Figure 1a

Sequence Alignment

Underlined, CDRs, as of EP1181318

HEAVY CHAIN:

mVHEP
EVKLMESGGGLVQPGGSLKLSCAASGFTFSTYTMSWARQTPEKRLEWVAYISKGGGSTYYPDTVKGRFTISRDNAKNTLYLQMSSLKSEDTALYYCARGAMYGNDFFYPMDYWGQQTSVTVSS
(SEQ IN No. 15)
3-23*01
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK.....
(SEQ IN No. 19)
JH4
.....YFDYWGQGTLVTVSS
(SEQ IN No. 20)
BXhVH1
EVQLLESGGGLVQPGGSLRLSCAASGFTFSTYTMSWVRQAPGKGLEWVSYISKGGGSTYYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGAMYGNDFFYPMDYWGQGTTVTVSS
(SEQ IN No. 1)
BXhVH2
EVKLLESGGGLVQPGGSLRLSCAASGFTFSTYTMSWVRQTPGKGLEWVAYISKGGGSTYYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGAMYGNDFFYPMDYWGQGTTVTVSS
(SEQ IN No. 2)
BXhVH3
EVQLLESGGGLVQPGGSLRLSCAASGFTFSTYTMSWVRQTPGKRLEWVAYISKGGGSTYYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGAMYGNDFFYPMDYWGQGTTVTVSS
(SEQ IN No. 3)
BXhVH4
EVQLLESGGGLVQPGGSLRLSCAASGFTFSTYTMSWVRQAPGKRLEWVAYISKGGGSTYYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGAMYGNDFFYPMDYWGQGTTVTVSS
(SEQ IN No. 4)
BXhVH5
EVKLLESGGGLVQPGGSLRLSCAASGFTFSTYTMSWVRQTPGKRLEWVAYISKGGGSTYYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGAMYGNDFFYPMDYWGQGTTVTVSS
(SEQ IN No. 5)
HuVHWO
EVQLLESGGGLVQPGGSLRLSCAASGFTFSTYTMSWARQAPGKGLEWVAYISKGGGSTYYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDSAVYYCARGAMFGNDFFFPMDRWGQGTLVTVSS
(SEQ IN No. 17)
HuVHWOv
EVQLLESGGGLVQPGGSLRLSCAASGFTFSTYTMSWARQAPGKGLEWVAYISKGGGSTYYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDSAVYYCARGAMYGNDFFYPMDYWGQGTLVTVSS
(SEQ IN No. 6)

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Figure 1b

LIGHT CHAIN:

mVLEP
DIVLSQSPAIMSASLGEEITLTCSASSSVSYMH-WYQQKSGTSPKLLITTTSNLASGVPSRFSGSGSGTFYSLTISSVEAEDAADYYCHQWSSYPWTFGGGTKLEIK
(SEQ IN No. 16)
L6*01
EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWP.....
(SEQ IN No. 21)
JK1
.....WTFGQGTKVEIK
(SEQ IN No. 22)
BXhVL1
EIVLTQSPATLSLSPGERATLSCSASSSVSYMH-WYQQKPGQAPRLLIYTTSNLASGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCHQWSSYPWTFGQGTKLEIK
(SEQ IN No. 7)
BXhVL2
EIVLTQSPATLSLSPGERATLSCSASSSVSYMH-WYQQKPGQSPRLLIYTTSNLASGIPSRFSGSGSGTDFTLTISSLEPEDAADYYCHQWSSYPWTFGQGTKLEIK
(SEQ IN No. 8)
BXhVL3
QIVLTQSPATLSLSPGERATLSCSASSSVSYMH-WYQQKPGQSPRLLIYTTSNLASGIPSRFSGSGSGTFYTLTISSLEPEDFAVYYCHQWSSYPWTFGGGTKLEIK
(SEQ IN No. 9)
BXhVL4
QIVLTQSPATLSLSPGERATLSCSASSSVSYMH-WYQQKPGQSPRLLIYTTSNLASGIPSRFSGSGSGTDFTLTISSLEPEDAADYYCHQWSSYPWTFGGGTKLEIK
(SEQ IN No. 10)
BXhVL5
QIVLTQSPATLSLSPGERATLSCSASSSVSYMH-WYQQKPGQSPRLLIYTTSNLASGIPSRFSGSGSGTDYTLTISSLEPEDAADYYCHQWSSYPWTFGQGTKLEIK
(SEQ IN No. 11)
BXhVL6
EIVLTQSPATLSLSPGEEATLSCSASSSVSYMH-WYQQKPGQSPRLLIYTTSNLASGIPSRFSGSGSGTFYTLTISSLEPEDAADYYCHQWSSYPWTFGGGTKLEIK
(SEQ IN No. 12)
BXhVL7
QIVLTQSPATLSLSPGERATLSCSASSSVSYMH-WYQQKPGQSPRLLIYTTSNLASGIPSRFSGSGSGTFYTLTISSLEPEDAADYYCHQWSSYPWTFGGGTKLEIK
(SEQ IN No. 13)
BXhVL8
QIVLTQSPATLSLSPGEEATLSCSASSSVSYMH-WYQQKSGTSPRLLIYTTSNLASGIPSRFSGSGSGTFYTLTISSLEPEDAADYYCHQWSSYPWTFGGGTKLEIK
(SEQ IN No. 14)
HuVLWO
DIVLTQSPSSLSASVGDRVTITCSASSSVSYMH-WYQQKPGQAPKLLIYTTSNLASGVPSRFSGSGSGTDYTLTISSLQPEDVATYYCHQWSSYPWTFGGGTKVEIK
(SEQ IN No. 18)

SUBSTITUTE SHEET (RULE 26)

Figure 2

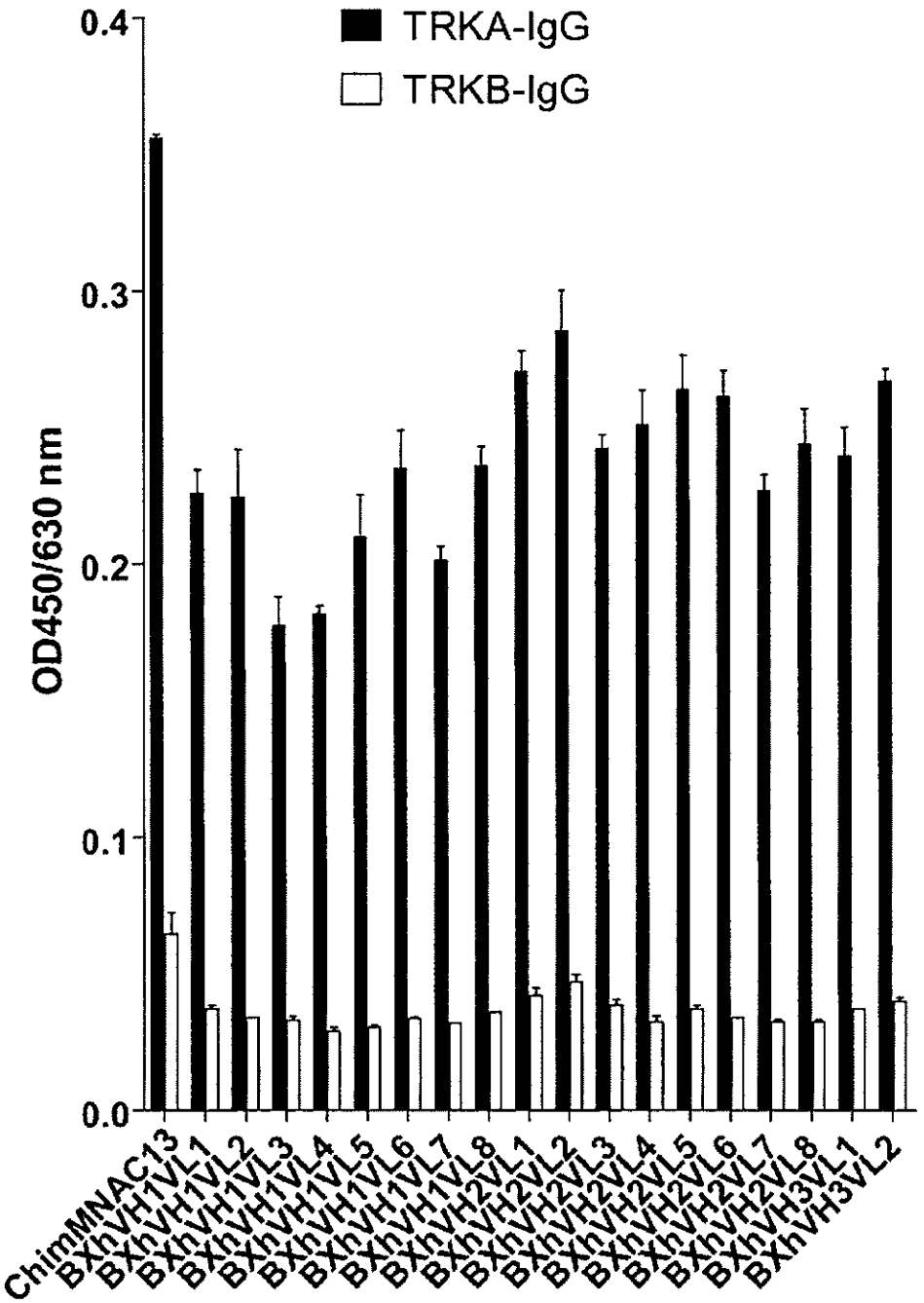

TRKA-IgG
TRKB-IgG
OD450/630 nm
0.4
0.3
0.2
0.1
0.0
ChimMNAC13
BXhVH1VL1
BXhVH1VL2
BXhVH1VL3
BXhVH1VL4
BXhVH1VL5
BXhVH1VL6
BXhVH1VL7
BXhVH1VL8
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BXhVH3VL1
BXhVH3VL2

Figure 2 (continued)

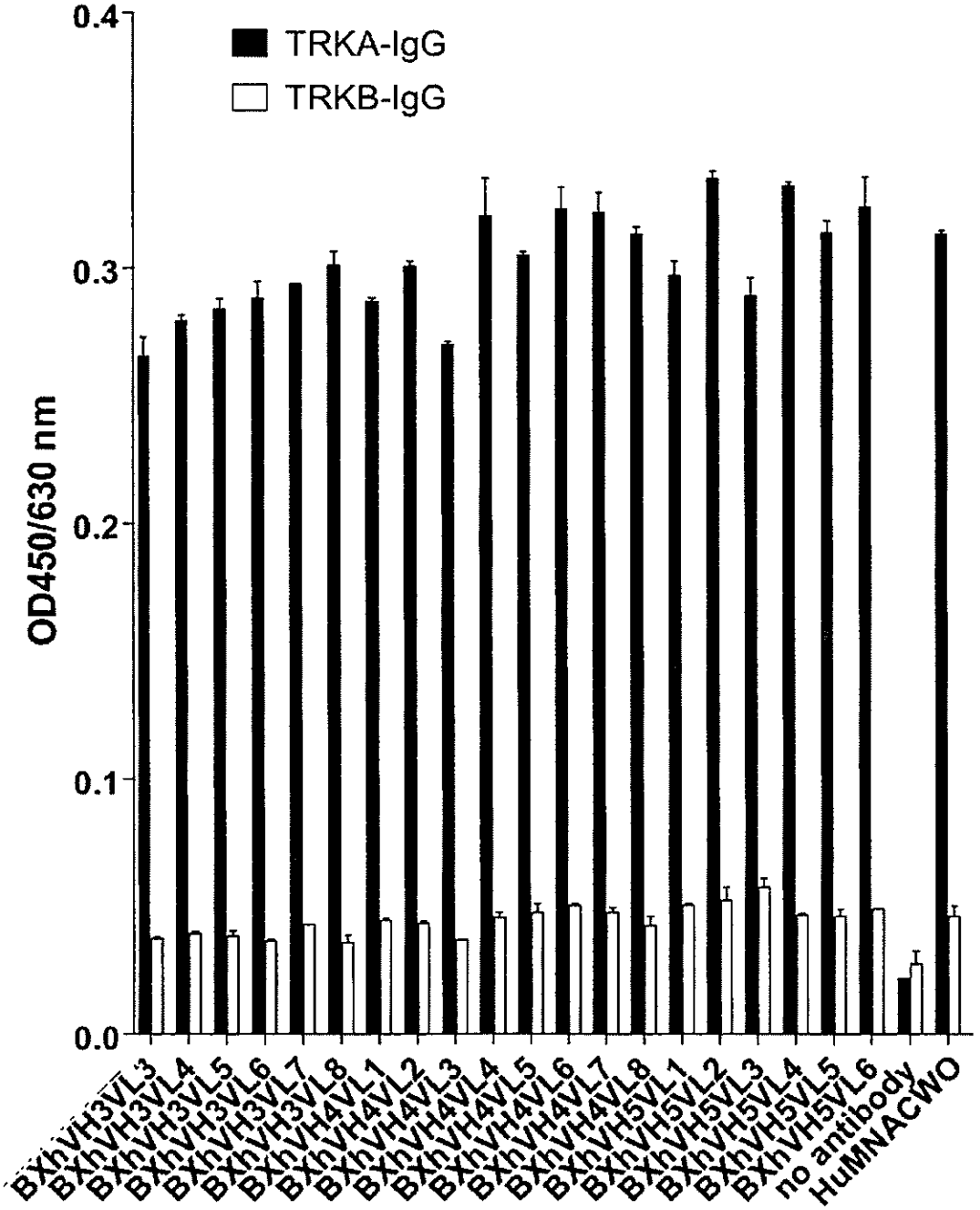


Figure 3

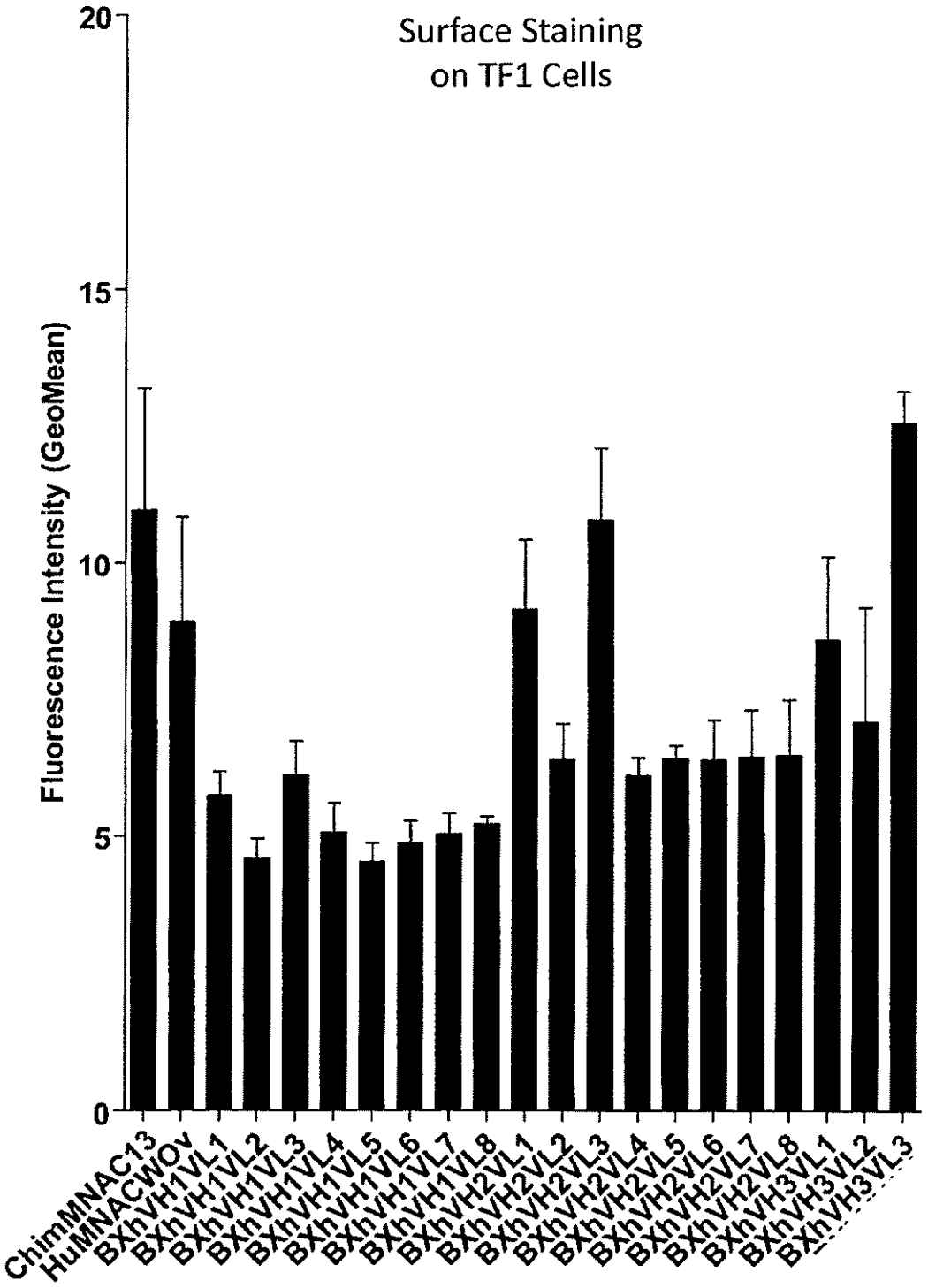
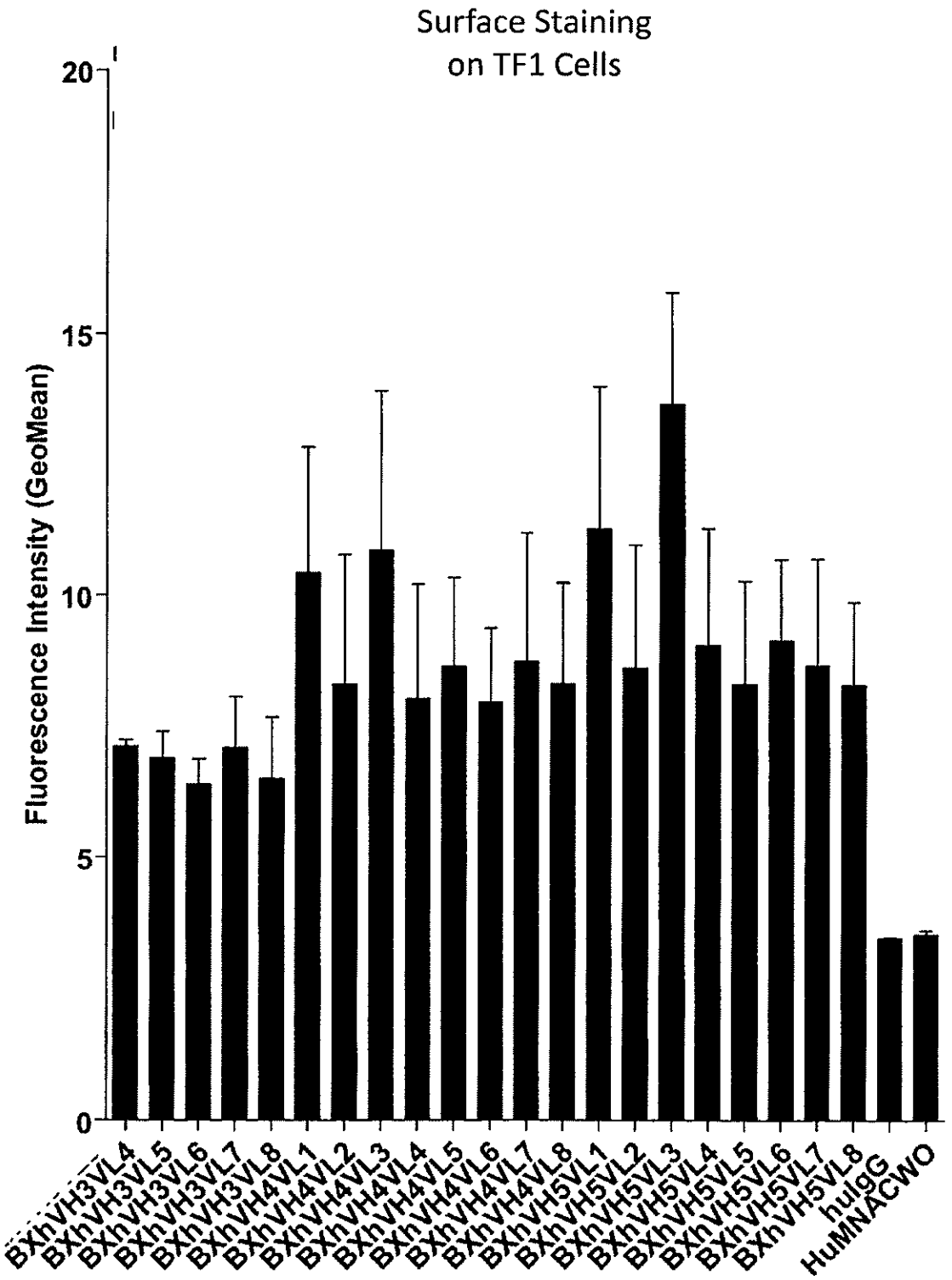

Surface Staining
on TF1 Cells
Fluorescence Intensity (GeoMean)
20
15
10
5
0
ChimMNAC13
HuMNACWOv
BXhVH1VL1
BXhVH1VL2
BXhVH1VL3
BXhVH1VL4
BXhVH1VL5
BXhVH1VL6
BXhVH1VL7
BXhVH1VL8
BXhVH2VL1
BXhVH2VL2
BXhVH2VL3
BXhVH2VL4
BXhVH2VL5
BXhVH2VL6
BXhVH2VL7
BXhVH2VL8
BXhVH3VL1
BXhVH3VL2
BXhVH3VL3

Figure 3 (continued)



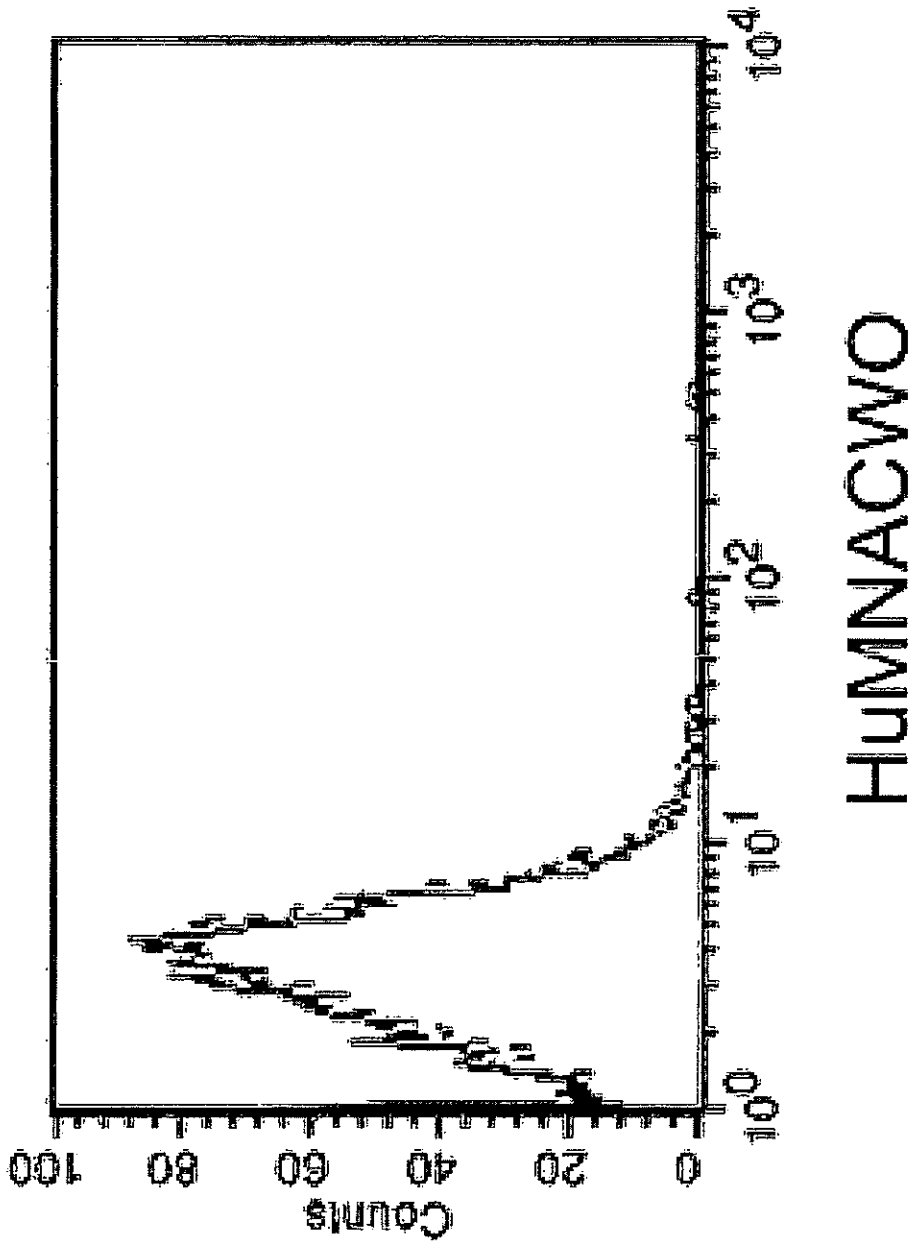
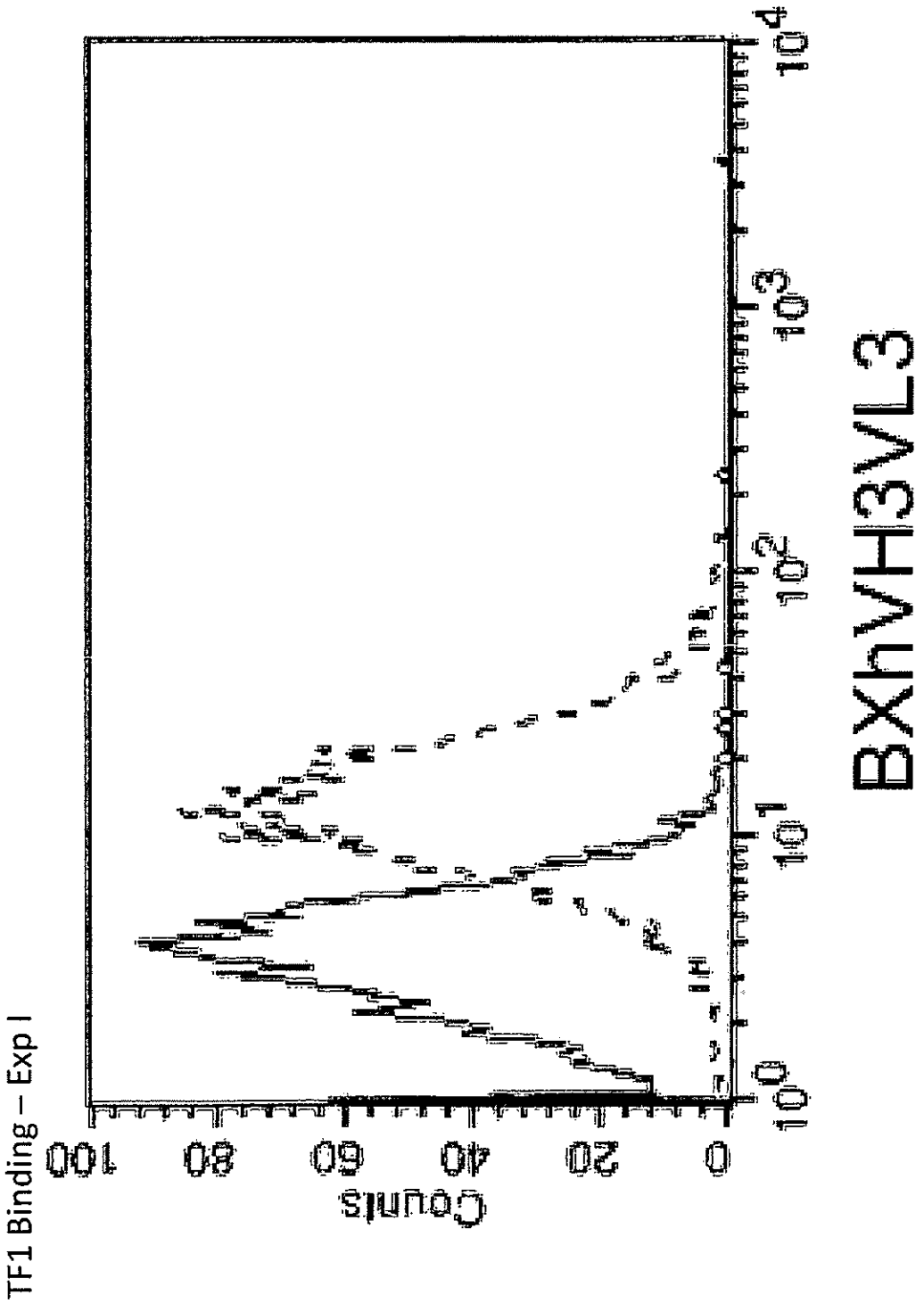
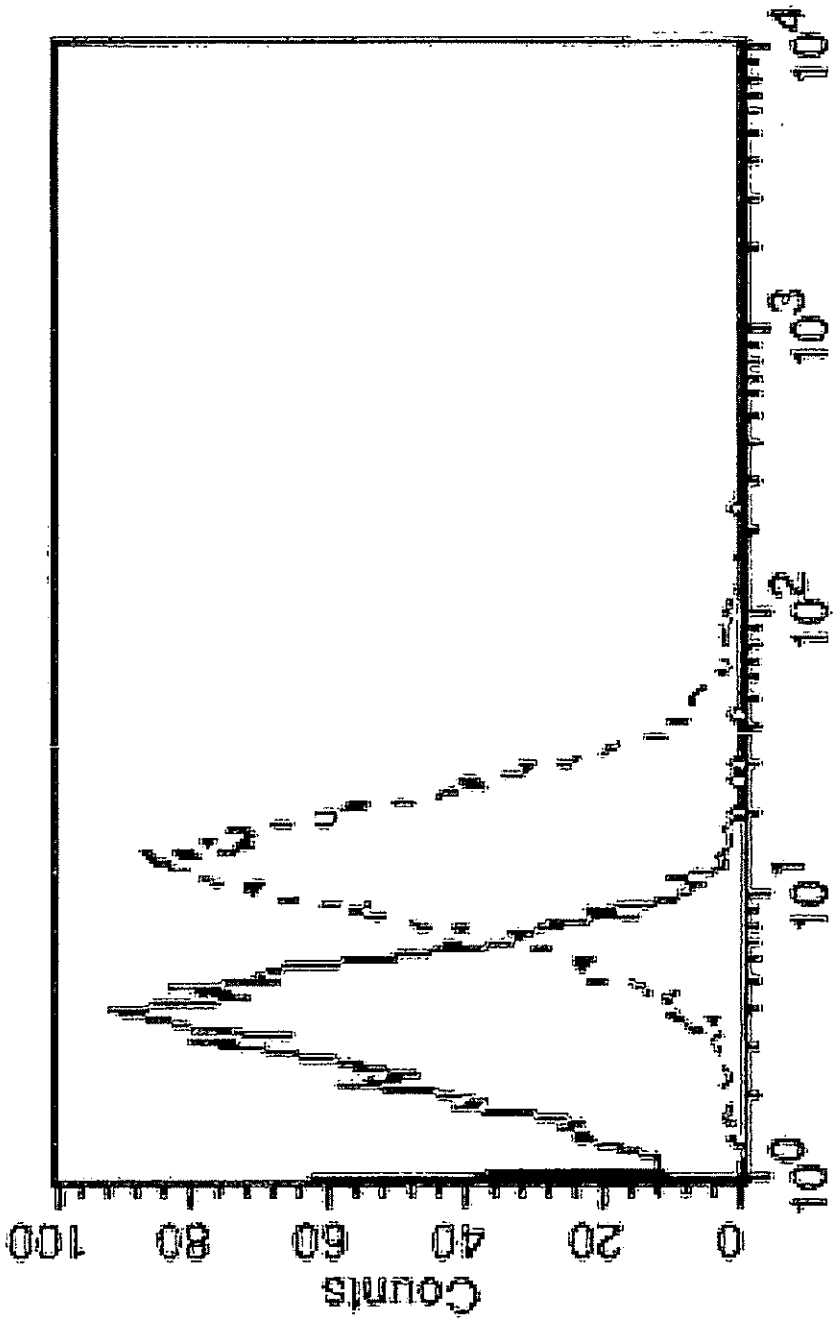


Figure 4

TF1 Binding

Figure 4 (continued)





TF1 Binding – Exp I

Figure 4 (continued)

Figure 4 (continued)

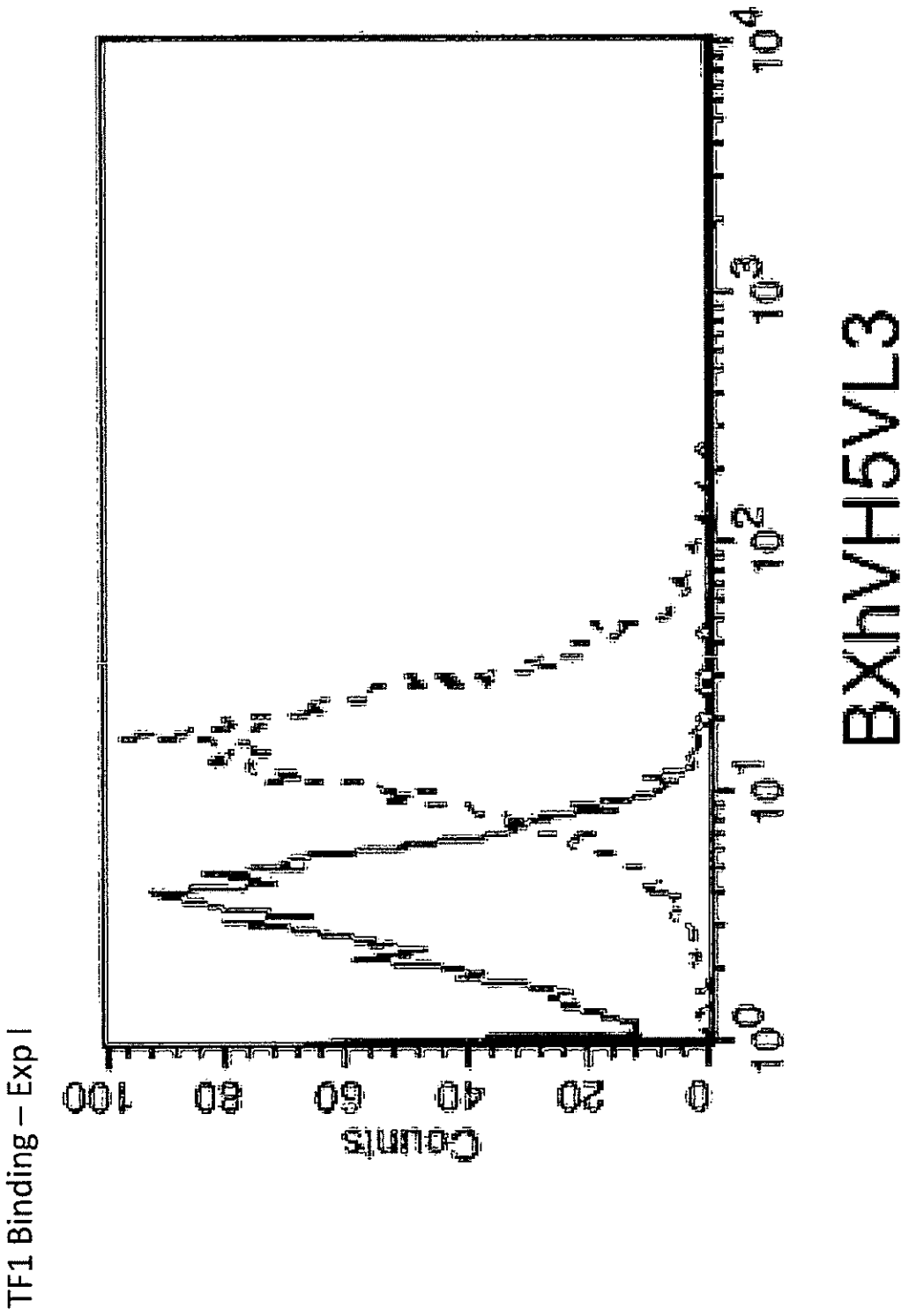
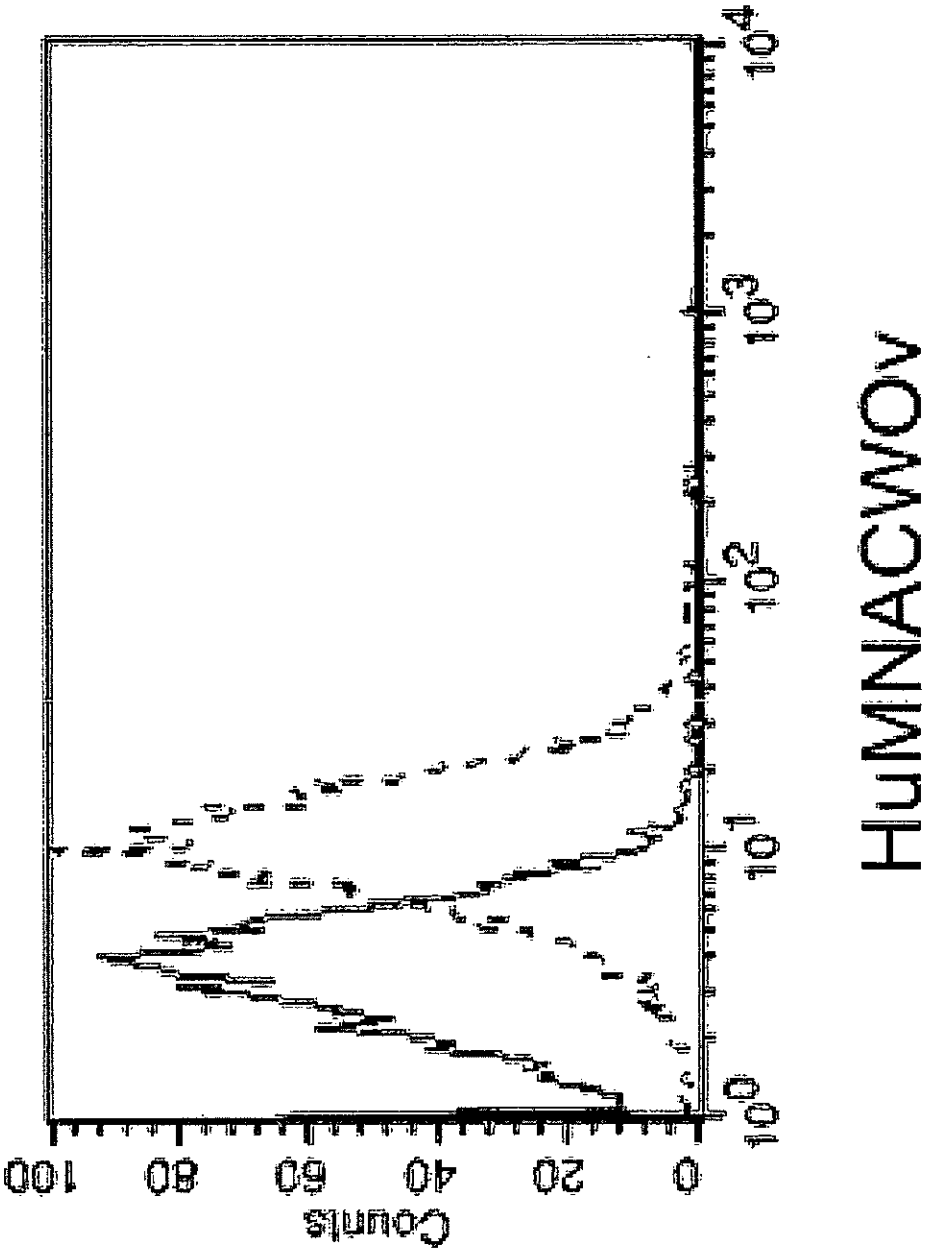


Figure 4 (continued)

TF1 Binding – Exp I



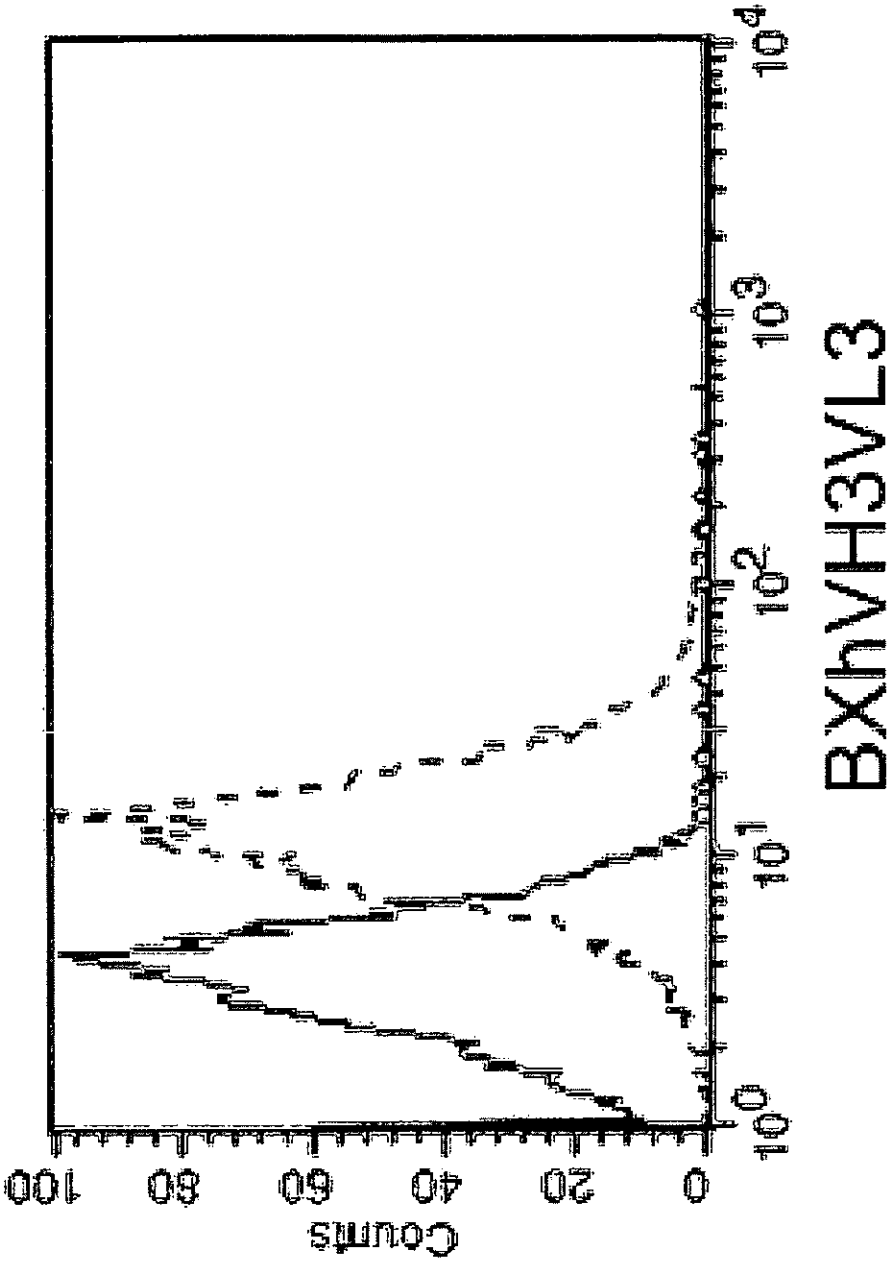


Figure 4 (continued)

TF1 Binding – Exp II

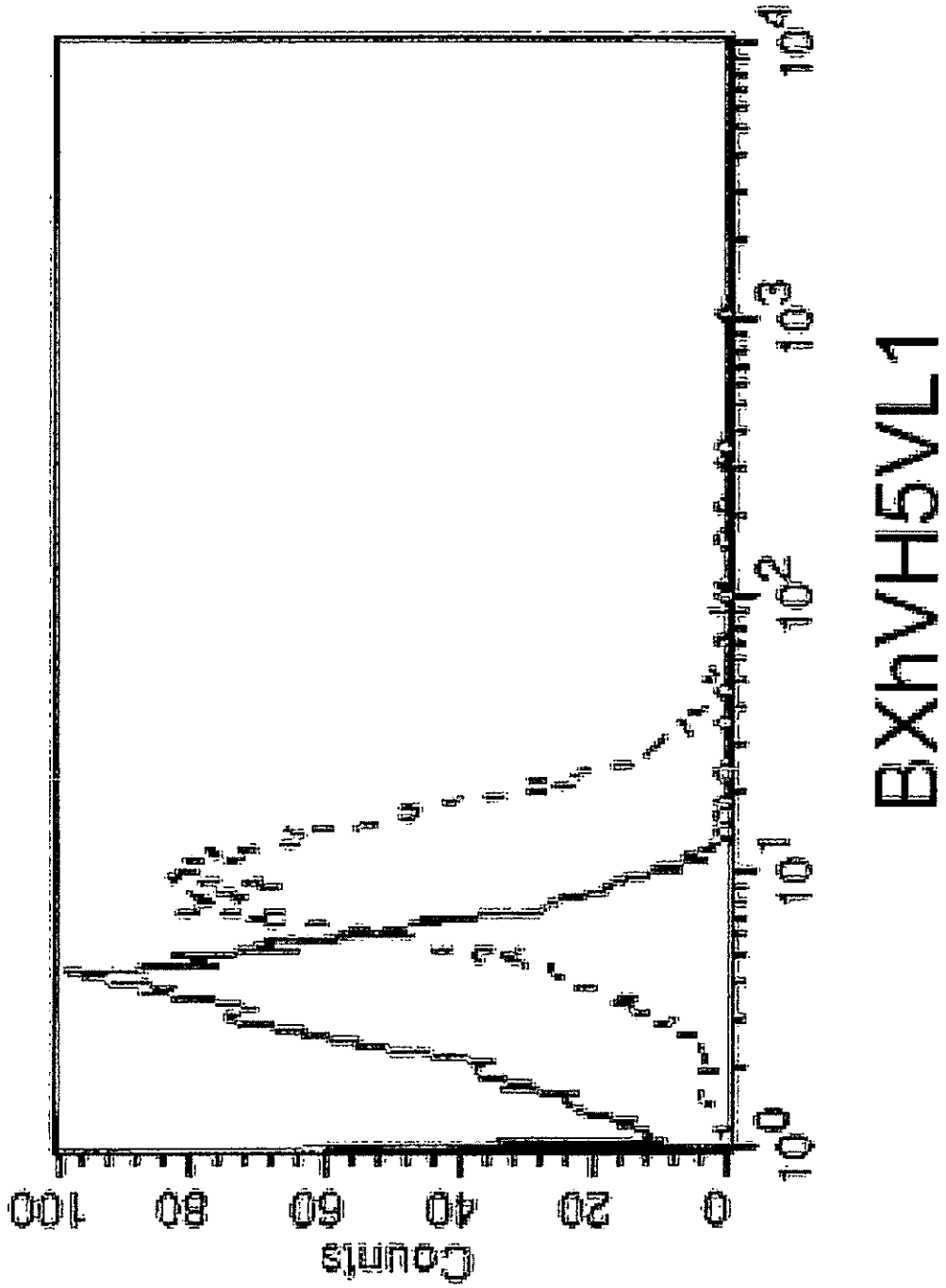


Figure 4 (continued)

TF1 Binding – Exp II

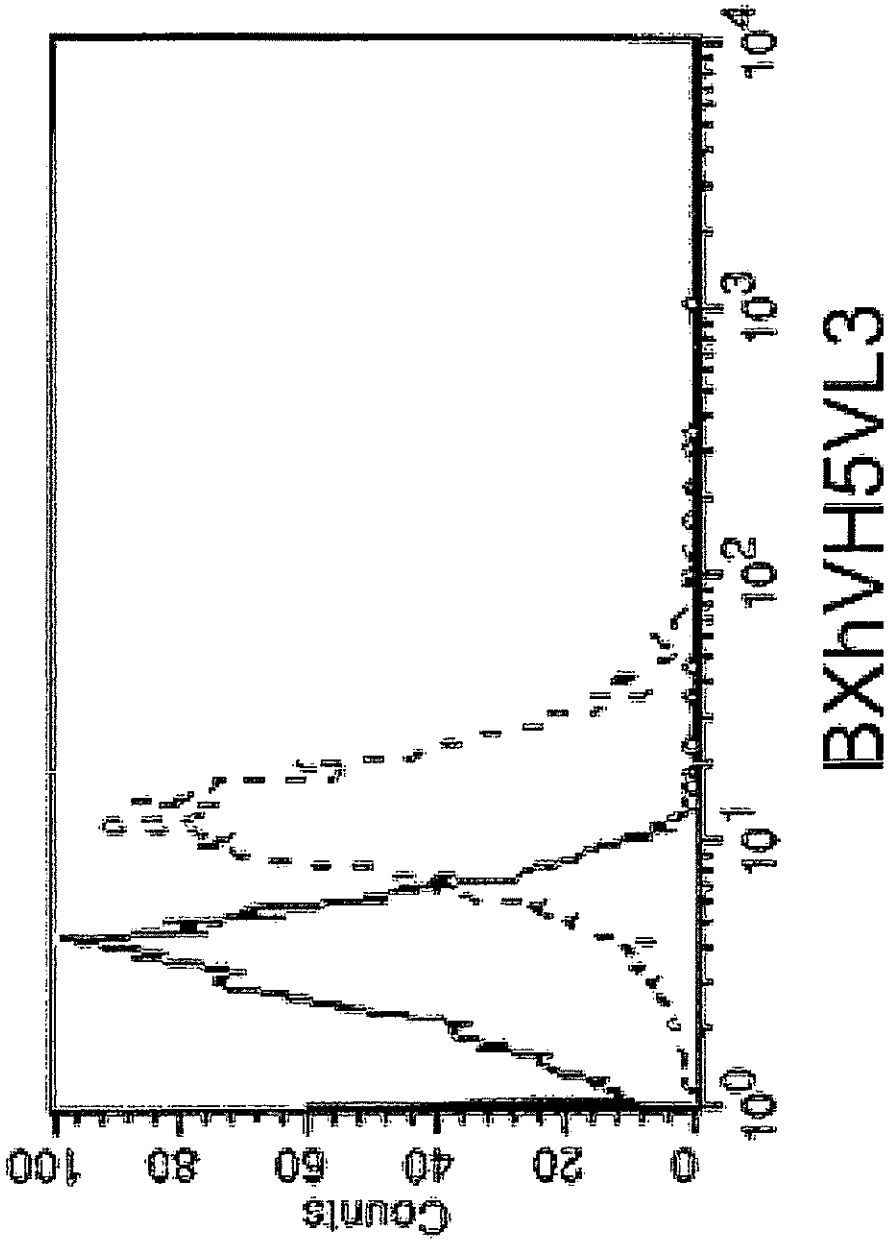
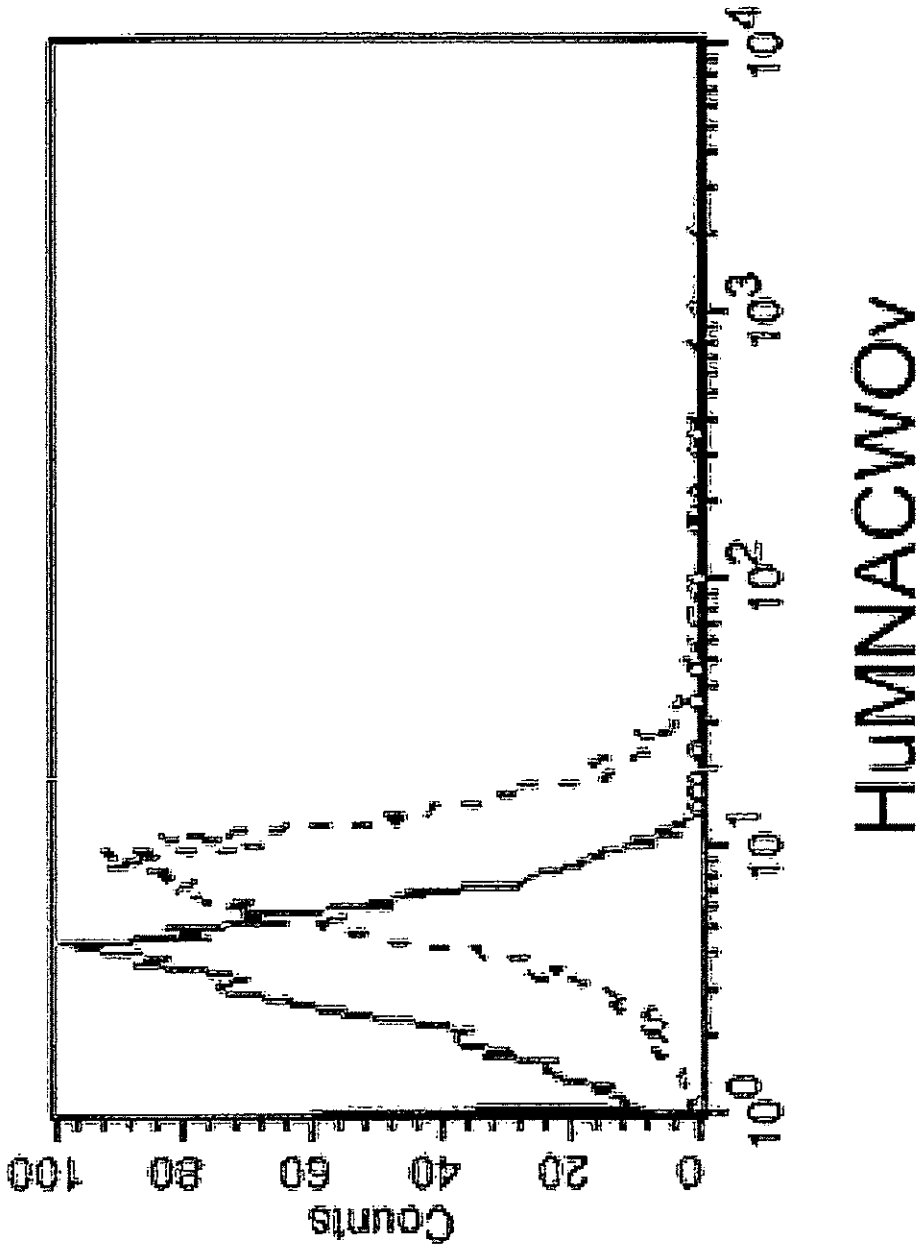


Figure 4 (continued)

TF1 Binding – Exp II



TF1 Binding – Exp II

Figure 4 (continued)

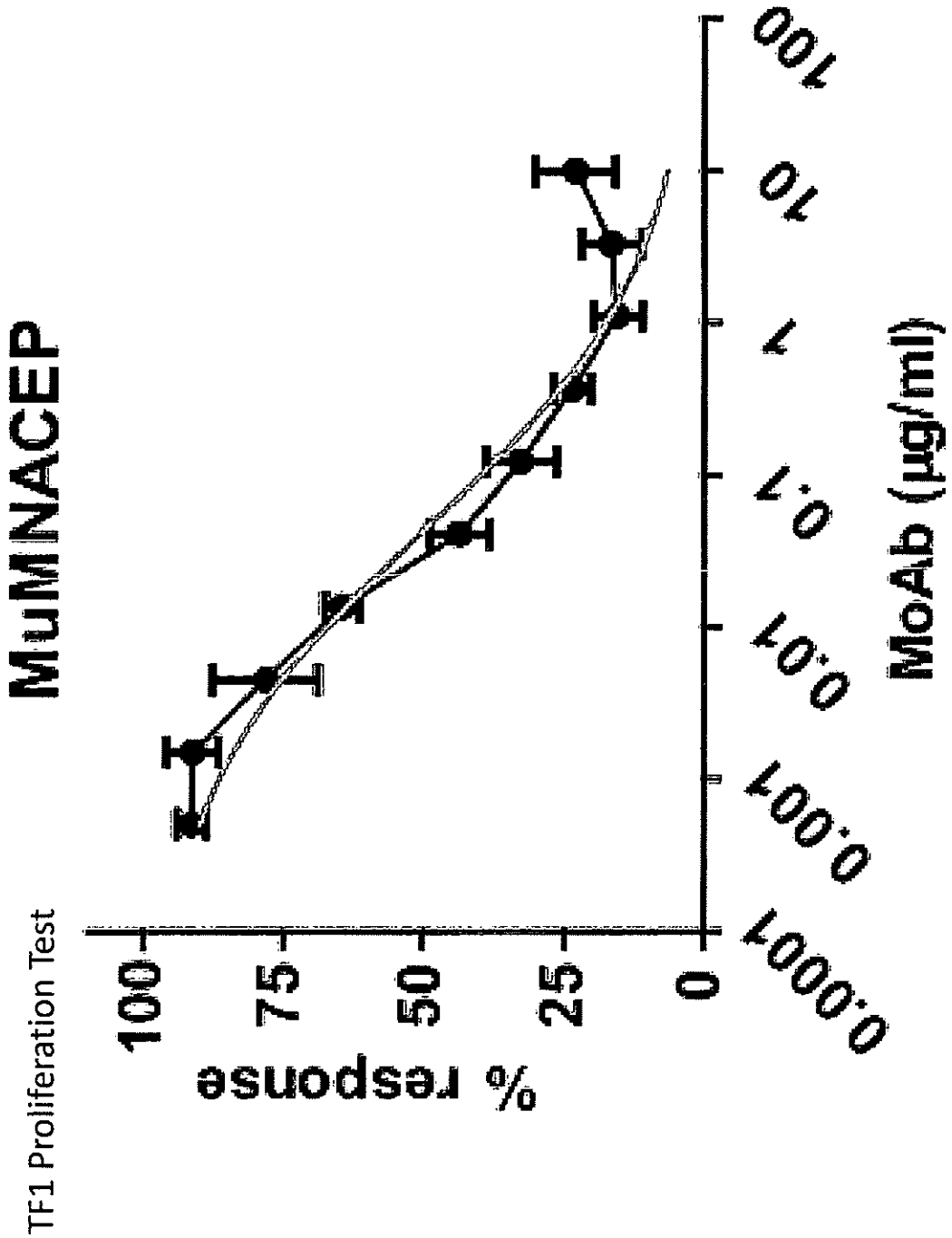

MuMNACEP
TF1 Proliferation Test
% response
100
75
50
25
0
MoAb (µg/ml)
100
10
1
0.1
0.01
0.001
0.0001

Figure 5

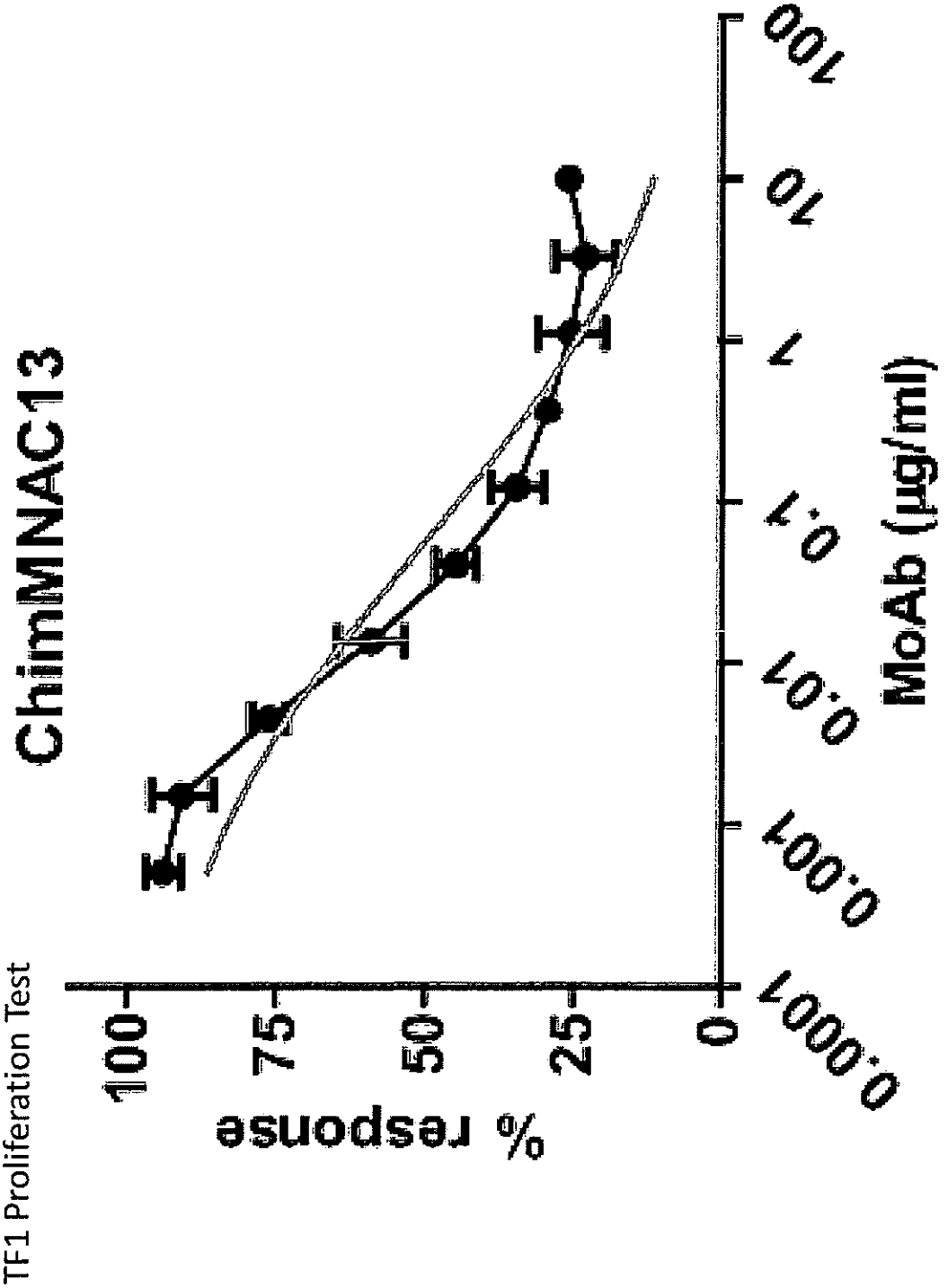


Figure 5 (continued)

TF1 Proliferation Test

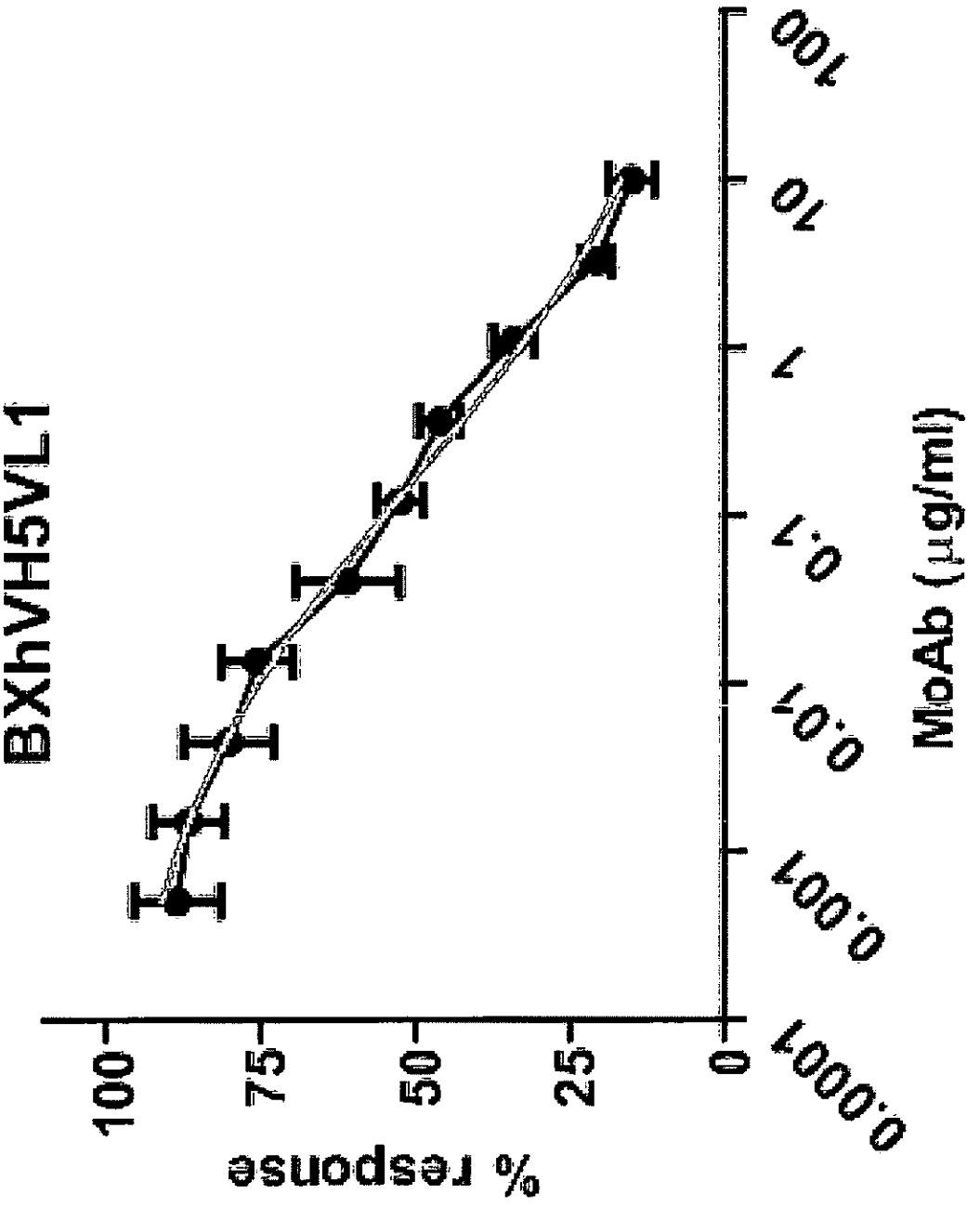


Figure 5 (continued)

TF1 Proliferation Test

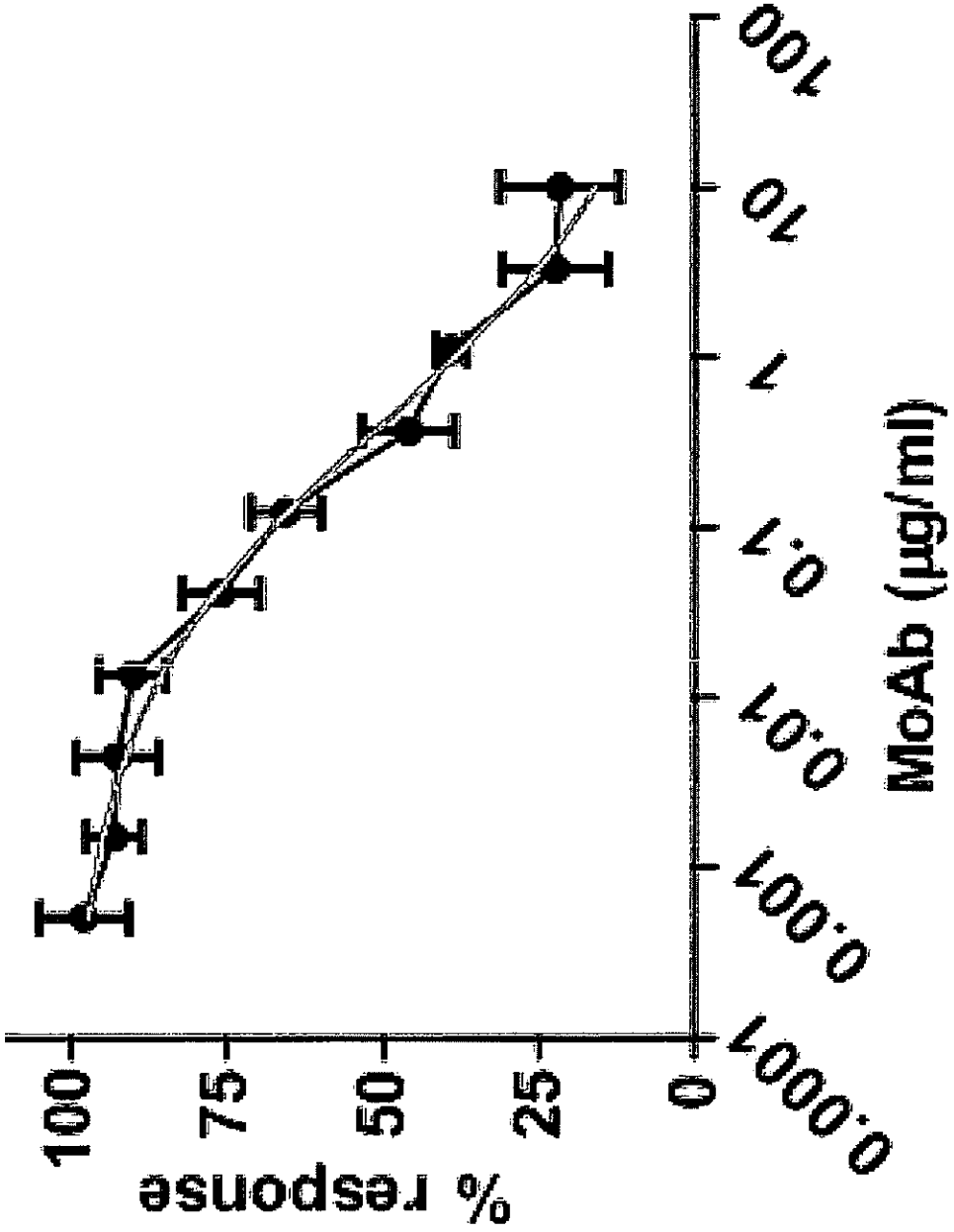


Figure 5 (continued)

TF1 Proliferation Test

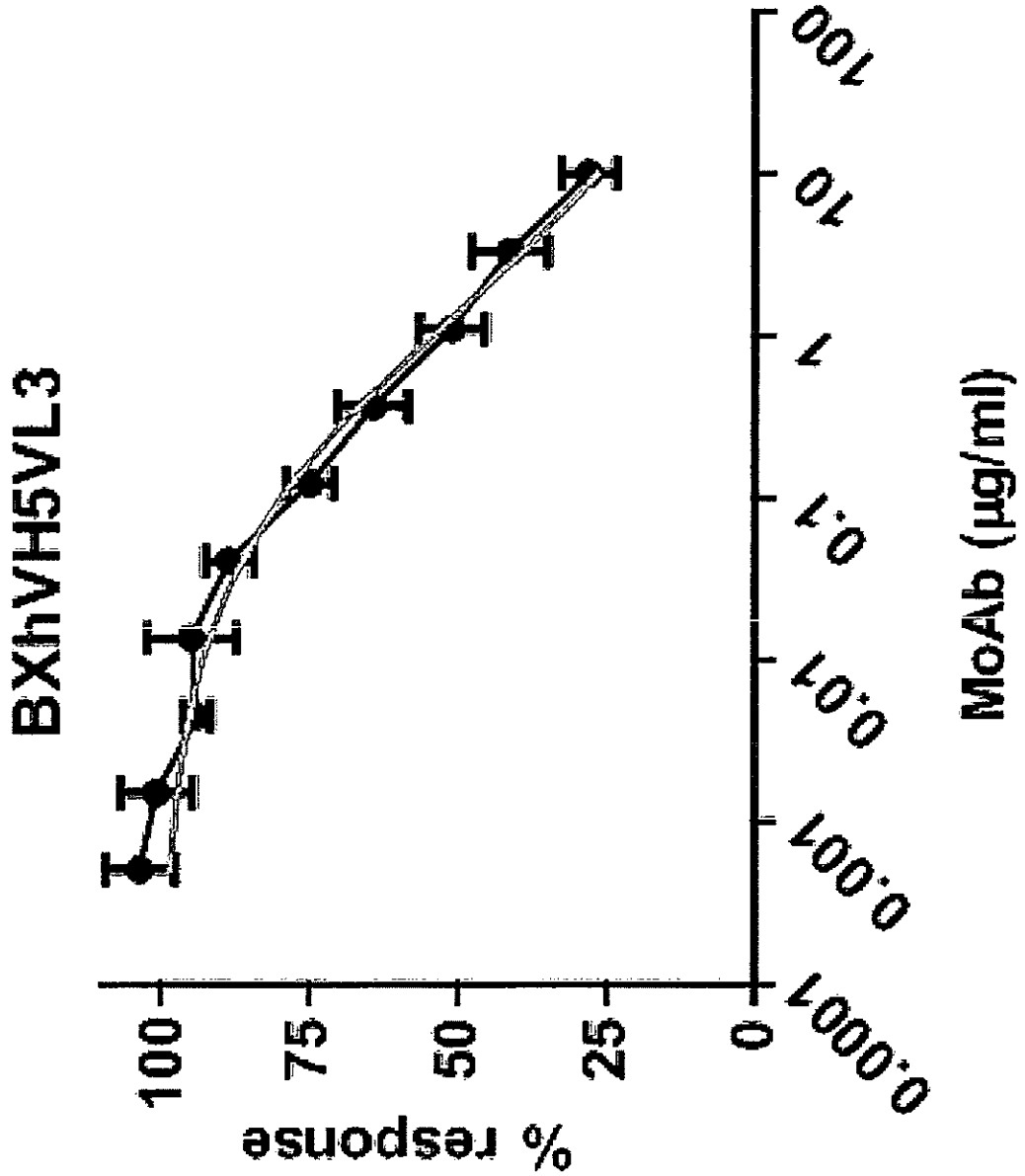


Figure 5 (continued)

TF1 Proliferation Test

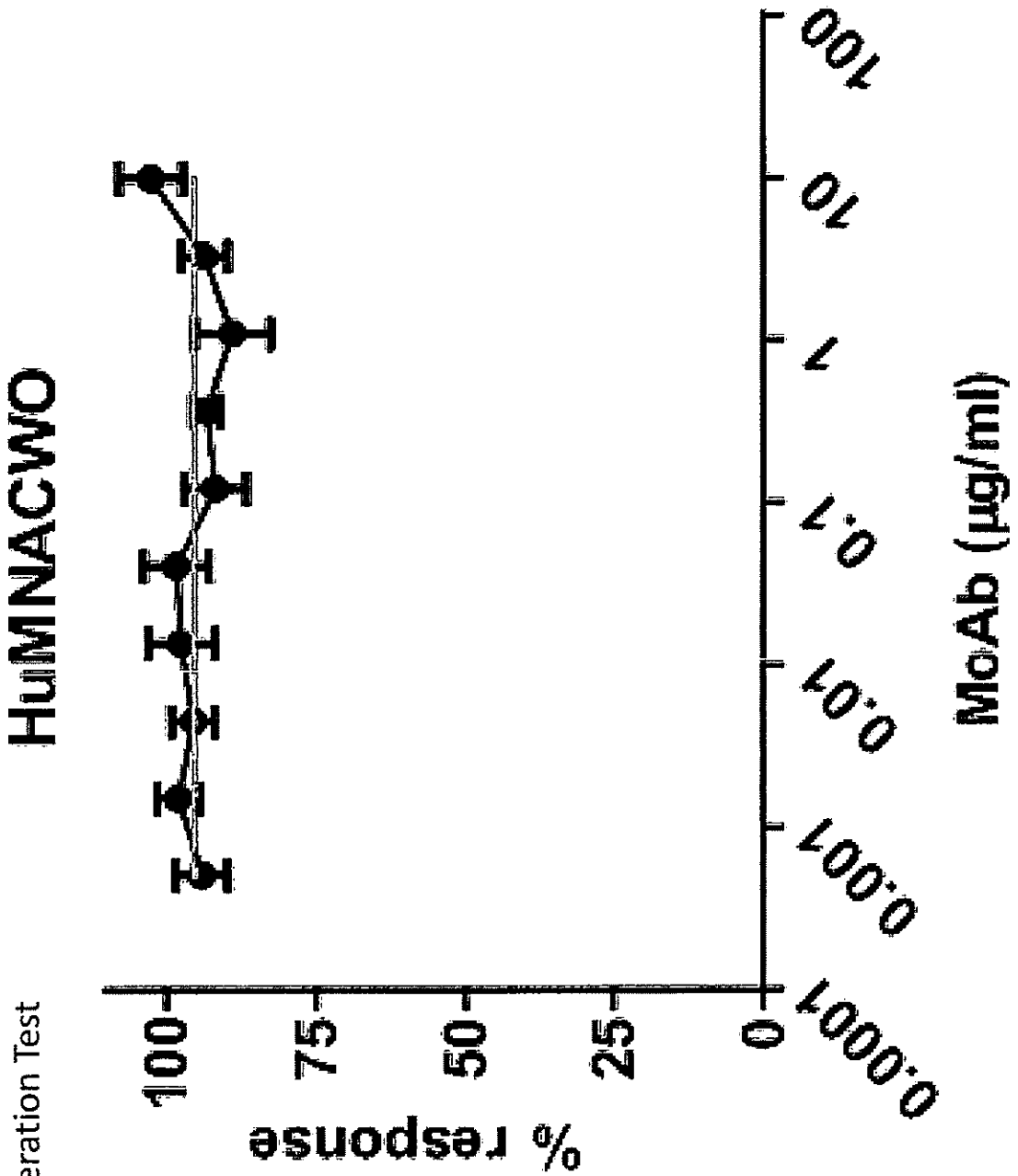


Figure 5 (continued)

TF1 Proliferation Test

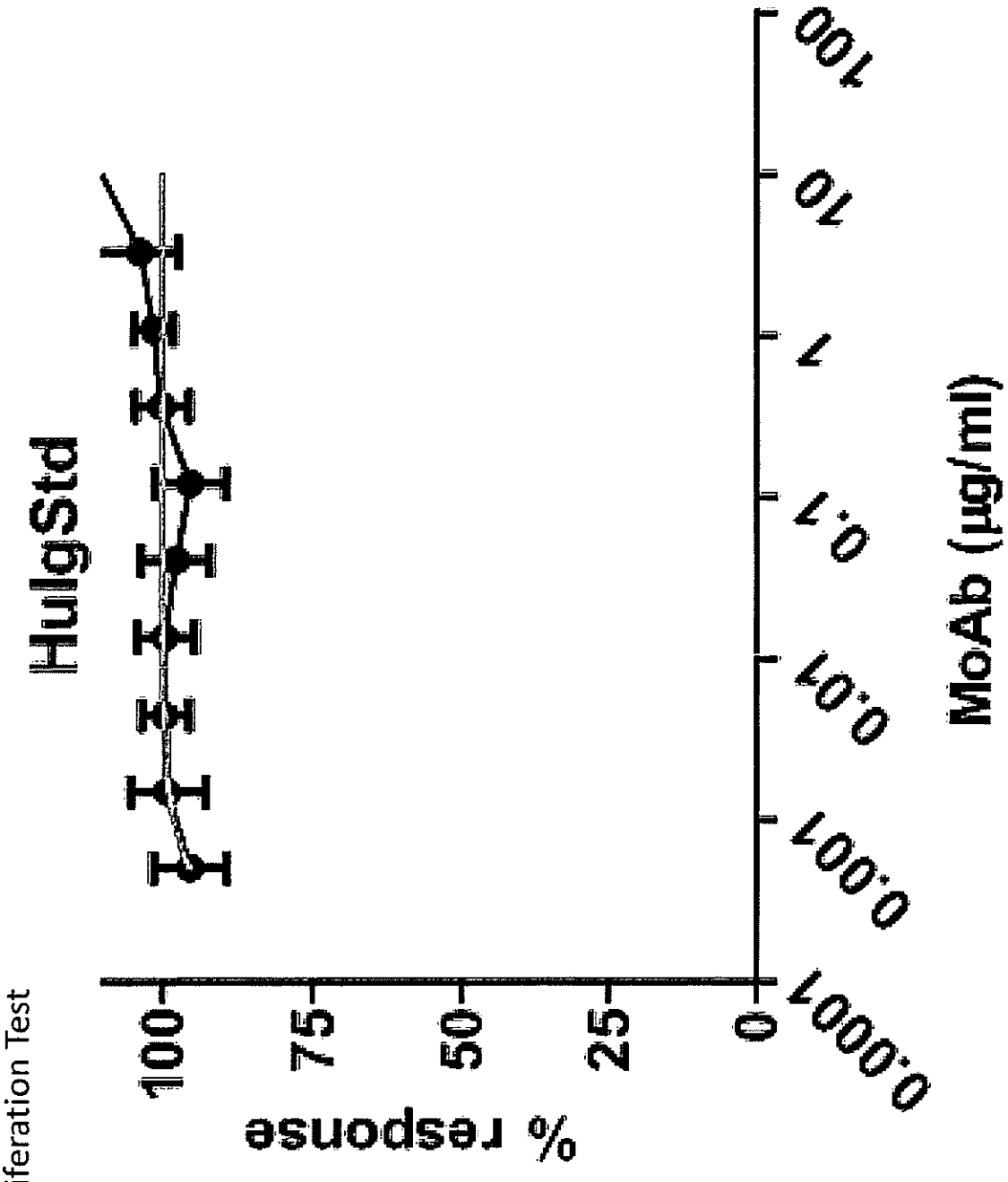


Figure 5 (continued)

TF1 Proliferation Test

Figure 6

BXhVH5 heavy chain with constant region

EVKLLESGGGLVQPGGSLRLSCAASGFTFSTYTMSWVRQTPGK
RLEWVAYISKGGGSTYYPDTVKGRFTISRDNSKNTLYLQMNSLRA
EDTAVYYCARGAMYGNDFFYPMDYWGQGTTVTVSSASTKGPSV
FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF
PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKV
EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT
CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV
SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT
TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEGLHNHYT
QKSLSLSPGK

BXhVL1 light chain with constant region

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGQAPRL
LIYTTSNLASGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCHQWS
SYPWTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLN
NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL
SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Figure 7

BXhVH5N297A heavy chain with constant region

EVKLLESGGGLVQPGGSLRLSCAASGFTFSTYTMSWVRQTPGKRLEWVAYISKGGGSTYYPDTV
KGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGAMYGNDFFYPMDYWGQGTTVTVSSASTKG
PSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVV
TVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDT
LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIA
VEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEGLHNHYTQKSLS
LSPGK

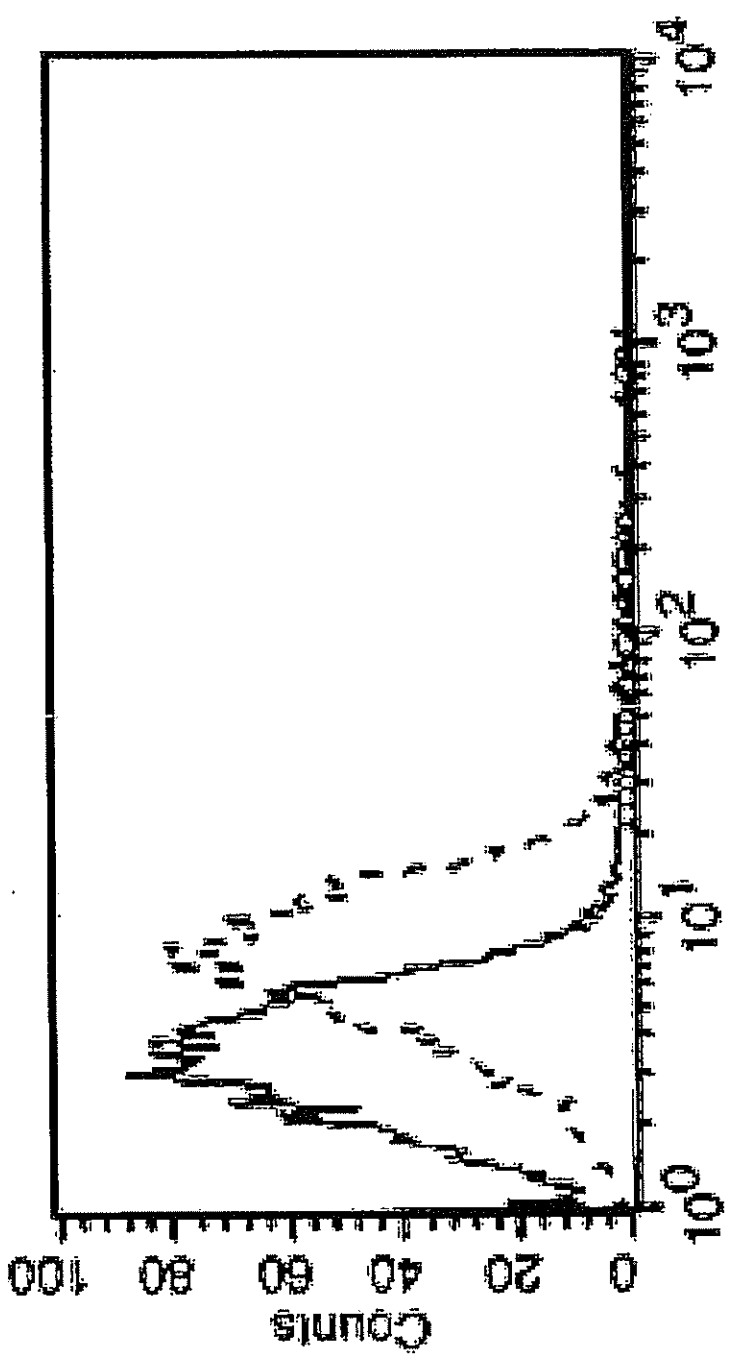


Figure 8

TF1

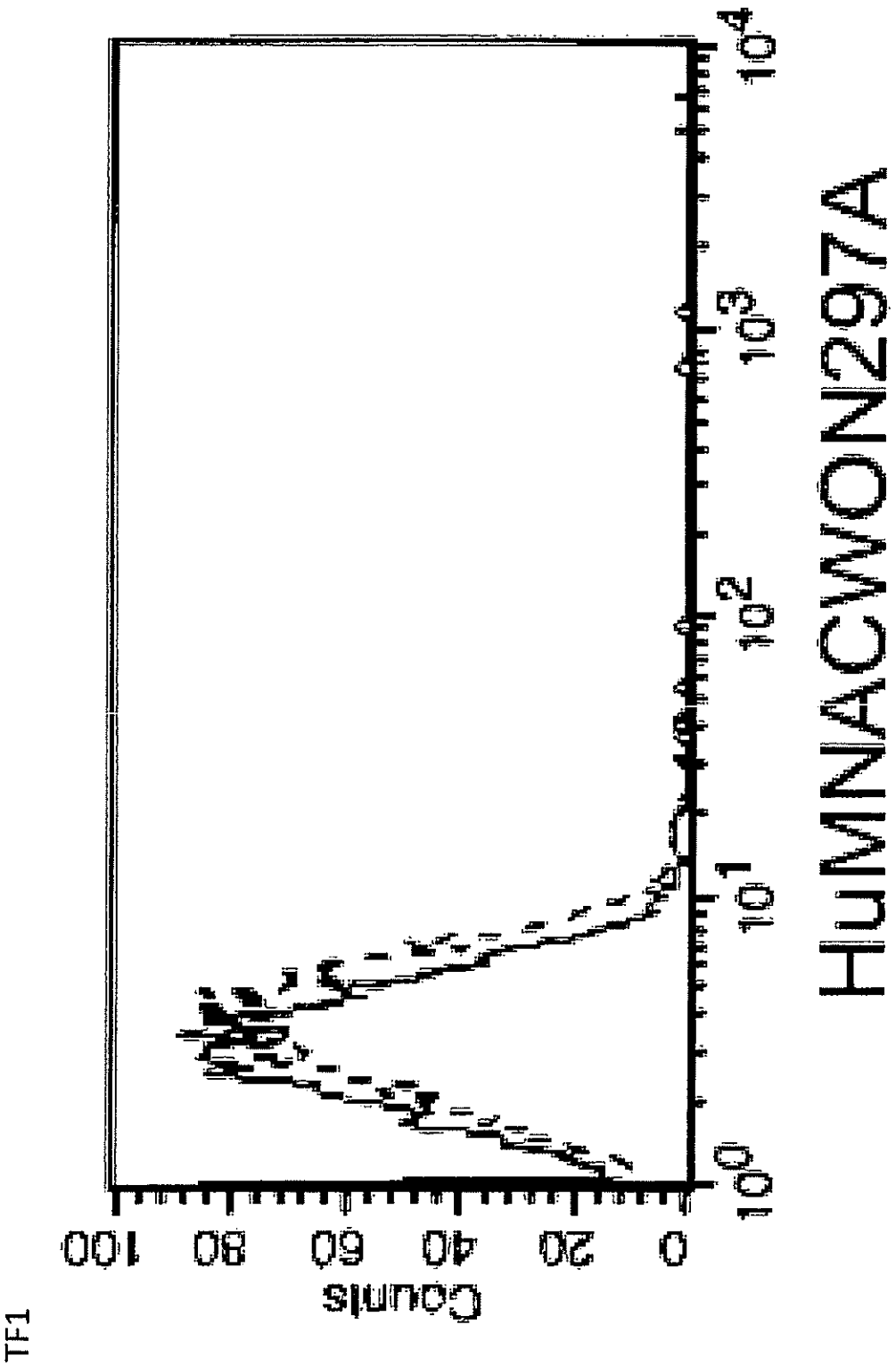


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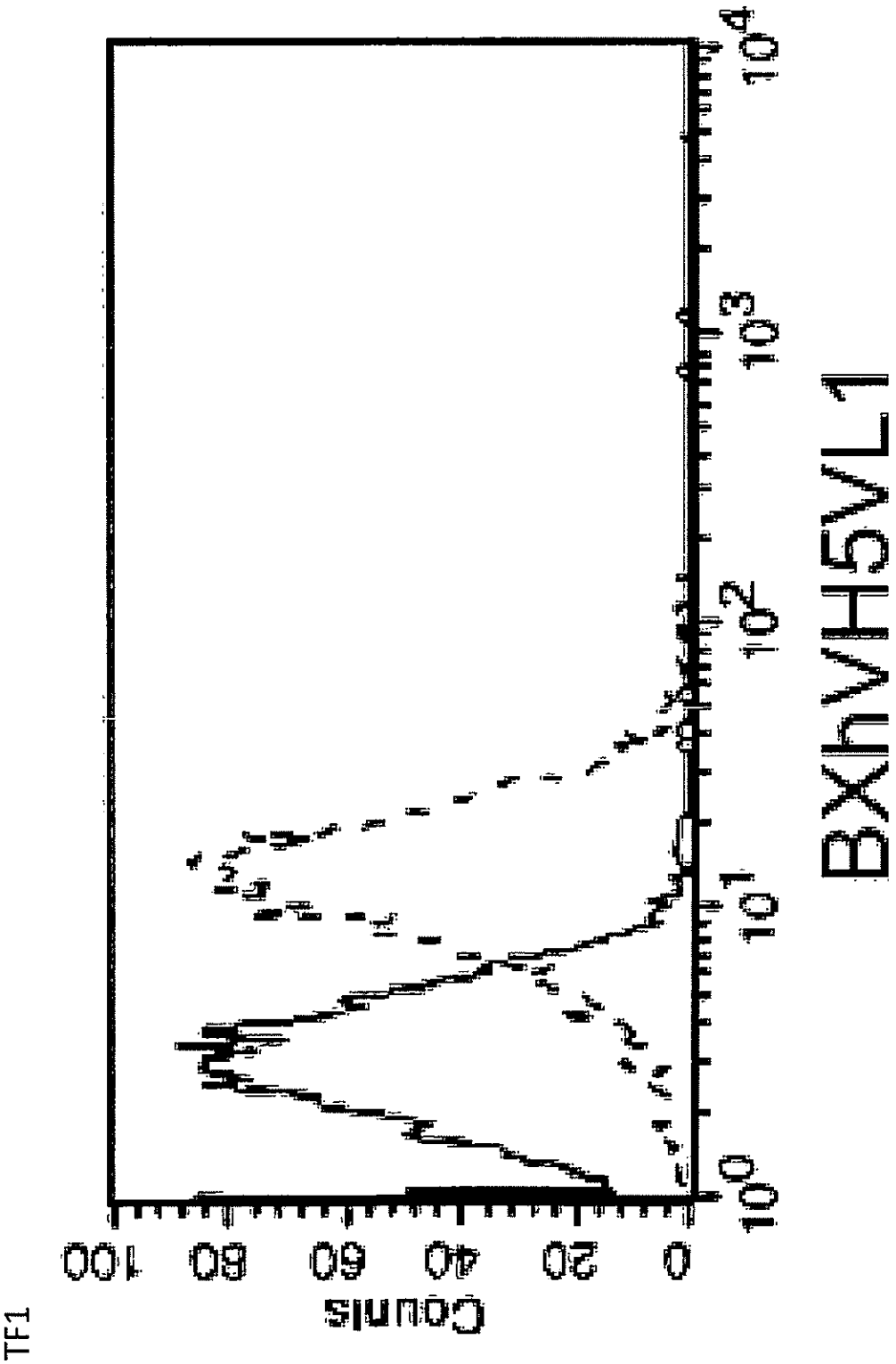


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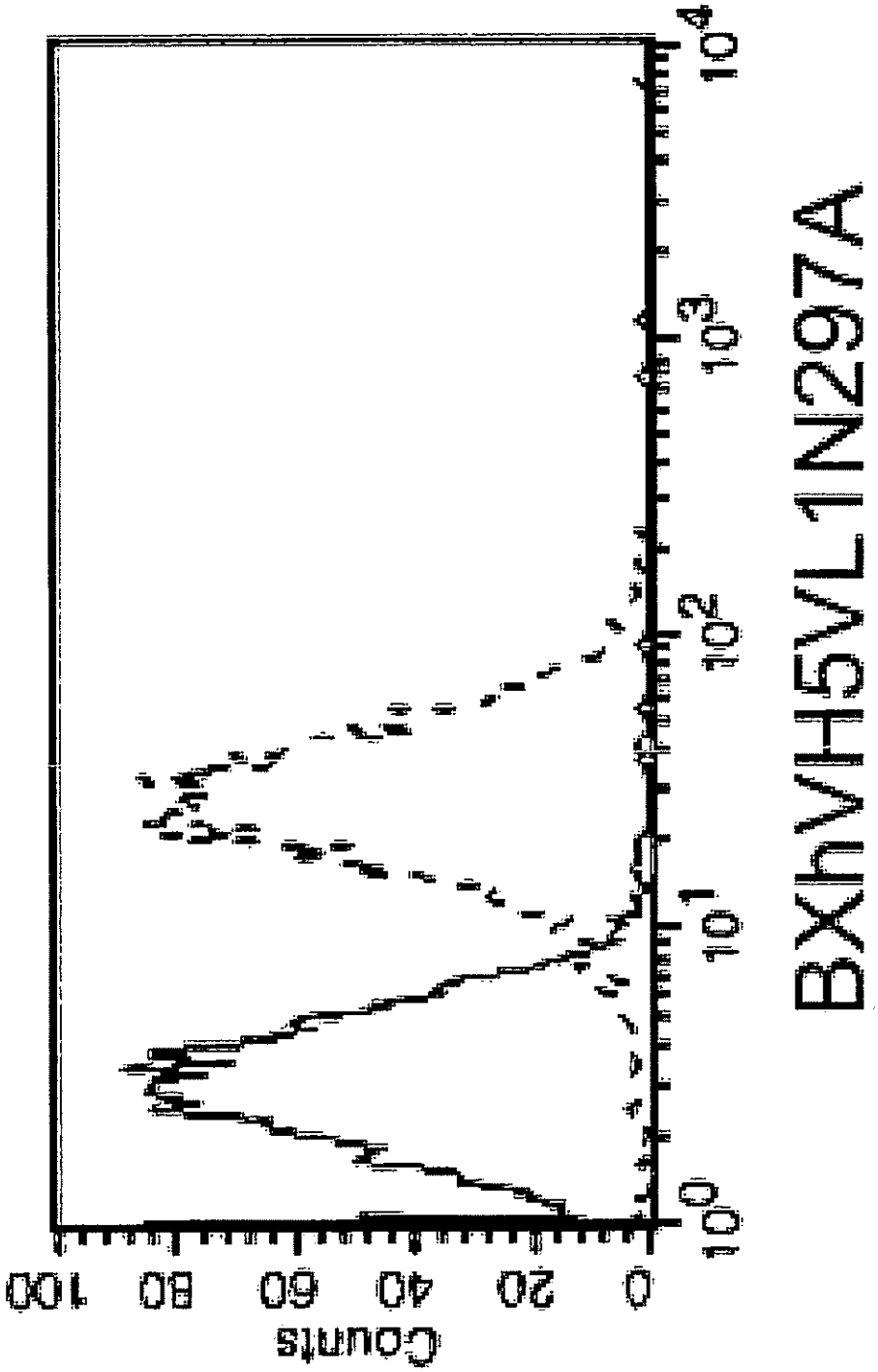
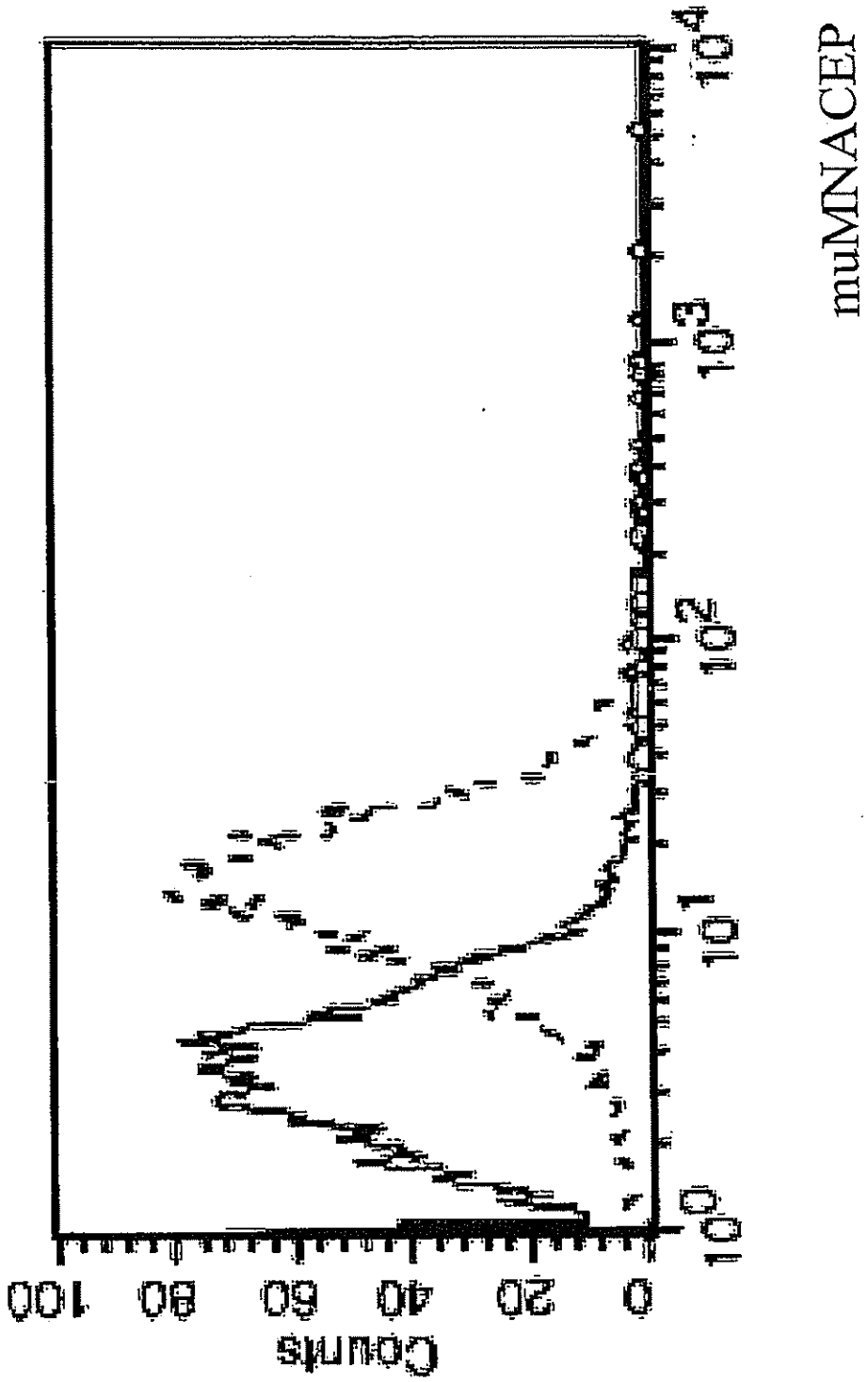


Figure 8 (continued)

TF1

Figure 8 (continued)

HMC1



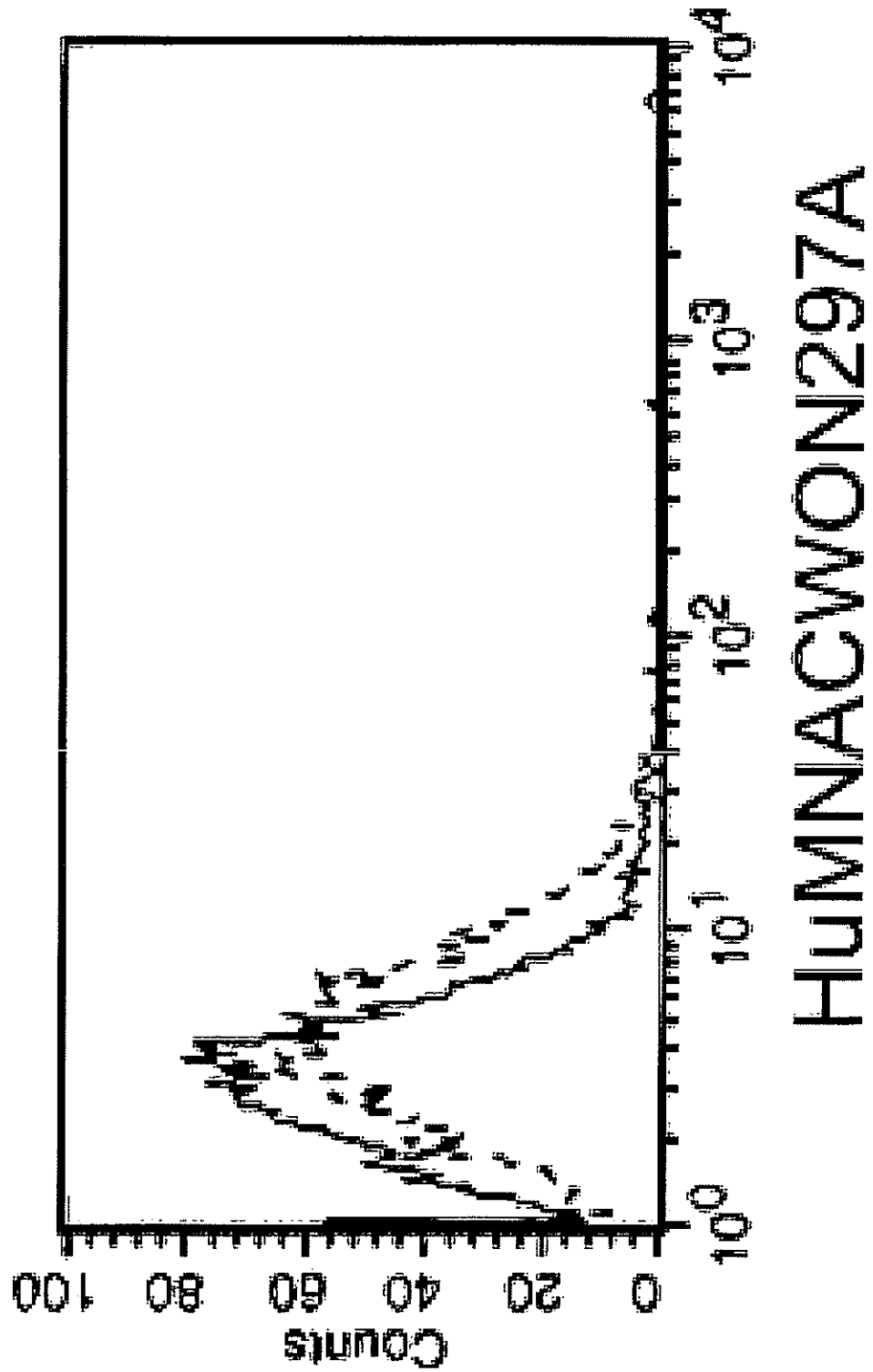


Figure 8 (continued)

HMC1

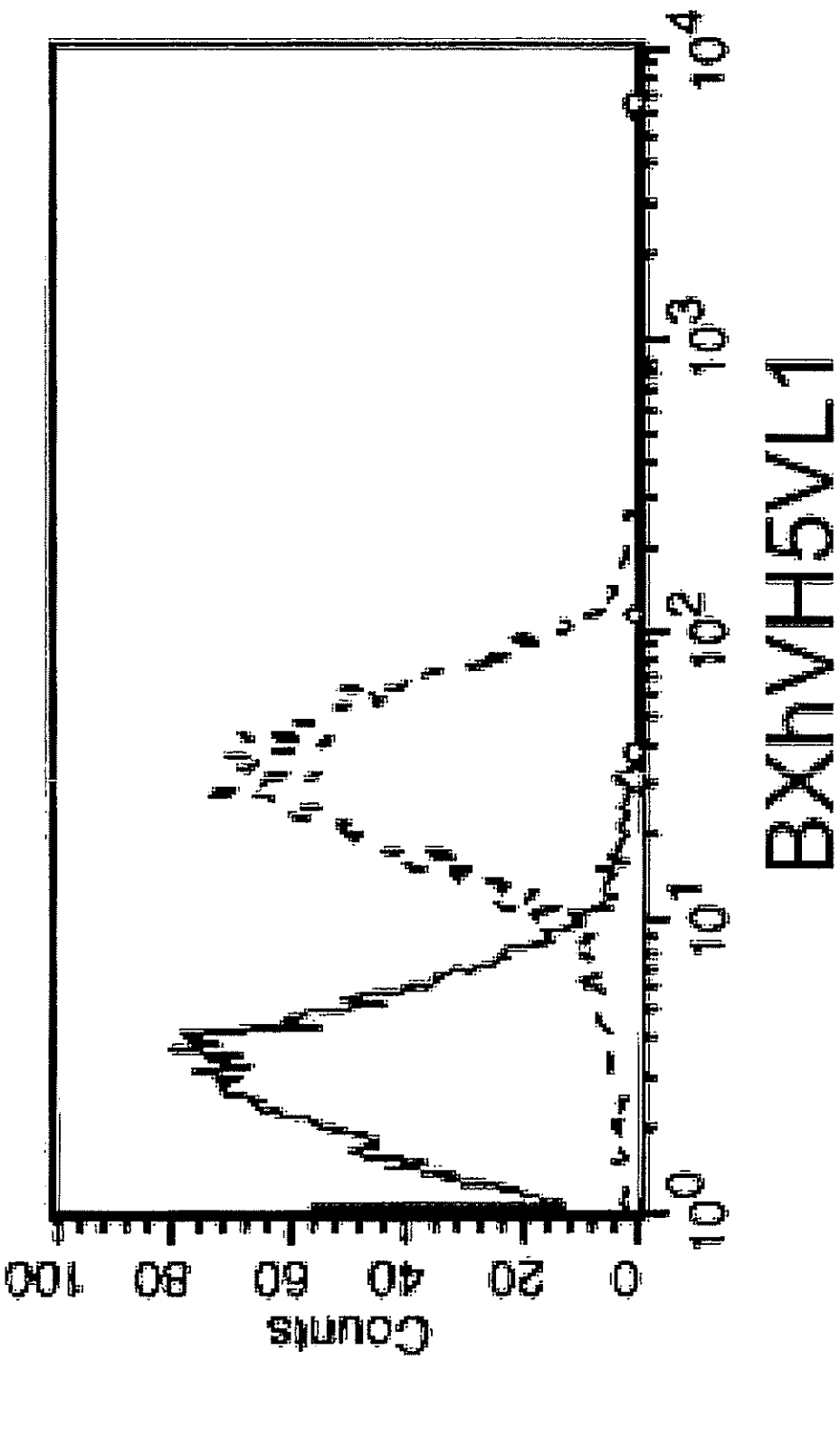


Figure 8 (continued)

HMC1

Figure 8 (continued)

HMC1

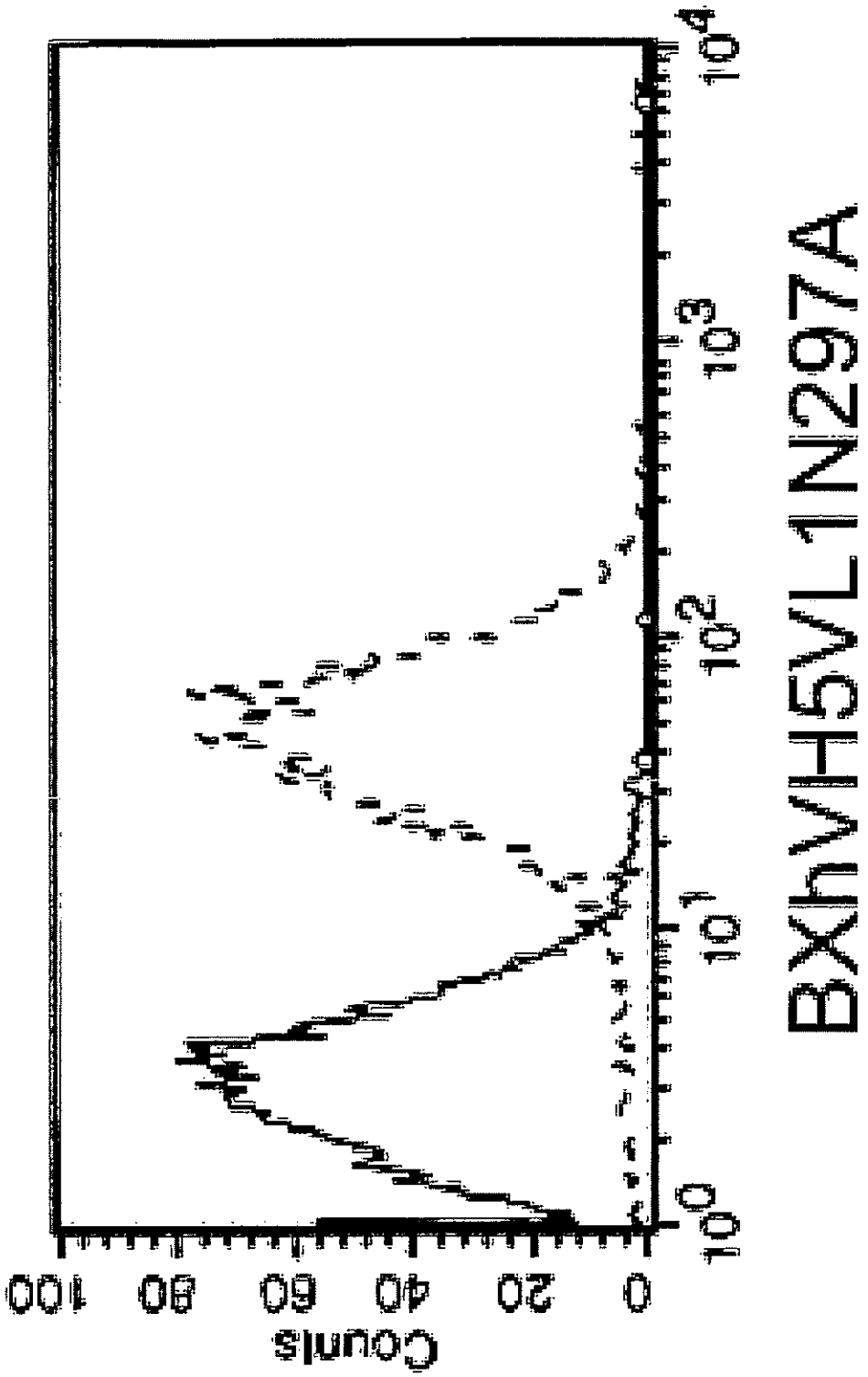
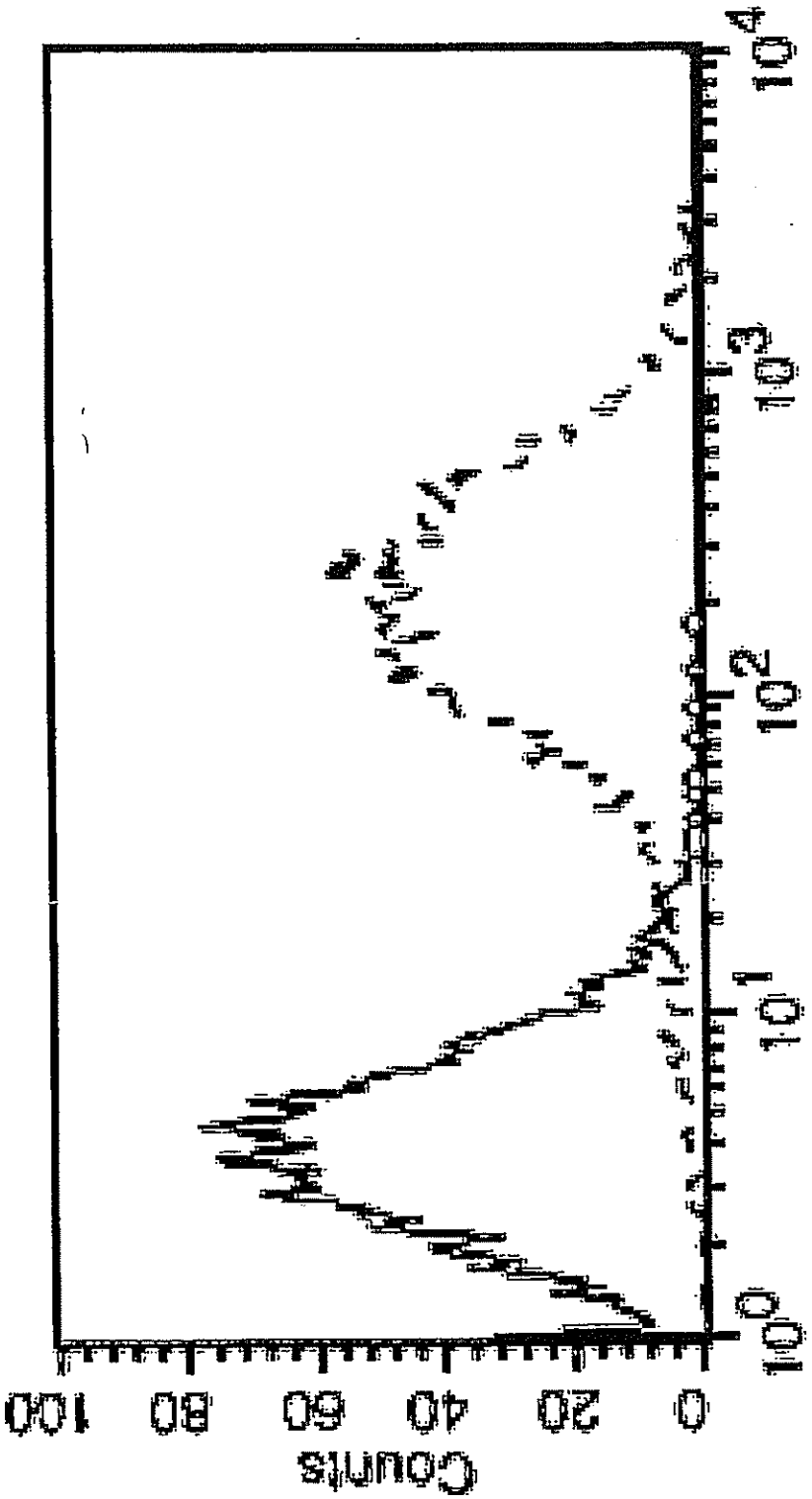


Figure 8 (continued)

PC12-huTrkA



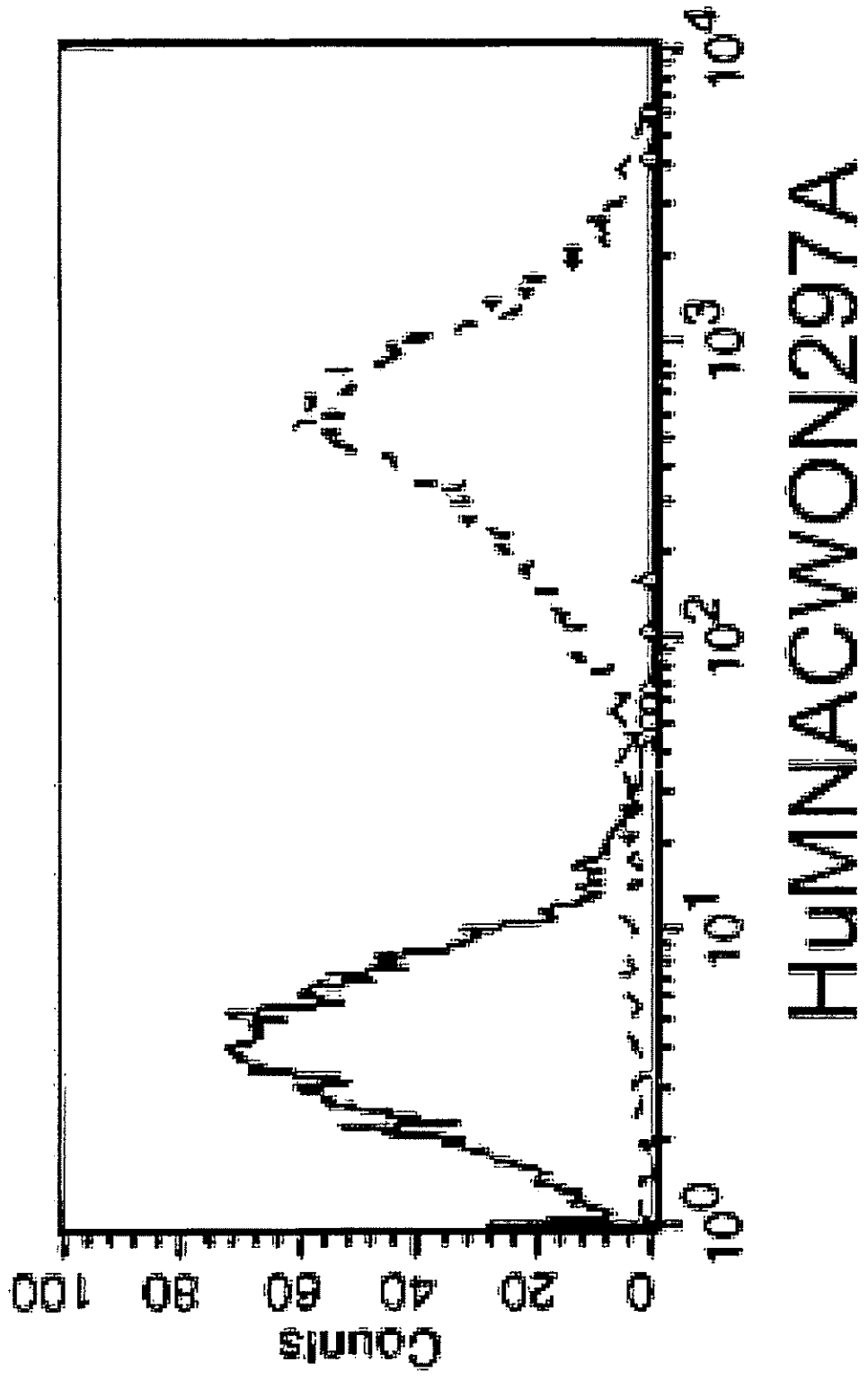
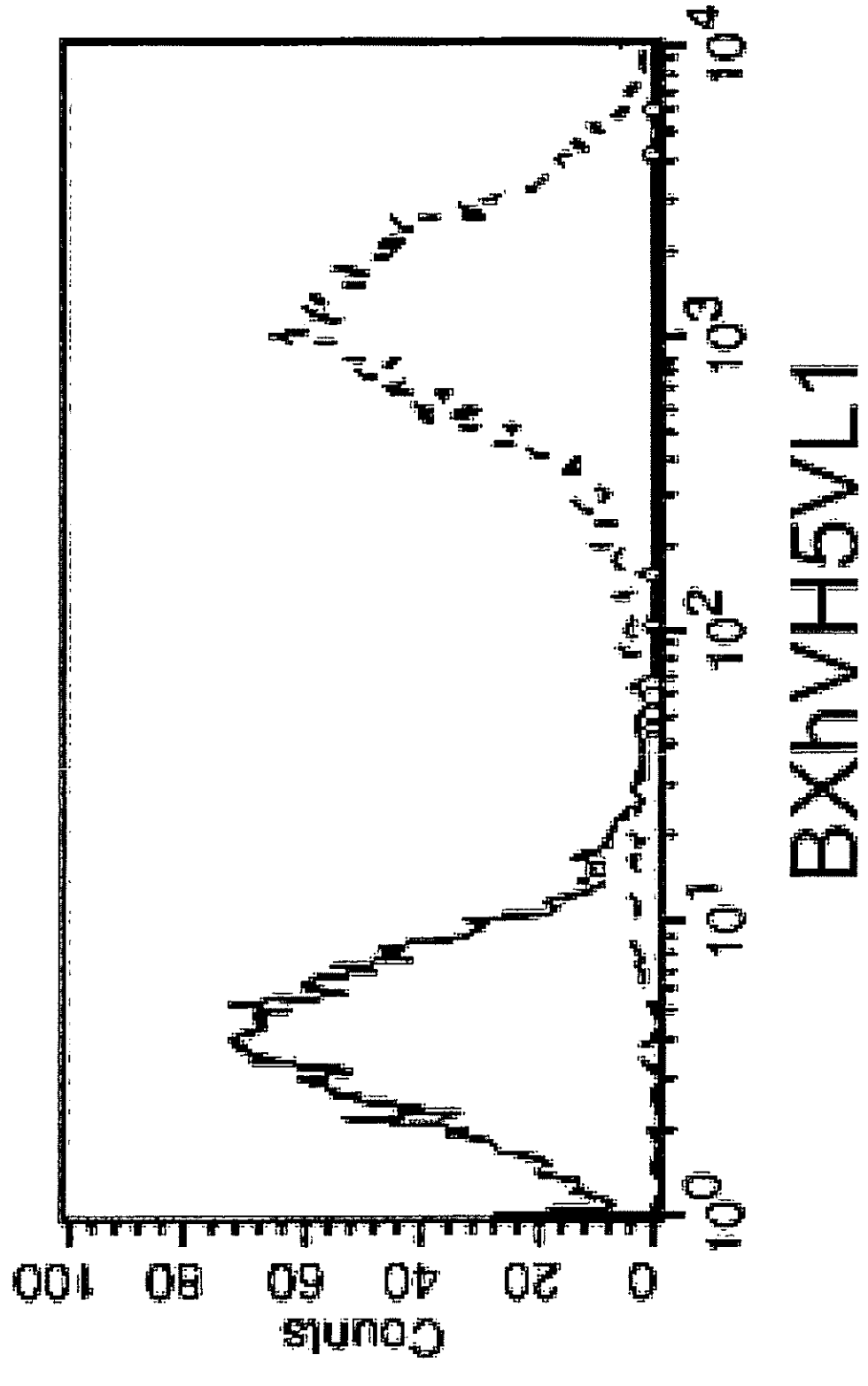
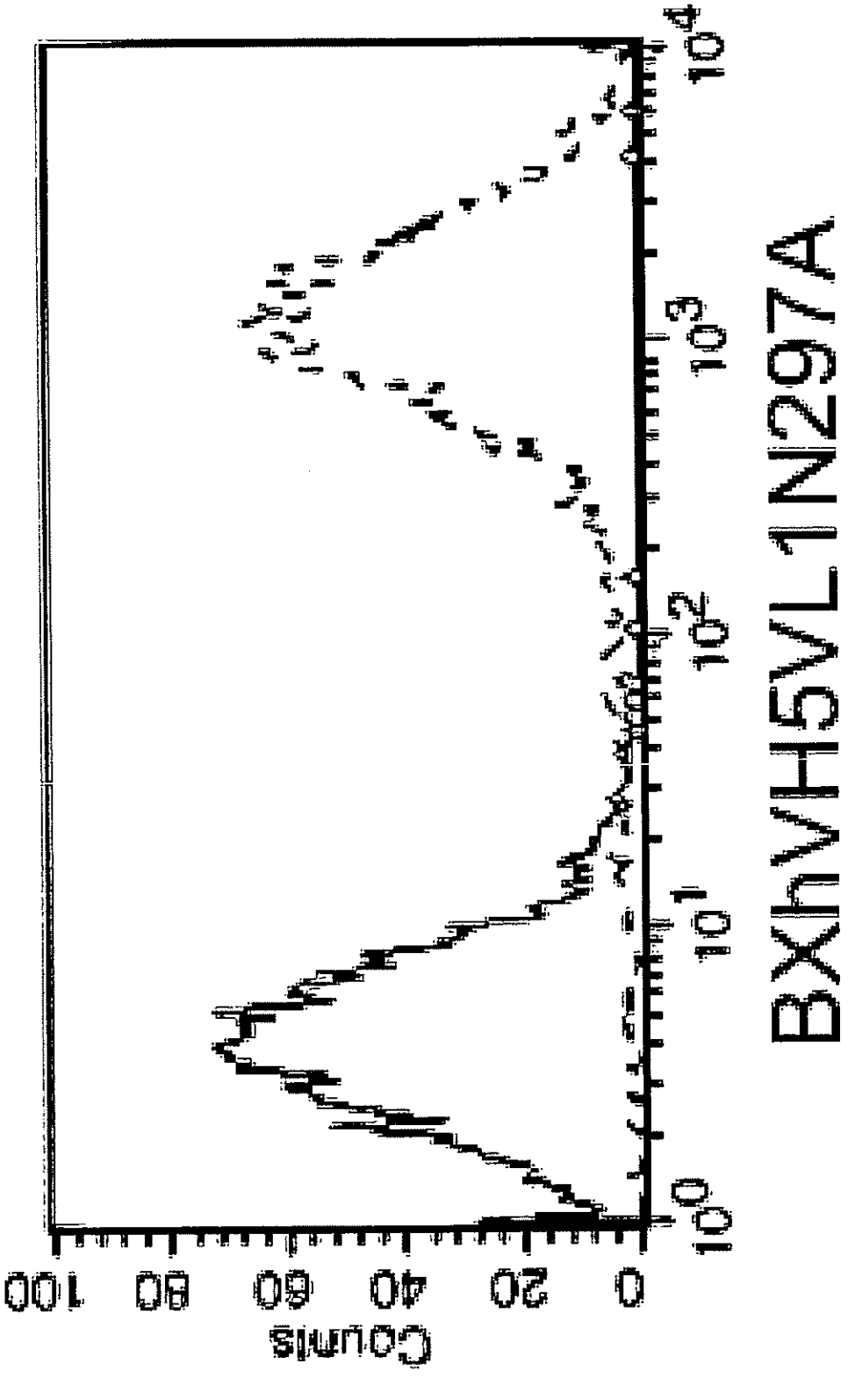


Figure 8 (continued)



PC12-huTrkA

Figure 8 (continued)



PC12-huTrkA

Figure 8 (continued)

Figure 9

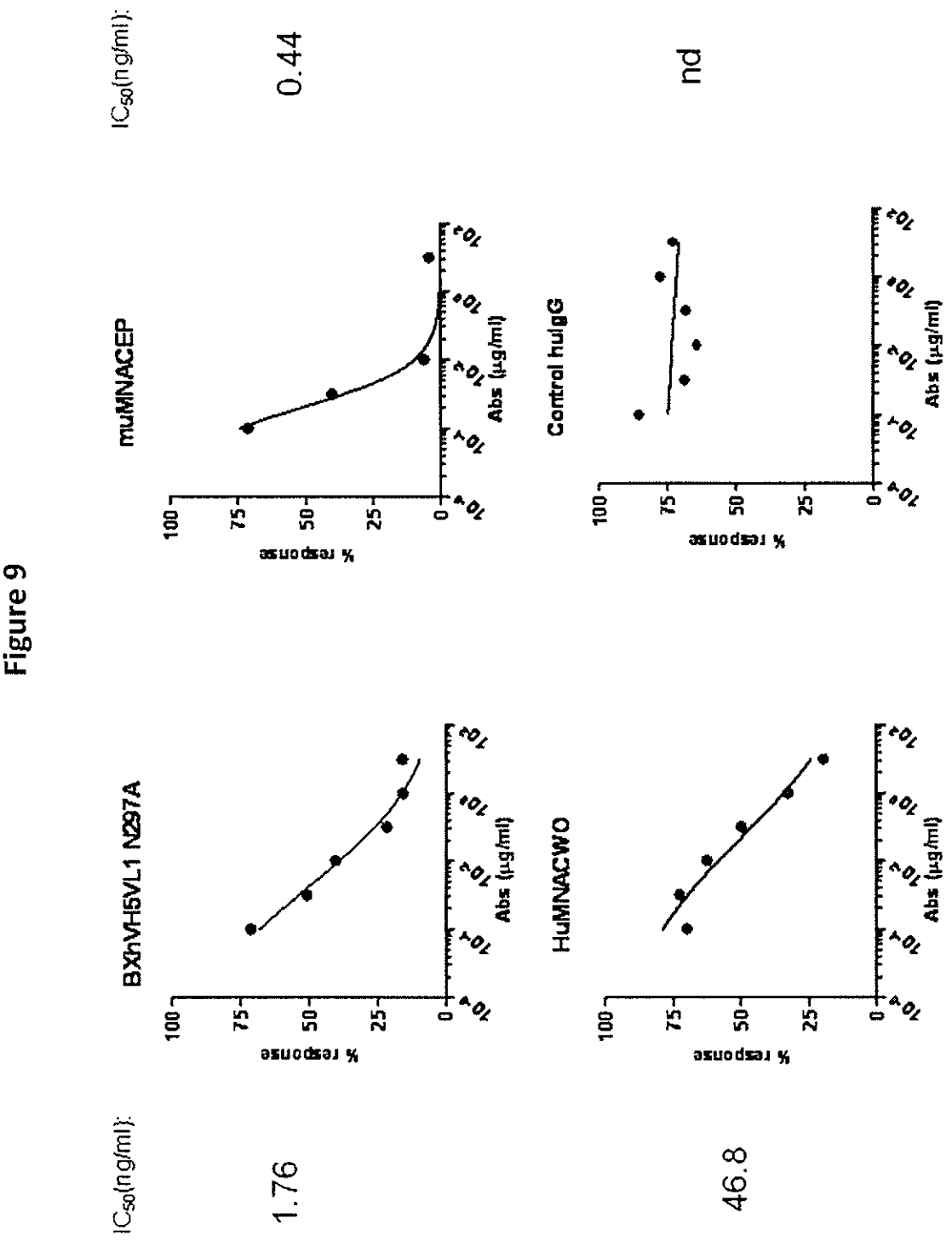

muMNACEP
IC50(ng/ml):
0.44
Control huIgG
nd
BXnVH5VL1 N297A
IC50(ng/ml):
1.76
HuMNACWO
46.8
% response
Abs (µg/ml)

Figure 10

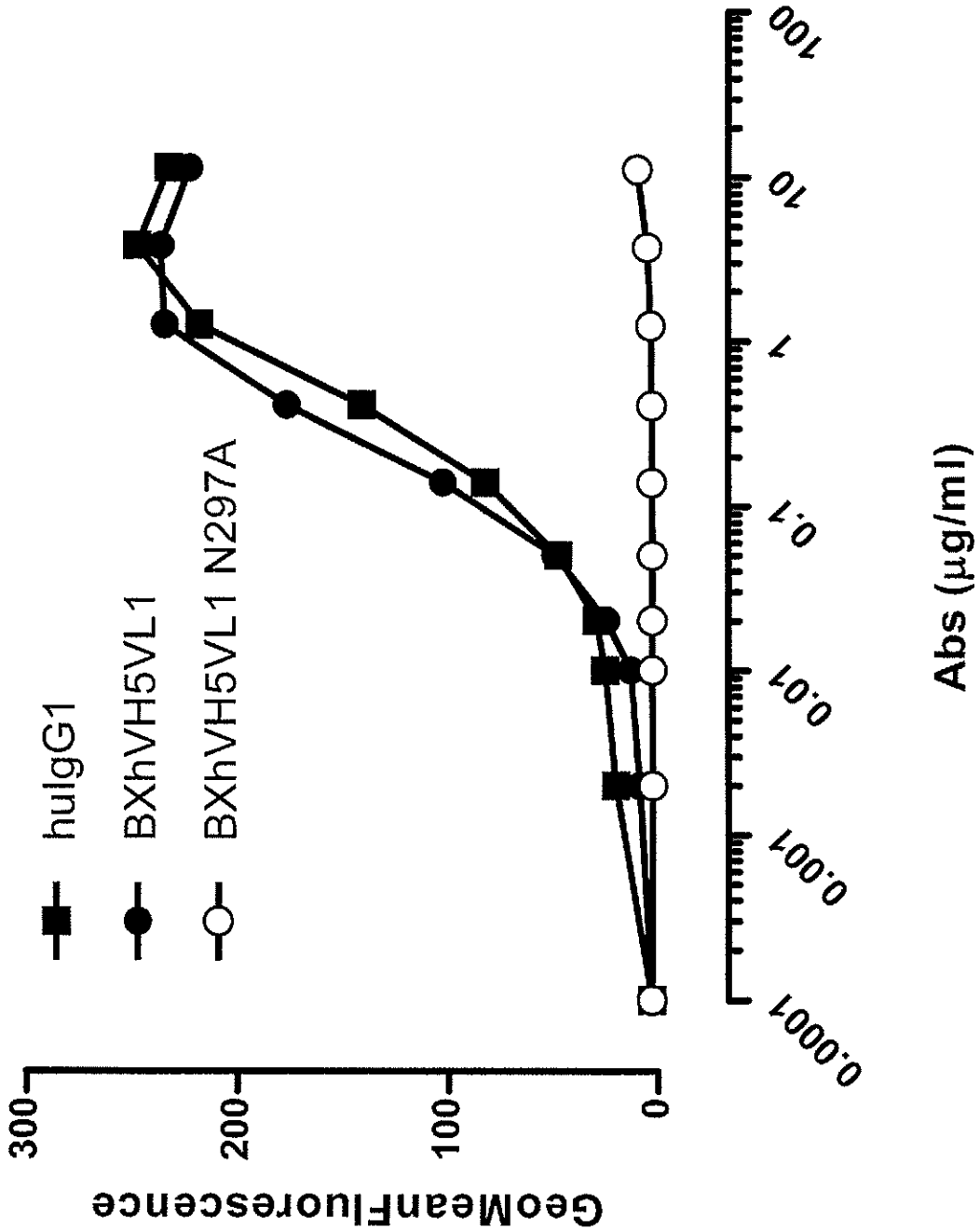
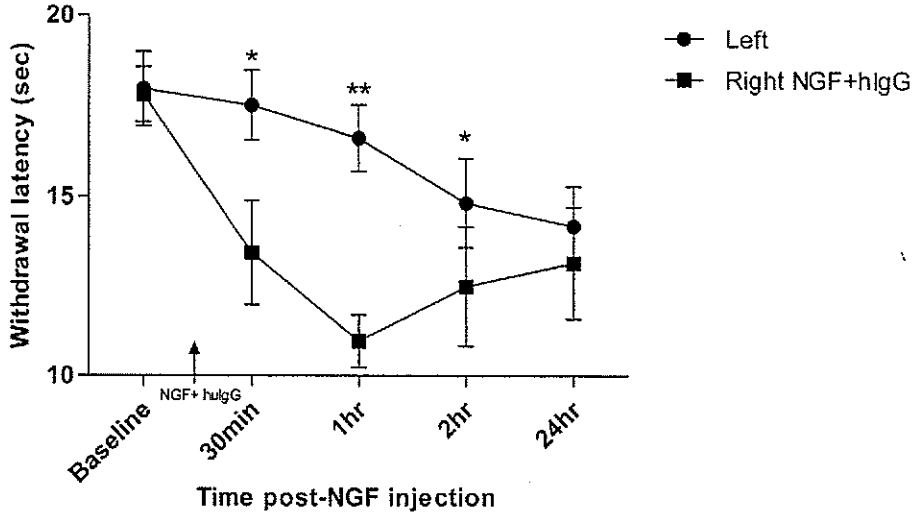

huIgG1
BXhVH5VL1
BXhVH5VL1 N297A
GeoMeanFluorescence
300
200
100
0
100
10
1
0.1
0.01
0.001
0.0001
Abs (µg/ml)

Figure 11


20
15
10
Withdrawal latency (sec)
*
**
*
NGF+ huIgG
Baseline
30min
1hr
2hr
24hr
Time post-NGF injection
Left
Right NGF+hIgG

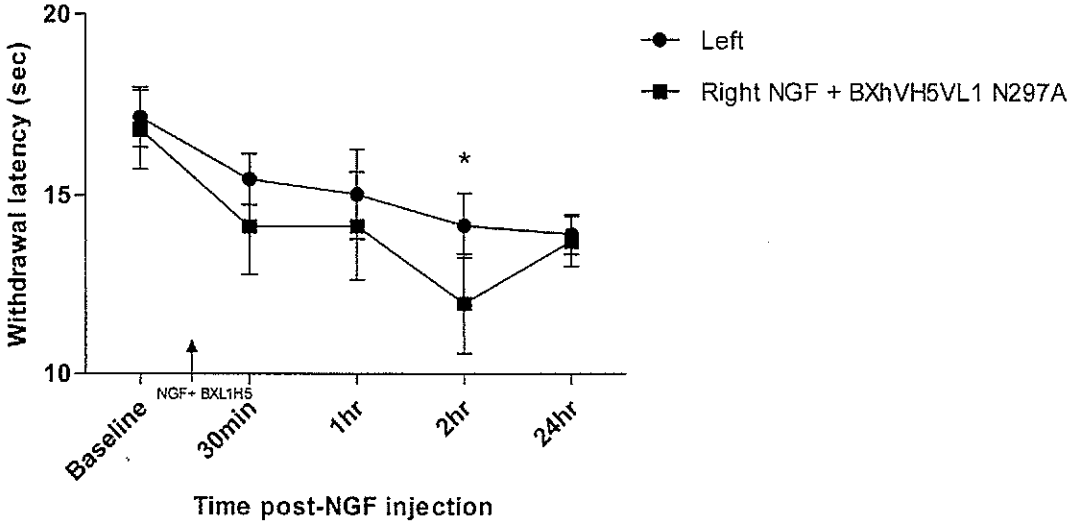
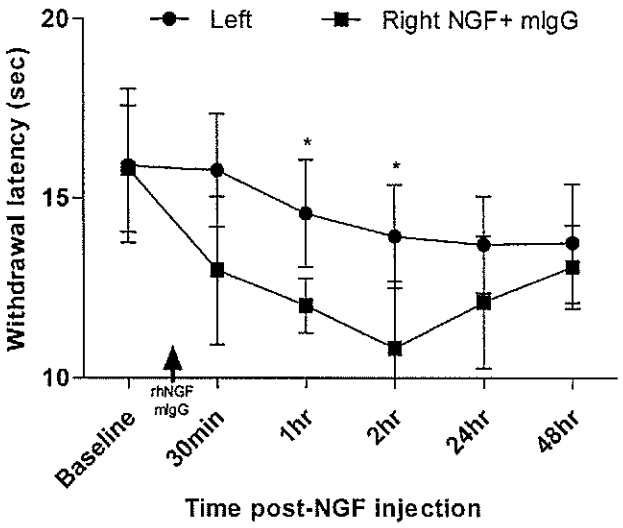
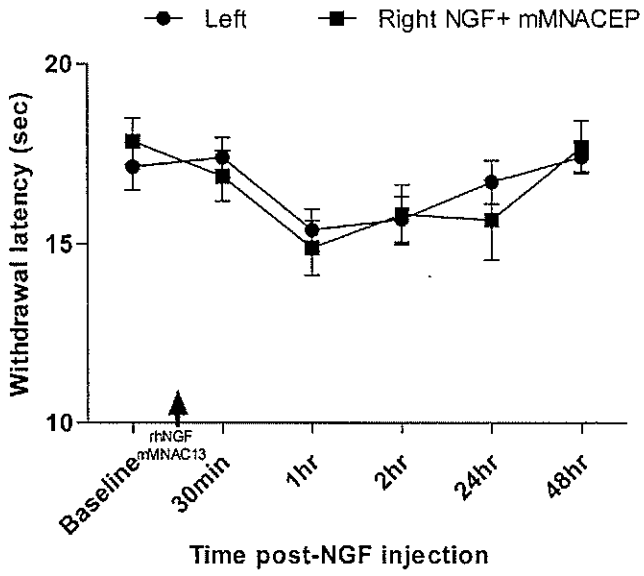

20
15
10
Withdrawal latency (sec)
*
NGF+ BXL1H5
Baseline
30min
1hr
2hr
24hr
Time post-NGF injection
Left
Right NGF + BXhVH5VL1 N297A

Figure 12


Left
Right NGF+ mIgG
Withdrawal latency (sec)
20
15
10
*
*
rhNGF
mIgG
Baseline
30min
1hr
2hr
24hr
48hr
Time post-NGF injection


Left
Right NGF+ mMNACEP
Withdrawal latency (sec)
20
15
10
rhNGF
αMNAC13
Baseline
30min
1hr
2hr
24hr
48hr
Time post-NGF injection

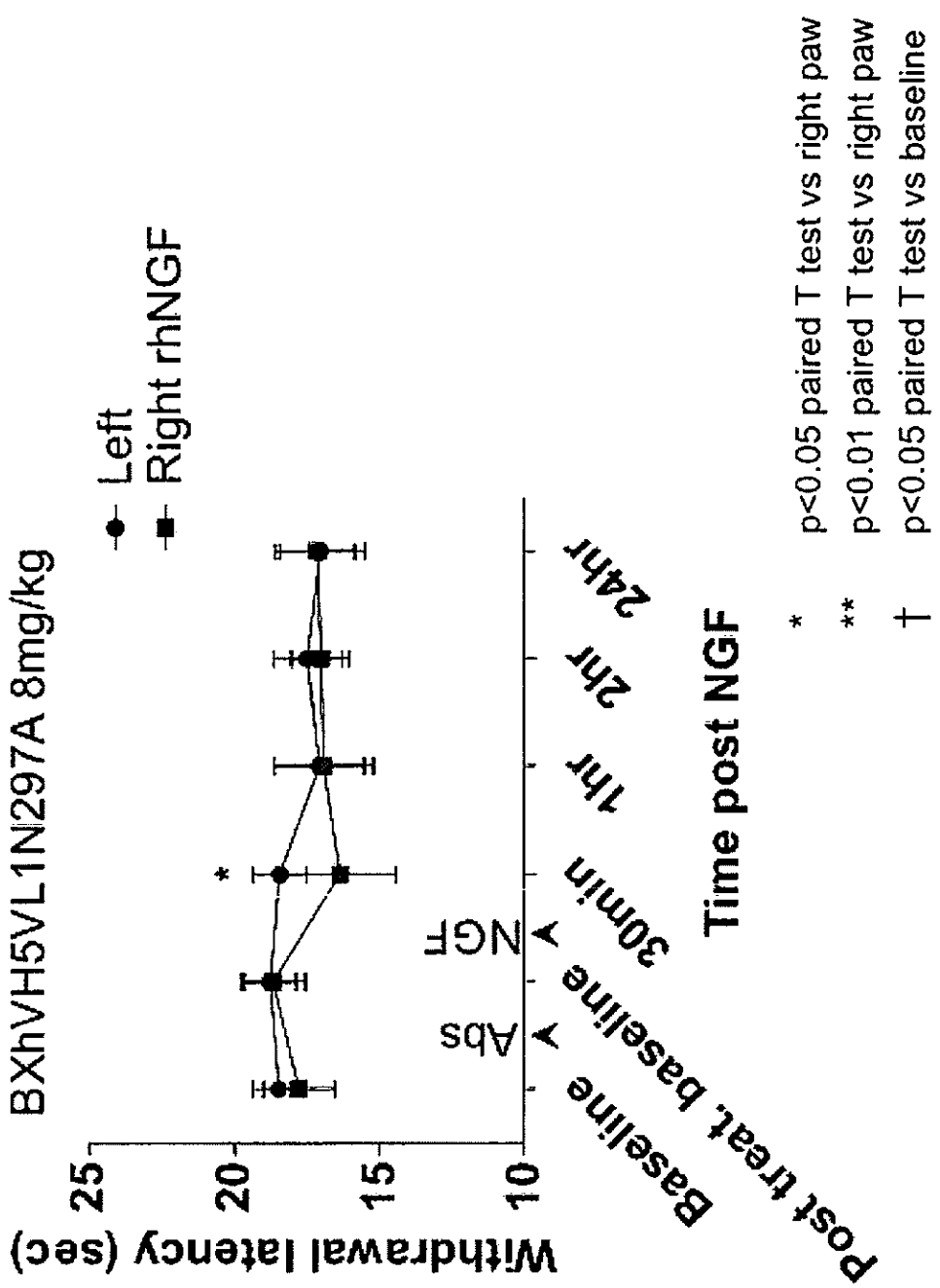

BXhVH5VL1N297A 8mg/kg
Left
Right rhNGF
Withdrawal latency (sec)
25
20
15
10
Baseline
Abs
NGF
30min
1hr
2hr
24hr
Post treat. baseline
Time post NGF
* p<0.05 paired T test vs right paw
** p<0.01 paired T test vs right paw
† p<0.05 paired T test vs baseline

Figure 13

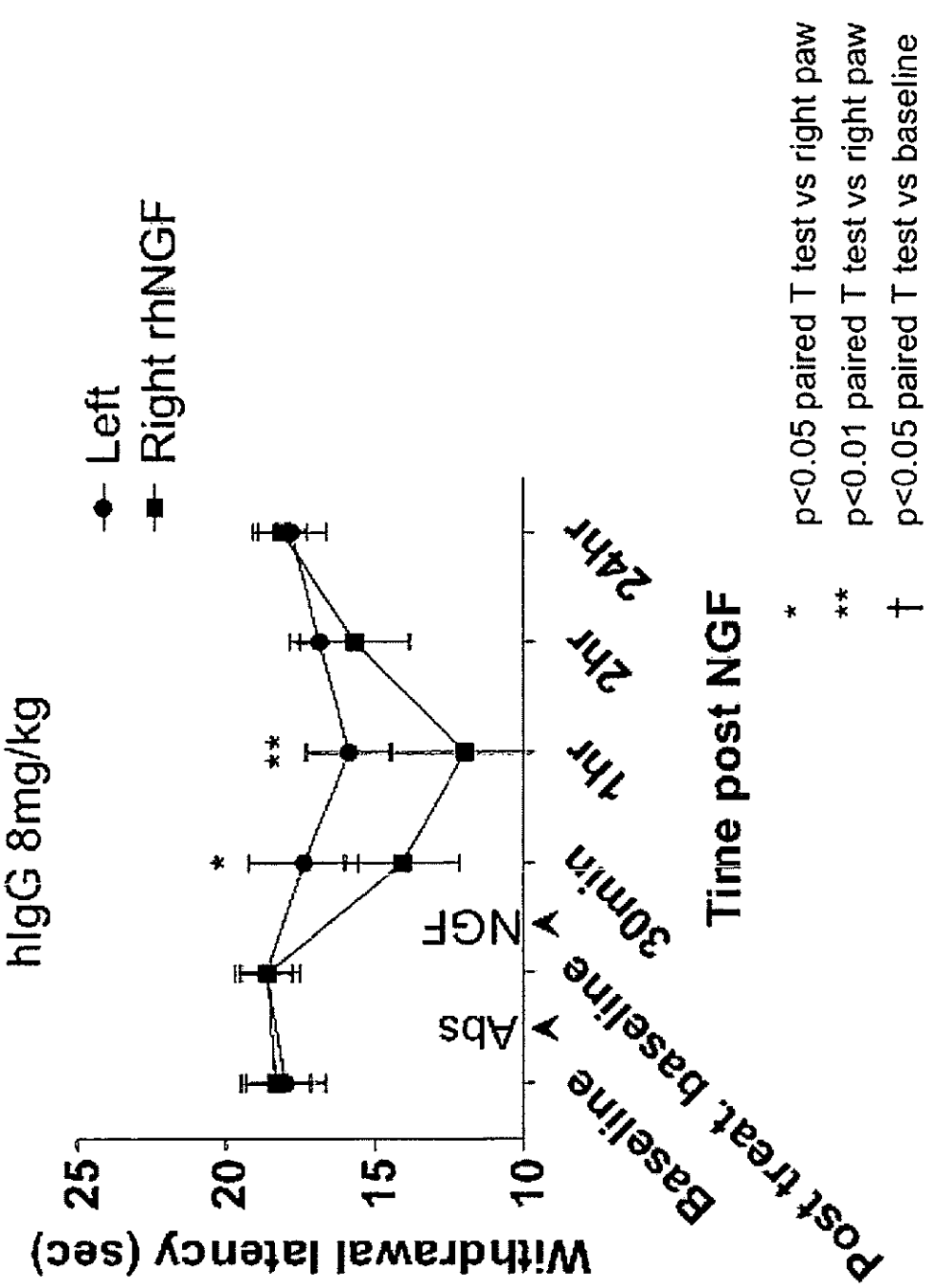


Figure 13 (continued)

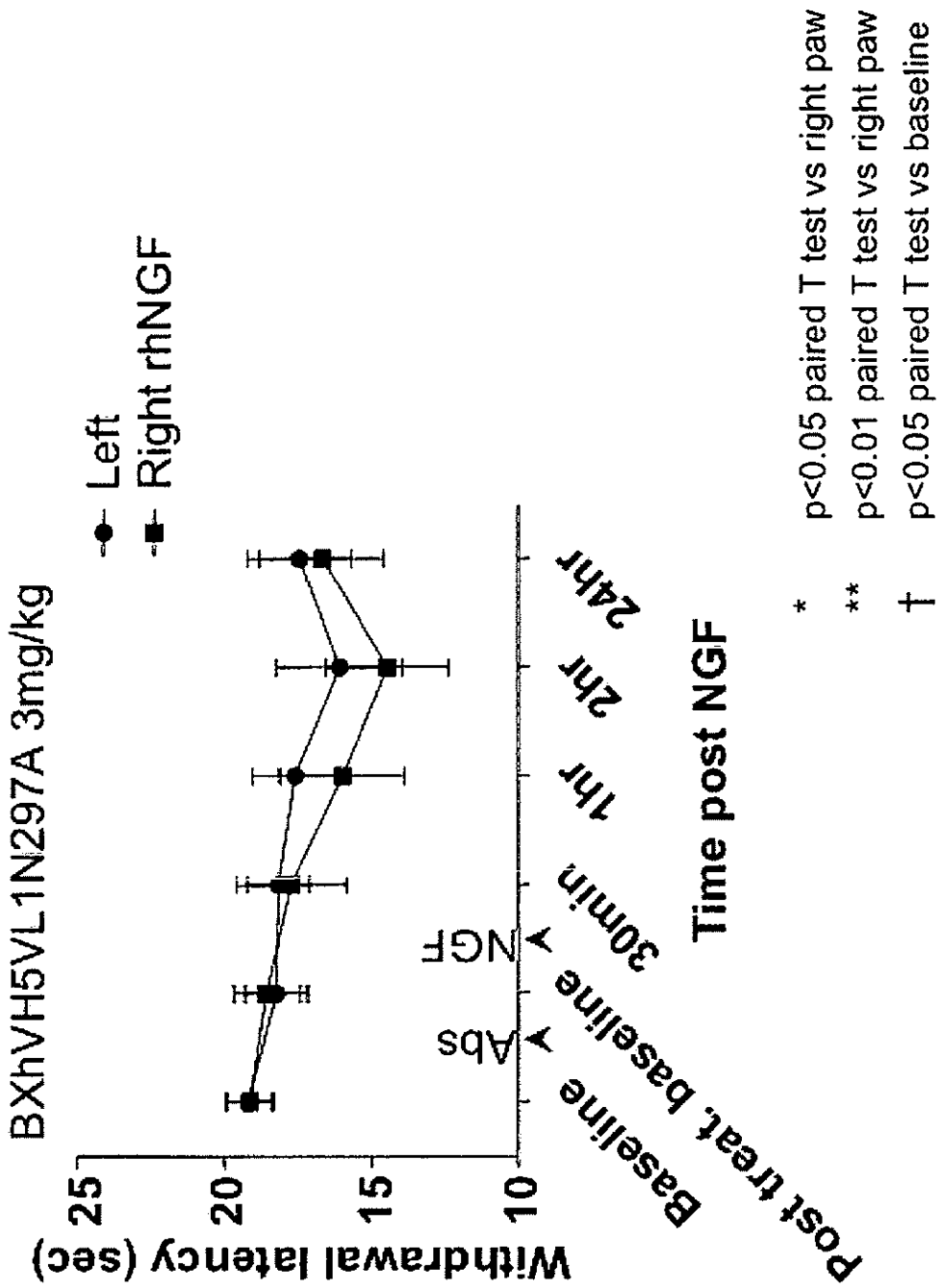


Figure 13 (continued)

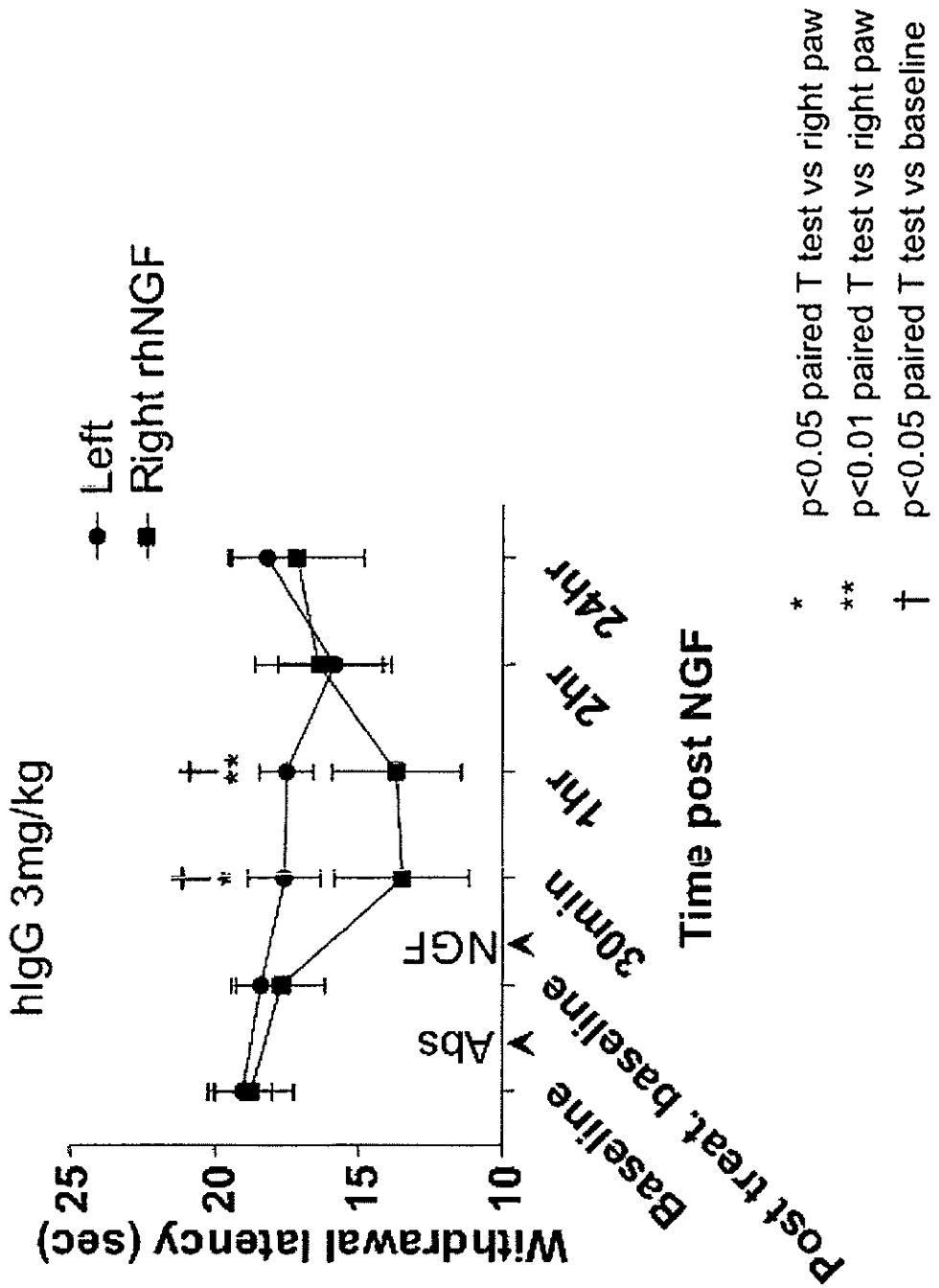


Figure 13 (continued)

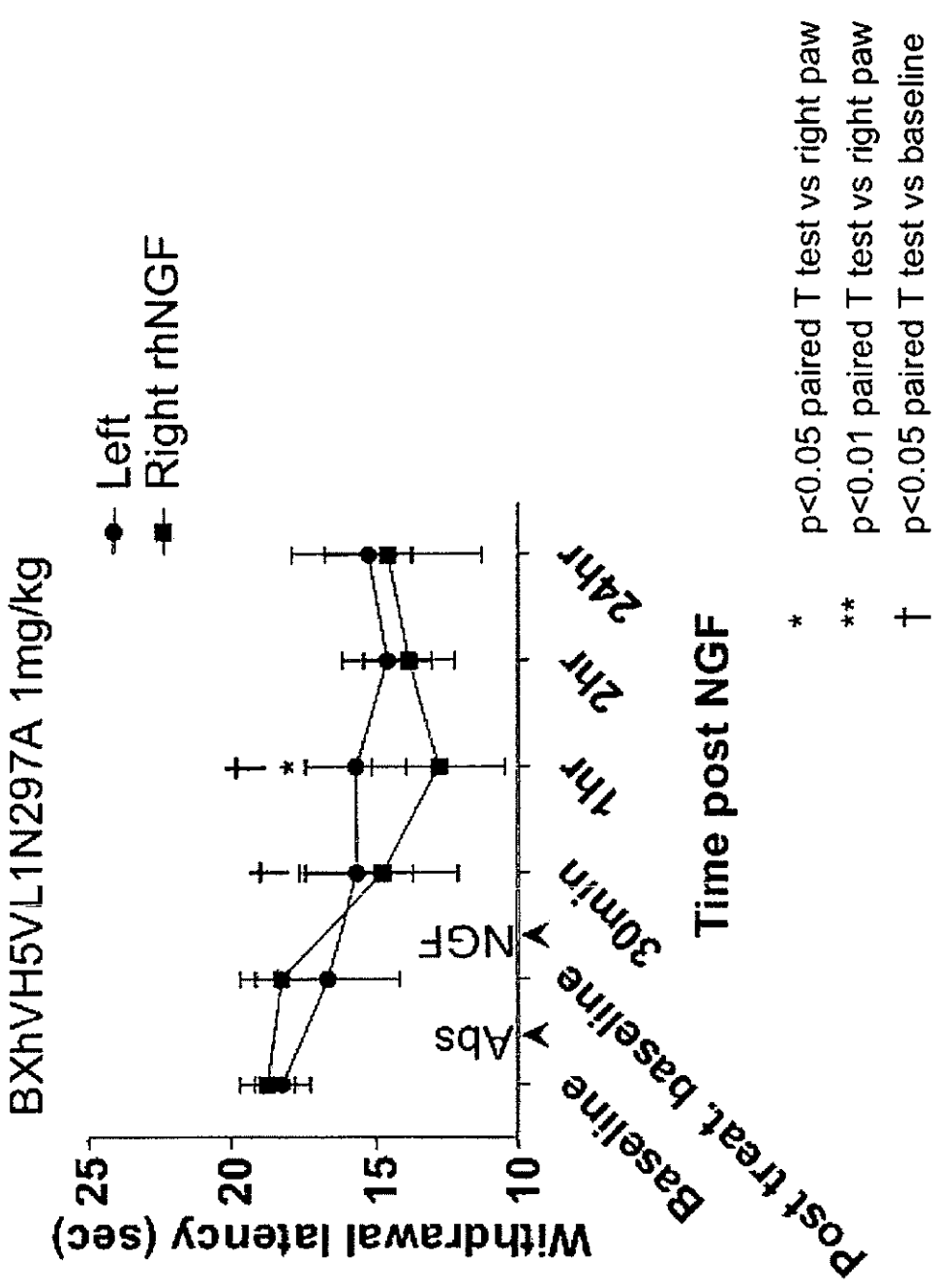


Figure 13 (continued)

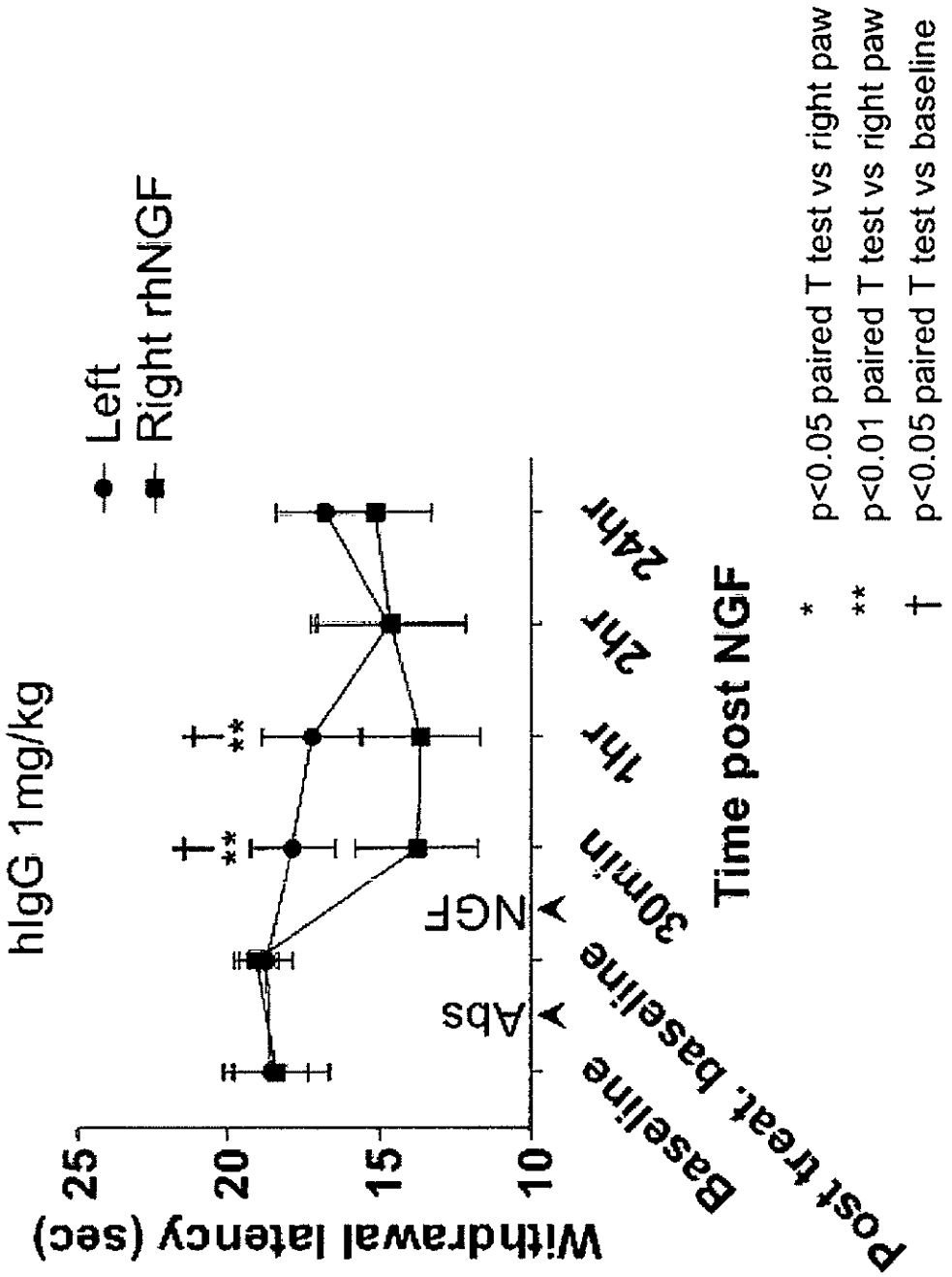


Figure 13 (continued)

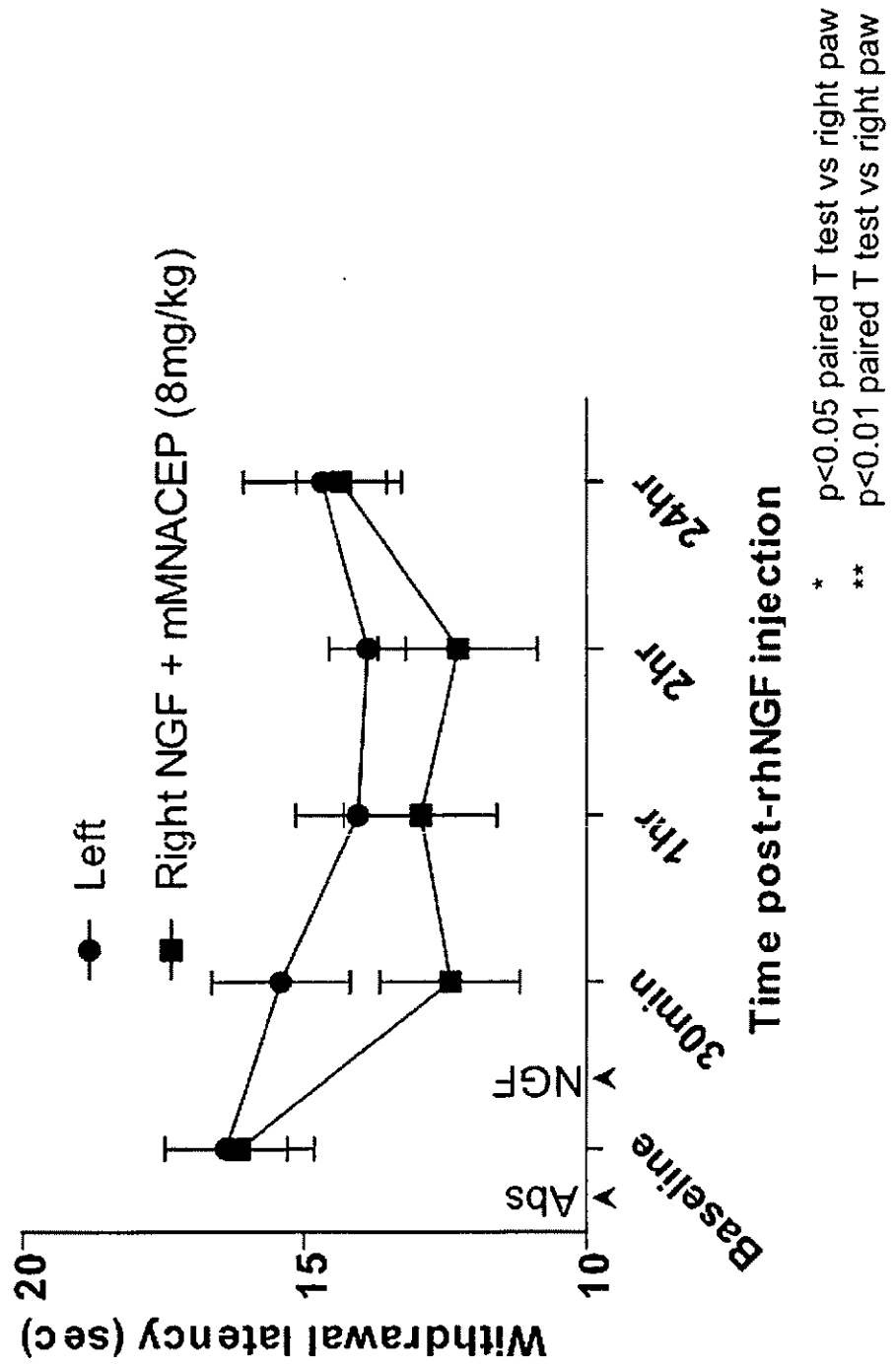

Withdrawal latency (sec)
20
15
10
Abs
NGF
Baseline
30min
1hr
2hr
24hr
Time post-rhNGF injection
Left
Right NGF + mMNACEP (8mg/kg)
* p<0.05 paired T test vs right paw
** p<0.01 paired T test vs right paw

Figure 14

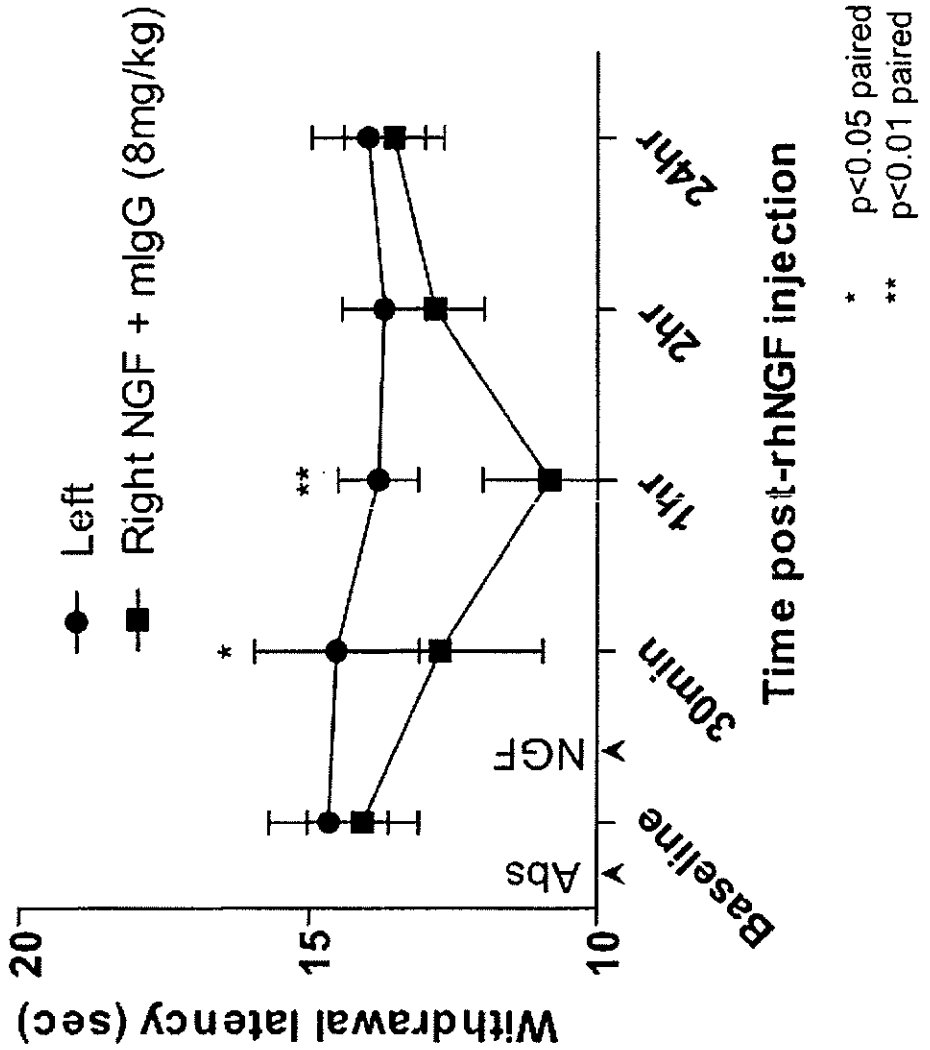


Figure 14 (continued)

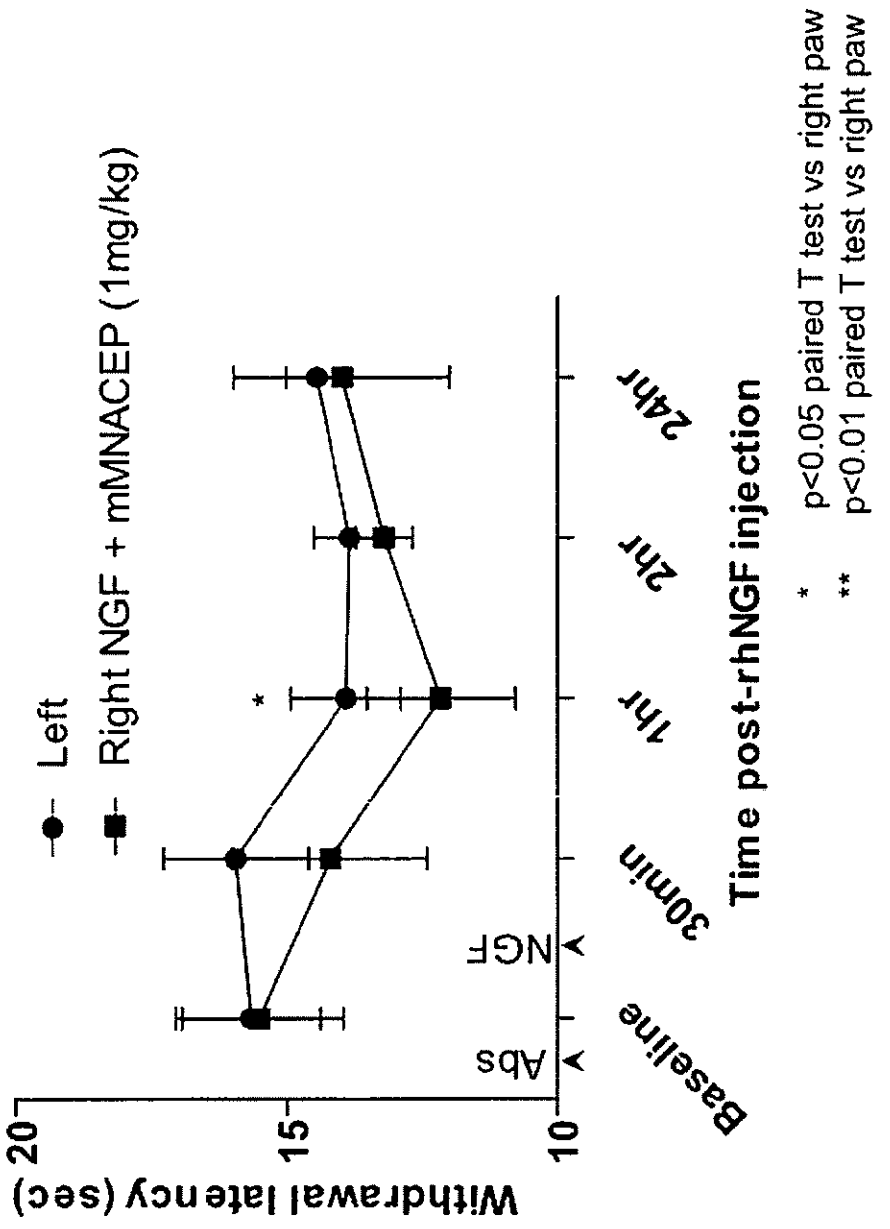


Figure 14 (continued)

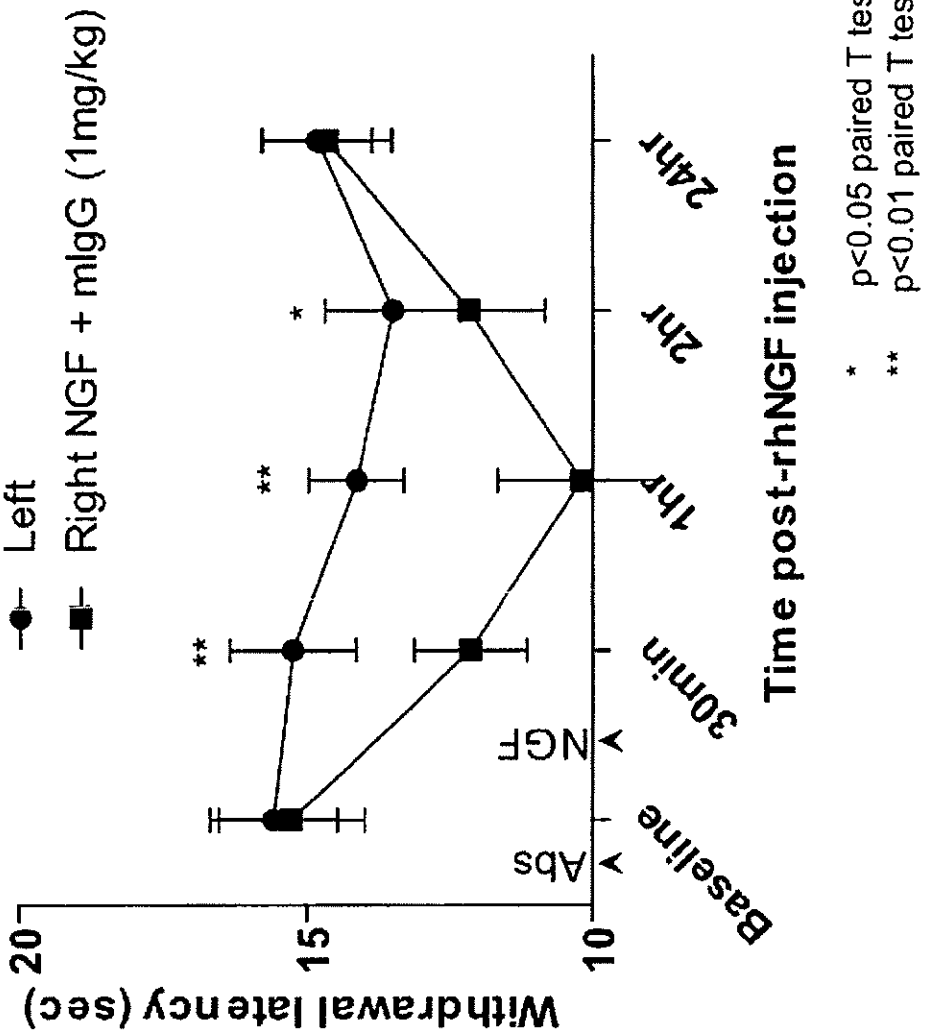


Figure 14 (continued)