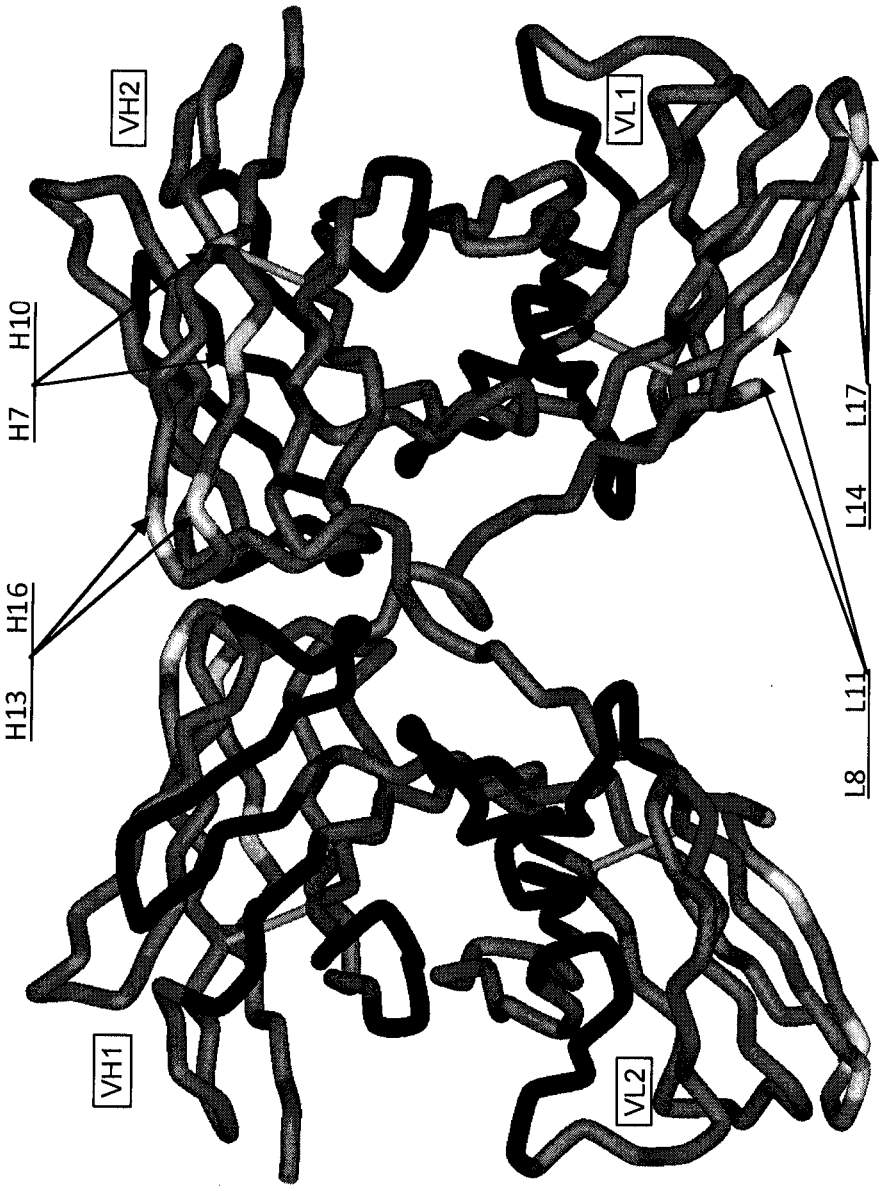


Figure 1

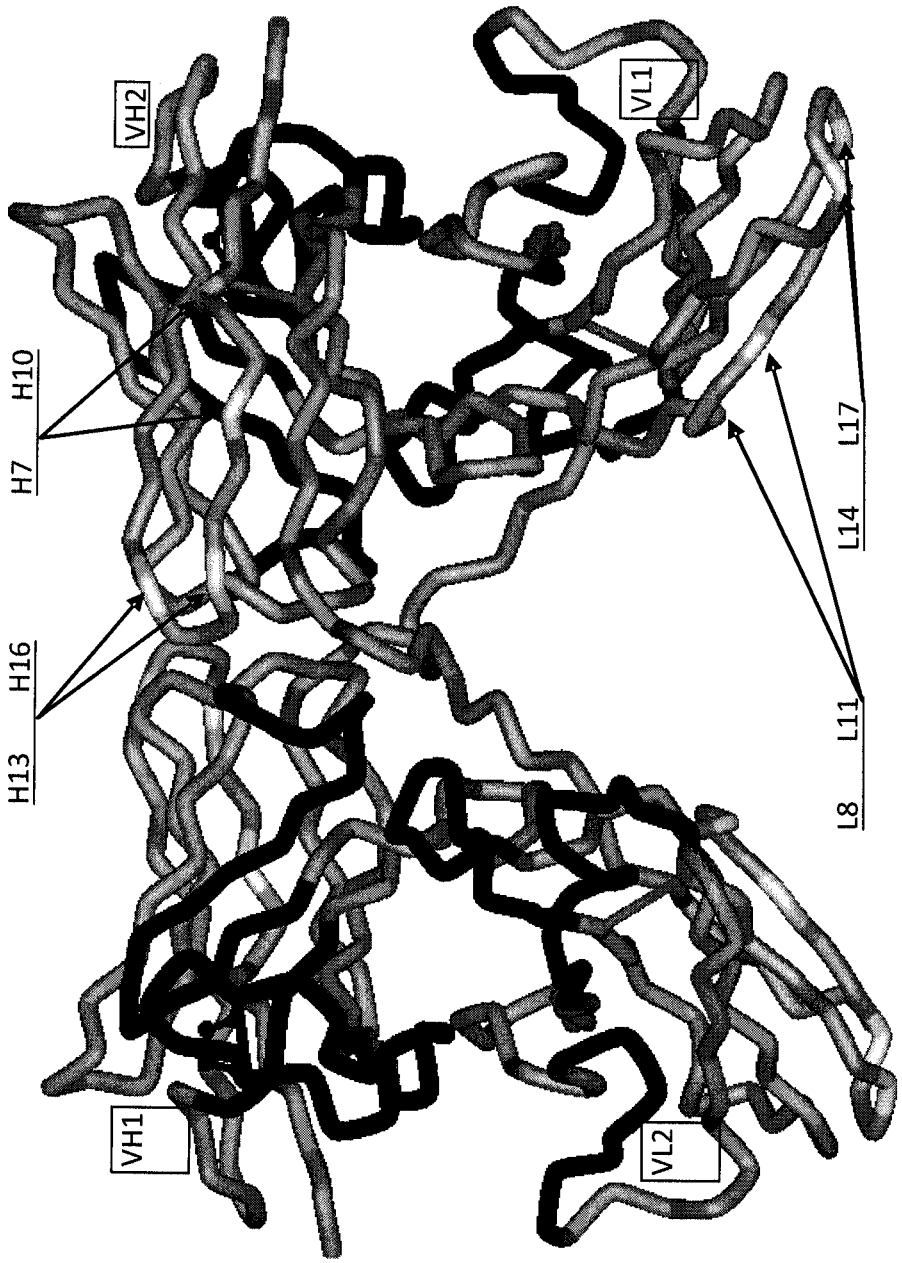


Figure 2

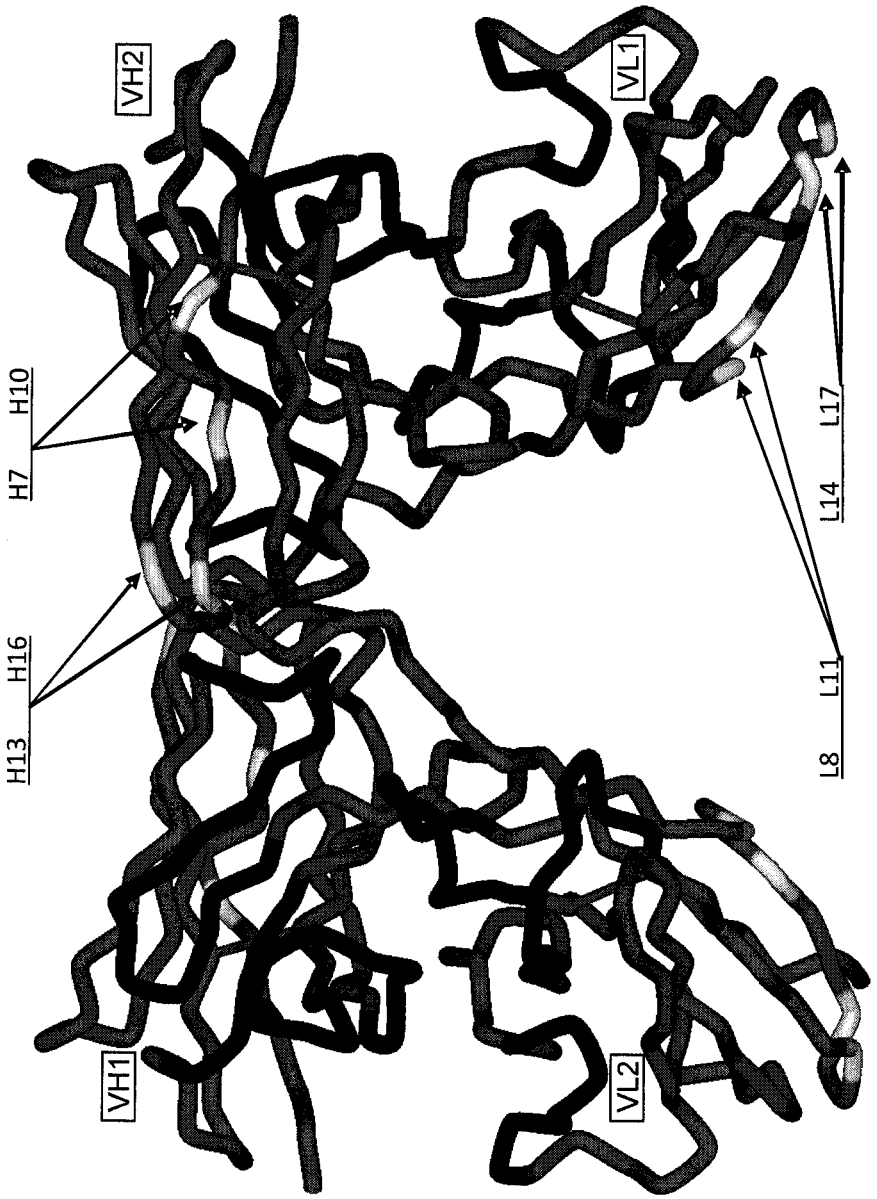


Figure 3



Figure 4A

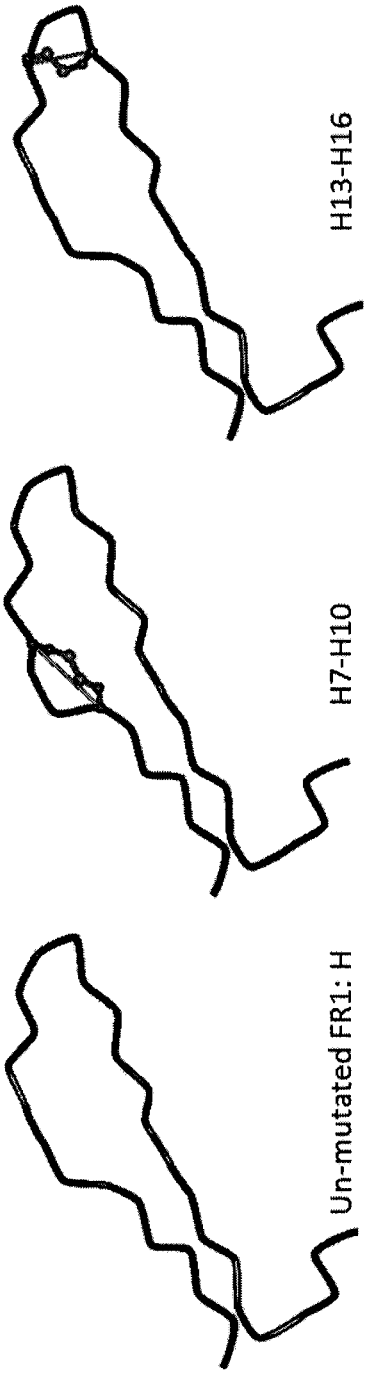


Figure 4B

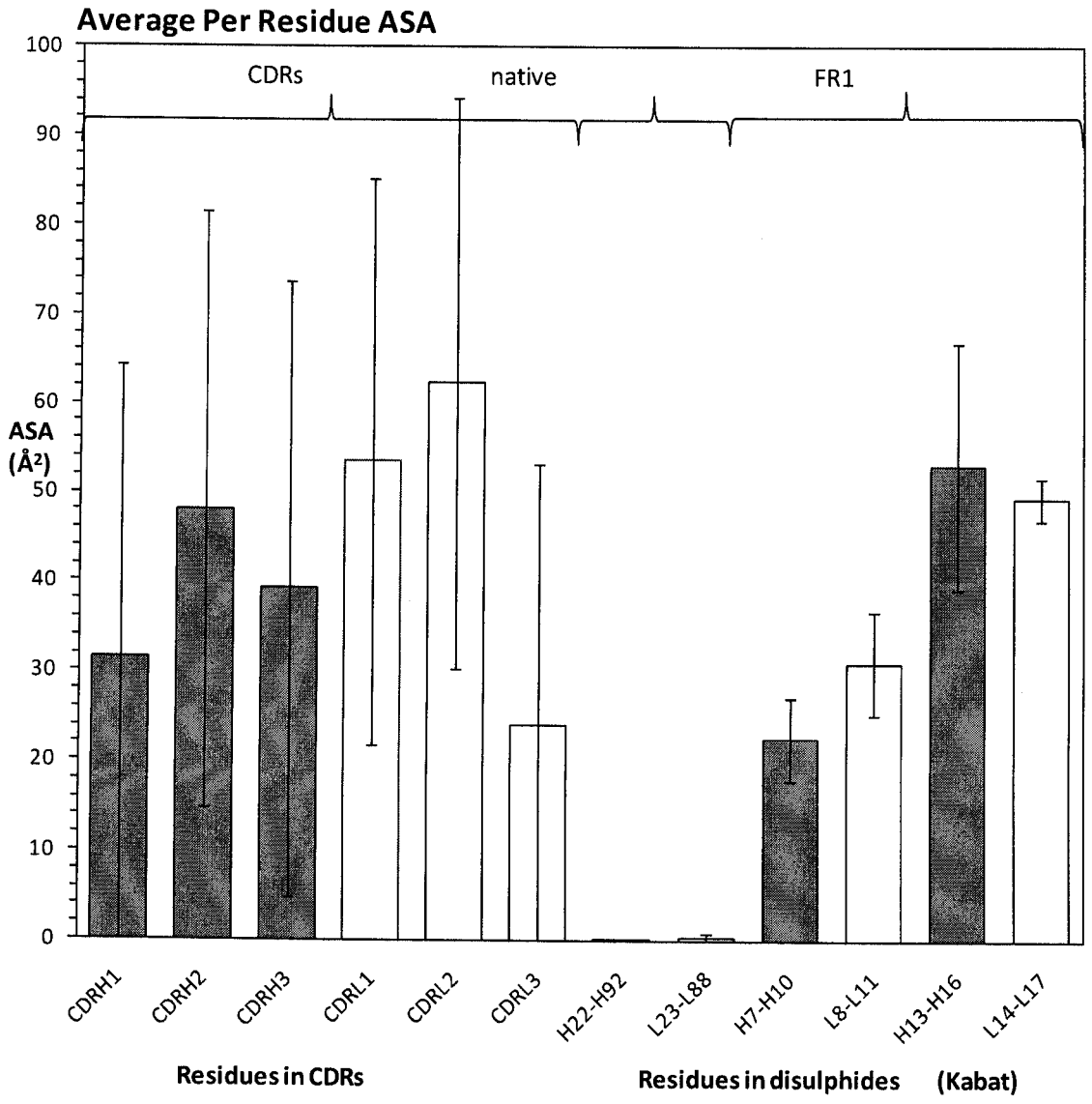

Average Per Residue ASA
CDRs
native
FR1
ASA (Å²)
100
90
80
70
60
50
40
30
20
10
0
CDRH1
CDRH2
CDRH3
CDRL1
CDRL2
CDRL3
H22-H92
L23-L88
H7-H10
L8-L11
H13-H16
L14-L17
Residues in CDRs
Residues in disulphides (Kabat)

Figure 5

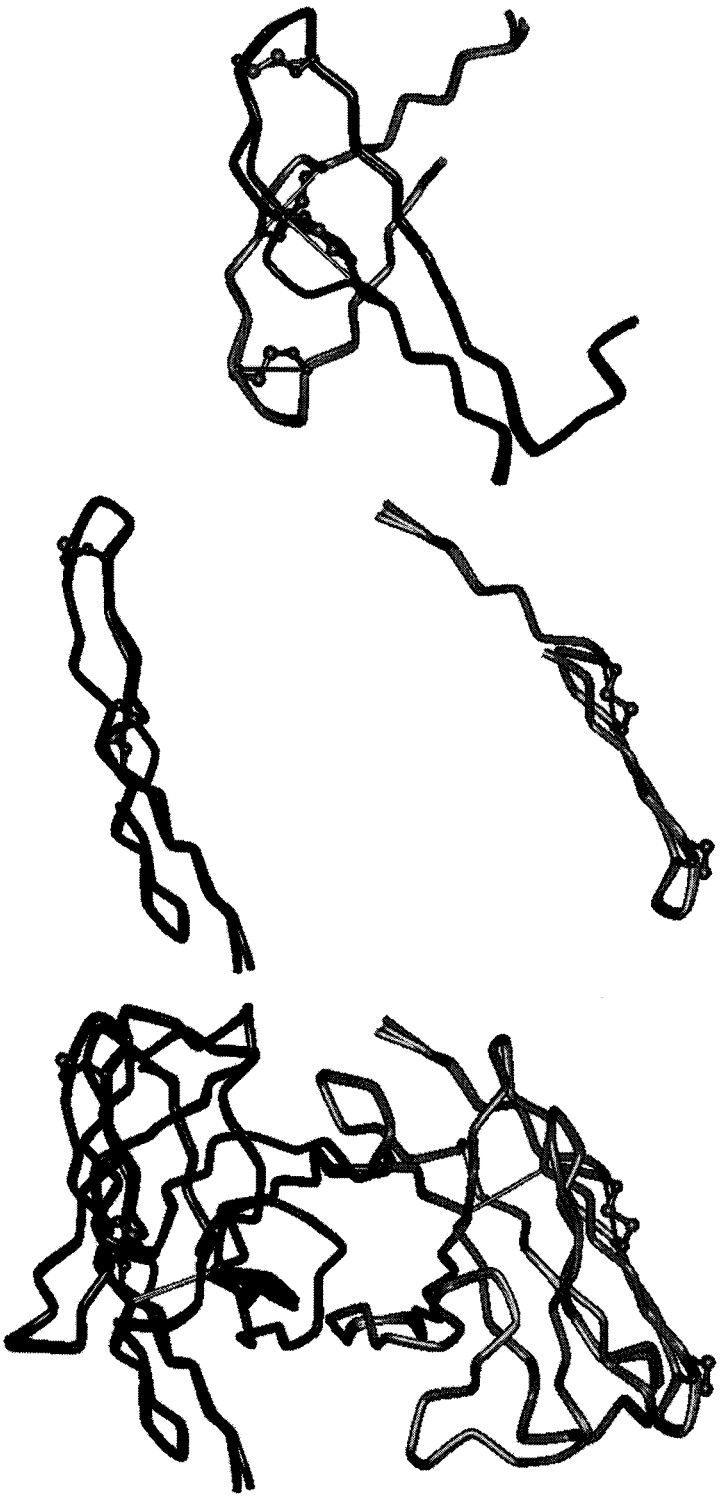


Figure 6A

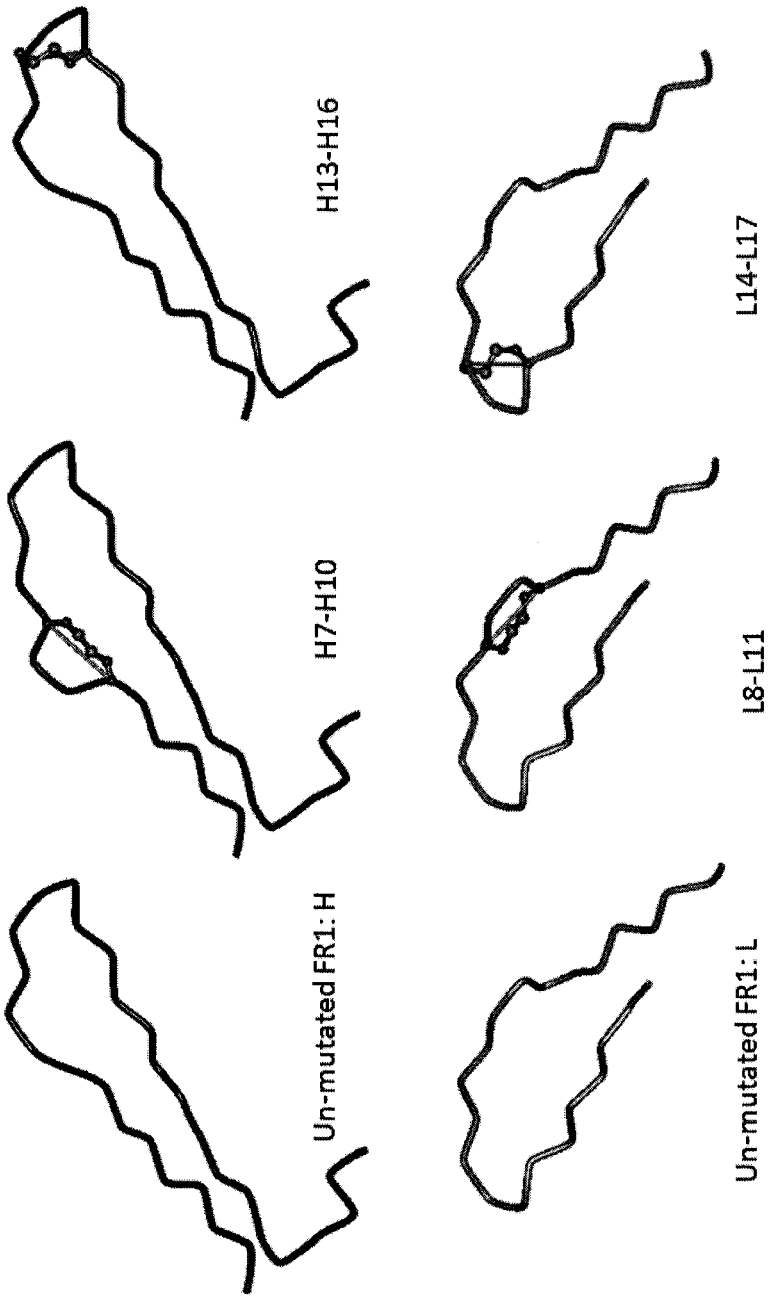


Figure 6B

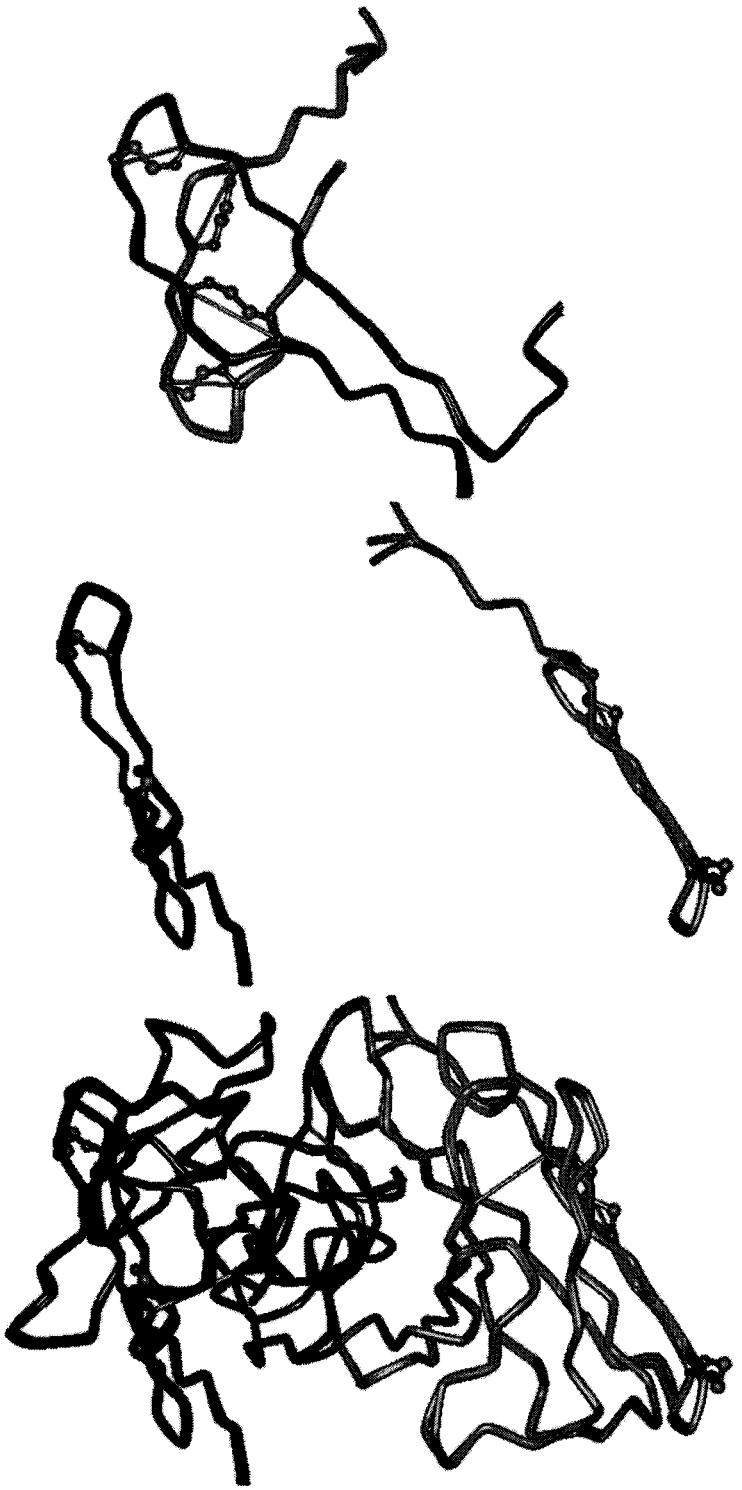


Figure 7A

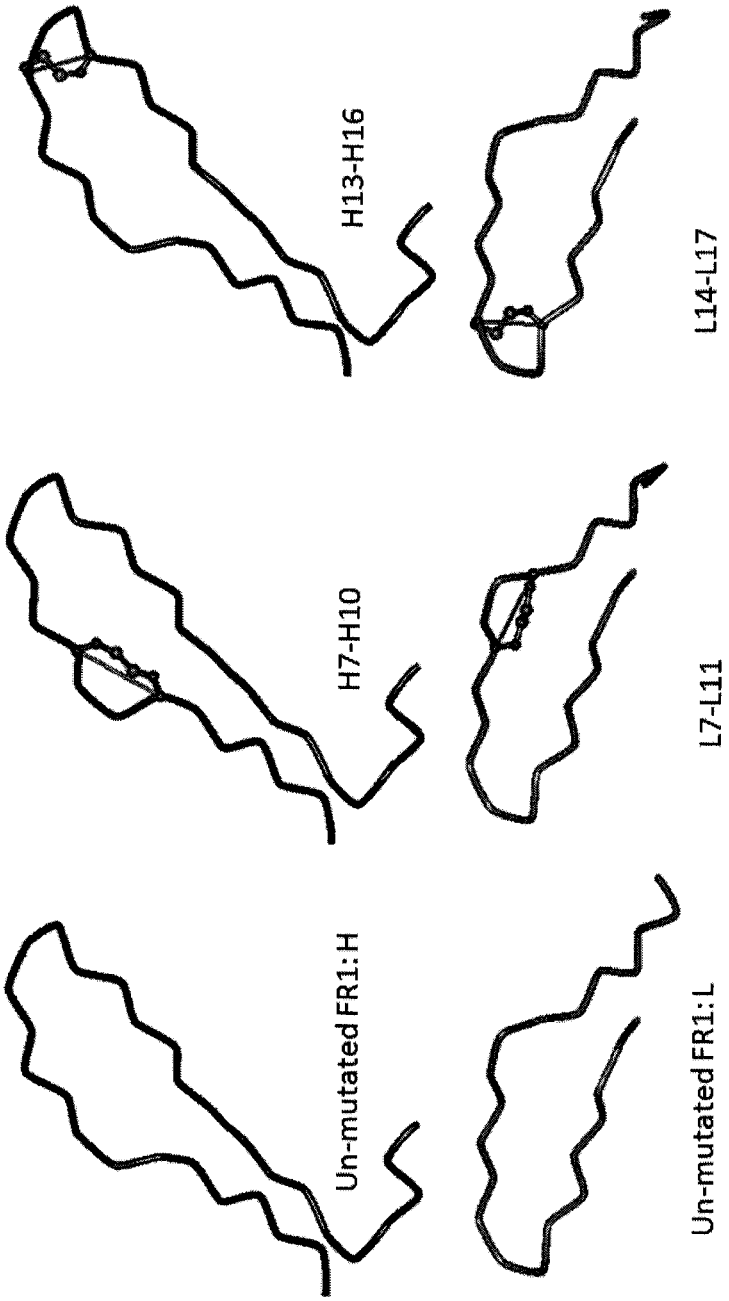


Figure 7B

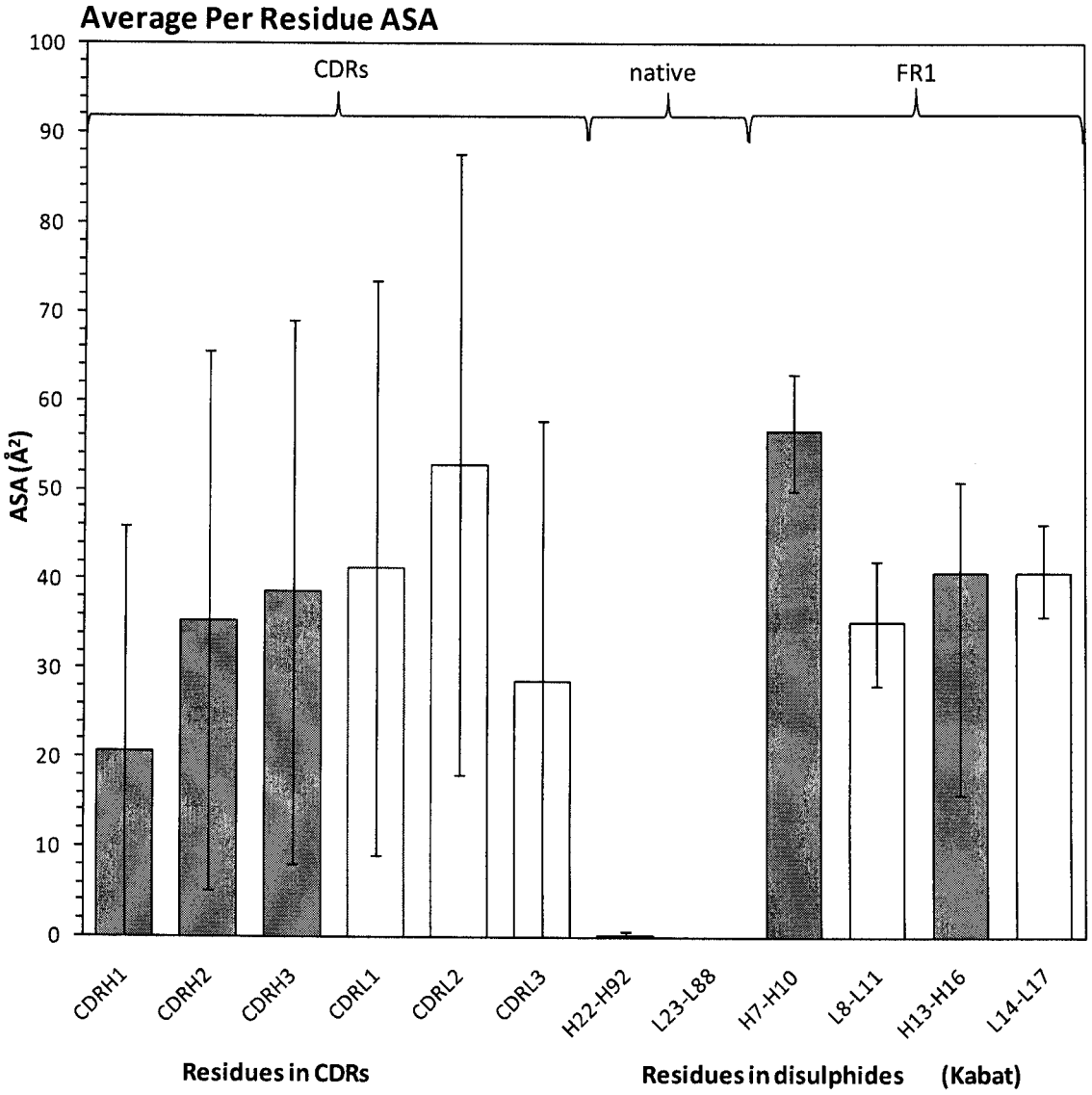

Average Per Residue ASA
CDRs
native
FR1
ASA (Å²)
100
90
80
70
60
50
40
30
20
10
0
CDRH1
CDRH2
CDRH3
CDRL1
CDRL2
CDRL3
H22-H92
L23-L88
H7-H10
L8-L11
H13-H16
L14-L17
Residues in CDRs
Residues in disulphides (Kabat)

Figure 8

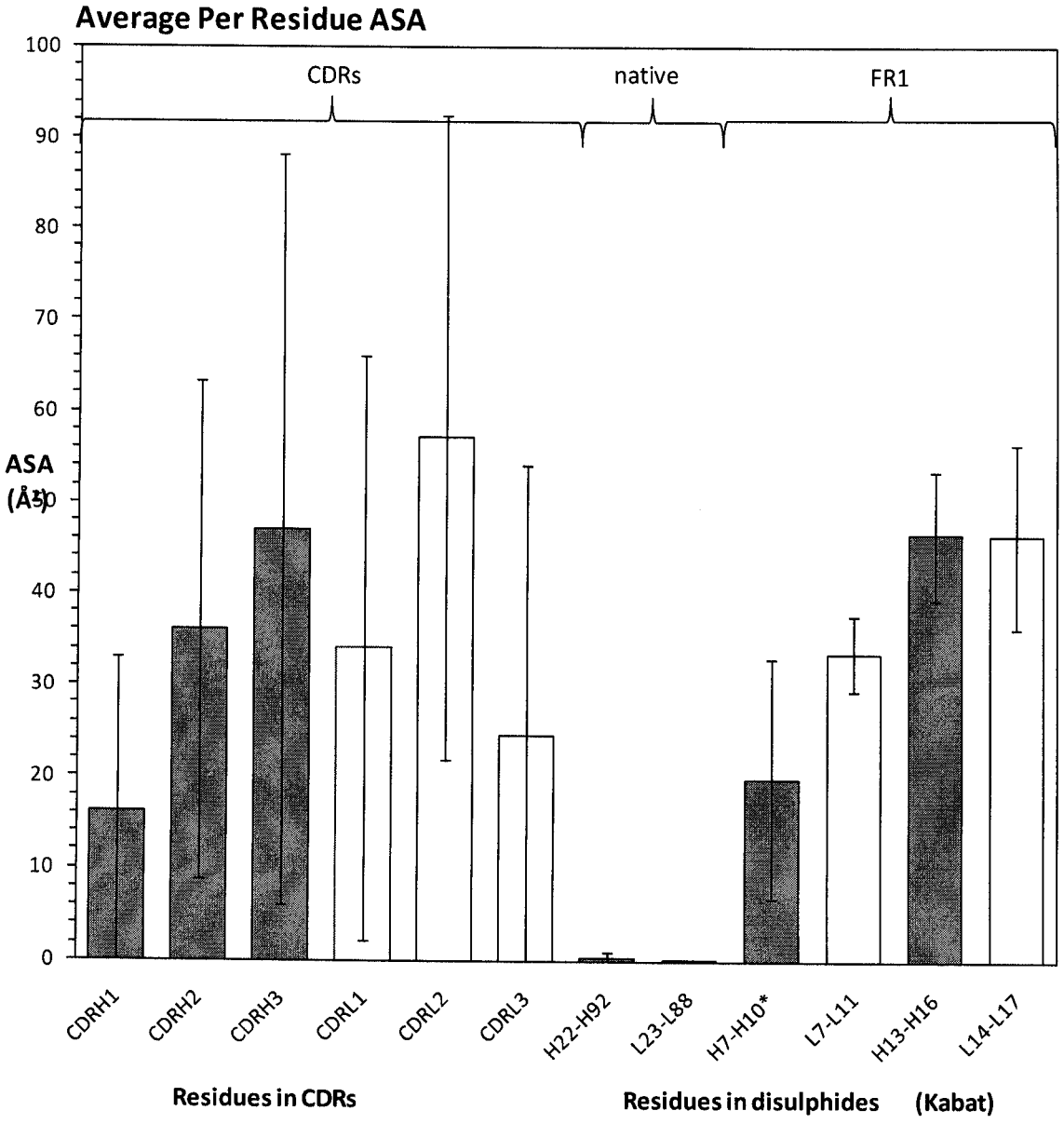

Average Per Residue ASA
CDRs
native
FR1
ASA (Å²)
100
90
80
70
60
50
40
30
20
10
0
CDRH1
CDRH2
CDRH3
CDRL1
CDRL2
CDRL3
H22-H92
L23-L88
H7-H10*
L7-L11
H13-H16
L14-L17
Residues in CDRs
Residues in disulphides (Kabat)

Figure 9

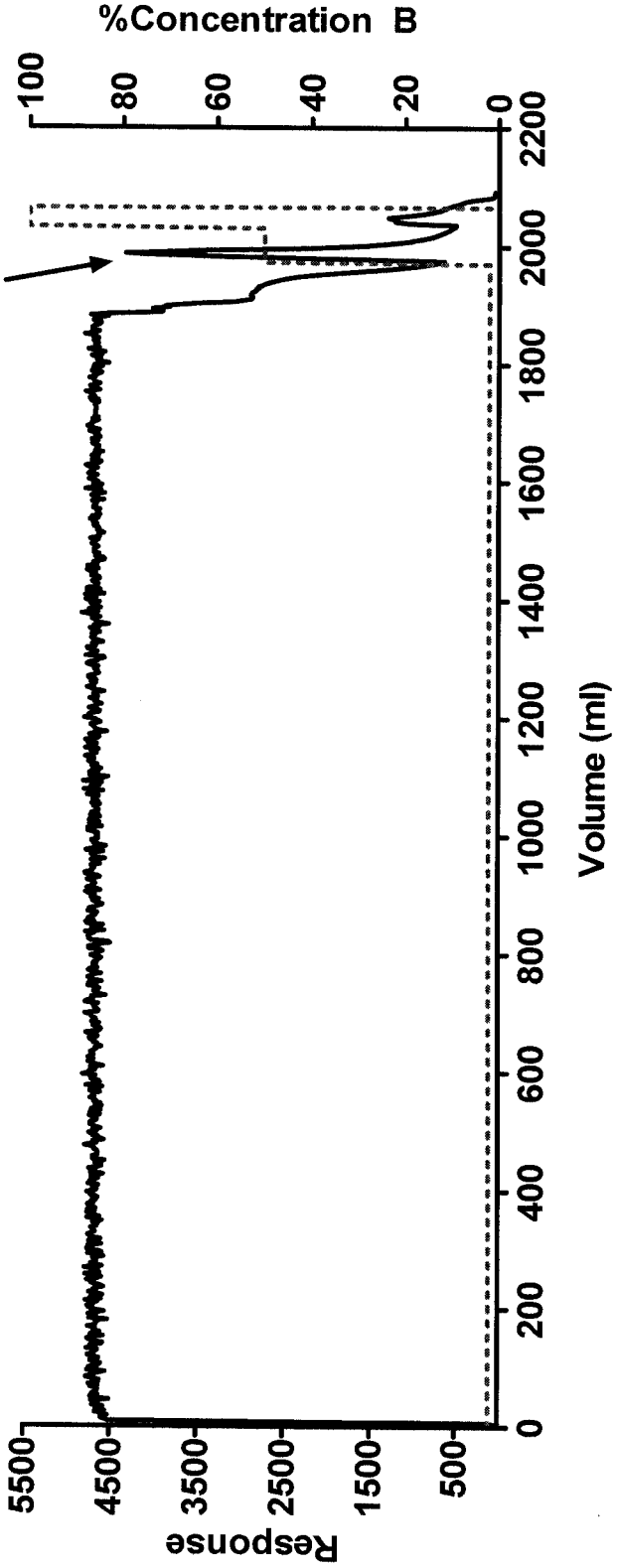

%Concentration B
100
80
60
40
20
0
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Volume (ml)
5500
4500
3500
2500
1500
500
Response

Figure 10A

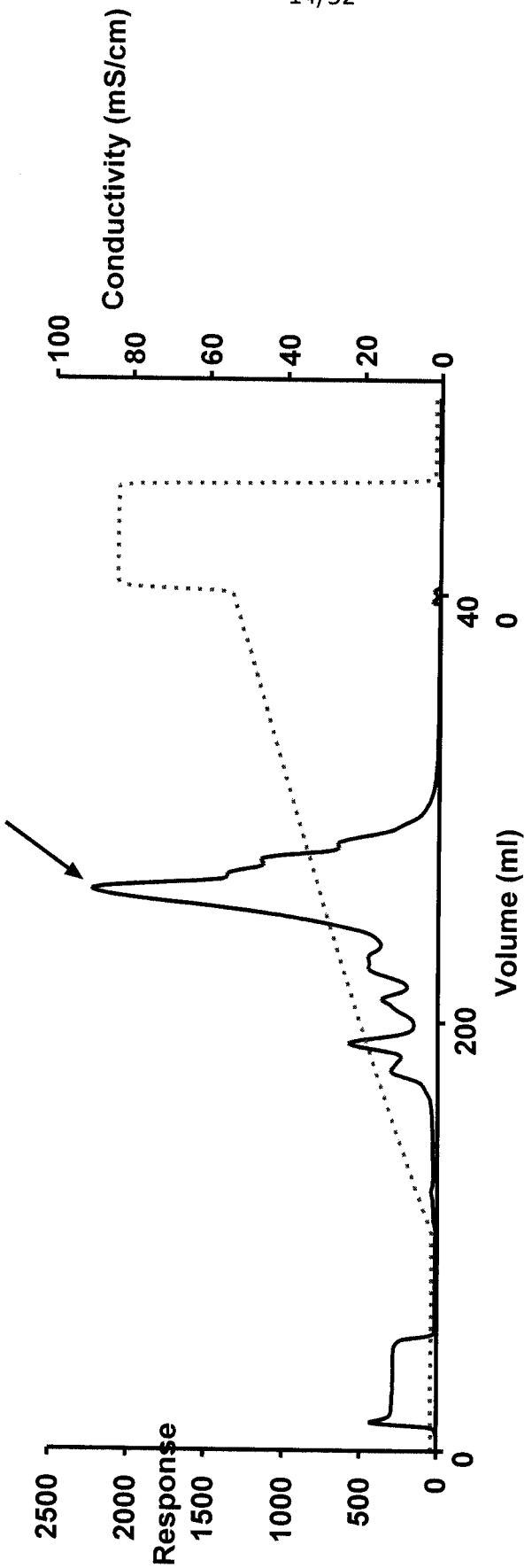

Conductivity (mS/cm)
100
80
60
40
20
0
Response
2500
2000
1500
1000
500
0
0
200
40
0
Volume (ml)

Figure 10B

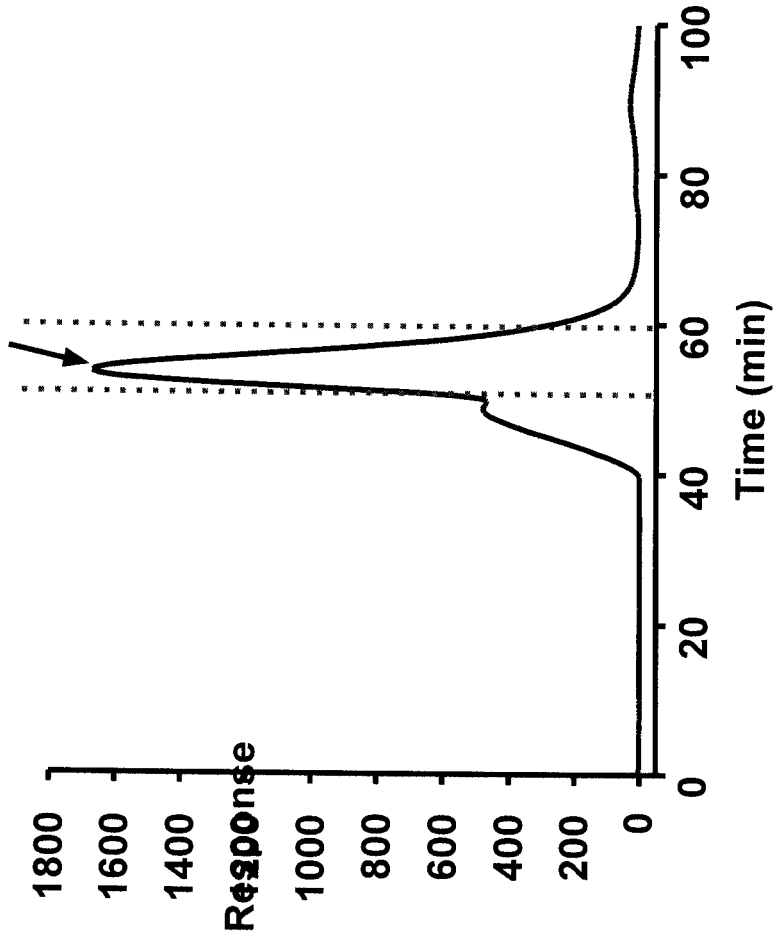

1800
1600
1400
1200
1000
800
600
400
200
0
Response
0
20
40
60
80
100
Time (min)

Figure 10C

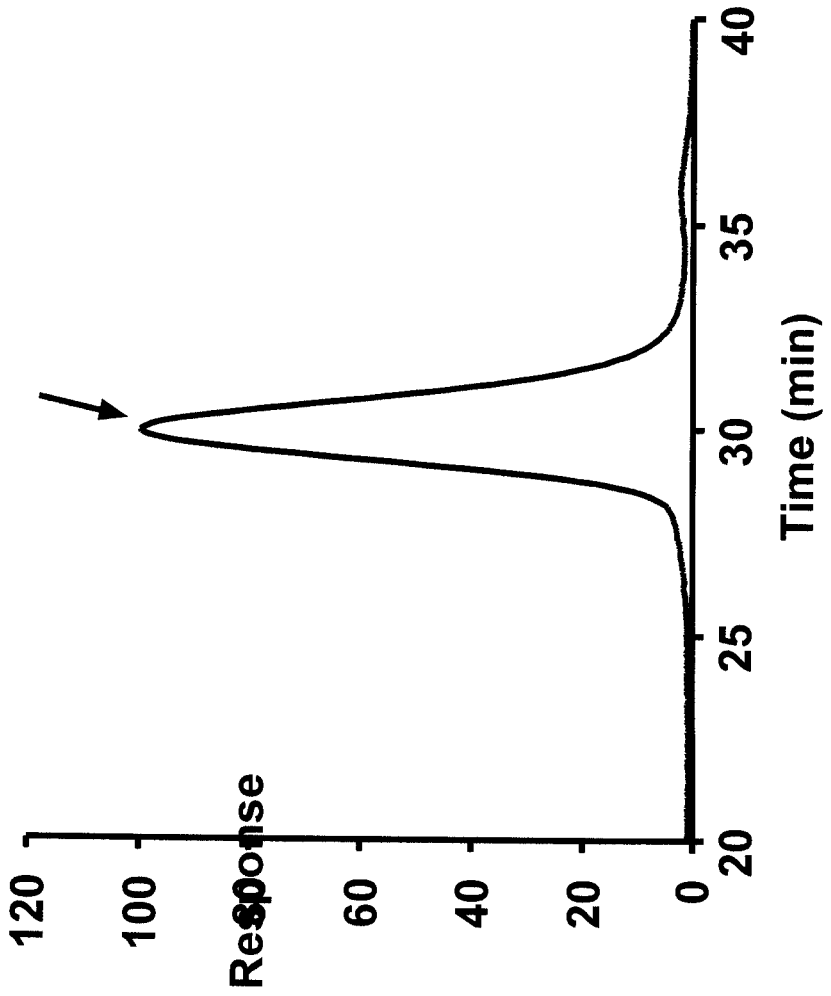


Figure 10D

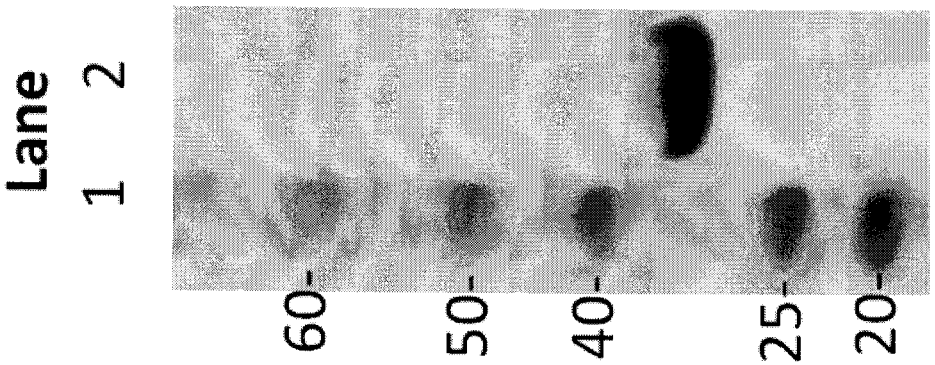


Figure 10E

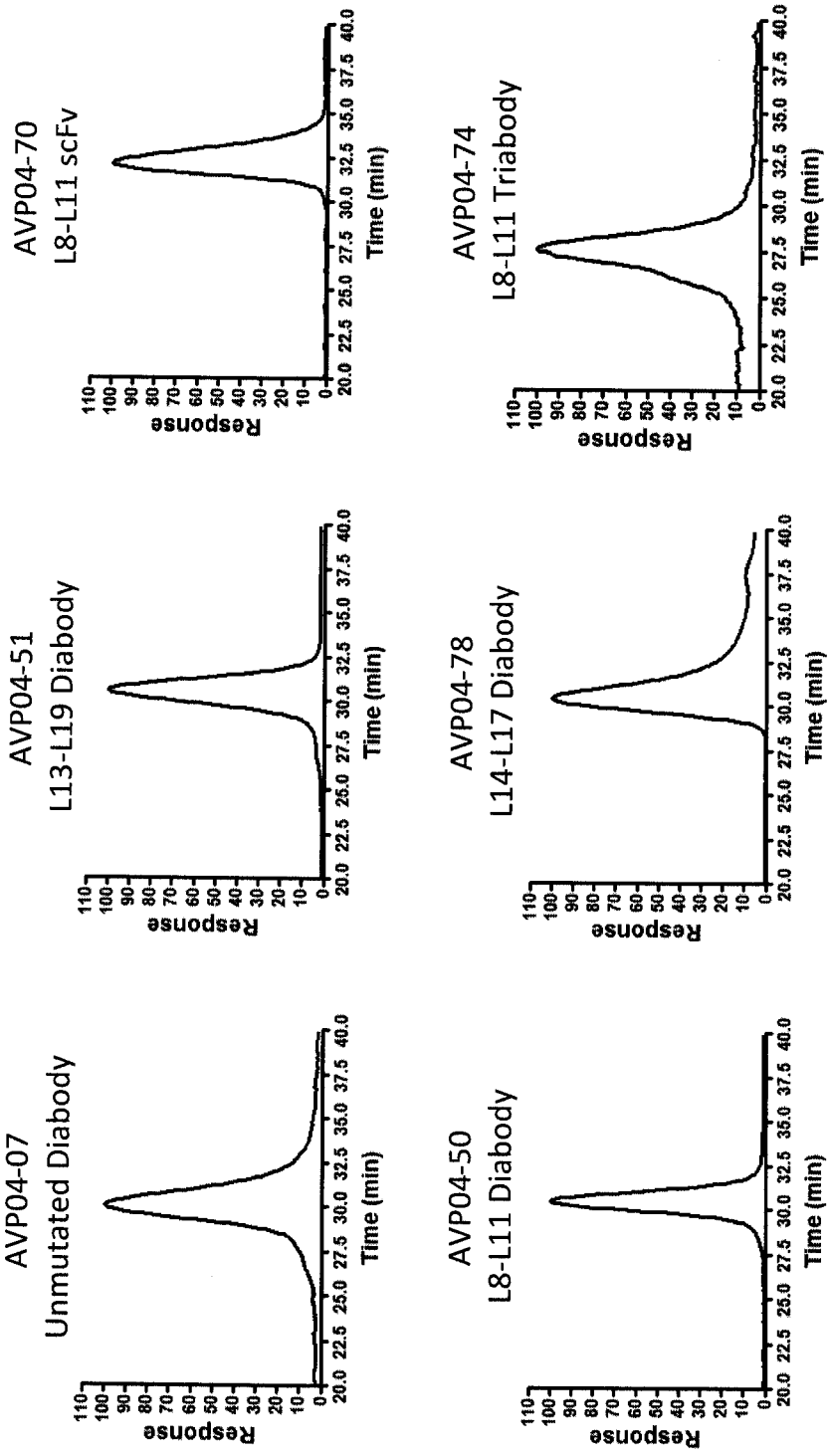

AVP04-07
Unmutated Diabody
AVP04-51
L13-L19 Diabody
AVP04-70
L8-L11 scFv
AVP04-50
L8-L11 Diabody
AVP04-78
L14-L17 Diabody
AVP04-74
L8-L11 Triabody
Response
Time (min)

Figure 11A

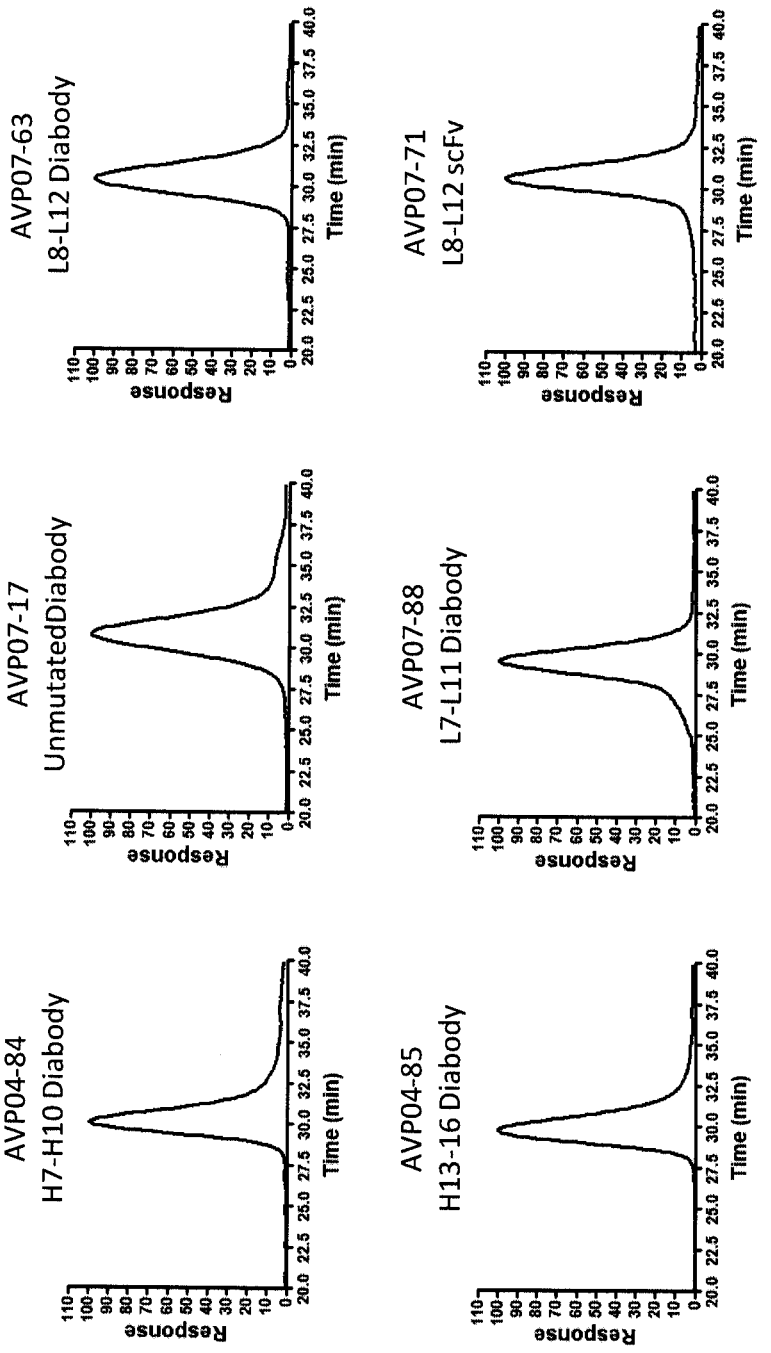

AVP07-63
L8-L12 Diabody
AVP07-71
L8-L12 scFv
AVP07-17
UnmutatedDiabody
AVP07-88
L7-L11 Diabody
AVP04-84
H7-H10 Diabody
AVP04-85
H13-16 Diabody
Response
Time (min)

Figure 11B

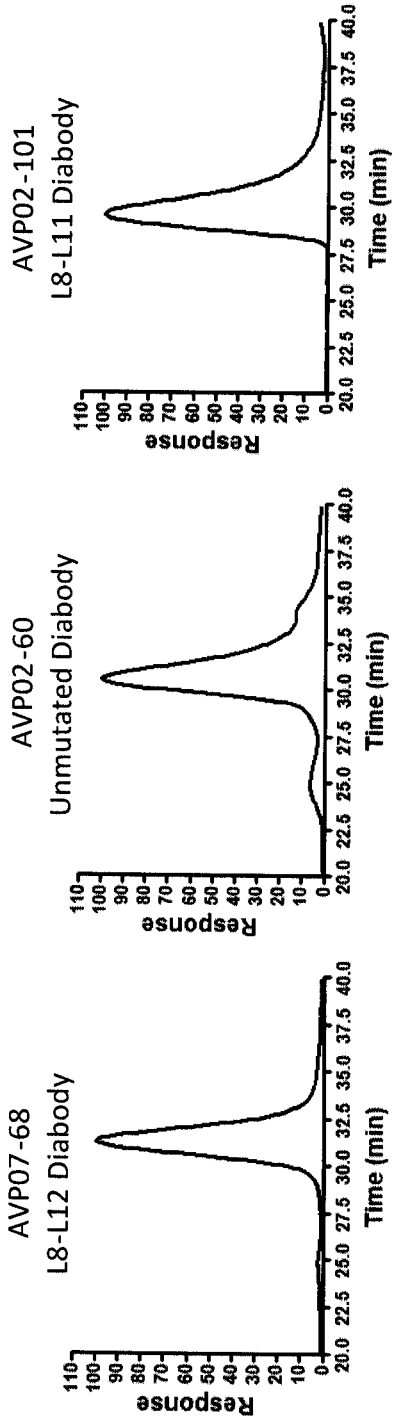

AVP07-68
L8-L12 Diabody
AVP02-60
Unmutated Diabody
AVP02-101
L8-L11 Diabody
Response
Time (min)

Figure 11C

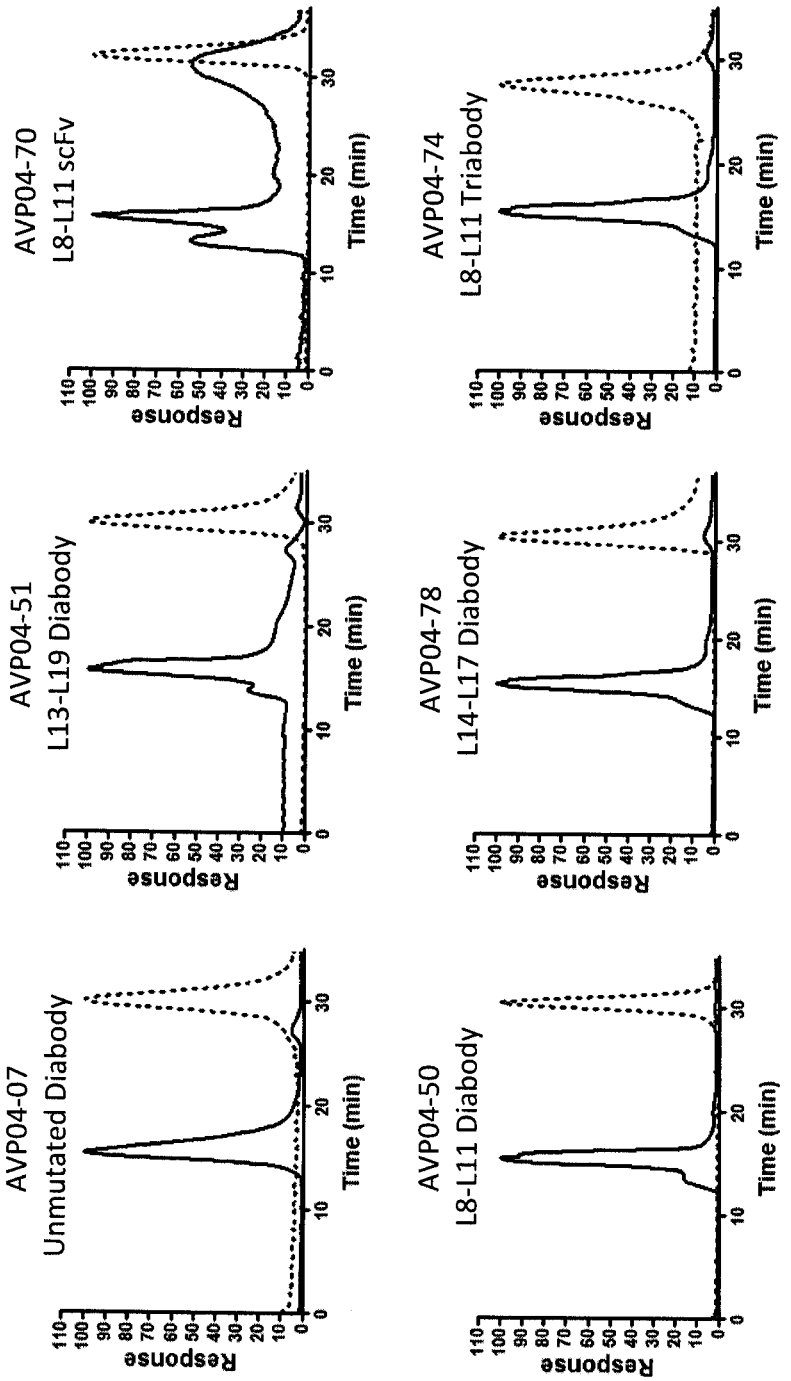

AVP04-70
L8-L11 scFv
AVP04-74
L8-L11 Triabody
AVP04-51
L13-L19 Diabody
AVP04-78
L14-L17 Diabody
AVP04-07
Unmutated Diabody
AVP04-50
L8-L11 Diabody
Response
Time (min)

Figure 12A

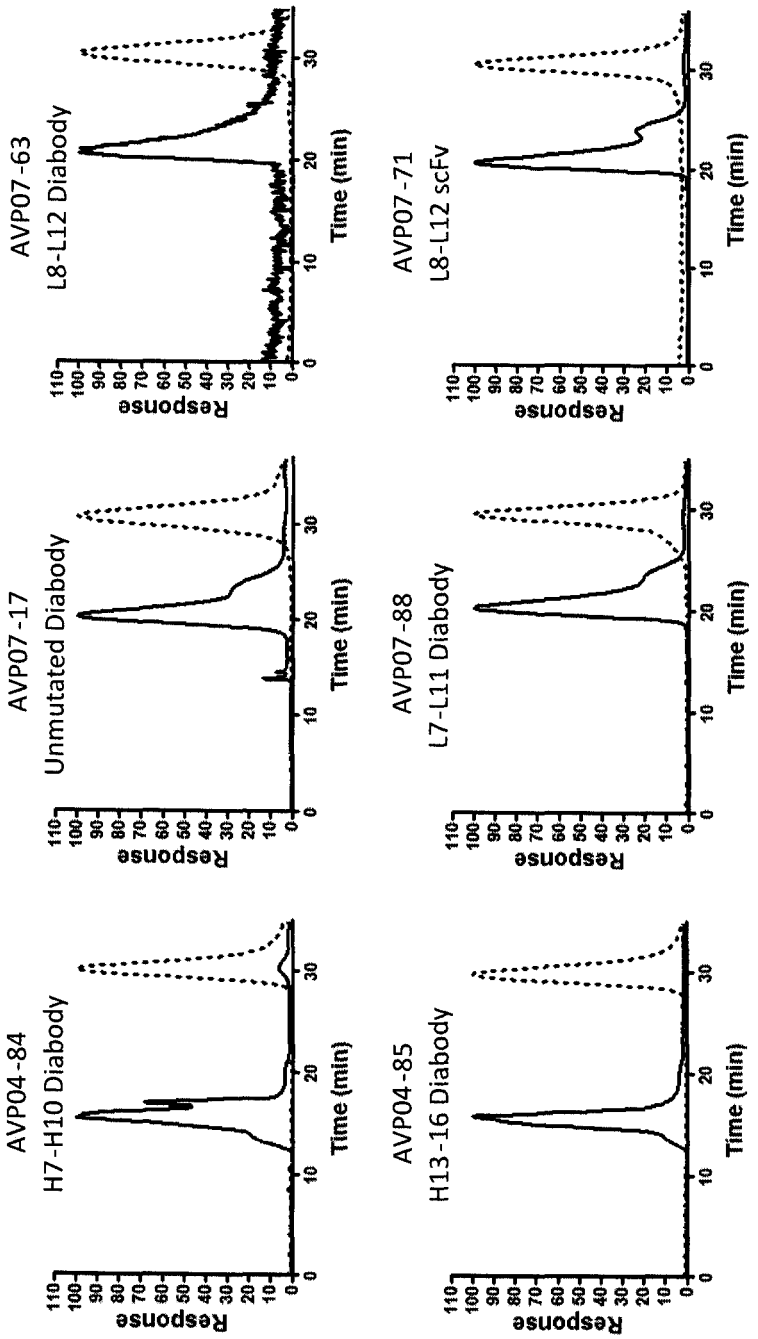

AVP07-63
L8-L12 Diabody
AVP07-17
Unmutated Diabody
AVP07-71
L8-L12 scFv
AVP07-88
L7-L11 Diabody
AVP04-84
H7-H10 Diabody
AVP04-85
H13-16 Diabody
Response
Time (min)

Figure 12B

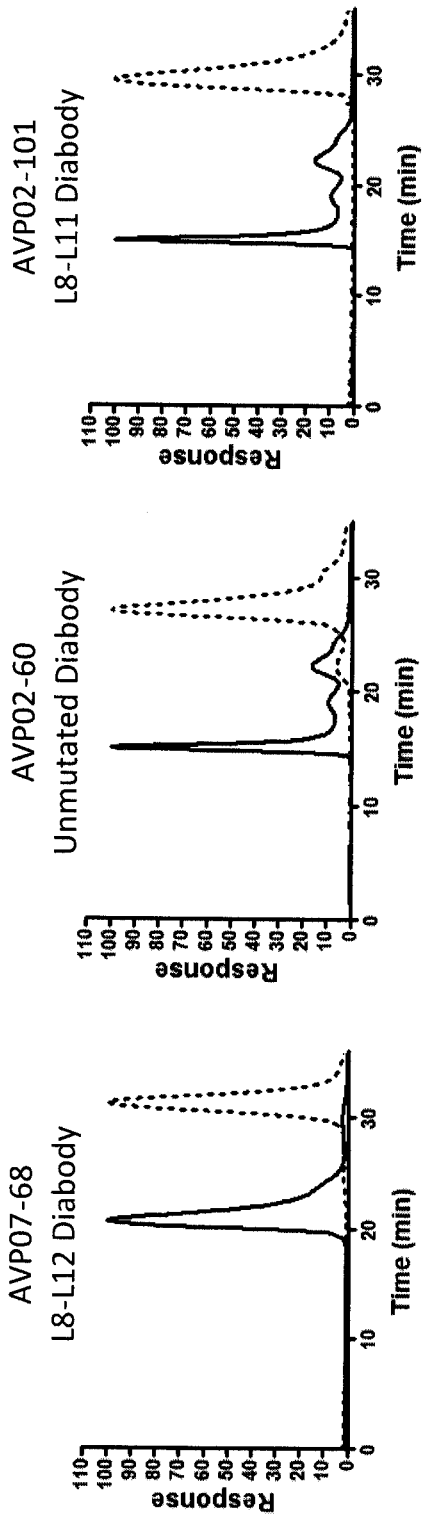

AVP02-101
L8-L11 Diabody
AVP02-60
Unmutated Diabody
AVP07-68
L8-L12 Diabody
Response
Time (min)

Figure 12C

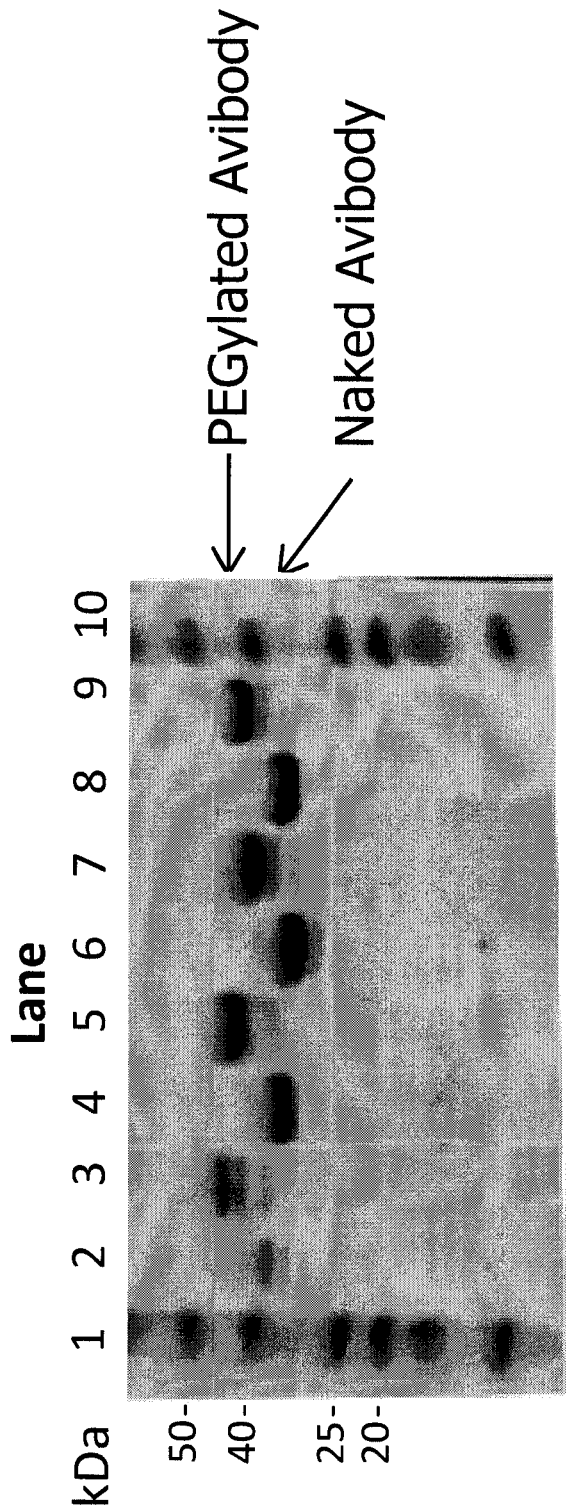

PEGylated Avibody
Naked Avibody
Lane
1 2 3 4 5 6 7 8 9 10
kDa
50-
40-
25-
20-

Figure 13A

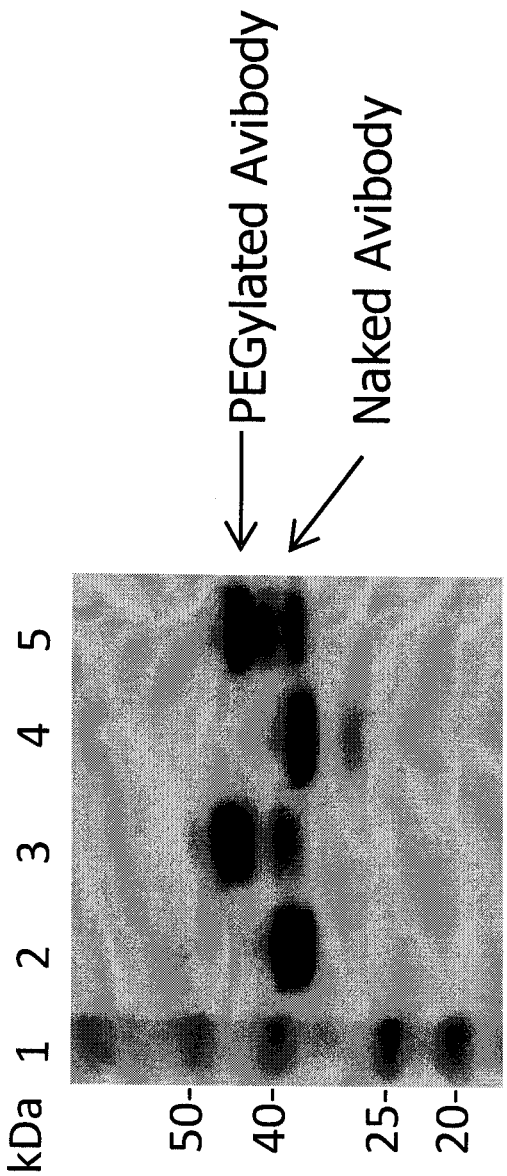


Figure 13B

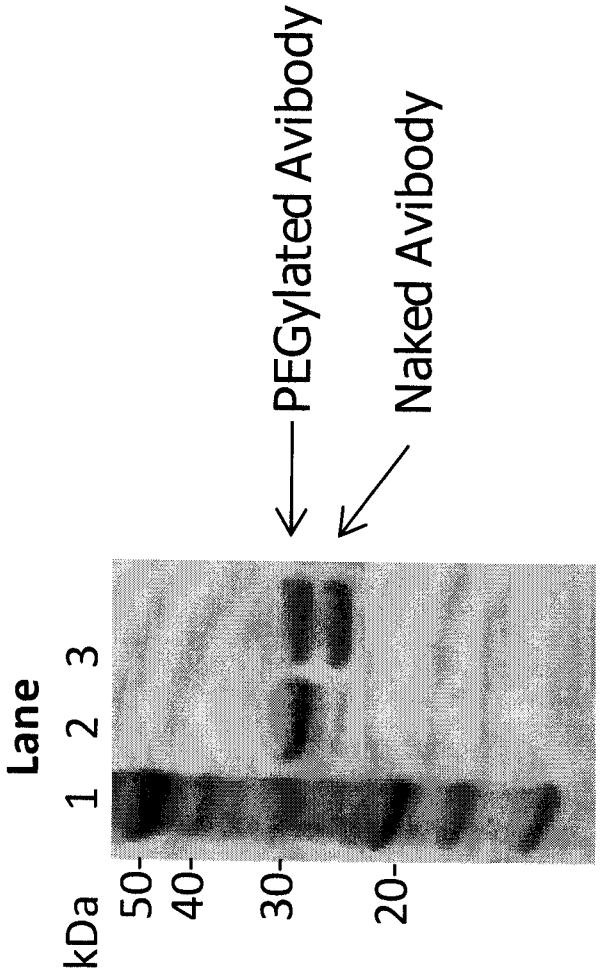


Figure 13C

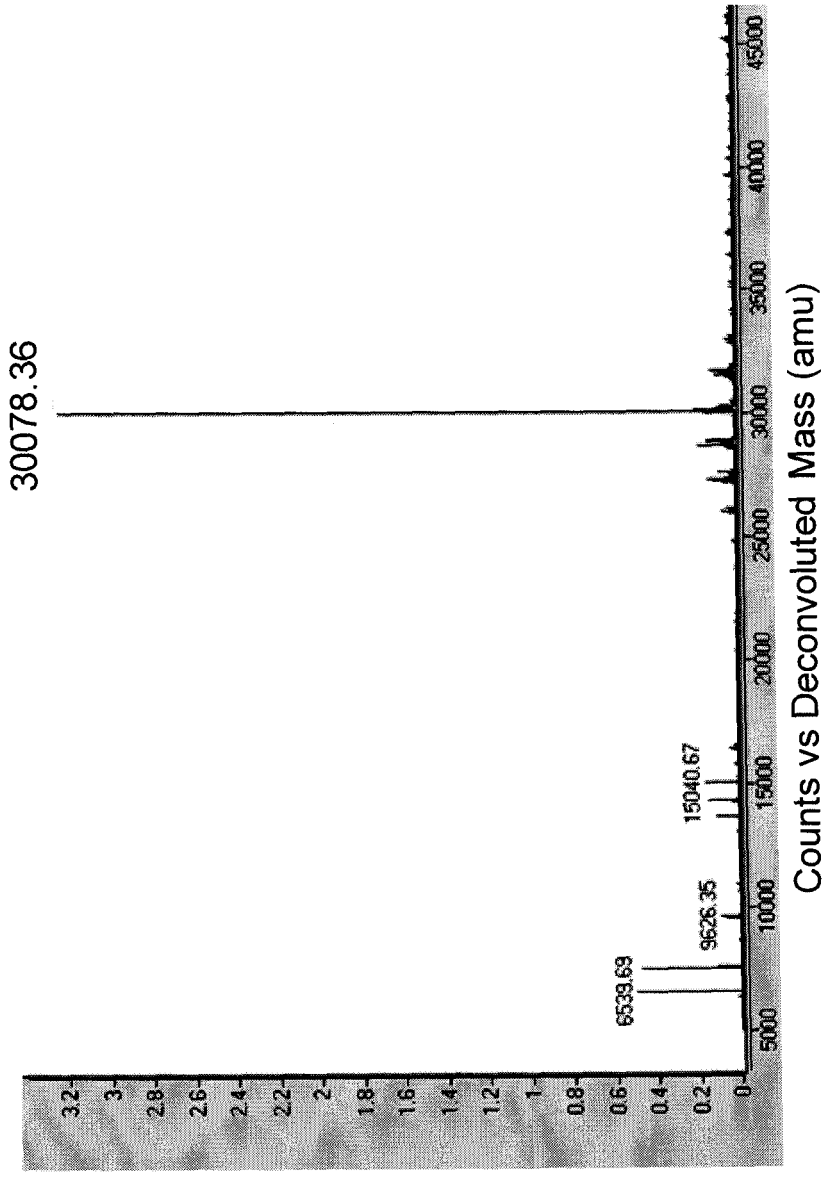

30078.36
15040.67
9628.35
6539.69
Counts vs Deconvoluted Mass (amu)

Figure 14A

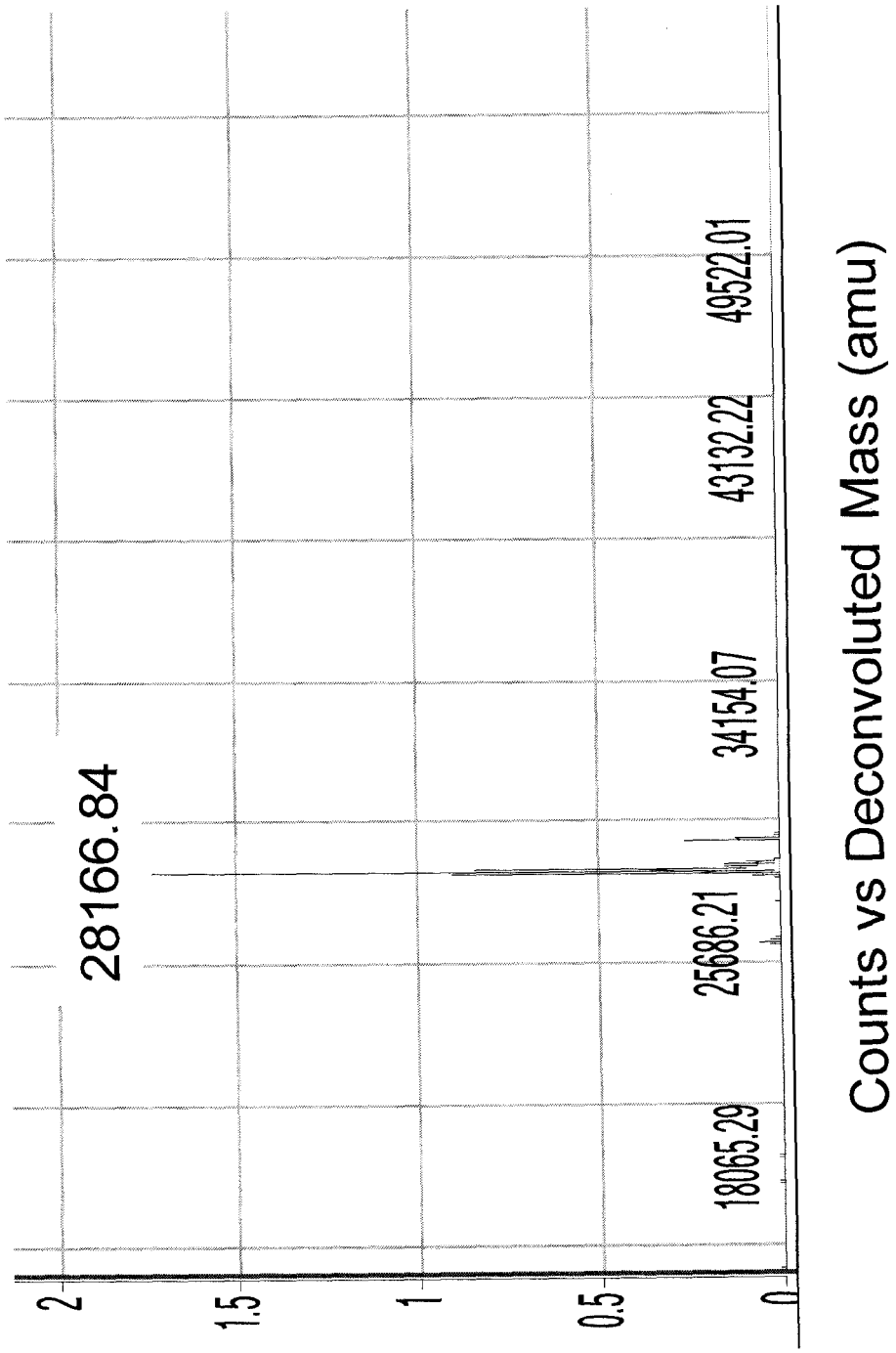

Counts vs Deconvoluted Mass (amu)
28166.84
18065.29
25686.21
34154.07
43132.22
49522.01
2
1.5
1
0.5
0

Figure 14B

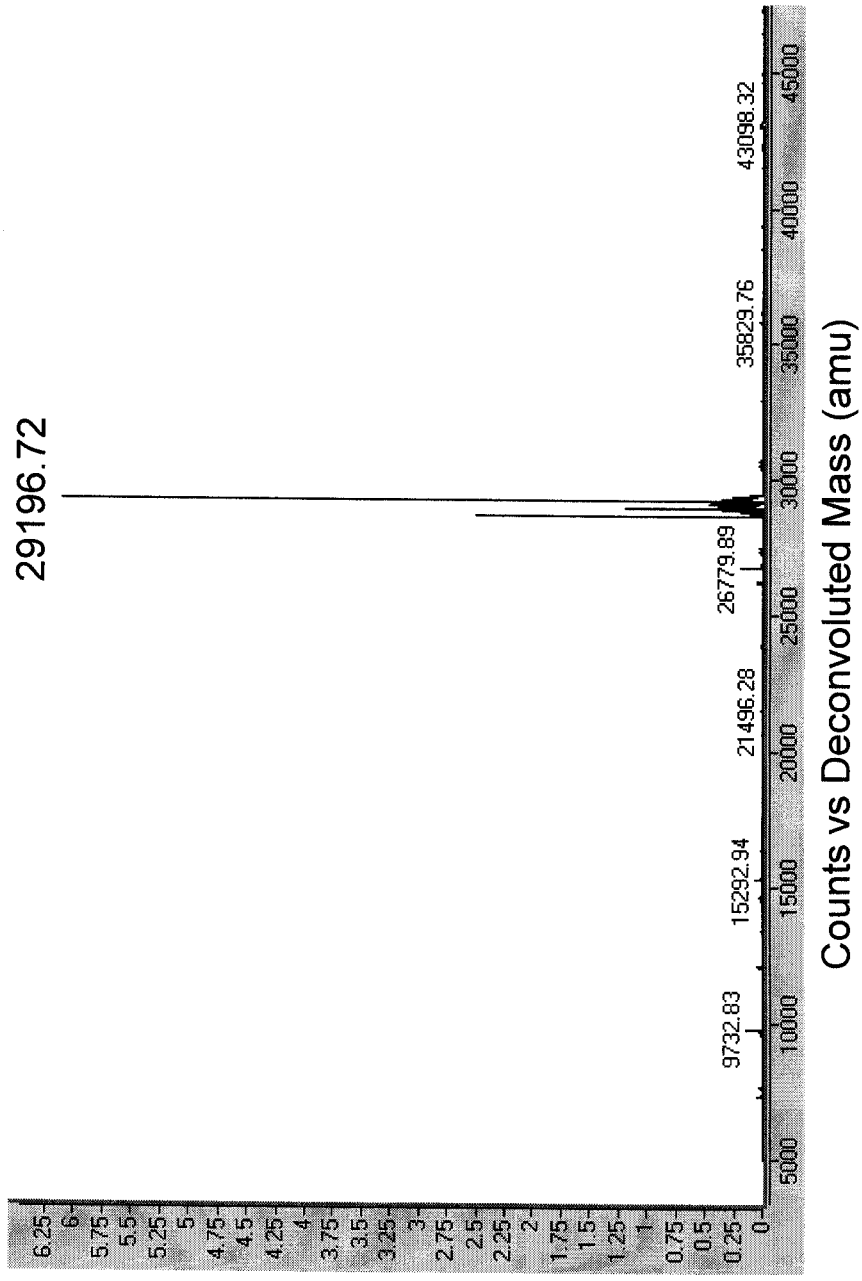

29196.72
9732.83
15232.94
21496.28
26779.89
35829.76
43098.32
Counts vs Deconvoluted Mass (amu)

Figure 14C

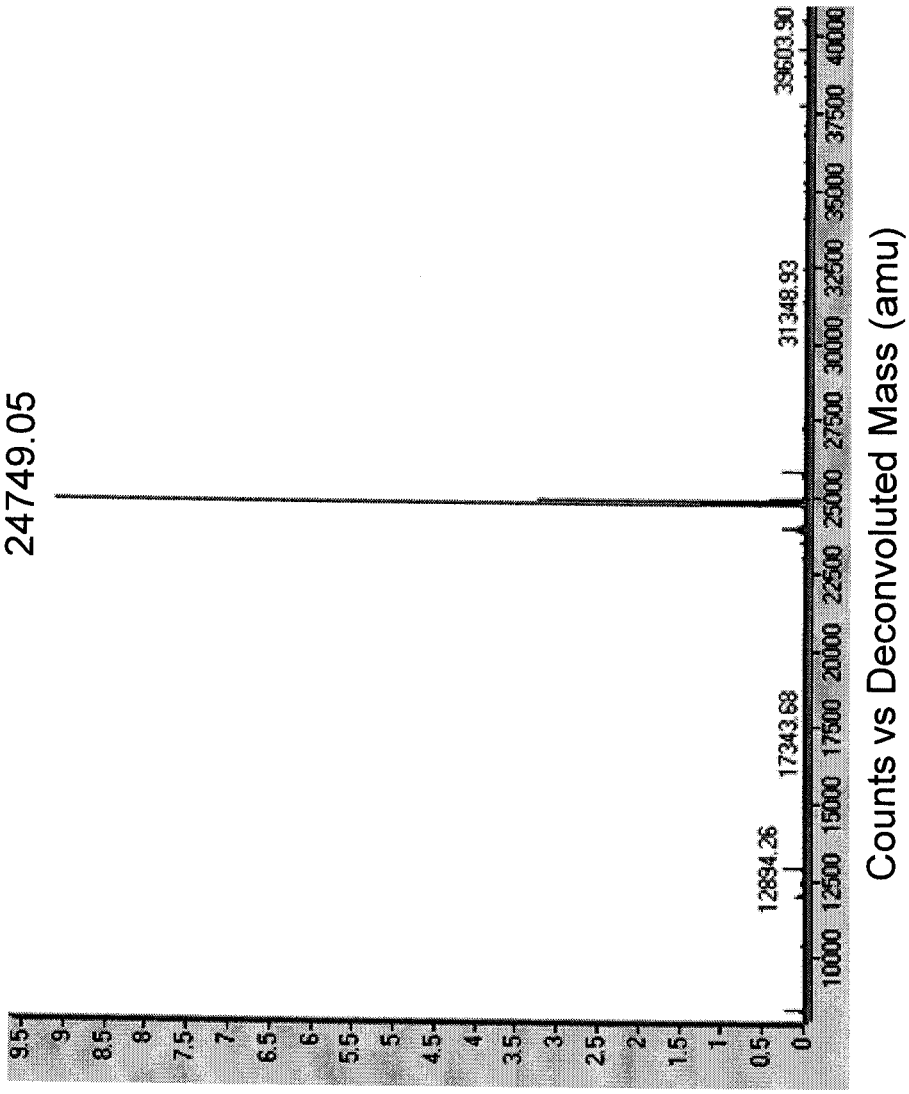

24749.05
12894.26
17343.68
31348.93
33603.90
Counts vs Deconvoluted Mass (amu)

Figure 14D

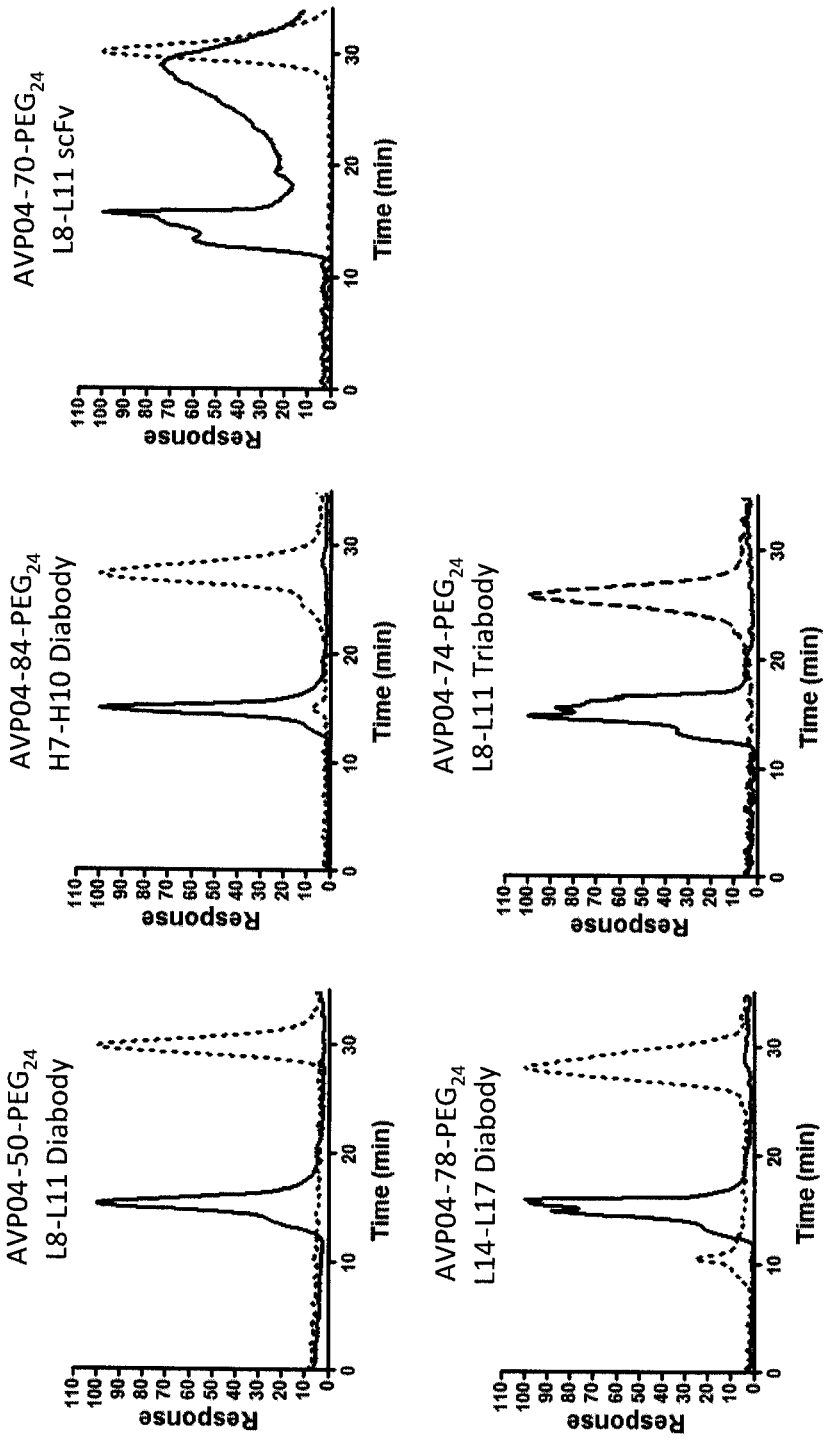

AVP04-50-PEG24
L8-L11 Diabody
AVP04-84-PEG24
H7-H10 Diabody
AVP04-74-PEG24
L8-L11 Triabody
AVP04-70-PEG24
L8-L11 scFv
AVP04-78-PEG24
L14-L17 Diabody
Response
Time (min)

Figure 15A

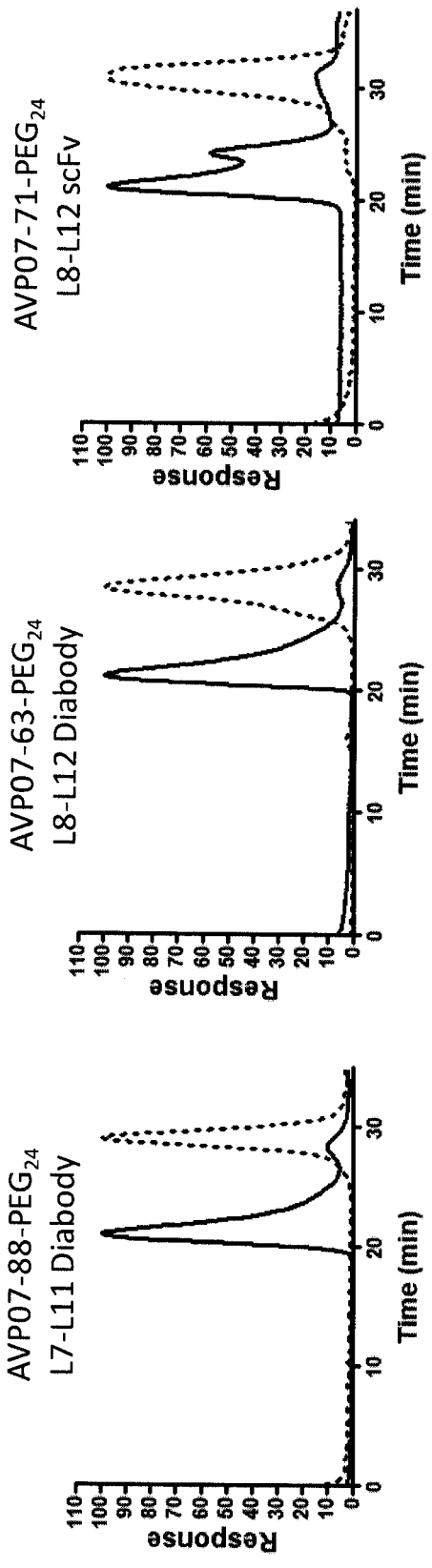

AVP07-88-PEG24
L7-L11 Diabody
AVP07-63-PEG24
L8-L12 Diabody
AVP07-71-PEG24
L8-L12 scFv
Response
Time (min)

Figure 15B

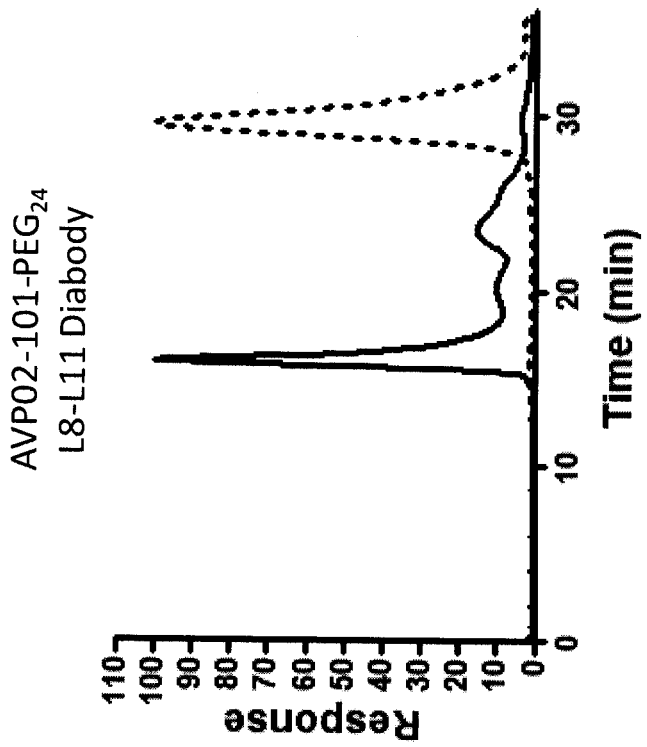

AVP02-101-PEG24
L8-L11 Diabody
Response
Time (min)
0
10
20
30
0
10
20
30
40
50
60
70
80
90
100
110

Figure 15C

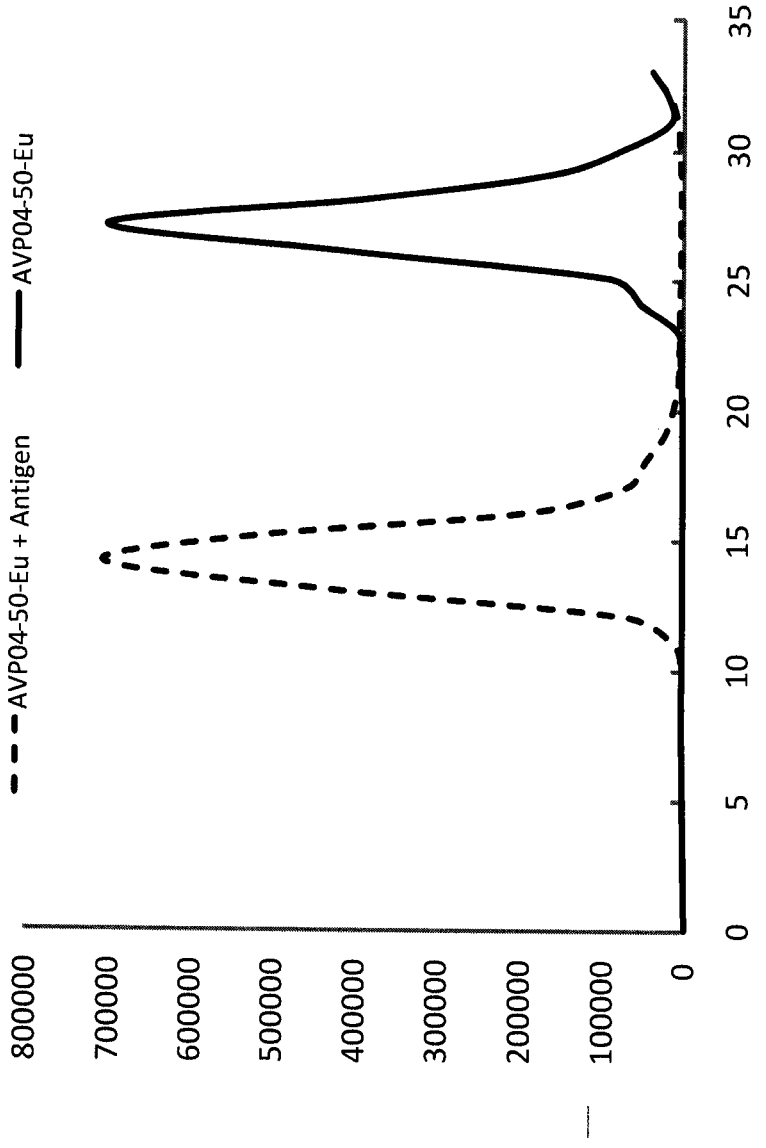

AVP04-50-Eu + Antigen
AVP04-50-Eu
800000
700000
600000
500000
400000
300000
200000
100000
0
0
5
10
15
20
25
30
35
Elution Time (min)

Figure 16

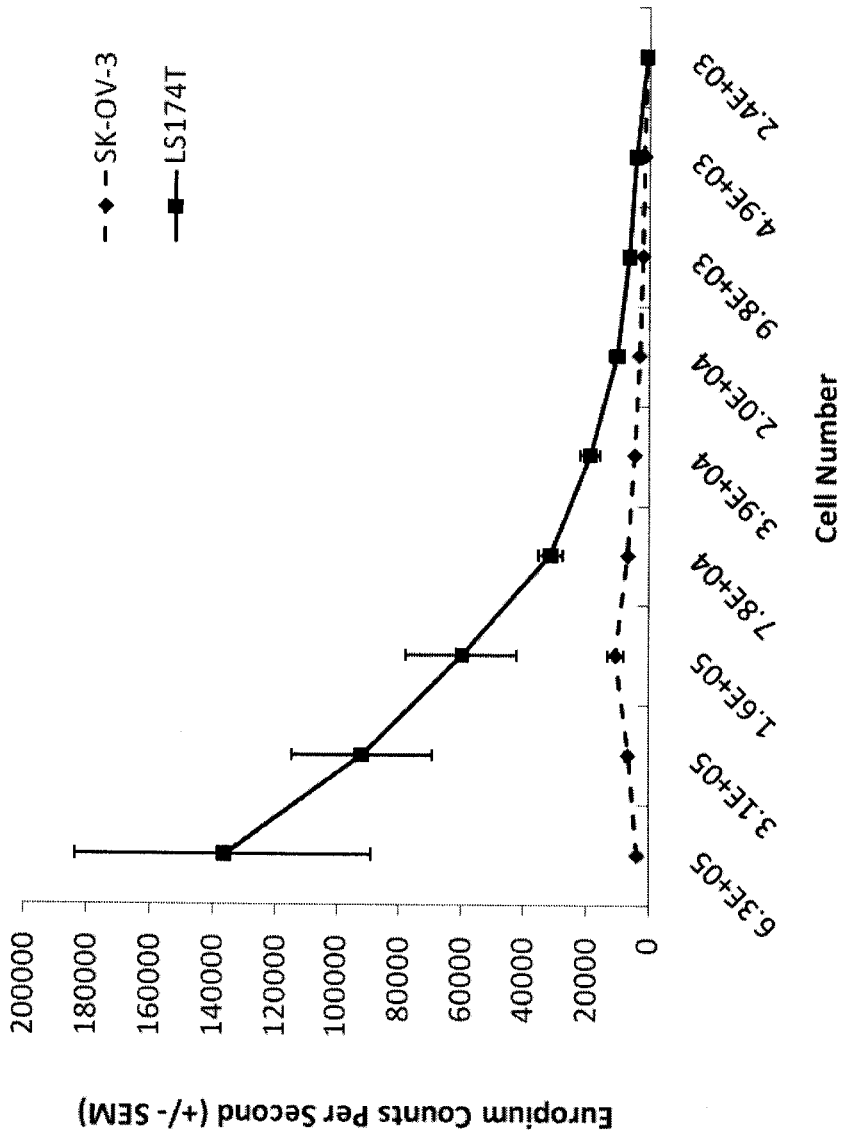

SK-OV-3
LS174T
Europium Counts Per Second (+/- SEM)
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
6.3E+05
3.1E+05
1.6E+05
7.8E+04
3.9E+04
2.0E+04
9.8E+03
4.9E+03
2.4E+03
Cell Number

Figure 17

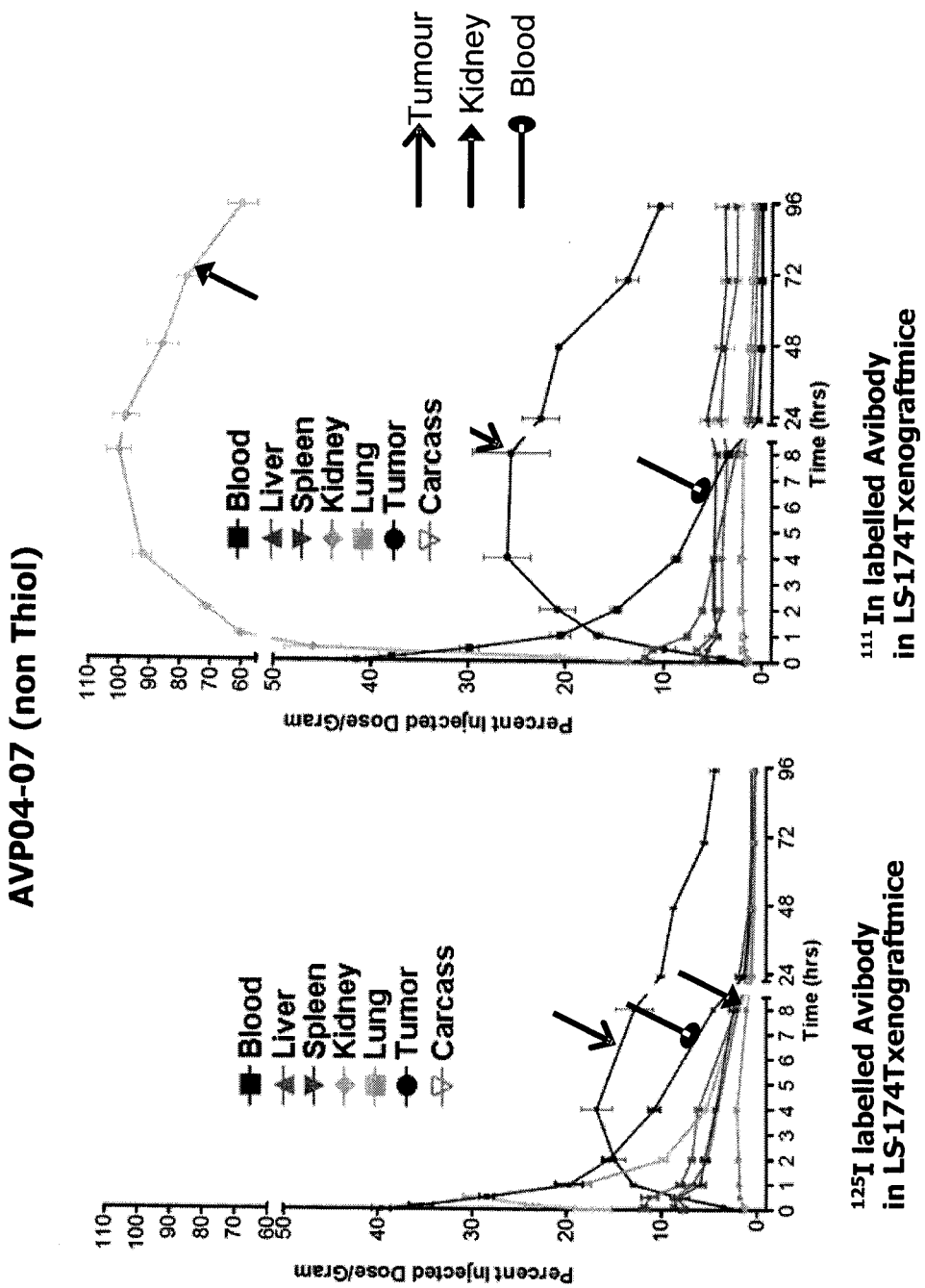

AVP04-07 (non Thiol)
Blood
Liver
Spleen
Kidney
Lung
Tumor
Carcass
Percent Injected Dose/Gram
Time (hrs)
125I labelled Avibody
in LS174Txenograftmice
111In labelled Avibody
in LS174Txenograftmice
Tumour
Kidney
Blood

Figure 18A

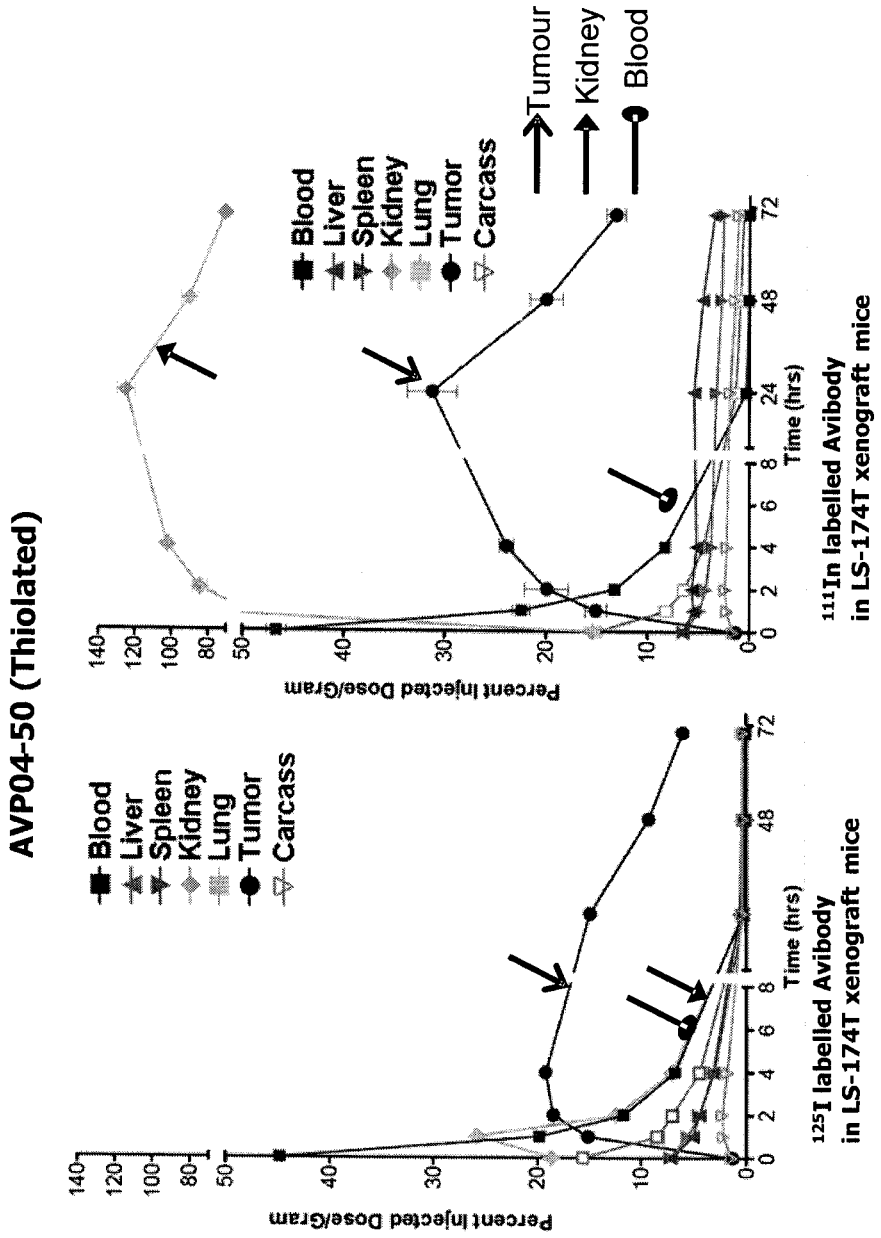

AVP04-50 (Thiolated)
Blood
Liver
Spleen
Kidney
Lung
Tumor
Carcass
Percent Injected Dose/Gram
Time (hrs)
125I labelled Avibody
in LS-174T xenograft mice
111In labelled Avibody
in LS-174T xenograft mice
Tumour
Kidney
Blood

Figure 18B

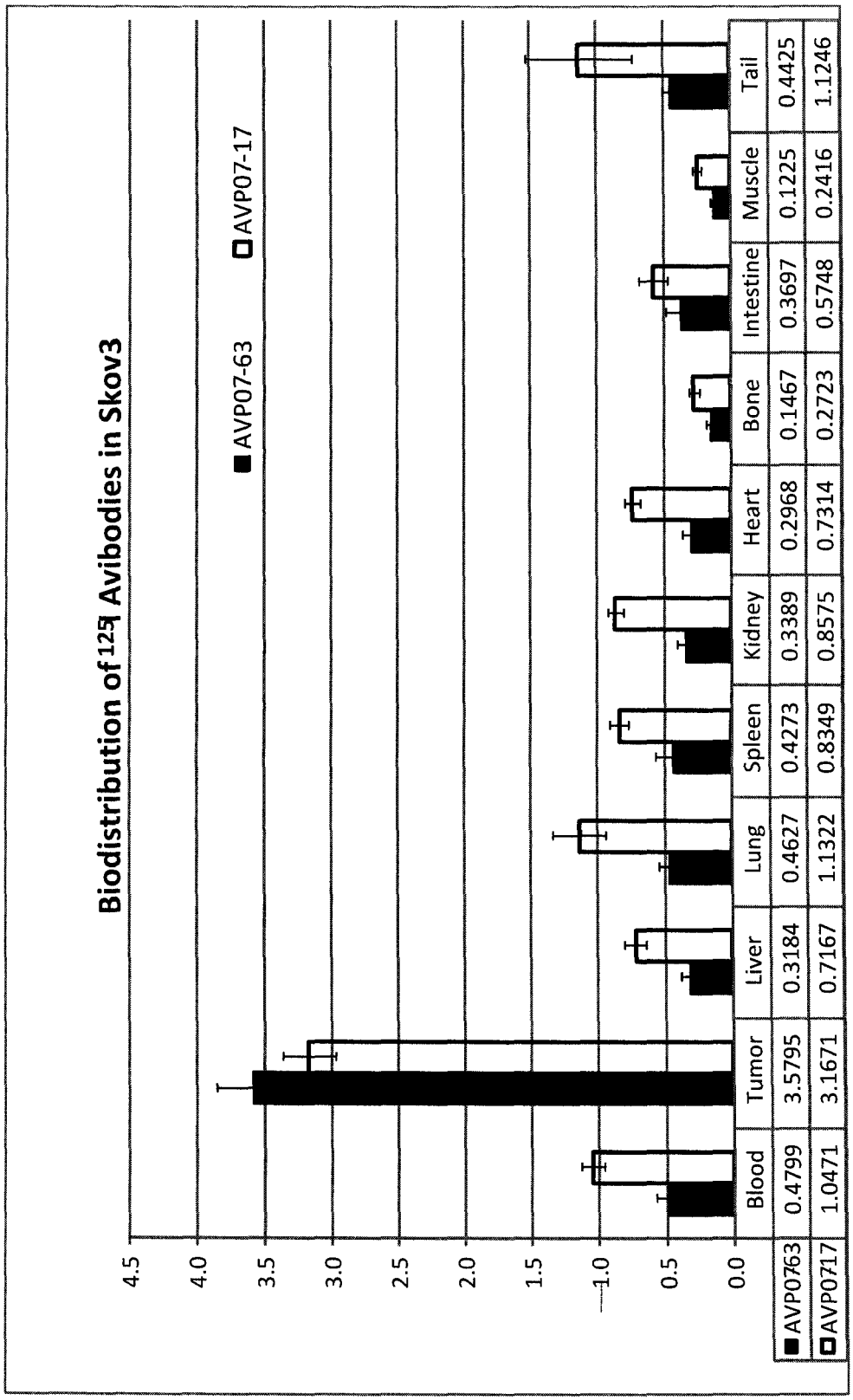

Biodistribution of 125I Avibodies in Skov3
AVP07-63
AVP07-17
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Blood Tumor Liver Lung Spleen Kidney Heart Bone Intestine Muscle Tail
AVP0763 0.4799 3.5795 0.3184 0.4627 0.4273 0.3389 0.2968 0.1467 0.3697 0.1225 0.4425
AVP0717 1.0471 3.1671 0.7167 1.1322 0.8349 0.8575 0.7314 0.2723 0.5748 0.2416 1.1246

Figure 19

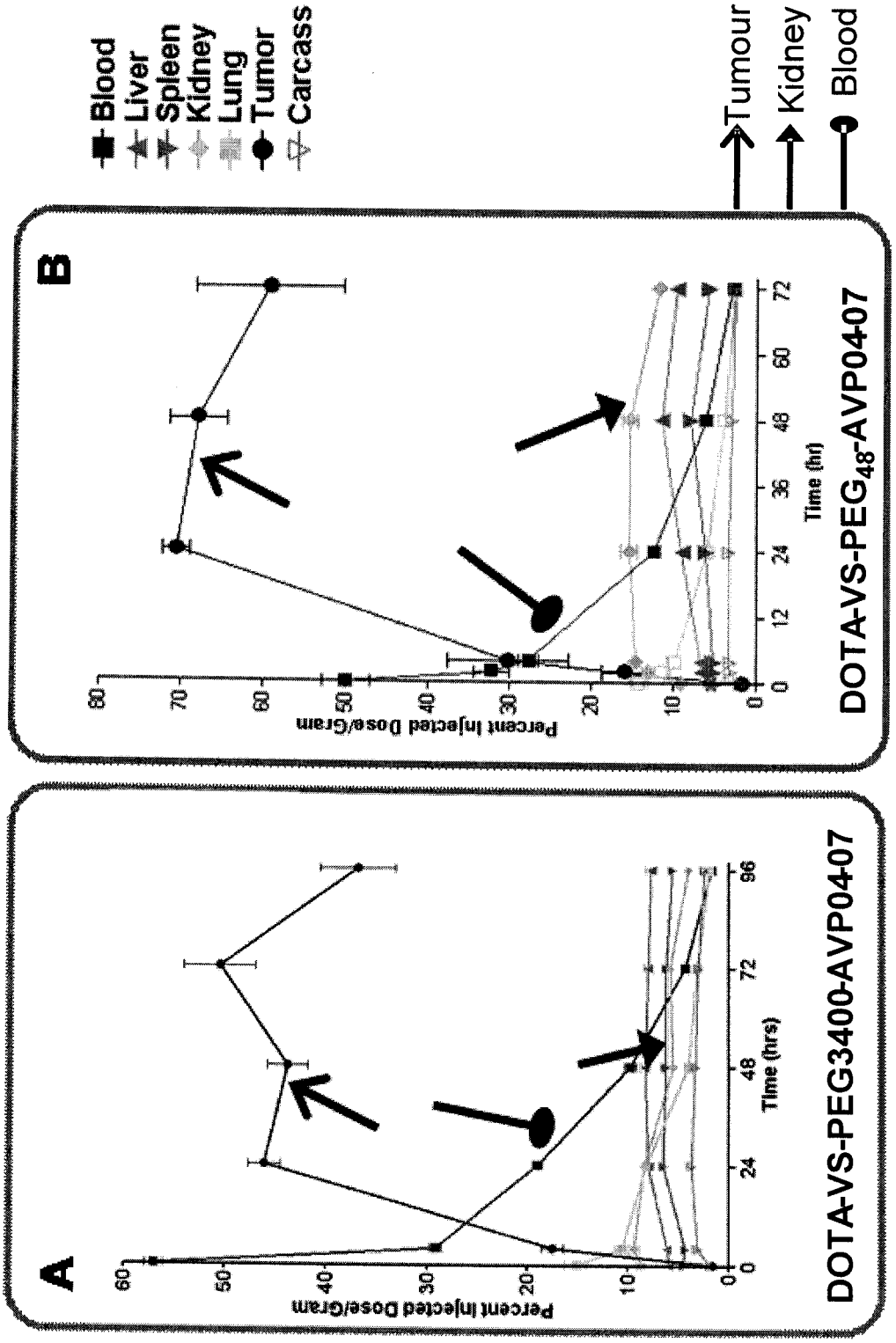

A
DOTA-VS-PEG3400-AVP0407
Percent Injected Dose/Gram
Time (hrs)
B
DOTA-VS-PEG48-AVP0407
Percent Injected Dose/Gram
Time (hr)
Blood
Liver
Spleen
Kidney
Lung
Tumor
Carcass
Tumour
Kidney
Blood

Figure 20

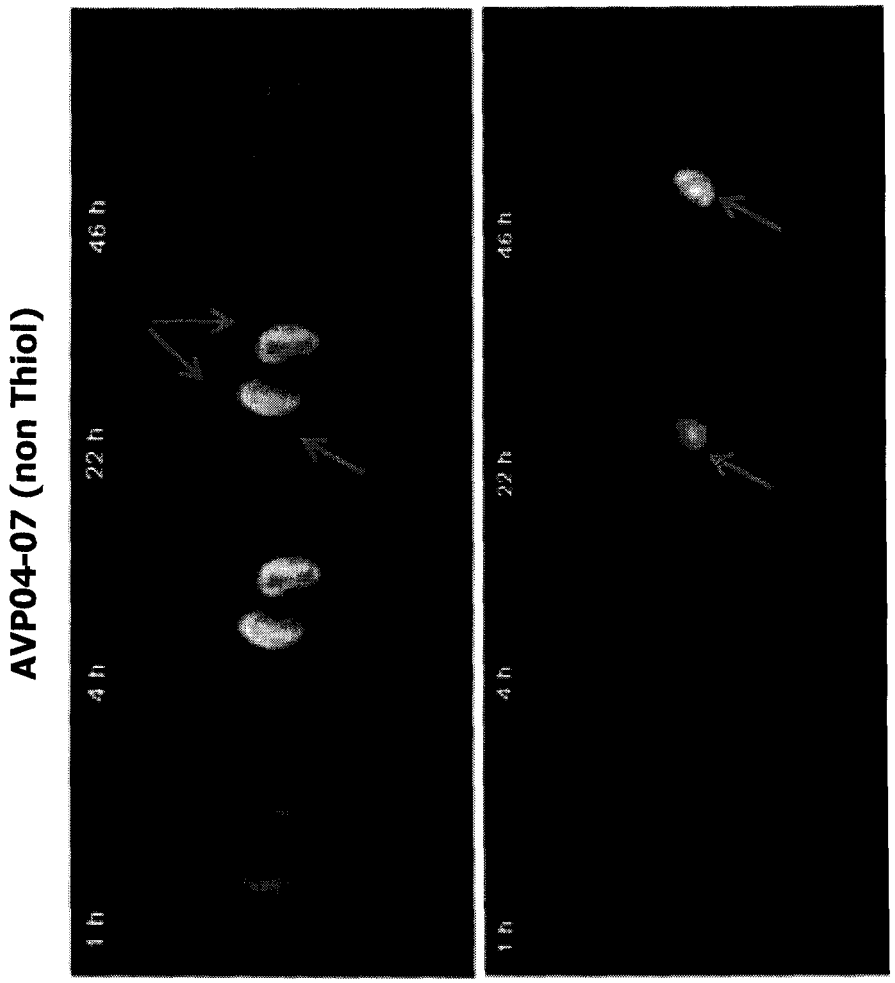

AVP04-07 (non Thiol)
1 h
4 h
22 h
46 h
No-PEGylation
PEGylation to Random Surface Lysines

Figure 21A

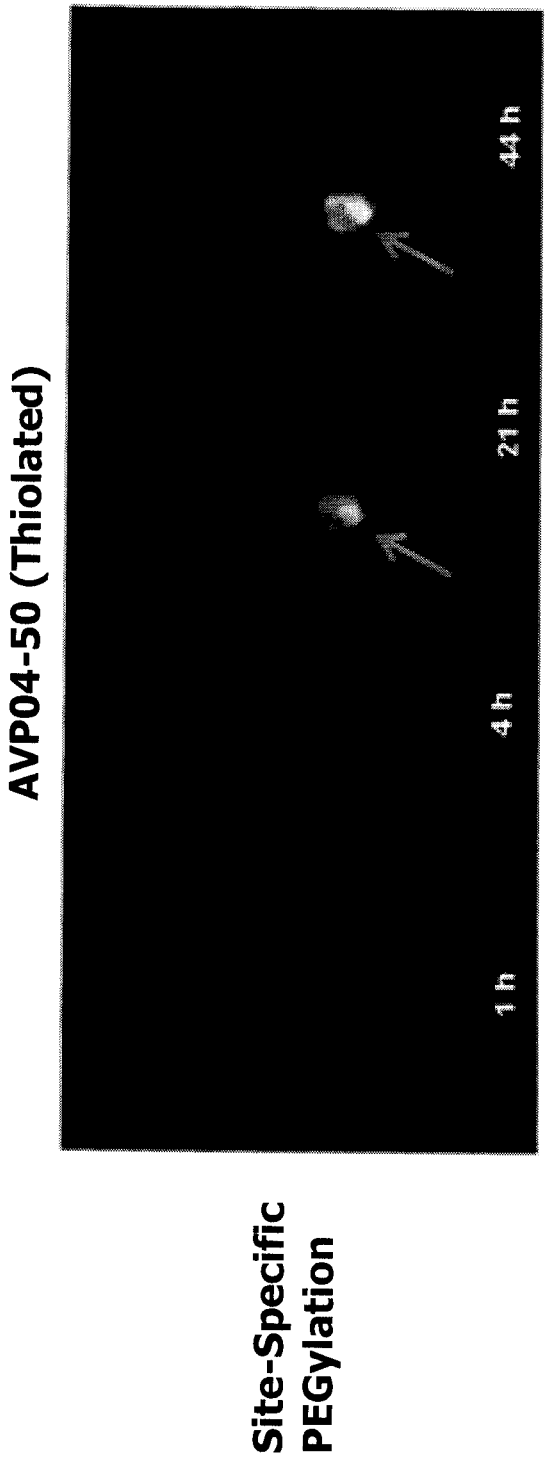


Figure 21B

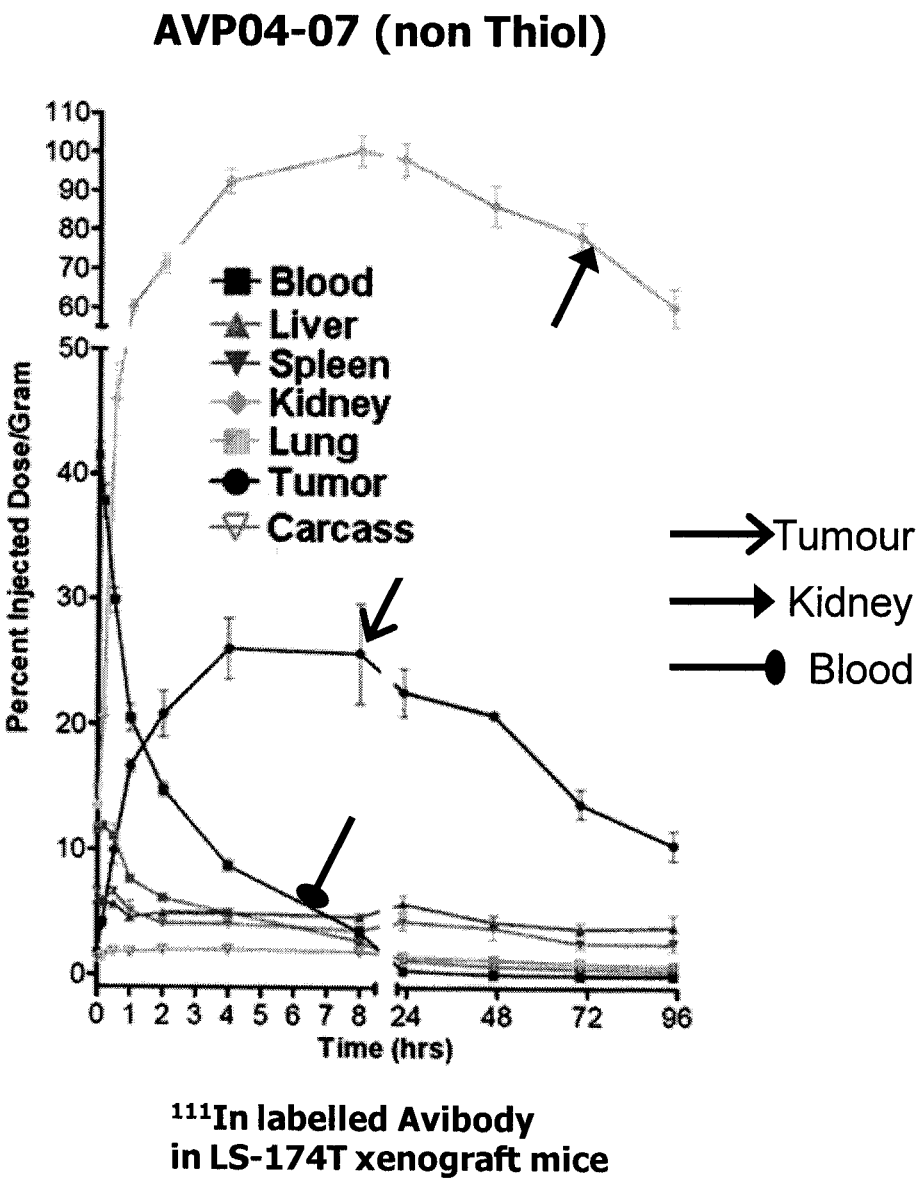

AVP04-07 (non Thiol)
Percent Injected Dose/Gram
Time (hrs)
Blood
Liver
Spleen
Kidney
Lung
Tumor
Carcass
Tumour
Kidney
Blood
111In labelled Avibody
in LS-174T xenograft mice

Figure 22A

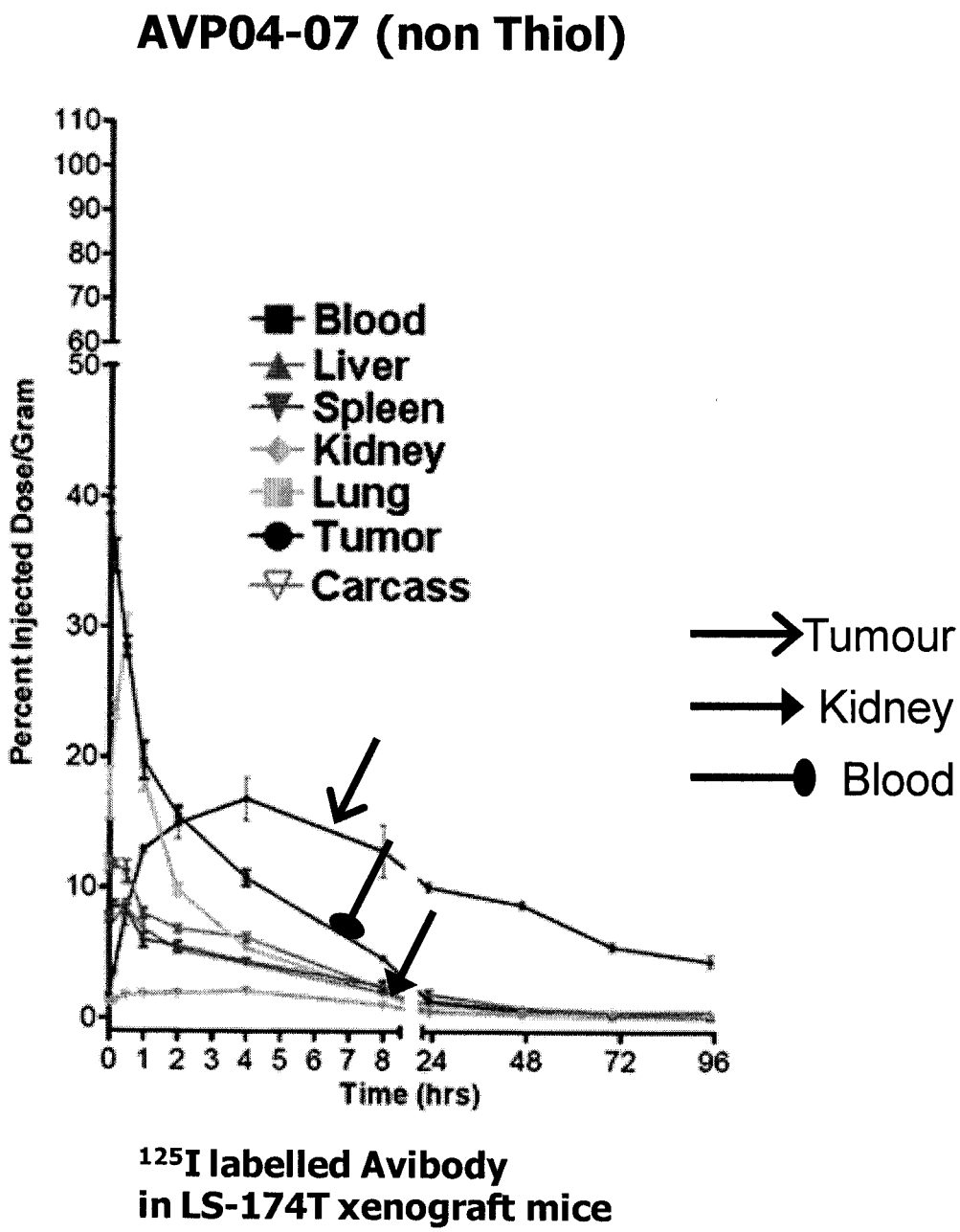
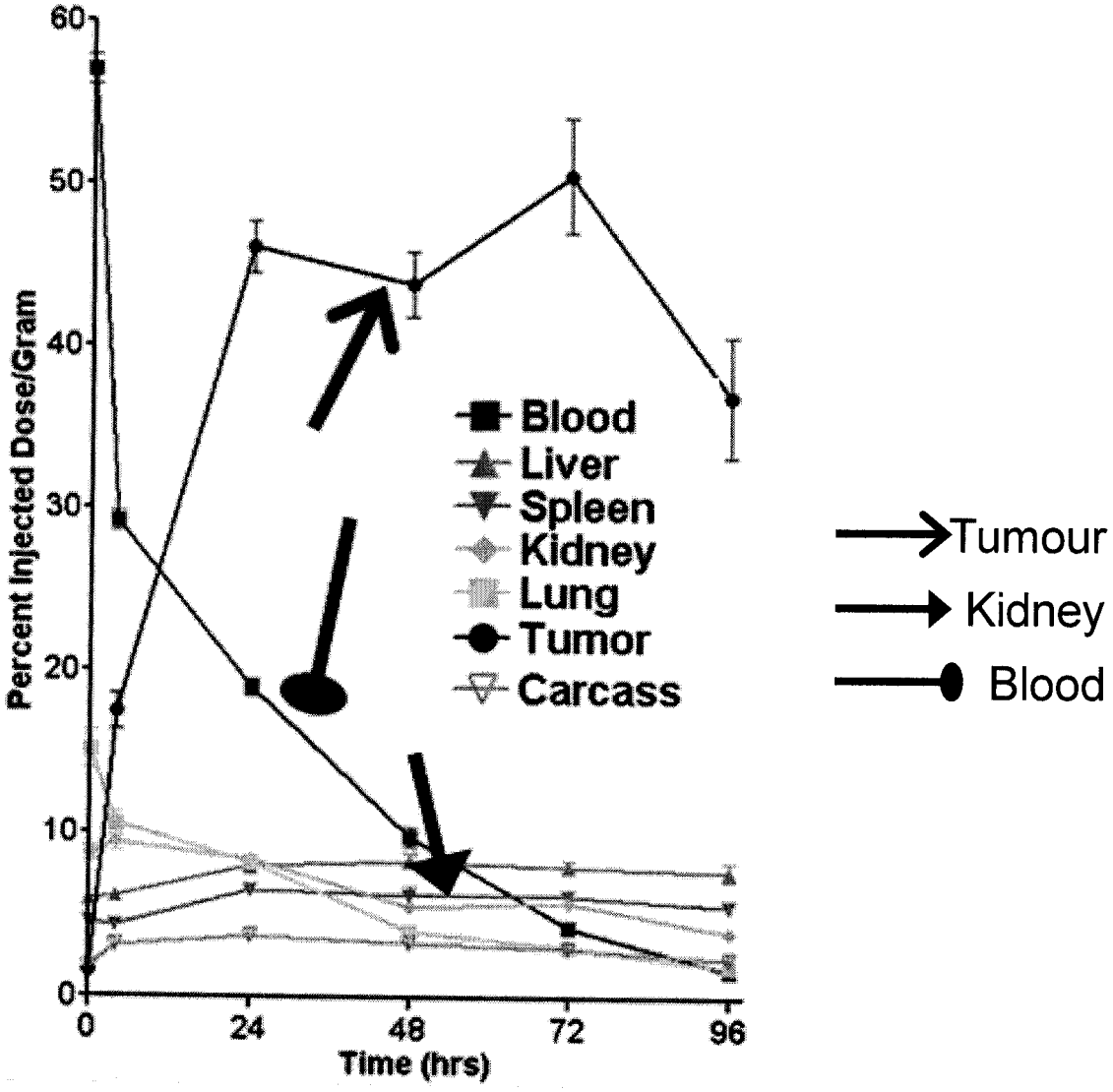

AVP04-07 (non Thiol)
Percent Injected Dose/Gram
110
100
90
80
70
60
50
40
30
20
10
0
Blood
Liver
Spleen
Kidney
Lung
Tumor
Carcass
0 1 2 3 4 5 6 7 8 24 48 72 96
Time (hrs)
Tumour
Kidney
Blood
125I labelled Avibody
in LS-174T xenograft mice

Figure 22B



^{111}In labelled DOTA-VS-PEG3400-AVP04-07 Avibody in LS-174T xenograft mice

Figure 22C

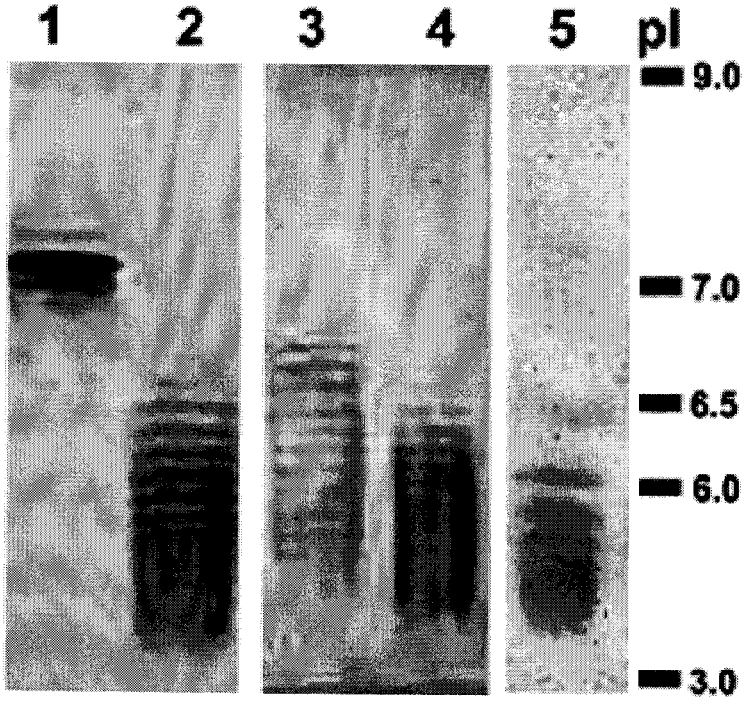


Figure 23A

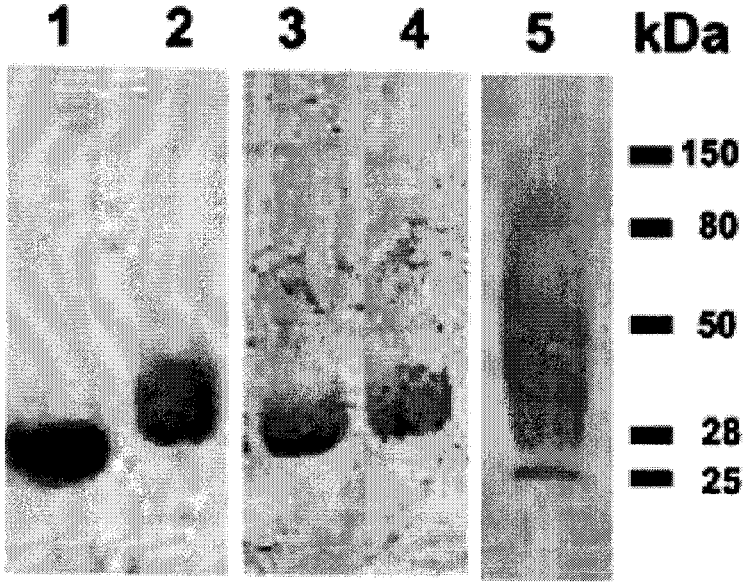


Figure 23B

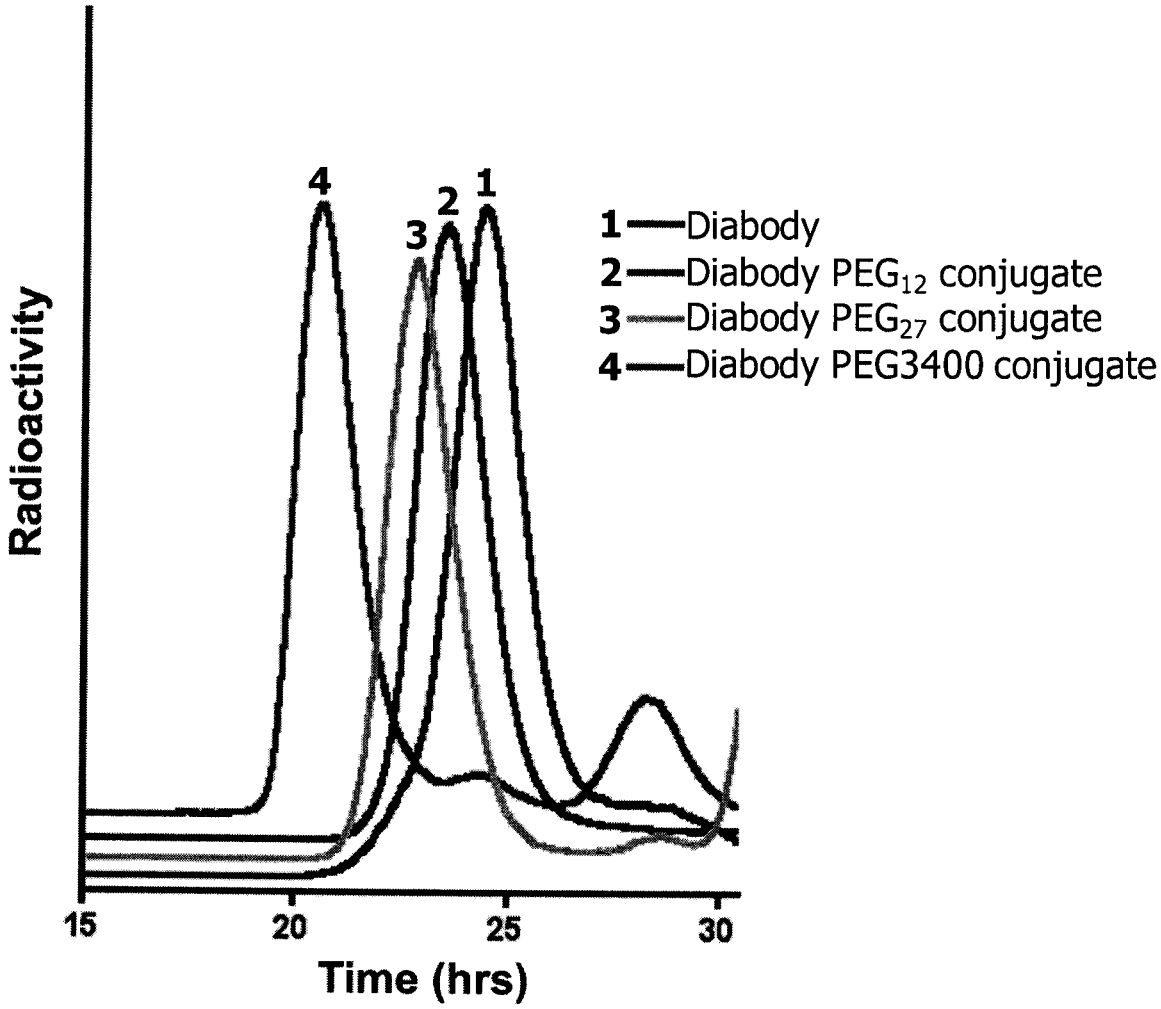

Radioactivity
4
3
2
1
1—Diabody
2—Diabody PEG12 conjugate
3—Diabody PEG27 conjugate
4—Diabody PEG3400 conjugate
15
20
25
30
Time (hrs)

Figure 24

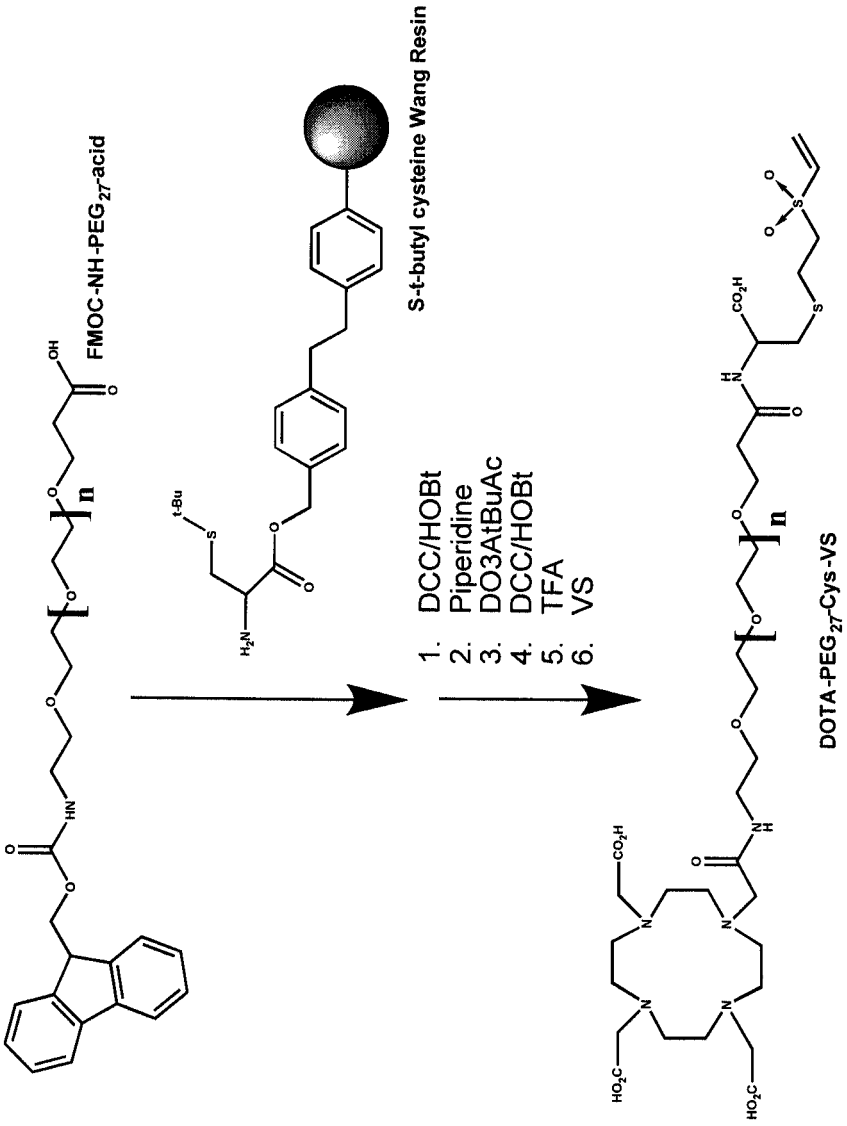

FMOC-NH-PEG27-acid
S-t-butyl cysteine Wang Resin
1. DCC/HOBt
2. Piperidine
3. DO3AtBuAc
4. DCC/HOBt
5. TFA
6. VS
DOTA-PEG27-Cys-VS

Figure 25

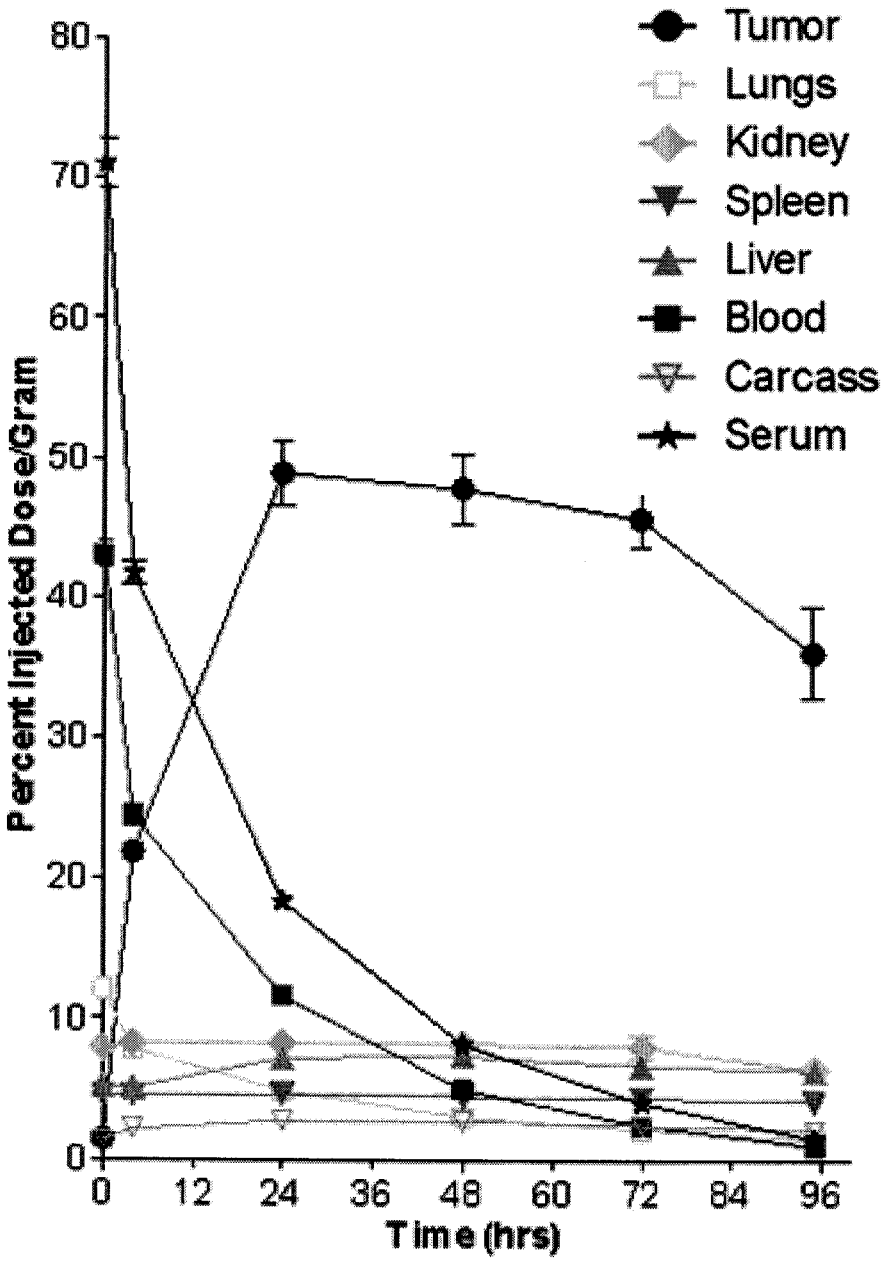

Tumor
Lungs
Kidney
Spleen
Liver
Blood
Carcass
Serum
Percent Injected Dose/Gram
0
10
20
30
40
50
60
70
80
0
12
24
36
48
60
72
84
96
Time (hrs)

Figure 26A

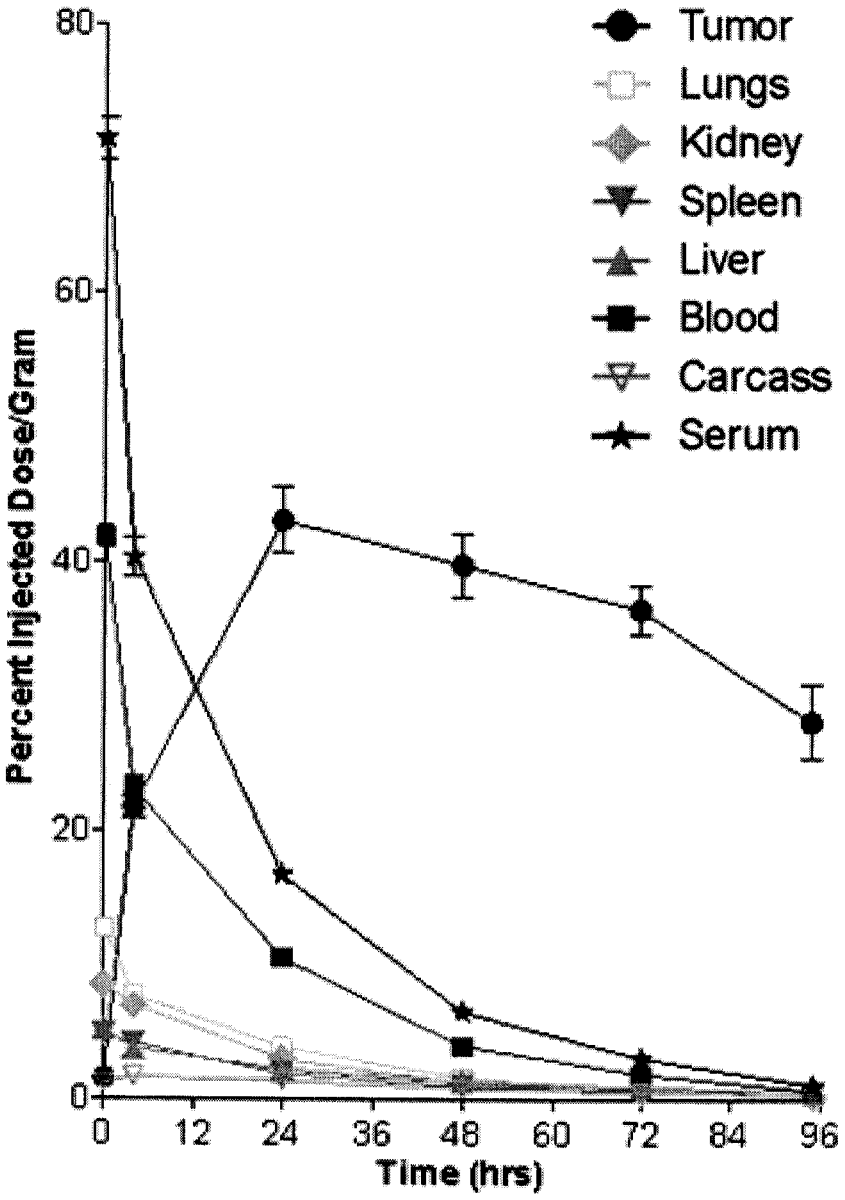

Tumor
Lungs
Kidney
Spleen
Liver
Blood
Carcass
Serum
Percent Injected Dose/Gram
80
60
40
20
0
0
12
24
36
48
60
72
84
96
Time (hrs)

Figure 26B

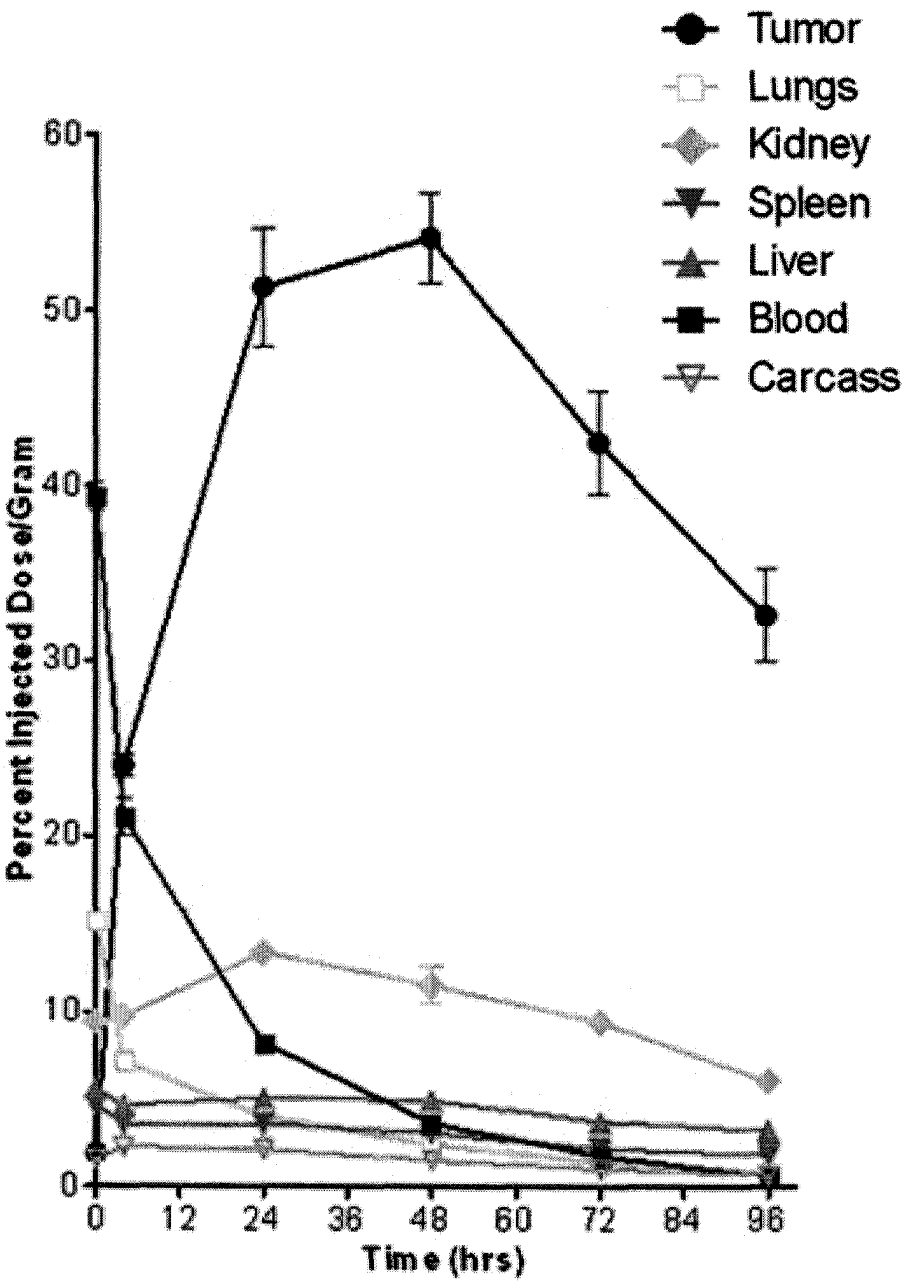

Tumor
Lungs
Kidney
Spleen
Liver
Blood
Carcass
Percent Injected Dose/Gram
60
50
40
30
20
10
0
0
12
24
36
48
60
72
84
96
Time (hrs)

Figure 26C

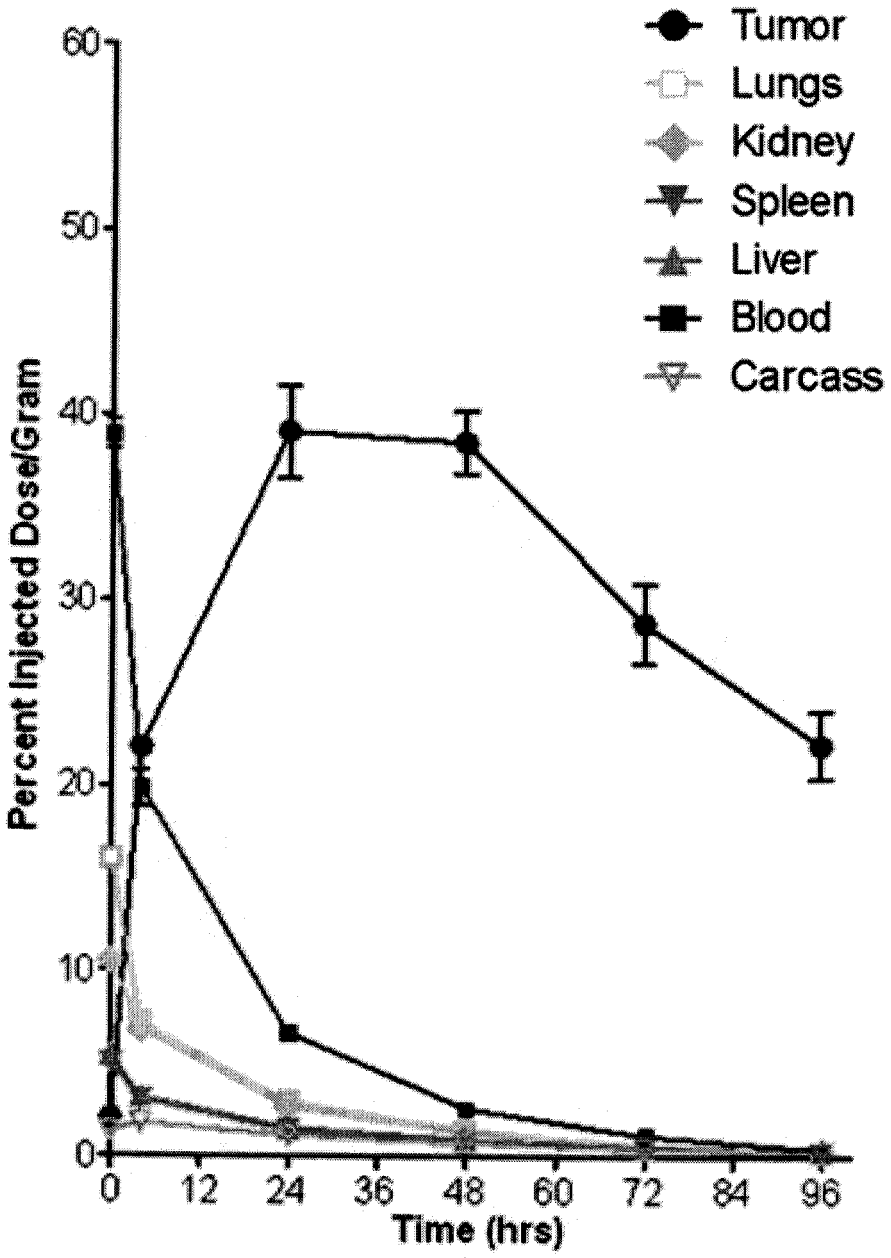

Tumor
Lungs
Kidney
Spleen
Liver
Blood
Carcass
Percent Injected Dose/Gram
60
50
40
30
20
10
0
0
12
24
36
48
60
72
84
96
Time (hrs)

Figure 26D

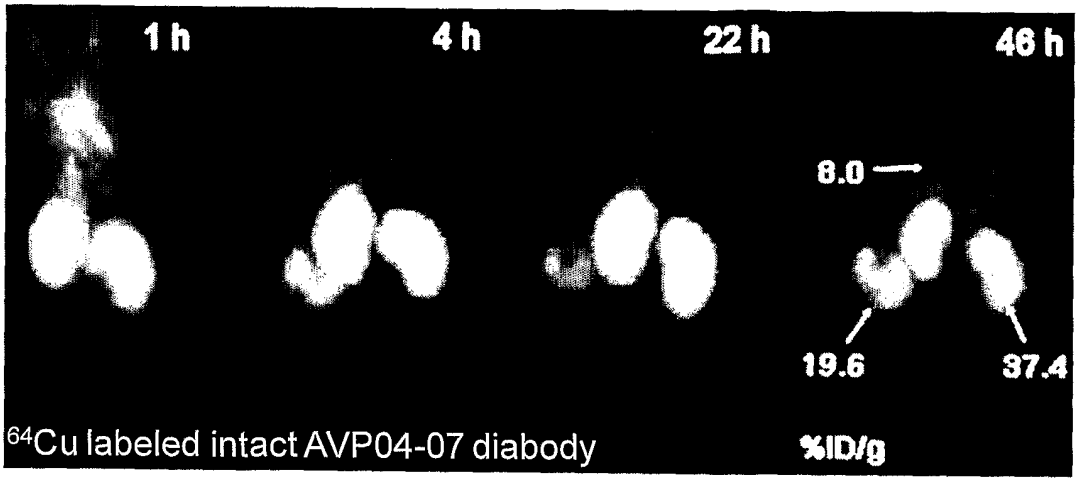


Figure 27A

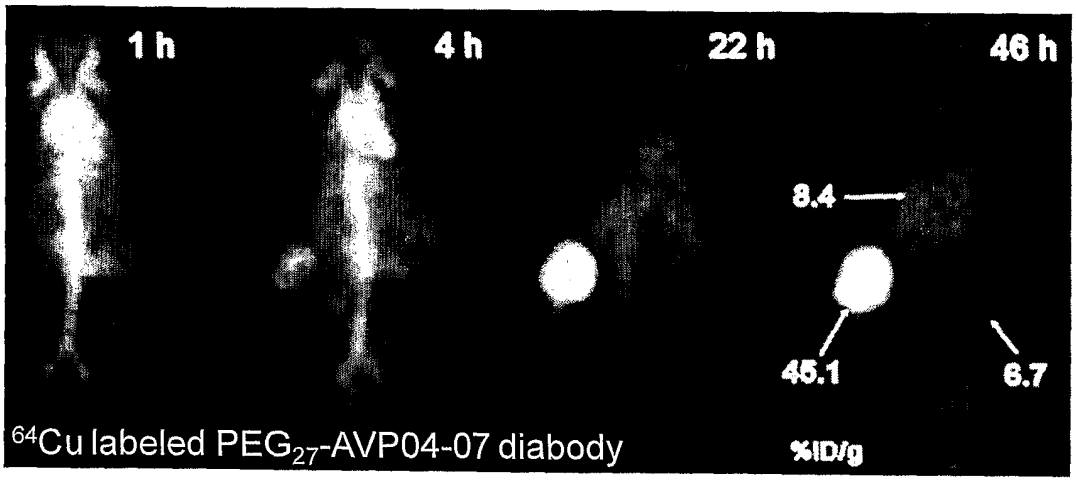


Figure 27B

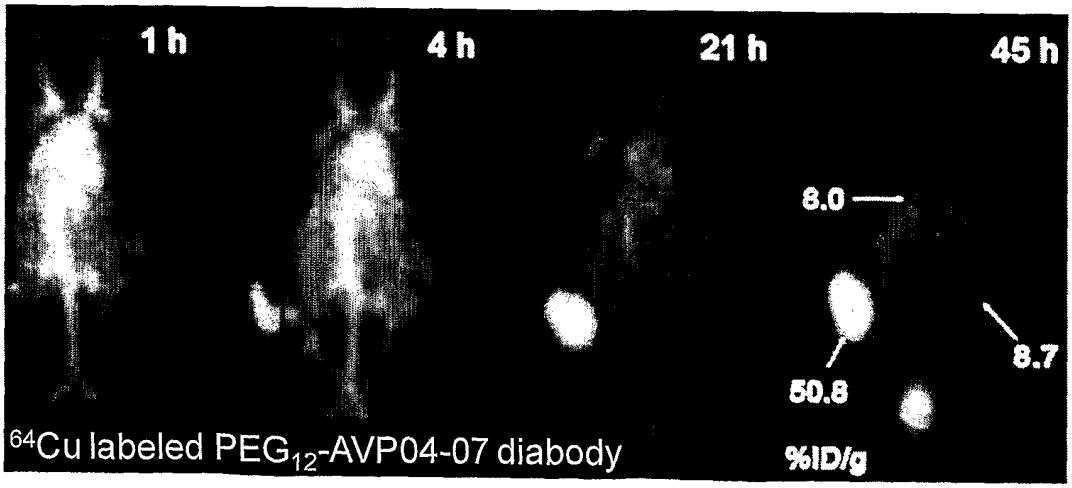


Figure 27C