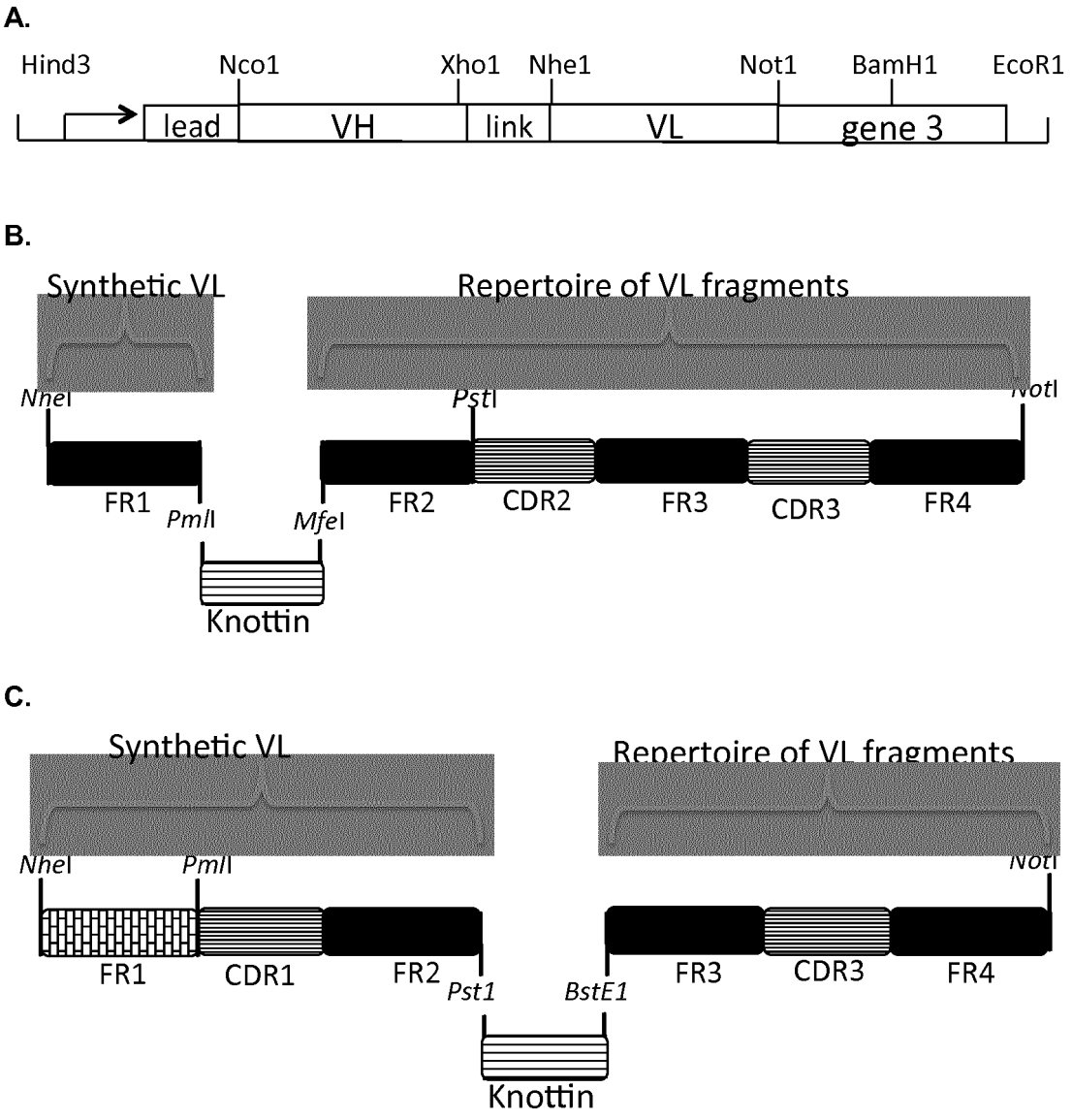

A.
Hind3
Nco1
Xho1
Nhe1
Not1
BamH1
EcoR1
lead
VH
link
VL
gene 3
B.
Synthetic VL
Repertoire of VL fragments
NheI
PstI
NotI
FR1
PmlI
MfeI
FR2
CDR2
FR3
CDR3
FR4
Knottin
C.
Synthetic VL
Repertoire of VL fragments
NheI
PmlI
NotI
FR1
CDR1
FR2
Pst1
BstE1
FR3
CDR3
FR4
Knottin

**Figure 1**

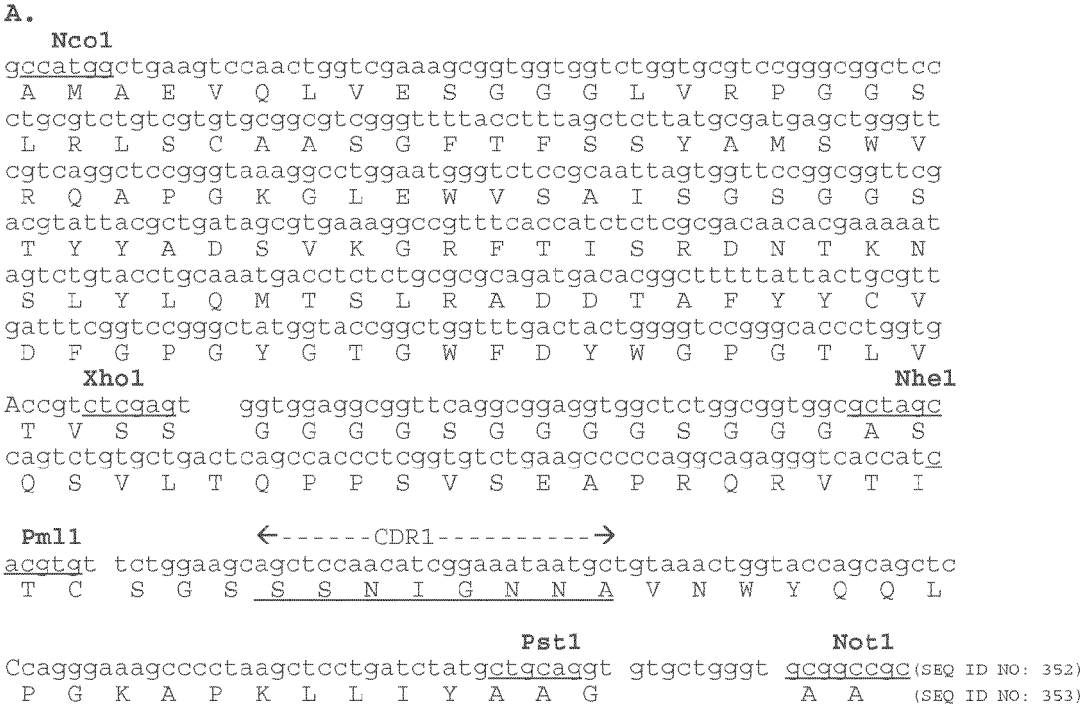



Figure 2A

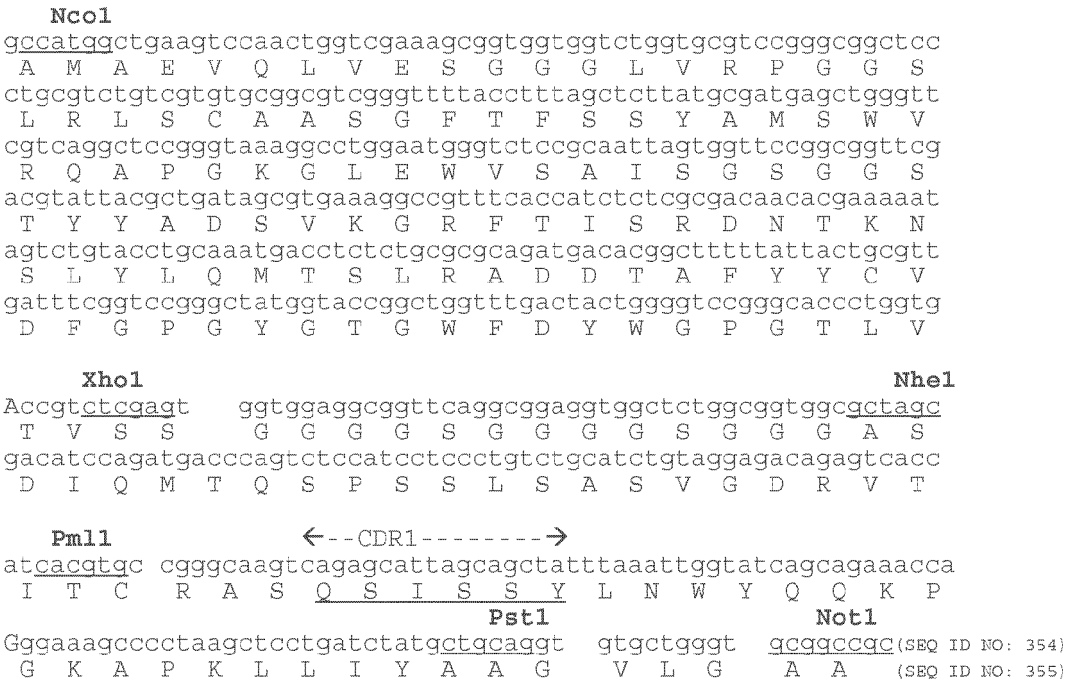



Figure 2B

```
ggctgcccgcgtatcctgatgcgttgcaaacaggactcagactgcctggccggctgcgta
 G  C  P  R  I  L  M  R  C  K  Q  D  S  D  C  L  A  G  C  V
tgcggtccgaacggcttctgcggg(SEQ ID NO: 356)
 C  G  P  N  G  F  C  G (SEQ ID NO: 357)
```

Figure 3A

```
i  RQRVTITCsgs          ssnignna              vNWYQQLP
ii RQRVTITCxxx -CPRILMRCKQDSDCLAGCVCGPNGFCG X xNWYQQLP
iiiRQRVTITCgxx xCPRILMRCKQDSDCLAGCVCGPNGFCG X xNWYQQLP
iv KAPKLLIY              ydd                llpSGVSDRFS
v  KAPKLLIY AAZ xCPRILMRCKQDSDCLAGCVCGPNGFCG -XXSGVSDRFS
(SEQ ID NOS: 358-362)
```

Figure 3B

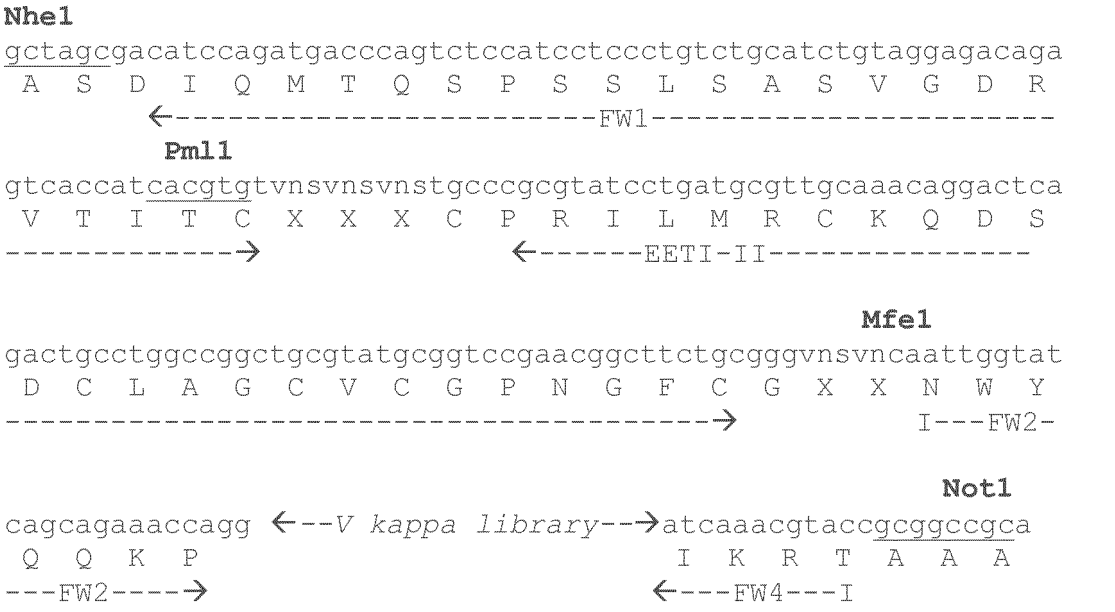
```
Nhe1
gctagccagtctgtgctgactcagccaccctcggtgtctgaagcccccaggcagagggtc
 A  S  Q  S  V  L  T  Q  P  P  S  V  S  E  A  P  R  Q  R  V
       ←------------------------FW1----------------------
     Pml1
accatcacgtgtvnsvnsvnstgcccgcgtatcctgatgcgttgcaaacaggactcagac
 T  I  T  C  X  X  X  C  P  R  I  L  M  R  C  K  Q  D  S  D
---------→          ←---------EETI-II-----------------

                                                  Mfe1
tgcctggccggctgcgtatgcggtccgaacggcttctgcgggvnsvncaattggtaccag
 C  L  A  G  C  V  C  G  P  N  G  F  C  G  X  X  N  W  Y  Q
-------------------------------------→          I----FW2---

                                                      Not1
cagctcccagga ←-Vlambda library-> accgtcctaggtcagcccgcggccgca
 Q  L  P  G                       T  V  L  G  Q  P  A  A  A
---FW2----→                      <--------FW4------I
```

(SEQ ID NOS: 319 & 320)

Figure 3C




(SEQ ID NOS: 321 & 322)

Figure 3D

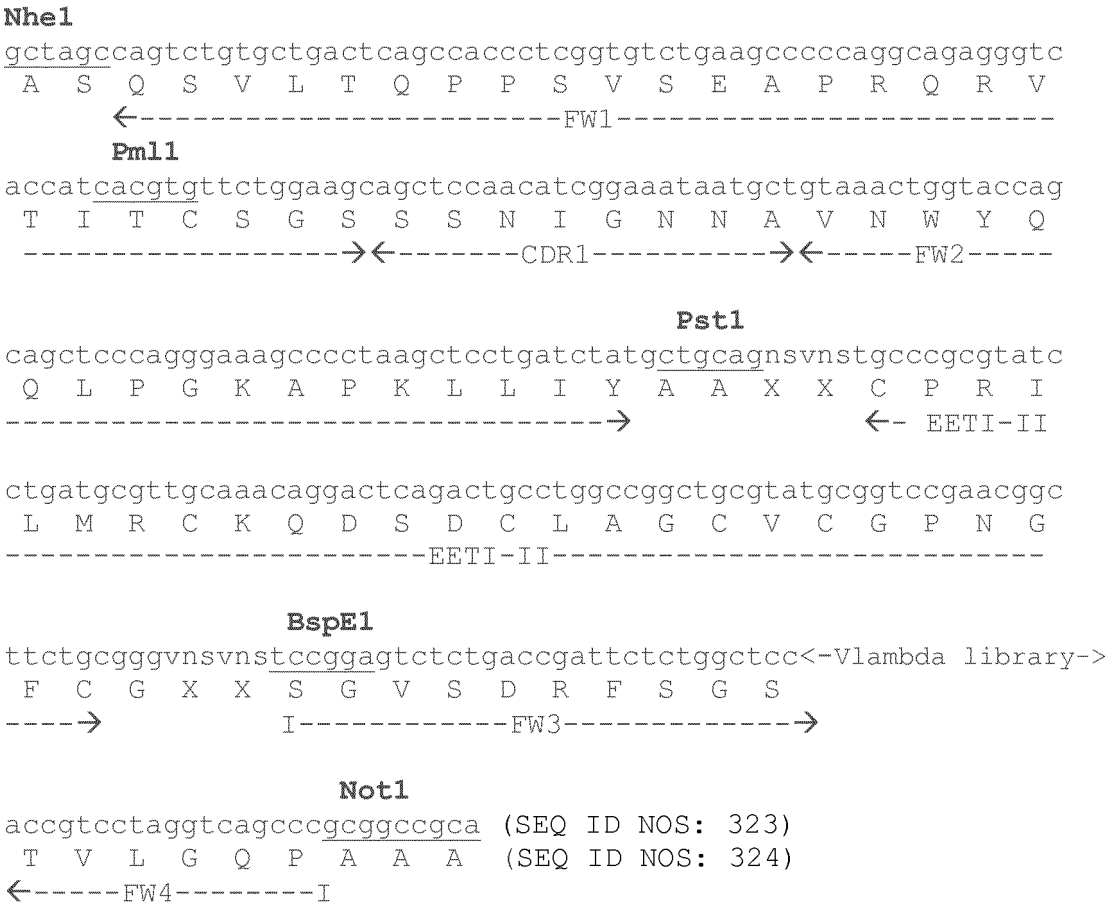



Figure 3E


Nhe1
gctagcgacatccagatgacccagtctccatcctccctgtctgcatctgtaggagacaga
A S D I Q M T Q S P S S L S A S V G D R
←FW1
Pml1
gtcaccatcacgtgccgggcaagtcagagcattagcagctatttaaattggtatcagcag
V T I T C R A S Q S I S S Y L N W Y Q Q
→←CDR1→←FW2
Pst1
aaaccagggaaagcccctaagctcctgatctatgctgcagnsvnstgcccgcgtatcctg
K P G K A P K L L I Y A A X X C P R I L
→
←- EETI-II
atgcgttgcaaacaggactcagactgcctggccggctgcgtatgcggtccgaacggcttc
M R C K Q D S D C L A G C V C G P N G F
EETI-II
BspE1
tgcgggvnsvnstccggagtcccatcaaggttcagtggcagt<-V kappa library->
C G X X S G V P S R F S G S
I-FW3→
Not1
Atcaaacgtaccgcggccgca (SEQ ID NOS: 325)
I K R T A A A (SEQ ID NOS: 326)
←FW4-I

**Figure 3F**

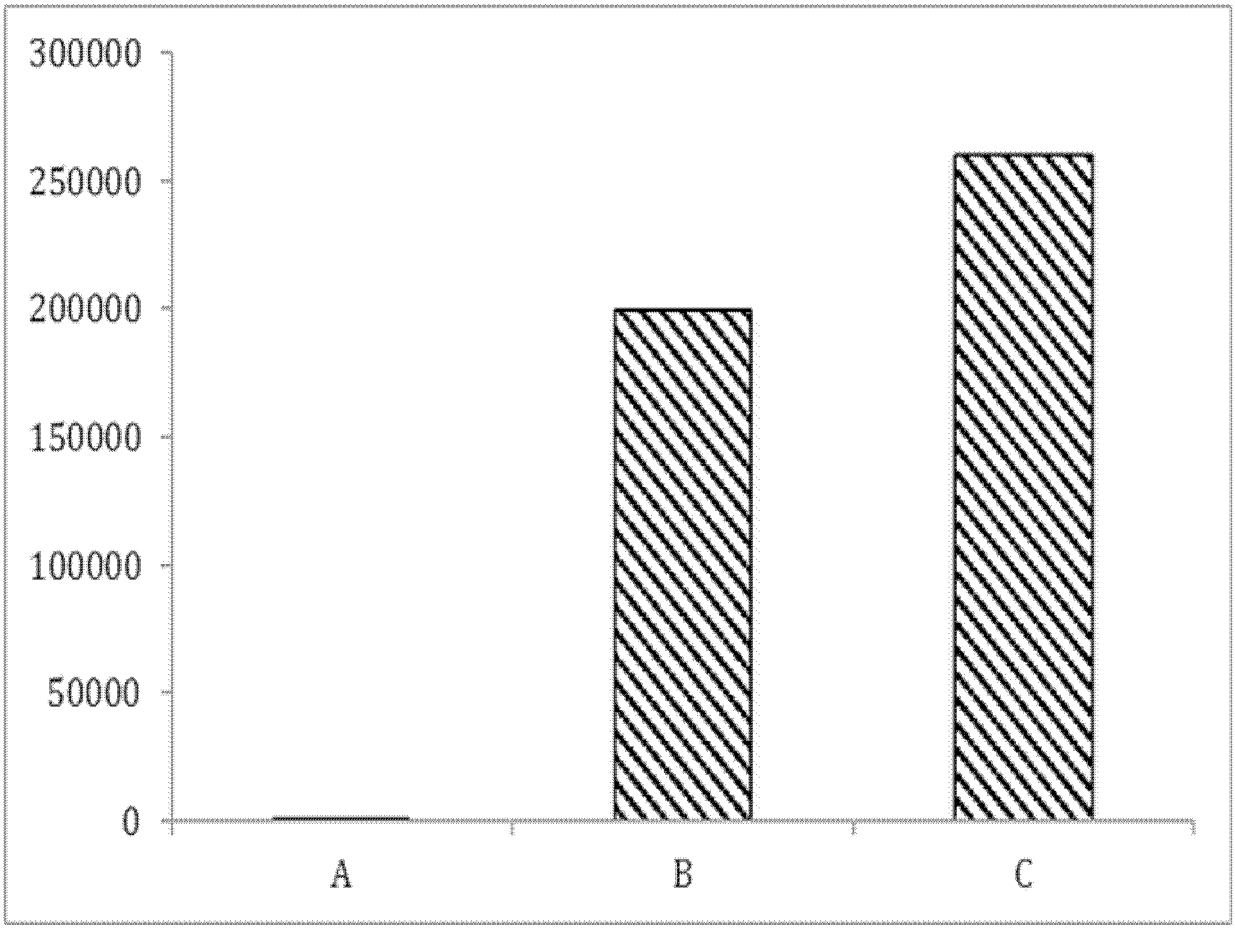



Figure 4

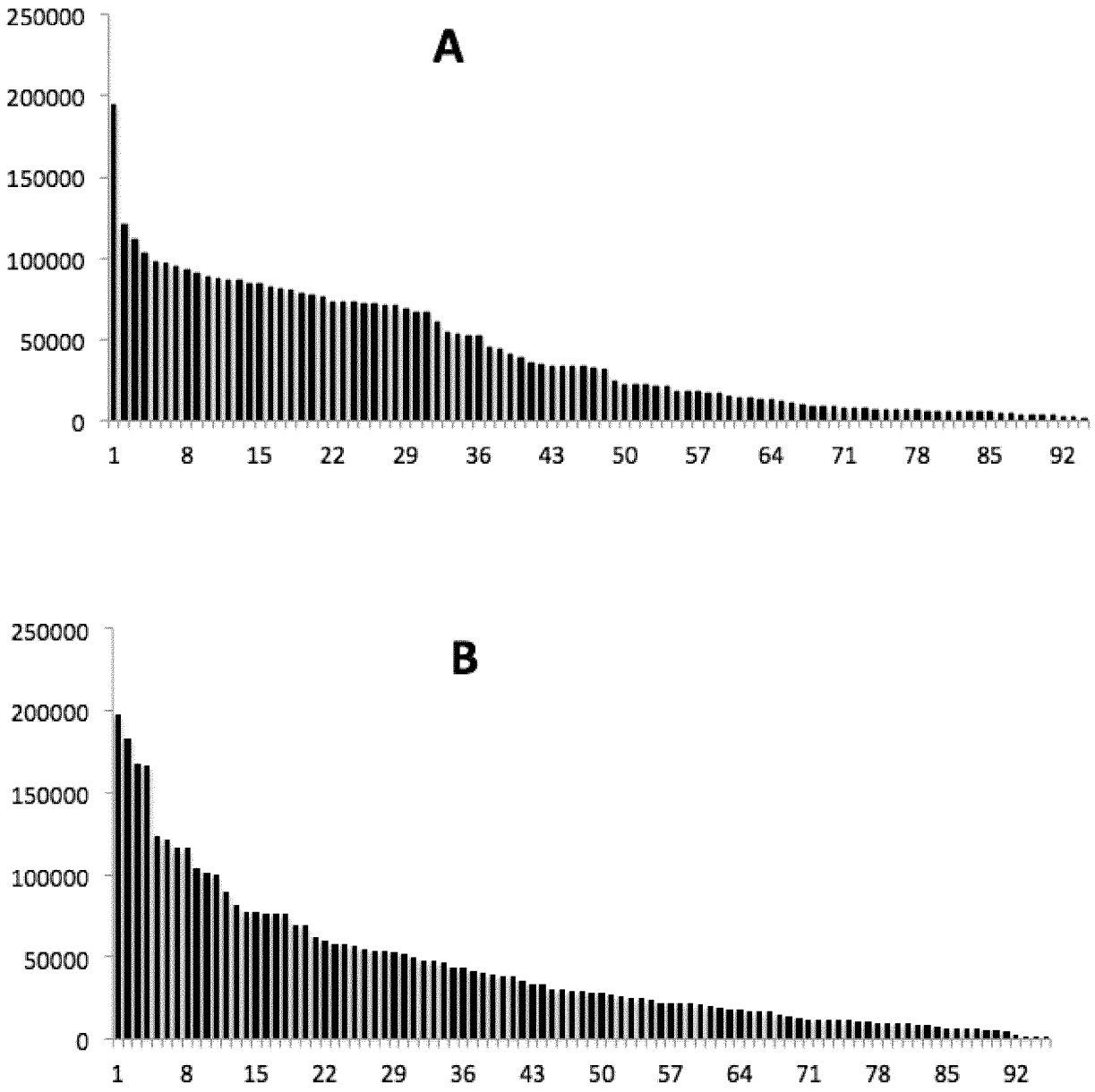

A
250000
200000
150000
100000
50000
0
1
8
15
22
29
36
43
50
57
64
71
78
85
92
B
250000
200000
150000
100000
50000
0
1
8
15
22
29
36
43
50
57
64
71
78
85
92

Figure 5

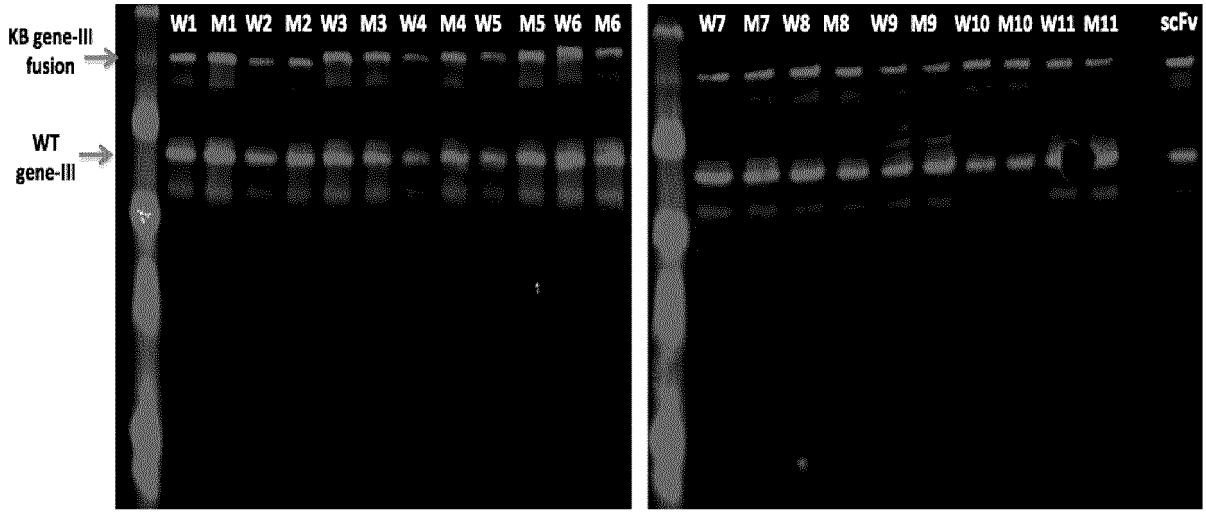



Figure 6

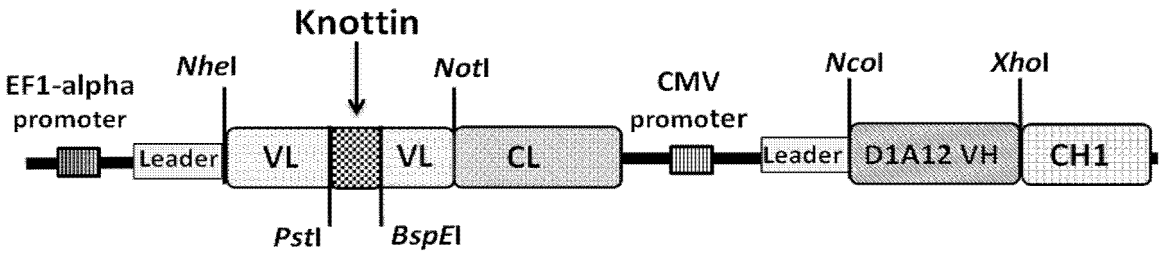



Figure 7

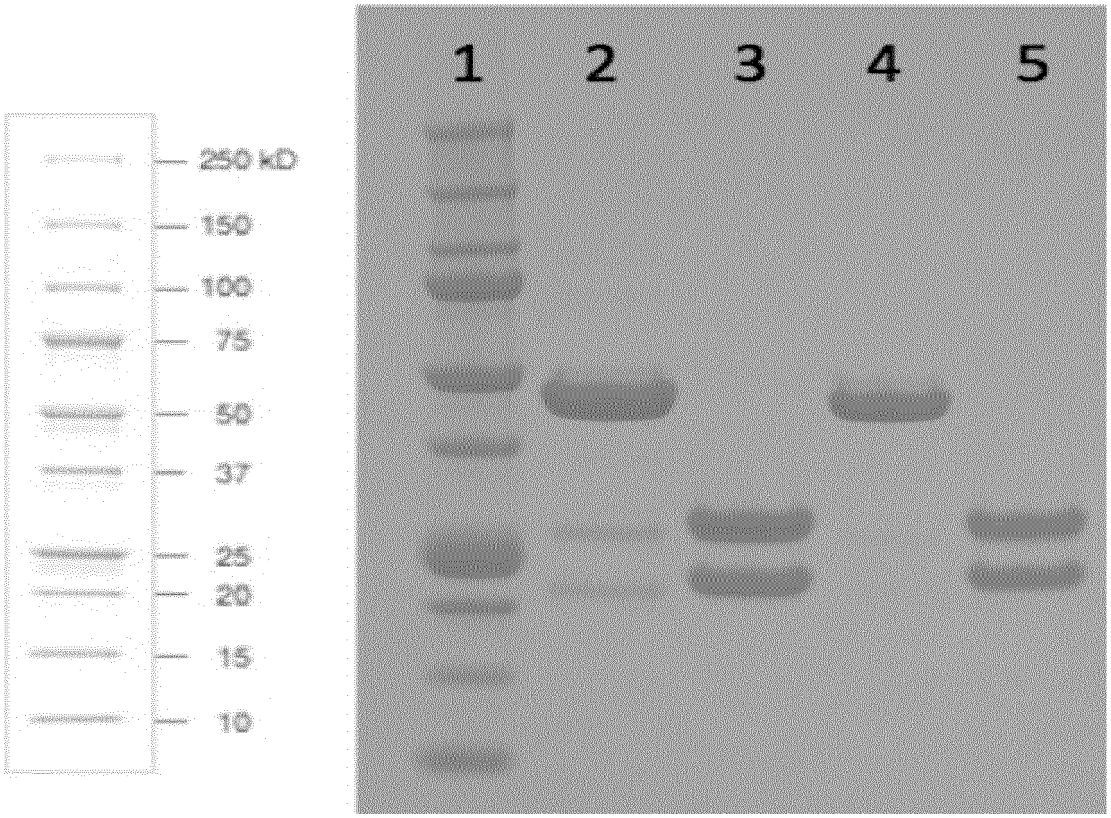



Figure 8A

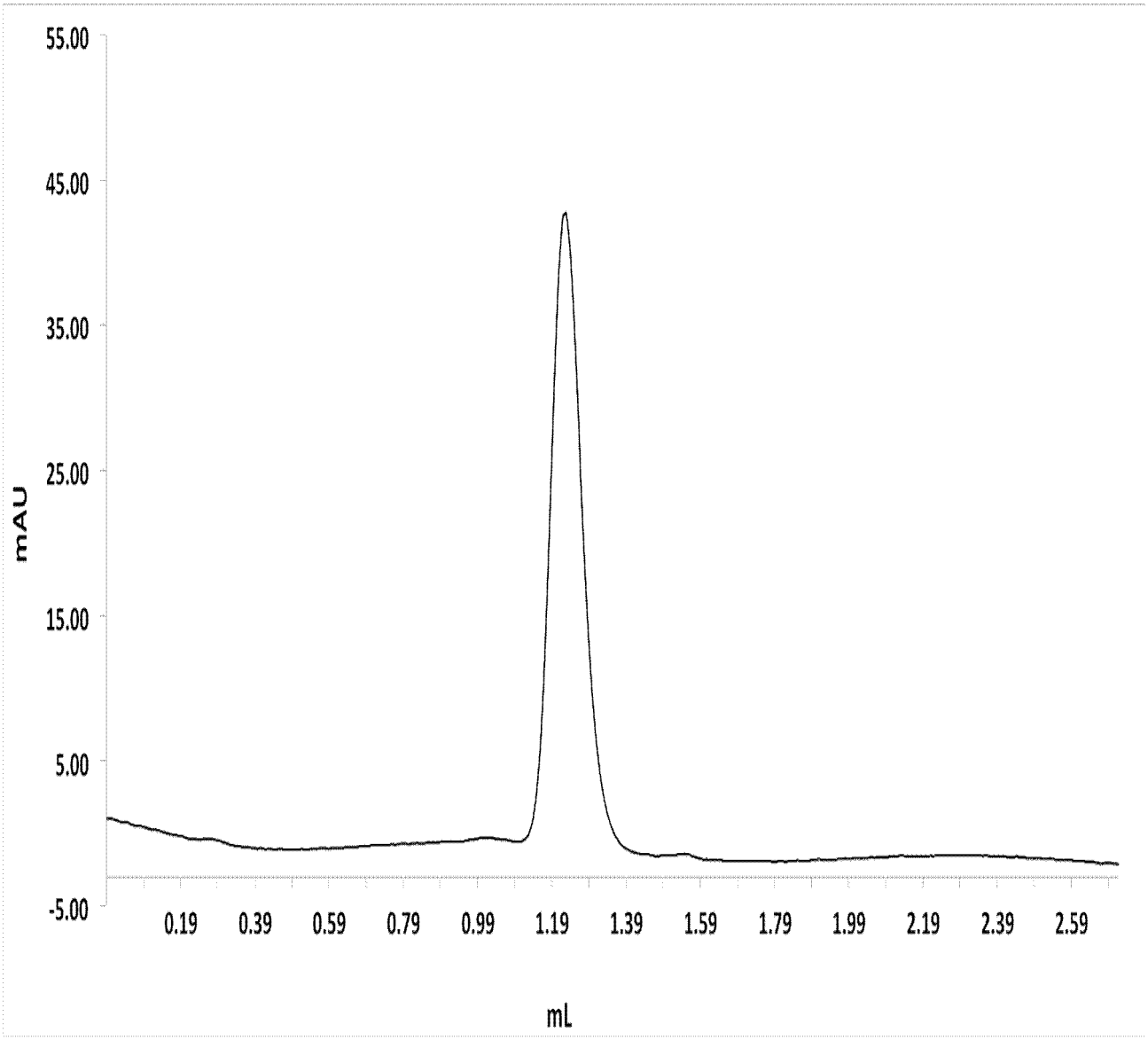
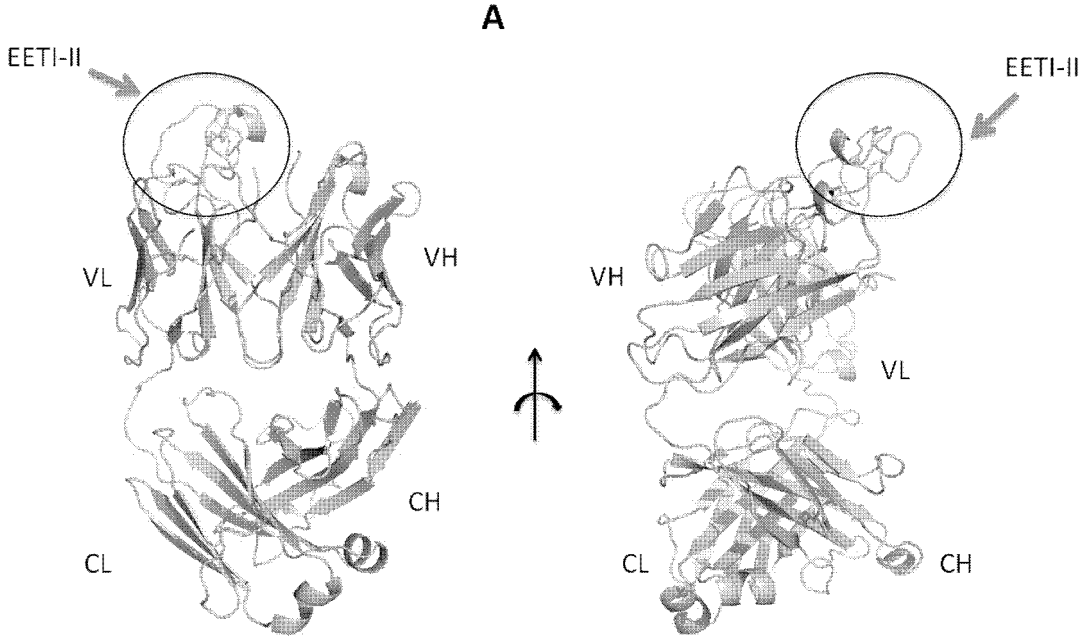

55.00
45.00
35.00
25.00
15.00
5.00
-5.00
mAU
0.19
0.39
0.59
0.79
0.99
1.19
1.39
1.59
1.79
1.99
2.19
2.39
2.59
mL

Figure 8B


A
EETI-II
VL
VH
CH
CL
EETI-II
VH
VL
CL
CH
KB_A05

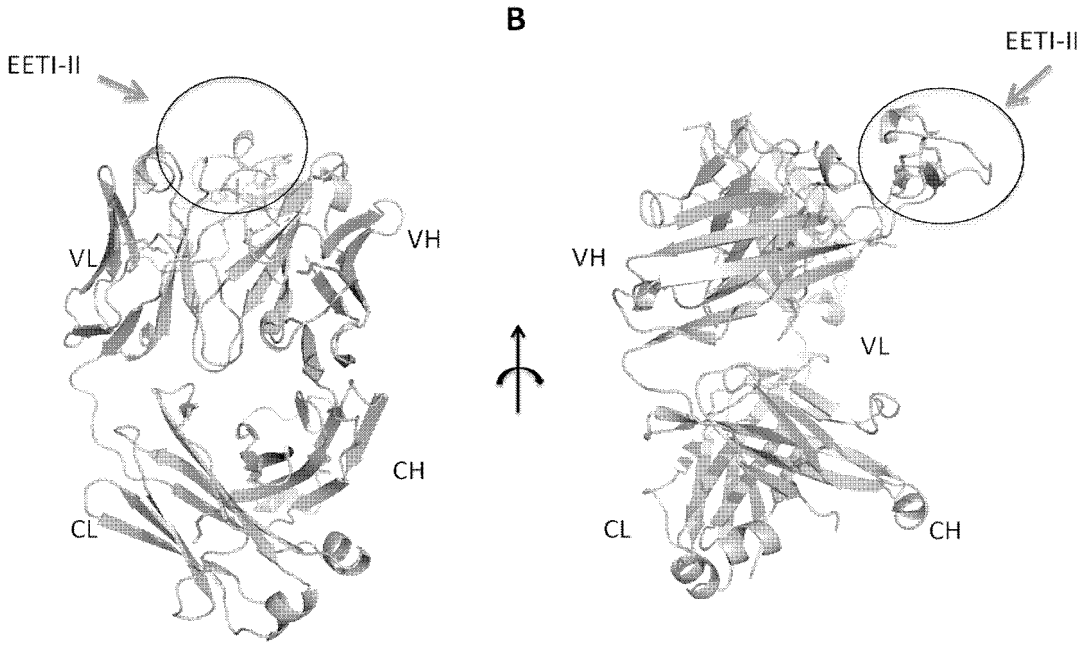
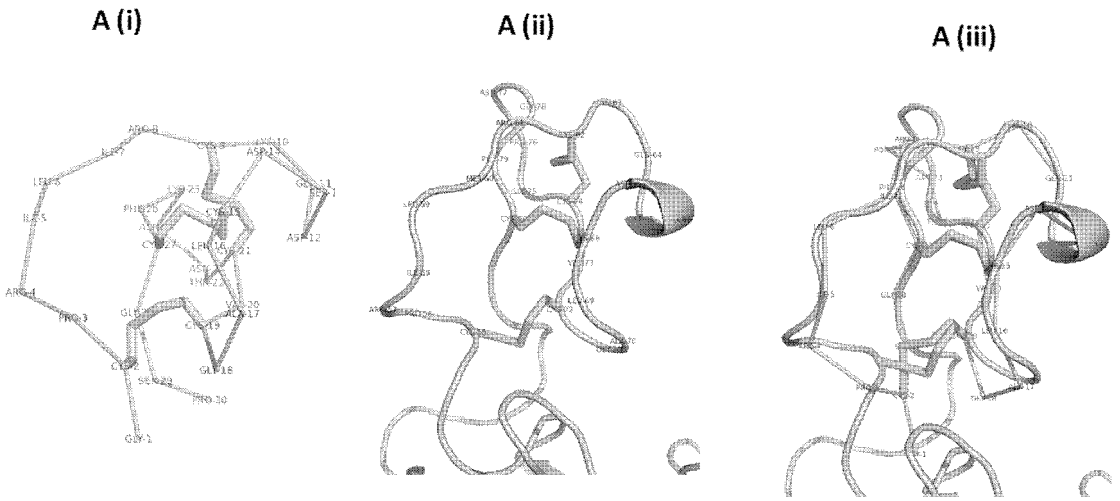

B
EETI-II
VL
VH
CH
CL
EETI-II
VH
VL
CL
CH
KB_A12

**Figure 9**



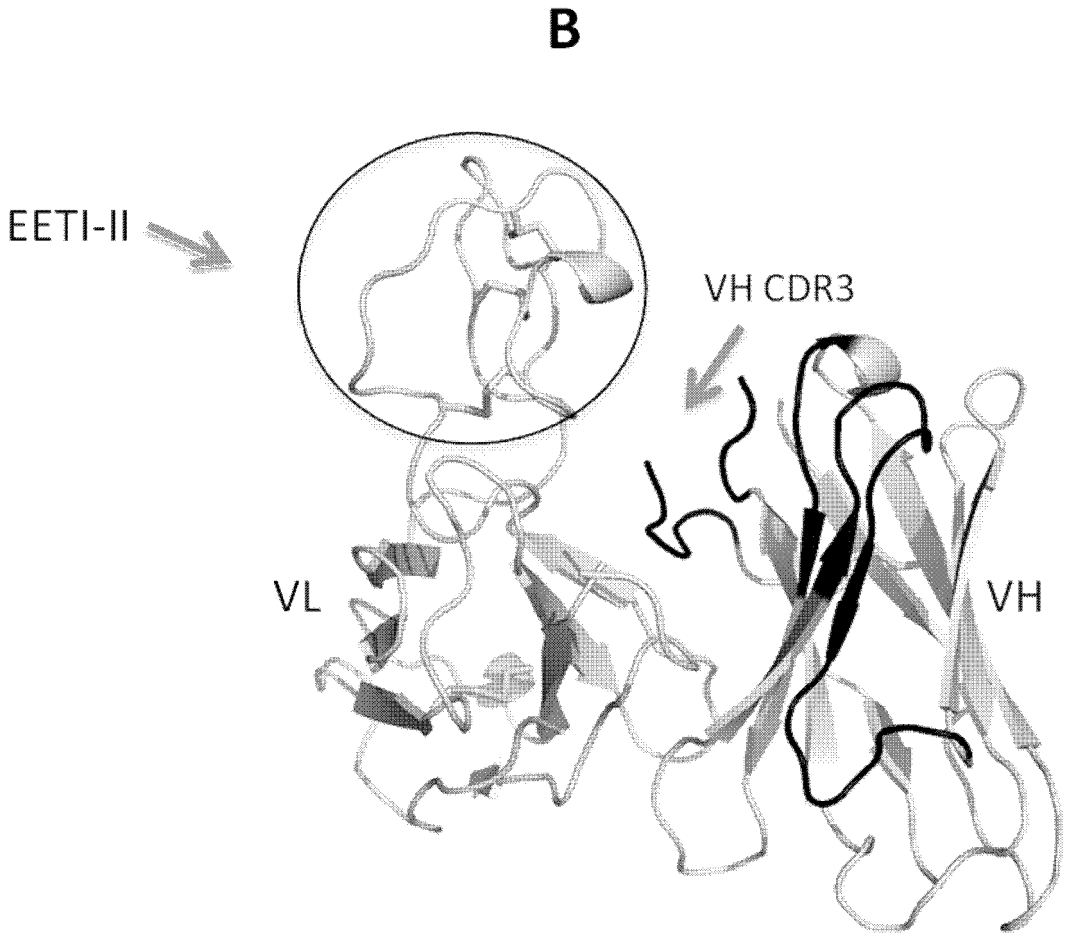




Figure 10

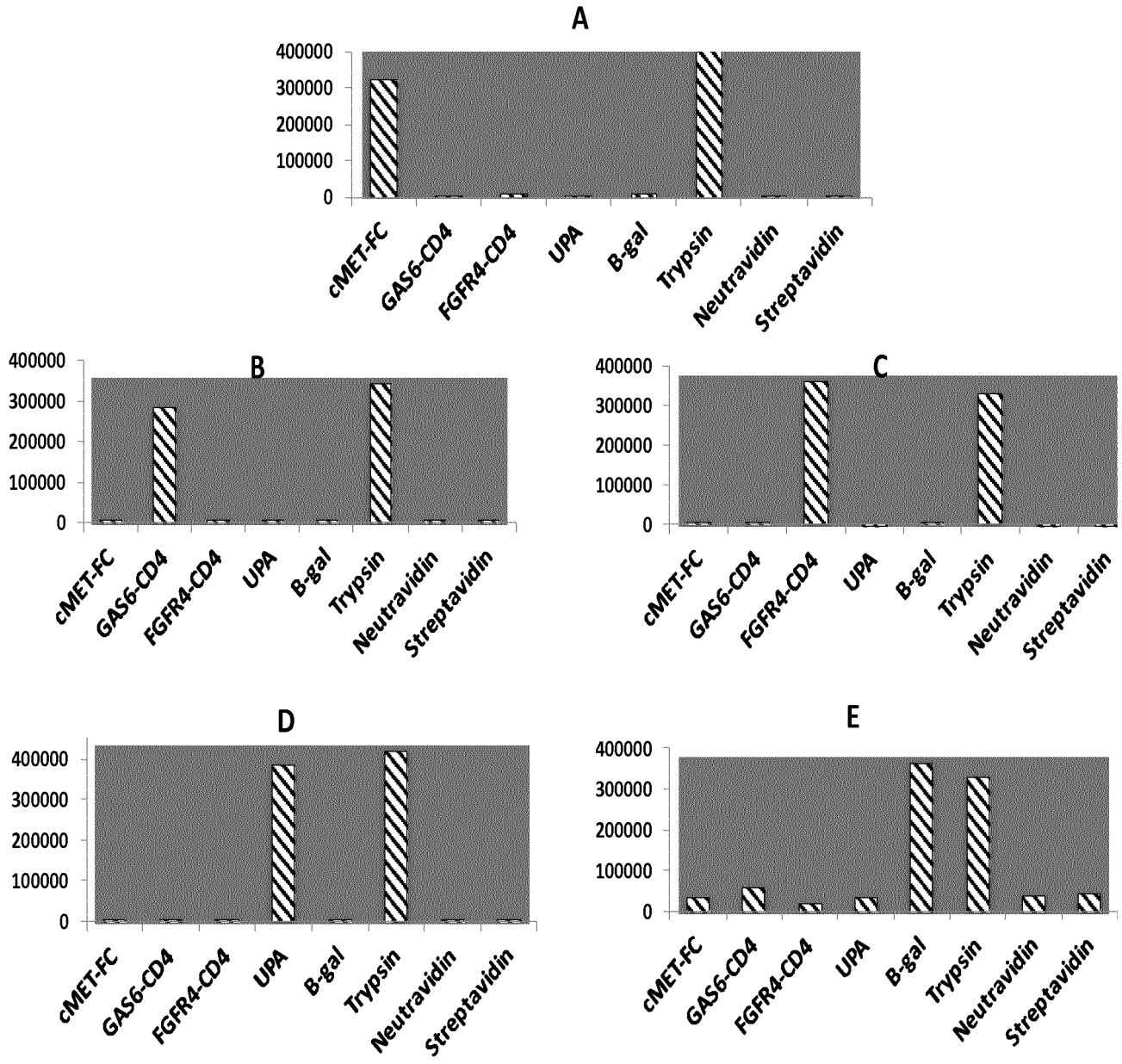

A
400000
300000
200000
100000
0
cMET-FC
GAS6-CD4
FGFR4-CD4
UPA
B-gal
Trypsin
Neutravidin
Streptavidin
B
C
D
E

Figure 11

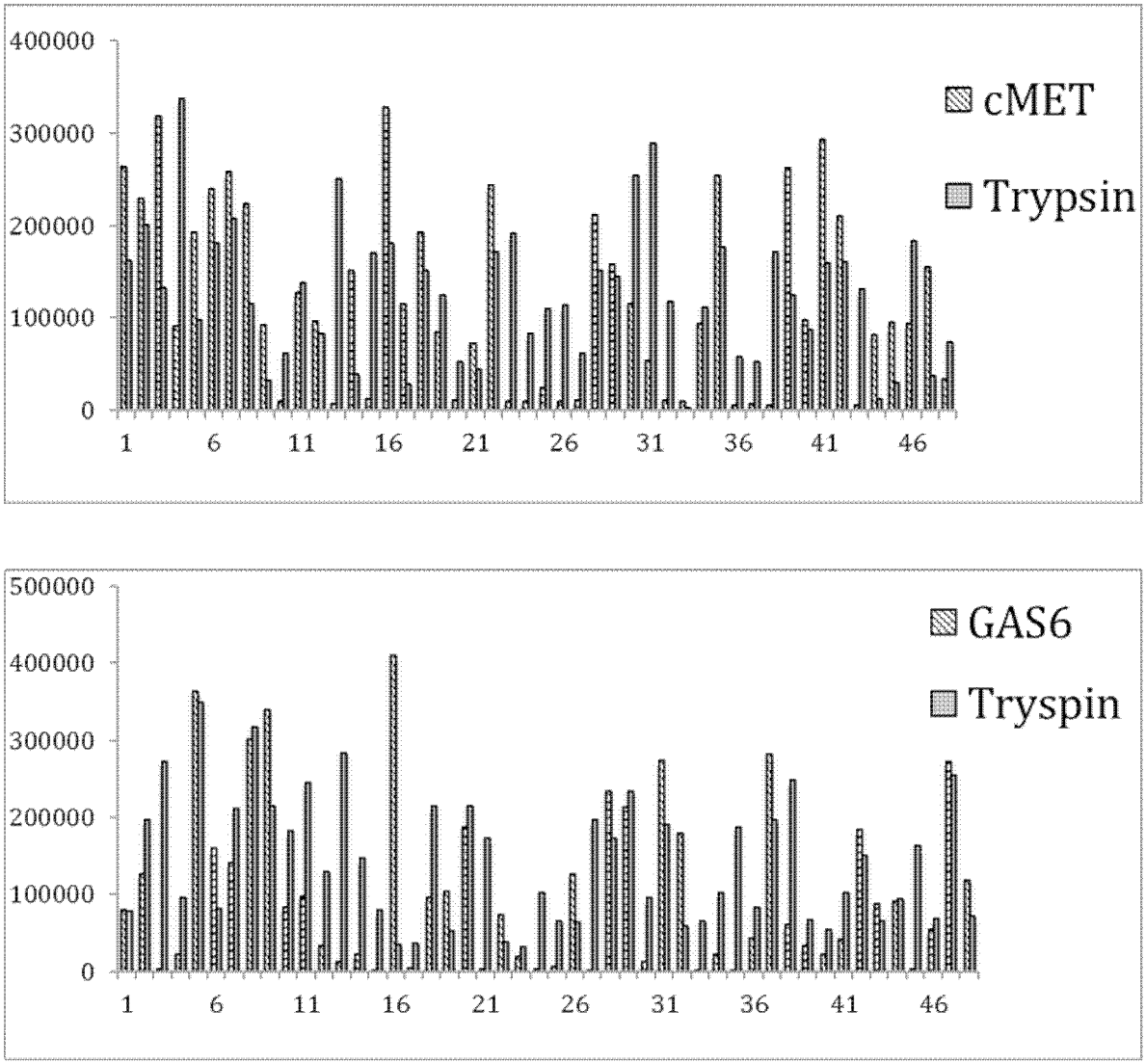

400000
300000
200000
100000
0
1
6
11
16
21
26
31
36
41
46
cMET
Trypsin
500000
400000
300000
200000
100000
0
1
6
11
16
21
26
31
36
41
46
GAS6
Tryspin

**Figure 12**

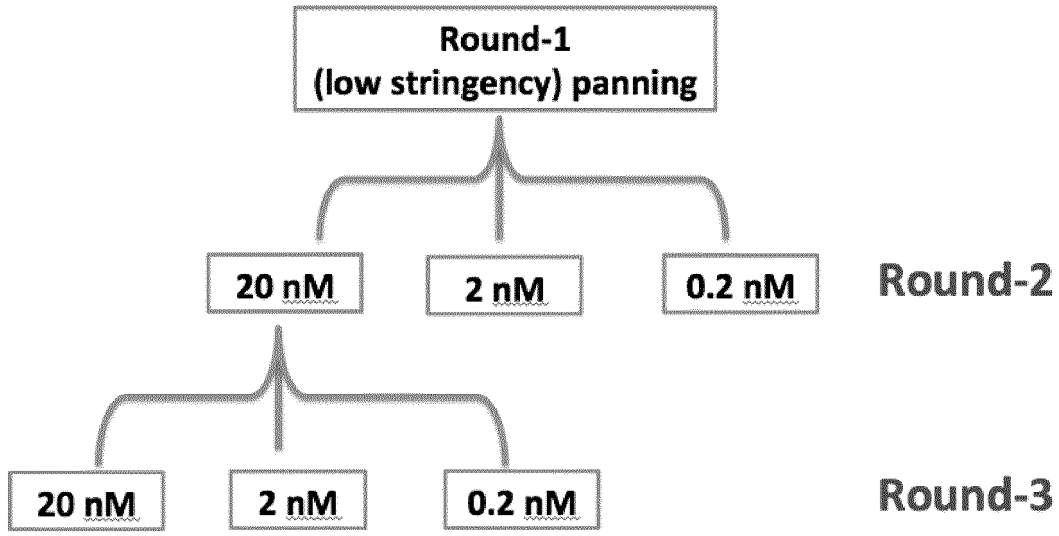



Figure 13

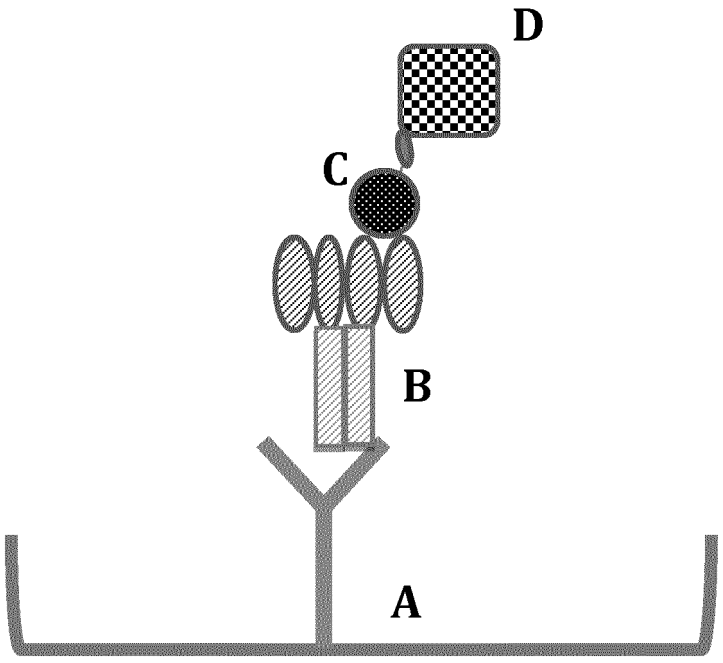



Figure 14

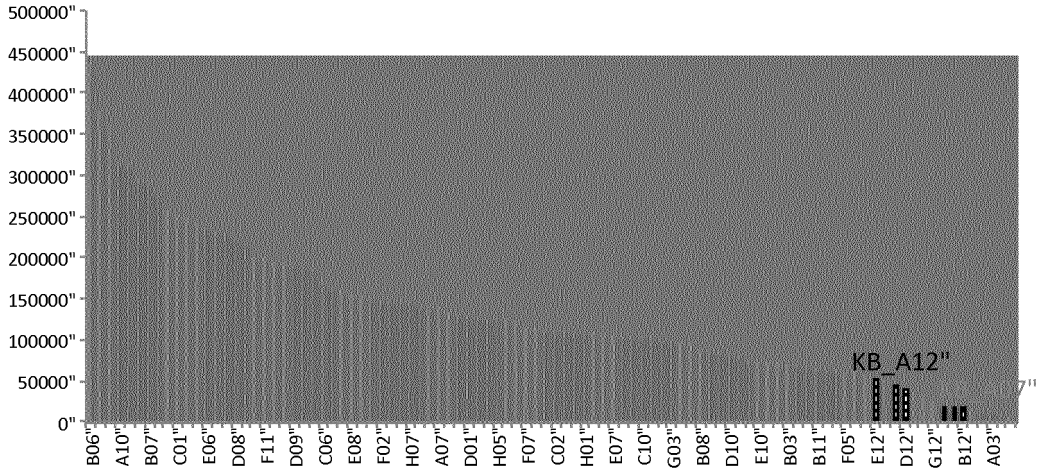



Figure 15

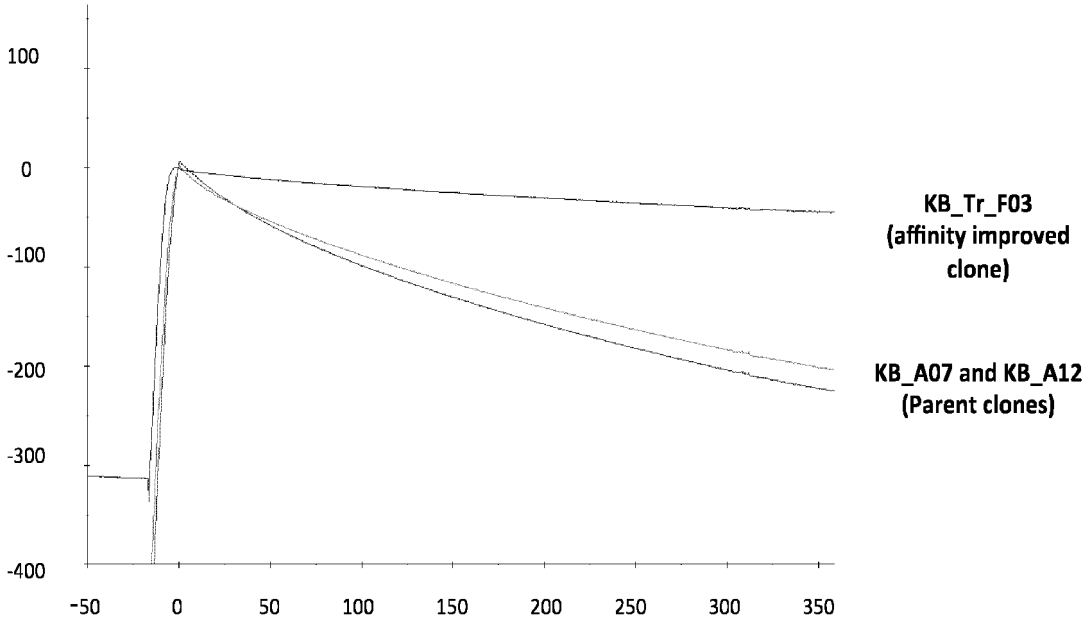



Figure 16

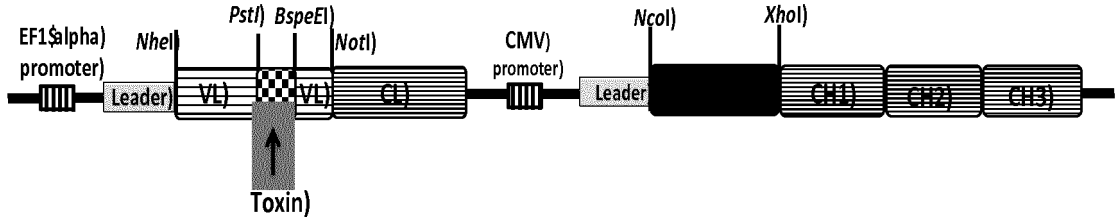



Figure 17

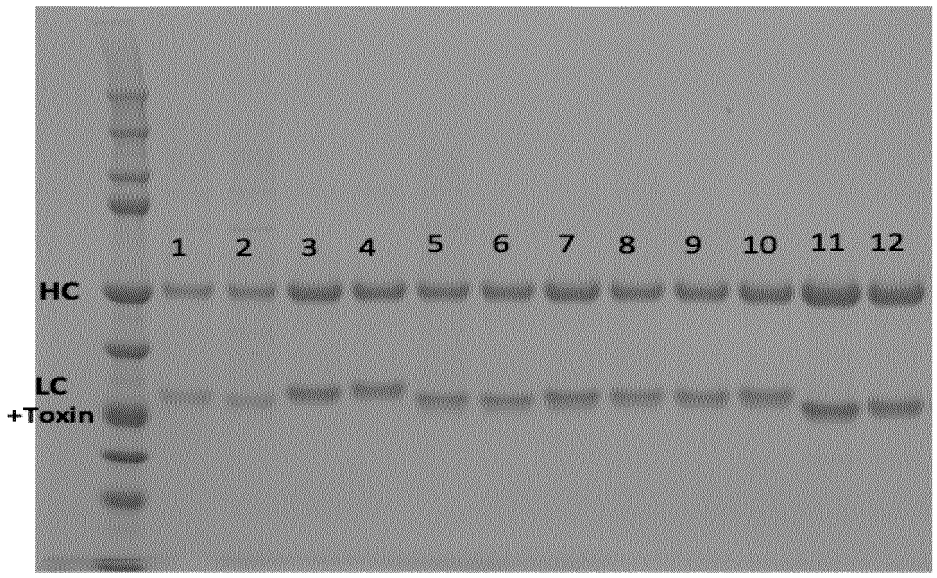



Figure 18

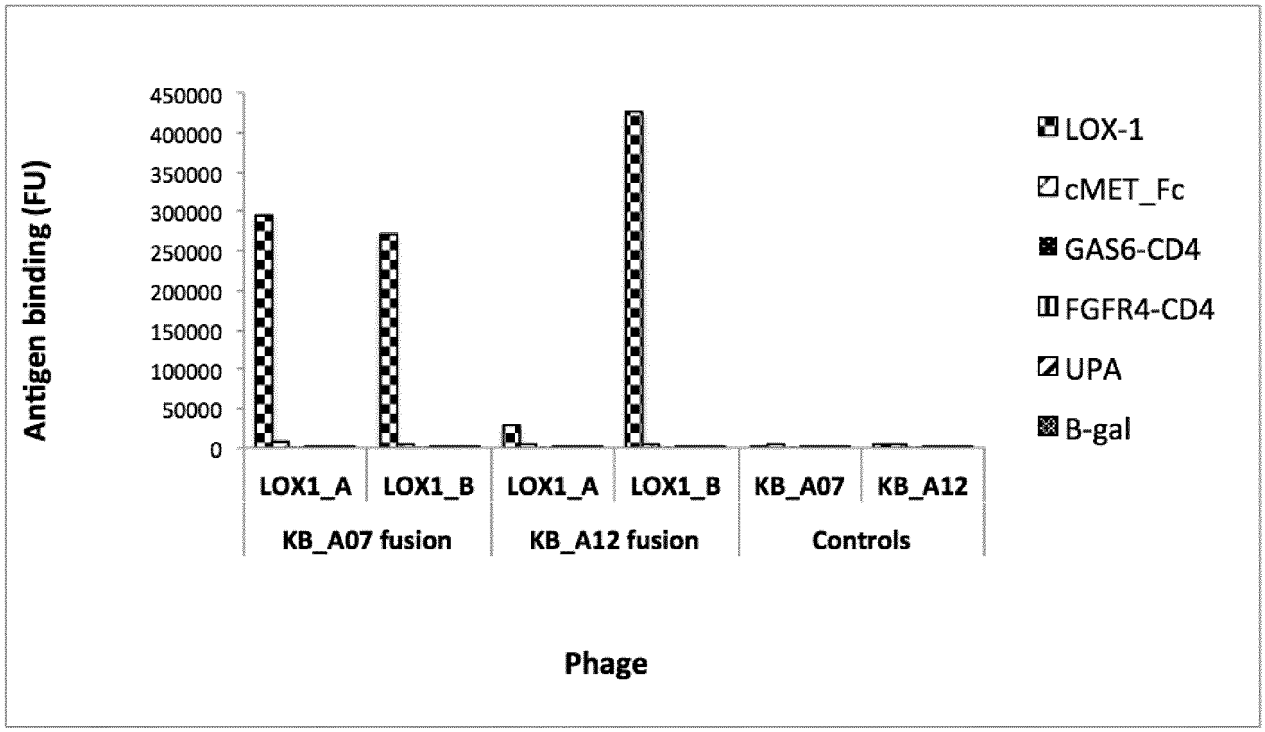



**Figure 19**

**A**

```
         10         20         30         40         50
RDLEVVAATPTSLLISwdapavtvrYYRITYGETGGNSPVQEFTVPgsks

         60         70         80         90
TATISGLKPGVDYTITVYAVtgrgdspasskpISINYRTEI (SEQID NO: 28)
```

**B.**

```
MSNVNTGSLSVDNKKFWATVEsseh SFEVPIYAETLDEALELAEWQYvpa
                beta       beta      alpha

gfEVTRVRPCVAPK (SEQ ID NO: 29)
   beta
```

**Figure 20**

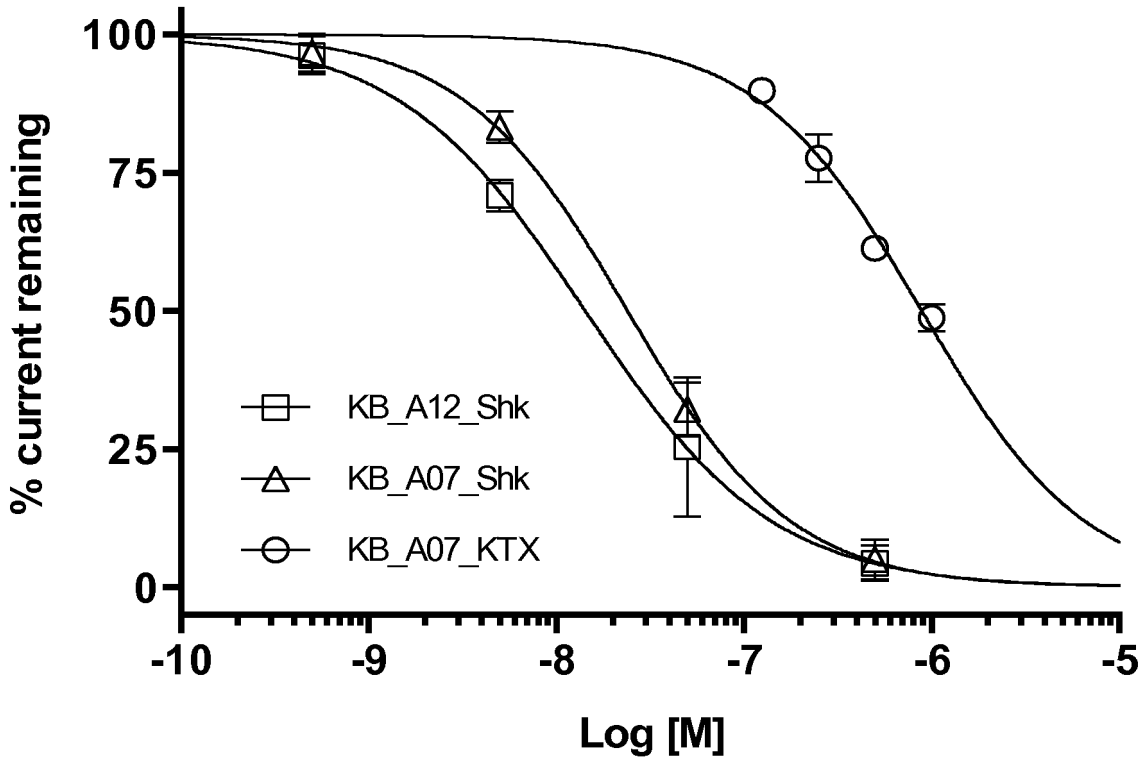

100
75
50
25
0
% current remaining
KB_A12_Shk
KB_A07_Shk
KB_A07_KTX
-10
-9
-8
-7
-6
-5
Log [M]

Figure 21

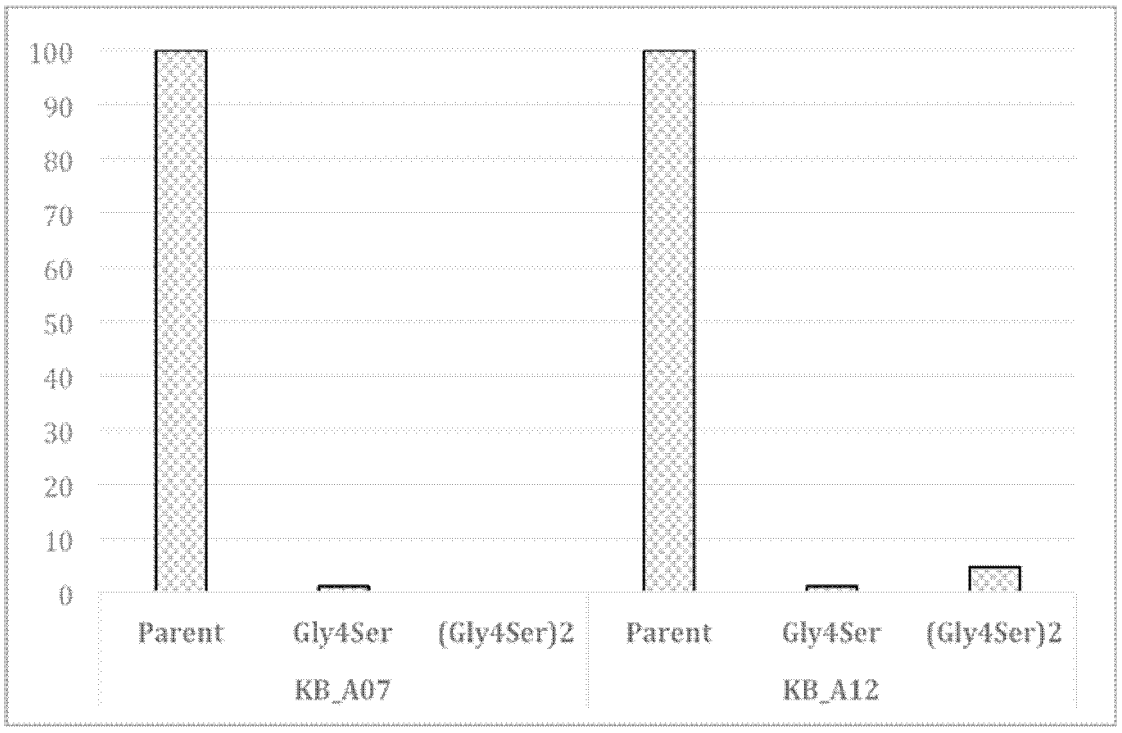



Figure 22

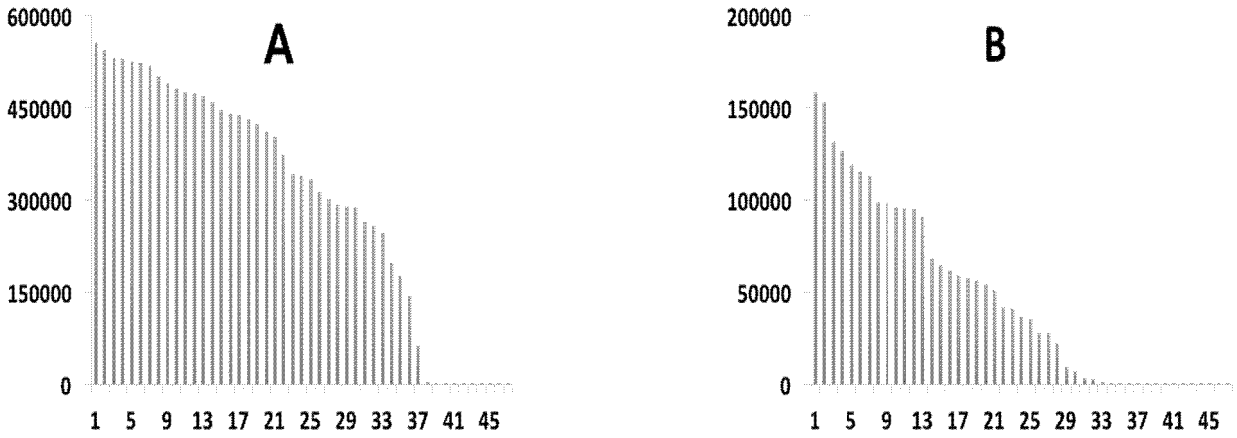



Figure 23

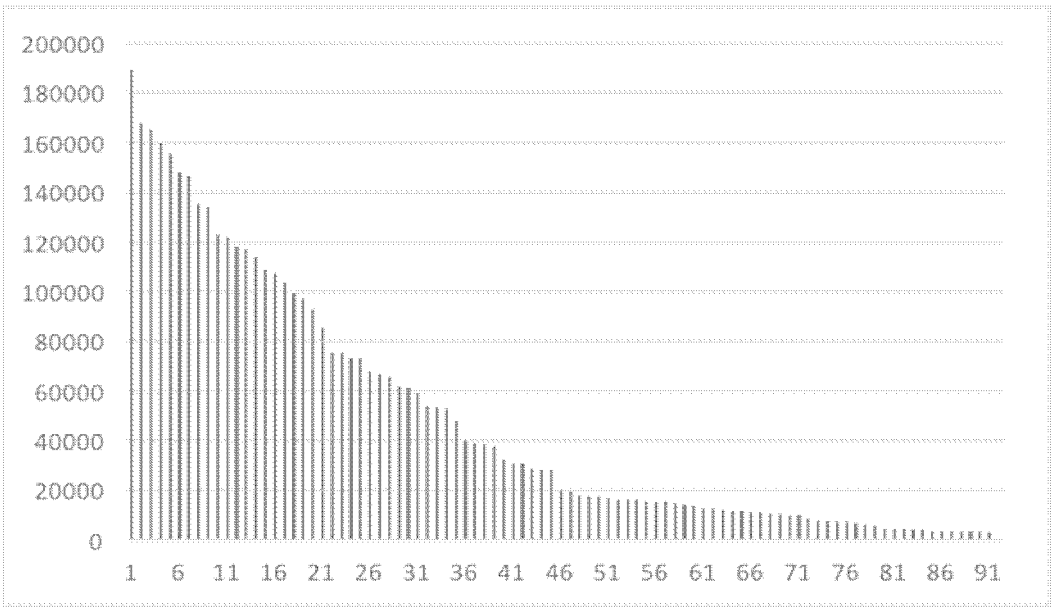



Figure 24

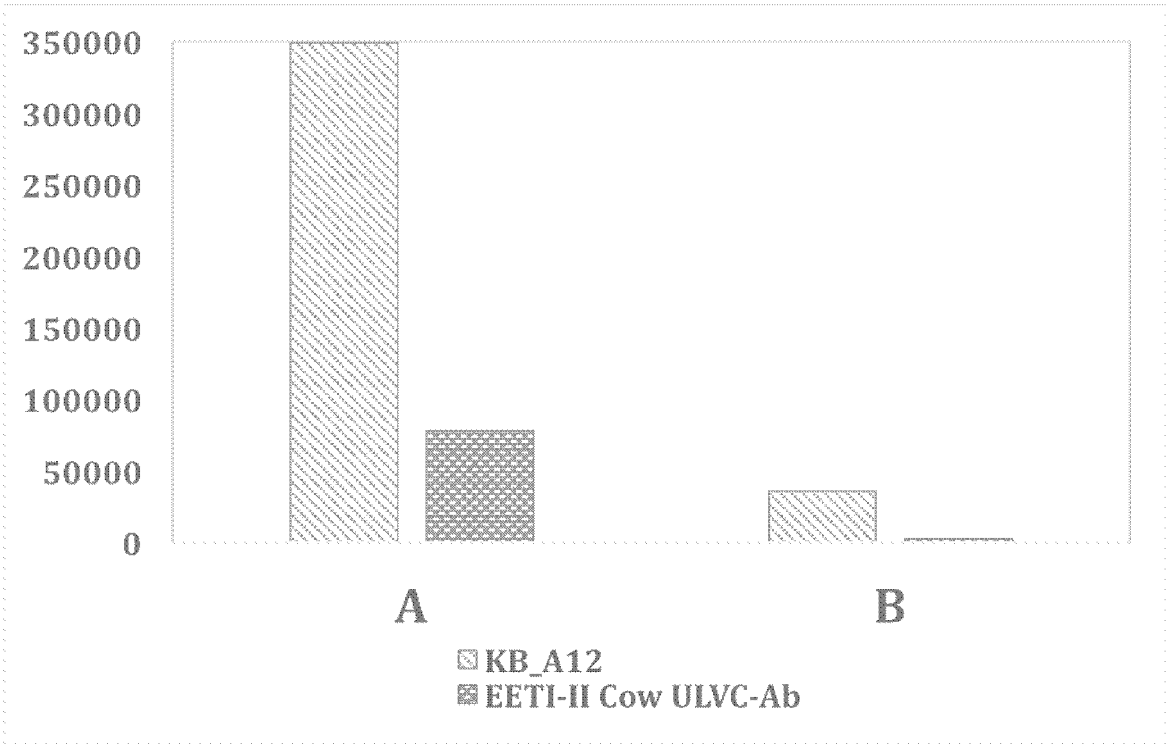



Figure 25

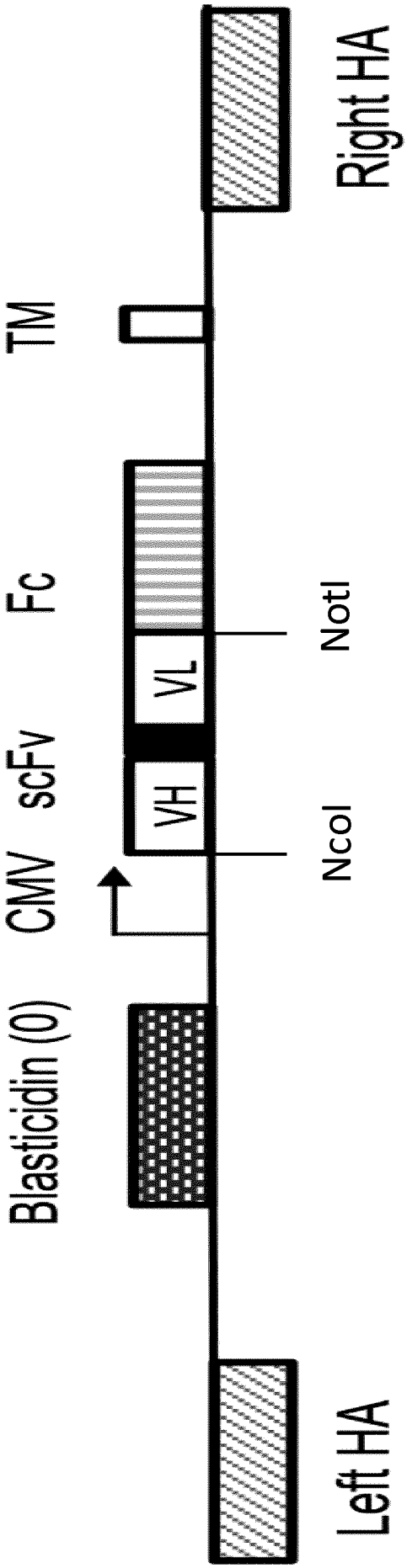



Figure 26

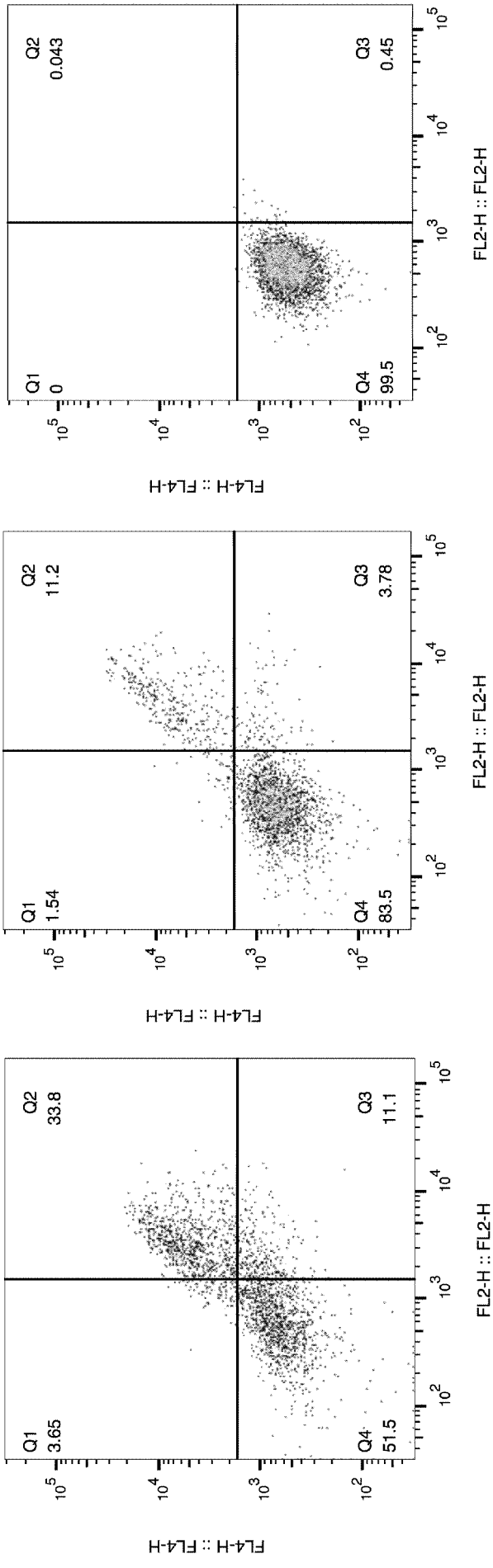

Q1
3.65
Q2
33.8
Q3
11.1
Q4
51.5
FL4-H :: FL4-H
FL2-H :: FL2-H
A
Q1
1.54
Q2
11.2
Q3
3.78
Q4
83.5
FL4-H :: FL4-H
FL2-H :: FL2-H
B
Q1
0
Q2
0.043
Q3
0.45
Q4
99.5
FL4-H :: FL4-H
FL2-H :: FL2-H
C

**Figure 27**

Ai CAASGFTFS syams WVRQAPGKG
(SEQ ID NO: 327)
Aii CAASGFTFS XX CPRILMRCKQDSDCLAGCVCGPNGFCG XX
WVRQAPGKG(SEQ ID NO: 328)

Bi PGKGLEWVS aisgsggstyyadsvkg RFTISRDNT
(SEQ ID NO: 329)
Bii PGKGLEWVS XX CPRILMRCKQDSDCLAGCVCGPNGFCG XX RFTISRDNT
(SEQ ID NO: 330)

Ci DTAFYYCVD fgpgygtgwfdy WGPGTLVTV
(SEQ ID NO: 331)
Cii DTAFYYCVD XX CPRILMRCKQDSDCLAGCVCGPNGFCG XX WGPGTLVTV
(SEQ ID NO: 332)

Di VGDRVTITC rasqsissyln WYQQKPGKA
(SEQ ID NO: 333)
Dii VGDRVTITC XX CPRILMRCKQDSDCLAGCVCGPNGFCG XX
WYQQKPGKA(SEQ ID NO: 334)

Ei KAPKLLIHD asslqs GVPSRFSGS
(SEQ ID NO: 335)
Eii KAPKLLIHD XX CPRILMRCKQDSDCLAGCVCGPNGFCG XX GVPSRFSGS
(SEQ ID NO: 336)

Fi PEDFATYYC qqsfsiplt FGGGTKMDI
(SEQ ID NO: 337)
Fii PEDFATYYC XX CPRILMRCKQDSDCLAGCVCGPNGFCG XX FGGGTKMDI
(SEQ ID NO: 338)

Gi APKLLIYAA GV CPRILMRCKQDSDCLAGCVCGPNGFCG SR SGVPSRFS
(SEQ ID NO: 339)
Gii APKLLIYAA XX CPRILMRCKQDSDCLAGCVCGPNGFCG XX SGVPSRFS
(SEQ ID NO: 340)

**Figure 28**

```
tgcggtccgaacggcttctgcggaagcggcagcgatggcggtgtgtgcccgcgtatcctg
 C  G  P  N  G  F  C  G  S  G  S  D  G  G  V  C  P  R  I  L
   ______LOOP5___>   <______LOOP6___________>    <__LOOP1___
atgcgttgcaaacaggactcagactgcctggccggctgc(SEQ ID NO: 341)
 M  R  C  K  Q  D  S  D  C  L  A  G  C(SEQ ID NO: 342)
_____>    <___LOOP2____>   <_LOOP3_>
```

Figure 29A

```
i  RVTITCsgs          ssnignna                    vNWYQQLP
(SEQ ID 343)
ii RVTITCxxx - CGPNGFCGSGSDGGVCPRILMRCKQDSDCLAGC X xNWYQQLP
iiiRVTITCgxx X CGPNGFCGSGSDGGVCPRILMRCKQDSDCLAGC X xNWYQQLP
(SEQ IDs 344 and 345)

iv KLLIY                  ydd                     llpSGVSDRFS
(SEQ ID NOS: 346)
v  KLLIY AAZ x CGPNGFCGSGSDGGVCPRILMRCKQDSDCLAGC gxxSGVSDRFS
(SEQ ID 347)
```

Figure 29B

```
Nhe1
gctagccagtctgtgctgactcagccaccctcggtgtctgaagcccccaggcagagggtc
 A  S  Q  S  V  L  T  Q  P  P  S  V  S  E  A  P  R  Q  R  V
       ←-----------------------FW1----------------------

      Pml1
accatcacgtgtvnsvnsvnstgcggtccgaacggcttctgcggaagcggcagcgatggc
 T  I  T  C  X  X  X  C  G  P  N  G  F  C  G  S  G  S  D  G
----------→          ←---------EETI-II-----------------

ggtgtgtgcccgcgtatcctgatgcgttgcaaacaggactcagactgcctggccggctgc
 G  V  C  P  R  I  L  M  R  C  K  Q  D  S  D  C  L  A  G  C
-------------------------------------------------------→
      Mfe 1                                          Not1
vnsvncaattggtaccagcagctcccagga ←-Vlambda library->
gcggccgc(SEQ ID NO: 348)
 X  X  N  W  Y  Q  Q  L  P  G  (SEQ ID NO: 349)
       I----FW2----------→
```

Figure 29C

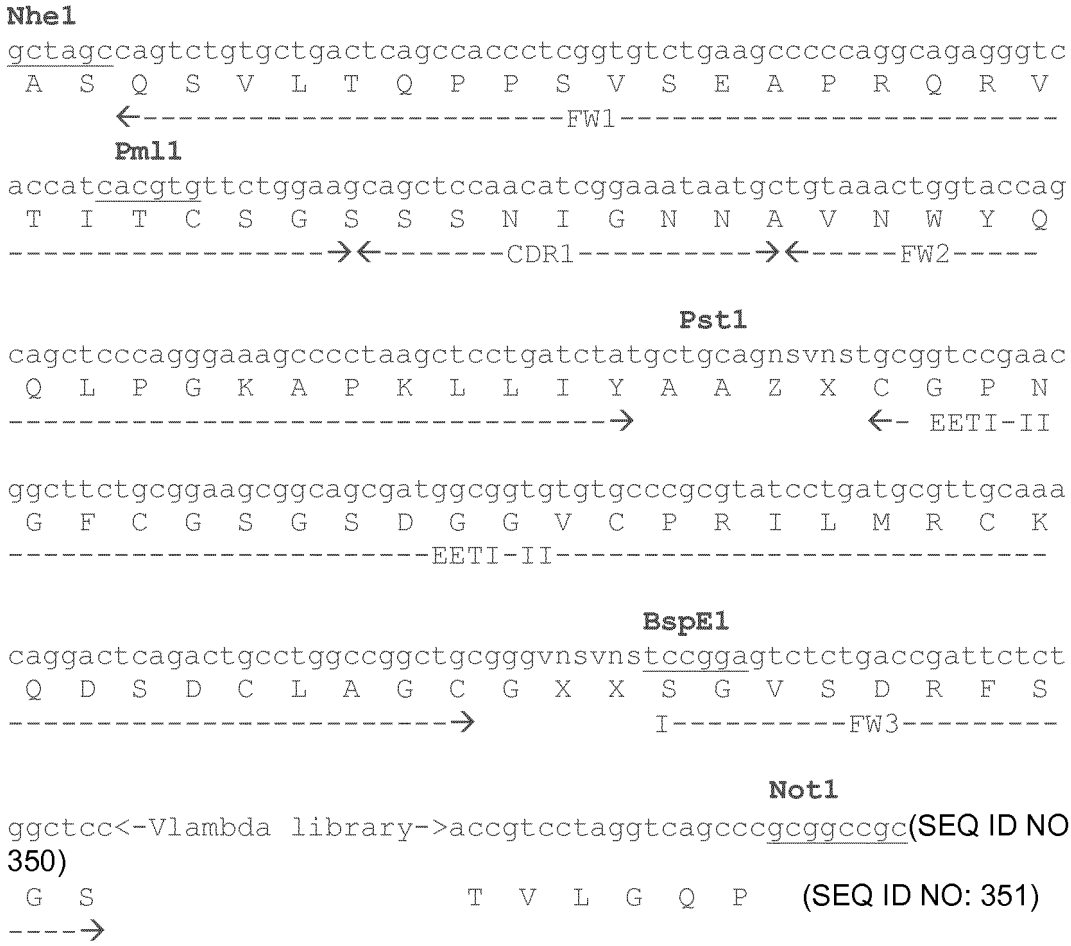

Nhe1
gctagccagtctgtgctgactcagccaccctcggtgtctgaagcccccaggcagagggtc
A S Q S V L T Q P P S V S E A P R Q R V
←-----------FW1-----------
Pml1
accatcacgtgttctggaagcagctccaacatcggaaataatgctgtaaactggtaccag
T I T C S G S S S N I G N N A V N W Y Q
----------→←-------CDR1----------→←-----FW2-----
Pst1
cagctcccagggaaagcccctaagctcctgatctatgctgcagnsvnstgcggtccgaac
Q L P G K A P K L L I Y A A Z X C G P N
----------→ ←- EETI-II
ggcttctgcggaagcggcagcgatggcggtgtgtgcccgcgtatcctgatgcgttgcaaa
G F C G S G S D G G V C P R I L M R C K
----------EETI-II----------
BspE1
caggactcagactgcctggccggctgcgggvnsvnstccggagtctctgaccgattctct
Q D S D C L A G C G X X S G V S D R F S
----------→ I----------FW3---------
Not1
ggctcc<-Vlambda library->accgtcctaggtcagcccgcggccgc(SEQ ID NO: 350)
G S T V L G Q P (SEQ ID NO: 351)
----→

Figure 29D

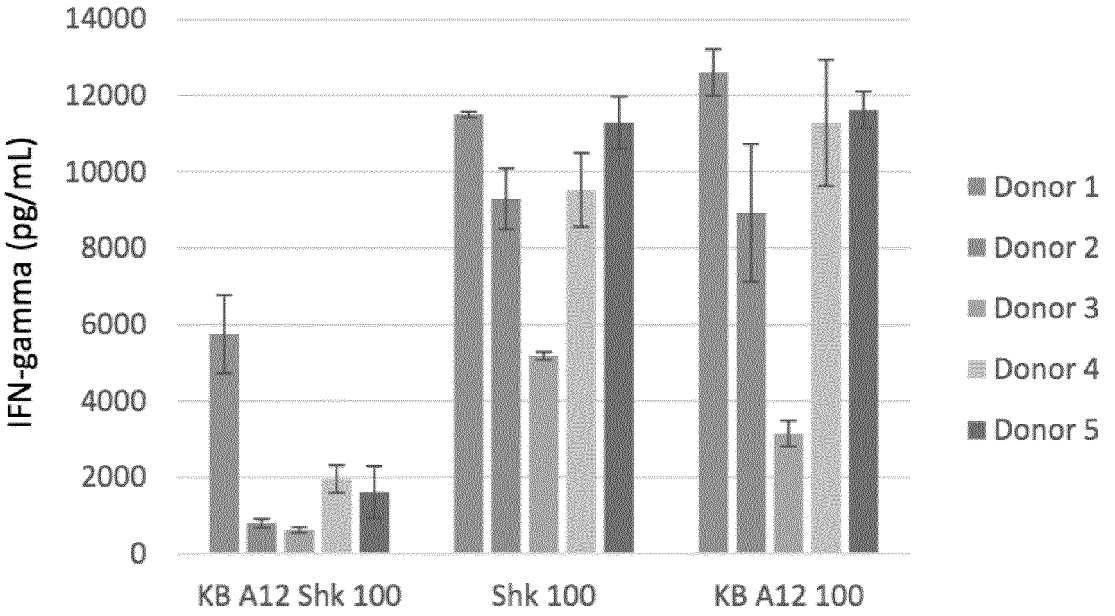



Figure 30A

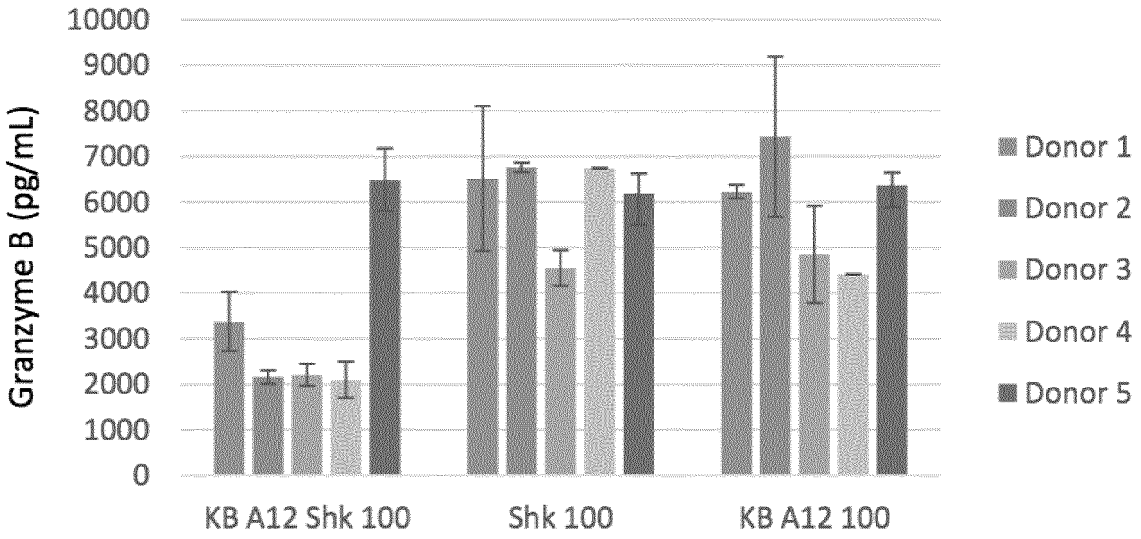



Figure 30B

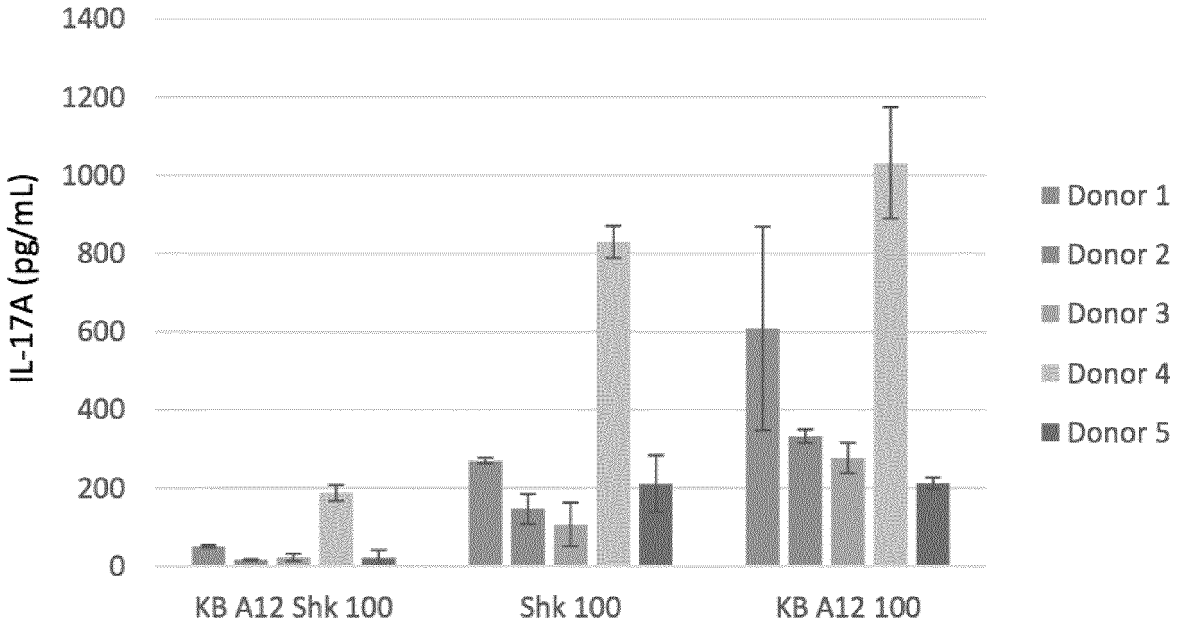



Figure 30C

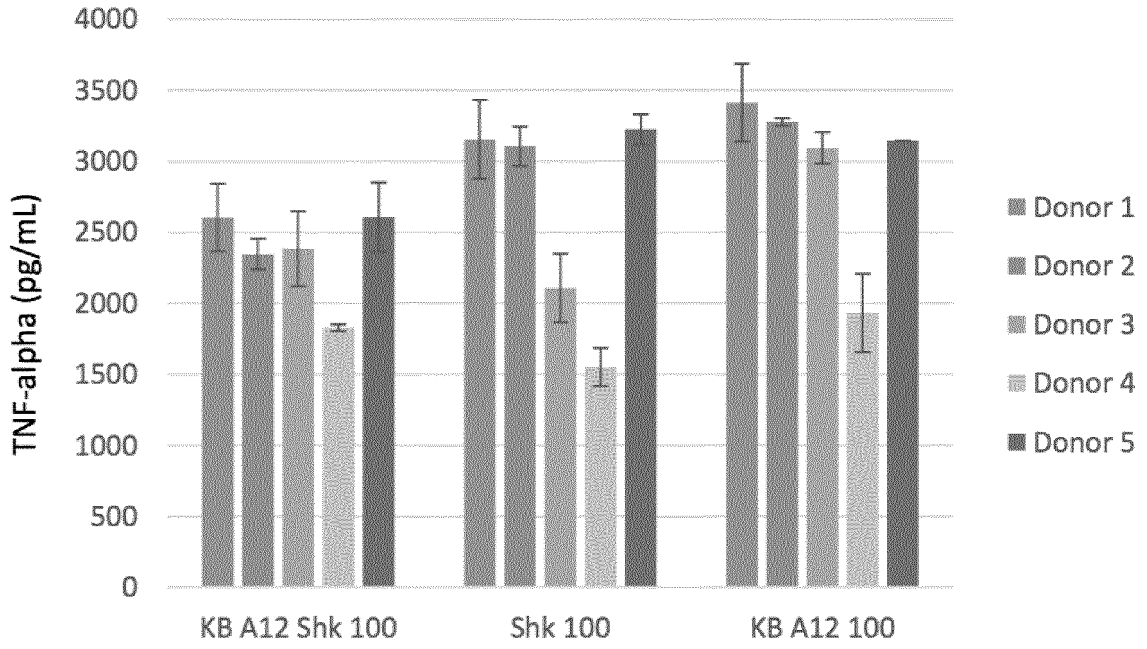



Figure 30D