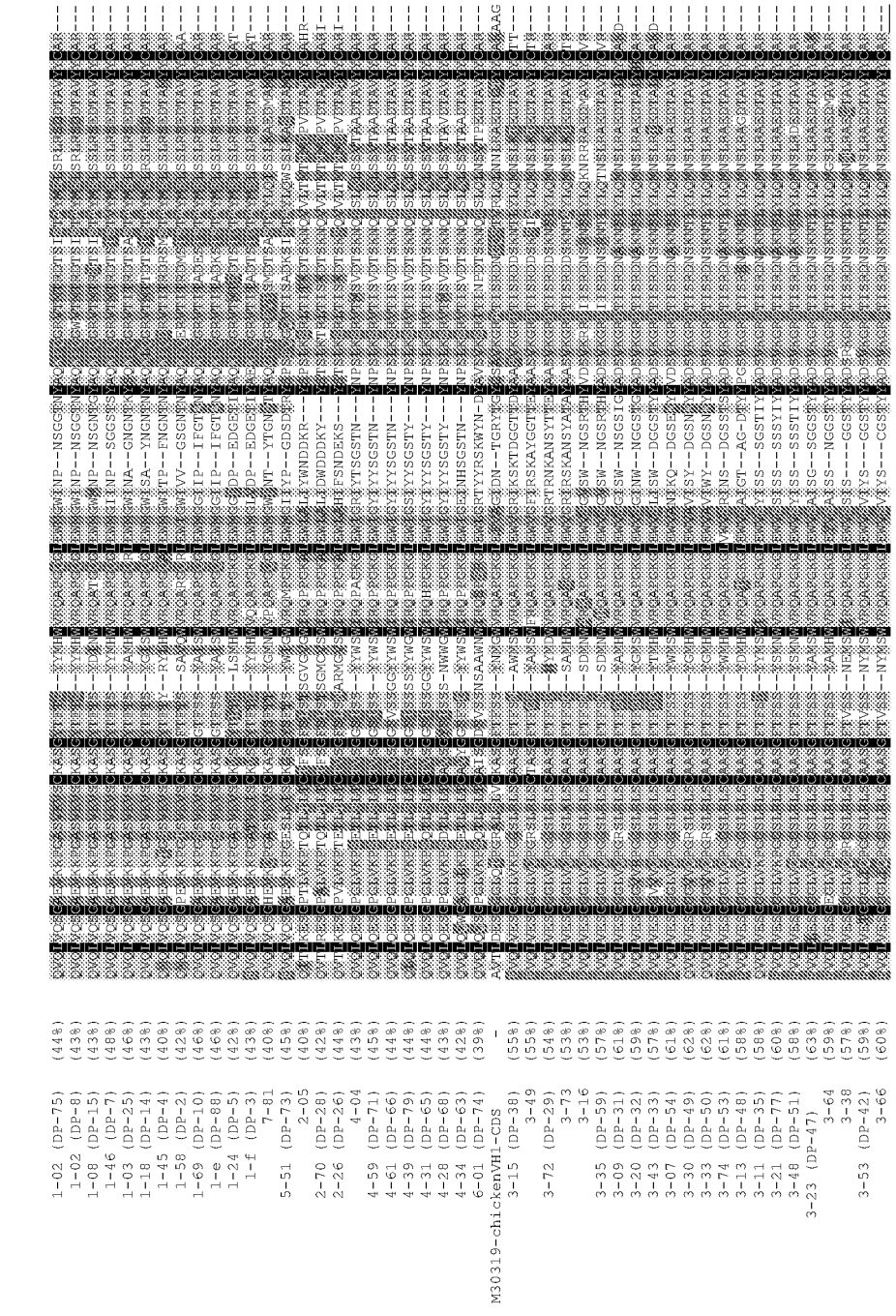


Fig. 1

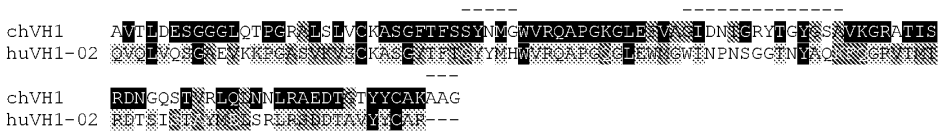

chVH1
huVH1-02
chVH1
huVH1-02

Fig. 2

chJH
huIGHJ1
huIGHJ2
huIGHJ3
huIGHJ4
huIGHJ5
huIGHJ6

Fig. 3

| | Hybrid Chicken | MF3178 | Identical | Equivalent |
|---|---|---|---|---|
| Total | 24 | 20 | 7 | 5 |
| Hydrogen Bond | 12 | 7 | 1 | 4 |
| Hydrophobic | 12 | 13 | 6 | 1 |

| # | Hybrid chicken (chicken VH-human VL) | MF3178 (human VH-human VL) | Category | Identical | Equivalent |
|---|---|---|---|---|---|
| 1 | A:ASN34:HD21 - B:GLY100H:O | A:ASN34:ND2 - B:TYR100D:O | Hydrogen Bond | | * |
| 2 | A:ASN34:HD22 - B:ALA100G:O | | Hydrogen Bond | | |
| 3 | A:TYR36:HH - B:GLY100H:O | A:TYR36:OH - B:PHE100G | Hydrogen Bond | | * |
| 4 | A:GLN38:HE21 - B:TYR91:OH | | Hydrogen Bond | | |
| 5 | A:GLN38:HE22 - B:GLN39:OE1 | A:GLN38:NE2 - B:GLN39:OE1 | Hydrogen Bond | * | |
| 6 | A:LEU46:HA - B:ILE100J:O | | Hydrogen Bond | | |
| 7 | A:GLN89:HE22 - B:GLY100H:O | A:GLN89:NE2 - B:TRP100E:O | Hydrogen Bond | | * |
| | | A:GLN89:NE2 - B:PHE100G | Hydrogen Bond | | |
| 8 | A:SER91:HG - B:ALA100G:O | | Hydrogen Bond | | |
| 9 | A:SER91:HB1 - B:ALA100G:O | B:GLN39:NE2 - A:GLN38:OE1 | Hydrogen Bond | | |
| 10 | B:ILE100J:HN - A:TYR36:OH | B:PHE100G:N - A:TYR36:OH | Hydrogen Bond | | * |
| 11 | B:CYS100I:HA - A:TYR36:OH | | Hydrogen Bond | | |
| 12 | B:TRP103:HD1 - A:PRO44:O | | Hydrogen Bond | | |
| | | A:TYR32 - B:TYR100D | Hydrophobic | | |
| | | A:PRO44 - B:LEU45 | Hydrophobic | | |
| 13 | A:TYR49 - B:CYS100I | | Hydrophobic | | |
| | | A:ALA50:CB - B:TYR100D | Hydrophobic | | |
| 14 | A:TYR87 - B:LEU45 | A:TYR87 - B:LEU45 | Hydrophobic | * | |
| 15 | A:PHE98 - B:VAL37 | | Hydrophobic | | |
| 16 | A:PHE98 - B:LEU45 | | Hydrophobic | | |
| | | B:LEU45:CD1 - A:PHE98 | Hydrophobic | | |
| 17 | B:TRP47 - A:PRO96 | B:TRP47 - A:PRO96 | Hydrophobic | * | |
| 18 | B:TRP47 - A:PRO96 | B:TRP47 - A:PRO96 | Hydrophobic | * | |
| 19 | B:TYR91 - A:ALA43 | B:TYR91 - A:ALA43 | Hydrophobic | * | |
| 20 | B:ALA96 - A:LEU46 | B:HIS96 - A:TYR49 | Hydrophobic | | * |
| 21 | B:CYS100I - A:LEU46 | B:TRP100E - A:PRO96 | Hydrophobic | | |
| 22 | B:TRP103 - A:ALA43 | B:TRP103 - A:ALA43 | Hydrophobic | | |
| 23 | B:TRP103 - A:PRO44 | B:TRP103 - A:PRO44 | Hydrophobic | * | |
| 24 | B:TRP103 - A:PRO44 | B:TRP103 - A:PRO44 | Hydrophobic | * | |

Fig. 4a

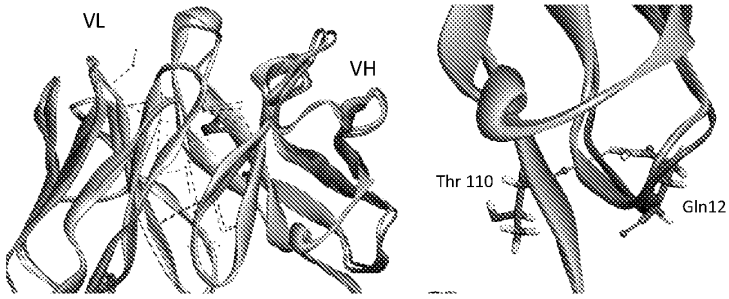



Fig. 4b

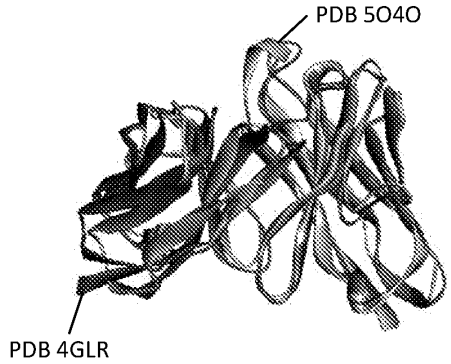



Fig. 4c

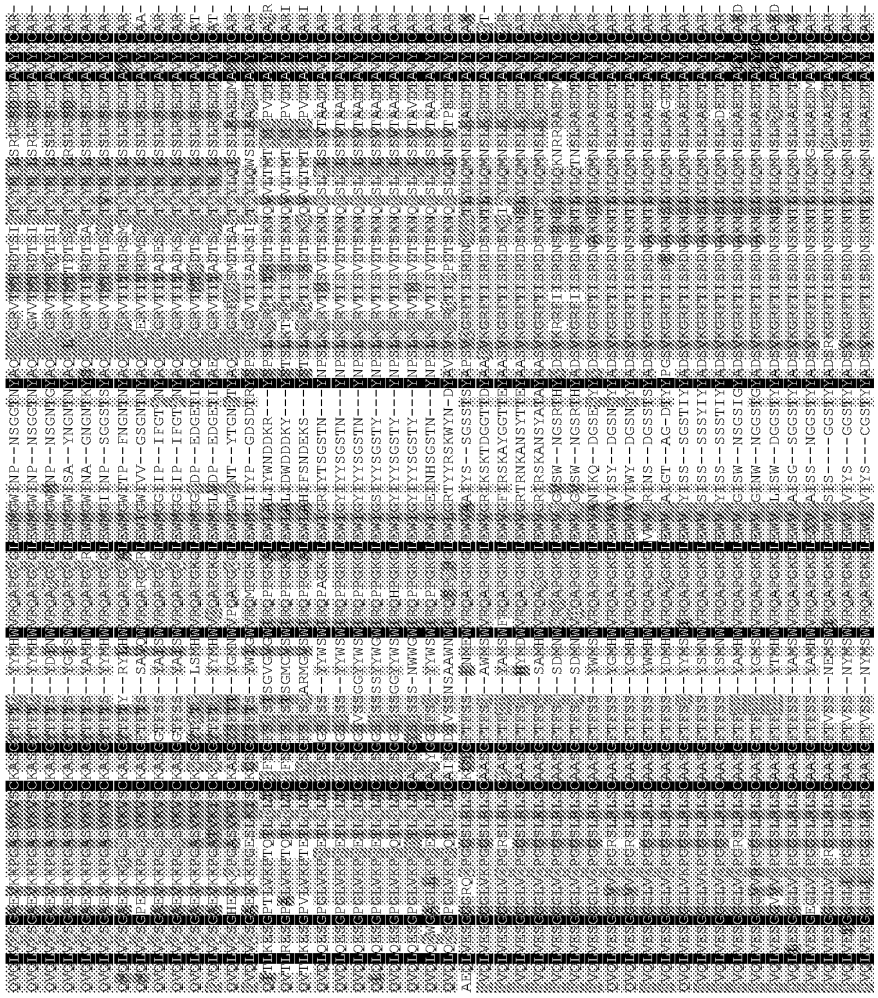


Fig. 5

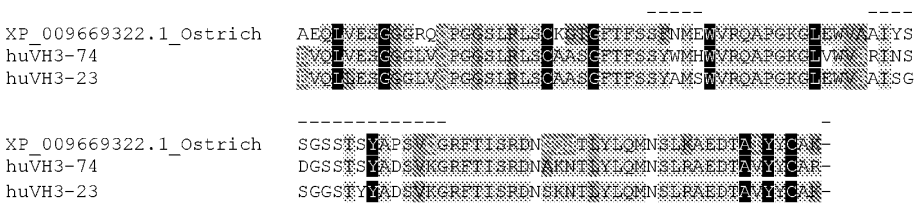



Fig. 6

| | Hybrid Ostrich | MF3178 | Identical | Equivalent |
|---|---|---|---|---|
| **Total** | 14 | 20 | 7 | 1 |
| **HBond** | 6 | 7 | 2 | 1 |
| **Hydrophobic** | 8 | 13 | 5 | 0 |

| # | Hybrid Ostrich | MF3178 | Category | Identical | Equivalent |
|---|---|---|---|---|---|
| | | A:ASN34:ND2 - B:TYR100D:O | Hydrogen Bond | | |
| **1** | A:TYR36:HH - B:ASN100F:OD1 | A:TYR36:OH - B:PHE100G | Hydrogen Bond | | * |
| **2** | A:GLN38:HE21 - B:GLN39:OE1 | A:GLN38:NE2 - B:GLN39:OE1 | Hydrogen Bond | * | |
| **3** | A:TYR87:HH - B:GLN39:OE1 | | Hydrogen Bond | | |
| | | A:GLN89:NE2 - B:TRP100E:O | Hydrogen Bond | | |
| | | A:GLN89:NE2 - B:PHE100G | Hydrogen Bond | | |
| **4** | A:SER91:HB1 - B:PRO100D:O | | Hydrogen Bond | | |
| **5** | A:SER91:HB2 - B:PRO100D:O | | Hydrogen Bond | | |
| **6** | B:GLN39:HE21 - A:GLN38:OE1 | B:GLN39:NE2 - A:GLN38:OE1 | Hydrogen Bond | * | |
| | | B:PHE100G:N - A:TYR36:OH | Hydrogen Bond | | |
| | | A:TYR32 - B:TYR100D | Hydrophobic | | |
| | | A:PRO44 - B:LEU45 | Hydrophobic | | |
| | | A:ALA50:CB - B:TYR100D | Hydrophobic | | |
| **7** | A:TYR87 - B:LEU45 | A:TYR87 - B:LEU45 | Hydrophobic | * | |
| **8** | A:PRO96 - B:PRO47 | | Hydrophobic | | |
| **9** | A:PHE98 - B:LEU45 | | Hydrophobic | | |
| | | B:LEU45:CD1 - A:PHE98 | Hydrophobic | | |
| | | B:TRP47 - A:PRO96 | Hydrophobic | | |
| | | B:TRP47 - A:PRO96 | Hydrophobic | | |
| **10** | B:TYR91 - A:ALA43 | B:TYR91 - A:ALA43 | Hydrophobic | * | |
| | | B:HIS96 - A:TYR49 | Hydrophobic | | |
| | | B:TRP100E - A:PRO96 | Hydrophobic | | |
| **11** | B:TRP103 - A:ALA43 | B:TRP103 - A:ALA43 | Hydrophobic | * | |
| **12** | B:TRP103 - A:PRO44 | B:TRP103 - A:PRO44 | Hydrophobic | * | |
| **13** | B:TRP103 - A:ALA43 | | Hydrophobic | | |
| **14** | B:TRP103 - A:PRO44 | B:TRP103 - A:PRO44 | Hydrophobic | * | |

Fig. 7a

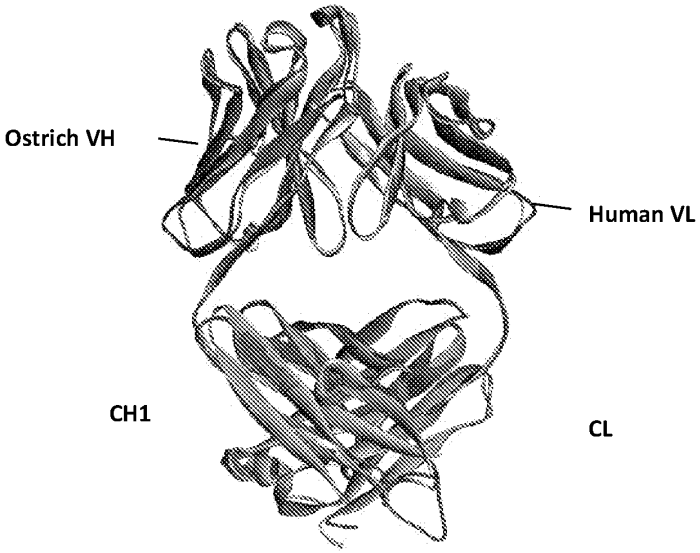



Fig. 7b

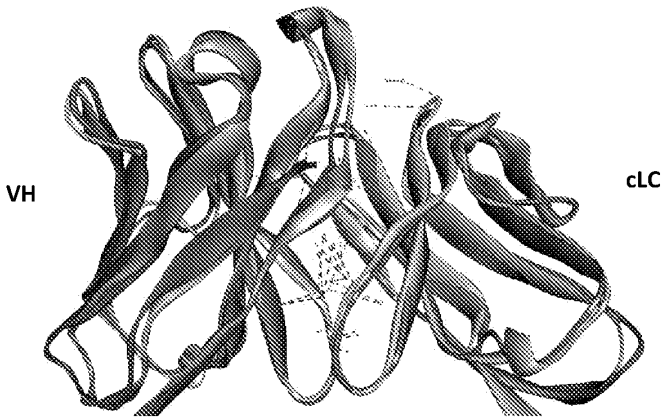



Fig. 7c

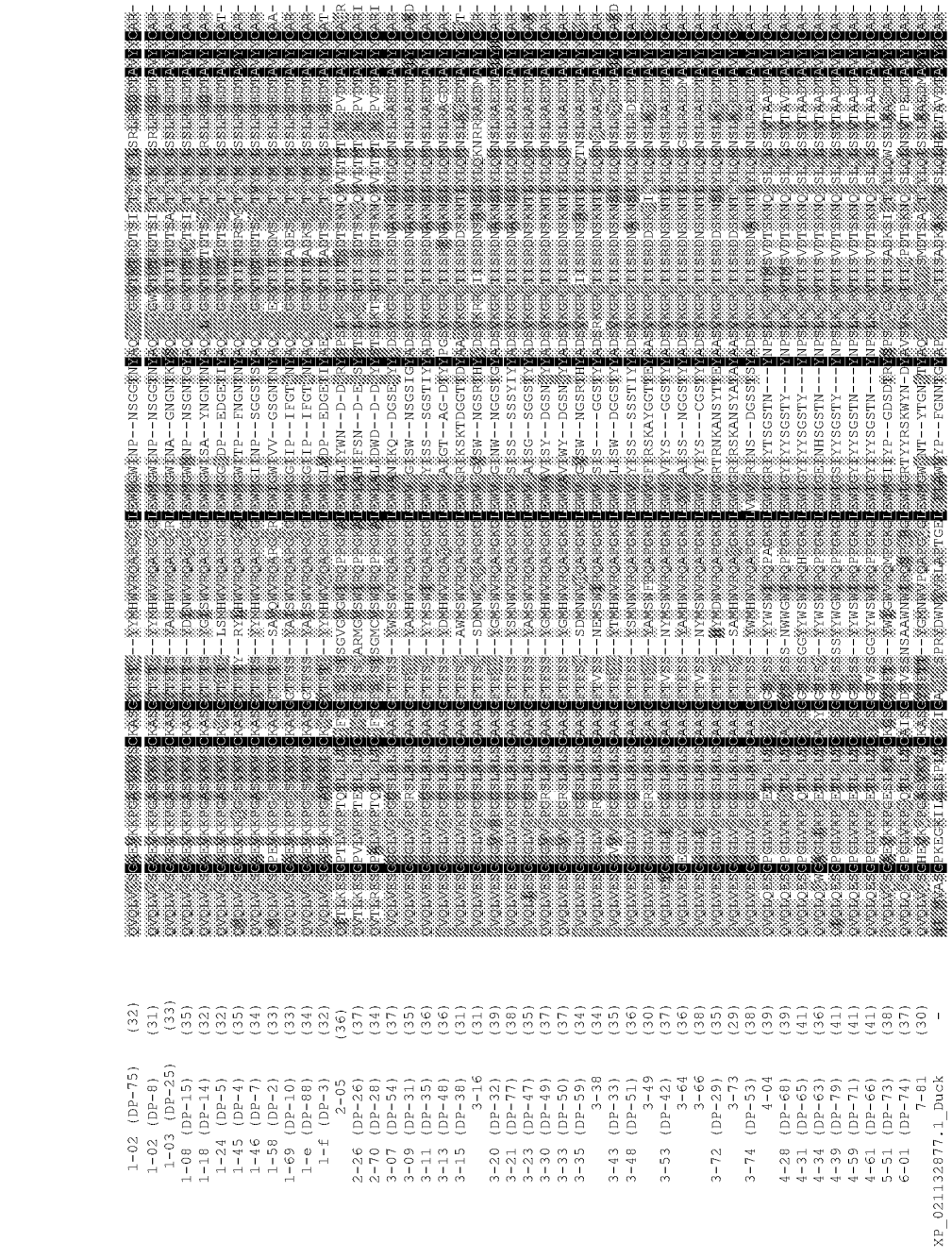


Fig. 8

Fig. 9

| | Hybrid Duck | MF3178 | Identical | Equivalent |
|---|---|---|---|---|
| Total | 28 | 20 | 12 | 1 |
| HBond | 12 | 7 | 3 | 0 |
| Hydrophobic | 15 | 13 | 9 | 0 |
| Electrostatic | 1 | 0 | 0 | 0 |

Fig. 10a

| # | Hybrid Duck | MF3178 | Category | Identical | Equivalent |
|---|---|---|---|---|---|
| | | A:ASN34:ND2 - B:TYR100D:O | Hydrogen Bond | | |
| 1 | A:TYR36:HH - B:ALA100H:O | A:TYR36:OH - B:PHE100G | Hydrogen Bond | | * |
| 2 | A:GLN38:HE21 - B:GLN39:OE1 | A:GLN38:NE2 - B:GLN39:OE1 | Hydrogen Bond | * | |
| 3 | A:TYR87:HH - B:GLN39:OE1 | | Hydrogen Bond | | |
| 4 | A:TYR87:HH - B:LYS43:O | | Hydrogen Bond | | |
| | | A:GLN89:NE2 - B:TRP100E:O | Hydrogen Bond | | |
| | | A:GLN89:NE2 - B:PHE100G | Hydrogen Bond | | |
| 5 | A:GLN89:HE21 - B:ALA100H:O | | | | |
| 6 | A:SER91:HB2 - B:TYR100D:O | | Hydrogen Bond | | |
| 7 | B:GLN39:HE21 - A:GLN38:OE1 | B:GLN39:NE2 - A:GLN38:OE1 | Hydrogen Bond | * | |
| 8 | B:GLY44:HA2 - A:TYR87:OH | | Hydrogen Bond | | |
| 9 | B:GLY100E:HA1 - A:SER91:O | | Hydrogen Bond | | |
| 10 | B:GLY100E:HA2 - A:SER91:O | | Hydrogen Bond | | |
| 11 | B:ASP100I:HA - A:TYR36:OH | B:PHE100G:N - A:TYR36:OH | Hydrogen Bond | * | |
| 12 | B:ILE100J:HN - A:TYR36:OH | | Hydrogen Bond | | |
| 13 | B:ASP100I:OD1 - A:TYR49 | | Electrostatic | | |
| 14 | A:TYR32 - B:TYR100D | A:TYR32 - B:TYR100D | Hydrophobic | * | |
| 15 | A:PRO44:C,O;LYS45:N - B:TRP103 | | Hydrophobic | | |
| 16 | A:PRO44:C,O;LYS45:N - B:TRP103 | | Hydrophobic | | |
| 17 | A:PRO44 - B:LEU45 | A:PRO44 - B:LEU45 | Hydrophobic | * | |
| | | A:ALA50:CB - B:TYR100D | Hydrophobic | | |
| 18 | A:TYR87 - B:LEU45 | A:TYR87 - B:LEU45 | Hydrophobic | * | |
| 19 | A:PHE98 - B:LEU45 | | Hydrophobic | | |
| | | B:LEU45:CD1 - A:PHE98 | Hydrophobic | | |
| 20 | B:TRP47 - A:PRO96 | B:TRP47 - A:PRO96 | Hydrophobic | * | |
| 21 | B:TRP47 - A:PRO95 | | Hydrophobic | | |
| 22 | B:TRP47 - A:PRO96 | B:TRP47 - A:PRO96 | Hydrophobic | * | |
| 23 | B:TYR91 - A:ALA43 | B:TYR91 - A:ALA43 | Hydrophobic | * | |
| | | B:HIS96 - A:TYR49 | Hydrophobic | | |
| 24 | B:ALA100H - A:PRO96 | | Hydrophobic | | |
| | | B:TRP100E - A:PRO96 | Hydrophobic | | |
| 25 | B:TYR100D - A:ALA50 | | Hydrophobic | | |
| 26 | B:TRP103 - A:ALA43 | B:TRP103 - A:ALA43 | Hydrophobic | * | |
| 27 | B:TRP103 - A:PRO44 | B:TRP103 - A:PRO44 | Hydrophobic | * | |
| 28 | B:TRP103 - A:PRO44 | B:TRP103 - A:PRO44 | Hydrophobic | * | |

Fig. 10a continued

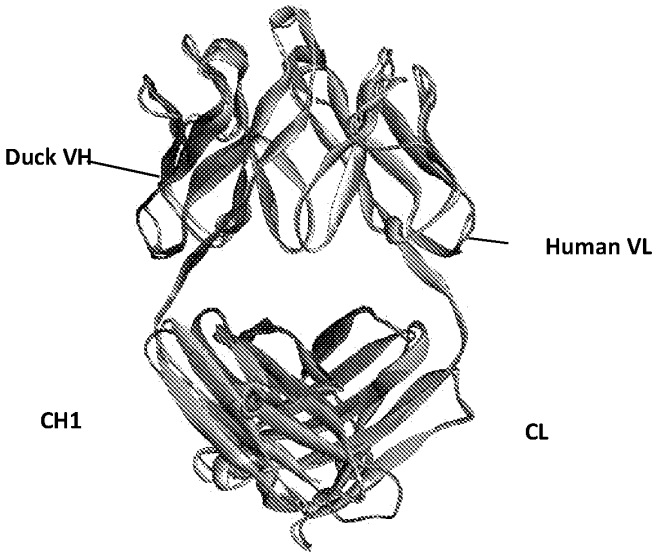



Fig. 10b

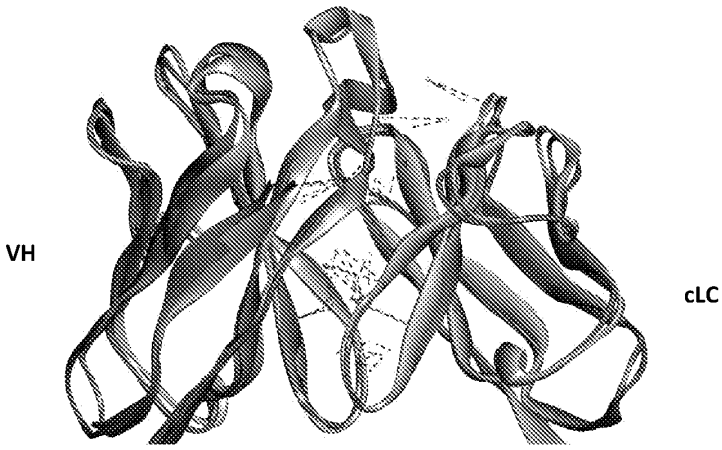



Fig. 10c

1 ACGCGCTAAC GAAGCCGGAG CCCTCCTTAT GCAAATTAGC CCCTCCAGAG GGCCATAAAA GCGCCGGCTC
VH1
M S P L V S S L L L L A A
71 TCCGACGGAG GAGCACCAGT CGGCTCCGCA ACCATGAGCC CACTCGTCTC CTCCCTCCTG CTCCTGGCCG
VH1
Intron_1
L P
141 CCCTGCCAGG TGAGGGCGCT GTGGGGCTCT ATGGGGCTCT ATGGGGTCTC AGCGGGGCTC TGCGGGCTCA
Intron_1
211 ATGGGGGCCA AAGGGGGGGT CTGCGGGCTC TATGGGGGGG TCAACGGGGG GTCTCACGGG GGGCCGGCTC
Intron_1
VH1
G L M A A V T
281 CGCGAGGCCG TGTGGCGGCG GCTCCGTCAG CGCTCTCTGT CCTTCCCCAC AGGGCTGATG GCGGCCGTCA
VH1
L D E S G G G L Q T P G R A L S L V C K A S G
351 CGTTGGACGA GTCCGGGGGC GGCCTCCAGA CGCCCGGTAG ACCGCTCAGC CTCGTCTGCA AGGCTTCCGG
VH1
F T F S S Y N M G W V R Q A P G K G L E F V A
421 GTTCACCTTC AGCAGTTACA ACATGGGTTG GGTGCGACAG GCGCCCGGCA AGGGGCTGGA GTTCGTCGCT
VH1
XhoI
G I D N T G R Y T G Y G S A V K G R A T I S R D
491 GGTATTGACA ACACTGGTAG ATACACAGGC TACGGGTCGG CGCTGAAGGG CCGTGCCACG ATCTCCAGGG
VH1
N G Q S T V R L Q L N N L R A E D T G T Y Y C
561 ACAACGGCCA GAGCACAGTG AGGCTGCAGC TGAACAACCT GAGGGCTGAG GACACCGGCA CCTACTACTG
VH1
A K A A G
631 CGCCAAAGCT GCTGGTCACG GTGACACCGA TCCCCAGCAC GGGTGGCACA AAACCCACCG TTGCAACCCA
701 AGGCGGTGAA

Fig. 11

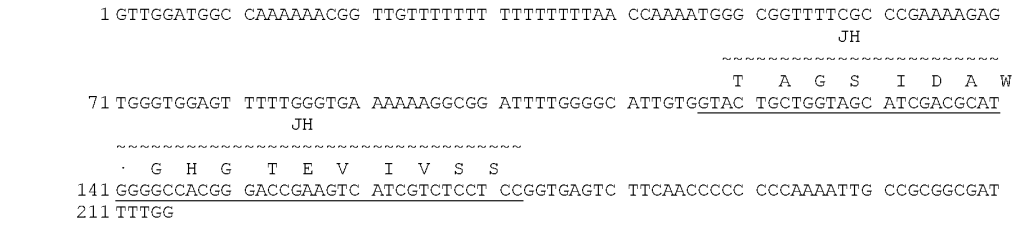



Fig. 12

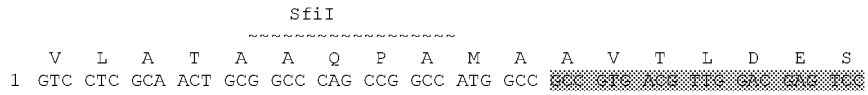



Fig. 13

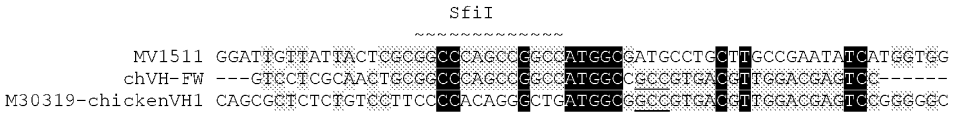
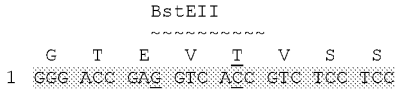



Fig. 14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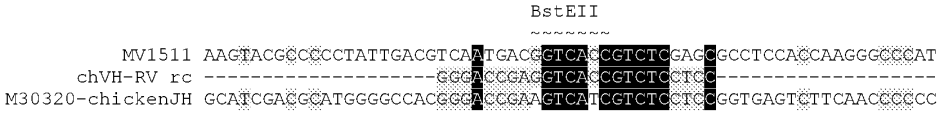
1 GGG ACC GAG GTC ACC GTC TCC TCC

Fig. 15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MV1511 AAGTACGCCCCCTATTGACGTCAATGACGGTCACCGTCTCGAGCGCCTCCACCAAGGGCCCAT
chVH-RV rc ----------GGGACCGAGGTCACCGTCTCCTCG----------
M30320-chickenJH GCATCGACGCATGGGGCCACGGGACCGAAGTCATCGTCTCCTCGGTGAGTCTTCAACCCCCC

Fig. 16

**Figure 17A (SEQ ID NO: 5)**

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGS
GSGTDFTLTISSLQPEDFATYYCQQSYSTPPTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTA
SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACE
VTHQGLSSPVTKSFNRGEC

**Figure 17B (SEQ ID NOs: 6 and 7)**

gacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacagagtcacc
D I Q M T Q S P S S L S A S V G D R V T
atcacttgccgggcaagtcagagcattagcagctacttaaattggtatcagcagaaacca
I T C R A S Q S I S S Y L N W Y Q Q K P
gggaaagcccctaagctcctgatctatgctgcatccagtttgcaaagtggggtcccatca
G K A P K L L I Y A A S S L Q S G V P S
aggttcagtggcagtggatctgggacagatttcactctcaccatcagcagtctgcaacct
R F S G S G S G T D F T L T I S S L Q P
gaagattttgcaacttactactgtcaacagagttacagtacccctccaacgttcggccaa
E D F A T Y Y C Q Q S Y S T P P T F G Q
gggaccaaggtggagatcaaa
G T K V E I K

**Figure 17C (SEQ ID NOs: 8 and 9)**

```
cgaactgtggctgcaccatctgtcttcatcttcccgccatctgatgagcagttgaaatct
 R  T  V  A  A  P  S  V  F  I  F  P  P  S  D  E  Q  L  K  S
ggaactgcctctgttgtgtgcctgctgaataacttctatcccagagaggccaaagtacag
 G  T  A  S  V  V  C  L  L  N  N  F  Y  P  R  E  A  K  V  Q
tggaaggtggataacgccctccaatcgggtaactcccaggagagtgtcacagagcaggac
 W  K  V  D  N  A  L  Q  S  G  N  S  Q  E  S  V  T  E  Q  D
agcaaggacagcacctacagcctcagcagcaccctgacgctgagcaaagcagactacgag
 S  K  D  S  T  Y  S  L  S  S  T  L  T  L  S  K  A  D  Y  E
aaacacaaagtctacgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaag
 K  H  K  V  Y  A  C  E  V  T  H  Q  G  L  S  S  P  V  T  K
agcttcaacaggggagagtgttag
 S  F  N  R  G  E  C  -
```

**Figure 17D (SEQ ID NO: 10)**

```
DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGS
GSGTDFTLTISSLQPEDFATYYCQQSYSTPPITFGQGTRLEIK
```

**Figure 17E (SEQ ID NO: 11)**

```
DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGS
GSGTDFTLTISSLQPEDFATYYCQQSYSTP
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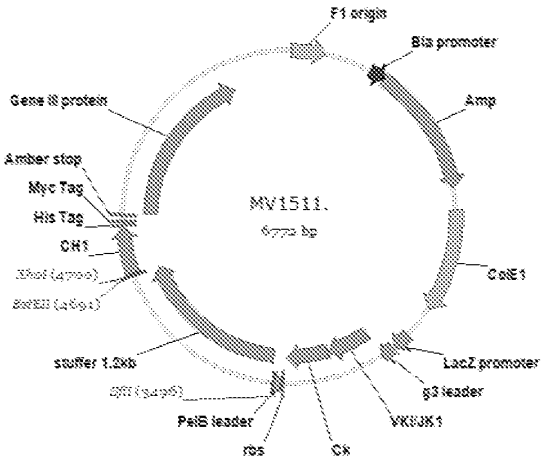

F1 origin
Bla promoter
Amp
Gene III protein
Amber stop
Myc Tag
His Tag
CH1
ColE1
stuffer 1.2kb
LacZ promoter
g3 leader
PelB leader
VK/JK1
rbs
Ck

Fig 18

**Figure 19A (SEQ ID NO: 87)** IgVκ3-15/IGJκ1

EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS
GSGTEFTLTISSLQSEDFAVYYCQQYNNWPWTFGQGTKVEIK

**Figure 19B (SEQ ID NO: 88)** IgVκ3-20/IGJκ1

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSG
SGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIK

**Figure 19C (SEQ ID NO: 89)** IgVλ3-21/IGJλ3

SYVLTQPPSVSVAPGETARITCGGDNIGRKSVYWYQQKSGQAPVLVIYYDSDRPSGIPERFSGSN
SGNTATLTISRVEAGDEADYYCQVWDGSSDHWVFGGGTKLTVL

**Figure 19D (SEQ ID NO: 90)** IgVκ3-15

EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS
GSGTEFTLTISSLQSEDFAVYYCQQYNNWP

**Figure 19E (SEQ ID NO: 91)** IgVκ3-20

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSG
SGSGTDFTLTISRLEPEDFAVYYCQQYGSSP

**Figure 19F (SEQ ID NO: 92)** VH 4GLR + Human CH1

AVTLDESGGGLQTPGGGLSLVCKASGFTLSSYQMMWVRQAPGKGLEWVAGITSRGGVTGYGSAVK
GRATISRDNGQSTVRLQLNNLRAEDTGTYYCAKPALDSDQCGFPEAGCIDAWGHGTEVTVSSAST
KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV
VTVPSSSLGTQTYICNVNHKPSNTKVDKRV

**Figure 19G (SEQ ID NO: 93)** VK1-39/IGJK5/Ckappa

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGS
GSGTDFTLTISSLQPEDFATYYCQQSYSTPPITFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGT
ASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC
EVTHQGLSSPVTKSFNRGEC

**Figure 19H (SEQ ID NO: 94)** IgVκ3-15/IGJκ1/Ckappa

EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGS
GSGTEFTLTISSLQSEDFAVYYCQQYNNWPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTA
SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACE
VTHQGLSSPVTKSFNRGEC

**Figure 19I (SEQ ID NO: 95)** IgVκ3-20/IGJκ1/Ckappa

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSG
SGSGTDFTLTISRLEPEDFAVYYCQQYGSSPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGT
ASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC
EVTHQGLSSPVTKSFNRGEC

**Figure 19J (SEQ ID NO: 96)** IgVλ3-21/IGJλ3/Clambda

SYVLTQPPSVSVAPGETARITCGGDNIGRKSVYWYQQKSGQAPVLVIYYDSDRPSGIPERFSGSN
SGNTATLTISRVEAGDEADYYCQVWDGSSDHWVFGGGTKLTVLGQPKAAPSVTLFPPSSEELQAN
KATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSLTPEQWKSHRSYSC
QVTHEGSTVEKTVAPTECS

**Figure 19K (SEQ ID NO: 97)** IgVλ3-21

SYVLTQPPSVSVAPGETARITCGGDNIGRKSVYWYQQKSGQAPVLVIYYDSDRPSGIPERFSGSN
SGNTATLTISRVEAGDEADYYCQVWDGSSDH

## Figure 20

| # | Human VH – Human VL | Chicken VH – Chicken VL | Vk3-15/JK1/Ckappa | VK3-20/JK1/Ckappa | VK1-39/JK5/Ckappa | VL3-21/JL3/Clambda |
|---|---|---|---|---|---|---|
| 1 | B:LYS319:HZ3 - A:GLU212:OE2 | H:LYS226:HZ2 - I:GLU213:OE1 | B:LYS319:HZ1 - A:GLU212:OE1 | B:LYS319:HZ2 - A:GLU212:OE1 | B:LYS212:HZ2 - A:GLU325:OE2 | A:LYS218:HZ3 - B:ASP227:OD1 |
| 2 | *A:ASN34:HD21 - B:TYR100D:O* | H:LYS319:HZ1 - I:GLU212:OE2 | *A:GLN38:HE21 - B:GLN39:OE1* | B:LYS212:NZ - A:GLU325:OE2 | B:LYS319:NZ - A:GLU212:OE1 | B:LYS226:HZ1 - A:GLU213:OE2 |
| 3 | *A:ASN34:HD22 - B:TRP100E:O* | *H:GLN39:HE21 - I:GLN38:OE1* | *A:TYR49:HH - B:ASP98:OD2* | *A:GLN38:HE21 - B:GLN39:OE1* | *A:ASN34:HD21 - B:ALA100G:O* | B:LYS319:HZ3 - A:GLU212:OE2 |
| 4 | *A:TYR36:HH - B:TRP100E:O* | *H:LYS64:HZ1 - I:ALA95:O* | *A:THR56:HN - B:ASP98:OD2* | *A:TYR87:HH - B:LYS43:O* | *A:ASN34:HD21 - B:CYS100I:SG* | *A:TYR36:HH - B:GLY100H:O* |
| 5 | *A:GLN38:HE21 - B:GLN39:OE1* | *H:TYR91:HH - I:GLN38:OE1* | *A:TYR87:HH - B:GLN39:OE1* | *A:TRP96:HE1 - B:ALA100G:O* | *A:GLN38:HE21 - B:GLN39:OE1* | *A:GLN38:HE21 - B:GLN39:OE1* |
| 6 | *A:GLN89:HE21 - B:TRP100E:O* | *H:TYR91:HH - I:SER42:O* | *A:TYR87:HH - B:LYS43:O* | A:GLN269:HE21 - B:LEU275:O | *A:TYR49:HH - B:ASP98:OD2* | *A:TRP91:HE1 - B:GLU100F:O* |
| 7 | A:SER271:HG - B:PRO272:O | H:LYS226:HZ2 - I:THR220:OG1 | *A:GLN89:HE21 - B:GLY100H:O* | *B:GLN39:HE21 - A:GLN38:OE1* | *A:SER56:HG - B:ASP98:OD1* | A:THR205:HG1 - B:THR214:OG1 |
| 8 | *B:GLN61:HE21 - A:ASP1:OD1* | H:SER277:HN - I:GLU269:OE2 | *A:TYR91:HH - B:PHE100D:O* | *B:ILE100J:HN - A:TYR36:OH* | *A:TYR87:HH - B:LYS43:O* | A:SER210:HG - B:PRO206:O |
| 9 | *B:GLN61:HE22 - A:ASP1:OD2* | H:LYS324:HZ1 - I:PRO209:O | A:SER271:HG - B:PRO272:O | B:SER211:HG - A:GLU325:OE1 | *A:GLN89:HE21 - B:GLY100H:O* | A:LYS218:HZ1 - B:GLN276:OE1 |
| 10 | *B:TYR91:HH - A:LYS42:O* | H:LYS324:HZ2 - I:PRO208:O | *B:GLN39:HE21 - A:GLN38:OE1* | B:SER211:HG - A:GLU325:O | *A:SER91:HG - B:ALA100G:O* | *B:GLN39:HE21 - A:GLN38:OE1* |
| 11 | *B:PHE100G:HN - A:TYR36:OH* | *I:GLN38:HE21 - H:GLN39:OE1* | *B:ILE100J:HN - A:TYR36:OH* | B:SER215:HG - A:SER320:O | A:ILE206:HN - B:SER215:O | *B:TYR91:HH - A:GLN42:O* |
| 12 | B:LYS226:HZ1 - A:THR290:OG1 | *I:THR46:HG1 - H:ILE100J:O* | B:LYS212:HN - A:CYS326:OCT1 | B:LYS226:HZ1 - A:THR288:OG1 | A:SER210:HG - B:PRO206:O | *B:ILE100J:HN - A:TYR36:OH* |
| 13 | B:LYS226:HZ2 - A:GLN213:OE1 | *I:THR46:HG1 - H:ASP101:O* | *B:TRP103:HD1 - A:PRO44:O* | B:LYS226:HZ3 - A:SER220:OG | A:ASP211:HN - B:SER210:O | B:SER211:HG - A:SER327:OCT1 |
| 14 | B:HIS269:HD1 - A:ASN226:OD1 | *I:TRP50:HN - H:GLY100H:O* | B:PRO209:HA - A:CYS326:OCT2 | A:SER210:HB2 - B:PRO206:O | A:ASN227:HD21 - B:HIS269:NE2 | B:LYS226:HZ3 - A:THR220:OG1 |
| 15 | *A:SER91:HB2 - B:TYR100D:O* | I:SER211:HG - H:SER325:O | B:PRO272:HD1 - A:SER271:OG | *B:CYS100I:HA - A:TYR36:OH* | A:LYS319:HZ1 - B:SER215:O | *B:GLY44:HA2 - A:TYR87:OH* |
| 16 | *B:GLY44:HA2 - A:TYR87:OH* | I:LYS319:HZ3 - H:SER213:OG | A:SER284:HG - B:HIS269 | *B:TRP103:HD1 - A:PRO44:O* | *B:GLN39:HE21 - A:GLN38:OE1* | *B:CYS100I:HA - A:TYR36:OH* |
| 17 | *B:TYR100D:HA - A:SER91:OG* | *H:GLY100H:HA1 - I:ASP32:O* | *A:TRP94 - B:TRP47* | B:SER210:HB2 - A:ILE206:O | *B:ILE100J:HN - A:TYR36:OH* | *B:TRP103:HD1 - A:PRO44:O* |
| 18 | *B:GLY100F:HA2 - A:TYR36:OH* | *H:GLY100H:HA2 - I:TYR36:OH* | *A:ALA34 - B:CYS100I* | B:SER211:HA - A:GLU325:O | B:SER215:HG - A:SER320:O | B:LYS226:HE2 - A:GLU213:OE2 |
| 19 | B:HIS269:HE1 - A:ASN227:OD1 | H:PRO206:HD2 - I:GLU212:OE1 | A:VAL222 - B:LEU207 | B:LYS212:HE1 - A:GLU325:OE2 | *A:SER56:HB2 - B:ASP98:OD2* | B:HIS269:HE1 - A:ASP227:OD1 |
| 20 | *B:LEU45:HB1 - A:PHE98* | H:GLN276:HA - I:GLU269:OE2 | B:VAL288 - A:LEU224 | B:LYS212:HE2 - A:GLU325:OE1 | A:PHE205:HA - B:SER215:O | B:SER286:HB1 - A:TYR288:OH |
| 21 | *A:TYR32 - B:TYR100D* | H:LYS319:HE1 - I:GLU212:OE1 | *A:TYR87 - B:LEU45* | B:LYS226:HE1 - A:THR288:OG1 | A:SER210:HA - B:SER210:O | B:SER286:HB2 - A:TYR288:OH |
| 22 | A:VAL222 - B:LEU207 | H:LYS319:HE2 - I:GLU212:OE1 | *A:PHE98 - B:LEU45* | B:LYS319:HE2 - A:GLU212:OE2 | A:CYS326:HA - B:SER211:O | B:LYS319:HE1 - |

| | | | | | | |
|---|---|---|---|---|---|---|
| 23 | B:VAL288 - A:LEU224 | *I:GLY41:HA2 - H:THR89:OG1* | A:PHE205 - B:ALA220 | *A:TRP96:HB1 - B:TRP47* | B:SER211:HB2 - A:PRO209:O | A:GLU212:OE1<br>B:LYS319:HE2 - A:GLU212:OE2 |
| 24 | A:PHE205 - B:ALA220 | *I:GLY41:HA2 - H:TYR91:OH* | A:PHE207 - B:LEU207 | *B:MET35:SD - A:TRP96* | B:GLY216:HA1 - A:ILE206:O | A:LYS275:NZ - B:HIS269 |
| 25 | A:PHE207 - B:LEU207 | *I:TYR49:HA - H:GLY100H:O* | A:PHE207 - B:PRO209 | *B:MET35:SD - A:TRP96* | B:GLY216:HA2 - A:ILE206:O | *A:TRP96:HN - B:TRP47* |
| 26 | *B:TRP47 - A:PRO96* | *I:GLY96:HA1 - H:PRO100E:O* | A:PHE207 - B:ALA220 | *A:TRP96 - B:TRP47* | B:HIS269:HE1 - A:ASN227:OD1 | *A:HIS95B - B:TRP47* |
| 27 | *B:TRP47 - A:PRO95* | *I:GLY96:HA2 - H:PRO100E:O* | *B:TYR91 - A:ALA43* | *A:TRP96 - B:TRP47* | B:LYS319:HE1 - A:GLU212:OE2 | *A:PRO44 - B:LEU45* |
| 28 | *B:TRP47 - A:PRO96* | *H:TRP103 - I:TYR36* | *B:TRP103 - A:ALA43* | *A:TRP96 - B:TRP47* | A:SER284:HG - B:HIS269 | A:VAL222 - B:LEU207 |
| 29 | *B:TYR91 - A:ALA43* | H:LEU207:C,O;ALA208:N - I:PHE207 | *B:TRP103 - A:PRO44* | *B:TRP47 - A:TRP96* | *A:TYR36 - B:TRP103* | A:VAL268 - B:VAL274 |
| 30 | *B:TYR100D - A:ALA50* | *I:PRO44 - H:LEU45* | *B:TRP103 - A:ALA43* | *A:PRO44 - B:LEU45* | *A:PRO44 - B:LEU45* | *B:CYS100I - A:LEU46* |
| 31 | *B:TRP100E - A:PRO96* | I:VAL222 - H:LEU207 | *B:TRP103 - A:PRO44* | A:VAL222 - B:LEU207 | A:PRO208 - B:LYS212 | B:ALA220 - A:LEU224 |
| 32 | *B:TRP103 - A:ALA43* | I:VAL222 - H:LEU224 | | A:VAL222 - B:LEU224 | A:VAL222 - B:LEU207 | *A:TYR34 - B:ALA100G* |
| 33 | *B:TRP103 - A:PRO44* | *H:TYR91 - I:PRO44* | | *B:CYS100I - A:LEU46* | *B:ALA62 - A:PRO95A* | *A:TYR34 - B:CYS100I* |
| 34 | *B:TRP103 - A:ALA43* | *H:TRP103 - I:PRO44* | | B:VAL288 - A:LEU224 | *B:CYS100I - A:LEU46* | *A:TYR87 - B:LEU45* |
| 35 | *B:TRP103 - A:PRO44* | *H:TRP103 - I:PRO44* | | *A:TYR32 - B:ALA100G* | B:VAL288 - A:LEU224 | *A:TRP91 - B:ALA100G* |
| 36 | | H:PHE205 - I:ALA216 | | *A:TYR36 - B:ILE100J* | *A:TYR32 - B:ALA100G* | *A:PHE98 - B:LEU45* |
| 37 | | H:HIS269 - I:ALA284 | | *A:TYR49 - B:CYS100I* | *A:TYR36 - B:ILE100J* | A:PHE207 - B:LEU207 |
| 38 | | H:PHE271 - I:LEU224 | | *A:TYR87 - B:LEU45* | *A:TYR87 - B:LEU45* | *B:TYR91 - A:ALA43* |
| 39 | | *I:TYR36 - H:ILE100J* | | *A:PHE98 - B:VAL37* | *A:PHE98 - B:LEU45* | *B:TRP103 - A:ALA43* |
| 40 | | *I:TYR49 - H:ALA96* | | *A:PHE98 - B:LEU45* | A:PHE205 - B:ALA220 | *B:TRP103 - A:PRO44* |
| 41 | | *I:TRP50 - H:CYS100B* | | A:PHE205 - B:ALA220 | *B:TRP47 - A:PRO95A* | *B:TRP103 - A:ALA43* |
| 42 | | *I:TRP50 - H:CYS100I* | | A:PHE207 - B:LEU207 | *B:TYR91 - A:ALA43* | *B:TRP103 - A:PRO44* |
| 43 | | *I:TYR87 - H:LEU45* | | A:PHE207 - B:ALA220 | B:TRP103 - A:ALA43 | B:HIS269 - A:LYS275 |
| 44 | | *I:TYR91 - H:PRO100E* | | *B:TRP103 - A:ALA43* | B:TRP103 - A:PRO44 | B:PHE271 - A:ALA284 |
| 45 | | *I:PHE98 - H:VAL37* | | *B:TRP103 - A:PRO44* | B:TRP103 - A:PRO44 | |
| 46 | | *I:PHE98 - H:LEU45* | | *B:TRP103 - A:PRO44* | | |
| 47 | | *I:PHE98 - H:ALA100G* | | B:PHE271 - A:LEU224 | | |
| 48 | | I:PHE207 - H:LEU207 | | | | |
| 49 | | I:PHE207 - H:ALA220 | | | | |
| 50 | | I:TYR288 - H:VAL274 | | | | |

**Figure 21**

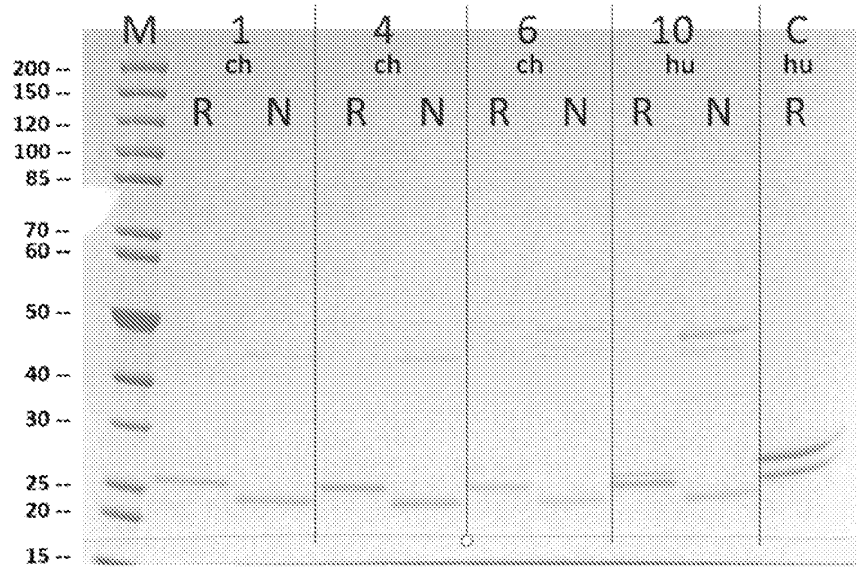
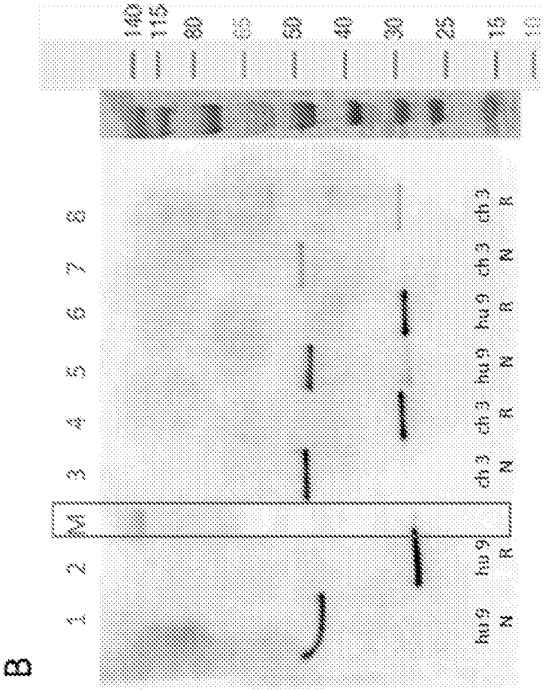



**Figure 22 (SEQ ID NO: 98)** Human control MF1025 VH sequence

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVK
GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARADWWATFDYWGQGTLVTVSS

Figure 23


B
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115
80
60
50
40
30
25
15
10
M
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hu 9 N
hu 9 R
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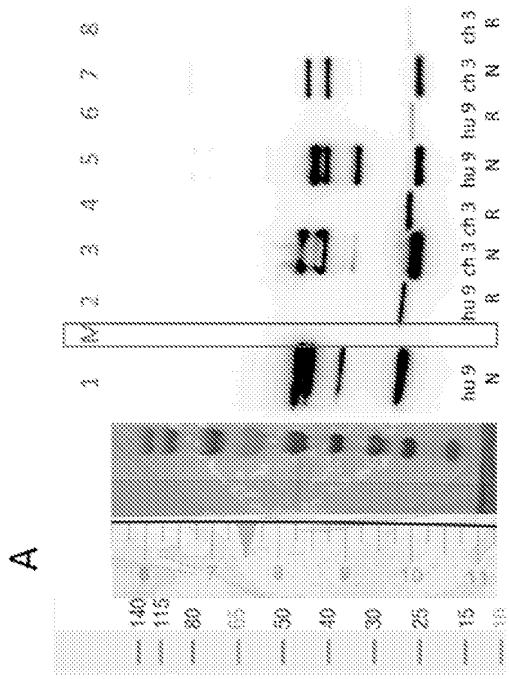
ch 3 N
ch 3 R


A
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115
80
60
50
40
30
25
15
10
M
1 2 3 4 5 6 7 8
hu 9 N
hu 9 R
ch 3 N
ch 3 R
hu 9 N
hu 9 R
ch 3 N
ch 3 R

**Figure 24 (SEQ ID NO: 99)** WT full length sequence mouse CXCR4 GenBank: AAH98322.1

MEPISVSIYT SDNYSEEVGS GDYDSNKEPC FRDENVHFNR IFLPTIYFII
FLTGIVGNGL VILVMGYQKK LRSMTDKYRL HLSVADLLFV ITLPFWAVDA
MADWYFGKFL CKAVHIIYTV NLYSSVLILA FISLDRYLAI VHATNSQRPR
KLLAEKAVYV GVWIPALLLT IPDFIFADVS QGDISQGDDR YICDRLYPDS
LWMVVFQFQH IMVGLILPGI VILSCYCIII SKLSHSKGHQ KRKALKTTVI LILAFFACWL
PYYVGISIDS FILLGVIKQG CDFESIVHKW ISITEALAFF HCCLNPILYA FLGAKFKSSA
QHALNSMSRG SSLKILSKGK RGGHSSVSTE SESSSFHSS

**Figure 25**

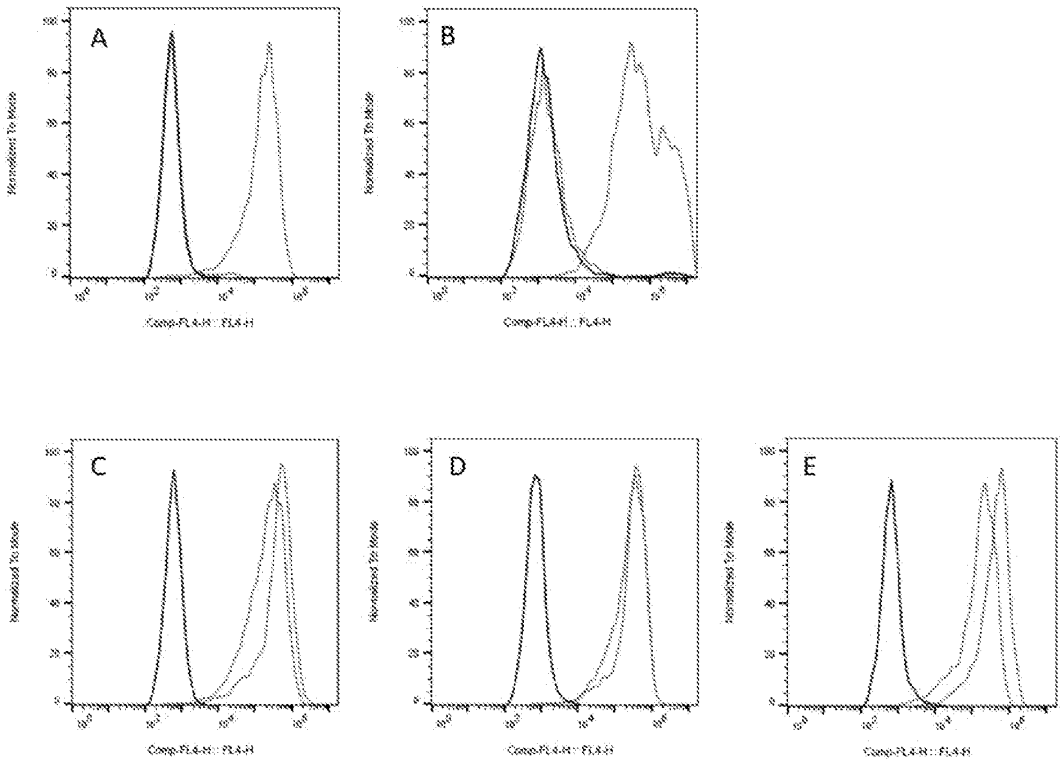

**Figure 26A (SEQ ID NO: 100)** cLC CXCR4 - 1

AVTLDESGGGLQTPGGALSLVCKASGFTFSSYRGMHWVRQAPGKGLEWVAGIYSSG
SSTAYGAAVKGRATISRDDGQSTVRLQLNNLRAEDTGTYYCAKDAGSCWYGRRSGFN
CDPYGGNIDAWGHGTEVIVSS

**Figure 26B (SEQ ID NO: 101)** cLC CXCR4 - 2

AVTLDESGGGLQTPGGALSLVCKASGFSFSSYDMSWVRQAPGKGLEWVAGIYSIGRD
AGYGAAVKGRATISRDNGQSTVRLQLNNLRAEDTGTYYCAKESGSACRYAARHGYICA
GYLGSIDAWGHGTEVIVSS

**Figure 26C (SEQ ID NO: 102)** cLC CXCR4 – 3

AVTLDESGGGLQTPGGALSLVCKASGFSIGSYGMGWVRQAPGKGLEFVAGISTIGGVT
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PGWNYGGRIDAWGHGTEVIVSS

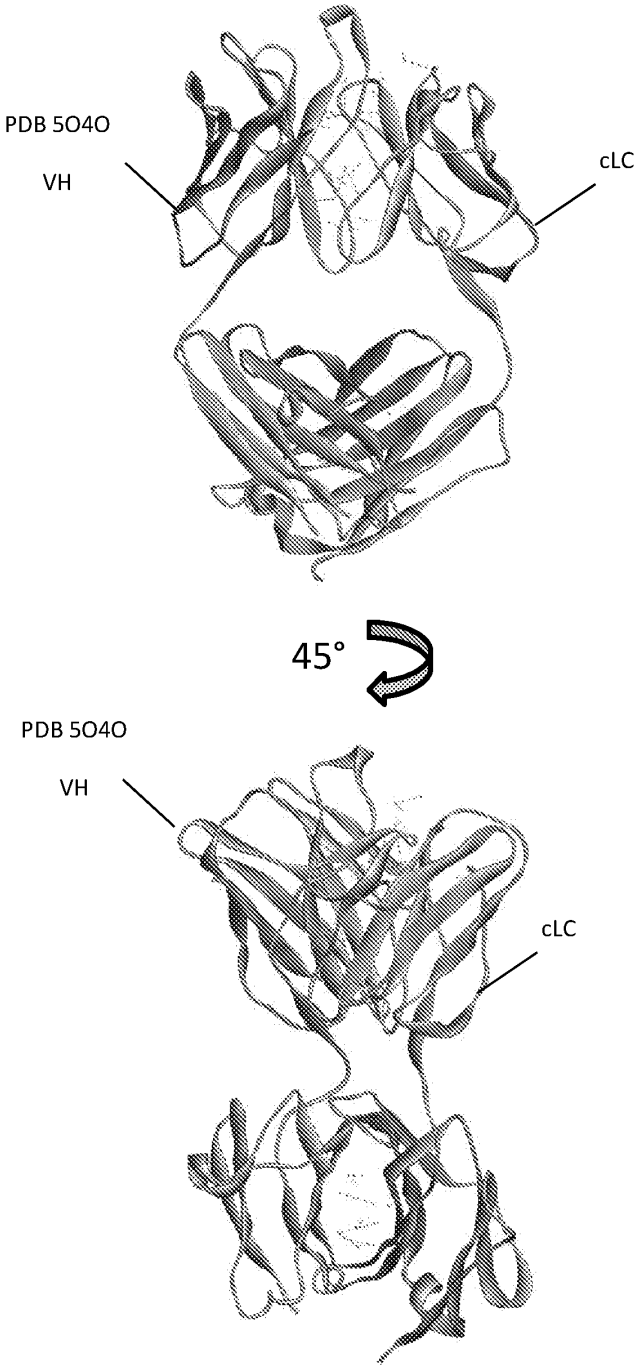



Fig. 27A

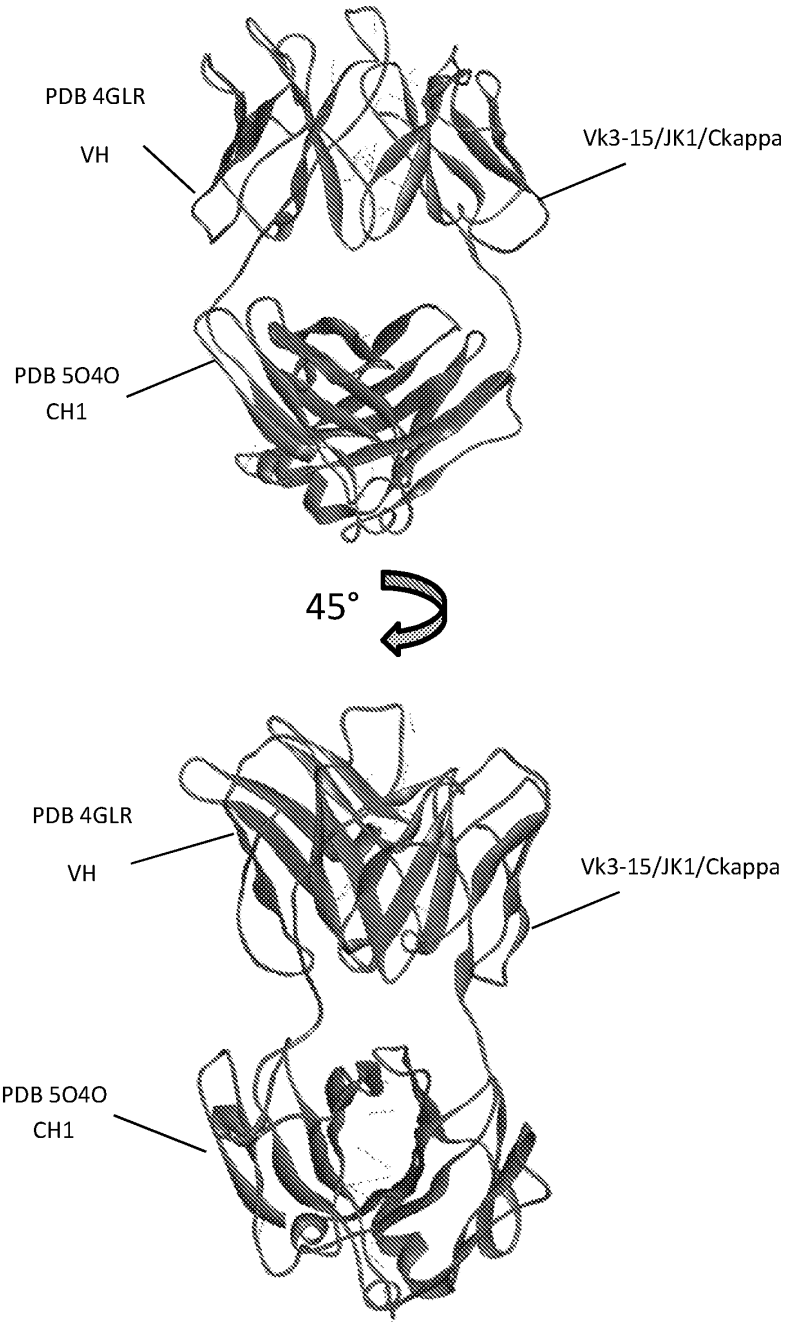
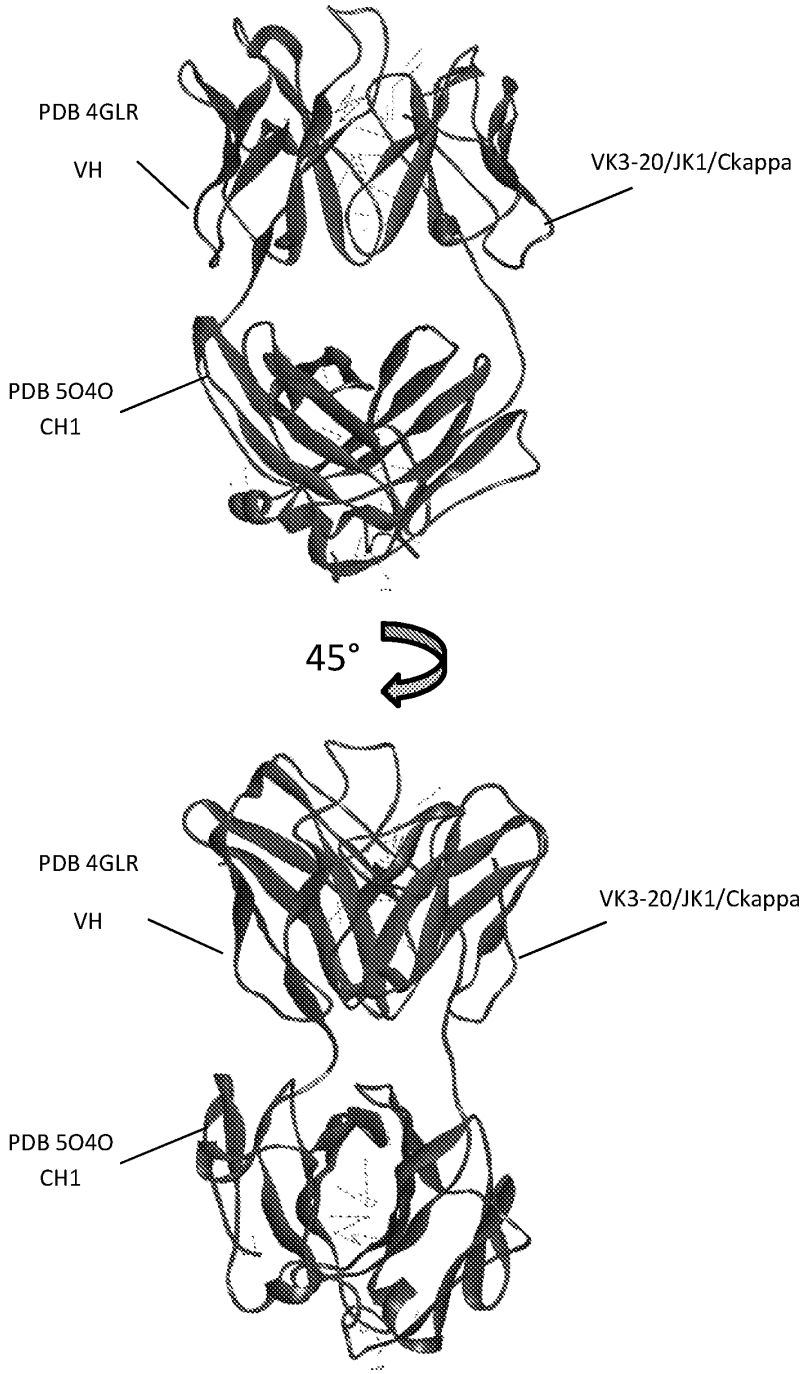

PDB 4GLR
VH
Vk3-15/JK1/Ckappa
PDB 5O4O
CH1
45°
PDB 4GLR
VH
Vk3-15/JK1/Ckappa
PDB 5O4O
CH1

Fig. 27B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VH
VK3-20/JK1/Ckappa
PDB 5O4O
CH1
45°
PDB 4GLR
VH
VK3-20/JK1/Ckappa
PDB 5O4O
CH1

Fig. 27C

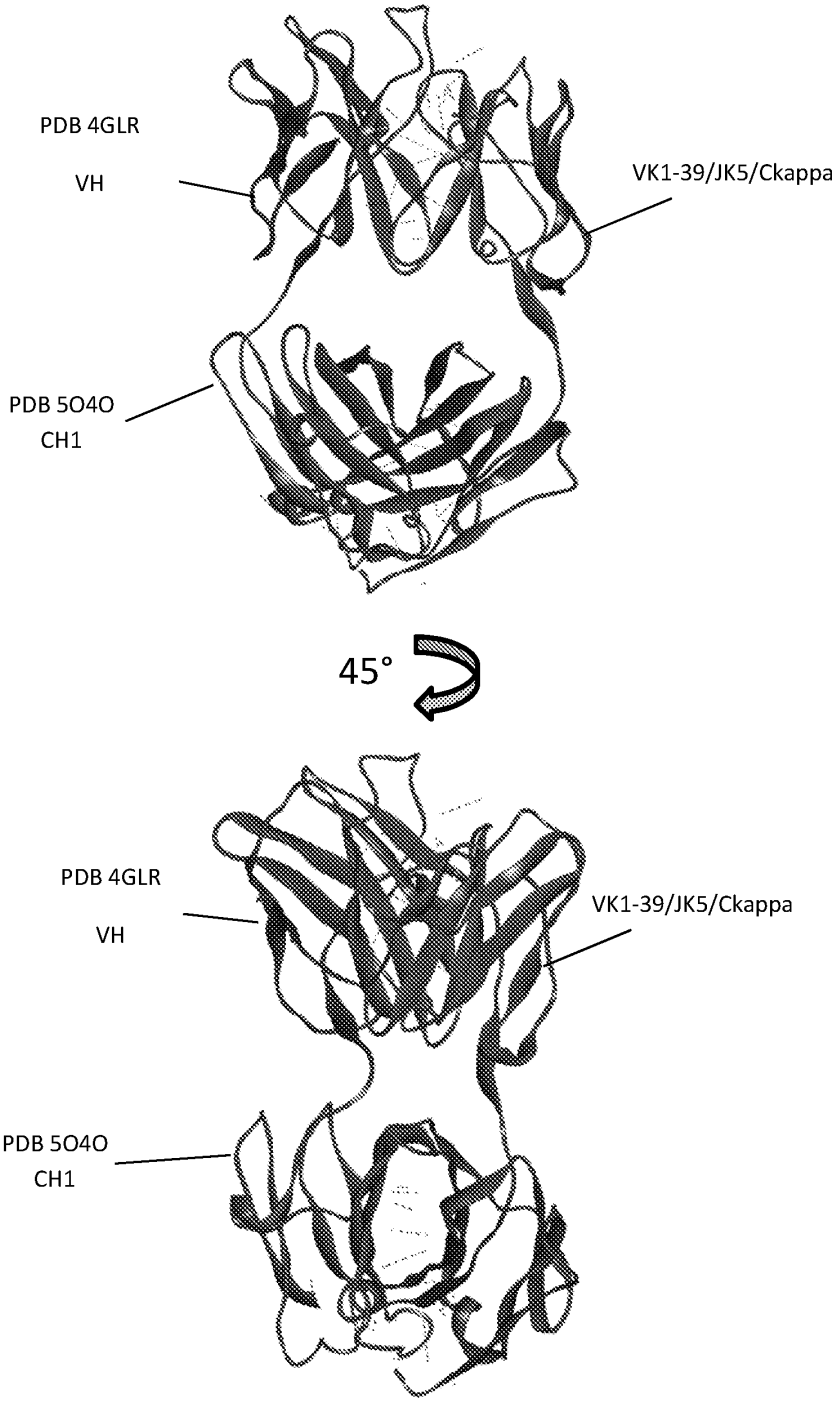
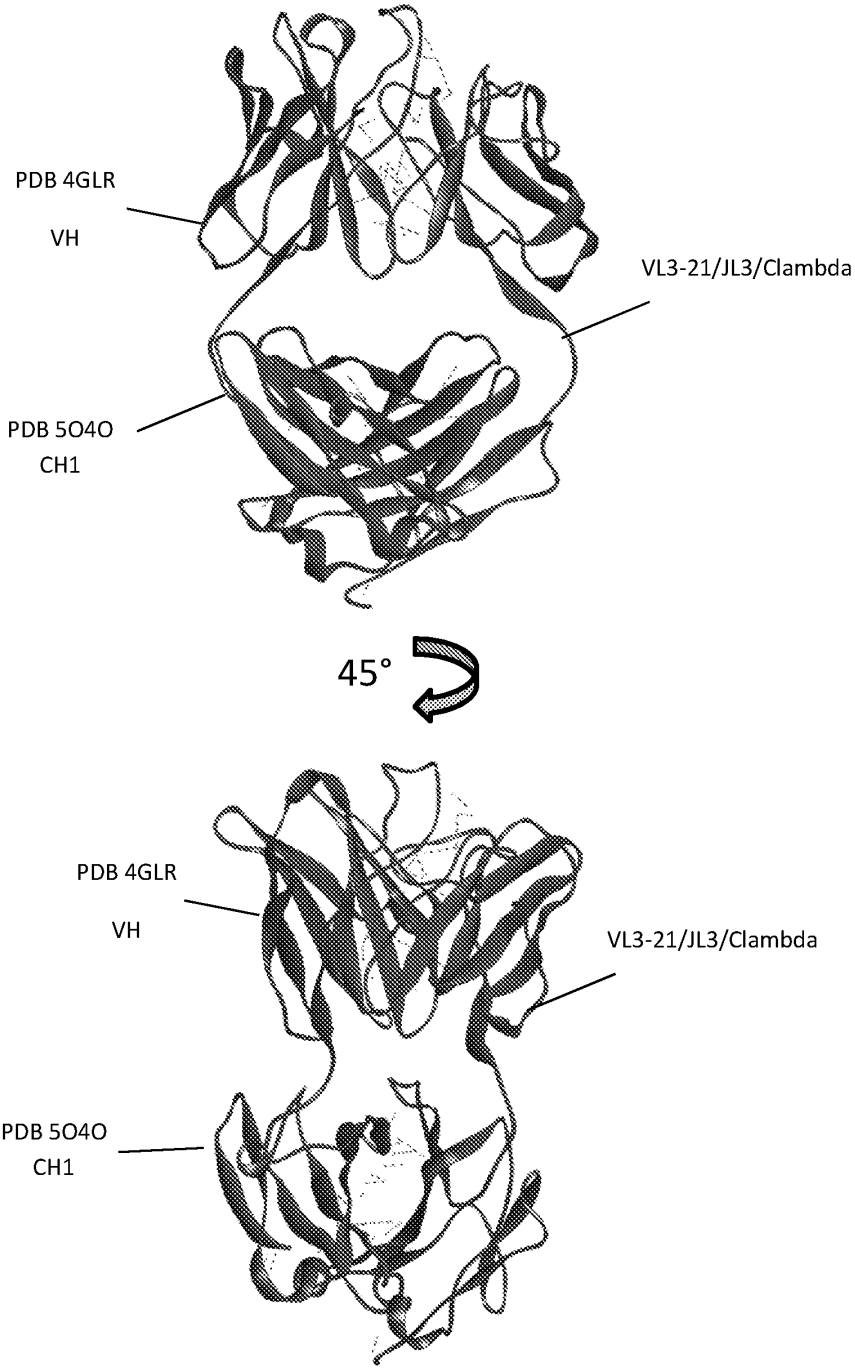

PDB 4GLR
VH
VK1-39/JK5/Ckappa
PDB 5O4O
CH1
45°
PDB 4GLR
VH
VK1-39/JK5/Ckappa
PDB 5O4O
CH1

Fig. 27D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VH
VL3-21/JL3/Clambda
PDB 5O4O
CH1
45°
PDB 4GLR
VH
VL3-21/JL3/Clambda
PDB 5O4O
CH1

Fig. 27E