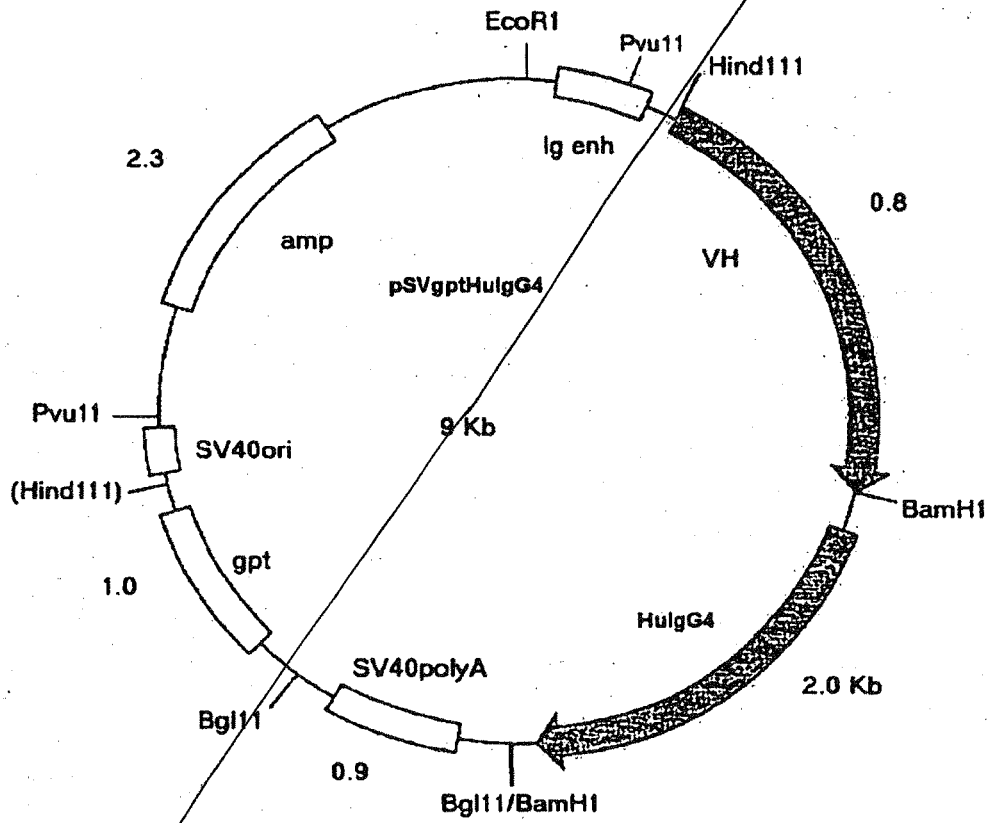


FIG 1
(example 2)

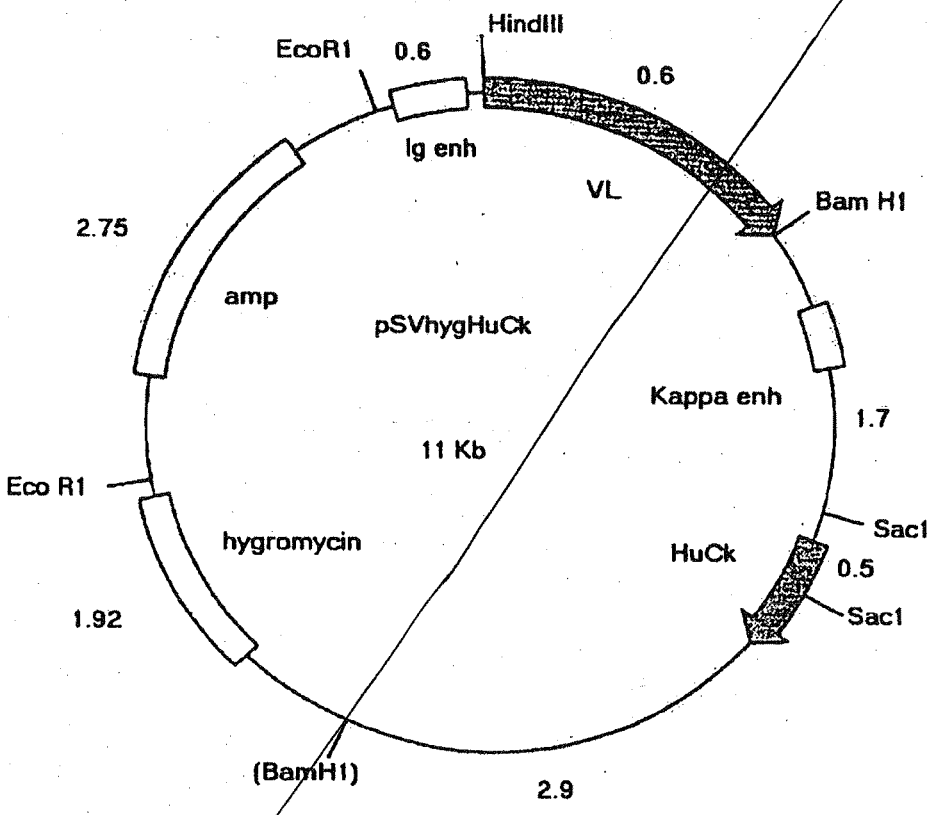


FIG 2(Example 2)

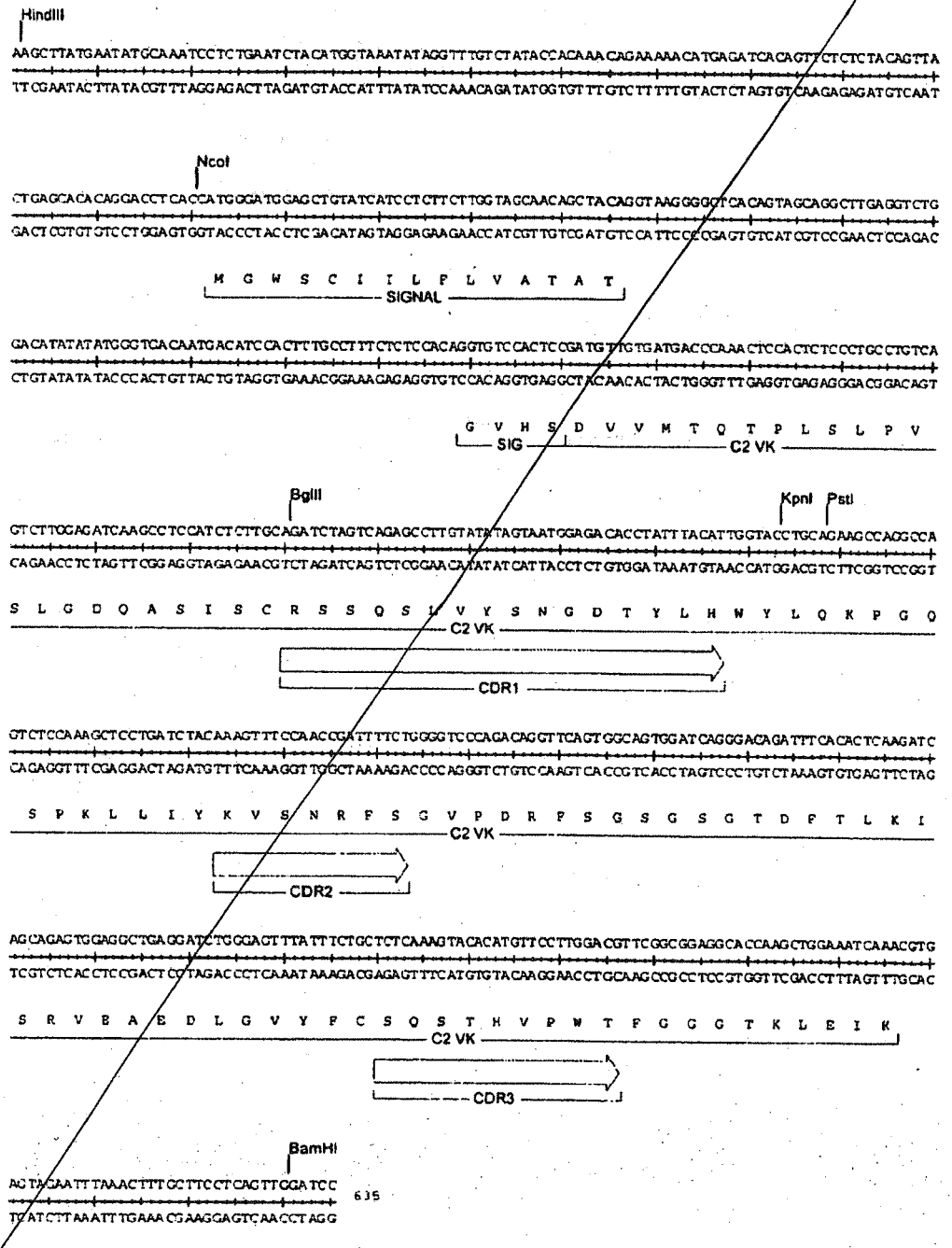


FIG 3
(Example 2)

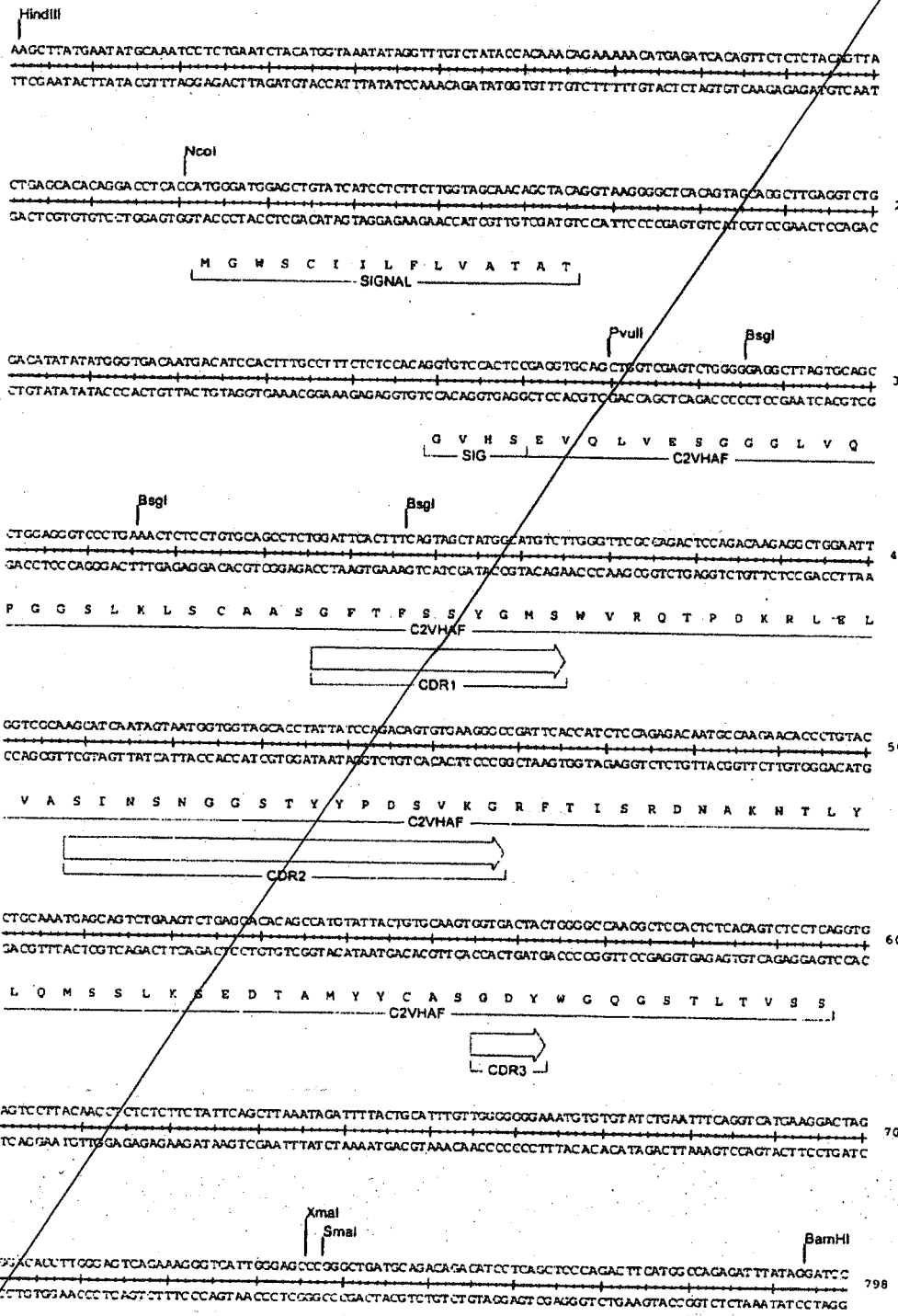


FIG 4
(Example 2)

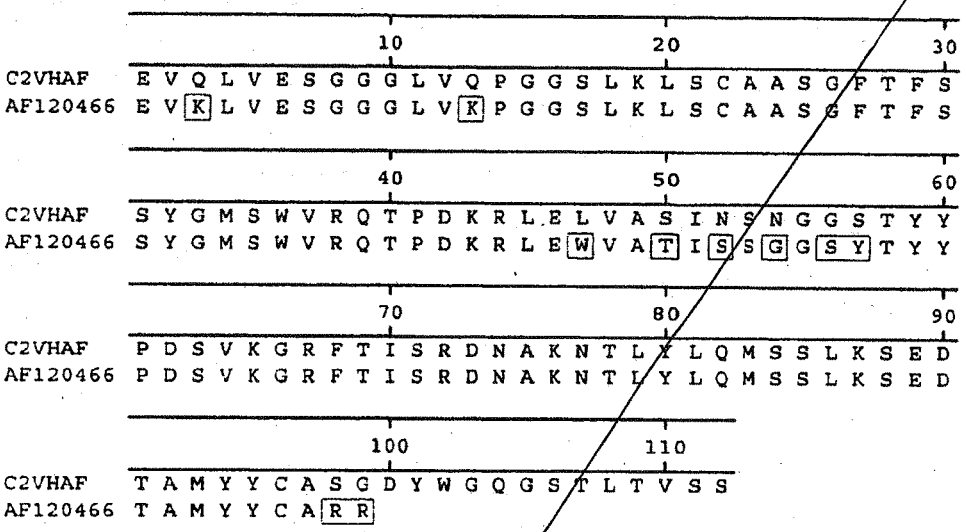


FIG 5
(Example 5.2)

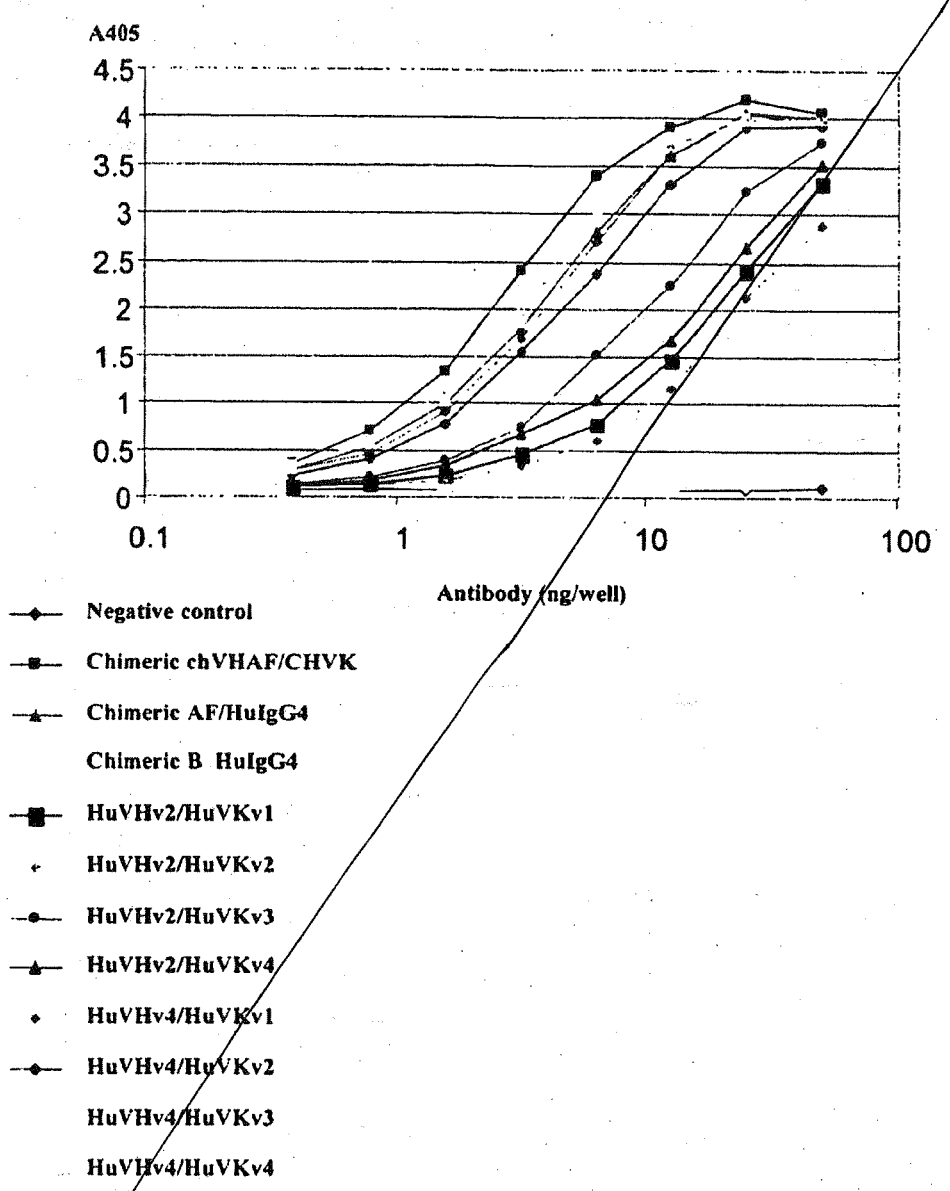


FIG 6
(Example 8)

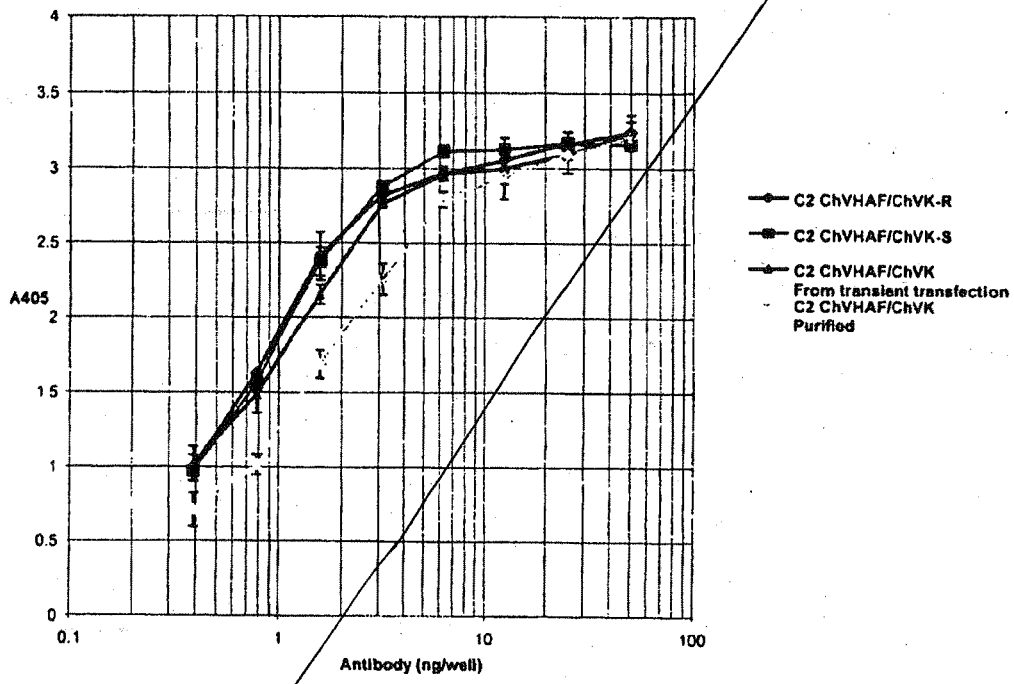


FIG 7
(Example 9)

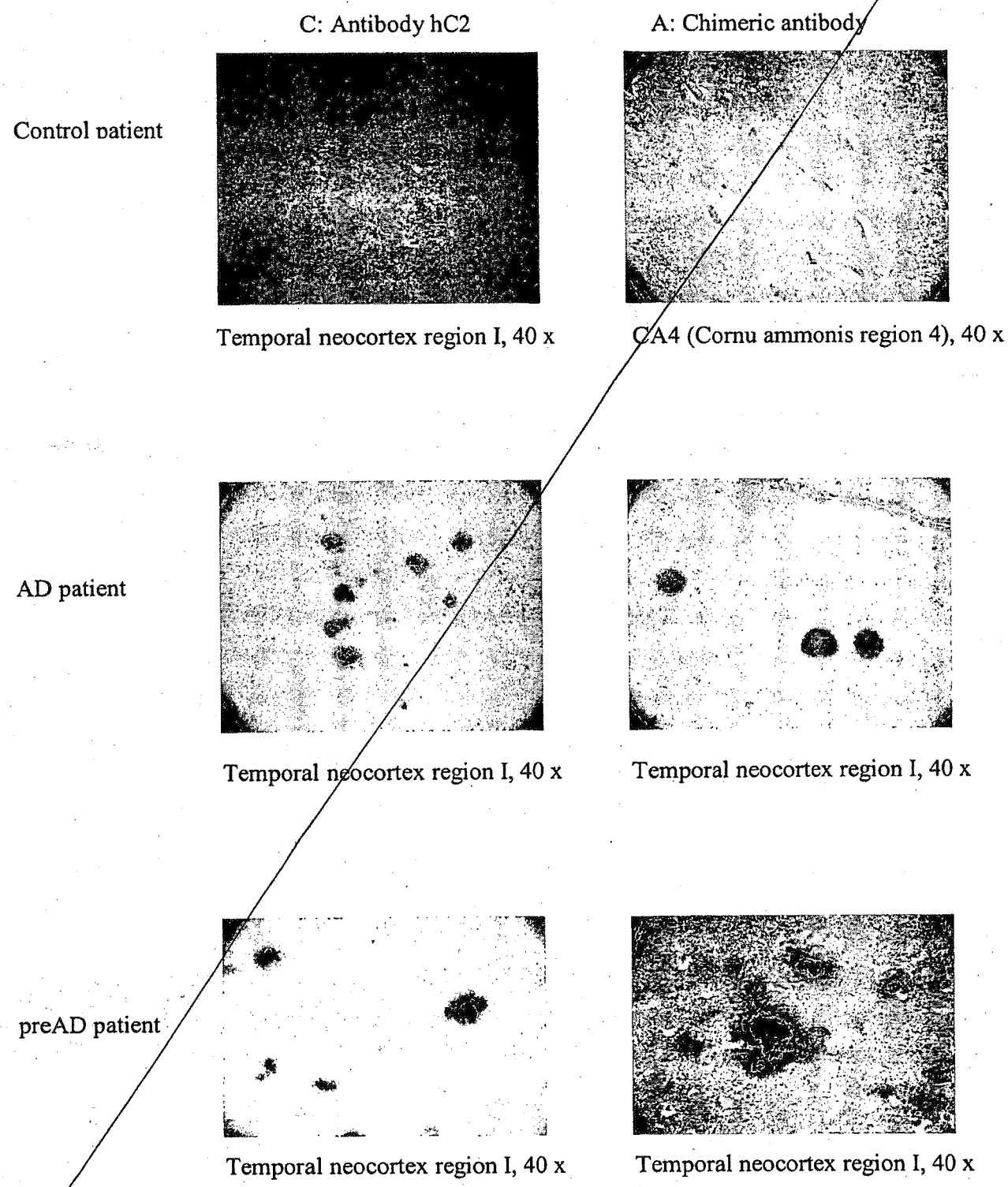
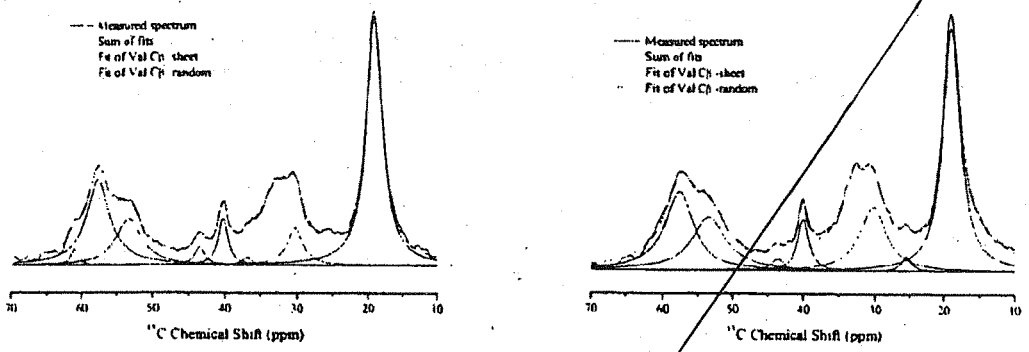


FIG. 8
(Example 11)

A)



B)

Resonance	PBS			Mouse C2		
	δ ISO (ppm)	FWHH (Hz)	% Integral Intensity	δ ISO (ppm)	FWHH (Hz)	% Integral Intensity
Val Cβ -sheet	32.60	479	81.7	33.09	366	53 5
Val Cβ -random	30.27	200	18.3	30.27	340	46.5

A) Comparison of ^{13}C CPMAS spectra and fits for U-^{13}C Tyr10 and Val12 labelled amyloid β1-42 fibres incubated with PBS (left; served as control) or ACI-7-C2 (right) for 24 hrs and then lyophilised. The fits for the two conformations of Val12 Cβ are shown in green (sheet) and blue (random coil). The peak at c33 ppm corresponds to the beta sheet conformation of the fibres whilst that at 30 ppm is a result of random coil conformation.

B): Comparison of the fitted parameters for the two conformations of Val 12 Cβ. The fitted chemical shifts for the two conformations are quite similar but the integral intensities are very different, reflecting a reduction in the original beta sheet conformation by approx 35% (1-(53.5/81.7)). This is in very close agreement with the value we obtained from the fluorescence measurement.

FIG 9
(Example 12)

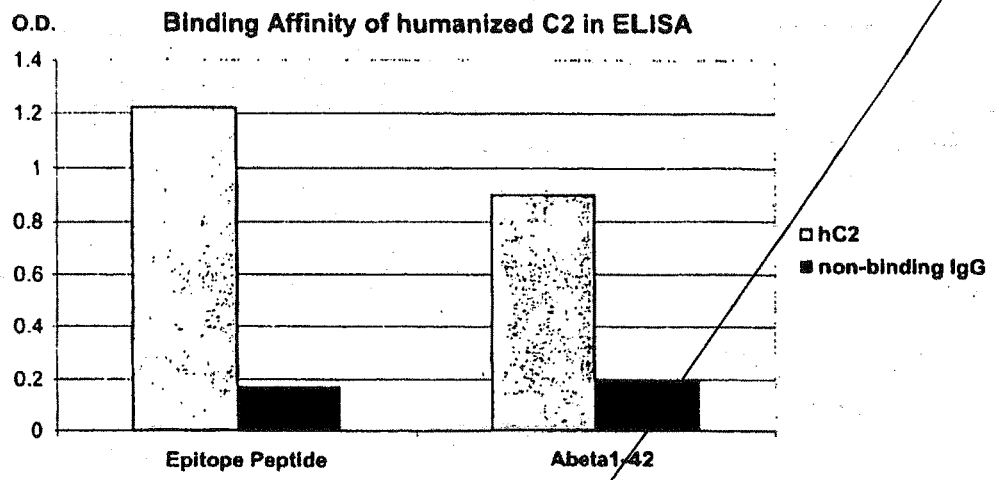


FIG 10
(Example 12)

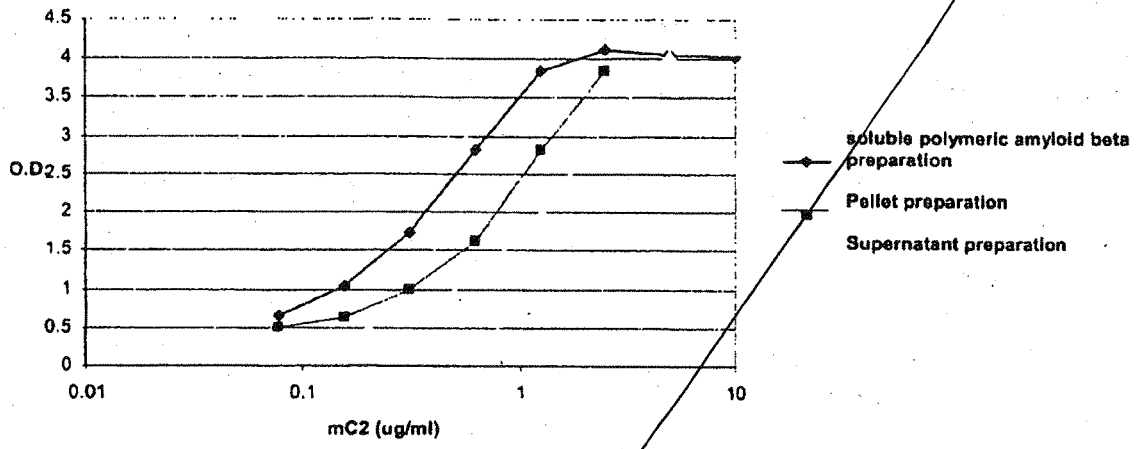


FIG 11
(Example 13)

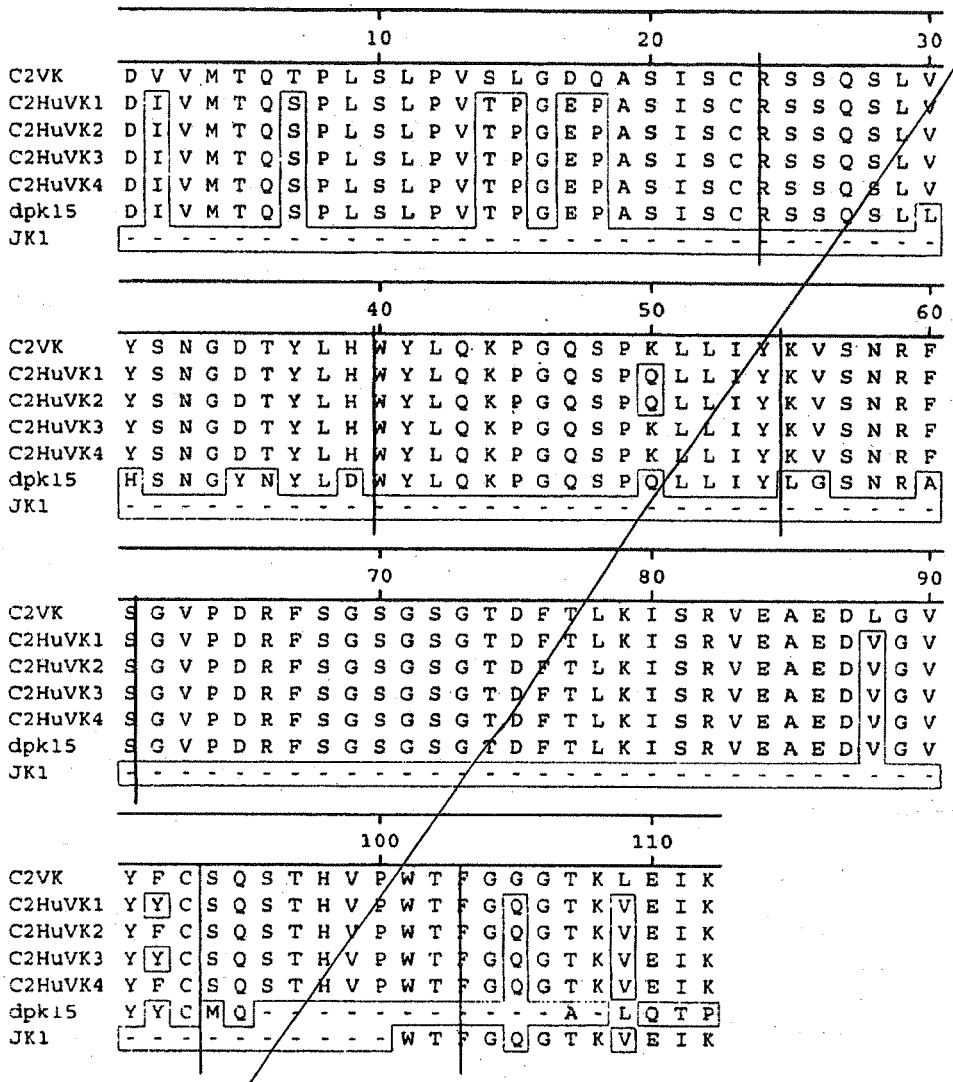

10 20 30
C2VK D V V M T Q T P L S L P V S L G D Q A S I S C R S S Q S L V
C2HuVK1 D I V M T Q S P L S L P V T P G E P A S I S C R S S Q S L V
C2HuVK2 D I V M T Q S P L S L P V T P G E P A S I S C R S S Q S L V
C2HuVK3 D I V M T Q S P L S L P V T P G E P A S I S C R S S Q S L V
C2HuVK4 D I V M T Q S P L S L P V T P G E P A S I S C R S S Q S L V
dpk15 D I V M T Q S P L S L P V T P G E P A S I S C R S S Q S L L
JK1
40 50 60
C2VK Y S N G D T Y L H W Y L Q K P G Q S P K L L I Y K V S N R F
C2HuVK1 Y S N G D T Y L H W Y L Q K P G Q S P Q L L I Y K V S N R F
C2HuVK2 Y S N G D T Y L H W Y L Q K P G Q S P Q L L I Y K V S N R F
C2HuVK3 Y S N G D T Y L H W Y L Q K P G Q S P K L L I Y K V S N R F
C2HuVK4 Y S N G D T Y L H W Y L Q K P G Q S P K L L I Y K V S N R F
dpk15 H S N G Y N Y L D W Y L Q K P G Q S P Q L L I Y L G S N R A
JK1
70 80 90
C2VK S G V P D R F S G S G S G T D F T L K I S R V E A E D L G V
C2HuVK1 S G V P D R F S G S G S G T D F T L K I S R V E A E D V G V
C2HuVK2 S G V P D R F S G S G S G T D F T L K I S R V E A E D V G V
C2HuVK3 S G V P D R F S G S G S G T D F T L K I S R V E A E D V G V
C2HuVK4 S G V P D R F S G S G S G T D F T L K I S R V E A E D V G V
dpk15 S G V P D R F S G S G S G T D F T L K I S R V E A E D V G V
JK1
100 110
C2VK Y F C S Q S T H V P W T F G G G T K L E I K
C2HuVK1 Y Y C S Q S T H V P W T F G Q G T K V E I K
C2HuVK2 Y F C S Q S T H V P W T F G Q G T K V E I K
C2HuVK3 Y Y C S Q S T H V P W T F G Q G T K V E I K
C2HuVK4 Y F C S Q S T H V P W T F G Q G T K V E I K
dpk15 Y Y C M Q A L Q T P
JK1 W T F G Q G T K V E I K

FIG 12.

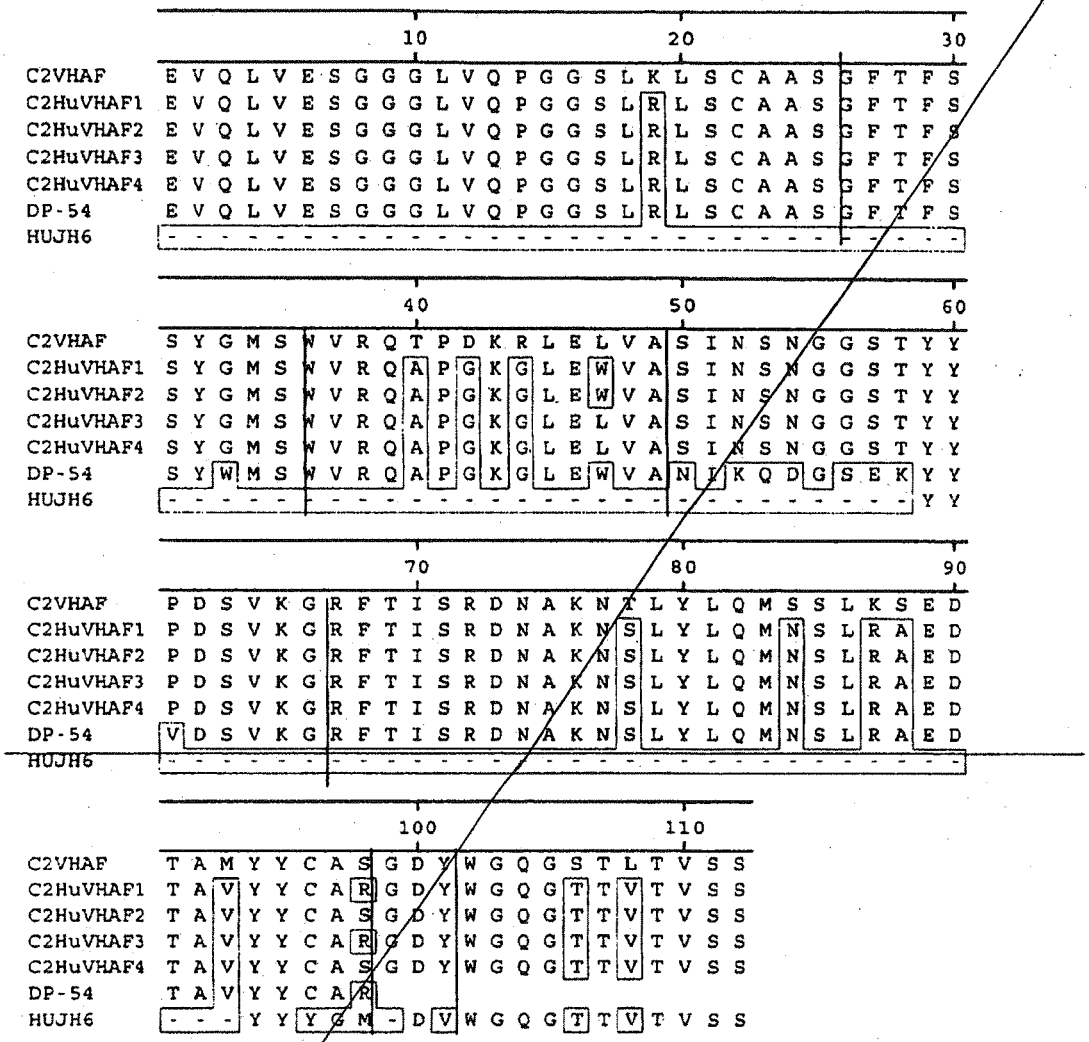

10 20 30
C2VHAF E V Q L V E S G G G L V Q P G G S L K L S C A A S G F T F S
C2HuVHAF1 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S
C2HuVHAF2 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S
C2HuVHAF3 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S
C2HuVHAF4 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S
DP-54 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S
HUJH6 -
40 50 60
C2VHAF S Y G M S W V R Q T P D K R L E L V A S I N S N G G S T Y Y
C2HuVHAF1 S Y G M S W V R Q A P G K G L E W V A S I N S N G G S T Y Y
C2HuVHAF2 S Y G M S W V R Q A P G K G L E W V A S I N S N G G S T Y Y
C2HuVHAF3 S Y G M S W V R Q A P G K G L E L V A S I N S N G G S T Y Y
C2HuVHAF4 S Y G M S W V R Q A P G K G L E L V A S I N S N G G S T Y Y
DP-54 S Y W M S W V R Q A P G K G L E W V A N I K Q D G S E K Y Y
HUJH6 - Y Y
70 80 90
C2VHAF P D S V K G R F T I S R D N A K N T L Y L Q M S S L K S E D
C2HuVHAF1 P D S V K G R F T I S R D N A K N S L Y L Q M N S L R A E D
C2HuVHAF2 P D S V K G R F T I S R D N A K N S L Y L Q M N S L R A E D
C2HuVHAF3 P D S V K G R F T I S R D N A K N S L Y L Q M N S L R A E D
C2HuVHAF4 P D S V K G R F T I S R D N A K N S L Y L Q M N S L R A E D
DP-54 V D S V K G R F T I S R D N A K N S L Y L Q M N S L R A E D
HUJH6 -
100 110
C2VHAF T A M Y Y C A S G D Y W G Q G S T L T V S S
C2HuVHAF1 T A V Y Y C A R G D Y W G Q G T T V T V S S
C2HuVHAF2 T A V Y Y C A S G D Y W G Q G T T V T V S S
C2HuVHAF3 T A V Y Y C A R G D Y W G Q G T T V T V S S
C2HuVHAF4 T A V Y Y C A S G D Y W G Q G T T V T V S S
DP-54 T A V Y Y C A R
HUJH6 - - - Y Y Y G M - D V W G Q G T T V T V S S

FIG 13.

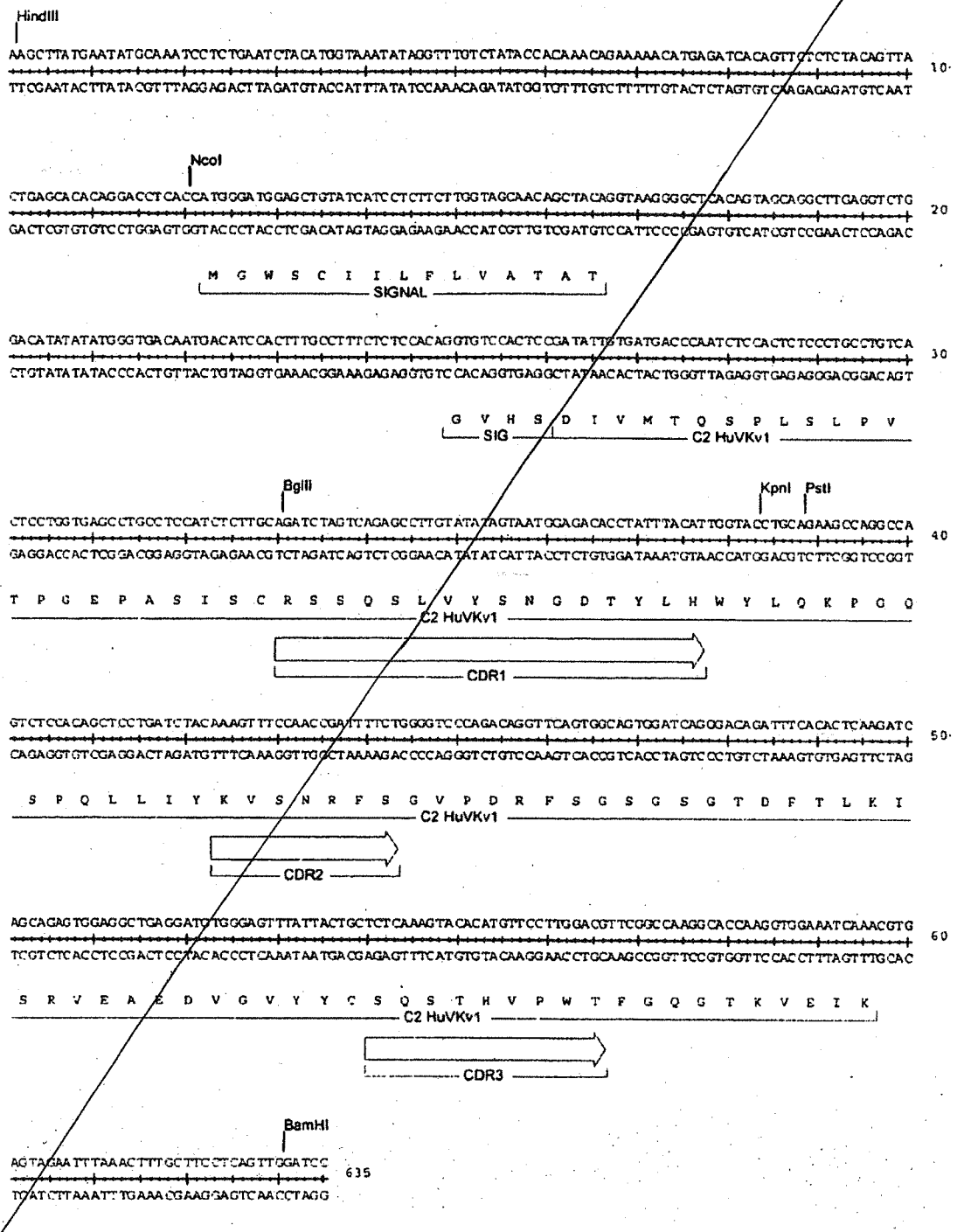

HindIII
NcoI
M G W S C I I L F L V A T A T
SIGNAL
G V H S D I V M T Q S P L S L P V
SIG
C2 HuVKv1
BglII
KpnI
PstI
T P G E P A S I S C R S S Q S L V Y S N G D T Y L H W Y L Q K P G Q
C2 HuVKv1
CDR1
S P Q L L I Y K V S N R F S G V P D R F S G S G S G T D F T L K I
C2 HuVKv1
CDR2
S R V E A E D V G V Y Y C S Q S T H V P W T F G Q G T K V E I K
C2 HuVKv1
CDR3
BamHI
635

FIG 14

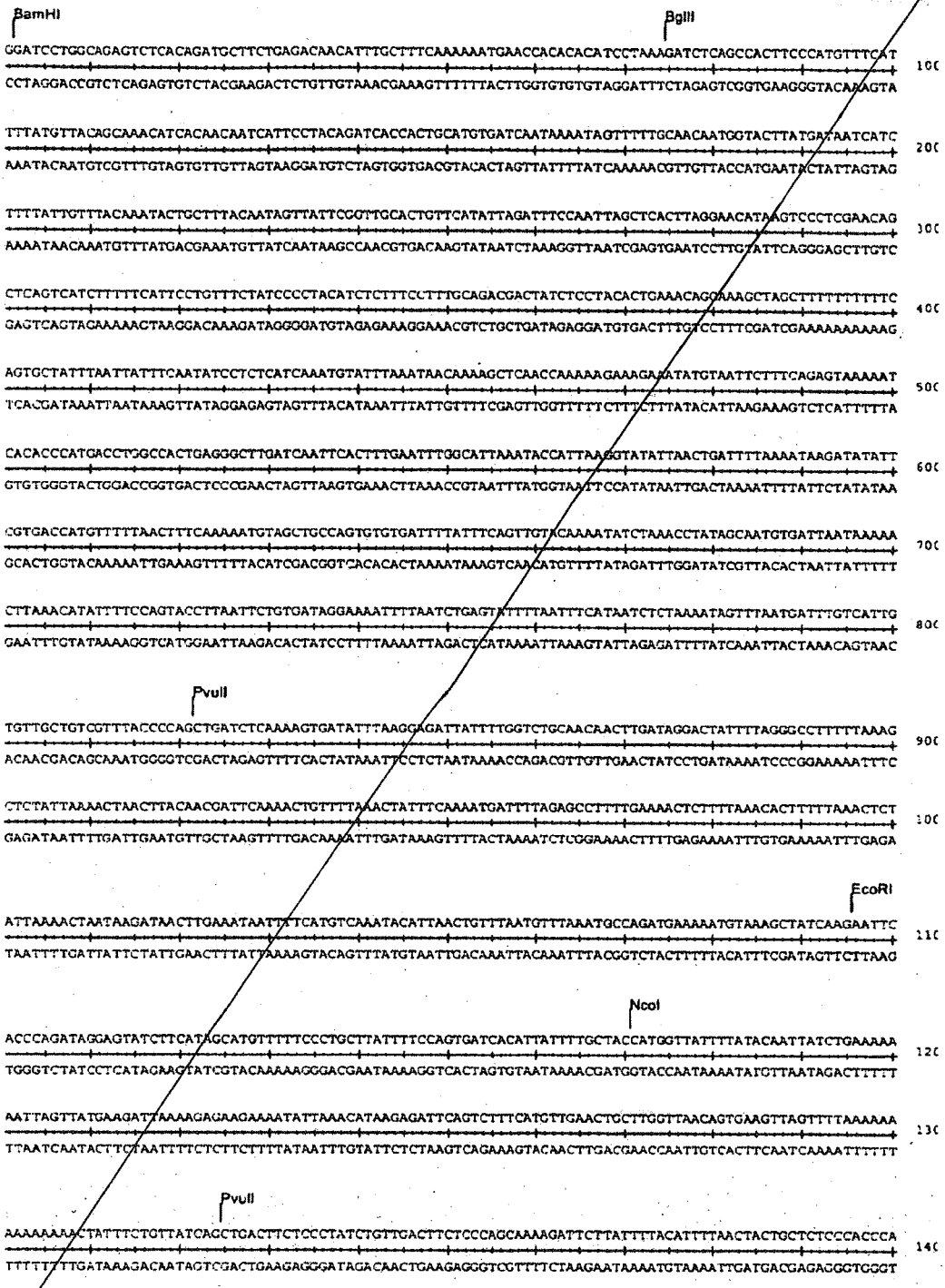


FIG 15-1

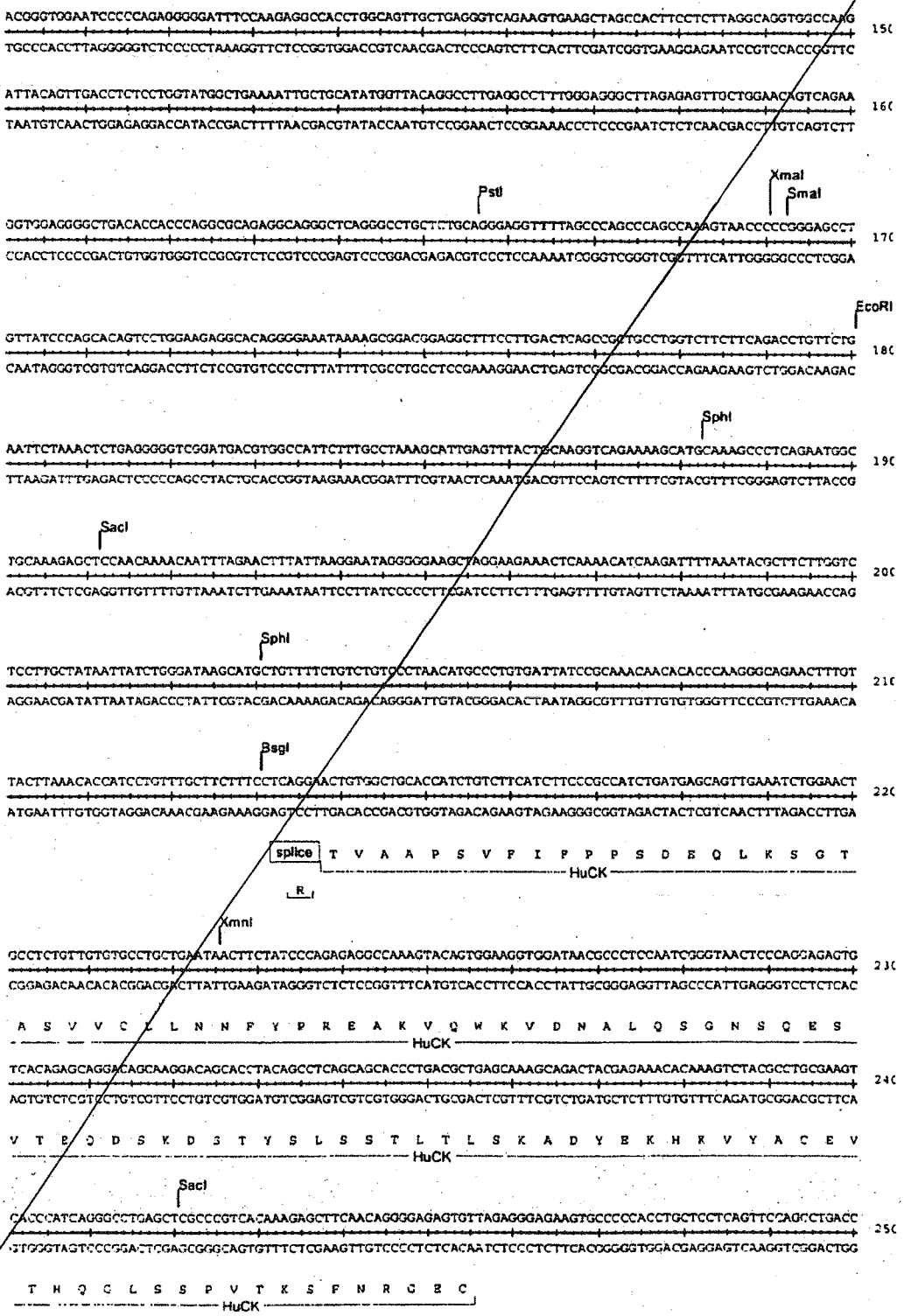

PstI
XmaI
SmaI
EcoRI
SphI
SacI
SphI
BsgI
splice
T V A A P S V F I F P P S D E Q L K S G T
HuCK
R
XmnI
A S V V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S
HuCK
V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V
HuCK
SacI
T H Q G L S S P V T K S F N R G E C
HuCK

FIG 15-2

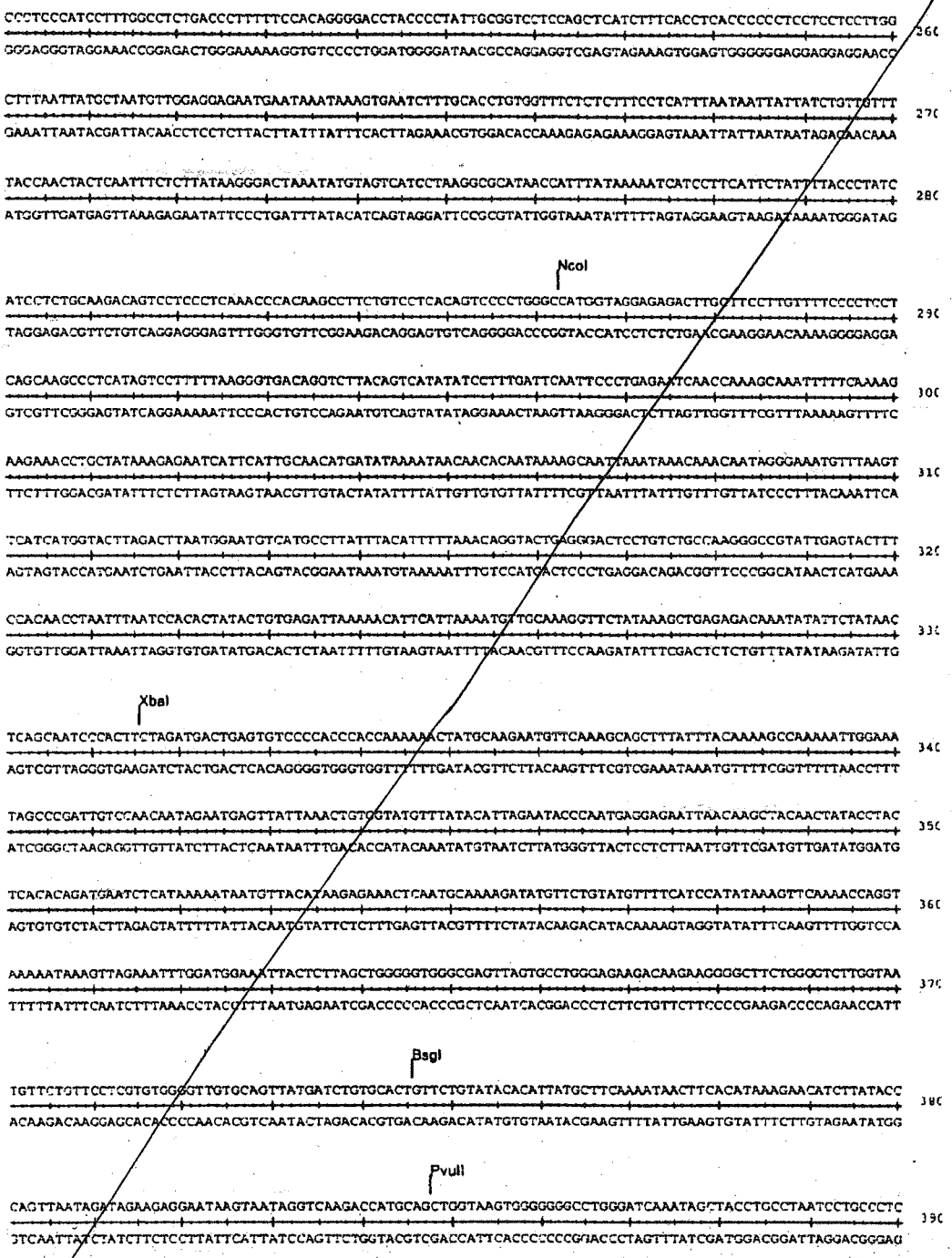


FIG 15-3

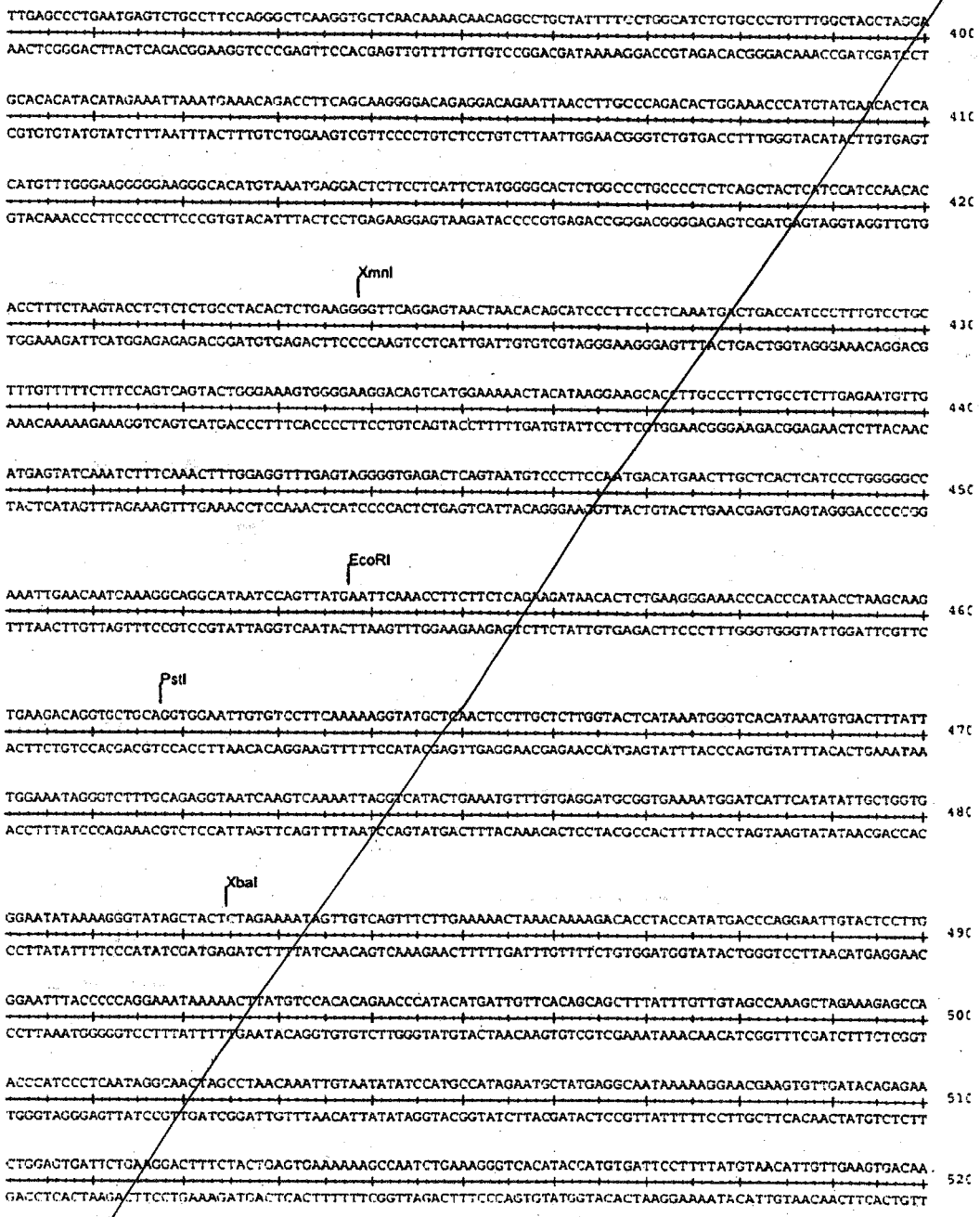


FIG 15-4

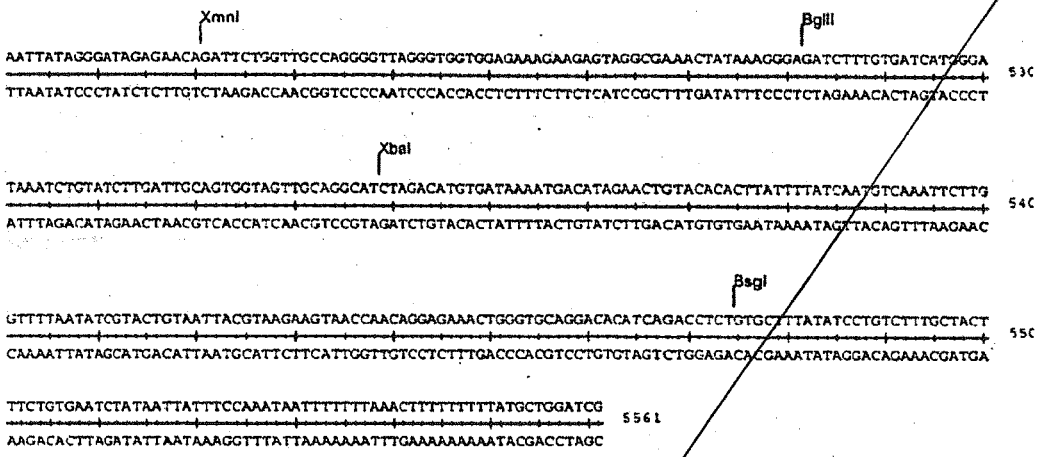

XmnI
BglII
AATTATAGGGATAGAGAACAGATTCTGGTTGCCAGGGGTTAGGGTGGTGGAGAAAGAAGAGTAGGCGAAACTATAAAGGGAGATCTTTGTGATCATGGGA
TTAATATCCCTATCTCTTGTCTAAGACCAACGGTCCCCAATCCCACCACCTCTTTCTTCTCATCCGCTTTGATATTTCCCTCTAGAAACACTAGTACCCT
530
XbaI
TAAATCTGTATCTTGATTGCAGTGGTAGTTGCAGGCATCTAGACATGTGATAAAATGACATAGAACTGTACACACTTATTTTATCAATGTCAAATTCTTG
ATTTAGACATAGAACTAACGTCACCATCAACGTCCGTAGATCTGTACACTATTTTACTGTATCTTGACATGTGTGAATAAAATAGTTACAGTTTAAGAAC
540
BsgI
GTTTTAATATCGTACTGTAATTACGTAAGAAGTAACCAACAGGAGAAACTGGGTGCAGGACACATCAGACCTCTGTGCTTTATATCCTGTCTTTGCTACT
CAAAATTATAGCATGACATTAATGCATTCTTCATTGGTTGTCCTCTTTGACCCACGTCCTGTGTAGTCTGGAGACACGAAATATAGGACAGAAACGATGA
550
TTCTGTGAATCTATAATTATTTCCAAATAATTTTTTTTAAACTTTTTTTTTTATGCTGGATCG
AAGACACTTAGATATTAATAAAGGTTTATTAAAAAAAATTTGAAAAAAAAAATACGACCTAGC
5561

FIG 15-5

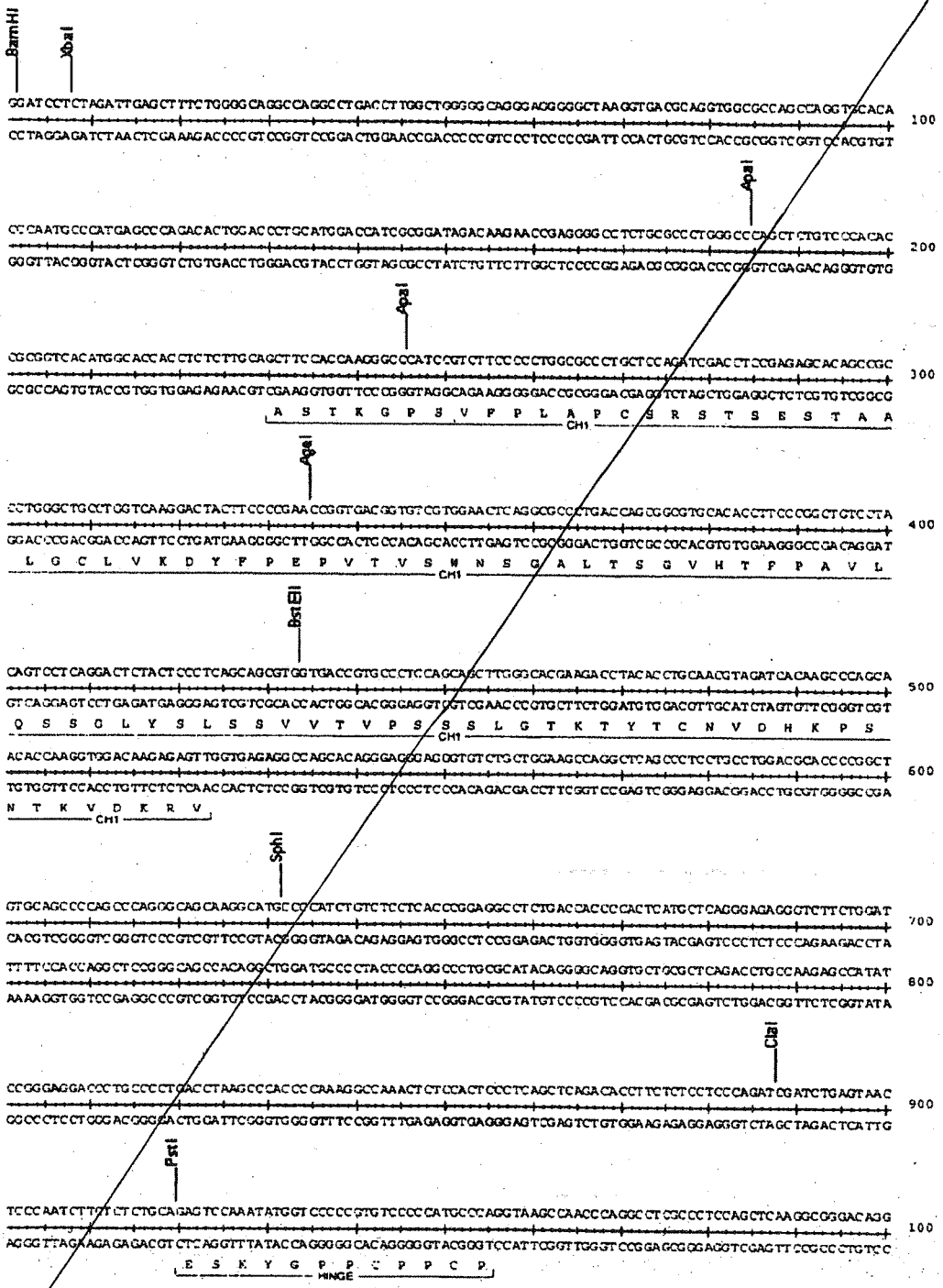

BamHI
XbaI
ApaI
ApaI
AgeI
BstEII
SphI
ClaI
PstI
CH1
CH1
CH1
HINGE

FIG 16 -1

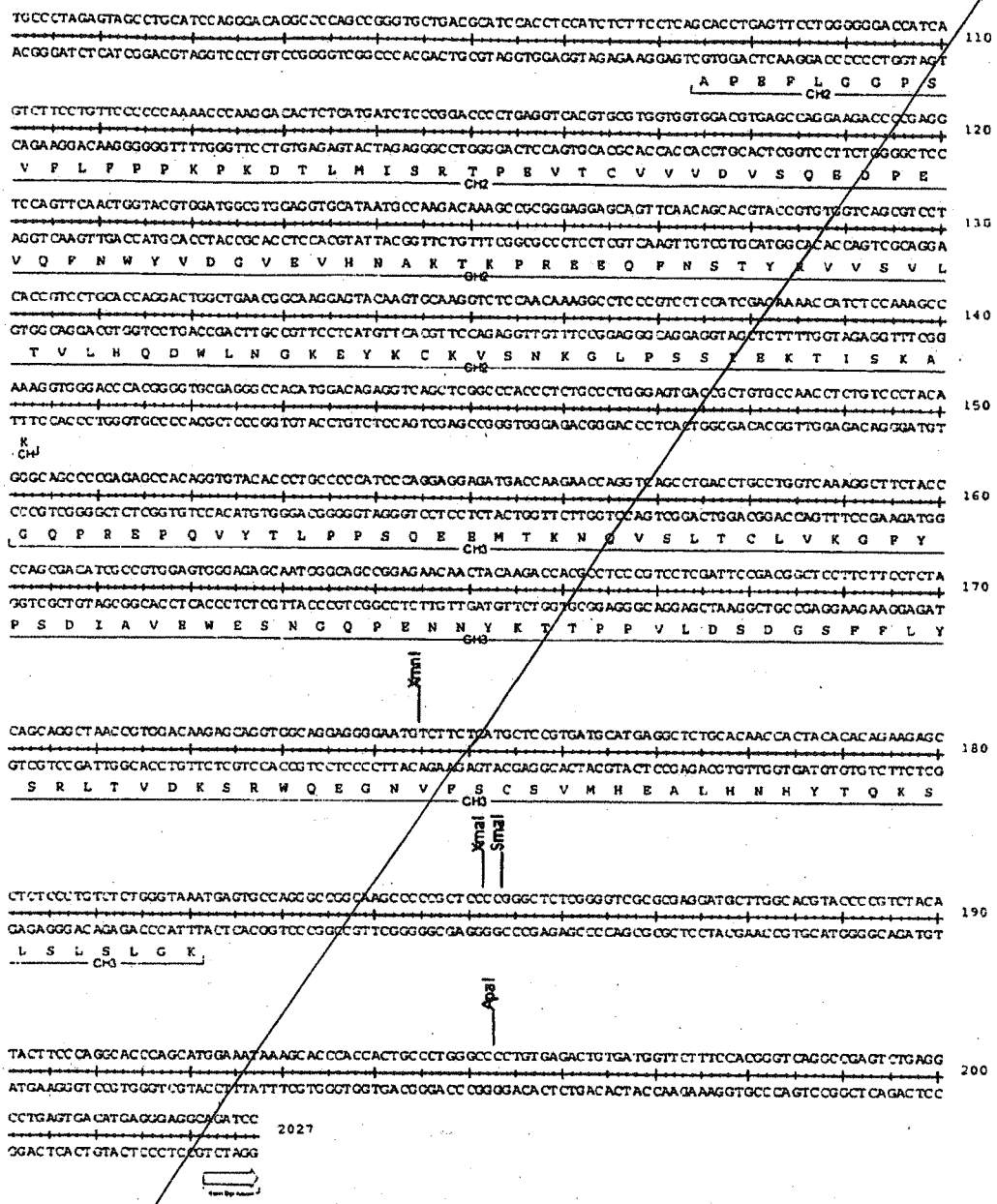

110
120
130
140
150
160
170
180
190
200
2027
XmaI
XmaI
SmaI
ApaI

FIG 16 -2

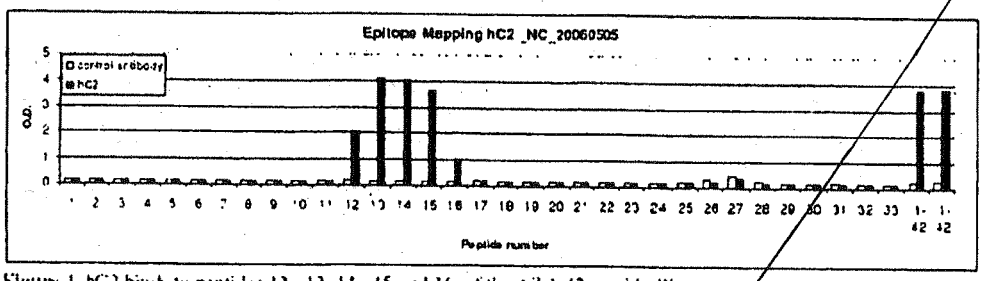


Figure 1. hC2 binds to peptides 12 , 13, 14 , 15 and 16 of the Aβ 1-42 peptide library.
Binding of hC2 to overlapping peptides of Aβ 1-42 was analyzed by ELISA. Binding to the complete Aβ 1-42 and binding of a non-binding chimeric antibody (control antibody) was used as positive and negative controls respectively. The peptide number corresponds to the amino acid in the Aβ 1-42 sequence on which the peptide starts. Results are expressed as OD.

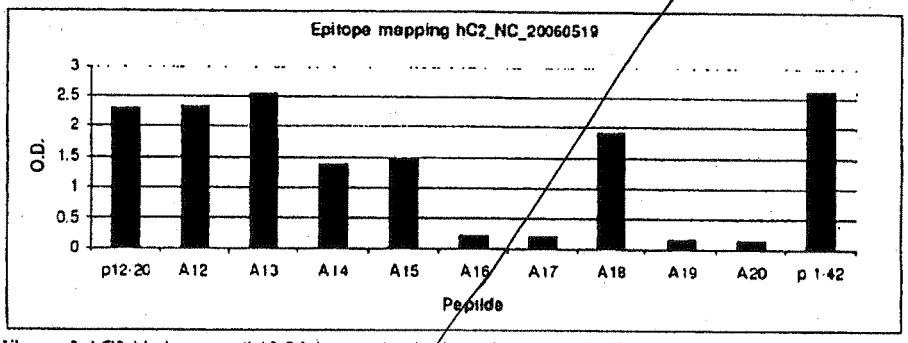


Figure 2. hC2 binding to Aβ 12-20 is completely dependent on aa 16,17,19 and 20 and partially dependent on aa 14,15 and 18.
Binding of hC2 to Aβ 12-20 and alanine substituted Aβ 12-20 was analyzed by ELISA. Binding to the complete Aβ 1-42 was used as positive control. The number corresponds to the aa that is substituted by alanine. Results are expressed as OD.

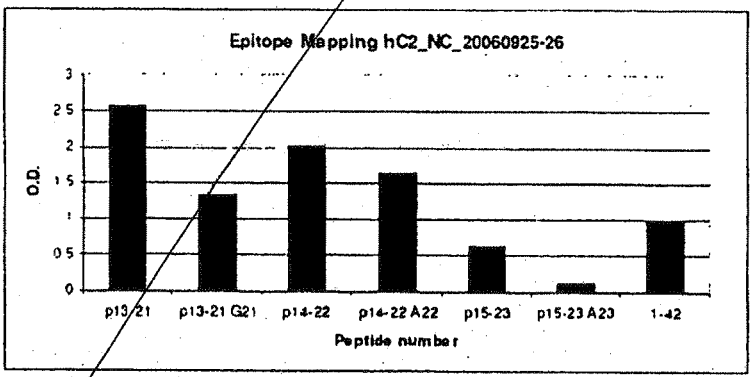


Figure 3. hC2 binding to Aβ 15-23 is dependent on aa 23 and partially on aa 21 and slightly dependent on aa 22.
Binding of hC2 to Aβ 13-21, 14-22 or 15-23 and to 13-21G21, 14-22A22 or 15-23A23 was analyzed by ELISA. Binding to the complete Aβ 1-42 was used as positive control. Results are expressed as OD

Fig 17:

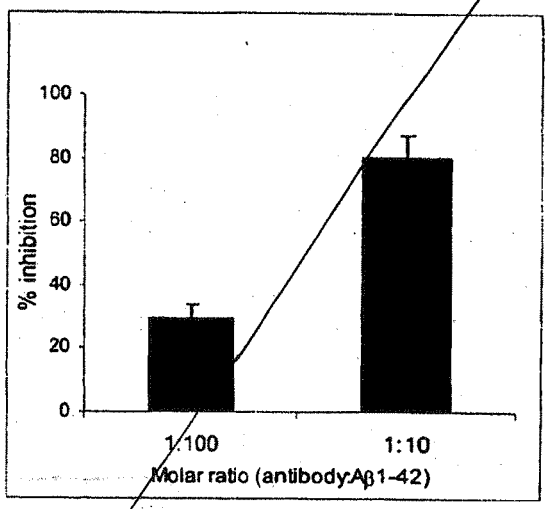

100
80
60
40
20
0
% inhibition
1:100
1:10
Molar ratio (antibody:Aβ1-42)

Fig 18

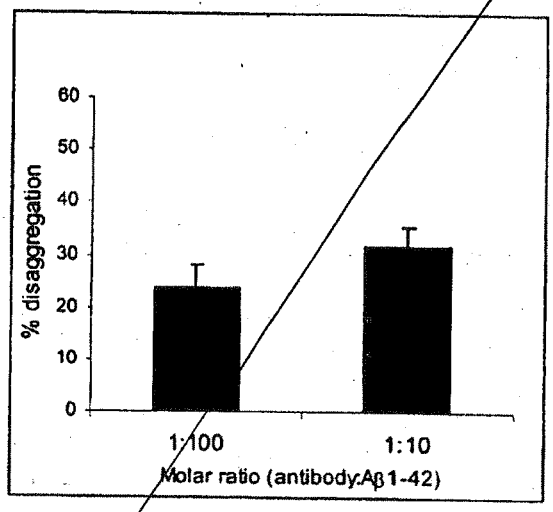

60
50
40
30
20
10
0
% disaggregation
1:100
1:10
Molar ratio (antibody:Aβ1-42)

FIG 19

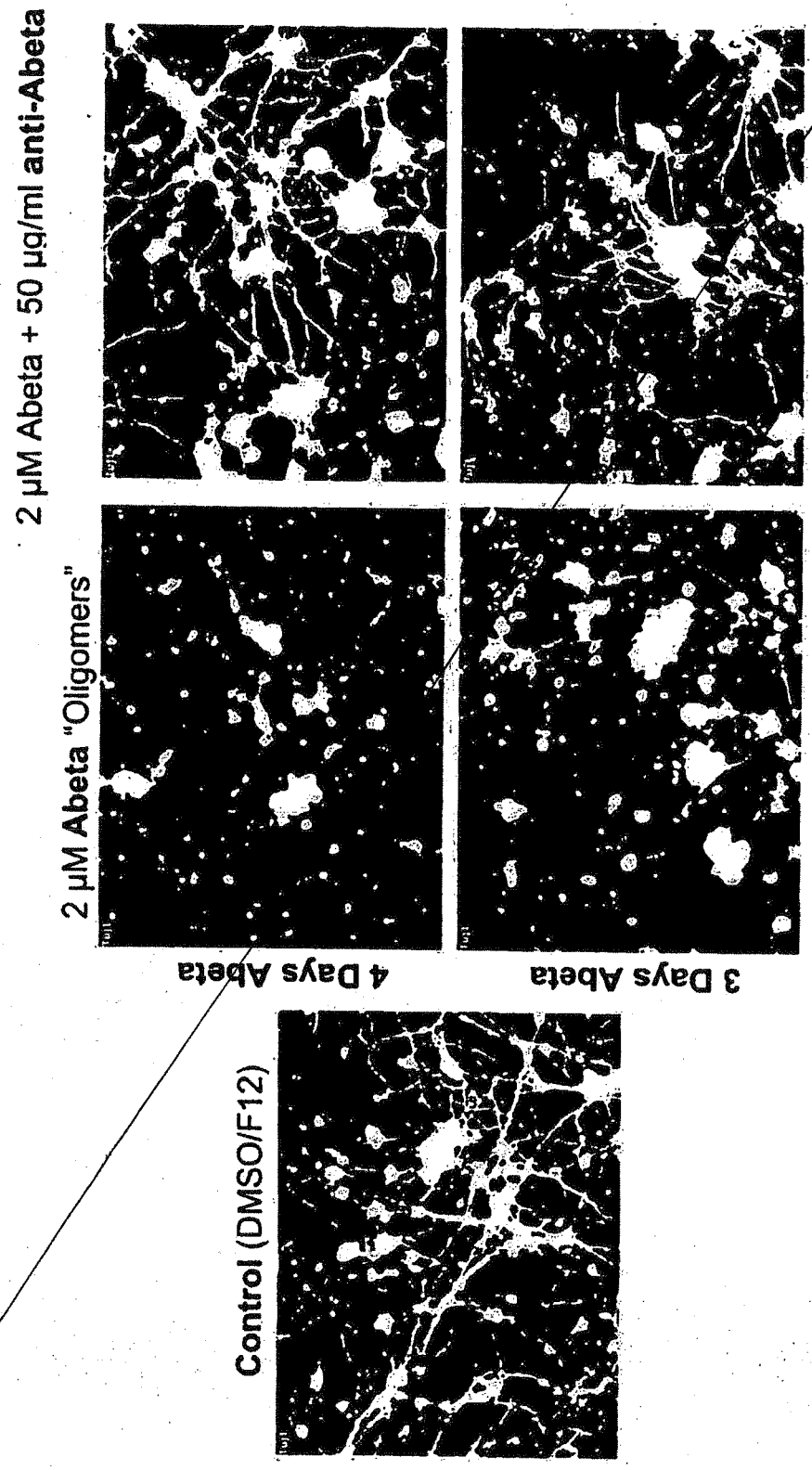

2 µM Abeta + 50 µg/ml anti-Abeta
2 µM Abeta "Oligomers"
4 Days Abeta
3 Days Abeta
Control (DMSO/F12)

FIG 20

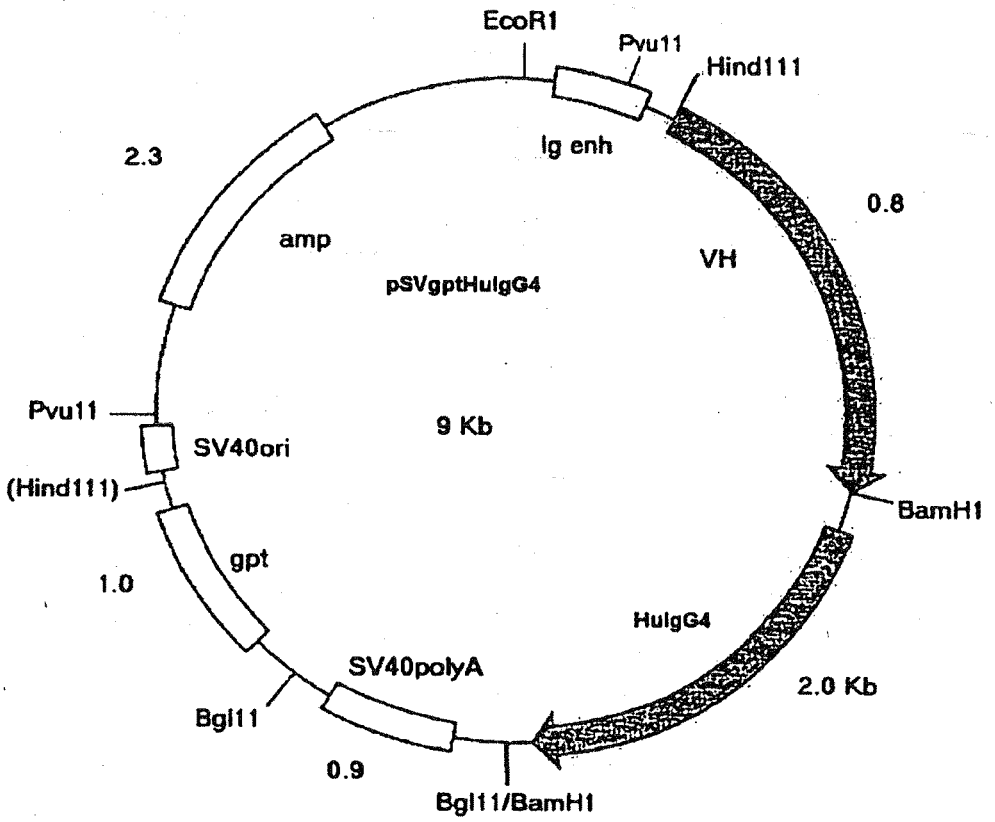


FIG 1
(example 2)

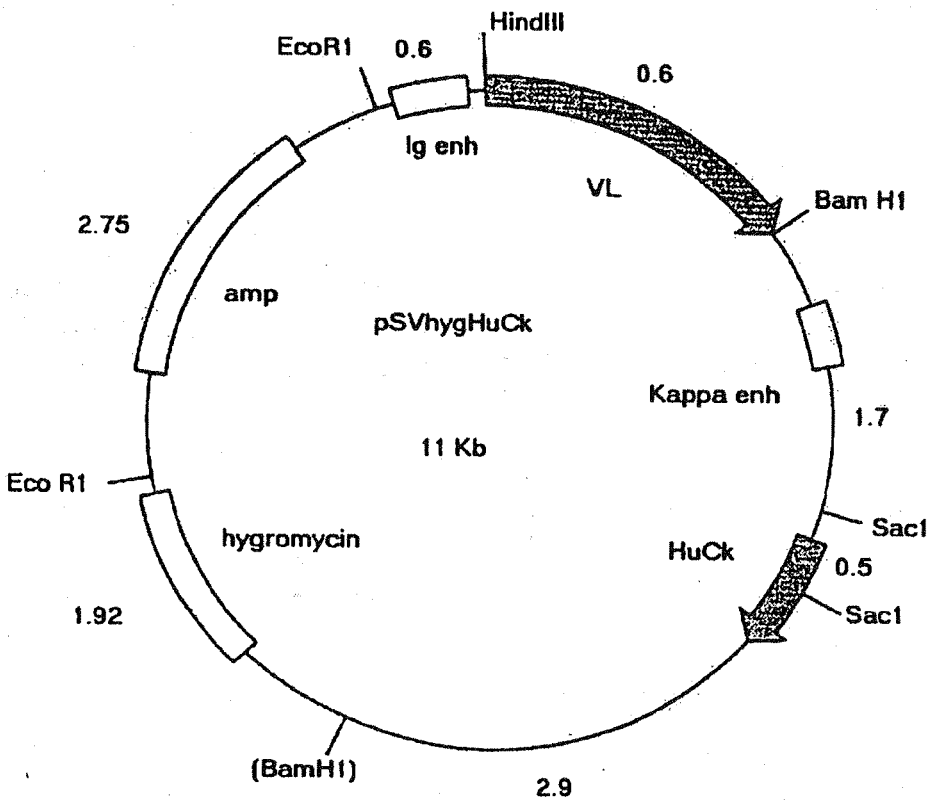


FIG 2(Example 2)

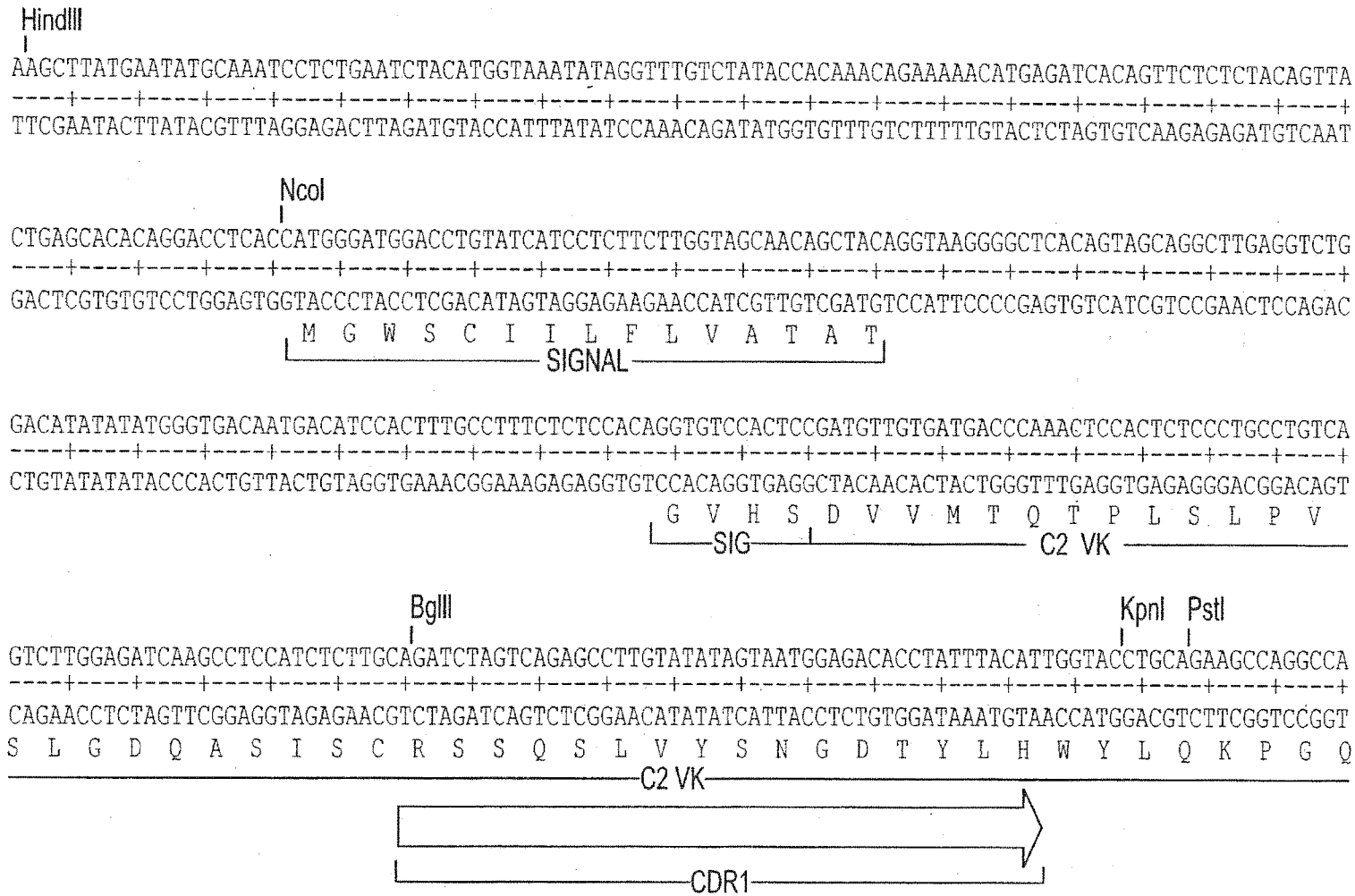

HindIII
AAGCTTATGAATATGCAAATCCTCTGAATCTACATGGTAAATATAGGTTTGTCTATACCACAAACAGAAAAACATGAGATCACAGTTCTCTCTACAGTTA
TTCGAATACTTATACGTTTAGGAGACTTAGATGTACCATTTATATCCAAACAGATATGGTGTTTGTCTTTTTGTACTCTAGTGTCAAGAGAGATGTCAAT
10
NcoI
CTGAGCACACAGGACCTCACCATGGGATGGACCTGTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTAAGGGGCTCACAGTAGCAGGCTTGAGGTCTG
GACTCGTGTGTCCTGGAGTGGTACCCTACCTCGACATAGTAGGAGAAGAACCATCGTTGTCGATGTCCATTCCCCGAGTGTCATCGTCCGAACTCCAGAC
20
M G W S C I I L F L V A T A T
SIGNAL
GACATATATATGGGTGACAATGACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCGATGTTGTGATGACCCAAACTCCACTCTCCCTGCCTGTCA
CTGTATATATACCCACTGTTACTGTAGGTGAAACGGAAAGAGAGGTGTCCACAGGTGAGGCTACAACACTACTGGGTTTGAGGTGAGAGGGACGGACAGT
30
G V H S D V V M T Q T P L S L P V
SIG
C2 VK
BglII
KpnI
PstI
GTCTTGGAGATCAAGCCTCCATCTCTTGCAGATCTAGTCAGAGCCTTGTATATAGTAATGGAGACACCTATTTACATTGGTACCTGCAGAAGCCAGGCCA
CAGAACCTCTAGTTCGGAGGTAGAGAACGTCTAGATCAGTCTCGGAACATATATCATTACCTCTGTGGATAAATGTAACCATGGACGTCTTCGGTCCGGT
40
S L G D Q A S I S C R S S Q S L V Y S N G D T Y L H W Y L Q K P G Q
C2 VK
CDR1

FIG. 3-1

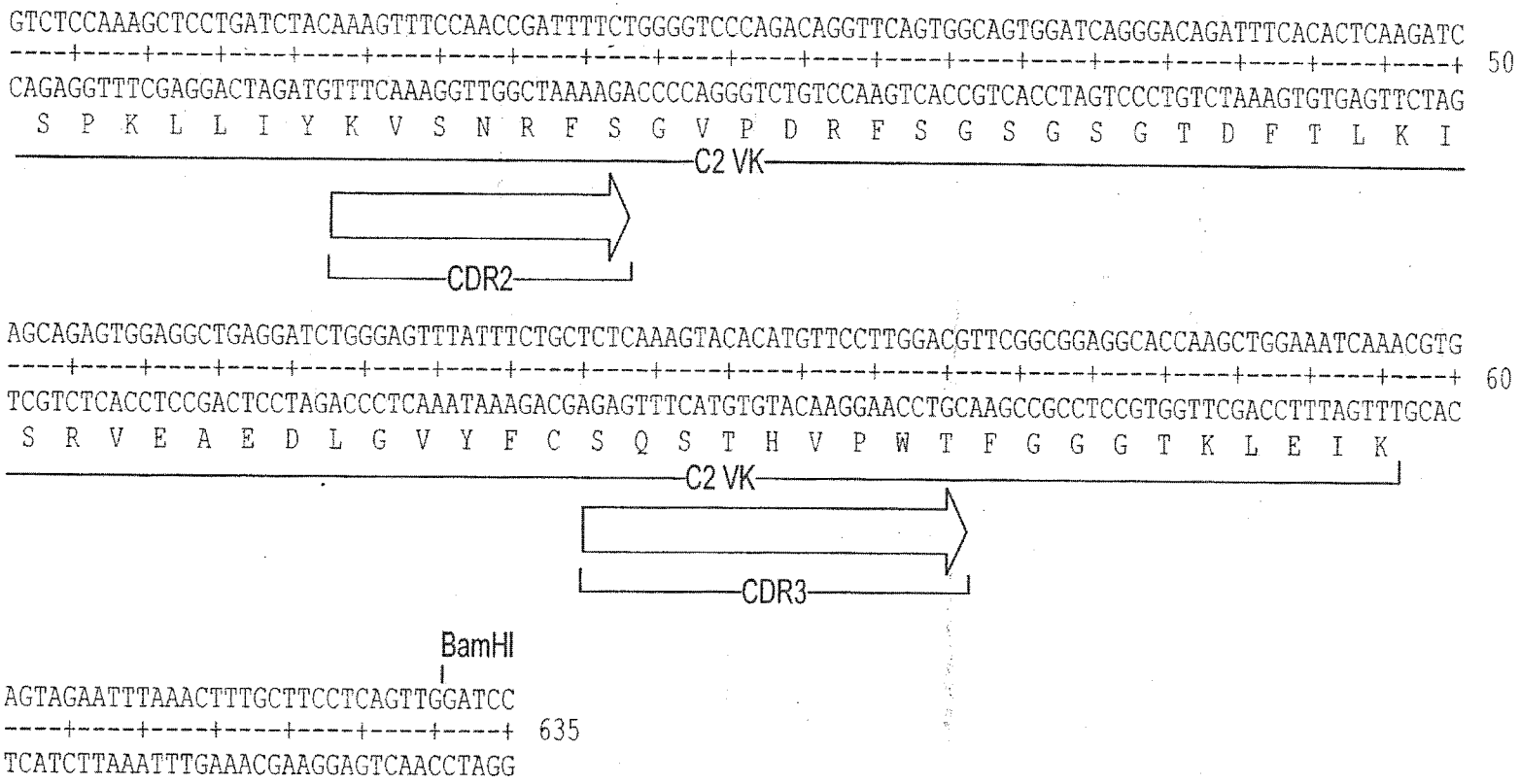

GTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGATTTTCTGGGGTCCCAGACAGGTTCAGTGGCAGTGGATCAGGGACAGATTTCACACTCAAGATC
CAGAGGTTTCGAGGACTAGATGTTTCAAAGGTTGGCTAAAAGACCCCAGGGTCTGTCCAAGTCACCGTCACCTAGTCCCTGTCTAAAGTGTGAGTTCTAG
50
S P K L L I Y K V S N R F S G V P D R F S G S G S G T D F T L K I
C2 VK
CDR2
AGCAGAGTGGAGGCTGAGGATCTGGGAGTTTATTTCTGCTCTCAAAGTACACATGTTCCTTGGACGTTCGGCGGAGGCACCAAGCTGGAAATCAAACGTG
TCGTCTCACCTCCGACTCCTAGACCCTCAAATAAAGACGAGAGTTTCATGTGTACAAGGAACCTGCAAGCCGCCTCCGTGGTTCGACCTTTAGTTTGCAC
60
S R V E A E D L G V Y F C S Q S T H V P W T F G G G T K L E I K
C2 VK
CDR3
BamHI
AGTAGAATTTAAACTTTGCTTCCTCAGTTGGATCC
TCATCTTAAATTTGAAACGAAGGAGTCAACCTAGG
635

FIG. 3-2

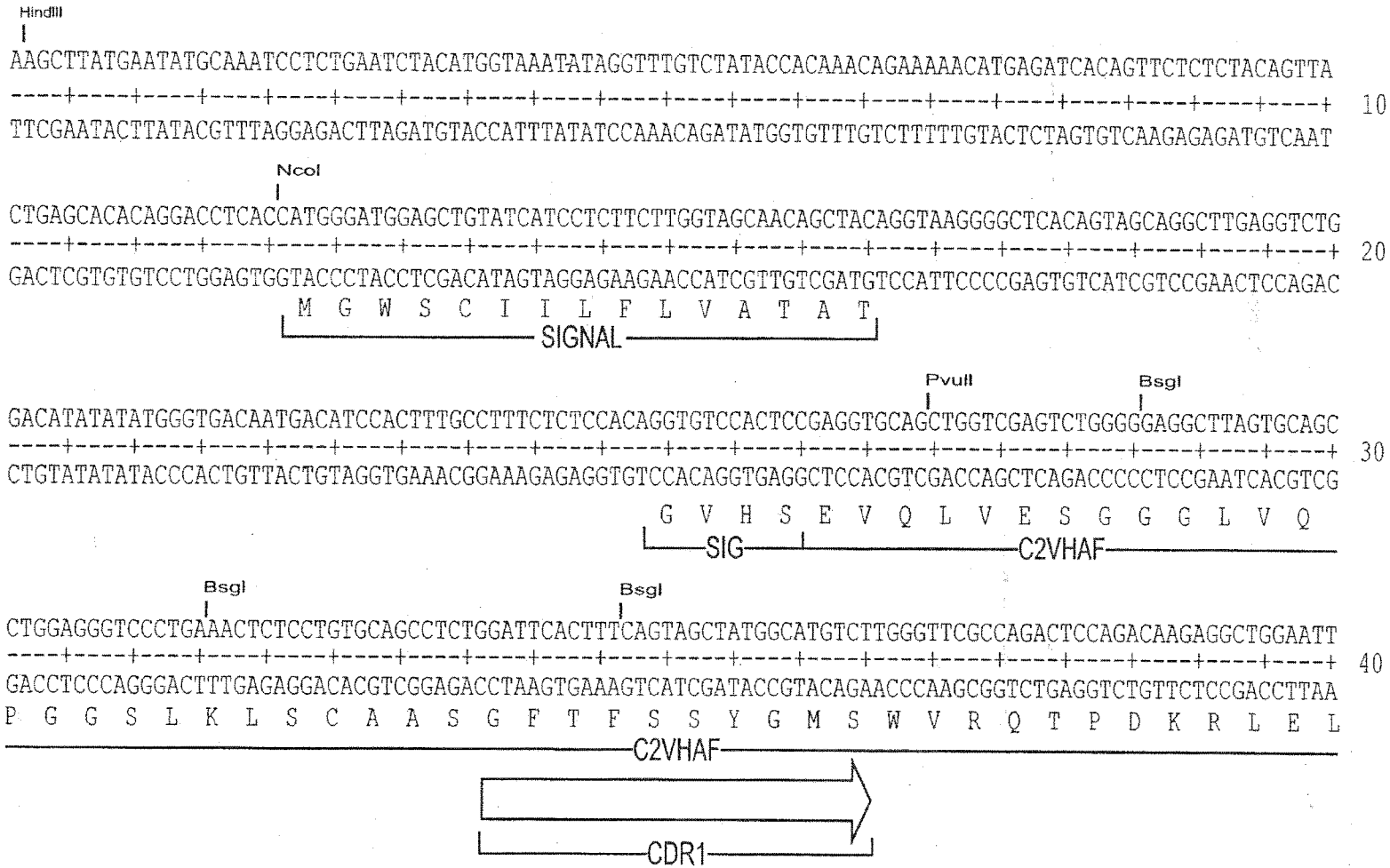

HindIII
AAGCTTATGAATATGCAAATCCTCTGAATCTACATGGTAAATATAGGTTTGTCTATACCACAAACAGAAAAACATGAGATCACAGTTCTCTCTACAGTTA
TTCGAATACTTATACGTTTAGGAGACTTAGATGTACCATTTATATCCAAACAGATATGGTGTTTGTCTTTTTGTACTCTAGTGTCAAGAGAGATGTCAAT
10
NcoI
CTGAGCACACAGGACCTCACCATGGGATGGAGCTGTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTAAGGGGCTCACAGTAGCAGGCTTGAGGTCTG
GACTCGTGTGTCCTGGAGTGGTACCCTACCTCGACATAGTAGGAGAAGAACCATCGTTGTCGATGTCCATTCCCCGAGTGTCATCGTCCGAACTCCAGAC
20
M G W S C I I L F L V A T A T
SIGNAL
PvuII
BsgI
GACATATATATGGGTGACAATGACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCGAGGTGCAGCTGGTCGAGTCTGGGGGAGGCTTAGTGCAGC
CTGTATATATACCCACTGTTACTGTAGGTGAAACGGAAAGAGAGGTGTCCACAGGTGAGGCTCCACGTCGACCAGCTCAGACCCCCTCCGAATCACGTCG
30
G V H S E V Q L V E S G G G L V Q
SIG
C2VHAF
BsgI
BsgI
CTGGAGGGTCCCTGAAACTCTCCTGTGCAGCCTCTGGATTCACTTTCAGTAGCTATGGCATGTCTTGGGTTCGCCAGACTCCAGACAAGAGGCTGGAATT
GACCTCCCAGGGACTTTGAGAGGACACGTCGGAGACCTAAGTGAAAGTCATCGATACCGTACAGAACCCAAGCGGTCTGAGGTCTGTTCTCCGACCTTAA
40
P G G S L K L S C A A S G F T F S S Y G M S W V R Q T P D K R L E L
C2VHAF
CDR1

FIG. 4-1

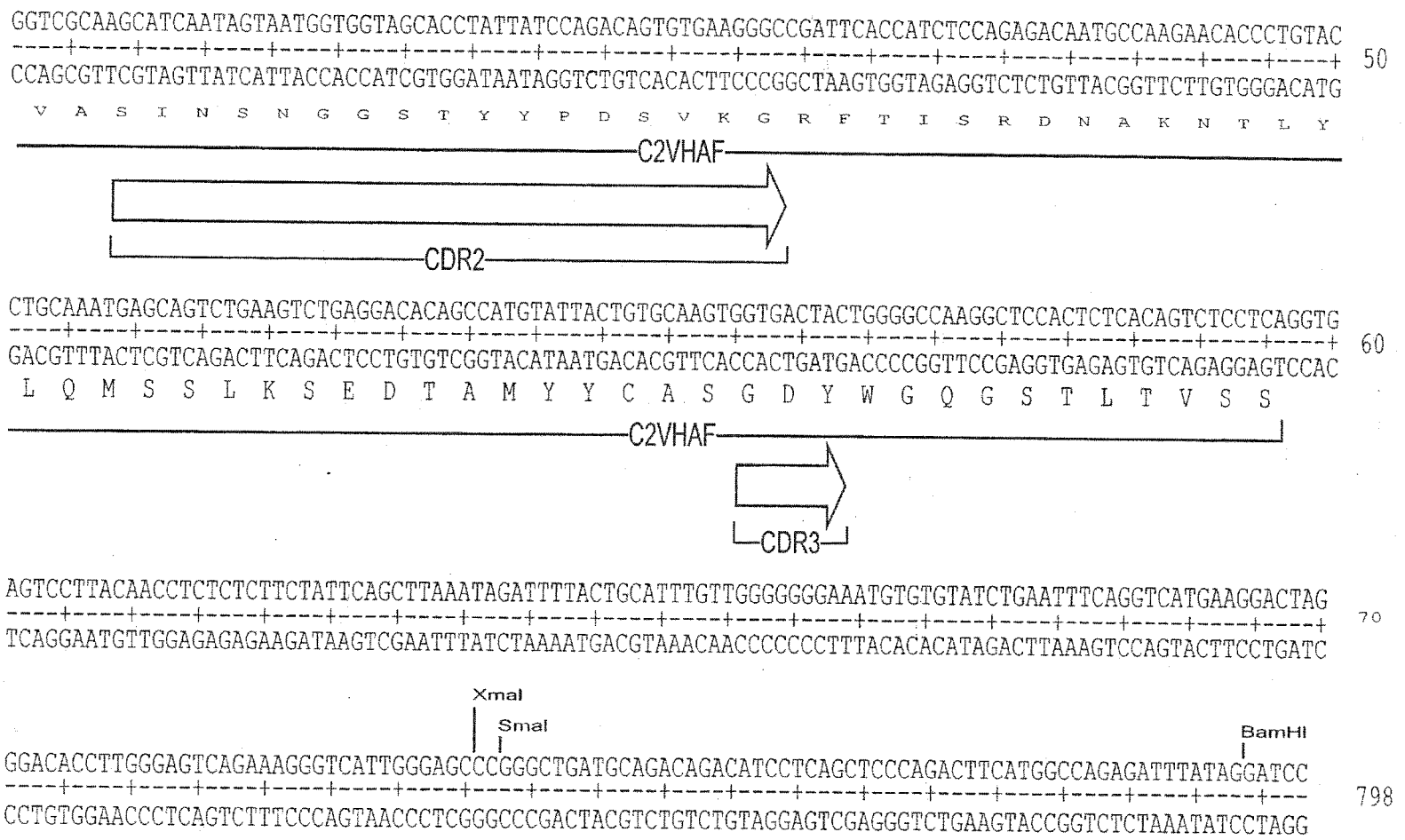

GGTCGCAAGCATCAATAGTAATGGTGGTAGCACCTATTATCCAGACAGTGTGAAGGGCCGATTCACCATCTCCAGAGACAATGCCAAGAACACCCTGTAC
CCAGCGTTCGTAGTTATCATTACCACCATCGTGGATAATAGGTCTGTCACACTTCCCGGCTAAGTGGTAGAGGTCTCTGTTACGGTTCTTGTGGGACATG
50
V A S I N S N G G S T Y Y P D S V K G R F T I S R D N A K N T L Y
C2VHAF
CDR2
CTGCAAATGAGCAGTCTGAAGTCTGAGGACACAGCCATGTATTACTGTGCAAGTGGTGACTACTGGGGCCAAGGCTCCACTCTCACAGTCTCCTCAGGTG
GACGTTTACTCGTCAGACTTCAGACTCCTGTGTCGGTACATAATGACACGTTCACCACTGATGACCCCGGTTCCGAGGTGAGAGTGTCAGAGGAGTCCAC
60
L Q M S S L K S E D T A M Y Y C A S G D Y W G Q G S T L T V S S
C2VHAF
CDR3
AGTCCTTACAACCTCTCTCTTCTATTCAGCTTAAATAGATTTTACTGCATTTGTTGGGGGGGAAATGTGTGTATCTGAATTTCAGGTCATGAAGGACTAG
TCAGGAATGTTGGAGAGAGAAGATAAGTCGAATTTATCTAAAATGACGTAAACAACCCCCCCTTTACACACATAGACTTAAAGTCCAGTACTTCCTGATC
70
XmaI
SmaI
BamHI
GGACACCTTGGGAGTCAGAAAGGGTCATTGGGAGCCCGGGCTGATGCAGACAGACATCCTCAGCTCCCAGACTTCATGGCCAGAGATTTATAGGATCC
CCTGTGGAACCCTCAGTCTTTCCCAGTAACCCTCGGGCCCGACTACGTCTGTCTGTAGGAGTCGAGGGTCTGAAGTACCGGTCTCTAAATATCCTAGG
798

FIG. 4-2

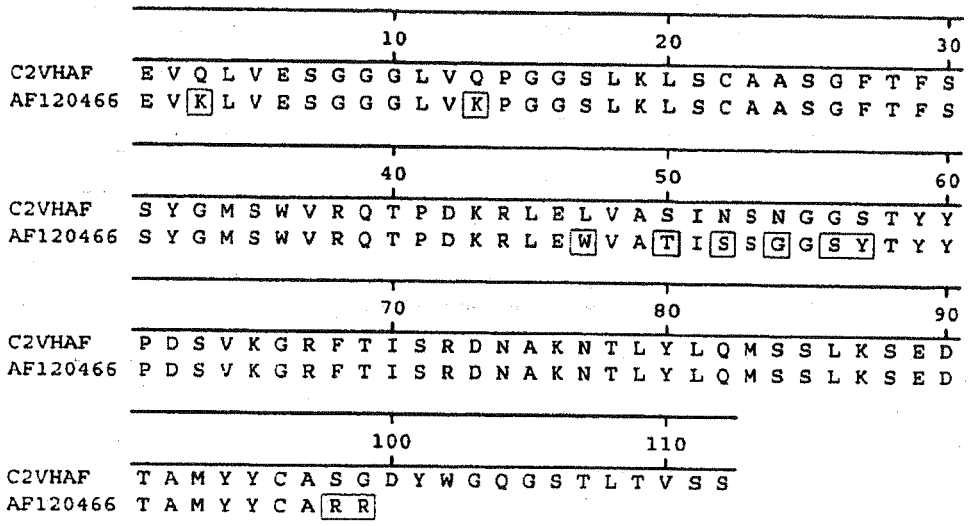
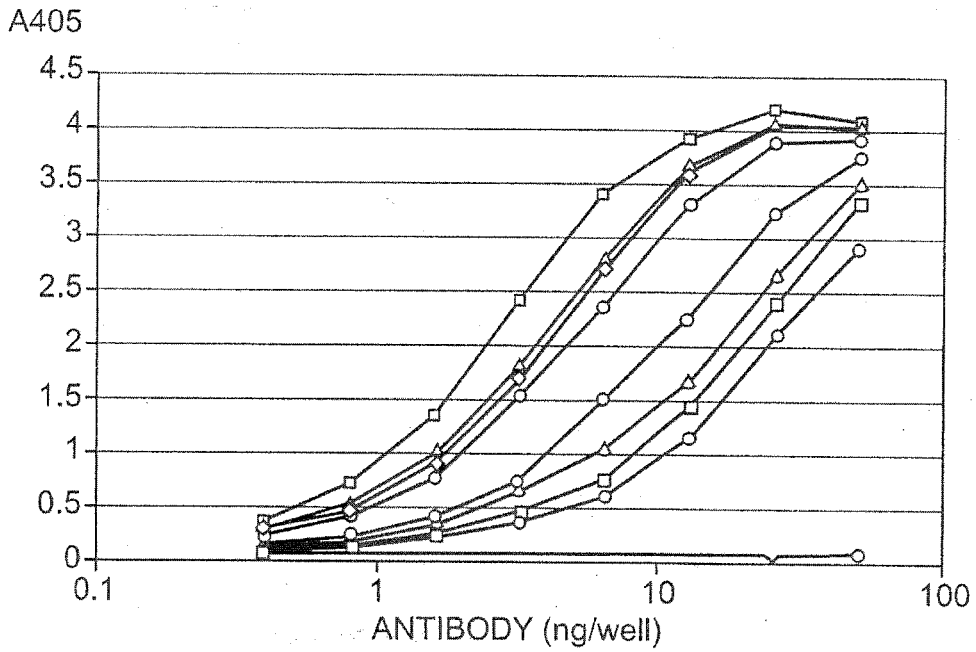


FIG 5
(Example 5.2)



NEGATIVE CONTROL

CHIMERIC ch VHAF/CHVK

CHIMERIC AT/HuIgG4

CHIMERIC B HuIgG4

HuVHv2/HuVKv1

HuVHv2/HuVKv2

HuVHv2/HuVKv3

HuVHv2/HuVKv4

HuVHv4/HuVKv1

HuVHv4/HuVKv2

HuVHv4/HuVKv3

HuVHv4/HuVKv4

FIG. 6

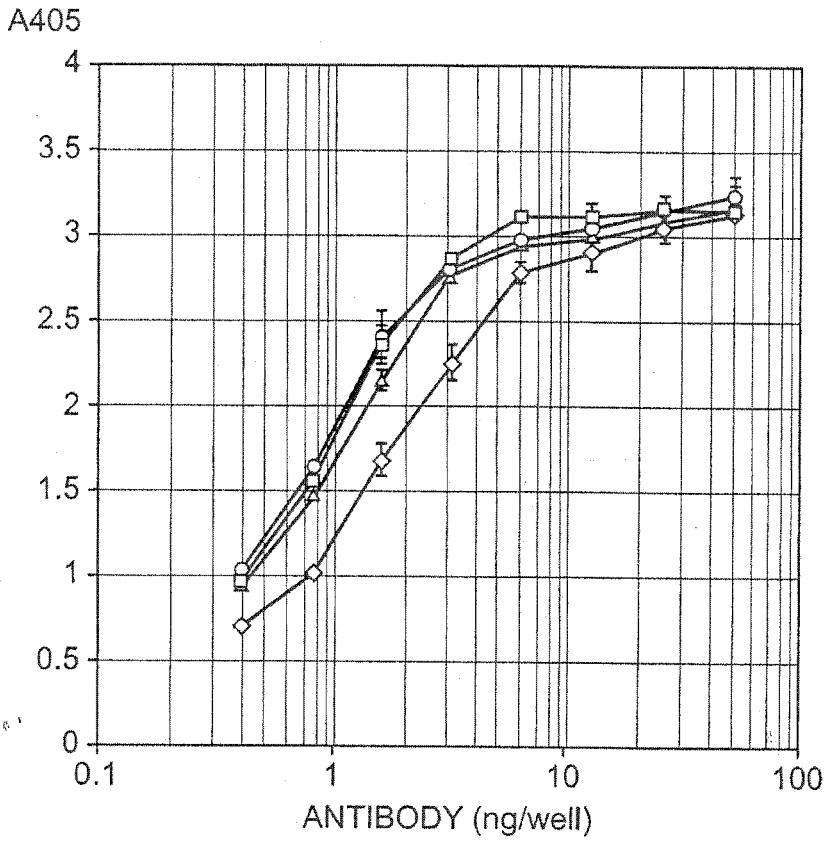

A405
4
3.5
3
2.5
2
1.5
1
0.5
0
0.1
1
10
100
ANTIBODY (ng/well)
C2 ChVHAF/ChVK-R
C2 ChVHAF/ChVK-S
C2 ChVHAF/ChVK
FROM TRANSLET TRANSFECTION
C2 ChVHAF/ChVK
PURIFIED

FIG. 7

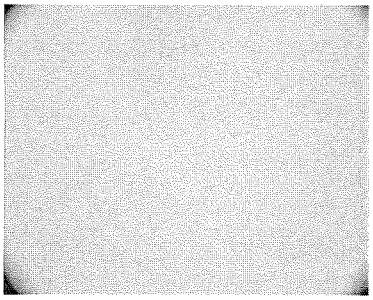
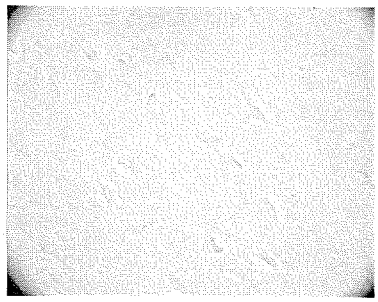
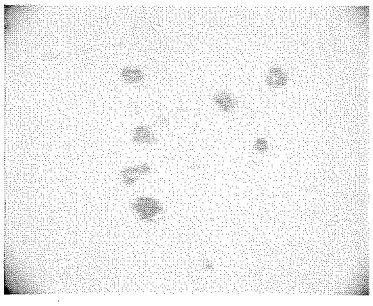
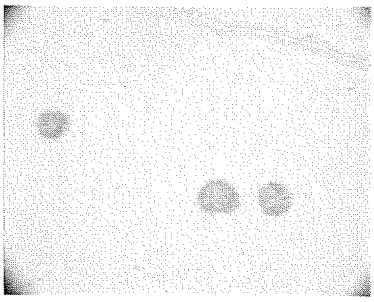
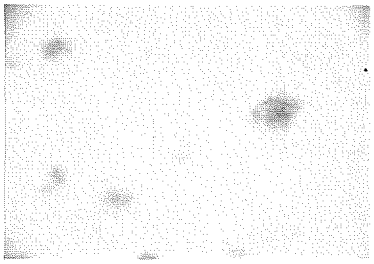
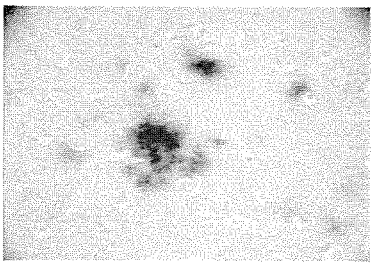
	C: Antibody hC2	A: Chimeric antibody
Control patient		
	Temporal neocortex region I, 40 x	CA4 (Cornu ammonis region 4), 40 x
AD patient		
	Temporal neocortex region I, 40 x	Temporal neocortex region I, 40 x
preAD patient		
	Temporal neocortex region I, 40 x	Temporal neocortex region I, 40 x

FIG. 8
(Example 11)

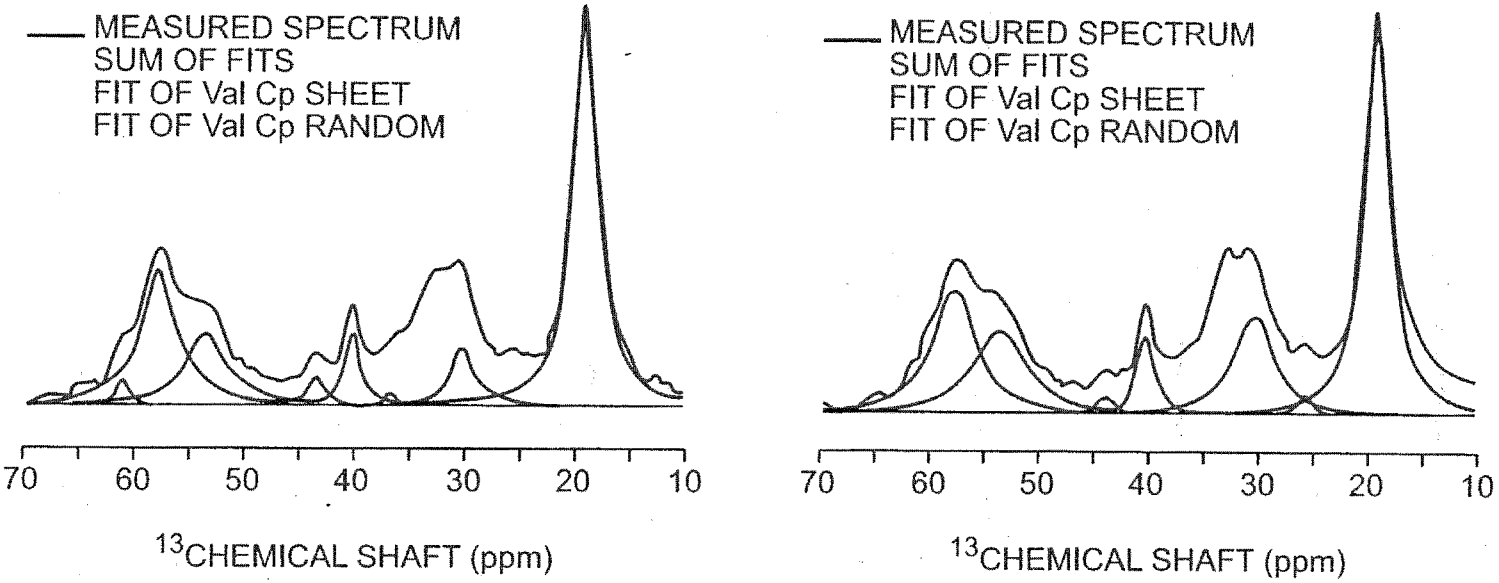


FIG. 9A

RESONANCE	PBS			MOUSE C2		
	δ ISO (ppm)	FWHH (Hz)	% INTEGRAL INTENSITY	δ ISO (ppm)	FWHH (Hz)	% INTEGRAL INTENSITY
Val Cβ -SHEET	32.60	479	81.7	33.09	366	53.5
Val Cβ -RANDOM	30.27	200	18.3	30.27	340	46.5

FIG. 9B

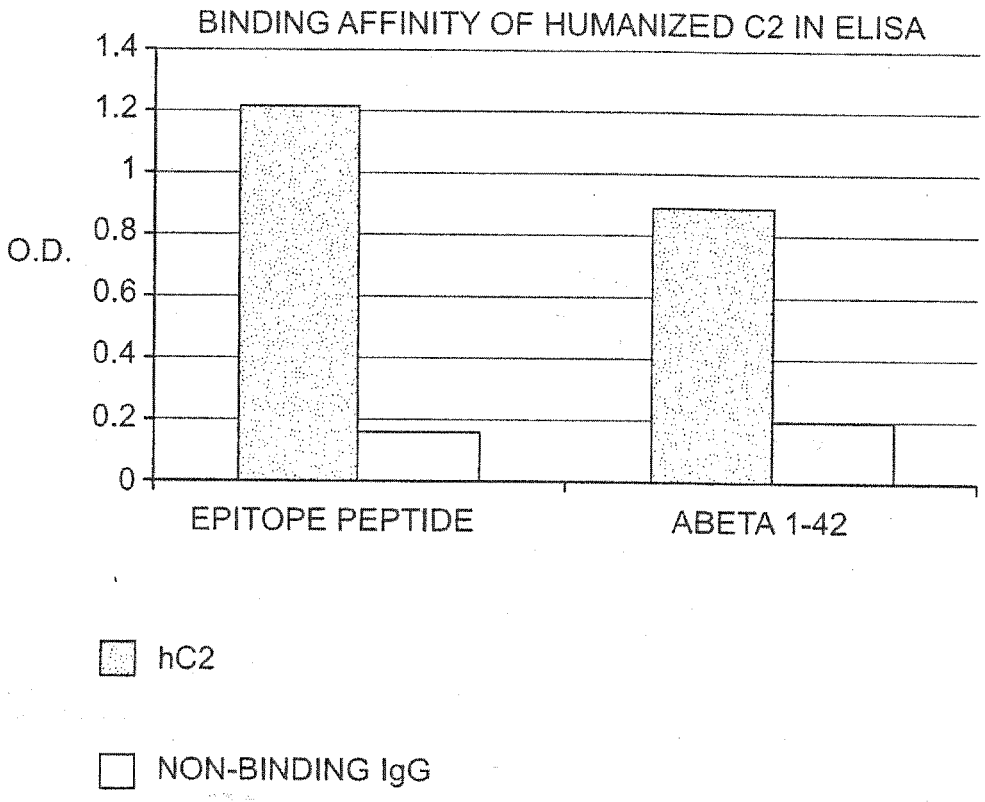

BINDING AFFINITY OF HUMANIZED C2 IN ELISA
1.4
1.2
1
0.8
0.6
0.4
0.2
0
O.D.
EPITOPE PEPTIDE
ABETA 1-42
hC2
NON-BINDING IgG

FIG. 10

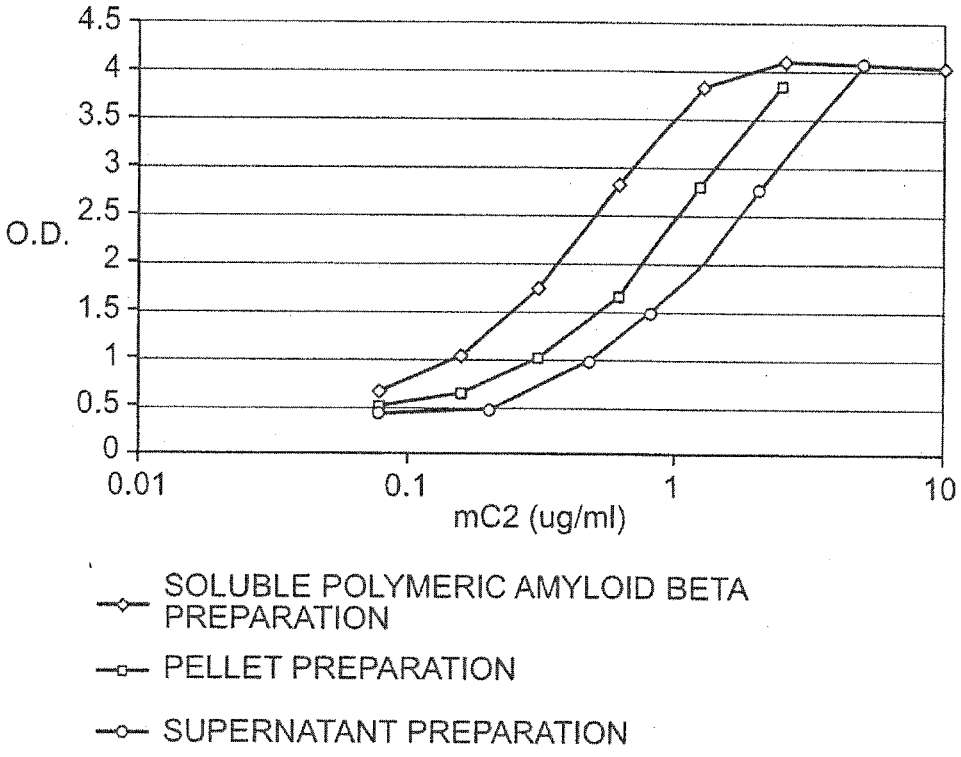

4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
O.D.
0.01
0.1
1
10
mC2 (ug/ml)
SOLUBLE POLYMERIC AMYLOID BETA PREPARATION
PELLET PREPARATION
SUPERNATANT PREPARATION

FIG. 11

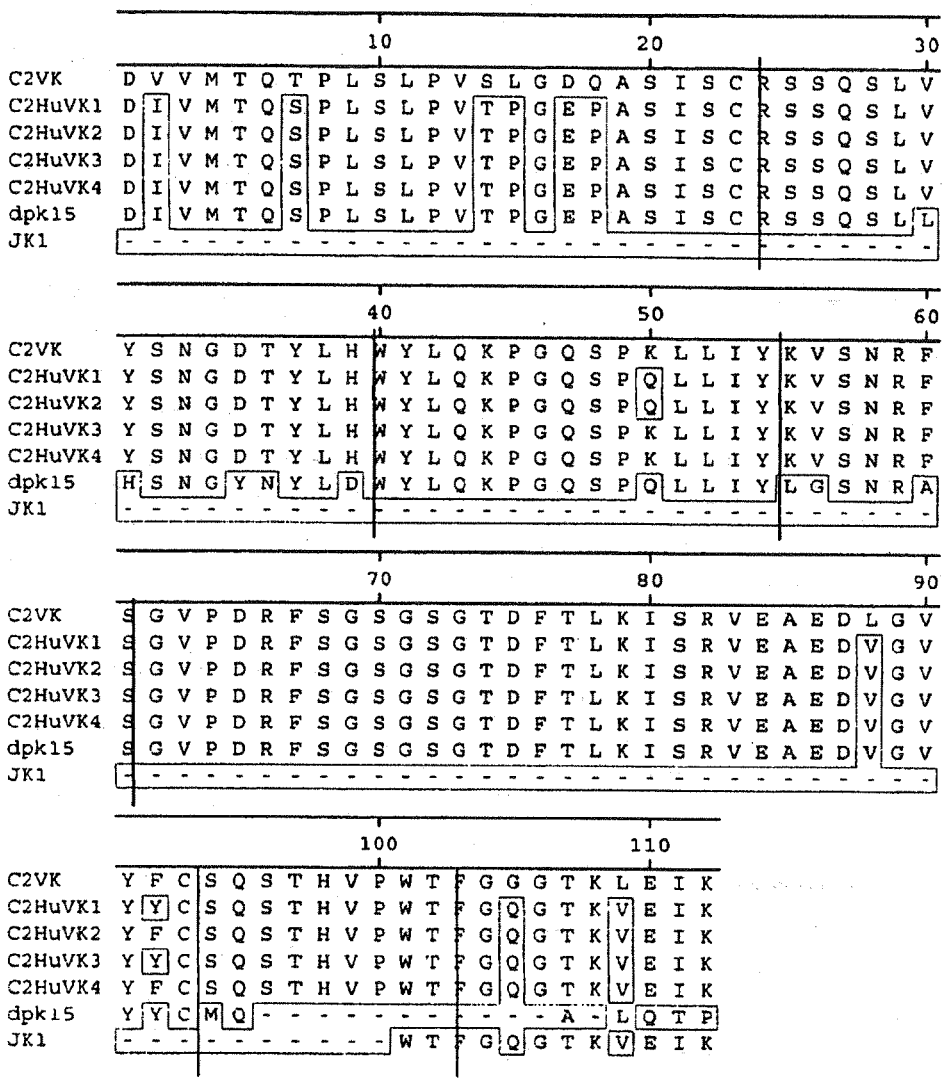

10 20 30
C2VK D V V M T Q T P L S L P V S L G D Q A S I S C R S S Q S L V
C2HuVK1 D I V M T Q S P L S L P V T P G E P A S I S C R S S Q S L V
C2HuVK2 D I V M T Q S P L S L P V T P G E P A S I S C R S S Q S L V
C2HuVK3 D I V M T Q S P L S L P V T P G E P A S I S C R S S Q S L V
C2HuVK4 D I V M T Q S P L S L P V T P G E P A S I S C R S S Q S L V
dpk15 D I V M T Q S P L S L P V T P G E P A S I S C R S S Q S L L
JK1 -
40 50 60
C2VK Y S N G D T Y L H W Y L Q K P G Q S P K L L I Y K V S N R F
C2HuVK1 Y S N G D T Y L H W Y L Q K P G Q S P Q L L I Y K V S N R F
C2HuVK2 Y S N G D T Y L H W Y L Q K P G Q S P Q L L I Y K V S N R F
C2HuVK3 Y S N G D T Y L H W Y L Q K P G Q S P K L L I Y K V S N R F
C2HuVK4 Y S N G D T Y L H W Y L Q K P G Q S P K L L I Y K V S N R F
dpk15 H S N G Y N Y L D W Y L Q K P G Q S P Q L L I Y L G S N R A
JK1 -
70 80 90
C2VK S G V P D R F S G S G S G T D F T L K I S R V E A E D L G V
C2HuVK1 S G V P D R F S G S G S G T D F T L K I S R V E A E D V G V
C2HuVK2 S G V P D R F S G S G S G T D F T L K I S R V E A E D V G V
C2HuVK3 S G V P D R F S G S G S G T D F T L K I S R V E A E D V G V
C2HuVK4 S G V P D R F S G S G S G T D F T L K I S R V E A E D V G V
dpk15 S G V P D R F S G S G S G T D F T L K I S R V E A E D V G V
JK1 -
100 110
C2VK Y F C S Q S T H V P W T F G G G T K L E I K
C2HuVK1 Y Y C S Q S T H V P W T F G Q G T K V E I K
C2HuVK2 Y F C S Q S T H V P W T F G Q G T K V E I K
C2HuVK3 Y Y C S Q S T H V P W T F G Q G T K V E I K
C2HuVK4 Y F C S Q S T H V P W T F G Q G T K V E I K
dpk15 Y Y C M Q - - - - - - - - - - A - L Q T P
JK1 - - - - - - - - - - W T F G Q G T K V E I K

FIG 12.

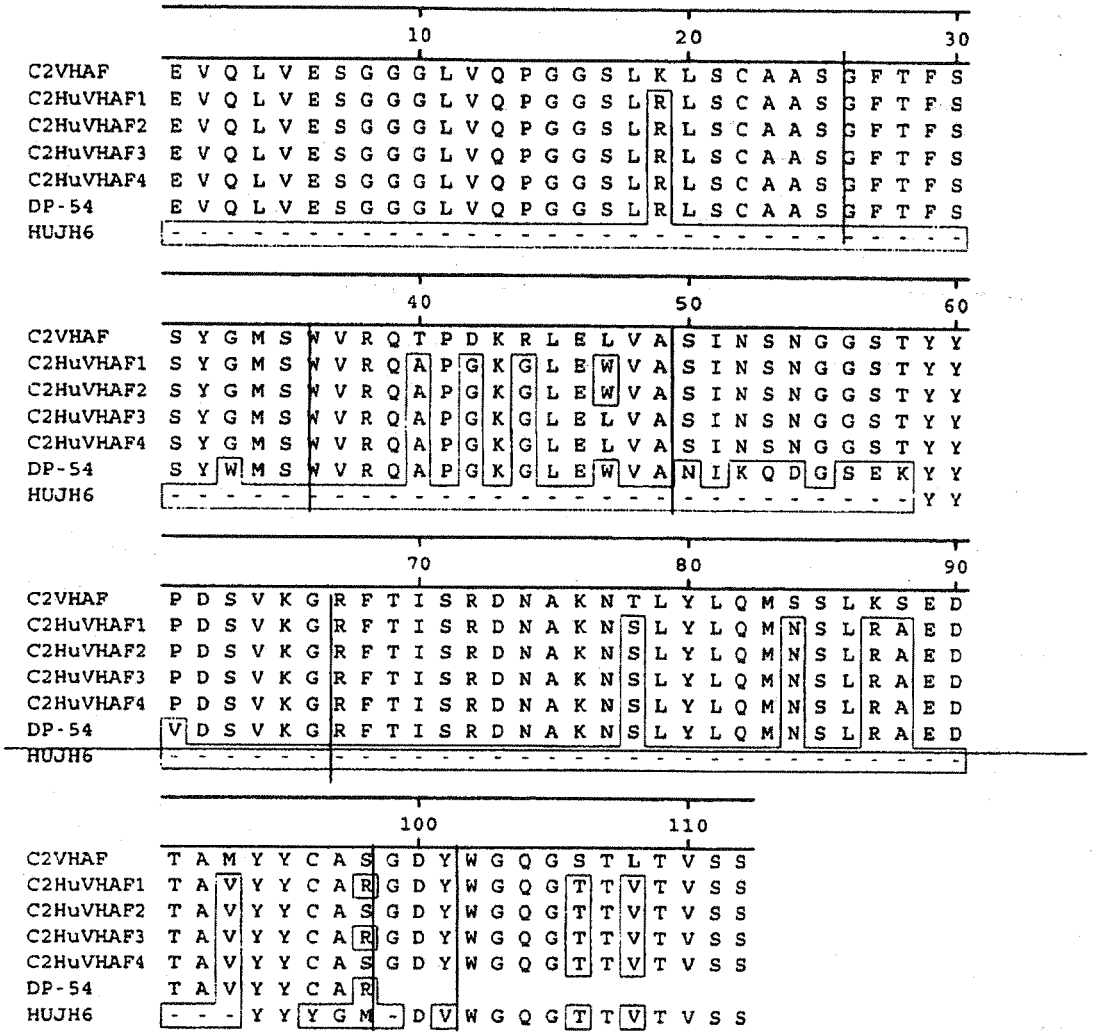

10 20 30
C2VHAF E V Q L V E S G G G L V Q P G G S L K L S C A A S G F T F S
C2HuVHAF1 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S
C2HuVHAF2 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S
C2HuVHAF3 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S
C2HuVHAF4 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S
DP-54 E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S
HUJH6 -
40 50 60
C2VHAF S Y G M S W V R Q T P D K R L E L V A S I N S N G G S T Y Y
C2HuVHAF1 S Y G M S W V R Q A P G K G L E W V A S I N S N G G S T Y Y
C2HuVHAF2 S Y G M S W V R Q A P G K G L E W V A S I N S N G G S T Y Y
C2HuVHAF3 S Y G M S W V R Q A P G K G L E L V A S I N S N G G S T Y Y
C2HuVHAF4 S Y G M S W V R Q A P G K G L E L V A S I N S N G G S T Y Y
DP-54 S Y W M S W V R Q A P G K G L E W V A N I K Q D G S E K Y Y
HUJH6 - Y Y
70 80 90
C2VHAF P D S V K G R F T I S R D N A K N T L Y L Q M S S L K S E D
C2HuVHAF1 P D S V K G R F T I S R D N A K N S L Y L Q M N S L R A E D
C2HuVHAF2 P D S V K G R F T I S R D N A K N S L Y L Q M N S L R A E D
C2HuVHAF3 P D S V K G R F T I S R D N A K N S L Y L Q M N S L R A E D
C2HuVHAF4 P D S V K G R F T I S R D N A K N S L Y L Q M N S L R A E D
DP-54 V D S V K G R F T I S R D N A K N S L Y L Q M N S L R A E D
HUJH6 -
100 110
C2VHAF T A M Y Y C A S G D Y W G Q G S T L T V S S
C2HuVHAF1 T A V Y Y C A R G D Y W G Q G T T V T V S S
C2HuVHAF2 T A V Y Y C A S G D Y W G Q G T T V T V S S
C2HuVHAF3 T A V Y Y C A R G D Y W G Q G T T V T V S S
C2HuVHAF4 T A V Y Y C A S G D Y W G Q G T T V T V S S
DP-54 T A V Y Y C A R
HUJH6 - - - Y Y Y G M - D V W G Q G T T V T V S S

FIG 13.

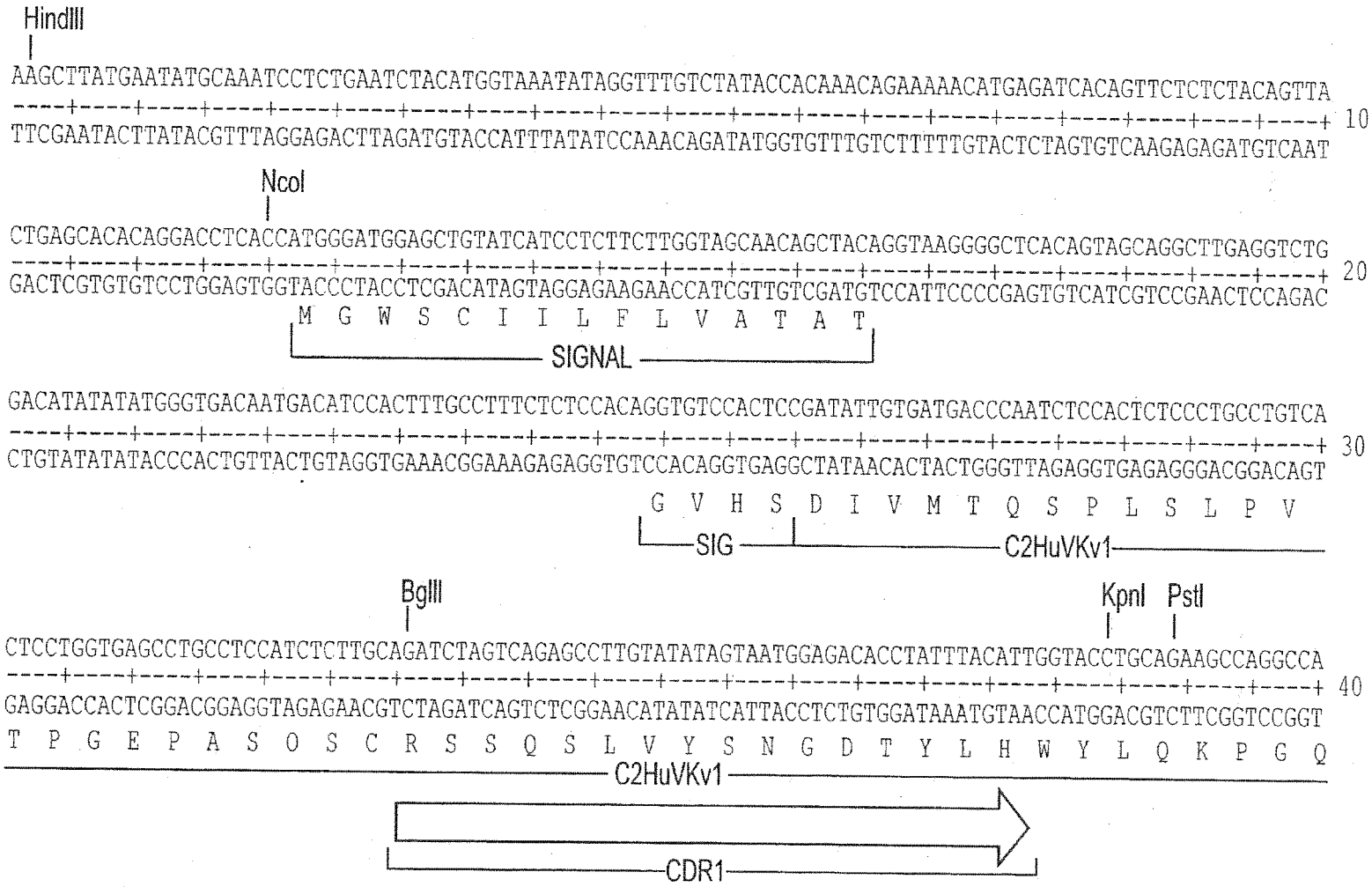

HindIII
AAGCTTATGAATATGCAAATCCTCTGAATCTACATGGTAAATATAGGTTTGTCTATACCACAAACAGAAAAACATGAGATCACAGTTCTCTCTACAGTTA
TTCGAATACTTATACGTTTAGGAGACTTAGATGTACCATTTATATCCAAACAGATATGGTGTTTGTCTTTTTGTACTCTAGTGTCAAGAGAGATGTCAAT
10
NcoI
CTGAGCACACAGGACCTCACCATGGGATGGAGCTGTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTAAGGGGCTCACAGTAGCAGGCTTGAGGTCTG
GACTCGTGTGTCCTGGAGTGGTACCCTACCTCGACATAGTAGGAGAAGAACCATCGTTGTCGATGTCCATTCCCCGAGTGTCATCGTCCGAACTCCAGAC
20
M G W S C I I L F L V A T A T
SIGNAL
GACATATATATGGGTGACAATGACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCGATATTGTGATGACCCAATCTCCACTCTCCCTGCCTGTCA
CTGTATATATACCCACTGTTACTGTAGGTGAAACGGAAAGAGAGGTGTCCACAGGTGAGGCTATAACACTACTGGGTTAGAGGTGAGAGGGACGGACAGT
30
G V H S D I V M T Q S P L S L P V
SIG
C2HuVKv1
BglII
KpnI
PstI
CTCCTGGTGAGCCTGCCTCCATCTCTTGCAGATCTAGTCAGAGCCTTGTATATAGTAATGGAGACACCTATTTACATTGGTACCTGCAGAAGCCAGGCCA
GAGGACCACTCGGACGGAGGTAGAGAACGTCTAGATCAGTCTCGGAACATATATCATTACCTCTGTGGATAAATGTAACCATGGACGTCTTCGGTCCGGT
40
T P G E P A S O S C R S S Q S L V Y S N G D T Y L H W Y L Q K P G Q
C2HuVKv1
CDR1

FIG. 14-1

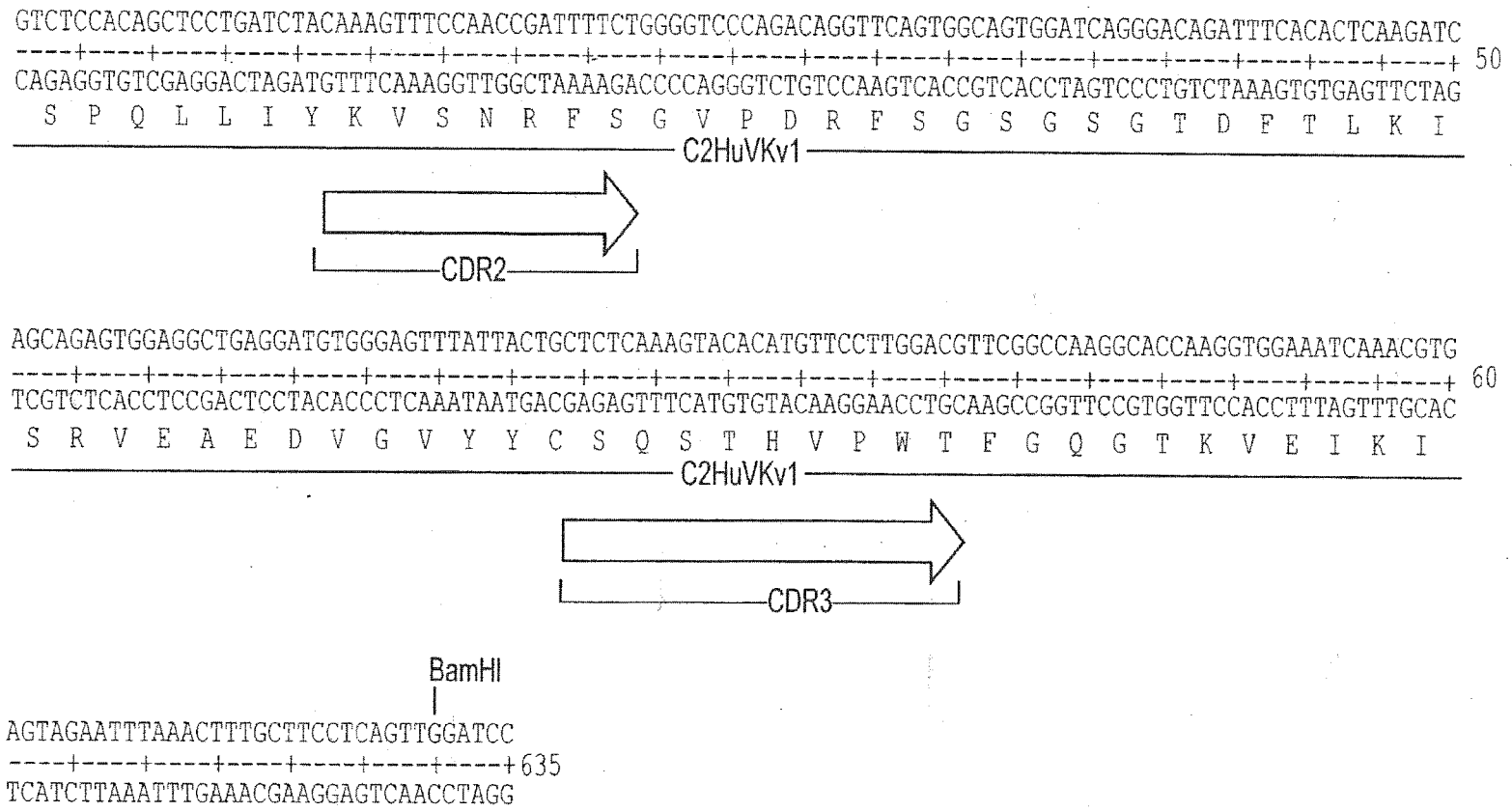

GTCTCCACAGCTCCTGATCTACAAAGTTTCCAACCGATTTTCTGGGGTCCCAGACAGGTTCAGTGGCAGTGGATCAGGGACAGATTTCACACTCAAGATC
50
CAGAGGTGTCGAGGACTAGATGTTTCAAAGGTTGGCTAAAAGACCCCAGGGTCTGTCCAAGTCACCGTCACCTAGTCCCTGTCTAAAGTGTGAGTTCTAG
S P Q L L I Y K V S N R F S G V P D R F S G S G S G T D F T L K I
C2HuVKv1
CDR2
AGCAGAGTGGAGGCTGAGGATGTGGGAGTTTATTACTGCTCTCAAAGTACACATGTTCCTTGGACGTTCGGCCAAGGCACCAAGGTGGAAATCAAACGTG
60
TCGTCTCACCTCCGACTCCTACACCCTCAAATAATGACGAGAGTTTCATGTGTACAAGGAACCTGCAAGCCGGTTCCGTGGTTCCACCTTTAGTTTGCAC
S R V E A E D V G V Y Y C S Q S T H V P W T F G Q G T K V E I K I
C2HuVKv1
CDR3
BamHI
AGTAGAATTTAAACTTTGCTTCCTCAGTTGGATCC
635
TCATCTTAAATTTGAAACGAAGGAGTCAACCTAGG

FIG. 14-2


BamHI
BglII
GGATCCTGGCAGAGTCTCACAGATGCTTCTGAGACAACATTTGCTTTCAAAAAATGAACCACACACATCCTAAAGATCTCAGCCACTTCCCATGTTTCAT
CCTAGGACCGTCTCAGAGTGTCTACGAAGACTCTGTTGTAAACGAAAGTTTTTTACTTGGTGTGTGTAGGATTTCTAGAGTCGGTGAAGGGTACAAAGTA
100
TTTATGTTACAGCAAACATCACAACAATCATTCCTACAGATCACCACTGCATGTGATCAATAAAATAGTTTTTGCAACAATGGTACTTATGATAATCATC
AAATACAATGTCGTTTGTAGTGTTGTTAGTAAGGATGTCTAGTGGTGACGTACACTAGTTATTTTATCAAAAACGTTGTTACCATGAATACTATTAGTAG
200
TTTTATTGTTTACAAATACTGCTTTACAATAGTTATTCGGTTGCACTGTTCATATTAGATTTCCAATTAGCTCACTTAGGAACATAAGTCCCTCGAACAG
AAAATAACAAATGTTTATGACGAAATGTTATCAATAAGCCAACGTGACAAGTATAATCTAAAGGTTAATCGAGTGAATCCTTGTATTCAGGGAGCTTGTC
300
CTCAGTCATCTTTTTCATTCCTGTTTCTATCCCCTACATCTCTTTCCTTTGCAGACGACTATCTCCTACACTGAAACAGGAAAGCTAGCTTTTTTTTTTC
GAGTCAGTAGAAAAAGTAAGGACAAAGATAGGGGATGTAGAGAAAGGAAACGTCTGCTGATAGAGGATGTGACTTTGTCCTTTCGATCGAAAAAAAAAAG
400
AGTGCTATTTAATTATTTCAATATCCTCTCATCAAATGTATTTAAATAACAAAAGCTCAACCAAAAAGAAAGAAATATGTAATTCTTTCAGAGTAAAAAT
TCACGATAAATTAATAAAGTTATAGGAGAGTAGTTTACATAAATTTATTGTTTTCGAGTTGGTTTTTCTTTCTTTATACATTAAGAAAGTCTCATTTTTA
500
CACACCCATGACCTGGCCACTGAGGGCTTGATCAATTCACTTTGAATTTGGCATTAAATACCATTAAGGTATATTAACTGATTTTAAAATAAGATATATT
GTGTGGGTACTCGACCGGTGACTCCCGAACTAGTTAAGTGAAACTTAAACCGTAATTTATGGTAATTCCATATAATTGACTAAAATTTTATTCTATATAA
600
CGTGACCATGTTTTTAACTTTCAAAAATGTAGCTGCCAGTGTGTGATTTTATTTCAGTTGTACAAAATATCTAAACCTATAGCAATGTGATTAATAAAAA
GCACTGGTACAAAAATTGAAAGTTTTTACATCGACGGTCACACACTAAAATAAAGTCAACATGTTTTATAGATTTGGATATCGTTACACTAATTATTTTT
700

FIG. 15-1


CTTAAACATATTTTCCAGTACCTTAATTCTGTGATAGGAAAATTTTAATCTGAGTATTTTAATTTCATAATCTCTAAAATAGTTTAATGATTTGTCATTG
GAATTTGTATAAAAGGTCATGGAATTAAGACACTATCCTTTTAAAATTAGACTCATAAAATTAAAGTATTAGAGATTTTATCAAATTACTAAACAGTAAC
PvuII
TGTTGCTGTCGTTTACCCCAGCTGATCTCAAAAGTGATATTTAAGGAGATTATTTTGGTCTGCAACAACTTGATAGGACTATTTTAGGGCCTTTTTAAAG
ACAACGACAGCAAATGGGGTCGACTAGAGTTTTCACTATAAATTCCTCTAATAAAACCAGACGTTGTTGAACTATCCTGATAAAATCCCGGAAAAATTTC
CTCTATTAAAACTAACTTACAACGATTCAAAACTGTTTTAAACTATTTCAAAATGATTTTAGAGCCTTTTGAAAACTCTTTTAAACACTTTTTAAACTCT
GAGATAATTTTGATTGAATGTTGCTAAGTTTTGACAAAATTTGATAAAGTTTTACTAAAATCTCGGAAAACTTTTGAGAAAATTTGTGAAAAATTTGAGA
EcoRI
ATTAAAACTAATAAGATAACTTGAAATAATTTTCATGTCAAATACATTAACTGTTTAATGTTTAAATGCCAGATGAAAAATGTAAAGCTATCAAGAATTC
TAATTTTGATTATTCTATTGAACTTTATTAAAAGTACAGTTTATGTAATTGACAAATTACAAATTTACGGTCTACTTTTTACATTTCGATAGTTCTTAAG
NcoI
ACCCAGATAGGAGTATCTTCATAGCATGTTTTTCCCTGCTTATTTTCCAGTGATCACATTATTTTGCTACCATGGTTATTTTATACAATTATCTGAAAAA
TGGGTCTATCCTCATAGAAGTATCGTACAAAAAGGGACGAATAAAAGGTCACTAGTGTAATAAAACGATGGTACCAATAAAATATGTTAATAGACTTTTT
AATTAGTTATGAAGATTAAAAGAGAAGAAAATATTAAACATAAGAGATTCAGTCTTTCATGTTGAACTGCTTGGTTAACAGTGAAGTTAGTTTTAAAAAA
TTAATCAATACTTCTAATTTTCTCTTCTTTTATAATTTGTATTCTCTAAGTCAGAAAGTACAACTTGACGAACCAATTGTCACTTCAATCAAAATTTTTT
PvuII
AAAAAAAACTATTTCTGTTATCAGCTGACTTCTCCCTATCTGTTGACTTCTCCCAGCAAAAGATTCTTATTTTACATTTTAACTACTGCTCTCCCACCCA
TTTTTTTTGATAAAGACAATAGTCGACTGAAGAGGGATAGACAACTGAAGAGGGTCGTTTTCTAAGAATAAAATGTAAAATTGATGACGAGAGGGTGGGT

FIG. 15-2


ACGGGTGGAATCCCCCAGAGGGGGATTTCCAAGAGGCCACCTGGCAGTTGCTGAGGGTCAGAAGTGAAGCTAGCCACTTCCTCTTAGGCAGGTGGCCAAG
TGCCCACCTTAGGGGGTCTCCCCCTAAAGGTTCTCCGGTGGACCGTCAACGACTCCCAGTCTTCACTTCGATCGGTGAAGGAGAATCCGTCCACCGGTTC
150
ATTACAGTTGACCTCTCCTGGTATGGCTGAAAATTGCTGCATATGGTTACAGGCCTTGAGGCCTTTGGGAGGGCTTAGAGAGTTGCTGGAACAGTCAGAA
TAATGTCAACTGGAGAGGACCATACCGACTTTTAACGACGTATACCAATGTCCGGAACTCCGGAAACCCTCCCGAATCTCTCAACGACCTTGTCAGTCTT
160
PstI
XmaI
SmaI
GGTGGAGGGGCTGACACCACCCAGGCGCAGAGGCAGGGCTCAGGGCCTGCTCTGCAGGGAGGTTTTAGCCCAGCCCAGCCAAAGTAACCCCCGGGAGCCT
CCACCTCCCCGACTGTGGTGGGTCCGCGTCTCCGTCCCGAGTCCCGGACGAGACGTCCCTCCAAAATCGGGTCGGGTCGGTTTCATTGGGGGCCCTCGGA
170
EcoRI
GTTATCCCAGCACAGTCCTGGAAGAGGCACAGGGGAAATAAAAGCGGACGGAGGCTTTCCTTGACTCAGCCGCTGCCTGGTCTTCTTCAGACCTGTTCTG
CAATAGGGTCGTGTCAGGACCTTCTCCGTGTCCCCTTTATTTTCGCCTGCCTCCGAAAGGAACTGAGTCGGCGACGGACCAGAAGAAGTCTGGACAAGAC
180

FIG. 15-3

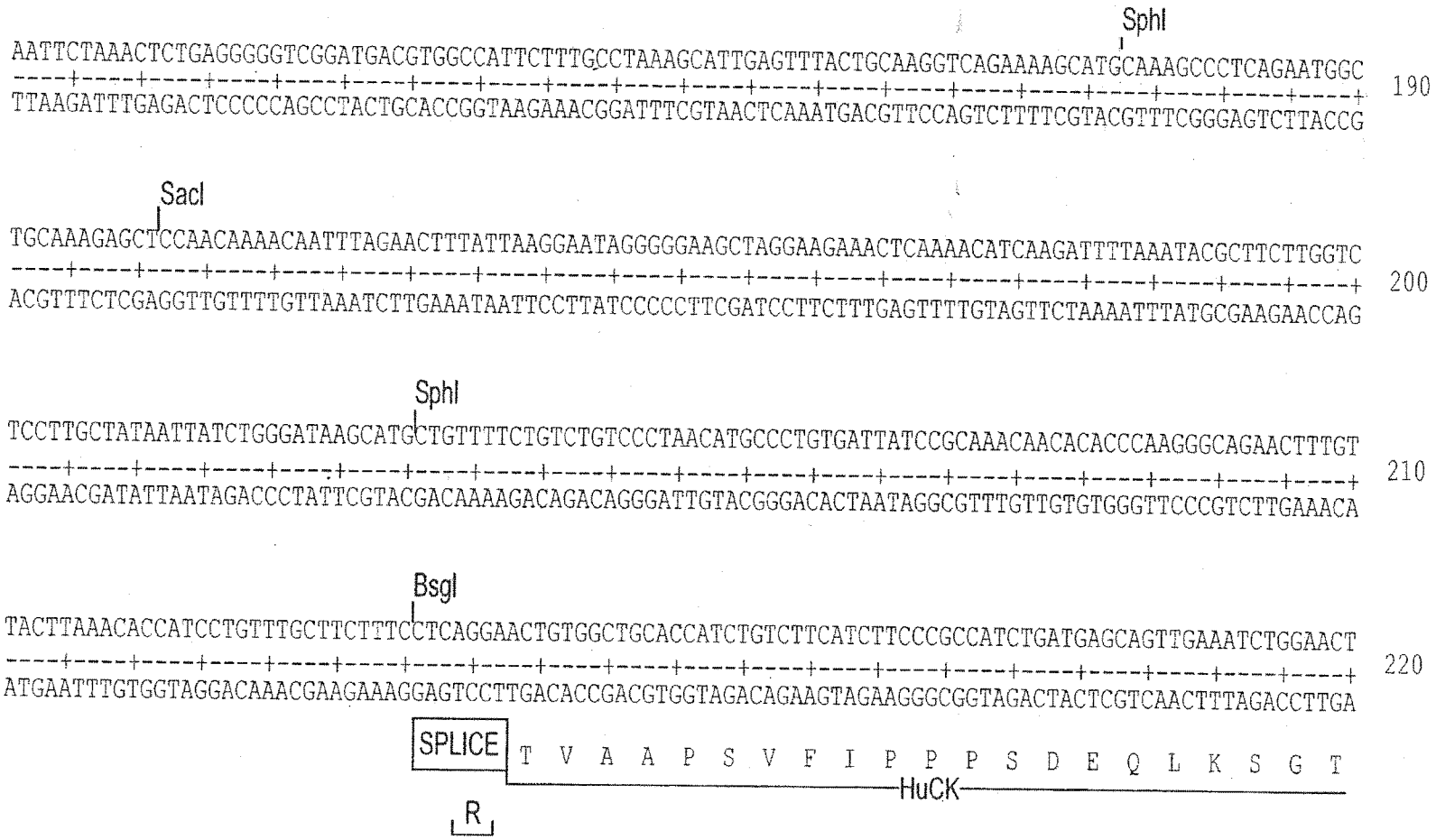

SphI
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TTAAGATTTGAGACTCCCCCAGCCTACTGCACCGGTAAGAAACGGATTTCGTAACTCAAATGACGTTCCAGTCTTTTCGTACGTTTCGGGAGTCTTACCG
190
SacI
TGCAAAGAGCTCCAACAAAACAATTTAGAACTTTATTAAGGAATAGGGGGAAGCTAGGAAGAAACTCAAAACATCAAGATTTTAAATACGCTTCTTGGTC
ACGTTTCTCGAGGTTGTTTTGTTAAATCTTGAAATAATTCCTTATCCCCCTTCGATCCTTCTTTGAGTTTTGTAGTTCTAAAATTTATGCGAAGAACCAG
200
SphI
TCCTTGCTATAATTATCTGGGATAAGCATGCTGTTTTCTGTCTGTCCCTAACATGCCCTGTGATTATCCGCAAACAACACACCCAAGGGCAGAACTTTGT
AGGAACGATATTAATAGACCCTATTCGTACGACAAAAGACAGACAGGGATTGTACGGGACACTAATAGGCGTTTGTTGTGTGGGTTCCCGTCTTGAAACA
210
BsgI
TACTTAAACACCATCCTGTTTGCTTCTTTCCTCAGGAACTGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACT
ATGAATTTGTGGTAGGACAAACGAAGAAAGGAGTCCTTGACACCGACGTGGTAGACAGAAGTAGAAGGGCGGTAGACTACTCGTCAACTTTAGACCTTGA
220
SPLICE
T V A A P S V F I P P P S D E Q L K S G T
HuCK
R

FIG. 15-4

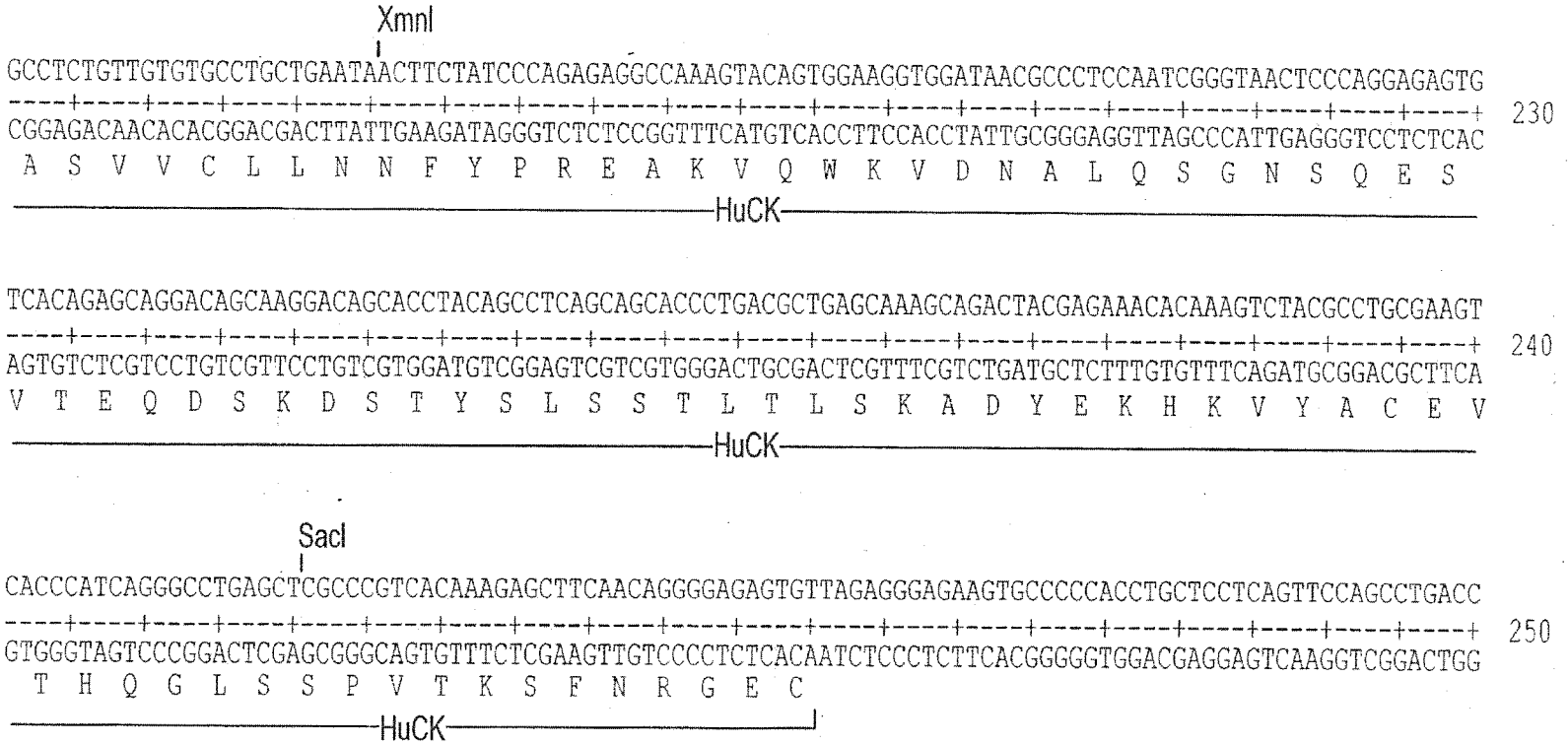

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CGGAGACAACACACGGACGACTTATTGAAGATAGGGTCTCTCCGGTTTCATGTCACCTTCCACCTATTGCGGGAGGTTAGCCCATTGAGGGTCCTCTCAC
230
A S V V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S
HuCK
TCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGT
AGTGTCTCGTCCTGTCGTTCCTGTCGTGGATGTCGGAGTCGTCGTGGGACTGCGACTCGTTTCGTCTGATGCTCTTTGTGTTTCAGATGCGGACGCTTCA
240
V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V
HuCK
SacI
CACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGTTAGAGGGAGAAGTGCCCCCACCTGCTCCTCAGTTCCAGCCTGACC
GTGGGTAGTCCCGGACTCGAGCGGGCAGTGTTTCTCGAAGTTGTCCCCTCTCACAATCTCCCTCTTCACGGGGGTGGACGAGGAGTCAAGGTCGGACTGG
250
T H Q G L S S P V T K S F N R G E C
HuCK

FIG. 15-5


CCCTCCCATCCTTTGGCCTCTGACCCTTTTTTCCACAGGGGACCTACCCCTATTGCGGTCCTCCAGCTCATCTTTCACCTCACCCCCCTCCTCCTCCTTGG
260
GGGAGGGTAGGAAACCGGAGACTGGGAAAAAGGTGTCCCCTGGATGGGGATAACGCCAGGAGGTCGAGTAGAAAGTGGAGTGGGGGGAGGAGGAGGAACC
CTTTAATTATGCTAATGTTGGAGGAGAATGAATAAATAAAGTGAATCTTTGCACCTGTGGTTTCTCTCTTTCCTCATTTAATAATTATTATCTGTTGTTT
270
GAAATTAATACGATTACAACCTCCTCTTACTTATTTATTTCACTTAGAAACGTGGACACCAAAGAGAGAAAGGAGTAAATTATTAATAATAGACAACAAA
TACCAACTACTCAATTTCTCTTATAAGGGACTAAATATGTAGTCATCCTAAGGCGCATAACCATTTATAAAAATCATCCTTCATTCTATTTTACCCTATC
280
ATGGTTGATGAGTTAAAGAGAATATTCCCTGATTTATACATCAGTAGGATTCCGCGTATTGGTAAATATTTTTAGTAGGAAGTAAGATAAAATGGGATAG
NcoI
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290
TAGGAGACGTTATGTCAGGAGGGAGTTTGGGTGTTCGGAAGACAGGAGTGTCAGGGGACCCGGTACCATCCTCTCTGAACGAAGGAACAAAAGGGGAGGA
CAGCAAGCCCTCATAGTCCTTTTTAAGGGTGACAGGTCTTACAGTCATATATCCTTTGATTCAATTCCCTGAGAATCAACCAAAGCAAATTTTTCAAAAG
300
GTCGTTCGGGAGTATCAGGAAAAATTCCCACTGTCCAGAATGTCAGTATATAGGAAACTAAGTTAAGGGACTCTTAGTTGGTTTCGTTTAAAAAGTTTTC
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310
TTCTTTGGACGATATTTCTCTTAGTAAGTAACGTTGTACTATATTTTATTGTTGTGTTATTTTCGTTAATTTATTTGTTTGTTATCCCTTTACAAATTCA
TCATCATGGTACTTAGACTTAATGGAATGTCATGCCTTATTTACATTTTTAAACAGGTACTGAGGGACTCCTGTCTGCCAAGGGCCGTATTGAGTACTTT
320
AGTAGTACCATGAATCTGAATTACCTTACAGTACGGAATAAATGTAAAAATTTGTCCATGACTCCCTGAGGACAGACGGTTCCCGGCATAACTCATGAAA
CCACAACCTAATTTAATCCACACTATACTGTGAGATTAAAAACATTCATTAAAATGTTGCAAAGGTTCTATAAAGCTGAGAGACAAATATATTCTATAAC
330
GGTGTTGGATTAAATTAGGTGTGATATGACACTCTAATTTTTGTAAGTAATTTTACAACGTTTCCAAGATATTTCGACTCTCTGTTTATATAAGATATTG

FIG. 15-6

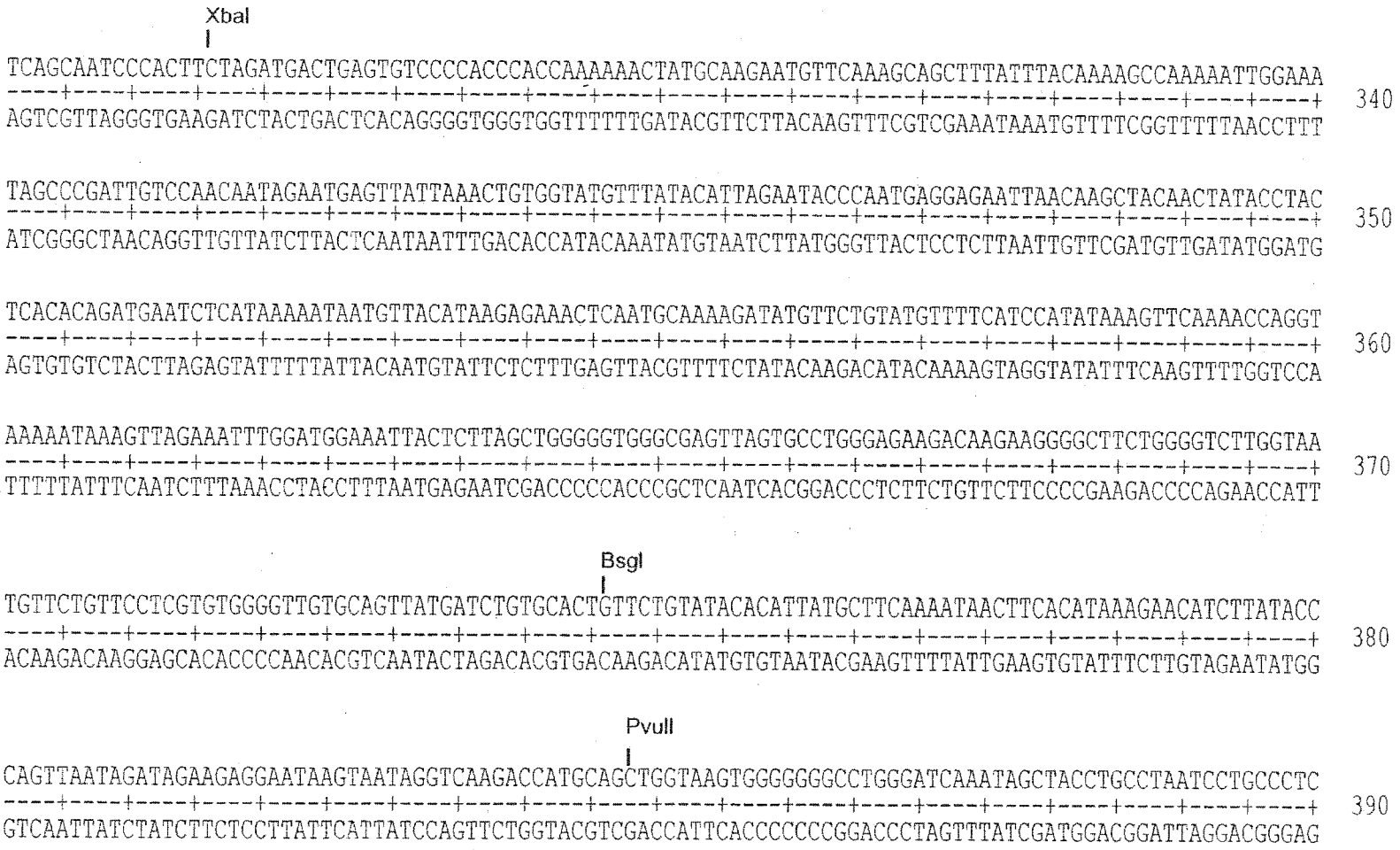

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AGTCGTTAGGGTGAAGATCTACTGACTCACAGGGGTGGGTGGTTTTTTGATACGTTCTTACAAGTTTCGTCGAAATAAATGTTTTCGGTTTTTAACCTTT
340
TAGCCCGATTGTCCAACAATAGAATGAGTTATTAAACTGTGGTATGTTTATACATTAGAATACCCAATGAGGAGAATTAACAAGCTACAACTATACCTAC
ATCGGGCTAACAGGTTGTTATCTTACTCAATAATTTGACACCATACAAATATGTAATCTTATGGGTTACTCCTCTTAATTGTTCGATGTTGATATGGATG
350
TCACACAGATGAATCTCATAAAAATAATGTTACATAAGAGAAACTCAATGCAAAAGATATGTTCTGTATGTTTTCATCCATATAAAGTTCAAAACCAGGT
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360
AAAAATAAAGTTAGAAATTTGGATGGAAATTACTCTTAGCTGGGGGTGGGCGAGTTAGTGCCTGGGAGAAGACAAGAAGGGGCTTCTGGGGTCTTGGTAA
TTTTTATTTCAATCTTTAAACCTACCTTTAATGAGAATCGACCCCCACCCGCTCAATCACGGACCCTCTTCTGTTCTTCCCCGAAGACCCCAGAACCATT
370
BsgI
TGTTCTGTTCCTCGTGTGGGGTTGTGCAGTTATGATCTGTGCACTGTTCTGTATACACATTATGCTTCAAAATAACTTCACATAAAGAACATCTTATACC
ACAAGACAAGGAGCACACCCCAACACGTCAATACTAGACACGTGACAAGACATATGTGTAATACGAAGTTTTATTGAAGTGTATTTCTTGTAGAATATGG
380
PvuII
CAGTTAATAGATAGAAGAGGAATAAGTAATAGGTCAAGACCATGCAGCTGGTAAGTGGGGGGGCCTGGGATCAAATAGCTACCTGCCTAATCCTGCCCTC
GTCAATTATCTATCTTCTCCTTATTCATTATCCAGTTCTGGTACGTCGACCATTCACCCCCCCGGACCCTAGTTTATCGATGGACGGATTAGGACGGGAG
390

FIG. 15-7

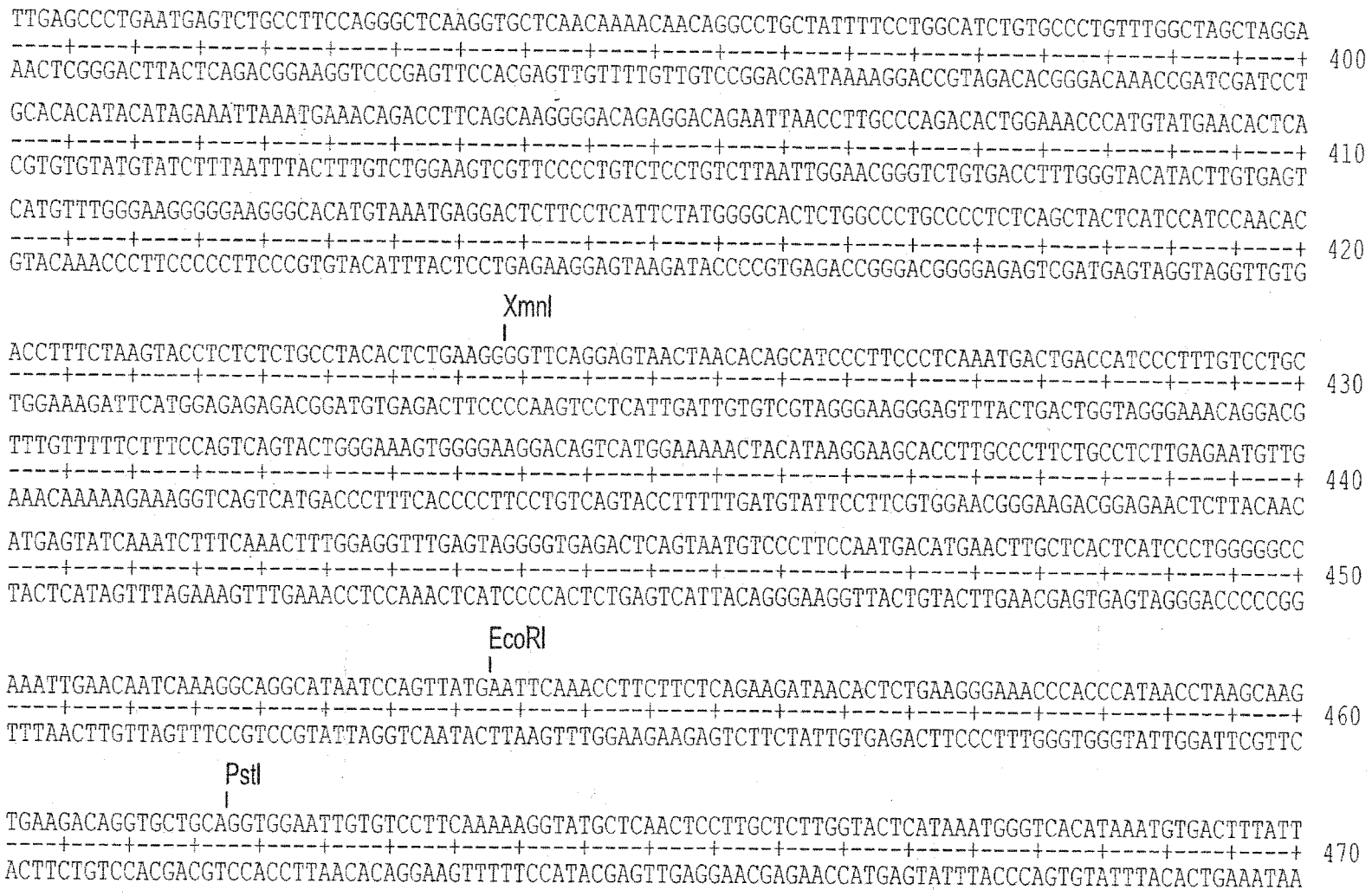

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GCACACATACATAGAAATTAAATGAAACAGACCTTCAGCAAGGGGACAGAGGACAGAATTAACCTTGCCCAGACACTGGAAACCCATGTATGAACACTCA
CGTGTGTATGTATCTTTAATTTACTTTGTCTGGAAGTCGTTCCCCTGTCTCCTGTCTTAATTGGAACGGGTCTGTGACCTTTGGGTACATACTTGTGAGT 410
CATGTTTGGGAAGGGGGAAGGGCACATGTAAATGAGGACTCTTCCTCATTCTATGGGGCACTCTGGCCCTGCCCCTCTCAGCTACTCATCCATCCAACAC
GTACAAACCCTTCCCCCTTCCCGTGTACATTTACTCCTGAGAAGGAGTAAGATACCCCGTGAGACCGGGACGGGGAGAGTCGATGAGTAGGTAGGTTGTG 420
XmnI
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TGGAAAGATTCATGGAGAGAGACGGATGTGAGACTTCCCCAAGTCCTCATTGATTGTGTCGTAGGGAAGGGAGTTTACTGACTGGTAGGGAAACAGGACG 430
TTTGTTTTTCTTTCCAGTCAGTACTGGGAAAGTGGGGAAGGACAGTCATGGAAAAACTACATAAGGAAGCACCTTGCCCTTCTGCCTCTTGAGAATGTTG
AAACAAAAAGAAAGGTCAGTCATGACCCTTTCACCCCTTCCTGTCAGTACCTTTTTGATGTATTCCTTCGTGGAACGGGAAGACGGAGAACTCTTACAAC 440
ATGAGTATCAAATCTTTCAAACTTTGGAGGTTTGAGTAGGGGTGAGACTCAGTAATGTCCCTTCCAATGACATGAACTTGCTCACTCATCCCTGGGGGCC
TACTCATAGTTTAGAAAGTTTGAAACCTCCAAACTCATCCCCACTCTGAGTCATTACAGGGAAGGTTACTGTACTTGAACGAGTGAGTAGGGACCCCCGG 450
EcoRI
AAATTGAACAATCAAAGGCAGGCATAATCCAGTTATGAATTCAAACCTTCTTCTCAGAAGATAACACTCTGAAGGGAAACCCACCCATAACCTAAGCAAG
TTTAACTTGTTAGTTTCCGTCCGTATTAGGTCAATACTTAAGTTTGGAAGAAGAGTCTTCTATTGTGAGACTTCCCTTTGGGTGGGTATTGGATTCGTTC 460
PstI
TGAAGACAGGTGCTGCAGGTGGAATTGTGTCCTTCAAAAAGGTATGCTCAACTCCTTGCTCTTGGTACTCATAAATGGGTCACATAAATGTGACTTTATT
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FIG. 15-8

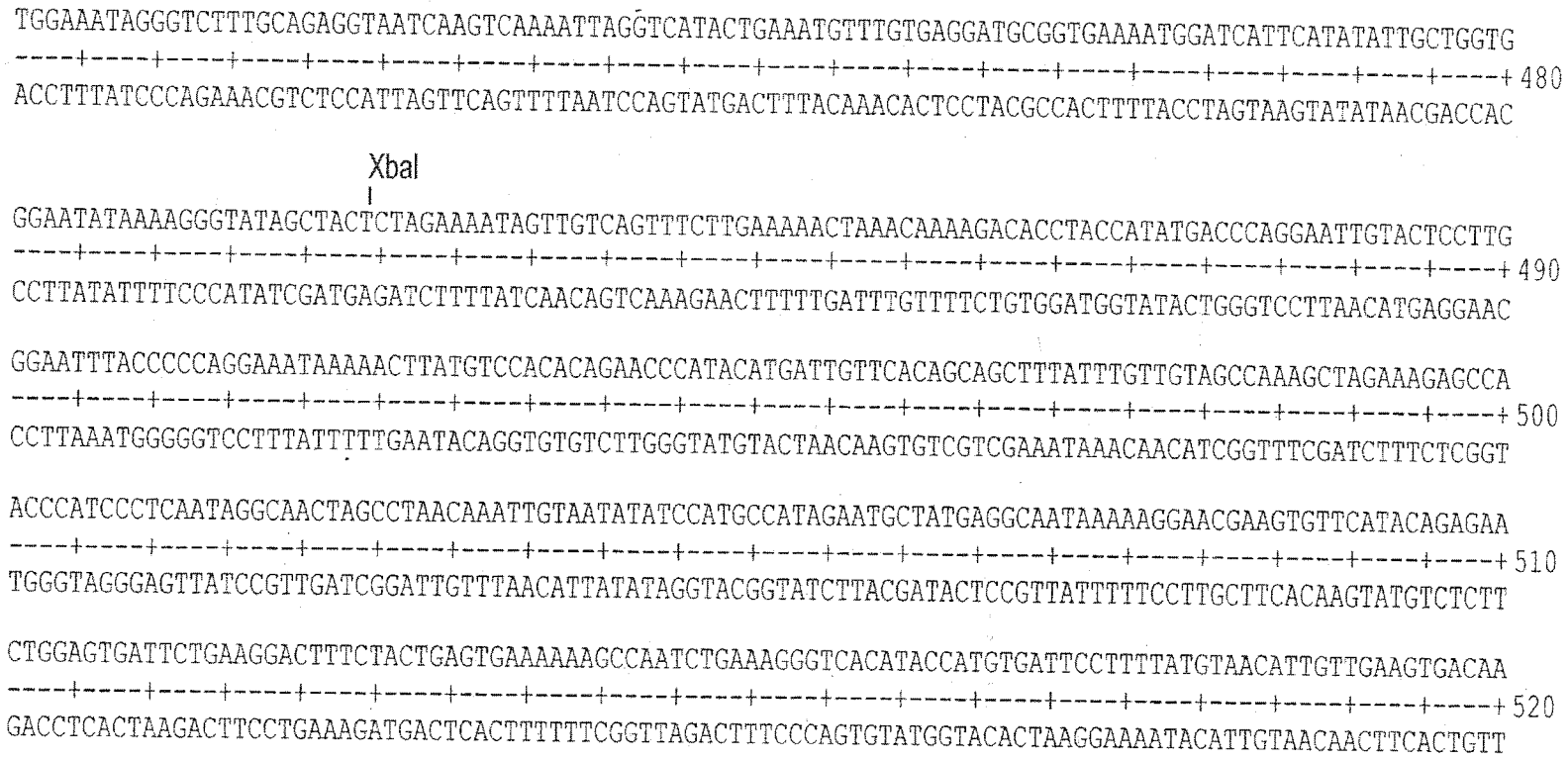

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480
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XbaI
GGAATATAAAAGGGTATAGCTACTCTAGAAAATAGTTGTCAGTTTCTTGAAAAACTAAACAAAAGACACCTACCATATGACCCAGGAATTGTACTCCTTG
490
CCTTATATTTTCCCATATCGATGAGATCTTTTATCAACAGTCAAAGAACTTTTTGATTTGTTTTCTGTGGATGGTATACTGGGTCCTTAACATGAGGAAC
GGAATTTACCCCCAGGAAATAAAAACTTATGTCCACACAGAACCCATACATGATTGTTCACAGCAGCTTTATTTGTTGTAGCCAAAGCTAGAAAGAGCCA
500
CCTTAAATGGGGGTCCTTTATTTTTGAATACAGGTGTGTCTTGGGTATGTACTAACAAGTGTCGTCGAAATAAACAACATCGGTTTCGATCTTTCTCGGT
ACCCATCCCTCAATAGGCAACTAGCCTAACAAATTGTAATATATCCATGCCATAGAATGCTATGAGGCAATAAAAAGGAACGAAGTGTTCATACAGAGAA
510
TGGGTAGGGAGTTATCCGTTGATCGGATTGTTTAACATTATATAGGTACGGTATCTTACGATACTCCGTTATTTTTCCTTGCTTCACAAGTATGTCTCTT
CTGGAGTGATTCTGAAGGACTTTCTACTGAGTGAAAAAAGCCAATCTGAAAGGGTCACATACCATGTGATTCCTTTTATGTAACATTGTTGAAGTGACAA
520
GACCTCACTAAGACTTCCTGAAAGATGACTCACTTTTTTCGGTTAGACTTTCCCAGTGTATGGTACACTAAGGAAAATACATTGTAACAACTTCACTGTT

FIG. 15-9

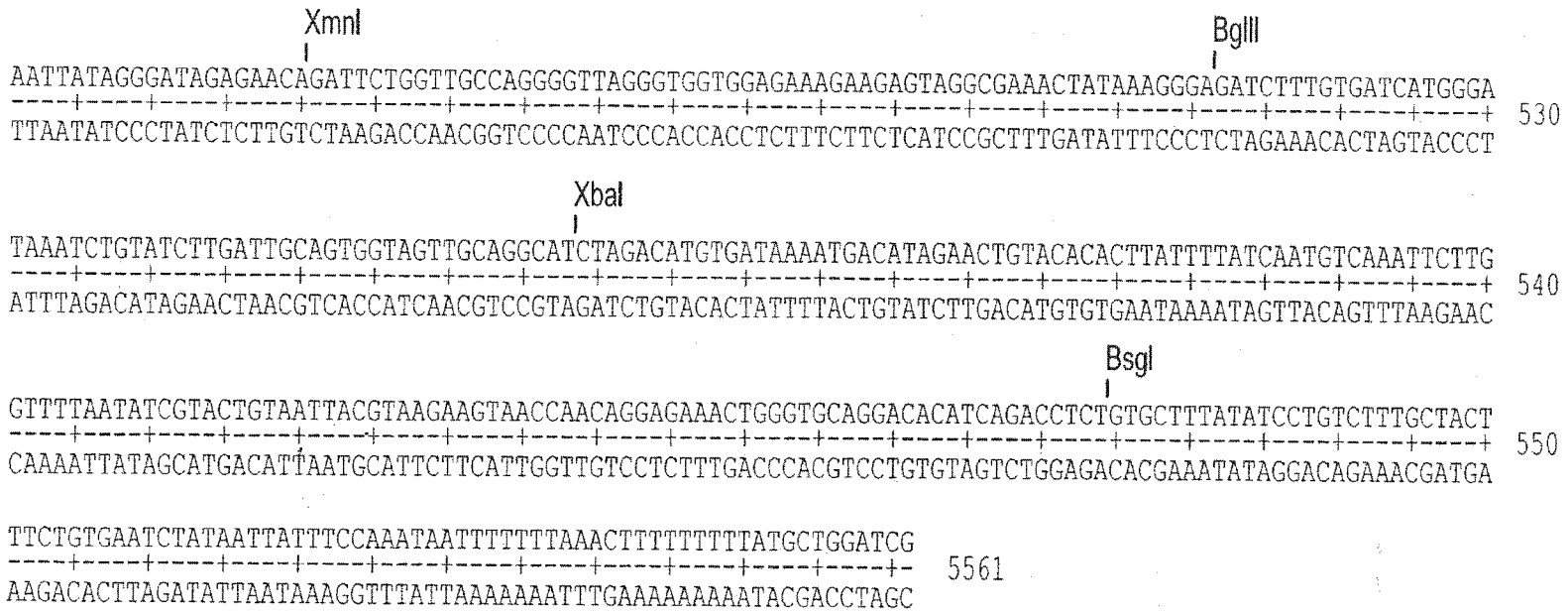

XmnI
BglII
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530
XbaI
TAAATCTGTATCTTGATTGCAGTGGTAGTTGCAGGCATCTAGACATGTGATAAAATGACATAGAACTGTACACACTTATTTTATCAATGTCAAATTCTTG
ATTTAGACATAGAACTAACGTCACCATCAACGTCCGTAGATCTGTACACTATTTTACTGTATCTTGACATGTGTGAATAAAATAGTTACAGTTTAAGAAC
540
BsgI
GTTTTAATATCGTACTGTAATTACGTAAGAAGTAACCAACAGGAGAAACTGGGTGCAGGACACATCAGACCTCTGTGCTTTATATCCTGTCTTTGCTACT
CAAAATTATAGCATGACATTAATGCATTCTTCATTGGTTGTCCTCTTTGACCCACGTCCTGTGTAGTCTGGAGACACGAAATATAGGACAGAAACGATGA
550
TTCTGTGAATCTATAATTATTTCCAAATAATTTTTTTAAACTTTTTTTTTATGCTGGATCG
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5561

FIG. 15-10

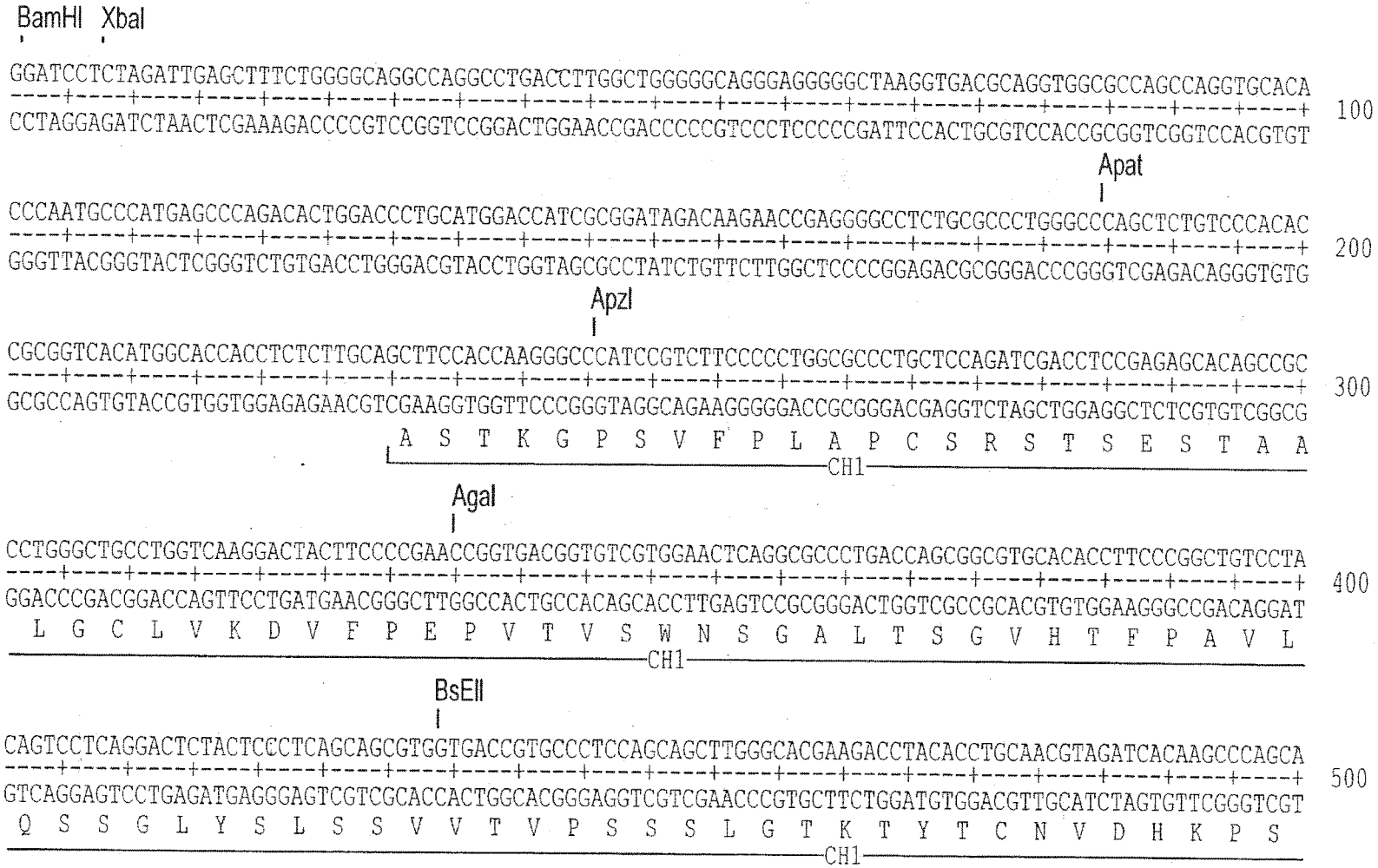

BamHI
XbaI
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CCTAGGAGATCTAACTCGAAAGACCCCGTCCGGTCCGGACTGGAACCGACCCCCGTCCCTCCCCCGATTCCACTGCGTCCACCGCGGTCGGTCCACGTGT
100
Apat
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200
ApzI
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300
A S T K G P S V F P L A P C S R S T S E S T A A
CH1
AgaI
CCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTA
GGACCCGACGGACCAGTTCCTGATGAACGGGCTTGGCCACTGCCACAGCACCTTGAGTCCGCGGGACTGGTCGCCGCACGTGTGGAAGGGCCGACAGGAT
400
L G C L V K D V F P E P V T V S W N S G A L T S G V H T F P A V L
CH1
BsEII
CAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACGAAGACCTACACCTGCAACGTAGATCACAAGCCCAGCA
GTCAGGAGTCCTGAGATGAGGGAGTCGTCGCACCACTGGCACGGGAGGTCGTCGAACCCGTGCTTCTGGATGTGGACGTTGCATCTAGTGTTCGGGTCGT
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CH1

FIG. 16-1

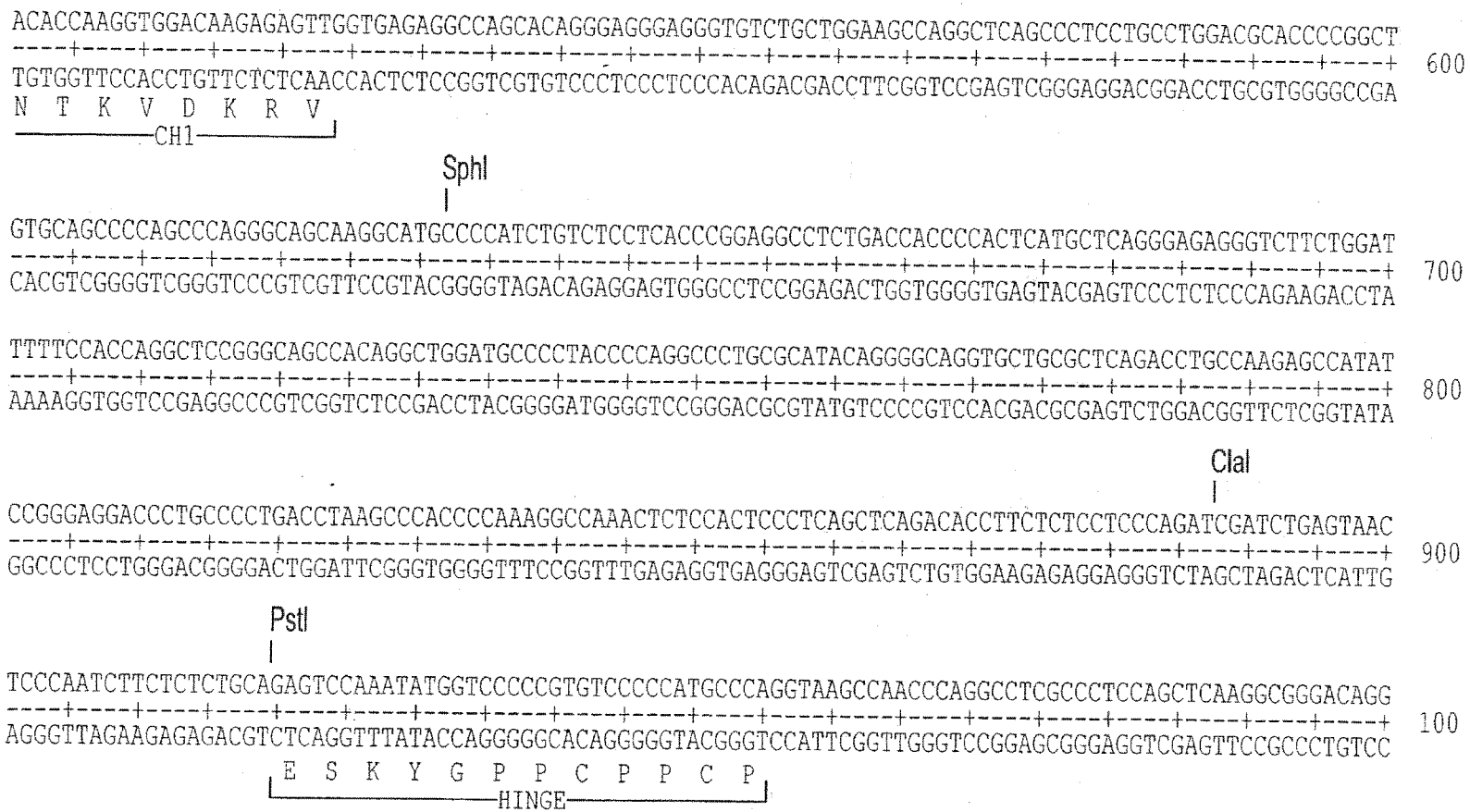

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600
N T K V D K R V
CH1
SphI
GTGCAGCCCCAGCCCAGGGCAGCAAGGCATGCCCCATCTGTCTCCTCACCCGGAGGCCTCTGACCACCCCACTCATGCTCAGGGAGAGGGTCTTCTGGAT
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700
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800
ClaI
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900
PstI
TCCCAATCTTCTCTCTGCAGAGTCCAAATATGGTCCCCCGTGTCCCCCATGCCCAGGTAAGCCAACCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGG
AGGGTTAGAAGAGAGACGTCTCAGGTTTATACCAGGGGGCACAGGGGGTACGGGTCCATTCGGTTGGGTCCGGAGCGGGAGGTCGAGTTCCGCCCTGTCC
100
E S K Y G P P C P P C P
HINGE

FIG. 16-2

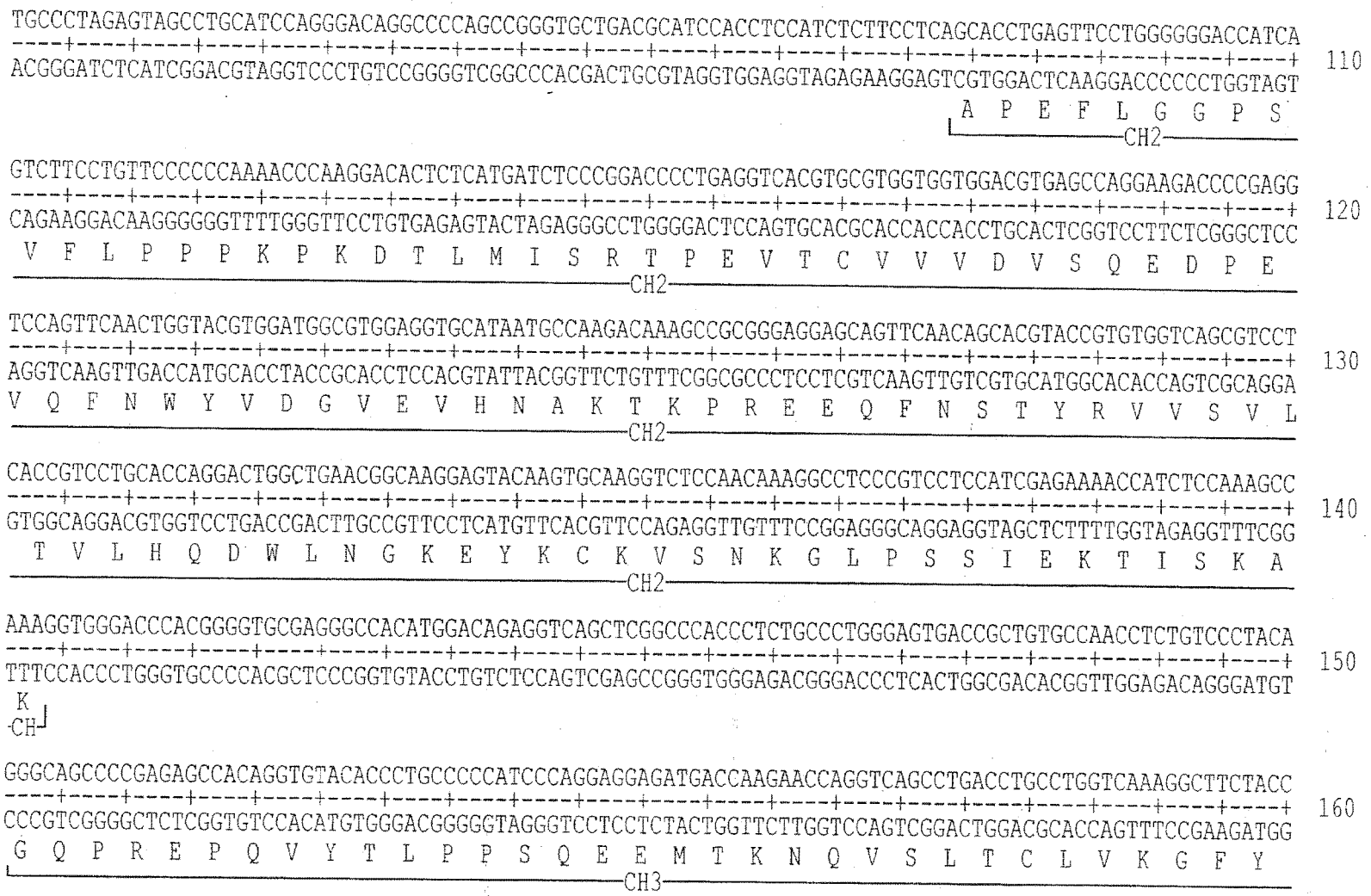

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ACGGGATCTCATCGGACGTAGGTCCCTGTCCGGGGTCGGCCCACGACTGCGTAGGTGGAGGTAGAGAAGGAGTCGTGGACTCAAGGACCCCCCTGGTAGT
110
A P E F L G G P S
CH2
GTCTTCCTGTTCCCCCCAAAACCCAAGGACACTCTCATGATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGGTGGACGTGAGCCAGGAAGACCCCGAGG
CAGAAGGACAAGGGGGGTTTTGGGTTCCTGTGAGAGTACTAGAGGGCCTGGGGACTCCAGTGCACGCACCACCACCTGCACTCGGTCCTTCTCGGGCTCC
120
V F L P P P K P K D T L M I S R T P E V T C V V V D V S Q E D P E
CH2
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AGGTCAAGTTGACCATGCACCTACCGCACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCAAGTTGTCGTGCATGGCACACCAGTCGCAGGA
130
V Q F N W Y V D G V E V H N A K T K P R E E Q F N S T Y R V V S V L
CH2
CACCGTCCTGCACCAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGGCCTCCCGTCCTCCATCGAGAAAACCATCTCCAAAGCC
GTGGCAGGACGTGGTCCTGACCGACTTGCCGTTCCTCATGTTCACGTTCCAGAGGTTGTTTCCGGAGGGCAGGAGGTAGCTCTTTTGGTAGAGGTTTCGG
140
T V L H Q D W L N G K E Y K C K V S N K G L P S S I E K T I S K A
CH2
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TTTCCACCCTGGGTGCCCCACGCTCCCGGTGTACCTGTCTCCAGTCGAGCCGGGTGGGAGACGGGACCCTCACTGGCGACACGGTTGGAGACAGGGATGT
150
K
CH
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CCCGTCGGGGCTCTCGGTGTCCACATGTGGGACGGGGGTAGGGTCCTCCTCTACTGGTTCTTGGTCCAGTCGGACTGGACGCACCAGTTTCCGAAGATGG
160
G Q P R E P Q V Y T L P P S Q E E M T K N Q V S L T C L V K G F Y
CH3

FIG. 16-3

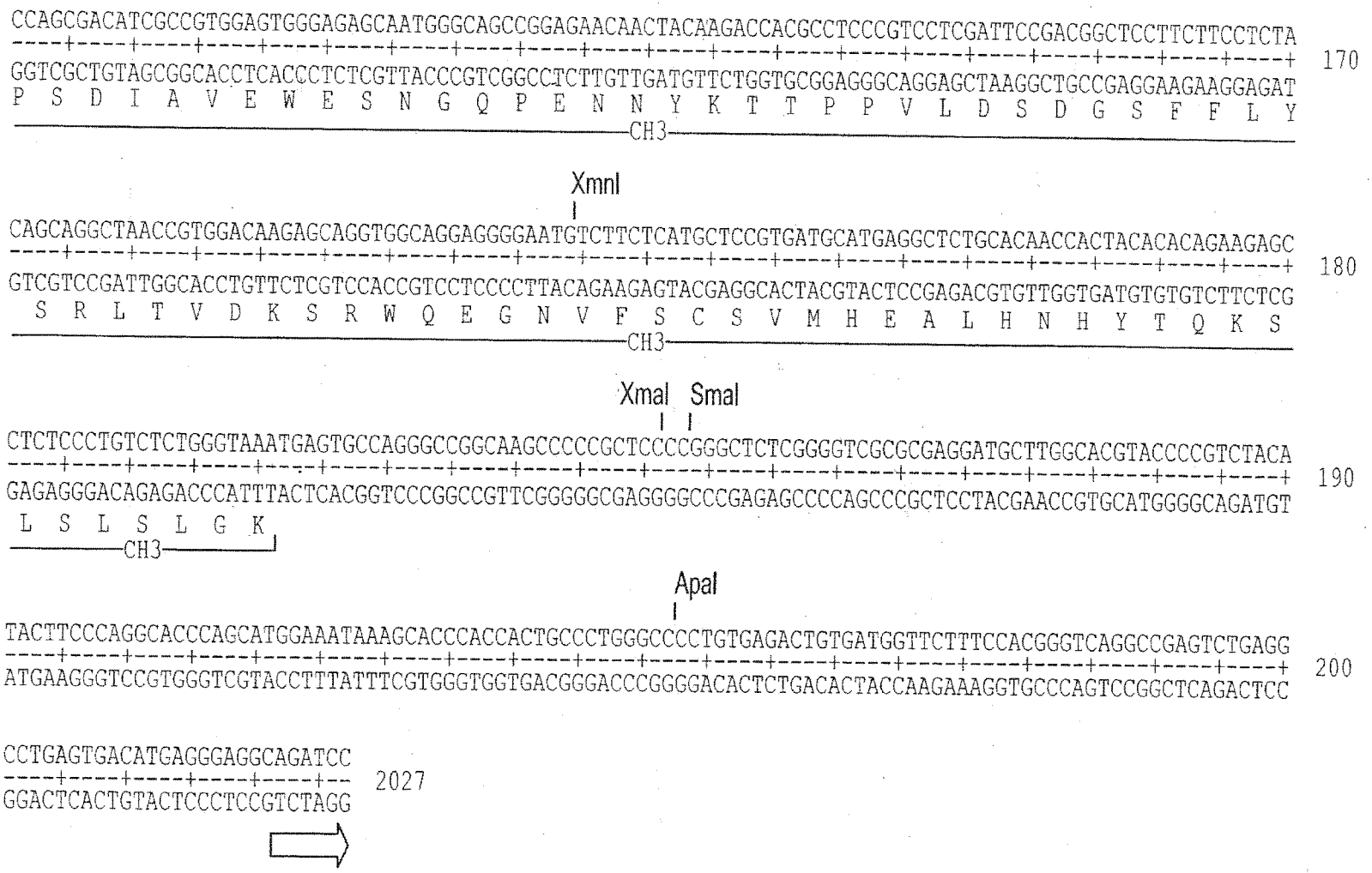

CCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTCCTCGATTCCGACGGCTCCTTCTTCCTCTA
GGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCAGGAGCTAAGGCTGCCGAGGAAGAAGGAGAT
170
P S D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y
CH3
Xmnl
CAGCAGGCTAACCGTGGACAAGAGCAGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACACAGAAGAGC
GTCGTCCGATTGGCACCTGTTCTCGTCCACCGTCCTCCCCTTACAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGTGTCTTCTCG
180
S R L T V D K S R W Q E G N V F S C S V M H E A L H N H Y T Q K S
CH3
XmaI
SmaI
CTCTCCCTGTCTCTGGGTAAATGAGTGCCAGGGCCGGCAAGCCCCCGCTCCCCGGGCTCTCGGGGTCGCGCGAGGATGCTTGGCACGTACCCCGTCTACA
GAGAGGGACAGAGACCCATTTACTCACGGTCCCGGCCGTTCGGGGGCGAGGGGCCCGAGAGCCCCAGCCCGCTCCTACGAACCGTGCATGGGGCAGATGT
190
L S L S L G K
CH3
ApaI
TACTTCCCAGGCACCCAGCATGGAAATAAAGCACCCACCACTGCCCTGGGCCCCTGTGAGACTGTGATGGTTCTTTCCACGGGTCAGGCCGAGTCTGAGG
ATGAAGGGTCCGTGGGTCGTACCTTTATTTCGTGGGTGGTGACGGGACCCGGGGACACTCTGACACTACCAAGAAAGGTGCCCAGTCCGGCTCAGACTCC
200
CCTGAGTGACATGAGGGAGGCAGATCC
GGACTCACTGTACTCCCTCCGTCTAGG
2027

FIG. 16-4

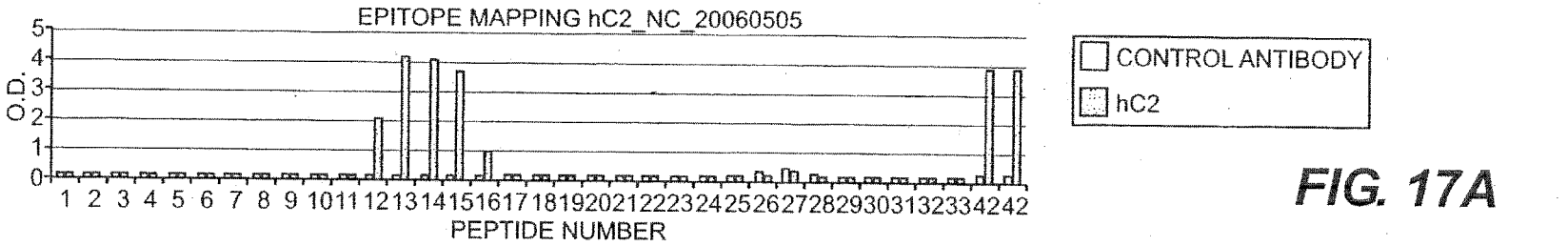
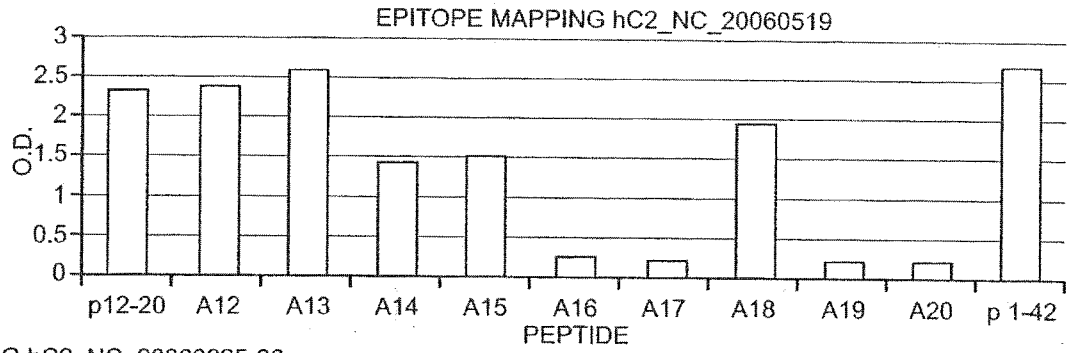


FIG. 17A

FIG. 17B



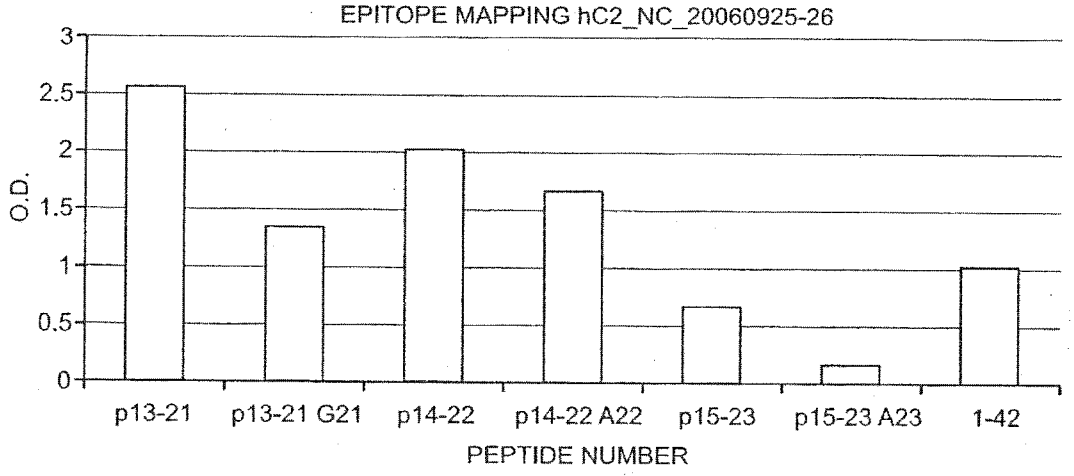


FIG. 17C

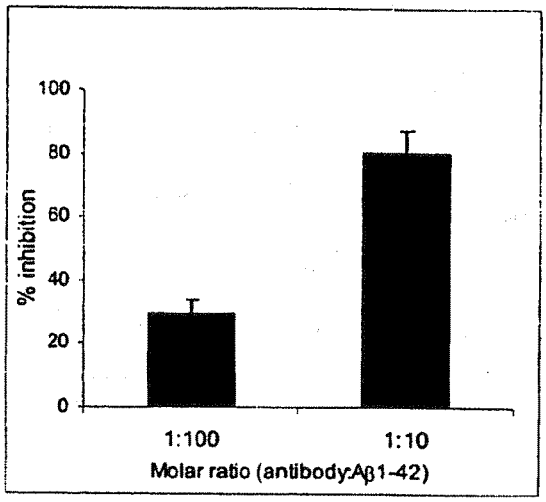

100
80
60
40
20
0
% inhibition
1:100
1:10
Molar ratio (antibody:Aβ1-42)

Fig. 18

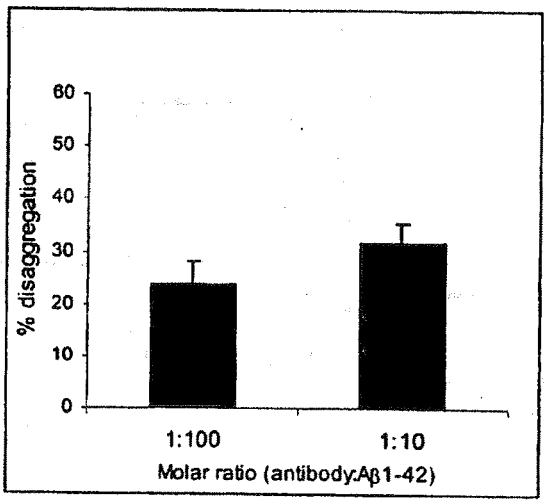

60
50
40
30
20
10
0
% disaggregation
1:100
1:10
Molar ratio (antibody:Aβ1-42)

FIG 19

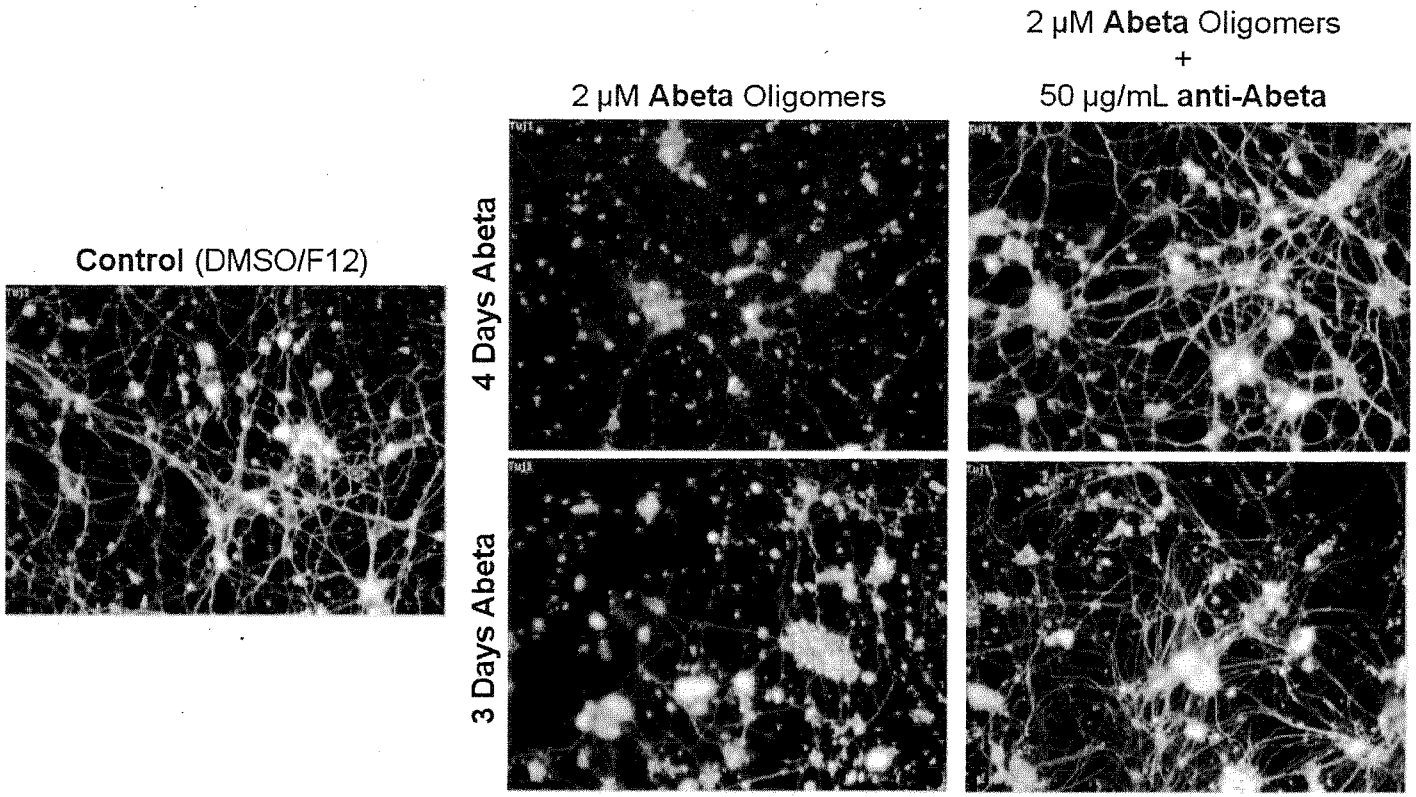

Control (DMSO/F12)
2 µM Abeta Oligomers
2 µM Abeta Oligomers
+
50 µg/mL anti-Abeta
4 Days Abeta
3 Days Abeta

FIG 20