K V N E \* F I \* I F S D  
- C S Y F P N S \* R S M S D S F K F L A T  
4741 - CCTCATTGAGGCGGTCAATTTCTTTTGAATGTTGACGACAGAAGCGTTAATGCCTGAAA - 4800  
- P H \* G G Q F L F E C \* R Q K R \* C L K  
- L I E A V N F F L N V D D R S V N A \* N  
- S L R R S I S F \* M L T T E A L M P E M  
4801 - TGTCGCCAAGATCAACATCTGGTGATGTATGATTTTTGAAGTACTTGTCCAGCTCTTCTT - 4860  
- C R Q D Q H L V M Y D F \* S T C P A L L  
- V A K I N I W \* C M I F E V L V Q L F F  
- S P R S T S G D V \* F L K Y L S S S S L  
4861 - TGAATGAGTCAAGCTCAGGTTCAGAGGATCATAAAGTGTGTTAATGATGCCAATAA - 4920  
- \* M S Q A Q V A E D H K L C C \* \* C Q \*  
- E \* V K L R L Q R I I N C V V N D A N N  
- N E S S S G C R G S \* T V L L M M P I T  
4921 - CGACATCACAATTTCCCTGAGACAAATGTAATTCCTGTAGTAATTTATTTGTGGAGAAAAGA - 4980  
- R H H N F L R Q M Y C L \* \* L F V E K R  
- D I T I S \* D K C I V C S N Y L W R K E  
- T S Q F P E T N V L S V V I I C G E K K  
4981 - AGTTCCTCTGTGTAATAAACCAAGAAGTGCCATTAAACACAAAAACACCTTCACGAGGGA - 5040  
- S S V \* \* T K K C H \* T Q K H L H E G  
- V P L C N K P R S A I K H K N T F T R E  
- F L C V I N Q E V P L N T K T P S R G K

FIG. 12 Con't

5041 - AGTATGCTTTGCCCTTCATGACAAAATTGCTGGCGCTGTGGTGAAGTTCCTCTCCTGGGGATG - 5100  
- S M L C L H D K L L A L W \* S S S P G M  
- V C F A F M T N C W R C G E V P L L G W  
- Y A L P S \* Q I A G A V V K F L S W D G  
5101 - GCACATACGTGACATGTAGGAAGACAACACCATGCGGGGCTGTGTGGGAAGGACATAA - 5160  
- A H T \* H V G R Q H H A G L L V G R T \*  
- H I R D M \* E D N T M R G C L W E G H K  
- T Y V T C R K T T P C G A A C G K D I R  
5161 - GGTGGTAGCCCTTTCCACAAAAGTCAACTCTTTTTGATTGTCCAAGAACACACTCAGACA - 5220  
- G G S P F H K S Q L F L I V Q E H T Q T  
- V V A L S T K V N S F \* L S K N T L R H  
- W \* P F P Q K S T L F D C P R T H S D I  
5221 - TTTTAGTAGCAGCAAGATTAGCAGAAGCCCTGATTCAGCAGCCCTGATTAGTTGTGTG - 5280  
- F \* \* Q Q D \* Q K P \* F Q Q P \* L V V V  
- F S S S K I S R S P D F S S P D \* L L C  
- L V A A R L A E A L I S A A L I S C C V  
5281 - TTACATAGGTTTGAAGGCTTTGAAGTCTGCCTGTAAATTAACCTGTCAATTTGTACCTCCG - 5340  
- L H R F E G F E V C L \* L T C Q F V P P  
- Y I G L K A L K S A C N \* P V N L Y L R  
- T \* V \* R L \* S L P V I N L S I C T S A  
5341 - CCTCGACTTATCAAGTCGCGAAAGGATATCATTAGCACACTTGAAATTCACCAAAAT - 5400  
- P R L Y Q V A K G Y H L A H L K L H Q N  
- L D F I K S R K D I I \* H T \* N C T K I  
- S T L S S R E R I S F S T L E I A P K L  
5401 - TAGAGCTAAGTTGTTAACAAGTGTGTTAATGCTTGAGCATTCTGGTTAACAACGCTCT - 5460  
- \* S \* V V \* Q V C L M L E H S G \* Q R L  
- R A K L F N K C V \* C L S I L V N N V L  
- E L S C L T S V F N A \* A F W L T T S C  
5461 - GCAGCTGCCCAATGCAGTTGATGTTGTTGTAAGTGATTCTTGAATTTGACTAATCGCCT - 5520  
- A A C P M Q L M L L \* V I L E F D \* S P  
- Q L A Q C S \* C C C K \* F L N L T N R L  
- S L P N A V D V V V S D S \* I \* L I A L  
5521 - TGTTAAATTTGGTTGCGGATTTGTTTTGTTTCTCATAGAGAACATTTTGGGTAACCTCAA - 5580  
- C \* I G W R F V F G S H R E H F G \* L Q  
- V K L V G D L F L V L I E N I L G N S N  
- L N W L A I C F W F S \* R T F W V T P M  
5581 - TGCCATTTGAACCTATATGCCATTTGCATAGCAAAAGGTATTTGAAGAGCAGCGCCAGCAC - 5640  
- C H \* T Y M P F A \* Q K V F E E Q R Q H  
- A I E P I C H L H S K R Y L K S S A S T  
- P L N L Y A I C I A K G I \* R A A P A P  
5641 - CAAATGTCCATCCAGCAGTGGCAGTACCCTAAGTAGAGCAGCAGTGTAGGCAGCAATCA - 5700  
- Q M S I Q Q W Q Y H \* L E Q Q C R Q Q S  
- K C P S S S G S T T N \* S S S V G S N H  
- N V H P A V A V P L T R A A V \* A A I I  
5701 - TATCATCAGTGAGCAGAGGTGGCAACACTGTAAGTCCATTGAACTTCTGCGCACAAATGA - 5760  
- Y H Q \* A E V A T L \* V H \* T S A H K \*  
- I I S E Q R W Q H C K S I E L L R T N E  
- S S V S R G N T V S P L N F C A Q M R  
5761 - GATCTCTAGCATTAAATATCACCTAGGCATTCGCCATATTGCTTCATGAAGCCAGCATCAG - 5820  
- D L \* H \* Y H L G I R H I A S \* S Q H Q  
- I S S I N I T \* A F A I L I H E A S I S  
- S L A L I S P R H S P Y C F M K P A S A  
5821 - CGAGTGTACCTTATTAAGAGCAAGTCCCTCAATAAAAGACCTCTTAGTTGGCTTTAGAG - 5880  
- R V S P Y \* R A S P Q \* K T S \* L A L E  
- E C H L I K E Q V L N K R P L S W L \* R  
- S V T L L K S K S S I K D L L V G F R G

FIG. 12 Con't

5881 - GGTCAGGTAATATTTGTGAAAAATTAACCACCAAAATATTTCAAAGTTGGGGTTTGT - 5940  
- G Q V I F V K N \* N H Q N I S K L G F C  
- V R \* Y L \* K I K T T K I F Q S W G F V  
- S G N I C E K L K P P K Y F K V G V L Y  
5941 - ACATTTGTTTACTTGTGCGAACACTTCACGTGTGTGCGATCCTGTTGAGCAGCAATAC - 6000  
- T F V \* L E R T L H V C C D P V Q Q Q Y  
- H L F D L S E H F T C V A I L F S S N T  
- I C L T \* A N T S R V L R S C S A A I P  
6001 - CTGAGAGTGCACGATTTAGTTGTGTGCAAAAGCTACCATATTGGAGAAGCAAATTAGCAC - 6060  
- L R V H D L V V C K S Y H I G E A N \* H  
- \* E C T I \* L C A K A T I L E K Q I S T  
- E S A R F S C V Q K L P Y W R S K L A H  
6061 - ATTCAGTAGAATCTCCGAGATGTACATATTACAATCTACGGAGGTTTGTAGCCATAGAAA - 6120  
- I Q \* N L R R C T Y Y N L R R F \* P \* K  
- F S R I S A D V H I T I Y G G F S H R N  
- S V E S P Q M Y I L Q S T E V L A I E T  
6121 - CAGGCATTACTTCTGTAGTAATGCTAATTGAAAAGTTAGTAGGTATAGCAATGGTGTAT - 6180  
- Q A L L L \* \* C \* L K S \* \* V \* Q W C Y  
- R H Y F C S N A N \* K V S R Y S N G V I  
- G I T S V V M L I E K L V G I A M V L L  
6181 - TAGAGTAAGCAATTGAACTATCAGCACCTAAAGACATAGTATAAGCCACAATAGATTTTT - 6240  
- \* S K Q L N Y Q H L K T \* Y K P Q \* I F  
- R V S N \* T I S T \* R H S I S H N R F L  
- E \* A I E L S A P K D I V \* A T I D F W  
6241 - GGCTAGTACTACGTAATAAAGAACTGTATGGTAACTAGCACAAATGCCAGCTCCAATAG - 6300  
- G \* Y Y V I K K L Y G N \* H K C Q L Q \*  
- A S T T \* \* R N C M V T S T N A S S N R  
- L V L R N K E T V W \* L A Q M P A P I G  
6301 - GAATGTCGCACATCATAAGAAGTGTGCGACATGCTCAGCTCCTATAAGACAGCCTGCTTGAG - 6360  
- E C R T H K K C R H A Q L L \* D S L L E  
- N V A L I R S V D M L S S Y K T A C L S  
- M S H S \* E V S T C S A P I R Q P A V  
6361 - TCTGGAATACATGTTTCCAGTAGAATATATCGGCCAAGCTGGTGTGAGTTGATCTGCAT - 6420  
- S G I H C F Q \* N I C A K L V \* V D L H  
- L E Y I V S S R I Y A P S W C E L I C M  
- W N T L F P V E Y M R Q A G V S \* S A \*  
6421 - GAATGCTGTAGAAAACATCAGTGCAGTTAACATCTTGATATAGAACAGCAACTTCAGATG - 6480  
- E L L \* K H Q C S \* H L D I E Q Q L Q M  
- N C C R N I S A V N I L I \* N S N F R \*  
- I A V E T S V Q L T S \* Y R T A T S D E  
6481 - AAGCATTTGTCCAGGTGAATTACACTTACACCCCAAGAGCAAGGTGAAATGTCTA - 6540  
- K H L F Q V \* L H L H P Q K S K V K C L  
- S I C S R C N Y T Y T P K R A R \* N V \*  
- A F V P G V I T L T P P K E Q G E M S N  
6541 - ATATTTGAGATGTTTTAGGATCTCGAACGGAATCAGTGAATCAGAAACATCAGGCCAA - 6600  
- I F Q M F \* D L E R N Q \* N Q K H H G Q  
- Y F R C F R I S N G I S E I R N I T A K  
- I S D V L G S R T E S V K S E T S R P N  
6601 - ATGTTGAAATGGTTGAAATCTCTTTGAAGAAGGAGTTAACACACCAGTACCAGTGAGTC - 6660  
- I V E M V E I S L K K E L T H Q Y Q \* V  
- L L K W L K S L \* R R S \* H T S T S E S  
- C \* N G \* N L F E E G V N T P V P V S P  
6661 - CATTAAAATTAAAATTGACACACTGGTTCTTAATAAGGTCAGTGGATAATTTTGGTCCAC - 6720  
- H \* N \* N \* H T G S \* \* G Q W I I L V H  
- I K I K I D T L V L N K V S G \* F W S T  
- L K L K L T H W F L I R S V D N F G P Q

FIG. 12 Con't

6721 - AAACCGTGGCCGGTGCATTTAAAAGTTCAAAGAAAGTACTACAACCTCTGTAAGGTTGGT - 6780  
 - K P W P V H L K V Q K K V L Q L C K V G  
 - N R G R C I \* K F K R K Y Y N S V R L V  
 - T V A G A F K S S K E S T T T L \* G W \*  
 6781 - AGCCAATGCCAGTAGTGGTGTAAAAACCATAATCATTTAATGGCCAATAACAATTAAGAG - 6840  
 - S Q C Q \* W C K N H N H L M A N N N \* E  
 - A N A S S G V K T I I I \* W P I T I K S  
 - P M P V V V \* K P \* S F N G Q \* Q L R A  
 6841 - CAGGTGGGGTGCAGGTTTGCCATCAGGGGAGAAAGGCACATTAGATATGTCTCTCTCAA - 6900  
 - Q V G C K V C H Q G R K A H \* I C L S Q  
 - R W G A R F A I R G E R H I R Y V S L K  
 - G G V Q G L P S G E K G T L D M S L S K  
 6901 - AGGGCCTAAGCTTGCCATGTCTAAGATACCTATATTTATAATTATAATTACCAGTTGAAG - 6960  
 - R A \* A C H V \* D T Y I Y N Y N Y Q L K  
 - G P K L A M S K I P I F I I I I T S \* S  
 - G L S L P C L R Y L Y L \* L \* L P V E V  
 6961 - TAGCATCAATGTTCTAGTATTCGAAGCAAGGACACAACCCATGAAATCATCTGGCAATT - 7020  
 - \* H Q C S \* Y S K Q G H N P \* N H L A I  
 - S I N V P S I P S K D T T H E I I W Q F  
 - A S M F L V F Q A R T Q P M K S S G N L  
 7021 - TATAATTATAATCAGCAATAACACCAGTTTGTCTGGCGCTATTTGTCTTACATCATCTC - 7080  
 - Y N Y N Q Q \* H Q F V L A L F V L H H L  
 - I I I I S N N T S L S W R Y L S Y I I S  
 - \* L \* S A I T P V C P G A I C L T S S P  
 7081 - CCTTGACTACAAAAGAATCTGCATAGACATTGGAGAAGCAAAGATCATTCAACTTAGTGG - 7140  
 - P \* L Q K N L H R H W R S K D H S T \* W  
 - L D Y K R I C I D I G E A K I I Q L S G  
 - L T T K E S A \* T L E K Q R S F N L V A  
 7141 - CAGAAACGCCATAGCACTTAAAGGTTGAAAAAATGTTGAGTTGTAGAGCACAGAGTART - 7200  
 - Q K R H S T \* R L K K M L S C R A Q S N  
 - R N A I A L K G \* K K C \* V V E H R V I  
 - E T P \* H L K V E K N V E L \* S T E \* S  
 7201 - CAGCAACACAATTAGAAATTTTTTCTCTCCCATGCATAGACAGAAGGGAATTTAGTAG - 7260  
 - Q Q H N \* K F F F S P M H R Q K G I \* \*  
 - S N T I R N F F S L P C I D R R E F S S  
 - A T Q L E I F F L S H A \* T E G N L V A  
 7261 - CATTAAAAACCTCTCCAAAAGGACACAAGTTTGTAAATATTAGGGAATCTCACAAACATCTC - 7320  
 - H \* K P L Q K D T S L \* Y \* G I S Q H L  
 - I K N L S K R T Q V C N I R E S H N I S  
 - L K T S P K G H K F V I L G N L T T S P  
 7321 - CTGAGGGAACAACCCCTGAAATTAGAGGTCTGGTAAATTCCTTTGTCAATCTCAAAGCTCT - 7380  
 - L R E Q P \* N \* R S G K F L C Q S Q S S  
 - \* G N N P E I R G L V N S F V N L K A L  
 - E G T F L K L E V W \* I P L S I S K L L  
 7381 - TAACAGAGCATTGAGTTCAGCAAGTGGATTTTGAGAACAATCAACAGCATCTGTGATG - 7440  
 - \* Q S I \* V Q Q V D F E N N Q Q H L \* L  
 - N R A F E F S K W I L R T I N S I C D C  
 - T E H L S S A S G F \* E Q S T A S V I V  
 7441 - TACCATTTTCATACACTTGAGCATAAATGTAGTTGGCTTTAAATAGCCAACAAAATAGG - 7500  
 - Y H F H H T \* A \* M \* L A L N S Q N R  
 - T I F I I L E H K C S W L \* I A N K I G  
 - P F S S Y L S I N V V G F K \* P T K \* A  
 7501 - CTGCAGCTGACGTGCCCCAAATGTCTTGAGCAGGTGAAAAGGCTGTAAGAATGGCTCTAA - 7560  
 - L Q L T C P K C L E Q V K R L \* E W L \*  
 - C S \* R A P N V L S R \* K G C K N G S K  
 - A A D V P Q M S \* A G E K A V R M A L K

FIG. 12 Con't

7561 - AATTTGTAATGTTAATACCAAGAGGCCAACTTAAAAATAGGTTTCAAAGTGTAAAAACCAG - 7620  
 - N L \* C \* Y Q E A T \* K \* V S K C \* N Q  
 - I C N V N T K R Q L K N R F Q S V K T R  
 - F V M L I P R G N L K I G F K V L K P E  
 7621 - AAGGTAGATCAGAACTACATCTATAGGTTGATAGCCCTTATAAACATAGAGAAACCCAT - 7680  
 - K V D H E L H L \* V D S P Y K H R E T H  
 - R \* I T N Y I Y R L I A L I N I E K P I  
 - G R S R T T S I G \* \* P L \* T \* R N P S  
 7681 - CTTTATTTTAAACACAAACTCTCGTAAGTGTAAAAATTACCTGACTTTTCTGAAACAT - 7740  
 - L Y F \* T Q T L V S V \* N Y L T F L K H  
 - F I F K H K L S \* V F K I T \* L F \* N I  
 - L F L N T N S R K C L K L P D F S E T S  
 7741 - CAAGCGAAAAGGCATCAGATATGTAAGTGAATTAATGCATTATCGAATATCA - 7800  
 - Q A K R H Q I C T R K C N \* M H Y R I S  
 - K R K G I R Y V L E S A I K C I I E Y H  
 - S E K A S D M Y S K V Q L N A L S N I I  
 7801 - TAGTATGTGTCTGTGTACCCATGGGTTTAGAAACAGCAAAGAAAGGGTTGTACACCAATT - 7860  
 - \* Y V S V Y P W V \* K Q Q R K G C H T I  
 - S M C L C T H G F R N S K E R V V T Q F  
 - V C V C V P M G L E T A K K G L S H N S  
 7861 - CAAAGTTACATGCTCGTATAACAACATTAGTAGAATTGTTAATAATAATCACCGACTGTG - 7920  
 - Q S Y M L V \* Q H \* \* N C \* \* \* S P T V  
 - K V T C S Y N N I S R I V N N N H R L \*  
 - K L H A R I T T L V E L L I I I T D C D  
 7921 - ACTTGTGTTCATGGTAGAACCAAAACCAACCACGGACAACATTGATTTCTCTGTGG - 7980  
 - T C C S W \* N Q K P N H G Q H L I S L W  
 - L V V H G R T K N P T T D N I \* F L C G  
 - L L F M V E P K T Q P R T T F D F S V A  
 7981 - CAGCAAATAAATAACCATCCTAAAAGGTATGACAGGGTTGCCAAACGTATGATTAATAG - 8040  
 - Q Q N K Y H P \* K V \* Q G C Q T Y D \* \*  
 - S K I N T I L K R Y D R V A K R M I N S  
 - A K \* I P S L K G M T G L P N V \* L I V  
 8041 - TATGAAACCCTGTAAACATTAGAATAAAAATGGAAGAAATAAATCCTGAGTTAAATAAAGAG - 8100  
 - Y E T L \* H \* N K M E E I N P E L N K E  
 - M K P C N I R I K W K K \* I L S \* I K S  
 - \* N P V T L E \* N G R N K S \* V K \* R V  
 8101 - TGTCTGATCTAAAAATTTTCATCAGGATAGTAAACCCCTCATAGATGAAGTATGTTGAG - 8160  
 - C L I \* K F E Q D S K P P S \* M K Y V E  
 - V \* S K N F I R I V N P P H R \* S M L S  
 - S D L K I S S G \* \* T P L I D E V C \* V  
 8161 - TGTAAATTAGGAGCTTGAACATCATCAAAGTGGTGCACCGGTCAAGGTCACCTACCCTAG - 8220  
 - C N \* E L E H H Q K W C T G Q G H Y H \*  
 - V I R S L N I I K S G A P V K V T T T S  
 - \* L G A \* T S S K V V H R S R S L P L V  
 8221 - TGAGAGTAAGAAAATAAAGAAAATAAACATGTTCTGTTTAGTTGTTAACAAGAATATCAC - 8280  
 - \* E \* E I I R K \* T C S F S C \* Q E Y H  
 - E S K K \* \* E N K H V R L V V N K N I T  
 - R V R N N K K I N M F V \* L L T R I S L  
 8281 - TTGAAACCACAACCTCTGTTGTTTCTCTAATGATAAGCCTACCTTTTCCAGAAGAGAAT - 8340  
 - L K P Q L C C F L \* \* \* A Y L F P E E N  
 - \* N H N S V V F S N D K P T F F Q K R I  
 - E T T T L L F S L M I S L P F F S R R E \*  
 8341 - AAATCATCATGATTTGATTTCTCCTAAGAGACATTACAGCAGTTTCTTAAATTTAA - 8400  
 - K S Y H \* F D S P \* E T L Q Q F L I \*  
 - N H I I D L I L L K R H Y S S S S \* F K  
 - I I S L I \* F S L R D I T A V P L N L R

FIG. 12 Con't

8401 - GAGGAAATTTGCTCATGTCAAAGAGTGAATAGGAAGACAACCTGGATAGGATTTGTGTTC - 8460  
 - E E I C S C Q R V N R K T T G \* D L C S  
 - R K F A H V K E \* I G R Q L D R I C V P  
 - G N L L M S K S E \* E D N W I G F V F L  
 8461 - TCCAGAAAATGTAGTTAGCATGCATGGTATAGCCATCAATTTGTTCCCTTCGGCTTGCCAA - 8520  
 - S R K C S \* H A W Y S H Q F V P S A C Q  
 - P E N V V S M H G I A I N L F L R L A K  
 - Q K M \* L A C M V \* P S I C S F G L P R  
 8521 - GATAGTTAGCCCCAATTA AAAATGCTTCCGATGATGATGCATTTACATTTGTAACAAAAG - 8580  
 - D S \* P Q L K M L P M M M H L H L \* Q K  
 - I V S P N \* K C F R \* \* C I Y I C N K S  
 - \* L A P I K N A S D D D A F T F V T K A  
 8581 - CTGTCCACCATGAGAAATGGCCATAAGCTTGTAAAGGTCAGCATTCCAAGAATGCTCTG - 8640  
 - L S T M R N G P \* A C K G Q H S K N A L  
 - C P P \* E M A H K L V K V S I P R M L C  
 - V H H E K W P I S L \* R S A F Q E C S V  
 8641 - TTATCTTTACAGCTATAGAACCACCCAGGGCTAGTTTTTGCTTTATAAATCCACACAGAT - 8700  
 - L S L Q L \* N H P G L V F A L \* I H T D  
 - Y L Y S Y R T T Q G \* F L L Y K S T Q I  
 - I F T A I E P P R A S F C F I N P H R \*  
 8701 - AAGTGAAAACCCCTCTTTAGAGTCATTCTCTTTTGTGACATGTTGGTCCTAGGGTCAT - 8760  
 - K \* K T L L \* S H S L L S H V W S \* G H  
 - S E K P F F R V I L F C H M F G P R V I  
 - V K N P S L E S F S F V T C L V L G S Y  
 8761 - ACATATCGCTAATAATAAGGTCCTTATAGCCGTATGTACTGTGCACAGTCTCCAA - 8820  
 - T Y R \* \* \* G P I Y \* P Y V L L H S L Q  
 - H I A N N K V P F I S R M Y C C T V S N  
 - I S L I I R S H L L A V C T V A Q S P I  
 8821 - TTAAGTAGAATCTCCCTCCGAGACGAAGTCATTAAGATCTGAATCGACAAGTAGTGTGC - 8880  
 - L K \* N L R R R R R S H \* D L N R Q V V C  
 - \* S R I C V G D E V I K I \* I D K \* C A  
 - K V E S A S E T K S L R S E S T S S V P  
 8881 - CAGTTGGCAACCATTGTCTGAGCACAGCTGTACCTGGTGCAACTCCTTTATCAGAGCCAG - 8940  
 - Q L A T I V \* A Q L Y L V Q L L Y Q S Q  
 - S W Q P L S E H S C T W C N S F I R A S  
 - V G N H C L S T A V P G A T P L S E P A  
 8941 - CACCAAAGTGAATAACTCTCATGTTGTAGGGTACAGCTAAAGTAAGTGTATTTAAGTATT - 9000  
 - H Q S E \* L S C C R V Q L K \* V Y L S I  
 - T K V N N S H V V G Y S \* S K C I \* V L  
 - P K \* I T L M L \* G T A K V S V F K Y \*  
 9001 - GACACAGTTGAGTATACTTTGGCAGATTTCATCATTATTCCTTTTGGTATAACAGCATTTT - 9060  
 - D T V E Y T L R H S S L F L L V \* Q H F  
 - T Q L S I L C D I H H Y S F W Y N S I F  
 - H S \* V Y F A T F I I I P F G I T A F S  
 9061 - CACCATAATTCIGAAGGTACACTTTTCAAGAAGCATTCTTTGCATCTTGTACAAGTTAG - 9120  
 - H H N S E G H T F Q E A F F A S C T S \*  
 - T I I L K V T L F K K H S L H L V Q V R  
 - P \* F \* R S H F S R S I L C I L Y K L G  
 9121 - GCATCGCAACACCTGGTTGCCACGCTTGACTTGCTTGTAGTTTTGGGTAGAAGGTTTCAA - 9180  
 - A S Q H L V A T L D L L V V L G R R F Q  
 - H R N T W L P R L T C L \* F W V E G F N  
 - I A T P G C H A \* L A C S F G \* K V S T  
 9181 - CAIGTCCATCCTTACCCAAAGCATGAATGAAATTTCCAGCATAGTCAATTGTAACCTTGA - 9240  
 - H V H P Y T K A \* M K F Q H S Q L \* P \*  
 - M S I L T P K H E \* N F S I V N C N L D  
 - C P S L H Q S M N E I S A \* S I V T L T

FIG. 12 Con't

9241 - CCACTTTTGAATCACTGACAAATCTTGTGACTTTATATCTCGACAAAGTCATCAAGTA - 9300  
- P L L K S L T N L V T L L S R Q S H Q V  
- H F \* N H \* Q I L \* L Y Y L D K V I K \*  
- T F E I T D K S C D F I I S T K S S S K  
9301 - AAAGATCAATCACAGAACACACACATTGTGATGAACCTGTTGCGCATCTGTATGAAGT - 9360  
- K D Q S Q N T H I L M N L F A H L L \* S  
- K I N H R T H T F \* \* T C L R I C Y E V  
- R S I T E H T H F D E P V C A S V M K \*  
9361 - AATTTTTCACGTGTGCTGTCCATAGGGATAAAATCCTCTAATTTAAGTGGTGAATCTTGTG - 9420  
- N F S L C C P \* G \* N P L I \* V V N L V  
- I F H C A V H R D K I L \* F K W \* I L \*  
- F F T V L S I G I K S S N L S G E S C E  
9421 - AGCGCTTGGCTAAGCCTATCATTAAATGAAGACCGCCAAGTTGTCATGACTGAAATCTC - 9480  
- S A W L S L S L N E D R Q V V H D \* N I  
- A L G \* A Y H \* M K T A K L S M T E I S  
- R L A K P I I K \* R P P S C P \* L K S P  
9481 - CATAAACGATGTGTTGGAAGGCATAGCCCTCGAGCTTATATCGCTGTATGAATTCATCCA - 9540  
- H K R C V R R H S P R A Y I A V \* I H P  
- I N D V F E G I A L E L I S L Y E F I H  
- \* T M C S K A \* P S S L Y R C M N S S I  
9541 - TAGCGAGCTCGAGAAAGTCAGTTTCCATTTGTGATCTGGGCTTAAATCCTCIAAGTCTC - 9600  
- \* R A R E S Q F P F V I W A \* N P L S L  
- S E L E K V S F H L \* S G L K I L \* V S  
- A S S R K S V S I C D L G L K S S K S L  
9601 - TGCTCTGAGTAAAGTAGGTTTCAGGCAACTGTTGAATAATGCCGTCTACTTCTTAAAGT - 9660  
- C S E \* S R F Q A T V E \* C R L L S \* S  
- A L S K V G F R Q L L N N A V Y F L K V  
- L \* V K \* V S G N C \* I M P S T F L K \*  
9661 - AGTTAAACTGTGTTTTTACTGATTCTCCAATTAATGTGACTCCATTGACGCTAGCTGTG - 9720  
- S \* T V F L L I L Q L M \* L H \* R \* L V  
- V K L C F Y \* F S N \* C D S I D A S L C  
- L N C V F T D S P I N V T P L T L A C A  
9721 - CTGGTCCCTTTGAAGGTGTTAGACCTTTGACTGAACCTTCTGTTATTAACACATTAC - 9780  
- L V P L K V L D L \* L N L L L K H H Y  
- W S L \* R C \* T F D \* T F C Y \* N T I T  
- G P F E G V R P L T E P S V I K T P L R  
9781 - GGGCGTTTCTAAAAGGTCTACCTGTCTTCCACTCTACCATCAAACAAGACAGTAAGTG - 9840  
- G R F \* K G L P V L P L Y H Q T R Q \* V  
- G V S K K V Y L S F H S T I K Q D S K \*  
- A F L K R S T C P S T L P S N K T V S E  
9841 - AAGAACAAGCACTCTCAGTAGGTTTCTTGGCAATGTCAGTCATTGTGCAGACACCTATG - 9900  
- K N K H S Q \* V S W Q C Q S L C R H L L  
- R T S T L S R F L G N V S H C A D T Y C  
- E Q A L S V G F L A M S V I V Q T P I V  
9901 - TAGATACATGTGCTGGGCTTCTCTTTGTAGTCCCAGATTACAGTATTAGCAGCGATAT - 9960  
- \* I H V L G L L F C S P R L Q Y \* Q R Y  
- R Y M C W G F S F V V P D Y S I S S D I  
- D T C A G A S L L \* S Q I T V L A A I S  
9961 - CAACACCCAAATTTAGTATCTTAATCTCTGGCACTGGTTTAAATGTTACGCTTAGCCC - 10020  
- Q H P N Y \* V S \* S L A L V \* C Y A \* P  
- N T Q I I E Y L N L W H W F N V T L S P  
- T P K L L S I L I S G T G L M L R L A Q  
10021 - AAAGCTCAAATGCAACATTAACAGGAGTGTGTCTTATTTTCAAAGATCTCCACATCAA - 10080  
- K A Q M Q H \* Q E V L S Y F Q R S P H Q  
- K L K C N I N R K C C L I F K D L H I N  
- S S N A T L T G S V V L F S K I S T S I

FIG. 12 Con't



10081 - TACCATCTACCTTTGTGTAACAGCATTATTAATGATGGAAACAGGTGCTTCGCCGGCGT - 1014C  
- Y H L P L C K Q E Y \* \* W K Q V L R R R  
- T I Y L C V N S I I N D G N R C F A G V  
- P S T F V \* T A L L M M E T G A S P A C  
10141 - GTCCATCAAAGTGTCCCTTTATTACAACATATAAGCCACATTTTCTAAACTCTGTAACC - 1020C  
- V H Q S V L Y \* Q H Y K P H F L N S V T  
- S I K V S F I N N I I S H I F \* T L \* P  
- T G T A A A T G T A T T C C A C A G T T A A G T A T C A A A T T G T T T G T A A A T C C A T A G G C T A A A T C  
10201 - TGCTAAATGTATTCCACAGTTATAAGTATCAAATGTTTGTAAATCCATAGGCTAAATC - 1026C  
- W \* M Y S T G Y K Y Q I V C K S I G \* I  
- G K C I P Q V I S I K L F V N P \* A K S  
- V N V F H R L \* V S N C L \* I H R L N P  
10261 - CAGCAGAAATCATCATATTATATGCATCCAAGTACTGTCCGTAICTCATTTGCATGGTGTGTC - 1032C  
- Q Q K S S Y Y M H P S T V G T H L H G V  
- S R N H H I I C I Q V L S V L I C M V S  
- A E I I I L Y A S K Y C R Y S F A W C L  
10321 - TGCAAACAGCACCACCTAAATTCATCGTGTAAATACACGTAGCAGATTTGAGTGGAAACAT - 1038C  
- C K Q H H L N C I V \* Y T \* Q I \* V E H  
- A N S T T \* I A S C N T R S R F E W N I  
- Q T A P P K L H R V I H V A D H S G T \*  
10381 - AATCAATATCCGACACTACTTGTGGCCATGAGACTCACAAGGACTATCAGAATAGTAAA - 1044C  
- N Q Y P T L L V C H E T H K D Y Q N S K  
- I N I R H Y L F A M R L T R T I R I V K  
- S I S D T T C L P \* D S Q G L S E \* \* K  
10441 - AGAAAGGCAATTGCTTTAAATTAGTAAATGCACITTTATCGAAAGCTGGAGTGTGGAATG - 1050C  
- R K A I A L N \* \* M H F Y R K L E C G M  
- E R Q L L \* I S K C T F I E S W S V E C  
- K G N C F K L V N A L L S K A G V W N A  
10501 - CATGCTTATTCACATACAAACTACCACCATCACAGCCTGGTAAGTTCAAGTTTGACAAGA - 1056C  
- H A Y S H T N Y H H H S L V S S S L T R  
- M L I H I Q T T T I T A W \* V Q V \* Q D  
- C L F T Y K L P P S Q P G K F K F D K T  
10561 - CTCTTGTGTCAAACCTACACACAATTGCATTGGCTGGGTAACGATCAACGTTACAATCC - 1062C  
- L L C Q T Y T Q L H W L G N D Q R Y N S  
- S C V K P T H N C I G W V T I N V T I P  
- L V S N L H T I A L A G \* R S T L Q F Q  
10621 - AAAACAACAAACACCATCAGTGAATTTATCGTGATGTGTAGCATAAGAATAGAAGGTT - 1068C  
- K T N K H H Q \* I Y R D V \* H K N R R V  
- K Q T N T I S E F I V M C S I R I E E F  
- N K Q T P S V N L S \* C V A \* E \* K S S  
10681 - CCTCTATTTGTAAAGCTTTGTCACTACAPGGCTGAGCATCGTAGAACTTCCATTCTACTT - 1074C  
- P L F C K L C H Y M A E H R R T S I L L  
- L Y F V S F V T T W L S I V E L P F Y F  
- S I L \* A L S L H G \* A S \* N F H S T S  
10741 - CAGCCTGAGGCACACACTTGATAGCCITTTGATTTCATGAAGAACTGGAAACT - 1080C  
- Q P E A H T \* \* P L D F Q C H E E L E T  
- S L R H T L D S L W I S N V M K N W K L  
- A \* G T H L I A F G F P M S \* R T G N L  
10801 - TATCAGCAAGCAATGCAGACTTACAACCATGTGTGTACTTTTCTGCAAGCAGAATTA - 1086C  
- Y Q Q A M Q T S Q P C V V L F C K Q N \*  
- I S A Q C R L H N H V L Y F S A S R I N  
- S A S N A D F T T M C C T F L Q A E L T  
10861 - CCCTCAGTTCATCTCTATAATAGGGTATTCAACAGACCAATCAACGGCTTAACAAAGC - 1092C  
- P S V R L L \* \* G I Q Q T N Q R A \* Q S  
- P Q F I S Y N R V F N R P I N A L N K A  
- L S S S P I I G Y S T D Q S T R L T K H

FIG. 12 Con't

10921 - ACTCATGGACTGCTAAACATCTAGTCATGATAGCATCACAAC TAGCCACATGTGCATTTTC - 10980  
 - T H G L L N I \* S \* \* H H N \* P H V H F  
 - L M D C \* T S S H D S I T T S H M C I S  
 - S W T A K H L V M I A S Q L A T C A F P  
 10981 - CATGTACCTGGCAATGTTGGTTCATGGTTACTCTGAAGTTACCGTAAAGCCCCACTGCT - 11040  
 - H V P G N V G H G Y S E G Y P \* S P T A  
 - M Y L A M L V M V T L K V T R K A P L L  
 - C T W Q C W S W L L \* R L P V K P H C \*  
 11041 - GAACATCAATCATAAATGGGTTATAGACATAGTCAAACCCACAGAATGATTCCAGCAGG - 11100  
 - E H Q S \* M G Y R H S Q N P Q N D S S R  
 - N I N H K W V I D I V K T H R M I P A G  
 - T S I N G L \* T \* S K P T E \* F Q Q A  
 11101 - CATAAGTATCTGATGAAGTAGAAAAGCAAGTTGACAGTTTGTACACAGACAACACGTTTC - 11160  
 - H K Y L M K \* K S K L H V C H T D N T F  
 - I S I \* \* S R K A S C T F V T Q T T R S  
 - \* V S D E V E K Q V A R L S E R Q H V L  
 11161 - TTTCAGGTCCAATCTTGACAAAGTACTTTCATTGATGTAAGCTCAAAGCCATGCGCCAAA - 11220  
 - F Q V Q S \* Q S T S L M \* A Q S H A P K  
 - F R S N L D K V L H \* C K L K A M R P K  
 - S G P I L T K Y F I D V S S K P C A Q R  
 11221 - GGACGAACACGACTCTGTCTGACAATCTTTCAGTGTATCACTGAGCATTGTACTATCT - 11280  
 - G R T R L C L T I L S V Y H \* A F V L S  
 - D E H D S V \* Q S F Q C I T E H L Y Y L  
 - T N T T L S D N P F S V S L S I C T I L  
 11281 - TAATACGCCTACATTCCAGGGCAAGCCTTTATACATGAGTGGTATAAGATGTTTAAACT - 11340  
 - \* Y A L H S R A S L Y T \* V V \* D V \* T  
 - N T H Y I P G Q A F I H E W Y K M F K L  
 - I R T T F Q G K P L Y M S G I R C L N W  
 11341 - GGTCACCTGGTGGAGGTTTTGCATTAACCTCTGGTGAATTCTGTGTTATTTTCAGTGTCAA - 11400  
 - G H L V E V L H \* L W \* I L C Y F Q C Q  
 - V T W W R F C I N S G E F C V I F S V N  
 - S P G G G F A L T L V N S V L F S V S T  
 11401 - CATAACCAGTCCGTACAGCTACTAAGTTAACACCTGTAGAAAATCCTAGCTGGAGAGGTA - 11460  
 - H N Q S V Q L L S \* H L \* K I L A G E V  
 - I T S R Y S Y \* V N T C R K S \* L E R \*  
 - \* P V G T A T K L T P V E N P S W R G R  
 11461 - GGTTAGTACCCACAGCATCTCTAGTTGCATGACAGCCCTCTACATCAAAGCCAAATCCAGC - 11520  
 - G \* Y P Q H L \* L H D S P L H Q S Q S T  
 - V S T H S I S S C M T A L Y I K A N P R  
 - L V P T A S L V A \* Q P S T S K P I H A  
 11521 - CACGAACGTGACGAATAGCTTCTCGGGGTGATAAACATATTAGGGTAACCATPGACTT - 11580  
 - H E R D E \* L L R G \* \* T Y \* G N H \* L  
 - T N V T N S F F A G D K H I R V T I D L  
 - R T \* R I A S S R V I N I L G \* P L T W  
 11581 - GGTAATTCATTTTGAACCCATCATAGAGATGAGTCTACGGTAGGTCATGTCCTTTGGTA - 11640  
 - G N S F \* N P S \* R \* V Y G R S C P L V  
 - V I H F E T H H R D E S T V G H V L W Y  
 - \* F I L K F I E M S L R \* V M S F G M  
 11641 - TGCCTGGTATGTCAACACATAATCCTTCAGTCTTGAATTTTATATCAACGCTGAGGTGTG - 11700  
 - C L V C Q H I I L Q S \* I L Y Q R \* G V  
 - A W Y V N T \* S F S L E F Y I N A E V C  
 - P G M S T H N P S V L N F I S T L R C V  
 11701 - TAGGTGCCTGTGTAGGATGAAGACCAGTAATGATCTTACTACAGTCCCTAAAAAGTCCAG - 11760  
 - \* V P V \* D E D Q \* \* S Y Y S P \* K V Q  
 - R C L C R M K T S N D L T T V L K K S S  
 - G A C V G \* R P V M I L L Q S L K S P V

FIG. 12 Con't

11761 - TTACATTTTCTGCTTGTAAATGTAGCCACATTGCGACGGTATTTCTAGACTTGTA AATT - 11820  
 - L H F L L V M \* P H C D V V F L D L \* I  
 - Y I F C L \* C S H I A T W Y F \* T C K L  
 - T F S A C N V A T L R R G I S R L V N C  
 11821 - GCAGTTTGTCAATAAGATCTCTATCAGACATTATGCACAAAATGCCAATTTTTCGCCCTTG - 11880  
 - A V C H K D L Y Q T L C T K C Q F L P L  
 - Q F V I K I S I R H Y A Q N A N F C P C  
 - S L S \* R S L S D I M H K M P I F A L V  
 11881 - TGATAGCCACATTGAAGCGGTTGACATTACAAGAGTGTGCTGTTTCAGTAGTTTGTGTGA - 11940  
 - \* \* P H \* S G \* H Y K S V L F Q \* F V \*  
 - D S H I E A V D I T R V C C F S S L C E  
 - I A T L K R L T L Q E C A V S V V C V N  
 11941 - ATATGACATACTCATATTCAGAACCCTGTGATGAATCAACAGTCTGCGTAGCCAATCCTA - 12000  
 - I \* H S H I Q N P V M N Q Q S A \* A I L  
 - Y D I V I F R T L \* \* I N S L R R Q S \*  
 - M T \* S Y S E P C D E S T V C V G N P K  
 12001 - AGATTTTGAAGCTACAGCGTCTGTGAATTATAAGGTGAGATAAAAACAGCTTTTCTCC - 12060  
 - R F L K L Q R S V N Y K V R \* K Q L F S  
 - D F \* S Y S V L \* I I R \* D K N S F S P  
 - I F E A T A F C E L \* G E I K T A F L Q  
 12061 - AAGCAGGATTCGCTGTAAGAAATTCTCTTACAACGCCTATTTGAGGTCTGTTGATTGCAG - 12120  
 - K Q D C V \* E I L L Q R L F E V C \* L Q  
 - S R I A C K K F S Y N A Y L R S V D C R  
 - A G L R V R N S L T T P I \* G L L I A D  
 12121 - ATGAAACATCATGTGTAATAACACCTTTGTAGAACATTTGAAGCATTGAGCTGACTTAT - 12180  
 - M K H H V \* \* H L C R T F \* S I E L T Y  
 - \* N I M C N N T F V E H F E A L S \* L I  
 - E T S C V I T P L \* N I L K H \* A D L S  
 12181 - CCTTGTGTGCTTTTAGCTTATTGTCAATAAACAAGCACTCACAGTGTCAACAATTTTCAG - 12240  
 - P C V L L A Y C H K L K H S Q C Q Q F Q  
 - L V C F \* L I V I N \* S T H S V N N F S  
 - L C A F S L L S \* T K A L T V S T I S A  
 12241 - CAGGACAACCGCGACAAGTCCAGGAACATCTCTGGACCTATTGTTTTCATAAGTCTGC - 12300  
 - Q D N G D K F Q G T C L D L L F S \* V C  
 - R T T A T S S K E H V W T Y C F H K S A  
 - G Q R R Q V P R N M S G P I V F I S L H  
 12301 - ACACTGAATTAATAATTTCTGGTTCTAGTGTGCCTTTAGTCAGCAATGTGCGGGGGGCTG - 12360  
 - T L N \* N I L V L V C L \* S A M C G G L  
 - H \* I K I F W F \* C A F S Q Q C A G G W  
 - T E L K Y S G S S V P L V S N V R G A G  
 12361 - GTAATTGAGCAGGATCGCCAATATAGACGTAGTGTGTTTGCACGAAGTCTAGCATTGACAA - 12420  
 - V I E Q D R Q Y R R S V L H E V \* H \* Q  
 - \* L S R I A N I D V V F C T K S S I D N  
 - N \* A G S P I \* T \* C F A R S L A L T T  
 12421 - CACTCAAGTCATAATTAGTAGCATAGAGATTTTCATCAAAGACTACAATGTCAGCAGTTG - 12480  
 - H S S H N \* \* P \* R F H Q R L Q C Q Q L  
 - T Q V I I S S H R D F I K D Y N V S S C  
 - L K S \* L V A I E I S S K T T M S A V V  
 12481 - TTTCTGGCAATGCATTTACAGTGCAGAAAACATACTGTCTAGTGTGAAATTCACCTTGA - 12540  
 - F L A M H L Q C R K H T V L V L N S L \*  
 - F W Q C I Y S A E N I L F \* C \* I H F E  
 - S G N A F T V Q K T Y C S S V E F T L N  
 12541 - ATTTATCAAACACTCTACGCGCGCAGGATGATTCTACTACATTATCTATGG - 12600  
 - I Y Q N T L R A H A Q V \* F Y Y I Y L W  
 - F I K T L Y A R T R R Y D S T T F I Y G  
 - L S K H S T R A R A G M I L L H L S M G

FIG. 12 Con't

12601 - GCAAATATTTTAAATGCCTTTTCACATAGGGCATCAACAGCTGCATGAGAGCATGCCGTAT - 12660  
 - A N I L M P F H I G H Q Q L E E S M P Y  
 - Q I F \* C L F T \* G I N S C M R A C R I  
 - K Y F N A F S H R A S T A A \* E H A V Y  
 12661 - ACACATATGCGAGCAGATGGGTAATAGAGAGCAAGTCCGATGGCAAATGACTCTTACCAG - 12720  
 - T L C E Q M G N R E Q V R W Q N D S Y Q  
 - H Y A S R W V I E S K S D G K M T L T S  
 - T M R A D G \* \* R A S P M A K \* L L P V  
 12721 - TACCAGGTGGTCTTGGAGTGTAGAGTACTTTTGCATGCCGACCTTTTGATAATTTGCAA - 12780  
 - Y Q V V L G V \* S T F A C R P F D N L Q  
 - T R W S L E C R V L L H A D L L I I C N  
 - P G G P W S V E Y F C M P T F \* \* F A T  
 12781 - CATTGCTAGAAAACATCATCTGAGATGTTGAGTCTTGGGTACAAGCCAGTAATTCACAT - 12840  
 - H C \* K T H L R C \* V L G T S Q \* F S H  
 - I A R K L I \* D V E C W V Q A S N S H I  
 - L L E N S S E M L S V G Y K P V I L T \*  
 12841 - AGTGTCTTGTGGCACTAGAGTAGGTGCACTAAGTGGCATTACAGTGTGAGATGTCAACA - 12900  
 - S A L V A L E \* V H \* V A L Q C E M S T  
 - V L L W H \* S R C T K W H Y S V R C Q H  
 - C S C G T R V G A L S G I T V \* D V N T  
 12901 - CAAAGTAATCACCACATTCAACTTGTATGTCGTAGTACCTCTGTACACAACAGCATCAC - 12960  
 - Q S N H Q H S T C M S \* Y L C T Q Q H H  
 - K V I T N I Q L V C R S T S V H N S I T  
 - K \* S P T F N L Y V V V P L Y T T A S P  
 12961 - CATAGTACCTTTTTCAAAGGTGTACTCTCCAATCTGTACTTTACTATTTTTAGTTACAC - 13020  
 - H S H L F Q R C T L Q S V L Y Y F \* L H  
 - I V T F F K G V L S N L Y F T I F S Y T  
 - \* S P F S K V Y S P I C T L L F L V T R  
 13021 - GGTAAACCAGTAAAGACATAGTTTCTGTTCAATGGTGGTCTAGGTTTTCCAACCTCCCATG - 13080  
 - G N Q \* R H S F C S M V V \* V F Q P P M  
 - V T S K D I V S V Q W W S R F S N L P \*  
 - \* P V K T \* F L F N G G L G F P T S H E  
 13081 - AAAGATGCAATCTCTGTGAGAGTACTTCGGGTACAGTGGCAATACCATATGACAGCT - 13140  
 - K D A I L C Q R V L R V Q W Q Y H M T A  
 - K M Q F S V R E Y F A Y S G N T I \* Q L  
 - R C N S L S E S T S R T V A I P Y D S L  
 13141 - TAAATGTTTCCCTCAGTGGCTTTGAGGTTTCTGCTGCGAAAAGCTTGAGTCTCAGTAC - 13200  
 - \* M F P Q W L \* A F L L R K A \* V S Q Y  
 - K C F L S G F E R F C C E K L E S L S T  
 - N V S S V A L S V S A A K S L S L S V Q  
 13201 - AAGTGTGGCAAGTATGTAATCGCCAGCATTAGTCCAATCACATGTTGCTATCGCATTGA - 13260  
 - K C W Q V C N R Q H \* S N H M L L S H \*  
 - S V G K Y V I A S I S P I T C C Y R I E  
 - V L A S M \* S P A L V Q S H V A I A L K  
 13261 - AGTCAGTGCATTTGTCCTGCCTACACATGTGTTTTGTATAAACCAAAAACCTGACCAT - 13320  
 - S Q \* H C H C L H M C F C I N Q K P D H  
 - V S D I V T A Y T C V F V \* T K N L T I  
 - S V T L S L P T E V F L Y K P K T \* P L  
 13321 - TAGCACATAATGGAAAACATAATGGGAGGCTTATGTGACTTGCAATAATAGCTCATACCTC - 13380  
 - \* H I M E N \* W E A Y V T C N N S S Y L  
 - S T \* W K T N G R L M \* L A I I A H T S  
 - A H N G K L M G G L C D L Q \* \* L I P P  
 13381 - CTAGATACAGTTGTGTACATCAGTGACATCACAACCTGGGGCATTGCAAACATAGGGAT - 13440  
 - L D T V V S H Q \* H H N L G H C K H R D  
 - \* I Q L C H I S D I F T W G I A N I G I  
 - R Y S C V T S V T S Q P G A L Q T \* G L

FIG. 12 Con't

13441 - TAACAGACAACACTAATTGTGTGATGTTGAAATGACATGGTCATAGCAGCACTTGCAAC - 13500  
 - \* Q T T L I C V M L K \* H G H S S T C N  
 - N R Q H \* F V \* C \* N D M V I A A L A T  
 - T D N T N L C D V E M T W S \* Q H L Q H  
 13501 - ATAGGAATGGTCTCCTAATACAGGCACCGCAACGAAGTGAAGTCTGTGAATTGCACAATA - 13560  
 - I G M V S \* Y R H R N E V K S V N C T I  
 - \* E W S P N T G T A T K \* S L \* I A Q Y  
 - R N G L L I Q A P Q R S E V C E L H N T  
 13561 - CACAAGCACCTACAGCCTGCAAGACTGTATGTGGTGTACATAGCCTCATAAAACTCAG - 13620  
 - H K H L Q P A R L Y V V C T \* P H K T Q  
 - T S T Y S L Q D C M W C V H S L I K L R  
 - Q A P T A C K T V C G V Y I A S \* N S G  
 13621 - GTTCCCAGTACCGTGGAGGTATTATCATTAGTTAGCATTACGGAATACATGTCCAACATGT - 13680  
 - V P S T V R C Y H \* L A L R N T C P T C  
 - F P V P \* G V I I S \* H Y G I H V Q H V  
 - S Q Y R E V L S L V S I F E Y M S N M W  
 13681 - GGCCAGTAAAGCTCATCATGTAACCTTCTAATGTATTGTAAATACAAGTGAAGACATCAG - 13740  
 - G Q \* A H H V T F \* C I V N T S E R H Q  
 - A S K L I M \* L S N V L \* I Q V K D I S  
 - P V S S S C N F L M Y C K Y K \* K T S A  
 13741 - CATACTCCTGATTAGGATGTTTTGTAAGTGGGTAAGCATCAATAGCCAGTGACACGAACC - 13800  
 - H T P D \* D V L \* V G K H Q \* P V T R T  
 - I L L I R M F C K W V S I N S Q \* H E P  
 - Y S \* L G C F V S G \* A S I A S D T N L  
 13801 - TTTCAATCATAAGTGTACCATCTGTTTTGACAATATCATCGACAAAACAGCCTGCCCTA - 13860  
 - F Q S \* V Y H L F \* Q Y H R Q N S L R L  
 - F N H K C T I C F D N I I D K T A C A \*  
 - S I I S V P S V L T I S S T K Q P A P N  
 13861 - ATATTCTTGATGGATCTGGGTAAGGCAGGTACACGTAATCATCTCCTTGTTTAAGTGA - 13920  
 - I F L M D L G K A G T R N H L L V \* L A  
 - Y S \* W I W V R Q V H V I I S L F N \* H  
 - I L D G S G \* G R Y T \* S S P C L T S I  
 13921 - TTGTATGCTGTGAGCAAAATTCGTGAGGTCCTTTAGTAAGGTCAGTCTCAGTCCAACATT - 13980  
 - L Y A V S K I R E V L \* \* G Q S Q S N I  
 - C M L \* A K F V R S F S K V S L S P T F  
 - V C C E Q N S \* G P L V R S V S V Q H F  
 13981 - TTGCCCTCAGACATGAACACATTATTTTGATAATAAAGAAGTGCCTTAAAGTTCTTAATGC - 14040  
 - L P Q T \* T H Y F D N K E L P \* S S \* C  
 - C L R H E H I I L I I K N C L K V L N A  
 - A S D M N T L F \* \* \* R T A L K F L M L  
 14041 - TAGCTACTAAACCTTGAGCCGCATAGTTACTGTTATAGCACACAACGGCATCATCAGAAA - 14100  
 - \* L L N L E P H S Y C Y S T Q R H H Q K  
 - S Y \* T L S R I V T V I A H N G I I R K  
 - A T K P \* A A \* L L L \* H T T A S S E R  
 14101 - GAATCATCATGGAGAAATGTTTACGCAGGTAAGCGTAAAACATCCACGAATTCATGAT - 14160  
 - E S S W R N V Y A G K R K T H P R I H D  
 - N H H G E M F T Q V S V K L I H E F M I  
 - I I M E K C L R R \* A \* N S S T N S \* S  
 14161 - CAACATCCCCTATTTCTATAGAGACACTCATAGAGCCTGTGTTGTAGATTGCGGACATA - 14220  
 - Q H P Y F Y R D T H R A C V V D C G H T  
 - N I P I S I E T L I E P V L \* I A D I L  
 - T S L F L \* R H S \* S L C C R L R T Y L  
 14221 - TGTCAGCTATCTTATTACCATCAGTTGAAAGAAGTGCATTTACATTGGCTGTAACAGCTT - 14280  
 - C Q L S Y Y H Q L K E V H L H W L \* Q L  
 - V S Y L I T I S \* K K C I Y I G C N S L  
 - S A I L L P S V E R S A F T L A V T A \*

FIG. 12 Con't

14281 - GACAAATGTTAAAGACACTATTAGCATAAGCAGTTGTAGCATCACCGGATGATGTTCCAC - 14340  
 - D K C \* R H Y \* H K Q L \* H H R M M F H  
 - T N V K D T I S I S S C S I T G \* C S T  
 - Q M L K T L L A \* A V V A S P D D V P P  
 14341 - CTGGTTTAAACATATAGTGAGCCGCCACACATGACCATCTCACTTAATACTTGCCGCACACT - 14400  
 - L V \* H I V S R H T \* P S H L I L A H T  
 - W F N I \* \* A A T H D H L T \* Y L R T L  
 - G L T Y S E P P H M T I S L N T C A H S  
 14401 - CGTTAGCTAACCTGTAGAAACGGTGTGATAAGTTACAGCAAGTGTATGTTTGGCGACAA - 14460  
 - R \* L T C R N G V I S Y S K C Y V C E Q  
 - V S \* P V E T V \* \* V T A S V M F A S K  
 - L A N L \* K R C D K L Q Q V L C L R A R  
 14461 - GAACAAGAGAGGCCATTATCCTAAGCATGTTAGGCATGGCTCTGTACATTTTGGATAAT - 14520  
 - E Q E R P L S \* A C \* A W L C H I L D N  
 - N K R G H Y P K H V R H G S V T F W I I  
 - T R E A I I L S M L G M A L S H F G \* S  
 14521 - CCCAACCCATAAGGTGTGGAGTTTCTACATCACTGTAACAGTTTTTAAACATATTATGCC - 14580  
 - P N P \* G V E F L H H C K Q F L T Y Y A  
 - P T H K V W S F Y I T V N S F \* H I M P  
 - Q P I R C G V S T S L \* T V F N I L C Q  
 14581 - AGCCACCGTAAAACCTGCTTGTCCAATTACCACAGTAGCTCCTCTAGTGGCGGCTATTG - 14640  
 - S H R K T C L F Q L P Q \* L L \* W R L L  
 - A T V K L A C S N Y H S S S S S G G Y \*  
 - P P \* N L L V P I T T V A P L V A A I D  
 14641 - ACTTCAATAATTTCTGATGAAACTGTCTATTTGTCTAGTACTACAGATAGACACCAG - 14700  
 - T S I I S D E T V Y I S \* Y Y R \* R H Q  
 - L Q \* F L M K L S I C H S T T D R D T S  
 - F N N F \* \* N C L F V I V L Q I E T P A  
 14701 - CTACGGTGGAGCTCTATTCTTTGCACTAATGGCATACTTAAGATTCAATTTGAGTTATAG - 14760  
 - L R C E L Y S L H \* W H T \* D S F E L \*  
 - Y G A S S I L C T N G I L K I H L S Y S  
 - T V R A L F F A L M A Y L R F I \* V I V  
 14761 - TAGGGATGACATTACGCTTAGTATACGCGAAAAGTGCATCTTGATCCTCATAACTCATTG - 14820  
 - \* G \* H Y A \* Y T R K V H L D P H N S L  
 - R D D I T L S I R E K C I L I L I T E \*  
 - G M T L R L V Y A K S A S \* S S \* L I E  
 14821 - AGTCATAATAAGTCTAGCCTACCCATTATTAATGGGAACCAGCTGATTATCCA - 14880  
 - S H N K V \* P Y P I Y \* M G N Q L I Y P  
 - V I I K S S L T P F I K W E T S \* F I Q  
 - S \* \* S L A L P H L L N G K P A D L S R  
 14881 - GATTGTTAACGATTACTTGGTTGGCATTAAATACAGCCACCATCGTAACAATCAAAGTATT - 14940  
 - D C \* R L L G W H \* Y S H H R N N Q S I  
 - I V N D Y L V G I N T A T I V T I K V F  
 - L L T I T W L A L I Q P P S \* Q S K Y L  
 14941 - TATCAACAACCTTCAACTACGAATAGGAGTTGTCTGATATCACACATTGTTGGCAGATTAT - 15000  
 - Y Q Q L Q L R I G V V \* Y H T L L A D Y  
 - I N N F N Y E \* E L S D I T H C W Q I I  
 - S T T S T T N R S C L I S H I V G R L \*  
 15001 - AACGATAATAGTCATAATCACTGATAGCAGCGTTGCCATCCTGAGCAAAGAAGAAGTGT - 15060  
 - N D N S H N H \* \* Q R C H P E Q R R S V  
 - T I I V I I T D S S V A I L S K E E V F  
 - R \* \* S \* S L I A A L P S \* A K K K C F  
 15061 - ETAGTTCAACAGAACTTCCTTAAAGAAACCTTAGACACAGCAAAGTCATAAAAGT - 15120  
 - L V Q Q N F L P \* R N L \* T Q Q S H K S  
 - \* F N R T S F L K E T F R H S K V I K V  
 - S S T E L P S L K K P L D T A K S \* K S

FIG. 12 Con't

15121 - CTTTATTAAAATTACCGGGTTTGACAGTTTGAAAAGCAACATTGTTTGTAGTGCAGCTA - 15180  
 - L Y \* N Y R V \* Q F E K Q H C L L V Q L  
 - F I K I T G F D S L K S N I V C \* C S Y  
 - L L K L P G L T V \* K A T L F V S A A T  
 15181 - CTGAAAAGCATGTAGTGC GTTTATCTAGCAATAAATTGCCAGAAGCTGCATGATAGCTG - 15240  
 - L K S M \* C V Y L A I N C Q K L H A \* L  
 - \* K A C S A F I \* Q \* I A R S C M H S W  
 - E K H V V R L S S N K L P E A A C I A G  
 15241 - GATCAGCAGCATACACTAAAAGTTCCTGAAACTGAGACGCGAGCTATGTAAGTTTACAT - 15300  
 - D Q Q H T L K V P \* N \* D A S Y V S L H  
 - I S S I H \* K F L E T E T R A M \* V Y I  
 - S A A Y T K S S L K L R R E L C K F T S  
 15301 - CCTGATTATGTACACTCCTACTCAGAAAATGGTATCCAGTTGAAACAACAAAAGGAA - 15360  
 - P D Y V R L L T H E N G I Q L K Q Q K E  
 - L I M Y D S \* L T K M V S S \* N N K R N  
 - \* L C T T P N S R K W Y P V E T T K G T  
 15361 - CACCATCTACAAATATTTTCTTACTAGTGGTCCAAAACCTGTAGGTGGAACACAGTAG - 15420  
 - H H L Q I F F L L V V Q N L \* V E T Q \*  
 - T I Y K Y F S Y \* W S K T C R W K H S R  
 - P S T N I F L T S G P K L V G G N T V E  
 15421 - AAAATAACACATTAAGTTTGCACAATGAAGGATACACCTATCATCAAACAGTTAATAC - 15480  
 - K I T H \* S L H N E G Y T Y H P N S \* Y  
 - K \* H I K V C T M K D T P I I Q T V N T  
 - N N T L K F A Q \* R I H L S S K Q L I Q  
 15481 - AATTGGGATGGTATGTCTGGTCCCAATATTTAAAATAACGGTCGAAGAGACAAAGTCTCT - 15540  
 - N W D G M S G P N I \* N N G R R D K V S  
 - I G M V C L V P I F K I T V E E T K S L  
 - L G W Y V W S Q Y L K \* R S K R Q S L S  
 15541 - CTTCGGTAAAATCATATTTTCAGCAAATCCCCTTAATAAGTGGTTTTGCGAGATCAGCAT - 15600  
 - L P \* N H I S A N P T \* \* V V L R D Q H  
 - F R K I I F Q Q I P L N K W F C E I S I  
 - S V K S Y F S K S H L I S G F A R S A S  
 15601 - CCATATGGGACTCAGCAGCCAATGCCCTAGTCAAAGTGAGGATGGGCATCAGCAATGAGT - 15660  
 - P Y G T Q Q P M P \* S K \* G W A S A M S  
 - H M G L S S Q C P S Q S E D G H Q Q \* V  
 - I W D S A A N A L V K V R M G I S N E \*  
 15661 - AATATGAATCCACAATAGGAACCTCCGCGCCTGGTGCTACTTGTACGAAATCACCAGAAAT - 15720  
 - N M N P Q \* E L R S L V L L V R N H R N  
 - I \* I H N R N S A A W C Y L Y E I T E I  
 - Y E S T I G T P Q P G A T C T K S P K S  
 15721 - CGTACCAGTTCOCATTAAGATCCTGATTATCTAATGTCAGTACGCCTACAATGCCTGCAT - 15780  
 - R T S S H \* D P D Y L M S V R L Q C L H  
 - V P V F I K I L I I \* C Q Y A Y N A C I  
 - Y Q F P L R S \* L S N V S T P T M P A S  
 15781 - CACGCATAGCATCGCAGAATTGTACAGTCTTTAATAATGATTGGCGTACACGCTCACCTA - 15840  
 - H A \* H R R I V Q S L I M I G V H A H L  
 - T H S I A E L Y S L \* \* \* L A Y T L T \*  
 - R I A S Q N C T V F N N D W R T R S P K  
 15841 - AGTTAGCATATACGCGTAAGATGTCAGGATTCTCTACGAAGTCATACCAATCCTTCTTAT - 15900  
 - S \* H I R V R C Q D S L R S H T N P S Y  
 - V S I Y A \* D V R I L Y E V I P I L I  
 - L A Y T R K M S G F S T K S Y Q S F L L  
 15901 - TGAATAATCATCATCACAGCAATTGTATGTGACGAGTATTTCTTTAATGTATCACAAT - 15960  
 - \* N N H H H S N C M \* R V F L L M Y H N  
 - E I I I I T A I V C D E Y F F \* C I T I  
 - K \* S S S Q Q L Y V T S I S F N V S Q L

FIG. 12 Con't

15961 - TACCCATCATCAAAAATGACGTAGAGCATAGACTAAATCAGCCATTGTGTATTTAGTTAGAC - 16020  
- Y P H Q N D V E H R L N Q P L C I \* L D  
- T L I K M T \* S I D \* I S H C V F S \* T  
- P S S K \* R R A \* T K S A I V Y L V R R  
16021 - GCTGACGTGATATATGTGGTACCATGTCACCATCTACTCTAAACTTGAAAAAGTCATGGA - 16080  
- A D V I Y V V P C H H L L \* T \* K S H G  
- L T \* Y M W Y H V T I Y S K L E K V M D  
- \* R D I C G T M S P S T L N L K K S W T  
16081 - CAGCAACCGCTGGACAATCTTTAACCAAGTTATAAATAGTCTCTTCATGTTGGTAGTTAG - 16140  
- Q Q P L D N L \* P S Y K \* S L H V G S \*  
- S N R W T I F N Q V I N S L F M L V V R  
- A T A G Q S L T K L \* I V S S C W \* L D  
16141 - ACATAGTATGCCTCTTAACCTACAAAGTAAGACTCTAATAAATGGCTTCCTCATCCTTCT - 16200  
- T \* Y A S \* L Q S K S L I N C L P H P S  
- H S M P L N Y K V R V \* \* I A F L I L L  
- I V C L L T T K \* E S N K L P S S S F S  
16201 - CCTGGAAGCGACAGCAATAGTTTTAGGAACTTTGCAAAACCAGCACTTTTTTCGTTGT - 16260  
- P G S D S N \* F L G T L Q N Q H F F R C  
- L E A T A I S F \* E L C K T S T F F V V  
- W K R Q Q L V F R N F A K P A L F S L \*  
16261 - AAATATCAAAAGCCCTGTAGACGACATCAGTACTAGTGCCTGTGCCGCACCGGTGAAGAC - 16320  
- K Y Q K P C R R H Q Y \* C L C R T V \* D  
- N I K S P V D D I S I S A C A A R C K T  
- I S K A L \* T T S V L V P V P H G V R R  
16321 - GGGCTGCACTTACACCGCAAACCCGTTAAAAACGTTGATGCATCCGCAGACTGCATCAA - 16380  
- G L H L H R K P V \* K R \* C I R R L H Q  
- G C T Y T A N P F K N V D A S A D C I K  
- A A L T P Q T R L K T L M H P Q T A S R  
16381 - GGGTTCGGGAGTTGGTCACAACACTACAGCCATAACCTTCCACATCCGCAGACGGTACA - 16440  
- G F A E L V T T T A I T F P H S A D G T  
- G S R S W S Q L Q P \* P F H I P Q T V Q  
- V R G V G H N Y S H N L S T F R R R Y R  
16441 - GACTGTGTTTCTAAGTGTAAAACCCACTGGGTCATTAGCACAAGTGGTAGGTATTTGGAC - 16500  
- D C V S K C K T H W V I S T S G R Y L D  
- T V F L S V K P T G S L A Q V V G I W T  
- L C F \* V \* N P L G H \* H K W \* V F G R  
16501 - GTACTTACCTTCAAGTCACAGAATCCTTTAGGATTTGGATGGTCAATGTGCCATCTACA - 16560  
- V L T F Q V T E S F R I W M V N V A S T  
- Y L P F K S Q N P L G F G W S M W H L Q  
- T Y L S S H R I L \* D L D G Q C G I Y N  
16561 - ATACAGACAACATGAAGCACCACCAAGGACTCTTGGTCCATGTAGCTTCTGGTGTAC - 16620  
- I Q T T \* S T T K G L L V H V S F W C Y  
- Y R Q H E A P P K D S W S M L A S G V T  
- T D N M K H H Q R T L G P C \* L L V L Q  
16621 - AGTAATTGCCTGTCCTGTACCAGTGTGTACACAACATCTTACACAGTTGGTGATTGG - 16680  
- S N C L S C T S V C T Q H L H T V G D W  
- V I A C P V P V C V E N I F T Q L V I G  
- \* L P V L Y Q C V Y T T S S H S W \* L V  
16681 - TTGTCCTCCACTTGCTAGGTAATCCTTATATGCTTTAGCAGGGTCTACTGCAAAAGCACA - 16740  
- L S S T C \* V I L I C F S R V Y C K S T  
- C P P L A R \* S L Y A L A G S T A K A Q  
- V L H L L G N P Y M L \* Q G L L Q K H R  
16741 - GAAGGAAAGCACAGTTGAATTGGCAGGTACTTCTGTAGCATTTCAGCCTGAAGACCTAC - 16800  
- E G K H S \* I G R Y F C S I S S L K T Y  
- K E S T V E L A G T S V A F P A \* R R T  
- R K A Q L N W Q V L L \* H F Q P E D V L

FIG. 12 Con't



16801 - TGTAGCAGCTAAACTGCCAGCACCATACCTCTATTTAGGTTGTTTAAAGCCTTTGATGAA - 16860  
 - C S S \* T A Q H H T S I \* V V \* A F D E  
 - V A A K L P S T I P L F R L F K P L M K  
 - \* Q L N C P A P Y L Y L G C L S L \* \* S  
 16861 - GTACAAGTATTTCACTTTAGGCCCTTTTGGTGTGTCTGTAACAAACCTACAAGTGGTTC - 16920  
 - V Q V F H F R P F W C V C N K P T R W F  
 - Y K Y F T L G P F G V S V T N L Q G G S  
 - T S I S L \* A L L V C L \* Q T Y K V V P  
 16921 - CAGTTCTGTGTAATTTGTACCTGTACCATCACTCTTAGGGAATCTAGCCCATTGAGATC - 16980  
 - Q F C V N C T C T I T L R E S S P F E I  
 - S S V \* I V P V P S L L G N L A H L R S  
 - V L C K L Y L Y H H S \* G I \* P I \* D L  
 16981 - TTGGTGGTCTGATAGTAATGCCAGCACAAACCTACCTCCCTTCGAATTGTTATAGTAGGC - 17040  
 - L V V \* \* \* C Q H K P T S L R I V I V G  
 - W W S D S N A S T N L P P F E L L \* \* A  
 - G G L I V M P A Q T Y L P S N C Y S R Q  
 17041 - AAGTGCATTGTGCATCAGTACAAGCTGTTTGTGGTACCAGCCGCACAGACATCTGTGC - 17100  
 - K C I V I S T S C L C G T S R T G H L S  
 - S A L S S V Q A V C V V P A A Q D I C R  
 - V H C H Q Y K L F V W Y Q P H R T S V V  
 17101 - TAGTGTACTGGACTCACTTCATTATCTGTAGTTTAAACAGCTGAGTTGGCTCTTAGAGC - 17160  
 - \* C Y W T Q F I I L \* F N S \* V G S \* S  
 - S A T G L S S L F C S L T A E L A L R A  
 - V L L D S V H Y S V V \* Q L S W L L E L  
 17161 - TGTAACAATAAGAGGCCAAGCCAAATTTGGTGAATTGTCCATGTTAATTTCACTAAGTTG - 17220  
 - C N N K R P S Q I W \* I V H V N F T K L  
 - V T I R G Q A K F G E L S M L I S L S \*  
 - \* Q \* E A K P N L V N C P C \* F H \* V E  
 17221 - AACAACTTGTCTATCCGCATCAACAACCTTGCTGGATTCCAGAGTGCAGATGCATATGT - 17280  
 - N N L A I R I N N L L D F P E C R C I C  
 - T I L L S A S T T C W I S Q S A D A Y V  
 - Q S C Y P H Q Q L A G F P R V Q M H M \*  
 17281 - AAAGTGTACCATCACAACCTGTTCTGTAGGTACCATAATCAGGGACAACAACCATGAG - 17340  
 - K G V T I T S V L V G T I I R D N N H E  
 - K V L P S Q V F L \* V P \* S G T T T M S  
 - R C Y H H K C S C R Y H N Q G Q Q P \* V  
 17341 - TTTGGCTGCTGTAGTCAATGGTATGATGTTGAGTGAACACAACCATCAGCGCATTGTT - 17400  
 - F G C C S Q W Y D V E W N T T I T R I V  
 - L A A V V N G M M L S G T Q P S R A L L  
 - W L L \* S M V \* C \* V E H N H H A H C \*  
 17401 - GATAATGTTGTTAAGTGCATCATTATCAAGCTTCCTAAGCATAGTGAAGAGCATTGTTG - 17460  
 - D N V V K C I I I K L P K H S E E H C L  
 - I M L L S A S L S S F L S I V K S I V C  
 - \* C C \* V H H Y Q A S \* A \* \* R A L F A  
 17461 - CATAGCACTAGTTACTTTTGCCTCTGTCCCTCAGATCTGCCTGTTGTACATTTGGGT - 17520  
 - H S T S Y F C P L V L R S C L F V H L G  
 - I A L V T F A L L S S D L A C L Y I W V  
 - \* H \* L L L P S C P Q I L P V C T F G S  
 17521 - CATAGCCTGATCTGCCATCTTTTCCAACCTTGCCTGGCAGCATCAGGTCAAACTC - 17580  
 - H S L I C H L F Q L A L H G S I T V K L  
 - I A \* S A I F S N L R C M A A S R S N S  
 - \* P D L P S F P T C V A W Q H H G Q T Q  
 17581 - AGATTTAGCCACATTCAAAGATTTCTTAACTTTTGGAGAACGACTTCAGAATCACCATT - 17640  
 - R F S H I Q R F L \* L F E N D F R I T I  
 - D L A T F K D F F N F L R T T S E S P L  
 - I \* P H S K I S L T F \* E R L Q N H H \*

FIG. 12 Con't

17641 - AGCTACAGCCTGCTCATAGGCCTCCTGGGCAGTGGCATAAGCGGCATATGATGGTAAAGA - 17700  
 - S Y S L L I G L L G S G I S G I \* W \* R  
 - A T A C S \* A S W A V A \* A A Y D G K E  
 - L Q P A H R P P G Q W H K R H M M V K N  
 17701 - ACTAAATTCTGAAGCAATAGCCTGAAGAGTAGCACGGTATCGAGCATTTCCTCGCACAA - 17760  
 - T K F \* S N S L K S S T V I E H F L A Q  
 - L N S E A I A \* R V A R L S S I S S H N  
 - \* I L K Q \* P E E \* H G Y R A F P R T T  
 17761 - CCTATTAATGTCTACAGCACCCCTGCATGGATAGCAAAACAGACAAAAGAGAAACCATCTT - 17820  
 - P I N V Y S T L H G \* Q N R Q K R N H L  
 - L L M S T A P C M D S K T D K R E T I F  
 - Y \* C L Q H P A W I A K Q T K E K P S S  
 17821 - CTCGAAAGCTTCAGTTGTGCTTTTGAAGAAGAATATCATTTGTGGAGTTGTACACATTG - 17880  
 - L E S F S C V F C K K N I I V E L Y T L  
 - S K A S V V S F A R R I S L W S C T H C  
 - R K L Q L C L L Q E E Y H C G V V H I V  
 17881 - TGCCACAAATTTAGAAGATGACTCTACTCTAAGTTGTTGAAGAACCGAGAGCAGTACCAC - 17940  
 - C P Q F R R \* L Y S K L L K N R E Q Y H  
 - A H N L E D D S T L S C \* R T E S S T T  
 - P T I \* K M T L L \* V V E E P R A V P Q  
 17941 - ASATGTGCACTTTACGTCAGACATTTAGACTGTACAGTAGCAACCTTCATACATGGTTT - 18000  
 - R C A L Y V R H F R L Y S S N L D T W F  
 - D V H F T S D I L D C T V A T L I H G L  
 - M C T L R Q T F \* T V Q \* Q F \* Y M V Y  
 18001 - ACCTCCAATACCCAACACTTAATGTTAAGCTTGAAGCATCAATACTACTCTTAGGAGG - 18060  
 - T S N T Q Q L N V K L E S I N T T L R R  
 - P P I P N N L M L S L K A S I L L L G G  
 - L Q Y P T T \* C \* A \* K H Q Y Y S \* E A  
 18061 - CAAAAGCCCTGGGAGTTCATATACCTAAATTCTTGTGTAGAGACCAAGTAGTCATAAAC - 18120  
 - Q K P L G V H I P K F L C R D Q V V I N  
 - K S P W E F I Y L N S C V E T K \* S \* T  
 - K A P G S S Y T \* I L V \* R P S S H K H  
 18121 - ACCAAGAGTAAGCCTGAAGTAACGGTTGAGTAAACAGAAAAGGCCAAAGTAGCAGCAGCA - 18180  
 - T K S K P E V T V E \* T E K A K V A A A  
 - P R V S L K \* R L S K Q K R P K \* Q Q Q  
 - Q E \* A \* S N G \* V N R K G Q S S S S N  
 18181 - ACAATAGCCTAAGAAACAATAACAAGCATGATACACTGTAAGGTGTTGCCAGTAATAAAA - 18240  
 - T I A \* E T I N K H D T L \* G V A S N K  
 - Q \* P K K Q \* T S M I H C K V L P V I N  
 - N S L R N N K Q A \* Y T V R C C Q \* \* I  
 18241 - TAACAATGGGTAATACTCAACACACAAACACTATAGCTCTAGCTAAAAACATGATAGT - 18300  
 - \* Q W V I L N T H K H Y S S S \* K H D S  
 - N N G \* Y S T H T N T I A L A K N M I V  
 - T M G N T Q H T Q T L \* L \* L K T \* \* S  
 18301 - CGTAACGACACCAGAATAGTTAGAGGTTACAGAAATAACTAAGGCCACATGGAAATAGC - 18360  
 - R N D T R I V R G Y R N N \* G P H G N S  
 - V T T P E \* L E V T E I T K A H M E I A  
 - \* R H Q N S \* R L Q K \* L R P T W K \* L  
 18361 - TTCATCTAAAGCATTACCATAGTAGACTTGTAAACAAGTGTAAATGACATTATCAGTGT - 18420  
 - L I \* S I T I V D F V N K C N D I H Q C  
 - \* S K A L P \* \* T L \* T S V M T F I S V  
 - D L K H Y H S R L C K Q V \* \* H S S V S  
 18421 - CCAAACAGTCTAGCAGCATCATAAACAGTGCAGCTGTCATGAGAAATAAGCAAAC - 18480  
 - P N T S S S I I N S A S C H E N K Q N  
 - Q I R L A A S S \* T V R A V M R I S K T  
 - K H V \* Q H H H K Q C E L S \* E \* A K L

FIG. 12 Con't

18481 - TAAAGCTGAAGCATACATAACACAATCCTTAAGCCTATAACCAGACAAGCTAGTGTGCAGC - 18540  
 - \* S \* S I H N T I L K P I T R Q A S V S  
 - K A E A Y I T Q S L S L \* P D K L V S A  
 - K L K H T \* H N P \* A Y N Q T S \* C Q P  
 18541 - CAATTC AAGCCATGTCATGATACGCATACCCAGCTAGCAGCCATGTAGACCATATTTAAA - 18600  
 - Q F K P C H D T H H P A S R H V D H I K  
 - N S S H V M I R I T Q L A G M \* T I L K  
 - I Q A M S \* Y A S P S \* Q A C R P Y \* S  
 18601 - GTAAGCAACTGTTGCAAGAGAAGGTAACAGAAACAAGCACAAGAATGCGTGCTTATGCTT - 18660  
 - V S N C C K R R \* Q K Q A Q E C V L M L  
 - \* A T V A R E G N R N K H K N A C L C L  
 - K Q L L Q E K V T E T S T R M R A Y A \*  
 18661 - AACAAAGCAGCATAGCACATGCAGCAATTGCCATAATACCAAGAGTAAATGGCAAGAAAGC - 18720  
 - N K Q H S T C S N C H N T K S K W Q E S  
 - T S S I A H A A I A I I P R V N G K K A  
 - Q A A \* H M Q Q L F \* Y Q E \* M A R K H  
 18721 - ATTCTCGTAAACAAAGAAAAACAGTGACCCTGTGTACTTTGAACAAGAATCAATAGTGA - 18780  
 - I L V N K E K Q \* P L C T L N K N Q \* \*  
 - F S \* T K K N S D H C V L \* T R I N S D  
 - S R K Q R K T V T T V Y F E Q E S I V M  
 18781 - TGTC AAGAAAGTTAAAAGCATCCAATGATGAGTGCCCTTAACAATTTCTTGAAGTACC - 18840  
 - C Q E S \* K H P M M S A L N N F L E L T  
 - V K K V K S I Q \* \* V P L T I F L N L P  
 - S R K L K A S N D E C P \* Q F S \* T Y L  
 18841 - TTGGAAGGTAACACCAGAGCATTGTCTAACAACATCAAATGGTGTAAGTCACTCTTAA - 18900  
 - L E G N T R A L S N N I K W C K L I F \*  
 - W K V T P E H C L T T S N G V N S S S K  
 - G R \* H Q S I V \* Q H Q M V \* T H L L K  
 18901 - AATAGTGTACCAAGGATAGTACGACCATTCAATCTGCAGCAGCTCTTTCAAAGC - 18960  
 - N S A T K D S T T I H T I L Q Q I F Q S  
 - I V L P R I V R P F I P F C S S S F K A  
 - \* C Y Q G \* Y D H S Y H S A A A L S K Q  
 18961 - AGCACATATCTAAGACGGCAATTCCTGTTGAGCAGAAAGAGGTCCCAATATGTCAAC - 19020  
 - S T H I \* D G N S C L S R K R S Q Y V N  
 - A H I S K T A I P V \* A E R G P N M S T  
 - H T Y L R R Q F L F E Q K E V P I C Q H  
 19021 - ATGATCTTGTGTCAAAGGTTTCATAGTTGTACTTCATTGCCACAAGGTTAAAGTCATTCAA - 19080  
 - M I L C Q R F I V V L H C H K V K V I Q  
 - \* S C V K G S \* L Y F I A T R L K S F K  
 - D L V S K V H S C T S L P Q G \* S H S K  
 19081 - AGTAGTGGTGAATCTATTAAGAAACCACCTATCACCATTGATAACAGCAGCATACAGCCA - 19140  
 - S S G E S I K K P P I T I D N S S I Q P  
 - V V V N L L R N H L S P L I T A A Y S H  
 - \* W \* I Y \* E T T Y H H \* \* Q Q H T A M  
 19141 - TGCCAAAACATTTAATGTTATGGTTGTGTACCTGCAGCCTGTGCAGTTGTCTGTGC - 19200  
 - C Q N I \* C Y G C V C T C S L C S L S V  
 - A K T F N V M V V S V P A A C A V C L S  
 - P K H L M L W L C L Y L Q P V Q F V C Q  
 19201 - AACAAATGGACCATAGAATTTACCTTCTAAGTCAGTACCAGCGTGTACTCCTGTTGGAAG - 19260  
 - N K W T I E F T F \* V S T S V Y S C W K  
 - T N G P \* N L P S K S V P A C T P V G S  
 - Q M D H R I Y L L S Q Y Q R V L L L E A  
 19261 - CTCCATATGATGCATATAGCAGAAAGACAGCAATCATAATCAATGTTAAAACCAACACT - 19320  
 - L H M M H I A E R H A I I I N V K T N T  
 - S I \* C I \* Q K D T Q S \* S M L K P T L  
 - P Y D A Y S R K T R N H N Q C \* N Q H Y

FIG. 12 Con't

19321 - ACCACATGATCCATTAAGGAAAGAACCTTTAATGGTATGATTAGGTCTCATGGCACACTG - 19380  
 - T T \* S I K E R T F N G M I R S H G T L  
 - P H D P L R K E P L M V \* L G L M A H \*  
 - H M I H \* G K N L \* W Y D \* V S W H T D  
 19381 - ATAAACACCAGATGGTGAACCATTGTAGCATGCTAGAAGTAAATGTTGACCAGGTTG - 19440  
 - I N T R W \* T I V A C \* N \* K C L T R L  
 - \* T P D G E P L \* H A R T E N V \* P G W  
 - K H Q M V N H C S M L E L K M F D Q V G  
 19441 - GATACGGACAAATTTATACTTGGGTGCTTAGGGTTAGAAGTATCAACTTTAAGCCTAAG - 19500  
 - D T D K F I L G C L R V R S I N F K P K  
 - I R T N L Y L G V L G L E V S T L S L S  
 - Y G Q I Y T W V S \* G \* K Y Q L \* A \* A  
 19501 - CAGACAATTTGCATAGAAATGGCCAATAACCGAAGTTGAACATTGCCAGCCTGAACAAG - 19560  
 - Q T I L H R M A N N T K L N I A S L N K  
 - R Q F C I E W P I T R S \* T L P A \* T R  
 - D N F A \* N G Q \* H E V E H C Q P E E  
 19561 - AAAGCTATGGTTGGATTGCGAATGAGCAGATCTTCATAGTTAGGATTAAGCATGCTCTC - 19620  
 - K A M V G F A N E Q I F I V R I K H V F  
 - K L W L D L R M S R S S \* L G L S M S S  
 - S Y G W I C E \* A D L H S \* D \* A C L L  
 19621 - TGCTGTGCAATGACATGTCTTGGACAGTATACTGTGTATCCAACCACAATCCATTAAG - 19680  
 - C C A N D M S W T V Y C V I Q P Q S I K  
 - A V Q M T C L G Q Y T V S S N H N P L R  
 - L C K \* H V L D S I L C H P T T I H \* E  
 19681 - AGTGTAGTCCACAGGTFACTTGTACCATGCACCCTTCAACTTTGCCTGACGGGAATGC - 19740  
 - S C S S T G Y L Y H A P F N F A \* R E C  
 - V V V P Q V T C T M H P S T L P D G N A  
 - L \* F H R L L V P C T L Q L C L T G M P  
 19741 - CATTTTCCTAAAACCACCTCTGCAGAACAGCAGAAGTGATTGATGTCTGTGGTGGTTGGTA - 19800  
 - H F P K T T L Q N S R S D \* C L W W L V  
 - I F L K P L C R T A E V I D V C G G W \*  
 - F S \* N H S A E Q K \* L M S V V V G R  
 19801 - GAGAACATCAGCACCTGAGTTGCTAAAGTCAATTTAGAGCCTTTGCTAAGTGGCAGCAAGC - 19860  
 - E N I S T \* V A K V I \* S L C \* V A A S  
 - R T S A P E L L K S F R A F A K W Q Q A  
 - E H Q H L S C \* S H L E P L L S G S K L  
 19861 - TGCTTCACGATAGCTGGTAGTATCTAAGGCTCCACTGAAATACTTGTACTTGTATATAG - 19920  
 - C F T I A G S I \* G S T E I L V L V I \*  
 - A S R \* L V V S K A P L K Y L Y L L Y R  
 - L H D S W \* Y L R L H \* N T C T C Y I E  
 19921 - AGCAAGATACCTGTTATACTGTGTAAGTGGCAACAGTGTCTCGCTACGCAATTTAGGTA - 19980  
 - S K I P V I L C K W Q Q C L A T Q F \* V  
 - A R Y L L Y C V S G N S V S L R N F R Y  
 - Q D T C Y T V \* V A T V S R Y A I L G T  
 19981 - CATTCCTTGTGAGCAAAAAGGTACACAAAGCAGCCTCCTCGAAGGTACTAAATGTAAC - 20040  
 - H F L V E Q K G T Q S S L L E G T K C N  
 - I S L S K K V H K A A S S K V L N V T  
 - F P C \* A K R Y T K Q P P R R Y \* M \* L  
 20041 - TCCATTAACATGACTCTTTTCTAAGATAGTTGTTAAAGAACCAATGGCAGTGCTTCAG - 20100  
 - S I K H D S F P K I V V K E P M A V L Q  
 - P L N M T L F L R \* L L K N Q W Q C F R  
 - H \* T \* L F S \* D S C \* R T N G S A S E  
 20101 - AGAAATACAGAATACATAGATTGCTGTTATCCAAAAAGGCACAATAGGAGAAAACATGGC - 20160  
 - R N T E Y I D C C Y P K R H N R R K H G  
 - E I Q N T \* I A V I Q K G T I G E N M A  
 - K Y R I H R L L L S K K A Q \* E K T W Q

FIG. 12 Con't

20161 - AAACCATTGAAGGTGAGCCAAGAATGAAACATCATTTGGTGAAATAGAATGTCAAGTACAA - 20220  
 - K P L K V S Q E \* N I I G E I E C Q V Q  
 - N H \* R \* A K N E T S L V K \* N V K Y K  
 - T I E G E P R M K H H W \* N R M S S T S  
 20221 - GTAAAAGACTGAGTAGACTCCCGGCAGAAAGCTGTAAGCTGGTACCAGACAGAGTATAGT - 20280  
 - V K D \* V D S R Q K A V S W Y Q T E Y S  
 - \* K T E \* T P G R K L \* A G T R Q S I V  
 - K R L S R L P A E S C K L V P D R V \* \*  
 20281 - GAAAGACATCAAAAACAAAAGTGCATTAGCAGCAACAACATGGTTGTACTCACAAAAAAC - 20340  
 - E R H Q K Q K C I S S N N M V V L T K N  
 - K D I K N K S A L A A T T W L Y S P K T  
 - K T S K T K V H \* Q Q Q H G C T H Q K H  
 20341 - ACGTCTGAATTTTCATAAAGTAGTAGGCAGCACAAAGTCACCAATATGGCAATAATACCACC - 20400  
 - T S E F H K V V G S T S H Q Y G N N T T  
 - R L N F I K \* \* A A Q V T N M A I I P  
 - V \* I S \* S S R Q H K S P I W Q \* Y H Q  
 20401 - AGCCACTACTGAAGCAGACACATCTAAAGCACCCACAGGTTGCACAAGAGGAGTAAAGAT - 20460  
 - S H Y \* S R H I \* S T H R L H K R S K D  
 - A T T E A D T S K A P T G C T R G V K M  
 - P L L K Q T H L K H P Q V A Q E E \* R C  
 20461 - GTTAGCTATGAGATTCATCGCATCAACACCACAGAAAACCTCCTGATAGAGCTCTGTAATG - 20520  
 - V S Y E I H R I N T T E N S \* \* S S V M  
 - L A M R F I A S T P Q K T P D R A L \* C  
 - \* L \* D S S H Q H H R K L L I E L C N A  
 20521 - CTCATTATTAAGAACCATCTACCCTGGTAGATAGGCCAAATACCTACTTCTGACCTTTC - 20580  
 - L I I K N P S T T G R \* A N T Y F \* P F  
 - S L L R T H L P L V D R Q I P T S D L S  
 - H Y \* E P I Y H W \* I G K Y L L L T F R  
 20581 - GCATGTACCATGTCTACAGTACTCAGCATCAAAAAGTTETTACTACTCTAACAGAACCCTC - 20640  
 - A C T M S T V L S I K S C Y Y S N R T L  
 - H V P C L Q Y S A S K V V T T L T E P S  
 - M Y H V Y S T Q H Q K L L L L \* Q N P P  
 20641 - CAGGTAAGTGTAGGAAACTGTATGATGGAACCATCCATAAGCACATAACGAGTGTCTGG - 20700  
 - Q V S V R K L Y D G T I H K H I T S V W  
 - R \* V L G N C M M E P S I S T \* R V S G  
 - G K C \* E T V \* W N H P \* A H N E C L D  
 20701 - ACGAAGCTCACTATAAGAAATGAACCTCTAGCAAATTAGTGTGATAACAATATGGCAC - 20760  
 - T K L T I R N R T L \* Q I S V I T I W H  
 - R S S L \* E I E P S S K L V S \* Q Y G T  
 - E A H Y K K \* N P L A N \* C H N N M A Q  
 20761 - AGGTTTGCCTATAGCATCCTTAAAAATTGTACACTCAGCAGCAAGAACGCAAGCAGAGGT - 20820  
 - R F A H S I L K N C T L S S K N A S R G  
 - G L P I A S L K I V H S A A R T Q A E V  
 - V C P \* H P \* K L Y T Q Q Q E R K Q R \*  
 20821 - AGCAAAATCACTATACTCAATGAGTTTGAAGGTGTGTAGCAAATGTTGCCAACAGCACT - 20880  
 - S K I T I L N E F G R C V A N V A N S T  
 - A K S L Y S M S L E G V \* Q M L P T A L  
 - Q N H Y T Q \* V W K V C S K C C Q Q H \*  
 20881 - AAAAACACGAGGTAGAAAATGCAAGAAGTCAACATGATTGCTCTCAGCACAGTACCCGG - 20940  
 - K N T R \* K M Q E V T I D C S Q H S T R  
 - K T R G R K C K K S P L I A L S T V P G  
 - K H E V E N A R S H H \* L L S A Q Y P V  
 20941 - TAAGCCAGGCACTATGAAACCAATCTCTTGTAAATGATAGCAGCTACTACAGGGCAGCT - 21000  
 - \* A R H Y E T N L S C N D S S Y Y R A A  
 - K P G T M K P C S L V M I A A T T G Q L  
 - S Q A L \* N Q S L L \* \* \* Q L L Q G S F

FIG. 12 Con't

21001 - TTTGTCAATTTTGTATGAACCACCACGCTGGCTAAACCATGGGTCAAAACCAGCATGTTT - 21060  
 - F V I F V \* T T T L A K P C V K T S M F  
 - L S F L Y E P P R W L N H A S K P A C L  
 - C H F C M N H H A G \* T M R Q N Q H V Y  
 21061 - ATTTGCAAAACAATCATCAGTAGAAATGATGTCACGAGTGACACCATCCTGAATGGCTTT - 21120  
 - I C K T I I S R N D V T S D T I L N G F  
 - F A K Q S S V E M M S R V T P S \* M A L  
 - L Q N N H Q \* K \* C H E \* E H P E W L C  
 21121 - GTAACCAATGATTTTCATTTGTGTAACCATCATGGATTGACAATGTATGTACTGGCATAAC - 21180  
 - V T N D F I C V T I M D \* Q C M Y W H N  
 - \* P M I S F V \* P S W I D N V C T G I T  
 - N Q \* F H L C N H H G L T M Y V L A \* R  
 21181 - GATATAACAAACCAATGCAGCAAGAAGCGACAATAATGTGGCCTTAAGCATAAGTTAAA - 21240  
 - D I T N Q C S K N A Q \* C G L K H K F K  
 - I \* Q T N A A R T H N N V A L S I S L K  
 - Y N K P M Q Q E R T I M W P \* A \* V \* N  
 21241 - ACAAGTACTAACAATCTACCACCCTTGAGTGAGATTTTAGTAGTTATGACATTGACAAC - 21300  
 - T S T N N L T T L E \* D F S S Y D I D N  
 - Q V L T I L P P L S E I L V V M T L T T  
 - K Y \* Q S Y H P \* V R F \* \* L \* H \* Q P  
 21301 - CTGTCTAGTTGTAGCACAAGTTAGTGTAAGGATGTTGTTCTTCTTGGCAGCAGTACG - 21360  
 - L S S C S T S \* C K R Y V V L L G S S T  
 - C L V V A Q V S V K G M L F F L A A V R  
 - V \* L \* H K L V \* K V C C S S W Q Q Y E  
 21361 - AATTTGTTIACGCAGCTGTTTCAGATAAAGACATGTAGTCTTTTACATTCCAGATGAGTGA - 21420  
 - N L F T Q L F R \* R H V V F Y I P D E \*  
 - I C L R S C S D K D M \* S F T F Q M S E  
 - F V Y A A V Q I K T C S L L H S R \* V K  
 21421 - AACATTGTGACTTTTGGCTACTTGGGCATTGATATGCCITGCATTACAGTCAATACATGC - 21480  
 - N I V T F C Y L G I D M P C I T V N T C  
 - T L \* L F A T W A L I C L A L Q S I H A  
 - H C D F L L L G H \* Y A L H Y S Q Y M R  
 21481 - GCCAAGATCTCTGGCGTCATGTTTCAACCTTATTATAGGTGAGCATGAAATTGTTACA - 21540  
 - A K I S G R H V F N L I I G E H E I V T  
 - P R S L G V M F S T L L \* V S M K L L Q  
 - Q D L W A S C F Q P Y Y R \* A \* N C Y N  
 21541 - ACTGTCACCTGTCACTTCTAAGTCAGACTGATGTGAAAGTTTGAGACATTCAATAACATC - 21600  
 - T V T C H F \* V R V M \* K F E T F N N I  
 - L S P V T S K S E \* C E S L R H S I T S  
 - C H L S L L S Q S D V K V \* D I Q \* H P  
 21601 - CTTTGTGTCAACATCGGTATCAACAACACCTTGTGGGCAGCTGACACGAATGTAGAAAG - 21660  
 - L C V N I G I N N T L S G S \* H E C R K  
 - F V S T S V S T T P C R A A D T N V E R  
 - L C Q H R Y Q Q H L V G Q L T R M \* K G  
 21661 - GACACCATCTAAAGCTACACCCTTGGCTAACTCGCTGTGAGCTGTAGCAACAAGTGCCTT - 21720  
 - D T I \* S Y T L C \* L A V S C S N K C L  
 - T P S K A T P F A N S L \* A V A T S A L  
 - H H L K L H P L L T R C E L \* Q Q V P \*  
 21721 - AAGTTTTTCCATAGGAACACTAAAAGTTGCTGAAAAGGTGTCGACATAAGCATCAAACAT - 21780  
 - K F F H R N T K S C \* K G V D I S I K H  
 - S F S I G T L K V A E K V S T \* A S N I  
 - V F P \* E H \* K L L K R C R H K H Q T S  
 21781 - CTTAACGGAAACTTCAGTACTCTCCAACGTTTGATACAAGAGCTTGGTCAAGCAACAG - 21840  
 - L N G N F S T I S N V \* Y K S L V K Q Q  
 - L T E T S V L S P T F D T R A W S S N R  
 - \* R K L Q Y Y L Q R L I Q E L G Q A T E

FIG. 12 Con't

21841 - AATAGGTTGGCACATCAGCTGACTGTAGTACACAGAAGCAGACTTAGAAGCAGACTCGTC - 21900  
 - N R L A H Q L T V V H R S R L R S R L V  
 - I G W H I S \* L \* Y T E A D L E A D S S  
 - \* V G T S A D C S T Q K Q T \* K Q T R R

21901 - GCATTTGGACTTGCCATCAAAAATGACATTAATAGGCAGTGAACCTTTAGTGTGTT - 21960  
 - A F G L A I K N Y D I N R Q \* T F S V V  
 - H L D L P S K T M T L I G S E P L V L L  
 - I W T C H Q K L \* H \* \* A V N L \* C C \*

21961 - AGCTCTCAAATGTCTAAATGACAAAATGGAGAGCGGATGTCTCTCATAGGTCTTTTG - 22020  
 - S S Q I V \* I D K M G E R M S L I G L L  
 - A L K L S K L T K W E S G C L S \* V F \*  
 - L S N C L N \* Q N G R A D V S H R S F D

22021 - ACCAGCCTTGTCAAAGTAGAGGTGAAGCGGCCATTTTCACAGCAACACTATCAACAAT - 22080  
 - T S L V K V E V K R A I F H S N T I N N  
 - P A L S K \* R \* S A P F F T A T L S T I  
 - Q P C Q S R G E A R H F S Q Q H Y Q Q Y

22081 - ATACGATGACTGGTCAGTAGGGTTGATGGTCTTTTAAACTGGAGTGACAATCACGAGC - 22140  
 - I R \* L V S R V D W S F K L E \* Q I T S  
 - Y D D L S V G L I G L L N W S D K S R A  
 - T M T G Q \* G \* L V F \* T G V T N H E Q

22141 - AACTTCATCACTAATGAATGTACTACCAGTGCAAAATGTGTACAATTGAGACAATCCA - 22200  
 - N F I T N E C T T S A K C V T I E T I P  
 - T S S L M N V L P V Q N V S Q L R Q F Q  
 - L H H \* \* M Y Y Q C K M C H N \* D N S N

22201 - ATGTGAGTCTTGAGAAGCCAGCGCTCCATTTGCATAGACATAGAAAGATCTCTTCAT - 22260  
 - I V S L A E A T A S I C I D I E R S L H  
 - L \* V L Q K P R P P F A \* T \* K D L F M  
 - C E S C R S H G L H L H R H R K I S S C

22261 - GCCATTAACAATAGTTGTACTCAACCGCTGTGGCAGGATTGGCTTATAGCACATCAT - 22320  
 - A I N N S C T L N A C G T I A L I A H H  
 - P L T I V V H S T R V A R L R L \* H I M  
 - H \* Q \* L Y T Q R V W H D C A Y S T S C

22321 - GCAAGTGAAGAGGTGCAACCATCCATGATATGAACATAGCTCTCCATATGTAGTAGAA - 22380  
 - A S R R G A T I H D M N I A L P Y V V E  
 - Q V E E V Q P S M I \* T \* L F H M \* \* K  
 - K S K R C N R P \* Y E H S S S I C S R K

22381 - AGAAGCAAAGAAGATGTACATCCTAACCATTGCAGAAACGGGTGCCATTTGTACAACT - 22440  
 - R S K E D V H P N H C R N G C H L Y N T  
 - E A K K M Y I L T I A E T G A I C T I L  
 - K Q R R C T S \* P L Q K R V P F V Q Y \*

22441 - AATGATAAACCCATGAGCCAAGAATTGCTGATGAAATGACTAGCAAAATAGCCAAGAA - 22500  
 - N D K P H E P R I A D E M T S K I A K E  
 - M I N H M S Q E L L M K \* L A K \* P K N  
 - \* \* T T \* A K N C \* \* N D \* Q N S Q R T

22501 - CACCTGCATTATAGCTGAAAGACCTAATAAATAAAAGAATTTTGTGAACAACATATGTC - 22560  
 - H L H Y S \* K T \* \* I K E F C E Q H I C  
 - T C I I A E R P N K \* K N F V N N I Y A  
 - P A L \* L K D L I N K R I L \* T T Y M P

22561 - CAAAACCCACTCAGCGGCCAGACCTAAAATGTCAAGTCTAGCTTGTACGATGAATCGT - 22620  
 - Q N P L S A G Q T \* N C Q V \* L V R \* N R  
 - K T H S A A R P K I V K S S L Y D E I V  
 - K P T Q R P D L K L S S L A C T M K S S

22621 - CACCTGAATGGTTTCAAGAGCTGGATAAGAATCAAGGGAGTCTAATCCACTTAAACAAAT - 22680  
 - H L N G F K S W I R I K G V \* S T \* T N  
 - T \* M V S R A G \* E S R E S N P L K Q M  
 - P E W F Q E L D K N Q G S L I H L N K C

FIG. 12 Con't

22681 - GCTGCAAGGAAAAGAACCTTCACAGAAATCCATAGTAGTAACGTTAGACGAATTAAGATA - 22740  
 - A A R K R T F T E I H S S N V R R I K I  
 - L Q G K E P S Q K S I V V T L D E L R Y  
 - C K E K N L H R N P \* \* \* R \* T N \* D T  
 22741 - CAATTCTCTAACGCCATTACAATAAGAAGGAGCACCAAAATAGATAAGAGTACACCAA - 22800  
 - Q F S N A I T I R R S T K I R \* E Y T K  
 - N S L T P L Q \* E G A P K L D K S T P K  
 - I L \* R H Y N K K E H Q N \* I R V H Q K  
 22801 - AGCAGCAGTTACACAGATTAGAGAACCTAAGCAAATACTTAACAACAATAGCCACATAGC - 22860  
 - S S S Y T D \* R T \* A N T \* Q Q \* P H S  
 - A A V T Q I R E P K Q I L N N N S H I A  
 - Q Q L H R L E N L S K Y L T T I A T \* R  
 22861 - GATTGTGAACAATTTAGAAAATTTGGGTGACTTCACATAATTAATGCCGGCATCCAAAACA - 22920  
 - D C E Q F R K F G \* L H I I N A G I Q T  
 - I V N N L E N L G D F T \* L M P A S K H  
 - L \* T I \* K I W V T S H N \* C R H P N I  
 22921 - TAATTTAGCAACACTCTTAACACTATTTTGTAGCAATAGTTGTAGGTAGTGAAGCTCTAAT - 22980  
 - \* F S N T L N T I F S N S C R \* \* S S N  
 - N L A T L L T L F L A I V V G S E A L I  
 - I \* Q H S \* H Y F \* Q \* L \* V V K L \* F  
 22981 - TCTAGAATGGTACTTTTGTAGTAAAGTACACAATTGGAACAATAATGTAAACACATAAGG - 23040  
 - S R I G T F S K S T Q L E Q \* C K H I R  
 - L E L V L L V K V H N W N N N V N T \* G  
 - \* N W Y F \* \* K Y T I G T I M \* T H K A  
 23041 - CATATAATGTTAAACACACGTTGTGCTAATCTCTTAGCGCAATTTGATGTTGTAATTGC - 23100  
 - H I I V K H T L C \* S L S A I \* C C N C  
 - I \* L L N T R C A N L L A Q F D V V I A  
 - Y N C \* T H V V L I S \* R N L M L \* L L  
 23101 - TGCTTGCTCTAAGAATGGTTTGACATAAGCCAAAATTTTACTCCAAGGAACACTATTAAT - 23160  
 - C L S \* E W F D I S Q N F T P R N T I N  
 - A C P K N G L T \* A K I L L Q G T L L I  
 - L V L R M V \* H K P K F Y S K E H Y \* L  
 23161 - TGCAGCAATACCATGAGTGGCAATGTTTTTAAACCTAAGGCTAGTGAAGCTCATTAGG - 23220  
 - C S N T M S G N C F \* T \* G \* \* K L I R  
 - A A I P \* V A I V F K P K A S E S S L G  
 - Q Q Y H E W Q L F L N L R L V K A H \* V  
 23221 - TTTCTTAATGGTAATGCTGTGTTTTCCACATAAGCAGCCATAAGATCCTCATGACCTAA - 23280  
 - F L N G N A C V F H I S S H K I L M T \*  
 - F L M V M L V F S T \* A A I R S S \* P N  
 - S \* W \* C L C F P H K Q P \* D P H D L T  
 23281 - CTCTTGCTTACTTTAACACCTTCATCTGATGGTTAAGTATGACATTGCCTACAACCTC - 23340  
 - L L C Y F N T F I \* W F K Y D I A Y N F  
 - S C V T L T P S S D G L S M T L P T T S  
 - L V L L \* H L H L M V \* V \* H C L Q L R  
 23341 - GGTAGTTTTACGTCACACTCTATGACTTCCTTCTGTATGGTAGGATTTCCACTACTTC - 23400  
 - G S F H V T L Y D F L L Y G R I F H Y F  
 - V V F T S H S M T S F C M V G F S T T S  
 - \* F S R H T L \* L P S V W \* D F P L L L  
 23401 - TTCAGAGGTGGGTGTTGACTTTCACAAGCAAGATTGTCCATTCTTGTGTCTTCTAC - 23460  
 - F R G G L L T F T S K I V H S L C V F Y  
 - S E V G C \* L S Q A R L S I P C V S S T  
 - Q R W V V D F H K Q D C P F L V C L L L  
 23461 - TGCCAGAACTCAAATGAATTTGAAGTATCTACTGGCTTTGTACTCAAAGACAACGTAA - 23520  
 - C Q N F K \* I \* S I Y W L C T P K T T \*  
 - A R T S N E F E V S T G F V L Q R Q R K  
 - P E L Q M N L K Y L L A L Y S K D N V N

FIG. 12 Con't



23521 - ACACCAAGTGTGTTGGTTGAACGTTGTCTTGGTTGTAGCCTGGTTAATGTGCCAAACAAT - 23580  
- T P S V W F E R C L G C S L V N V P N N  
- H Q V F G L N V V L V V A W L M C Q T I  
- T K C L V \* T L S W L \* P G \* C A K Q L  
23581 - TGGCTTATGCAGTAATTTAGCACCTTCTTGAAACTCGCTGAATAGTGTCTATAGTCAAT - 23640  
- W L M Q \* F S T F L E T R \* I V S I V N  
- G L C S N L A P F L K L A E \* C L \* S I  
- A Y A V I \* H L S \* N S L N S V Y S Q \*  
23641 - AGCCACTACATCGCCATTCAAGTCTGGGAAGAATGTGACAGATAGCTCTCGTGAAGCTGG - 23700  
- S H Y I A I Q V W E E C D R \* L S \* S W  
- A T T S P F K S G K N V T D S S R E A G  
- P L H R H S S L G R M \* Q I A L V K L A  
23701 - CTTTGTGAAGCCTGTCATTTGATTTAAATCATCAGCAAATTTTGTGTTAGAACATGTGAG - 23760  
- L C E A C H L I \* I I S K F C V R T C E  
- F V K P V I \* E K S S A N F V L E H V S  
- L \* S L S F D L N H Q Q I L C \* N M \* V  
23761 - TTTGAAATATCAAAACTCGCATTGGTAATGGTTGAGTTGGTACAAGGTCTATAGGCTG - 23820  
- F E I I K T R I W \* W L S W Y K V Y R L  
- L K L S K L A F G N G \* V G T R S I G C  
- \* N Y Q N S H L V M V E L V Q G L \* A A  
23821 - CTCTGTATAGTAAGCATTTATCCTTTTATAATACCCATCCAATTTTGGTTCAATCTCTGT - 23880  
- L C T V S I I L F I I P I Q F W F N L C  
- S V \* \* A L S F L \* Y P S N F G S I S V  
- L Y S K H Y P F Y N T H P I L V Q S L C  
23881 - GTAAGTAACTCCATCGAGTTTATACGACACAGGCTTGTGGTTGTAGTGTAAAGATGTTTC - 23940  
- V S N S I E F I R H R L D G C S V R C F  
- \* V T P S S L Y D T G L M V V V \* D V S  
- K \* L H R V Y T T Q A \* W L \* C K M F P  
23941 - CTTGTAGAAAACATCAGTCACTGCTCTTGTACTCTGACATCTTTGTAAGGTGAGCTCC - 24000  
- L V E N I S H W S F V L \* H L C K V S S  
- L \* K T S V T G P L Y S D I F V R \* A P  
- C R K H Q S L V L C T L T S L \* G E L R  
24001 - GTCAATACGATAGGGTCTCCTTAGCAGTTATATGAGTGTAAATGACCACACTGATAGTT - 24060  
- V N T I E G L L S S Y M S V M T T L I V  
- S I R \* R V S L A V I \* V \* \* P H \* \* L  
- Q Y D R G S P \* Q L Y E C N D H T D S Y  
24061 - ACCAGTGTACTCATTCCACATAAGAATGTACCTTGCTGTAATTTATACTCAGCAGGTGG - 24120  
- T S V L I R T \* E C T L L \* F I L S R W  
- P V Y S F A H K N V P C C N L Y S A G G  
- Q C T H S H I R M Y L A V I Y T Q Q V V  
24121 - TGCAGACATCATAACAAAAGAAGACTCTTGTGTACTAGATATTGTGTAGCATCAGCACC - 24180  
- C R H H N K R R L L L Y \* I L C S I T T  
- A D I I T K E D S C C T R Y C V A S R P  
- Q T S \* Q K K T L V V L D I V \* H H D H  
24181 - ACACACACATGGAATGGAACACCTGTCTTAAGATTATCATAAGATAGAGTACCCATATA - 24240  
- T H T W N G N T C L K I I I R \* S T H I  
- H T H G M E T P V L R L S \* D R V P I Y  
- T H M E W K H L S \* D Y H K I E Y P Y T  
24241 - CATCAGCTTCTACACCCGTTAAGGTAGTAGTTTCTGACCACAATGTTTACACACCAC - 24300  
- H H S F Y T R \* G S S F L T T M F T H H  
- I T A S T P V K V V F \* P Q C L H T T  
- S Q L L H P L R \* \* F S D H N V Y T P H  
24301 - ATTAAGAACTCGCTTGCAGATTCCAAATTAGCATGCTGTAGAAGATGGGTCATAGTTTC - 24360  
- I K N S L C R F Q I S M L \* K M G H S F  
- L R T R F A D S K L A C C R R W V I V S  
- \* E L A L Q I P N \* H A V E D G S \* F L

FIG. 12 Con't

24361 - TCTGACATCACCAAGCTCGCCAACAGTTTTATTACTGTAAGCGAGTATGAGTGCACAAAA - 24420  
 - S D I T K L A N S F I T V S E Y E C T K  
 - L T S P S S P T V L L L \* A S M S A Q K  
 - \* H H Q A R Q Q F Y Y C K R V \* V H K S  
 24421 - GTTAGCAGCATCACCGACGGGCTCTATAATAAGCCTCTTGAAGTGCCTGGTGCATTGAA - 24480  
 - V S S I T S T G S I I S L L K C W C I E  
 - L A A S P A R A L \* \* A S \* S A G A L N  
 - \* Q E H Q H G L Y N K P L E V L V H \* I  
 24481 - TTTGACTTCAAGCTGTTGAAGTGCTAATAAAACACTAGACAAATAACAATTGTTATCAGC - 24540  
 - F D F K L L K C \* \* N T R Q I T I V I S  
 - L T S S C \* S A N K T L D K \* Q L L S A  
 - \* L Q A V E V L I K H \* T N N N C Y Q P  
 24541 - CCATTTAATTGAAGTTAAACCACCAACTTGAGGAAATTTCCATTTCTTTGTGGTTTAA - 24600  
 - P F N \* S \* T T N L R K F P F L C V V \*  
 - H L I E V K P P T \* G N F H F F V W F K  
 - I \* L K L N H Q L E E I S I S L C G L K  
 24601 - AGCAGACATGTACCTACCAAGAAAACCTCTCATCAAGAGTATGGTAGTACTCGAAAGCTTC - 24660  
 - S R H V P T K K T L I K S M V V L E S F  
 - A D M Y L P R K L S S R V W \* Y S K A S  
 - Q T C T Y Q E N S H Q E Y G S T R K L H  
 24661 - ACTACGTAGTGTGCATCACTAGGTAGTACAAAGAAAGTCTTACCCTCATGATTTACATG - 24720  
 - T T \* C V I T R \* Y K E S L T L M I Y M  
 - L R S V S S L G S T K K V L P S \* F T \*  
 - Y V V C H H \* V V Q R K S Y P H D L H E  
 24721 - AGGTTTAATTTTGTAAACATCAGCACCACTCCAAGTATGTTGGACCAAACTGCTGTCCATA - 24780  
 - R F N F C N I S T I Q V C W T K L L S I  
 - G L I F V T S A P S K Y V G P N C C P Y  
 - V \* F L \* H Q H H P S M L D Q T A V H M  
 24781 - TGTCAATAGACATATCCACAAGCTGTGTGTGGAGATTAGTGTGTCCACAGTTGTGAACAC - 24840  
 - C H R H I H K L C V E I S V V H S C E H  
 - V I D I S T S C V W R L V L S T V V N T  
 - S \* T Y P Q A V C G D \* C C P Q L \* T L  
 24841 - TTTTATAGTCTTAACTCCCGCAGGGATAAGAGACTCTTTAGITTTGTCAAGTGAAGAAC - 24900  
 - F Y S L N L P Q G \* E T L \* F V K \* K N  
 - F I V L T S R R D K R L F S L S S E R T  
 - L \* S \* P P A G I R D S L V C Q V K E P  
 24901 - CTCACCGTCAAGATGAAACTCGACGGGCTCTCCAGAGTGTGGTACACAATTTTGTACC - 24960  
 - L T V K M K L D G A L Q S V V H N F V T  
 - S P S R \* N S T G L S R V W Y T I L S P  
 - H R Q D E T R R G S P E C G T Q F C H H  
 24961 - ACGCTTAAGAAATTC AACACCTA ACTCTGTAGCTGTCTG AATAGGACCAATCTCTGTA - 25020  
 - T L K K F N T \* L C T L S \* I G P I S V  
 - R L R N S T P N S V R C P E \* D Q S L \*  
 - A \* E I Q H L T L Y A V L N R T N L C K  
 25021 - AGAGCCAGCCAAAGAAACTGTTTCTACAAAGTGCTCCTCAGATGTCTTTGATGACGAAGT - 25080  
 - R A S Q R N C F Y K V L L R C L \* \* R S  
 - E P A K E T V S T K C S S D V F D D E V  
 - S Q P K K L F L Q S A P Q M S L M T K \*  
 25081 - GAGGTATCCATATATGTAGTAACAGCATCTGGTGTGATACTGACACTACGGCAGGAGC - 25140  
 - E V S I I C S N S I W \* \* Y \* H Y G R S  
 - R Y P L Y V V T A S G D D T D T A G A  
 - G I H Y M \* \* Q H L V M I L T L R Q E L  
 25141 - TTTAAGAGAACGCATACAGCGCGCAGCCTCTTCAAGATTAACCATGTGTCACATAACC - 25200  
 - F K R T H T A R S L F K I K T M C H I T  
 - L R E R I Q R A A S S R L K P C V T \* P  
 - \* E N A Y S A Q P L Q D \* N H V S H N Q

FIG. 12 Con't

25201 - AATTGGCATTGTGACAAGCGGCTCATTAGAGAGTTCAGCTTCGTAATAATAGAAGCTAC - 25260  
 - N W H C D K R L I \* R V Q L R N N R S Y  
 - I G I V T S G S F R E F S F V I I E A T  
 - L A L \* Q A A H L E S S A S \* \* \* K L Q  
 25261 - AGGCTCTTTACTAGTATAAAAAGAAGAATCGGACACCATAGTCAACGATGCCCTCTTGAAT - 25320  
 - R L F T S I K E E S D T I V N D A L L N  
 - G S L L V \* K K N R T P \* S T M P S \* I  
 - A L Y \* Y K R R I G H H S Q R C P L E F  
 25321 - TTTAATTCCTTTACTTACGTGGATGGTTGCCATTATGGCTCTAACATCCATGCATAT - 25380  
 - F N S F I L T L D G C H Y G S N I H A Y  
 - L I P L Y L R W M V A I M A L T S M H I  
 - \* F L Y T Y V G W L P L W L \* H P C I \*  
 25381 - AGGCATTAATTTTCTGTCTCTCAGCATGAGCAAGCATTCTCTCAAATCCAGGATAC - 25440  
 - R H \* F S C L F S M S K H F S Q I P G Y  
 - G I N F L V S S A \* A S I S L K F Q D T  
 - A L I F L S L Q H E Q A F L S N S R I Q  
 25441 - AGTTCCTAGAAATCTCTTCTTAGCATTAGTGTCTCTGAAGGTAGTACATAAAATGCAGA - 25500  
 - S S \* N L F L S I R C F \* R \* Y I K C R  
 - V P R I S S L A L G A S E G S T \* N A D  
 - F L E S L P \* H \* V L L K V V H K M Q I  
 25501 - TTTGCATTTCCTAAGAGCAGTCTTAGCTTCCTCAAGTGTATAACCAGCACATCCTTGTC - 25560  
 - F A F L K S S L S F L K C I T S T S L S  
 - L H F L R A V L A S S S V \* P A H P C P  
 - C I S \* E Q S \* L P Q V Y N Q H I L V Q  
 25561 - AGGGTACCTGGTTATATACTCATCAACTGGCACTTCTTCAAAGCTCTTGAGAGCATCTC - 25620  
 - R V R G Y I L I N W H F L Q S S \* E H L  
 - G Y V V I Y S S T G T F F K A L E S I S  
 - S T W L Y T H Q L A L S S K L L R A S Q  
 25621 - AGTAGTGCACCAGCCTTTTTGGAGGGTATTACAACACAAGTGATATCACCCTAGTGAT - 25680  
 - S S A T S L F G G Y Y N T S D I T T S D  
 - V V P P A F L E G I T T Q V I S P L V I  
 - \* C H Q P F W R V L Q H K \* Y H H \* \* \*  
 25681 - AACATCACCTACCATGTAAGGTGCATCCTTCTCAAGGAAAGACATATCTTCACCTCTAAG - 25740  
 - N I T Y H V R C I L L K E R H I F T S K  
 - T S P T M \* G A S F S R K D I S S P L S  
 - H H L P C K V H P S Q G K T Y L H L \* A  
 25741 - CATGTTCTGAGAATCATGGTAAAGCTTACCATTGATATCAGCAAACAAGAGTAACTTATT - 25800  
 - H V L R I M V K L T I D I S K Q E \* L I  
 - M F \* E S W \* S L P L I S A N K S N L L  
 - C S E N H G K A Y H \* Y Q Q T R V T Y W  
 25801 - GGTAAGAAACTTAGTTTCTTCCAGTGTGTGGTAACTCATCAATGCAGGCCTTAATTTT - 25860  
 - G K K L S F F Q C C G N L I N A G L N F  
 - V R N L V S S S V V V T S S M Q A L I F  
 - \* E T \* F L P V L W \* P H Q C R P \* F L  
 25861 - TGGCTTCACATCSACAGGCTTCTGTACGACAGATTCTCCTCAGTTTGGAAATCTTCTGT - 25920  
 - W L H I D R L L Y D R F L L S F G I F C  
 - G F T S T G F C T T D F S S V L E S S V  
 - A S H R Q A S V R Q I S P Q F W N L L C  
 25921 - GTTTGGTGGCTCCTCTTGTGTTAGGTGCTCCACTCTAGGCTTCAGGTTATCAAGATAATC - 25980  
 - V W W L L L F R C F H S R L Q V I K I I  
 - F G G S S C L G A S T L G F R L S R \* S  
 - L V A P L V \* V L P L \* A S G Y Q D N P  
 25981 - CATGACAACCTGCTCATAAAGAGCTTTGTCATTGACTGCAATATAAACCTGTGTACGAAC - 26040  
 - H D N L L I K S F V I D C N I N L C T N  
 - M T T C S \* R A L S L T A I \* T C V R T  
 - \* Q P A H X E L C H \* L Q Y K P V Y E P

FIG. 12 Con't



26881 - ACCGGATTCAACAGTGTAGACAGAGCACTTTTCATTAAGCACTTTGTCAACACGGTTCATC - 26940  
- T G F N S V D R A L F I K H F V N T F I  
- P D S T V \* T E H F S L S T L S T R S S  
- R I Q Q C R Q S T F H \* A L C Q H V H Q  
26941 - AAGCTCAAATGTGATTCTCACATTCTTGTAACCTTGAACCTCCCAAACAGTATCTTCTCC - 27000  
- K L K C D S H I L V T L N F P N S I F S  
- S S N V I L T F L \* P \* T S Q T V S S P  
- A Q M \* F S H S C N L E L P K Q Y L L Q  
27001 - AAAGTTACACCTTTAATTGGTGCACCCCTTTTAAGCGAAAGACATTGTTTGTAGCCAG - 27060  
- K G Y T F N W C T P F \* A K D I V C S Q  
- K V T P L I G A P P F K R K T L F V A S  
- R L H L \* L V H P L L S E R H C L \* P V  
27061 - TAAACCAGGAGACAATGCGCAGTATTGTTCTTTGTCCTTAATCTCTAAGAGCATGAGGCC - 27120  
- \* T R R Q C A V L F F V L N L \* E H E A  
- K P G D N A Q Y C S L S L I S K S M R P  
- N Q E T M R S I V L C P \* S L R A \* G H  
27121 - ATTTACACAGACTGGTGTGCCGACGATAGCTCCATTTGTGAAGCTATCAACGGGCGTCTC - 27180  
- I Y T D W C A D D S S I C E A I N G R L  
- F T Q T G V P T I A P F V K L S T G V S  
- L H R L V C R R \* L H L \* S Y Q R A S R  
27181 - GAGTGCCTCGAGTTCACCGTTCCTTGAGAACAACCTCCTCAGAGGTAAGTACTGTGTCATG - 27240  
- E C F E F T V L E N N L L R G K Y C V M  
- S A S S S P F L R T T S S E V S T V S C  
- V L R V E R S \* E Q P P Q R \* V L C H V  
27241 - TGAATCACCTTCAAGAAAGGTTACTTCTTTGGTGCCTTAAGAGGCATGAGTAGTTGCAG - 27300  
- \* I T F K K G Y F F W C L K R H E \* L Q  
- E S P S R K V T S F G A L R G M S S C S  
- N H L Q E R L L L L V P \* E A \* V V A A  
27301 - CTGCTCCTTGCCACGTATACTGACGGTAAAGTCCCTTGCTTTGAGCGATGAAGACTTC - 27360  
- L L L A T Y T L T V K S L A L S D E D F  
- C S L P R I H \* R \* S P L L \* A M K T S  
- A P C H V Y T D G K V P C F E R \* R L H  
27361 - ACCTAAGTGTGAGTGTGCAACTTTGCGCCAGCGATAGTACTGACTTGATCAATGCACATTC - 27420  
- T \* V E \* S Q L C A S D S D L I N A H F  
- P K L S D R N E A P A I V T \* S M H I S  
- L S \* V I A T L R Q R \* \* L D Q C T F R  
27421 - GAGTGCCTTGTTAACAACATCAATGAAGCATTTTACACAATCCTTGATGTTATCTGAAGC - 27480  
- E C L V N N I N E A F Y T I L D V I \* S  
- S A L L T T S M K H F T Q S L M L S E A  
- V P C \* Q H Q \* S I L H N P \* C Y L K Q  
27481 - AACCTGTATTTGACCCTTGACGATGTCAAAAACACCTGTAATGAGAAATTTGAGAATCTC - 27540  
- N L Y L T L D D V K N T C N E K F E N L  
- T C I \* P L T M S K T P V M R N L R I S  
- P V F D P \* R C Q K H L \* \* E I \* E S P  
27541 - CCAAGCATCCTTGAGAAATTCAACTCCTGCACTAAGTTTCGCCTCAATCCATTCAAAGAT - 27600  
- P S I L E K F N S C T K F R L N P F K D  
- Q A S L R N S T P A L S F A S I H S K I  
- K H P \* E I Q L L H \* V S P Q S I Q R \*  
27601 - AGGCCTGAGTTTTTCAACAGTAGTGCCCAAAGATTAGACAACCACTGAGAAGTCTGTG - 27660  
- R P E F F N S S A Q K I R Q P L R S L L  
- G L S F S T V V P K R L D N H \* E V C C  
- A \* V F Q Q \* C P K D \* T T T E K S V V  
27661 - TACAAGACCACCAGTTACATATGCCATAATAATGACACTGTTGGTGAGCAGGTCTGAAGT - 27720  
- Y K T T S Y I C H N N D T V G E Q V \* S  
- T R P P V T Y A I I M T L L V S R S E V  
- Q D H Q L H M P \* \* \* H C W \* A G L K Y

FIG. 12 Con't

27721 - ATAAACCATGGCGTCGACAAGACGTAATGACTGTTCAGAAATACCATCAAGTATGGTGAC - 27780  
 - I N H G V D K T \* \* L F R N T I K Y G D  
 - \* T M A S T R R N D C S E I P S S M V T  
 - K P W R R Q D V M T V Q K Y H Q V W \* Q  
 27781 - AGCTGCTCTTTGCAAATCAGGAATTGAGTGGTTTCTGCATCAAGTGTGCGCGCAAAAAT - 27840  
 - S C S L Q I R N \* V V C C I K C A R K N  
 - A A L C K S G I E W F A A S S V R A K I  
 - L L F A N Q E L S G L L H Q V C A Q K L  
 27841 - TGATCTGATAACACCAGCAGCCTGTGAGGGAAAACCACACAGTGGTGTAAAACTGATCT - 27900  
 - \* S D N T S S L \* G K T T Q W C \* N \* S  
 - D L I T P A A C E G K P H S G V K T D L  
 - I \* \* H Q Q P V R E N H T V V L K L I S  
 27901 - CTGTTGTCCAATGTTCCAAGCACCTTTACGGGCTTTCCCTTGGTAACTTTATAGTTACC - 27960  
 - L L S N V P S T F Y G L S L G N F I V T  
 - C C P M F Q A P F T G F P L V T L \* L P  
 - V V Q C S K H L L R A F P W \* L Y S R  
 27961 - GCAGACTCAACAATGGTTTGAAGACTTGTAAATCAAGACTCTTTATAGTGTCAATAAA - 28020  
 - A G L N N G F E R L V I K T L Y S V N K  
 - Q D S T M V L K D L \* S R L F I V S I K  
 - R T Q Q W F \* K T C N Q D S L \* C Q \* R  
 28021 - GGCACCTGTAGAAGCAGAGAAAGATGCCAAAATGATGGCAACCTCTTCATTCAAATGAAA - 28080  
 - G T C R S R E R C Q N D G N L F I Q M K  
 - A L V E A E K D A K M M A T S S F K \* K  
 - H L \* K Q R K M P K \* W Q P L H S N E N  
 28081 - ATCGCCAACAATGTTAATGTTAACACGTTACAGACTCAGTATCTCAAGGAGATCCTCATT - 28140  
 - I A N N V N V N T F T T Q Y L K E I L I  
 - S P T M L M L T R S R L S I S R R S S F  
 - R Q Q C \* C \* H V H D S V S Q G D P H S  
 28141 - CAAGTCTCCACATTGTCACCAGTAATGCCAGTATGGCCTGAGCCAATATCAGCATTAGC - 28200  
 - Q G L H I V T S N A S M A \* A N I S T S  
 - K V S T L S P V M P V W P E P I S A L A  
 - R S P H C H Q \* C Q Y G L S Q Y Q H \* E  
 28201 - ACGAGCAACCCAGTAGGCAGCCTTATTATAGCAGCCAACATAGGCAAACACACAGCCTCC - 28260  
 - T R N P V G T L I I A A N I G K H T A S  
 - R G T Q \* A R L L \* Q P T \* A N T Q P P  
 - E E P S R H A Y Y S S Q H R Q T H S Q  
 28261 - AAAACATCTAGTCTACCTCCCTTGCGGAGTCAGTTTCAATGTTGAGTGGTTGTGATA - 28320  
 - K T S S P T S L A E S S F N V \* V V V I  
 - K H L V L P P L R S R V S M F E W L \* \*  
 - N I \* S Y L P C G V E F Q C L S G C D N  
 28321 - ATCTGCAACACTATGCTCAGGTCCAATCTCTGGGTCTTGACAGGCAGCACATGGCATTTC - 28380  
 - I C N T M L R S N L W V L T G R T W H F  
 - S A T L C S G P I S G S \* Q A G H G I F  
 - L Q H Y A Q V Q S L G L D R Q D M A F S  
 28381 - CACTACAGCATTAGTAGGTAGGTACCCACATGTAGTAGGTCTTCAATAACTAAATTTTC - 28440  
 - H Y S I S R \* V P T C S R S F N N \* I F  
 - T T A L V G R Y P H V V G P S I T K F S  
 - L Q H \* \* V G T H M \* \* V L Q \* L N F Q  
 28441 - AGTGCCACAATGTTCAAGTGGCTTTCAGAAAAGTCGACAGTCTGCCATGAAACTTCATC - 28500  
 - S A T M F T S G F Q K V A R L P \* N F I  
 - V P Q C S Q V A F R K S H V C H E T S S  
 - C H N V H K W L S E S R T S A M K L H R  
 28501 - GCAATGATTACATTCATCAAGGTAGACAAGTGCATATGTTACACTCCTGTGGAGATGC - 28560  
 - A M I T F H Q G R Q V H I V T L L W R C  
 - Q \* L H F I K V D K C I L L H S C G D A  
 - N D Y I S S R \* T S A Y C Y T P V E M Q

FIG. 12 Con't

28561 - AACAGGGTACACAGAGCGGTATACGCCCATGAAACCCTCAGTCTTTTTCTTTTCAACACG - 28620  
 - N R V H R A Y T P H E T L S L F L F N T  
 - T G Y T E R I R P M K P S V F F F S T R  
 - Q G T Q S V Y A P \* N P Q S F S F Q H V  
 28621 - TGGTTGAATGACTTTGACTTTTGAGTTAAGAGGAAACACAAACTTTGGGCATTCCCCTTT - 28680  
 - W L N D F D F \* V K R K H K L W A F P F  
 - G \* M T L T F E L R G N T N F G H S P L  
 - V E \* L \* L L S \* E E T Q T L G I P L \*  
 28681 - GAAAGTGTCAAATTTCTTGGCACTCTTAATTCGAAGGGTGTCTGGTGCTCGTAGCTCTT - 28740  
 - E S V K F L G T L N F E G C L V L V A L  
 - K V S N F L A L L I S K G V W C S \* L L  
 - K C Q I S W H S \* F R R V S G A R S Y  
 28741 - ATCAGAGCGCTCAGTGAACCAGGCAATTTTCATGCTCATGGTCACGGCAGTAGACACC - 28800  
 - I R A L S E P G N F M L M V T A A V D T  
 - S E R S V N Q A I S C S W S R Q Q \* T P  
 - Q S A Q \* T R Q F H A H G H G S S R H L  
 28801 - TCTCTCGACTCGATGTAATCAAGTTGTTCCGAAAGAGTGCACATTGACTTGCCCCGCGG - 28860  
 - S L R L D V I K L F G K S A H \* L A R A  
 - L F D S M \* S S C S E R V H I D L P A R  
 - S S T R C N Q V V R K E C T L T C P R V  
 28861 - TGGAGAAAATCTTTGATGCAATCAAGAGGGTACCCATCTGGGCCACAGAAATGTTGTC - 28920  
 - C E K I F D A I K R V P I W A T E I V V  
 - A R K S L M Q S R G Y P S G P Q K L L S  
 - R E N L \* C N Q E G T H L G H R N C C R  
 28921 - GACATAGCGAGTGACTGCACCTCCATTGAGCTCAGGAGTTCACGGAGTGCACCACT - 28980  
 - D I A S D C T S I E L T S E F T E C T T  
 - T \* R V T A P P L S S R V S S R S A P L  
 - H S E \* L H L H \* A H E \* V H G V H H C  
 28981 - GCCATGCTTAGTGTCCAGTTTGTTCATAATCTTCAATGGGATCAGTCCCAAGCTCGTC - 29040  
 - A M L S V P V L F I I F N G I S A K L V  
 - P C L V F Q F C S \* S S M G S V P S S S  
 - H A \* C S S F V H N L Q W D Q C Q A R H  
 29041 - ACCTAAGTCATAAGACTTTAGATCGATGCCATAGCTATGACCACCGGCTCCCTTATTACC - 29100  
 - T \* V I R L \* I D A I A M T T G S L I T  
 - P K S \* D F R S M P \* L \* P P A P L L P  
 - L S H K T L D R C H S Y D H R L P Y Y R  
 29101 - GTTCTTACGAAGAAGCAATTCGCGGTATGCAATTTGGGGTTTCGCCACATGTGGCAGCAG - 29160  
 - V L T K K N I A V C N W G F A H M W H E  
 - F L R R R T L R Y A I G V S P T C G T S  
 - S Y E E E H C G M Q L G F R P H V A R V  
 29161 - TACTCCCAGTGTATACCGCTACGACCGTACTGAATGCCGTCATTCTGCAACCAGCTC - 29220  
 - Y S Q C Y T A T T V L N A V H F C N Q L  
 - T P S V I P L R P Y \* M P S I S A T S S  
 - L P V L Y R Y D R T E C R P F L Q P A Q  
 29221 - AACGACCTTGTGGCCGTGATTGGTGCTTAAGGCATCAGAACGTTTAAATGAACACATAGGG - 29280  
 - N D L V A V I G A \* G I R T F N E H I G  
 - T T L W P \* L V L K A S E R L M N T \* G  
 - R P C G R D W C L R H Q N V \* \* T H R A  
 29281 - CTGTTCAAGCTGGGGCAGTACGCCTTTTCCAGCTCTACTAGACCACAAGTGCATTTTT - 29340  
 - L F K L G Q Y A F F Q L Y \* T T S A I F  
 - C S S W G S T P F S S S T R P Q V P F F L  
 - V Q A G A V I G A L L D H K C H F \*  
 29341 - GAGTGTTCACGTGCCTCCGATAGGGCCCTTCCACAGAGTCCCGAAGCCACGCACTAG - 29400  
 - E V F T C L R \* G L F H R V P E A T H \*  
 - R C S R A S D R A S S T E S P K P R T S  
 - G V H V P P I G P L P Q S P R S H A L A

FIG. 12 Con't

29401 - CACGTCTCTAACCTGAAGGACAGGCCAAACTGAGTTGGACGTGTGTTTTCTCGTTGACACC - 29460  
- H V S N L K D R Q T E L D V C F L V D T  
- T S L T \* R T G K L S W T C V F S L T P  
- R L \* P E G Q A N \* V G R V F S R \* H Q  
29461 - AAGAACAAGGCTCTCCATCTTACCTTTTCGGTCACACCCCGACGAAACCTAGGTATGCTGA - 29520  
- K N K A L H L T F R S H P D E T \* V C \*  
- R T R L S I L P F G H T R T K P R Y A D  
- E Q G S P S Y L S V T P G R N L G M L M  
29521 - TGATCGACTGCAACACGGACGAAACCGTAAGCAGTCTGCAGAAGAGGGACGAGTTACTCG - 29580  
- \* S T A T R T K P \* A V C R R G T S Y S  
- D R L Q H G R N R K Q S A E E G R V T R  
- I D C N T D E T V S S L Q K R D E L L V  
29581 - TTTCTTGTCAACGACAGTAAAATTTATTATTGTTTATACTGCGTAGGTGCACTAGGCATG - 29640  
- F L V N D S K I Y Y C L Y C V G A L G M  
- F L S T T V K F I I V Y T A \* V H \* A C  
- S C Q R Q \* N L L L F I L R R C T R H A  
29641 - CAGCCGAGCGACAGCTACACAGATTTTAAAGTTCGTTTAGAGAACAGATCTACAAGAGAT - 29700  
- Q P S D S Y T D F K V R L E N R S T R D  
- S R A T A T Q I L K F V \* R T D L Q E I  
- A E R Q L H R F \* S S F R E Q I Y K R S  
29701 - CGAGGTTGGTTGGCTTTTCCTGGGTAGGTAAAAACCTAATAT - 29742  
- R G W L A F P G \* V K T \* Y X  
- E V G W L F L G R \* K P N X  
- R L V G F S W V G K N L I X

FIG. 12 Con't



**HUMAN VIRUS CAUSING SEVERE ACUTE  
RESPIRATORY SYNDROME (SARS) AND  
USES THEREOF**

This application is a continuation application of U.S. patent application Ser. No. 11/808,408, filed Jun. 8, 2007 now U.S. Pat. No. 7,785,775; which is a divisional application of U.S. patent application Ser. No. 10/808,121, filed Mar. 24, 2004, now U.S. Pat. No. 7,375,202; which claims priority benefit to U.S. provisional Application No. 60/457,031, filed Mar. 24, 2003; U.S. provisional Application No. 60/457,730, filed Mar. 26, 2003; U.S. provisional Application No. 60/459,931, filed Apr. 2, 2003; U.S. provisional Application No. 60/460,357, filed Apr. 3, 2003; U.S. provisional Application No. 60/461,265, filed Apr. 8, 2003; U.S. provisional Application No. 60/462,805, filed Apr. 14, 2003; and U.S. provisional Application No. 60/464,886 filed Apr. 23, 2003, each of which is incorporated herein by reference in its entirety.

The Sequence Listing for this application is labeled "SeqListing.txt", which was created on Feb. 10, 2010, and is 1,624 KB. The entire content is incorporated herein by reference in its entirety.

### 1. INTRODUCTION

The present invention relates to an isolated novel virus causing Severe Acute Respiratory Syndrome (SARS) in humans ("hSARS virus"). The hSARS virus is identified to be morphologically and phylogenetically similar to known members of Coronaviridae. The present invention relates to a nucleotide sequence comprising the complete genomic sequence of the hSARS virus. The invention further relates to nucleotide sequences comprising a portion of the genomic sequence of the hSARS virus. The invention also relates to the deduced amino acid sequences of the complete genome of the hSARS virus. The invention further relates to the nucleic acids and peptides encoded by and/or derived from these sequences and their use in diagnostic methods and therapeutic methods, such as for immunogens. The invention further encompasses chimeric or recombinant viruses encoded by said nucleotide sequences and antibodies directed against polypeptides encoded by the nucleotide sequence. Furthermore, the invention relates to vaccine preparations comprising the hSARS virus, including recombinant and chimeric forms of said virus as well as protein extracts and subunits of said virus.

### 2. BACKGROUND OF THE INVENTION

Recently, there has been an outbreak of atypical pneumonia in Guangdong province in mainland China. Between November 2002 and March 2003, there were 792 reported cases with 31 fatalities (WHO. Severe Acute Respiratory Syndrome (SARS) *Weekly Epidemiol Rec.* 2003; 78: 86). In response to this crisis, the Hospital Authority in Hong Kong has increased the surveillance on patients with severe atypical pneumonia. In the course of this investigation, a number of clusters of health care workers with the disease were identified. In addition, there were clusters of pneumonia incidents among persons in close contact with those infected. The disease was unusual in its severity and its progression in spite of the antibiotic treatment typical for the bacterial pathogens that are known to be commonly associated with atypical pneumonia. The present inventors were one of the groups involved in the investigation of these patients. All tests for identifying commonly recognized viruses and bacteria were negative in these patients. The disease was given the acronym

Severe Acute Respiratory Syndrome ("SARS"). The etiologic agent responsible for this disease was not known until the isolation of hSARS virus from the SARS patients by the present inventors as disclosed herein. Namely, the present invention discloses a novel human virus that has been isolated and identified from the patients suffering from SARS. The invention is useful in both clinical and scientific research applications.

### 3. SUMMARY OF INVENTION

The present invention is based upon the inventor's isolation and identification of a novel virus causing Severe Acute Respiratory Syndrome in humans ("hSARS virus"). The virus was isolated from the patients suffering from SARS in the recent outbreak of severe atypical pneumonia in China. The isolated virus is an enveloped, single-stranded RNA virus of positive polarity which belongs to the order, Nidovirales, of the family, Coronaviridae. Accordingly, the invention relates to the isolated hSARS virus that morphologically and phylogenetically relates to known members of Coronaviridae. In a specific embodiment, the isolated hSARS virus is that which was deposited with China Center for Type Culture Collection (CCTCC) on Apr. 2, 2003 and accorded an accession number, CCTCC-V200303, as described in Section 7, *infra*. In another specific embodiment, the invention provides complete genomic sequence of the hSARS virus. In a preferred embodiment, the virus comprises a nucleotide sequence of SEQ ID NO:15. In another specific embodiment, the invention provides nucleic acids isolated from the virus. The virus preferably comprises a nucleotide sequence of SEQ ID NO:1, 11 and/or 13 in its genome. In a specific embodiment, the present invention provides isolated nucleic acid molecules comprising or, alternatively, consisting of the nucleotide sequence of SEQ ID NO:1, a complement thereof or a portion thereof, preferably at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. In another specific embodiment, the present invention provides isolated nucleic acid molecules comprising or, alternatively, consisting of the nucleotide sequence of SEQ ID NO:11, a complement thereof or a portion thereof, preferably at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:11, or a complement thereof. In yet another specific embodiment, the present invention provides isolated nucleic acid molecules comprising or, alternatively, consisting of the nucleotide sequence of SEQ ID NO:13, a complement thereof or a portion thereof, preferably at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:13, or a complement thereof. In another specific embodiment, the present invention provides isolated nucleic acid molecules comprising or, alternatively, consisting of the nucleotide sequence of SEQ ID NO:15, a complement thereof or a portion thereof, preferably at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 11000, 13,000, 14,000, 15,000, 16,000, 17,000, 18,000, 19,000, 20,000, 21,000, 22,000, 23,000, 24,000, 25,000, 26,000, 27,000, 28,000, 29,000 or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:15, or a complement thereof. Furthermore, in another specific

embodiment, the invention provides isolated nucleic acid molecules which hybridize under stringent conditions, as defined herein, to a nucleic acid molecule having the sequence of SEQ ID NO:1, 11, 13, 15, 16, 240, 737, 1108, 1590 or 1965 or a complement thereof. In one embodiment, the invention provides an isolated nucleic acid molecule which is antisense to the coding strand of a nucleic acid of the invention. In another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising or, alternatively consisting of a nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. In yet another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising or, alternatively consisting of a nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200 or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:11, or a complement thereof. In yet another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising or, alternatively consisting of a nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:13, or a complement thereof. In yet another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising or, alternatively consisting of a nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, 17,000, 18,000, 19,000, 20,000, 21,000, 22,000, 23,000, 24,000, 25,000, 26,000, 27,000, 28,000, 29,000 or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:15, or a complement thereof. The invention further provides proteins or polypeptides that are isolated from the hSARS virus, including viral proteins isolated from cells infected with the virus but not present in comparable uninfected cells. The invention further provides proteins or polypeptides of SEQ ID NOS:2, 12 and 14 and those shown in FIGS. 11 (SEQ ID NOS:17-239, 241-736 and 738-1107) and 12 (1109-1589, 1591-1964, 1966-2470). The polypeptides or the proteins of the present invention preferably have a biological activity of the protein (including antigenicity and/or immunogenicity) encoded by the sequence of SEQ ID NO:1, 11, 13, 16, 240, 737, 1108, 1590 or 1965. In other embodiments, the polypeptides or the proteins of the present invention have a biological activity of the protein (including antigenicity and/or immunogenicity) encoded by a nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, 17,000, 18,000, 19,000, 20,000, 21,000, 22,000, 23,000, 24,000, 25,000, 26,000, 27,000, 28,000, 29,000 or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:15, or a complement thereof. In other embodiments, the polypeptides or the proteins of the present invention have a biological activity of the protein (including antigenicity and/

or immunogenicity) of FIGS. 11 (SEQ ID NOS:17-239, 241-736 and 738-1107) and 12 (SEQ ID NOS:1109-1589, 1591-1964 and 1966-2470).

In one aspect, the invention provides a method for propagating the hSARS virus in host cells comprising infecting the host cells with the isolated hSARS virus, culturing the host cells to allow the virus to multiply, and harvesting the resulting virions. Also provided by the present invention are host cells that are infected with the hSARS virus. In another aspect, the invention relates to the use of the isolated hSARS virus for diagnostic and therapeutic methods. In a specific embodiment, the invention provides a method of detecting in a biological sample an antibody immunospecific for the hSARS virus using the isolated hSARS virus or any proteins or polypeptides thereof. In another specific embodiment, the invention provides a method of screening for an antibody which immunospecifically binds and neutralizes hSARS. Such an antibody is useful for a passive immunization or immunotherapy of a subject infected with hSARS.

The invention further relates to the use of the sequence information of the isolated virus for diagnostic and therapeutic methods. In a specific embodiment, the invention provides nucleic acid molecules which are suitable for use as primers consisting of or comprising the nucleotide sequence of SEQ ID NO:1, 11, 13, or 15, a complement thereof, or at least a portion of the nucleotide sequence thereof. In another specific embodiment, the invention provides nucleic acid molecules which are suitable for hybridization to hSARS nucleic acid, including, but not limited to, as PCR primers, Reverse Transcriptase primers, probes for Southern analysis or other nucleic acid hybridization analysis for the detection of hSARS nucleic acids, e.g., consisting of or comprising the nucleotide sequence of SEQ ID NO:1, 11, 13, or 15, a complement thereof, or a portion thereof. The invention further encompasses chimeric or recombinant viruses encoded in whole or in part by said nucleotide sequences.

The invention further provides antibodies that specifically bind a polypeptide of the invention encoded by the nucleotide sequence of SEQ ID NO:1, 11, 13, 16, 240, 737, 1108, 1590 or 1965, or a fragment thereof, or encoded by a nucleic acid comprising a nucleotide sequence that hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO:1, 11, or 13, and/or any hSARS epitope, having one or more biological activities of a polypeptide of the invention. The invention further provides antibodies that specifically bind polypeptides of the invention encoded by the nucleotide sequence of SEQ ID NO:15 or a complement thereof, or a fragment thereof. These polypeptides include those shown in FIGS. 11 (SEQ ID NOS:17-239, 241-736 and 738-1107) and 12 (SEQ ID NOS:1109-1589, 1591-1964 and 1966-2470). The invention further provides antibodies that specifically bind polypeptides of the invention encoded by a nucleic acid comprising a nucleotide sequence that hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO:15, and/or any hSARS epitope, having one or more biological activities of a polypeptide of the invention. Such antibodies include, but are not limited to polyclonal, monoclonal, bi-specific, multi-specific, human, humanized, chimeric antibodies, single chain antibodies, Fab fragments, F(ab')<sub>2</sub> fragments, disulfide-linked Fvs, intrabodies and fragments containing either a VL or VH domain or even a complementary determining region (CDR) that specifically binds to a polypeptide of the invention.

In one embodiment, the invention provides methods for detecting the presence, activity or expression of the hSARS virus of the invention in a biological material, such as cells, blood, saliva, urine, and so forth. The increased or decreased

activity or expression of the hSARS virus in a sample relative to a control sample can be determined by contacting the biological material with an agent which can detect directly or indirectly the presence, activity or expression of the hSARS virus. In a specific embodiment, the detecting agents are the antibodies or nucleic acid molecules of the present invention. Antibodies of the invention may also be used to treat SARS.

In another embodiment, the invention provides vaccine preparations, comprising the hSARS virus, including recombinant and chimeric forms of said virus, or protein subunits of the virus. In a specific embodiment, the vaccine preparations of the present invention comprise live but attenuated hSARS virus with or without adjuvants. In another specific embodiment, the vaccine preparations of the invention comprise an inactivated or killed hSARS virus. Such attenuated or inactivated viruses may be prepared by a series of passages of the virus through the host cells or by preparing recombinant or chimeric forms of virus. Accordingly, the present invention further provides methods of preparing recombinant or chimeric forms of hSARS. In another specific invention, the vaccine preparations of the present invention comprise a nucleic acid or fragment of the hSARS virus, e.g., the virus having accession no. CCTCC-V200303, or nucleic acid molecules having the sequence of SEQ ID NO. 1, 11, 13, or 15, or a fragment thereof. In another embodiment, the invention provides vaccine preparations comprising one or more polypeptides isolated from or produced from nucleic acid of hSARS virus, for example, of deposit accession no. CCTCC-V200303. In a specific embodiment, the vaccine preparations comprise a polypeptide of the invention encoded by the nucleotide sequence of SEQ ID NO:1, 11, 13, 16, 240, 737, 1108, 1590 or 1965, or a fragment thereof. In a specific embodiment, the vaccine preparations comprise polypeptides of the invention as shown in FIGS. 11 (SEQ ID NOS:17-239, 241-736 and 738-1107) and 12 (SEQ ID NOS:1109-1589, 1591-1964 and 1966-2470) or encoded by the nucleotide sequence of SEQ ID NO:15, or a fragment thereof. Furthermore, the present invention provides methods for treating, ameliorating, managing or preventing SARS by administering the vaccine preparations or antibodies of the present invention alone or in combination with adjuvants, or other pharmaceutically acceptable excipients.

In another aspect, the present invention provides pharmaceutical compositions comprising anti-viral agents of the present invention and a pharmaceutically acceptable carrier. In a specific embodiment, the anti-viral agent of the invention is an antibody that immunospecifically binds hSARS virus or any hSARS epitope. In another specific embodiment, the anti-viral agent is a polypeptide or protein of the present invention or nucleic acid molecule of the invention. The invention also provides kits containing a pharmaceutical composition of the present invention.

### 3.1 Definitions

The term "an antibody or an antibody fragment that immunospecifically binds a polypeptide of the invention" as used herein refers to an antibody or a fragment thereof that immunospecifically binds to the polypeptide encoded by the nucleotide sequence of SEQ ID NO:1, 11, 13 or 15, or a fragment thereof, and does not non-specifically bind to other polypeptides. An antibody or a fragment thereof that immunospecifically binds to the polypeptide of the invention may cross-react with other antigens. Preferably, an antibody or a fragment thereof that immunospecifically binds to a polypeptide of the invention does not cross-react with other antigens. An antibody or a fragment thereof that immunospecifically

binds to the polypeptide of the invention, can be identified by, for example, immunoassays or other techniques known to those skilled in the art.

An "isolated" or "purified" peptide or protein is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of a polypeptide/protein in which the polypeptide/protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, a polypeptide/protein that is substantially free of cellular material includes preparations of the polypeptide/protein having less than about 30%, 20%, 10%, 5%, 2.5%, or 1%, (by dry weight) of contaminating protein. When the polypeptide/protein is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When polypeptide/protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly, such preparations of the polypeptide/protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than polypeptide/protein fragment of interest. In a preferred embodiment of the present invention, polypeptides/proteins are isolated or purified.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid molecule. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. In a preferred embodiment of the invention, nucleic acid molecules encoding polypeptides/proteins of the invention are isolated or purified. The term "isolated" nucleic acid molecule does not include a nucleic acid that is a member of a library that has not been purified away from other library clones containing other nucleic acid molecules.

The term "portion" or "fragment" as used herein refers to a fragment of a nucleic acid molecule containing at least about 25, 30, 35, 40, 45, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, 17,000, 18,000, 19,000, 20,000, 21,000, 22,000, 23,000, 24,000, 25,000, 26,000, 27,000, 28,000, 29,000, or more contiguous nucleic acids in length of the relevant nucleic acid molecule and having at least one functional feature of the nucleic acid molecule (or the encoded protein has one functional feature of the protein encoded by the nucleic acid molecule); or a fragment of a protein or a polypeptide containing at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 90, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, 320, 340, 360, 400, 500, 600, 700, 800, 900, 1,000, 1,500, 2,000, 2,500, 3,000, 3,500, 4,000, 4,100, 4,200, 4,300, 4,350, 4,360, 4,370, 4,380 amino acid residues in length of the relevant protein or polypeptide and having at least one functional feature of the protein or polypeptide.

The term "having a biological activity of the protein" or "having biological activities of the polypeptides of the invention" refers to the characteristics of the polypeptides or pro-

teins having a common biological activity similar or identical structural domain and/or having sufficient amino acid identity to the polypeptide encoded by the nucleotide sequence of SEQ ID NO:1, 11, 13, 15, 16, 240, 737, 1108, 1590 or 1965. Such common biological activities of the polypeptides of the invention include antigenicity and immunogenicity.

The term "under stringent condition" refers to hybridization and washing conditions under which nucleotide sequences having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% identity to each other remain hybridized to each other. Such hybridization conditions are described in, for example but not limited to, Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6.; Basic Methods in Molecular Biology, Elsevier Science Publishing Co. Inc., N.Y. (1986), pp. 75-78, and 84-87; and Molecular Cloning, Cold Spring Harbor Laboratory, N.Y. (1982), pp. 387-389, and are well known to those skilled in the art. A preferred, non-limiting example of stringent hybridization conditions is hybridization in 6x sodium chloride/sodium citrate (SSC), 0.5% SDS at about 68° C. followed by one or more washes in 2xSSC, 0.5% SDS at room temperature. Another preferred, non-limiting example of stringent hybridization conditions is hybridization in 6xSSC at about 45° C. followed by one or more washes in 0.2xSSC, 0.1% SDS at about 50-65° C.

The term "variant" as used herein refers either to a naturally occurring genetic mutant of hSARS or a recombinantly prepared variation of hSARS each of which contain one or more mutations in its genome compared to the hSARS of CCTCC-V200303. The term "variant" may also refer either to a naturally occurring variation of a given peptide or a recombinantly prepared variation of a given peptide or protein in which one or more amino acid residues have been modified by amino acid substitution, addition, or deletion.

#### 4. DESCRIPTION OF THE FIGURES

FIG. 1 shows a partial DNA sequence (SEQ ID NO:1) and its deduced amino acid sequence (SEQ ID NO:2) obtained from the SARS virus that has 57% homology to the RNA-dependent RNA polymerase protein of known Coronaviruses.

FIG. 2 shows an electron micrograph of the novel hSARS virus that has similar morphological characteristics of coronaviruses.

FIG. 3 shows an immunofluorescent staining for IgG antibodies that are specifically bound to the FrHK-4 cells infected with the novel human respiratory virus of Coronaviridae.

FIG. 4 shows an electron micrograph of ultra-centrifuged deposit of hSARS virus that was grown in the cell culture and negatively stained with 3% potassium phospho-tungstate at pH 7.0.

FIG. 5A shows a thin-section electron micrograph of lung biopsy of a patient with SARS; and FIG. 5B shows a thin section electron micrograph of hSARS-infected cells.

FIG. 6 shows the result of phylogenetic analysis for the partial protein sequence (215 amino acids; SEQ ID NO:2) of the hSARS virus (GenBank accession number AY268070). The phylogenetic tree is constructed by the neighbor-joining method. The horizontal-line distance represents the number of sites at which the two sequences compared are different. Bootstrap values are deducted from 500 replicates.

FIG. 7A shows an amplification plot of fluorescence intensity against the PCR cycle in a real-time quantitative PCR assay that can detect a hSARS virus in samples quantitatively. The copy numbers of input plasmid DNA in the reactions are indicated. The X-axis denotes the cycle number of a quanti-

tative PCR assay and the Y-axis denotes the fluorescence intensity (FI) over the background. FIG. 7B shows the result of a melting curve analysis of PCR products from clinical samples. Signals from positive (+ve) samples, negative (-ve) samples and water control (water) are indicated. The X-axis denotes the temperature (° C.) and the Y-axis denotes the fluorescence intensity (FI) over the background.

FIG. 8 shows another partial DNA sequence (SEQ ID NO:11) and its deduced amino acid sequence (SEQ ID NO:12) obtained from the SARS virus.

FIG. 9 shows yet another partial DNA sequence (SEQ ID NO:13) and its deduced amino acid sequence (SEQ ID NO:14) obtained from the SARS virus.

FIG. 10 shows the entire genomic DNA sequence (SEQ ID NO:15) of the SARS virus.

FIG. 11 shows the deduced amino acid sequences obtained from SEQ ID NO:15 in three frames (see SEQ ID NOS:16, 240 and 737). An asterisk (\*) indicates a stop codon which marks the end of a peptide. The first-frame amino acid sequences: SEQ ID NOS:17-239; the second-frame amino acid sequences: SEQ ID NOS:241-736; and the third-frame amino acid sequences: SEQ ID NO:738-1107.

FIG. 12 shows the deduced amino acid sequences obtained from the complement of SEQ ID NO:15 in three frames (see SEQ ID NOS:1108, 1590 and 1965). An asterisk (\*) indicates a stop codon which marks the end of a peptide. The first-frame amino acid sequences: SEQ ID NOS:1109-1589; the second-frame amino acid sequences: SEQ ID NOS:1591-1964; and the third-frame amino acid sequences: SEQ ID NO:1966-2470.

#### 5. DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to the isolated hSARS virus that morphologically and phylogenetically relates to known Coronaviruses. In a specific embodiment, the isolated hSARS virus is that of CCTCC-V200303. In another specific embodiment, the virus comprises a nucleotide sequence of SEQ ID NO:1, 11, 13, and/or 15. In a specific embodiment, the present invention provides isolated nucleic acid molecules of the hSARS virus, comprising, or, alternatively, consisting of the nucleotide sequence of SEQ ID NO:1, 11, 13, and/or 15, a complement thereof or a portion thereof. In another specific embodiment, the invention provides isolated nucleic acid molecules which hybridize under stringent conditions, as defined herein, to a nucleic acid molecule having the sequence of SEQ ID NO:1, 11, 13, or 15, or specific genes of known member of Coronaviridae, or a complement thereof. In another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising a nucleotide sequence that is at least about 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:1, or a complement thereof. In another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising a nucleotide sequence that is at least about 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:11, or a complement thereof. In yet another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising a nucleotide sequence that is at least about 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650,

700, or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:13, or a complement thereof. In yet another specific embodiment, the invention provides isolated polypeptides or proteins that are encoded by a nucleic acid molecule comprising or, alternatively consisting of a nucleotide sequence that is at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 100, 150, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1,000, 1,050, 1,100, 1,150, 1,200, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, 17,000, 18,000, 19,000, 20,000, 21,000, 22,000, 23,000, 24,000, 25,000, 26,000, 27,000, 28,000, 29,000 or more contiguous nucleotides of the nucleotide sequence of SEQ ID NO:15, or a complement thereof. The polypeptides include those shown in FIGS. 11 (SEQ ID NOS:17-239, 241-736 and 738-1107) and 12 (SEQ ID NOS:1109-1589, 1591-1964 and 1966-2470). The polypeptides or the proteins of the present invention preferably have one or more biological activities of the proteins encoded by the sequence of SEQ ID NO:1, 11, 13, 15, or the native viral proteins containing the amino acid sequences encoded by the sequence of SEQ ID NO:1, 11, 13, or 15, or those shown in FIGS. 11 (SEQ ID NOS:17-239, 241-736 and 738-1107) and 12 (SEQ ID NOS:1109-1589, 1591-1964 and 1966-2470).

The present invention also relates to a method for propagating the hSARS virus in host cells.

The invention further relates to the use of the sequence information of the isolated virus for diagnostic and therapeutic methods. In a specific embodiment, the invention provides the entire nucleotide sequence of hSARS virus, CCTCC-V200303, SEQ ID NO:15, or fragments, or complement thereof. Furthermore, the present invention relates to a nucleic acid molecule that hybridizes any portion of the genome of the hSARS virus, CCTCC-V200303, SEQ ID NO:15, under the stringent conditions. In a specific embodiment, the invention provides nucleic acid molecules which are suitable for use as primers consisting of or comprising the nucleotide sequence of SEQ ID NO:1, 11, 13, or 15, or a complement thereof, or a portion thereof. In a non-limiting embodiment, the invention provides the primers consisting of or comprising the nucleotide sequence of SEQ ID NOS:3 and/or 4. In another specific embodiment, the invention provides nucleic acid molecules which are suitable for use as hybridization probes for the detection of nucleic acids encoding a polypeptide of the invention, consisting of or comprising the nucleotide sequence of SEQ ID NO:1, 11, 13, or 15, a complement thereof, or a portion thereof. The invention further encompasses chimeric or recombinant viruses or viral proteins encoded by said nucleotide sequences.

The invention further provides antibodies that specifically bind a polypeptide of the invention encoded by the nucleotide sequence of SEQ ID NO:1, 11, 13, 16, 240, 737, 1108, 1590 or 1965, or a fragment thereof, or any hSARS epitope. The invention further provides antibodies that specifically bind the polypeptides of the invention encoded by the nucleotide sequence of SEQ ID NO:15, or a fragment thereof, or any hSARS epitope. Such antibodies include, but are not limited to polyclonal, monoclonal, bi-specific, multi-specific, human, humanized, chimeric antibodies, single chain antibodies, Fab fragments, F(ab')<sub>2</sub> fragments, disulfide-linked Fvs, intrabodies and fragments containing either a VL or VH domain or even a complementary determining region (CDR) that specifically binds to a polypeptide of the invention.

In one embodiment, the invention provides methods for detecting the presence, activity or expression of the hSARS virus of the invention in a biological material, such as cells, blood, saliva, urine, sputum, nasopharyngeal aspirates, and so

forth. The presence of the hSARS virus in a sample can be determined by contacting the biological material with an agent which can detect directly or indirectly the presence of the hSARS virus. In a specific embodiment, the detection agents are the antibodies of the present invention. In another embodiment, the detection agent is a nucleic acid of the present invention.

In another embodiment, the invention provides vaccine preparations comprising the hSARS virus, including recombinant and chimeric forms of said virus, or subunits of the virus. In a specific embodiment, the vaccine preparations comprise live but attenuated hSARS virus with or without pharmaceutically acceptable carriers, including adjuvants. In another specific embodiment, the vaccine preparations comprise an inactivated or killed hSARS virus with or without pharmaceutically acceptable carriers, including adjuvants.

The present invention further provides methods of preparing recombinant or chimeric forms of hSARS. In another specific invention, the vaccine preparations of the present invention comprise one or more nucleic acid molecules comprising or consisting of the sequence of SEQ ID NO. 1, 11, 13, and/or, 15, or a fragment thereof. In another embodiment, the invention provides vaccine preparations comprising one or more polypeptides of the invention encoded by a nucleotide sequence comprising or consisting of the nucleotide sequence of SEQ ID NO:1, 11, 13, 16, 240, 737, 1108, 1590 and/or 1965, or a fragment thereof. In another embodiment, the invention provides vaccine preparations comprising one or more polypeptides of the invention encoded by a nucleotide sequence comprising or consisting of the nucleotide sequence of SEQ ID NO:15, or a fragment thereof. Furthermore, the present invention provides methods for treating, ameliorating, managing, or preventing SARS by administering the vaccine preparations or antibodies of the present invention alone or in combination with antivirals [e.g., amantadine, rimantadine, gancyclovir, acyclovir, ribavirin, penciclovir, oseltamivir, foscarnet zidovudine (AZT), didanosine (ddI), lamivudine (3TC), zalcitabine (ddC), stavudine (d4T), nevirapine, delavirdine, indinavir, ritonavir, vidarabine, nelfinavir, saquinavir, relenza, tamiflu, pleconaril, interferons, etc.], steroids and corticosteroids such as prednisone, cortisone, fluticasone and glucocorticoid, antibiotics, analgesics, bronchodilators, or other treatments for respiratory and/or viral infections.

Furthermore, the present invention provides pharmaceutical compositions comprising anti-viral agents of the present invention and a pharmaceutically acceptable carrier. The present invention also provides kits comprising pharmaceutical compositions of the present invention.

In another aspect, the present invention provides methods for screening anti-viral agents that inhibit the infectivity or replication of hSARS virus or variants thereof.

### 5.1 Recombinant and Chimeric hSARS Viruses

The present invention encompasses recombinant or chimeric viruses encoded by viral vectors derived from the genome of hSARS virus or natural variants thereof. In a specific embodiment, a recombinant virus is one derived from the hSARS virus of deposit accession no. CCTCC-V200303. In a specific embodiment, the virus has a nucleotide sequence of SEQ ID NO:15. In another specific embodiment, a recombinant virus is one derived from a natural variant of hSARS virus. A natural variant of hSARS has a sequence that is different from the genomic sequence (SEQ ID NO:15) of the hSARS virus, CCTCC-V200303, due to one or more naturally occurred mutations, including, but not limited to, point

mutations, rearrangements, insertions, deletions etc., to the genomic sequence that may or may not result in a phenotypic change. In accordance with the present invention, a viral vector which is derived from the genome of the hSARS virus, CCTCC-V200303, is one that contains a nucleic acid sequence that encodes at least a part of one ORF of the hSARS virus. In a specific embodiment, the ORF comprises or consists of a nucleotide sequence of SEQ ID NO:1, 11 or 13, or a fragment thereof. In a specific embodiment, there are more than one ORF within the nucleotide sequence of SEQ ID NO:15 or a complement thereof, as shown in FIGS. 11 (SEQ ID NOS:16, 240 and 737) and 12 (SEQ ID NOS:1108, 1590 and 1965), or a fragment thereof. In another embodiment, the polypeptide encoded by the ORF comprises or consists of an amino acid sequence of SEQ ID NO:2, 12, or 14, or a fragment thereof, or shown in FIGS. 11 (SEQ ID NOS:17-239, 241-736 and 738-1107) and 12 (SEQ ID NOS:1109-1589, 1591-1964 and 1966-2470), or a fragment thereof. In accordance with the present invention these viral vectors may or may not include nucleic acids that are non-native to the viral genome.

In another specific embodiment, a chimeric virus of the invention is a recombinant hSARS virus which further comprises a heterologous nucleotide sequence. In accordance with the invention, a chimeric virus may be encoded by a nucleotide sequence in which heterologous nucleotide sequences have been added to the genome or in which endogenous or native nucleotide sequences have been replaced with heterologous nucleotide sequences.

According to the present invention, the chimeric viruses are encoded by the viral vectors of the invention which further comprise a heterologous nucleotide sequence. In accordance with the present invention a chimeric virus is encoded by a viral vector that may or may not include nucleic acids that are non-native to the viral genome. In accordance with the invention a chimeric virus is encoded by a viral vector to which heterologous nucleotide sequences have been added, inserted or substituted for native or non-native sequences. In accordance with the present invention, the chimeric virus may be encoded by nucleotide sequences derived from different strains or variants of hSARS virus. In particular, the chimeric virus is encoded by nucleotide sequences that encode antigenic polypeptides derived from different strains or variants of hSARS virus.

A chimeric virus may be of particular use for the generation of recombinant vaccines protecting against two or more viruses (Tao et al., *J. Virol.* 72, 2955-2961; Durbin et al 2000, *J. Virol.* 74, 6821-6831; Skiadopoulos et al. 1998, *J. Virol.* 72, 1762-1768 (1998); Teng et al., 2000, *J. Virol.* 74, 9317-9321). For example, it can be envisaged that a virus vector derived from the hSARS virus expressing one or more proteins of variants of hSARS virus, or vice versa, will protect a subject vaccinated with such vector against infections by both the native hSARS and the variant. Attenuated and replication-defective viruses may be of use for vaccination purposes with live vaccines as has been suggested for other viruses. (See, PCT WO 02/057302, at pp. 6 and 23, incorporated by reference herein).

In accordance with the present invention the heterologous sequence to be incorporated into the viral vectors encoding the recombinant or chimeric viruses of the invention include sequences obtained or derived from different strains or variants of hSARS.

In certain embodiments, the chimeric or recombinant viruses of the invention are encoded by viral vectors derived from viral genomes wherein one or more sequences, intergenic regions, termini sequences, or portions or entire ORF

have been substituted with a heterologous or non-native sequence. In certain embodiments of the invention, the chimeric viruses of the invention are encoded by viral vectors derived from viral genomes wherein one or more heterologous sequences have been inserted or added to the vector.

The selection of the viral vector may depend on the species of the subject that is to be treated or protected from a viral infection. If the subject is human, then an attenuated hSARS virus can be used to provide the antigenic sequences.

In accordance with the present invention, the viral vectors can be engineered to provide antigenic sequences which confer protection against infection by the hSARS and natural variants thereof. The viral vectors may be engineered to provide one, two, three or more antigenic sequences. In accordance with the present invention the antigenic sequences may be derived from the same virus, from different strains or variants of the same type of virus, or from different viruses.

The expression products and/or recombinant or chimeric virions obtained in accordance with the invention may advantageously be utilized in vaccine formulations. The expression products and chimeric virions of the present invention may be engineered to create vaccines against a broad range of pathogens, including viral and bacterial antigens, tumor antigens, allergen antigens, and auto antigens involved in autoimmune disorders. In particular, the chimeric virions of the present invention may be engineered to create vaccines for the protection of a subject from infections with hSARS virus and variants thereof.

In certain embodiments, the expression products and recombinant or chimeric virions of the present invention may be engineered to create vaccines against a broad range of pathogens, including viral antigens, tumor antigens and autoantigens involved in autoimmune disorders. One way to achieve this goal involves modifying existing hSARS genes to contain foreign sequences in their respective external domains. Where the heterologous sequences are epitopes or antigens of pathogens, these chimeric viruses may be used to induce a protective immune response against the disease agent from which these determinants are derived.

Thus, the present invention relates to the use of viral vectors and recombinant or chimeric viruses to formulate vaccines against a broad range of viruses and/or antigens. The present invention also encompasses recombinant viruses comprising a viral vector derived from the hSARS or variants thereof which contains sequences which result in a virus having a phenotype more suitable for use in vaccine formulations, e.g., attenuated phenotype or enhanced antigenicity. The mutations and modifications can be in coding regions, in intergenic regions and in the leader and trailer sequences of the virus.

The invention provides a host cell comprising a nucleic acid or a vector according to the invention. Plasmid or viral vectors containing the polymerase components of hSARS virus are generated in prokaryotic cells for the expression of the components in relevant cell types (bacteria, insect cells, eukaryotic cells). Plasmid or viral vectors containing full-length or partial copies of the hSARS genome will be generated in prokaryotic cells for the expression of viral nucleic acids in-vitro or in-vivo. The latter vectors may contain other viral sequences for the generation of chimeric viruses or chimeric virus proteins, may lack parts of the viral genome for the generation of replication defective virus, and may contain mutations, deletions or insertions for the generation of attenuated viruses. In addition, the present invention provides a host cell infected with hSARS virus, for example, of deposit no. CCTCC-V200303.

Infectious copies of hSARS (being wild type, attenuated, replication-defective or chimeric) can be produced upon co-expression of the polymerase components according to the state-of-the-art technologies described above.

In addition, eukaryotic cells, transiently or stably expressing one or more full-length or partial hSARS proteins can be used. Such cells can be made by transfection (proteins or nucleic acid vectors), infection (viral vectors) or transduction (viral vectors) and may be useful for complementation of mentioned wild type, attenuated, replication-defective or chimeric viruses.

The viral vectors and chimeric viruses of the present invention may be used to modulate a subject's immune system by stimulating a humoral immune response, a cellular immune response or by stimulating tolerance to an antigen. As used herein, a subject means: humans, primates, horses, cows, sheep, pigs, goats, dogs, cats, avian species and rodents.

### 5.2 Formulation of Vaccines and Antivirals

In a preferred embodiment, the invention provides a proteinaceous molecule or hSARS virus specific viral protein or functional fragment thereof encoded by a nucleic acid according to the invention. Useful proteinaceous molecules are for example derived from any of the genes or genomic fragments derivable from the virus according to the invention, including envelop protein (E protein), integral membrane protein (M protein), spike protein (S protein), nucleocapsid protein (N protein), hemagglutinin esterase (HE protein), and RNA-dependent RNA polymerase. Such molecules, or antigenic fragments thereof, as provided herein, are for example useful in diagnostic methods or kits and in pharmaceutical compositions such as subunit vaccines. Particularly useful are polypeptides encoded by the nucleotide sequence of SEQ ID NO: 1, 11, 13, or 15, or as shown in FIGS. 11 (SEQ ID NOS:17-239, 241-736 and 738-1107) and 12 (SEQ ID NOS: 1109-1589, 1591-1964 and 1966-2470), or antigenic fragments thereof for inclusion as antigen or subunit immunogen, but inactivated whole virus can also be used. Particularly useful are also those proteinaceous substances that are encoded by recombinant nucleic acid fragments of the hSARS genome, of course preferred are those that are within the preferred bounds and metes of ORFS, in particular, for eliciting hSARS specific antibody or T cell responses, whether in vivo (e.g. for protective or therapeutic purposes or for providing diagnostic antibodies) or in vitro (e.g. by phage display technology or another technique useful for generating synthetic antibodies).

The invention provides vaccine formulations for the prevention and treatment of infections with hSARS virus. In certain embodiments, the vaccine of the invention comprises recombinant and chimeric viruses of the hSARS virus. In certain embodiments, the virus is attenuated.

In another embodiment of this aspect of the invention, inactivated vaccine formulations may be prepared using conventional techniques to "kill" the chimeric viruses. Inactivated vaccines are "dead" in the sense that their infectivity has been destroyed. Ideally, the infectivity of the virus is destroyed without affecting its immunogenicity. In order to prepare inactivated vaccines, the chimeric virus may be grown in cell culture or in the allantois of the chick embryo, purified by zonal ultracentrifugation, inactivated by formaldehyde or  $\beta$ -propiolactone, and pooled. The resulting vaccine is usually inoculated intramuscularly.

Inactivated viruses may be formulated with a suitable adjuvant in order to enhance the immunological response. Such adjuvants may include but are not limited to mineral gels, e.g.,

aluminum hydroxide; surface active substances such as lysolecithin, pluronic polyols, polyanions; peptides; oil emulsions; and potentially useful human adjuvants such as BCG and *Corynebacterium parvum*.

In another aspect, the present invention also provides DNA vaccine formulations comprising a nucleic acid or fragment of the hSARS virus, e.g., the virus having accession no. CCTCC-V200303, or nucleic acid molecules having the sequence of SEQ ID NO:1, 11, 13, or 15, or a fragment thereof. In another specific embodiment, the DNA vaccine formulations of the present invention comprises a nucleic acid or fragment thereof encoding the antibodies which immunospecifically binds hSARS viruses. In DNA vaccine formulations, a vaccine DNA comprises a viral vector, such as that derived from the hSARS virus, bacterial plasmid, or other expression vector, bearing an insert comprising a nucleic acid molecule of the present invention operably linked to one or more control elements, thereby allowing expression of the vaccinating proteins encoded by said nucleic acid molecule in a vaccinated subject. Such vectors can be prepared by recombinant DNA technology as recombinant or chimeric viral vectors carrying a nucleic acid molecule of the present invention (see also Section 5.1, supra).

Various heterologous vectors are described for DNA vaccinations against viral infections. For example, the vectors described in the following references may be used to express hSARS sequences instead of the sequences of the viruses or other pathogens described; in particular, vectors described for hepatitis B virus (Michel, M. L. et al., 1995, DAN-mediated immunization to the hepatitis B surface antigen in mice: Aspects of the humoral response mimic hepatitis B viral infection in humans, *Proc. Natl. Aca. Sci. USA* 92:5307-5311; Davis, H. L. et al., 1993, DNA-based immunization induces continuous secretion of hepatitis B surface antigen and high levels of circulating antibody, *Human Molec. Genetics* 2:1847-1851), HIV virus (Wang, B. et al., 1993, Gene inoculation generates immune responses against human immunodeficiency virus type 1, *Proc. Natl. Acad. Sci. USA* 90:4156-4160; Lu, S. et al., 1996, Simian immunodeficiency virus DNA vaccine trial in macques, *J. Virol.* 70:3978-3991; Letvin, N. L. et al., 1997, Potent, protective anti-HIV immune responses generated by bimodal HIV envelope DNA plus protein vaccination, *Proc Natl Acad Sci USA.* 94(17):9378-83), and influenza viruses (Robinson, H L et al., 1993, Protection against a lethal influenza virus challenge by immunization with a haemagglutinin-expressing plasmid DNA, *Vaccine* 11:957-960; Ulmer, J. B. et al., Heterologous protection against influenza by injection of DNA encoding a viral protein, *Science* 259:1745-1749), as well as bacterial infections, such as tuberculosis (Tascon, R. E. et al., 1996, Vaccination against tuberculosis by DNA injection, *Nature Med* 2:888-892; Huygen, K. et al., 1996, Immunogenicity and protective efficacy of a tuberculosis DNA vaccine, *Nature Med.*, 2:893-898), and parasitic infection, such as malaria (Sedegah, M., 1994, Protection against malaria by immunization with plasmid DNA encoding circumsporozoite protein, *Proc. Natl. Acad. Sci. USA* 91:9866-9870; Doolan, D. L. et al., 1996, Circumventing genetic restriction of protection against malaria with multigene DNA immunization: CD8+ T cell-interferon  $\delta$ , and nitric oxide-dependent immunity, *J. Exper. Med.*, 1183:1739-1746).

Many methods may be used to introduce the vaccine formulations described above. These include, but are not limited to, oral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, and intranasal routes. Alternatively, it may be preferable to introduce the chimeric virus vaccine formulation via the natural route of infection of the pathogen



for which the vaccine is designed. The DNA vaccines of the present invention may be administered in saline solutions by injections into muscle or skin using a syringe and needle (Wolff J. A. et al., 1990, Direct gene transfer into mouse muscle in vivo, *Science* 247:1465-1468; Raz, E., 1994, Intradermal gene immunization: The possible role of DNA uptake in the induction of cellular immunity to viruses, *Proc. Natl. Acad. Sci. USA* 91:9519-9523). Another way to administer DNA vaccines is called "gene gun" method, whereby microscopic gold beads coated with the DNA molecules of interest is fired into the cells (Tang, D. et al., 1992, Genetic immunization is a simple method for eliciting an immune response, *Nature* 356:152-154). For general reviews of the methods for DNA vaccines, see Robinson, H. L., 1999, DNA vaccines: basic mechanism and immune responses (Review), *Int. J. Mol. Med.* 4(5):549-555; Barber, B., 1997, Introduction: Emerging vaccine strategies, *Seminars in Immunology* 9(5):269-270; and Robinson, H. L. et al., 1997, DNA vaccines, *Seminars in Immunology* 9(5):271-283.

### 5.3 Attenuation of hSARS Virus or Variants Thereof

The hSARS virus or variants thereof of the invention can be genetically engineered to exhibit an attenuated phenotype. In particular, the viruses of the invention exhibit an attenuated phenotype in a subject to which the virus is administered as a vaccine. Attenuation can be achieved by any method known to a skilled artisan. Without being bound by theory, the attenuated phenotype of the viruses of the invention can be caused, e.g., by using a virus that naturally does not replicate well in an intended host species, for example, by reduced replication of the viral genome, by reduced ability of the virus to infect a host cell, or by reduced ability of the viral proteins to assemble to an infectious viral particle relative to the wild type strain of the virus.

The attenuated phenotypes of hSARS virus or variants thereof can be tested by any method known to the artisan. A candidate virus can, for example, be tested for its ability to infect a host or for the rate of replication in a cell culture system. In certain embodiments, growth curves at different temperatures are used to test the attenuated phenotype of the virus. For example, an attenuated virus is able to grow at 35° C., but not at 39° C. or 40° C. In certain embodiments, different cell lines can be used to evaluate the attenuated phenotype of the virus. For example, an attenuated virus may only be able to grow in monkey cell lines but not the human cell lines, or the achievable virus titers in different cell lines are different for the attenuated virus. In certain embodiments, viral replication in the respiratory tract of a small animal model, including but not limited to, hamsters, cotton rats, mice and guinea pigs, is used to evaluate the attenuated phenotypes of the virus. In other embodiments, the immune response induced by the virus, including but not limited to, the antibody titers (e.g., assayed by plaque reduction neutralization assay or ELISA) is used to evaluate the attenuated phenotypes of the virus. In a specific embodiment, the plaque reduction neutralization assay or ELISA is carried out at a low dose. In certain embodiments, the ability of the hSARS virus to elicit pathological symptoms in an animal model can be tested. A reduced ability of the virus to elicit pathological symptoms in an animal model system is indicative of its attenuated phenotype. In a specific embodiment, the candidate viruses are tested in a monkey model for nasal infection, indicated by mucous production.

The viruses of the invention can be attenuated such that one or more of the functional characteristics of the virus are impaired. In certain embodiments, attenuation is measured in

comparison to the wild type strain of the virus from which the attenuated virus is derived. In other embodiments, attenuation is determined by comparing the growth of an attenuated virus in different host systems. Thus, for a non-limiting example, hSARS virus or a variant thereof is said to be attenuated when grown in a human host if the growth of the hSARS or variant thereof in the human host is reduced compared to the non-attenuated hSARS or variant thereof.

In certain embodiments, the attenuated virus of the invention is capable of infecting a host, is capable of replicating in a host such that infectious viral particles are produced. In comparison to the wild type strain, however, the attenuated strain grows to lower titers or grows more slowly. Any technique known to the skilled artisan can be used to determine the growth curve of the attenuated virus and compare it to the growth curve of the wild type virus.

In certain embodiments, the attenuated virus of the invention (e.g., a recombinant or chimeric hSARS) cannot replicate in human cells as well as the wild type virus (e.g., wild type hSARS) does. However, the attenuated virus can replicate well in a cell line that lack interferon functions, such as Vero cells.

In other embodiments, the attenuated virus of the invention is capable of infecting a host, of replicating in the host, and of causing proteins of the virus of the invention to be inserted into the cytoplasmic membrane, but the attenuated virus does not cause the host to produce new infectious viral particles. In certain embodiments, the attenuated virus infects the host, replicates in the host, and causes viral proteins to be inserted in the cytoplasmic membrane of the host with the same efficiency as the wild type hSARS. In other embodiments, the ability of the attenuated virus to cause viral proteins to be inserted into the cytoplasmic membrane into the host cell is reduced compared to the wild type virus. In certain embodiments, the ability of the attenuated hSARS virus to replicate in the host is reduced compared to the wild type virus. Any technique known to the skilled artisan can be used to determine whether a virus is capable of infecting a mammalian cell, of replicating within the host, and of causing viral proteins to be inserted into the cytoplasmic membrane of the host.

In certain embodiments, the attenuated virus of the invention is capable of infecting a host. In contrast to the wild type hSARS, however, the attenuated hSARS cannot be replicated in the host. In a specific embodiment, the attenuated hSARS virus can infect a host and can cause the host to insert viral proteins in its cytoplasmic membranes, but the attenuated virus is incapable of being replicated in the host. Any method known to the skilled artisan can be used to test whether the attenuated hSARS has infected the host and has caused the host to insert viral proteins in its cytoplasmic membranes.

In certain embodiments, the ability of the attenuated virus to infect a host is reduced compared to the ability of the wild type virus to infect the same host. Any technique known to the skilled artisan can be used to determine whether a virus is capable of infecting a host.

In certain embodiments, mutations (e.g., missense mutations) are introduced into the genome of the virus, for example, into the sequence of SEQ ID NO:1, 11, 13, or 15, or to generate a virus with an attenuated phenotype. Mutations (e.g., missense mutations) can be introduced into the structural genes and/or regulatory genes of the hSARS. Mutations can be additions, substitutions, deletions, or combinations thereof. Such variant of hSARS can be screened for a predicted functionality, such as infectivity, replication ability, protein synthesis ability, assembling ability, as well as cytopathic effect in cell cultures. In a specific embodiment, the



missense mutation is a cold-sensitive mutation. In another embodiment, the missense mutation is a heat-sensitive mutation. In another embodiment, the missense mutation prevents a normal processing or cleavage of the viral proteins.

In other embodiments, deletions are introduced into the genome of the hSARS virus, which result in the attenuation of the virus.

In certain embodiments, attenuation of the virus is achieved by replacing a gene of the wild type virus with a gene of a virus of a different species, of a different subgroup, or of a different variant. In another aspect, attenuation of the virus is achieved by replacing one or more specific domains of a protein of the wild type virus with domains derived from the corresponding protein of a virus of a different species. In certain other embodiments, attenuation of the virus is achieved by deleting one or more specific domains of a protein of the wild type virus.

When a live attenuated vaccine is used, its safety must also be considered. The vaccine must not cause disease. Any techniques known in the art that can make a vaccine safe may be used in the present invention. In addition to attenuation techniques, other techniques may be used. One non-limiting example is to use a soluble heterologous gene that cannot be incorporated into the virion membrane. For example, a single copy of the soluble version of a viral transmembrane protein lacking the transmembrane and cytosolic domains thereof, can be used.

Various assays can be used to test the safety of a vaccine. For example, sucrose gradients and neutralization assays can be used to test the safety. A sucrose gradient assay can be used to determine whether a heterologous protein is inserted in a virion. If the heterologous protein is inserted in the virion, the virion should be tested for its ability to cause symptoms in an appropriate animal model since the virus may have acquired new, possibly pathological, properties.

#### 5.4 Adjuvants and Carrier Molecules

hSARS-associated antigens are administered with one or more adjuvants. In one embodiment, the hSARS-associated antigen is administered together with a mineral salt adjuvants or mineral salt gel adjuvant. Such mineral salt and mineral salt gel adjuvants include, but are not limited to, aluminum hydroxide (ALHYDROGEL, REHYDRAGEL), aluminum phosphate gel, aluminum hydroxyphosphate (ADJU-PHOS), and calcium phosphate.

In another embodiment, hSARS-associated antigen is administered with an immunostimulatory adjuvant. Such class of adjuvants, include, but are not limited to, cytokines (e.g., interleukin-2, interleukin-7, interleukin-12, granulocyte-macrophage colony stimulating factor (GM-CSF), interferon- $\gamma$  interleukin-1 $\beta$  (IL-1 $\beta$ ), and IL-1 $\beta$  peptide or Selavo Peptide), cytokine-containing liposomes, triterpenoid glycosides or saponins (e.g., QuilA and QS-21, also sold under the trademark STIMULON, ISCOPREP), Muramyl Dipeptide (MDP) derivatives, such as N-acetyl-muramyl-L-threonyl-D-isoglutamine (Threonyl-MDP, sold under the trademark TERMURTIDE), GMDP, N-acetyl-nor-muramyl-L-alanyl-D-isoglutamine, N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3-hydroxy phosphoryloxy)-ethylamine, muramyl tripeptide phosphatidylethanolamine (MTP-PE), unmethylated CpG dinucleotides and oligonucleotides, such as bacterial DNA and fragments thereof, LPS, monophosphoryl Lipid A (3D-MLA sold under the trademark MPL), and polyphosphazenes.

In another embodiment, the adjuvant used is a particular adjuvant, including, but not limited to, emulsions, e.g., Fre-

und's Complete Adjuvant, Freund's Incomplete Adjuvant, squalene or squalane oil-in-water adjuvant formulations, such as SAF and MF59, e.g., prepared with block-copolymers, such as L-121 (polyoxypropylene/polyoxyethylene) sold under the trademark PLURONIC L-121, Liposomes, Virosomes, cochleates, and immune stimulating complex, which is sold under the trademark ISCOM.

In another embodiment, a microparticulate adjuvant is used. Microparticulate adjuvants include, but are not limited to biodegradable and biocompatible polyesters, homo- and copolymers of lactic acid (PLA) and glycolic acid (PGA), poly(lactide-co-glycolides) (PLGA) microparticles, polymers that self-associate into particulates (poloxamer particles), soluble polymers (polyphosphazenes), and virus-like particles (VLPs) such as recombinant protein particulates, e.g., hepatitis B surface antigen (HbsAg).

Yet another class of adjuvants that may be used include mucosal adjuvants, including but not limited to heat-labile enterotoxin from *Escherichia coli* (LT), cholera holotoxin (CT) and cholera Toxin B Subunit (CTB) from *Vibrio cholerae*, mutant toxins (e.g., LTK63 and LTR72), microparticles, and polymerized liposomes.

In other embodiments, any of the above classes of adjuvants may be used in combination with each other or with other adjuvants. For example, non-limiting examples of combination adjuvant preparations that can be used to administer the hSARS-associated antigens of the invention include liposomes containing immunostimulatory protein, cytokines, or T-cell and/or B-cell peptides, or microbes with or without entrapped IL-2 or microparticles containing enterotoxin. Other adjuvants known in the art are also included within the scope of the invention (see *Vaccine Design: The Subunit and Adjuvant Approach*, Chap. 7. Michael F. Powell and Mark J. Newman (eds.), Plenum Press, New York, 1995, which is incorporated herein in its entirety).

The effectiveness of an adjuvant may be determined by measuring the induction of antibodies directed against an immunogenic polypeptide containing a hSARS polypeptide epitope, the antibodies resulting from administration of this polypeptide in vaccines which are also comprised of the various adjuvants.

The polypeptides may be formulated into the vaccine as neutral or salt forms. Pharmaceutically acceptable salts include the acid additional salts (formed with free amino groups of the peptide) and which are formed with inorganic acids, such as, for example, hydrochloric or phosphoric acids, or organic acids such as acetic, oxalic, tartaric, maleic, and the like. Salts formed with free carboxyl groups may also be derived from inorganic bases, such as, for example, sodium potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine and the like.

The vaccines of the invention may be multivalent or univalent. Multivalent vaccines are made from recombinant viruses that direct the expression of more than one antigen.

Many methods may be used to introduce the vaccine formulations of the invention; these include but are not limited to oral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal routes, and via scarification (scratching through the top layers of skin, e.g., using a bifurcated needle).

The patient to which the vaccine is administered is preferably a mammal, most preferably a human, but can also be a non-human animal including but not limited to cows, horses, sheep, pigs, fowl (e.g., chickens), goats, cats, dogs, hamsters, mice and rats.

## 5.5 Preparation of Antibodies

Antibodies which specifically recognize a polypeptide of the invention, such as, but not limited to, polypeptides comprising the sequence of SEQ ID NO:2, 12, and 14, and polypeptides as shown in FIGS. 11 (SEQ ID NOS:17-239, 241-736 and 738-1107) and 12 (SEQ ID NOS:1109-1589, 1591-1964 and 1966-2470), or hSARS epitope or antigen-binding fragments thereof can be used for detecting, screening, and isolating the polypeptide of the invention or fragments thereof, or similar sequences that might encode similar enzymes from the other organisms. For example, in one specific embodiment, an antibody which immunospecifically binds hSARS epitope, or a fragment thereof, can be used for various in vitro detection assays, including enzyme-linked immunosorbent assays (ELISA), radioimmunoassays, Western blot, etc., for the detection of a polypeptide of the invention or, preferably, hSARS, in samples, for example, a biological material, including cells, cell culture media (e.g., bacterial cell culture media, mammalian cell culture media, insect cell culture media, yeast cell culture media, etc.), blood, plasma, serum, tissues, sputum, nasopharyngeal aspirates, etc.

Antibodies specific for a polypeptide of the invention or any epitope of hSARS may be generated by any suitable method known in the art. Polyclonal antibodies to an antigen-of-interest, for example, the hSARS virus from deposit no. CCTCC-V200303, or comprises a nucleotide sequence of SEQ ID NO:15, can be produced by various procedures well known in the art. For example, an antigen can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc., to induce the production of antisera containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete) adjuvant, mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful adjuvants for humans such as BCG (*Bacille Calmette-Guerin*) and *Corynebacterium parvum*. Such adjuvants are also well known in the art.

Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: *Monoclonal Antibodies and T-Cell Hybridomas*, pp. 563-681 (Elsevier, N.Y., 1981) (both of which are incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art. In a non-limiting example, mice can be immunized with an antigen of interest or a cell expressing such an antigen. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells. Hybridomas are selected and cloned

by limiting dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding the antigen. Ascites fluid, which generally contains high levels of antibodies, can be generated by inoculating mice intraperitoneally with positive hybridoma clones.

Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, Fab and F(ab')<sub>2</sub> fragments may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')<sub>2</sub> fragments). F(ab')<sub>2</sub> fragments contain the complete light chain, and the variable region, the CH1 region and the hinge region of the heavy chain.

The antibodies of the invention or fragments thereof can be also produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques.

The nucleotide sequence encoding an antibody may be obtained from any information available to those skilled in the art (i.e., from Genbank, the literature, or by routine cloning and sequence analysis). If a clone containing a nucleic acid encoding a particular antibody or an epitope-binding fragment thereof is not available, but the sequence of the antibody molecule or epitope-binding fragment thereof is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

Once the nucleotide sequence of the antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., *supra*; and Ausubel et al., eds., 1998, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence by, for example, introducing amino acid substitutions, deletions, and/or insertions into the epitope-binding domain regions of the antibodies or any portion of antibodies which may enhance or reduce biological activities of the antibodies.

Recombinant expression of an antibody requires construction of an expression vector containing a nucleotide sequence that encodes the antibody. Once a nucleotide sequence encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art as discussed in the previous sections. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. The nucleotide sequence encoding the heavy-chain variable region, light-chain variable region, both the heavy-chain and light-chain variable regions,

an epitope-binding fragment of the heavy- and/or light-chain variable region, or one or more complementarity determining regions (CDRs) of an antibody may be cloned into such a vector for expression. Thus-prepared expression vector can be then introduced into appropriate host cells for the expres-

sion of the antibody. Accordingly, the invention includes host cells containing a polynucleotide encoding an antibody specific for the polypeptides of the invention or fragments thereof.

The host cell may be co-transfected with two expression vectors of the invention, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides or different selectable markers to ensure maintenance of both plasmids. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, *Nature*, 322:52, 1986; and Kohler, *Proc. Natl. Acad. Sci. USA*, 77:2197, 1980). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

In another embodiment, antibodies can also be generated using various phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains, such as Fab and Fv or disulfide-bond stabilized Fv, expressed from a repertoire or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage, including fd and M13. The antigen binding domains are expressed as a recombinantly fused protein to either the phage gene III or gene VIII protein. Examples of phage display methods that can be used to make the immunoglobulins, or fragments thereof, of the present invention include those disclosed in Brinkman et al., *J. Immunol. Methods*, 182:41-50, 1995; Ames et al., *J. Immunol. Methods*, 184:177-186, 1995; Kettleborough et al., *Eur. J. Immunol.*, 24:952-958, 1994; Persic et al., *Gene*, 187:9-18, 1997; Burton et al., *Advances in Immunology*, 57:191-280, 1994; PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Pat. Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired fragments, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab')<sub>2</sub> fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., *BioTechniques*, 12(6):864-869, 1992; and Sawai et al., *AJRI*, 34:26-34, 1995; and Better et al., *Science*, 240:1041-1043, 1988 (each of which is incorporated by reference in its entirety). Examples of techniques

which can be used to produce single-chain Fvs and antibodies include those described in U.S. Pat. Nos. 4,946,778 and 5,258,498; Huston et al., *Methods in Enzymology*, 203:46-88, 1991; Shu et al., *PNAS*, 90:7995-7999, 1993; and Skerra et al., *Science*, 240:1038-1040, 1988.

Once an antibody molecule of the invention has been produced by any methods described above, it may then be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A or Protein G purification, and sizing column chromatography), centrifugation, differential solubility, or by any other standard techniques for the purification of proteins. Further, the antibodies of the present invention or fragments thereof may be fused to heterologous polypeptide sequences described herein or otherwise known in the art to facilitate purification.

For some uses, including in vivo use of antibodies in humans and in vitro detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a constant region derived from a human immunoglobulin. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, *Science*, 229:1202, 1985; Oi et al., *BioTechniques*, 4:214 1986; Gillies et al., *J. Immunol. Methods*, 125:191-202, 1989; U.S. Pat. Nos. 5,807,715; 4,816,567; and 4,816,397, which are incorporated herein by reference in their entireties. Humanized antibodies are antibody molecules from non-human species that bind the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. See, e.g., Queen et al., U.S. Pat. No. 5,585,089; Riechmann et al., *Nature*, 332:323, 1988, which are incorporated herein by reference in their entireties. Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Pat. Nos. 5,225,539; 5,530,101 and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, *Molecular Immunology*, 28(4/5):489-498, 1991; Studnicka et al., *Protein Engineering*, 7(6):805-814, 1994; Roguska et al., *Proc Natl. Acad. Sci. USA*, 91:969-973, 1994), and chain shuffling (U.S. Pat. No. 5,565,332), all of which are hereby incorporated by reference in their entireties.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See U.S. Pat. Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645; WO 98/50433; WO 98/24893; WO 98/16654; WO 96/34096; WO 96/33735; and WO 91/10741, each of which is incorporated herein by reference in its entirety.

Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endog-

enous immunoglobulins, but which can express human immunoglobulin genes. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, *Int. Rev. Immunol.*, 13:65-93, 1995. For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent No. 0 598 877; U.S. Pat. Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; and 5,939,598, which are incorporated by reference herein in their entireties. In addition, companies such as Abgenix, Inc. (Fremont, Calif.), Medarex (NJ) and Genpharm (San Jose, Calif.) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespersen et al., *Bio/technology*, 12:899-903, 1988).

Antibodies fused or conjugated to heterologous polypeptides may be used in *in vitro* immunoassays and in purification methods (e.g., affinity chromatography) well known in the art. See e.g., PCT publication Number WO 93/21232; EP 439,095; Naramura et al., *Immunol. Lett.*, 39:91-99, 1994; U.S. Pat. No. 5,474,981; Gillies et al., *PNAS*, 89:1428-1432, 1992; and Fell et al., *J. Immunol.*, 146:2446-2452, 1991, which are incorporated herein by reference in their entireties.

Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the polypeptides of the invention or fragments, derivatives, analogs, or variants thereof, or similar molecules having the similar enzymatic activities as the polypeptide of the invention. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

### 5.6 Pharmaceutical Compositions and Kits

The present invention encompasses pharmaceutical compositions comprising anti-viral agents of the present invention. In a specific embodiment, the anti-viral agent is an antibody which immunospecifically binds and neutralize the hSARS virus or variants thereof, or any proteins derived therefrom (see Section 5.5). In another specific embodiment, the anti-viral agent is a polypeptide or nucleic acid molecule of the invention (see, for example, Sections 5.1 and 5.2). The pharmaceutical compositions have utility as an anti-viral prophylactic agent and may be administered to a subject where the subject has been exposed or is expected to be exposed to a virus.

Various delivery systems are known and can be used to administer the pharmaceutical composition of the invention, e.g., encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the mutant viruses, receptor mediated endocytosis (see, e.g., Wu and Wu, 1987, *J. Biol. Chem.* 262:4429-4432). Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active

agents. Administration can be systemic or local. In a preferred embodiment, it may be desirable to introduce the pharmaceutical compositions of the invention into the lungs by any suitable route. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

In a specific embodiment, it may be desirable to administer the pharmaceutical compositions of the invention locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, by means of nasal spray, or by means of an implant, said implant being of a porous, non porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. In one embodiment, administration can be by direct injection at the site (or former site) infected tissues.

In another embodiment, the pharmaceutical composition can be delivered in a vesicle, in particular a liposome (see Langer, 1990, *Science* 249:1527-1533; Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989); Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*).

In yet another embodiment, the pharmaceutical composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, *supra*; Sefton, 1987, *CRC Crit. Ref. Biomed. Eng.* 14:201; Buchwald et al., 1980, *Surgery* 88:507; and Saudek et al., 1989, *N. Engl. J. Med.* 321:574). In another embodiment, polymeric materials can be used (see *Medical Applications of Controlled Release*, Langer and Wise (eds.), CRC Pres., Boca Raton, Fla. (1974); *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, *J. Macromol. Sci. Rev. Macromol. Chem.* 23:61 (1983); see also Levy et al., 1985, *Science* 228:190; During et al., 1989, *Ann. Neurol.* 25:351; Howard et al., 1989, *J. Neurosurg.* 71:105). In yet another embodiment, a controlled release system can be placed in proximity of the composition's target, i.e., the lung, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in *Medical Applications of Controlled Release*, *supra*, vol. 2, pp. 115-138 (1984)).

Other controlled release systems are discussed in the review by Langer (*Science* 249:1527-1533 (1990)).

The pharmaceutical compositions of the present invention comprise a therapeutically effective amount of a live attenuated, inactivated or killed hSARS virus, or recombinant or chimeric hSARS virus, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the pharmaceutical composition is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc,

sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form in of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E. W. Martin. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The pharmaceutical compositions of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with free amino groups such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with free carboxyl groups such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2 ethylamino ethanol, histidine, procaine, etc.

The amount of the pharmaceutical composition of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, suitable dosage ranges for intravenous administration are generally about 20 500 micrograms of active compound per kilogram body weight. Suitable dosage ranges for intranasal administration are generally about 0.01 pg/kg body weight to 1 mg/kg body weight. Effective doses may be extrapolated from dose response curves derived from in vitro or animal model test systems.

Suppositories generally contain active ingredient in the range of 0.5% to 10% by weight; oral formulations preferably contain 10% to 95% active ingredient.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or

biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In a preferred embodiment, the kit contains an anti-viral agent of the invention, e.g., an antibody specific for the polypeptides encoded by a nucleotide sequence of SEQ ID NO:1, 11, 13, or 15, or as shown in FIGS. 11 (SEQ ID NOS:17-239, 241-736 and 738-1107) and 12 (SEQ ID NOS:1109-1589, 1591-1964 and 1966-2470), or any hSARS epitope, or a polypeptide or protein of the present invention, or a nucleic acid molecule of the invention, alone or in combination with adjuvants, antivirals, antibiotics, analgesic, bronchodilators, or other pharmaceutically acceptable excipients.

The present invention further encompasses kits comprising a container containing a pharmaceutical composition of the present invention and instructions to for use.

### 5.7 Detection Assays

The present invention provides a method for detecting an antibody, which immunospecifically binds to the hSARS virus, in a biological sample, for example blood, serum, plasma, saliva, urine, etc., from a patient suffering from SARS. In a specific embodiment, the method comprising contacting the sample with the hSARS virus, for example, of deposit no. CCTCC-V200303, or having a genomic nucleic acid sequence of SEQ ID NO:15, directly immobilized on a substrate and detecting the virus-bound antibody directly or indirectly by a labeled heterologous anti-isotype antibody. In another specific embodiment, the sample is contacted with a host cell which is infected by the hSARS virus, for example, of deposit no. CCTCC-V200303, or having a genomic nucleic acid sequence of SEQ ID NO:15, and the bound antibody can be detected by immunofluorescent assay as described in Section 6.5, *infra*.

An exemplary method for detecting the presence or absence of a polypeptide or nucleic acid of the invention in a biological sample involves obtaining a biological sample from various sources and contacting the sample with a compound or an agent capable of detecting an epitope or nucleic acid (e.g., mRNA, genomic DNA) of the hSARS virus such that the presence of the hSARS virus is detected in the sample. A preferred agent for detecting hSARS mRNA or genomic RNA of the invention is a labeled nucleic acid probe capable of hybridizing to mRNA or genomic RNA encoding a polypeptide of the invention. The nucleic acid probe can be, for example, a nucleic acid molecule comprising or consisting of the nucleotide sequence of SEQ ID NO:1, 11, 13, or 15, or a portion thereof, such as an oligonucleotide of at least 15, 20, 25, 30, 50, 100, 250, 500, 750, 1,000 or more contiguous nucleotides in length and sufficient to specifically hybridize under stringent conditions to a hSARS mRNA or genomic RNA.

In another preferred specific embodiment, the presence of hSARS virus is detected in the sample by an reverse transcription polymerase chain reaction (RT-PCR) using the primers that are constructed based on a partial nucleotide sequence of the genome of hSARS virus, for example, that of deposit accession no. CCTCC-V200303, or having a genomic nucleic acid sequence of SEQ ID NO:15, or based on a nucleotide sequence of SEQ ID NO:1, 11, 13, or 15. In a non-limiting specific embodiment, preferred primers to be used in a RT-PCR method are: 5'-TACACACCTCAGC-GTTG-3' (SEQ ID NO:3) and 5'-CACGAACGTGACG-AAT-3' (SEQ ID NO:4), in the presence of 2.5 mM MgCl<sub>2</sub> and the thermal cycles are, for example, but not limited to, 94° C. for 8 min followed by 40 cycles of 94° C. for 1 min, 50° C. for 1 min, 72° C. for 1 min (also see Section 6.7, *infra*). In more

preferred specific embodiment, the present invention provides a real-time quantitative PCR assay to detect the presence of hSARS virus in a biological sample by subjecting the cDNA obtained by reverse transcription of the extracted total RNA from the sample to PCR reactions using the specific primers, such as those having nucleotide sequences of SEQ ID NOS:3 and 4, and a fluorescence dye, such as SYBR® Green I, which fluoresces when bound non-specifically to double-stranded DNA. The fluorescence signals from these reactions are captured at the end of extension steps as PCR product is generated over a range of the thermal cycles, thereby allowing the quantitative determination of the viral load in the sample based on an amplification plot (see Section 6.7, *infra*).

A preferred agent for detecting hSARS is an antibody that specifically binds a polypeptide of the invention or any hSARS epitope, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')<sub>2</sub>) can be used.

The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin. The detection method of the invention can be used to detect mRNA, protein (or any epitope), or genomic RNA in a sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of mRNA include northern hybridizations, *in situ* hybridizations, RT-PCR, and RNase protection. *In vitro* techniques for detection of an epitope of hSARS include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. *In vitro* techniques for detection of genomic RNA include northern hybridizations, RT-PCT, and RNase protection. Furthermore, *in vivo* techniques for detection of hSARS include introducing into a subject organism a labeled antibody directed against the polypeptide. For example, the antibody can be labeled with a radioactive marker whose presence and location in the subject organism can be detected by standard imaging techniques, including autoradiography.

In a specific embodiment, the methods further involve obtaining a control sample from a control subject, contacting the control sample with a compound or agent capable of detecting hSARS, e.g., a polypeptide of the invention or mRNA or genomic RNA encoding a polypeptide of the invention, such that the presence of hSARS or the polypeptide or mRNA or genomic RNA encoding the polypeptide is detected in the sample, and comparing the absence of hSARS or the polypeptide or mRNA or genomic RNA encoding the polypeptide in the control sample with the presence of hSARS, or the polypeptide or mRNA or genomic DNA encoding the polypeptide in the test sample.

The invention also encompasses kits for detecting the presence of hSARS or a polypeptide or nucleic acid of the invention in a test sample. The kit, for example, can comprise a labeled compound or agent capable of detecting hSARS or the polypeptide or a nucleic acid molecule encoding the polypeptide in a test sample and, in certain embodiments, a means for determining the amount of the polypeptide or mRNA in the sample (e.g., an antibody which binds the

polypeptide or an oligonucleotide probe which binds to DNA or mRNA encoding the polypeptide). Kits can also include instructions for use.

For antibody-based kits, the kit can comprise, for example: (1) a first antibody (e.g., attached to a solid support) which binds to a polypeptide of the invention or hSARS epitope; and, optionally, (2) a second, different antibody which binds to either the polypeptide or the first antibody and is conjugated to a detectable agent.

For oligonucleotide-based kits, the kit can comprise, for example: (1) an oligonucleotide, e.g., a detectably labeled oligonucleotide, which hybridizes to a nucleic acid sequence encoding a polypeptide of the invention or to a sequence within the hSARS genome or (2) a pair of primers useful for amplifying a nucleic acid molecule containing an hSARS sequence. The kit can also comprise, e.g., a buffering agent, a preservative, or a protein stabilizing agent. The kit can also comprise components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit can also contain a control sample or a series of control samples which can be assayed and compared to the test sample contained. Each component of the kit is usually enclosed within an individual container and all of the various containers are within a single package along with instructions for use.

#### 5.8 Screening Assays to Identify Anti-Viral Agents

The invention provides methods for the identification of a compound that inhibits the ability of hSARS virus to infect a host or a host cell. In certain embodiments, the invention provides methods for the identification of a compound that reduces the ability of hSARS virus to replicate in a host or a host cell. Any technique well-known to the skilled artisan can be used to screen for a compound that would abolish or reduce the ability of hSARS virus to infect a host and/or to replicate in a host or a host cell.

In certain embodiments, the invention provides methods for the identification of a compound that inhibits the ability of hSARS virus to replicate in a mammal or a mammalian cell. More specifically, the invention provides methods for the identification of a compound that inhibits the ability of hSARS virus to infect a mammal or a mammalian cell. In certain embodiments, the invention provides methods for the identification of a compound that inhibits the ability of hSARS virus to replicate in a mammalian cell. In a specific embodiment, the mammalian cell is a human cell.

In another embodiment, a cell is contacted with a test compound and infected with the hSARS virus. In certain embodiments, a control culture is infected with the hSARS virus in the absence of a test compound. The cell can be contacted with a test compound before, concurrently with, or subsequent to the infection with the hSARS virus. In a specific embodiment, the cell is a mammalian cell. In an even more specific embodiment, the cell is a human cell. In certain embodiments, the cell is incubated with the test compound for at least 1 minute, at least 5 minutes at least 15 minutes, at least 30 minutes, at least 1 hour, at least 2 hours, at least 5 hours, at least 12 hours, or at least 1 day. The titer of the virus can be measured at any time during the assay. In certain embodiments, a time course of viral growth in the culture is determined. If the viral growth is inhibited or reduced in the presence of the test compound, the test compound is identified as being effective in inhibiting or reducing the growth or infection of the hSARS virus. In a specific embodiment, the compound that inhibits or reduces the growth of the hSARS virus is tested for its ability to inhibit or reduce the growth rate of other viruses to test its specificity for the hSARS virus.

In one embodiment, a test compound is administered to a model animal and the model animal is infected with the hSARS virus. In certain embodiments, a control model animal is infected with the hSARS virus without the administration of a test compound. The test compound can be administered before, concurrently with, or subsequent to the infection with the hSARS virus. In a specific embodiment, the model animal is a mammal. In an even more specific embodiment, the model animal can be, but is not limited to, a cotton rat, a mouse, or a monkey. The titer of the virus in the model animal can be measured at any time during the assay. In certain embodiments, a time course of viral growth in the culture is determined. If the viral growth is inhibited or reduced in the presence of the test compound, the test compound is identified as being effective in inhibiting or reducing the growth or infection of the hSARS virus. In a specific embodiment, the compound that inhibits or reduces the growth of the hSARS in the model animal is tested for its ability to inhibit or reduce the growth rate of other viruses to test its specificity for the hSARS virus.

## 6. EXAMPLES

The following examples illustrate the isolation and identification of the novel hSARS virus. These examples should not be construed as limiting.

### Methods and Results

As a general reference, Wiedbrauk DL & Johnston SL G. (Manual of Clinical Virology, Raven Press, New York, 1993) was used.

#### 6.1 Clinical Subjects

The study included all 50 patients who fitted a modified World Health Organization (WHO) definition of SARS and were admitted to 2 acute regional hospitals in Hong Kong Special Administrative Region (HKSAR) between Feb. 26 to Mar. 26, 2003 (WHO. Severe acute respiratory syndrome (SARS) *Weekly Epidemiol Rec.* 2003; 78: 81-83). A lung biopsy from an additional patient, who had typical SARS and was admitted to a third hospital, was also included in the study. Briefly, the case definition for SARS was: (i) fever of 38° C. or more; (ii) cough or shortness of breath; (iii) new pulmonary infiltrates on chest radiograph; and (iv) either a history of exposure to a patient with SARS or absence of response to empirical antimicrobial coverage for typical and atypical pneumonia (beta-lactams and macrolides, fluoroquinolones or tetracyclines).

Nasopharyngeal aspirates and serum samples were collected from all patients. Paired acute and convalescent sera and feces were available from some patients. Lung biopsy tissue from one patient was processed for a viral culture, RT-PCR, routine histopathological examination, and electron microscopy. Nasopharyngeal aspirates, feces and sera submitted for microbiological investigation of other diseases were included in the study under blinding and served as controls.

The medical records were reviewed retrospectively by the attending physicians and clinical microbiologists. Routine hematological, biochemical and microbiological examinations, including bacterial culture of blood and sputum, serological study and collection of nasopharyngeal aspirates for virological tests, were carried out.

### 6.2 Cell Line

FRhK-4 (fetal rhesus monkey kidney) cells were maintained in minimal essential medium (MEM) with 1% fetal calf serum, 1% streptomycin and penicillin, 0.2% nystatin and 0.05% garamycin.

### 6.3 Viral Infection

Two-hundred µl of clinical (nasopharyngeal aspirates) samples, from two patients (see the Result section, infra), in virus transport medium were used to infect FRhK-4 cells. The inoculated cells were incubated at 37° C. for 1 hour. One ml of MEM containing 1 µg trypsin was then added to the culture and the infected cells were incubated in a 37° C. incubator supplied with 5% carbon dioxide. Cytopathic effects were observed in the infected cells after 2 to 4 days of incubation. The infected cells were passaged into new FRhK-4 cells and cytopathic effects were observed within 1 day after the inoculation. The infected cells were tested by an immunofluorescent assay for influenza A., influenza B, respiratory syncytial virus, parainfluenza types 1, 2 and 3, adenovirus and human metapneumovirus (hMPV) and negative results were obtained for all cases. The infected cells were also tested by RT-PCR for influenza A and human metapneumovirus with negative results.

### 6.4 Virus Morphology

The infected cells prepared as described above were harvested, pelleted by centrifugation and the cell pellets were processed for thin-section transmitted electron microscopic visualization. Viral particles were identified in the cells infected with both clinical specimens, but not in control cells which were not infected with the virus. Virions isolated from the infected cells were about 70-100 nanometers (FIG. 2). Viral capsids were found predominantly within the vesicles of the golgi and endoplasmic reticulum and were not free in the cytoplasm. Virus particles were also found at the cell membrane.

One virus isolate was ultracentrifuged and the cell pellet was negatively stained using phosphotungstic acid. Virus particles characteristic of Coronaviridae were thus visualized. Since the human Coronaviruses hitherto recognized are not known to cause a similar disease, the present inventors postulated that the virus isolates represent a novel virus that infects humans.

### 6.5 Antibody Response to the Isolated Virus

To further confirm that this novel virus is responsible for causing SARS in the infected patients, blood serum samples from the patients who were suffering from SARS were obtained and a neutralization test was performed. Typically diluted serum (×50, ×200, ×800 and ×1600) was incubated with acetone-fixed FRhK-4 cells infected with hSARS at 37° C. for 45 minutes. The incubated cells were then washed with phosphate-buffered saline and stained with anti-human IgG-FITC conjugated antibody. The cells were then washed and examined under a fluorescent microscope. In these experiments, positive signals were found in 8 patients who had SARS (FIG. 3), indicating that these patients had an IgG antibody response to this novel human respiratory virus of Coronaviridae. By contrast, no signal was detected in 4 negative-control paired sera. The serum titers of anti-hSARS antibodies of the tested patients are shown in Table 1.



TABLE 1

Name	Date	Lab No.	Anti-SARS
Patient A	25 Feb. 2003	S2728	<50
	6 Mar. 2003	S2728	1600
Patient B	26 Feb. 2003	S2441	50
	3 Mar. 2003	S2441	200
Patient C	4 Mar. 2003	S3279	200
	14 Mar. 2003	S3279	1600
Patient D	6 Mar. 2003	M41045	<50
	11 Mar. 2003	MB943703	800
Patient E	4 Mar. 2003	M38953	<50
	18 Mar. 2003	KWH03/3601	800
Control F	13 Feb. 2003	M27124	<50
	1 Mar. 2003	MB942968	<50
Patient G	3 Mar. 2003	M38685	<50
	7 Mar. 2003	KWH03/2900	Equivocal
Blinded samples:			
1a *	Acute		<50
1b	Convalescent		1600
2a *	Acute		50
2b	Convalescent		>1600
3a *	Acute		50
3b	Convalescent		>1600
4a *	Acute		<50
4b	Convalescent		<50
5a *	Acute		<50
5b	Convalescent		<50
6a *	Acute		<50
6b	Convalescent		<50

NB: \* patients with SARS

These results indicated that this novel member of Coronaviridae is a key pathogen in SARS.

#### 6.6 Sequences of the hSARS Virus

Total RNA from infected or uninfected FrHK-4 cells was harvested two days post-infection. One-hundred ng of purified RNA was reverse transcribed using Superscript® II reverse transcriptase (Invitrogen) in a 20 µl reaction mixture containing 10 pg of a degenerated primer (5'-GCCG-GAGCTCTGCAGAATTCNNNNNNN-3'; SEQ ID NO:5; T, G or C) as recommended by the manufacturer. Reverse transcribed products were then purified by a QIAquick® PCR purification kit as instructed by the manufacturer and eluted in 30 µl of 10 mM Tris-HCl, pH 8.0. Three µl of purified cDNA products were added in a 25 µl reaction mixture containing 2.5 µl of 10×PCR buffer, 4 µl of 25 mM MgCl<sub>2</sub>, 0.5 µl of 10 mM dNTP, 0.25 µl of AmpliTaq Gold® DNA polymerase (Applied Biosystems), 2.5 µCi of [α-<sup>32</sup>P]CTP (Amersham), 2 µl of 10 µM primer (5'-GCCGAGCTCTGCAGAATT-C-3'; SEQ ID NO:6). Reactions were thermal cycled through the following profile: 94° C. for 8 min followed by 2 cycles of 94° C. for 1 min, 40° C. for 1 min, 72° C. for 2 min. This temperature profile was followed by 35 cycles of 94° C. for 1 min, 60° C. for 1 min, 72° C. for 1 min. 6 µl of the PCR products were analyzed in a 5% denaturing polyacrylamide gel electrophoresis. Gel was exposed to X-ray film and the film was developed after an over-night exposure. Unique PCR products which were only identified in infected cell samples were isolated from the gel and eluted in a 50 µl of 1×TE buffer. Eluted PCR products were then re-amplified in 25 µl of reaction mixture containing 2.5 µl of 10×PCR buffer, 4 µl of 25 mM MgCl<sub>2</sub>, 0.5 µl of 10 mM dNTP, 0.25 µl of AmpliTaq Gold® DNA polymerase (Applied Biosystems), 1 µl of 10 µM primer (5'-GCCGAGCTCTGCAGAATTC-3'; SEQ ID NO:6). Reaction mixtures were thermal cycled through the following profile: 94° C. for 8 min followed by 35 cycles of 94° C. for 1 min, 60° C. for 1 min, 72° C. for 1 min. PCR products were cloned using a TOPO TA Cloning® kit (Invit-

rogen) and ligated plasmids were transformed into TOP10 *E. coli* competent cells (Invitrogen). PCR inserts were sequenced by a BigDye cycle sequencing kit as recommended by the manufacturer (Applied Biosystems) and sequencing products were analyzed by an automatic sequencer (Applied Biosystems, model number 3770). The obtained sequence (SEQ ID NO:1) is shown in FIG. 1. The deduced amino acid sequence (SEQ ID NO:2) from the obtained DNA sequence showed 57% homology to the polymerase protein of identified coronaviruses.

Similarly, two other partial sequences (SEQ ID NOS:11 and 13) and deduced amino acid sequences (SEQ ID NOS:12 and 14, respectively) were obtained from the hSARS virus and are shown in FIGS. 8 (SEQ ID NOS:11 and 12) and 9 (SEQ ID NOS:13 and 14).

The entire genomic sequence of hSARS virus is shown in FIG. 10 (SEQ ID NO:15). The deduced amino acid sequences of SEQ ID NO:15 in all three frames are shown in FIG. 11 (nucleotide sequences shown in SEQ ID NOS:16, 240 and 737; for amino acid sequences, see SEQ ID NO:17-239, 241-736 and 738-1107). The deduced amino acid sequences of the complement of SEQ ID NO:15 in all three frames are shown in FIG. 12 (nucleotide sequences shown in SEQ NOS: 1108, 1590 and 1965; for amino acid sequences, see SEQ ID NOS:1109-1589, 1591-1964 and 1966-2470).

#### 6.7 Detection of hSARS Virus in Nasopharyngeal Aspirates

First, the nasopharyngeal aspirates (NPA) were examined by rapid immunofluorescent antigen detection for influenza A and B, parainfluenza types 1, 2 and 3, respiratory syncytial virus and adenovirus (Chan K H, Maldeis N, Pope W, Yup A, Ozinskas A, Gill J, Seto W H, Shortridge K F, Peiris J S M. Evaluation of Directigen Fly A+B test for rapid diagnosis of influenza A and B virus infections. *J Clin Microbiol.* 2002; 40: 1675-1680) and were cultured for conventional respiratory pathogens on Mardin Darby Canine Kidney, LLC-Mk2, RDE, Hep-2 and MRC-5 cells (Wiedbrauk D L, Johnston S L G. *Manual of clinical virology.* Raven Press, New York. 1993). Subsequently, fetal rhesus kidney (FRhk-4) and A-549 cells were added to the panel of cell lines used. Reverse transcription polymerase chain reaction (RT-PCR) was performed directly on the clinical specimen for influenza A (Fouchier R A, Bestebroer T M, Herfst S, Van Der Kemp L, Rimmelzwan G F, Osterhaus A D. Detection of influenza A virus from different species by PCR amplification of conserved sequences in the matrix gene. *J Clin Microbiol.* 2000; 38: 4096-101) and human metapneumovirus (HMPV). The primers used for HMPV were: for first round, 5'-AARGT-S AATGCATCAGC-3' (SEQ ID NO. 7) and 5'-CAKATTYT-GCTTATGCTTTC-3' (SEQ ID NO:8); and nested primers: 5'-ACACCTGTTACAATACCAGC-3' (SEQ ID NO:9) and 5'-GACTTGAGTCCCAGCTCCA-3' (SEQ ID NO:10). The size of the nested PCR product was 201 bp. An ELISA for mycoplasma was used to screen cell cultures (Roche Diagnostics GmbH, Roche, Indianapolis, USA).

#### RT-PCR Assay

Subsequent to culturing and genetic sequencing of the hSARS virus from two patients (see Section 6.6, supra), an RT-PCR was developed to detect the hSARS virus sequence from NPA samples. Total RNA from clinical samples was reverse transcribed using random hexamers and cDNA was amplified using primers 5'-TACACACCTCAGC-GTTG-3' (SEQ ID NO:3) and 5'-CACGAACGTGACGAAT-3' (SEQ ID NO:4), which are constructed based on the RNA-dependent RNA polymerase-encoding sequence (SEQ ID NO:1) of



the hSARS virus in the presence of 2.5 mM MgCl<sub>2</sub> (94° C. for 8 min followed by 40 cycles of 94° C. for 1 min, 50° C. for 1 min, 72° C. for 1 min).

The summary of a typical RT-PCR protocol is as follows:

#### 1. RNA Extraction

RNA from 140 µl of NPA samples is extracted by QIAquick viral RNA extraction kit and is eluted in 50 µl of elution buffer.

#### 2. Reverse Transcription

RNA	11.5 µl
0.1 M DTT	2 µl
5x buffer	4 µl
10 mM dNTP	1 µl
Superscript II, 200 U/µl (Invitrogen)	1 µl
Random hexamers, 0.3 µg/µl	0.5 µl
Reaction condition	42° C., 50 min 94° C., 3 min 4° C.

#### 3. PCR

cDNA generated by random primers is amplified in a 50 µl reaction as follows:

cDNA	2 µl
10 mM dNTP	0.5 µl
10x buffer	5 µl
25 mM MgCl <sub>2</sub>	5 µl
25 µM Forward primer	0.5 µl
25 µM Reverse primer	0.5 µl
AmpliTaq Gold® polymerase, 5 U/µl (Applied Biosystems)	0.25 µl
Water	36.25 µl

Thermal-cycle condition: 95° C., 10 min, followed by 40 cycles of 95° C., 1 min; 50° C. 1 min; 72° C., 1 min.

#### 4. Primer Sequences

Primers were designed based on the RNA-dependent RNA polymerase encoding sequence (SEQ ID NO:1) of the hSARS virus.

Forward primer: 5' TACACACCTCAGCGTTG 3' (SEQ ID NO: 3)

Reverse primer: 5' CACGAACGTGACGAAT 3' (SEQ ID NO: 4)

Product size: 182 bps

#### Real-Time Quantitative PCR Assay

Total RNA from 140 µl of nasopharyngeal aspirate (NPA) was extracted by QIAamp® virus RNA mini kit (Qiagen) as instructed by the manufacturer. Ten µl of eluted RNA samples were reverse transcribed by 200 U of Superscript® II reverse transcriptase (Invitrogen) in a 20 µl reaction mixture containing 0.15 µg of random hexamers, 10 mmol/L DTT, and 0.5 mmol/L dNTP, as instructed. Complementary DNA was then amplified in a SYBR® Green I fluorescence reaction (Roche) mixtures. Briefly, 20 µl reaction mixtures containing 2 µl of cDNA, 3.5 mmol/L MgCl<sub>2</sub>, 0.25 µmol/L of forward primer (5'-TACACACCTCAGCGTTG-3'; SEQ ID NO:3) and 0.25 µmol/L reverse primer (5'-CACGAACGTGACGAAT-3'; SEQ ID NO:4) were thermal-cycled by a Light-Cycler (Roche) with the PCR program, [95° C., 10 min followed by 50 cycles of 95° C. 10 min; 57° C., 5 sec; 72° C. 9 sec]. Plasmids containing the target sequence were used as positive controls. Fluorescence signals from these reactions were cap-

ured at the end of extension step in each cycle (see FIG. 7A). To determine the specificity of the assay, PCR products (184 base pairs) were subjected to a melting curve analysis at the end of the assay (65° C. to 95° C., 0.1° C. per second; see FIG. 7B).

#### Clinical Results

##### Clinical Findings:

All 50 patients with SARS were ethnic Chinese. They represented 5 different epidemiologically linked clusters as well as additional sporadic cases fitting the case definition. They were hospitalized at a mean of 5 days after the onset of symptoms. The median age was 42 years (range of 23 to 74) and the female to male ratio was 1.3. Fourteen (28%) were health care workers and five (10%) had a history of visit to a hospital experiencing a major outbreak of SARS. Thirteen (26%) patients had household contacts and 12 (24%) others had social contacts with patients with SARS. Four (8%) had a history of recent travel to mainland China.

The major complaints from most patients were fever (90%) and shortness of breath. Cough and myalgia were present in more than half the patients (Table 2). Upper respiratory tract symptoms such as rhinorrhea (24%) and sore throat (20%) were present in a minority of patients. Diarrhea (10%) and anorexia (10%) were also reported. At initial examination, auscultatory findings, such as crepitations and decreased air entry, were present in only 38% of patients. Dry cough was reported by 62% of patients. All patients had radiological evidence of consolidation, at the time of admission, involving 1 zone (in 36), 2 zones (13) and 3 zones (1).

TABLE 2

Clinical symptoms	Number (percentage)
Fever	50 (100%)
Chill or rigors	37 (74%)
Cough	31 (62%)
Myalgia	27 (54%)
Malaise	25 (50%)
Running nose	12 (24%)
Sore throat	10 (20%)
Shortness of breath	10 (20%)
Anorexia	10 (20%)
Diarrhea	5 (10%)
Headache	10 (20%)
Dizziness	6 (12%)

\* Truncal maculopapular rash was noted in 1 patient.

In spite of the high fever, most patients (98%) had no evidence of a leukocytosis. Lymphopenia (68%), leucopenia (26%), thrombocytopenia (40%) and anemia (18%) were present in peripheral blood examination (Table 3). Parenchymal liver enzyme, alanine aminotransferase (ALT) and muscle enzyme, creatinine kinase (CPK) were elevated in 34% and 26% respectively.

TABLE 3

Laboratory parameter	Mean (range)	Percentage of abnormal	Normal range
Haemoglobin	12.9 (8.9-15.9)		11.5-16.5 g/dl
Anaemia		9 (18%)	
White cell count	5.17 (1.1-11.4)		4-11 × 10 <sup>9</sup> /L
Leucopenia		13 (26%)	
Lymphocyte count	0.78 (0.3-1.5)		1.5-4.0 × 10 <sup>9</sup> /L
Significant lymphopenia (<1.0 × 10 <sup>9</sup> /L)		34 (68%)	
Platelet count	174 (88-351)		150-400 × 10 <sup>9</sup> /L
Thrombocytopenia		20 (40%)	

TABLE 3-continued

Laboratory parameter	Mean (range)	Percentage of abnormal	Normal range
Alanine aminotransaminase (ALT)	63 (11-350)		6-53 U/L
Elevated ALT		17 (34%)	
Albumin	37 (26-50)		42-54 g/L
Low albumin		34 (68%)	
Globulin	33 (21-42)		24-36 g/L
Elevated globulin		10 (20%)	
Creatinine kinase	244 (31-1379)		34-138 U/L
Elevated creatinine kinase		13 (26%)	

Routine microbiological investigations for known viruses and bacteria by culture, antigen detection, and PCR were negative in most cases. Blood culture was positive for *Escherichia coli* in a 74-year-old male patient, who was admitted to intensive care unit, and was attributed to hospital acquired urinary tract infection. *Klebsiella pneumoniae* and *Hemophilus influenzae* were isolated from the sputum specimens of 2 other patients on admission.

Oral levofloxacin 500 mg q24 h was given in 9 patients and intravenous (1.2 g q8 h)/oral (375 mg tid) amoxicillin-clavulanate and intravenous/oral clarithromycin 500 mg q12 h were given in another 40 patients. Four patients were given oral oseltamivir 75 mg bid. In one patient, intravenous ceftriaxone 2 gm q24 h, oral azithromycin 500 mg q24 h, and oral amantadine 100 mg bid were given for empirical coverage of typical and atypical pneumonia.

Nineteen patients progressed to severe disease with oxygen desaturation and were required intensive care and ventilatory support. The mean number of days of deterioration from the onset of symptoms was 8.3 days. Intravenous ribavirin 8 mg/kg q8 h and steroid was given in 49 patients at a mean day of 6.7 after onset of symptoms.

The risk factors associated with severe complicated disease requiring intensive care and ventilatory support were older age, lymphopenia, impaired ALT, and delayed initiation of ribavirin and steroid (Table 4). All the complicated cases were treated with ribavirin and steroid after admission to the intensive care unit whereas all the uncomplicated cases were started on ribavirin and steroid in the general ward. As expected, 31 uncomplicated cases recovered or improved whereas 8 complicated cases deteriorated with one death at the time of writing. All 50 patients were monitored for a mean of 12 days at the time of writing.

TABLE 4

	Complicated case (n = 19)	Uncomplicated case (n = 31)	P value
Mean (SD) age (range)	49.5 ± 12.7	39.0 ± 10.7	P < 0.01
Male/Female ratio	8/11	14/17	N.S.
Underlying illness	5 †	1 ‡	P < 0.05
Mode of contact			
Travel to China	1	3	N.S.
Health care worker	5	9	N.S.
Hospital visit	1	4	N.S.
Household contact	8	5	P < 0.05
Social contact	4	10	N.S.
Mean (SD) duration of symptoms to admission (days)	5.2 ± 2.0	4.7 ± 2.5	N.S.
Mean (SD) admission temperature (° C.)	38.8 ± 0.9	38.7 ± 0.8	N.S.

TABLE 4-continued

	Complicated case (n = 19)	Uncomplicated case (n = 31)	P value
Mean (SD) initial total peripheral WBC count (×10 <sup>9</sup> /L)	5.1 ± 2.4	5.2 ± 1.8	N.S.
Mean (SD) initial lymphocyte count (×10 <sup>9</sup> /L)	0.66 ± 0.3	0.85 ± 0.3	P < 0.05
Presence of thrombocytopenia (<150 × 10 <sup>9</sup> /L)	8	12	N.S.
Impaired liver function test	11	6	P < 0.01
CXR changes (number of zone affected)	1.4	1.2	N.S.
Mean (SD) day of deterioration from the onset of symptoms §	8.3 ± 2.6	Not applicable	
Mean (SD) day of initiation of Ribavirin & steroid from the onset of symptoms	7.7 ± 2.9	5.7 ± 2.6	P < 0.05
Initiation of ribavirin & steroid after deterioration	12	0	P < 0.001
Response to ribavirin & steroid	11	28	P < 0.05
Outcome			
Improved or recovered	10	31	P < 0.01
Not improving	8	0	P < 0.01

\* Multi-variant analysis is not performed due to low number of cases;

† 2 patients had diabetic mellitus, 1 had hypertrophic obstructive cardiomyopathy, 1 had chronic active hepatitis B, and 1 had brain tumour;

‡ 1 patient had essential hypertension;

§ desaturation requiring intensive care support;

|| 1 died.

Two virus isolates, subsequently identified as a member of Coronaviridae (see below), were isolated from two patients. One was from an open lung biopsy tissue of a 53-year-old Hong Kong Chinese resident and the other from a nasopharyngeal aspirate of a 42 year-old female with good previous health. The 53-year old male had a history of 10-hour household contact with a Chinese visitor who came from Guangzhou and later died from SARS. Two days after this exposure, he presented with fever, malaise, myalgia, and headache. Crepitations were present over the right lower zone and there was a corresponding alveolar shadow on the chest radiograph. Hematological investigation revealed lymphopenia of 0.7×10<sup>9</sup>/L with normal total white cell and platelet counts. Both ALT (41 U/L) and CPK (405 U/L) were impaired. Despite a combination of oral azithromycin, amantadine, and intravenous ceftriaxone, there was increasing bilateral pulmonary infiltrates and progressive oxygen desaturation. Therefore, an open lung biopsy was performed 9 days after admission. Histopathological examination showed a mild interstitial inflammation with scattered alveolar pneumocytes showing cytomegaly, granular amphophilic cytoplasm and enlarged nuclei with prominent nucleoli. No cells showed inclusions typical of herpesvirus or adenovirus infection. The patient required ventilation and intensive care after the operative procedure. Empirical intravenous ribavirin and hydrocortisone were given. He succumbed 20 days after admission. In retrospect, coronavirus-like RNA was detected in his nasopharyngeal aspirate, lung biopsy and post-mortem lung. He had a significant rise in titer of antibodies against his own hSARS isolate from 1/200 to 1/1600.

The second patient from whom a hSARS virus was isolated, was a 42-year-old female with good past health. She had a history of travel to Guangzhou in mainland China for 2

days. She presented with fever and diarrhea 5 days after her return to Hong Kong. Physical examination showed crepitation over the right lower zone which had a corresponding alveolar shadow on the chest radiograph. Investigation revealed leucopenia ( $2.7 \times 10^9/L$ ), lymphopenia ( $0.6 \times 10^9/L$ ), and thrombocytopenia ( $104 \times 10^9/L$ ). Despite the empirical antimicrobial coverage with amoxicillin-clavulanate, clarithromycin, and oseltamivir, she deteriorated 5 days after admission and required mechanical ventilation and intensive care for 5 days. She gradually improved without receiving treatment with ribavirin or steroid. Her nasopharyngeal aspirate was positive for the virus in the RT-PCR and she was seroconverted from antibody titre  $<1/50$  to  $1/1600$  against the hSARS isolate.

#### Virological Findings:

Viruses were isolated on FRhk-4 cells from the lung biopsy and nasopharyngeal aspirate respectively, of two patients described above. The initial cytopathic effect appeared between 2 and 4 days after inoculation, but on subsequent passage, cytopathic effect appeared in 24 hours. Both virus isolates did not react with the routine panel of reagents used to identify virus isolates including those for influenza A, B parainfluenza types 1,2,3, adenovirus and respiratory syncytial virus (DAKO, Glostrup, Denmark). They also failed to react in RT-PCR assays for influenza A and HMPV or in PCR assays for mycoplasma. The virus was ether sensitive, indicating that it was an enveloped virus. Electron microscopy of negatively stained (2% potassium phospho-tungstate, pH 7.0) cell culture extracts obtained by ultracentrifugation showed the presence of pleomorphic enveloped viral particles, of about 80-90 nm (ranging 70-130 nm) in diameter, whose surface morphology appeared comparable to members of Coronaviridae (FIG. 5A). Thin section electron microscopy of infected cells revealed virus particles of 55-90 nm diameter within the smooth-walled vesicles in the cytoplasm (FIGS. 5A and 5B). Virus particles were also seen at the cell surface. The overall findings were compatible with infections in the cells caused by viruses of Coronaviridae.

A thin section electron micrograph of the lung biopsy of the 53 year old male contained 60-90-nm viral particles in the cytoplasm of desquamated cells. These viral particles were similar in size and morphology to those observed in the cell-cultured virus isolate from both patients (FIG. 4).

The RT-PCR products generated in a random primer RT-PCR assay were analyzed and unique bands found in the virus infected specimen was cloned and sequenced. Of 30 clones examined, a clone containing 646 base pairs (SEQ ID NO:1) of unknown origin was identified. Sequence analysis of this DNA fragment suggested this sequence had a weak homology to viruses of the family of Coronaviridae (data not shown). Deducted amino acid sequence (215 amino acids: SEQ ID NO:2) from this unknown sequence, however, had the highest homology (57%) to the RNA polymerase of bovine coronavirus and murine hepatitis virus, confirming that this virus belongs to the family of Coronaviridae. Phylogenetic analysis of the protein sequences showed that this virus, though most closely related to the group II coronaviruses, was a distinct virus (FIGS. 5A and 5B).

Based on the 646 by sequence of the isolate, specific primers for detecting the new virus was designed for RT-PCR detection of this hSARS virus genome in clinical specimens. Of the 44 nasopharyngeal specimens available from the 50 SARS patients, 22 had evidence of hSARS RNA. Viral RNA was detectable in 10 of 18 fecal samples tested. The specificity of the RT-PCR reaction was confirmed by sequencing selected positive RT-PCR amplified products. None of 40

nasopharyngeal and fecal specimens from patients with unrelated diseases were reactive in the RT-PCR assay.

To determine the dynamic range of real-time quantitative PCR, serial dilutions of plasmid DNA containing the target sequence were made and subjected to the real-time quantitative PCR assay. As shown in FIG. 7A, the assay was able to detect as little as 10 copies of the target sequence. By contrast, no signal was observed in the water control (FIG. 7A). Positive signals were observed in 23 out of 29 serologically confirmed SARS patients. In all of these positive cases, a unique PCR product ( $T_m = 82^\circ C.$ ) corresponding to the signal from the positive control was observed (FIG. 7B, and data not shown). These results indicated this assay is highly specific to the target. The copy numbers of the target sequence in these reactions range from 4539 to less than 10. Thus, as high as  $6.48 \times 10^5$  copies of this viral sequence could be found in 1 ml of NPA sample. In 5 of the above positive cases, it was possible to collect NPA samples before seroconversion. Viral RNA was detected in 3 of these samples, indicating that this assay can detect the virus even at the early onset of infection.

To further validate the specificity of this assay, NPA samples from healthy individuals (n=11) and patients suffered from adenovirus (n=11), respiratory syncytial virus (n=11), human metapneumovirus (n=11), influenza A virus (n=13) or influenza B virus (n=1) infection were recruited as negative controls. All of these samples, except one, were negative in the assay. The false positive case was negative in a subsequent test. Taken together, including the initial false positive case, the real-time quantitative PCR assay has sensitivity of 79% and specificity of 98%.

Epidemiological data suggest that droplet transmission is one of the major route of transmission of this virus. The detection of live virus and the detection of high copies of viral sequence from NPA samples in the current study clearly support that cough and sneeze droplets from SARS patients might be the major source of this infectious agent. Interestingly, 2 out of 4 available stool samples from the SARA patients in this study were positive in the assay (data not shown). The detection of the virus in feces suggests that there might be other routes of transmission. It is relevant to note that a number of animal coronaviruses are spread via the fecal-oral route (McIntosh K., 1974, *Coronaviruses: a comparative review. Current Top Microbiol Immunol.* 63: 85-112). However, further studies are required to test whether the virus in feces is infectious or not.

Currently, apart from this hSARS virus, there are two known serogroups of human coronaviruses (229E and OC43) (Hruskova J. et al., 1990, *Antibodies to human coronaviruses 229E and OC43 in the population of C.R., Acta Virol.* 34:346-52). The primer set used in the present assay does not have homology to the strain 229E. Due to the lack of available corresponding OC43 sequence in the Genebank, it is not known whether these primers would cross-react with this strain. However, sequence analyses of available sequences in other regions of OC43 polymerase gene indicate that the novel human virus associated with SARS is genetically distinct from OC43. Furthermore, the primers used in this study do not have homology to any of sequences from known coronaviruses. Thus, it is very unlikely that these primers would cross-react with the strain OC43.

Apart from the novel pathogen, metapneumovirus was reported to be identified in some of SARS patients (Center for Disease Control and Prevention, 2003, *Morbidity and Mortality Weekly Report* 52: 269-272). No evidence of metapneumovirus infection was detected in any of the patients in this

study (data not shown), suggesting that the novel hSARS virus of the invention is the key player in the pathogenesis of SARS.

#### Immunofluorescent Antibody Detection:

Thirty-five of the 50 most recent serum samples from patients with SARS had evidence of antibodies to the hSARS (see FIG. 3). Of 27 patients from whom paired acute and convalescent sera were available, all were seroconverted or had >4 fold increase in antibody titer to the virus. Five other pairs of sera from additional SARS patients from clusters outside this study group were also tested to provide a wider sampling of SARS patients in the community and all of them were seroconverted. None of 80 sera from patients with respiratory or other diseases as well as none of 200 normal blood donors had detectable antibody.

When either seropositivity to HP-CV in a single serum or viral RNA detection in the NPA or stool are considered evidence of infection with the hSARS, 45 of the 50 patients had evidence of infection. Of the 5 patients without any virological evidence of Coronaviridae viral infection, only one of these patients had their sera tested >14 days after onset of clinical disease.

#### Discussion

The outbreak of SARS is unusual in a number of aspects, in particular, in the appearance of clusters of patients with pneumonia in health care workers and family contacts. In this series of patients with SARS, investigations for conventional pathogens of atypical pneumonia proved negative. However, a virus that belongs to the family Coronaviridae was isolated from the lung biopsy and nasopharyngeal aspirate obtained from two SARS patients, respectively. Phylogenetically, the virus was not closely related to any known human or animal coronavirus or torovirus. The present analysis is based on a 646 bp fragment (SEQ ID NO:1) of the polymerase gene and the entire genome of the isolated hSARS virus, which indicates that the virus relates to antigenic group 2 of the coronaviruses along with murine hepatitis virus and bovine coronavirus. However, viruses of the Coronaviridae can undergo heterologous recombination within the virus family and genetic analysis of other parts of the genome needs to be carried out before the nature of this new virus is more conclusively defined (Holmes KV. Coronaviruses. Eds Knipe D M, Howley P M Fields Virology, 4th Edition, Lippincott Williams & Wilkins, Philadelphia, 1187-1203). The biological, genetic and clinical data, taken together, indicate that the new virus is not one of the two known human coronaviruses.

The majority (90%) of patients with clinically defined SARS had either serological or RT-PCR evidence of infection by this virus. In contrast, neither antibody nor viral RNA was detectable in healthy controls. All 27 patients from whom acute and convalescent sera were available demonstrated rising antibody titers to hSARS virus, strengthening the contention that a recent infection with this virus is a necessary factor in the evolution of SARS. In addition, all five pairs of acute and convalescent sera tested from patients from other hospitals in Hong Kong also showed seroconversion to the virus. The five patients who has not shown serological or virological evidence of hSARS virus infection, need to have later convalescent sera tested to define if they are also seroconverted. However, the concordance of the hSARS virus with the clinical definition of SARS appears remarkable, given that clinical case definitions are never perfect.

No evidence of HMPV infection, either by RT-PCR or rising antibody titer against HMPV, was detected in any of these patients. No other pathogen was consistently detected in our group of patients with SARS. It is therefore highly likely that this hSARS virus is either the cause of SARS or a

necessary pre-requisite for disease progression. Whether or not other microbial or other co-factors play a role in progression of the disease remains to be investigated.

The family Coronaviridae includes the genus Coronavirus and Torovirus. They are enveloped RNA viruses which cause disease in humans and animals. The previously known human coronaviruses, types 229E and OC43 are the major causes of the common cold (Holmes K V. Coronaviruses. Eds Knipe D M, Howley P M Fields Virology, 4th Edition, Lippincott Williams & Wilkins, Philadelphia, 1187-1203). But, while they can occasionally cause pneumonia in older adults, neonates or immunocompromised patient (El-Sahly H M, Atmar R L, Glezen W P, Greenberg S B. Spectrum of clinical illness in hospitalized patients with "common cold" virus infections. *Clin Infect Dis.* 2000; 31: 96-100; and Foltz E J, Elkordy MA. Coronavirus pneumonia following autologous bone marrow transplantation for breast cancer. *Chest* 1999; 115: 901-905), Coronaviruses have been reported to be an important cause of pneumonia in military recruits, accounting for up to 30% of cases in some studies (Wenzel R P, Hendley J O, Davies J A, Gwaltney J M, Coronavirus infections in military recruits: Three-year study with coronavirus strains OC43 and 229E. *Am Rev Respir Dis.* 1974; 109: 621-624). Human coronaviruses can infect neurons and viral RNA has been detected in the brain of patients with multiple sclerosis (Talbot P J, Cote G, Arbour N. Human coronavirus OC43 and 229E persistence in neural cell cultures and human brains. *Adv Exp Med Biol.*—in press). On the other hand, a number of animal coronaviruses (e.g. Porcine Transmissible Gastroenteritis Virus, Murine Hepatitis Virus, Avian Infectious Bronchitis Virus) cause respiratory, gastrointestinal, neurological or hepatic disease in their respective hosts (McIntosh K. Coronaviruses: a comparative review. *Current Top Microbiol Immunol.* 1974; 63: 85-112).

We describe for the first time the clinical presentation and complications of SARS. Less than 25% of patients with coronavirus pneumonia had upper respiratory tract symptoms. As expected in atypical pneumonia, both respiratory symptoms and positive auscultatory findings were very disproportional to the chest radiographic findings. Gastrointestinal symptoms were present in 10%. It is relevant that the virus RNA is detected in faeces of some patients and that coronaviruses have been associated with diarrhoea in animals and humans (Caul E O, Egglestone S I. Further studies on human enteric coronaviruses *Arch Virol.* 1977; 54: 107-17). The high incidence of deranged liver function test, leucopenia, significant lymphopenia, thrombocytopenia and subsequent evolution into adult respiratory distress syndrome suggests a severe systemic inflammatory damage induced by this hSARS virus. Thus immuno-modulation by steroid may be important to complement the antiviral therapy by ribavirin. In this regard, it is pertinent that severe human disease associated with the avian influenza subtype H5N1, another virus that recently crossed from animals to humans, has also been postulated to have an immuno-pathological component (Cheung C Y, Poon L L M, Lau A S Y et al. Induction of proinflammatory cytokines in human macrophages by influenza A (H5N1) viruses: a mechanism for the unusual severity of human disease. *Lancet* 2002; 360: 1831-1837). In common with H5N1 disease, patients with severe SARS are adults, are significantly more lymphopenic and have parameters of organ dysfunction beyond the respiratory tract (Table 4) (Yuen K Y, Chan P K S, Peiris J S M, et al. Clinical features and rapid viral diagnosis of human disease associated with avian influenza A H5N1 virus. *Lancet* 1998; 351: 467-471). It is important to note that a window of opportunity of around 8 days exists from the onset of symptoms to respiratory failure. Severe complicated

cases are strongly associated with both underlying disease and delayed use of ribavirin and steroid therapy. Following our clinical experience in the initial cases, this combination therapy was started very early in subsequent cases which were largely uncomplicated cases at the time of admission. The overall mortality at the time of writing is only 2% with this treatment regimen. There were still 8 out of 19 complicated cases who had not shown significant response. It is not possible to a detail analysis of the therapeutic response to this combination regimen due to the heterogeneous dosing and time of initiation of therapy.

Other factors associated with severe disease is acquisition of the disease through household contact which may be attributed to a higher dose or duration of viral exposure and the presence of underlying diseases.

The clinical description reported here pertains largely to the more severe cases admitted to hospital. We presently have no data on the full clinical spectrum of the emerging Coronaviridae infection in the community or in an out-patient-setting. The availability of diagnostic tests as described here will help address these questions. In addition, it will allow questions pertaining to the period of virus shedding (and communicability) during convalescence, the presence of virus in other body fluids and excreta and the presence of virus shedding during the incubation period, to be addressed.

The epidemiological data at present appears to indicate that the virus is spread by droplets or by direct and indirect contact although airborne spread cannot be ruled out in some instances. The finding of infectious virus in the respiratory tract supports this contention. Preliminary evidence also suggests that the virus may be shed in the feces. However, it is important to note that detection of viral RNA does not prove that the virus is viable or transmissible. If viable virus is detectable in the feces, this would be a potentially additional route of transmission that needs to be considered. It is relevant to note that a number of animal coronaviruses are spread via the fecal-oral route (McIntosh K. Coronaviruses: a comparative review. *Current Top Microbiol Immunol.* 1974; 63: 85-112).

In conclusion, this report provides evidence that a virus in the Coronaviridae family is the etiological agent of SARS.

#### 7. DEPOSIT

A sample of isolated hSARS virus was deposited with China Center for Type Culture Collection (CCTCC) at Wuhan University, Wuhan 430072 in China on Apr. 2, 2003 in accordance with the Budapest Treaty on the Deposit of Microorganisms, and accorded accession No. CCTCC-V200303, which is incorporated herein by reference in its entirety.

#### 8. MARKET POTENTIAL

The hSARS virus can now be grown on a large scale, which allows the development of various diagnostic tests as described hereinabove as well as the development of vaccines and antiviral agents that are effective in preventing, ameliorating or treating SARS. Given the severity of the disease and its rapid global spread, it is highly likely that significant demands for diagnostic tests, therapies and vaccines to battle against the disease, will arise on a global scale. In addition, this virus contains genetic information which is extremely important and valuable for clinical and scientific research applications.

#### 9. EQUIVALENTS

Those skilled in the art will recognize, or be able to ascertain many equivalents to the specific embodiments of the invention described herein using no more than routine experimentation. Such equivalents are intended to be encompassed by the following claims.

All publications, patents and patent applications mentioned in this specification are herein incorporated by reference into the specification to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated herein by reference.

Citation or discussion of a reference herein shall not be construed as an admission that such is prior art to the present invention.

#### SEQUENCE LISTING

The patent contains a lengthy "Sequence Listing" section. A copy of the "Sequence Listing" is available in electronic form from the USPTO web site (<http://seqdata.uspto.gov/?pageRequest=docDetail&DocID=US08361708B2>). An electronic copy of the "Sequence Listing" will also be available from the USPTO upon request and payment of the fee set forth in 37 CFR 1.19(b)(3).

What is claimed:

1. A method for detecting the presence of a hSARS virus in a biological sample, said method comprising:

(a) contacting the sample with a primer or probe that binds to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1, 11, 13 or 15; or with an antibody, or antigen-binding fragment thereof, to a polypeptide encoded by the nucleotide sequence of SEQ ID NO: 1, 11, 13 or 15; and

(b) detecting whether said primer or probe, or antibody or antigen-binding fragment thereof, binds to said nucleic acid molecule or polypeptide in the sample,

wherein binding of said primer or probe to said nucleic acid molecule or binding of said antibody, or antigen-binding fragment thereof, to said polypeptide indicates the presence of said hSARS virus.

2. The method of claim 1, wherein the biological sample is selected from the group consisting of cells, blood, serum, plasma, saliva, urine, stool, sputum, and nasopharyngeal aspirates.

3. The method of claim 1, wherein said sample is contacted with an antibody, or antigen-binding fragment thereof.

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