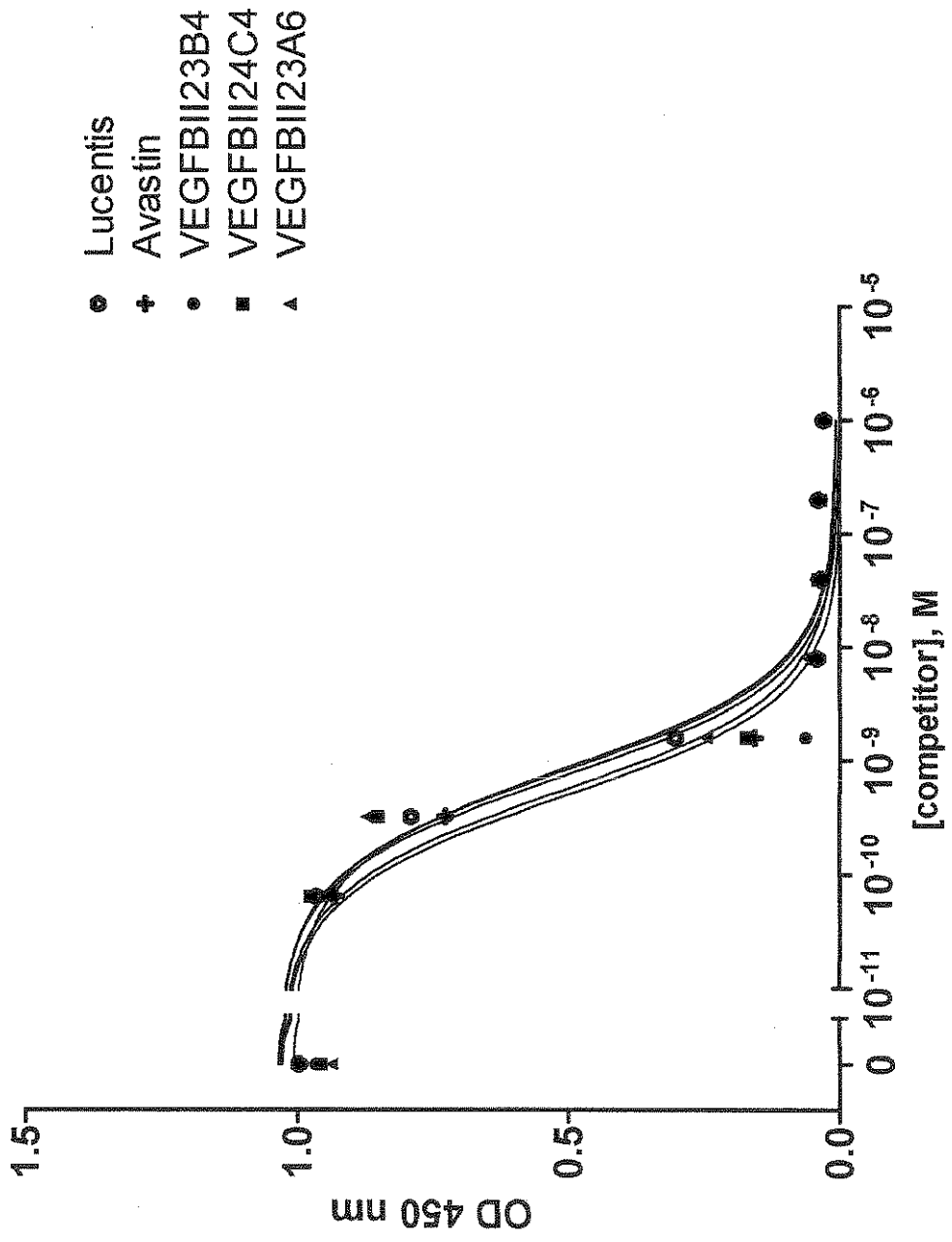
Figure 1


Lucentis
Avastin
VEGFBII23B4
VEGFBII24C4
VEGFBII23A6
OD 450 nm
1.5
1.0
0.5
0.0
0
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[competitor], M

2 / 125

**Figure 2**

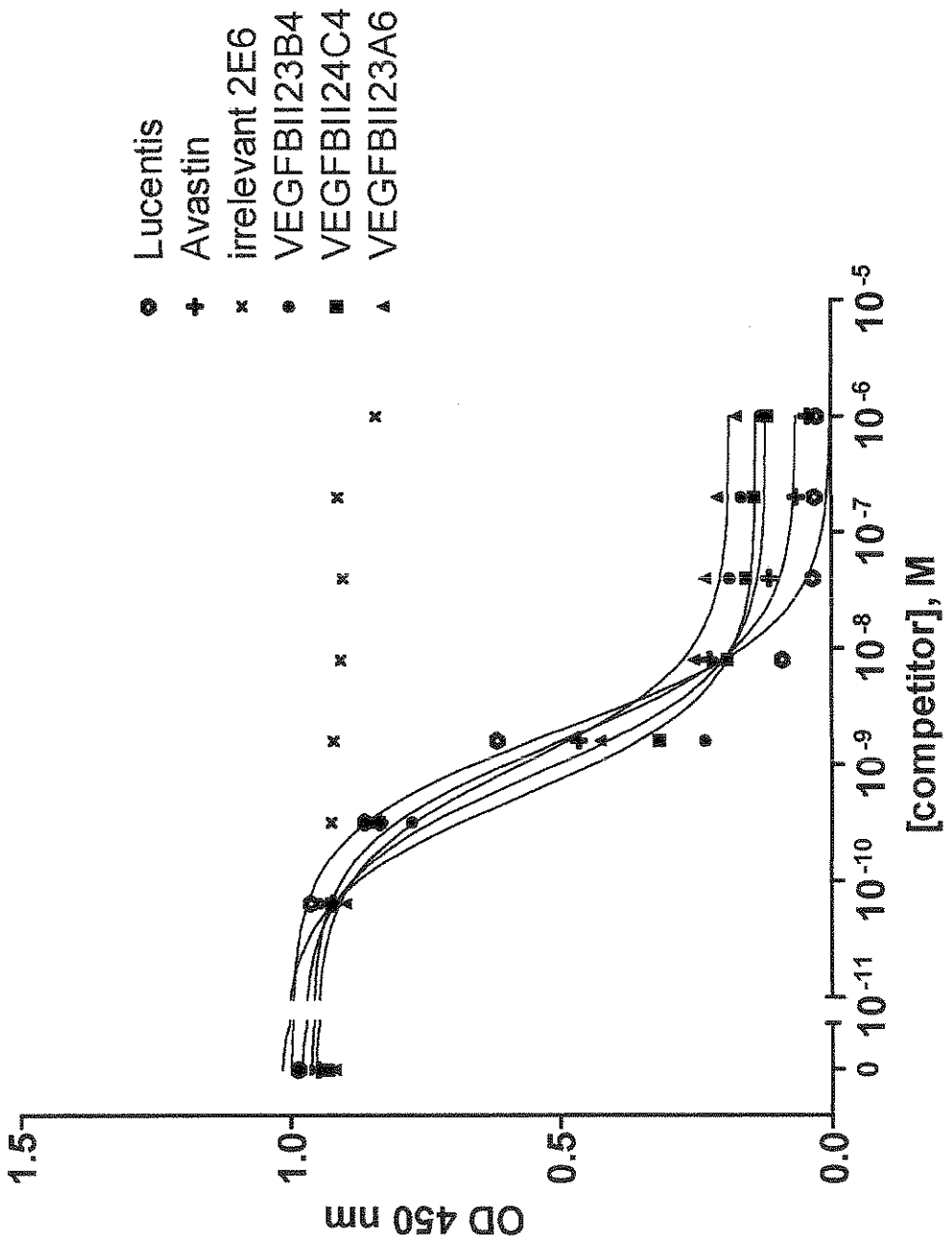


Figure 3

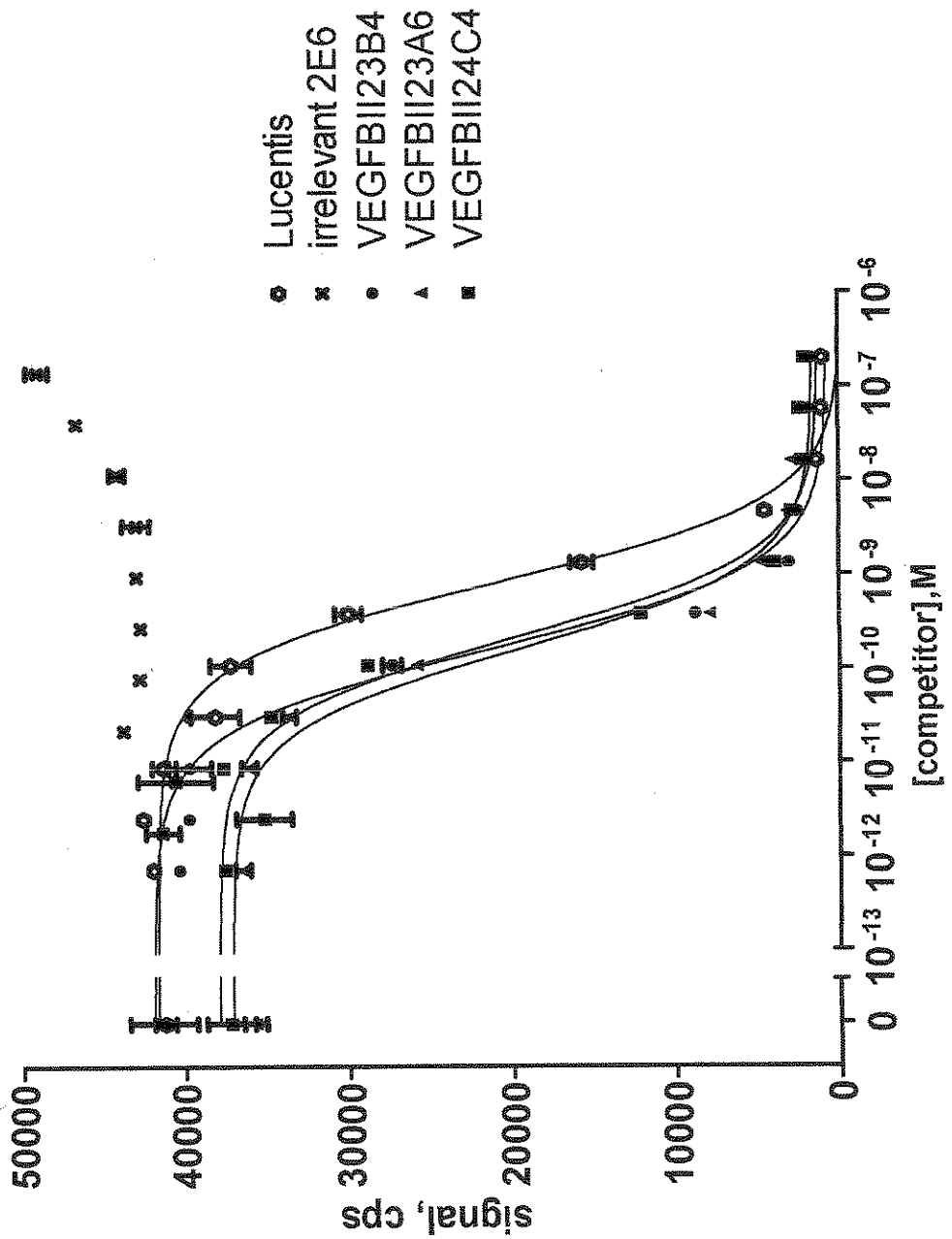
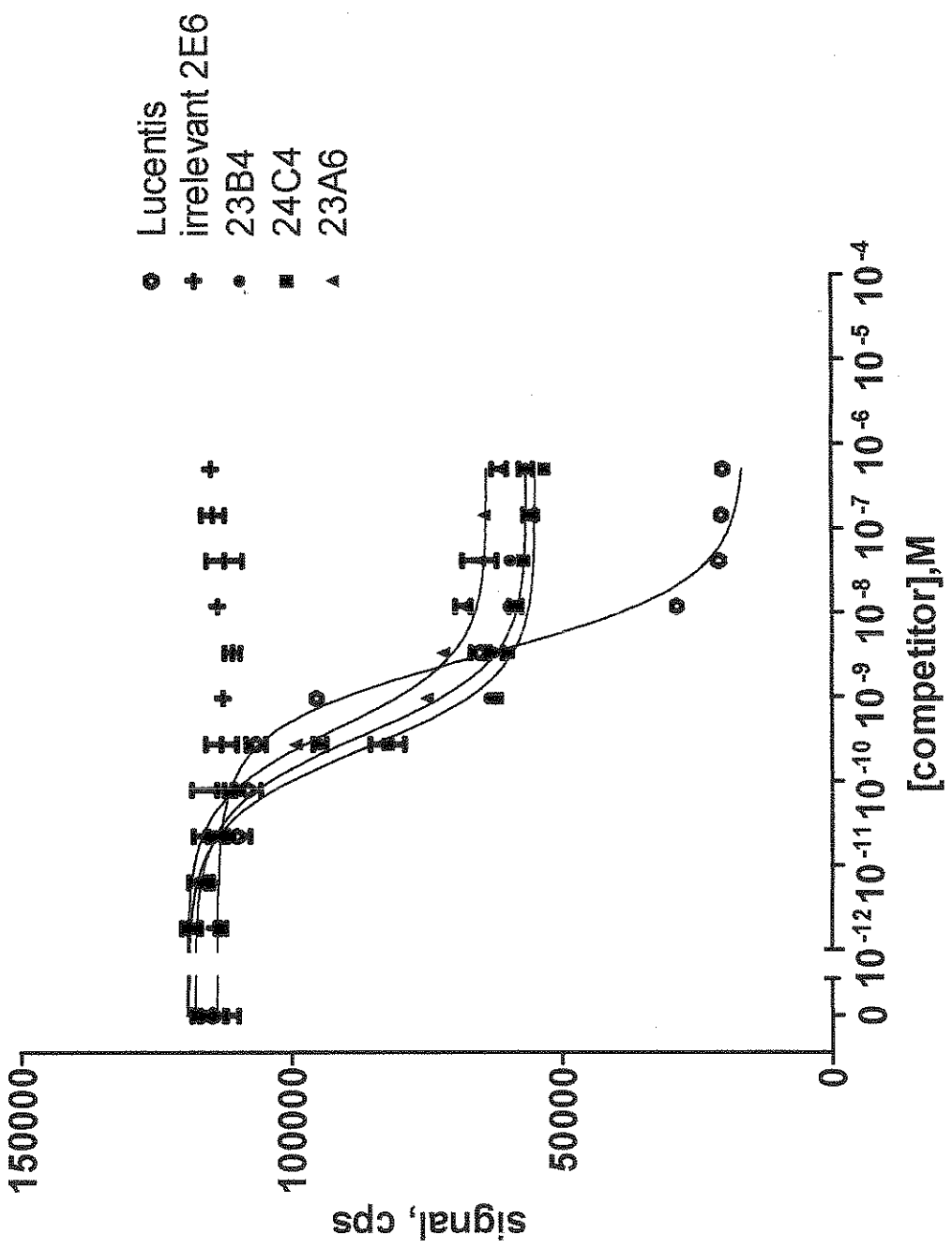

Lucentis
irrelevant 2E6
VEGFBII23B4
VEGFBII23A6
VEGFBII24C4
signal, cps
50000
40000
30000
20000
10000
0
0 10-13 10-12 10-11 10-10 10-9 10-8 10-7 10-6
[competitor],M

Figure 4


Lucentis
irrelevant 2E6
23B4
24C4
23A6
signal, cps
150000
100000
50000
0
0 10-12 10-11 10-10 10-9 10-8 10-7 10-6 10-5 10-4
[competitor],M

5 / 125

**Figure 5**

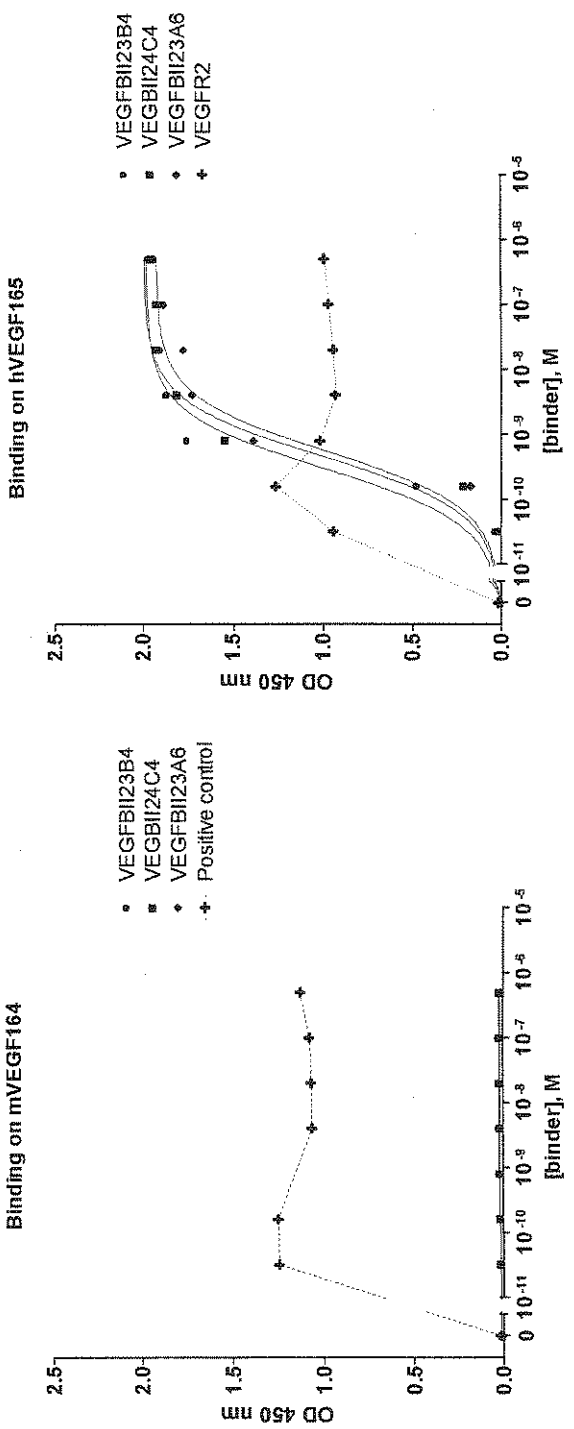


Figure 6

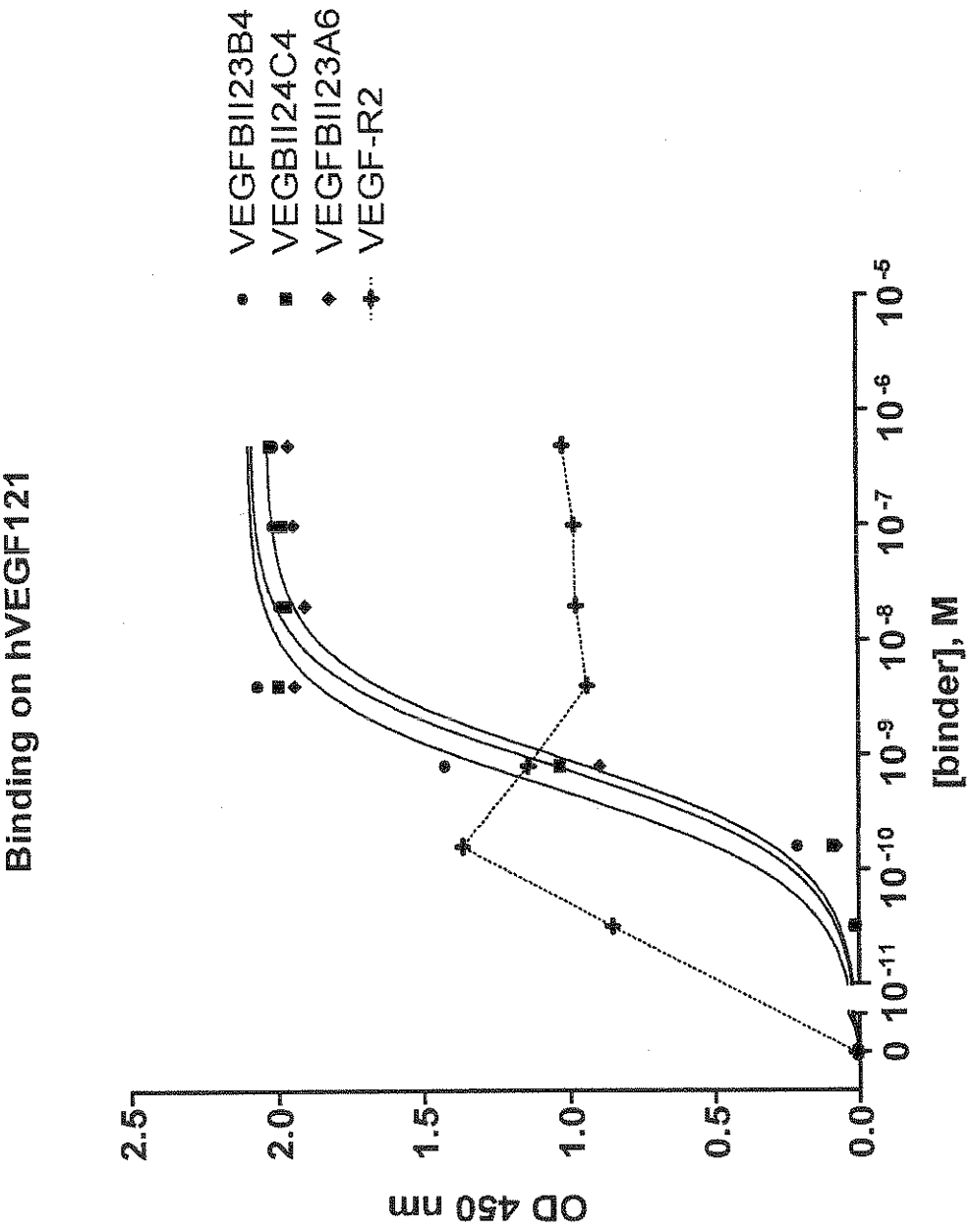

Binding on hVEGF121
VEGFBII23B4
VEGBII24C4
VEGFBII23A6
VEGF-R2
OD 450 nm
0.0
0.5
1.0
1.5
2.0
2.5
0
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[binder], M

**Figure 7**

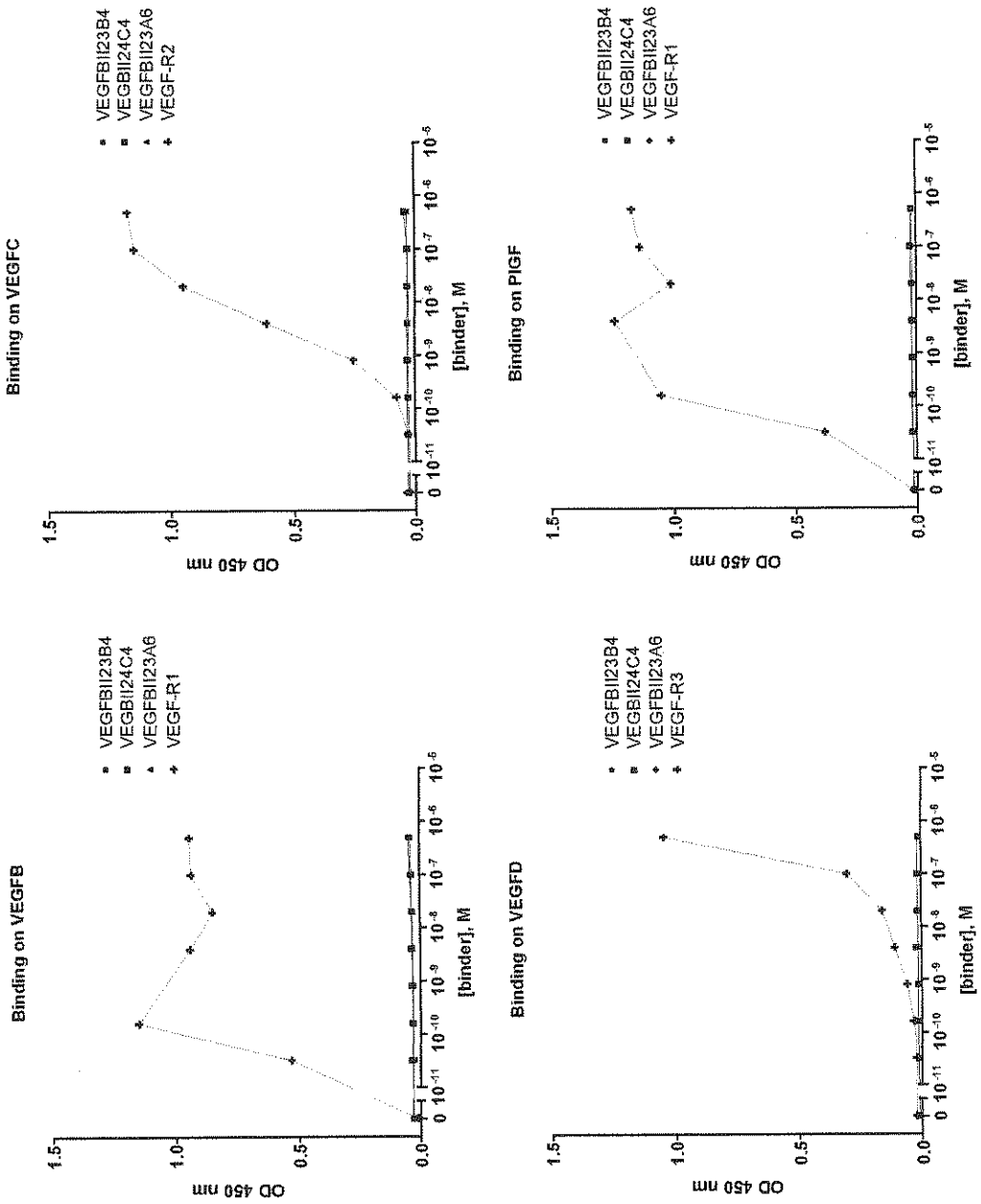

Binding on VEGFC
VEGFBII23B4
VEGBII24C4
VEGFBII23A6
VEGF-R2
OD 450 nm
[binder], M
Binding on PlGF
VEGFBII23B4
VEGBII24C4
VEGFBII23A6
VEGF-R1
OD 450 nm
[binder], M
Binding on VEGFB
VEGFBII23B4
VEGBII24C4
VEGFBII23A6
VEGF-R1
OD 450 nm
[binder], M
Binding on VEGFD
VEGFBII23B4
VEGBII24C4
VEGFBII23A6
VEGF-R3
OD 450 nm
[binder], M

**Figure 8**

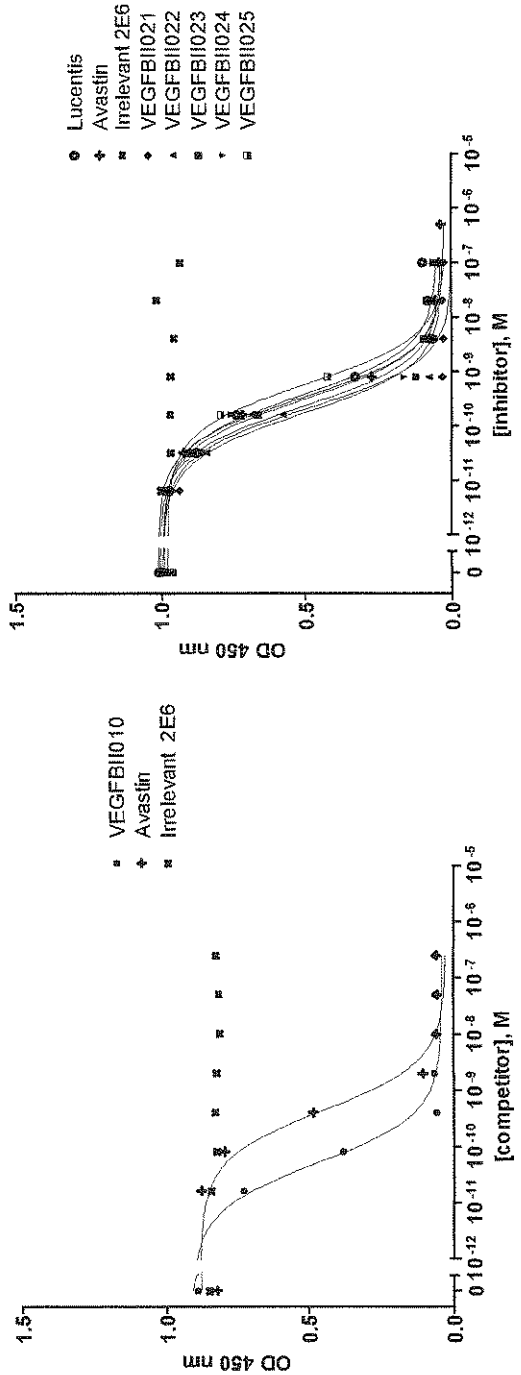
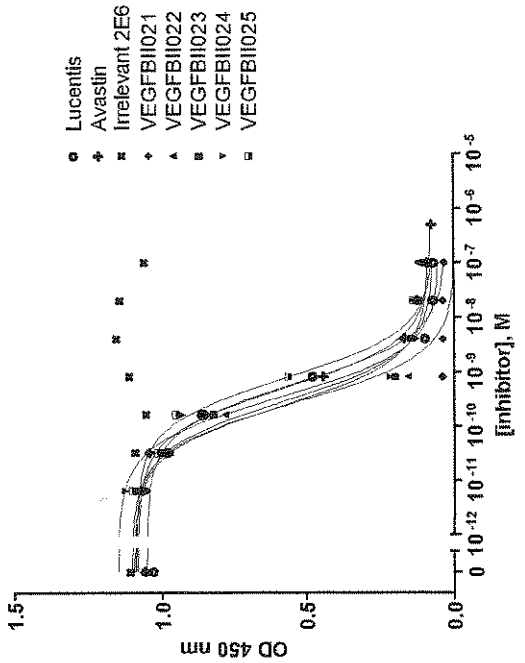

Lucentis
Avastin
Irrelevant 2E6
VEGFBII021
VEGFBII022
VEGFBII023
VEGFBII024
VEGFBII025
OD 450 nm
[inhibitor], M
VEGFBII010
Avastin
Irrelevant 2E6
OD 450 nm
[competitor], M

**Figure 9**


Lucentis
Avastin
Irrelevant 2E6
VEGFBII021
VEGFBII022
VEGFBII023
VEGFBII024
VEGFBII025
OD 450 nm
[inhibitor], M

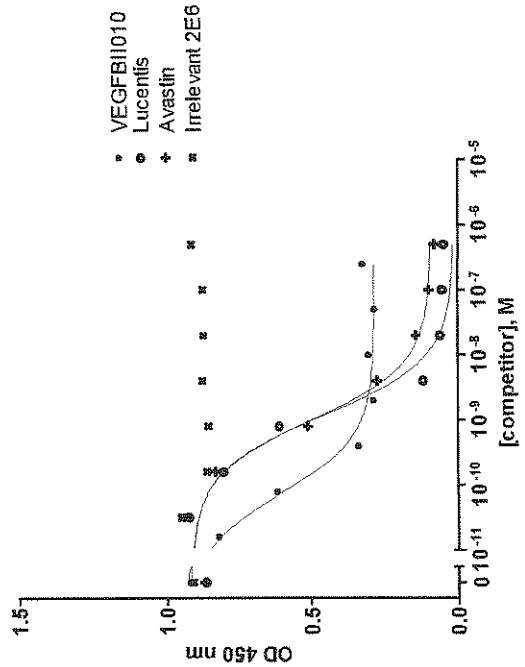
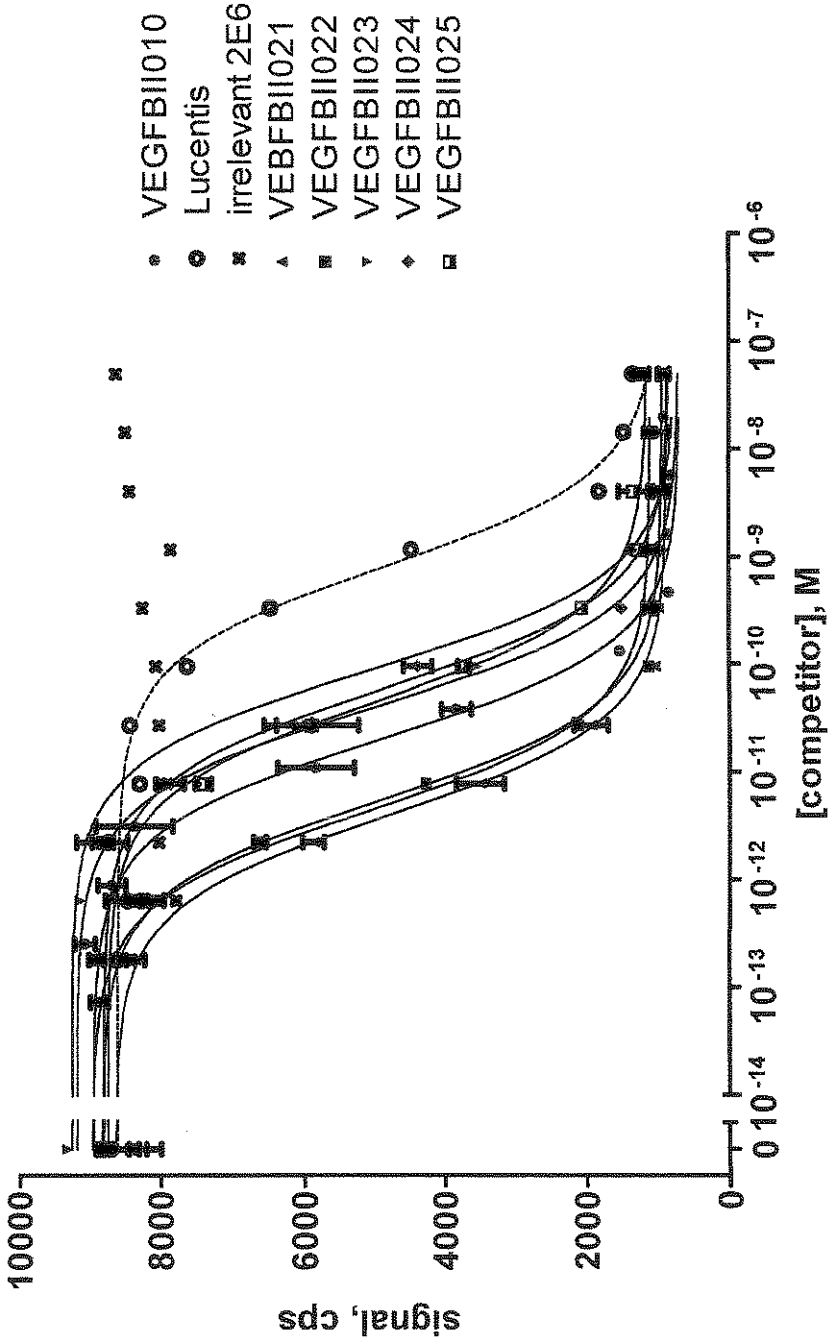

VEGFBII010
Lucentis
Avastin
Irrelevant 2E6
OD 450 nm
[competitor], M

Figure 10


VEGFBII010
Lucentis
irrelevant 2E6
VEBFBII021
VEGFBII022
VEGFBII023
VEGFBII024
VEGFBII025
signal, cps
10000
8000
6000
4000
2000
0
0 10-14 10-13 10-12 10-11 10-10 10-9 10-8 10-7 10-6
[competitor], M

11 / 125

Figure 11

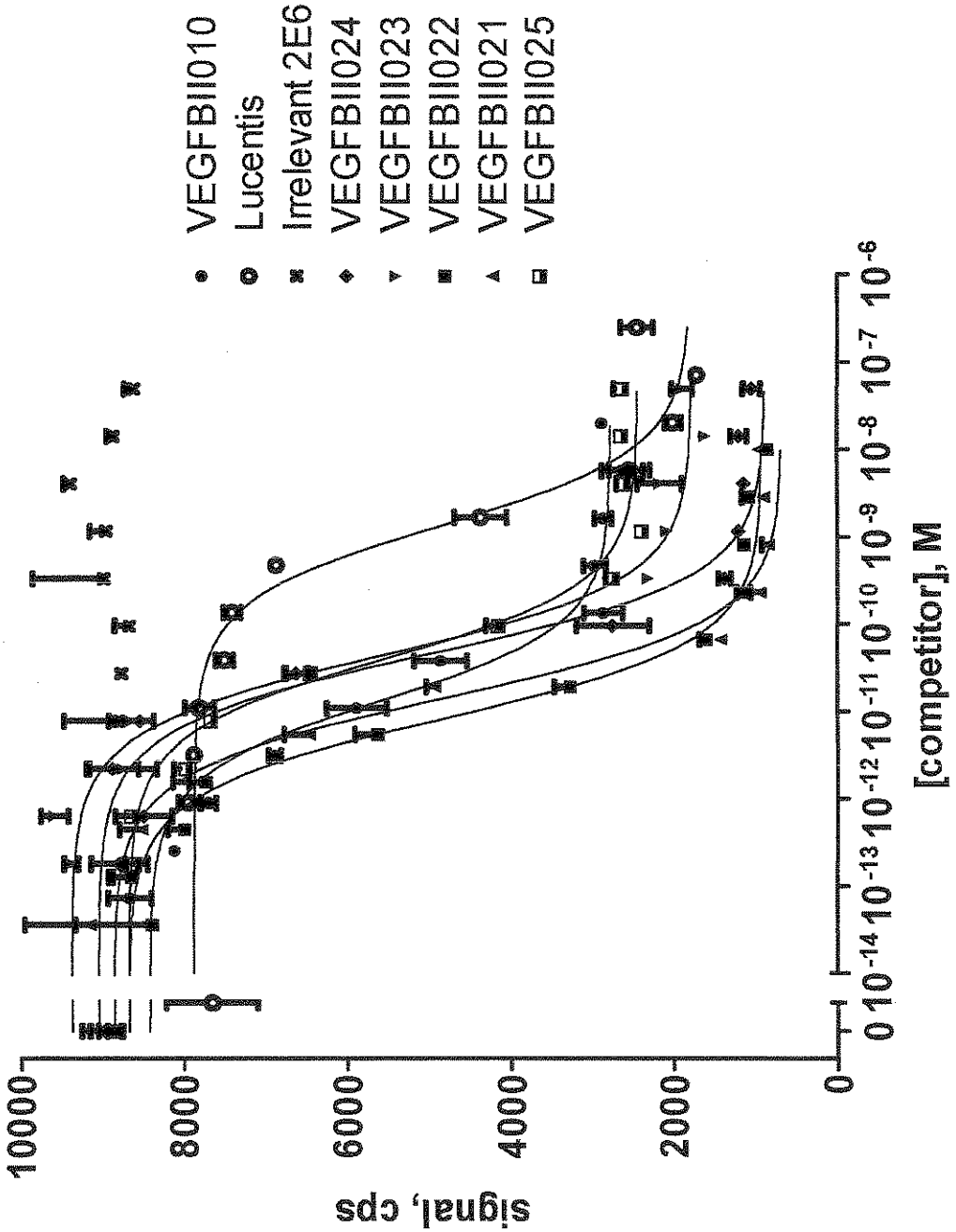


Figure 12

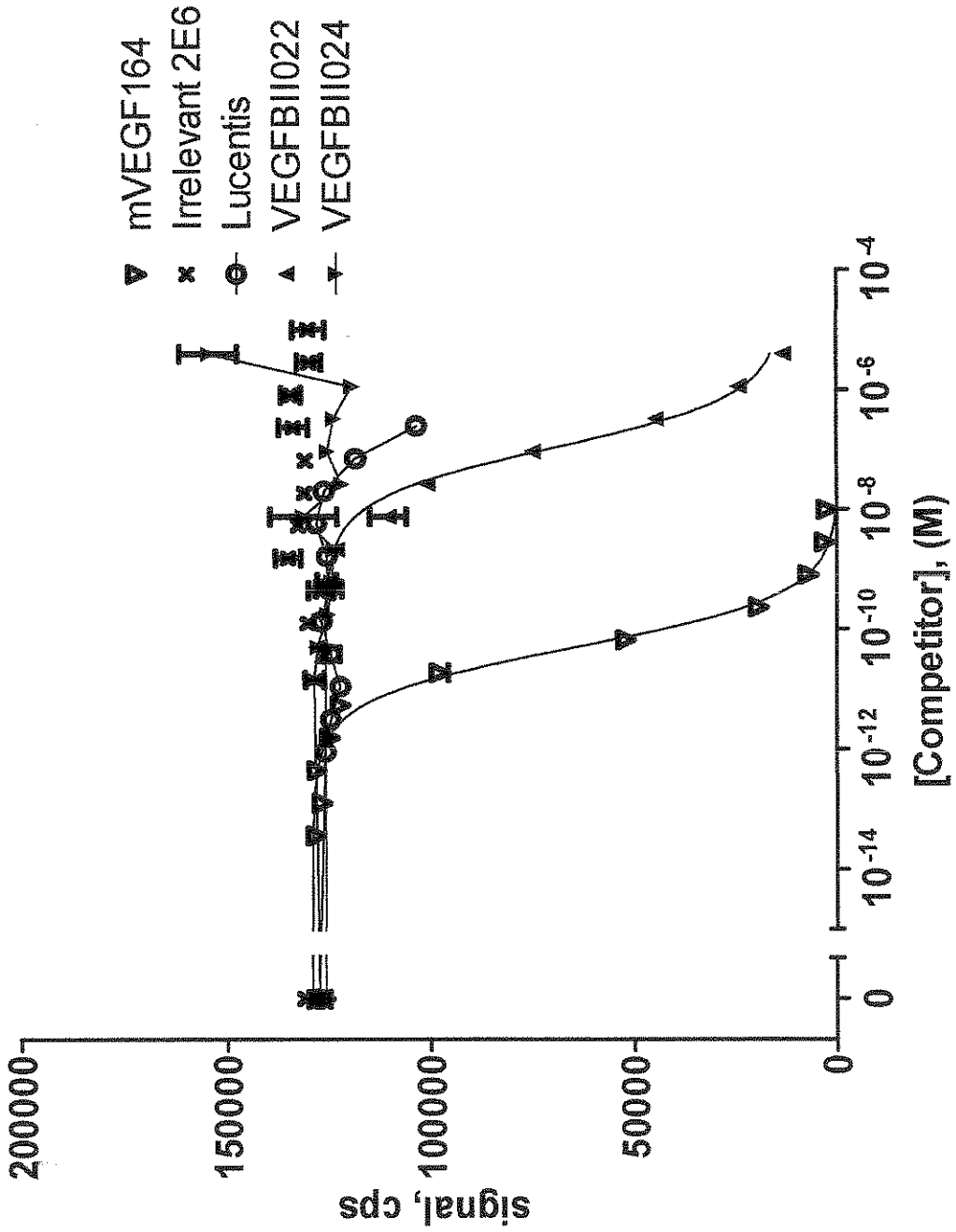
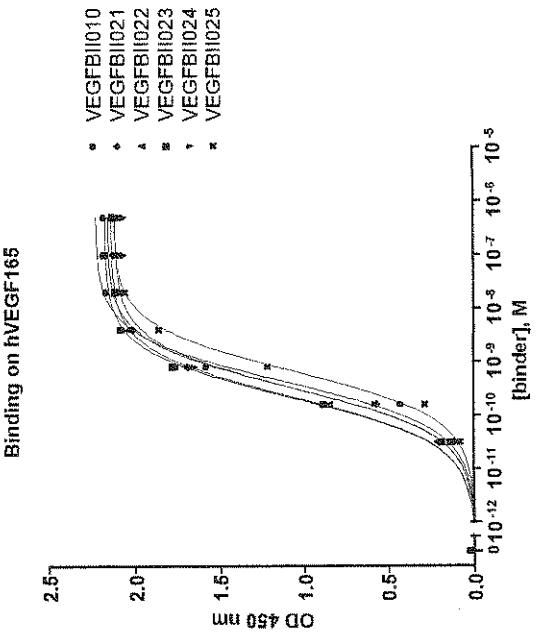

mVEGF164
Irrelevant 2E6
Lucentis
VEGFBII022
VEGFBII024
signal, cps
200000
150000
100000
50000
0
0
10-14
10-12
10-10
10-8
10-6
10-4
[Competitor], (M)

**Figure 13**


Binding on hVEGF165
VEGFBII010
VEGFBII021
VEGFBII022
VEGFBII023
VEGFBII024
VEGFBII025
OD 450 nm
[binder], M

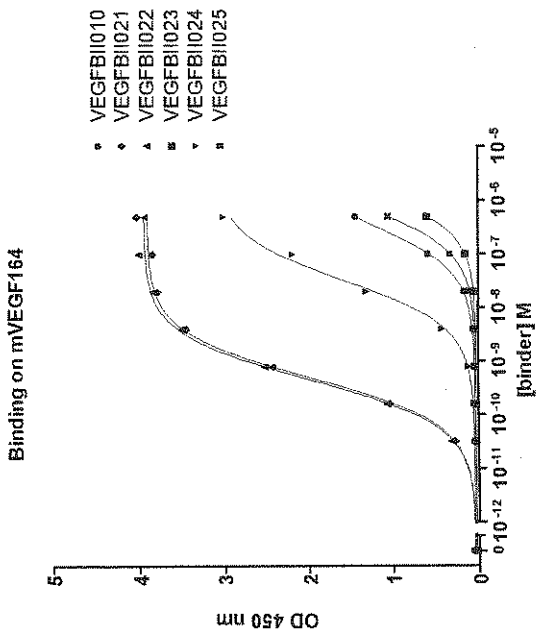

Binding on mVEGF164
VEGFBII010
VEGFBII021
VEGFBII022
VEGFBII023
VEGFBII024
VEGFBII025
OD 450 nm
[binder] M

Figure 14-1

A

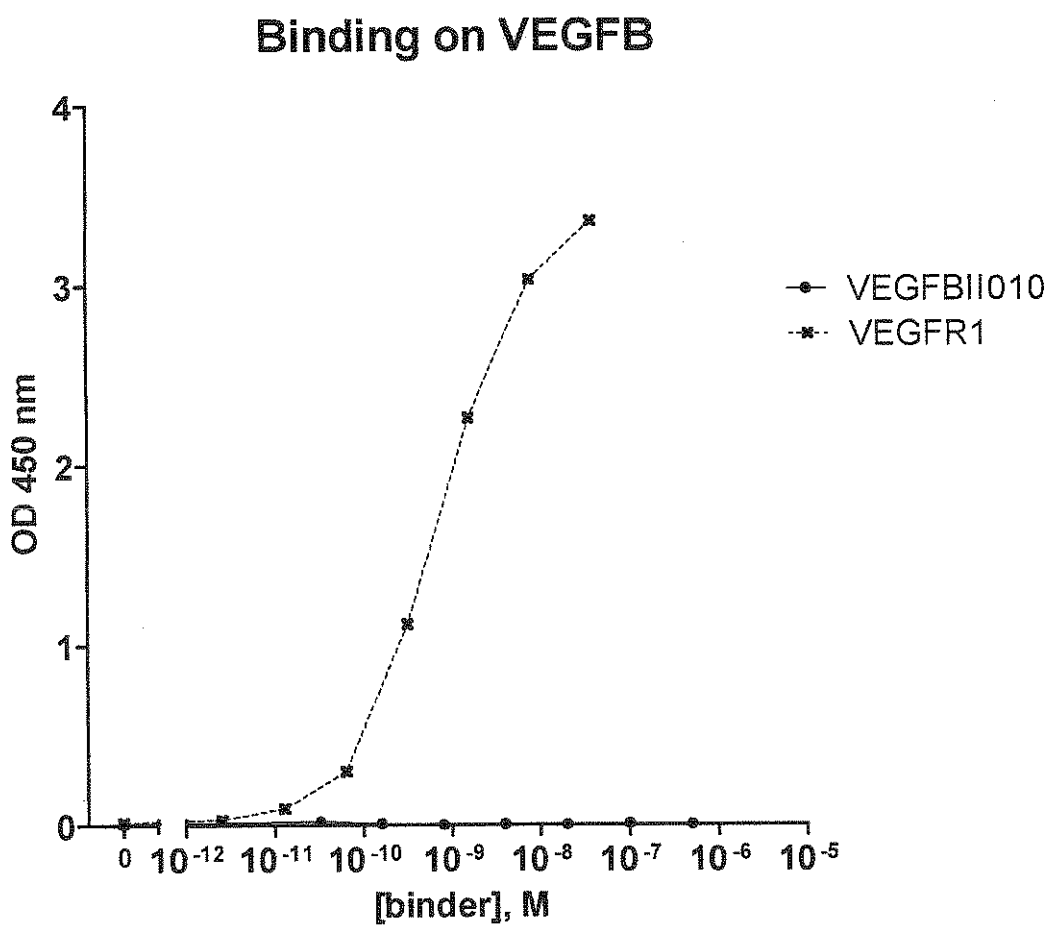

Binding on VEGFB
OD 450 nm
4
3
2
1
0
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[binder], M
VEGFBII010
VEGFR1

Figure 14-2

B

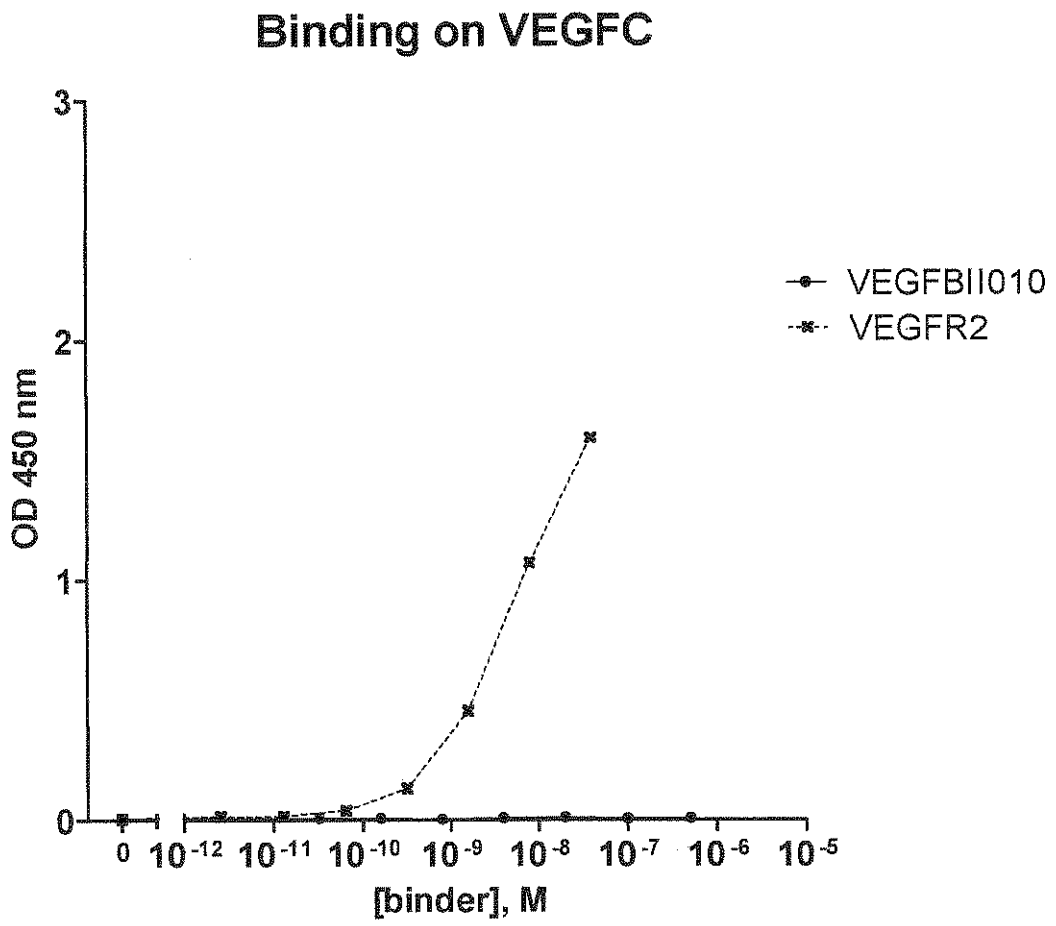

Binding on VEGFC
OD 450 nm
3
2
1
0
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[binder], M
VEGFBII010
VEGFR2

Figure 14-3

C

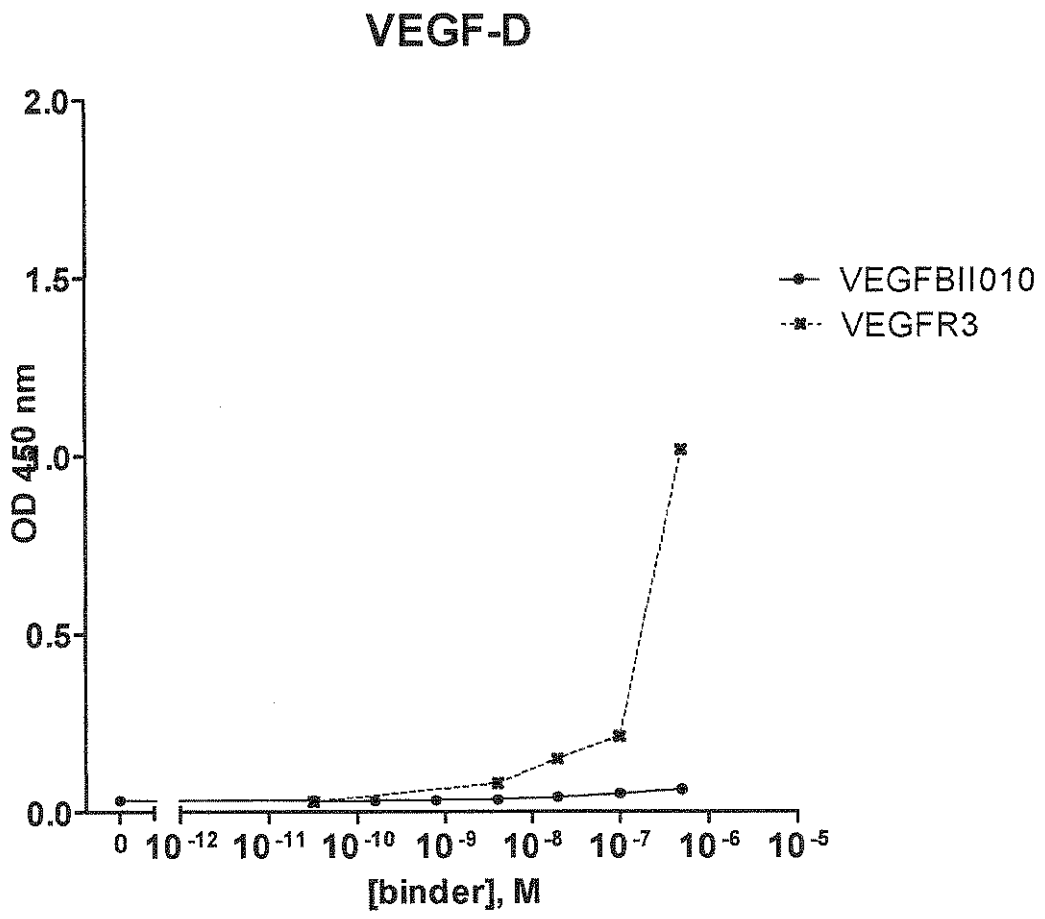

VEGF-D
2.0
1.5
1.0
0.5
0.0
OD 450 nm
VEGFBII010
VEGFR3
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[binder], M

Figure 14-4

D

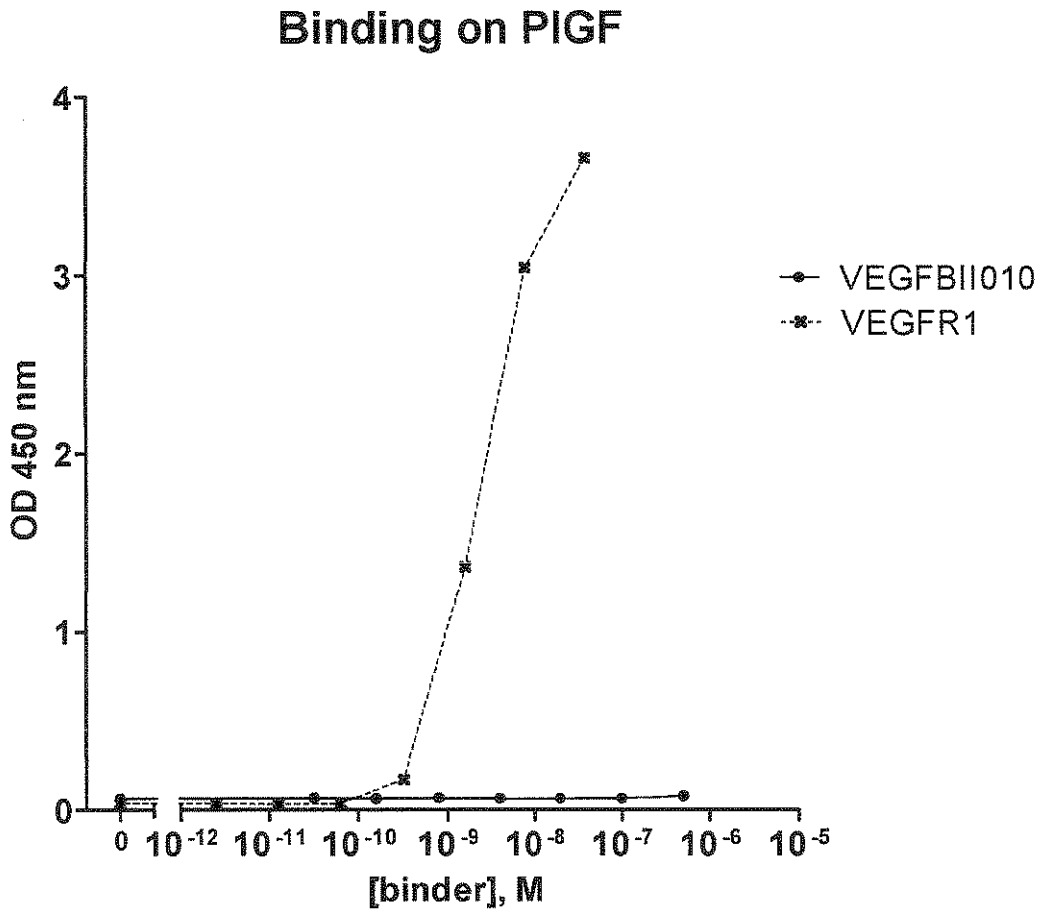

Binding on PlGF
OD 450 nm
0
1
2
3
4
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[binder], M
VEGFBII010
VEGFR1

Figure 14-5

E

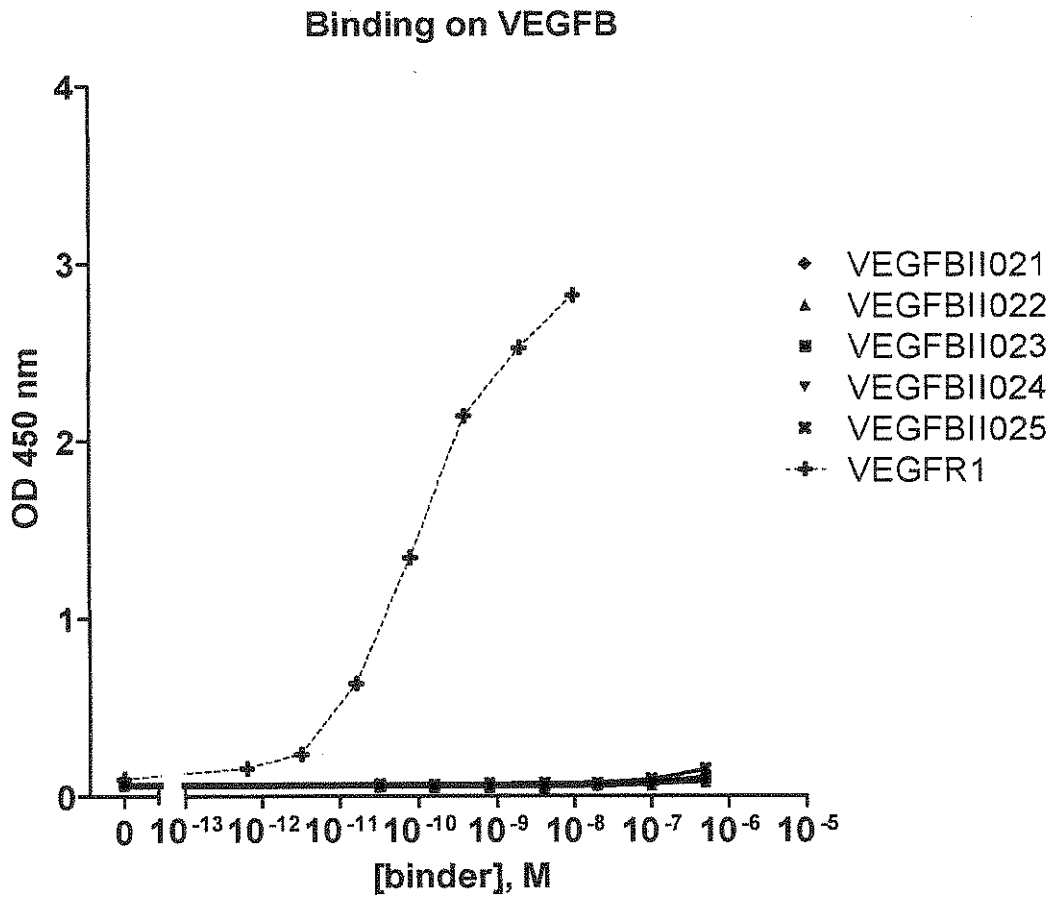

Binding on VEGFB
OD 450 nm
4
3
2
1
0
0 10-13 10-12 10-11 10-10 10-9 10-8 10-7 10-6 10-5
[binder], M
VEGFBII021
VEGFBII022
VEGFBII023
VEGFBII024
VEGFBII025
VEGFR1

Figure 14-6

F

Binding on VEGFC

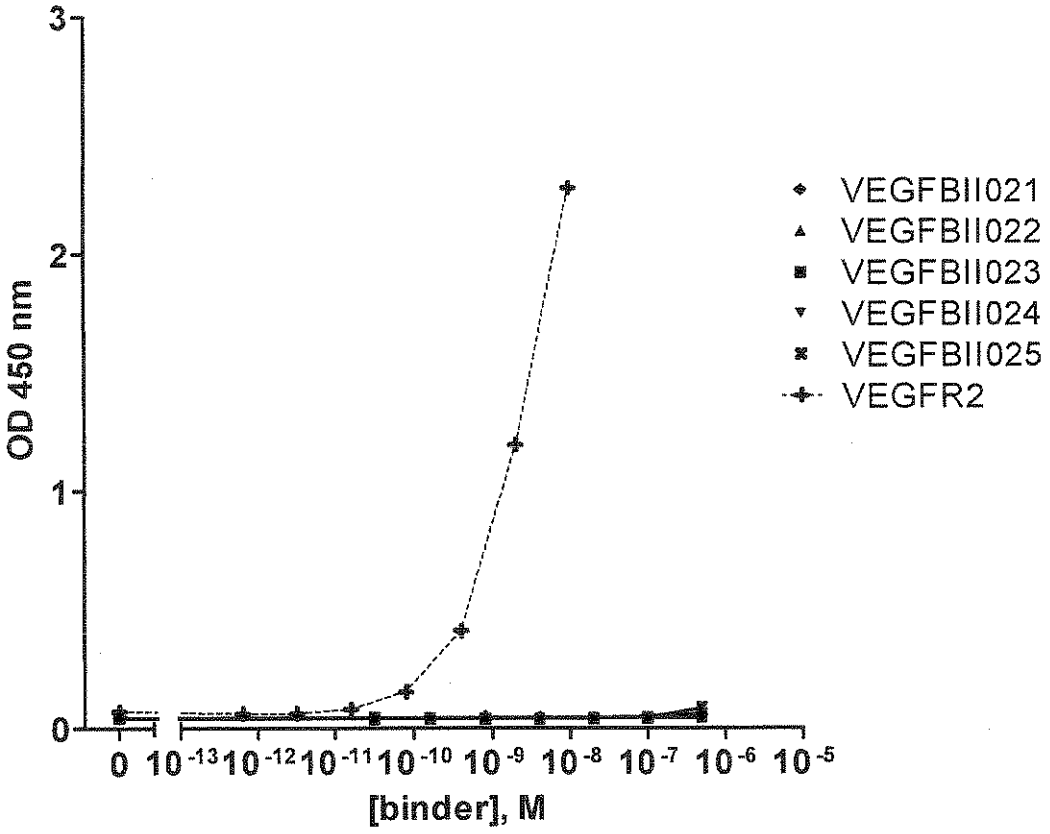


Figure 14-7

G

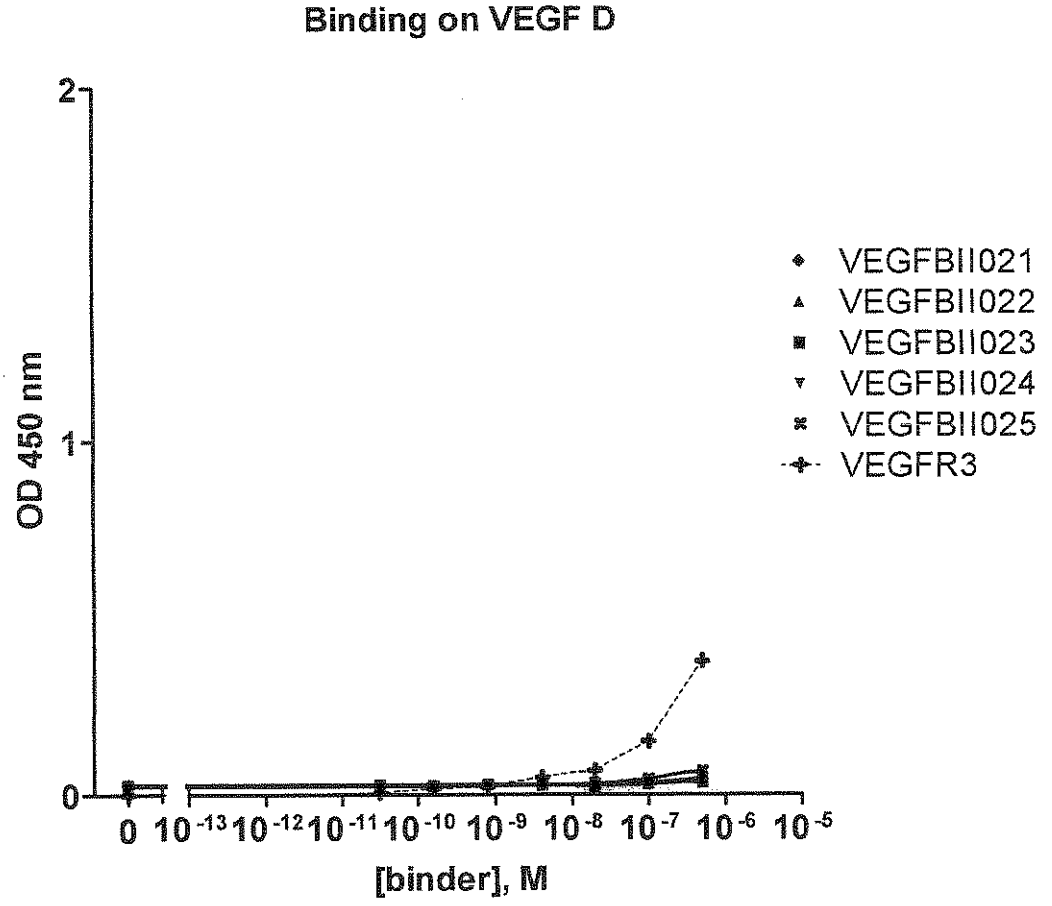

Binding on VEGF D
OD 450 nm
2
1
0
0 10-13 10-12 10-11 10-10 10-9 10-8 10-7 10-6 10-5
[binder], M
VEGFBII021
VEGFBII022
VEGFBII023
VEGFBII024
VEGFBII025
VEGFR3

Figure 14-8

H

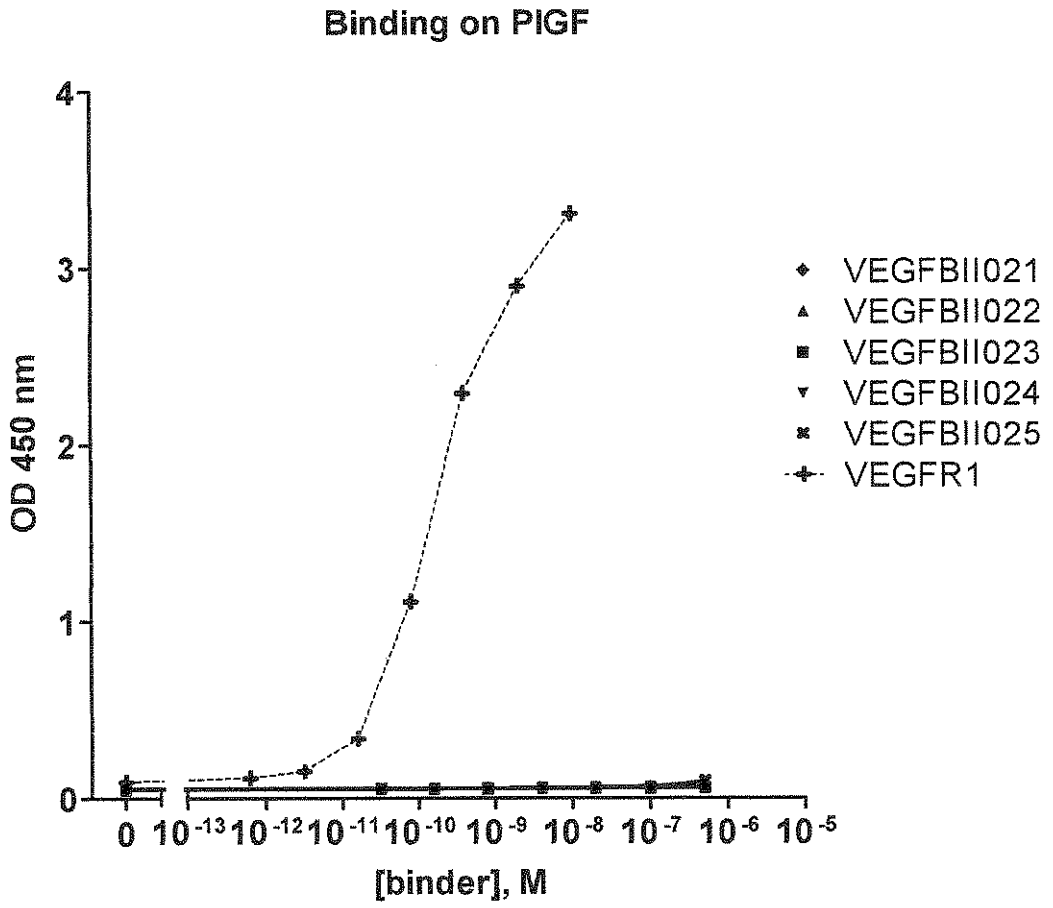

Binding on PlGF
OD 450 nm
4
3
2
1
0
0 10-13 10-12 10-11 10-10 10-9 10-8 10-7 10-6 10-5
[binder], M
VEGFBII021
VEGFBII022
VEGFBII023
VEGFBII024
VEGFBII025
VEGFR1

Figure 15

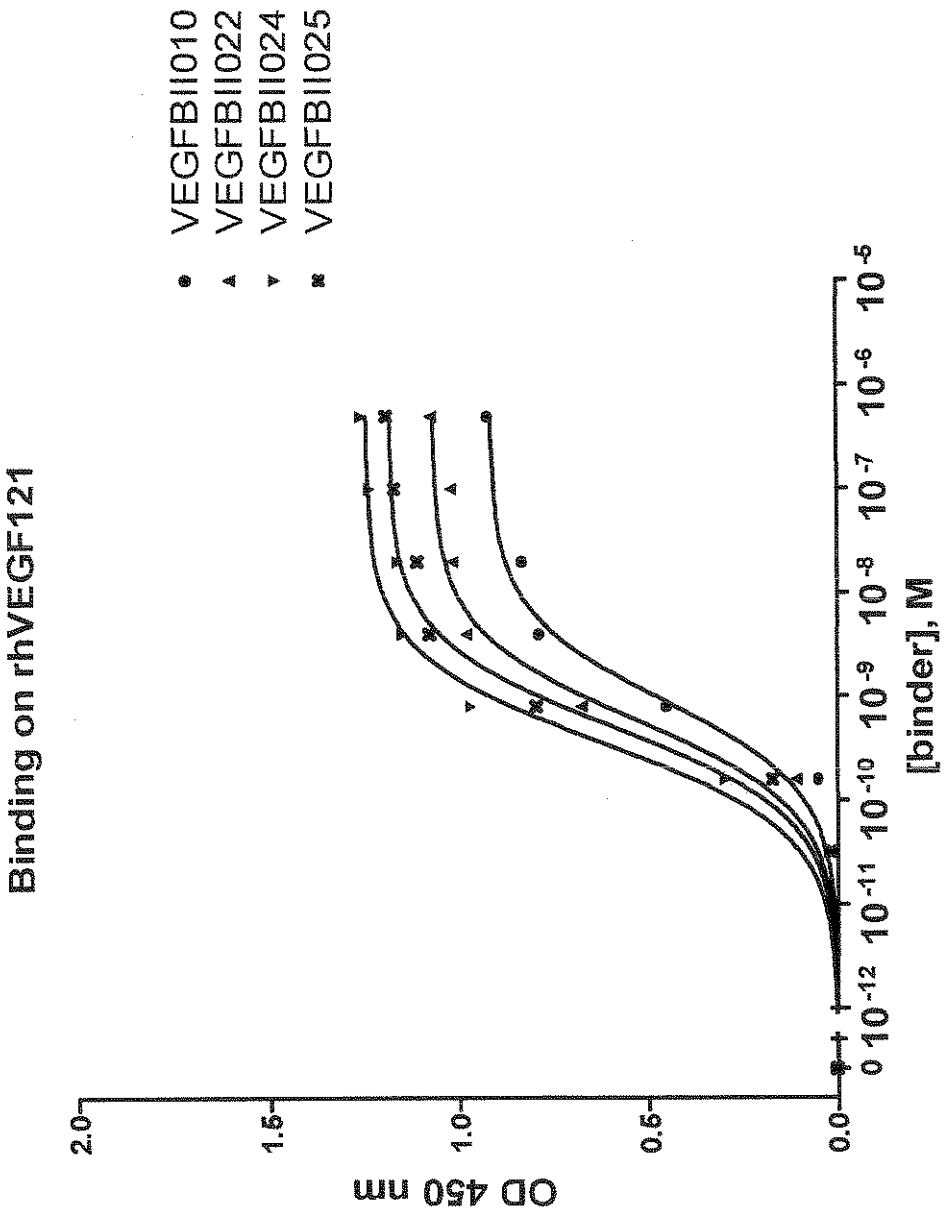

Binding on rhVEGF121
VEGFBII010
VEGFBII022
VEGFBII024
VEGFBII025
OD 450 nm
2.0
1.5
1.0
0.5
0.0
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[binder], M

Figure 16

```
                10        20        30        40
                |.........|.........|.........|.........|
Kabat#      :   .........|.........|.........|.........|
VH3-23/JH5  :   EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQA
VEGFBII23B04 :  ...............T.D.......EV..R.....S.G.F...

                50        60        70        80
                |.........|.........|.........|.........|
Kabat#      :   .........|..a......|.........|.........|
VH3-23/JH5  :   PGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYL
VEGFBII23B04 :  Q..ER.F.V....-K..YK.DSV.LE.......K..A...V..

                90        100       110
                |.........|.........|abcdefghi.........|....
Kabat#      :   ..abc.....|.........|.........|.........|....
VH3-23/JH5  :   QMNSLRAEDTAVYYCAK----------WGQGTLVTVSS
VEGFBII23B04 :  .I...KP.........SSRAYGSSRLRLADTYEY.....Q.....
```

Figure 17

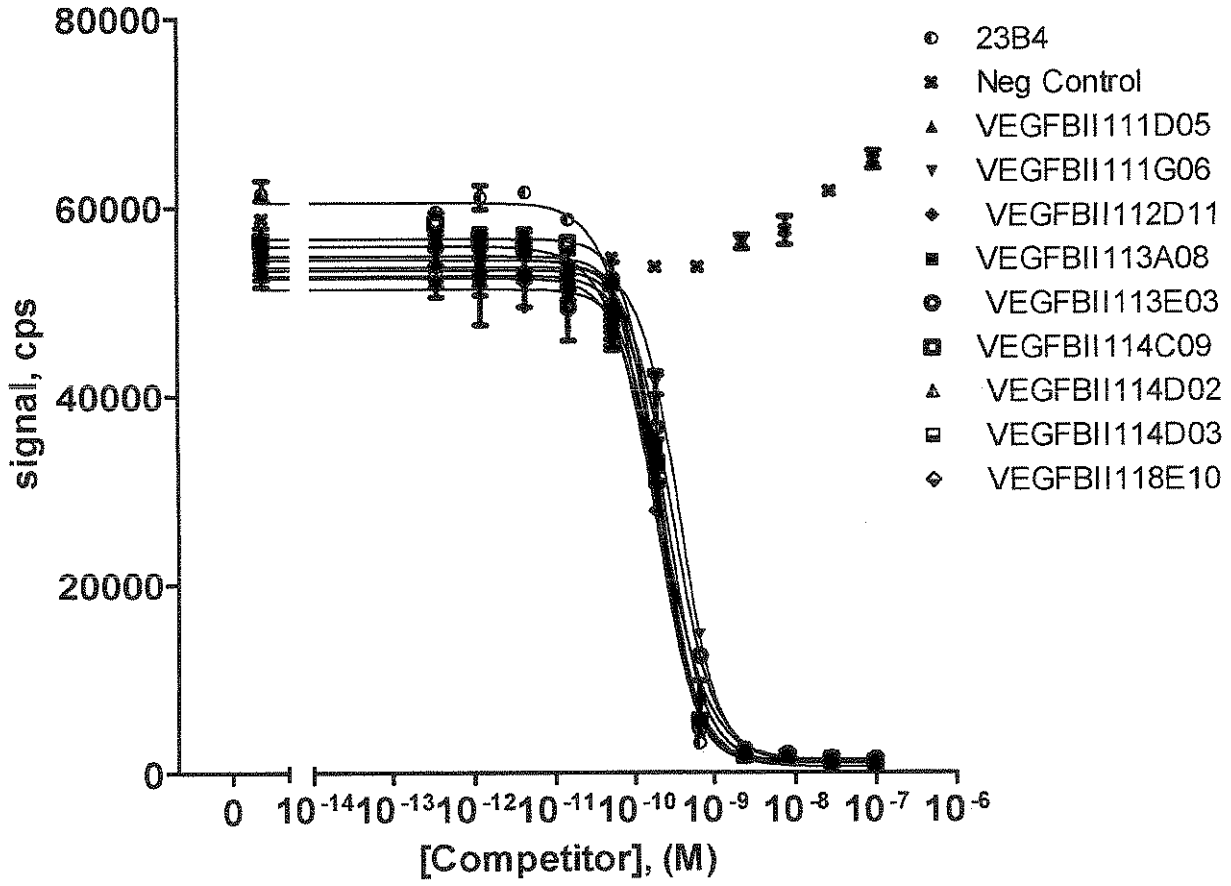

80000
60000
40000
20000
0
signal, cps
0
10-14
10-13
10-12
10-11
10-10
10-9
10-8
10-7
10-6
[Competitor], (M)
23B4
Neg Control
VEGFBII111D05
VEGFBII111G06
VEGFBII112D11
VEGFBII113A08
VEGFBII113E03
VEGFBII114C09
VEGFBII114D02
VEGFBII114D03
VEGFBII118E10

**Figure 18**

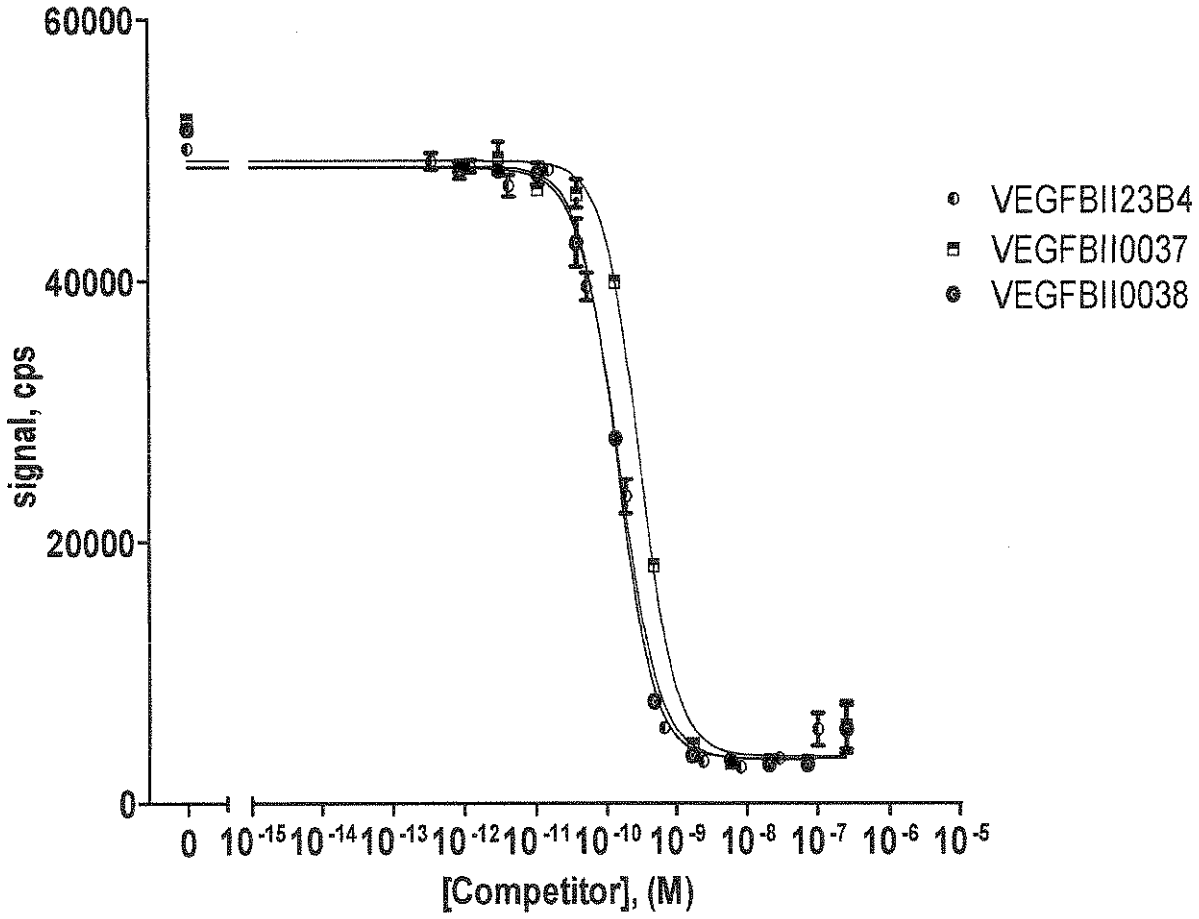

60000
40000
20000
0
signal, cps
0 10-15 10-14 10-13 10-12 10-11 10-10 10-9 10-8 10-7 10-6 10-5
[Competitor], (M)
VEGFBII23B4
VEGFBII0037
VEGFBII0038

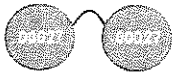
Figure 19

```
                10        20        30        40
Kabat#     : ..........|..........|..........|..........|
VH3-23/JH5 : EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQA
PVEGFBIIPMP5B5 : ..............V...IR.MSM.--.Y....

                50        60        70        80
Kabat#     : ..........|..a.....|..........|..........|
VH3-23/JH5 : PGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYL
PVEGFBIIPMP5B5 : ...HR.L.AR..-....T.A.V.....................V..

                90        101       110
Kabat#     : ..abc.....|..........|..........|...
VH3-23/JH5 : QMNSLRAEDTAVYYCAK----------WGQGTLVTVSS
PVEGFBIIPMP5B5 : .....KA.........NTFSSRPNP..A..Q.....
```

**Figure 20**

| VHH ID | Format | Description |
|---|---|---|
| ANGBII00001 |  | 1D01-9gs-1D01 |
| ANGBII00002 |  | 1D01-40gs-1D01 |
| ANGBII00003 |  | 11B07-9gs-11B07 |
| ANGBII00004 |  | 00027-9gs-00027 |
| ANGBII00005 |  | 00027-40gs-00027 |
| ANGBII00006 |  | 00908-9gs-00908 |

Legend:

| | Description |
|---|---|
|  | 1D01 |
|  | 11B07 |
|  | 00027 |
|  | 00908 |
|  | *9 GlySer* linker |
|  | *40 GlySer* linker |

Figure 21-1A

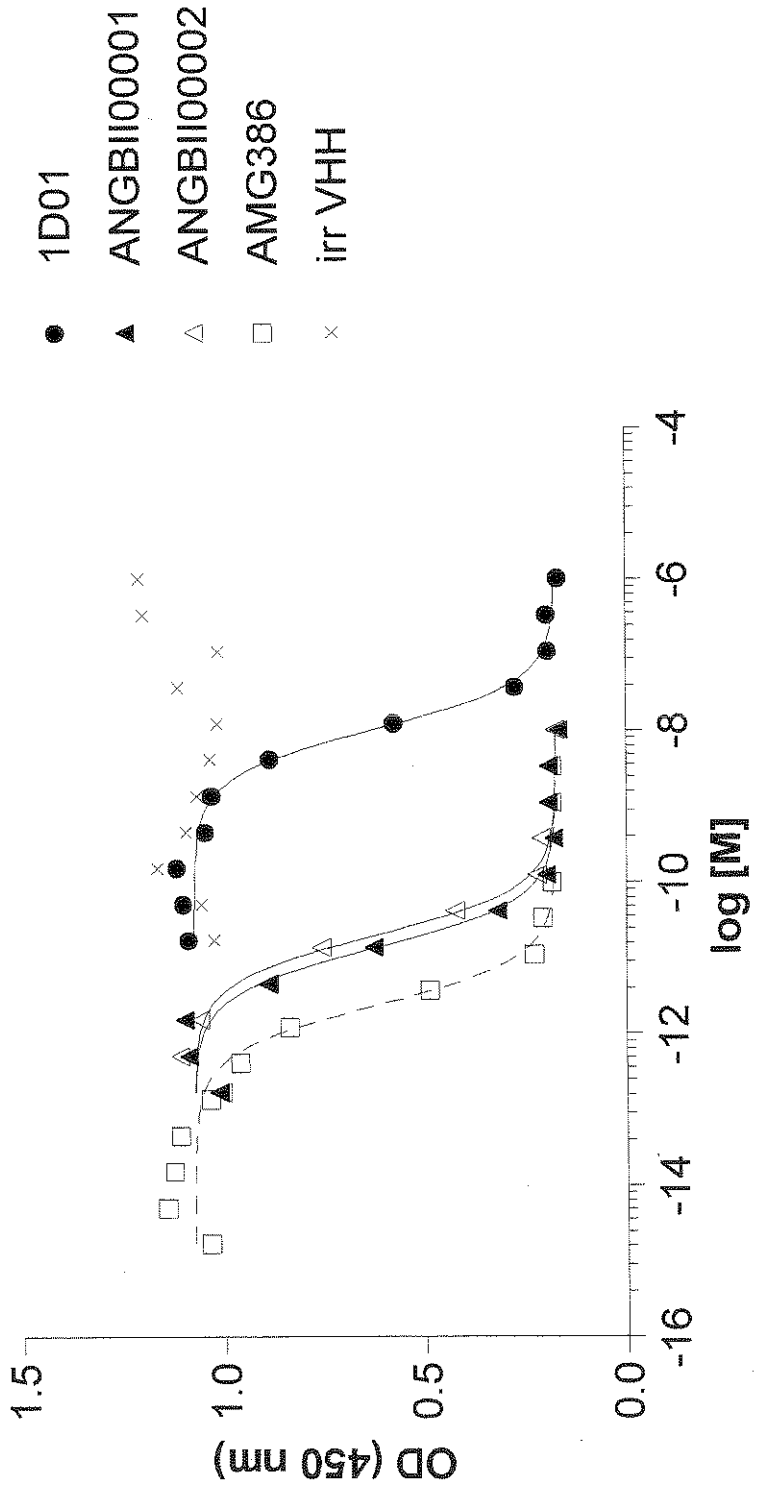

1D01
ANGBII00001
ANGBII00002
AMG386
irr VHH
OD (450 nm)
1.5
1.0
0.5
0.0
-4
-6
-8
-10
-12
-14
-16
log [M]

**Figure 21-1B**

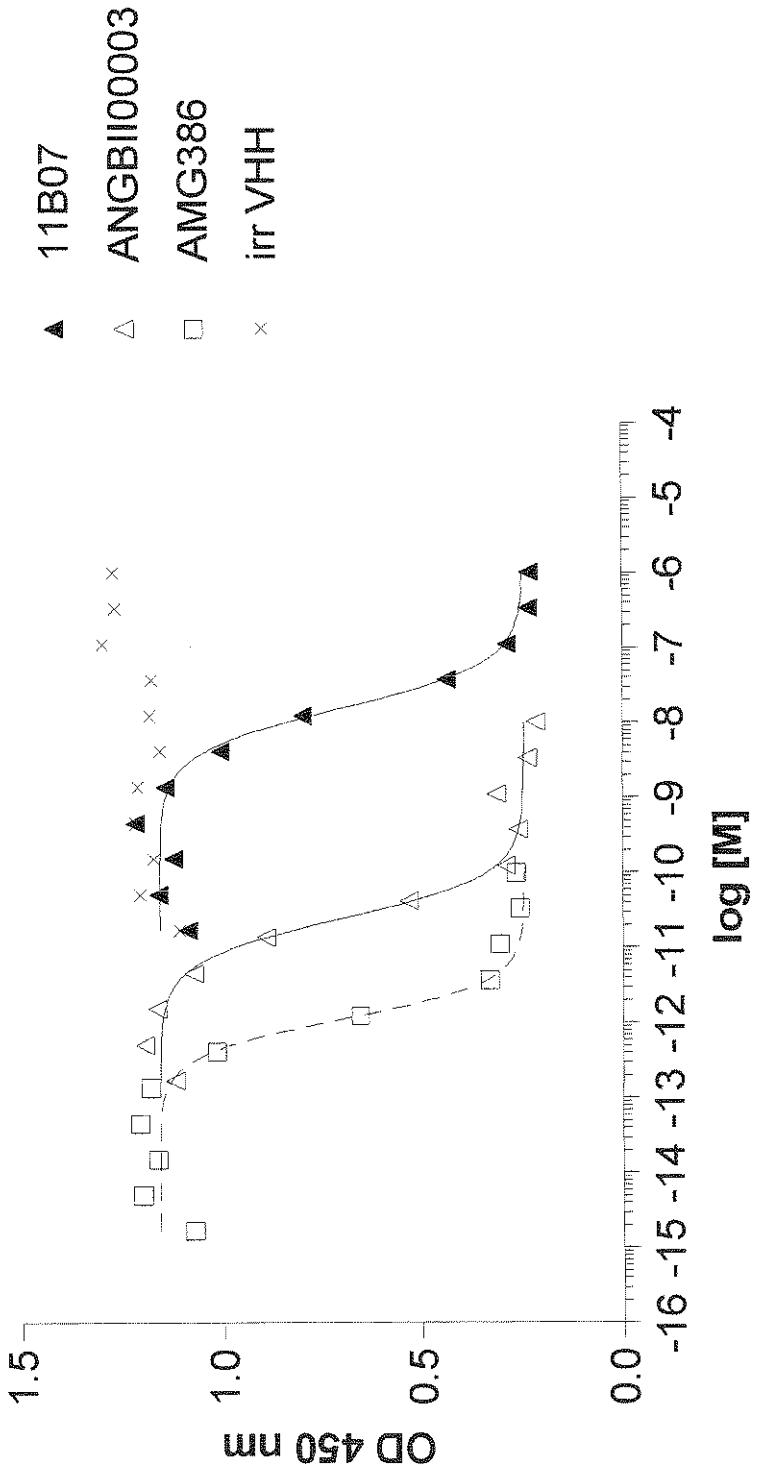

11B07
ANGBII00003
AMG386
irr VHH
OD 450 nm
1.5
1.0
0.5
0.0
-16 -15 -14 -13 -12 -11 -10 -9 -8 -7 -6 -5 -4
log [M]

Figure 21-1C

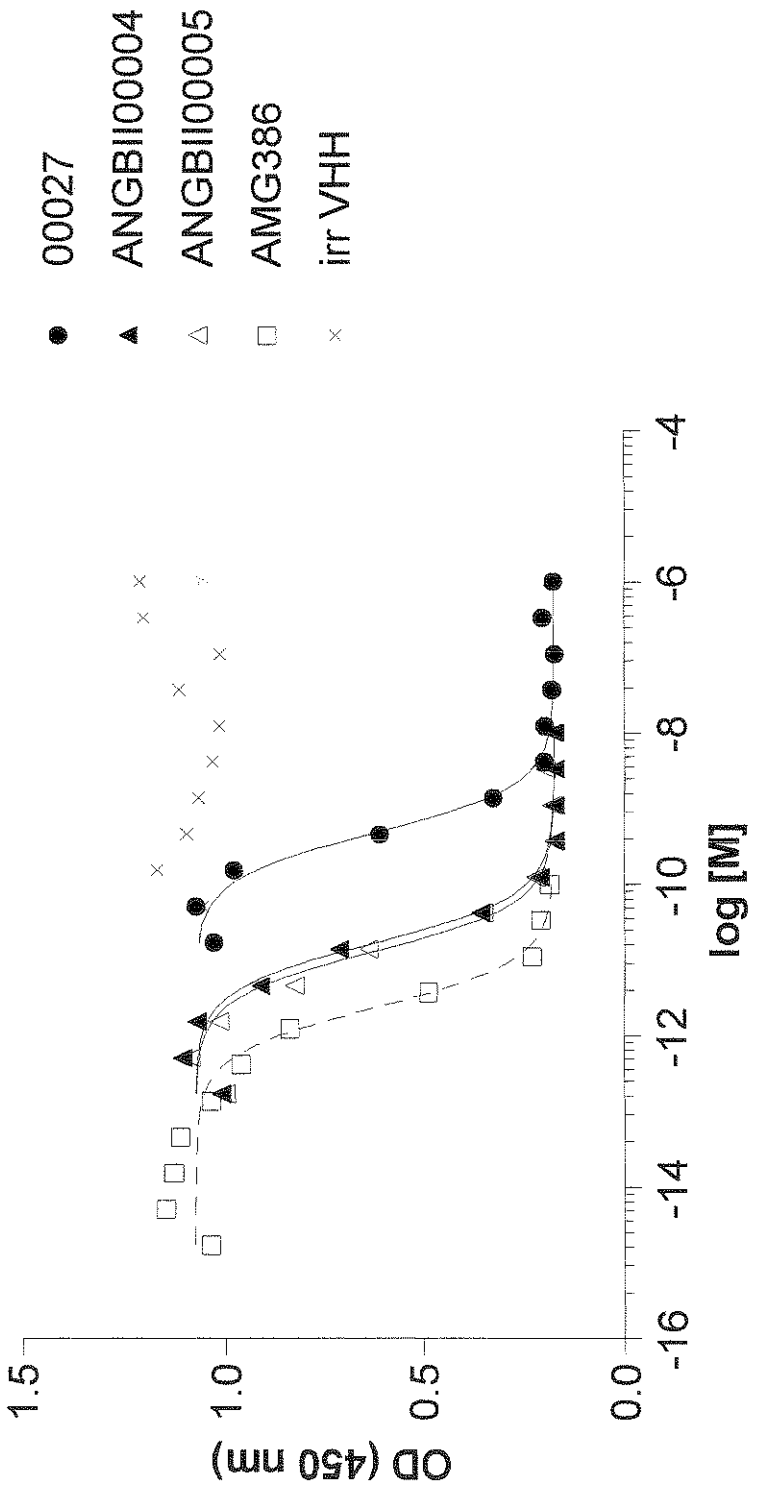

00027
ANGBII00004
ANGBII00005
AMG386
irr VHH
OD (450 nm)
1.5
1.0
0.5
0.0
-4
-6
-8
-10
-12
-14
-16
log [M]

Figure 21-1D

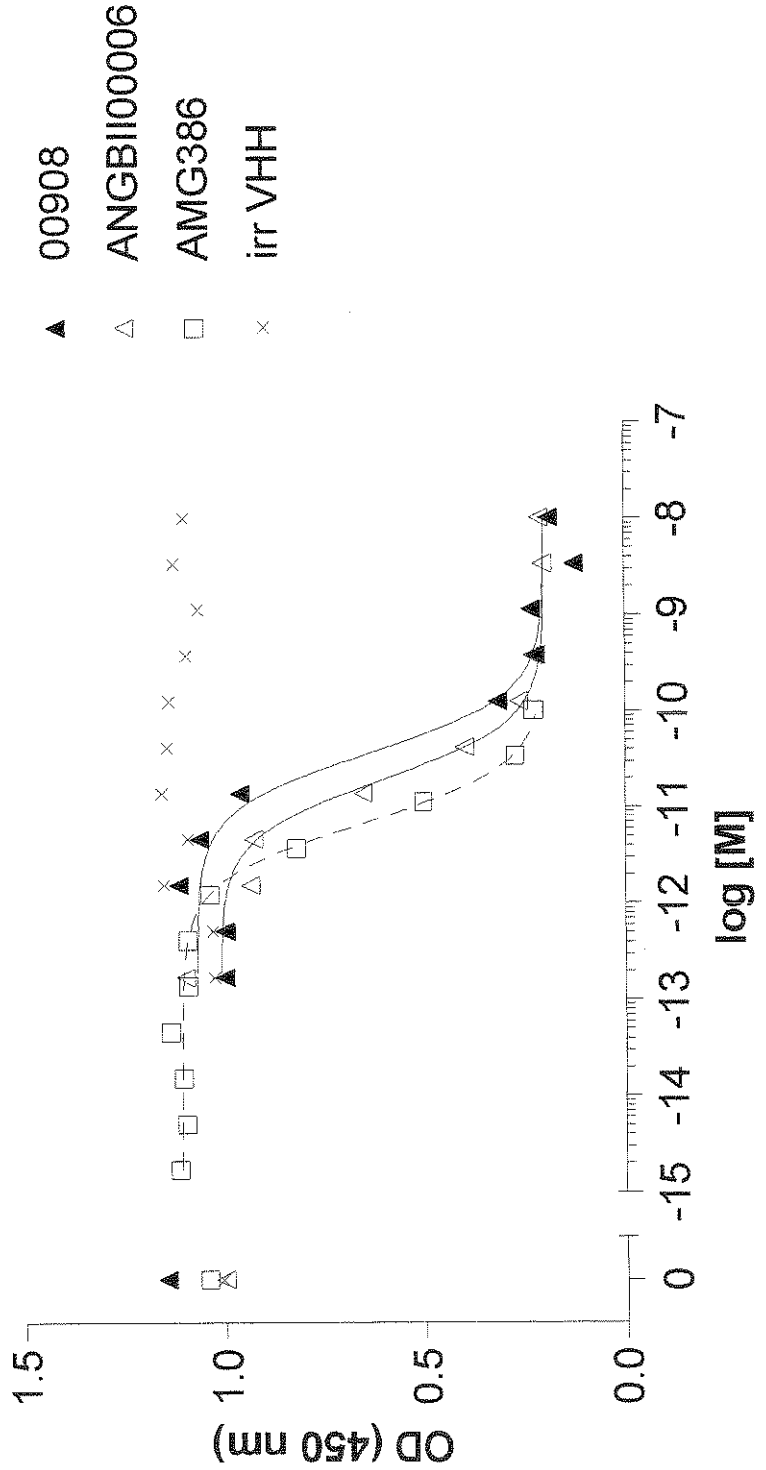

00908
ANGBII00006
AMG386
irr VHH
OD (450 nm)
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
log [M]

Figure 21-2A

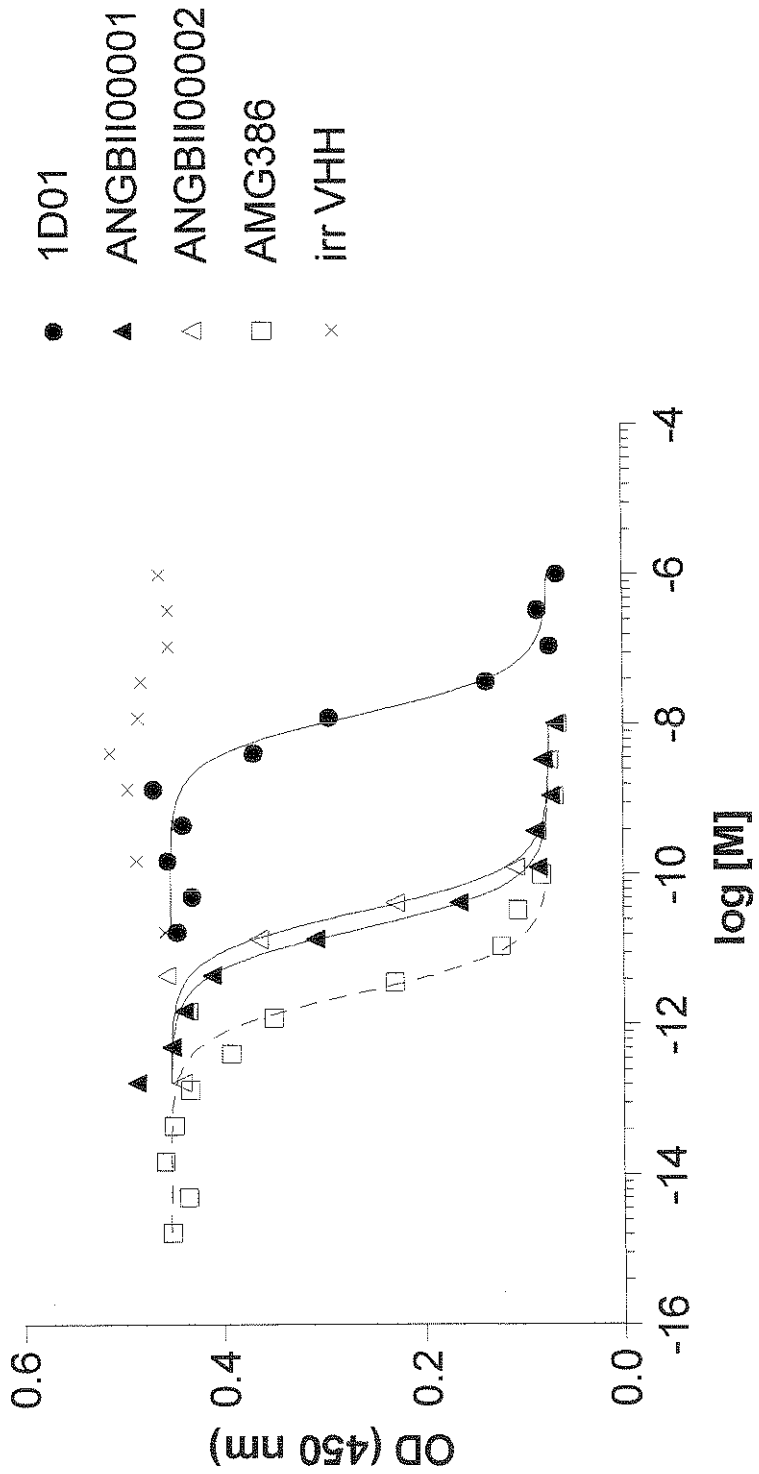

1D01
ANGBII00001
ANGBII00002
AMG386
irr VHH
OD (450 nm)
0.0
0.2
0.4
0.6
log [M]
-4
-6
-8
-10
-12
-14
-16

Figure 21-2B

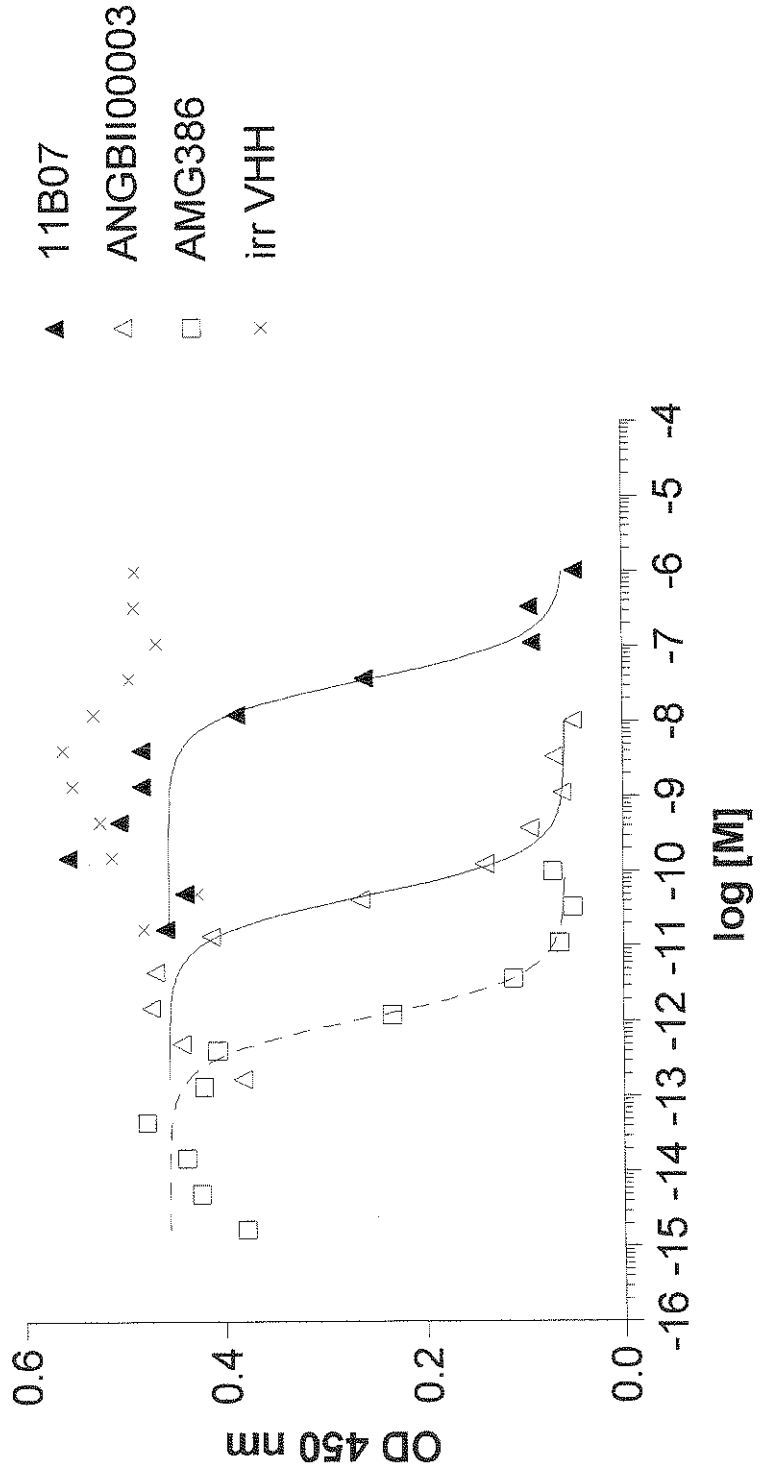

11B07
ANGBII00003
AMG386
irr VHH
OD 450 nm
0.0
0.2
0.4
0.6
log [M]
-4
-5
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15
-16

Figure 21-2C

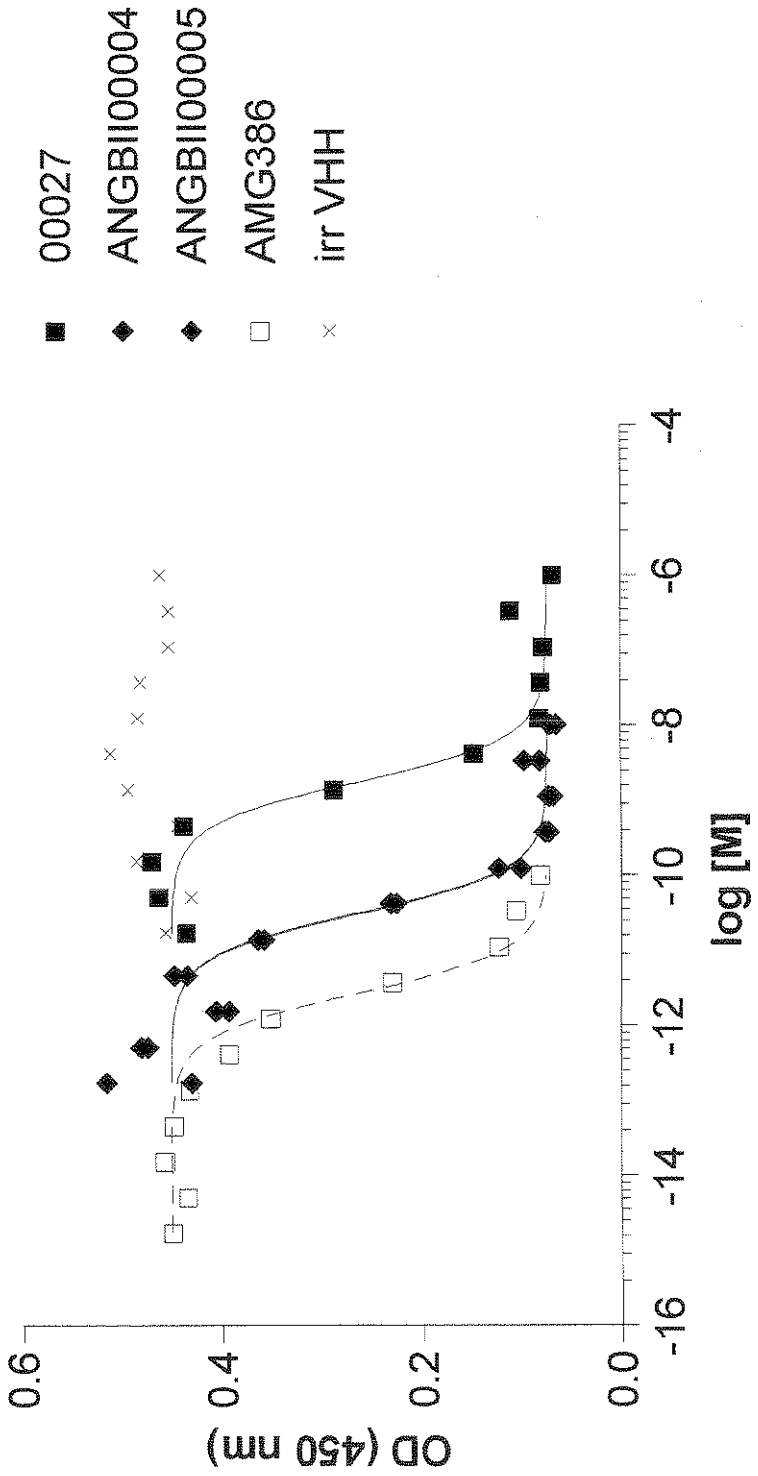

00027
ANGBII00004
ANGBII00005
AMG386
irr VHH
OD (450 nm)
0.0
0.2
0.4
0.6
log [M]
-4
-6
-8
-10
-12
-14
-16

**Figure 21-2D**

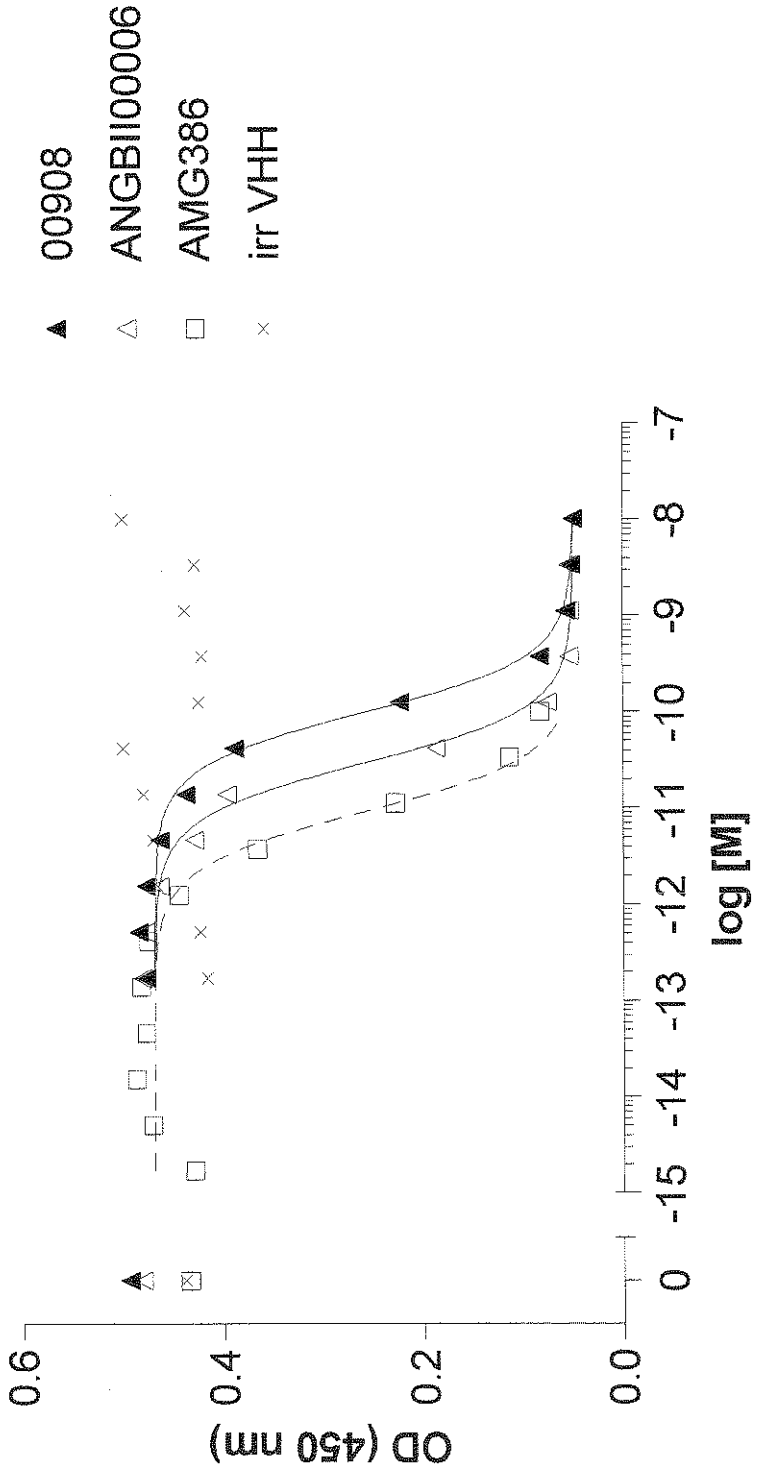

00908
ANGBII00006
AMG386
irr VHH
OD (450 nm)
0.0
0.2
0.4
0.6
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7

Figure 21-3A

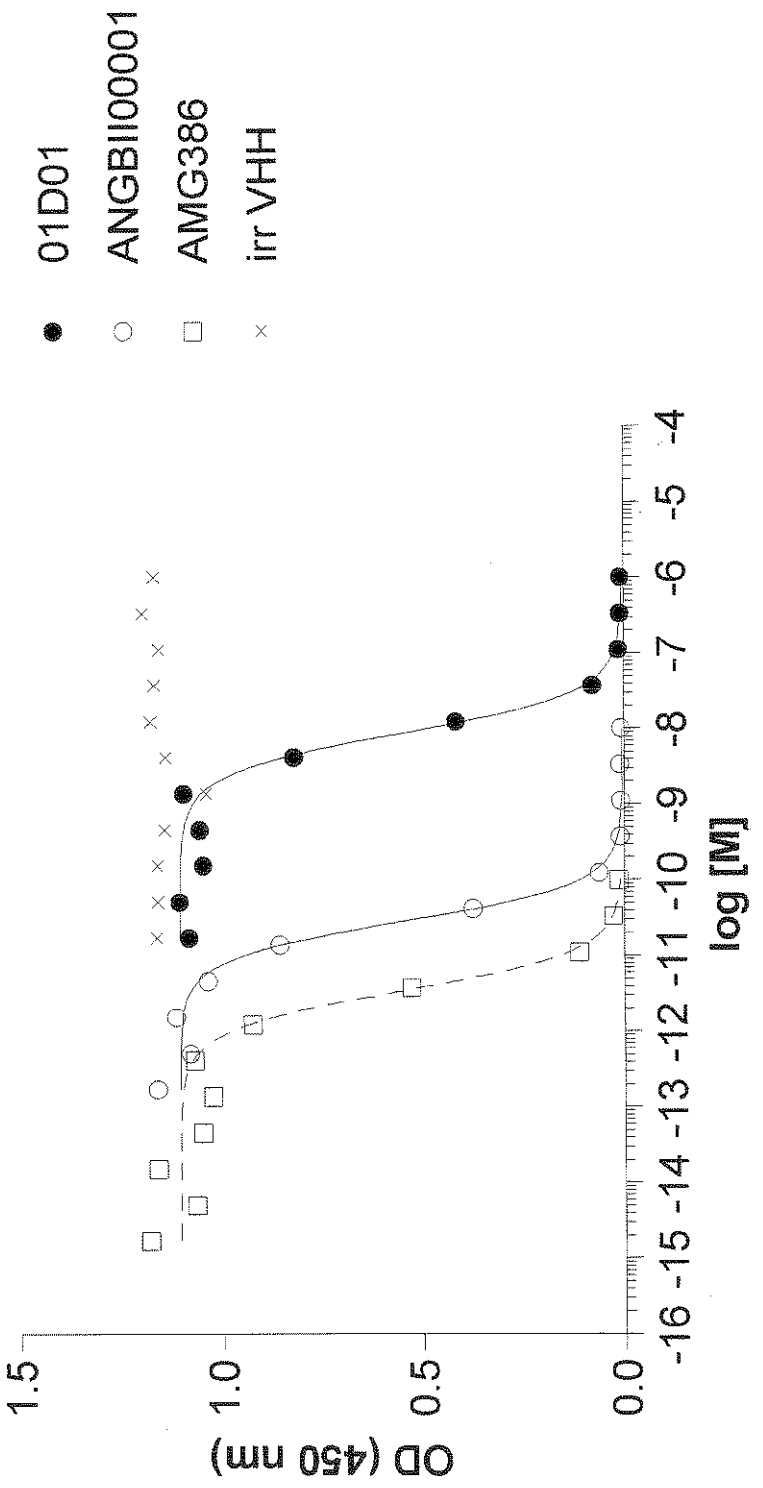

01D01
ANGBII00001
AMG386
irr VHH
OD (450 nm)
1.5
1.0
0.5
0.0
-16 -15 -14 -13 -12 -11 -10 -9 -8 -7 -6 -5 -4
log [M]

**Figure 21-3B**

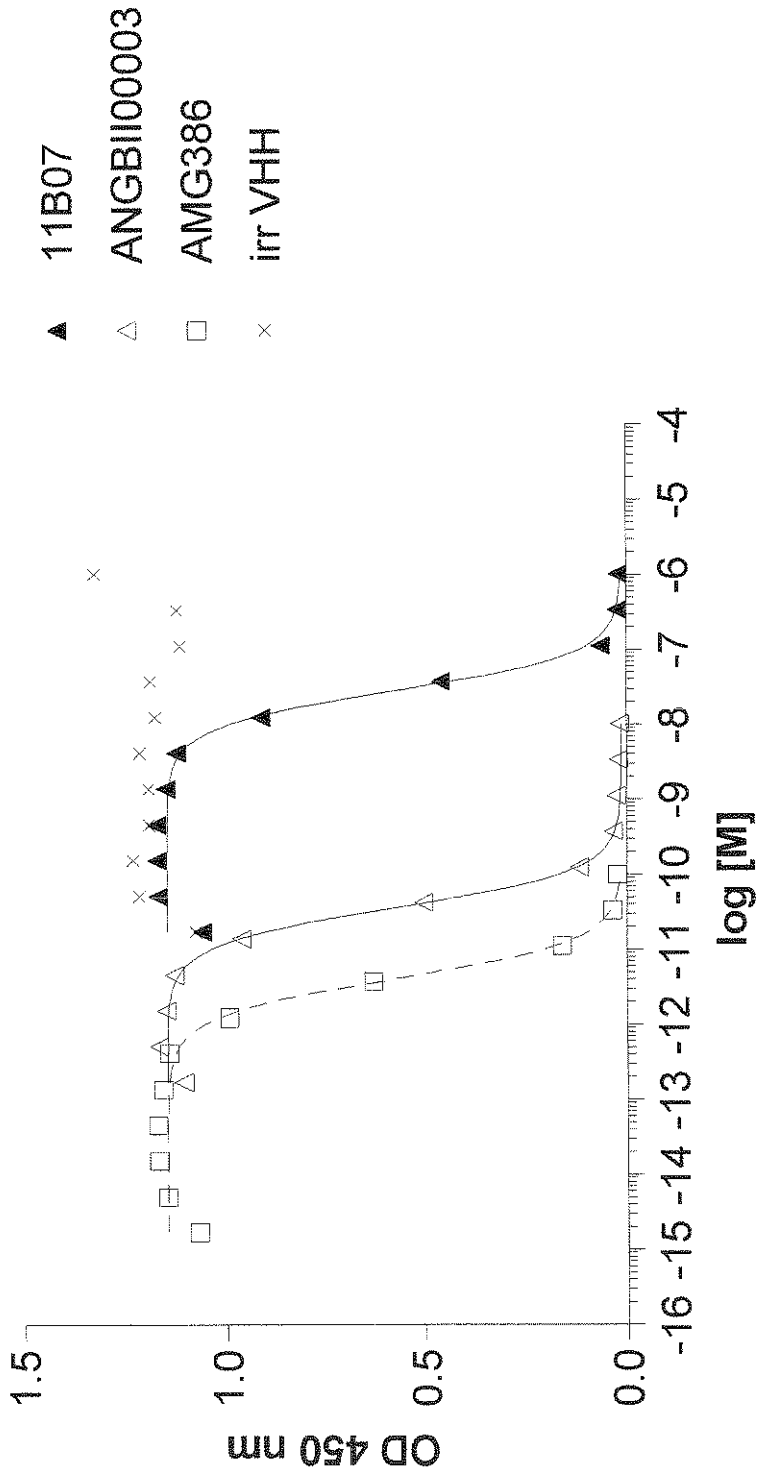

11B07
ANGBII00003
AMG386
irr VHH
OD 450 nm
1.5
1.0
0.5
0.0
-16 -15 -14 -13 -12 -11 -10 -9 -8 -7 -6 -5 -4
log [M]

Figure 21-3C

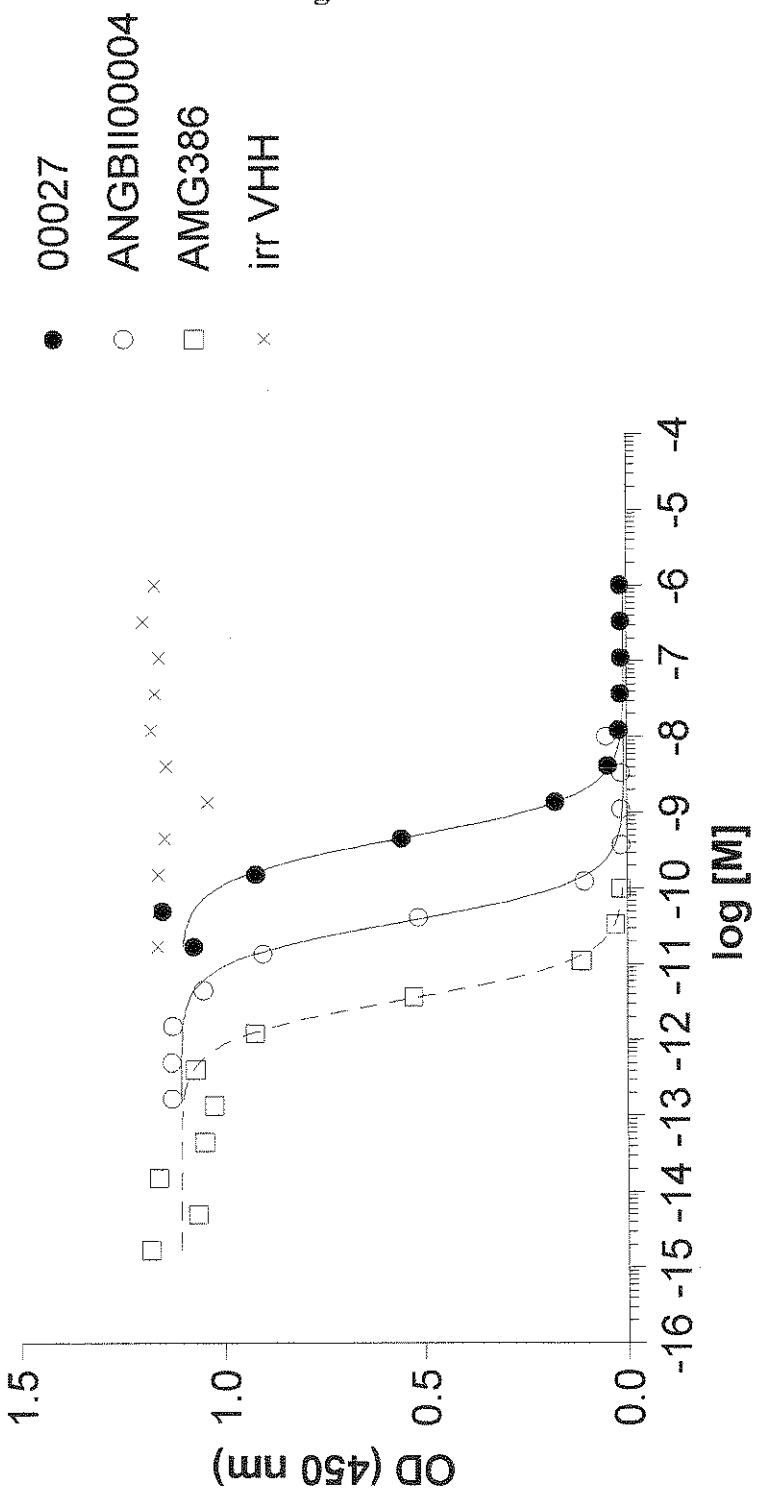

00027
ANGBII00004
AMG386
irr VHH
OD (450 nm)
1.5
1.0
0.5
0.0
log [M]
-4
-5
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15
-16

Figure 21-3D

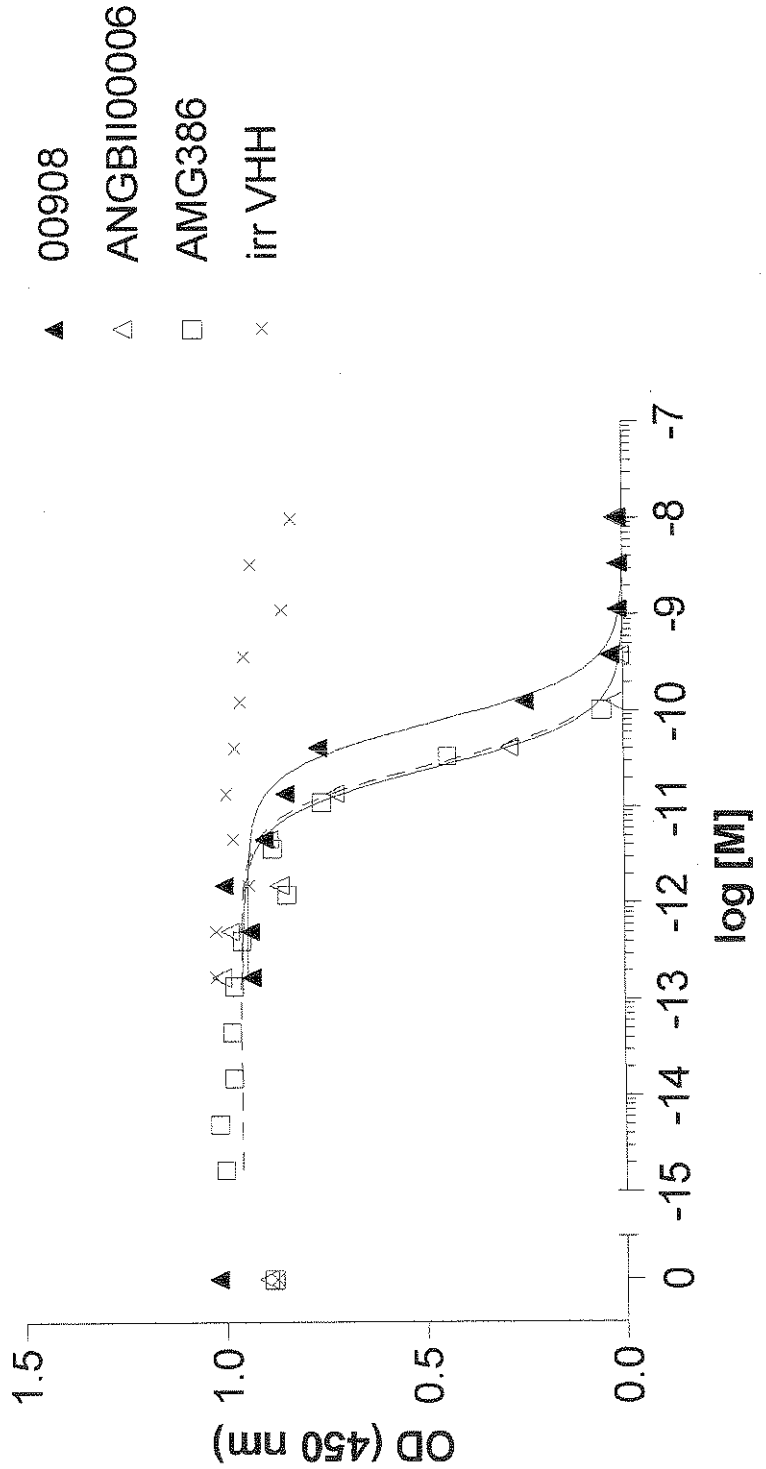

00908
ANGBII00006
AMG386
irr VHH
OD (450 nm)
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
log [M]

Figure 22

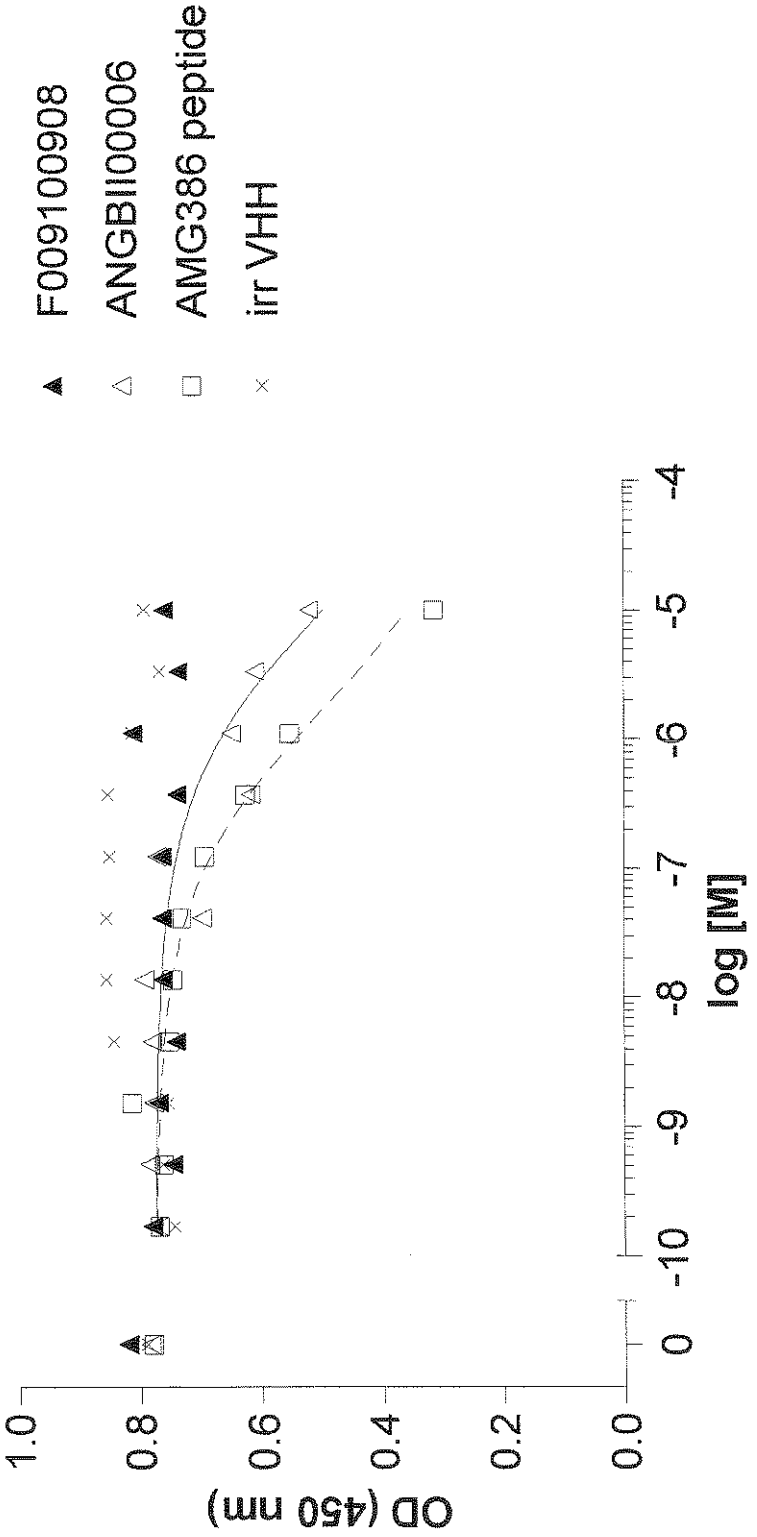

F009100908
ANGBII00006
AMG386 peptide
irr VHH
OD (450 nm)
1.0
0.8
0.6
0.4
0.2
0.0
0
-10
-9
-8
-7
-6
-5
-4
log [M]

**Figure 23**

| VHH ID | Format | Description |
|---|---|---|
| VEGFANGBII00001 |  | VEGFBII00038-9gs-ALB11-9gs-00027 |
| VEGFANGBII00002 |  | 00027-9gs-ALB11-9gs-VEGFBII00038 |
| VEGFANGBII00003 |  | 00027-9gs-VEGFBII00038-9gs-ALB11 |
| VEGFANGBII00004 |  | VEGFBII00038-*AAA*-ALB11-*AAA*-00027 |

Legend:

| | Description |
|---|---|
|  | VEGFBII00038 |
|  | 00027 |
|  | ALB11 |
| AAA | *triple Ala* linker |
|  | *9 GlySer* linker |

Figure 24A

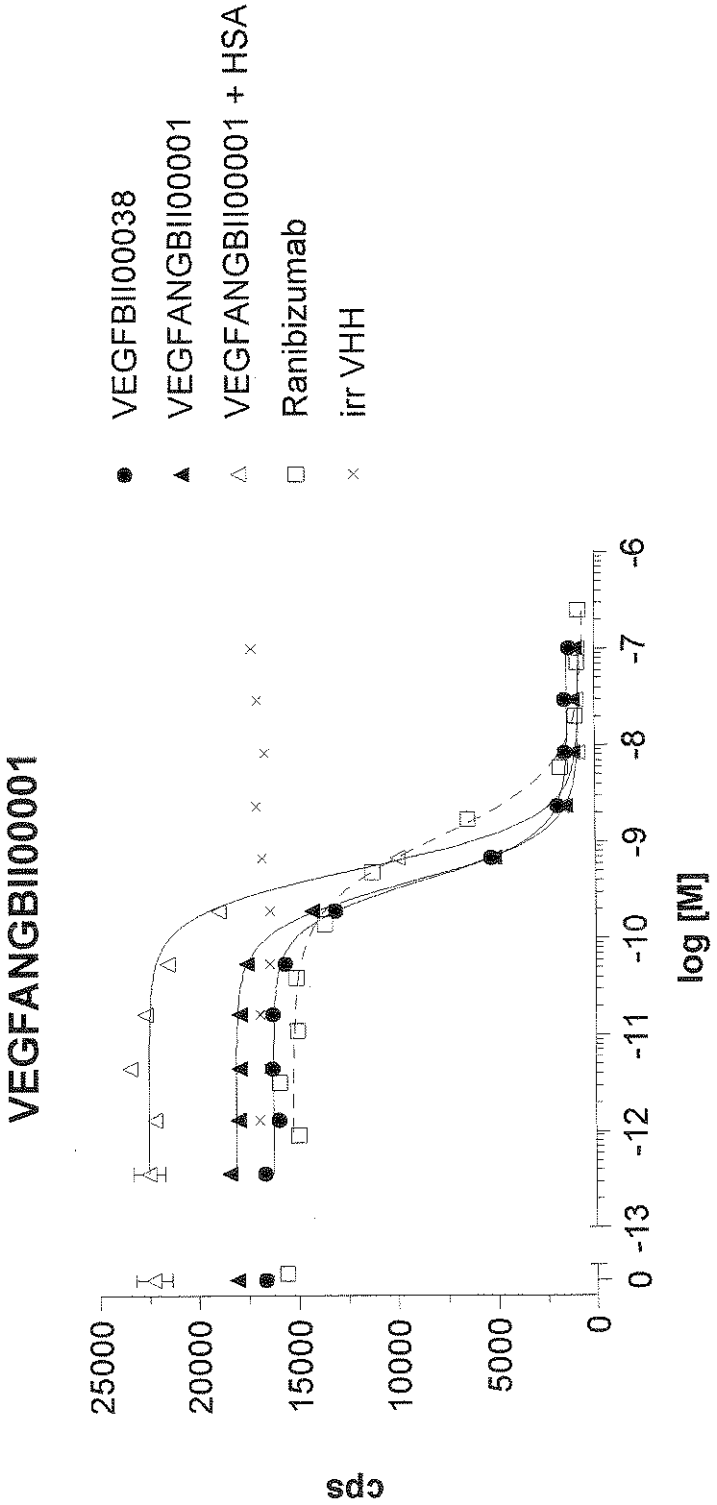

VEGFBII00038
VEGFANGBII00001
VEGFANGBII00001 + HSA
Ranibizumab
irr VHH
VEGFANGBII00001
cps
25000
20000
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 24B**

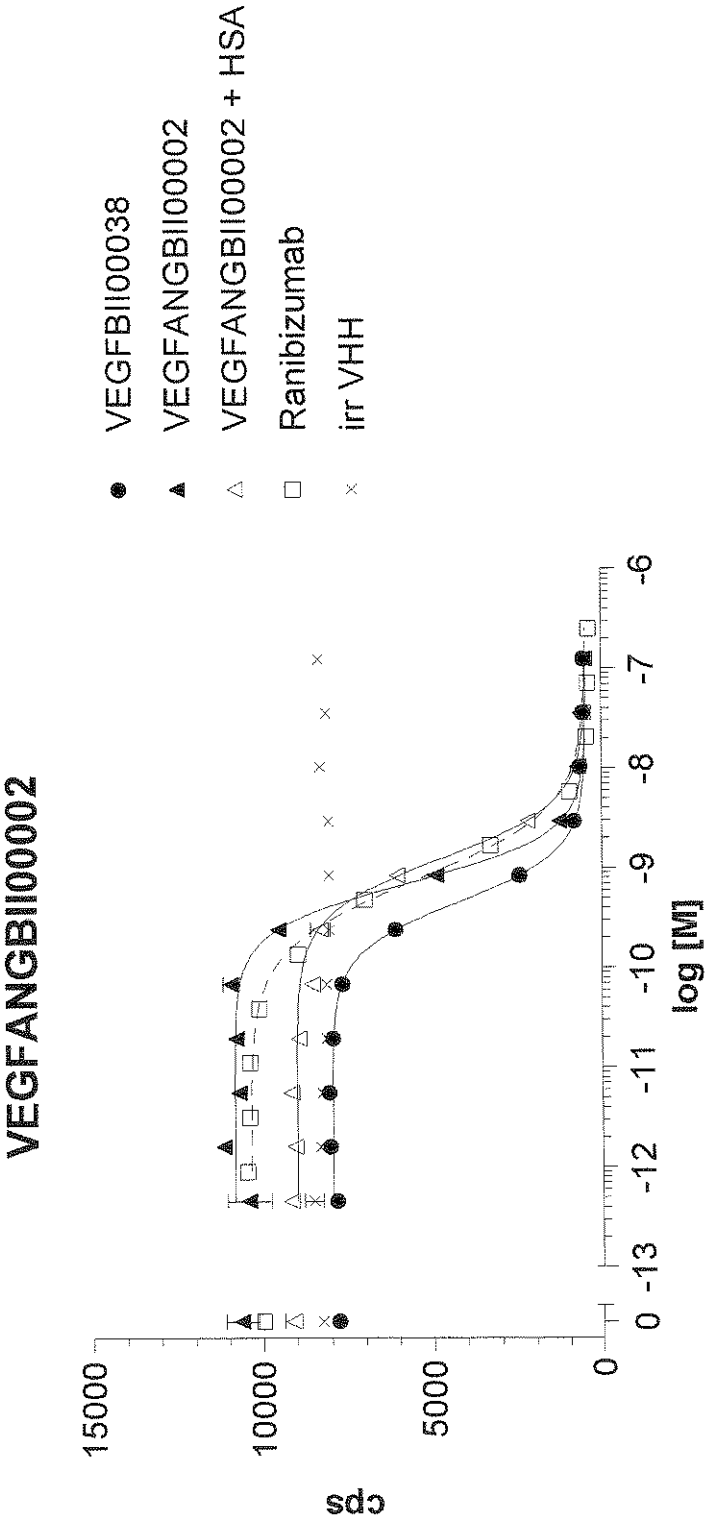

VEGFBII00038
VEGFANGBII00002
VEGFANGBII00002 + HSA
Ranibizumab
irr VHH
VEGFANGBII00002
cps
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 24C**

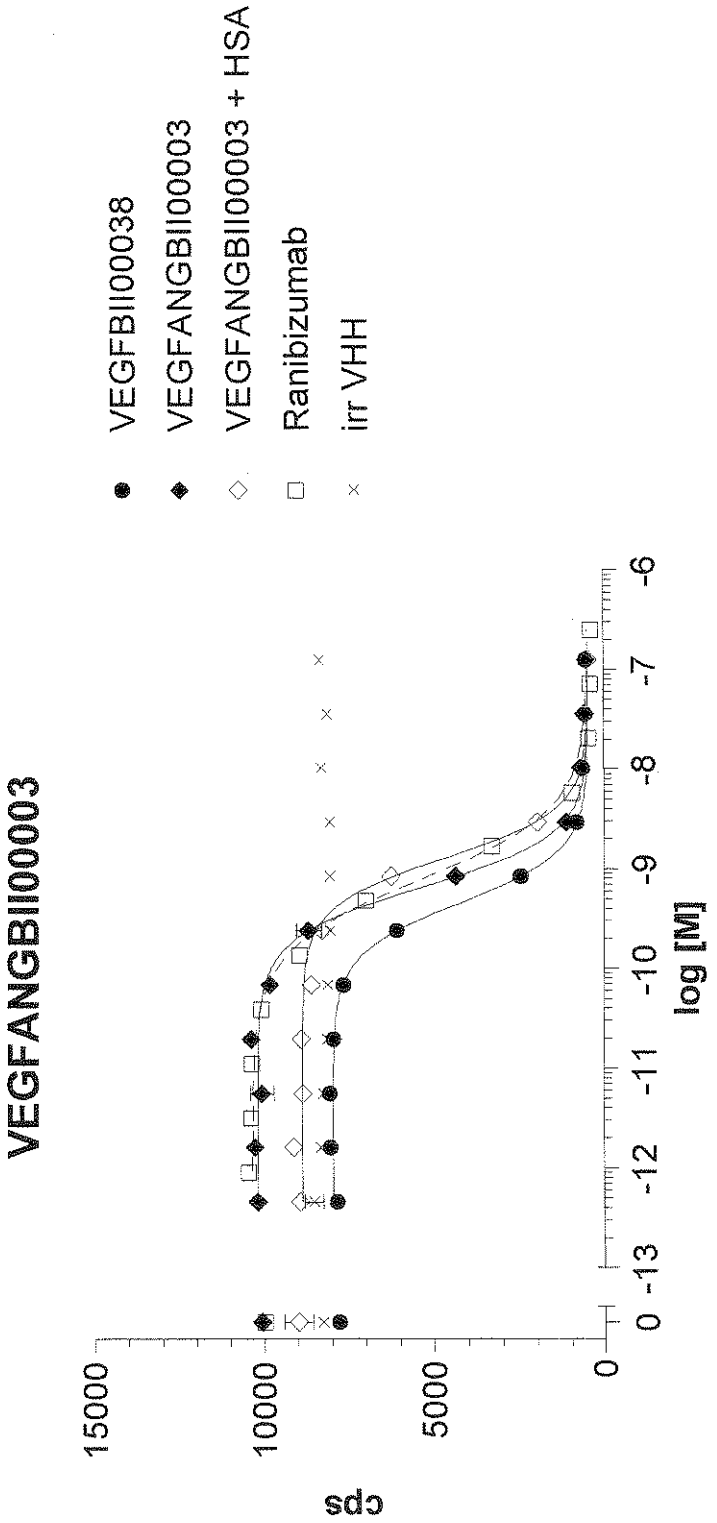

VEGFBII00038
VEGFANGBII00003
VEGFANGBII00003 + HSA
Ranibizumab
irr VHH
VEGFANGBII00003
cps
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 24D**

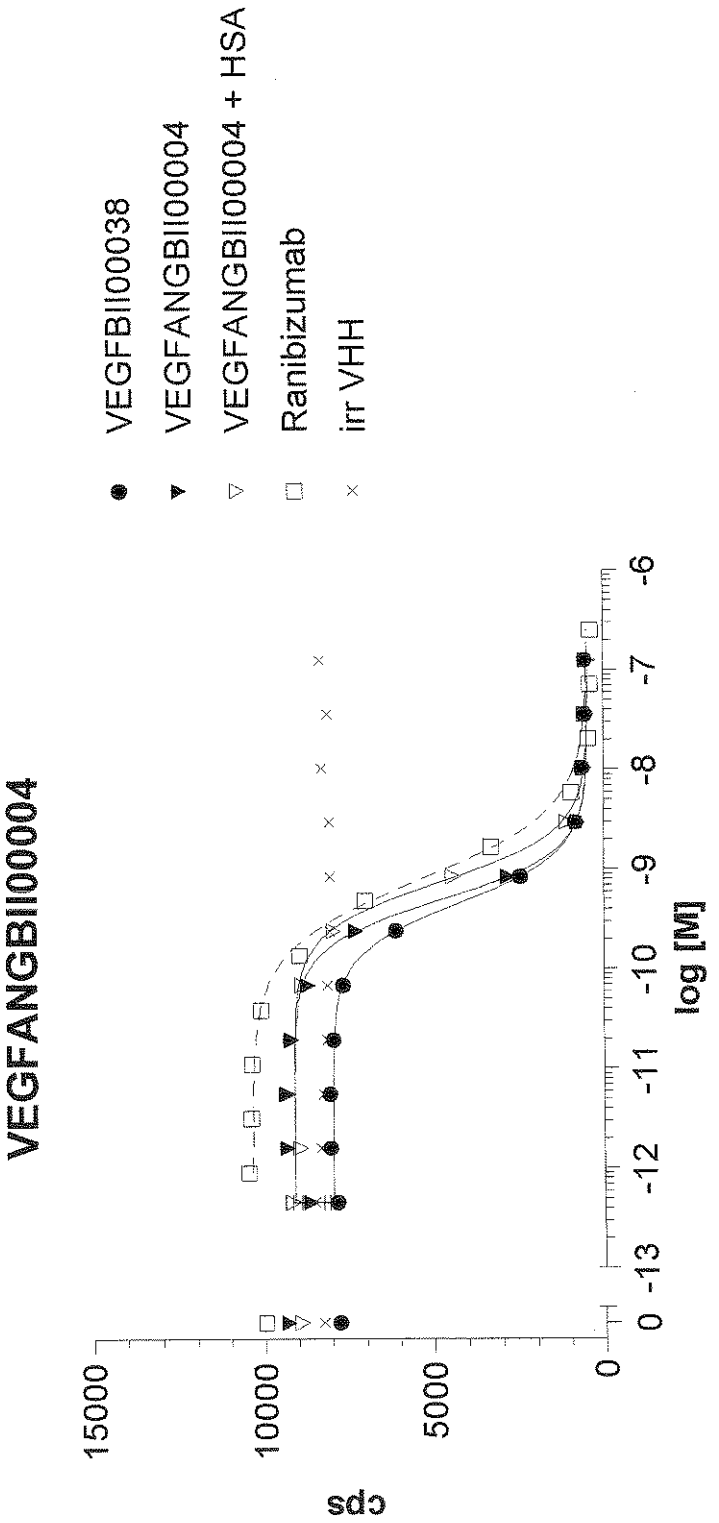

VEGFBII00038
VEGFANGBII00004
VEGFANGBII00004 + HSA
Ranibizumab
irr VHH
VEGFANGBII00004
cps
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 25A**

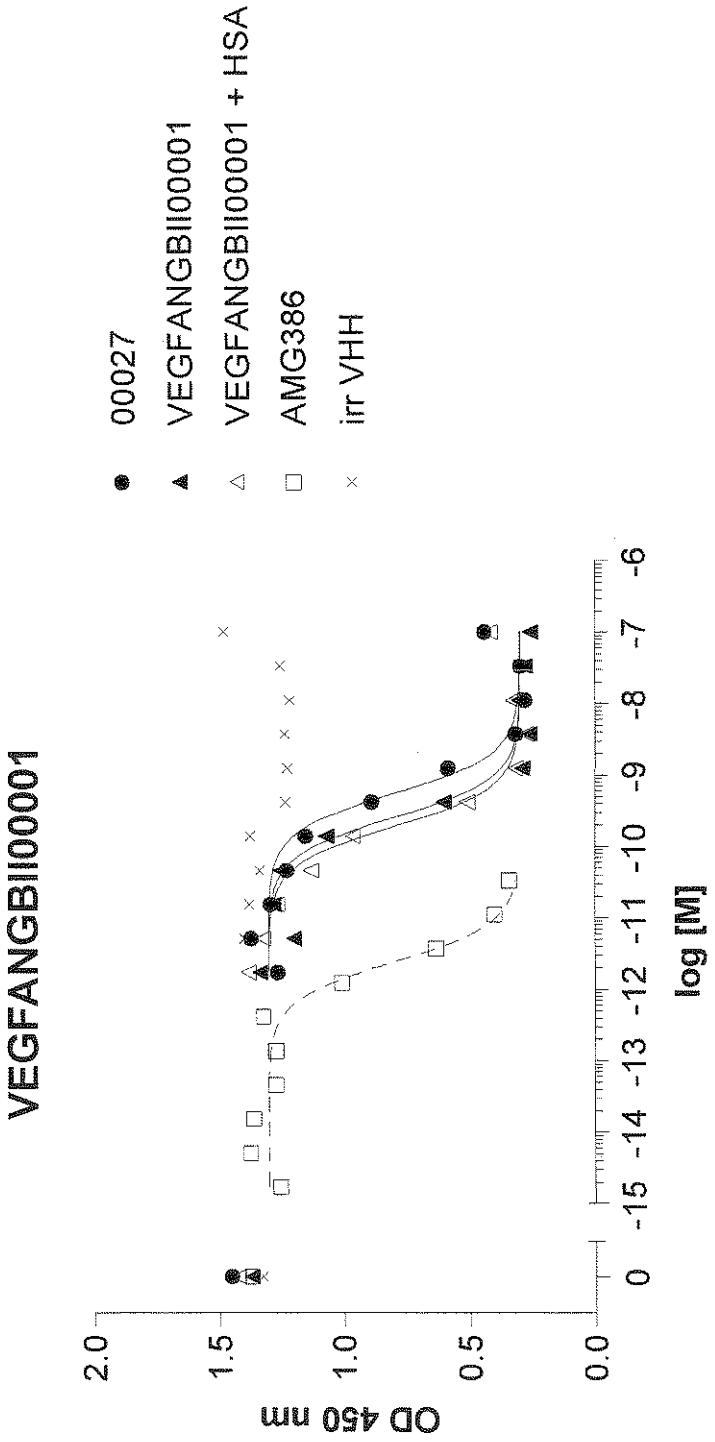

VEGFANGBII00001
00027
VEGFANGBII00001
VEGFANGBII00001 + HSA
AMG386
irr VHH
OD 450 nm
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 25B**

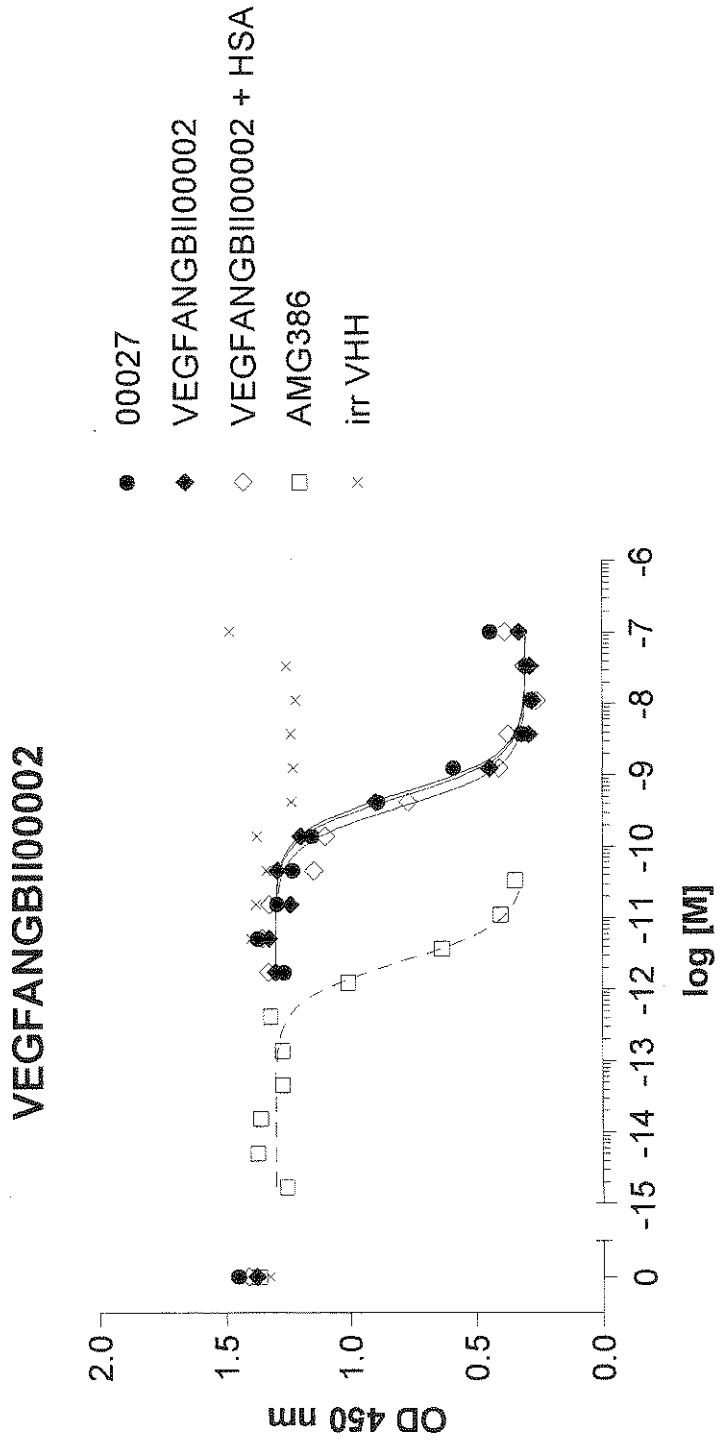

VEGFANGBII00002
00027
VEGFANGBII00002
VEGFANGBII00002 + HSA
AMG386
irr VHH
OD 450 nm
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 25C**

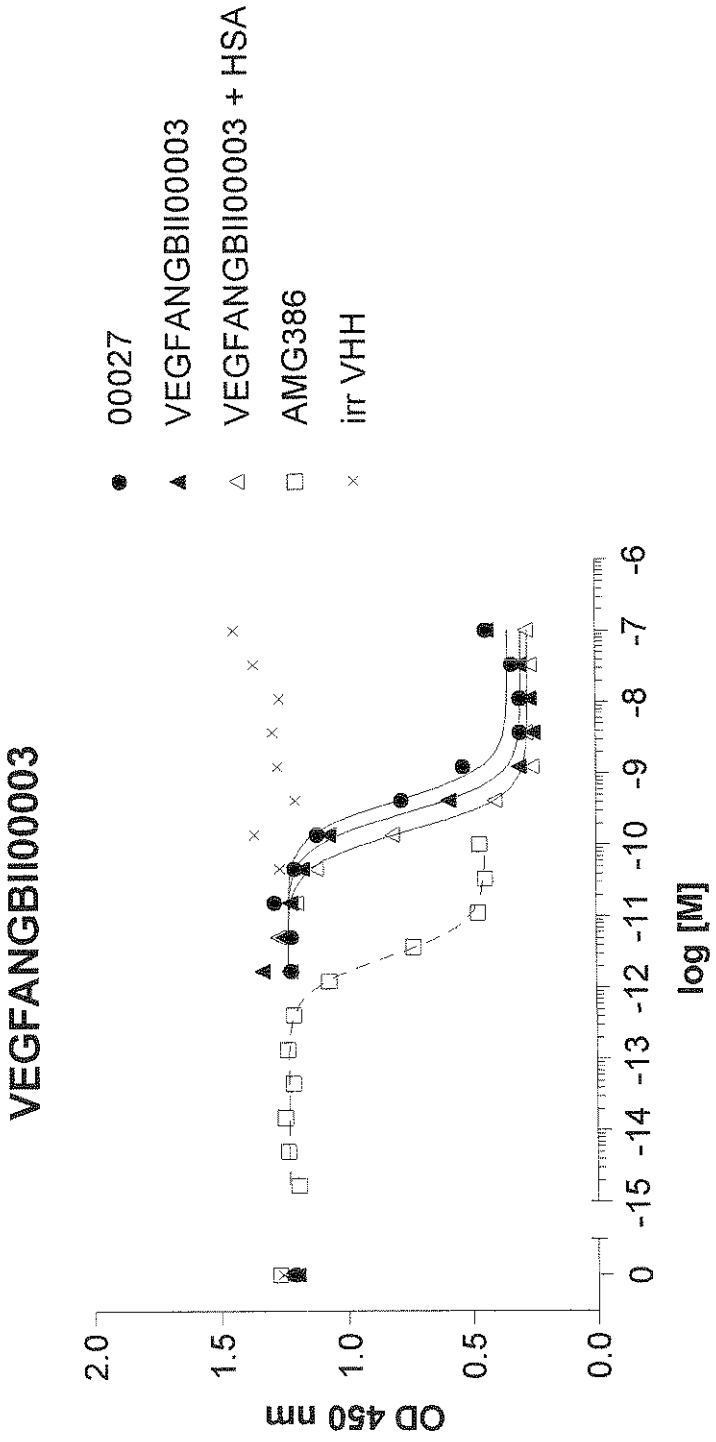
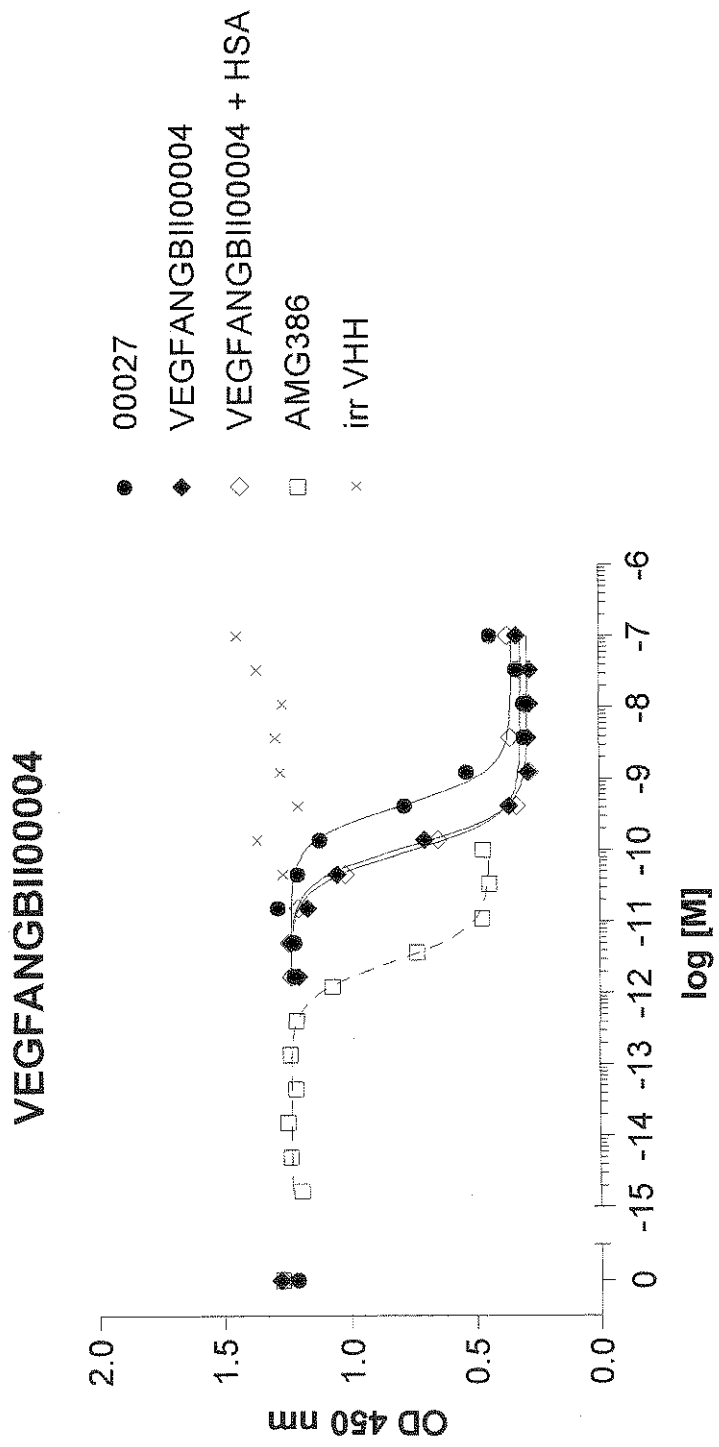
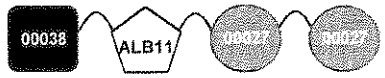

VEGFANGBII00003
00027
VEGFANGBII00003
VEGFANGBII00003 + HSA
AMG386
irr VHH
OD 450 nm
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 25D**


VEGFANGBII00004
00027
VEGFANGBII00004
VEGFANGBII00004 + HSA
AMG386
irr VHH
OD 450 nm
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

## Figure 26

| VHH ID | Format | Description |
|---|---|---|
| VEGFANGBII00005 |  | VEGFBII00038-9gs-7G08-9gs-ALB11 |
| VEGFANGBII00006 |  | VEGFBII00038-9gs-ALB11-9gs-7G08 |
| VEGFANGBII00007 |  | VEGFBII00038-9gs-7G08-9gs-ALB11-9gs-7G08 |
| VEGFANGBII00008 |  | VEGFBII00038-9gs-00027-9gs-00027-9gs-ALB11 |
| VEGFANGBII00009 |  | VEGFBII00038-9gs-ALB11-9gs-00027-9gs-00027 |
| VEGFANGBII00010 |  | VEGFBII00038-9gs-00027-9gs-ALB11-9gs-00027 |
| VEGFANGBII00011 |  | VEGFBII00038-9gs-1D01-9gs-1D01-9gs-ALB11 |
| VEGFANGBII00012 |  | VEGFBII00038-9gs-ALB11-9gs-1D01-9gs-1D01 |
| VEGFANGBII00013 |  | VEGFBII00038-9gs-1D01-9gs-ALB11-9gs-1D01 |
| VEGFANGBII00014 |  | VEGFBII00038-9gs-ALB11-9gs-1D01 |

Legend:

| | Description | | Description |
|---|---|---|---|
|  | VEGFBII00038 |  | ALB11 |
|  | 00027 | AAA | *triple Ala* linker |
|  | 1D01 |  | *9 GlySer* linker |
|  | 7G08 | | |

**Figure 27-1A**

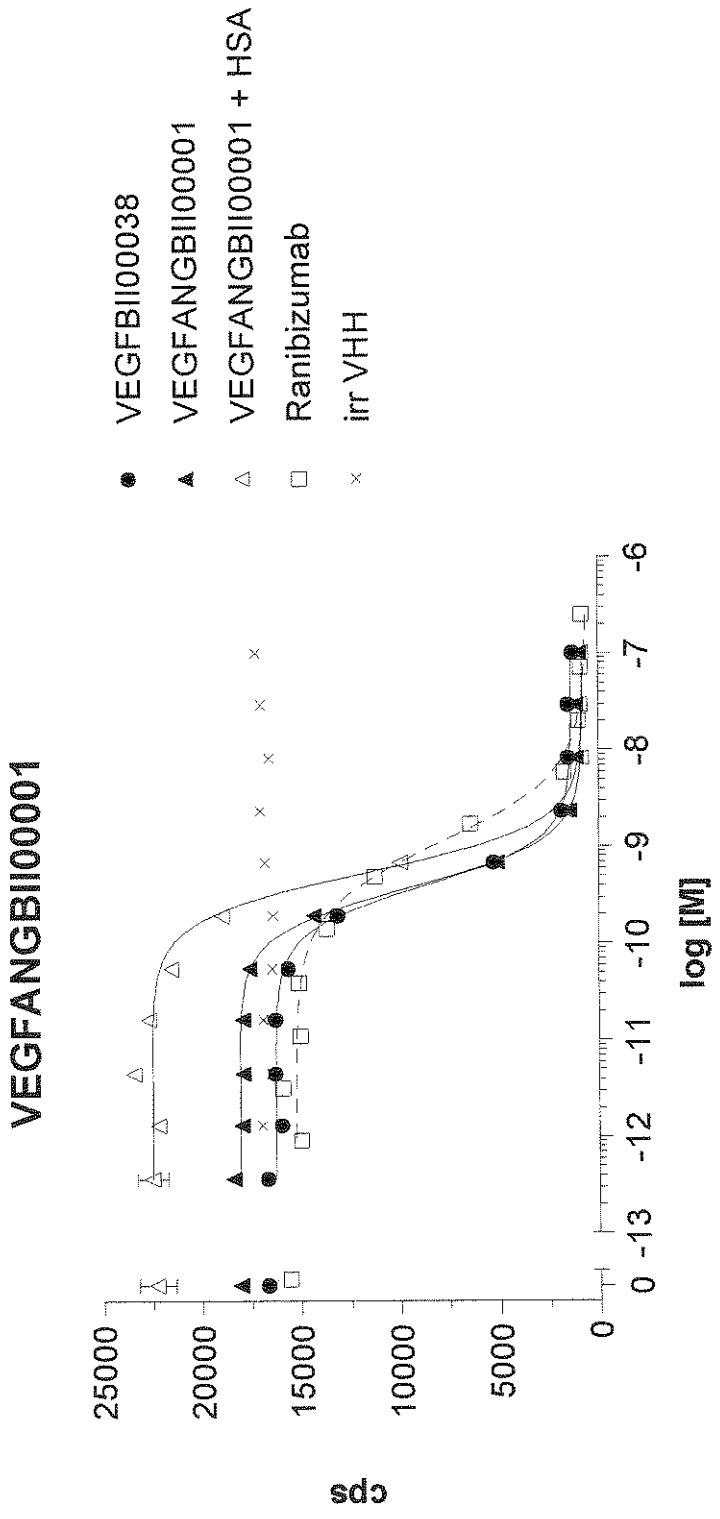

VEGFBII00038
VEGFANGBII00001
VEGFANGBII00001 + HSA
Ranibizumab
irr VHH
VEGFANGBII00001
cps
25000
20000
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

Figure 27-1B

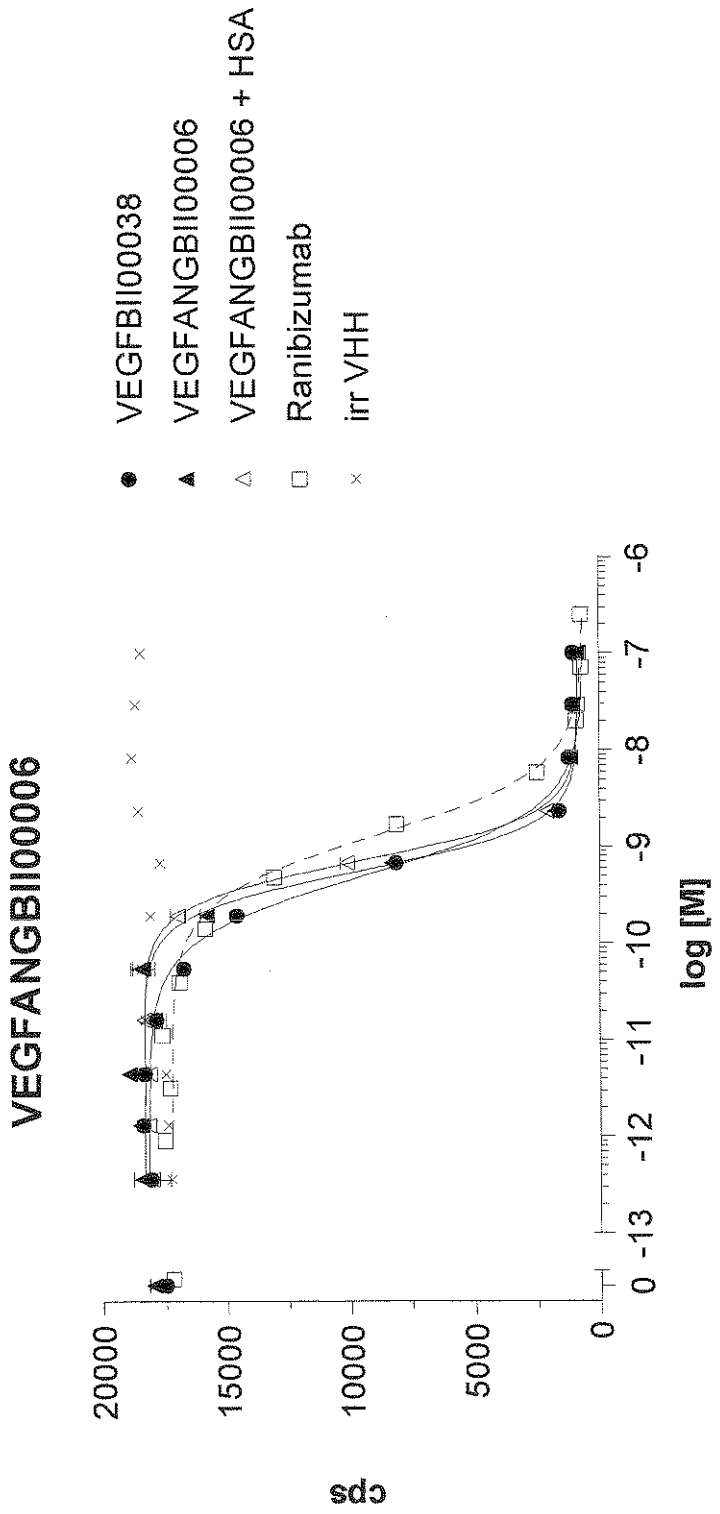

VEGFBII00038
VEGFANGBII00006
VEGFANGBII00006 + HSA
Ranibizumab
irr VHH
VEGFANGBII00006
cps
20000
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

Figure 27-1C

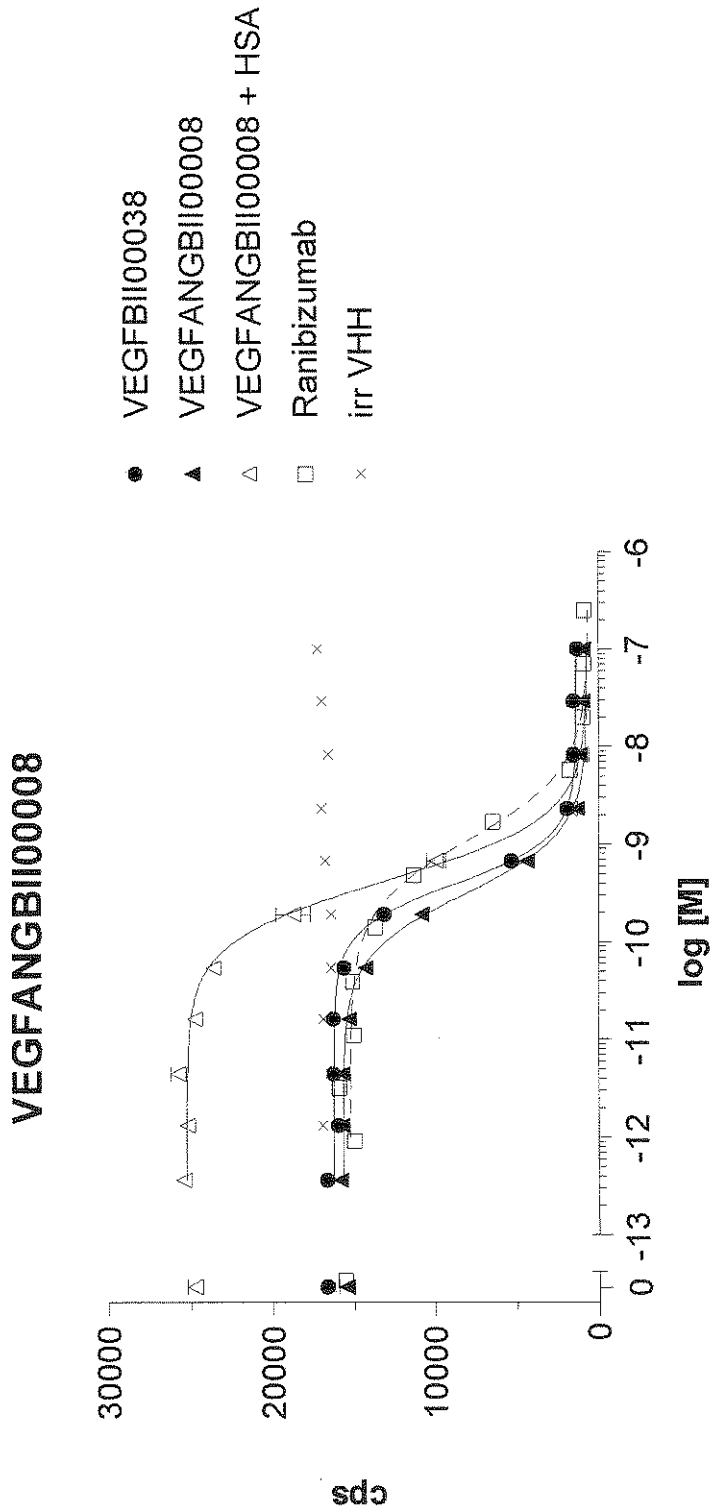

VEGFBII00038
VEGFANGBII00008
VEGFANGBII00008 + HSA
Ranibizumab
irr VHH
VEGFANGBII00008
cps
30000
20000
10000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 27-1D**

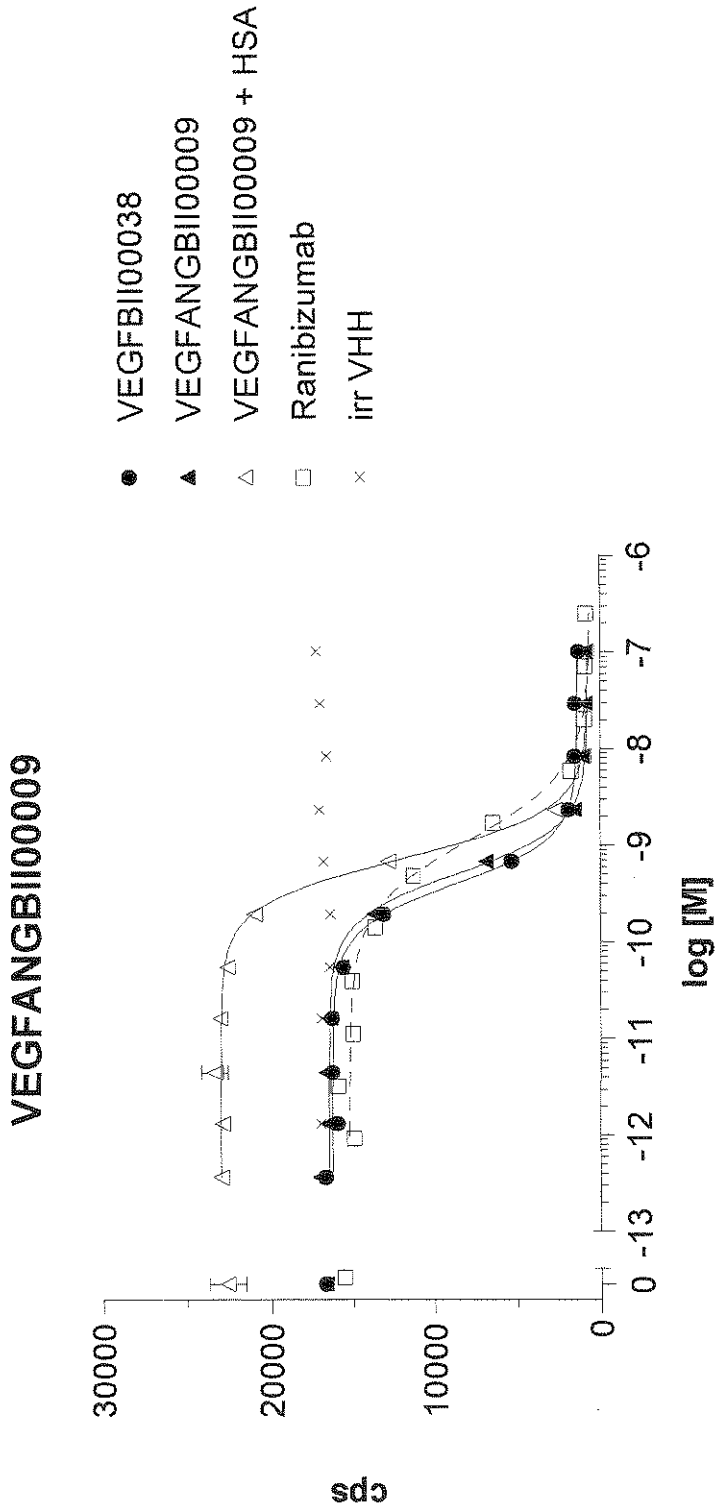

VEGFBII00038
VEGFANGBII00009
VEGFANGBII00009 + HSA
Ranibizumab
irr VHH
VEGFANGBII00009
cps
30000
20000
10000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

Figure 27-1E

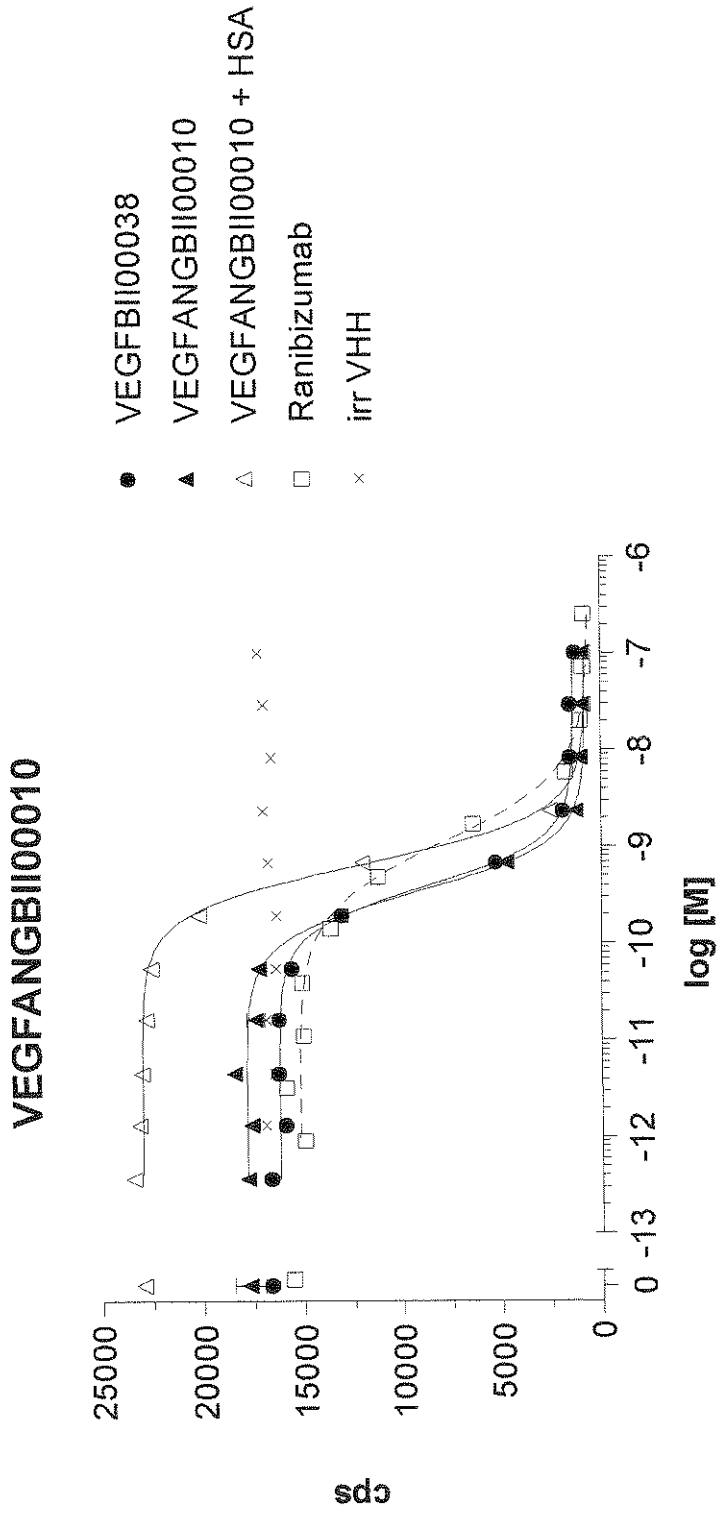

VEGFBII00038
VEGFANGBII00010
VEGFANGBII00010 + HSA
Ranibizumab
irr VHH
VEGFANGBII00010
cps
25000
20000
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 27-1F**

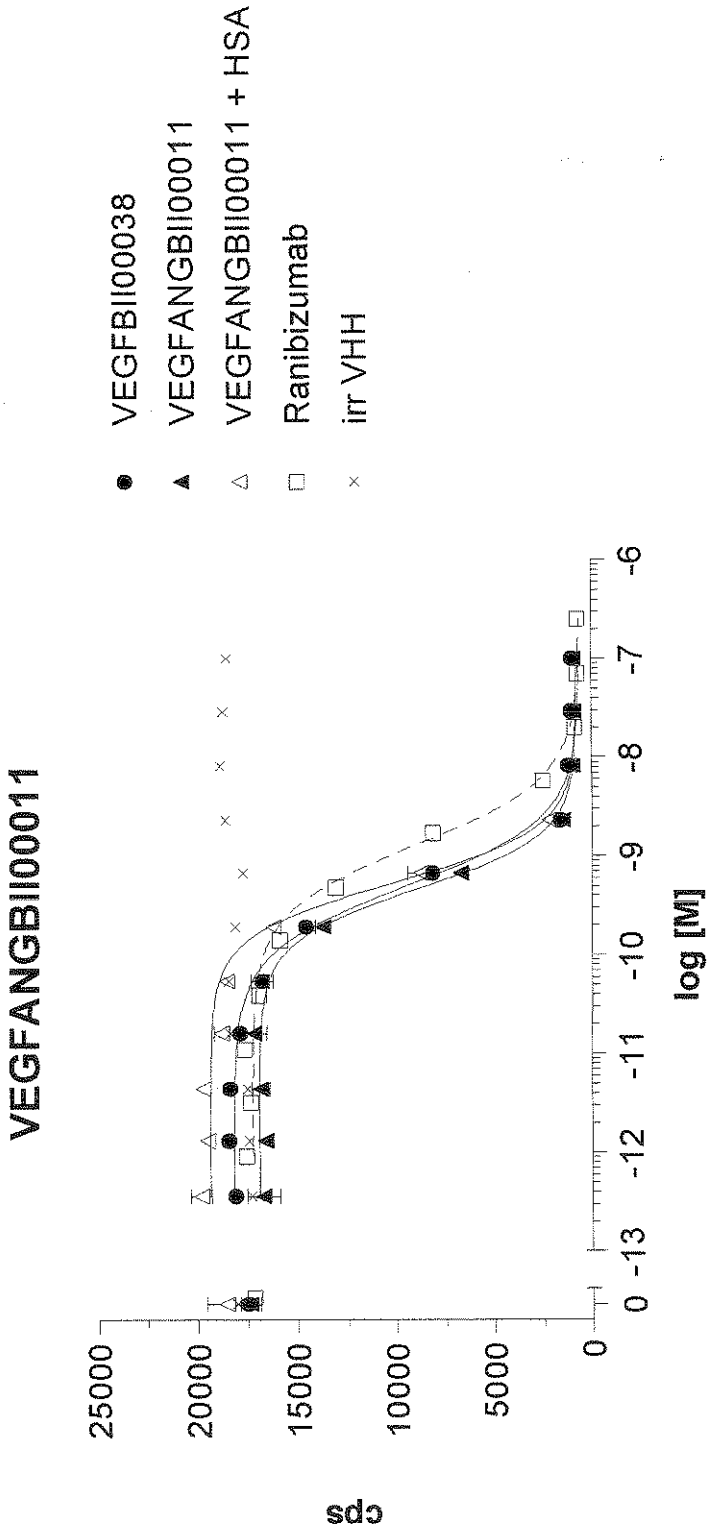

VEGFBII00038
VEGFANGBII00011
VEGFANGBII00011 + HSA
Ranibizumab
irr VHH
VEGFANGBII00011
cps
25000
20000
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 27-1G**

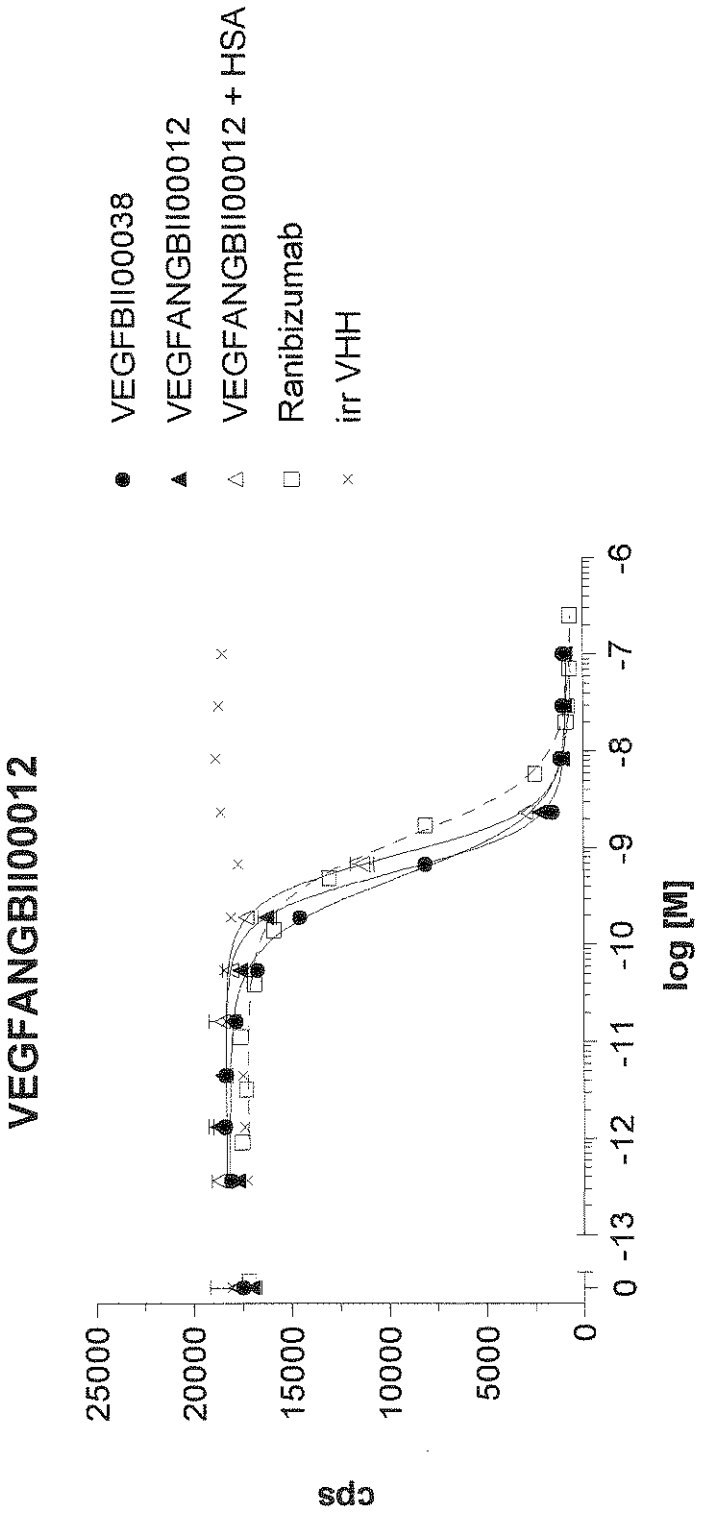

VEGFBII00038
VEGFANGBII00012
VEGFANGBII00012 + HSA
Ranibizumab
irr VHH
VEGFANGBII00012
cps
25000
20000
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 27-1H**

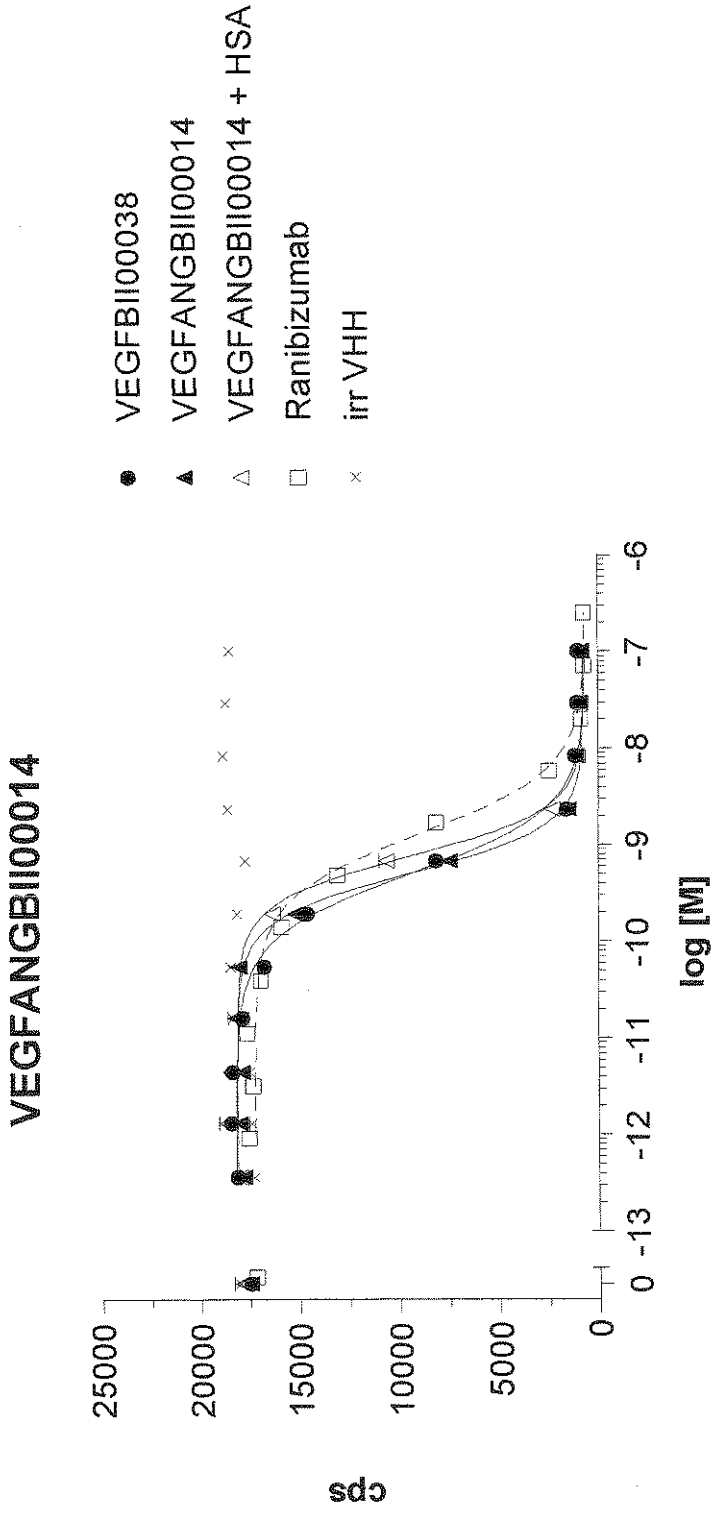

VEGFANGBII00014
VEGFBII00038
VEGFANGBII00014
VEGFANGBII00014 + HSA
Ranibizumab
irr VHH
cps
25000
20000
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 27-2A**

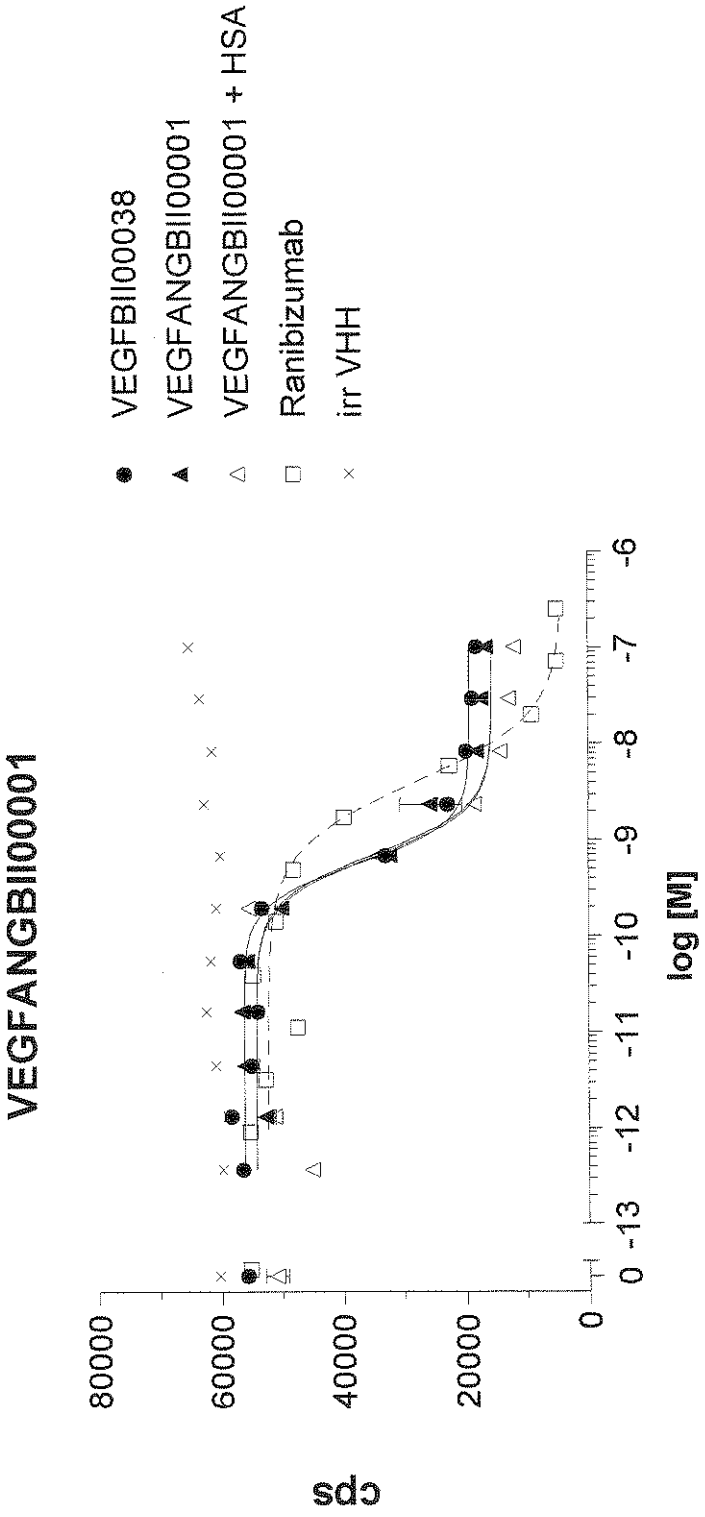

VEGFBII00038
VEGFANGBII00001
VEGFANGBII00001 + HSA
Ranibizumab
irr VHH
VEGFANGBII00001
cps
80000
60000
40000
20000
0
0
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 27-2B**

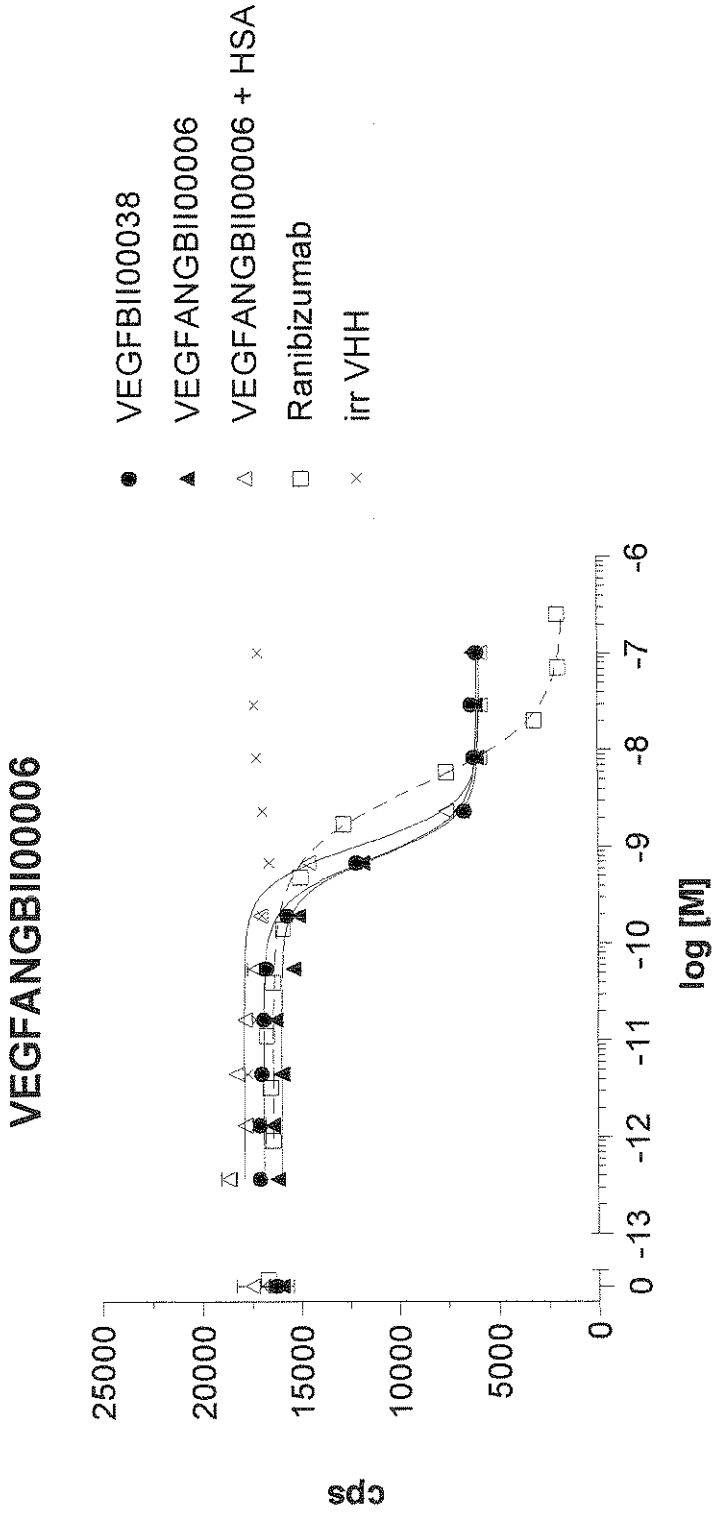

VEGFBII00038
VEGFANGBII00006
VEGFANGBII00006 + HSA
Ranibizumab
irr VHH
VEGFANGBII00006
cps
25000
20000
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

Figure 27-2C

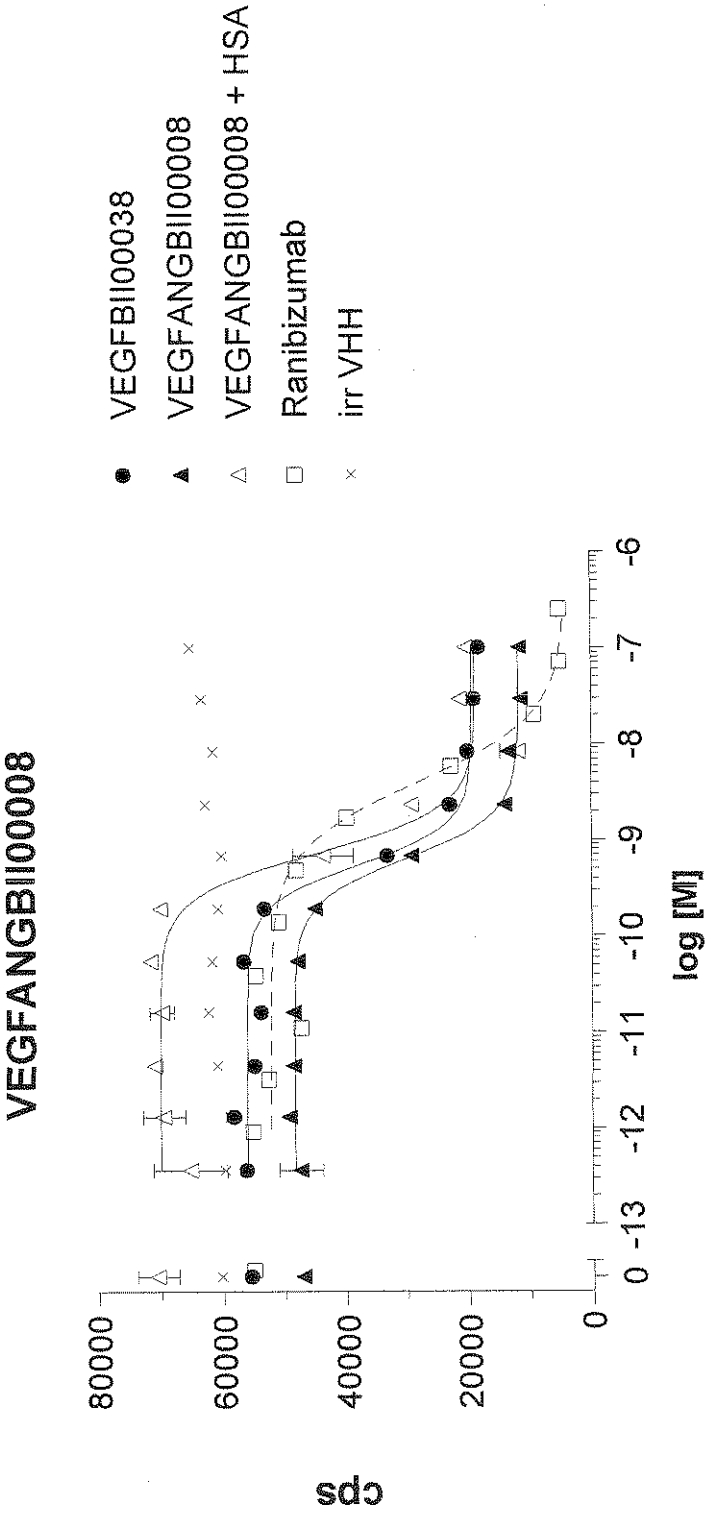

VEGFBII00038
VEGFANGBII00008
VEGFANGBII00008 + HSA
Ranibizumab
irr VHH
VEGFANGBII00008
cps
80000
60000
40000
20000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 27-2D**

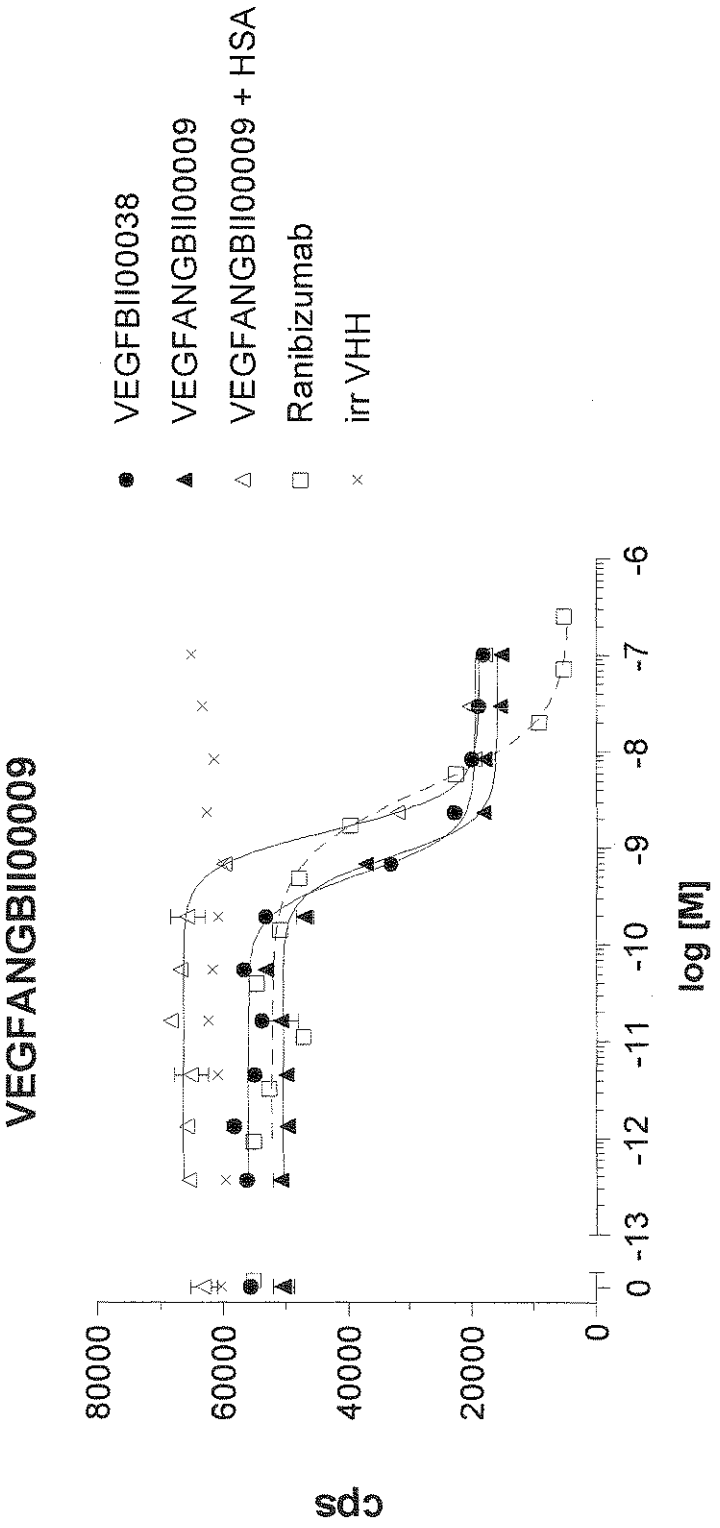

VEGFBII00038
VEGFANGBII00009
VEGFANGBII00009 + HSA
Ranibizumab
irr VHH
VEGFANGBII00009
cps
80000
60000
40000
20000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 27-2E**

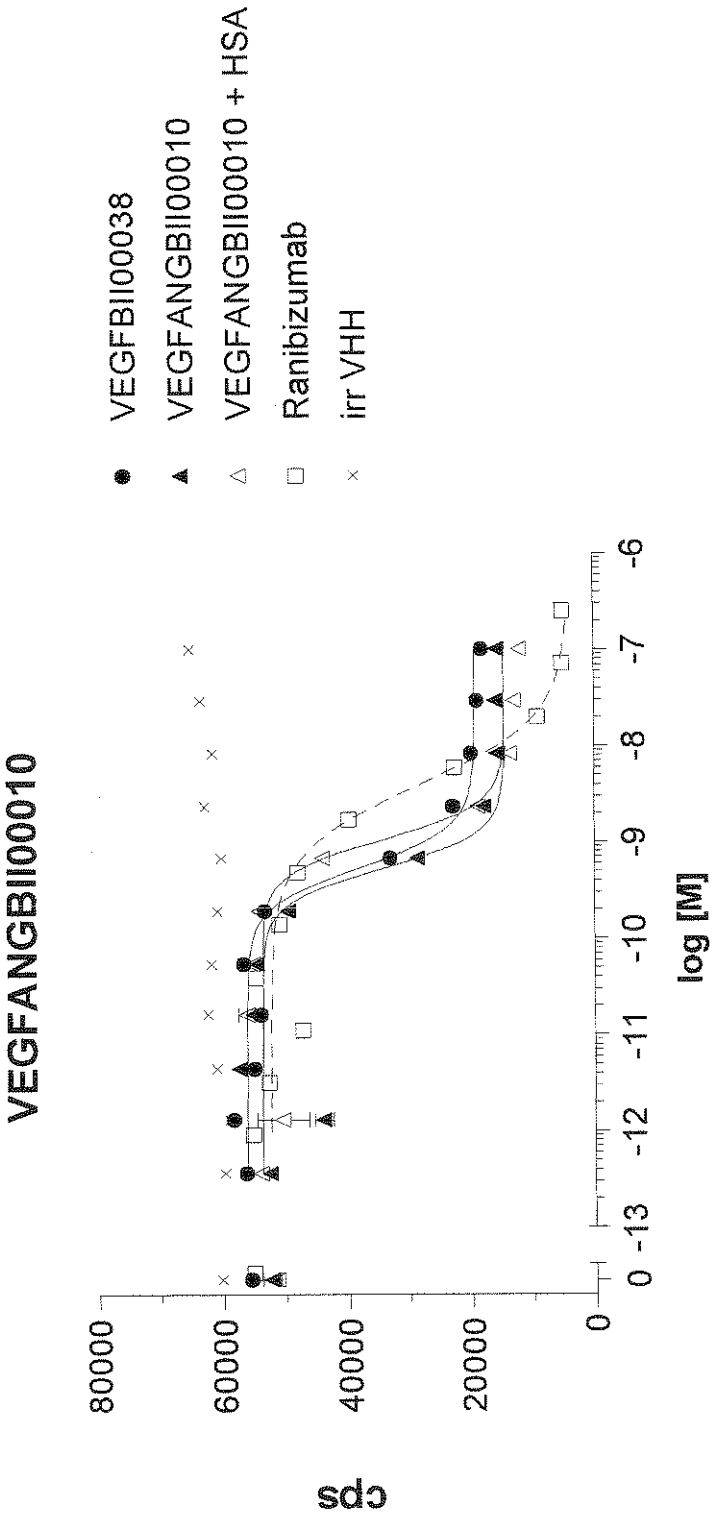

VEGFBII00038
VEGFANGBII00010
VEGFANGBII00010 + HSA
Ranibizumab
irr VHH
VEGFANGBII00010
cps
80000
60000
40000
20000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

Figure 27-2F

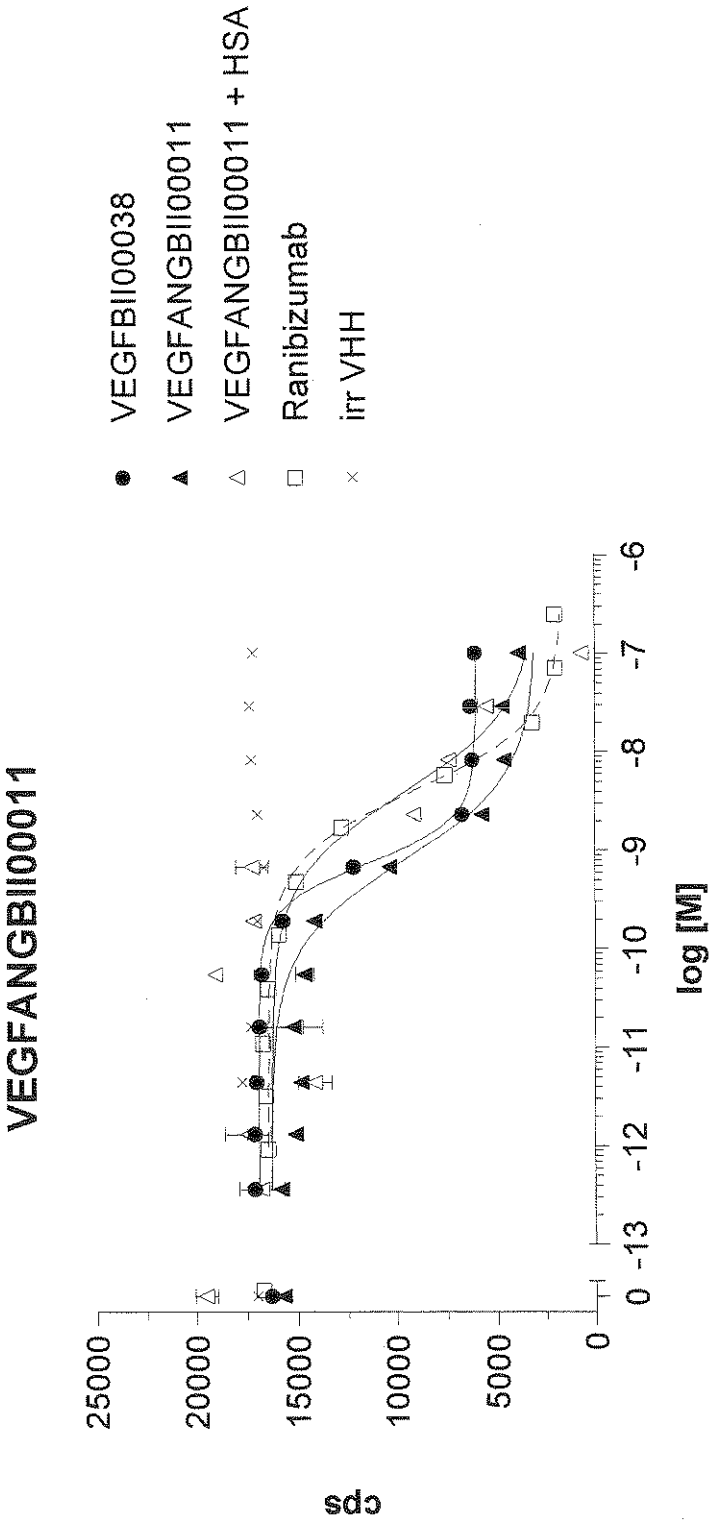

VEGFBII00038
VEGFANGBII00011
VEGFANGBII00011 + HSA
Ranibizumab
irr VHH
VEGFANGBII00011
cps
25000
20000
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 27-2G**

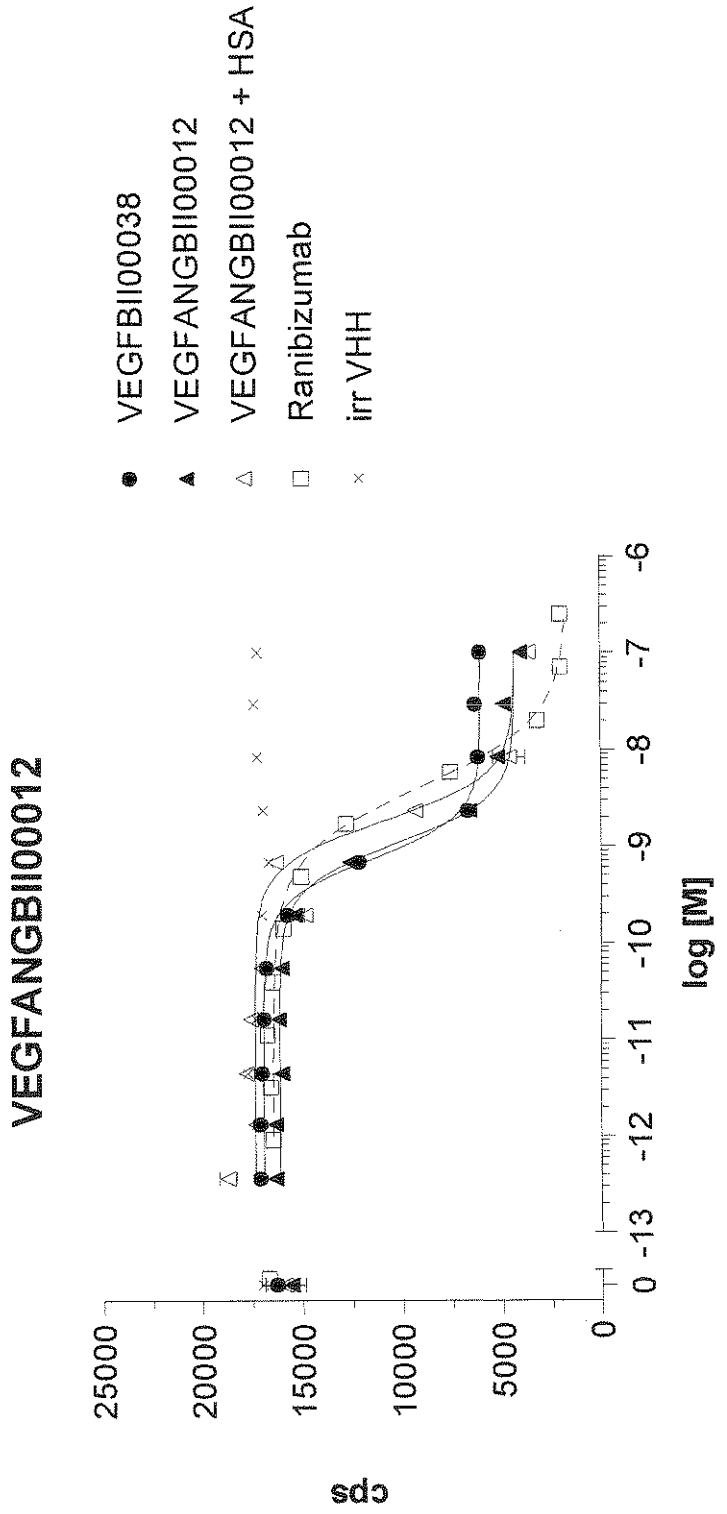

VEGFANGBII00012
VEGFBII00038
VEGFANGBII00012
VEGFANGBII00012 + HSA
Ranibizumab
irr VHH
cps
25000
20000
15000
10000
5000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 27-2H**

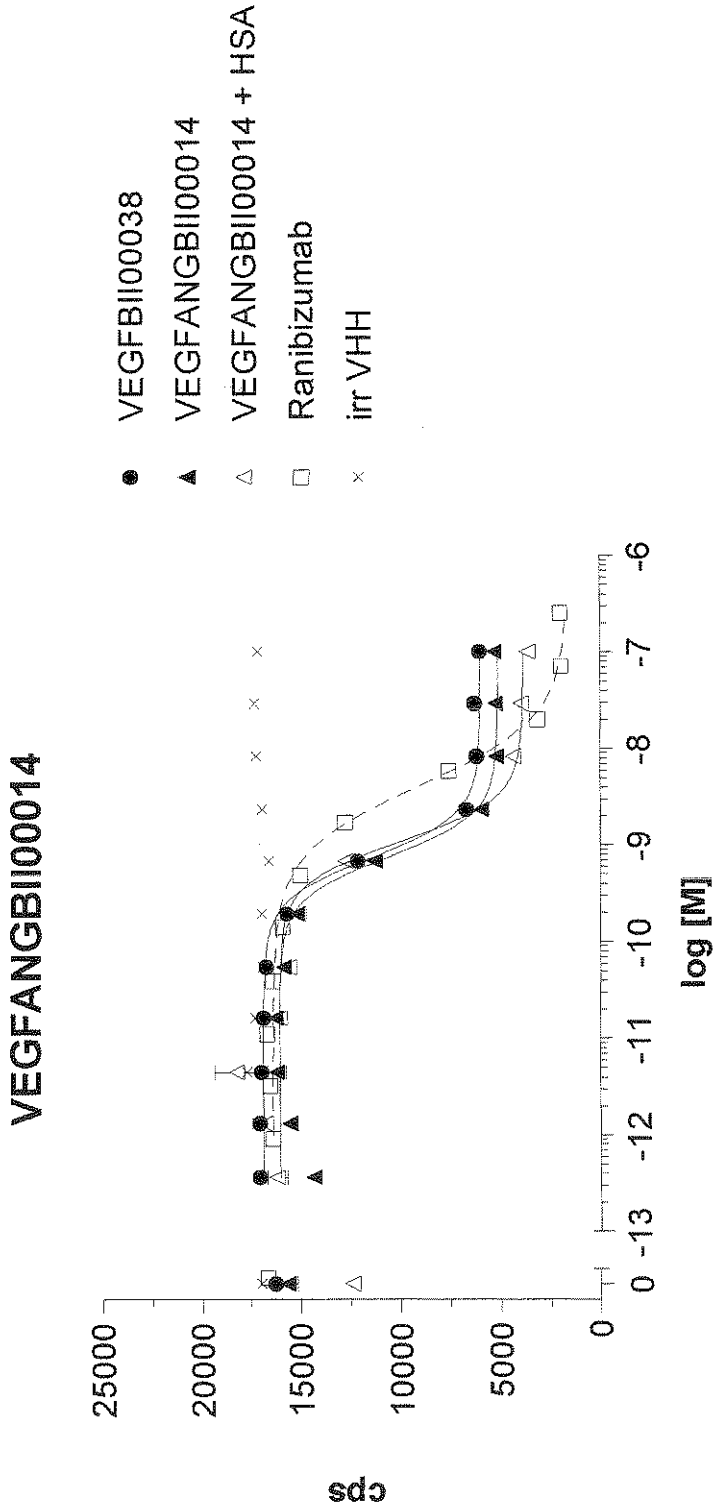

VEGFANGBII00014
VEGFBII00038
VEGFANGBII00014
VEGFANGBII00014 + HSA
Ranibizumab
irr VHH
cps
25000
20000
15000
10000
5000
0
0
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 28-1A

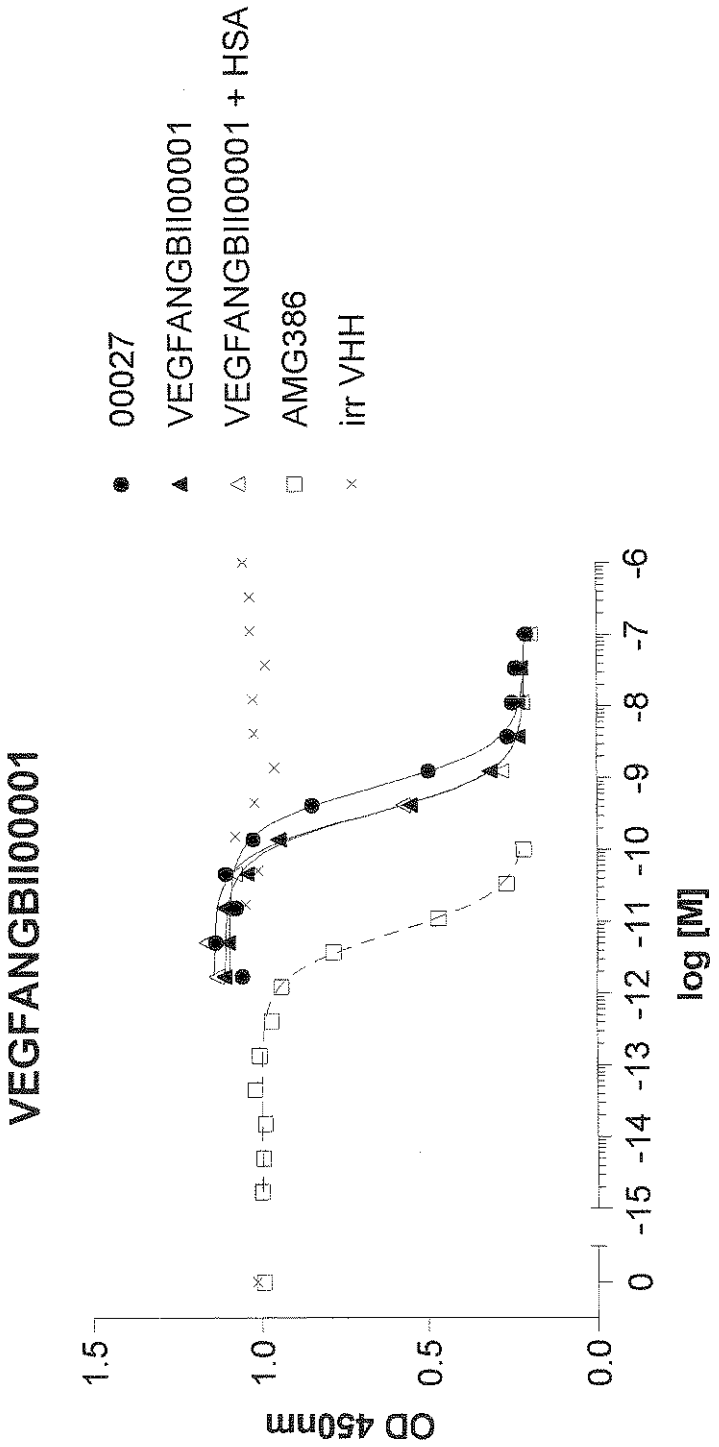

00027
VEGFANGBII00001
VEGFANGBII00001 + HSA
AMG386
irr VHH
VEGFANGBII00001
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-1B**

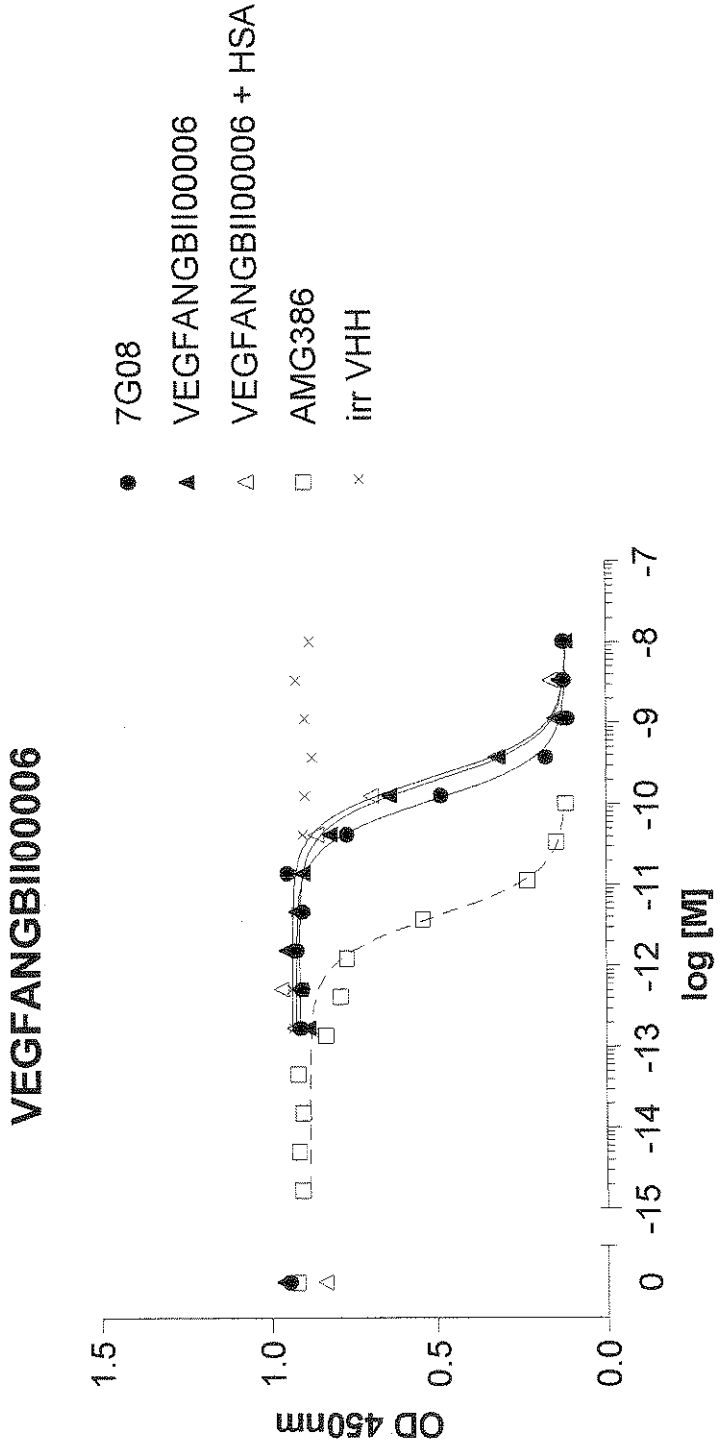

VEGFANGBII00006
7G08
VEGFANGBII00006
VEGFANGBII00006 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
log [M]

**Figure 28-1C**

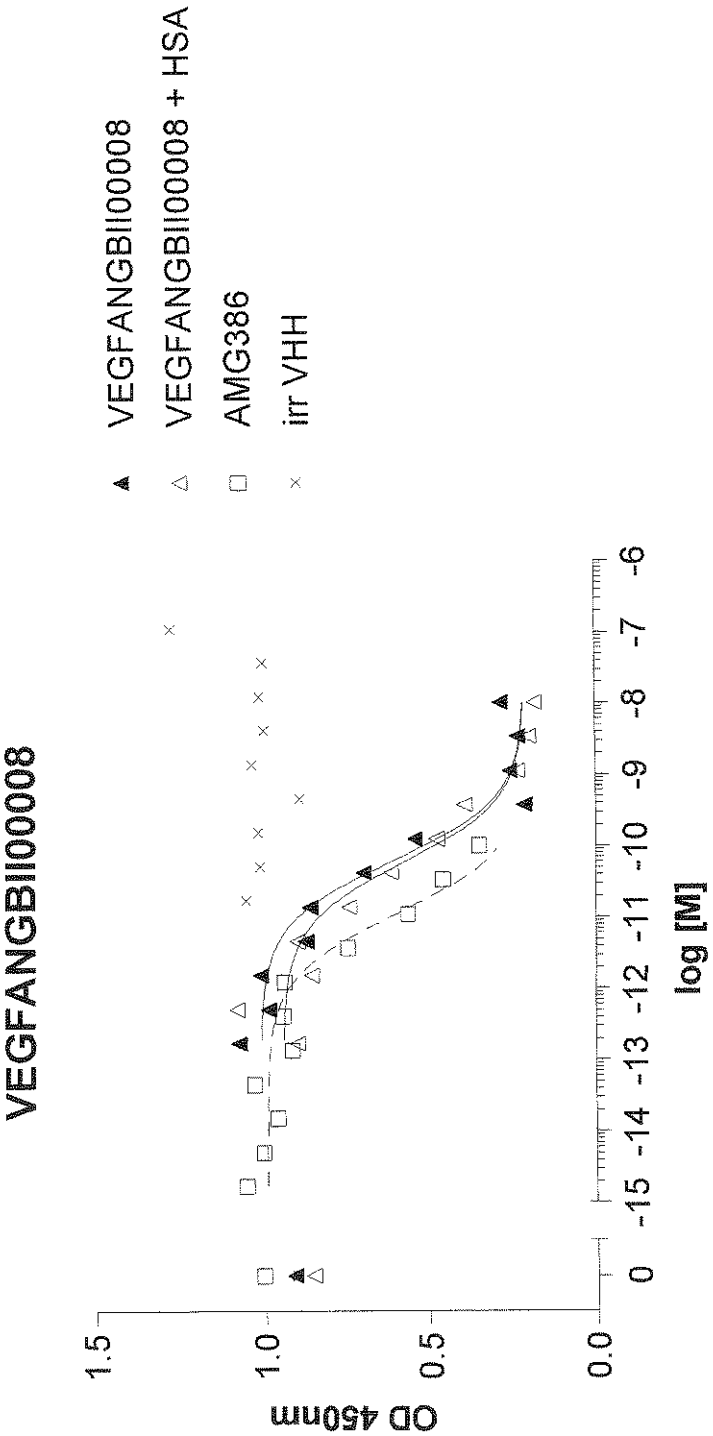

VEGFANGBII00008
VEGFANGBII00008
VEGFANGBII00008 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-1D**

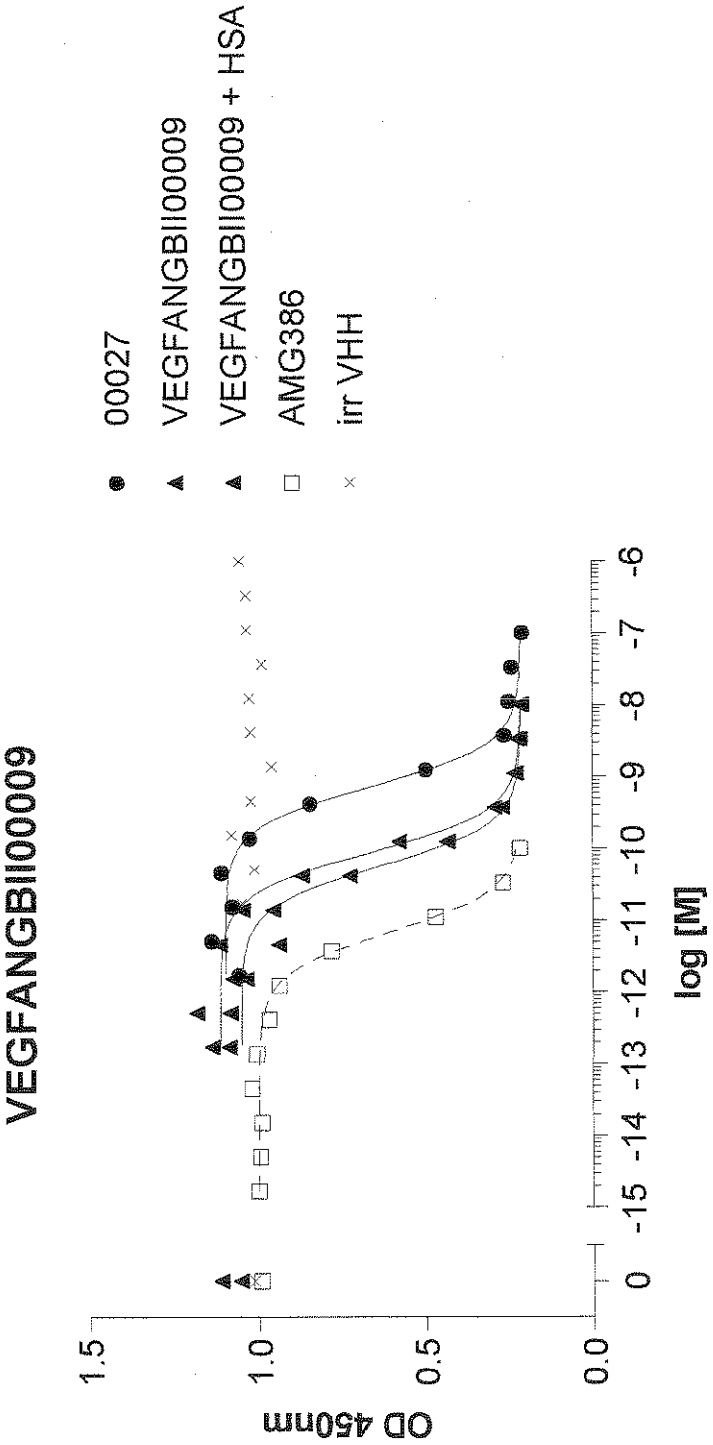

VEGFANGBII00009
00027
VEGFANGBII00009
VEGFANGBII00009 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-1E**

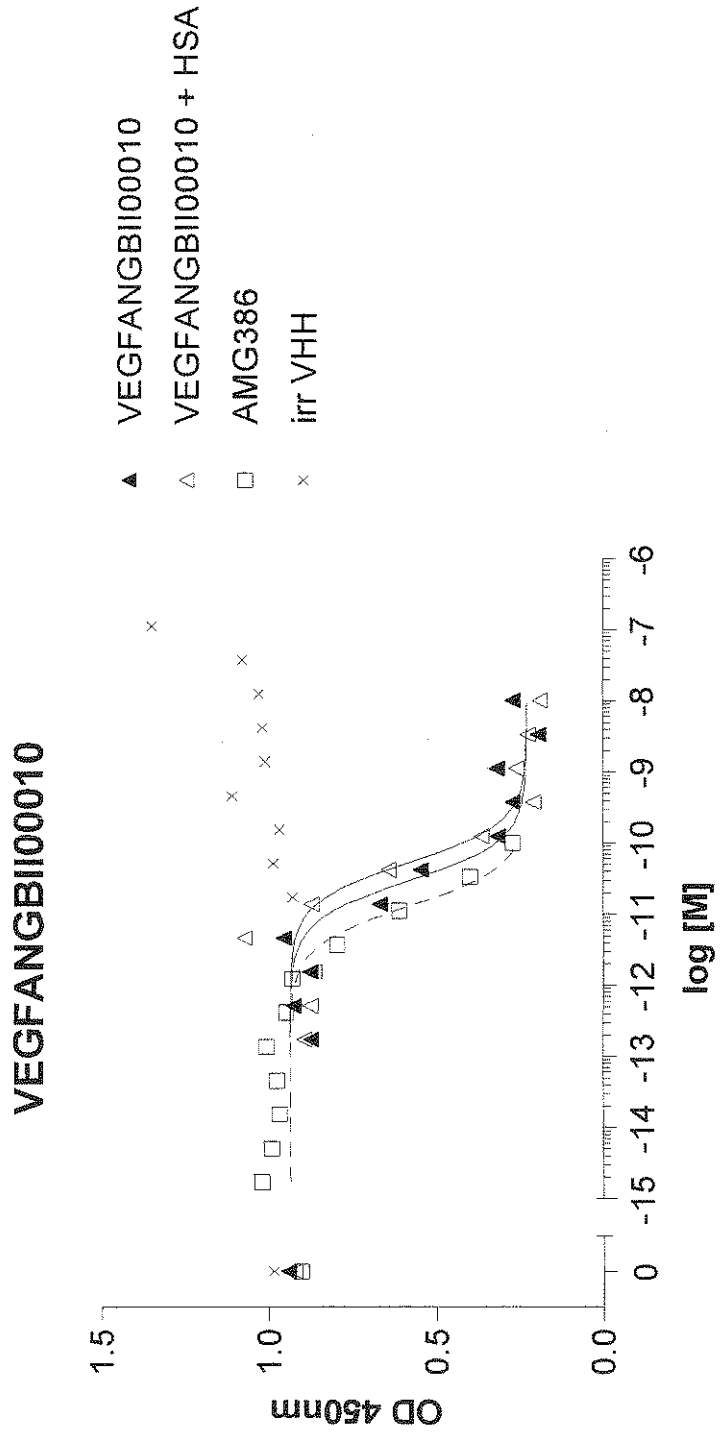

VEGFANGBII00010
VEGFANGBII00010 + HSA
AMG386
irr VHH
VEGFANGBII00010
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-1F**

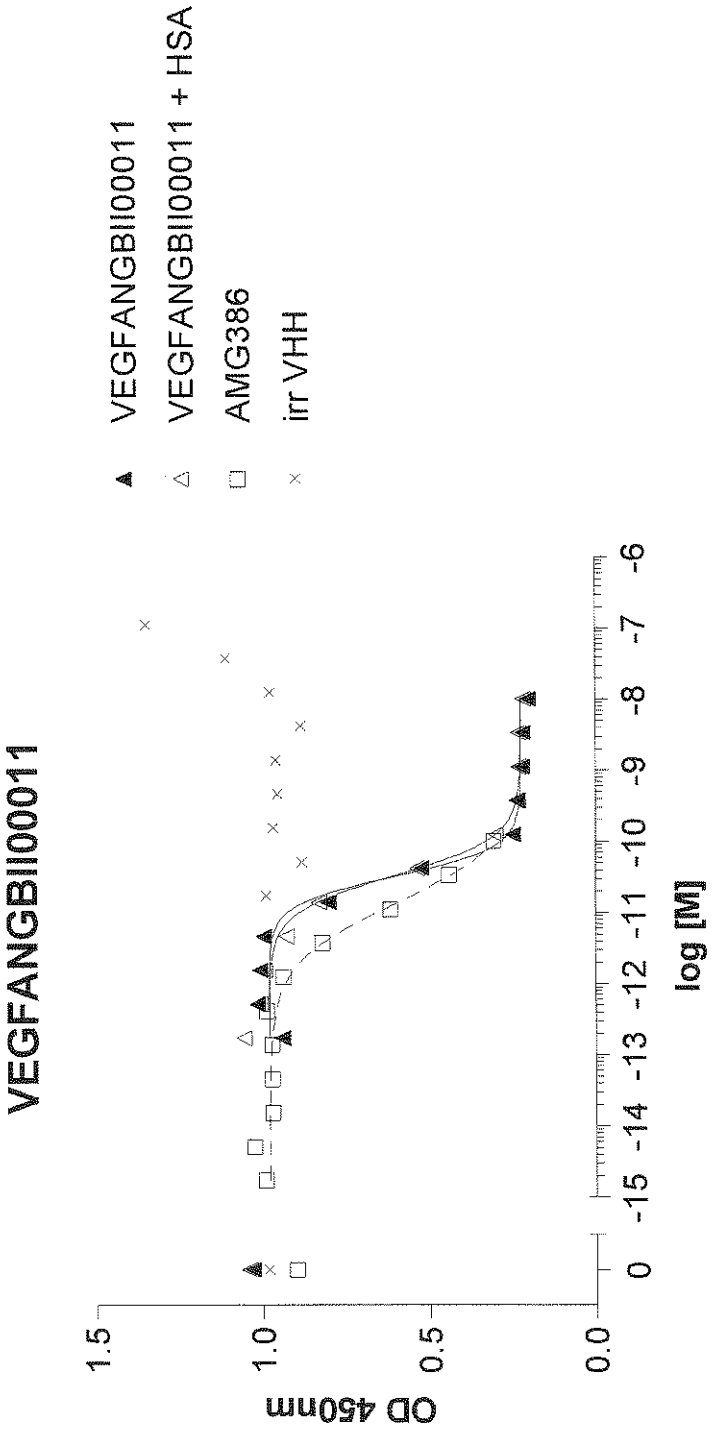

VEGFANGBII00011
VEGFANGBII00011
VEGFANGBII00011 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-1G**

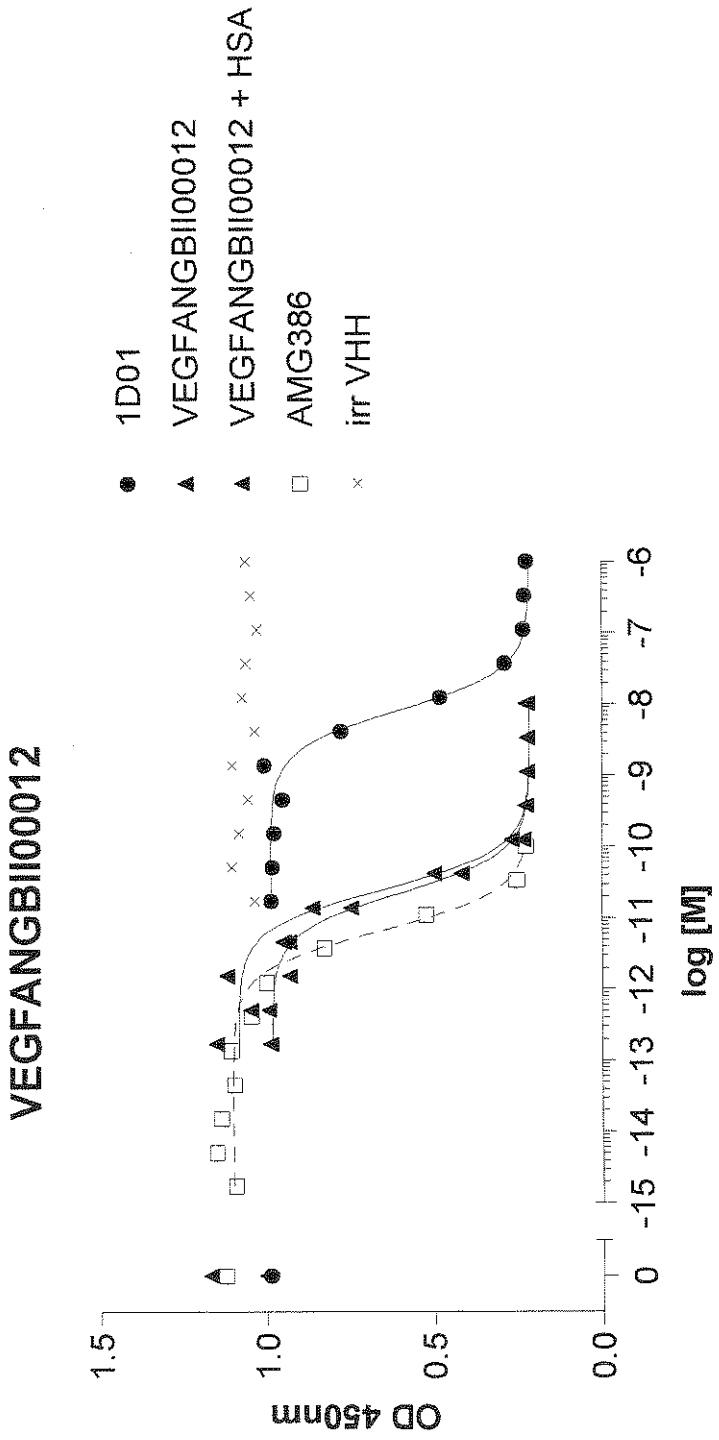

VEGFANGBII00012
1D01
VEGFANGBII00012
VEGFANGBII00012 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-1H**

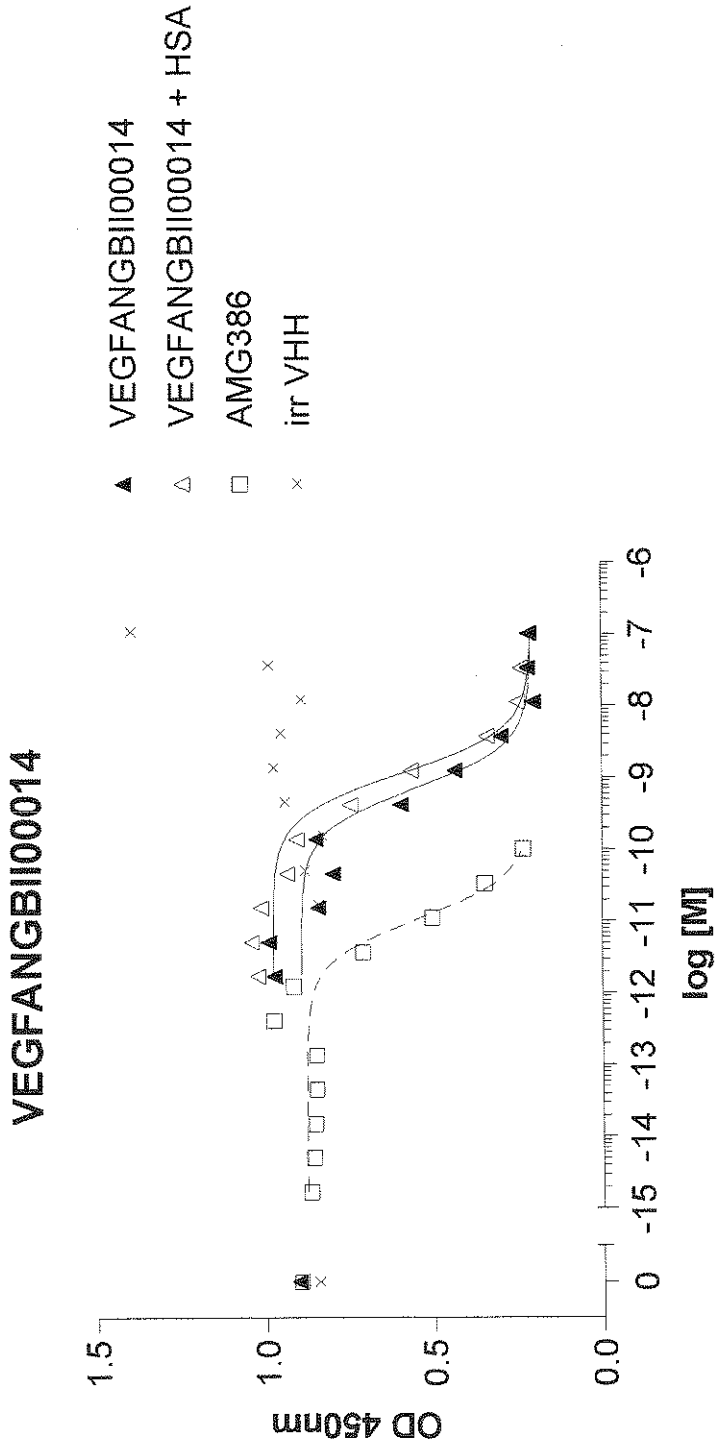

VEGFANGBII00014
VEGFANGBII00014
VEGFANGBII00014 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 28-2A

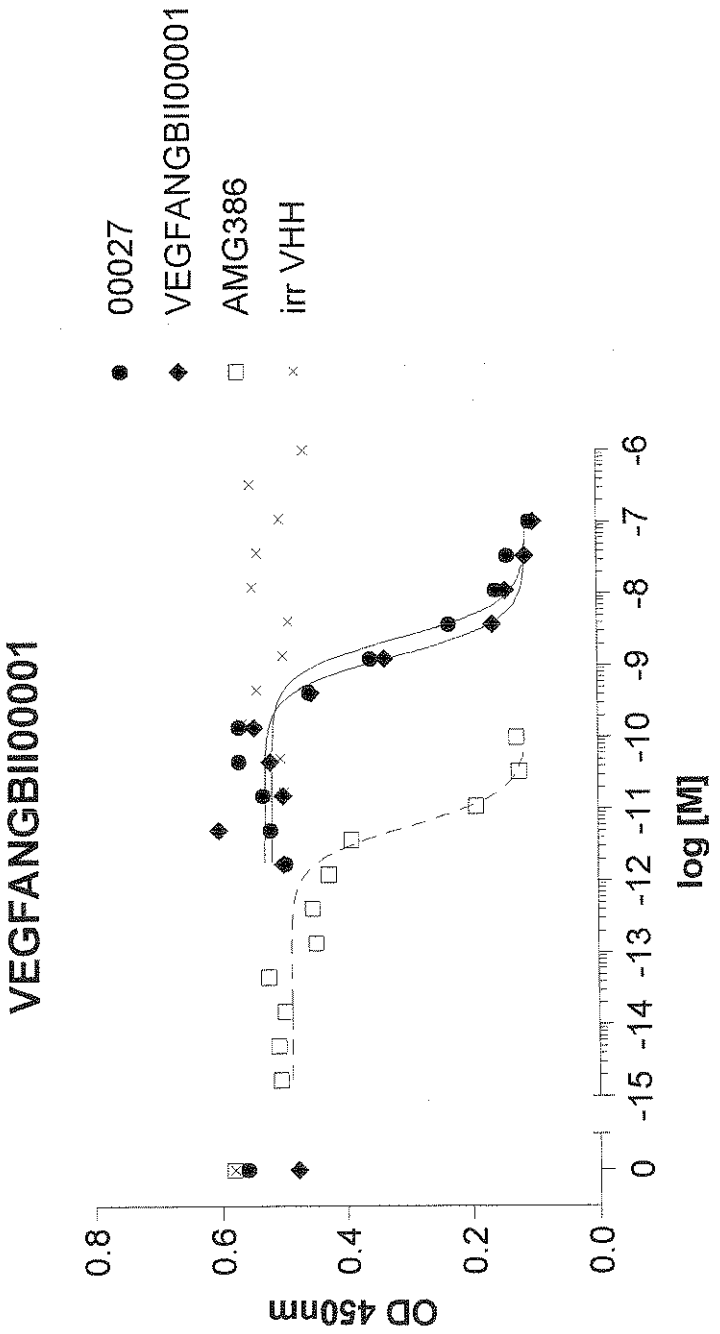

VEGFANGBII00001
00027
VEGFANGBII00001
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-2B**

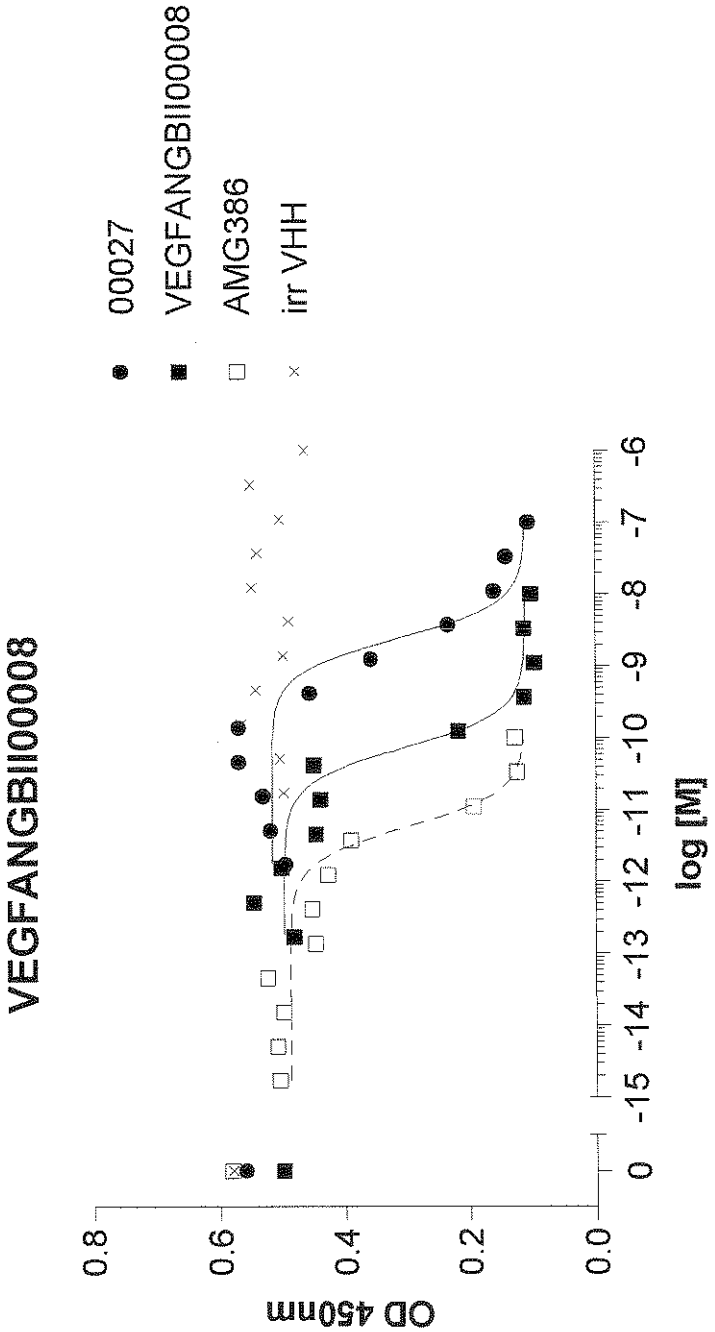

VEGFANGBII00008
00027
VEGFANGBII00008
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6

**Figure 28-2C**

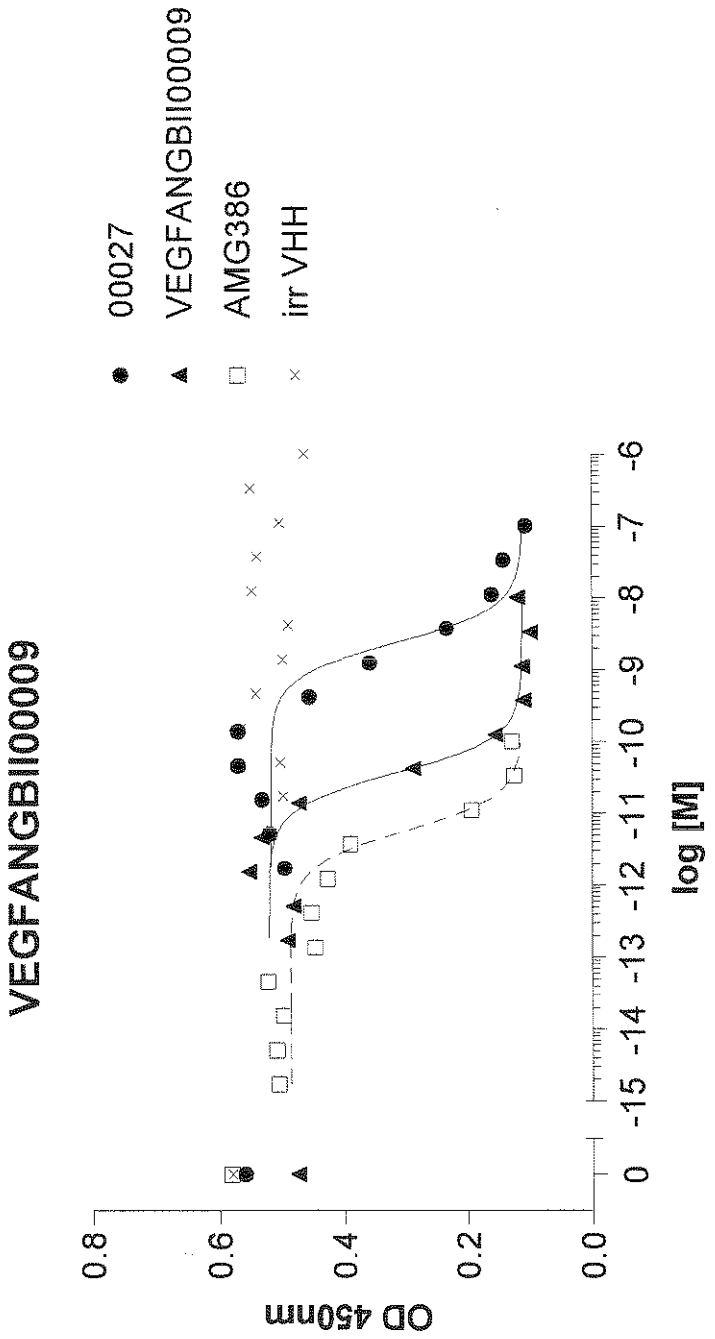

VEGFANGBII00009
00027
VEGFANGBII00009
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-2D**

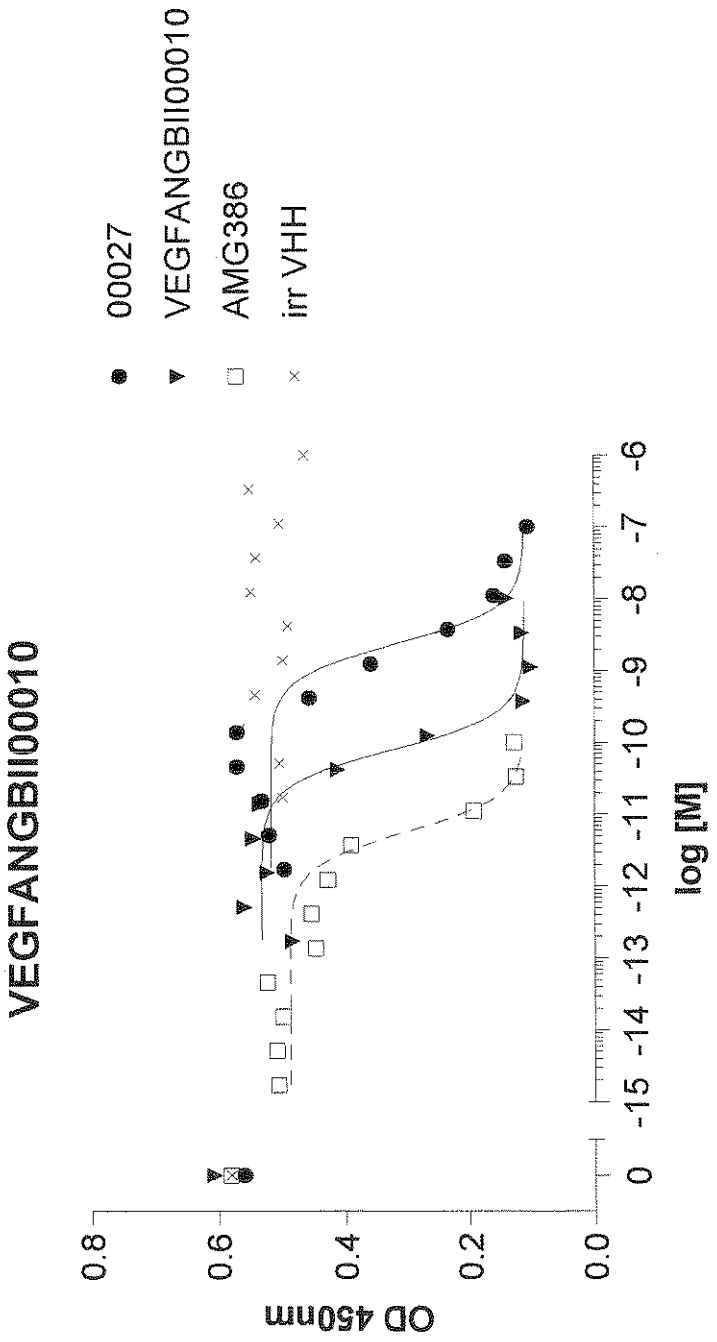

VEGFANGBII00010
00027
VEGFANGBII00010
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-2E**

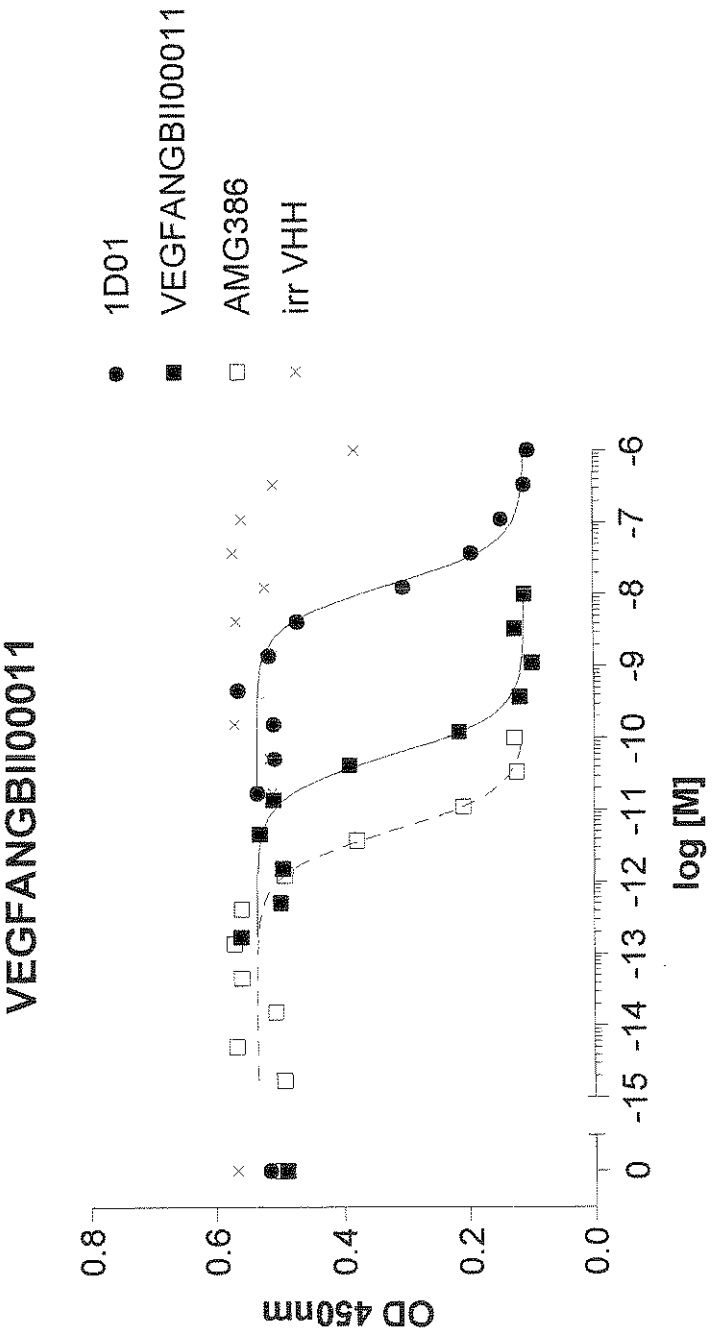

VEGFANGBII00011
1D01
VEGFANGBII00011
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-2F**

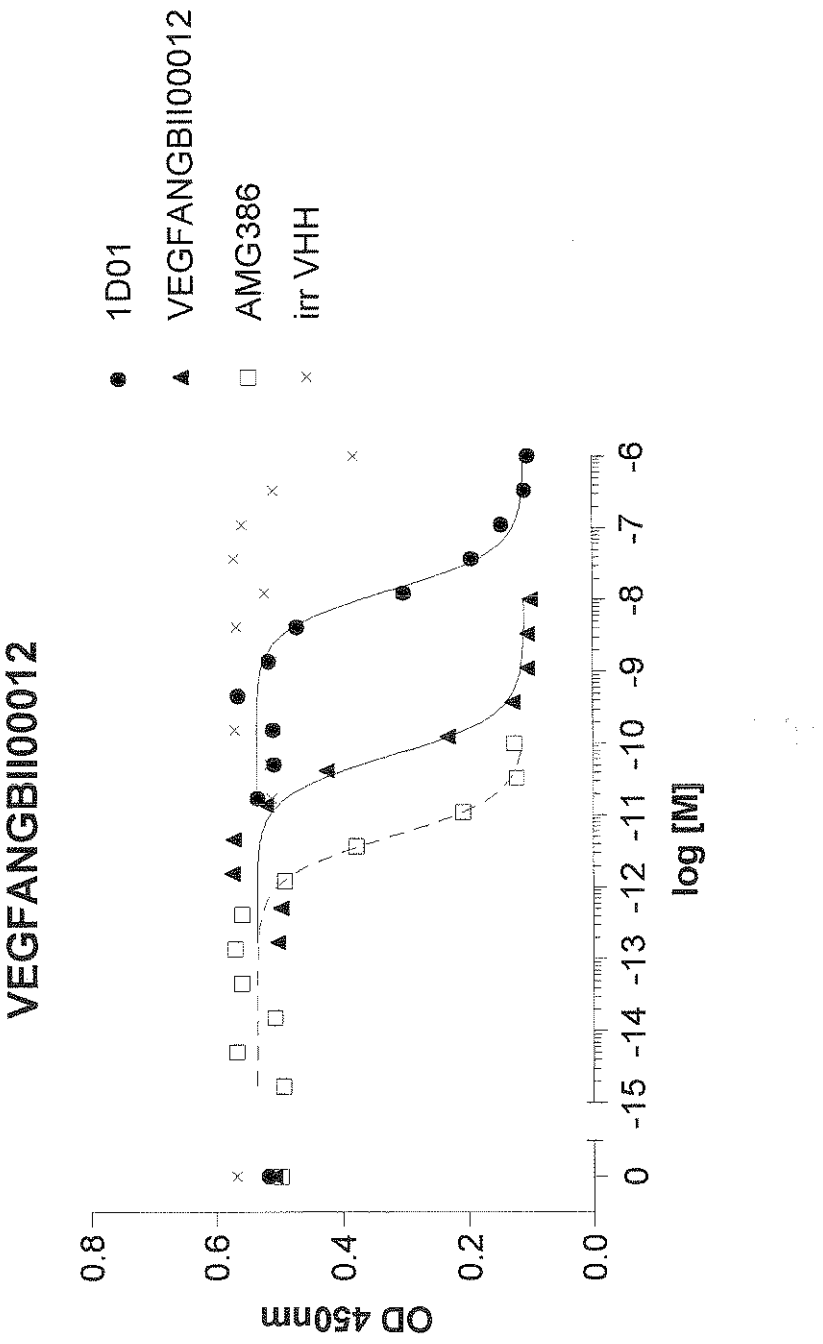

VEGFANGBII00012
1D01
VEGFANGBII00012
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 28-2G

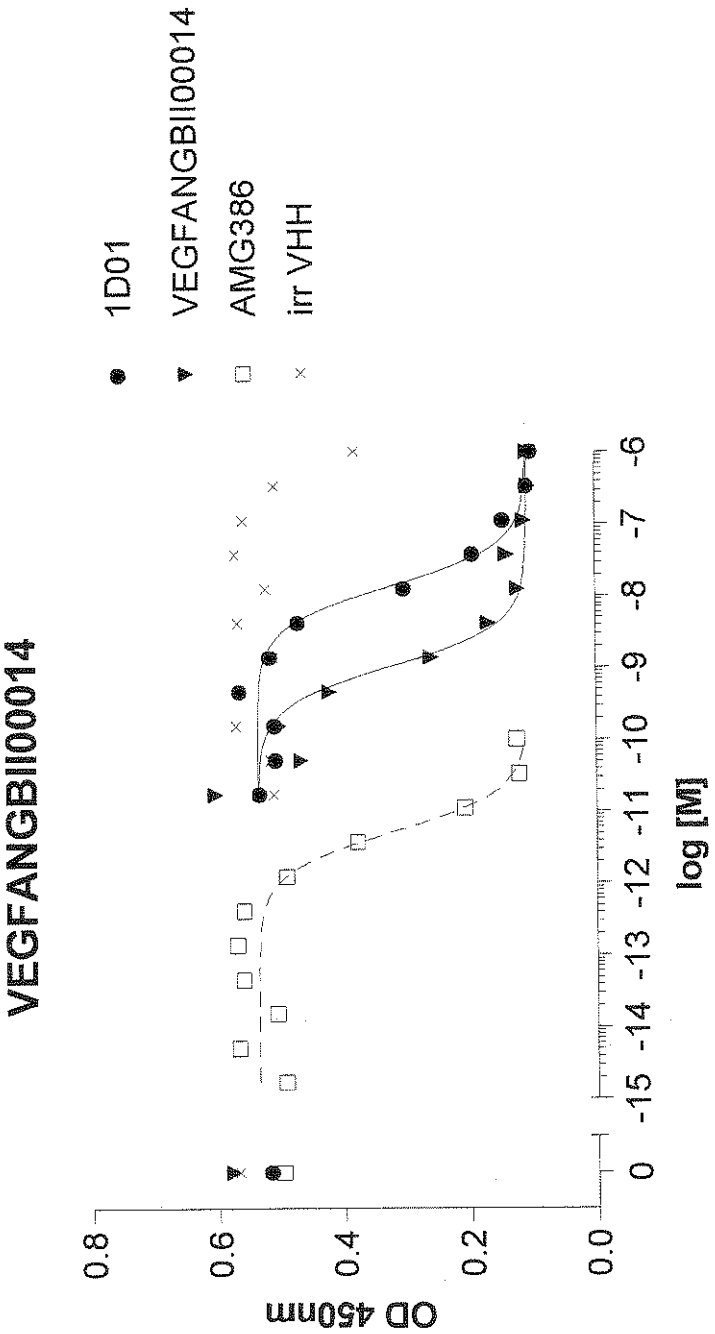

VEGFANGBII00014
1D01
VEGFANGBII00014
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6

Figure 28-3A

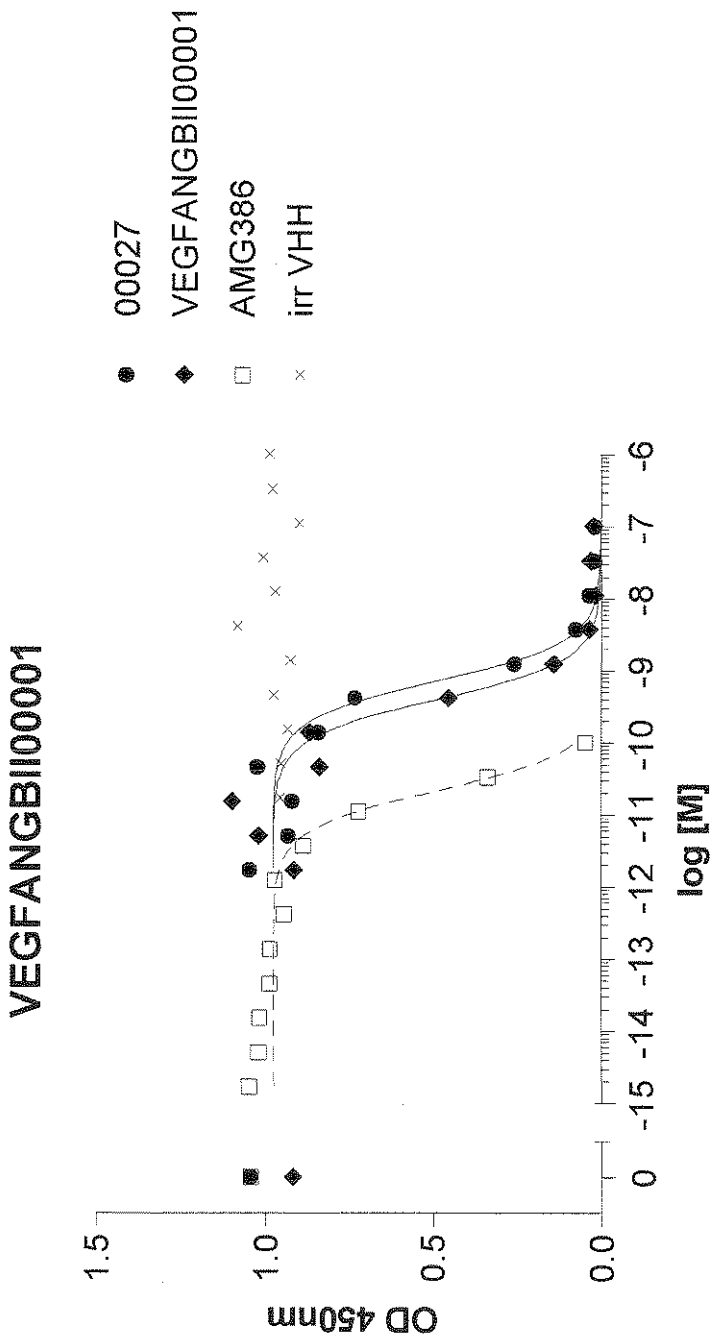

VEGFANGBII00001
00027
VEGFANGBII00001
AMG386
irr VHH
OD 450nm
0.0
0.5
1.0
1.5
log [M]
0
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15

**Figure 28-3B**

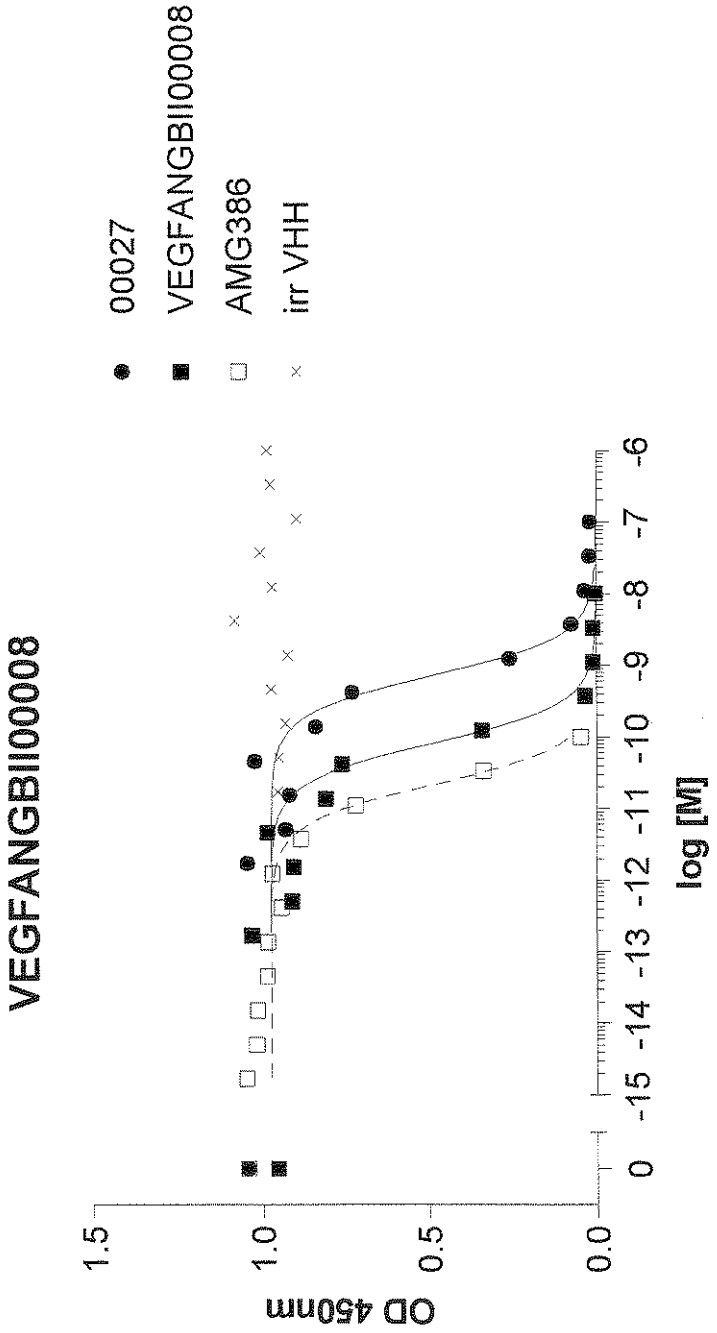

00027
VEGFANGBII00008
AMG386
irr VHH
VEGFANGBII00008
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-3C**

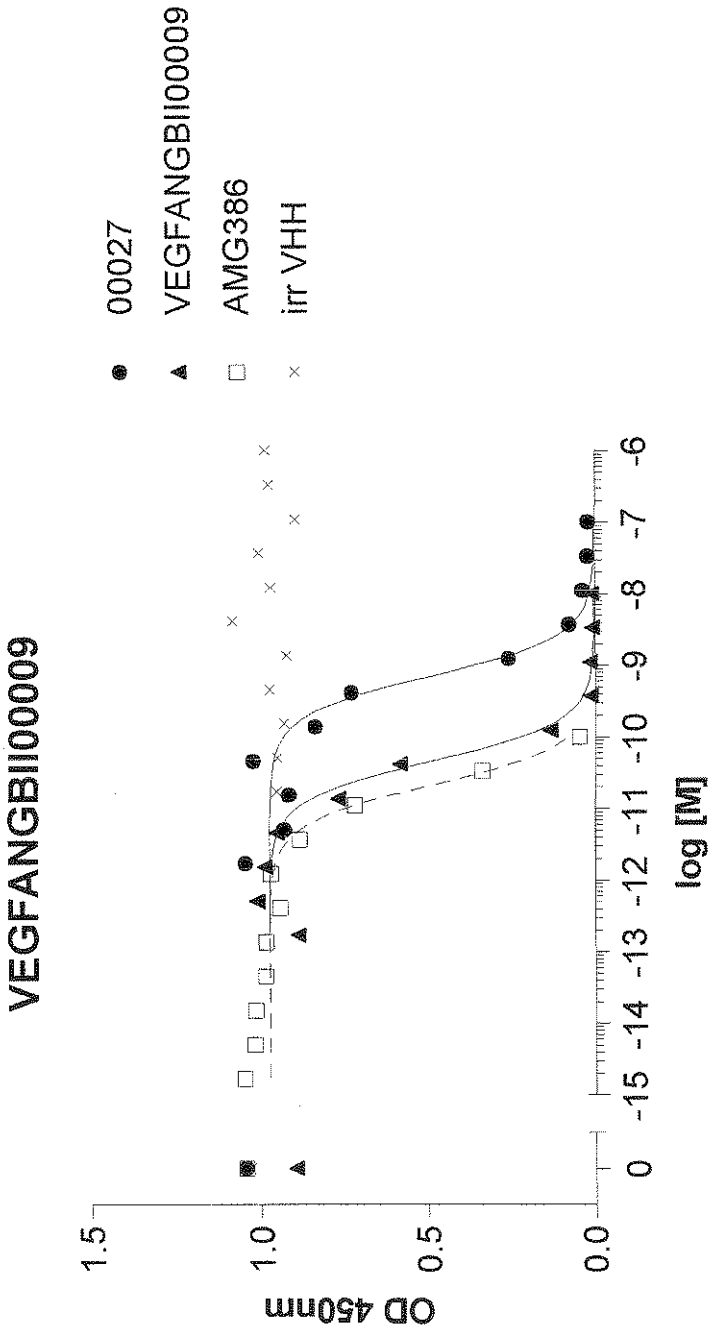

VEGFANGBII00009
00027
VEGFANGBII00009
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-3D**

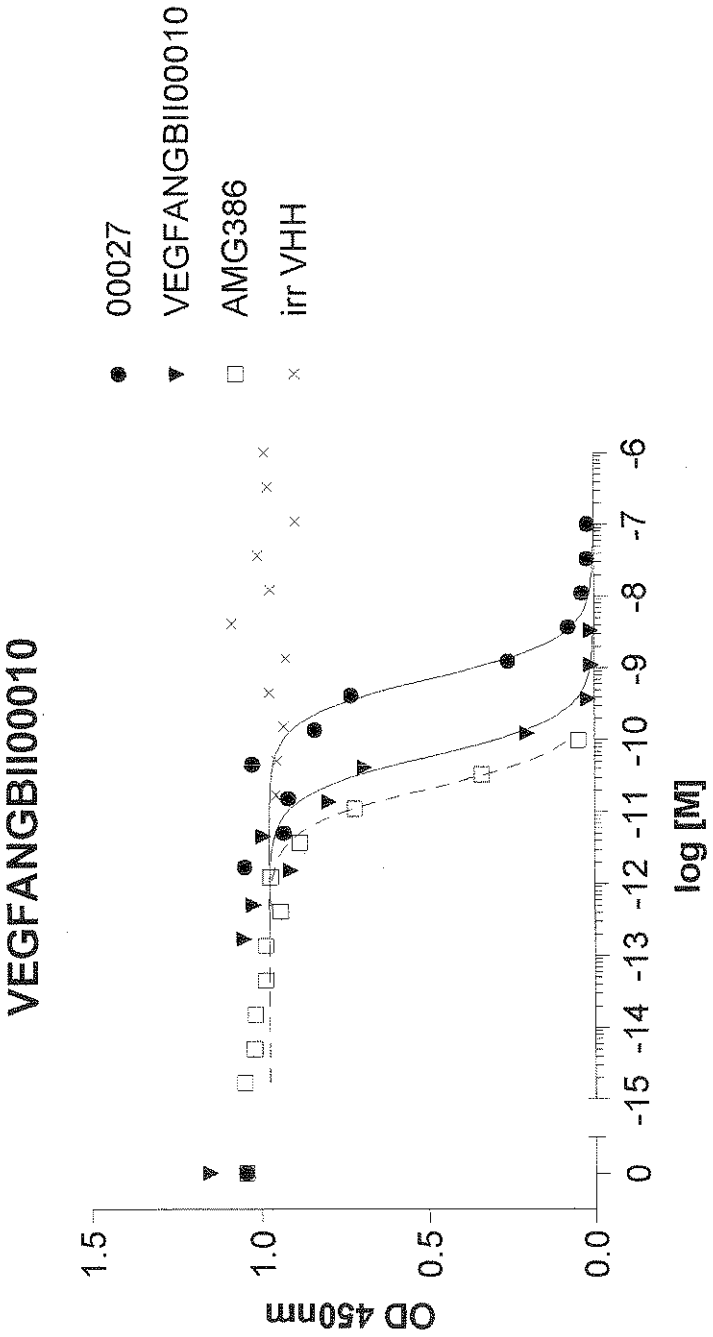

VEGFANGBII00010
00027
VEGFANGBII00010
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 28-3E**

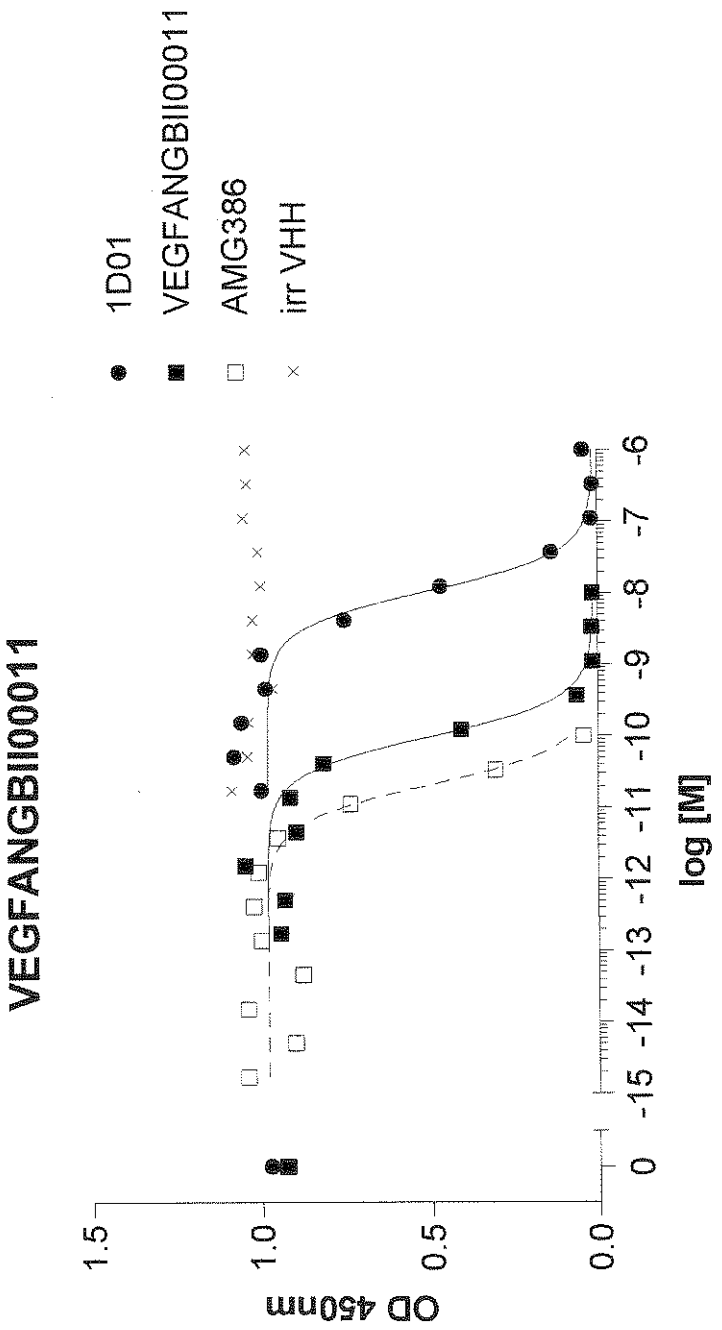

1D01
VEGFANGBII00011
AMG386
irr VHH
VEGFANGBII00011
OD 450nm
0.0
0.5
1.0
1.5
log [M]
0
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15

**Figure 28-3F**

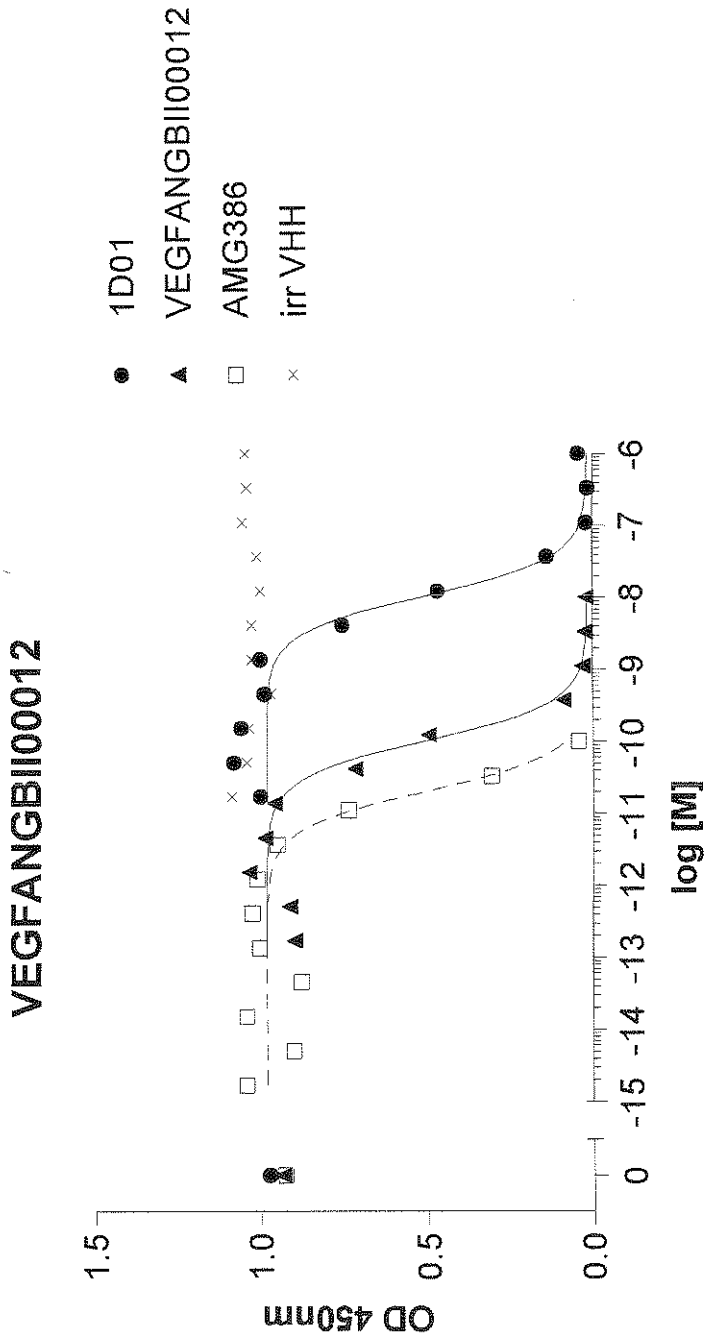

VEGFANGBII00012
1D01
VEGFANGBII00012
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 28-3G

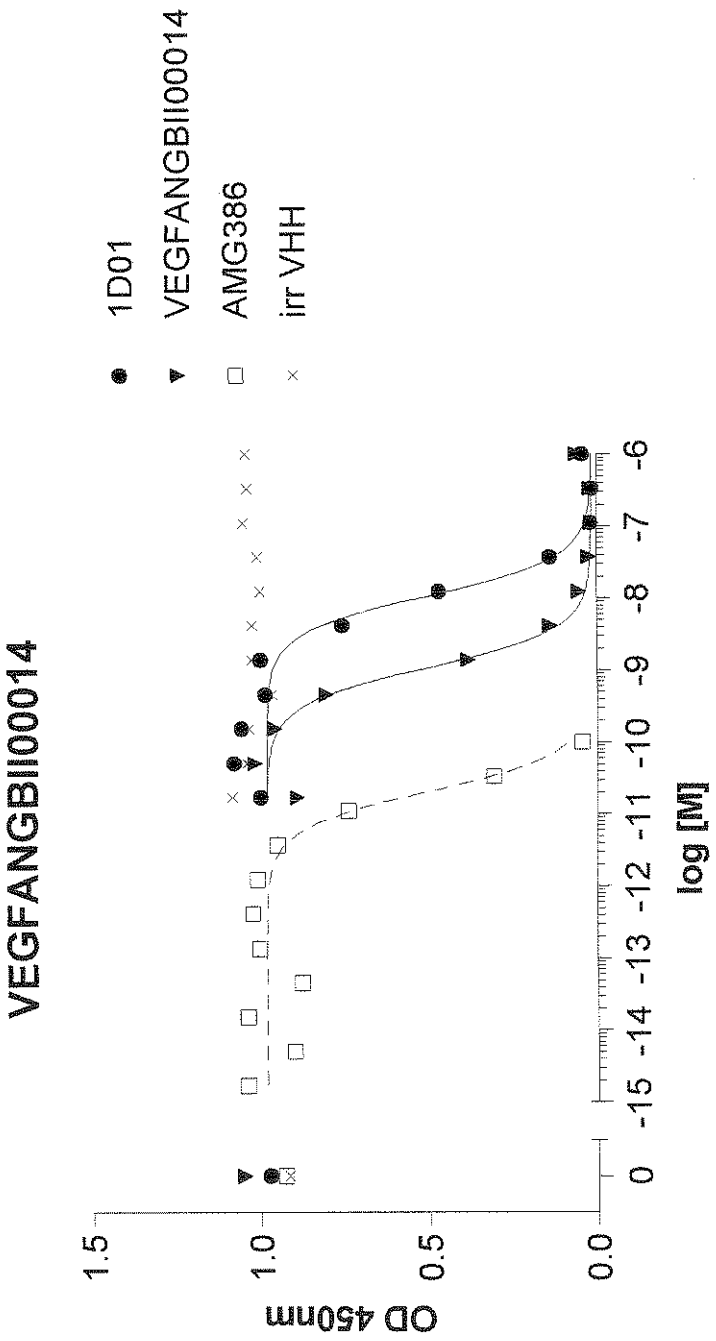

VEGFANGBII00014
1D01
VEGFANGBII00014
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 29A

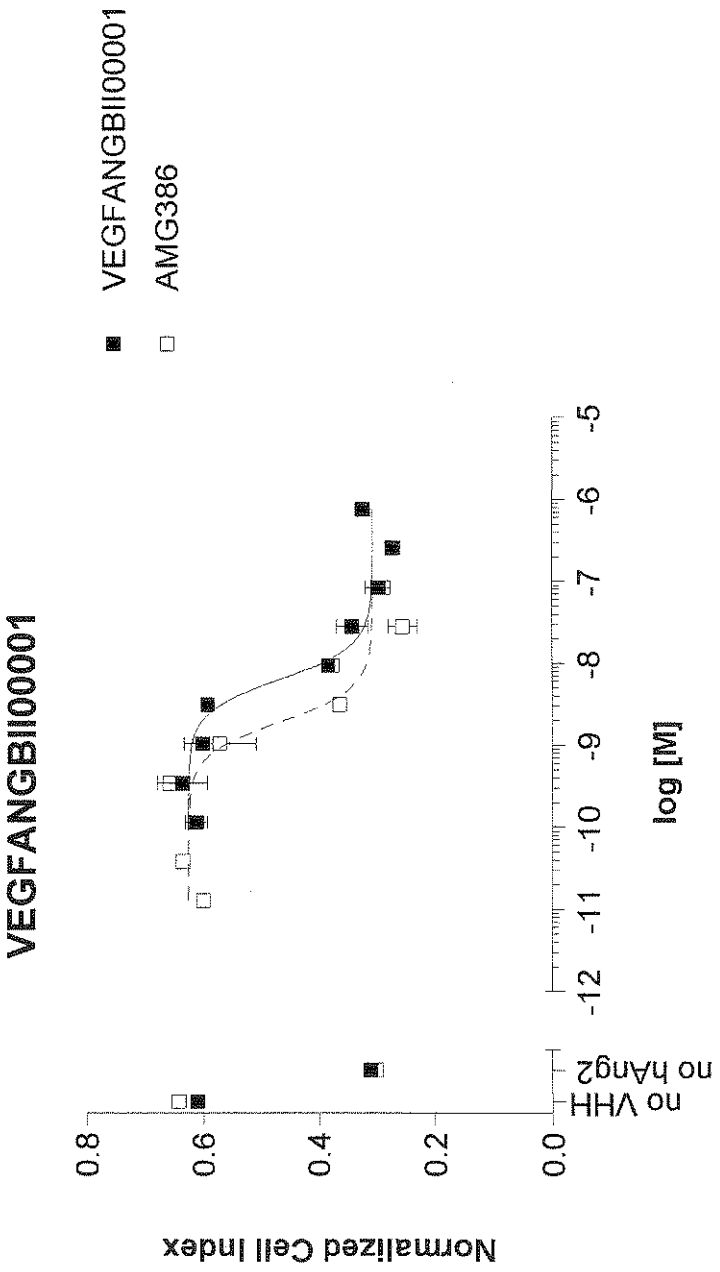

VEGFANGBII00001
AMG386
VEGFANGBII00001
Normalized Cell Index
0.0
0.2
0.4
0.6
0.8
no VHH
no hAng2
-12
-11
-10
-9
-8
-7
-6
-5
log [M]

**Figure 29B**

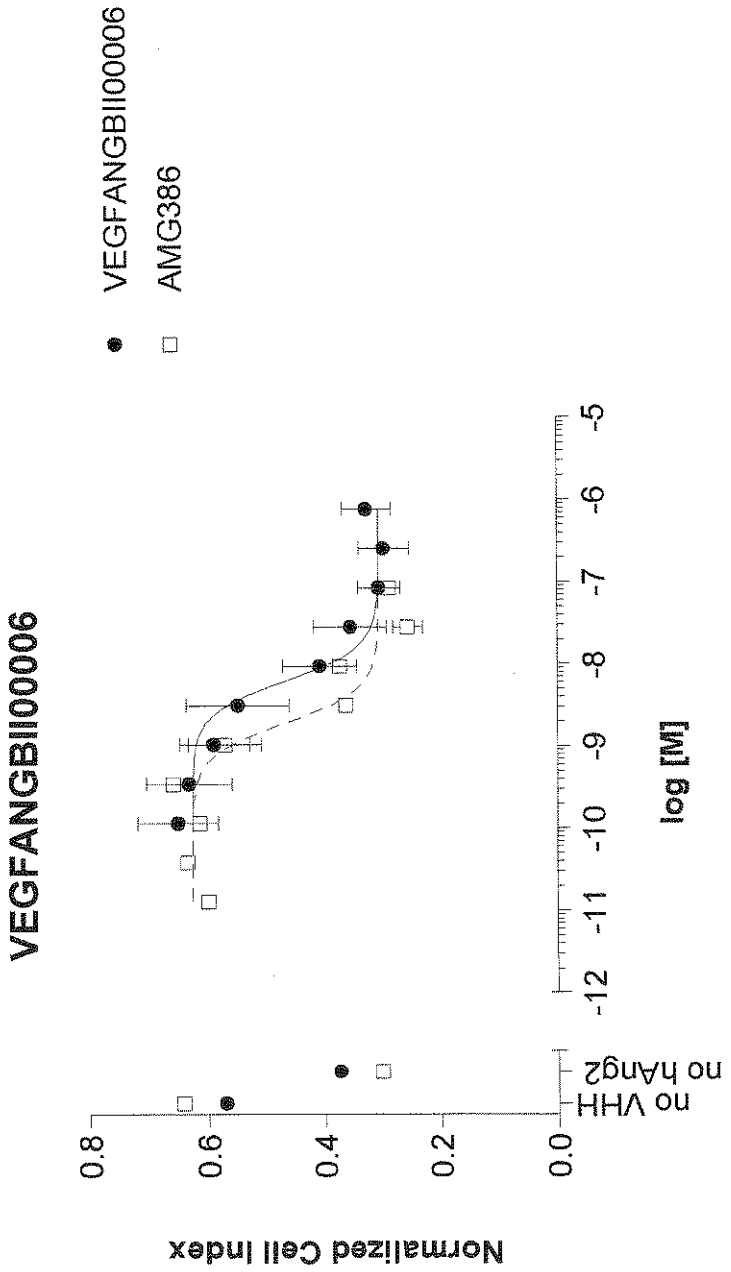

VEGFANGBII00006
VEGFANGBII00006
AMG386
Normalized Cell Index
0.0
0.2
0.4
0.6
0.8
no VHH
no hAng2
-12
-11
-10
-9
-8
-7
-6
-5
log [M]

**Figure 29C**

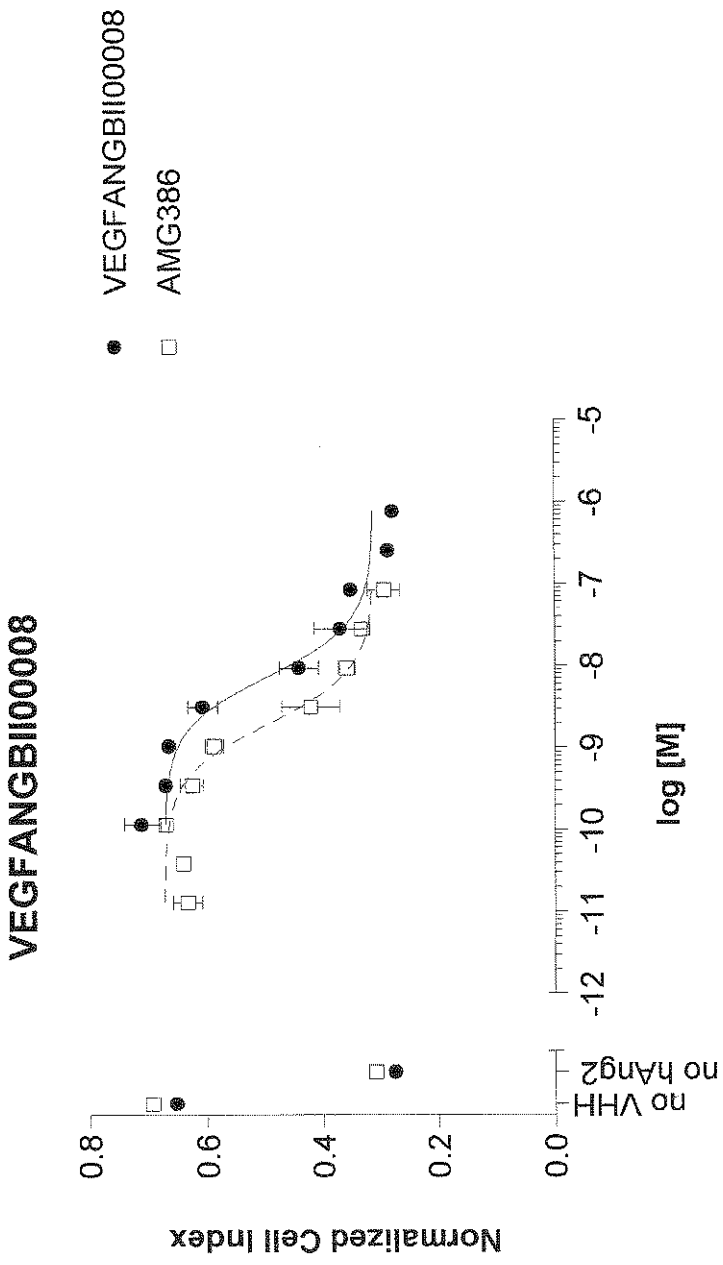

VEGFANGBII00008
VEGFANGBII00008
AMG386
Normalized Cell Index
0.0
0.2
0.4
0.6
0.8
no VHH
no hAng2
-12
-11
-10
-9
-8
-7
-6
-5
log [M]

**Figure 29D**

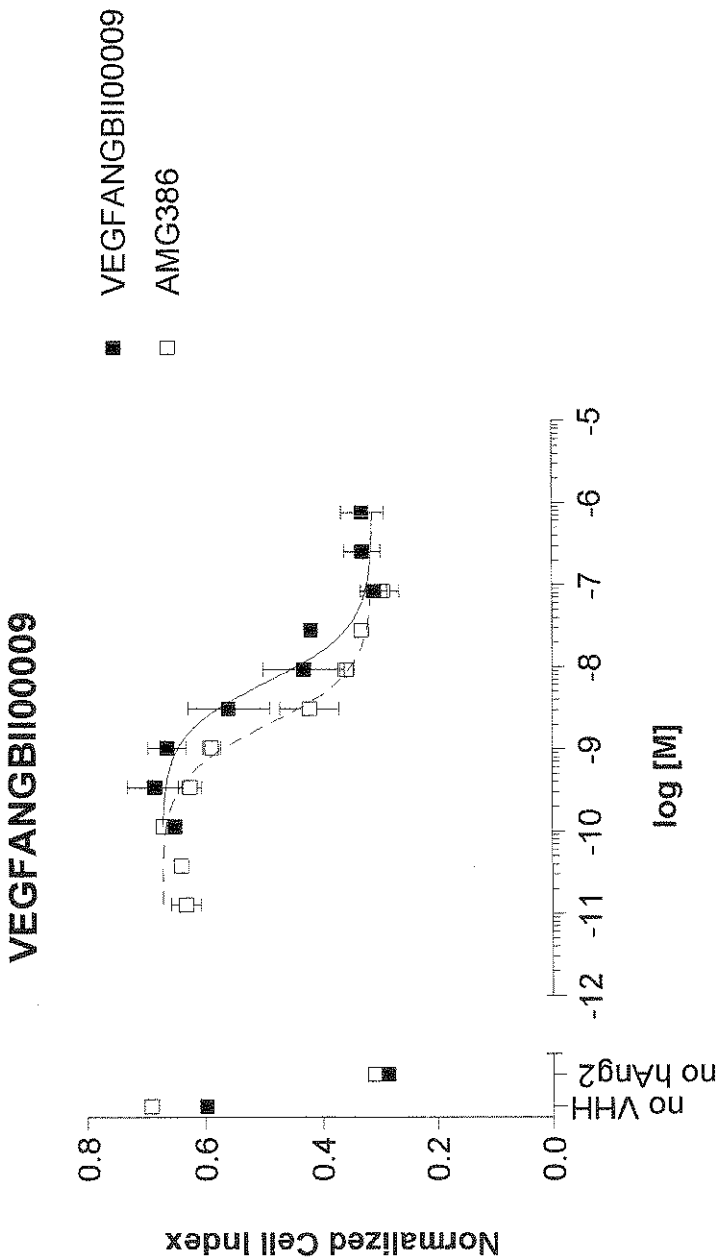

VEGFANGBII00009
VEGFANGBII00009
AMG386
Normalized Cell Index
0.0
0.2
0.4
0.6
0.8
no VHH
no hAng2
-12
-11
-10
-9
-8
-7
-6
-5
log [M]

**Figure 29E**

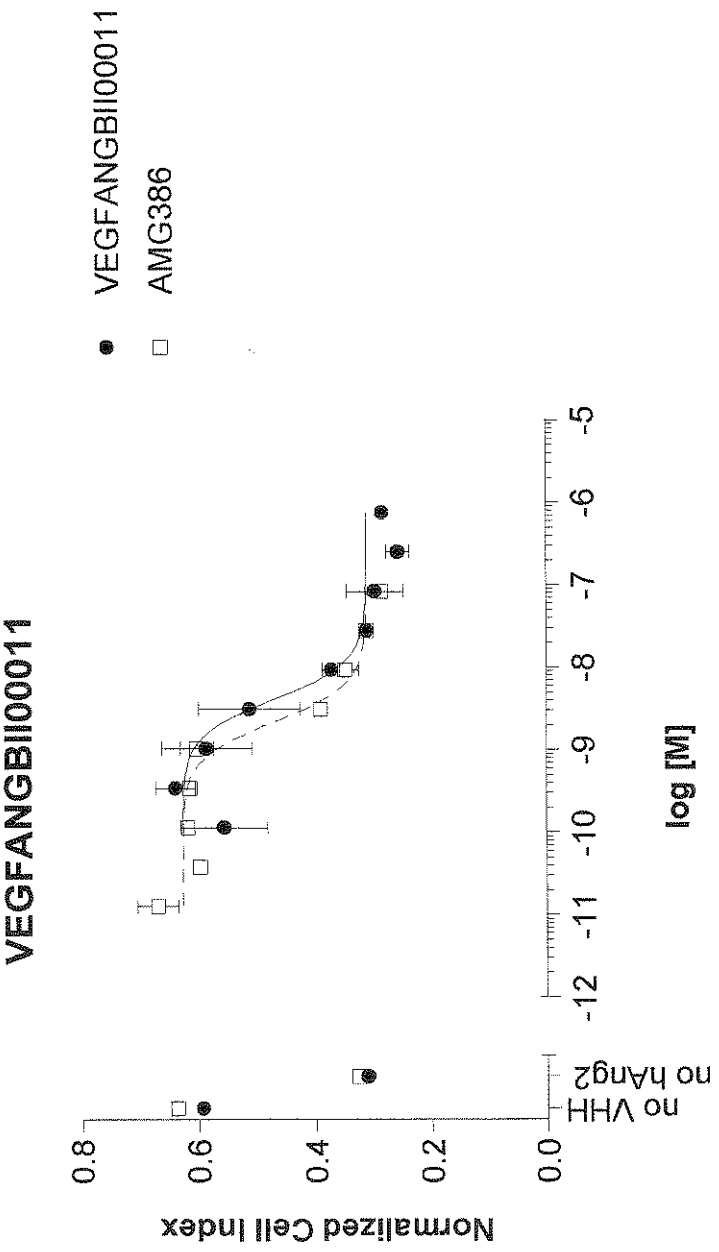

VEGFANGBII00011
VEGFANGBII00011
AMG386
Normalized Cell Index
0.0
0.2
0.4
0.6
0.8
no VHH
no hAng2
-12
-11
-10
-9
-8
-7
-6
-5
log [M]

**Figure 29F**

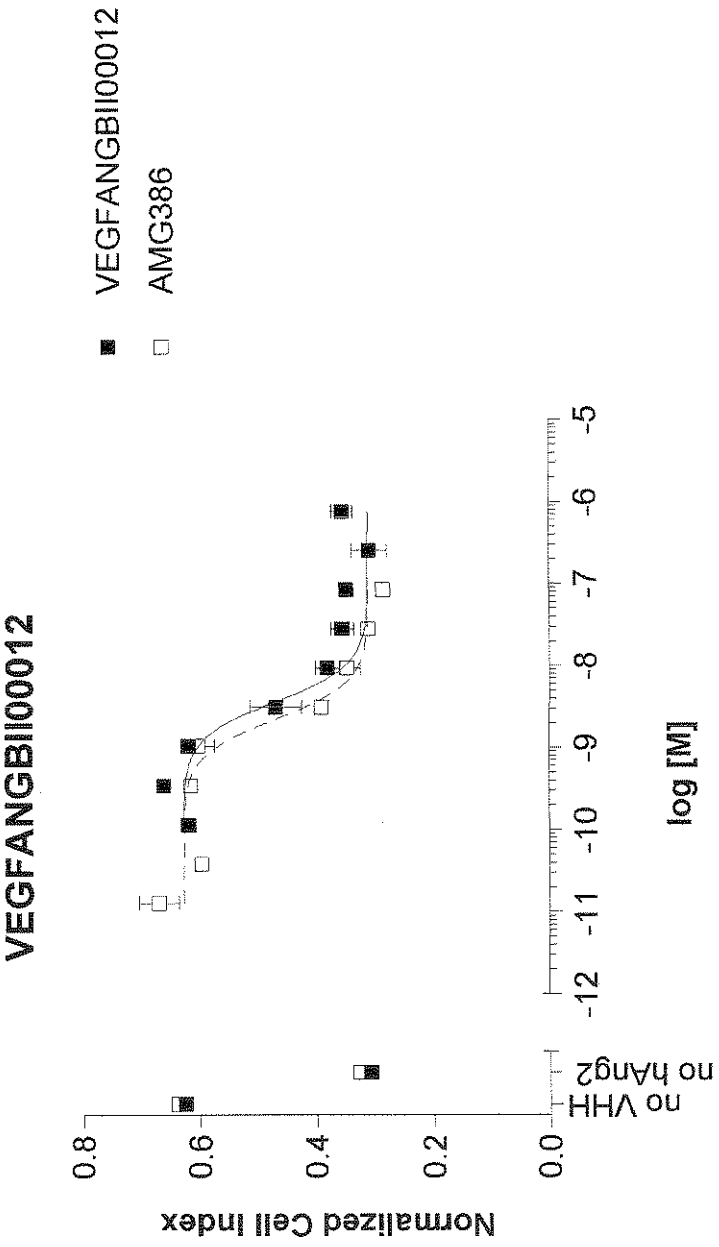
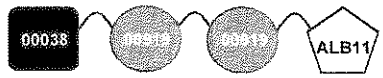
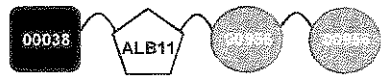

VEGFANGBII00012
VEGFANGBII00012
AMG386
Normalized Cell Index
0.0
0.2
0.4
0.6
0.8
no VHH
no hAng2
-12
-11
-10
-9
-8
-7
-6
-5
log [M]

**Figure 30**

| VHH ID | Format | Description |
|---|---|---|
| VEGFANGBII00015 |  | VEGFBII00038-9gs-ALB11-9gs-00908 |
| VEGFANGBII00016 |  | VEGFBII00038-9gs-ALB11-9gs-00932 |
| VEGFANGBII00017 |  | VEGFBII00038-9gs-ALB11-9gs-00933 |
| VEGFANGBII00018 |  | VEGFBII00038-9gs-ALB11-9gs-00934 |
| VEGFANGBII00019 |  | VEGFBII00038-9gs-ALB11-9gs-00935 |
| VEGFANGBII00020 |  | VEGFBII00038-9gs-ALB11-9gs-00936 |
| VEGFANGBII00021 |  | VEGFBII00038-9gs-ALB11-9gs-00937 |
| VEGFANGBII00022 |  | VEGFBII00038-9gs-ALB11-9gs-00938 |
| VEGFANGBII00023 |  | VEGFBII00038-9gs-ALB11-9gs-00919-9gs-00919 |
| VEGFANGBII00024 |  | VEGFBII00038-9gs-00919-9gs-00919-9gs-ALB11 |
| VEGFANGBII00025 |  | VEGFBII00038-9gs-ALB11-9gs-00921-9gs-00921 |
| VEGFANGBII00026 |  | VEGFBII00038-9gs-00921-9gs-00921-9gs-ALB11 |
| VEGFANGBII00027 |  | VEGFBII00038-9gs-ALB11-9gs-00928 |
| VEGFANGBII00028 |  | VEGFBII00038-9gs-ALB11-9gs-00956-9gs-00956 |

## Figure 30 (cont'd)

Legend:

| | Description | | Description |
|---|---|---|---|
|  | VEGFBII00038 |  | 00937 |
|  | 00908 |  | 00938 |
|  | 00919 |  | 00956 |
|  | 00932 |  | 00921 |
|  | 00933 |  | 00928 |
|  | 00934 |   | ALB11 |
|  | 00935 |  | *9 GlySer* linker |
|  | 00936 | | |

**Figure 31-1A**

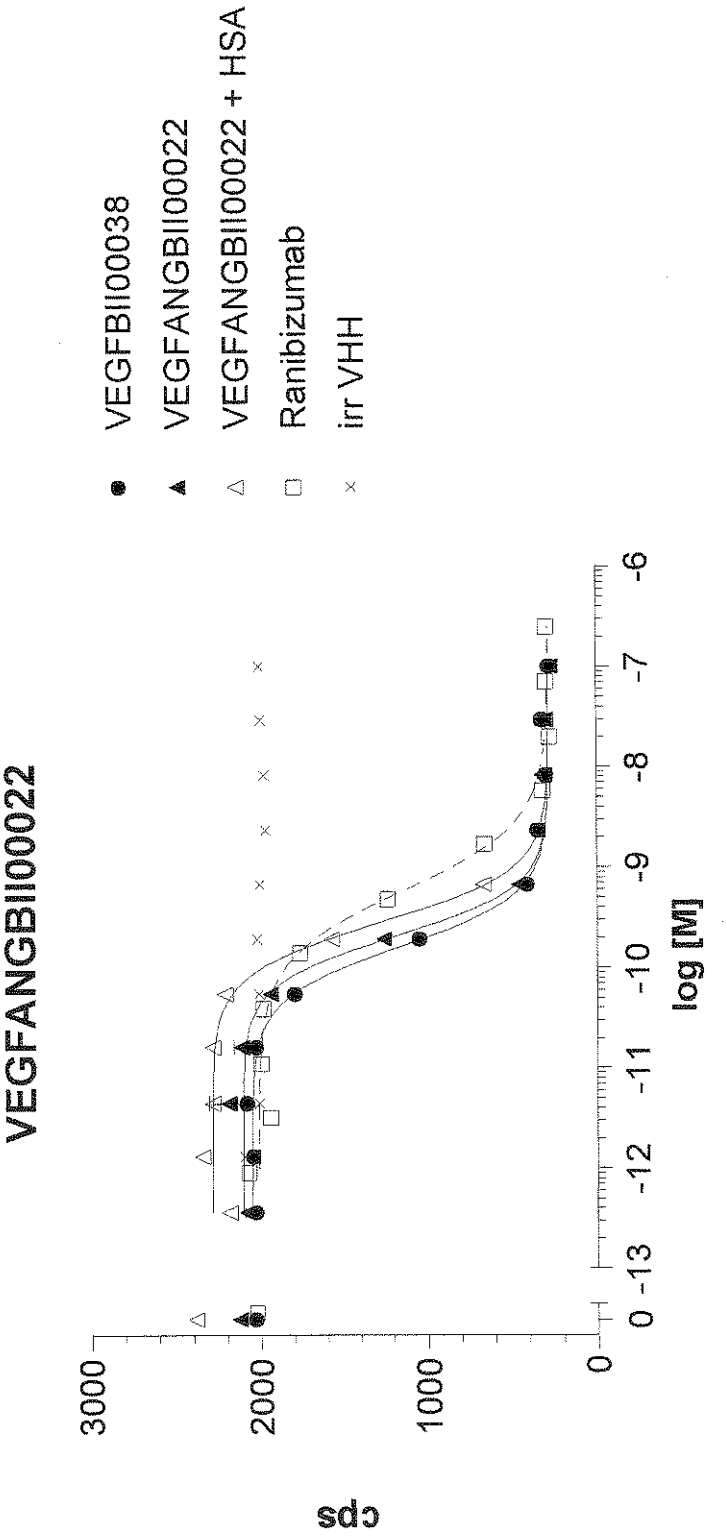

VEGFBII00038
VEGFANGBII00022
VEGFANGBII00022 + HSA
Ranibizumab
irr VHH
VEGFANGBII00022
cps
3000
2000
1000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 31-1B**

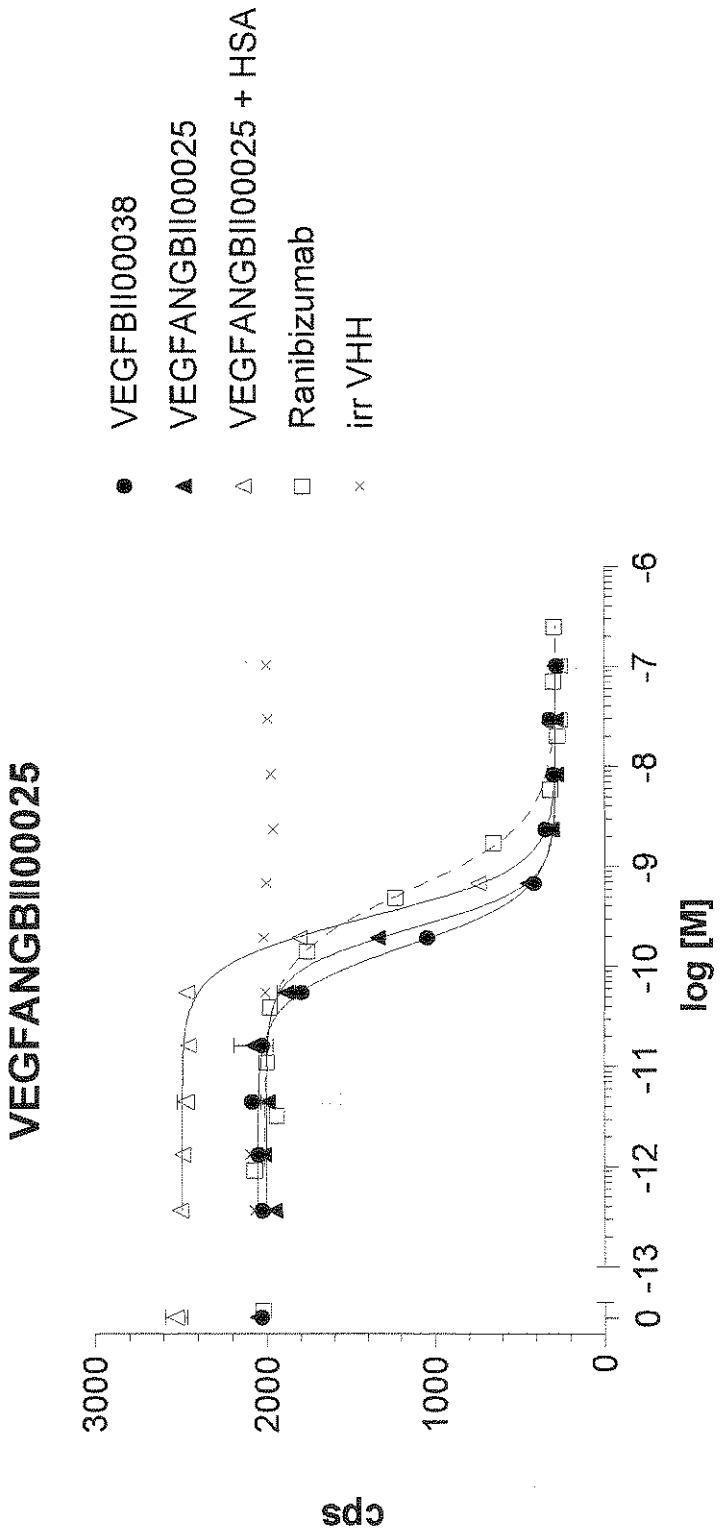
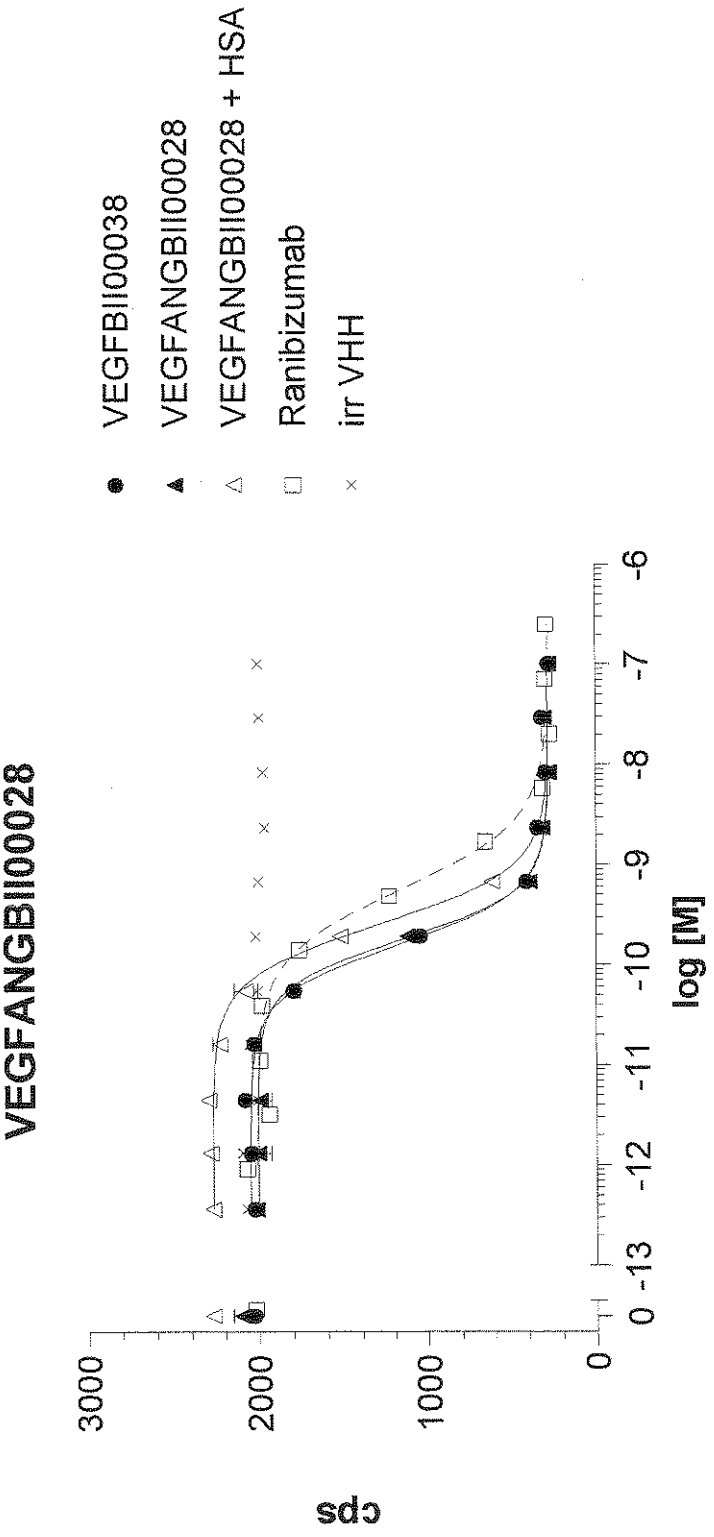

VEGFBII00038
VEGFANGBII00025
VEGFANGBII00025 + HSA
Ranibizumab
irr VHH
VEGFANGBII00025
cps
3000
2000
1000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 31-1C**


VEGFANGBII00028
VEGFBII00038
VEGFANGBII00028
VEGFANGBII00028 + HSA
Ranibizumab
irr VHH
cps
3000
2000
1000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

100 / 125

**Figure 31-2A**

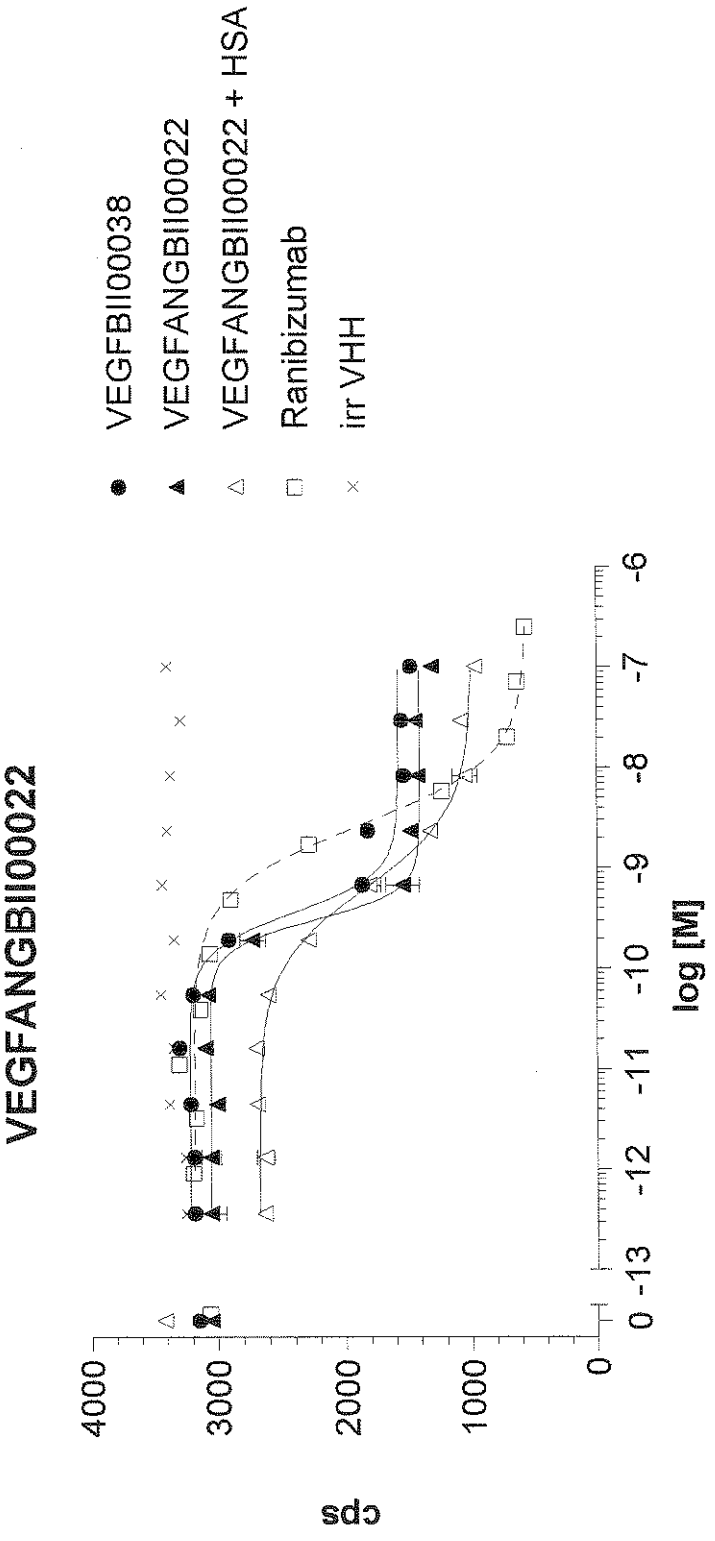


**Figure 31-2B**

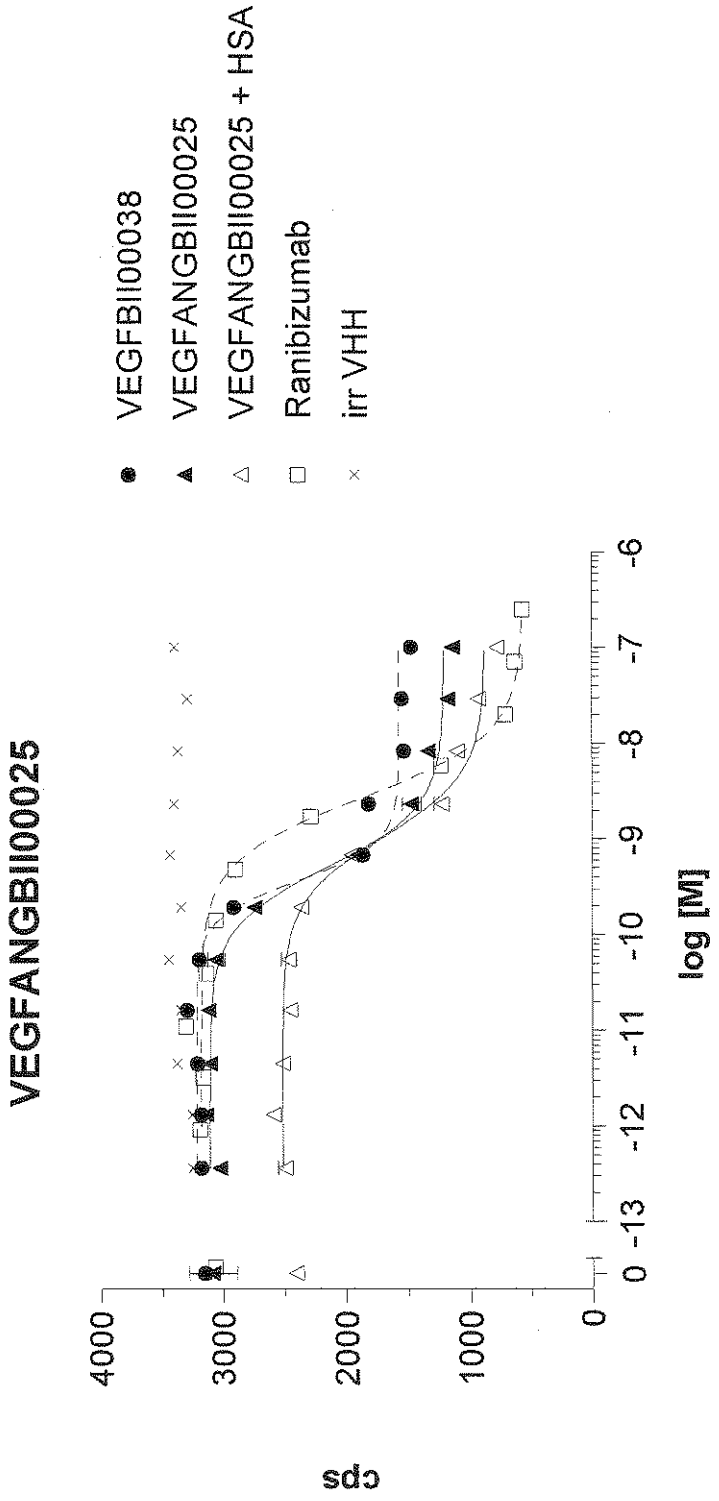

VEGFANGBII00025
VEGFBII00038
VEGFANGBII00025
VEGFANGBII00025 + HSA
Ranibizumab
irr VHH
cps
4000
3000
2000
1000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

**Figure 31-2C**

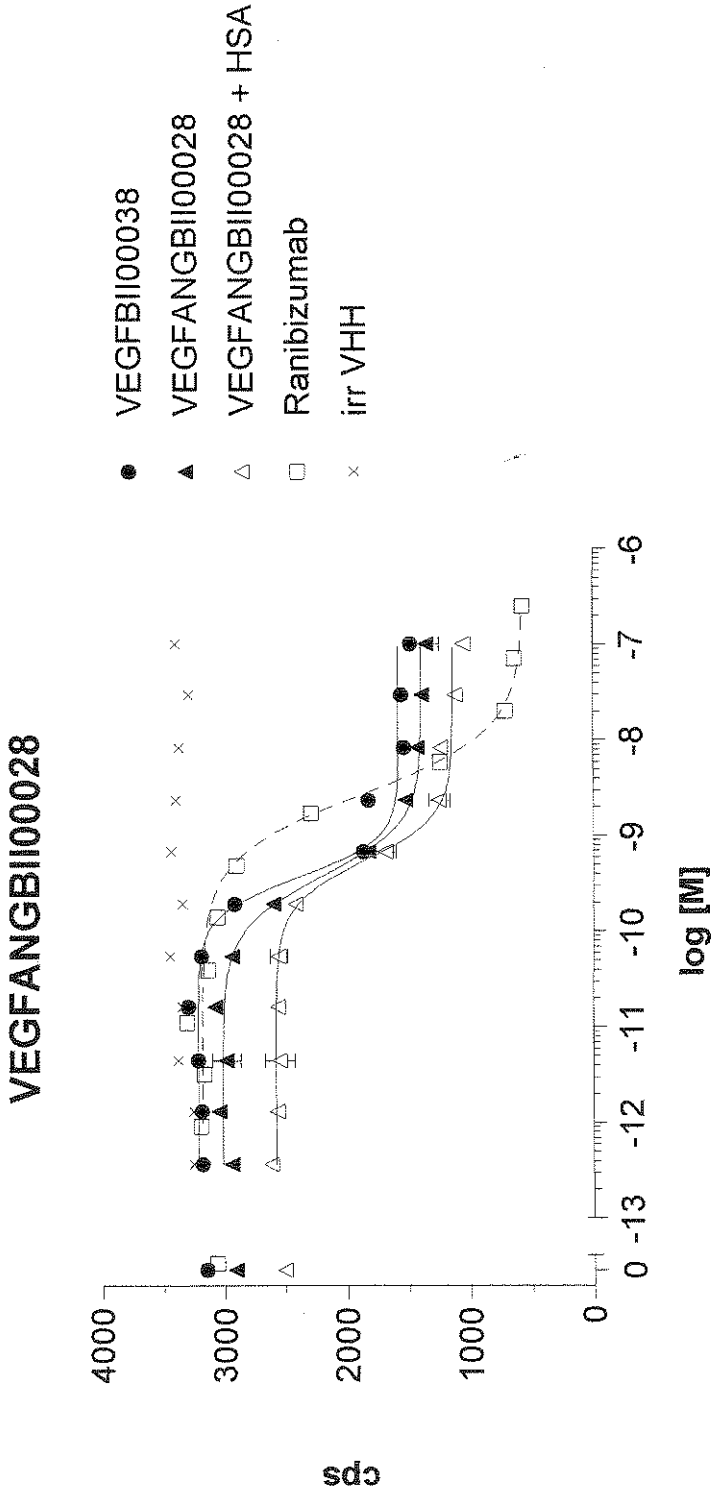

VEGFBII00038
VEGFANGBII00028
VEGFANGBII00028 + HSA
Ranibizumab
irr VHH
VEGFANGBII00028
cps
4000
3000
2000
1000
0
0 -13 -12 -11 -10 -9 -8 -7 -6
log [M]

Figure 32A

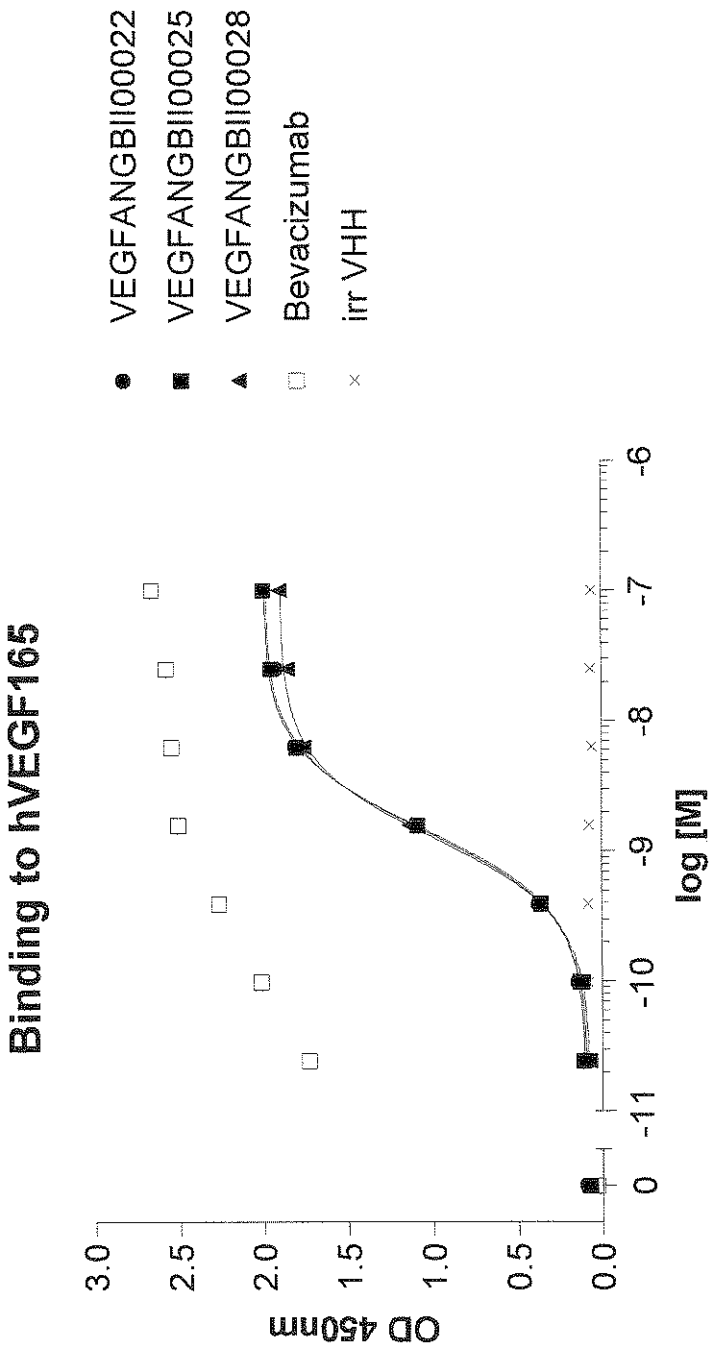

Binding to hVEGF165
VEGFANGBII00022
VEGFANGBII00025
VEGFANGBII00028
Bevacizumab
irr VHH
OD 450nm
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 32B

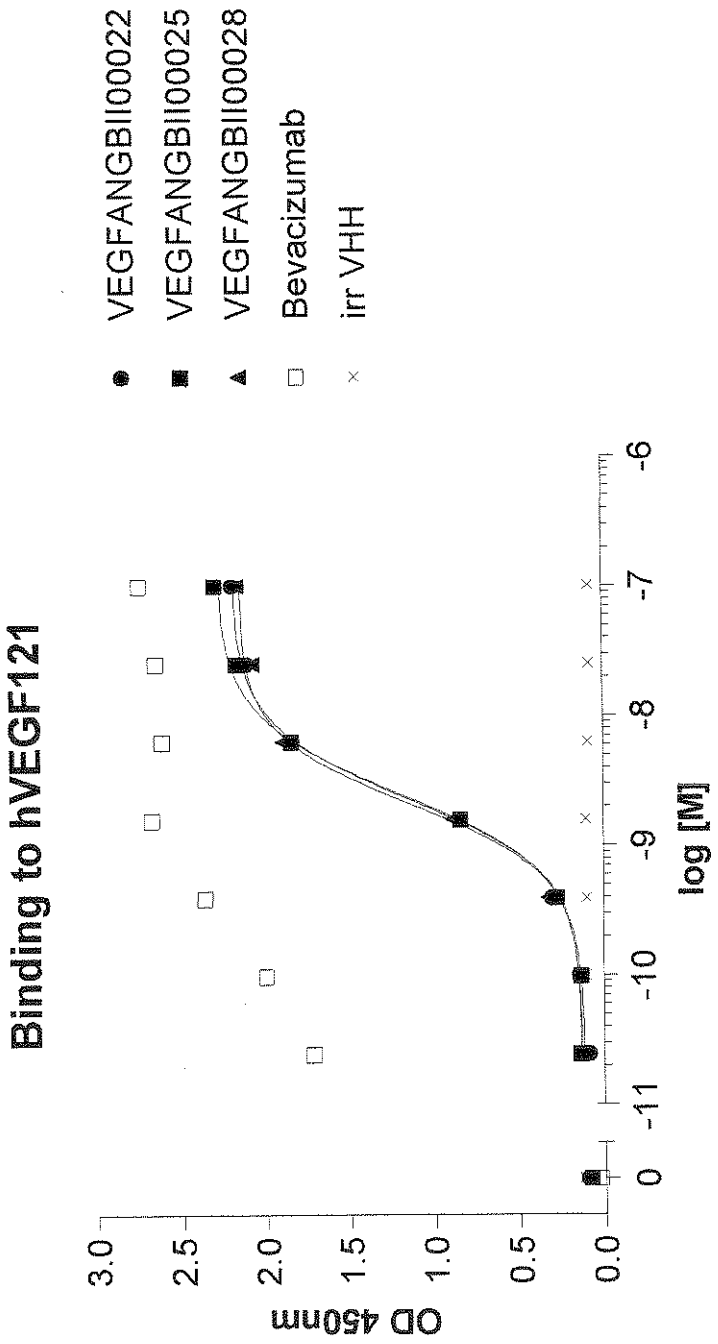

Binding to hVEGF121
VEGFANGBII00022
VEGFANGBII00025
VEGFANGBII00028
Bevacizumab
irr VHH
OD 450nm
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 33A

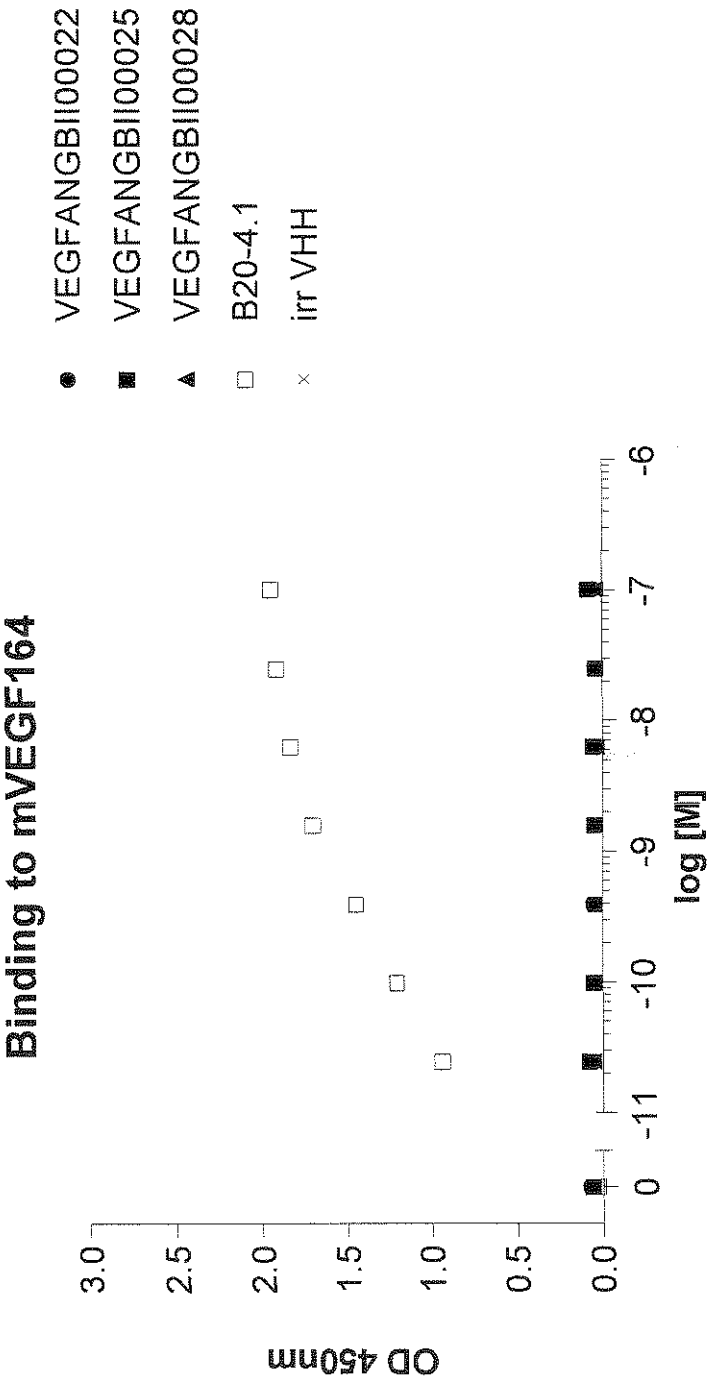

VEGFANGBII00022
VEGFANGBII00025
VEGFANGBII00028
B20-4.1
irr VHH
Binding to mVEGF164
OD 450nm
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

**Figure 33B**

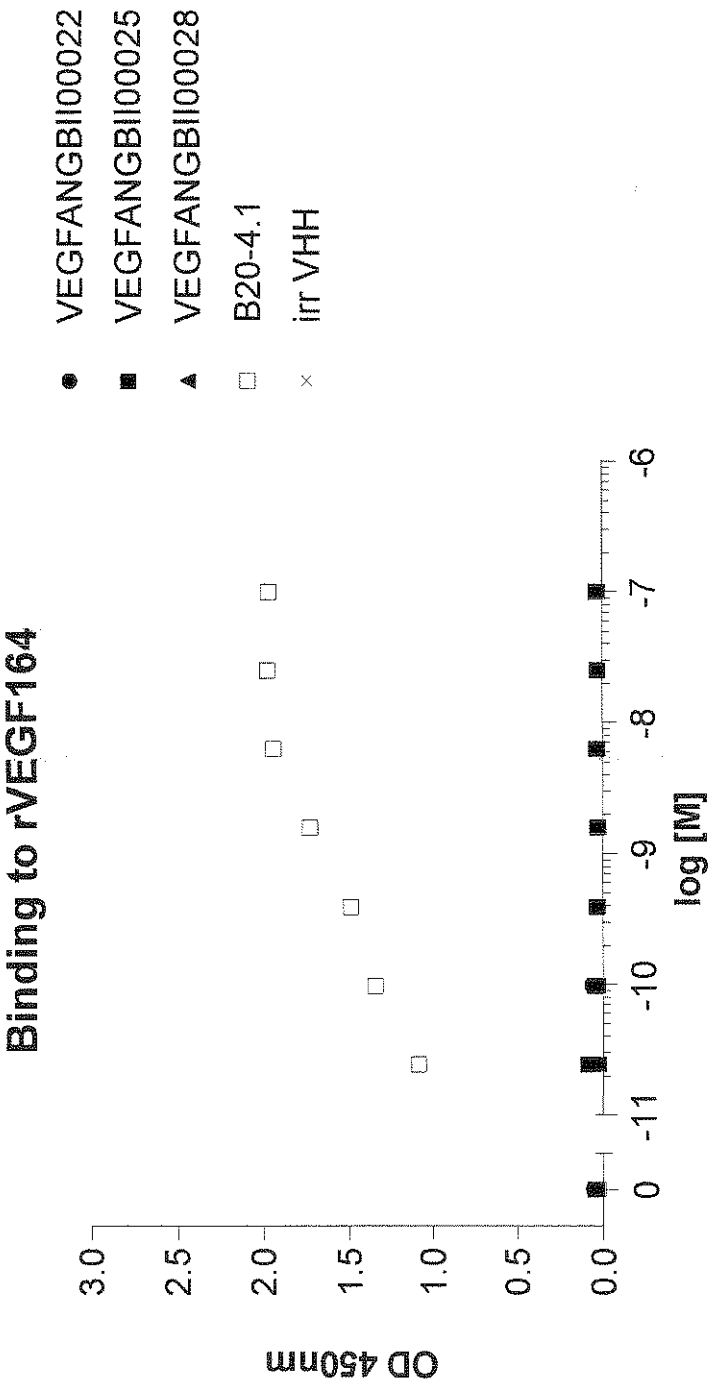

VEGFANGBII00022
VEGFANGBII00025
VEGFANGBII00028
B20-4.1
irr VHH
Binding to rVEGF164
OD 450nm
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

**Figure 34A**

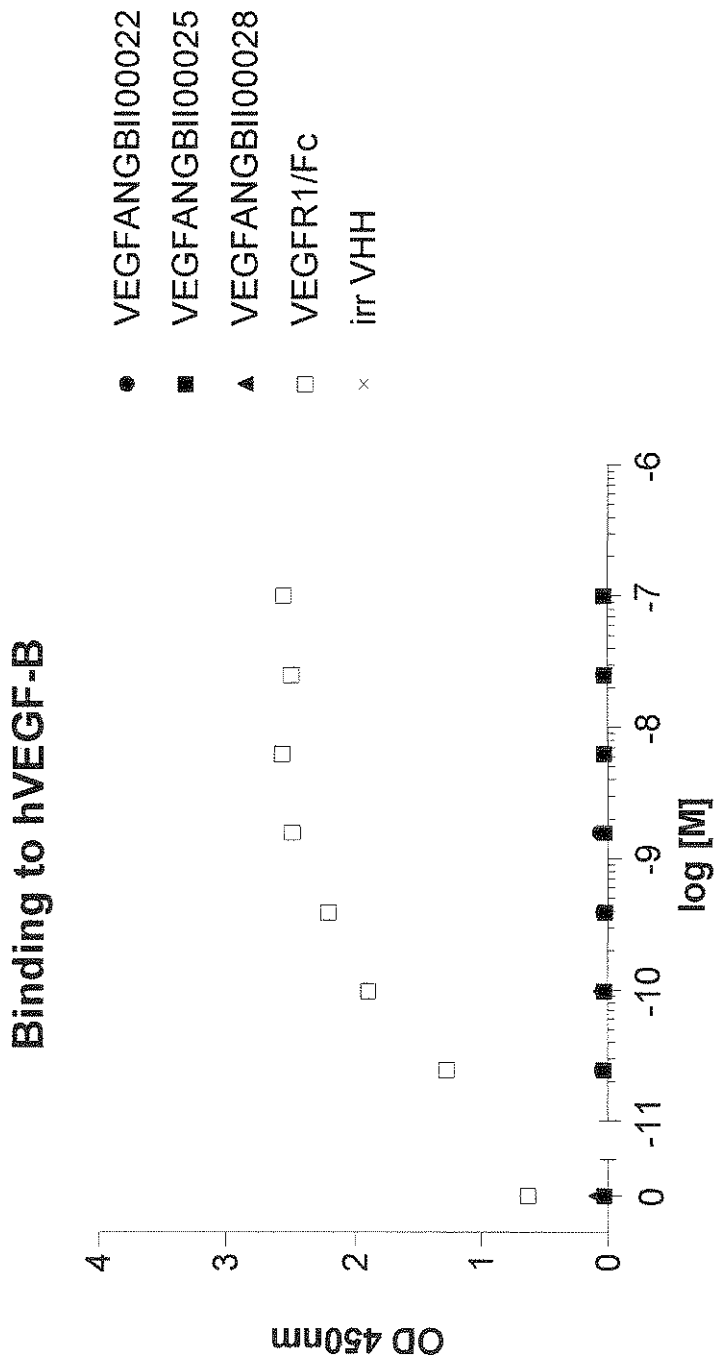

Binding to hVEGF-B
VEGFANGBII00022
VEGFANGBII00025
VEGFANGBII00028
VEGFR1/Fc
irr VHH
OD 450nm
0
1
2
3
4
log [M]
-11
-10
-9
-8
-7
-6

**Figure 34B**

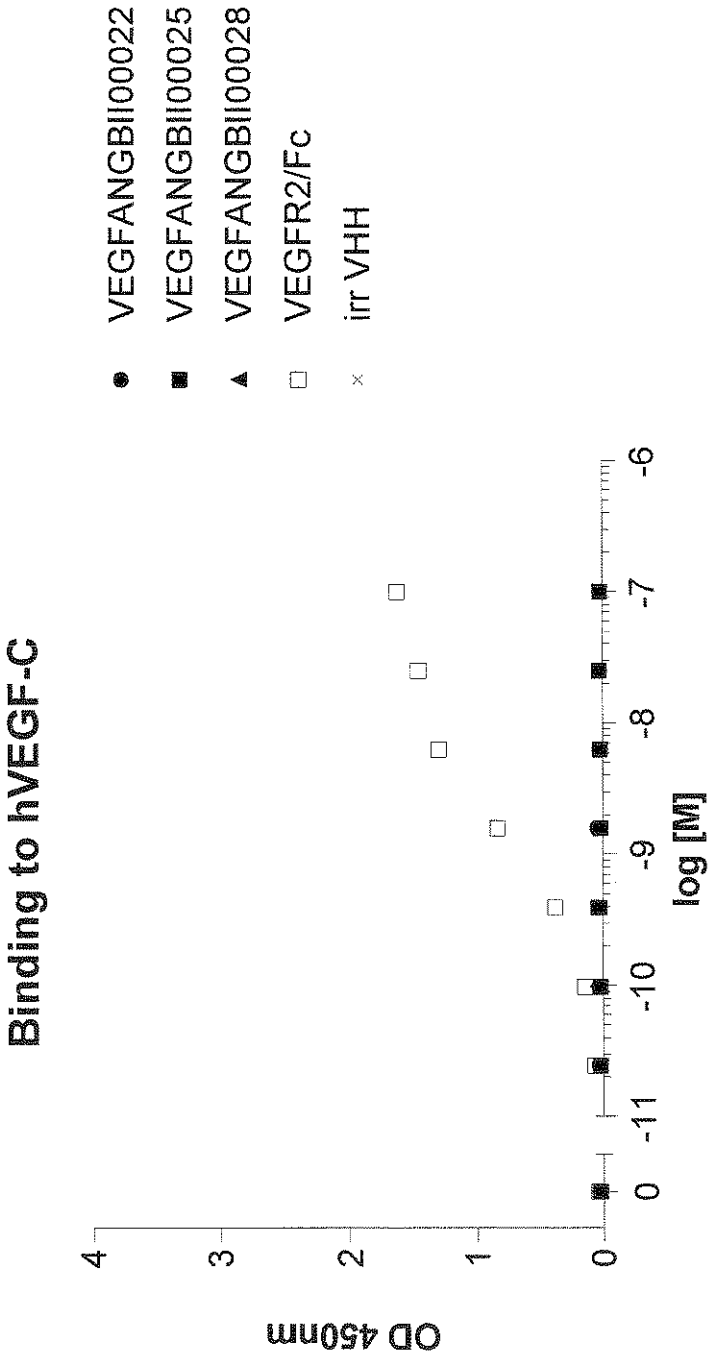

VEGFANGBII00022
VEGFANGBII00025
VEGFANGBII00028
VEGFR2/Fc
irr VHH
Binding to hVEGF-C
OD 450nm
0
1
2
3
4
log [M]
-6
-7
-8
-9
-10
-11
0

Figure 34C

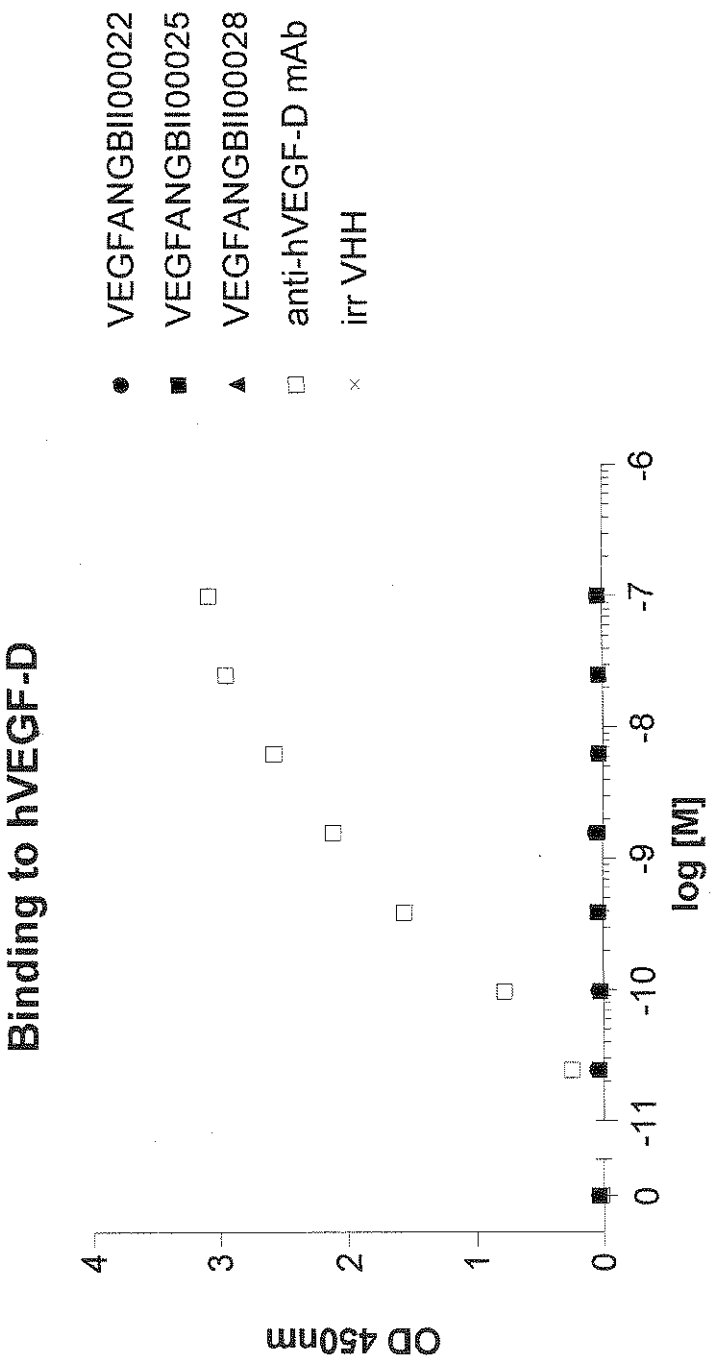

Binding to hVEGF-D
OD 450nm
log [M]
VEGFANGBII00022
VEGFANGBII00025
VEGFANGBII00028
anti-hVEGF-D mAb
irr VHH
0
1
2
3
4
-11
-10
-9
-8
-7
-6

**Figure 34D**

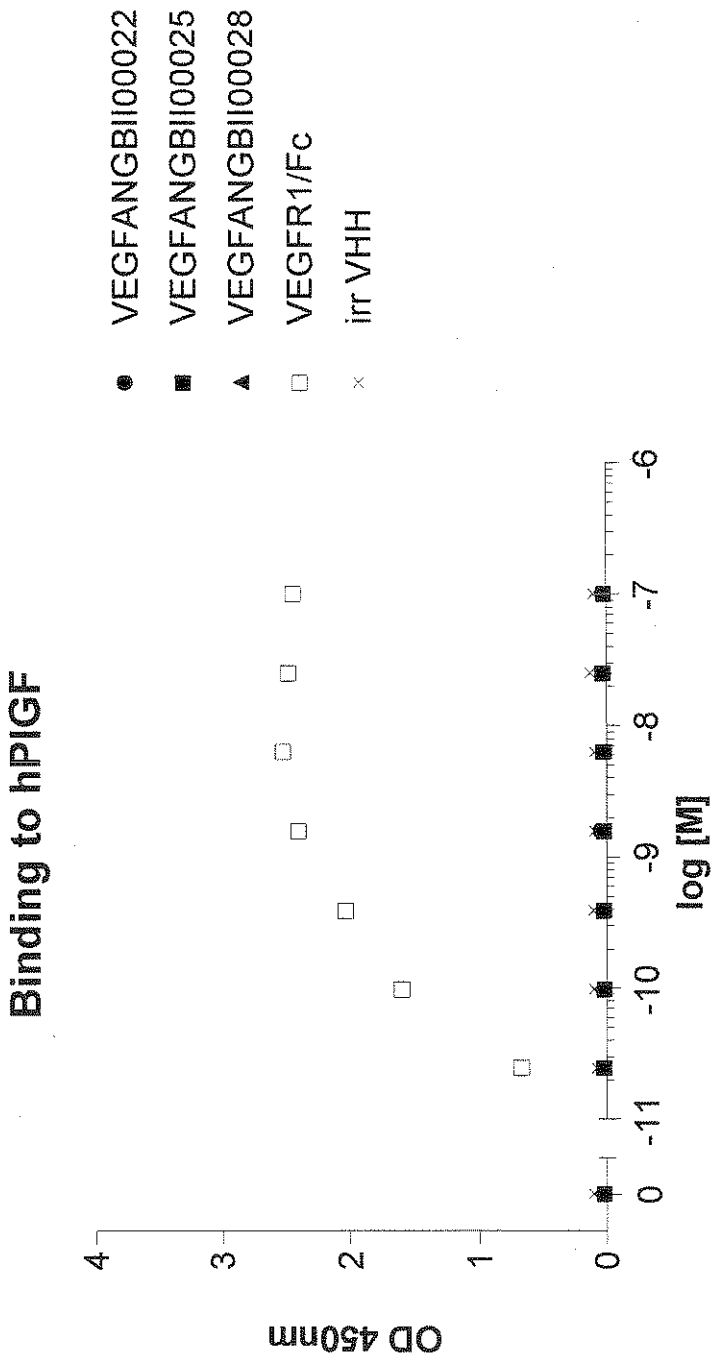

Binding to hPlGF
VEGFANGBII00022
VEGFANGBII00025
VEGFANGBII00028
VEGFR1/Fc
irr VHH
OD 450nm
0
1
2
3
4
log [M]
-6
-7
-8
-9
-10
-11
0

Figure 35-1A

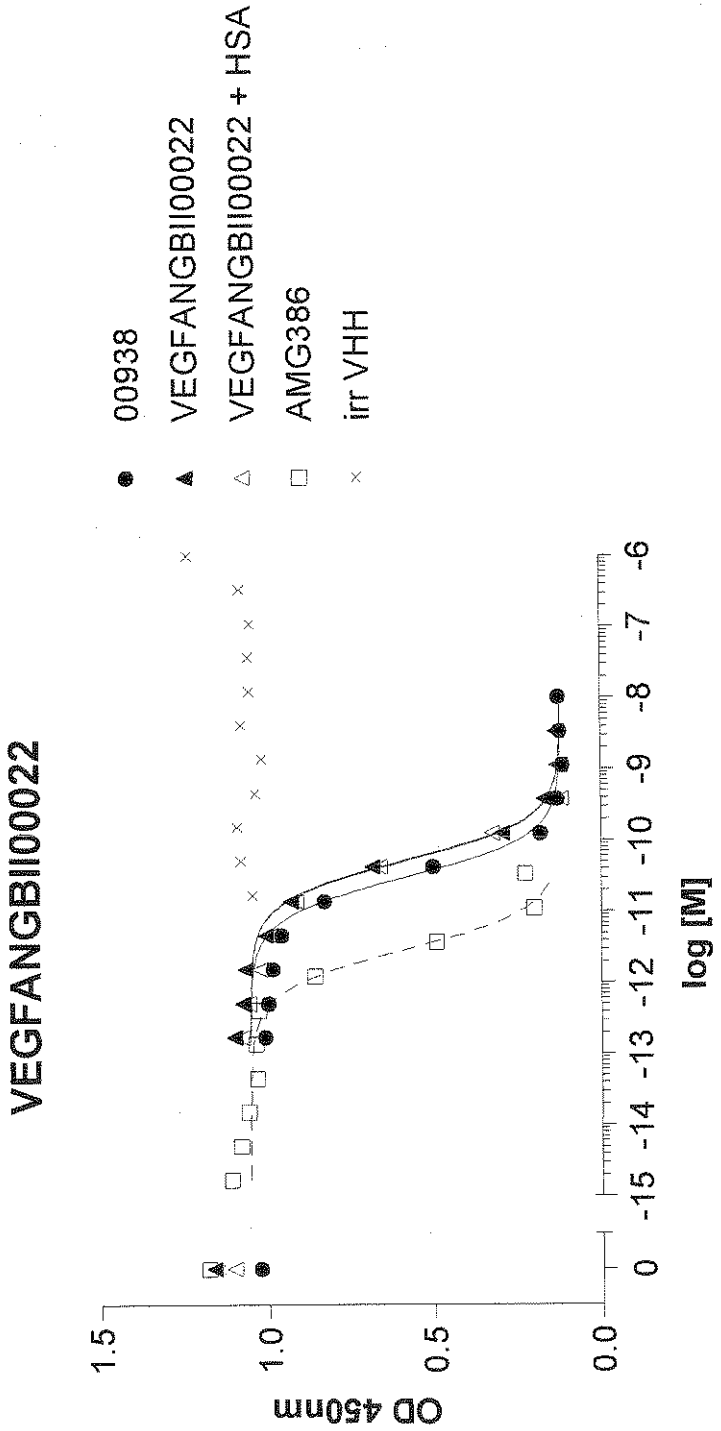

VEGFANGBII00022
00938
VEGFANGBII00022
VEGFANGBII00022 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 35-1B**

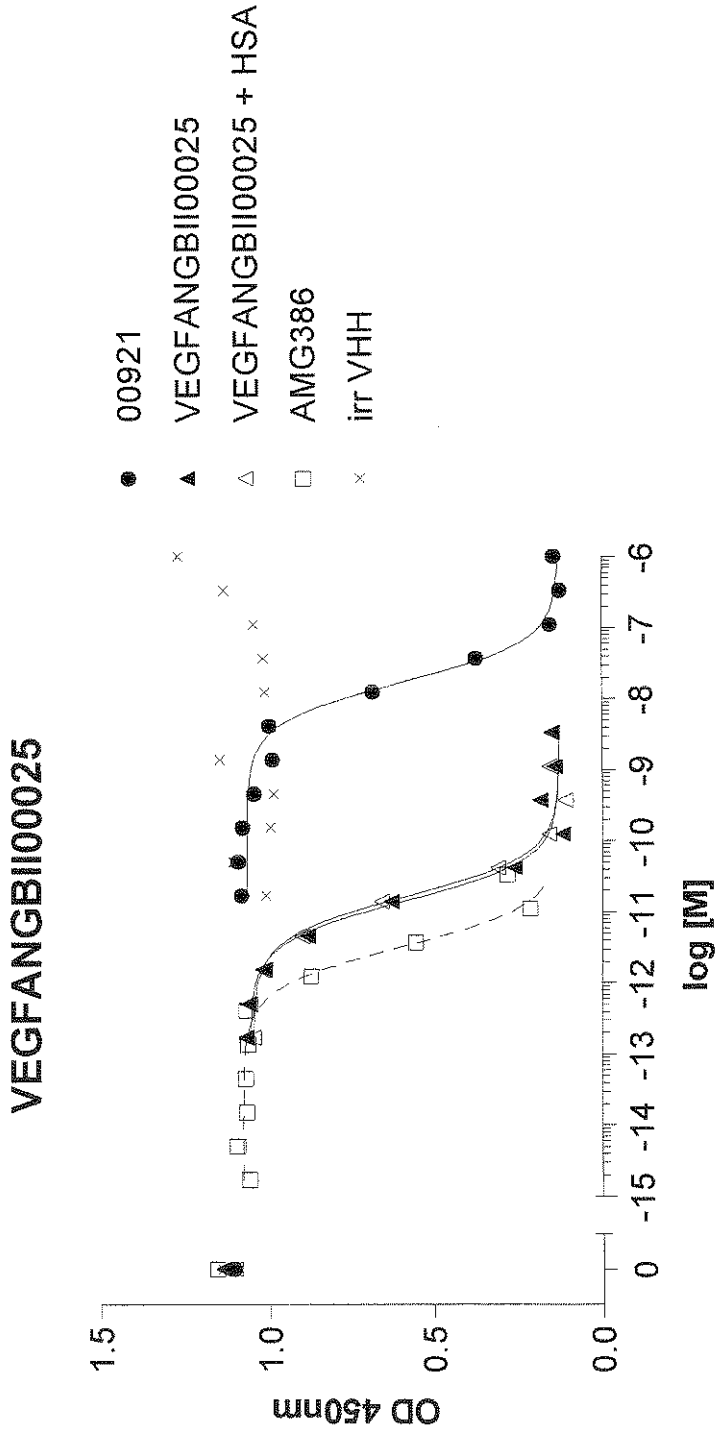

VEGFANGBII00025
00921
VEGFANGBII00025
VEGFANGBII00025 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 35-1C

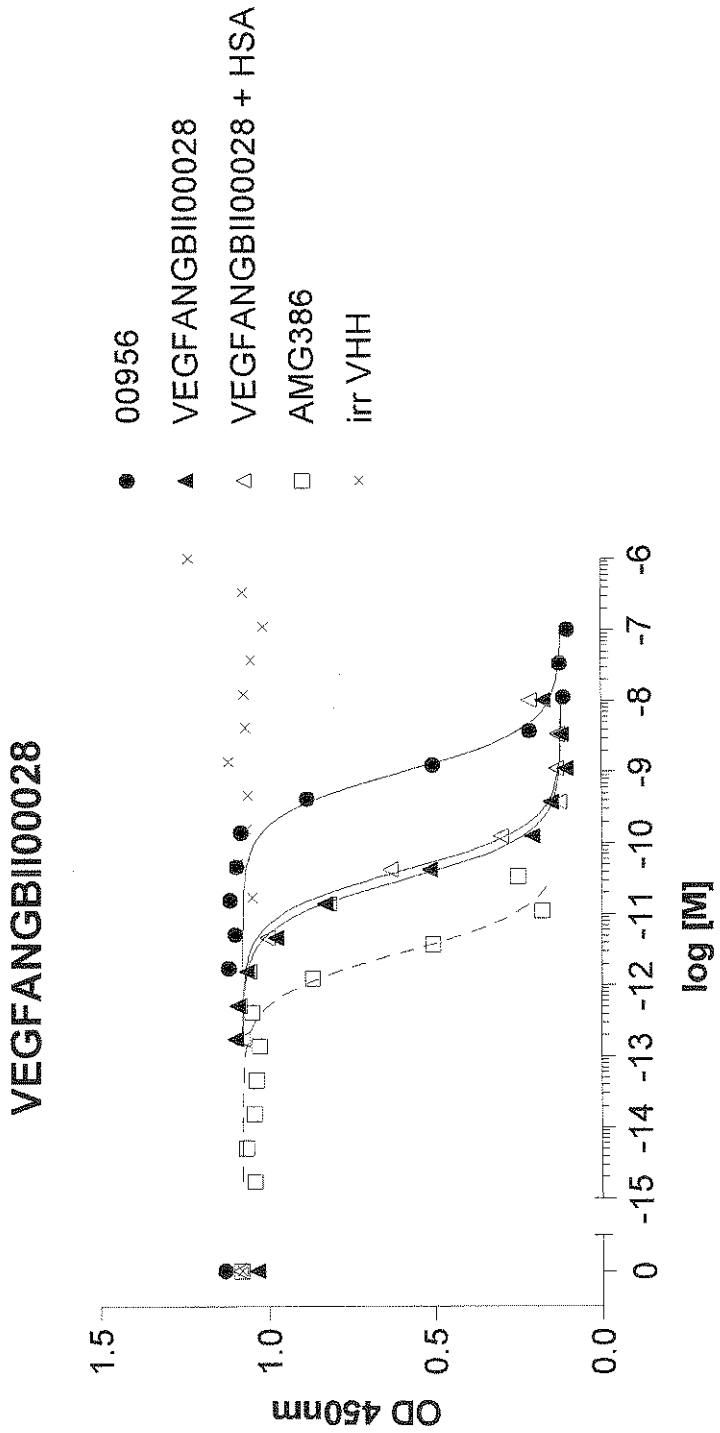

VEGFANGBII00028
00956
VEGFANGBII00028
VEGFANGBII00028 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 35-2A

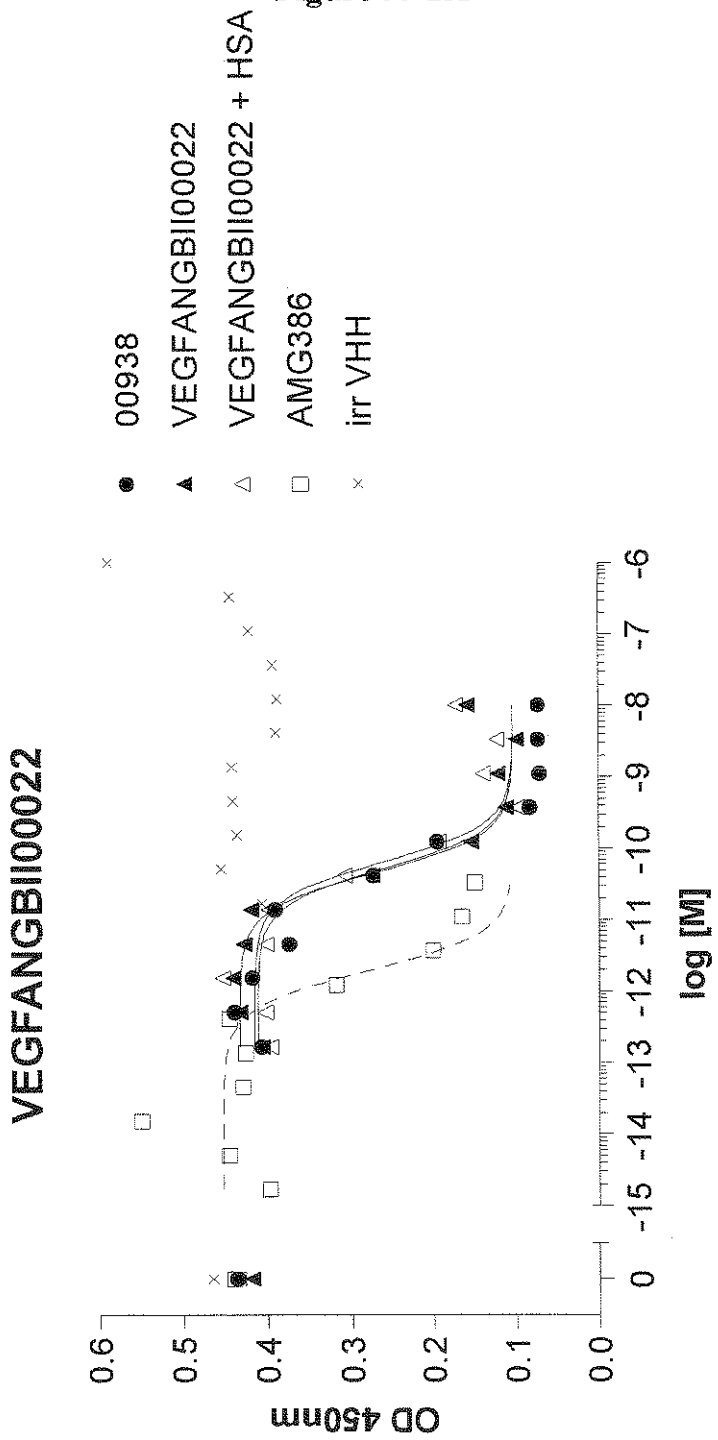

VEGFANGBII00022
00938
VEGFANGBII00022
VEGFANGBII00022 + HSA
AMG386
irr VHH
OD 450nm
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 35-2B**

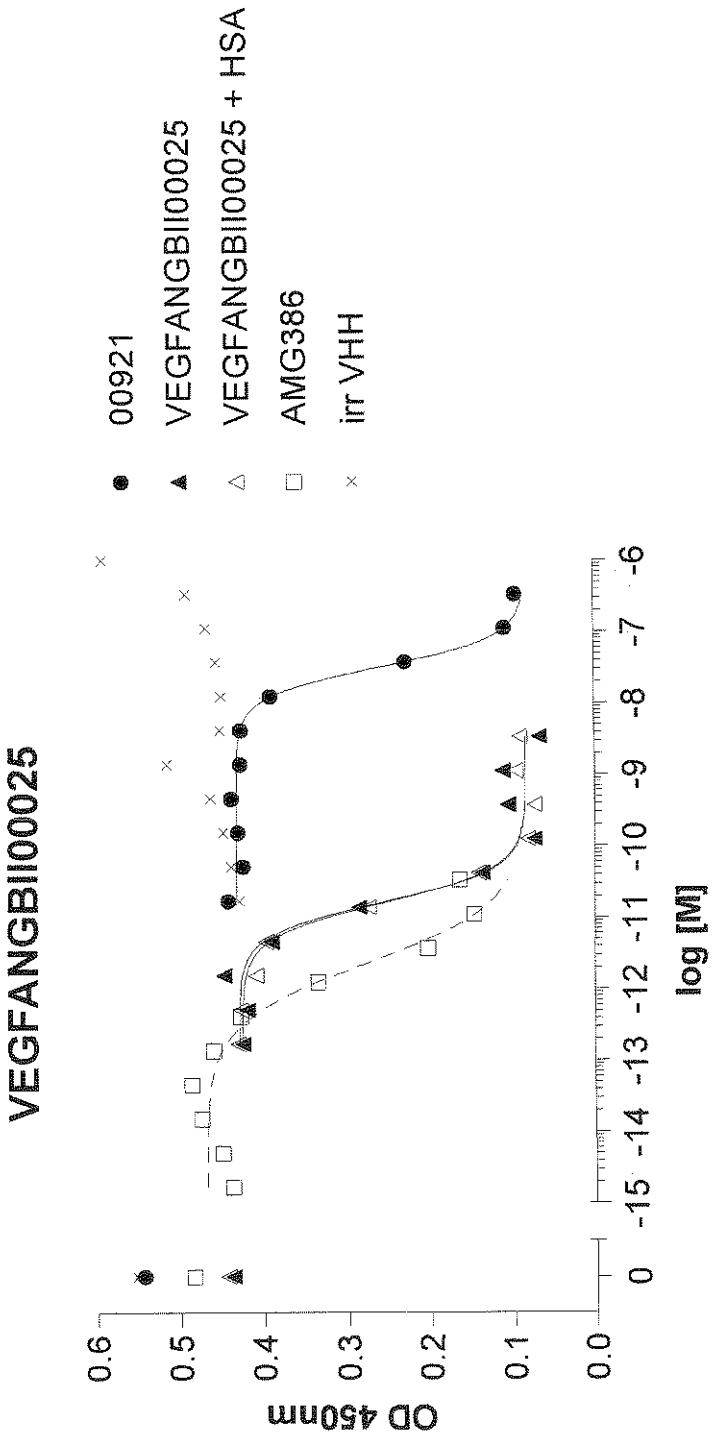

VEGFANGBII00025
00921
VEGFANGBII00025
VEGFANGBII00025 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.1
0.2
0.3
0.4
0.5
0.6
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6

Figure 35-2C

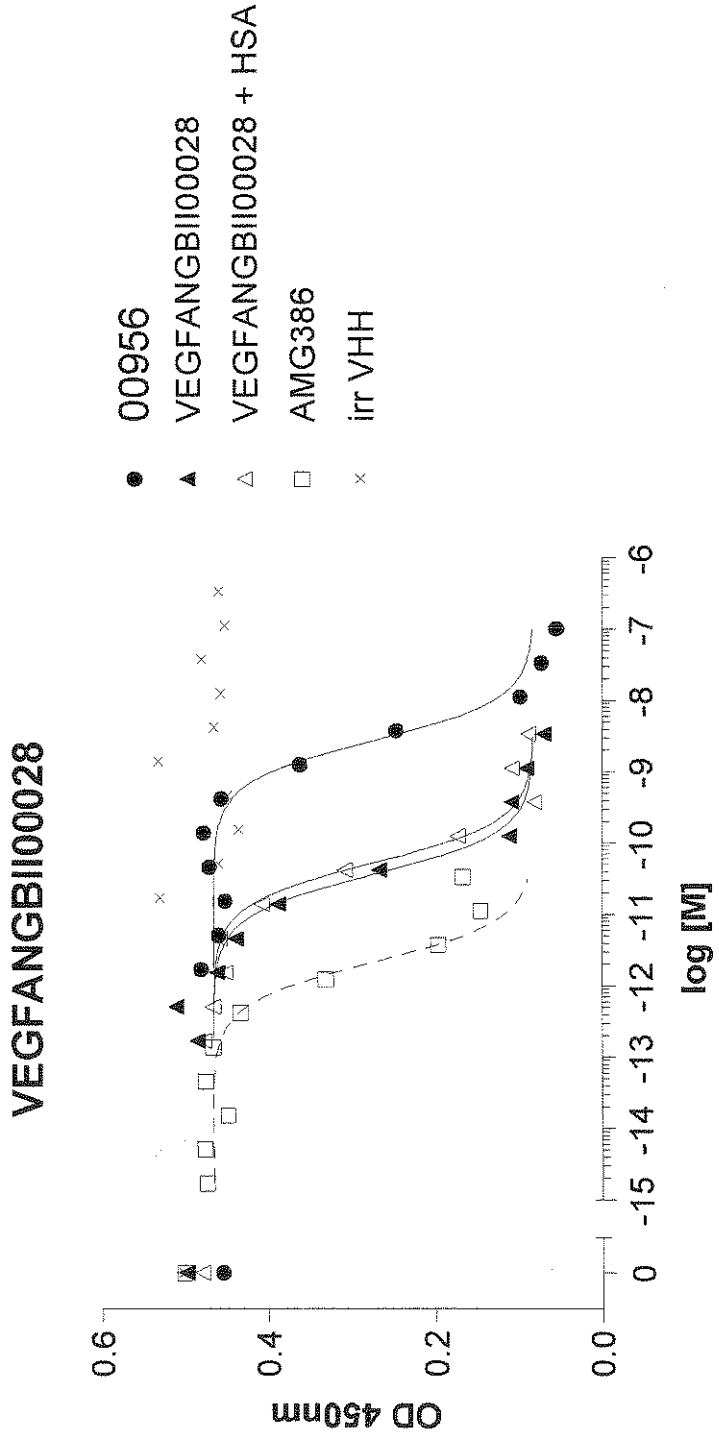

00956
VEGFANGBII00028
VEGFANGBII00028 + HSA
AMG386
irr VHH
VEGFANGBII00028
OD 450nm
0.0
0.2
0.4
0.6
0
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15
log [M]

**Figure 35-3A**

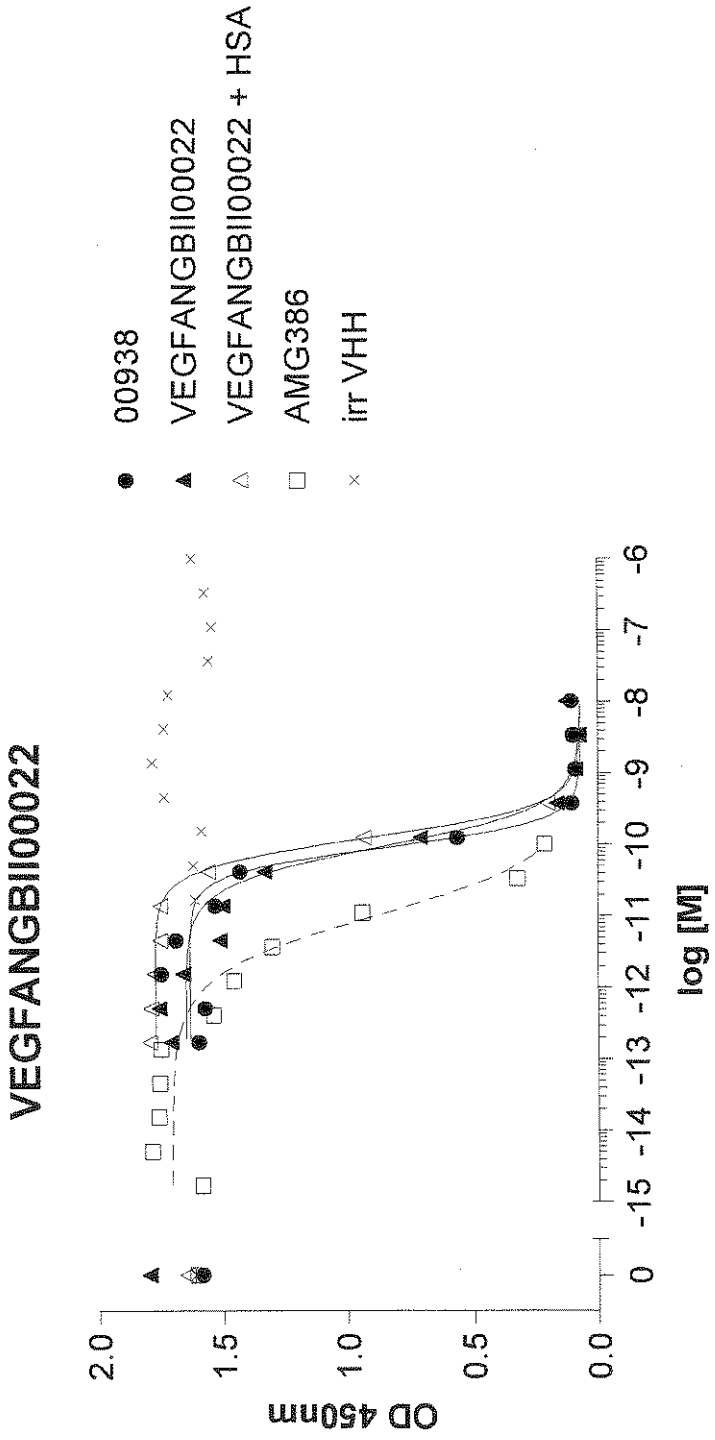

00938
VEGFANGBII00022
VEGFANGBII00022 + HSA
AMG386
irr VHH
VEGFANGBII00022
OD 450nm
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 35-3B

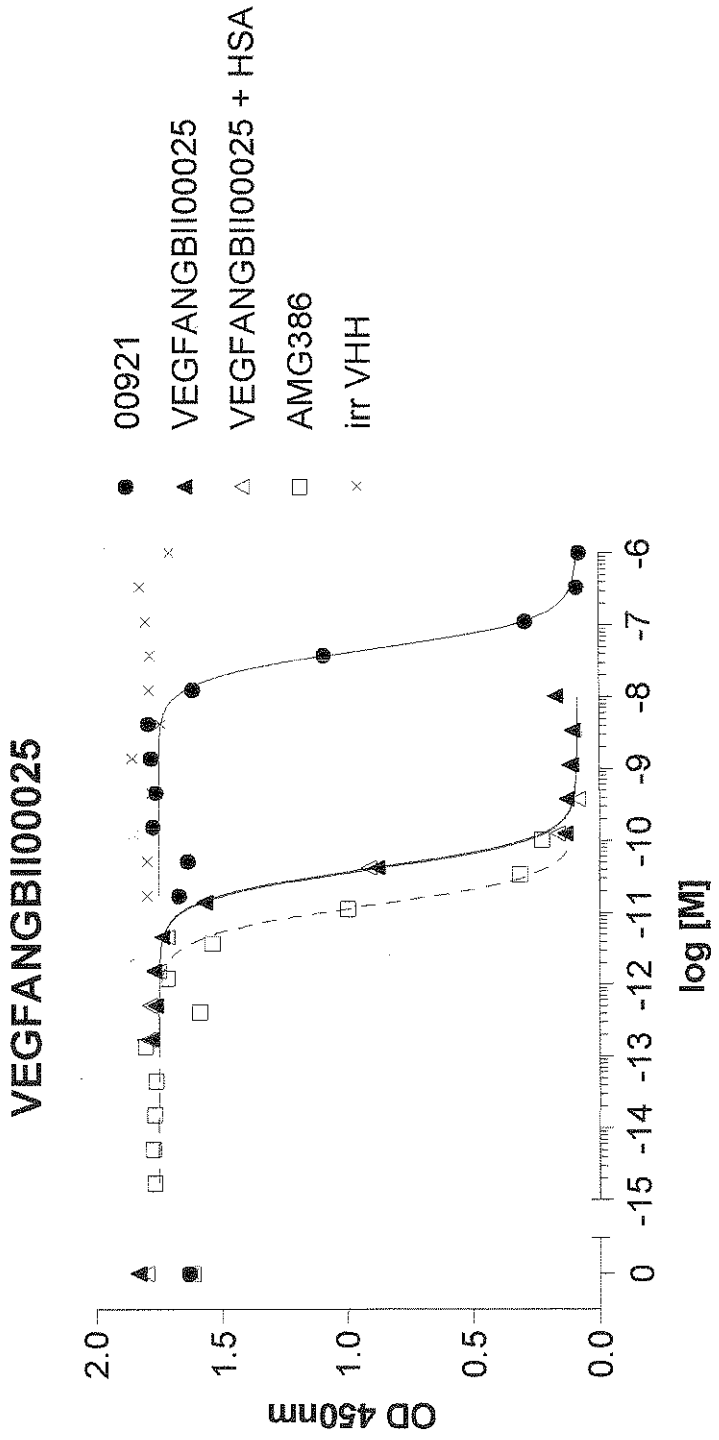

VEGFANGBII00025
00921
VEGFANGBII00025
VEGFANGBII00025 + HSA
AMG386
irr VHH
OD 450nm
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 35-3C

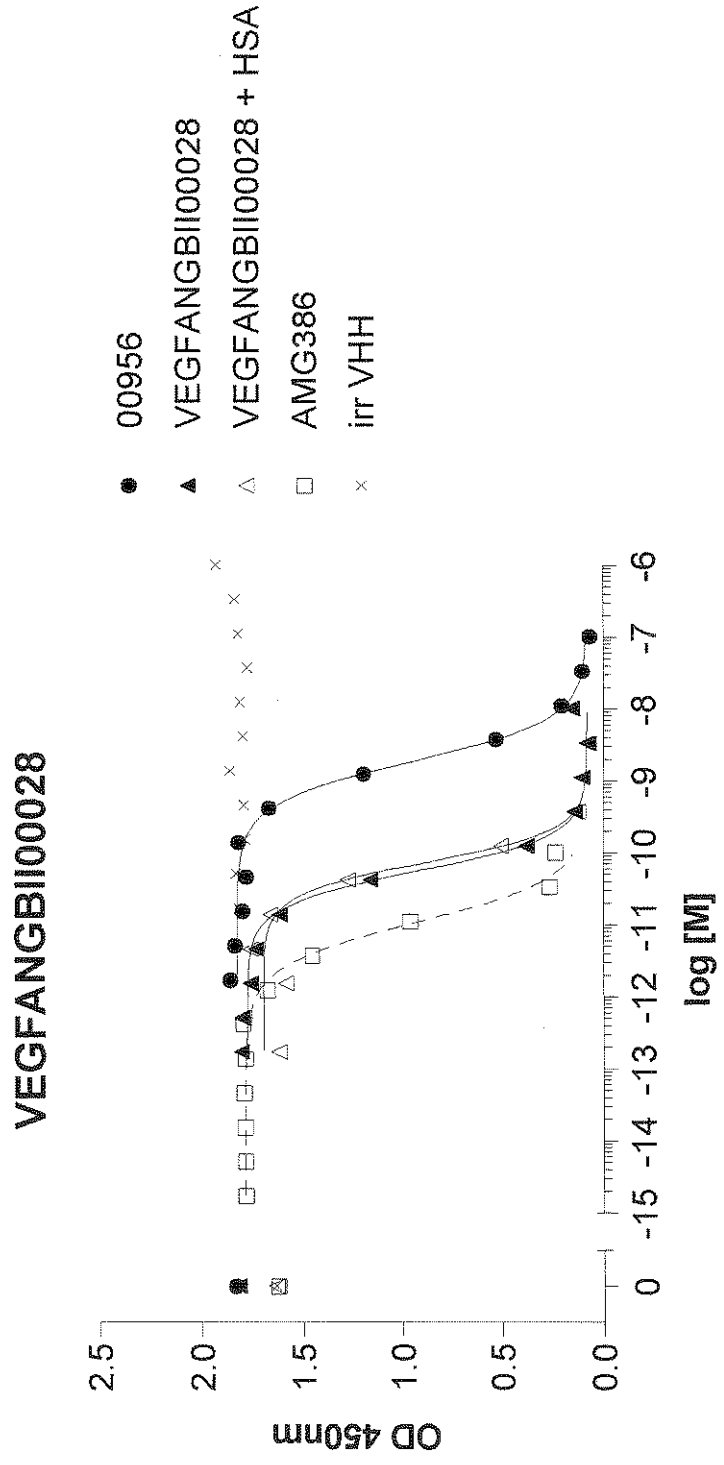

VEGFANGBII00028
00956
VEGFANGBII00028
VEGFANGBII00028 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

**Figure 36A**

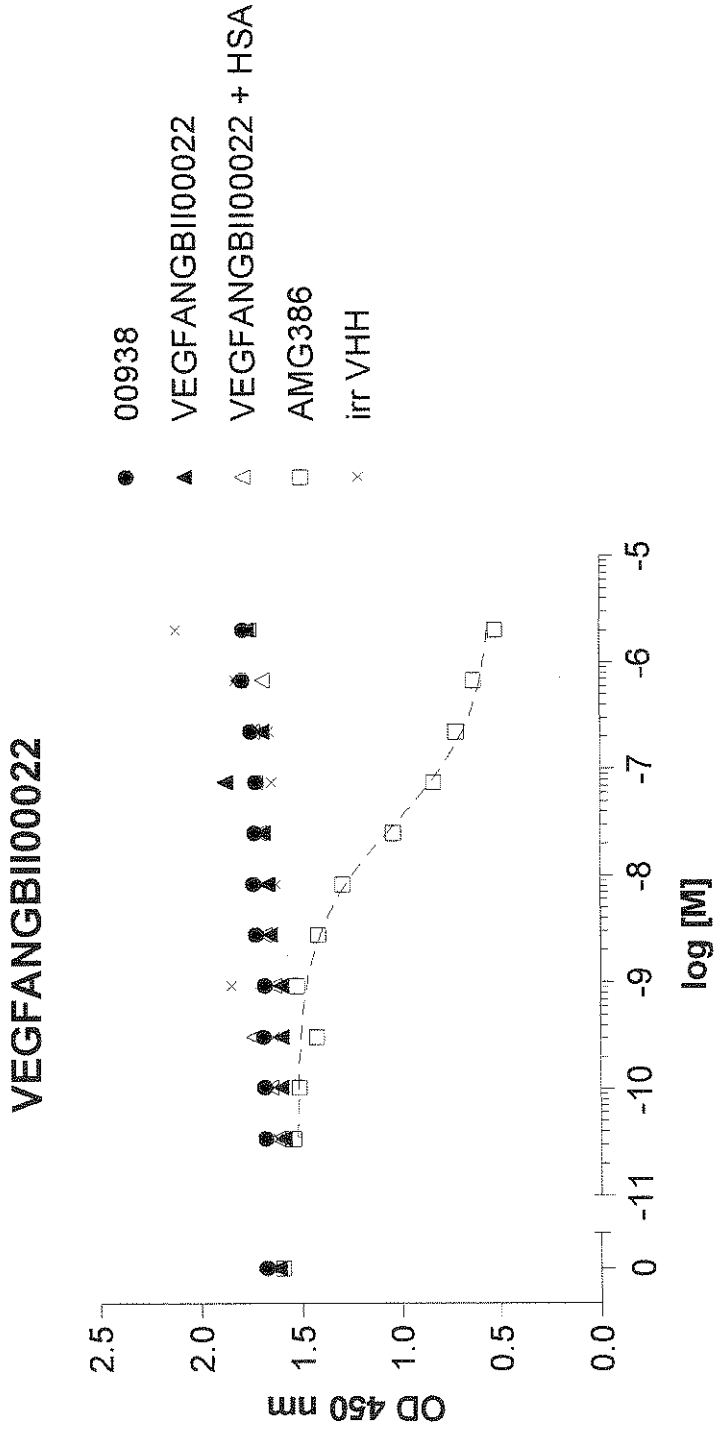

VEGFANGBII00022
00938
VEGFANGBII00022
VEGFANGBII00022 + HSA
AMG386
irr VHH
OD 450 nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
-5
log [M]

**Figure 36B**

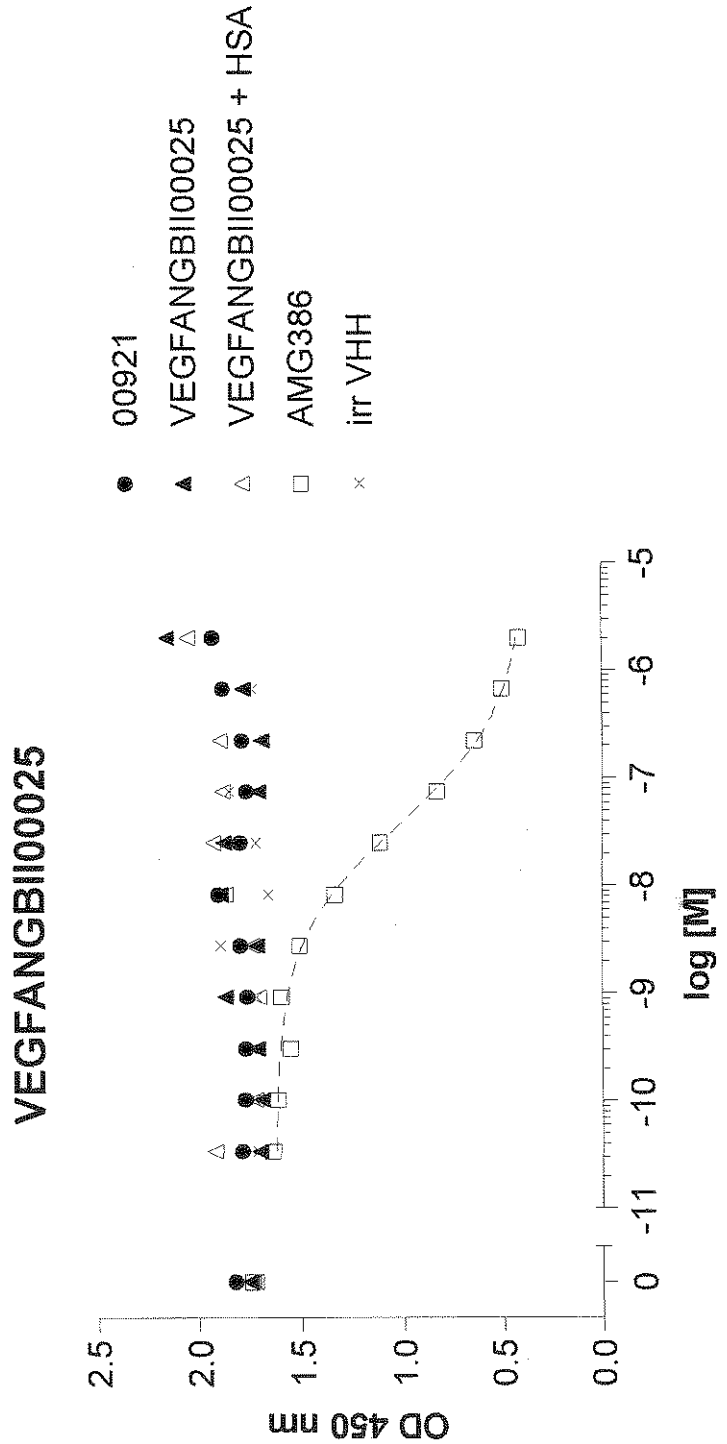

VEGFANGBII00025
00921
VEGFANGBII00025
VEGFANGBII00025 + HSA
AMG386
irr VHH
OD 450 nm
0.0
0.5
1.0
1.5
2.0
2.5
log [M]
0
-11
-10
-9
-8
-7
-6
-5

**Figure 36C**

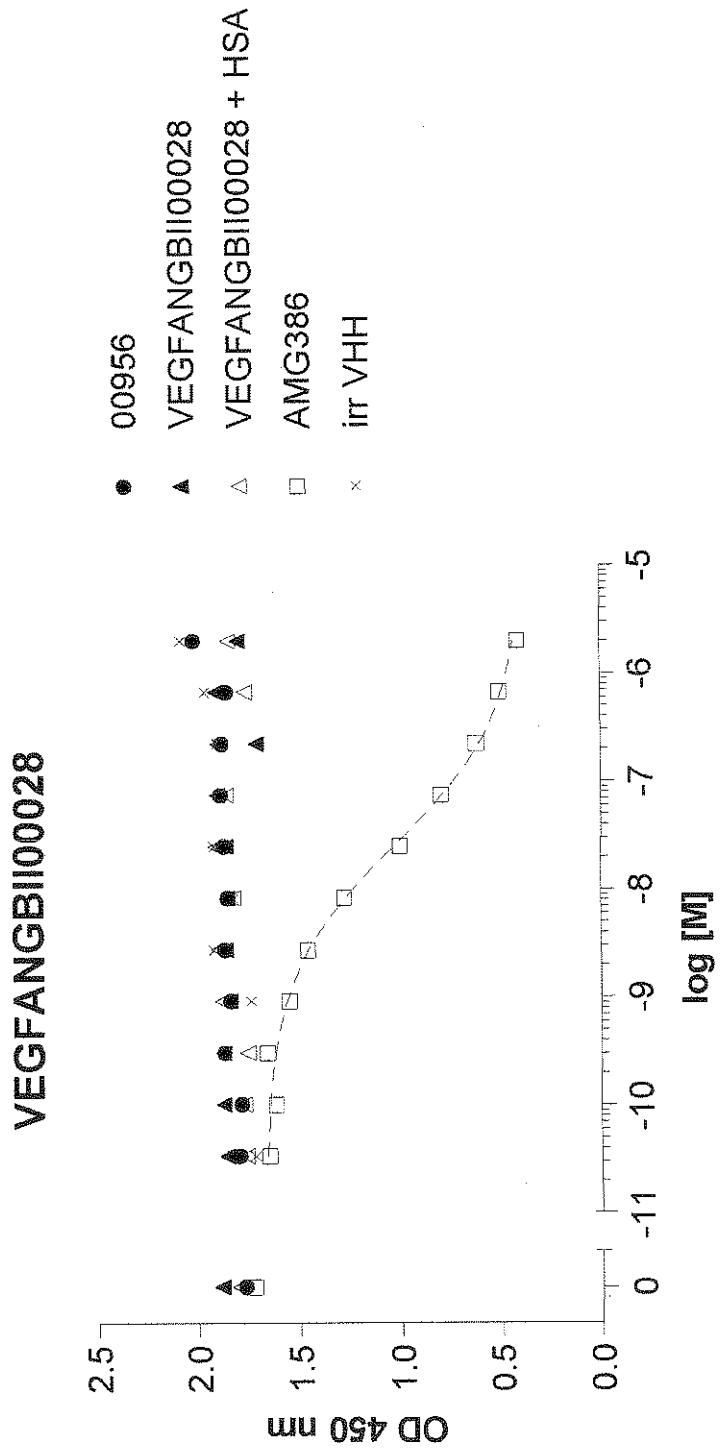

VEGFANGBII00028
00956
VEGFANGBII00028
VEGFANGBII00028 + HSA
AMG386
irr VHH
OD 450 nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
-5
log [M]

Figure 37A

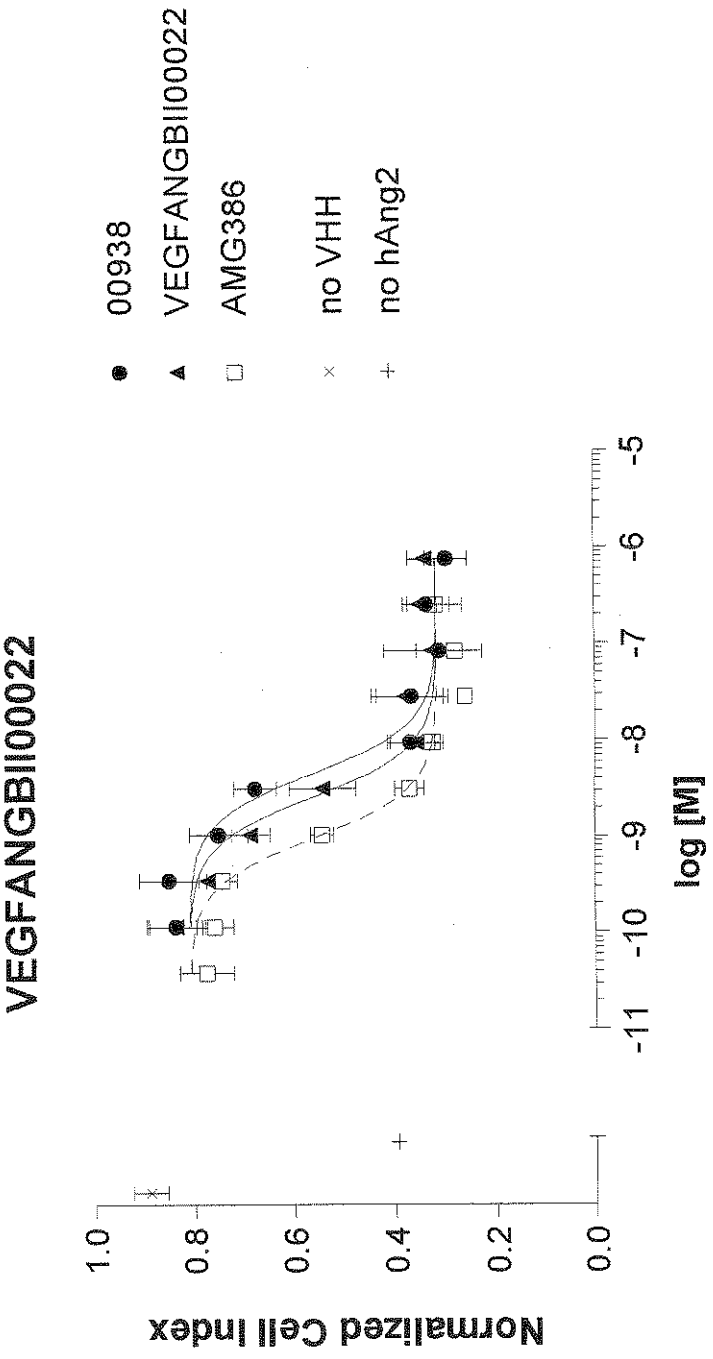

VEGFANGBII00022
00938
VEGFANGBII00022
AMG386
no VHH
no hAng2
Normalized Cell Index
1.0
0.8
0.6
0.4
0.2
0.0
-11
-10
-9
-8
-7
-6
-5
log [M]

**Figure 37B**

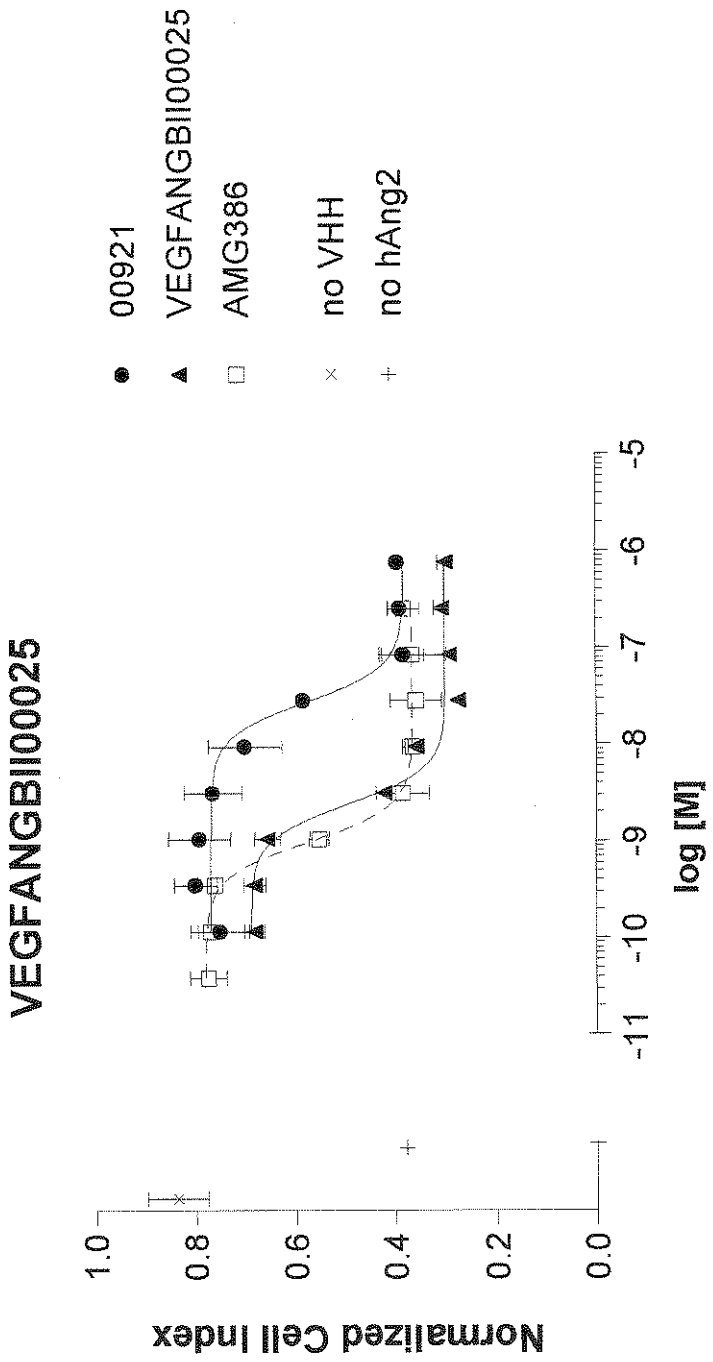
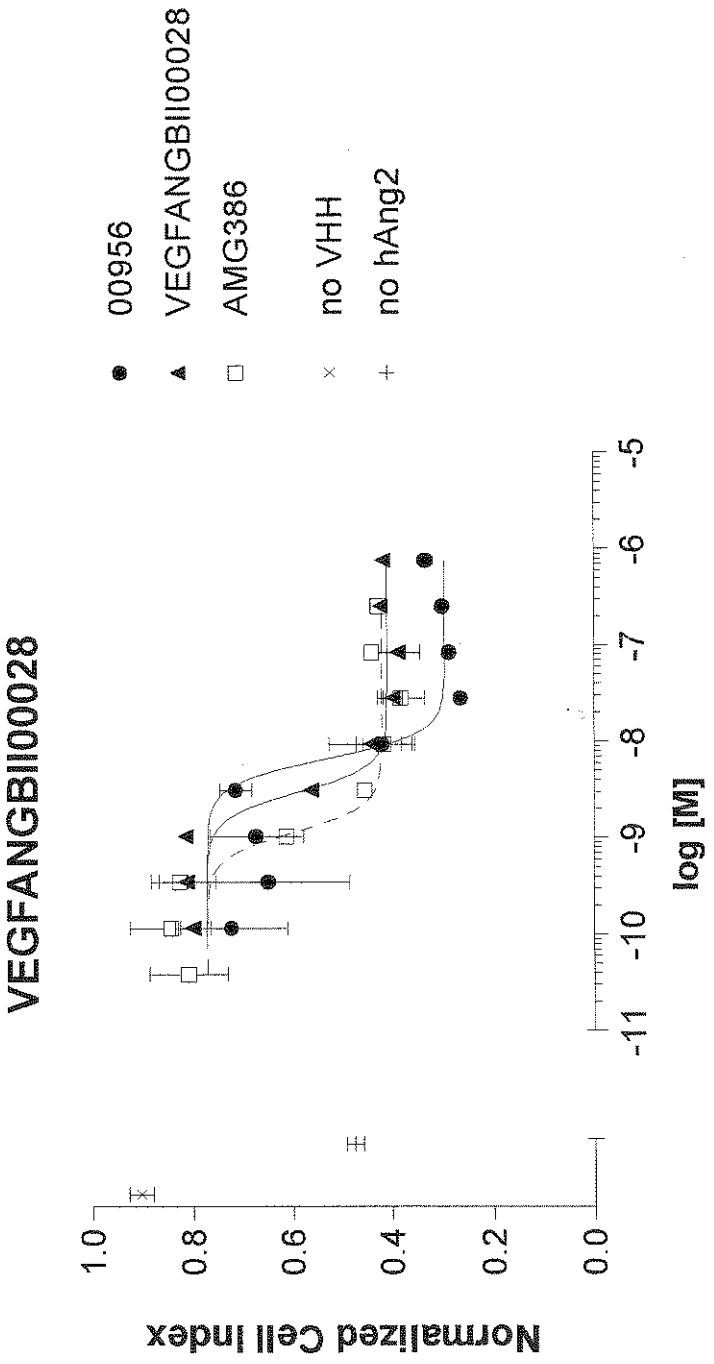

VEGFANGBII00025
00921
VEGFANGBII00025
AMG386
no VHH
no hAng2
Normalized Cell Index
1.0
0.8
0.6
0.4
0.2
0.0
-11
-10
-9
-8
-7
-6
-5
log [M]

**Figure 37C**


00956
VEGFANGBII00028
AMG386
no VHH
no hAng2
VEGFANGBII00028
Normalized Cell Index
1.0
0.8
0.6
0.4
0.2
0.0
-11
-10
-9
-8
-7
-6
-5
log [M]