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Fig. 1

```
                1                                                   100
DLL4 human    (1) MAAASRSASGWALLLLVALWQQRAAGSGVFQLQLQEFTNERGVLASGRPCEPGCRTFFRVCLKHFQAVVSPGPCTFGTVSTPVLGTNSFAVRDDSSGGGR
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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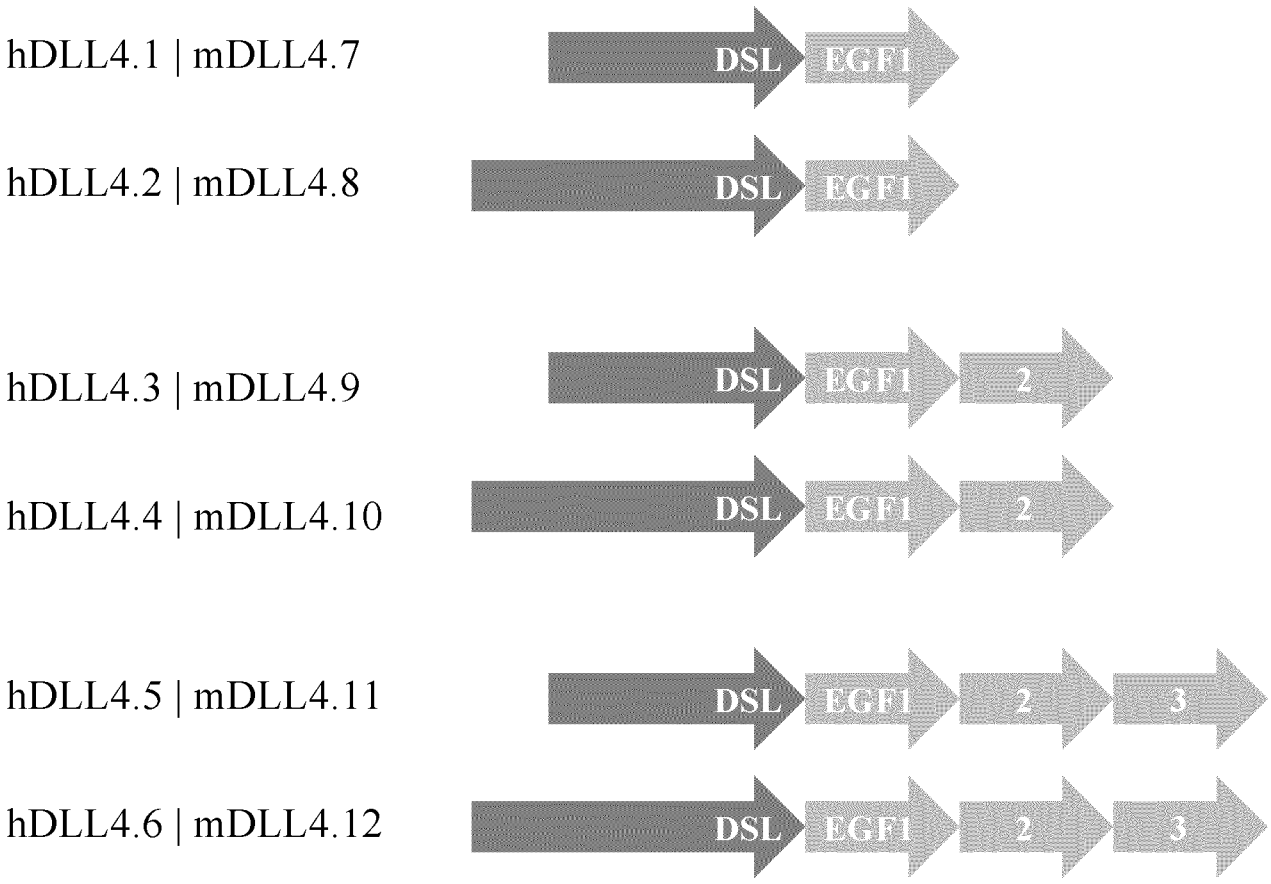
Fig. 2

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: $DSL^{1152-218} – EGF1^{219-252} – EGF2^{252-282} – EGF3^{285-323} – (His)6$



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Fig. 3-1

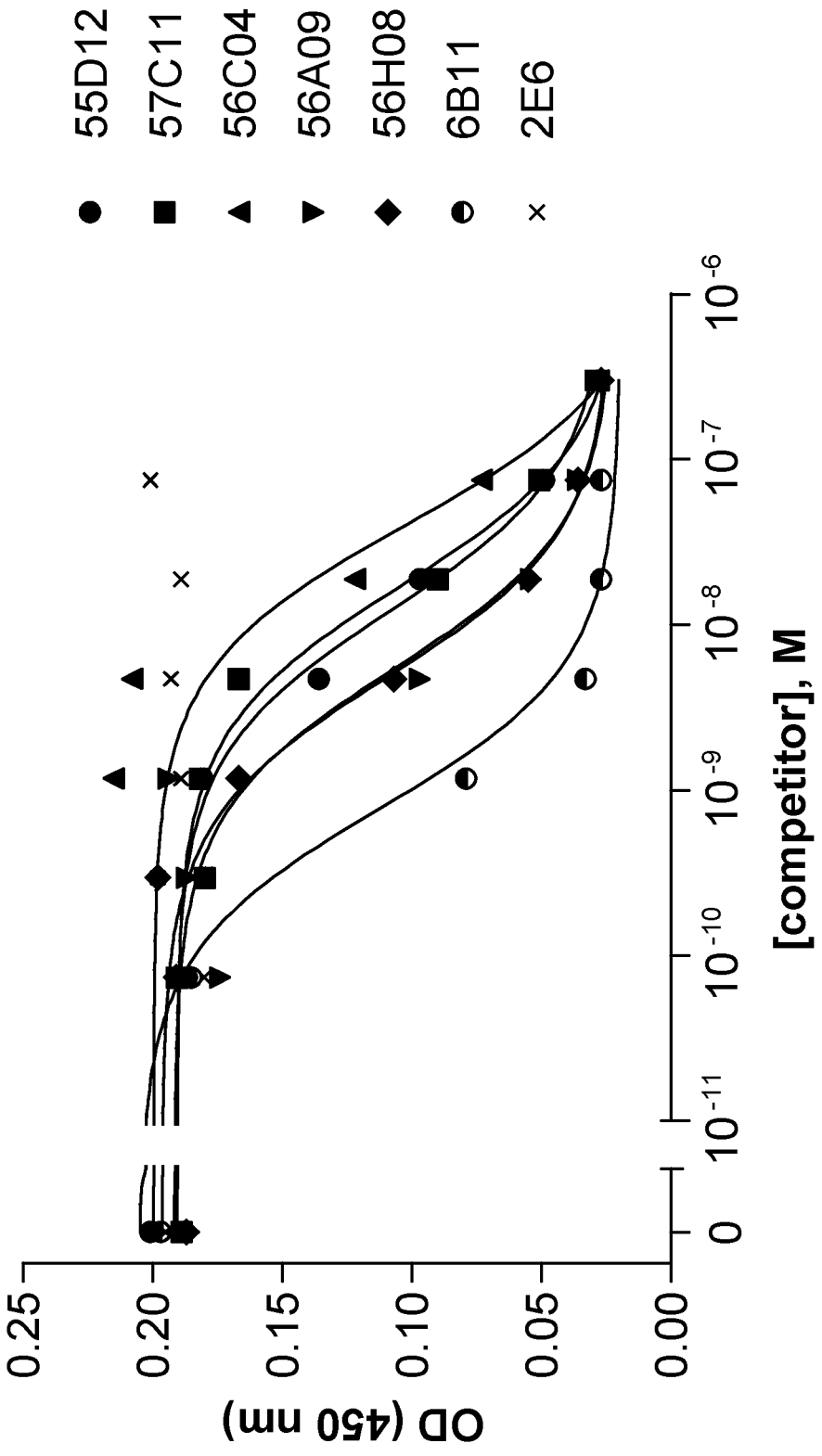

55D12
57C11
56C04
56A09
56H08
6B11
2E6
OD (450 nm)
0.25
0.20
0.15
0.10
0.05
0.00
0
10-11
10-10
10-9
10-8
10-7
10-6
[competitor], M

Fig. 3-2

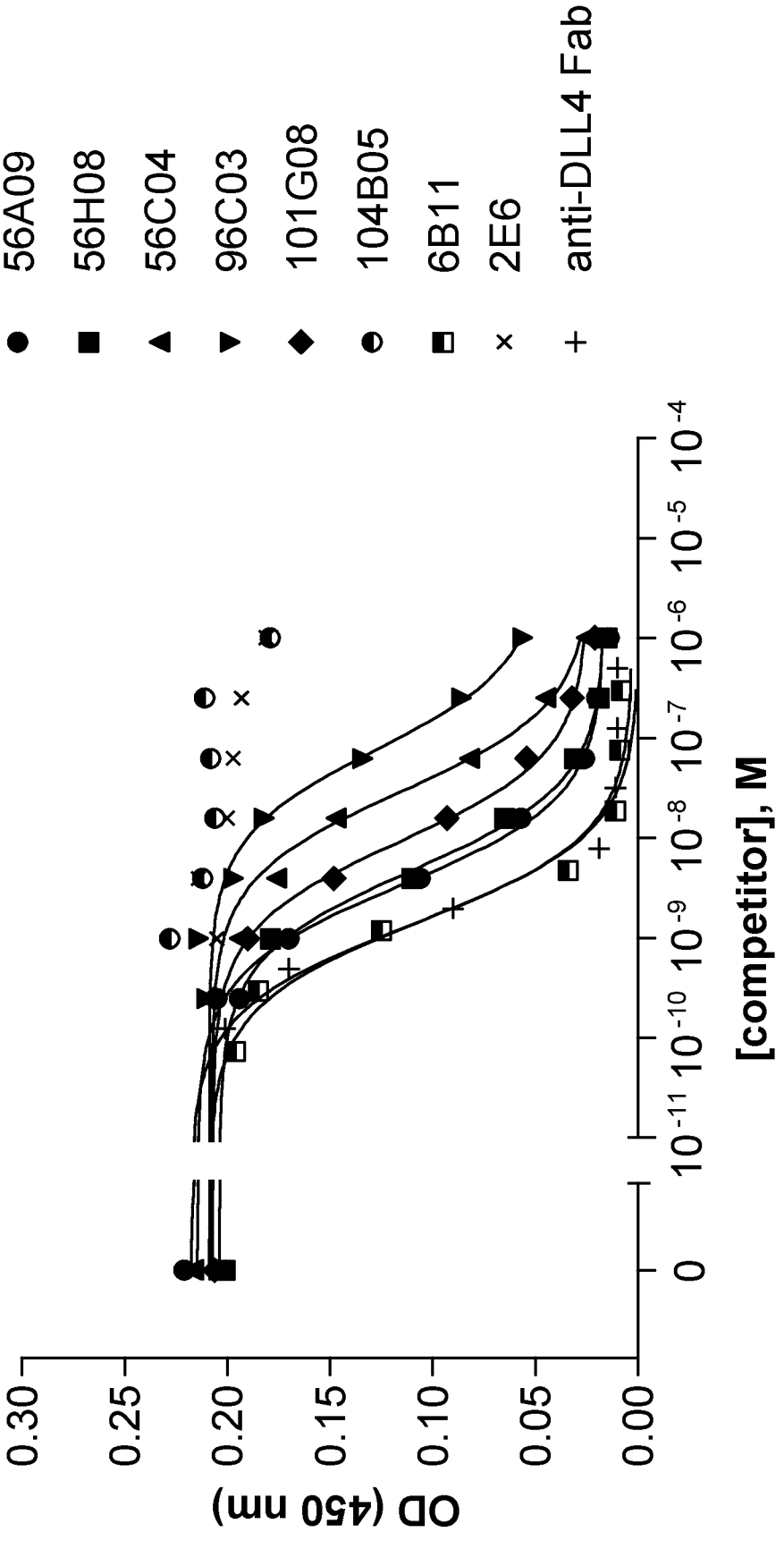

56A09
56H08
56C04
96C03
101G08
104B05
6B11
2E6
anti-DLL4 Fab
OD (450 nm)
0.30
0.25
0.20
0.15
0.10
0.05
0.00
0
10-11
10-10
10-9
10-8
10-7
10-6
10-5
10-4
[competitor], M

Fig. 3-3

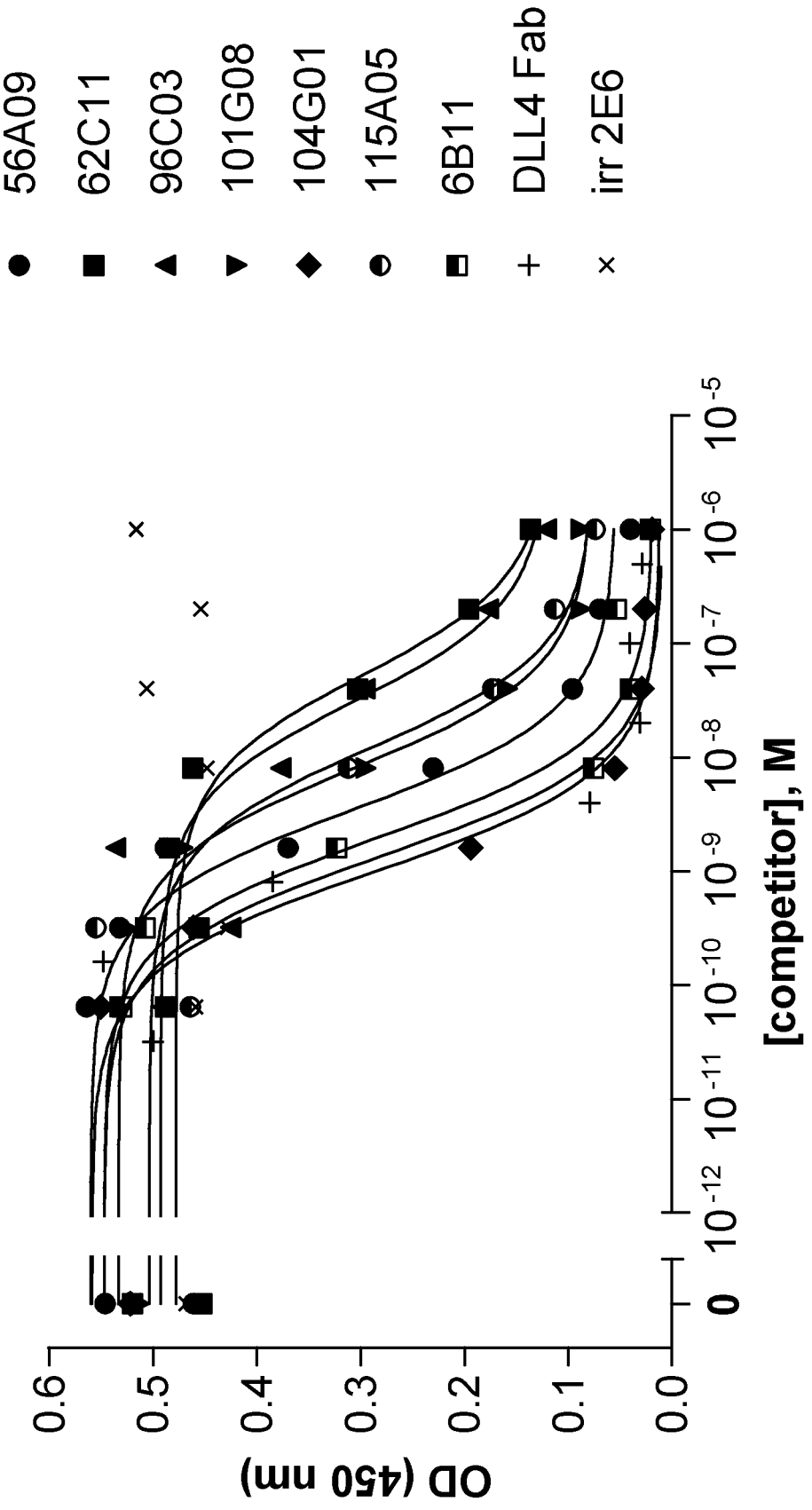

56A09
62C11
96C03
101G08
104G01
115A05
6B11
DLL4 Fab
irr 2E6
OD (450 nm)
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[competitor], M

Fig. 4-1

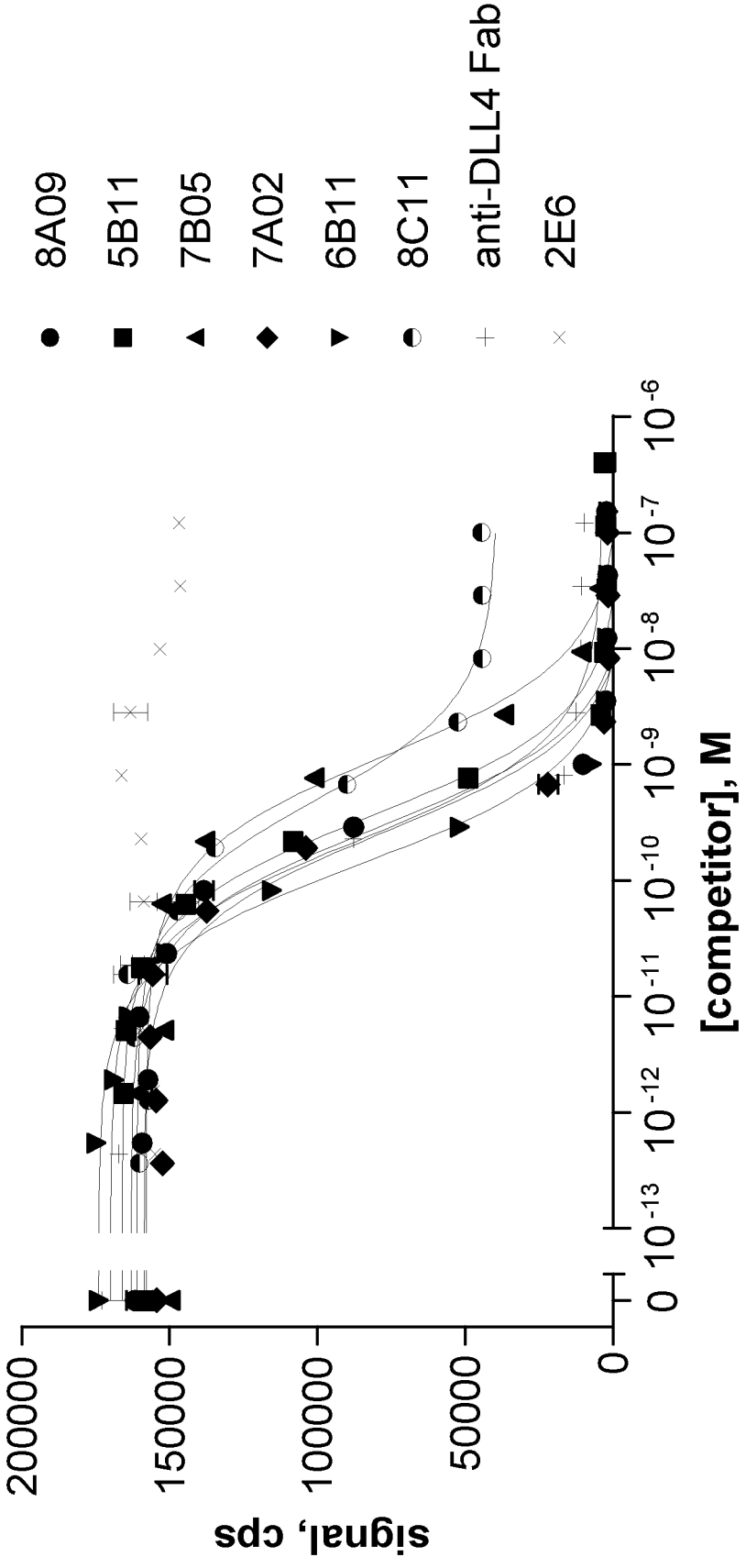

8A09
5B11
7B05
7A02
6B11
8C11
anti-DLL4 Fab
2E6
signal, cps
200000
150000
100000
50000
0
0
10-13
10-12
10-11
10-10
10-9
10-8
10-7
10-6
[competitor], M

Fig. 4-2

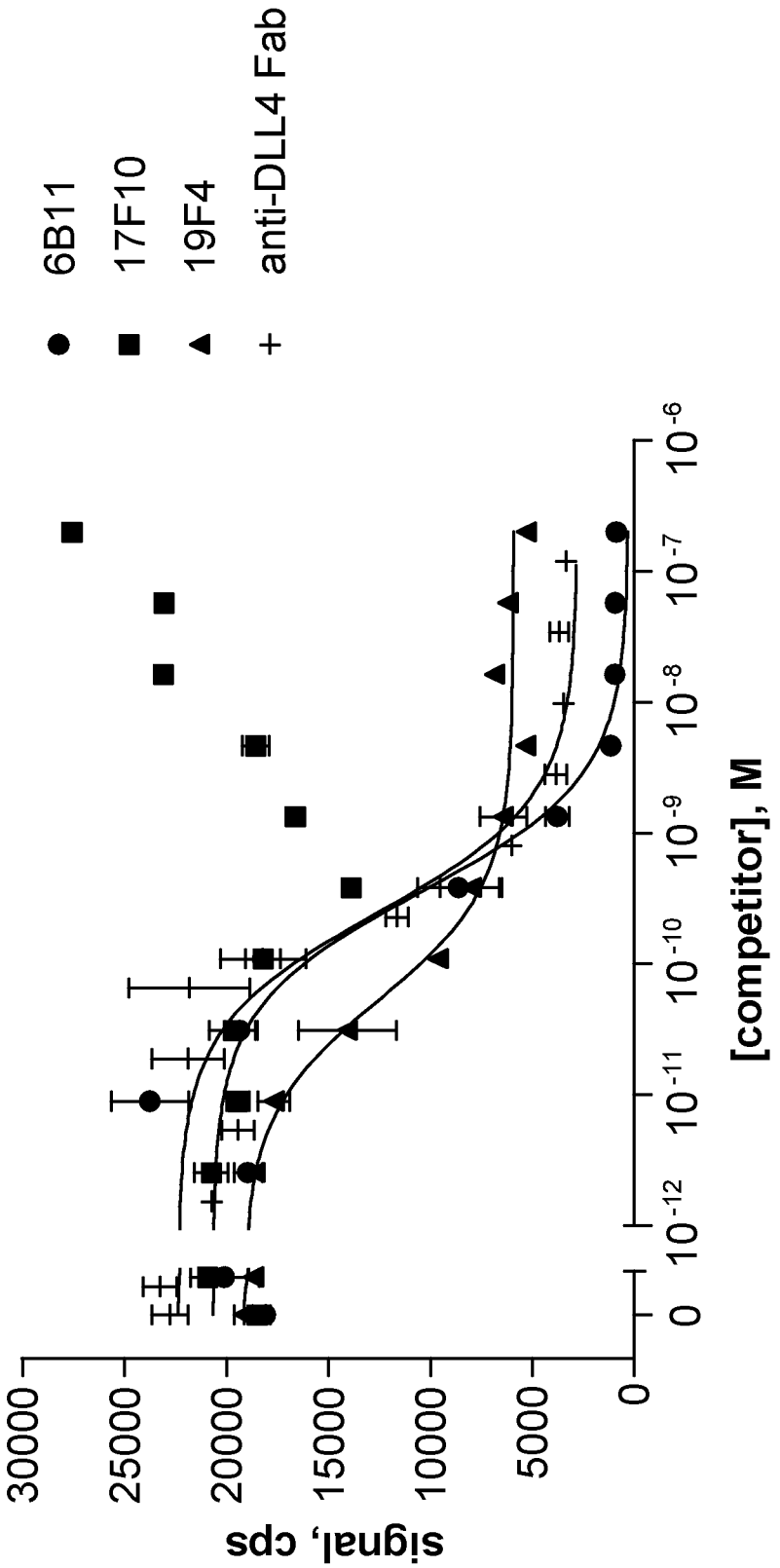

6B11
17F10
19F4
anti-DLL4 Fab
signal, cps
30000
25000
20000
15000
10000
5000
0
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
[competitor], M

Fig. 4-3

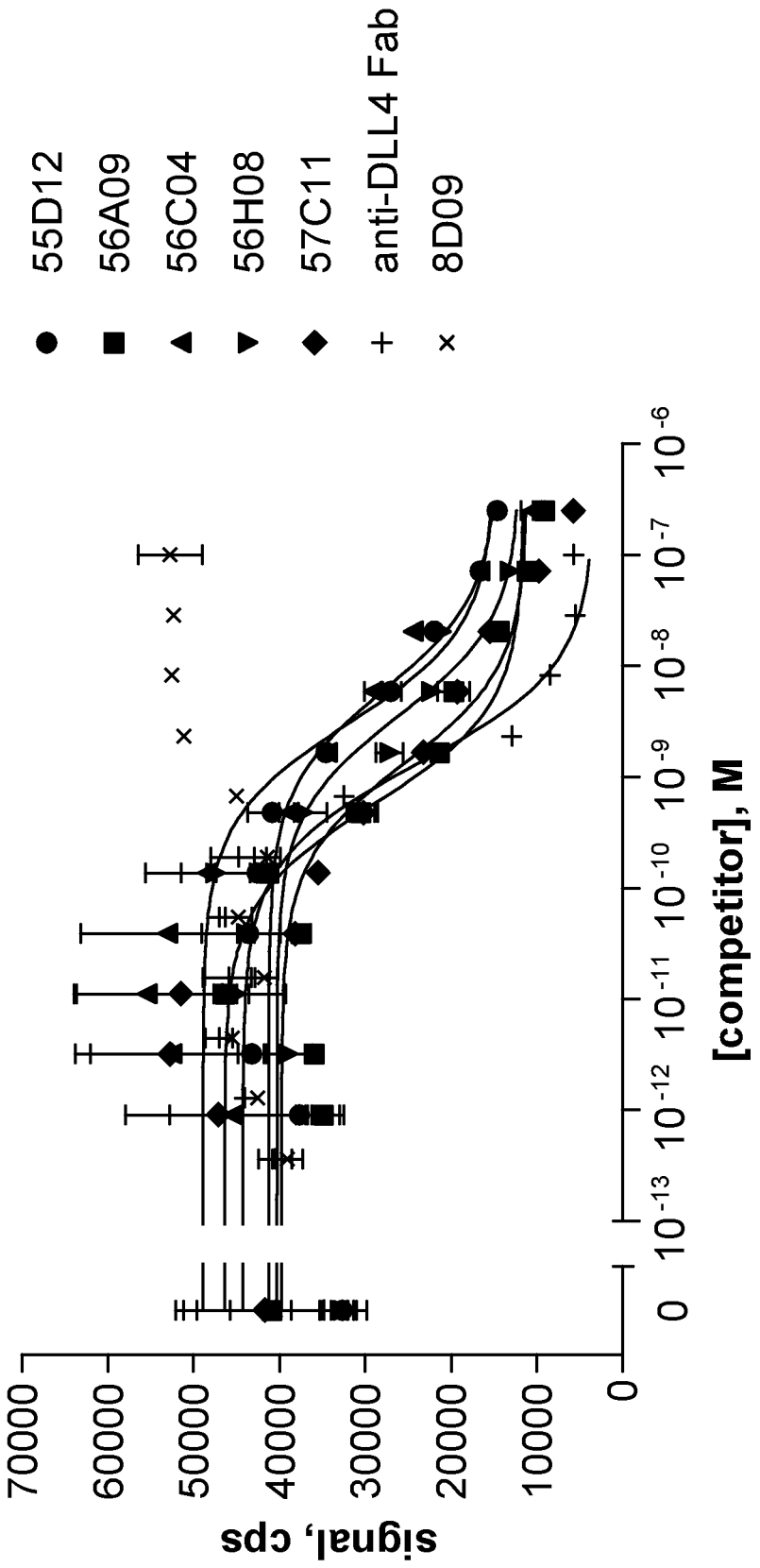

55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab
8D09
signal, cps
0
10000
20000
30000
40000
50000
60000
70000
0
10^-13
10^-12
10^-11
10^-10
10^-9
10^-8
10^-7
10^-6
[competitor], M

Fig. 4-4

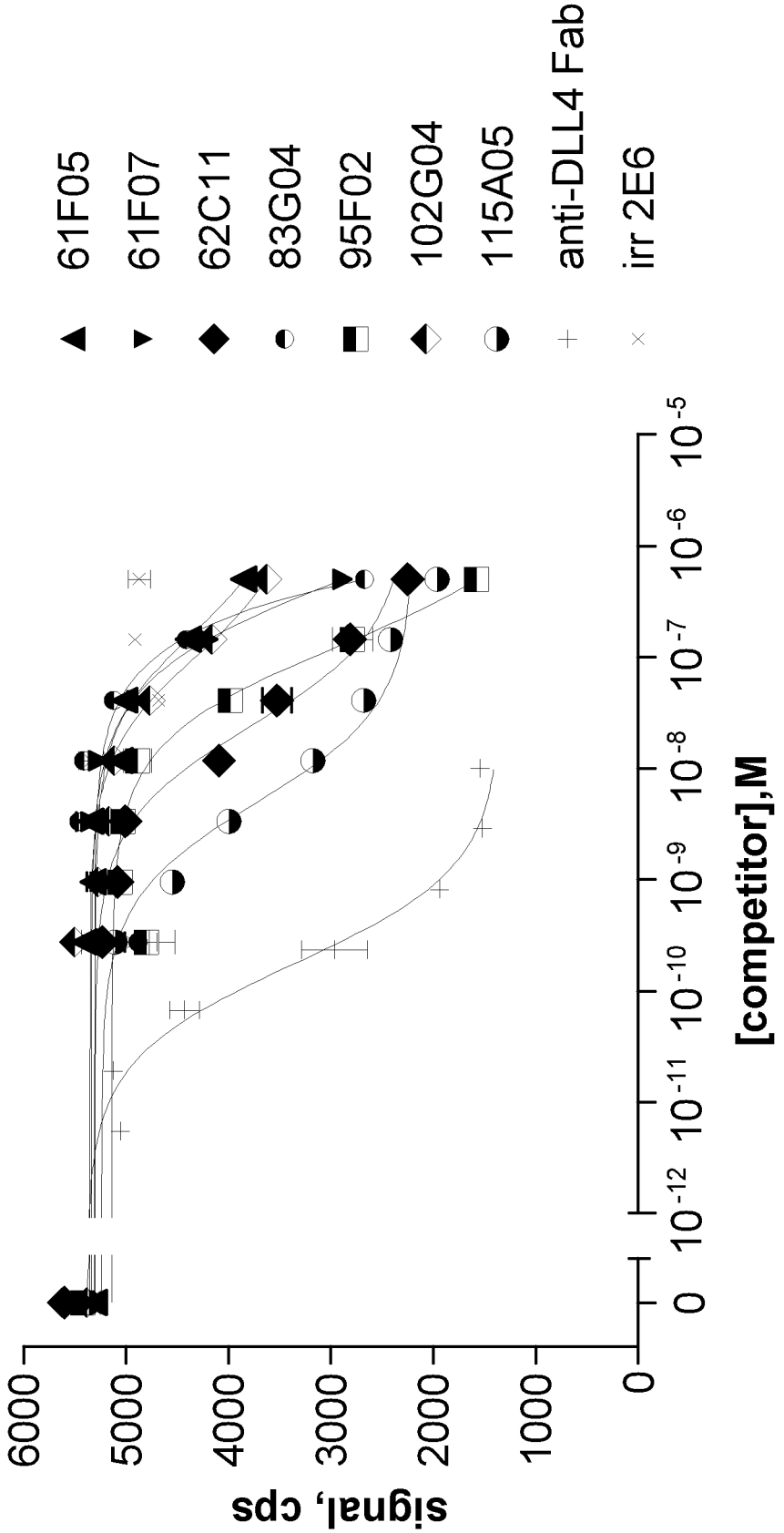

61F05
61F07
62C11
83G04
95F02
102G04
115A05
anti-DLL4 Fab
irr 2E6
signal, cps
6000
5000
4000
3000
2000
1000
0
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[competitor],M

Fig. 4-5

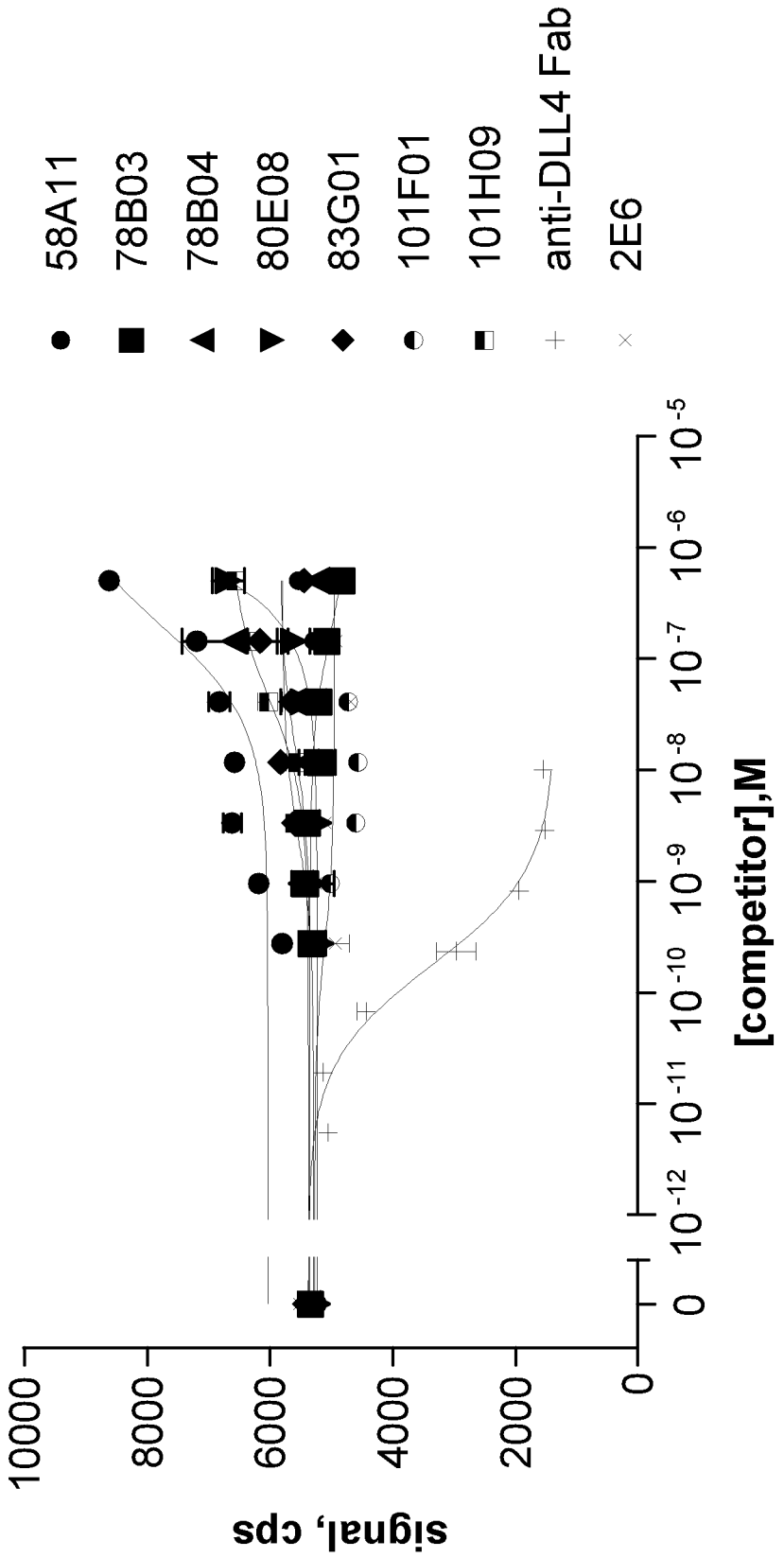

58A11
78B03
78B04
80E08
83G01
101F01
101H09
anti-DLL4 Fab
2E6
signal, cps
10000
8000
6000
4000
2000
0
0
10-12
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[competitor],M

Fig. 5-1

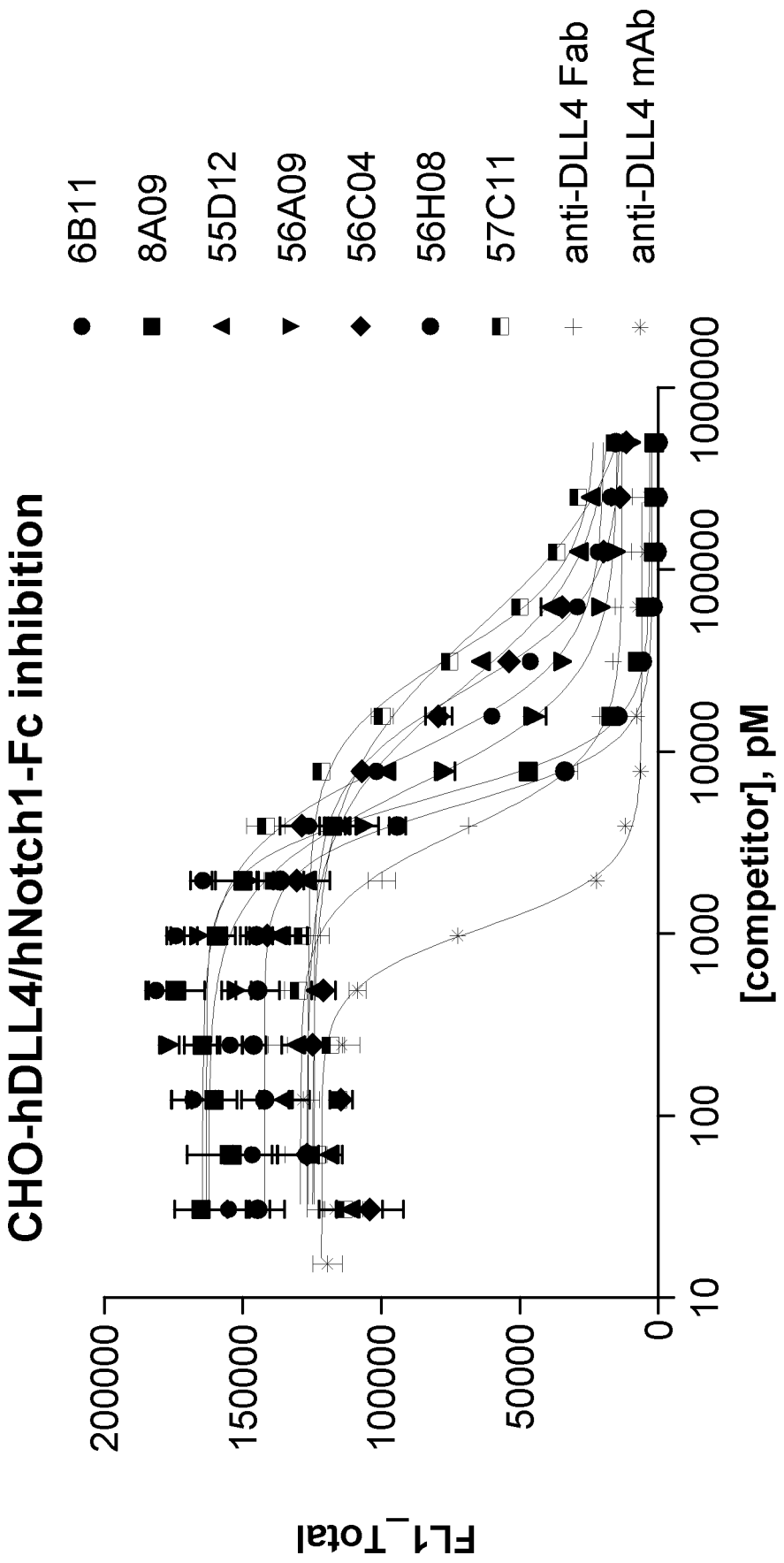
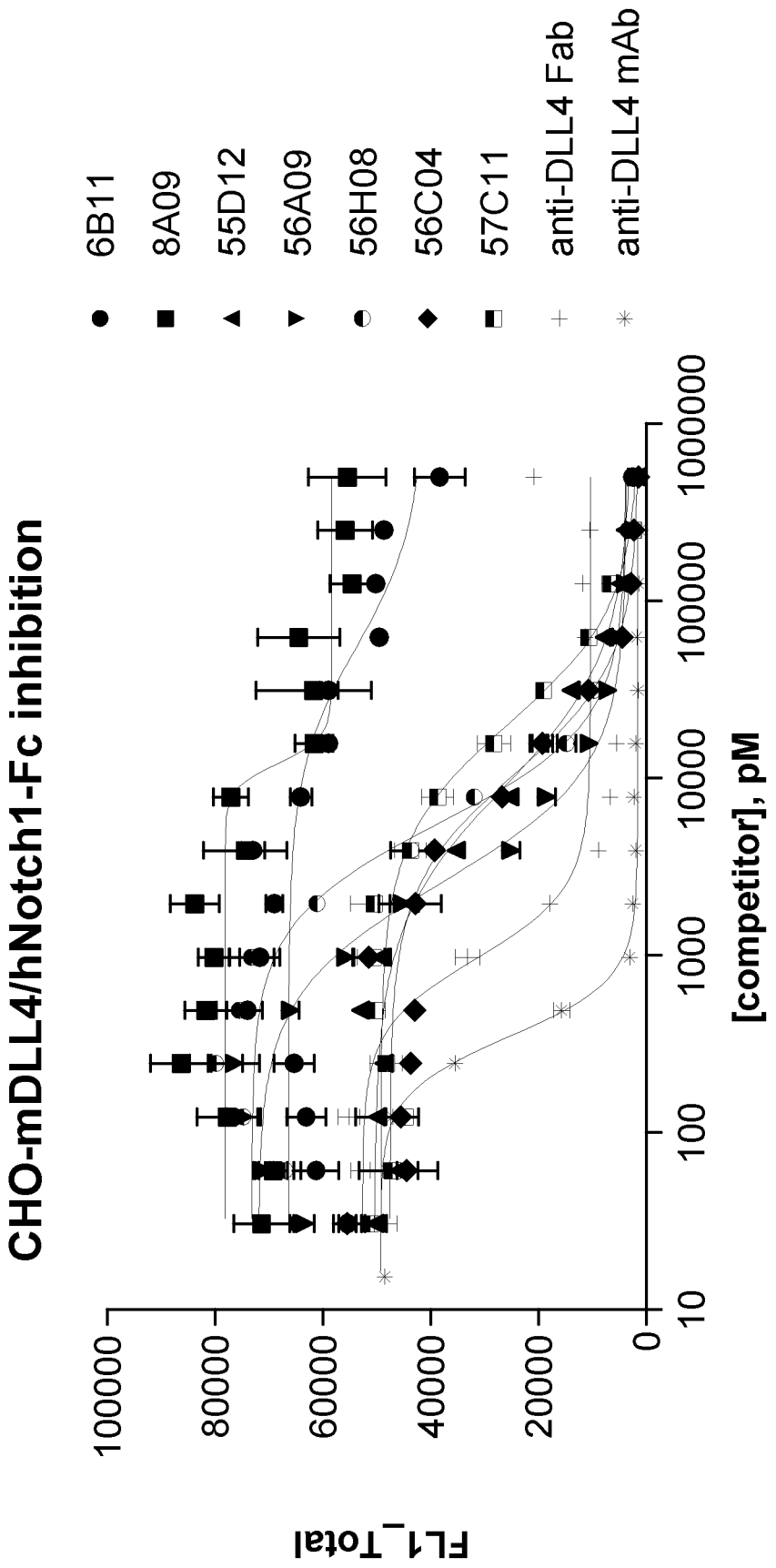

CHO-hDLL4/hNotch1-Fc inhibition
6B11
8A09
55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab
anti-DLL4 mAb
FL1_Total
200000
150000
100000
50000
0
10
100
1000
10000
100000
1000000
[competitor], pM

Fig. 5-2


CHO-mDLL4/hNotch1-Fc inhibition
6B11
8A09
55D12
56A09
56H08
56C04
57C11
anti-DLL4 Fab
anti-DLL4 mAb
FL1_Total
100000
80000
60000
40000
20000
0
10
100
1000
10000
100000
1000000
[competitor], pM

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Fig. 5-3

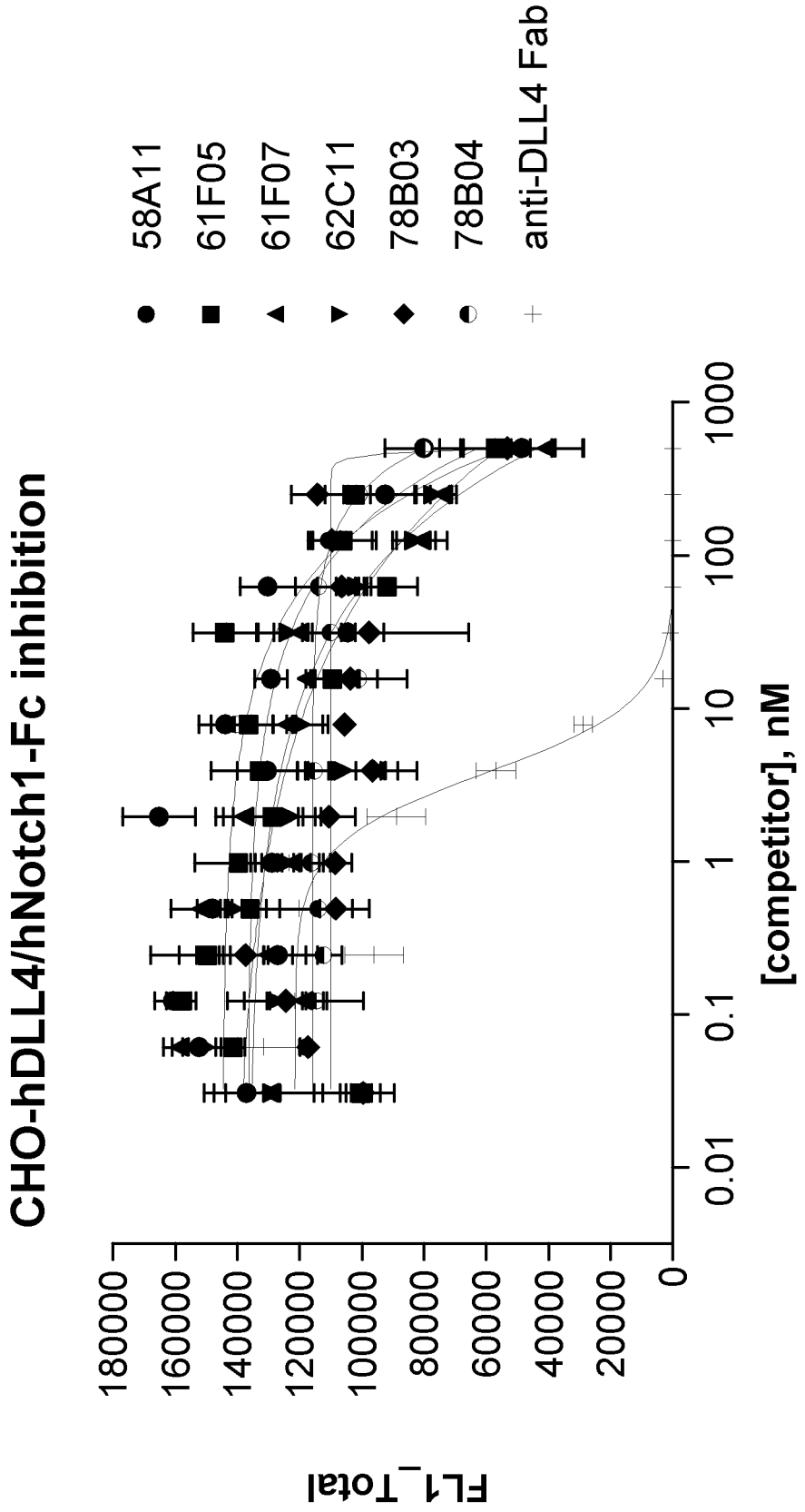

CHO-hDLL4/hNotch1-Fc inhibition
58A11
61F05
61F07
62C11
78B03
78B04
anti-DLL4 Fab
FL1_Total
[competitor], nM
0
20000
40000
60000
80000
100000
120000
140000
160000
180000
0.01
0.1
1
10
100
1000

Fig. 5-4

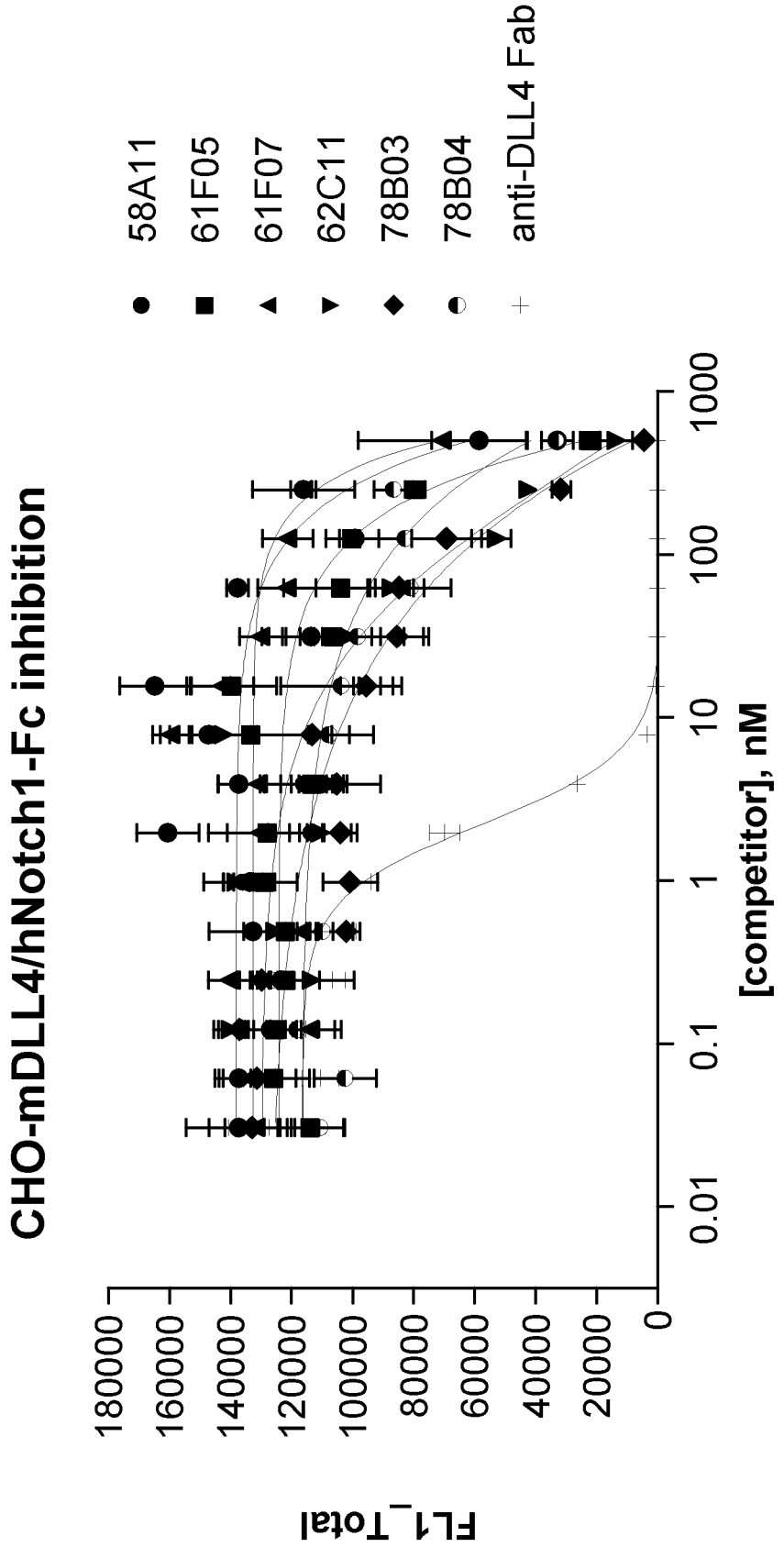

CHO-mDLL4/hNotch1-Fc inhibition
58A11
61F05
61F07
62C11
78B03
78B04
anti-DLL4 Fab
FL1_Total
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
0.01
0.1
1
10
100
1000
[competitor], nM

Fig. 5-5

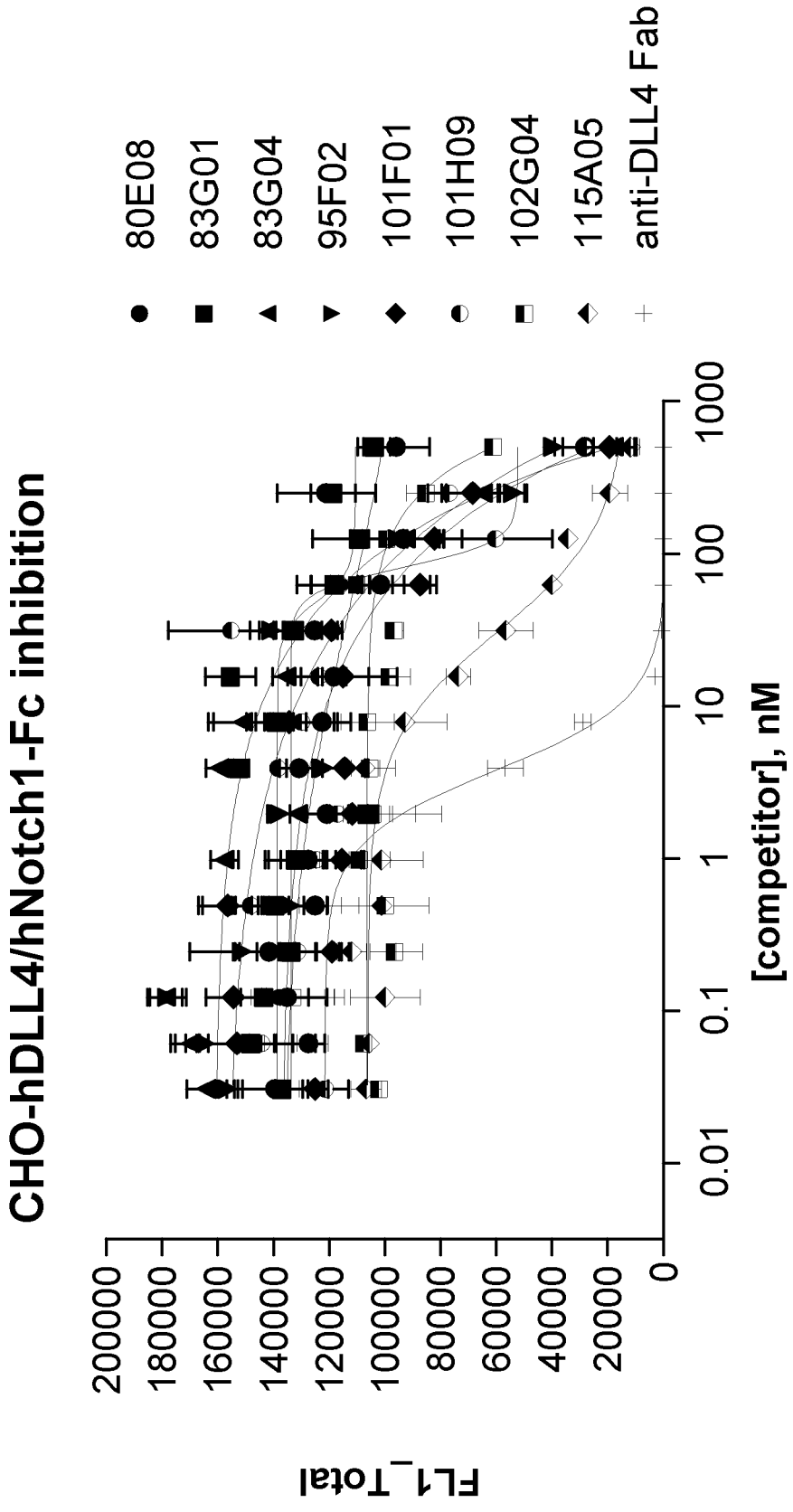
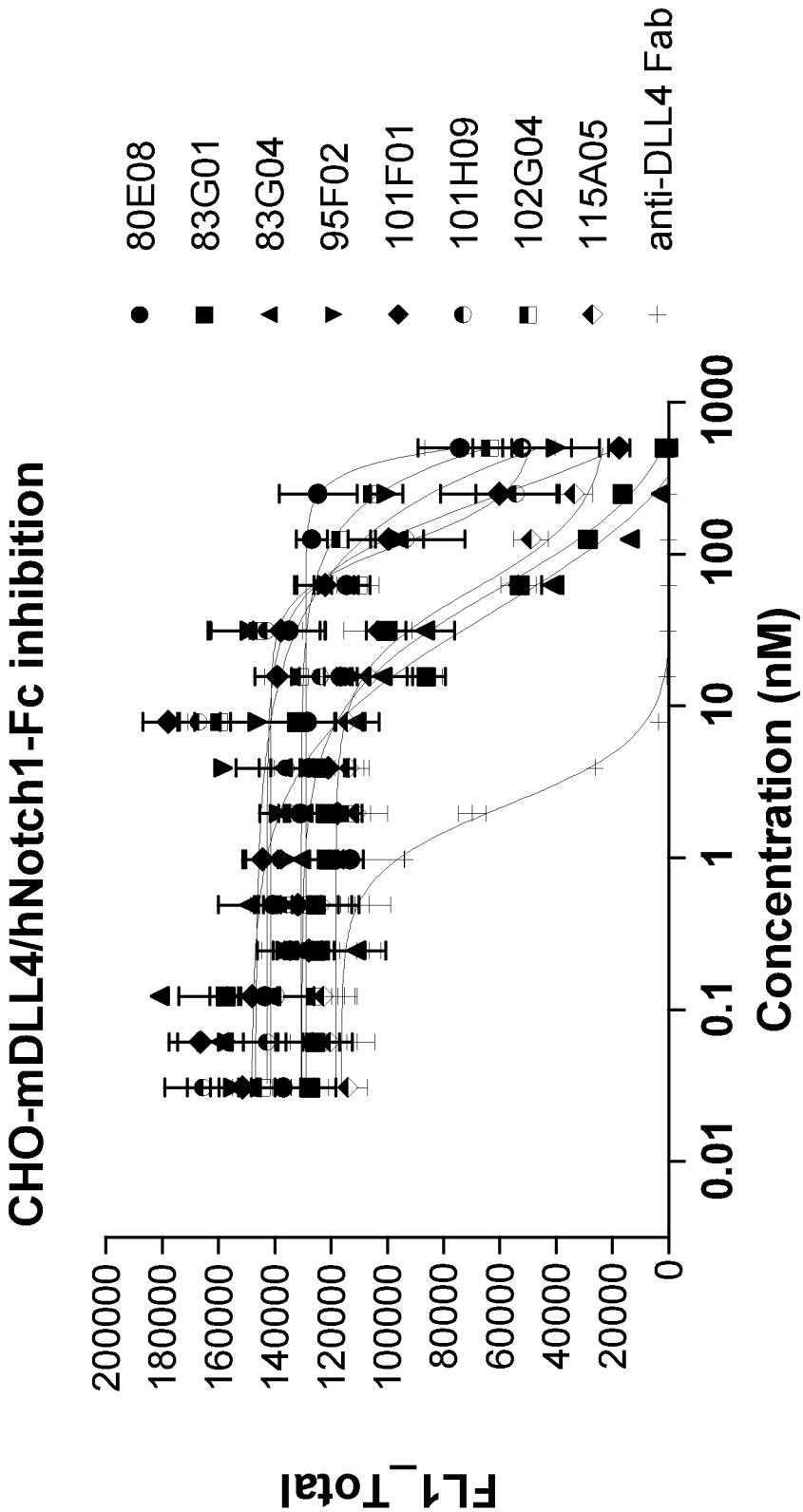

CHO-hDLL4/hNotch1-Fc inhibition
80E08
83G01
83G04
95F02
101F01
101H09
102G04
115A05
anti-DLL4 Fab
FL1_Total
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
0.01
0.1
1
10
100
1000
[competitor], nM

Fig. 5-6


CHO-mDLL4/hNotch1-Fc inhibition
80E08
83G01
83G04
95F02
101F01
101H09
102G04
115A05
anti-DLL4 Fab
FL1_Total
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
0.01
0.1
1
10
100
1000
Concentration (nM)

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Fig. 5-7

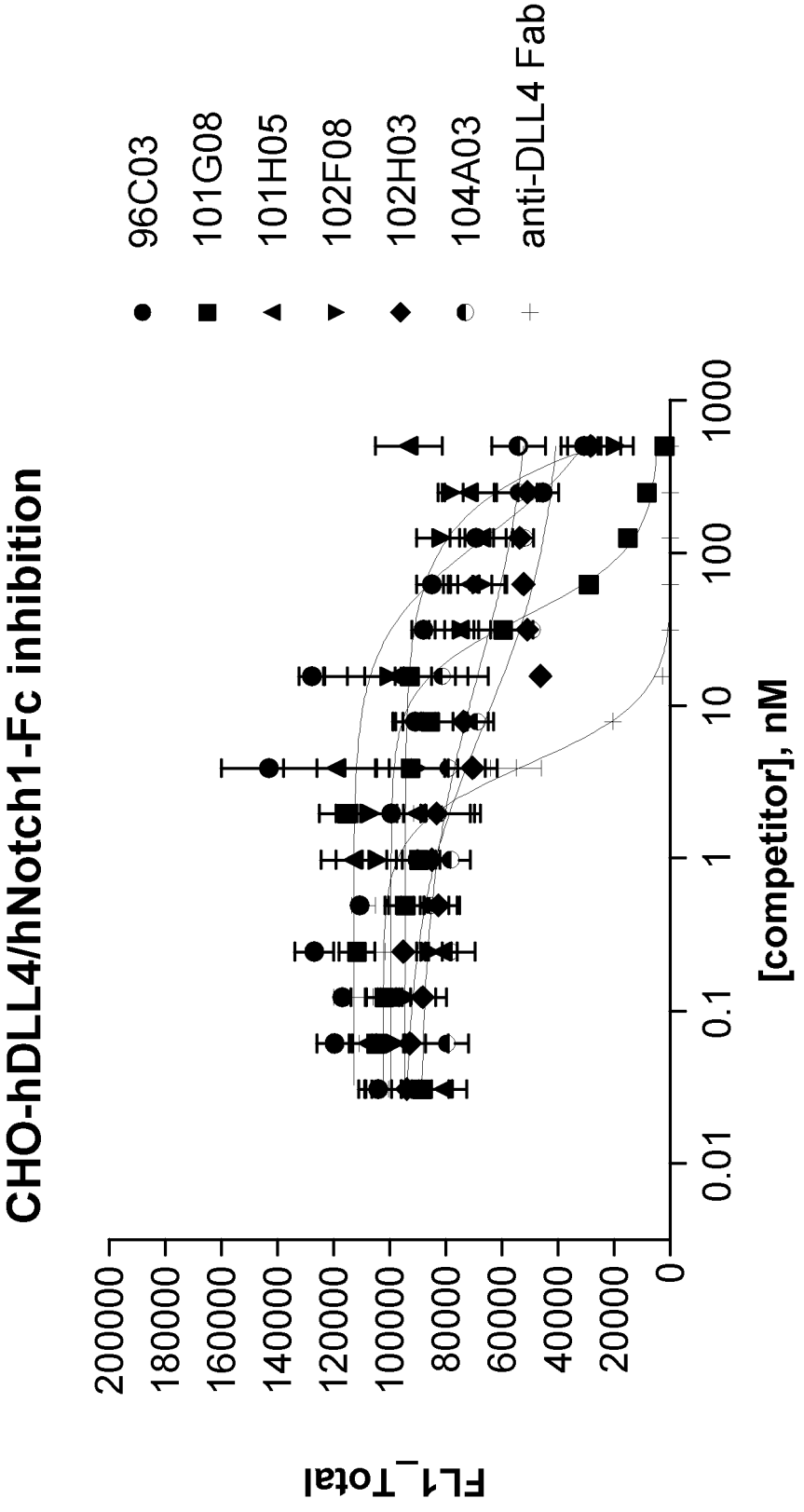

CHO-hDLL4/hNotch1-Fc inhibition
96C03
101G08
101H05
102F08
102H03
104A03
anti-DLL4 Fab
FL1_Total
[competitor], nM
0
20000
40000
60000
80000
100000
120000
140000
160000
180000
200000
0.01
0.1
1
10
100
1000

Fig. 5-8

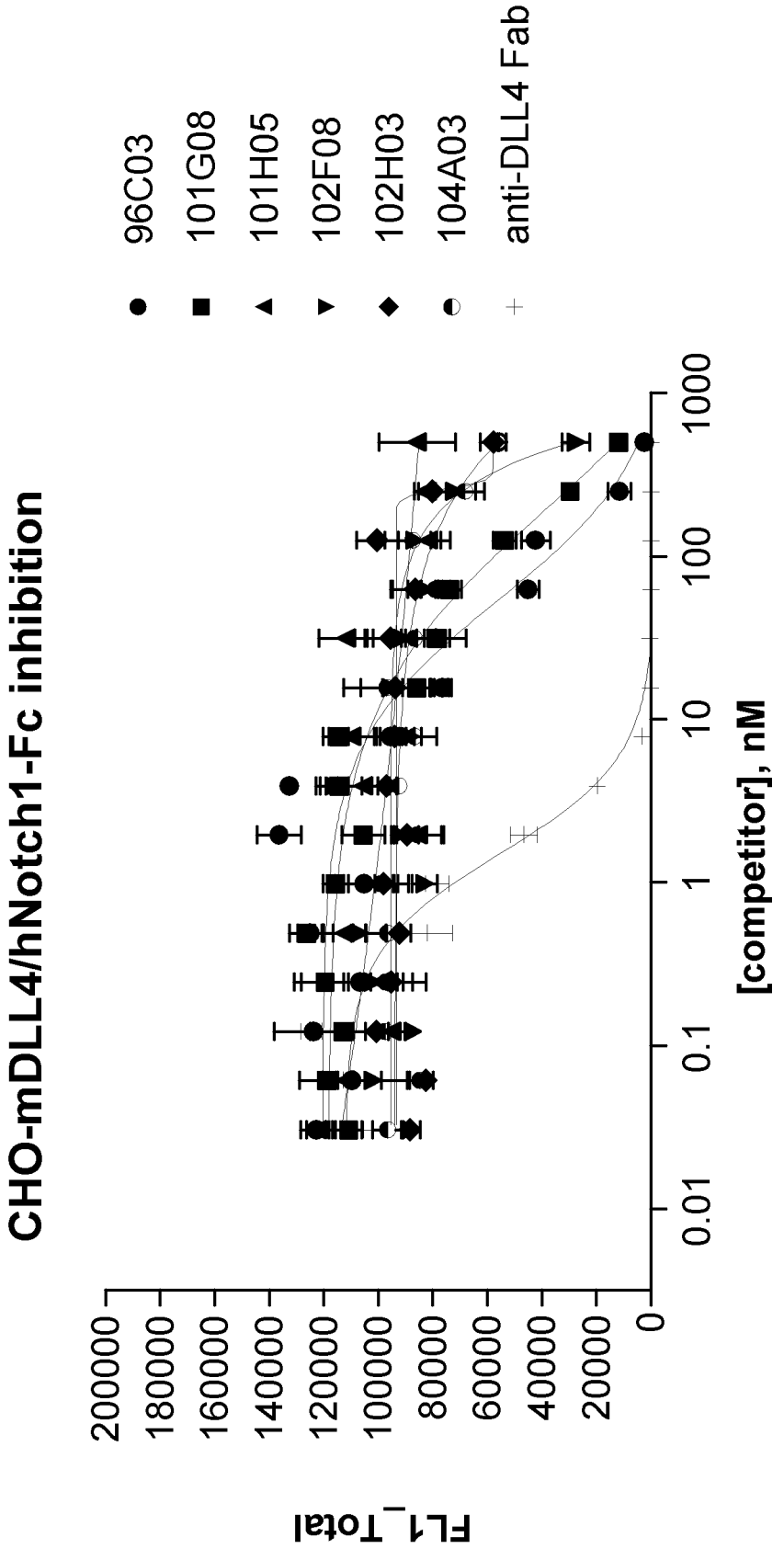

CHO-mDLL4/hNotch1-Fc inhibition
96C03
101G08
101H05
102F08
102H03
104A03
anti-DLL4 Fab
FL1_Total
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
0.01
0.1
1
10
100
1000
[competitor], nM

Fig. 5-9

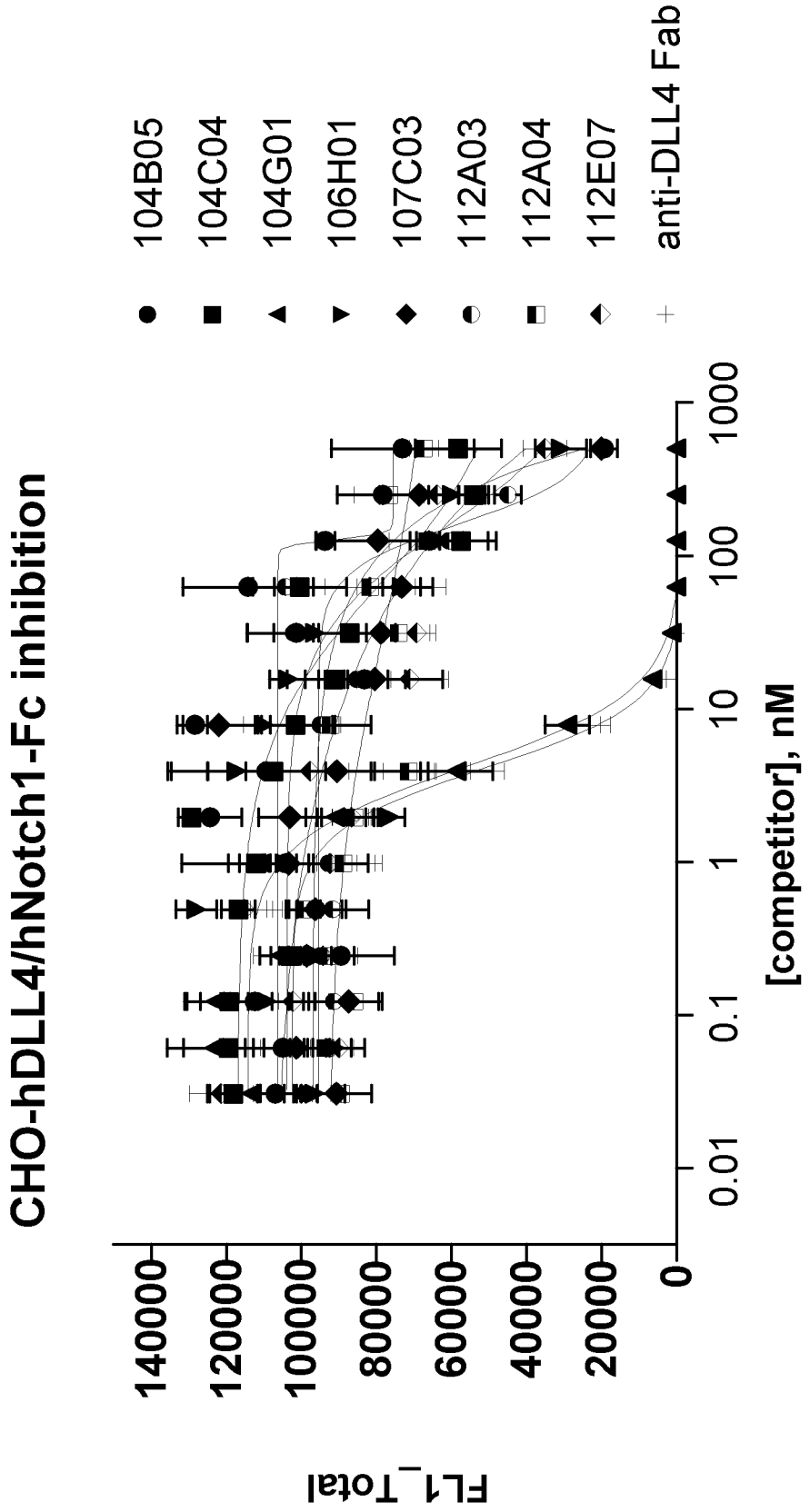

CHO-hDLL4/hNotch1-Fc inhibition
104B05
104C04
104G01
106H01
107C03
112A03
112A04
112E07
anti-DLL4 Fab
FL1_Total
140000
120000
100000
80000
60000
40000
20000
0
0.01
0.1
1
10
100
1000
[competitor], nM

Fig. 5-10

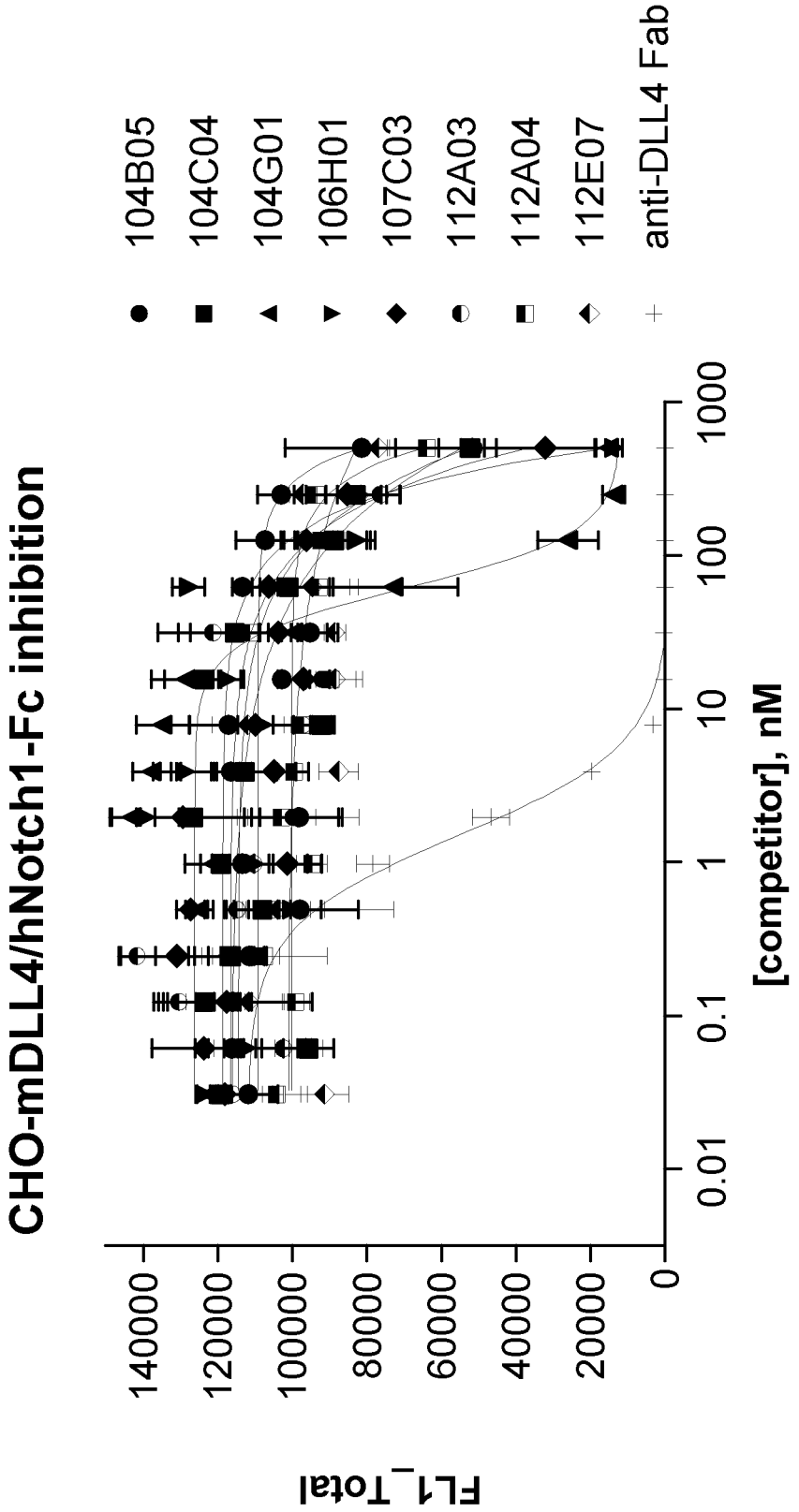

CHO-mDLL4/hNotch1-Fc inhibition
104B05
104C04
104G01
106H01
107C03
112A03
112A04
112E07
anti-DLL4 Fab
FL1_Total
140000
120000
100000
80000
60000
40000
20000
0
0.01
0.1
1
10
100
1000
[competitor], nM

Fig. 6-1

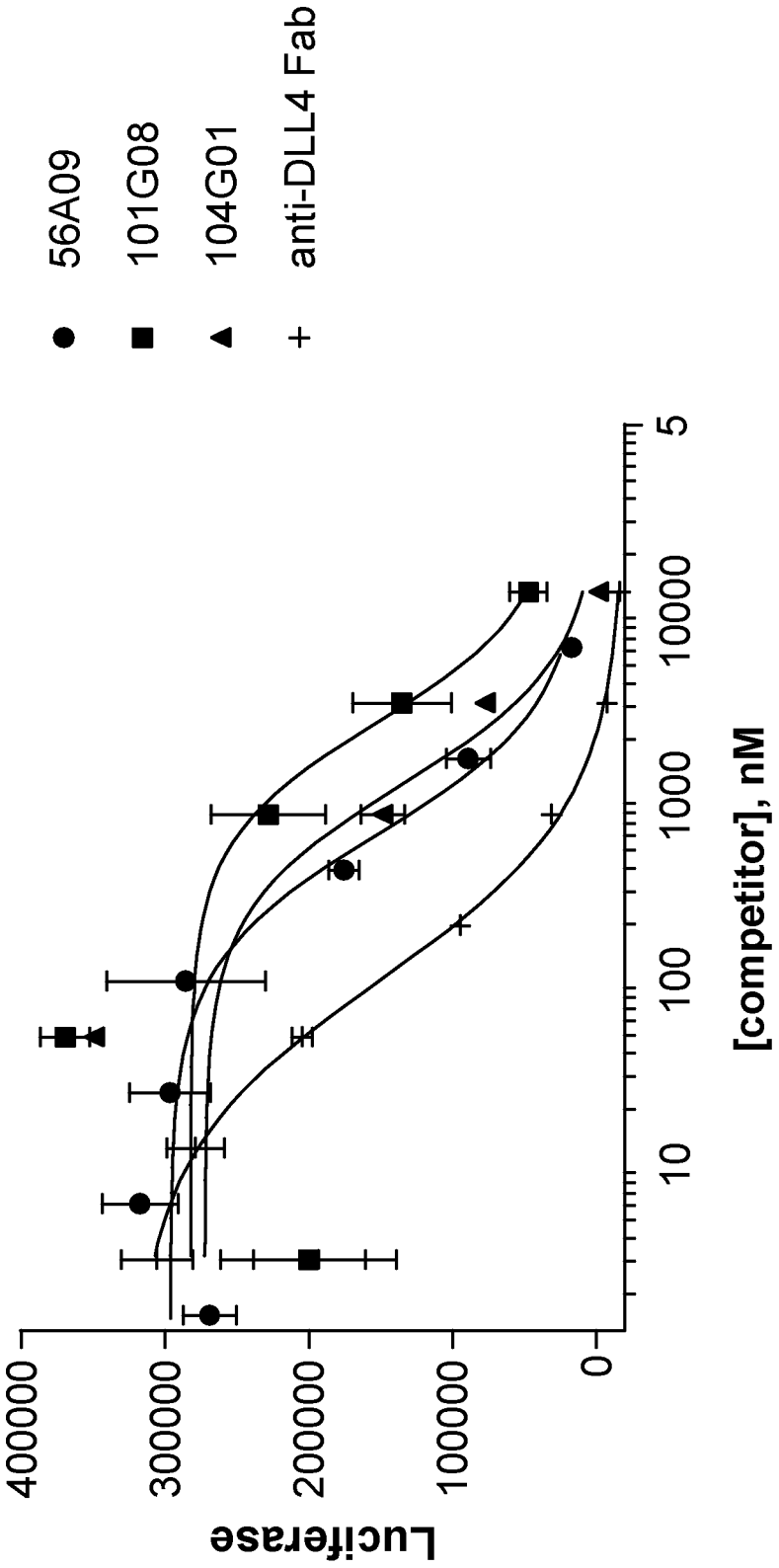

56A09
101G08
104G01
anti-DLL4 Fab
Luciferase
400000
300000
200000
100000
0
10
100
1000
10000
5
[competitor], nM

Fig. 6-2

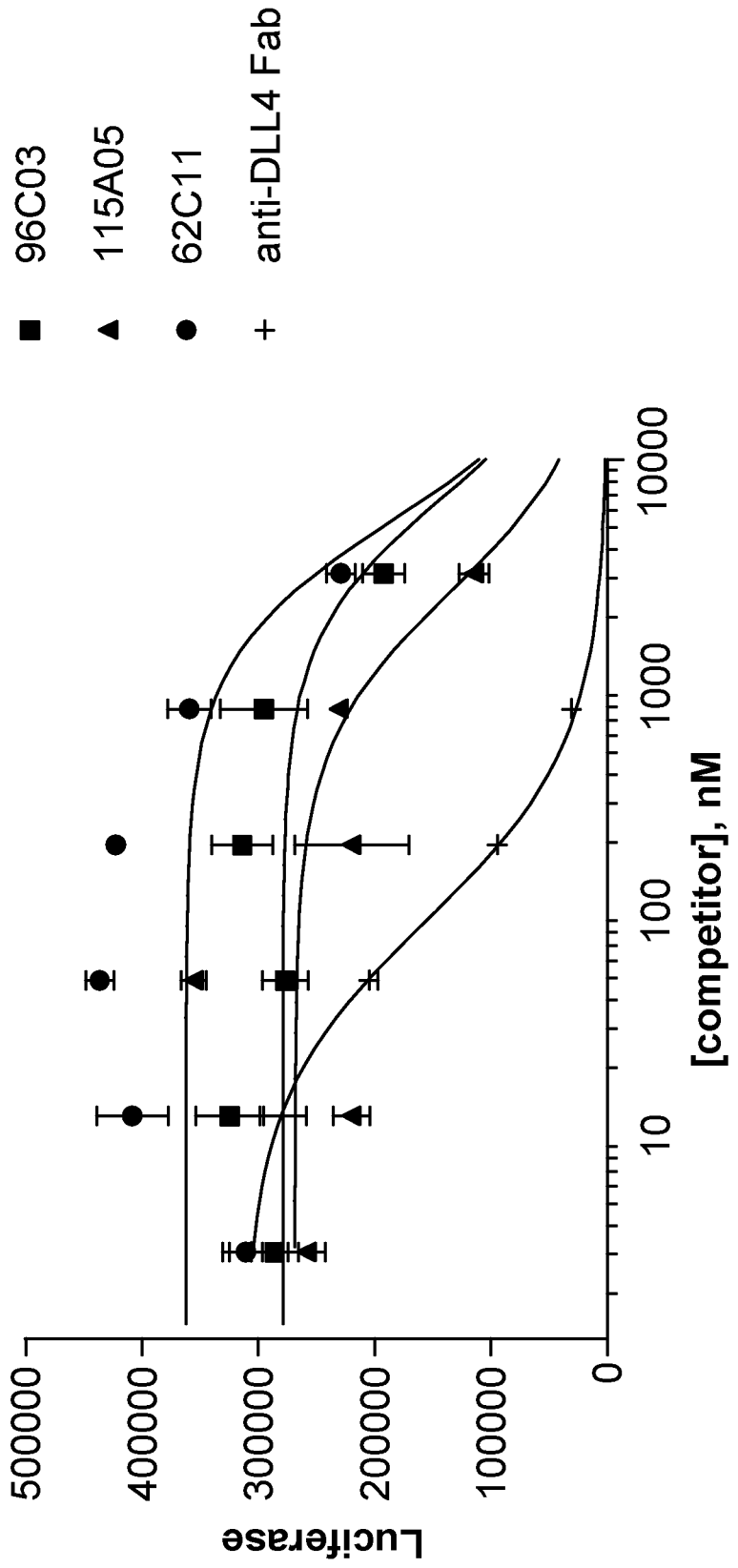

96C03
115A05
62C11
anti-DLL4 Fab
Luciferase
500000
400000
300000
200000
100000
0
10
100
1000
10000
[competitor], nM

Fig. 6-3

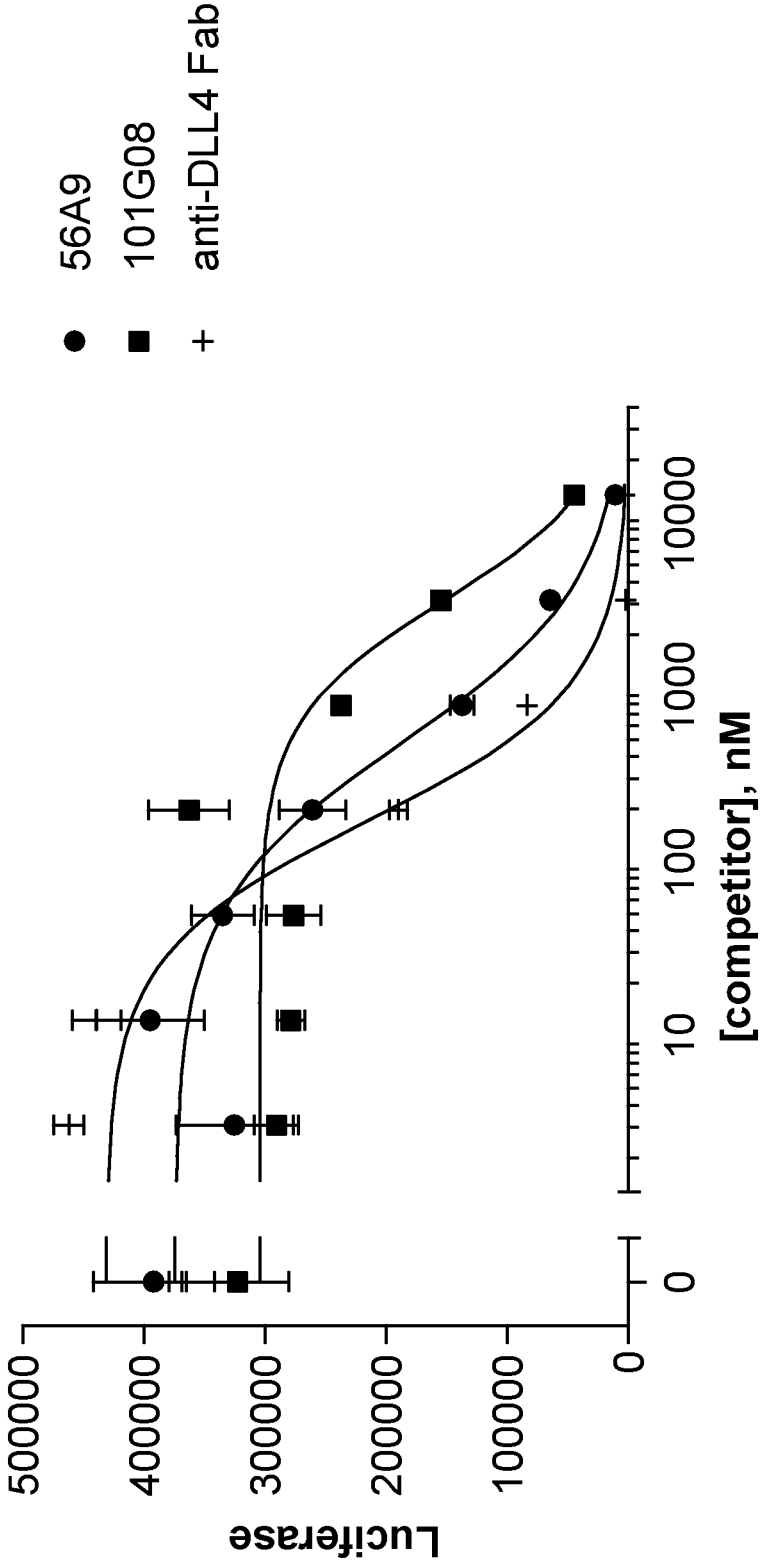

56A9
101G08
anti-DLL4 Fab
Luciferase
500000
400000
300000
200000
100000
0
0
10
100
1000
10000
[competitor], nM

Fig. 6-4

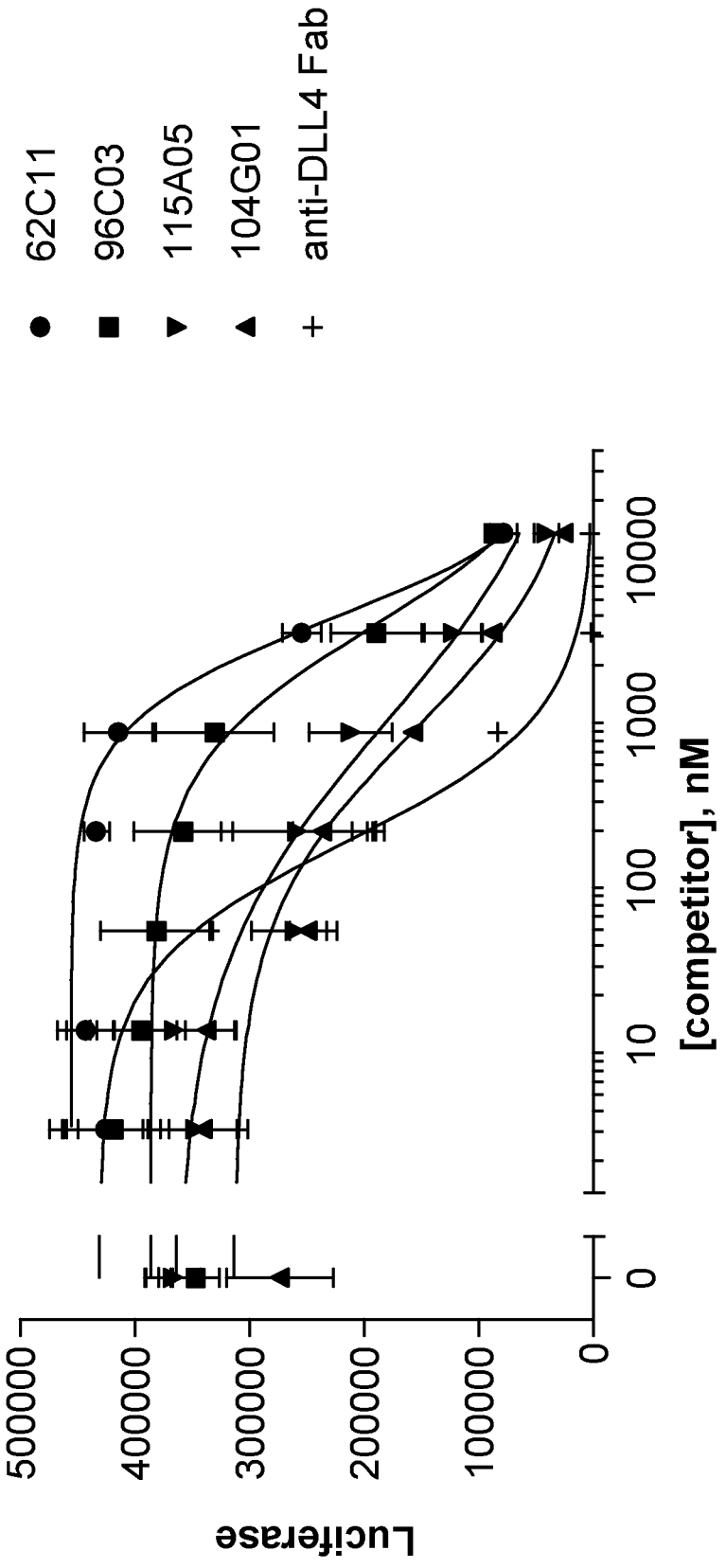
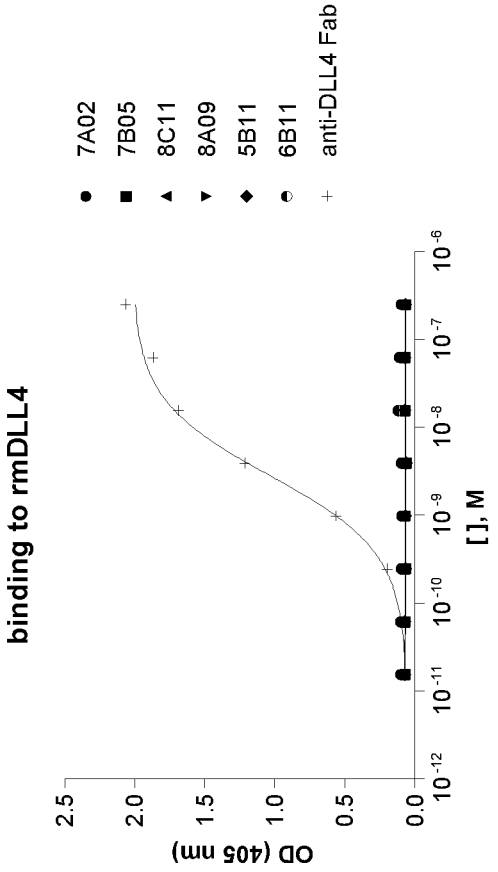

62C11
96C03
115A05
104G01
anti-DLL4 Fab
Luciferase
500000
400000
300000
200000
100000
0
0
10
100
1000
10000
[competitor], nM

Fig. 7-1


binding to rmDLL4
OD (405 nm)
[], M
7A02
7B05
8C11
8A09
5B11
6B11
anti-DLL4 Fab

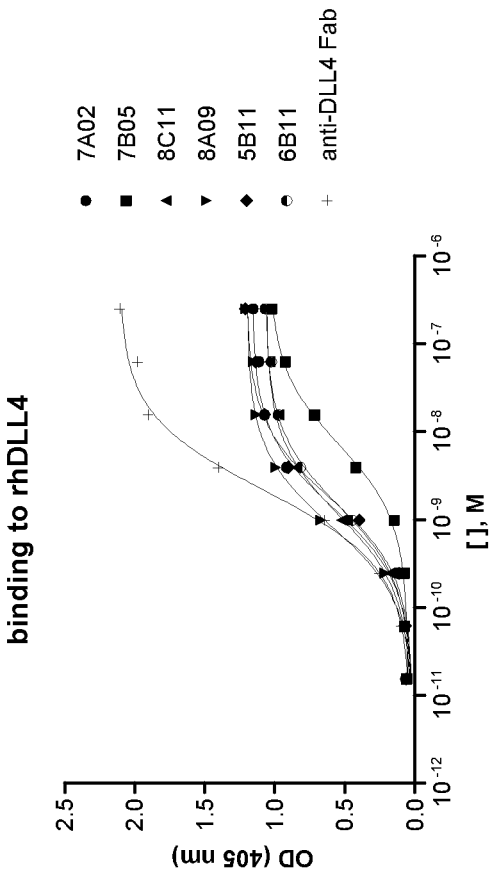
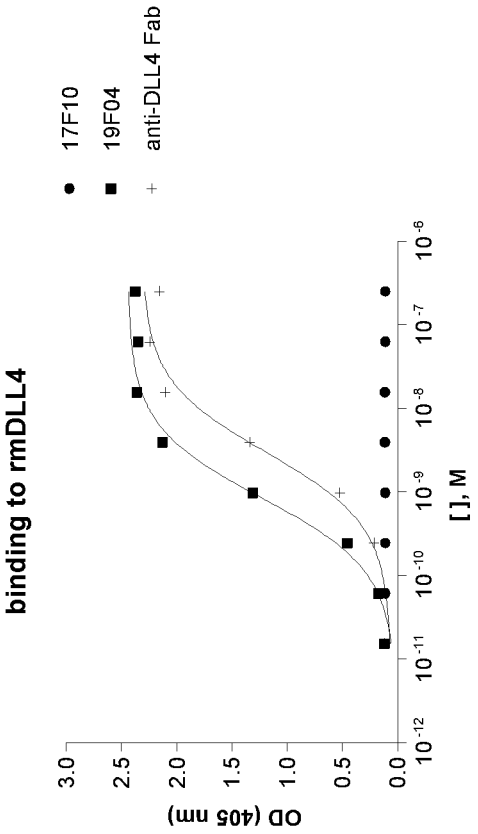

binding to rhDLL4
OD (405 nm)
[], M
7A02
7B05
8C11
8A09
5B11
6B11
anti-DLL4 Fab

Fig. 7-2


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

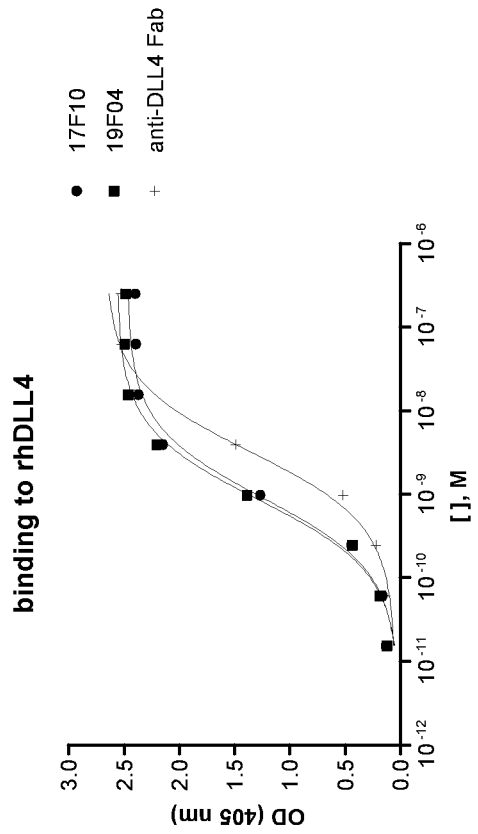
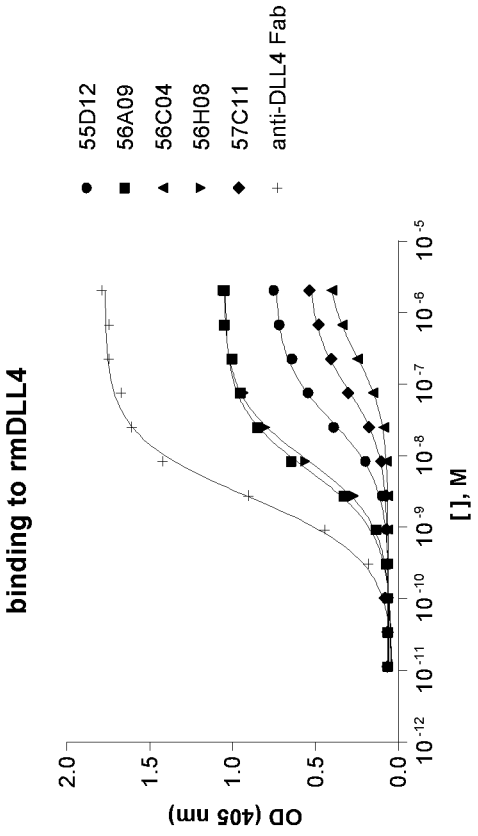

binding to rhDLL4
17F10
19F04
anti-DLL4 Fab
OD (405 nm)
[ ], M

Fig. 7-3


binding to rmDLL4
55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab
OD (405 nm)
[], M

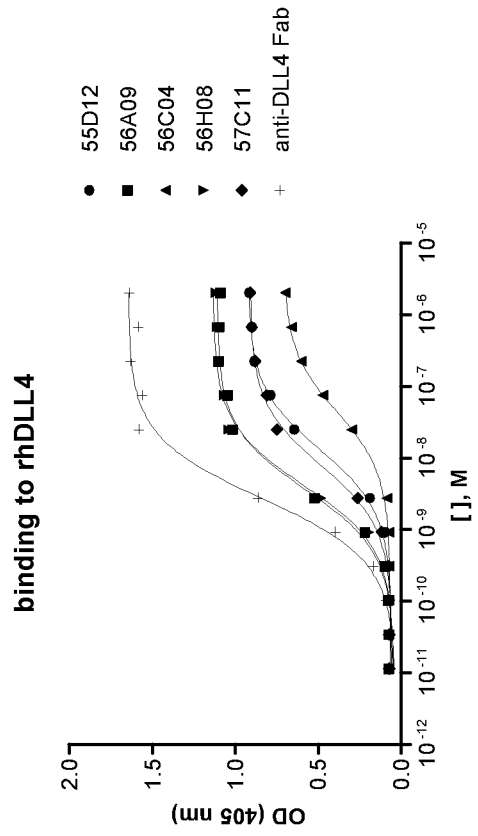
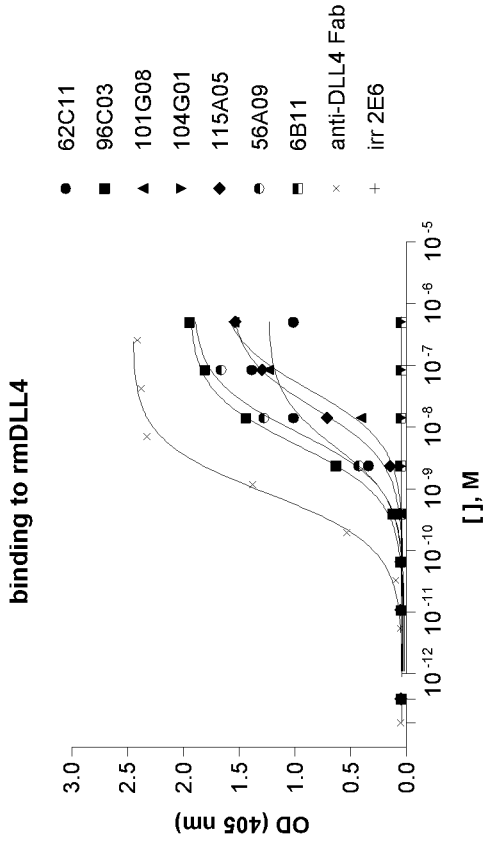

binding to rhDLL4
55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab
OD (405 nm)
[], M

Fig. 7-4


binding to rmDLL4
OD (405 nm)
[], M
62C11
96C03
101G08
104G01
115A05
56A09
6B11
anti-DLL4 Fab
irr 2E6

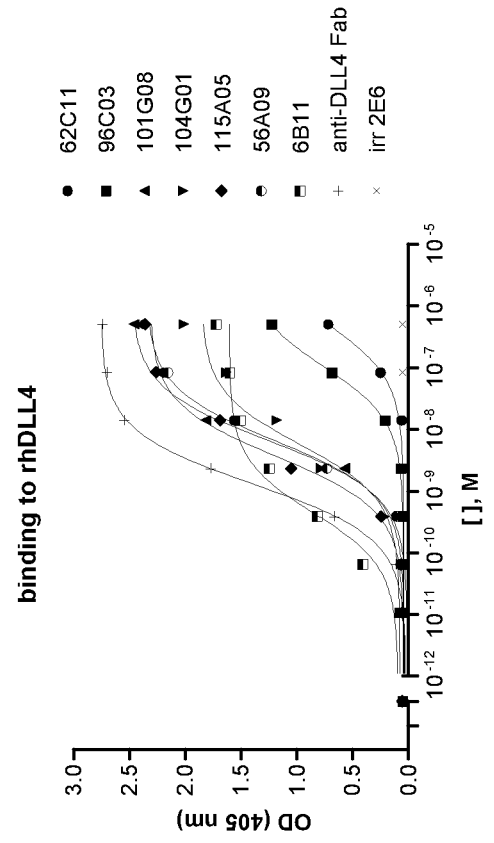
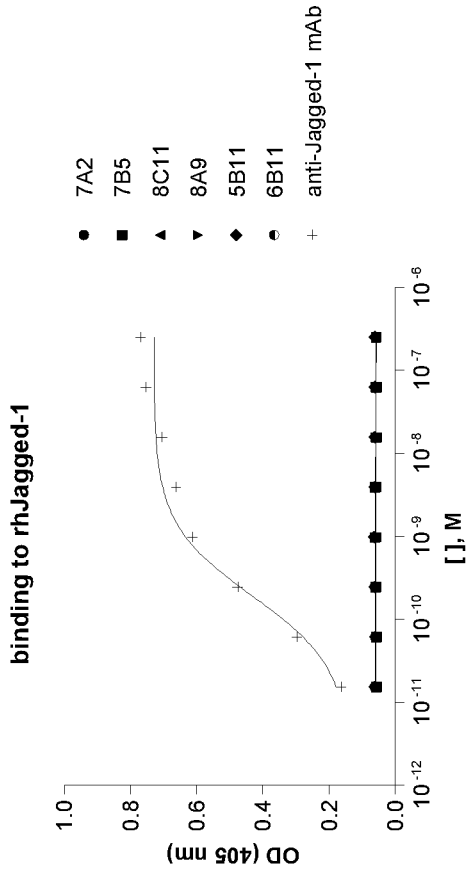

binding to rhDLL4
OD (405 nm)
[], M
62C11
96C03
101G08
104G01
115A05
56A09
6B11
anti-DLL4 Fab
irr 2E6

Fig. 8-1


binding to rhJagged-1
OD (405 nm)
[ ], M
7A2
7B5
8C11
8A9
5B11
6B11
anti-Jagged-1 mAb

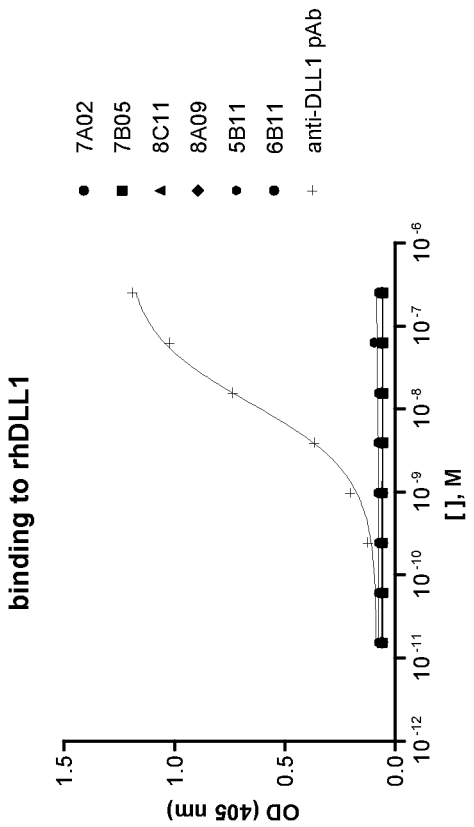
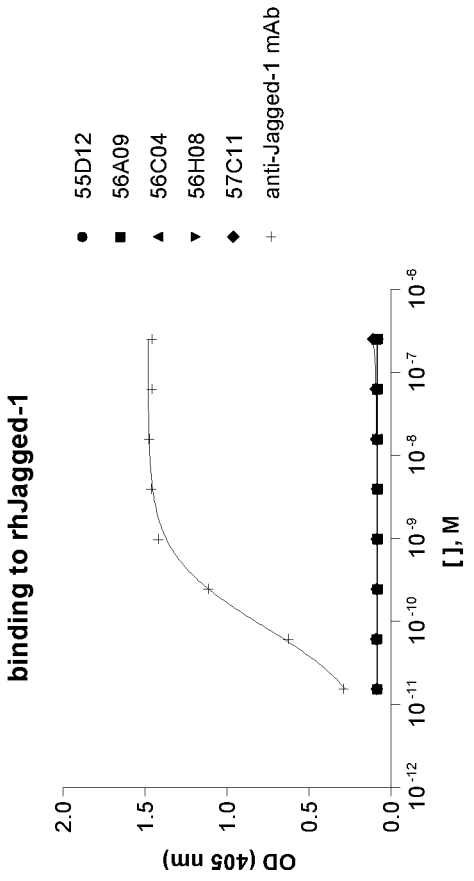

binding to rhDLL1
OD (405 nm)
[ ], M
7A02
7B05
8C11
8A09
5B11
6B11
anti-DLL1 pAb

Fig. 8-2


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

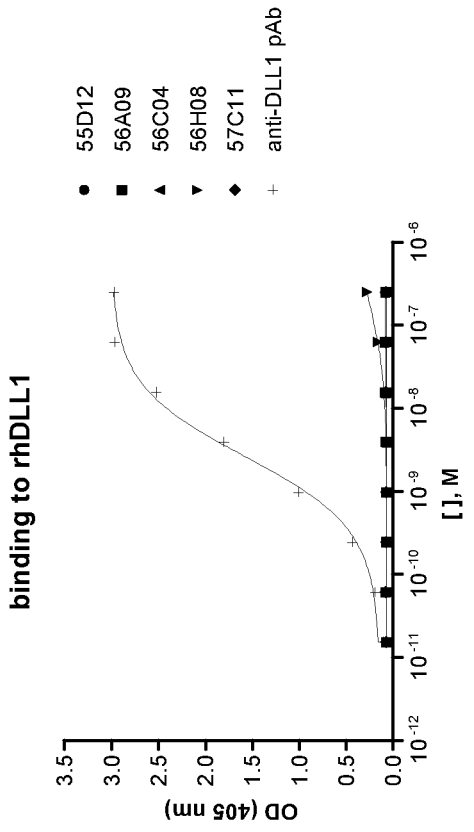
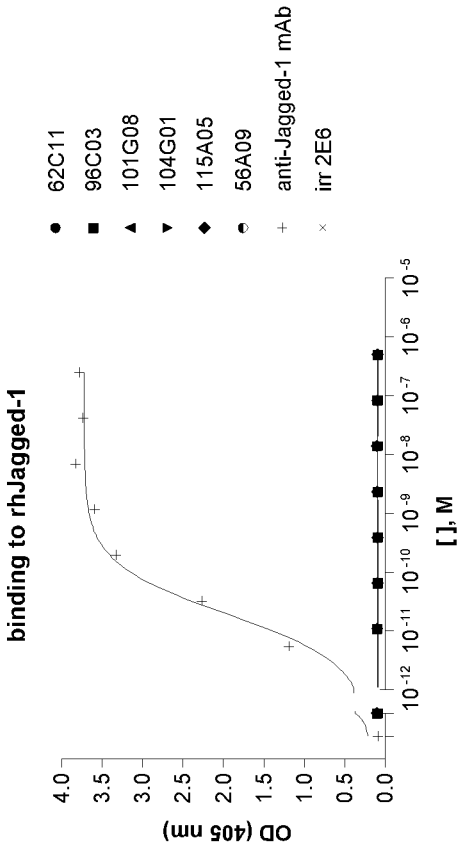

binding to rhDLL1
55D12
56A09
56C04
56H08
57C11
anti-DLL1 pAb
OD (405 nm)
[ ], M

Fig. 8-3


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

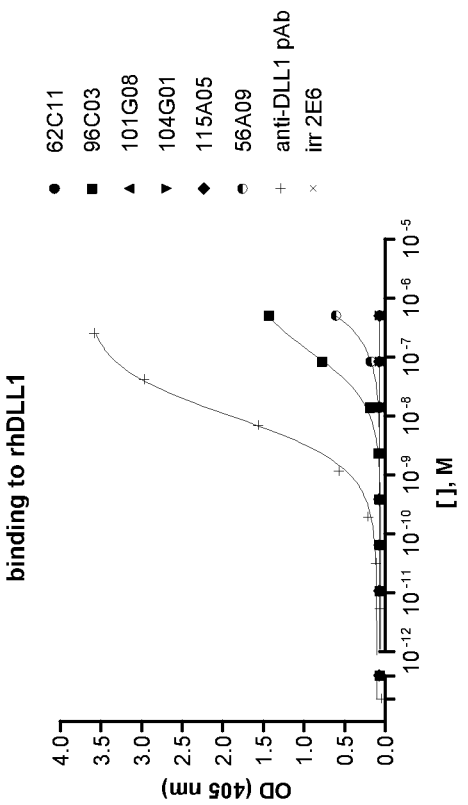
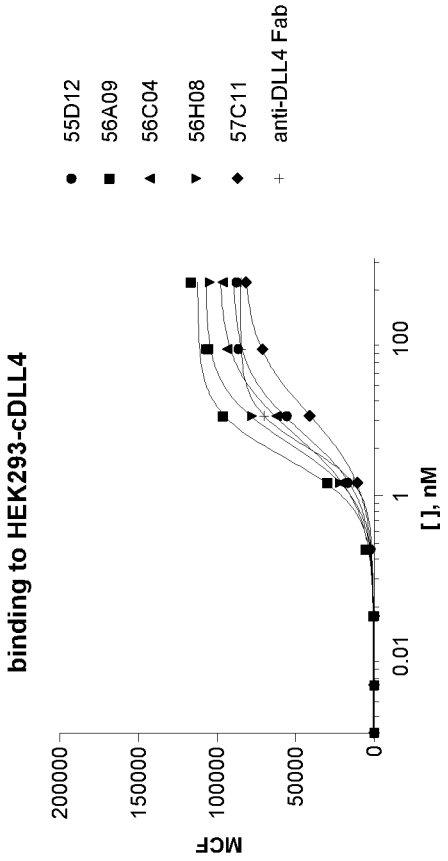

binding to rhDLL1
OD (405 nm)
[], M
62C11
96C03
101G08
104G01
115A05
56A09
anti-DLL1 pAb
irr 2E6

Fig. 9-1


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

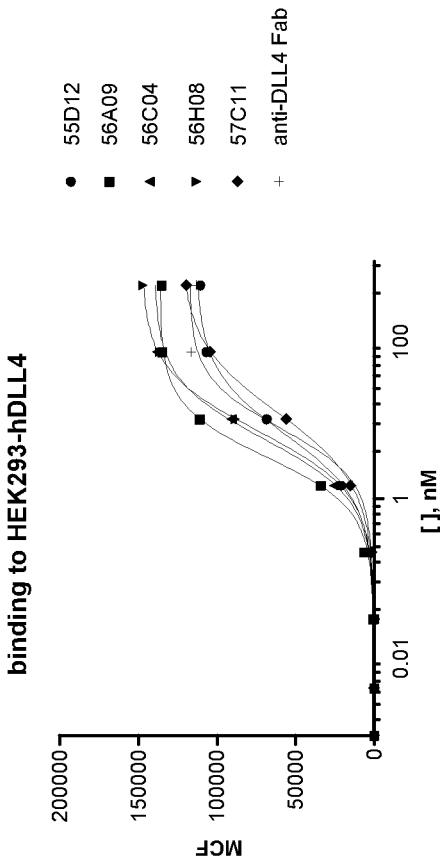

binding to HEK293-hDLL4
MCF
200000
150000
100000
50000
0
0.01
1
100
[ ], nM
55D12
56A09
56C04
56H08
57C11
anti-DLL4 Fab

Fig. 9-2

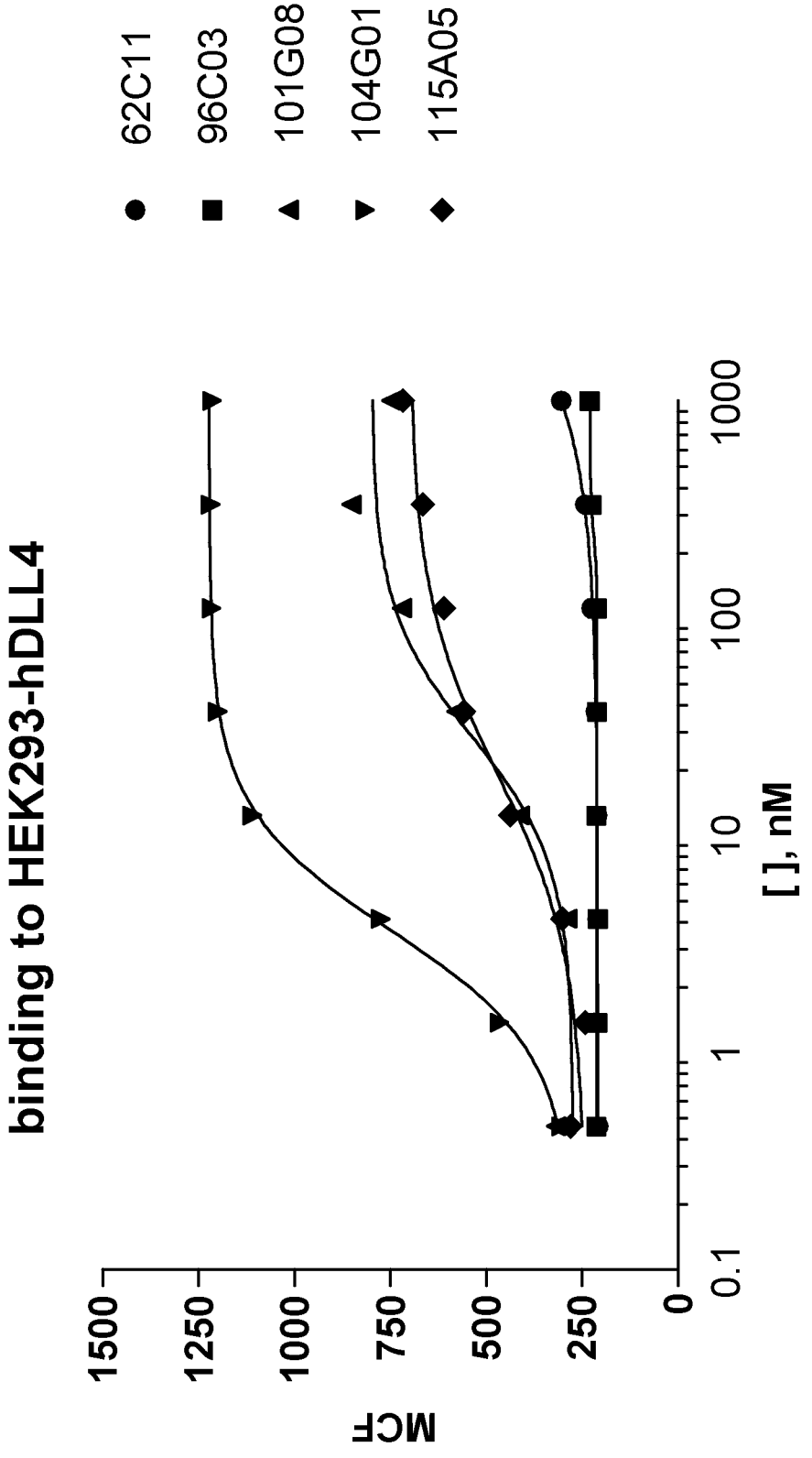

binding to HEK293-hDLL4
62C11
96C03
101G08
104G01
115A05
MCF
1500
1250
1000
750
500
250
0
0.1
1
10
100
1000
[ ], nM

Fig. 9-3

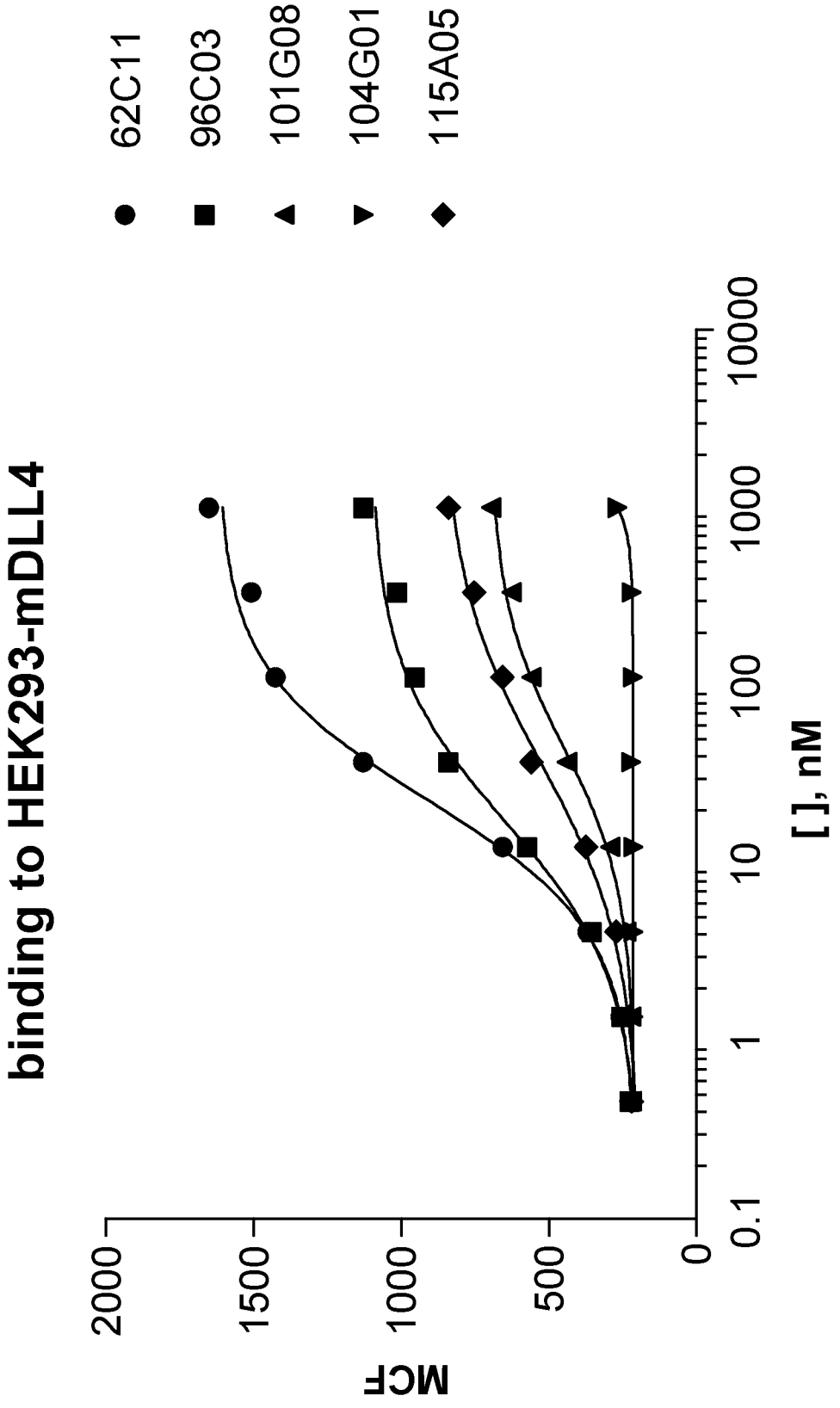

binding to HEK293-mDLL4
62C11
96C03
101G08
104G01
115A05
MCF
2000
1500
1000
500
0
0.1
1
10
100
1000
10000
[ ], nM

Fig. 9-4

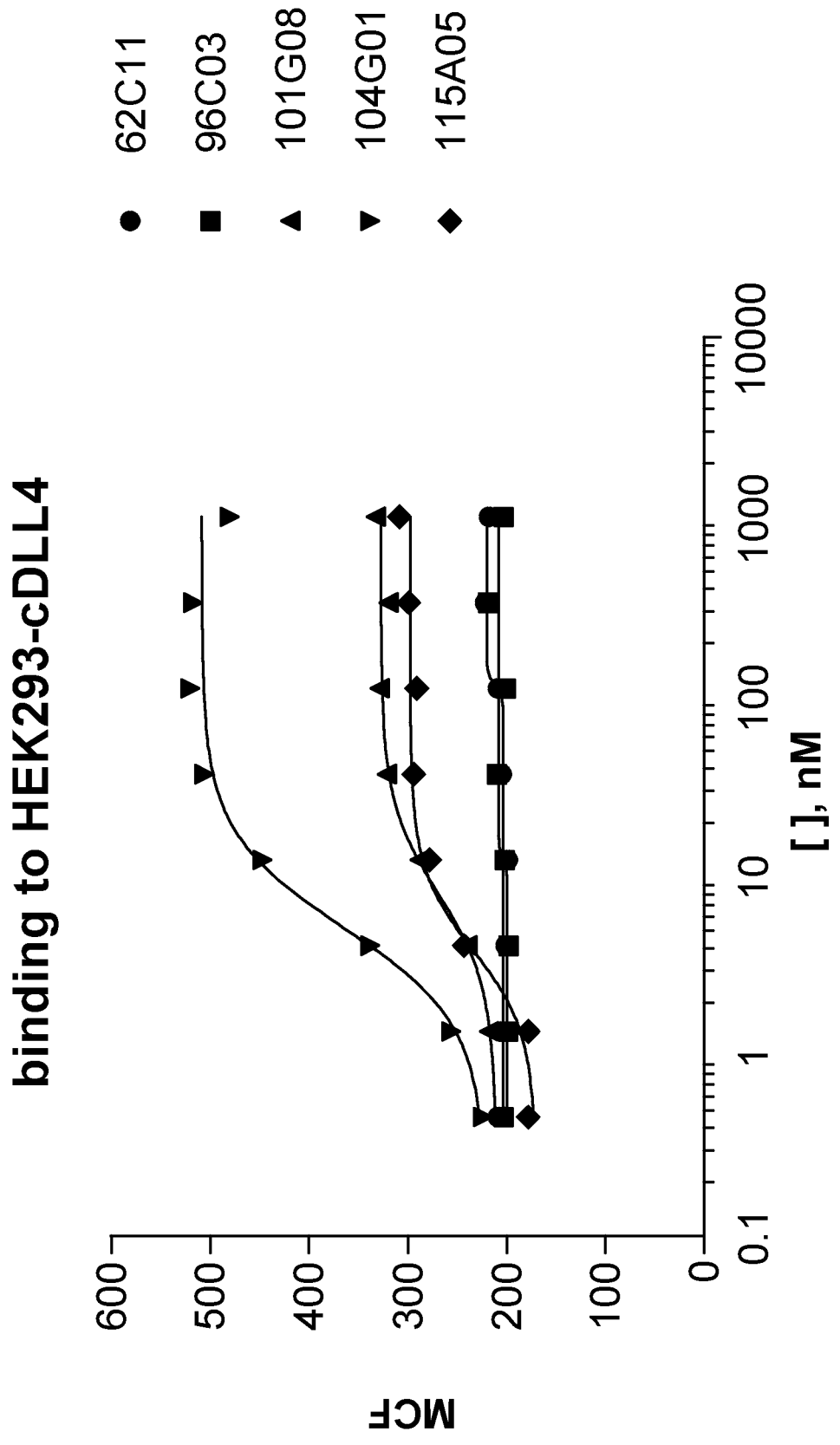
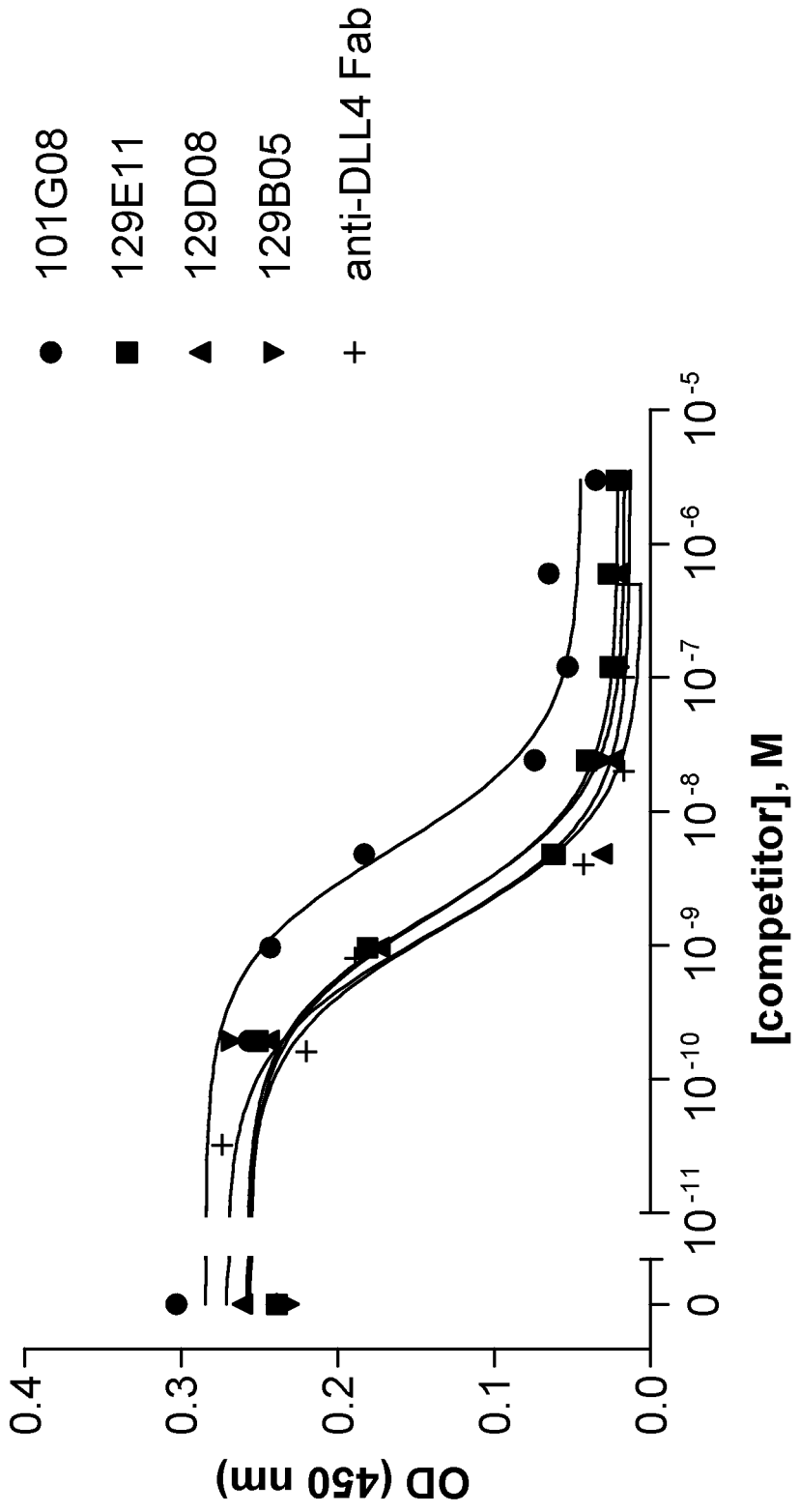

binding to HEK293-cDLL4
62C11
96C03
101G08
104G01
115A05
MCF
600
500
400
300
200
100
0
0.1
1
10
100
1000
10000
[ ], nM

Fig. 10-1


101G08
129E11
129D08
129B05
anti-DLL4 Fab
OD (450 nm)
0.0
0.1
0.2
0.3
0.4
0
10-11
10-10
10-9
10-8
10-7
10-6
10-5
[competitor], M

37 / 152
Fig. 10-2

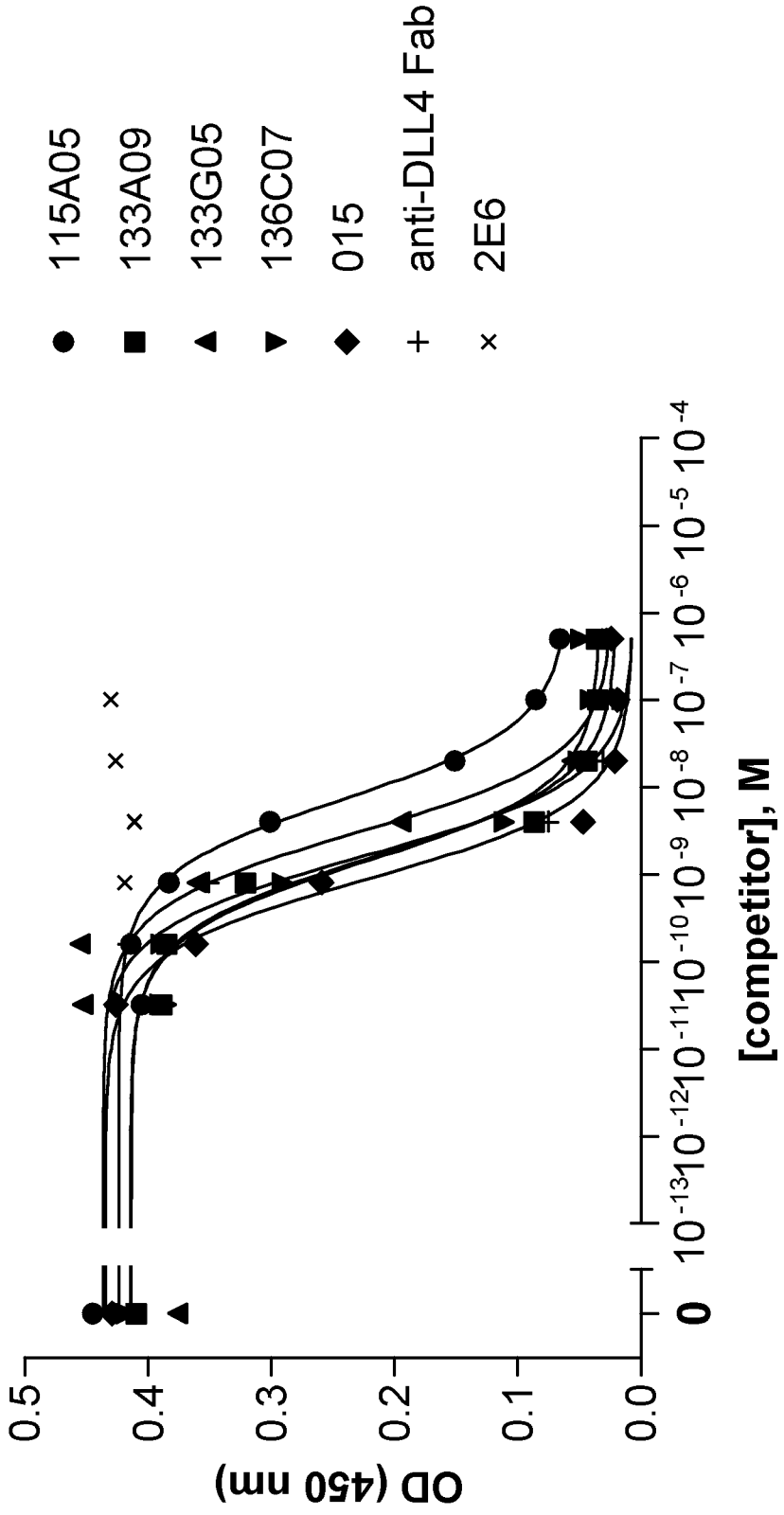


Fig. 11-1

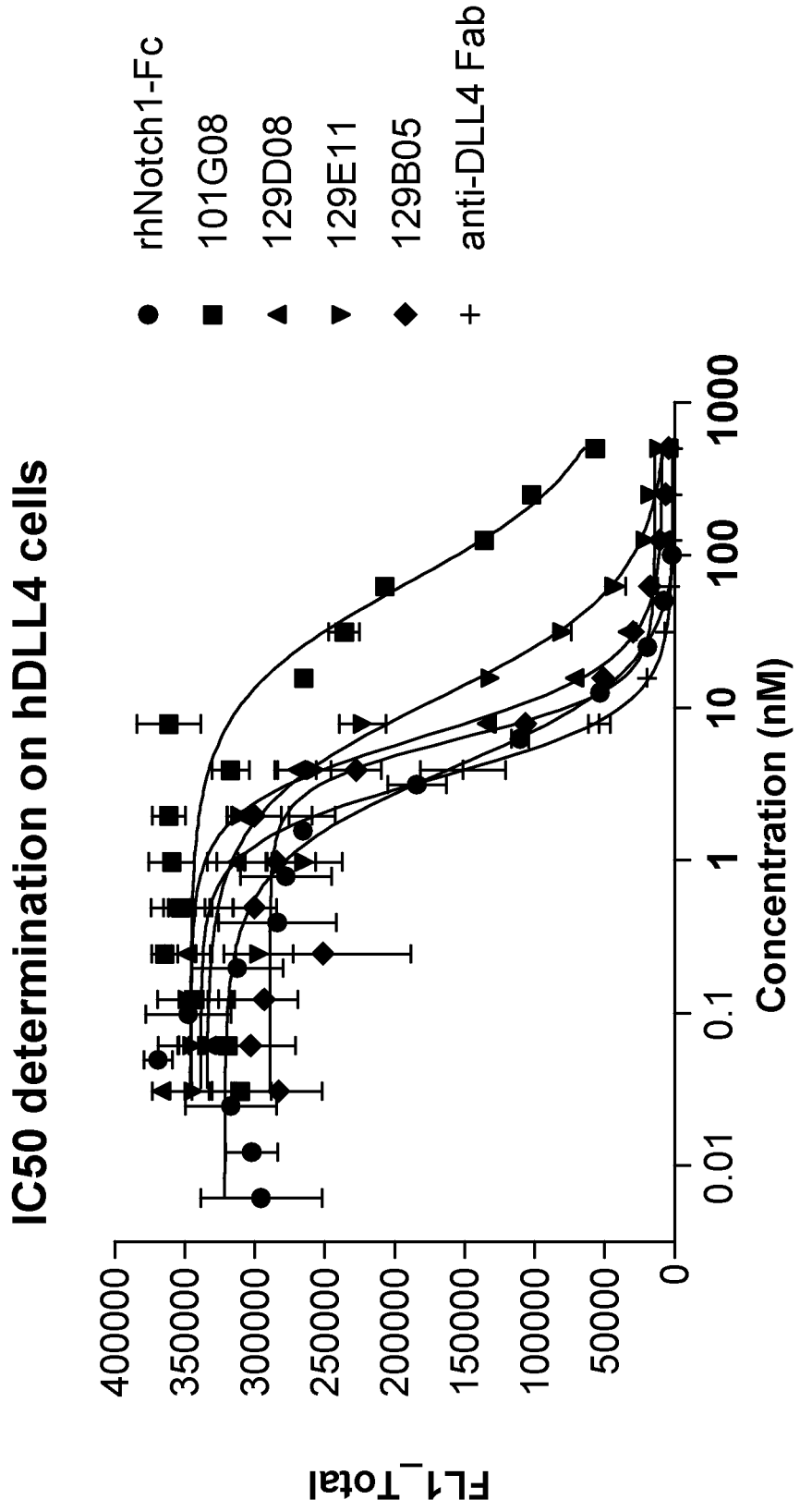

IC50 determination on hDLL4 cells
rhNotch1-Fc
101G08
129D08
129E11
129B05
anti-DLL4 Fab
FL1_Total
Concentration (nM)
0
50000
100000
150000
200000
250000
300000
350000
400000
0.01
0.1
1
10
100
1000

Fig. 11-2

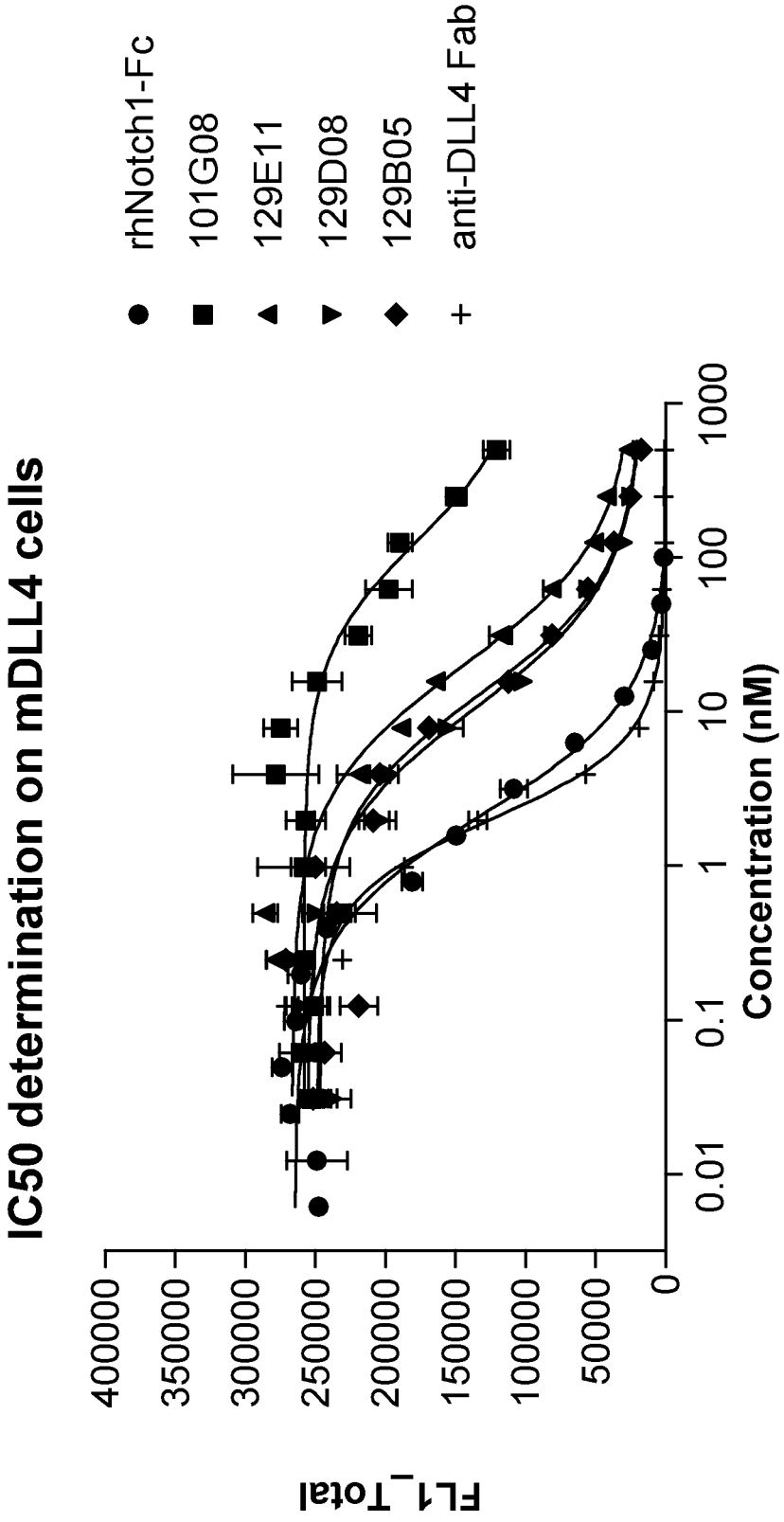

IC50 determination on mDLL4 cells
rhNotch1-Fc
101G08
129E11
129D08
129B05
anti-DLL4 Fab
FL1_Total
400000
350000
300000
250000
200000
150000
100000
50000
0
0.01
0.1
1
10
100
1000
Concentration (nM)

Fig. 11-3

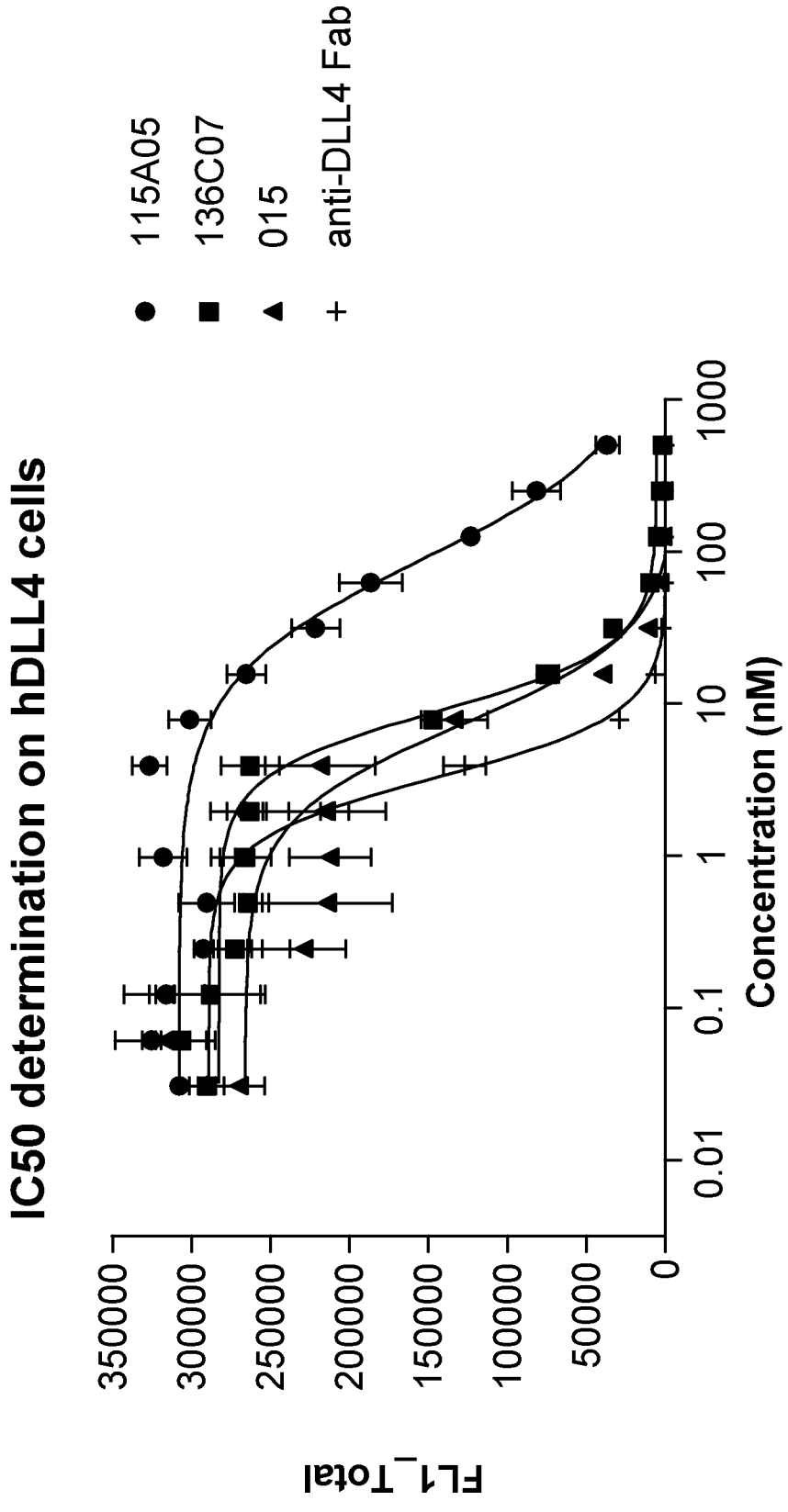

IC50 determination on hDLL4 cells
115A05
136C07
015
anti-DLL4 Fab
FL1_Total
Concentration (nM)
0
50000
100000
150000
200000
250000
300000
350000
0.01
0.1
1
10
100
1000

Fig. 11-4

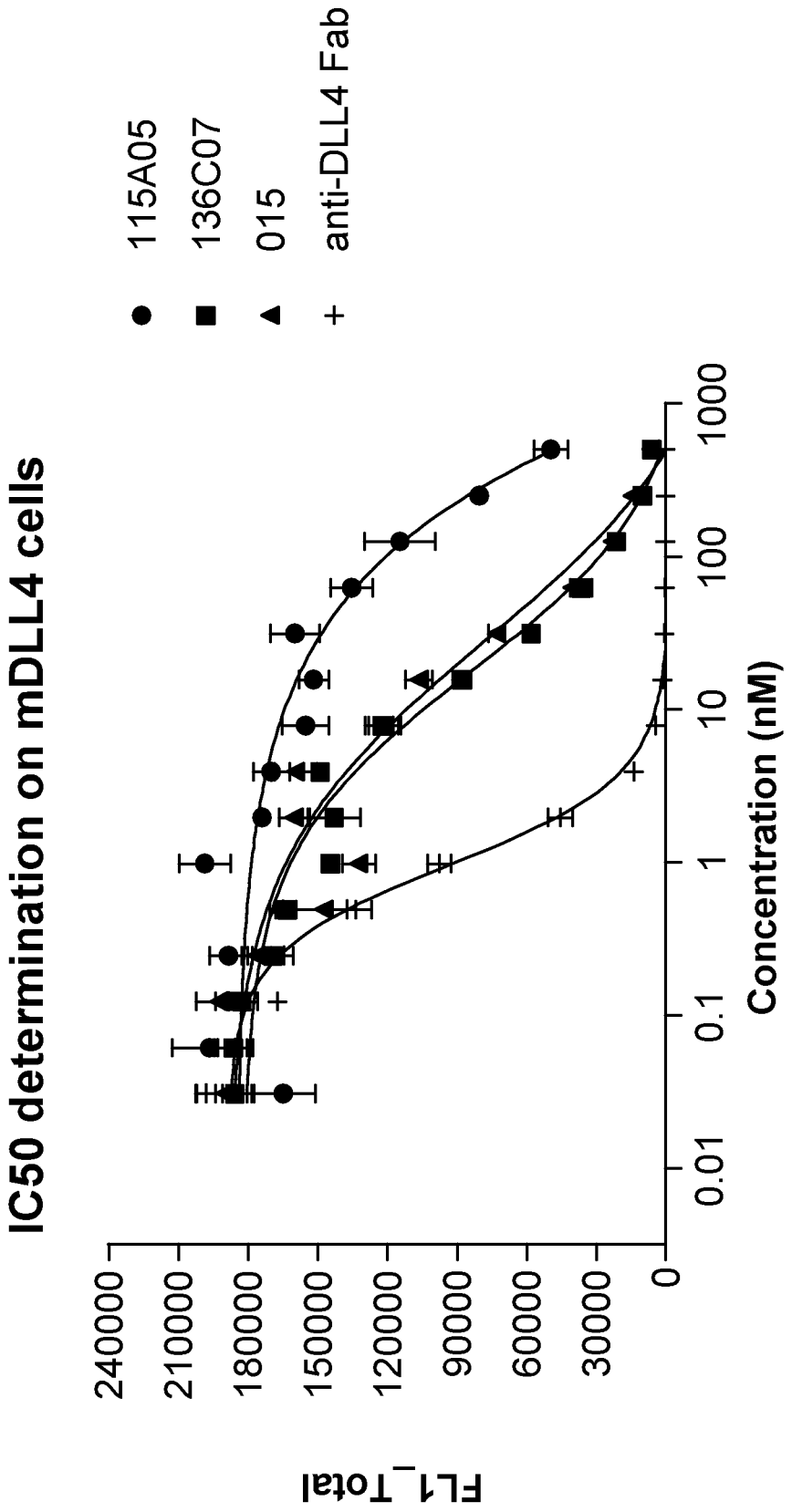

IC50 determination on mDLL4 cells
115A05
136C07
015
anti-DLL4 Fab
FL1_Total
240000
210000
180000
150000
120000
90000
60000
30000
0
0.01
0.1
1
10
100
1000
Concentration (nM)

Fig. 12-1

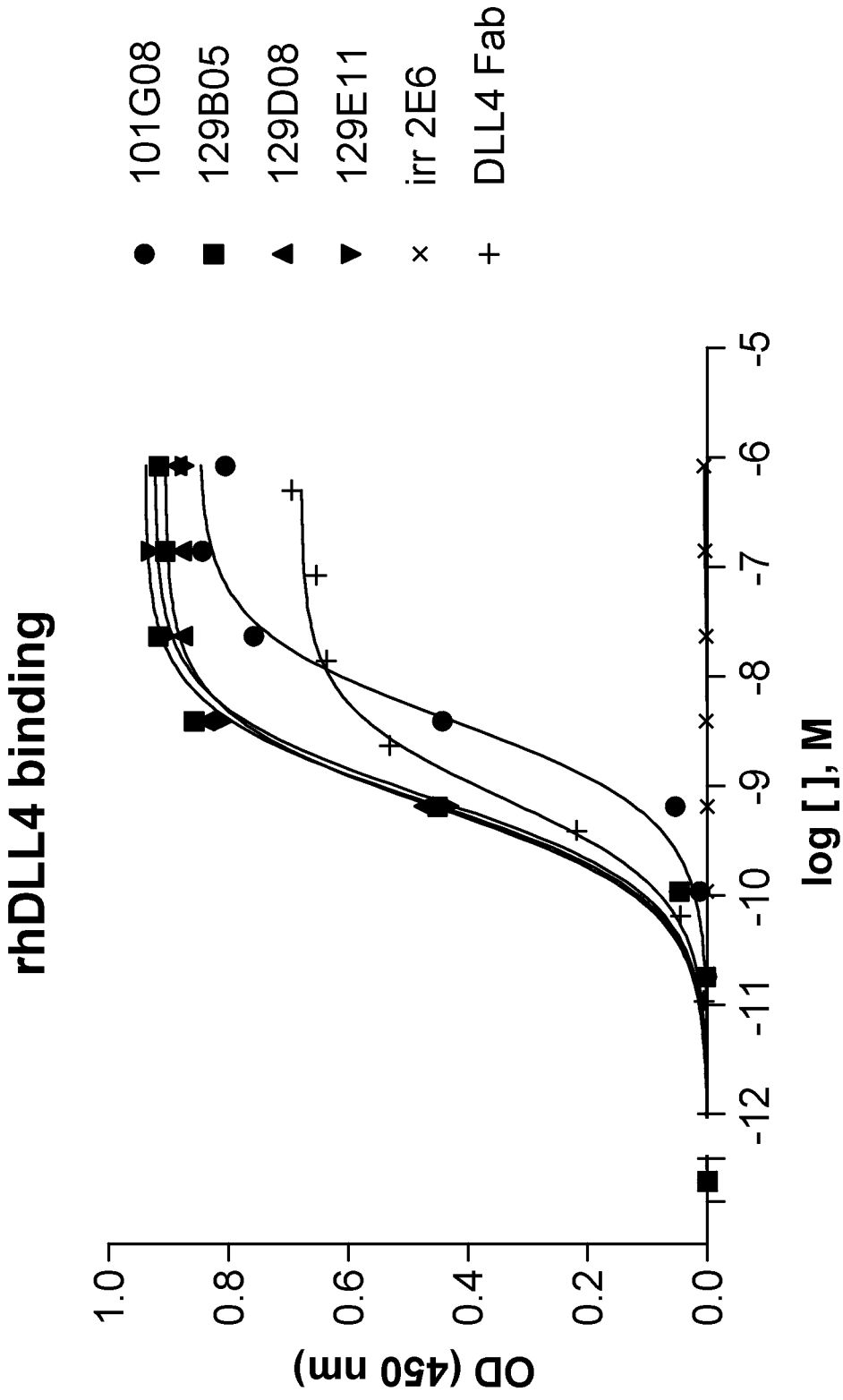

rhDLL4 binding
OD (450 nm)
1.0
0.8
0.6
0.4
0.2
0.0
-12
-11
-10
-9
-8
-7
-6
-5
log [ ], M
101G08
129B05
129D08
129E11
irr 2E6
DLL4 Fab

Fig. 12-2

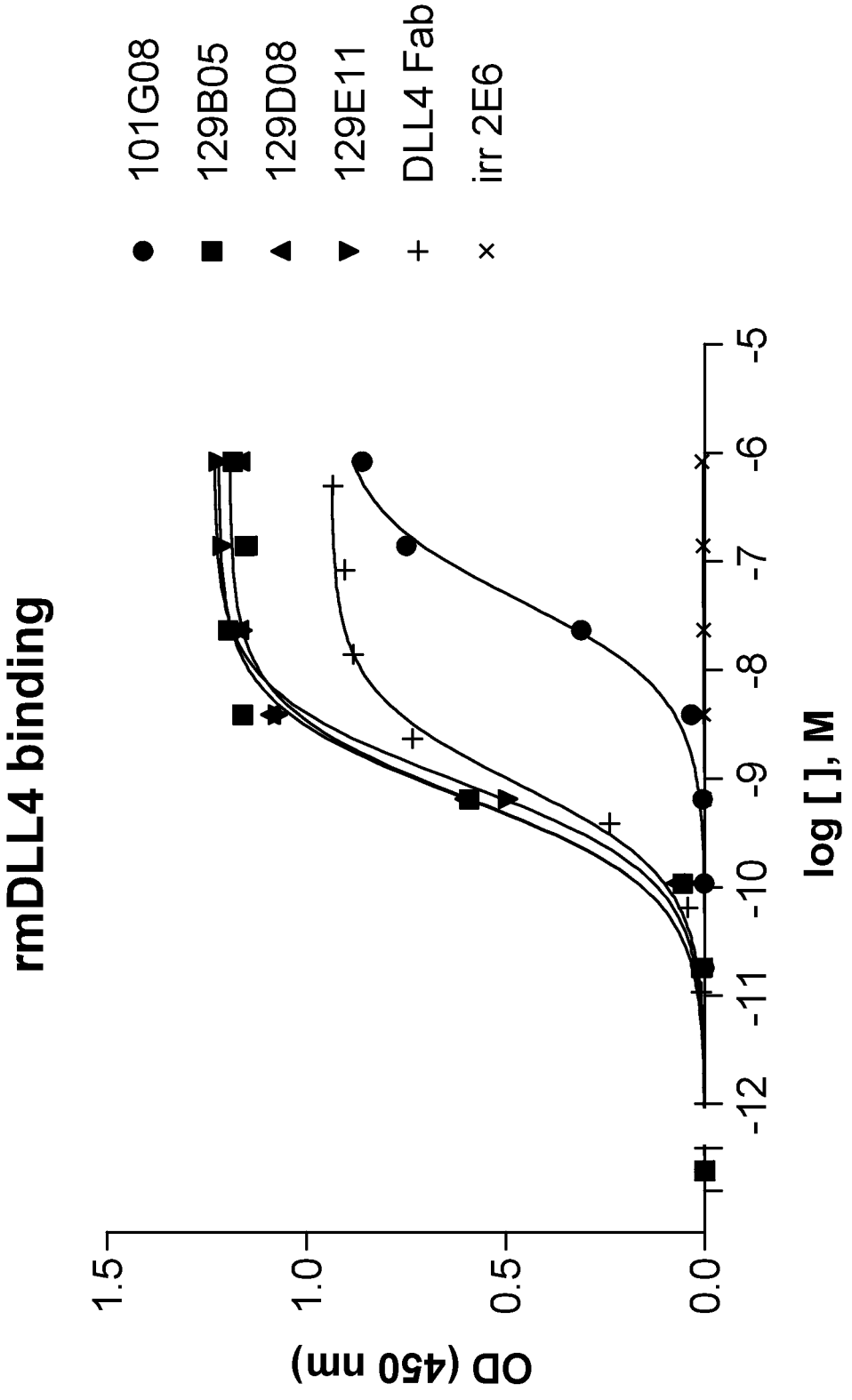

rmDLL4 binding
OD (450 nm)
1.5
1.0
0.5
0.0
-12
-11
-10
-9
-8
-7
-6
-5
log [ ], M
101G08
129B05
129D08
129E11
DLL4 Fab
irr 2E6

Fig. 12-3

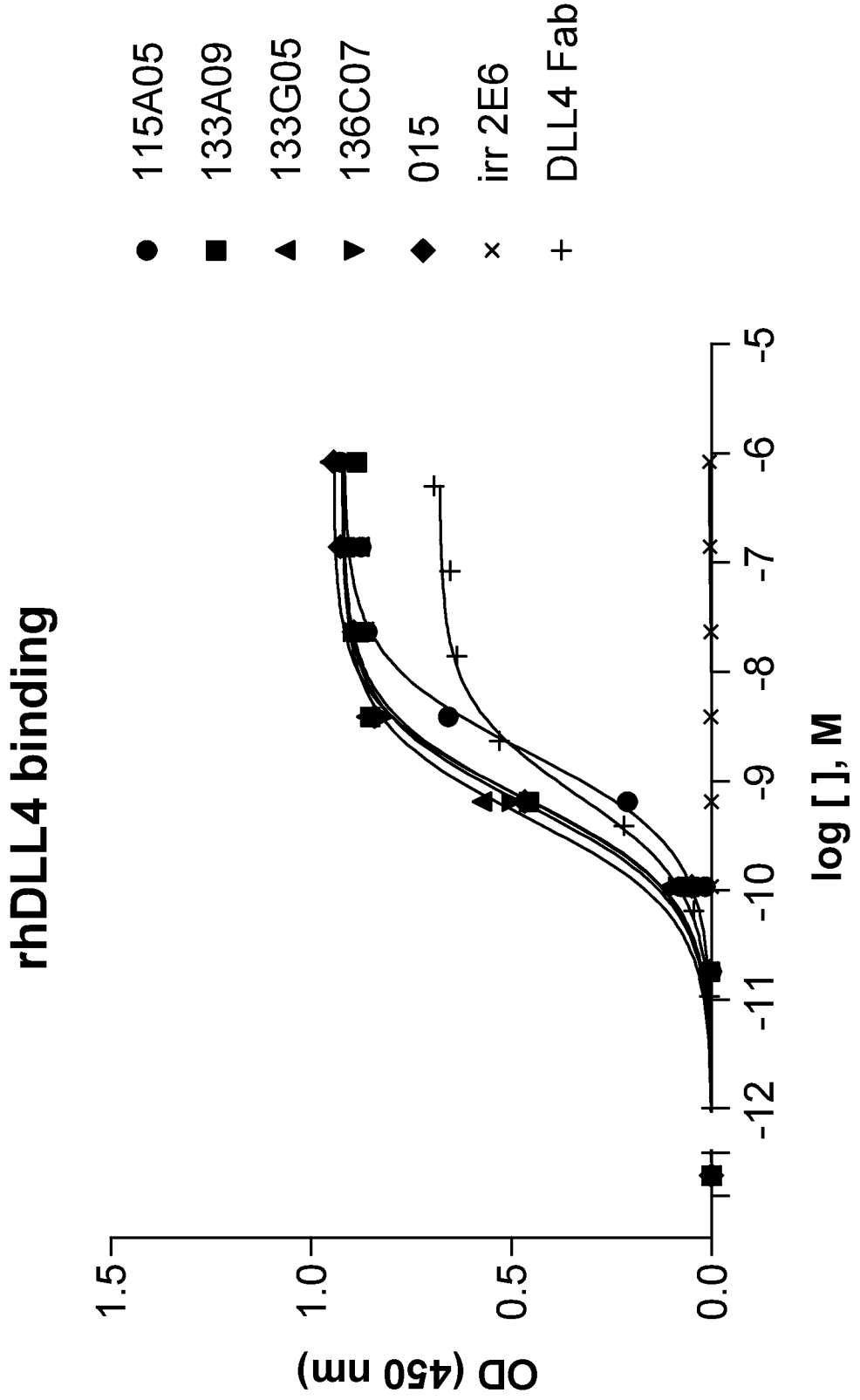

rhDLL4 binding
OD (450 nm)
1.5
1.0
0.5
0.0
-12
-11
-10
-9
-8
-7
-6
-5
log [ ], M
115A05
133A09
133G05
136C07
015
irr 2E6
DLL4 Fab

Fig. 12-4

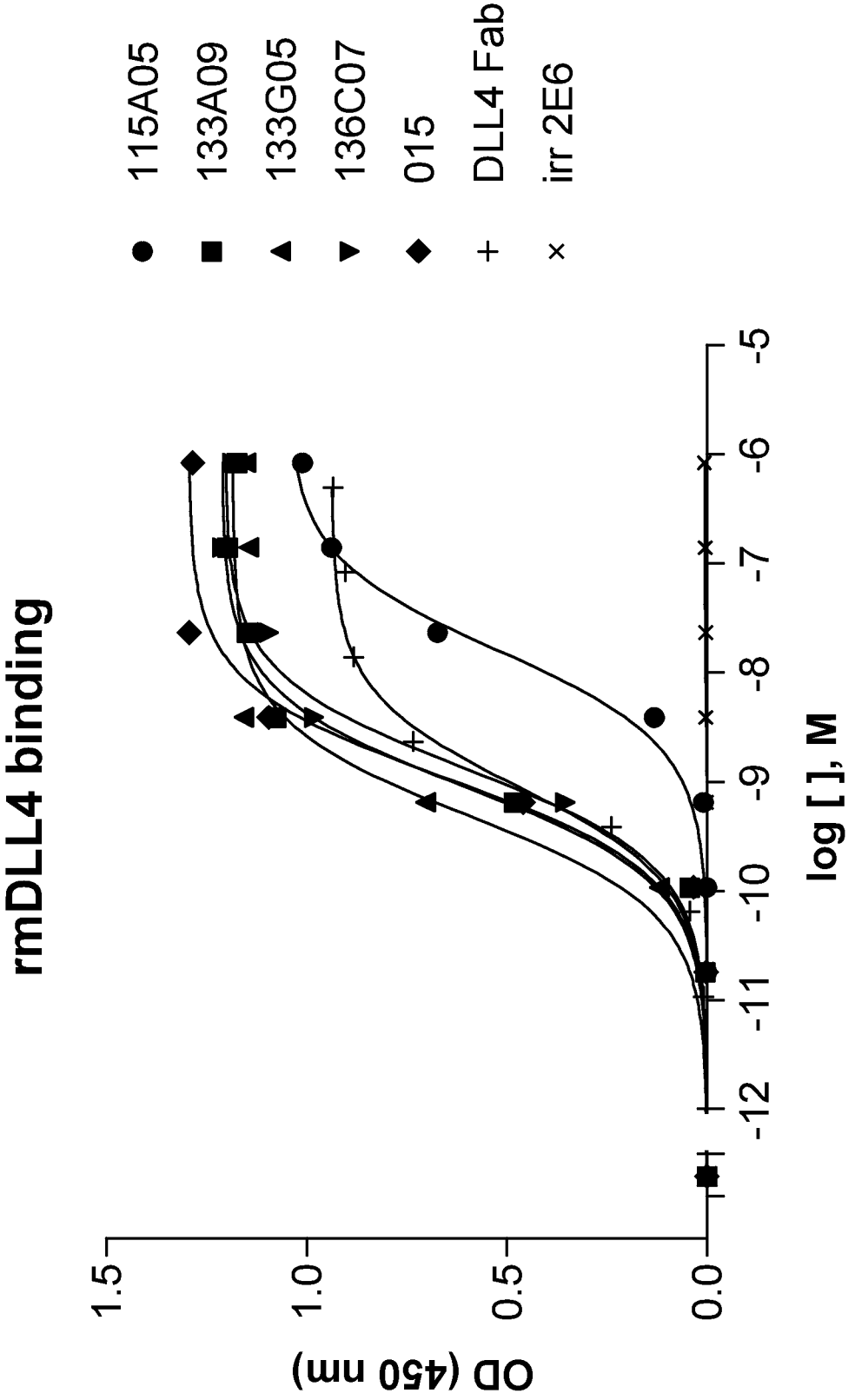

rmDLL4 binding
OD (450 nm)
1.5
1.0
0.5
0.0
-12
-11
-10
-9
-8
-7
-6
-5
log [ ], M
115A05
133A09
133G05
136C07
015
DLL4 Fab
irr 2E6

Fig. 13-1

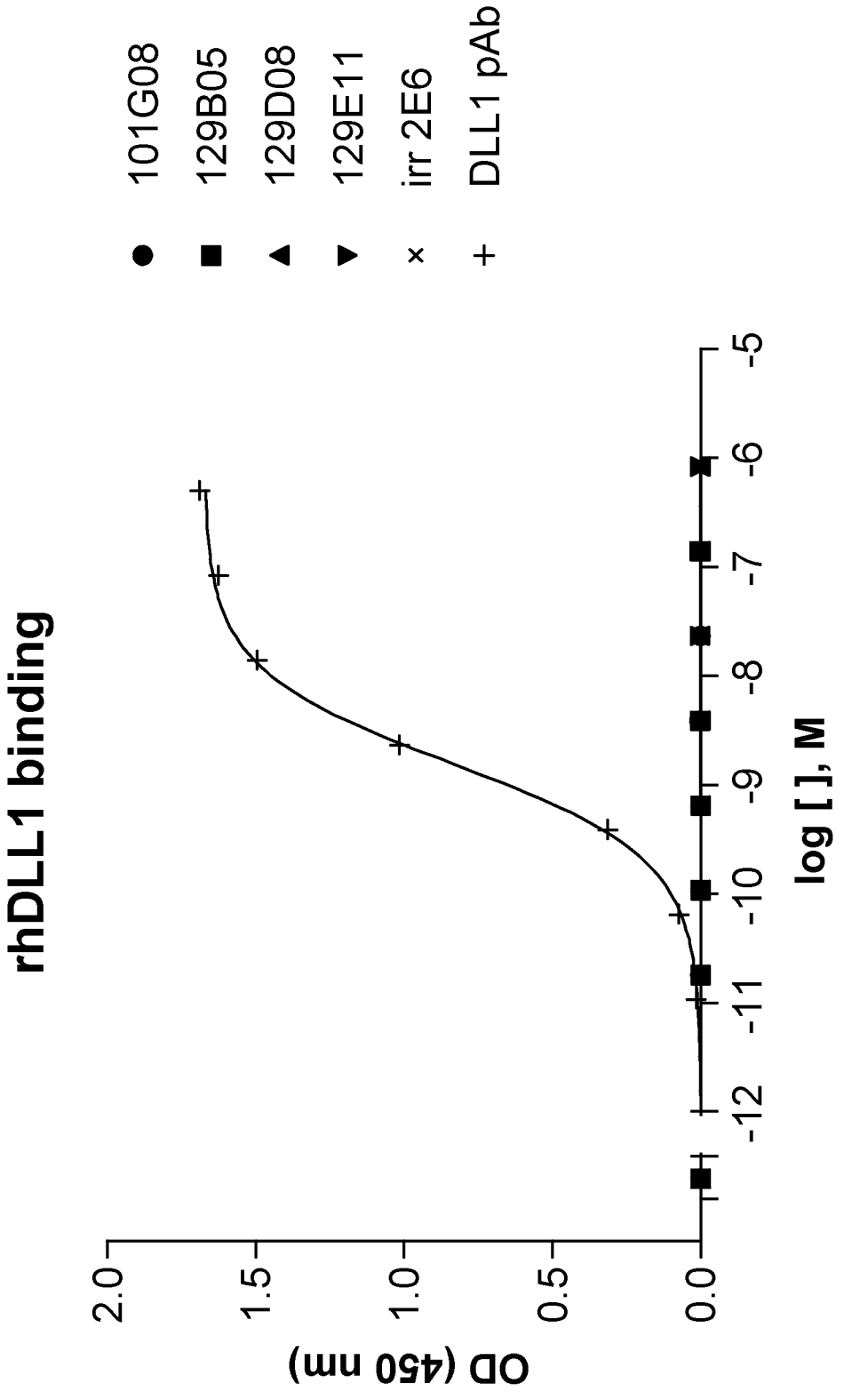

rhDLL1 binding
101G08
129B05
129D08
129E11
irr 2E6
DLL1 pAb
OD (450 nm)
2.0
1.5
1.0
0.5
0.0
-12
-11
-10
-9
-8
-7
-6
-5
log [ ], M

Fig. 13-2

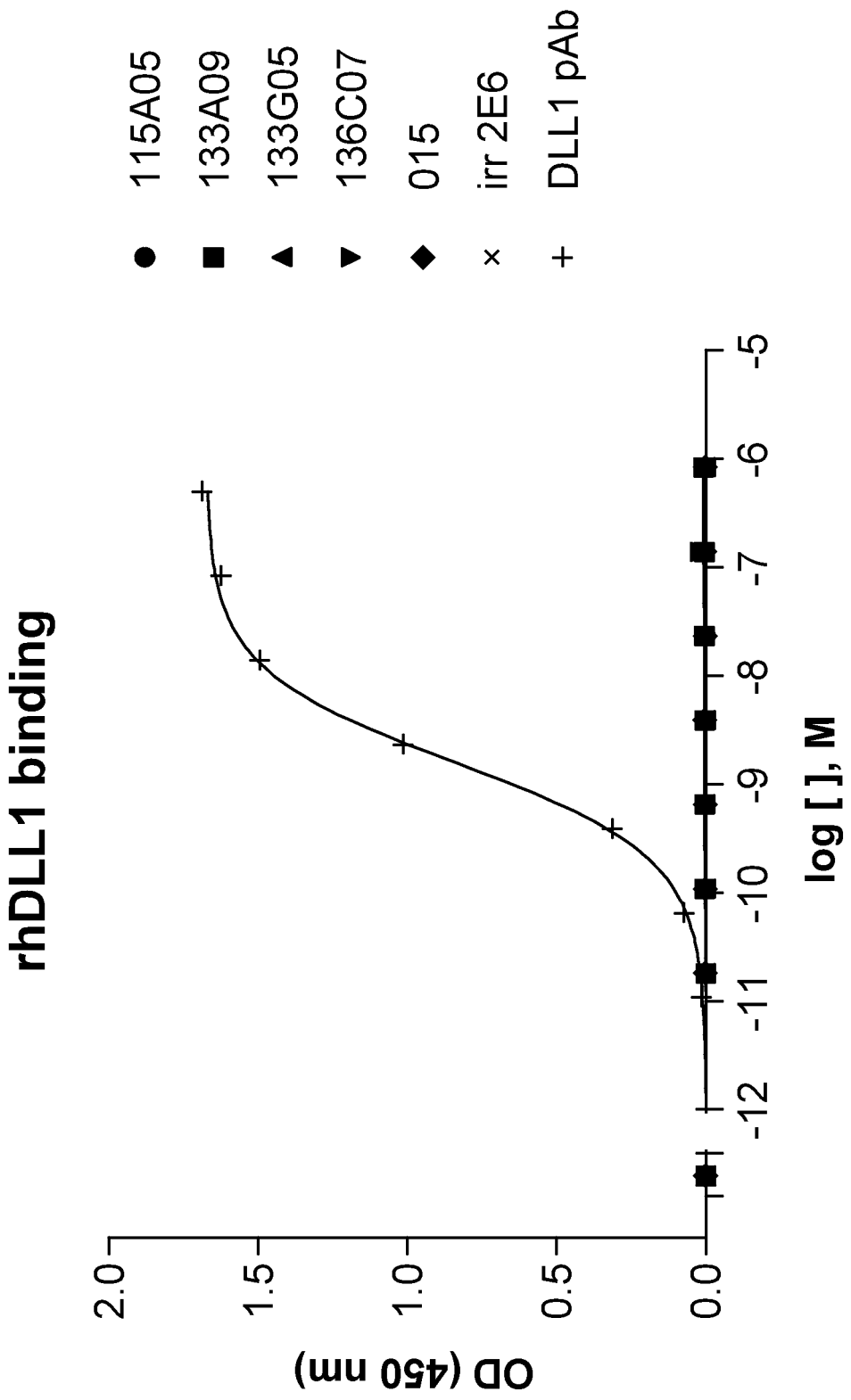

rhDLL1 binding
OD (450 nm)
2.0
1.5
1.0
0.5
0.0
-12
-11
-10
-9
-8
-7
-6
-5
log [ ], M
115A05
133A09
133G05
136C07
015
irr 2E6
DLL1 pAb

Fig. 13-3

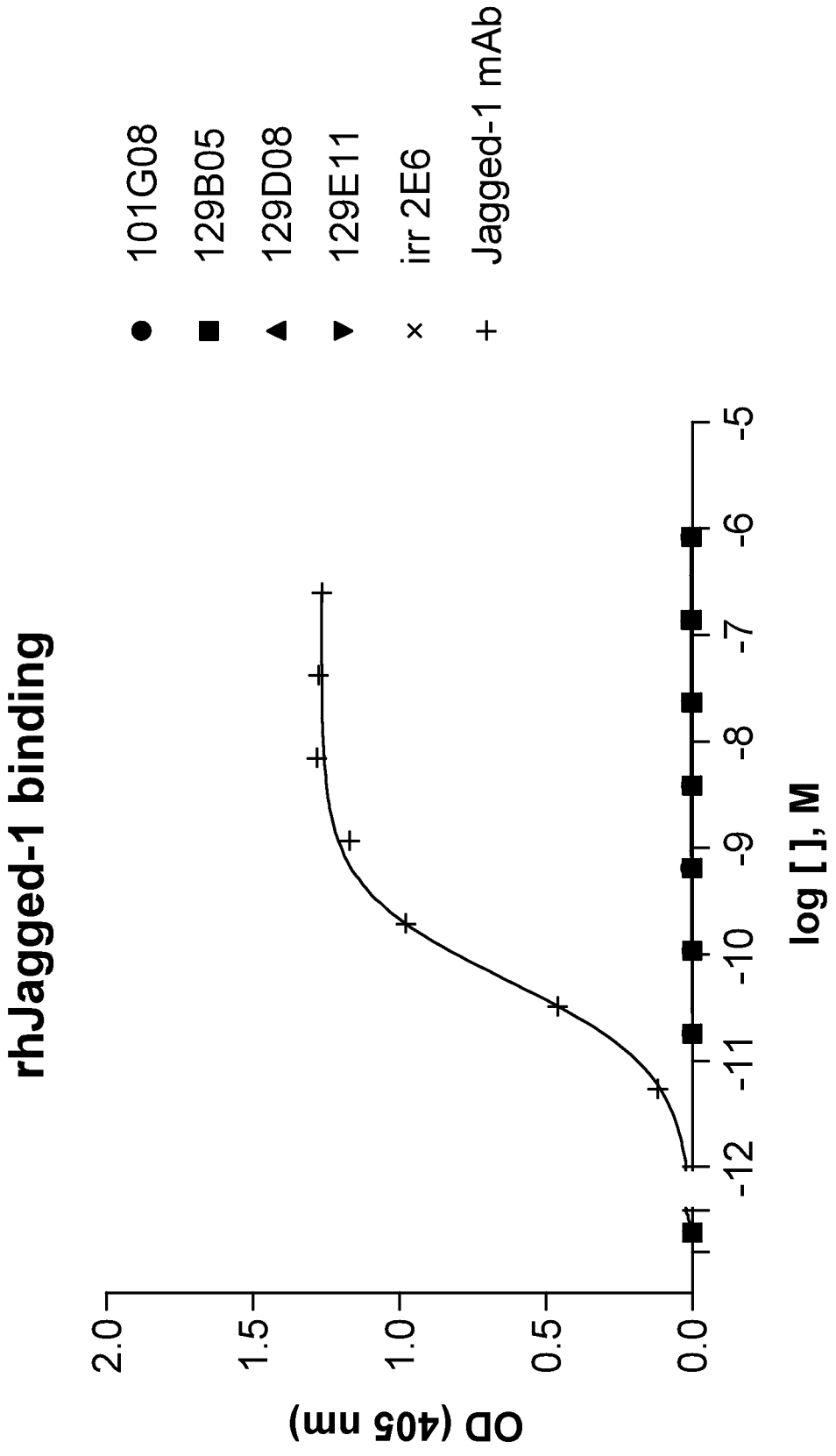

rhJagged-1 binding
OD (405 nm)
2.0
1.5
1.0
0.5
0.0
-12
-11
-10
-9
-8
-7
-6
-5
log [ ], M
101G08
129B05
129D08
129E11
irr 2E6
Jagged-1 mAb

Fig. 13-4

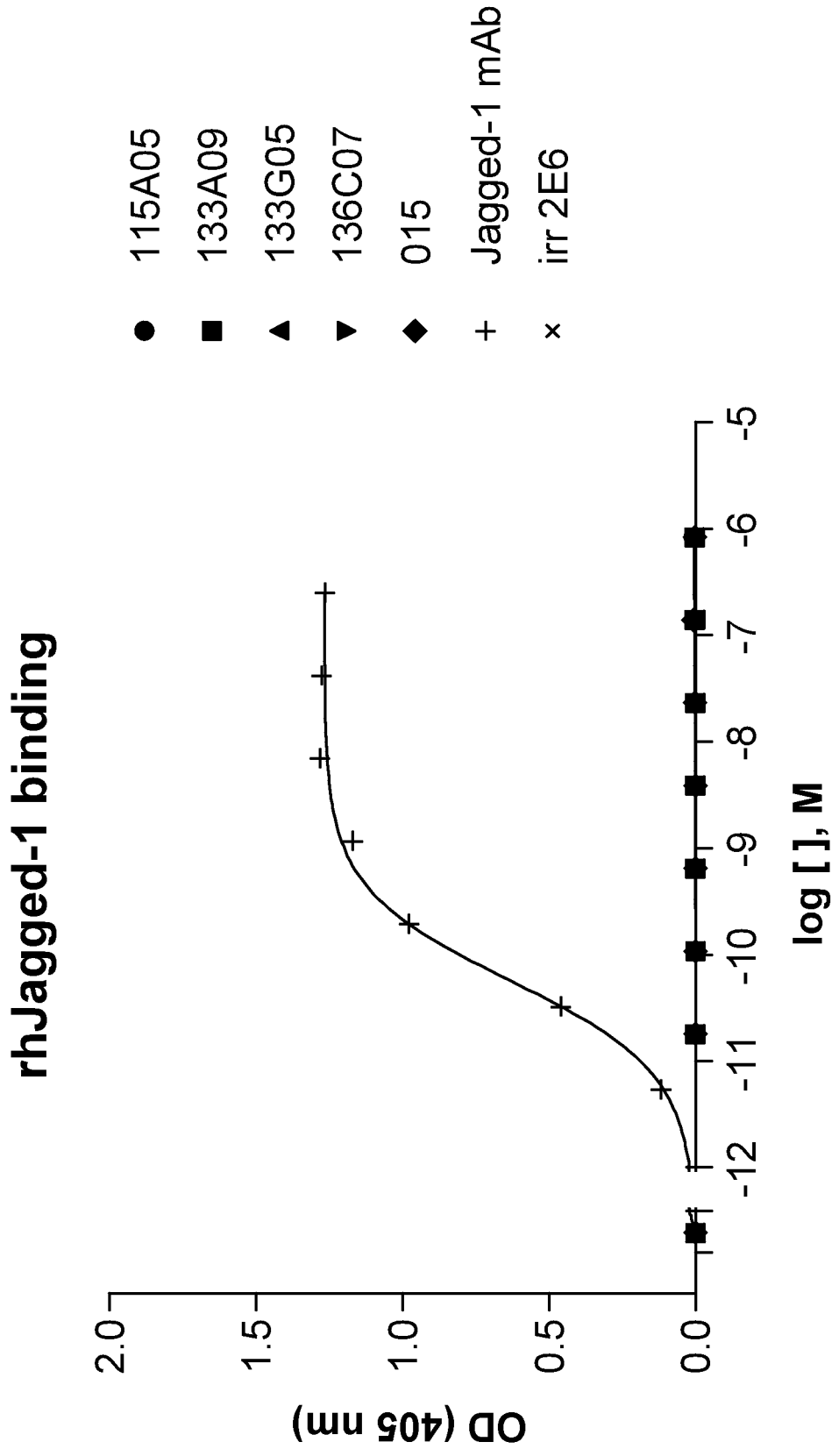

rhJagged-1 binding
OD (405 nm)
2.0
1.5
1.0
0.5
0.0
-12
-11
-10
-9
-8
-7
-6
-5
log [ ], M
115A05
133A09
133G05
136C07
015
Jagged-1 mAb
irr 2E6

Fig. 14-1

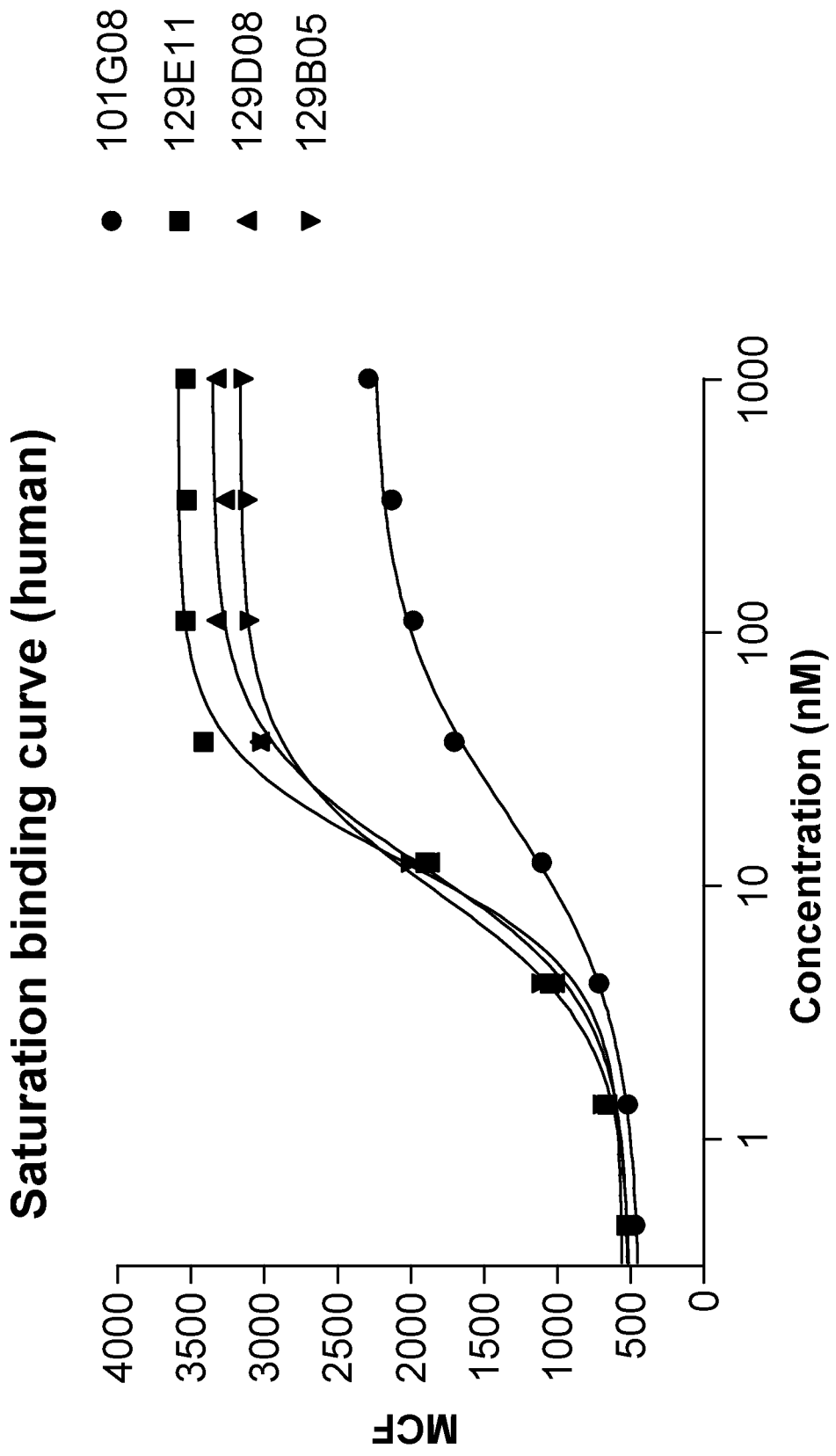

Saturation binding curve (human)
101G08
129E11
129D08
129B05
MCF
4000
3500
3000
2500
2000
1500
1000
500
0
1
10
100
1000
Concentration (nM)

Fig. 14-2

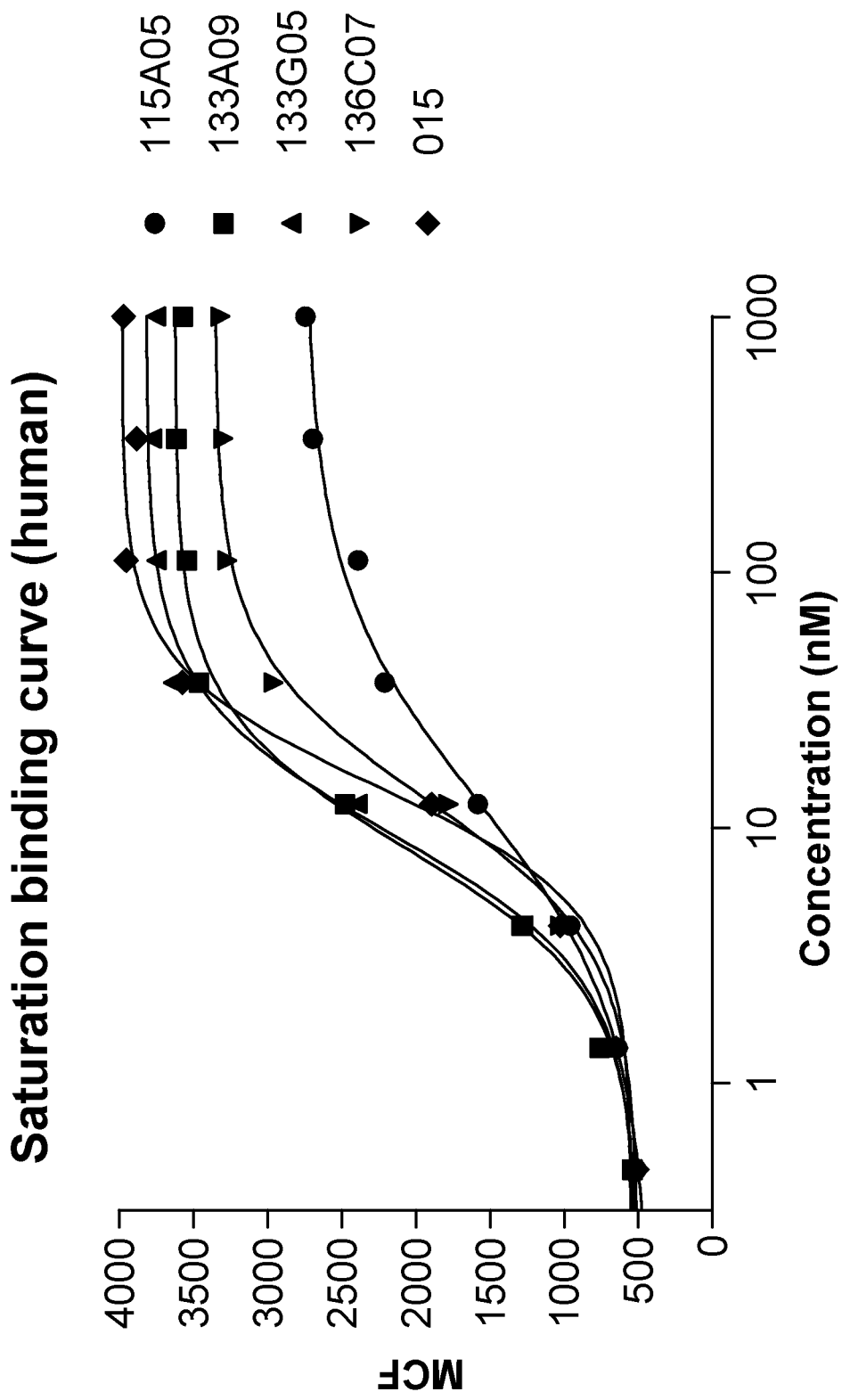

Saturation binding curve (human)
115A05
133A09
133G05
136C07
015
MCF
4000
3500
3000
2500
2000
1500
1000
500
0
1
10
100
1000
Concentration (nM)

Fig. 14-3

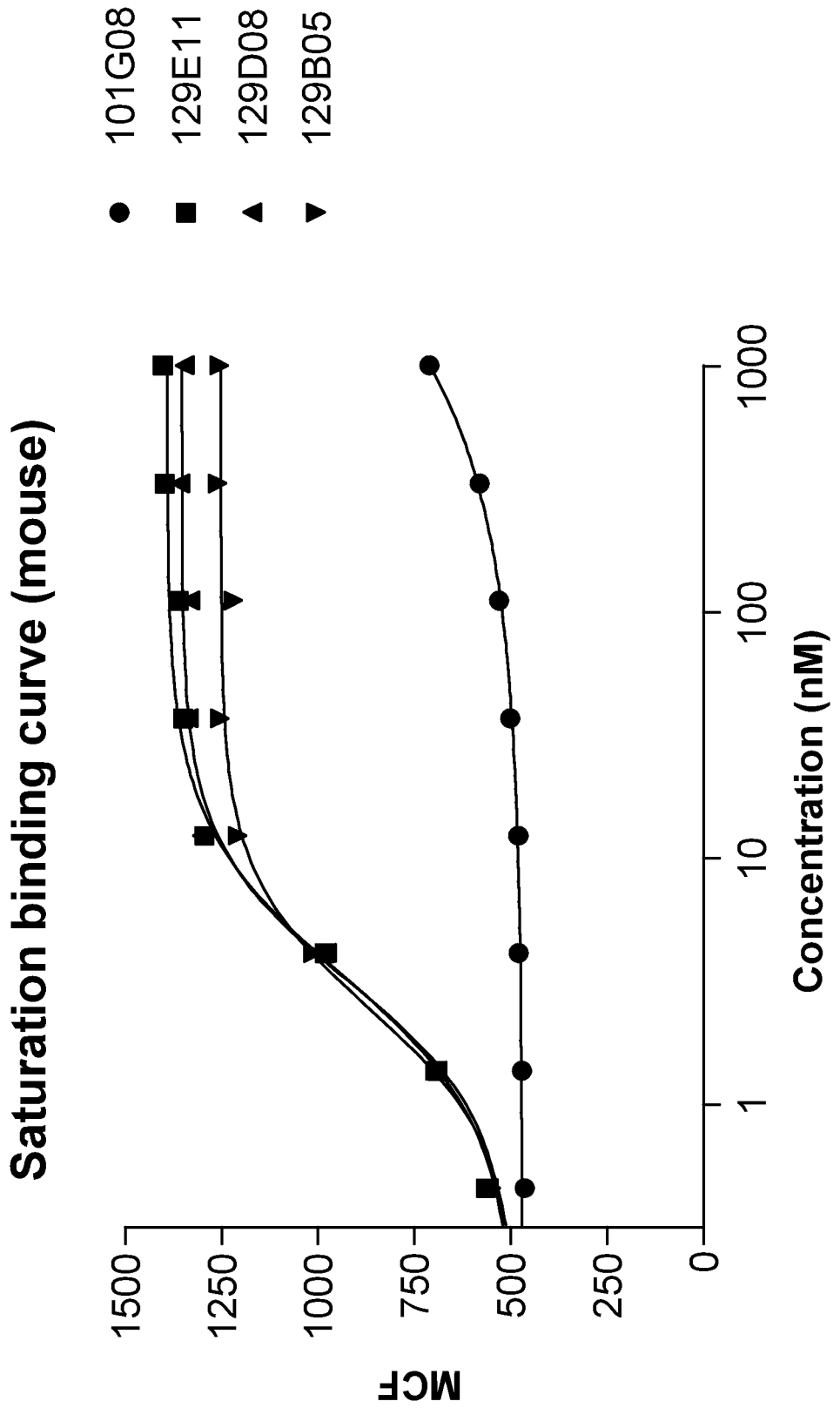

Saturation binding curve (mouse)
101G08
129E11
129D08
129B05
MCF
1500
1250
1000
750
500
250
0
1
10
100
1000
Concentration (nM)

Fig. 14-4

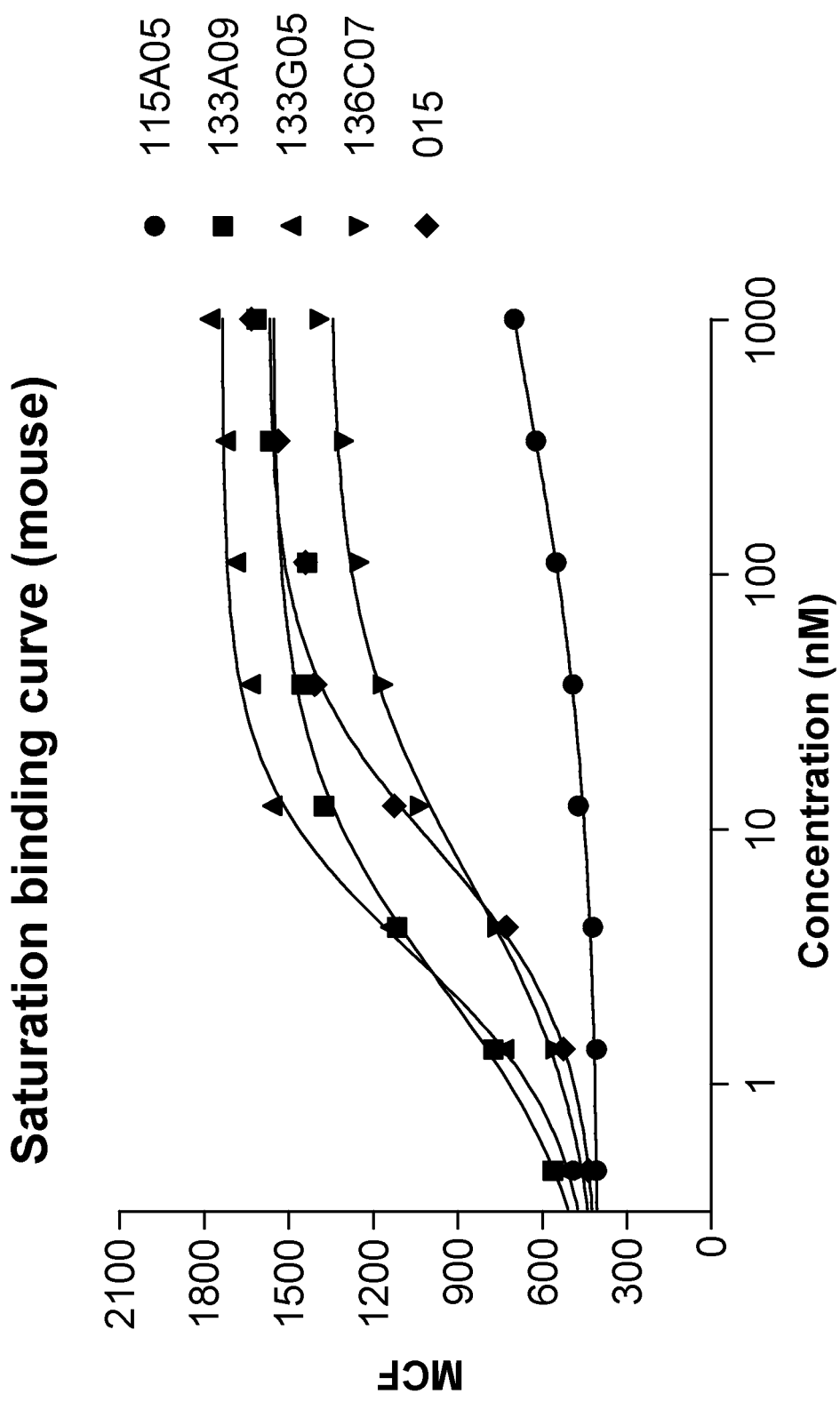

Saturation binding curve (mouse)
115A05
133A09
133G05
136C07
015
MCF
2100
1800
1500
1200
900
600
300
0
1
10
100
1000
Concentration (nM)

Fig. 14-5

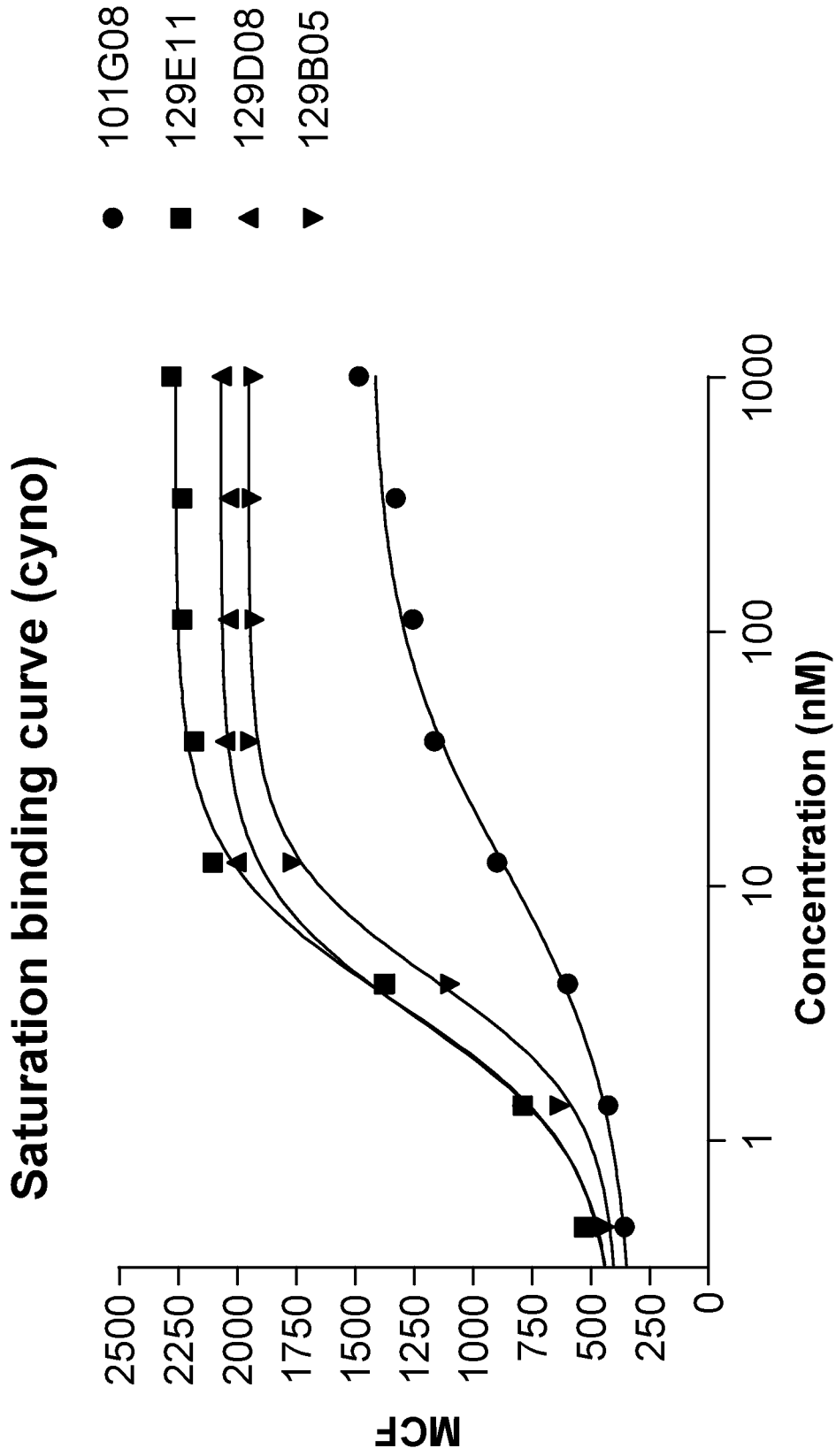

Saturation binding curve (cyno)
101G08
129E11
129D08
129B05
MCF
2500
2250
2000
1750
1500
1250
1000
750
500
250
0
1
10
100
1000
Concentration (nM)

Fig. 14-6

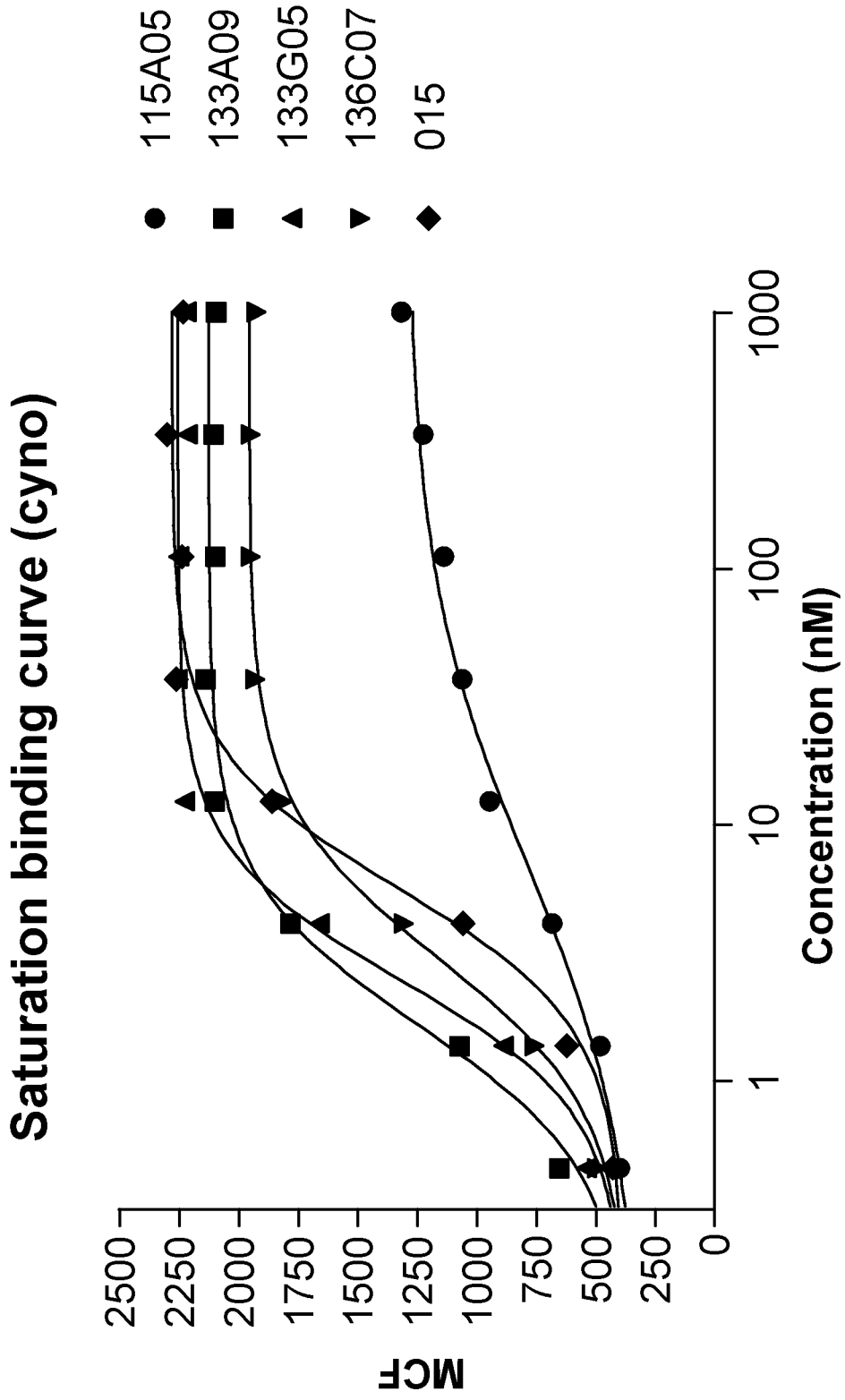

Saturation binding curve (cyno)
115A05
133A09
133G05
136C07
015
MCF
2500
2250
2000
1750
1500
1250
1000
750
500
250
0
1
10
100
1000
Concentration (nM)

Fig. 15

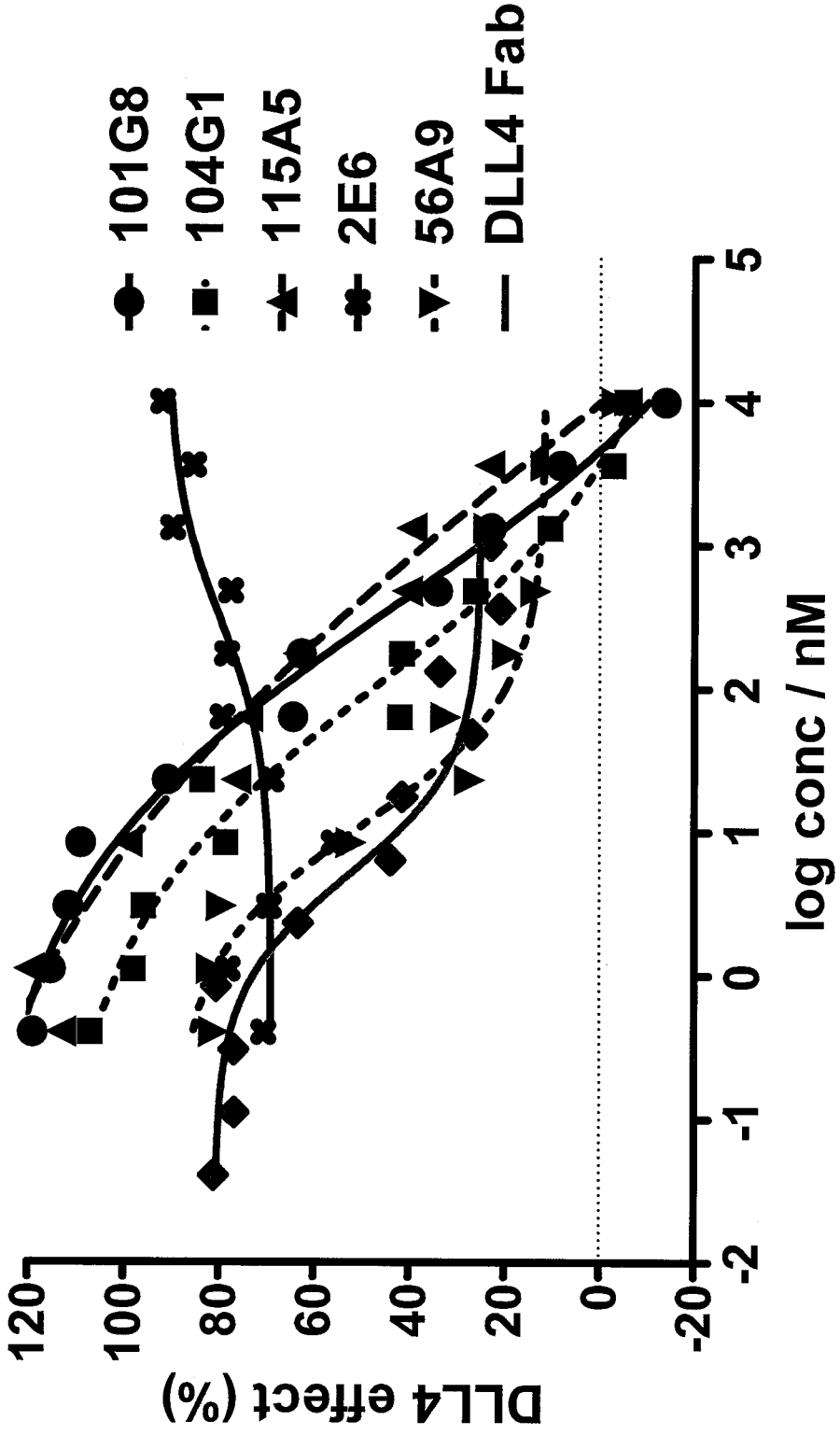
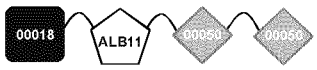
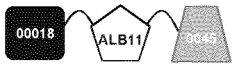
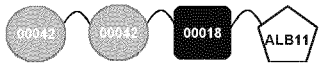

101G8
104G1
115A5
2E6
56A9
DLL4 Fab
DLL4 effect (%)
120
100
80
60
40
20
0
-20
-2
-1
0
1
2
3
4
5
log conc / nM

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

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Fig. 16 cont'd

Legend:

	Description
	DLLBII00018
	00042
	00045
	00050
	ALB11
	*9 GlySer* linker

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Fig. 17A

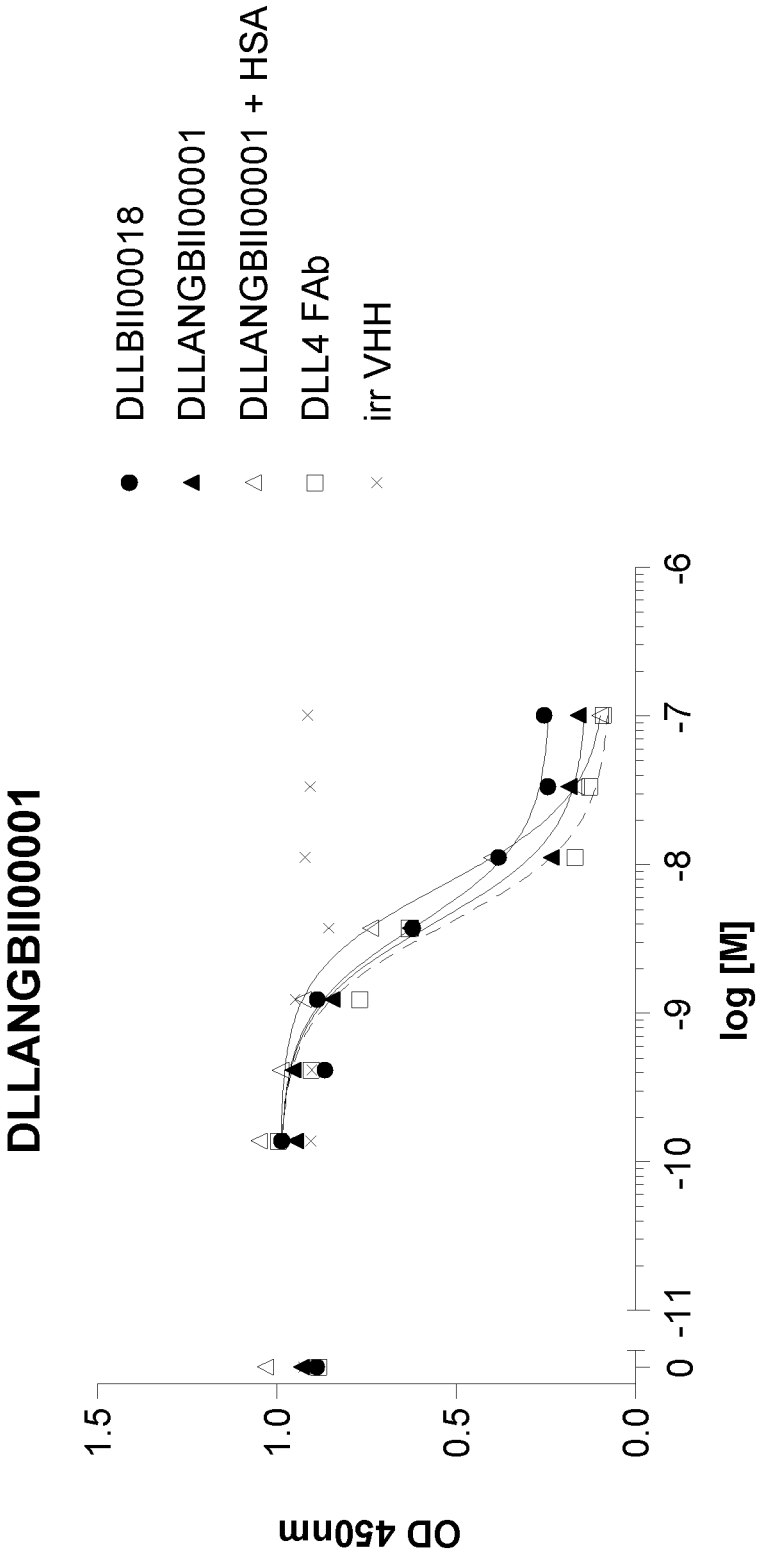
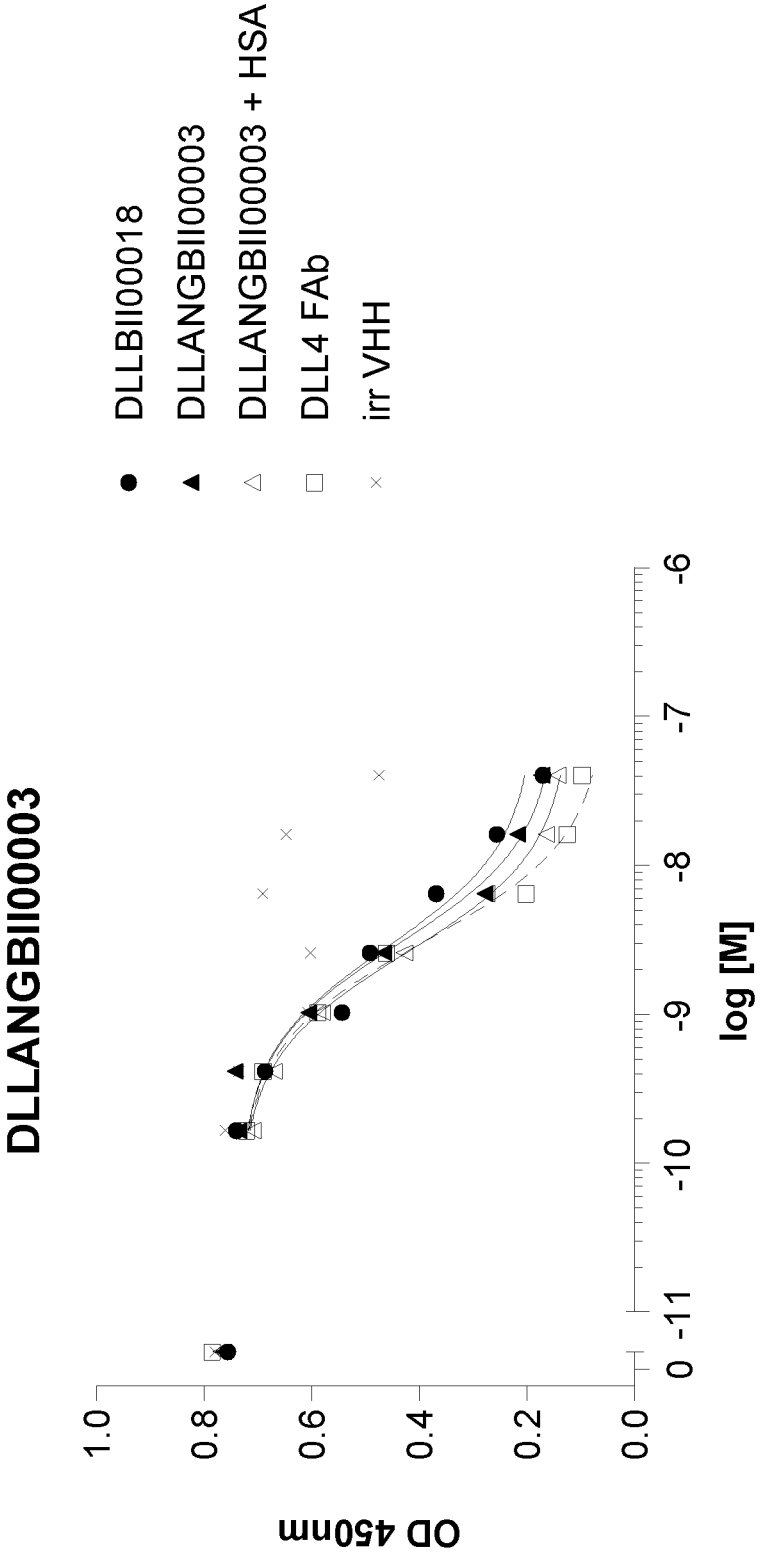


Figure 17B


DLLANGBII00003
DLLBII00018
DLLANGBII00003
DLLANGBII00003 + HSA
DLL4 FAb
irr VHH
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

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Fig. 17C

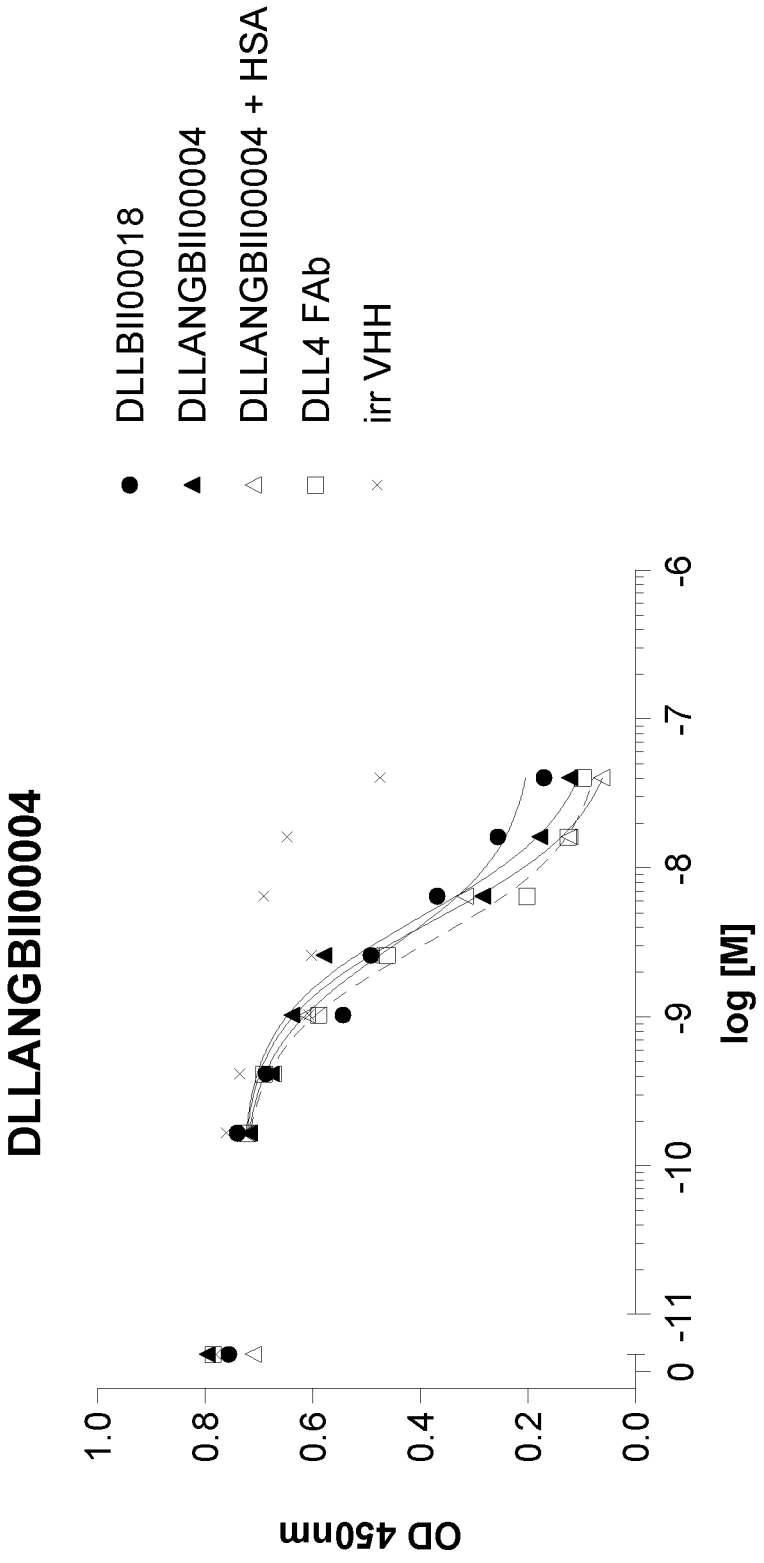


Fig. 17D

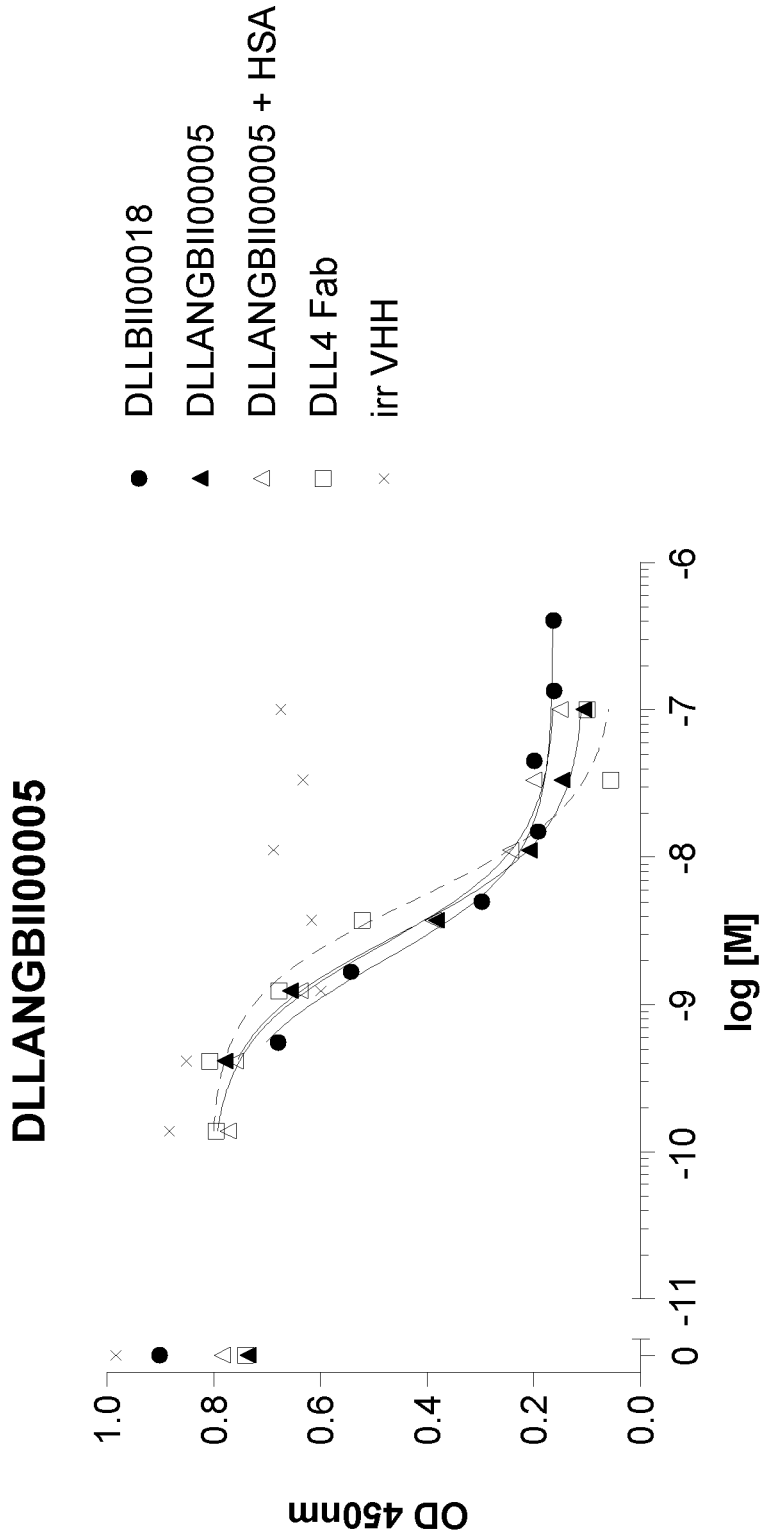

DLLANGBII00005
DLLBII00018
DLLANGBII00005
DLLANGBII00005 + HSA
DLL4 Fab
irr VHH
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17E

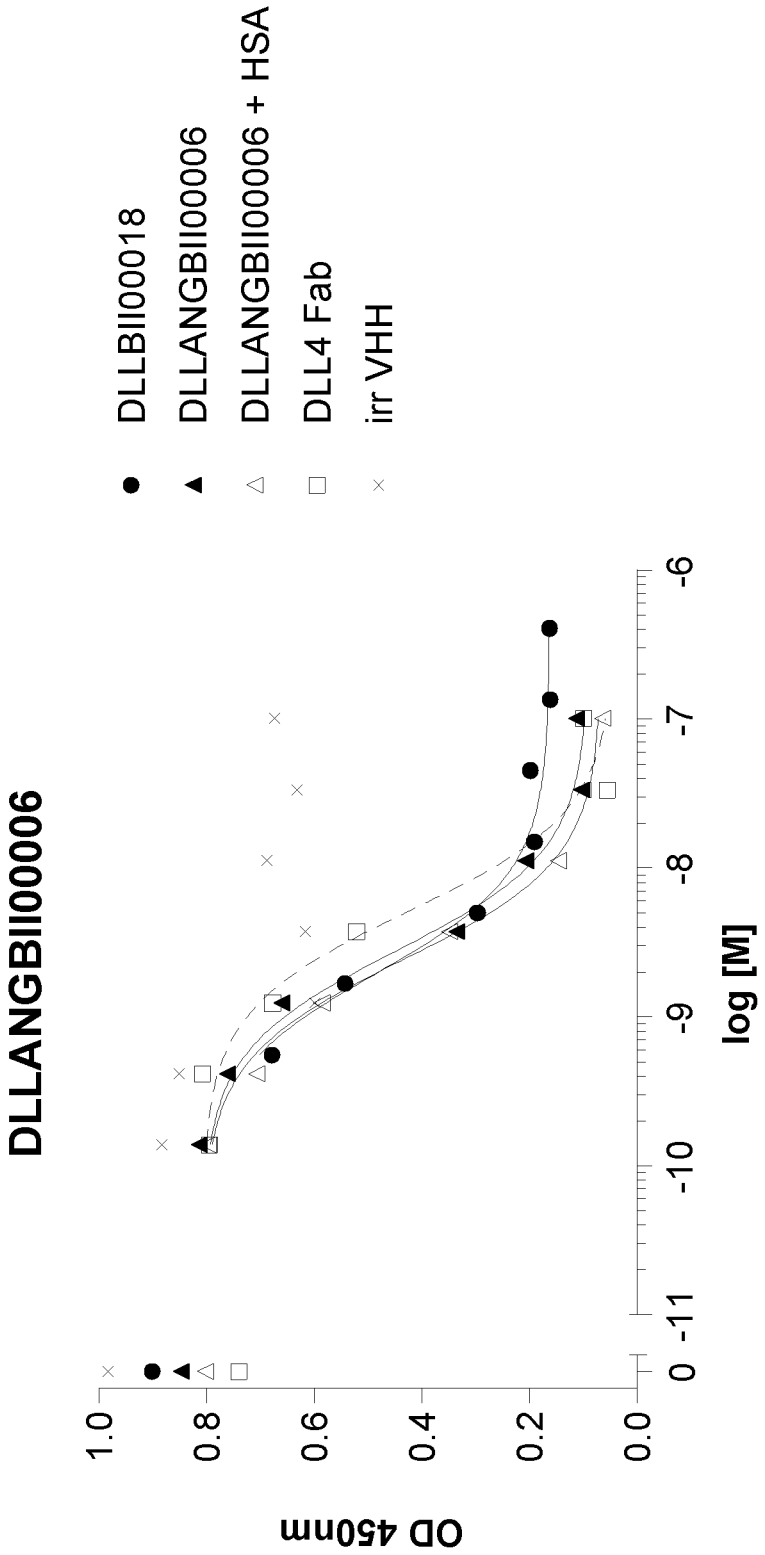

DLLANGBII00006
DLLBII00018
DLLANGBII00006
DLLANGBII00006 + HSA
DLL4 Fab
irr VHH
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17F

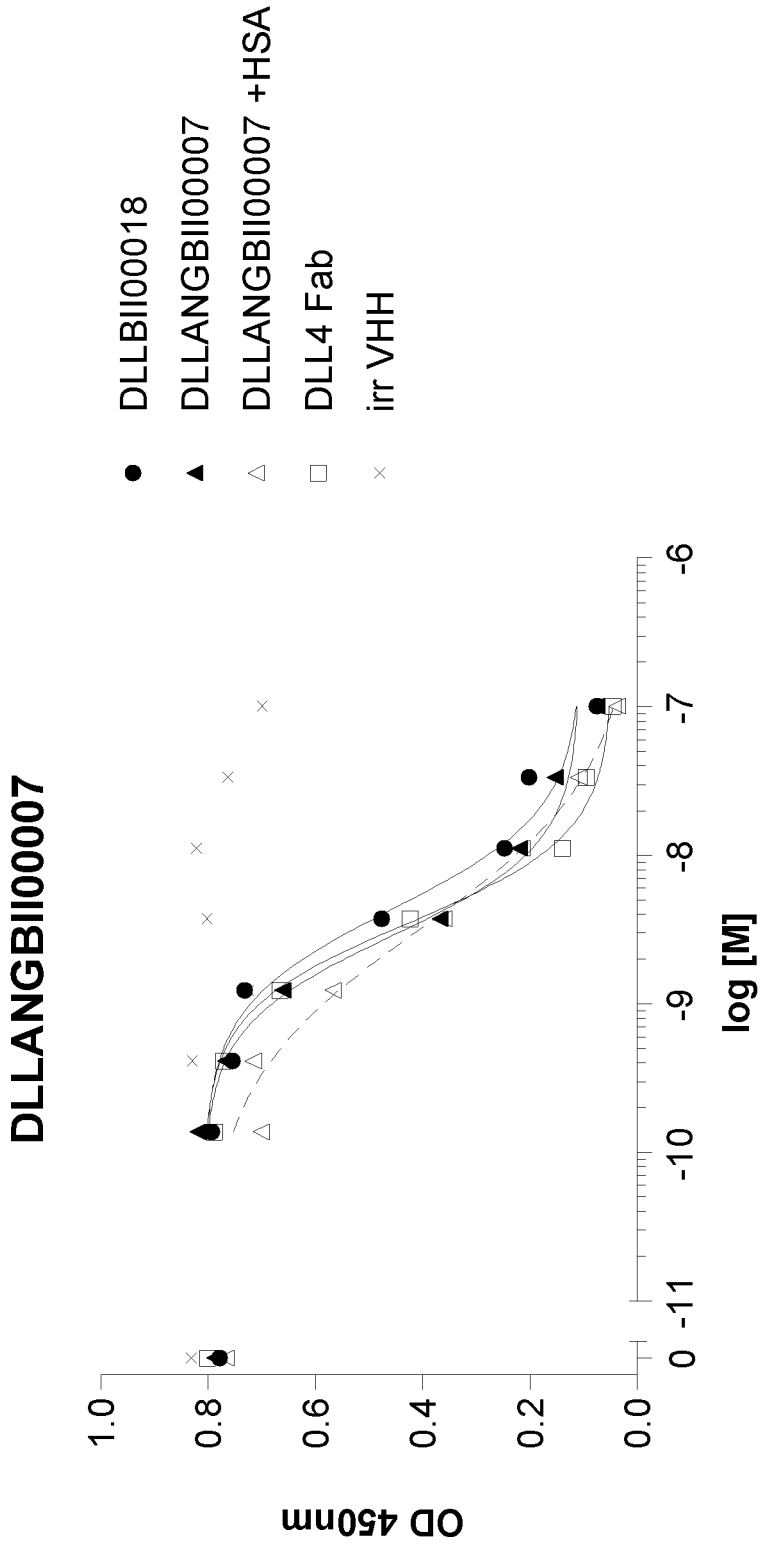

DLLANGBII00007
DLLBII00018
DLLANGBII00007
DLLANGBII00007 +HSA
DLL4 Fab
irr VHH
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17G

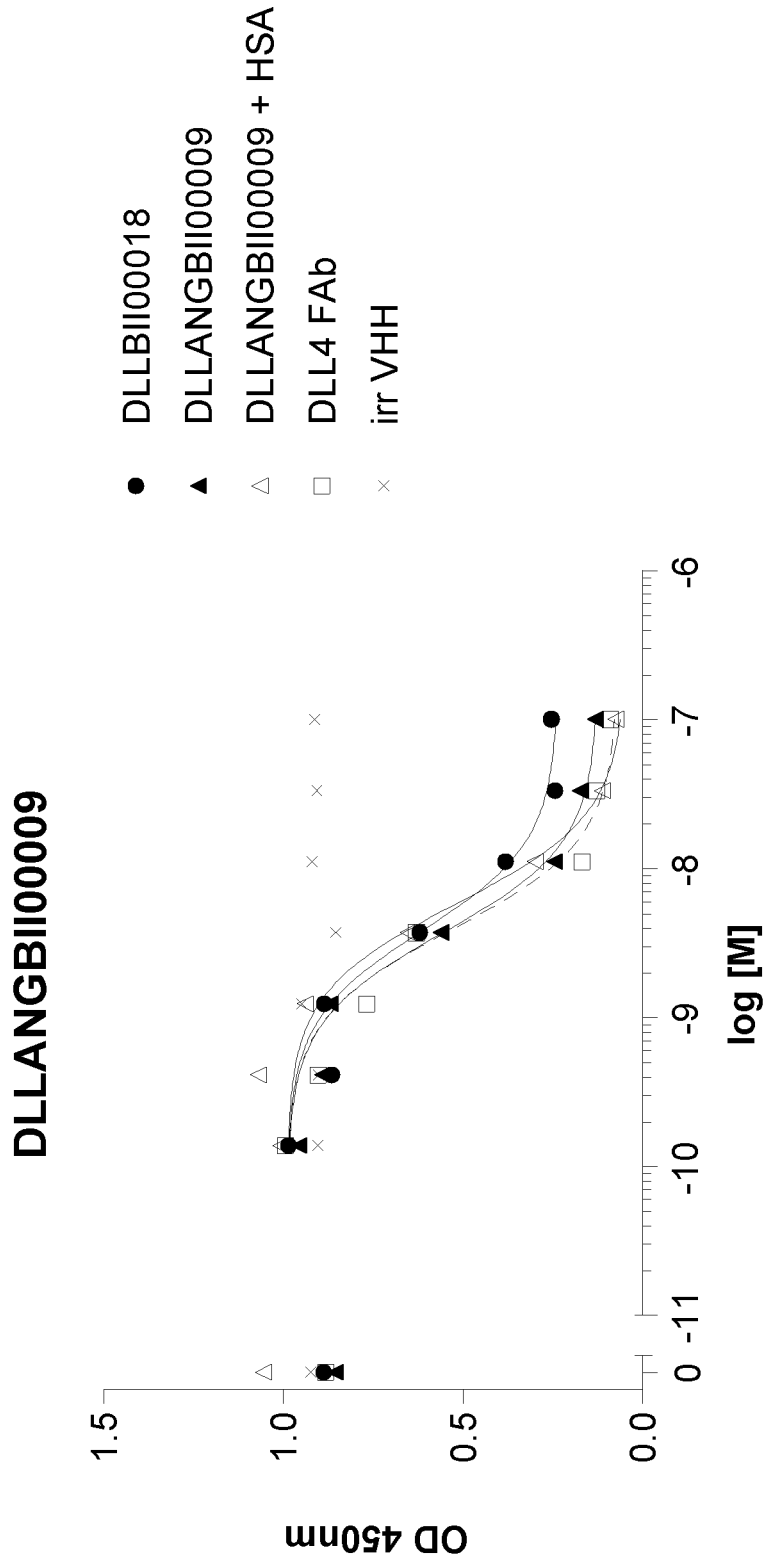

DLLANGBII00009
DLLBII00018
DLLANGBII00009
DLLANGBII00009 + HSA
DLL4 FAb
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17H

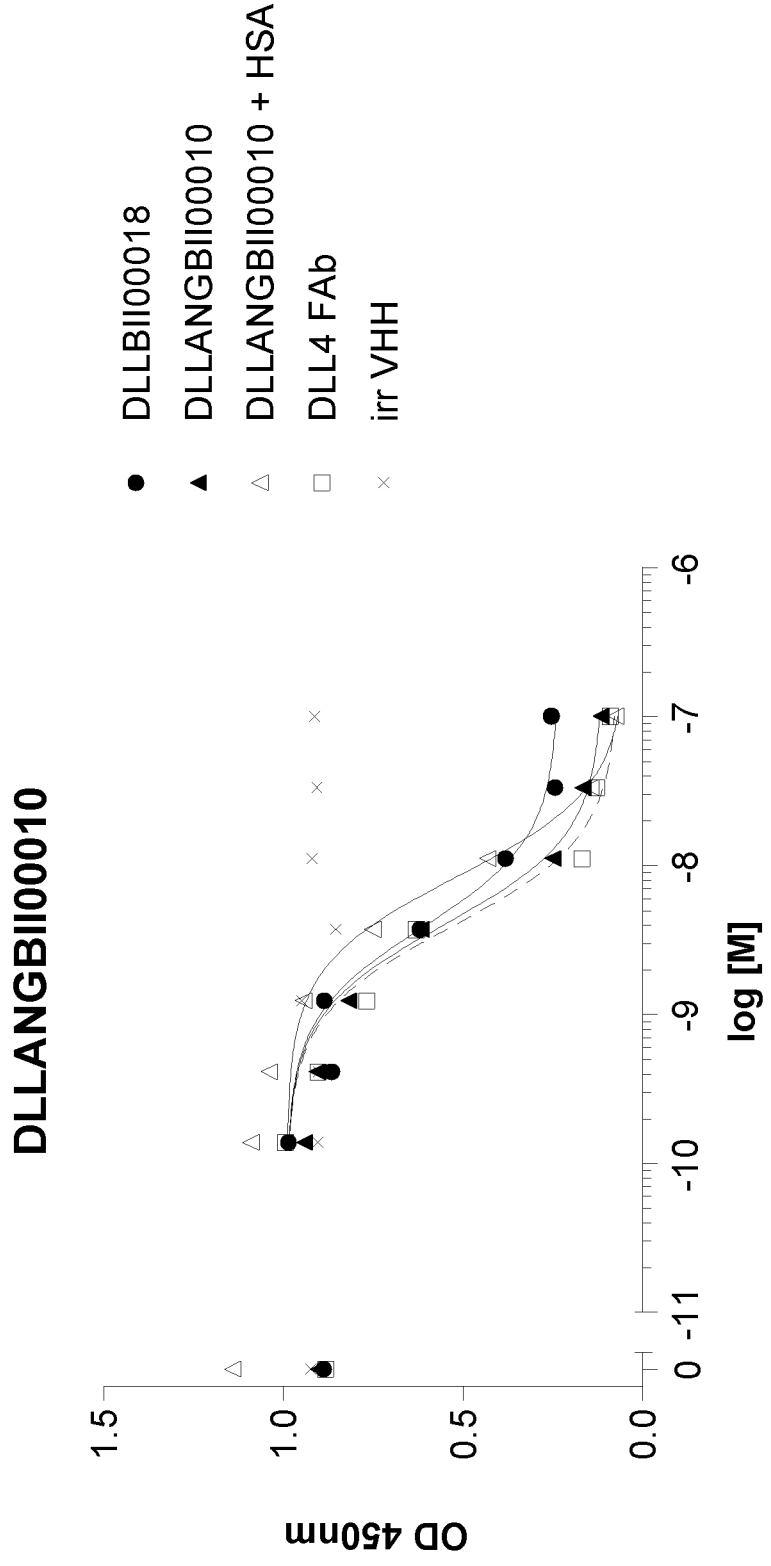

DLLANGBII00010
DLLBII00018
DLLANGBII00010
DLLANGBII00010 + HSA
DLL4 FAb
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17I

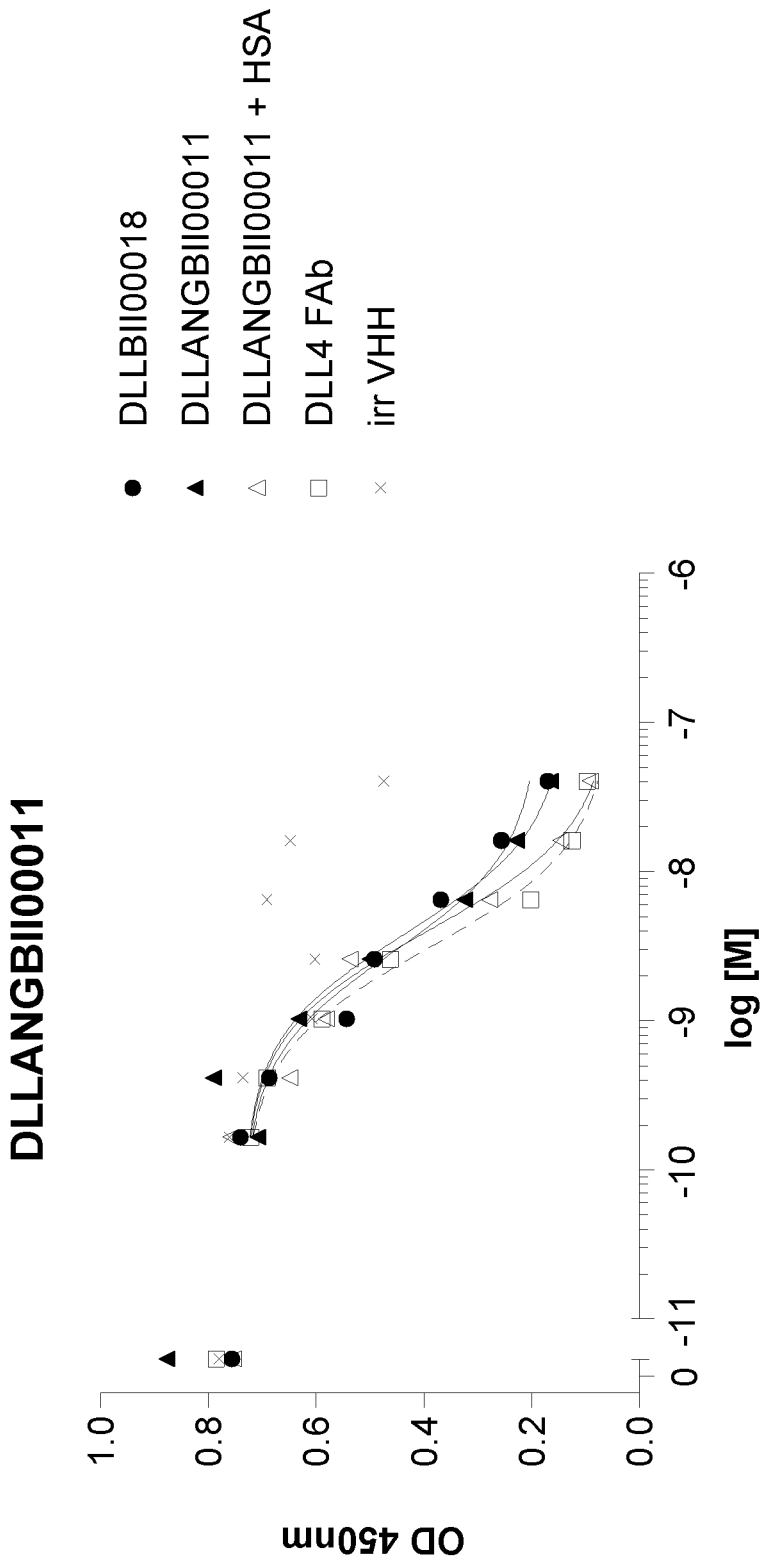

DLLANGBII00011
DLLBII00018
DLLANGBII00011
DLLANGBII00011 + HSA
DLL4 FAb
irr VHH
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17J

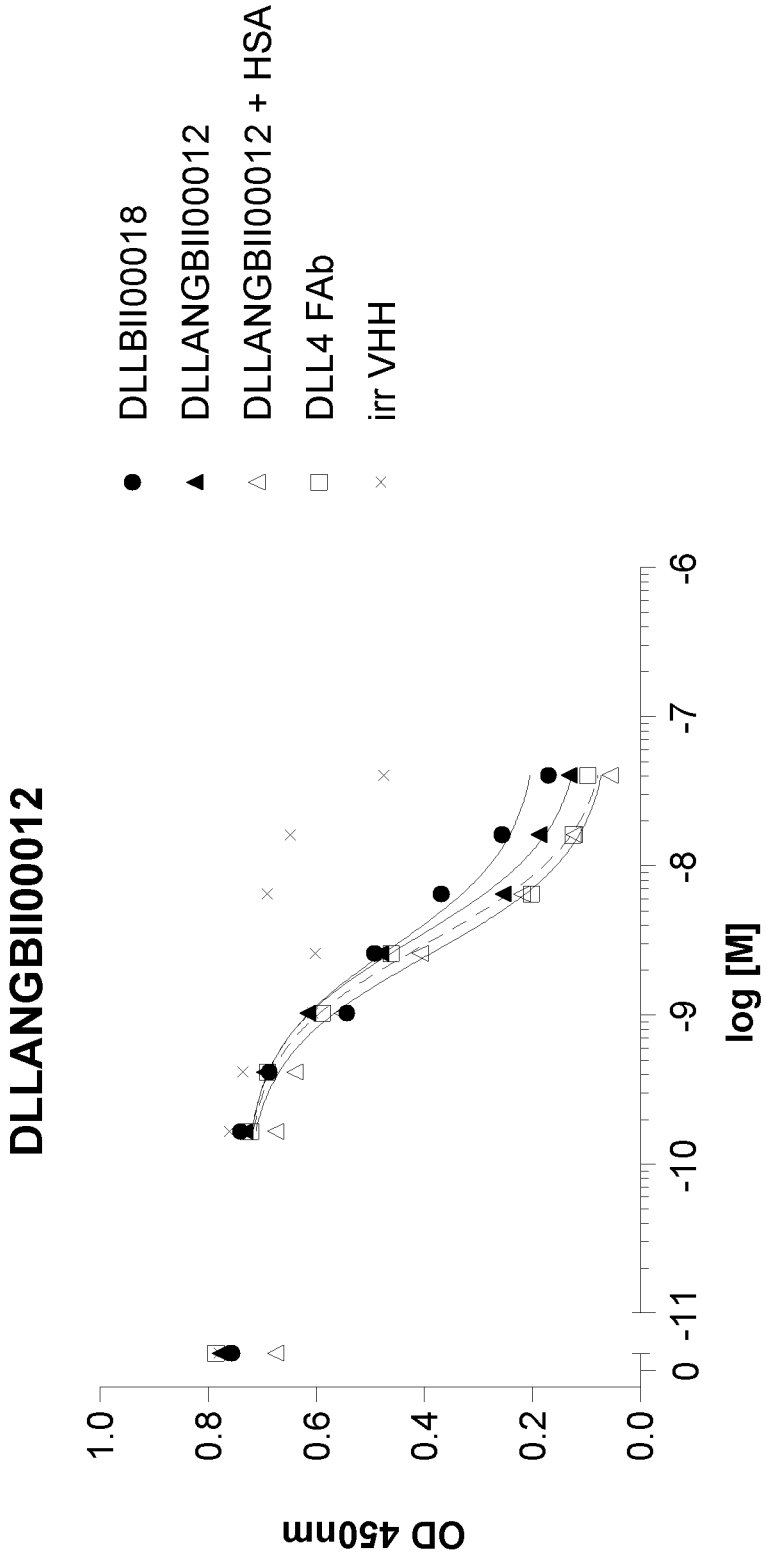

DLLANGBII00012
DLLBII00018
DLLANGBII00012
DLLANGBII00012 + HSA
DLL4 FAb
irr VHH
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17K

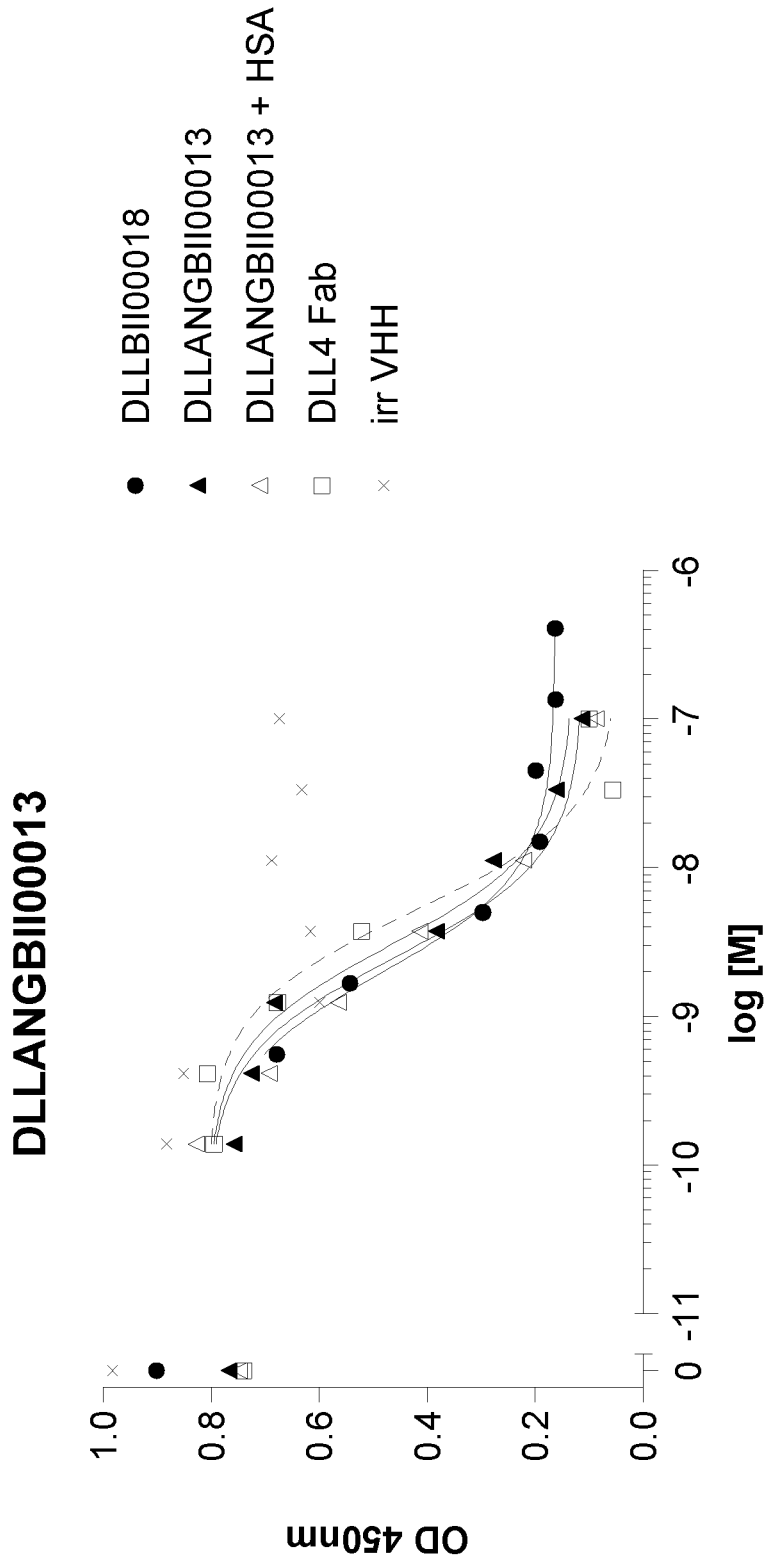

DLLANGBII00013
DLLBII00018
DLLANGBII00013
DLLANGBII00013 + HSA
DLL4 Fab
irr VHH
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17L

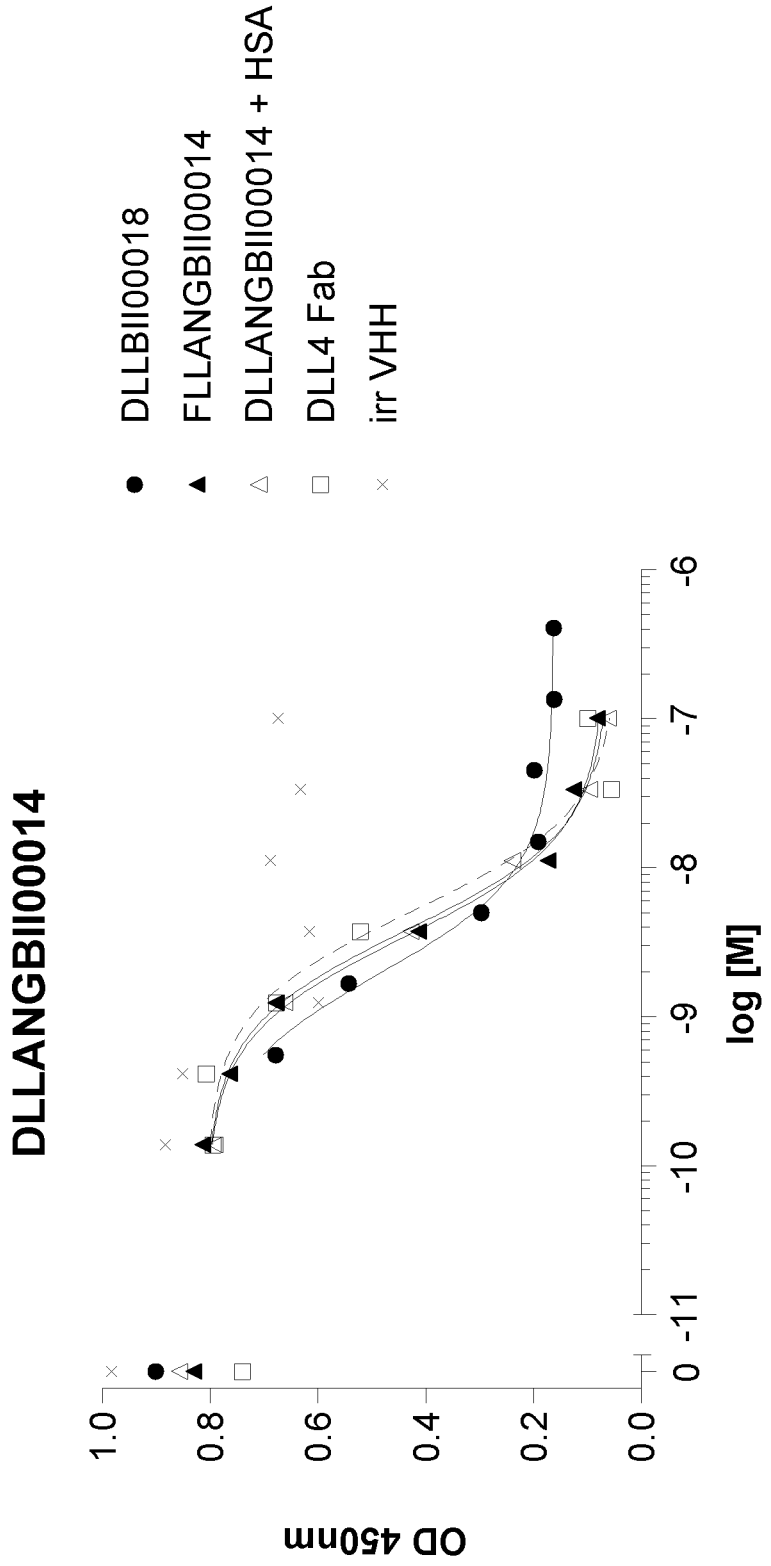

DLLANGBII00014
DLLBII00018
FLLANGBII00014
DLLANGBII00014 + HSA
DLL4 Fab
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
1.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 17M

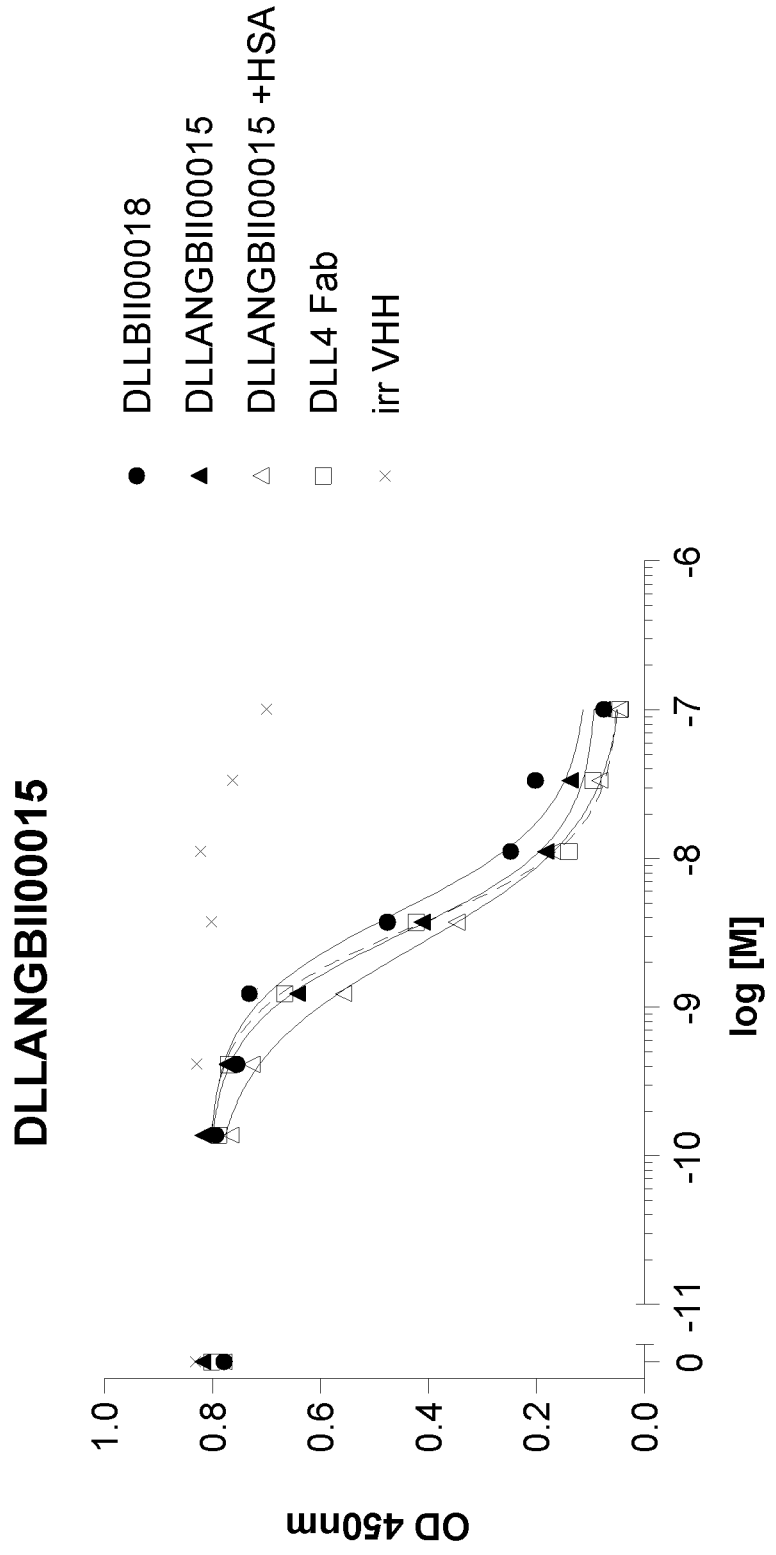

DLLANGBII00015
DLLBII00018
DLLANGBII00015
DLLANGBII00015 +HSA
DLL4 Fab
irr VHH
OD 450nm
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 18-1A

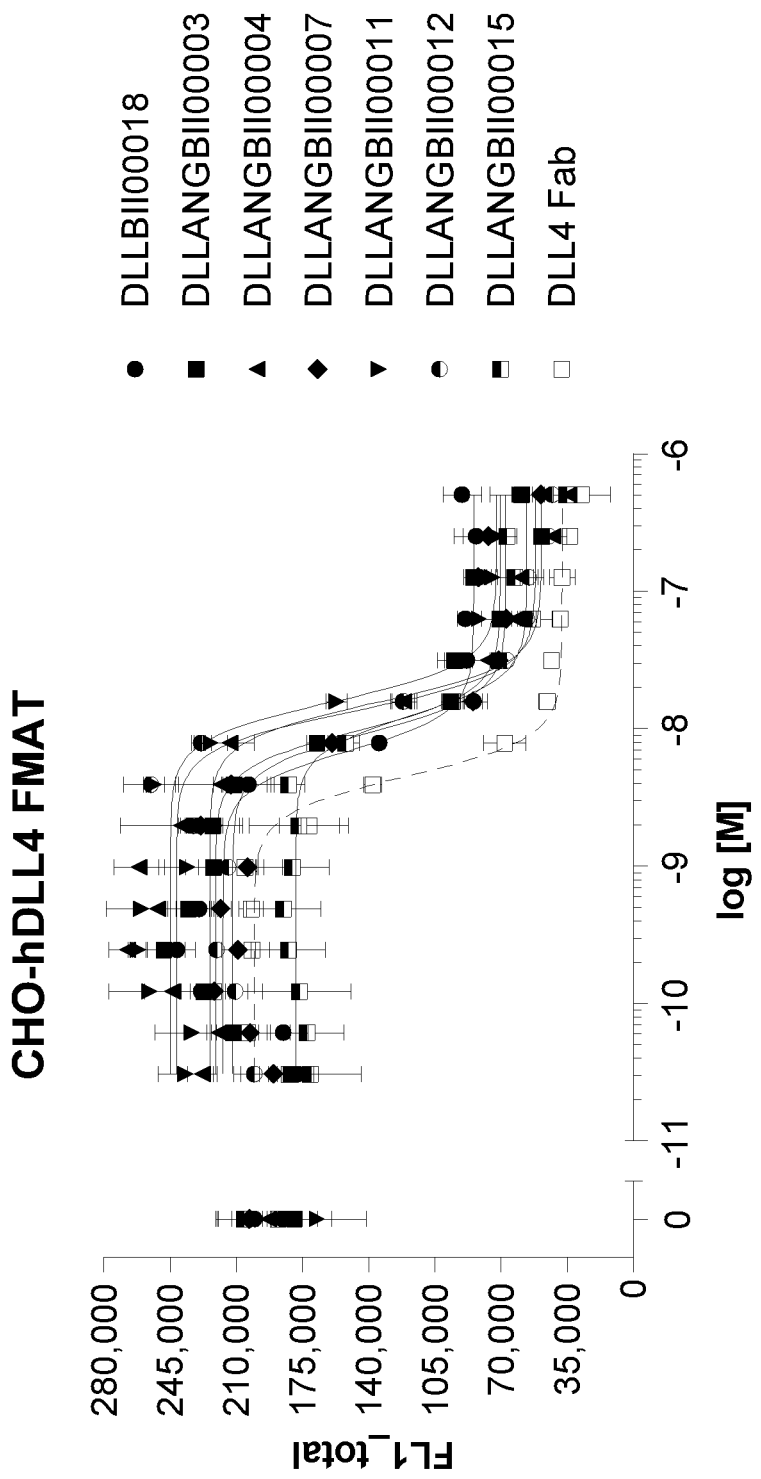

DLLBII00018
DLLANGBII00003
DLLANGBII00004
DLLANGBII00007
DLLANGBII00011
DLLANGBII00012
DLLANGBII00015
DLL4 Fab
CHO-hDLL4 FMAT
FL1_total
280,000
245,000
210,000
175,000
140,000
105,000
70,000
35,000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 18-1A (continued)

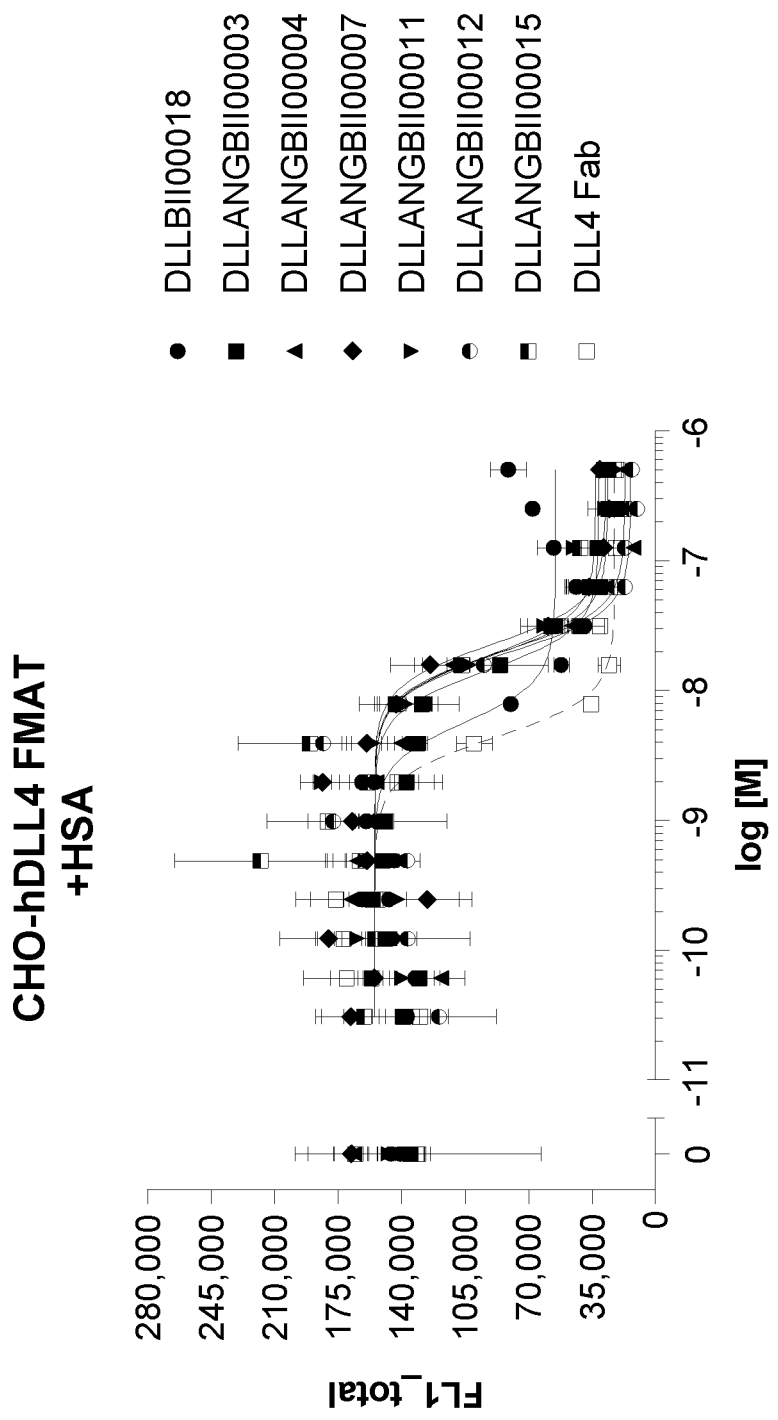


Figure 18-1B

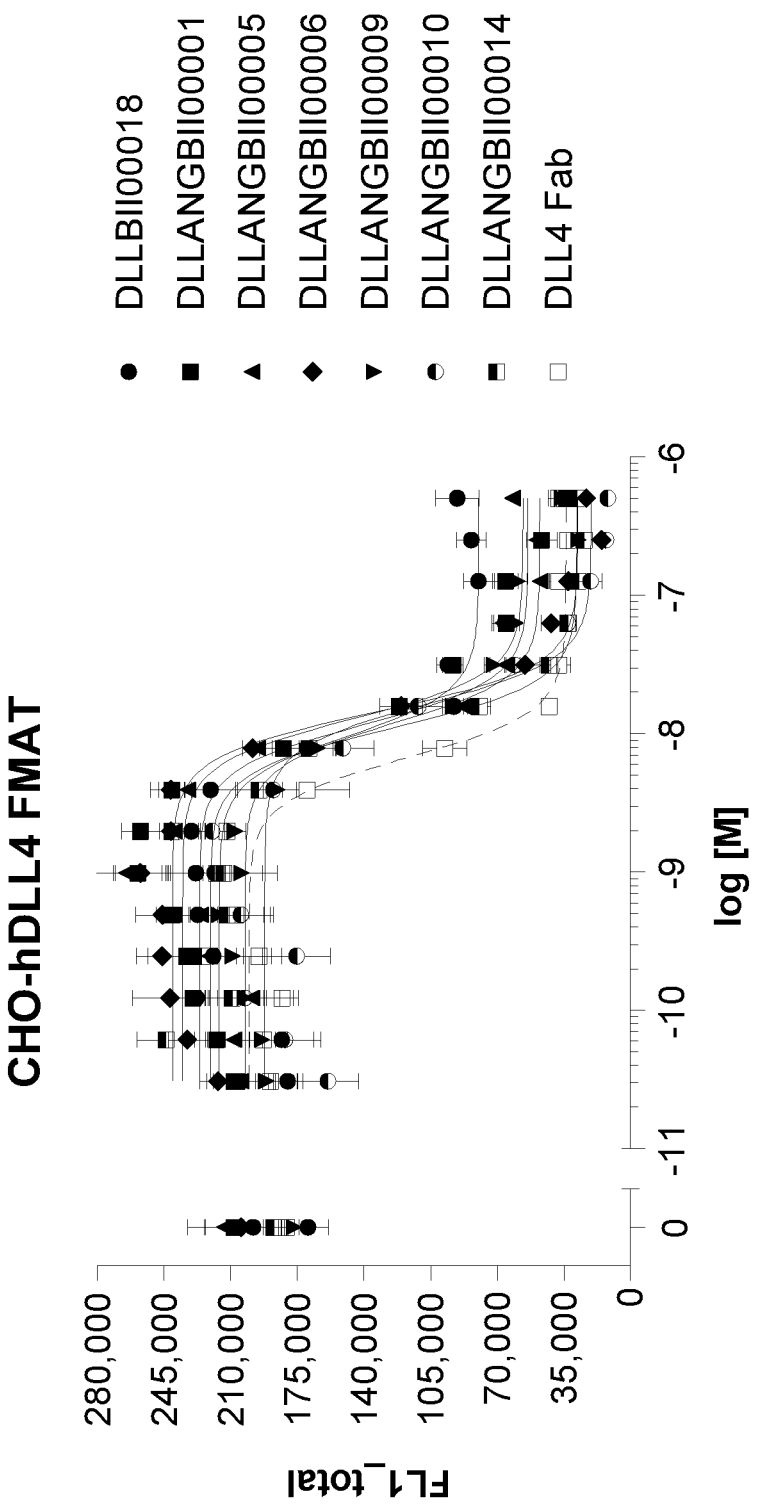

DLLBII00018
DLLANGBII00001
DLLANGBII00005
DLLANGBII00006
DLLANGBII00009
DLLANGBII00010
DLLANGBII00014
DLL4 Fab
CHO-hDLL4 FMAT
FL1_total
280,000
245,000
210,000
175,000
140,000
105,000
70,000
35,000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 18-1B (continued)

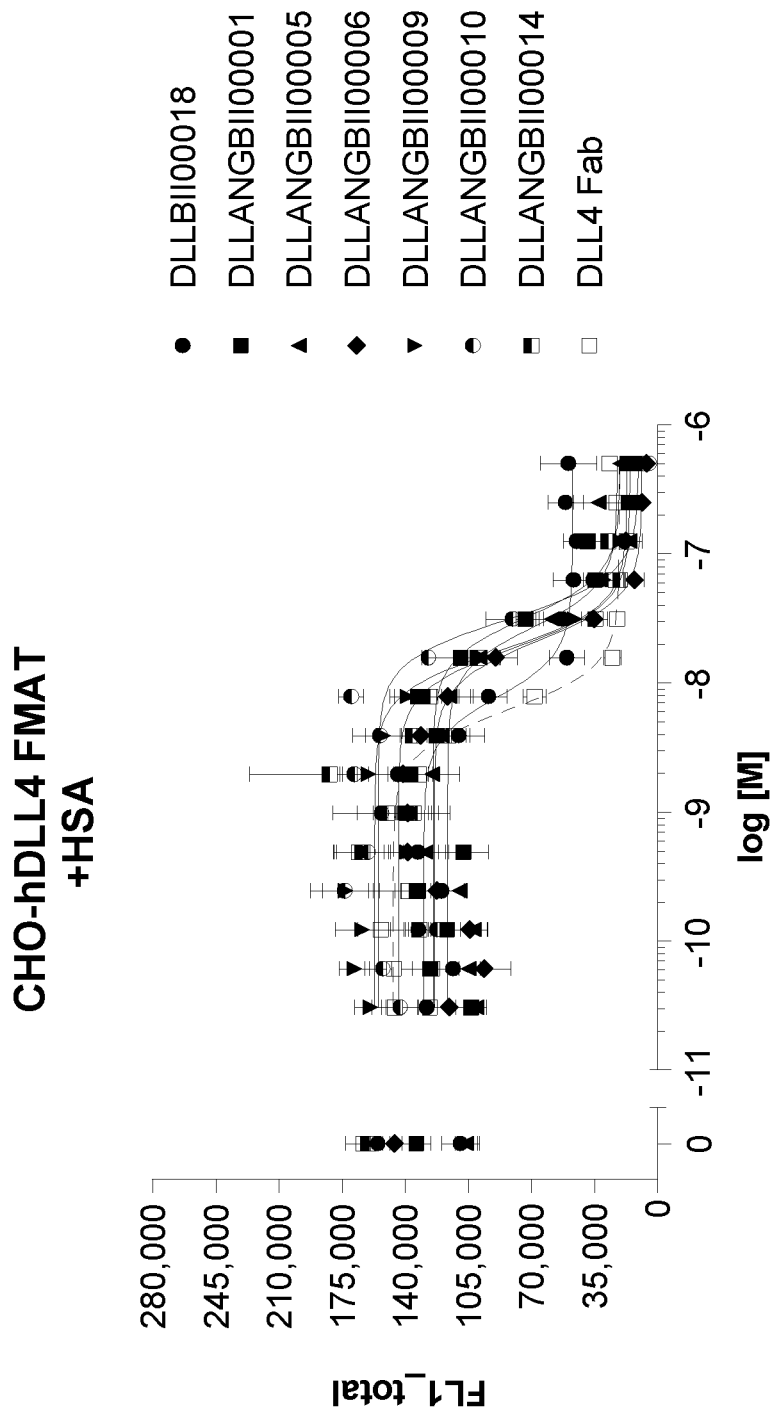


Figure 18-2A

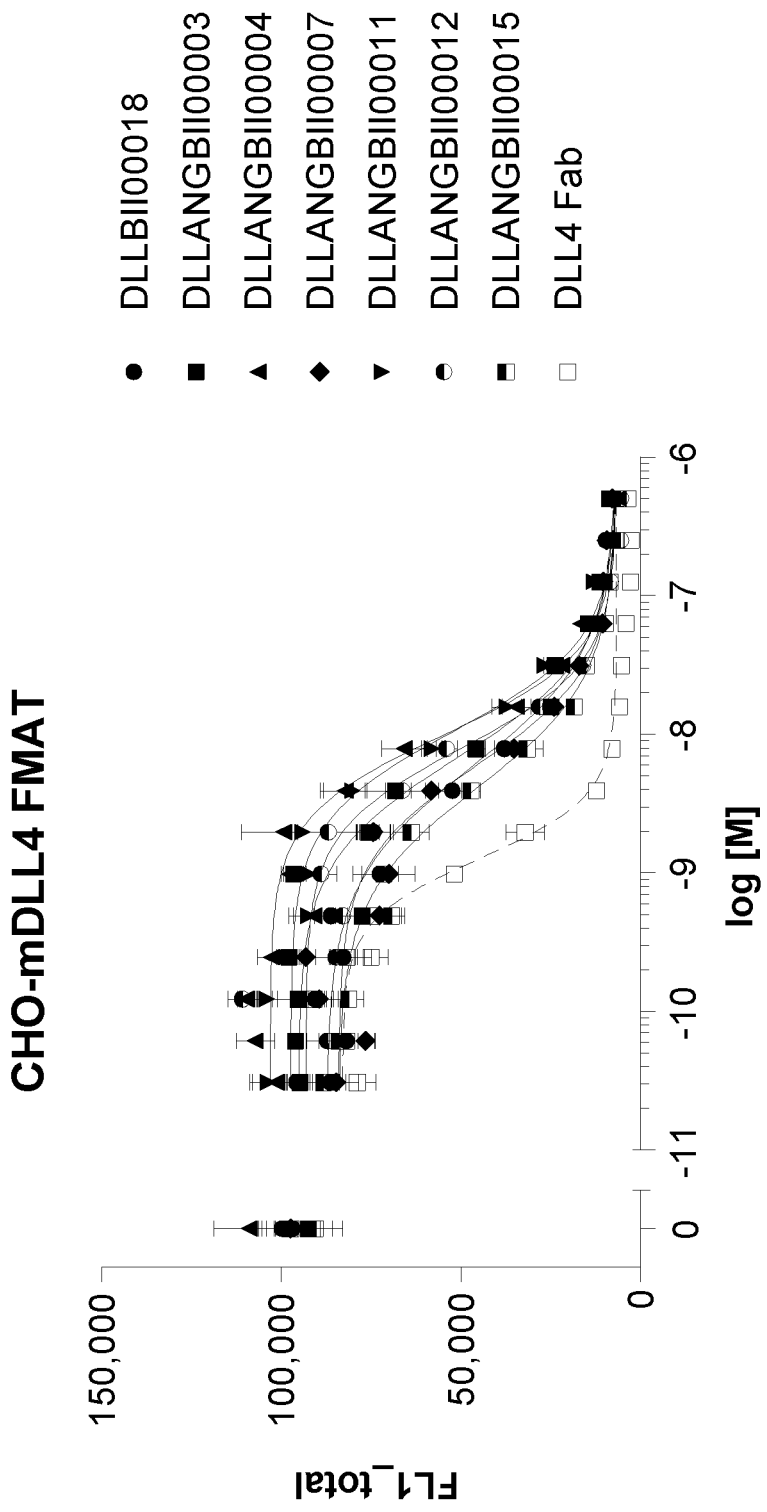

DLLBII00018
DLLANGBII00003
DLLANGBII00004
DLLANGBII00007
DLLANGBII00011
DLLANGBII00012
DLLANGBII00015
DLL4 Fab
CHO-mDLL4 FMAT
FL1_total
150,000
100,000
50,000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 18-2A (continued)

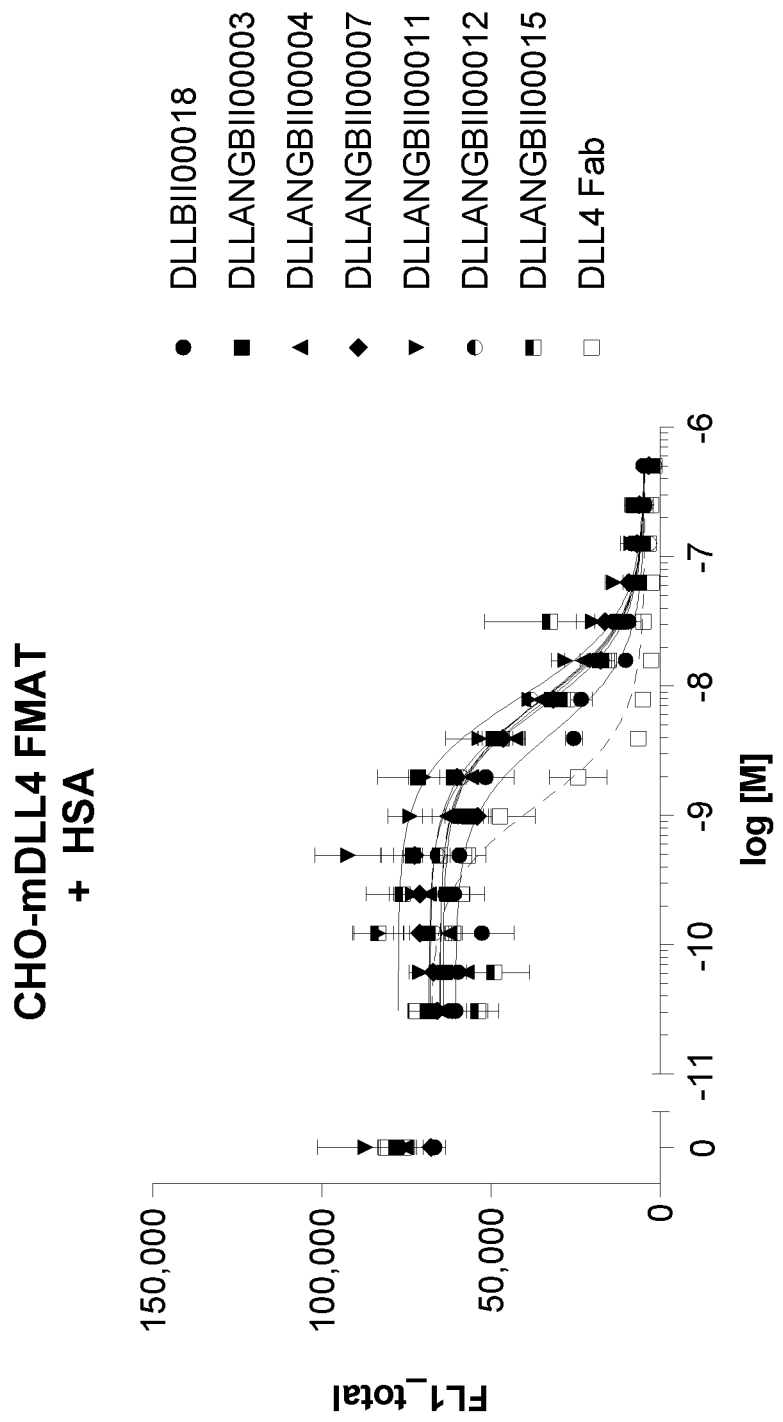


Figure 18-2B

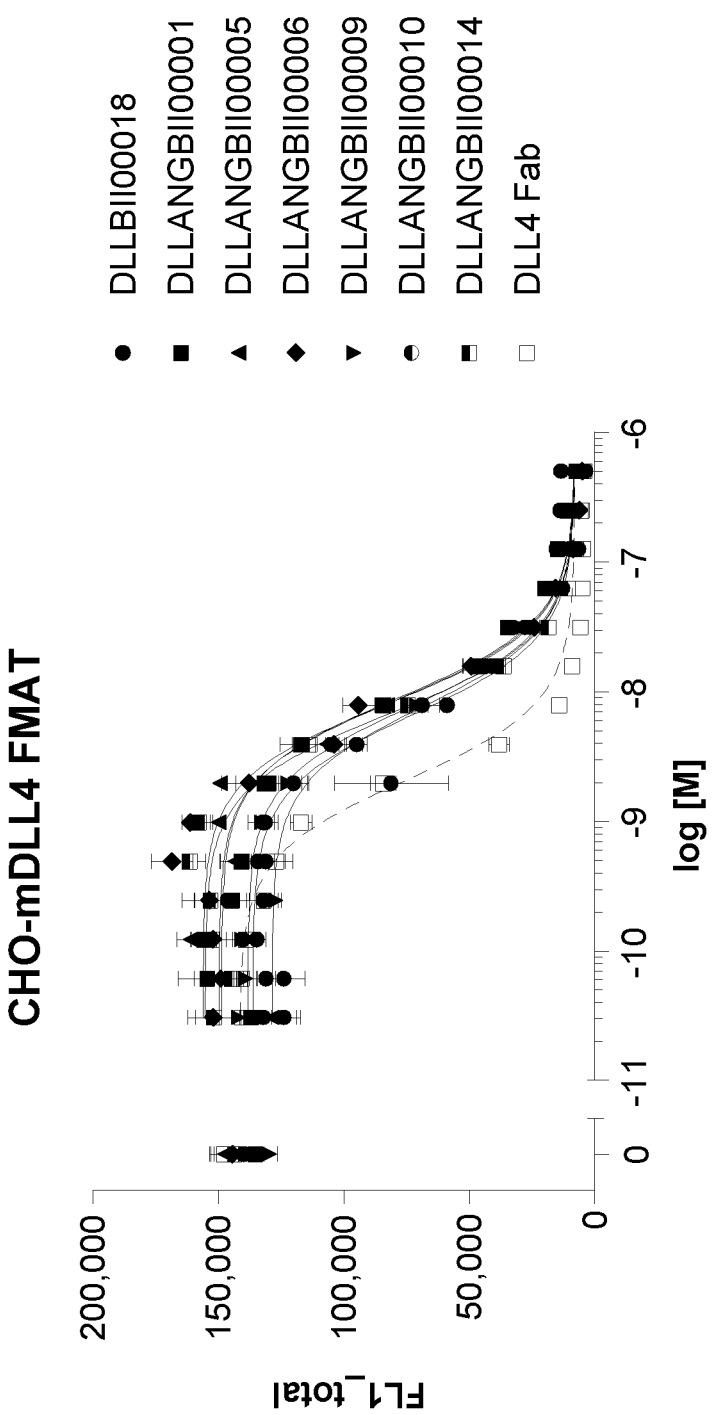

DLLBII00018
DLLANGBII00001
DLLANGBII00005
DLLANGBII00006
DLLANGBII00009
DLLANGBII00010
DLLANGBII00014
DLL4 Fab
CHO-mDLL4 FMAT
FL1_total
200,000
150,000
100,000
50,000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 18-2B (continued)

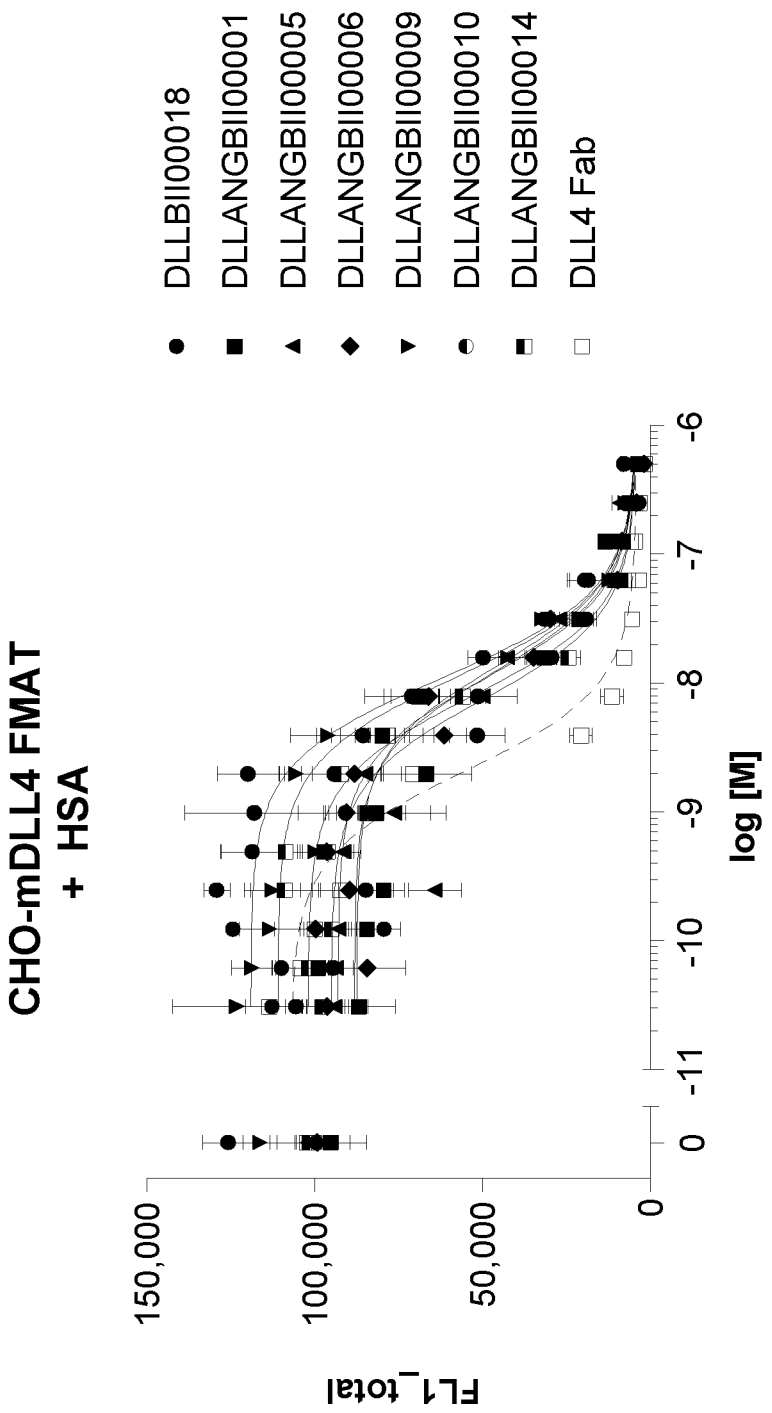


Figure 19A

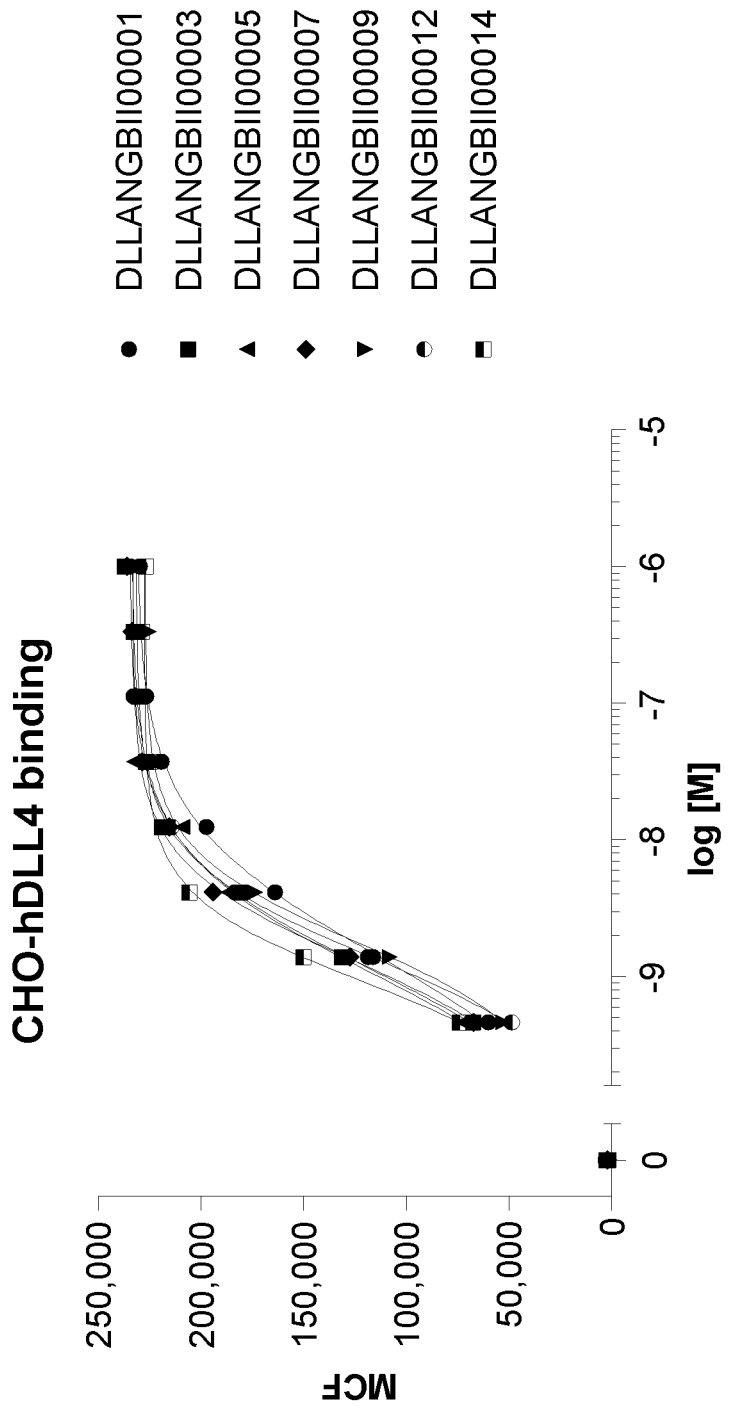

DLLANGBII00001
DLLANGBII00003
DLLANGBII00005
DLLANGBII00007
DLLANGBII00009
DLLANGBII00012
DLLANGBII00014
CHO-hDLL4 binding
MCF
250,000
200,000
150,000
100,000
50,000
0
0
-5
-6
-7
-8
-9
log [M]

Figure 19B

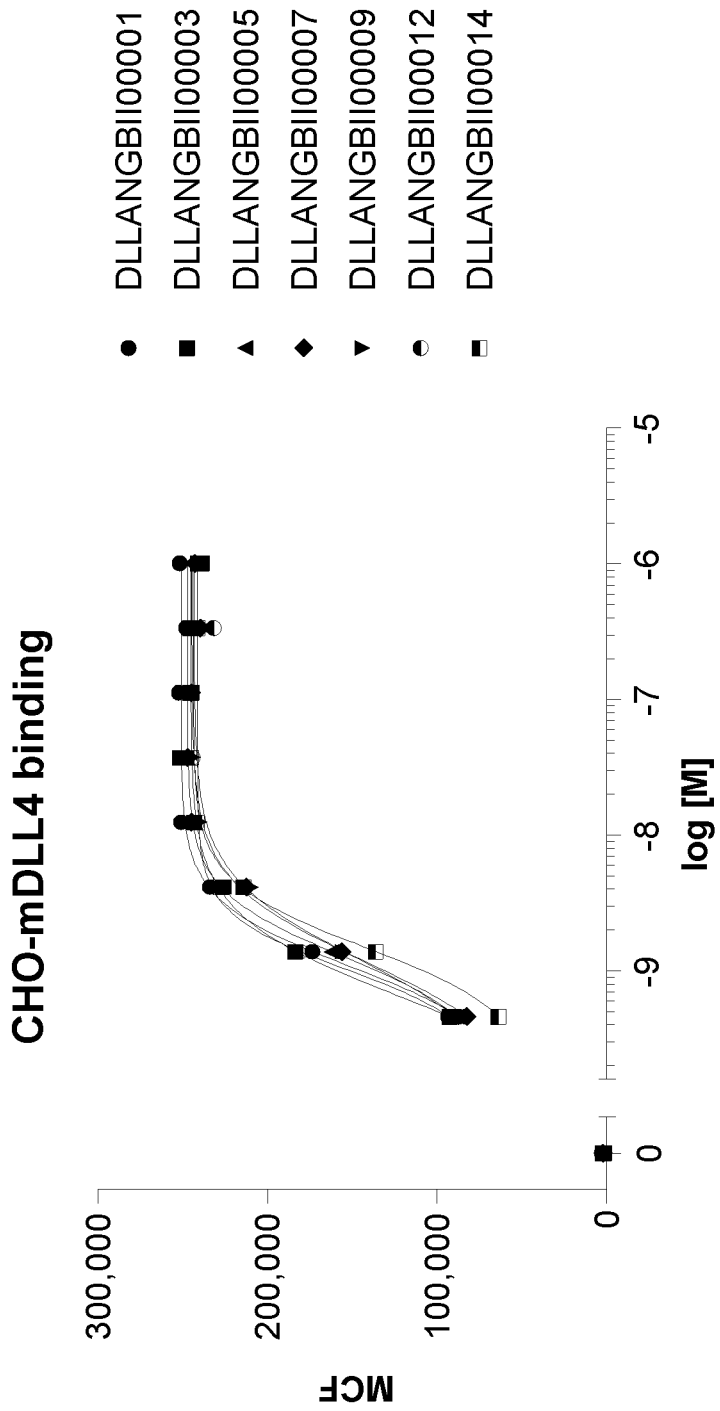

DLLANGBII00001
DLLANGBII00003
DLLANGBII00005
DLLANGBII00007
DLLANGBII00009
DLLANGBII00012
DLLANGBII00014
CHO-mDLL4 binding
MCF
300,000
200,000
100,000
0
0
-5
-6
-7
-8
-9
log [M]

Figure 19C

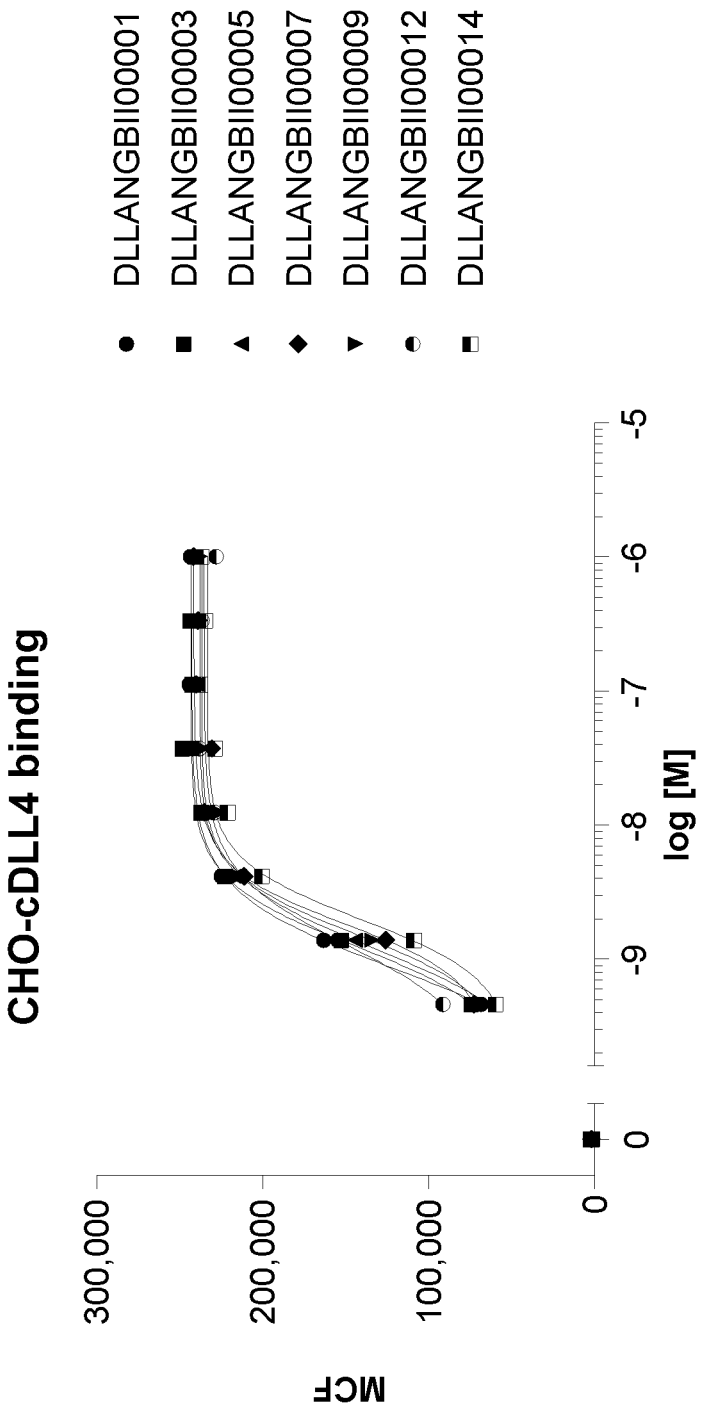

DLLANGBII00001
DLLANGBII00003
DLLANGBII00005
DLLANGBII00007
DLLANGBII00009
DLLANGBII00012
DLLANGBII00014
CHO-cDLL4 binding
MCF
300,000
200,000
100,000
0
0
-5
-6
-7
-8
-9
log [M]

Figure 20A

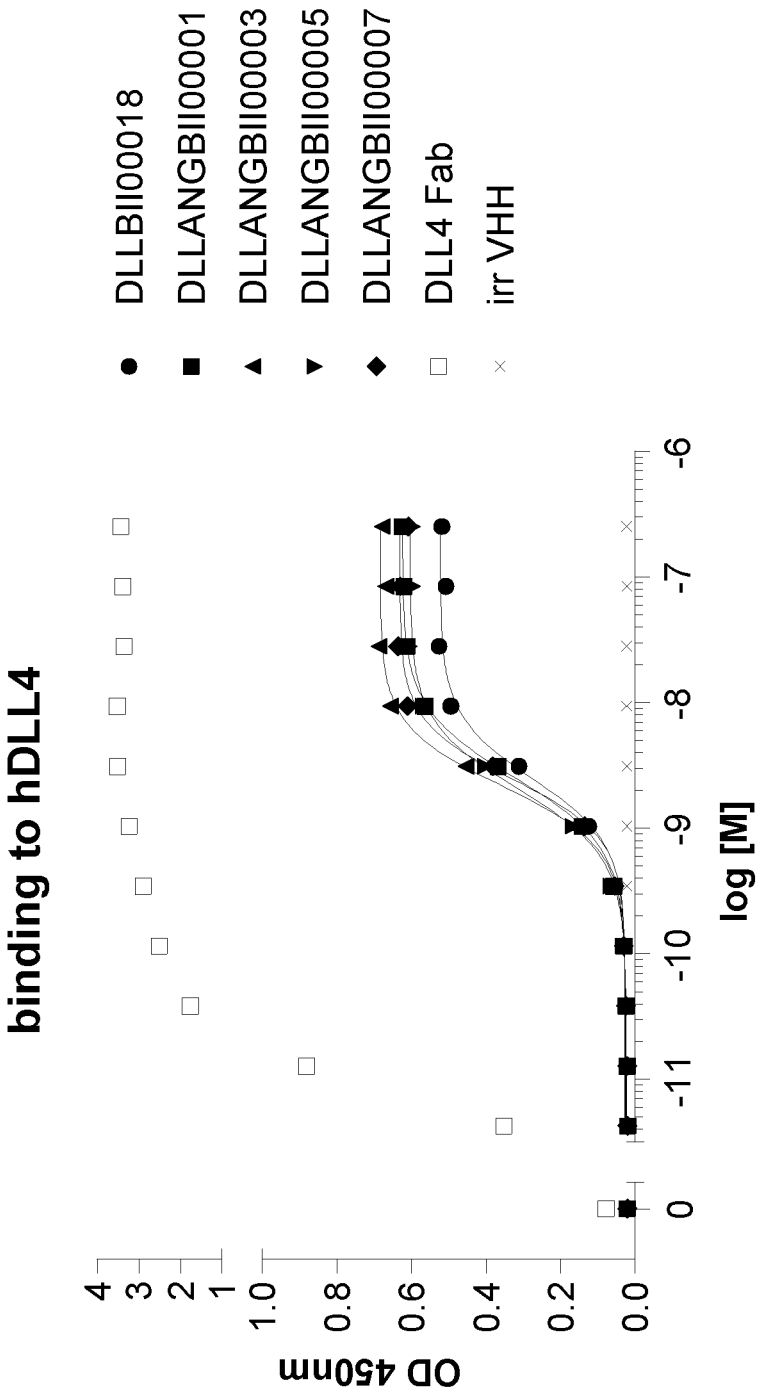

binding to hDLL4
OD 450nm
log [M]
DLLBII00018
DLLANGBII00001
DLLANGBII00003
DLLANGBII00005
DLLANGBII00007
DLL4 Fab
irr VHH

Figure 20A (continued)

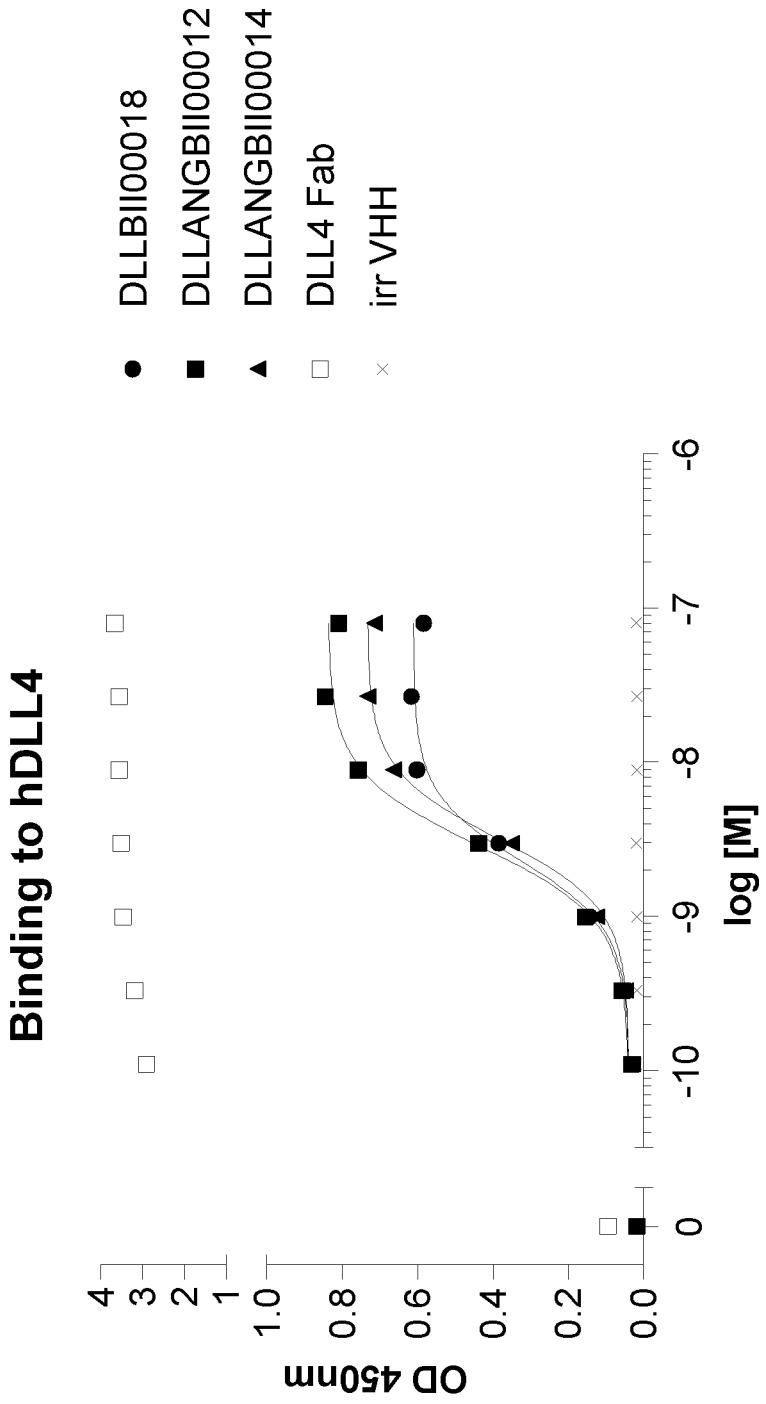


Figure 20B

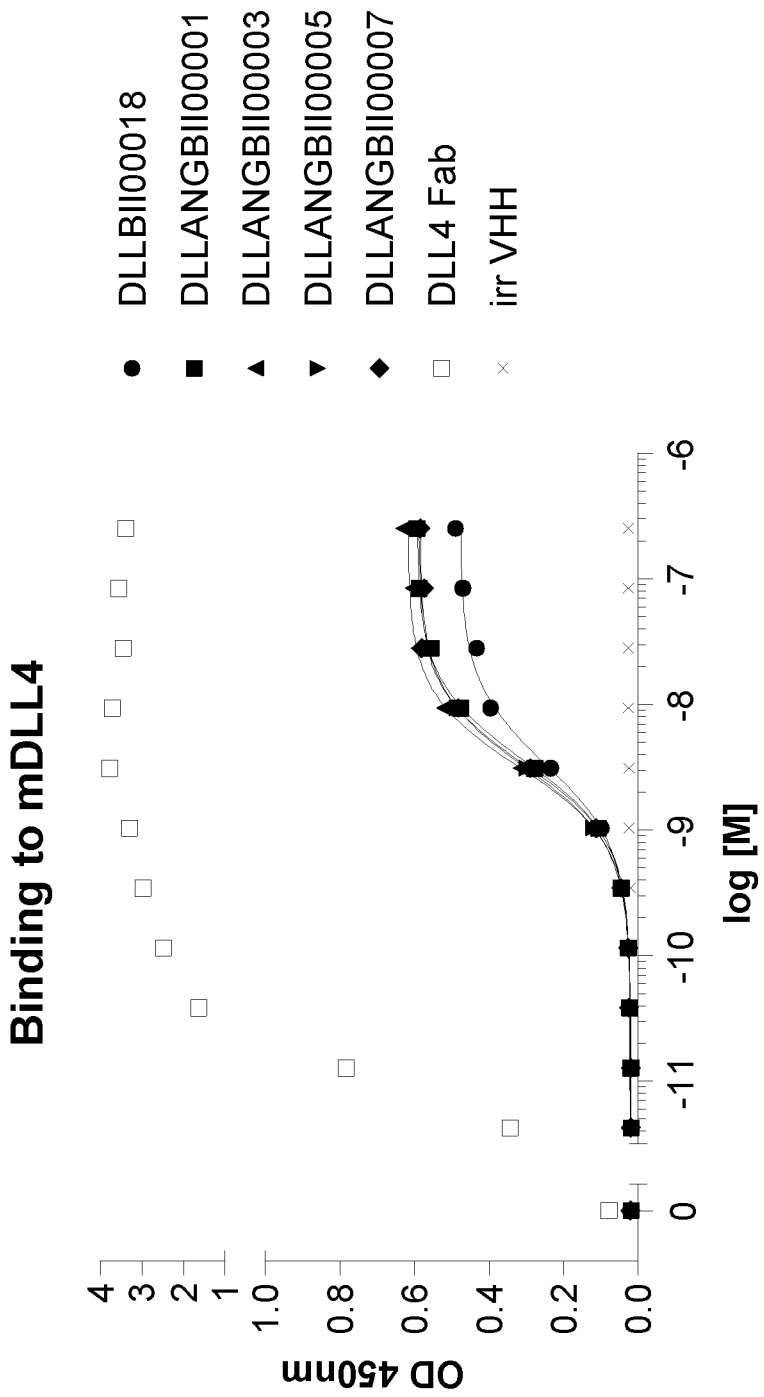

Binding to mDLL4
DLLBII00018
DLLANGBII00001
DLLANGBII00003
DLLANGBII00005
DLLANGBII00007
DLL4 Fab
irr VHH
OD 450nm
4
3
2
1
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 20B (continued)

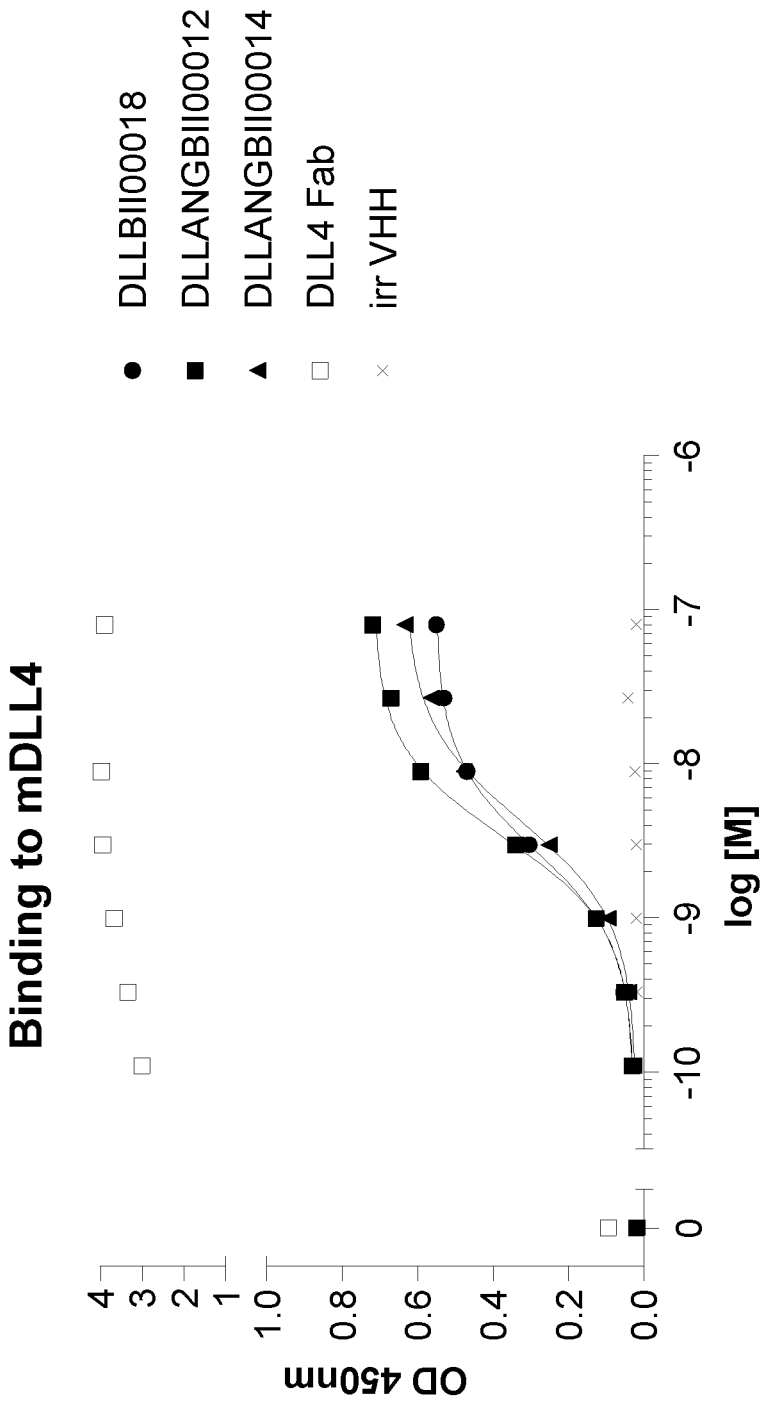


Figure 20C

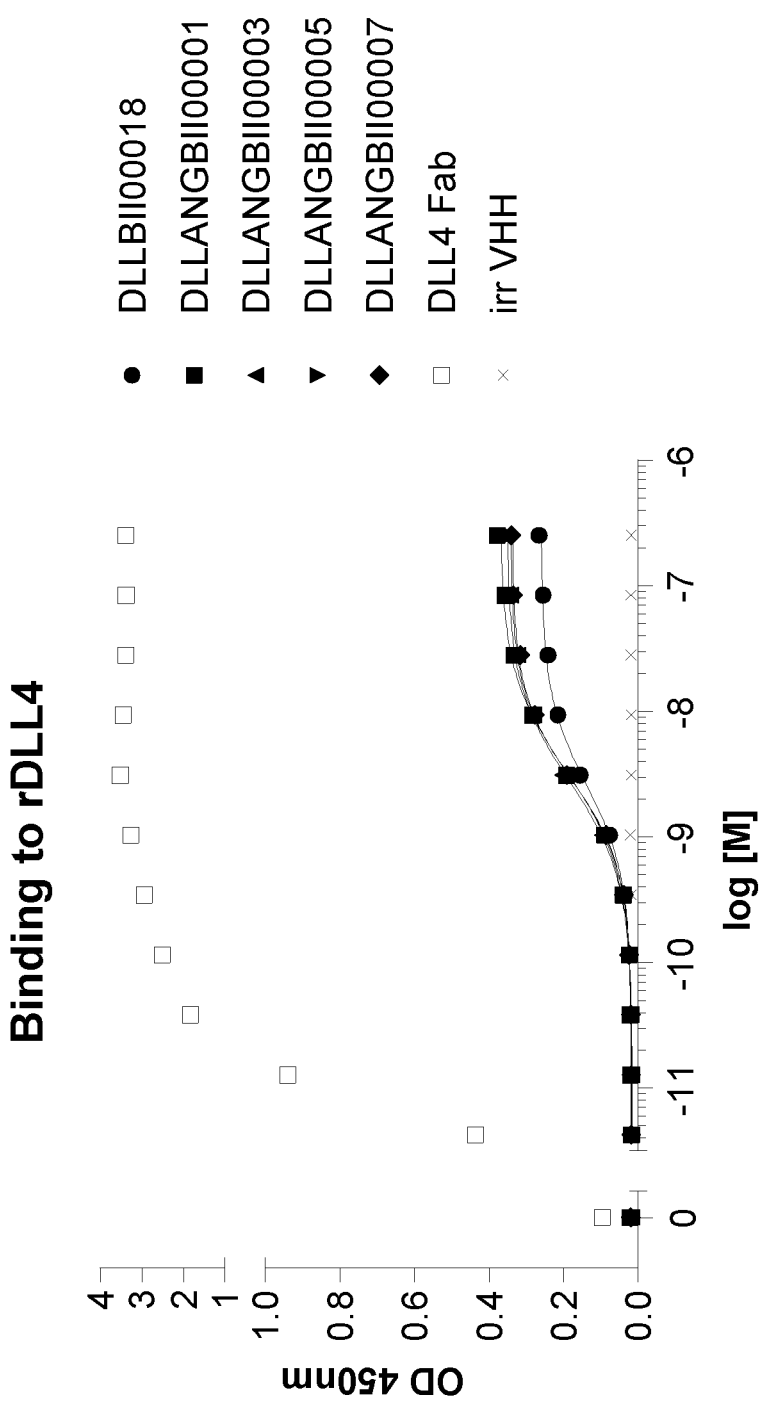

Binding to rDLL4
OD 450nm
log [M]
DLLBII00018
DLLANGBII00001
DLLANGBII00003
DLLANGBII00005
DLLANGBII00007
DLL4 Fab
irr VHH

Figure 20C (continued)

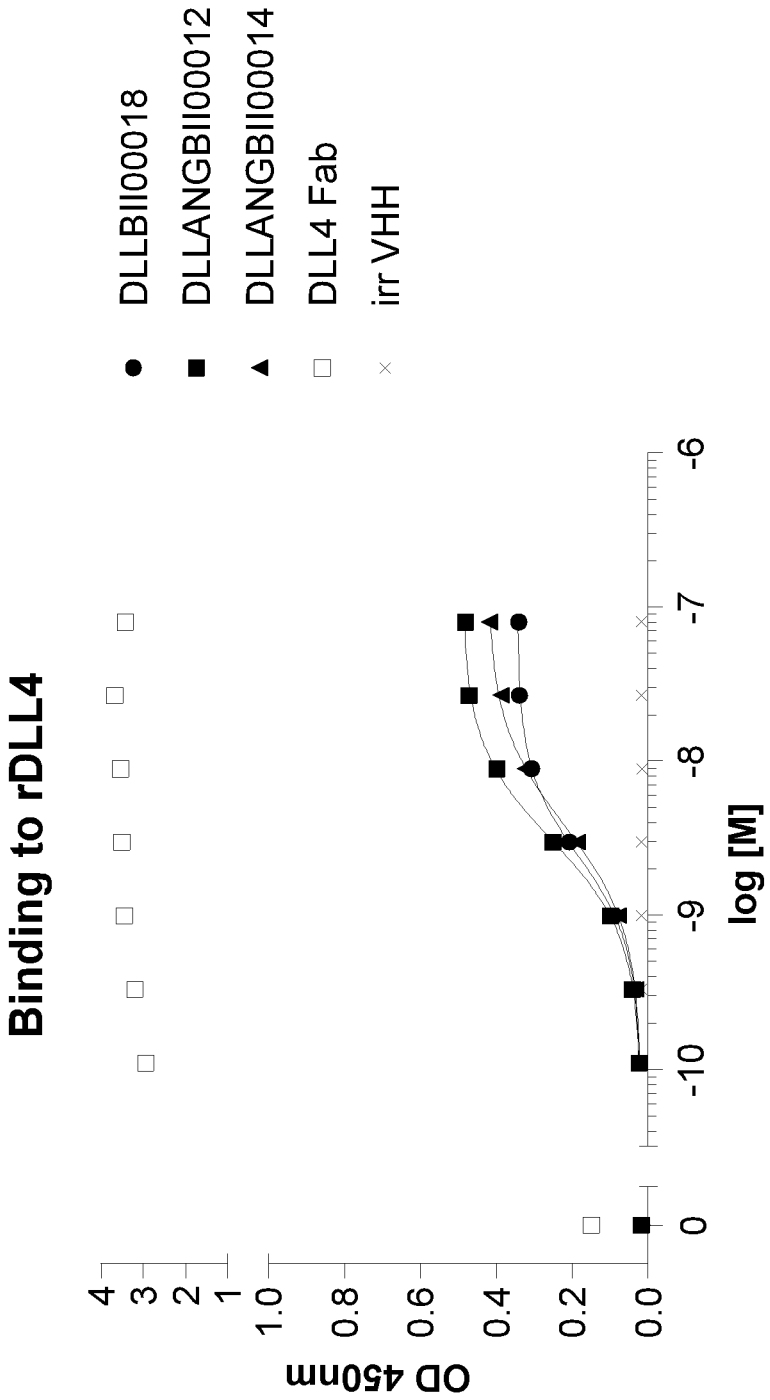


Figure 21A

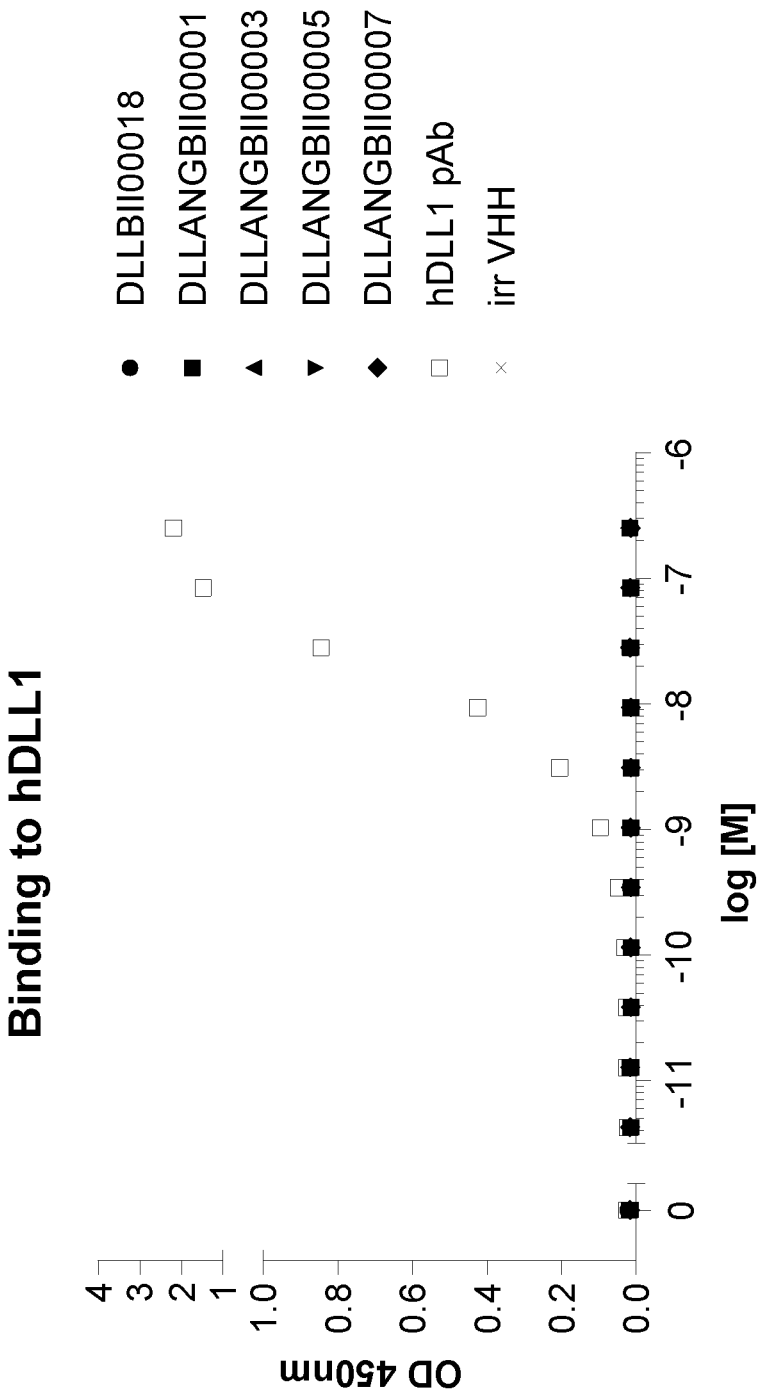

Binding to hDLL1
DLLBII00018
DLLANGBII00001
DLLANGBII00003
DLLANGBII00005
DLLANGBII00007
hDLL1 pAb
irr VHH
OD 450nm
4
3
2
1
1.0
0.8
0.6
0.4
0.2
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 21A (continued)

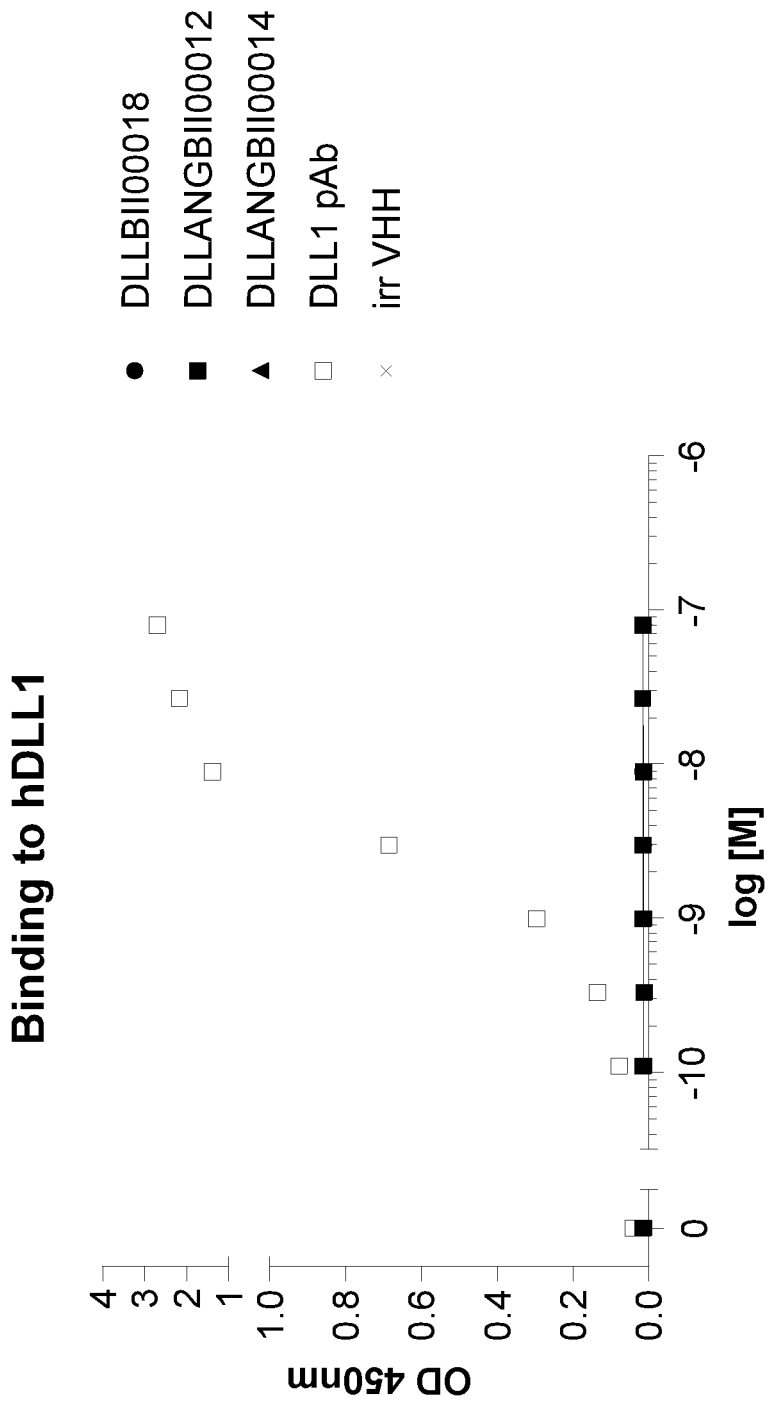


Figure 21B

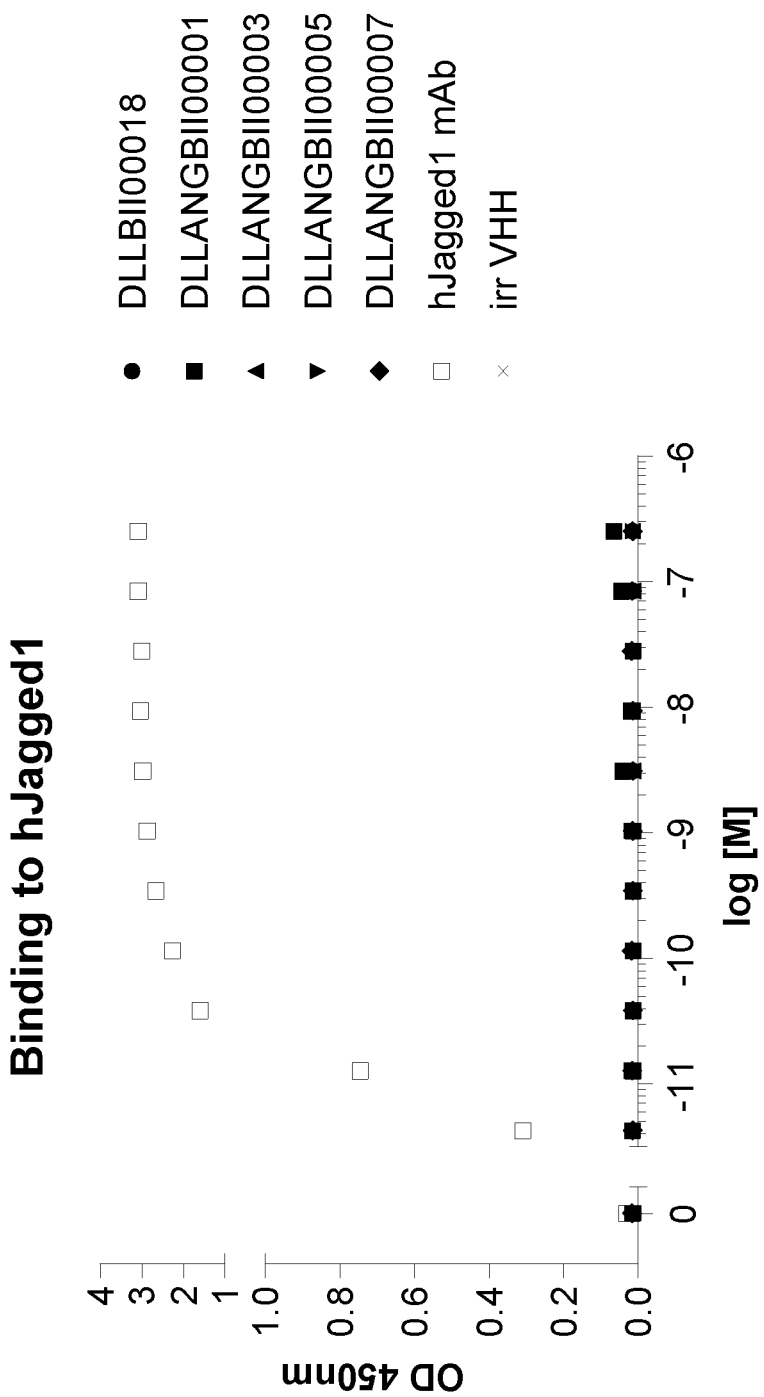

Binding to hJagged1
OD 450nm
log [M]
DLLBII00018
DLLANGBII00001
DLLANGBII00003
DLLANGBII00005
DLLANGBII00007
hJagged1 mAb
irr VHH

Figure 21B (continued)

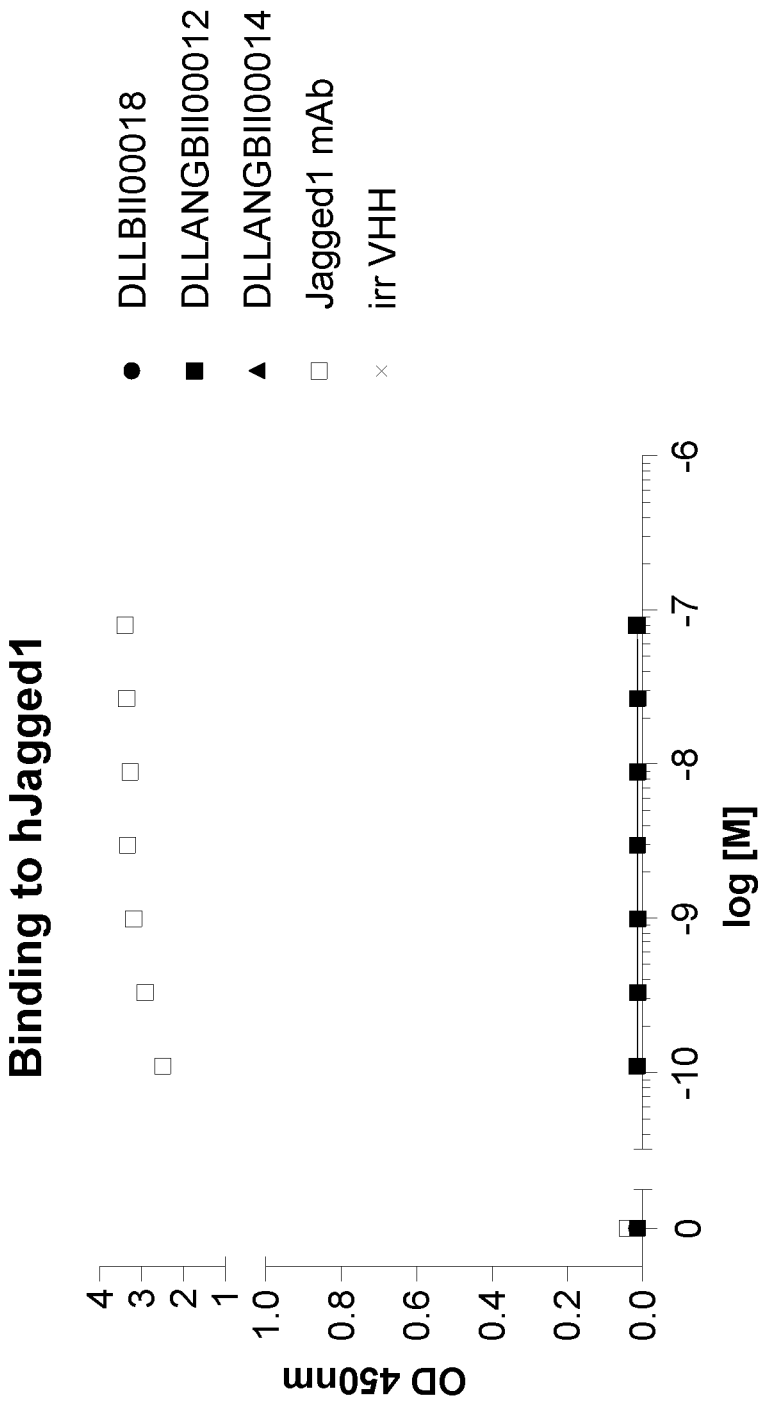


Figure 22-1A

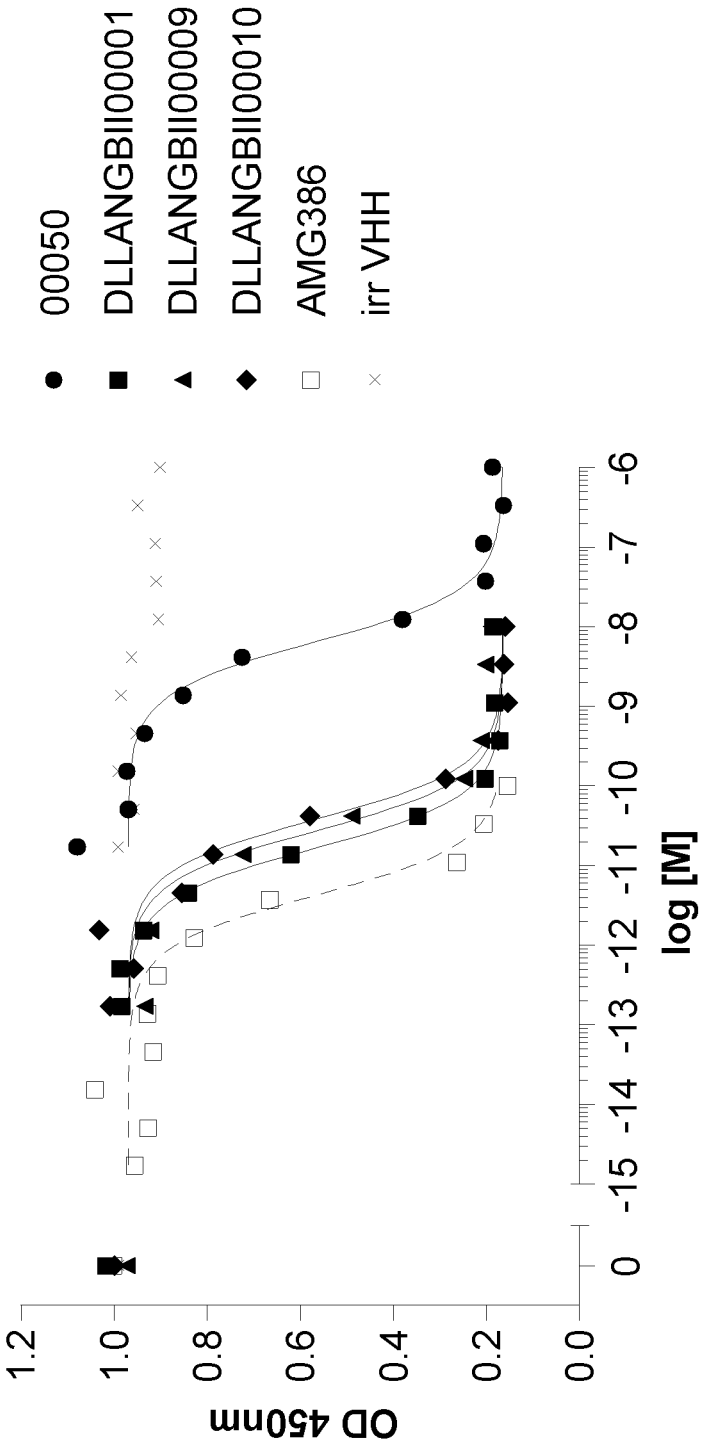

00050
DLLANGBII00001
DLLANGBII00009
DLLANGBII00010
AMG386
irr VHH
OD 450nm
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 22-1A (continued)

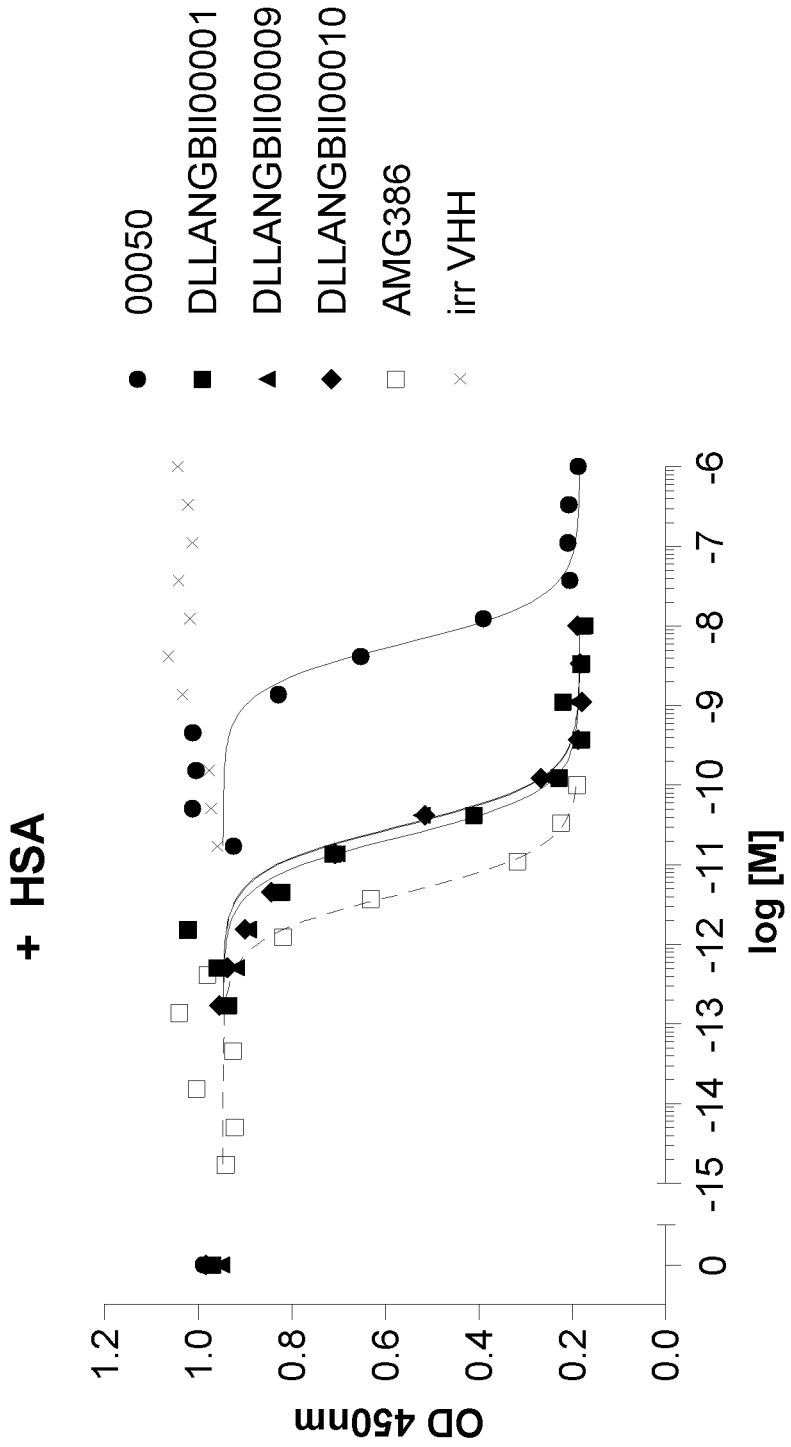


Figure 22-1B

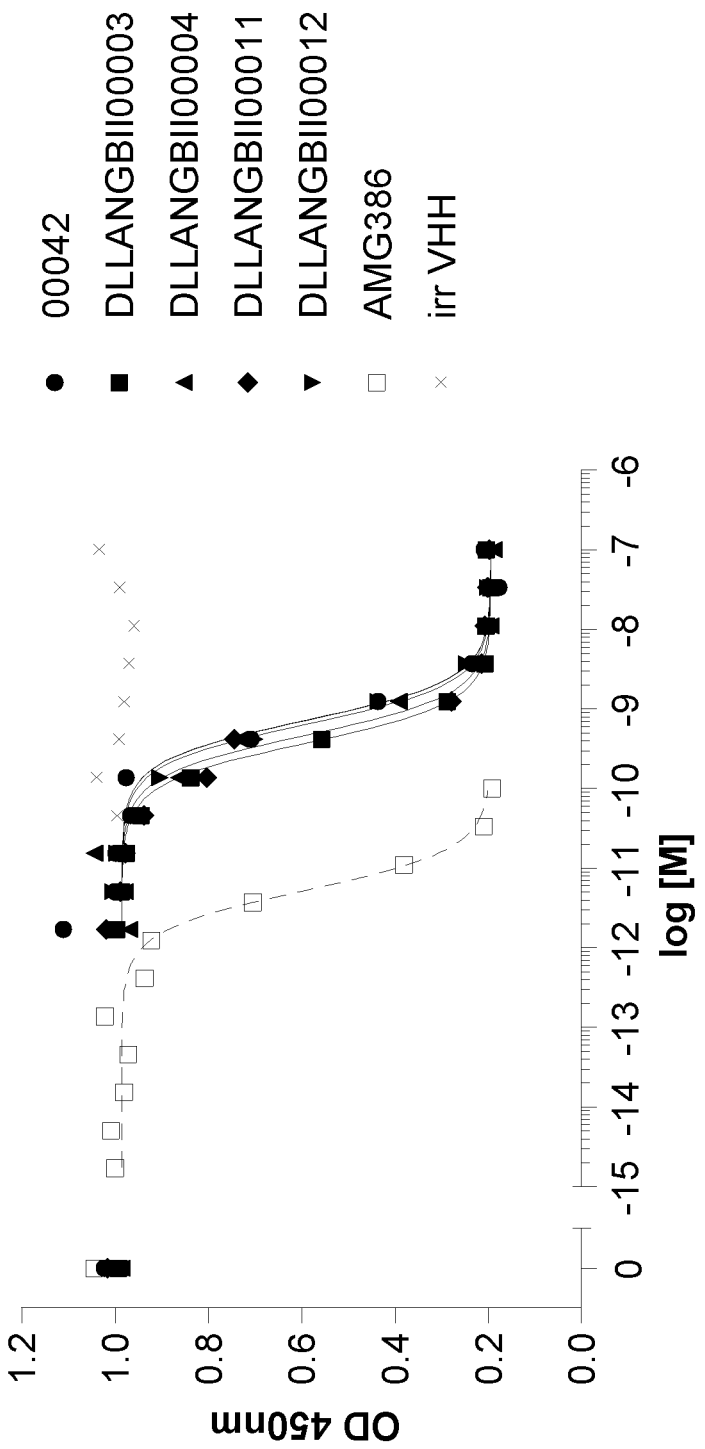

00042
DLLANGBII00003
DLLANGBII00004
DLLANGBII00011
DLLANGBII00012
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
1.0
1.2
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6

Figure 22-1B (continued)

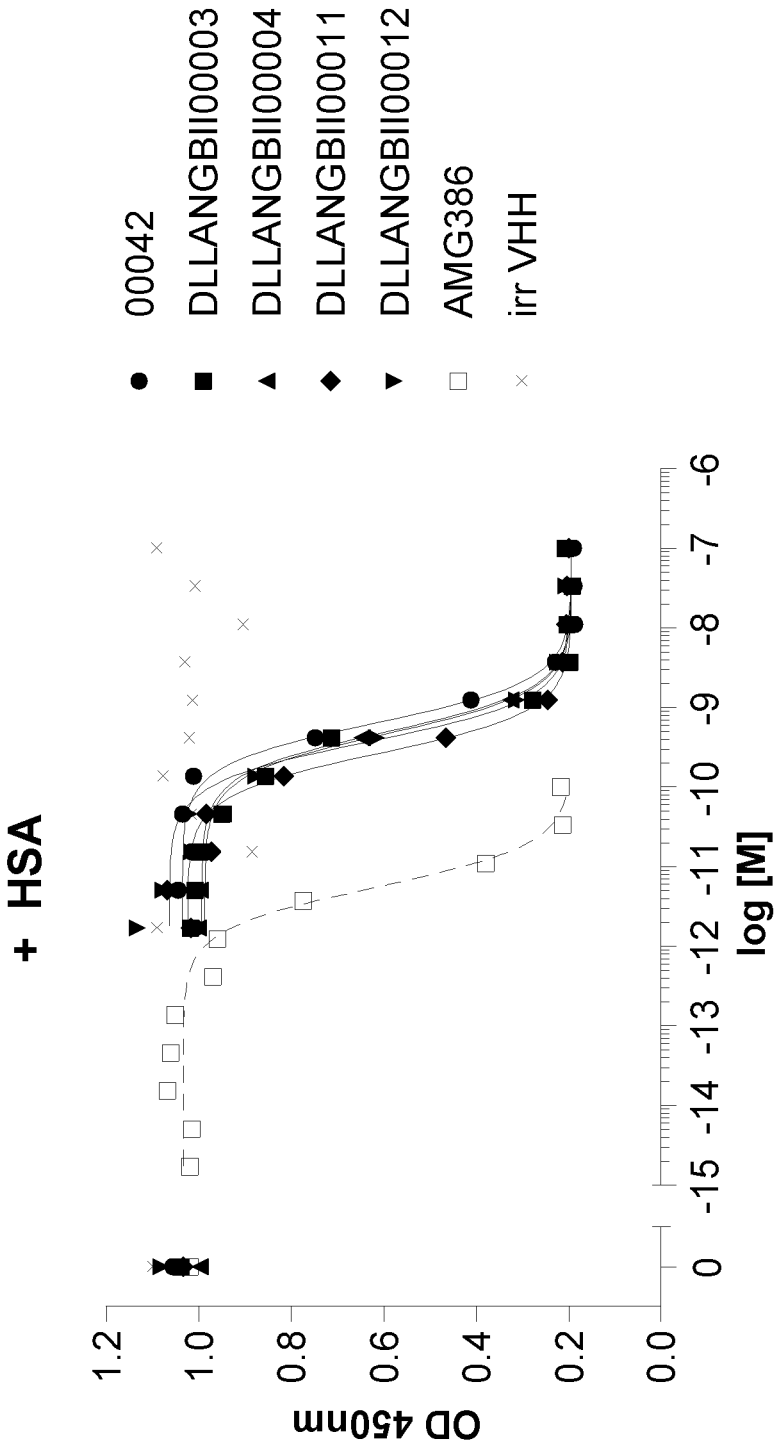


Figure 22-1C

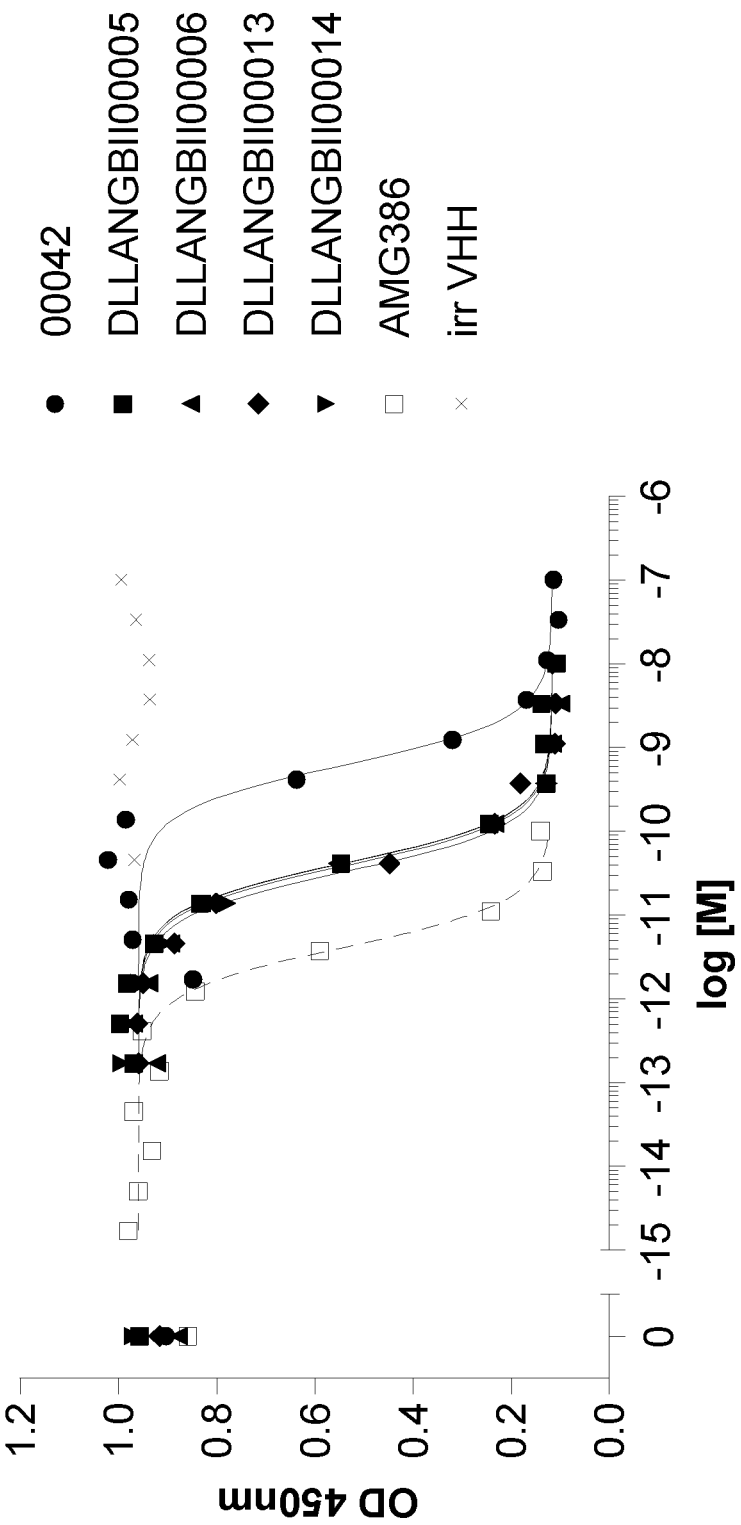

00042
DLLANGBII00005
DLLANGBII00006
DLLANGBII00013
DLLANGBII00014
AMG386
irr VHH
OD 450nm
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 22-1C (continued)

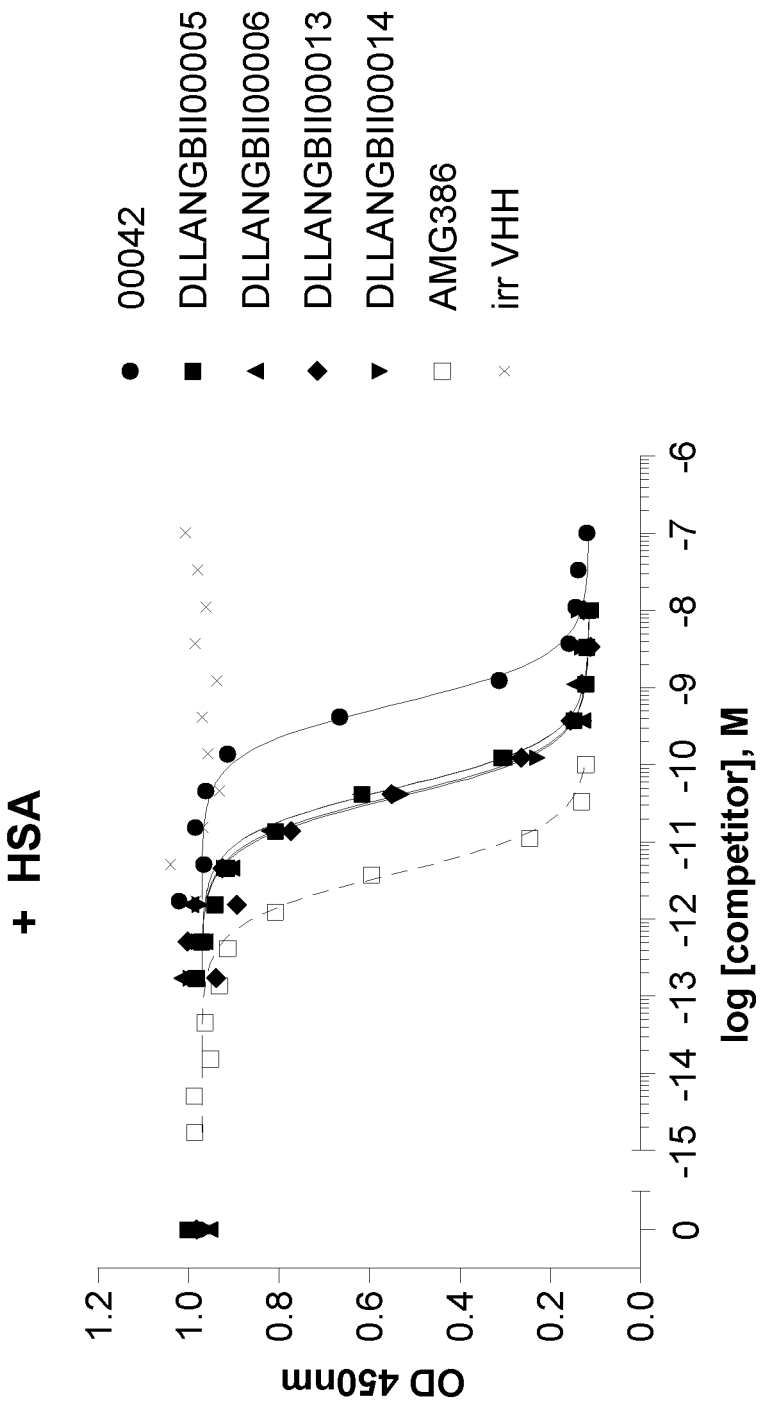


Figure 22-1D

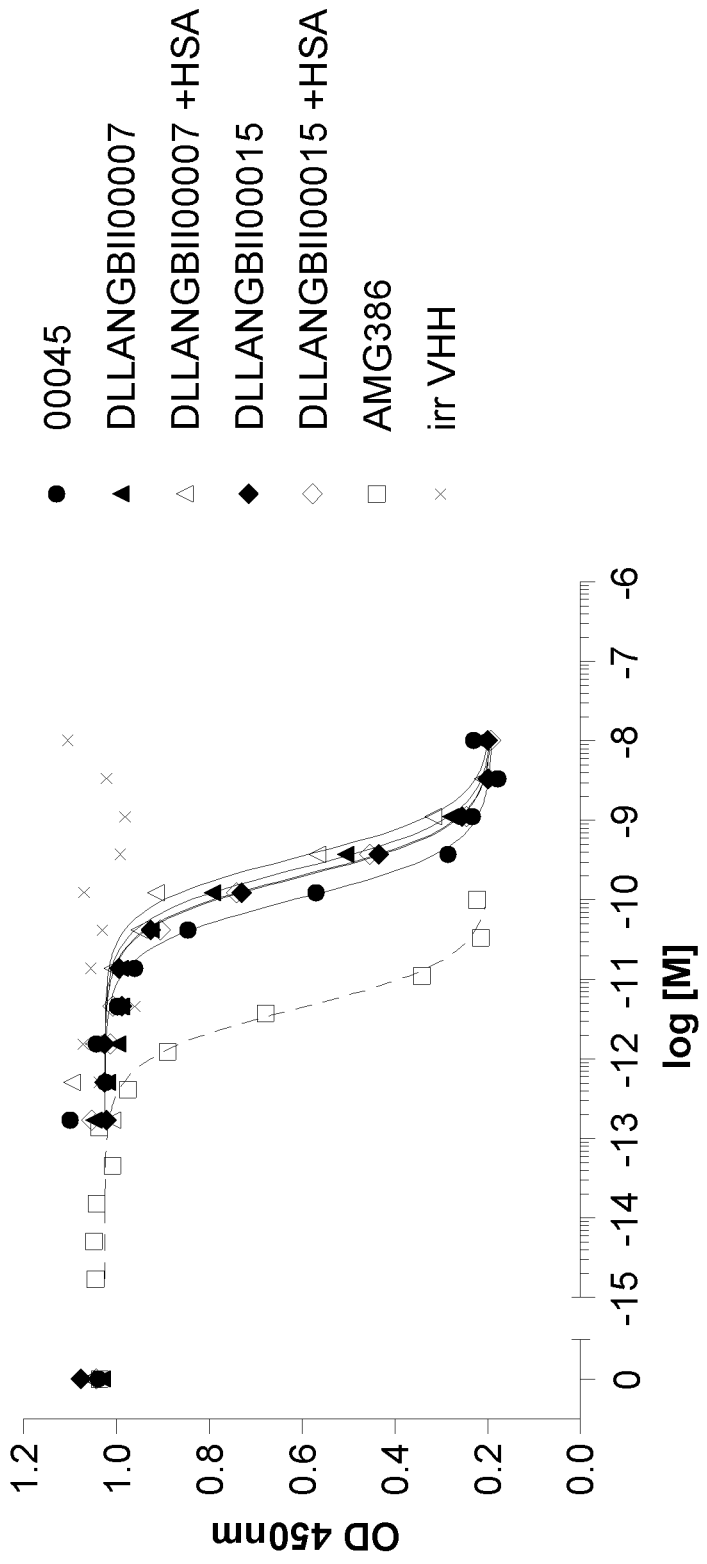

00045
DLLANGBII00007
DLLANGBII00007 +HSA
DLLANGBII00015
DLLANGBII00015 +HSA
AMG386
irr VHH
OD 450nm
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 22-2A

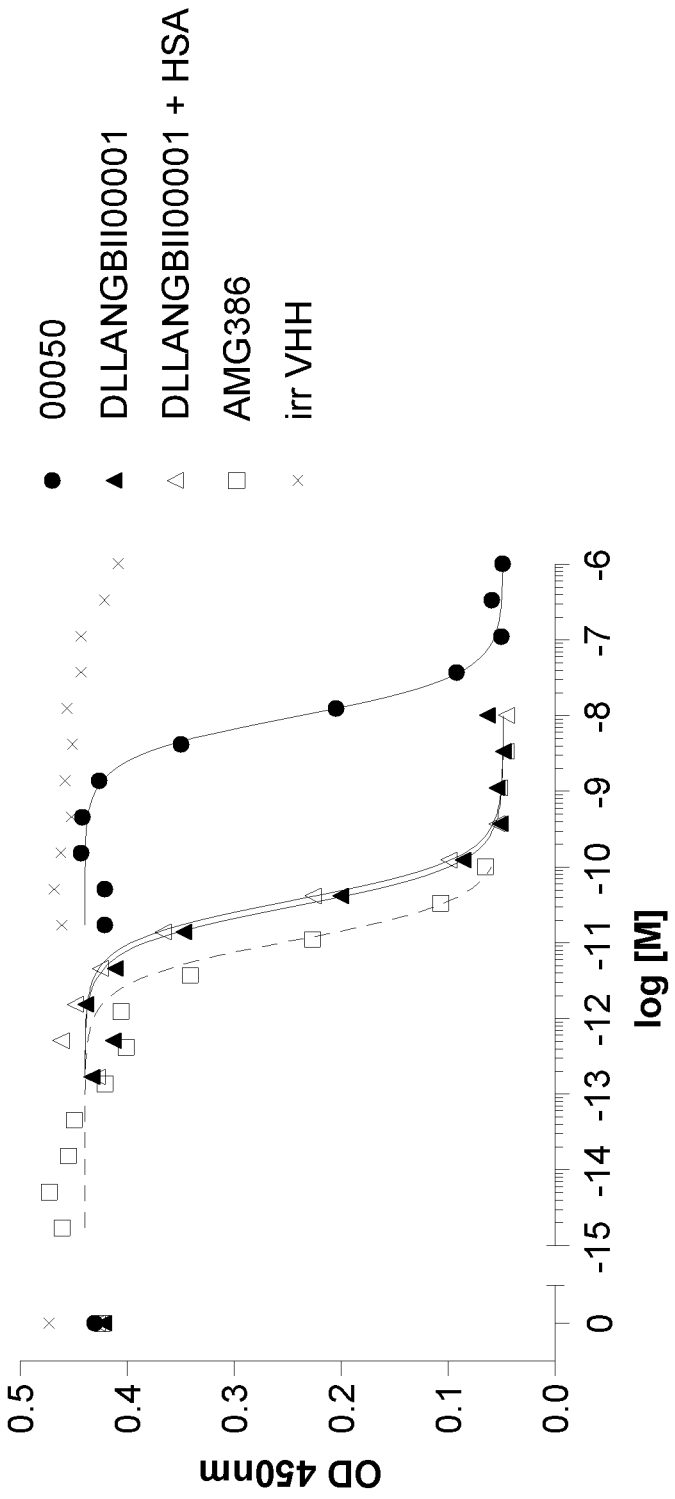

00050
DLLANGBII00001
DLLANGBII00001 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.1
0.2
0.3
0.4
0.5
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6

Figure 22-2B

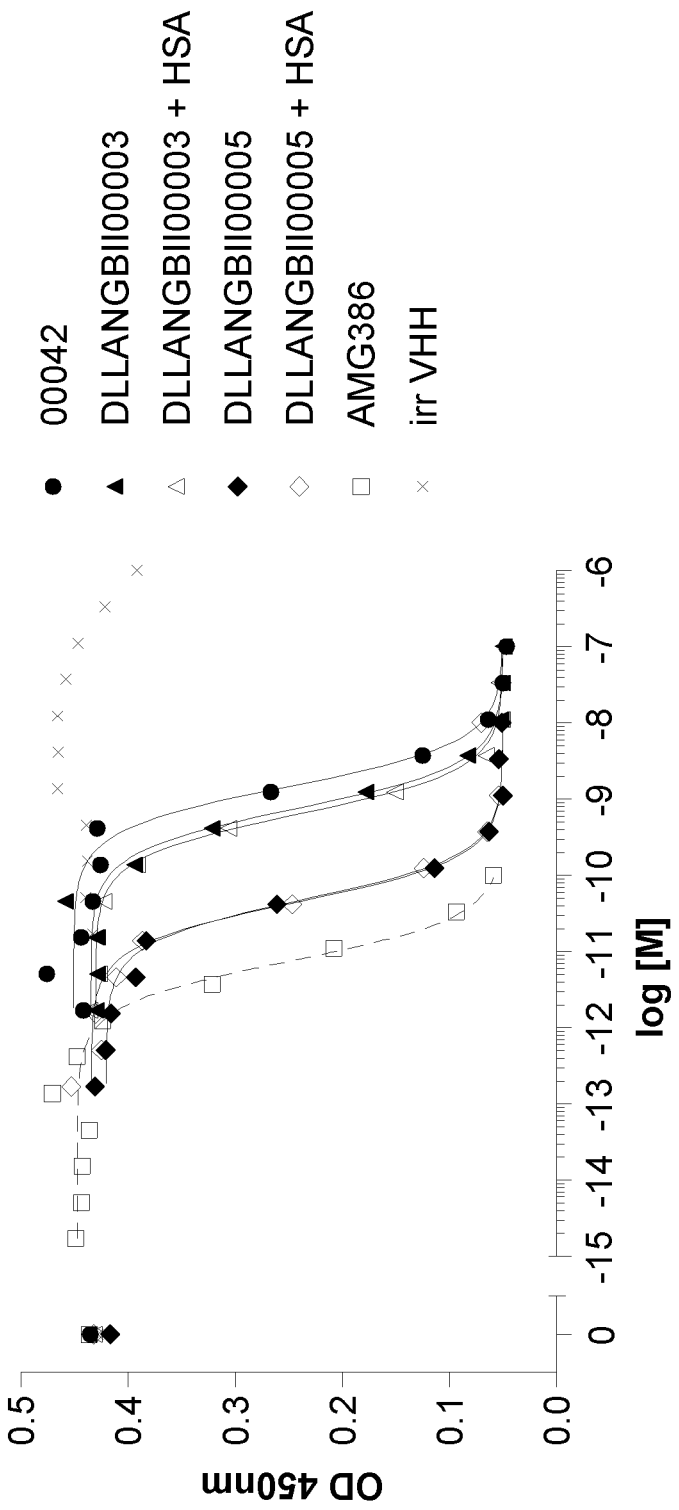

00042
DLLANGBII00003
DLLANGBII00003 + HSA
DLLANGBII00005
DLLANGBII00005 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.1
0.2
0.3
0.4
0.5
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6

Figure 22-2C

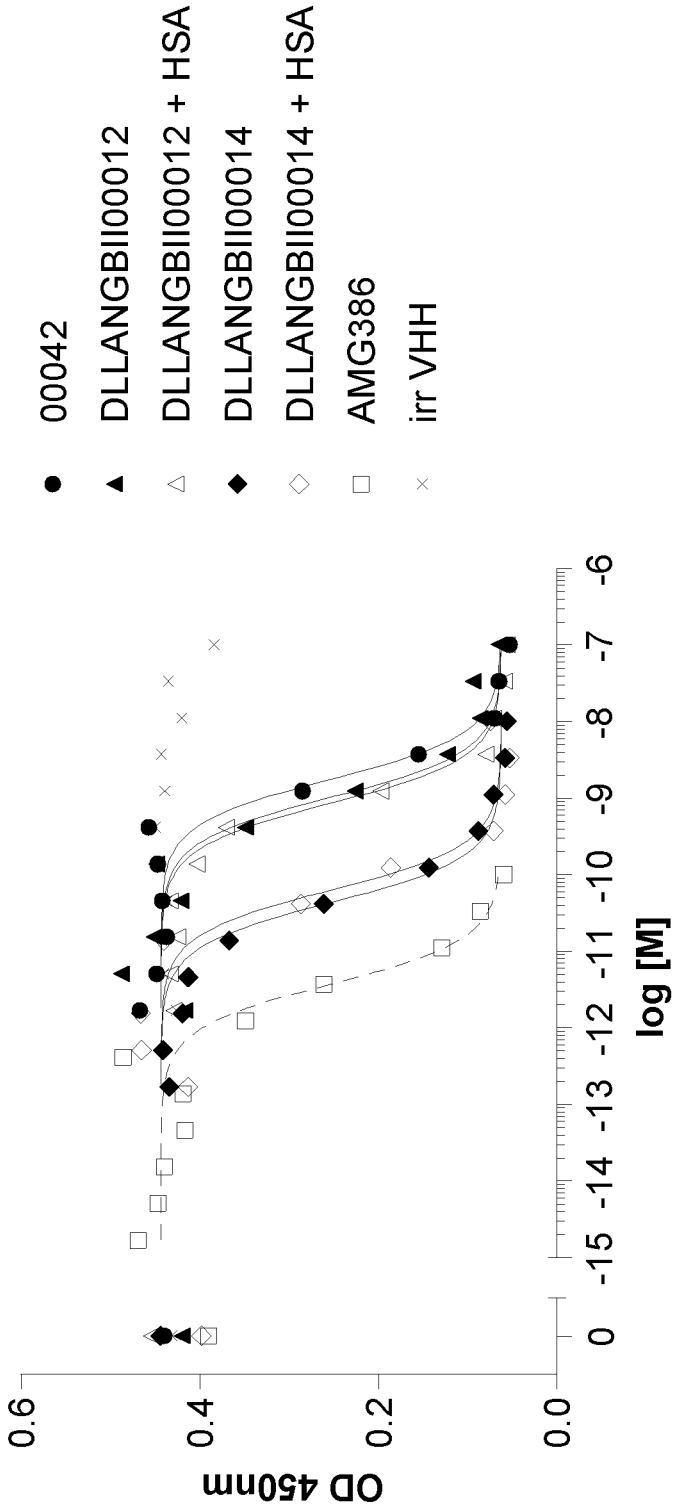

00042
DLLANGBII00012
DLLANGBII00012 + HSA
DLLANGBII00014
DLLANGBII00014 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
log [M]
0
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15

Figure 22-2D

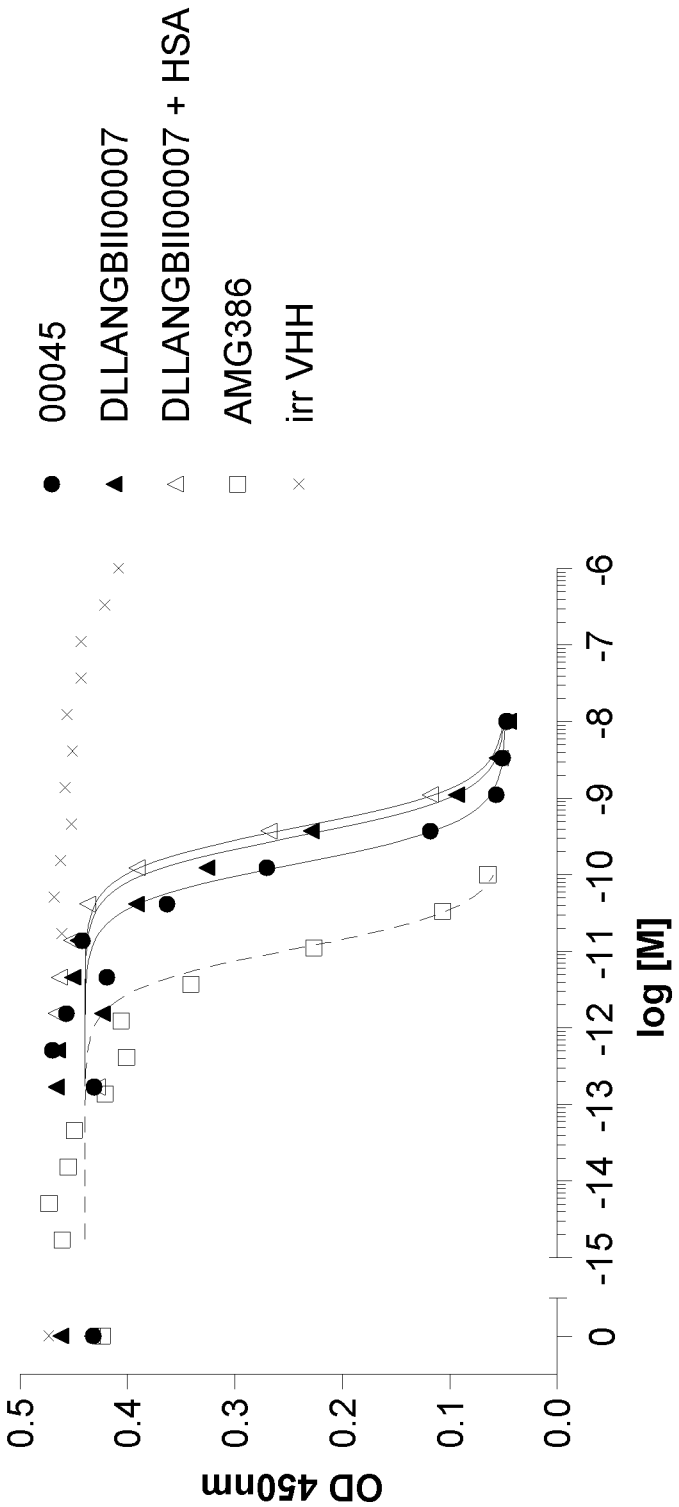

00045
DLLANGBII00007
DLLANGBII00007 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.1
0.2
0.3
0.4
0.5
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6

Figure 22-3A

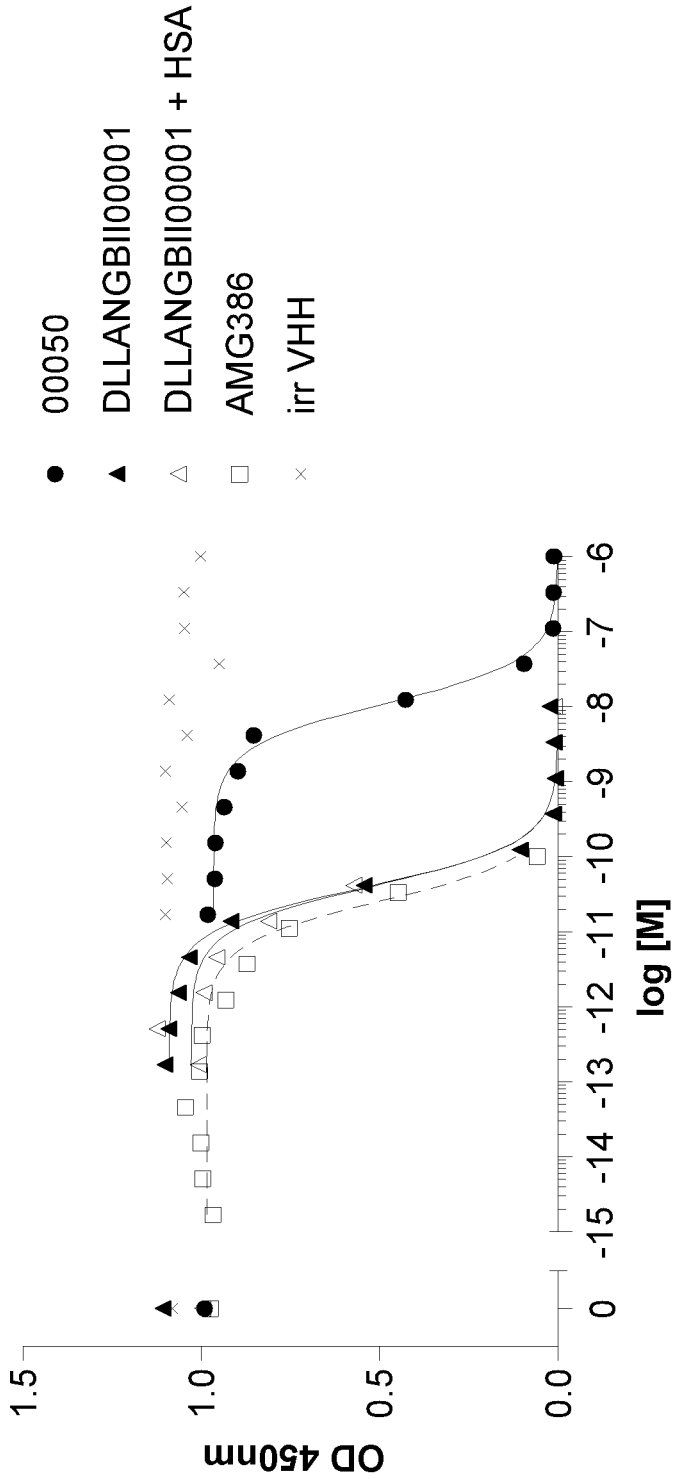

00050
DLLANGBII00001
DLLANGBII00001 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 22-3B

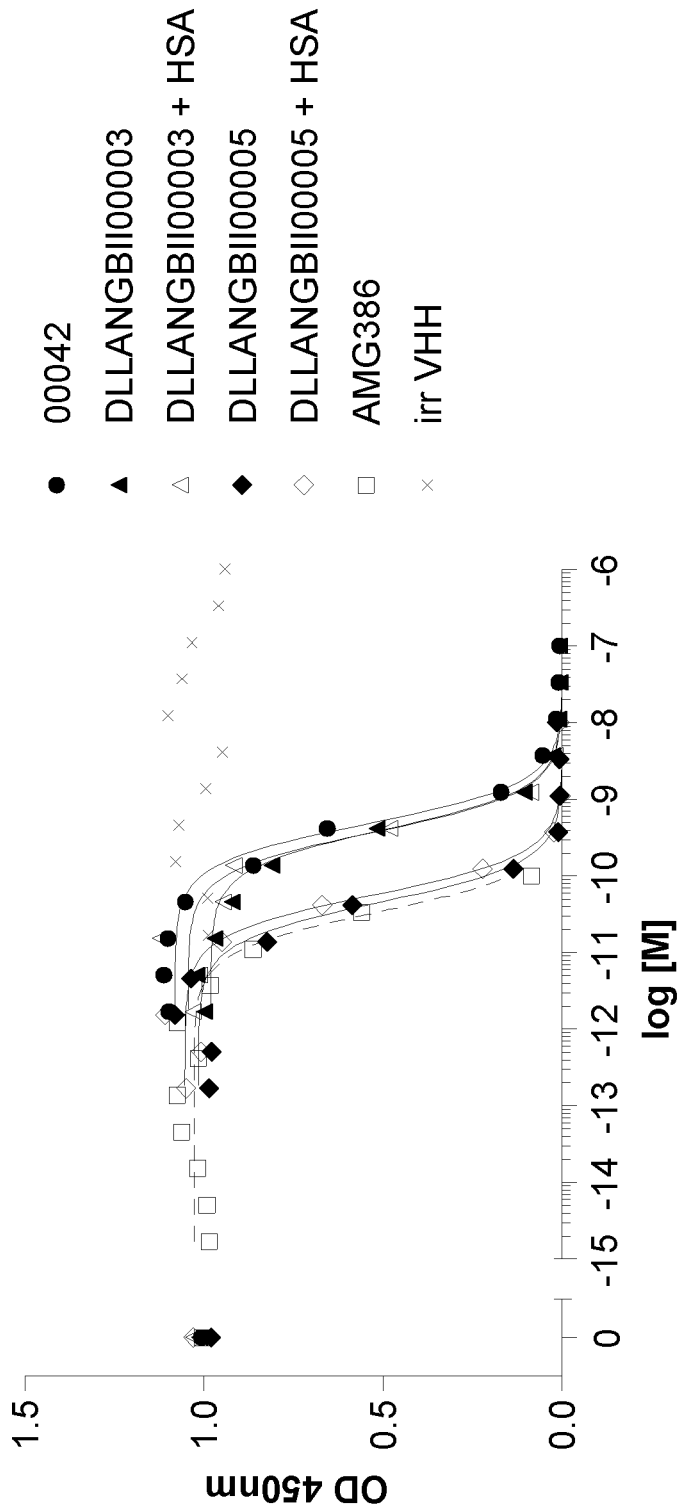

00042
DLLANGBII00003
DLLANGBII00003 + HSA
DLLANGBII00005
DLLANGBII00005 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 22-3C

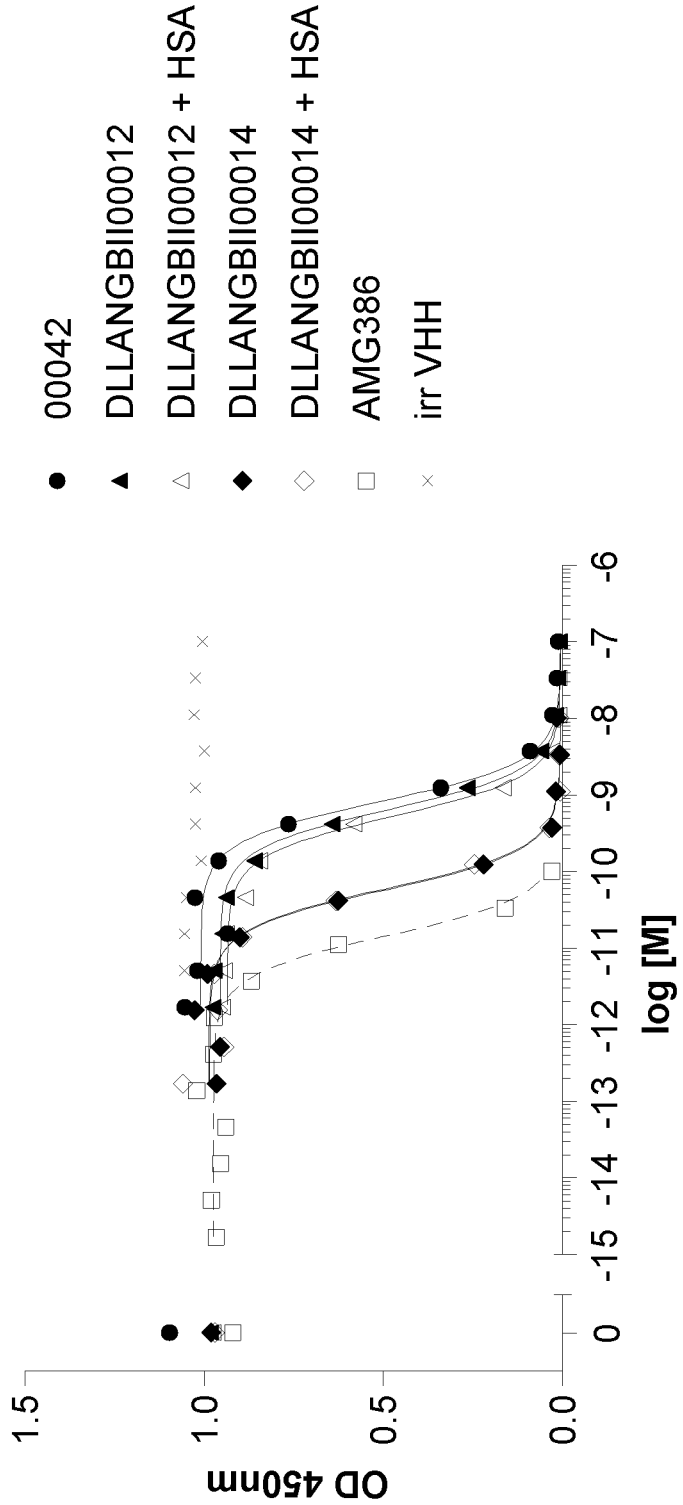

00042
DLLANGBII00012
DLLANGBII00012 + HSA
DLLANGBII00014
DLLANGBII00014 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 22-3D

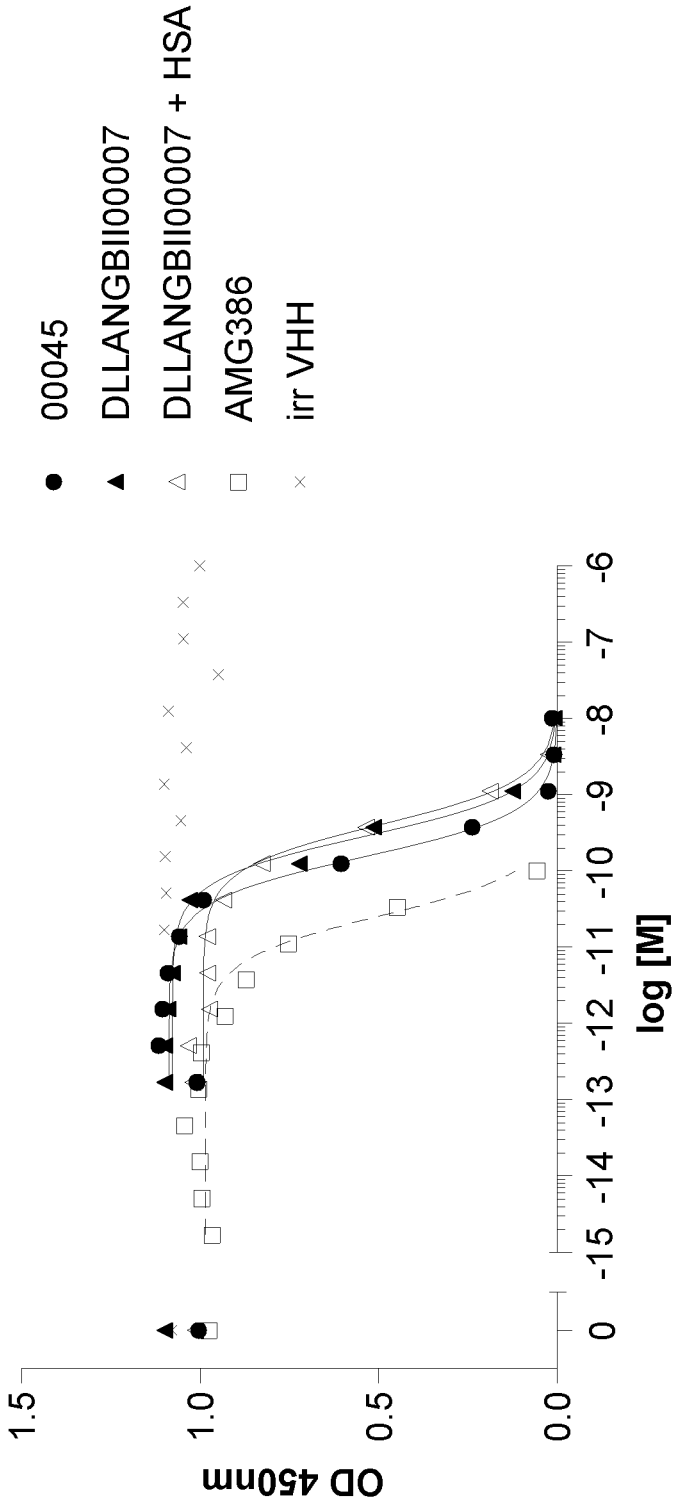
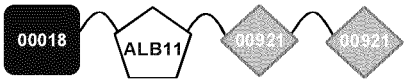
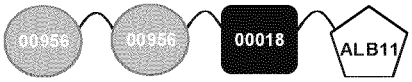

00045
DLLANGBII00007
DLLANGBII00007 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

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

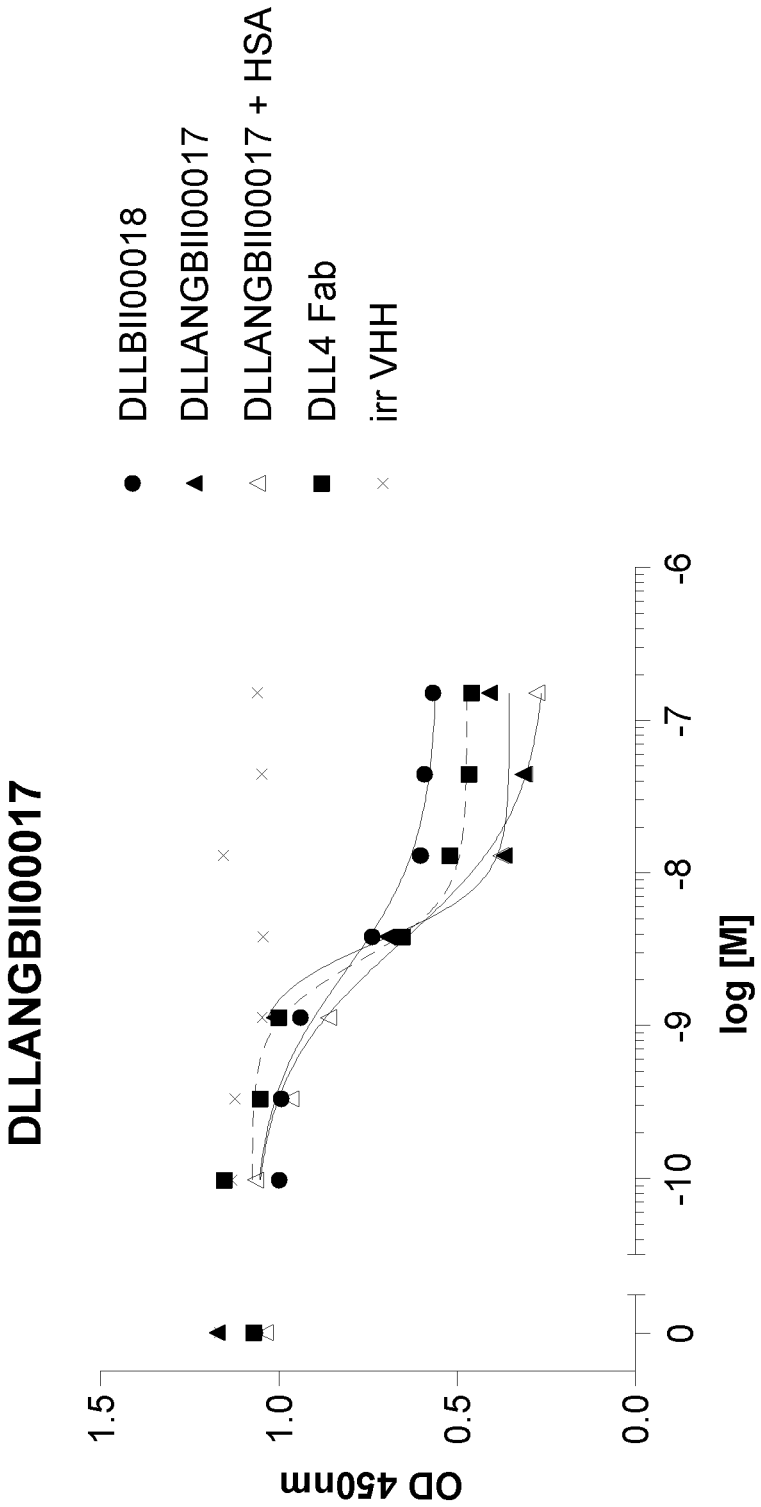

DLLANGBII00017
DLLBII00018
DLLANGBII00017
DLLANGBII00017 + HSA
DLL4 Fab
irr VHH
OD 450nm
0.0
0.5
1.0
1.5
0
-10
-9
-8
-7
-6
log [M]

Figure 24B

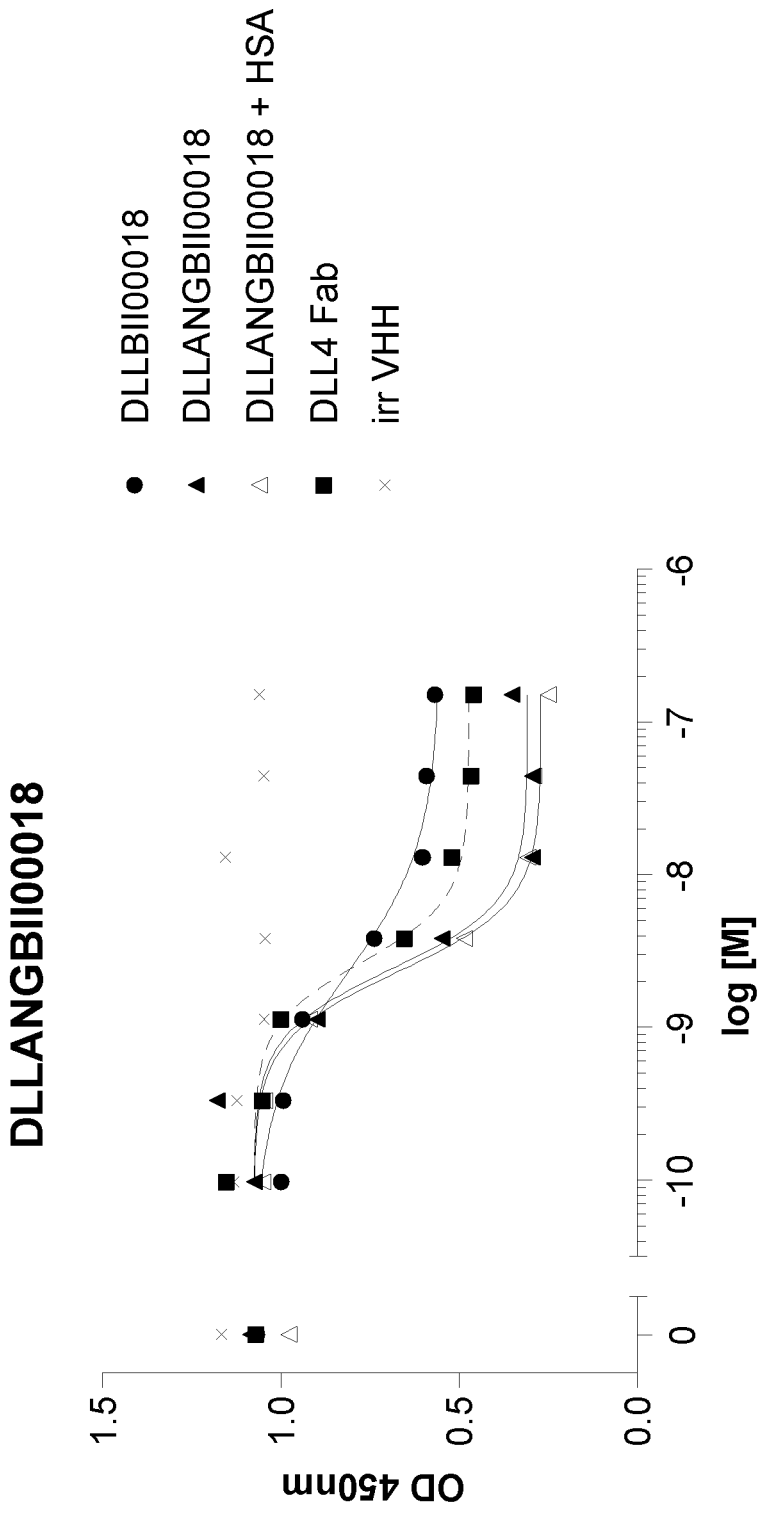

DLLANGBII00018
DLLBII00018
DLLANGBII00018
DLLANGBII00018 + HSA
DLL4 Fab
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-10
-9
-8
-7
-6
log [M]

Figure 24C

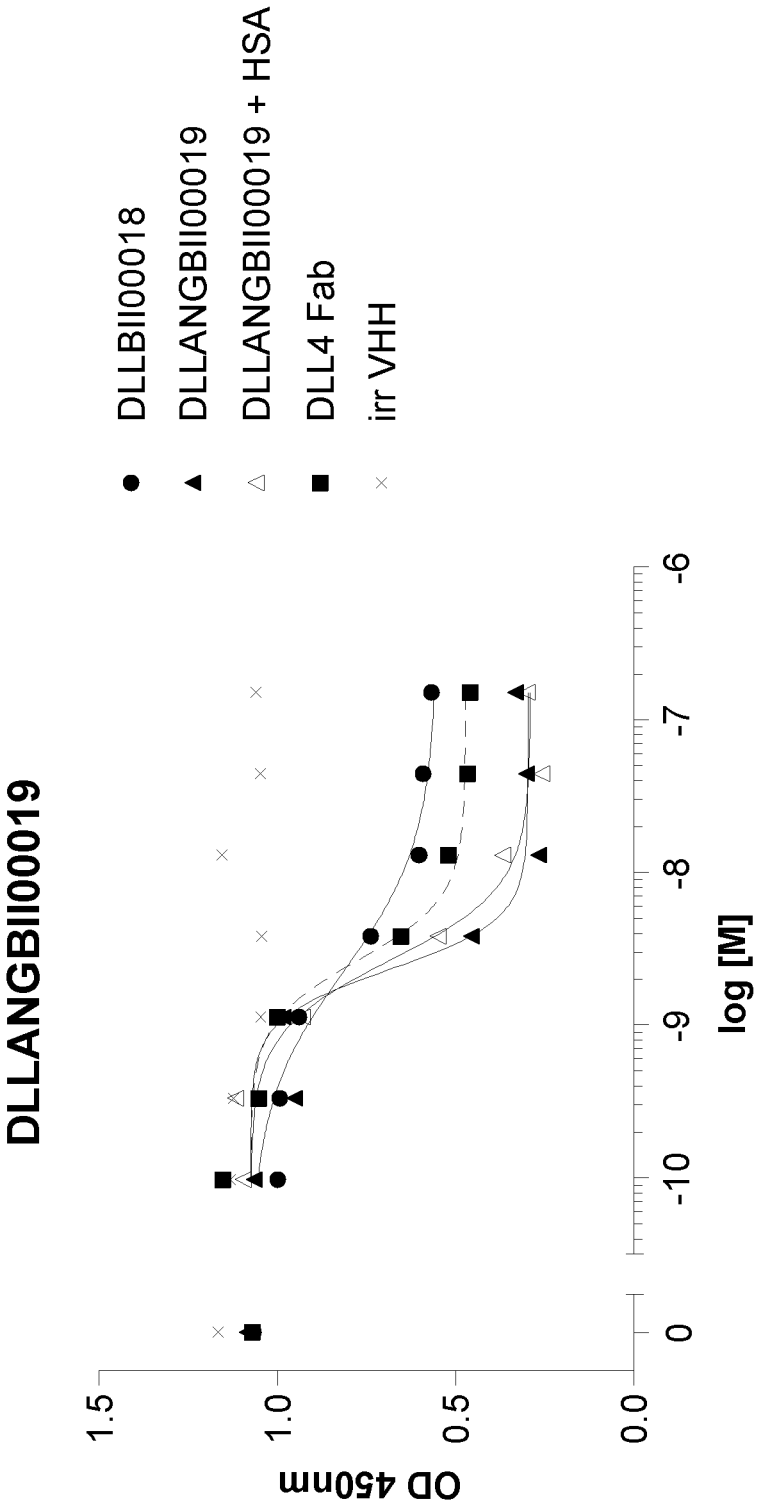

DLLANGBII00019
DLLBII00018
DLLANGBII00019
DLLANGBII00019 + HSA
DLL4 Fab
irr VHH
OD 450nm
0.0
0.5
1.0
1.5
0
-10
-9
-8
-7
-6
log [M]

Figure 25-1A

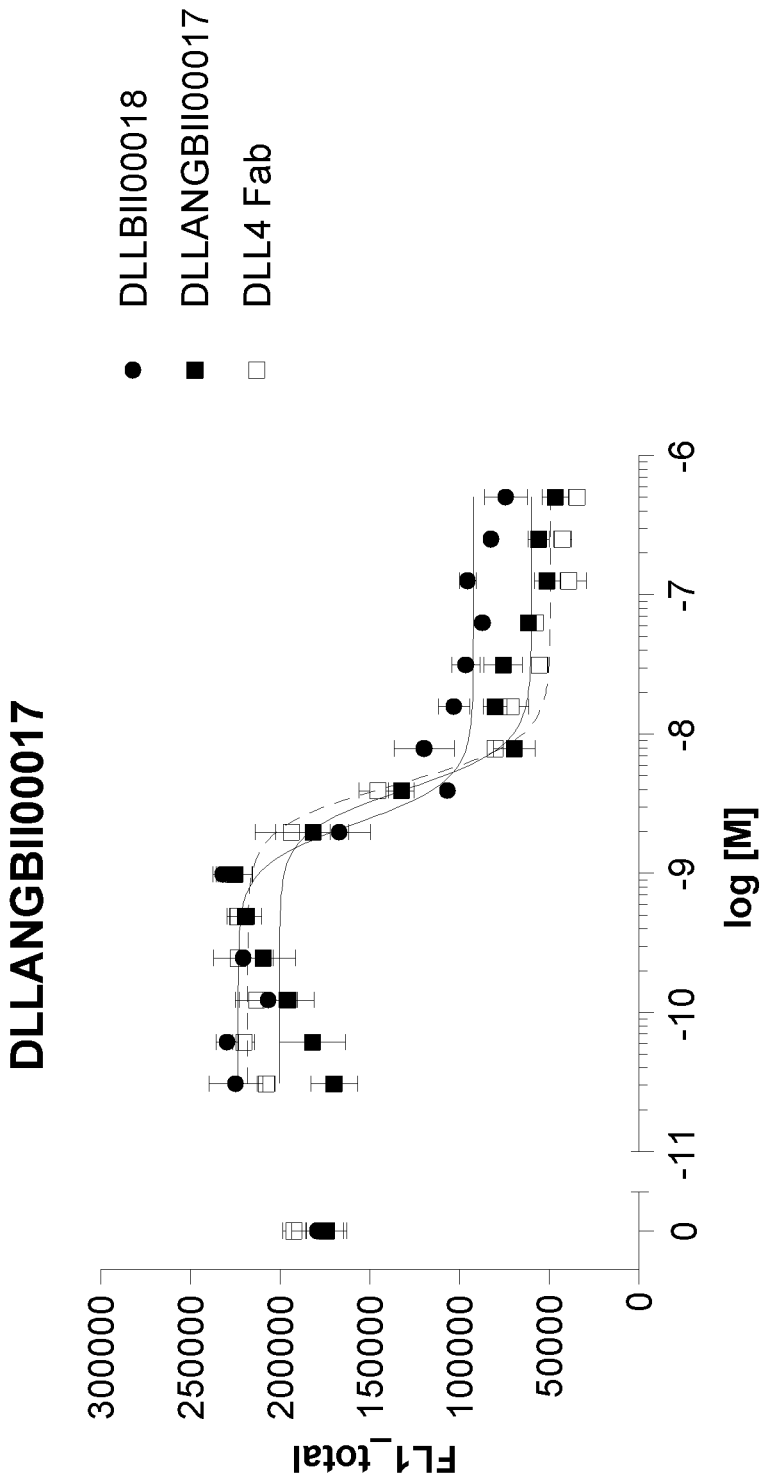

DLLBII00018
DLLANGBII00017
DLL4 Fab
DLLANGBII00017
FL1_total
300000
250000
200000
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-1A (continued)

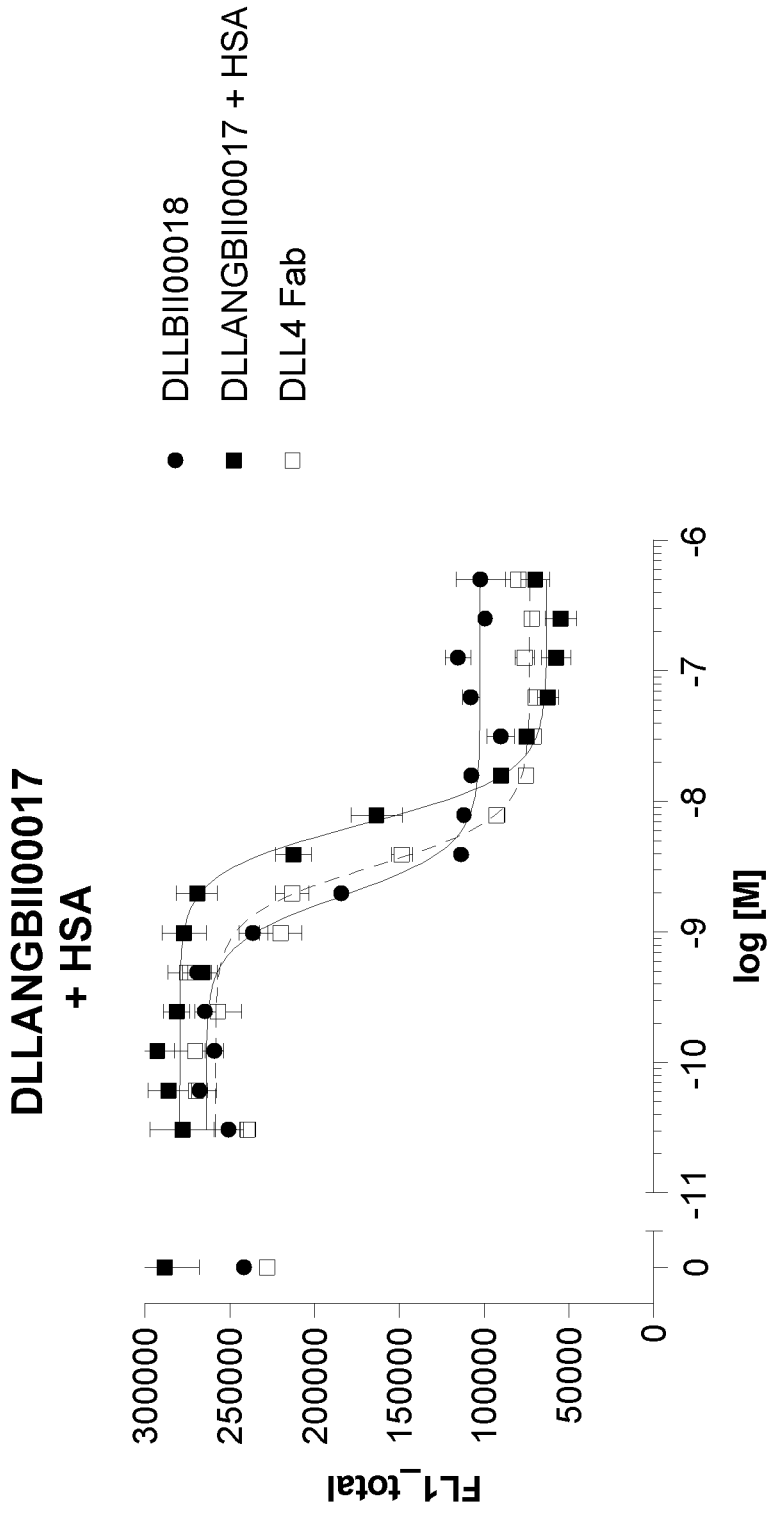


Figure 25-1B

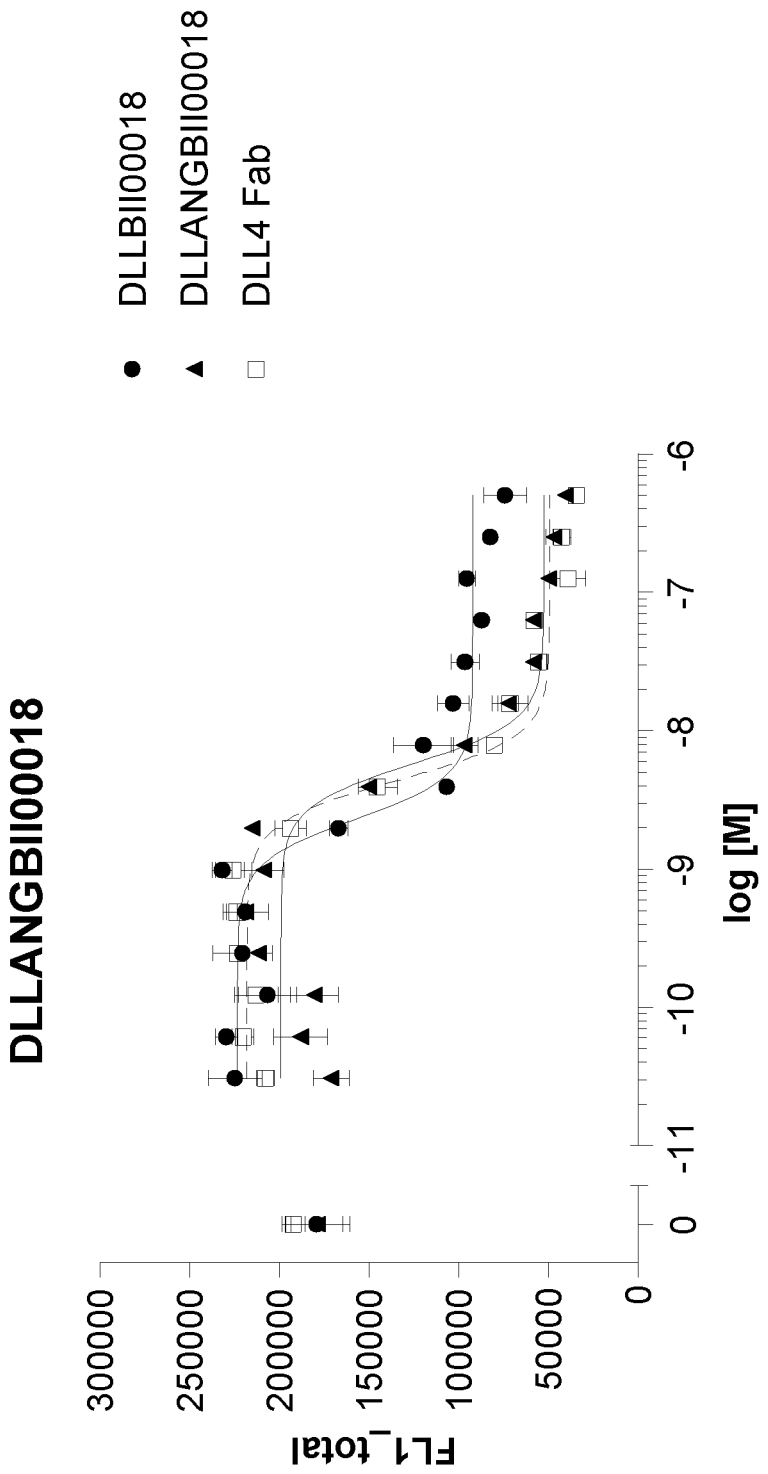

DLLBII00018
DLLANGBII00018
DLL4 Fab
DLLANGBII00018
FL1_total
300000
250000
200000
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-1B (continued)

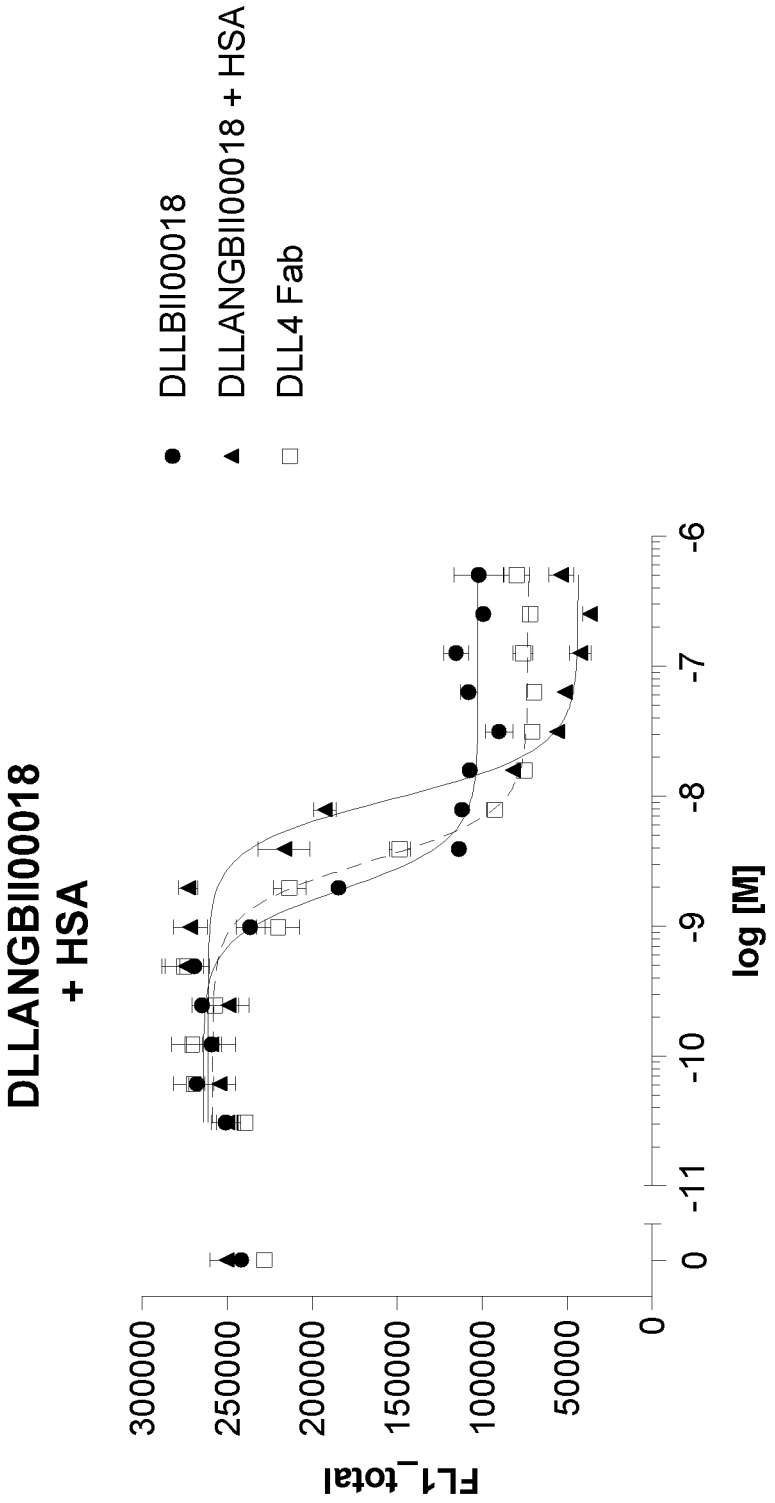


Figure 25-1C

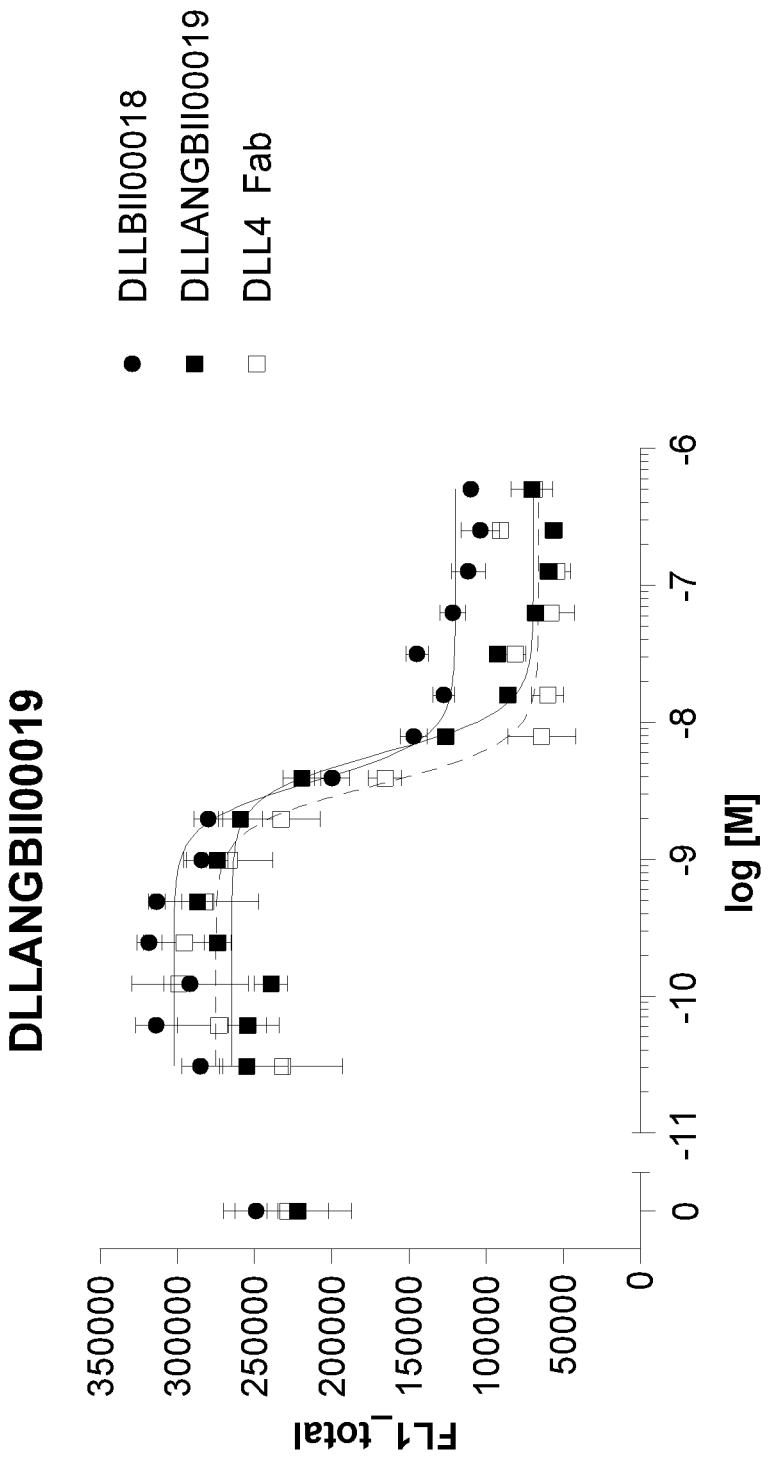

DLLBII00018
DLLANGBII00019
DLL4 Fab
DLLANGBII00019
FL1_total
350000
300000
250000
200000
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-1C (continued)

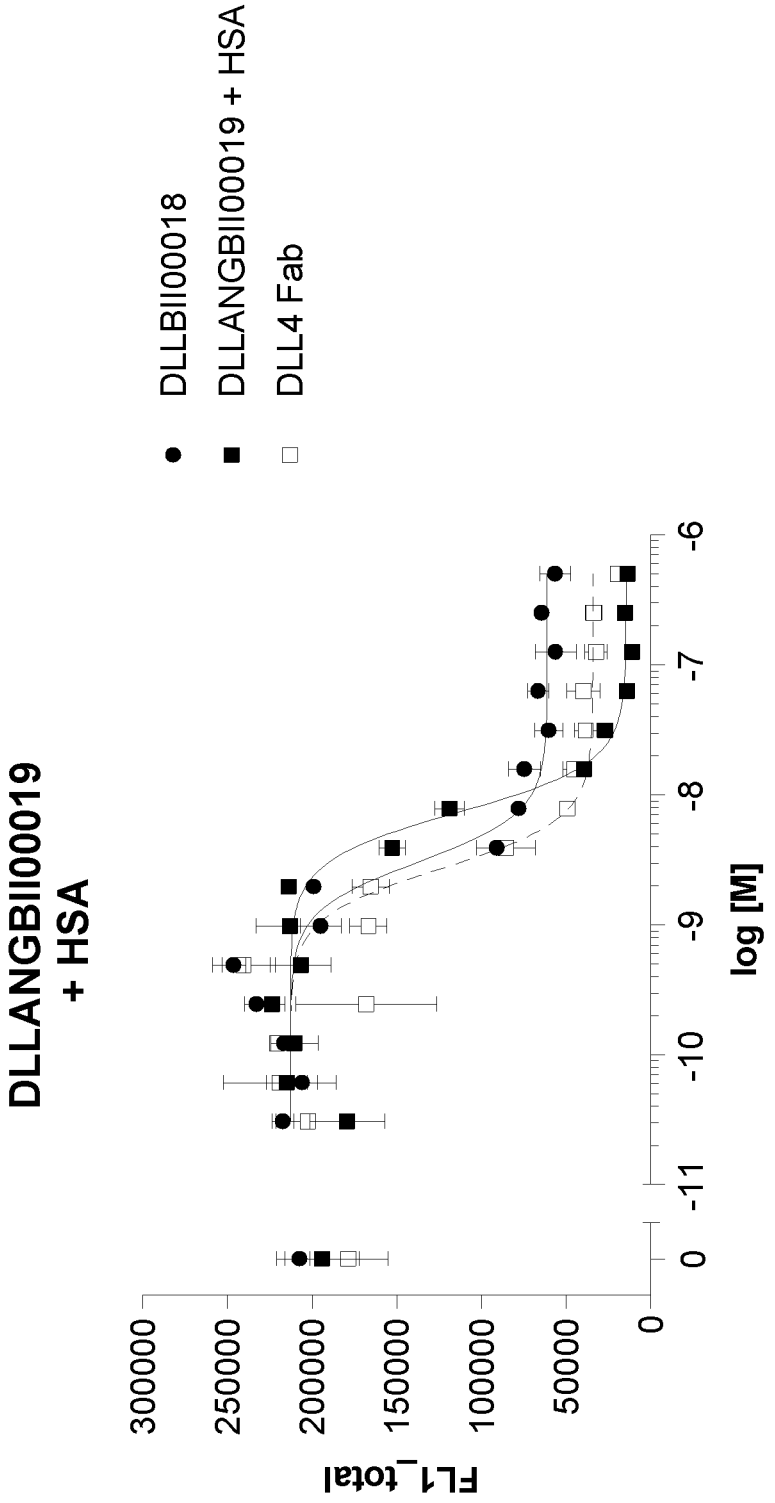


Figure 25-2A

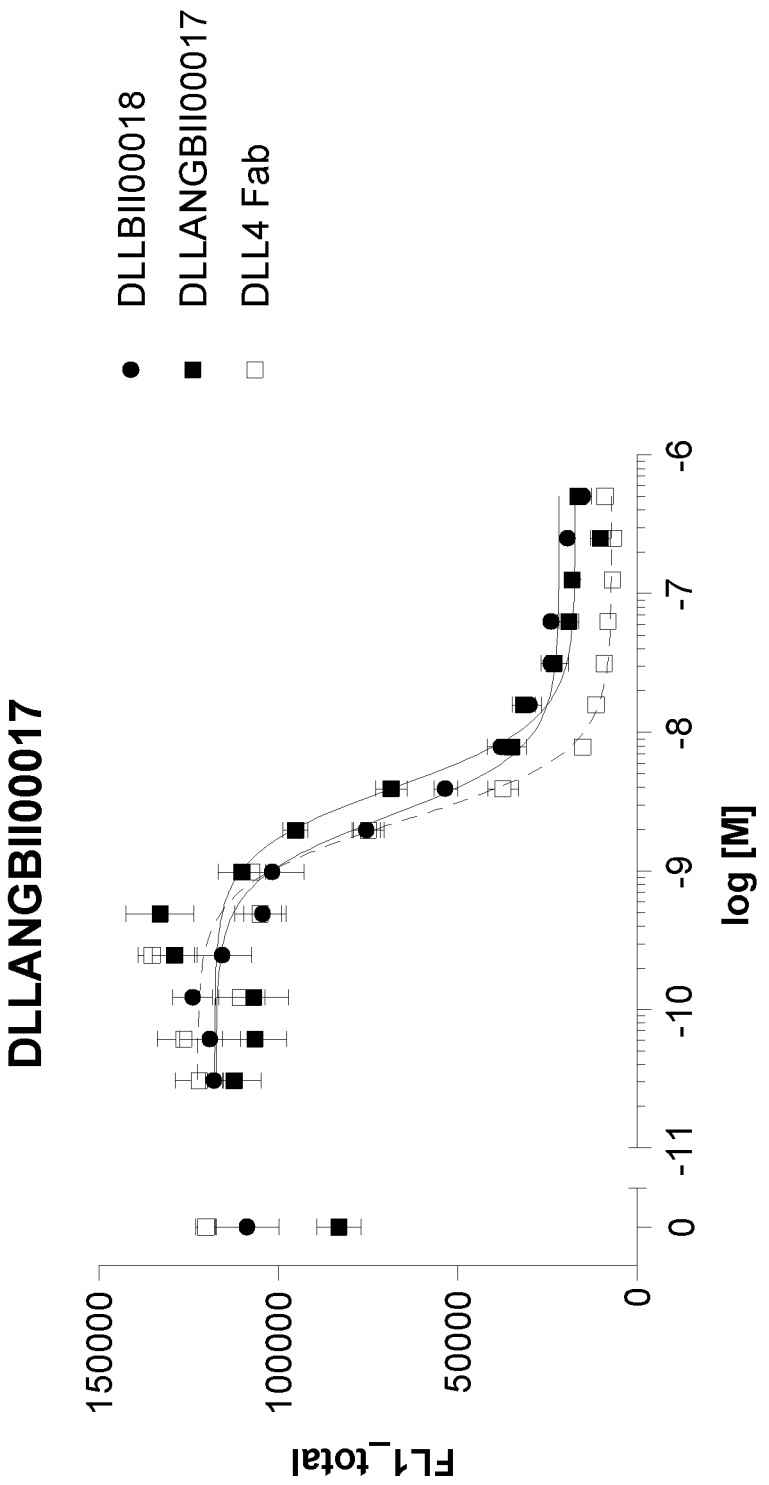

DLLBII00018
DLLANGBII00017
DLL4 Fab
DLLANGBII00017
FL1_total
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-2A (continued)

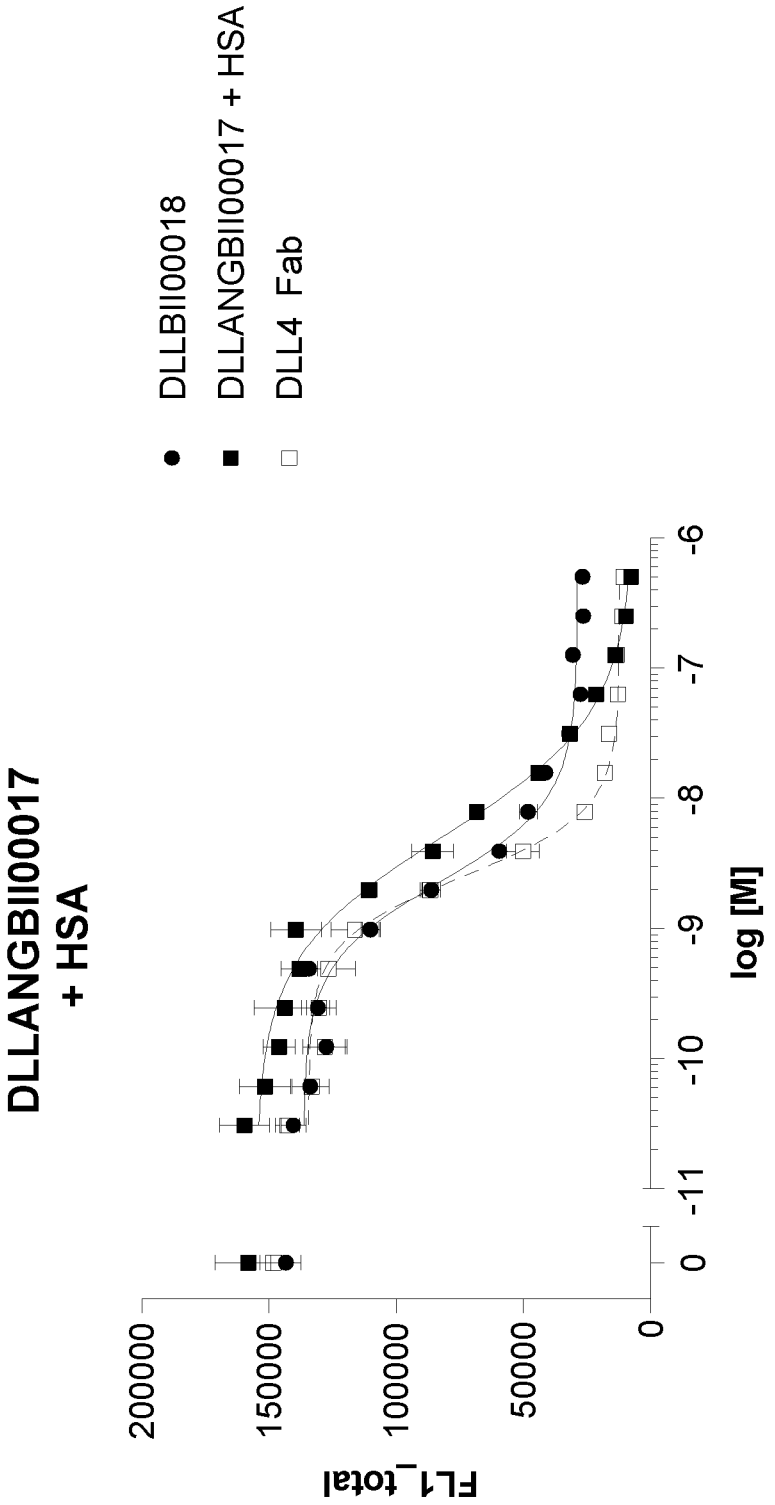


Figure 25-2B

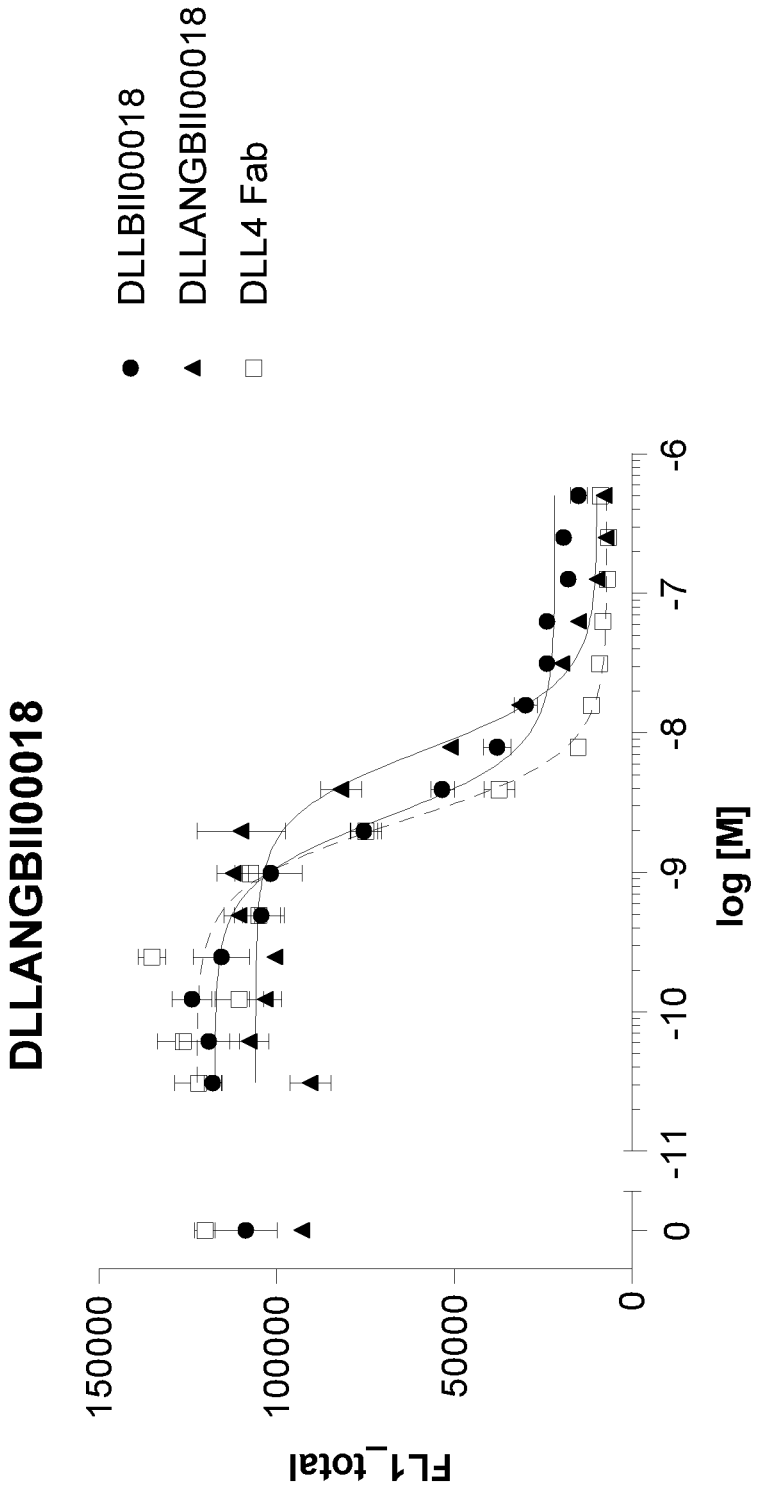

DLLBII00018
DLLANGBII00018
DLL4 Fab
DLLANGBII00018
FL1_total
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-2B (continued)

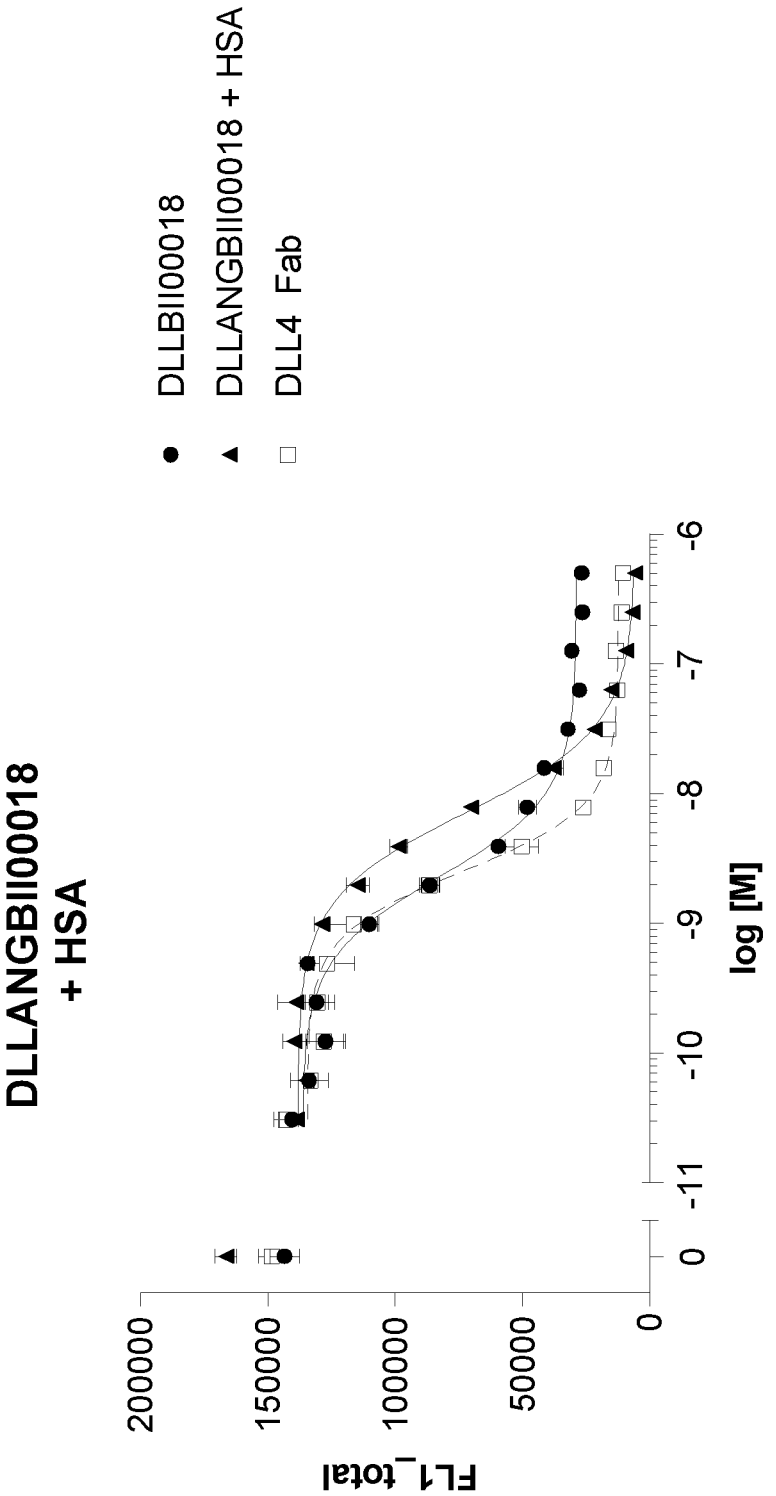


Figure 25-2C

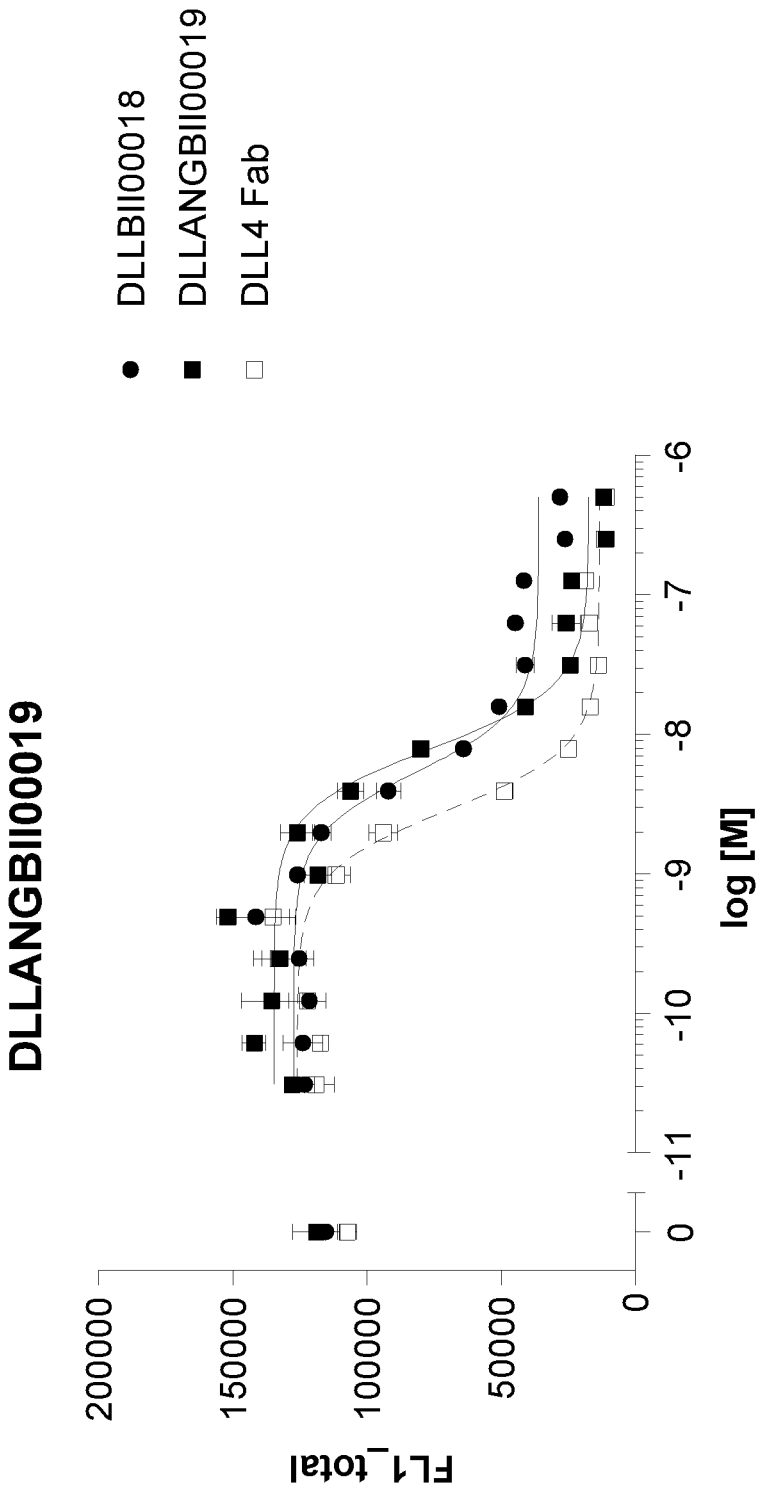

DLLBII00018
DLLANGBII00019
DLL4 Fab
DLLANGBII00019
FL1_total
200000
150000
100000
50000
0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 25-2C (continued)

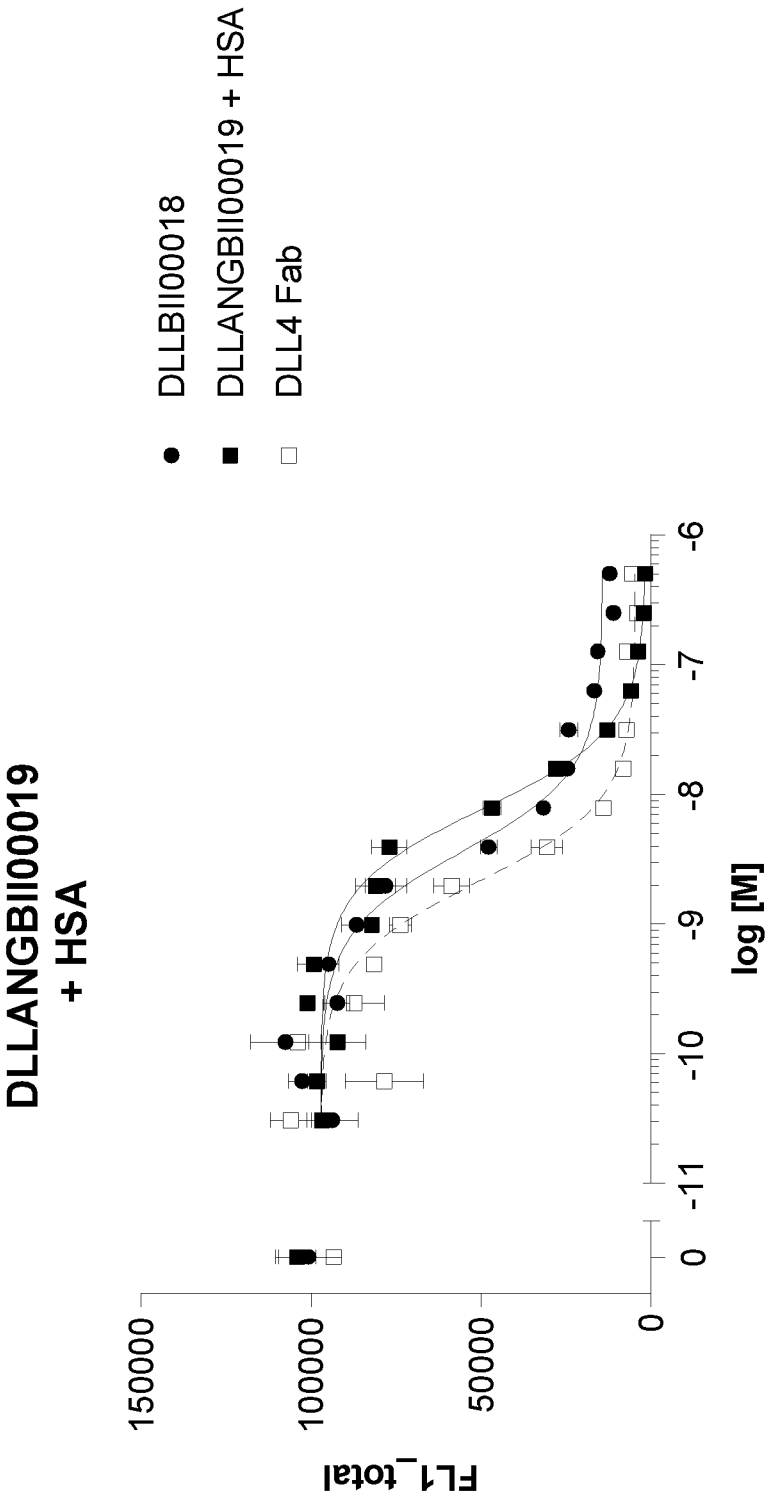


Figure 26A

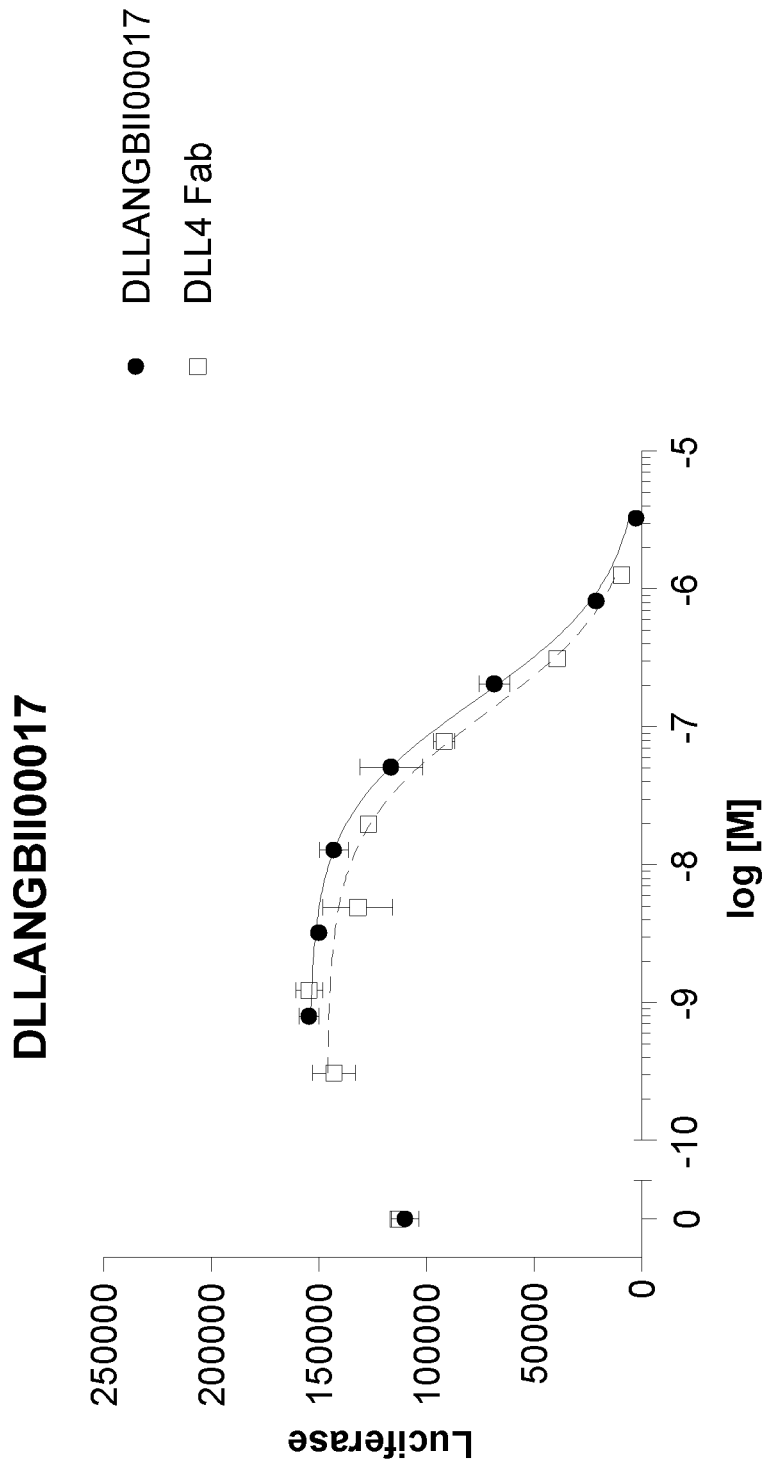

DLLANGBII00017
DLL4 Fab
DLLANGBII00017
Luciferase
250000
200000
150000
100000
50000
0
0
-10
-9
-8
-7
-6
-5
log [M]

Figure 26A (continued)

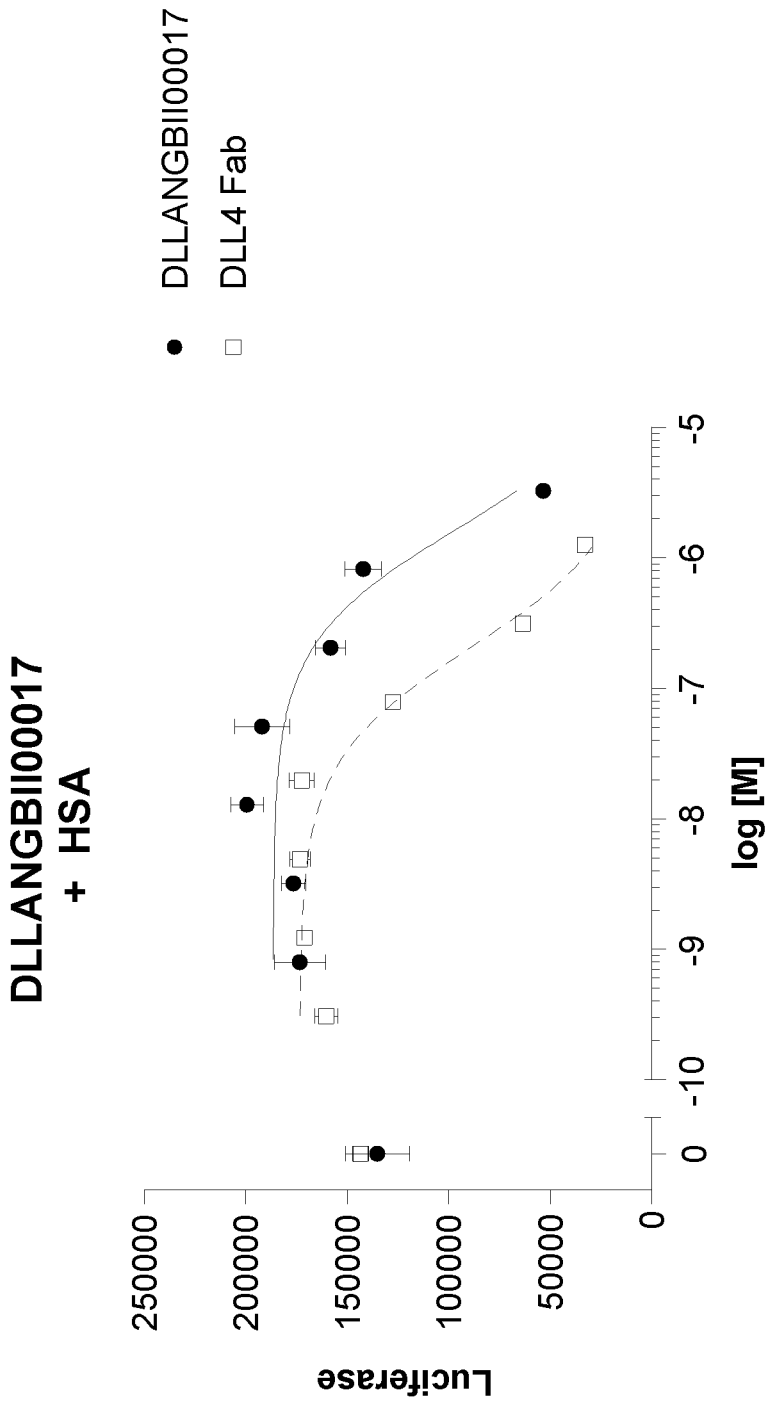


Figure 26B

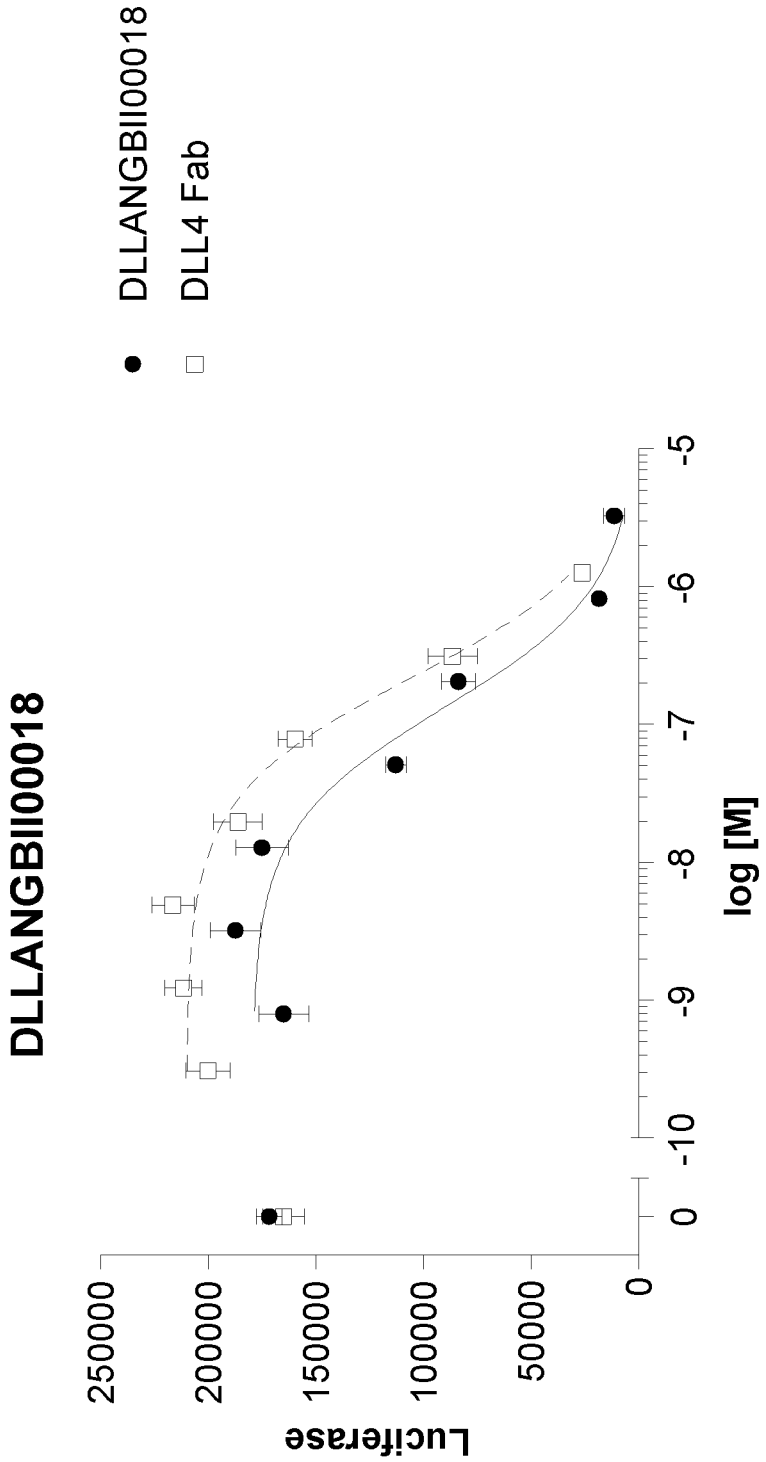

DLLANGBII00018
DLL4 Fab
DLLANGBII00018
Luciferase
250000
200000
150000
100000
50000
0
0
-10
-9
-8
-7
-6
-5
log [M]

Figure 26B (continued)

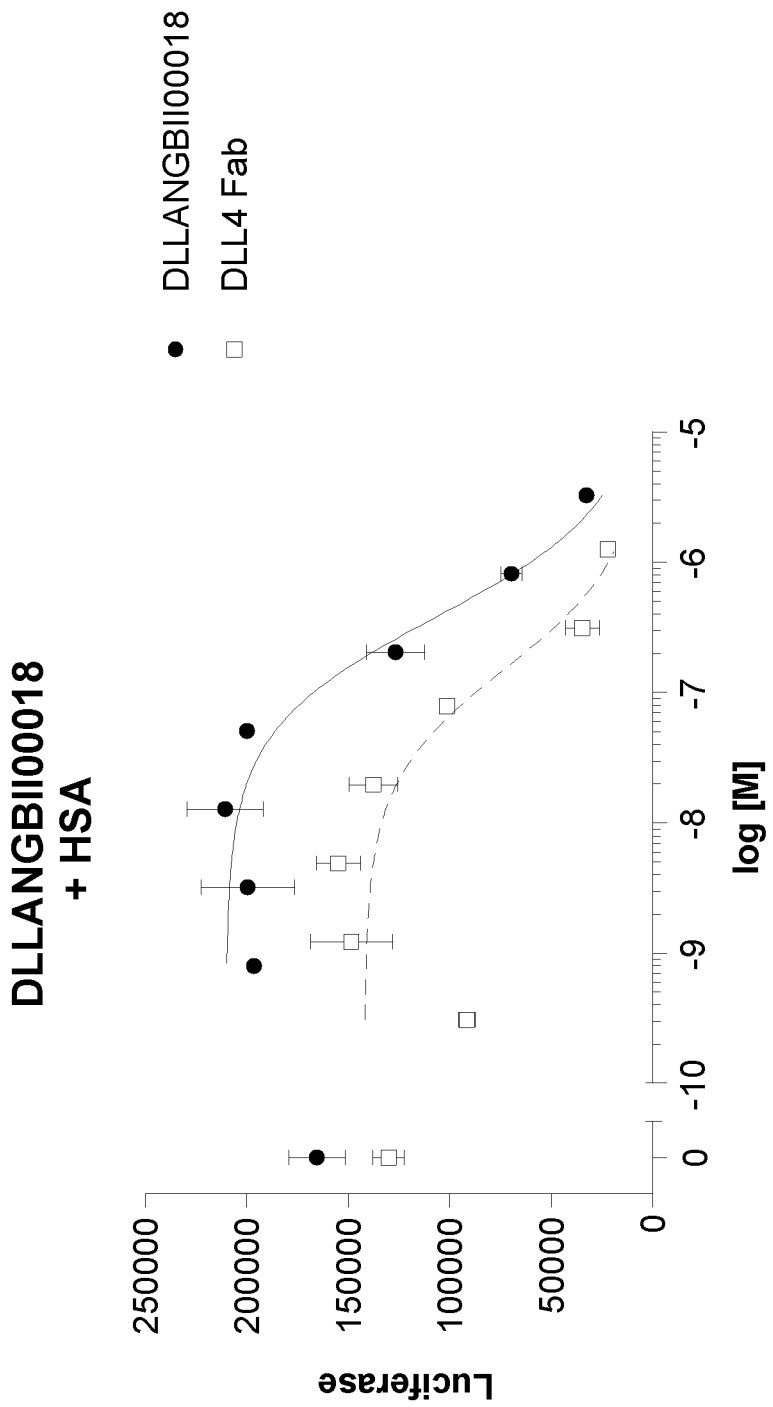


Figure 26C

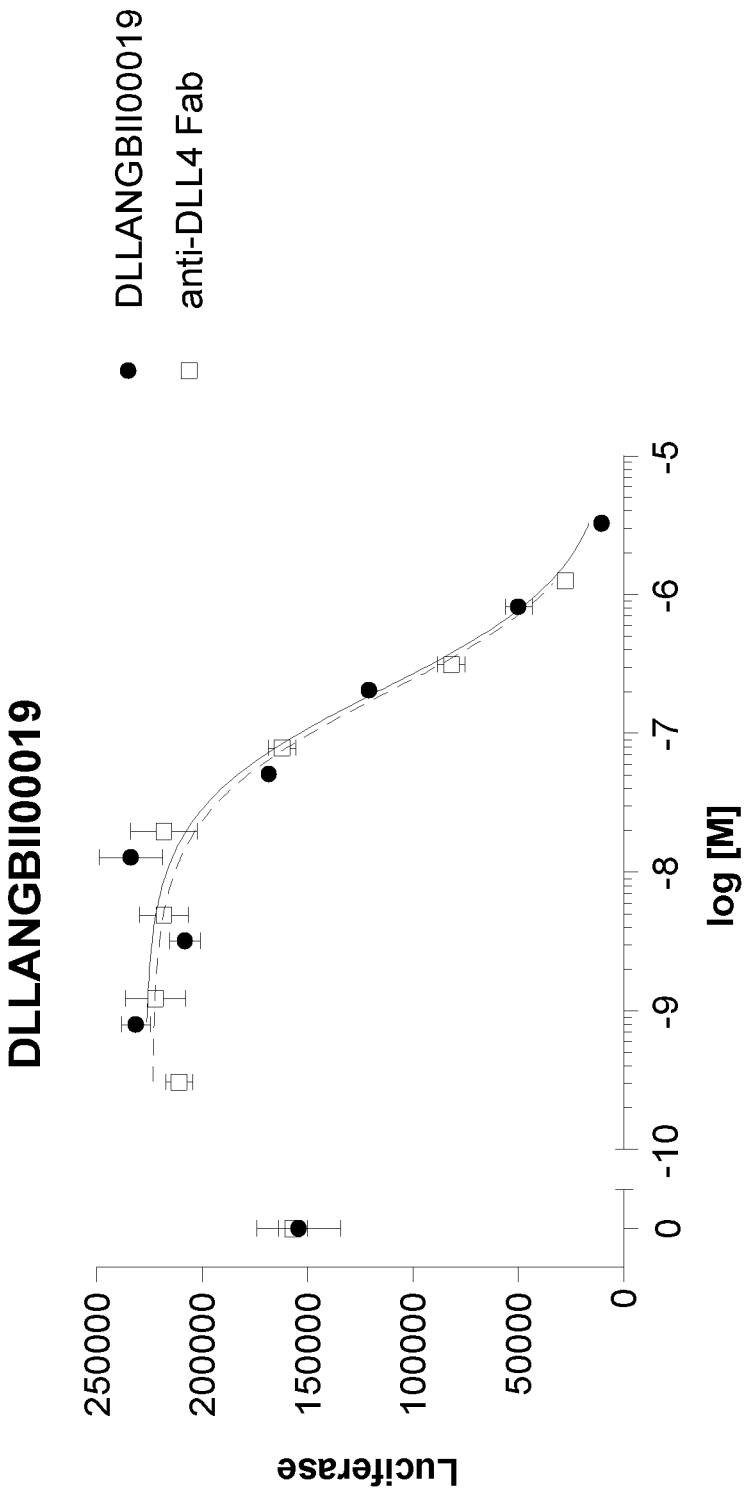

DLLANGBII00019
DLLANGBII00019
anti-DLL4 Fab
Luciferase
250000
200000
150000
100000
50000
0
0
-10
-9
-8
-7
-6
-5
log [M]

Figure 26C (continued)

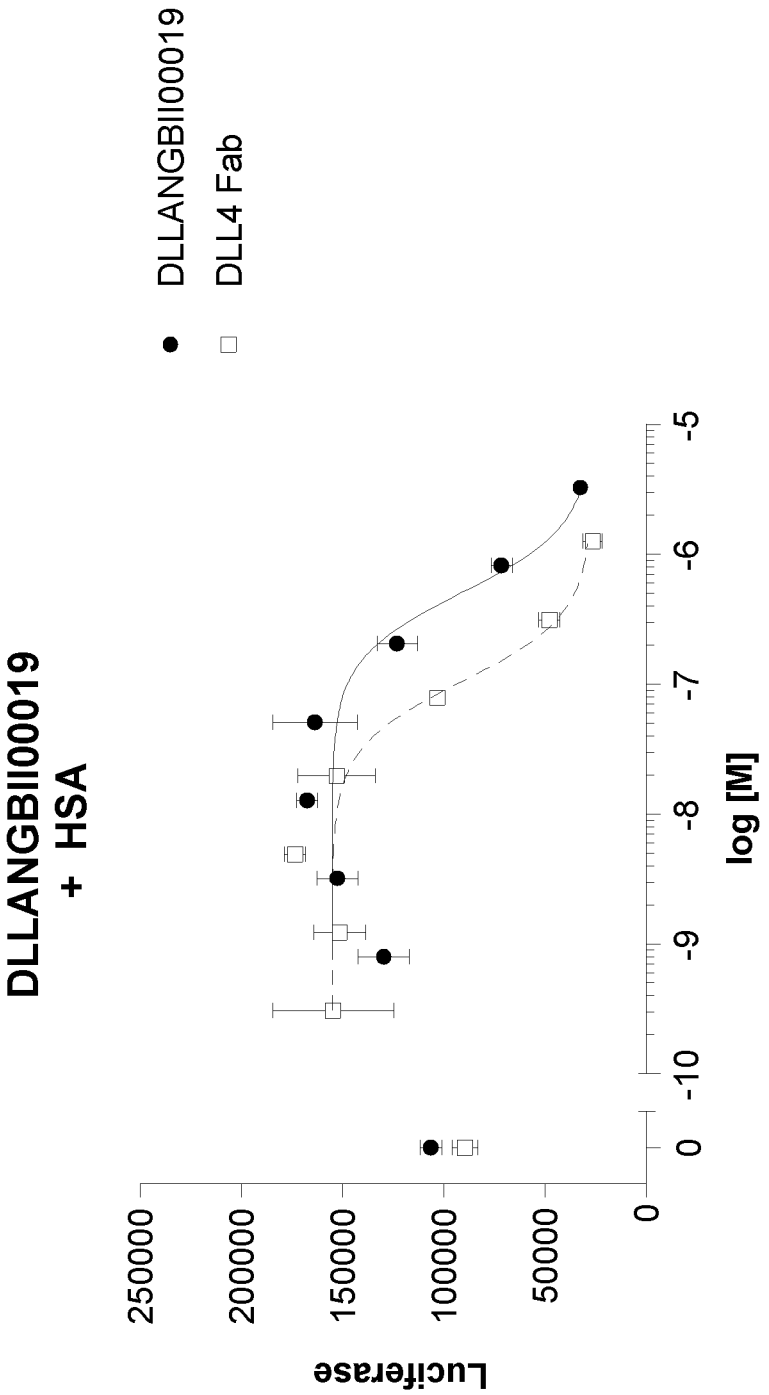


Figure 27A

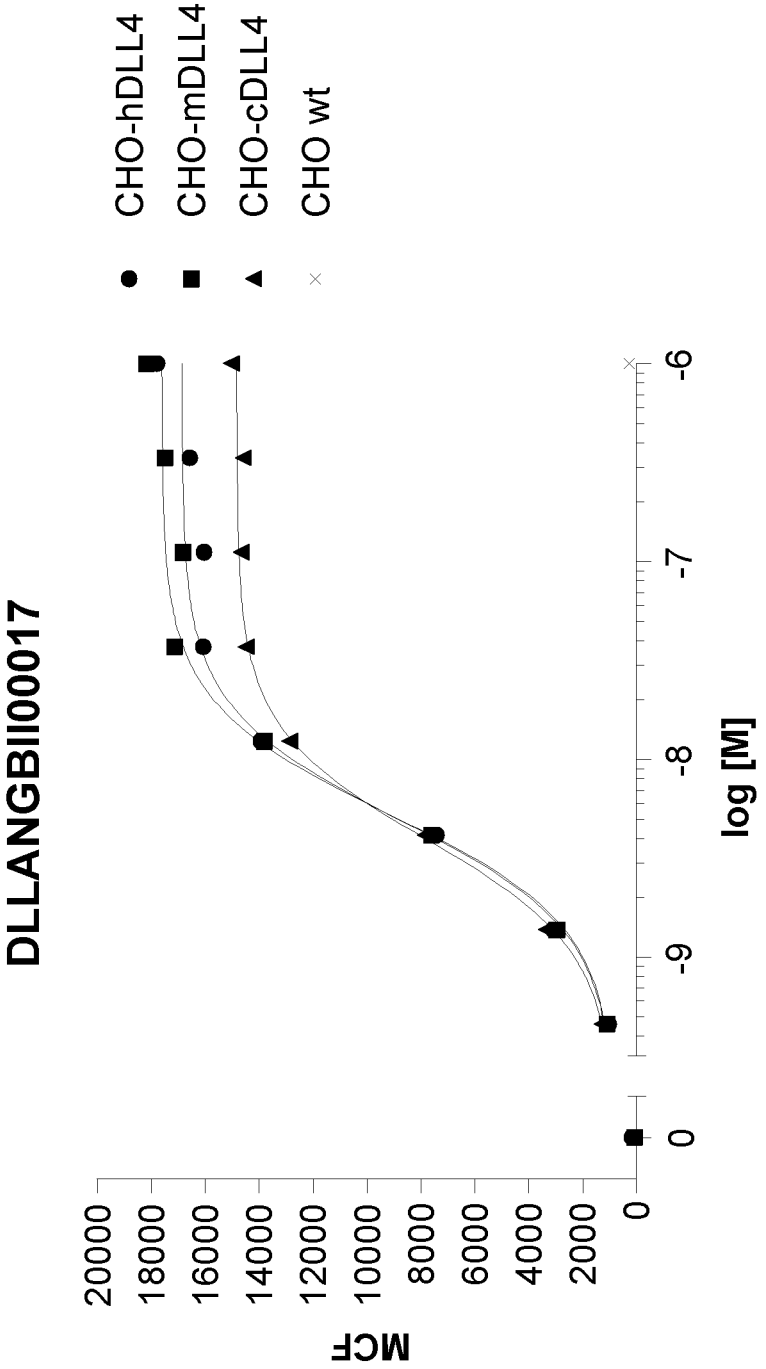

DLLANGBII00017
CHO-hDLL4
CHO-mDLL4
CHO-cDLL4
CHO wt
MCF
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
0
-9
-8
-7
-6
log [M]

Figure 27B

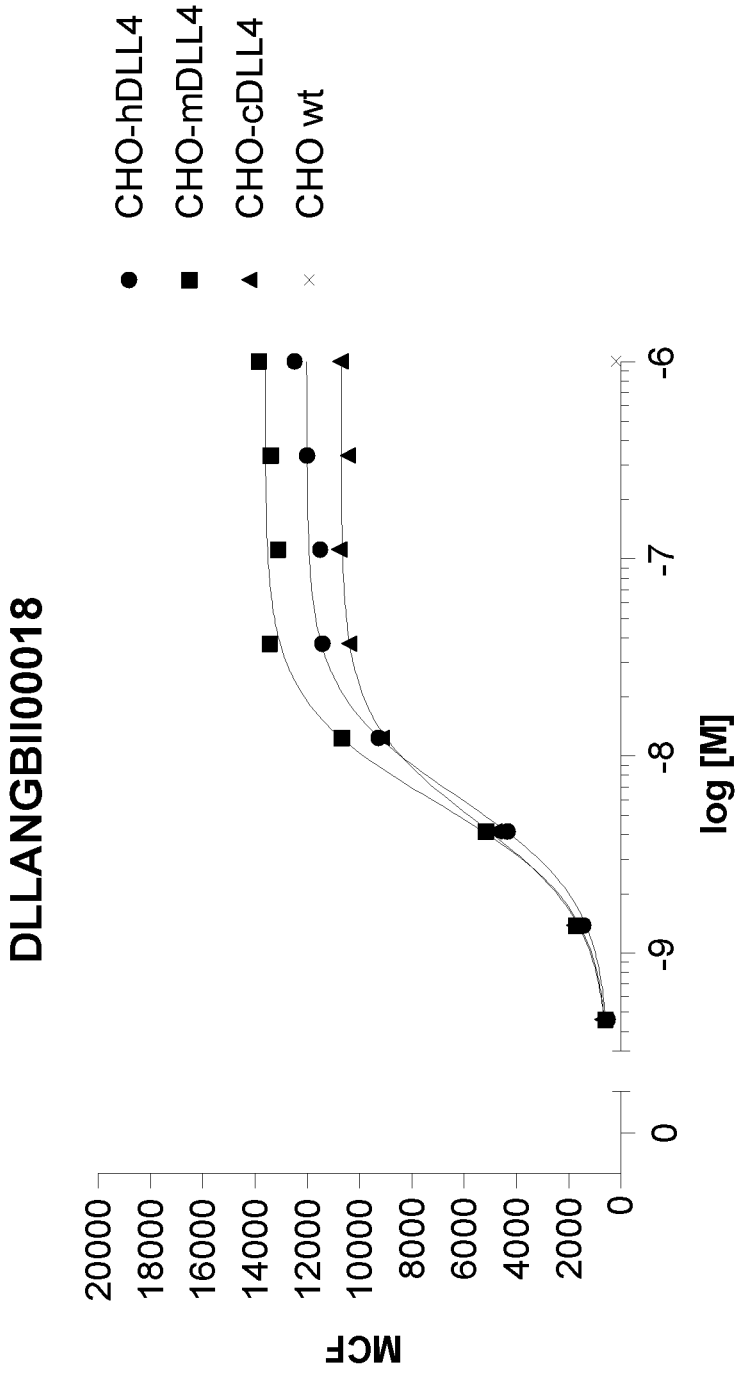

DLLANGBII00018
CHO-hDLL4
CHO-mDLL4
CHO-cDLL4
CHO wt
MCF
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
0
-6
-7
-8
-9
log [M]

Figure 27C

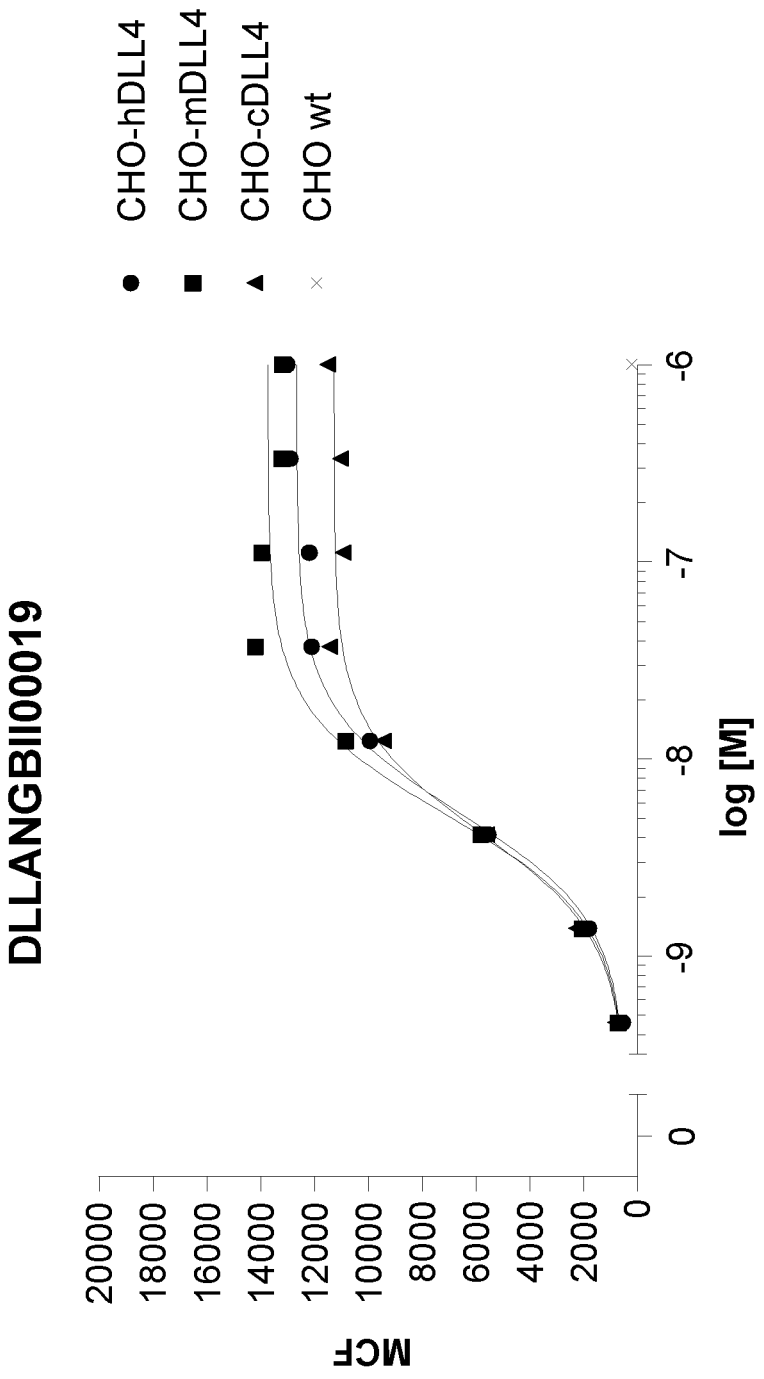

DLLANGBII00019
CHO-hDLL4
CHO-mDLL4
CHO-cDLL4
CHO wt
MCF
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
0
-9
-8
-7
-6
log [M]

Figure 28A

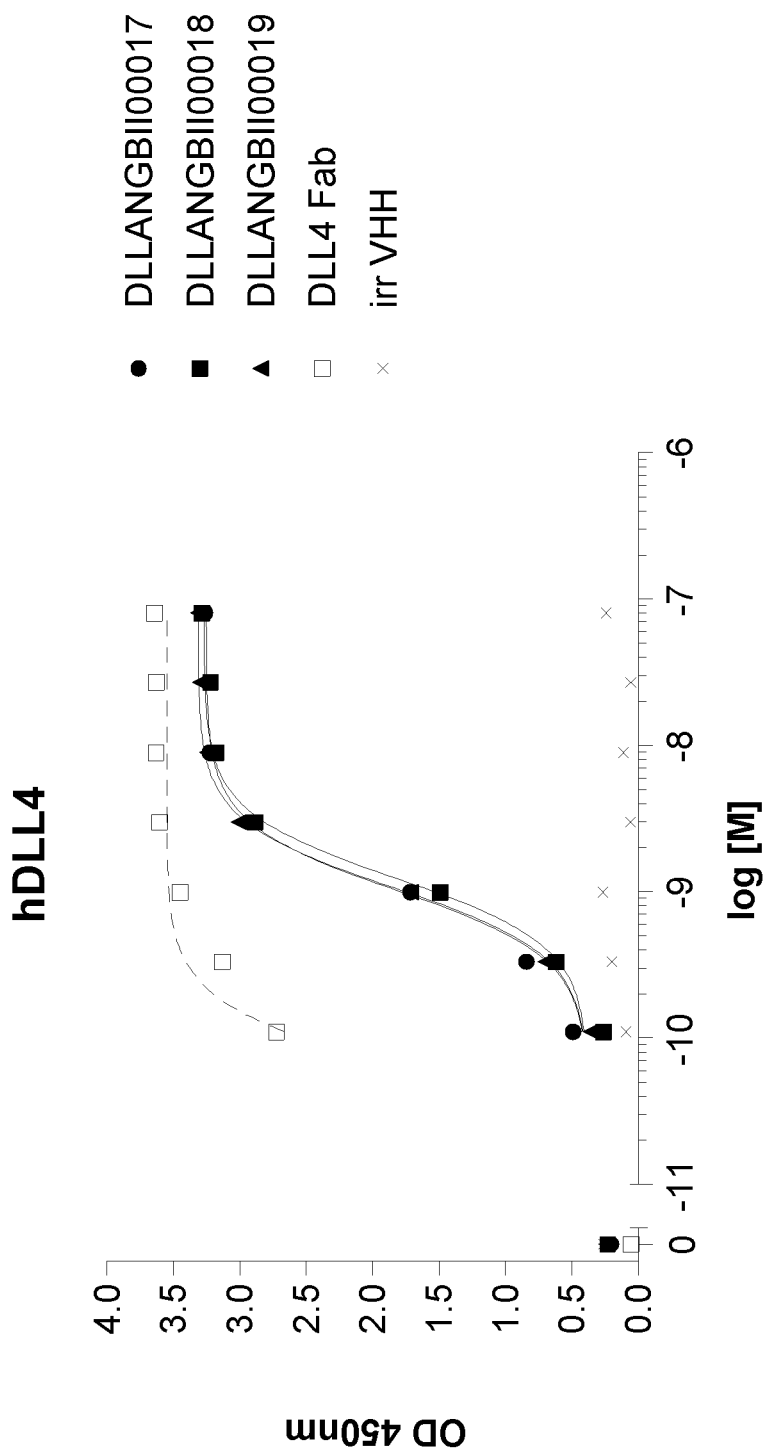

DLLANGBII00017
DLLANGBII00018
DLLANGBII00019
DLL4 Fab
irr VHH
hDLL4
OD 450nm
log [M]
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6

Figure 28B

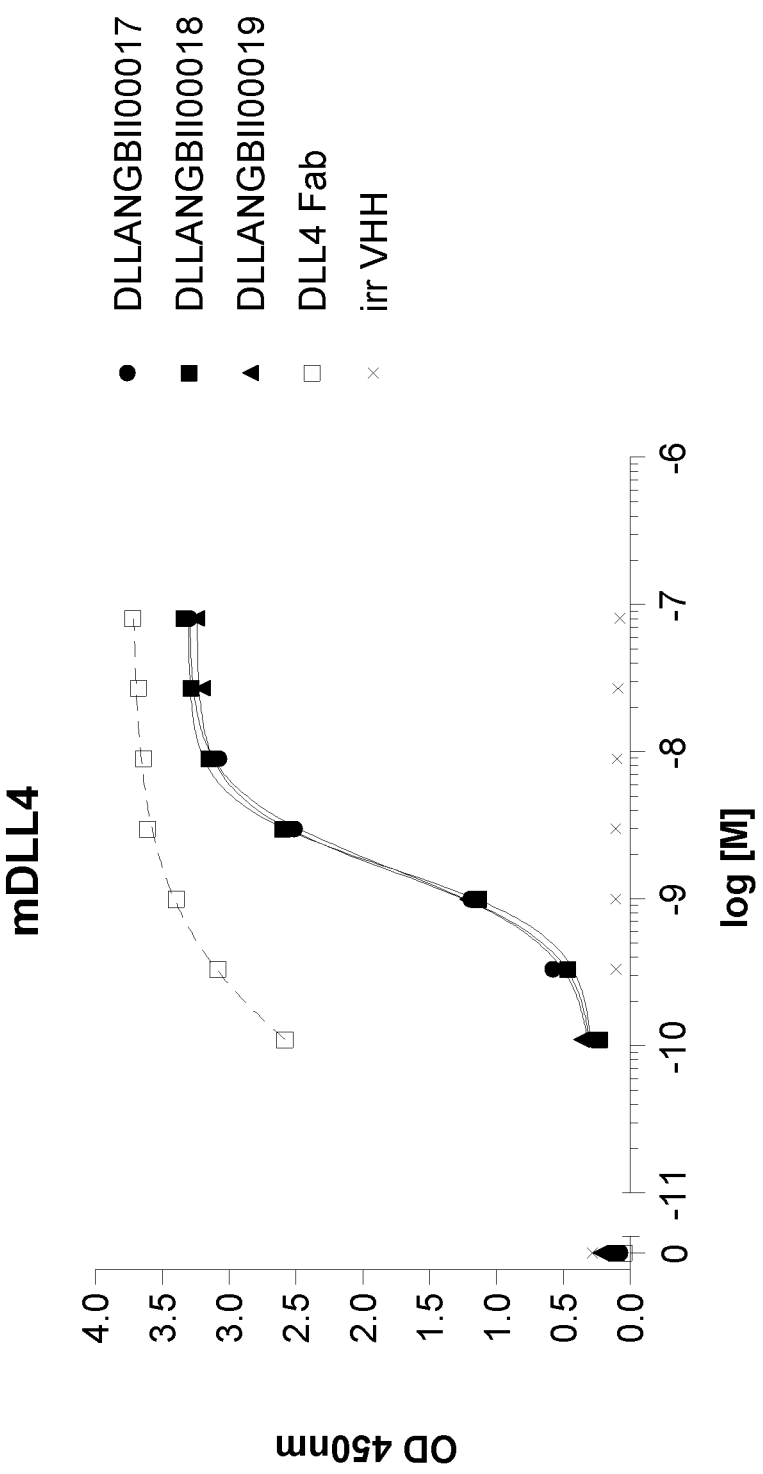

DLLANGBII00017
DLLANGBII00018
DLLANGBII00019
DLL4 Fab
irr VHH
mDLL4
OD 450nm
log [M]
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
0
-11
-10
-9
-8
-7
-6

Figure 28C

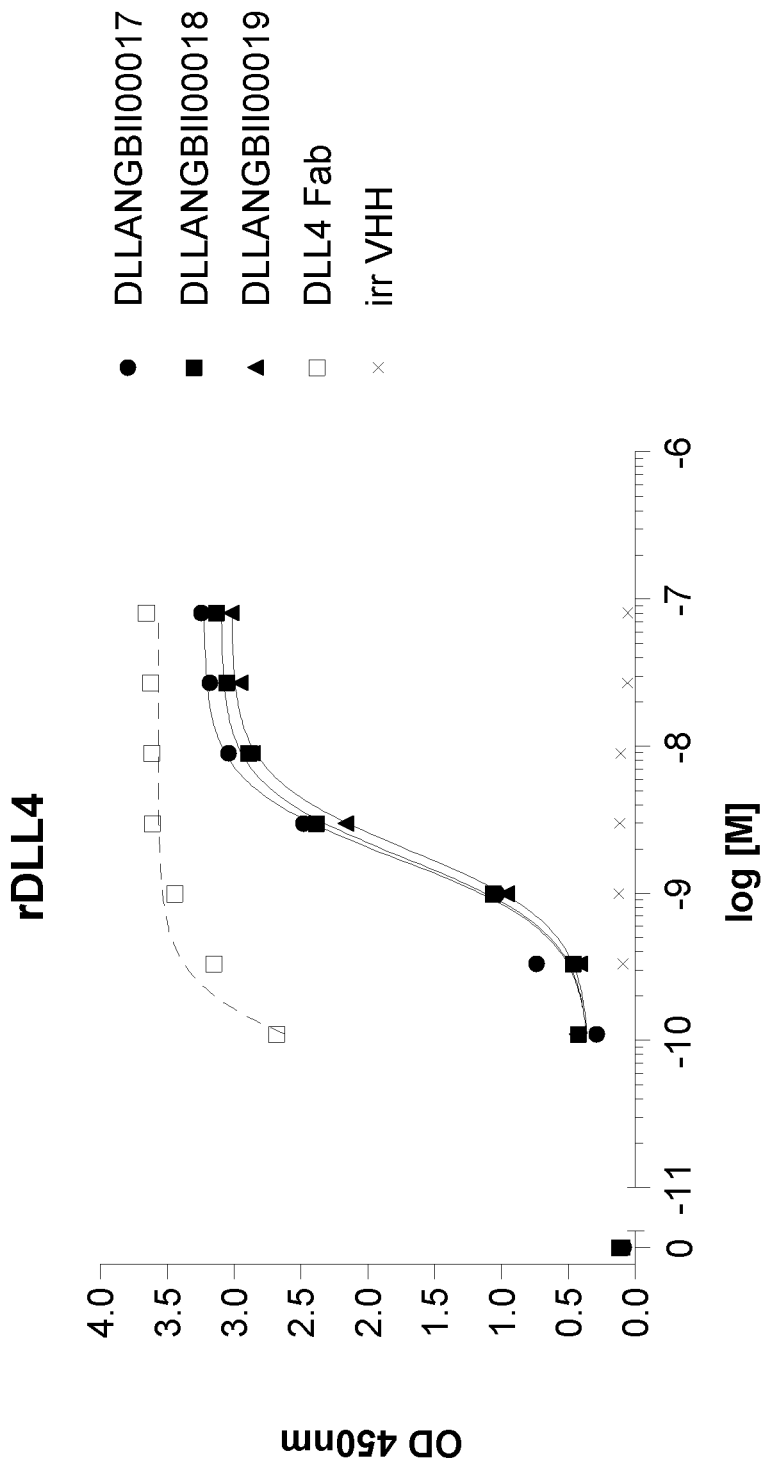

DLLANGBII00017
DLLANGBII00018
DLLANGBII00019
DLL4 Fab
irr VHH
rDLL4
OD 450nm
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 29A

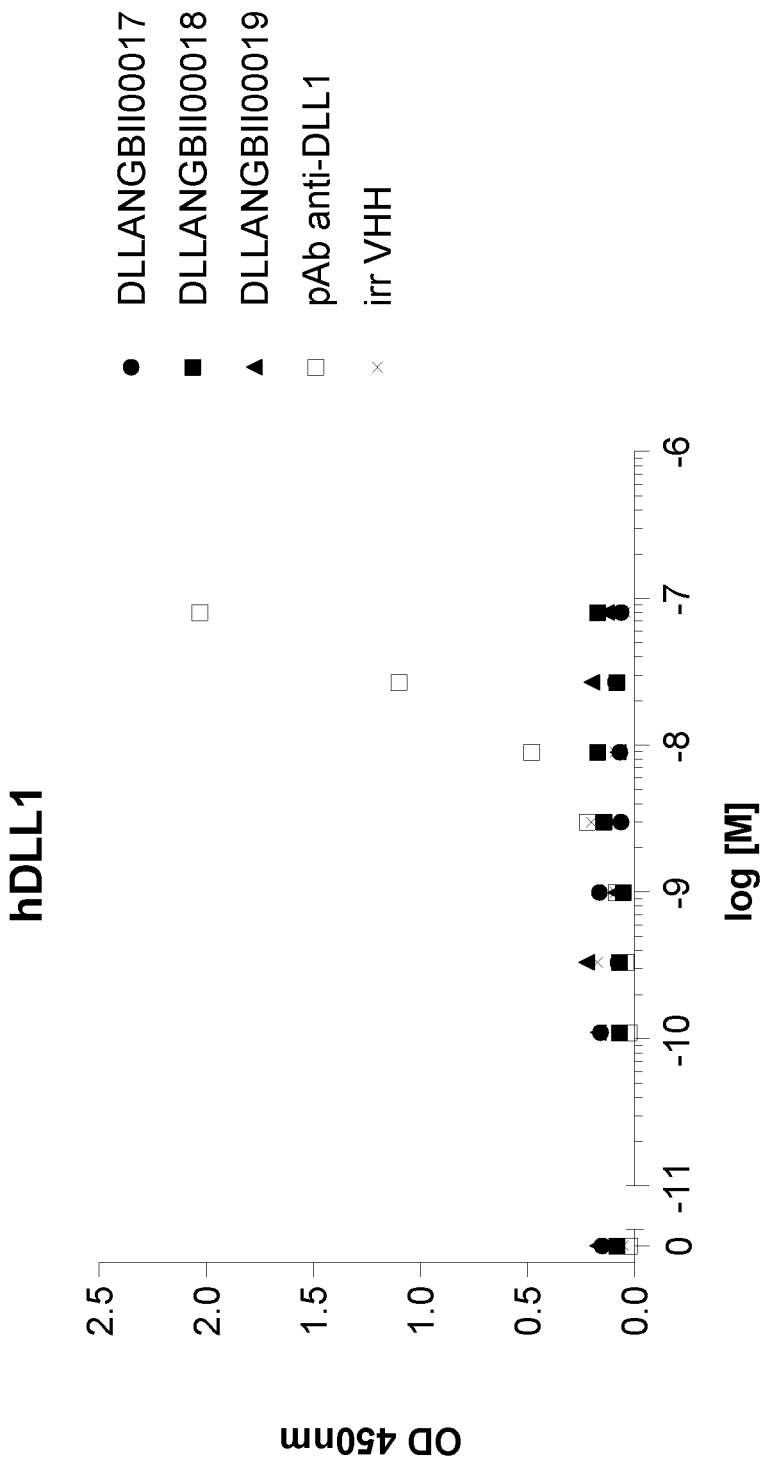

DLLANGBII00017
DLLANGBII00018
DLLANGBII00019
pAb anti-DLL1
irr VHH
hDLL1
OD 450nm
0.0
0.5
1.0
1.5
2.0
2.5
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 29B

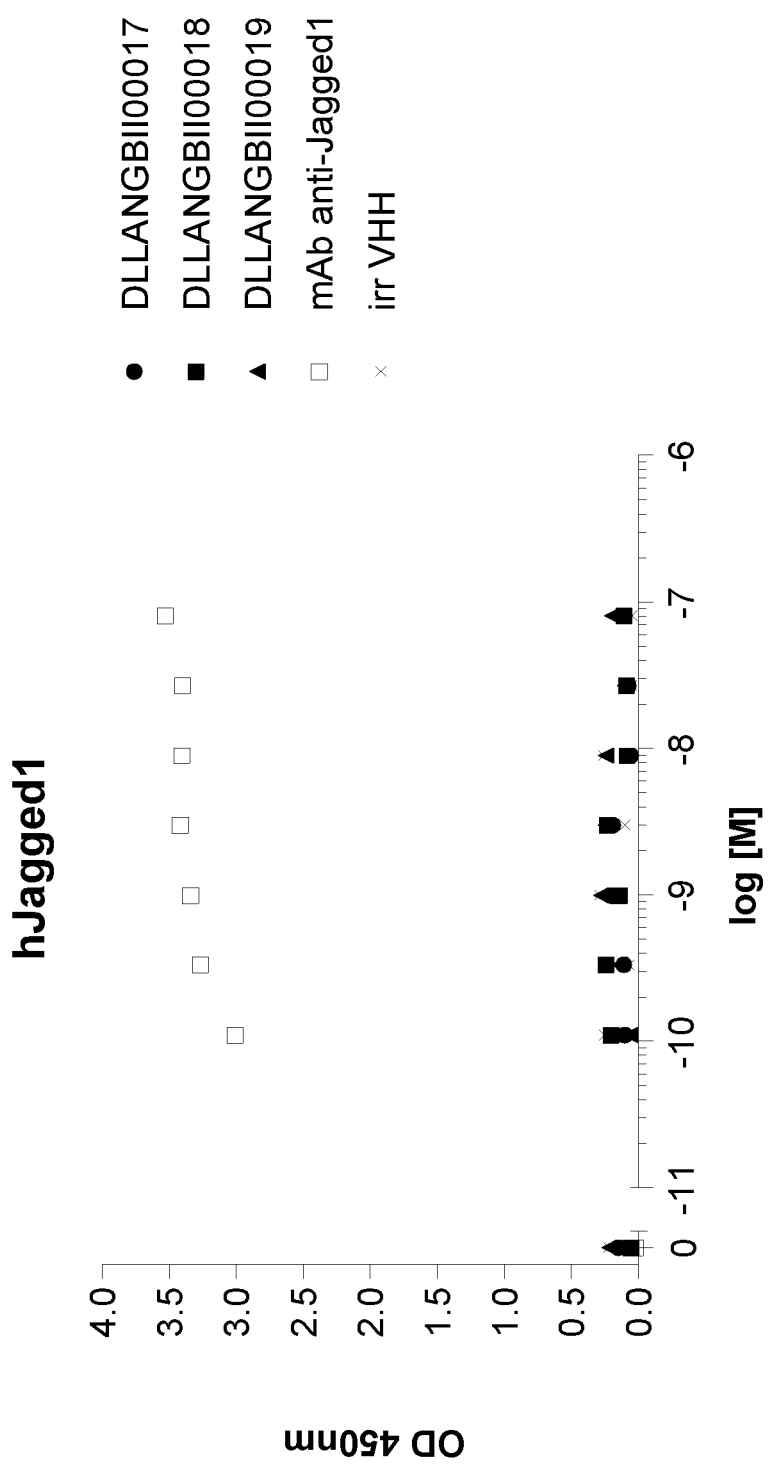

DLLANGBII00017
DLLANGBII00018
DLLANGBII00019
mAb anti-Jagged1
irr VHH
hJagged1
OD 450nm
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-1A

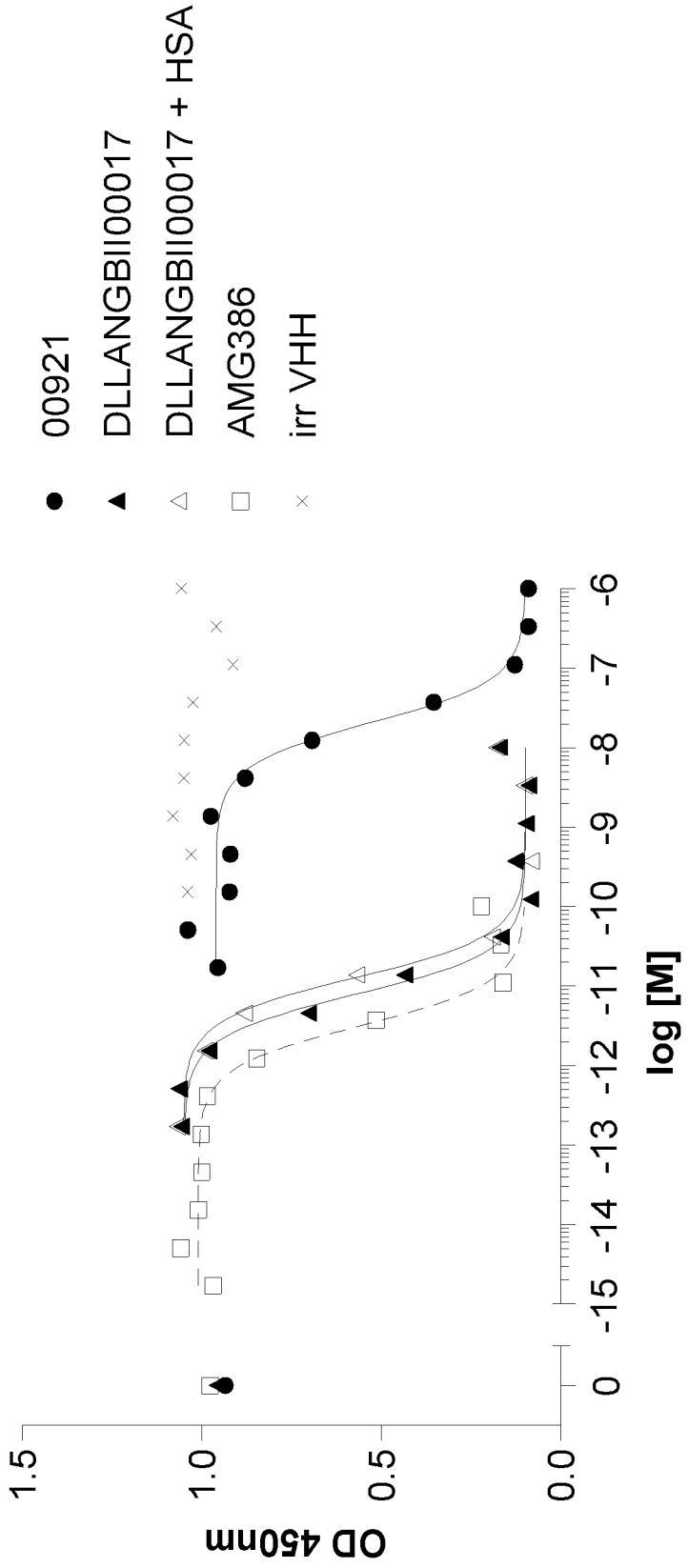

00921
DLLANGBII00017
DLLANGBII00017 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-1B

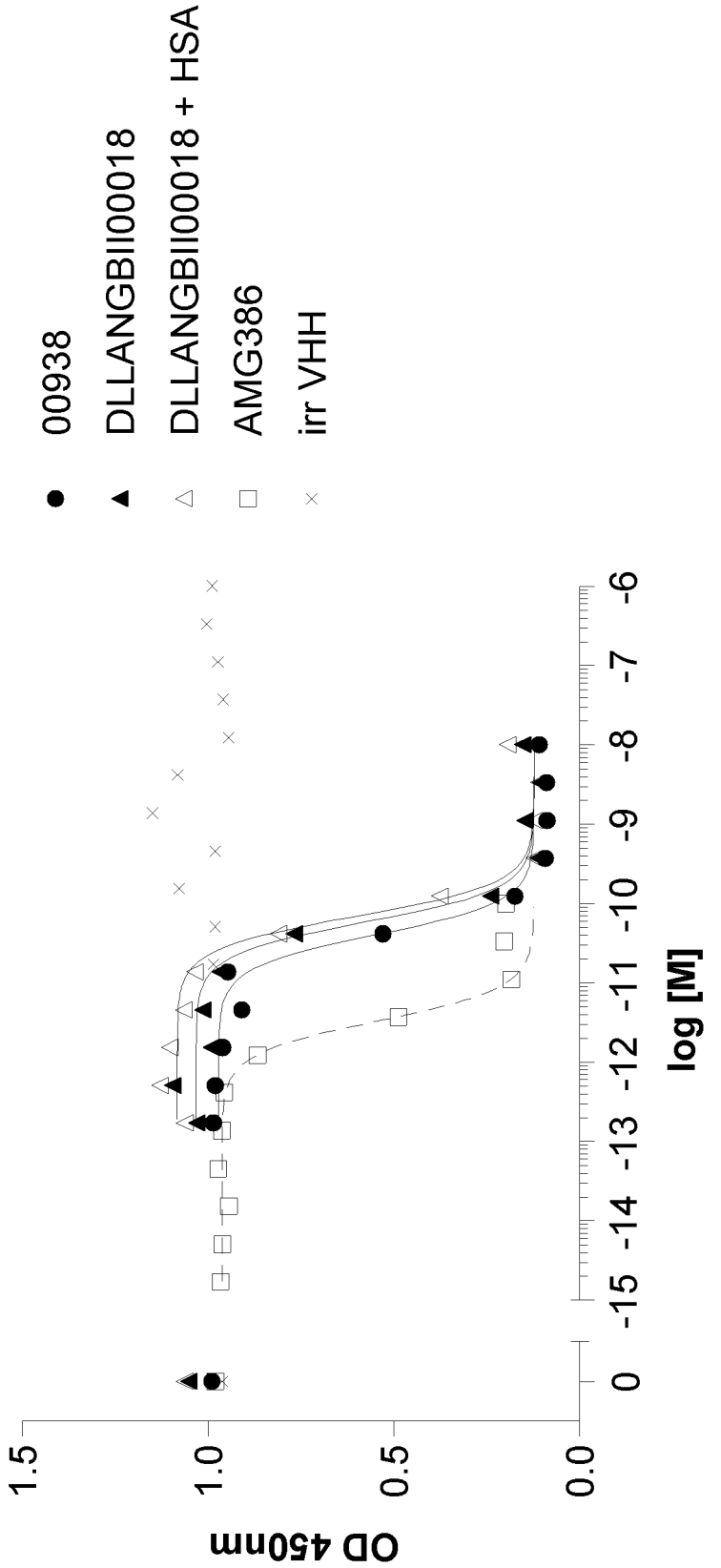

00938
DLLANGBII00018
DLLANGBII00018 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-1C

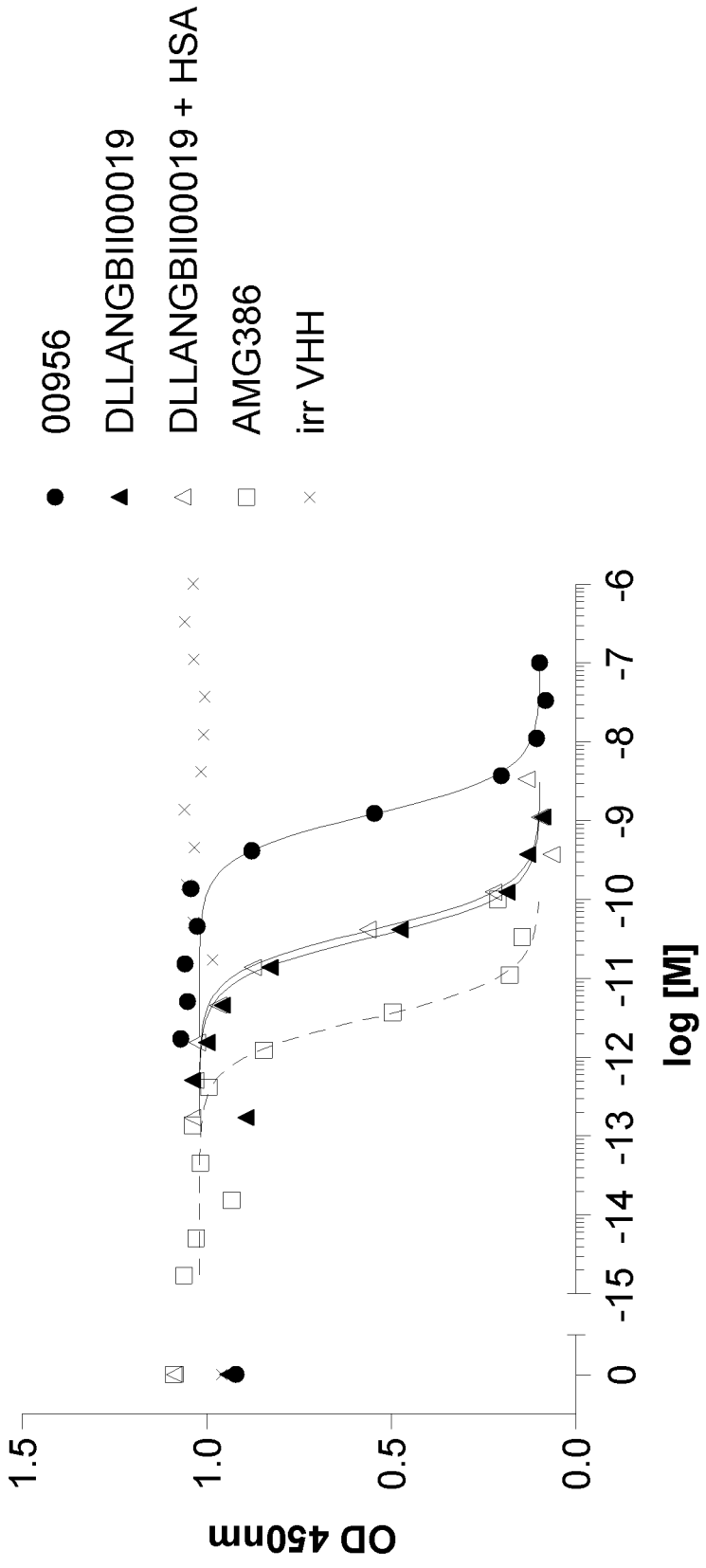

00956
DLLANGBII00019
DLLANGBII00019 + HSA
AMG386
irr VHH
OD 450nm
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-2A

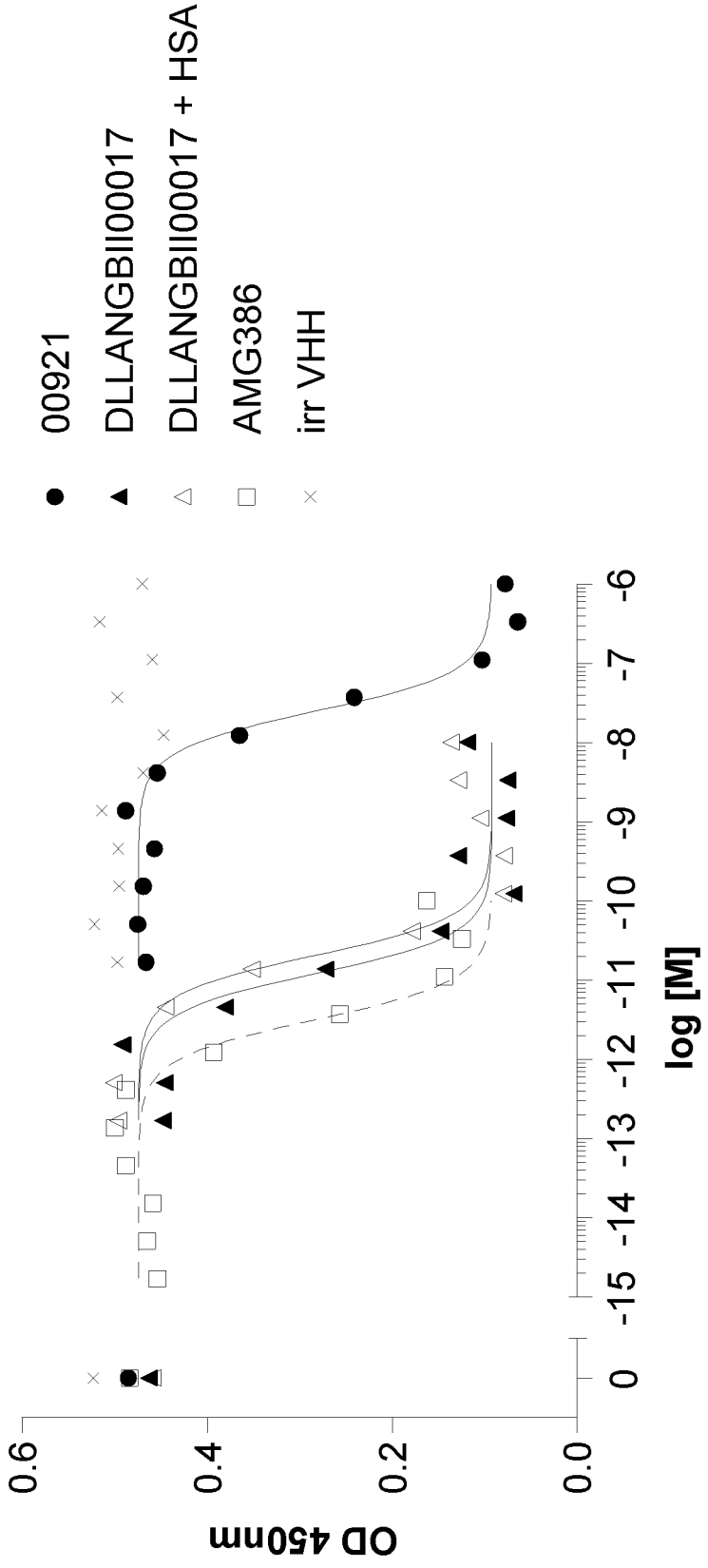

00921
DLLANGBII00017
DLLANGBII00017 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
log [M]
0
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15

Figure 30-2B

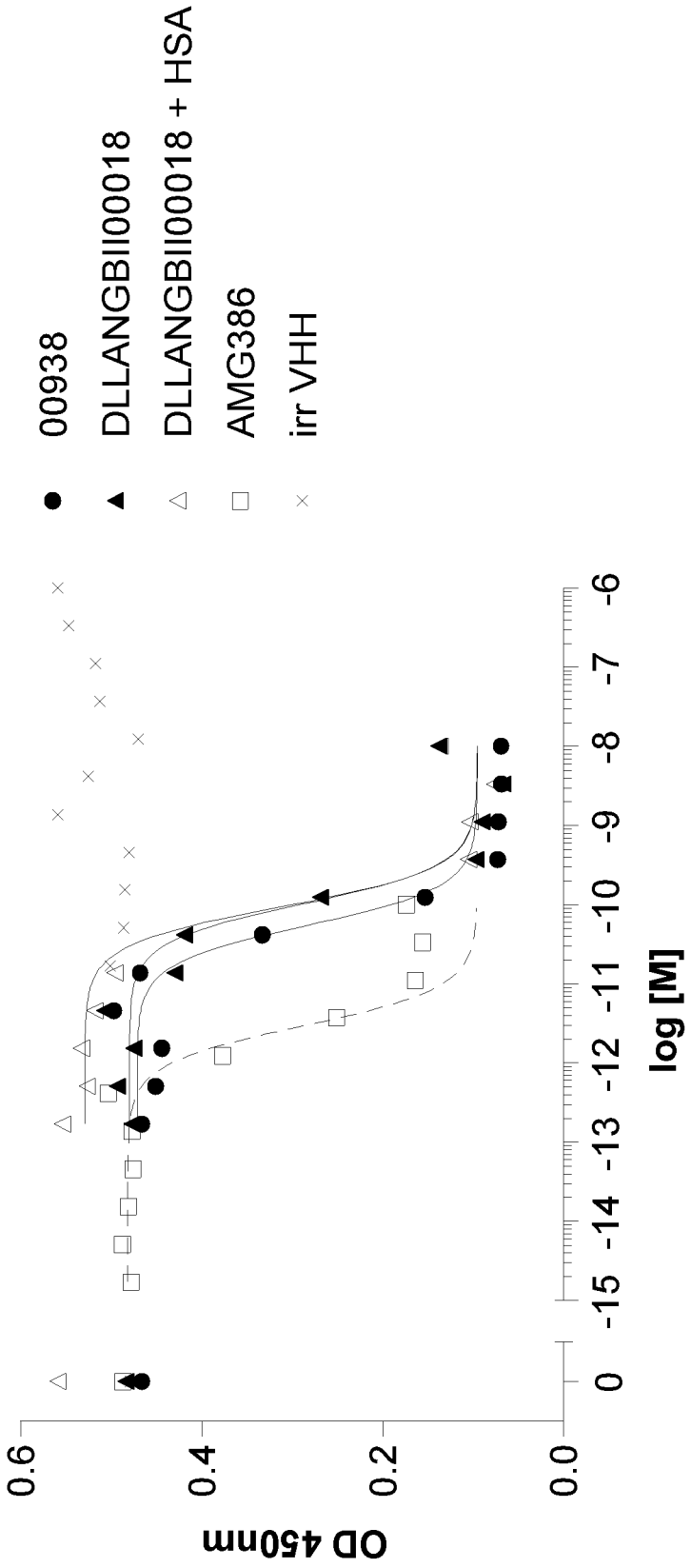

00938
DLLANGBII00018
DLLANGBII00018 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
log [M]
0
-6
-7
-8
-9
-10
-11
-12
-13
-14
-15

Figure 30-2C

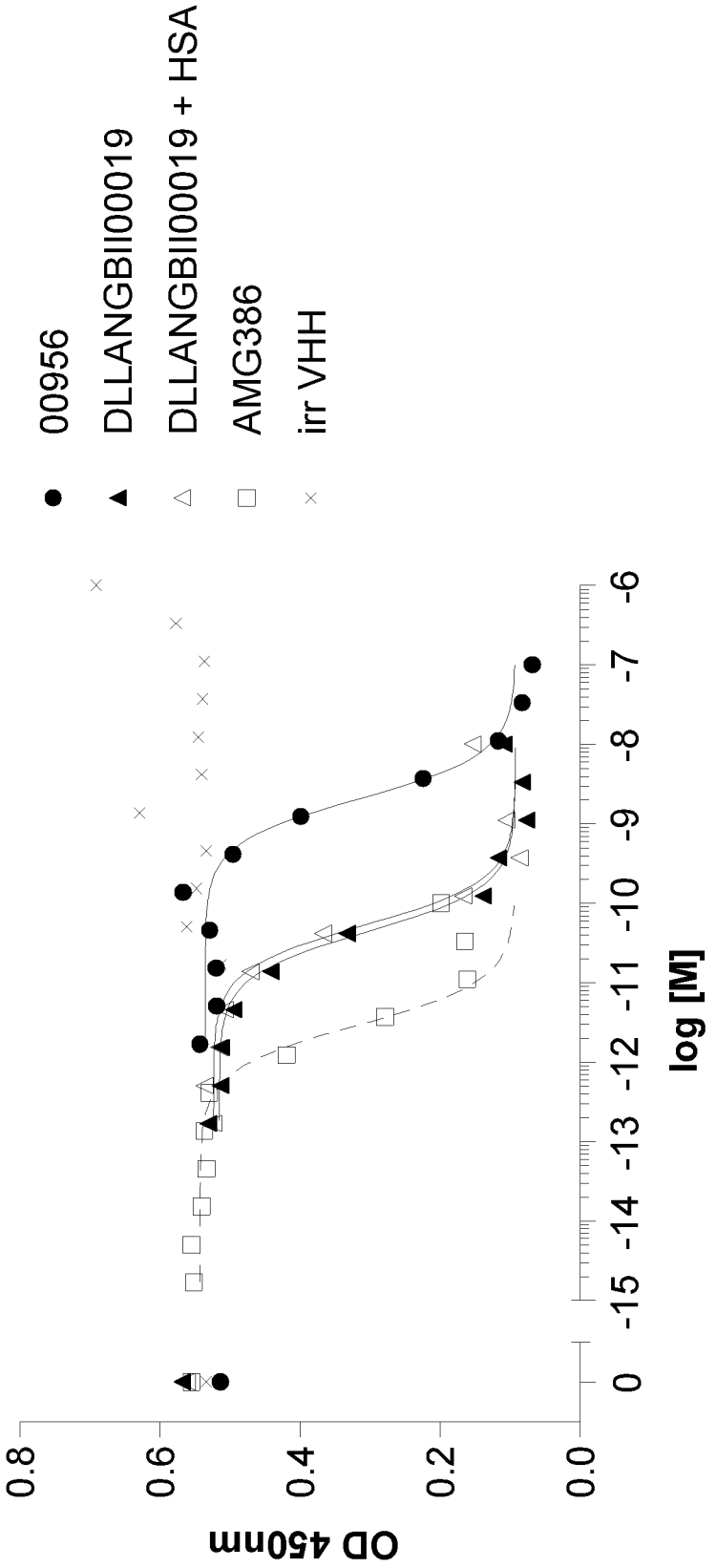

00956
DLLANGBII00019
DLLANGBII00019 + HSA
AMG386
irr VHH
OD 450nm
0.0
0.2
0.4
0.6
0.8
log [M]
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6

Figure 30-3A

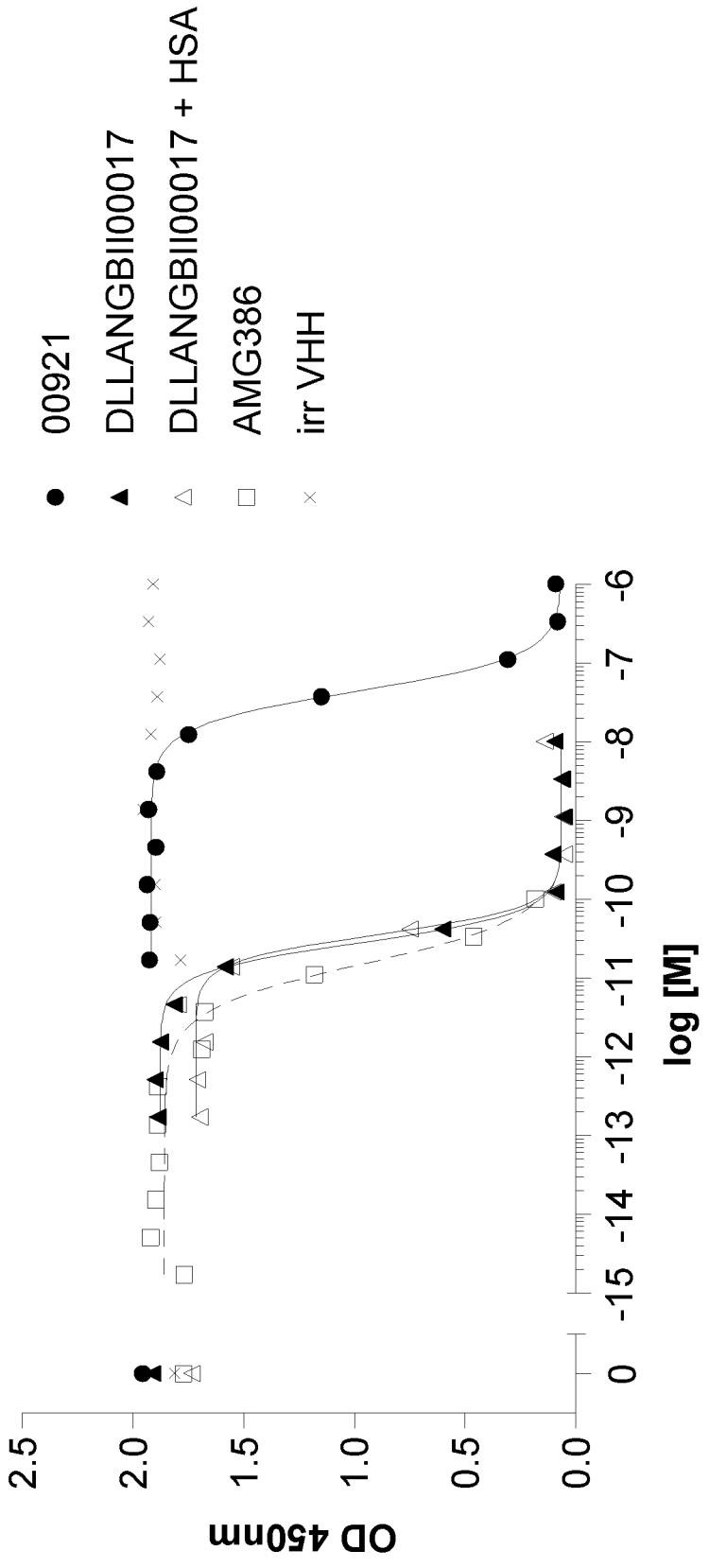

00921
DLLANGBII00017
DLLANGBII00017 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-3B

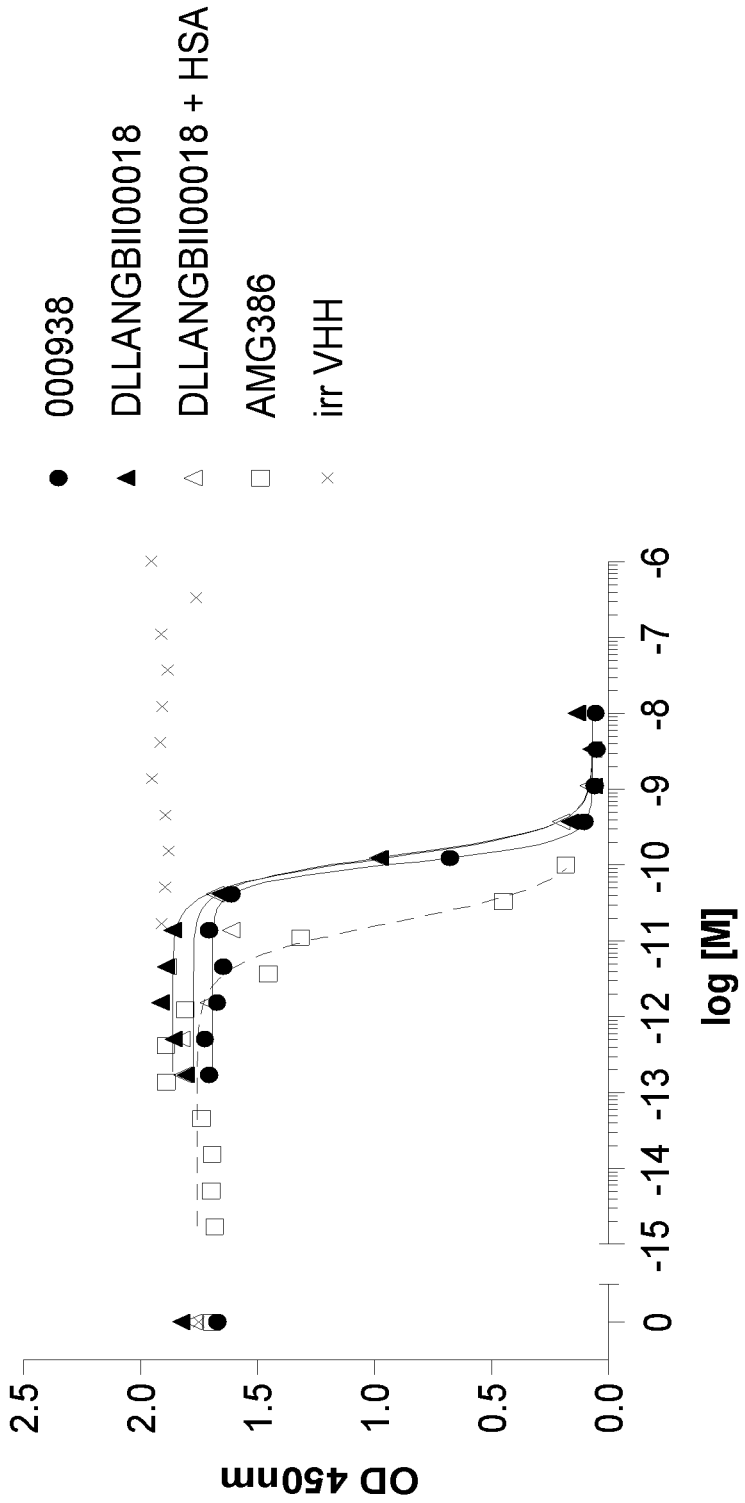
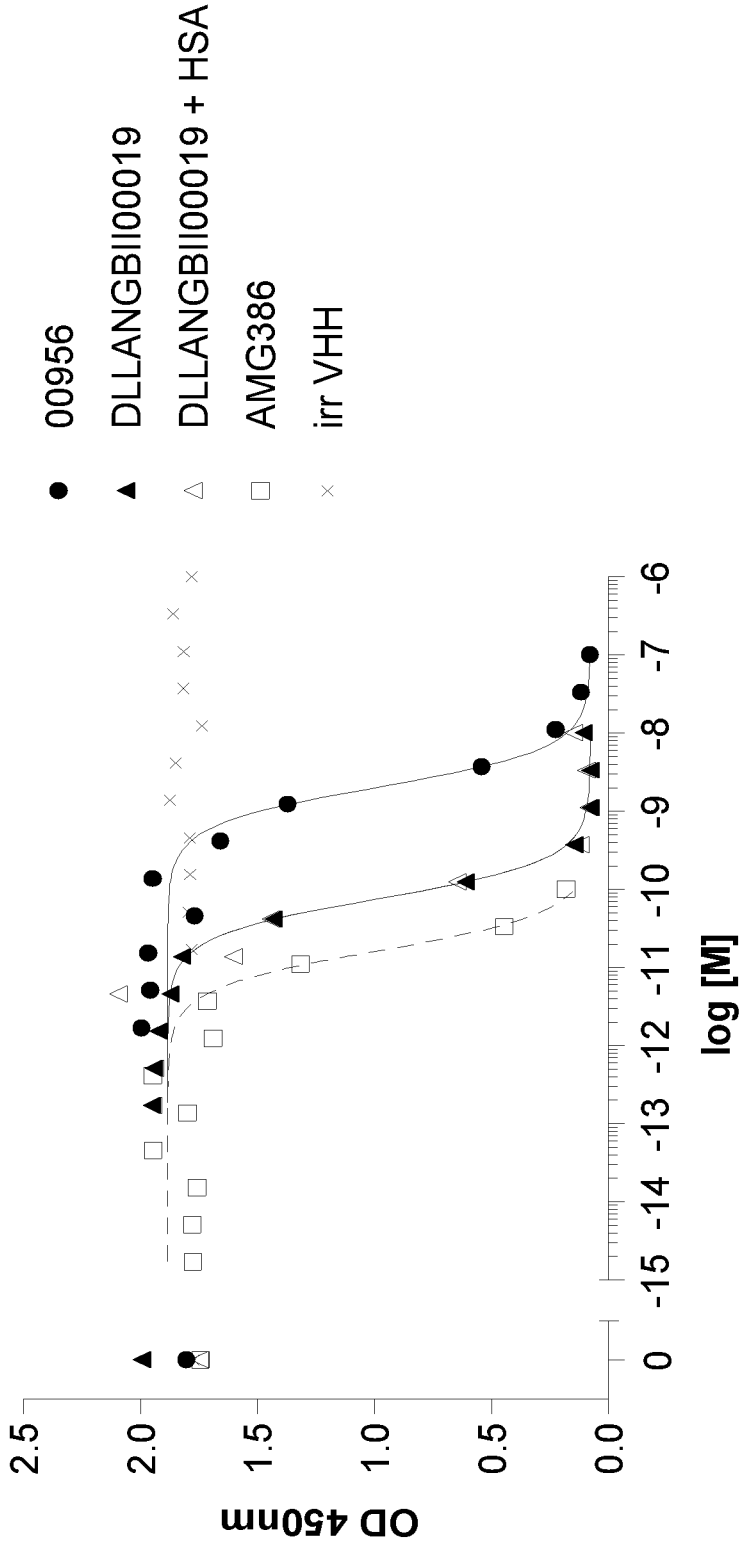

000938
DLLANGBII00018
DLLANGBII00018 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-15
-14
-13
-12
-11
-10
-9
-8
-7
-6
log [M]

Figure 30-3C


00956
DLLANGBII00019
DLLANGBII00019 + 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]

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Figure 31A

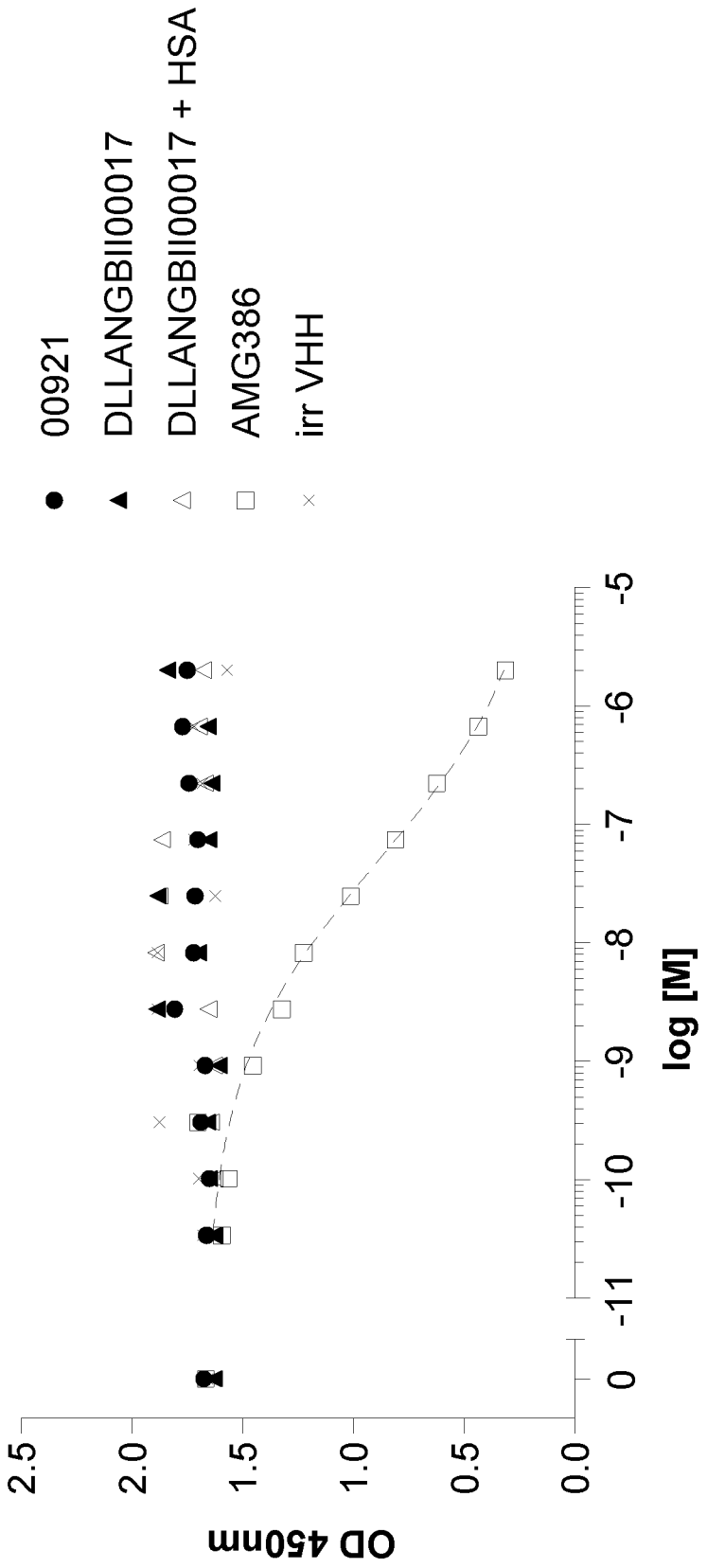


Figure 31B

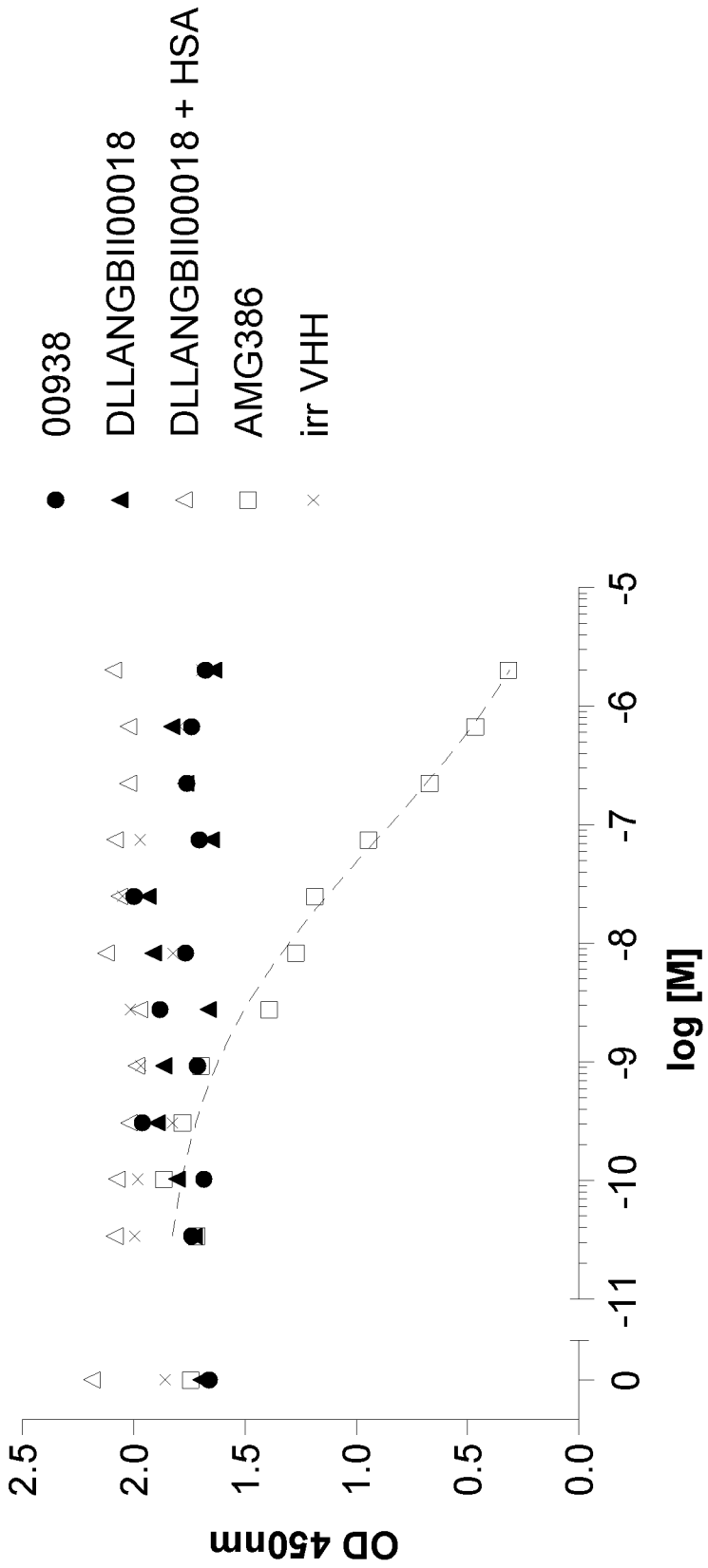

00938
DLLANGBII00018
DLLANGBII00018 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
-5
log [M]

Figure 31C

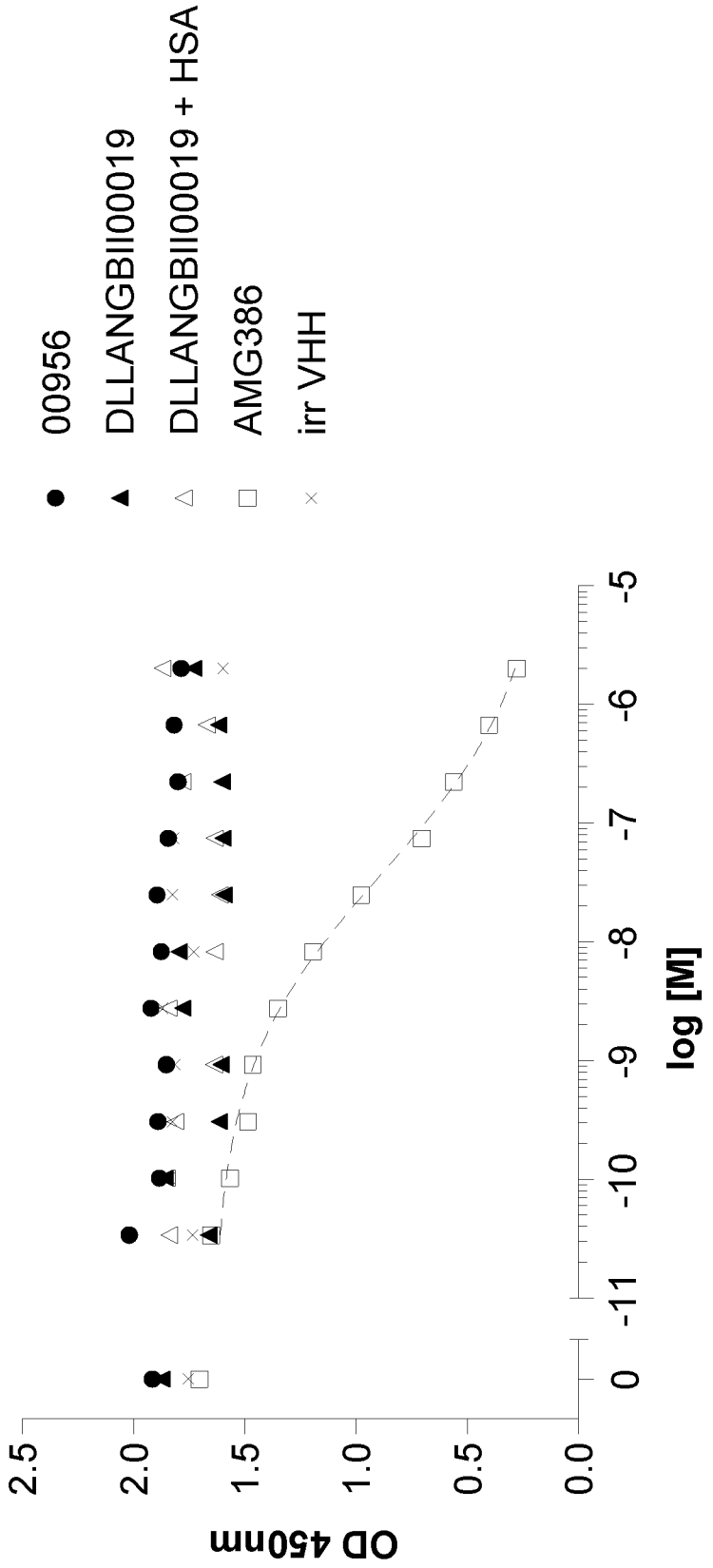

00956
DLLANGBII00019
DLLANGBII00019 + HSA
AMG386
irr VHH
OD 450nm
2.5
2.0
1.5
1.0
0.5
0.0
0
-11
-10
-9
-8
-7
-6
-5
log [M]

Figure 32A

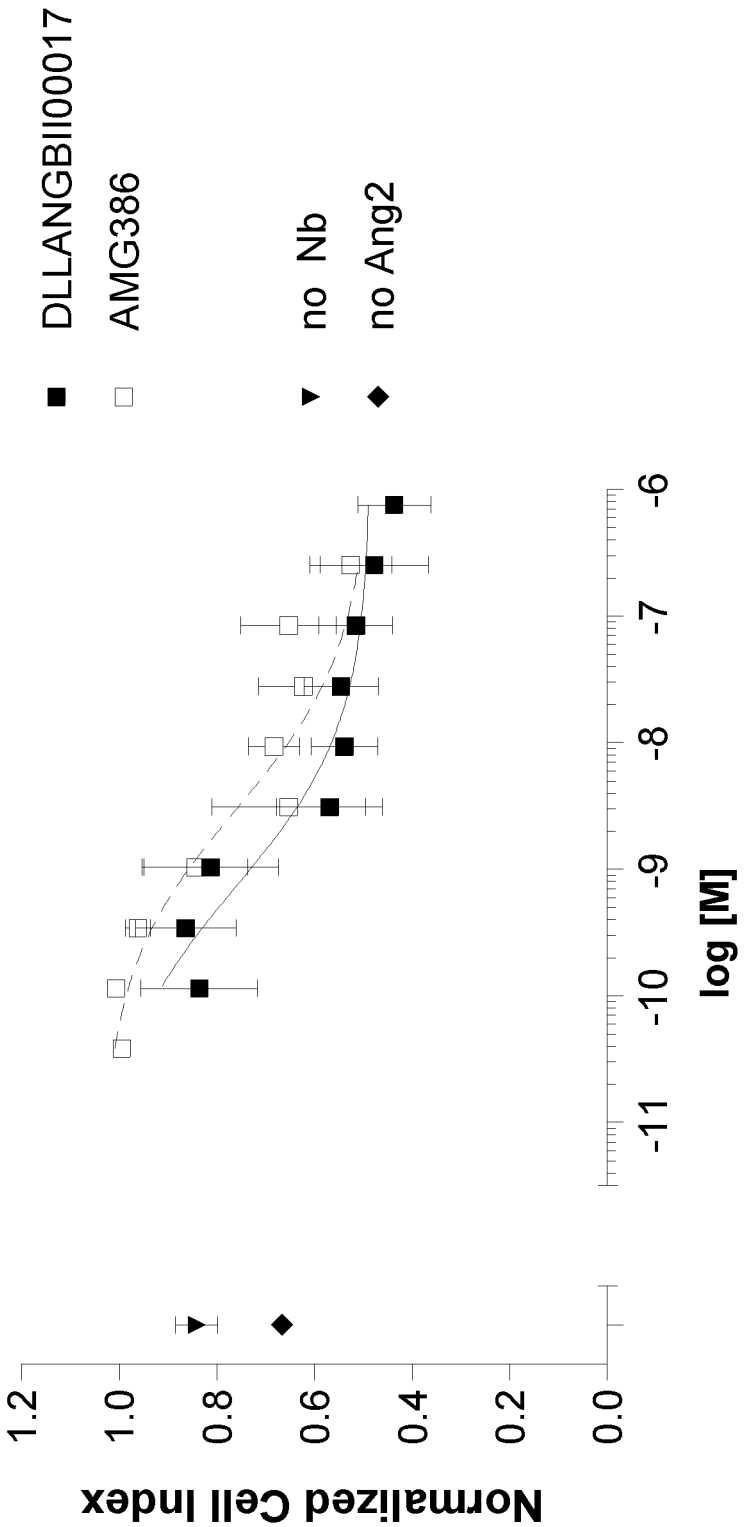

DLLANGBII00017
AMG386
no Nb
no Ang2
Normalized Cell Index
1.2
1.0
0.8
0.6
0.4
0.2
0.0
log [M]
-6
-7
-8
-9
-10
-11

Figure 32B

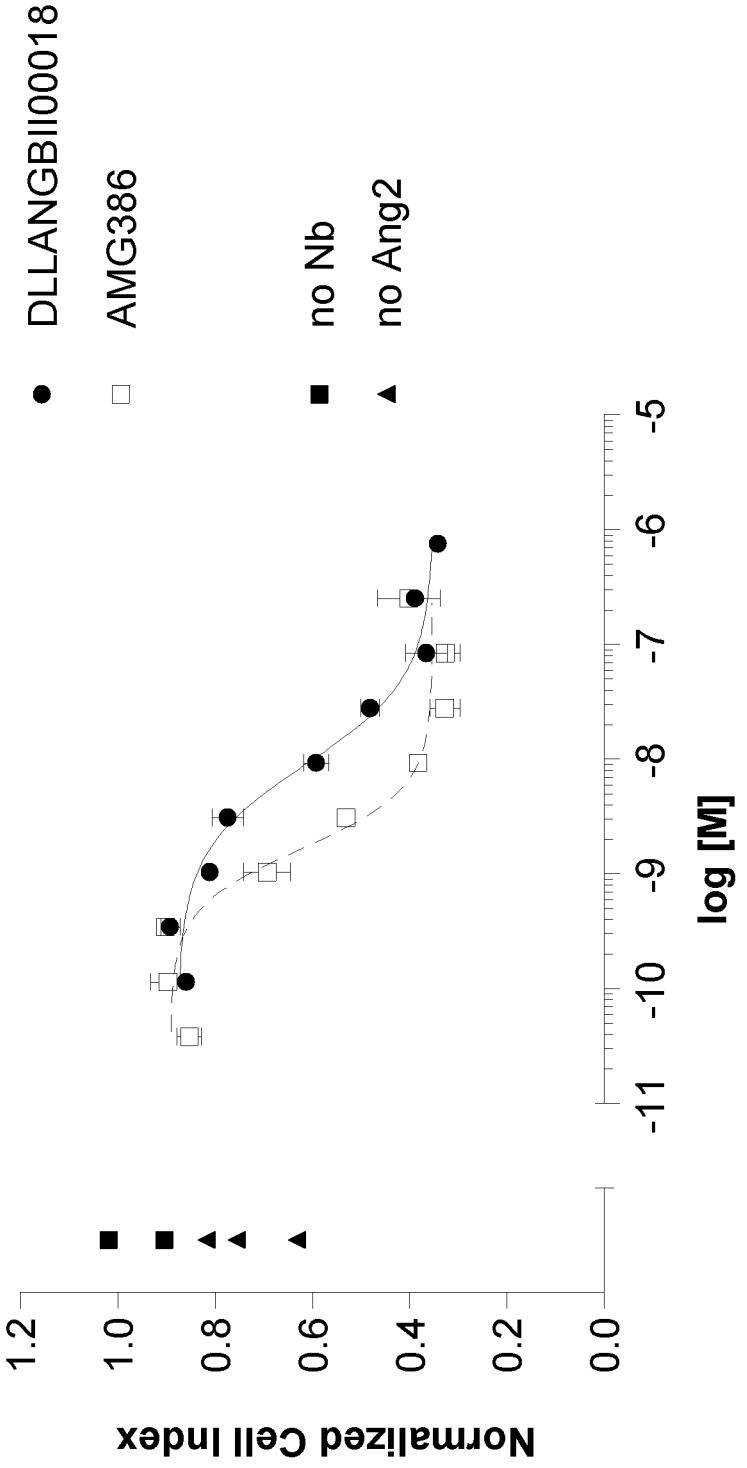
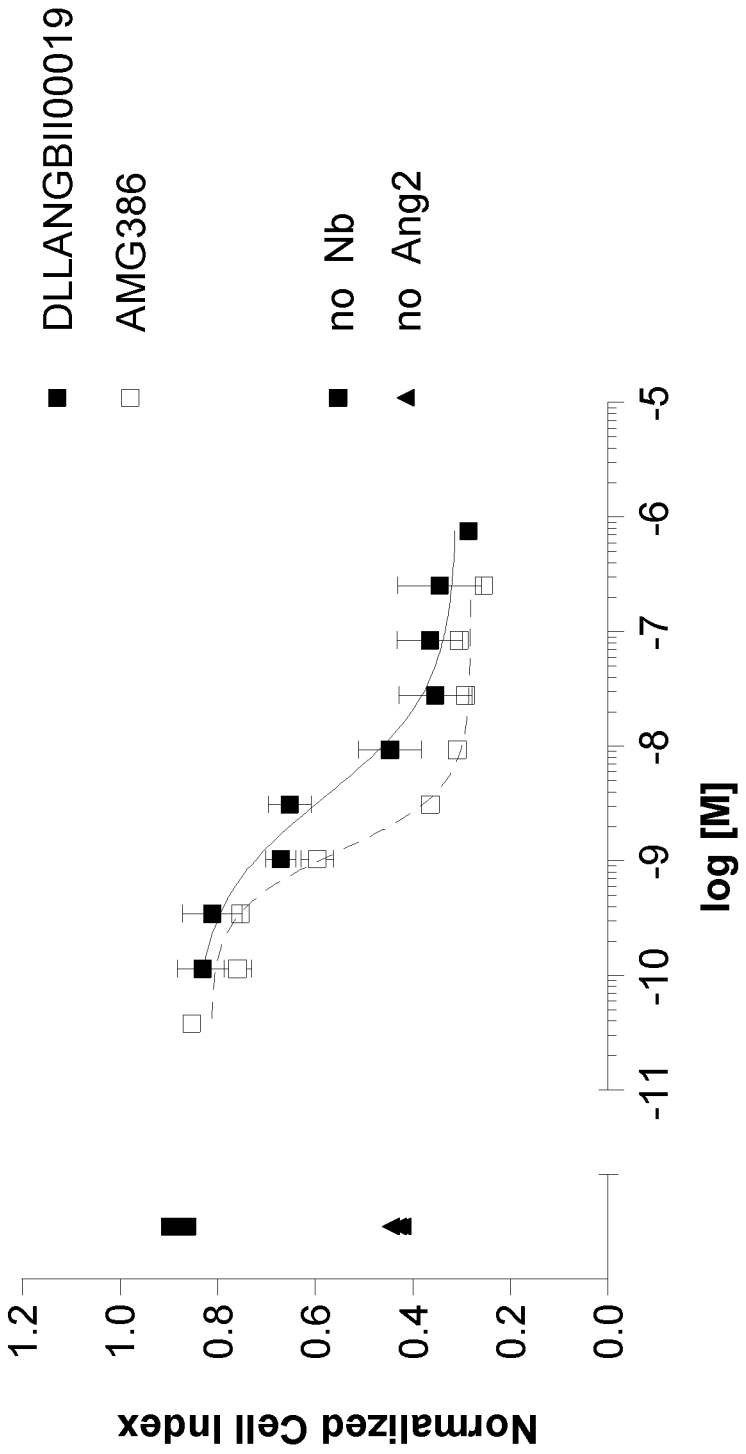

DLLANGBII00018
AMG386
no Nb
no Ang2
Normalized Cell Index
1.2
1.0
0.8
0.6
0.4
0.2
0.0
log [M]
-5
-6
-7
-8
-9
-10
-11

Figure 32C


DLLANGBII00019
AMG386
no Nb
no Ang2
Normalized Cell Index
1.2
1.0
0.8
0.6
0.4
0.2
0.0
log [M]
-5
-6
-7
-8
-9
-10
-11