
Breast Tumour Models
A
B
C
D
E
50 Kda
37 Kda
43 Kda

FIG. 1A

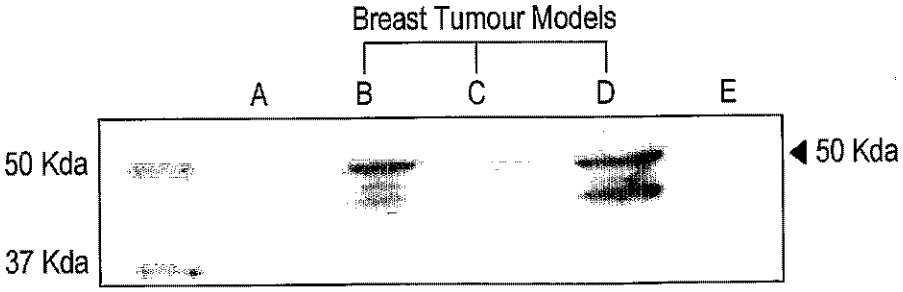

Breast Tumour Models
A
B
C
D
E
50 Kda
37 Kda
50 Kda

FIG. 1B

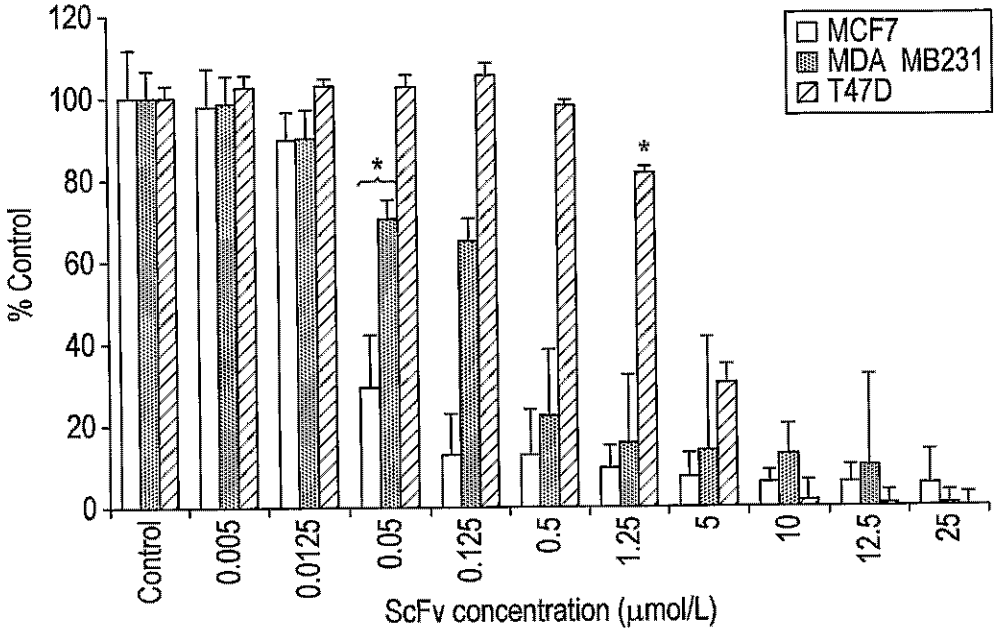

MCF7
MDA MB231
T47D
% Control
120
100
80
60
40
20
0
*
*
Control
0.005
0.0125
0.05
0.125
0.5
1.25
5
10
12.5
25
ScFv concentration (μmol/L)

FIG. 2A

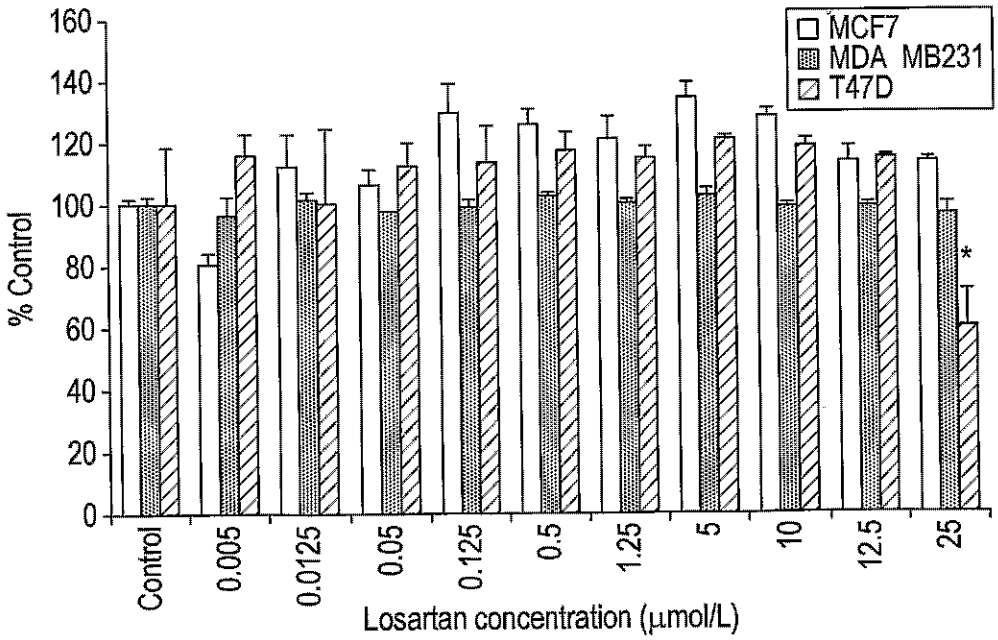

MCF7
MDA MB231
T47D
% Control
160
140
120
100
80
60
40
20
0
*
Control
0.005
0.0125
0.05
0.125
0.5
1.25
5
10
12.5
25
Losartan concentration (μmol/L)

FIG. 2B

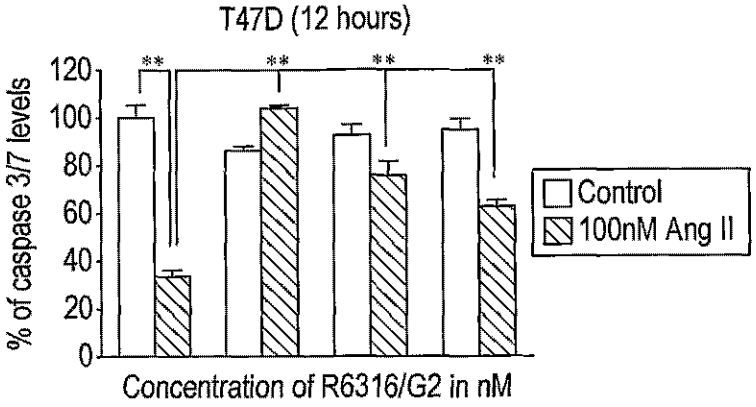


FIG. 3A

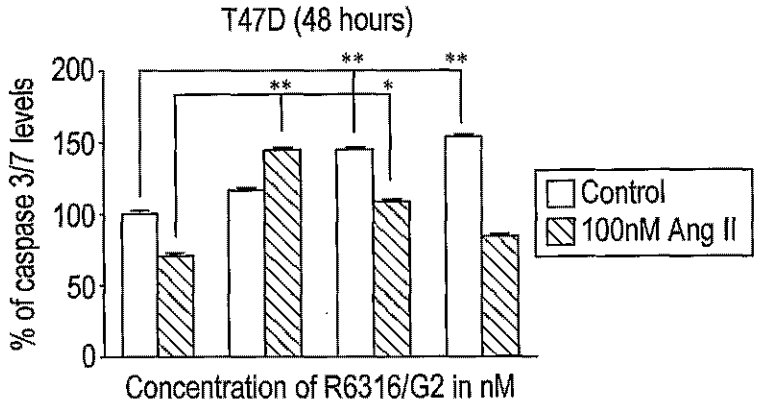


FIG. 3B

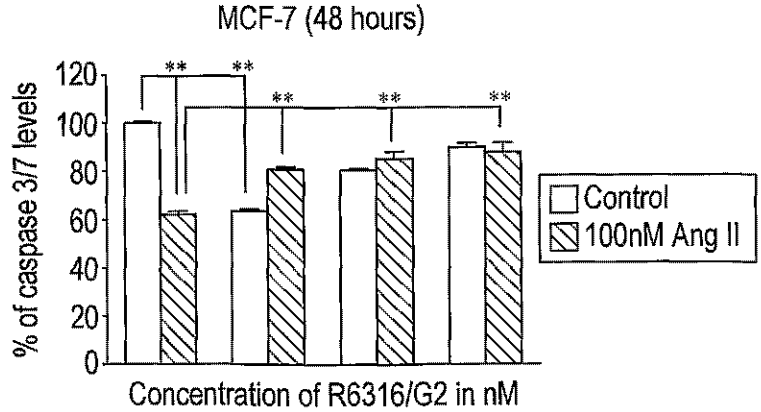


FIG. 3C

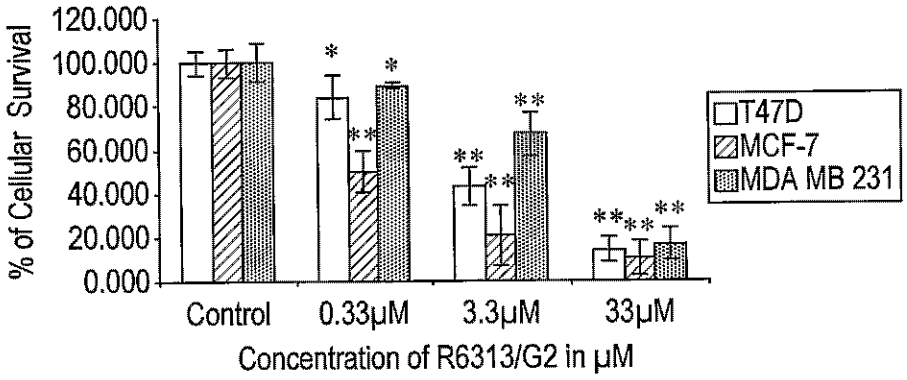

120.000
100.000
80.000
60.000
40.000
20.000
0.000
% of Cellular Survival
Control
0.33µM
3.3µM
33µM
Concentration of R6313/G2 in µM
T47D
MCF-7
MDA MB 231

FIG. 4A

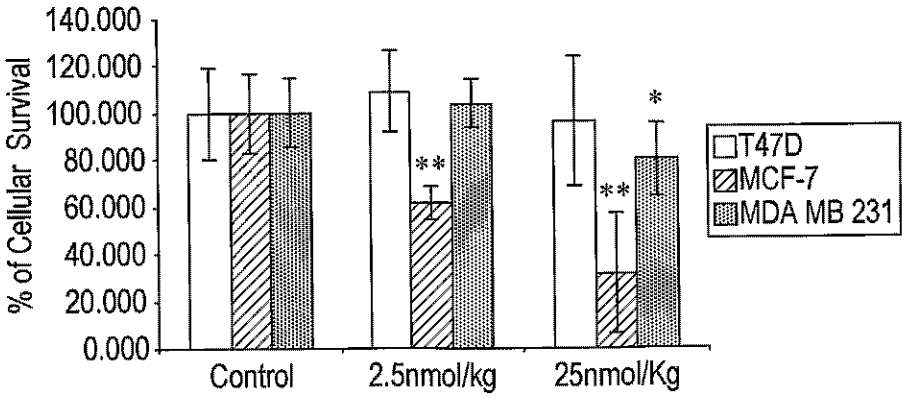

140.000
120.000
100.000
80.000
60.000
40.000
20.000
0.000
% of Cellular Survival
Control
2.5nmol/kg
25nmol/Kg
T47D
MCF-7
MDA MB 231

FIG. 4B

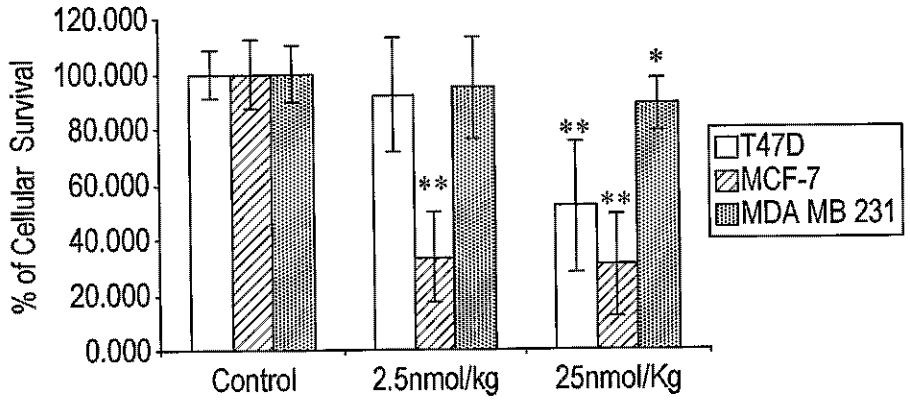

120.000
100.000
80.000
60.000
40.000
20.000
0.000
% of Cellular Survival
**
**
**
*
Control
2.5nmol/kg
25nmol/Kg
T47D
MCF-7
MDA MB 231

FIG. 4C

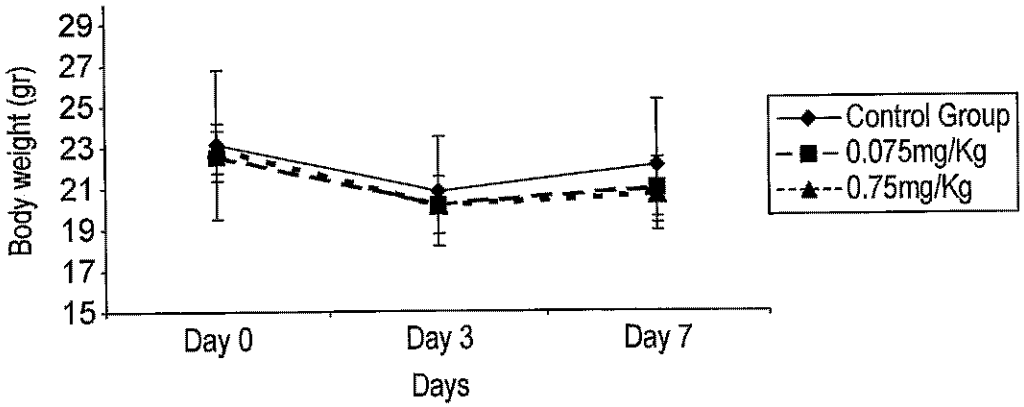

29
27
25
23
21
19
17
15
Body weight (gr)
Day 0
Day 3
Day 7
Days
Control Group
0.075mg/Kg
0.75mg/Kg

FIG. 4D

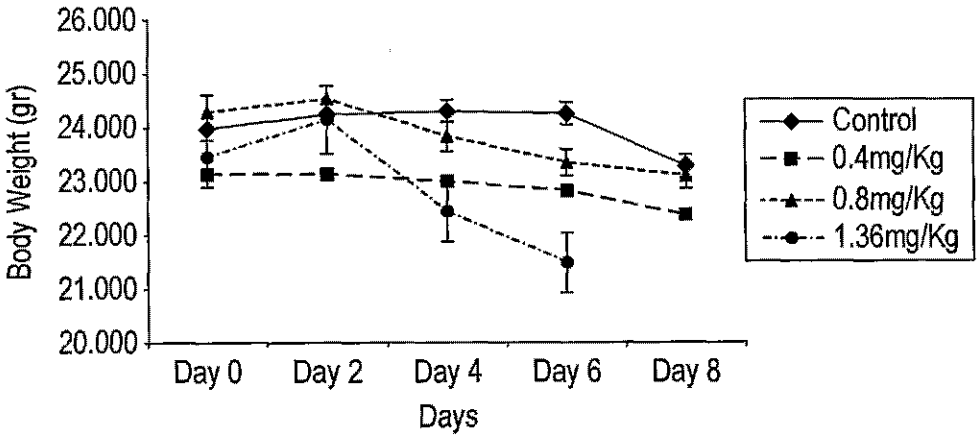


FIG. 5

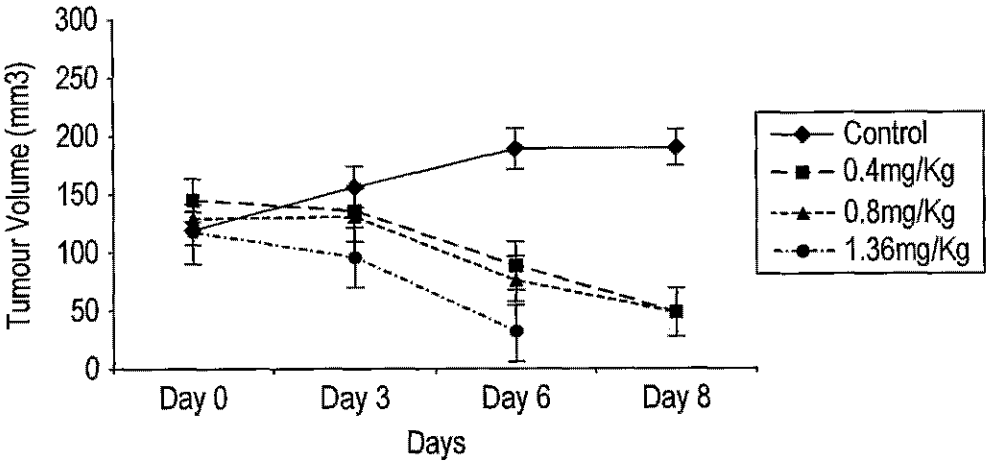


FIG. 6A

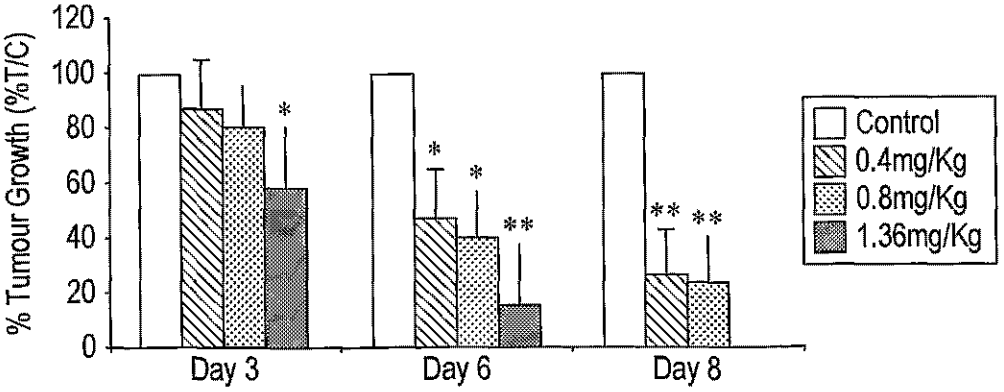


FIG. 6B

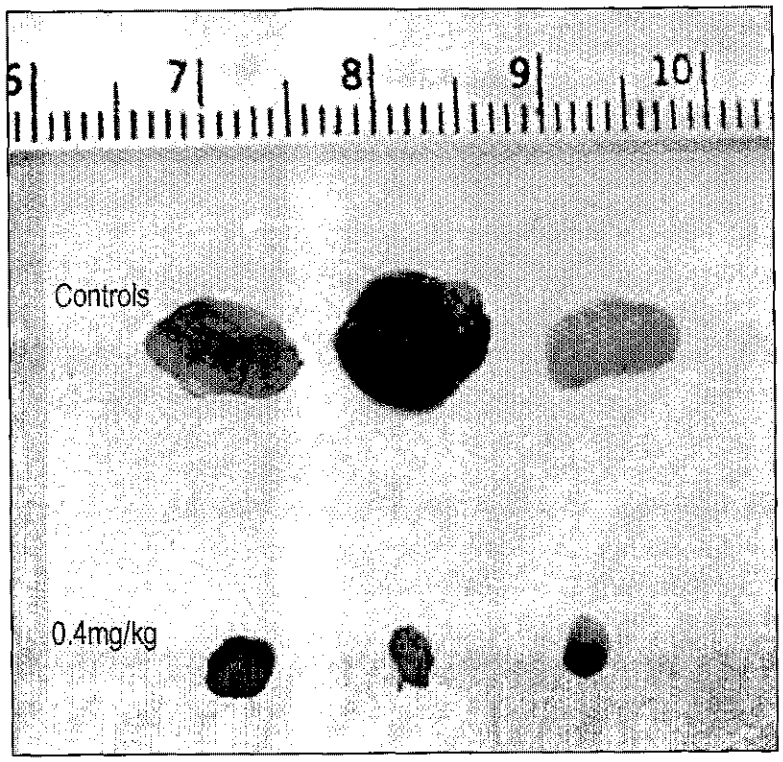

7
8
9
10
Controls
0.4mg/kg

FIG. 7

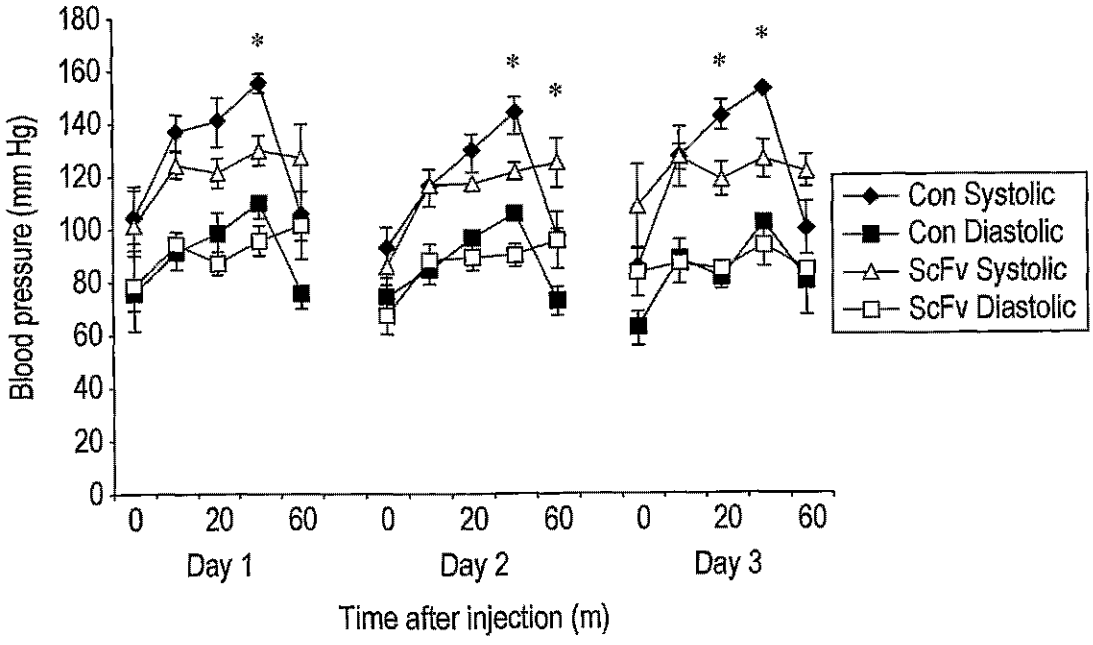

Blood pressure (mm Hg)
180
160
140
120
100
80
60
40
20
0
0
20
60
Day 1
Day 2
Day 3
Time after injection (m)
Con Systolic
Con Diastolic
ScFv Systolic
ScFv Diastolic

FIG. 8

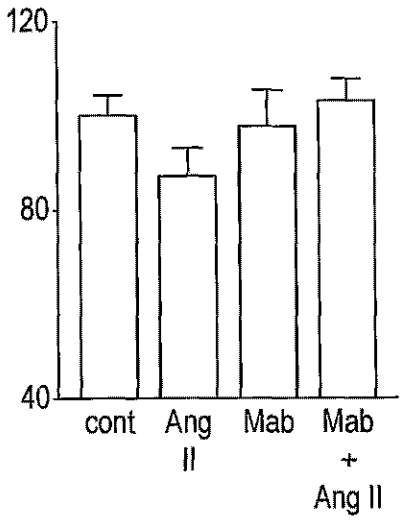

120
80
40
cont
Ang II
Mab
Mab + Ang II

FIG. 9A

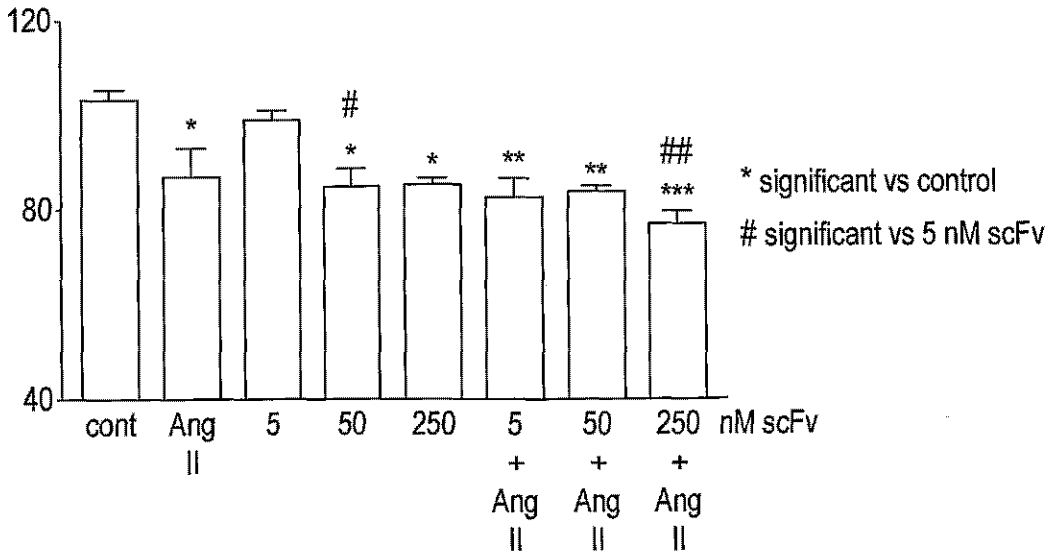

120
80
40
*
#
*
*
**
**
##
***
cont
Ang II
5
50
250
5 + Ang II
50 + Ang II
250 + Ang II
nM scFv
* significant vs control
# significant vs 5 nM scFv

FIG. 9B

```
CLUSTAL W (1.82) multiple sequence alignment

R6313clone12D   YAAQPAMAQVKLQQSGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNID
R6313clone11B   YAAQPAMAQVQLQESGPELEKPGASVKISCKASGYSFTGYNMSWVKQSNGKSLEWIGNID
                **********:**:****************************.*****************

R6313clone12D   PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
R6313clone11B   PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
                ************************************************************

R6313clone12D   SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
R6313clone11B   SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
                ************************************************************

R6313clone12D   GQPPRLLIYLVSNLESGVPARFSGSGSGTDFTLNIHPVEEEDAATYYCQHIRELTRSEGT
R6313clone11B   GQPPRLLIYLVSNLESGVPARFSGSGSGTDFTLNIHPVEEEDAATYYCQHIRELTRSEGT
                ************************************************************

R6313clone12D   KLEIKRAAAGAPVPY
R6313clone11B   KLEIKRAAAGAPVPY
                ***************
```

FIG. 10

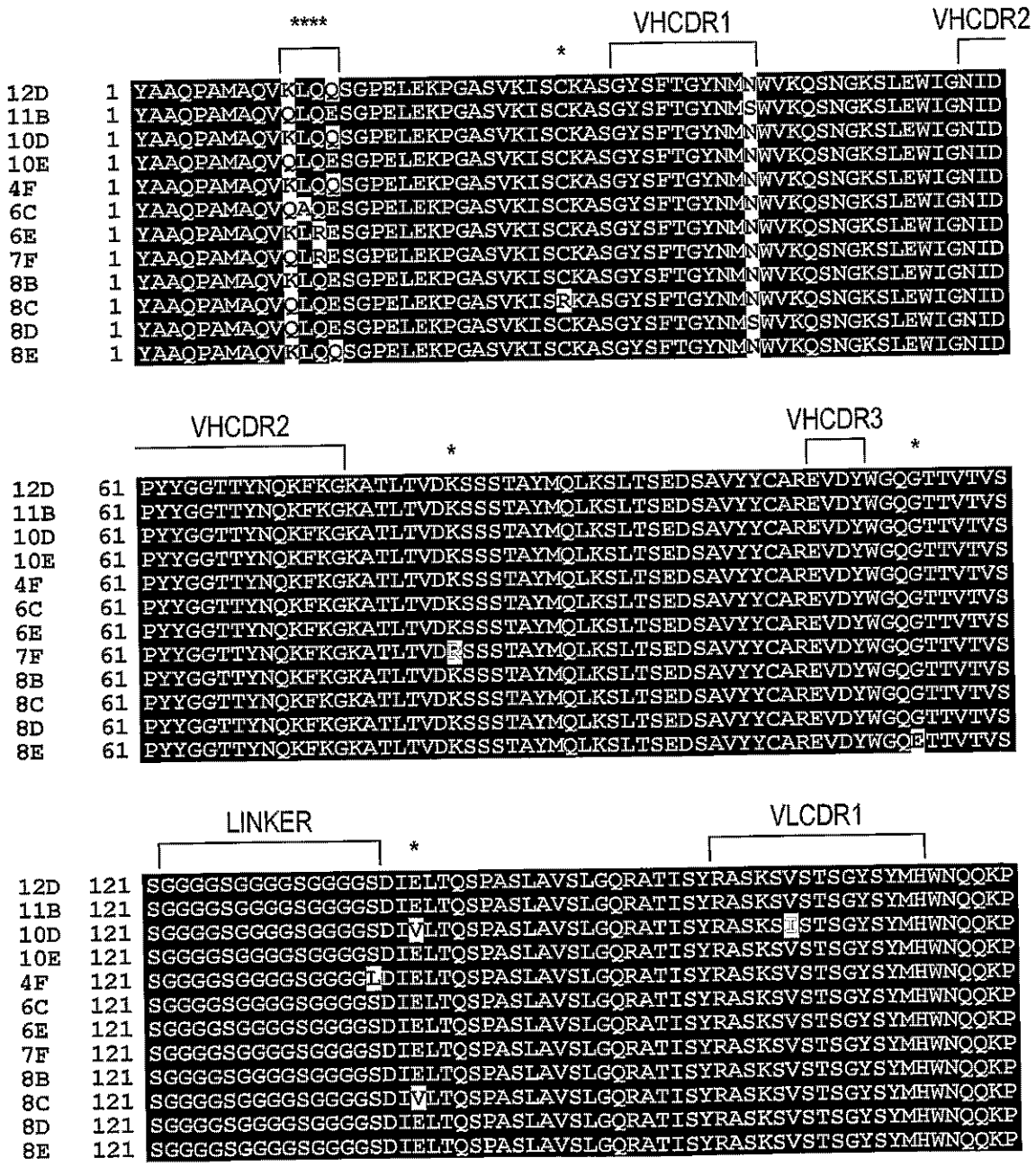

****
VHCDR1
VHCDR2
12D 1 YAAQPAMAQVKLQQSGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNID
11B 1 YAAQPAMAQVQLQESGPELEKPGASVKISCKASGYSFTGYNMSWVKQSNGKSLEWIGNID
10D 1 YAAQPAMAQVKLQQSGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNID
10E 1 YAAQPAMAQVQLQESGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNID
4F 1 YAAQPAMAQVKLQQSGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNID
6C 1 YAAQPAMAQVQAQESGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNID
6E 1 YAAQPAMAQVKLRESGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNID
7F 1 YAAQPAMAQVQLRESGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNID
8B 1 YAAQPAMAQVKLQESGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNID
8C 1 YAAQPAMAQVQLQESGPELEKPGASVKISRKASGYSFTGYNMNWVKQSNGKSLEWIGNID
8D 1 YAAQPAMAQVQLQESGPELEKPGASVKISCKASGYSFTGYNMSWVKQSNGKSLEWIGNID
8E 1 YAAQPAMAQVKLQQSGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNID
VHCDR2
VHCDR3
12D 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
11B 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
10D 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
10E 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
4F 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
6C 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
6E 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
7F 61 PYYGGTTYNQKFKGKATLTVDRSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
8B 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
8C 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVS
8D 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQETTVTVS
8E 61 PYYGGTTYNQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQETTVTVS
LINKER
VLCDR1
12D 121 SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
11B 121 SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
10D 121 SGGGGSGGGGSGGGGSDIVLTQSPASLAVSLGQRATISYRASKSISTSGYSYMHWNQQKP
10E 121 SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
4F 121 SGGGGSGGGGSGGGGLDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
6C 121 SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
6E 121 SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
7F 121 SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
8B 121 SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
8C 121 SGGGGSGGGGSGGGGSDIVLTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
8D 121 SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP
8E 121 SGGGGSGGGGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKP

FIG. 11A

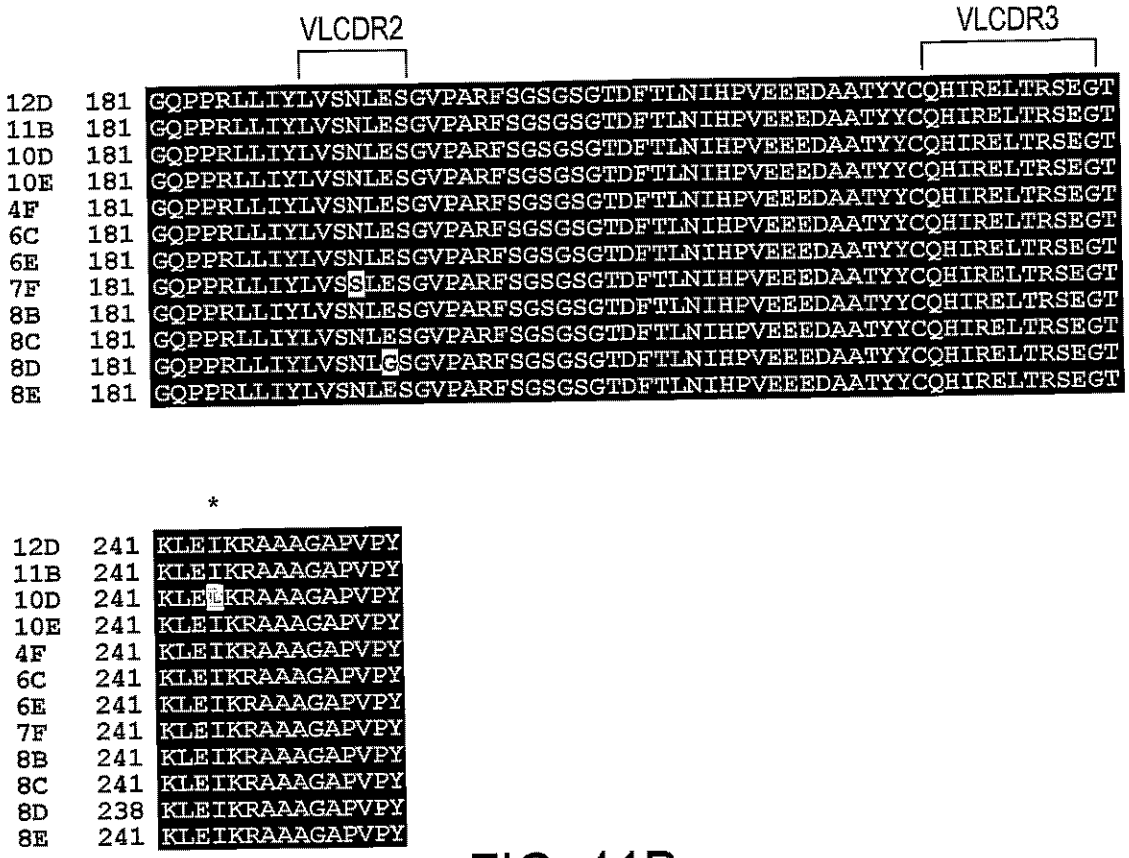


FIG. 11B

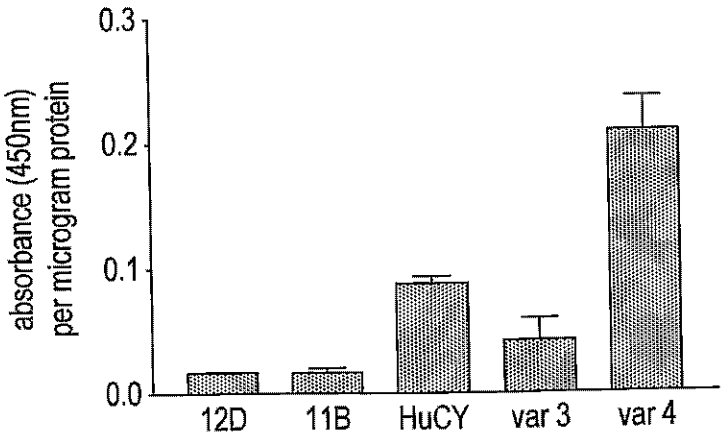


FIG. 12A

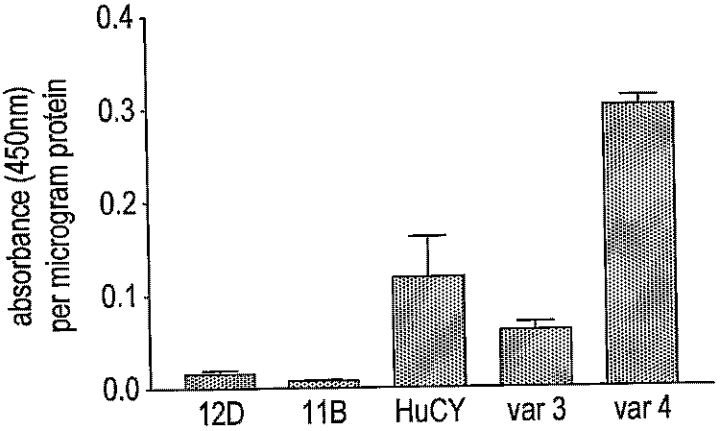


FIG. 12B

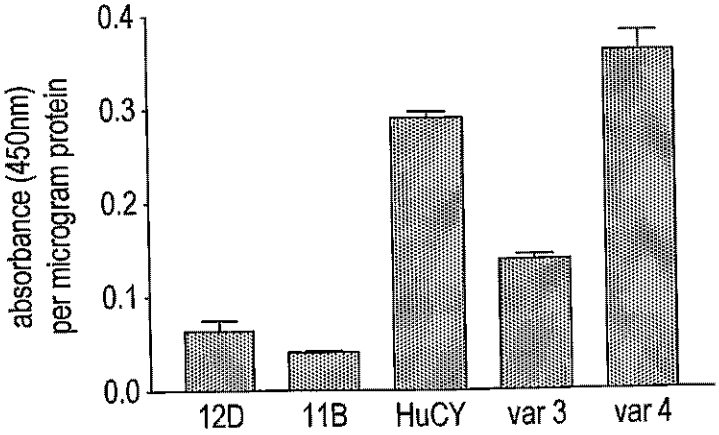


FIG. 12C

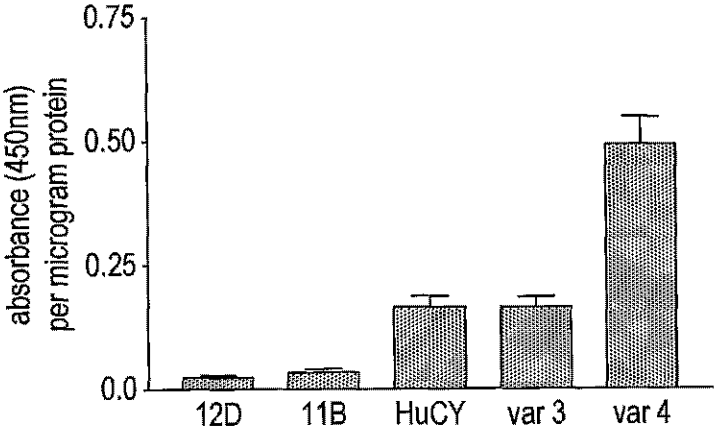


FIG. 12D

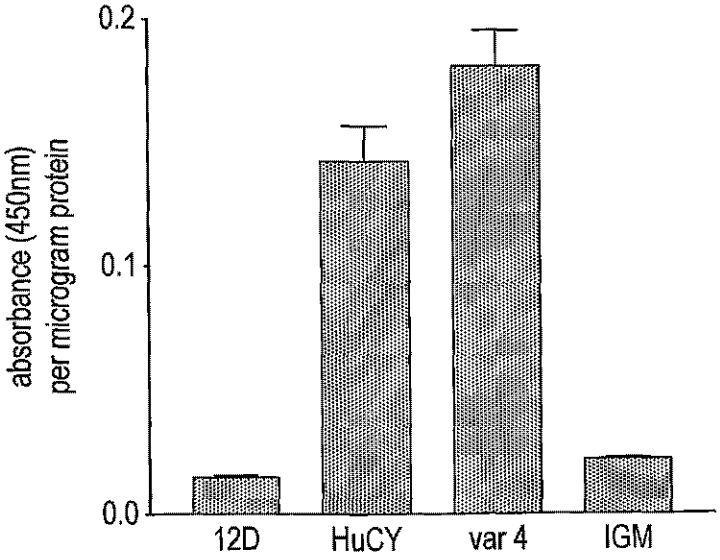


FIG. 13


12D 1 QVKLQQSGPELEKPGASVKISCKASGYSFTGYNMNWVKQSNGKSLEWIGNIDPYYGGTTY
11B 1 QVQLQESGPELEKPGASVKISCKASGYSFTGYNMSWVKQSNGKSLEWIGNIDPYYGGTTY
HuCY 1 QVQLVQSGPELVKPGASVKISCKASGYSFTGYNMNWVKQAPGKSLEWIGNIDPYYGGTTY
var3 1 QVQLVQSGPELVKPGASVKISCKASGYSFTGYNMNWVKQAPGKGLEWIGNIDPYYGGTTY
var4 1 QVQLVQSGPELVKPGASVKISCKASGYSFTGYNMNWVKQAPGKGLEWIGNIDPYYGGTTY
12D 61 NQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVSSGGGSGG
11B 61 NQKFKGKATLTVDKSSSTAYMQLKSLTSEDSAVYYCAREVDYWGQGTTVTVSSGGGSGG
HuCY 61 NQKFKGKATLTVDKSSSTAYMQLKSLRSEDTAVYYCAREVDYWGQGTTVTVSSGGGSGG
var3 61 NQKFKGKATLTVDKSSSTAYMQLKSLRSEDTAVYYCAREVDYWGQGTTVTVSSGGGSGG
var4 61 NQKFKGKATLTVDKSSSTAYMQLKSLRSEDTAVYYCAREVDYWGQGTTVTVSSGGGSGG
12D 121 GGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKPGQPPRLLI
11B 121 GGSGGGGSDIELTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKPGQPPRLLI
HuCY 121 GGSGGGGSDIVLTQSPASLAVSLGERATISCRASKSVSTSGYSYMHWYQQKPGQPPRLLI
var3 121 GGSGGGGSDIVLTQSPASLAVSLGERATISCRASKSVSTSGYSYMHWYQQKPGQPPRLLI
var4 121 GGSGGGGSDIVLTQSPASLAVSLGERATISCRASKSVSTSGYSYMHWYQQKPGQPPRLLI
12D 181 YLVSNLESGVPARFSGSGSGTDFTLNIHPVEEEDAATYYCQHIRELTRSEGTKLEIKR
11B 181 YLVSNLESGVPARFSGSGSGTDFTLNIHPVEEEDAATYYCQHIRELTRSEGTKLEIKR
HuCY 181 YLVSNLESGVPDRFSGSGSGTDFTLTISSVEAEDVAVYYCQHIRELTRSEGTKLEIKR
var3 181 YLVSNLESGVPDRFSGSGSGTDFTLTISSVEAEDVAVYYCQHIRELTRSEGTKLEIKR
var4 181 YLVSDLEDGVPDRFSGSGSGTDFTLTISSVEAEDVAVYYCQHIRELTRSEGTKLEIKR

FIG. 14

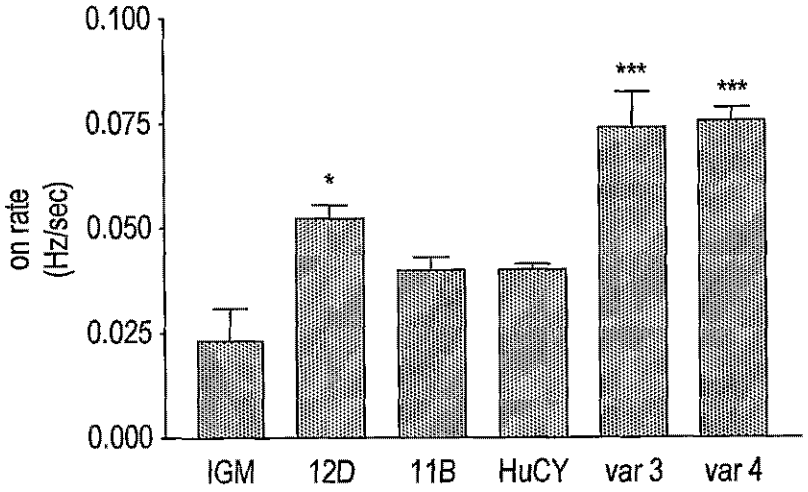


FIG. 15A

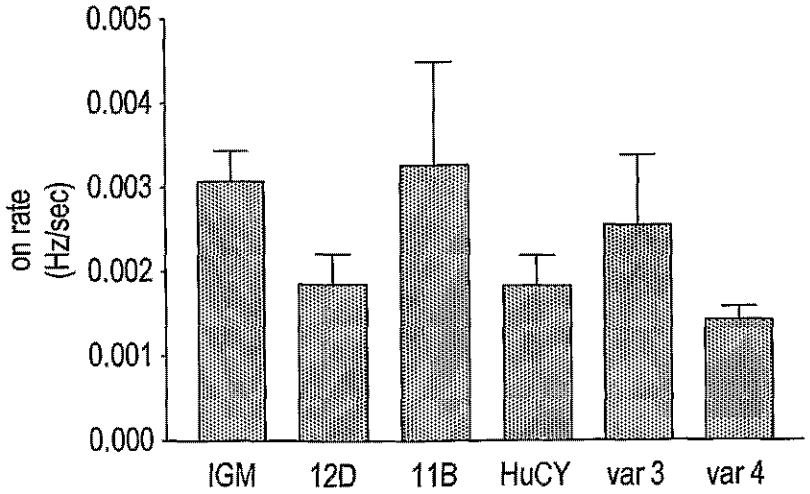


FIG. 15B