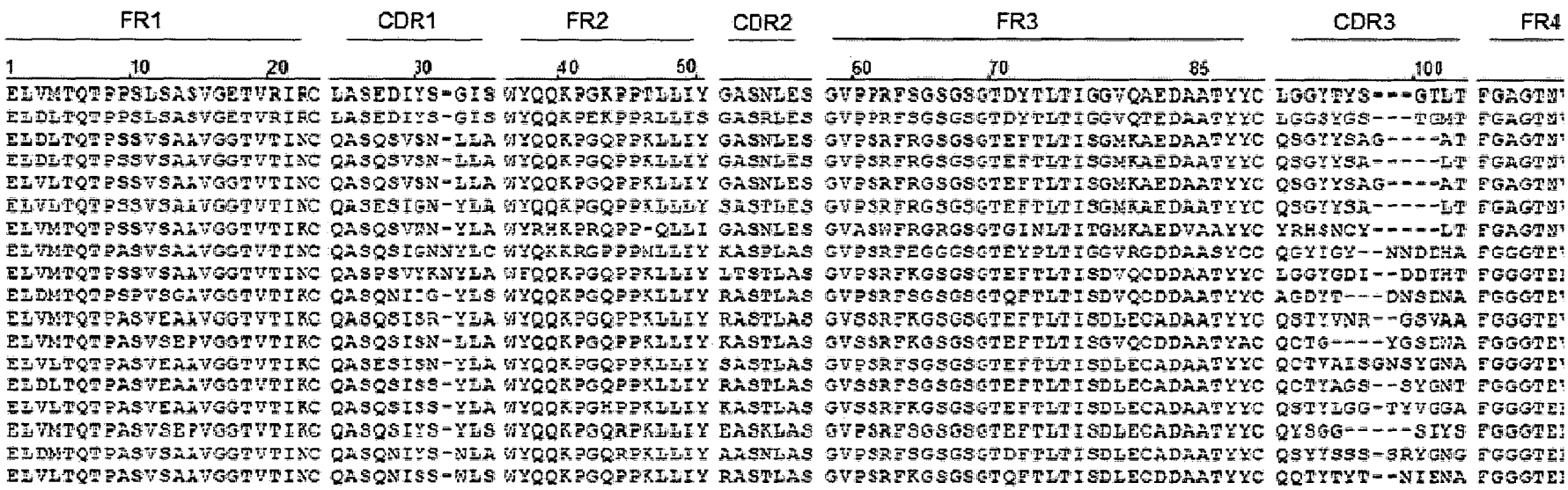

FR1
CDR1
FR2
CDR2
FR3
CDR3
FR4
1 10 20 30 40 50 60 70 85 100
VL100 ELVMTQTPPSLSASVGETVRITC LASEDIYS-GIS WYQQKPGKPPTLLIY GASNLES GVPPRFSGSGSGTDYTLTIGGVQAEDAATYYC LGGYTYS---GTLT FGAGTN
VL94 ELDLTQTPPSLSASVGETVRITC LASEDIYS-GIS WYQQKPEKPPRLLIS GASRLES GVPPRFSGSGSGTDYTLTIGGVQTEDAATYYC LGGSYGS---TGMT FGAGTN
VL121 ELDLTQTPSSVSAAVGGTVTINC QASQSVSN-LLA WYQQKPGQPPKLLIY GASNLES GVPSRFRGSGSGTEFTLTISGMKAEDAATYYC QSGYYSAG----AT FGAGTN
VL89 ELDLTQTPSSVSAAVGGTVTINC QASQSVSN-LLA WYQQKPGQPPKLLIY GASNLES GVPSRFRGSGSGTEFTLTISGMKAEDAATYYC QSGYYSA-----LT FGAGTN
VL88 ELVLTQTPSSVSAAVGGTVTINC QASQSVSN-LLA WYQQKPGQPPKLLIY GASNLES GVPSRFRGSGSGTEFTLTISGMKAEDAATYYC QSGYYSAG----AT FGAGTN
VL12A ELVLTQTPSSVSAAVGGTVTINC QASESIGN-YLA WYQQKPGQPPKLLIY SASTLES GVPSRFRGSGSGTEFTLTISGMKAEDAATYYC QSGYYSA-----LT FGAGTN
VL91 ELVMTQTPSSVSAAVGGTVTIKC QASQSVWN-YLA WYRHKPRQPP-QLLI GASNLES GVASWFRGRGSGTGINLTITGMKAEDVAAYYC YRHSNCY-----LT FGAGTN
VL109 ELVMTQTPASVSAAVGGTVTINC QASQSIGNNYLC WYQKKRGPPPMLLIY KASPLAS GVPSRFEGGGSGTEYPLTIGGVRGDDAASYCC QGYIGY--NNDIHA FGGGTE
VL89-3 ELVMTQTPSSVSAAVGGTVTINC QASPSVYKNYLA WFQQKPGQPPKLLIY LTSTLAS GVPSRFKGSGSGTEFTLTISDVQCDDAATYYC LGGYGDI--DDIHT FGGGTE
VL152 ELDMTQTPSPVSGAVGGTVTIKC QASQNIIG-YLS WYQQKPGQPPKLLIY RASTLAS GVPSRFSGSGSGTQFTLTISDVQCDDAATYYC AGDYT---DNSINA FGGGTE
VL11 ELVMTQTPASVEAAVGGTVTIKC QASQSISR-YLA WYQQKPGQPPKLLIY RASTLAS GVSSRFKGSGSGTEFTLTISDLECADAATYYC QSIYVNR--GSVAA FGGGTE
VL78 ELVMTQTPASVSEPVGGTVTIKC QASQSISN-LLA WYQQKPGQPPKLLIY KASTLAS GVSSRFKGSGSGTEFTLTISGVQCDDAATYAC QCTG----YGSINA FGGGTE
VL115 ELVLTQTPASVEAAVGGTVTIKC QASESISN-YLA WYQQKPGQPPKLLIY SASTLAS GVPSRFSGSGSGTEFTLTISDLECADAATYYC QCTYAISGNSYGNA FGGGTE
VL141 ELDLTQTPASVEAAVGGTVTIKC QASQSISS-YLA WYQQKPGQPPKLLIY RASTLAS GVSSRFSGSGSGTEFTLTISDLECADAATYYC QCTYAGS--SYGNT FGGGTE
VL18 ELVLTQTPASVEAAVGGTVTIKC QASQSISS-YLA WYQQKPGHPPKLLIY KASTLAS GVSSRFKGSGSGTEFTLTISDLECADAATYYC QSTYLGG-TYVGGA FGGGTE
VL137 ELVMTQTPASVSEPVGGTVTIKC QASQSIYS-YLS WYQQKPGQRPKLLIY EASKLAS GVPSRFSGSGSGTEFTLTISDLECADAATYYC QYSGG-----SIYS FGGGTE
VL74 ELDMTQTPASVSAAVGGTVTINC QASQNIYS-NLA WYQQKPGQRPKLLIY AASNLAS GVPSRFSGSGSGTDFTLTISDLECADAATYYC QSYYSSS-SRYGNG FGGGTE
VL76 ELVLTQTPASVSAAVGGTVTINC QASQNISS-WLS WYQQKPGQPPKLLIY RASTLAS GVPSRFKGSGSGTQFTLTISDLECDDAATYYC QQTYTYT--NIENA FGGGTE

FIG. 1

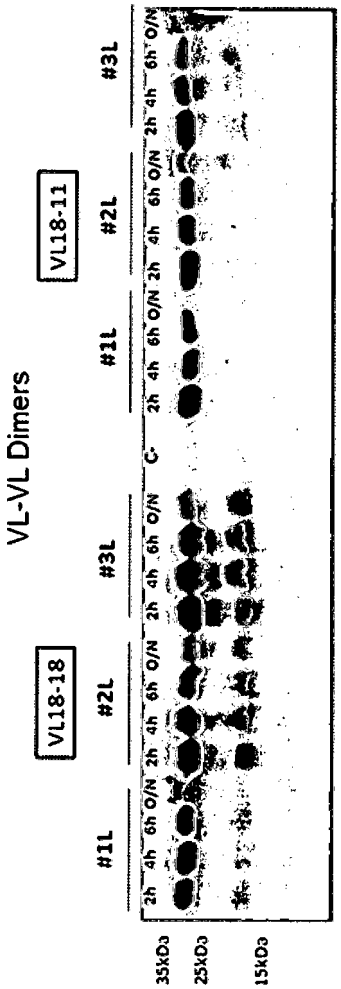


FIG. 2A

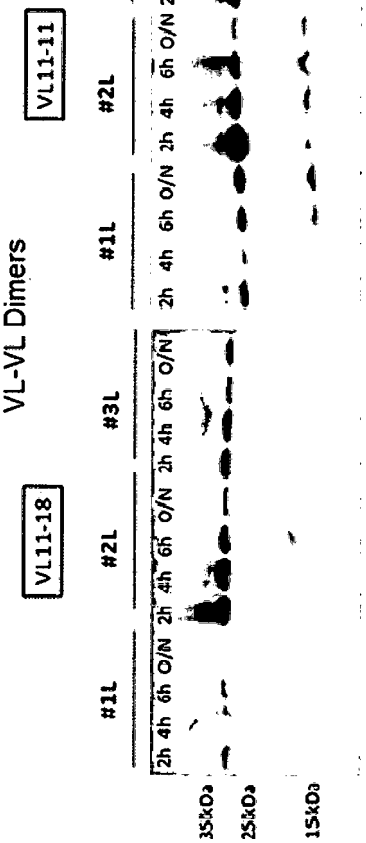


FIG. 2B

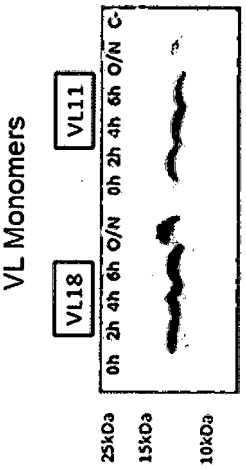


FIG. 2C

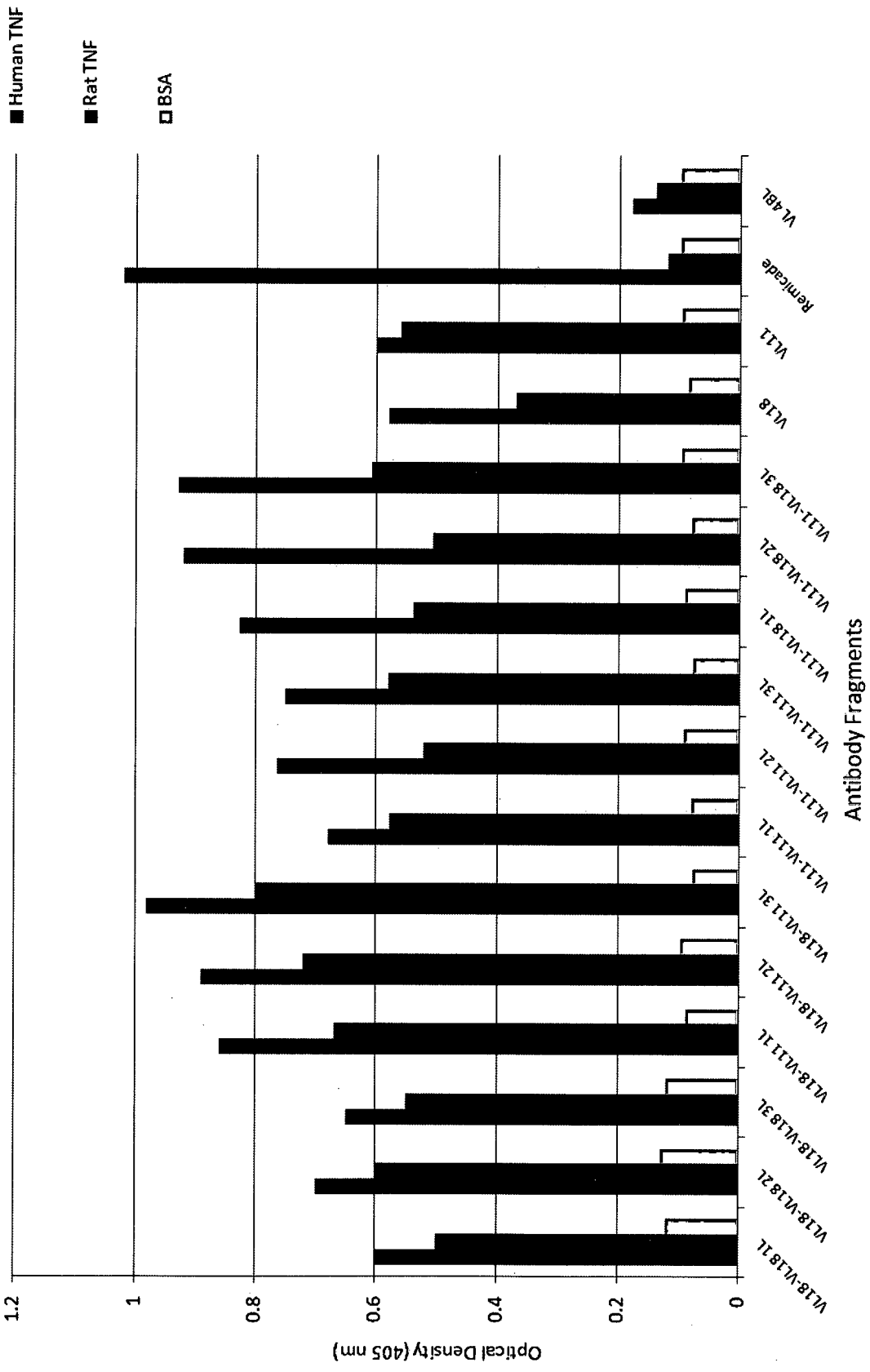

Human TNF
Rat TNF
BSA
Optical Density (405 nm)
1.2
1
0.8
0.6
0.4
0.2
0
Antibody Fragments
VL18-VL18.1L
VL18-VL18.2L
VL18-VL18.3L
VL18-VL11.1L
VL18-VL11.2L
VL18-VL11.3L
VL11-VL11.1L
VL11-VL11.2L
VL11-VL11.3L
VL11-VL18.1L
VL11-VL18.2L
VL11-VL18.3L
VL18
VL11
Remicade
VL4BL

FIG. 2D

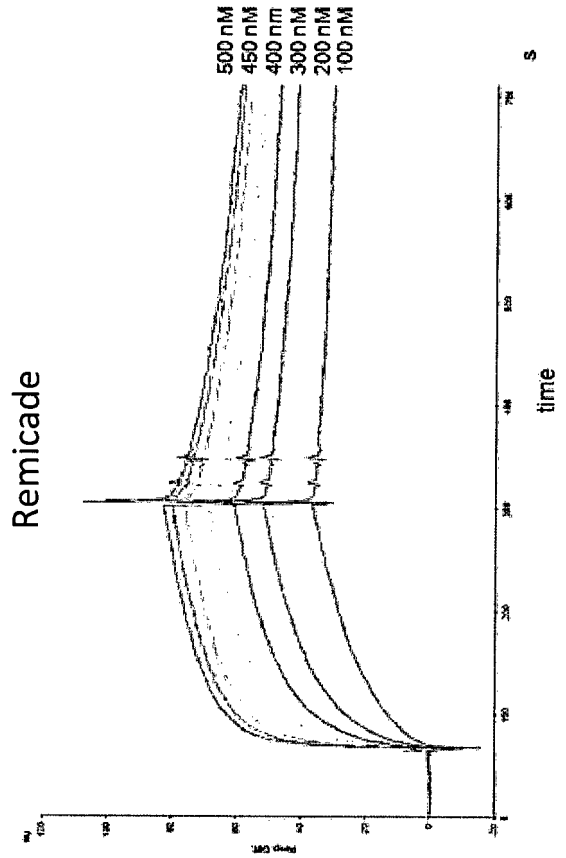

Remicade
500 nM
450 nM
400 nm
300 nM
200 nM
100 nM
time
S

FIG. 3B

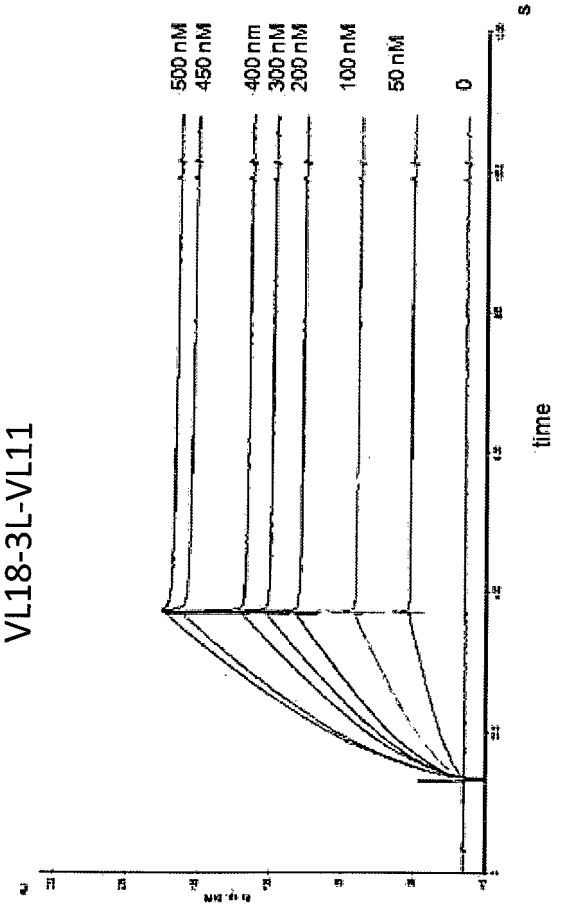

VL18-3L-VL11
500 nM
450 nM
400 nm
300 nM
200 nM
100 nM
50 nM
0
time
S

FIG. 3A

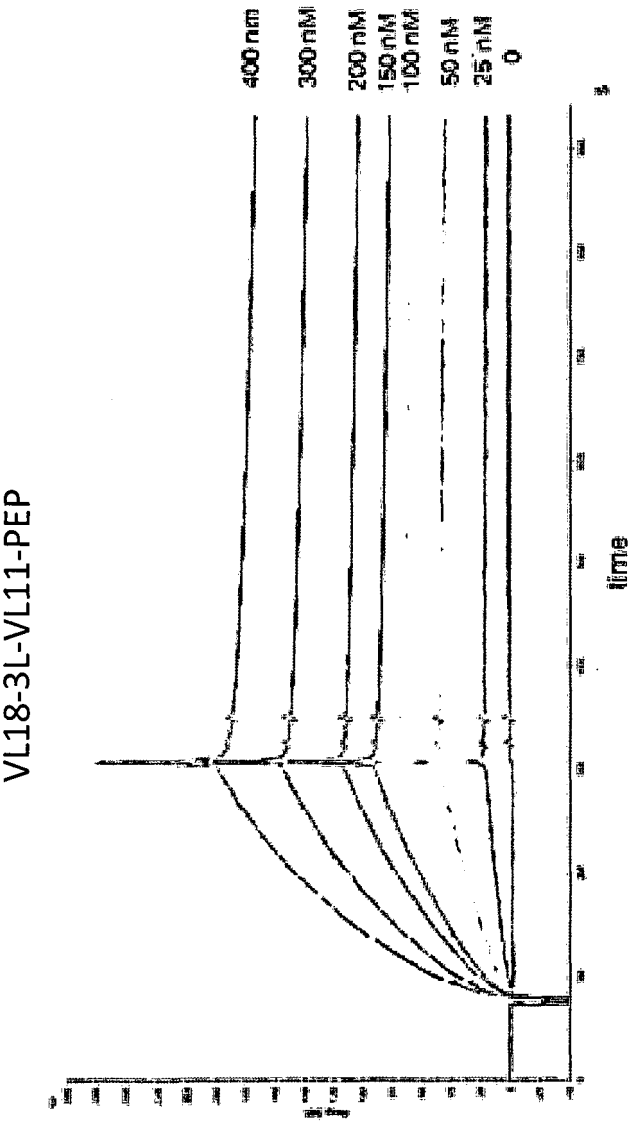

VL18-3L-VL11-PEP
400 nM
300 nM
200 nM
150 nM
100 nM
50 nM
25 nM
0
time

FIG. 3C

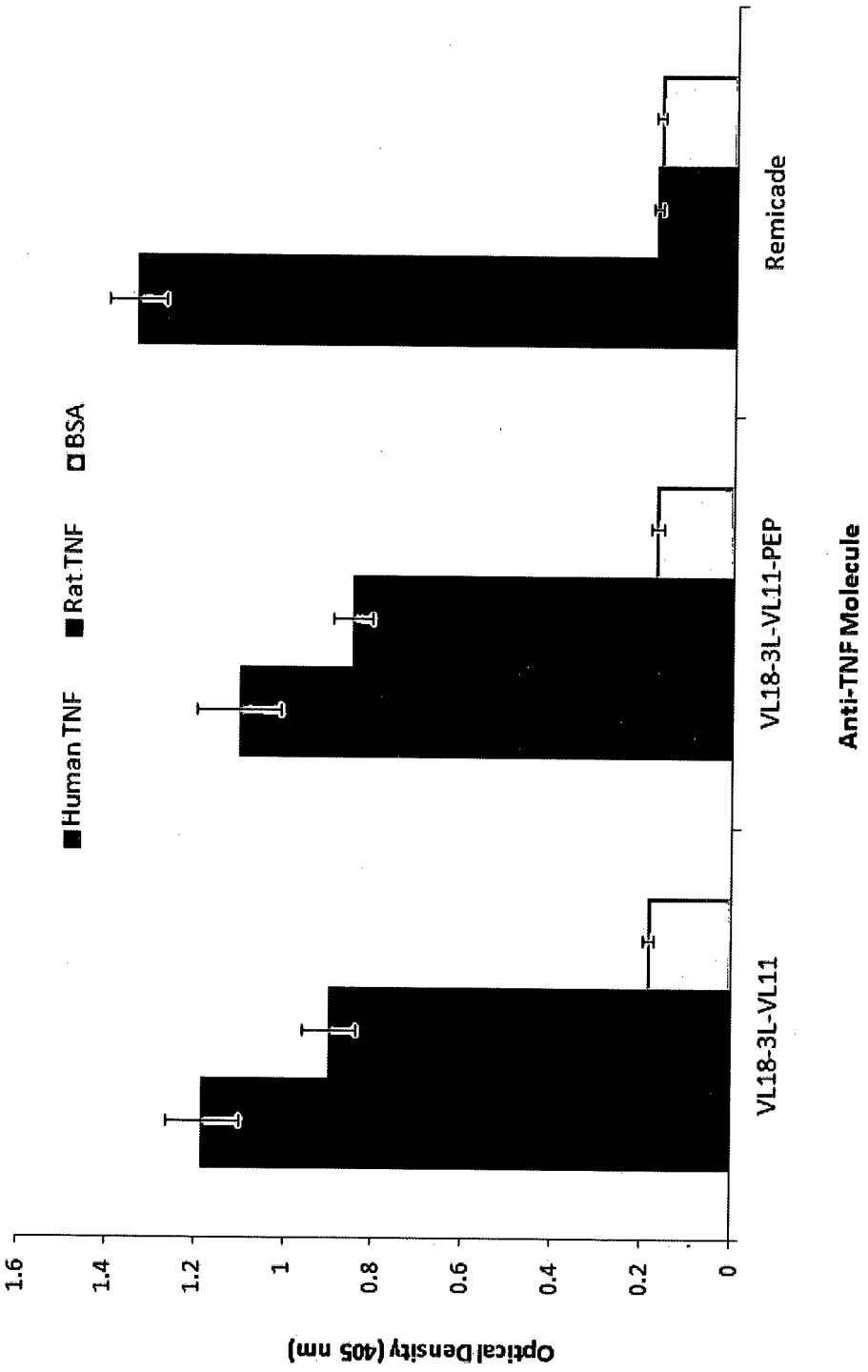

Optical Density (405 nm)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Human TNF
Rat TNF
BSA
VL18-3L-VL11
VL18-3L-VL11-PEP
Remicade
Anti-TNF Molecule

FIG. 3D

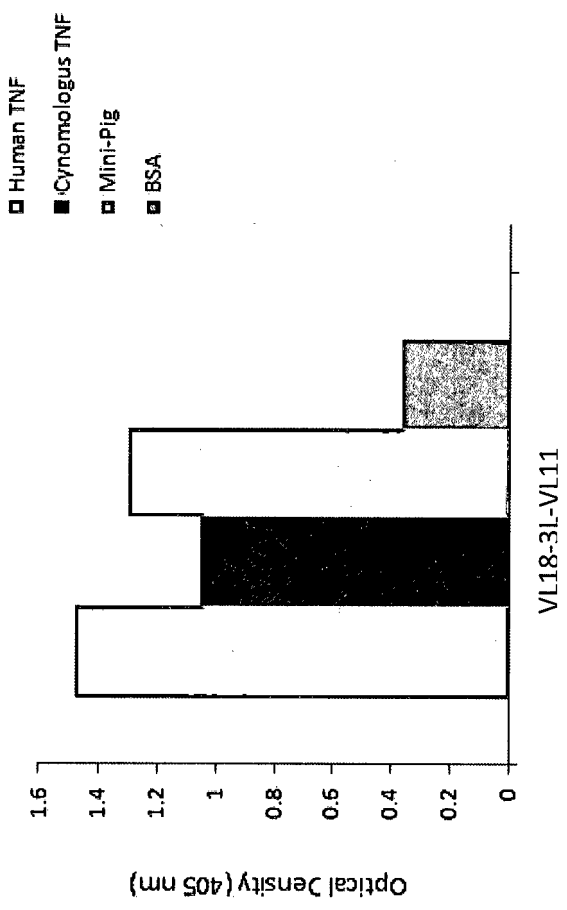

Human TNF
Cynomologus TNF
Mini-Pig
BSA
Optical Density (405 nm)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
VL18-3L-VL11

FIG. 3E

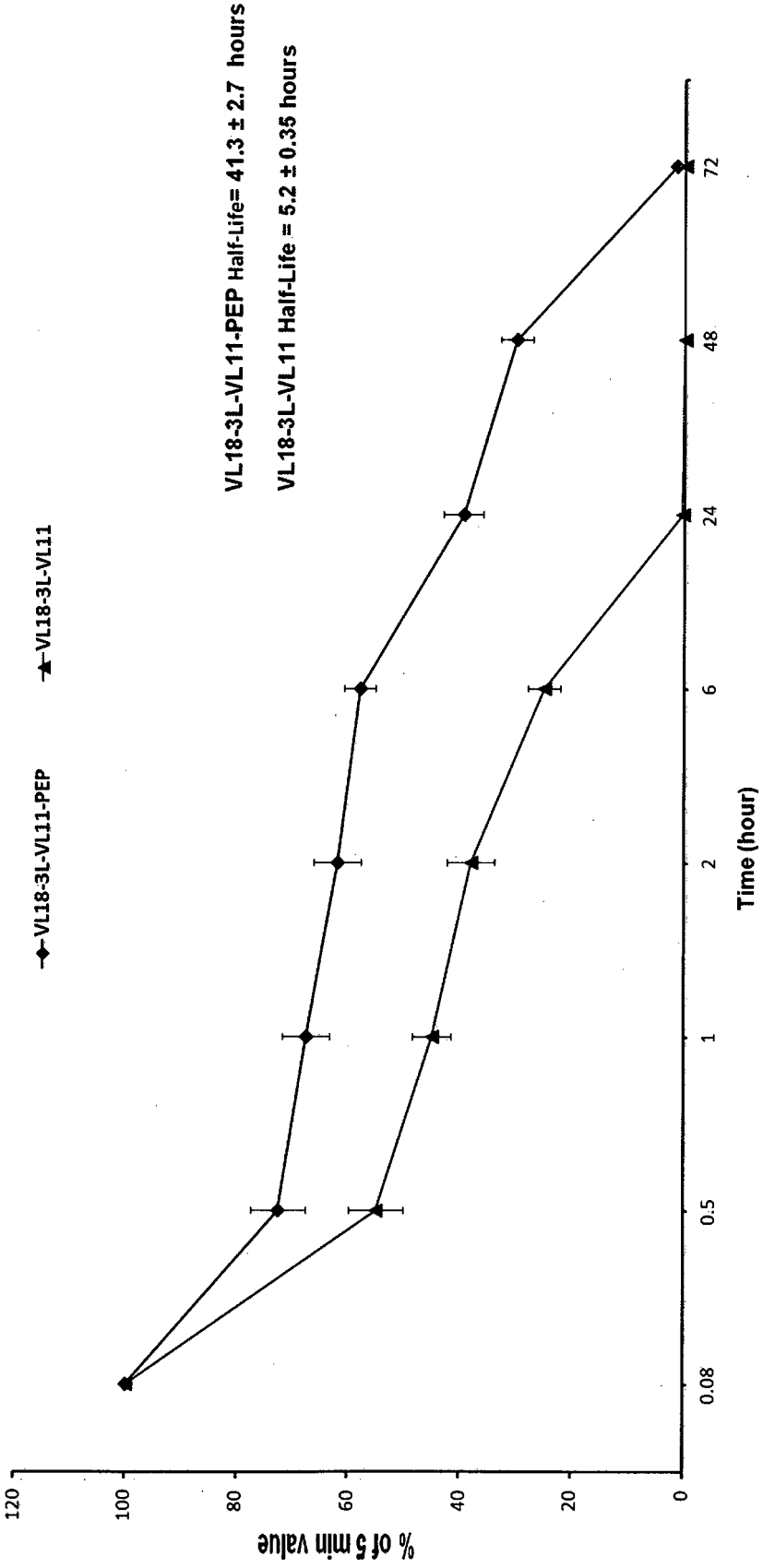

VL18-3L-VL11-PEP Half-Life= 41.3 ± 2.7 hours
VL18-3L-VL11 Half-Life = 5.2 ± 0.35 hours
VL18-3L-VL11-PEP
VL18-3L-VL11
% of 5 min value
Time (hour)
120
100
80
60
40
20
0
0.08
0.5
1
2
6
24
48
72

FIG. 3F

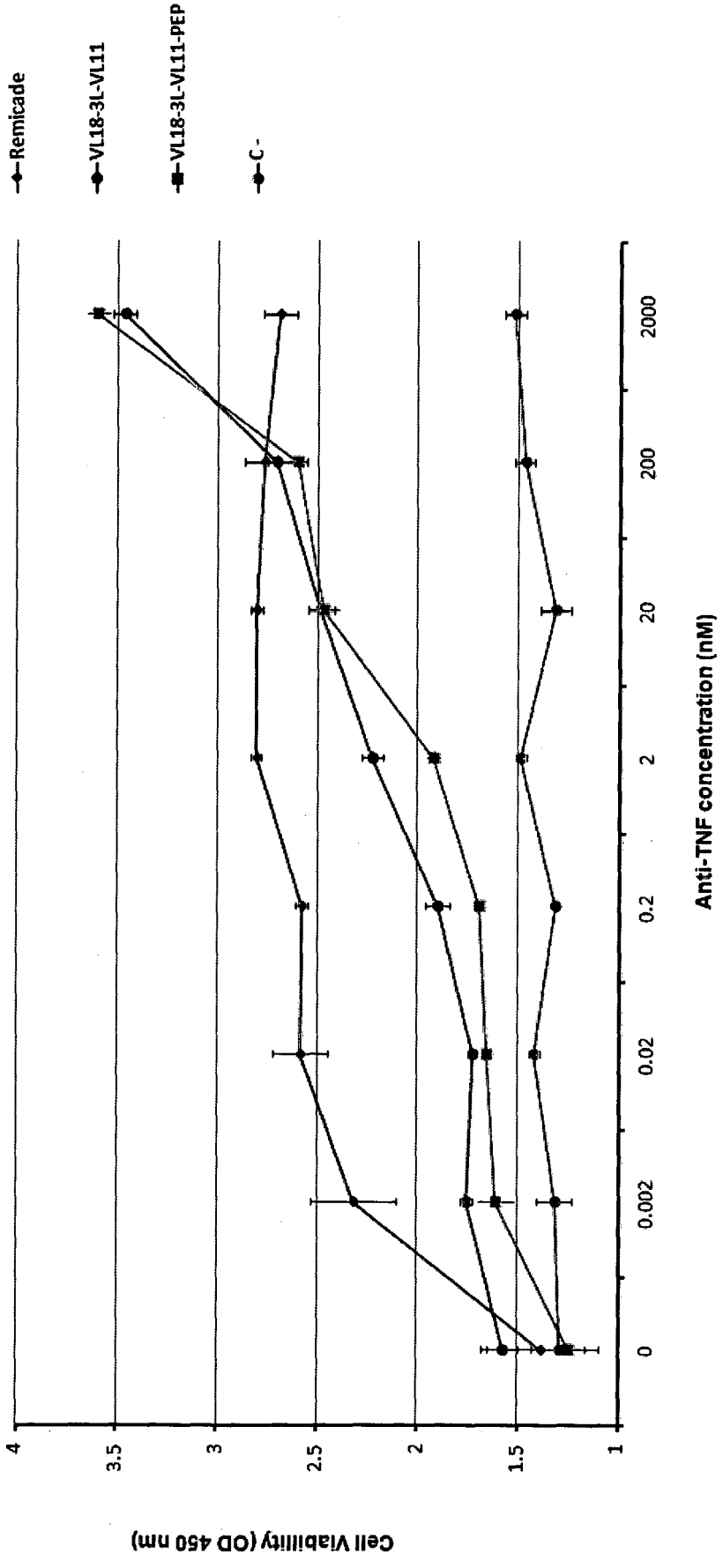

Remicade
VL18-3L-VL11
VL18-3L-VL11-PEP
C-
Cell Viability (OD 450 nm)
4
3.5
3
2.5
2
1.5
1
0
0.002
0.02
0.2
2
20
200
2000
Anti-TNF concentration (nM)

FIG. 4

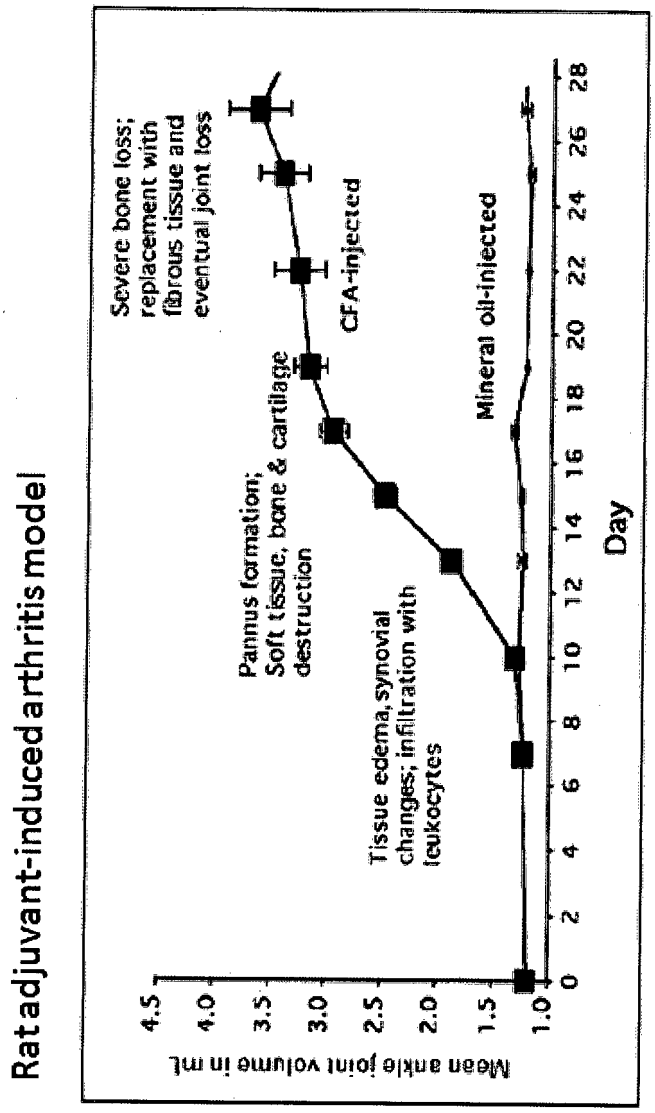

Rat adjuvant-induced arthritis model
Mean ankle joint volume in mL
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Day
Severe bone loss; replacement with fibrous tissue and eventual joint loss
Pannus formation; Soft tissue, bone & cartilage destruction
Tissue edema, synovial changes; infiltration with leukocytes
CFA-injected
Mineral oil-injected

FIG. 5

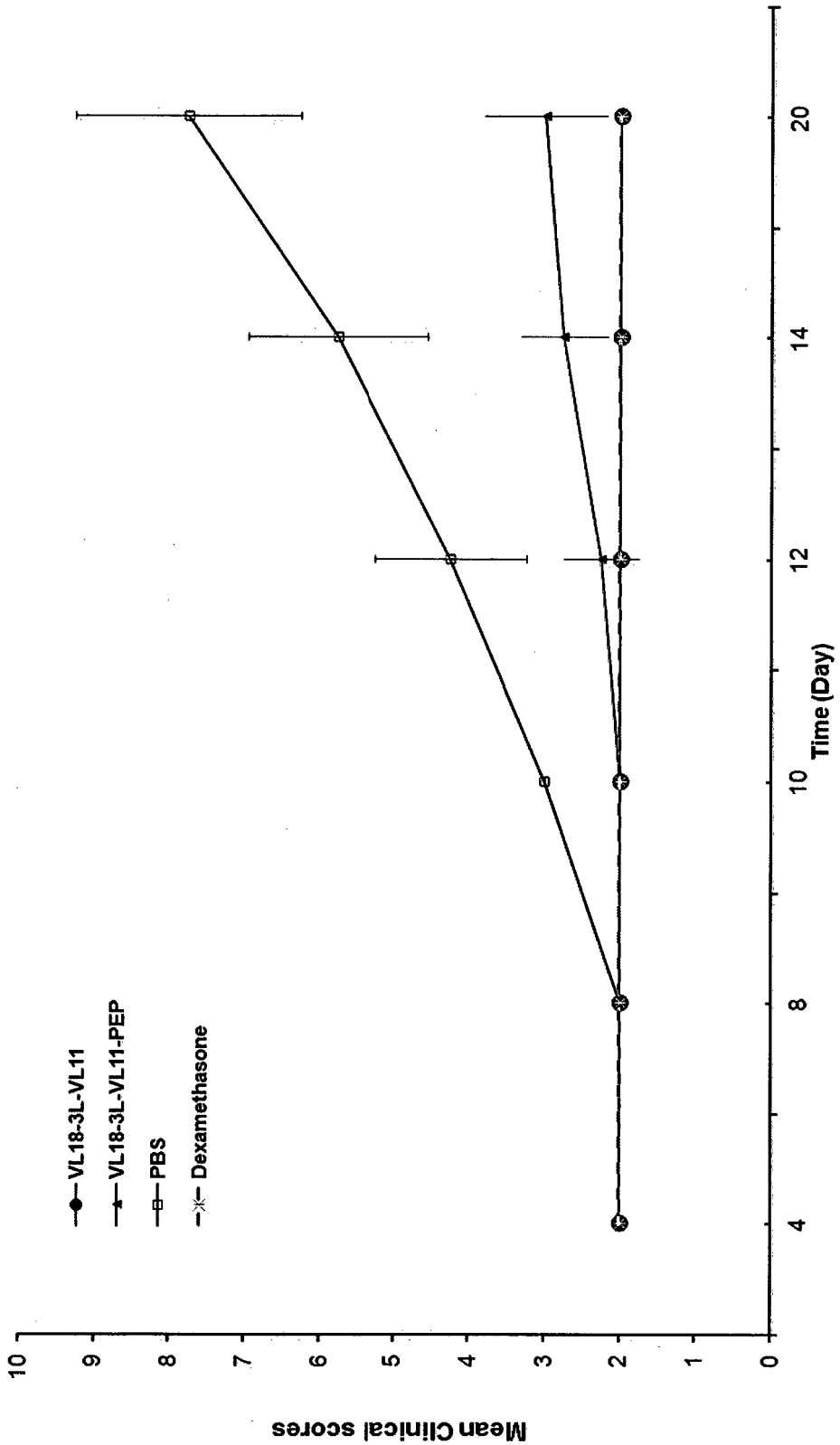

Mean Clinical scores
Time (Day)
VL18-3L-VL11
VL18-3L-VL11-PEP
PBS
Dexamethasone
0
1
2
3
4
5
6
7
8
9
10
4
8
10
12
14
20

FIG. 6

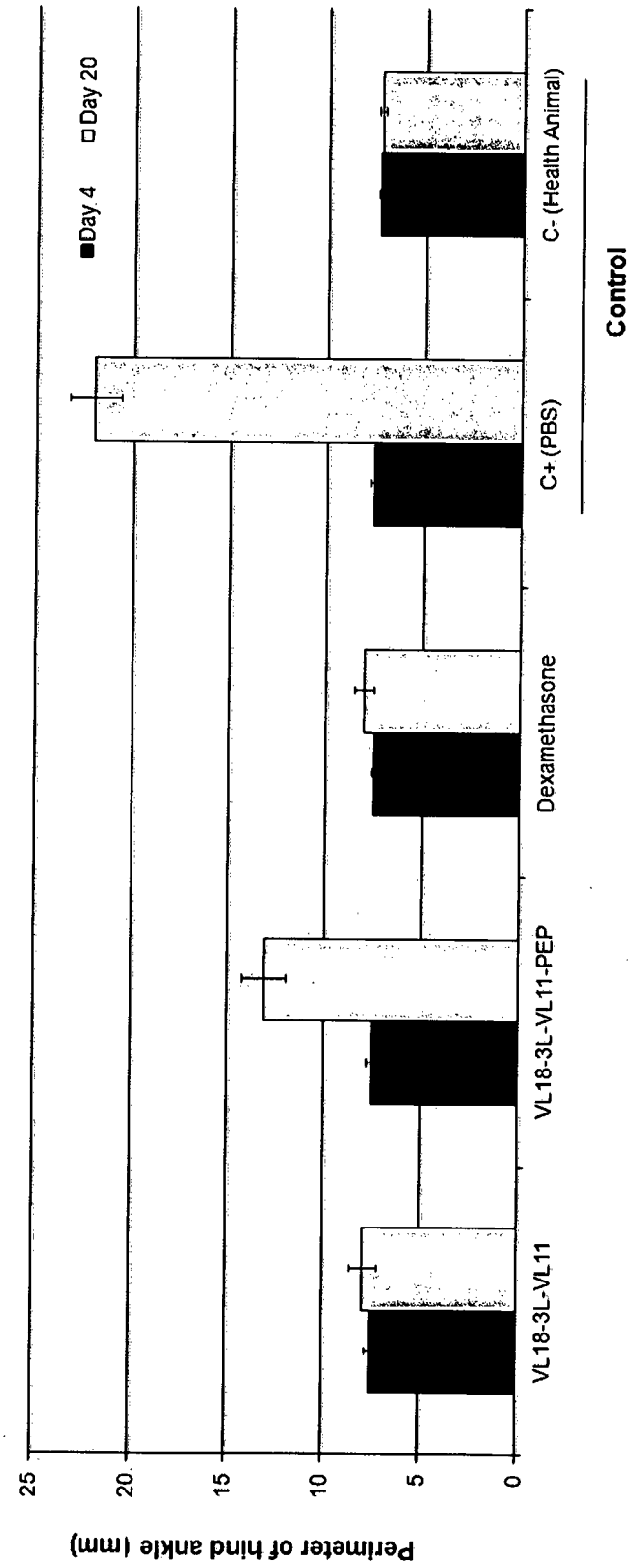

Perimeter of hind ankle (mm)
25
20
15
10
5
0
Day 4
Day 20
VL18-3L-VL11
VL18-3L-VL11-PEP
Dexamethasone
C+ (PBS)
C- (Health Animal)
Control

FIG. 7

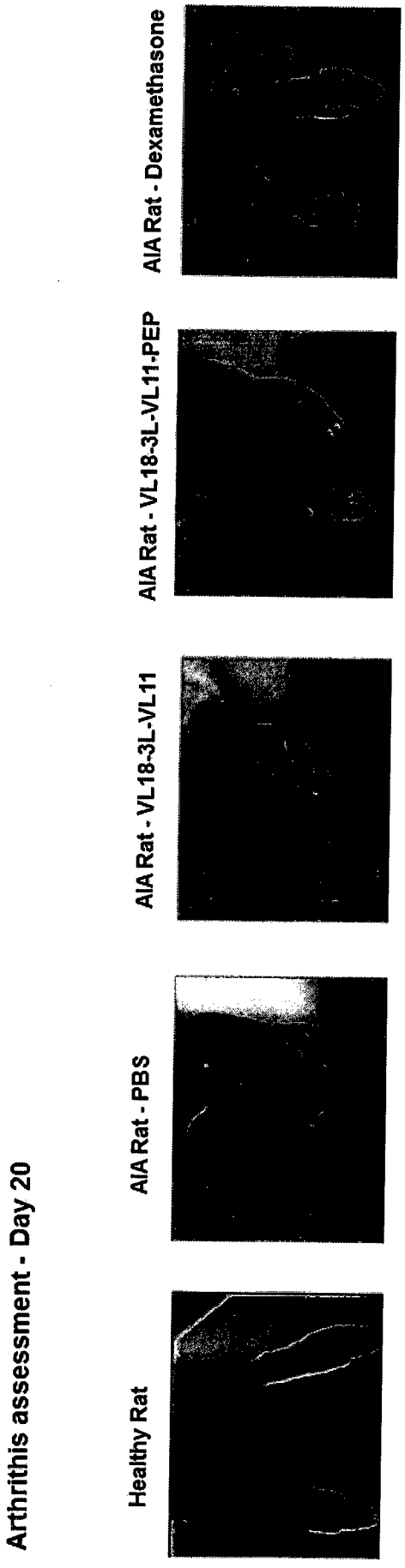


FIG. 8A FIG. 8B FIG. 8C FIG. 8D FIG. 8E

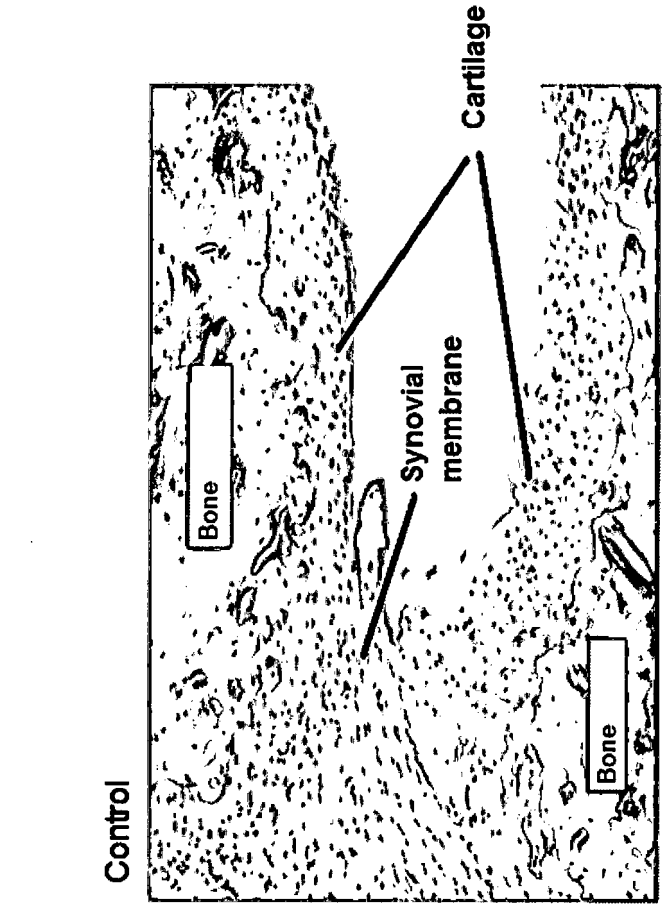

Control
Bone
Synovial membrane
Cartilage
Bone

FIG. 9B

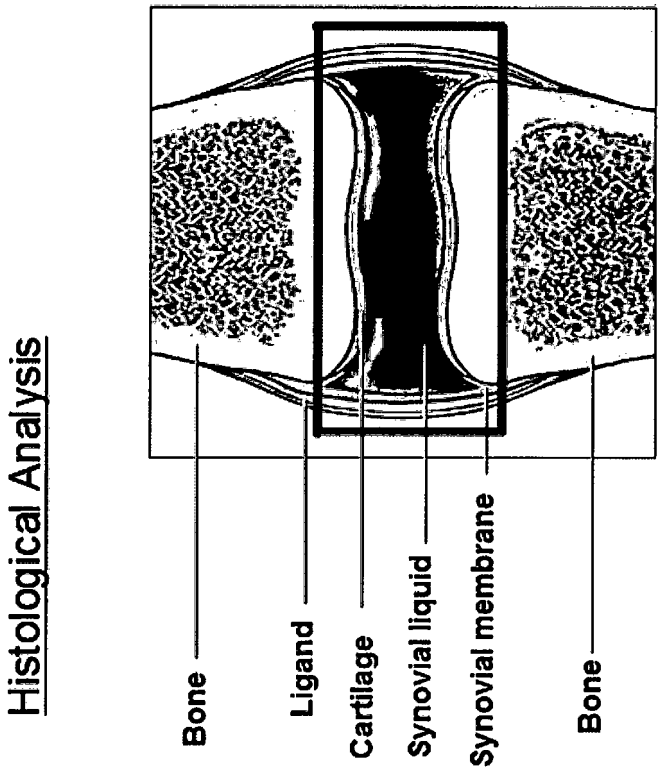

Histological Analysis
Bone
Ligand
Cartilage
Synovial liquid
Synovial membrane
Bone

FIG. 9A

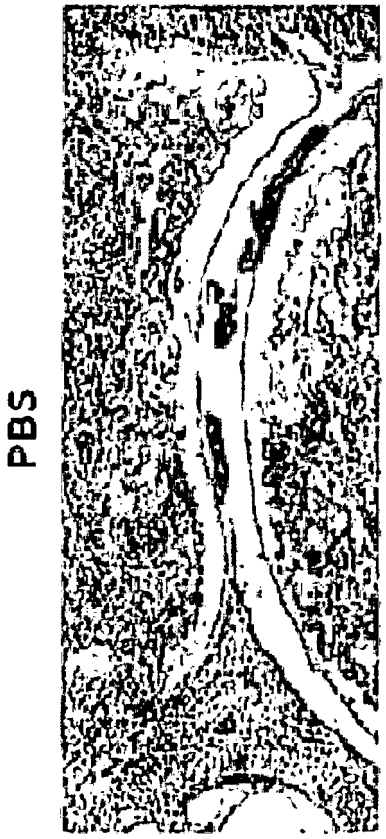


FIG. 9D

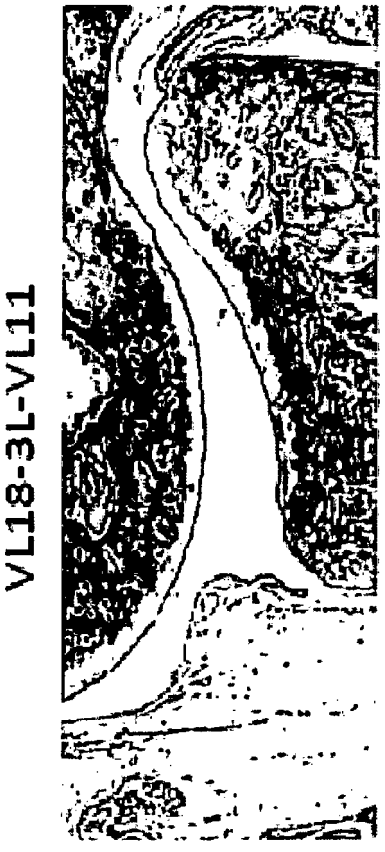


FIG. 9C

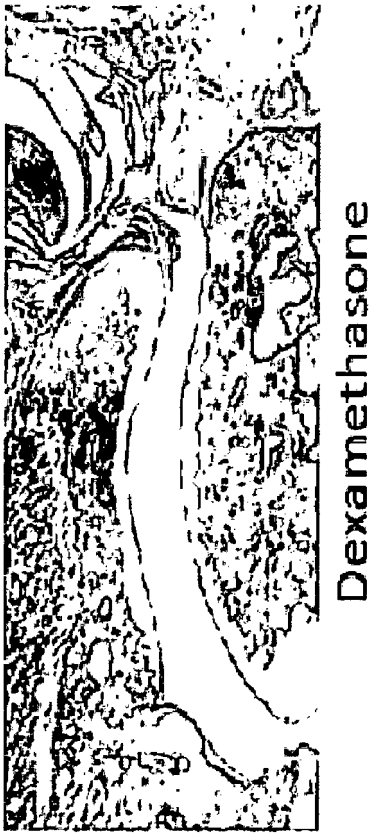


FIG. 9F

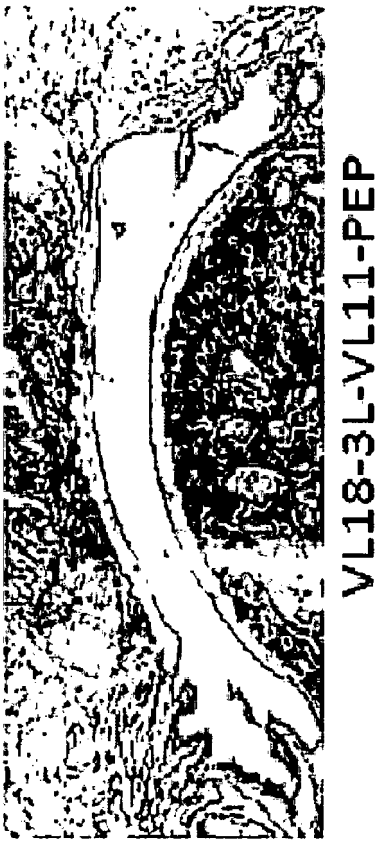


FIG. 9E



FIG. 10A



FIG. 10B

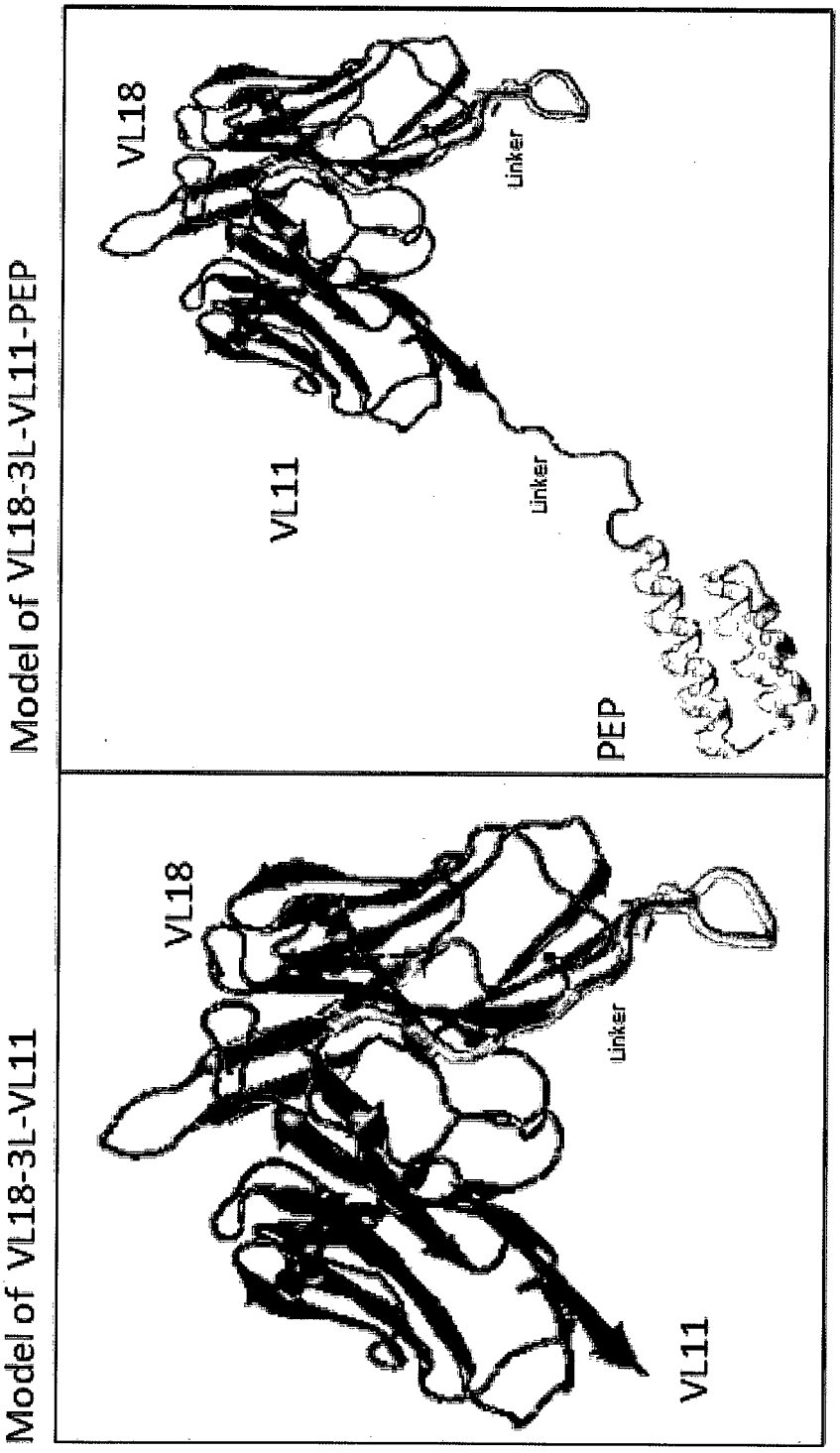


FIG. 11A

FIG 11B

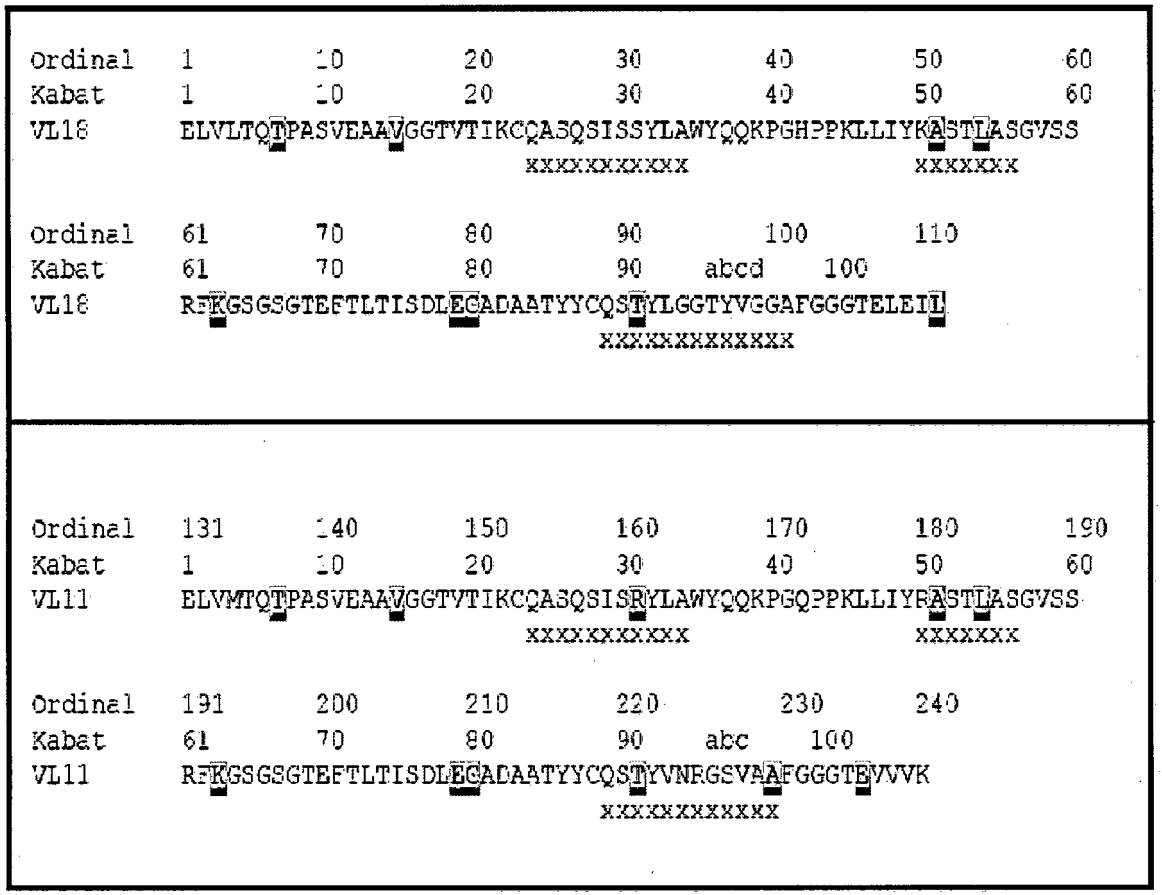


FIG. 12A

FIG. 12B

```
pep
Ordinal    250       260       270       280       290       300
pep        DITGAALLEAKEAAINELKQYGISDYYVELINKAKTVEGVNALKAEILSALP
```

FIG. 12C

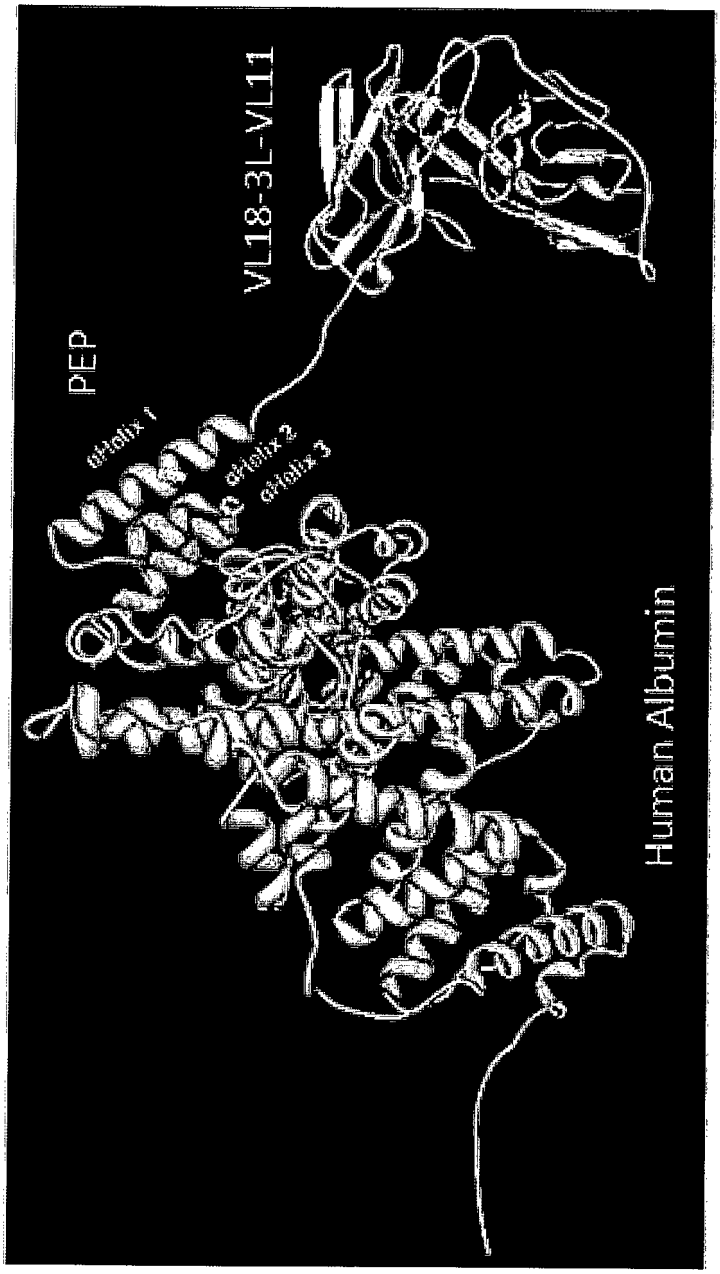


FIG. 13

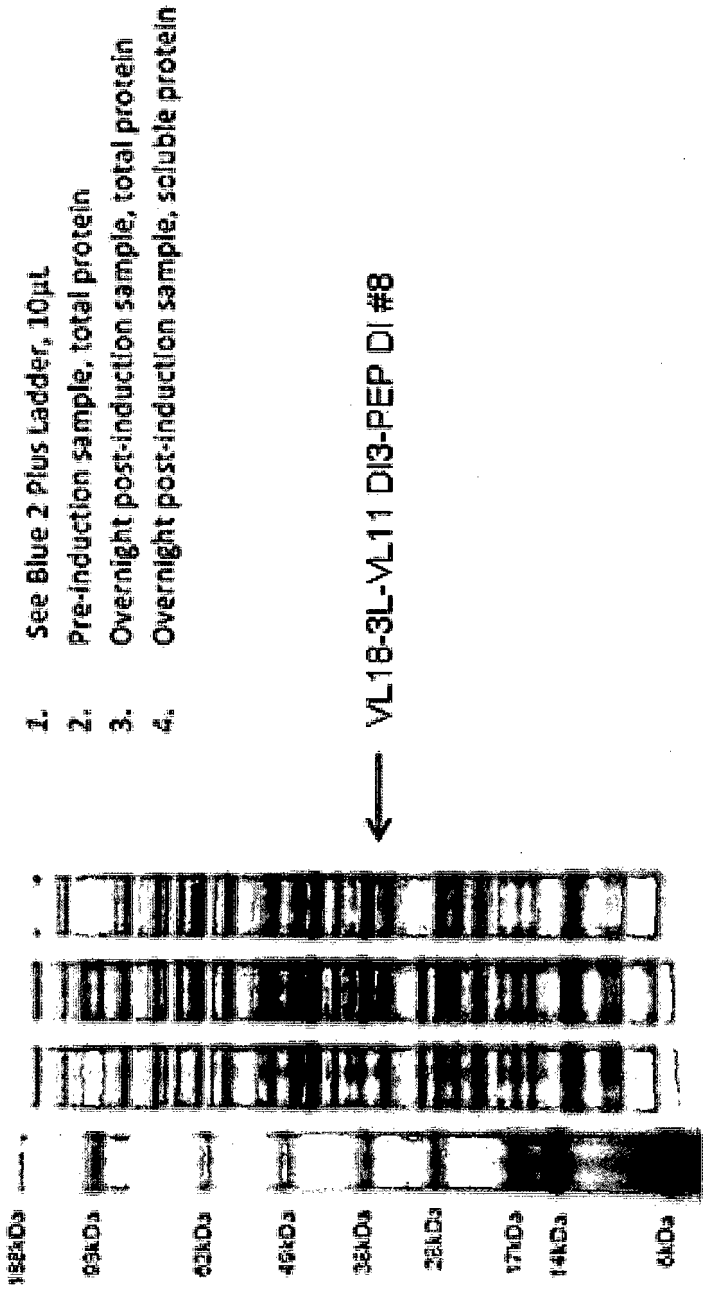

1. See Blue 2 Plus Ladder, 10µL
2. Pre-induction sample, total protein
3. Overnight post-induction sample, total protein
4. Overnight post-induction sample, soluble protein
VL18-3L-VL11 DI3-PEP DI #8
1 2 3 4
188kDa
98kDa
62kDa
49kDa
38kDa
28kDa
17kDa
14kDa
6kDa

FIG. 14

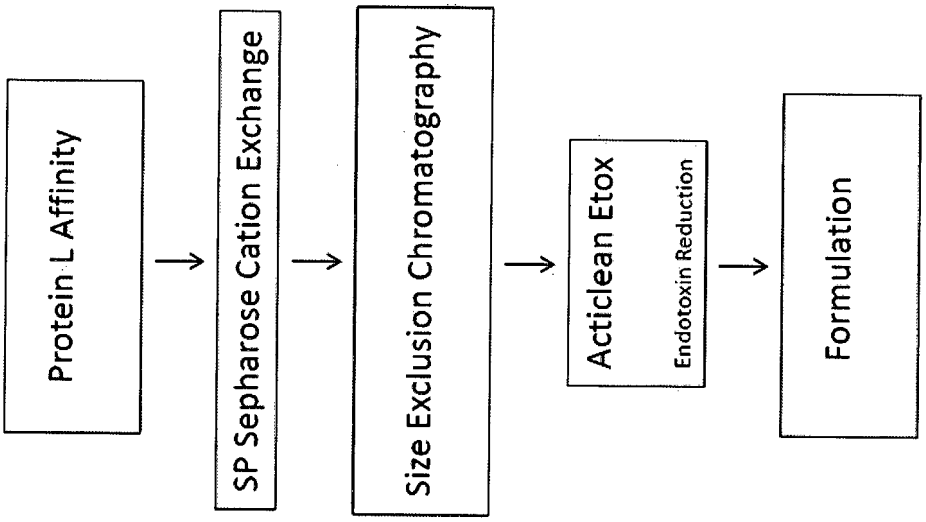
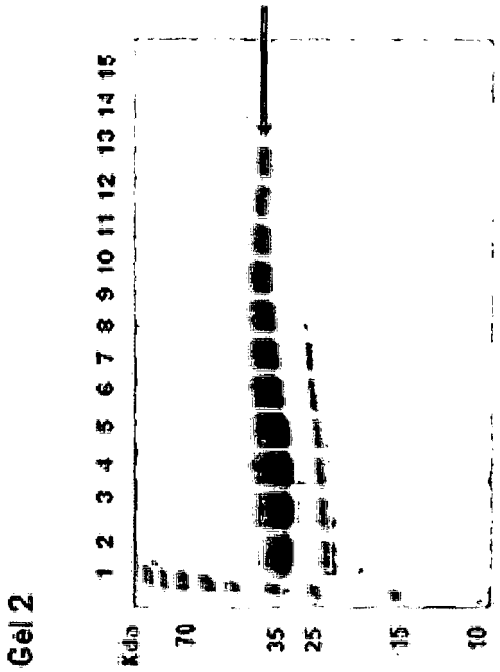

Protein L Affinity
SP Sepharose Cation Exchange
Size Exclusion Chromatography
Acticlean Etox
Endotoxin Reduction
Formulation

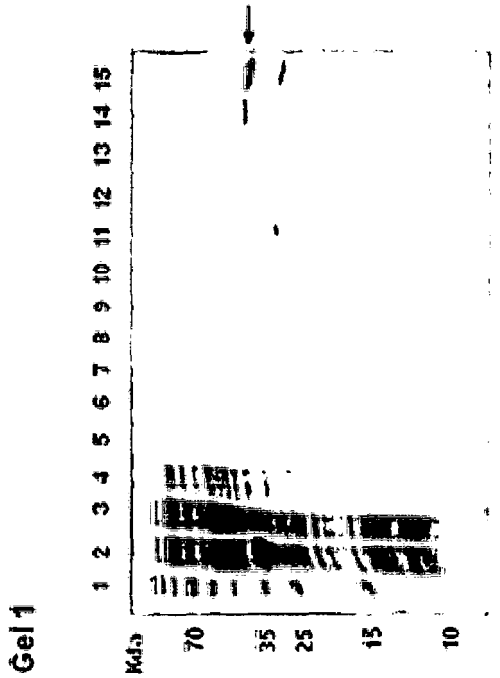
FIG. 15A



Gel 2 - SDS-PAGE coomassie Legend

Lane 1 – Marker
Lane 2 – Elution 22
Lane 3 – Elution 23
Lane 4 – Elution 24
Lane 5 – Elution 25
Lane 6 – Elution 26
Lane 7 – Elution 27
Lane 8 – Elution 28
Lane 9 – Elution 29
Lane 10 – Elution 30
Lane 11 – Elution 31
Lane 12 – Elution 32
Lane 13 – Elution 33
Lane 14 – Elution 34
Lane 14 – Elution 38

FIG. 15C



Gel 1 - SDS-PAGE coomassie Legend

Lane 1 – Marker
Lane 2 – Soluble Lysate = Protein Load
Lane 3 – Flow Through
Lane 4 – Wash 1
Lane 5 – Wash 2
Lane 6 – Wash 4
Lane 7 – Wash 6
Lane 8 – Wash 8
Lane 9 – Wash 10
Lane 10 – Elution 1
Lane 11 – Elution 3
Lane 12 – Elution 5
Lane 13 – Elution 7
Lane 14 – Elution 9
Lane 15 – Elution 10

FIG. 15B

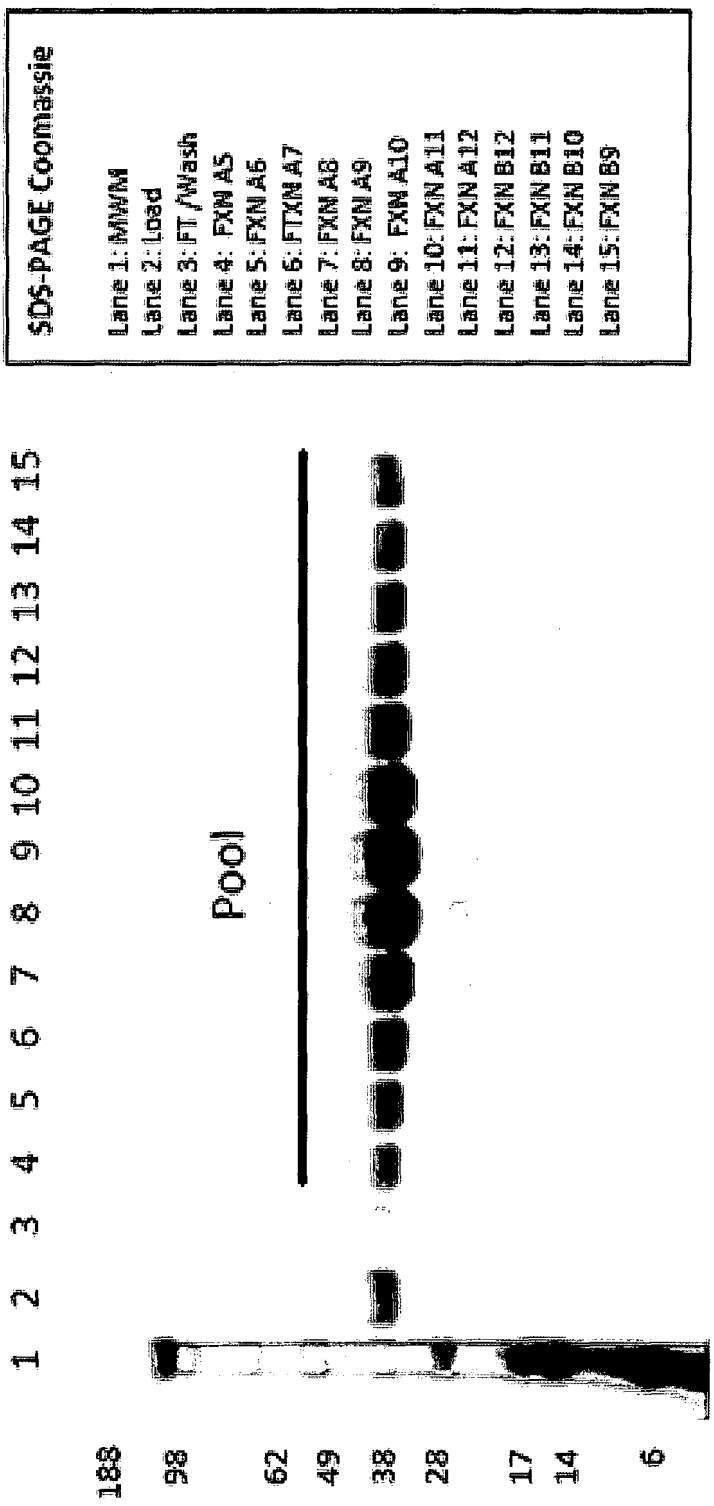

SDS-PAGE Coomassie
Lane 1: MWM
Lane 2: Load
Lane 3: FT /Wash
Lane 4: FXN A5
Lane 5: FXN A6
Lane 6: FTXN A7
Lane 7: FXN A8
Lane 8: FXN A9
Lane 9: FXN A10
Lane 10: FXN A11
Lane 11: FXN A12
Lane 12: FXN B12
Lane 13: FXN B11
Lane 14: FXN B10
Lane 15: FXN B9
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Pool
188
98
62
49
38
28
17
14
6

FIG. 15D

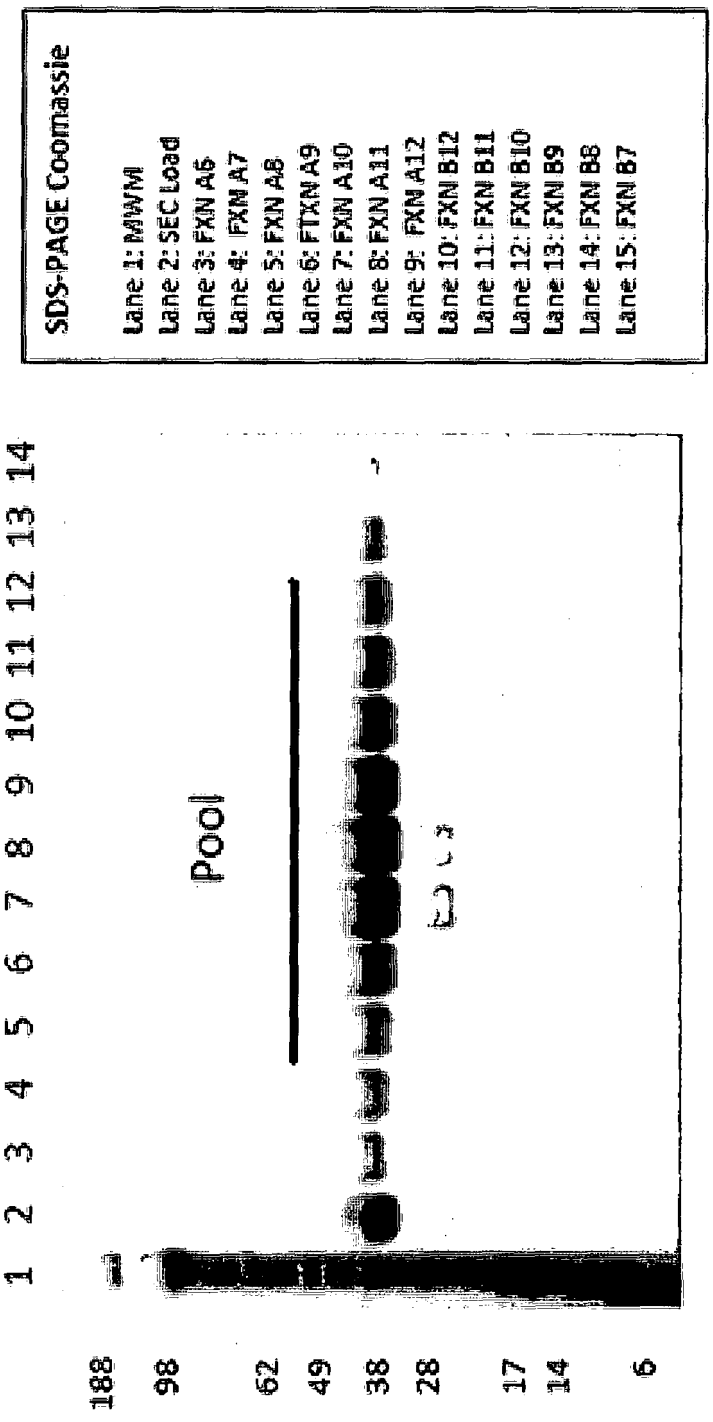

SDS-PAGE Coomassie
Lane 1: MWM
Lane 2: SEC Load
Lane 3: FXN A6
Lane 4: FXN A7
Lane 5: FXN A8
Lane 6: FTXN A9
Lane 7: FXN A10
Lane 8: FXN A11
Lane 9: FXN A12
Lane 10: FXN B12
Lane 11: FXN B11
Lane 12: FXN B10
Lane 13: FXN B9
Lane 14: FXN B8
Lane 15: FXN B7
1 2 3 4 5 6 7 8 9 10 11 12 13 14
Pool
188
98
62
49
38
28
17
14
6

FIG. 15E

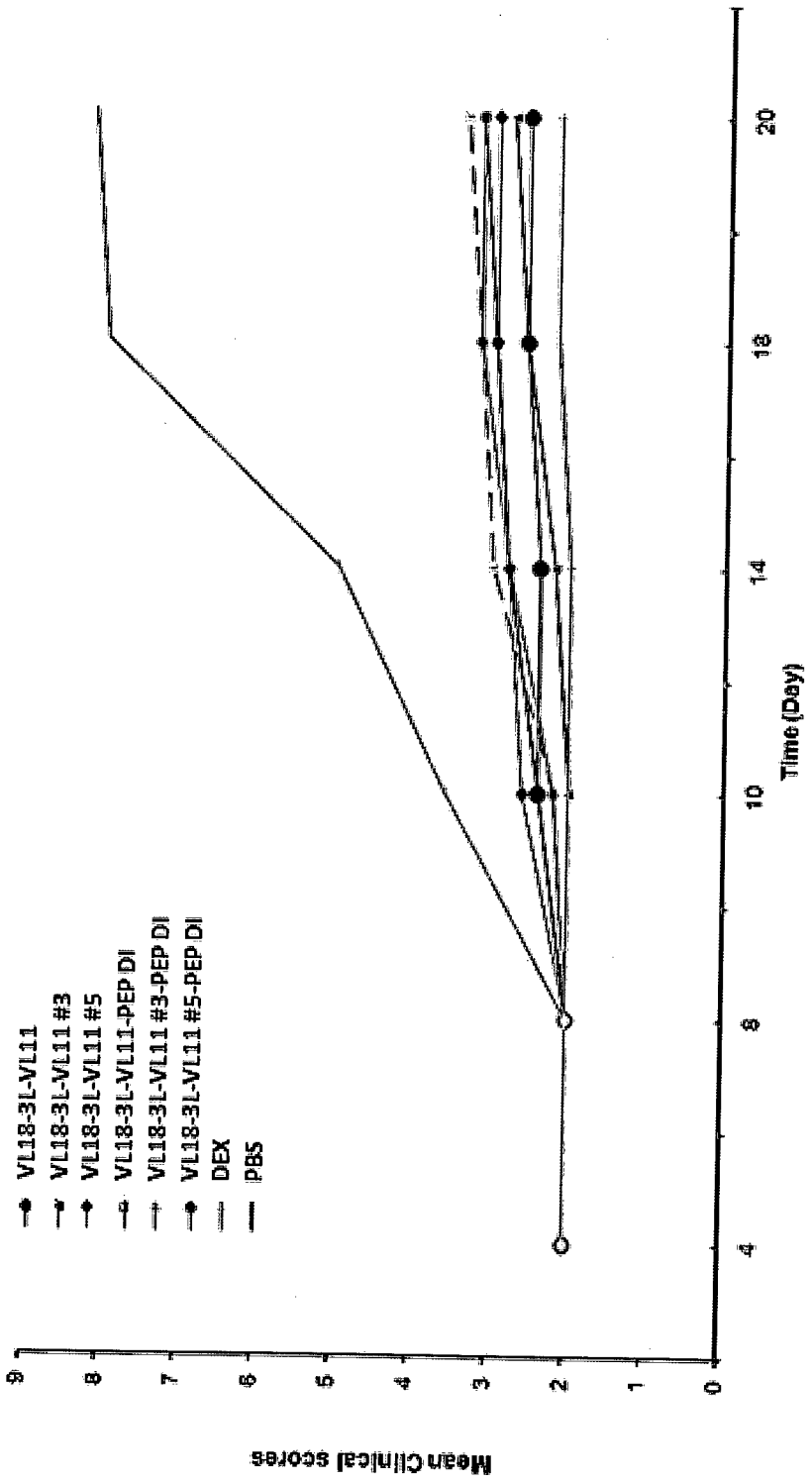

Mean Clinical scores
Time (Day)
VL18-3L-VL11
VL18-3L-VL11 #3
VL18-3L-VL11 #5
VL18-3L-VL11-PEP DI
VL18-3L-VL11 #3-PEP DI
VL18-3L-VL11 #5-PEP DI
DEX
PBS

FIG. 16

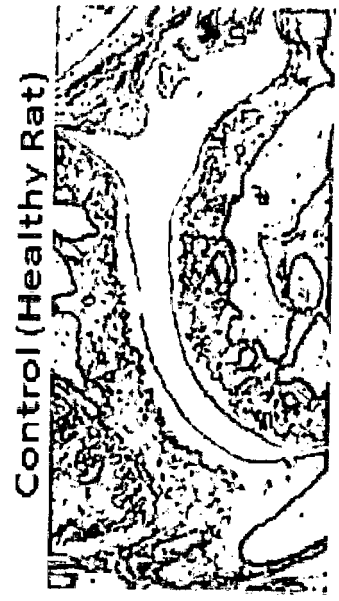


FIG. 17C

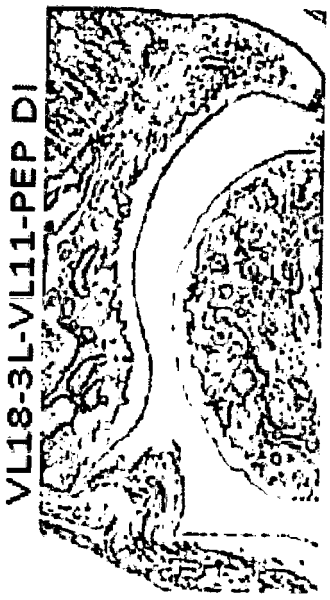


FIG. 17B



FIG. 17A



FIG. 17F

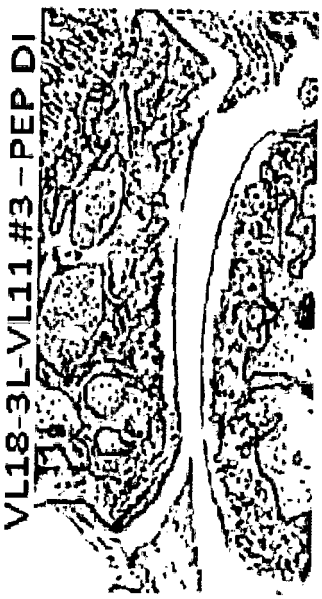


FIG. 17E



FIG. 17D

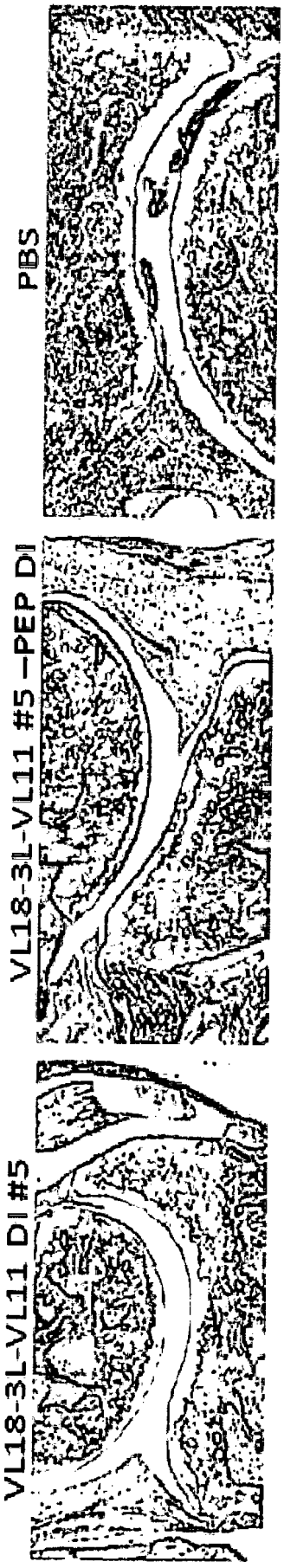


FIG. 17G

FIG. 17H

FIG. 17I

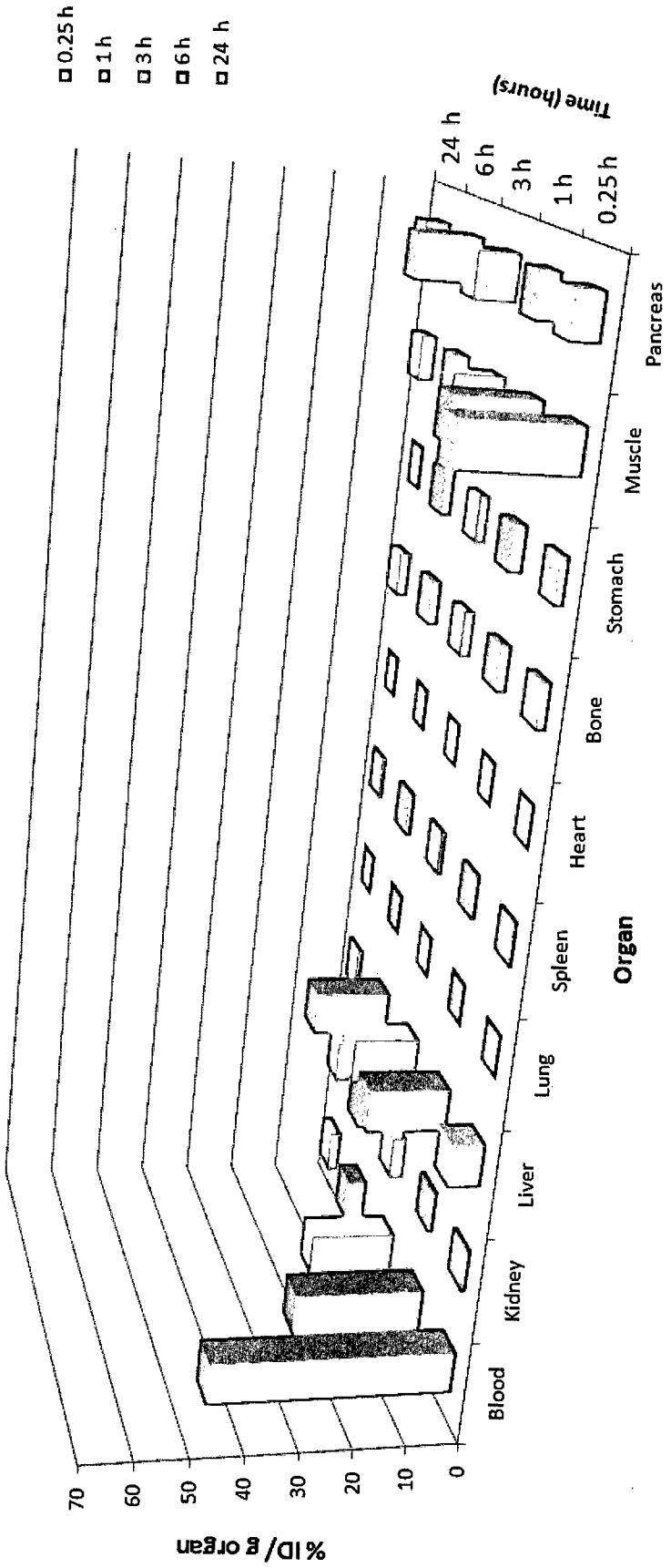

0.25 h
1 h
3 h
6 h
24 h
Time (hours)
24 h
6 h
3 h
1 h
0.25 h
% ID/ g organ
70
60
50
40
30
20
10
0
Blood
Kidney
Liver
Lung
Spleen
Heart
Bone
Stomach
Muscle
Pancreas
Organ

FIG. 18A

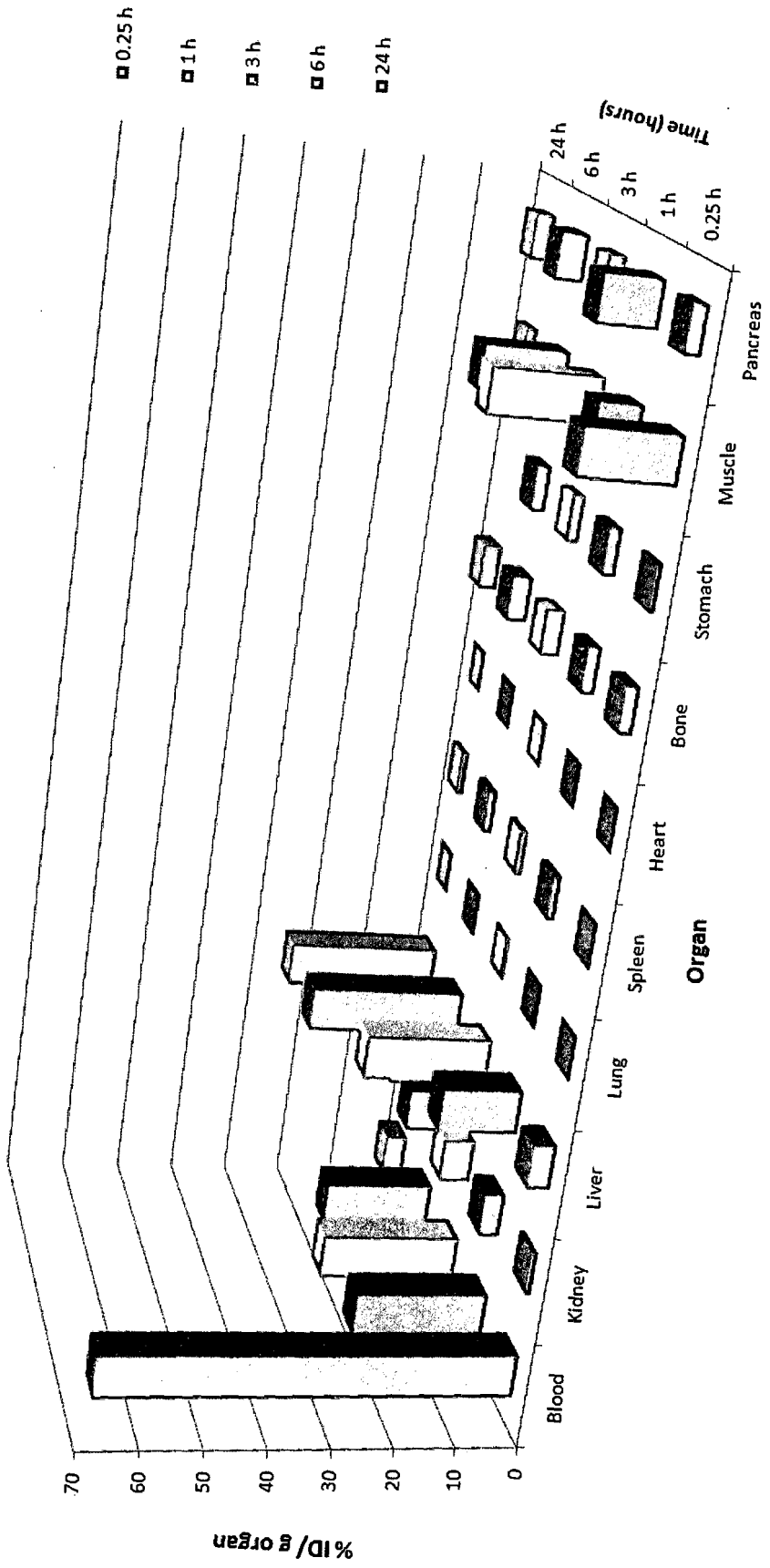

0.25 h
1 h
3 h
6 h
24 h
Time (hours)
24 h
6 h
3 h
1 h
0.25 h
% ID/ g organ
70
60
50
40
30
20
10
0
Blood
Kidney
Liver
Lung
Spleen
Heart
Bone
Stomach
Muscle
Pancreas
Organ

FIG. 18B