WO 03/014383 PCT/CA02/01230

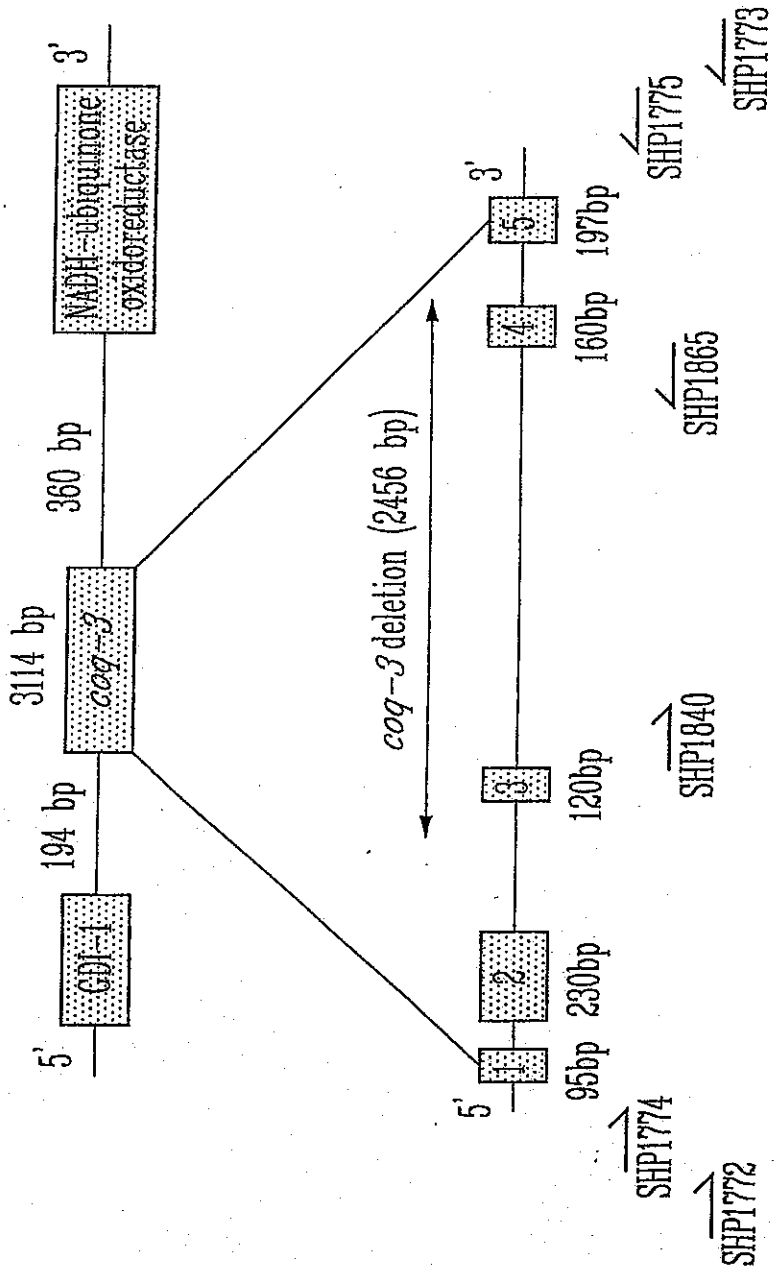


Fig. 1

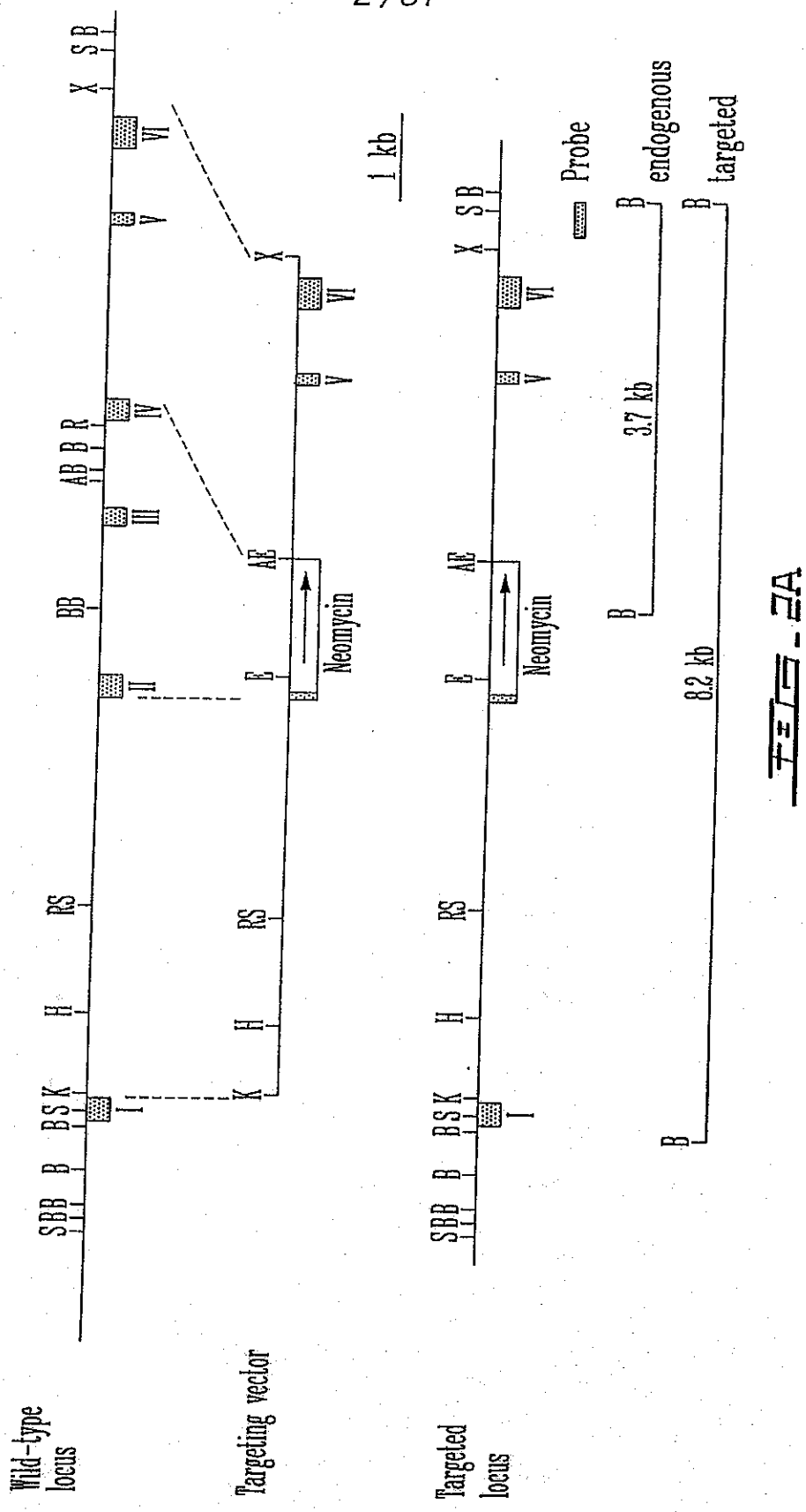
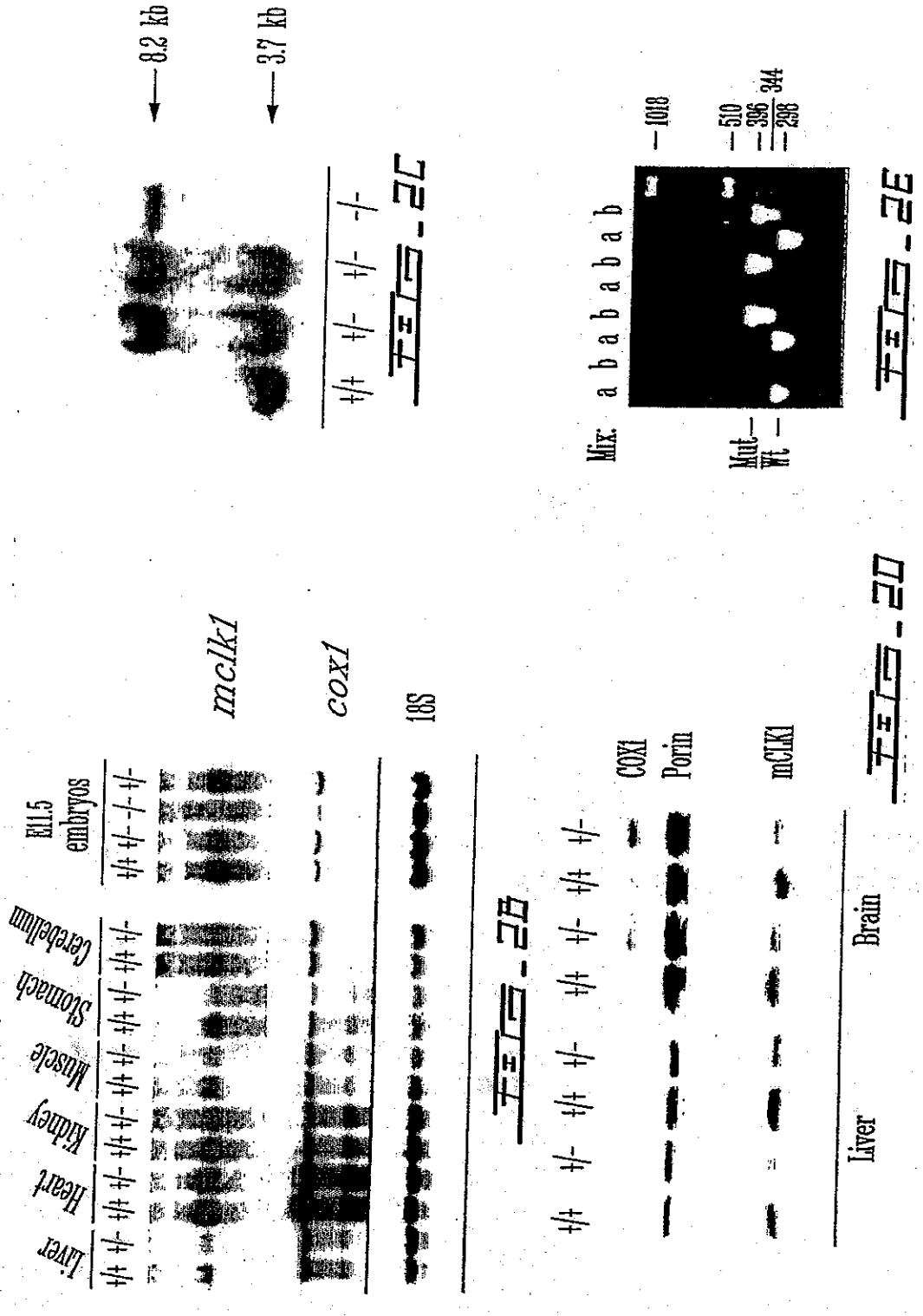

X S B
VI
V
IV
AB B R
III
BB
II
I
RS
H
BS K
SBB B
1 kb
X
VI
V
AE
E
Neomycin
K
RS
H
Wild-type locus
Targeting vector
Probe
B endogenous
3.7 kb
B targeted
8.2 kb
Targeted locus

FIG. 2A


8.2 kb
3.7 kb
+/+ +/- -/-
2C
Mix: a b a b a b a b
1018
510
396
344
298
Mut
Wt
2E
Liver Heart Kidney Muscle Stomach Cerebellum E11.5 embryos
mclk1
cox1
18S
+/+ +/- -/- -/-
2B
+/+ +/- +/+ +/- +/-
COXI
Porin
mCLK1
Liver Brain
2D

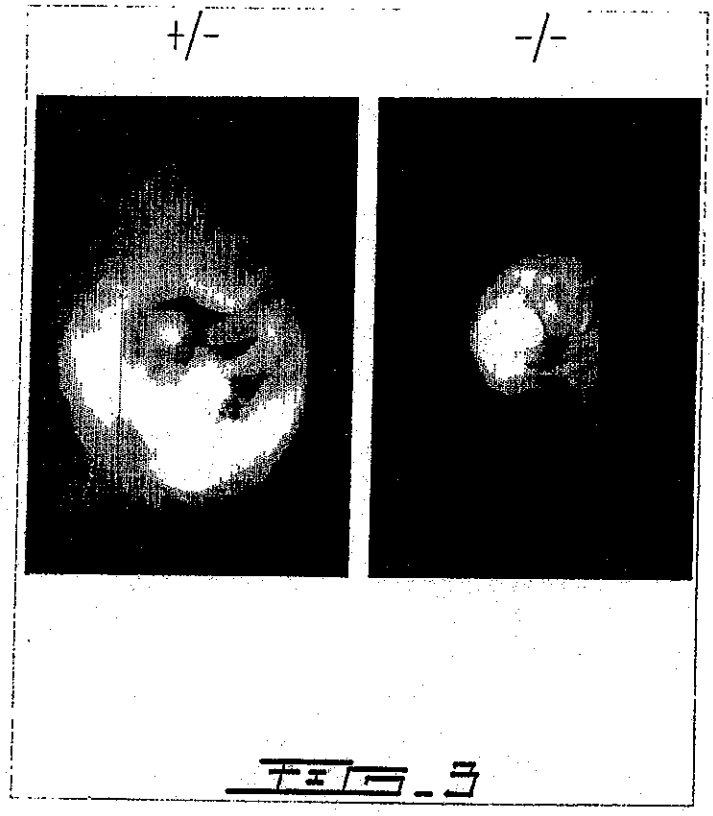


FIG. 3

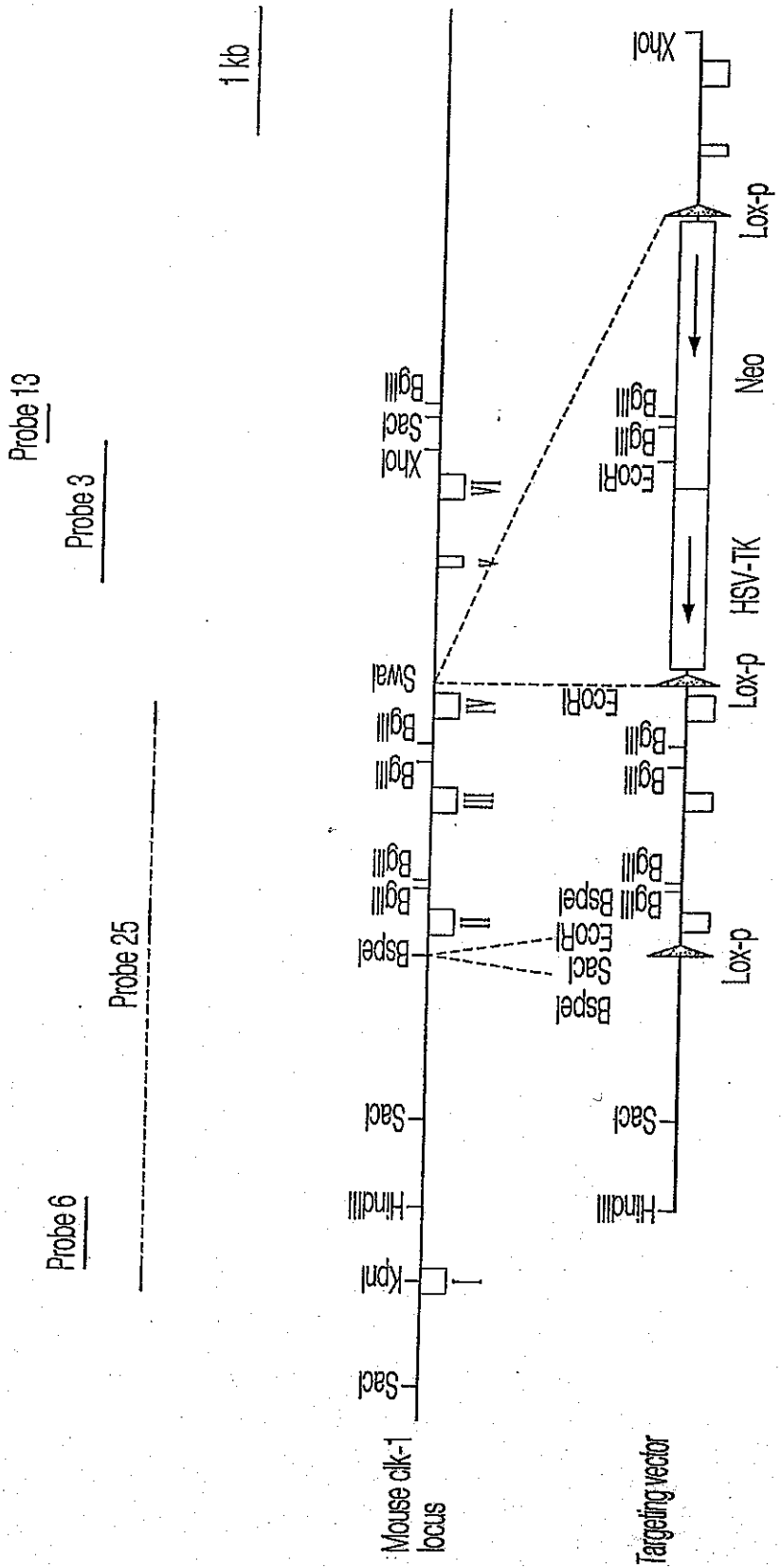

1 kb
Probe 13
Probe 3
Probe 25
Probe 6
XhoI
Lox-p
Neo
BglII
SacI
XhoI
VI
EcoRI
BglII
BglII
HSV-TK
Lox-p
SwaI
EcoRI
AI
BglII
BglII
III
BglII
BglII
BglII
BspeI
II
BglII
BspeI
EcoRI
SacI
BspeI
Lox-p
SacI
HindIII
KpnI
I
SacI
SacI
HindIII
Mouse clk-1 locus
Targeting vector

FIG - 4A

Enzyme	Allele	Probe 3	Probe 6	Probe Neo	Probe 25
EcoRI	*mclk1 WT*	~ 12 kb	~ 12 kb	0	~ 12 kb
	mclk1 flox neo flox	5.7 kb	6 kb	2 kb	6 kb + 2.8 kb
	mclk1 flox	5.7 kb	6 kb	0	6 kb + 2.8 kb
	mclk1 Δ	5.7 kb	9 kb	0	~ 10 kb
BglII	*mclk1 WT*	3.7 kb	4.7 kb	0	4.7 kb + 1.1 kb + 3.7 kb
	mclk1 flox neo flox	4.3 kb	4.8 kb	2.6 kb	4.8 kb + 1.1 kb + 3.3 kb
	mclk1 flox	4 kb	4.8 kb	0	4.8 kb + 1.1 kb + 3.9 kb
	mclk1 Δ	6.8 kb	6.8 kb	0	6.8 kb
SacI	*mclk1 WT*	7.2 kb	-	0	
	mclk1 flox neo flox	9.8 kb	-	9.8 kb	
	mclk1 flox	5.6 kb	-	0	
	mclk1 Δ	4 kb	-	0	

FIG. 4B

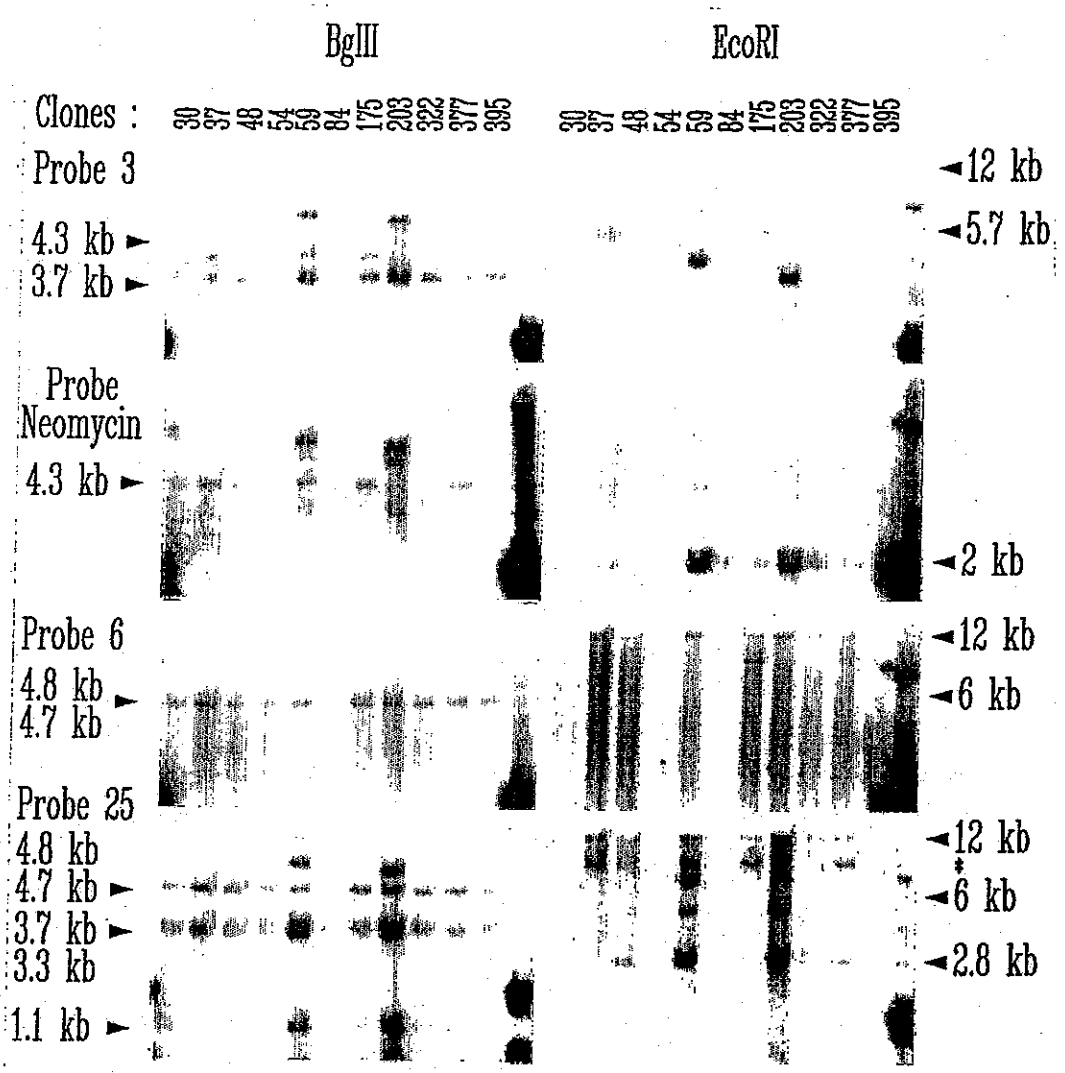

BglII
EcoRI
Clones : 30 37 48 54 59 84 175 203 322 377 395
30 37 48 54 59 84 175 203 322 377 395
Probe 3
4.3 kb
3.7 kb
12 kb
5.7 kb
Probe Neomycin
4.3 kb
2 kb
Probe 6
4.8 kb
4.7 kb
12 kb
6 kb
Probe 25
4.8 kb
4.7 kb
3.7 kb
3.3 kb
1.1 kb
12 kb
6 kb
2.8 kb

FIG_4C

The dark boxes highlight the fully conserved amino acids.

The light boxes highlight the amino acids conserved in at least three species.

FIG - 5A

C. elegans
S. cerevisiae
E. coli
H. sapiens
C. elegans
S. cerevisiae
E. coli
H. sapiens
C. elegans
S. cerevisiae
E. coli
H. sapiens
199
243
171
145
261
308
233
207
268
316
240
250

Fig. 5B

NTTAGGNTCC CGGCNGGGGG TTTCGGGGGN ATTCAAACCC AGGTTCTTTA
ACAGGGNGCA GGGAATGTTT TTCAACTTCT GAGCTCTCTC TAGCTCTAAT
TTTTTAAACA CTTTACTTCC AAAAATTTCC AGTAATAACT AGGACATACA
CCTCAACATT CTTTTATCTC TTTAGGACAG ATCTAGAAGT GGAATGCACG
GGAAAGGTTC TGAACATTTG AAGGCTTTGA GAGCCAGATT TAGGCTGAGT
ATTCCACAGG AATATTTAAG TACCCTCACT GCCGCTAAGG CCCAGTACTT
GGGCTCGTCT TAATTTTAAG TTACTGTAGT ATACTAACTT GAACACTATA
ATTATATAGA ATGGGTTAGT AGTTTCATTT ATTTTACAGT AGCTATGAAT
CAAATACATA CCCCCCCGCC AAGGGTGCAA ACTCTAGTTT TCCTAAAGCC
ACAGTCTCTA GTGATCCTAT AATAGGCACT GATTATGCCT TGCAGGTATG
GTTTTTCCCC TTATATACTT ATCTGACTTG GAAATTTTAT TTCTATTGGC
TAGATCTAGC TGTCATATTA ATGGATATGC ACTTTAAAAT GTTTAATGTA
TGCTACTAAA TTTTCCTTCC CTCAACACAC AGCTATGTTC ATCACTAATG
TGCCCTAGGC CATGAATAAT CCAGTAAAGG ATGAACAATG AAGCAAATCT
CAATATAAAA ATTGAGAAGG AACGGAAAGT AACGGGAAAC AAACTGGGAA
ACCCACAATT ACACCGAAAA CTGGCATGTT TTACCAGGTA ATTGCTGACT
TTCAGGTGTA AATCGGCTCT TAATAGAGAA AAATAATCTC CGTAACGTGG
AGGAAACAGT GACCTGCGGG TCGCCTTTCC AAGACAGGGA GAAACCCTAA
CCTAAACTGC CTCTCCAGGA CAGCTCTGCA TCAACCCTAA GAGCCGACCG
GGCGCCTTCA CTACGTTCCA ATGATCGACA GGGGGCAGAC CAAATAGAGT
ACGTGAATTG GTCATTTCTA ACCAATCGGG TTTAATCCAG GGCCTAGGGG
CGTTTCCTCT GGCTCTCGGT CCGCGGCATC TATGCGTCAT CACCCTGAGT
CGAGAGCACG ATTGGCGGGG CGTTTGGACC ATAGCTGCAT TGTCCGCAGC
GATGAGCGCC GCCGGAGCCA TAGCGGCTGC TTCCGTGGGA CGCCTGCGCA
CTGGTGTCCG GAGGCCCTTC TCAGGTACCG GCCGCTCGGG GTCGTGGTTC
GGCGCGGGGT TCTTCGCTGG TGACTATTTG CAGTGGAGGT CACGGATGTC
ACGGGGAGGA CGTCTATACG TCACAAGCGC GCGACATGGG GGTGGGGTTT
GTAGTACGTC TAGTTGATTG ACAGGAATGG GTGAACTTCT GCAGGATGCC

FIG. 6A

CTGCCGGGGG AACAAGTGAT TACCAGCCTG TGATGTGACG TCAGTGCAAG
GCACATCACA GTGCAACTTG AGTGTCCTGC AGTGTCCCTC CGGTCTCCAC
TCGGGACTTT CTCAAGCAAA GTAGCCTTCC GACGACAGCA TCAATCTGTT
ATAAATGCAG ATTTTCGGGT CCCCCTCATT ATCCACTGGA TTGATAGGTT
TTAGAGTTTT AAAAAGTGTG TGTGTGTGTG TGTGTGTGTG TGTGTGTGTG
TGTGTGTGTG TGCGCGCGCG CGTGCGTGCG CACAATAATT AAATTCTAGA
GAGGCCAGAA TTGGGGTTTG AATCTGCAAC TAGAGTAACA GGCAGTTTGT
GAATCCCTAT ATATGGGTGC TGGGAGCCCA ACTCAAGTCA TTTGCAAGTG
CAGTACACAT TCTTAACTGC TGAGCCTTCT TTTGAGCCGT AGAGTCTCTG
TTTTTATCAA GCCTCTCATG GGACTGTTTG TATTGCAAAA TATGGTAAGC
TTTGAATTTG GAATGGAGAG AGGTAGGTTT GGATTCAGGT CTGATTCATC
CGAGCTGCCC CAGAAAATCG TGGTCATTTT CTTGAAACTA AATCTTCAAG
CATTAGATTT CTATTTTGCC TGAAGGCAAT ATTGTTTGGA GGTTTGAGAT
GTGTTTTTGT TTAACTACAA CTTATTAAGT AATTTAATTG AAACTACATC
CTTTTGGTAA ATAATAAGCC AGAATTGCCT GCCCCCAAAT GGATGAGTAA
TCACCCCCCC CACACACACA CACCACCACC ACCACCACCA CCACCACCAA
TACCTTGAGA ACAGCTATGA AACTTCATTA GATATTGTTG TGTGTGCCTT
CCAAGGCTTG AGTCCAAGGC TGTTTTTCTT TCTGGAAGAG AAGARTGCTT
AGCAAGTGTT TGGATATTAT TCAAGACATG CCAGTTATAG AGATGTTTCC
CTTGGTGATA ATGATTCAGA AGAGACTTTT TAAGAGCCTC TTAGTATGTA
ATTTATGTGT CCATAAGCCA CTTAAAATCT TCTCATTTGC CACTTAAAAT
CTCCCAGATA CCATGGCTGG AACAGCACGC TTGAGAGCTT CTAGCTCTGC
GATTCAGCTT TATTTTAAAG TGTGTAACAA GGCAGTCAGG TCTCAGGGAT
GTGGATTTTA AGGTTCCTTG CTAACCCAGT GAACAGGTTA ACAATAAGAA
TCACTTGTTT TCATTTATGA AGTAACTTAG TTTCCTTTGT TTCATATACC
CTCATGATAA TAATAATAAT AAAAAACCCT TAAGTGTGTG TCTCCTTAAA
AAAATAAAAC TAGCCTTGCT ACTGGGTAGG TTTTAATTTG GTTTTGAGAC
AGCCTCTAGC GCTGGCTGAC CTGGACCTTG CTTGTTCACC AGGATATCCT
TCAATTCACA GAGCTCTGCC AACTCATGCT GGGATTAATA CCTATACTGA
TTTCTTAGGT AAAAGGACAA ATACTACCCT CTCCCAGTCA TTGAGTGCAG
AAGTTGTGTT TTAGAGAACA TTCCAGTGTG TTCTCAGTTA TAAAGAATCC

FIG. 6B

TGTTTATCAC ACCTCAAAAG CCAGCCATAT AAACTTGGCC CACCTGCTCA
GCTCCTTGTT ATTCTTCTTT TAAAAAAAAG ATTTATTTTA TATATGTGAA
CACACTGTAG CTGTCTTCAG ACACACCAGA AGAGGGAATC AGATCCCATT
ACAAATGGTC CTGAGCCACC ATGTAGTTGC TGGGAATTGA CCTCAGGACC
TCTGGAAGAG CAGTCAGTGC TTTTAACCGC TGAGCCACCT CCCCAGGCCC
CTTGTTATTC CTTAATATAC TTTTTAAAAA GGAGTACTGG GTTGCCTTGA
ACTTTCTTTG CTAAAAAGTA AGAGCACAAG CAAACAAGAT TGTGTTGAGA
AATACAACTG GCTCACCAAG TCTGTCTCCA GACCCTGCTT TCTGCAAGGA
GACAAGCTGG CCAGAAGCAT AAGCCCTTGA ACTTGGACAC AGAAATGCAA
CAAGTTCCTG ATTGTGTCCC ATCACTGTCC CATAAAATAT GGGCCTCAAA
CCGTAGAGCC CCACTGTCTG AAGACAGTTT GGAATGGTTG GTGTCTTACA
CTCGGCAGGA GAGCTGAGGT GCCGTGTCTG CTCCACAGAC TCTGTCCAGT
TAGAGTCAGT GAGCTGAGTG AGGCAGAGCA TGCCATGCGC AGTAGACCAA
AGCCATTCTC CCTCCTGCAG AATCCACGTG CCTTTGCACA CACAGCGCTA
TTTGTCCCAG GACTGTTGAT GTAGCTCAGC ATTTAAAATT CTACTTGGTA
GCAAAGCTCA CGTTCCCAAC GACTGCATGC ATACACACCA GATACTCCAA
TCCTGCCCCG TGGCCTTGTG TCCAAAGACC TTAAGCCTTG GTTGATGAAA
GAGCCAAAGA CATATGGGAC TTTTCCACCC GTTTTCTGGA TGTTGAAGTT
TGCTTAGGTG AAAAGAAGTG TCTTCCAAAG ACATGGTGGT CATAGCAAGC
AGAGAGCCTG CAGCACTTTA AACAGGGTGC AGCTAGAGTG ACAAACCAGA
GGGCCTGTGG GTTTCCGTTT TTATATGGAA TAAACACACA TTACTACAGG
ACCCTTCTGG GATGAGGTAA ACATTCAAGA TCCTCTAATC TGGAGCTTGG
AAGTATAGTG AAGTGTTTAC ATTTGAAGAA GAGTTTAGTC TGAGGTCAAA
CCTTGTCAGG CAGGGTCTCA GTCACCTGCC CGTGGAATTG GTGTATTAAA
AGAACGTTGA AGCCCCAACT TGGGATGCCA GGCTTTGTCC CCTGAGCCTT
TTCAGAACAT CAACACTGGC CGCTTCCCAG GGAGACTTAG GGAGAGCATT
ATAGATAGCT TTGGGTGCAC TCCAGGGGCT TCTGTACAGC TTGAGAGGGG
AGCCTCCCTT TCCTGAAACA GCTGTCACGT CAGCTGCCTT GTGAGGACAG
ATTTCGGTCC TTCCAGATCG CCATATGTTT AAAGTAAATC CGGAAGCCCT
AGTCTTTAGG TGAAGTCTTT TGGGTTTGAG CATTGCAGGT GACAAAGAAC
ACACACTGGT AGATGTGTCC AGCCCTCAGG CTTGTCTTTC ATTCTGTCGG

FIG. 6C

CAAAAAGGCA ACAGGCCAGC GATATGACTC AGTGGGTAAA GGTGCTTGCT
TTCCAGCACA AGGGCCTGAG TTCCATCCCT GGACCCCACA ACTCCGTTTT
CAGGAATGTC AGTGTCCTGT GTGGATAATG AGACGGACAC TTGCTTTTTC
ATTGCAGAGT ATGGAAGAGG CCTCATCATC AGGTGTCACA GTTCGGGGAT
GACCTTAGAC AATATTAACC GGGCAGCCGT GGATCKAATA ATTCGGGTGG
ATCACGCTGG TGAATATGGA GCAAACCGCA TCTATGCAGG GCAAATGGCT
GTGCTCGGTC GGACCAGTGT TGGCCCTGTC ATTCAGGTGG GTTCTTTCCT
GAGTCTCAGC CCAGTCTGTT GCCCTGGCAG TGTATCTGAA GCCCTCGGGC
ATCACTTTTG GCTGTGTGCT CCAAAGGGAG GCACTTGGAA CAAAGCACTT
GCTCTGTTGT CTAAAAGCAC AGATATGCAT TGACTCTGGC TGGGTGTGGT
GGTGCATGCC TATAATCCCA GCACTTGGGA GCTGGAGATA GGGTGATCGC
TGGGACTTTG AGGCCAGCCT GGTCTACATA GGAAGTTCCA GGTCAGAAAG
AAAAAAATGG AGAGAGGGGG AAAGAAAGTA AGAGAGAAAG AAATTGGGTC
TGGAAATTGG GTGTATTTGT GGTGTTAATG TTTCATTGCA GAAAAGGCTG
AAAGTCCCTC CATTAGAAGA ATGTTCCATG TGCCAGGAGG TTGTTGTAGG
CTTGTCCTAG CACAGAGTAT CAGAGAGAGG GGTTAACAGC CCCGAAGATC
TAGGTTTCCT TTCCAGATCT CTCATCTACT TCTGCGACCC TGAAGAGGTC
ACCTGACCTC TAGGTTTTCA TTTCCCTGTG TGCACACTAG CCTGGTAACC
CCCACCTCCC TGGGTCTGGC TGGGGAATAA ACCAGATCCT GTTGTCACCA
TGACACATGG CAGCTTAGAT CCCCGCAGAT CCCAGTCCCC AGTGCTCATC
CCATGTGTAA GATGGTGGGT GTCTGCTTGT GGCCCTGCAC AACTCTCCTG
TGAAGAGTCC TTCATGCCAG GAGAATGCCT CTCATTGGCT GTCCTGTTTT
CTATTGAGAA CATTCTGCGA GTTTTCAGGA CACAGTTTTG TTGTTGTTGT
TGTTGTTAGT TTTTTTCATT ATTTTCTCTT GTGGTTGCTT GAGCCGGTGG
CTCAGAACCT GGAGTTCTAT ATGGCTCACT ATGCAAGCTG ATTGTGTGGT
CACTGAGGTG TGTGTGGCTC TGGAGGTGGA ACACTTAGCT CTGTCCAAGG
CCTTGGTTCT TCATTTACTT GGCAGGTGCT TTTCTTTTTT GAGAGATTCT
TCTGTGGTTT GCTTTTATCT CATGGATATT TAAGGGGATG GAAGACAGCA
TTGCACCAAT TCCTTCTTAC CTCTTGTGTG CTCAGCGAGC CGTGTCCCTG
TGATGCCTCT TTTTATGTTT CCCCCCCCAG AAAATGTGGG ATCAAGAGAA
GAACCATTTG AAAAAGTTCA ACGAGTTGAT GATTGCATTC AGGGTCCGAC
CTACGGTTTT GATGCCCTTG TGGAACGTGG CAGGCTTTGC CCTGGGTATG

FIG. 60

TGTCTGTCCA GCAGCCGCTT GGGCTCTAAT GATGGGCTGT TCCTGCCTCT
GGAGCCCTTG TCAGGGCTGC ATCCAACCTT TTAAAATTTA CTGTGTGTTT
TCCTAAAGCT AAATTGAAGT TGATGAAGTT GATKGAATTT TCTTTGTTTA
TATTACTTTA AGATAGAGCC ATCACTTTTA TAAATAGATG GTATAATAAC
TCACAGAGGG AAGCTAGGAT CGTGCCACCA CTGCCAGAAT CCATGTCCTG
AGGATCCTGA CCTCAGAGCA ACCTGACTGT GAGAGTGCTG GTGCCCACCT
TTAACCCCAG CACTCGGGAG ACAGAGGCAG GCAGATCTCT GAGTTTGAGG
CCAGCATGGT CTACAAATCG AGTTCCATAA CACACACACA CACACACACA
CACACACACA CACACACACA CACACACAGA AGAACAGCAG AGAACCCAGA
TAGCACTCTC AGCTCTCTGC AGAGGGTCAA GTCTCATTGA GCCCATGTGT
TAACTTGGGT TTCATAGTGA GATCTTGTCT CAAACAAAAC AAACCAACCA
AATAAAATAA AAATCCATTC AGAAAGAGCT TTGTGACTGG CATCTGATAT
AAGCTCCAGC CGCTTCTCAA CTAGGCGTGA CTGTTTCAAG GGATTCATGG
GAATATCTGA ATGCCCAGTG GTCATGATCA GCAGGTACTG CTGACATCCA
GAGGGTGGAT ATCGGGTGCC ATTAGACACC CTGAGAAACA CGTCACAGCC
CTCCCAGAGA GTTACCAACC CAGGTGTCAG GACGCCTCAC AGATGACCAG
CAGCCTGTGG CTTGACTTTG TTTGTTTGAC GGTTGCAGGG GCAGGAACTG
CCTTGCTGGG GAAGGAAGGA GCAATGGCCT GCACCGTGGC GGTAGAAGAG
TCTATCGCTA ATCACTACAA CAACCAGATC CGCATGCTGA TGGAAGAGGA
CCCTGAGAAG TATGAGGAGC TGCTGCAGGT GATGACTGTG CGCTGCTTGA
GGAGAGAAAG GGCAGGTGAC AGGAGATGGG TACTAAGGAG GCAGGGACTT
AGACAGCTGG GGAAGGGGGC GTATCTTTTA CGTGAGACAC AGACAGATCA
TACAGCTCAG AACTGTTCCC AGTCCAGGTC TGTGTGGCCT CTGCACATCC
ATGACTCAGC AGCACGAGGT GAACAAGGAT GATGTCAGCT AACACACTAA
CTAGACAGAG AAAAATCCAC AAGGCCTGAC CCCTACACAA AGAACCATAG
TGATGCAGGA AGGTCGAGAT GGGAGGGGTG GCCTTCTGTT TGTCCAGTGC
CAGAAGGTCA GCCTGAAAGC ATACATACAG GTGGCATTAT GCGGACAGAA
GAGACTAGAT TTAAATATGT ATAAGCAAAT ACATACACAC AGGCAACAGC
AACTAATGAA AAGAGAAGCC ATGAACTTGA AGGAGAGCAG AGAGGGGTAT
ATGGGAGGAA GGAAAGGGAC AGGAAAAAAT GCTGTGGTTA ACTAATAATC
CCAAAAATAA AATAAAAAAA ATGATGATCA ACTCTTCAGG TTGAGTGATT
TTCCTCAGGT TTCTCTATAG AAAAGAAGGA ACTATTTGGC CCTGGGCTGG

FIG. 6E

TCTTAAAACT AGCGTCTACA GAGGTCCTCC TGCCTGGTTG CCATCCTCCA
GCACTCTCCC TAACAGCAGT TCATTTACTT AGATTCTGTT TGGTTTACTT
TTGAGACAAA GGCTTGTCTT GACTCTTGGC CCTCCTGCCT CTGCCTTCCA
AGGGCTGGGG ATGTCAGTGT GTATTGCTGT ACTTGGCCAT GTGGTGGTTT
GAATAAGCGC AGGCCCCCAC AGTTTCACAT ATCTGAATGC TTAGATGTGG
GGGAGTGGCA TTATTTGAGA AGGGTTAGGA GGCTCAGGAT TAGCCTTGTT
GGAGGAAGTA TGTTGTTGGA GGGTGGGGCT TTAAGCCCAT GCCAGGCCCA
GGGTCTGTCT CTTGGTCTGC AAGTCAGGAT GTAGCTCTCG GCTACTGCTC
CAGCACCAAA GTGCTGCCCT GCTCCCTGCT AAGCTGATAG TGAGCTAAAC
CTCTGAAACC TCAGGCAAGC CCCCAGTTAA ATGCTTTCCT TTCTAAGAGT
TGCTTTCCTC ATGGTGTCTC TTCACAGCAA CAGAGCAGGG ACTAAGACAG
GCAACAACTC TCACTTTTTA AAACCTAAAG TCAGCCACTG GCTGACCCTA
GCCTGTGGCC ATGCTCGTTT CGTAAATAAG TCTCATTAGA GCCACAGCTA
TGGGTTACTC TTGCAAGGCT GTTCACCCCA CTGGAGTGCC AGGGTAGAAA
AAGCATGAGA GCCTTTGACA GCTGTATGTG AGGACACAGG CTCTGGCCTG
GAAACAGGAT GAGCTGCCGG CAACCTGGGG TGCCGACTCA CCCCAGTCTG
CGATTCCTTT CTTCCCAGGT CATCAAGCAG TTTCGCGATG AGGAGCTTGA
ACACCACGAC ACAGGCCTGG ACCACGATGC AGAGCTGGTA GGGCCAACTC
TTCTTGTGCT GCTCTCGGGC CATTTTAAAG GTTGTGGGGG ACAAAGGTTT
CTGTTCCCAA AAGGAGACAT TTGAAAGTAC AGGTCAGAAG GCAGGGAAAC
GGGTACTTGA CAGAAAGCAC CCAAGCTCAG CCTTGGTCCA TGGTGAGGCT
CCTGTGTCCT GCTCTGTTAC TAACACAAGA AACAACCCAG CAGTTCAGTG
TCCATAGATG CTTCTAGAAT TTCAAATGGC TTTTGTTTCA AATTAAATCA
TTTCCCARAT CCTCTTTTTA TCCAGAGGAG CCCAAACCCT GCCCTACCAG
TGAGTCCAGG TCTGAACATC TGAAAATAGA TGCATCTCGT GGGGGTTTCC
TTGCTGTTTG TTTAGGGGCT GGCATTGAAT CCAGGGCCTT GCTAGGCAAG
CGCTCTACCA CTTAACAGAC CACTTGCCCG TTTGCTTATT TTCCCAGCTC
AGGGTGCCGC CGTGCATGTT AGACAATACT CTACCATCTA GTACATCGCA
GCCTTTTGTT CTCCGCAGGC TCCCGCGTAT GCCTTGTTGA AGAGGATTAT
CCAGGCCGGA TGCAGTGCAG CCATATATTT ATCAGAAAGG TTTTAGAGTA
TGTCTATTGA TCCATTTCTA GAAAAGATGG TCGTAACTTA AGGAGTGATG
TTTGTGGAGG AGGTGCTGTA CAGTTATCAC TGTGTGTGTT TTGTTAATAC

FIG. 8F

AAAAGGCCGG GTTTGGGGCT TGTGTTTGTC AATAAACTCT TTGGCGCTGG
ATTCCTTGGT TTTCTTGTGC TGTGAGGTTG GCAGTTAACT AACTCTGCTC
ACCTTACAGT ACCTGCAGCT GGTCTTCCCT TGGTCTTATA GTTAATTTGG
GCCTAAGACA TCAAGAACAA ACCATTCGTC AGTTAACAGG AATCCTTTTT
TAAAGATTTA TTTTACTTCT ATTTCTAGAG TTTAAAAACA TTAGACTGTA
TAAGATGGGC TAAGCAAGAC TGGGAAGTCT CTCGAGGGAG GTGCTGTGCA
TTCTGATGTC AGCATGATGC CGCAAAGCAC TGTGGTAGCT ATGGCTCCTG
AAAATCCTCA CCCAGAGTCG ATGGTAGGAG GTGGTAAATC CCTCACCCCA
GAGGAGACAC CTGAAGGGAG AGGAGGCTGG GAGGTGGCAG ATAAGGGGCA
GAGACCTCAG GAGTGGGGTT AGTGCCCTTA TAGAAACGAG GCCTAGGGAG
ACCCAGTCTG TTCCACATCA CTGGACACCA ACCTGTTGGC ACCCTGATAT
TGGACTTCAT AGCCTCCAGA ACTGCAAACA AGTTTTTGTT GTTCATGAGC
TCCTGAGCCT ACAGTATTTT AATAGCAGTC CTGGCAGACT AAGGCAGGAT
GGCATTATCC CAATCAAAAA TATACTTAAG TTGGGTGTGG TGATGCAGGC
CTGTAATCCT AGCACCATGG GAGGCAGAGG CAAGAAGATC TGCAGGAGTC
CCAGGGCTAT CCTCAGCACA CGTCAAGTTT GAGGACAGCG TACATGACAC
CCGGCCCCAG CAAACAACCA CAATAACATA CAGAGCTGTG GGTTATTTAC
AATTGAATTA TAATTTCTGC AAGGTCTGCT ATCTCCAAAT AAGCCAGACT
GACAAAAATT TAGTATTTCT GTGAACTATT TTATTATTTT AAATTTTCAA
AATATATTTA AAGAAAAACA AACAAACAAA CAAAGAACCC AGGATCAAGC
AGAGTGTGGT GATACATGCC TGTAATCCCA GCCGTGGGAG CAGAGGGAGA
GAGATCTTCA TGAGCCAGTT GGTTACGTAG CAAGACCCTG TCAAATACAA
AAGCCAAAAA AAAAAAAAAA AAAACCTCAG TTCTCCTCAG AATGTCCTTT
CAAACTTCCC TGGGAGGCTG AGGCAGGAGT TAAAGGTCAG TCTGAGCAAT
ACMGCAAGAA AAAAAAACMA ATGAATTTGC AGACCAAAAT CTGACCTAGT
TGCACTGGTC AGTGGTCCCT ATAGCGARCC TGAGATGACT GGGGCTT

FIG. 6G

NTTAGGNTCC CGGCNGGGGG TTTCGGGGGN ATTCAAACCC AGGTTCTTTA
ACAGGGNGCA GGGAATGTTT TTCAACTTCT GAGCTCTCTC TAGCTCTAAT
TTTTTAAACA CTTTACTTCC AAAAATTTCC AGTAATAACT AGGACATACA
CCTCAACATT CTTTTATCTC TTTAGGACAG ATCTAGAAGT GGAATGCACG
GGAAAGGTTC TGAACATTTG AAGGCTTTGA GAGCCAGATT TAGGCTGAGT
ATTCCACAGG AATATTTAAG TACCCTCACT GCCGCTAAGG CCCAGTACTT
GGGCTCGTCT TAATTTTAAG TTACTGTAGT ATACTAACTT GAACACTATA
ATTATATAGA ATGGGTTAGT AGTTTCATTT ATTTTACAGT AGCTATGAAT
CAAATACATA CCCCCCCGCC AAGGGTGCAA ACTCTAGTTT TCCTAAAGCC
ACAGTCTCTA GTGATCCTAT AATAGGCACT GATTATGCCT TGCAGGTATG
GTTTTTCCCC TTATATACTT ATCTGACTTG GAAATTTTAT TTCTATTGGC
TAGATCTAGC TGTCATATTA ATGGATATGC ACTTTAAAAT GTTTAATGTA
TGCTACTAAA TTTTCCTTCC CTCAACACAC AGCTATGTTC ATCACTAATG
TGCCCTAGGC CATGAATAAT CCAGTAAAGG ATGAACAATG AAGCAAATCT
CAATATAAAA ATTGAGAAGG AACGGAAAGT AACGGGAAAC AAACTGGGAA
ACCCACAATT ACACCGAAAA CTGGCATGTT TTACCAGGTA ATTGCTGACT
TTCAGGTGTA AATCGGCTCT TAATAGAGAA AAATAATCTC CGTAACGTGG
AGGAAACAGT GACCTGCGGG TCGCCTTTCC AAGACAGGGA GAAACCCTAA
CCTAAACTGC CTCTCCAGGA CAGCTCTGCA TCAACCCTAA GAGCCGACCG
GGCGCCTTCA CTACGTTCCA ATGATCGACA GGGGGCAGAC CAAATAGAGT
ACGTGAATTG GTCATTTCTA ACCAATCGGG TTTAATCCAG GGCCTAGGGG
CGTTTCCTCT GGCTCTCGGT CCGCGGCATC TATGCGTCAT CACCCTGAGT
CGAGAGCACG ATTGGCGGGG CGTTTGGACC ATAGCTGCAT TGTCCGCAGC
GATGAGCGCC GCCGGAGCCA TAGCGGCTGC TTCCGTGGGA CGCCTGCGCA
CTGGTGTCCG GAGGCCCTTC TCAGGTACCG GCCGCTCGGG GTCGTGGTTC
GGCGCGGGGT TCTTCGCTGG TGACTATTTG CAGTGGAGGT CACGGATGTC
ACGGGGAGGA CGTCTATACG TCACAAGCGC GCGACATGGG GGTGGGGTTT
GTAGTACGTC TAGTTGATTG ACAGGAATGG GTGAACTTCT GCAGGATGCC
CTGCCGGGGG AACAAGTGAT TACCAGCCTG TGATGTGACG TCAGTGCAAG
GCACATCACA GTGCAACTTG AGTGTCCTGC AGTGTCCCTC CGGTCTCCAC
TCGGGACTTT CTCAAGCAAA GTAGCCTTCC GACGACAGCA TCAATCTGTT

FIG. 7A

ATAAATGCAG ATTTTCGGGT CCCCCTCATT ATCCACTGGA TTGATAGGTT
TTAGAGTTTT AAAAAGTGTG TGTGTGTGTG TGTGTGTGTG TGTGTGTGTG
TGTGTGTGTG TGCGCGCGCG CGTGCGTGCG CACAATAATT AAATTCTAGA
GAGGCCAGAA TTGGGGTTTG AATCTGCAAC TAGAGTAACA GGCAGTTTGT
GAATCCCTAT ATATGGGTGC TGGGAGCCCA ACTCAAGTCA TTTGCAAGTG
CAGTACACAT TCTTAACTGC TGAGCCTTCT TTTGAGCCGT AGAGTCTCTG
TTTTTATCAA GCCTCTCATG GGACTGTTTG TATTGCAAAA TATGGTAAGC
TTTGAATTTG GAATGGAGAG AGGTAGGTTT GGATTCAGGT CTGATTCATC
CGAGCTGCCC CAGAAAATCG TGGTCATTTT CTTGAAACTA AATCTTCAAG
CATTAGATTT CTATTTTGCC TGAAGGCAAT ATTGTTTGGA GGTTTGAGAT
GTGTTTTTGT TTAACTACAA CTTATTAAGT AATTTAATTG AAACTACATC
CTTTTGGTAA ATAATAAGCC AGAATTGCCT GCCCCCAAAT GGATGAGTAA
TCACCCCCCC CACACACACA CACCACCACC ACCACCACCA CCACCACCAA
TACCTTGAGA ACAGCTATGA AACTTCATTA GATATTGTTG TGTGTGCCTT
CCAAGGCTTG AGTCCAAGGC TGTTTTTCTT TCTGGAAGAG AAGARTGCTT
AGCAAGTGTT TGGATATTAT TCAAGACATG CCAGTTATAG AGATGTTTCC
CTTGGTGATA ATGATTCAGA AGAGACTTTT TAAGAGCCTC TTAGTATGTA
ATTTATGTGT CCATAAGCCA CTTAAAATCT TCTCATTTGC CACTTAAAAT
CTCCCAGATA CCATGGCTGG AACAGCACGC TTGAGAGCTT CTAGCTCTGC
GATTCAGCTT TATTTTAAAG TGTGTAACAA GGCAGTCAGG TCTCAGGGAT
GTGGATTTTA AGGTTCCTTG CTAACCCAGT GAACAGGTTA ACAATAAGAA
TCACTTGTTT TCATTTATGA AGTAACTTAG TTTCCTTTGT TTCATATACC
CTCATGATAA TAATAATAAT AAAAAACCCT TAAGTGTGTG TCTCCTTAAA
AAAATAAAAC TAGCCTTGCT ACTGGGTAGG TTTTAATTTG GTTTTGAGAC
AGCCTCTAGC GCTGGCTGAC CTGGACCTTG CTTGTTCACC AGGATATCCT
TCAATTCACA GAGCTCTGCC AACTCATGCT GGGATTAATA CCTATACTGA
TTTCTTAGGT AAAAGGACAA ATACTACCCT CTCCCAGTCA TTGAGTGCAG
AAGTTGTGTT TTAGAGAACA TTCCAGTGTG TTCTCAGTTA TAAAGAATCC
TGTTTATCAC ACCTCAAAAG CCAGCCATAT AAACTTGGCC CACCTGCTCA
GCTCCTTGTT ATTCTTCTTT TAAAAAAAAG ATTTATTTTA TATATGTGAA
CACACTGTAG CTGTCTTCAG ACACACCAGA AGAGGGAATC AGATCCCATT

FIG. 7B

ACAAATGGTC CTGAGCCACC ATGTAGTTGC TGGGAATTGA CCTCAGGACC
TCTGGAAGAG CAGTCAGTGC TTTTAACCGC TGAGCCACCT CCCCAGGCCC
CTTGTTATTC CTTAATATAC TTTTTAAAAA GGAGTACTGG GTTGCCTTGA
ACTTTCTTTG CTAAAAAGTA AGAGCACAAG CAAACAAGAT TGTGTTGAGA
AATACAACTG GCTCACCAAG TCTGTCTCCA GACCCTGCTT TCTGCAAGGA
GACAAGCTGG CCAGAAGCAT AAGCCCTTGA ACTTGGACAC AGAAATGCAA
CAAGTTCCTG ATTGTGTCCC ATCACTGTCC CATAAAATAT GGGCCTCAAA
CCGTAGAGCC CCACTGTCTG AAGACAGTTT GGAATGGTTG GTGTCTTACA
CTCGGCAGGA GAGCTGAGGT GCCGTGTCTG CTCCACAGAC TCTGTCCAGT
TAGAGTCAGT GAGCTGAGTG AGGCAGAGCA TGCCATGCGC AGTAGACCAA
AGCCATTCTC CCTCCTGCAG AATCCACGTG CCTTTGCACA CACAGCGCTA
TTTGTCCCAG GACTGTTGAT GTAGCTCAGC ATTTAAAATT CTACTTGGTA
GCAAAGCTCA CGTTCCCAAC GACTGCATGC ATACACACCA GATACTCCAA
TCCTGCCCCG TGGCCTTGTG TCCAAAGACC TTAAGCCTTG GTTGATGAAA
GAGCCAAAGA CATATGGGAC TTTTCCACCC GTTTTCTGGA TGTTGAAGTT
TGCTTAGGTG AAAAGAAGTG TCTTCCAAAG ACATGGTGGT CATAGCAAGC
AGAGAGCCTG CAGCACTTTA AACAGGGTGC AGCTAGAGTG ACAAACCAGA
GGGCCTGTGG GTTTCCGTTT TTATATGGAA TAAACACACA TTACTACAGG
ACCCTTCTGG GATGAGGTAA ACATTCAAGA TCCTCTAATC TGGAGCTTGG
AAGTATAGTG AAGTGTTTAC ATTTGAAGAA GAGTTTAGTC TGAGGTCAAA
CCTTGTCAGG CAGGGTCTCA GTCACCTGCC CGTGGAATTG GTGTATTAAA
AGAACGTTGA AGCCCCAACT TGGGATGCCA GGCTTTGTCC CCTGAGCCTT
TTCAGAACAT CAACACTGGC CGCTTCCCAG GGAGACTTAG GGAGAGCATT
ATAGATAGCT TTGGGTGCAC TCCAGGGGCT TCTGTACAGC TTGAGAGGGG
AGCCTCCCTT TCCTGAAACA GCTGTCACGT CAGCTGCCTT GTGAGGACAG
ATTTCGGTCC TTCCAGATCG CCATATGTTT AAAGTAAATC CGGAAGCCCT
AGTCTTTAGG TGAAGTCTTT TGGGTTTGAG CATTGCAGGT GACAAAGAAC
ACACACTGGT AGATGTGTCC AGCCCTCAGG CTTGTCTTTC ATTCTGTCGG
CAAAAAGGCA ACAGGCCAGC GATATGACTC AGTGGGTAAA GGTGCTTGCT
TTCCAGCACA AGGGCCTGAG TTCCATCCCT GGACCCCACA ACTCCGTTTT
CAGGAATGTC AGTGTCCTGT GTGGATAATG AGACGGACAC TTGCTTTTTC

FIG. 7C

ATTGCAGAGT ATGGAAGAGG ctcgagcagt gtggttttgc aagaggaagc
aaaaagcctc tccacccagg cctggaatgt ttccacccaa
tgtcgagcag tgtggttttg caagaggaag caaaaagcct
ctccacccag gcctggaatg tttccaccca atgtcgagca
aaccccgccc agcgtcttgt cattggcgaa ttcgaacacg
cagatgcagt cggggcggcg cggtcccagg tccacttcgc
atattaaggt gacgcgtgtg gcctcgaaca ccgagcgacc
ctgcagccaa tatgggatcg gccattgaac aagatggatt
gcacgcaggt tctccggccg cttgggtgga gaggctattc
ggctatgact gggcacaaca gacaatcggc tgctctgatg
ccgccgtgtt ccggctgtca gcgcaggggc gcccggttct
ttttgtcaag accgacctgt ccggtgccct gaatgaactg
caggacgagg cagcgcggct atcgtggctg gccacgacgg
gcgttccttg cgcagctgtg ctcgacgttg tcactgaagc
gggaagggac tggctgctat tgggcgaagt gccggggcag
gatctcctgt catctcacct tgctcctgcc gagaaagtat
ccatcatggc tgatgcaatg cggcggctgc atacgcttga
tccggctacc tgcccattcg accaccaagc gaaacatcgc
atcgagcgag cacgtactcg gatggaagcc ggtcttgtcg
atcaggatga tctggacgaa gagcatcagg ggctcgcgcc
agccgaactg ttcgccaggc tcaaggcgcg catgcccgac
ggcgaggatc tcgtcgtgac ccatggcgat gcctgcttgc
cgaatatcat ggtggaaaat ggccgctttt ctggattcat
cgactgtggc cggctgggtg tggcggaccg ctatcaggac
atagcgttgg ctacccgtga tattgctgaa gagcttggcg
gcgaatgggc tgaccgcttc ctcgtgcttt acggtatcgc
cgctcccgat tcgcagcgca tcgccttcta tcgccttctt
gacgagttct tctgagggga tcggcaataa aaagacagaa
taaaacgcac gggtgttggg tcgtttgttc ggatccccca tcgaattcCT
GCAGGT GATGACTGTG CGCTGCTTGA GGAGAGAAAG GGCAGGTGAC
AGGAGATGGG TACTAAGGAG GCAGGGACTT AGACAGCTGG

FIG. 70

GGAAGGGGGC	GTATCTTTTA	CGTGAGACAC	AGACAGATCA
TACAGCTCAG	AACTGTTCCC	AGTCCAGGTC	TGTGTGGCCT
CTGCACATCC	ATGACTCAGC	AGCACGAGGT	GAACAAGGAT
GATGTCAGCT	AACACACTAA	CTAGACAGAG	AAAAATCCAC
AAGGCCTGAC	CCCTACACAA	AGAACCATAG	TGATGCAGGA
AGGTCGAGAT	GGGAGGGGTG	GCCTTCTGTT	TGTCCAGTGC
CAGAAGGTCA	GCCTGAAAGC	ATACATACAG	GTGGCATTAT
GCGGACAGAA	GAGACTAGAT	TTAAATATGT	ATAAGCAAAT
ACATACACAC	AGGCAACAGC	AACTAATGAA	AAGAGAAGCC
ATGAACTTGA	AGGAGAGCAG	AGAGGGGTAT	ATGGGAGGAA
GGAAAGGGAC	AGGAAAAAAT	GCTGTGGTTA	ACTAATAATC
CCAAAAATAA	AATAAAAAAA	ATGATGATCA	ACTCTTCAGG
TTGAGTGATT	TTCCTCAGGT	TTCTCTATAG	AAAAGAAGGA
ACTATTTGGC	CCTGGGCTGG	TCTTAAAACT	AGCGTCTACA
GAGGTCCTCC	TGCCTGGTTG	CCATCCTCCA	GCACTCTCCC
TAACAGCAGT	TCATTTACTT	AGATTCTGTT	TGGTTTACTT
TTGAGACAAA	GGCTTGTCTT	GACTCTTGGC	CCTCCTGCCT
CTGCCTTCCA	AGGGCTGGGG	ATGTCAGTGT	GTATTGCTGT
ACTTGGCCAT	GTGGTGGTTT	GAATAAGCGC	AGGCCCCCAC
AGTTTCACAT	ATCTGAATGC	TTAGATGTGG	GGGAGTGGCA
TTATTTGAGA	AGGGTTAGGA	GGCTCAGGAT	TAGCCTTGTT
GGAGGAAGTA	TGTTGTTGGA	GGGTGGGGCT	TTAAGCCCAT
GCCAGGCCCA	GGGTCTGTCT	CTTGGTCTGC	AAGTCAGGAT
GTAGCTCTCG	GCTACTGCTC	CAGCACCAAA	GTGCTGCCCT
GCTCCCTGCT	AAGCTGATAG	TGAGCTAAAC	CTCTGAAACC
TCAGGCAAGC	CCCCAGTTAA	ATGCTTTCCT	TTCTAAGAGT
TGCTTTCCTC	ATGGTGTCTC	TTCACAGCAA	CAGAGCAGGG
ACTAAGACAG	GCAACAACTC	TCACTTTTTA	AAACCTAAAG
TCAGCCACTG	GCTGACCCTA	GCCTGTGGCC	ATGCTCGTTT
CGTAAATAAG	TCTCATTAGA	GCCACAGCTA	TGGGTTACTC
TTGCAAGGCT	GTTCACCCCA	CTGGAGTGCC	AGGGTAGAAA

FIG. 7E

AAGCATGAGA GCCTTTGACA GCTGTATGTG AGGACACAGG
CTCTGGCCTG GAAACAGGAT GAGCTGCCGG CAACCTGGGG
TGCCGACTCA CCCCAGTCTG CGATTCCTTT CTTCCCAGGT CATCAAGCAG
TTTCGCGATG AGGAGCTTGA ACACCACGAC ACAGGCCTGG ACCACGATGC
AGAGCTGGTA GGGCCAACTC TTCTTGTGCT GCTCTCGGGC CATTTTAAAG
GTTGTGGGGG ACAAAGGTTT CTGTTCCCAA AAGGAGACAT
TTGAAAGTAC AGGTCAGAAG GCAGGGAAAC GGGTACTTGA
CAGAAAGCAC CCAAGCTCAG CCTTGGTCCA TGGTGAGGCT
CCTGTGTCCT GCTCTGTTAC TAACACAAGA AACAACCCAG
CAGTTCAGTG TCCATAGATG CTTCTAGAAT TTCAAATGGC
TTTTGTTTCA AATTAAATCA TTTCCCARAT CCTCTTTTTA
TCCAGAGGAG CCCAAACCCT GCCCTACCAG TGAGTCCAGG
TCTGAACATC TGAAAATAGA TGCATCTCGT GGGGGTTTCC
TTGCTGTTTG TTTAGGGGCT GGCATTGAAT CCAGGGCCTT
GCTAGGCAAG CGCTCTACCA CTTAACAGAC CACTTGCCCG
TTTGCTTATT TTCCCAGCTC AGGGTGCCGC CGTGCATGTT
AGACAATACT CTACCATCTA GTACATCGCA GCCTTTTGTT CTCCGCAGGC
TCCCGCGTAT GCCTTGTTGA AGAGGATTAT CCAGGCCGGA TGCAGTGCAG
CCATATATTT ATCAGAAAGG TTTTAGAGTA TGTCTATTGA TCCATTTCTA
GAAAAGATGG TCGTAACTTA AGGAGTGATG TTTGTGGAGG AGGTGCTGTA
CAGTTATCAC TGTGTGTGTT TTGTTAATAC AAAAGGCCGG GTTTGGGGCT
TGTGTTTGTC AATAAACTCT TTGGCGCTGG ATTCCTTGGT TTTCTTGTGC
TGTGAGGTTG GCAGTTAACT AACTCTGCTC ACCTTACAGT
ACCTGCAGCT GGTCTTCCCT TGGTCTTATA GTTAATTTGG
GCCTAAGACA TCAAGAACAA ACCATTCGTC AGTTAACAGG
AATCCTTTTT TAAAGATTTA TTTTACTTCT ATTTCTAGAG
TTTAAAAACA TTAGACTGTA TAAGATGGGC TAAGCAAGAC

TGGGAAGTCT CTCGAGGGAG GTGCTGTGCA TTCTGATGTC
AGCATGATGC CGCAAAGCAC TGTGGTAGCT ATGGCTCCTG
AAAATCCTCA CCCAGAGTCG ATGGTAGGAG GTGGTAAATC
CCTCACCCCA GAGGAGACAC CTGAAGGGAG AGGAGGCTGG
GAGGTGGCAG ATAAGGGGCA GAGACCTCAG GAGTGGGGTT

FIG_7F

AGTGCCCTTA	TAGAAACGAG	GCCTAGGGAG	ACCCAGTCTG
TTCCACATCA	CTGGACACCA	ACCTGTTGGC	ACCCTGATAT
TGGACTTCAT	AGCCTCCAGA	ACTGCAAACA	AGTTTTTGTT
GTTCATGAGC	TCCTGAGCCT	ACAGTATTTT	AATAGCAGTC
CTGGCAGACT	AAGGCAGGAT	GGCATTATCC	CAATCAAAAA
TATACTTAAG	TTGGGTGTGG	TGATGCAGGC	CTGTAATCCT
AGCACCATGG	GAGGCAGAGG	CAAGAAGATC	TGCAGGAGTC
CCAGGGCTAT	CCTCAGCACA	CGTCAAGTTT	GAGGACAGCG
TACATGACAC	CCGGCCCCAG	CAAACAACCA	CAATAACATA
CAGAGCTGTG	GGTTATTTAC	AATTGAATTA	TAATTTCTGC
AAGGTCTGCT	ATCTCCAAAT	AAGCCAGACT	GACAAAAATT
TAGTATTTCT	GTGAACTATT	TTATTATTTT	AAATTTTCAA
AATATATTTA	AAGAAAAACA	AACAAACAAA	CAAAGAACCC
AGGATCAAGC	AGAGTGTGGT	GATACATGCC	TGTAATCCCA
GCCGTGGGAG	CAGAGGGAGA	GAGATCTTCA	TGAGCCAGTT
GGTTACGTAG	CAAGACCCTG	TCAAATACAA	AAGCCAAAAA
AAAAAAAAAA	AAAACCTCAG	TTCTCCTCAG	AATGTCCTTT
CAAACTTCCC	TGGGAGGCTG	AGGCAGGAGT	TAAAGGTCAG
TCTGAGCAAT	ACMGCAAGAA	AAAAAAACMA	ATGAATTTGC
AGACCAAAAT	CTGACCTAGT	TGCACTGGTC	AGTGGTCCCT
ATAGCGARCC	TGAGATGACT	GGGGCTT	

FIG. 7G

NTTAGGNTCC CGGCNGGGGG TTTCGGGGGN ATTCAAACCC AGGTTCTTTA
ACAGGGNGCA GGGAATGTTT TTCAACTTCT GAGCTCTCTC TAGCTCTAAT
TTTTTAAACA CTTTACTTCC AAAAATTTCC AGTAATAACT AGGACATACA
CCTCAACATT CTTTTATCTC TTTAGGACAG ATCTAGAAGT GGAATGCACG
GGAAAGGTTC TGAACATTTG AAGGCTTTGA GAGCCAGATT TAGGCTGAGT
ATTCCACAGG AATATTTAAG TACCCTCACT GCCGCTAAGG CCCAGTACTT
GGGCTCGTCT TAATTTTAAG TTACTGTAGT ATACTAACTT GAACACTATA
ATTATATAGA ATGGGTTAGT AGTTTCATTT ATTTTACAGT AGCTATGAAT
CAAATACATA CCCCCCCGCC AAGGGTGCAA ACTCTAGTTT TCCTAAAGCC
ACAGTCTCTA GTGATCCTAT AATAGGCACT GATTATGCCT TGCAGGTATG
GTTTTTCCCC TTATATACTT ATCTGACTTG GAAATTTTAT TTCTATTGGC
TAGATCTAGC TGTCATATTA ATGGATATGC ACTTTAAAAT GTTTAATGTA
TGCTACTAAA TTTTCCTTCC CTCAACACAC AGCTATGTTC ATCACTAATG
TGCCCTAGGC CATGAATAAT CCAGTAAAGG ATGAACAATG AAGCAAATCT
CAATATAAAA ATTGAGAAGG AACGGAAAGT AACGGGAAAC AAACTGGGAA
ACCCACAATT ACACCGAAAA CTGGCATGTT TTACCAGGTA ATTGCTGACT
TTCAGGTGTA AATCGGCTCT TAATAGAGAA AAATAATCTC CGTAACGTGG
AGGAAACAGT GACCTGCGGG TCGCCTTTCC AAGACAGGGA GAAACCCTAA
CCTAAACTGC CTCTCCAGGA CAGCTCTGCA TCAACCCTAA GAGCCGACCG
GGCGCCTTCA CTACGTTCCA ATGATCGACA GGGGGCAGAC CAAATAGAGT
ACGTGAATTG GTCATTTCTA ACCAATCGGG TTTAATCCAG GGCCTAGGGG
CGTTTCCT**CT GGCTCTCGGT CCGCGGCATC TATGCGTCAT CACCCTGAGT**
CGAGAGCACG ATTGGCGGGG CGTTTGGACC ATAGCTGCAT TGTCCGCAGC
GATGAGCGCC GCCGGAGCCA TAGCGGCTGC TTCCGTGGGA CGCCTGCGCA
CTGGTGTCCG GAGGCCCTTC TCAGGTACCG GCCGCTCGGG GTCGTGGTTC
GGCGCGGGGT TCTTCGCTGG TGACTATTTG CAGTGGAGGT CACGGATGTC
ACGGGGAGGA CGTCTATACG TCACAAGCGC GCGACATGGG GGTGGGGTTT
GTAGTACGTC TAGTTGATTG ACAGGAATGG GTGAACTTCT GCAGGATGCC
CTGCCGGGGG AACAAGTGAT TACCAGCCTG TGATGTGACG TCAGTGCAAG
GCACATCACA GTGCAACTTG AGTGTCCTGC AGTGTCCCTC CGGTCTCCAC
TCGGGACTTT CTCAAGCAAA GTAGCCTTCC GACGACAGCA TCAATCTGTT

FIG. 8A

ATAAATGCAG ATTTTCGGGT CCCCCTCATT ATCCACTGGA TTGATAGGTT
TTAGAGTTTT AAAAAGTGTG TGTGTGTGTG TGTGTGTGTG TGTGTGTGTG
TGTGTGTGTG TGCGCGCGCG CGTGCGTGCG CACAATAATT AAATTCTAGA
GAGGCCAGAA TTGGGGTTTG AATCTGCAAC TAGAGTAACA GGCAGTTTGT
GAATCCCTAT ATATGGGTGC TGGGAGCCCA ACTCAAGTCA TTTGCAAGTG
CAGTACACAT TCTTAACTGC TGAGCCTTCT TTTGAGCCGT AGAGTCTCTG
TTTTTATCAA GCCTCTCATG GGACTGTTTG TATTGCAAAA TATGGTAAGC
TTTGAATTTG GAATGGAGAG AGGTAGGTTT GGATTCAGGT CTGATTCATC
CGAGCTGCCC CAGAAAATCG TGGTCATTTT CTTGAAACTA AATCTTCAAG
CATTAGATTT CTATTTTGCC TGAAGGCAAT ATTGTTTGGA GGTTTGAGAT
GTGTTTTTGT TTAACTACAA CTTATTAAGT AATTTAATTG AAACTACATC
CTTTTGGTAA ATAATAAGCC AGAATTGCCT GCCCCCAAAT GGATGAGTAA
TCACCCCCCC CACACACACA CACCACCACC ACCACCACCA CCACCACCAA
TACCTTGAGA ACAGCTATGA AACTTCATTA GATATTGTTG TGTGTGCCTT
CCAAGGCTTG AGTCCAAGGC TGTTTTTCTT TCTGGAAGAG AAGARTGCTT
AGCAAGTGTT TGGATATTAT TCAAGACATG CCAGTTATAG AGATGTTTCC
CTTGGTGATA ATGATTCAGA AGAGACTTTT TAAGAGCCTC TTAGTATGTA
ATTTATGTGT CCATAAGCCA CTTAAAATCT TCTCATTTGC CACTTAAAAT
CTCCCAGATA CCATGGCTGG AACAGCACGC TTGAGAGCTT CTAGCTCTGC
GATTCAGCTT TATTTTAAAG TGTGTAACAA GGCAGTCAGG TCTCAGGGAT
GTGGATTTTA AGGTTCCTTG CTAACCCAGT GAACAGGTTA ACAATAAGAA
TCACTTGTTT TCATTTATGA AGTAACTTAG TTTCCTTTGT TTCATATACC
CTCATGATAA TAATAATAAT AAAAAACCCT TAAGTGTGTG TCTCCTTAAA
AAAATAAAAC TAGCCTTGCT ACTGGGTAGG TTTTAATTTG GTTTTGAGAC
AGCCTCTAGC GCTGGCTGAC CTGGACCTTG CTTGTTCACC AGGATATCCT
TCAATTCACA GAGCTCTGCC AACTCATGCT GGGATTAATA CCTATACTGA
TTTCTTAGGT AAAAGGACAA ATACTACCCT CTCCCAGTCA TTGAGTGCAG
AAGTTGTGTT TTAGAGAACA TTCCAGTGTG TTCTCAGTTA TAAAGAATCC
TGTTTATCAC ACCTCAAAAG CCAGCCATAT AAACTTGGCC CACCTGCTCA
GCTCCTTGTT ATTCTTCTTT TAAAAAAAAG ATTTATTTTA TATATGTGAA
CACACTGTAG CTGTCTTCAG ACACACCAGA AGAGGGAATC AGATCCCATT

Fig - 8B

ACAAATGGTC CTGAGCCACC ATGTAGTTGC TGGGAATTGA CCTCAGGACC
TCTGGAAGAG CAGTCAGTGC TTTTAACCGC TGAGCCACCT CCCCAGGCCC
CTTGTTATTC CTTAATATAC TTTTTAAAAA GGAGTACTGG GTTGCCTTGA
ACTTTCTTTG CTAAAAAGTA AGAGCACAAG CAAACAAGAT TGTGTTGAGA
AATACAACTG GCTCACCAAG TCTGTCTCCA GACCCTGCTT TCTGCAAGGA
GACAAGCTGG CCAGAAGCAT AAGCCCTTGA ACTTGGACAC AGAAATGCAA
CAAGTTCCTG ATTGTGTCCC ATCACTGTCC CATAAAATAT GGGCCTCAAA
CCGTAGAGCC CCACTGTCTG AAGACAGTTT GGAATGGTTG GTGTCTTACA
CTCGGCAGGA GAGCTGAGGT GCCGTGTCTG CTCCACAGAC TCTGTCCAGT
TAGAGTCAGT GAGCTGAGTG AGGCAGAGCA TGCCATGCGC AGTAGACCAA
AGCCATTCTC CCTCCTGCAG AATCCACGTG CCTTTGCACA CACAGCGCTA
TTTGTCCCAG GACTGTTGAT GTAGCTCAGC ATTTAAAATT CTACTTGGTA
GCAAAGCTCA CGTTCCCAAC GACTGCATGC ATACACACCA GATACTCCAA
TCCTGCCCCG TGGCCTTGTG TCCAAAGACC TTAAGCCTTG GTTGATGAAA
GAGCCAAAGA CATATGGGAC TTTTCCACCC GTTTTCTGGA TGTTGAAGTT
TGCTTAGGTG AAAAGAAGTG TCTTCCAAAG ACATGGTGGT CATAGCAAGC
AGAGAGCCTG CAGCACTTTA AACAGGGTGC AGCTAGAGTG ACAAACCAGA
GGGCCTGTGG GTTTCCGTTT TTATATGGAA TAAACACACA TTACTACAGG
ACCCTTCTGG GATGAGGTAA ACATTCAAGA TCCTCTAATC TGGAGCTTGG
AAGTATAGTG AAGTGTTTAC ATTTGAAGAA GAGTTTAGTC TGAGGTCAAA
CCTTGTCAGG CAGGGTCTCA GTCACCTGCC CGTGGAATTG GTGTATTAAA
AGAACGTTGA AGCCCCAACT TGGGATGCCA GGCTTTGTCC CCTGAGCCTT
TTCAGAACAT CAACACTGGC CGCTTCCCAG GGAGACTTAG GGAGAGCATT
ATAGATAGCT TTGGGTGCAC TCCAGGGGCT TCTGTACAGC TTGAGAGGGG
AGCCTCCCTT TCCTGAAACA GCTGTCACGT CAGCTGCCTT GTGAGGACAG
ATTTCGGTCC TTCCAGATCG CCATATGTTT AAAGTAAA

TCCGGAGCTAGCGAGCTCGGA**ATAACTTCGTATAATGTATGCTATACGAAGTTAT**GGCGAA
T

TC CGGAAGCCCT

FIG. 8C

AGTCTTTAGG TGAAGTCTTT TGGGTTTGAG CATTGCAGGT GACAAAGAAC
ACACACTGGT AGATGTGTCC AGCCCTCAGG CTTGTCTTTC ATTCTGTCGG
CAAAAAGGCA ACAGGCCAGC GATATGACTC AGTGGGTAAA GGTGCTTGCT
TTCCAGCACA AGGGCCTGAG TTCCATCCCT GGACCCCACA ACTCCGTTTT
CAGGAATGTC AGTGTCCTGT GTGGATAATG AGACGGACAC TTGCTTTTTC
ATTGCAG**AGT ATGGAAGAGG CCTCATCATC AGGTGTCACA GTTCGGGGAT**
GACCTTAGAC AATATTAACC GGGCAGCCGT GGATCKAATA ATTCGGGTGG
ATCACGCTGG TGAATATGGA GCAAACCGCA TCTATGCAGG GCAAATGGCT
GTGCTCGGTC GGACCAGTGT TGGCCCTGTC ATTCAGGTGG GTTCTTTCCT
GAGTCTCAGC CCAGTCTGTT GCCCTGGCAG TGTATCTGAA GCCCTCGGGC
ATCACTTTTG GCTGTGTGCT CCAAAGGGAG GCACTTGGAA CAAAGCACTT
GCTCTGTTGT CTAAAAGCAC AGATATGCAT TGACTCTGGC TGGGTGTGGT
GGTGCATGCC TATAATCCCA GCACTTGGGA GCTGGAGATA GGGTGATCGC
TGGGACTTTG AGGCCAGCCT GGTCTACATA GGAAGTTCCA GGTCAGAAAG
AAAAAAATGG AGAGAGGGGG AAAGAAAGTA AGAGAGAAAG AAATTGGGTC
TGGAAATTGG GTGTATTTGT GGTGTTAATG TTTCATTGCA GAAAAGGCTG
AAAGTCCCTC CATTAGAAGA ATGTTCCATG TGCCAGGAGG TTGTTGTAGG
CTTGTCCTAG CACAGAGTAT CAGAGAGAGG GGTTAACAGC CCCGAAGATC
TAGGTTTCCT TTCCAGATCT CTCATCTACT TCTGCGACCC TGAAGAGGTC
ACCTGACCTC TAGGTTTTCA TTTCCCTGTG TGCACACTAG CCTGGTAACC
CCCACCTCCC TGGGTCTGGC TGGGGAATAA ACCAGATCCT GTTGTCACCA
TGACACATGG CAGCTTAGAT CCCCGCAGAT CCCAGTCCCC AGTGCTCATC
CCATGTGTAA GATGGTGGGT GTCTGCTTGT GGCCCTGCAC AACTCTCCTG
TGAAGAGTCC TTCATGCCAG GAGAATGCCT CTCATTGGCT GTCCTGTTTT
CTATTGAGAA CATTCTGCGA GTTTTCAGGA CACAGTTTTG TTGTTGTTGT
TGTTGTTAGT TTTTTTCATT ATTTTCTCTT GTGGTTGCTT GAGCCGGTGG
CTCAGAACCT GGAGTTCTAT ATGGCTCACT ATGCAAGCTG ATTGTGTGGT
CACTGAGGTG TGTGTGGCTC TGGAGGTGGA ACACTTAGCT CTGTCCAAGG
CCTTGGTTCT TCATTTACTT GGCAGGTGCT TTTCTTTTTT GAGAGATTCT
TCTGTGGTTT GCTTTTATCT CATGGATATT TAAGGGGATG GAAGACAGCA
TTGCACCAAT TCCTTCTTAC CTCTTGTGTG CTCAGCGAGC CGTGTCCCTG

FIG. 8D

TGATGCCTCT TTTTATGTTT CCCCCCCCAG **AAAATGTGGG ATCAAGAGAA**
GAACCATTTG AAAAAGTTCA ACGAGTTGAT GATTGCATTC AGGGTCCGAC
CTACGGTTTT GATGCCCTTG TGGAACGTGG CAGGCTTTGC CCTGGGTATG
TGTCTGTCCA GCAGCCGCTT GGGCTCTAAT GATGGGCTGT TCCTGCCTCT
GGAGCCCTTG TCAGGGCTGC ATCCAACCTT TTAAAATTTA CTGTGTGTTT
TCCTAAAGCT AAATTGAAGT TGATGAAGTT GATKGAATTT TCTTTGTTTA
TATTACTTTA AGATAGAGCC ATCACTTTTA TAAATAGATG GTATAATAAC
TCACAGAGGG AAGCTAGGAT CGTGCCACCA CTGCCAGAAT CCATGTCCTG
AGGATCCTGA CCTCAGAGCA ACCTGACTGT GAGAGTGCTG GTGCCCACCT
TTAACCCCAG CACTCGGGAG ACAGAGGCAG GCAGATCTCT GAGTTTGAGG
CCAGCATGGT CTACAAATCG AGTTCCATAA CACACACACA CACACACACA
CACACACACA CACACACACA CACACACAGA AGAACAGCAG AGAACCCAGA
TAGCACTCTC AGCTCTCTGC AGAGGGTCAA GTCTCATTGA GCCCATGTGT
TAACTTGGGT TTCATAGTGA GATCTTGTCT CAAACAAAAC AAACCAACCA
AATAAAATAA AAATCCATTC AGAAAGAGCT TTGTGACTGG CATCTGATAT
AAGCTCCAGC CGCTTCTCAA CTAGGCGTGA CTGTTTCAAG GGATTCATGG
GAATATCTGA ATGCCCAGTG GTCATGATCA GCAGGTACTG CTGACATCCA
GAGGGTGGAT ATCGGGTGCC ATTAGACACC CTGAGAAACA CGTCACAGCC
CTCCCAGAGA GTTACCAACC CAGGTGTCAG GACGCCTCAC AGATGACCAG
CAGCCTGTGG CTTGACTTTG TTTGTTTGAC GGTTGCAG**GG GCAGGAACTG**
CCTTGCTGGG GAAGGAAGGA GCAATGGCCT GCACCGTGGC GGTAGAAGAG
TCTATCGCTA ATCACTACAA CAACCAGATC CGCATGCTGA TGGAAGAGGA
CCCTGAGAAG TATGAGGAGC TGCTGCAGGT GATGACTGTG CGCTGCTTGA
GGAGAGAAAG GGCAGGTGAC AGGAGATGGG TACTAAGGAG GCAGGGACTT
AGACAGCTGG GGAAGGGGGC GTATCTTTTA CGTGAGACAC AGACAGATCA
TACAGCTCAG AACTGTTCCC AGTCCAGGTC TGTGTGGCCT CTGCACATCC
ATGACTCAGC AGCACGAGGT GAACAAGGAT GATGTCAGCT AACACACTAA
CTAGACAGAG AAAAATCCAC AAGGCCTGAC CCCTACACAA AGAACCATAG
TGATGCAGGA AGGTCGAGAT GGGAGGGGTG GCCTTCTGTT TGTCCAGTGC
CAGAAGGTCA GCCTGAAAGC ATACATACAG GTGGCATTAT GCGGACAGAA
GAGACTAGAT TT

FIG. 8E

TCGAGG TCGACGCATG CCTGTACATC CGGAGACGCG TCACGGCCGA
AGCTAGCGAA TTCCGATCAT ATTCAATAAC CCTTAATA**TAACTTCGT ATAATGTATG**
CTATACGAAG TTATTAGGTC TGAAGAGGAG TTTACGTCCA GCCAAGCTAG
CTTGGCTGCA GCCCGGGGGA TCCACTAGTT CTAGAGCGGC C

AAATATGT ATAAGCAAAT ACATACACAC AGGCAACAGC
AACTAATGAA AAGAGAAGCC ATGAACTTGA AGGAGAGCAG AGAGGGGTAT
ATGGGAGGAA GGAAAGGGAC AGGAAAAAAT GCTGTGGTTA ACTAATAATC
CCAAAAATAA AATAAAAAAA ATGATGATCA ACTCTTCAGG TTGAGTGATT
TTCCTCAGGT TTCTCTATAG AAAAGAAGGA ACTATTTGGC CCTGGGCTGG
TCTTAAAACT AGCGTCTACA GAGGTCCTCC TGCCTGGTTG CCATCCTCCA
GCACTCTCCC TAACAGCAGT TCATTTACTT AGATTCTGTT TGGTTTACTT
TTGAGACAAA GGCTTGTCTT GACTCTTGGC CCTCCTGCCT CTGCCTTCCA
AGGGCTGGGG ATGTCAGTGT GTATTGCTGT ACTTGGCCAT GTGGTGGTTT
GAATAAGCGC AGGCCCCCAC AGTTTCACAT ATCTGAATGC TTAGATGTGG
GGGAGTGGCA TTATTTGAGA AGGGTTAGGA GGCTCAGGAT TAGCCTTGTT
GGAGGAAGTA TGTTGTTGGA GGGTGGGGCT TTAAGCCCAT GCCAGGCCCA
GGGTCTGTCT CTTGGTCTGC AAGTCAGGAT GTAGCTCTCG GCTACTGCTC
CAGCACCAAA GTGCTGCCCT GCTCCCTGCT AAGCTGATAG TGAGCTAAAC
CTCTGAAACC TCAGGCAAGC CCCCAGTTAA ATGCTTTCCT TTCTAAGAGT
TGCTTTCCTC ATGGTGTCTC TTCACAGCAA CAGAGCAGGG ACTAAGACAG
GCAACAACTC TCACTTTTTA AAACCTAAAG TCAGCCACTG GCTGACCCTA
GCCTGTGGCC ATGCTCGTTT CGTAAATAAG TCTCATTAGA GCCACAGCTA
TGGGTTACTC TTGCAAGGCT GTTCACCCCA CTGGAGTGCC AGGGTAGAAA
AAGCATGAGA GCCTTTGACA GCTGTATGTG AGGACACAGG CTCTGGCCTG
GAAACAGGAT GAGCTGCCGG CAACCTGGGG TGCCGACTCA CCCCAGTCTG
CGATTCCTTT CTTCCCAG**GT CATCAAGCAG TTTCGCGATG AGGAGCTTGA**
ACACCACGAC ACAGGCCTGG ACCACGATGC AGAGCTGGTA GGGCCAACTC
TTCTTGTGCT GCTCTCGGGC CATTTTAAAG GTTGTGGGGG ACAAAGGTTT
CTGTTCCCAA AAGGAGACAT TTGAAAGTAC AGGTCAGAAG GCAGGGAAAC

FIG. 8F

GGGTACTTGA CAGAAAGCAC CCAAGCTCAG CCTTGGTCCA TGGTGAGGCT
CCTGTGTCCT GCTCTGTTAC TAACACAAGA AACAACCCAG CAGTTCAGTG
TCCATAGATG CTTCTAGAAT TTCAAATGGC TTTTGTTTCA AATTAAATCA
TTTCCCARAT CCTCTTTTTA TCCAGAGGAG CCCAAACCCT GCCCTACCAG
TGAGTCCAGG TCTGAACATC TGAAAATAGA TGCATCTCGT GGGGGTTTCC
TTGCTGTTTG TTTAGGGGCT GGCATTGAAT CCAGGGCCTT GCTAGGCAAG
CGCTCTACCA CTTAACAGAC CACTTGCCCG TTTGCTTATT TTCCCAGCTC
AGGGTGCCGC CGTGCATGTT AGACAATACT CTACCATCTA GTACATCGCA
GCCTTTTGTT CTCCGCAGGC **TCCCGCGTAT GCCTTGTTGA AGAGGATTAT**
CCAGGCCGGA TGCAGTGCAG CCATATATTT ATCAGAAAGG TTTTAGAGTA
TGTCTATTGA TCCATTTCTA GAAAAGATGG TCGTAACTTA AGGAGTGATG
TTTGTGGAGG AGGTGCTGTA CAGTTATCAC TGTGTGTGTT TTGTTAATAC
AAAAGGCCGG GTTTGGGGCT TGTGTTTGTC AATAAACTCT TTGGCGCTGG
ATTCCTTGGT TTTCTTGTGC TGTGAGGTTG GCAGTTAACT AACTCTGCTC
ACCTTACAGT ACCTGCAGCT GGTCTTCCCT TGGTCTTATA GTTAATTTGG
GCCTAAGACA TCAAGAACAA ACCATTCGTC AGTTAACAGG AATCCTTTTT
TAAAGATTTA TTTTACTTCT ATTTCTAGAG TTTAAAAACA TTAGACTGTA
TAAGATGGGC TAAGCAAGAC TGGGAAGTCT CTCGAGGGAG GTGCTGTGCA
TTCTGATGTC AGCATGATGC CGCAAAGCAC TGTGGTAGCT ATGGCTCCTG
AAAATCCTCA CCCAGAGTCG ATGGTAGGAG GTGGTAAATC CCTCACCCCA
GAGGAGACAC CTGAAGGGAG AGGAGGCTGG GAGGTGGCAG ATAAGGGGCA
GAGACCTCAG GAGTGGGGTT AGTGCCCTTA TAGAAACGAG GCCTAGGGAG
ACCCAGTCTG TTCCACATCA CTGGACACCA ACCTGTTGGC ACCCTGATAT
TGGACTTCAT AGCCTCCAGA ACTGCAAACA AGTTTTTGTT GTTCATGAGC
TCCTGAGCCT ACAGTATTTT AATAGCAGTC CTGGCAGACT AAGGCAGGAT
GGCATTATCC CAATCAAAAA TATACTTAAG TTGGGTGTGG TGATGCAGGC
CTGTAATCCT AGCACCATGG GAGGCAGAGG CAAGAAGATC TGCAGGAGTC
CCAGGGCTAT CCTCAGCACA CGTCAAGTTT GAGGACAGCG TACATGACAC
CCGGCCCCAG CAAACAACCA CAATAACATA CAGAGCTGTG GGTTATTTAC
AATTGAATTA TAATTTCTGC AAGGTCTGCT ATCTCCAAAT AAGCCAGACT
GACAAAAATT TAGTATTTCT GTGAACTATT TTATTATTTT AAATTTTCAA

FIG_8G

AATATATTTA AAGAAAAACA AACAAACAAA CAAAGAACCC AGGATCAAGC
AGAGTGTGGT GATACATGCC TGTAATCCCA GCCGTGGGAG CAGAGGGAGA
GAGATCTTCA TGAGCCAGTT GGTTACGTAG CAAGACCCTG TCAAATACAA
AAGCCAAAAA AAAAAAAAAA AAAACCTCAG TTCTCCTCAG AATGTCCTTT
CAAACTTCCC TGGGAGGCTG AGGCAGGAGT TAAAGGTCAG TCTGAGCAAT
ACMGCAAGAA AAAAAAACMA ATGAATTTGC AGACCAAAAT CTGACCTAGT
TGCACTGGTC AGTGGTCCCT ATAGCGARCC TGAGATGACT GGGGCTT

FIG_8H