Figure 1

Human RTP801 polynucleotide (SEQ ID NO:1)

```
TTTGGCCCTC GAGGCCAAGA ATTCGGCACG AGGGGGGGAG GTGCGAGCGT GGACCTGGGA 60
CGGGTCTGGG CGGCTCTCGG TGGTTGGCAC GGGTTCGCAC ACCCATTCAA GCGGCAGGAC 120
GCACTTGTCT TAGCAGTTCT CGCTGACCGC GCTAGCTGCG GCTTCTACGC TCCGGCACTC 180
TGAGTTCATC AGCAAACGCC CTGGCGTCTG TCCTCACCAT GCCTAGCCTT TGGGACCGCT 240
TCTCGTCGTC GTCCACCTCC TCTTCGCCCT CGTCCTTGCC CCGAACTCCC ACCCCAGATC 300
GGCCGCCGCG CTCAGCCTGG GGGTCGGCGA CCCGGGAGGA GGGGTTTGAC CGCTCCACGA 360
GCCTGGAGAG CTCGGACTGC GAGTCCCTGG ACAGCAGCAA CAGTGGCTTC GGGCCGGAGG 420
AAGACACGGC TTACCTGGAT GGGGTGTCGT TGCCCGACTT CGAGCTGCTC AGTGACCCTG 480
AGGATGAACA CTTGTGTGCC AACCTGATGC AGCTGCTGCA GGAGAGCCTG GCCCAGGCGC 540
GGCTGGGCTC TCGACGCCCT GCGCGCCTGC TGATGCCTAG CCAGTTGGTA AGCCAGGTGG 600
GCAAAGAACT ACTGCGCCTG GCCTACAGCG AGCCGTGCGG CCTGCGGGGG GCGCTGCTGG 660
ACGTCTGCGT GGAGCAGGGC AAGAGCTGCC ACAGCGTGGG CCAGCTGGCA CTCGACCCCA 720
GCCTGGTGCC CACCTTCCAG CTGACCCTCG TGCTGCGCCT GGACTCACGA CTCTGGCCCA 780
AGATCCAGGG GCTGTTTAGC TCCGCCAACT CTCCCTTCCT CCCTGGCTTC AGCCAGTCCC 840
TGACGCTGAG CACTGGCTTC CGAGTCATCA AGAAGAAGCT GTACAGCTCG GAACAGCTGC 900
TCATTGAGGA GTGTTGAACT TCAACCTGAG GGGGCCGACA GTGCCCTCCA AGACAGAGAC 960
GACTGAACTT TTGGGGTGGA GACTAGAGGC AGGAGCTGAG GGACTGATTC CTGTGGTTGG 1020
AAAACTGAGG CAGCCACCTA AGGTGGAGGT GGGGGAATAG TGTTTCCCAG GAAGCTCATT 1080
GAGTTGTGTG CGGGTGGCTG TGCATTGGGG ACACATACCC CTCAGTACTG TAGCATGAAA 1140
CAAAGGCTTA GGGGCCAACA AGGCTTCCAG CTGGATGTGT GTGTAGCATG TACCTTATTA 1200
TTTTTGTTAC TGACAGTTAA CAGTGGTGTG ACATCCAGAG AGCAGCTGGG CTGCTCCCGC 1260
CCCAGCCCGG CCCAGGGTGA AGGAAGAGGC ACGTGCTCCT CAGAGCAGCC GGAGGGAGGG 1320
GGGAGGTCGG AGGTCGTGGA GGTGGTTTGT GTATCTTACT GGTCTGAAGG GACCAAGTGT 1380
GTTTGTTGTT TGTTTTGTAT CTTGTTTTTC TGATCGGAGC ATCACTACTG ACCTGTTGTA 1440
GGCAGCTATC TTACAGACGC ATGAATGTAA GAGTAGGAAG GGGTGGGTGT CAGGGATCAC 1500
TTGGGATCTT TGACACTTGA AAAATTACAC CTGGCAGCTG CGTTTAAGCC TTCCCCCATC 1560
GTGTACTGCA GAGTTGAGCT GGCAGGGGAG GGGCTGAGAG GGTGGGGGCT GGAACCCCTC 1620
CCCGGGAGGA GTGCCATCTG GGTCTTCCAT CTAGAACTGT TTACATGAAG ATAAGATACT 1680
CACTGTTCAT GAATACACTT GATGTTCAAG TATTAAGACC TATGCAATAT TTTTTACTTT 1740
TCTAATAAAC ATGTTTGTTA AAACAAAAAA AAAAAAAAAA AA  1782
```

Figure 2

Human RTP801 polypeptide (SEQ ID NO:2)

```
MPSLWDRFSS SSTSSSPSSL PRTPTPDRPP RSAWGSATRE EGFDRSTSLE 50
SSDCESLDSS NSGFGPEEDT AYLDGVSLPD FELLSDPEDE HLCANLMQLL 100
QESLAQARLG SRRPARLLMP SQLVSQVGKE LLRLAYSEPC GLRGALLDVC 150
VEQGKSCHSV GQLALDPSLV PTFQLTLVLR LDSRLWPKIQ GLFSSANSPF 200
LPGFSQSLTL STGFRVIKKK LYSSEQLLIE EC  232
```

Figure 3

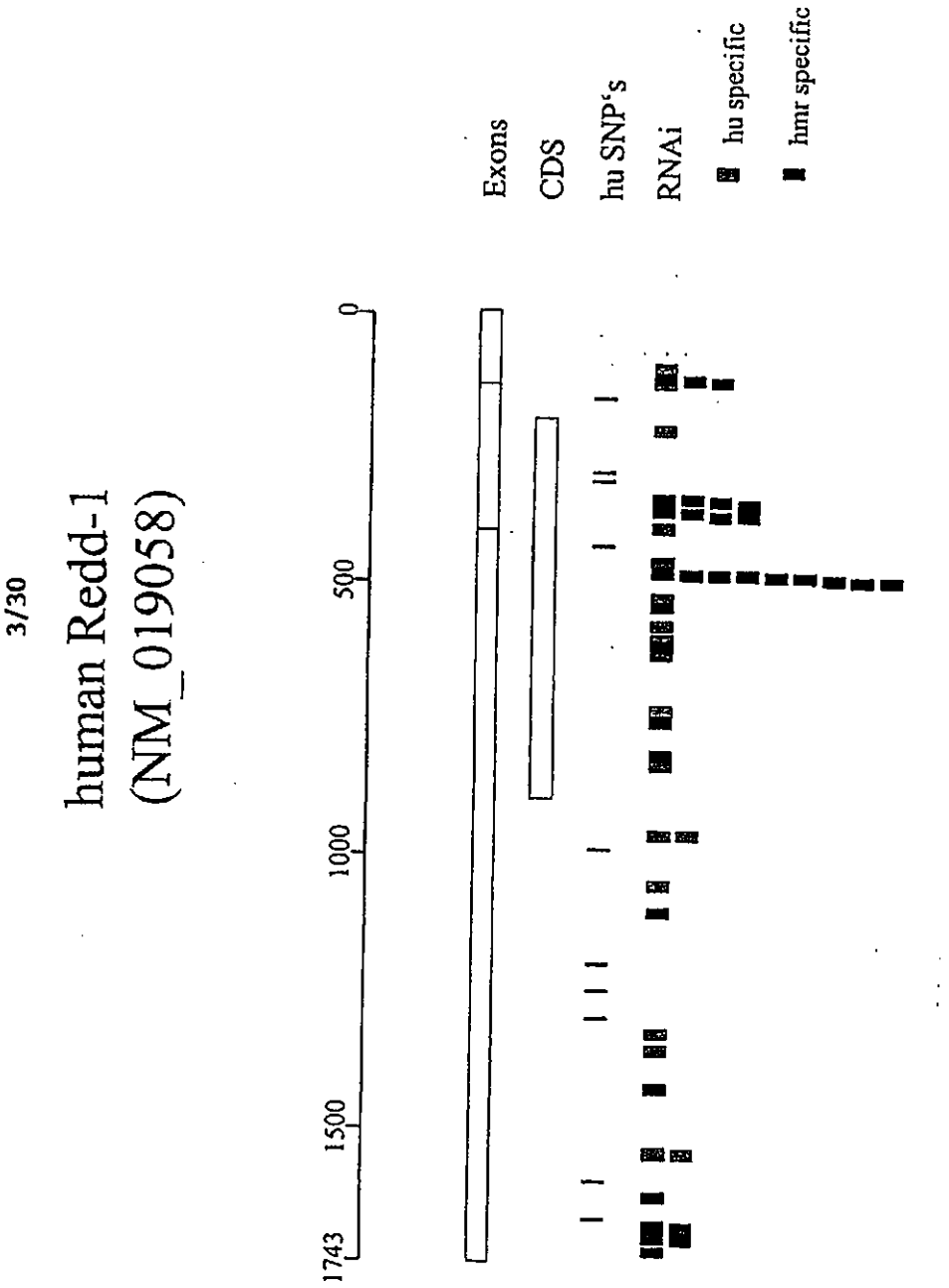

3/30
human Redd-1
(NM_019058)
0
500
1000
1500
1743
Exons
CDS
hu SNP's
RNAi
hu specific
hmr specific

Figure 4 part I

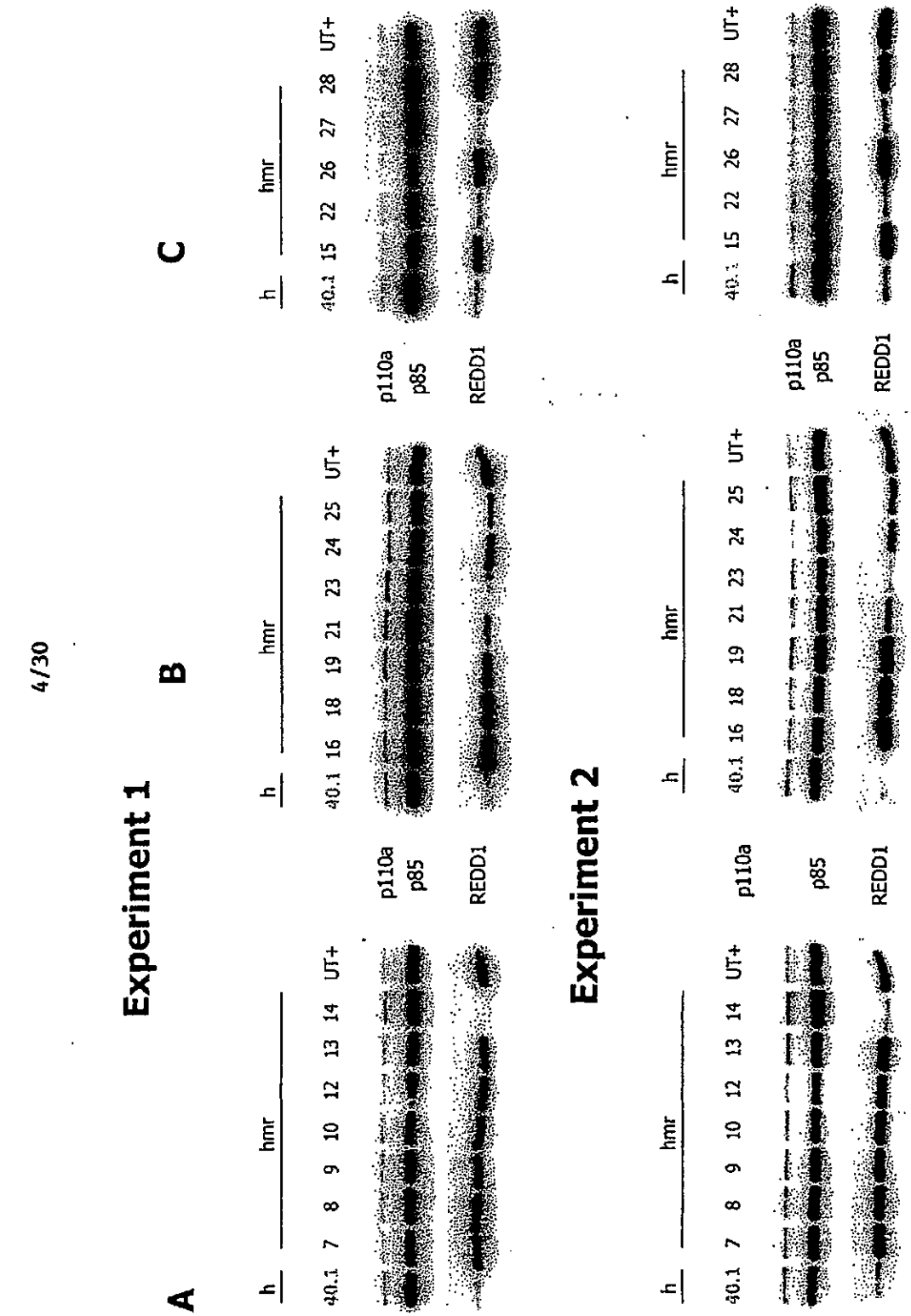


Figure 4 part II

Figure 4 part III

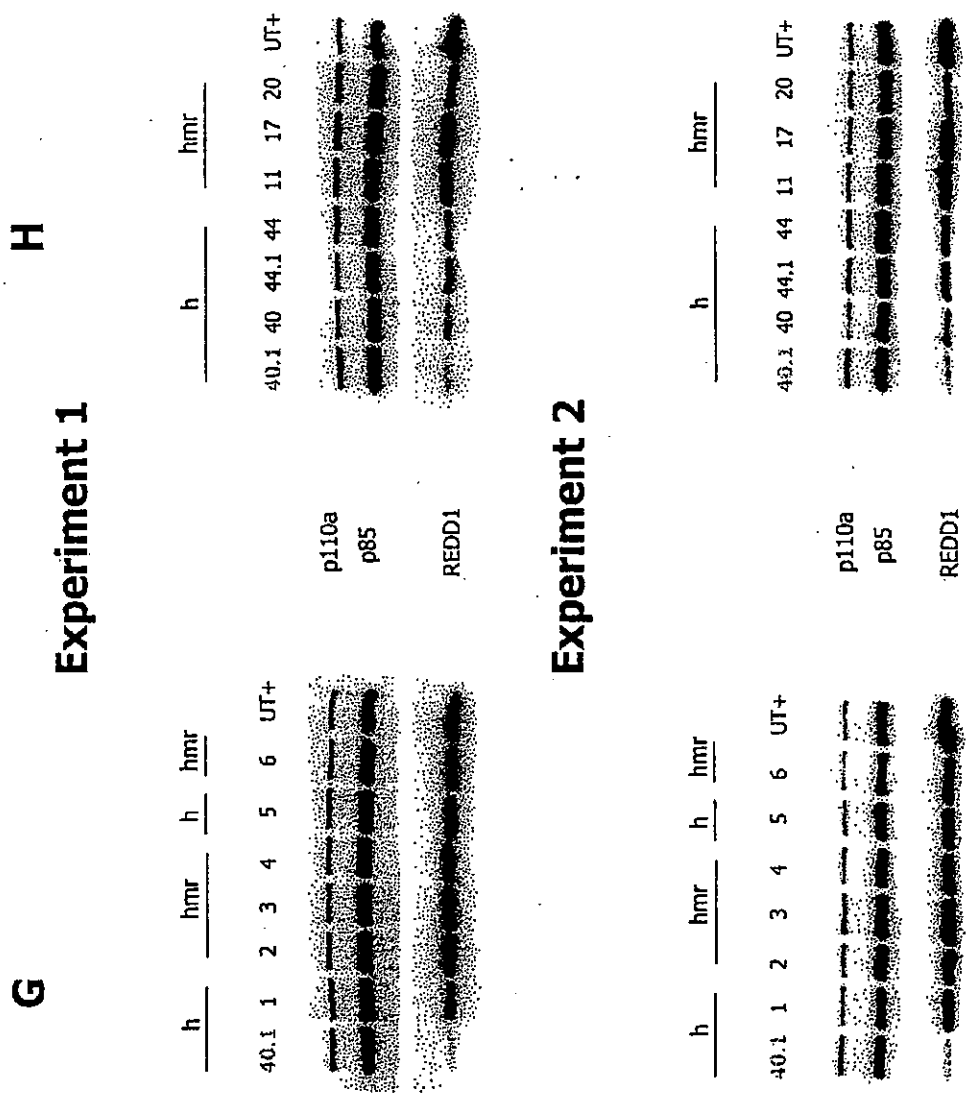


Figure 5 part I

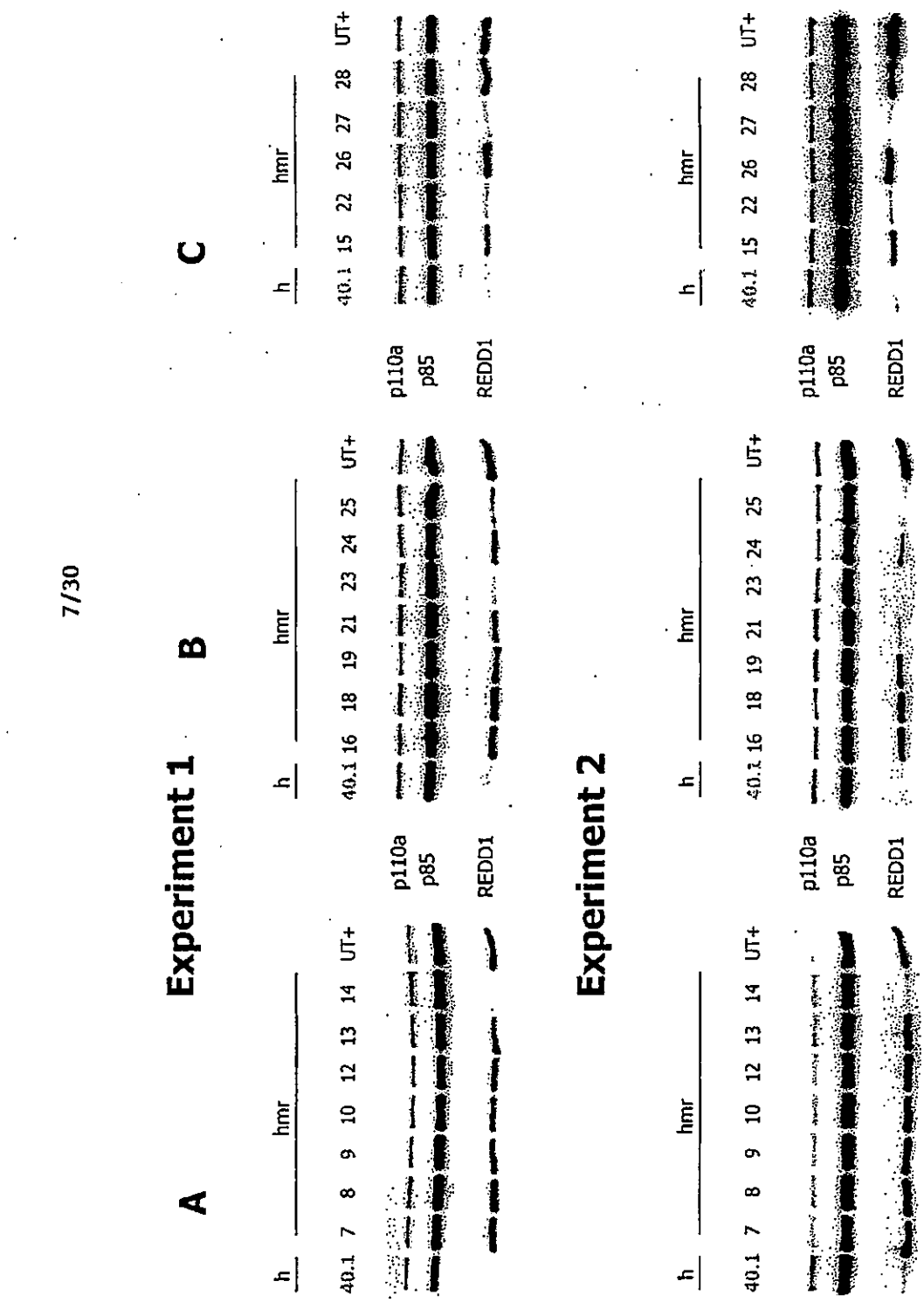


Figure 5 part II

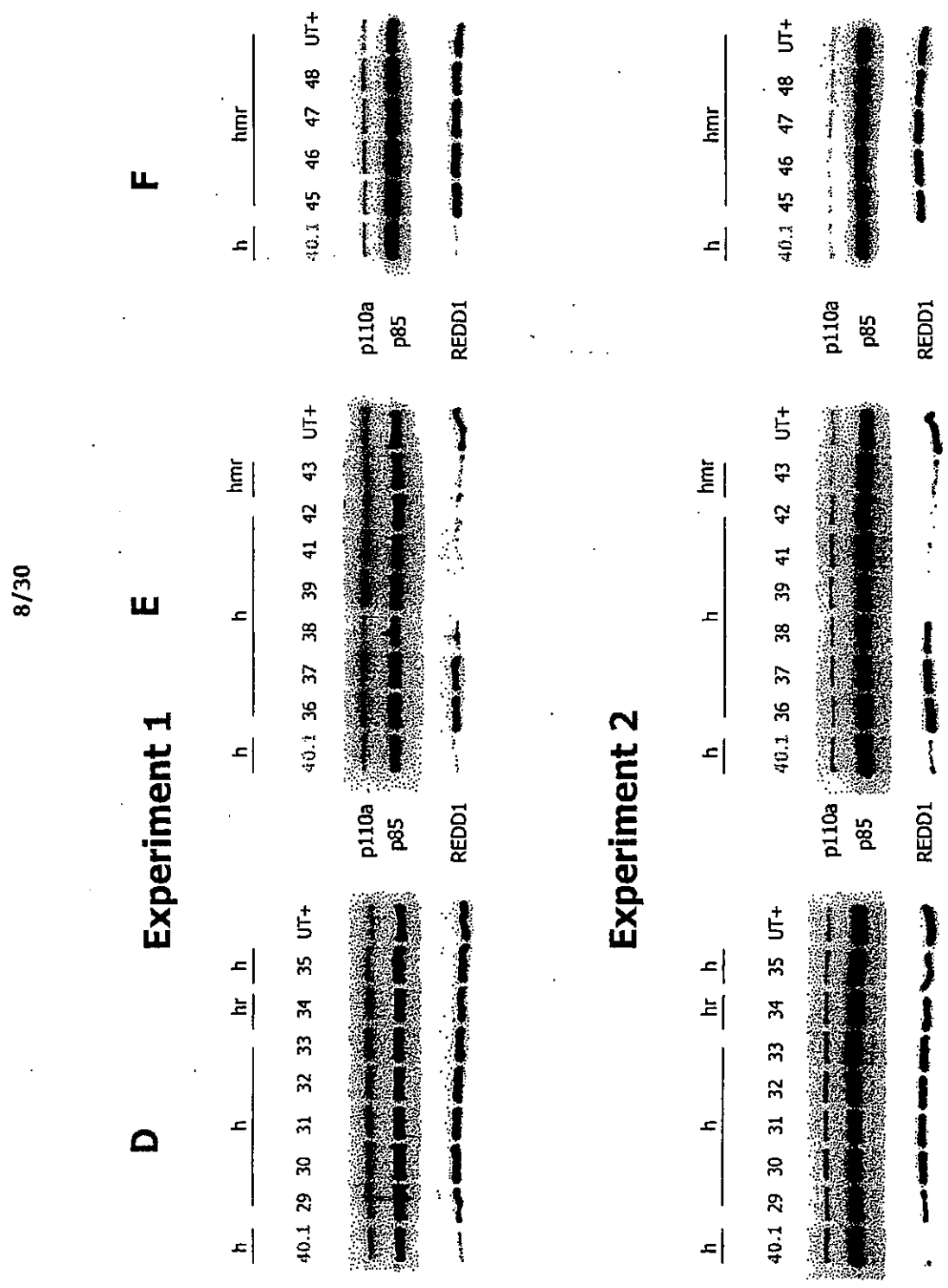


Figure 6

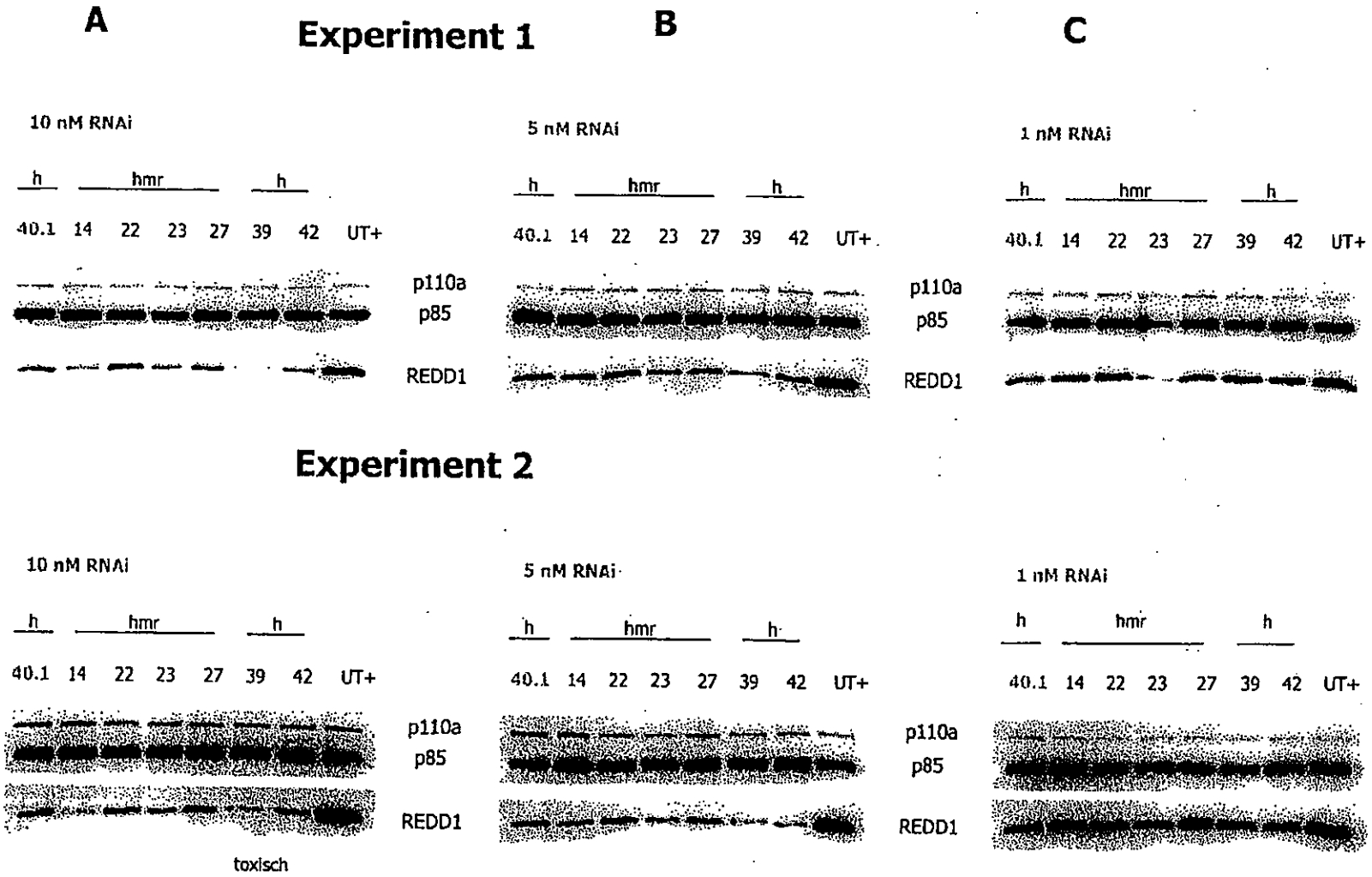

A
Experiment 1
B
C
10 nM RNAi
5 nM RNAi
1 nM RNAi
h
hmr
h
40.1 14 22 23 27 39 42 UT+
p110a
p85
REDD1
Experiment 2
10 nM RNAi
5 nM RNAi
1 nM RNAi
toxIsch

Figure 7

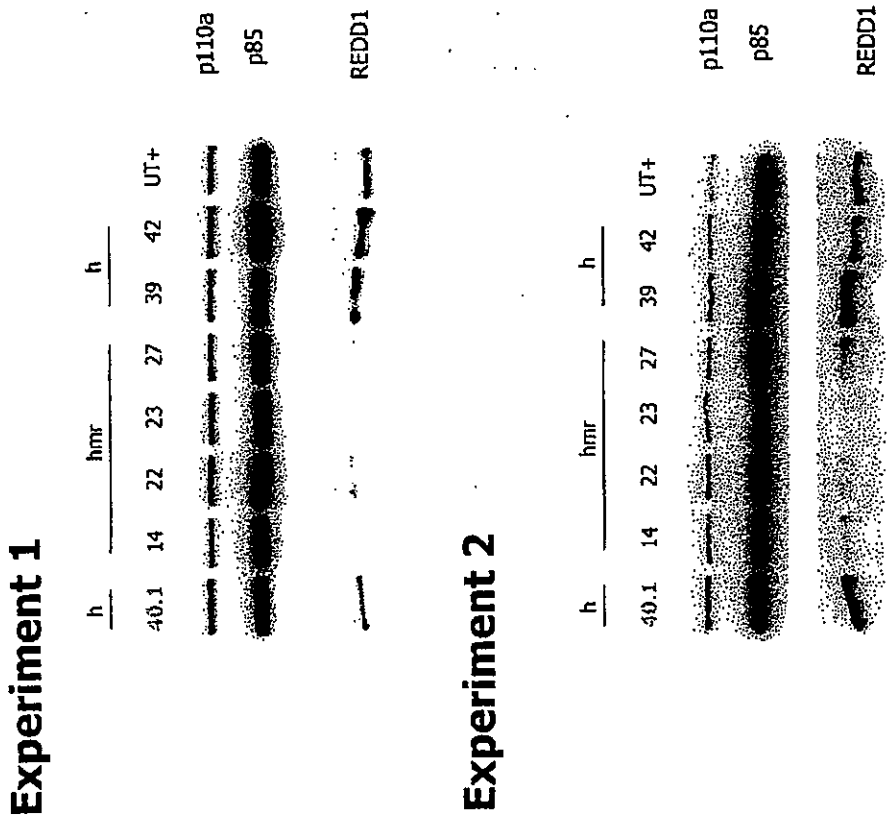

Experiment 1
h
hmr
h
40.1 14 22 23 27 39 42 UT+
p110a
p85
REDD1
Experiment 2
h
hmr
h
40.1 14 22 23 27 39 42 UT+
p110a
p85
REDD1

Figure 8

Blood vessel leakage in RTP801 KO mice as compared to control following CNV induction

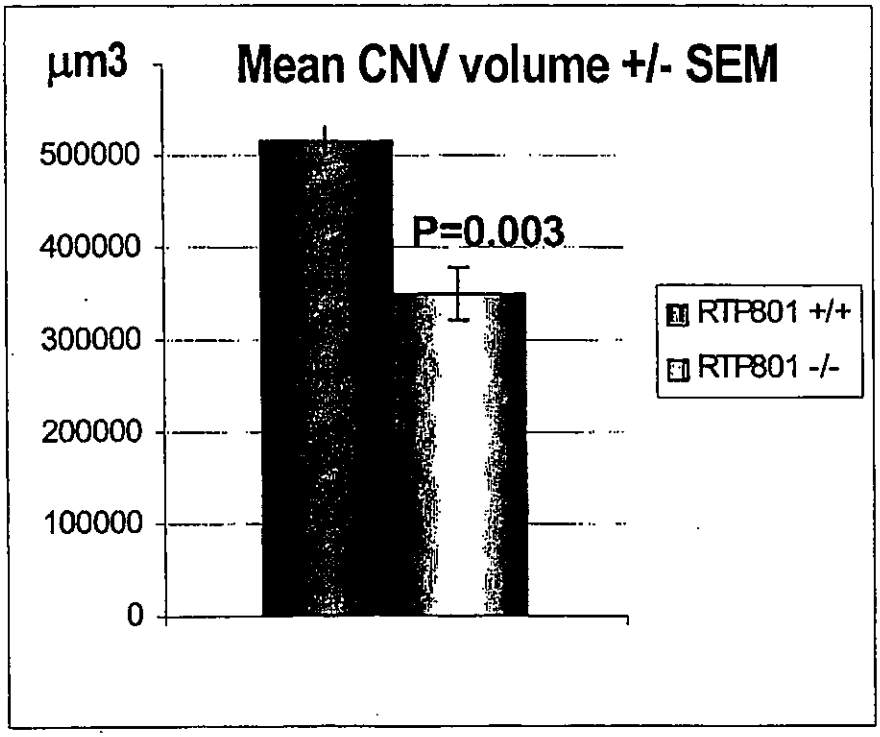


Figure 9

Reduction of CNV volume in response to RTP801 siRNA (REDD14) as compared to controls

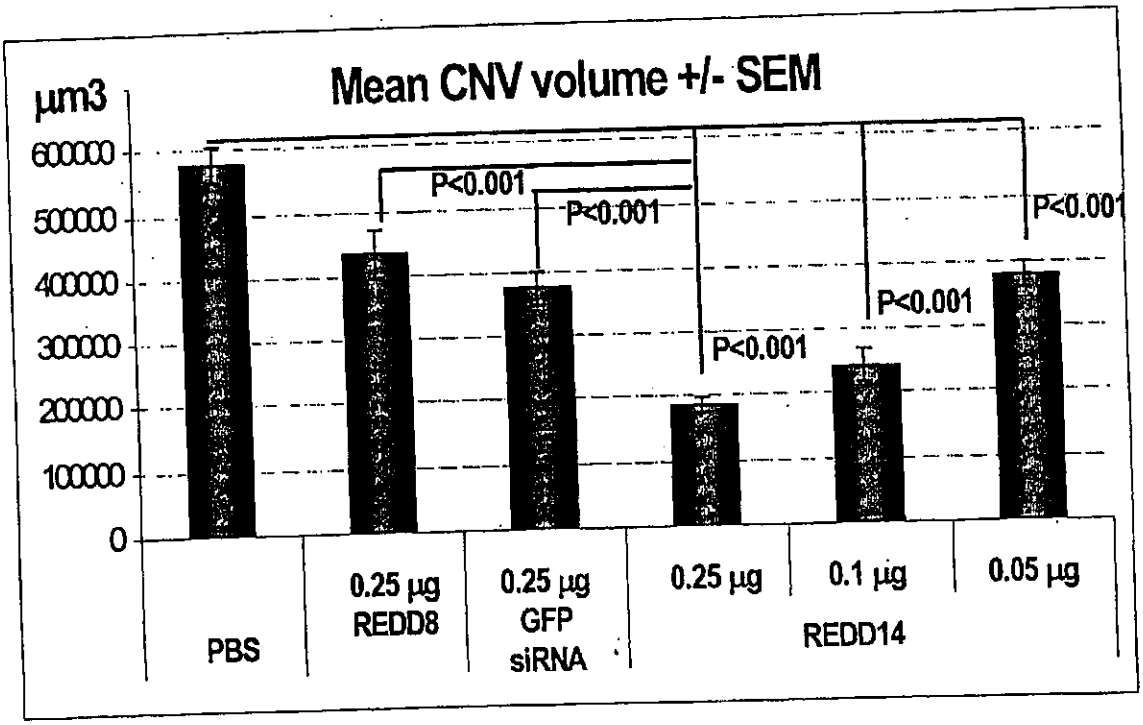


Figure 10

Reduction of RTP801 expression in the choroids of laser-treated monkeys in response to RTP801 siRNA as compared to a control, measured by Real - Time PCR

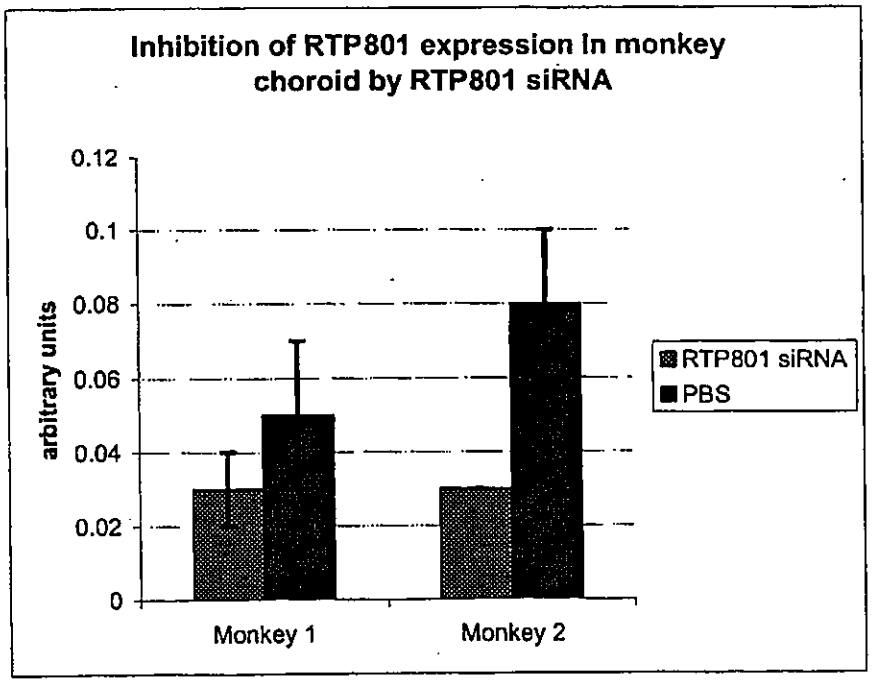
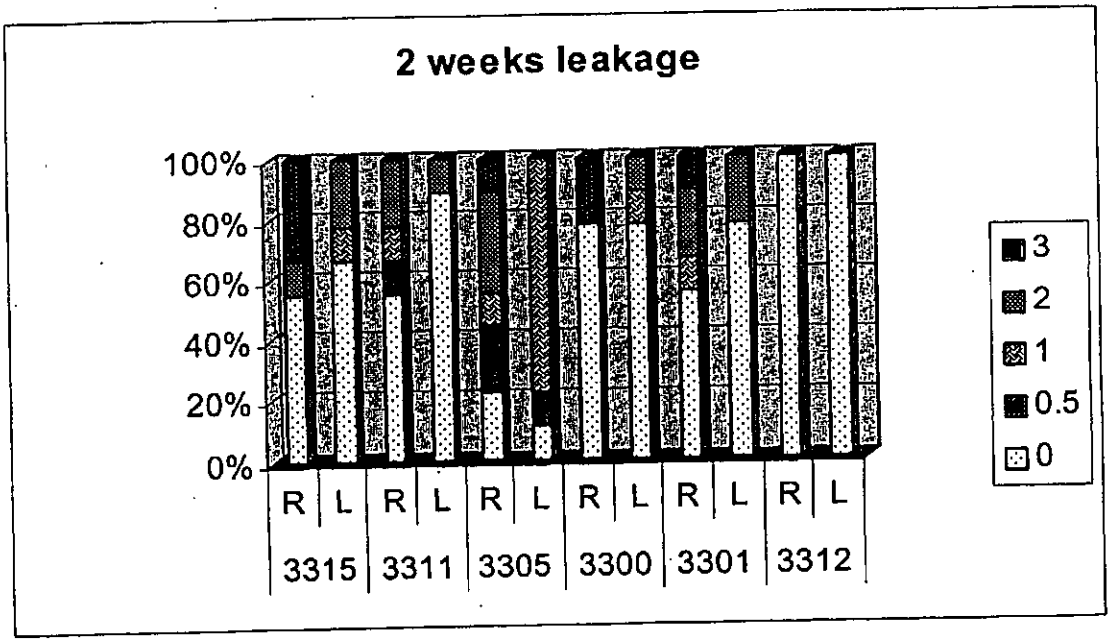


Figure 11

Reduction of leakage in a non-primate CNV model in response to RTP801 siRNA as compared to a control

a)



b)

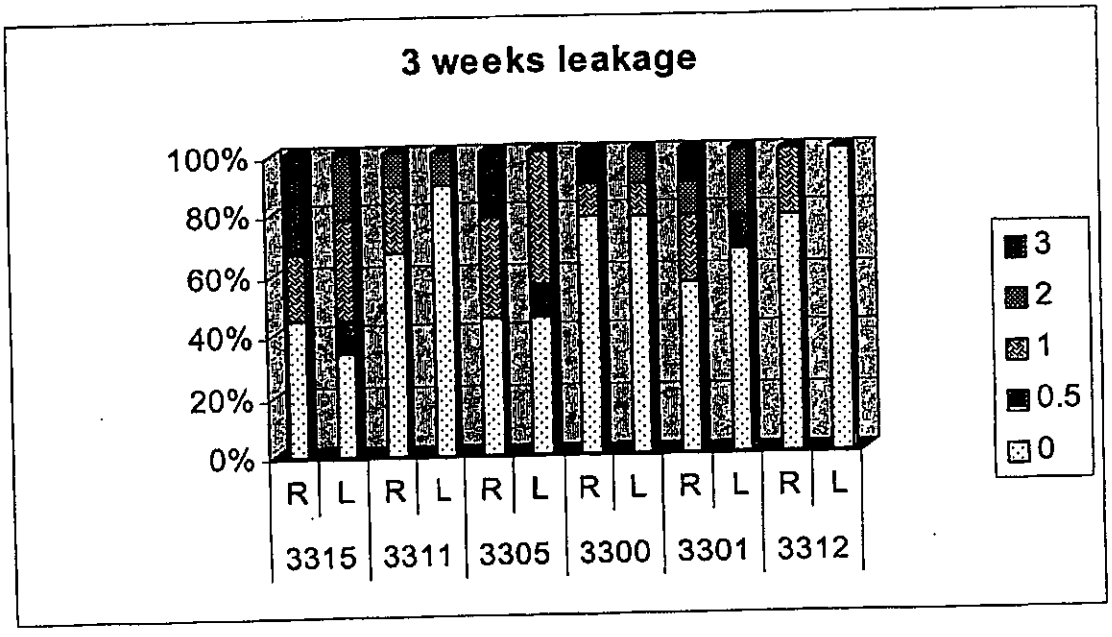
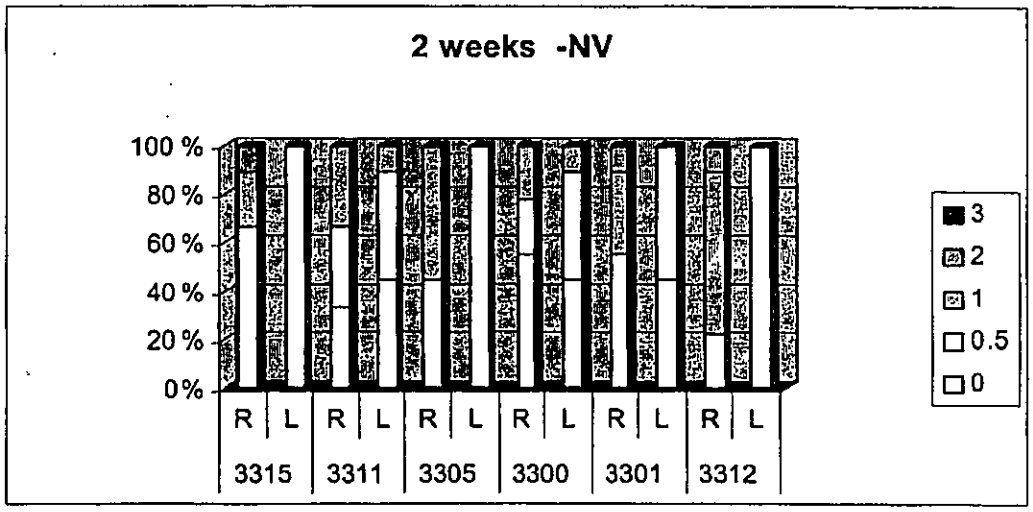


Figure 12

Reduction of neovascularization in a non-primate CNV model in response to RTP801 siRNA as compared to a control

a)



b)

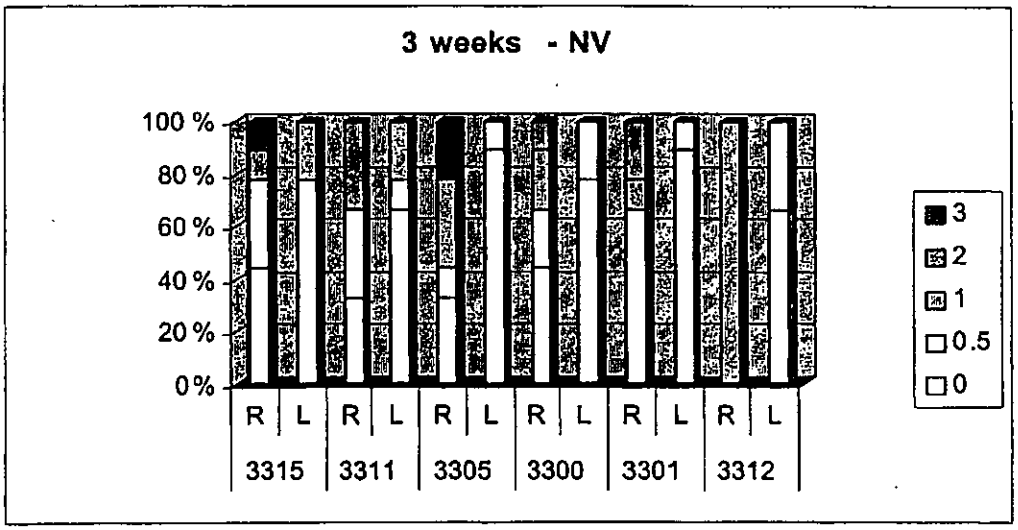
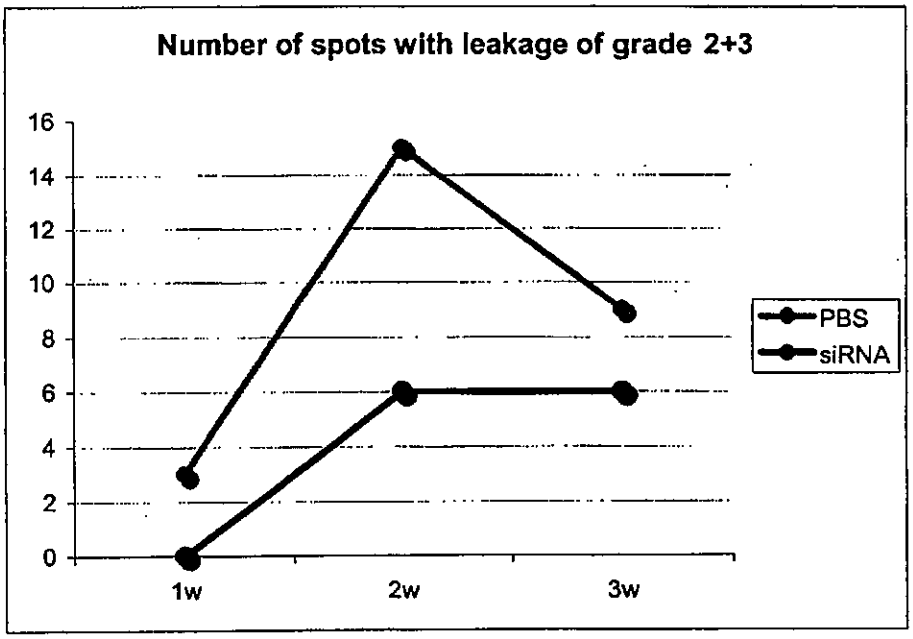


Figure 13

a)


Number of spots with leakage of grade 2+3
16
14
12
10
8
6
4
2
0
1w
2w
3w
PBS
siRNA

b)

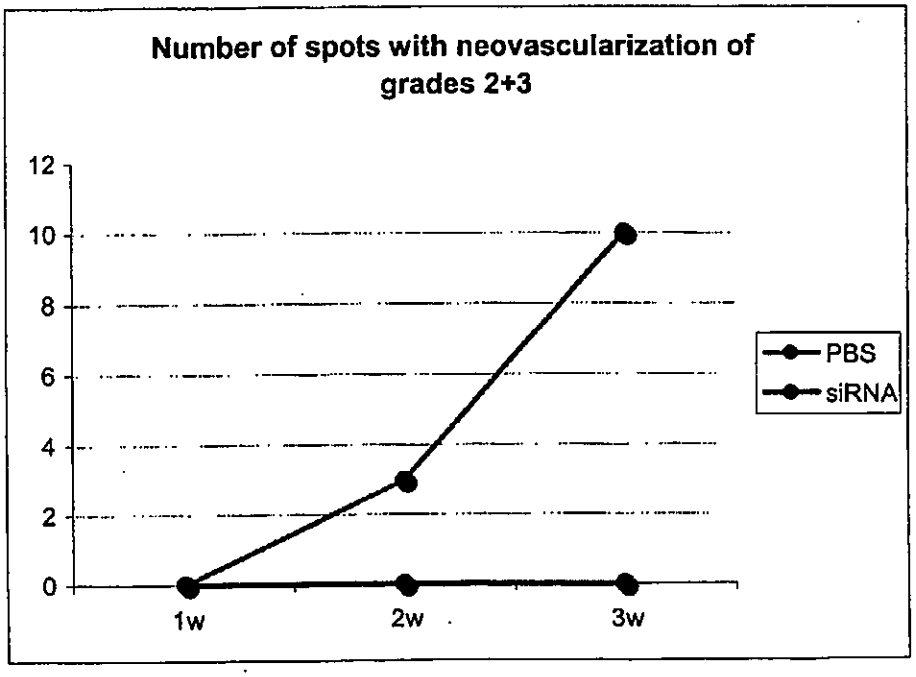

Number of spots with neovascularization of grades 2+3
12
10
8
6
4
2
0
1w
2w
3w
PBS
siRNA

Figure 14

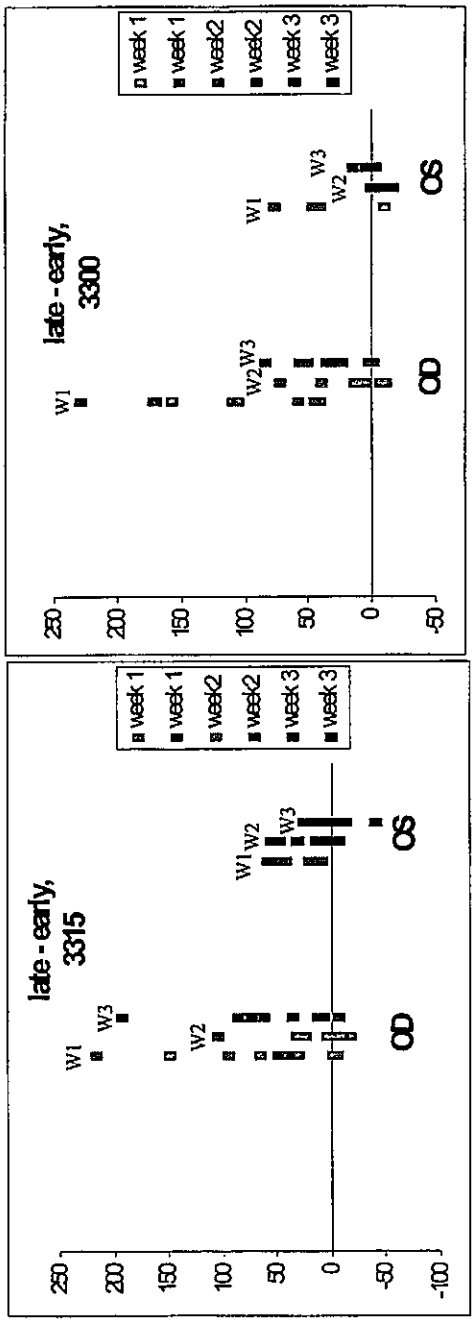
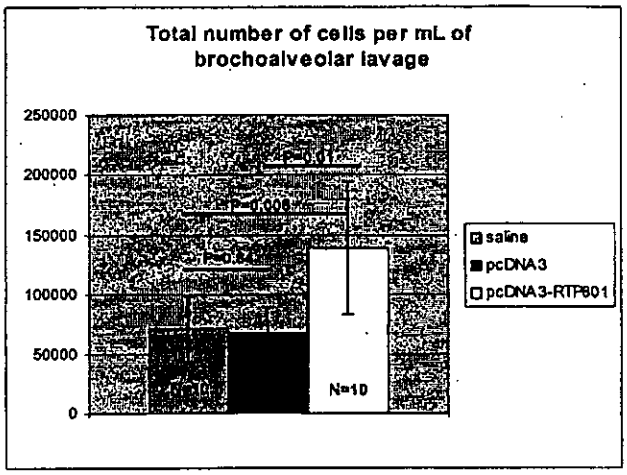
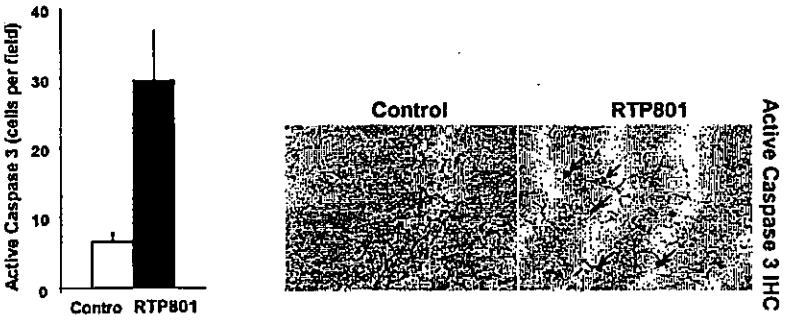

late - early,
3315
late - early,
3300
week 1
week 1
week2
week2
week 3
week 3
250
200
150
100
50
0
-50
-100
W1
W2
W3

Figure 15

a.



b.



c.

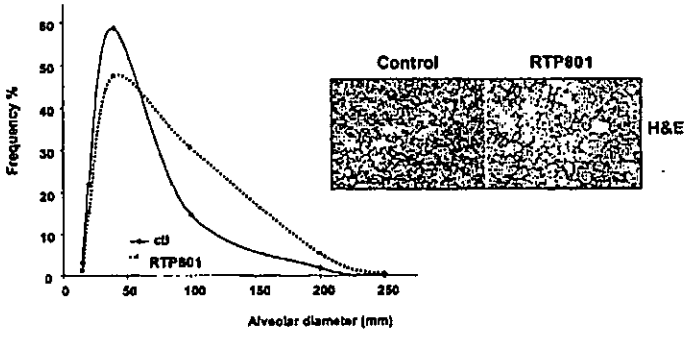
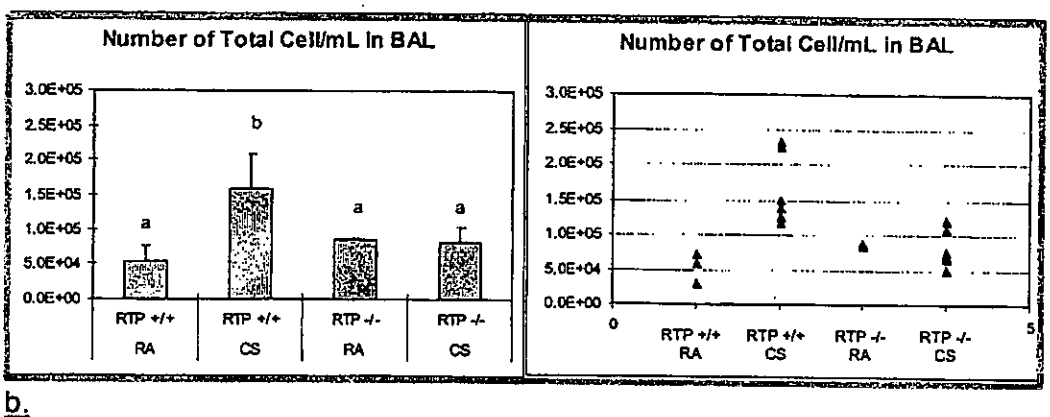
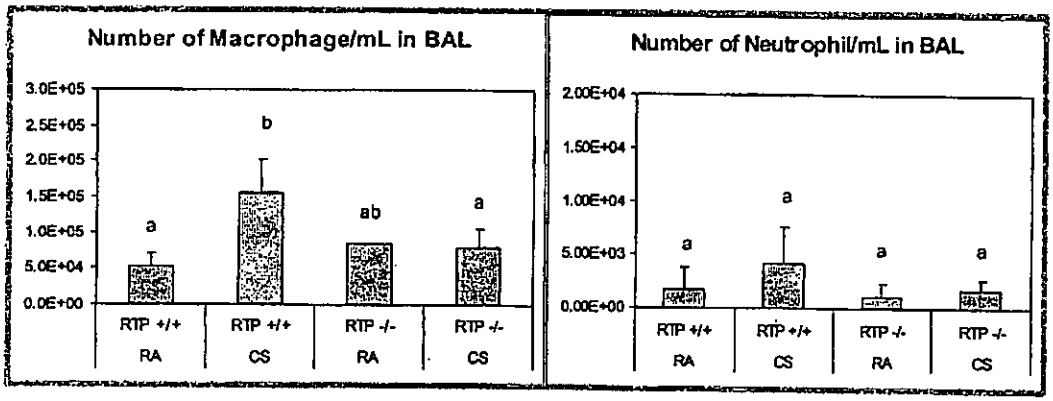


Figure 16

a.



b.



c.

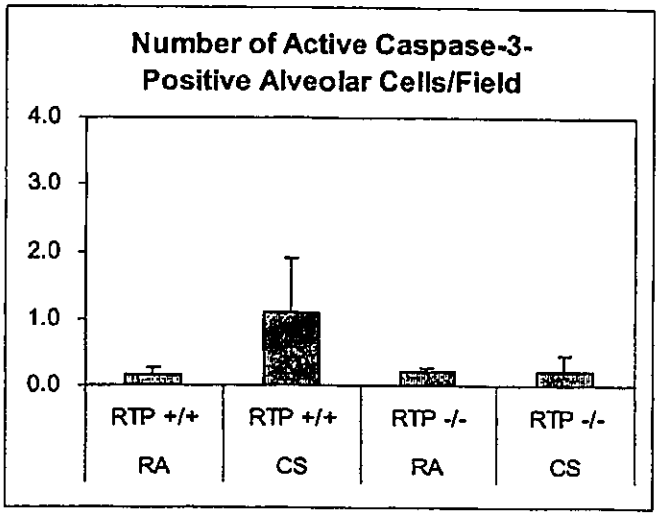
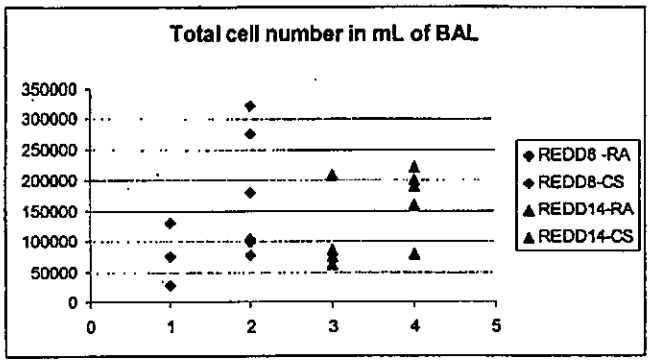
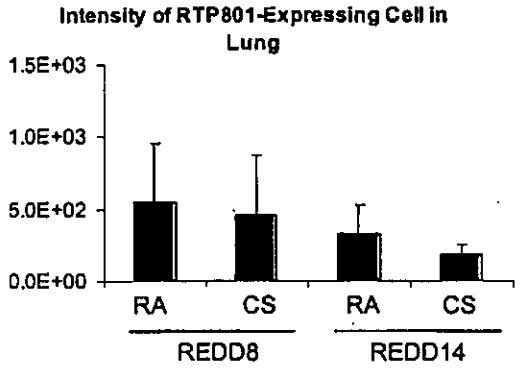


Figure 17

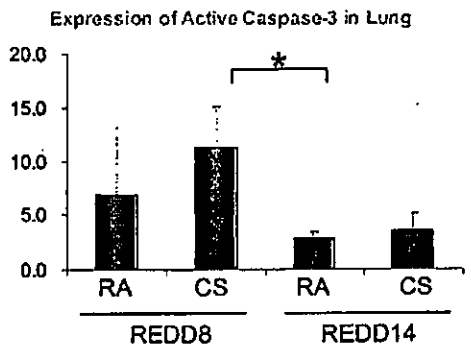
a.



b.



c.



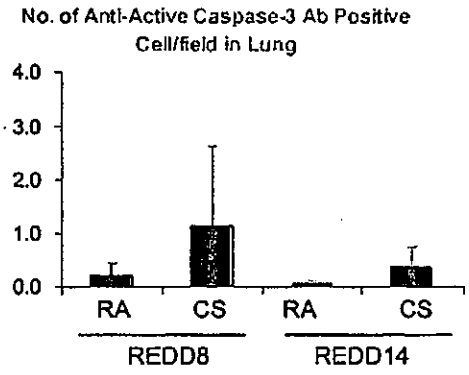


Figure 18

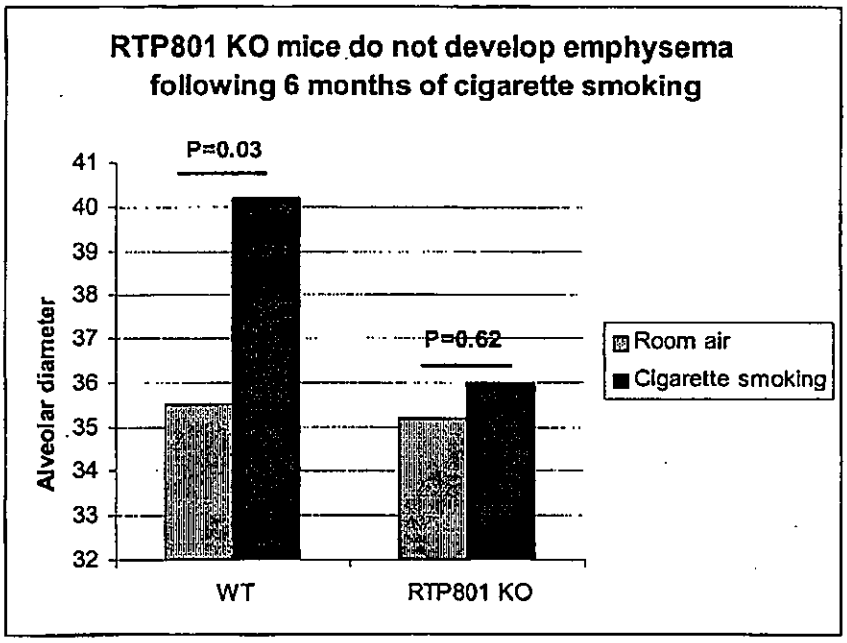

RTP801 KO mice do not develop emphysema following 6 months of cigarette smoking
P=0.03
P=0.62
Alveolar diameter
41
40
39
38
37
36
35
34
33
32
WT
RTP801 KO
Room air
Cigarette smoking

Figure 19

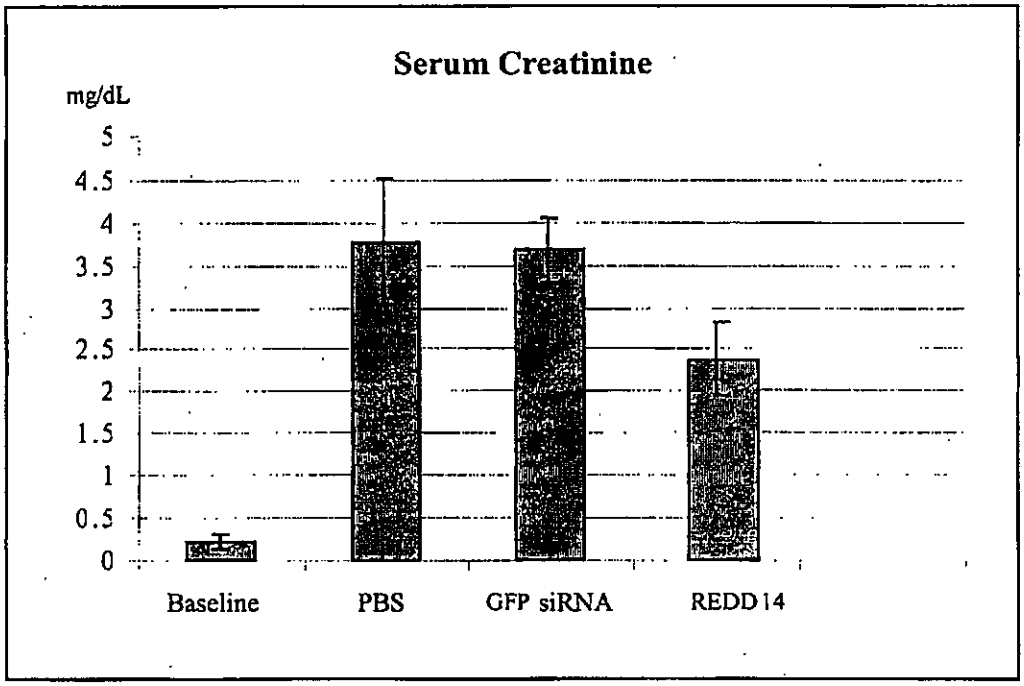

Serum Creatinine
mg/dL
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
Baseline
PBS
GFP siRNA
REDD14

Figure 20

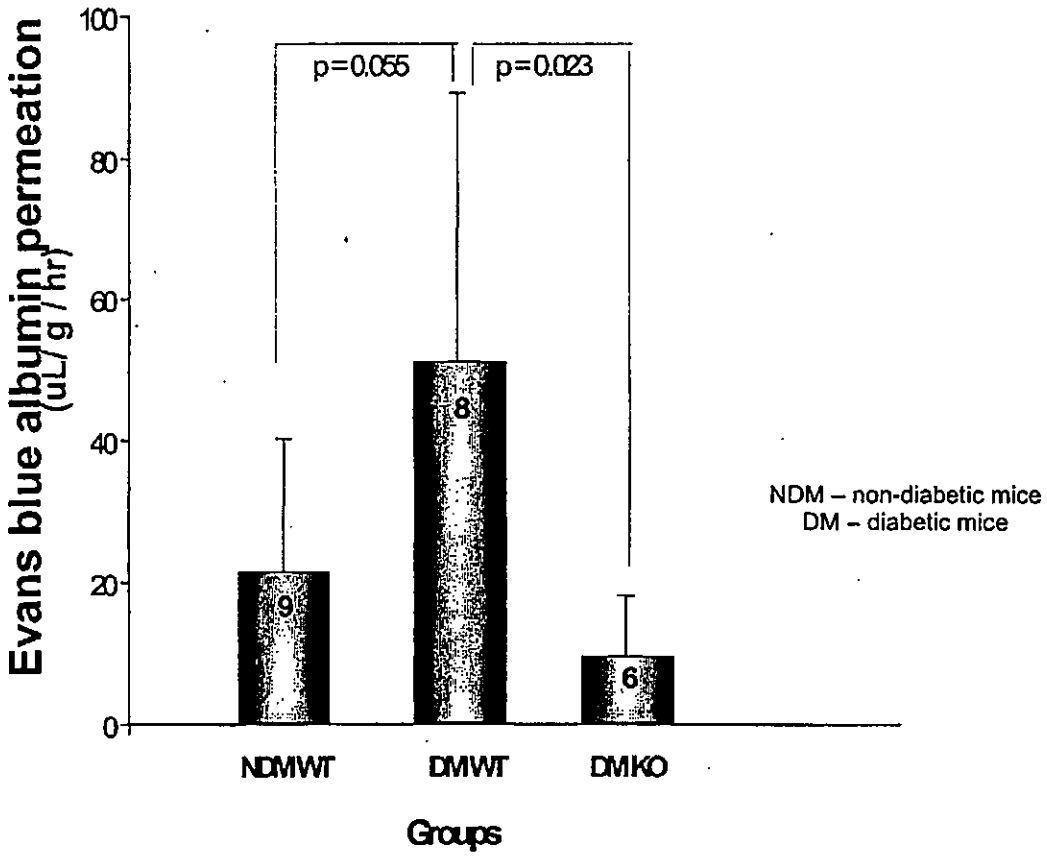

Evans blue albumin permeation (uL/g/hr)
100
80
60
40
20
0
p=0.055
p=0.023
9
8
6
NDMWT
DMWT
DMKO
Groups
NDM – non-diabetic mice
DM – diabetic mice

Figure 21

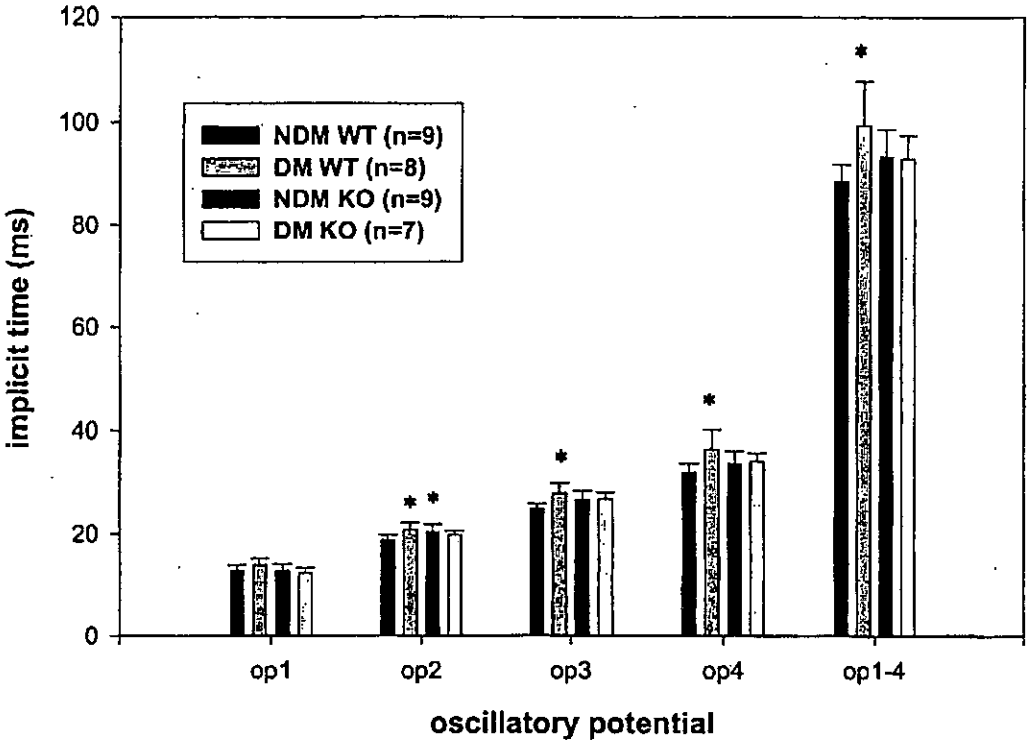

120
100
80
60
40
20
0
implicit time (ms)
NDM WT (n=9)
DM WT (n=8)
NDM KO (n=9)
DM KO (n=7)
*
* *
*
*
*
op1
op2
op3
op4
op1-4
oscillatory potential

Figure 22

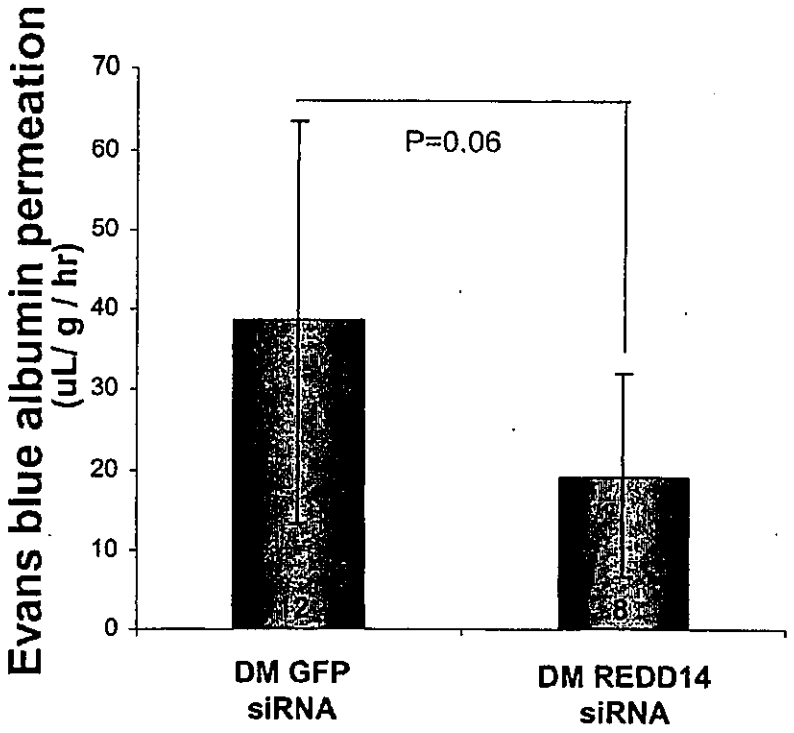

Evans blue albumin permeation
(uL/ g / hr)
70
60
50
40
30
20
10
0
P=0.06
2
3
DM GFP siRNA
DM REDD14 siRNA

Figure 23

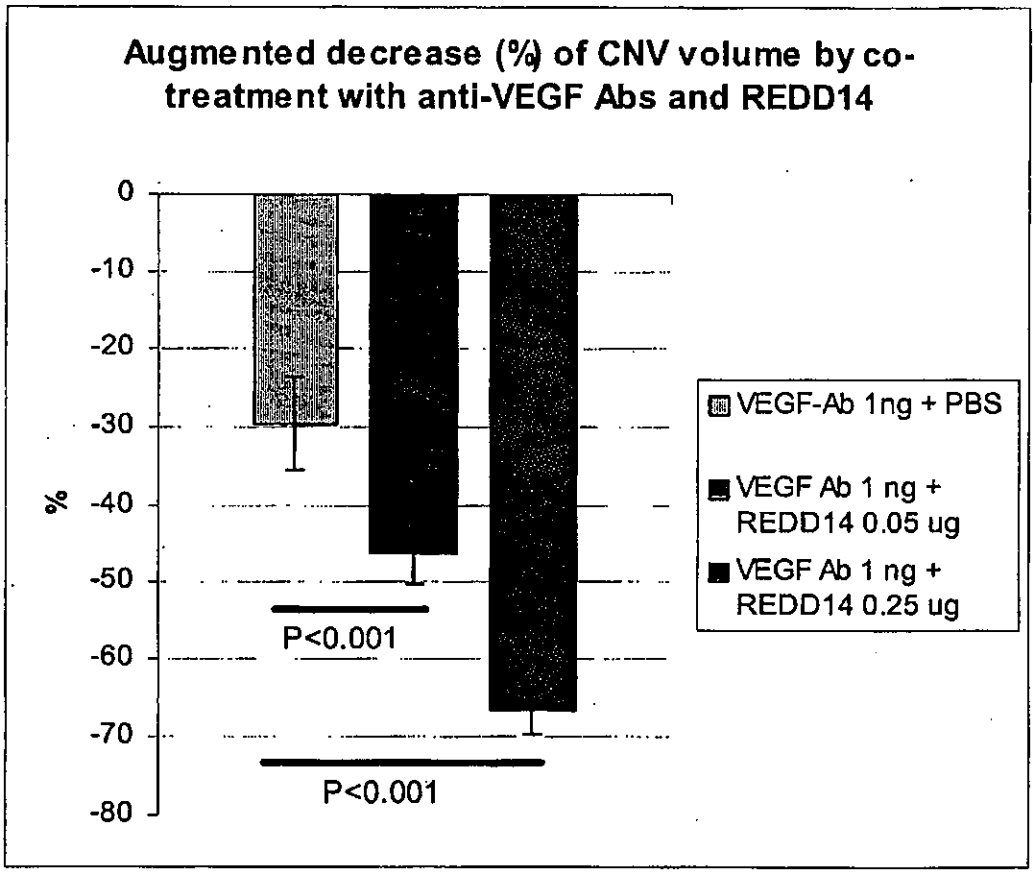

Augmented decrease (%) of CNV volume by co-treatment with anti-VEGF Abs and REDD14
0
-10
-20
-30
-40
-50
-60
-70
-80
%
P<0.001
P<0.001
VEGF-Ab 1ng + PBS
VEGF Ab 1 ng + REDD14 0.05 ug
VEGF Ab 1 ng + REDD14 0.25 ug

Figure 24

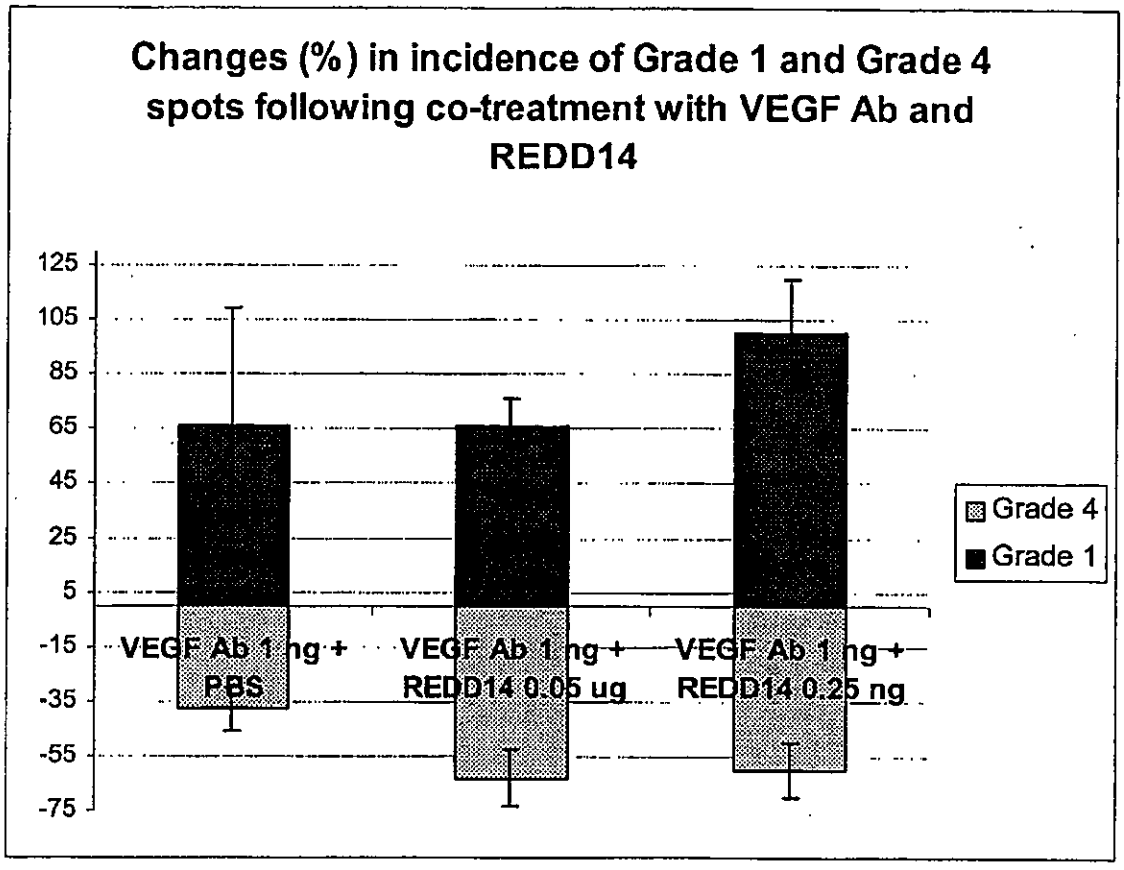

Changes (%) in incidence of Grade 1 and Grade 4 spots following co-treatment with VEGF Ab and REDD14
125
105
85
65
45
25
5
-15
-35
-55
-75
VEGF Ab 1 ng + PBS
VEGF Ab 1 ng + REDD14 0.05 ug
VEGF Ab 1 ng + REDD14 0.25 ng
Grade 4
Grade 1

Figure 25

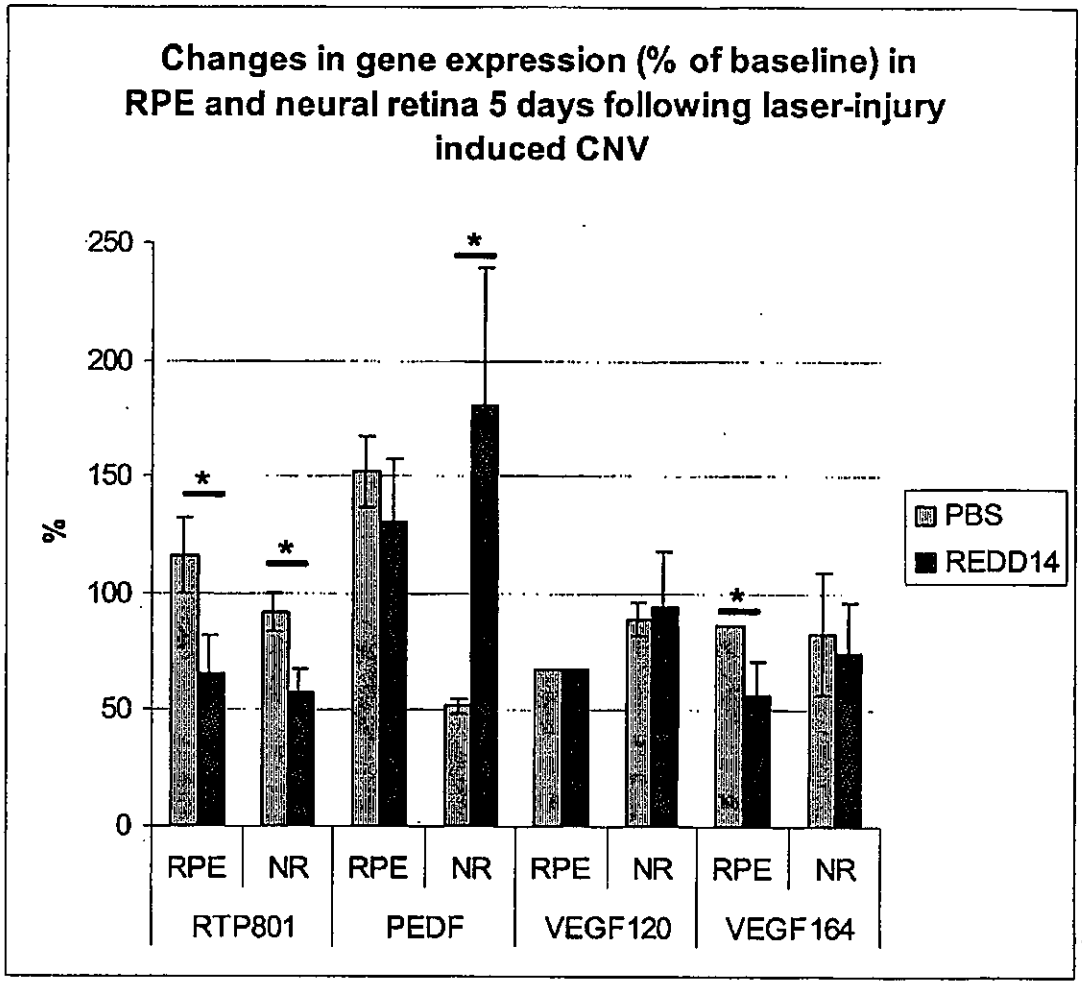
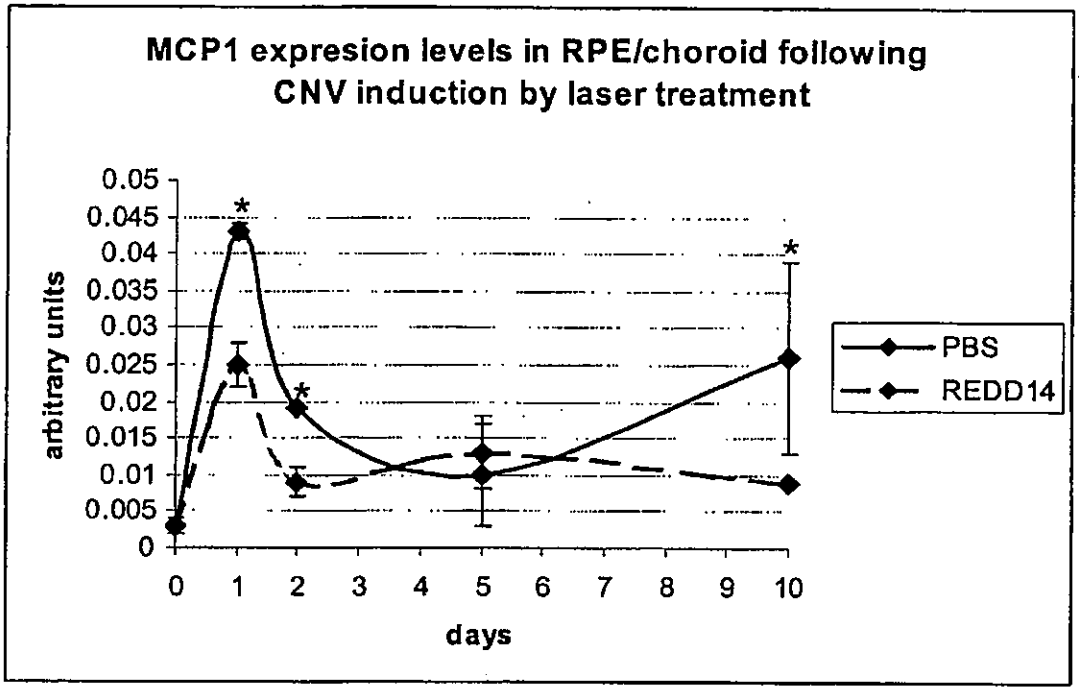

Changes in gene expression (% of baseline) in RPE and neural retina 5 days following laser-injury induced CNV
250
200
150
100
50
0
%
*
*
*
*
PBS
REDD14
RPE
NR
RPE
NR
RPE
NR
RPE
NR
RTP801
PEDF
VEGF120
VEGF164

Figure 26

a)


MCP1 expresion levels in RPE/choroid following CNV induction by laser treatment
arbitrary units
0.05
0.045
0.04
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0
0 1 2 3 4 5 6 7 8 9 10
days
PBS
REDD14
*
*
*

b)

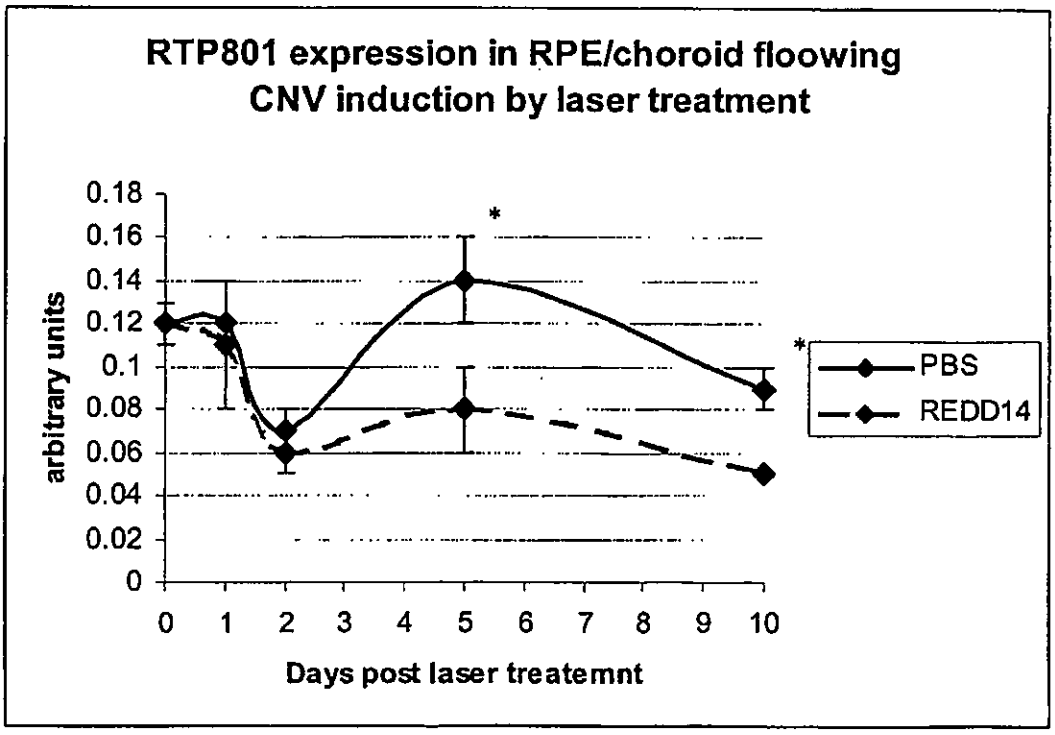
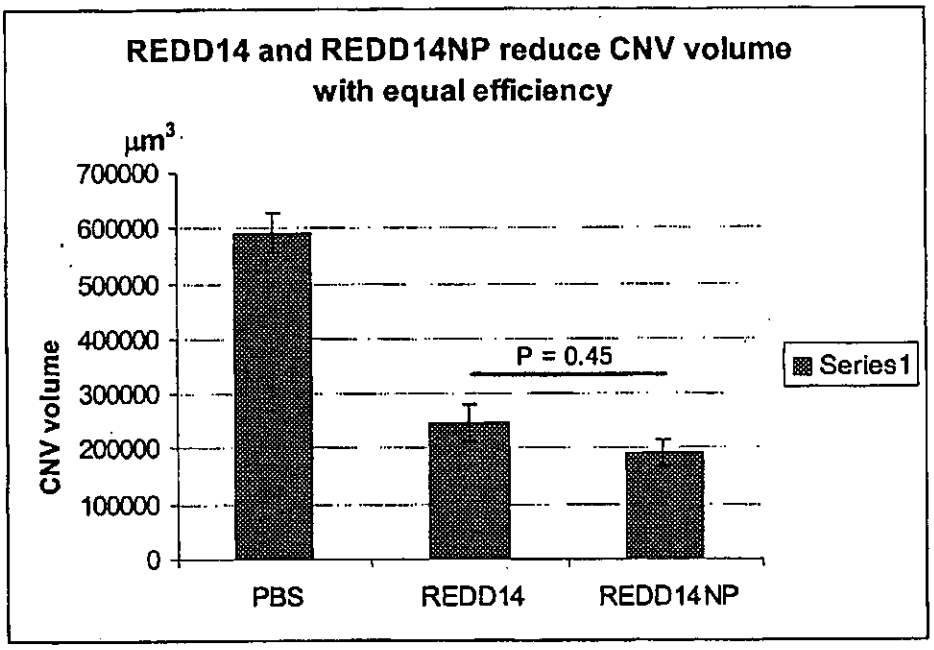

RTP801 expression in RPE/choroid floowing CNV induction by laser treatment
arbitrary units
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0 1 2 3 4 5 6 7 8 9 10
Days post laser treatemnt
PBS
REDD14
*
*

Figure 27


REDD14 and REDD14NP reduce CNV volume with equal efficiency
µm3
700000
600000
500000
400000
300000
200000
100000
0
CNV volume
P = 0.45
Series1
PBS
REDD14
REDD14NP