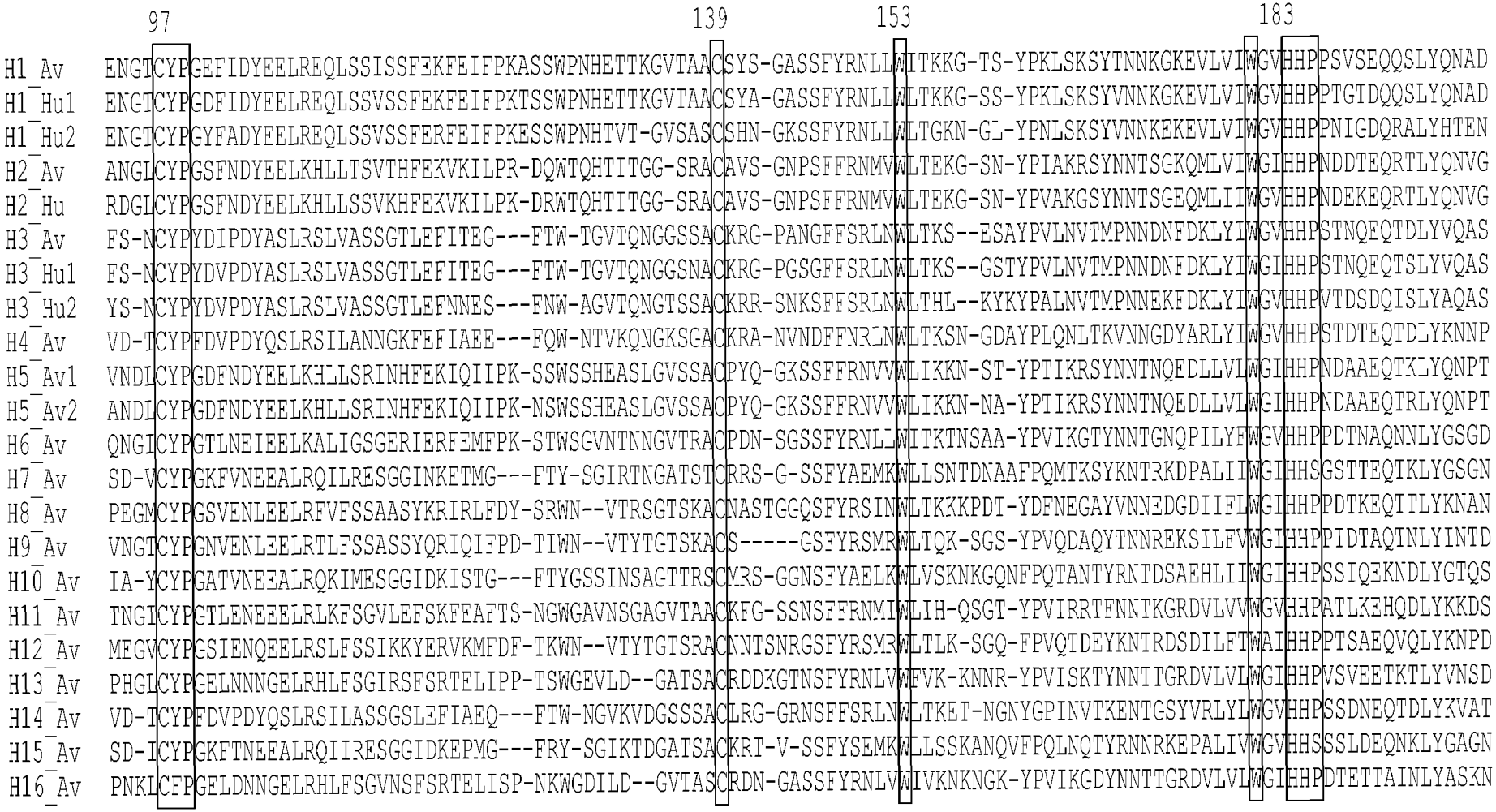
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H2_Av ANGLCYPGSFNDYEELKHLLTSVTHFEKVKILPR-DQWTQHTTTGG-SRACAVS-GNPSFFRNMVWLTEKG-SN-YPIAKRSYNNTSGKQMLVIWGIHHPNDDTEQRTLYQNVG
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H3_Av FS-NCYPYDIPDYASLRSLVASSGTLEFITEG---FTW-TGVTQNGGSSACKRG-PANGFFSRLNWLTKS--ESAYPVLNVTMPNNDNFDKLYIWGVHHPSTNQEQTDLYVQAS
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H10_Av IA-YCYPGATVNEEALRQKIMESGGIDKISTG---FTYGSSINSAGTTRSCMRS-GGNSFYAELKWLVSKNKGQNFPQTANTYRNTDSAEHLIIWGIHHPSSTQEKNDLYGTQS
H11_Av TNGICYPGTLENEEELRLKFSGVLEFSKFEAFTS-NGWGAVNSGAGVTAACKFG-SSNSFFRNMIWLIH-QSGT-YPVIRRTFNNTKGRDVLVVWGVHHPATLKEHQDLYKKDS
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H14_Av VD-TCYPFDVPDYQSLRSILASSGSLEFIAEQ---FTW-NGVKVDGSSSACLRG-GRNSFFSRLNWLTKET-NGNYGPINVTKENTGSYVRLYLWGVHHPSSDNEQTDLYKVAT
H15_Av SD-ICYPGKFTNEEALRQIIRESGGIDKEPMG---FRY-SGIKTDGATSACKRT-V-SSFYSEMKWLLSSKANQVFPQLNQTYRNNRKEPALIVWGVHHSSSLDEQNKLYGAGN
H16_Av PNKLCFPGELDNNGELRHLFSGVNSFSRTELISP-NKWGDILD--GVTASCRDN-GASSFYRNLVWIVKNKNGK-YPVIKGDYNNTTGRDVLVLWGIHHPDTETTAINLYASKN

FIG. 1A

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H2_Av    TYVSVGTSTLNKRSIPEIATRPKVNGQGGRMEFSWTLLETWDVINFESTGNLIAPEYGFKISKRGS--------SGIMKT-EKTLE-NCETKCQTPLGAINTTLPFHNIHPLT
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H4_Av    GRVTVSTKTSQTSVVPNIGSRPWVRGQSGRISFYWTIVDPGDIIVFNTIGNLIAPRGHYKLNSQK--------KSTILNT-AVPIG-SCVSKCHTDRGSITTTKPFQNISRIS
H5_Av1   TYISVGTSTLNQRLVPRIATRSKVNGQSGRMEFFWTILKPNDAINFESNGNFIAPEYAYKIVKKGD--------STIMKS-ELEYG-NCNTKCQTPMGAINSSMPFHNIHPLT
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H10_Av   LSISVGSSTYQNNFVPVVGARPQVNGQSGRIDFHWTMVQPGDNITFSHNGGLIAPSRVSKLK----------GRGLGIQS-GASVDNDCESKCFWKGGSINTKLPFQNLSPRT
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H14_Av   GRVTVSTRSDQISIVPNIGSRPRVRNQSGRISIYWTLVNPGDSIIFNSIGNLIAPRGHYKISKST--------KSTVLKS-DKRIG-SCTSPCLTDKGSIQSDKPFQNVSRIA
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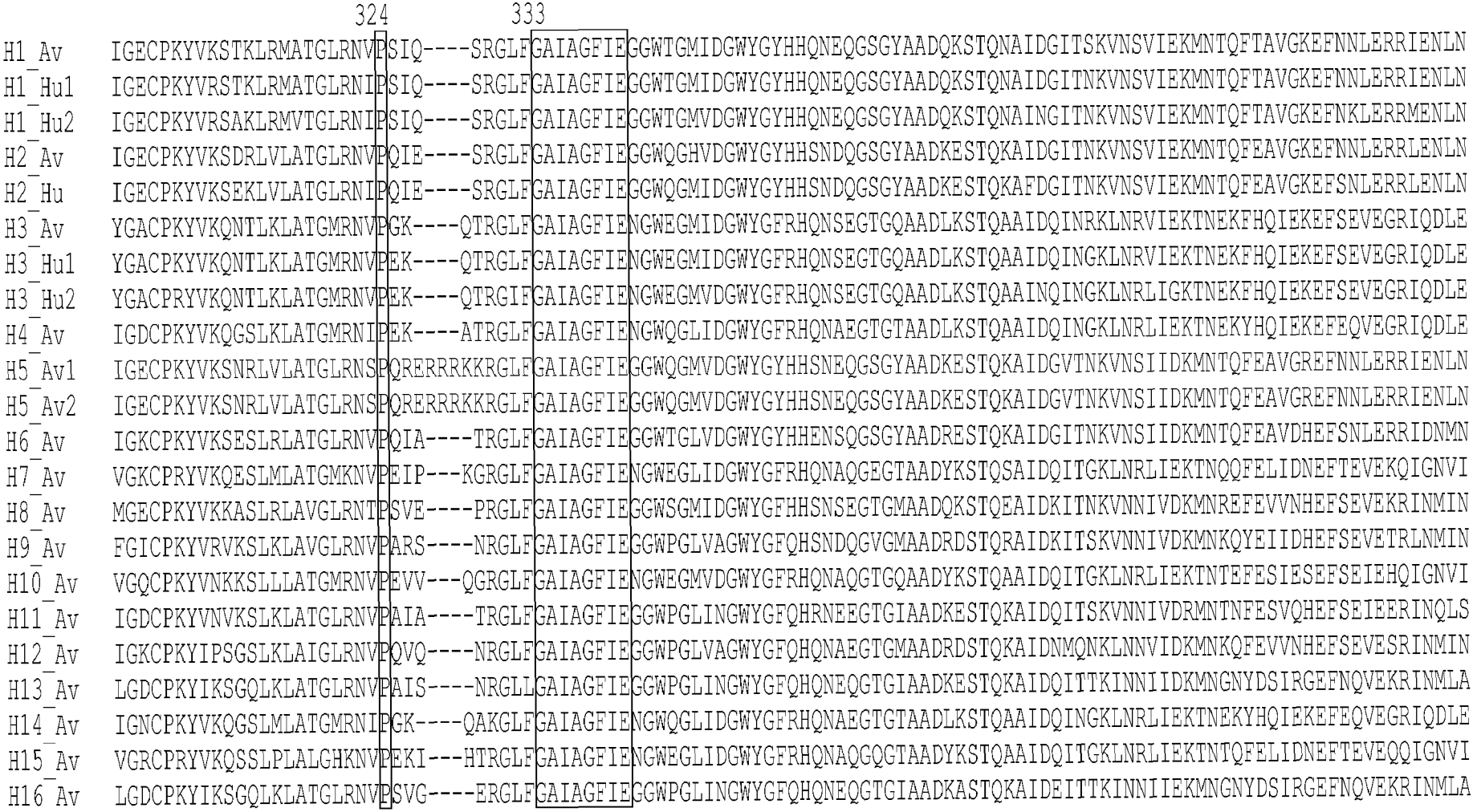
FIG. 1B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H15_Av VGRCPRYVKQSSLPLALGHKNVPEKI---HTRGLFGAIAGFIENGWEGLIDGWYGFRHQNAQGQGTAADYKSTQAAIDQITGKLNRLIEKTNTQFELIDNEFTEVEQQIGNVI
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FIG. 1C

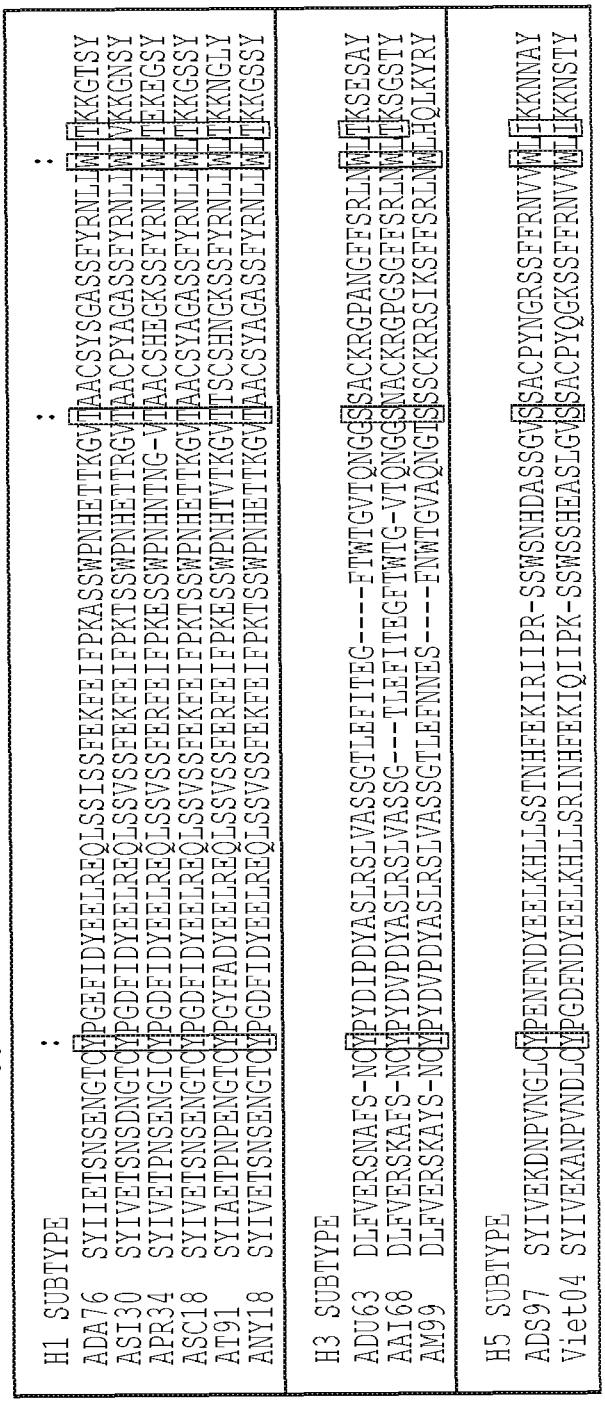
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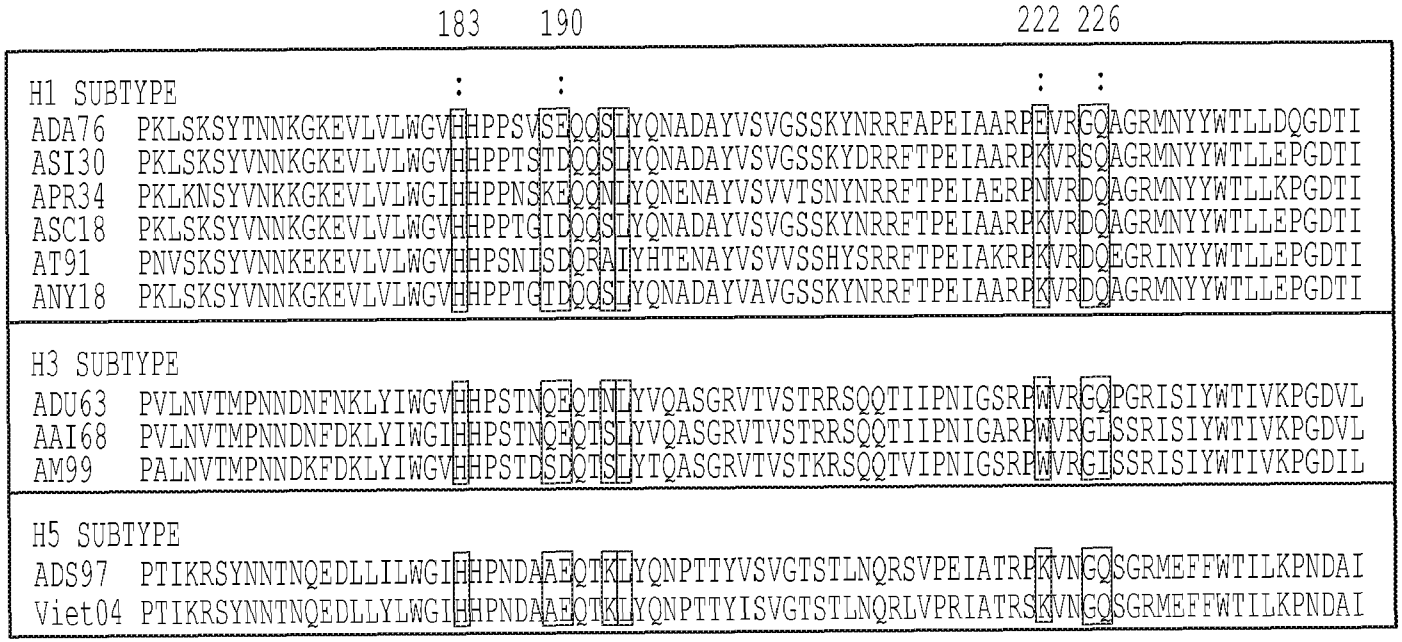
FIG. 2A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ANY18 PKLSKSYVNNKGKEVLVLWGVHHPPTGTDQQSLYQNADAYVAVGSSKYNRRFTPEIAARPKVRDQAGRMNYYWTLLEPGDTI
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AAI68 PVLNVTMPNNDNFDKLYIWGIHHPSTNQEQTSLYVQASGRVTVSTRRSQQTIIPNIGARPWVRGLSSRISIYWTIVKPGDVL
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FIG. 2B

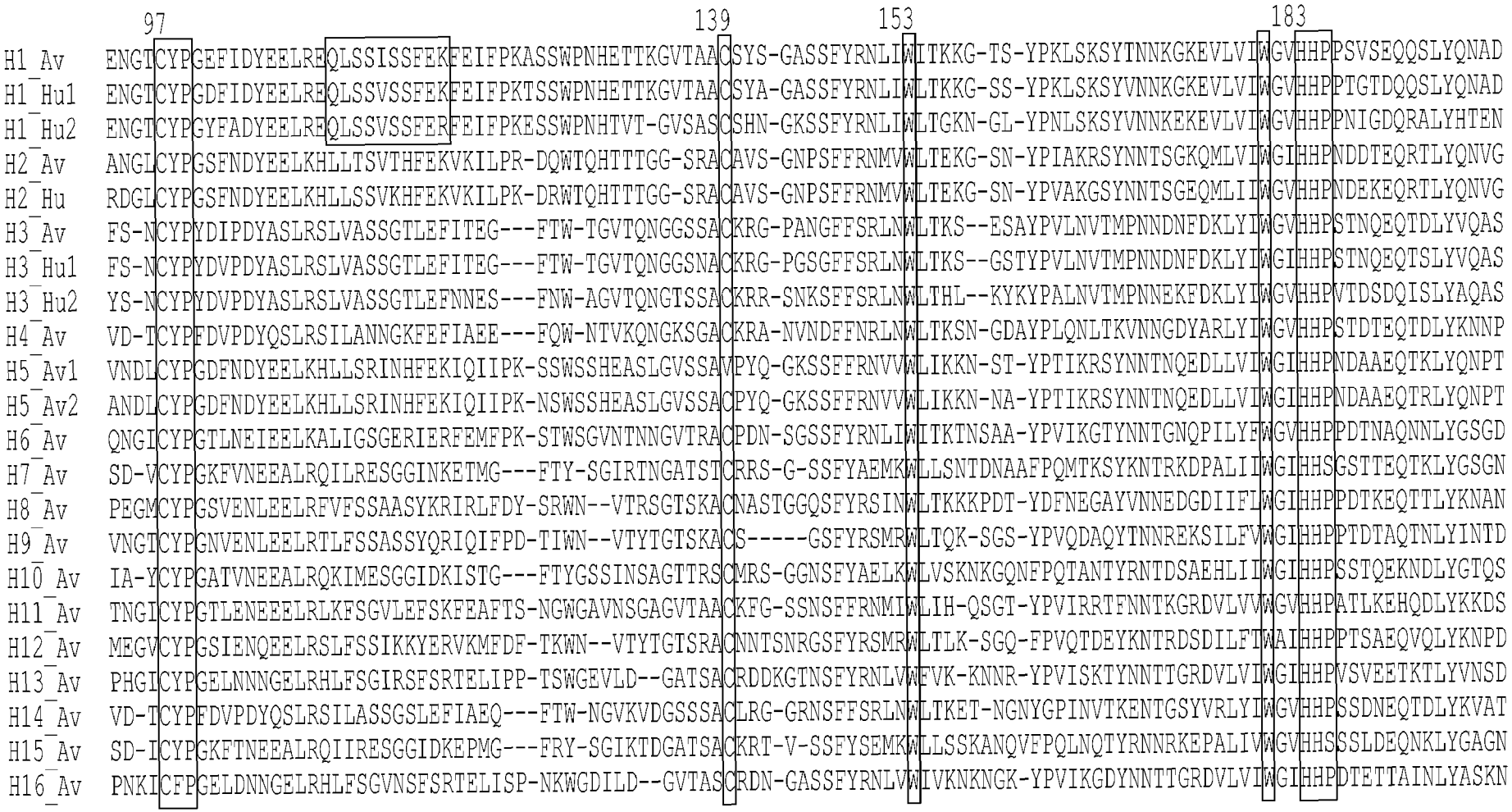
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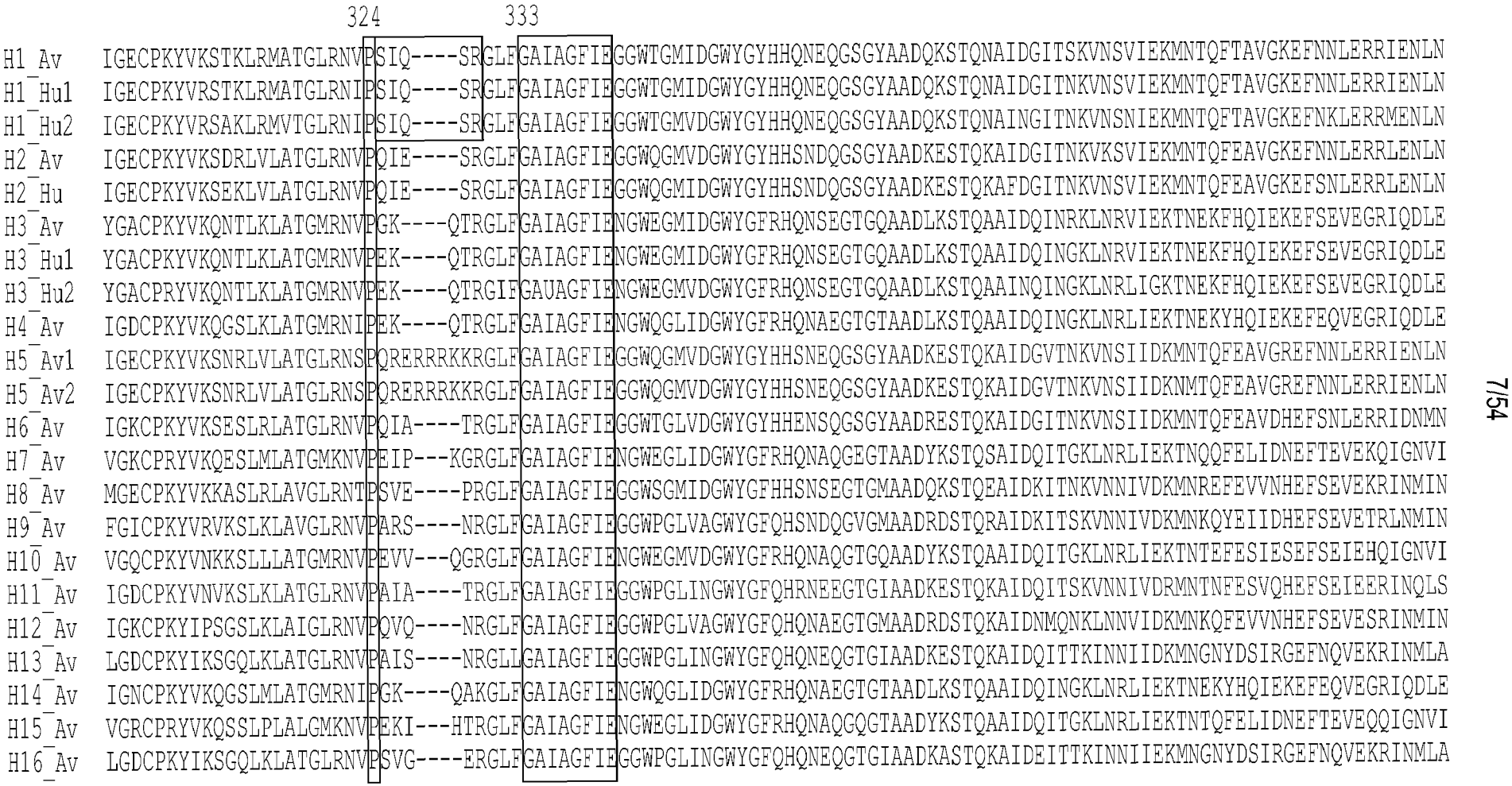
FIG. 3A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H3_Av YGACPKYVKQNTLKLATGMRNVPGK----QTRGLFGAIAGFIENGWEGMIDGWYGFRHQNSEGTGQAADLKSTQAAIDQINRKLNRVIEKTNEKFHQIEKEFSEVEGRIQDLE
H3_Hu1 YGACPKYVKQNTLKLATGMRNVPEK----QTRGLFGAIAGFIENGWEGMIDGWYGFRHQNSEGTGQAADLKSTQAAIDQINGKLNRVIEKTNEKFHQIEKEFSEVEGRIQDLE
H3_Hu2 YGACPRYVKQNTLKLATGMRNVPEK----QTRGIFGAUAGFIENGWEGMVDGWYGFRHQNSEGTGQAADLKSTQAAINQINGKLNRLIGKTNEKFHQIEKEFSEVEGRIQDLE
H4_Av IGDCPKYVKQGSLKLATGMRNIPEK----QTRGLFGAIAGFIENGWQGLIDGWYGFRHQNAEGTGTAADLKSTQAAIDQINGKLNRLIEKTNEKYHQIEKEFEQVEGRIQDLE
H5_Av1 IGECPKYVKSNRLVLATGLRNSPQRERRRKKRGLFGAIAGFIEGGWQGMVDGWYGYHHSNEQGSGYAADKESTQKAIDGVTNKVNSIIDKMNTQFEAVGREFNNLERRIENLN
H5_Av2 IGECPKYVKSNRLVLATGLRNSPQRERRRKKRGLFGAIAGFIEGGWQGMVDGWYGYHHSNEQGSGYAADKESTQKAIDGVTNKVNSIIDKNMTQFEAVGREFNNLERRIENLN
H6_Av IGKCPKYVKSESLRLATGLRNVPQIA----TRGLFGAIAGFIEGGWTGLVDGWYGYHHENSQGSGYAADRESTQKAIDGITNKVNSIIDKMNTQFEAVDHEFSNLERRIDNMN
H7_Av VGKCPRYVKQESLMLATGMKNVPEIP---KGRGLFGAIAGFIENGWEGLIDGWYGFRHQNAQGEGTAADYKSTQSAIDQITGKLNRLIEKTNQQFELIDNEFTEVEKQIGNVI
H8_Av MGECPKYVKKASLRLAVGLRNTPSVE----PRGLFGAIAGFIEGGWSGMIDGWYGFHHSNSEGTGMAADQKSTQEAIDKITNKVNNIVDKMNREFEVVNHEFSEVEKRINMIN
H9_Av FGICPKYVRVKSLKLAVGLRNVPARS----NRGLFGAIAGFIEGGWPGLVAGWYGFQHSNDQGVGMAADRDSTQRAIDKITSKVNNIVDKMNKQYEIIDHEFSEVETRLNMIN
H10_Av VGQCPKYVNKKSLLLATGMRNVPEVV---QGRGLFGAIAGFIENGWEGMVDGWYGFRHQNAQGTGQAADYKSTQAAIDQITGKLNRLIEKTNTEFESIESEFSEIEHQIGNVI
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H12_Av IGKCPKYIPSGSLKLAIGLRNVPQVQ----NRGLFGAIAGFIEGGWPGLVAGWYGFQHQNAEGTGMAADRDSTQKAIDNMQNKLNNVIDKMNKQFEVVNHEFSEVESRINMIN
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H14_Av IGNCPKYVKQGSLMLATGMRNIPGK----QAKGLFGAIAGFIENGWQGLIDGWYGFRHQNAEGTGTAADLKSTQAAIDQINGKLNRLIEKTNEKYHQIEKEFEQVEGRIQDLE
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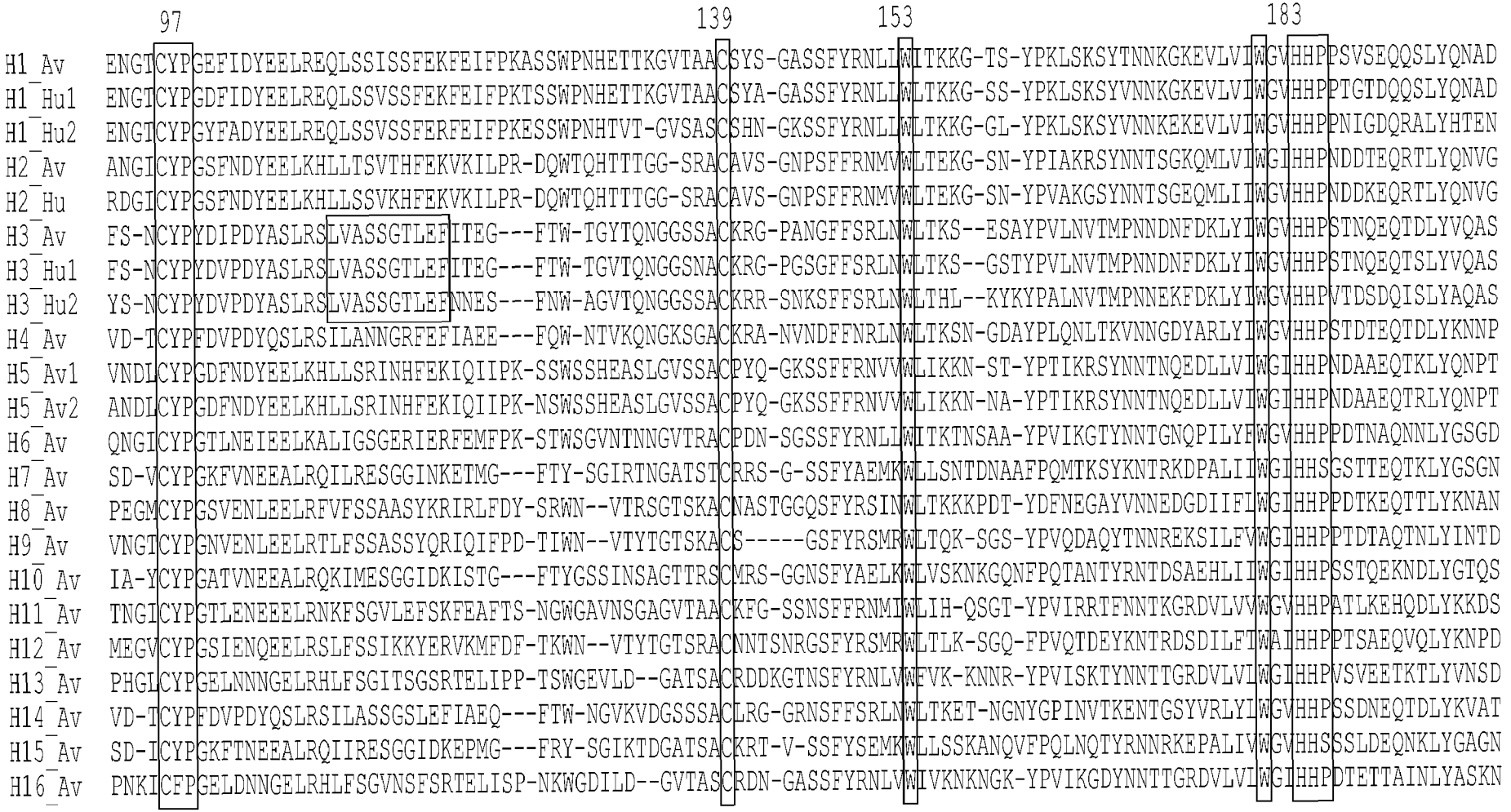
FIG. 3B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H1_Hu2 ENGTCYPGYFADYEELREQLSSVSSFERFEIFPKESSWPNHTVT-GVSASCSHN-GKSSFYRNLLWLTKKG-GL-YPKLSKSYVNNKEKEVLVIWGVHHPPNIGDQRALYHTEN
H2_Av ANGICYPGSFNDYEELKHLLTSVTHFEKVKILPR-DQWTQHTTTGG-SRACAVS-GNPSFFRNMVWLTEKG-SN-YPIAKRSYNNTSGKQMLVIWGIHHPNDDTEQRTLYQNVG
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H3_Hu2 YS-NCYPYDVPDYASLRSLVASSGTLEFNNES---FNW-AGVTQNGGSSACKRR-SNKSFFSRLNWLTHL--KYKYPALNVTMPNNEKFDKLYIWGVHHPVTDSDQISLYAQAS
H4_Av VD-TCYPFDVPDYQSLRSILANNGRFEFIAEE---FQW-NTVKQNGKSGACKRA-NVNDFFNRLNWLTKSN-GDAYPLQNLTKVNNGDYARLYIWGVHHPSTDTEQTDLYKNNP
H5_Av1 VNDLCYPGDFNDYEELKHLLSRINHFEKIQIIPK-SSWSSHEASLGVSSACPYQ-GKSSFFRNVVWLIKKN-ST-YPTIKRSYNNTNQEDLLVIWGIHHPNDAAEQTKLYQNPT
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H7_Av SD-VCYPGKFVNEEALRQILRESGGINKETMG---FTY-SGIRTNGATSTCRRS-G-SSFYAEMKWLLSNTDNAAFPQMTKSYKNTRKDPALIIWGIHHSGSTTEQTKLYGSGN
H8_Av PEGMCYPGSVENLEELRFVFSSAASYKRIRLFDY-SRWN--VTRSGTSKACNASTGGQSFYRSINWLTKKKPDT-YDFNEGAYVNNEDGDIIFLWGIHHPPDTKEQTTLYKNAN
H9_Av VNGTCYPGNVENLEELRTLFSSASSYQRIQIFPD-TIWN--VTYTGTSKACS-----GSFYRSMRWLTQK-SGS-YPVQDAQYTNNREKSILFVWGIHHPPTDTAQTNLYINTD
H10_Av IA-YCYPGATVNEEALRQKIMESGGIDKISTG---FTYGSSINSAGTTRSCMRS-GGNSFYAELKWLVSKNKGQNFPQTANTYRNTDSAEHLIIWGIHHPSSTQEKNDLYGTQS
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H15_Av SD-ICYPGKFTNEEALRQIIRESGGIDKEPMG---FRY-SGIKTDGATSACKRT-V-SSFYSEMKWLLSSKANQVFPQLNQTYRNNRKEPALIVWGVHHSSSLDEQNKLYGAGN
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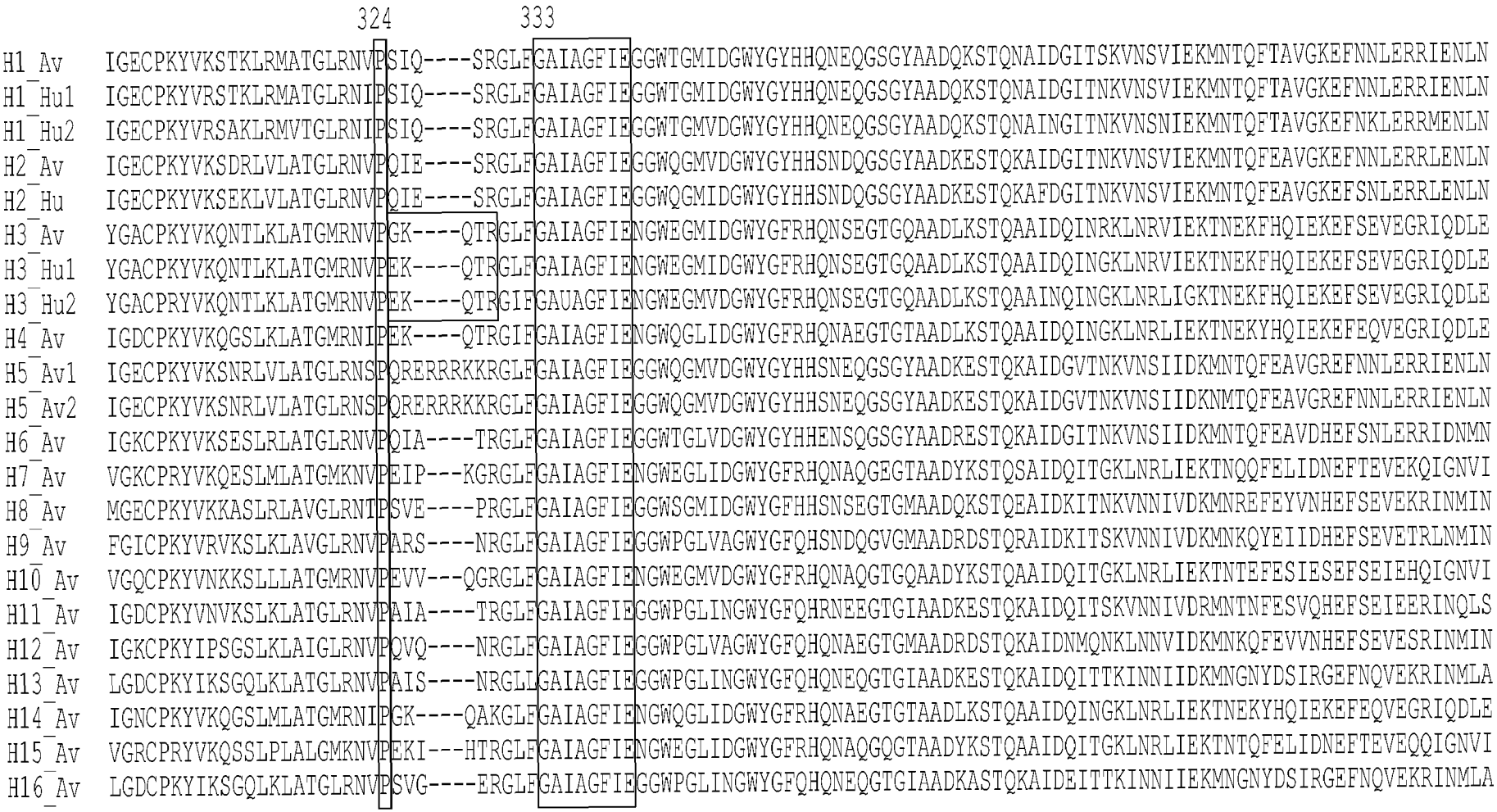
FIG. 4A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H8_Av MGECPKYVKKASLRLAVGLRNTPSVE----PRGLFGAIAGFIEGGWSGMIDGWYGFHHSNSEGTGMAADQKSTQEAIDKITNKVNNIVDKMNREFEYVNHEFSEVEKRINMIN
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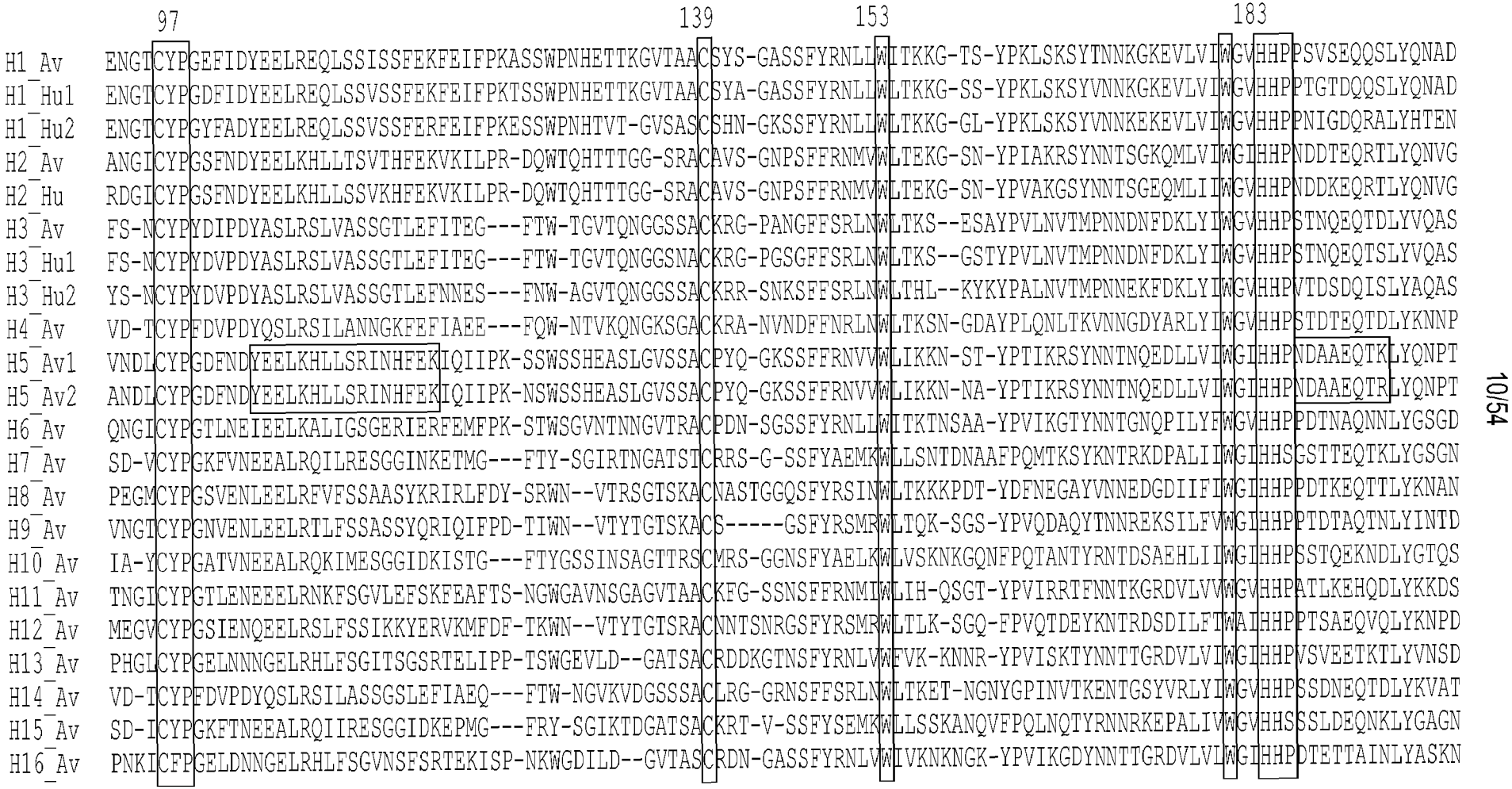
FIG. 4B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H2_Av ANGICYPGSFNDYEELKHLLTSVTHFEKVKILPR-DQWTQHTTTGG-SRACAVS-GNPSFFRNMVWLTEKG-SN-YPIAKRSYNNTSGKQMLVLWGIHHPNDDTEQRTLYQNVG
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H3_Av FS-NCYPYDIPDYASLRSLVASSGTLEFITEG---FTW-TGVTQNGGSSACKRG-PANGFFSRLNWLTKS--ESAYPVLNVTMPNNDNFDKLYIWGVHHPSTNQEQTDLYVQAS
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H4_Av VD-TCYPFDVPDYQSLRSILANNGKFEFIAEE---FQW-NTVKQNGKSGACKRA-NVNDFFNRLNWLTKSN-GDAYPLQNLTKVNNGDYARLYIWGVHHPSTDTEQTDLYKNNP
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H5_Av2 ANDLCYPGDFNDYEELKHLLSRINHFEKIQIIPK-NSWSSHEASLGVSSACPYQ-GKSSFFRNVVWLIKKN-NA-YPTIKRSYNNTNQEDLLVIWGIHHPNDAAEQTRLYQNPT
H6_Av QNGICYPGTLNEIEELKALIGSGERIERFEMFPK-STWSGVNTNNGVTRACPDN-SGSSFYRNLLWITKTNSAA-YPVIKGTYNNTGNQPILYFWGVHHPPDTNAQNNLYGSGD
H7_Av SD-VCYPGKFVNEEALRQILRESGGINKETMG---FTY-SGIRTNGATSTCRRS-G-SSFYAEMKWLLSNTDNAAFPQMTKSYKNTRKDPALIIWGIHHSGSTTEQTKLYGSGN
H8_Av PEGMCYPGSVENLEELRFVFSSAASYKRIRLFDY-SRWN--VTRSGTSKACNASTGGQSFYRSINWLTKKKPDT-YDFNEGAYVNNEDGDIIFIWGIHHPPDTKEQTTLYKNAN
H9_Av VNGTCYPGNVENLEELRTLFSSASSYQRIQIFPD-TIWN--VTYTGTSKACS-----GSFYRSMRWLTQK-SGS-YPVQDAQYTNNREKSILFVWGIHHPPTDTAQTNLYINTD
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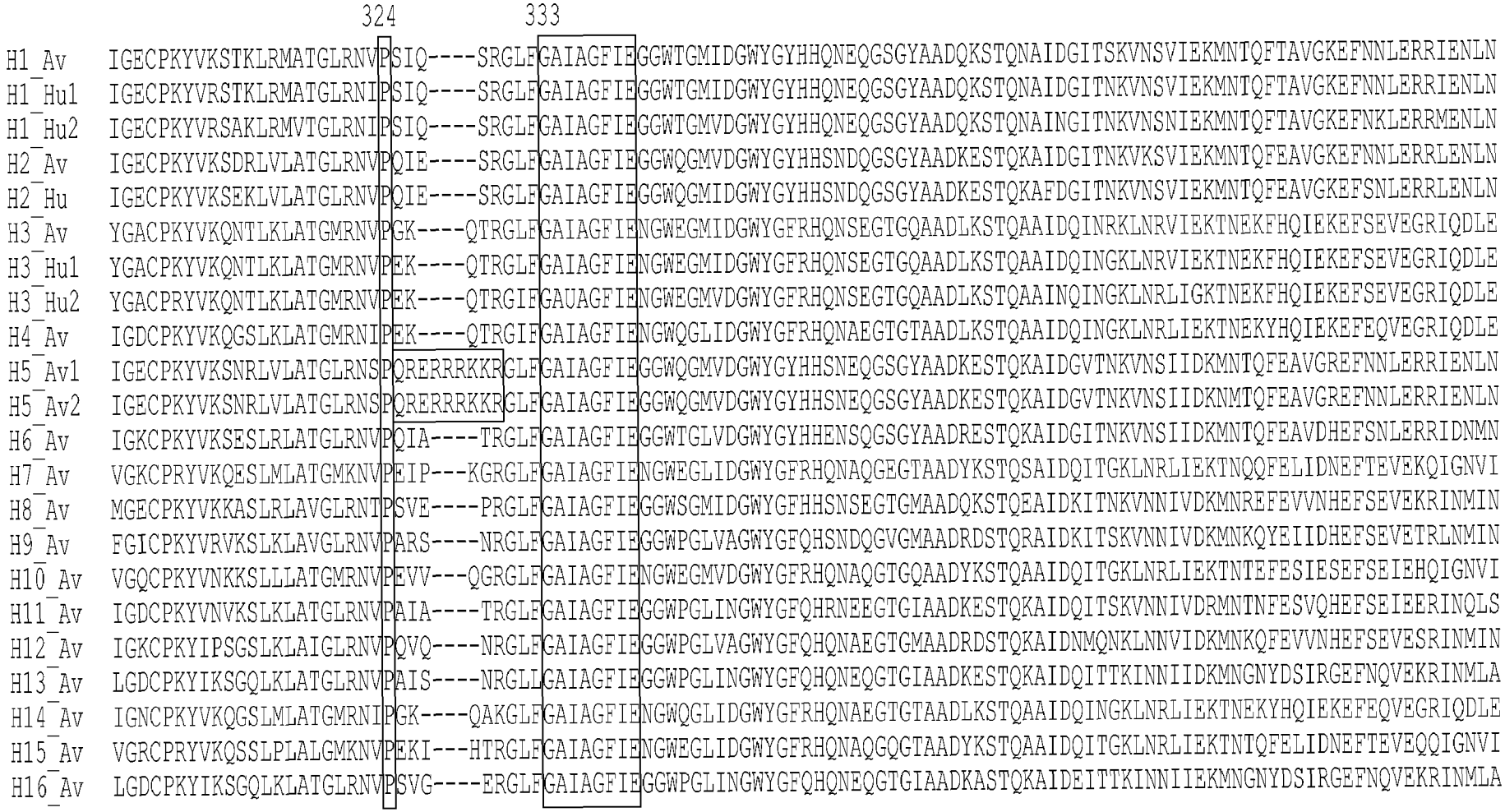
FIG. 5A-1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H6_Av IGKCPKYVKSESLRLATGLRNVPQIA----TRGLFGAIAGFIEGGWTGLVDGWYGYHHENSQGSGYAADRESTQKAIDGITNKVNSIIDKMNTQFEAVDHEFSNLERRIDNMN
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H13_Av LGDCPKYIKSGQLKLATGLRNVPAIS----NRGLLGAIAGFIEGGWPGLINGWYGFQHQNEQGTGIAADKESTQKAIDQITTKINNIIDKMNGNYDSIRGEFNQVEKRINMLA
H14_Av IGNCPKYVKQGSLMLATGMRNIPGK----QAKGLFGAIAGFIENGWQGLIDGWYGFRHQNAEGTGTAADLKSTQAAIDQINGKLNRLIEKTNEKYHQIEKEFEQVEGRIQDLE
H15_Av VGRCPRYVKQSSLPLALGMKNVPEKI---HTRGLFGAIAGFIENGWEGLIDGWYGFRHQNAQGQGTAADYKSTQAAIDQITGKLNRLIEKTNTQFELIDNEFTEVEQQIGNVI
H16_Av LGDCPKYIKSGQLKLATGLRNVPSVG----ERGLFGAIAGFIEGGWPGLINGWYGFQHQNEQGTGIAADKASTQKAIDEITTKINNIIEKMNGNYDSIRGEFNQVEKRINMLA

FIG. 5A-2

```
POSITIONS FROM 1 TILL 60
CONSENSUS      MEKIVLLLAIVSLVKSDQICIGYHANNSTEQVDTIMEKNVTVTHAQDILEKTHNGKLCDL
AAL59142       ............................................................
AAZ29963       .......F....................................................
ABA70758       .......F....................................................
ABB87042       ..R..IA...I.I..G.............K.....................E......S.
ABD14810       ............................................................
ABD46740       ----........................................................
ABD85144       -------F....................................................
ABE97569       ............................................................

POSITIONS FROM 61 TILL 120
CONSENSUS      DGVKPLILRDCSVAGWLLGNPMCDEFINVPEWSYIVEKANPANDLCYPGDFNDYEELKEL
AAL59142       ......................................S.D...................
AAZ29963       ........................................V...................
ABA70758       ........................................V...................
ABB87042       K..R...K..................L...........D..I.G................
ABD14810       .......K.........................................I..........
ABD46740       ..........................L...........I..........N..........
ABD85144       ..........................L...........I..........N..........
ABE97569       ...............................................N..........
```

FIG. 5B-1

```
POSITIONS FROM 121 TILL 180
CONSENSUS       LSRINHFEKIQIIPKSSWSDHEASSGVSSACPYQGKSSFFRNVVWLIKKNSAYPTIKRSY
AAL59142        ..................N.............H.........................
AAZ29963        ..................S....L.........................T........
ABA70758        ..................S....L..........P.............T........
ABB87042        M.ST.........R....N.D..........N.R.............N.......T.
ABD14810        ..................................................I..
ABD46740        ...................................R.............DN.........
ABD85144        ...................................R.............DN.........
ABE97569        ..................................L..........................

POSITIONS FROM 181 TILL 240
CONSENSUS       NNTNQEDLLVLWGIHHPNDAAEQTKLYQNPTTYISVGTSTLNQRLVPKIATRSKVNGQSG
AAL59142        ................................................................
AAZ29963        ...............................................R............
ABA70758        ........V.......................................R............
ABB87042        ....I....I..................SN..V..........SI.E....P.......
ABD14810        ........................R.......................................
ABD46740        ........................R.......................................
ABD85144        ........................R.......................................
ABE97569        ........................R.......................................
```

FIG. 5B-2

```
POSITIONS FROM 241 TILL 300
CONSENSUS      RMEFFWTILKPNDAINFESNGNFIAPEYAYKIVKKGDSTIMKSBLEYGNCNTKCQTPMGA
AAL59142       ....................................A.....................
AAZ29963       ............................................................
ABA70758       ............................................................
ABB87042       ...............S.......................A...........D......V..
ABD14810       ..............V..................................D...........
ABD46740       ............................N.............................I..
ABD85144       ..........S................N.............................I..
ABE97569       ....................................A.....................

POSITIONS FROM 301 TILL 360
CONSENSUS      INSSMPFHNIHPLTIGECPKYVKSNRLVLATGLRNSPQRERRRKKRGLFGAIAGFIEGGW
AAL59142       ..................................T....G...................
AAZ29963       ............................................................
ABA70758       ........................................K...................
ABB87042       .........V..............DK.........V....----T...............
ABD14810       ........................................-...................
ABD46740       ....................................G.....................
ABD85144       ....................................G.....................
ABE97569       ............................................................
```

FIG. 5B-3

```
POSITIONS FROM 361 TILL 420
CONSENSUS       QGMVDGWYGYHHSNEQGSGYAADKESTQKAIDGVTNKVNSIIDKMNTQFEAVGREFNNLE
AAL59142        ..........................................................K..
AAZ29963        ..........................................................
ABA70758        ..............K...........................................
ABB87042        ................................I................T..K......
ABD14810        ..........................................................
ABD46740        ..........................................................
ABD85144        ..........................................................
ABE97569        ..........................................................

POSITIONS FROM 421 TILL 480
CONSENSUS       RRIENLNKKMEDGFLDVWTYNAELLVLMENERTLDFHDSNVKNLYDKVRLQLRDNAKELG
AAL59142        ..........................................................
AAZ29963        ..........................................................
ABA70758        ..........................................................
ABB87042        ..........................................................
ABD14810        ..........................................................
ABD46740        ..........................................................
ABD85144        ..........................................................
ABE97569        ..........................................................
```

FIG. 5B-4

```
POSITIONS FROM 481 TILL 540
CONSENSUS       NGCFEFYHKCDNECMESVRNGTYDYPQYSEEARLKREEISGVKLESIGTYQILSIYSTVA
AAL59142        .................K.............N..........M.............
AAZ29963        ................................................I...........
ABA70758        ................................................I...........
ABB87042        ..............................S..N....D......M.............
ABD14810        ..................................................................
ABD46740        ........R.........................................................
ABD85144        ........R.........................................................
ABE97569        .................I....N.......................I...........

POSITIONS FROM 541 TILL 568
CONSENSUS       SSLALAIMVAGLSLWMCSNGSLQCRICI
AAL59142        ............................
AAZ29963        .............------------
ABA70758        ............................
ABB87042        ............F...............
ABD14810        ............................
ABD46740        .................--------
ABD85144        ............F........VTM----
ABE97569        ........M....---------------
```

FIG. 5B-5

AAL59142: 568 Avian 4 (HA) H5N1 Hong Kong 2000 Influenza A virus (A/Goose/Hong Kong/385.3.2000(H5N1))

AAZ29963: 556 Avian 4 (HA) H5N1 Thailand 2004 Influenza A virus (A/Ostrich/Samut Prakan/Thailand/CU-19/04(H5N1))

ABA70758: 568 Avian 4 (HA) H5N1 Belgium 2004 Influenza A virus (A/crested eagle/Belgium/01/2004(H5N1))

ABB87042: 564 Avian 4 (HA) H5N2 Canada 1976/08/12 Influenza A virus (A/mallard duck/ALB/57/1976(H5N2))

ABD14810: 567 Avian 4 (HA) H5N1 China 2004 Influenza A virus (A/duck/Guangxi/13/2004(H5N1))

ABD46740: 556 Avian 4 (HA) H5N1 Nigeria 2006/01/17 Influenza A virus (A/chicken/Nigeria/641/2006(H5N1))

ABD85144: 557 Avian 4 (HA) H5N1 Egypt 2006 Influenza A virus (A/chicken/Egypt/960N3-004/2006(H5N1))

ABE97569: 553 Avian 4 (HA) H5N1 Indonesia 2004 Influenza A virus (A/turkey/Kedaton/BPPV3/2004(H5N1))

FIG. 5B-6

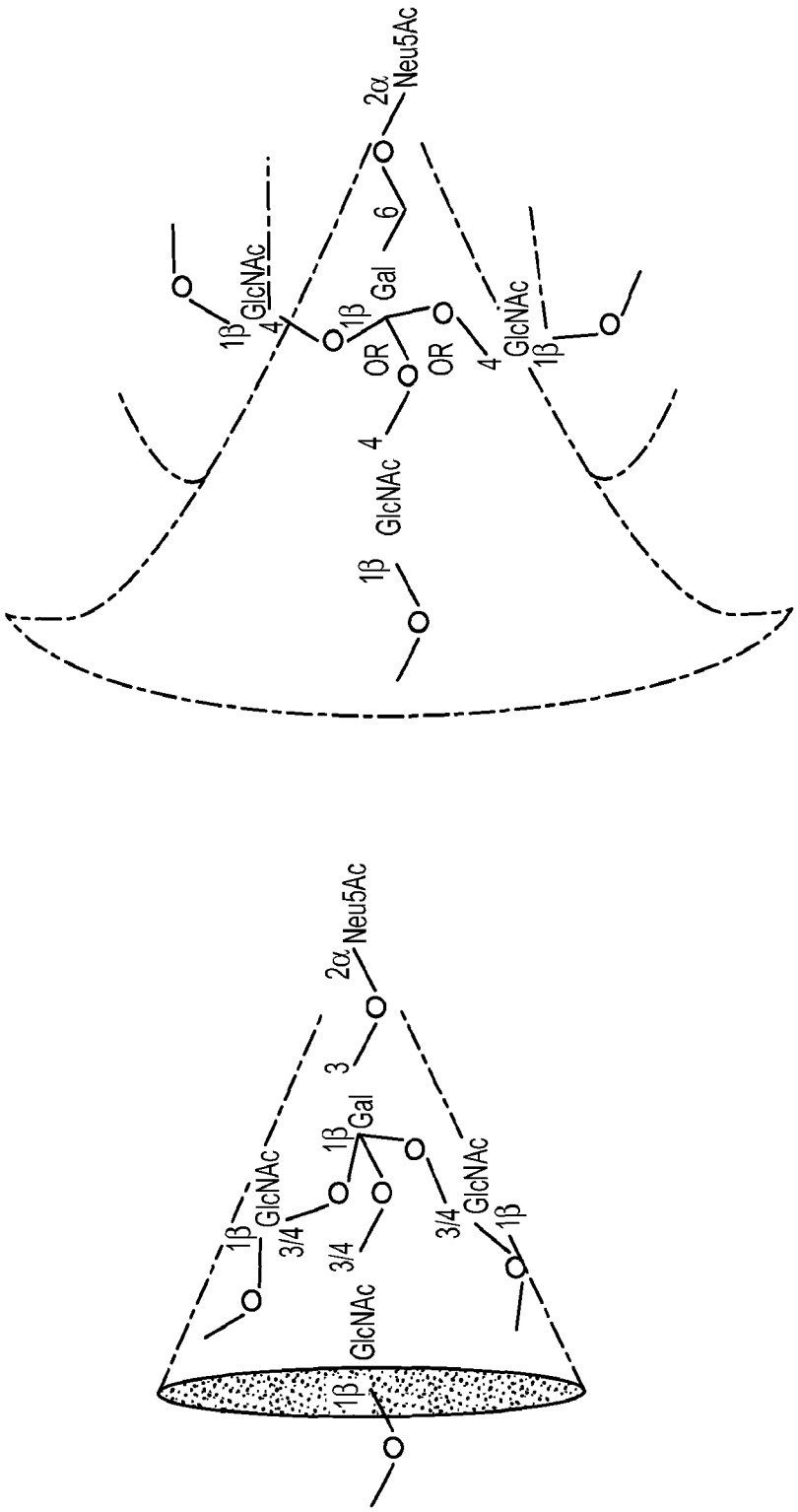

2α Neu5Ac
6
1β GlcNAc 4
1β Gal
OR
OR
4 GlcNAc 1β
4 GlcNAc 1β
2α Neu5Ac
3
1β GlcNAc 3/4
1β Gal
3/4 GlcNAc 1β
3/4 GlcNAc 1β

FIG. 6A

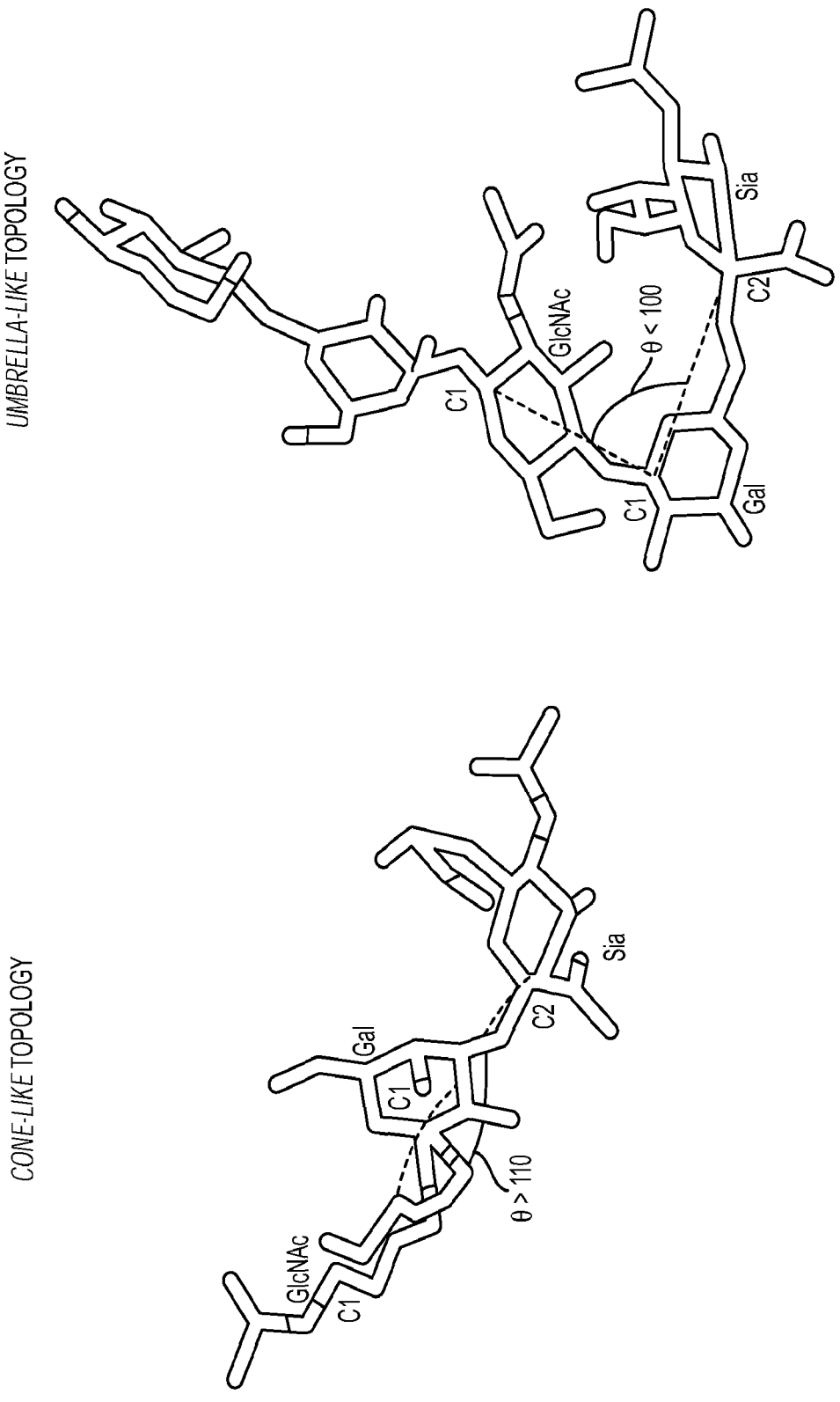

UMBRELLA-LIKE TOPOLOGY
CONE-LIKE TOPOLOGY
GlcNAc
C1
Gal
C1
C2
Sia
θ > 110
GlcNAc
C1
θ < 100
C2
Sia
C1
Gal

FIG. 6B-1

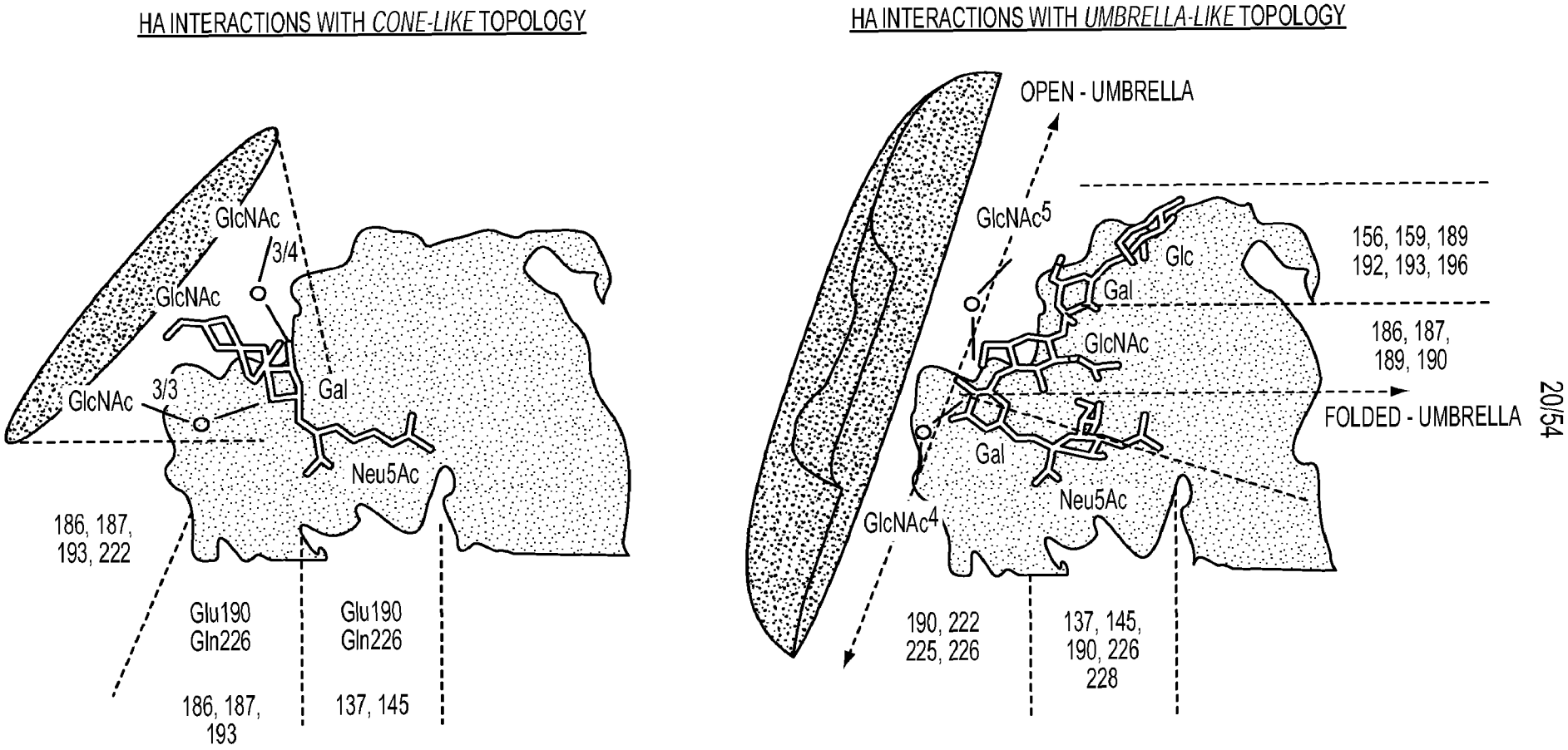

HA INTERACTIONS WITH *CONE-LIKE* TOPOLOGY
GlcNAc
3/4
GlcNAc
GlcNAc
3/3
Gal
Neu5Ac
186, 187,
193, 222
Glu190
Gln226
186, 187,
193
Glu190
Gln226
137, 145
HA INTERACTIONS WITH *UMBRELLA-LIKE* TOPOLOGY
OPEN - UMBRELLA
GlcNAc5
Glc
Gal
GlcNAc
Gal
Neu5Ac
GlcNAc4
156, 159, 189
192, 193, 196
186, 187,
189, 190
FOLDED - UMBRELLA
190, 222
225, 226
137, 145,
190, 226
228

FIG. 6B-2

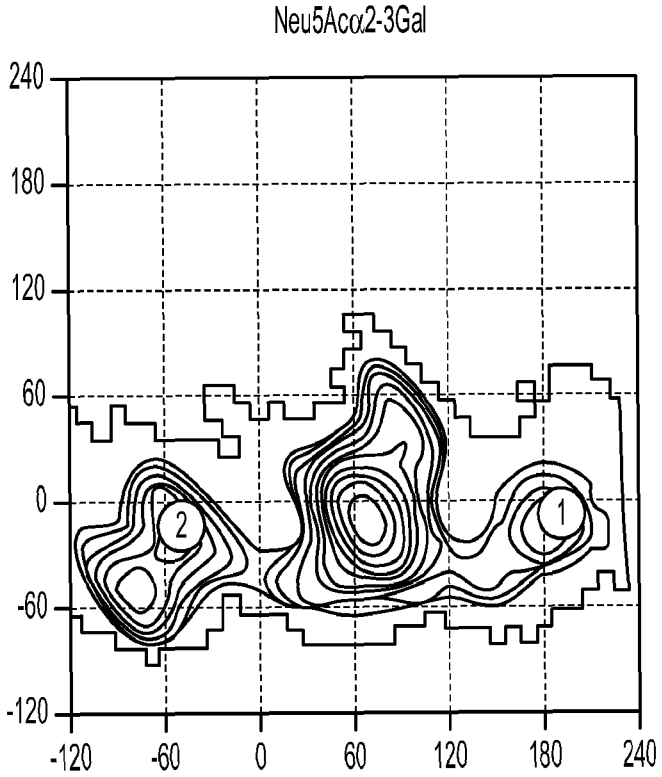


FIG. 6C-A

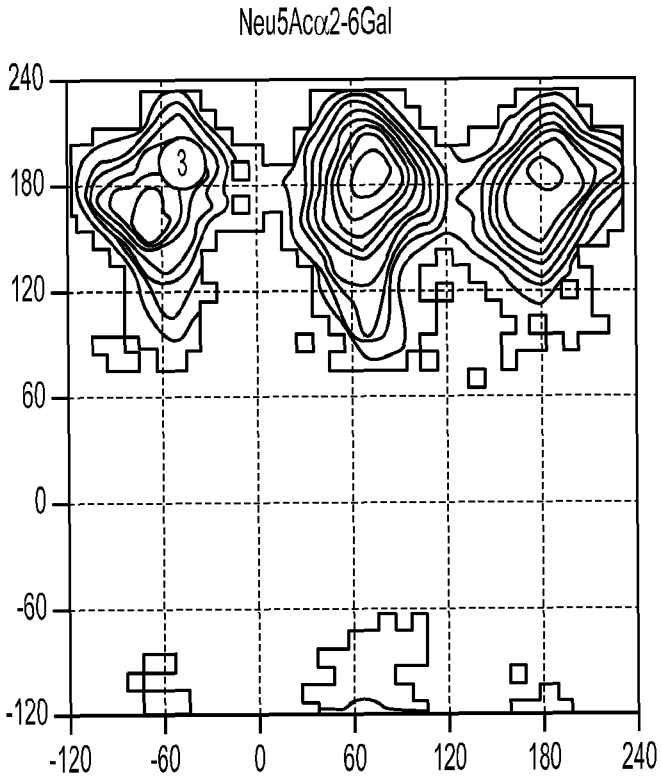


FIG. 6C-B

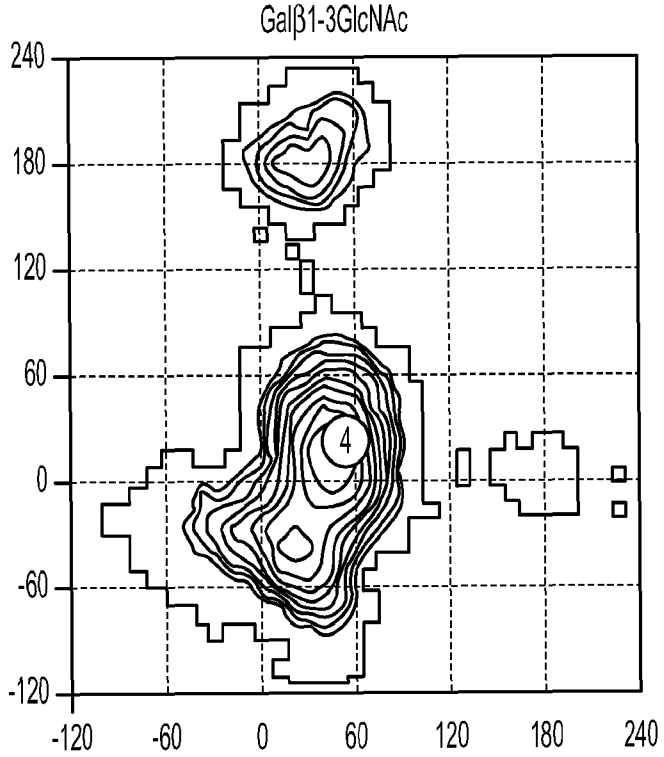


FIG. 6C-C

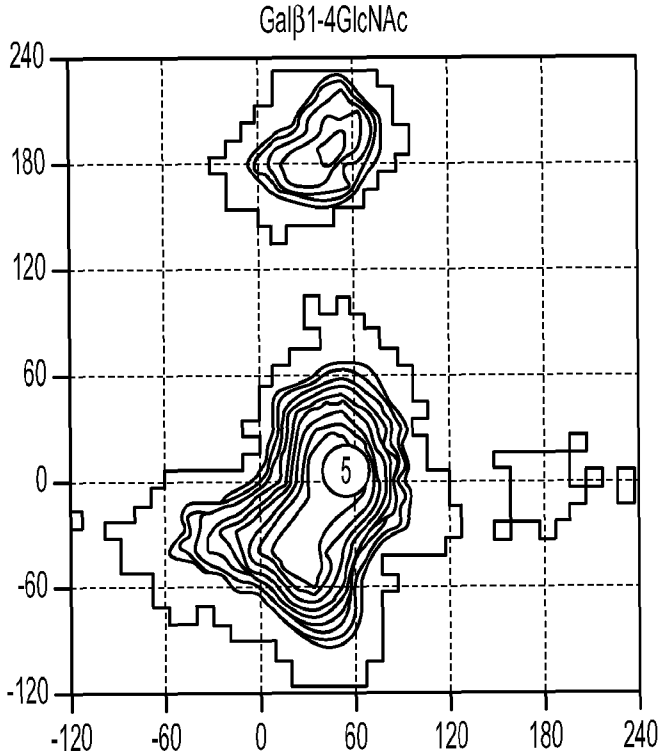


FIG. 6C-D

CONFORMATIONAL SAMPLING OF α2-3 LINKAGE

CONE-LIKE	100%
UMBRELLA-LIKE	0%

FIG. 6C-E

CONFORMATIONAL SAMPLING OF α2-6 LINKAGE

	UMBRELLA-LIKE (%) : *CONE*-LIKE (%)
$\omega = -60^{\circ}$	60 : 20
$\omega = +60^{\circ}$	10 : 40
$\omega = 180^{\circ}$	30 : 30

FIG. 6C-F

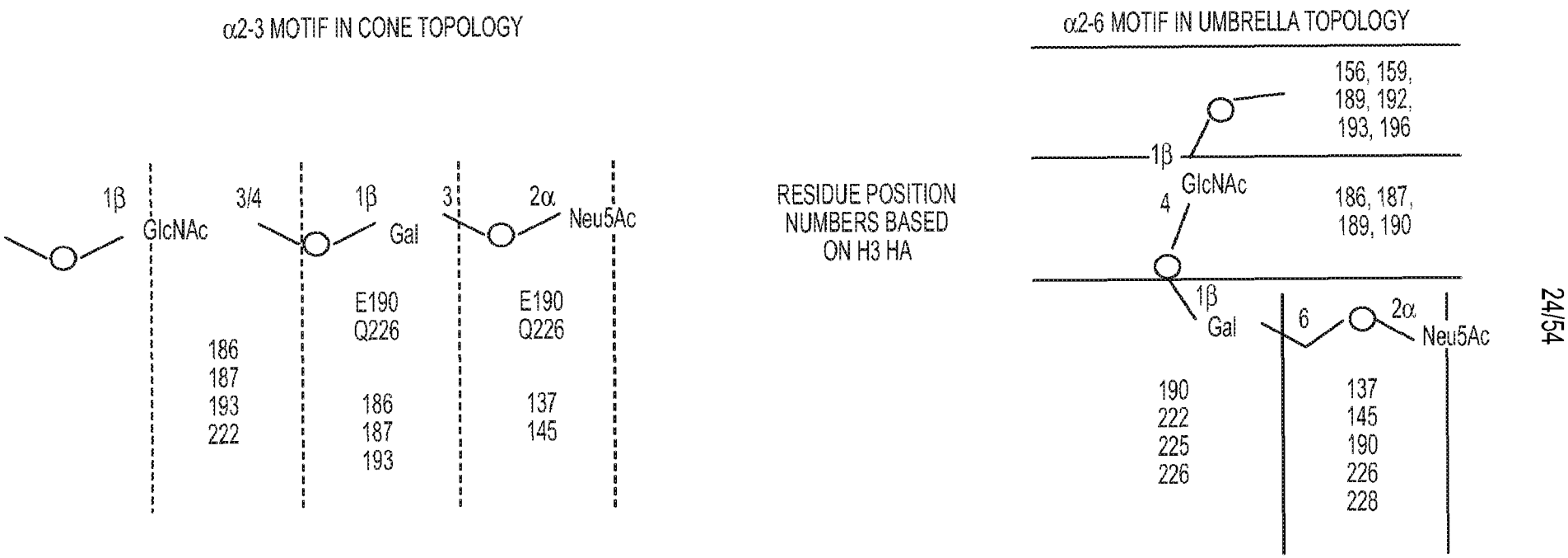

α2-3 MOTIF IN CONE TOPOLOGY
1β
GlcNAc
3/4
1β
Gal
3
2α
Neu5Ac
E190
Q226
186
187
193
222
E190
Q226
186
187
193
137
145
RESIDUE POSITION NUMBERS BASED ON H3 HA
α2-6 MOTIF IN UMBRELLA TOPOLOGY
156, 159,
189, 192,
193, 196
1β
GlcNAc
4
186, 187,
189, 190
1β
Gal
6
2α
Neu5Ac
190
222
225
226
137
145
190
226
228

FIG. 7

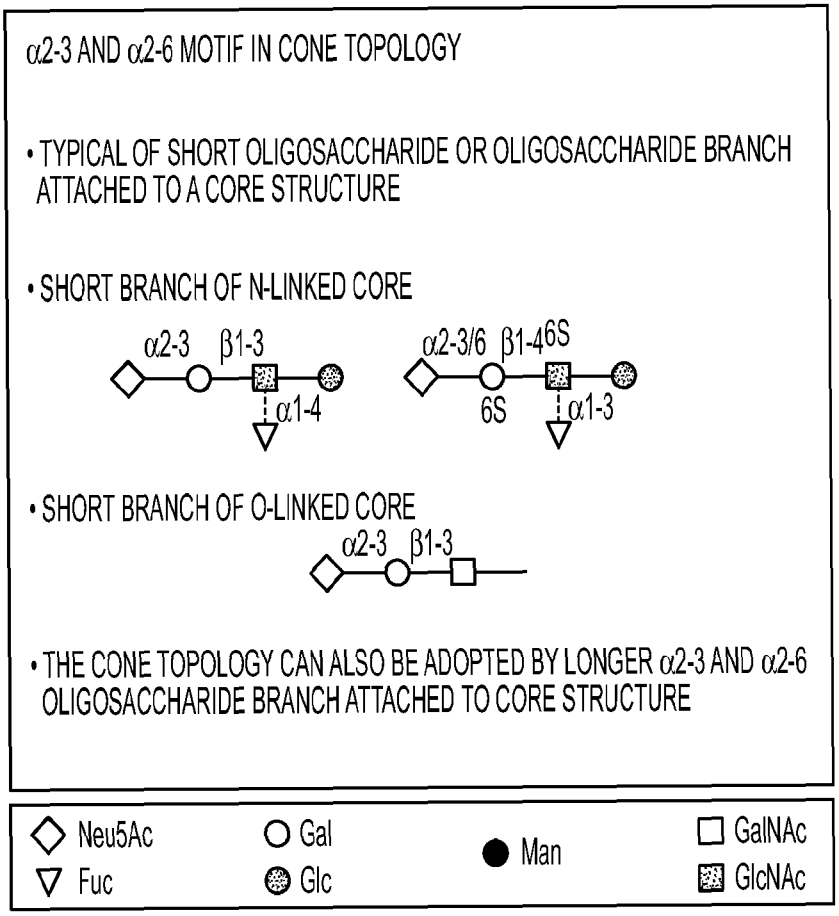

α2-3 AND α2-6 MOTIF IN CONE TOPOLOGY
• TYPICAL OF SHORT OLIGOSACCHARIDE OR OLIGOSACCHARIDE BRANCH ATTACHED TO A CORE STRUCTURE
• SHORT BRANCH OF N-LINKED CORE
α2-3
β1-3
α1-4
α2-3/6
β1-4
6S
6S
α1-3
• SHORT BRANCH OF O-LINKED CORE
α2-3
β1-3
• THE CONE TOPOLOGY CAN ALSO BE ADOPTED BY LONGER α2-3 AND α2-6 OLIGOSACCHARIDE BRANCH ATTACHED TO CORE STRUCTURE
Neu5Ac
Fuc
Gal
Glc
Man
GalNAc
GlcNAc
DOTTED GRAY LINES, 4S AND 6S INDICATE POTENTIAL SITES FOR FUCOSYLATION AND SULFATION MODIFICATIONS

FIG. 8

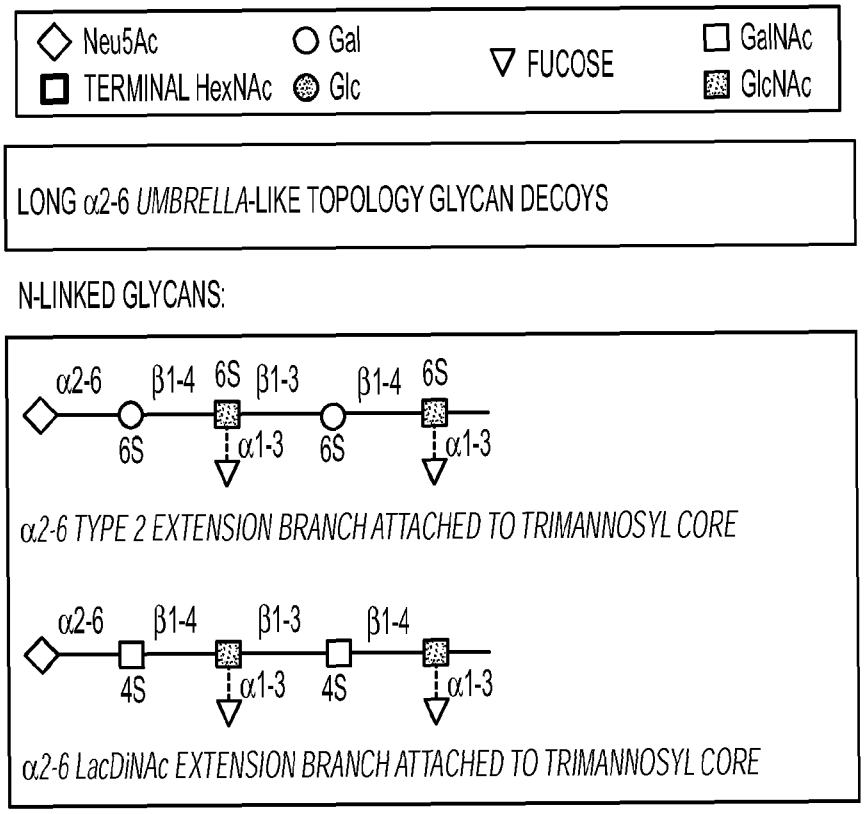
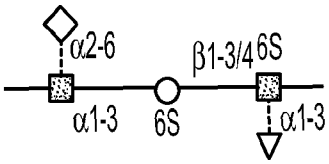

Neu5Ac
Gal
FUCOSE
GalNAc
TERMINAL HexNAc
Glc
GlcNAc
LONG α2-6 UMBRELLA-LIKE TOPOLOGY GLYCAN DECOYS
N-LINKED GLYCANS:
α2-6
β1-4
6S
β1-3
β1-4
6S
6S
α1-3
6S
α1-3
α2-6 TYPE 2 EXTENSION BRANCH ATTACHED TO TRIMANNOSYL CORE
α2-6
β1-4
β1-3
β1-4
4S
α1-3
4S
α1-3
α2-6 LacDiNAc EXTENSION BRANCH ATTACHED TO TRIMANNOSYL CORE

FIG. 9A-1

LONG α2-6 *UMBRELLA*-LIKE TOPOLOGY GLYCANS THAT ARE NOT DECOYS

N-LINKED GLYCANS:

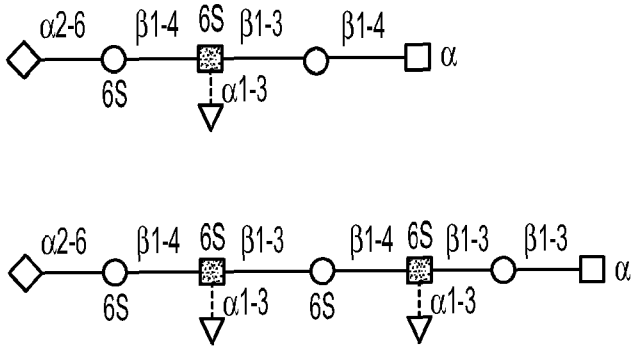


α2-6 LINKAGE ON GlcNAc OF TYPE 1/TYPE 2 EXTENSION

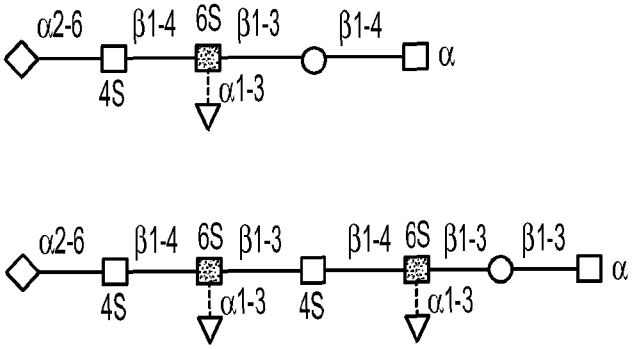
FIG. 9A-2

LONG α2-6 *UMBRELLA*-LIKE TOPOLOGY GLYCAN DECOYS

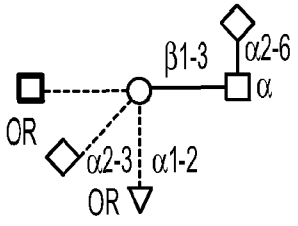
O-LINKED GLYCANS:



α2-6 TYPE 2 EXTENSION BRANCH IN A CORE 1 TYPE STRUCTURE



α2-6 LacDiNAc EXTENSION BRANCH IN A CORE 1 TYPE STRUCTURE

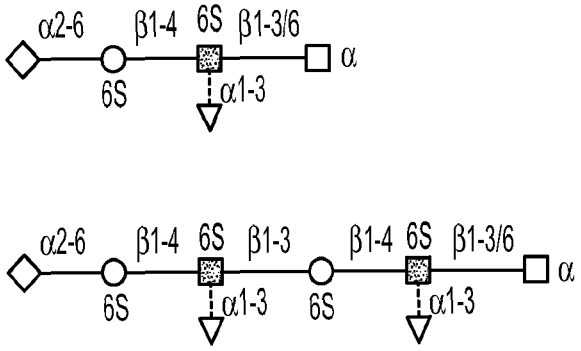


α2-6 ATTACHED TO CORE GalNAc IN CORE 1 TYPE STRUCTURE

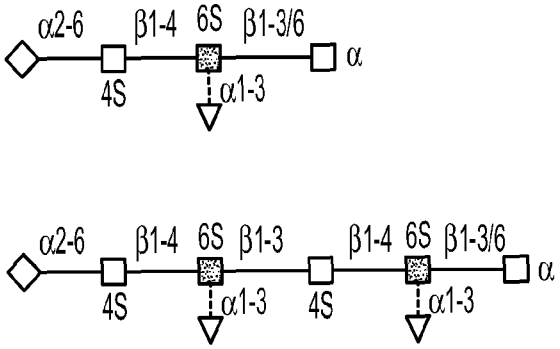
FIG. 9A-3

LONG α2-6 *UMBRELLA*-LIKE TOPOLOGY GLYCAN DECOYS

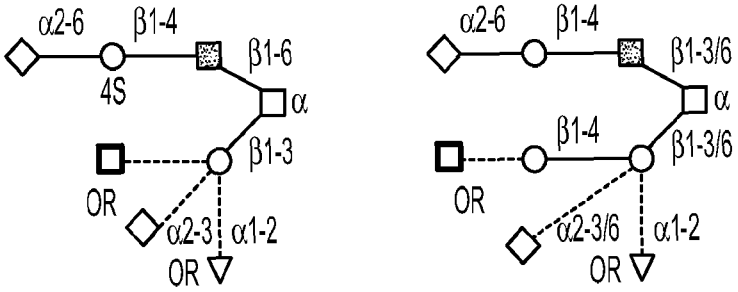
O-LINKED GLYCANS:



α2-6 TYPE 2 EXTENSION BRANCH IN A CORE 2 OR 3 OR 4 TYPE STRUCTURE



α2-6 LacDiNAc EXTENSION BRANCH IN A CORE 2 OR 3 OR 4 TYPE STRUCTURE

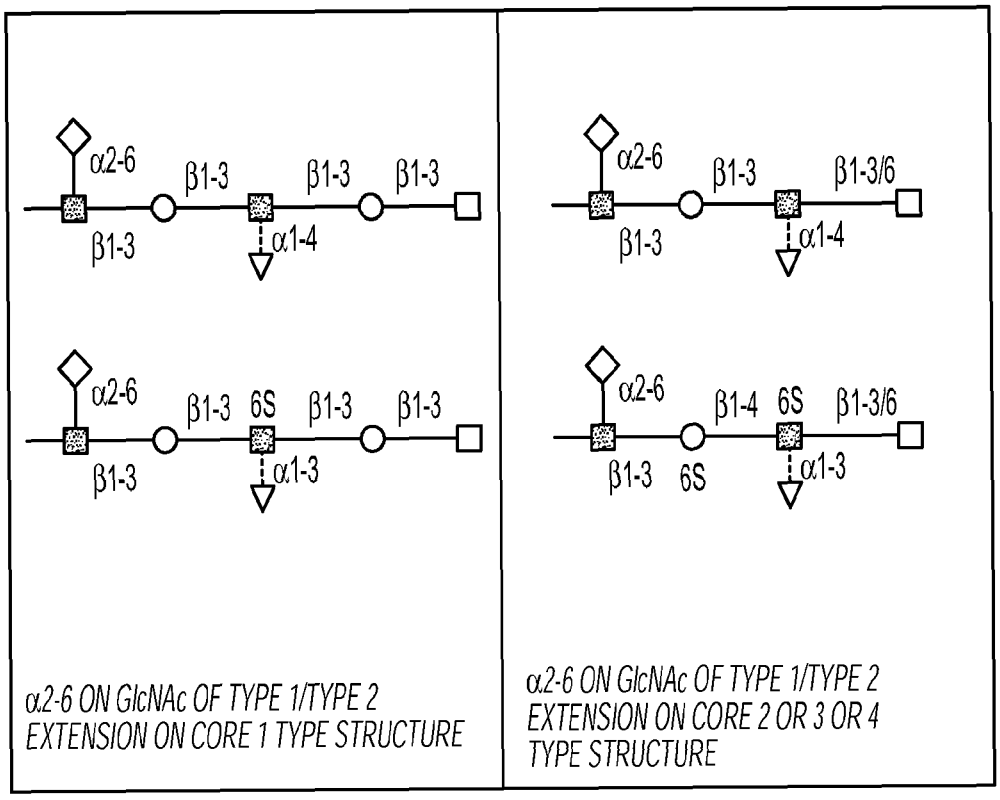


α2-6 ATTACHED TO BRANCHED CORE 2 AND CORE 4 STRUCTURES

FIG. 9A-4

LONG α2-6 *UMBRELLA*-LIKE TOPOLOGY GLYCAN THAT ARE NOT DECOYS

O-LINKED GLYCANS:



α2-6 ON GlcNAc OF TYPE 1/TYPE 2 EXTENSION ON CORE 1 TYPE STRUCTURE

α2-6 ON GlcNAc OF TYPE 1/TYPE 2 EXTENSION ON CORE 2 OR 3 OR 4 TYPE STRUCTURE

FIG. 9A-5

LONG α2-6 *UMBRELLA*-LIKE TOPOLOGY GLYCAN DECOYS

GLYCOLIPIDS:

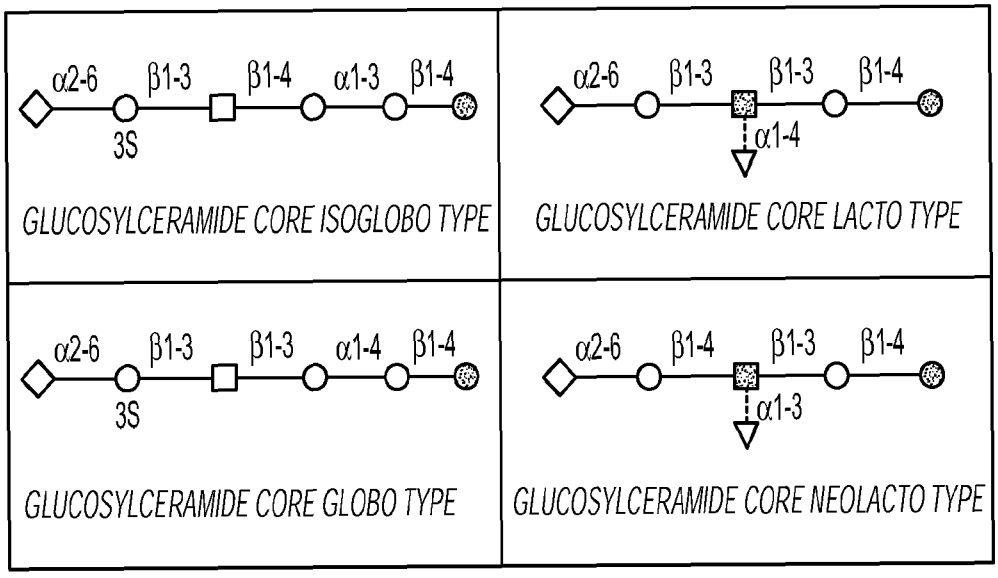
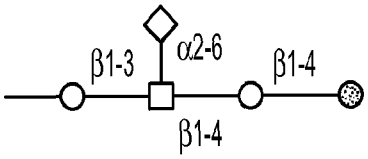


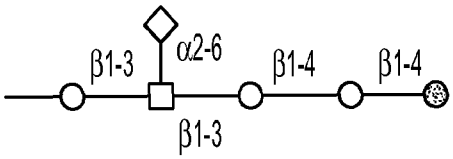
FIG. 9A-6

LONG α2-6 *UMBRELLA*-LIKE TOPOLOGY GLYCAN THAT ARE NOT DECOYS

GLYCOLIPIDS:



GLUCOSYLCERAMIDE CORE GANGLIO TYPE



GLUCOSYLCERAMIDE CORE GLOBO TYPE

FIG. 9A-7

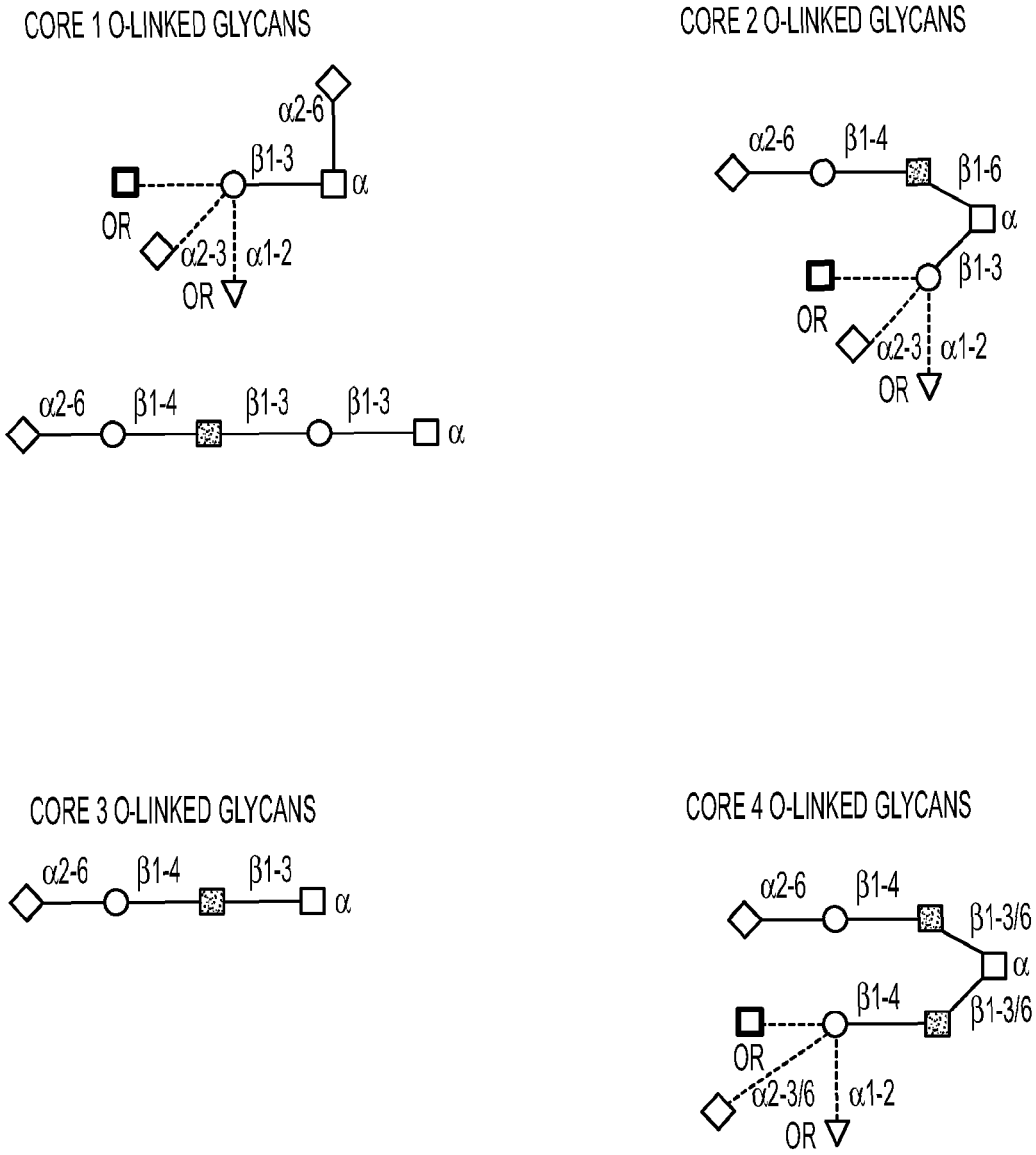

CORE 1 O-LINKED GLYCANS
α2-6
β1-3
α
OR
α2-3
α1-2
OR
α2-6
β1-4
β1-3
β1-3
α
CORE 2 O-LINKED GLYCANS
α2-6
β1-4
β1-6
α
β1-3
OR
α2-3
α1-2
OR
CORE 3 O-LINKED GLYCANS
α2-6
β1-4
β1-3
α
CORE 4 O-LINKED GLYCANS
α2-6
β1-4
β1-3/6
α
β1-4
β1-3/6
OR
α2-3/6
α1-2
OR
GlcNAc
α GalNAc O-LINKED TO PROTEIN
Neu5Ac
FUCOSE
Gal
TERMINAL HexNAc

FIG. 9B

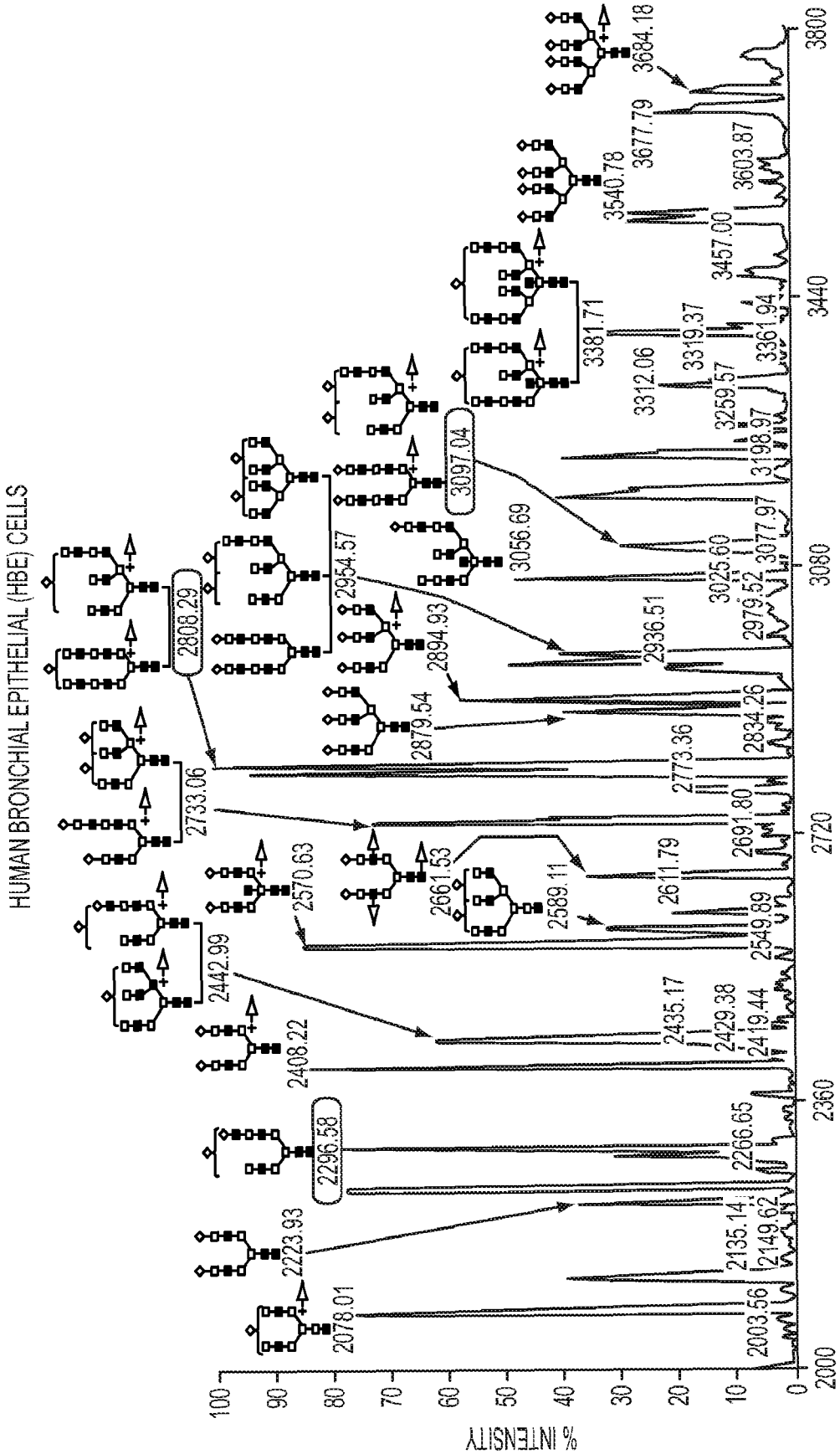

HUMAN BRONCHIAL EPITHELIAL (HBE) CELLS
% INTENSITY
MASS (m/z)
2000
2360
2720
3080
3440
3800
2078.01
2003.56
2135.14
2149.62
2223.93
2296.58
2266.65
2408.22
2442.99
2435.17
2429.38
2419.44
2549.89
2570.63
2661.53
2589.11
2611.79
2691.80
2733.06
2773.36
2808.29
2834.26
2879.54
2894.93
2954.57
2936.51
3025.60
2979.52
3077.97
3056.69
3097.04
3198.97
3259.57
3312.06
3319.37
3361.94
3381.71
3457.00
3540.78
3603.87
3677.79
3684.18

FIG. 10A

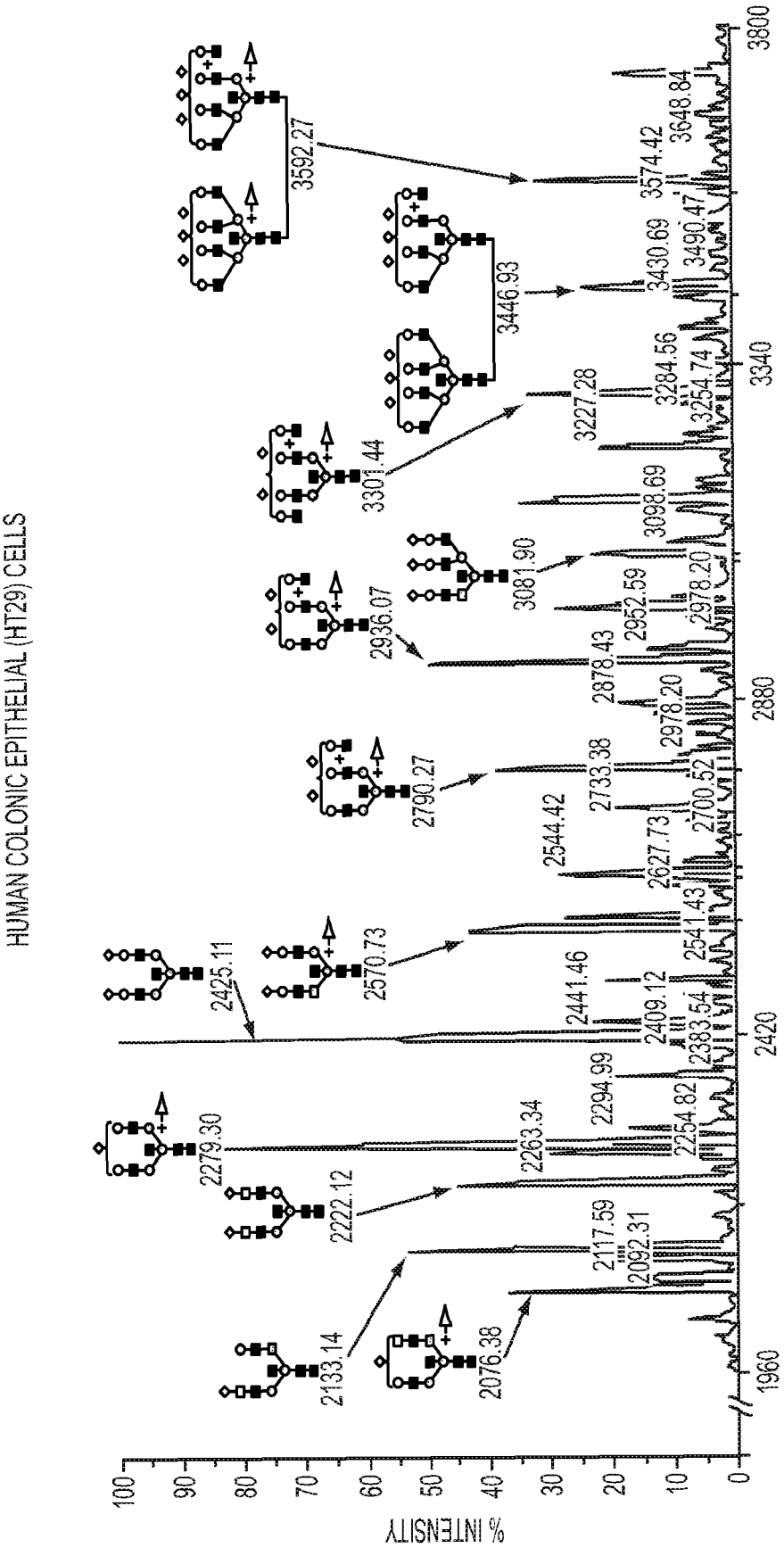

HUMAN COLONIC EPITHELIAL (HT29) CELLS
% INTENSITY
MASS (m/z)
100
90
80
70
60
50
40
30
20
10
0
1960
2420
2880
3340
3800
2133.14
2076.38
2279.30
2222.12
2425.11
2570.73
2790.27
2936.07
3301.44
3446.93
3592.27
2117.59
2092.31
2263.34
2294.99
2254.82
2441.46
2409.12
2383.54
2541.43
2544.42
2733.38
2627.73
2700.52
2978.20
2878.43
2952.59
3081.90
3098.69
3227.28
3284.56
3254.74
3430.69
3490.47
3574.42
3648.84

FIG. 10B

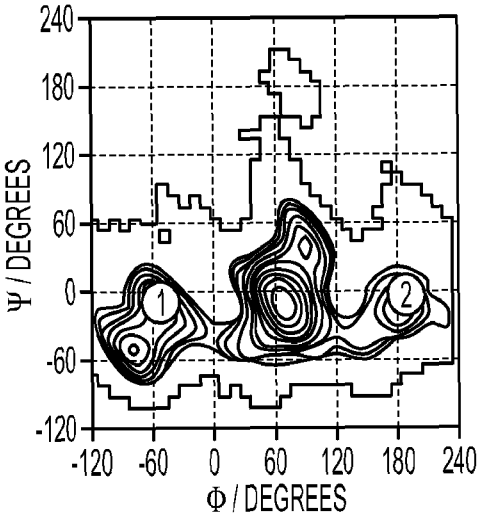


FIG. 11A

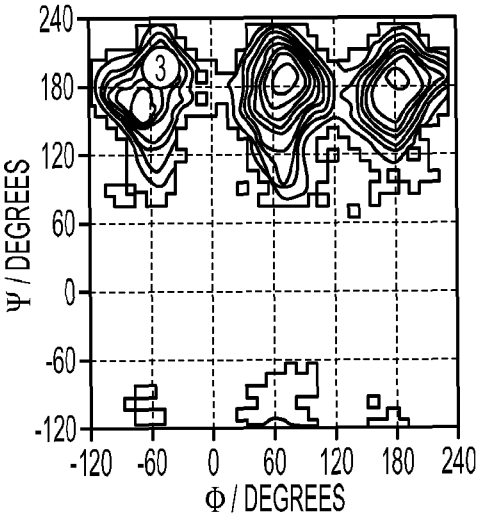


FIG. 11B

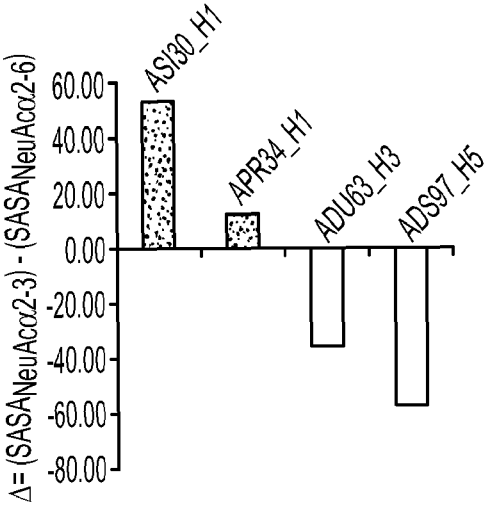


FIG. 11C

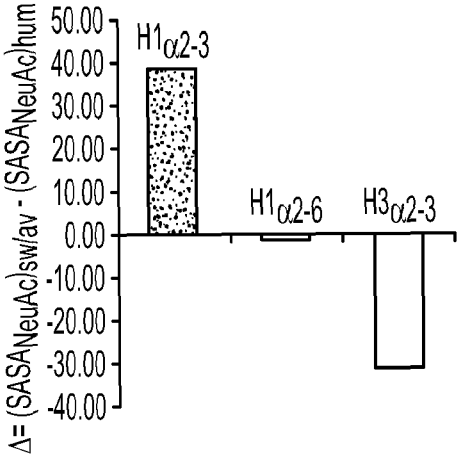
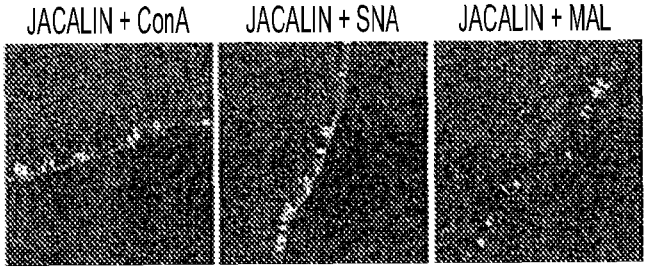


FIG. 11D



LECTIN STAINING OF UPPER RESPIRATORY TISSUE SECTIONS

FIG. 12A

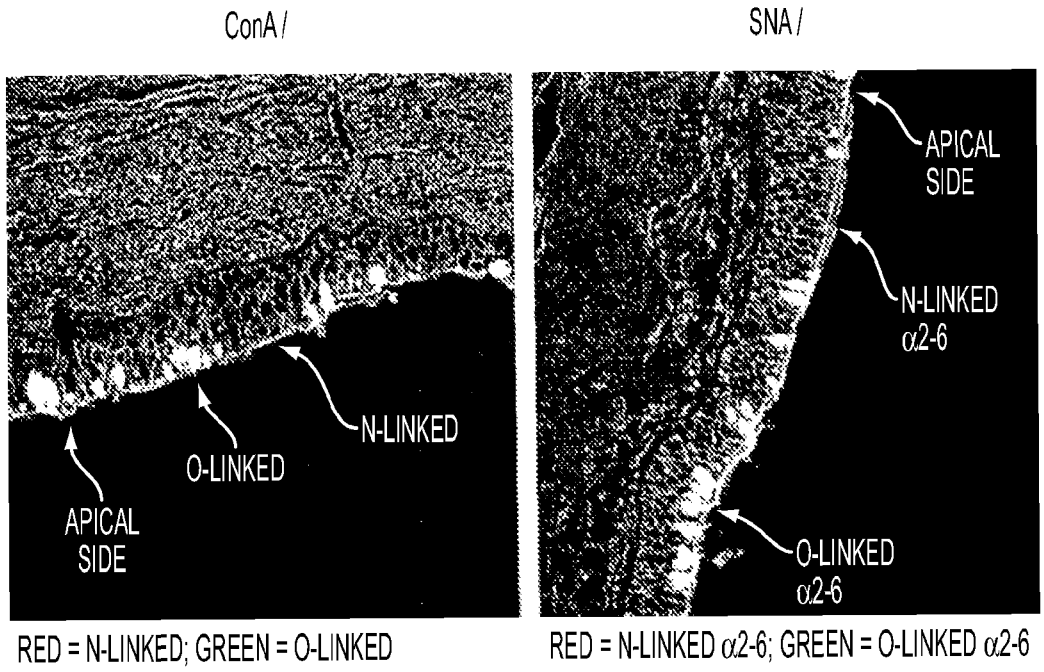

ConA /
SNA /
APICAL SIDE
O-LINKED
N-LINKED
APICAL SIDE
N-LINKED α2-6
O-LINKED α2-6
RED = N-LINKED; GREEN = O-LINKED
RED = N-LINKED α2-6; GREEN = O-LINKED α2-6

FIG. 12B

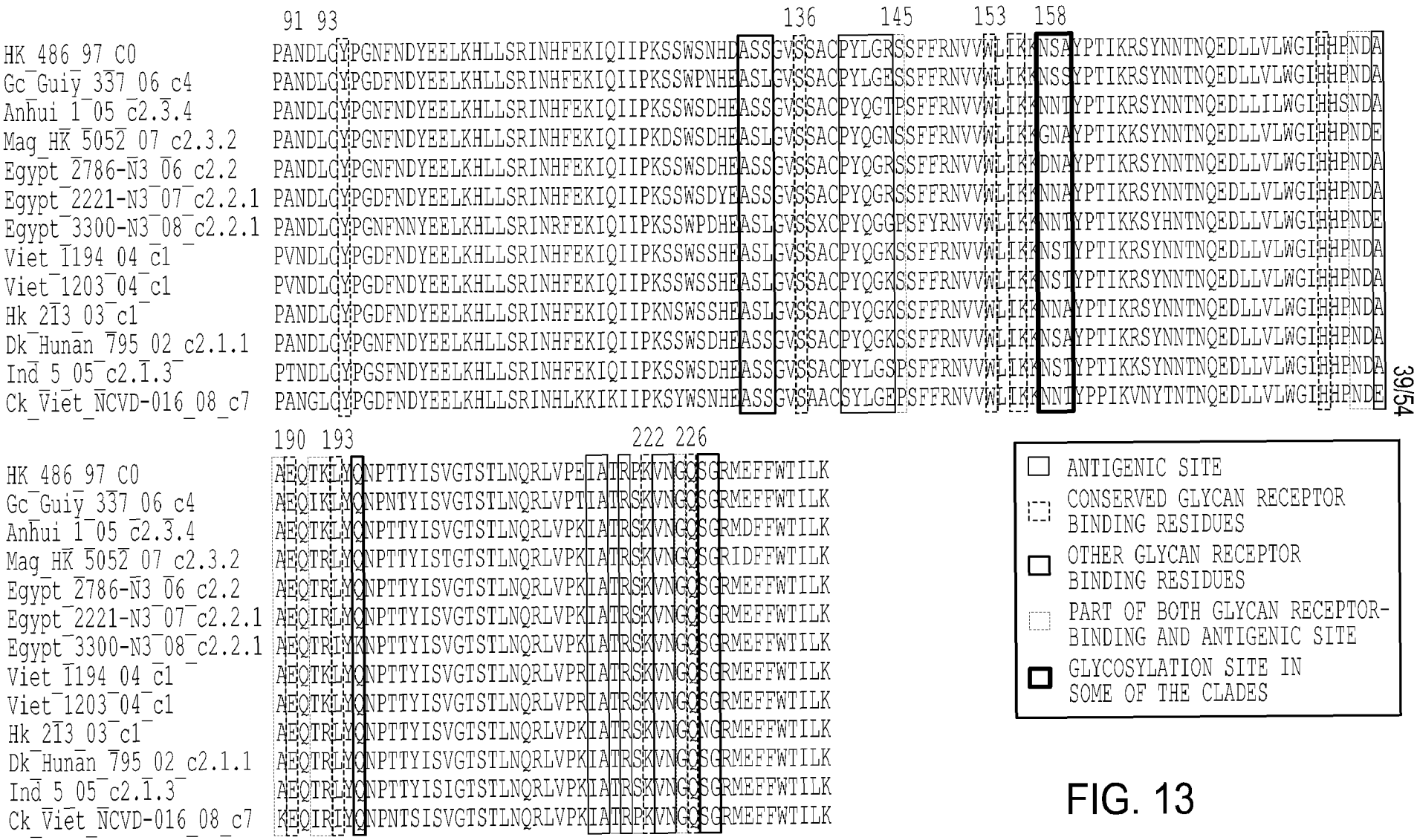

91 93
136
145
153
158
HK_486_97_C0
Gc_Guiy_337_06_c4
Anhui_1_05_c2.3.4
Mag_HK_5052_07_c2.3.2
Egypt_2786-N3_06_c2.2
Egypt_2221-N3_07_c2.2.1
Egypt_3300-N3_08_c2.2.1
Viet_1194_04_c1
Viet_1203_04_c1
Hk_213_03_c1
Dk_Hunan_795_02_c2.1.1
Ind_5_05_c2.1.3
Ck_Viet_NCVD-016_08_c7
39/54
190 193
222 226
ANTIGENIC SITE
CONSERVED GLYCAN RECEPTOR BINDING RESIDUES
OTHER GLYCAN RECEPTOR BINDING RESIDUES
PART OF BOTH GLYCAN RECEPTOR-BINDING AND ANTIGENIC SITE
GLYCOSYLATION SITE IN SOME OF THE CLADES

FIG. 13

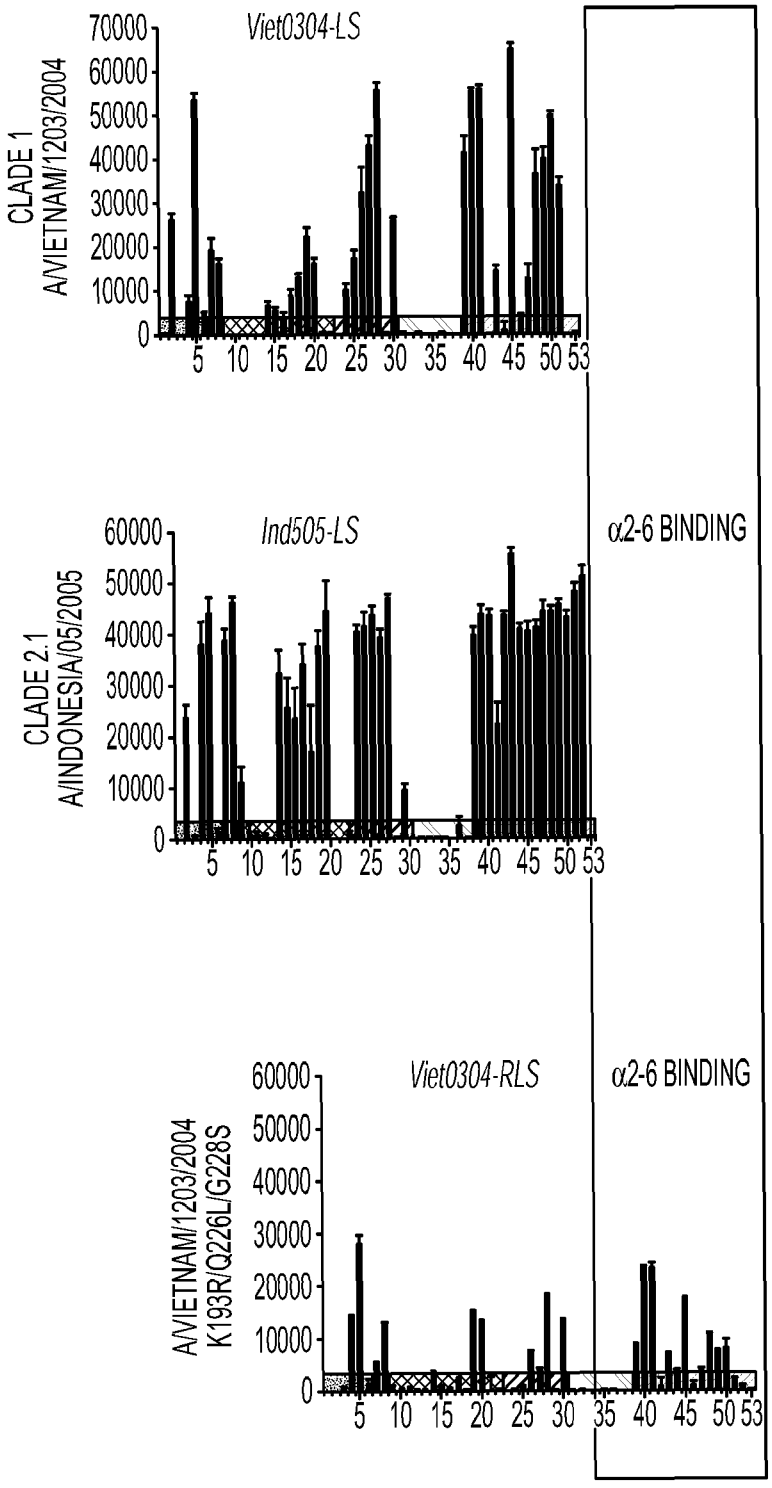

CLADE 1
A/VIETNAM/1203/2004
Viet0304-LS
70000
60000
50000
40000
30000
20000
10000
0
5 10 15 20 25 30 35 40 45 50 53
CLADE 2.1
A/INDONESIA/05/2005
Ind505-LS
α2-6 BINDING
60000
50000
40000
30000
20000
10000
0
5 10 15 20 25 30 35 40 45 50 53
A/VIETNAM/1203/2004
K193R/Q226L/G228S
Viet0304-RLS
α2-6 BINDING
60000
50000
40000
30000
20000
10000
0
5 10 15 20 25 30 35 40 45 50 53

FIG. 14

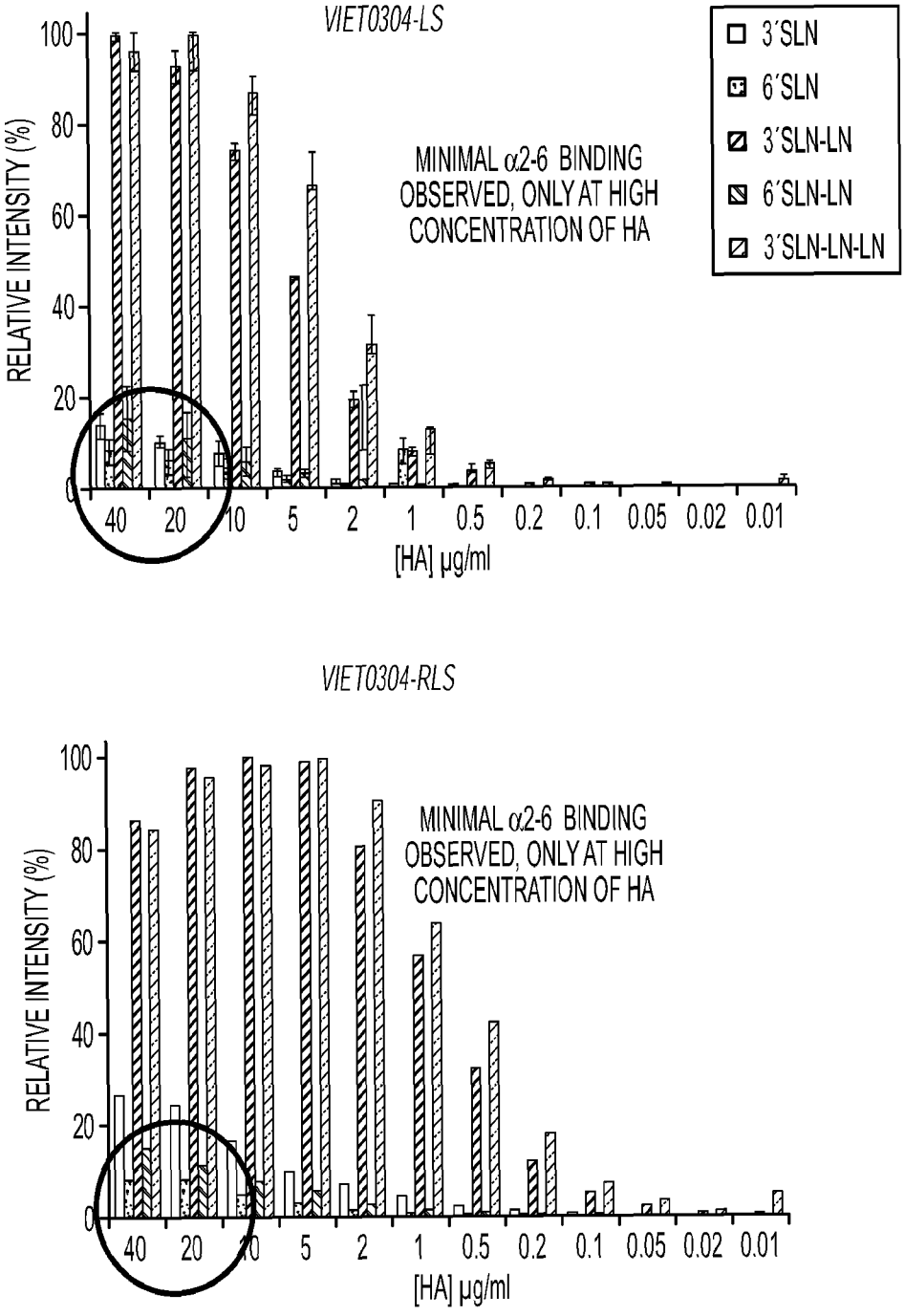

VIET0304-LS
3´SLN
6´SLN
3´SLN-LN
6´SLN-LN
3´SLN-LN-LN
MINIMAL α2-6 BINDING OBSERVED, ONLY AT HIGH CONCENTRATION OF HA
RELATIVE INTENSITY (%)
100
80
60
40
20
0
40 20 10 5 2 1 0.5 0.2 0.1 0.05 0.02 0.01
[HA] µg/ml
VIET0304-RLS
MINIMAL α2-6 BINDING OBSERVED, ONLY AT HIGH CONCENTRATION OF HA
RELATIVE INTENSITY (%)
100
80
60
40
20
0
40 20 10 5 2 1 0.5 0.2 0.1 0.05 0.02 0.01
[HA] µg/ml

FIG. 15

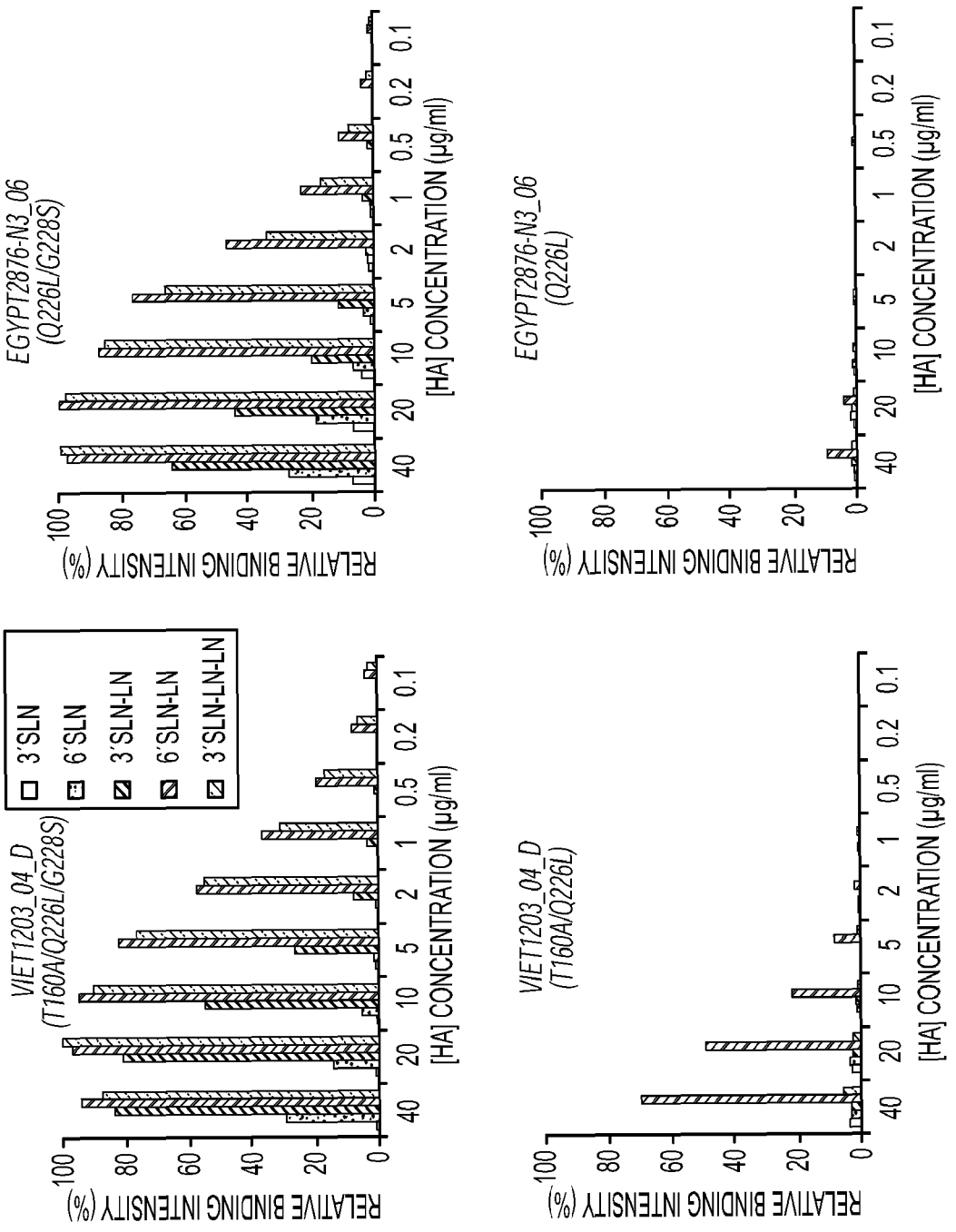

VIET1203_04_D
(T160A/Q226L/G228S)
EGYPT2876-N3_06
(Q226L/G228S)
VIET1203_04_D
(T160A/Q226L)
EGYPT2876-N3_06
(Q226L)
3'SLN
6'SLN
3'SLN-LN
6'SLN-LN
3'SLN-LN-LN
RELATIVE BINDING INTENSITY (%)
[HA] CONCENTRATION (µg/ml)
0
20
40
60
80
100
40
20
10
5
2
1
0.5
0.2
0.1

FIG. 16

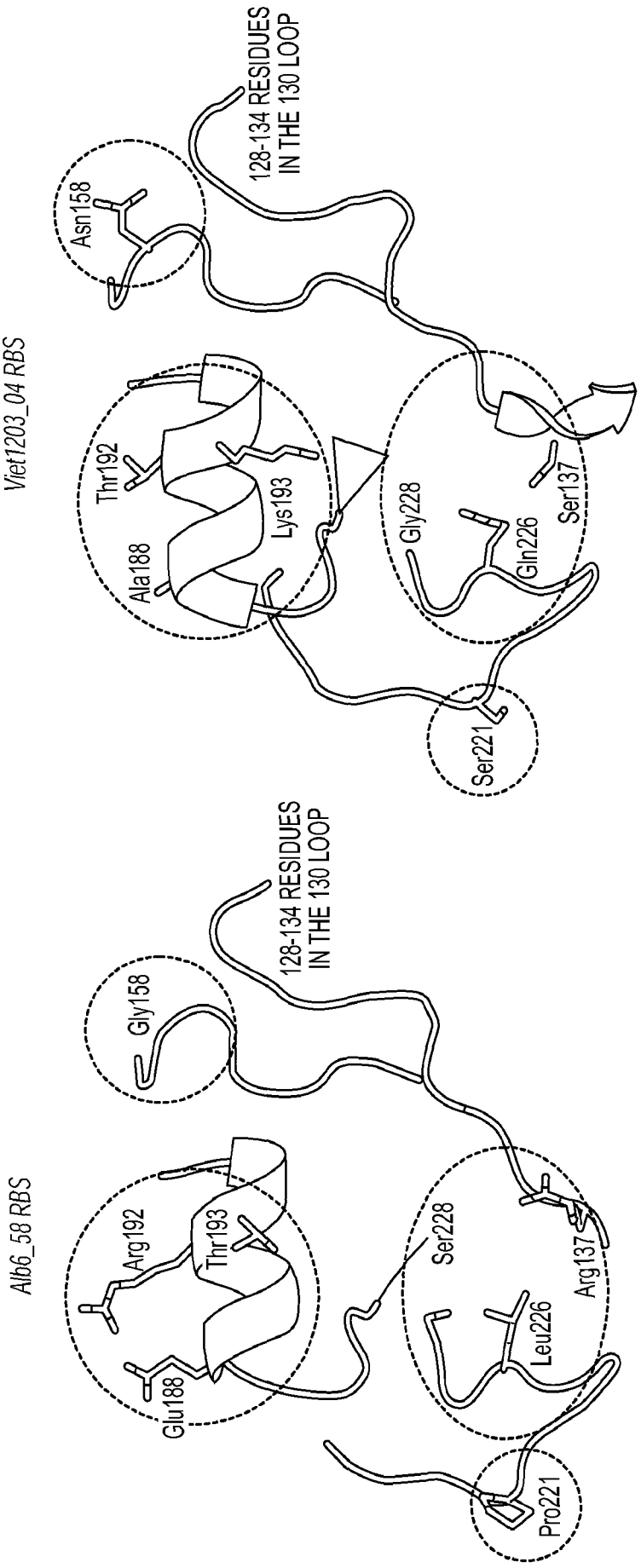

Alb6_58 RBS
Glu188
Arg192
Thr193
Gly158
128-134 RESIDUES
IN THE 130 LOOP
Pro221
Ser228
Leu226
Arg137
Viet1203_04 RBS
Ala188
Thr192
Lys193
Asn158
128-134 RESIDUES
IN THE 130 LOOP
Ser221
Gly228
Gln226
Ser137

FIG. 17

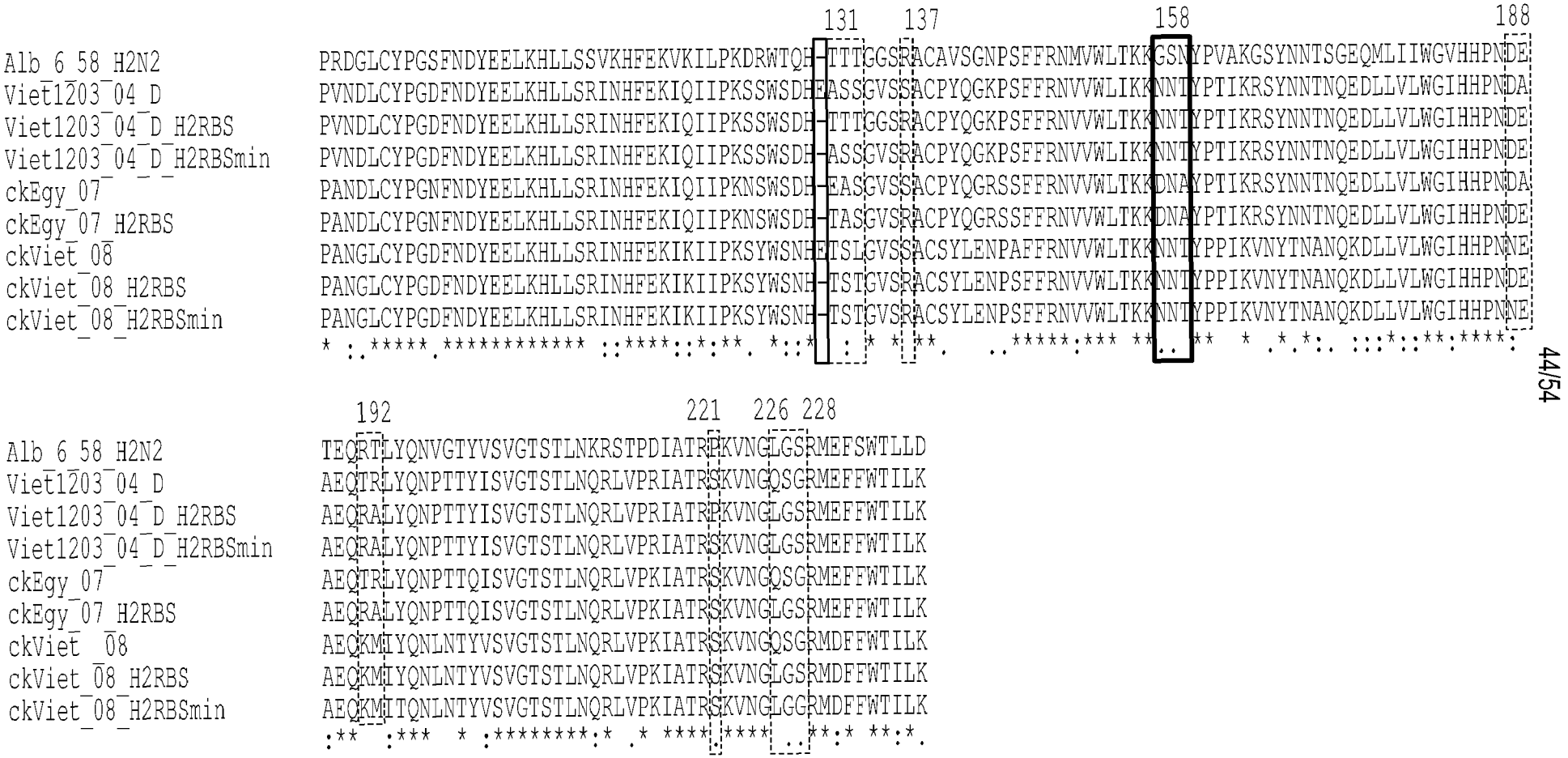

131
137
158
188
Alb_6_58_H2N2
Viet1203_04_D
Viet1203_04_D_H2RBS
Viet1203_04_D_H2RBSmin
ckEgy_07
ckEgy_07_H2RBS
ckViet_08
ckViet_08_H2RBS
ckViet_08_H2RBSmin
192
221
226
228
Alb_6_58_H2N2
Viet1203_04_D
Viet1203_04_D_H2RBS
Viet1203_04_D_H2RBSmin
ckEgy_07
ckEgy_07_H2RBS
ckViet_08
ckViet_08_H2RBS
ckViet_08_H2RBSmin

FIG. 18

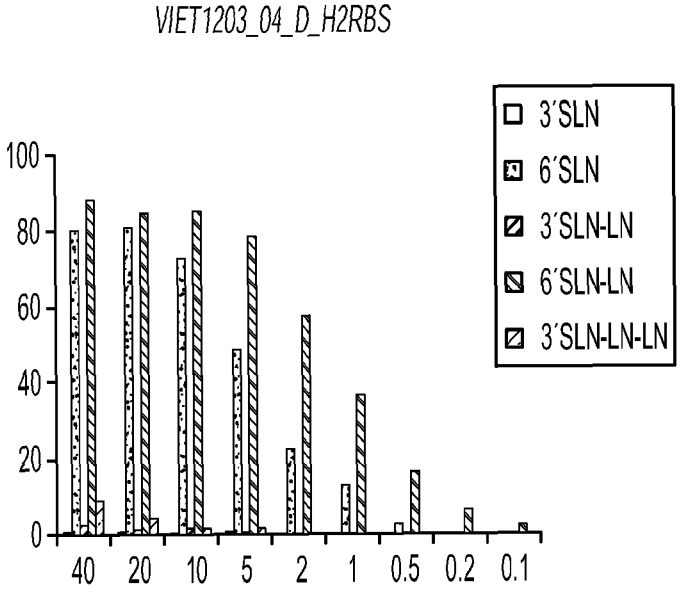

VIET1203_04_D_H2RBS
3´SLN
6´SLN
3´SLN-LN
6´SLN-LN
3´SLN-LN-LN
100
80
60
40
20
0
40
20
10
5
2
1
0.5
0.2
0.1

FIG. 19

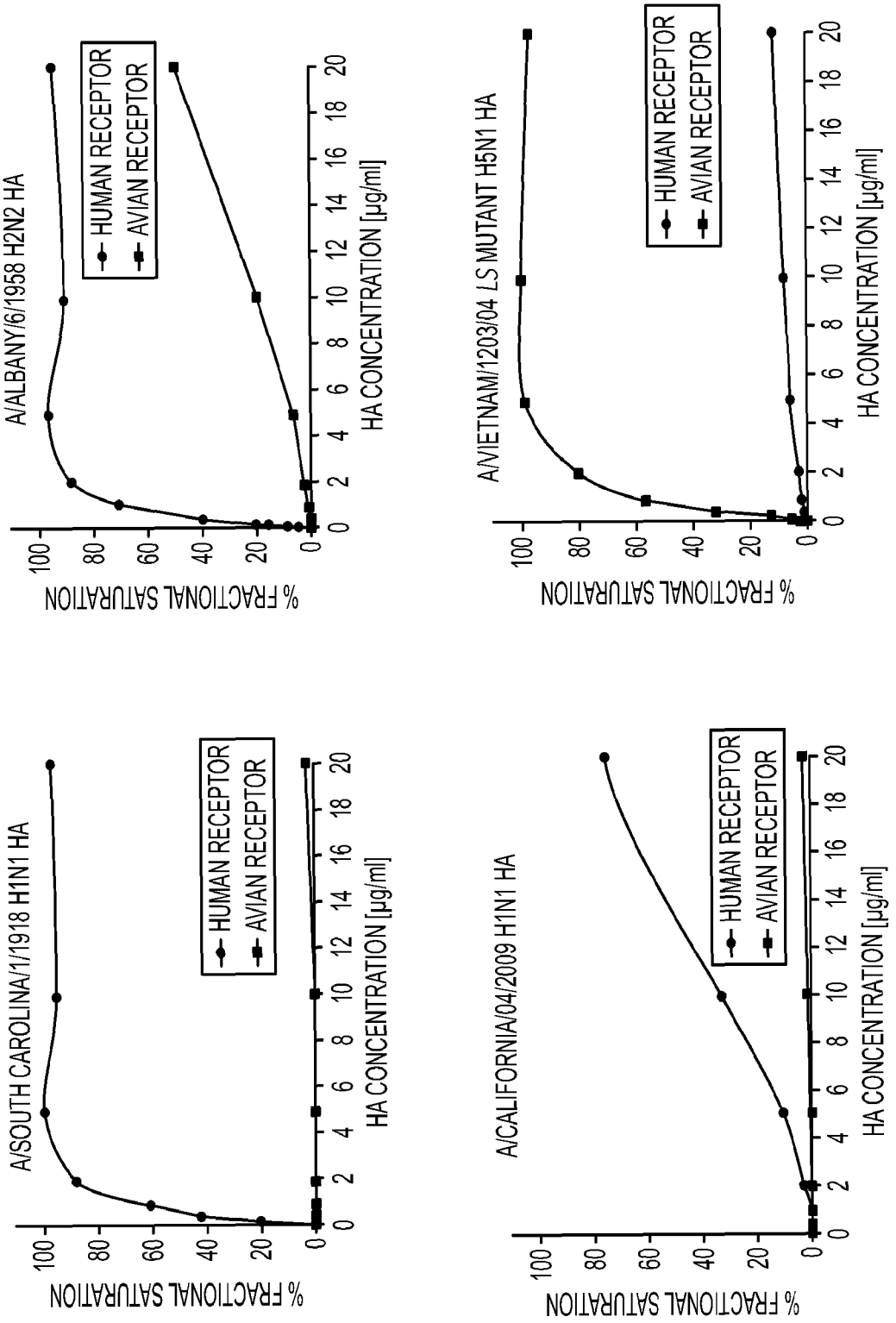

A/ALBANY/6/1958 H2N2 HA
A/VIETNAM/1203/04 LS MUTANT H5N1 HA
A/SOUTH CAROLINA/1/1918 H1N1 HA
A/CALIFORNIA/04/2009 H1N1 HA
HUMAN RECEPTOR
AVIAN RECEPTOR
% FRACTIONAL SATURATION
HA CONCENTRATION [µg/ml]
0
20
40
60
80
100
0
2
4
6
8
10
12
14
16
18
20

FIG. 20

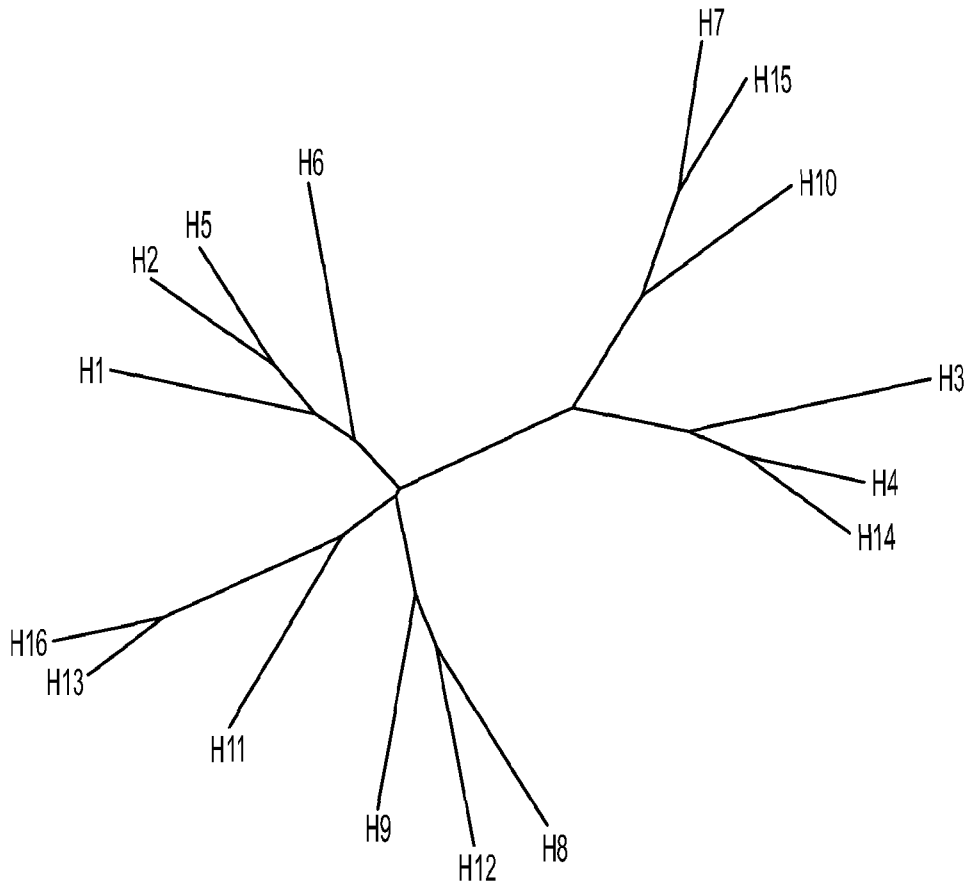


FIG. 21

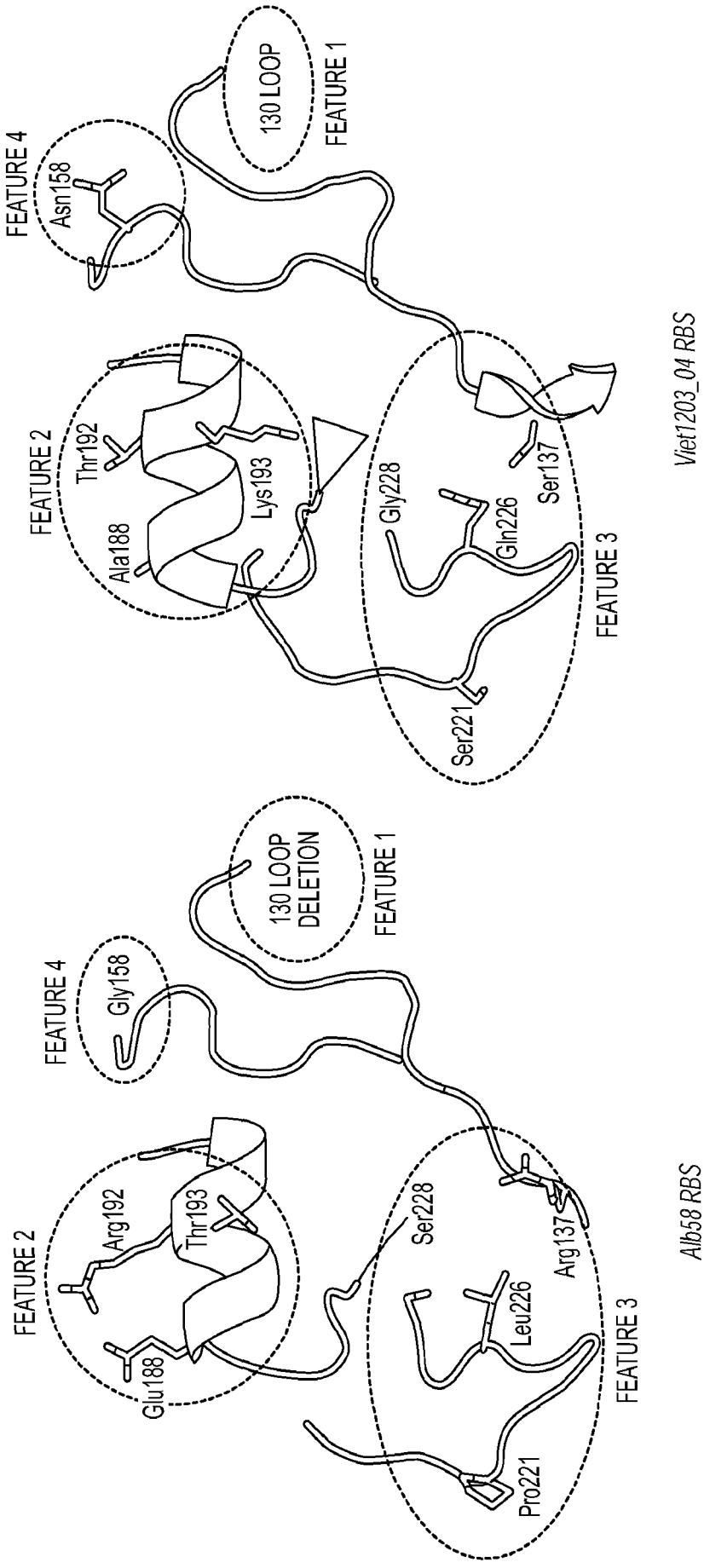

FEATURE 4
Asn158
130 LOOP
FEATURE 1
FEATURE 2
Thr192
Ala188
Lys193
Gly228
Gln226
Ser137
FEATURE 3
Ser221
Viet1203_04 RBS
FEATURE 4
Gly158
130 LOOP
DELETION
FEATURE 1
FEATURE 2
Arg192
Thr193
Ser228
Arg137
Leu226
Glu188
FEATURE 3
Pro221
Alb58 RBS

FIG. 22

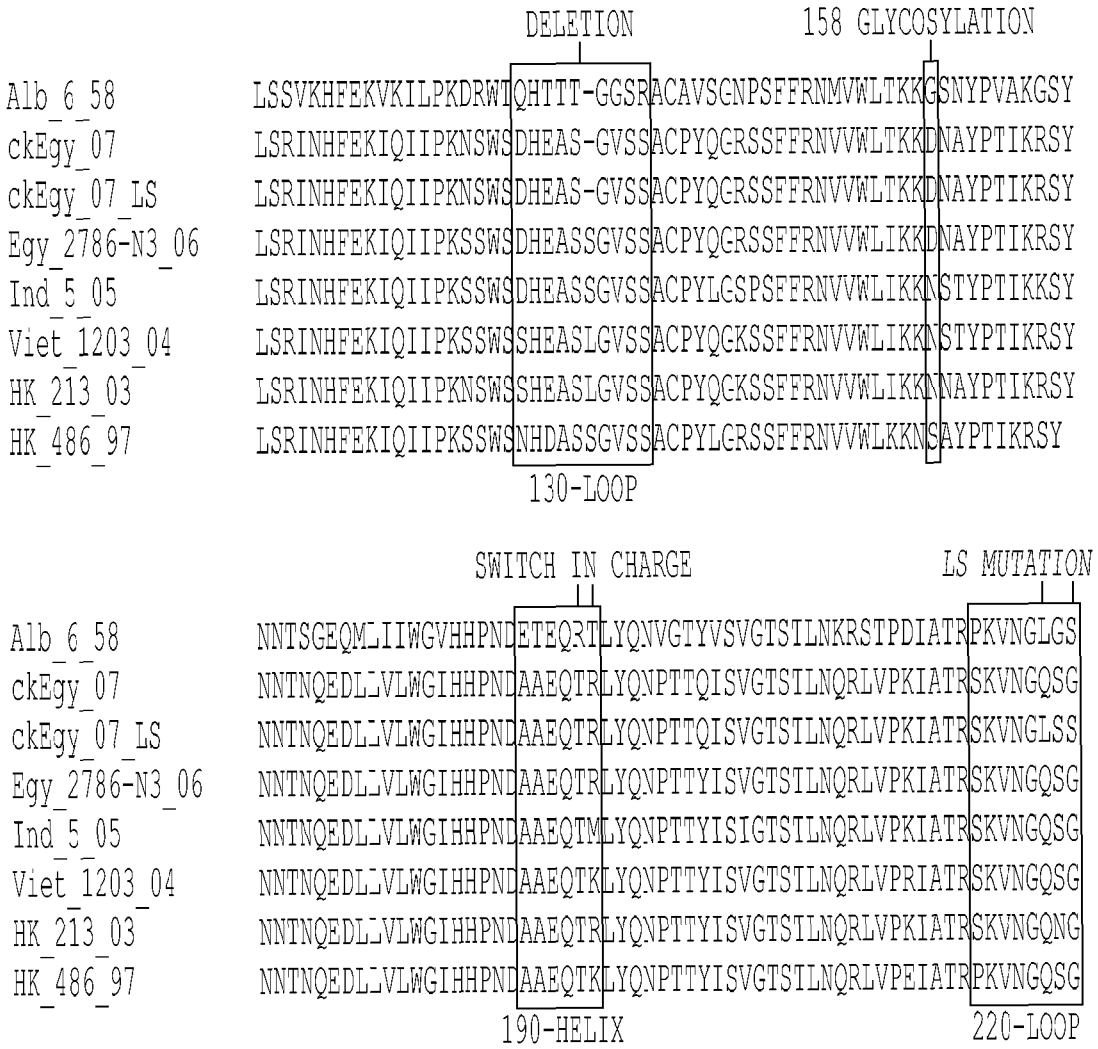

DELETION
158 GLYCOSYLATION
Alb_6_58 LSSVKHFEKVKILPKDRWTQHTTT-GGSRACAVSGNPSFFRNMVWLTKKGSNYPVAKGSY
ckEgy_07 LSRINHFEKIQIIPKNSWSDHEAS-GVSSACPYQGRSSFFRNVVWLTKKDNAYPTIKRSY
ckEgy_07_LS LSRINHFEKIQIIPKNSWSDHEAS-GVSSACPYQGRSSFFRNVVWLTKKDNAYPTIKRSY
Egy_2786-N3_06 LSRINHFEKIQIIPKSSWSDHEASSGVSSACPYQGRSSFFRNVVWLIKKDNAYPTIKRSY
Ind_5_05 LSRINHFEKIQIIPKSSWSDHEASSGVSSACPYLGSPSFFRNVVWLIKKNSTYPTIKKSY
Viet_1203_04 LSRINHFEKIQIIPKSSWSSHEASLGVSSACPYQGKSSFFRNVVWLIKKNSTYPTIKRSY
HK_213_03 LSRINHFEKIQIIPKNSWSSHEASLGVSSACPYQGKSSFFRNVVWLIKKNNAYPTIKRSY
HK_486_97 LSRINHFEKIQIIPKSSWSNHDASSGVSSACPYLGRSSFFRNVVWLKKNSAYPTIKRSY
130-LOOP
SWITCH IN CHARGE
LS MUTATION
Alb_6_58 NNTSGEQMLIIWGVHHPNDETEQRTLYQNVGTYVSVGTSILNKRSTPDIATRPKVNGLGS
ckEgy_07 NNTNQEDLLVLWGIHHPNDAAEQTRLYQNPTTQISVGTSILNQRLVPKIATRSKVNGQSG
ckEgy_07_LS NNTNQEDLLVLWGIHHPNDAAEQTRLYQNPTTQISVGTSILNQRLVPKIATRSKVNGLSS
Egy_2786-N3_06 NNTNQEDLLVLWGIHHPNDAAEQTRLYQNPTTYISVGTSILNQRLVPKIATRSKVNGQSG
Ind_5_05 NNTNQEDLLVLWGIHHPNDAAEQTMLYQNPTTYISIGTSILNQRLVPKIATRSKVNGQSG
Viet_1203_04 NNTNQEDLLVLWGIHHPNDAAEQTKLYQNPTTYISVGTSILNQRLVPRIATRSKVNGQSG
HK_213_03 NNTNQEDLLVLWGIHHPNDAAEQTRLYQNPTTYISVGTSILNQRLVPKIATRSKVNGQNG
HK_486_97 NNTNQEDLLVLWGIHHPNDAAEQTKLYQNPTTYISVGTSILNQRLVPEIATRPKVNGQSG
190-HELIX
220-LOOP

FIG. 23

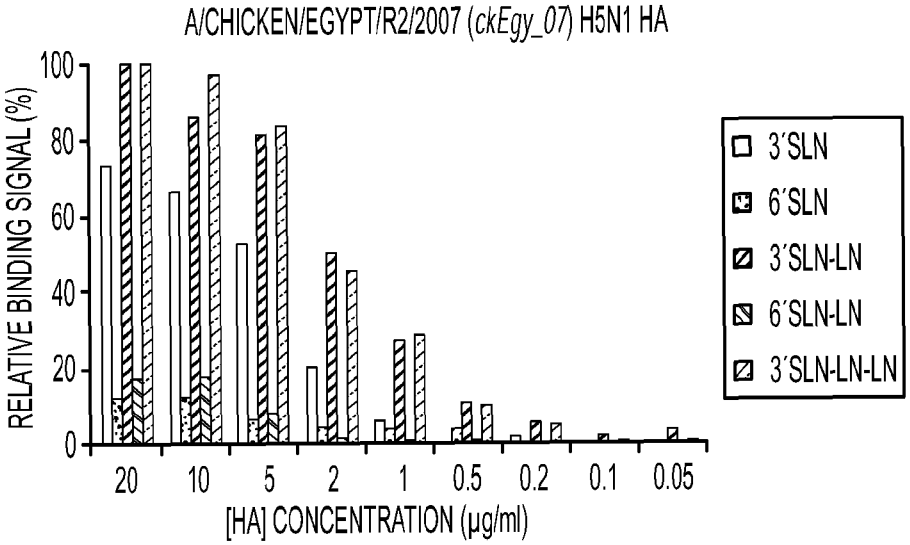


FIG. 24A

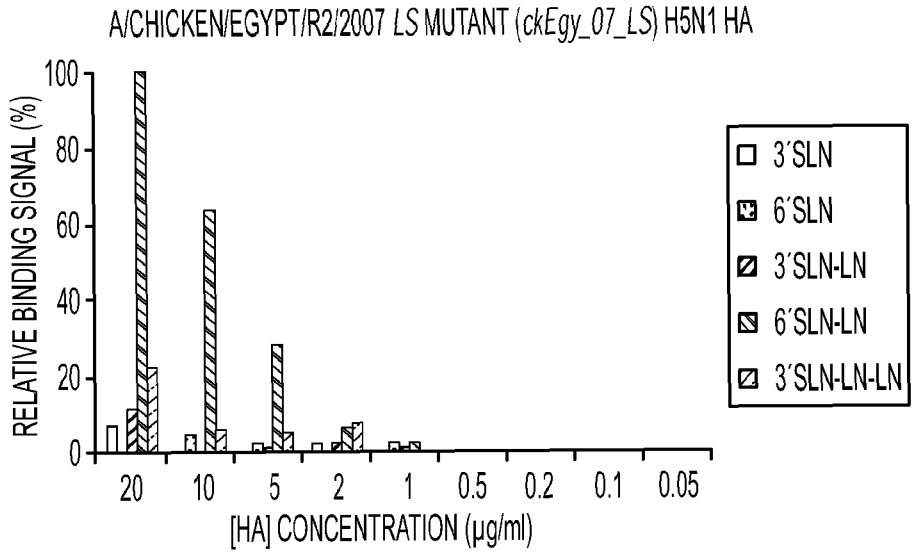
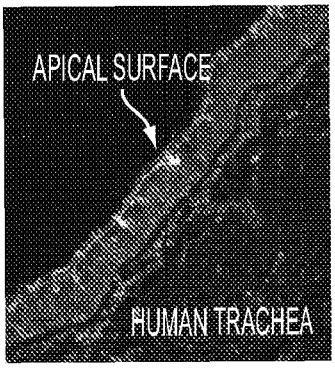


FIG. 24B



ckEgy_07_LS MUTANT HA/ PI

FIG. 24C

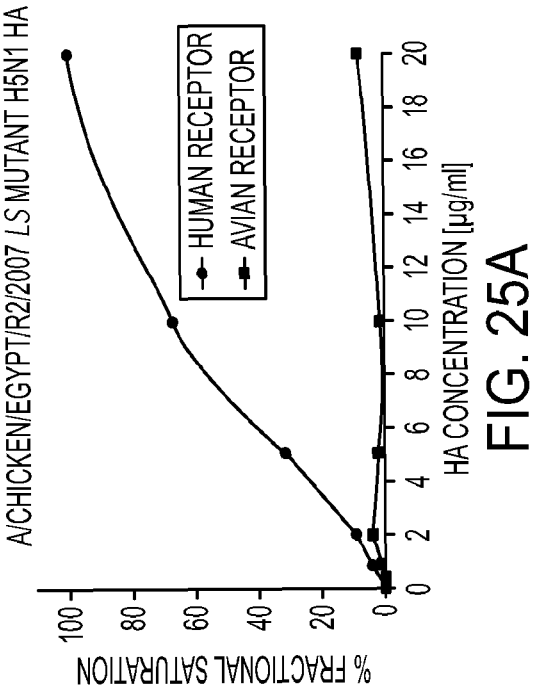


FIG. 25A

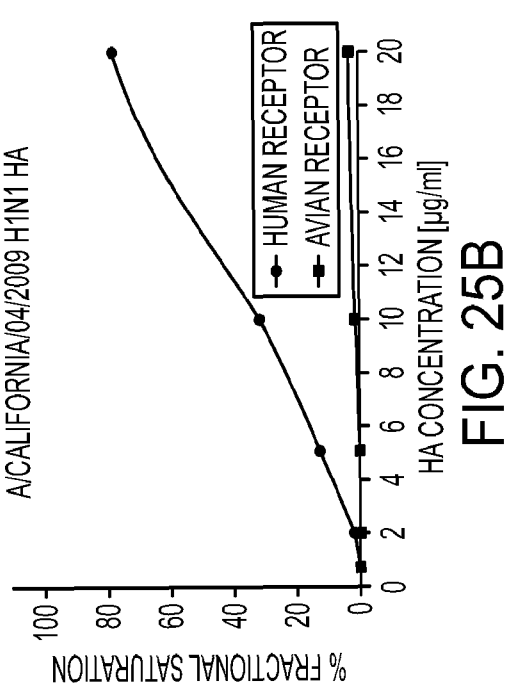


FIG. 25B

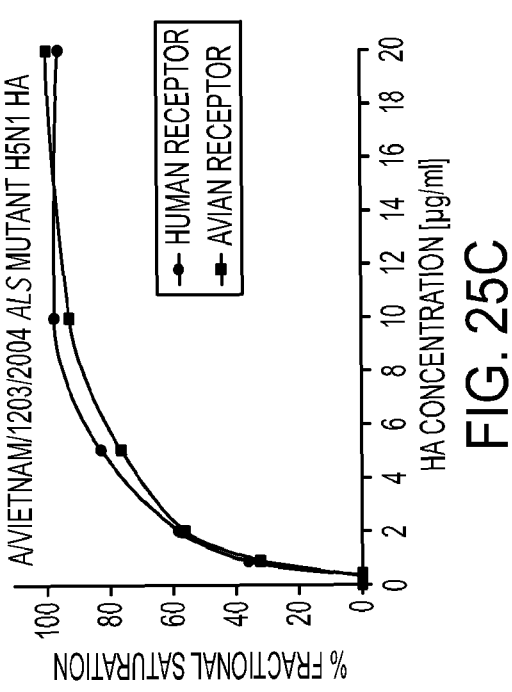


FIG. 25C

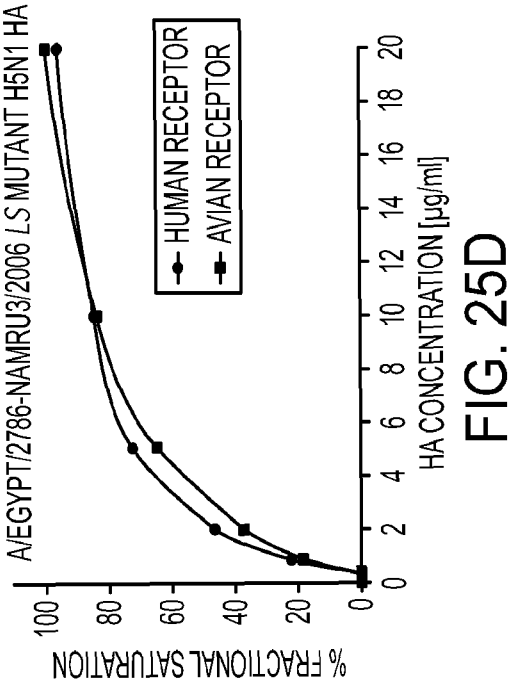


FIG. 25D

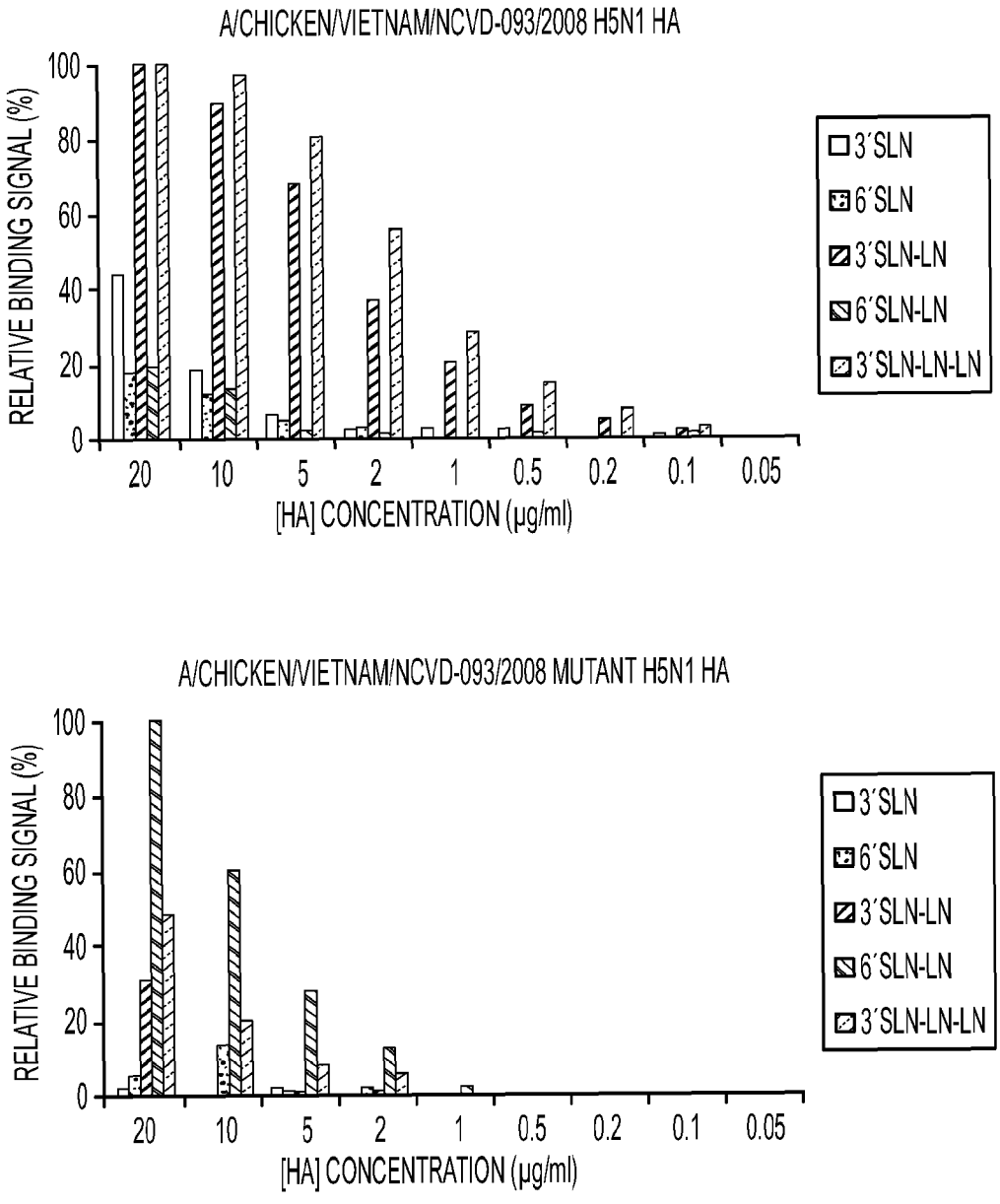

A/CHICKEN/VIETNAM/NCVD-093/2008 H5N1 HA
RELATIVE BINDING SIGNAL (%)
100
80
60
40
20
0
20
10
5
2
1
0.5
0.2
0.1
0.05
[HA] CONCENTRATION (µg/ml)
3´SLN
6´SLN
3´SLN-LN
6´SLN-LN
3´SLN-LN-LN
A/CHICKEN/VIETNAM/NCVD-093/2008 MUTANT H5N1 HA
RELATIVE BINDING SIGNAL (%)
100
80
60
40
20
0
20
10
5
2
1
0.5
0.2
0.1
0.05
[HA] CONCENTRATION (µg/ml)
3´SLN
6´SLN
3´SLN-LN
6´SLN-LN
3´SLN-LN-LN

FIG. 26

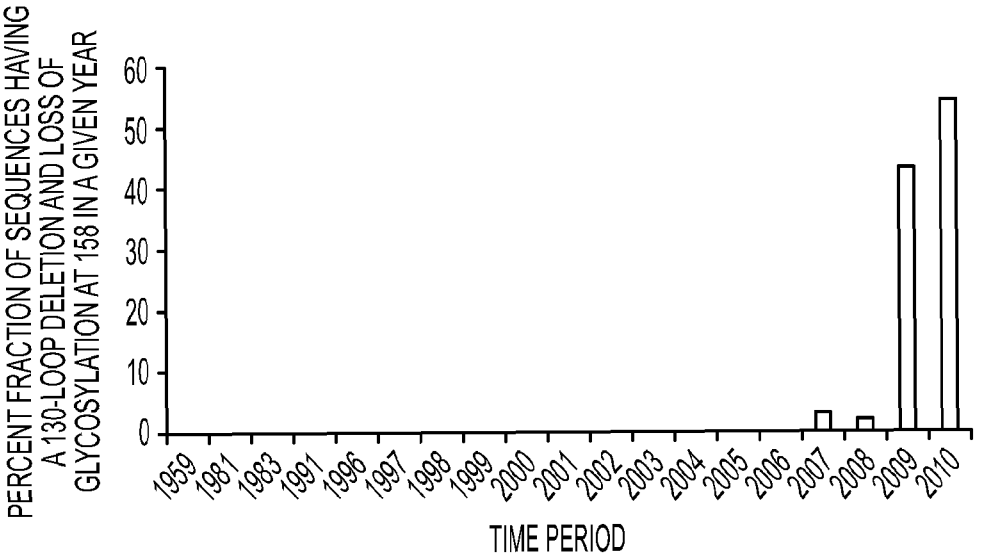


FIG. 27A

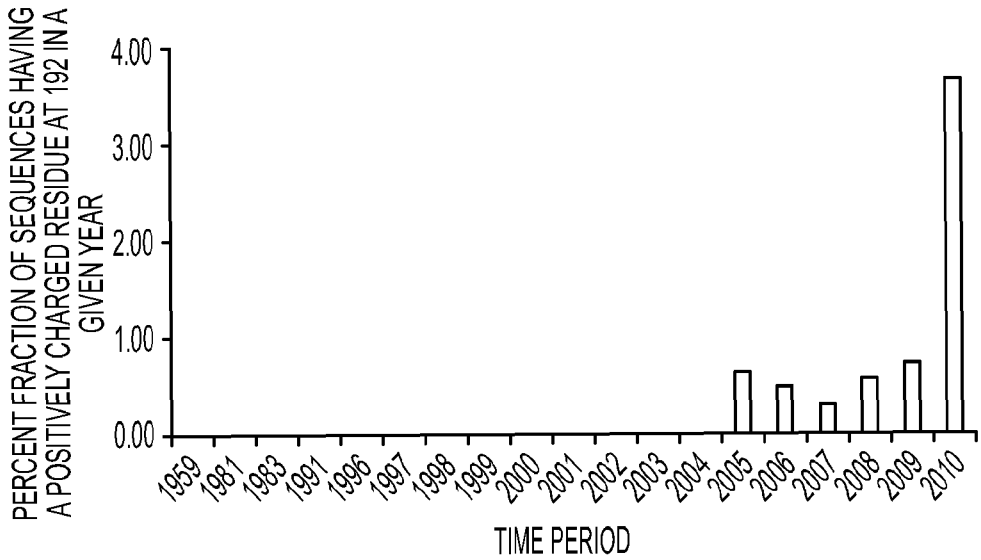


FIG. 27B

EXPANDED NOMENCLATURE OF GLYCANS USED IN THE GLYCAN ARRAY

GLYCAN	EXPANDED NOMENCLATURE
3´SLN	Neu5Acα2-3Galβ1-4GlcNAcβ1-
6´SLN	Neu5Acα2-6Galβ1-4GlcNAcβ1-
3´SLN-LN	Neu5Acα2-3Galβ1-4GlcNAcβ1-3Galβ1-4GlcNAcβ1-
6´SLN-LN	Neu5Acα2-6Galβ1-4GlcNAcβ1-3Galβ1-4GlcNAcβ1-
3´SLN-LN-LN	Neu5Acα2-3Galβ1-4GlcNAcβ1-3Galβ1-4GlcNAcβ1-3Galβ1-4GlcNAcβ1

KEY: Neu5Ac: N-ACETYL D-NEURAMINIC ACID; Gal: D-GALACTOSE; GlcNAc: N-ACETYL D-GLUCOSAMINE. α / β: ANOMERIC CONFIGURATION OF THE PYRANOSE SUGARS. ALL THE SUGARS ARE LINKED VIA A SPACER TO BIOTIN (-Sp-LC-LC-BIOTIN AS DESCRIBED IN http://www.functionalglycomics.org/static/consortium/resources/resourcecored5.shtml)

FIG. 28