Figure 1

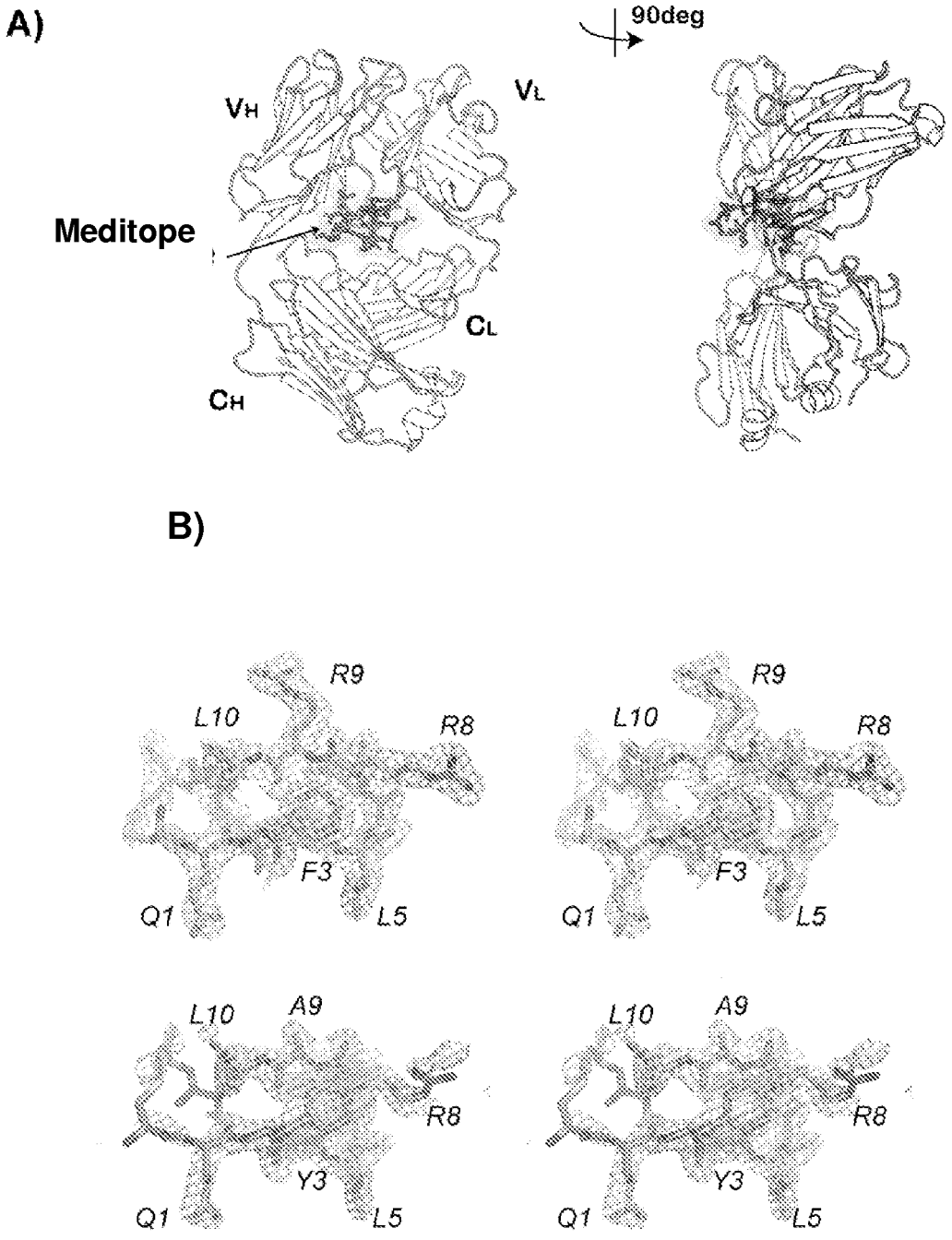

A)
90deg
VH
VL
Meditope
CL
CH
B)
R9
L10
R8
F3
Q1
L5
R9
L10
R8
F3
Q1
L5
L10
A9
R8
Y3
Q1
L5
L10
A9
R8
Y3
Q1
L5

Figure 2

A)

Light Chain

Kabat Number	10	38-------43	83-----87	100----105	165
cetuximab	I	QRTNGS	IADYY	AGTKLE	E
ch 14.18	S	QKPGQS	LGVYF	AGTKLE	E
trastuzumab	S	QKPGKA	FATYY	QGTKVE	E

Heavy Chain

Kabat Number	39--------44	87-89	105-108	150	175-176
cetuximab	QSPGKG	TAI	QGTL	E	PA
ch 14.18	QNIGKS	SAV	QGTS	E	PA
trastuzumab	QAPGKG	TAV	QGTL	E	PA

B)

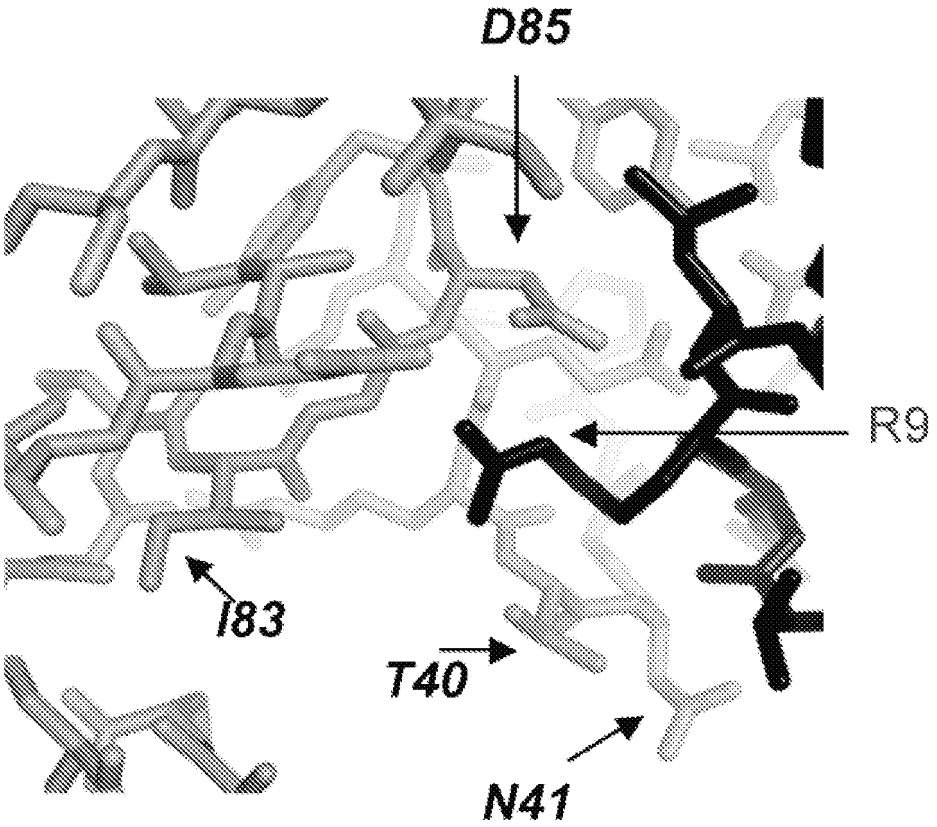


Figure 3

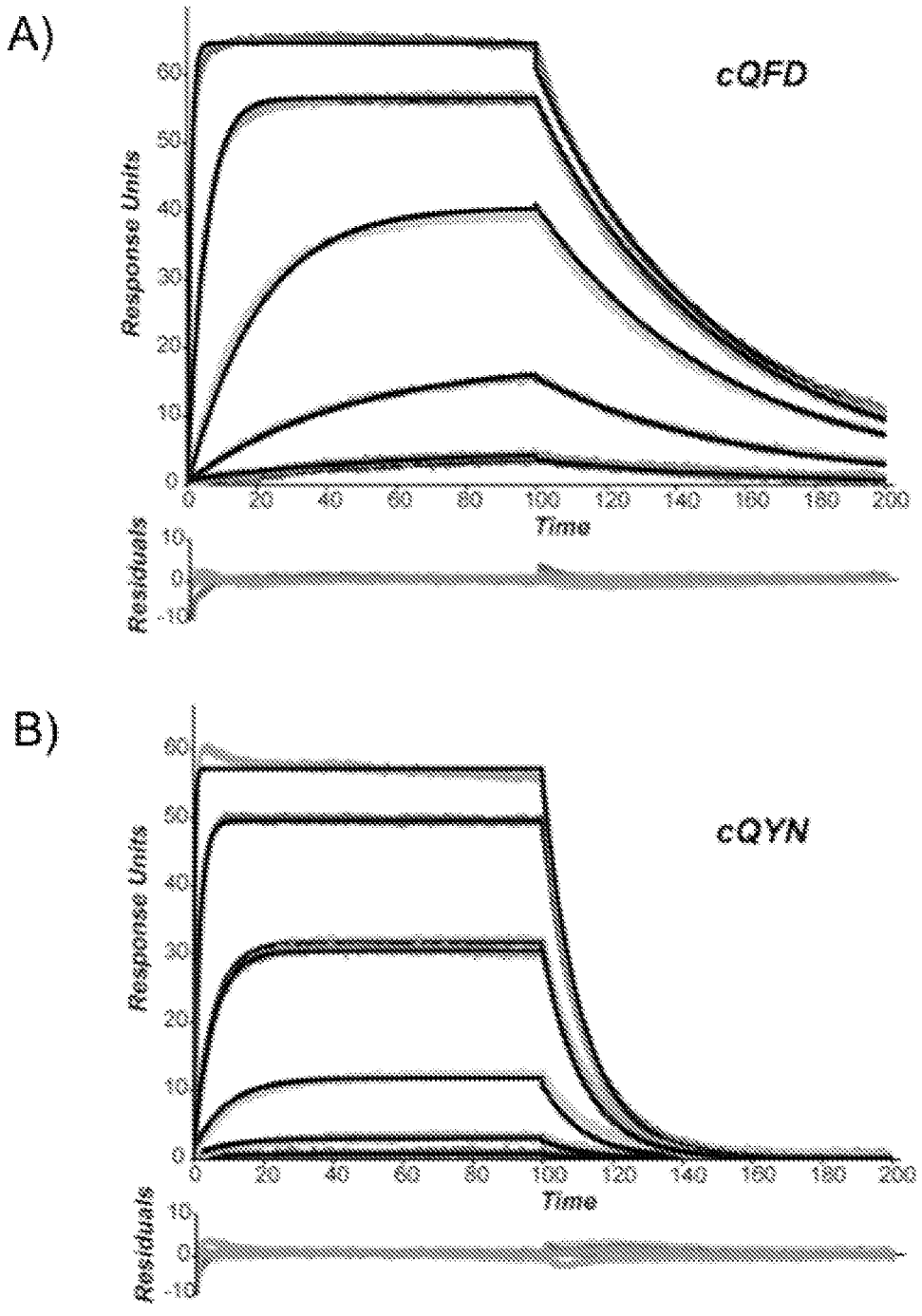

A)
cQFD
Response Units
Time
Residuals
B)
cQYN
Response Units
Time
Residuals

Figure 4 A-C

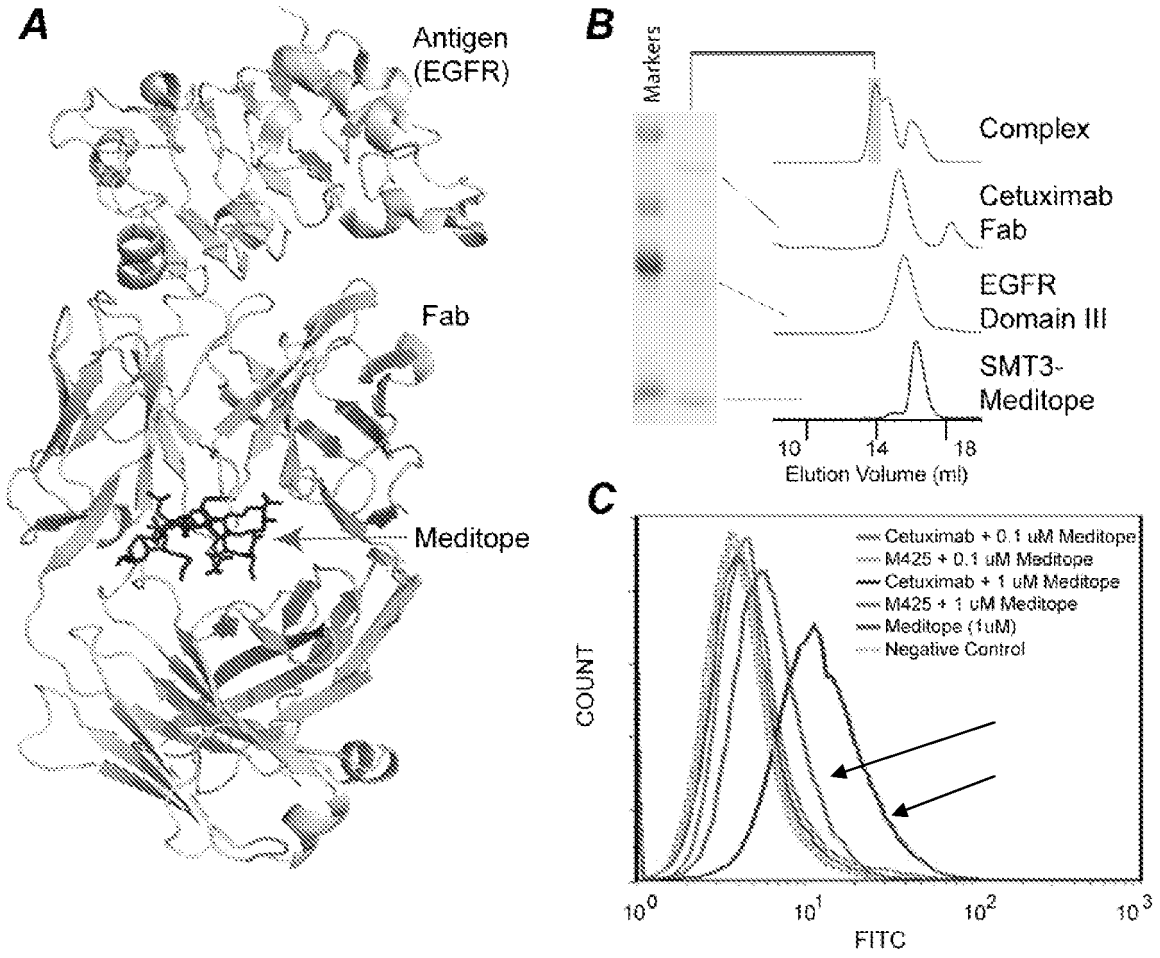

A
Antigen (EGFR)
Fab
Meditope
B
Markers
Complex
Cetuximab Fab
EGFR Domain III
SMT3-Meditope
10
14
18
Elution Volume (ml)
C
Cetuximab + 0.1 uM Meditope
M425 + 0.1 uM Meditope
Cetuximab + 1 uM Meditope
M425 + 1 uM Meditope
Meditope (1uM)
Negative Control
COUNT
10^0
10^1
10^2
10^3
FITC

Figure 4D

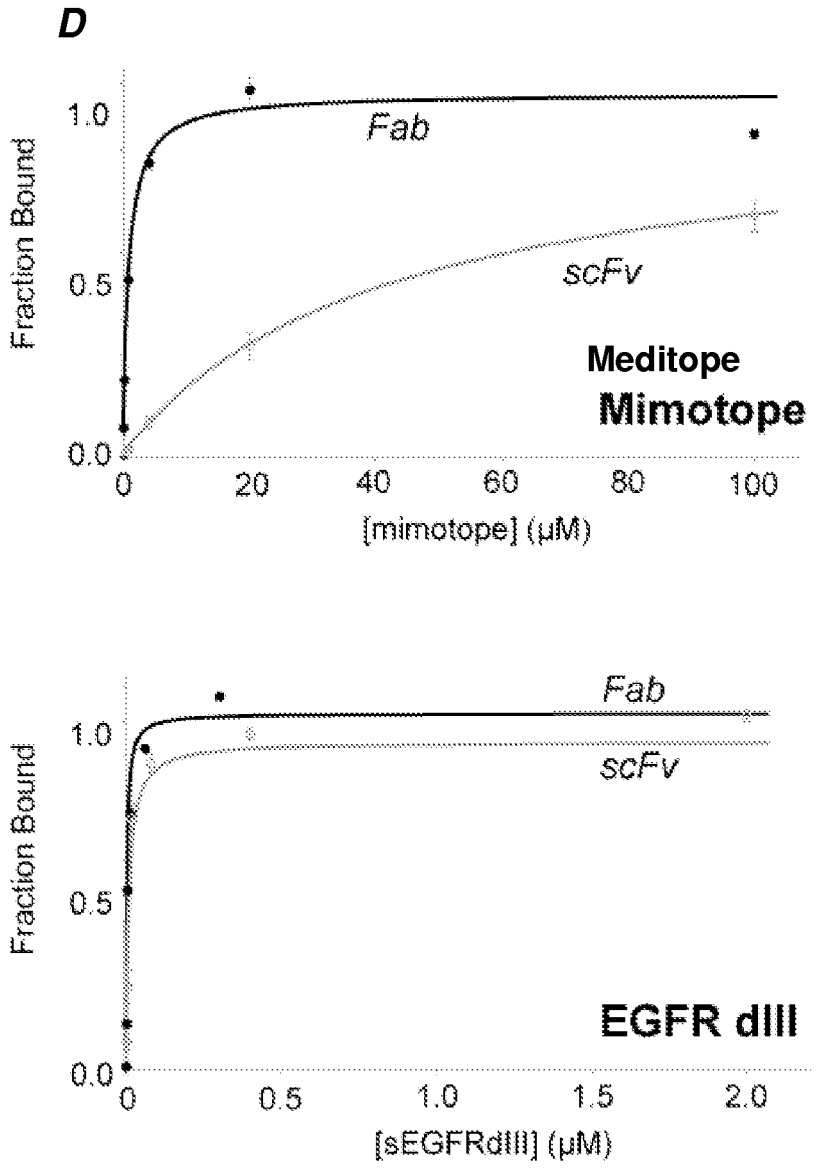

D
Fraction Bound
1.0
0.5
0.0
Fab
scFv
Meditope
Mimotope
0
20
40
60
80
100
[mimotope] (μM)
Fraction Bound
1.0
0.5
0.0
Fab
scFv
EGFR dIII
0
0.5
1.0
1.5
2.0
[sEGFRdIII] (μM)

Figure 5

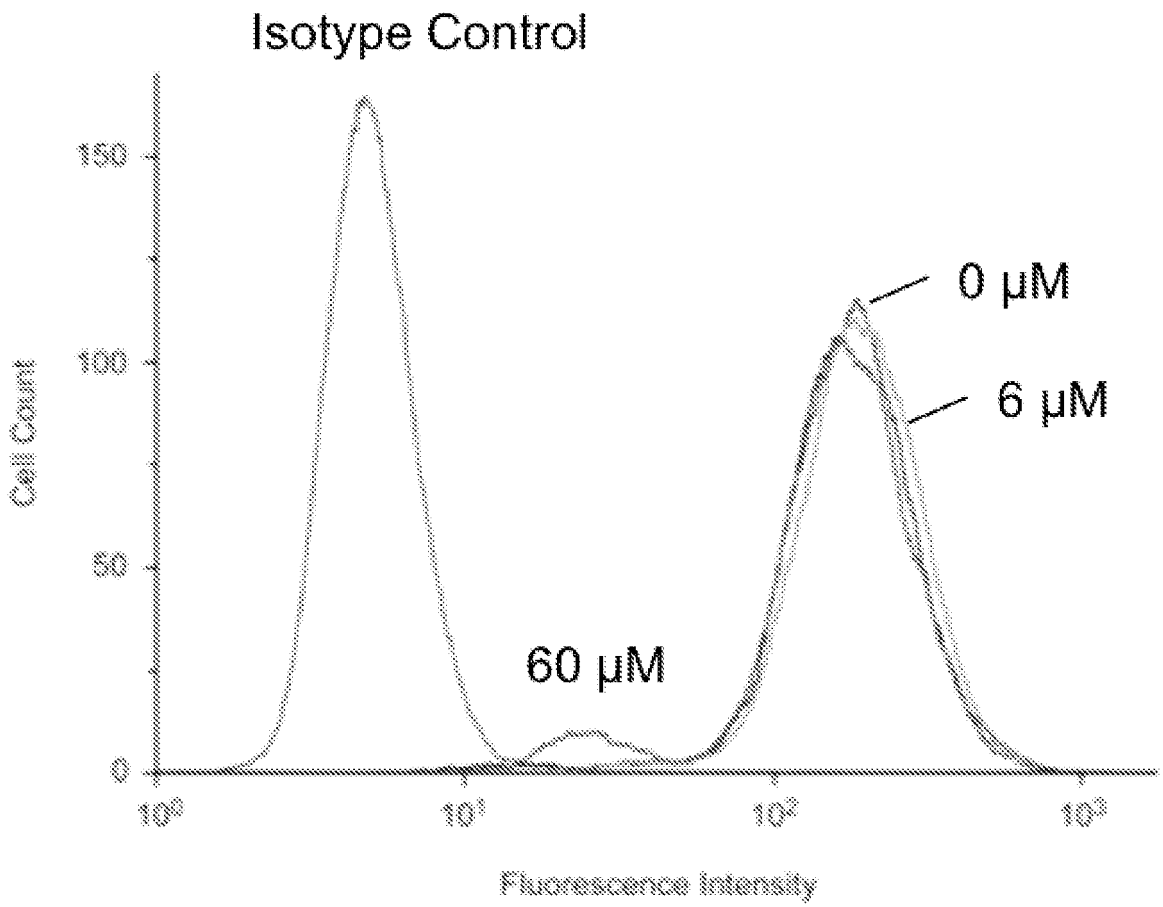

Isotype Control
150
100
50
0
Cell Count
0 µM
6 µM
60 µM
10^0
10^1
10^2
10^3
Fluorescence Intensity

Figure 6

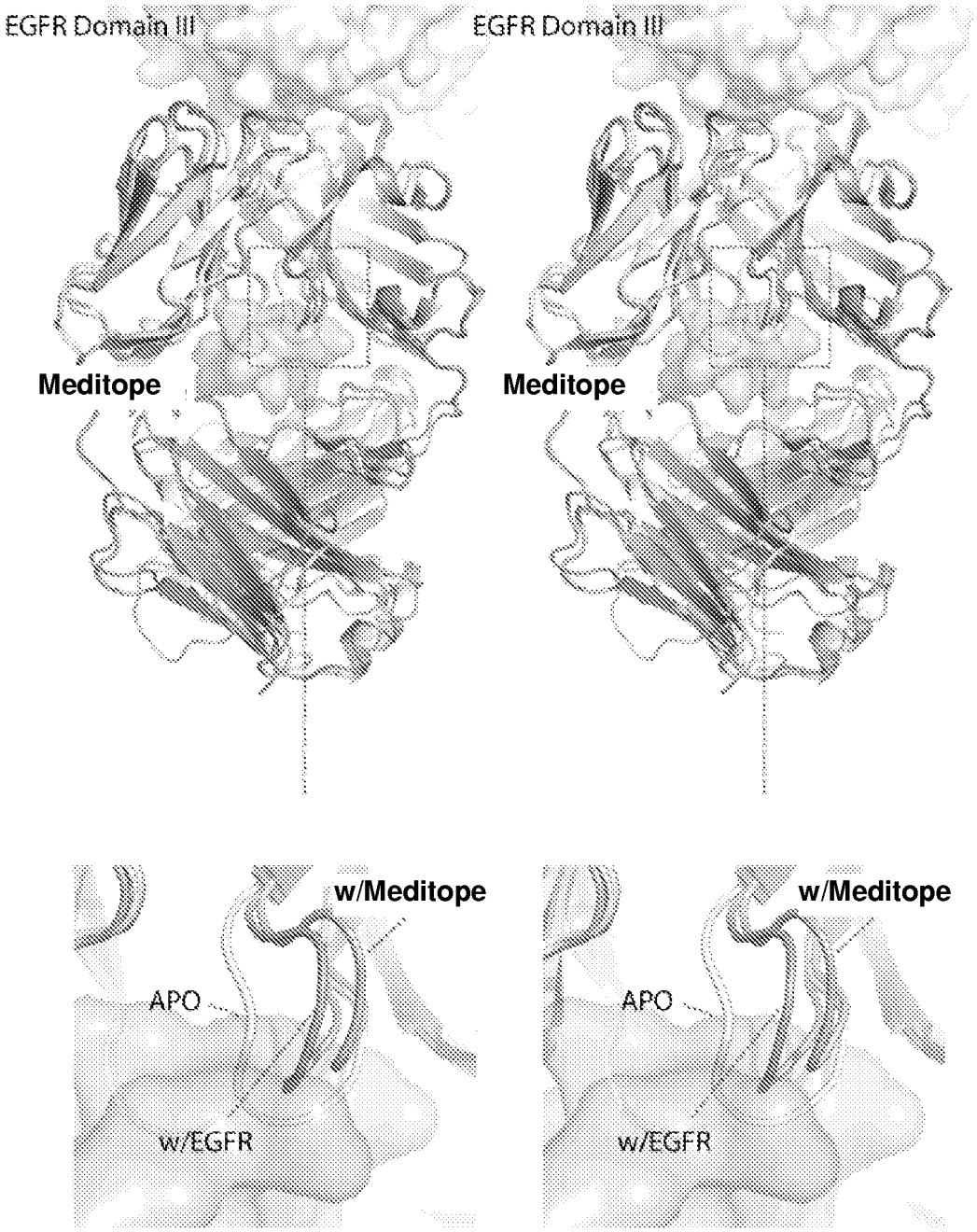

EGFR Domain III
Meditope
EGFR Domain III
Meditope
w/Meditope
APO
w/EGFR
w/Meditope
APO
w/EGFR

Figure 7

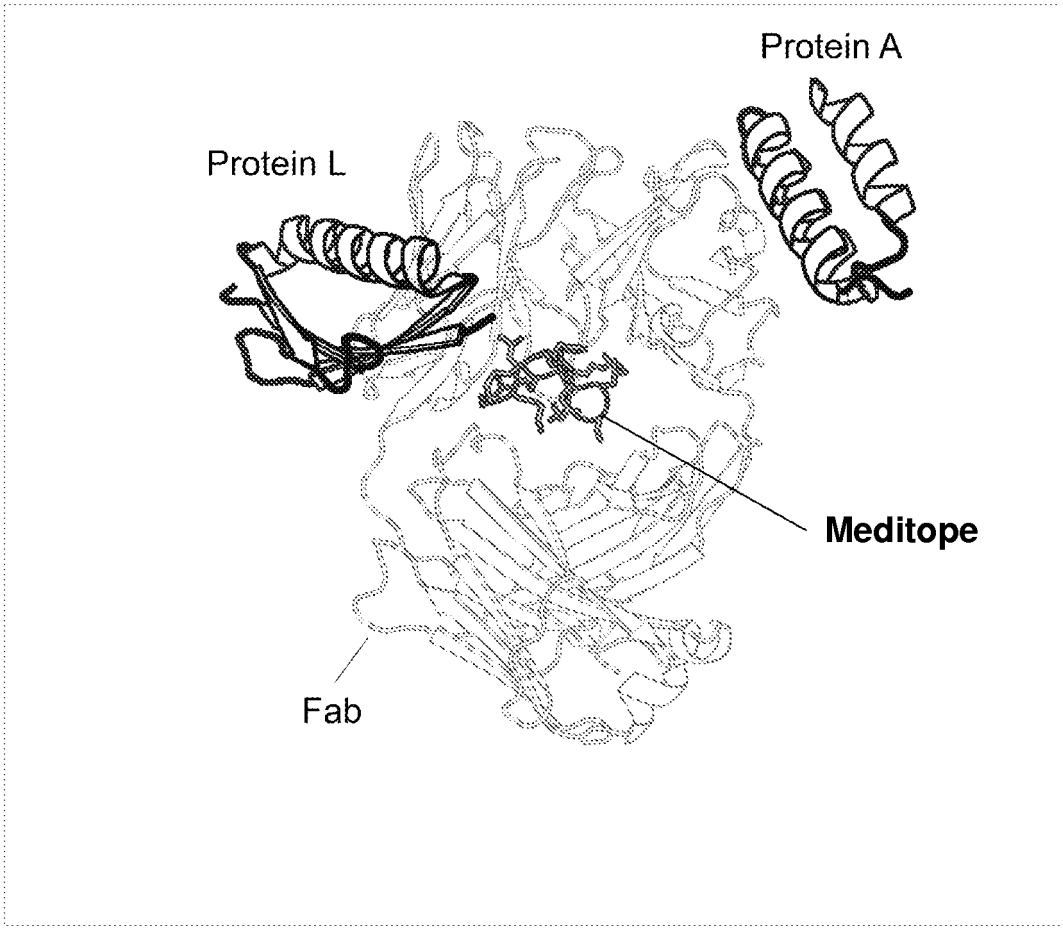


Figure 8

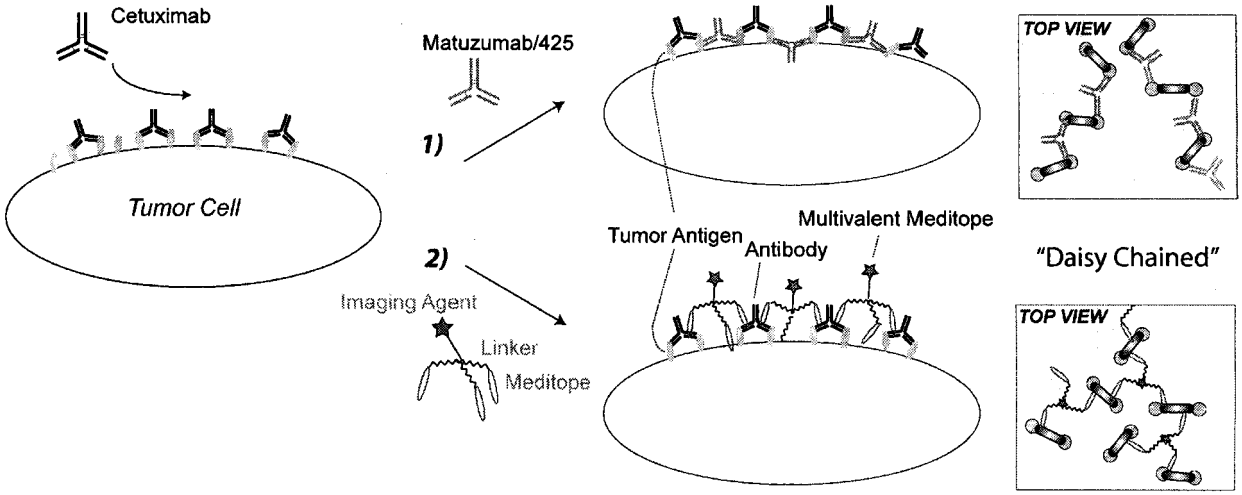

Cetuximab
Tumor Cell
Matuzumab/425
1)
2)
Imaging Agent
Linker
Meditope
Tumor Antigen
Antibody
Multivalent Meditope
TOP VIEW
"Daisy Chained"
TOP VIEW

Figure 9

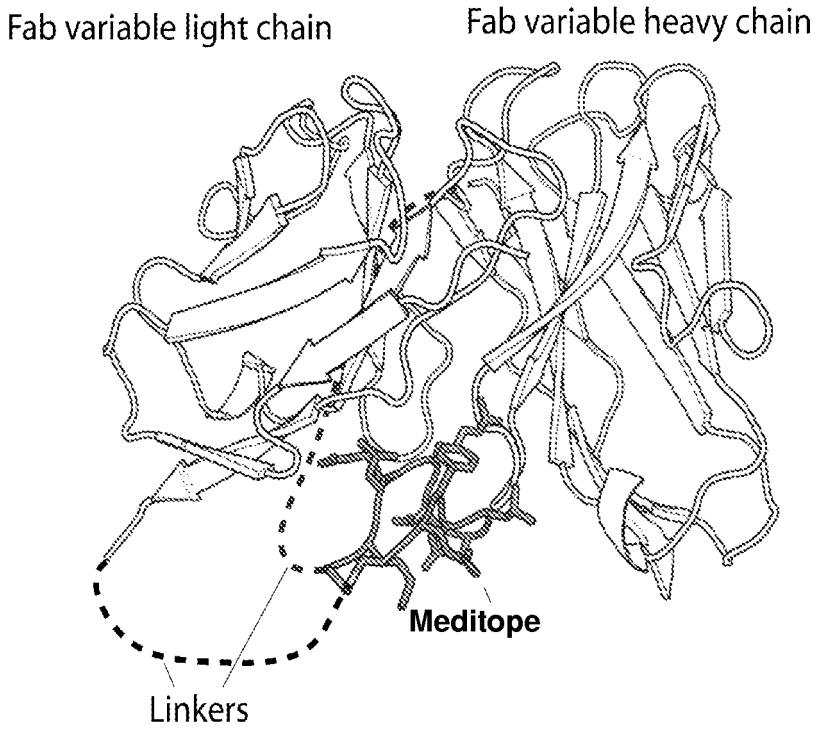

Fab variable light chain
Fab variable heavy chain
Meditope
Linkers

Figure 10

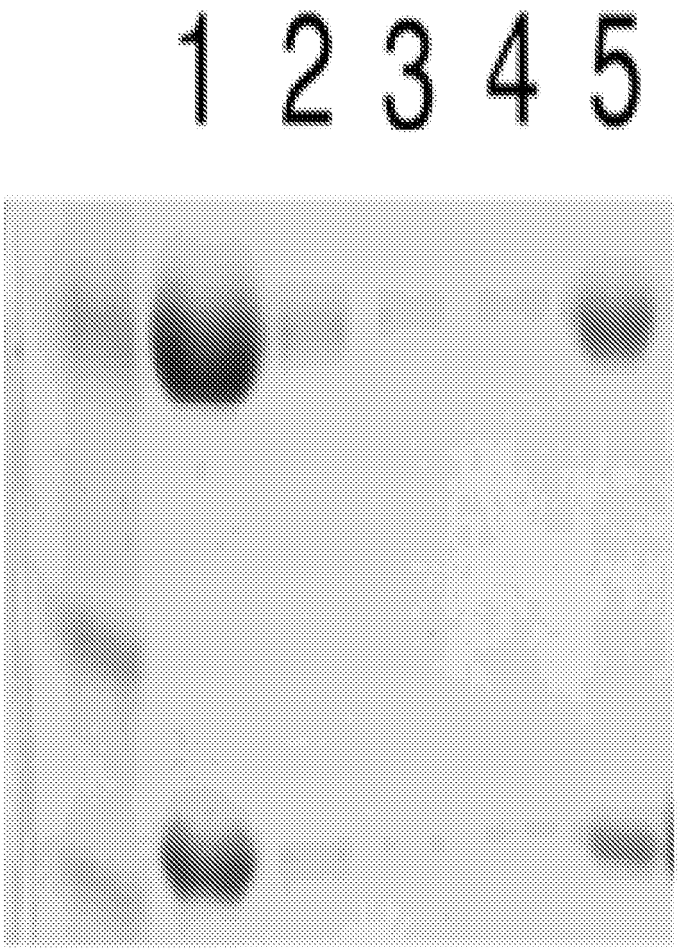


Figure 11

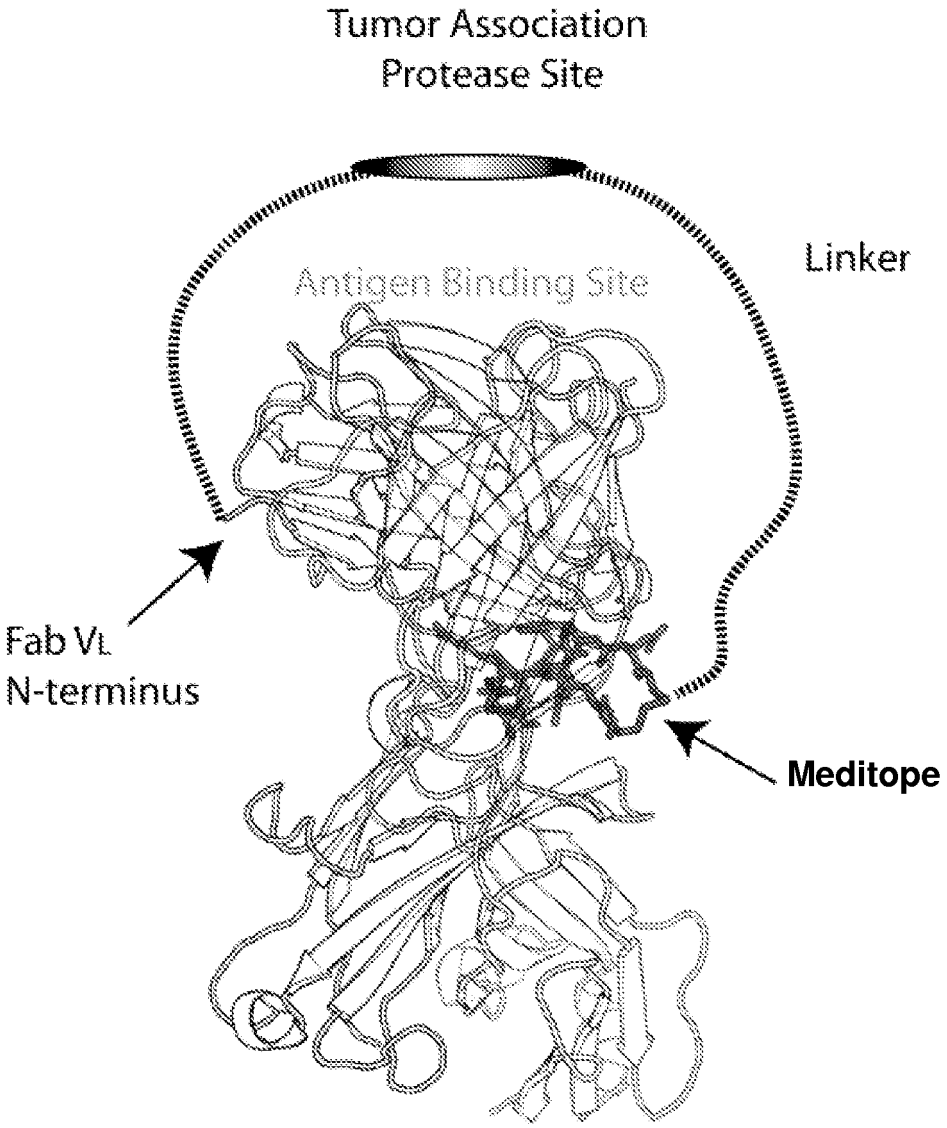

Tumor Association
Protease Site
Linker
Antigen Binding Site
Fab VL
N-terminus
Meditope

Figure 12

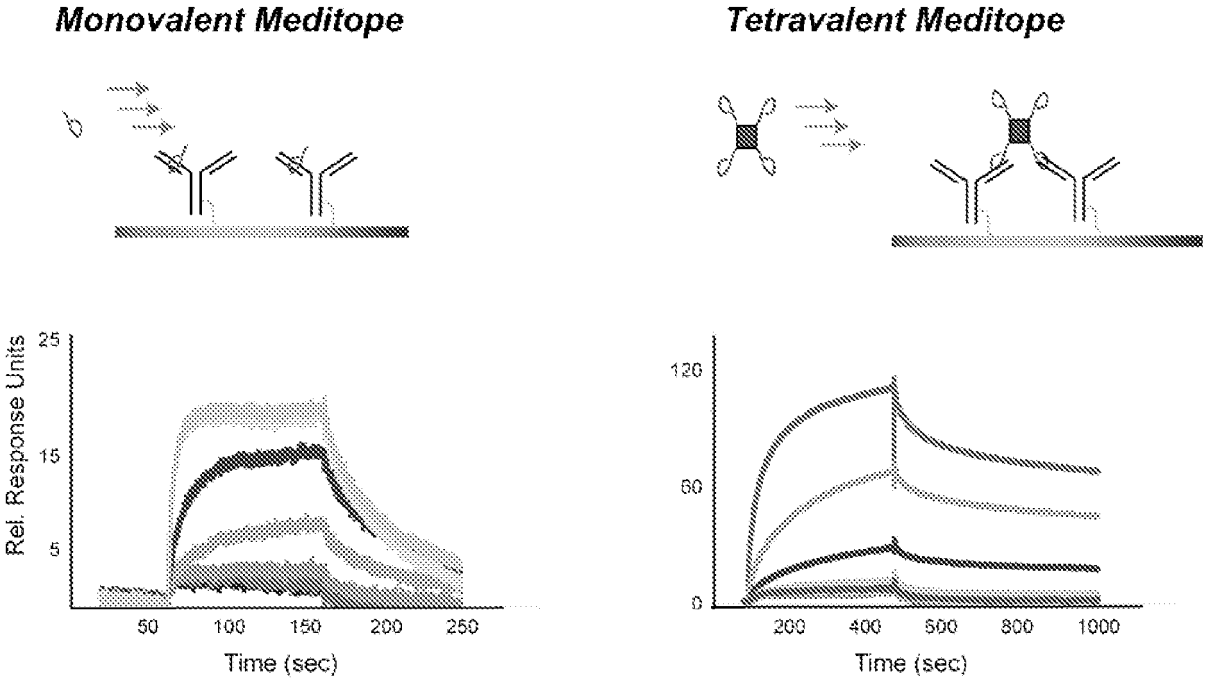
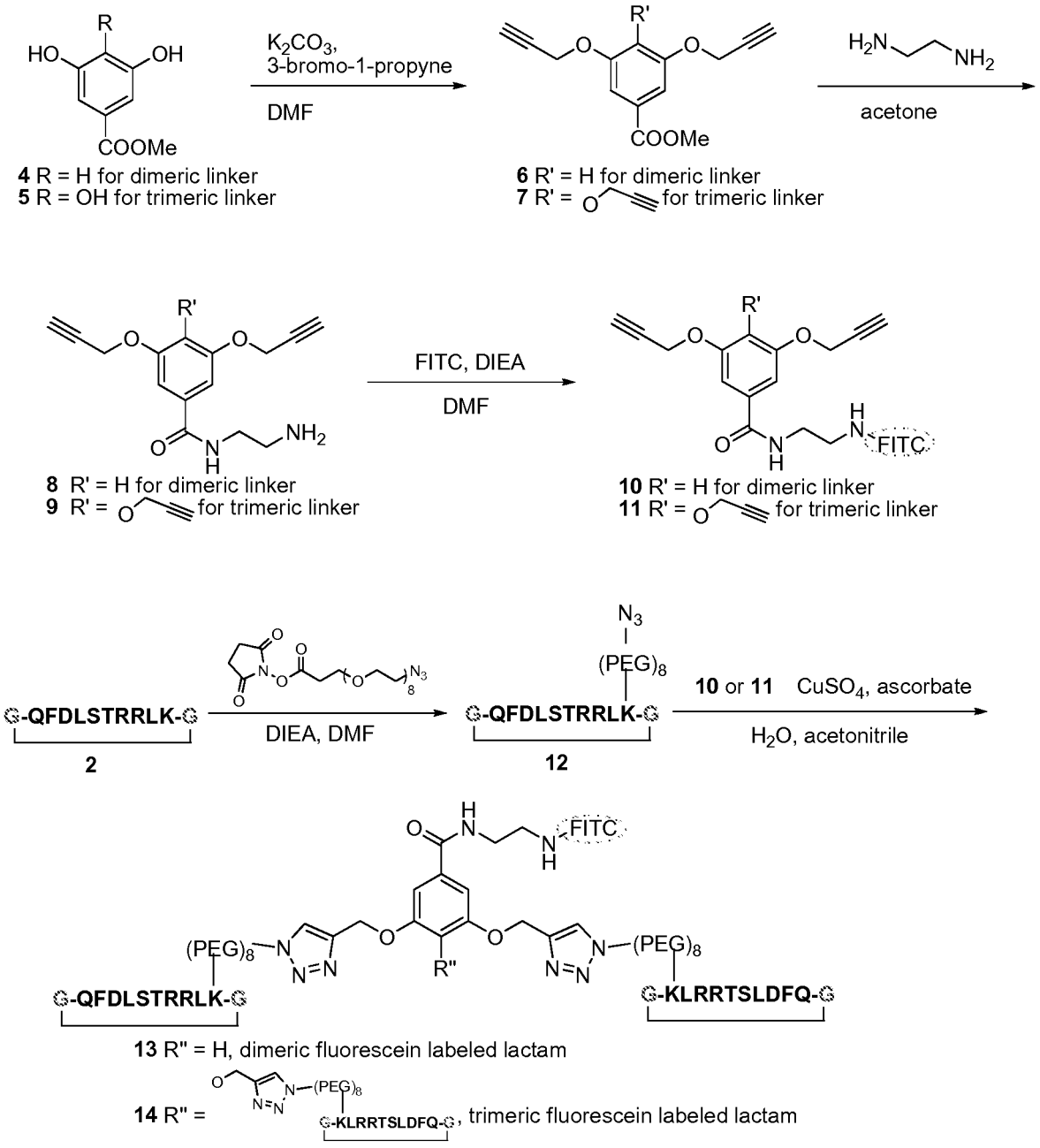

Monovalent Meditope
Tetravalent Meditope
Rel. Response Units
25
15
5
50
100
150
200
250
Time (sec)
120
60
0
200
400
500
800
1000
Time (sec)

Figure 13



4 R = H for dimeric linker
5 R = OH for trimeric linker

6 R' = H for dimeric linker
7 R' = for trimeric linker

8 R' = H for dimeric linker
9 R' = for trimeric linker

10 R' = H for dimeric linker
11 R' = for trimeric linker

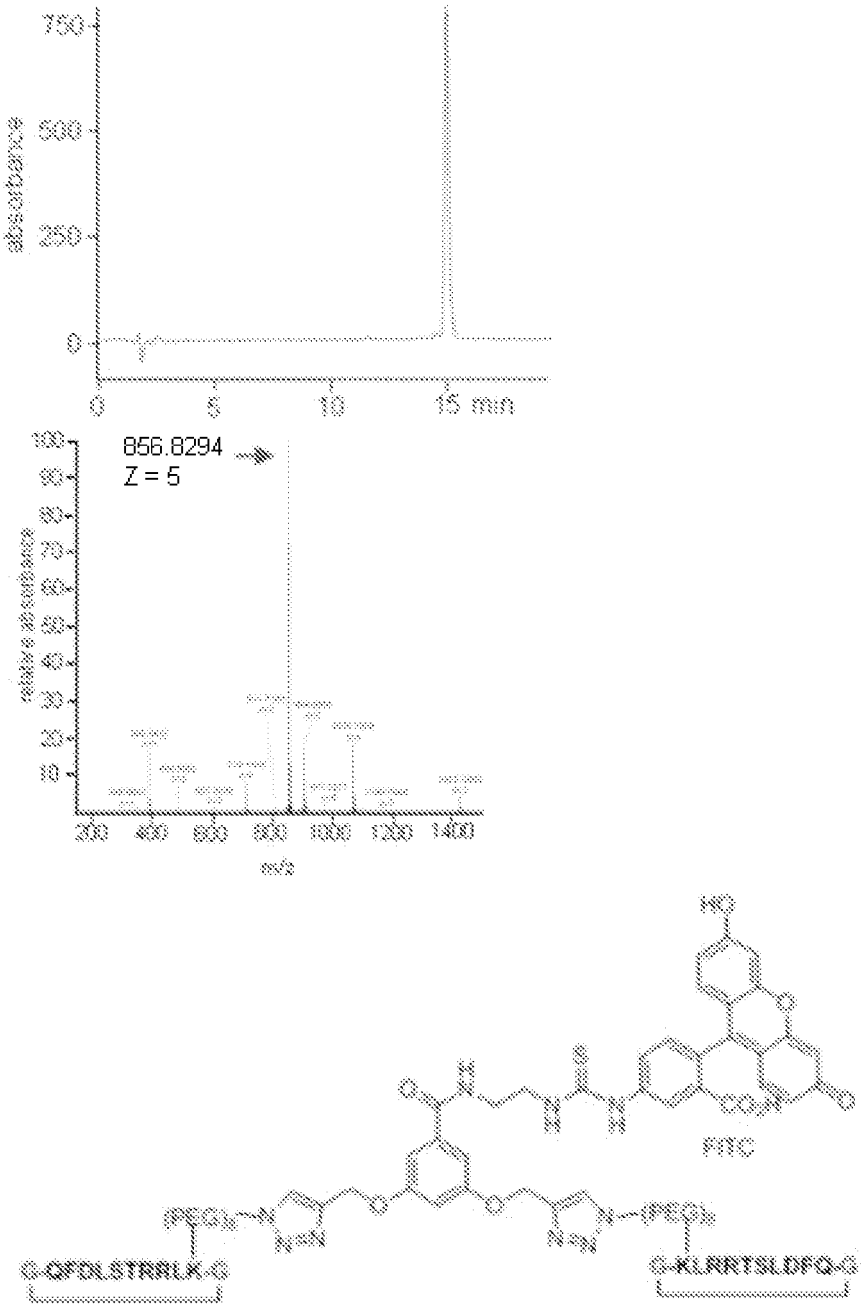
2

12

13 R" = H, dimeric fluorescein labeled lactam

14 R" = , trimeric fluorescein labeled lactam

Figure 14



for Z = 5
Expected MW: 856.8328
Found MW: 856.8294

Figure 15

Meditope-Fc (SEQ ID NO:3 nucleic acid and SEQ ID NO: 4 amino acid)

```
                        tgccagtttgacctgtcaactcggcgactgaaatgcggt
                         C  Q  F  D  L  S  T  R  R  L  K  C  G
ggggggctccggttcaggctcgggcggttcatcgggaggaggggggaggggaacctaagtca
 G  G  S  G  S  G  S  G  G  S  S  G  G  G  G  G  E  P  K  S
tgcgataagacgcacacctgtcctccatgcccagccccgagttgcttggtgggccctca
 C  D  K  T  H  T  C  P  P  C  P  A  P  E  L  L  G  G  P  S
gtattcctcttcccctccaaaacccaaagacaccttgatgatttcccgcacgcccggaagtc
 V  F  L  F  P  P  K  P  K  D  T  L  M  I  S  R  T  P  E  V
acgtgtgtggtcgtggatgtgagccatgaggatcccgaggtgaagttcaattggtacgtg
 T  C  V  V  V  D  V  S  H  E  D  P  E  V  K  F  N  W  Y  V
gatggagtagaggtacacaacgcgaaaacgaagcccagggaggaacagtacaattccaca
 D  G  V  E  V  H  N  A  K  T  K  P  R  E  E  Q  Y  N  S  T
tatcgcgtggtgtccgtgcttactgtgttgcatcaagactggctgaatgggaaggagtat
 Y  R  V  V  S  V  L  T  V  L  H  Q  D  W  L  N  G  K  E  Y
aagtgcaaagtatcaaacaaggcgctgcctgctccaatcgaaaagaccatctcgaaggcg
 K  C  K  V  S  N  K  A  L  P  A  P  I  E  K  T  I  S  K  A
aaaggacaacccagagaaccccaagtctacacgcttccgcccctcgcgggatgagctcacc
 K  G  Q  P  R  E  P  Q  V  Y  T  L  P  P  S  R  D  E  L  T
aaaaaccaggtatccctcacttgtttggtaaaaggattctacccgtcggacattgcagtc
 K  N  Q  V  S  L  T  C  L  V  K  G  F  Y  P  S  D  I  A  V
gagtgggagtcgaatgggcagccggaaaacaactacaaaacaacaccgcccgtcttggac
 E  W  E  S  N  G  Q  P  E  N  N  Y  K  T  T  P  P  V  L  D
tccgatggttcgttctttctctattcgaagctcaccgtagacaagtcgaggtggcagcag
 S  D  G  S  F  F  L  Y  S  K  L  T  V  D  K  S  R  W  Q  Q
ggcaacgtcttttcgtgctcagtgatgcatgaggccctttcacaatcactatacgcagaaa
 G  N  V  F  S  C  S  V  M  H  E  A  L  H  N  H  Y  T  Q  K
agcctgagcctgtcaccggggaagtaa
 S  L  S  L  S  P  G  K  -
```

Figure 16

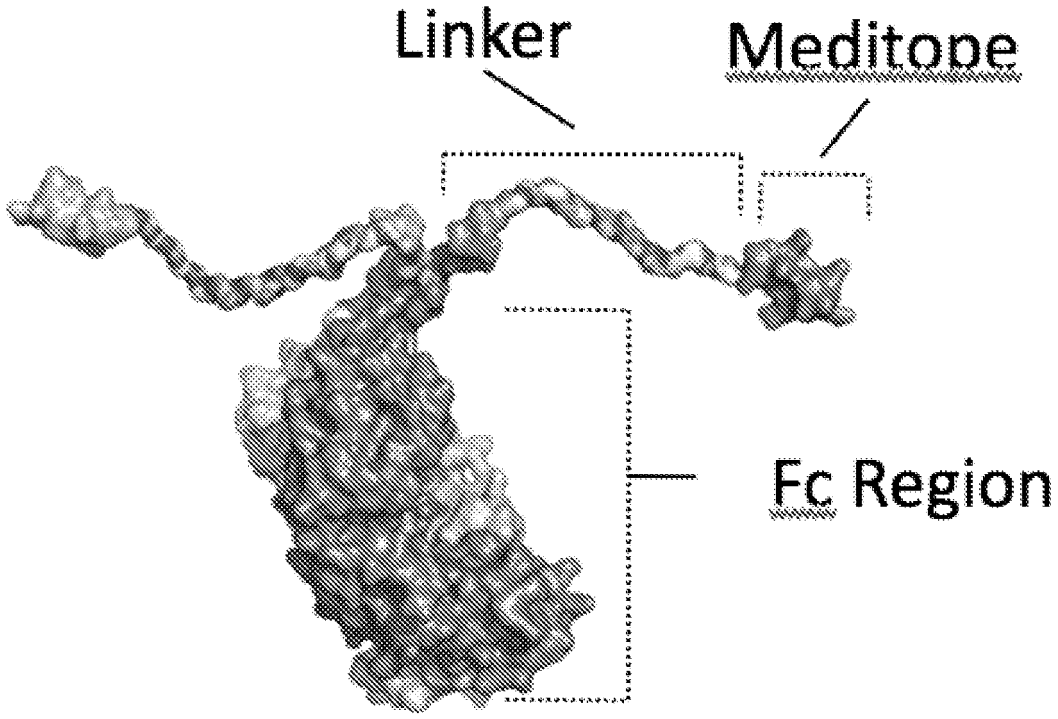


Figure 17

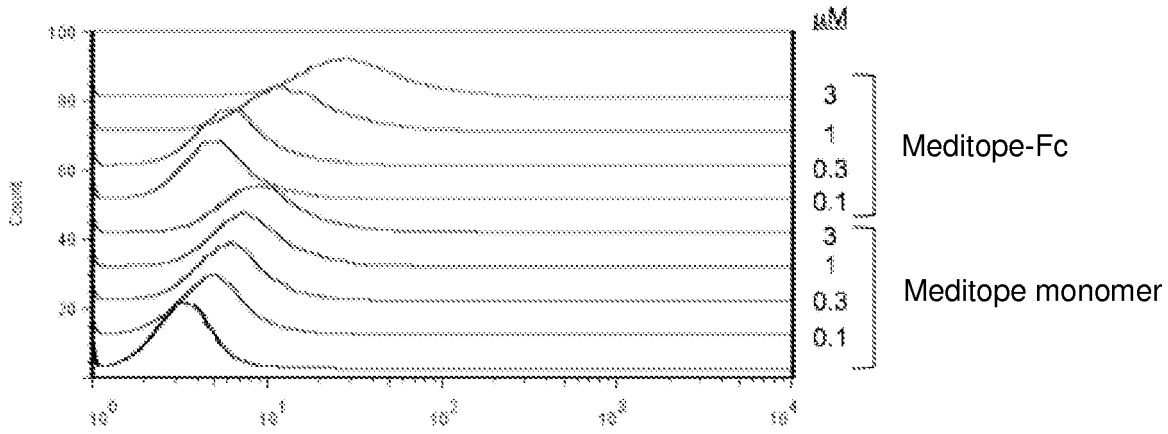


Figure 18

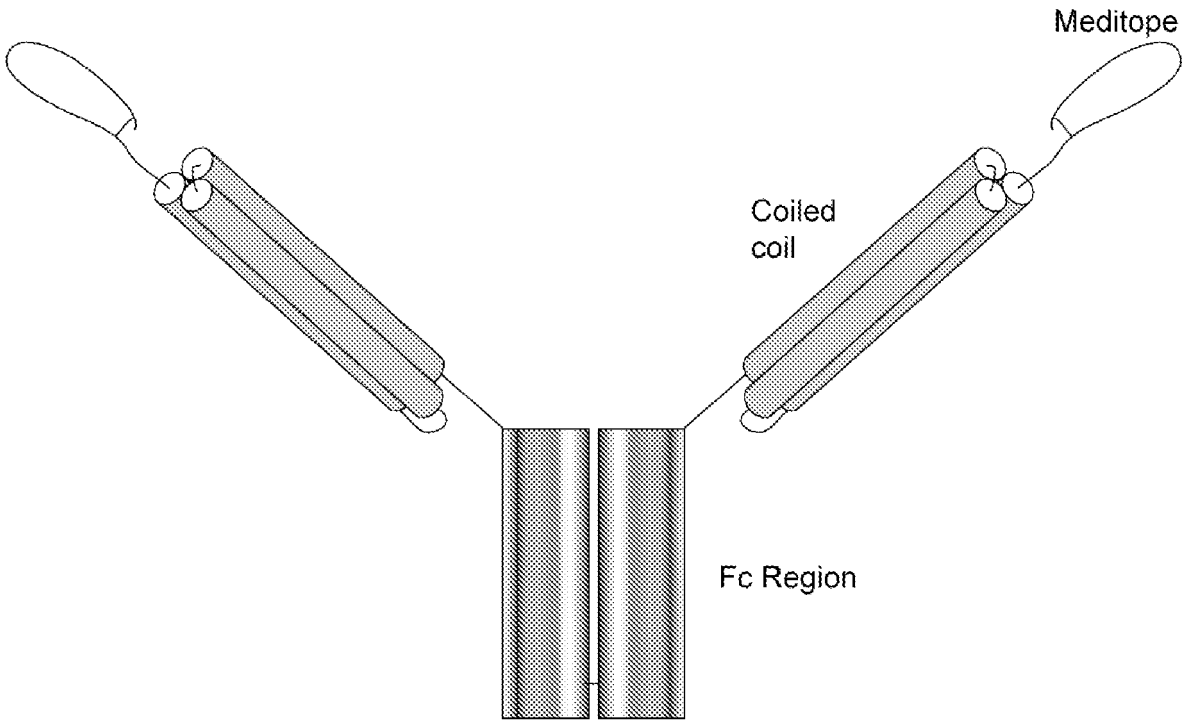


Figure 19

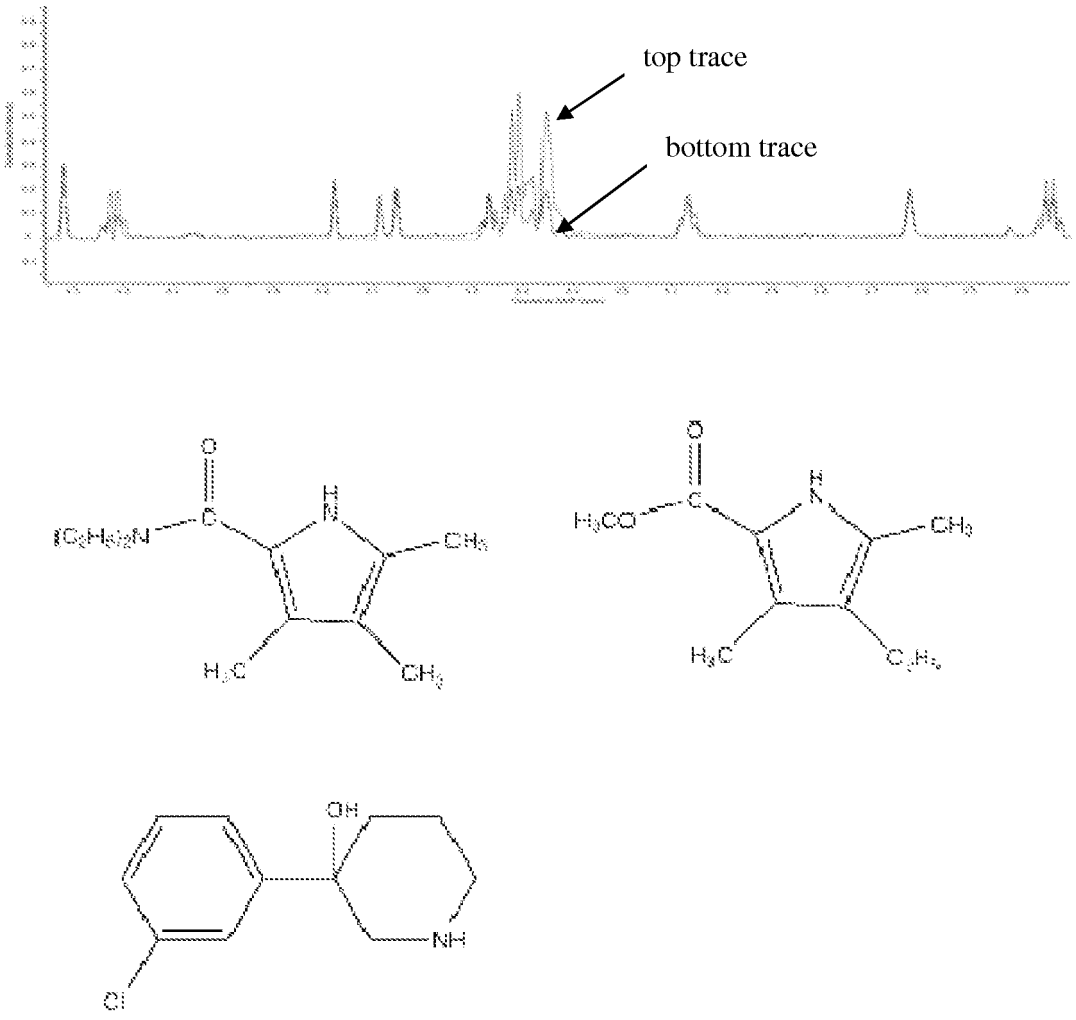


Figure 20

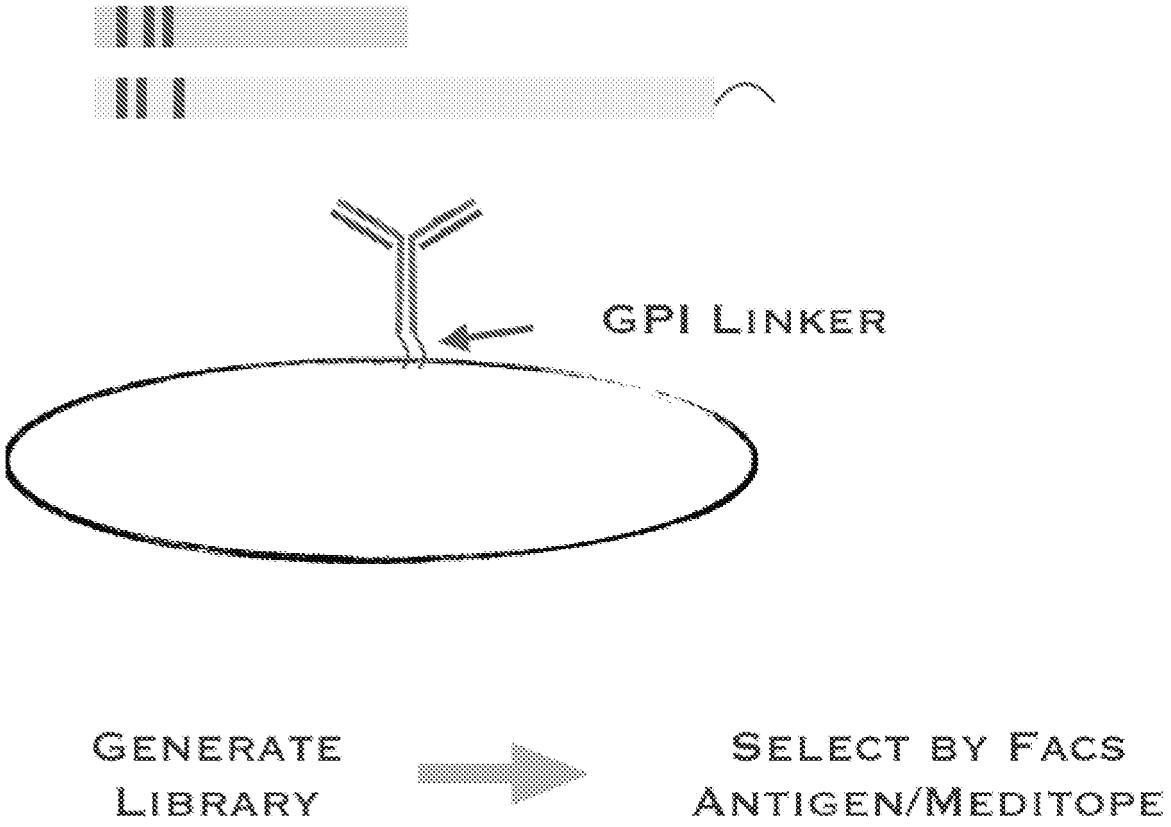

GPI LINKER
GENERATE LIBRARY
SELECT BY FACS ANTIGEN/MEDITOPE

Figure 21

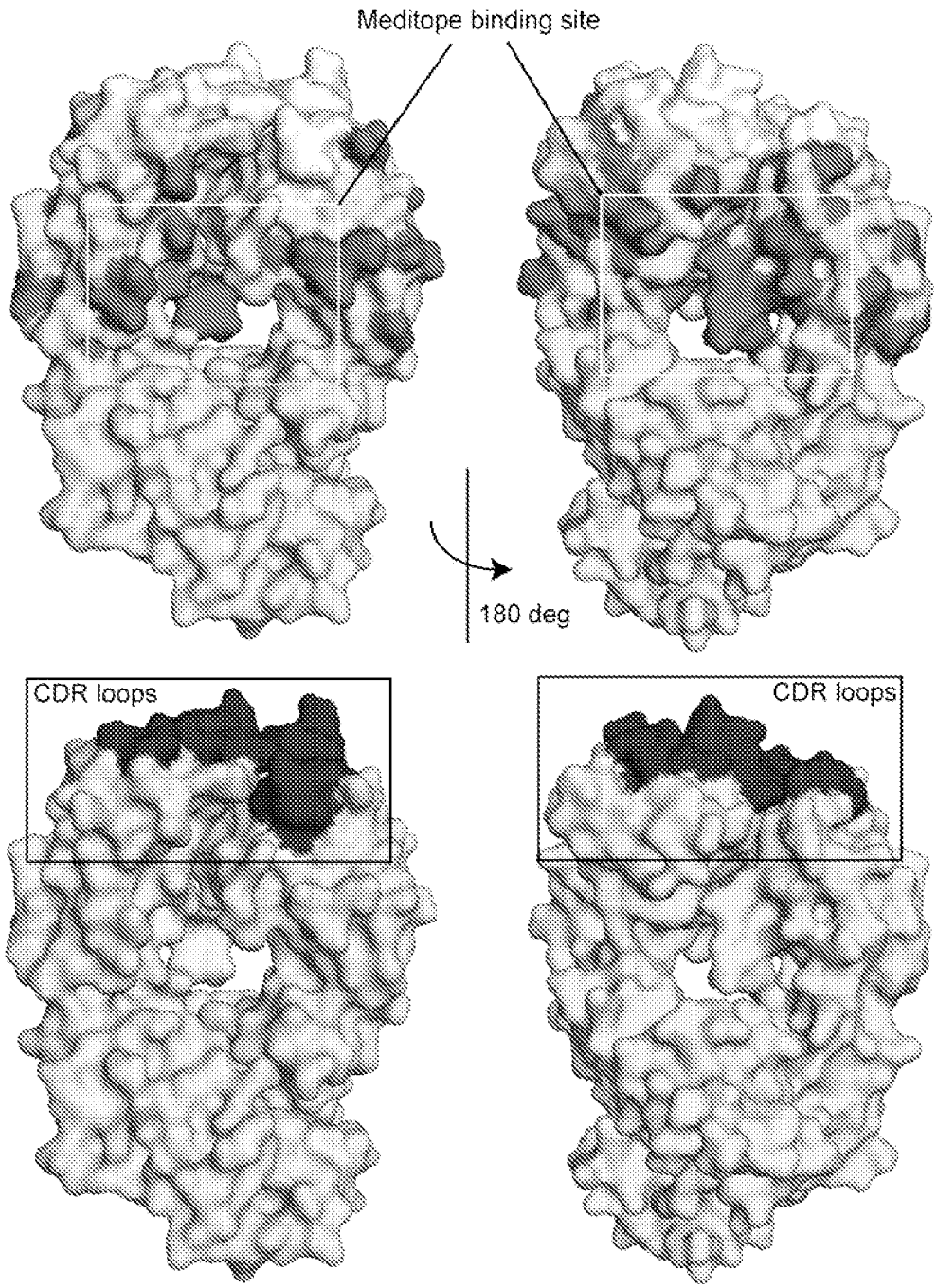
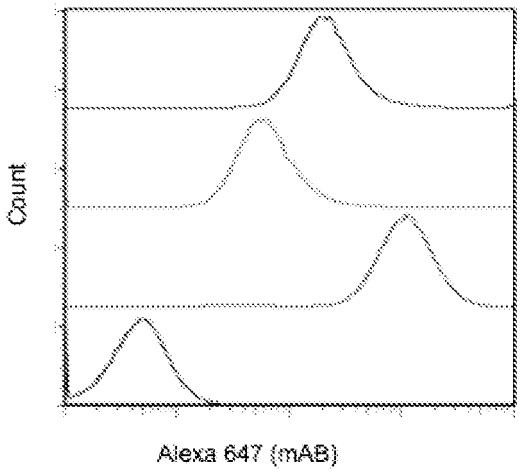


Figure 22

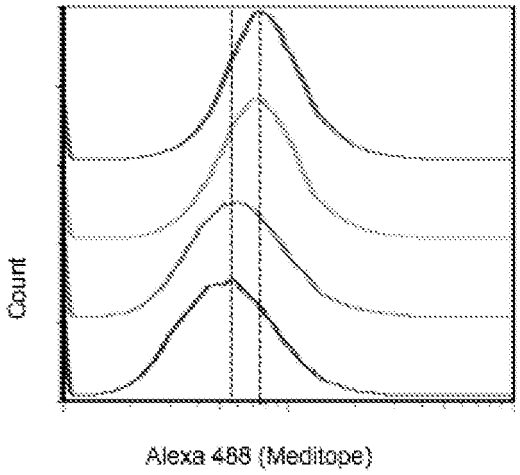


5 μM meditope-enabled trastuzumab

1 μM meditope-enabled trastuzumab

1 μM wild-type trastuzumab

negative control



5 μM meditope-enabled trastuzumab

1 μM meditope-enabled trastuzumab

1 μM wild-type trastuzumab

negative control

Figure 23A

```
ATGAAATGCT CGTGGGTGAT CTTTTTCCTT ATGGCGGTAG TAACCGGAGT AAACTCCGAG
GTCCAGCTCG
TCGAATCCGG TGGCGGCTTG GTGCAGCCGG GTGGGTCGTT GCGACTGTCG TGCGCAGCGT
CGGGGTTTAA
CATCAAAGAC ACCTATATCC ACTGGGTGAG GCAATCGCCC GGAAAGGGGC TCGAATGGGT
AGCCAGAATC
TACCCTACGA ATGGTTATAC TCGATATGCG GACTCCGTGA AAGGAAGATT CACCATCAGC
GCAGATACGT
CCAAAAACAC TGCATACCTC CAGATGAATA GCCTTCGGGC GGAGGACACG GCGATCTACT
ACTGTAGCCG
GTGGGGTGGG GACGGGTTCT ATGCGATGGA CTACTGGGGA CAGGGGACGC TTGTAACGGT
CAGCTCGGCG
TCAACAAAGG GACCTAGCGT GTTTCCCTTG GCTCCCTCAT CGAAATCAAC GTCCGGTGGG
ACGGCGGCAT TGGGGTGTCT TGTCAAGGAC TATTTCCCCG AGCCCGTGAC AGTCTCGTGG
AACTCGGGTG CCCTTACAAG CGGCGTACAT ACGTTTCCCG CCGTGCTCCA ATCATCCGGA
CTGTATTCCC TTTCATCCGT CGTGACTGTG CCGTCCTCGT CACTCGGAAC GCAAACTTAC
ATTTGCAATG TCAACCACAA ACCGTCAAAT ACAAAGGTCG ATAAGAAGGT CGAGCCAAAG
TCGTGTGATA AGACCCACAC ATGCCCTCCC TGTCCAGCGC CGGAGCTGTT GGGAGGGCCT
TCAGTGTTCC TCTTCCCGCC CAAACCCAAG GACACCCTGA TGATTAGCCG CACACCCGAG
GTGACGTGTG TCGTCGTCGA TGTCTCACAT GAGGACCCGG AGGTAAAGTT CAACTGGTAC
GTGGATGGAG TCGAAGTGCA CAACGCAAAA ACAAAACCTC GGGAAGAGCA GTACAATAGC
ACGTACAGAG TAGTCAGCGT GCTCACCGTG CTGCACCAGG ATTGGCTCAA TGGAAAGGAG
TACAAGTGTA AAGTGTCGAA TAAGGCGCTG CCTGCCCCCA TCGAAAAGAC AATTTCCAAA
GCTAAAGGGC AACCCCGCGA GCCGCAAGTA TACACCCTCC CACCCTCGCG CGATGAACTG
ACCAAGAACC AGGTGTCATT GACGTGTCTC GTCAAGGGCT TCTATCCGAG CGACATTGCA
GTAGAATGGG AAAGCAACGG ACAGCCGGAA AACAACTACA AGACTACACC GCCTGTCCTT
GATTCGGATG GTTCCTTCTT TCTTTACTCA AAACTTACAG TCGACAAATC GAGGTGGCAG
CAGGGAAATG TGTTTTCGTG CAGCGTGATG CACGAGGCCT TGCATAATCA CTATACACAG
AAGTCGTTGT CACTGTCGCC GGGAAAGTAA
```

Figure 23B

```
Medi    EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQSPGKGLEWVARIYPTNGYTRYADSV
        ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
WT      EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSV


Medi    KGRFTISADTSKNTAYLQMNSLRAEDTAIYYCSRWGGDGFYAMDYWGQGTLVTVSSASTK
        :::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
WT      KGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSSASTK


Medi    GPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
        ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
WT      GPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
```

Figure 23C

```
ATGGAGACAG ACACGCTTTT GCTTTGGGTG TTGTTGTTGT GGGTCCCCGG TTCGACGGGG
GATATTCAGA TGACCCAGTC ACCGATCCTT CTCTCGGCGA GCGTGGGGGA TAGAGTAACG
ATCACGTGTA GAGCGTCCCA AGACGTCAAC ACAGCTGTCG CGTGGTATCA GCAGCGGACA
AATGGATCGC CGAGGCTCCT GATCTACAGC GCATCATTTC TCTATTCGGG AGTCCCCTCC
CGATTTTCCG GATCGCGCAG CGGTACTGAC TTCACCCTCA CGATTTCCTC CCTTCAACCG
GAAGATATCG CTGATTACTA CTGTCAGCAG CACTATACAA CACCTCCCAC TTTCGGAGCA
GGGACAAAAG TGGAGATTAA GCGCACTGTA GCAGCCCCCT CGGTCTTTAT CTTCCCTCCT
AGCGACGAAC AATTGAAGTC AGGGACCGCC TCGGTGGTAT GCCTGCTTAA CAACTTTTAC
CCACGGGAAG CCAAAGTACA GTGGAAGGTG GATAATGCGC TCCAGAGCGG AAACTCCCAA
GAGAGCGTGA CAGAACAGGA CTCGAAGGAT TCGACGTACT CACTCAGCTC AACGCTGACC
CTGTCGAAAG CGGACTATGA GAAACACAAG GTCTACGCGT GCGAGGTGAC CCATCAGGGC
CTGAGCTCCC CCGTAACTAA GTCATTCAAC CGGGGTGAAT GCTAA
```

Figure 23D

```
            10         20         30         40         50         60
medi    DIQMTQSPILLSASVGDRVTITCRASQDVNTAVAWYQQRTNGSPRLLIYSASFLYSGVPS
        :::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
WT      DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPS
                10         20         30         40         50         60

                70         80         90        100        110        120
medi    RFSGSRSGTDFTLTISSLQPEDIADYYCQQHYTTPPTFGAGTKVEIKRTVAAPSVFIFPP
        :::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
WT      RFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIKRTVAAPSVFIFPP
                70         80         90        100        110        120

               130        140        150        160        170        180
medi    SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT
        :::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
WT      SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT
               130        140        150        160        170        180

               190        200        210
medi    LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
        :::::::::::::::::::::::::::::::::
WT      LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
               190        200        210
```

Figure 24

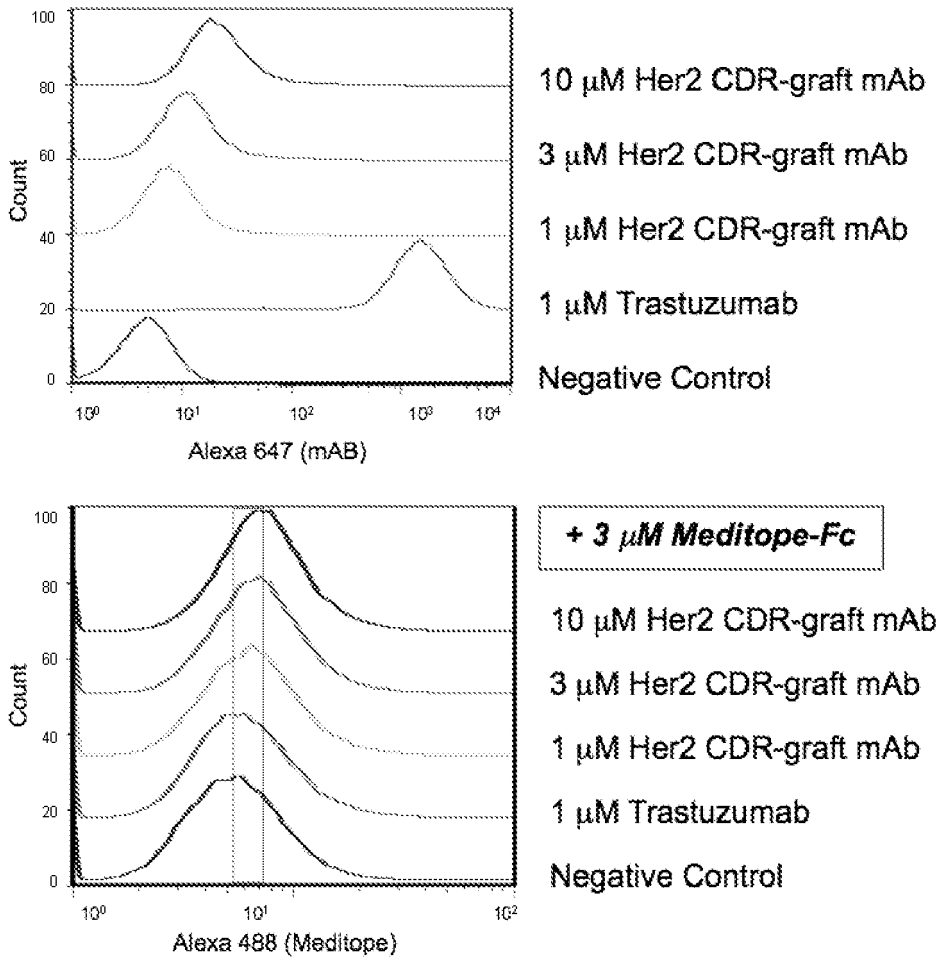

Count
Alexa 647 (mAB)
10 μM Her2 CDR-graft mAb
3 μM Her2 CDR-graft mAb
1 μM Her2 CDR-graft mAb
1 μM Trastuzumab
Negative Control
+ 3 μM Meditope-Fc
Count
Alexa 488 (Meditope)
10 μM Her2 CDR-graft mAb
3 μM Her2 CDR-graft mAb
1 μM Her2 CDR-graft mAb
1 μM Trastuzumab
Negative Control

Figure 25A

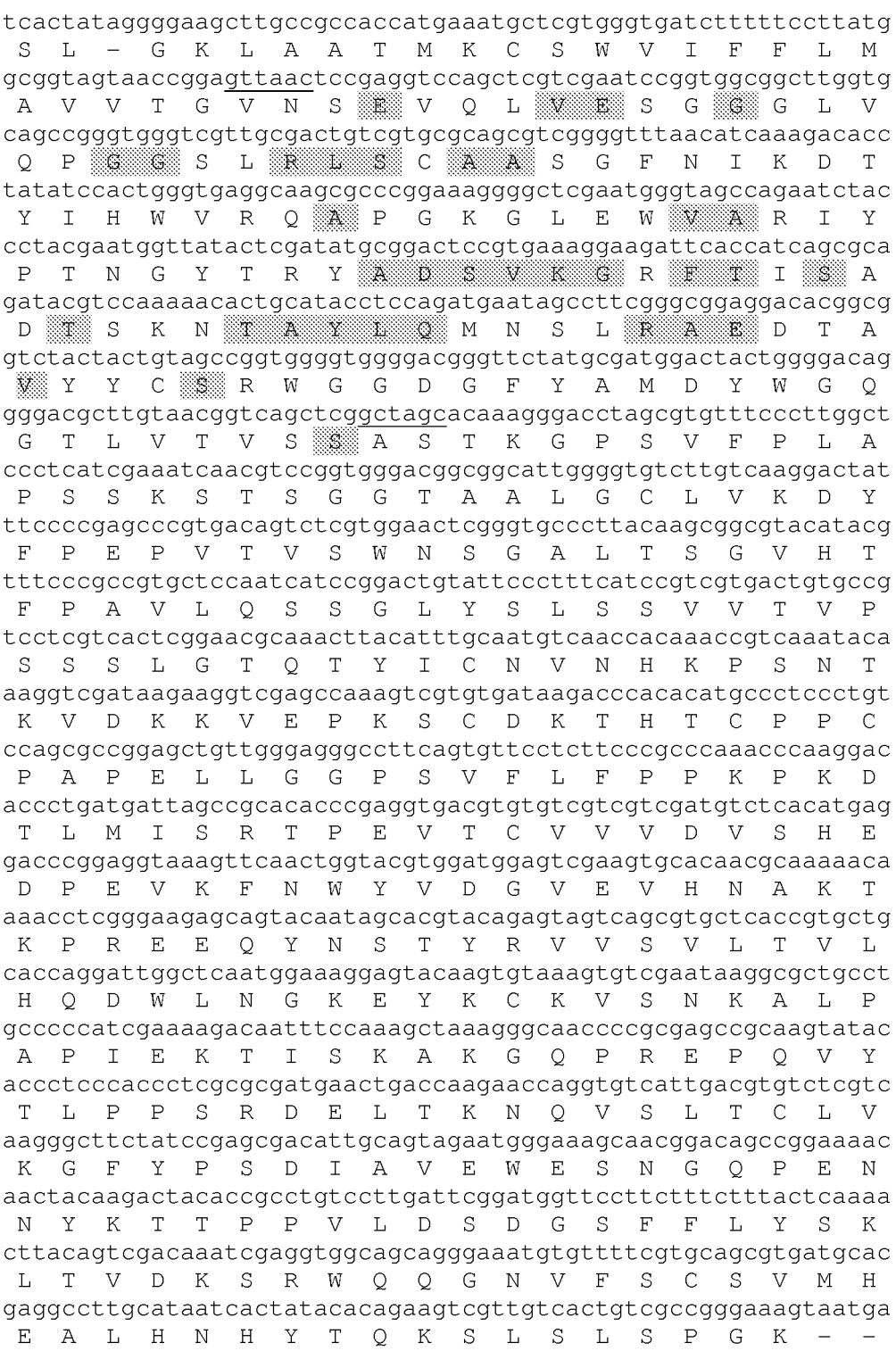

tcactataggggaagcttgccgccaccatgaaatgctcgtgggtgatcttttttccttatg
S L - G K L A A T M K C S W V I F F L M
gcggtagtaaccggagttaactccgaggtccagctcgtcgaatccggtggcggcttggtg
A V V T G V N S E V Q L V E S G G G L V
cagccgggtgggtcgttgcgactgtcgtgcgcagcgtcggggtttaacatcaaagacacc
Q P G G S L R L S C A A S G F N I K D T
tatatccactgggtgaggcaagcgcccggaaaggggctcgaatgggtagccagaatctac
Y I H W V R Q A P G K G L E W V A R I Y
cctacgaatggttatactcgatatgcggactccgtgaaaggaagattcaccatcagcgca
P T N G Y T R Y A D S V K G R F T I S A
gatacgtccaaaaacactgcatacctccagatgaatagccttcgggcggaggacacggcg
D T S K N T A Y L Q M N S L R A E D T A
gtctactactgtagccggtggggtggggacgggttctatgcgatggactactggggacag
V Y Y C S R W G G D G F Y A M D Y W G Q
gggacgcttgtaacggtcagctcggctagcacaaagggacctagcgtgtttcccttggct
G T L V T V S S A S T K G P S V F P L A
ccctcatcgaaatcaacgtccggtgggacggcggcattggggtgtcttgtcaaggactat
P S S K S T S G G T A A L G C L V K D Y
ttccccgagcccgtgacagtctcgtggaactcgggtgcccttacaagcggcgtacatacg
F P E P V T V S W N S G A L T S G V H T
tttcccgccgtgctccaatcatccggactgtattccctttcatccgtcgtgactgtgccg
F P A V L Q S S G L Y S L S S V V T V P
tcctcgtcactcggaacgcaaacttacatttgcaatgtcaaccacaaaccgtcaaataca
S S S L G T Q T Y I C N V N H K P S N T
aaggtcgataagaaggtcgagccaaagtcgtgtgataagacccacacatgccctccctgt
K V D K K V E P K S C D K T H T C P P C
ccagcgccggagctgttgggagggccttcagtgttcctcttcccgcccaaacccaaggac
P A P E L L G G P S V F L F P P K P K D
accctgatgattagccgcacacccgaggtgacgtgtgtcgtcgtcgatgtctcacatgag
T L M I S R T P E V T C V V V D V S H E
gacccggaggtaaagttcaactggtacgtggatggagtcgaagtgcacaacgcaaaaaca
D P E V K F N W Y V D G V E V H N A K T
aaacctcgggaagagcagtacaatagcacgtacagagtagtcagcgtgctcaccgtgctg
K P R E E Q Y N S T Y R V V S V L T V L
caccaggattggctcaatggaaaggagtacaagtgtaaagtgtcgaataaggcgctgcct
H Q D W L N G K E Y K C K V S N K A L P
gcccccatcgaaaagacaatttccaaagctaaagggcaaccccgcgagccgcaagtatac
A P I E K T I S K A K G Q P R E P Q V Y
accctcccaccctcgcgcgatgaactgaccaagaaccaggtgtcattgacgtgtctcgtc
T L P P S R D E L T K N Q V S L T C L V
aagggcttctatccgagcgacattgcagtagaatgggaaagcaacggacagccggaaaac
K G F Y P S D I A V E W E S N G Q P E N
aactacaagactacaccgcctgtccttgattcggatggttccttctttctttactcaaaa
N Y K T T P P V L D S D G S F F L Y S K
cttacagtcgacaaatcgaggtggcagcagggaaatgtgttttcgtgcagcgtgatgcac
L T V D K S R W Q Q G N V F S C S V M H
gaggccttgcataatcactatacacagaagtcgttgtcactgtcgccgggaaagtaatga
E A L H N H Y T Q K S L S L S P G K - -

Figure 25B

atagggaagcttgccgccaccatggagacagacacgcttttgctttgggtgttgttgttg
– G K L A A T M E T D T L L L W V L L L
tgggtccccggttcgaccggtgatattcagatgacccagtcaccgtcatccctttcggcg
W V P G S T G D I Q M T Q S P S S L S A
agcgtgggggatagagtaacgatcacgtgtagagcgtcccaagacgtcaacacagctgtc
S V G D R V T I T C R A S Q D V N T A V
gcgtggtatcagcagaagccaggaaaagcgccgaagctcctgatctacagcgcatcattt
A W Y Q Q K P G K A P K L L I Y S A S F
ctctattcgggagtcccctcccgattttccggatcgcgcagcggtactgacttcaccctc
L Y S G V P S R F S G S R S G T D F T L
acgatttcctcccttcaaccggaagattttgctacttactactgtcagcagcactataca
T I S S L Q P E D F A T Y Y C Q Q H Y T
acacctcccactttcggacaggggacaaaagtggagattaagcggaccgtagcagccccc
T P P T F G Q G T K V E I K R T V A A P
tcggtctttatcttccctcctagcgacgaacaattgaagtcagggaccgcctcggtggta
S V F I F P P S D E Q L K S G T A S V V
tgcctgcttaacaacttttacccacgggaagccaaagtacagtggaaggtggataatgcg
C L L N N F Y P R E A K V Q W K V D N A
ctccagagcggaaactcccaagagagcgtgacagaacaggactcgaaggattcgacgtac
L Q S G N S Q E S V T E Q D S K D S T Y
tcactcagctcaacgctgaccctgtcgaaagcggactatgagaaacacaaggtctacgcg
S L S S T L T L S K A D Y E K H K V Y A
tgcgaggtgacccatcagggcctgagctcccccgtaactaagtcattcaaccggggtgaa
C E V T H Q G L S S P V T K S F N R G E
tgctaatga
C – –

Figure 26

```
1YY9_D|PDBID|CHAIN|SEQUENCE   QVQLKQSGPGLVQPSQSLSITCTVSGFSLTNYGVHWV[redacted]GLEWLG- 49
2R56_H|PDBID|CHAIN|SEQUENCE   QVSLRESGGGLVQPGRSLRLSCTASGFTFRHHGMIWVRQAPGKGLEWVAS 50
                              **.*::** *****.:** ::**.***:: ::*: ****:*******:.

1YY9_D|PDBID|CHAIN|SEQUENCE   VIWSGGNTDYNTPFTSRLSINKDNSKSQVFFKMNSLQSNDTAIYYCARAL 99
2R56_H|PDBID|CHAIN|SEQUENCE   LSGSGTKTHFADSVKGRFTISRDNSNNTLYLQMDNVRDEDTAIYYCAKAK
100
                              :  ** :*.:  ....*::*.:***:. ::::*:.::.:********:*

1YY9_D|PDBID|CHAIN|SEQUENCE   TYYDY-EFAYWGQGTLVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLV
148
2R56_H|PDBID|CHAIN|SEQUENCE   RVGATGYFDLWGRGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLV
150
                                     *  **:*******:*****************************

1YY9_D|PDBID|CHAIN|SEQUENCE   KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQ
198
2R56_H|PDBID|CHAIN|SEQUENCE   KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQ
200
                              **************************************************

1YY9_D|PDBID|CHAIN|SEQUENCE   TYICNVNHKPSNTKVDKRVEPKS 221
2R56_H|PDBID|CHAIN|SEQUENCE   TYICNVNHKPSNTKVDKKAEP-- 221
                              ******************:.**
```

Figure 27

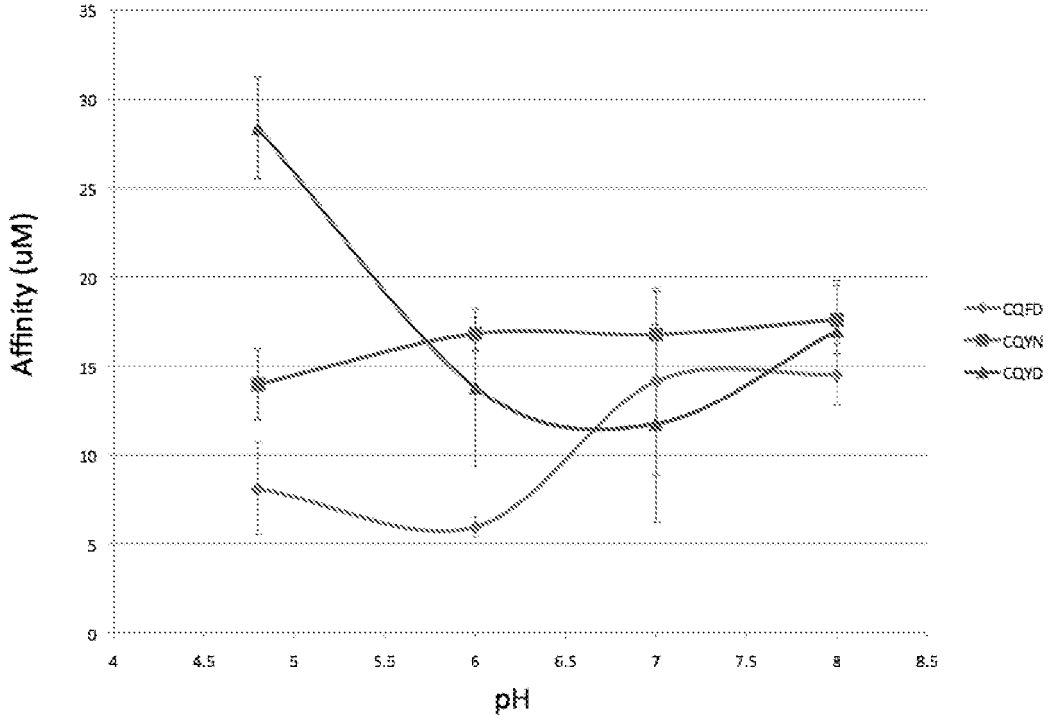
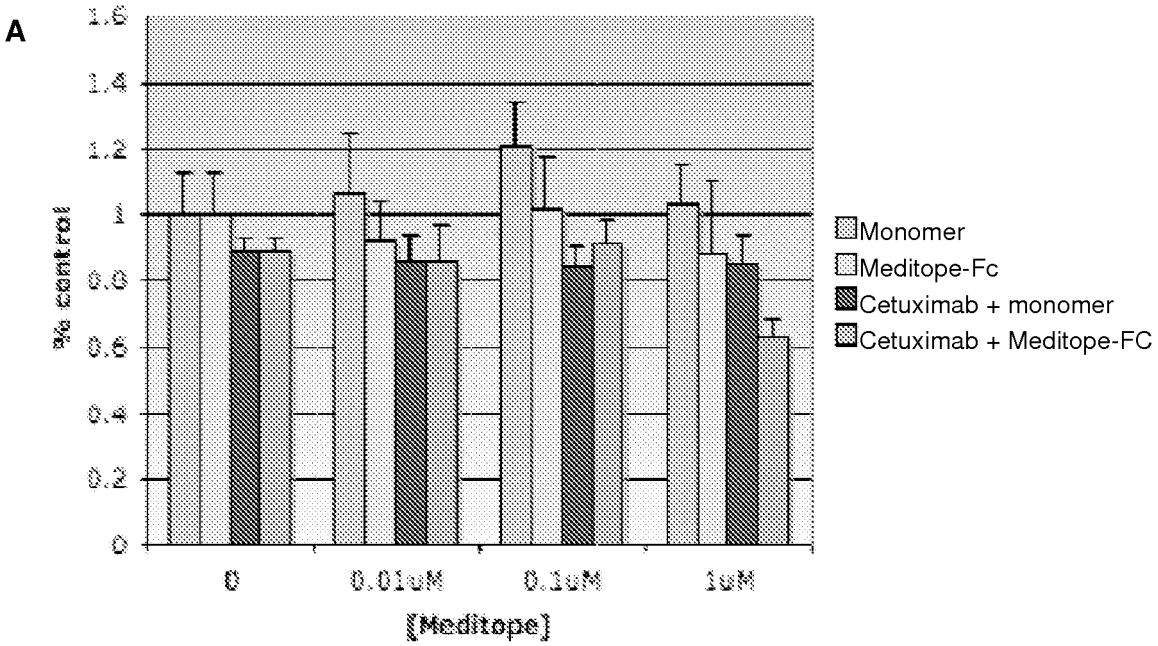

Affinity (uM)
35
30
25
20
15
10
5
0
4
4.5
5
5.5
6
6.5
7
7.5
8
8.5
pH
CQFD
CQYN
CQYD

Figure 28


A
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
% control
0
0.01uM
0.1uM
1uM
[Meditope]
Monomer
Meditope-Fc
Cetuximab + monomer
Cetuximab + Meditope-FC

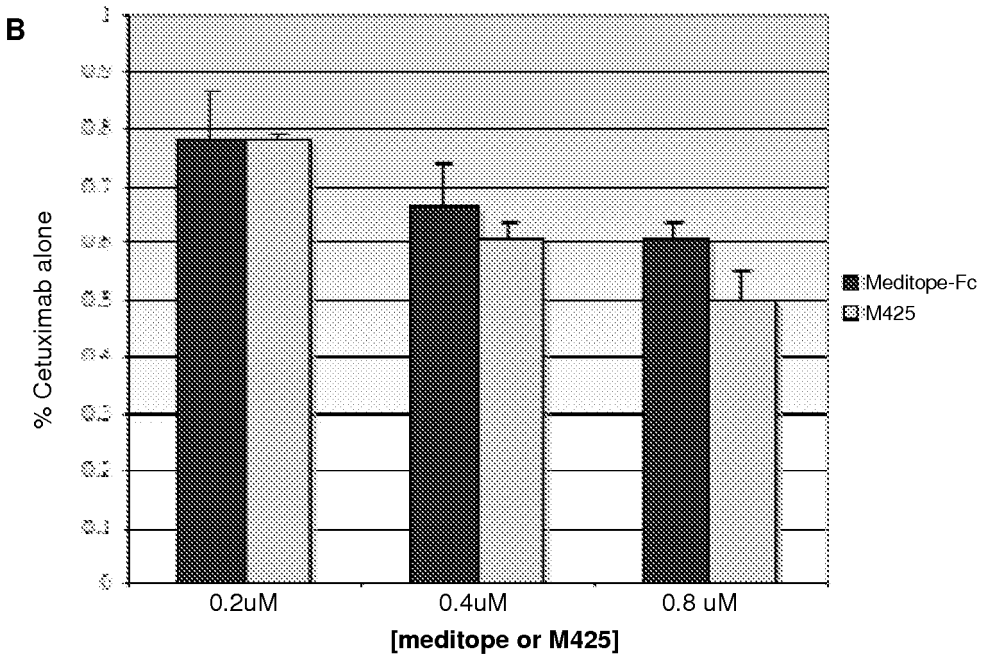

B
% Cetuximab alone
0.2uM
0.4uM
0.8 uM
[meditope or M425]
:Meditope-Fc
:M425

Figure 29

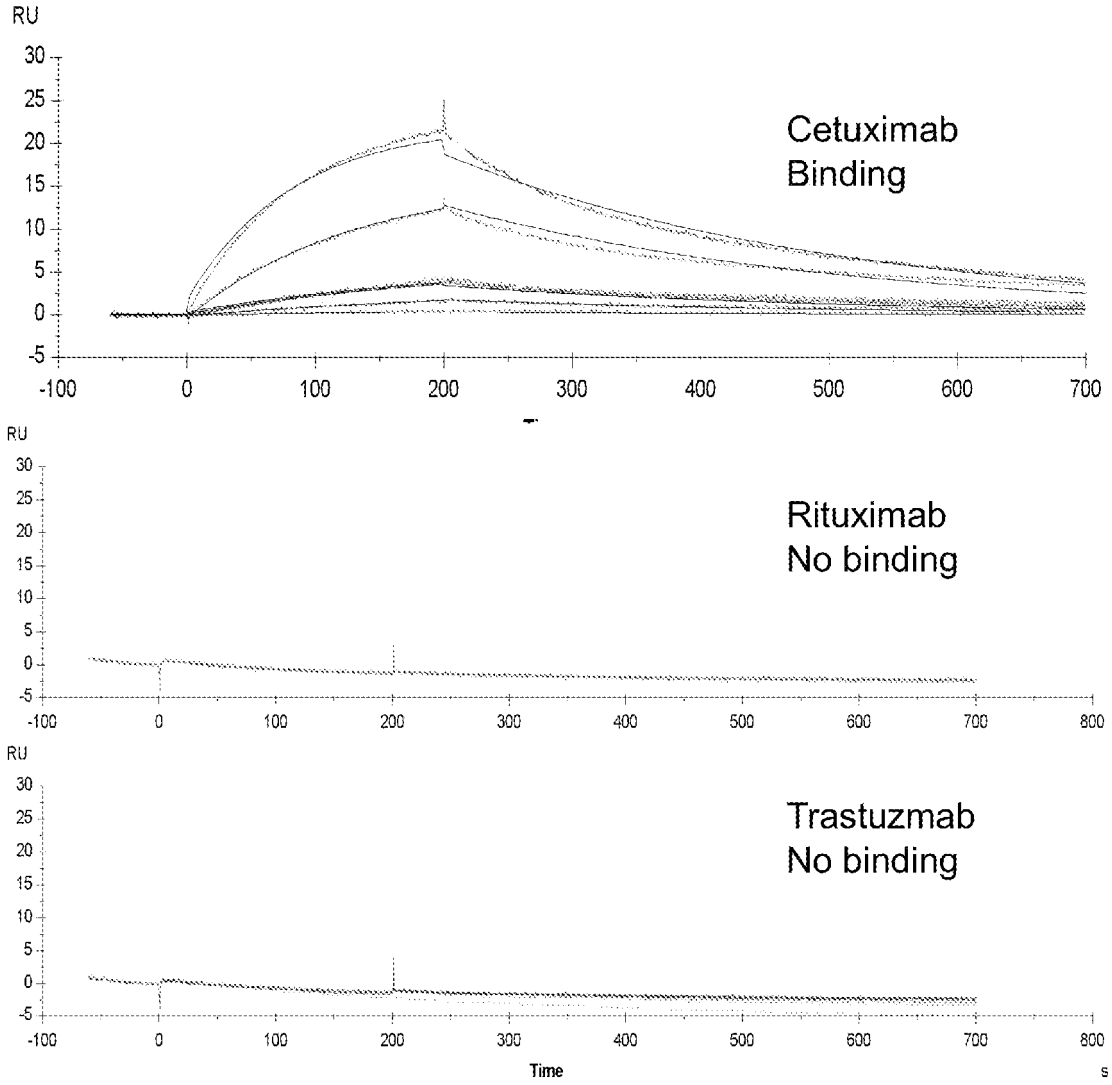

RU
Cetuximab
Binding
Rituximab
No binding
Trastuzmab
No binding
Time
s

Figure 30

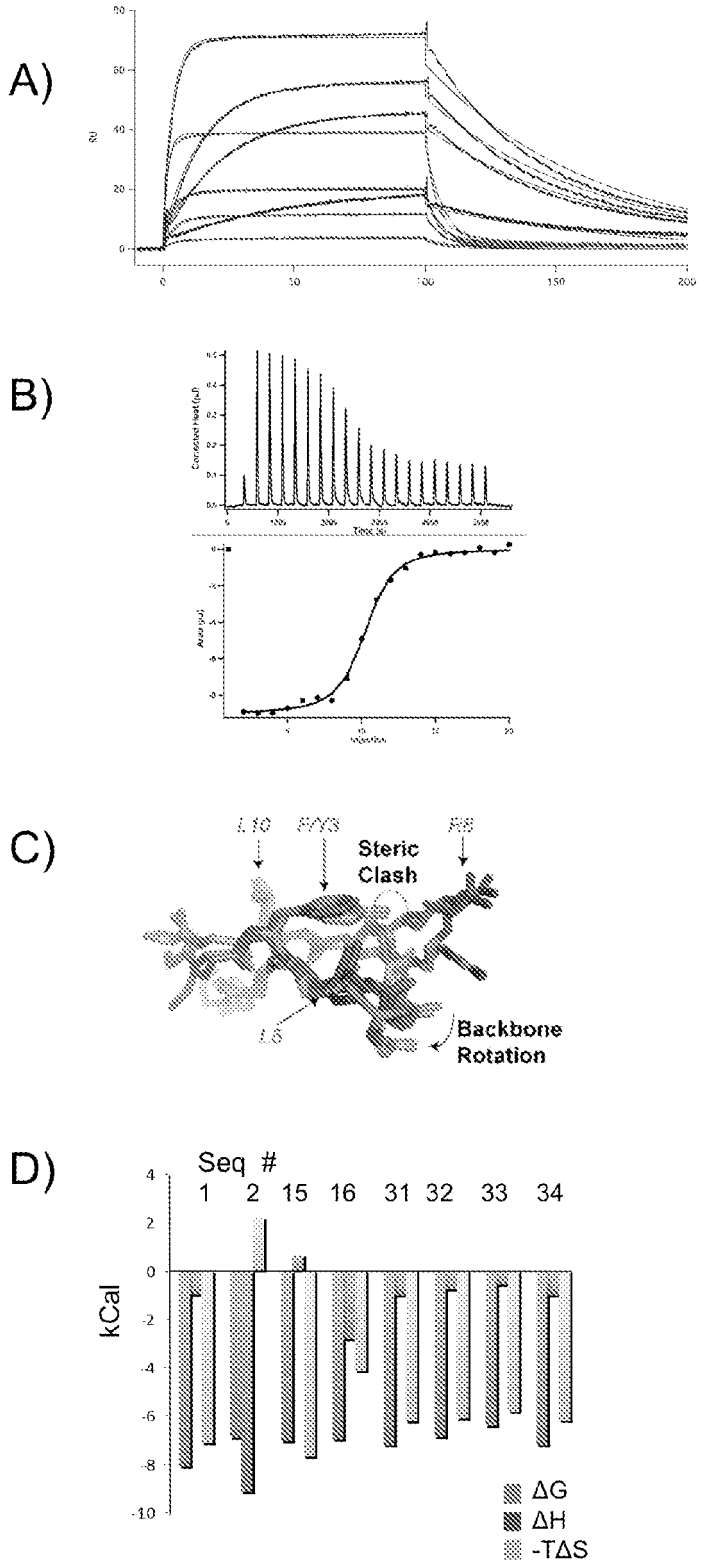

A)
B)
C)
L10
P/Y3
R8
Steric Clash
L6
Backbone Rotation
D)
Seq #
1 2 15 16 31 32 33 34
kCal
ΔG
ΔH
-TΔS

Figure 31

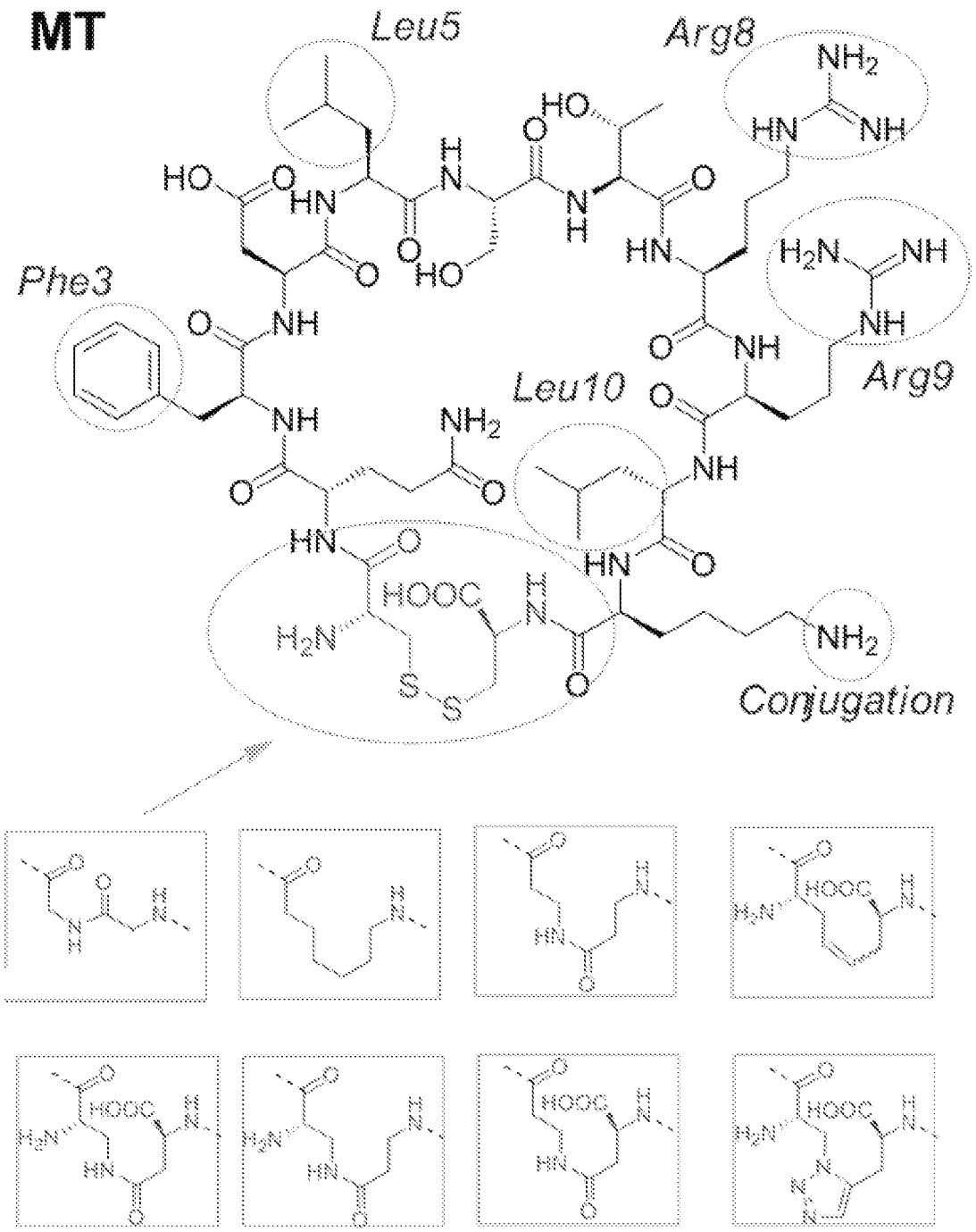


Figure 32

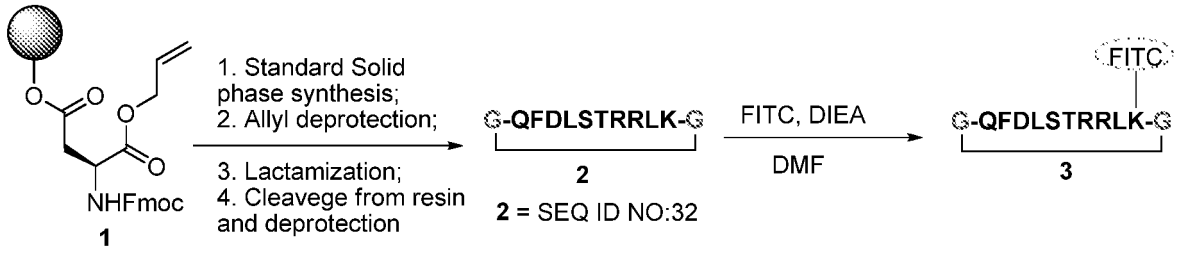

NHFmoc
1
1. Standard Solid phase synthesis;
2. Allyl deprotection;
3. Lactamization;
4. Cleavege from resin and deprotection
G-QFDLSTRRLK-G
2
2 = SEQ ID NO:32
FITC, DIEA
DMF
FITC
G-QFDLSTRRLK-G
3

Figure 33

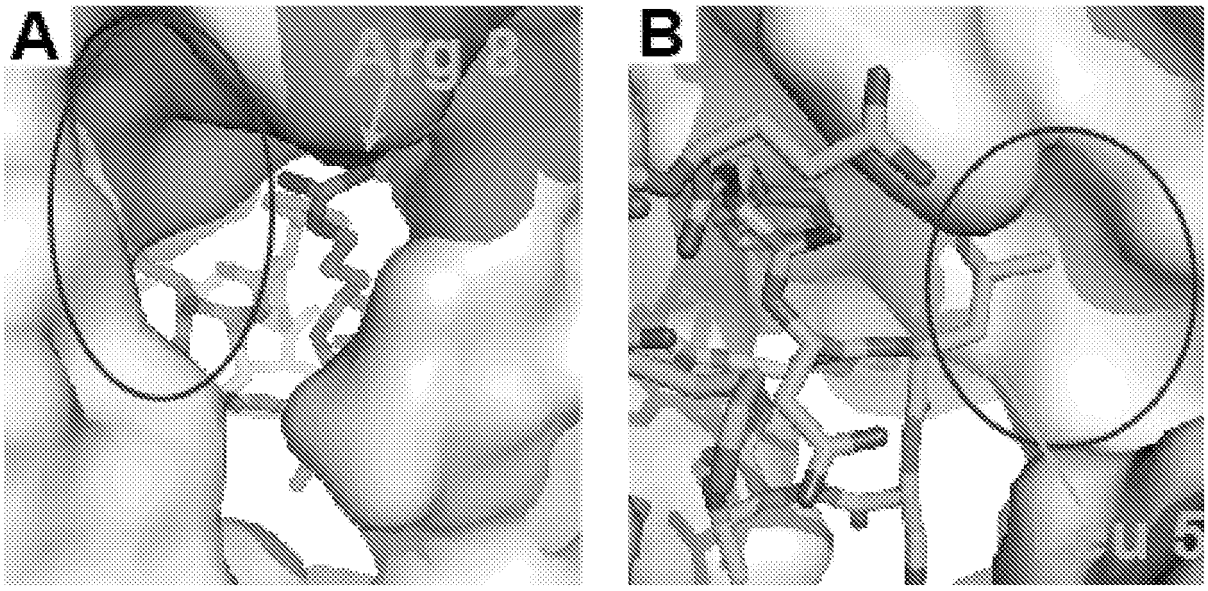
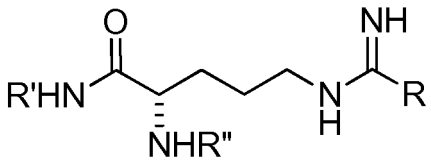


Figure 34



Modified Arg8

R = alkyl, substituted alkyl, aromatic or NHR'''
where R''' = alkyl, substituted alkyl, aromatic

Figure 35

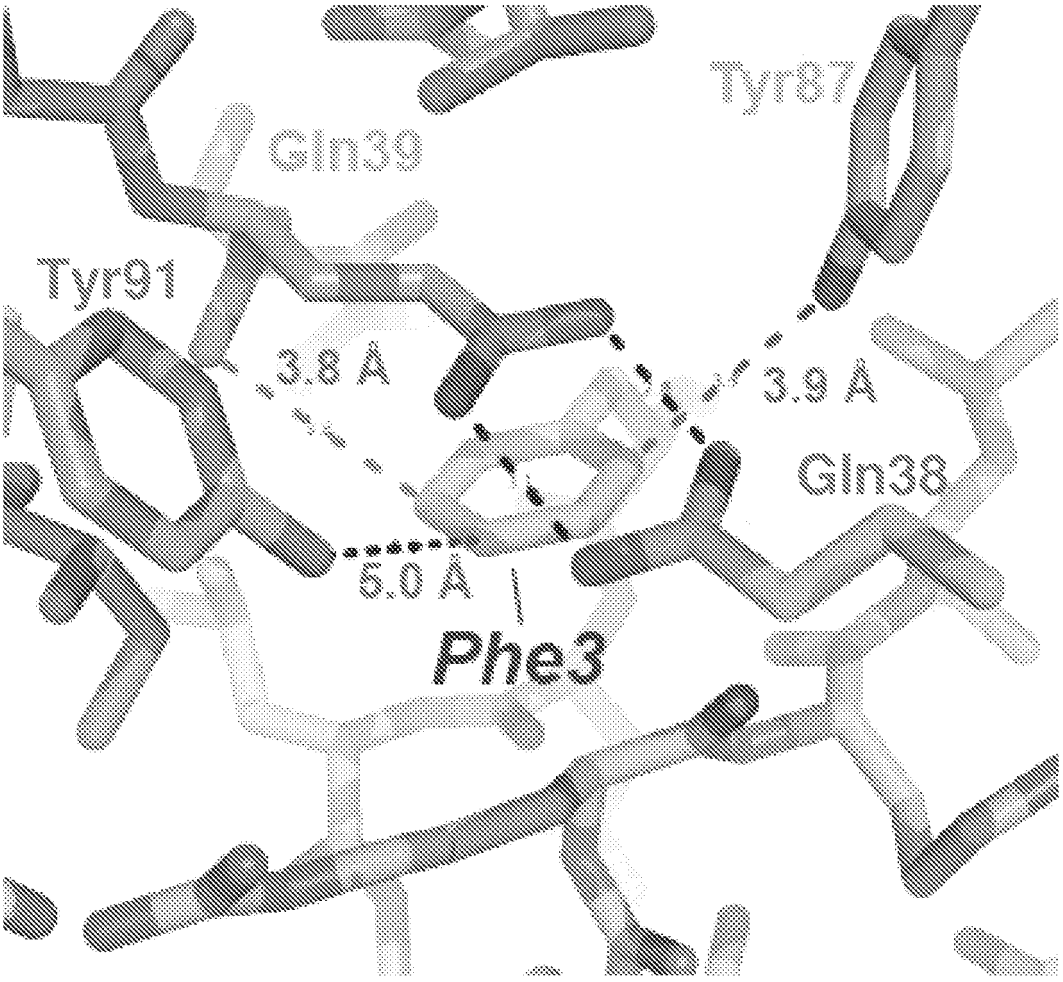


Figure 36

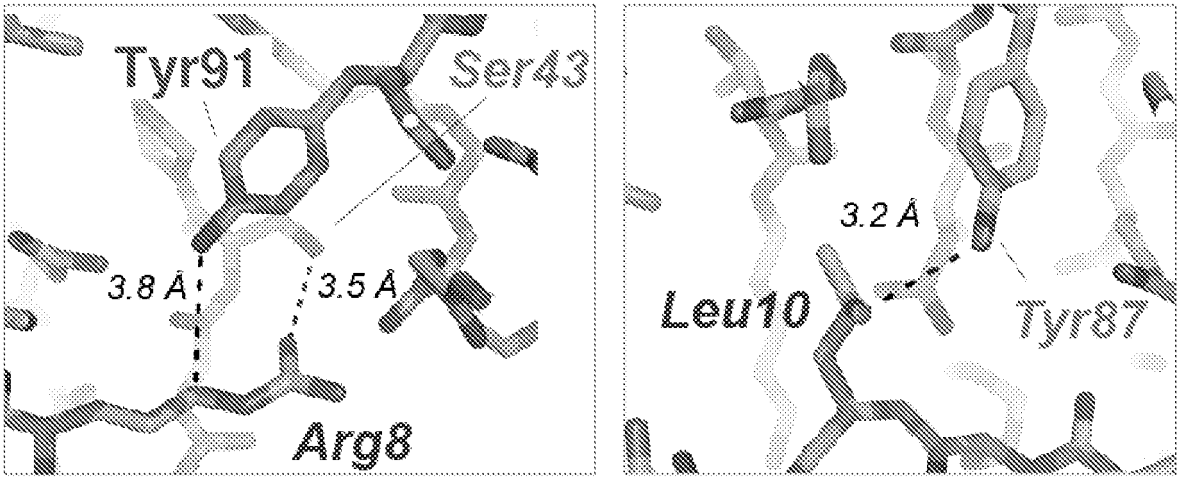


Figure 37

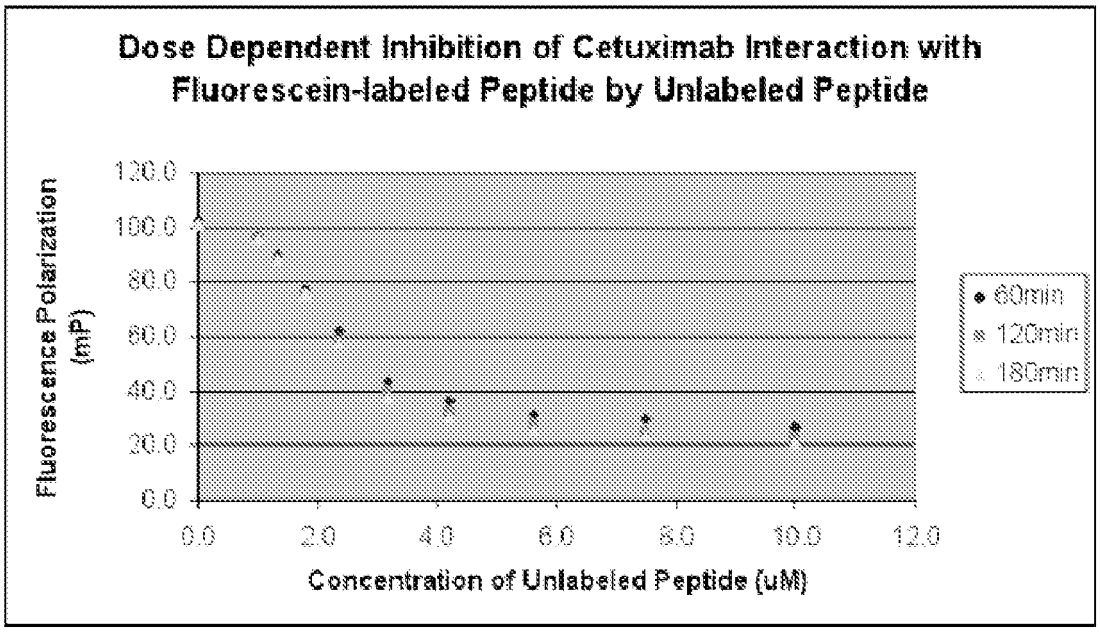
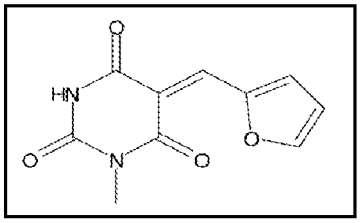
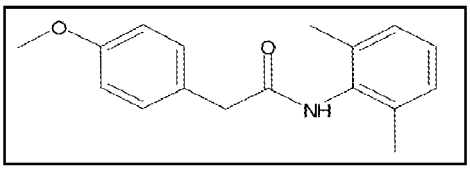
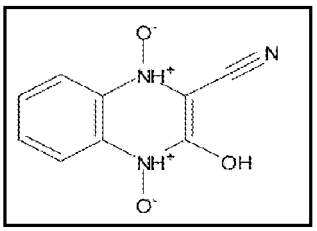
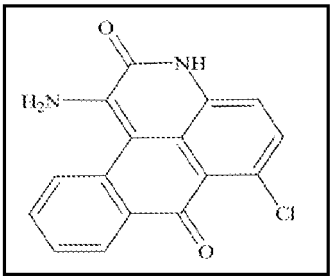

Dose Dependent Inhibition of Cetuximab Interaction with Fluorescein-labeled Peptide by Unlabeled Peptide
Fluorescence Polarization (mP)
120.0
100.0
80.0
60.0
40.0
20.0
0.0
0.0
2.0
4.0
6.0
8.0
10.0
12.0
Concentration of Unlabeled Peptide (uM)
60min
120min
180min

Figure 38









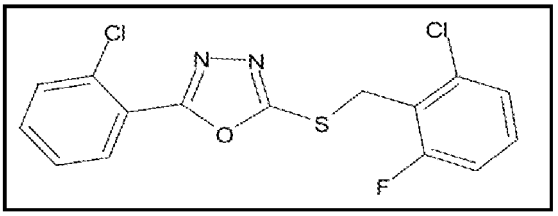
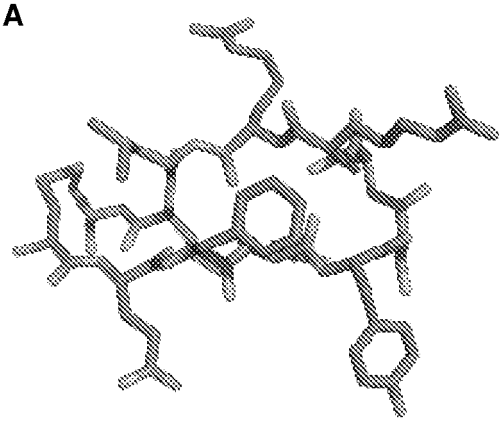


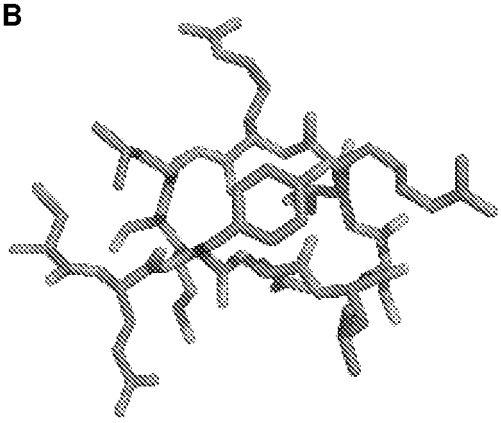
Figure 39

A



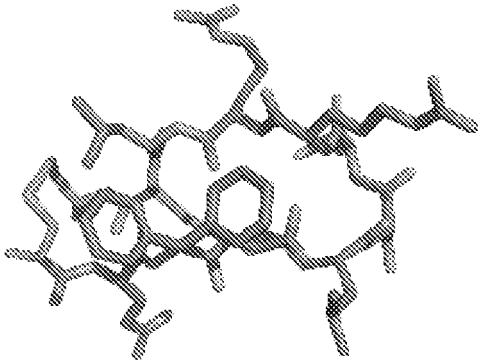
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B



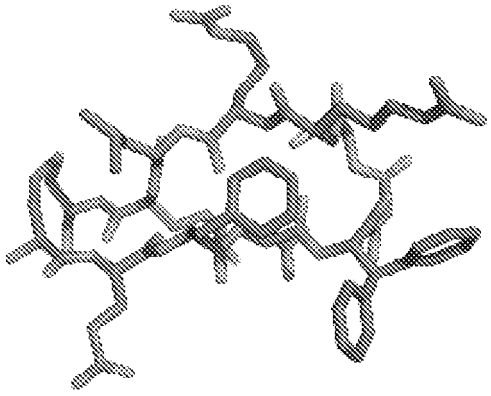
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C



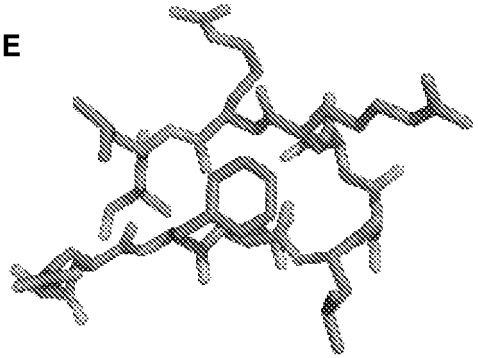
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D



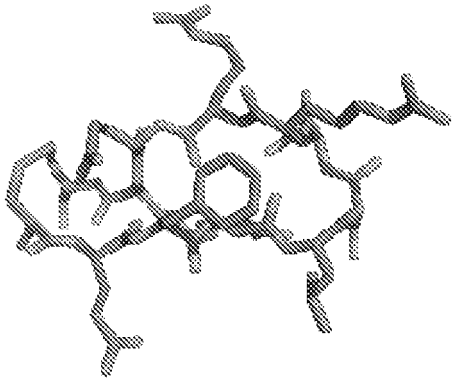
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E



15

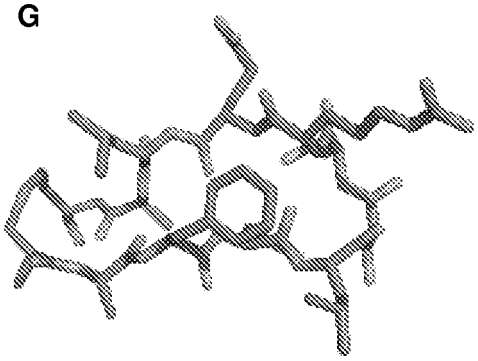
F



23

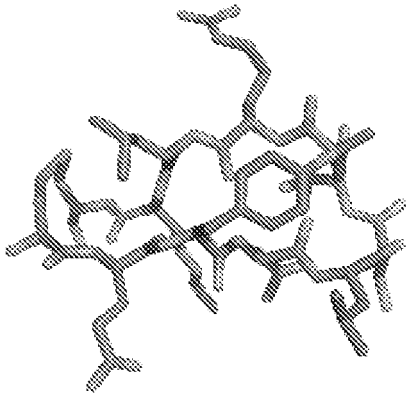
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G



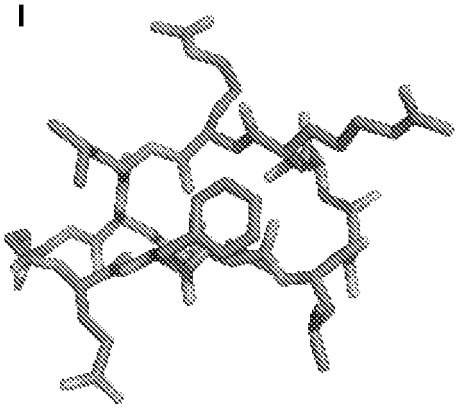
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H



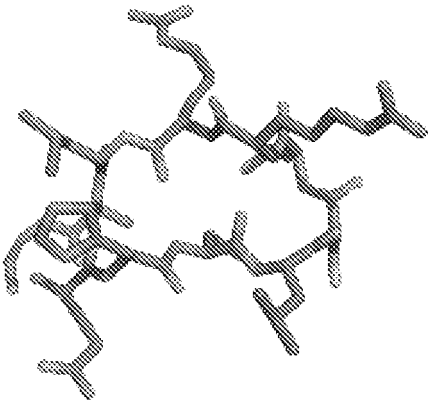
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I



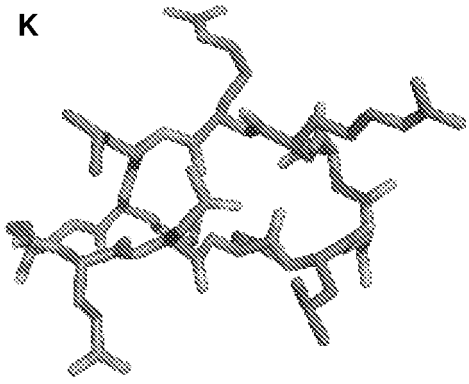
32

J



33

K



L

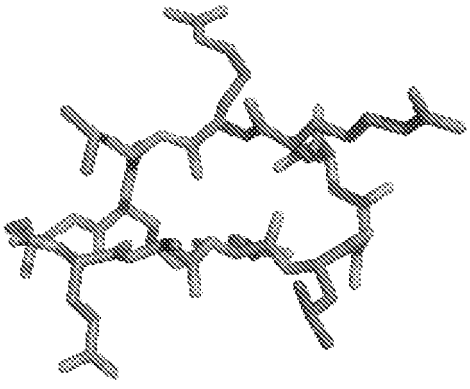
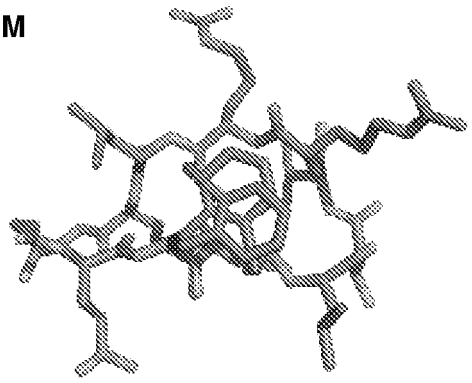


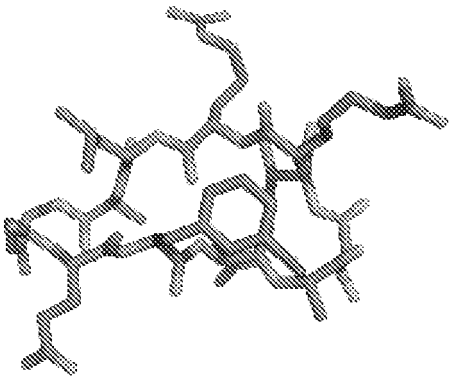
Figure 39 (cont'd)

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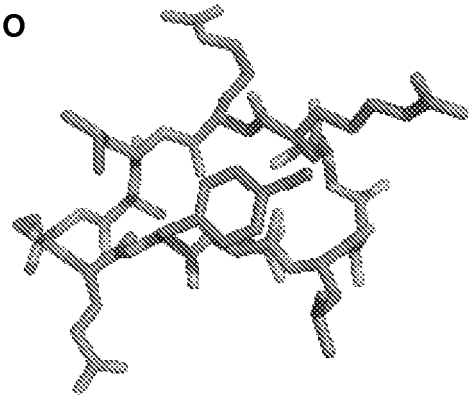
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N



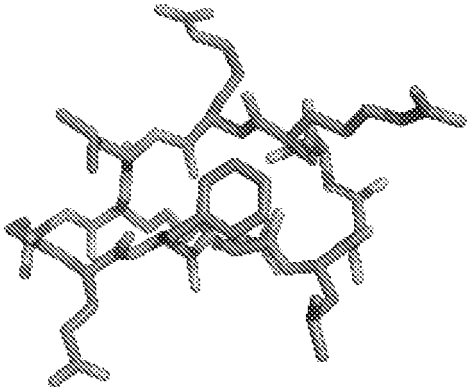
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O



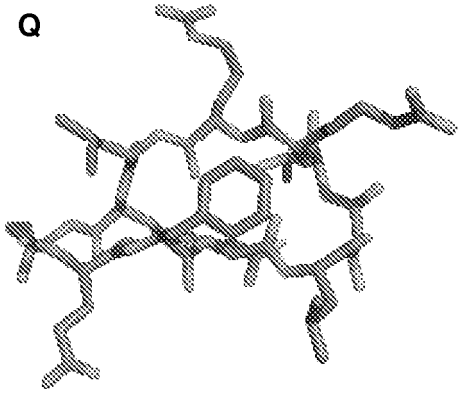
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P



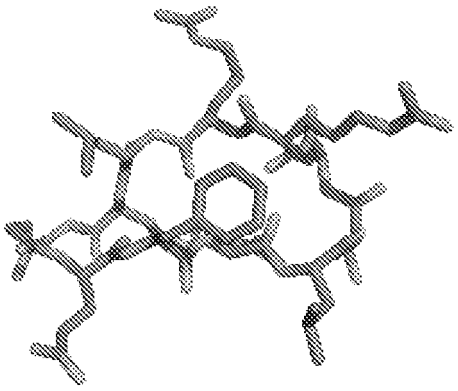
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Q



40

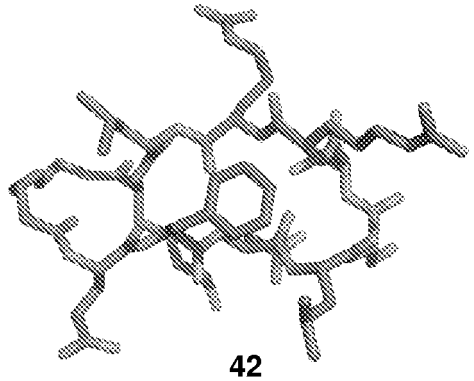
R



41

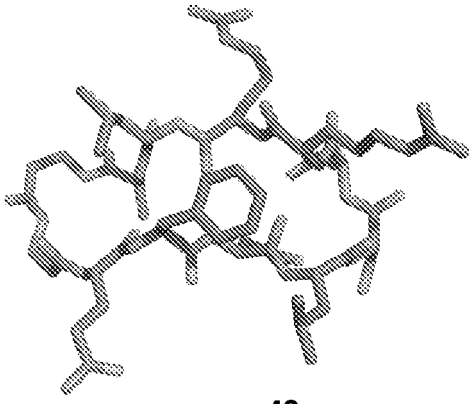
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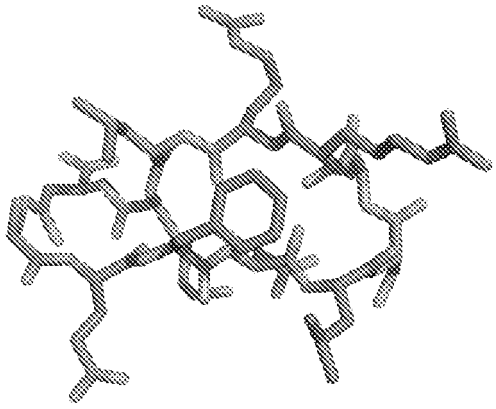
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T



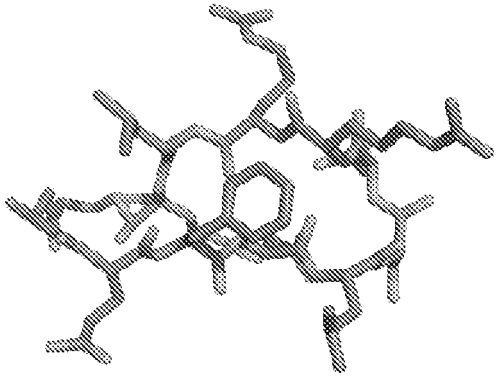
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U



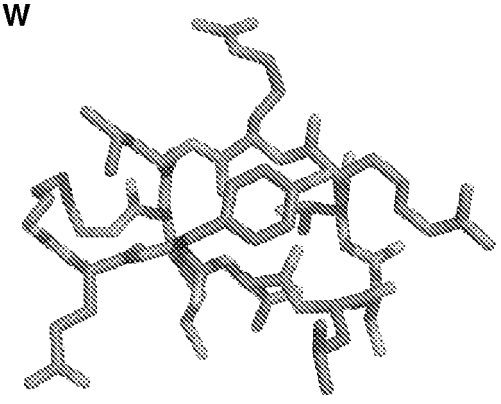
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V



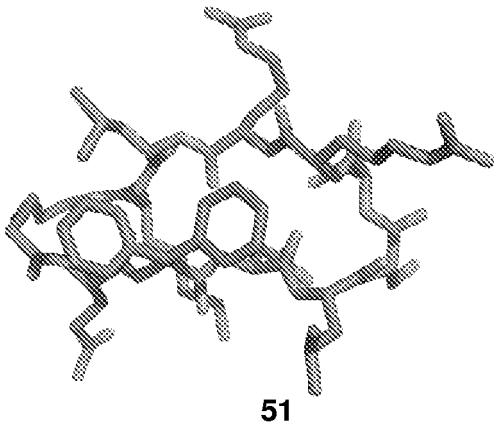
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W



49

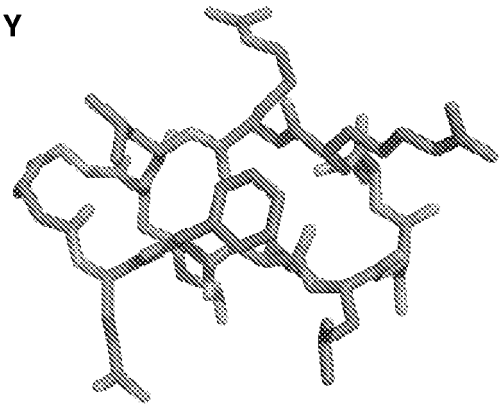
X



51

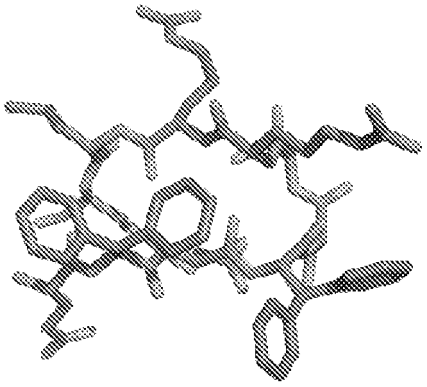
Figure 39 (cont'd)

Y



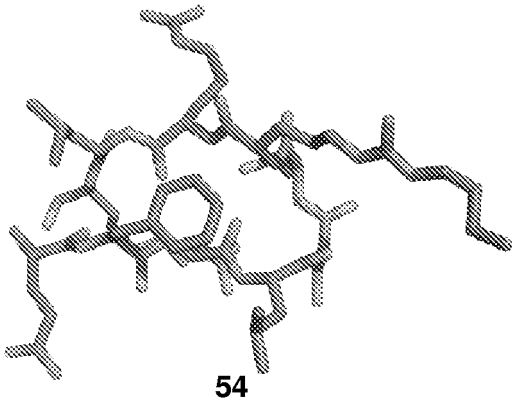
52

Z



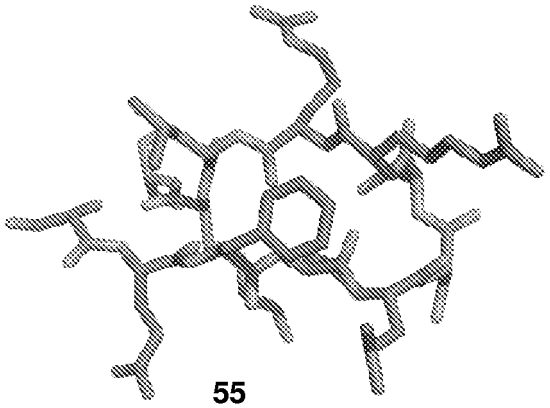
53

AA



54

BB



55

Figure 40

SEQ ID NO:	15	16	17	18
Data Collection				
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions				
a, b, c (Å)	64.33, 82.84, 212.32	64.20, 82.50, 212.49	64.02, 82.83, 212.10	64.28, 83.25, 212.30
α, β, γ (°)	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0
Resolution (Å)	30.00-2.24 (2.45-2.24)	32.99-2.53 (2.60-2.53)	34.36-2.48 (2.54-2.48)	33.19–2.48 (2.54-2.48)
R_{mrgd-F}	0.070 (0.281)	0.066 (0.334)	0.065 (0.312)	0.072 (0.331)
I/σ(I)	19.05 (5.92)	24.74 (5.21)	24.88 (4.97)	23.52 (4.68)
Completeness (%)	99.1 (99.1)	97.6 (91.3)	99.4 (92.6)	99.1 (90.3)
Redundancy	5.2 (5.4)	4.9 (4.5)	6.19 (4.27)	4.61 (3.16)
Refinement				
Resolution (Å)	2.24	2.53	2.48	2.48
No. reflections	55,026	37,650	40,641	41,098
R_{work}/R_{free}	18.0/22.6	17.2/23.6	17.6/22.0	17.4/22.9
No. atoms				
Protein	6526	6514	6551	6541
Meditope	174	291 (198)*	212	218
Water	507	392	511	469
B-factors				
Protein				
Fab	38.16	27.79	25.74	25.23
Meditope	49.08	43.40 (27.51)*	31.78	31.52
Water	41.78	28.05	28.32	29.65
r.m.s.d				
Bond lengths (Å)	0.007	0.005	0.007	0.008
Bond angles (°)	1.093	0.903	1.091	1.106
Ramachandran favored/allowed/disallowed	96.9/3.1/0.0	96.8/3.2/0.0	97.6/2.4/0.0	97.2/2.7/0.1

* 3 meditopes in asymmetric unit. Data in parenthesis refer to the meditopes in the meditope binding pocket characteristic for the WT meditope

Figure 40 (cont'd)

SEQ ID NO:	21	22	23	24
Data Collection				
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions				
a, b, c (Å)	64.38, 82.87, 213.00	64.24, 83.14, 211.94	64.30, 83.39, 212.73	64.46, 83.21, 212.44
α, β, γ (°)	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0
Resolution (Å)	32.65-2.53 (2.60-2.53)	33.15-2.48 (2.55-2.48)	33.23-2.49 (2.55-2.49)	34.96-2.62 (2.69-2.62)
R_{mrgd-F}	0.129 (0.637)	0.044 (0.153)	0.056 (0.219)	0.125 (0.470)
I/σ(I)	23.46 (7.34)	25.24 (9.23)	19.83 (6.03)	15.21 (3.87)
Completeness (%)	99.6 (98.1)	95.1 (72.3)	99.6 (95.4)	98.6 (97.7)
Redundancy	3.91 (3.41)	5.2 (4.6)	5.0 (3.66)	4.95 (5.05)
Refinement				
Resolution (Å)	2.53	2.48	2.49	2.62
No. reflections	38,821	39,080	40,816	34,738
R_{work}/R_{free}	19.1/24.7	17.9/22.6	17.1/22.3	18.4/23.5
No. atoms				
Protein	6535	6554	6525	6529
Meditope	202	208	198	174
Water	327	493	511	380
B-factors				
Protein				
Fab	26.57	24.08	24.69	25.47
Meditope	31.61	27.64	30.40	26.45
Water	28.48	29.37	29.15	28.75
r.m.s.d				
Bond lengths (Å)	0.008	0.003	0.007	0.002
Bond angles (°)	1.185	0.742	1.103	0.618
Ramachandran favored/allowed/disallowed	97.2/2.7/0.1	96.9/3.1/0.0	97.1/2.9/0.0	96.3/3.7/0.0

Figure 40 (cont'd)

SEQ ID NO:	25	31	32	33
Data Collection				
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions				
a, b, c (Å)	64.10, 83.16, 212.32	64.22, 82.53, 212.53	64.28, 82.64, 212.50	64.16, 82.46, 212.05
α, β, γ (°)	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0
Resolution (Å)	33.14-2.55 (2.62-2.55)	33.00-2.60 (2.67-2.60)	30.00-2.55 (2.62-2.55)	32.51–2.49 (2.55-2.49)
R_{mrgd-F}	0.094 (0.374)	0.093 (0.385)	0.085 (0.365)	0.039 (0.163)
I/σ(I)	19.13 (4.60)	16.79 (4.65)	20.27 (4.54)	31.38 (9.58)
Completeness (%)	99.4 (94.1)	95.8 (93.7)	96.7 (91.5)	99.6 (96.1)
Redundancy	4.33 (3.96)	4.35 (4.36)	5.1 (5.1)	5.01 (3.61)
Refinement				
Resolution (Å)	2.55	2.60	2.55	2.49
No. reflections	37701	34,156	36,560	40,266
R_{work}/R_{free}	17.8/22.5	18.8/23.1	18.7/22.7	16.9/22.0
No. atoms				
Protein	6517	6527	6545	6509
Meditope	190	192	188	174
Water	404	338	332	471
B-factors				
Protein				
Fab	25.98	21.36	27.94	25.70
Meditope	26.64	24.70	29.73	53.33
Water	28.08	22.78	29.40	31.55
r.m.s.d				
Bond lengths (Å)	0.008	0.003	0.002	0.003
Bond angles (°)	1.122	0.777	0.631	0.771
Ramachandran favored/allowed/disallowed	96.5/3.4/0.1	97.4/2.6/0.0	96.2/3.8/0.0	97.2/2.8/0.0

Figure 40 (cont'd)

SEQ ID NO:	34	35	36	37
Data Collection				
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions				
a, b, c (Å)	64.18, 82.66, 211.91	63.97, 82.50, 211.88	64.01, 82.21, 211.90	64.04, 82.51, 211.54
α, β, γ (°)	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0
Resolution (Å)	33.02-2.50 (2.56-2.50)	32.95-2.50 (2.62-2.55)	34.14-2.51 (2.58-2.51)	34.22–2.48 (2.55-2.48)
R_{mrgd-F}	0.047 (0.177)	0.094 (0.405)	0.046 (0.238)	0.039 (0.144)
I/σ(I)	30.78 (9.25)	17.76 (3.68)	25.22 (6.50)	30.13 (8.86)
Completeness (%)	99.8 (99.0)	99.0 (90.1)	98.5 (92.3)	99.4 (92.5)
Redundancy	6.02 (4.70)	4.00 (3.70)	4.12 (3.52)	5.77 (4.14)
Refinement				
Resolution (Å)	2.50	2.55	2.51	2.48
No. reflections	39,848	37,028	38,565	40,290
R_{work}/R_{free}	16.9/22.5	16.9/21.4	19.0/23.9	17.9/23.5
No. atoms				
Protein	6507	6555	6528	6535
Meditope	182	190	218	187
Water	503	285	338	454
B-factors				
Protein				
Fab	21.62	32.02	34.24	26.67
Meditope	40.13	38.42	47.05	48.78
Water	27.78	33.79	32.96	31.14
r.m.s.d				
Bond lengths (Å)	0.004	0.005	0.003	0.008
Bond angles (°)	0.876	0.904	0.749	1.120
Ramachandran favored/allowed/disallowed	97.3/2.7/0.0	96.4/3.6/0.0	96.4/3.5/0.1	96.0/4.0/0.0

Figure 40 (cont'd)

SEQ ID NO:	38	39	40	41
Data Collection				
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions				
a, b, c (Å)	64.05, 83.16, 212.26	64.14, 83.19, 212.46	64.21, 83.04, 212.26	64.34, 82.57, 212.05
α, β, γ (°)	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0
Resolution (Å)	33.13–2.50 (2.56-2.50)	33.16-2.48 (2.55-2.48)	34.40-2.48 (2.54-2.48)	34.29-2.48 (2.54-2.48)
R_{mrgd-F}	0.084 (0.375)	0.054 (0.186)	0.051 (0.184)	0.035 (0.147)
I/σ(I)	20.51 (4.31)	29.15 (8.34)	30.80 (7.93)	38.15 (11.37)
Completeness (%)	99.2 (92.2)	99.3 (93.2)	99.4 (93.6)	98.2 (91.1)
Redundancy	6.26 (4.94)	5.79 (4.10)	5.40 (3.86)	6.17 (4.25)
Refinement				
Resolution (Å)	2.50	2.48	2.48	2.48
No. reflections	39,826	40,872	40,869	40,195
R_{work}/R_{free}	19.1/24.0	18.1/23.3	17.8/22.4	18.6/23.8
No. atoms				
Protein	6524	6539	6499	6539
Meditope	190	192	192	192
Water	361	485	466	475
B-factors				
Protein				
Fab	26.19	19.15	20.04	20.24
Meditope	33.05	26.02	26.61	27.05
Water	28.90	24.13	24.30	24.57
r.m.s.d				
Bond lengths (Å)	0.004	0.003	0.007	0.007
Bond angles (°)	0.822	0.760	1.071	1.125
Ramachandran favored/allowed/disallowed	96.6/3.4/0.0	96.8/3.1/0.1	97.0/2.9/0.1	96.9/3.0/0.1

Figure 40 (cont'd)

SEQ ID NO:	42	43	44	46
Data Collection				
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions				
a, b, c (Å)	64.06, 82.71, 212.39	64.14, 82.57, 212.07	64.28, 83.05, 212.37	63.95, 82.38, 211.54
α, β, γ (°)	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0
Resolution (Å)	34.74-2.48 (2.54-2.48)	34.26-2.55 (2.61-2.55)	32.71-2.55 (2.62-2.55)	34.17–2.50 (2.56-2.50)
R_{mrgd-F}	0.045 (0.209)	0.101 (0.482)	0.078 (0.313)	0.066 (0.337)
I/σ(I)	28.89 (7.15)	20.57 (3.85)	21.03 (4.48)	20.98 (4.11)
Completeness (%)	98.7 (89.6)	99.2 (93.0)	97.6 (95.1)	99.1 (90.6)
Redundancy	5.85 (4.14)	5.49 (4.89)	4.47 (4.69)	3.92 (3.01)
Refinement				
Resolution (Å)	2.48	2.55	2.55	2.50
No. reflections	40,599	37,507	37,078	39,231
R_{work}/R_{free}	17.2/21.8	19.8/25.2	18.2/22.3	18.2/22.9
No. atoms				
Protein	6539	6531	6522	6520
Meditope	185	182	190	198
Water	490	338	459	412
B-factors				
Protein				
Fab	21.04	31.73	23.90	27.12
Meditope	26.53	39.04	37.29	37.46
Water	24.76	31.88	28.49	29.83
r.m.s.d				
Bond lengths (Å)	0.007	0.004	0.003	0.004
Bond angles (°)	1.136	0.755	0.767	0.921
Ramachandran favored/allowed/disallowed	97.1/2.9/0.0	96.6/3.4/0.0	96.5/3.5/0.0	96.9/3.1/0.0

Figure 40 (cont'd)

SEQ ID NO:	49	51	52	53
Data Collection				
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions				
a, b, c (Å)	64.24, 82.94, 212.4	64.11, 82.47, 212.49	64.27, 82.74, 212.37	64.15, 82.75, 211.67
α, β, γ (°)	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0	90.0, 90.0, 90.0
Resolution (Å)	34.38-2.52 (2.59-2.52)	34.23-2.48 (2.54-2.48)	34.79-2.49 (2.55-2.49)	33.03-2.50 (2.56-2.50)
R_{mrgd-F}	0.057 (0.196)	0.087 (0.374)	0.067 (0.308)	0.059 (0.238)
I/σ(I)	26.03 (7.14)	18.64 (4.04)	27.61 (5.79)	21.92 (5.96)
Completeness (%)	97.4 (91.4)	99.1 (90.3)	99.1 (94.2)	98.4 (91.0)
Redundancy	4.60 (3.89)	4.76 (3.19)	4.54 (3.53)	4.30 (3.12)
Refinement				
Resolution (Å)	2.52	2.48	2.49	2.50
No. reflections	38,211	40,649	40,191	39,261
R_{work}/R_{free}	18.6/22.9	18.1/22.9	17.3/22.9	18.0/23.4
No. atoms				
Protein	6587	6544	6529	6549
Meditope	196	197	185	206
Water	363	438	454	361
B-factors				
Protein				
Fab	23.36	23.05	21.47	25.78
Meditope	27.69	33.77	27.91	47.45
Water	25.75	26.89	25.45	28.54
r.m.s.d				
Bond lengths (Å)	0.006	0.008	0.007	0.005
Bond angles (°)	1.079	1.164	1.076	0.970
Ramachandran favored/allowed/disallowed	96.9/3.1/0.0	97.3/2.7/0.0	96.9/3.1/0.0	96.9/3.0/0.1

Figure 40 (cont'd)

SEQ ID NO:	54	55
Data Collection		
Space group	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions		
a, b, c (Å)	64.58, 83.06, 211.83	64.18, 82.89, 212.90
α, β, γ (°)	90.0, 90.0, 90.0	90.0, 90.0, 90.0
Resolution (Å)	33.17-2.48 (2.55-2.48)	34.82-2.50 (2.57-2.50)
R_{mrgd-F}	0.036 (0.169)	0.064 (0.245)
I/σ(I)	34.78 (9.23)	20.15 (5.87)
Completeness (%)	98.0 (85.0)	99.6 (96.1)
Redundancy	5.47 (4.28)	4.68 (3.53)
Refinement		
Resolution (Å)	2.48	2.50
No. reflections	40,269	40,034
R_{work}/R_{free}	19.0/23.0	16.8/21.6
No. atoms		
Protein	6577	6569
Meditope	184	194
Water	294	501
B-factors		
Protein		
Fab	37.76	20.94
Meditope	50.14	28.28
Water	36.97	25.34
r.m.s.d		
Bond lengths (Å)	0.004	0.007
Bond angles (°)	0.864	1.095
Ramachandran favored/allowed/disallowed	97.1/2.8/0.1	96.9/3.1/0.0

Figure 41

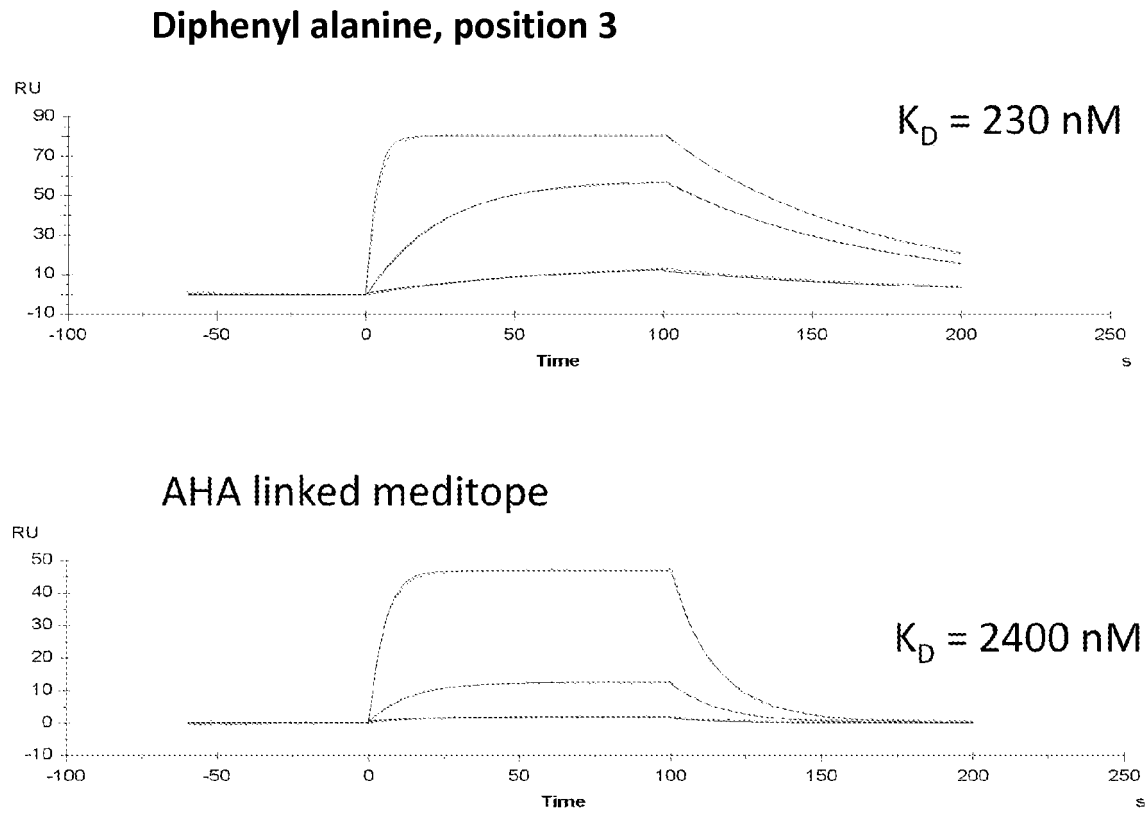

Diphenyl alanine, position 3
RU
90
70
50
30
10
-10
-100
-50
0
50
100
150
200
250
Time
s
K_D = 230 nM
AHA linked meditope
RU
50
40
30
20
10
0
-10
-100
-50
0
50
100
150
200
250
Time
s
K_D = 2400 nM

Figure 42

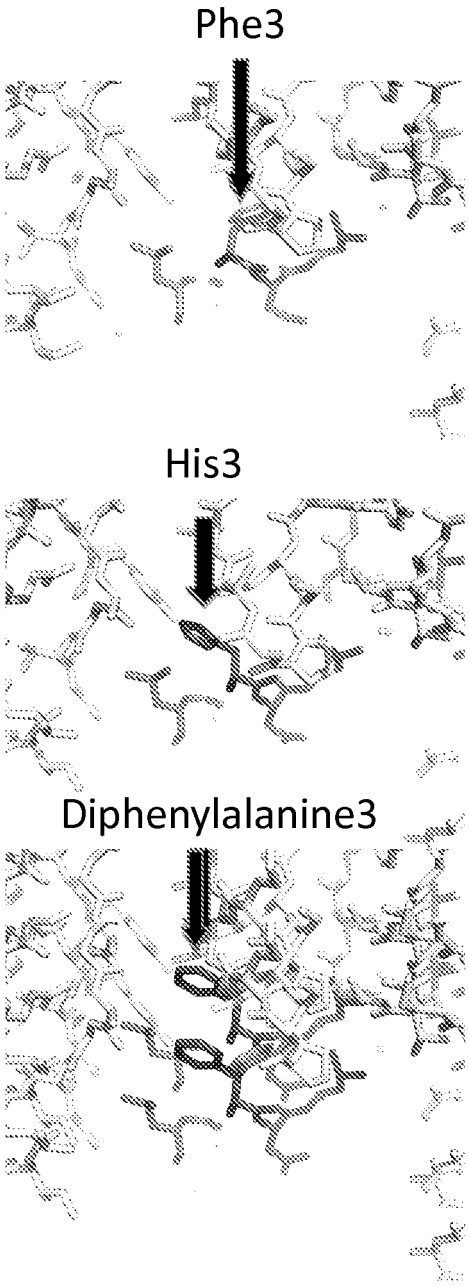


Figure 43

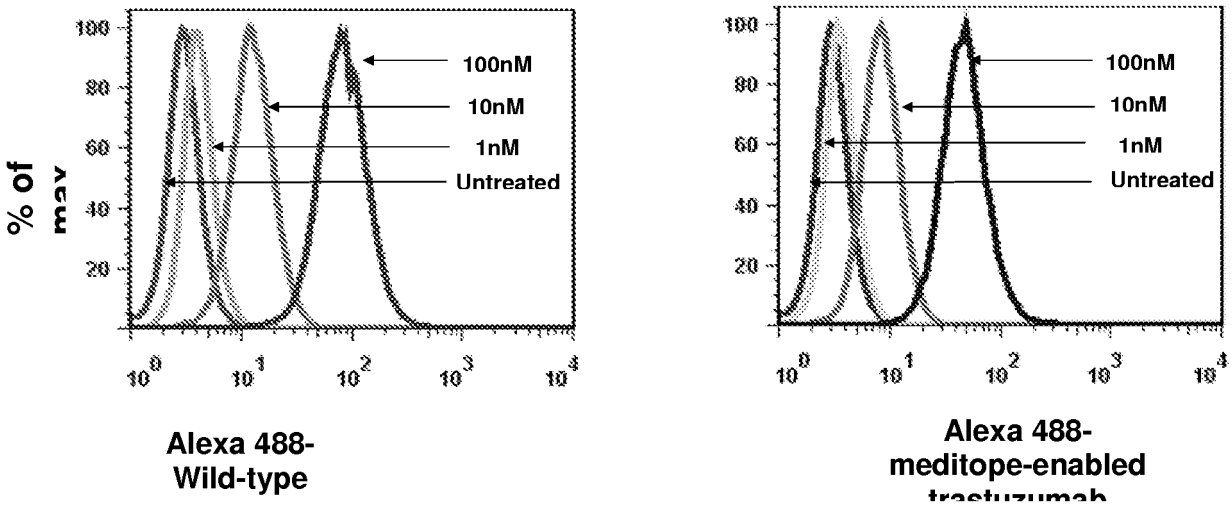

% of max
100nM
10nM
1nM
Untreated
Alexa 488-Wild-type
Alexa 488-meditope-enabled

Figure 44

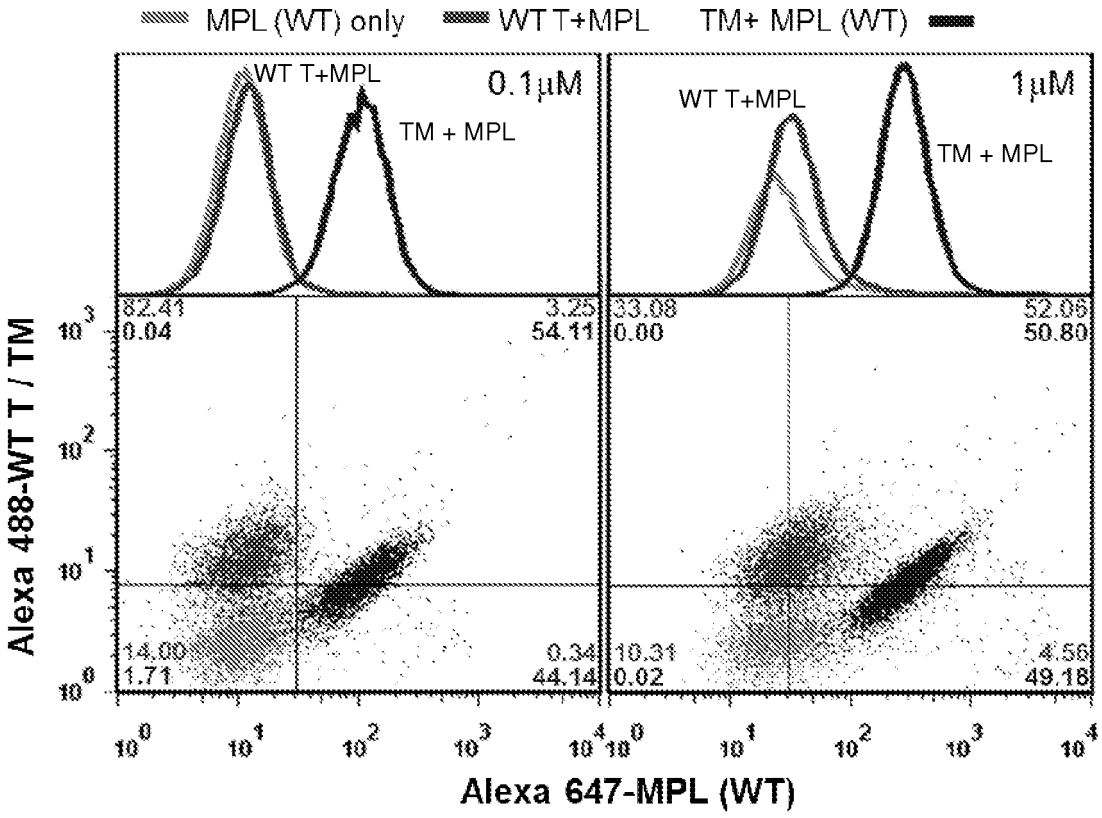

MPL (WT) only
WT T+MPL
TM+ MPL (WT)
WT T+MPL
0.1μM
TM + MPL
WT T+MPL
1μM
TM + MPL
82.41
0.04
3.25
54.11
33.08
0.00
52.06
50.80
14.00
1.71
0.34
44.14
10.31
0.02
4.56
49.18
Alexa 488-WT T / TM
Alexa 647-MPL (WT)

Figure 45

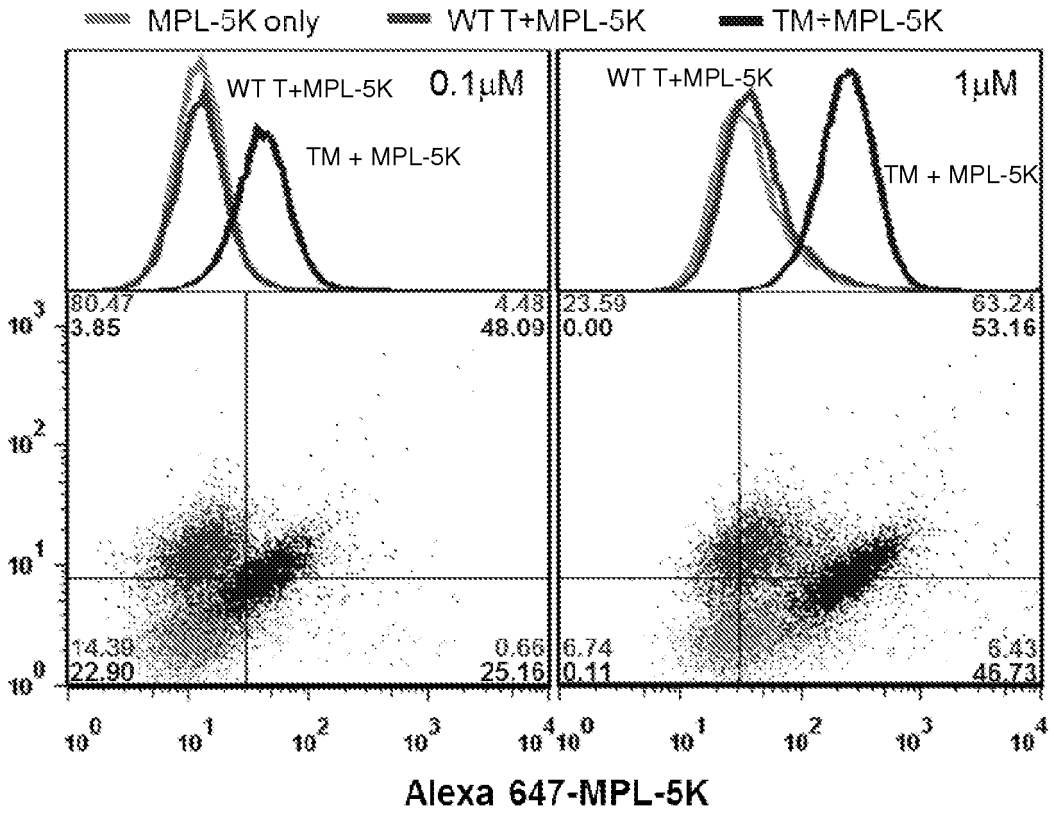

MPL-5K only
WT T+MPL-5K
TM÷MPL-5K
WT T+MPL-5K 0.1μM
TM + MPL-5K
WT T+MPL-5K 1μM
TM + MPL-5K
80.47
3.85
4.48
48.09
23.59
0.00
63.24
53.16
14.39
22.90
0.66
25.16
6.74
0.11
6.43
46.73
Alexa 647-MPL-5K

Figure 46

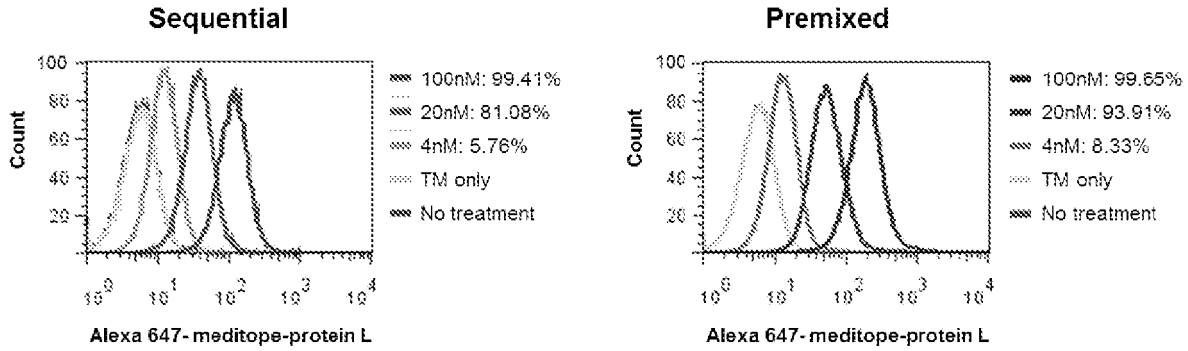

Sequential
Count
100
80
60
40
20
10^0 10^1 10^2 10^3 10^4
Alexa 647-meditope-protein L
100nM: 99.41%
20nM: 81.08%
4nM: 5.76%
TM only
No treatment
Premixed
Count
100
80
60
40
20
10^0 10^1 10^2 10^3 10^4
Alexa 647-meditope-protein L
100nM: 99.65%
20nM: 93.91%
4nM: 8.33%
TM only
No treatment

Figure 47A

A) Light chain nucleic acid (SEQ ID NO: 60) and amino acid (SEQ ID NO: 61) sequences

```
aagcttgccgccaccatggagacagacacgcttttgctttgggtgttgttgttgtgggtc
 K  L  A  A  T  M  E  T  D  T  L  L  L  W  V  L  L  L  W  V  P
ccccggttcgaccggtaccggtgacatcttgttgacgcagtccccgtcattctgagcgtg
 G  S  T  G  D  I  L  L  T  Q  S  P  V  I  L  S  V
tccccgggagagccgggtatcgttttcctgccgagcctcgcaaagatatcaacactgcgatt
 S  P  G  E  R  V  S  F  S  C  R  A  S  Q  D  I  N  T  A  I
gcatggtatcaacagcgcacaaacgggtcgccgagactgtcatctactcagcctcgttc
 A  W  Y  Q  Q  R  T  N  G  S  P  R  L  L  I  Y  S  A  S  F
ctttatagcggtgtgccttcgaggttctcgggatcacggtcaggaacggattttacactc
 L  Y  S  G  V  P  S  P  F  S  G  S  P  S  G  T  D  F  T  L
agcatcaattccgtggaatcagaggacattgcggactactattgtcagcagcactacacc
 S  I  N  S  V  E  S  E  D  I  A  D  Y  Y  C  Q  Q  H  Y  T
acaccaccgacctteggcgctgggacgaaagtcgaaatcaagcggacggtagcagccccc
 T  P  P  T  F  G  A  G  T  K  V  E  I  K  R  T  V  A  A  P
tcggtctttatcttccctcctagcgacgaacaattgaagtcagggaccgcctcggtggta
 S  V  F  I  F  P  P  S  D  E  Q  L  K  S  G  T  A  S  V  V
tgcctgcttaacaacttttacccacgggaagccaaagtacagtggaaggtggataatgcg
 C  L  L  N  N  F  Y  P  R  E  A  K  V  Q  W  K  V  D  N  A
ctccagagcggaaactcccaagagagcgtgacagaacaggactcgaaggattcgacgtac
 L  Q  S  G  N  S  Q  E  S  V  T  E  Q  D  S  K  D  S  T  Y
tcactcagctcaacgctgaccctgtcgaaagcggactatgagaaacacaaggtctacgcg
 S  L  S  S  T  L  T  L  S  K  A  D  Y  E  K  H  K  V  Y  A
tgcgaggtgacccatcagggcctgagctccccgtaactaagtcattcaaccggggtgaa
 C  E  V  T  H  Q  G  L  S  S  P  V  T  K  S  F  N  R  G  E
tgctaa
 C  -
```

Figure 47B

B) Heavy chain nucleic acid (SEQ ID NO: 62) and amino acid (SEQ ID NO: 63) sequences

```
aagcttgccgccaccatgaaaatgctcgtgggtgatcttttccttatggcggtagtaacc
 M  K  M  L  V  G  D  L  F  S  L  W  R  W  S  N  T  A  V  T
ggagttaactcccaagtacagcttaagcagtcgggtccgggggctggtgcagccatcgcag
 G  V  N  S  Q  V  Q  L  K  Q  S  G  P  G  L  V  Q  P  S  Q
tcgttgtcaatcacatgcacggtgtcgggattcaacattaaagacacctatatccactgg
 S  L  S  I  T  C  T  V  S  G  F  N  I  K  D  T  Y  I  H  W
gtccgacaatcccctggtaaagggctggagtggctcggtcggatctaccccacgaacgga
 V  R  Q  S  P  G  K  G  L  E  W  L  G  R  I  Y  P  T  N  G
tacaccaggtataacacgccctttacatcgagactttcaattaacgcggataatagcaag
 Y  T  R  Y  N  T  P  F  T  S  R  L  S  I  N  A  D  N  S  K
aatcaggtgttcttcaagatgaatagcctccagtcaaatgacactgcaatctactactgt
 N  Q  V  F  F  K  M  N  S  L  Q  S  N  D  T  A  I  Y  Y  C
gcccgctggggaggggatggcttttatgcgatggactattgggggcagggaactttggtc
 A  R  W  G  G  D  G  F  Y  A  M  D  Y  W  G  Q  G  T  L  V
acagtaagctccgctagcacaaagggacctagcgtgtttccccttggctccctcatcgaaa
 T  V  S  S  A  S  T  K  G  P  S  V  F  P  L  A  P  S  S  K
tcaacgtccggtgggacggcggcattggggtgtcttgtcaaggactatttccccgagccc
 S  T  S  G  G  T  A  A  L  G  C  L  V  K  D  Y  F  P  E  P
gtgacagtctcgtggaactcgggtgccctcacaagcggcgtacatacgtttcccgccgtg
 V  T  V  S  W  N  S  G  A  L  T  S  G  V  H  T  F  P  A  V
ctccaatcatccggactgtattccctttcatccgtcgtgactgtgccgtcctcgtcactc
 L  Q  S  S  G  L  Y  S  L  S  S  V  V  T  V  P  S  S  S  L
ggaacgcaaacttacatttgcaatgtcaacccacaaaccgtcaaatacaaaggtcgataag
 G  T  Q  T  Y  I  C  N  V  N  H  K  P  S  N  T  K  V  D  K
aaggtcgagccaaagtcgtgtgataagacccacacatgcccctcccctgtccagcgccggag
 K  V  E  P  K  S  C  D  K  T  H  T  C  P  P  C  P  A  P  E
ctgttgggagggccttcagtgttcctcttcccgccccaaacccaaggacaccctgatgatt
 L  L  G  G  P  S  V  F  L  F  P  P  K  P  K  D  T  L  M  I
agcccgcacacccgaggtgacgtgtgtcgtcgtgatgtctcacatgaggaccccggaggta
 S  R  T  P  E  V  T  C  V  V  V  D  V  S  H  E  D  P  E  V
aagttcaactggtacgtggatggagtcgaagtgcacaacgcaaaaacaaaaacctcgggaa
 K  F  N  W  Y  V  D  G  V  E  V  H  N  A  K  T  K  P  R  E
gagcagtacaatagcacgtacagagtagtcagcgtgctcaccgtgctgcaccaggattgg
 E  Q  Y  N  S  T  Y  R  V  V  S  V  L  T  V  L  H  Q  D  W
ctcaatggaaaggagtacaagtgtaaagtgtccaataaggcgctgcctgccccccatcgaa
 L  N  G  K  E  Y  K  C  K  V  S  N  K  A  L  P  A  P  I  E
aagacaatttccaaagctaaagggcaaccccgcgagccgcaagtatacacccctcccaccc
 K  T  I  S  K  A  K  G  Q  P  R  E  P  Q  V  Y  T  L  P  P
tcgcgcgatgaactgaccaagaaccaggtgtcattgacgtgtctcgtcaagggcttctat
 S  R  D  E  L  T  K  N  Q  V  S  L  T  C  L  V  K  G  F  Y
ccgagcgacattgcagtagaatgggaaagcaacggacagccggaaaacaactacaagact
 P  S  D  I  A  V  E  W  E  S  N  G  Q  P  E  N  N  Y  K  T
acaccgcctgtccttgattcggatggttccttctttctttactcaaaacttacagtcgac
 T  P  P  V  L  D  S  D  G  S  F  F  L  Y  S  K  L  T  V  D
aaatcgaggtggcagcagggaaatgtgttttcgtgcagcgtgatgcacgaggccttgcat
 K  S  R  W  Q  Q  G  N  V  F  S  C  S  V  M  H  E  A  L  H
aatcactatacacagaagtcgttgtcactgtcgccgggaaagtaa
 N  H  Y  T  Q  K  S  L  S  L  S  P  G  K  -
```

Figure 48

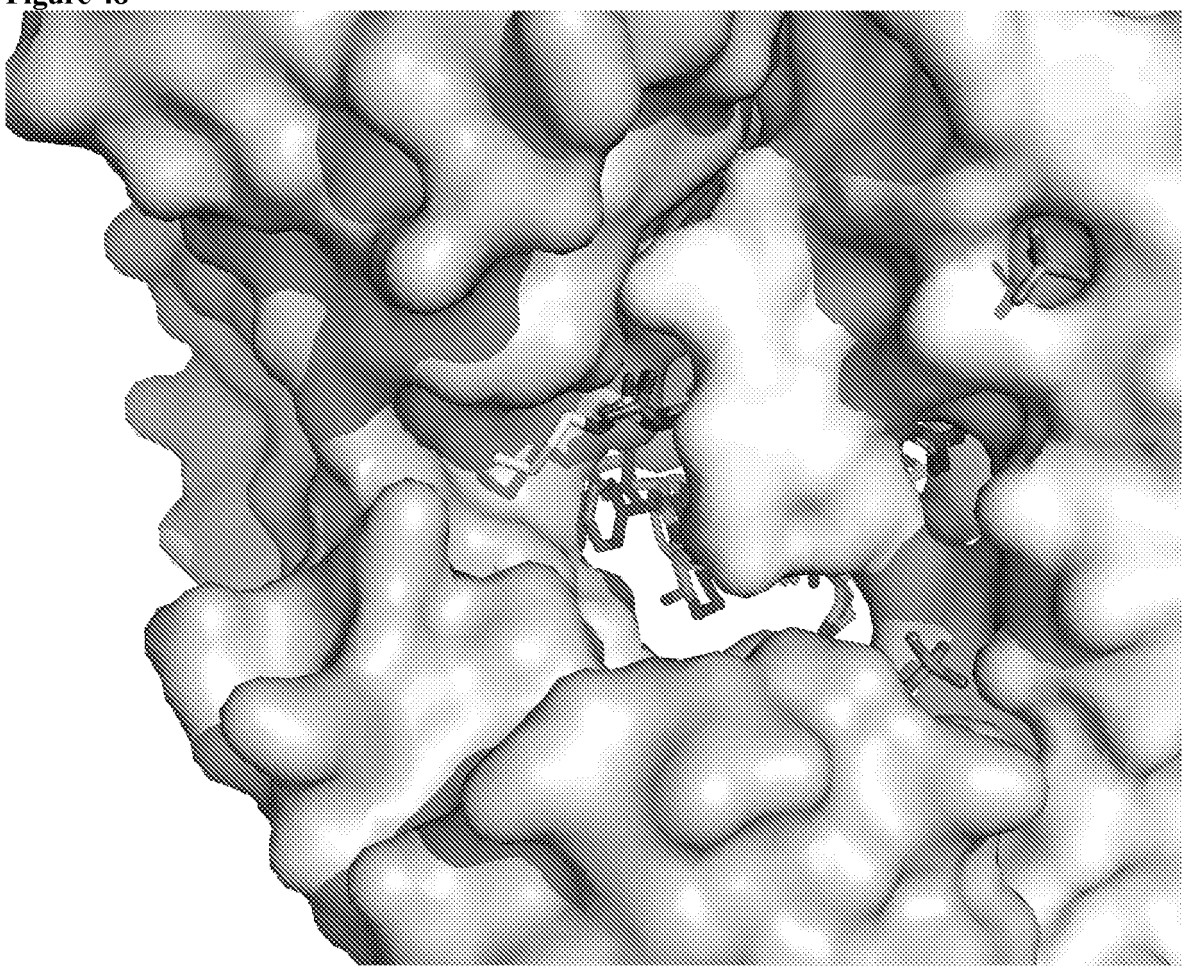


Figure 49

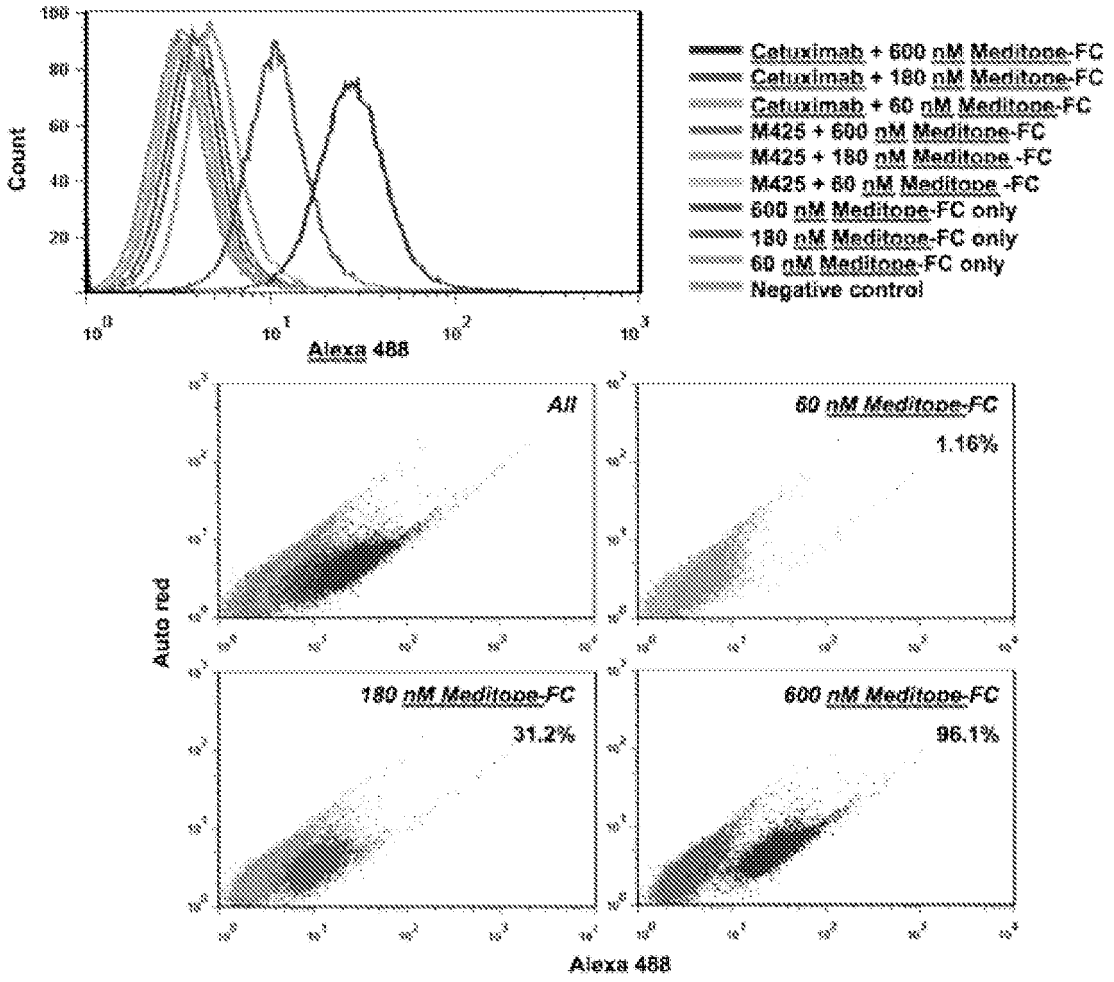

Count
Alexa 488
Cetuximab + 600 nM Meditope-FC
Cetuximab + 180 nM Meditope-FC
Cetuximab + 60 nM Meditope-FC
M425 + 600 nM Meditope-FC
M425 + 180 nM Meditope-FC
M425 + 60 nM Meditope-FC
600 nM Meditope-FC only
180 nM Meditope-FC only
60 nM Meditope-FC only
Negative control
All
60 nM Meditope-FC
1.16%
180 nM Meditope-FC
31.2%
600 nM Meditope-FC
96.1%
Auto red
Alexa 488

Figure 50

White Sticks: 5-dipheylalanine meditope bound to trastuzumab MeMab;
Dark Grey Sticks: 5-diphenylalanine meditope bound to cetuximab;
Outlined Sticks show Fab residues.

b

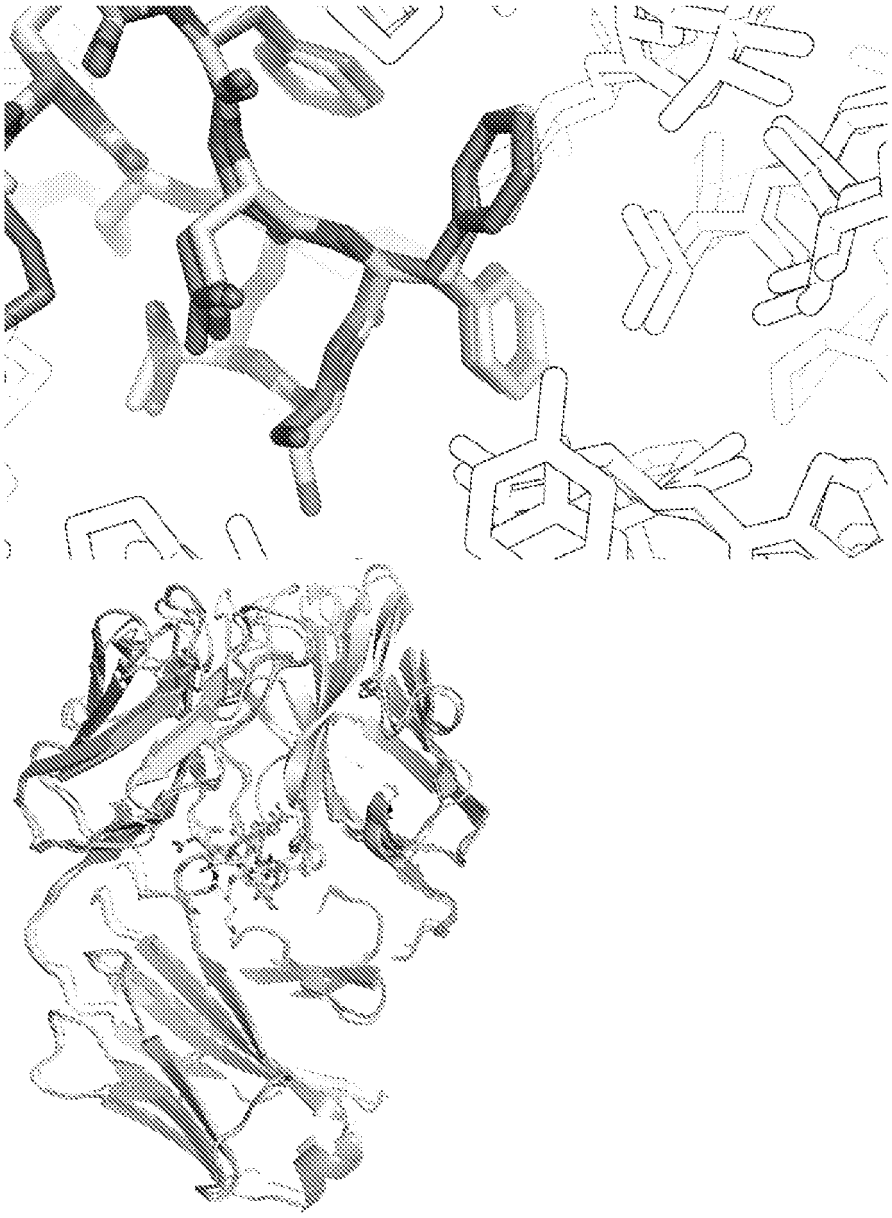


Figure 51

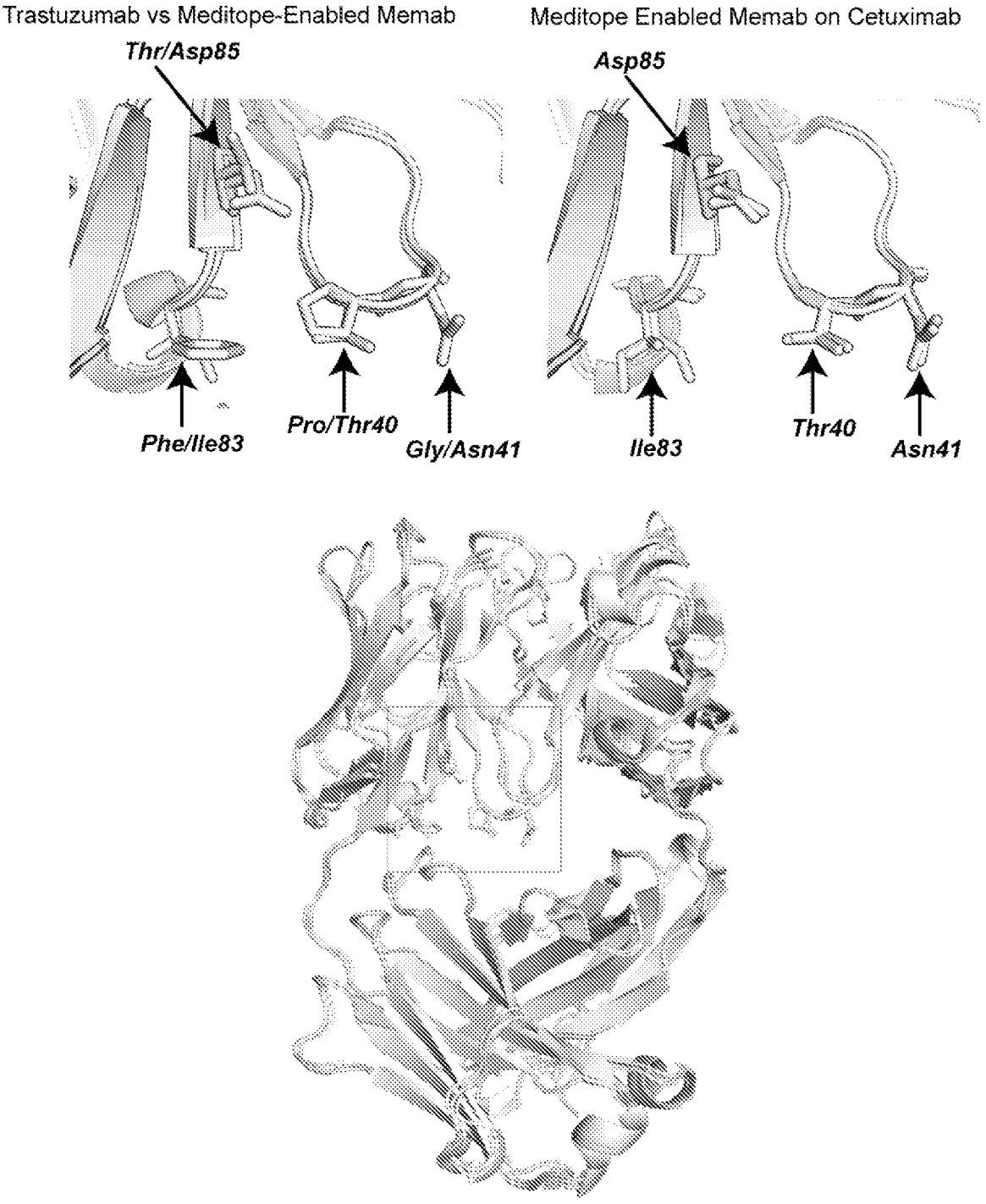

Trastuzumab vs Meditope-Enabled Memab
Thr/Asp85
Phe/Ile83
Pro/Thr40
Gly/Asn41
Meditope Enabled Memab on Cetuximab
Asp85
Ile83
Thr40
Asn41

Figure 52

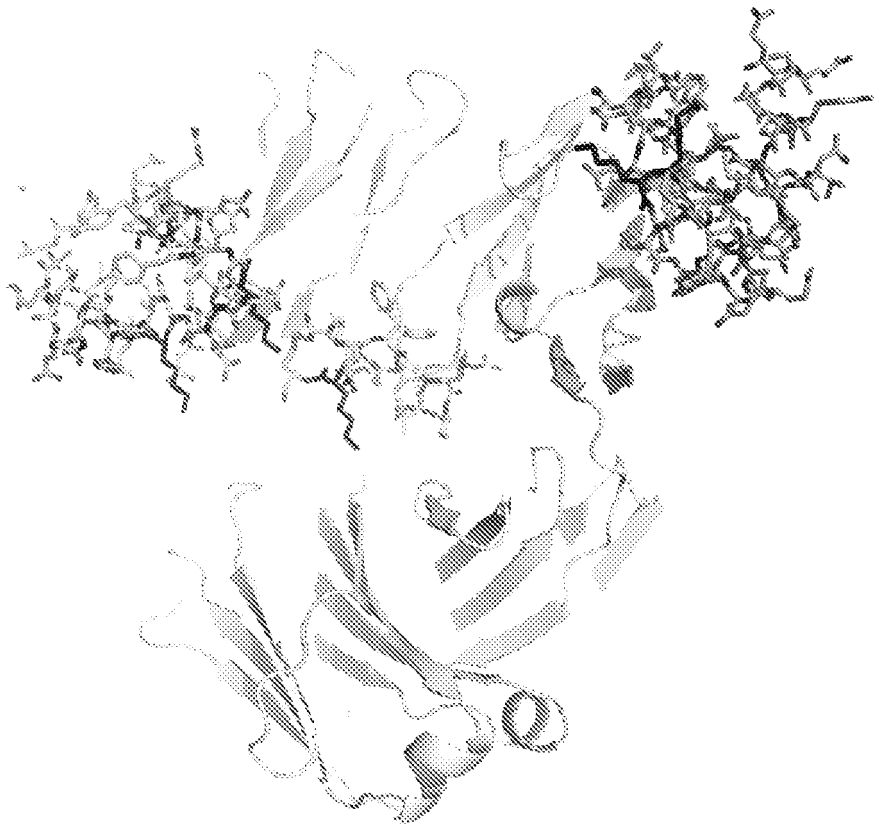


Figure 53

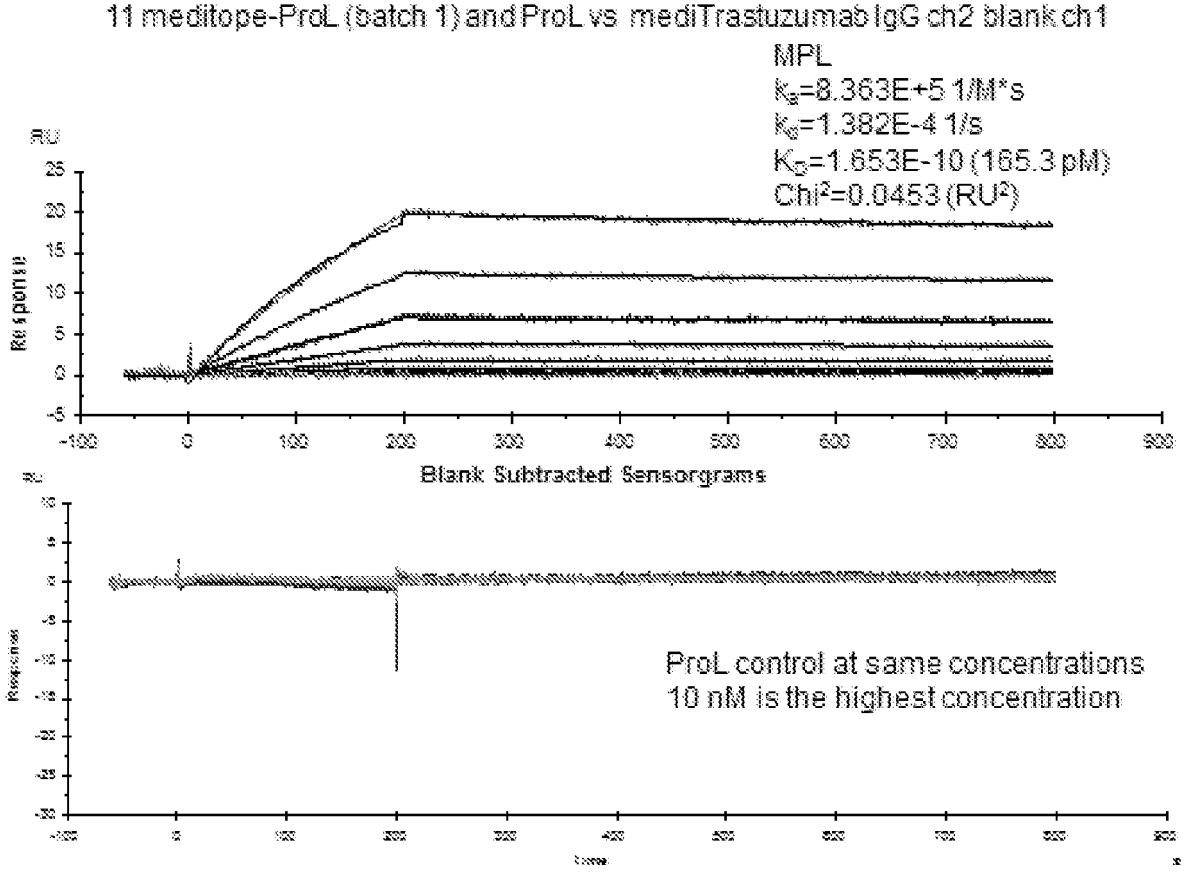

11 meditope-ProL (batch 1) and ProL vs mediTrastuzumab IgG ch2 blank ch1
MPL
k_a=8.363E+5 1/M*s
k_d=1.382E-4 1/s
K_D=1.653E-10 (165.3 pM)
Chi²=0.0453 (RU²)
RU
Response
Blank Subtracted Sensorgrams
ProL control at same concentrations
10 nM is the highest concentration

Figure 54

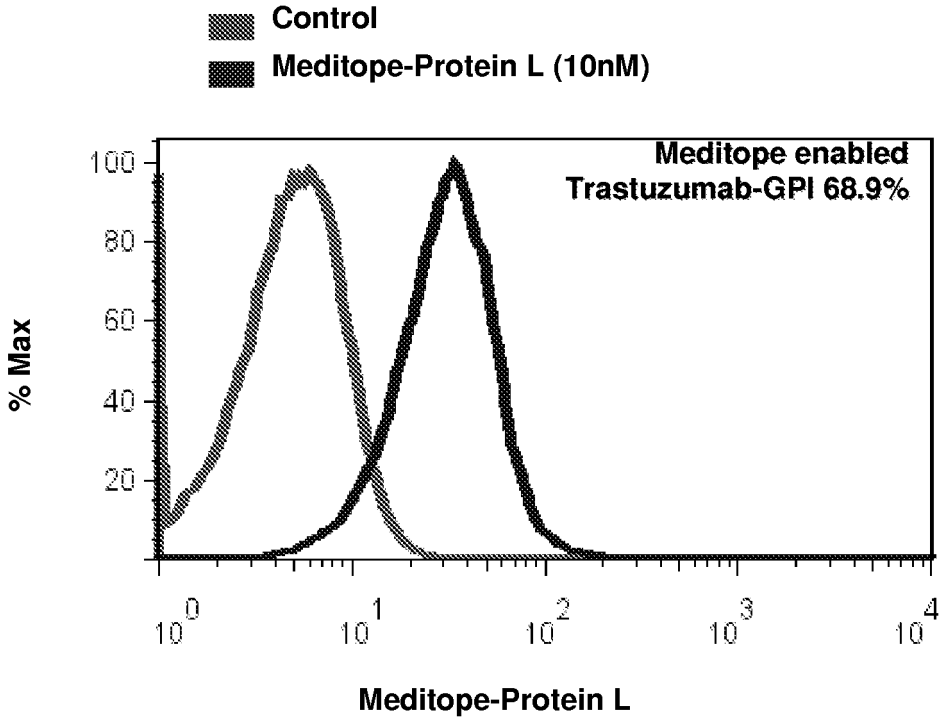

Control
Meditope-Protein L (10nM)
Meditope enabled
Trastuzumab-GPI 68.9%
% Max
100
80
60
40
20
10^0
10^1
10^2
10^3
10^4
Meditope-Protein L

Figure 55

A.

```
IgG2|P01859|1-98    ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS 60
IgG4|P01861|1-98    ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS 60
IgG3|P01860|1-98    ASTKGPSVFPLAPCSRSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS 60
IgG1|P01857|1-98    ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS 60
                    *************.*:*** .****************************************

sp|P01859|1-98      GLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTV 98 (SEQ ID NO: 64)
sp|P01861|1-98      GLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRV 98 (SEQ ID NO: 65)
sp|P01860|1-98      GLYSLSSVVTVPSSSLGTQTYTCNVNHKPSNTKVDKRV 98 (SEQ ID NO: 66)
sp|P01857|1-98      GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKV 98 (SEQ ID NO: 67)
                    ***************.**.******.**********.*
```

B.

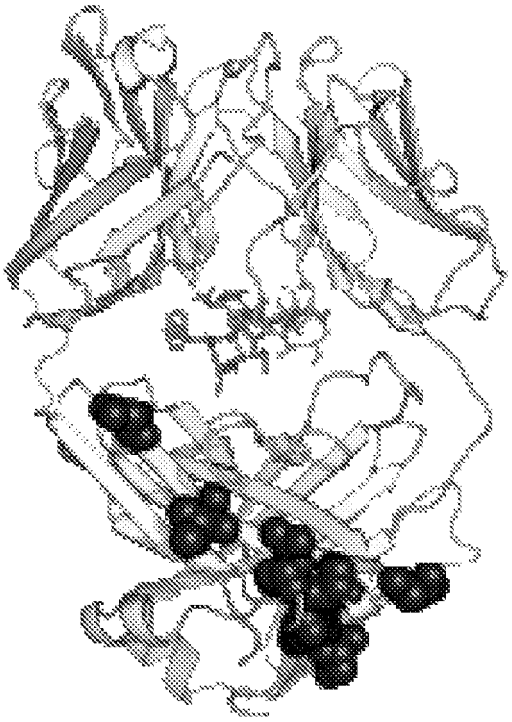


Figure 56

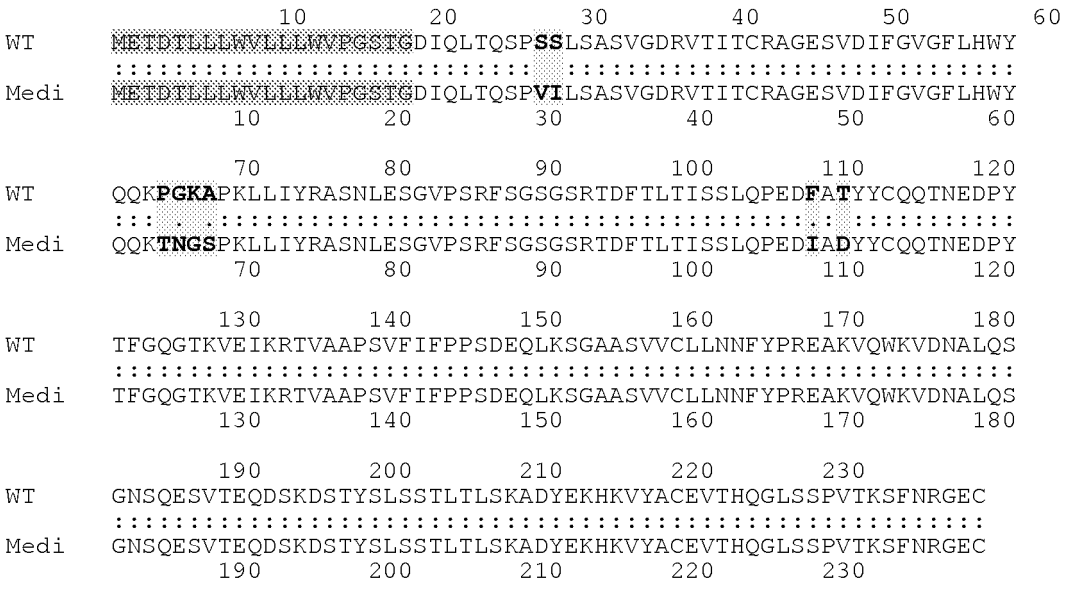

10 20 30 40 50 60
WT METDTLLLWVLLLWVPGSTGDIQLTQSPSSLSASVGDRVTITCRAGESVDIFGVGFLHWY
Medi METDTLLLWVLLLWVPGSTGDIQLTQSPVILSASVGDRVTITCRAGESVDIFGVGFLHWY
10 20 30 40 50 60
70 80 90 100 110 120
WT QQKPGKAPKLLIYRASNLESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQTNEDPY
Medi QQKTNGSPKLLIYRASNLESGVPSRFSGSGSRTDFTLTISSLQPEDIADYYCQQTNEDPY
70 80 90 100 110 120
130 140 150 160 170 180
WT TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGAASVVCLLNNFYPREAKVQWKVDNALQS
Medi TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGAASVVCLLNNFYPREAKVQWKVDNALQS
130 140 150 160 170 180
190 200 210 220 230
WT GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
Medi GNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
190 200 210 220 230

Figure 57

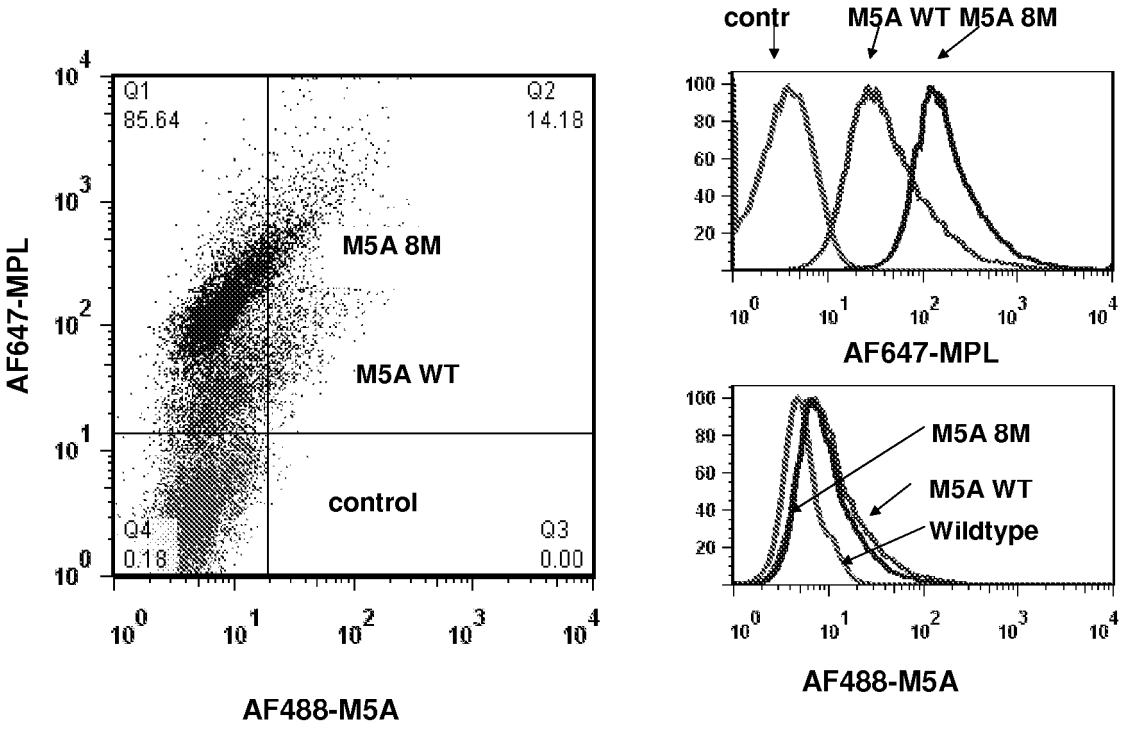

Q1
85.64
Q2
14.18
M5A 8M
M5A WT
control
Q4
0.18
Q3
0.00
AF647-MPL
AF488-M5A
contr
M5A WT
M5A 8M
AF647-MPL
M5A 8M
M5A WT
Wildtype
AF488-M5A

Figure 58

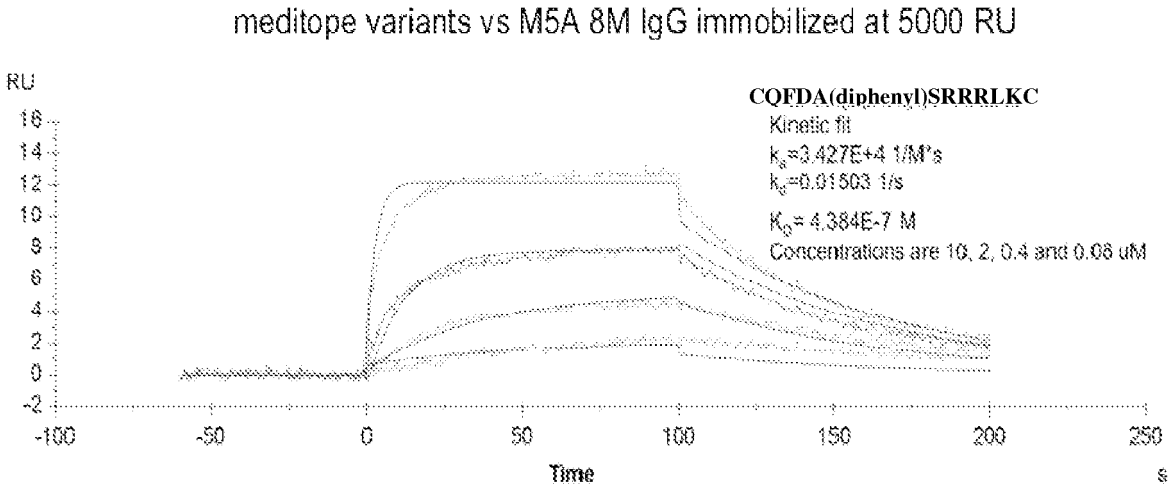
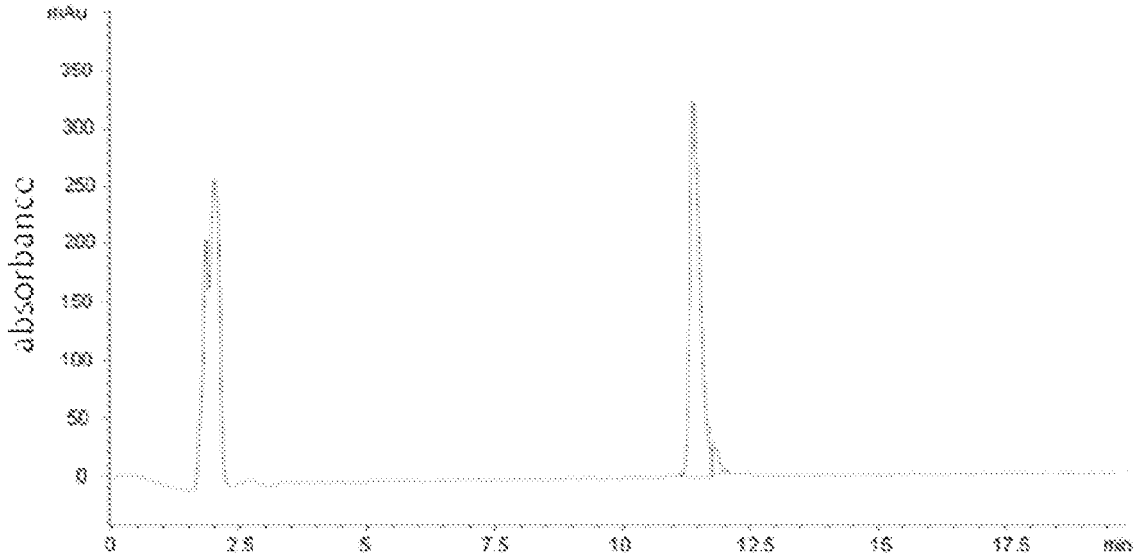

meditope variants vs M5A 8M IgG immobilized at 5000 RU
RU
16
14
12
10
8
6
4
2
0
-2
-100
-50
0
50
100
150
200
250
Time
s
CQFDA(diphenyl)SRRRLKC
Kinetic fit
k_a=3.427E+4 1/M*s
k_d=0.01503 1/s
K_D= 4.384E-7 M
Concentrations are 10, 2, 0.4 and 0.08 uM

Figure 59

HPLC



Mass Spectrum

$C_{66}H_{113}N_{19}O_{16}$, ESI-MS, calculated m/z 714.94 $[M+2H]^{2+}$, found 714.94 $[M+2H]^{2+}$.

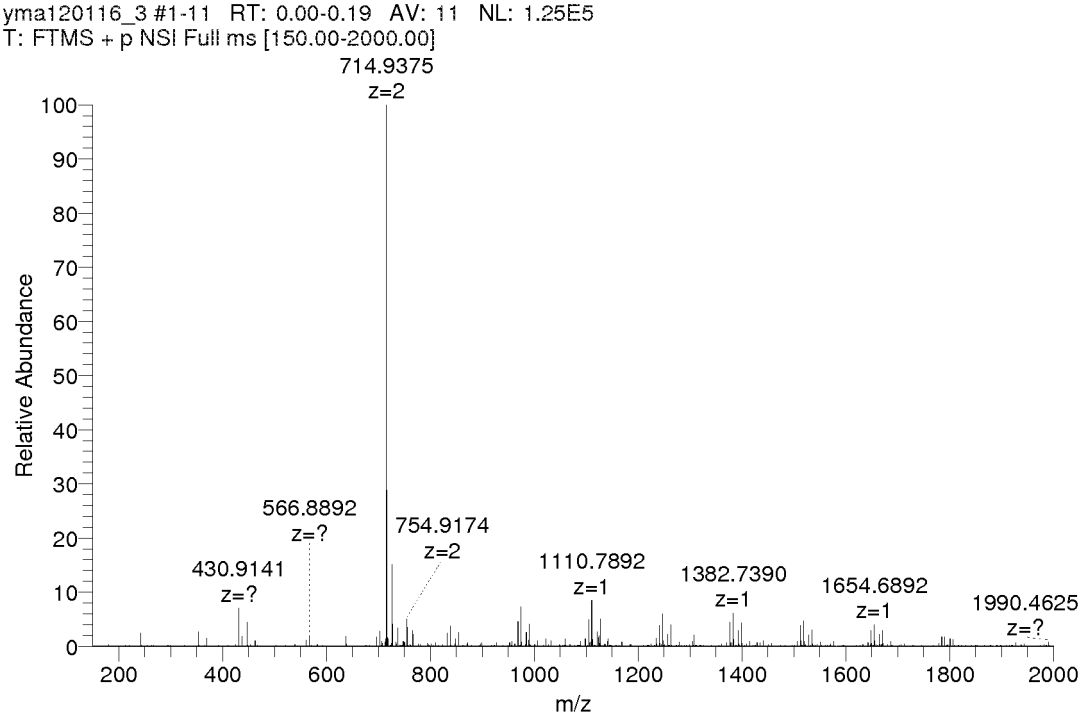


Figure 60

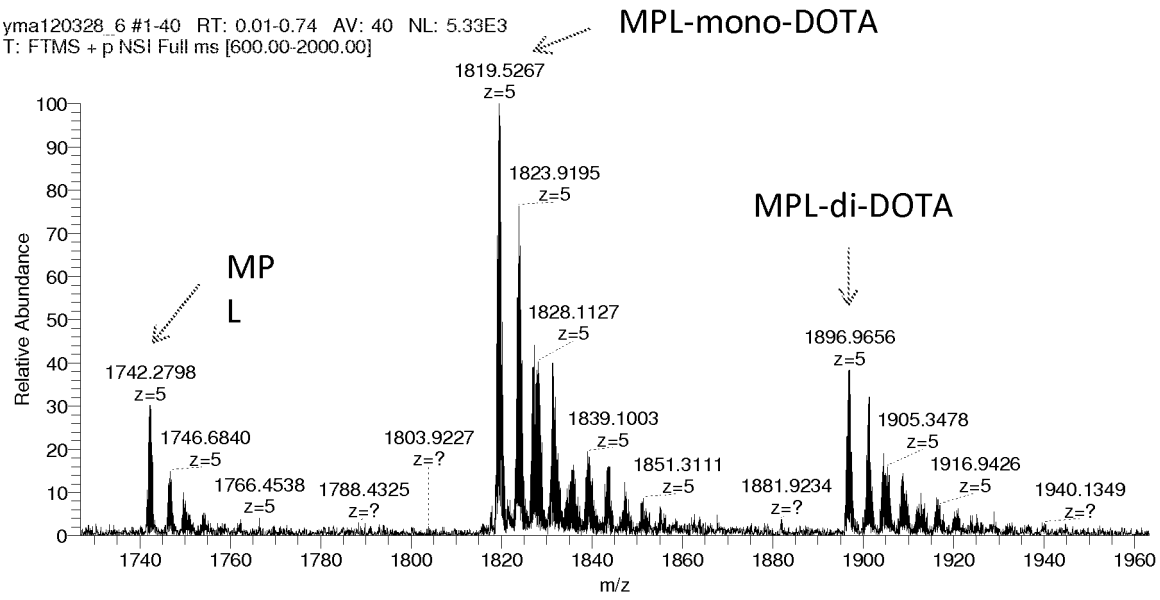
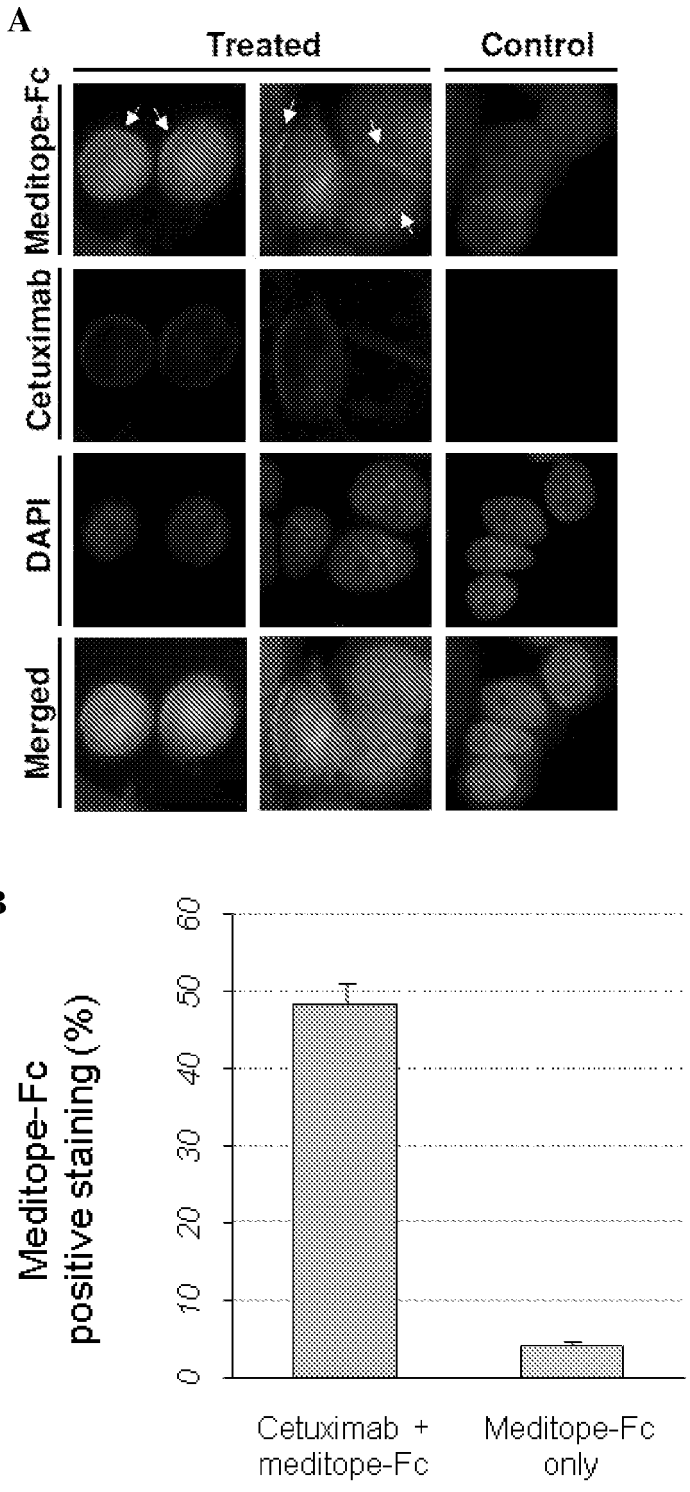

yma120328_6 #1-40 RT: 0.01-0.74 AV: 40 NL: 5.33E3
T: FTMS + p NSI Full ms [600.00-2000.00]
MPL-mono-DOTA
MPL-di-DOTA
MPL
1819.5267
z=5
1823.9195
z=5
1828.1127
z=5
1839.1003
z=5
1851.3111
z=5
1742.2798
z=5
1746.6840
z=5
1766.4538
z=5
1788.4325
z=?
1803.9227
z=?
1881.9234
z=?
1896.9656
z=5
1905.3478
z=5
1916.9426
z=5
1940.1349
z=?
Relative Abundance
m/z

Figure 61


A
Treated
Control
Meditope-Fc
Cetuximab
DAPI
Merged
B
Meditope-Fc positive staining (%)
0
10
20
30
40
50
60
Cetuximab + meditope-Fc
Meditope-Fc only