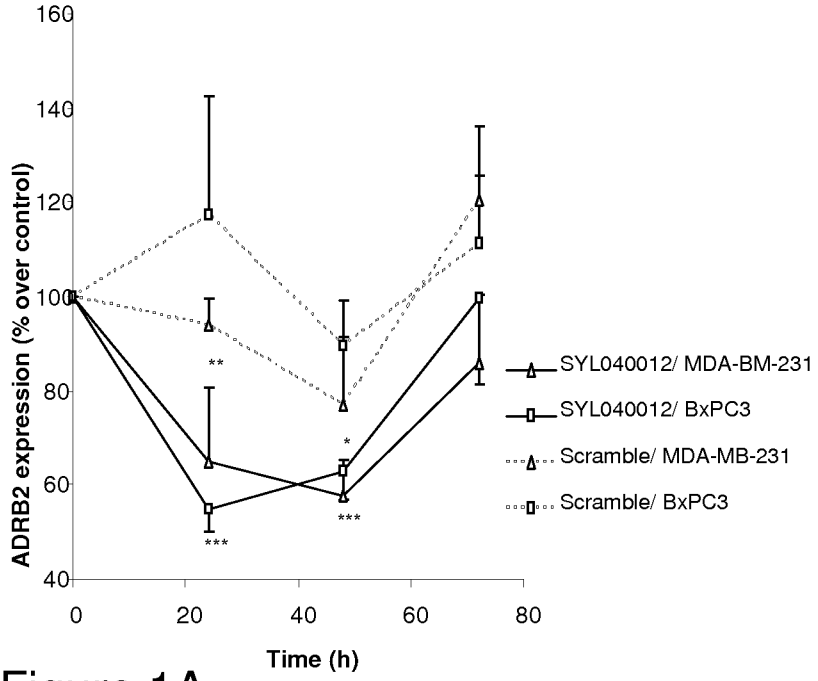

160
140
120
100
80
60
40
ADRB2 expression (% over control)
0
20
40
60
80
Time (h)
**
*
***
***
SYL040012/ MDA-BM-231
SYL040012/ BxPC3
Scramble/ MDA-MB-231
Scramble/ BxPC3

Figure 1A

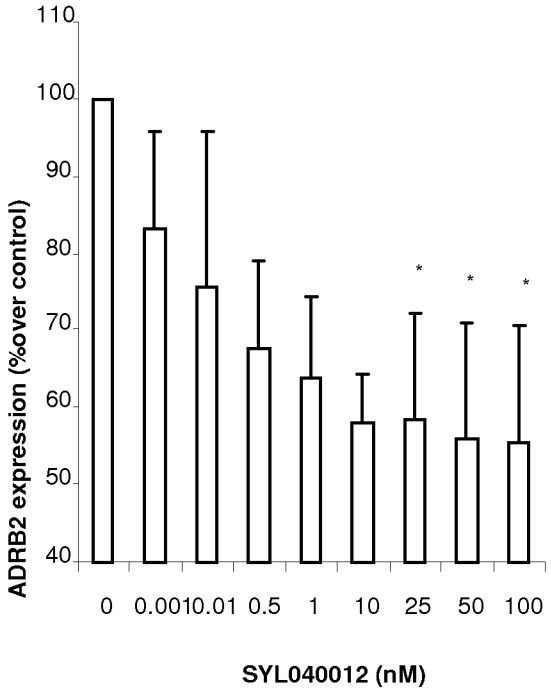

110
100
90
80
70
60
50
40
ADRB2 expression (%over control)
0
0.001
0.01
0.5
1
10
25
50
100
*
*
*
SYL040012 (nM)

Figure 1B

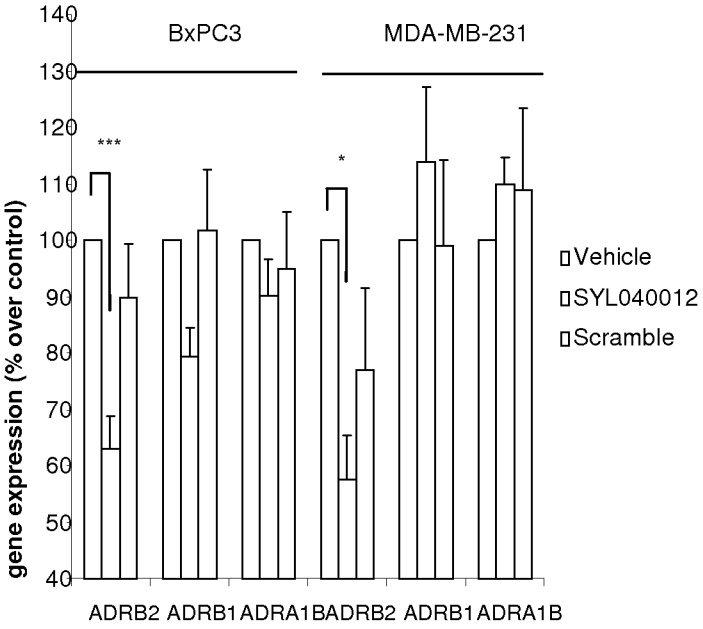
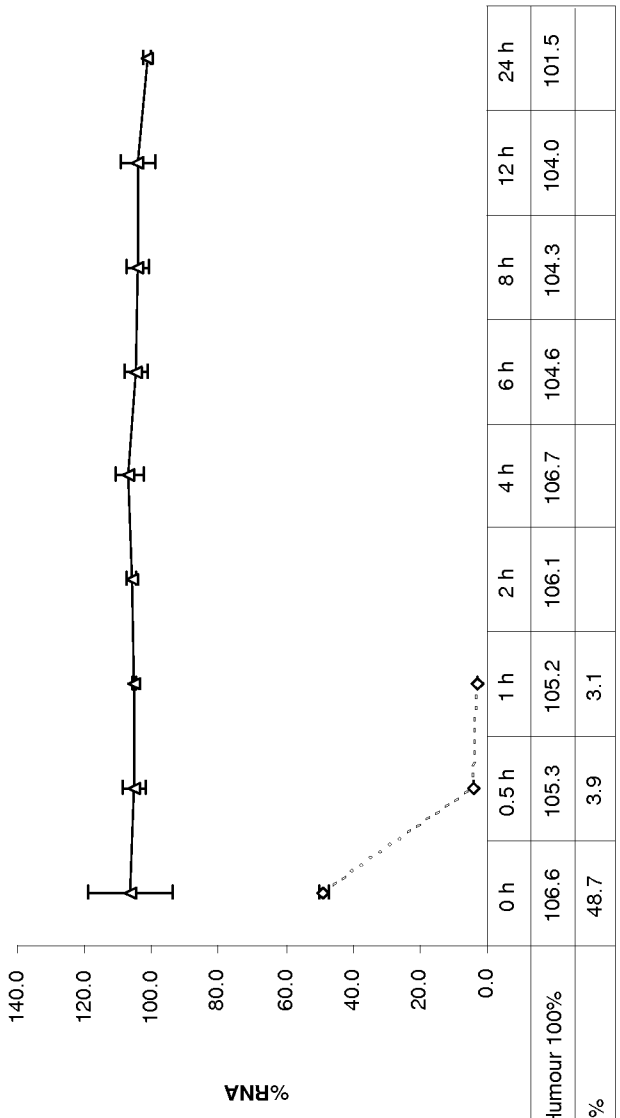

BxPC3
MDA-MB-231
***
*
gene expression (% over control)
140
130
120
110
100
90
80
70
60
50
40
Vehicle
SYL040012
Scramble
ADRB2 ADRB1 ADRA1B ADRB2 ADRB1 ADRA1B

Figure 1C



	0 h	0.5 h	1 h	2 h	4 h	6 h	8 h	12 h	24 h
Rabbit Aqueous Humour 100%	106.6	105.3	105.2	106.1	106.7	104.6	104.3	104.0	101.5
Rabbit serum 100%	48.7	3.9	3.1						

Figure 2

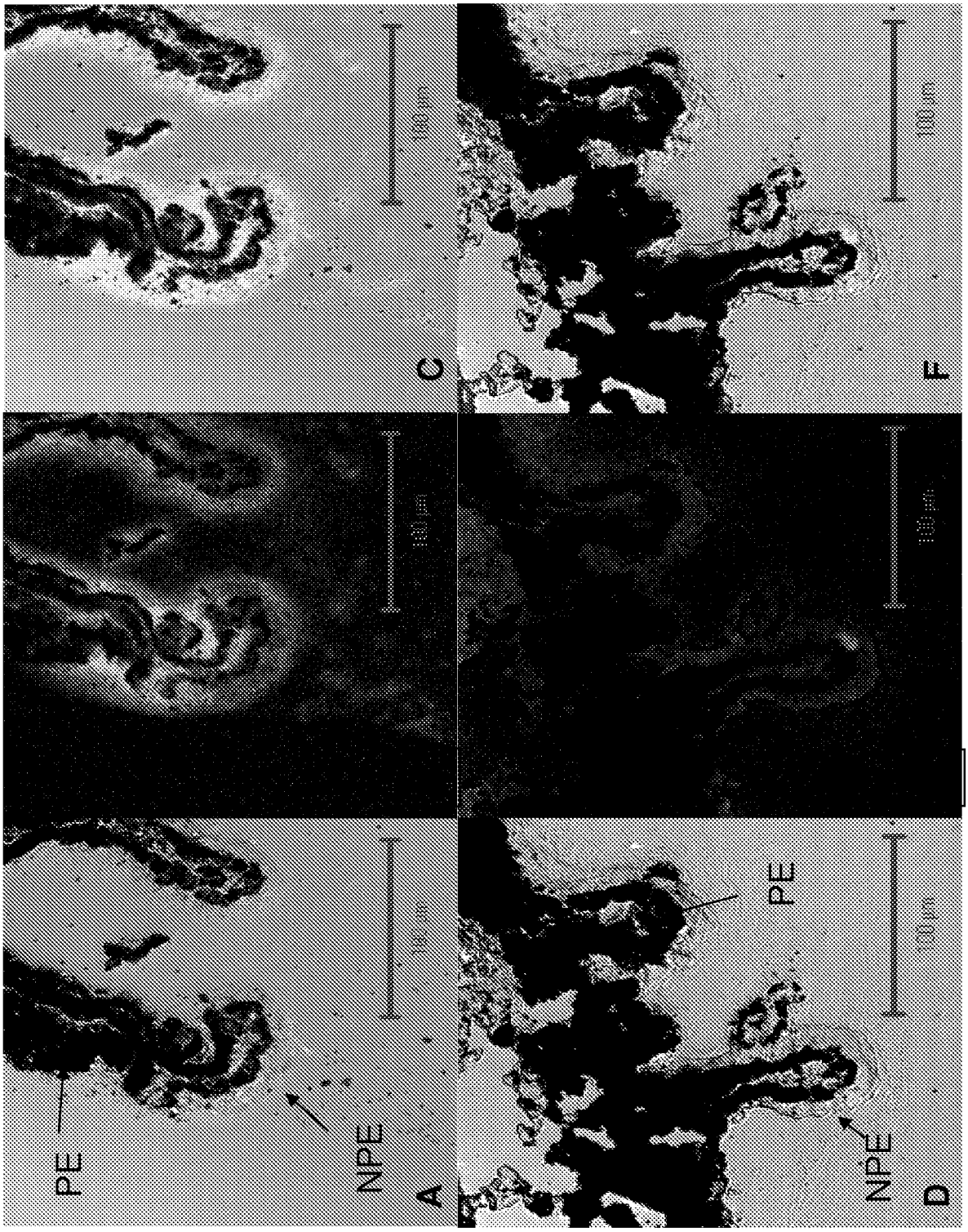


Figure 3A to 3F

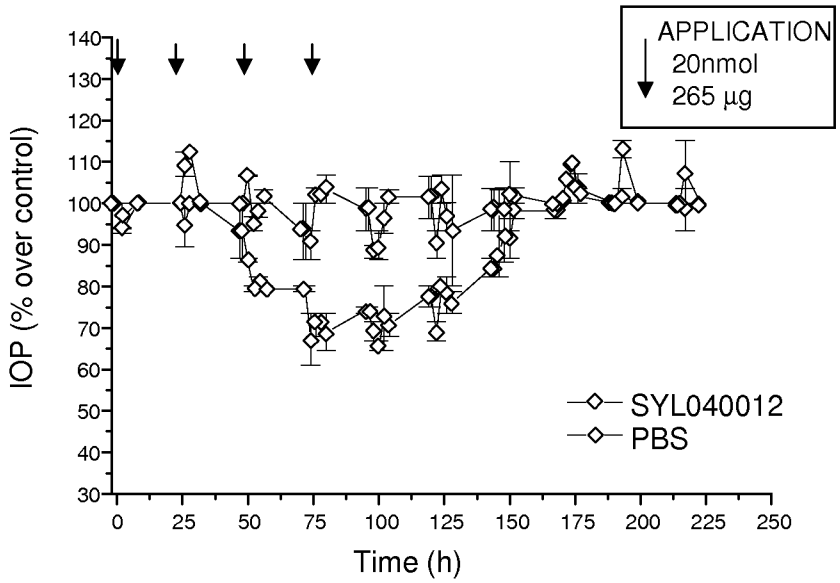

APPLICATION
20nmol
265 µg
IOP (% over control)
Time (h)
SYL040012
PBS
140
130
120
110
100
90
80
70
60
50
40
30
0
25
50
75
100
125
150
175
200
225
250

Figure 4A

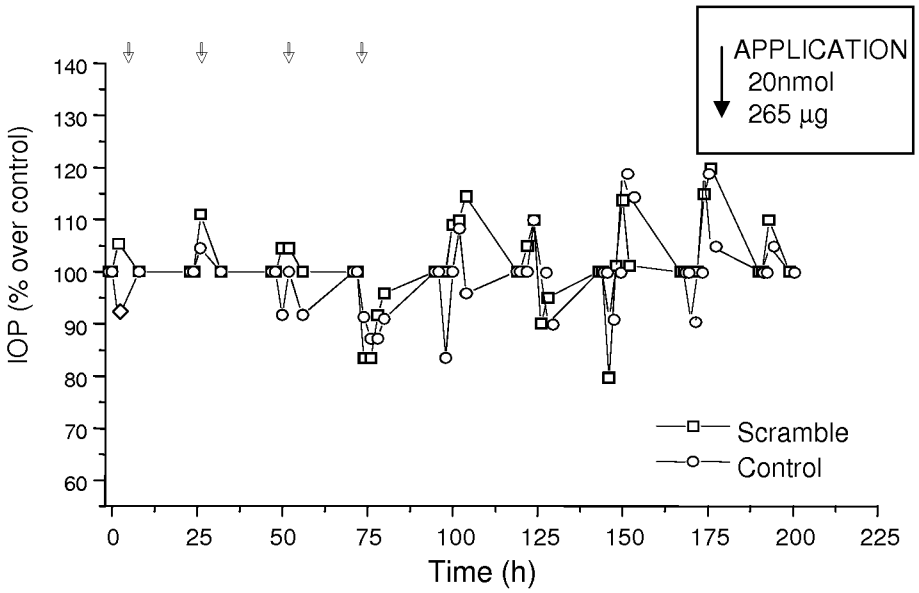

APPLICATION
20nmol
265 µg
IOP (% over control)
140
130
120
110
100
90
80
70
60
0
25
50
75
100
125
150
175
200
225
Time (h)
Scramble
Control

Figure 4B

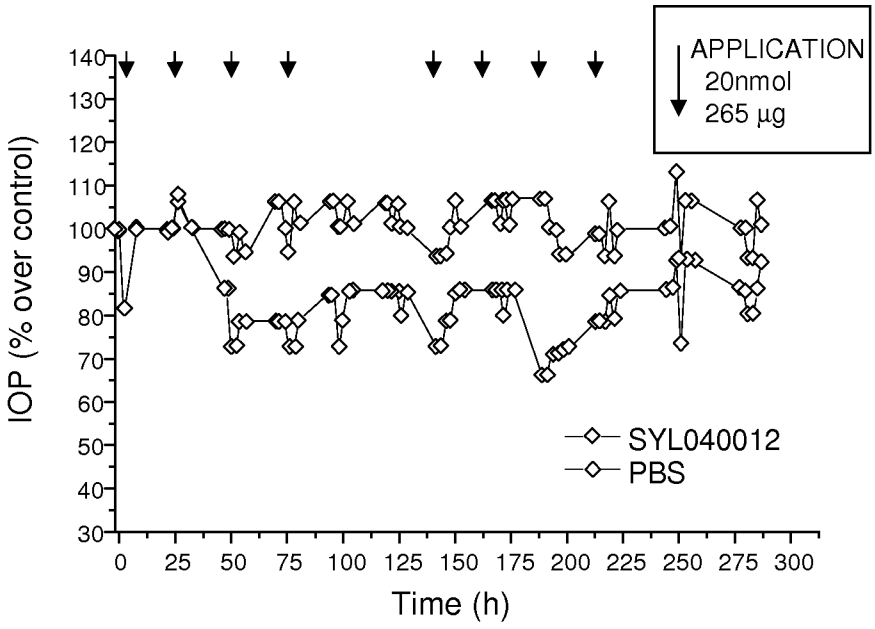

APPLICATION
20nmol
265 µg
IOP (% over control)
140
130
120
110
100
90
80
70
60
50
40
30
0
25
50
75
100
125
150
175
200
225
250
275
300
Time (h)
SYL040012
PBS

Figure 4C

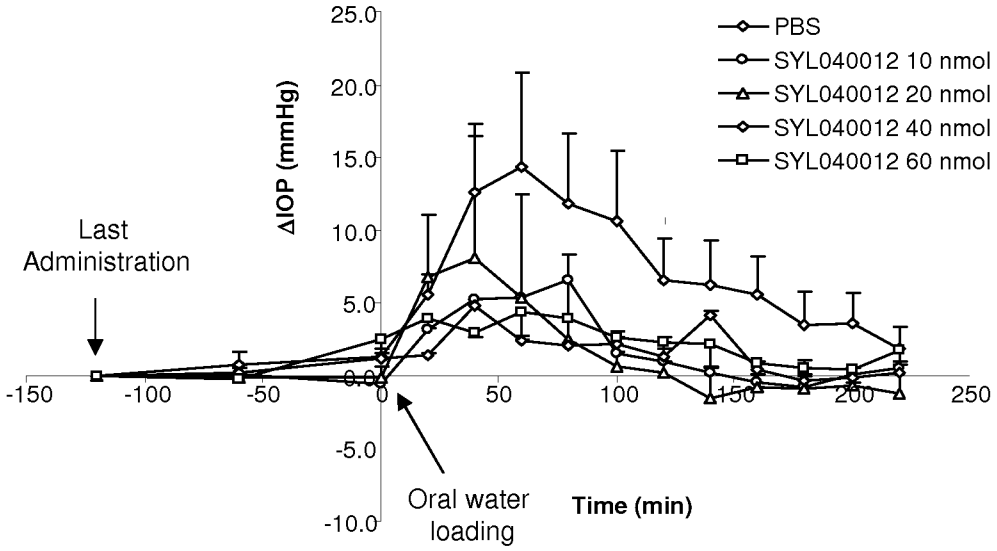

25.0
20.0
15.0
10.0
5.0
0.0
-5.0
-10.0
ΔIOP (mmHg)
-150
-100
-50
0
50
100
150
200
250
Time (min)
PBS
SYL040012 10 nmol
SYL040012 20 nmol
SYL040012 40 nmol
SYL040012 60 nmol
Last Administration
Oral water loading

Figure 5A

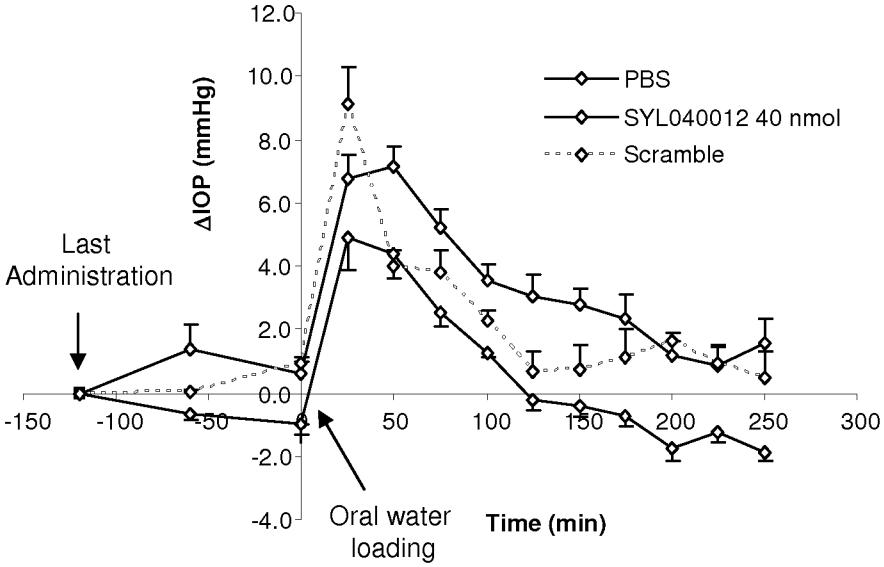

12.0
10.0
8.0
6.0
4.0
2.0
0.0
-2.0
-4.0
ΔIOP (mmHg)
PBS
SYL040012 40 nmol
Scramble
Last Administration
Oral water loading
Time (min)
-150
-100
-50
50
100
150
200
250
300

Figure 5B

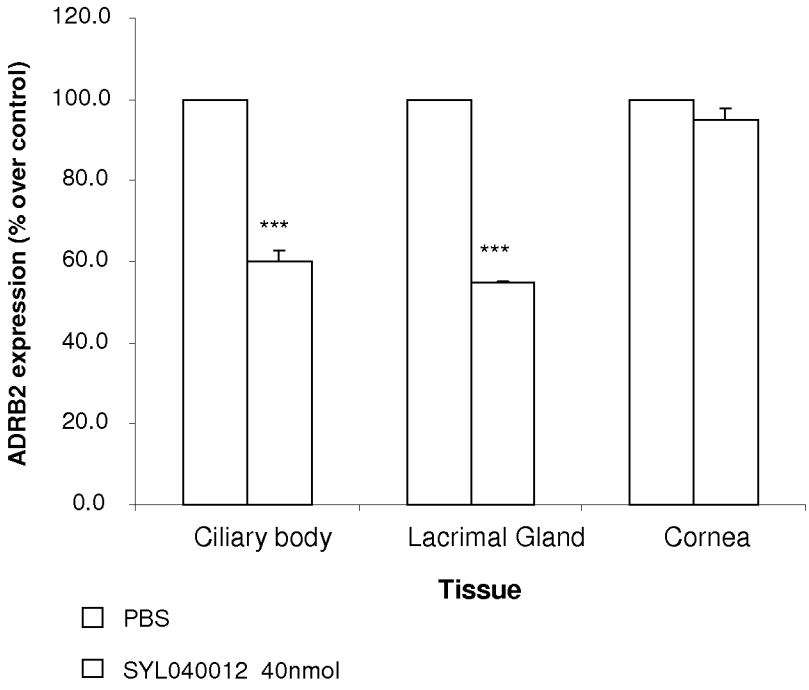

120.0
100.0
80.0
60.0
40.0
20.0
0.0
ADRB2 expression (% over control)
***
***
Ciliary body
Lacrimal Gland
Cornea
Tissue
PBS
SYL040012 40nmol

Figure 5C

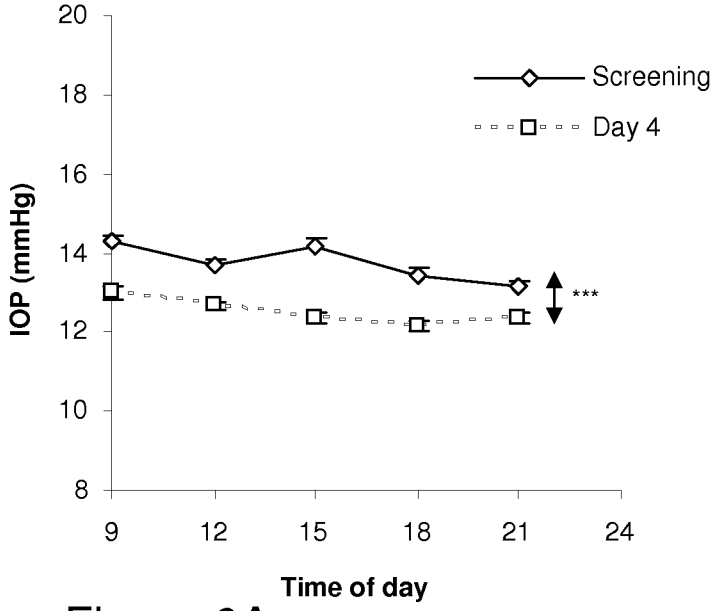


Figure 6A

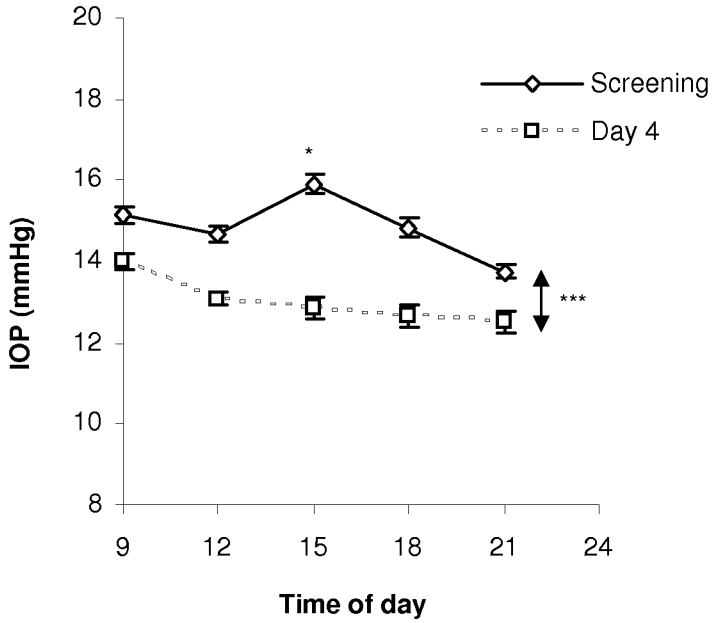


Figure 6B

SEQ ID NO: 1

Human ADRB2 mRNA target sequence: CAUUGUGCAUGUGAUCCAG

SEQ ID NO: 2

SYL040012: Sense	5' - CAUUGUGCAUGUGAUCCAG dT dT - 3'
Antisense	3'- dT dT GUAACACGUACACUAGGUC - 5'

SEQ ID NO: 3

Sense	5' - CAUUGUGCAUGUGAUCCAG- 3'
Antisense	3'- GUAACACGUACACUAGGUC - 5'

SEQ ID NO: 4

Sense	5' - CAUUGUGCAUGUGAUCCAG - 3'
Antisense	3'- dT dT GUAACACGUACACUAGGUC - 5'

SEQ ID NO: 5

Sense	5' - CAUUGUGCAUGUGAUCCAG dT dT - 3'
Antisense	3'- GUAACACGUACACUAGGUC - 5'

SEQ ID NO: 6

Sense	5' - CAUUGUGCAUGUGAUCCAG dU dU - 3'
Antisense	3'- dU dU GUAACACGUACACUAGGUC - 5'

Underline represents hybridization region

Figure 7