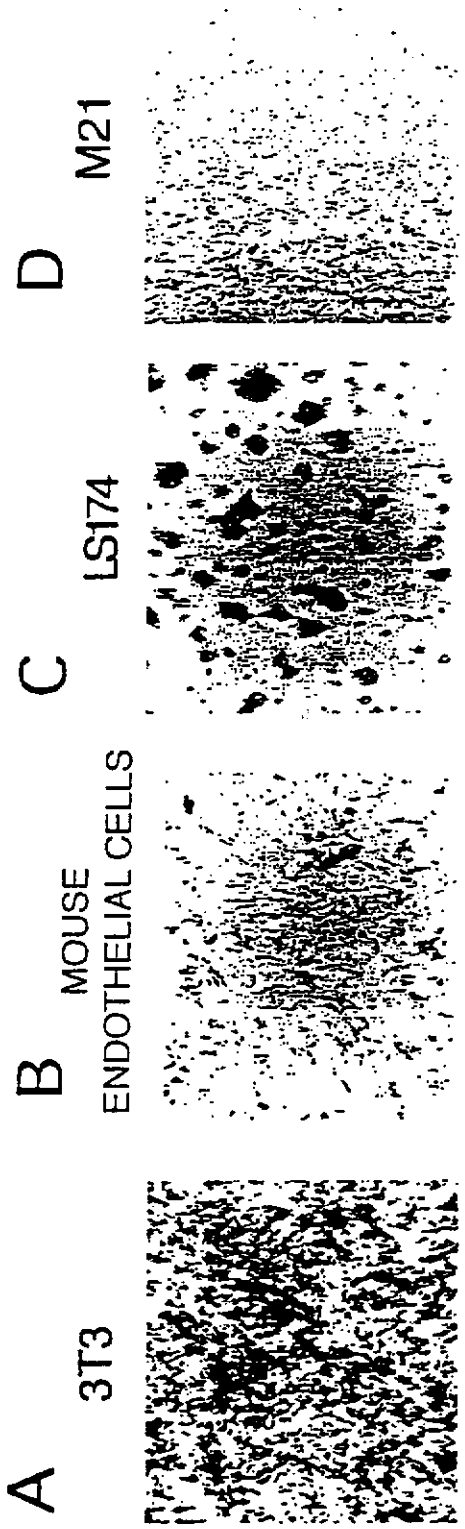
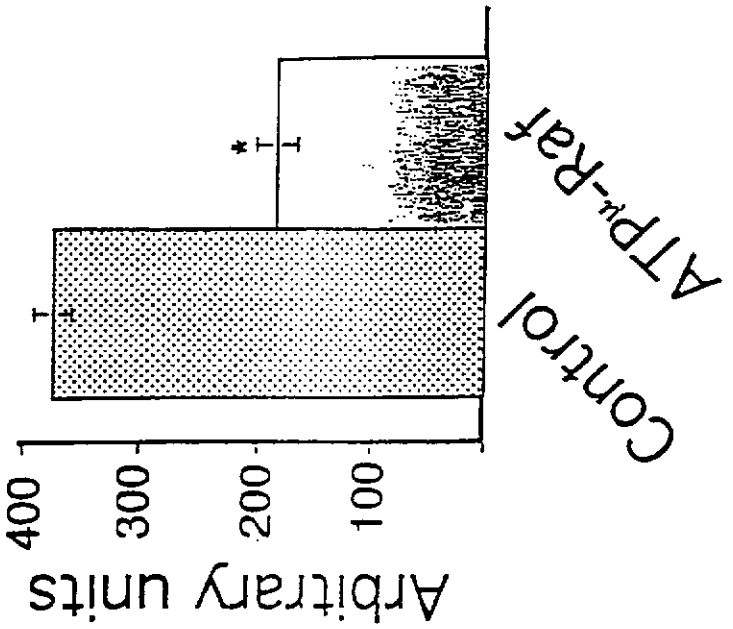


FIGURE 1


Arbitrary units
400
300
200
100
Control
ATPμ-Raf
*


Control
ATPμ-Raf

FIGURE 2

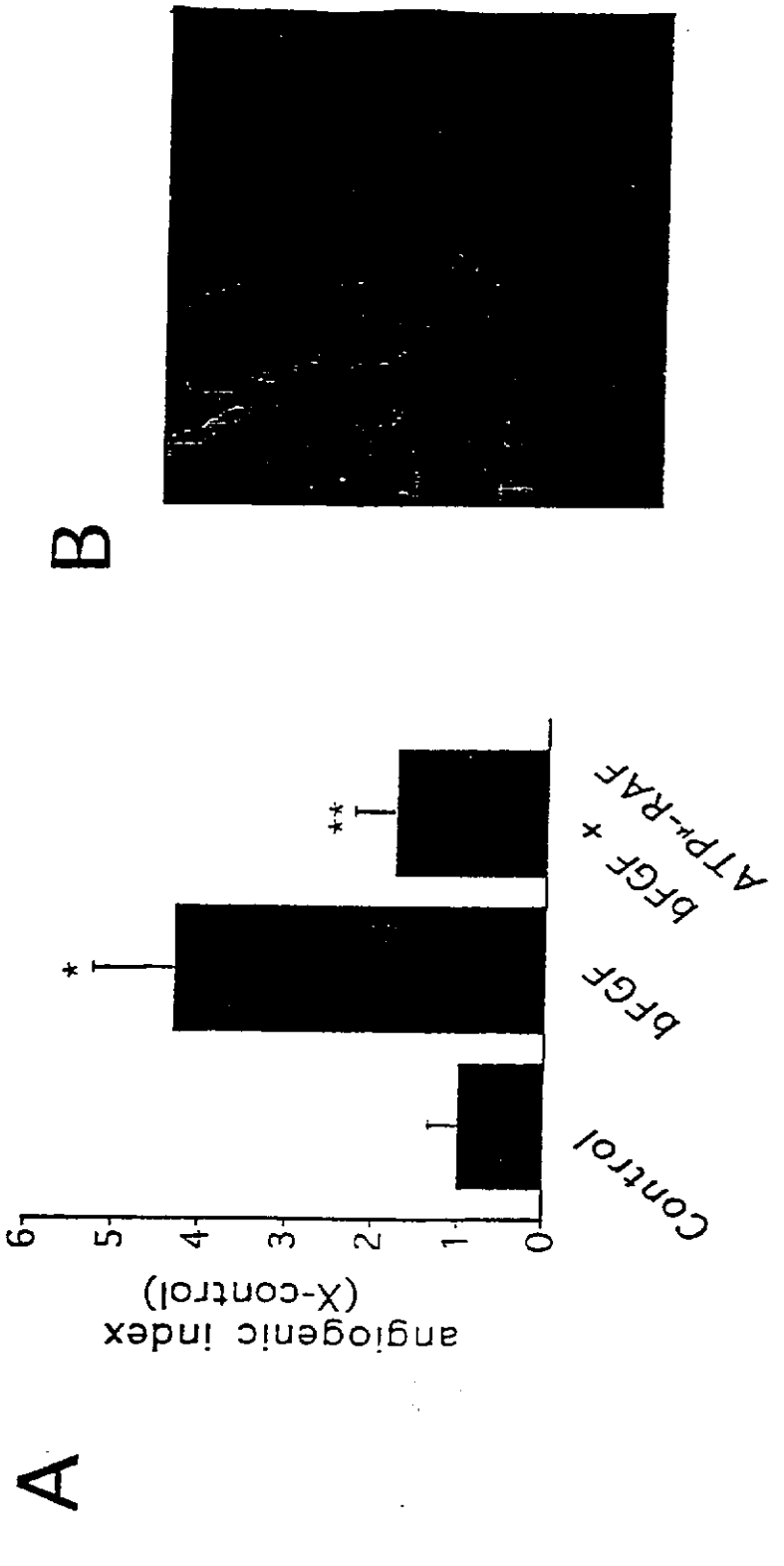

A
angiogenic index
(X-control)
0
1
2
3
4
5
6
*
**
control
bFGF
bFGF +
ATP-RAF
B

FIGURE 3

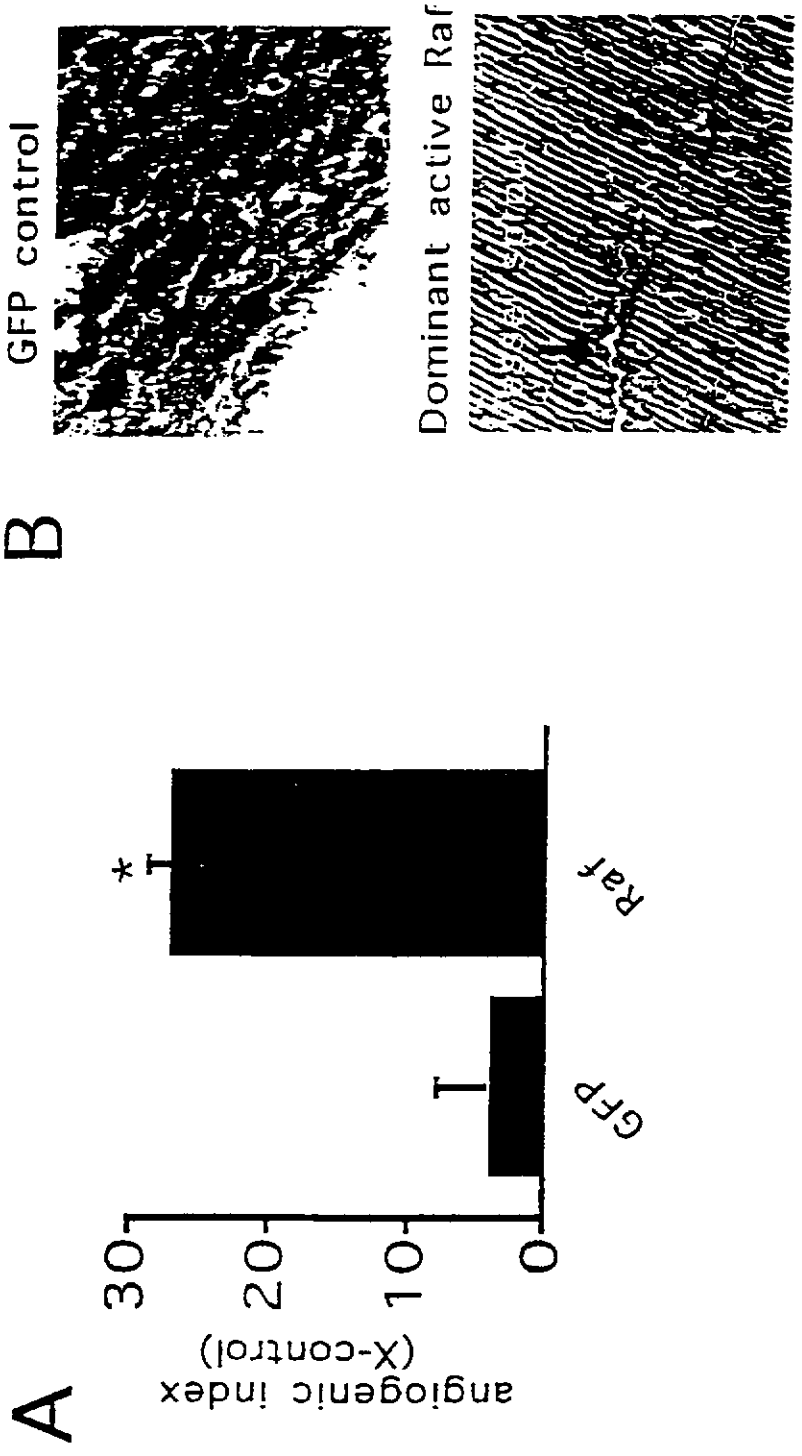

A
angiogenic index
(X-control)
30
20
10
0
GFP
Raf
*
B
GFP control
Dominant active Raf

FIGURE 4

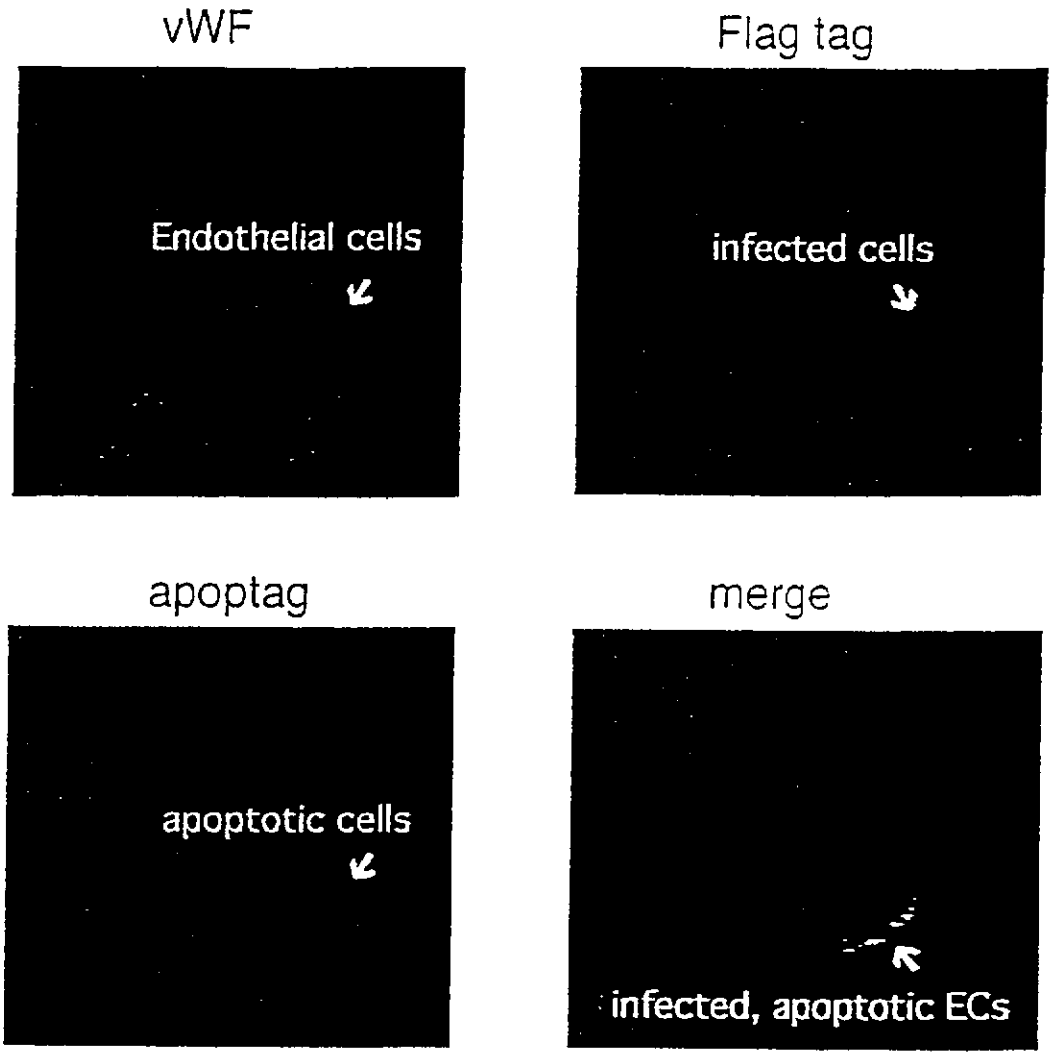

vWF
Endothelial cells
Flag tag
infected cells
apoptag
apoptotic cells
merge
infected, apoptotic ECs

FIGURE 5

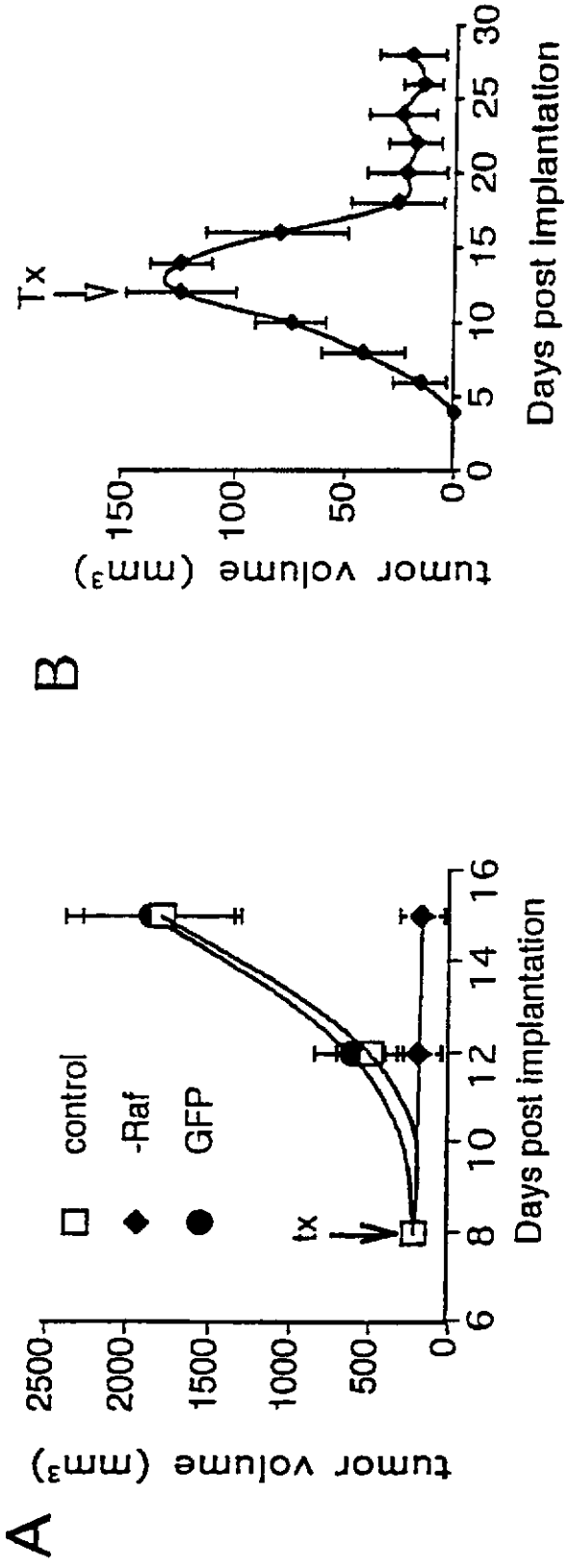

A
tumor volume (mm³)
2500
2000
1500
1000
500
0
6
8
10
12
14
16
Days post implantation
tx
control
-Raf
GFP
B
tumor volume (mm³)
150
100
50
0
0
5
10
15
20
25
30
Days post implantation
Tx

FIGURE 6

HUMAN c-RAF cDNA

ccgaatgtgaccgcctcccgctccctcacccgccgcggggaggaggagcgggcgagaagctgccgccgaacgacaggacg
ttggggcggcctggctccctcaggtttaagaattgtttaagctgcatcaatggagcacatacagggagcttggaagacga
tcagcaatggttttggattcaaagatgccgtgtttgatggctccagctgcatctctcctacaatagttcagcagtttggc
tatcagcgccgggcatcagatgatggcaaactcacagatccttctaagacaagcaacactatccgtgttttcttgccgaa
caagcaaagaacagtggtcaatgtgcgaaatggaatgagcttgcatgactgccttatgaaagcactcaaggtgaggggcc
tgcaaccagagtgctgtgcagtgttcagacttctccacgaacacaaaggtaaaaaagcacgcttagattggaatactgat
gctgcgtctttgattggagaagaacttcaagtagatttcctggatcatgttcccctcacaacacacaactttgctcggaa
gacgttcctgaagcttgccttctgtgacatctgtcagaaattcctgctcaatggatttcgatgtcagacttgtggctaca
aatttcatgagcactgtagcaccaaagtacctactatgtgtgtggactggagtaacatcagacaactcttattgtttcca
aattccactattggtgatagtggagtcccagcactaccttctttgactatgcgtcgtatgcgagagtctgtttccaggat
gcctgttagttctcagcacagatattctacacctcacgccttcacctttaacacctccagtccctcatctgaaggttccc
tctcccagaggcagaggtcgacatccacacctaatgtccacatggtcagcaccacgctgcctgtggacagcaggatgatt
gaggatgcaattcgaagtcacagcgaatcagcctcaccttcagccctgtccagtagccccaacaatctgagcccaacagg
ctggtcacagccgaaaaccccctgtccagcacaaagagagcgggcaccagtatctgggacccaggagaaaaacaaaatta
ggcctcgtggacagagagattcaagctattattgggaaatagaagccagtgaagtgatgctgtccactcggattgggtca
ggctcttttggaactgtttataagggtaaatggcacggagatgttgcagtaaagatcctaaaggttgtcgacccaaccccc
agagcaattccaggccttcaggaatgaggtggctgttctgcgcaaaacacggcatgtgaacattctgcttttcatggggt
acatgacaaaggacaacctggcaattgtgacccagtggtgcgagggcagcagcctctacaaacacctgcatgtccaggag
accaagtttcagatgttccagctaattgacattgcccggcagacggctcagggaatggactatttgcatgcaaagaacat
catccatagagacatgaaatccaacaatatatttctccatgaaggcttaacagtgaaaattggagattttggtttggcaa
cagtaaagtcacgctggagtggttctcagcaggttgaacaacctactggctctgtcctctggatggccccagaggtgatc
cgaatgcaggataacaacccattcagtttccagtcggatgtctactcctatggcatcgtattgtatgaactgatgacggg
ggagcttccttattctcacatcaacaaccgagatcagatcatcttcatggtgggccgaggatatgcctccccagatctta
gtaagctatataagaactgccccaaagcaatgaagaggctggtagctgactgtgtgaagaaagtaaaggaagagaggcct
ctttttccccagatcctgtcttccattgagctgctccaacactctctaccgaagatcaaccggagcgcttccgagccatc
cttgcatcgggcagcccacactgaggatatcaatgcttgcacgctgaccacgtccccgaggctgcctgtcttctagttga
ctttgcacctgtcttcaggctgccaggggaggaggagaagccagcaggcaccacttttctgctccctttctccagaggca
gaacacatgttttcagagaagctctgctaaggaccttctagactgctcacagggccttaacttcatgttgccttctttc
tatccctttgggccctgggagaaggaagccatttgcagtgctggtgtgtcctgctcccctccccacattccccatgctcaa
ggcccagccttctgtagatgcgcaagtggatgttgatggtagtacaaaaagcaggggcccagccccagctgttggctaca
tgagtatttagaggaagtaaggtagcaggcagtccagccctgatgtggagacacatgggattttggaaatcagcttctgg
aggaatgcatgtcacaggcgggactttcttcagagagtggtgcagcgccagacattttgcacataaggcaccaaacagcc
caggactgccgagactctggccgcccgaaggagcctgctttggtactatggaacttttcttaggggacacgtcctccttt
cacagcttctaaggtgtccagtgcattgggatggttttccaggcaaggcactcggccaatccgcatctcagccctctcag
gagcagtcttccatcatgctgaattttgtcttccaggagctgcccctatggggcgggccgcagggccagcctgtttctct
aacaaacaaacaaacaaacagccttgtttctctagtcacatcatgtgtatacaaggaagccaggaatacaggttttcttg
atgatttgggttttaattttgtttttattgcacctgacaaaatacagttatctgatggtccctcaattatgttattttaa
taaaataaattaaattt

FIGURE 7

HUMAN c-RAF ENCODED PROTEIN

MEHIQGAWKTISNGFGFKDAVFDGSSCISPTIVQQFGYQRRASDDGKLTD
PSKTSNTIRVFLPNKQRTVVNVRNGMSLHDCLMKALKVRGLQPECCAV
FRLLHEHKGKKARLDWNTDAASLIGEELQVDFLDHVPLTTHNFARKTFL
KLAFCDICQKFLLNGFRCQTCGYKFHEHCSTKVPTMCVDWSNIRQLLLFP
NSTIGDSGVPALPSLTMRRMRESVSRMPVSSQHRYSTPHAFTFNTSSPS
SEGSLSQRQRSTSTPNVHMVSTTLPVDSRMIEDAIRSHSESASPSALSSS
PNNLSPTGWSQPKTPVPAQRERAPVSGTQEKNKIRPRGQRDSSYYWEIE
ASEVMLSTRIGSGSFGTVYKGKWHGDVAVKILKVVDPTPEQFQAFRNE
VAVLRKTRHVNILLFMGYMTKDNLAIVTQWCEGSSLYKHLHVQETKF
QMFQLIDIARQTAQGMDYLHAKNIIHRDMKSNNIFLHEGLTVKIGDFGL
ATVKSRWSGSQQVEQPTGSVLWMAPEVIRMQDNNPFSFQSDVYSYGIV
LYELMTGELPYSHINNRDQIIFMVGRGYASPDLSKLYKNCPKAMKRLVA
DCVKKVKEERPLFPQILSSIELLQHSLPKINRSASEPSLHRAAHTEDINAC
TLTTSPRLPVF

FIGURE 8

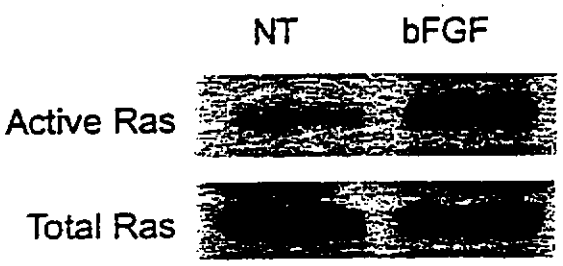


FIGURE 9

atgacggaatataagctggtggtggtgggcgccggcggtgtgggcaagagtgcgctgaccatccagctgatccagaacca

ttttgtggacgaatacgaccccactatagaggattcctaccggaagcaggtggtcattgatggggagacgtgcctgttgg

acatcctggataccgccggccaggaggagtacagcgccatgcgggaccagtacatgcgcaccggggagggcttcctgtgt

gtgtttgccatcaacaacaccaagtcttttgaggacatccaccagtacagggagcagatcaaacgggtgaaggactcgga

tgacgtgcccatggtgctggtggggaacaagtgtgacctggctgcacgcactgtggaatctcggcaggctcaggacctcg

cccgaagctacggcatccctacatcgagacctcggccaagacccggcagggagtggaggatgccttctacacgttggtg

cgtgagatccggcagcacaagctgcggaagctgaaccctcctgatgagagtggccccggctgcatgagctgcaagtgtgt

gctctcctga

FIGURE 10

MTEYKLVVVGAGGVGKSALTIQLIQNHFVDEYDPTIEDSY
RKQVVIDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLC
VFAINNTKSFEDIHQYREQIKRVKDSDDVPMVLVGNKCDL
AARTVESRQAQDLARSYGIPYIETSAKTRQGVEDAFYTLV
REIRQHKLRKLNPPDESGPGCMSCKCVLS

FIGURE 11

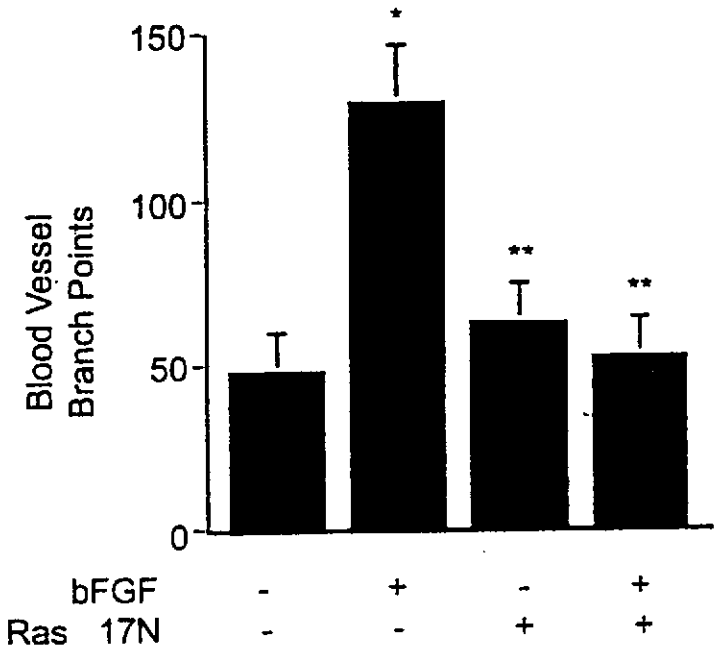


FIGURE 12

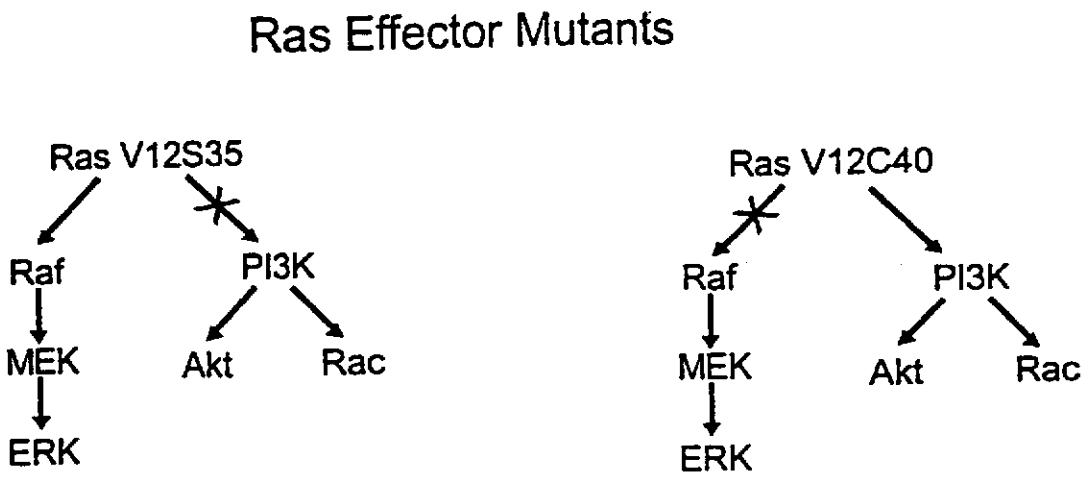


FIGURE 13A

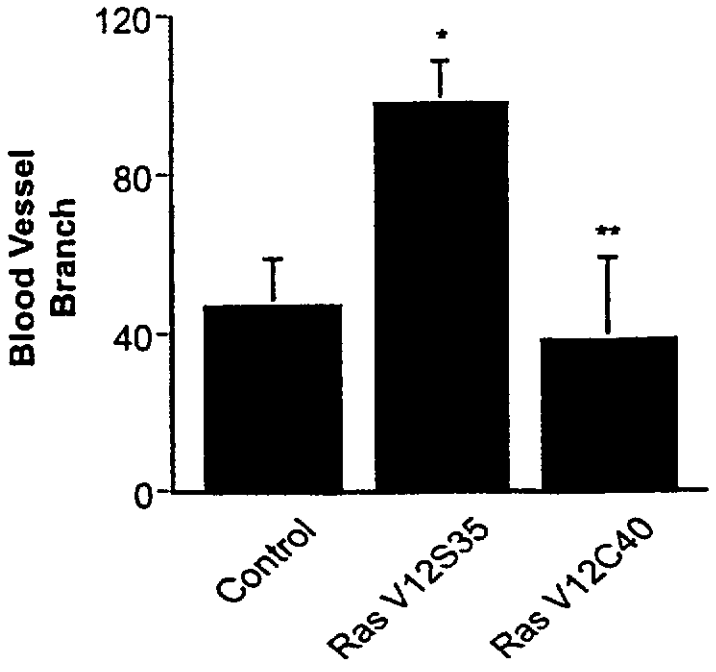


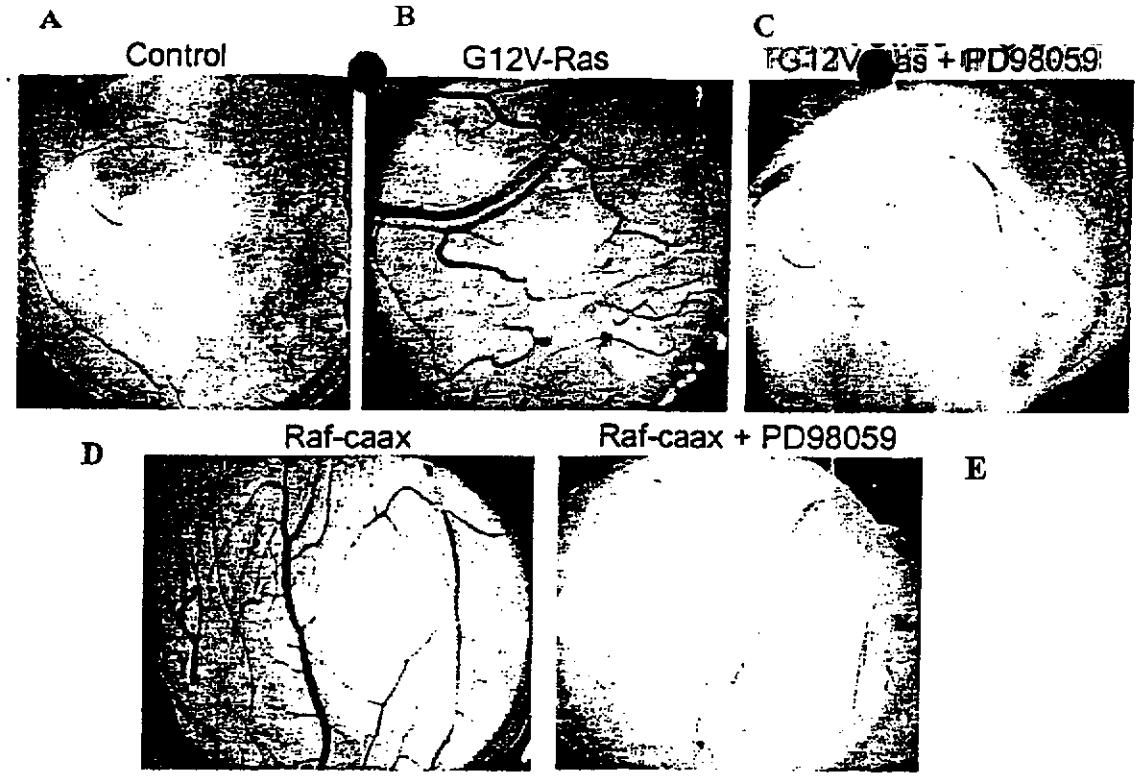
FIGURE 13B

atggagcacatacagggagcttggaagacgatcagcaatggttttggattcaaagatgccgtgtttgatggctccagctg
catctctcctacaatagttcagcagtttggctatcagcgccgggcatcagatgatggcaaactcacagatccttctaaga
caagcaacactatccgtgttttcttgccgaacaagcaaagaacagtggtcaatgtgcgaaatggaatgagcttgcatgac
tgccttatgaaagcactcaaggtgaggggcctgcaaccagagtgctgtgcagtgttcagacttctccacgaacacaaagg
taaaaaagcacgcttagattggaatactgatgctgcgtctttgattggagaagaacttcaagtagatttcctggatcatg
ttcccctcacaacacacaacttgctcggaagacgttcctgaagcttgccttctgtgacatctgtcagaaattcctgctc
aatggatttcgatgtcagacttgtggctacaaatttcatgagcactgtagcaccaaagtacctactatgtgtgtggactg
gagtaacatcagacaactcttattgtttccaaattccactattggtgatagtggagtcccagcactaccttctttgacta
tgcgtcgtatgcgagagtctgtttccaggatgcctgttagttctcagcacagatattctacacctcacgccttcaccttt
aacacctccagtccctcatctgaaggttccctctcccagaggcagaggtcgacatccacacctaatgtccacatggtcag
caccacgctgcctgtggacagcaggatgattgaggatgcaattcgaagtcacagcgaatcagcctcaccttcagccctgt
ccagtagccccaacaatctgagcccaacaggctggtcacagccgaaaaccccgtgccagcacaaagagagcgggcacca
gtatctgggacccaggagaaaaacaaaattaggcctcgtggacagagagattcaagctattattgggaaatagaagccag
tgaagtgatgctgtccactcggattgggtcaggctcttttggaactgtttataagggtaaatggcacggagatgttgcag
taaagatcctaaaggttgtcgacccaaccccagagcaattccaggccttcaggaatgaggtggctgttctgcgcaaaaca
cggcatgtgaacattctgcttttcatggggtacatgacaaaggacaacctggcaattgtgacccagtggtgcgagggcag
cagcctctacaaacacctgcatgtccaggagaccaagtttcagatgttccagctaattgacattgcccggcagacggctc
agggaatggactatttgcatgcaaagaacatcatccatagagacatgaaatccaacaatatatttctccatgaaggctta
acagtgaaaattggagattttggtttggcaacagtaaagtcacgctggagtggttctcagcaggttgaacaacctactgg
ctctgtcctctggatggccccagaggtgatccgaatgcaggataacaacccattcagtttccagtcggatgtctactcct
atggcatcgtattgtatgaactgatgacgggggagcttccttattctcacatcaacaaccgagatcagatcatcttcatg
gtgggccgaggatatgcctccccagatcttagtaagctatataagaactgccccaaagcaatgaagaggctggtagctga
ctgtgtgaagaaagtaaaggaagagaggcctcttttccccagatcctgtcttccattgagctgctccaacactctctac
cgaagatcaaccggagcgcttccgagccatccttgcatcgggcagcccacactgaggatatcaatgcttgcacgctgacc
acgtccccgaggctgcctgtcttc tactcgttcctgccgttcttcttcttcttctctcgttctgtttcacgcctagtacattc

FIGURE 14

MEHIQGAWKTISNGFGFKDAVFDGSSCISPTIVQQFGYQR
RASDDGKLTDPSKTSNTIRVFLPNKQRTVVNVRNGMSLHD
CLMKALKVRGLQPECCAVFRLLHEHKGKKARLDWNTDAAS
LIGEELQVDFLDHVPLTTHNFARKTFLKLAFCDICQKFLL
NGFRCQTCGYKFHEHCSTKVPTMCVDWSNIRQLLLFPNST
IGDSGVPALPSLTMRRMRESVSRMPVSSQHRYSTPHAFTF
NTSSPSSEGSLSQRQRSTSTPNVHMVSTTLPVDSRMIEDA
IRSHSESASPSALSSSPNNLSPTGWSQPKTPVPAQRERAP
VSGTQEKNKIRPRGQRDSSYYWEIEASEVMLSTRIGSGSF
GTVYKGKWHGDVAVKILKVVDPTPEQFQAFRNEVAVLRKT
RHVNILLFMGYMTKDNLAIVTQWCEGSSLYKHLHVQETKF
QMFQLIDIARQTAQGMDYLHAKNIIHRDMKSNNIFLHEGL
TVKIGDFGLATVKSRWSGSQQVEQPTGSVLWMAPEVIRMQ
DNNPFSFQSDVYSYGIVLYELMTGELPYSHINNRDQIIFM
VGRGYASPDLSKLYKNCPKAMKRLVADCVKKVKEERPLFP
QILSSIELLQHSLPKINRSASEPSLHRAAHTEDINACTLT
TSPRLPVFYSFLPFFFFFSFCFTPSTF

FIGURE 15


A
Control
B
G12V-Ras
C
G12V-Ras + PD98059
D
Raf-caax
Raf-caax + PD98059
E

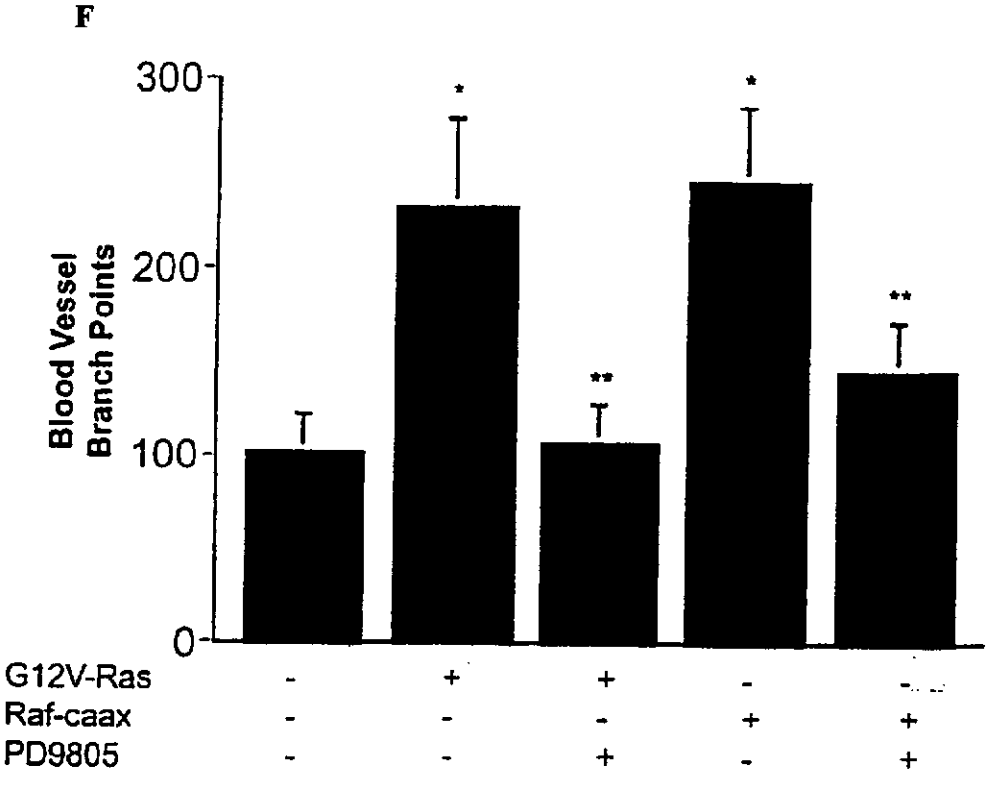
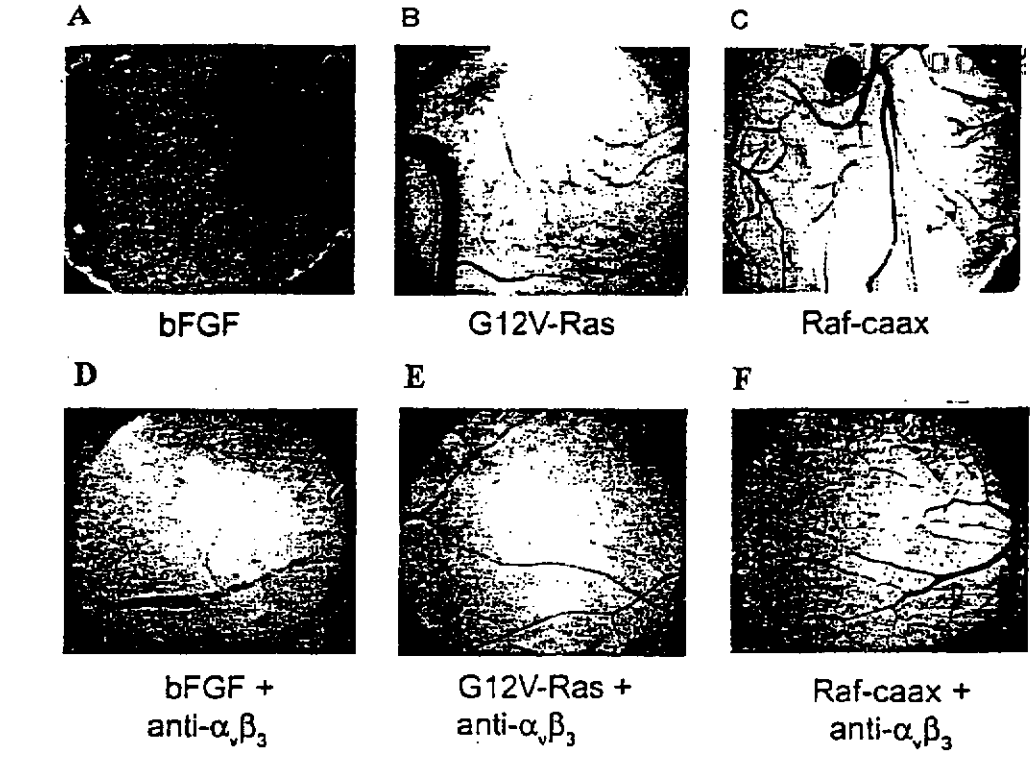

F
Blood Vessel Branch Points
300
200
100
0
*
**
*
**
G12V-Ras - + + - -
Raf-caax - - - + +
PD9805 - - + - +

FIGURE 16


A
B
C
bFGF
G12V-Ras
Raf-caax
D
E
F
bFGF +
anti-$\alpha_v\beta_3$
G12V-Ras +
anti-$\alpha_v\beta_3$
Raf-caax +
anti-$\alpha_v\beta_3$

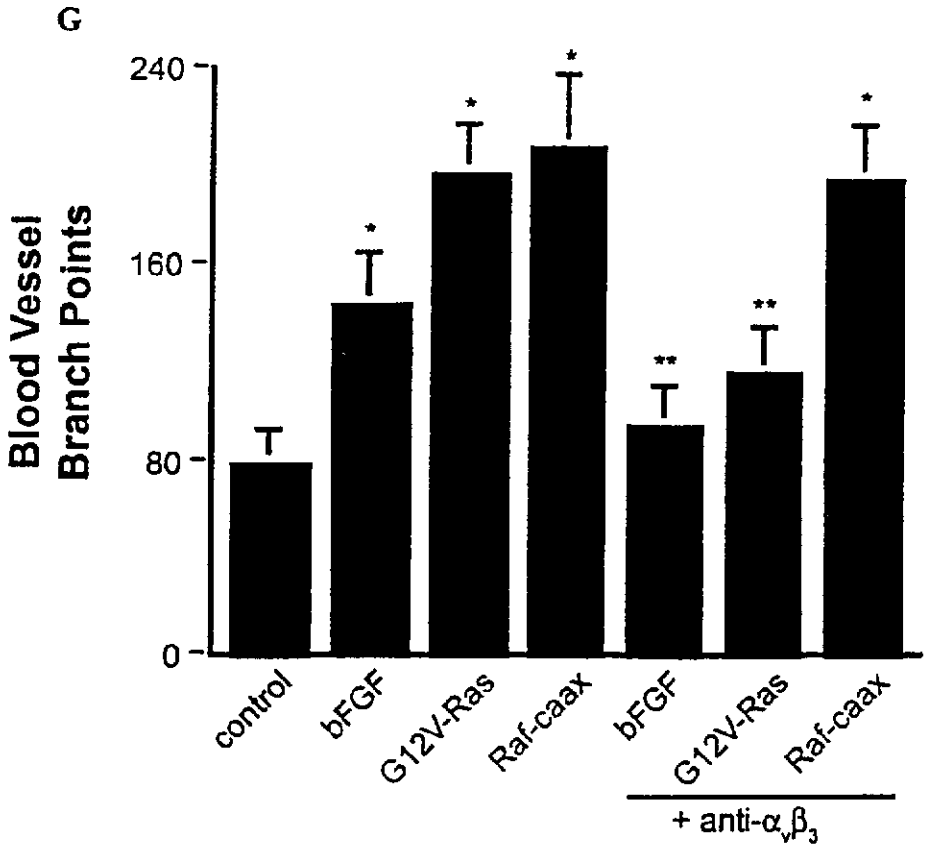
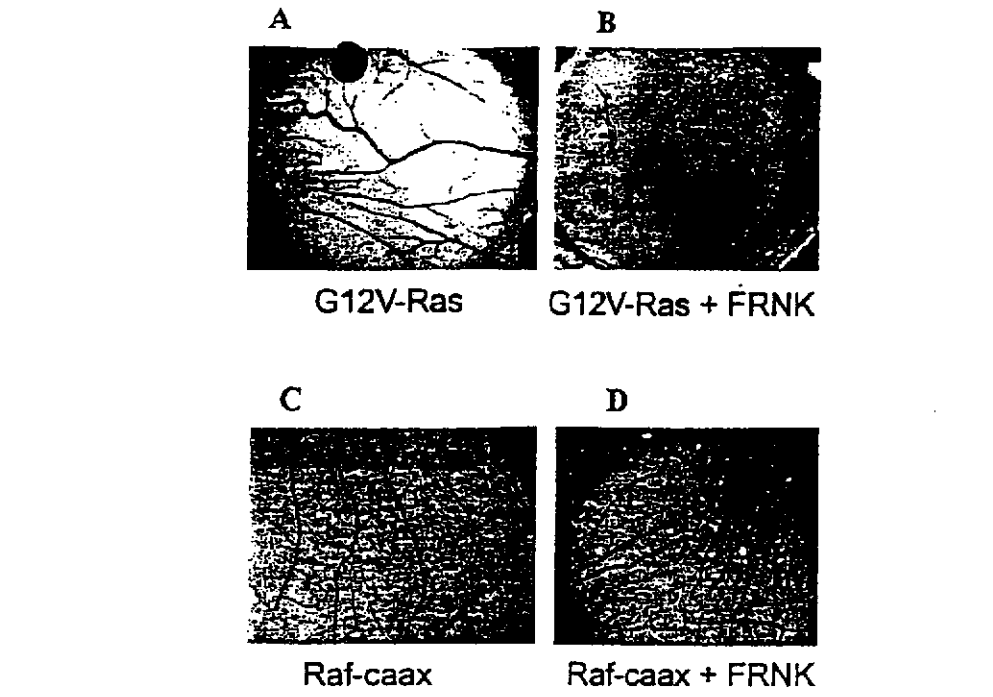

G
Blood Vessel Branch Points
240
160
80
0
control
bFGF
G12V-Ras
Raf-caax
bFGF
G12V-Ras
Raf-caax
+ anti-$\alpha_v\beta_3$

FIGURE 17


A
B
G12V-Ras
G12V-Ras + FRNK
C
D
Raf-caax
Raf-caax + FRNK

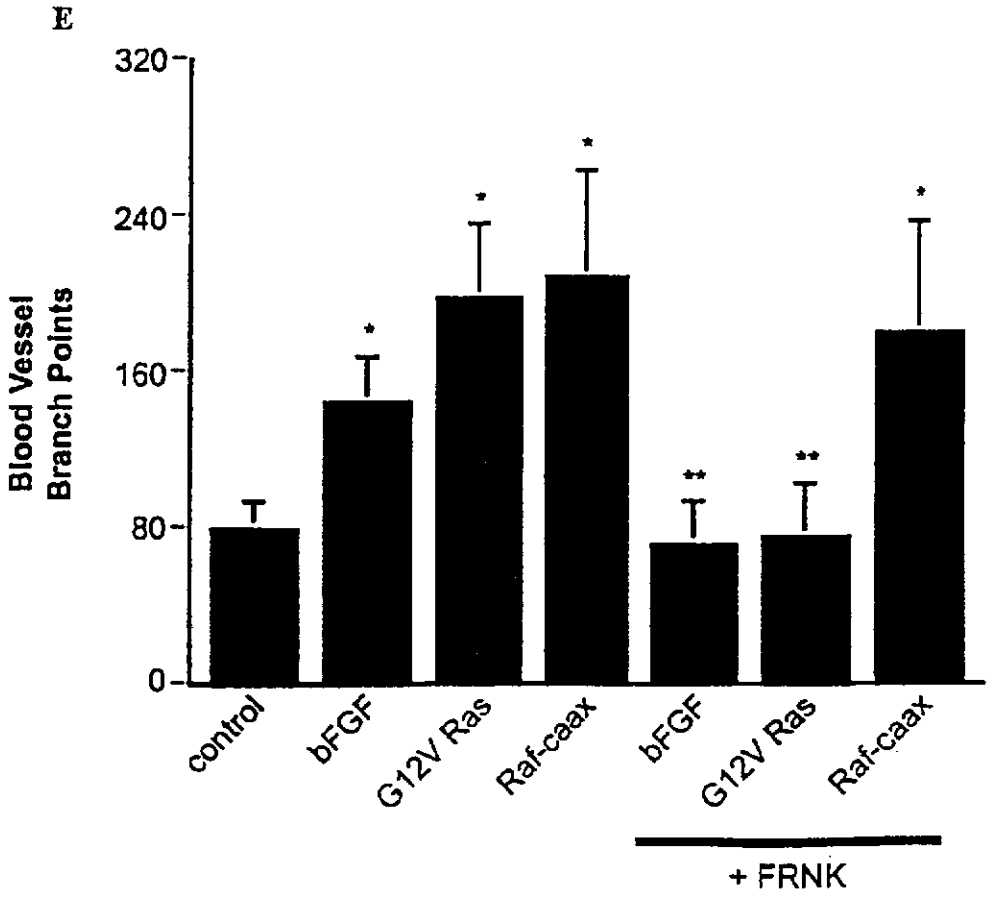

E
Blood Vessel Branch Points
320
240
160
80
0
control
bFGF
G12V Ras
Raf-caax
bFGF
G12V Ras
Raf-caax
+ FRNK

FIGURE 18

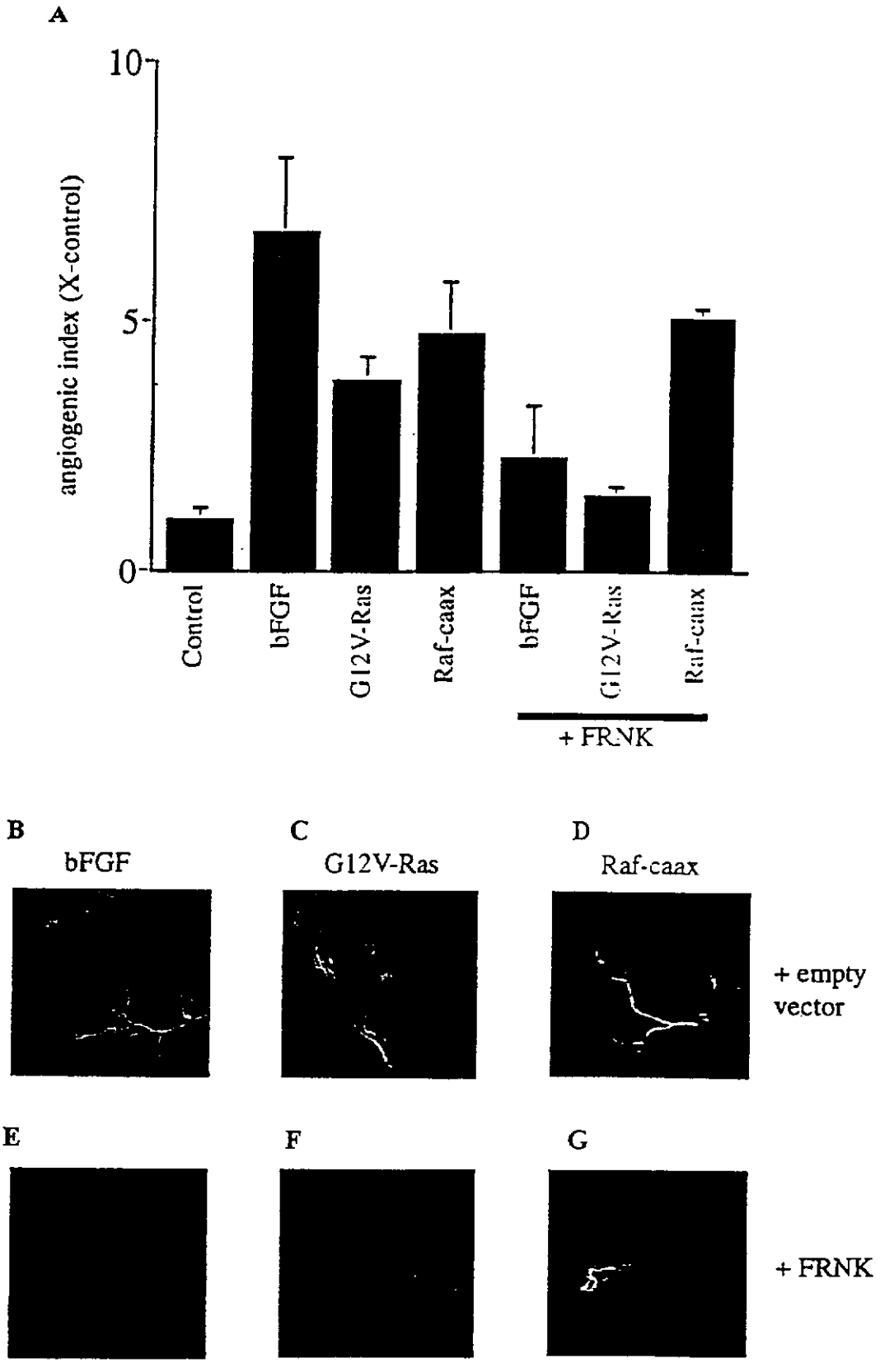

A
10
5
0
angiogenic index (X-control)
Control
bFGF
G12V-Ras
Raf-caax
bFGF
G12V-Ras
Raf-caax
+ FRNK
B
bFGF
C
G12V-Ras
D
Raf-caax
+ empty vector
E
F
G
+ FRNK

FIGURE 19

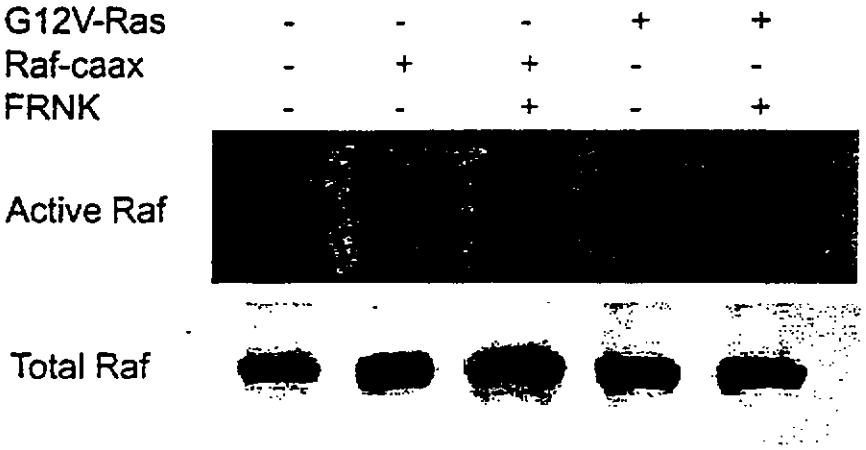


FIGURE 20A

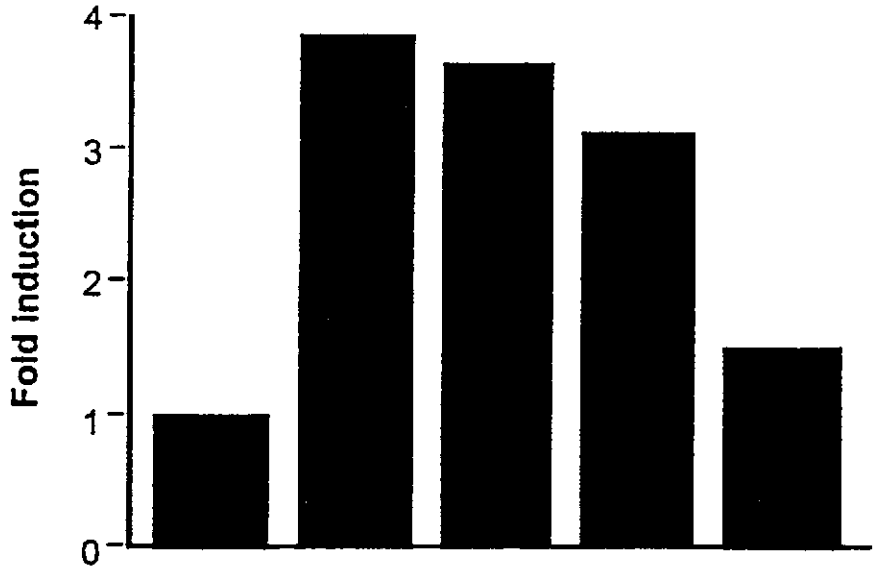


FIGURE 20B