Fig. 1

```
                    1                                                   100
DLL4 human      (1) MAAASRSASGWALLLLVALWQQRAAGSGVFQLQLQEFINERGVLASGRPCEPGCRTFFRVCLKHFQAVVSPGPCTFGTVSTPVLGTNSFAVRDDSSGGGR
DLL4 rhesus     (1) MAAASWSASGWALLLLVALWQQRAAGSGVFQLQLQEFVNERGVLASGRPCEPGCRTFFRVCLKHFQAVVSPGPCTFGSVSTPVLGTNSFAVRDDSSGGGR
DLL4 cyno       (1) MAAASWSASGWALLLLVALWQQRAAGSGVFQLQLQEFVNERGVLASGRPCEPGCRTFFRVCLKHFQAVVSPGPCTFGSVSTPVLGTNSFAVRDDSSGGGR

                  101                                                   200
DLL4 human    (101) NPLQLPFNFTWPGTFSLIIEAWHAPGDDLRPEALPPDALISKIAIQGSLAVGQNWLLDEQTSTLTRLRYSYRVICSDNYYGDNCSRLCKKRNDHFGHYVC
DLL4 rhesus   (101) NPLQLPFNFTWPGTFSLIIEAWHAPGDDLRPEALPPDALISKIAIQGSLAVGQNWLLDEQTSTLTRLRYSYRVICSDNYYGDNCSRLCKKRNDHFGHYVC
DLL4 cyno     (101) NPLQLPFNFTWPGTFSLIIEAWHAPGDDLRPEALPPDALISKIAIQGSLAVGQNWLLDEQTSTLTRLRYSYRVICSDNYYGDNCSRLCKKRNDHFGHYVC

                  201                                                   300
DLL4 human    (201) QPDGNLSCLPGWTGEYCQQPICLSGCHEQNGYCSKPAECLCRPGWQGRLCNECIPHNGCRHGTCSTPWQCTCDEGWGGLFCDQDLNYCTHHSPCKNGATC
DLL4 rhesus   (201) QPDGNLSCLPGWTGEYCQQPICLSGCHEQNGYCSKPAECLCRPGWQGRLCNECIPHNGCRHGTCSTPWQCTCDEGWGGLFCDQDLNYCTHHSPCKNGATC
DLL4 cyno     (201) QPDGNLSCLPGWTGEYCQQPICLSGCHEQNGYCSKPAECLCRPGWQGRLCNECIPHNGCRHGTCSTPWQCTCDEGWGGLFCDQDLNYCTHHSPCKNGATC

                  301                                                   400
DLL4 human    (301) SNSGQRSYTCTCRPGYTGVDCELELSECDSNPCRNGGSCKDQEDGYHCLCPPGYYGLHCEHSTLSCADSPCFNGGSCRERNQGANYACECPPNFTGSNCE
DLL4 rhesus   (301) SNSGQRSYTCTCRPGYTGVDCELELSECDSNPCRNGGSCKDQEDGYHCLCPPGYYGLHCEHSTLSCADSPCFNGGSCRERNQGASYACECPPNFTGSNCE
DLL4 cyno     (301) SNSGQRSYTCTCRPGYTGVDCELELSECDSNPCRNGGSCKDQEDGYHCLCPPGYYGLHCEHSTLSCADSPCFNGGSCRERNQGASYACECPPNFTGSNCE

                  401                                                   500
DLL4 human    (401) KKVDRCTSNPCANGGQCLNRGPSRMCRCRPGFTGTYCELHVSDCARNPCAHGGTCHDLENGLMCTCPAGFSGRRCEVRTSIDACASSPCFNRATCYTDLS
DLL4 rhesus   (401) KKVDRCTSNPCANGGQCLNRGPSRMCRCRPGFTGTYCERHVSDCARNPCAHGGTCHDLESGLMCTCPAGFSGRRCEVRTSIDACASSPCFNRATCYTDLS
DLL4 cyno     (401) KKVDRCTSNPCANGGQCLNRGPSRMCRCRPGFTGTYCERHVSDCARNPCAHGGTCHDLESGLMCTCPAGFSGRRCEVRTSIDACASSPCFNRATCYTDLS

                  501                                                   600
DLL4 human    (501) TDTFVCNCPYGFVGSRCEFPVGLPPSFPWVAVSLGVGLAVLLVLLGMVAVAVRQLRLRRPDDGSREAMNNLSDFQKDNLIPAAQLKNTNQKKELEVDCGL
DLL4 rhesus   (501) TDTFVCNCPYGFVGSRCEFPVGLPPSFPWVAVSLGVGLAVLLVLLGMVAVAVRQLRLRRPDDGSREAMNNLSDFQKDNLIPAAQLKNTNQKKELEVDCGL
DLL4 cyno     (501) TDTFVCNCPYGFVGSRCEFPVGLPPSFPWVAVSLGVGLAVLLVLLGMVAVAVRQLRLRRPDDGSREAMNNLSDFQKDNLIPAAQLKNTNQKKELEVDCGL

                  601                                                   685
DLL4 human    (601) DKSNCGKQQNHTLDYNLAPGPLGRGTMPGKFPHSDKSLGEKAPLRLHSEKPECRISAICSPRDSMYQSVCLISEERNECVIATEV
DLL4 rhesus   (601) DKSNCGKQQNHTLDYNLAPGPLGRGTMPGKFPHSDKSLGEKAPLRLHSEKPECRISAICSPRDSMYQSVCLISEERNECVIATEV
DLL4 cyno     (601) DKSNCGKQQNHTLDYNLAPGPLGRGTMPGKFPHSDKSLGEKAPLRLHSEKPECRISAICSPRDSMYQSVCLISEERNECVIATEV
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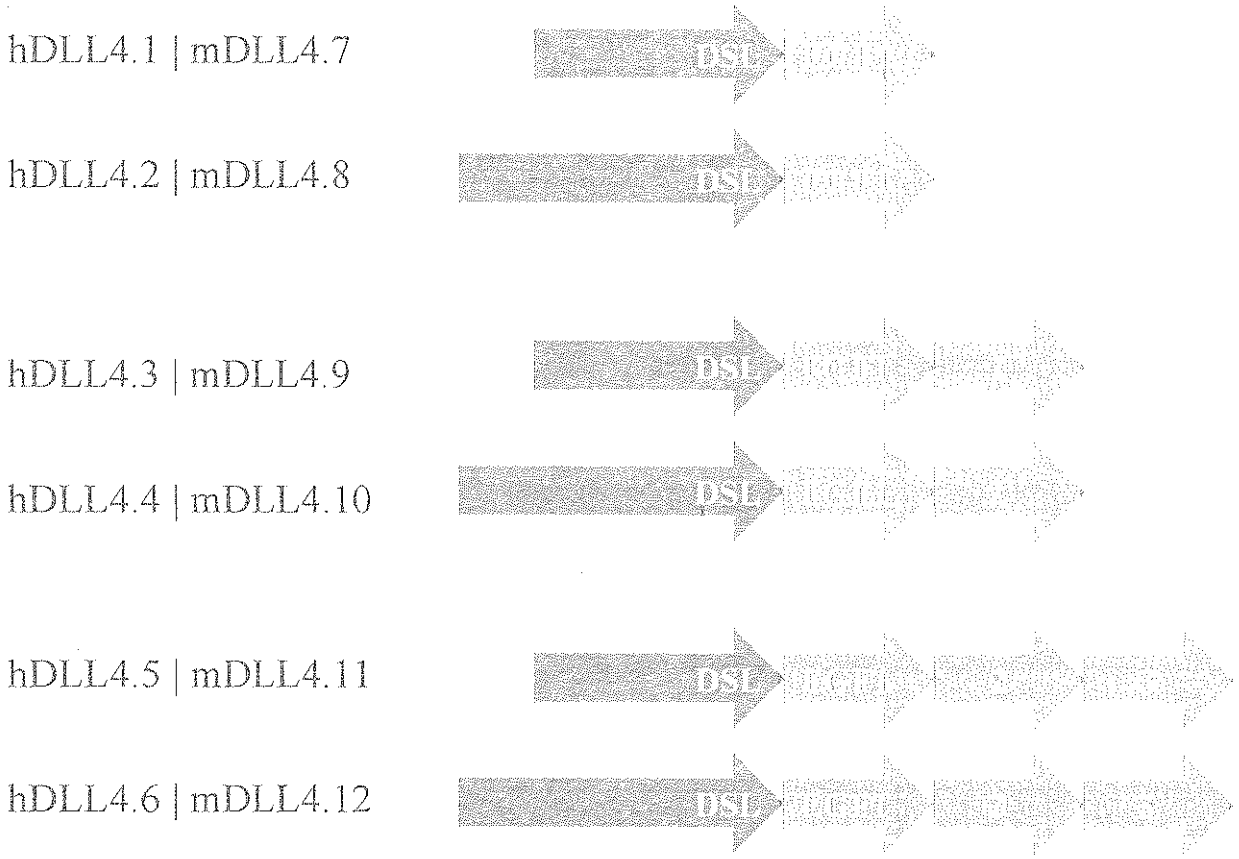
Fig. 2

hDLL4 constructs

hDLL4.1: $DSL^{173-217}$ – $EGF1^{218-251}$ – (His)6
hDLL4.2: $DSL^{155-217}$ – $EGF1^{218-251}$ – (His)6
hDLL4.3: $DSL^{173-217}$ – $EGF1^{218-251}$ – $EGF2^{252-282}$ – (His)6
hDLL4.4: $DSL^{155-217}$ – $EGF1^{218-251}$ – $EGF2^{252-282}$ – (His)6
hDLL4.5: $DSL^{173-217}$ – $EGF1^{218-251}$ – $EGF2^{252-282}$ – $EGF3^{284-322}$ – (His)6
hDLL4.6: $DSL^{155-217}$ – $EGF1^{218-251}$ – $EGF2^{252-282}$ – $EGF3^{284-322}$ – (His)6

mDLL4 constructs

mDLL4.7: $DSL^{174-218}$ – $EGF1^{219-252}$ – (His)6
mDLL4.8: $DSL^{1152-218}$ – $EGF1^{219-252}$ – (His)6
mDLL4.9: $DSL^{174-218}$ – $EGF1^{219-252}$ – $EGF2^{252-282}$ – (His)6
mDLL4.10: $DSL^{1152-218}$ – $EGF1^{219-252}$ – $EGF2^{252-282}$ – (His)6
mDLL4.11: $DSL^{174-218}$ – $EGF1^{219-252}$ – $EGF2^{252-282}$ – $EGF3^{285-323}$ – (His)6
mDLL4.12: $DSL^{1152-218}$ – $EGF1^{219-252}$ – $EGF2^{252-282}$ – $EGF3^{285-323}$ – (His)6



3 / 152
Fig. 3-1

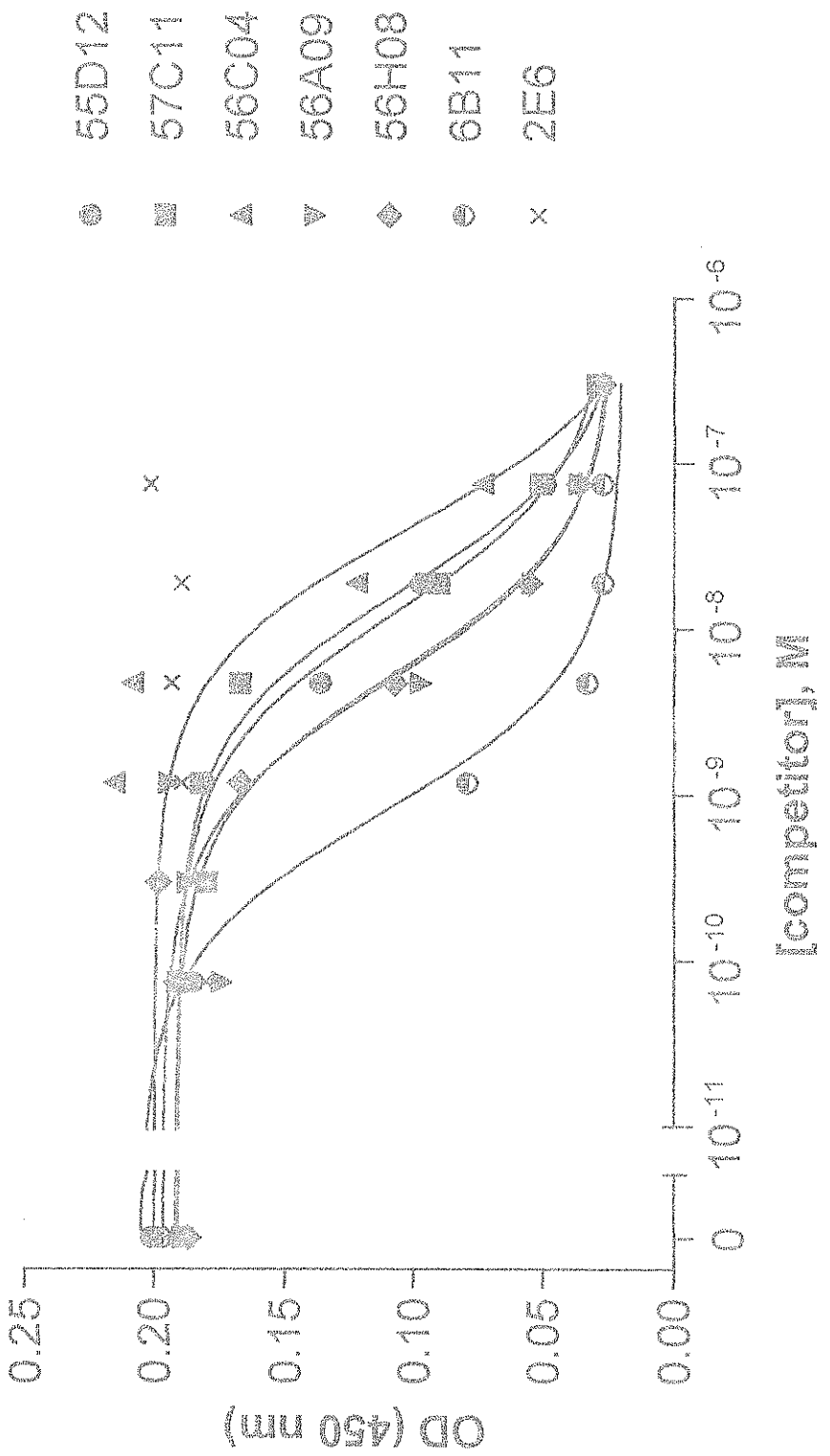
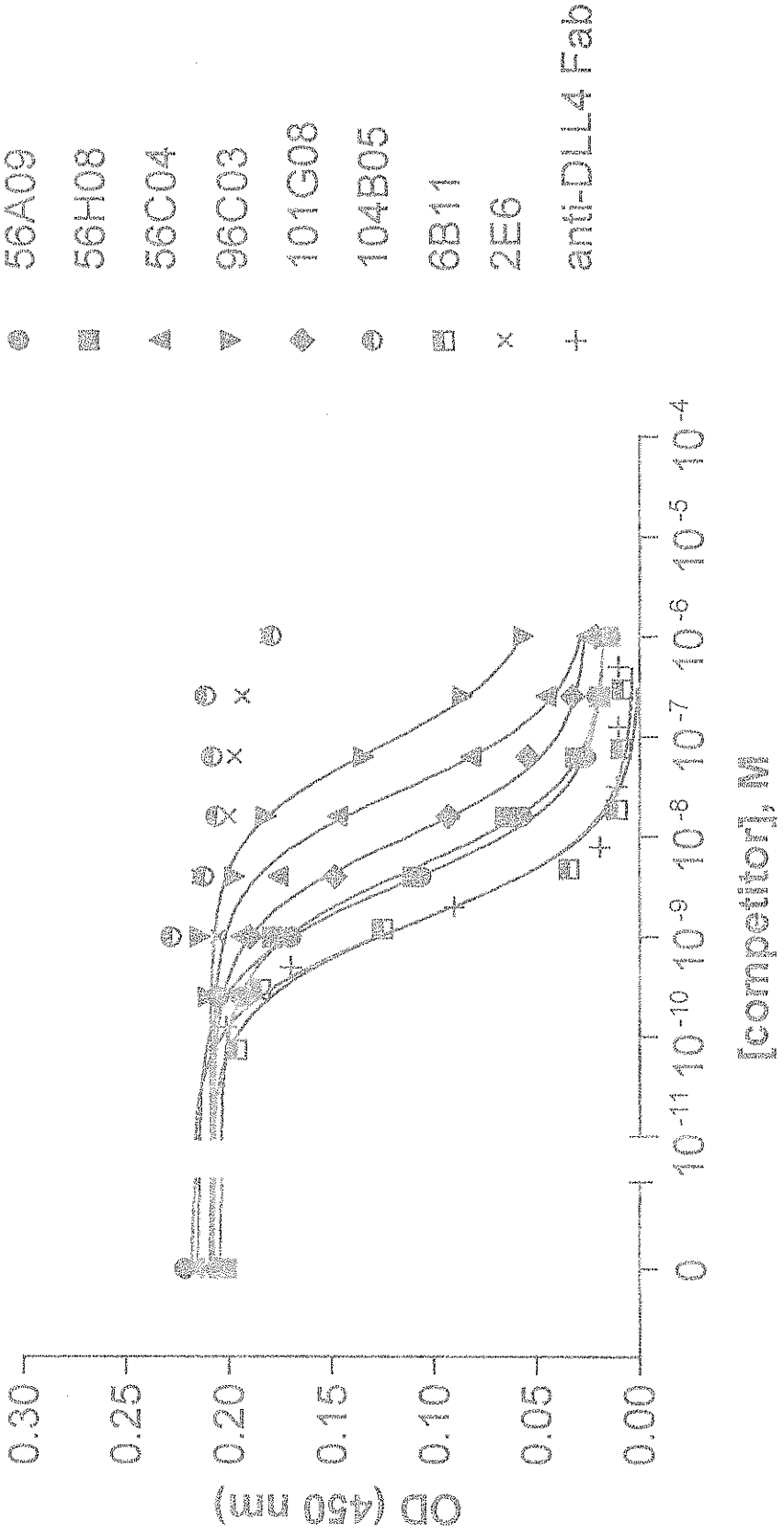

5D12
57C11
56C04
56A09
56H08
6B11
2E6
OD (450 nm)
0.25
0.20
0.15
0.10
0.05
0.00
0
10-11
10-10
10-9
10-8
10-7
10-6
[competitor], M

Fig. 3-2


56A03
56H08
56C04
96C03
101G08
104B05
6B1/1
2E6
anti-DLL4 Fab
OD (450 nm)
0.30
0.25
0.20
0.15
0.10
0.05
0.00
0
10-11
10-10
10-9
10-8
10-7
10-6
10-5
10-4
Concentration, M

5 / 152
Fig. 3-3

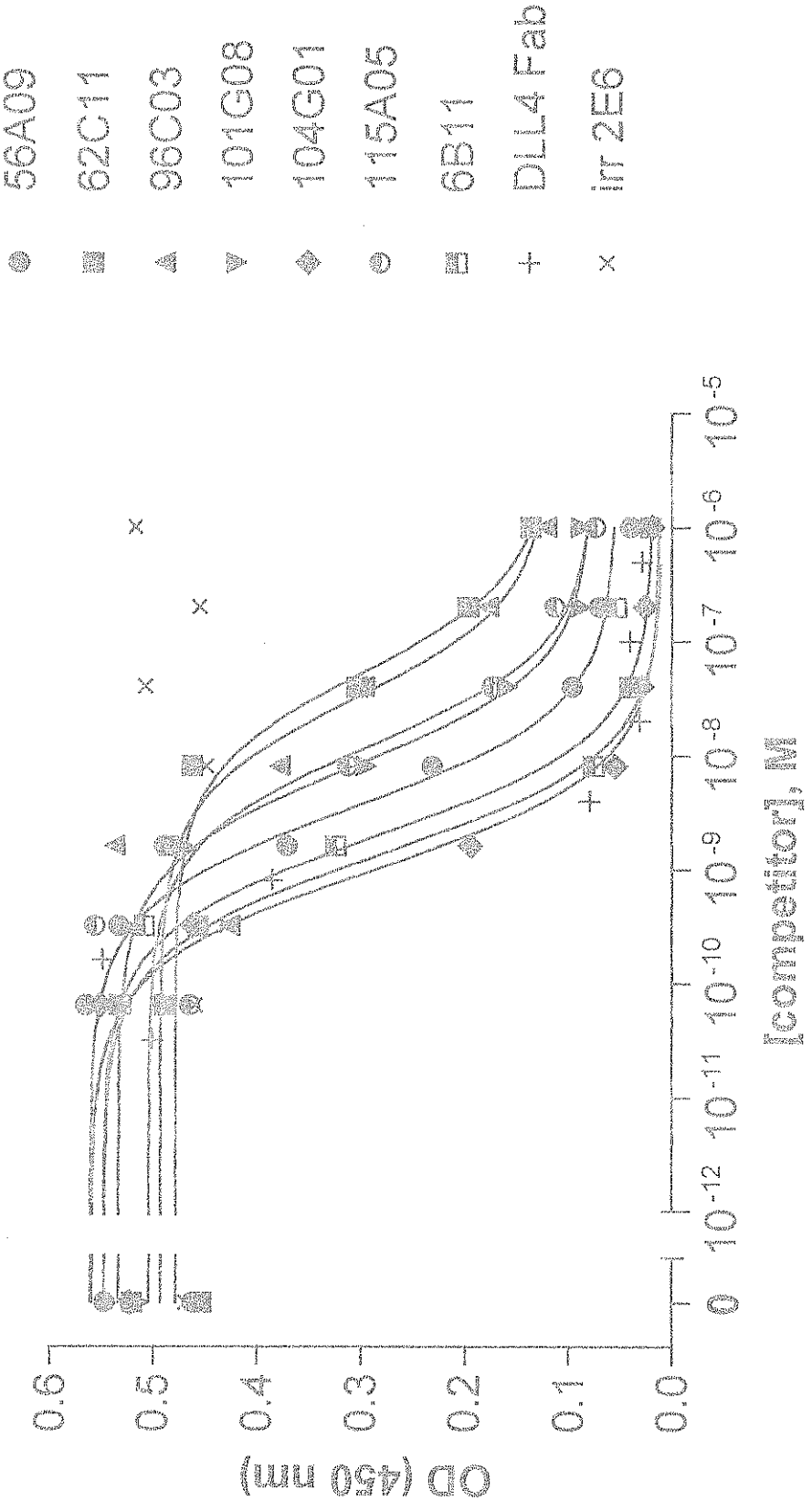

56A09
82C11
98C03
101G08
104G01
115A05
6B11
DL14 Fab
Irr 2E6
OD (450 nm)
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
Konzentration [M]

Fig. 4-1

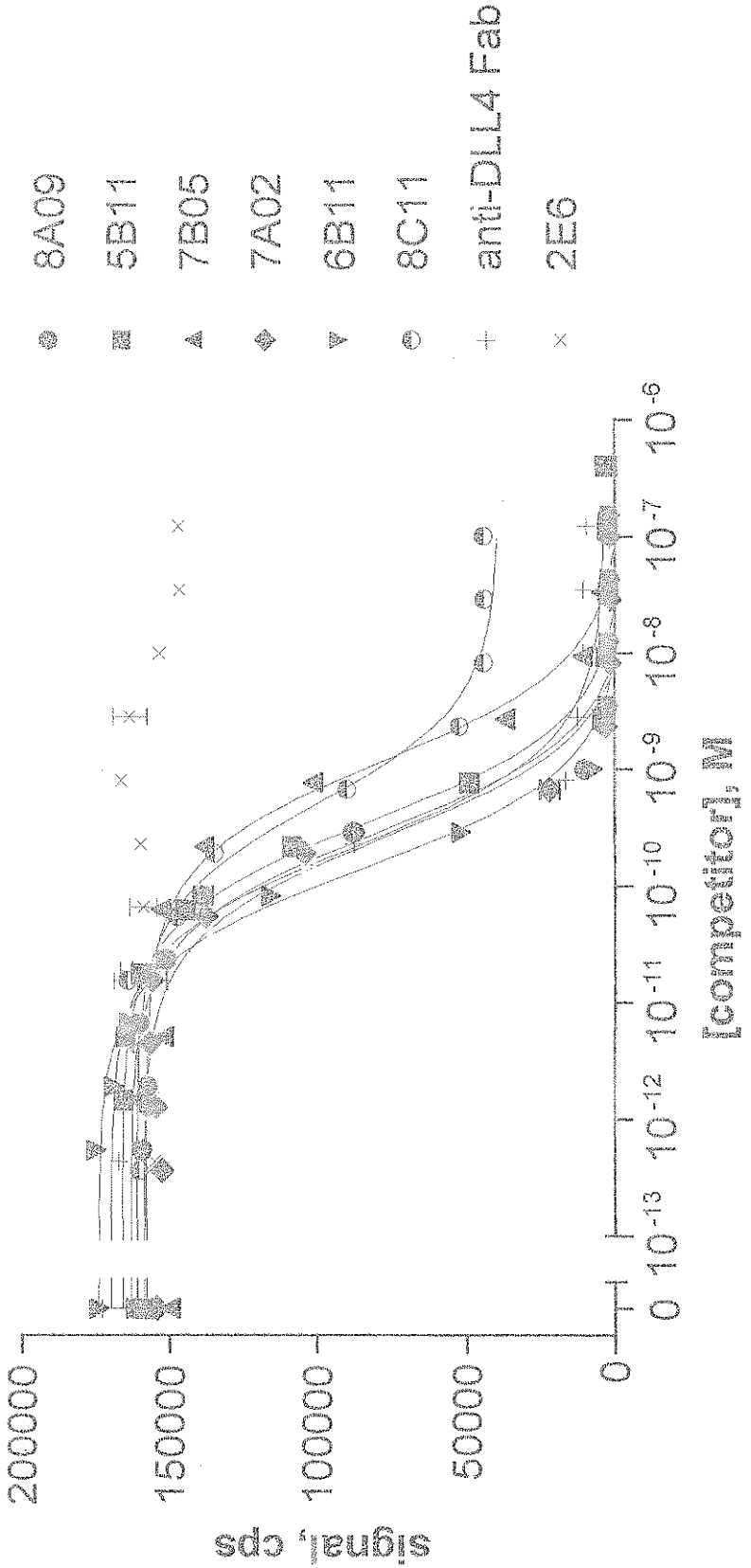

8A09
5B11
7B05
7A02
6B11
8C11
anti-DLL4 Fab
2E6
signal, cps
200000
150000
100000
50000
0
0 10-13 10-12 10-11 10-10 10-9 10-8 10-7 10-6
concentration, M

Fig. 4-2

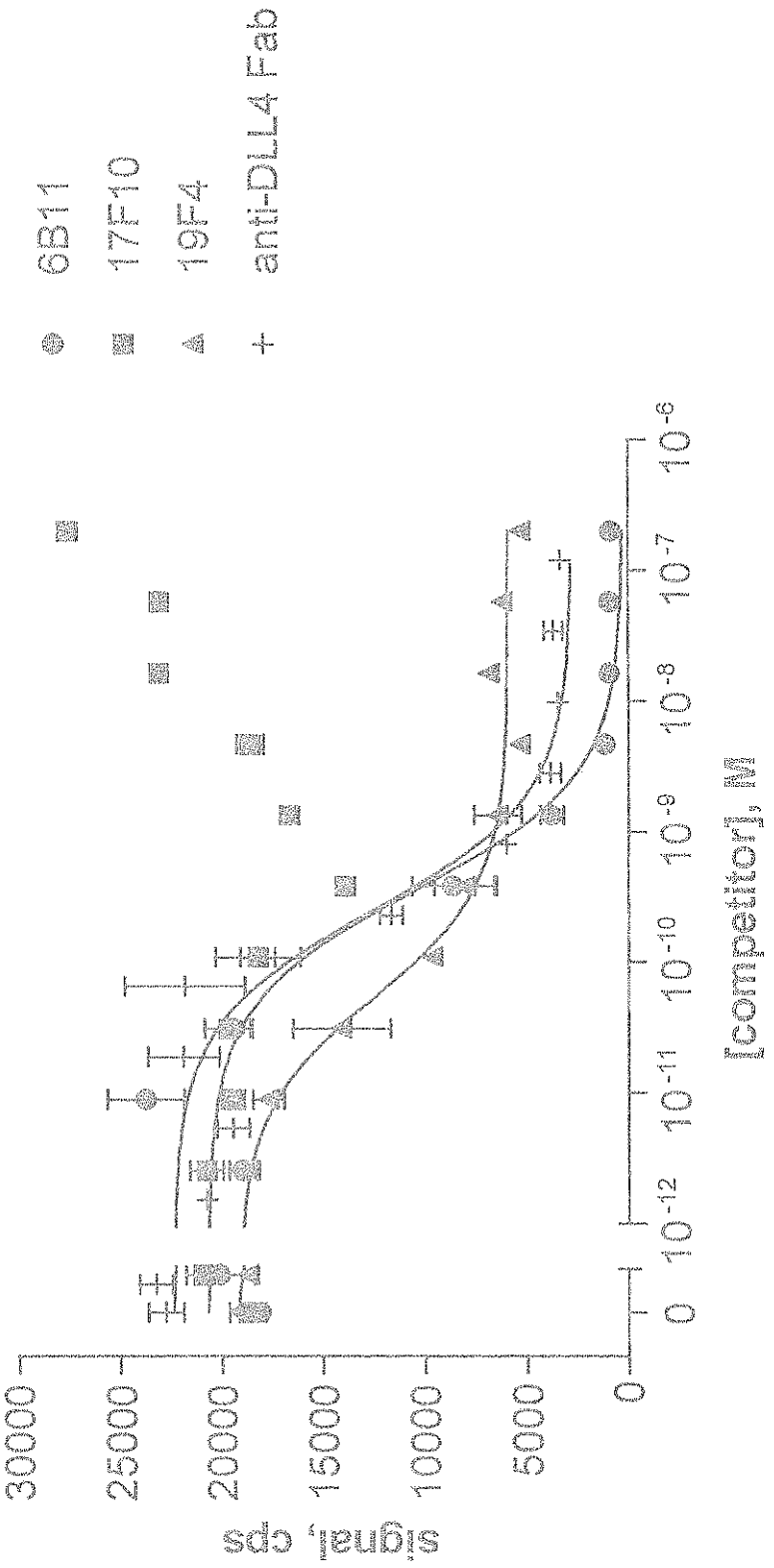

6B11
17F10
19F4
anti-DLL4 Fab
signal, cps
30000
25000
20000
15000
10000
5000
0
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
[competitor], M

Fig. 4-3

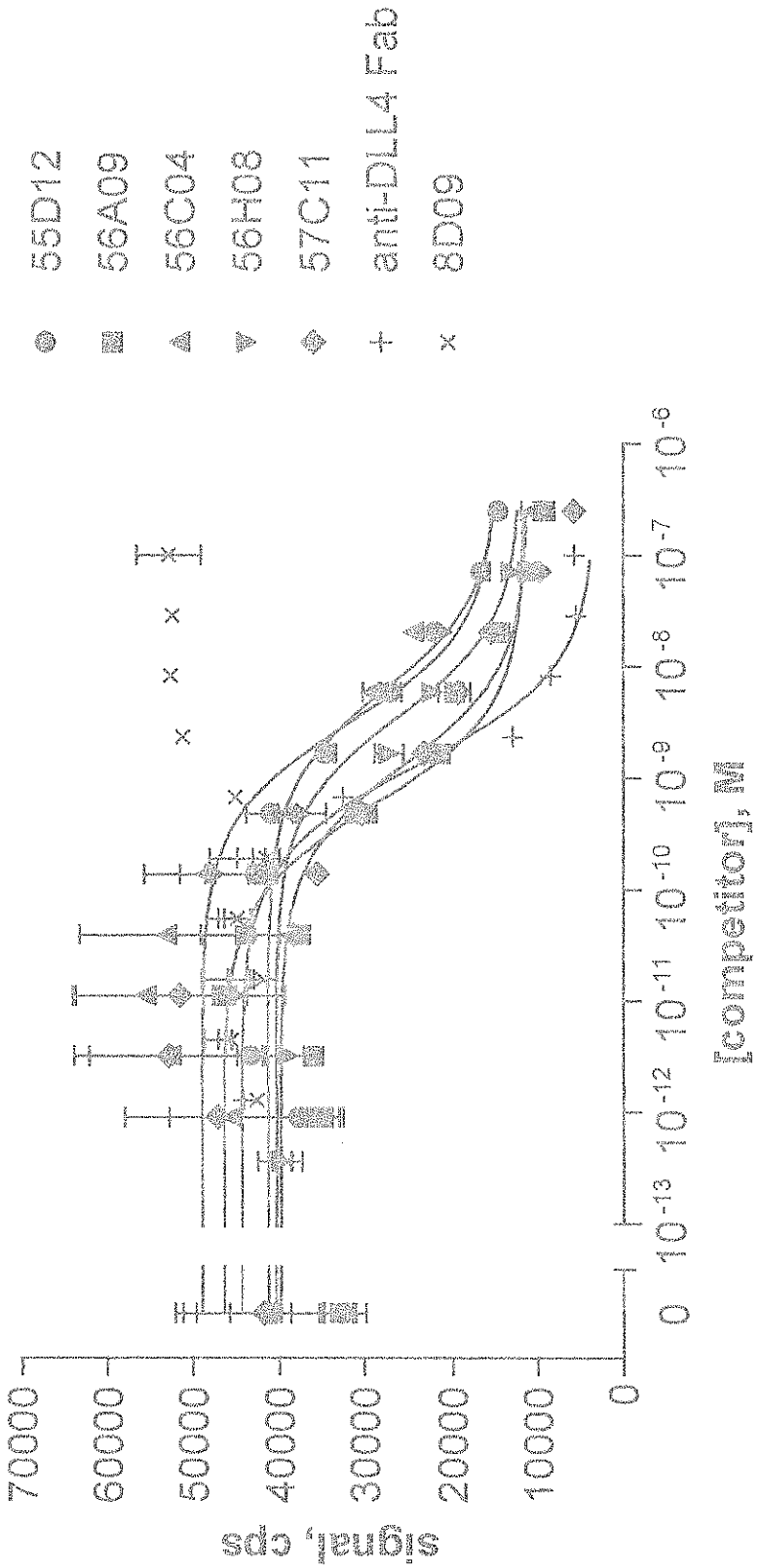

55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab
8D09
signal, cps
70000
60000
50000
40000
30000
20000
10000
0
competitor, M
0
10-13
10-12
10-11
10-10
10-9
10-8
10-7
10-6

Fig. 4-4

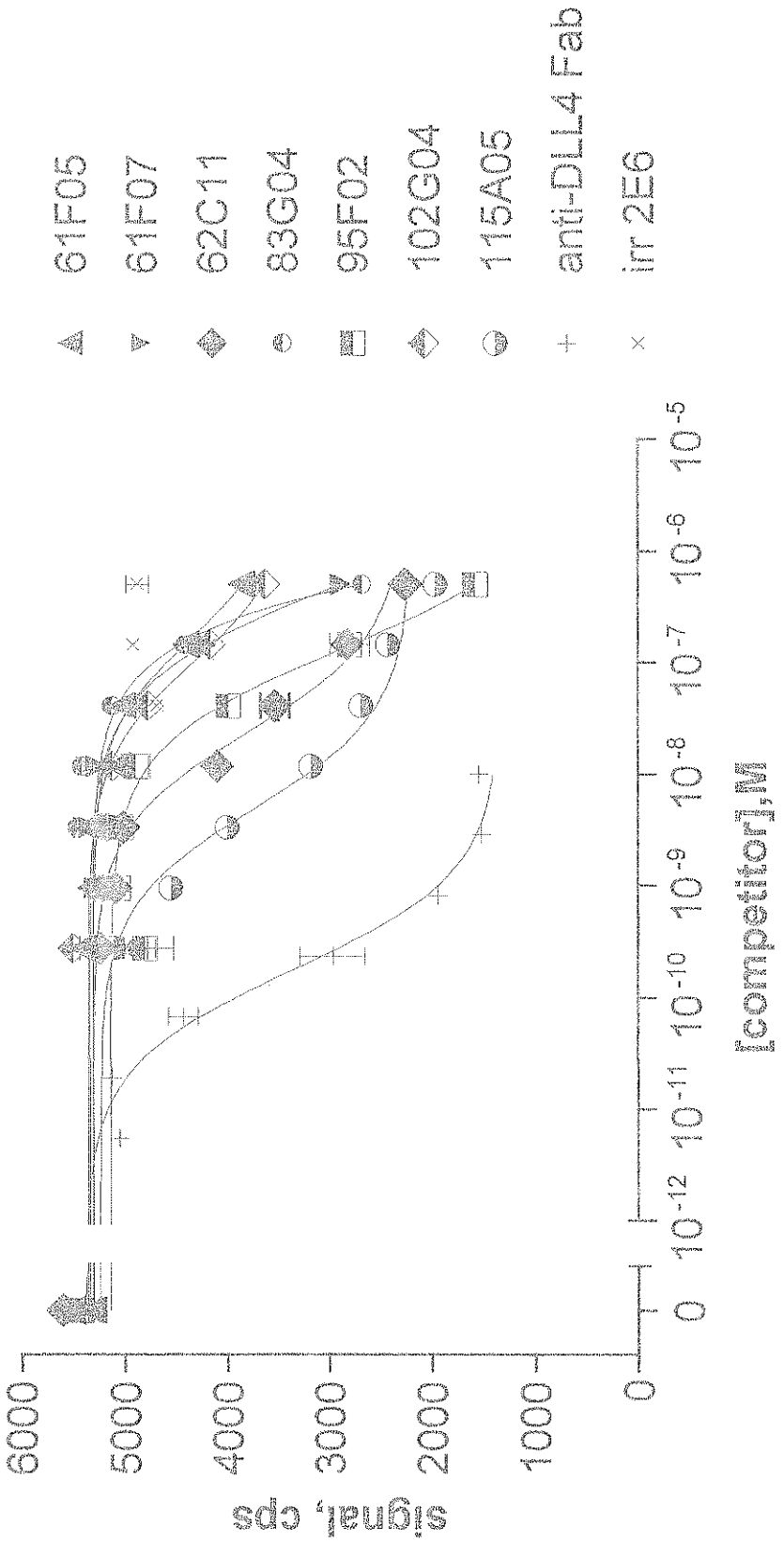

61F05
61F07
62C11
83G04
95F02
102G04
115A05
anti-DLL4 Fab
irr 2E6
signal, cps
6000
5000
4000
3000
2000
1000
0
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
concentration, M

Fig. 4-5

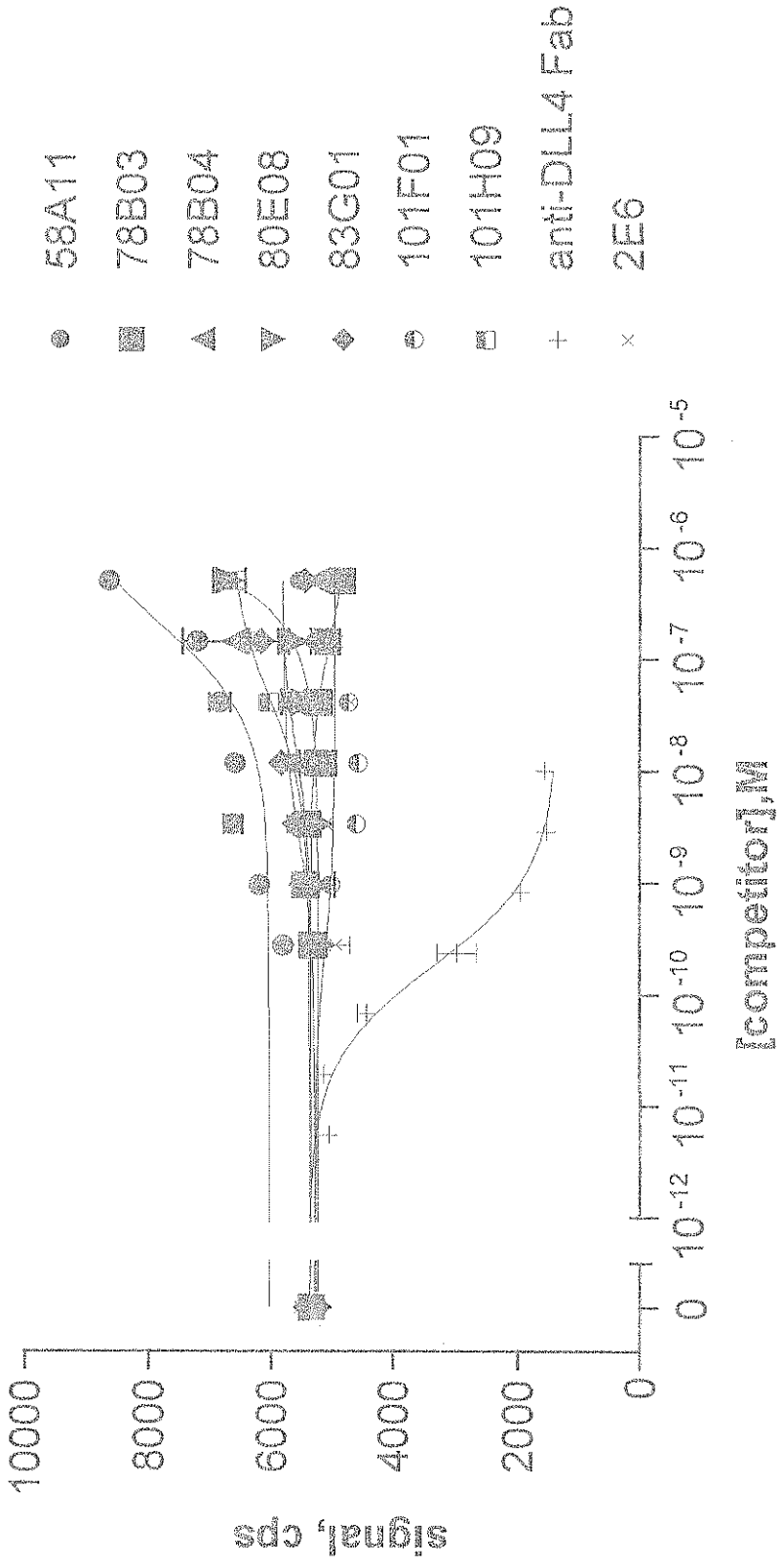
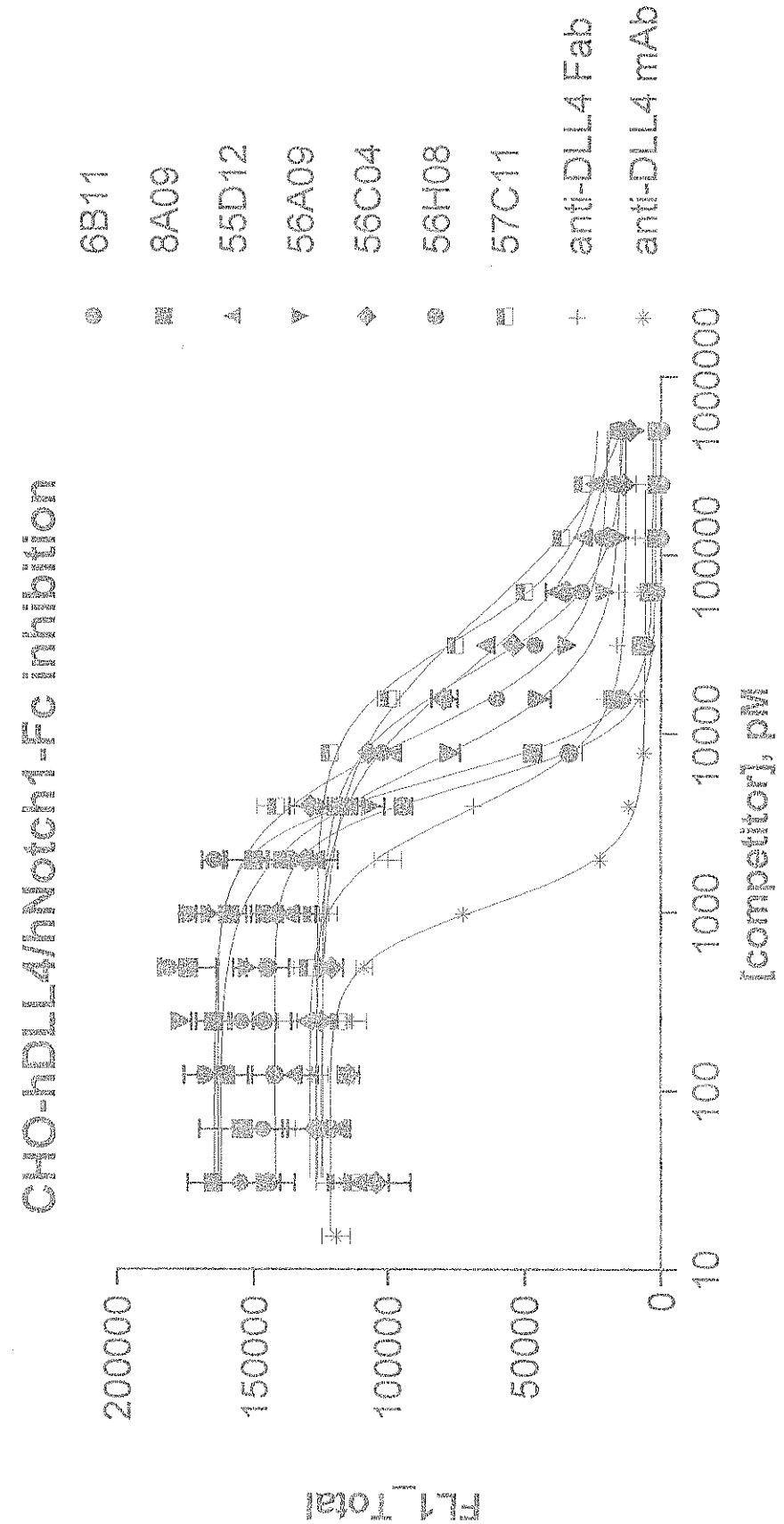

58A11
78B03
78B04
80E08
83C01
101F01
101H09
anti-DLL4 Fab
2E6
signal, cps
10000
8000
6000
4000
2000
0
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
competitor, M

Fig. 5-1


CHO-hDLL4hNotch1-Fc inhibition
6B11
8A09
55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab
anti-DLL4 mAb
FL1_Total
200000
150000
100000
50000
0
10
100
1000
10000
100000
1000000
concentration, pM

12 / 152
Fig. 5-2

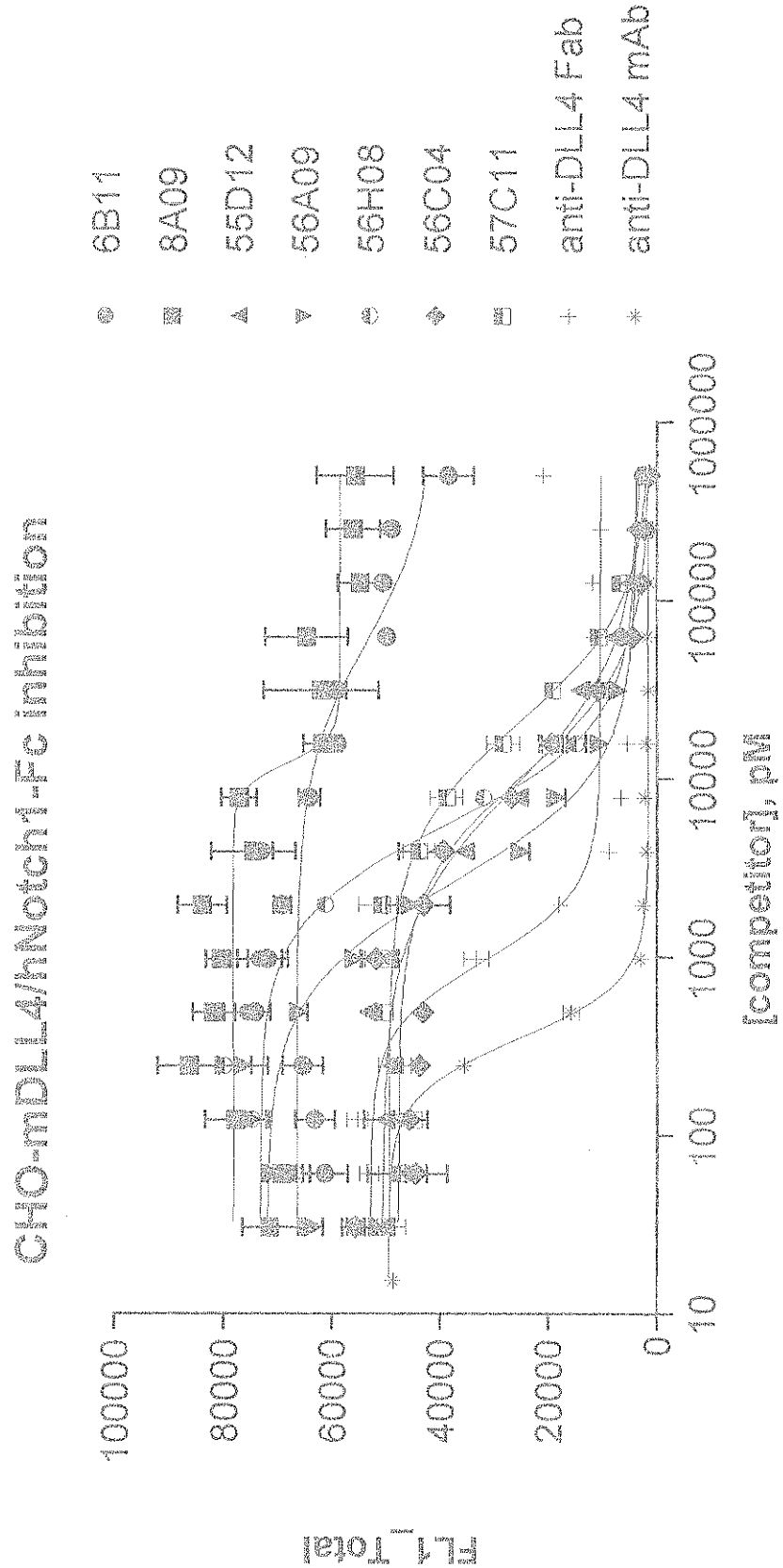
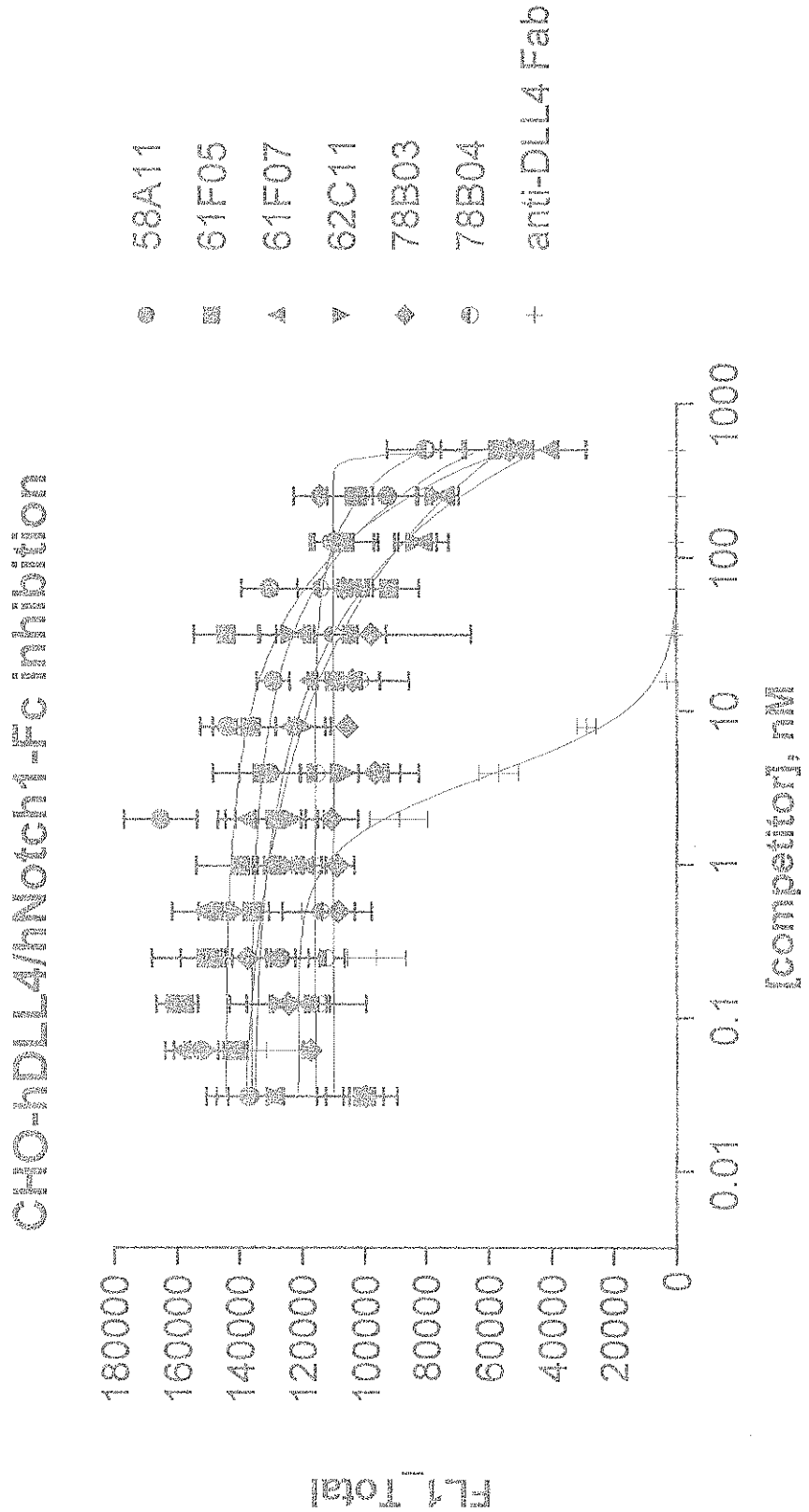

6B11
8A09
55D12
56A09
56H08
56C04
57C11
anti-DL4 Fab
anti-DL4 mAb
CHO-mDL4/mNotch1-Fc inhibition
FL1_Total
competitor, pM
100000
80000
60000
40000
20000
0
10
100
1000
10000
100000
1000000

Fig. 5-3


58A11
61F05
61F07
62C11
78B03
78B04
anti-DLL4 Fab
CHO-hDLL4/Notch1-Fc empression
FL-1_Total
Concentration, nM
0.01
0.1
1
10
100
1000
0
20000
40000
60000
80000
100000
120000
140000
160000
180000

14 / 152

Fig. 5-4

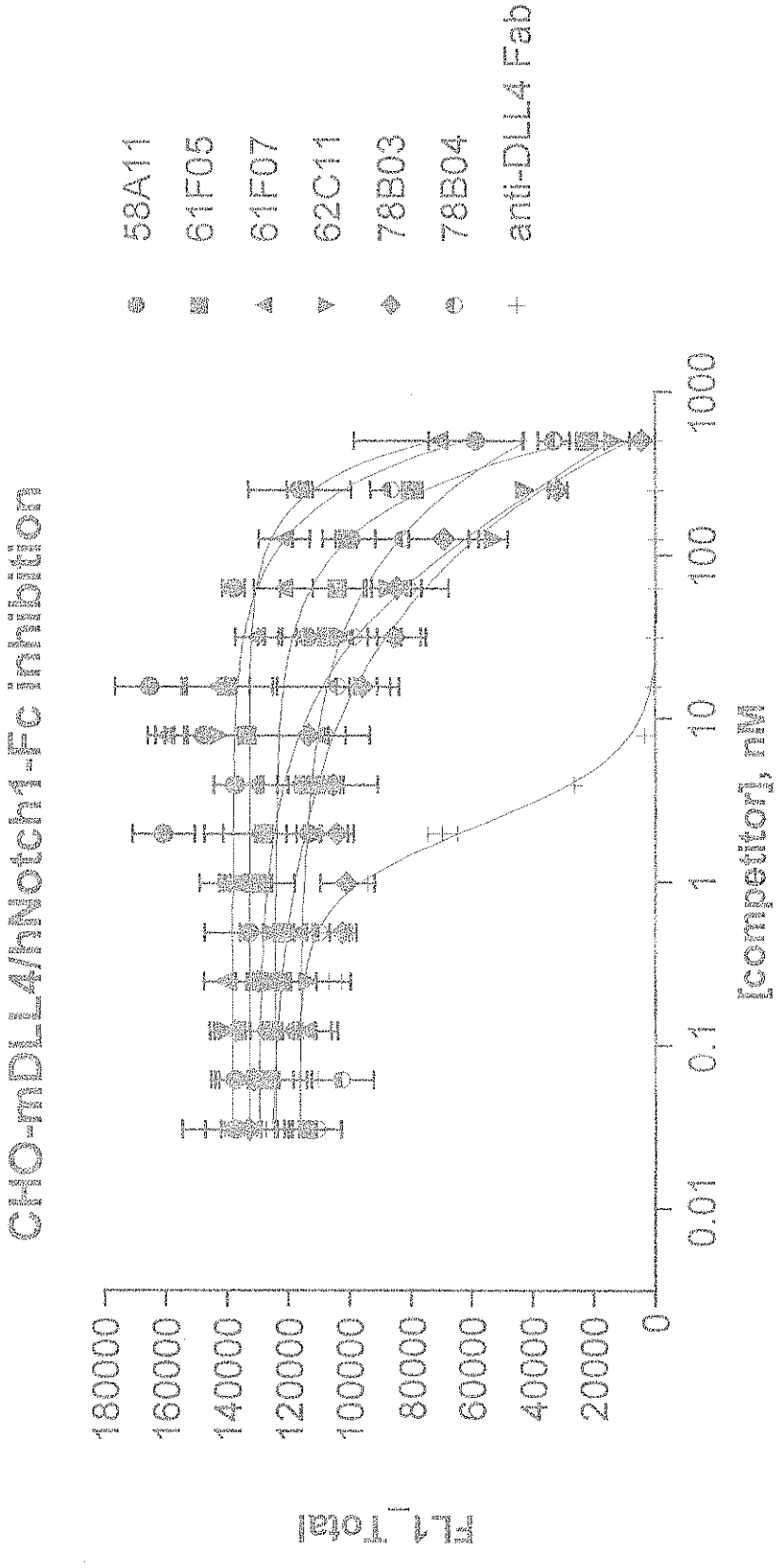
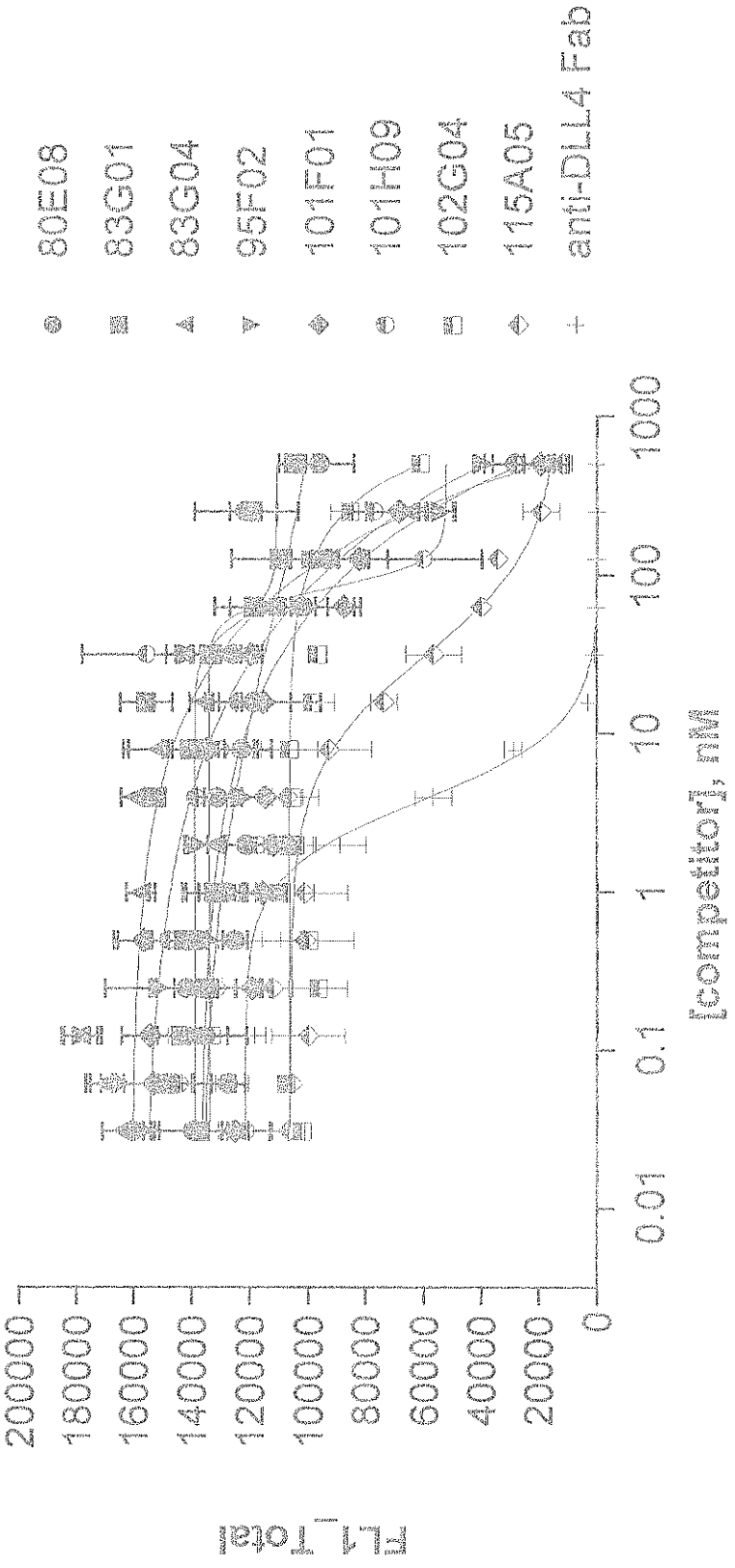

58A11
61F05
61F07
62C11
78B03
78B04
anti-DLL4 Fab
CHO-mDLL4/hNotch1-FC Inhibition
FL4_Total
Concentration, nM
0.01
0.1
1
10
100
1000
0
20000
40000
60000
80000
100000
120000
140000
160000
180000

Fig. 5-5


CHO-hDLL4/hNotch1-Fc inhibition
FL1_Total
Concentration nM
0.01
0.1
1
10
100
1000
0
20000
40000
60000
80000
100000
120000
140000
160000
180000
200000
80E08
83G01
83G04
95F02
101F01
101H09
102G04
115A05
anti-DLL4 Fab

16 / 152
Fig. 5-6

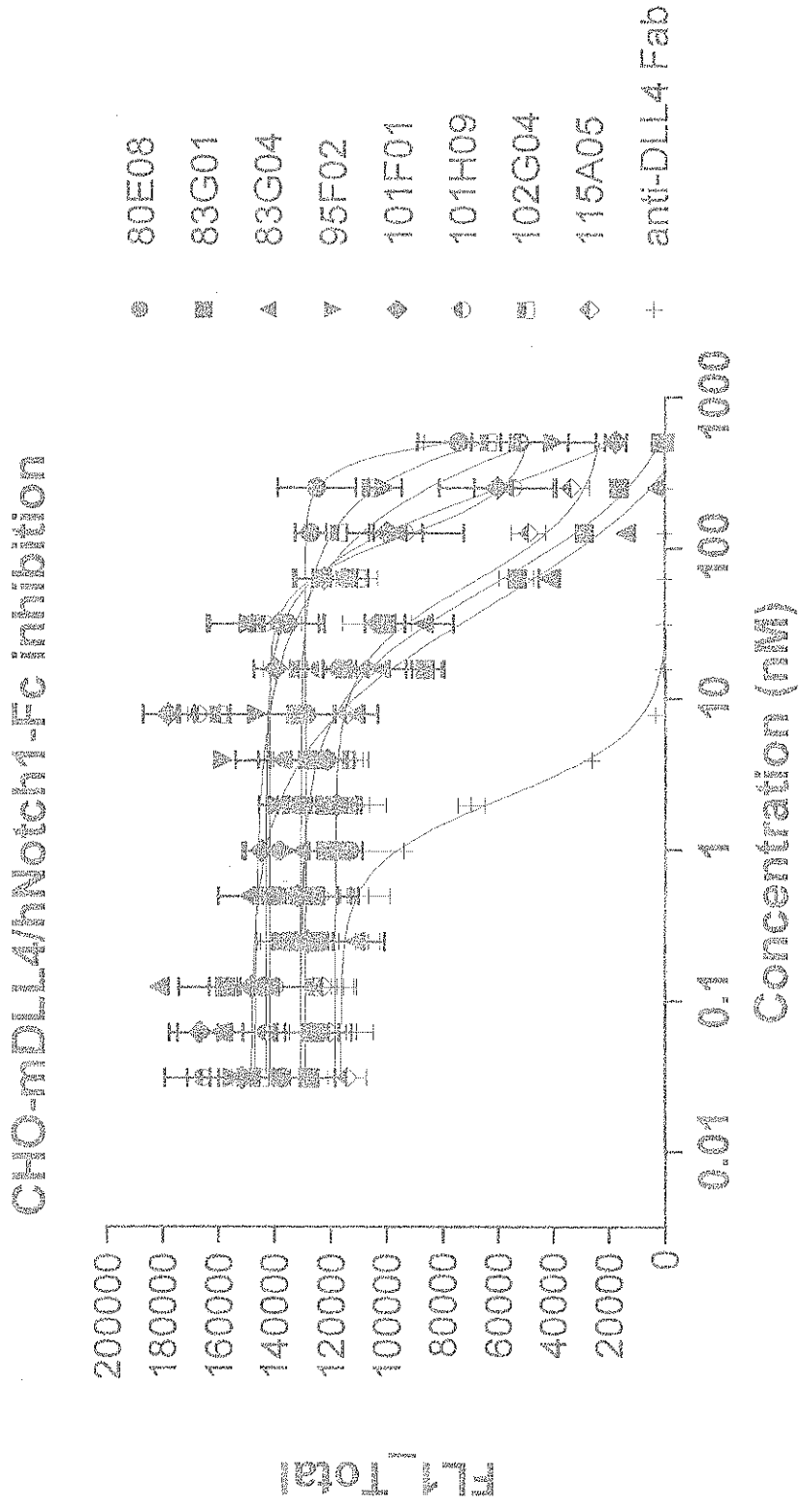

CHO-mDLL4/Notch1-Fc binding
80E08
83G01
83G04
95F02
101F01
101H09
102G04
115A05
anti-DLL4 Fab
FL-1_Total
Concentration (nM)
0.01
0.1
1
10
100
1000
0
20000
40000
60000
80000
100000
120000
140000
160000
180000
200000

Fig. 5-7

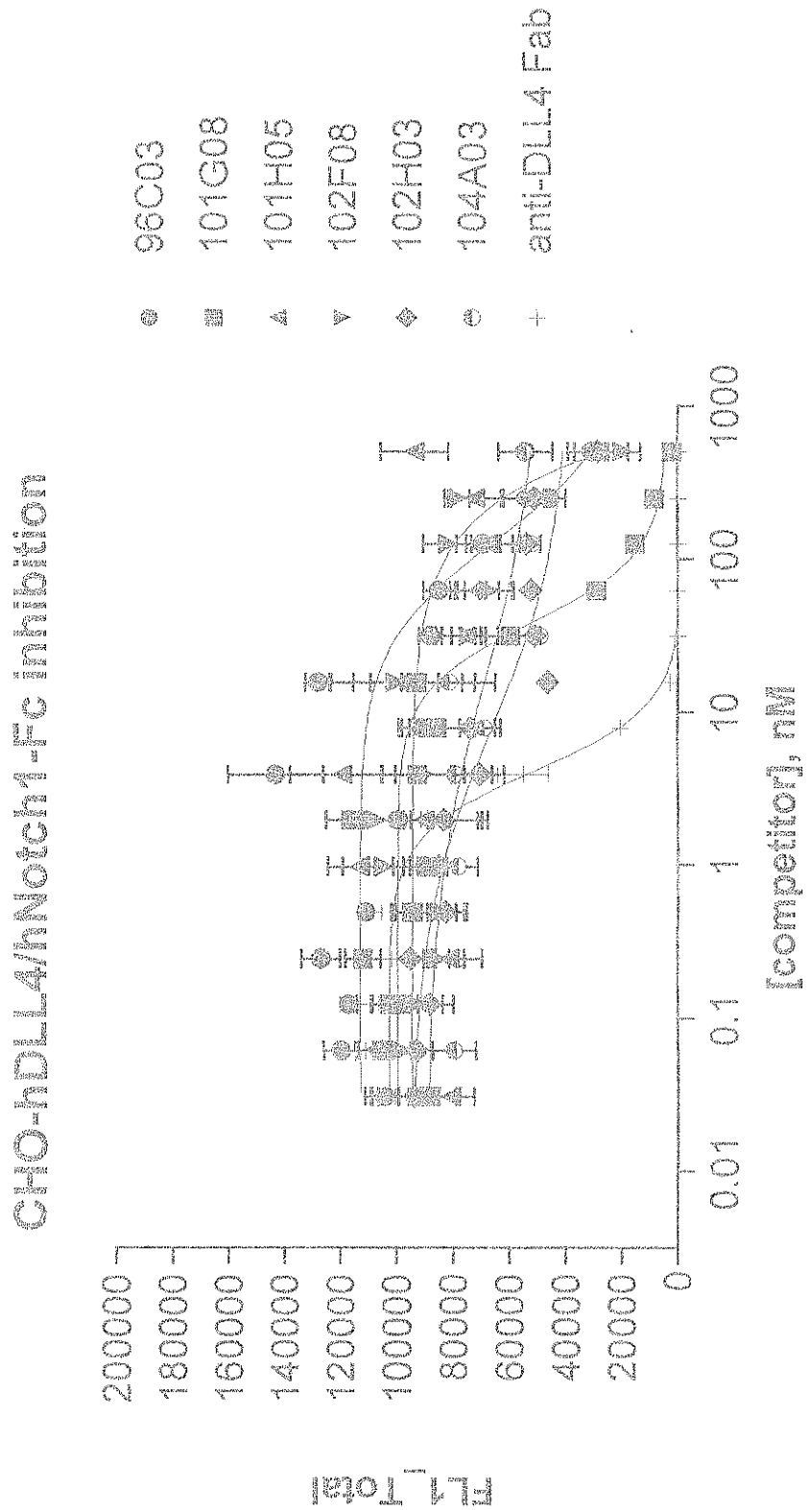

96C03
101C08
101H05
102F08
102H03
104A03
anti-DLL4 Fab
CHO-hDLL4/Notch1-EC binding inhibition
FL1_Total
Concentration, nM
0.01
0.1
1
10
100
1000
0
20000
40000
60000
80000
100000
120000
140000
160000
180000
200000

Fig. 5-8

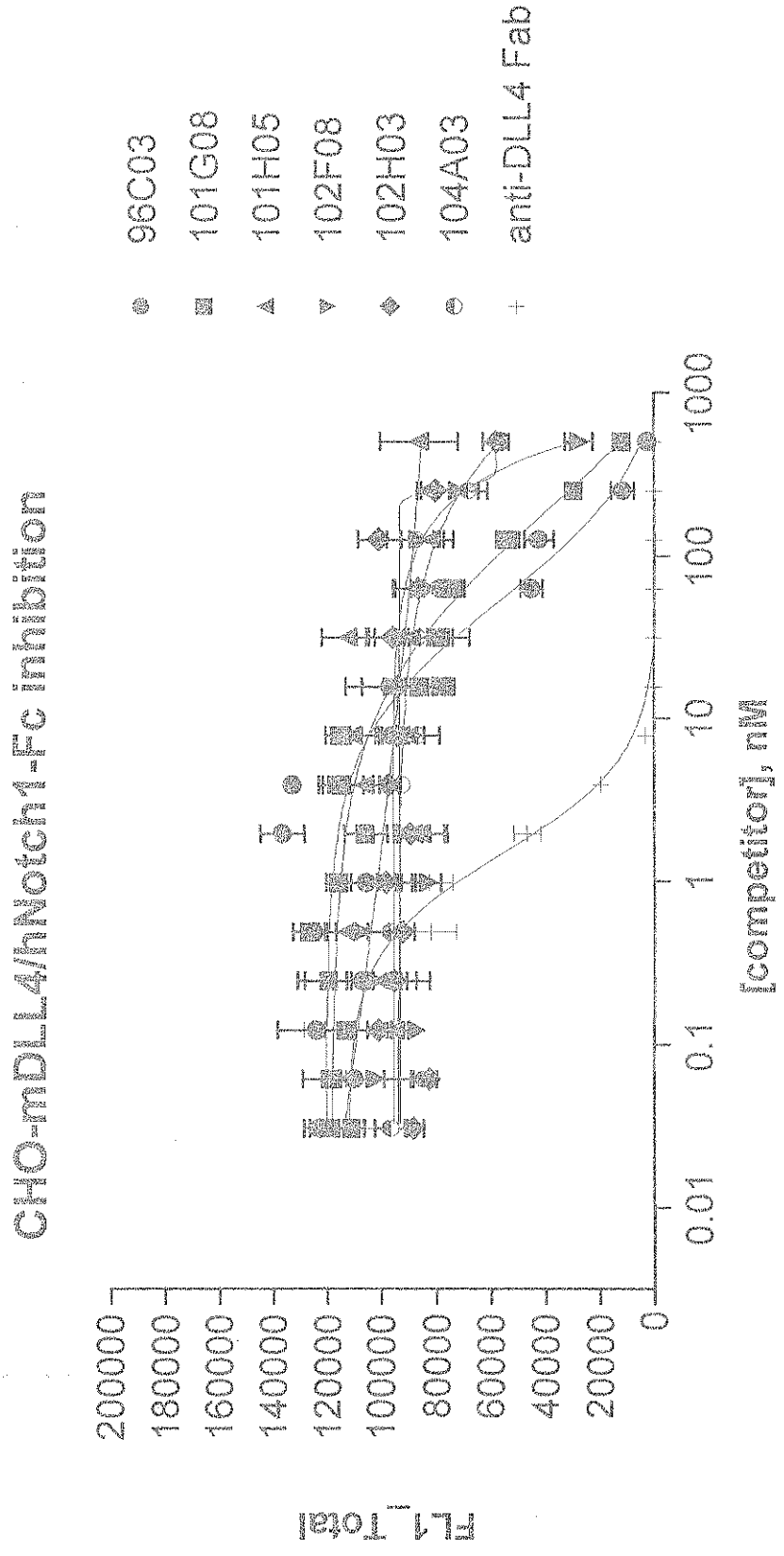

96C03
101G08
101H05
102F08
102H03
104A03
anti-DLL4 Fab
CHO-mDLL4/hVEGFR2-Fc binding
competitor, nM
FL1_Total
0.01
0.1
1
10
100
1000
0
20000
40000
60000
80000
100000
120000
140000
160000
180000
200000

Fig. 5-9

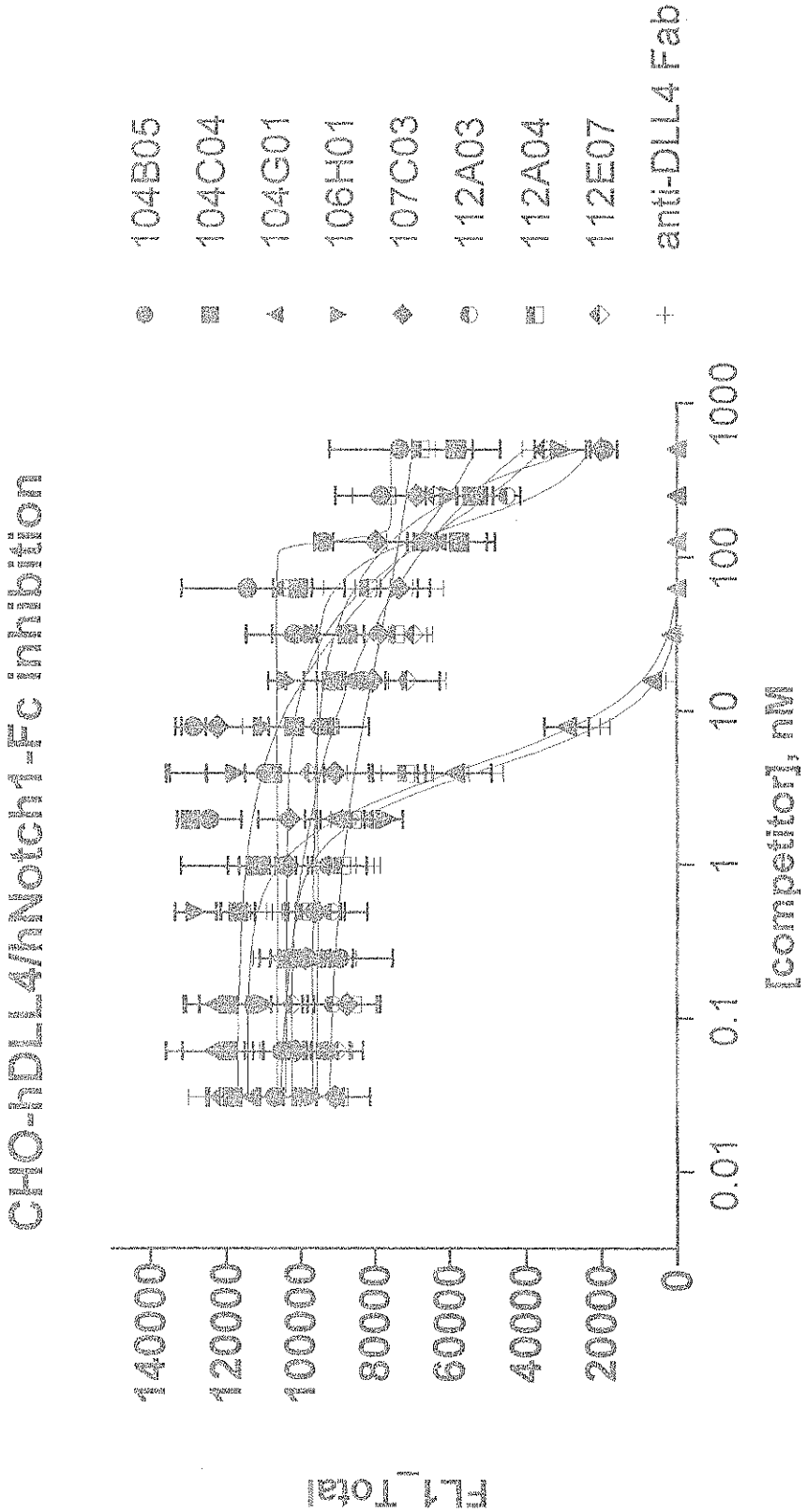

CHO-hDLL4/hNotch1-Fc inhibition
104B05
104C04
104G01
106H01
107C03
112A03
112A04
112E07
anti-DLL4 Fab
FL1_Total
40000
30000
20000
10000
80000
60000
40000
20000
0
0.01
0.1
1
10
100
1000
concentration nM

Fig. 5-10

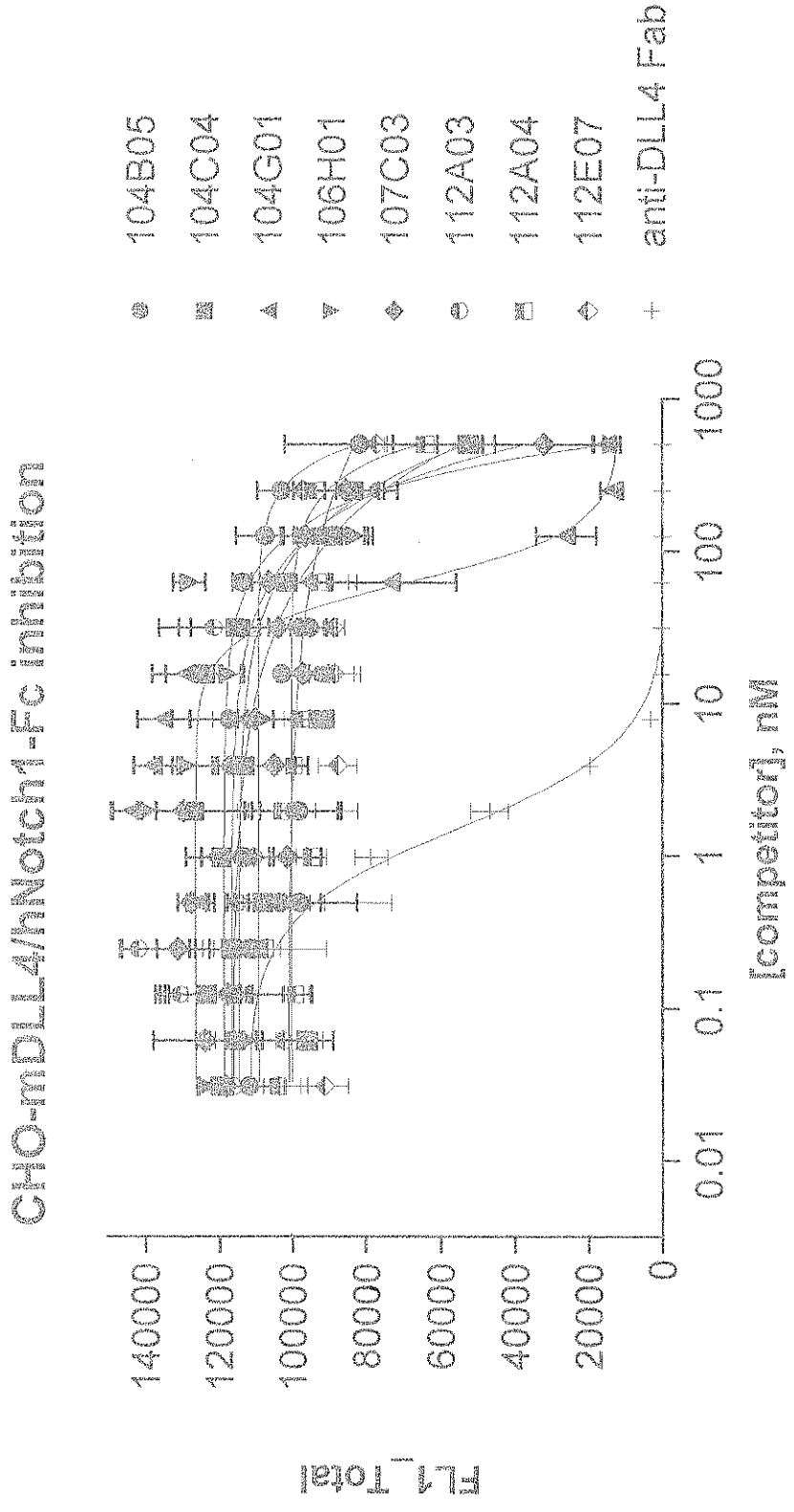

CHO-mDLL4/hNotch1-Fc inhibition
104B05
104C04
104G01
106H01
107C03
112A03
112A04
112E07
anti-DLL4 Fab
FL1_Total
140000
120000
100000
80000
60000
40000
20000
0
0.01
0.1
1
10
100
1000
concentration, nM

Fig. 6-1

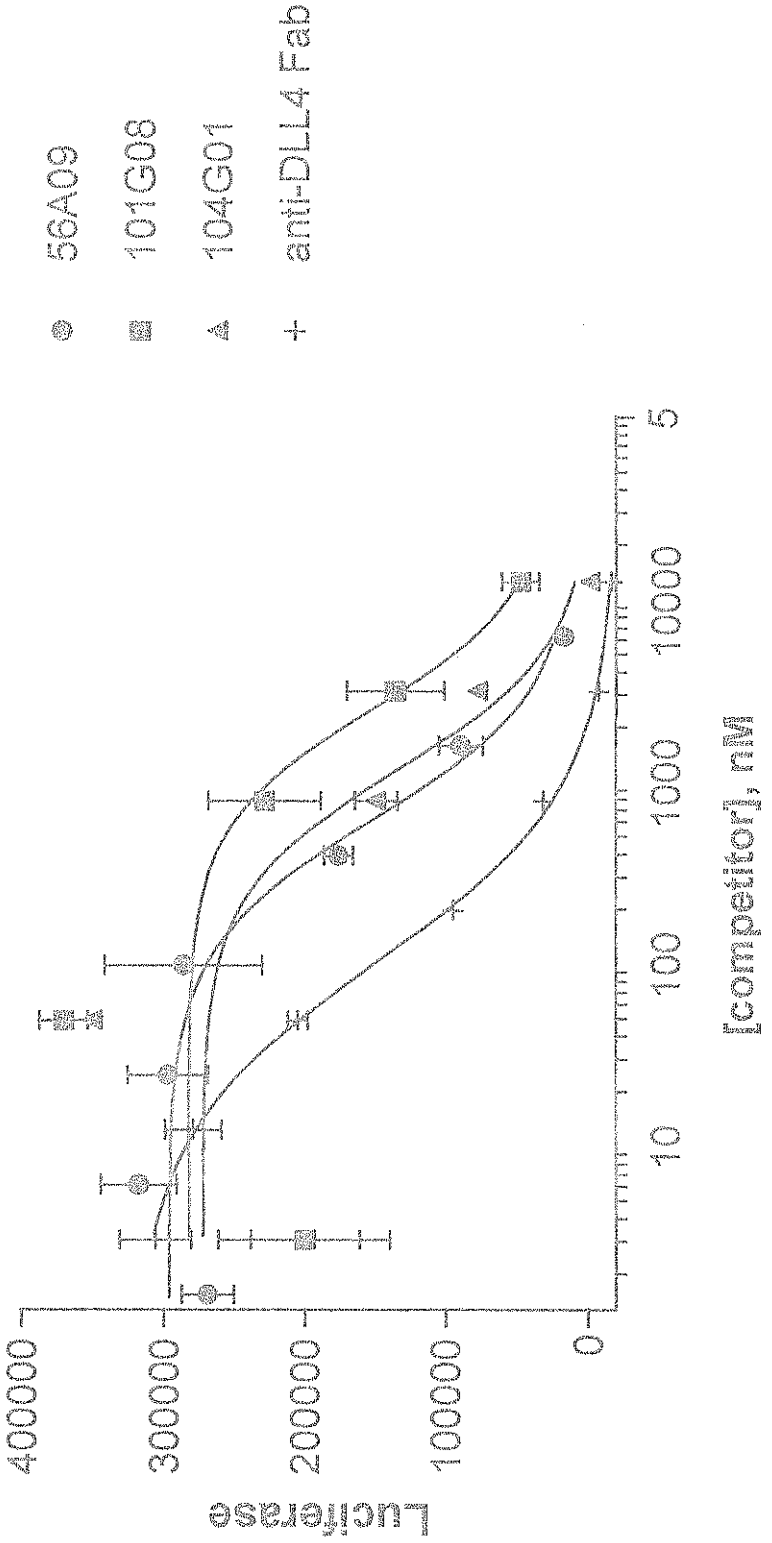

56A09
101G08
104G01
anti-DLL4 Fab
Luciferase
400000
300000
200000
100000
0
competitor1, nM
1
10
100
1000
10000
5

Fig. 6-2

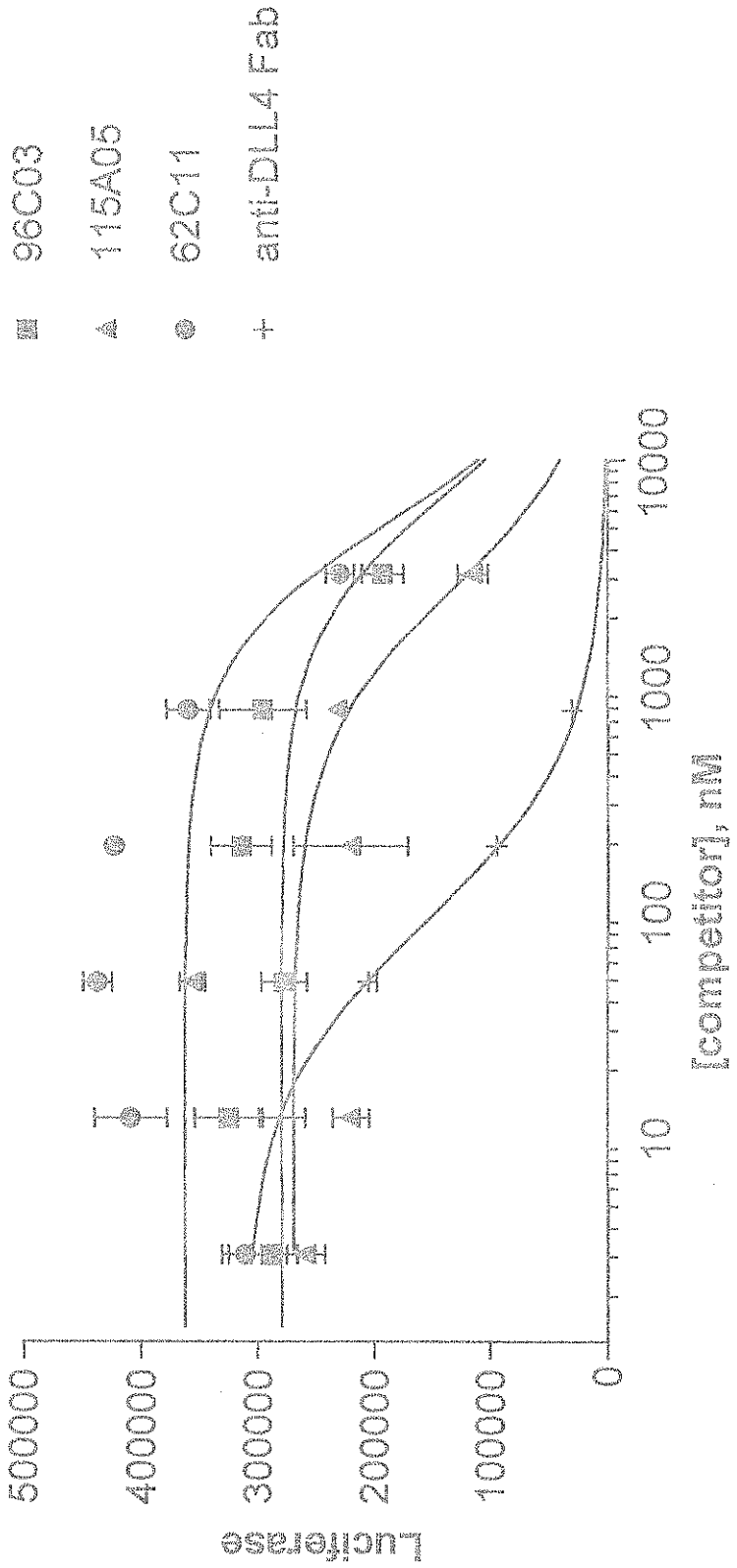

96C03
115A05
62C11
anti-DLL4 Fab
Luciferase
500000
400000
300000
200000
100000
0
10
100
1000
10000
Competitor, nM

Fig. 6-3

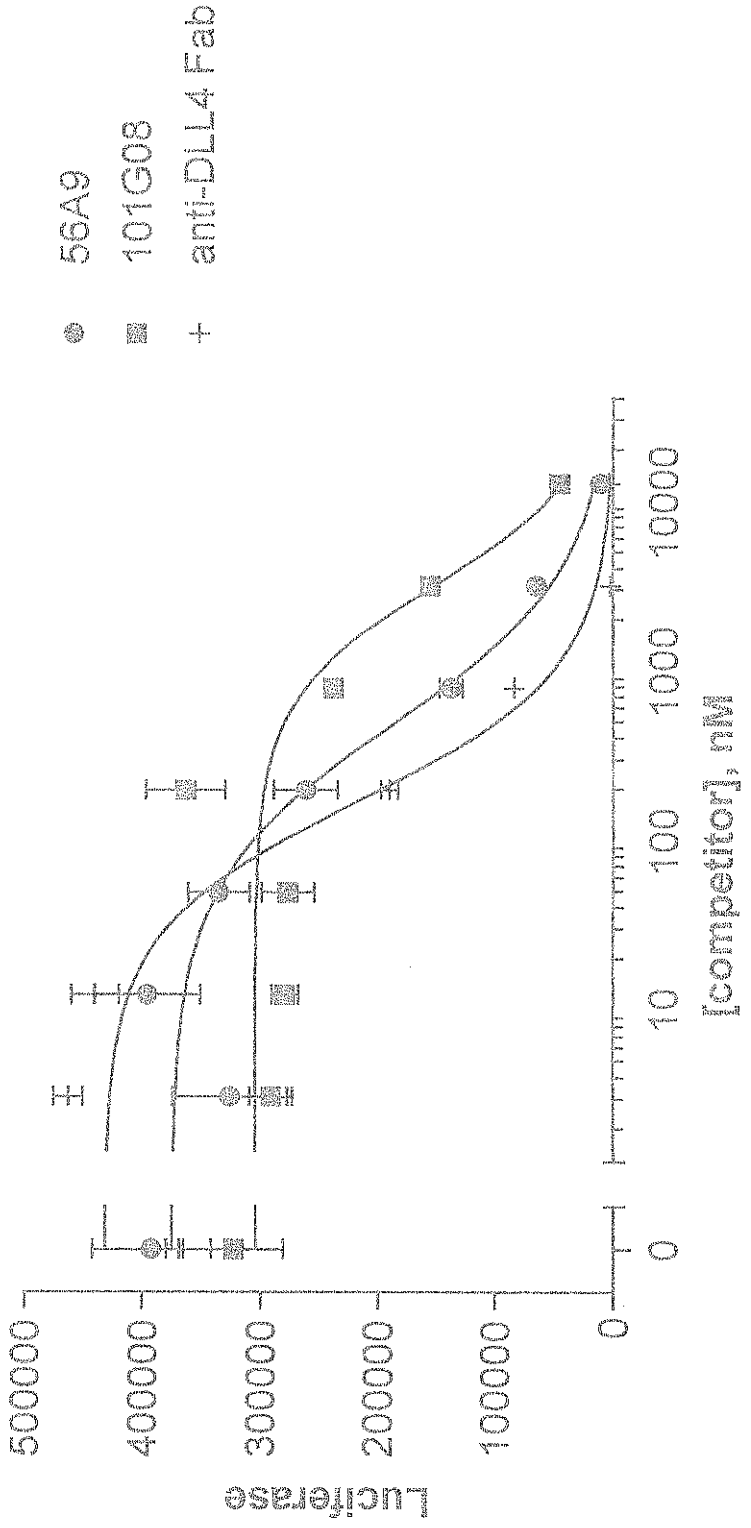

56A9
10.G08
anti-DLL4 Fab
Luciferase
500000
400000
300000
200000
100000
0
0
10
100
1000
10000
Concentration nM

Fig. 6-4

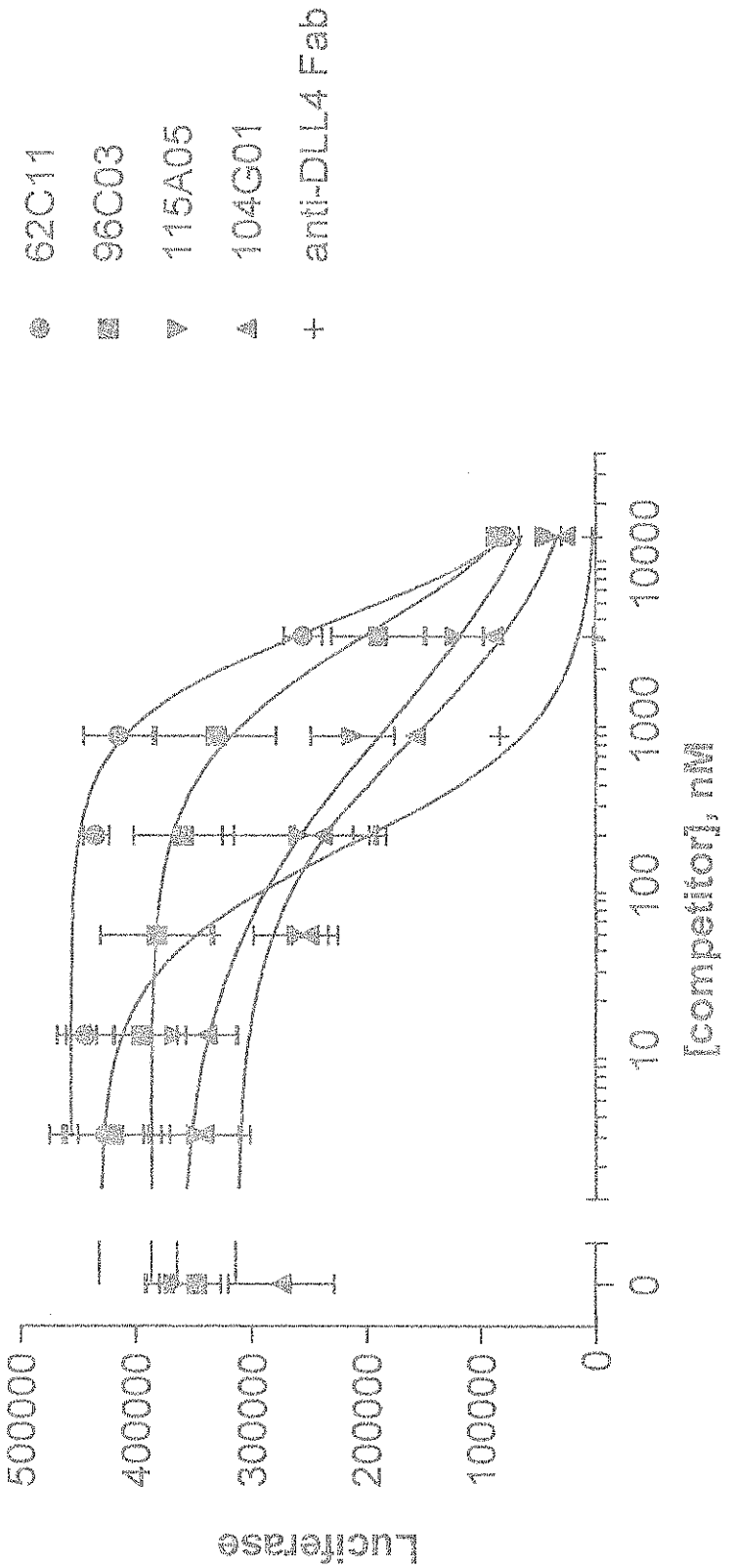

62C11
96C03
115A05
104G01
anti-DLL4 Fab
Luciferase
500000
400000
300000
200000
100000
0
0
10
100
1000
10000
competitor, nM

Fig. 7-1

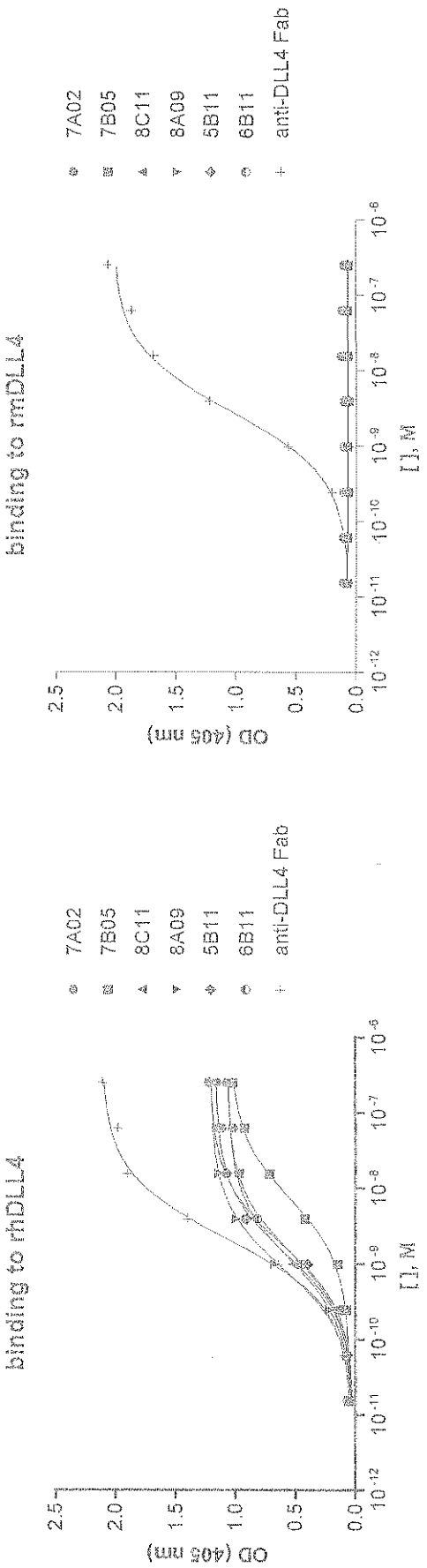
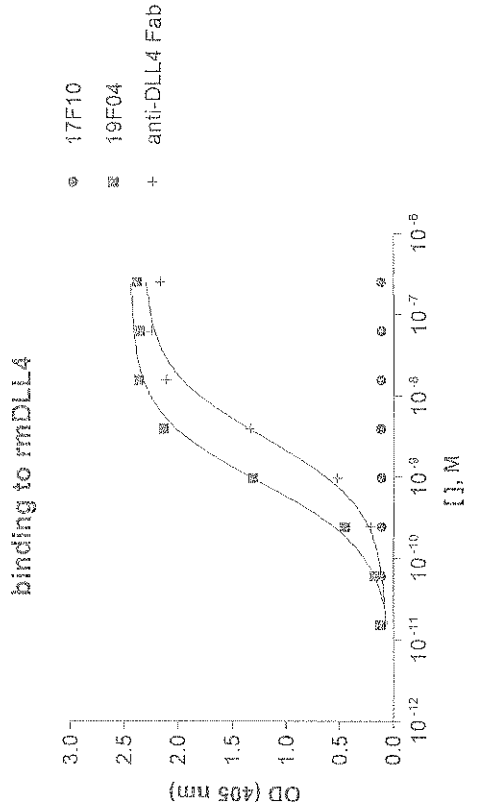

binding to rhDLL4
OD (405 nm)
2.5
2.0
1.5
1.0
0.5
0.0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
[], M
7A02
7B05
8C11
8A09
5B11
6B11
anti-DLL4 Fab
binding to rmDLL4
OD (405 nm)
2.5
2.0
1.5
1.0
0.5
0.0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
[], M
7A02
7B05
8C11
8A09
5B11
6B11
anti-DLL4 Fab

Fig. 7-2


binding to rmDLL4
17F10
19F04
anti-DLL4 Fab
OD (405 nm)
[1], M

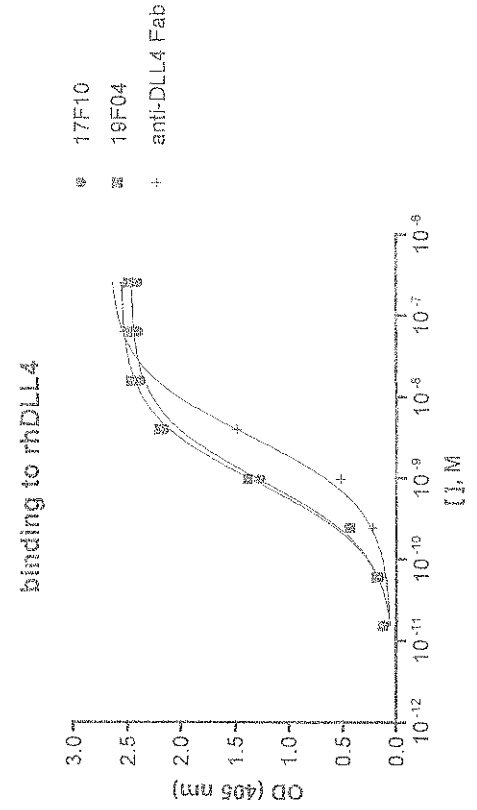
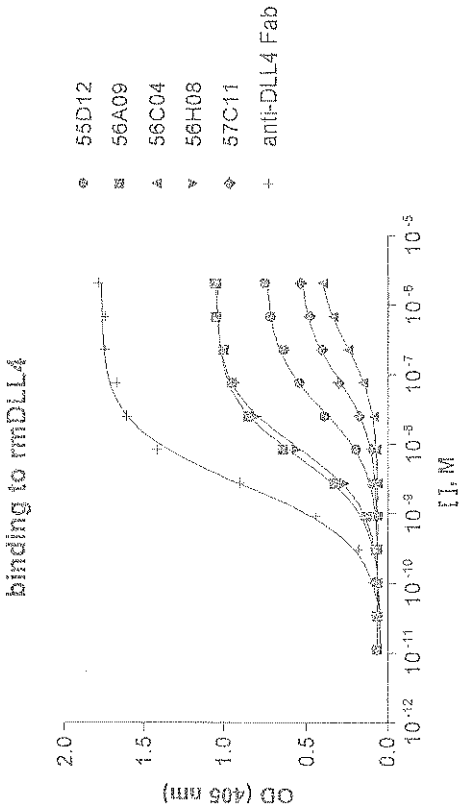
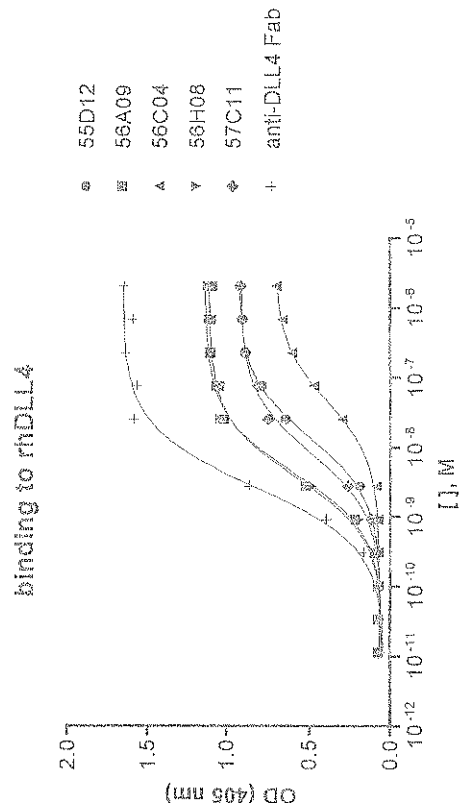

binding to rhDLL4
17F10
19F04
anti-DLL4 Fab
OD (405 nm)
[1], M

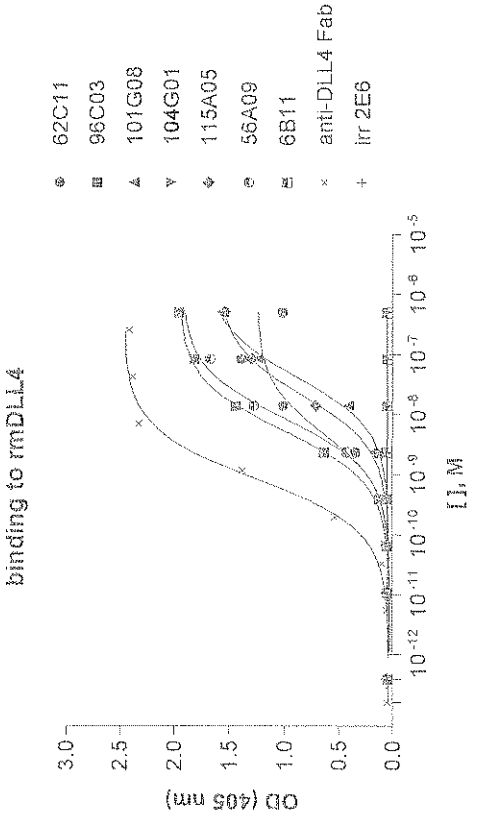
Fig. 7-3


binding to rhDLL4
OD (405 nm)
2.0
1.5
1.0
0.5
0.0
10-12 10-11 10-10 10-9 10-8 10-7 10-6 10-5
[], M
55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab


binding to rmDLL4
OD (405 nm)
2.0
1.5
1.0
0.5
0.0
10-12 10-11 10-10 10-9 10-8 10-7 10-6 10-5
[], M
55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab

28 / 152

Fig. 7-4


binding to rmDLL4
OD (405 nm)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
10^-12 10^-11 10^-10 10^-9 10^-8 10^-7 10^-6 10^-5
[], M
62C11
96C03
101G08
104G01
115A05
56A09
6B11
anti-DLL4 Fab
irr 2E6

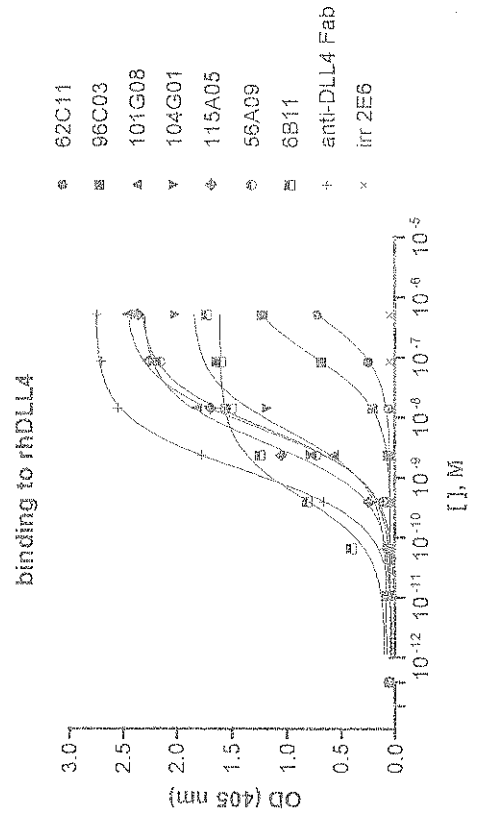
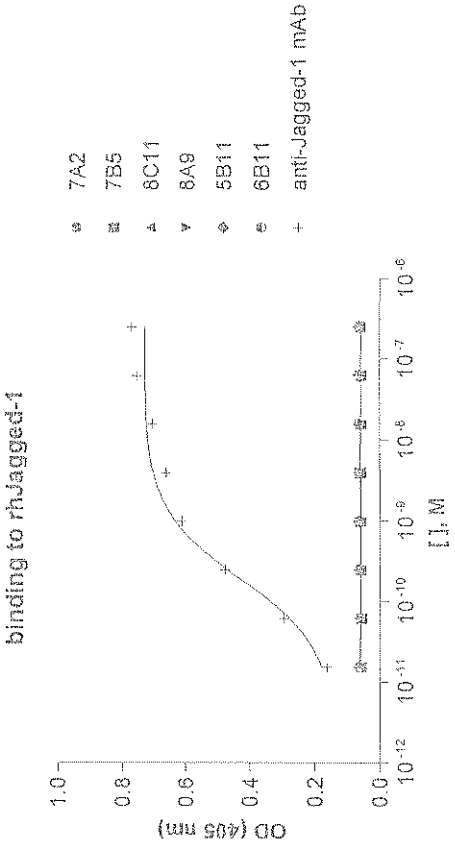

binding to rhDLL4
OD (405 nm)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
10^-12 10^-11 10^-10 10^-9 10^-8 10^-7 10^-6 10^-5
[], M
62C11
96C03
101G08
104G01
115A05
56A09
6B11
anti-DLL4 Fab
irr 2E6

Fig. 8-1


binding to rhJagged-1
OD (405 nm)
1.0
0.8
0.6
0.4
0.2
0.0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
[], M
7A2
7B5
8C11
8A9
5B11
6B11
anti-Jagged-1 mAb

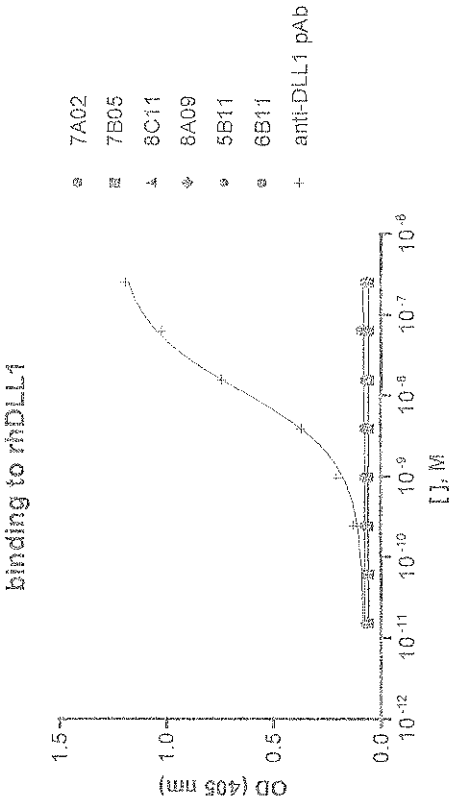
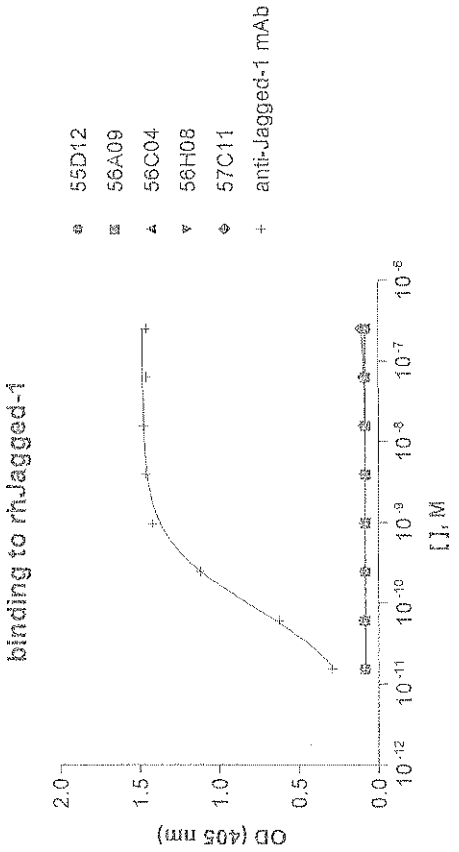

binding to rhDLL1
OD (405 nm)
1.5
1.0
0.5
0.0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
[], M
7A02
7B05
8C11
8A09
5B11
6B11
anti-DLL1 pAb

Fig. 8-2


binding to rhJagged-1
55D12
56A09
56C04
56H08
57C11
anti-Jagged-1 mAb
OD (405 nm)
[], M

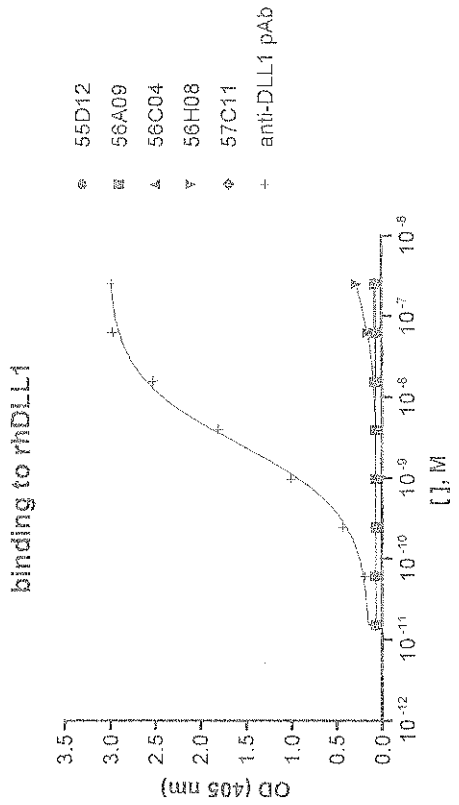
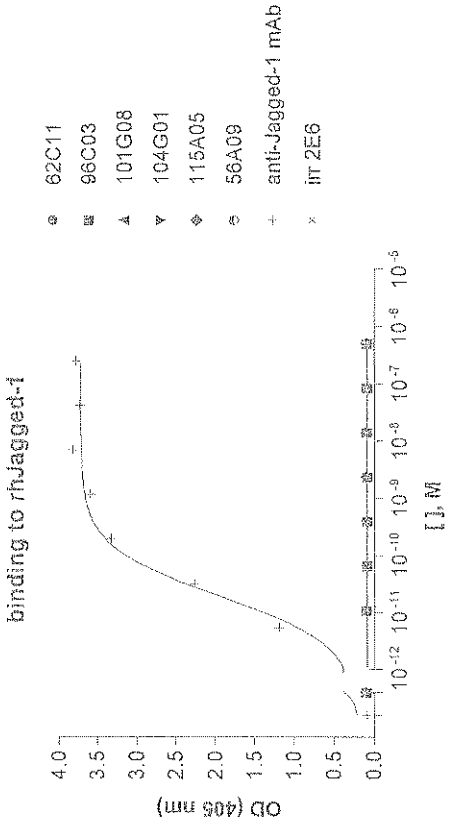

binding to rhDLL1
55D12
56A09
56C04
56H08
57C11
anti-DLL1 pAb
OD (405 nm)
[], M

Fig. 8-3


binding to rhJagged-1
62C11
96C03
101G08
104G01
115A05
56A09
anti-Jagged-1 mAb
irr 2E6
OD (405 nm)
[ ], M

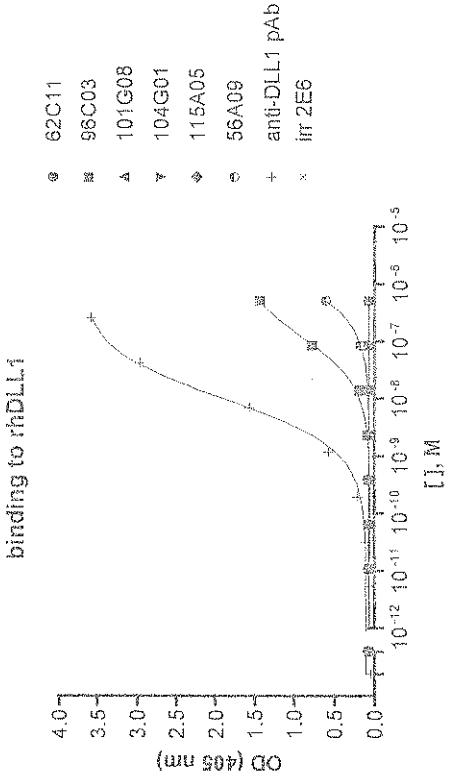
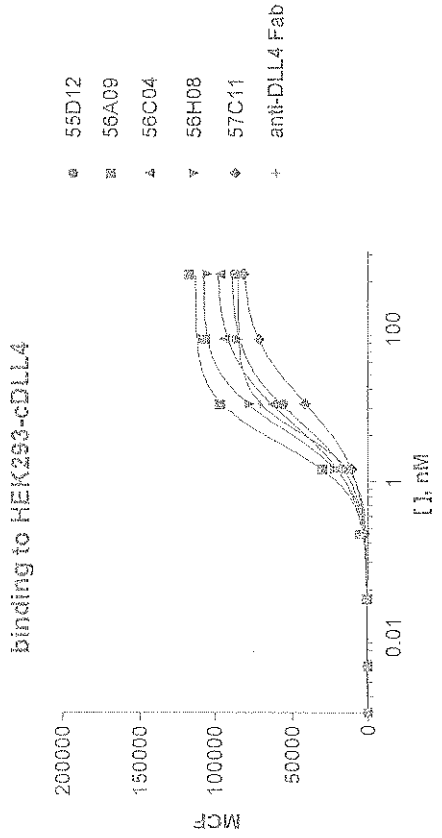

binding to rhDLL1
62C11
96C03
101G08
104G01
115A05
56A09
anti-DLL1 pAb
irr 2E6
OD (405 nm)
[ ], M

Fig. 9-1


binding to HEK293-cDLL4
55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab
MCF
200000
150000
100000
50000
0
0.01
1
100
[], nM

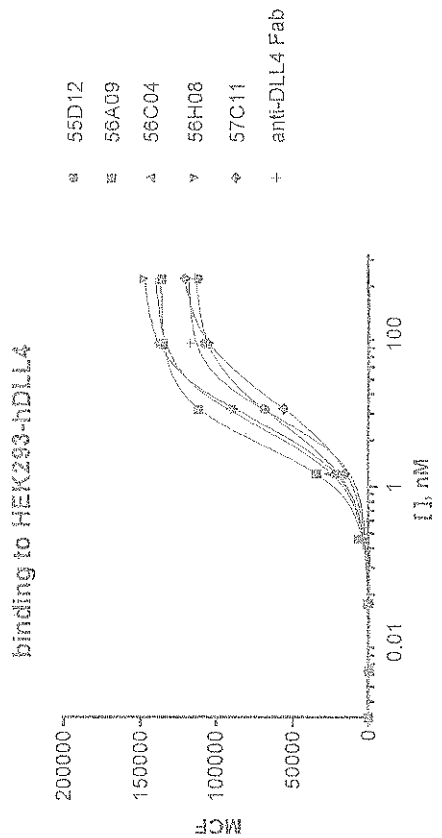

binding to HEK293-hDLL4
55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab
MCF
200000
150000
100000
50000
0
0.01
1
100
[], nM

Fig. 9-2

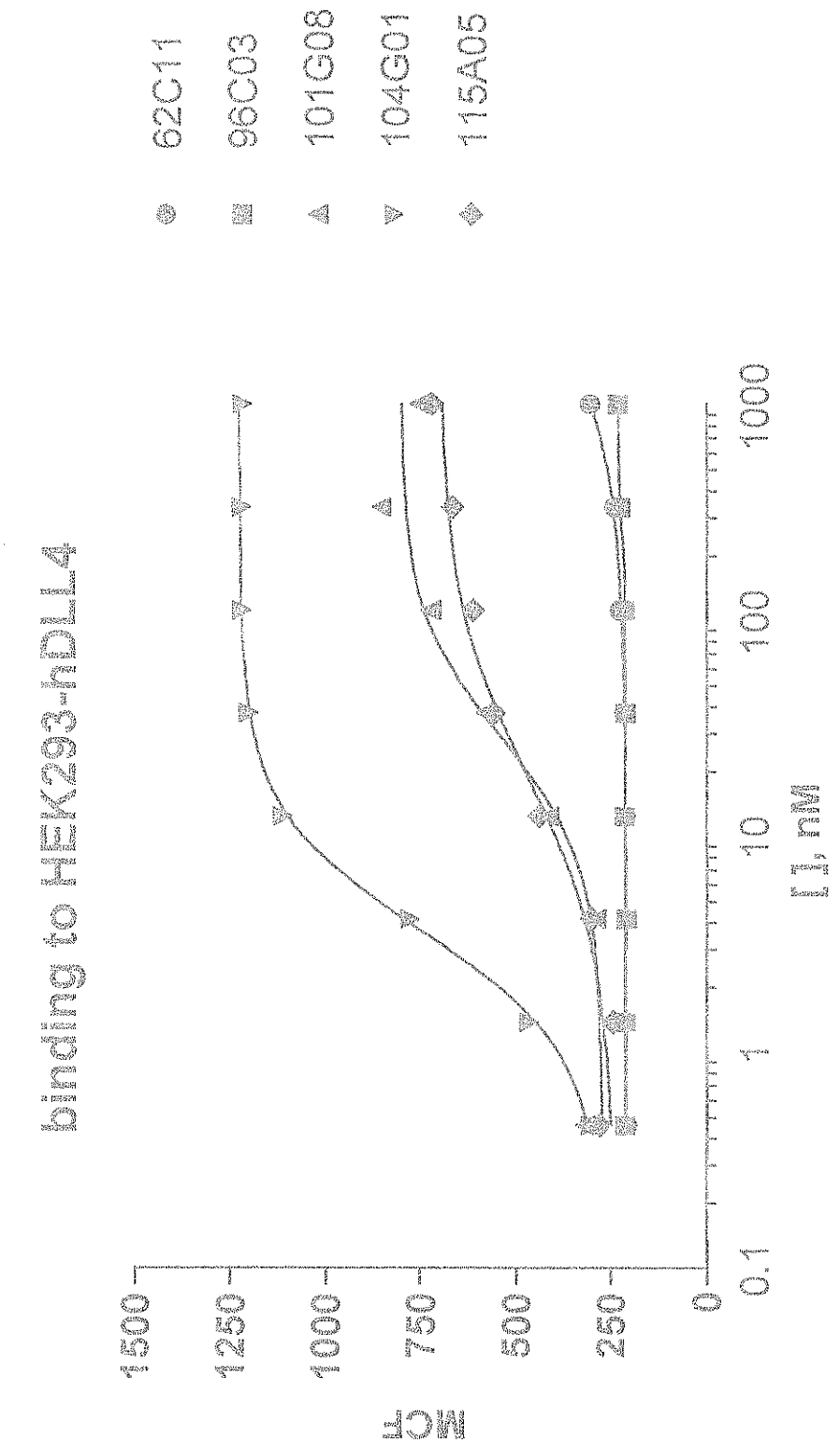

binding to HEK293-hDLL4
MCF
500
1250
1000
750
500
250
0
0.1
1
10
100
1000
EU, nM
62C11
96C03
101G08
104G01
115A05

Fig. 9-3

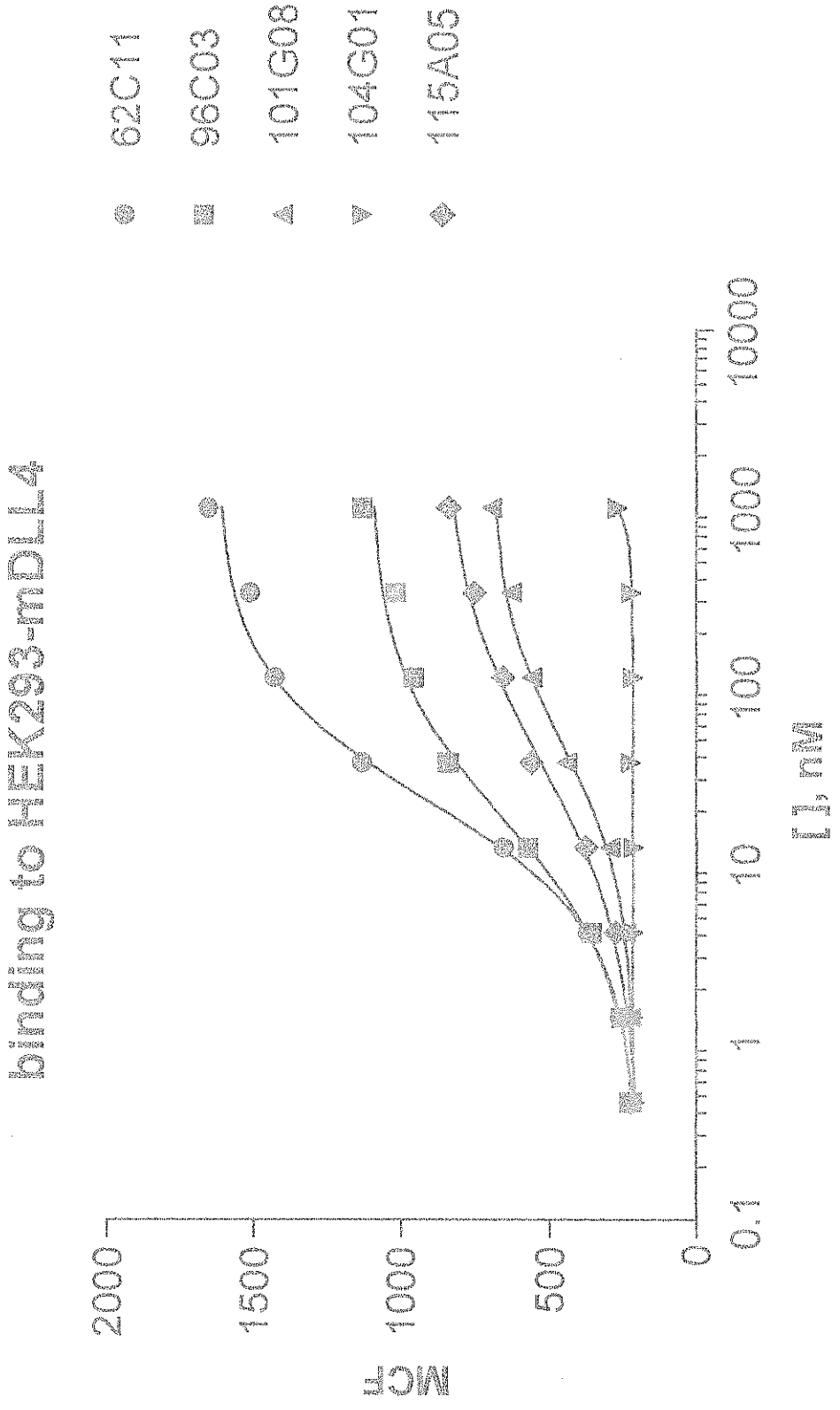
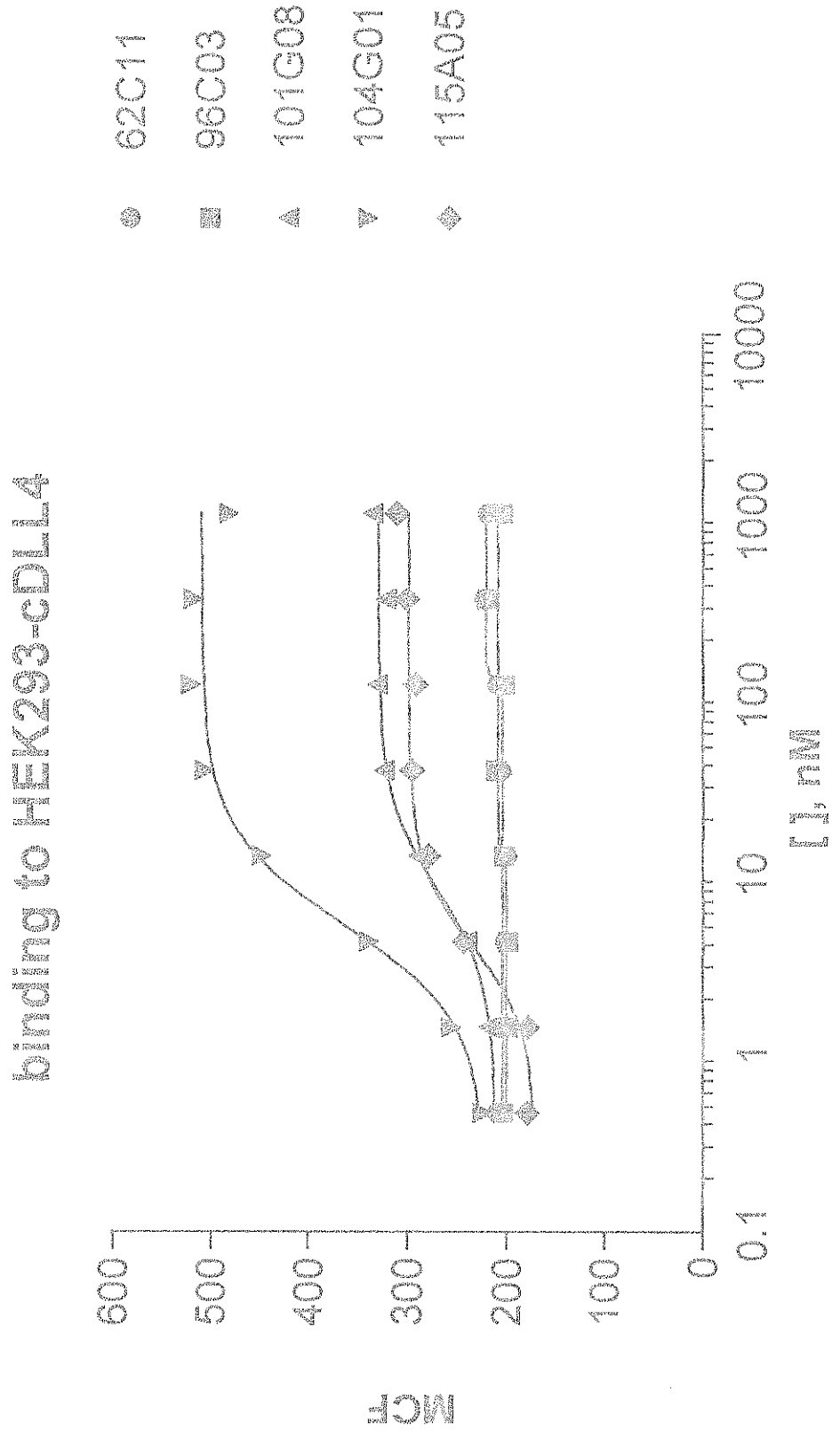
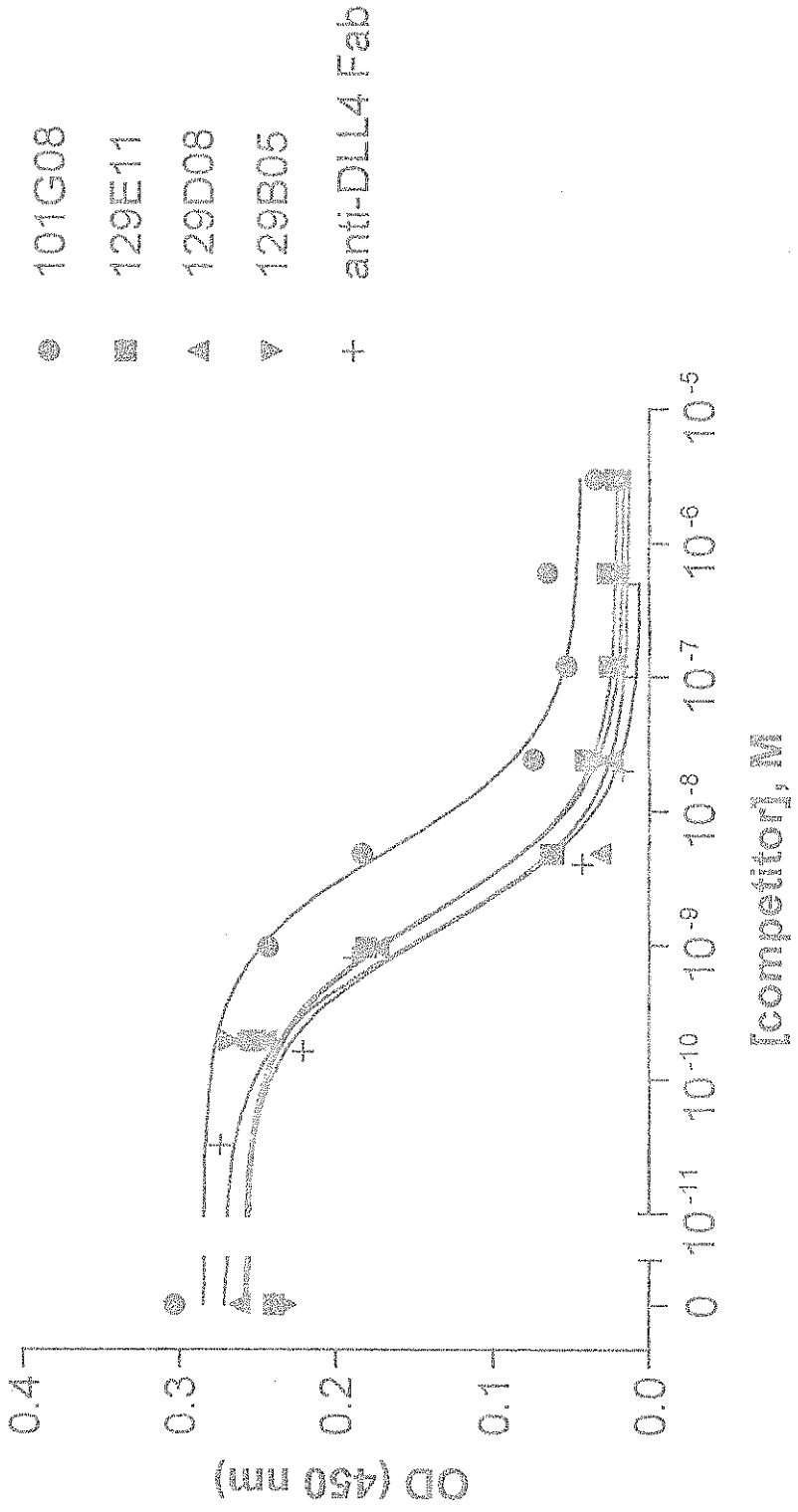

binding to HEK293-mDLL4
62C11
96C03
101G08
104G01
115A05
MCF
2000
1500
1000
500
0
0,1
1
10
100
1000
nM

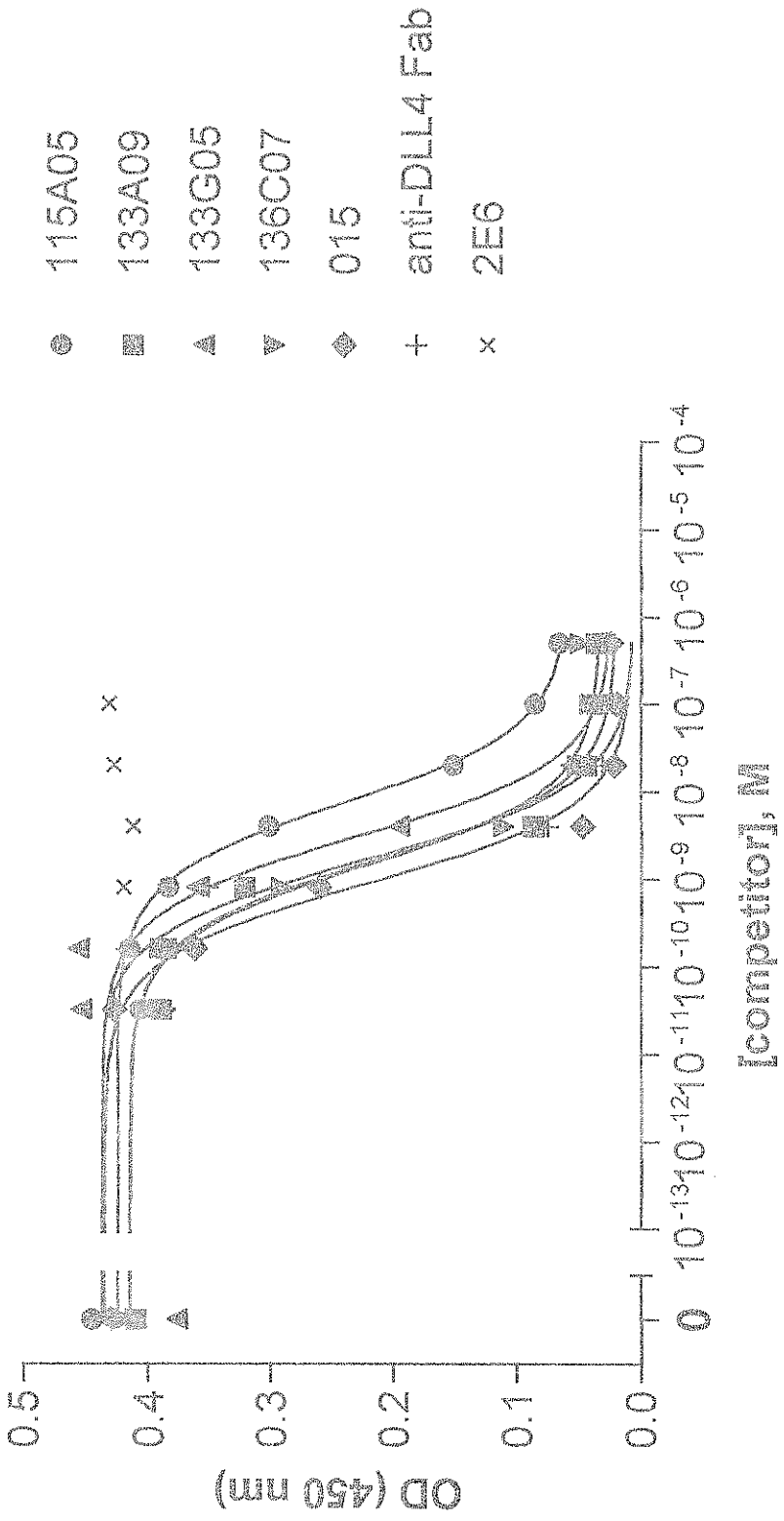
Fig. 9-4


binding to hFcRn-293-cDL4
62C11
66C03
104C08
104G01
115A05
MCF
600
500
400
300
200
100
0
0.1
1
10
100
1000
10000
nM

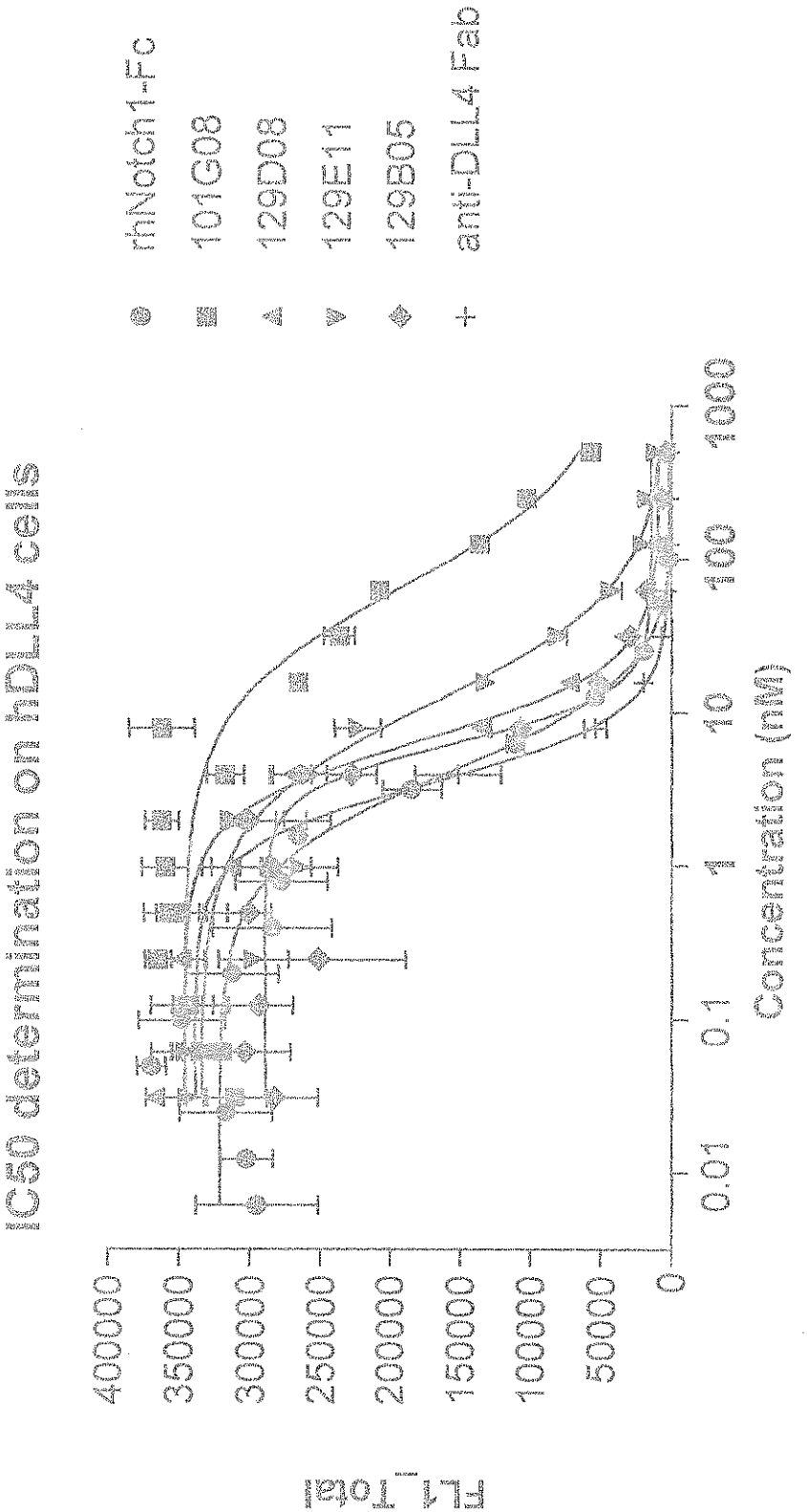
36 / 152
Fig. 10-1



37 / 152
Fig. 10-2



38 / 152
Fig. 11-1



39 / 152
Fig. 11-2

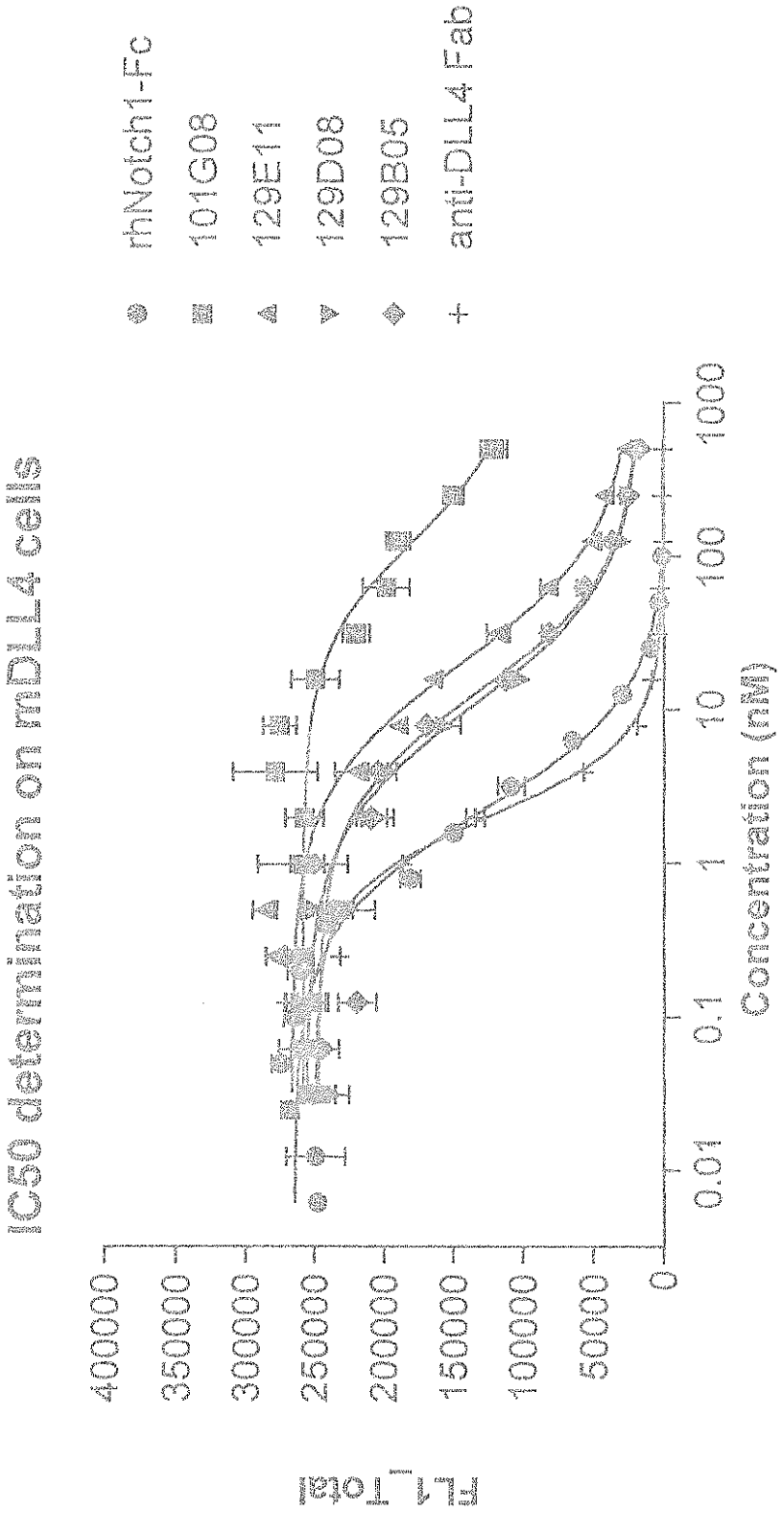
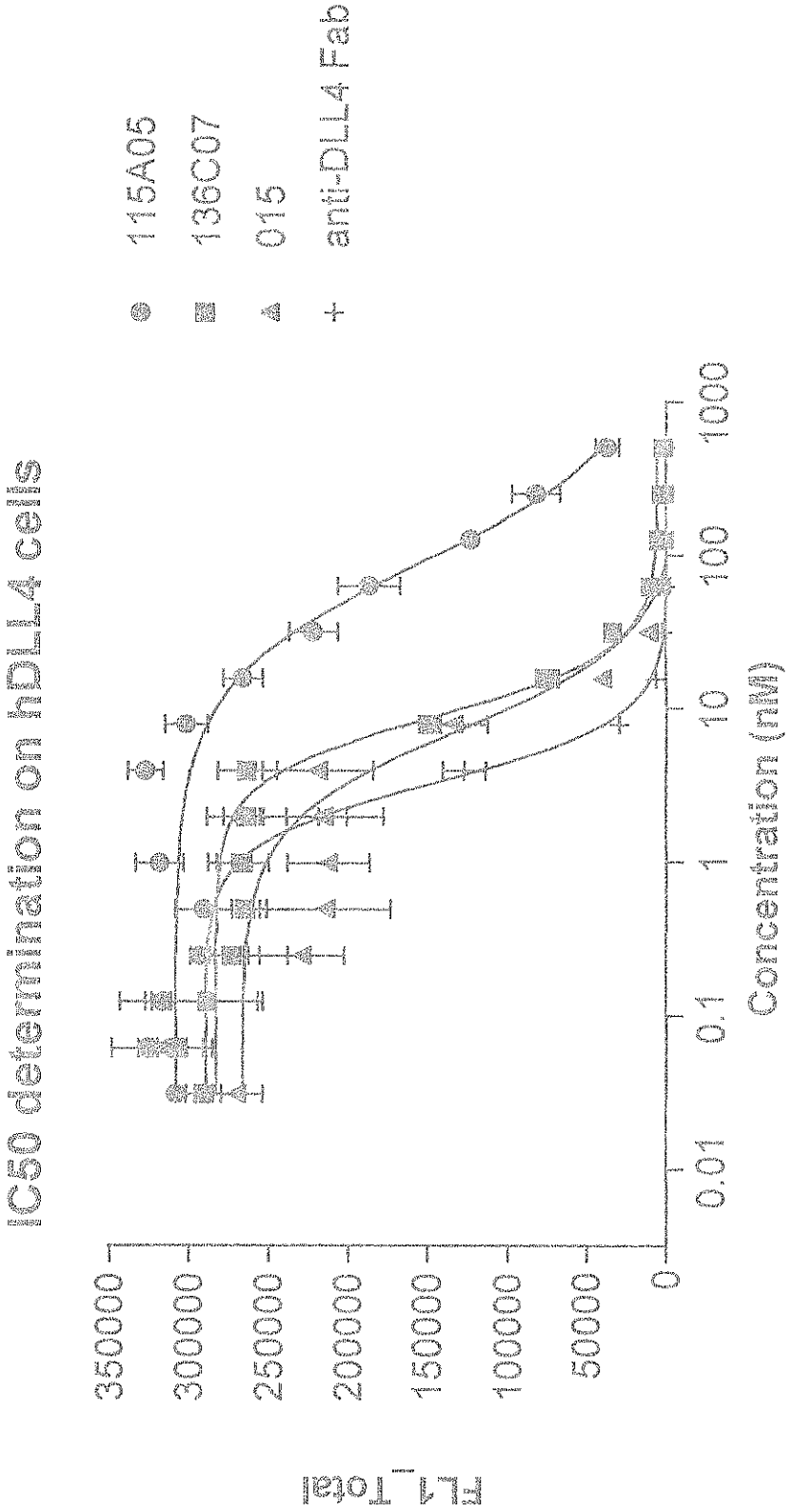
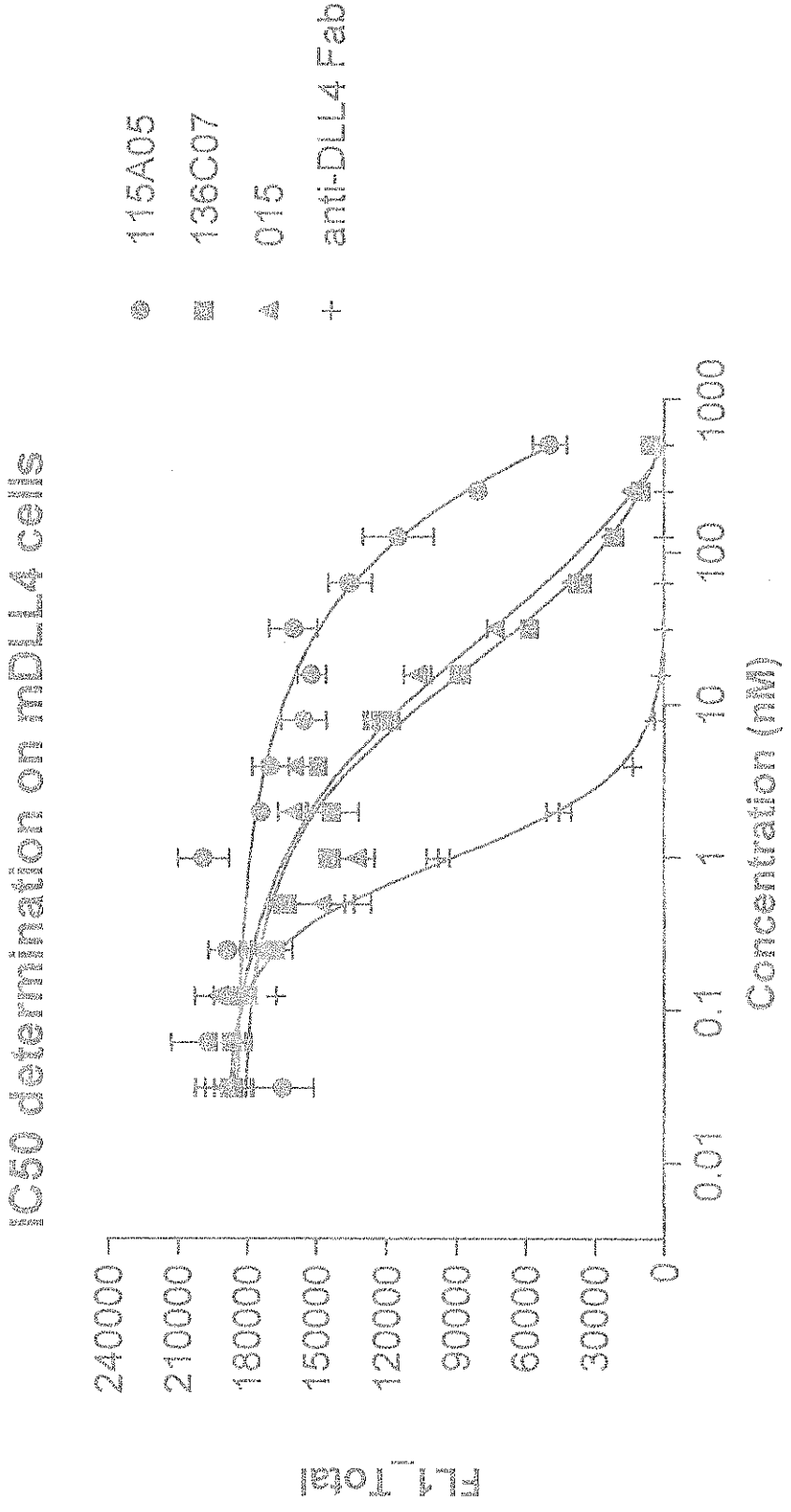


Fig. 11-3


C50 determination on hDLL4 cells
115A05
136C07
015
anti-DLL4 Fab
FL4_Total
350000
300000
250000
200000
150000
100000
50000
0
0,01
0,1
1
10
100
1000
Concentration (nM)

41 / 152
Fig. 11-4



42 / 152
Fig. 12-1

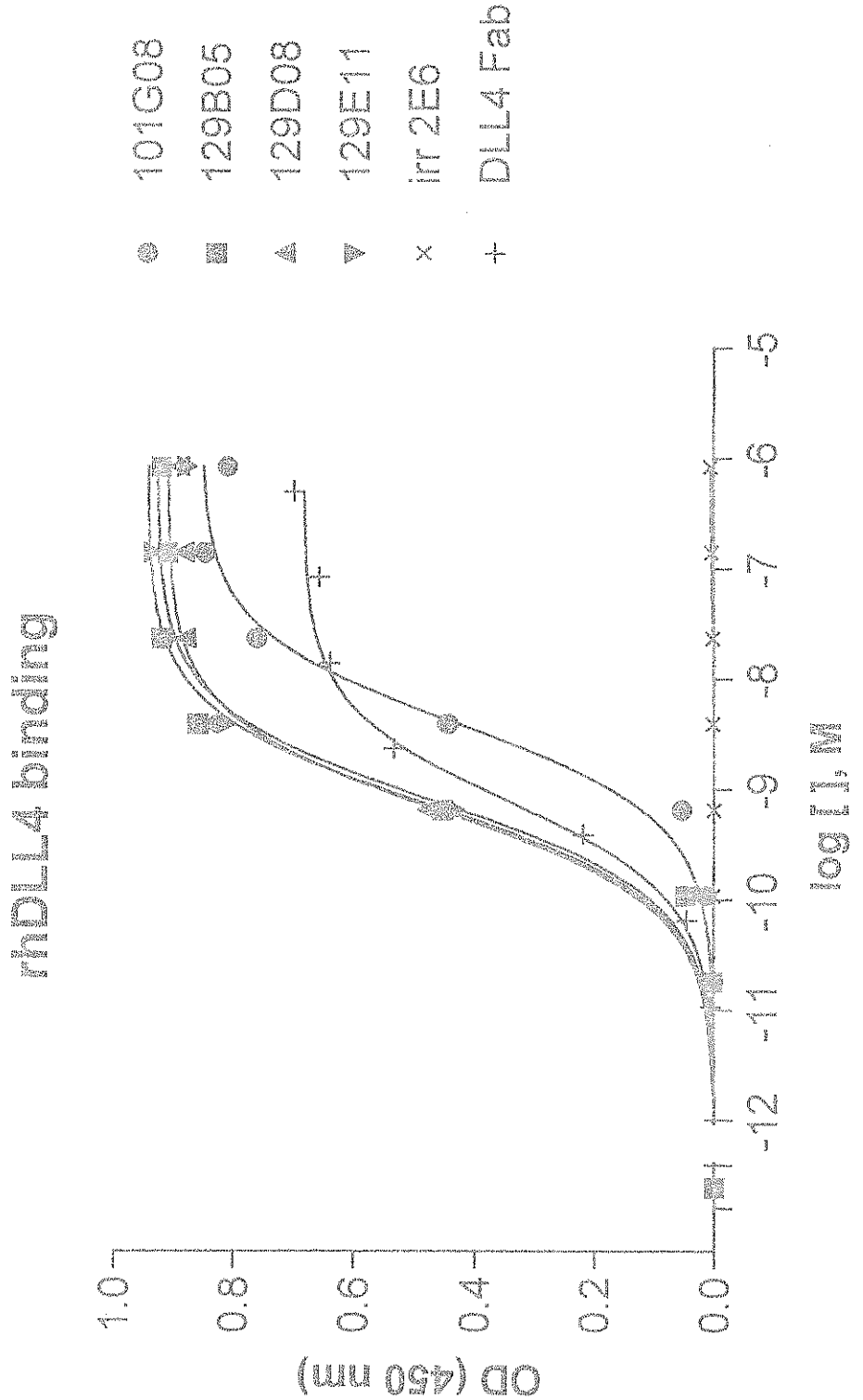


Fig. 12-2

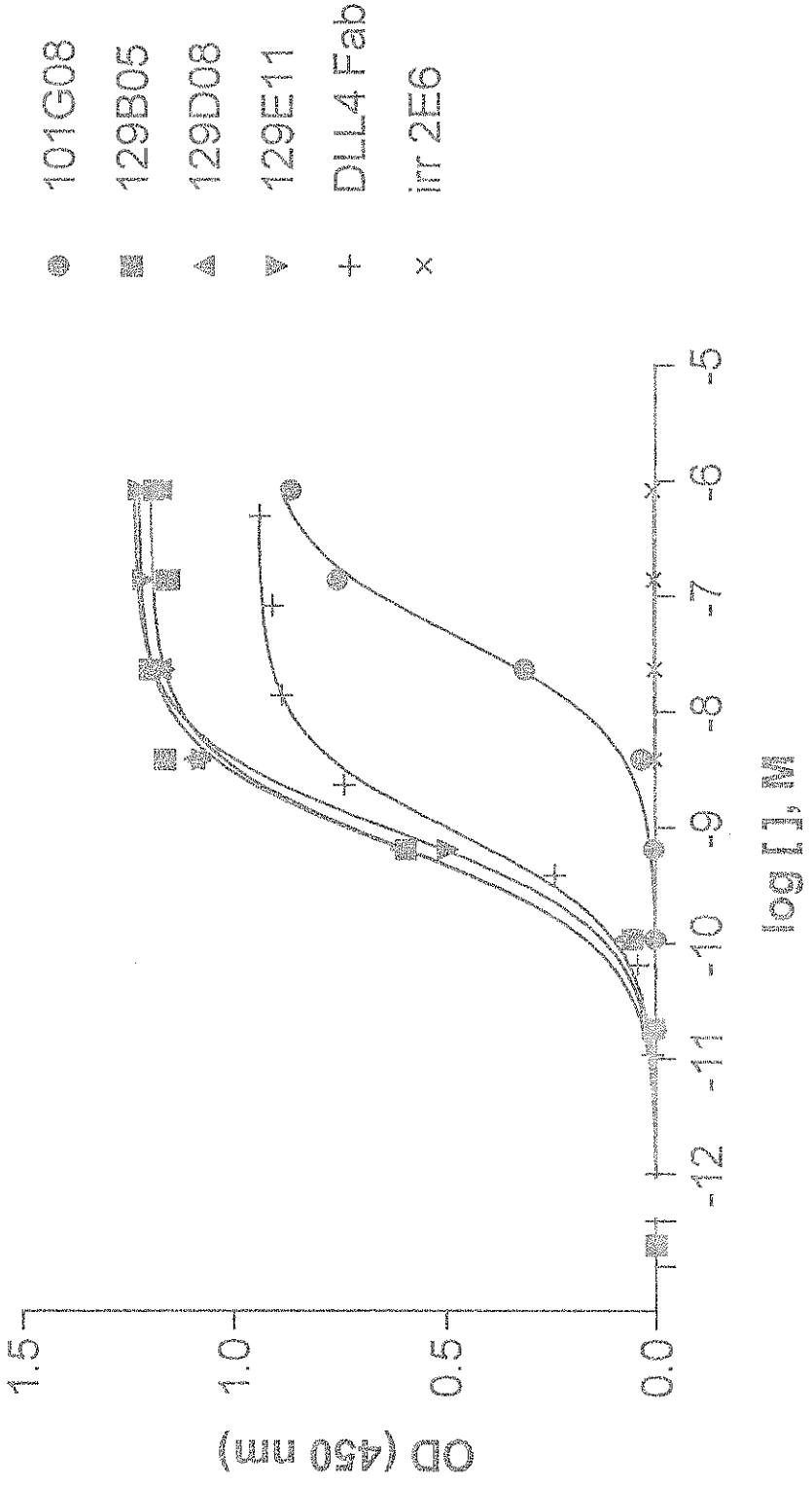
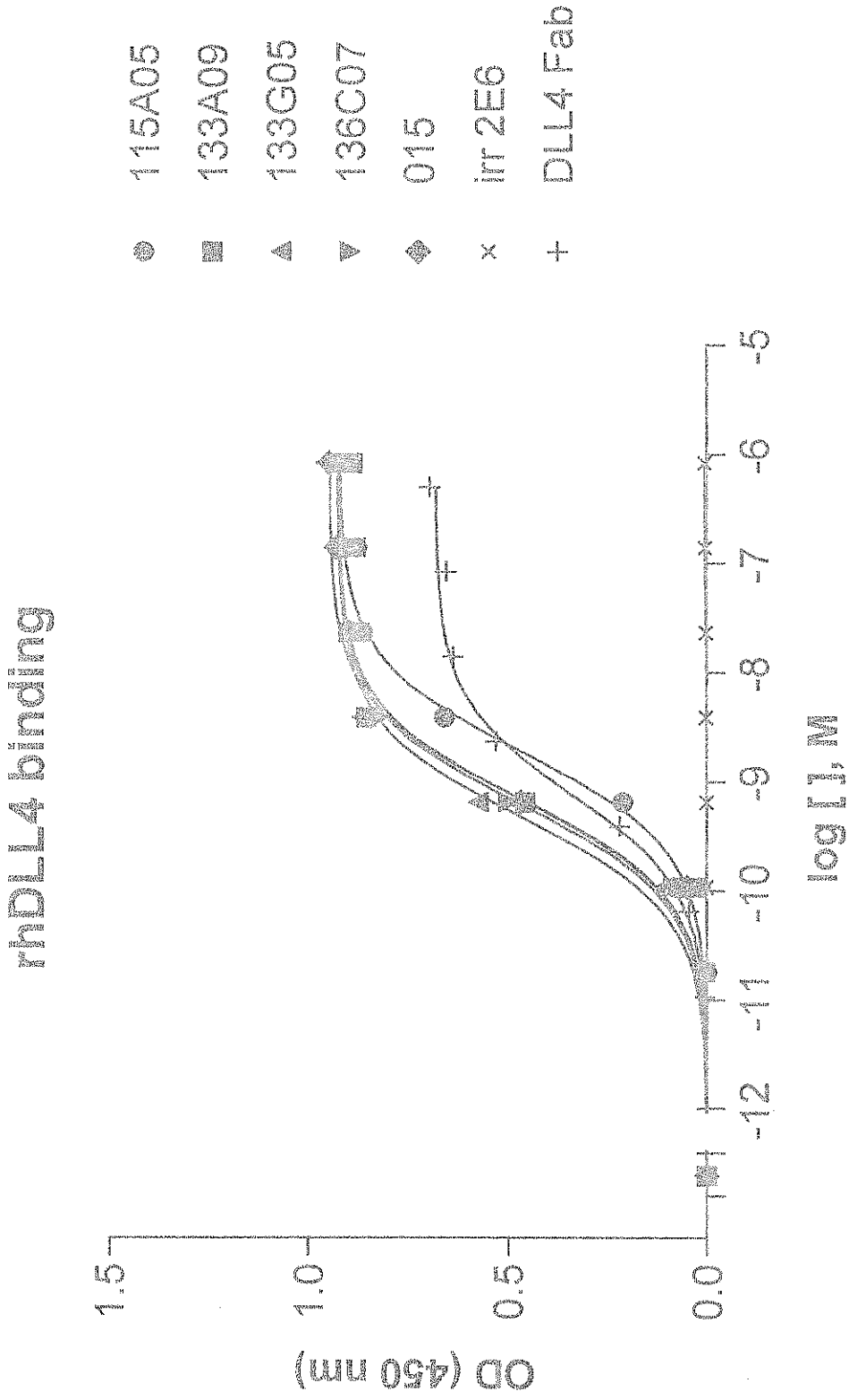

101G08
129B05
129D08
129E11
DLL4 Fab
irr 2E6
vsDLL4 binding
OD (450 nm)
log f1, M
0.0
0.5
1.0
1.5
-5
-6
-7
-8
-9
-10
-11
-12

Fig. 12-3


hDLL4 binding
OD (450 nm)
0.0
0.5
1.0
1.5
-5
-6
-7
-8
-9
-10
-11
-12
log[Ab] M
15A05
13A09
13G05
13C07
015
hr2E6
DLL4 Fab

45 / 152
Fig. 12-4

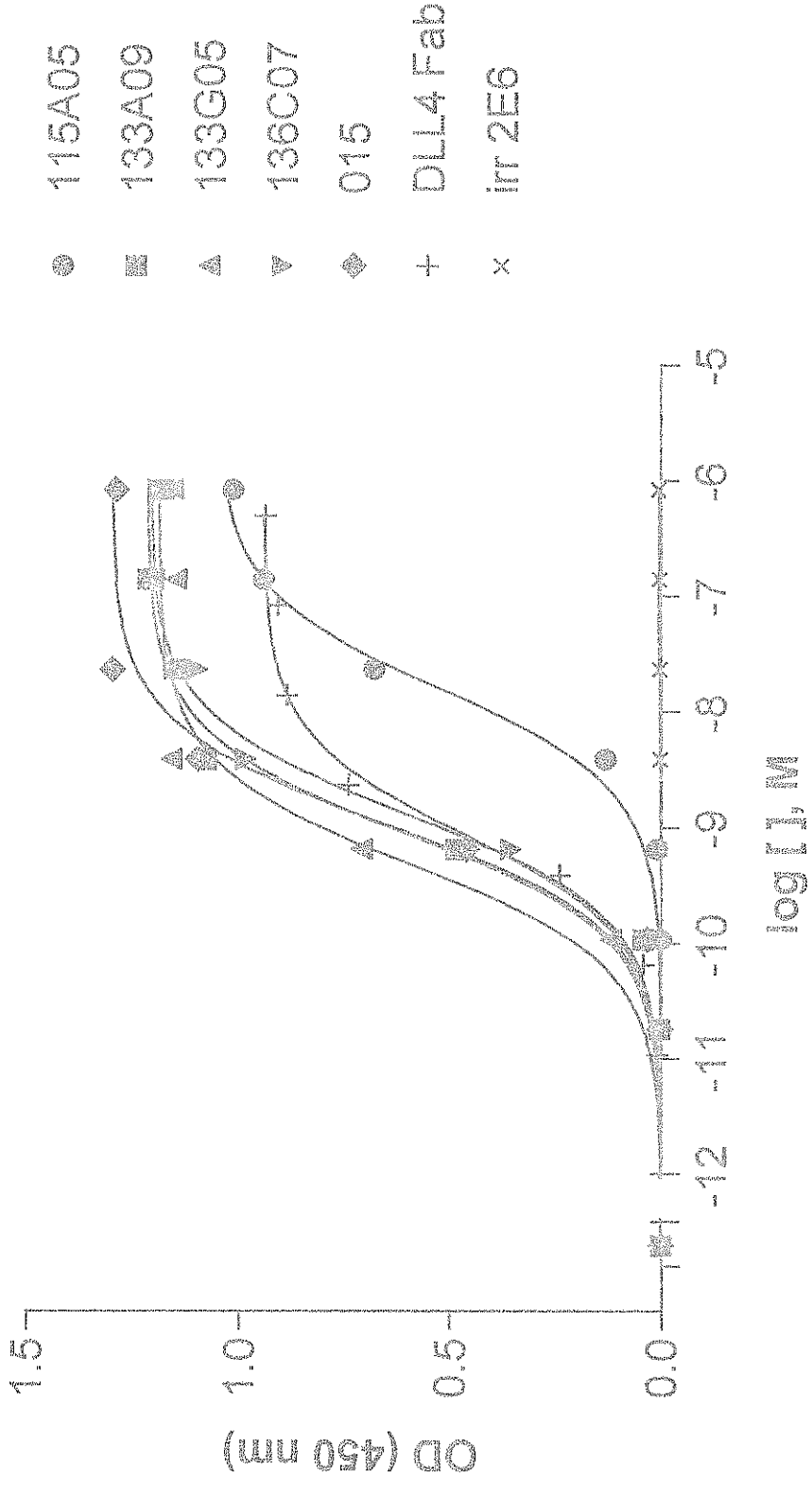


Fig. 13-1

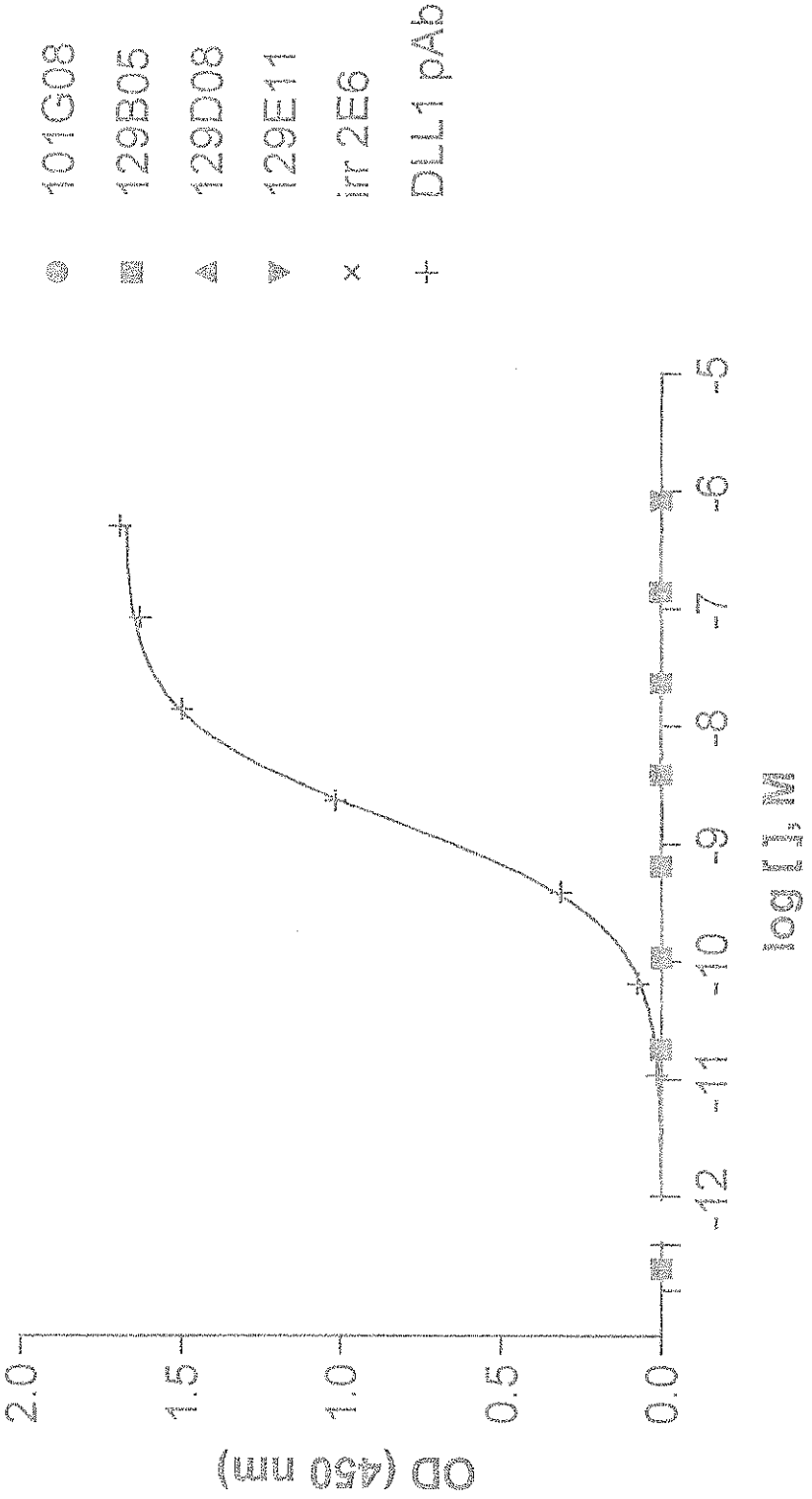
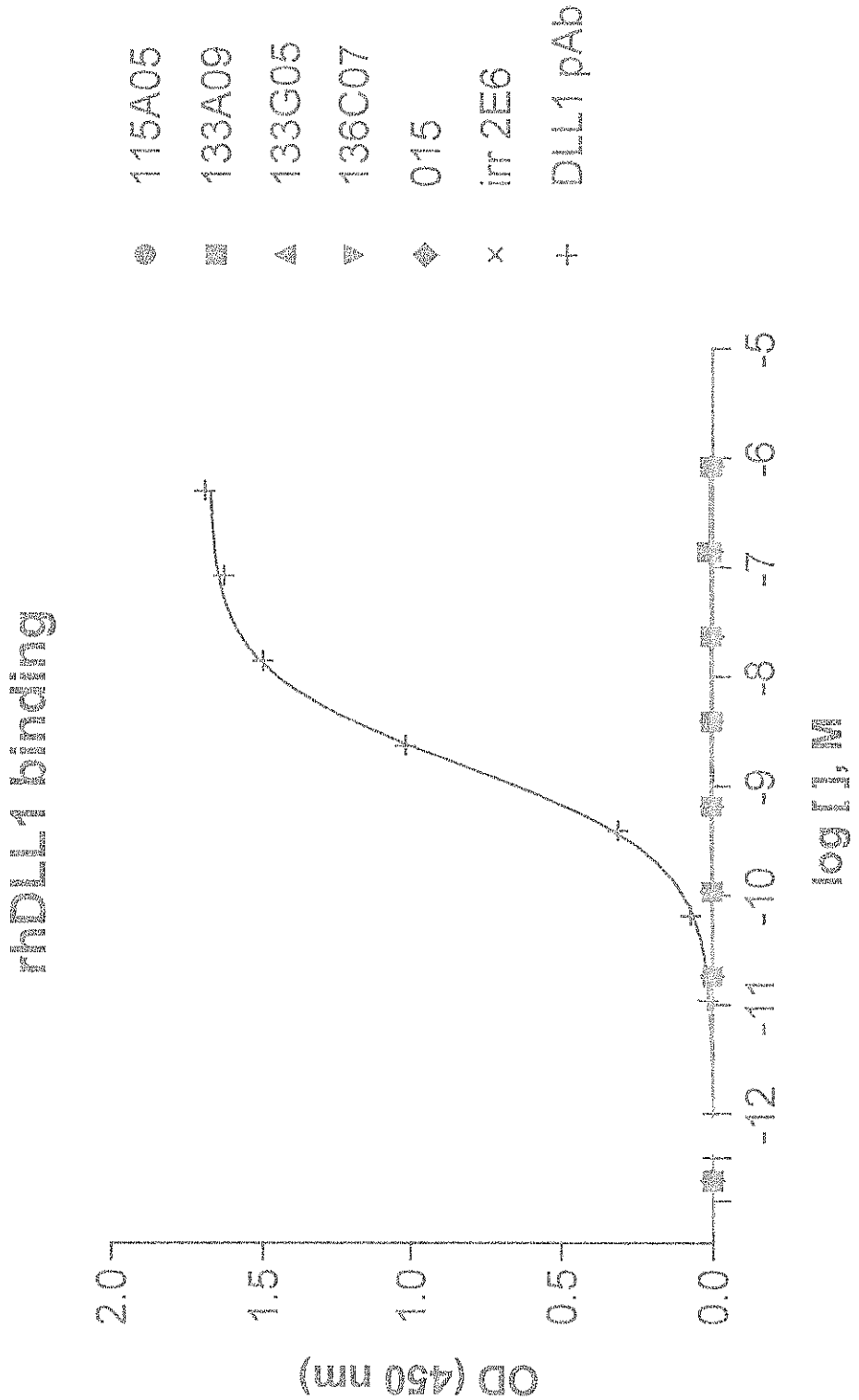

10'C08
129B05
129D08
129E11
hr 2E6
DLL1 pAb
OD (450 nm)
2.0
1.5
1.0
0.5
0.0
-12
-11
-10
-9
-8
-7
-6
-5
log [nM]

Fig. 13-2


115A05
133A09
133C05
136C07
015
int 2E6
DsL1 pAb
rhDLL4 binding
OD (450 nm)
2.0
1.5
1.0
0.5
0.0
-5
-6
-7
-8
-9
-10
-11
-12
log [mAb]

48 / 152
Fig. 13-3

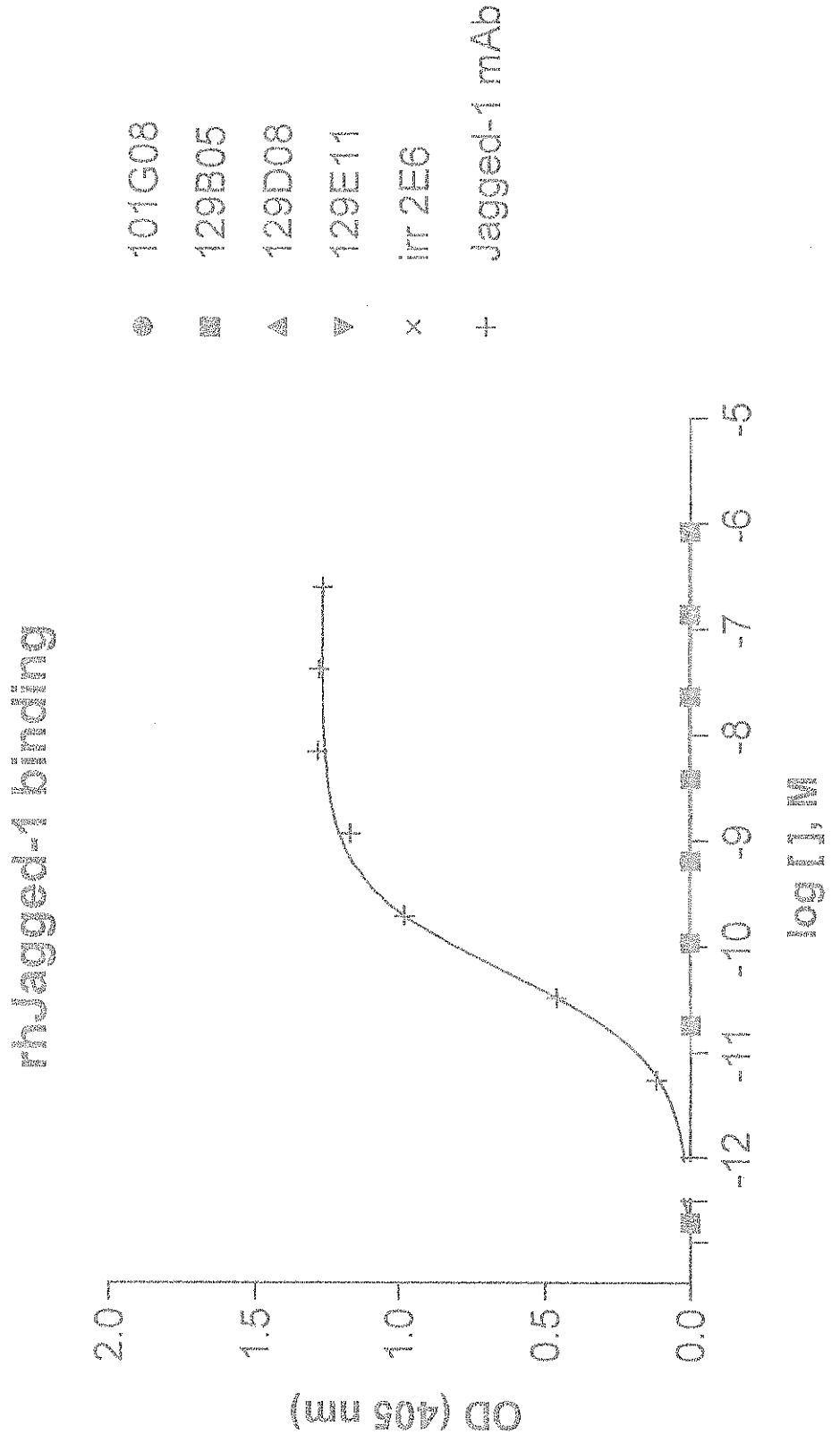


Fig. 13-4

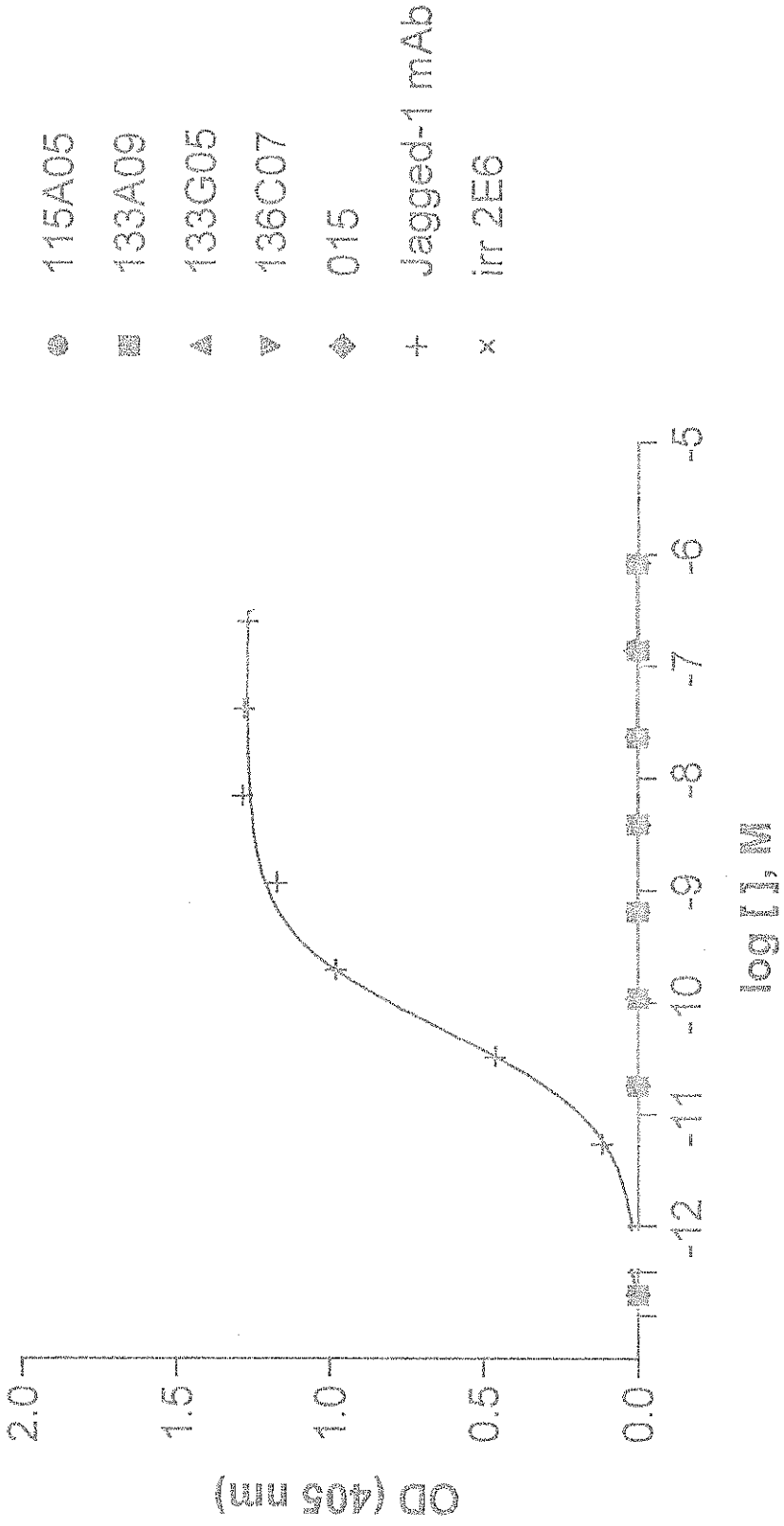

Jagged-1 binding
OD (405 nm)
2.0
1.5
1.0
0.5
0.0
-12
-11
-10
-9
-8
-7
-6
-5
log [mAb] M
115A05
133A09
133G05
136C07
015
Jagged-1 mAb
hr 2E6

Fig. 14-1

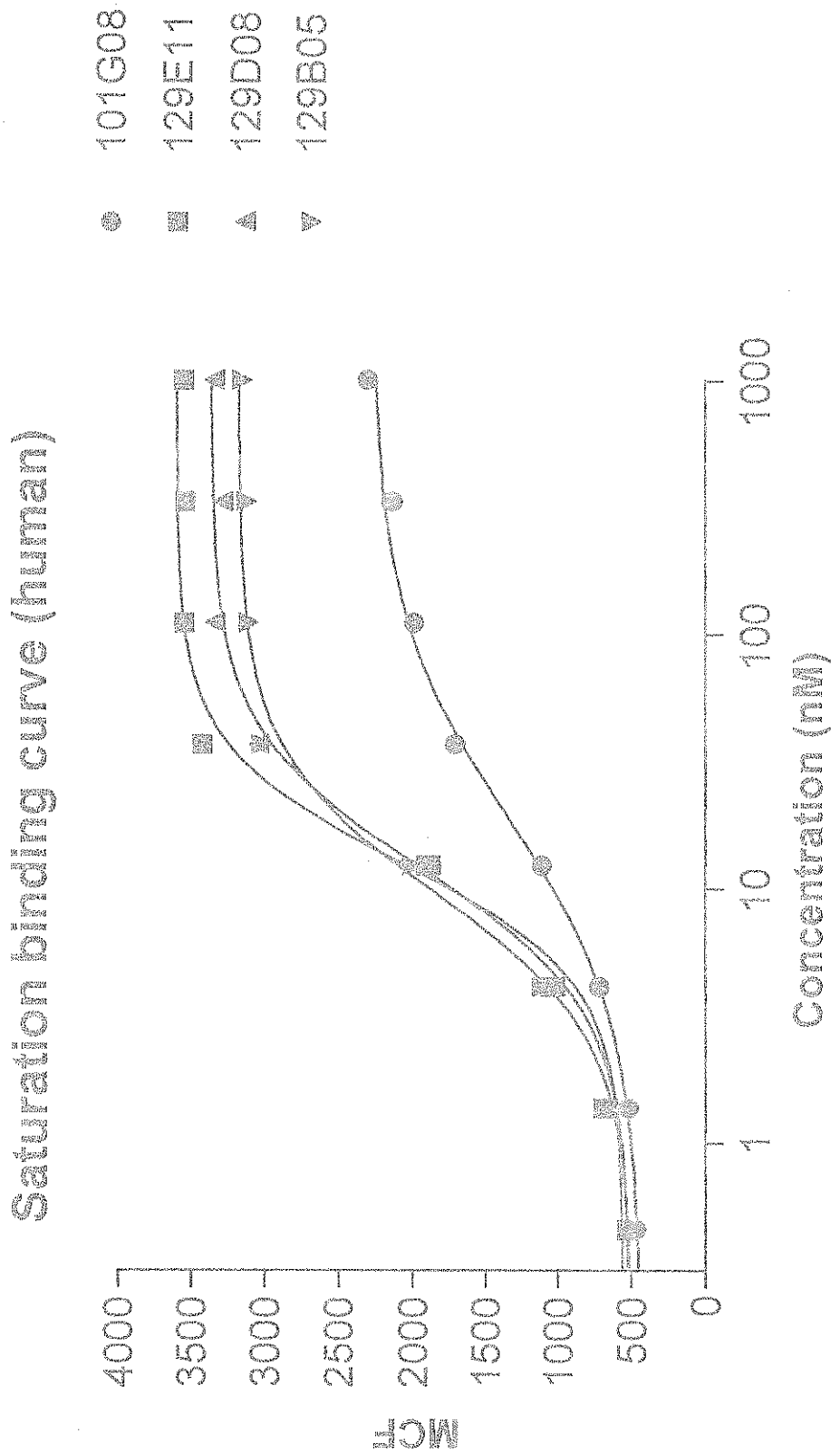

101G08
129E11
129D08
129B05
Saturation binding curve (human)
MCF
4000
3500
3000
2500
2000
1500
1000
500
0
1
10
100
1000
Concentration (nM)

Fig. 14-2

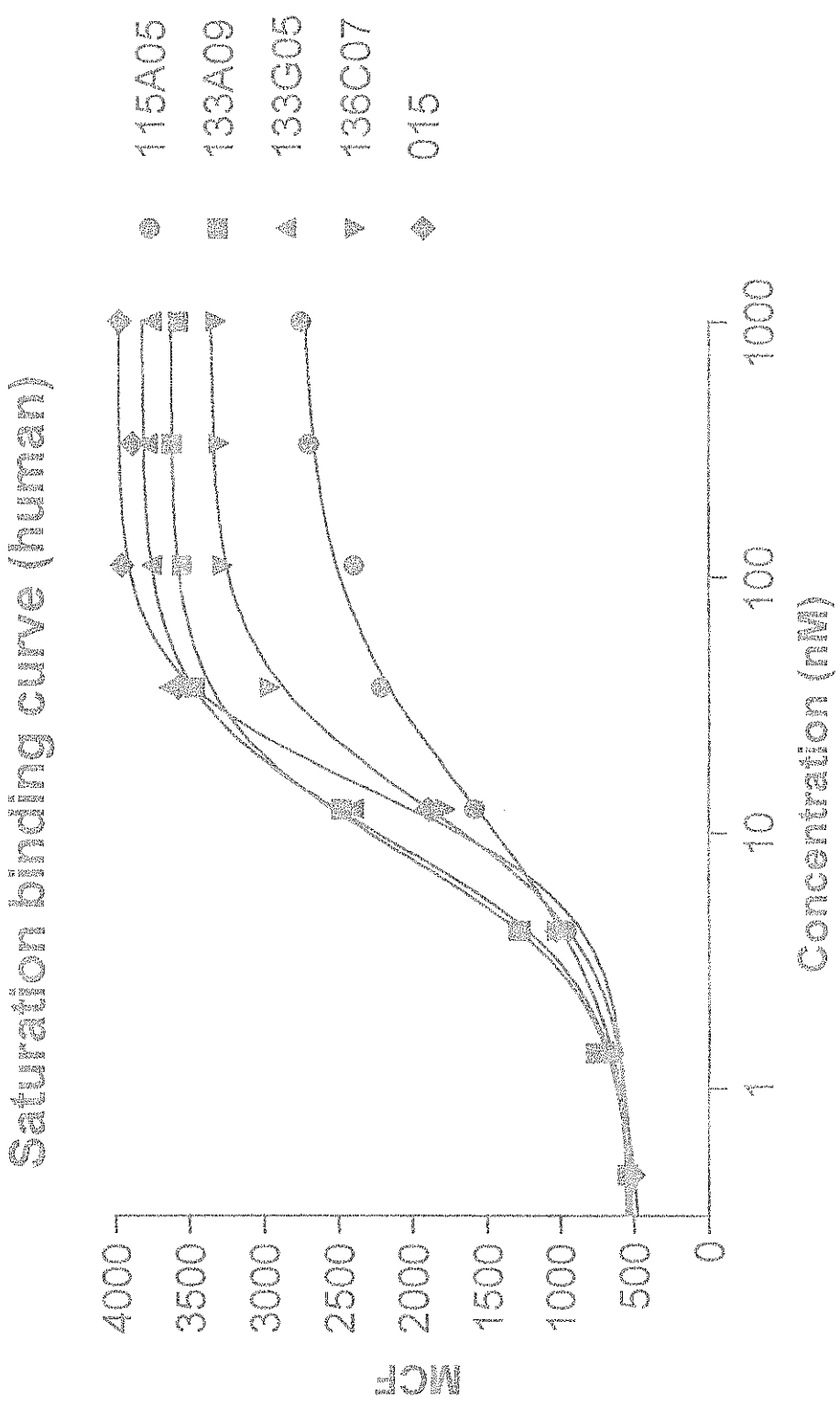

Saturation binding curve (human)
115A05
133A09
133C05
136C07
015
MCF
4000
3500
3000
2500
2000
1500
1000
500
0
1
10
100
1000
Concentration (nM)

Fig. 14-3

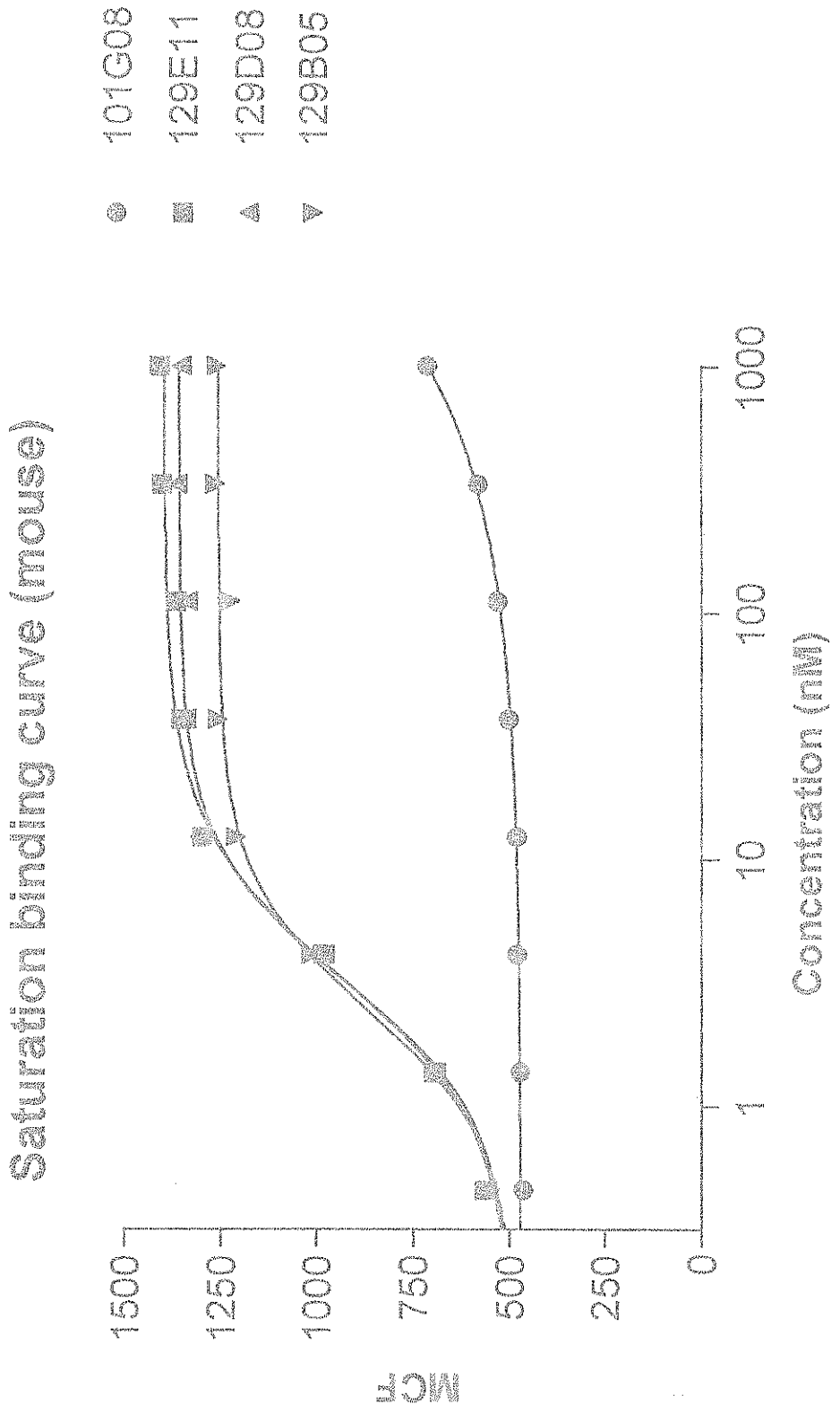

101G08
129E11
129D08
129B05
Saturation binding curve (mouse)
MCF
1500
1250
1000
750
500
250
0
1
10
100
1000
Concentration (nM)

Fig. 14-4

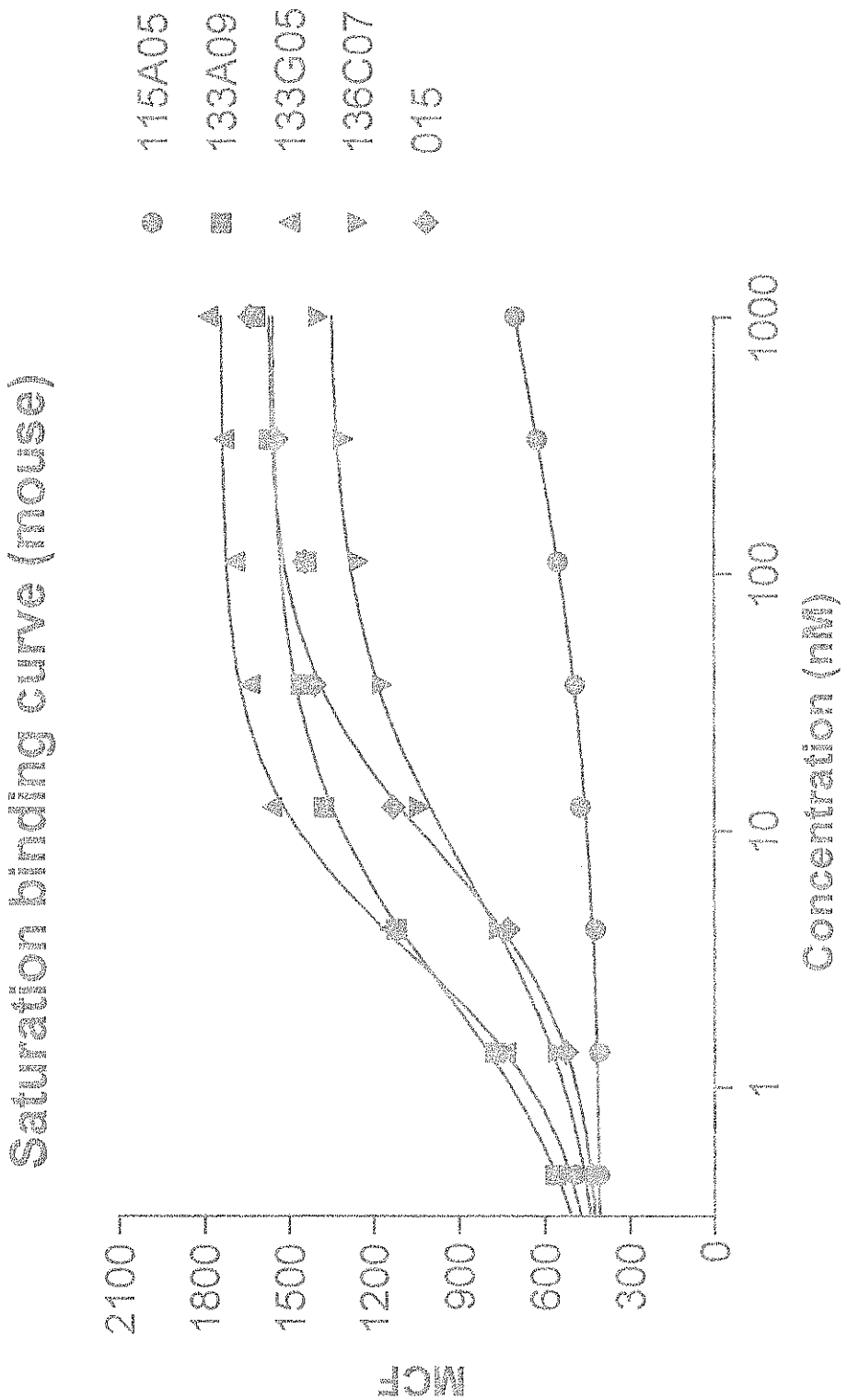

115A05
133A09
133C05
136C07
015
Saturation binding curve (mouse)
MCF
2100
1800
1500
1200
900
600
300
0
1
10
100
1000
Concentration (nM)

Fig. 14-5

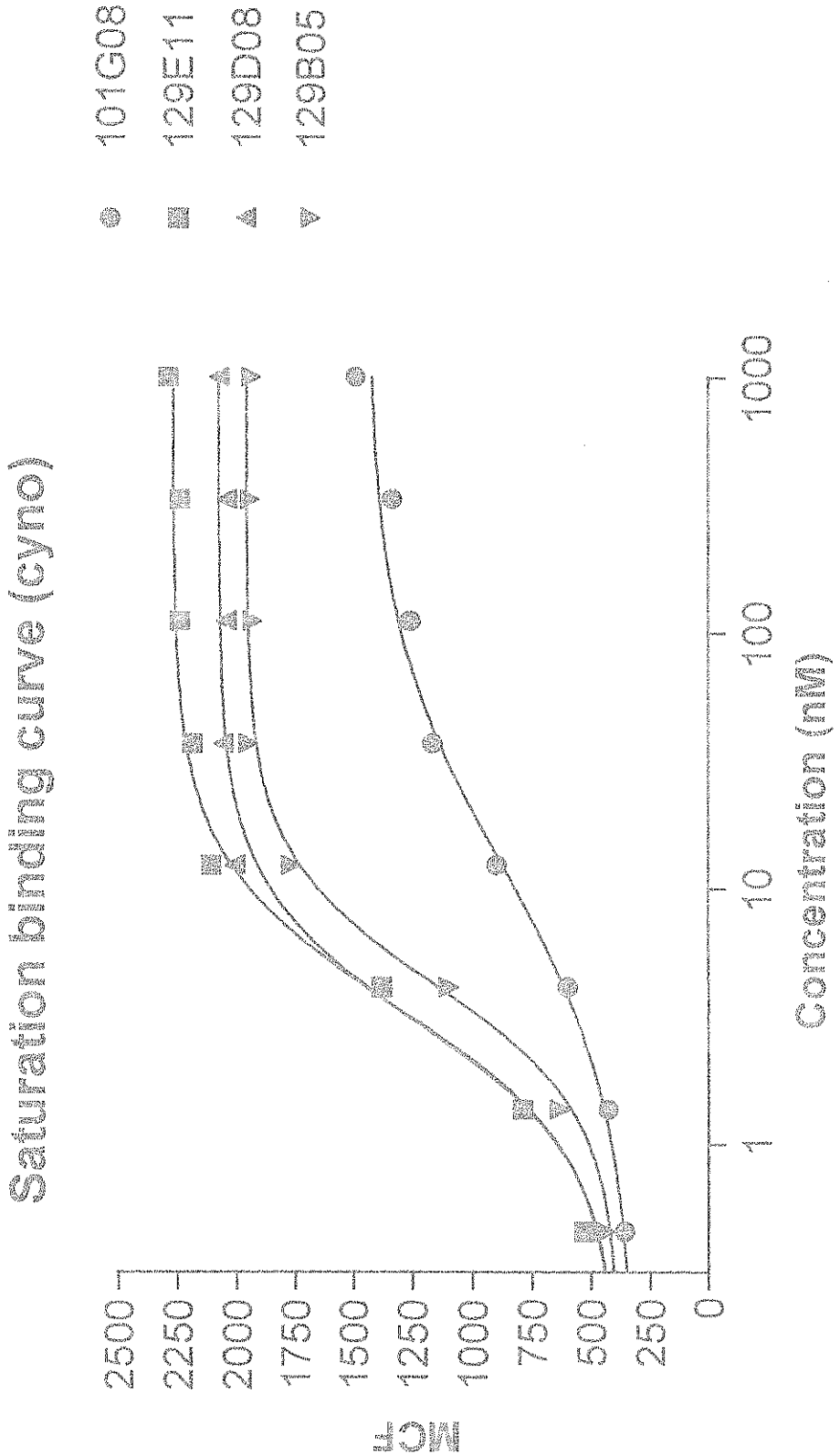

101G08
129E11
129D08
129B05
Saturation binding curve (cyno)
MCF
2500
2250
2000
1750
1500
1250
1000
750
500
250
0
1
10
100
1000
Concentration (nM)

Fig. 14-6

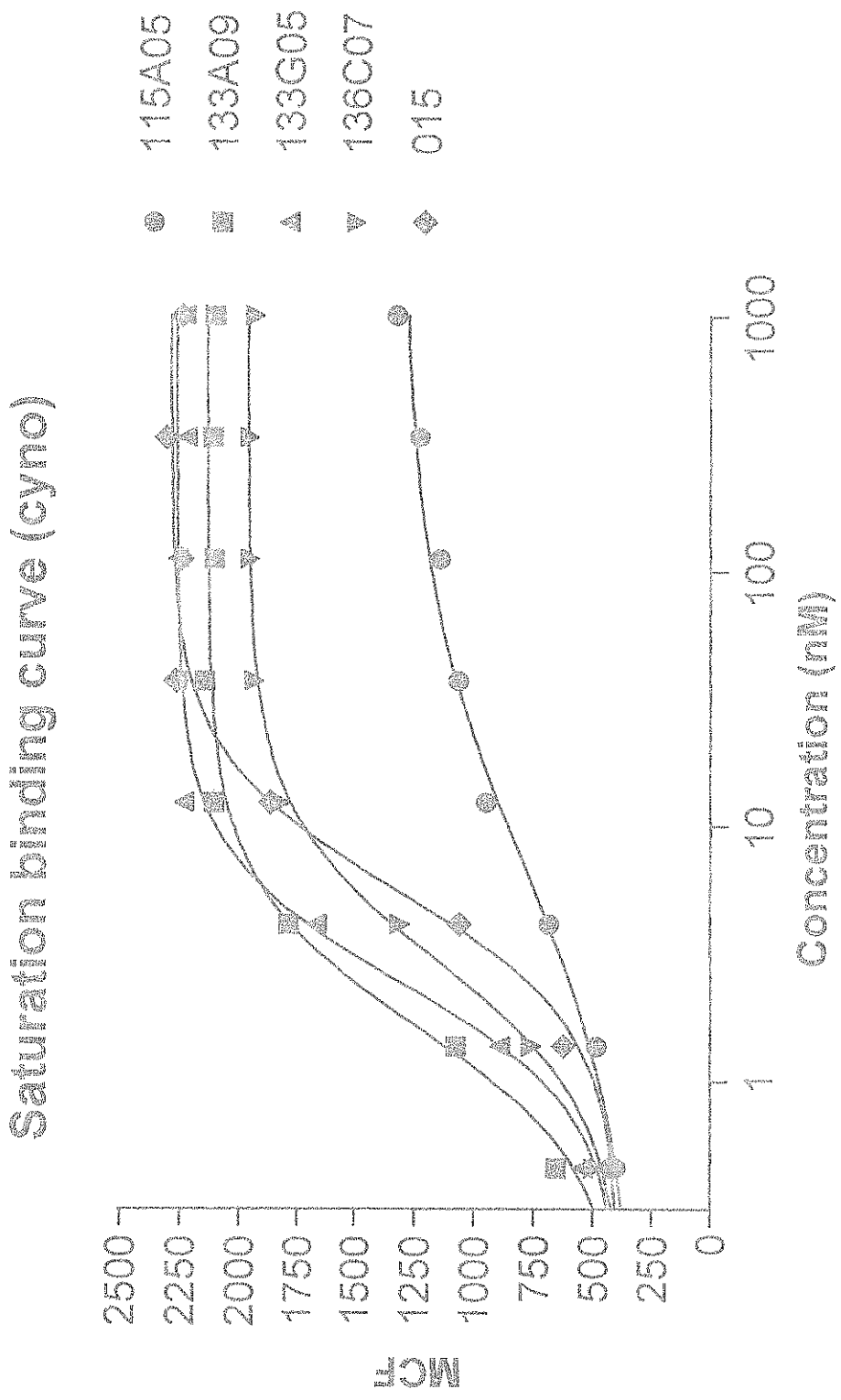

Saturation binding curve (cyno)
MCF
Concentration (nM)
115A05
133A09
133G05
136C07
015
2500
2250
2000
1750
1500
1250
1000
750
500
250
0
1
10
100
1000

Fig. 15

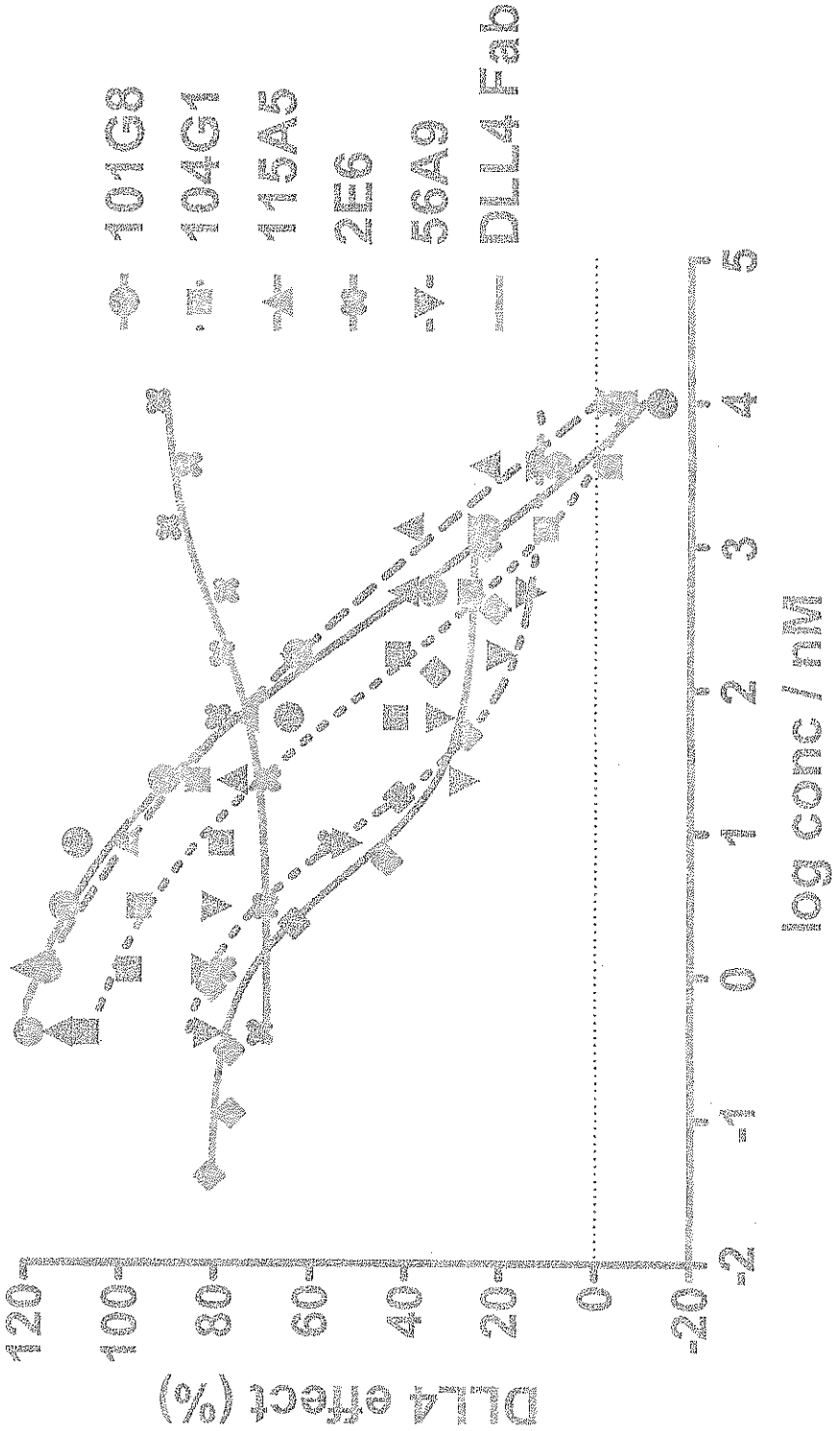
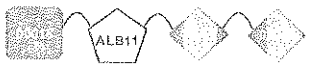
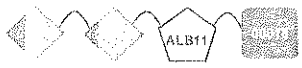
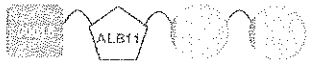

DLL4 effect (%)
120
100
80
60
40
20
0
-20
log conc / nM
5
4
3
2
1
0
-1
-2
hDLL4-Fc
5649
2166
15445
10451
10268

Fig. 16

VHH ID	Format	Description
DLLANGBII00001		DLLBII00018-9gs-ALB11-9gs-00050-9gs-00050
DLLANGBII00002		00050-9gs-00050-9gs-ALB11-9gs-DLLBII00018
DLLANGBII00003		DLLBII00018-9gs-ALB11-9gs-00042
DLLANGBII00004		00042-9gs-ALB11-9gs-DLLBII00018
DLLANGBII00005		DLLBII00018-9gs-ALB11-9gs-00042-9gs-00042
DLLANGBII00006		00042-9gs-00042-9gs-ALB11-9gs-DLLBII00018
DLLANGBII00007		DLLBII00018-9gs-ALB11-9gs-00045
DLLANGBII00008		00045-9gs-ALB11-9gs-DLLBII00018
DLLANGBII00009		DLLBII00018-9gs-00050-9gs-00050-9gs-ALB11
DLLANGBII00010		00050-9gs-00050-9gs-DLLBII00018-9gs-ALB11
DLLANGBII00011		DLLBII00018-9gs-00042-9gs-ALB11
DLLANGBII00012		00042-9gs-DLLBII00018-9gs-ALB11
DLLANGBII00013		DLLBII00018-9gs-00042-9gs-00042-9gs-ALB11
DLLANGBII00014		00042-9gs-00042-9gs-DLLBII00018-9gs-ALB11
DLLANGBII00015		DLLBII00018-9gs-00045-9gs-ALB11
DLLANGBII00016		00045-9gs-DLLBII00018-9gs-ALB11

58 / 152

Fig. 16 cont'd

Legend:

	Description
	DLLBII00018
	00042
	00045
	00050
	ALB11
	9 GlySer linker

59 / 152
Fig. 17A

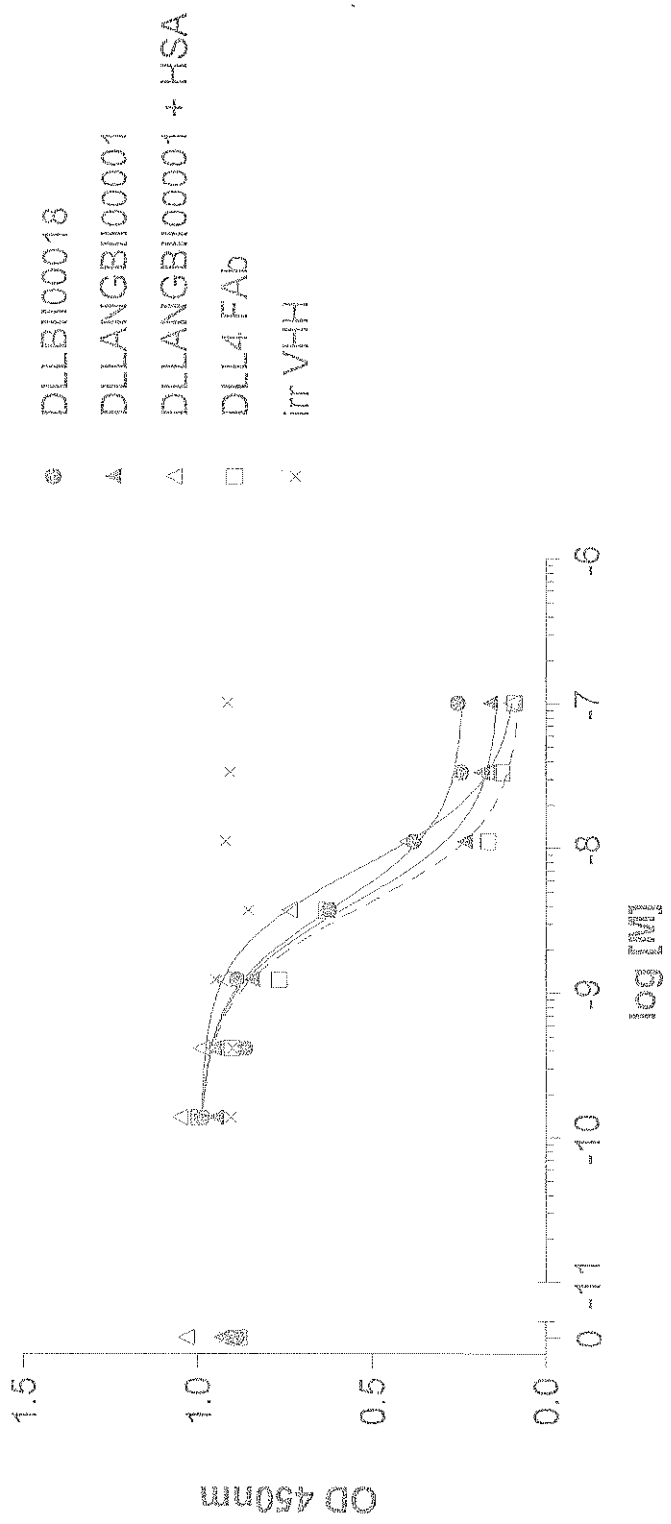


Figure 17B

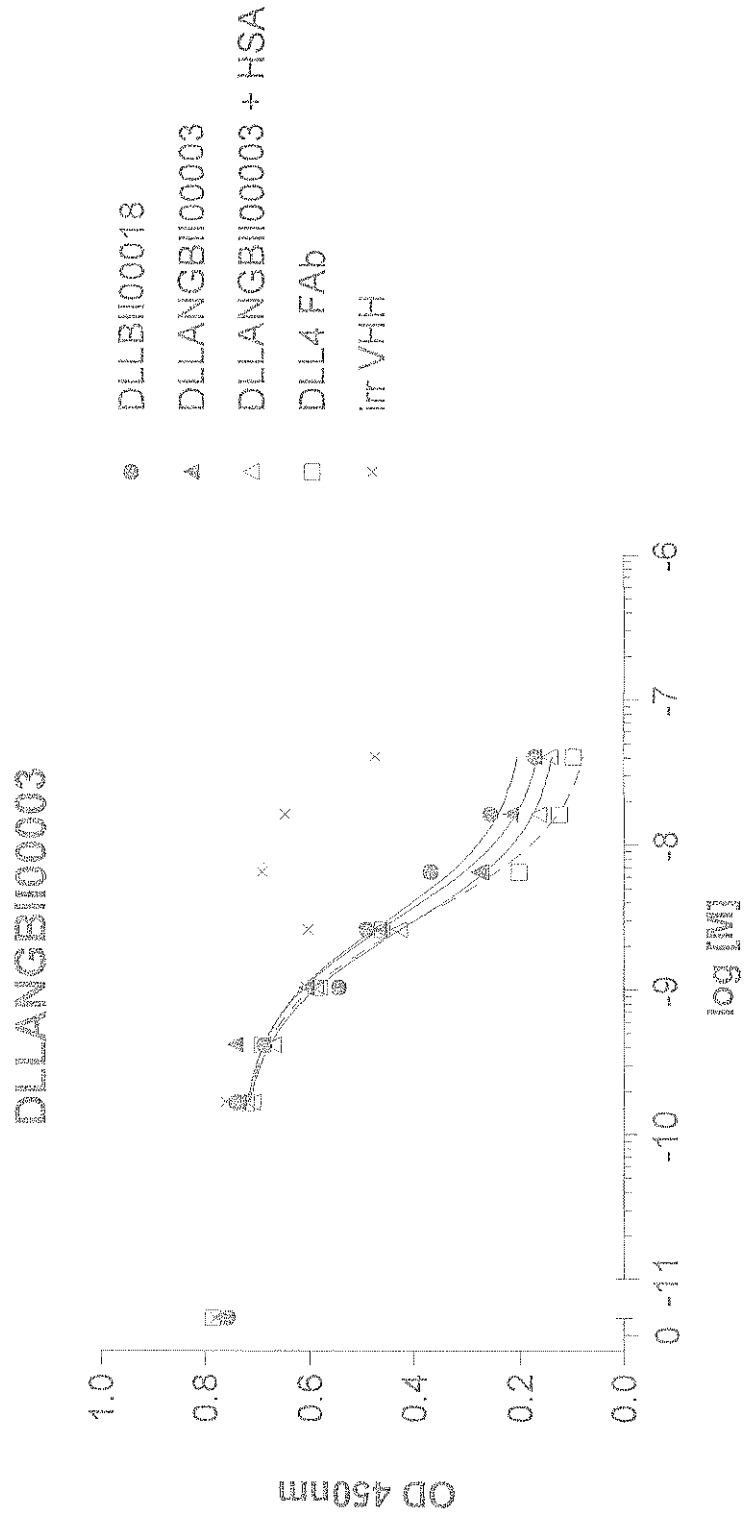

DLLBI100018
DLLANGBI00003
DLLANGBI00003 + HSA
DLL4 FAb
Irr VHH
DLLANGBI00003
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Fig. 17C

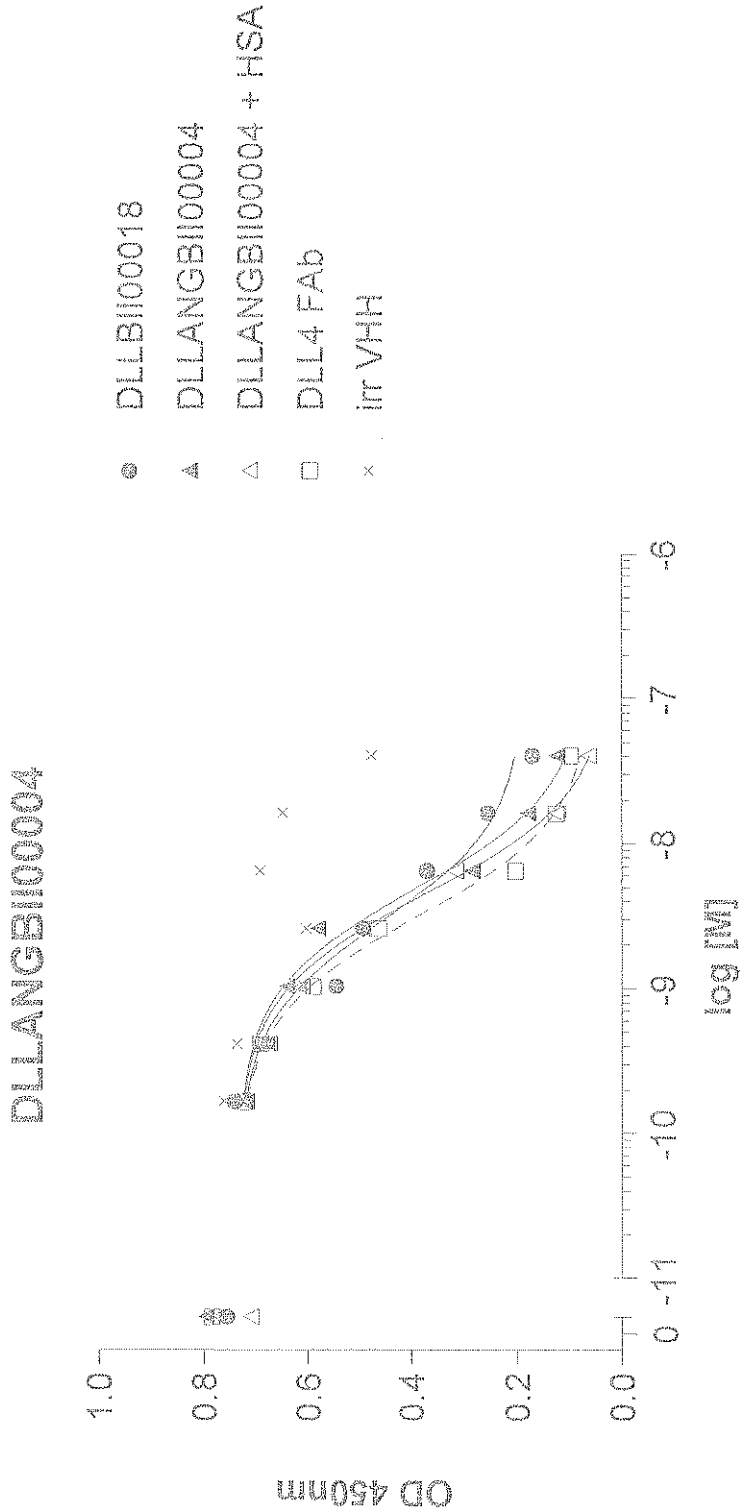

DLLBII00018
DLLANGBII00004
DLLANGBII00004 + HSA
DLL4 FAb
irr VHH
DLLANGBII00004
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Fig. 17D

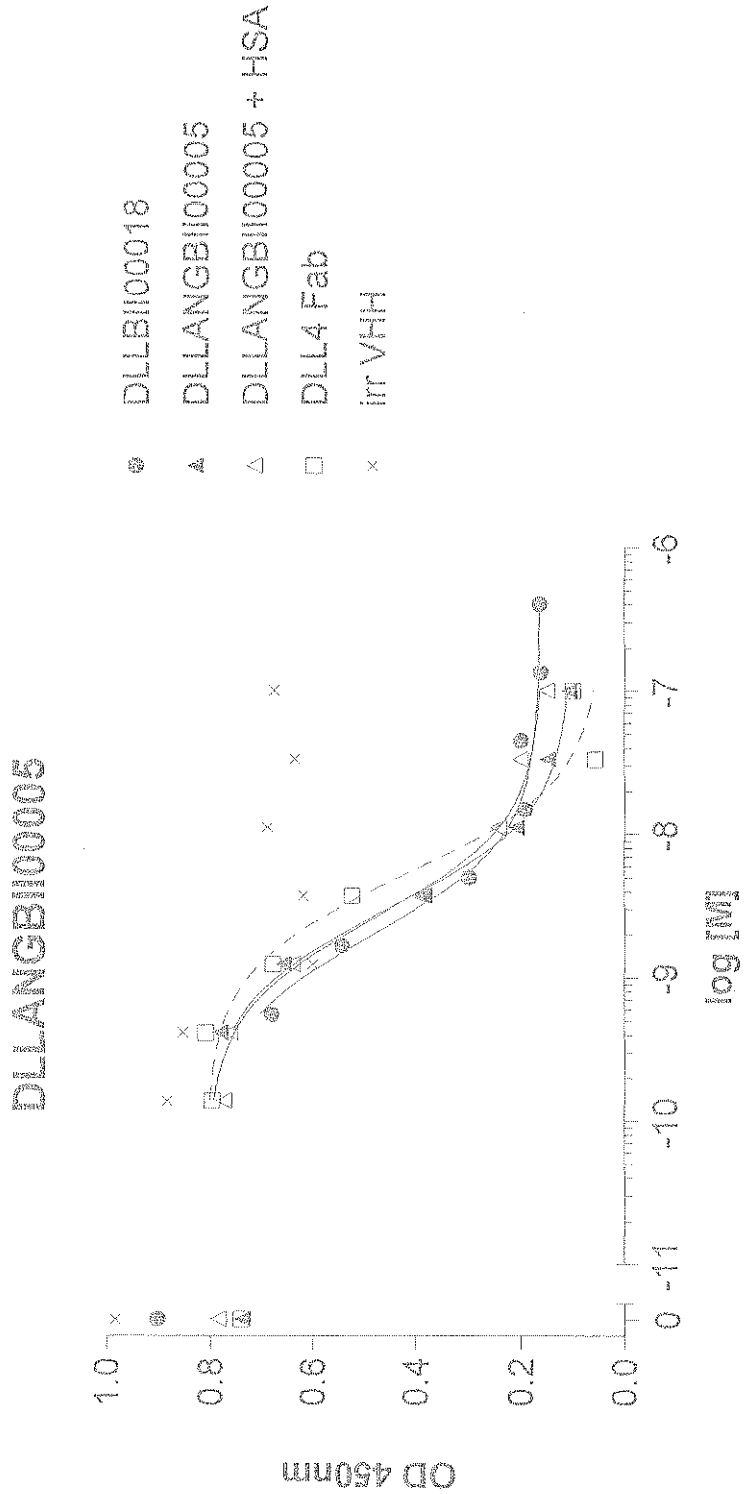
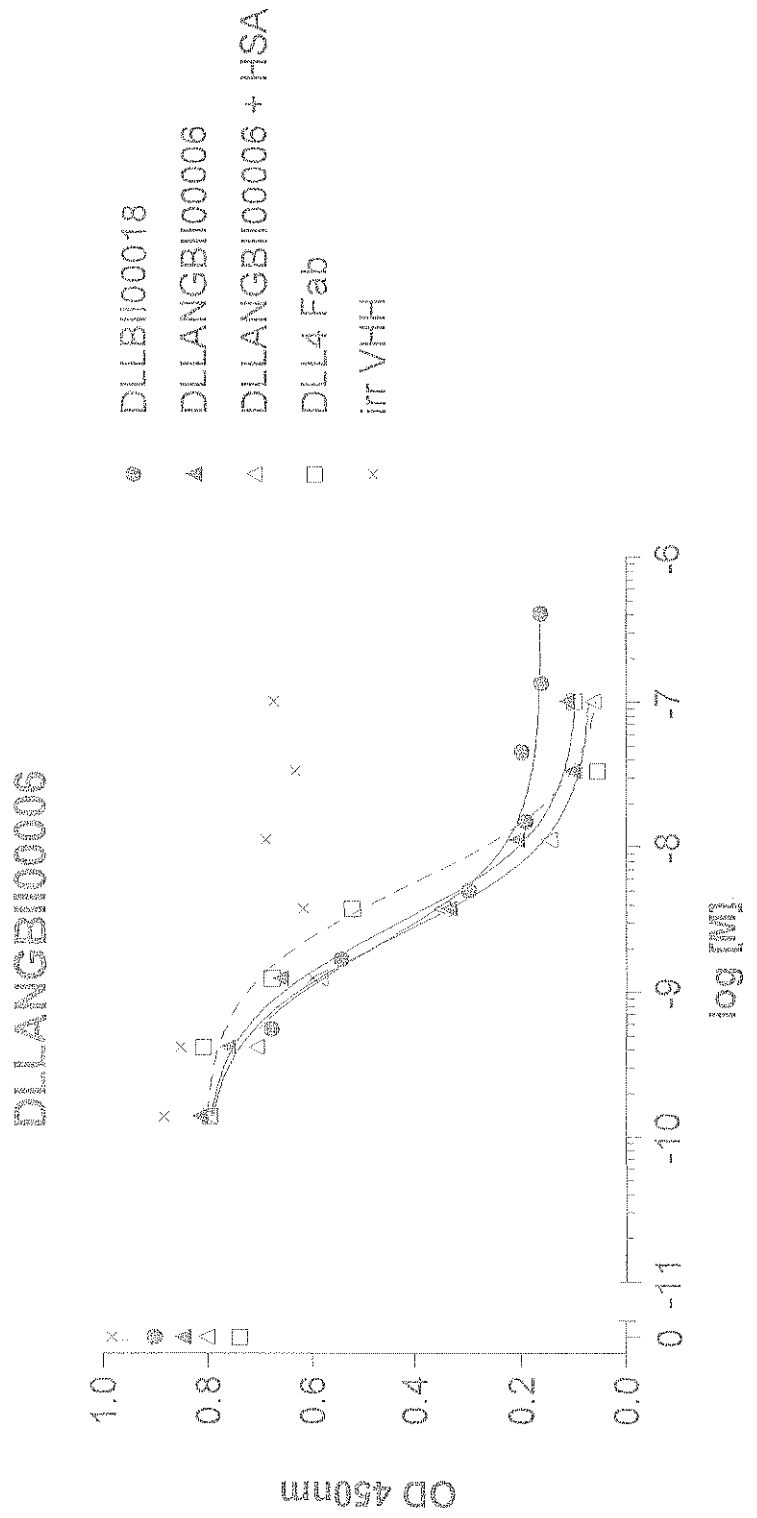

DLBI00018
DLANGBI00005
DLANGBI00005 + HSA
DL4 Fab
irr VHH
DLANGBI00005
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
-6
-7
-8
-9
-10
-11
log [M]

Figure 17E


DLBli00018
DLANGBli00006
DLANGBli00006 + HSA
DL4 Fab
irr VHH
DLANGBli00006
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
-5
-7
-8
-9
-10
-11
-log [M]

64 / 152

Figure 17F

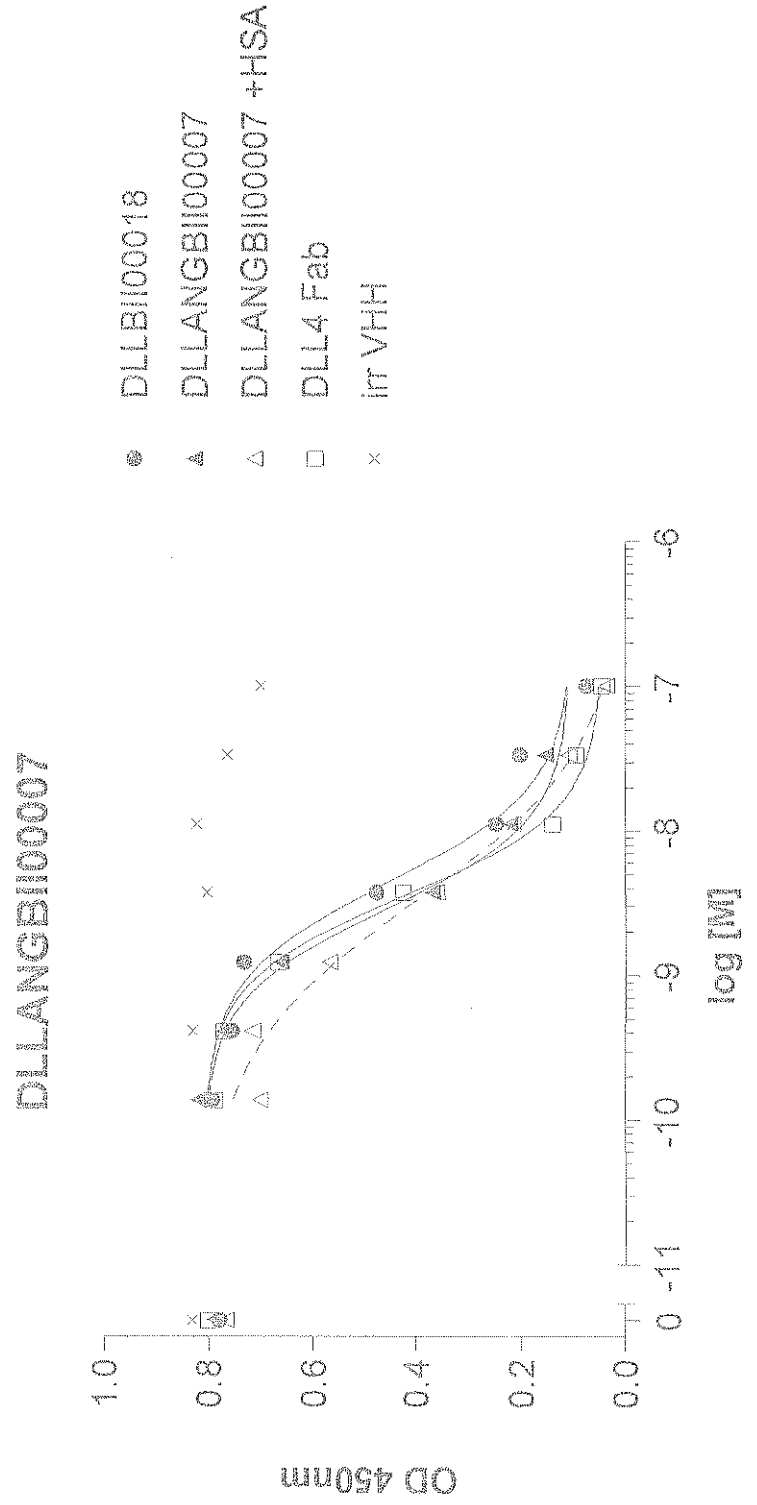


Figure 17G

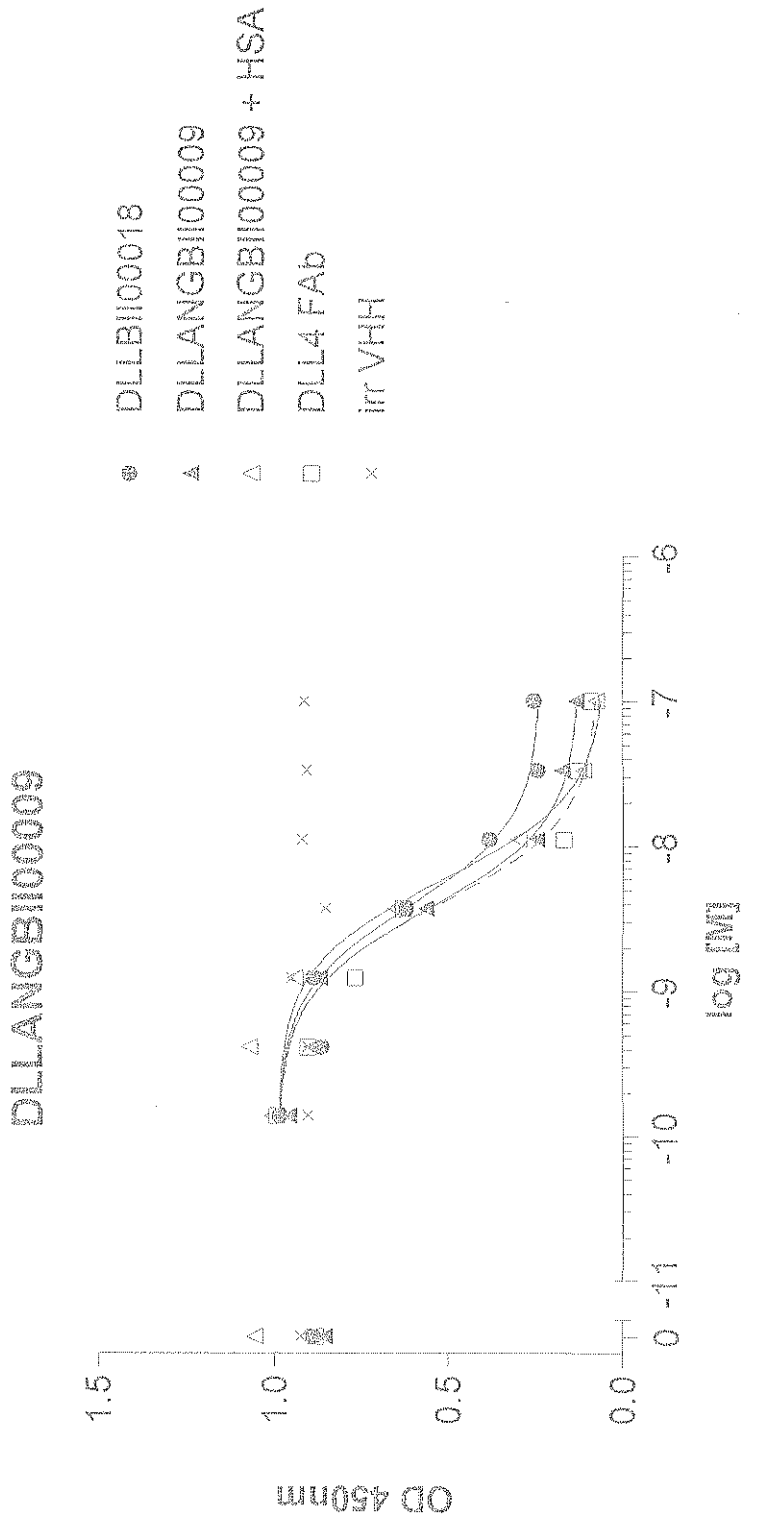

DLBI00018
DLANGBI00009
DLANGBI00009 + HSA
DL4 FAb
Irr VHH
DLANGBI00009
OD 450nm
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17H

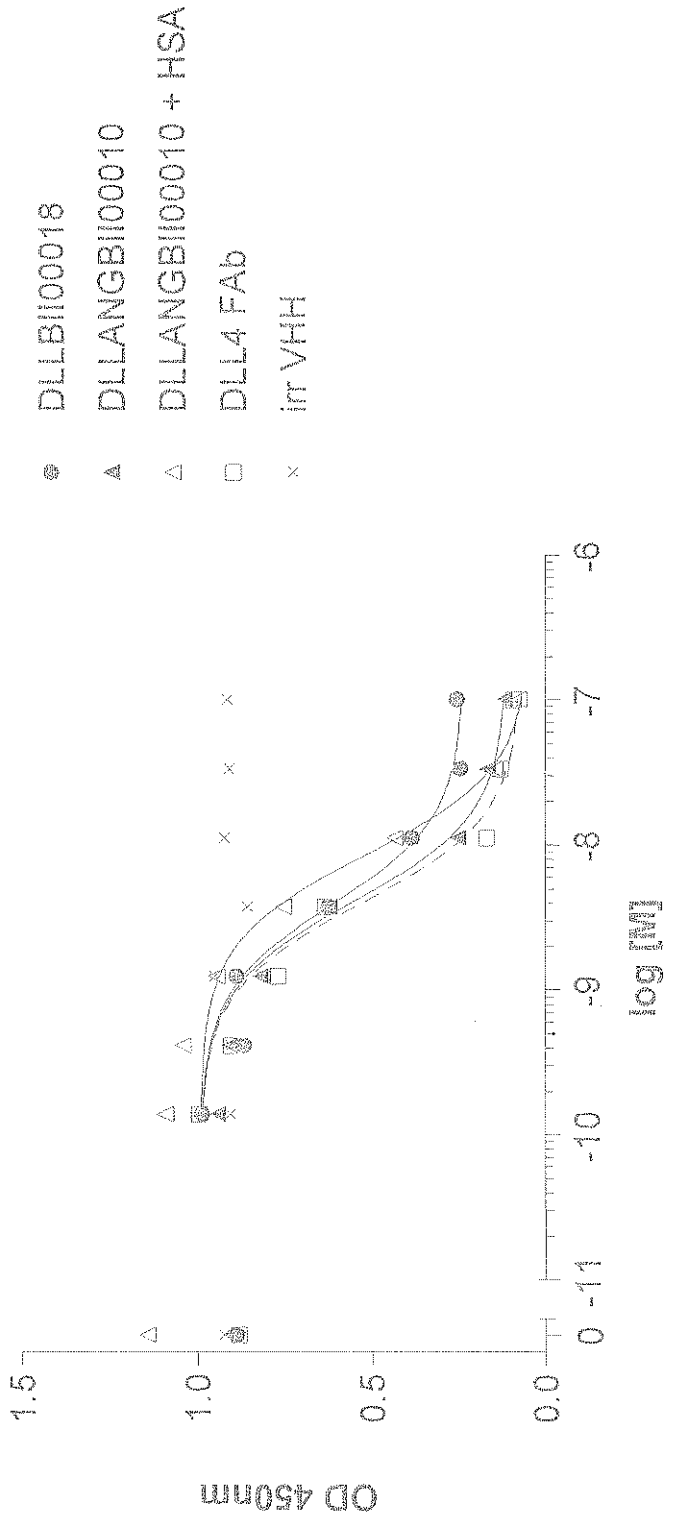

DLLBI100018
DLLANGBI00010
DLLANGBI00010 + HSA
DLL4 FAb
irr VHH
DLLANGBI00010
OD 450nm
1.5
1.0
0.5
0.0
-6
-7
-8
-9
-10
-11
log [M]

Figure 17I

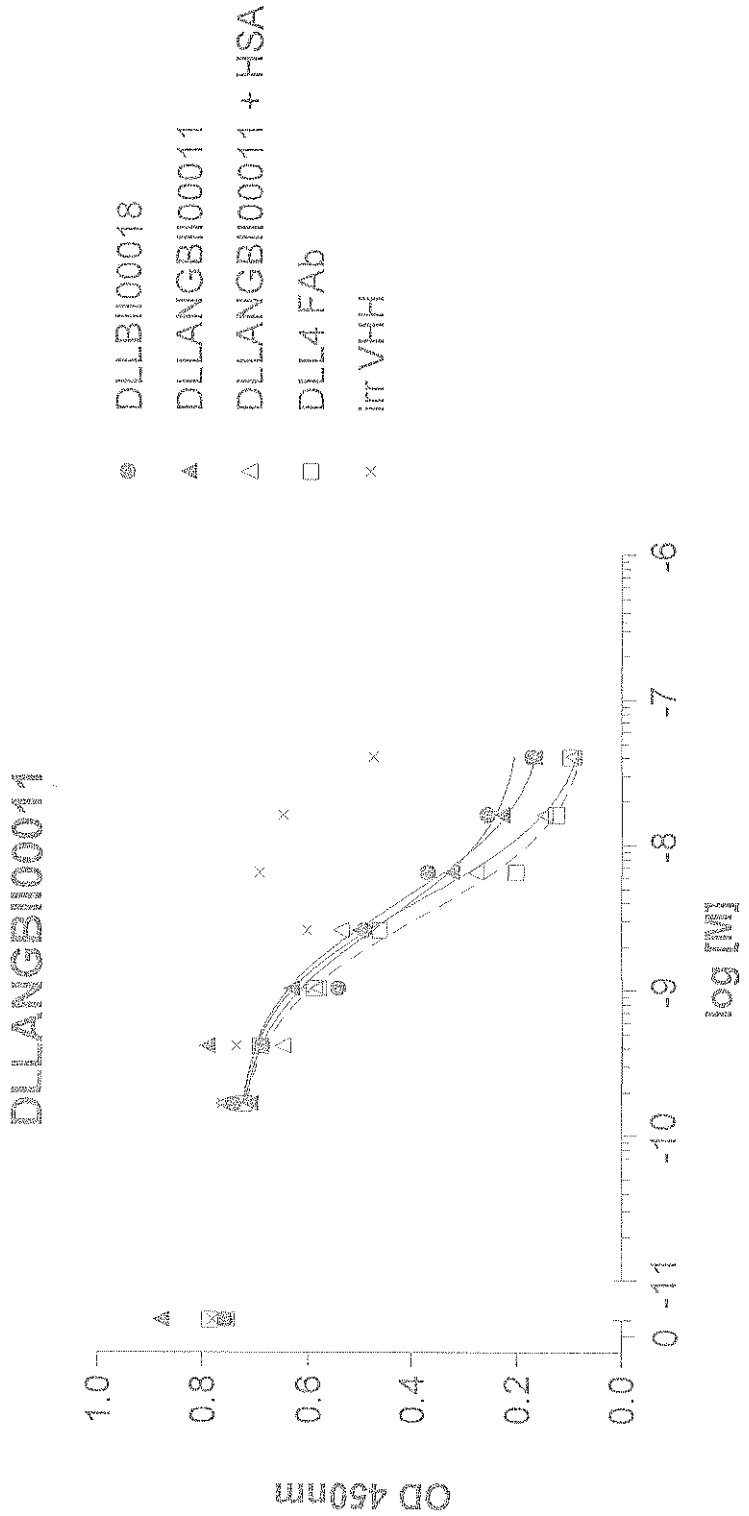

DLLBI00018
DLLANGBI00011
DLLANGBI00011 + HSA
DL4 FAb
irr VHH
DLLANGBI00011
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log

Figure 17J

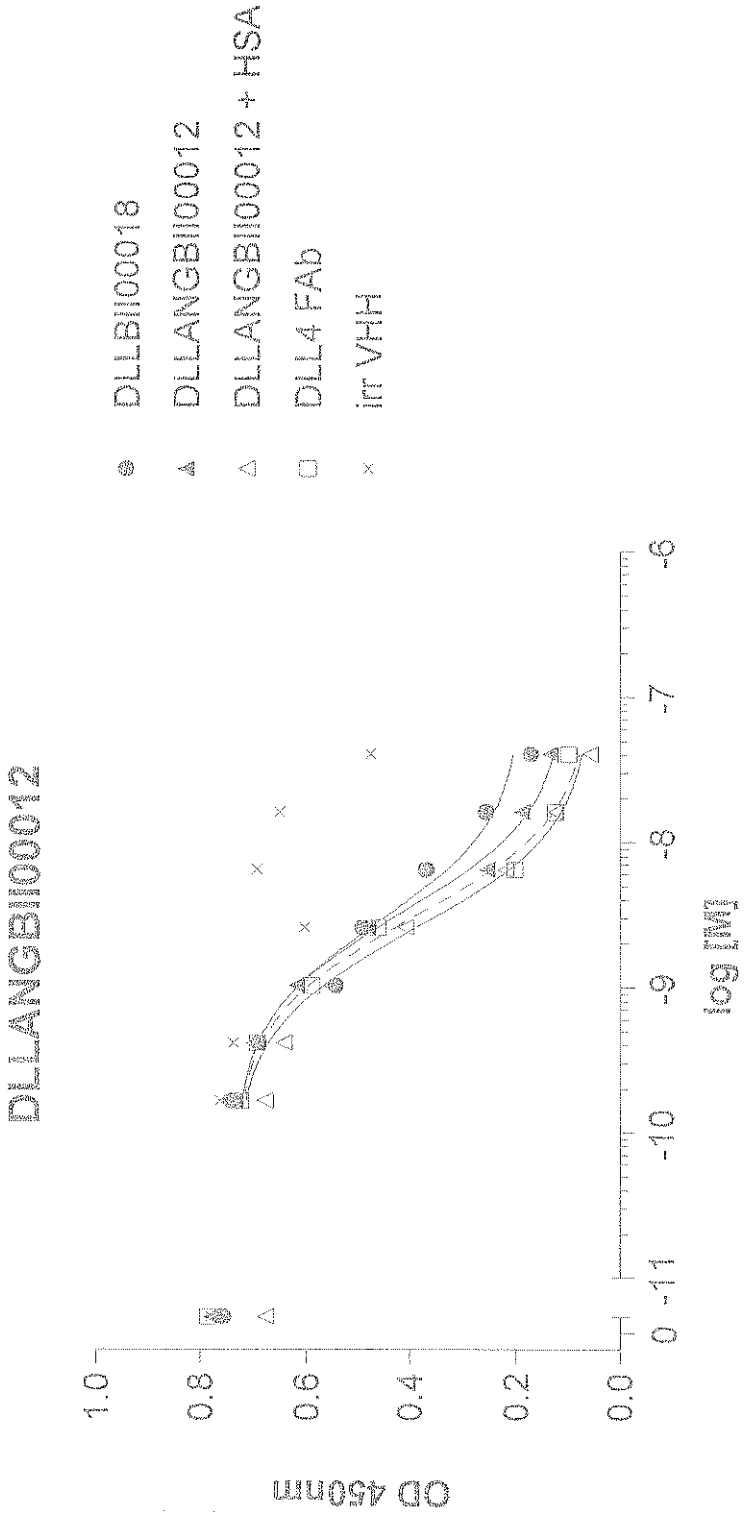

DLBI000018
DLLANGBI00012
DLLANGBI00012 + HSA
DLL4 FAb
irr VHH
DLLANGBI00012
OD 450nm
log [M]

Figure 17K

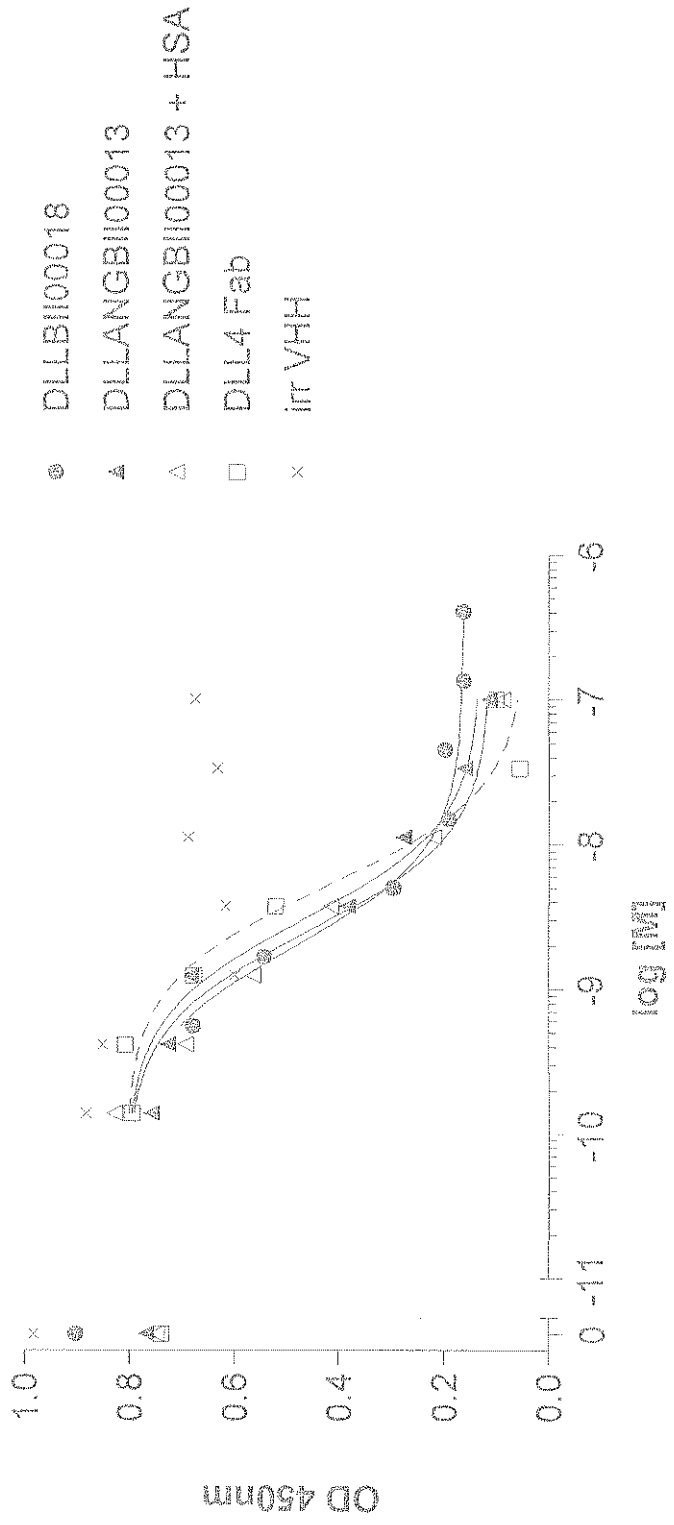
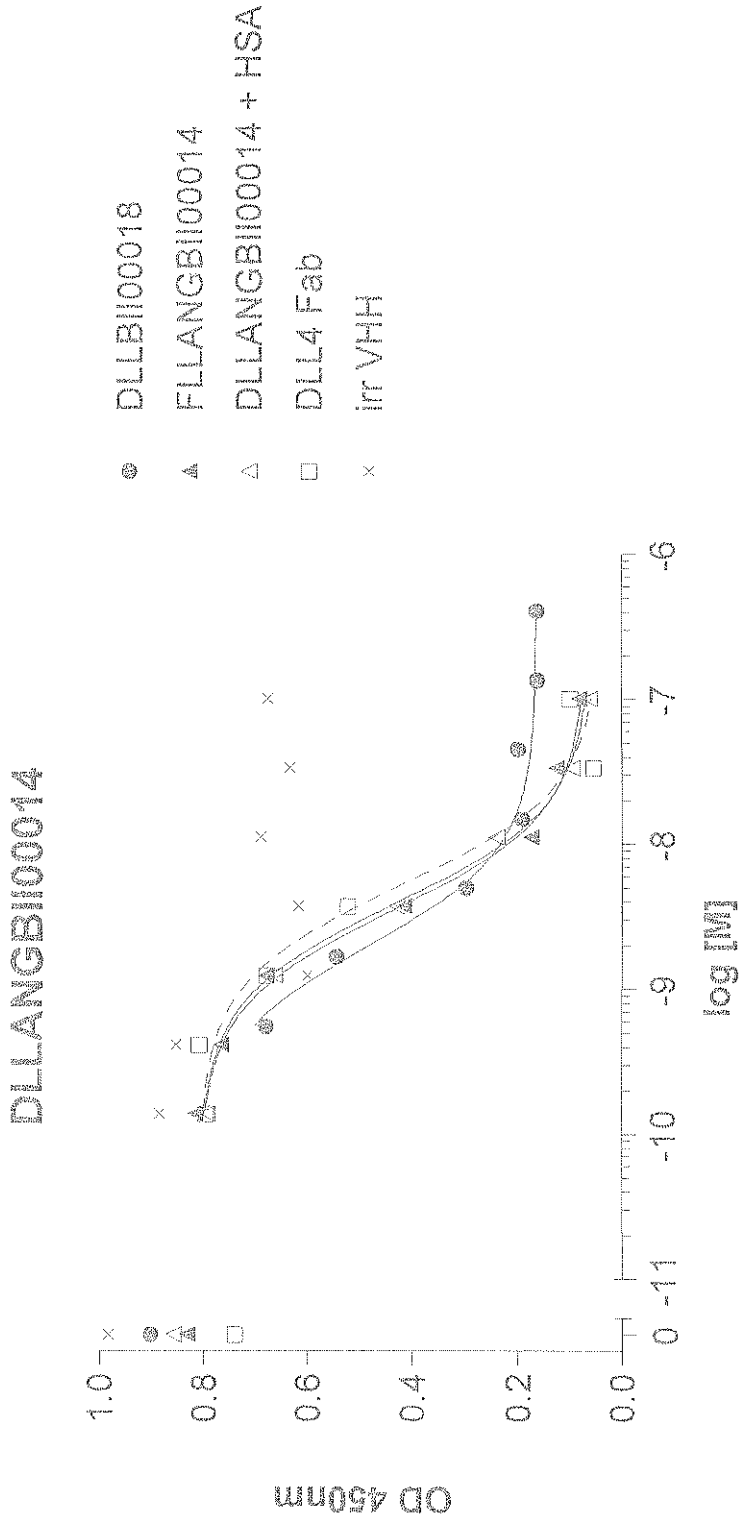

DLB100018
DLLANGBI00013
DLLANGBI00013 + HSA
DLL4 Fab
irr VHH
DLLANGBI00013
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17L


DLBli00018
FLANGBli00014
DLANGBli00014 + HSA
DL4 Fab
Irr VHH
DLANGBli00014
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

71 / 152

Figure 17M

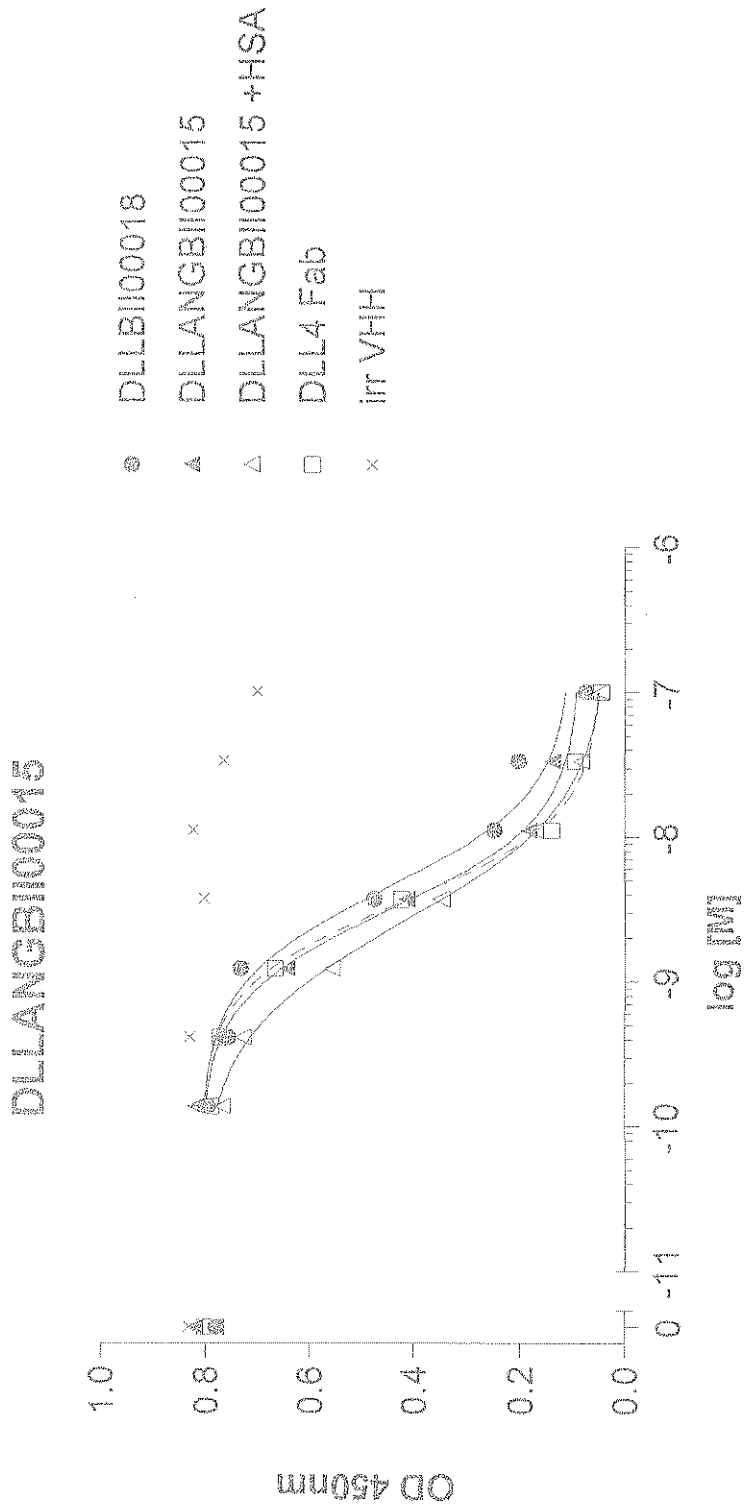


Figure 18-1A

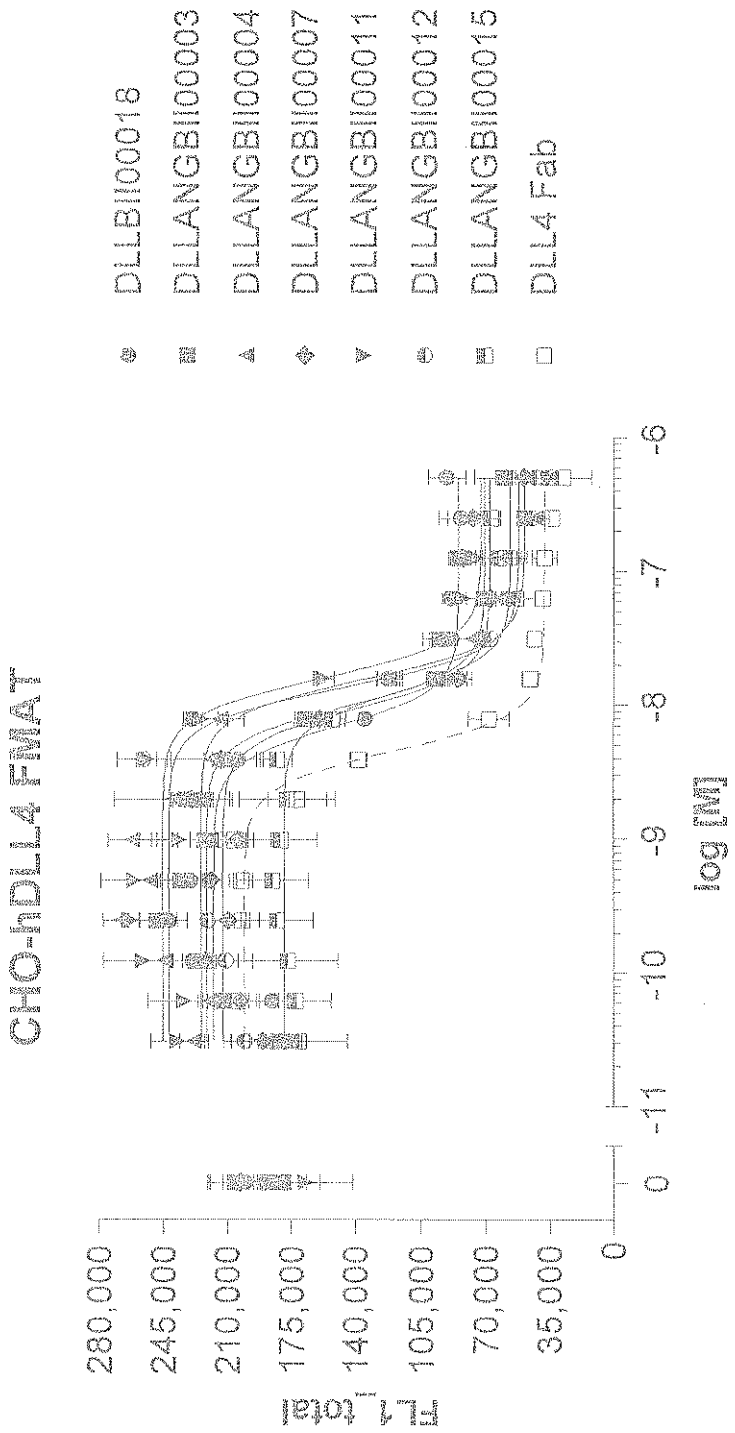
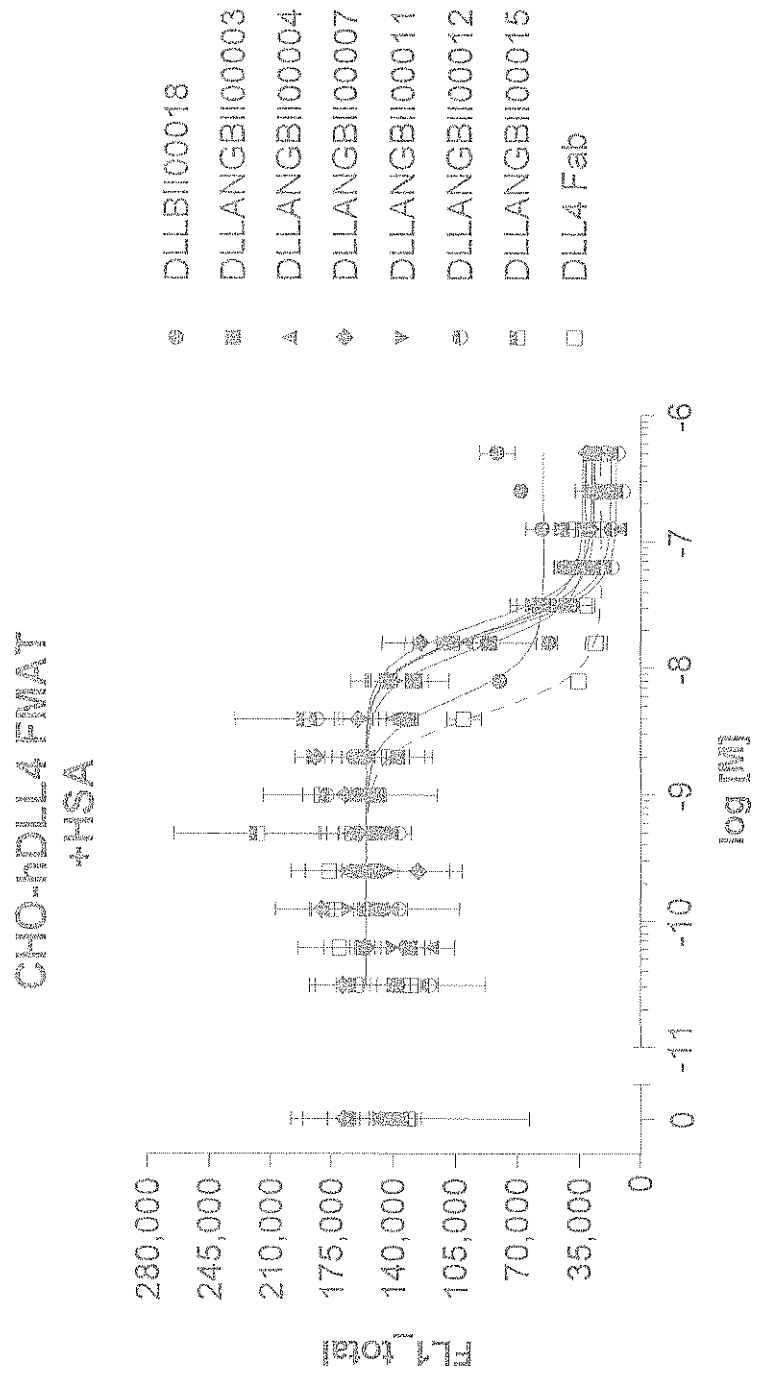

DLLBI00018
DLLANGBI00003
DLLANGBI00004
DLLANGBI00007
DLLANGBI00011
DLLANGBI00012
DLLANGBI00015
DL4 Fab
CHO-hDLL4 FMAT
FL4_Total
280,000
245,000
210,000
175,000
140,000
105,000
70,000
35,000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 18-1A (continued)



74 / 152

Figure 18-1B

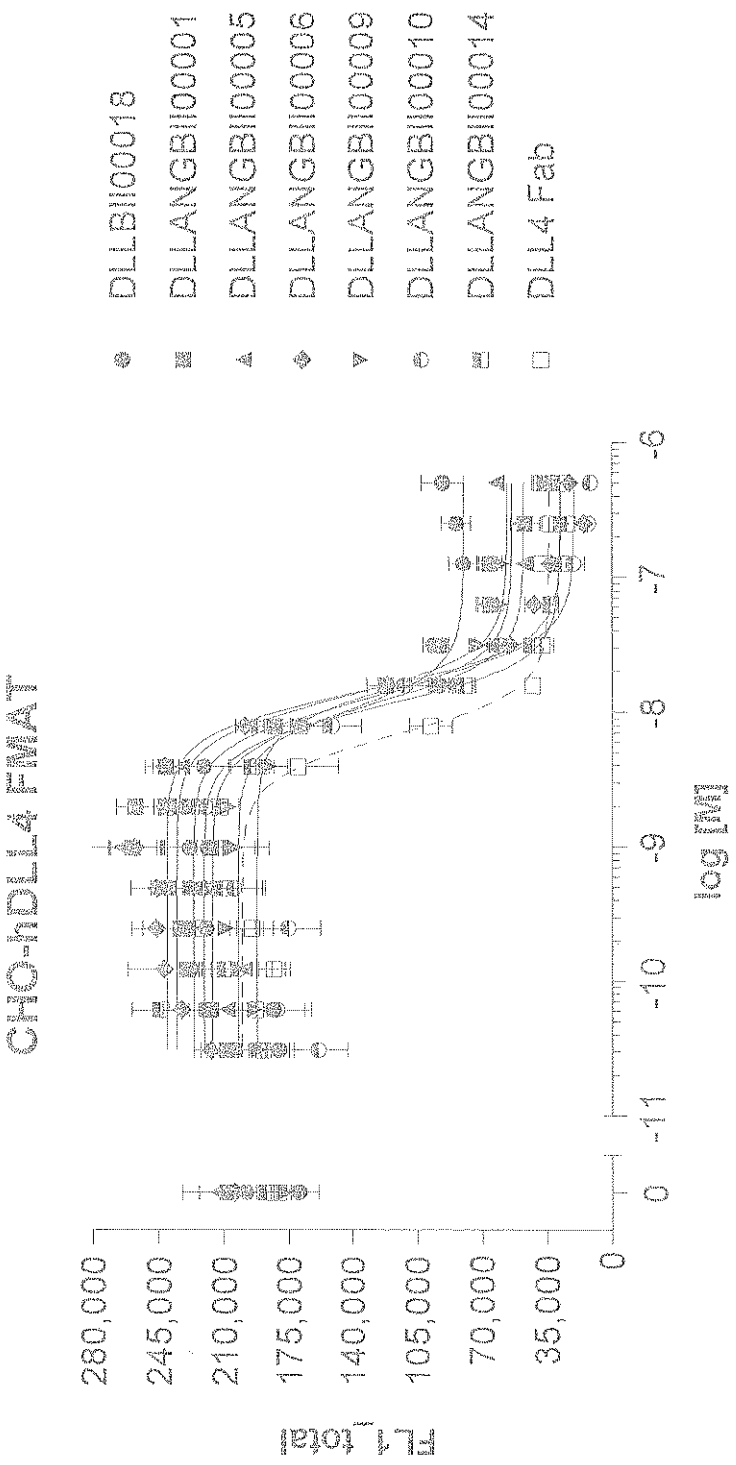


Figure 18-1B (continued)

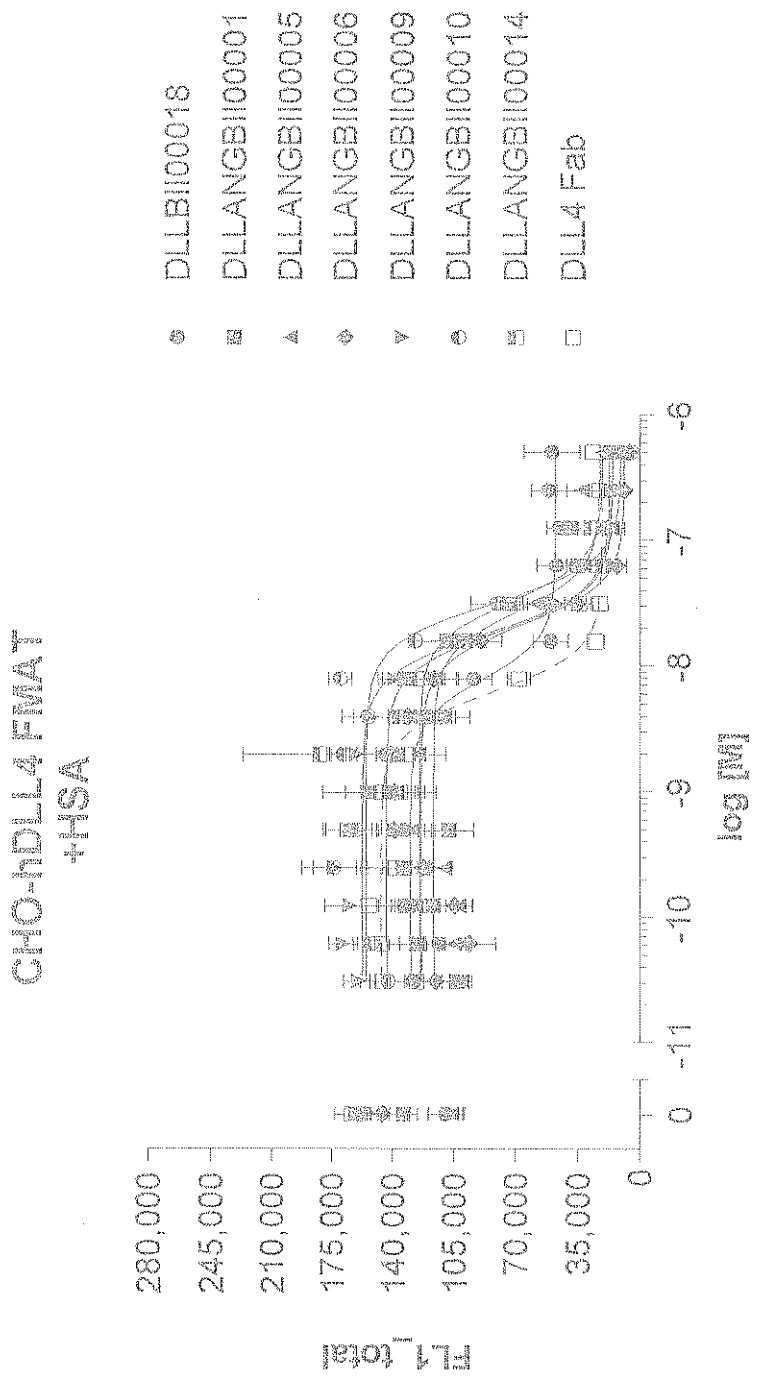
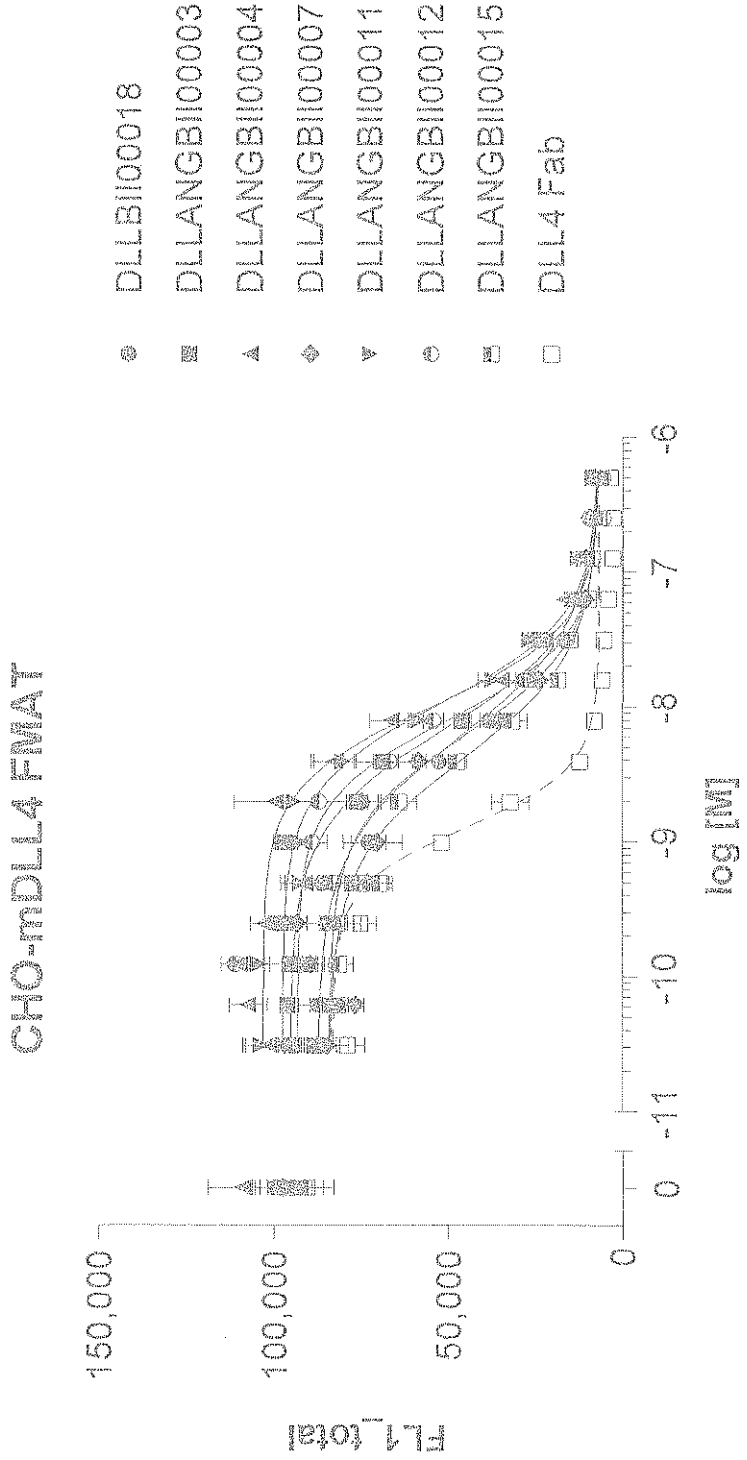


Figure 18-2A


DLLBI00018
DLLANGBI00003
DLLANGBI00004
DLLANGBI00007
DLLANGBI00011
DLLANGBI00012
DLLANGBI00015
DLL4 Fab
CHO-mDLL4 FMAT
FL1_total
150,000
100,000
50,000
0
0
-11
-10
-9
-8
-7
-6
log [M]

77 / 152

Figure 18-2A (continued)

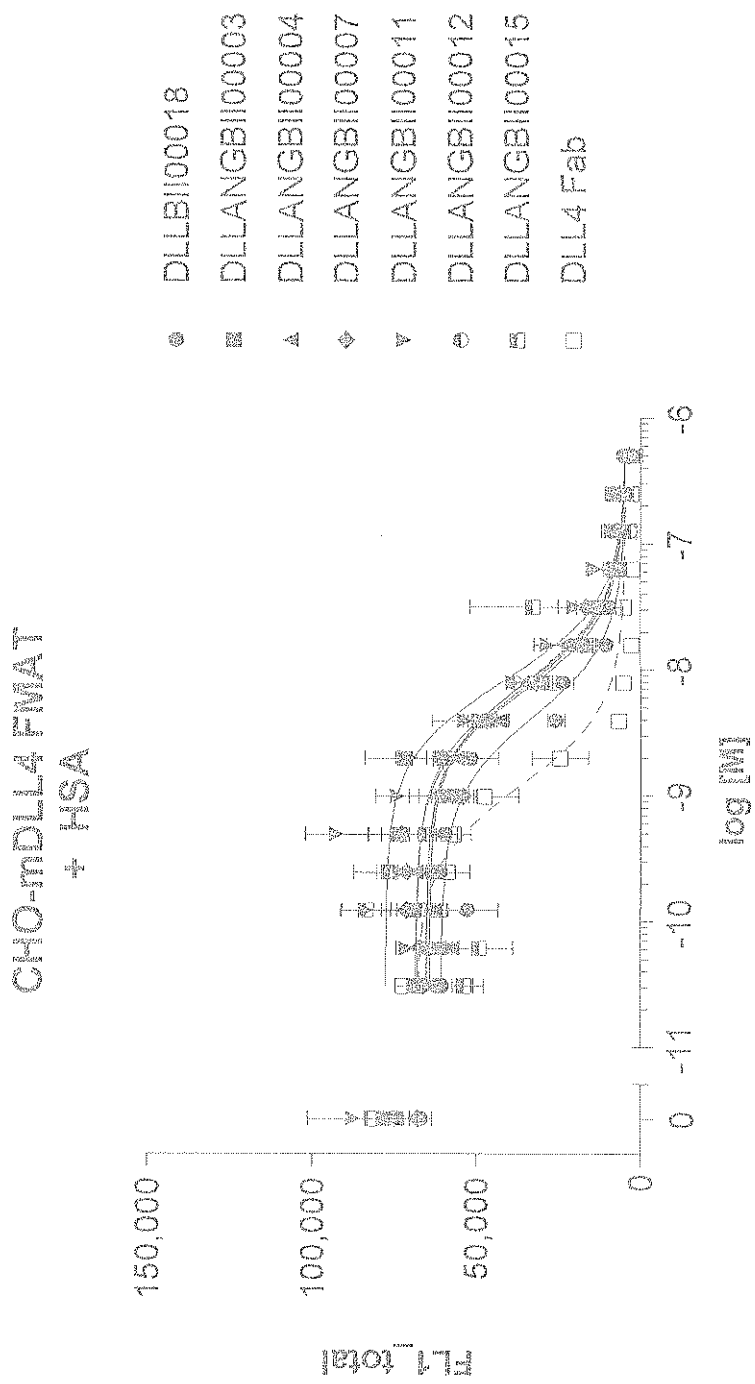
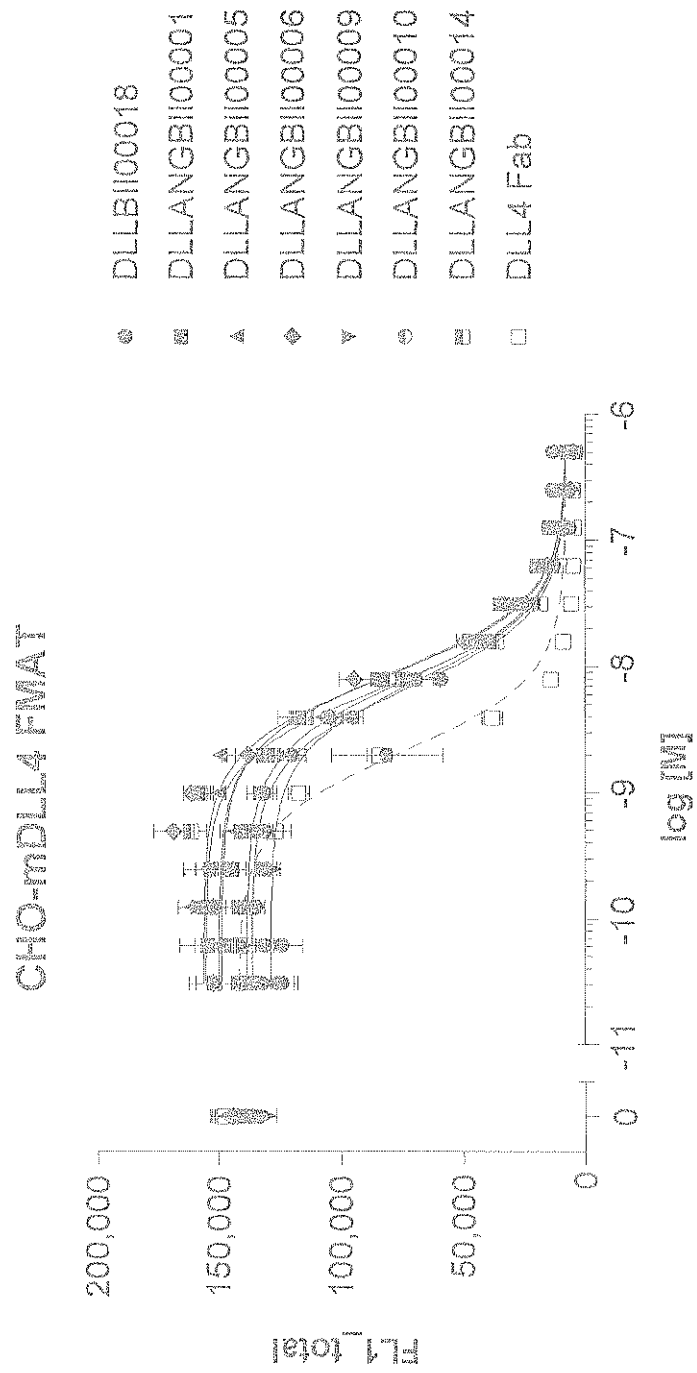


Figure 18-2B


DLLBI100018
DLLANGBI100001
DLLANGBI100005
DLLANGBI100006
DLLANGBI100009
DLLANGBI100010
DLLANGBI100014
DLL4 Fab
CHO-hDLL4 FMAT
FLI_total
200,000
150,000
100,000
50,000
0
0
-11
-10
-9
-8
-7
-6
log [nM]

79 / 152

Figure 18-2B (continued)

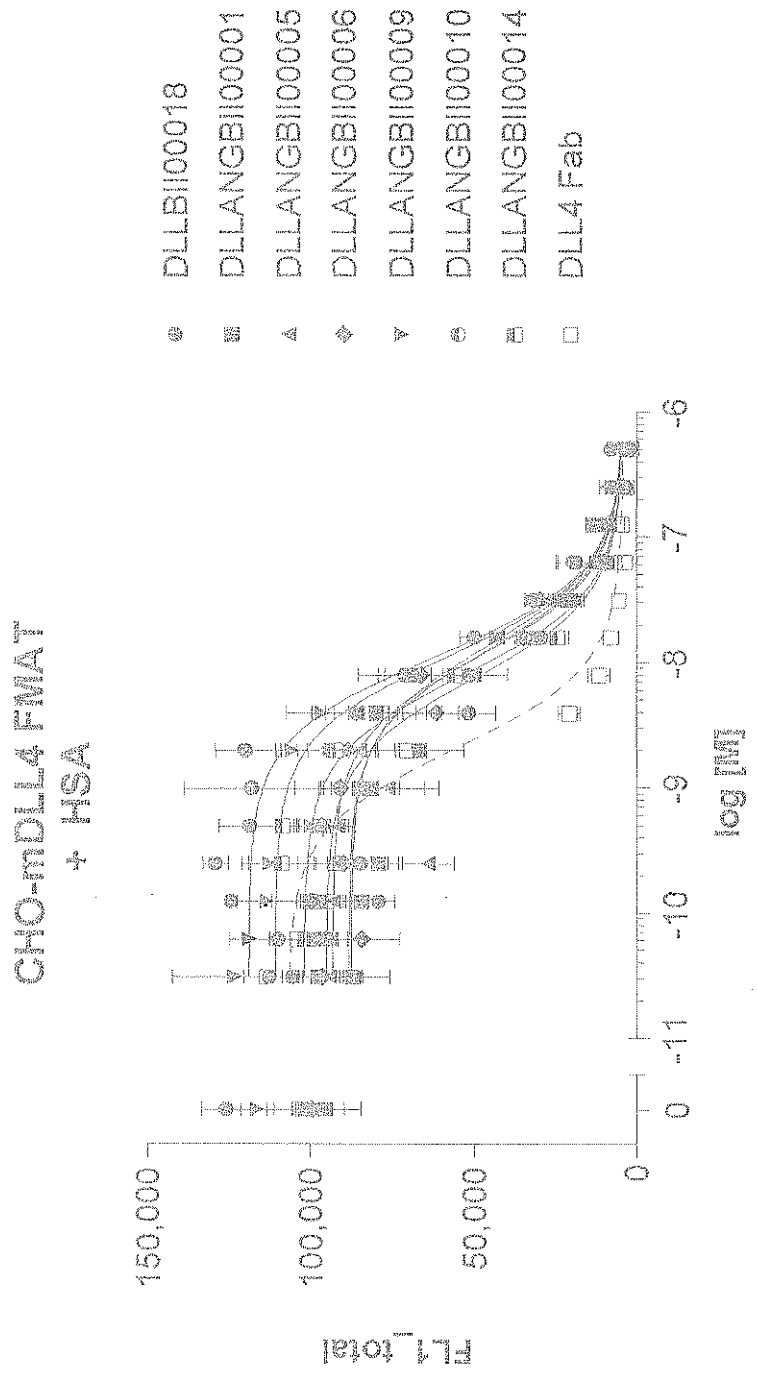


Figure 19A

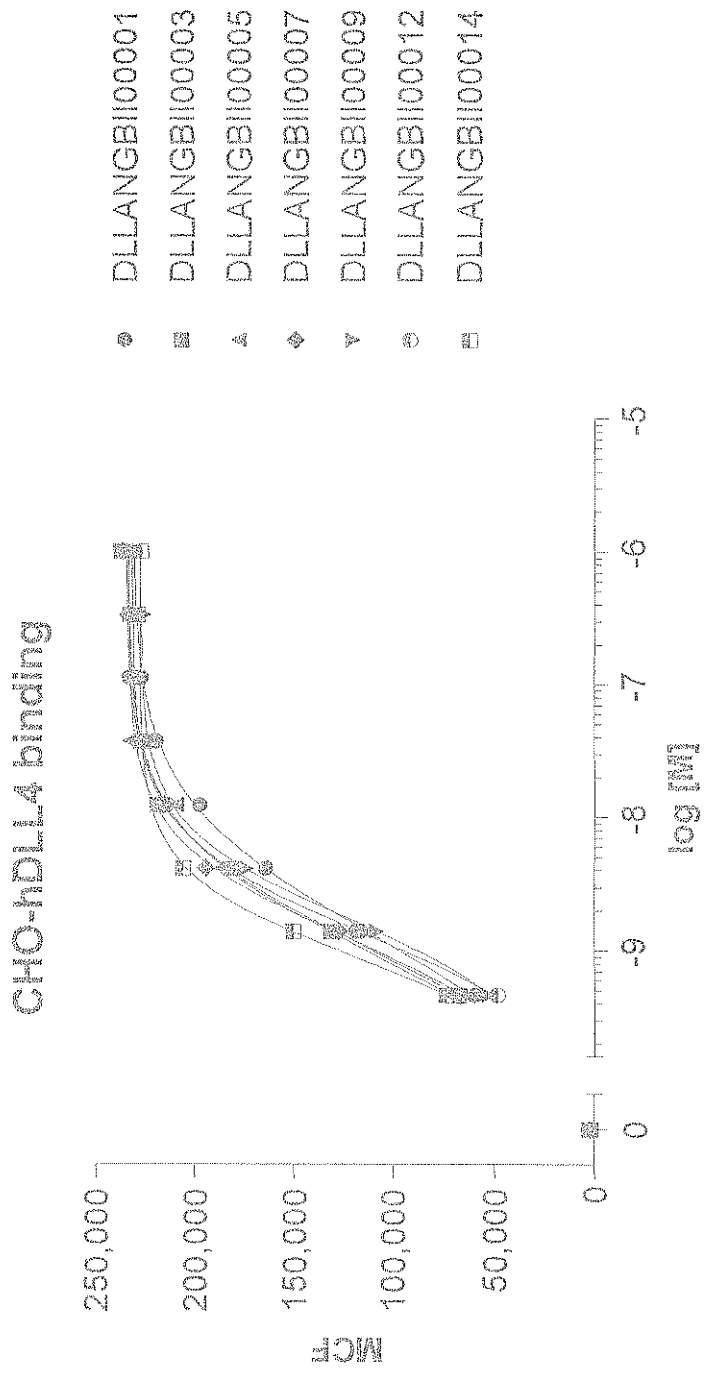

DLLANGBI00001
DLLANGBI00003
DLLANGBI00005
DLLANGBI00007
DLLANGBI00009
DLLANGBI00012
DLLANGBI00014
CHO-hDLL4 binding
MCF
250,000
200,000
150,000
100,000
50,000
0
0
-5
-6
-7
-8
-9
log [M]

Figure 19B

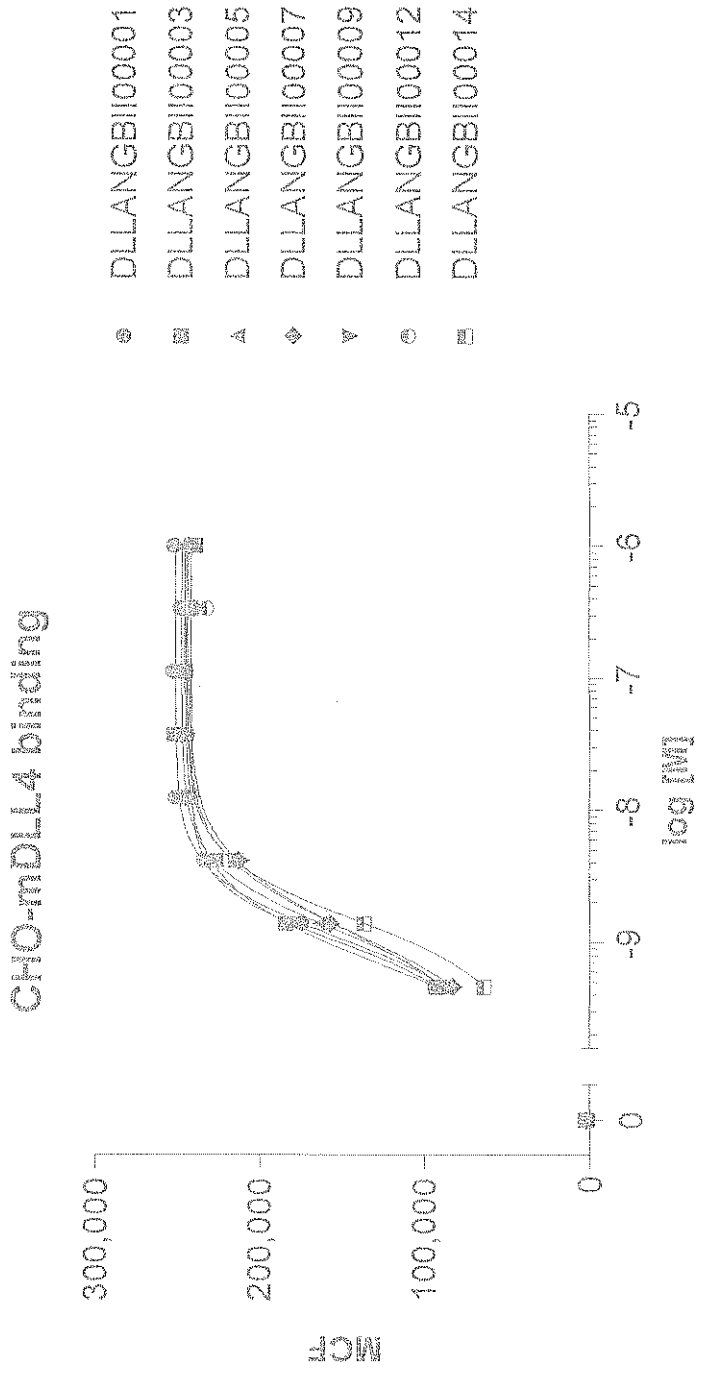

DLLANGBI00001
DLLANGBI00003
DLLANGBI00005
DLLANGBI00007
DLLANGBI00009
DLLANGBI00012
DLLANGBI00014
MCF
300,000
200,000
100,000
0
0
-5
-6
-7
-8
-9
log [M]

Figure 19C

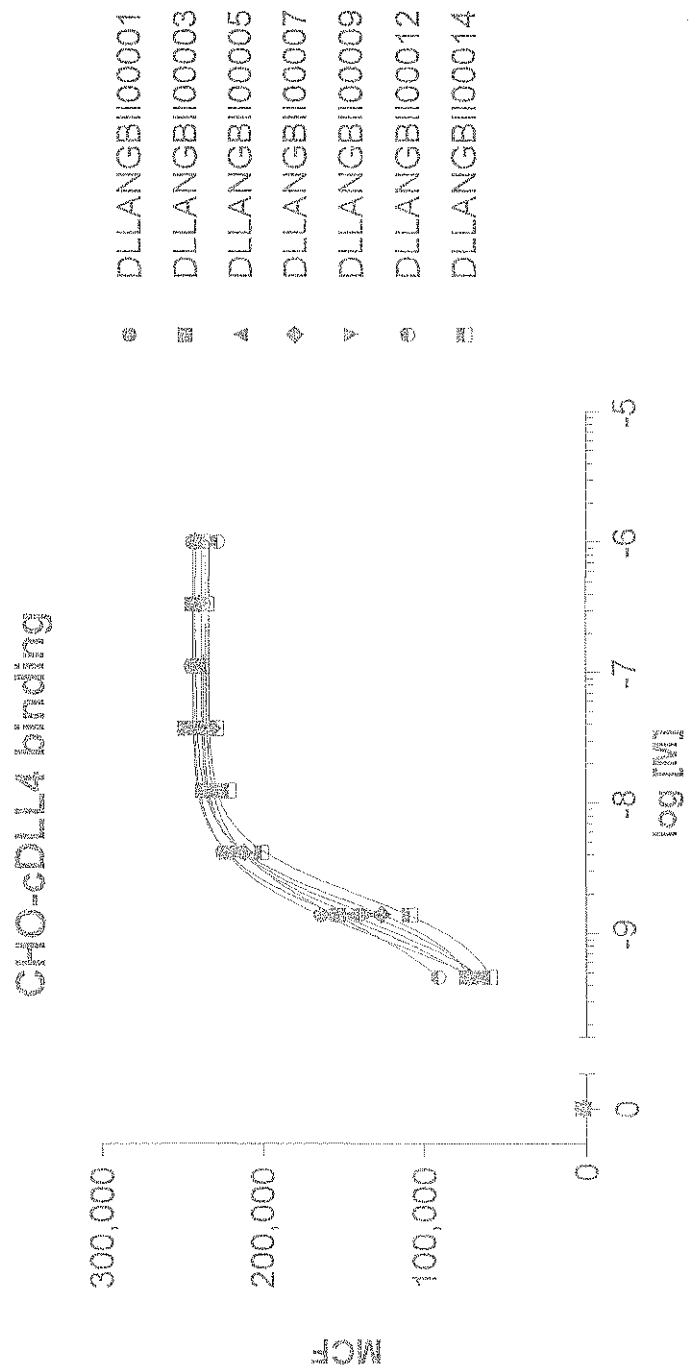

DLLANGBI00001
DLLANGBI00003
DLLANGBI00005
DLLANGBI00007
DLLANGBI00009
DLLANGBI00012
DLLANGBI00014
CHO-cDLL4 titration
MCF
300,000
200,000
100,000
0
0
-5
-6
-7
-8
-9
log [M]

Figure 20A

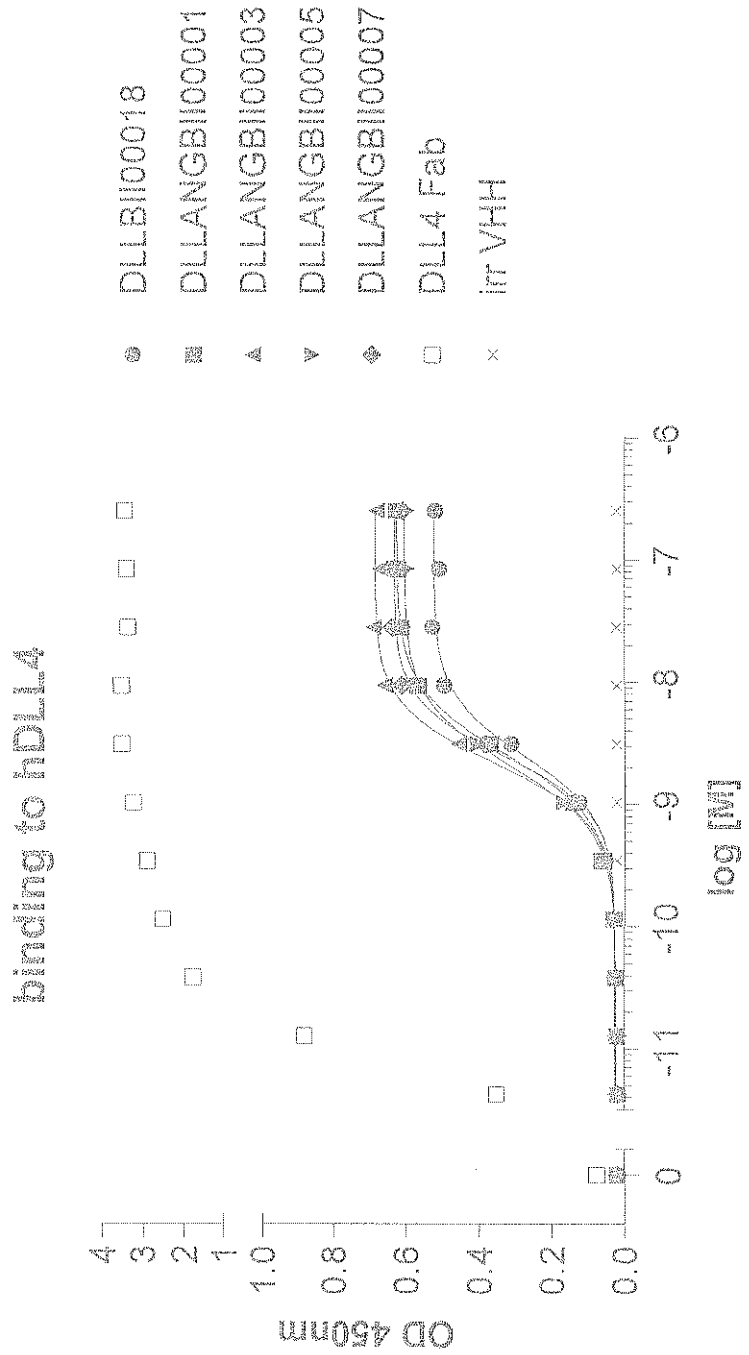

DLB100018
DLANGB00001
DLANGB00003
DLANGB00005
DLANGB00007
DLL4 Fab
irr VHH
binding to hDLL4
OD 450nm
4
3
2
1
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 20A (continued)

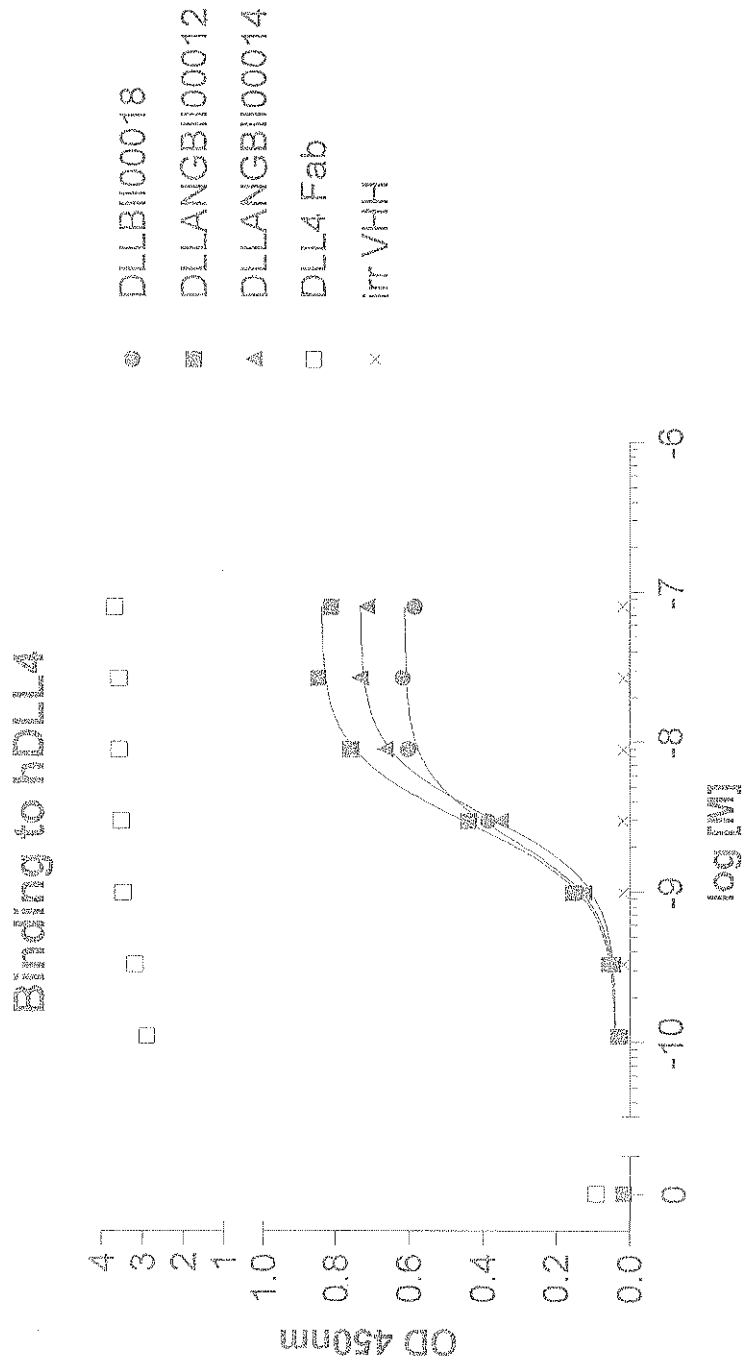


Figure 20B

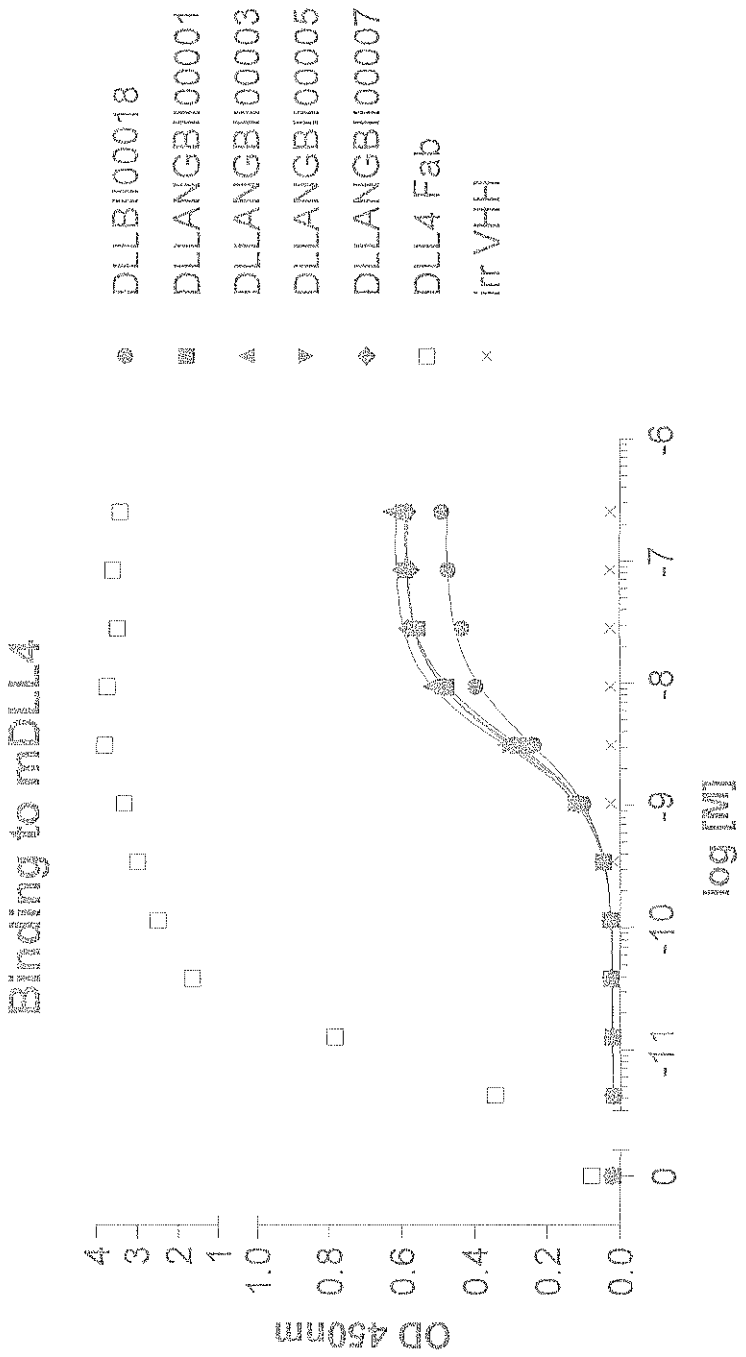
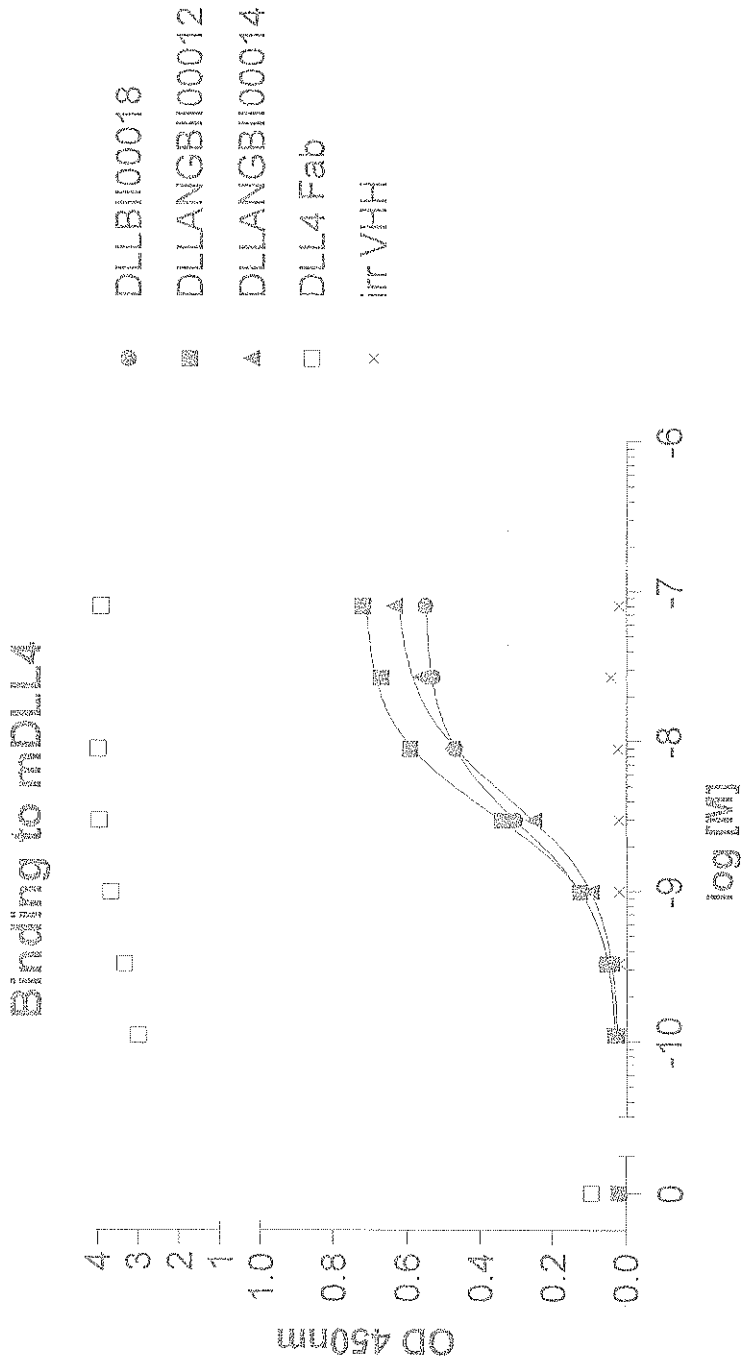
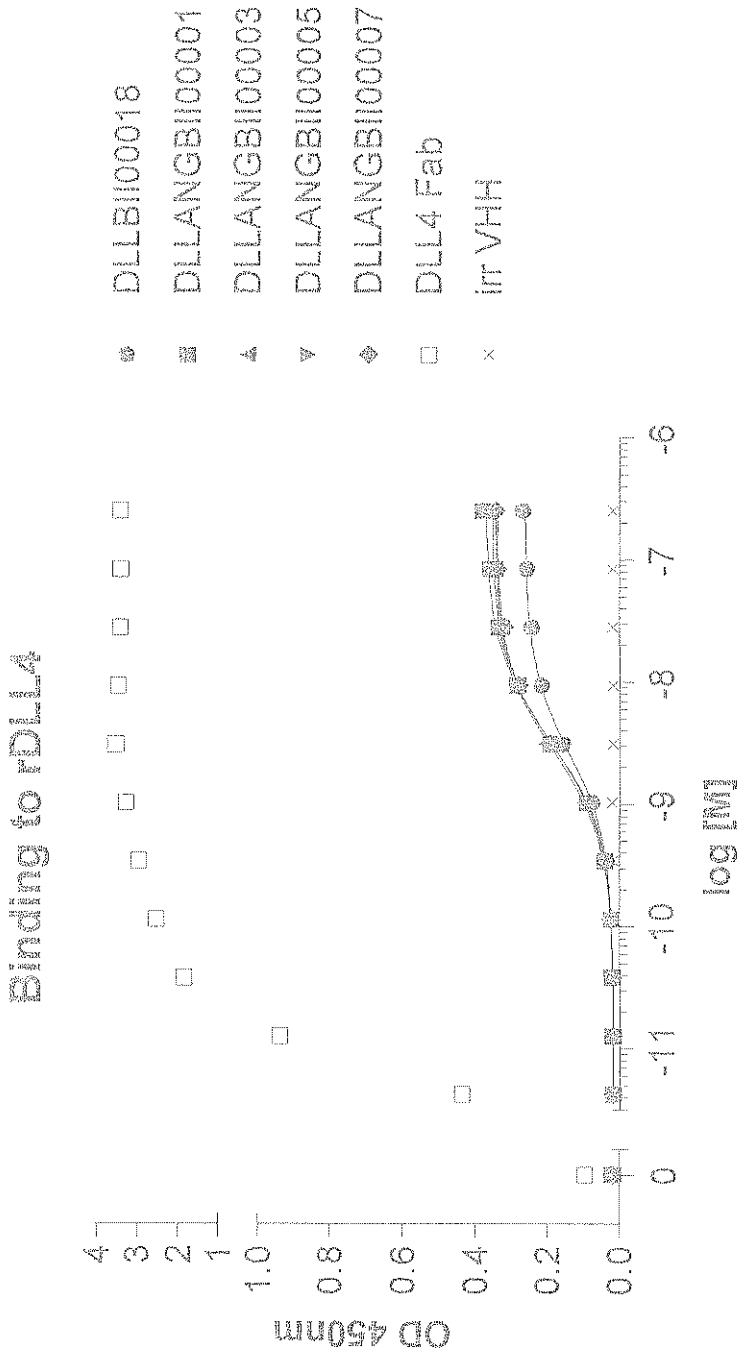

Binding to hDLL4
DLLBI00018
DLLANGBI00001
DLLANGBI00003
DLLANGBI00005
DLLANGBI00007
DLL4 Fab
irr VHH
OD 450nm
log [M]

Figure 20B (continued)



87 / 152

Figure 20C



88 / 152

Figure 20C (continued)

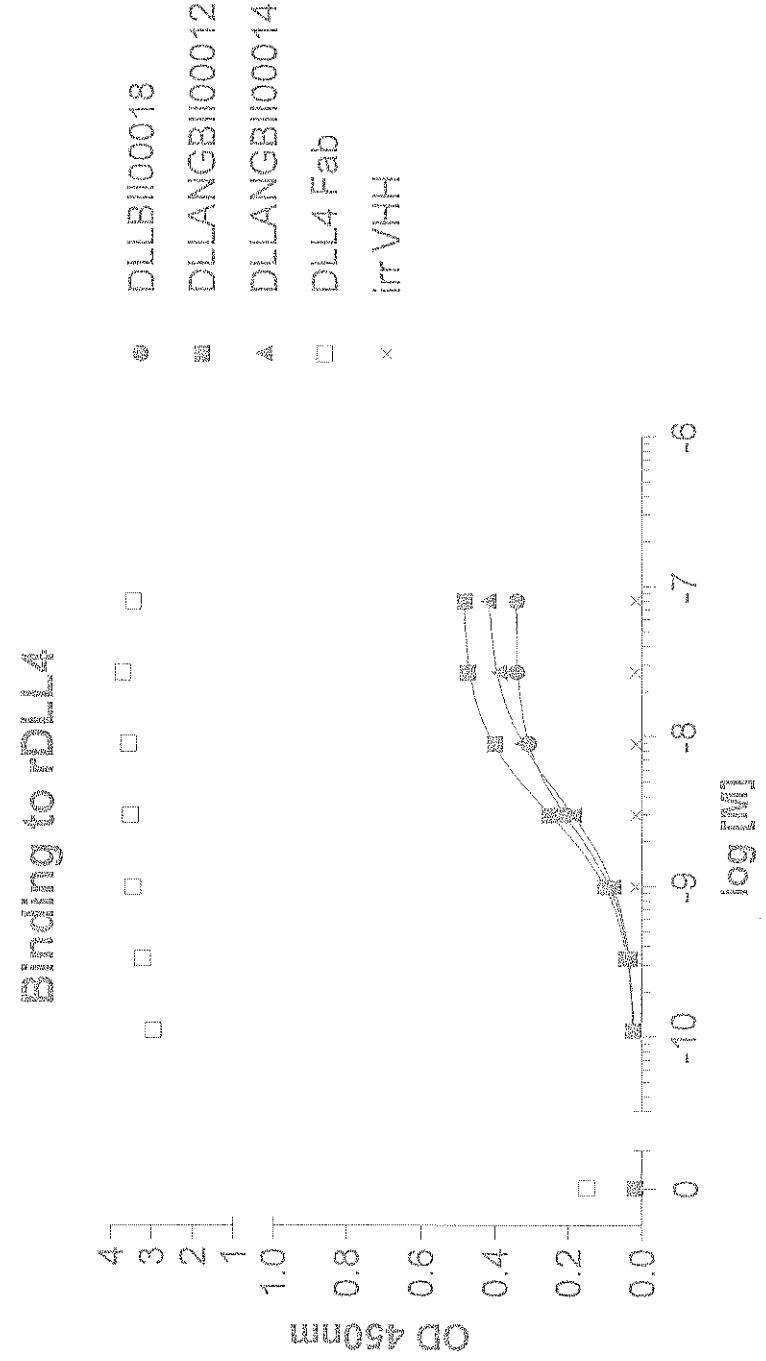


Figure 21A

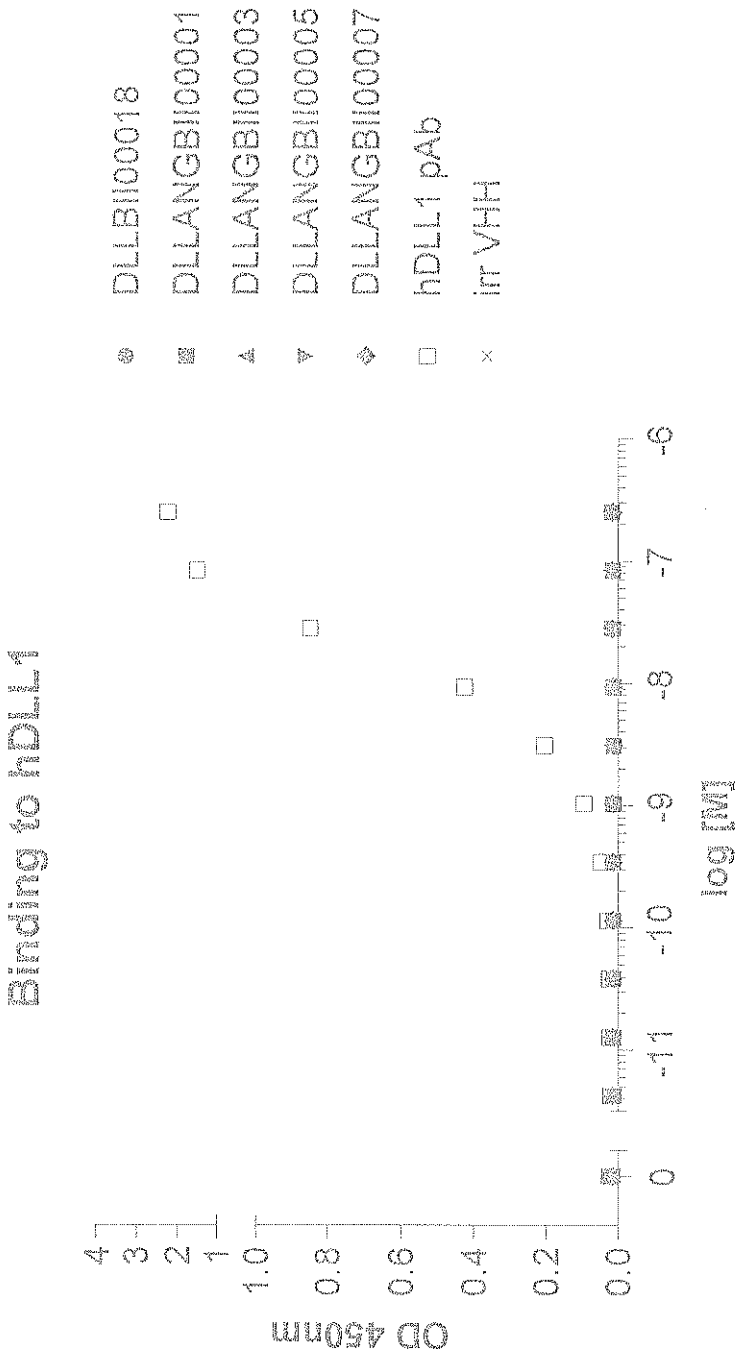

DLLB100018
DLLANGB00001
DLLANGB00003
DLLANGB00005
DLLANGB00007
hDLL1 pAb
mr VHH
Binding to hDLL1
OD 450nm
0.0
0.2
0.4
0.6
0.8
1.0
1
2
3
4
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 21A (continued)

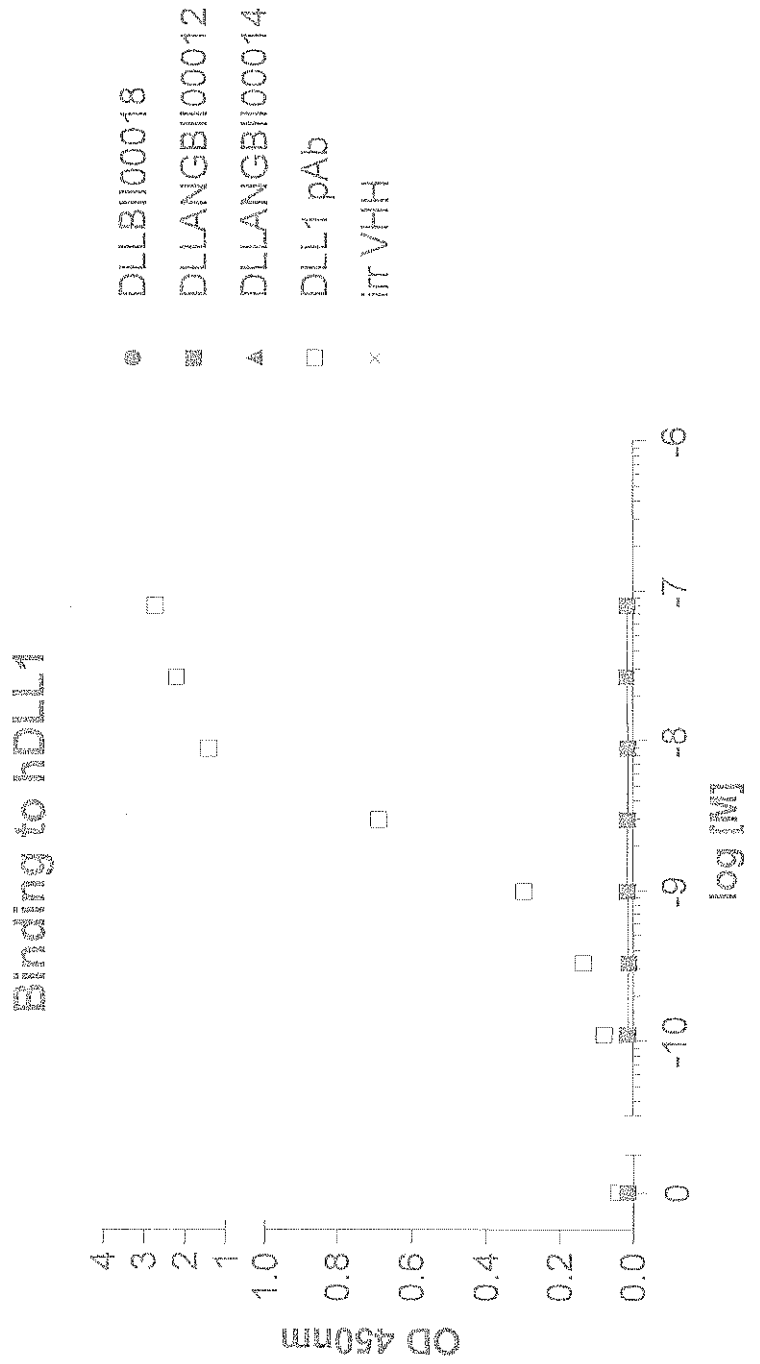
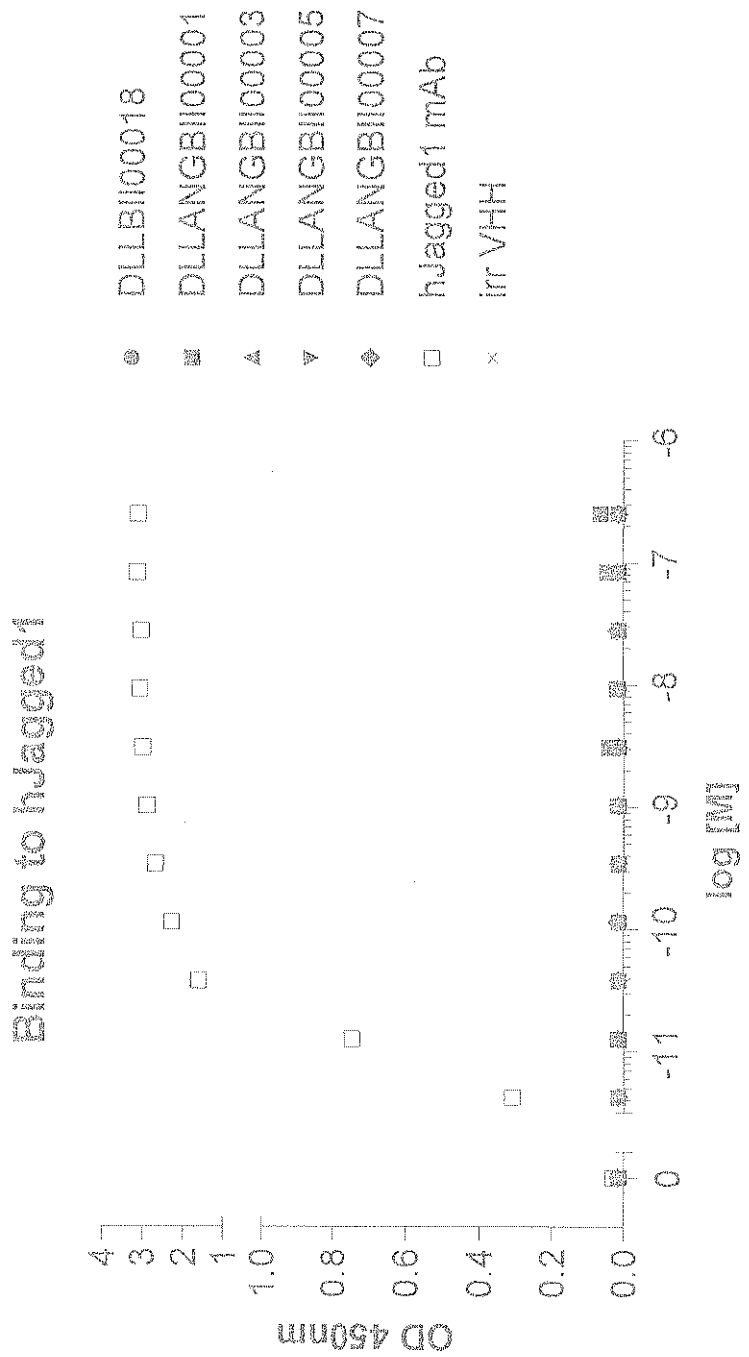


Figure 21B


Binding to hJagged1
OD 450nm
4
3
2
1
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log M
DLBli00018
DLLANGBI00001
DLLANGBI00003
DLLANGBI00005
DLLANGBI00007
hJagged1 mAb
irr VHH

92 / 152

Figure 21B (continued)

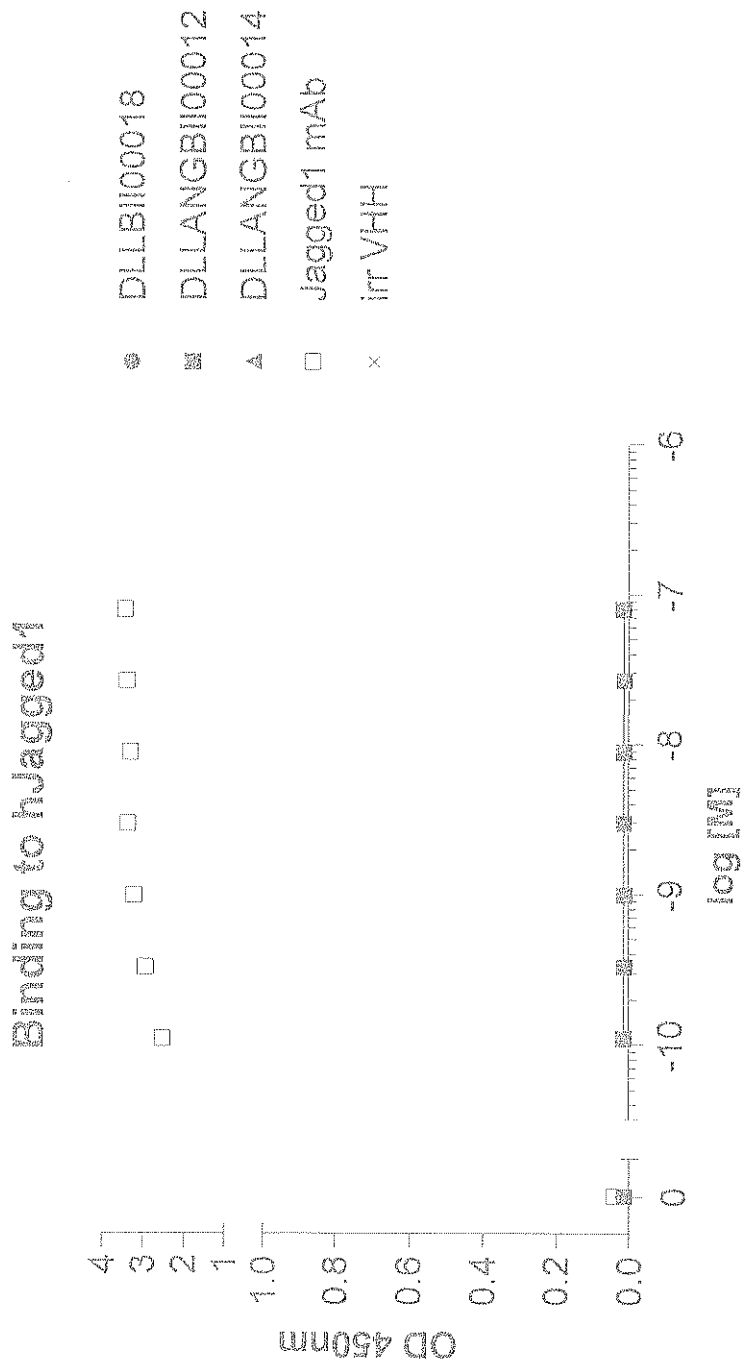


Figure 22-1A

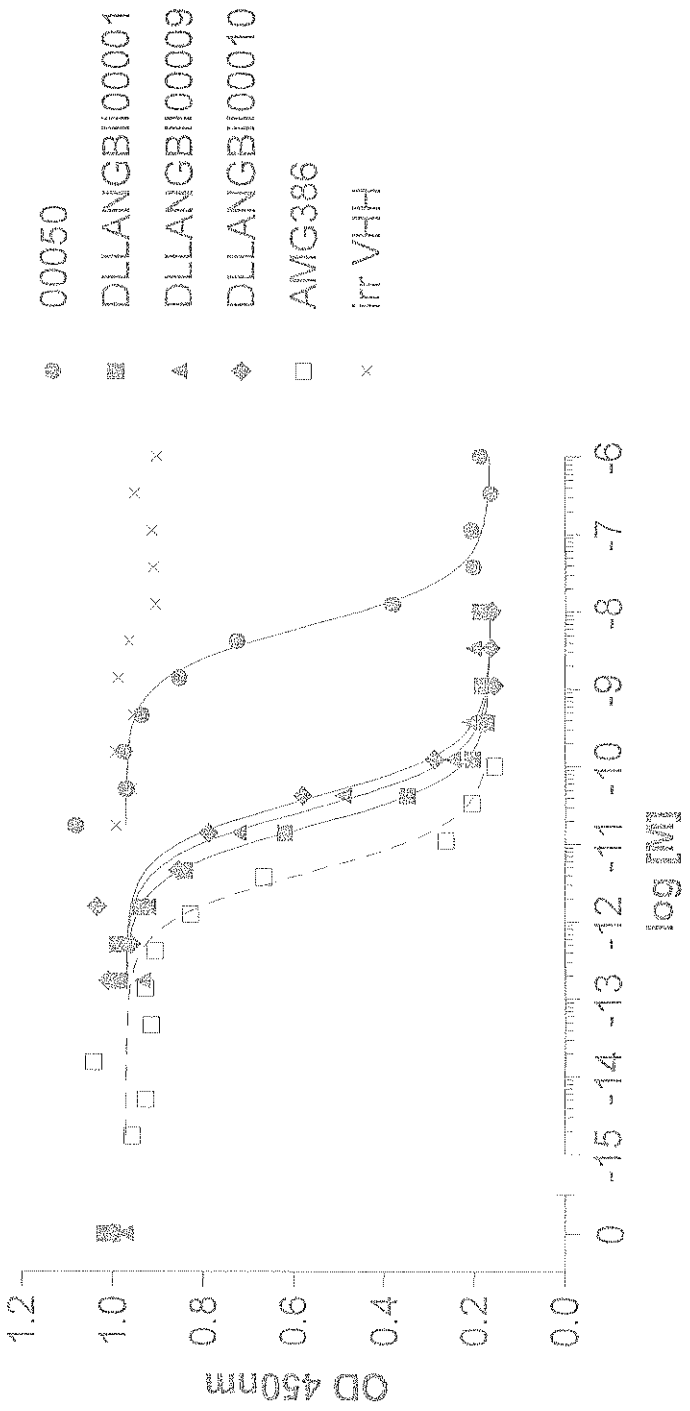

00050
DLLANGBI00001
DLLANGBI00003
DLLANGBI00010
AMG386
irr VHH
OD 450nm
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 22-1A (continued)

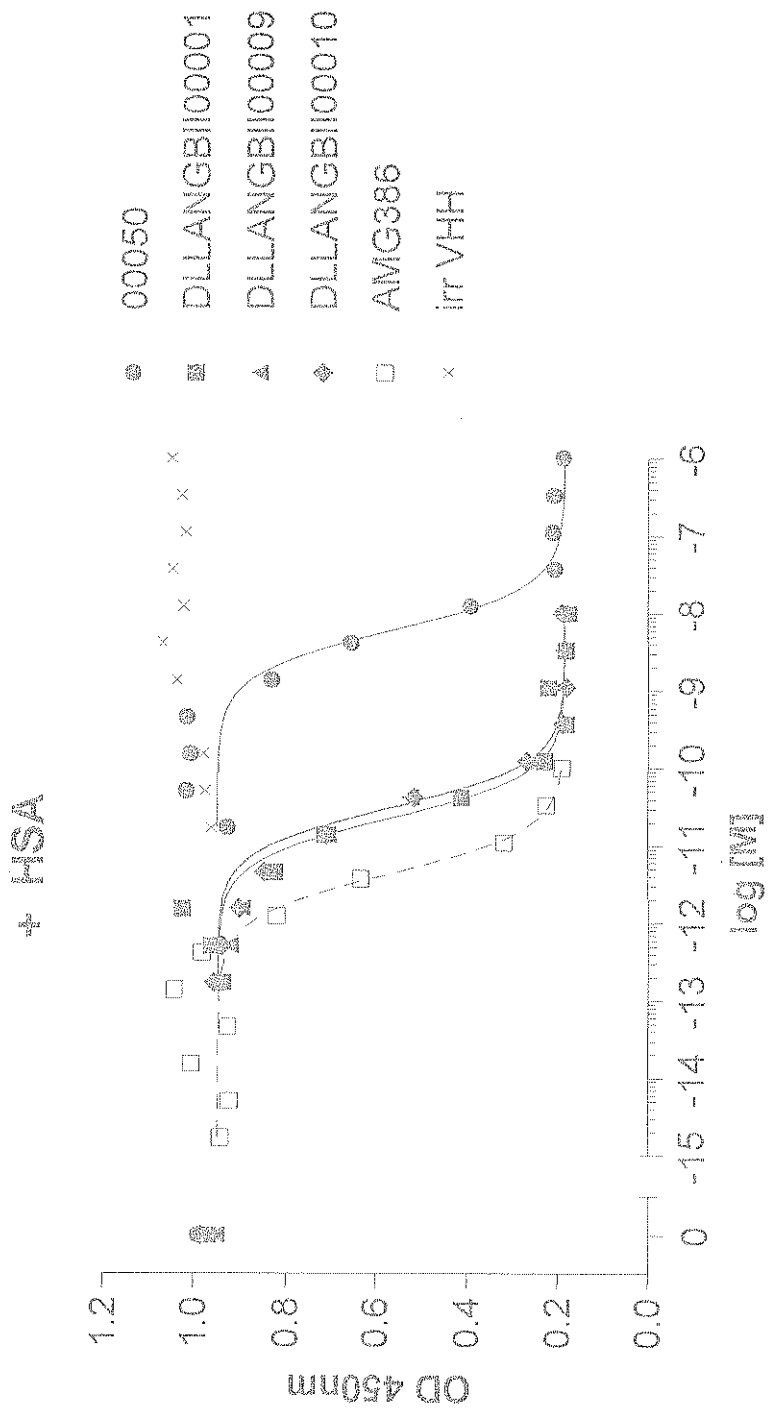


Figure 22-1B

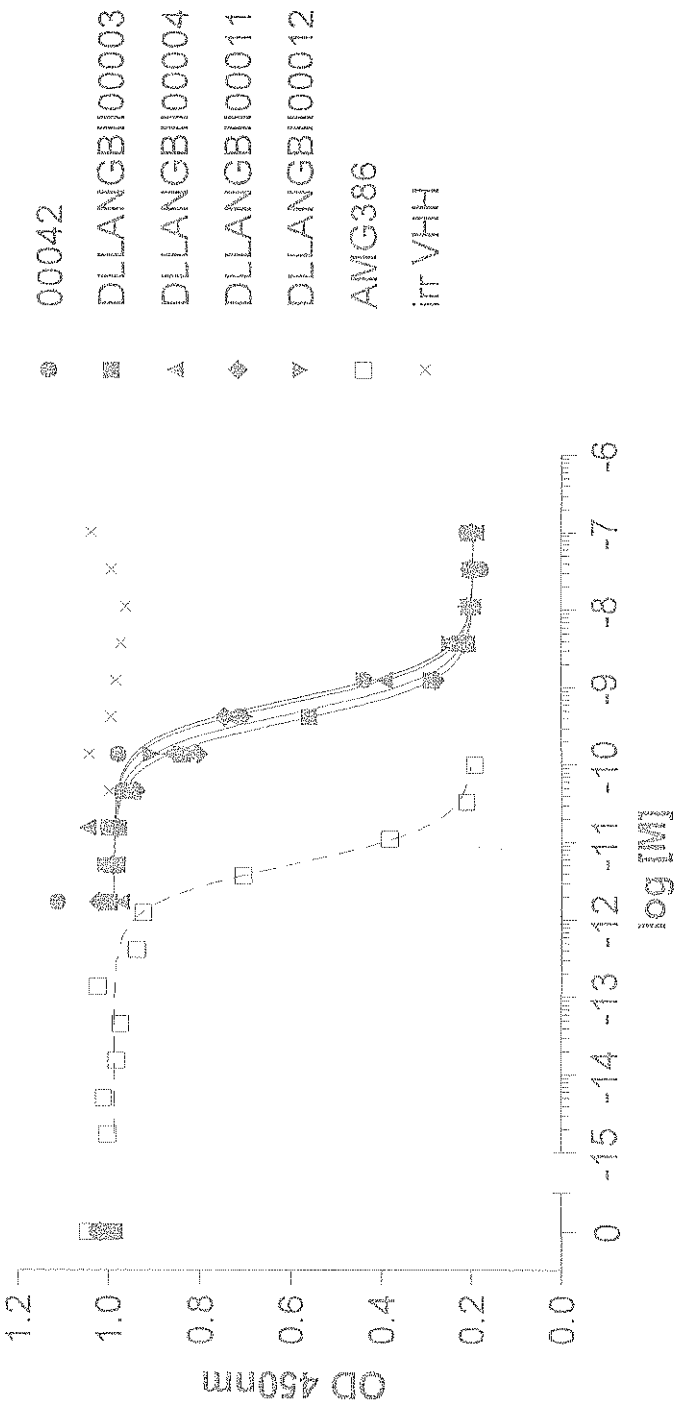
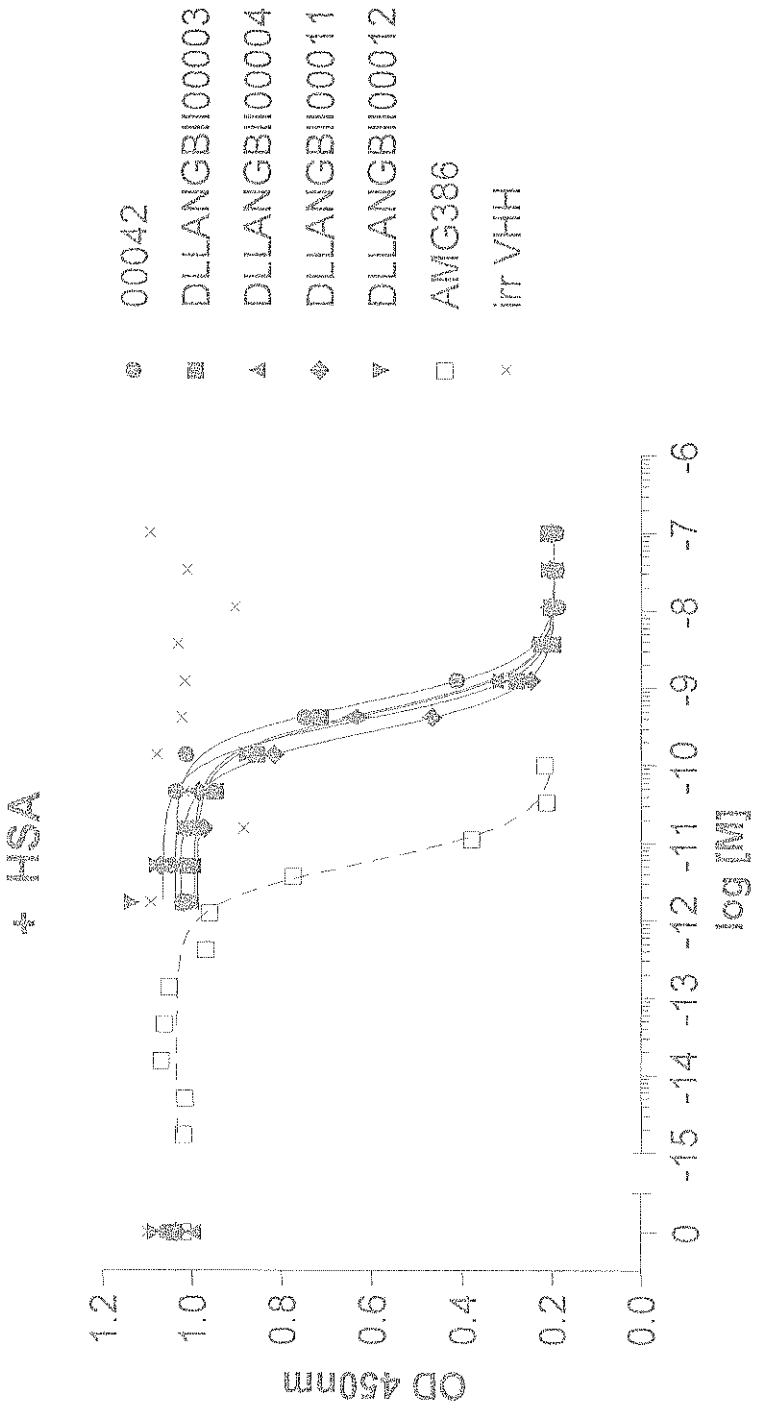

00042
DLLANGBI00003
DLLANGBI00004
DLLANGBI00011
DLLANGBI00012
AMG386
irr VHH
OD 450nm
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log M

Figure 22-1B (continued)



97 / 152

Figure 22-1C

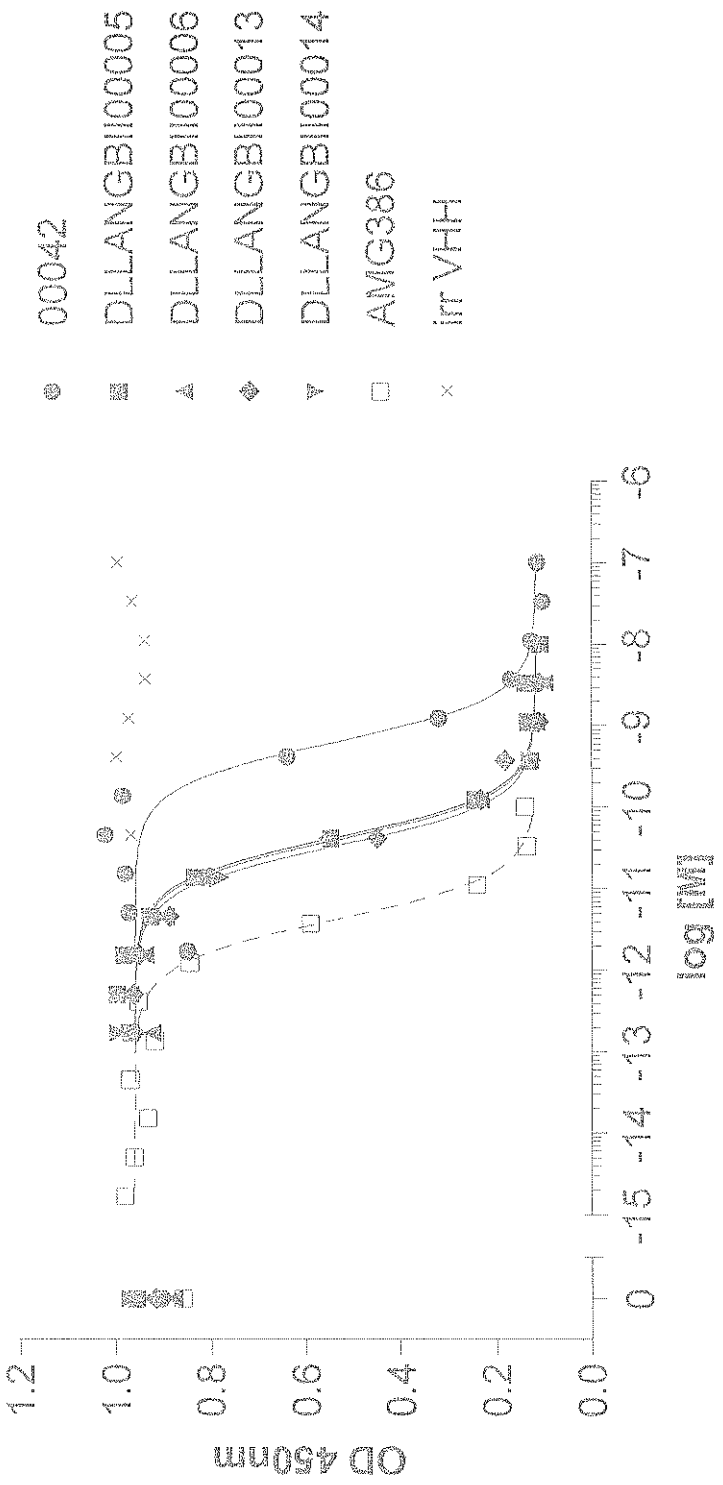


Figure 22-1C (continued)

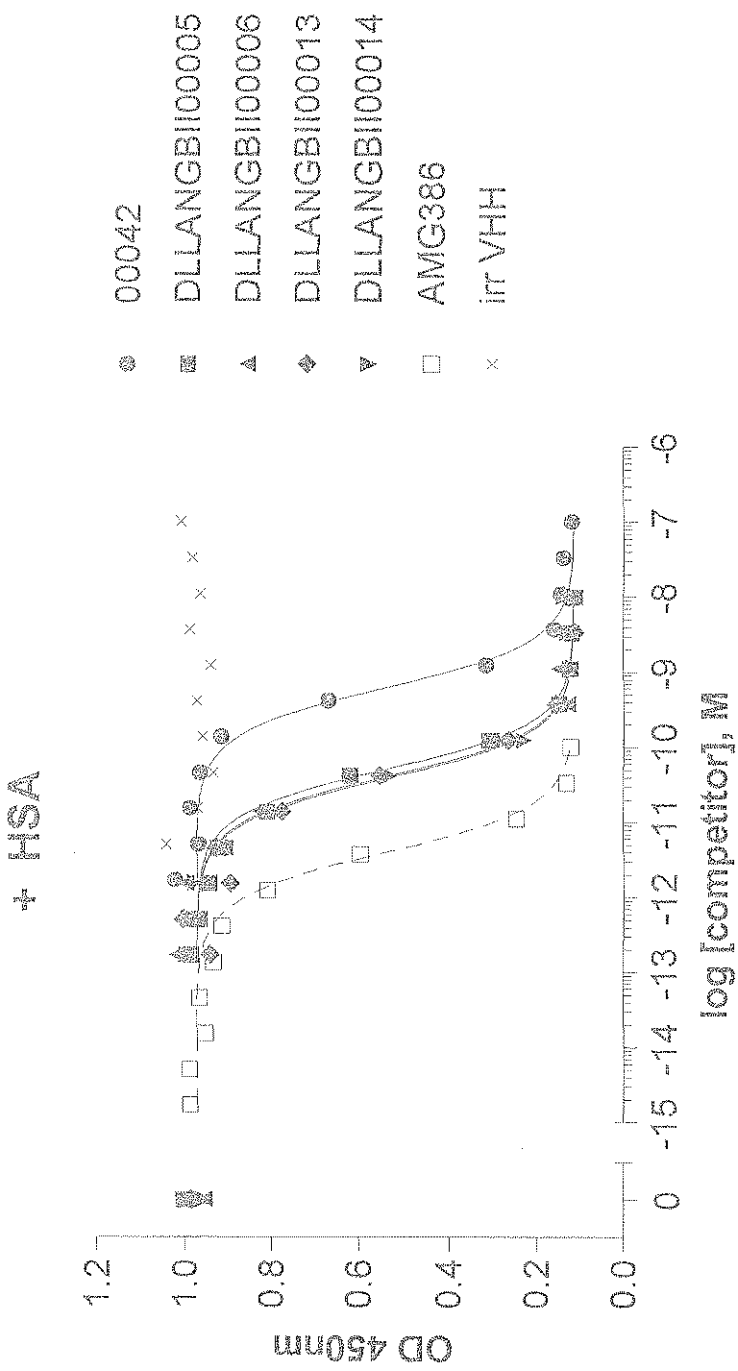


Figure 22-1D

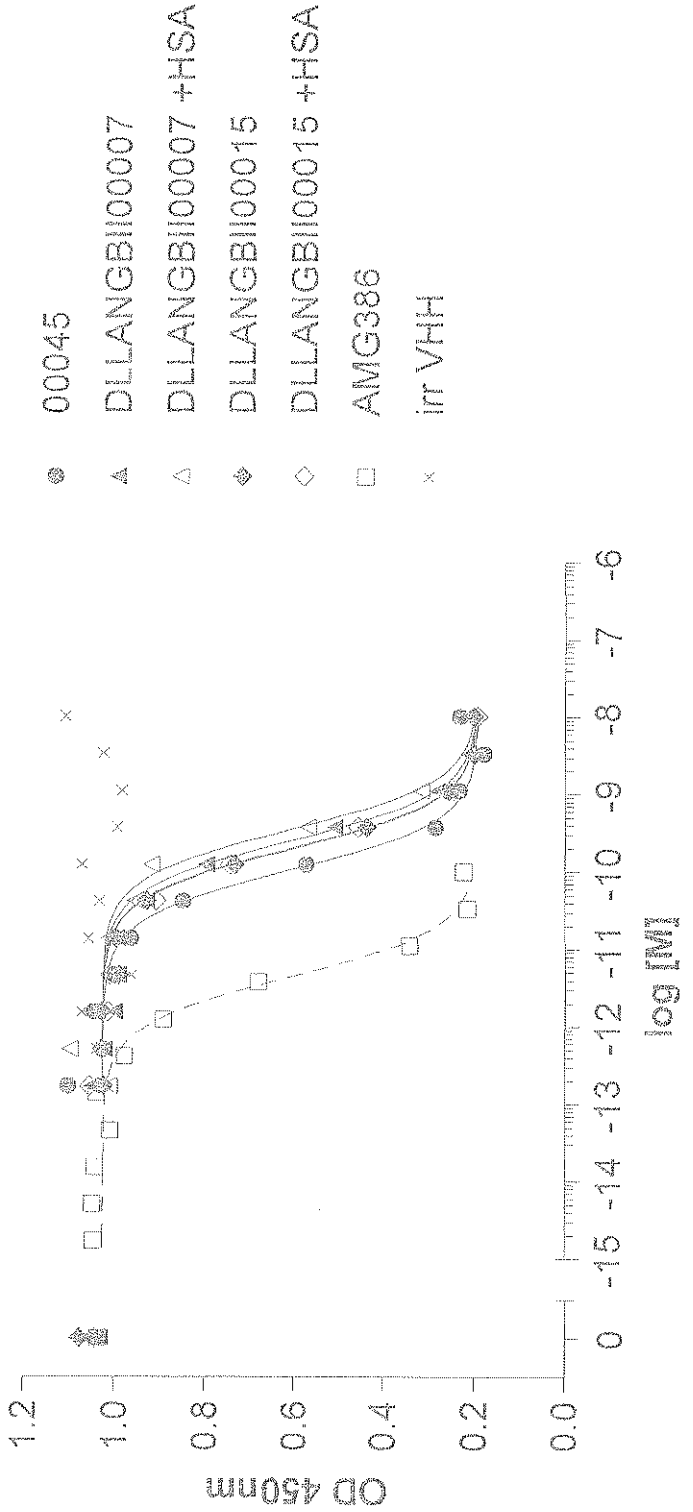

00045
DLLANGBI00007
DLLANGBI00007 +HSA
DLLANGBI00015
DLLANGBI00015 +HSA
AMG386
irr VHH
OD 450nm
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log M/L

Figure 22-2A

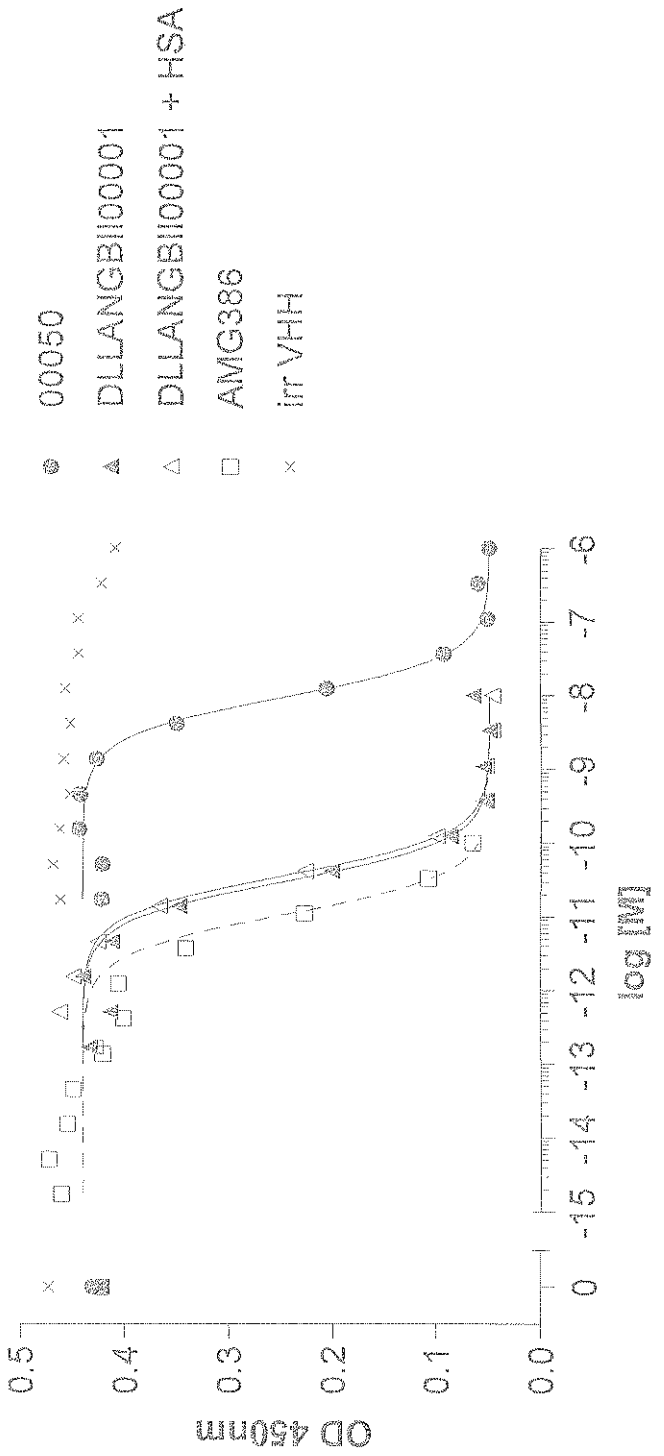

00050
DLLANGBI100001
DLLANGBI100001 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.1
0.2
0.3
0.4
0.5
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6

Figure 22-2B

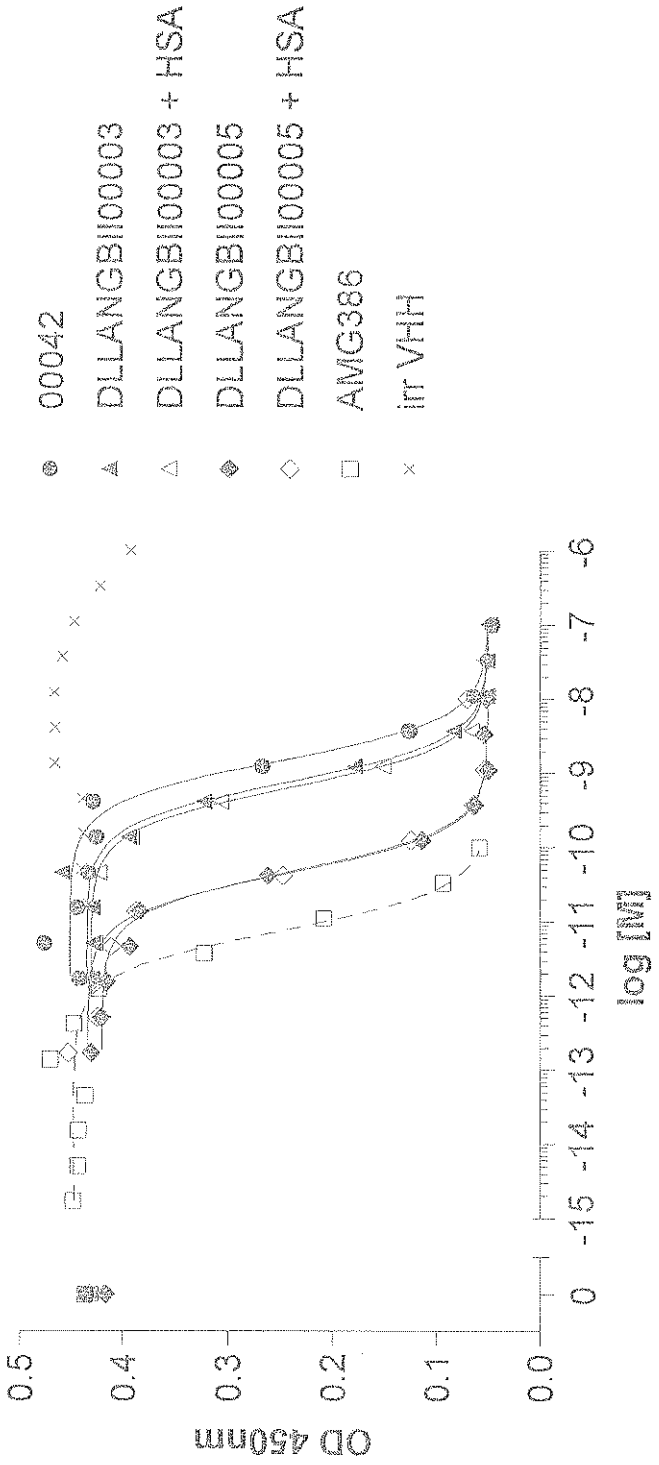

00042
DLLANGBI00003
DLLANGBI00003 + HSA
DLLANGBI00005
DLLANGBI00005 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.1
0.2
0.3
0.4
0.5
log [M]
0
-5
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15

Figure 22-2C

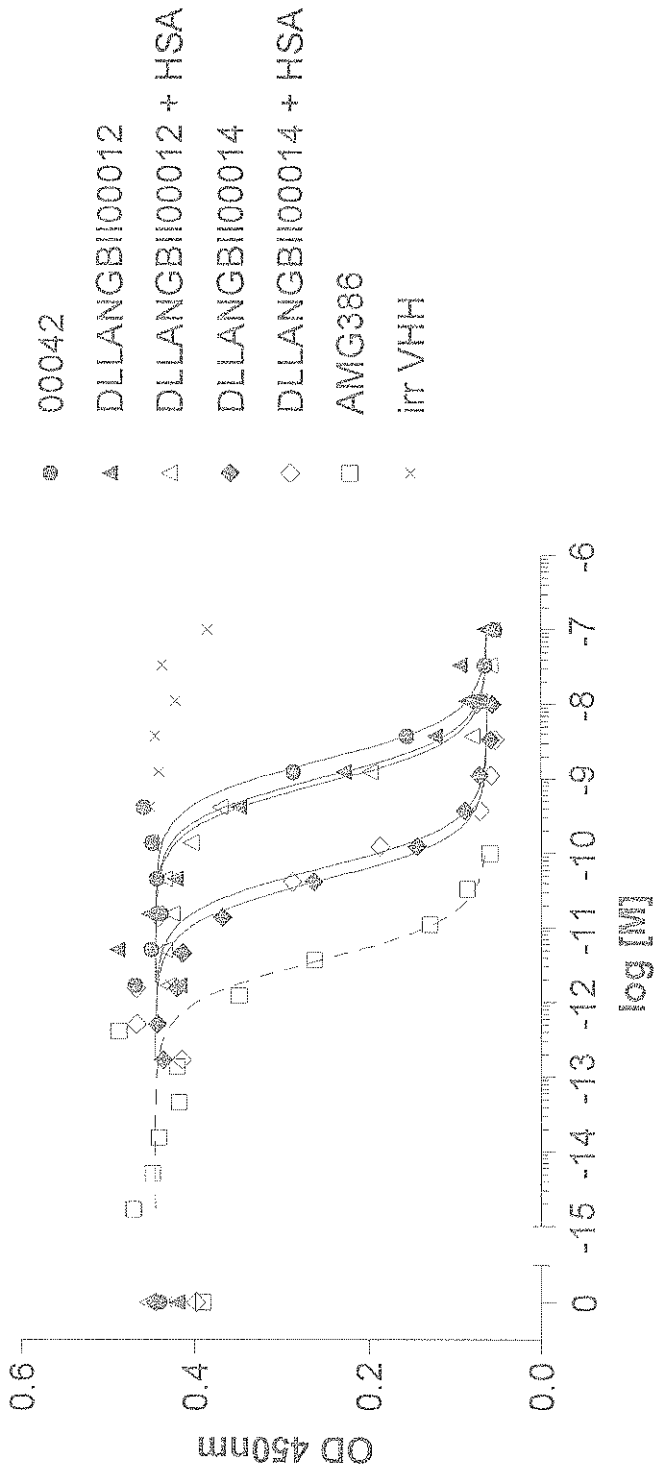

00042
DLLANGBI00012
DLLANGBI00012 + HSA
DLLANGBI00014
DLLANGBI00014 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
log [M]
0
-5
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15

Figure 22-2D

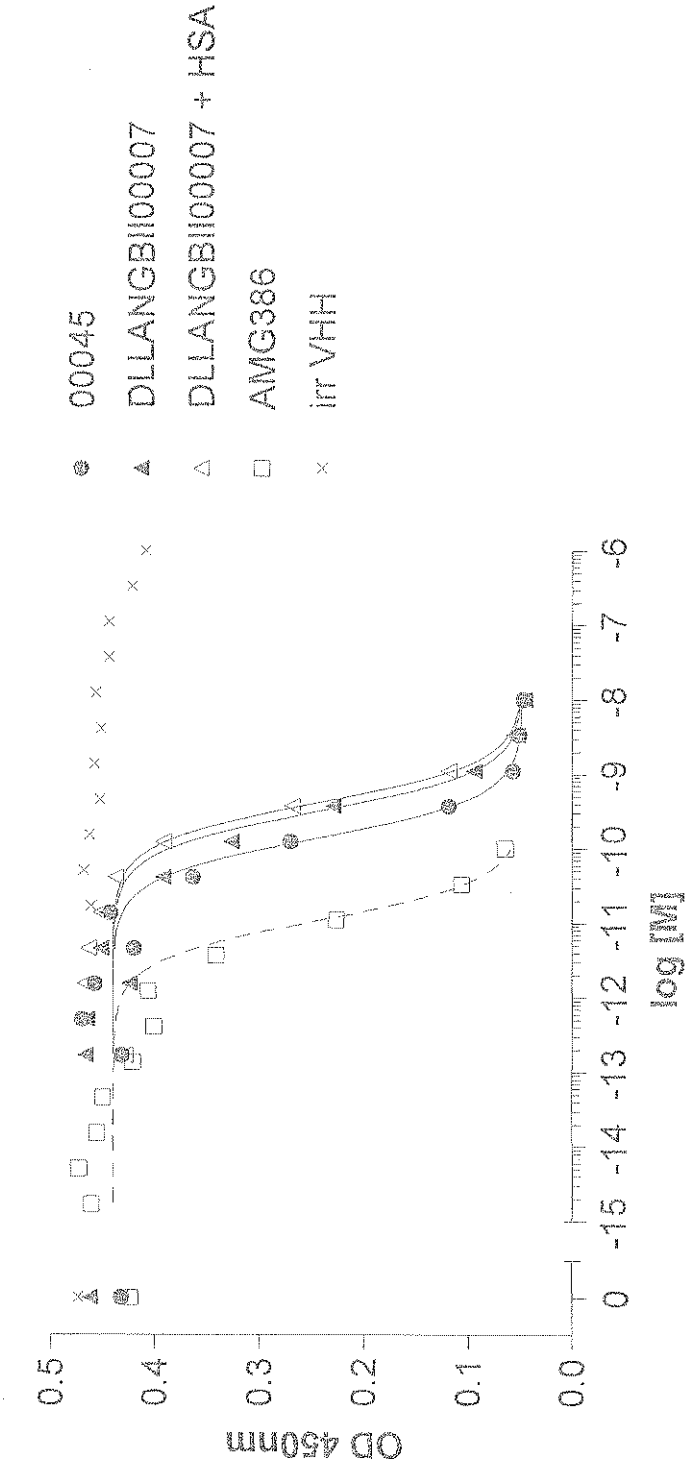

00045
DLLANGBI00007
DLLANGBI00007 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.1
0.2
0.3
0.4
0.5
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6

Figure 22-3A

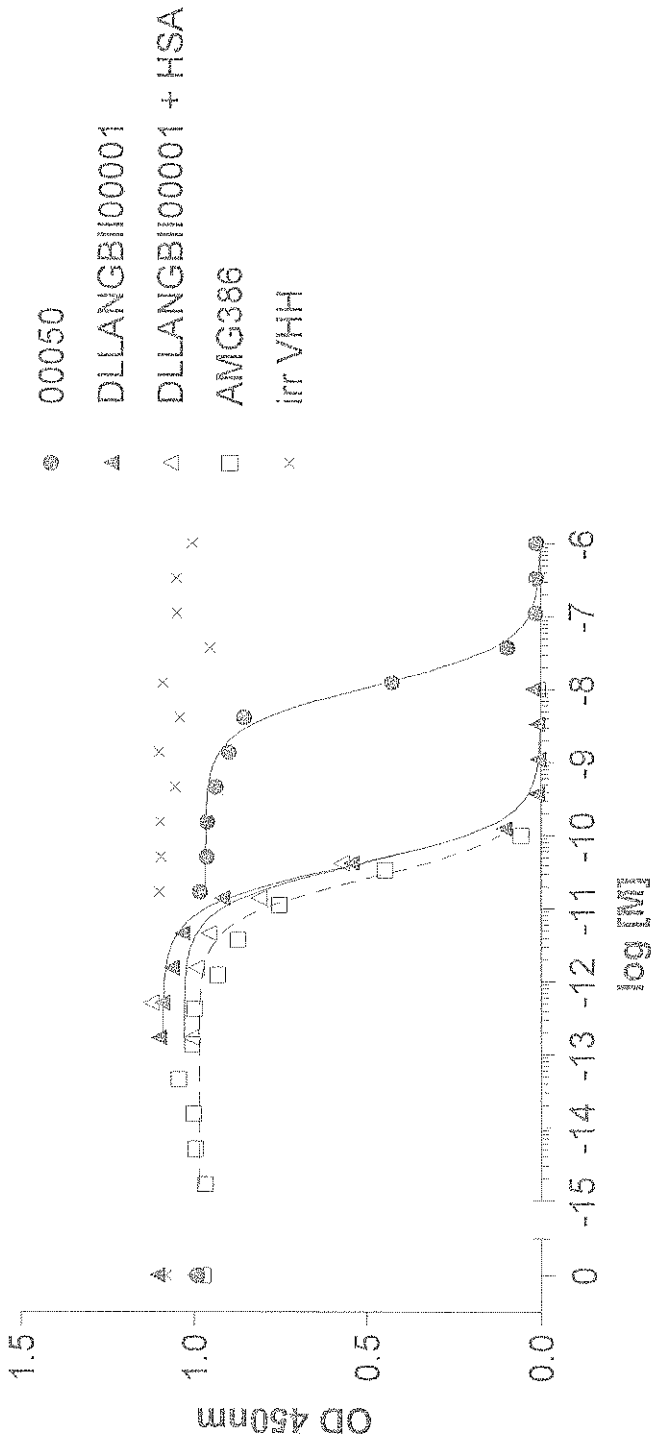

00050
DLLANGBII00001
DLLANGBII00001 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 22-3B

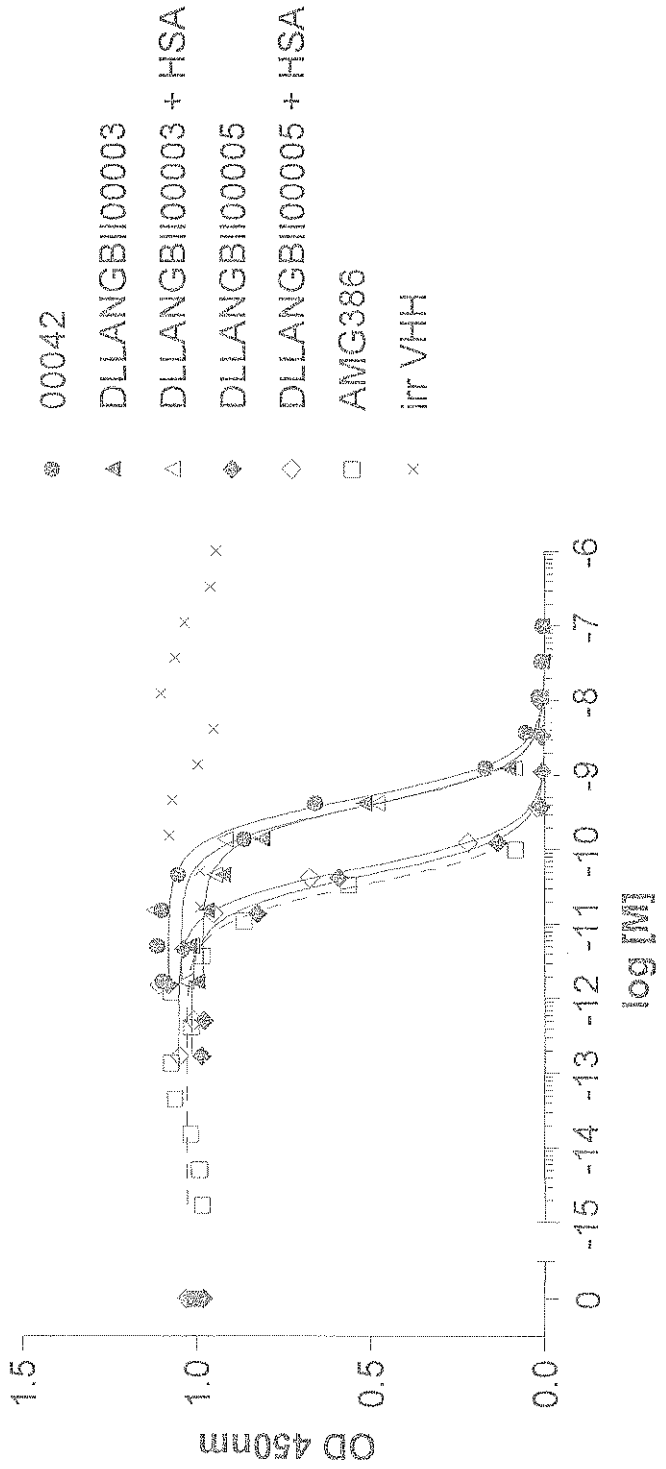

00042
DLLANGBI00003
DLLANGBI00003 + HSA
DLLANGBI00005
DLLANGBI00005 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 22-3C

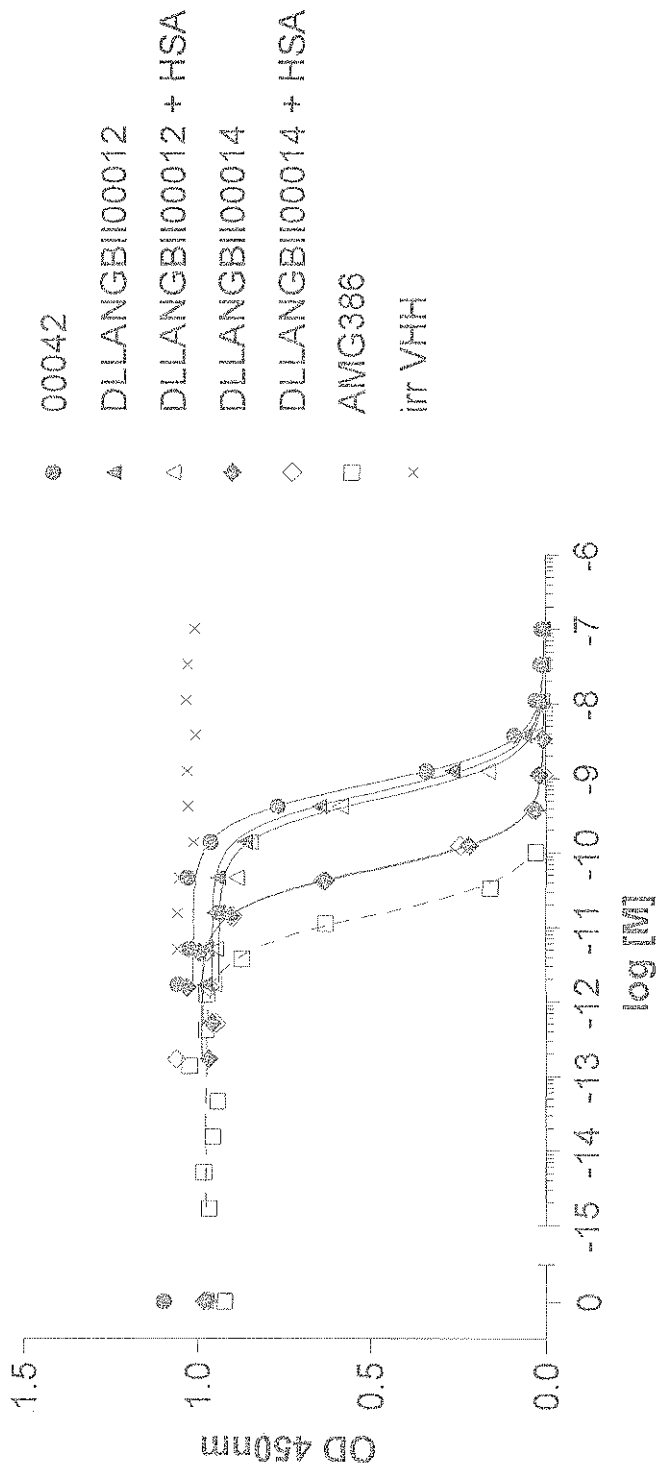

00042
DLLANGBI00012
DLLANGBI00012 + HSA
DLLANGBI00014
DLLANGBI00014 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 22-3D

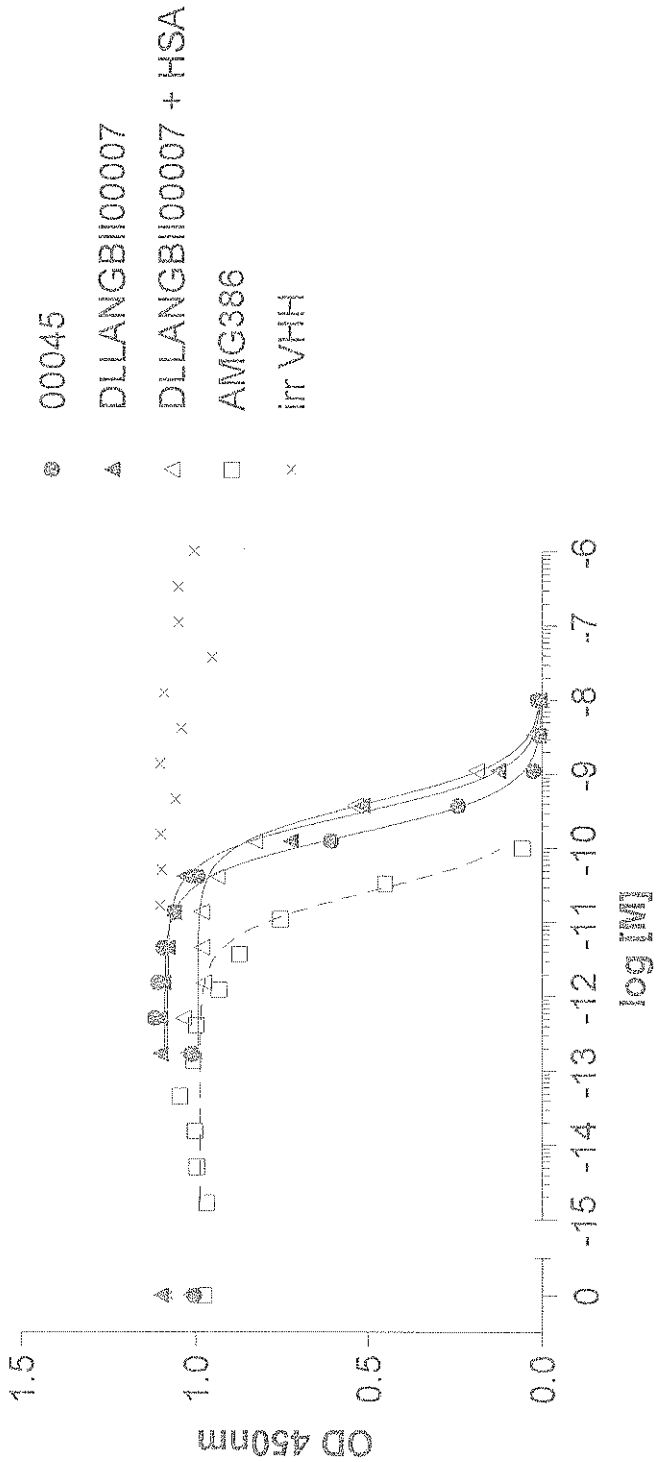
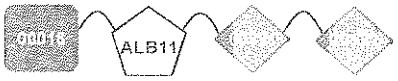
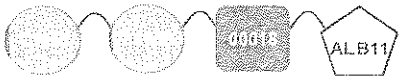

00045
DLLANGBI00007
DLLANGBI00007 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 23

VHH ID	Format	Description
DLLANGBII00017		DLLBII00018-9gs-ALB11-9gs-00921-9gs-00921
DLLANGBII00018		00938-9gs-DLLBII00018-9gs-ALB11
DLLANGBII00019		009152-9gs-009152-9gs-DLLBII00018-9gs-ALB11

Legend:

	Description		Description
	DLLBII00018		009152
	00921		ALB11
	00938		*9 GlySer* linker

Figure 24A

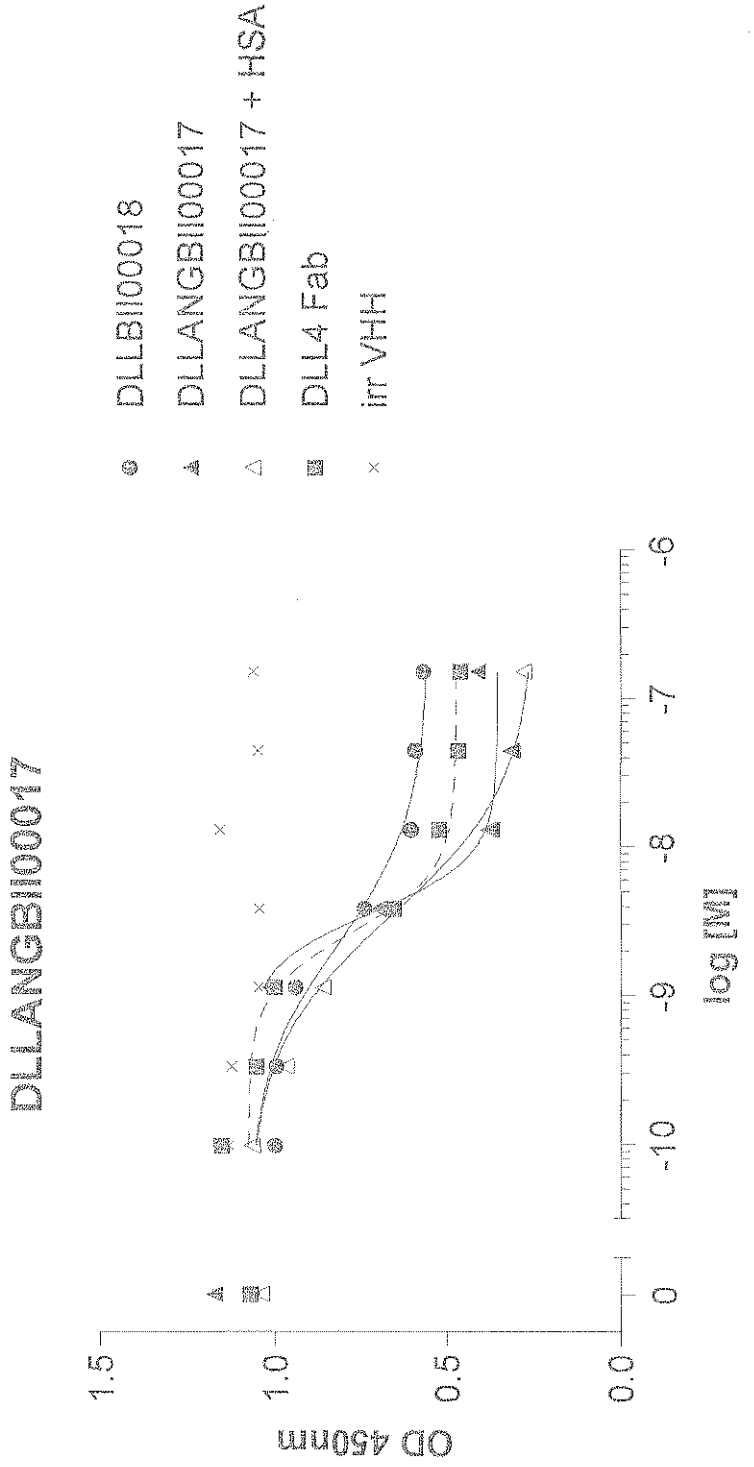

DLLBI00018
DLLANGBI00017
DLLANGBI00017 + HSA
DLL4 Fab
irr VHH
DLLANGBI00017
OD 450nm
1.5
1.0
0.5
0.0
0
-10
-9
-8
-7
-6
log [M]

Figure 24B

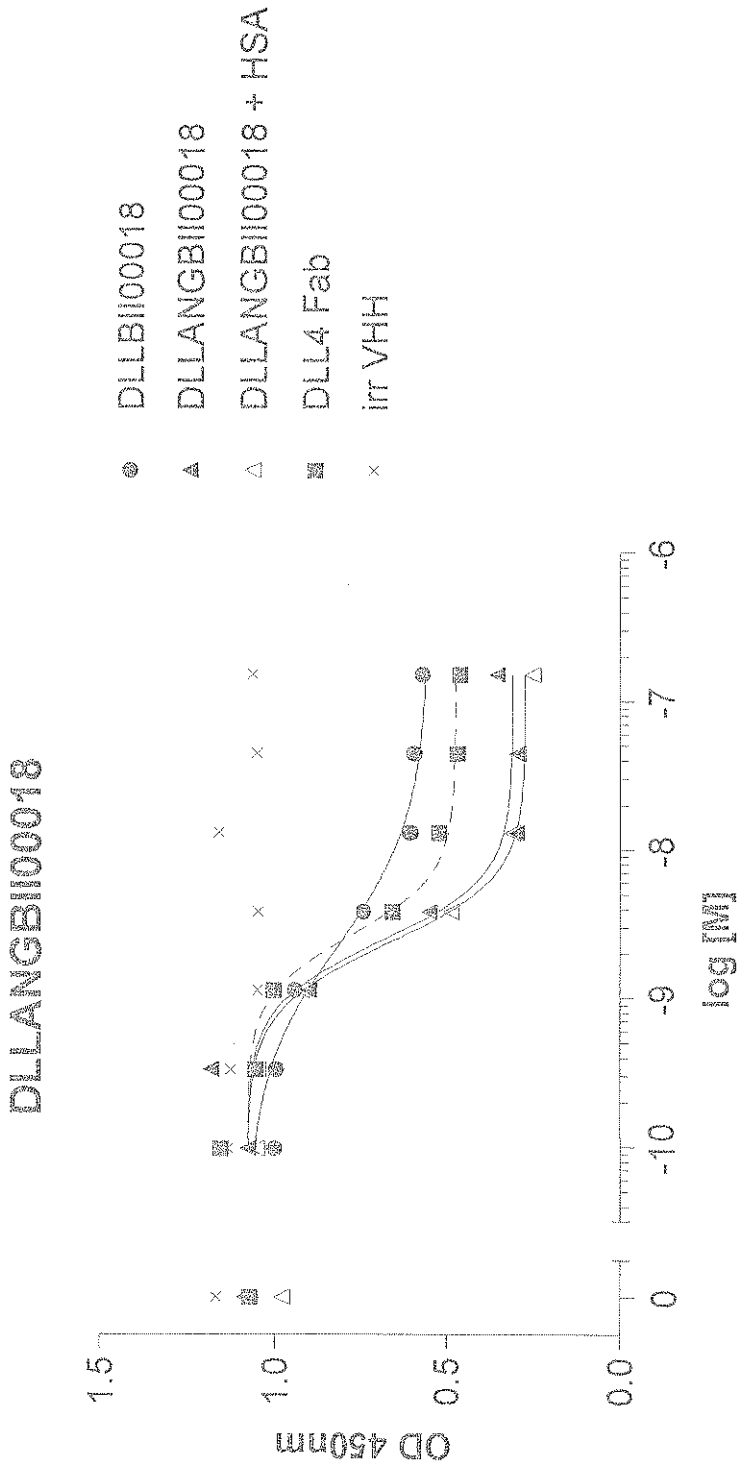

DLLBI100018
DLLANGBI100018
DLLANGBI100018 + HSA
DLL4 Fab
irr VHH
DLLANGBI100018
OD 450nm
1.5
1.0
0.5
0.0
0
-10
-9
-8
-7
-6
log M

Figure 24C

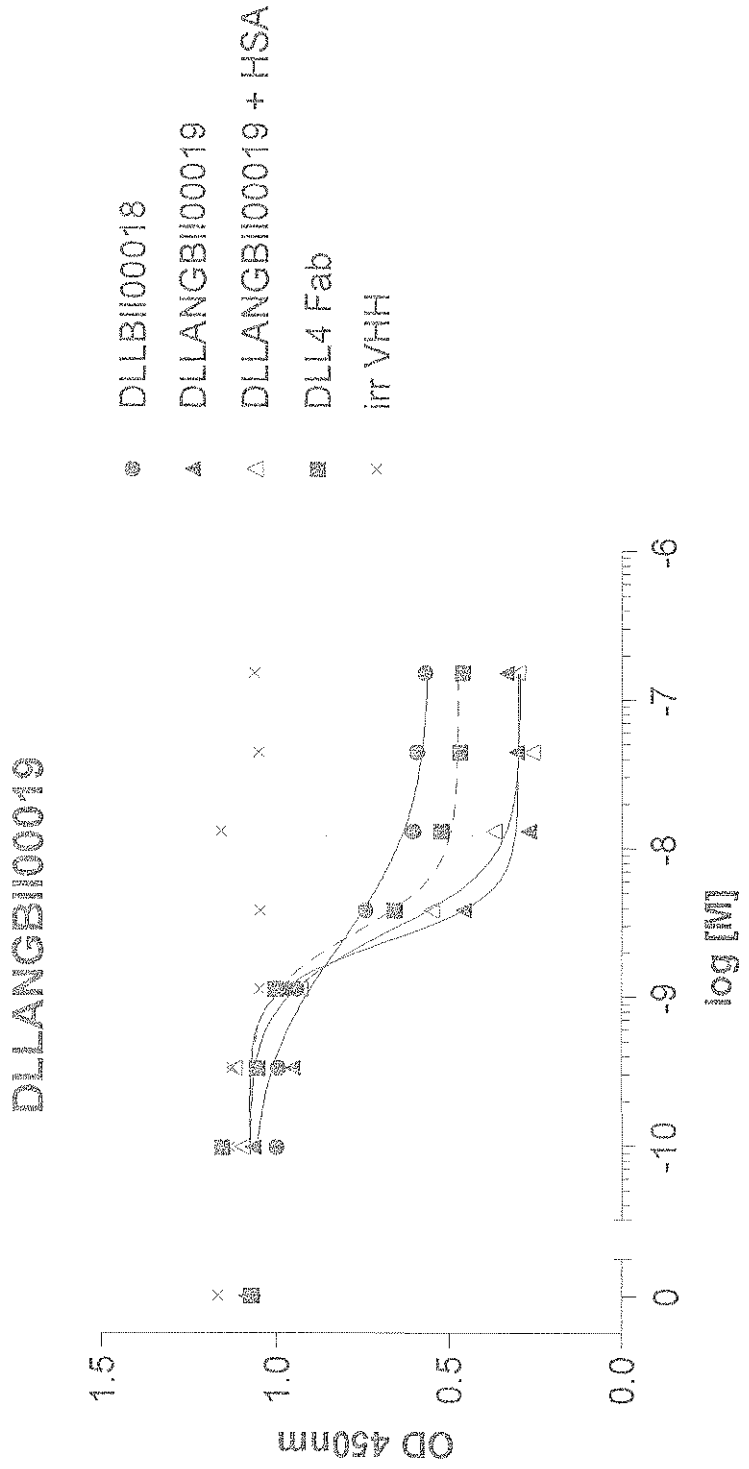

DLLBI100018
DLLANGBI100019
DLLANGBI100019 + HSA
DLL4 Fab
irr VHH
DLLANGBI100019
OD 450nm
1.5
1.0
0.5
0.0
0
-10
-9
-8
-7
-6
log [M]

Figure 25-1A

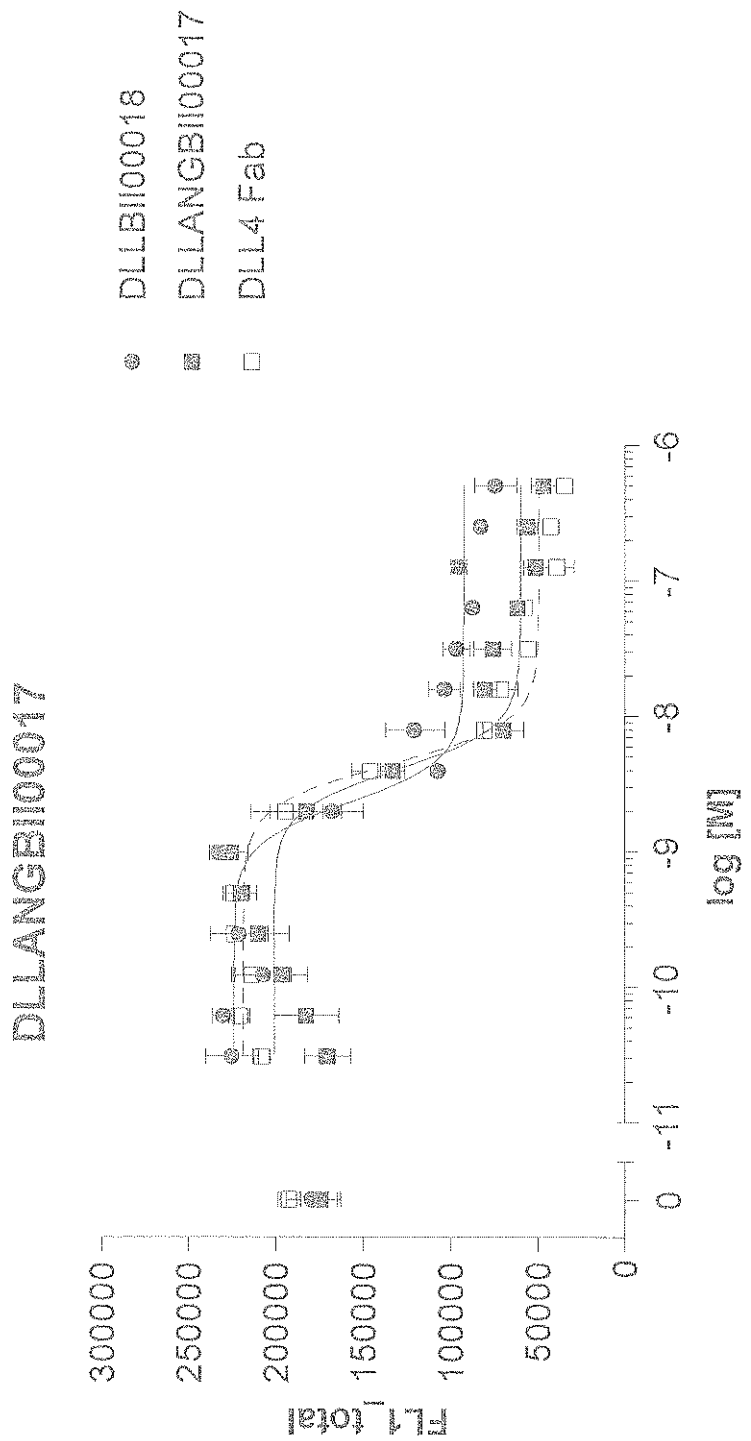

DLLBI100018
DLLANGBI100017
DLL4 Fab
DLLANGBI00017
FL_total
300000
250000
200000
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-1A (continued)

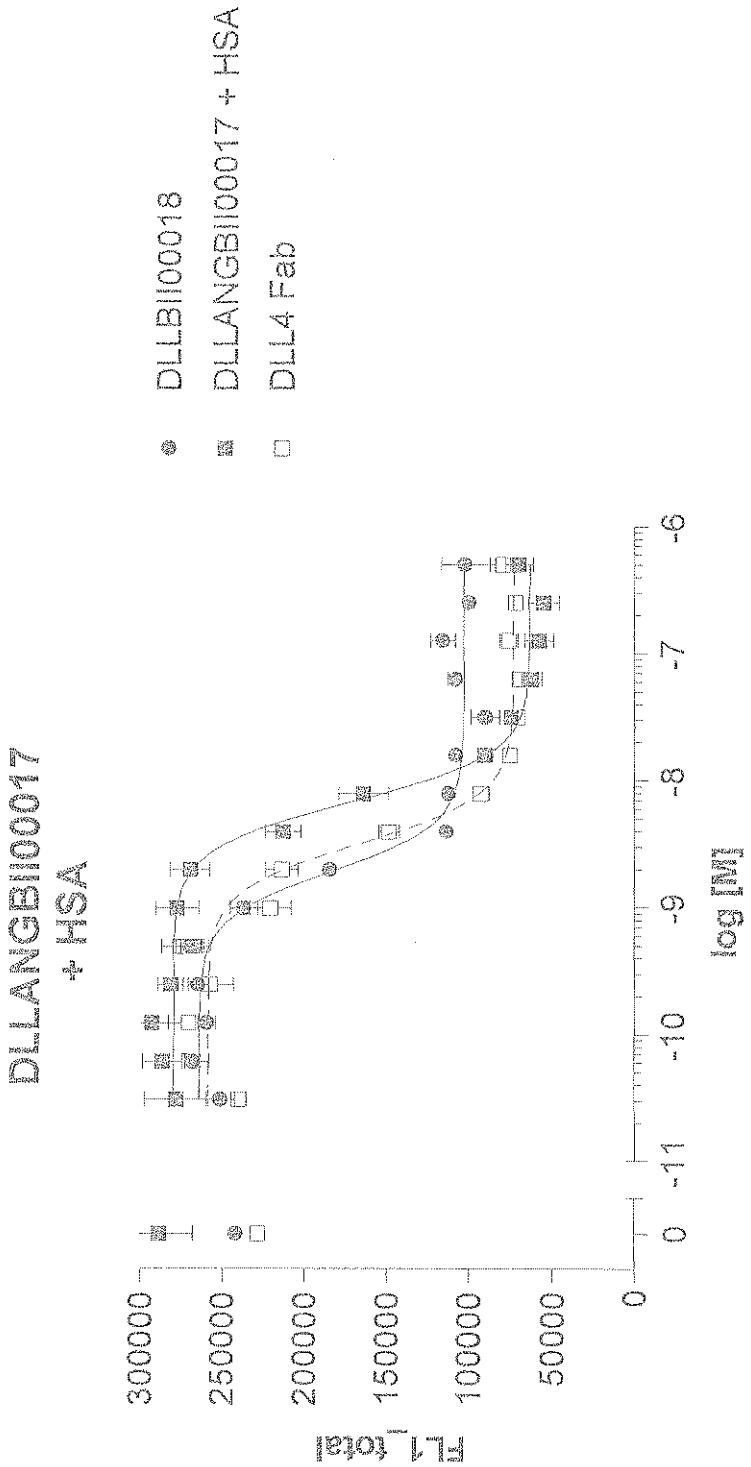


Figure 25-1B

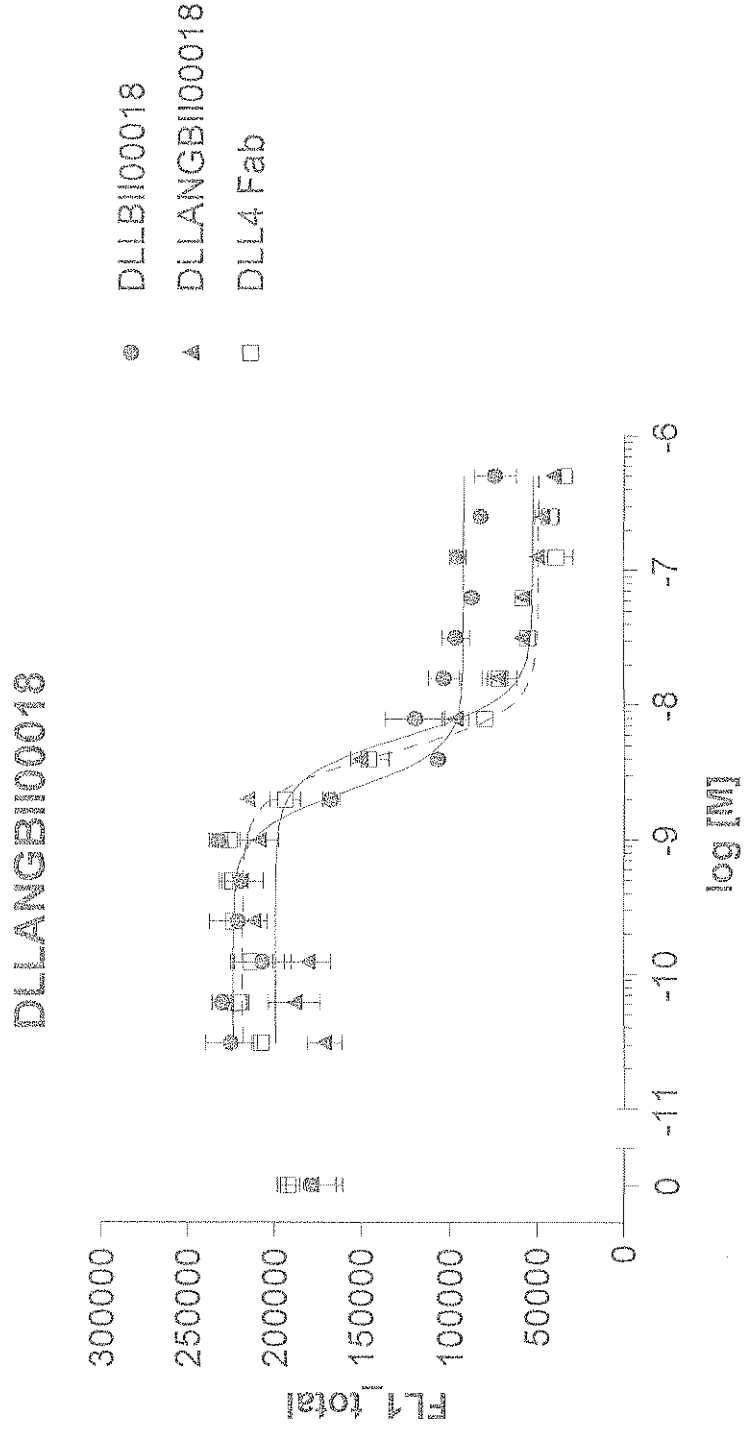

DLLBI100018
DLLANGBI100018
DLL4 Fab
DLLANGBI100018
FL1_total
300000
250000
200000
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-1B (continued)

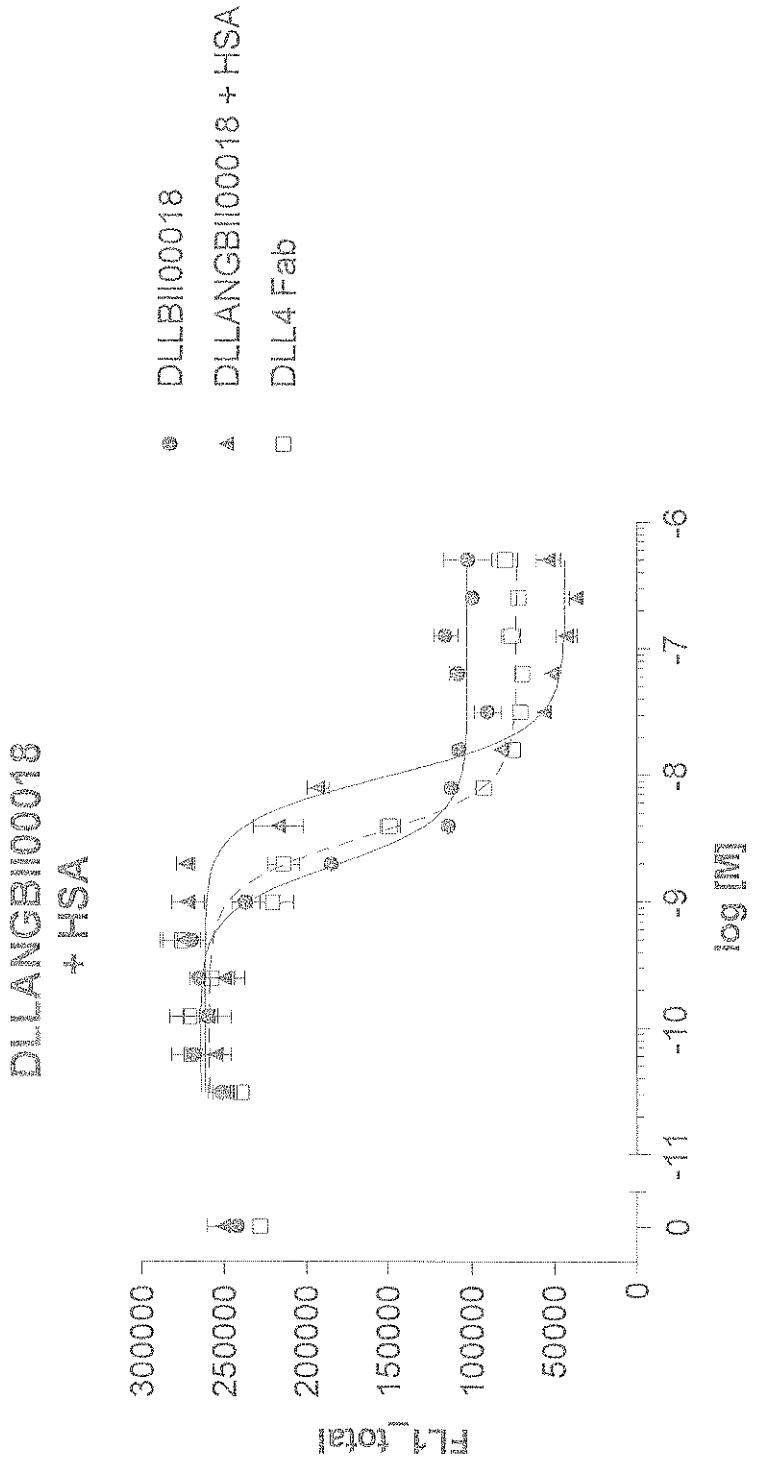


Figure 25-1C

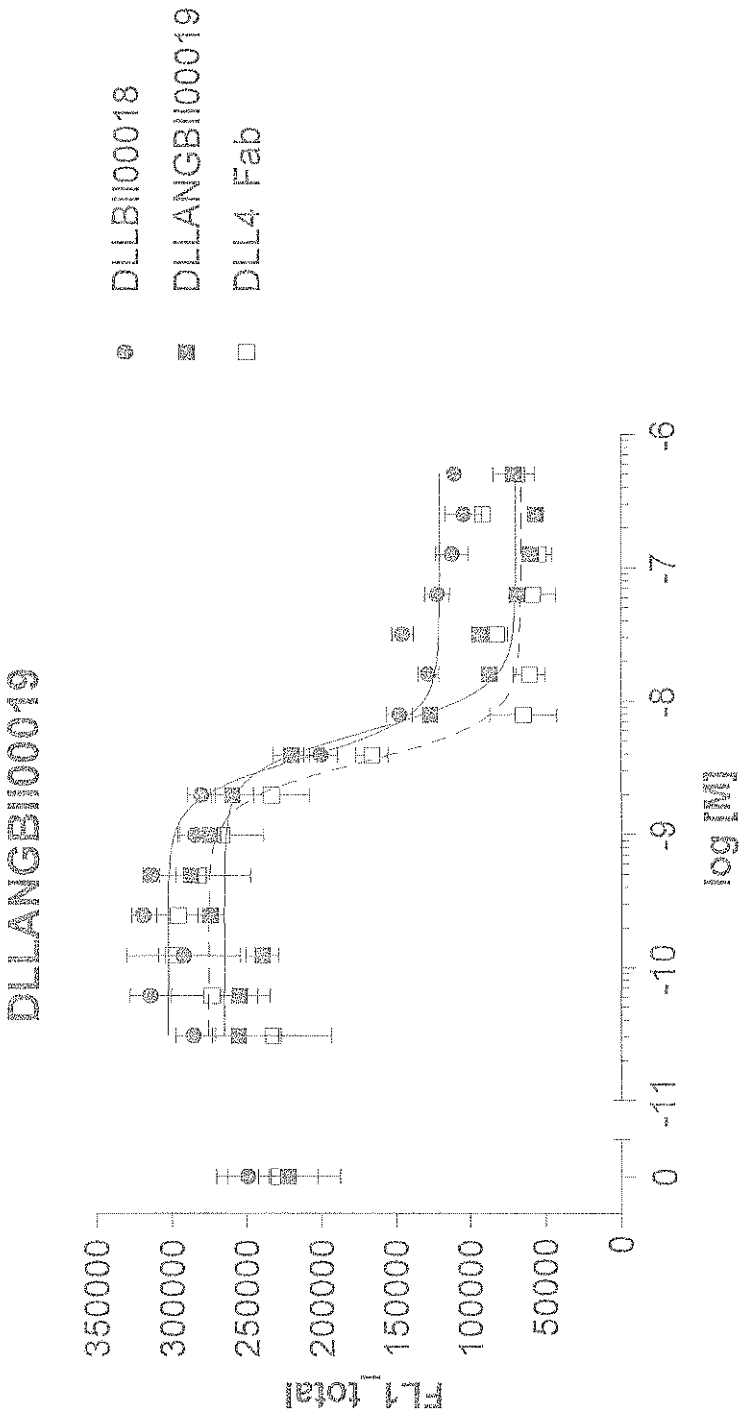

DLLBI100018
DLLANGBI100019
DLL4 Fab
DLLANGBI100019
FL1_total
350000
300000
250000
200000
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-1C (continued)

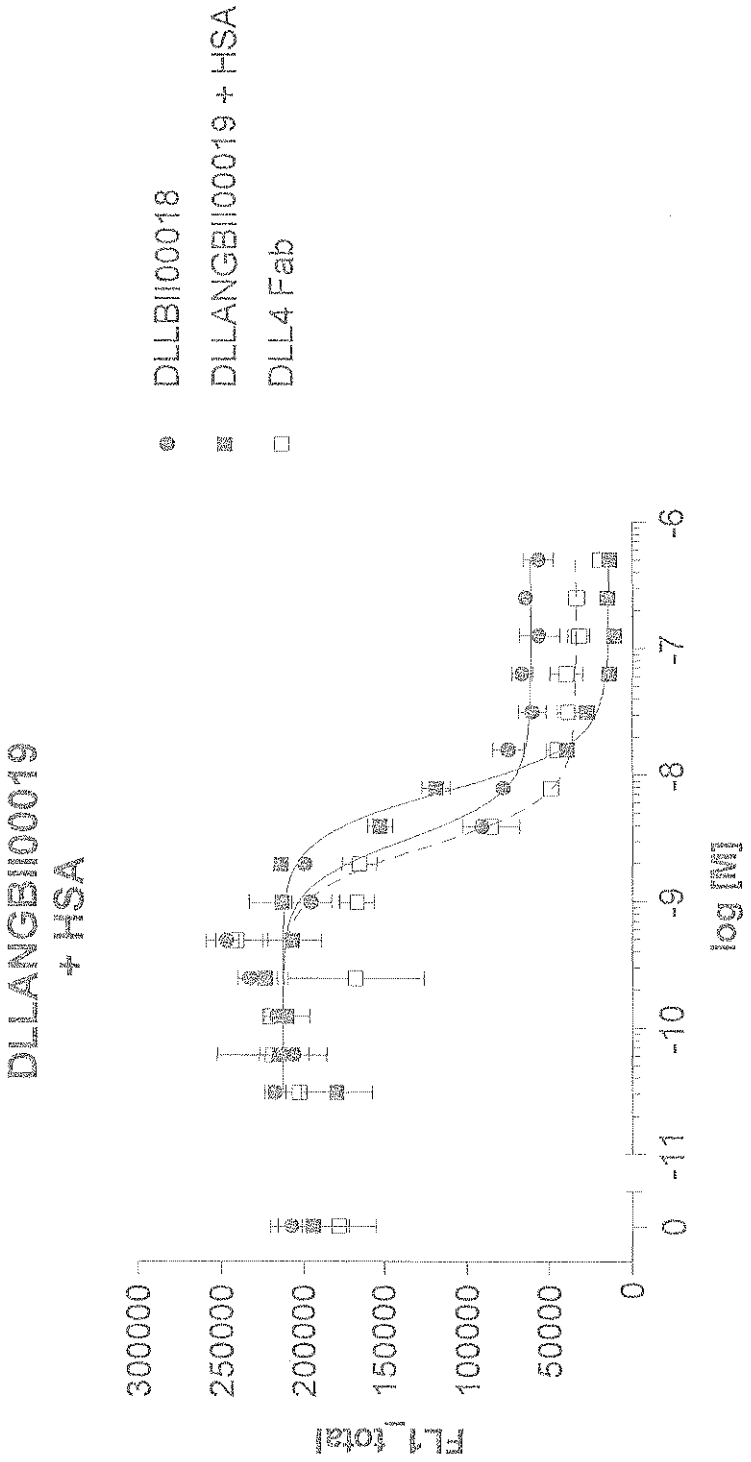


Figure 25-2A

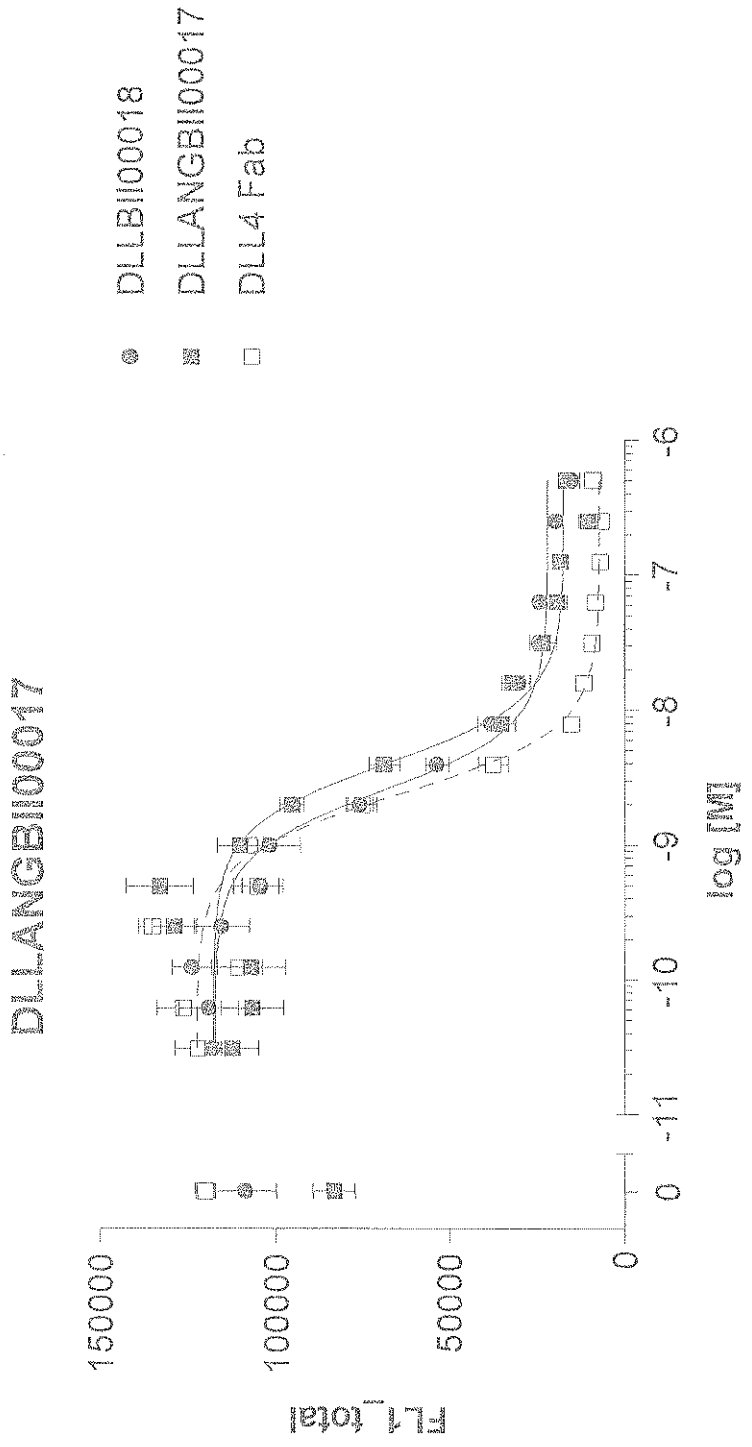

DLLBI100018
DLLANGBI100017
DLL4 Fab
DLLANGBI100017
FL1_total
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-2A (continued)

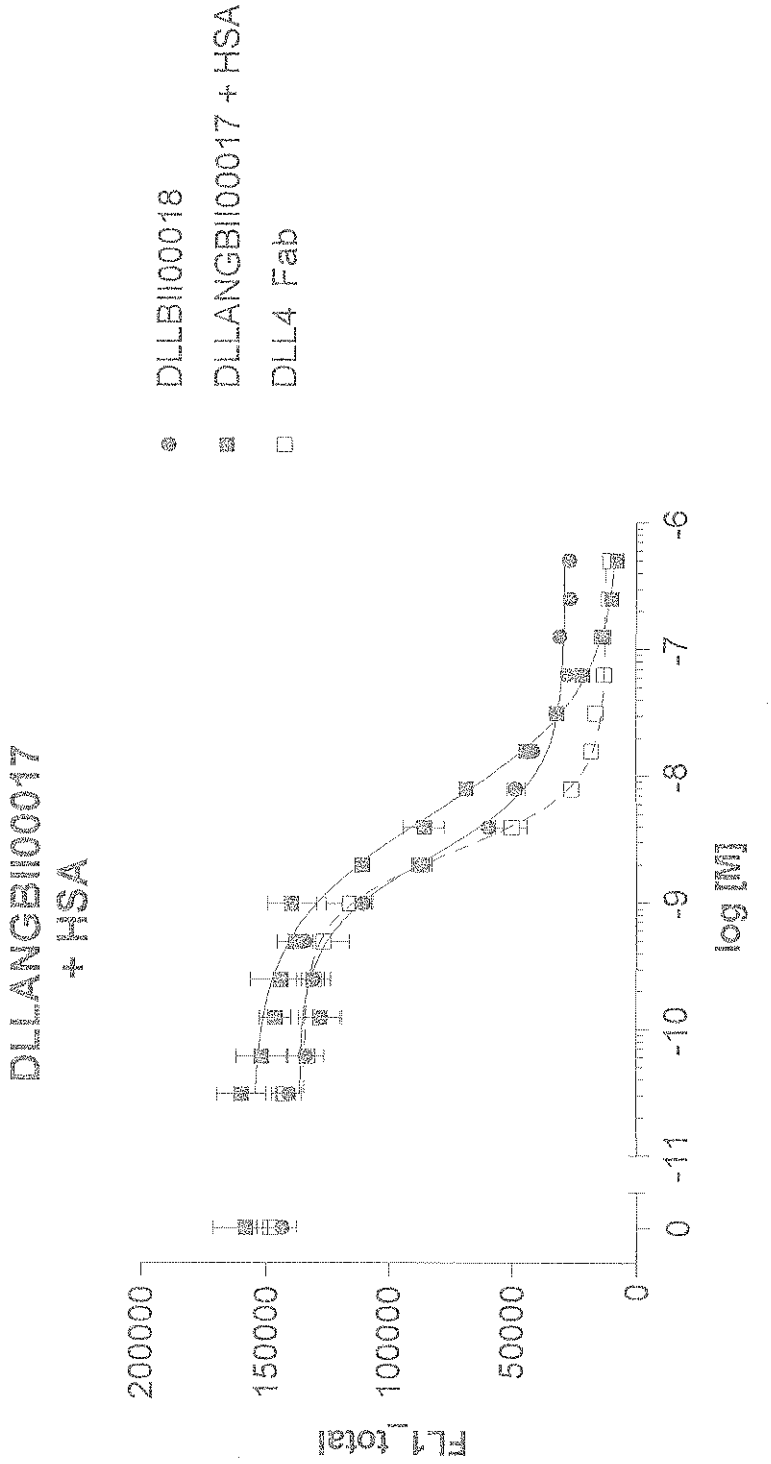


Figure 25-2B

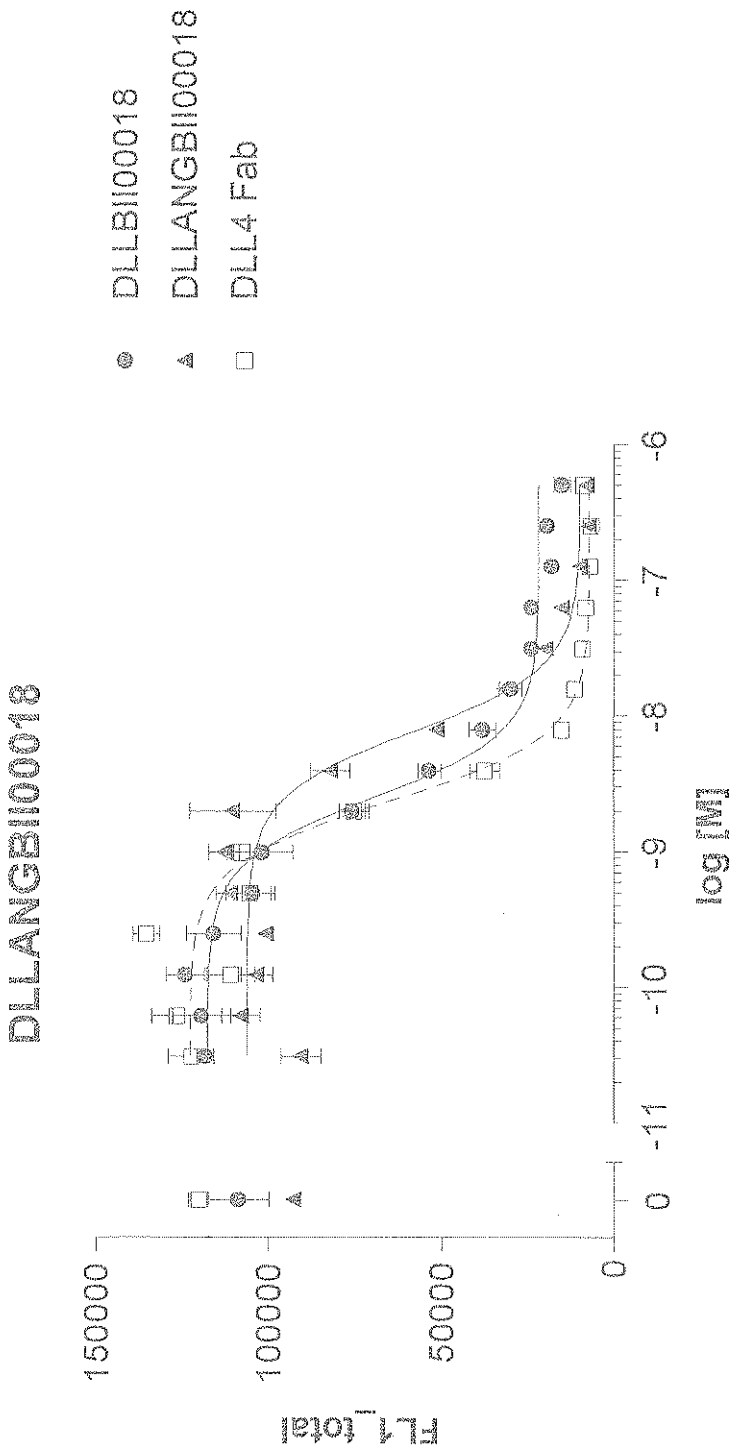

DLLBI100018
DLLANGBI100018
DLL4 Fab
DLLANGBI100018
FL1_total
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-2B (continued)

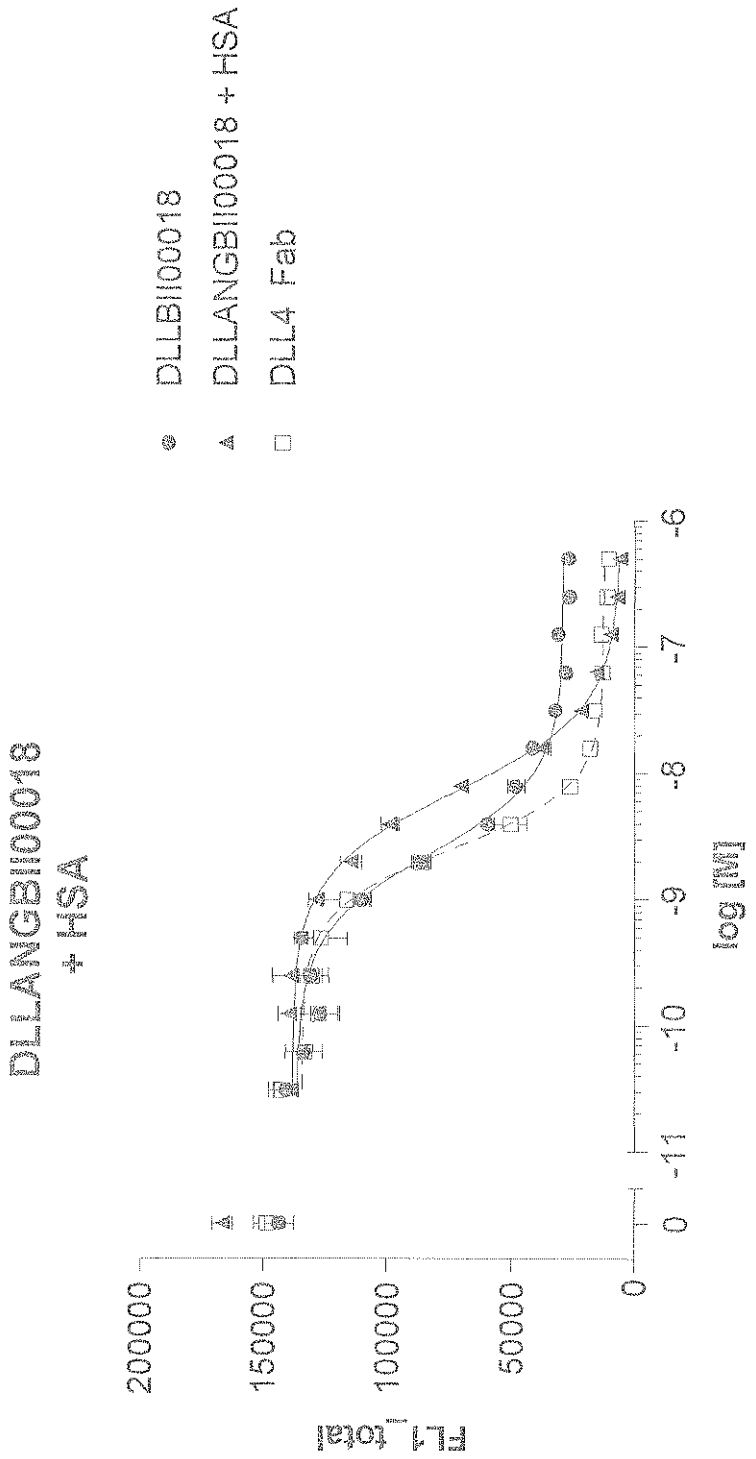


Figure 25-2C

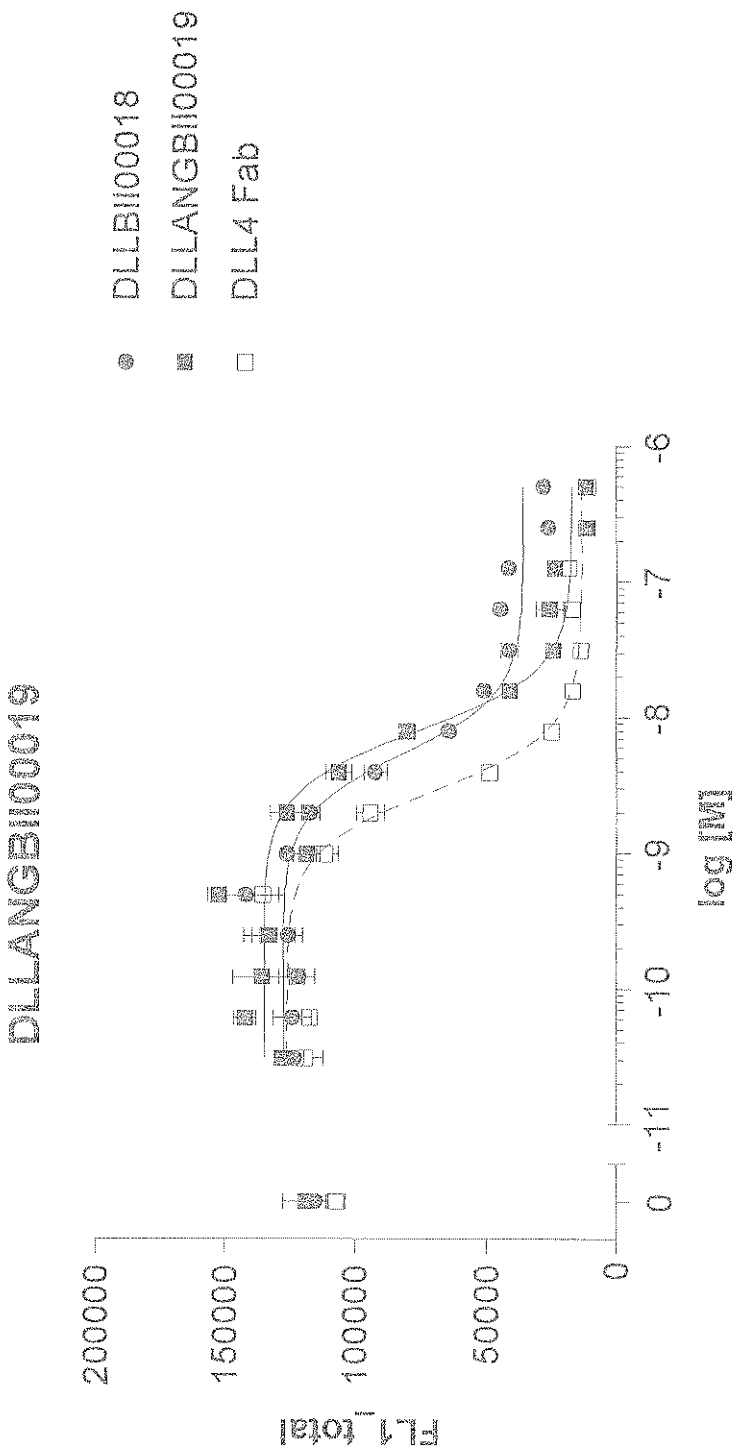

DLLBI00018
DLLANGBI00019
DLL4 Fab
DLLANGBI00019
FL1_total
200000
150000
100000
50000
0
0
-6
-7
-8
-9
-10
-11
log [M]

Figure 25-2C (continued)

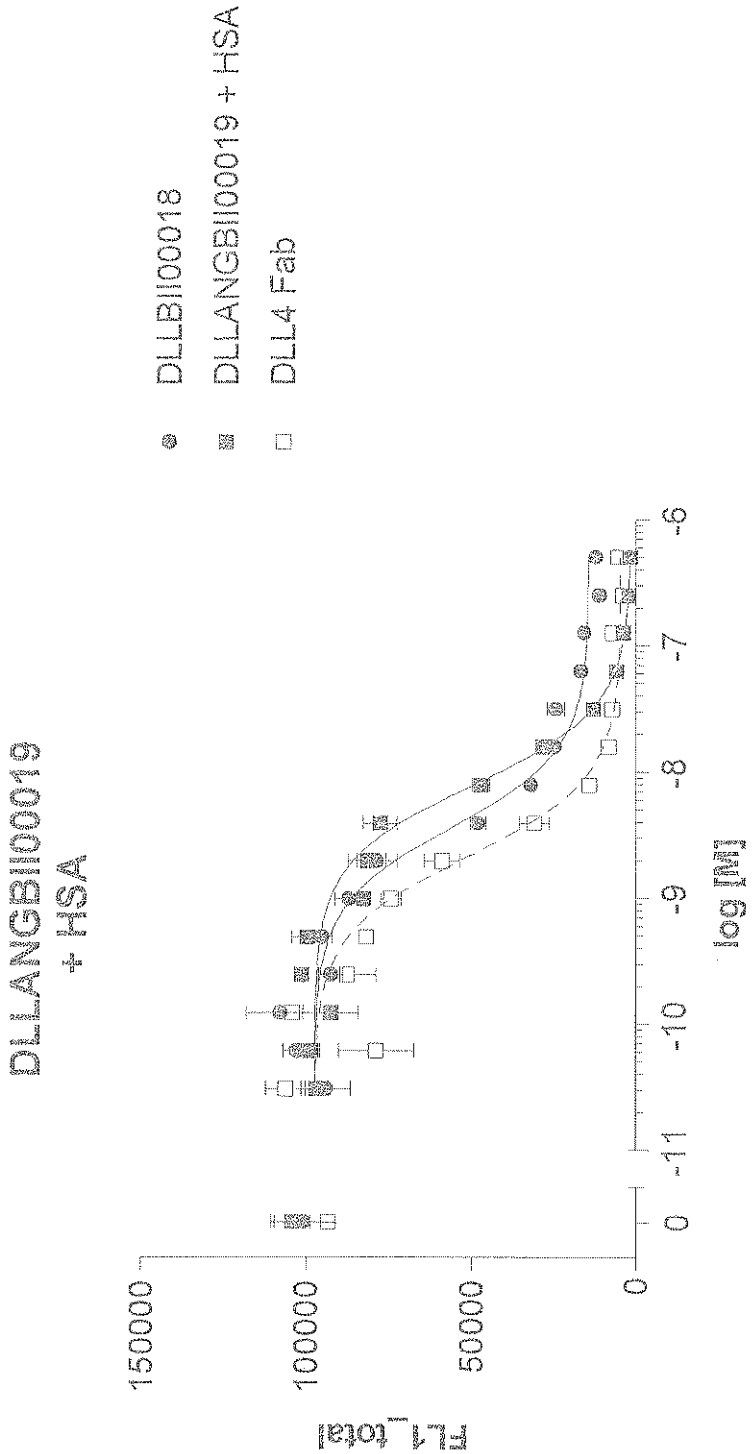


Figure 26A

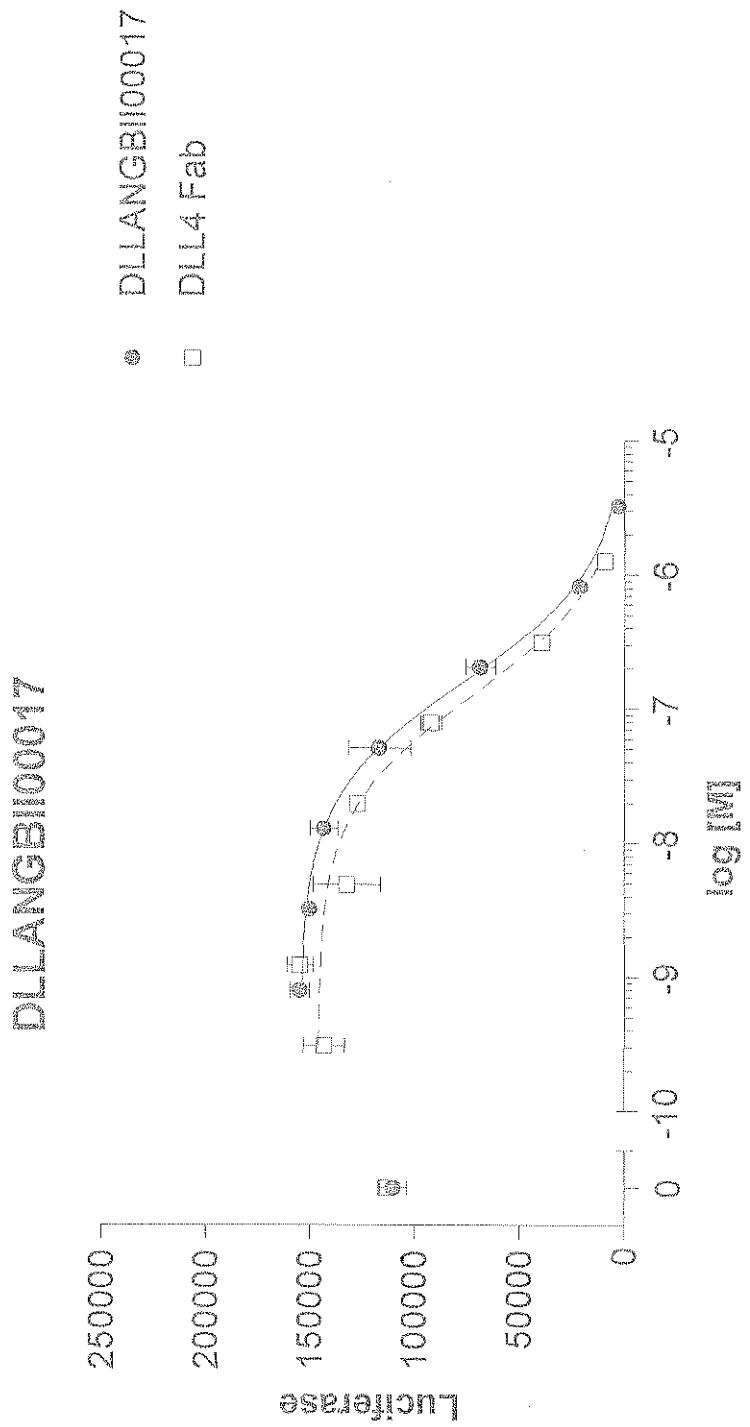

DLLANGBI00017
DLL4 Fab
DLLANGBI00017
Luciferase
250000
200000
150000
100000
50000
0
0
-10
-9
-8
-7
-6
-5
log [M]

Figure 26A (continued)

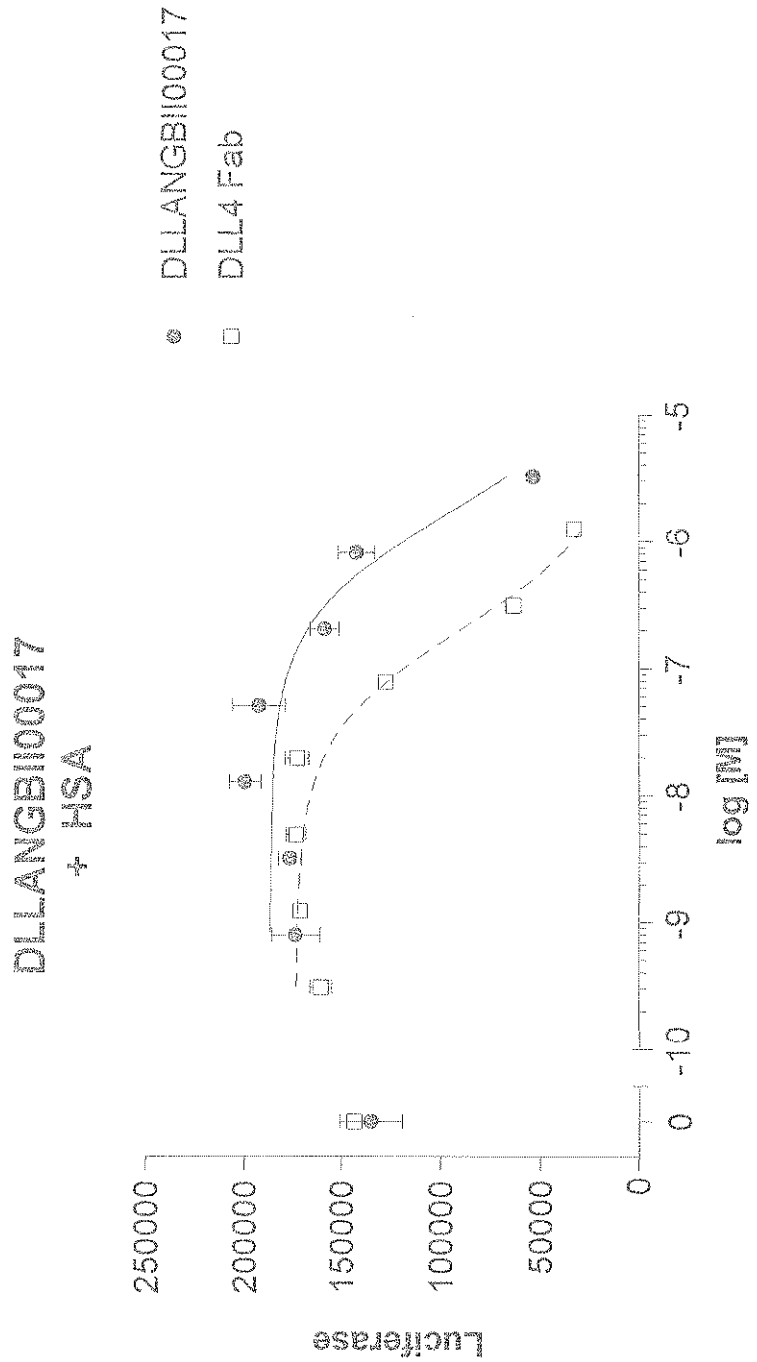
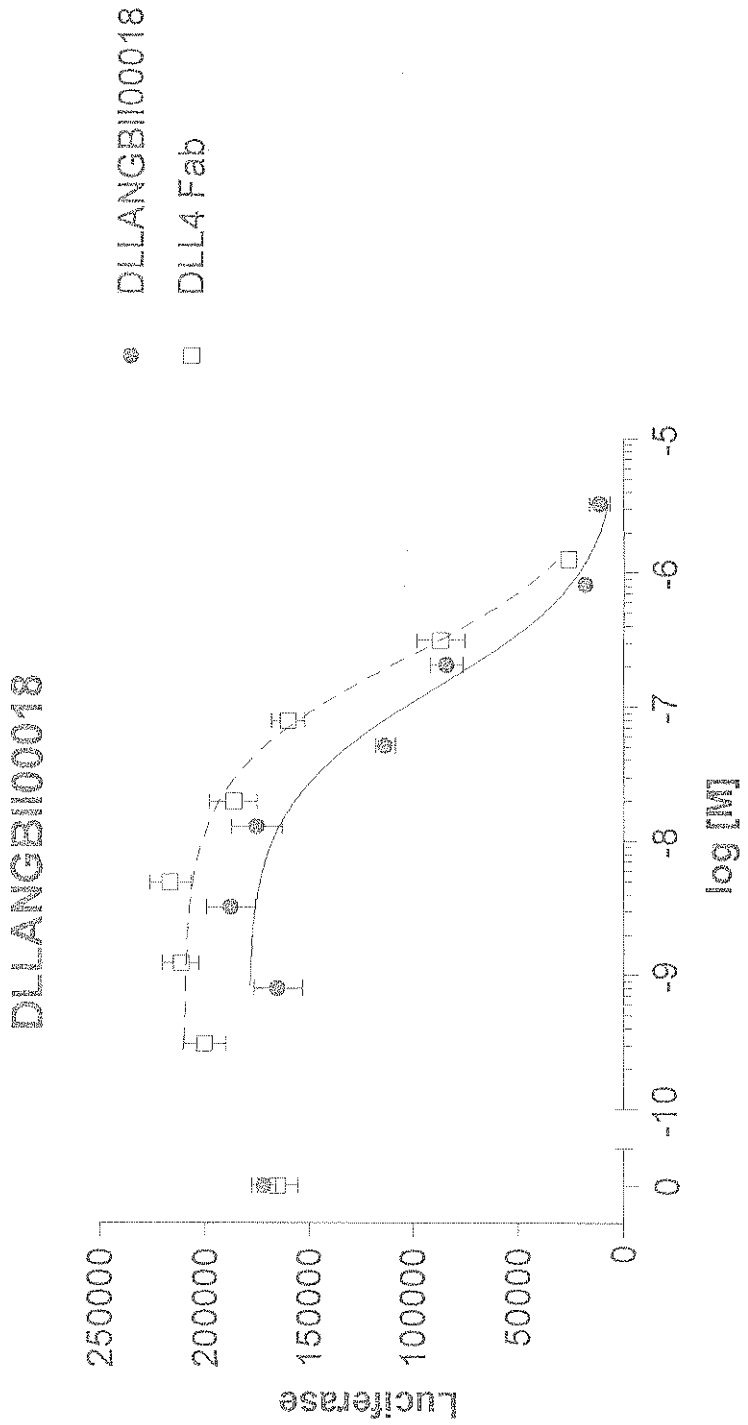


Figure 26B


DLLANGBI00018
DLL4 Fab
DLLANGBI00018
Luciferase
250000
200000
150000
100000
50000
0
0
-5
-6
-7
-8
-9
-10
log [M]

127 / 152

Figure 26B (continued)

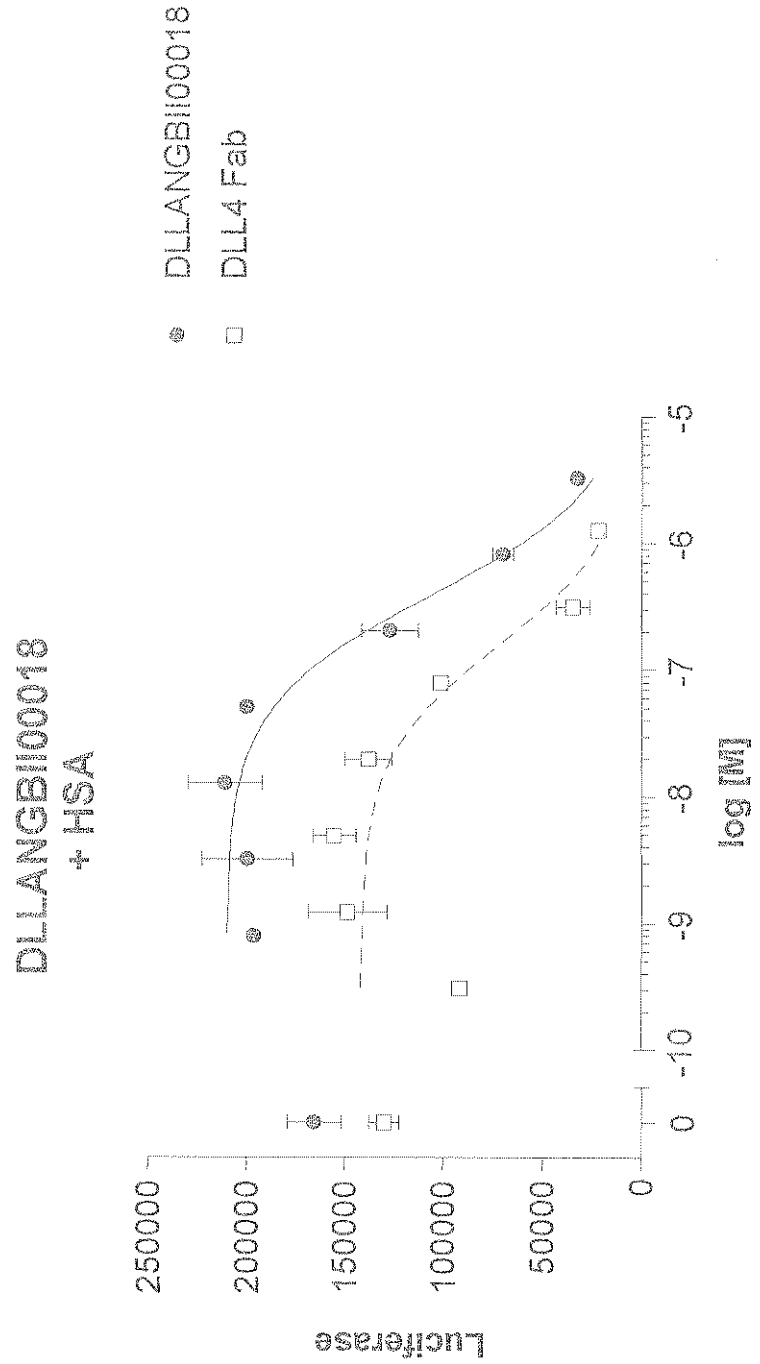


Figure 26C

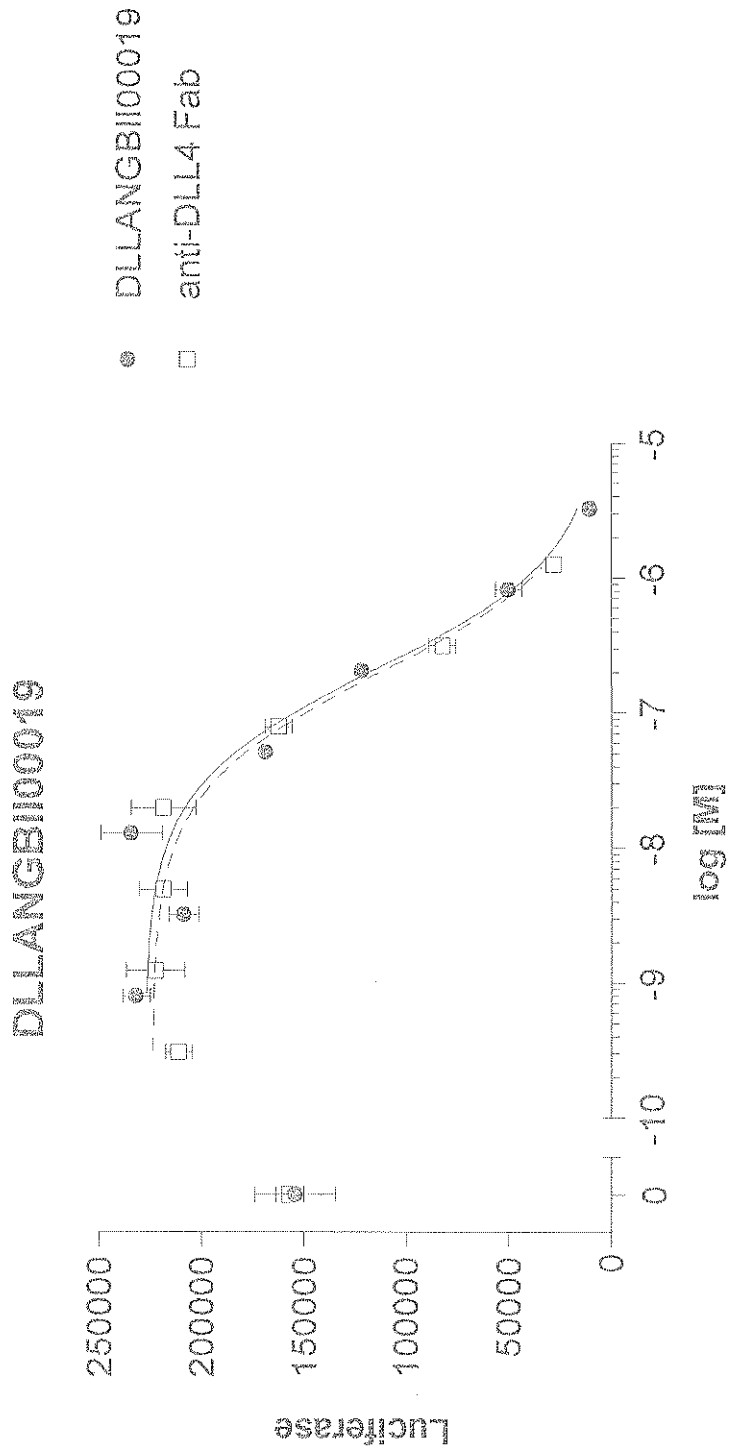

DLLANGBII00019
anti-DLL4 Fab
DLLANGBII00019
Luciferase
250000
200000
150000
100000
50000
0
0
-10
-9
-8
-7
-6
-5
log [M]

Figure 26C (continued)

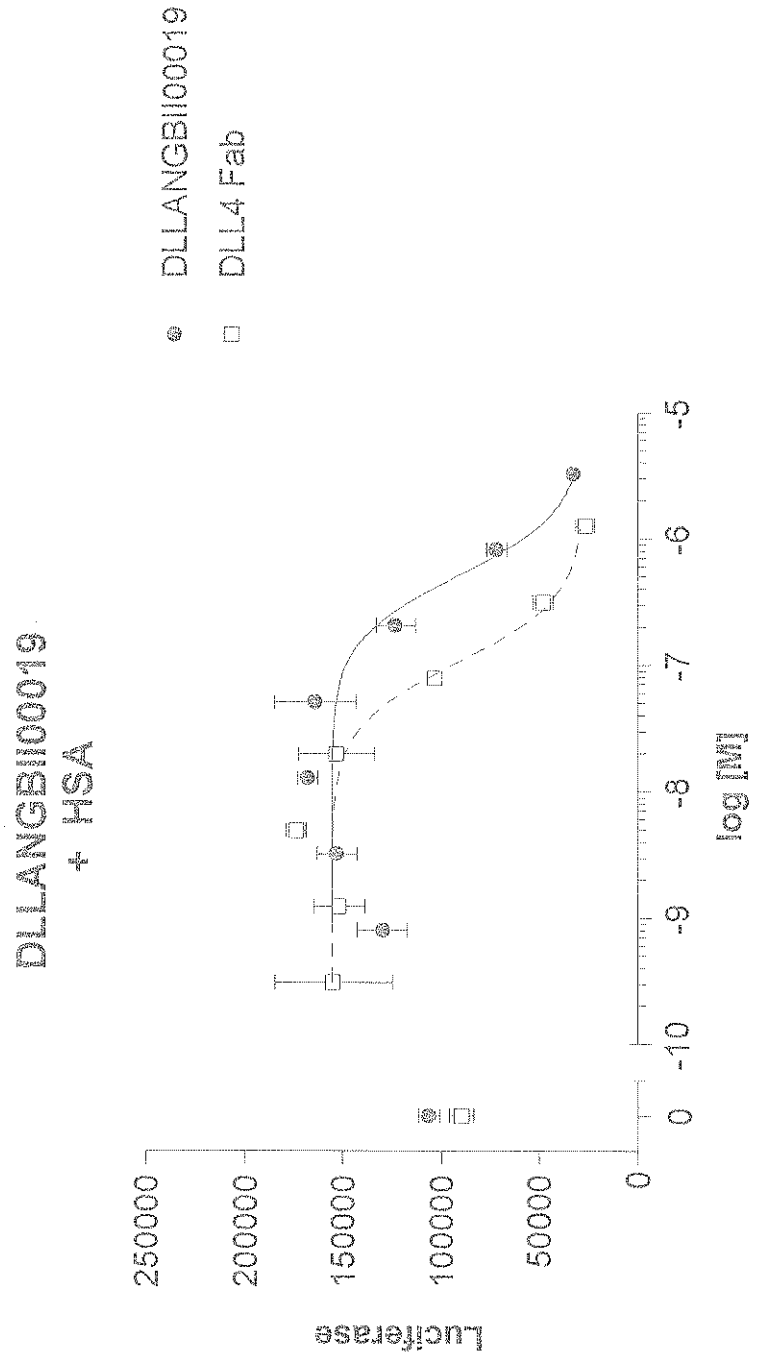


Figure 27A

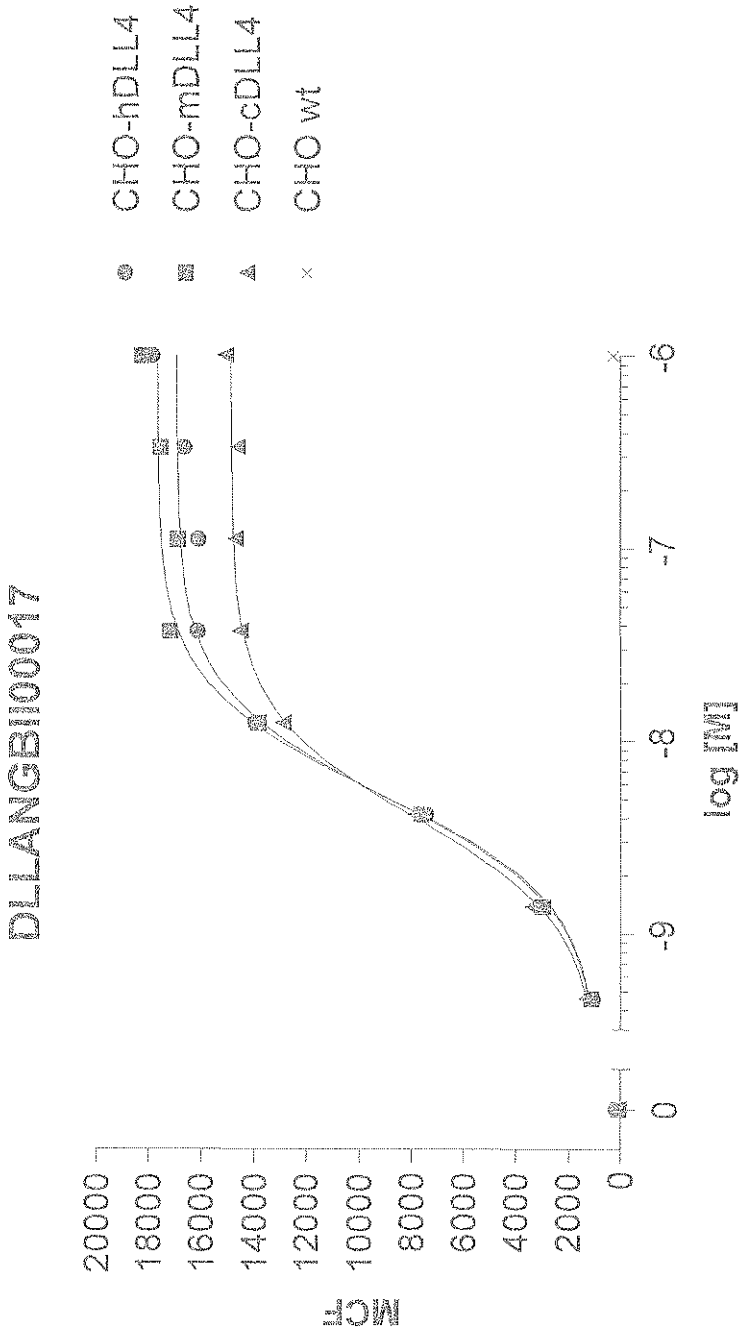

DLLANGB10017
CHO-hDLL4
CHO-mDLL4
CHO-cDLL4
CHO wt
MCF
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
0
-6
-7
-8
-9
log [M]

Figure 27B

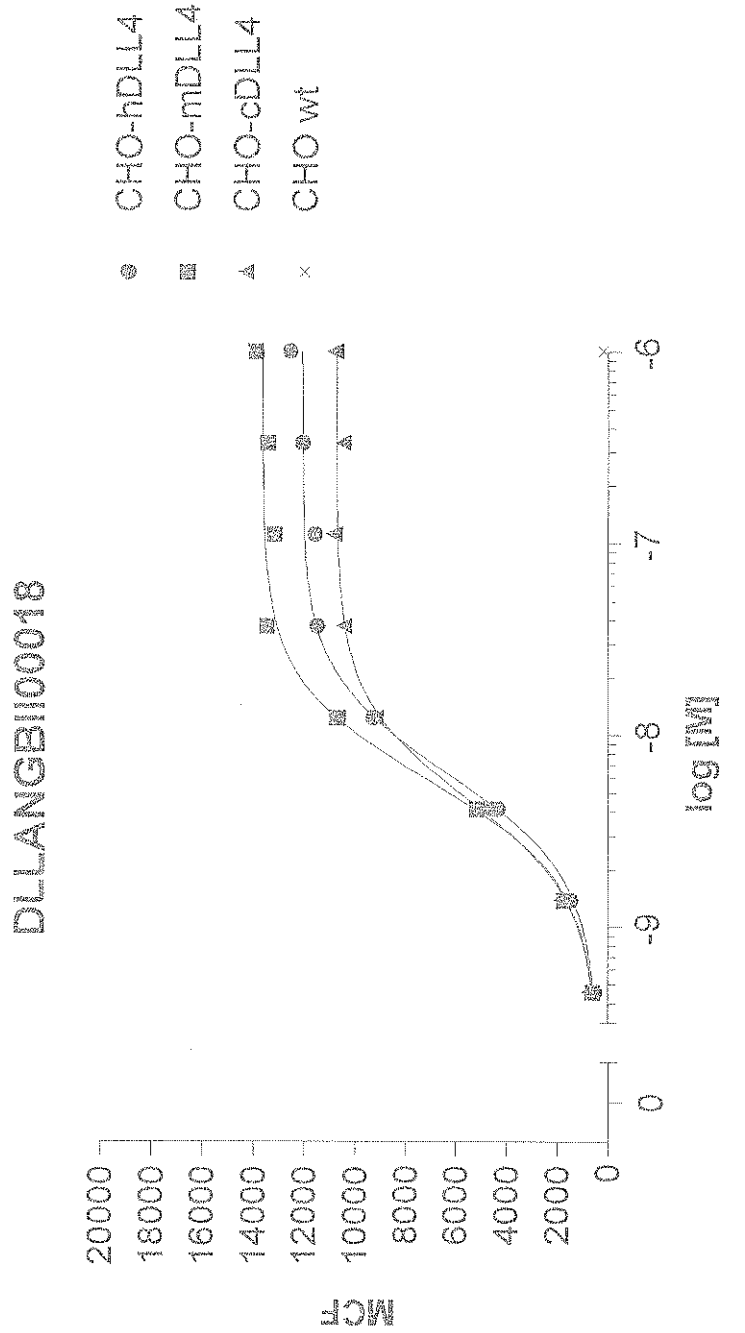

DLLANGBI00018
CHO-hDLL4
CHO-mDLL4
CHO-cDLL4
CHO wt
MCFI
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
0
-6
-7
-8
-9
log [M]

Figure 27C

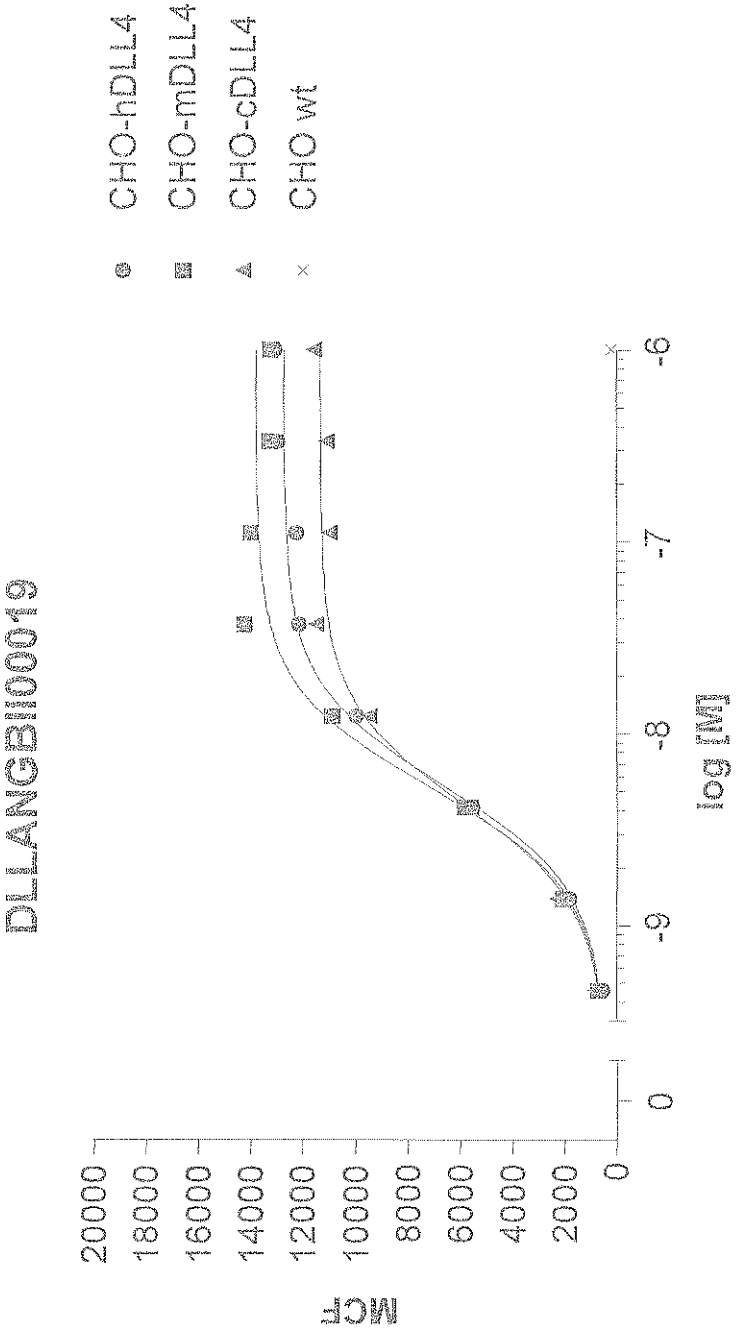

DLL4NOTCH1
CHO-hDLL4
CHO-mDLL4
CHO-cDLL4
CHO wt
MCF
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
0
-6
-7
-8
-9
log EMT

Figure 28A

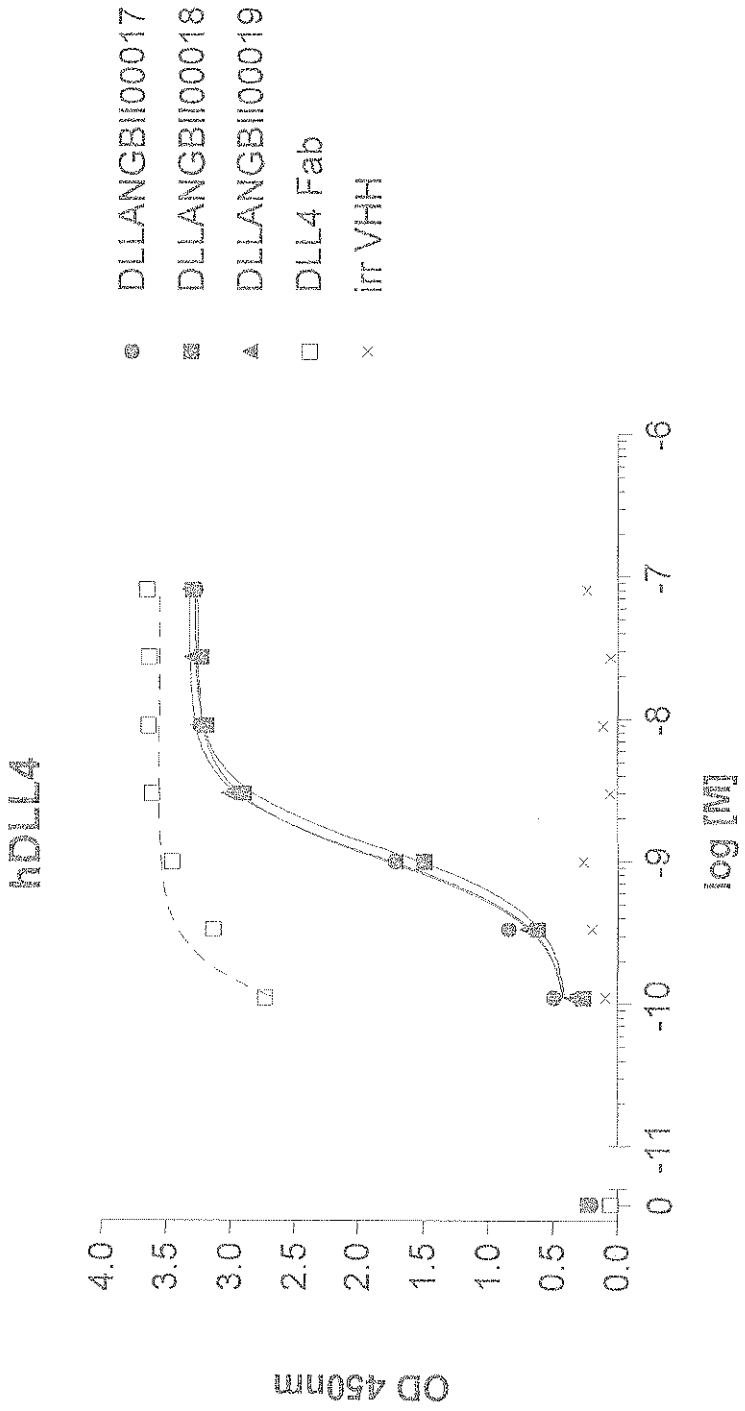

DLLANGBI00017
DLLANGBI00018
DLLANGBI00019
DLL4 Fab
irr VHH
hDLL4
OD 450nm
log [M]
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6

Figure 28B

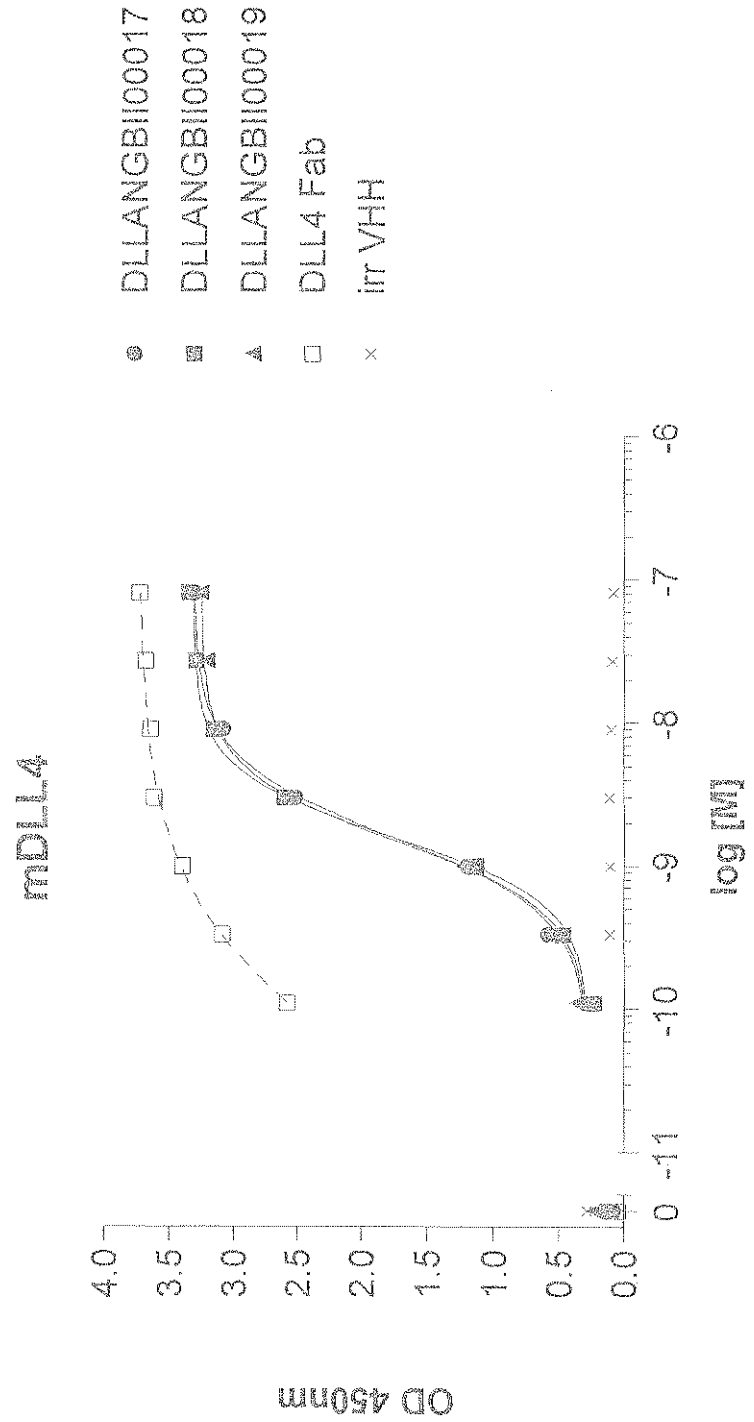

DLLANGBI00017
DLLANGBI00018
DLLANGBI00019
DLL4 Fab
irr VHH
anDLL4
log [M]
OD 450nm
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6

Figure 28C

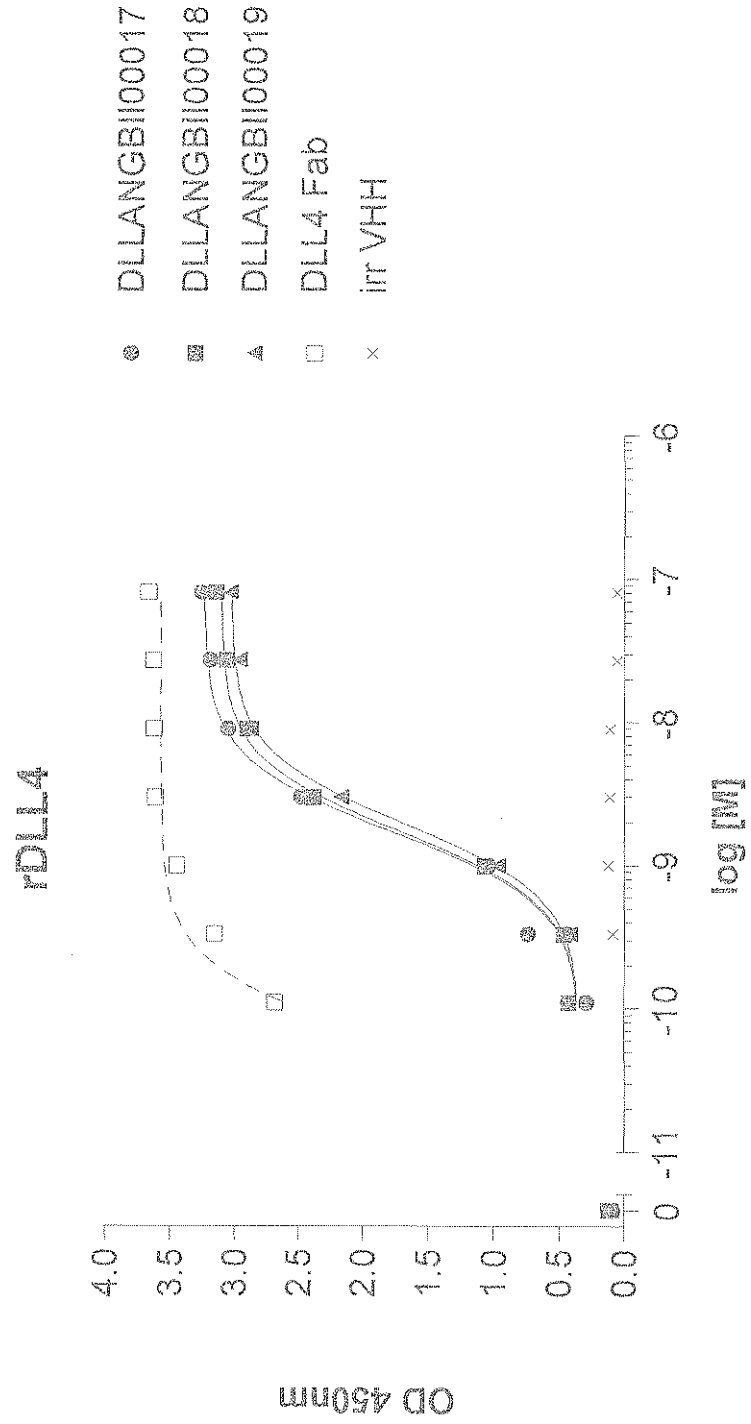

DLLANGBII00017
DLLANGBII00018
DLLANGBII00019
DLL4 Fab
irr VHH
rDLL4
log [M]
OD 450nm
0
-11
-10
-9
-8
-7
-6
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0

Figure 29A

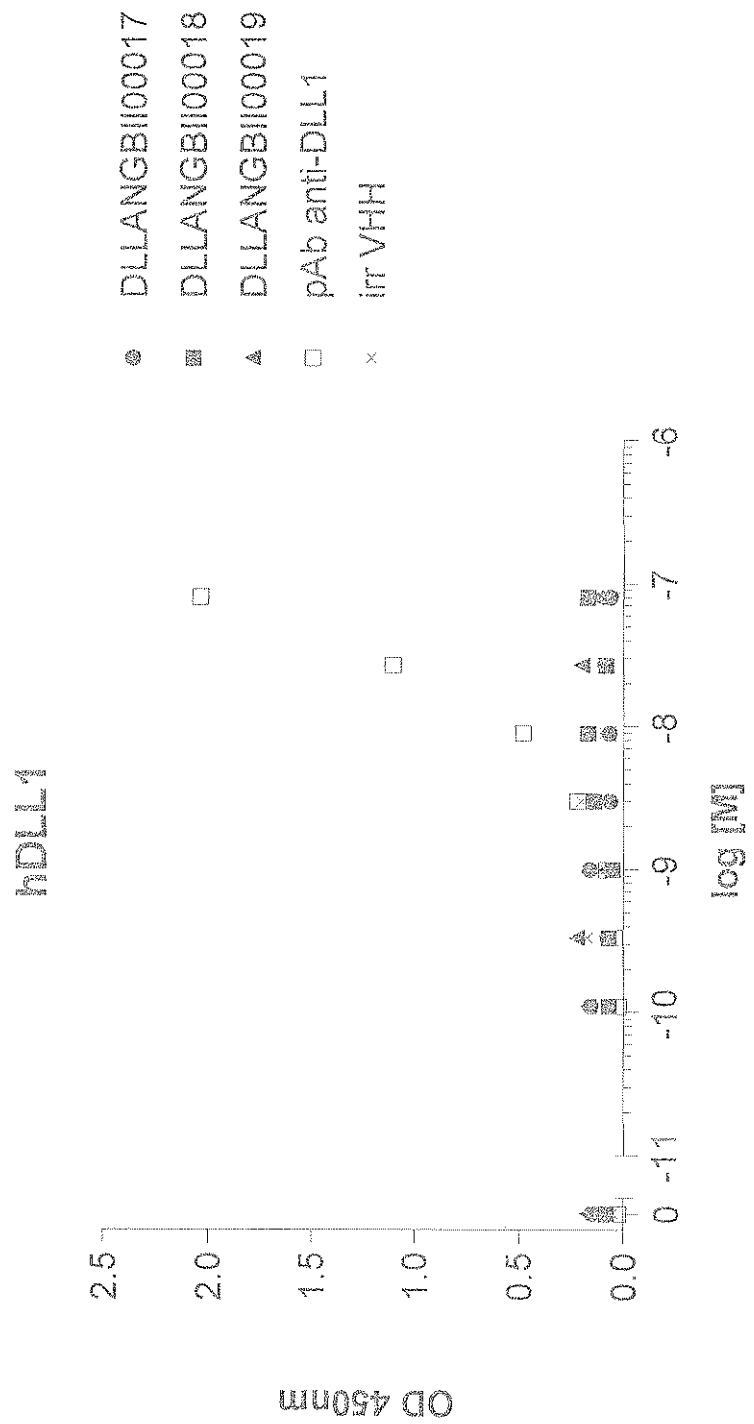

DLLANGBI00017
DLLANGBI00018
DLLANGBI00019
pAb anti-DLL1
irr VHH
hDLL1
log [M]
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6

Figure 29B

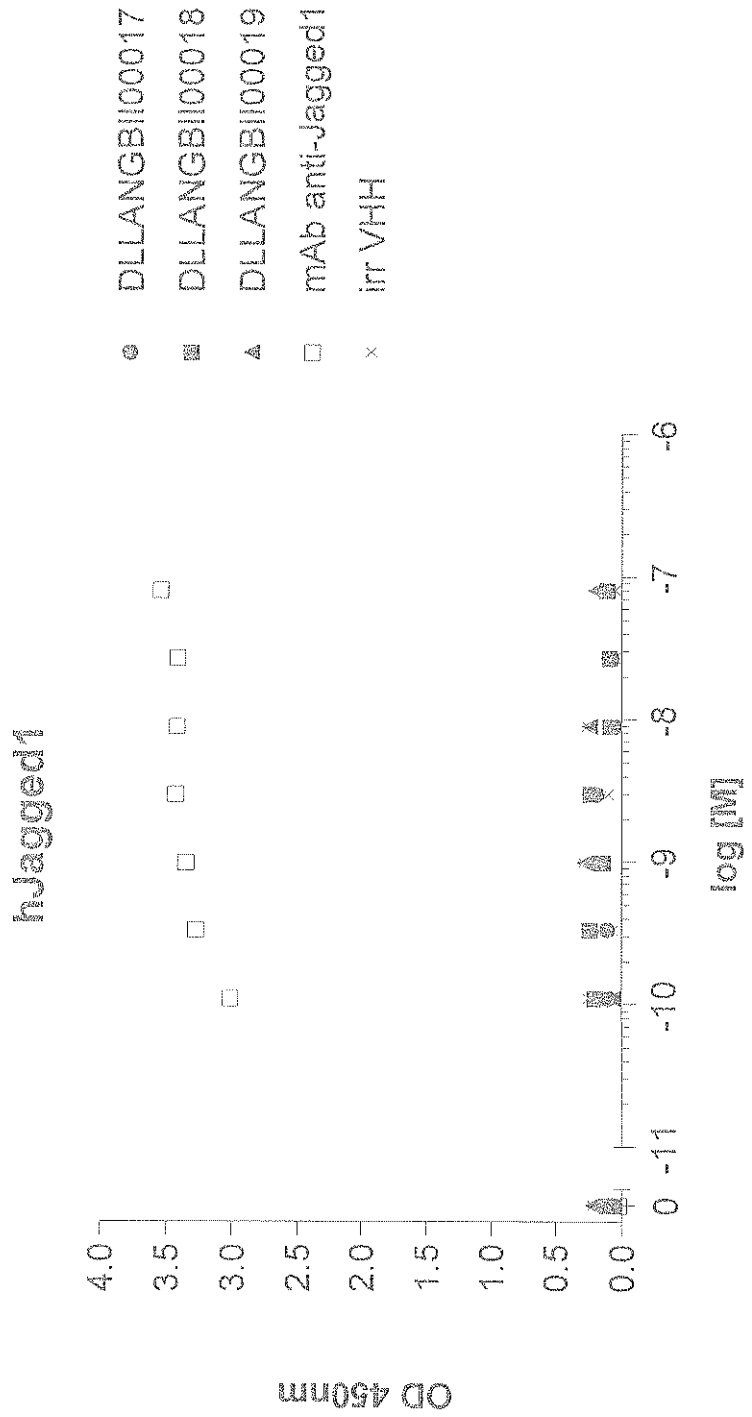

DLLANGBI00017
DLLANGBI00018
DLLANGBI00019
mAb anti-Jagged1
irr VHH
hJagged1
OD 450nm
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-1A

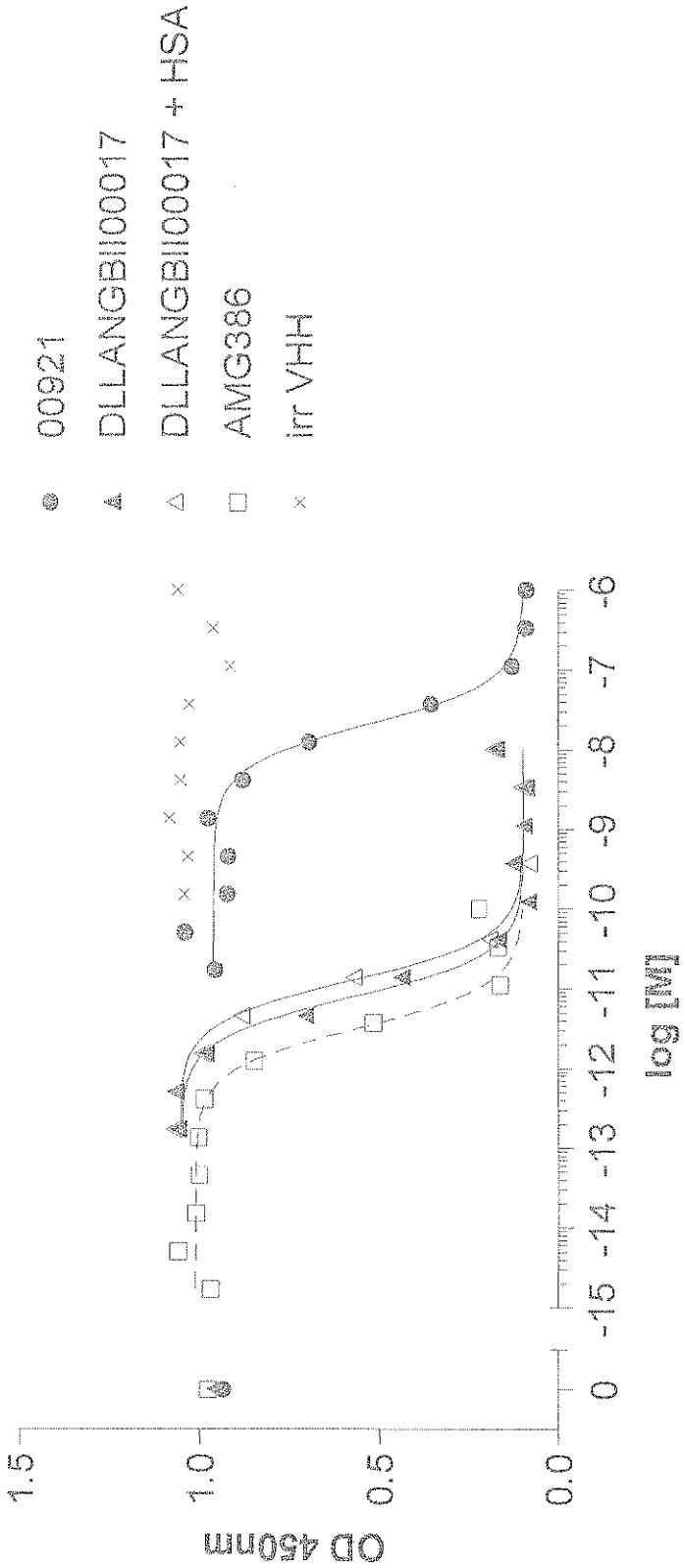

00921
DLLANGBII00017
DLLANGBII00017 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-1B

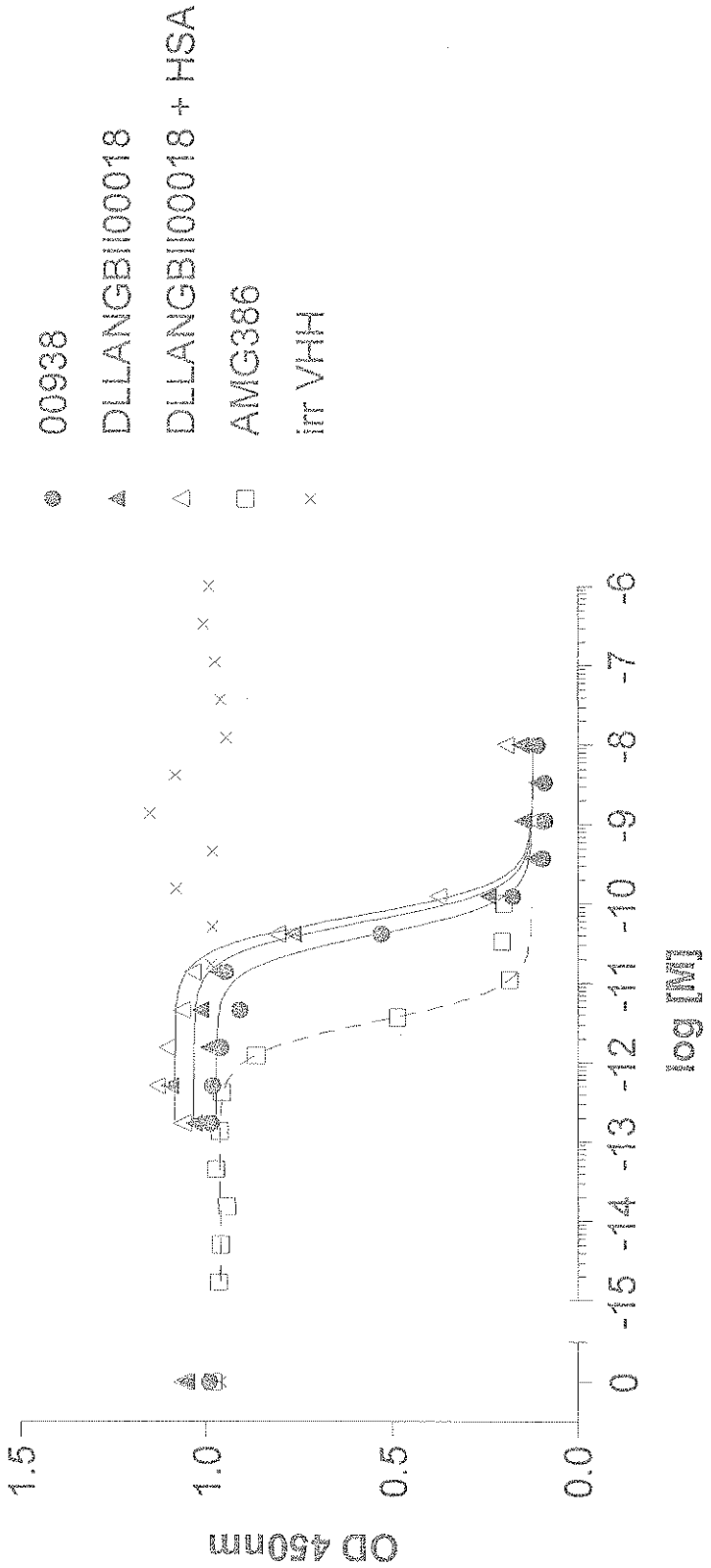

00938
DLLANGBI00018
DLLANGBI00018 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-5
-4
-3
-2
-1
-10
-9
-8
-7
-6
log [M]

Figure 30-1C

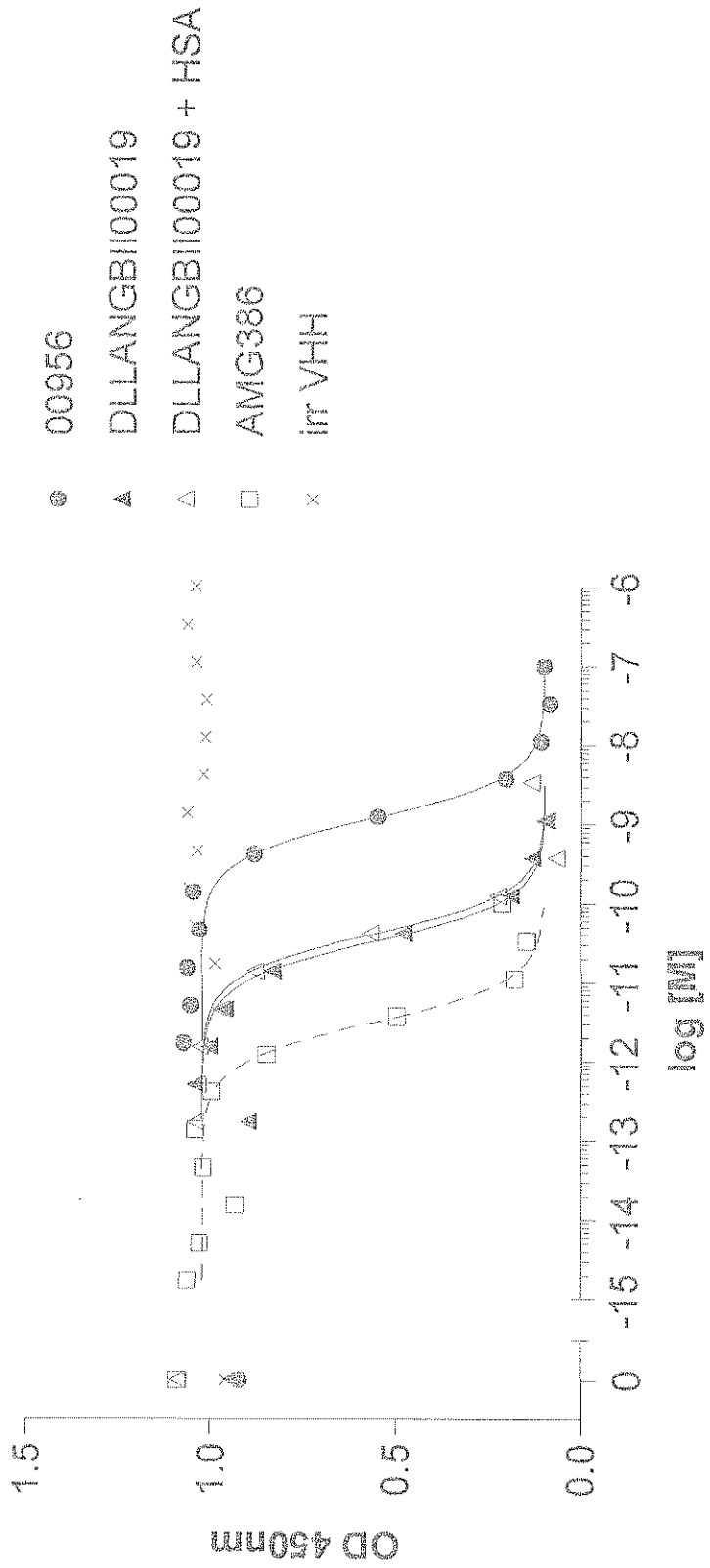

00956
DLLANGBI00019
DLLANGBI00019 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.5
1.0
1.5
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log nM

Figure 30-2A

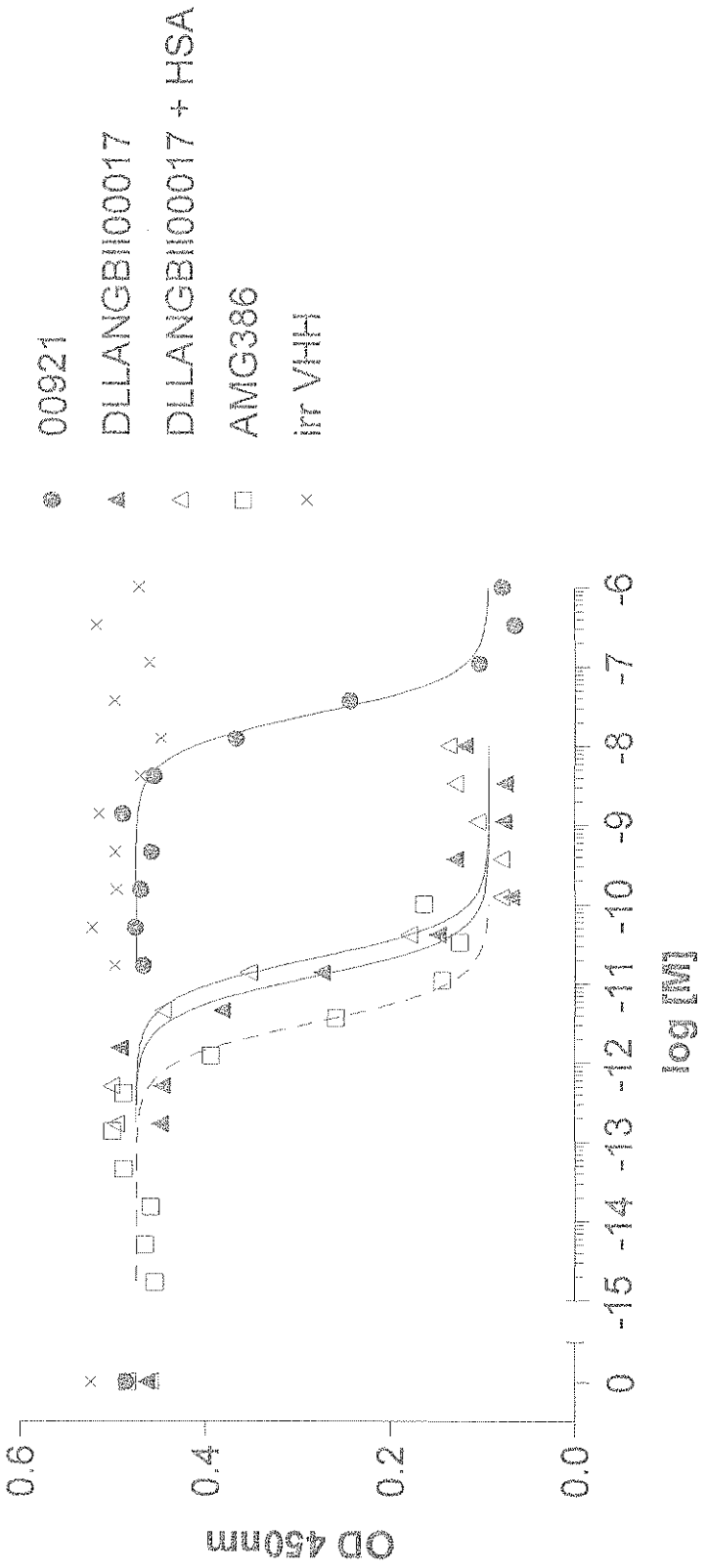

00921
DLLANGBI00017
DLLANGBI00017 + HSA
AMG386
Irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15
log [M]

Figure 30-2B

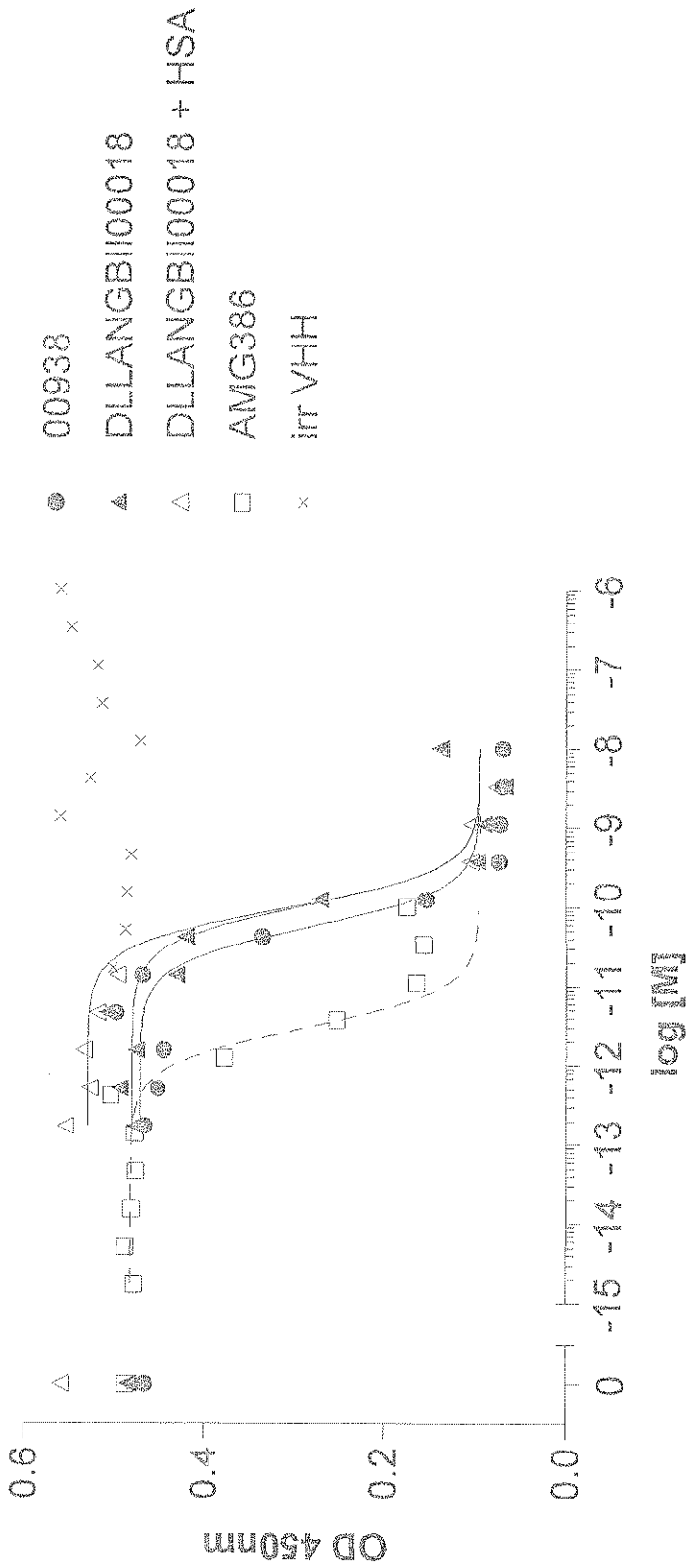

00938
DLLANGBI00018
DLLANGBI00018 + HSA
AMG386
irr VHH
OD 450nm
0.6
0.4
0.2
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-2C

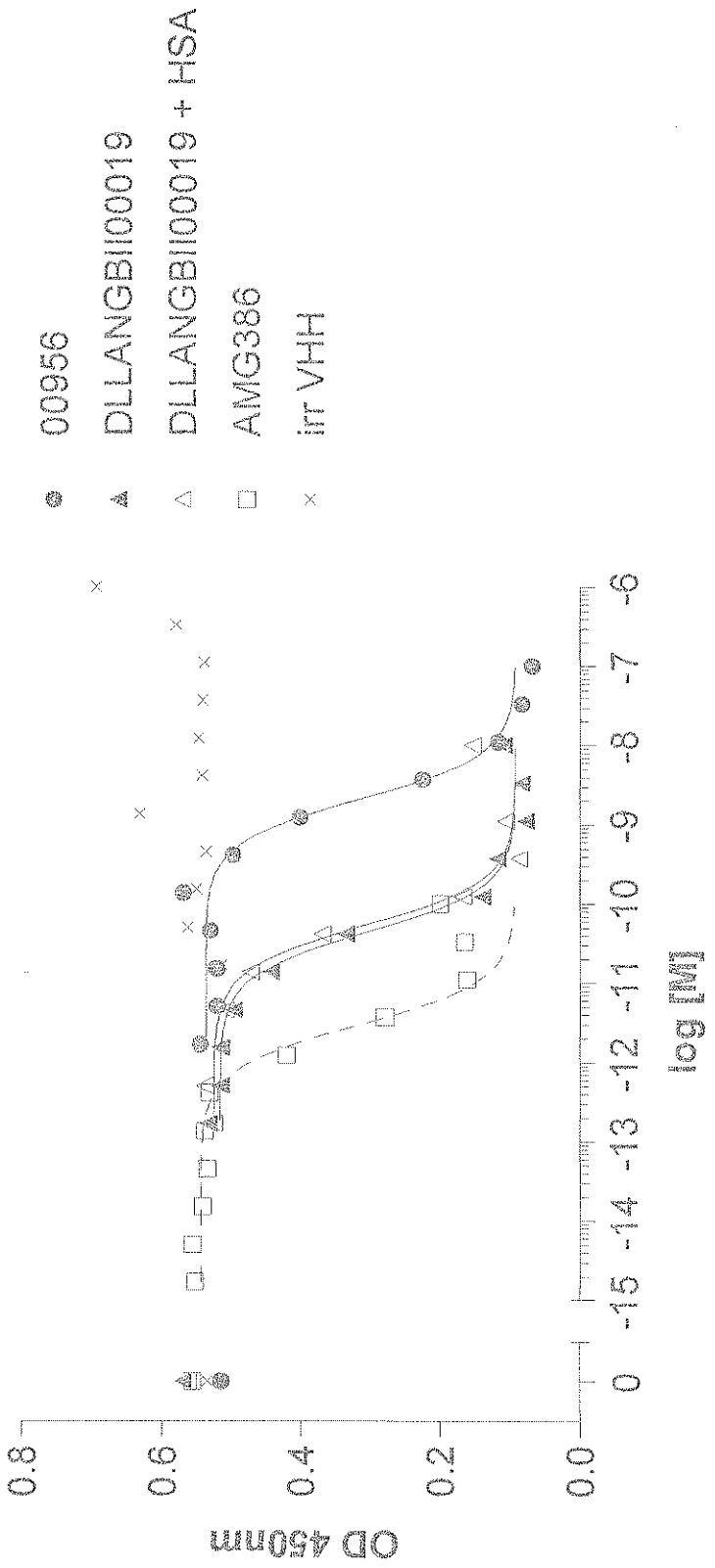

00956
DLLANGBI00019
DLLANGBI00019 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-3A

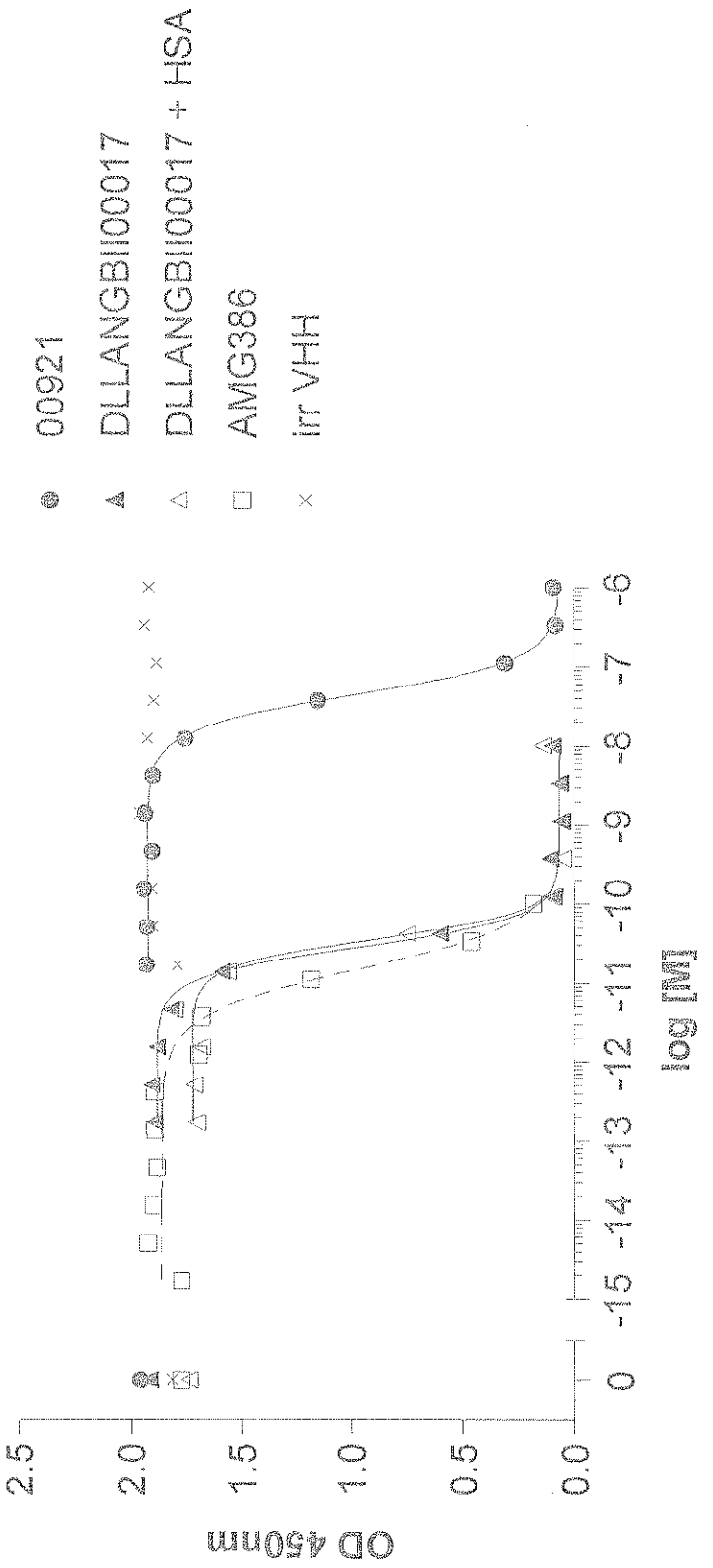

00921
DLLANGBI00017
DLLANGBI00017 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-3B

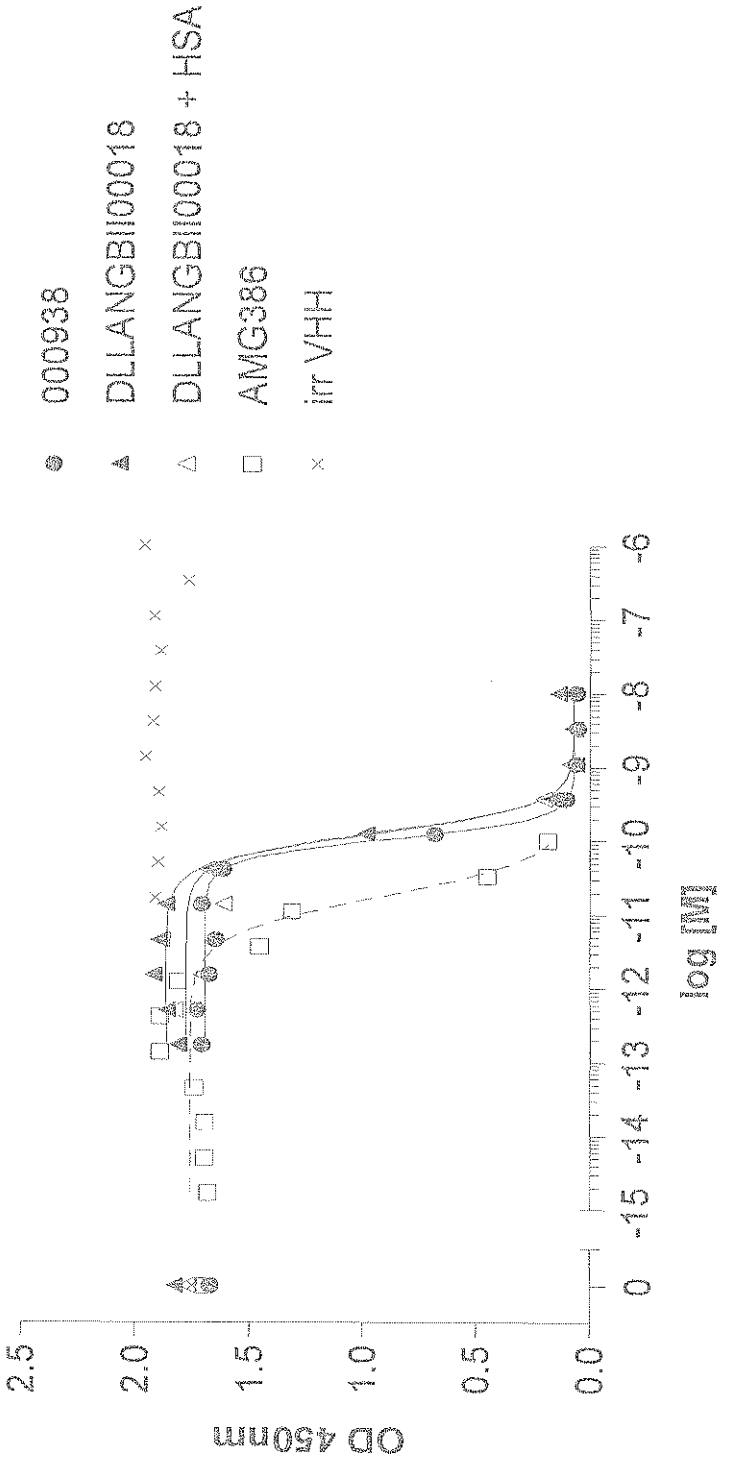

000938
DLLANGBI000018
DLLANGBI000018 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-3C

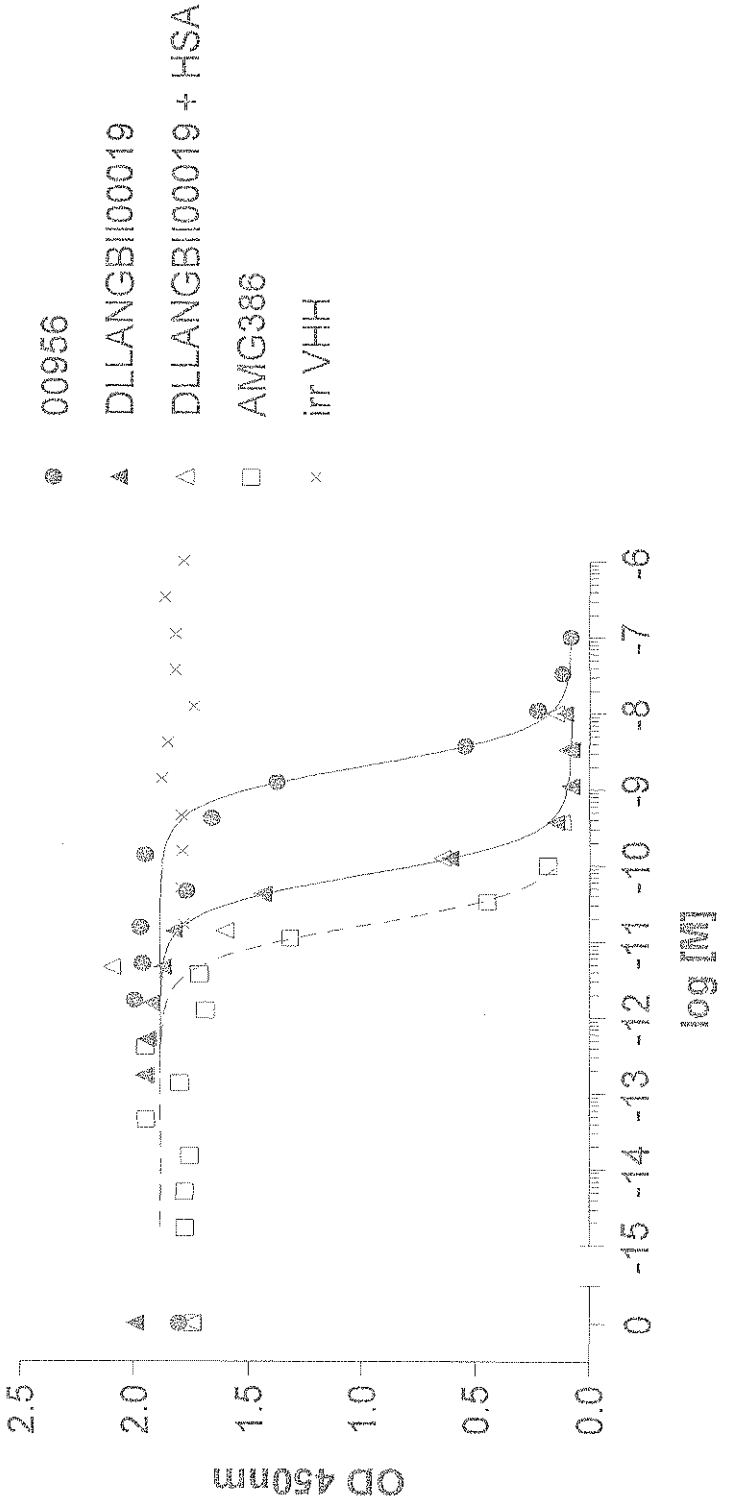

00956
DLLANGBI00019
DLLANGBI00019 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log M

Figure 31A

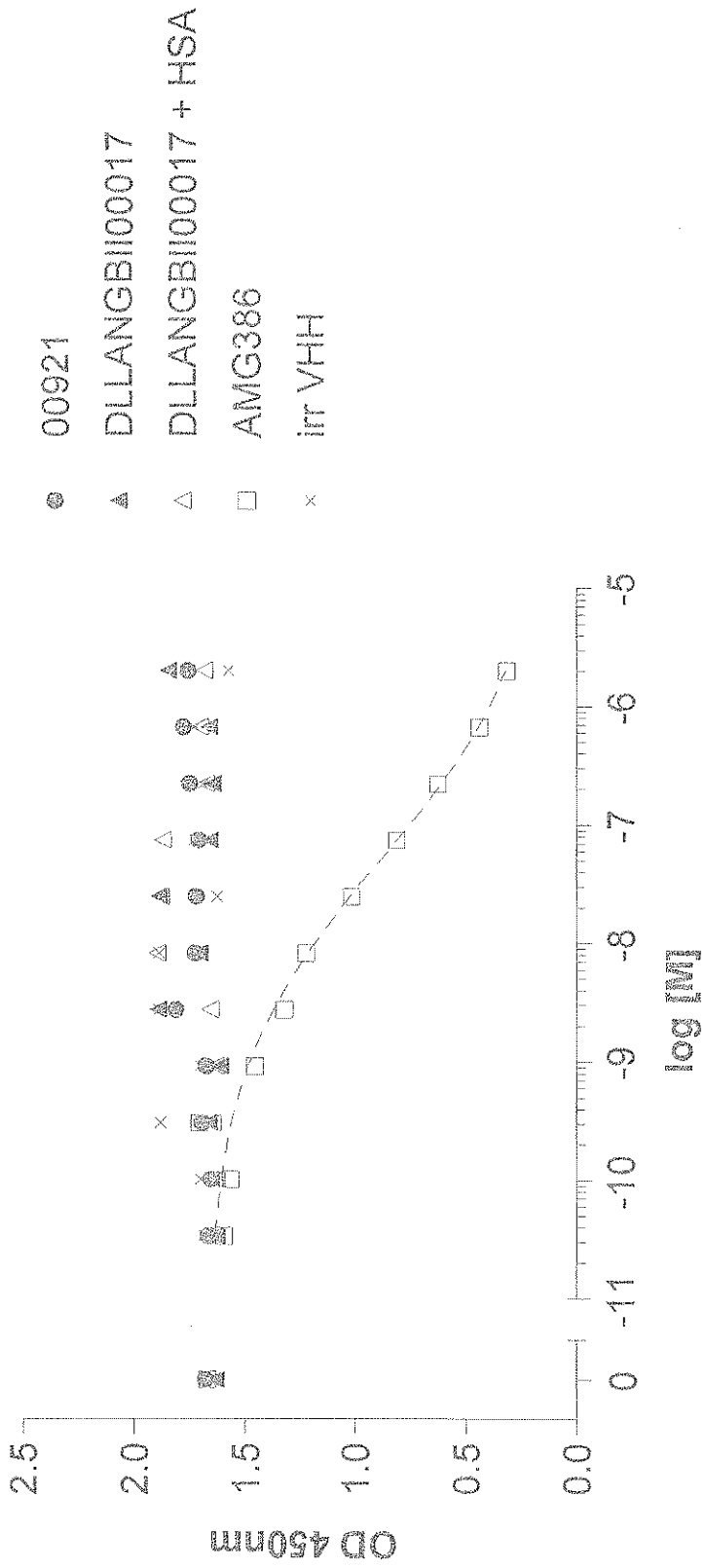

00921
DLLANGBI00017
DLLANGBI00017 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-5
-6
-7
-8
-9
-10
-11
log [M]

Figure 31B

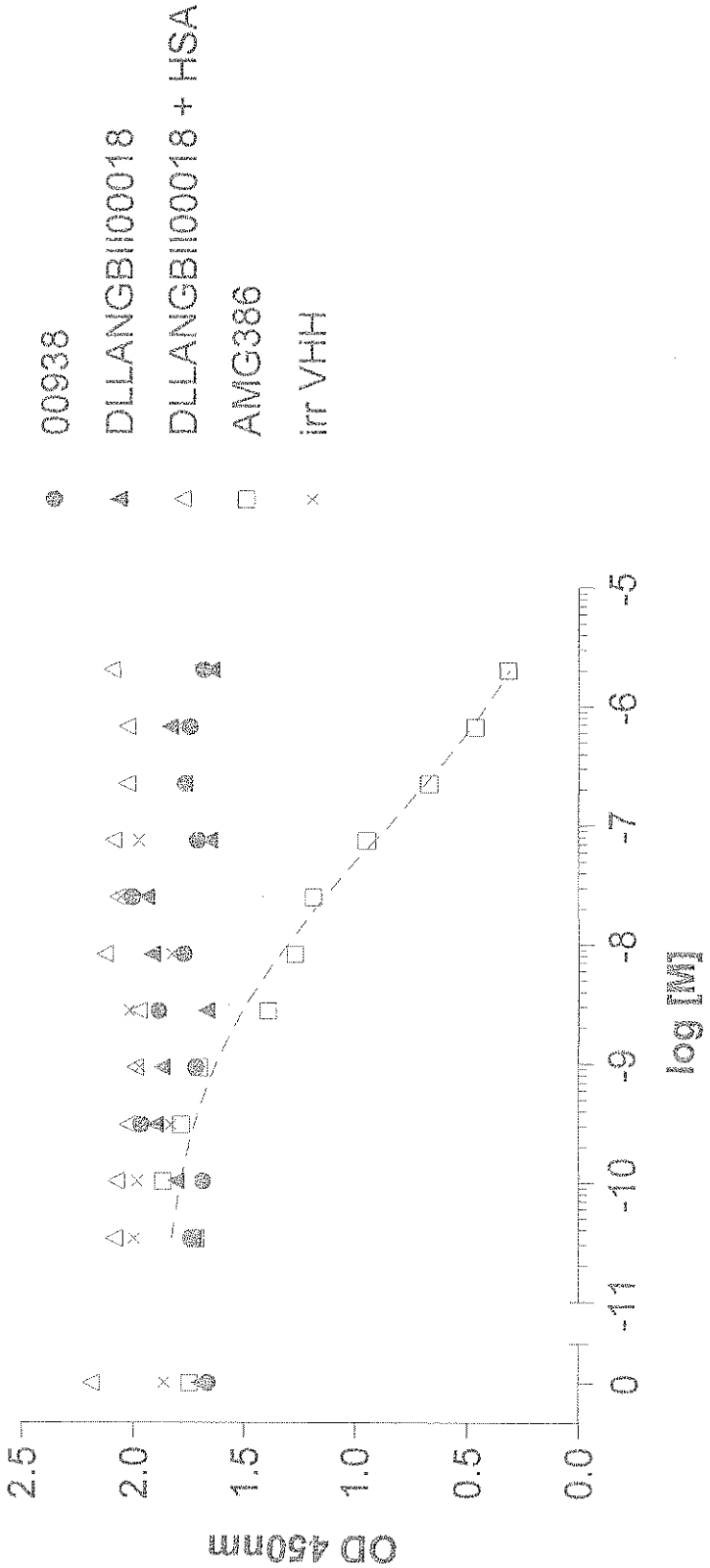

00938
DLLANGBI00018
DLLANGBI00018 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-5
-6
-7
-8
-9
-10
-11
log M1

Figure 31C

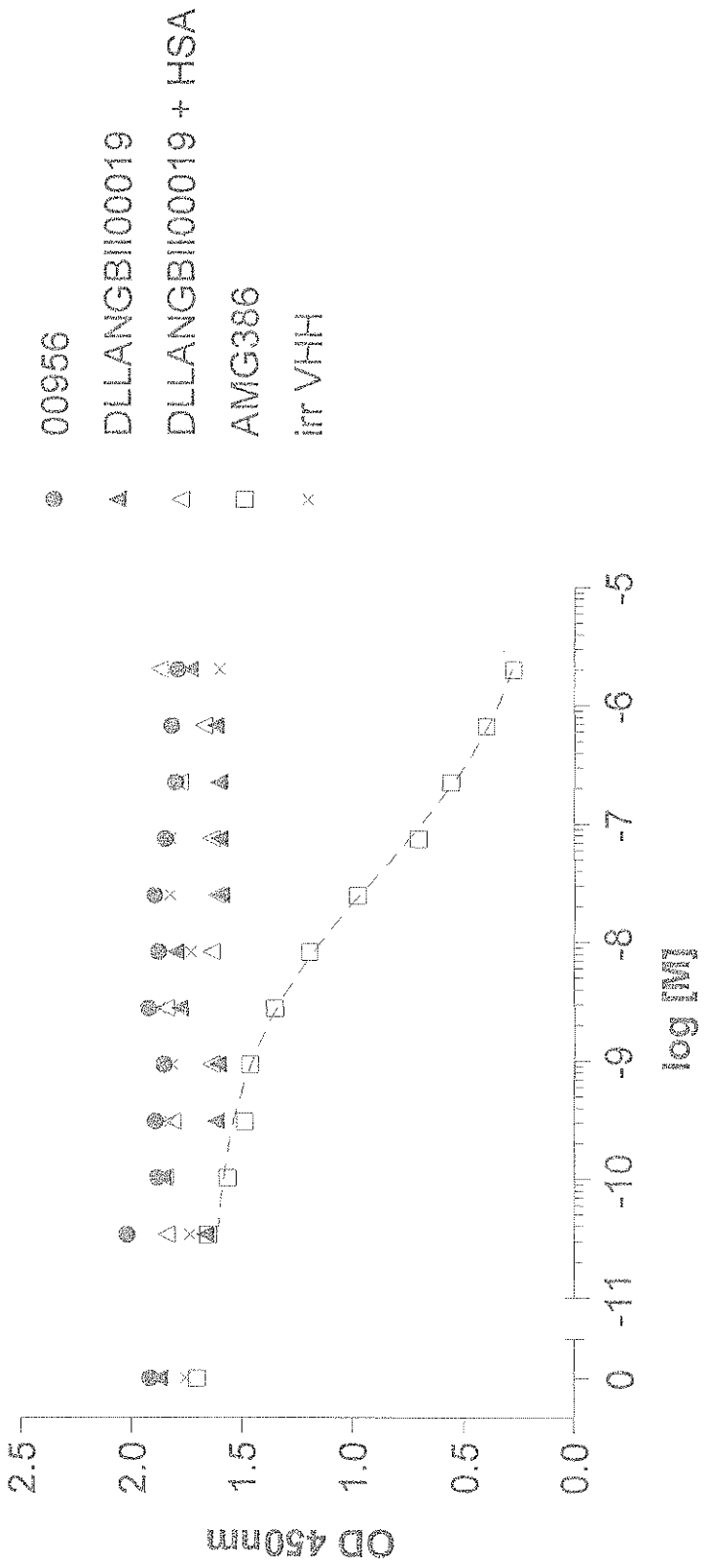

00956
DLLANGBI00019
DLLANGBI00019 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
-5
log [M]

Figure 32A

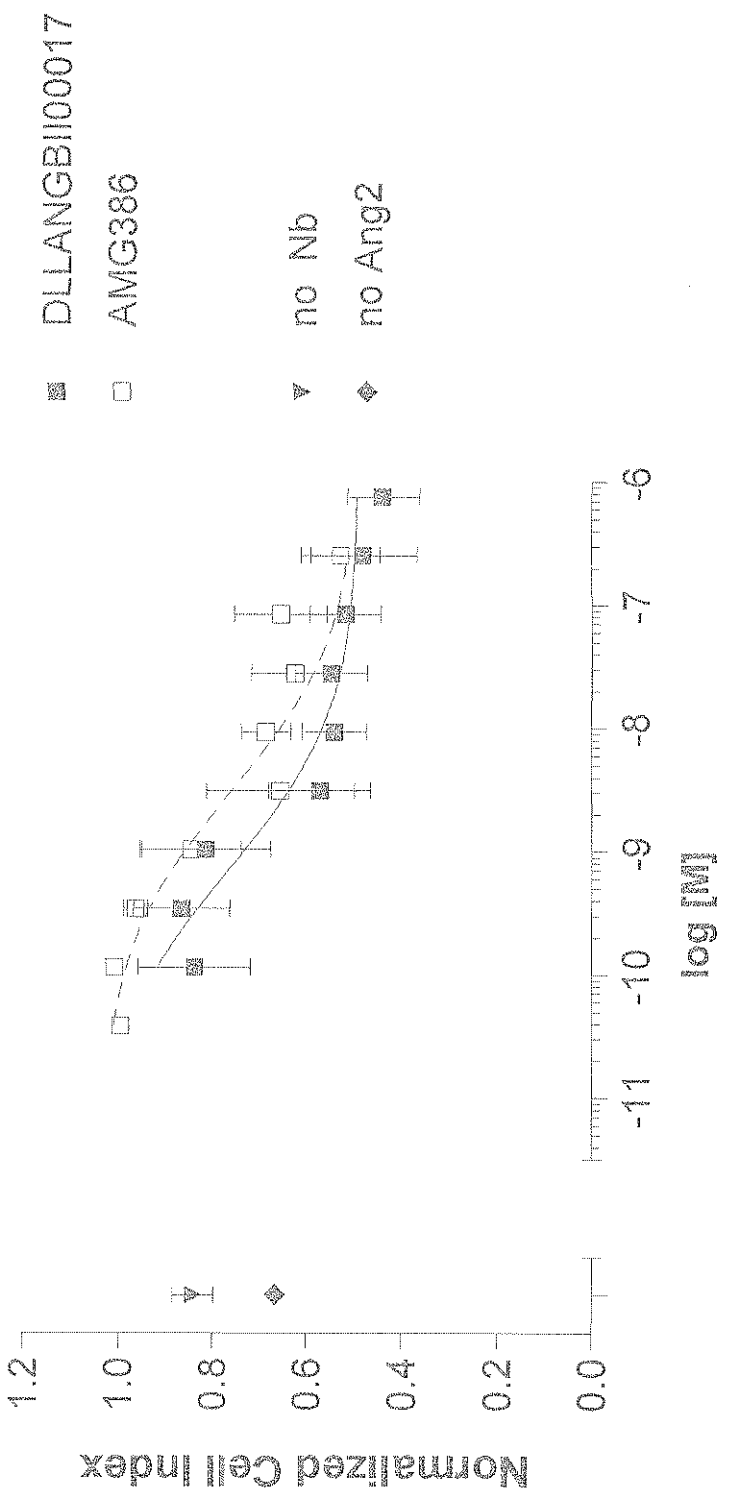

DLLANGBI00017
AMG386
no Nb
no Ang2
Normalized Cell Index
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-6
-7
-8
-9
-10
-11
log [M]

Figure 32B

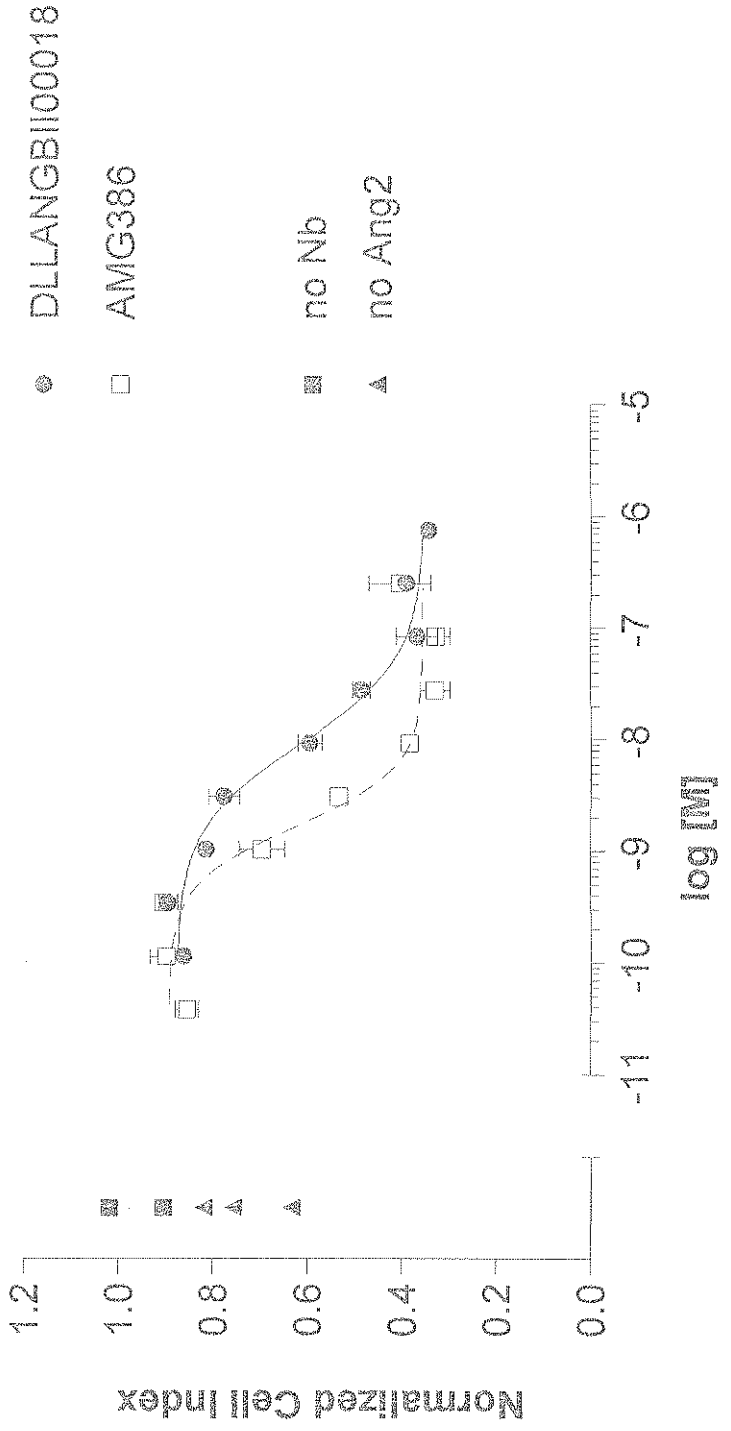
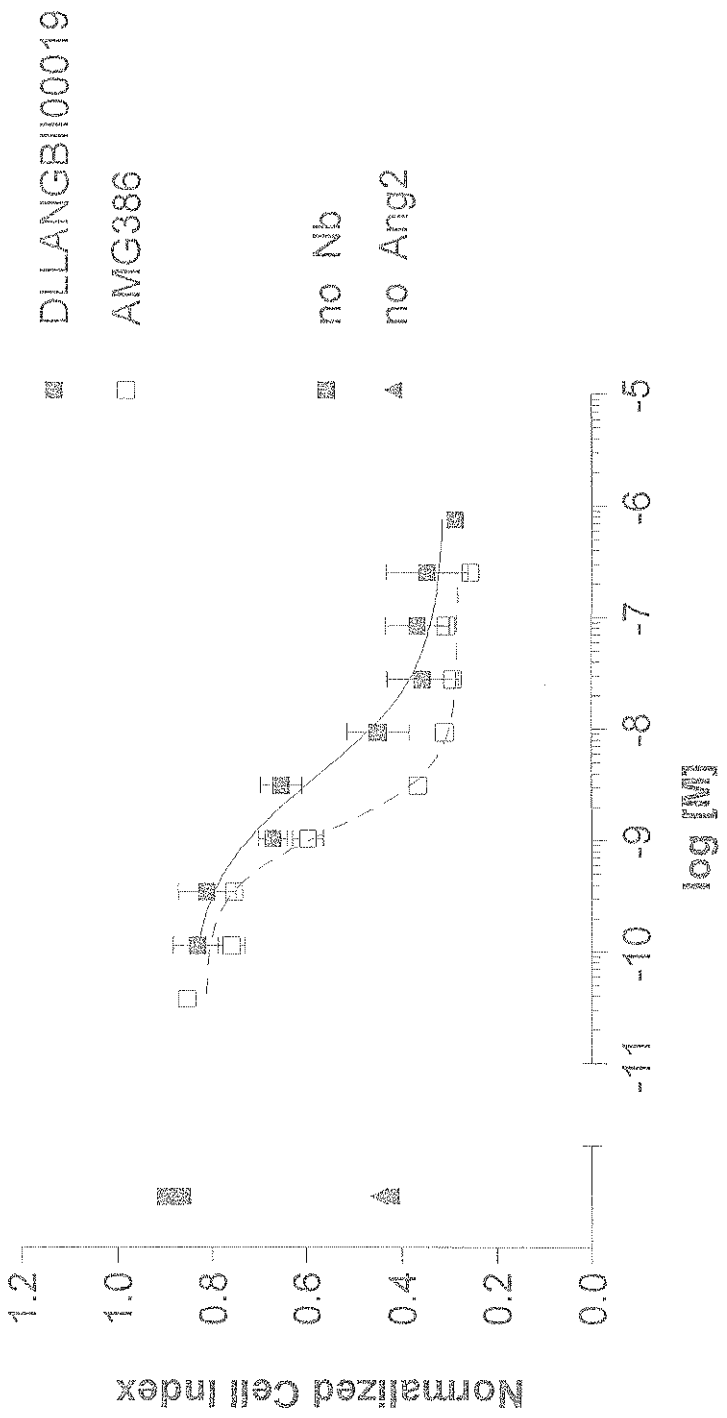

DLLANGBI00018
AMG386
no Nb
no Ang2
Normalized Cell Index
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-11
-10
-9
-8
-7
-6
-5
log [M]

Figure 32C


DLLANGBI00019
AMG386
no Nb
no Ang2
Normalized Cell Index
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-5
-6
-7
-8
-9
-10
-11
log [M]