Figure 1A

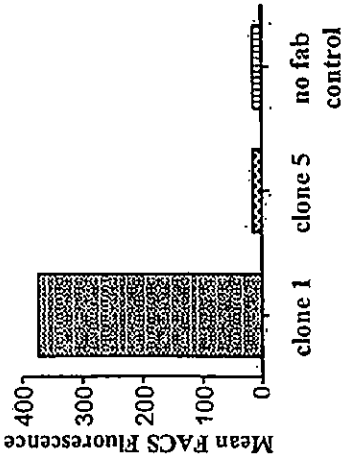


Figure 1B

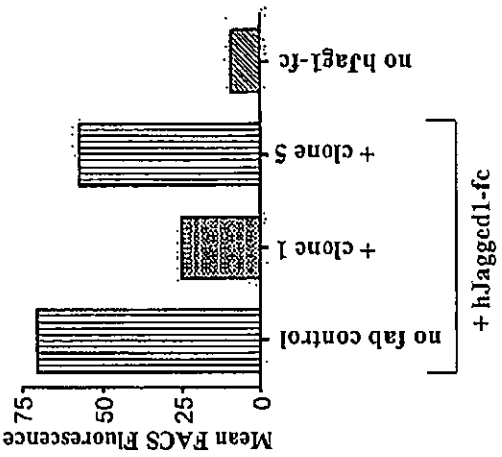


Figure 1D

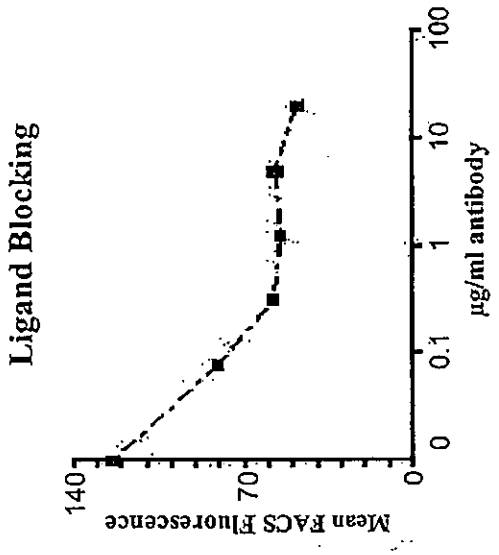


Figure 1C

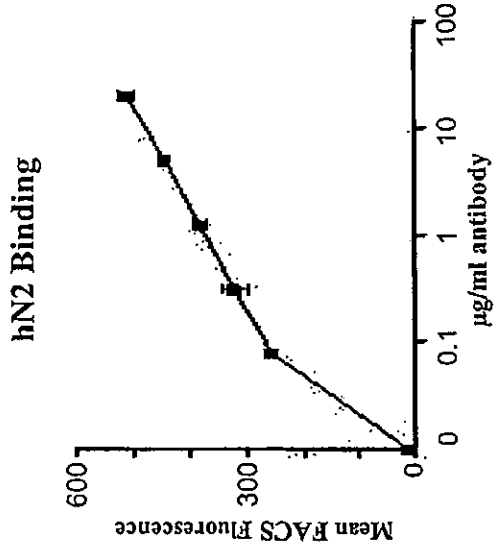


Figure 1E

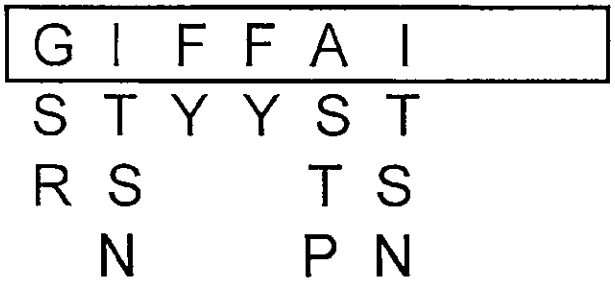


Figure 1F

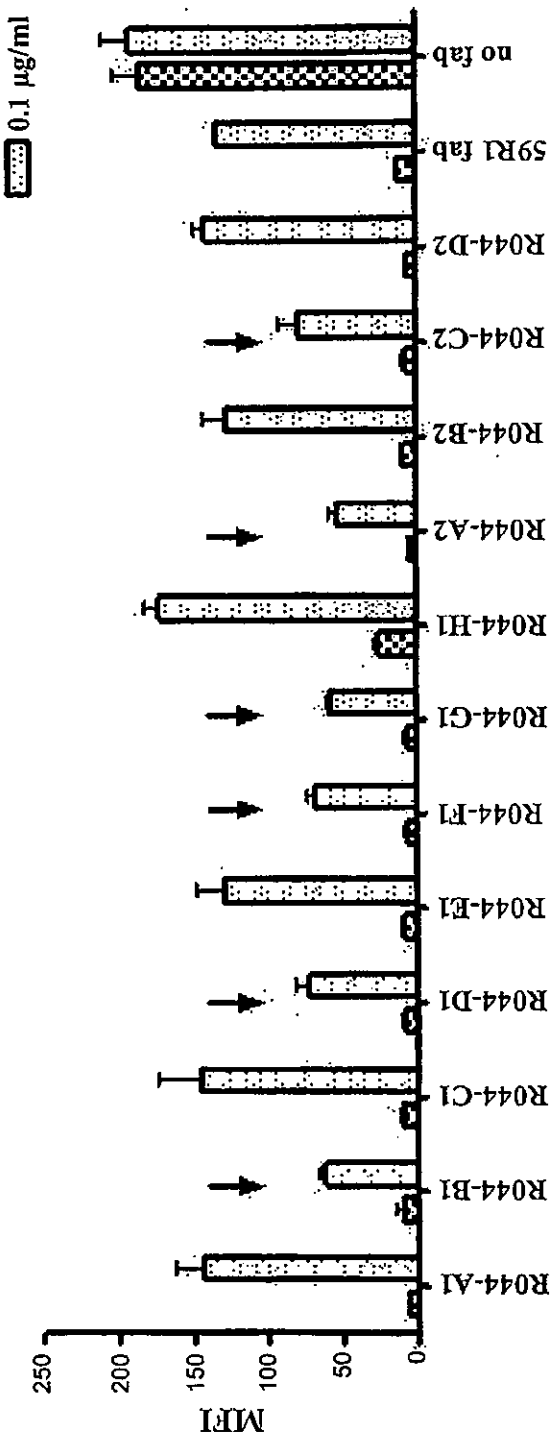

10 µg/ml
0.1 µg/ml
MFI
250
200
150
100
50
0
no fab
59R1 fab
R044-D2
R044-C2
R044-B2
R044-A2
R044-H1
R044-G1
R044-F1
R044-E1
R044-D1
R044-C1
R044-B1
R044-A1

Figure 2

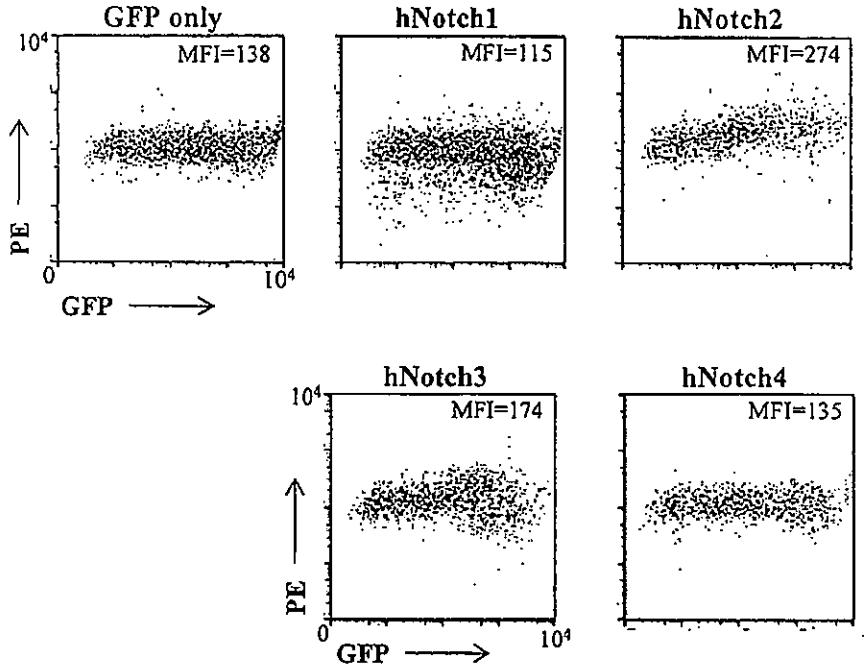
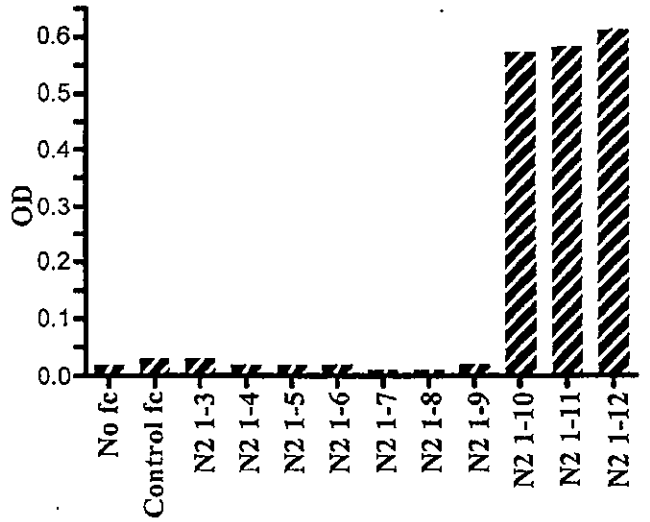

GFP only
MFI=138
hNotch1
MFI=115
hNotch2
MFI=274
hNotch3
MFI=174
hNotch4
MFI=135
PE
GFP
0
10⁴

Figure 3A


OD
0.0
0.1
0.2
0.3
0.4
0.5
0.6
No fc
Control fc
N2 1-3
N2 1-4
N2 1-5
N2 1-6
N2 1-7
N2 1-8
N2 1-9
N2 1-10
N2 1-11
N2 1-12

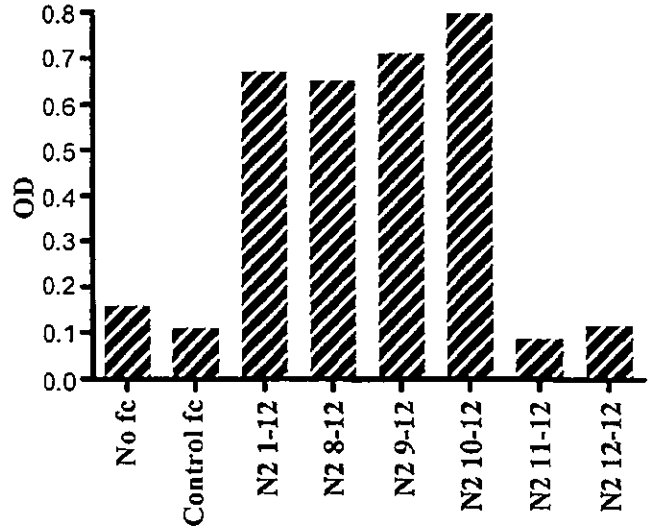
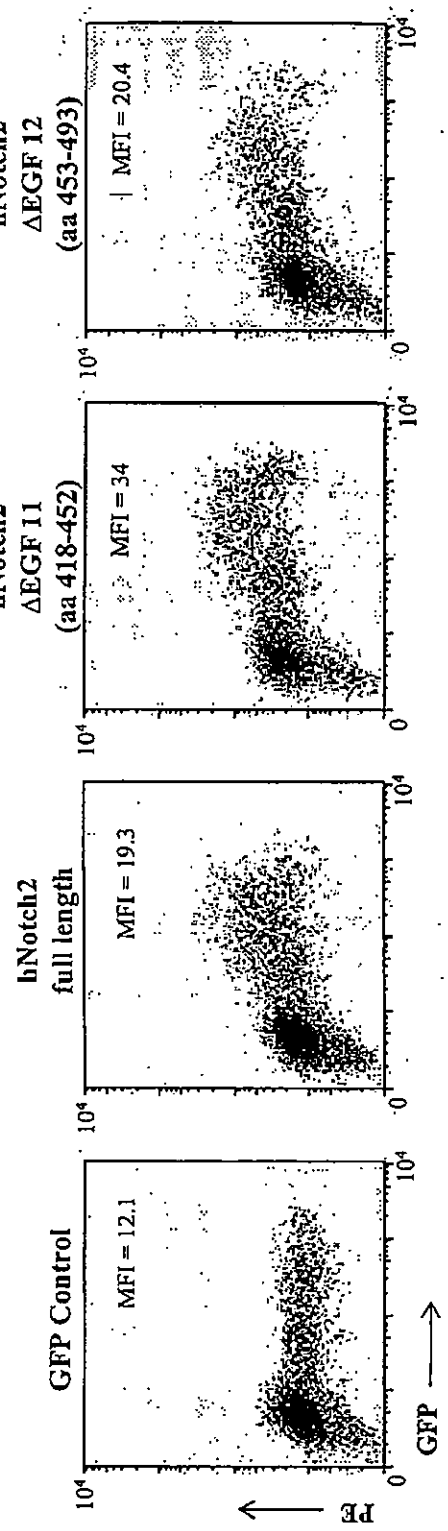

OD
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
No fc
Control fc
N2 1-12
N2 8-12
N2 9-12
N2 10-12
N2 11-12
N2 12-12

Figure 3B



SUBSTITUTE SHEET (RULE 26)

Figure 3C

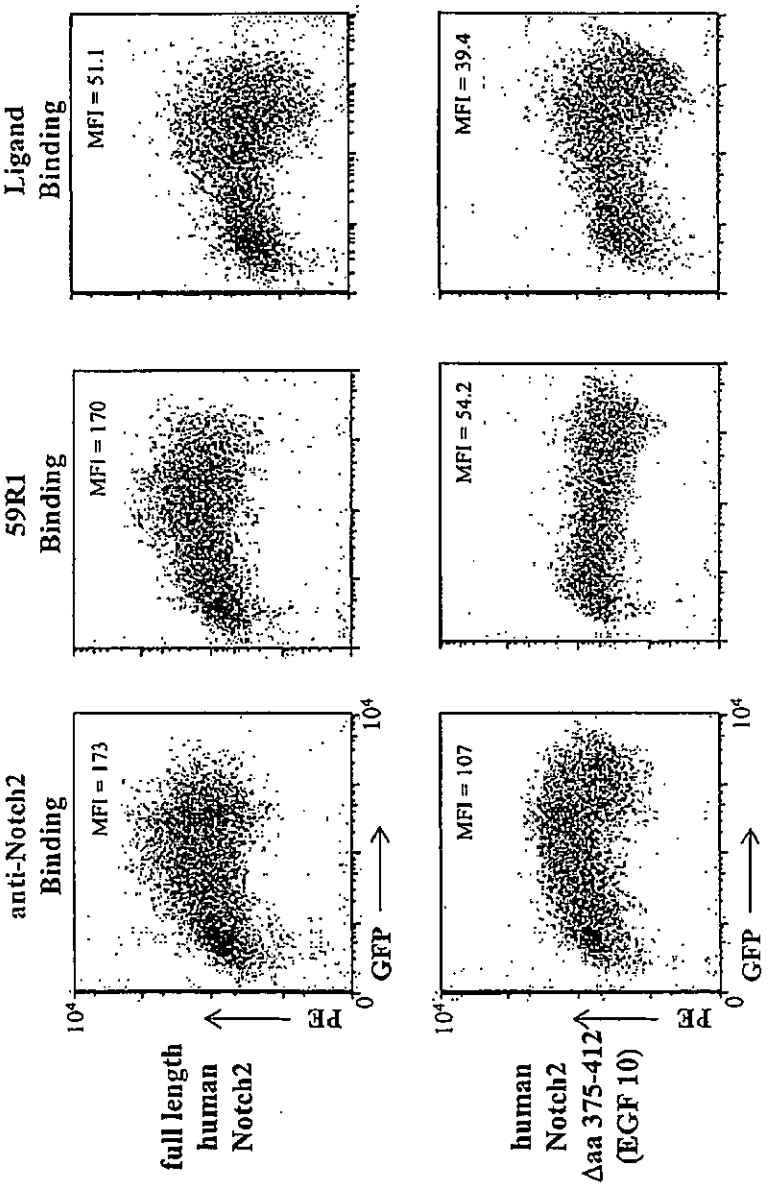

anti-Notch2 Binding
59R1 Binding
Ligand Binding
MFI = 173
MFI = 170
MFI = 51.1
MFI = 107
MFI = 54.2
MFI = 39.4
full length human Notch2
human Notch2 Δaa 375-412 (EGF 10)
PE
GFP
0
10^4

Figure 4A

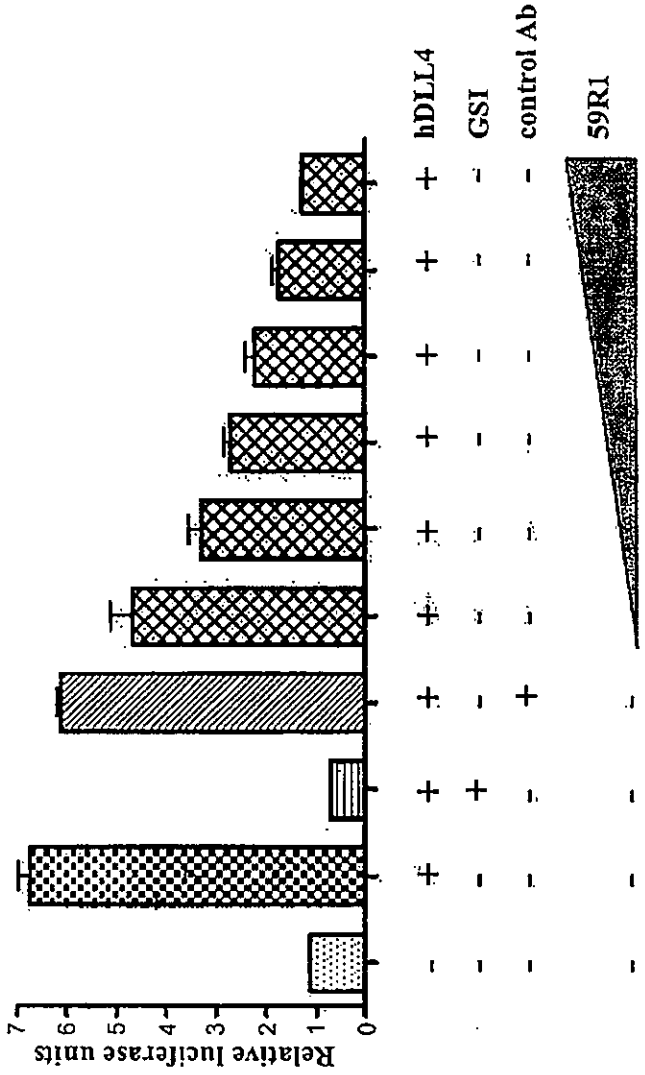

Relative luciferase units
0
1
2
3
4
5
6
7
hDLL4
GSI
control Ab
59R1

Figure 4B

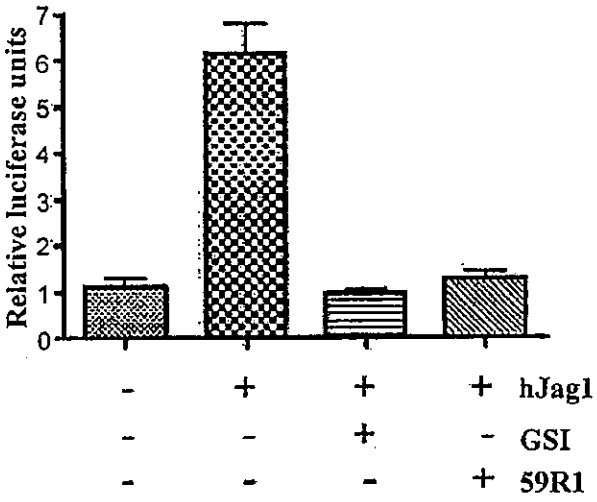


Figure 4C

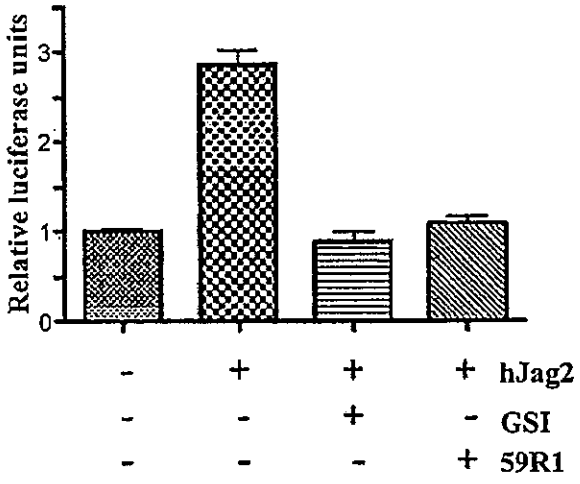


Figure 5A

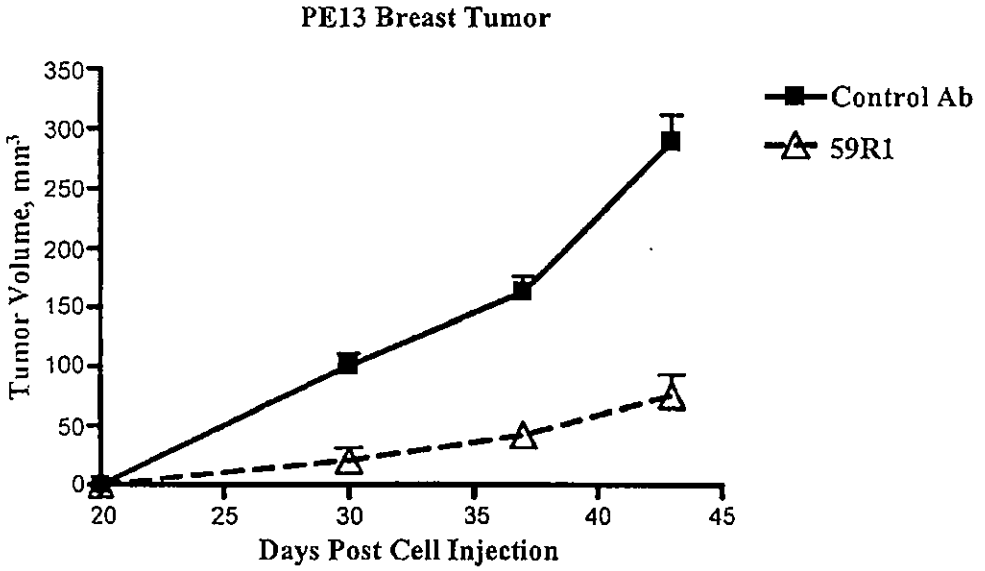

PE13 Breast Tumor
Tumor Volume, mm³
350
300
250
200
150
100
50
0
20
25
30
35
40
45
Days Post Cell Injection
Control Ab
59R1

Figure 5B

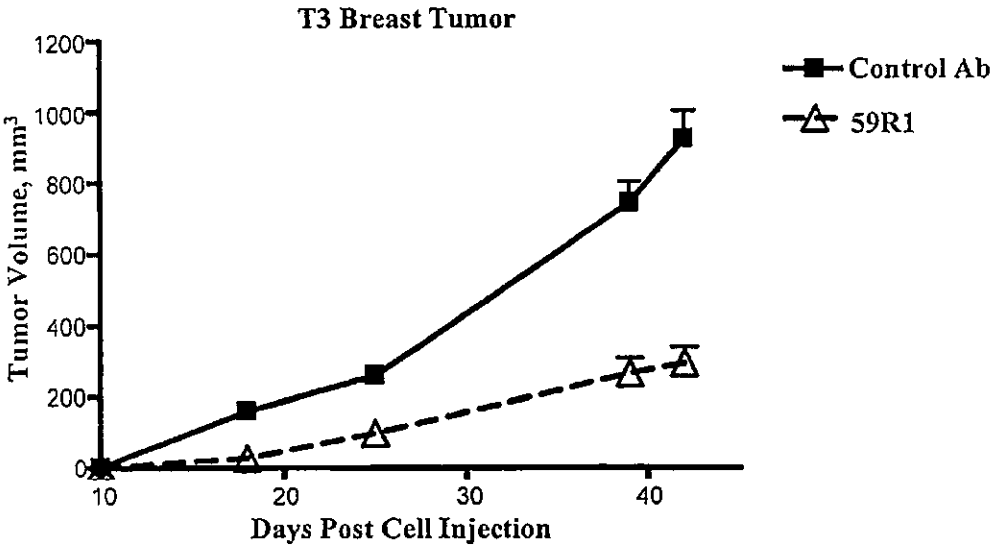
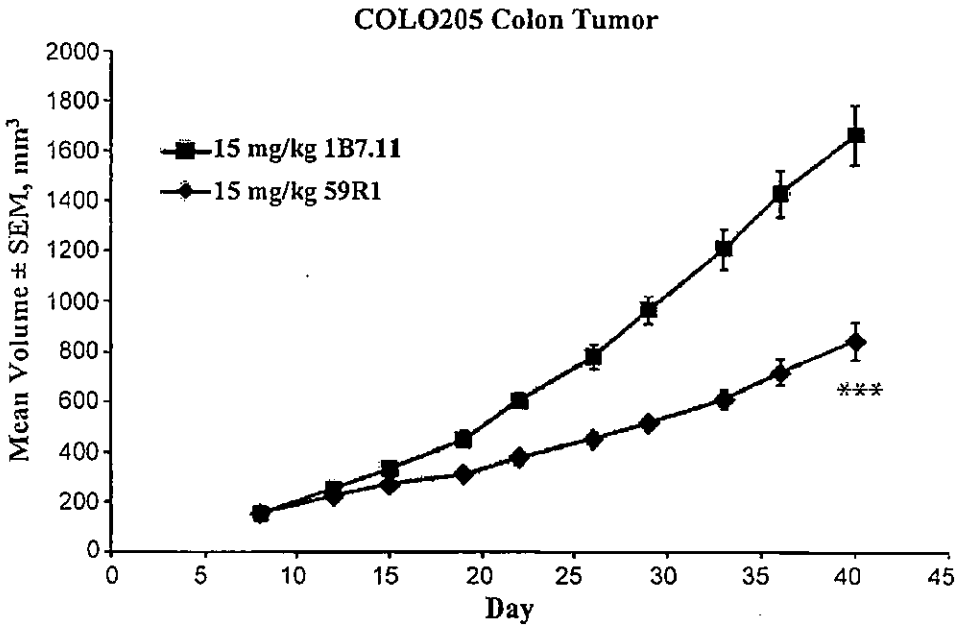
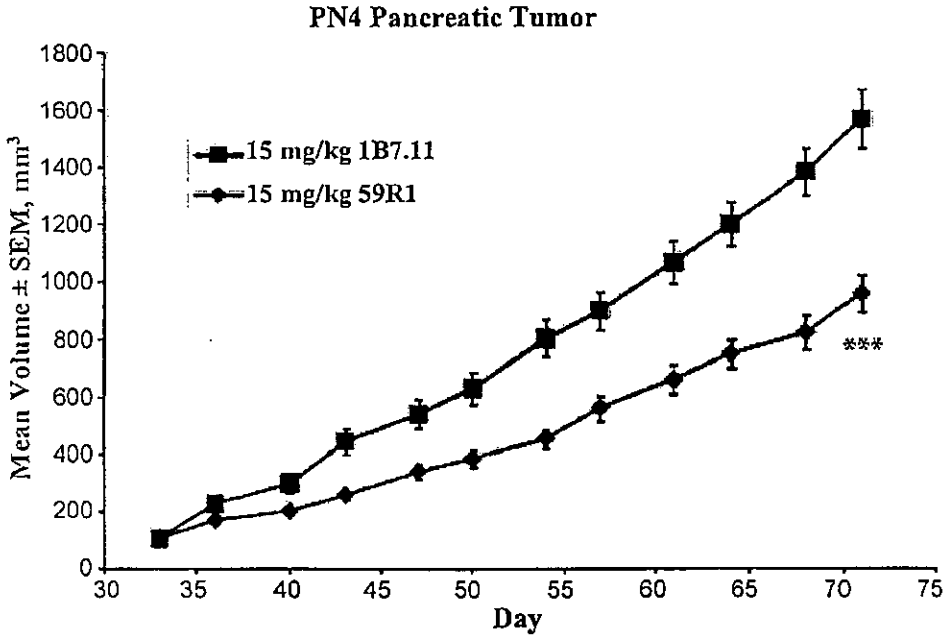

T3 Breast Tumor
Tumor Volume, mm³
1200
1000
800
600
400
200
0
10
20
30
40
Days Post Cell Injection
Control Ab
59R1

Figure 5C



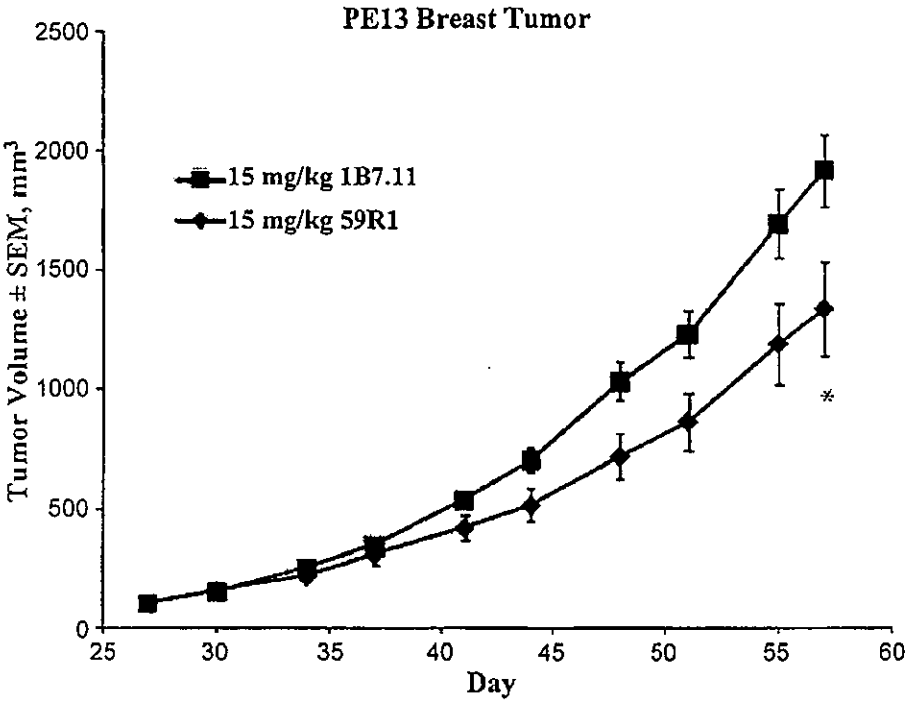
*** $p < 0.001$, 59R1 relative to 1B7.11

Figure 5D



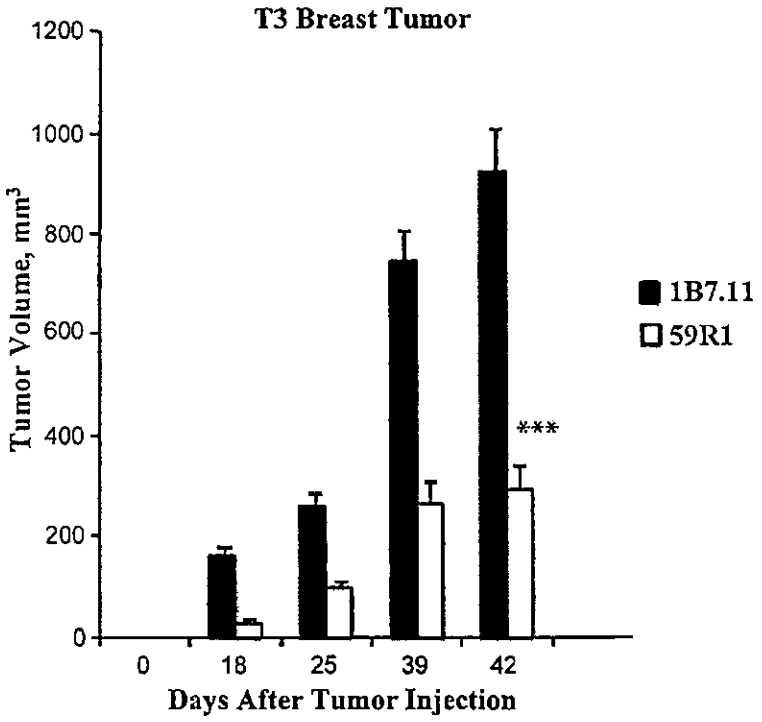
*** $p < 0.001$, 59R1 relative to 1B7.11

Figure 5E



* $p < 0.05$, 59R1 relative to 1B7.11

Figure 5F



*** p < 0.001, 59R1 relative to 1B7.11

Figure 6

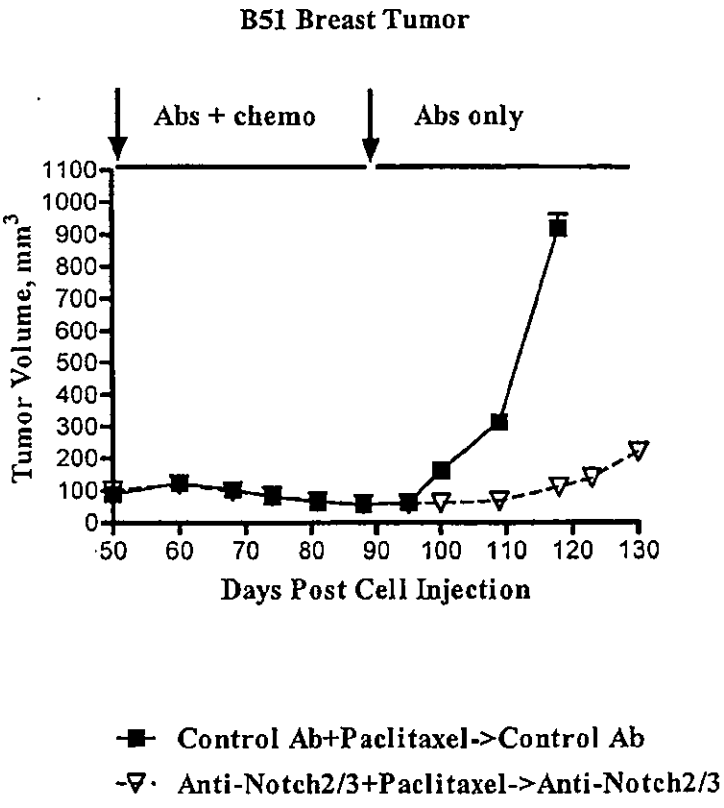

B51 Breast Tumor
Abs + chemo
Abs only
Tumor Volume, mm3
1100
1000
900
800
700
600
500
400
300
200
100
0
50
60
70
80
90
100
110
120
130
Days Post Cell Injection
Control Ab+Paclitaxel->Control Ab
Anti-Notch2/3+Paclitaxel->Anti-Notch2/3

Figure 7

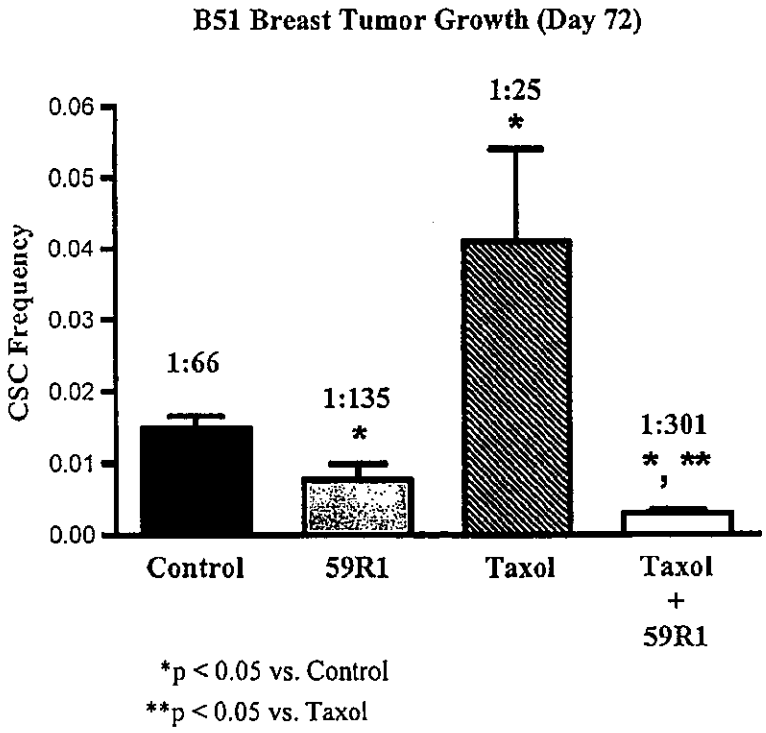

B51 Breast Tumor Growth (Day 72)
CSC Frequency
0.06
0.05
0.04
0.03
0.02
0.01
0.00
1:66
1:135
*
1:25
*
1:301
*, **
Control
59R1
Taxol
Taxol
+
59R1
*p < 0.05 vs. Control
**p < 0.05 vs. Taxol

Figure 8

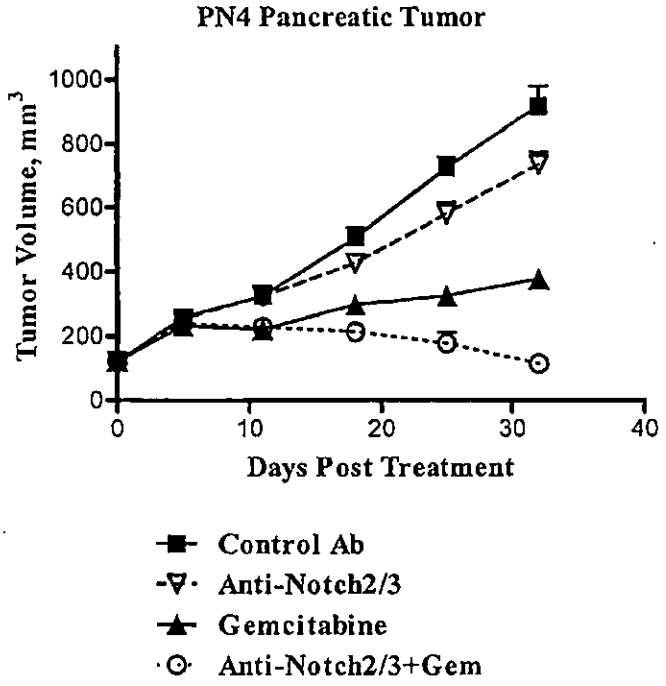

PN4 Pancreatic Tumor
Tumor Volume, mm3
1000
800
600
400
200
0
0
10
20
30
40
Days Post Treatment
Control Ab
Anti-Notch2/3
Gemcitabine
Anti-Notch2/3+Gem

Figure 9

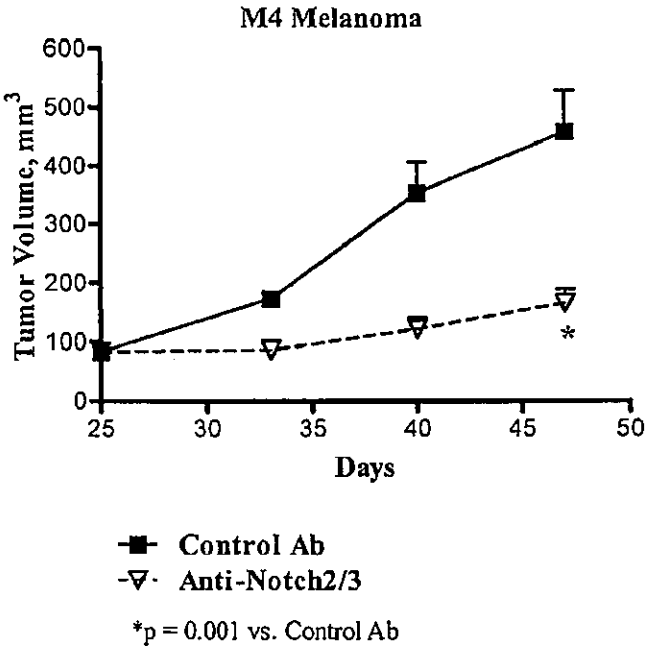
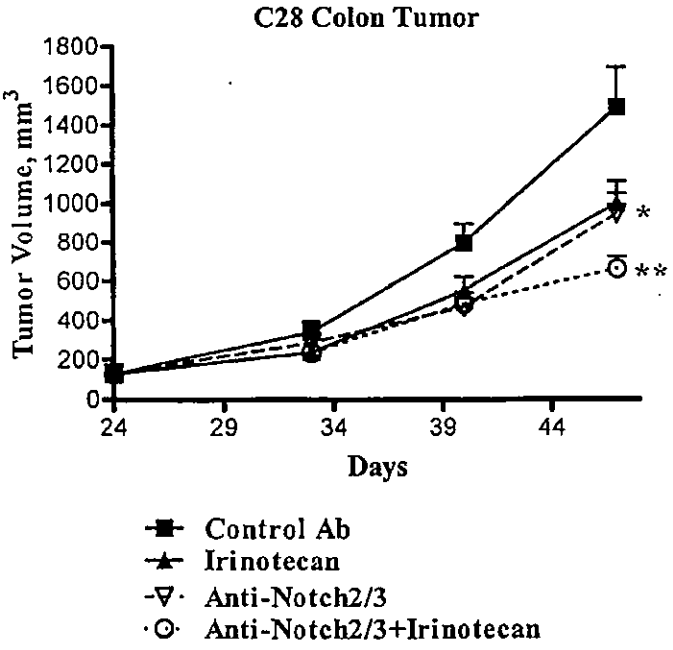

M4 Melanoma
Tumor Volume, mm3
600
500
400
300
200
100
0
25
30
35
40
45
50
Days
*
Control Ab
Anti-Notch2/3
*p = 0.001 vs. Control Ab

Figure 10



*p = 0.03 vs. Control Ab
**p = 0.01 vs. Irinotecan

Figure 11A

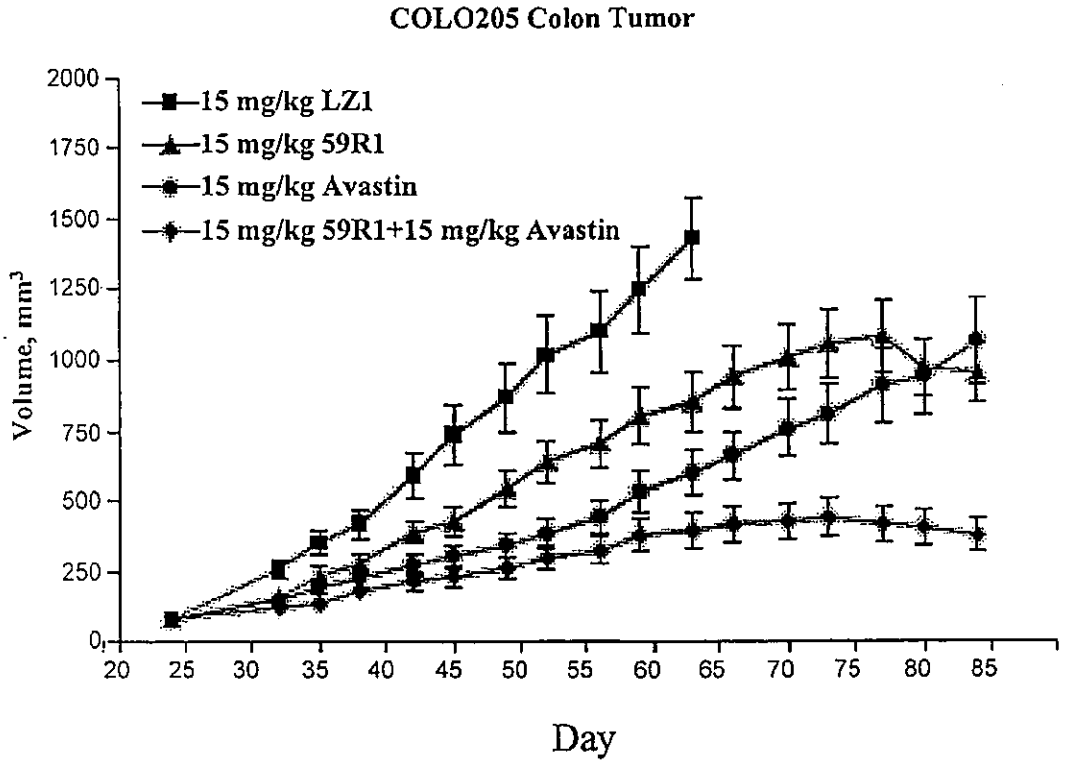

COLO205 Colon Tumor
15 mg/kg LZ1
15 mg/kg 59R1
15 mg/kg Avastin
15 mg/kg 59R1+15 mg/kg Avastin
Volume, mm3
2000
1750
1500
1250
1000
750
500
250
0
20
25
30
35
40
45
50
55
60
65
70
75
80
85
Day

Figure 11B

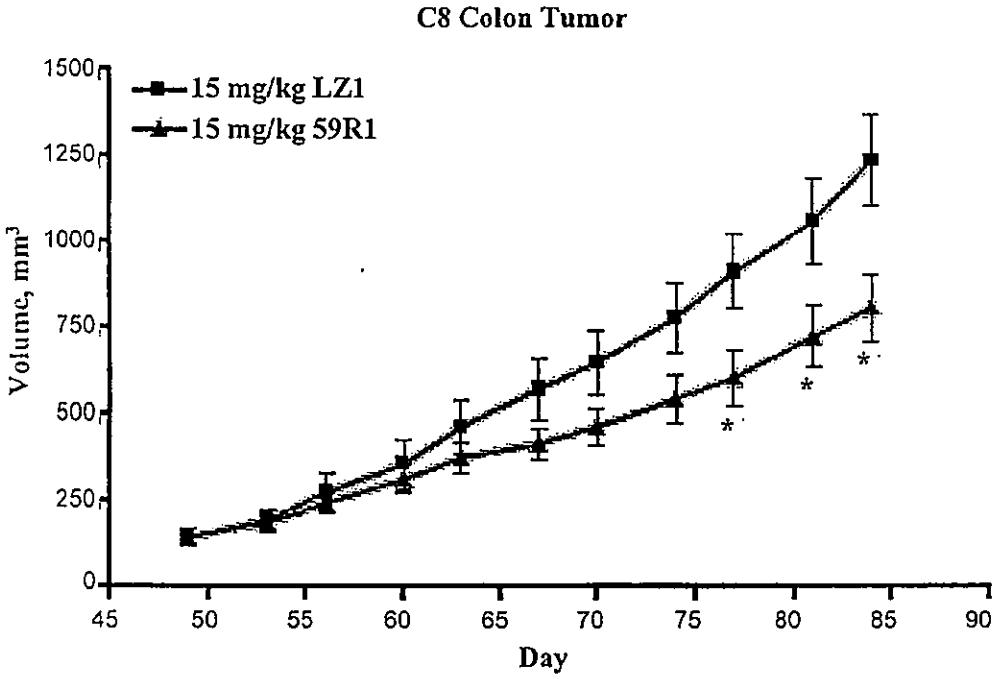

C8 Colon Tumor
15 mg/kg LZ1
15 mg/kg 59R1
Volume, mm3
1500
1250
1000
750
500
250
0
45
50
55
60
65
70
75
80
85
90
Day
*
*
*

Figure 11C

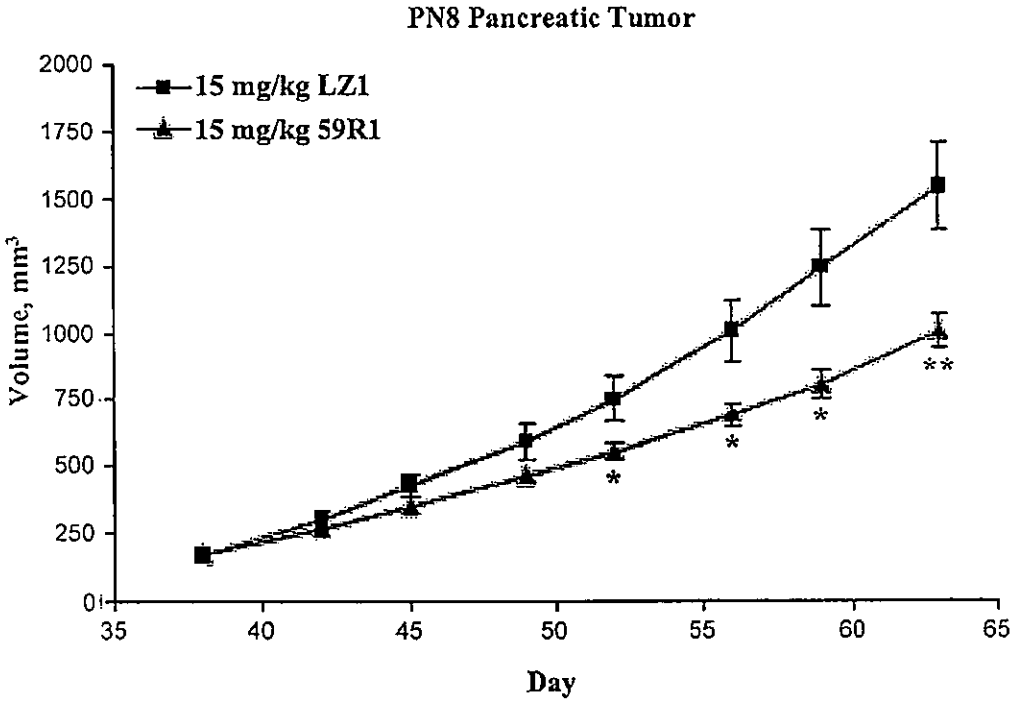

PN8 Pancreatic Tumor
15 mg/kg LZ1
15 mg/kg 59R1
Volume, mm³
2000
1750
1500
1250
1000
750
500
250
0
35
40
45
50
55
60
65
Day
*
*
*
*
**

Figure 11D

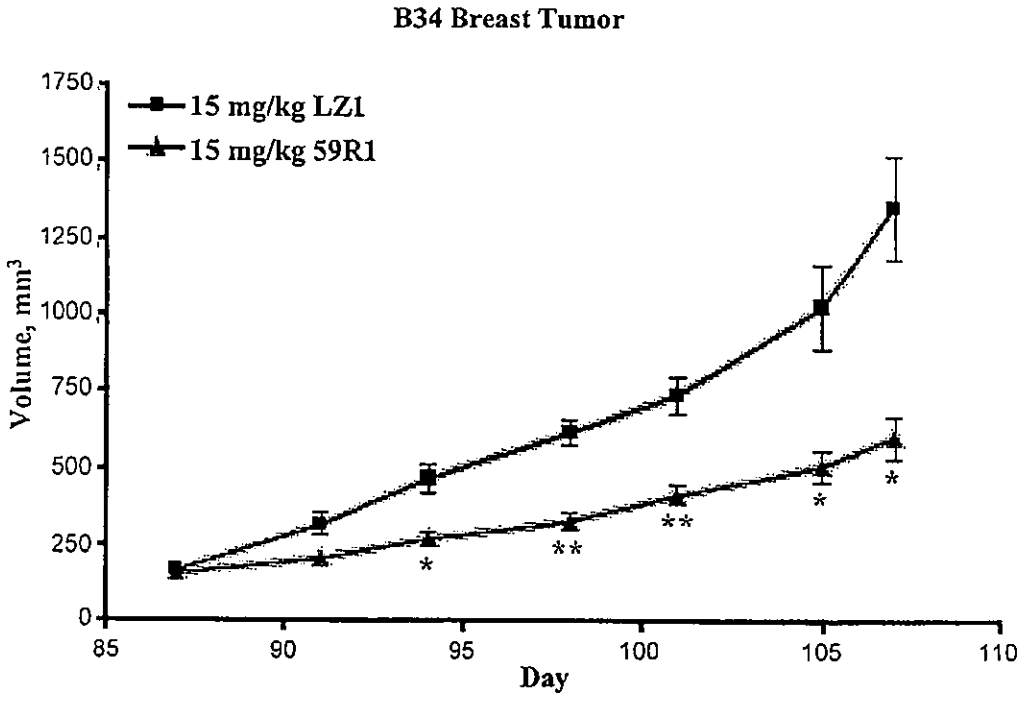

B34 Breast Tumor
15 mg/kg LZ1
15 mg/kg 59R1
Volume, mm3
1750
1500
1250
1000
750
500
250
0
85
90
95
100
105
110
Day
*
**
**
*
*
*

Figure 11E

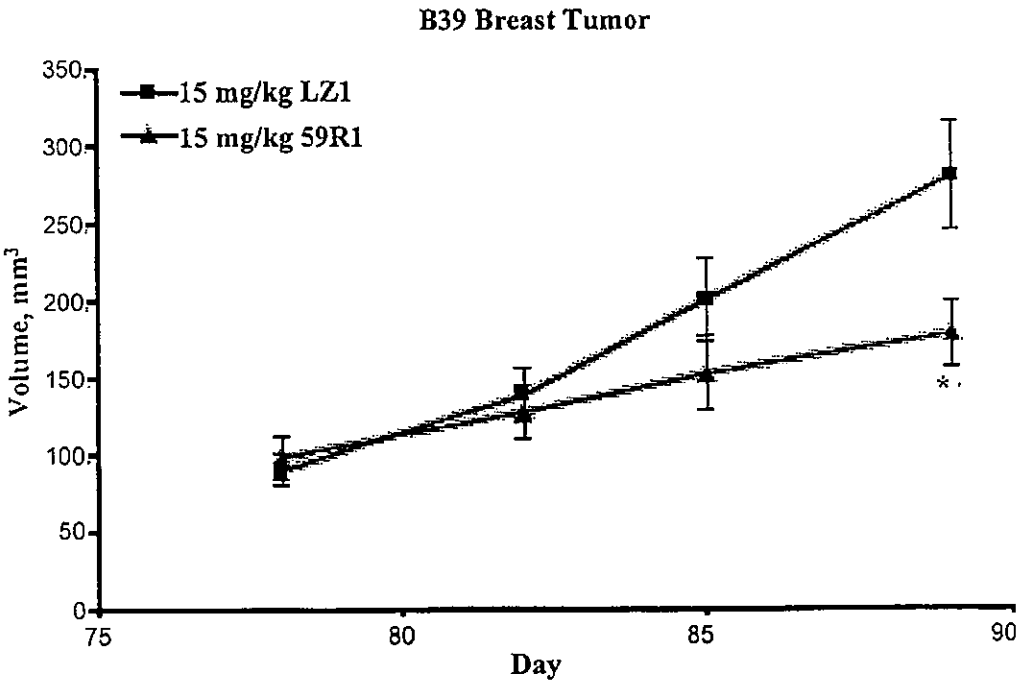

B39 Breast Tumor
15 mg/kg LZ1
15 mg/kg 59R1
Volume, mm3
350
300
250
200
150
100
50
0
75
80
85
90
Day
*

Figure 11F

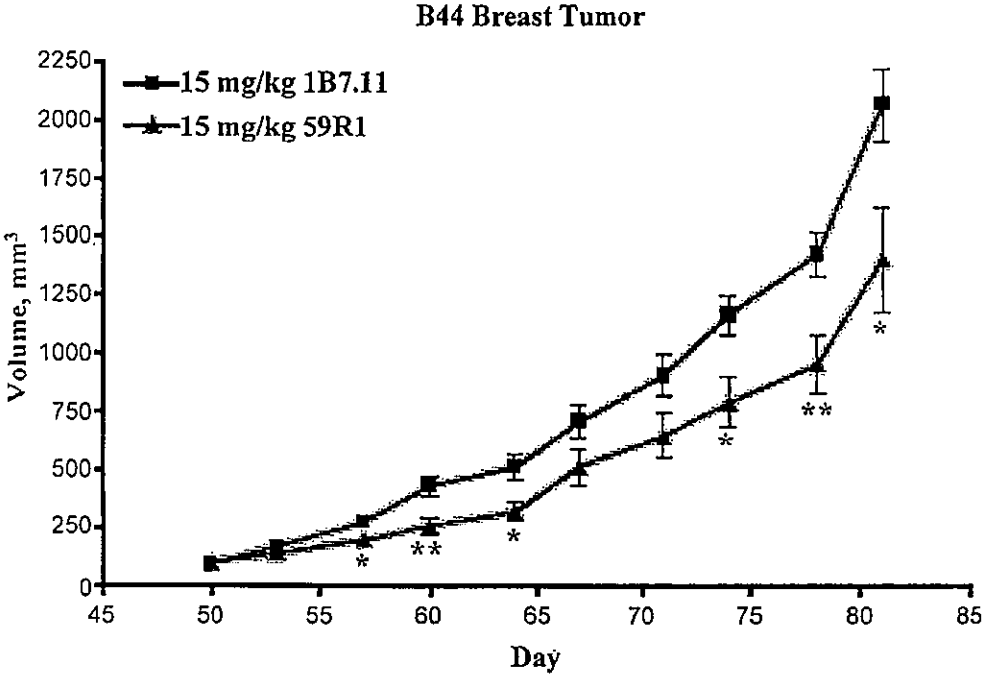

B44 Breast Tumor
15 mg/kg 1B7.11
15 mg/kg 59R1
Volume, mm3
Day
2250
2000
1750
1500
1250
1000
750
500
250
0
45
50
55
60
65
70
75
80
85
*
**
*
*
**
*

Figure 11G

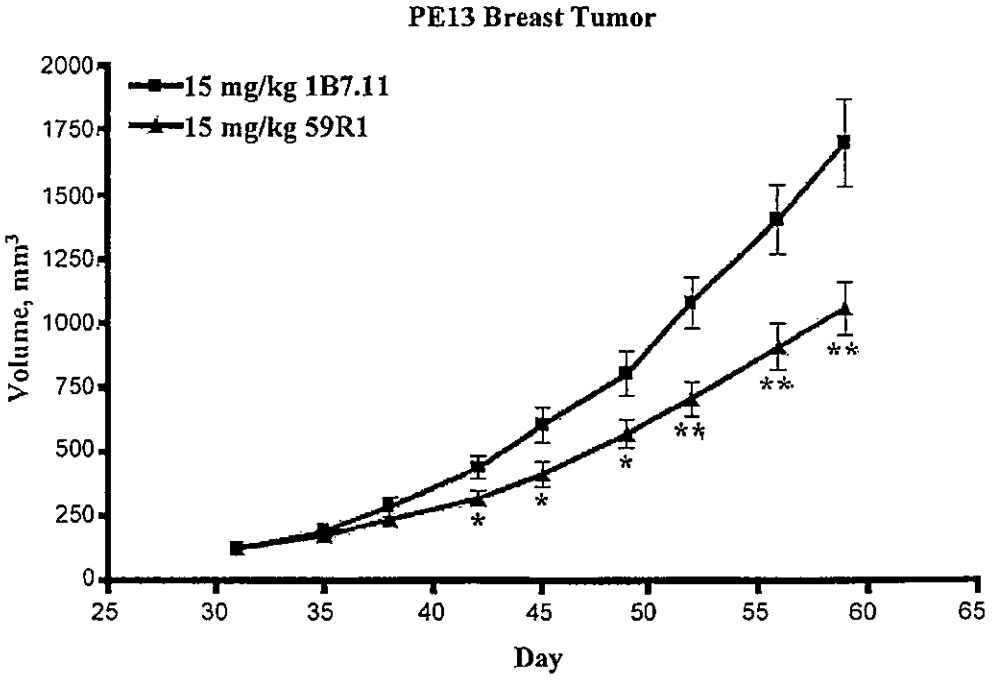

PE13 Breast Tumor
15 mg/kg 1B7.11
15 mg/kg 59R1
Volume, mm3
Day
2000
1750
1500
1250
1000
750
500
250
0
25
30
35
40
45
50
55
60
65
*
*
*
**
**
**

Figure 11H

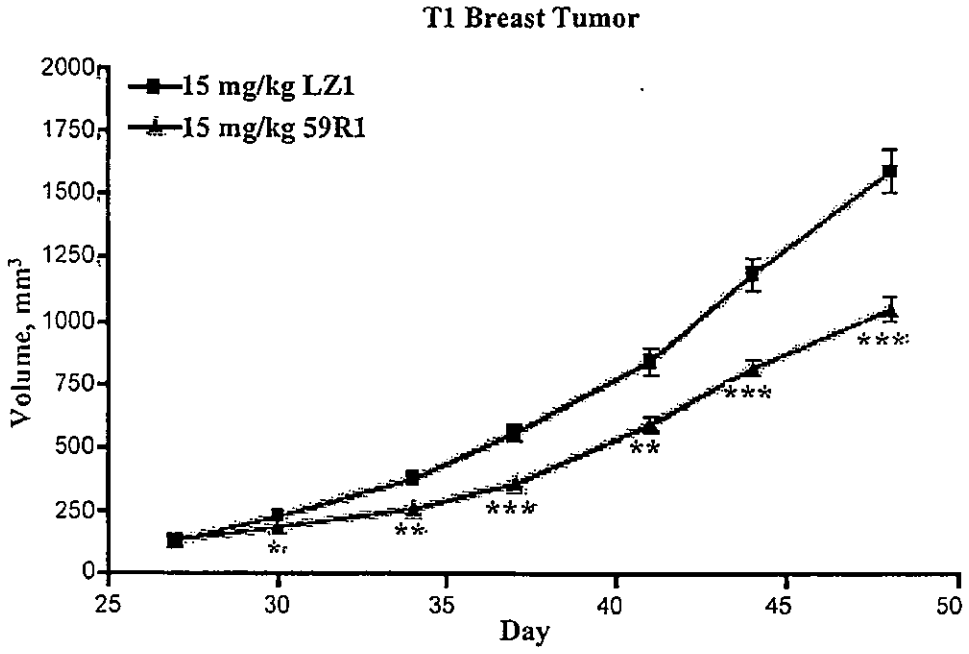

T1 Breast Tumor
15 mg/kg LZ1
15 mg/kg 59R1
Volume, mm3
2000
1750
1500
1250
1000
750
500
250
0
25
30
35
40
45
50
Day
*
**
***
**
***
***

Figure 12A

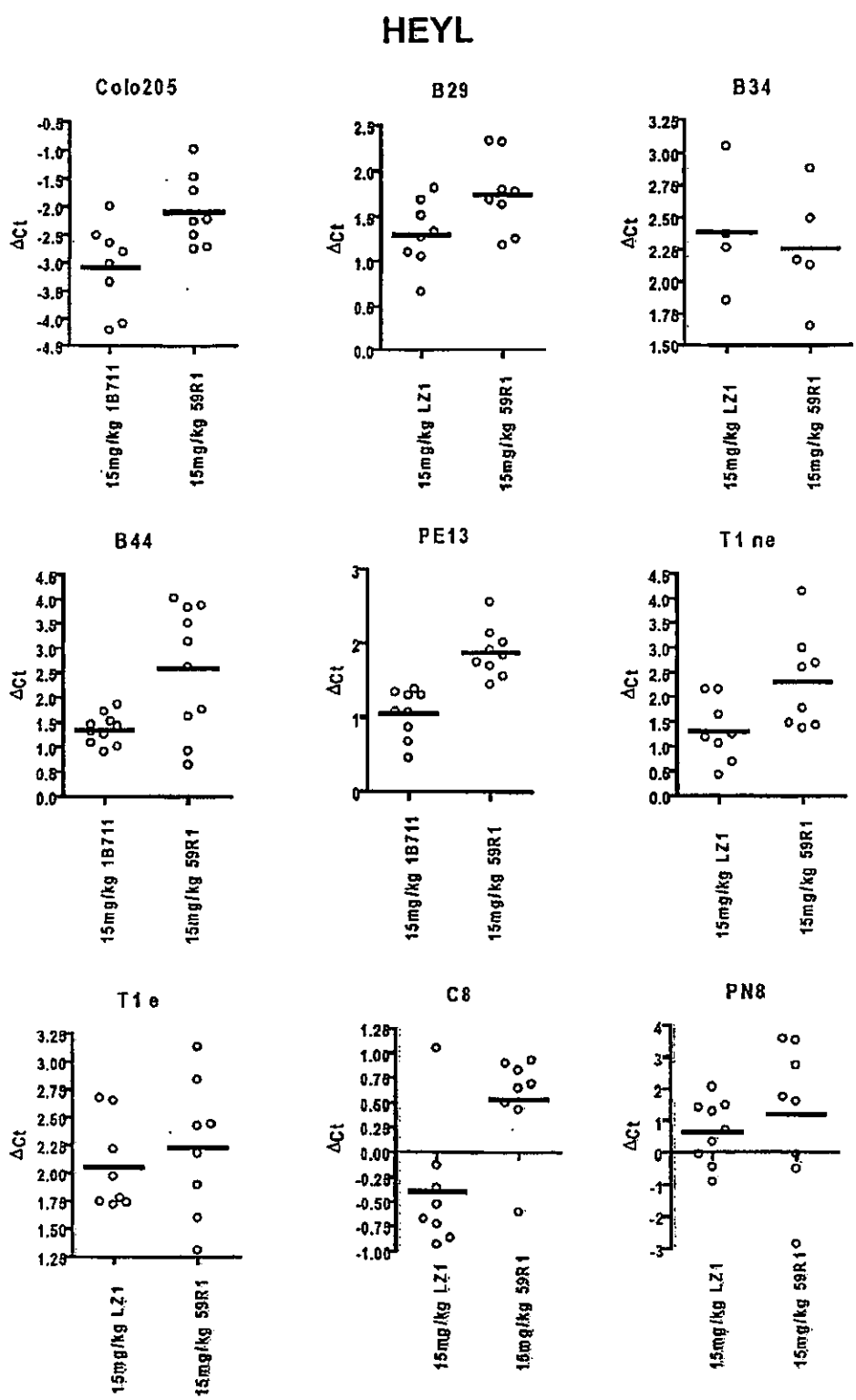

HEYL
Colo205
B29
B34
B44
PE13
T1 ne
T1 e
C8
PN8
ΔCt
15mg/kg 1B711
15mg/kg 59R1
15mg/kg LZ1

Figure 12B

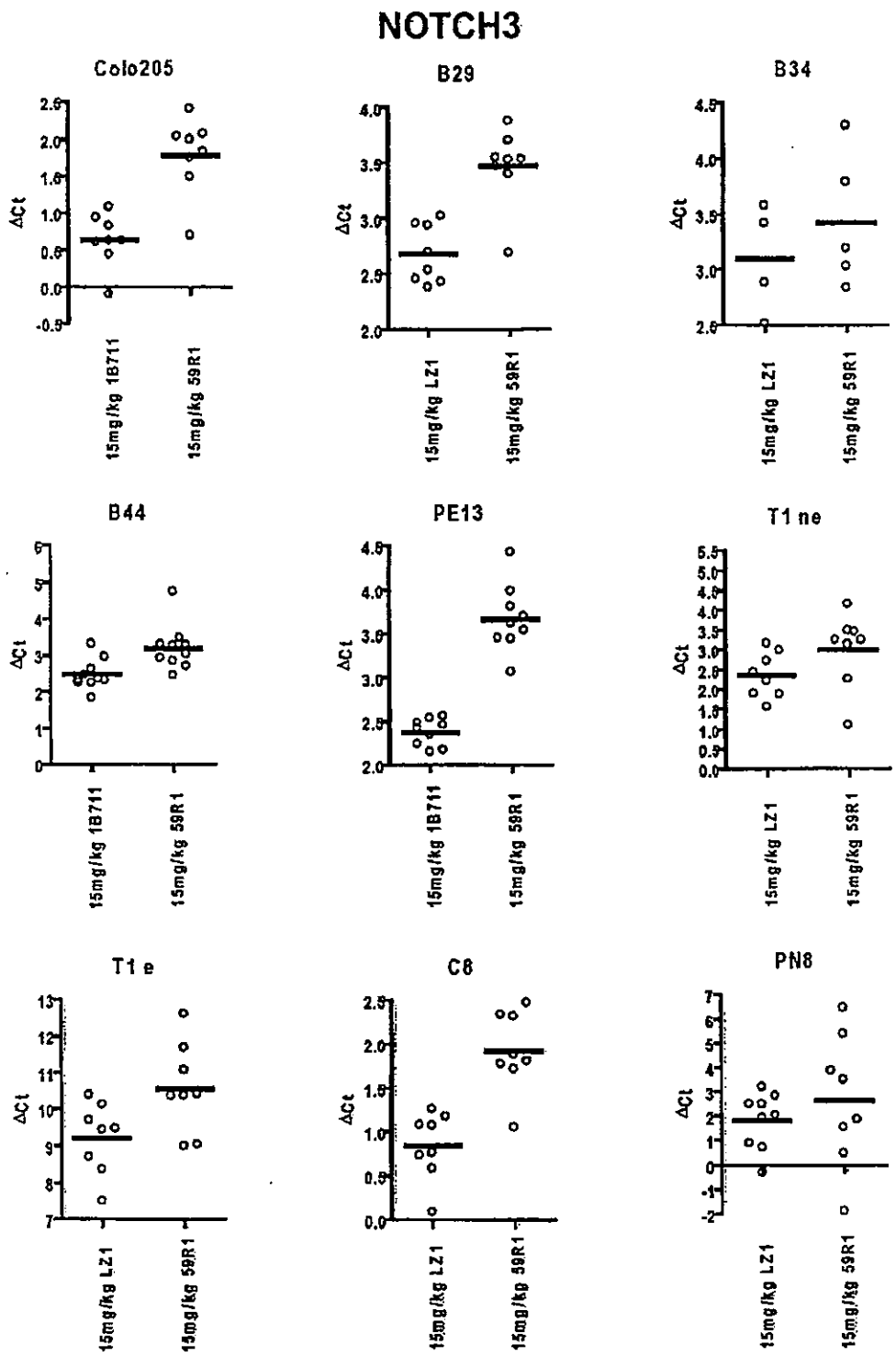

NOTCH3
Colo205
B29
B34
B44
PE13
T1 ne
T1 e
C8
PN8
ΔCt
15mg/kg 1B711
15mg/kg 59R1
15mg/kg LZ1

Figure 12C

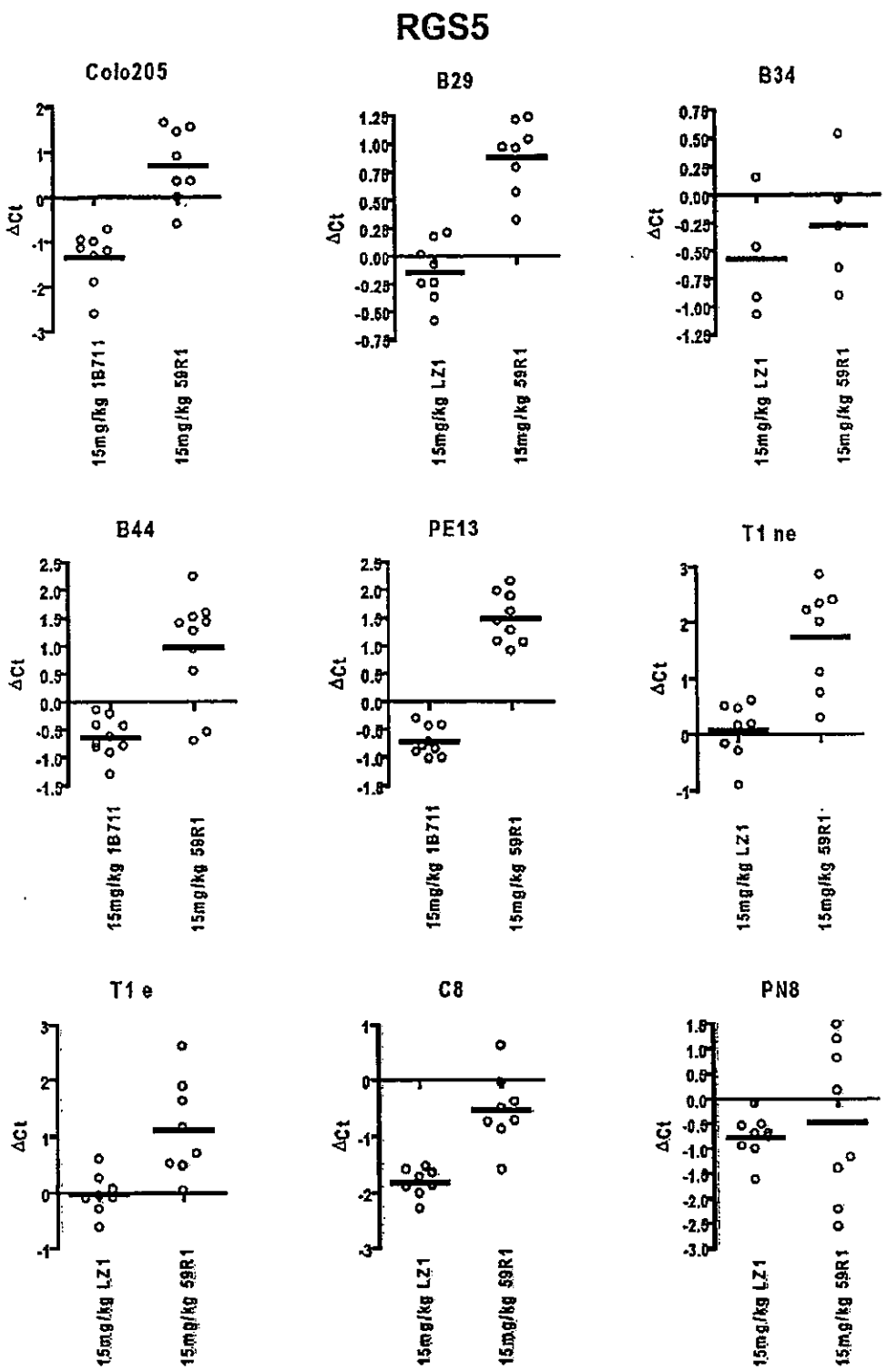

RGS5
Colo205
B29
B34
B44
PE13
T1 ne
T1 e
C8
PN8
ΔCt
15mg/kg 1B711
15mg/kg 59R1
15mg/kg LZ1

Figure 12D

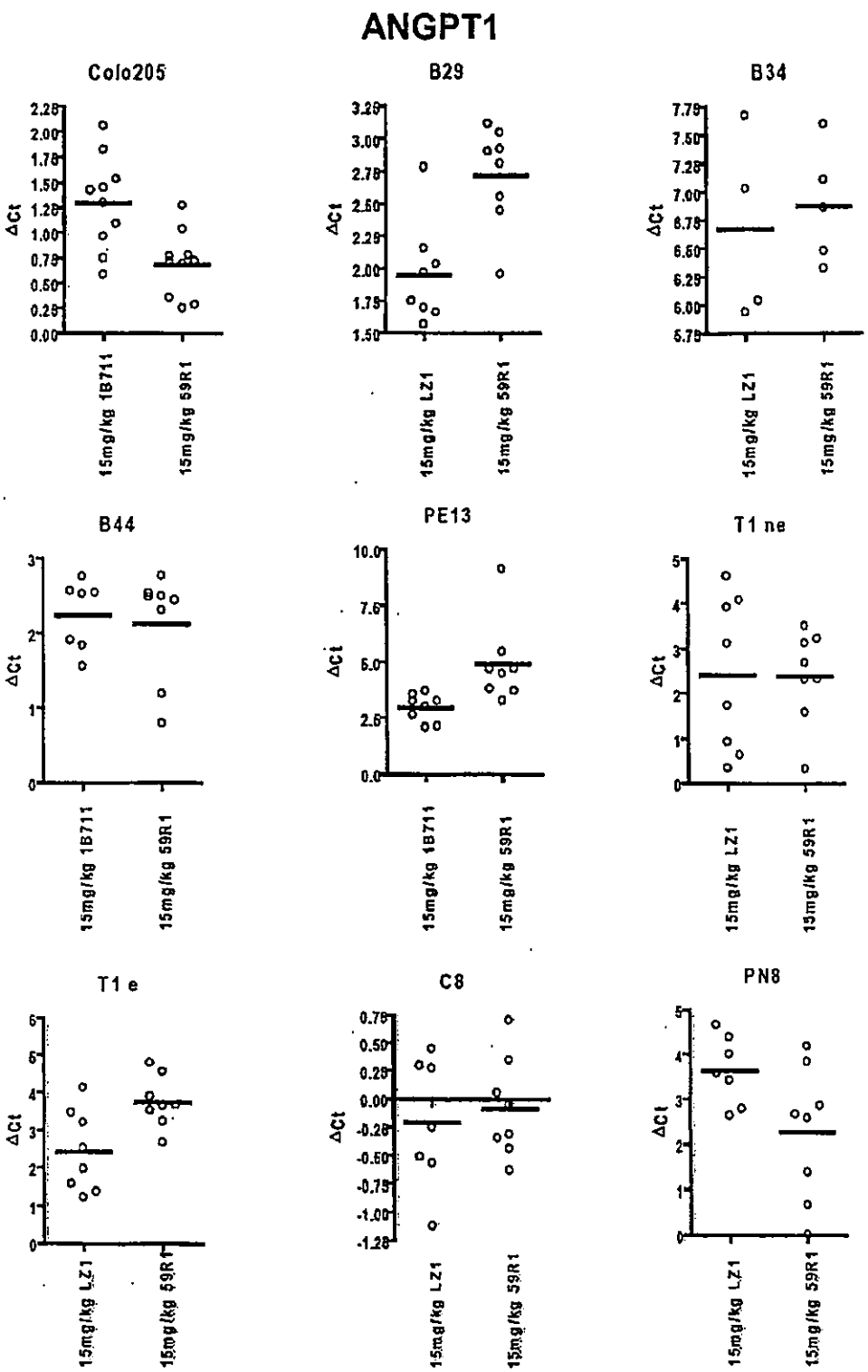

ANGPT1
Colo205
B29
B34
B44
PE13
T1 ne
T1 e
C8
PN8
ΔCt
15mg/kg 1B711
15mg/kg 59R1
15mg/kg LZ1

Figure 12E

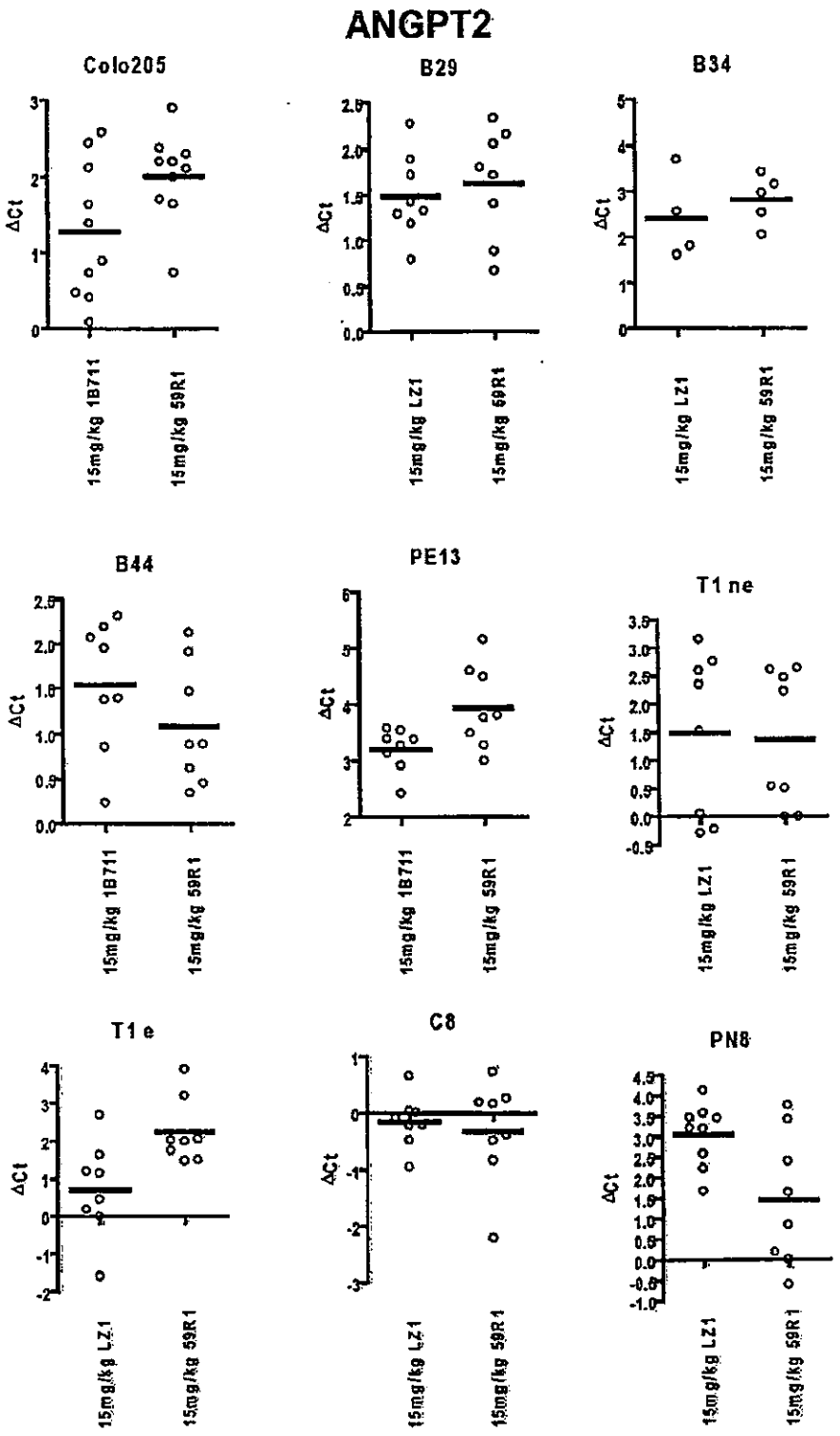

ANGPT2
Colo205
B29
B34
B44
PE13
T1 ne
T1 e
C8
PN8
ΔCt
15mg/kg 1B711
15mg/kg 59R1
15mg/kg LZ1

Figure 13

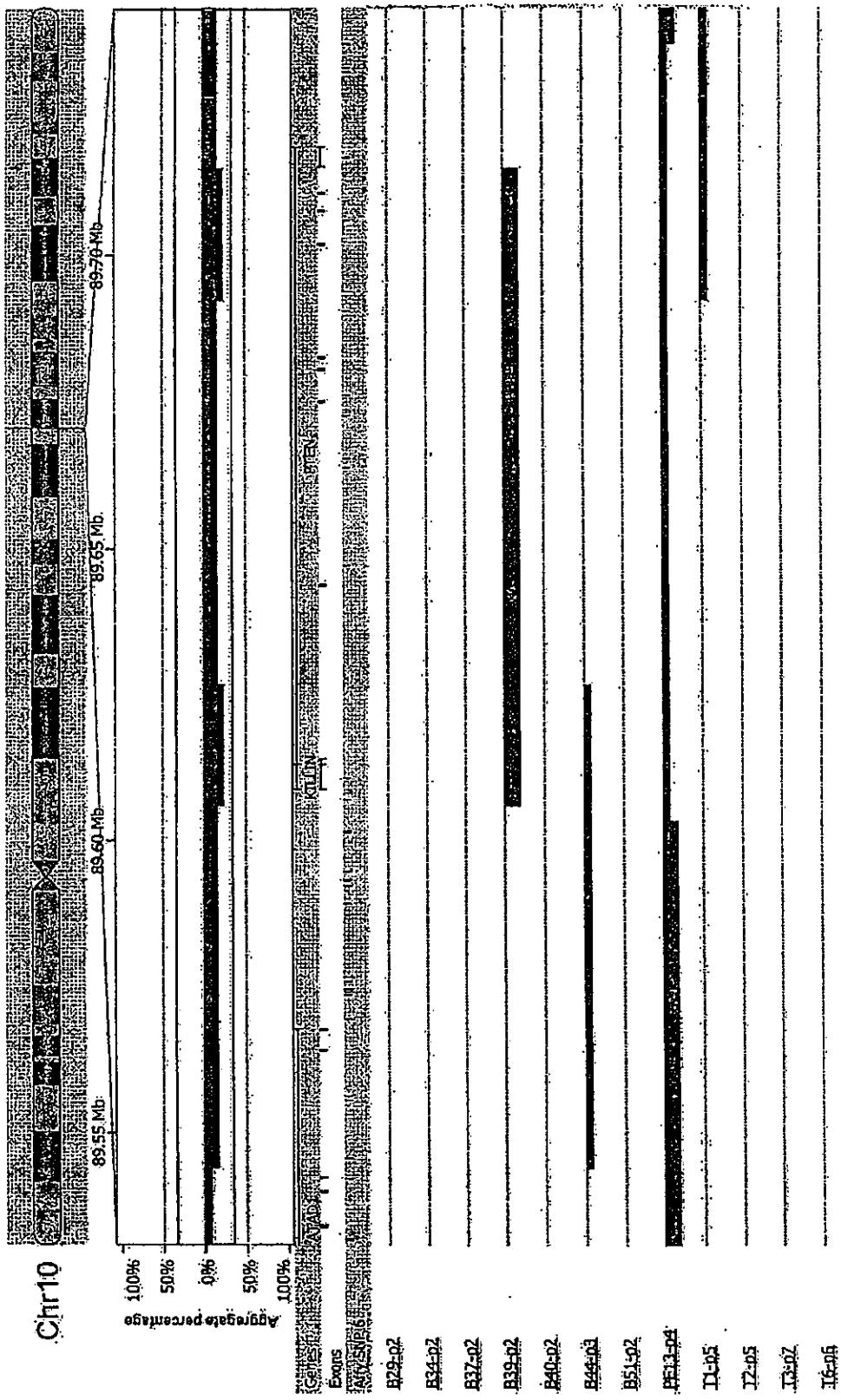

Chr10
89.55 Mb
89.60 Mb
89.65 Mb
89.70 Mb
100%
50%
0%
50%
100%
Aggregate percentage
Genes
Exons
B29-p2
B34-p2
B37-p2
B39-p2
B40-p2
B44-p3
B51-p2
PE13-p4
T1-p5
T2-p5
T3-p7
T6-p6

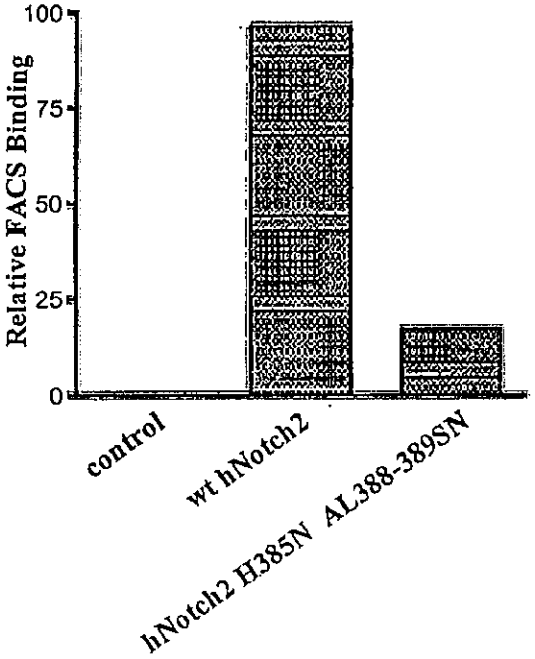
Figure 14

14A

EGF10 (or equivalent)

```
h-NOTCH1    356 sfycecphgrtglichlndacisnpcnegsncdcnpvngkaictcpsgytgpacsqdvdecsl-
h-NOTCH2    359 sfscmcpegkaglichlddacisnpchkgalcdcnplngqyictcpqgykgadctedvdecam-
h-NOTCH3    335 sfycacpmgktglichlddacvsnpchedaicdcnpvngraictcppgftggacdqdvdecsi-
h-NOTCH4    376 sfsclcppgrtglichledmclsqpchgdaqcscnpltgstlclcqpgyvgptchqdldeclma
```

14B



14C

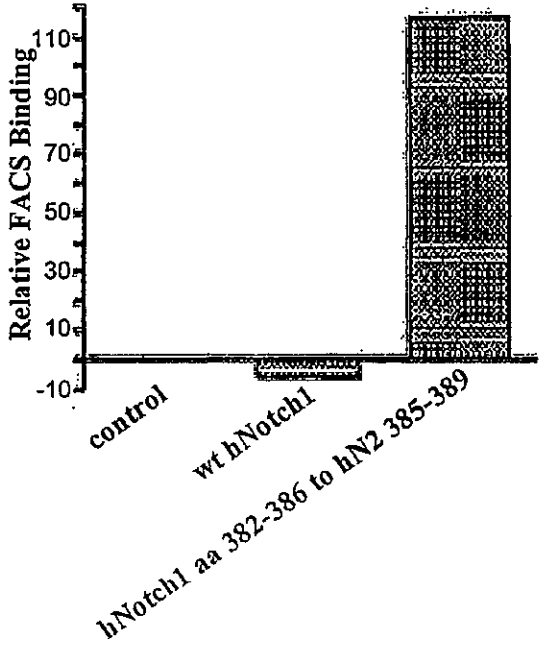


Figure 15A

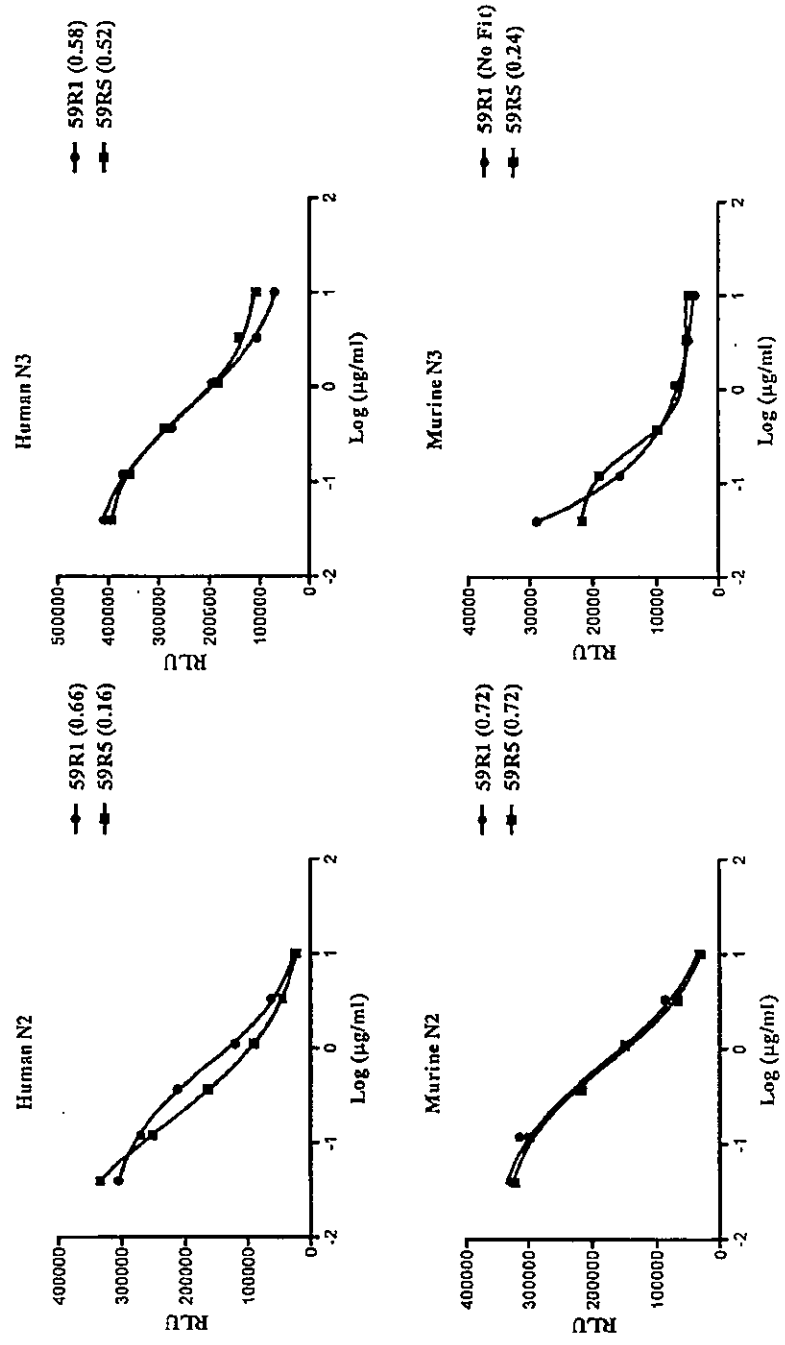

Human N3
59R1 (0.58)
59R5 (0.52)
RLU
Log (µg/ml)
Murine N3
59R1 (No Fit)
59R5 (0.24)
RLU
Log (µg/ml)
Human N2
59R1 (0.66)
59R5 (0.16)
RLU
Log (µg/ml)
Murine N2
59R1 (0.72)
59R5 (0.72)
RLU
Log (µg/ml)

Figure 15B

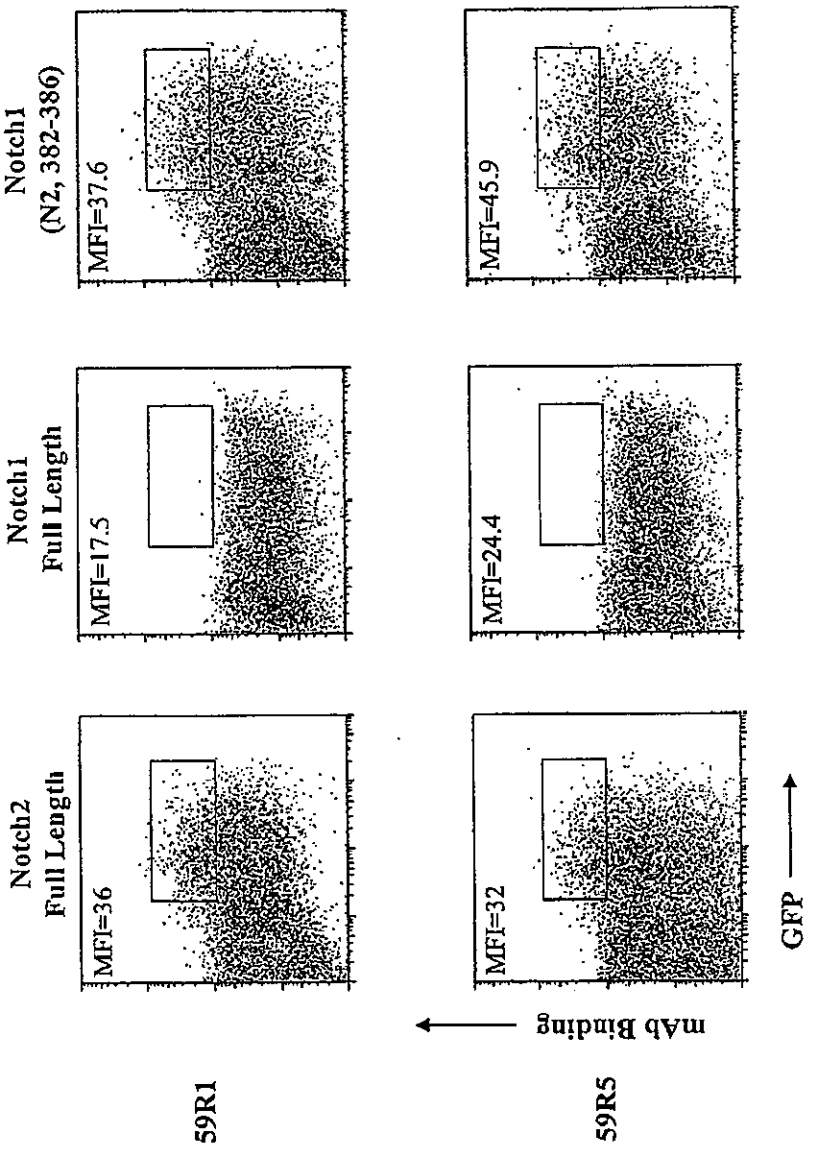
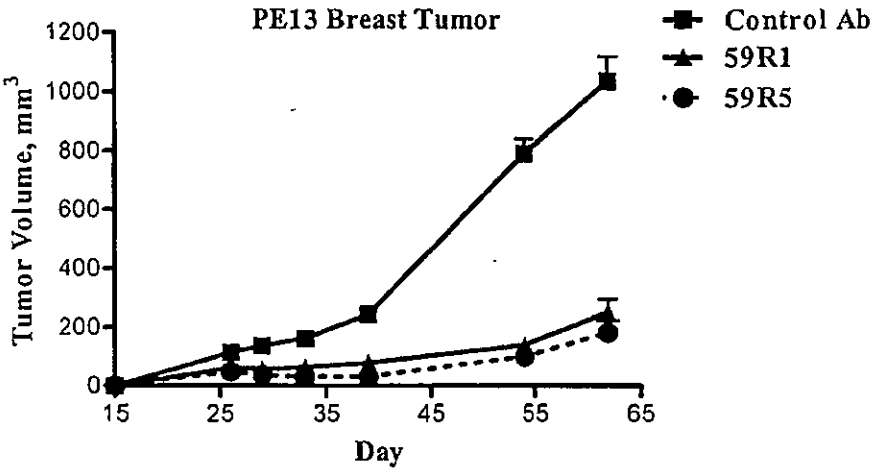

Notch2
Full Length
MFI=36
Notch1
Full Length
MFI=17.5
Notch1
(N2, 382-386)
MFI=37.6
MFI=32
MFI=24.4
MFI=45.9
59R1
59R5
mAb Binding
GFP

Figure 16

16A



16B

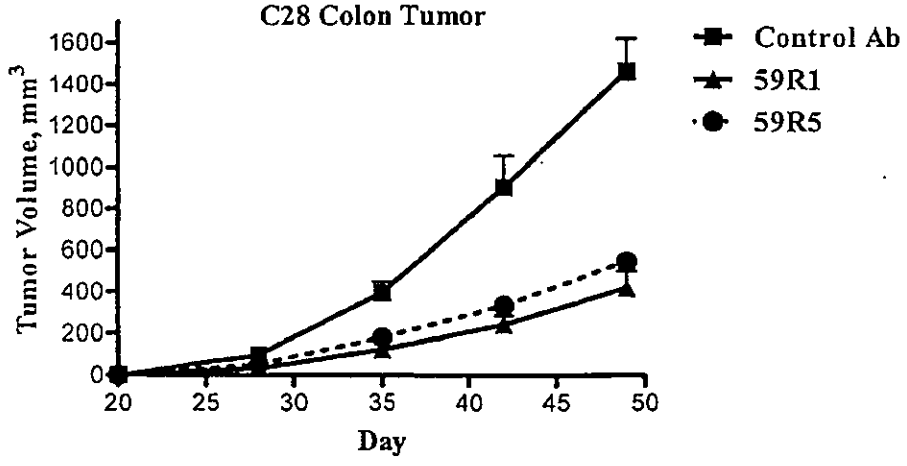


Figure 16

16C

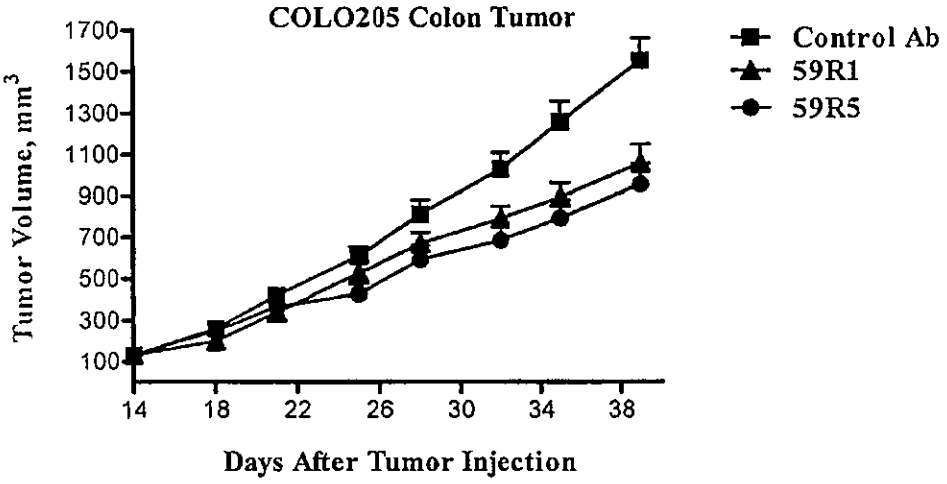
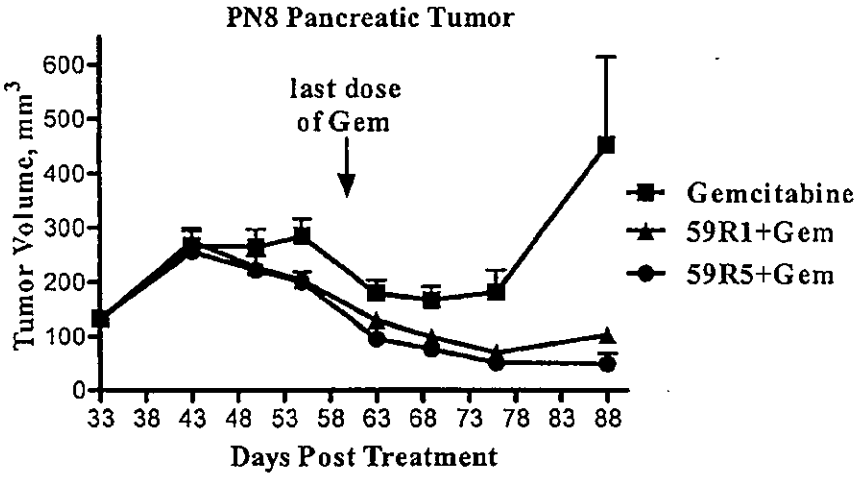


Figure 17

17A



17B

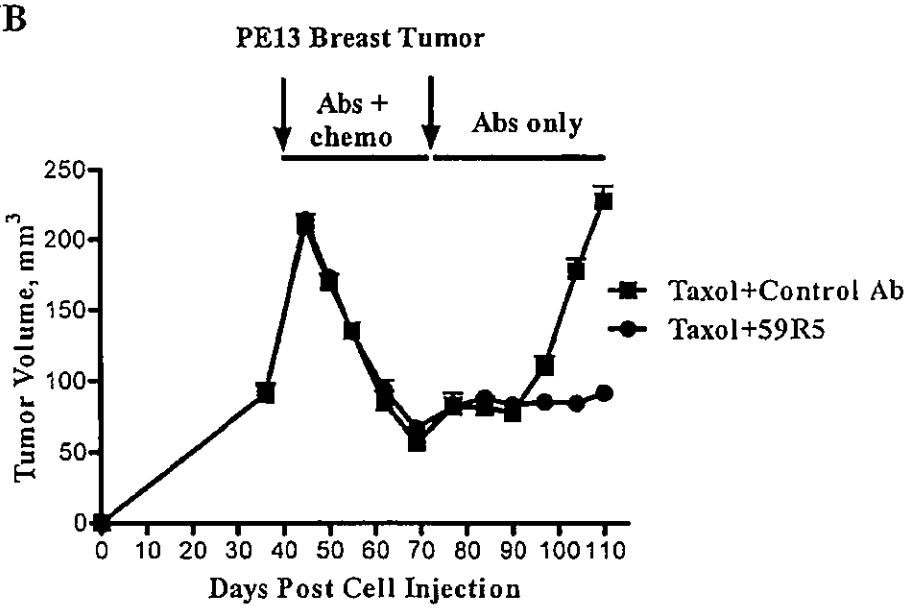
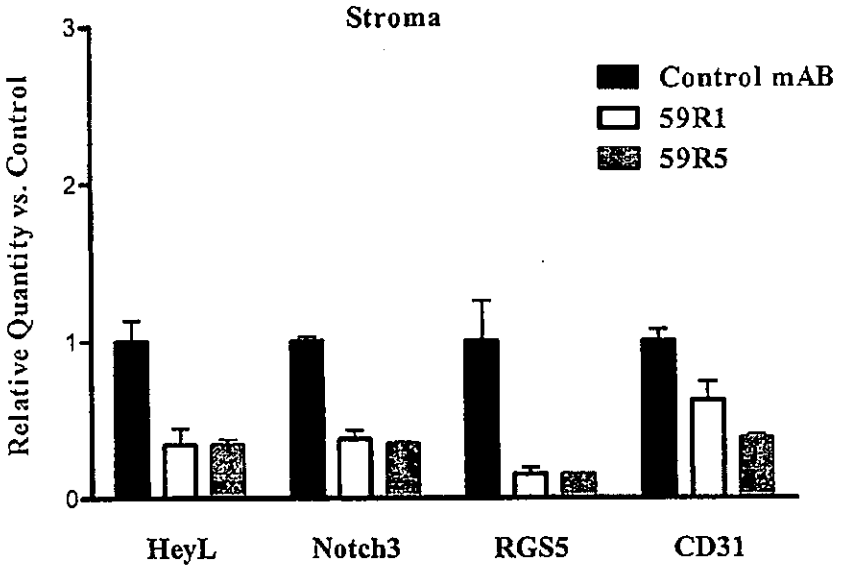


Figure 18


Stroma
Control mAB
59R1
59R5
Relative Quantity vs. Control
3
2
1
0
HeyL
Notch3
RGS5
CD31

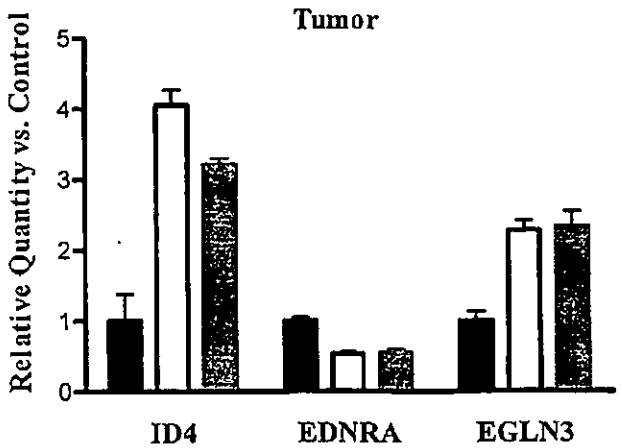
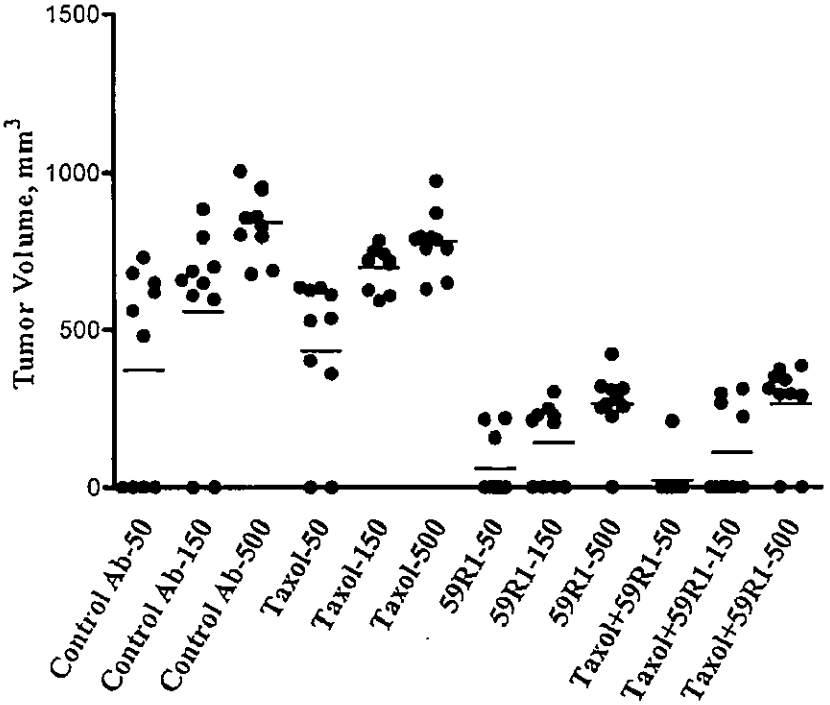

Tumor
Relative Quantity vs. Control
5
4
3
2
1
0
ID4
EDNRA
EGLN3

Figure 19

19A



19B

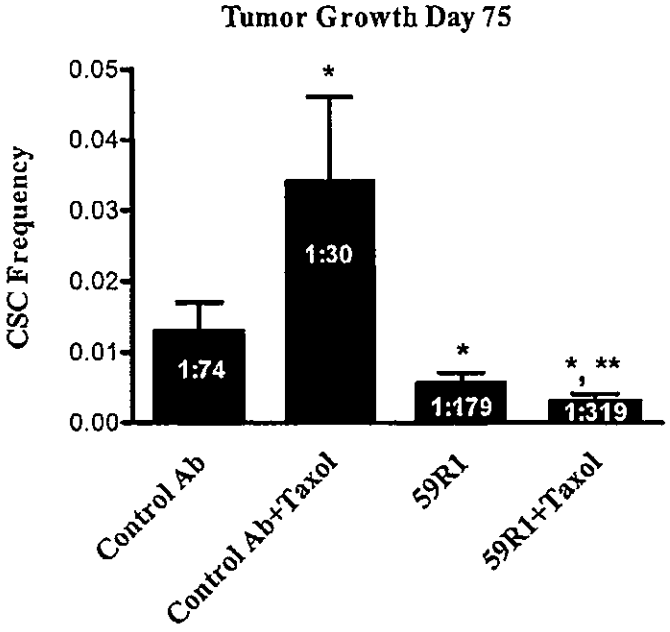
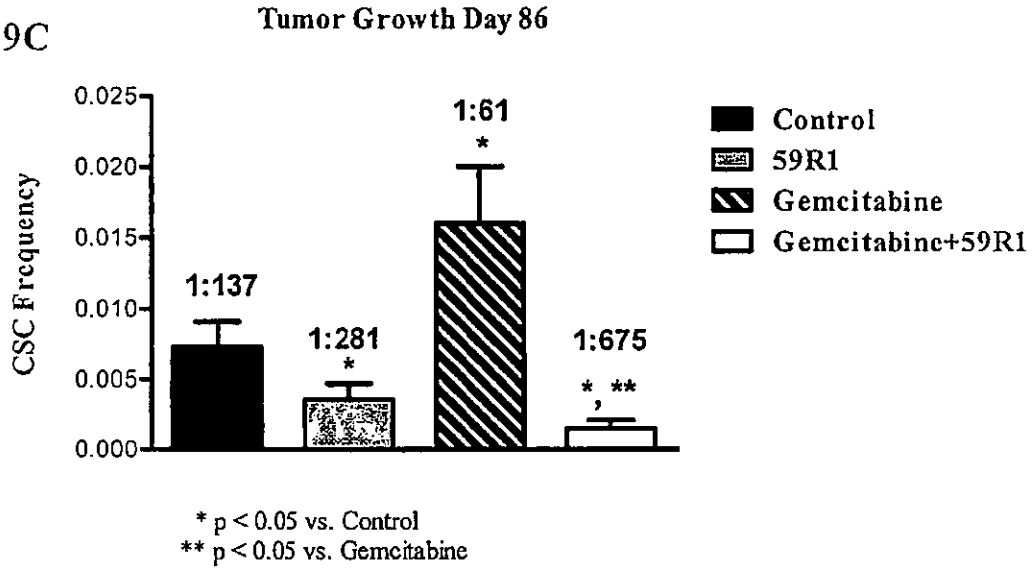


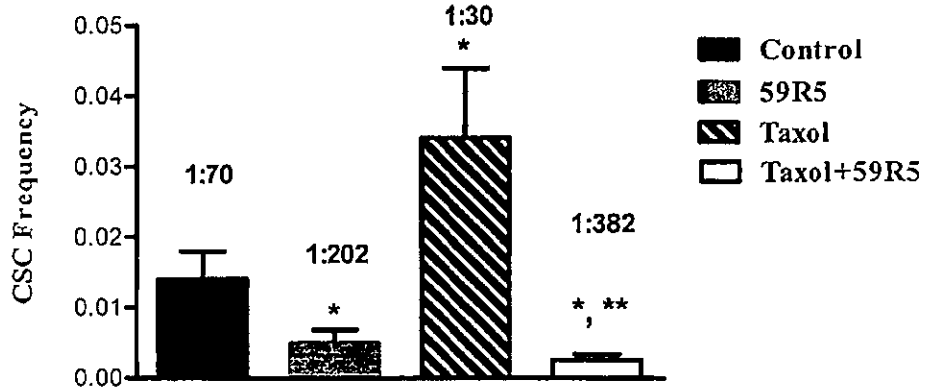
Figure 19

19C



* $p < 0.05$ vs. Control
** $p < 0.05$ vs. Gemcitabine

19D



* $p < 0.05$ vs. Control
** $p < 0.05$ vs. Taxol