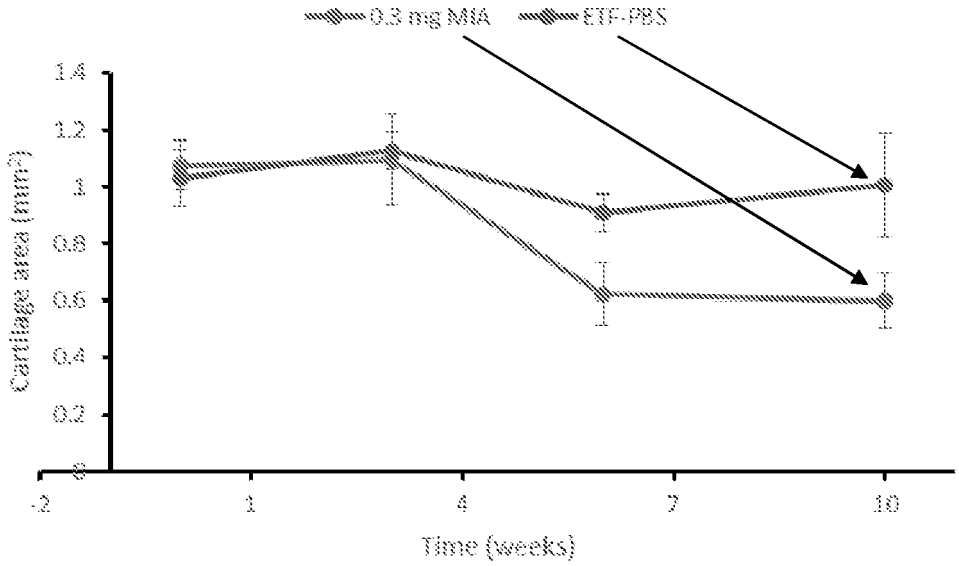

0.3 mg MIA
ETF-PBS
Cartilage area (mm²)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
-2
1
4
7
10
Time (weeks)

Figure 1

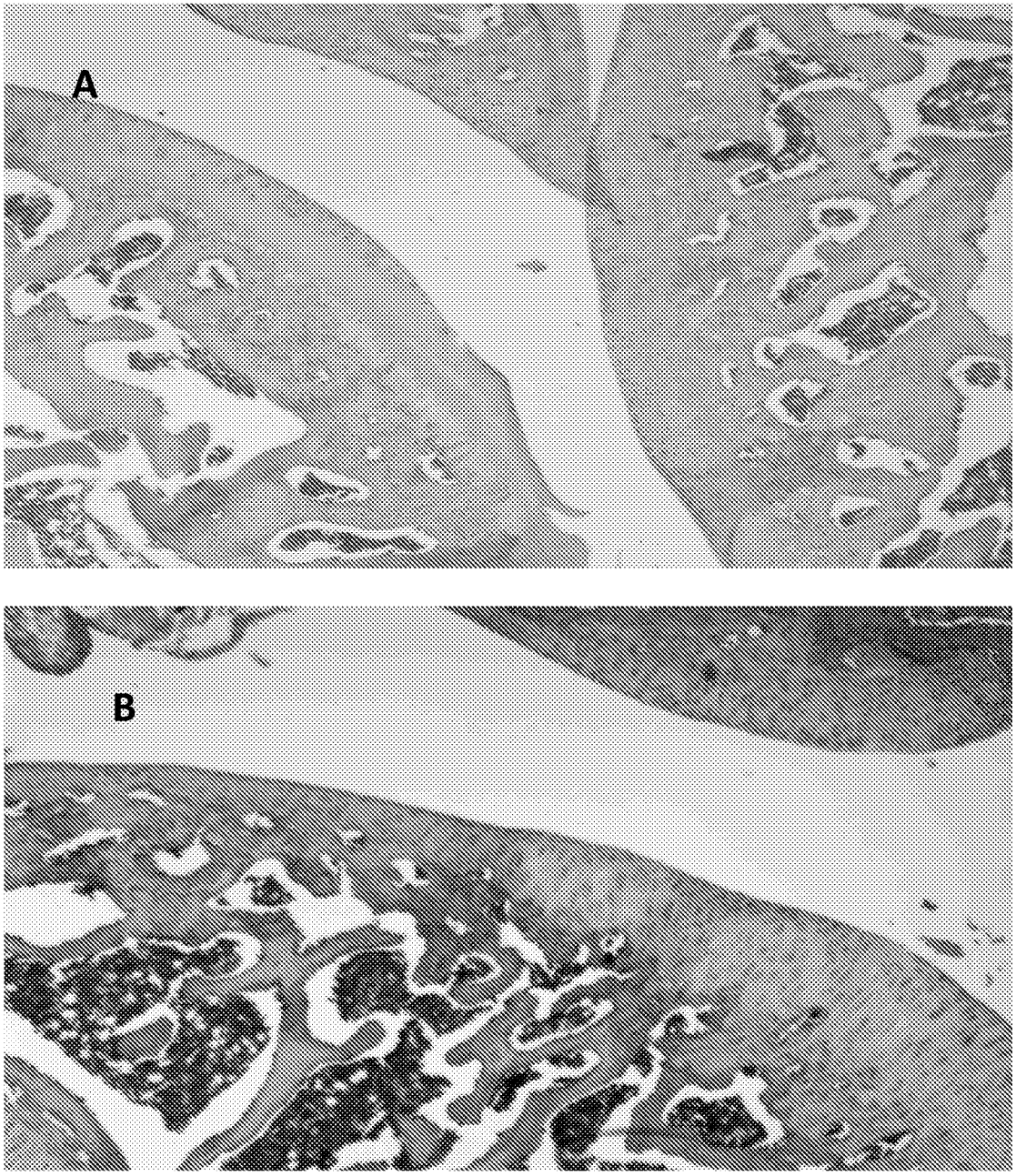


Figure 2

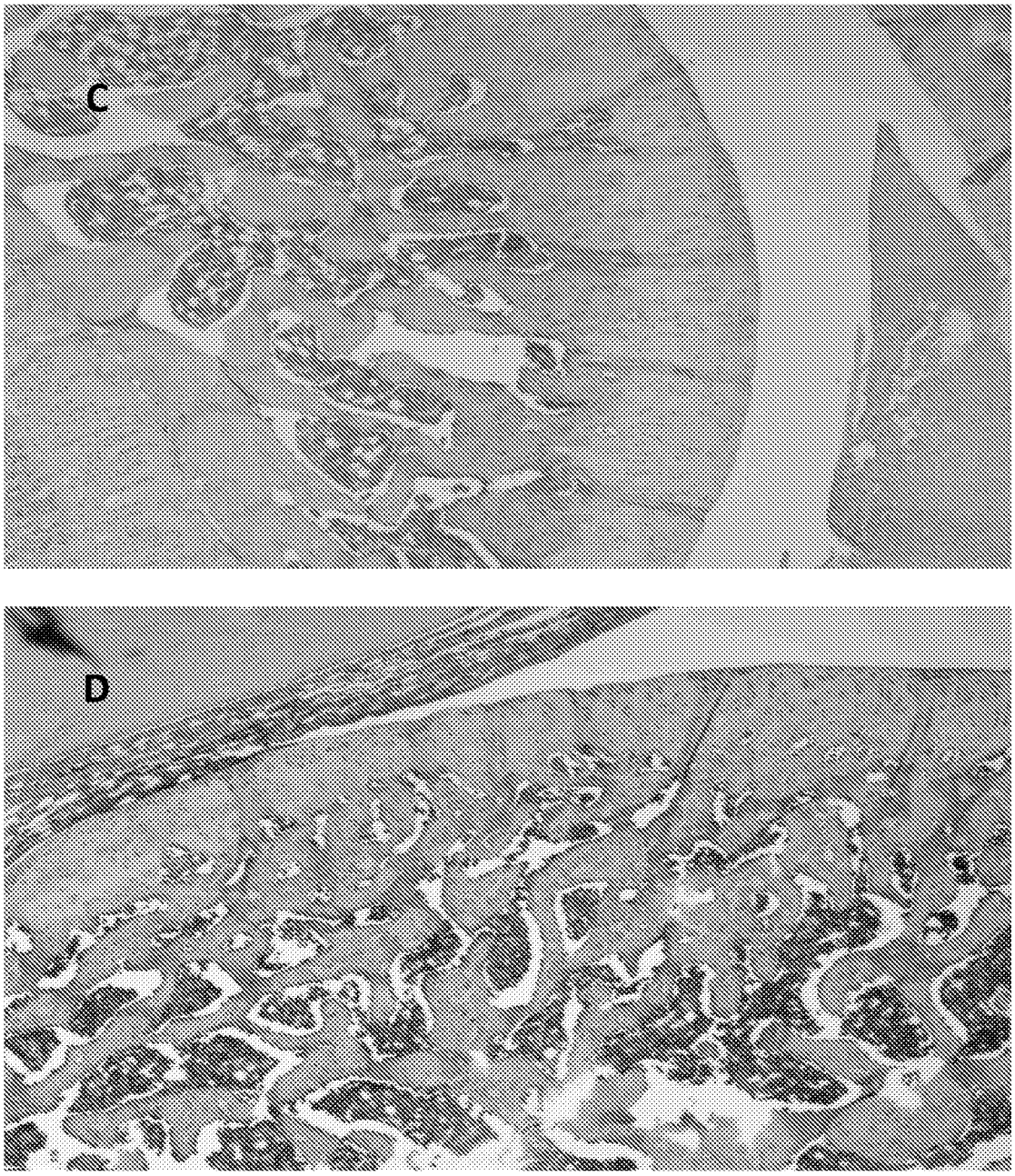


Figure 2

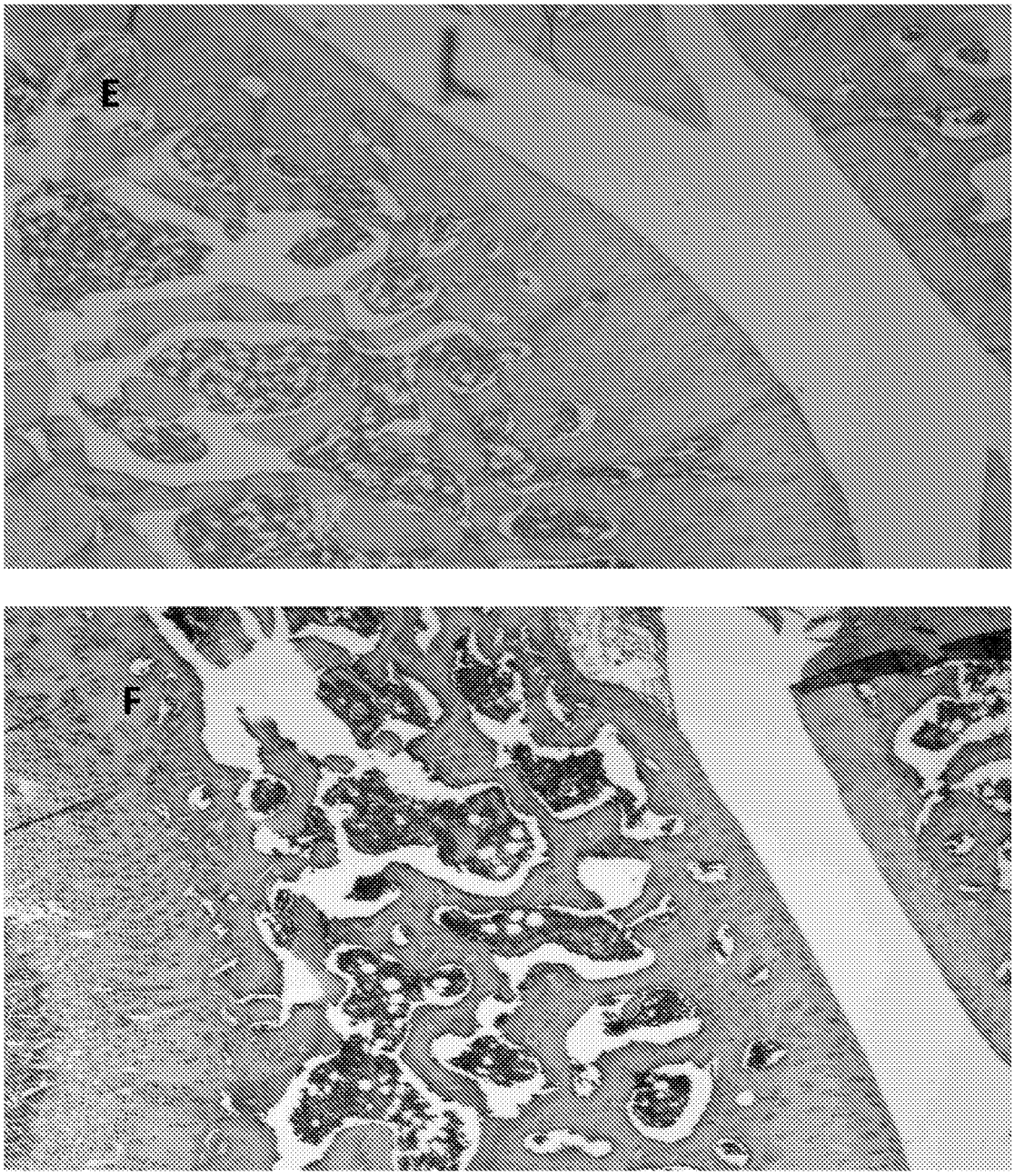


Figure 2

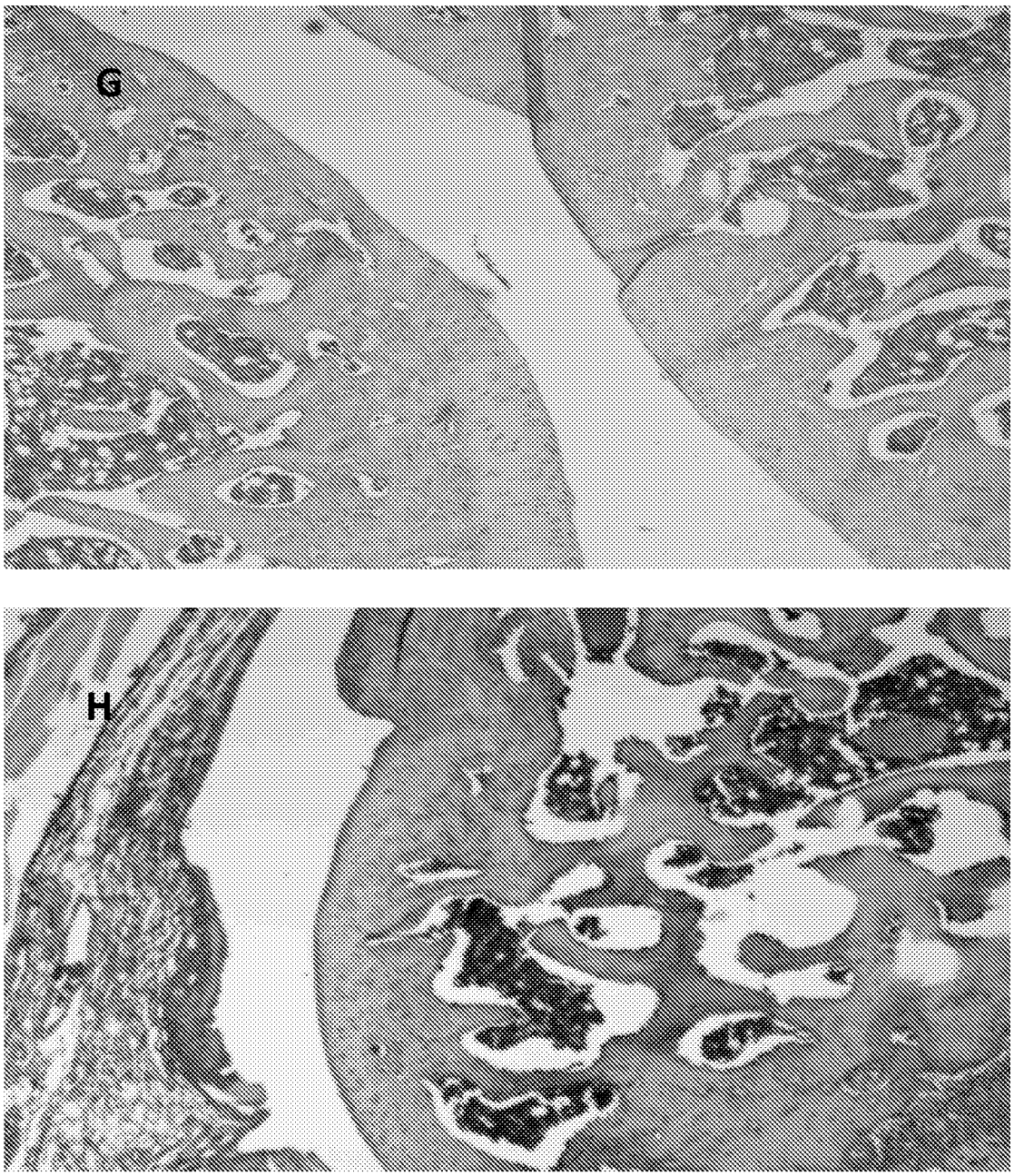


Figure 2

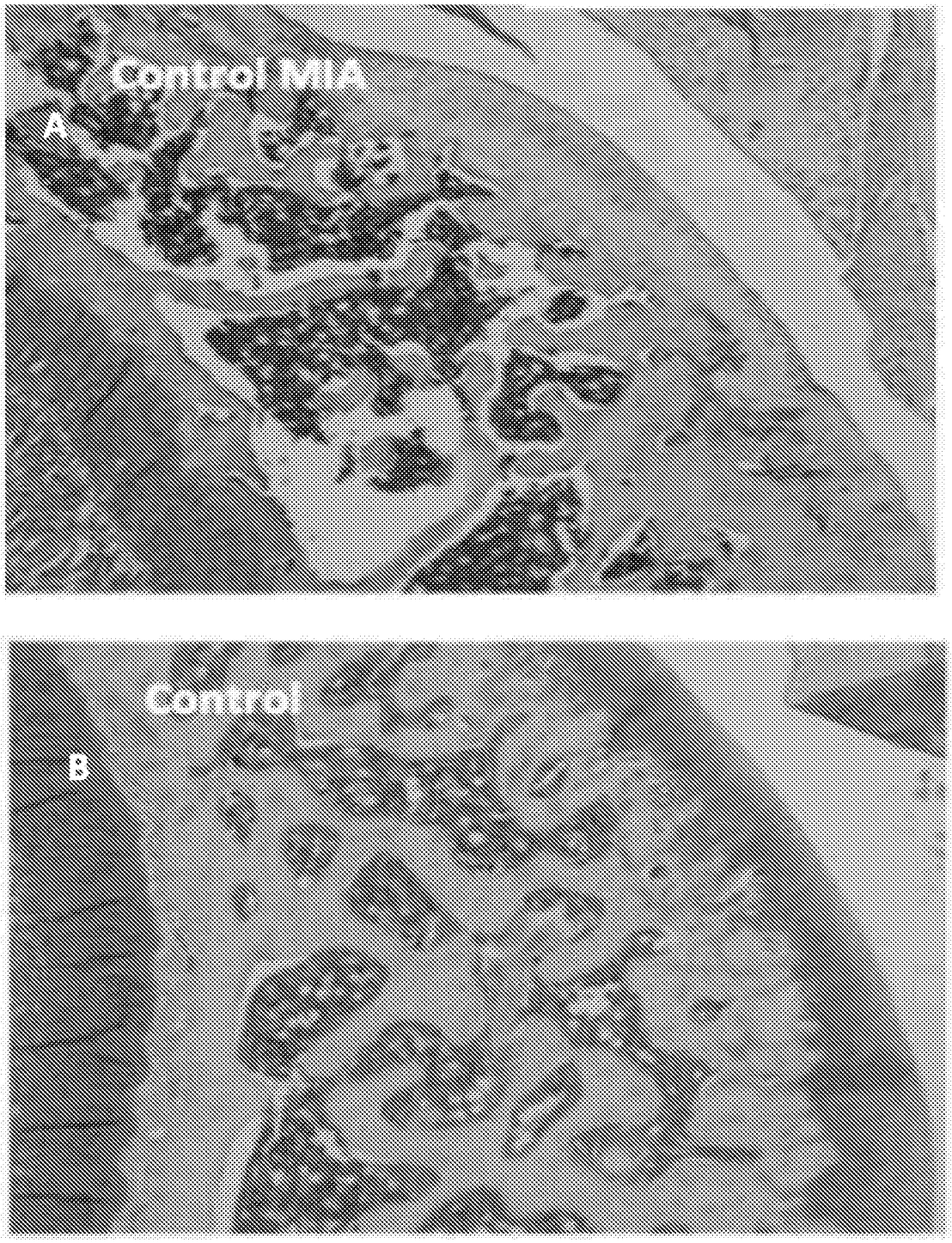


Figure 3

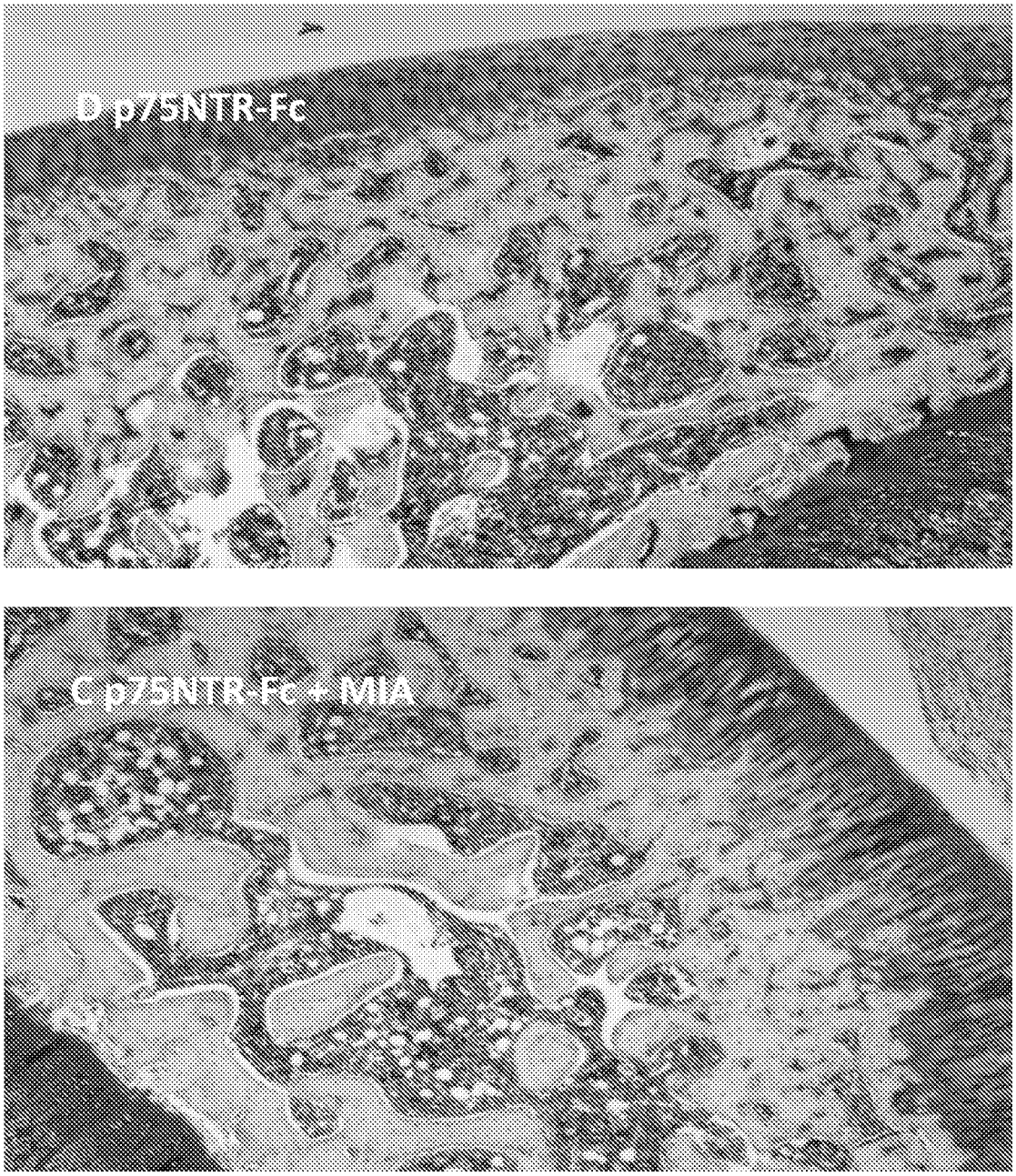


Figure 3

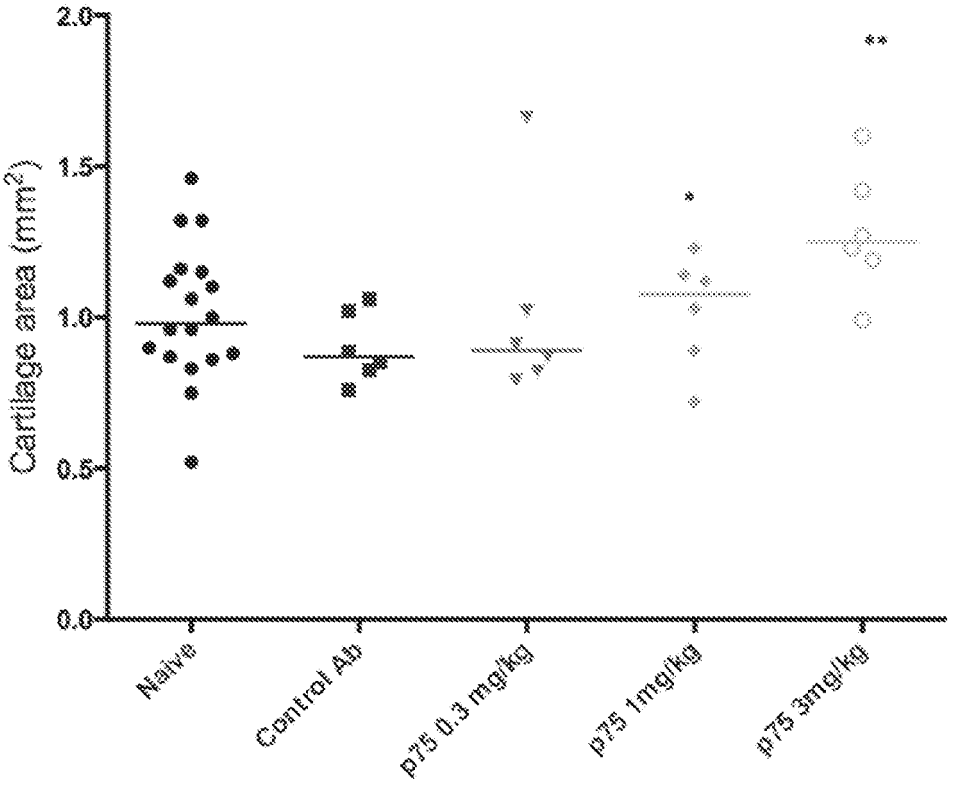

Cartilage area (mm2)
2.0
1.5
1.0
0.5
0.0
Naive
Control Ab
p75 0.3 mg/kg
p75 1mg/kg
p75 3mg/kg

Figure 4

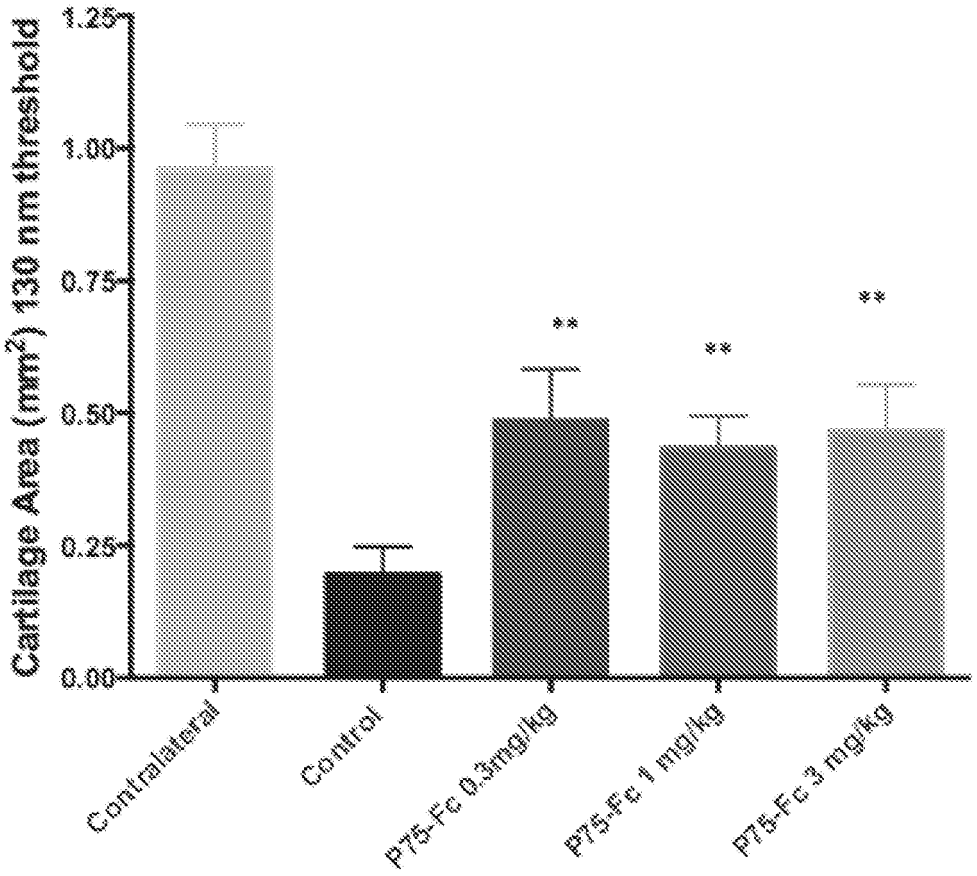

Cartilage Area (mm²) 130 nm threshold
1.25
1.00
0.75
0.50
0.25
0.00
**
**
**
Contralateral
Control
P75-Fc 0.3mg/kg
P75-Fc 1 mg/kg
P75-Fc 3 mg/kg

Figure 5

KEACPTGLYTHSGECCKACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGLQSMS
APCVEADDAVCRCAYGYYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEECPDGTYSDEANHVD
PCLPCTVCEDTERQLRECTRWADAECEEIPGRWITRSTPPEGSDSTAPSTQEPEAPPEQDLIASTVAGVV
TTVM**GSSQPVVTRGTTDNDIEGRMD***PKS**C**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC
VVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL
YSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*

Figure 6 – SEQ ID No. 1

MEWSWVFLFFLSVTTGVHSKEACPTGLYTHSGECCKACNLGEGVAQPCGANQTVCEPCLDSVTFSDV
VSATEPCKPCTECVGLQSMSAPCVEADDAVCRCAYGYYQDETTGRCEACRVCEAGSGLVFSCQDKQN
TVCEECPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWADAECEEIPGRWITRSTPPEGSDSTAPST
QEPEAPPEQDLIASTVAGVVTTVMGGGGEPKSSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTP
EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG

Figure 7 – SEQ ID No. 2

KEACPTGLYTHSGECCKACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGLQSMS
APCVEADDAVCRCAYGYYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEECPDGTYSDEANHVD
PCLPCTVCEDTERQLRECTRWADAECEEIPGRWITRSTPPEGSDSTAPSTQEPEAPPEQDLIASTVAGVV
TTVMGGGG*EPKS**S**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY
VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPG*

Figure 8 – SEQ ID No. 3

AAGCTTGCCGCCACCATGGAATGGTCCTGGGTGTTCCTGTTCTTCCTGTCCGTGACCACCGGCGTG
CACTCCAAAGAGGCTTGTCCCACCGGCCTGTACACCCACTCTGGCGAGTGTTGCAAGGCCTGTAAC
CTGGGAGAAGGCGTGGCCCAGCCTTGTGGCGCTAATCAGACAGTGTGCGAGCCCTGCCTGGACTC
CGTGACCTTCTCCGATGTGGTGTCCGCCACCGAGCCTTGCAAGCCCTGCACAGAGTGTGTGGGCCT
GCAGTCCATGTCCGCCCCTTGCGTGGAAGCCGACGACGCCGTGTGTAGATGCGCCTACGGCTACTA
CCAGGACGAGACAACCGGCAGATGCGAGGCCTGCAGAGTGTGCGAAGCTGGCTCTGGCCTGGTGT
TCAGTTGTCAAGACAAGCAGAACACCGTGTGCGAGGAATGCCCCGACGGCACCTACTCTGACGAG
GCCAATCACGTGGACCCCTGCCTGCCTTGCACCGTGTGTGAAGATACCGAGCGGCAGCTGCGCGA
GTGCACCAGATGGGCTGATGCCGAGTGCGAAGAGATCCCTGGCCGGTGGATCACCAGATCCACCC
CTCCAGAGGGCTCCGACTCTACCGCTCCCTCTACCCAGGAACCTGAGGCCCCTCCTGAGCAGGACC
TGATCGCTTCTACAGTGGCCGGCGTCGTGACCACAGTGATGGGCGGAGGCGGCGAGCCTAAGTCC
TCCGACAAGACCCACACCTGTCCCCCTTGTCCTGCCCCTGAACTGCTGGGCGGACCTTCCGTGTTTC
TGTTCCCCCCAAAGCCCAAGGACACCCTGATGATCTCCCGGACCCCCGAAGTGACCTGCGTGGTGG
TGGATGTGTCCCACGAGGACCCTGAAGTGAAGTTCAATTGGTACGTGGACGGCGTGGAAGTGCAC
AACGCCAAGACCAAGCCCAGAGAGGAACAGTACAACTCCACCTACCGGGTGGTGTCTGTGCTGAC
CGTGCTGCACCAGGACTGGCTGAACGGCAAAGAGTACAAGTGCAAGGTGTCCAACAAGGCCCTGC
CAGCCCCCATCGAAAAGACCATCTCCAAGGCCAAGGGCCAGCCCCGGGAACCCCAGGTGTACACA
CTGCCCCCTAGCAGGGACGAGCTGACCAAGAACCAGGTGTCCCTGACCTGTCTCGTGAAGGGCTTC
TACCCCTCCGATATCGCCGTGGAATGGGAGTCCAACGGCCAGCCTGAGAACAACTACAAGACCAC
CCCCCCTGTGCTGGACAGCGACGGCTCATTCTTTCTGTACTCCAAGCTGACAGTGGACAAGTCCCG
GTGGCAGCAGGGCAACGTGTTCTCCTGCAGCGTGATGCACGAGGCTCTGCACAACCACTACACCC
AGAAGTCCCTGTCCCTGAGCCCCGGCTGATGAATTC

Figure 9 – SEQ ID No. 4

P75NTR	IASTVAGVVTTVMGSSQPVVTRGTTDNLIPVYCSILAAVVVGLVAYIAFKR	(SEQ ID 6)
Commercial p75-Fc	IASTVAGVVTTVMGIPKVDKKV-EPKSCDKTHTCPPCPAPELLGGPSVFLF	(SEQ ID 7)
p75-Fc	IASTVAGVVTTVMGIPKVDKKV-EPKSCDKTHTCPPCPAPELLGGPSVFLF	(SEQ ID 8)
p75-Fc C222S	IASTVAGVVTTVMGIPKVDKKV-EPKS**S**DKTHTCPPCPAPELLGGPSVFLF	(SEQ ID 9)
p75-Fc G4x1	IASTVAGVVTTVMG*GGG*------EPKS**S**DKTHTCPPCPAPELLGGPSVFLF	(SEQ ID 10)
p75-Fc G4Sx1	IASTVAGVVTTVMG*GGGS*-----EPKS**S**DKTHTCPPCPAPELLGGPSVFLF	(SEQ ID 11)
p75-Fc G4Sx2	IASTVAGVVTTVMG*GGGSGGGGS*EPKS**S**DKTHTCPPCPAPELLGGPSVFLF	(SEQ ID 12)
Lonza IgG1za	----------NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLF	(SEQ ID 13)

Figure 10 – SEQ ID Nos. 6 to 13

```
1   mgagatgram dgprllllll lgvslggake acptglyths gecckacnlg egvaqpcgan
61  qtvcepclds vtfsdvvsat epckpctecv glqsmsapcv eaddavcrca ygyyqdettg
121 rceacrvcea gsglvfscqd kqntvceecp dgtysdeanh vdpclpctvc edterqlrec
181 trwadaecee ipgrwitrst ppegsdstap stqepeappe qdliastvag vvttvmgssq
241 pvvtrgttdn lipvycsila avvvglvayi afkrwnsckq nkqgansrpv nqtpppegek
301 lhsdsgisvd sqslhdqqph tqtasgqalk gdgglysslp pakreevekl lngsagdtwr
361 hlagelgyqp ehidsfthea cpvrallasw atqdsatlda llaalrriqr adlveslcse
421 statspv
```

Figure 11 – SEQ ID NO. 14 Human p75NTR full amino acid sequence

```
1   mgagatgram dgprllllll lgvslggake acptglyths gecckacnlg egvaqpcgan
61  qtvcepclds vtfsdvvsat epckpctecv glqsmsapcv eaddavcrca ygyyqdettg
121 rceacrvcea gsglvfscqd kqntvceecp dgtysdeanh vdpclpctvc edterqlrec
181 trwadaecee ipgrwitrst ppegsdstap stqepeappe qdliastvag vvttvmgssq
241 pvvtrgttdn
```

Figure 12: SEQ ID NO. 15 Human p75NTR extracellular domain including signal sequence

ke acptglyths gecckacnlg egvaqpcgan qtvcepclds vtfsdvvsat epckpctecv glqsmsapcv eaddavcr**ca ygyyqdettg r**ceacr**vcea gsglvfscqd kqntvceecp gtysdeanh vdpclpctvc edter**qlrec tr**wadaecee ipgr**witrst ppegsdstap stqepeappe qdliastvag vvttvmgssq pvvtrgttdn

Figure 13: SEQ ID NO. 16 Human p75NTR extracellular domain without signal sequence

CAYGYYQDETTGR

Figure 14 SEQ ID NO. 17 Human p75NTR(NBP) neurotrophin binding domain 1

VCEAGSGLVFSCQD KQNTVCEECP GGTYSDEANH VDPCLPCTVCEDTER

Figure 15 SEQ ID NO. 18 Human p75NTR(NBP) neurotrophin binding domain 2

VCEAGSGLVFSCQDK

Figure 16 SEQ ID NO.19 Human p75NTR(NBP) neurotrophin binding domain 3

WADAECEEIPGR

Figure 17 SEQ ID NO. 20 Human p75NTR(NBP) neurotrophin binding domain 4

LDSVTSDVVSATEPCKP

Figure 18 SEQ ID NO. 21 Human p75NTR(NBP) neurotrophin binding domain 5

```
  1 mrlavgallv cavlglclav pdktvrwcav seheatkcqs frdhmksvip sdgpsvacvk
 61 kasyldcira iaaneadavt ldaglvyday lapnnlkpvv aefygskedp qtfyyavavv
121 kkdsgfqmnq lrgkkschtg lgrsagwnip igllycdlpe prkplekava nffsgscapc
181 adgtdfpqlc qlcpgcgcst lnqyfgysga fkclkdgagd vafvkhstif enlankadrd
241 qyellcldnt rkpvdeykdc hlaqvpshtv varsmggked liwellnqaq ehfgkdkske
301 fqlfssphgk dllfkdsahg flkvpprmda kmylgyeyvt airnlregtc peaptdeckp
361 vkwcalshhe rlkcdewsvn svgkiecvsa ettedciaki mngeadamsl dggfvyiagk
421 cglvpvlaen ynksdncedt peagyfavav vkksasdltw dnlkgkksch tavgrtagwn
481 ipmgllynki nhcrfdeffs egcapgskkd sslcklcmgs glnlcepnnk egyygytgaf
541 rclvekgdva fvkhqtvpqn tggknpdpwa knlnekdyel lcldgtrkpv eeyanchlar
601 apnhavvtrk dkeacvhkil rqqqhlfgsn vtdcsgnfcl frsetkdllf rddtvclakl
661 hdrntyekyl geeyvkavgn lrkcstssll eactfrrp
```

Figure 19 SEQ ID NO. 22 Human Transferrin

```
  1 mkwvtfisll flfssaysrg vfrrdahkse vahrfkdlge enfkalvlia faqylqqcpf
 61 edhvklvnev tefaktcvad esaencdksl htlfgdklct vatlretyge madccakqep
121 ernecflqhk ddnpnlprlv rpevdvmcta fhdneetflk kylyeiarrh pyfyapellf
181 fakrykaaft eccqaadkaa cllpkldelr degkassakq rlkcaslqkf gerafkawav
241 arlsqrfpka efaevsklvt dltkvhtecc hgdllecadd radlakyice nqdsissklk
301 eccekpllek shciaevend empadlpsla adfveskdvc knyaeakdvf lgmflyeyar
361 rhpdysvvll lrlaktyett lekccaaadp hecyakvfde fkplveepqn likqncelfe
421 qlgeykfqna llvrytkkvp qvstptlvev srnlgkvgsk cckhpeakrm pcaedylsvv
481 lnqlcvlhek tpvsdrvtkc cteslvnrrp cfsalevdet yvpkefnaet ftfhadictl
541 sekerqikkq talvelvkhk pkatkeqlka vmddfaafve kcckaddket cfaeegkklv
601 aasqaalgl
```

Figure 20 SEQ ID NO. 23 Human Albumin

```
  1 ggpsvflfpp kpkdtlmisr tpevtcvvvd vshedpevkf nwyvdgvevh naktkpreeq
 61 ydstyrvvsv ltvlhqdwln gkeykckvsn kalpapiekt iskakgqpre pqvytlppsr
121 eemtknqvsl tclvkgfyps diavewesng qpennykttp pvldsdgsff lyskltvdks
181 rwqqgnvfsc svmhealhnh ytqkslslsp gk
```

Figure 21. SEQ ID NO. 24 Human Fc IgG1

```
  1 astkgpsvfp lapcsrstse staalgclvk dyfpepvtvs wnsgaltsgv htfpavlqss
 61 glyslssvvt vtssnfgtqt ytcnvdhkps ntkvdktver kccvecppcp appvagpsvf
121 lfppkpkdtl misrtpevtc vvvdvshedp evqfnwyvdg mevhnaktkp reeqfnstfr
181 vvsvltvvhq dwlngkeykc kvsnkglpap iektisktkg qprepqvytl ppsreemtkn
241 qvsltclvkg fypsdiavew esngqpenny kttppmldsd gsfflysklt vdksrwqqgn
301 vfscsvmhea lhnhytqksl slspgk
```

Figure 22. SEQ ID NO. 25 Human Fc IgG2

```
  1 cytllllttp swvlsqvtlk esgpvlvkpt etltltctvs gfslsnakmg vswirqppgk
 61 alewlahifs ndeksystsl ksrltiskdt sksqvvltmt nmdpvdtaty ycariftity
121 snyvlqyyyy mdvwgkgttv tvssastkgp svfplapcsr stsgg
```

Figure 23. SEQ ID NO. 26 Human Fc IgG3

```
  1 apeflggpsv flfppkpkdt lmisrtpevt cvvvdvsqed pevqfnwyvd gvevhnaktk
 61 preeqfnsty rvvsvltvlh qdwlngkeyk ckvsnkglps siektiskak gqprepqvyt
121 lppsqeemtk nqvsltclvk gfypsdiave wesngqpenn ykttppvlds dgsfflyskl
181 tvdksrwqeg nvfscsvmhe alhnhytqks lslslgk
```

Figure 24. SEQ ID NO. 27 Human Fc IgG4

```
  1 ggpsvflfpp kpkdtlyitr epevtcvvvd vshedpevkf nwyvdgvevh naktkpreeq
 61 ynstyrvvsv ltvlhqdwln gkeykckvsn kalpapiekt iskakgqpre pqvytlppsr
121 deltknqvsl tclvkgfyps diavewesng qpennykttp pvldsdgsff lyskltvdks
181 rwqqgnvfsc svmhealhnh ytqkslsls
```

Figure 25. SEQ ID NO. 28 Human Fc Fragment Engineered For Extended Serum Half-Life

```
  1 thtcppcpap efeggpsvfl fppkpkdtlm isrtpevtcv vvdvshedpe vkfnwyvdgv
 61 evhnaktkpr eeqynstyrv vsvltvlhqd wlngkeykck vsnkalpasi ektiskakgq
121 prepqvytlp psreemtknq vsltclvkgf ypsdiavewe sngqpennyk ttppvldsdg
181 sfflyskltv dksrwqqgnv fscsvmheal hnhytqksls lspgk
```

Figure 26. SEQ ID NO. 29 Human Fc Fragment Engineered For Lack Of Effector Functions

$(GGGGS)n$ $(n = 1 \text{ to } 4)$

Figure 27: SEQ ID NO. 30 p75NTR(NBP)-Fc linker

$(EAAAK)n$ $(n = 2 \text{ to } 5)$

Figure 28: SEQ ID NO. 31 p75NTR(NBP)-Fc linker

GGGGS

Figure 29: SEQ ID NO. 32 p75NTR(NBP)-Fc linker

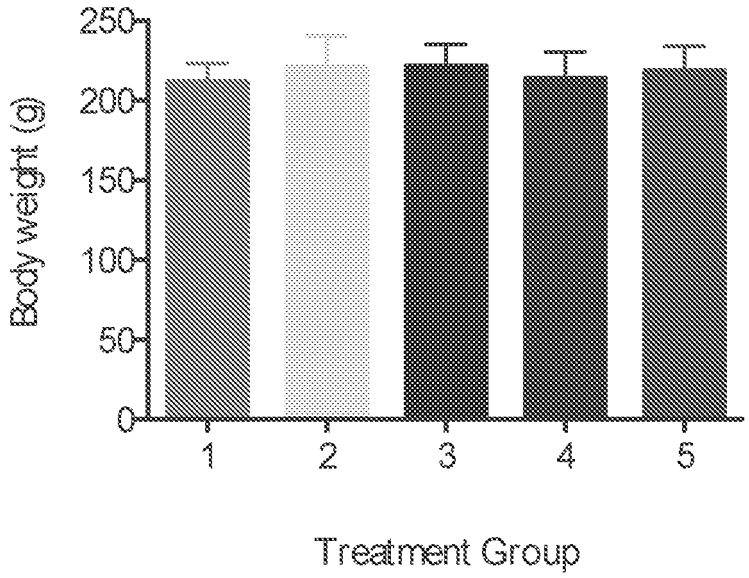


Figure 30

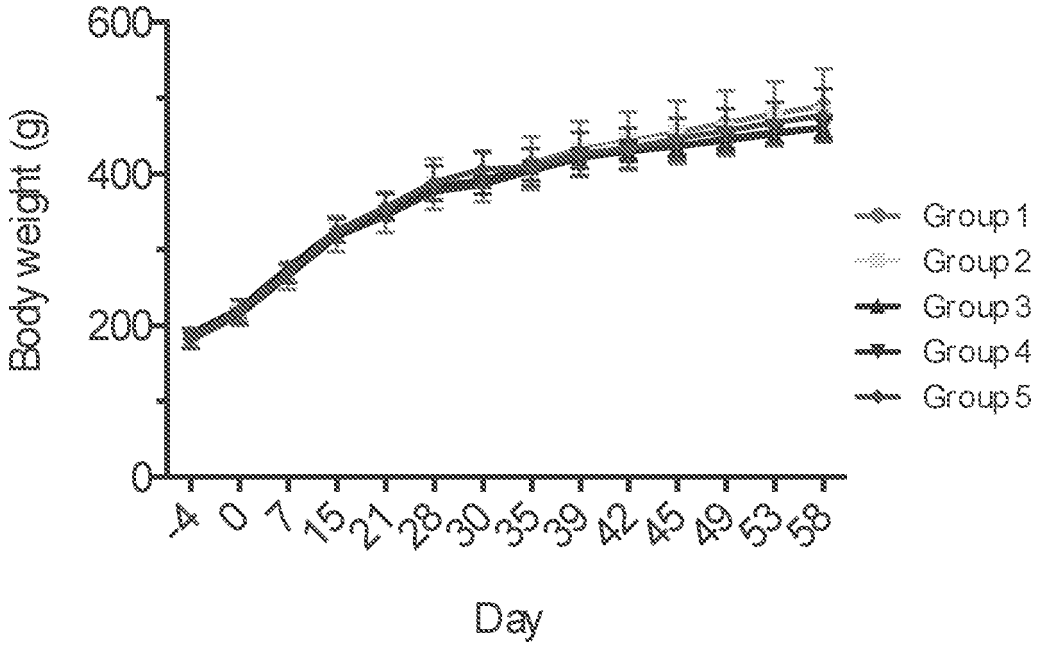


Figure 31

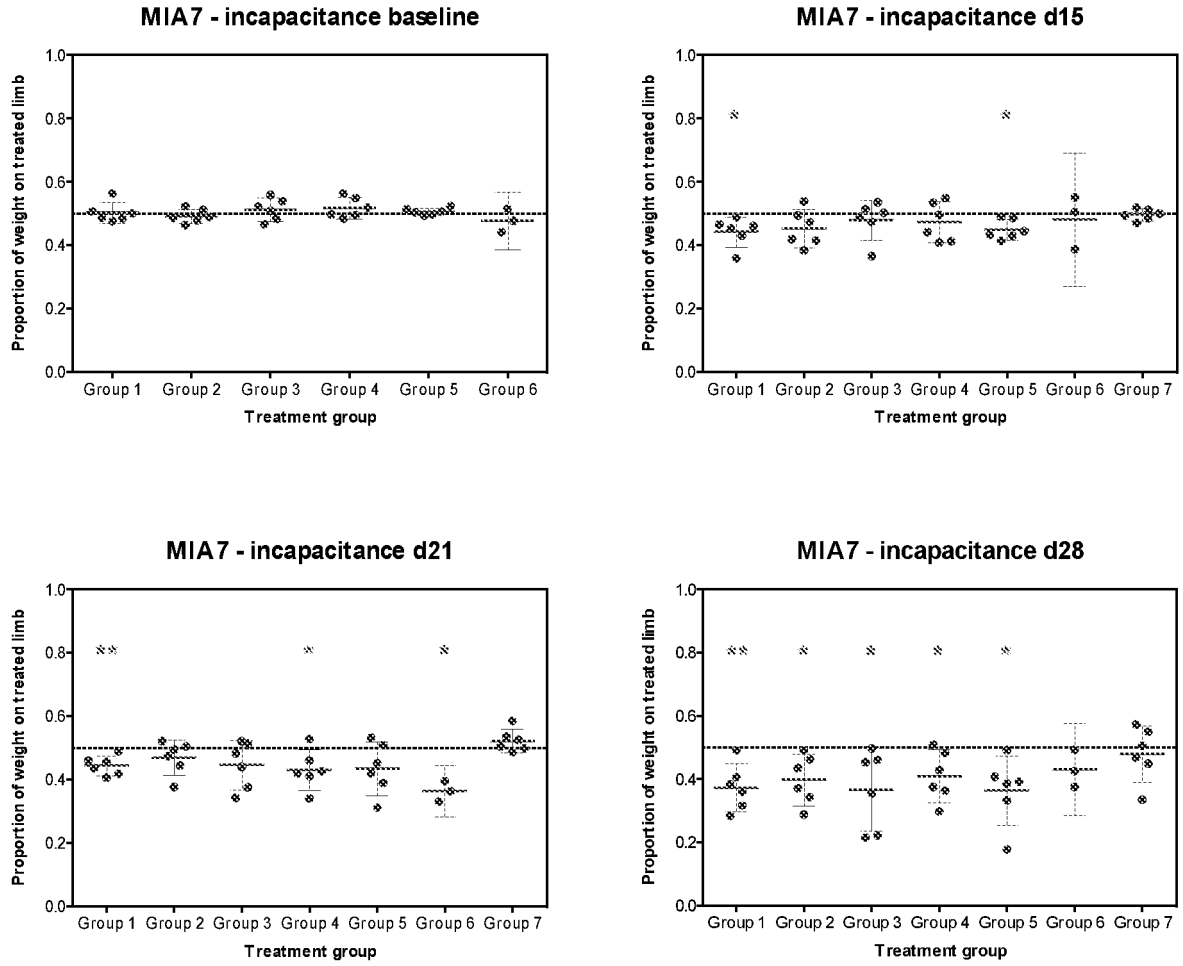

MIA7 - incapacitance baseline
Proportion of weight on treated limb
1.0
0.8
0.6
0.4
0.2
0.0
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Treatment group
MIA7 - incapacitance d15
Proportion of weight on treated limb
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
Treatment group
MIA7 - incapacitance d21
Proportion of weight on treated limb
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
Treatment group
MIA7 - incapacitance d28
Proportion of weight on treated limb
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7
Treatment group

Figure 32

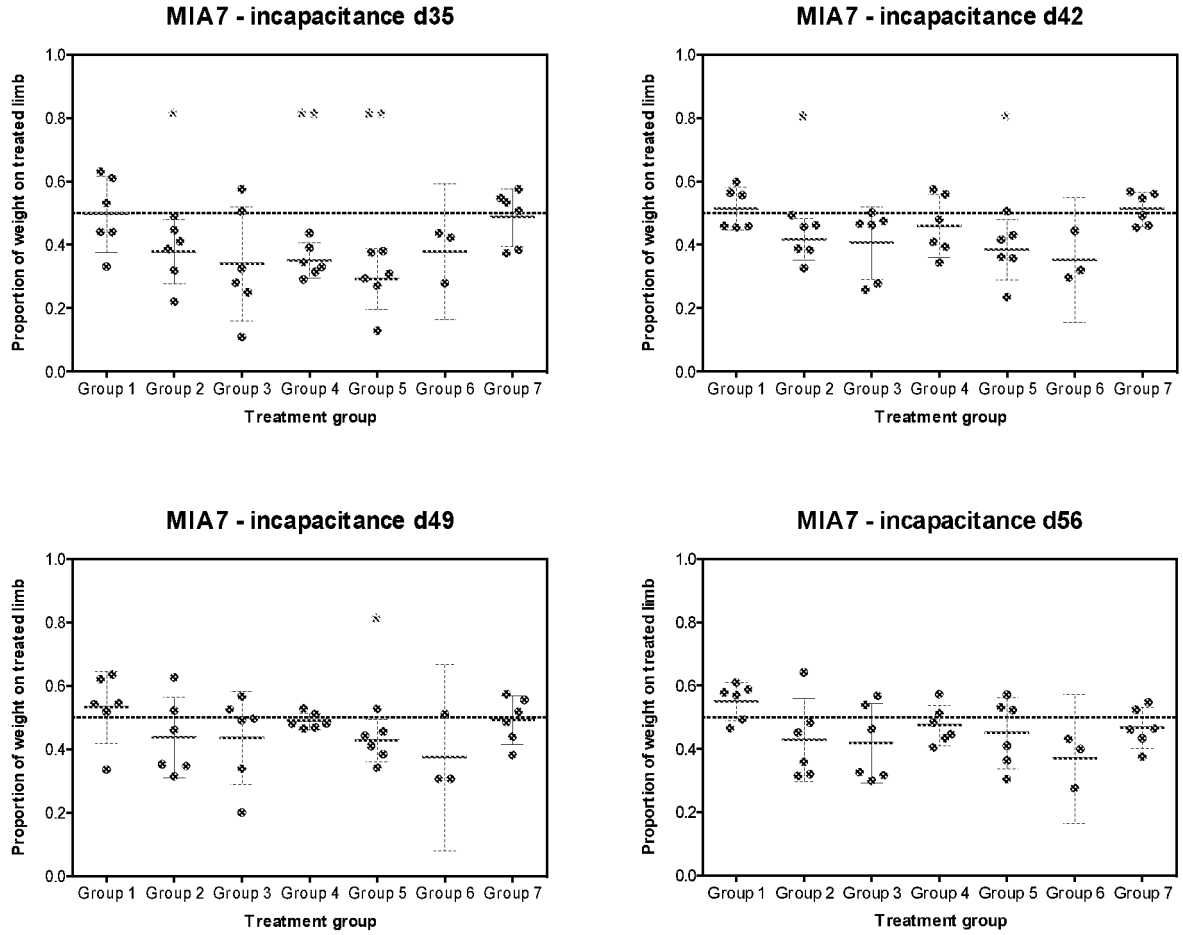

MIA7 - incapacitance d35
MIA7 - incapacitance d42
MIA7 - incapacitance d49
MIA7 - incapacitance d56
Proportion of weight on treated limb
1.0
0.8
0.6
0.4
0.2
0.0
Group 1 Group 2 Group 3 Group 4 Group 5 Group 6 Group 7
Treatment group

Figure 33

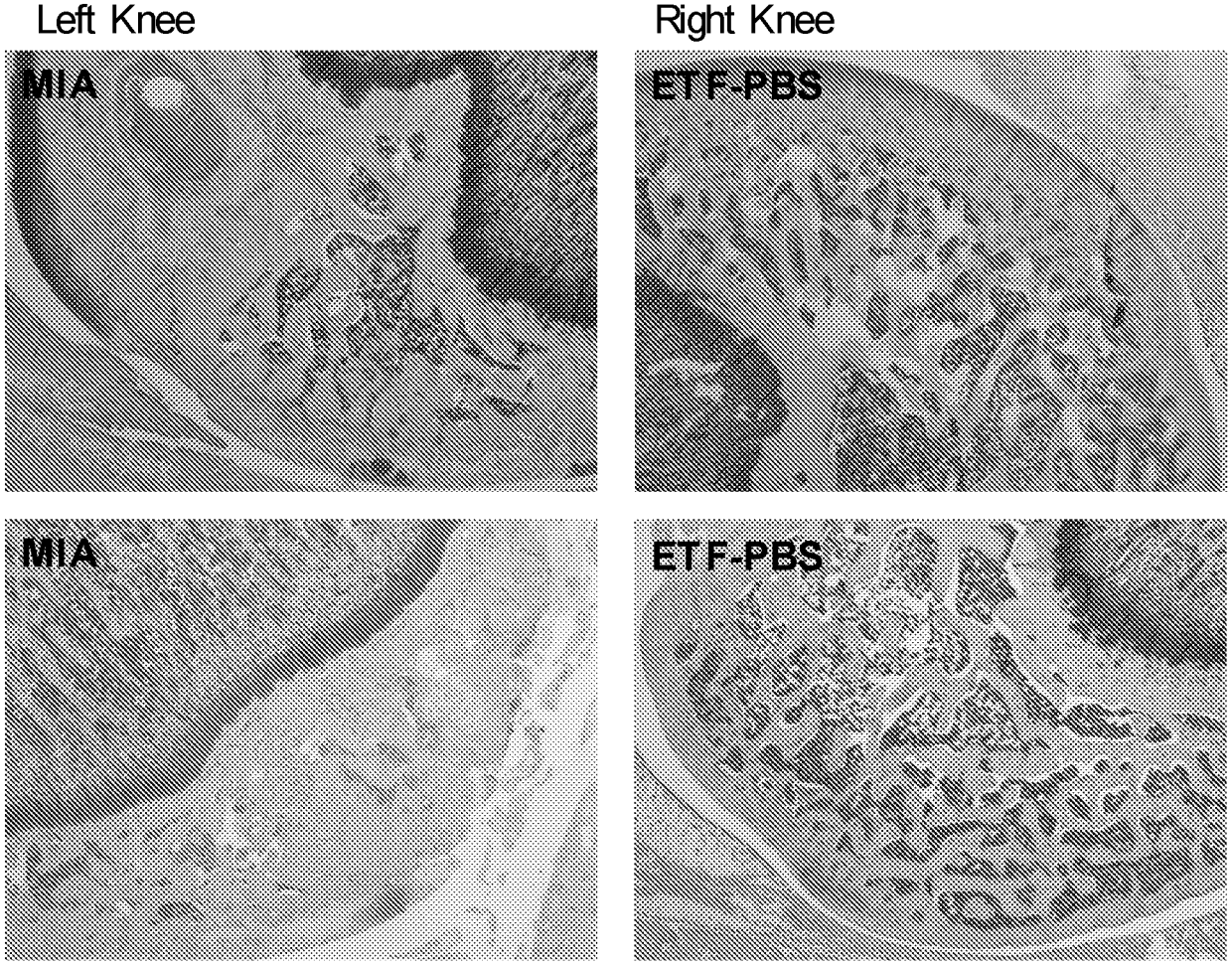

Left Knee
Right Knee
MIA
ETF-PBS
MIA
ETF-PBS
Control IgG-Fc treated animals - Day 56

Figure 34

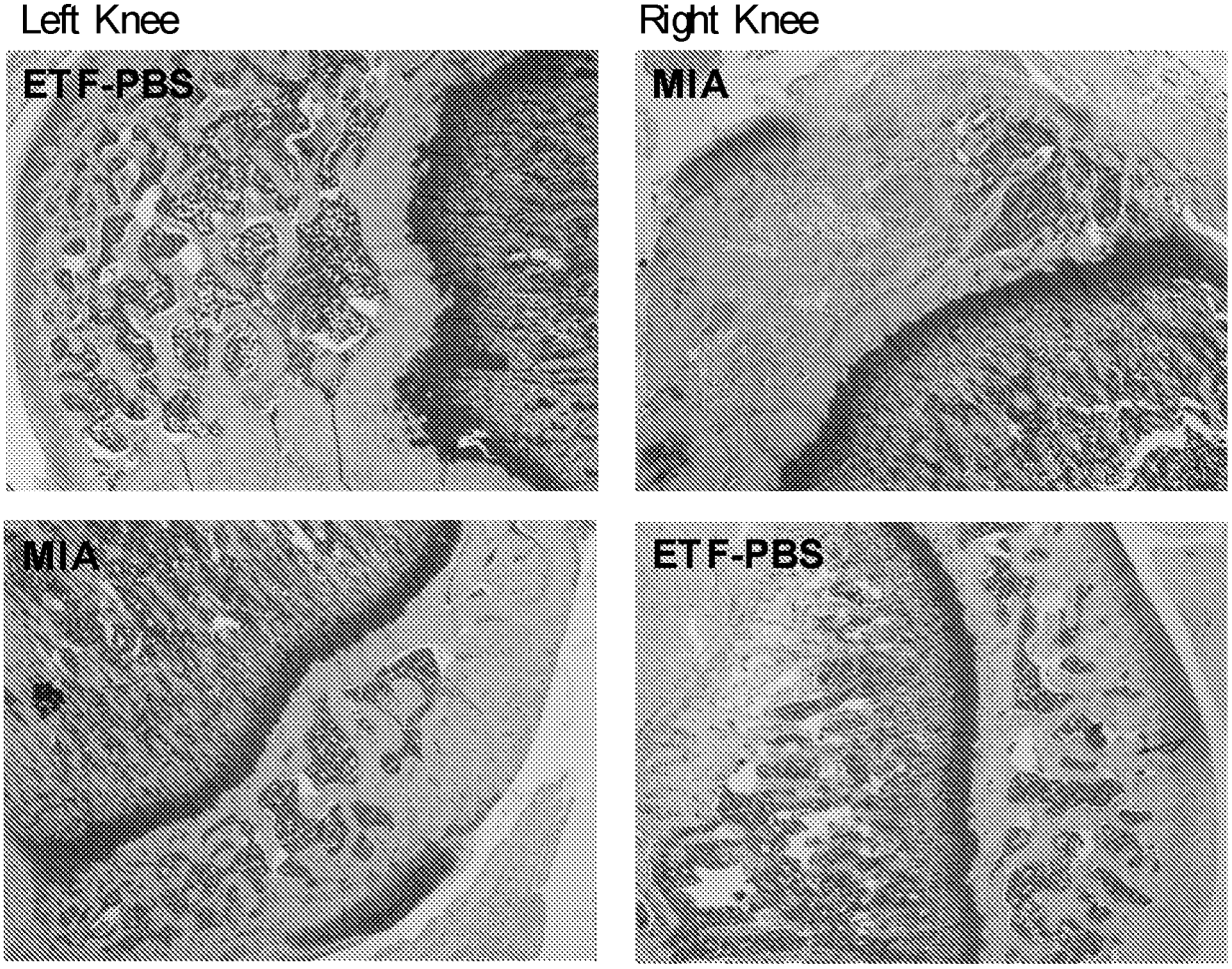

Left Knee
Right Knee
ETF-PBS
MIA
MIA
ETF-PBS
3 mg/kg PG-007 treated animals - Day 56

Figure 35

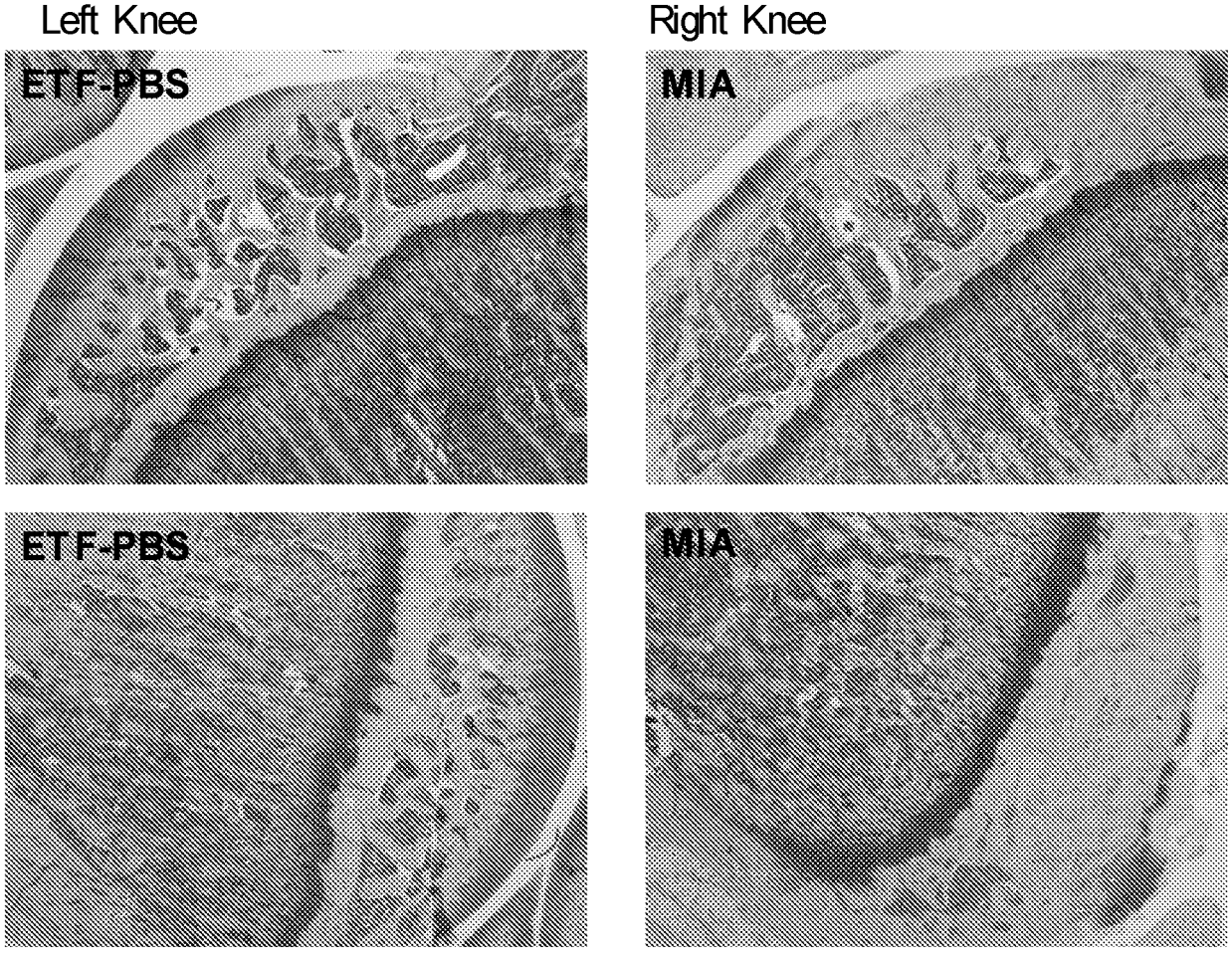

Left Knee
Right Knee
ETF-PBS
MIA
ETF-PBS
MIA
3 mg/kg p75NTR-Fc treated animals – Day 56

Figure 36

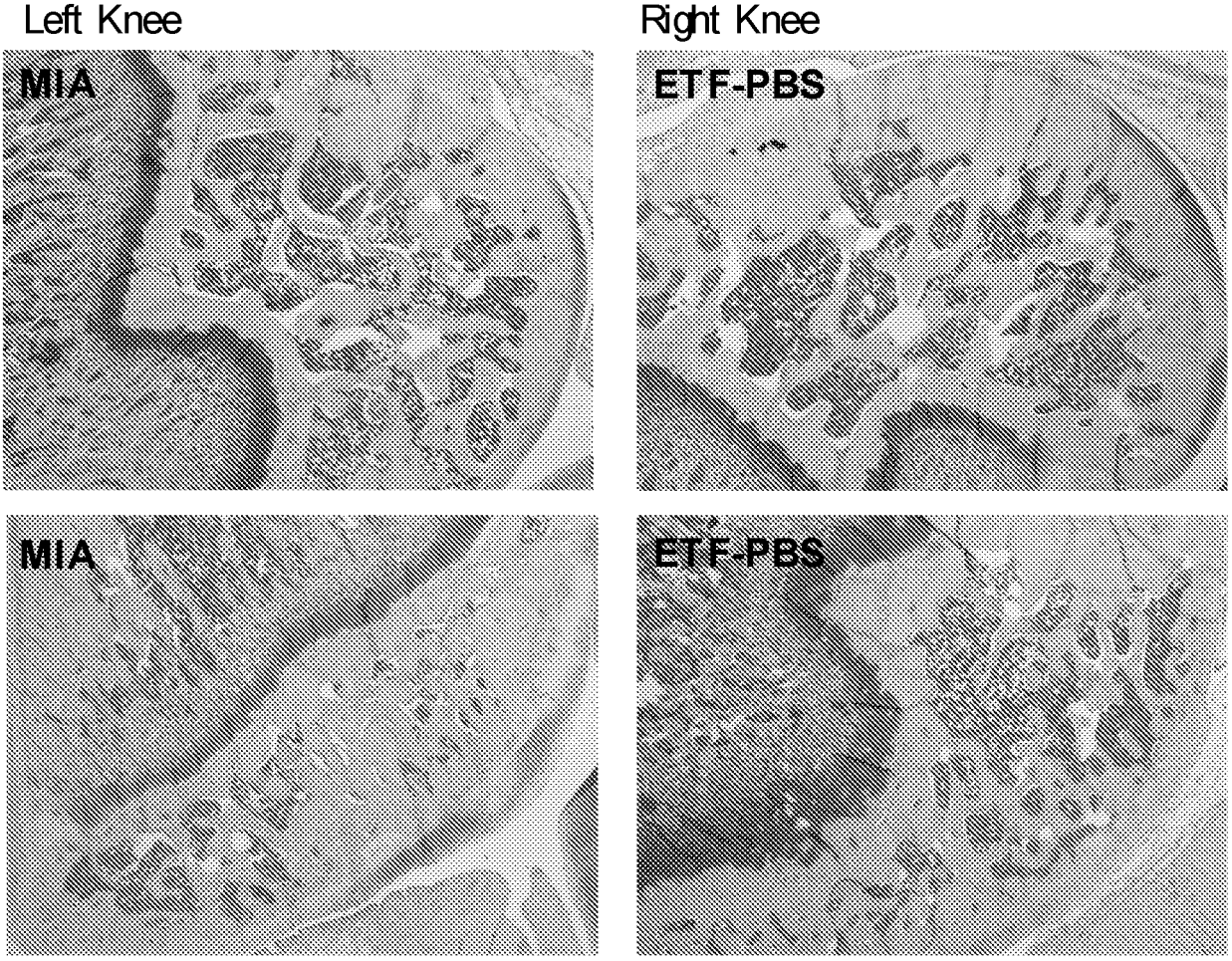

Left Knee
Right Knee
MIA
ETF-PBS
MIA
ETF-PBS
1 mg/kg p75NTR-Fc treated animals – Day 56

Figure 37

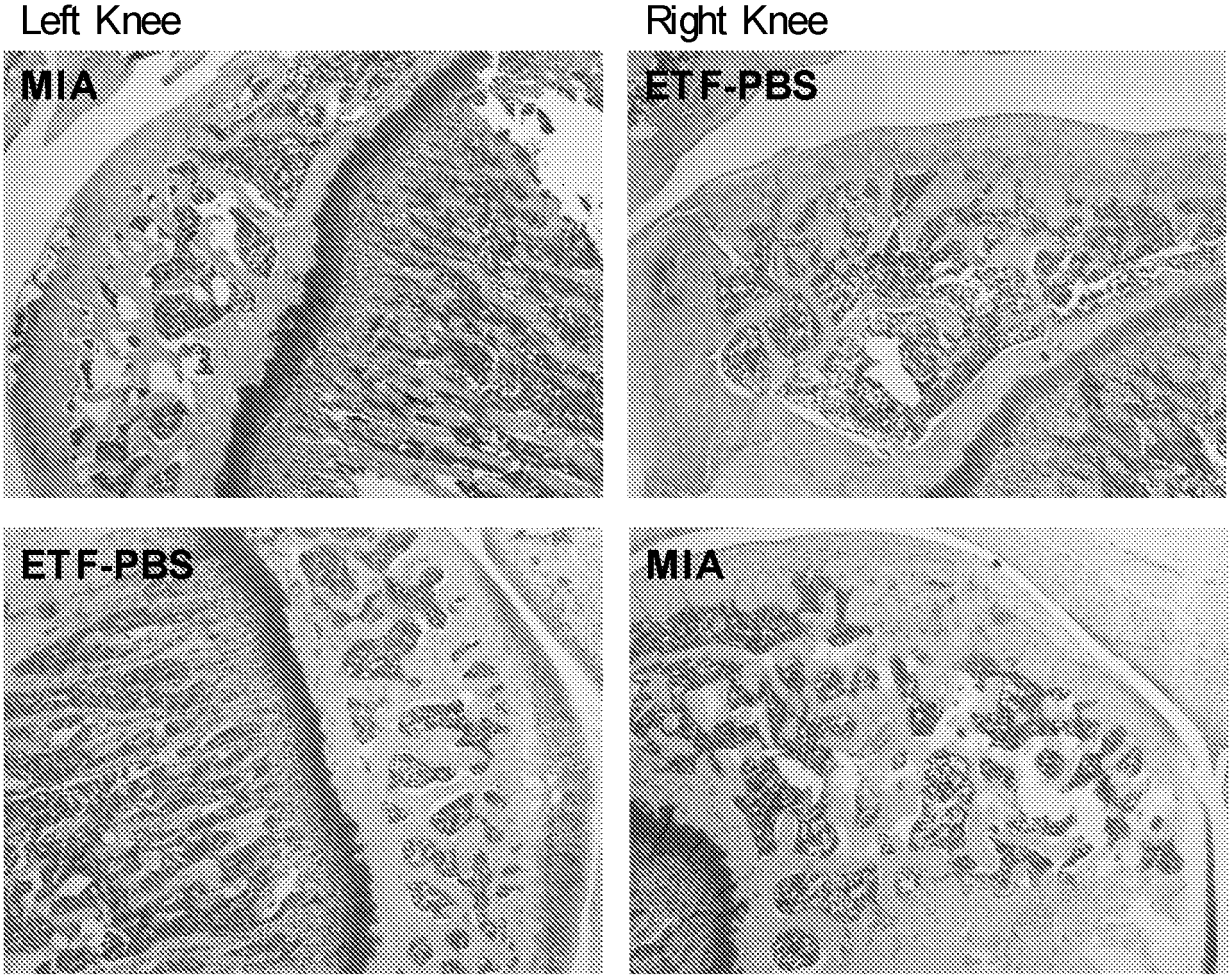

Left Knee
Right Knee
MIA
ETF-PBS
ETF-PBS
MIA
0.3 mg/kg p75NTR-Fc treated animals – Day 56

Figure 38

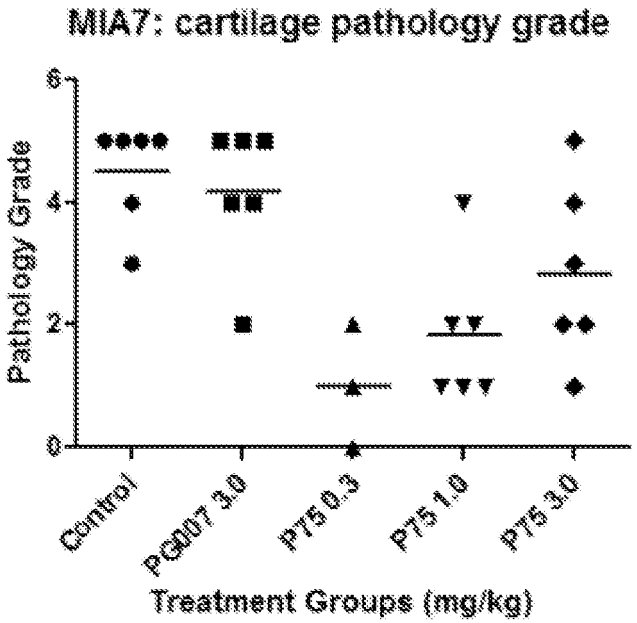


Figure 39

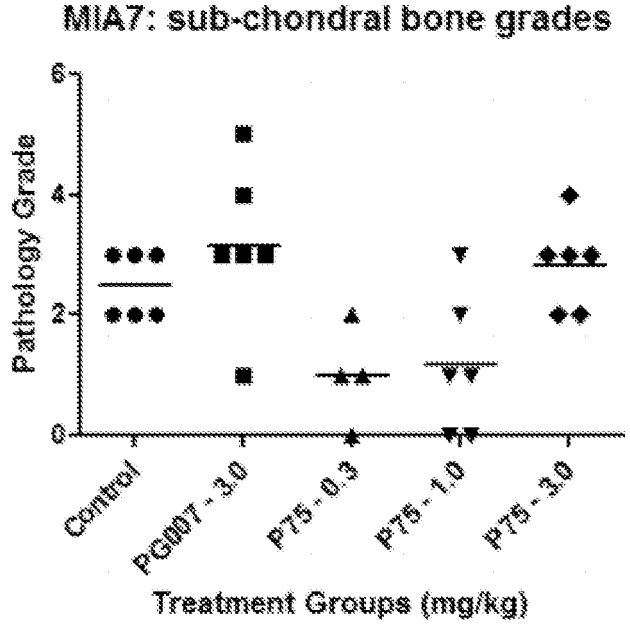


Figure 40

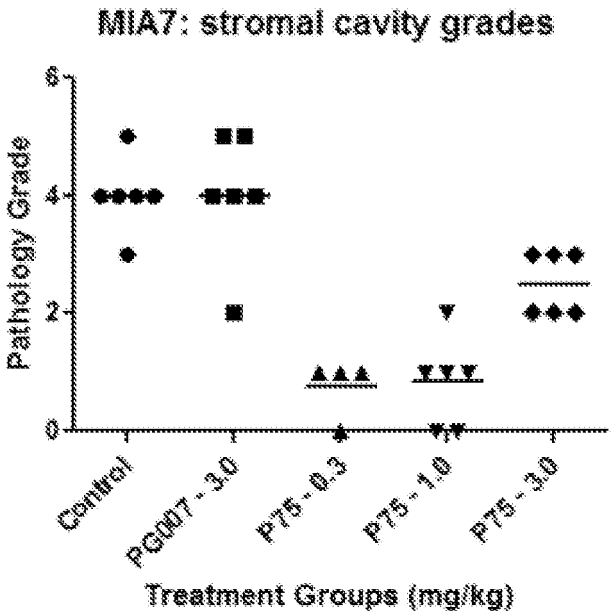


Figure 41

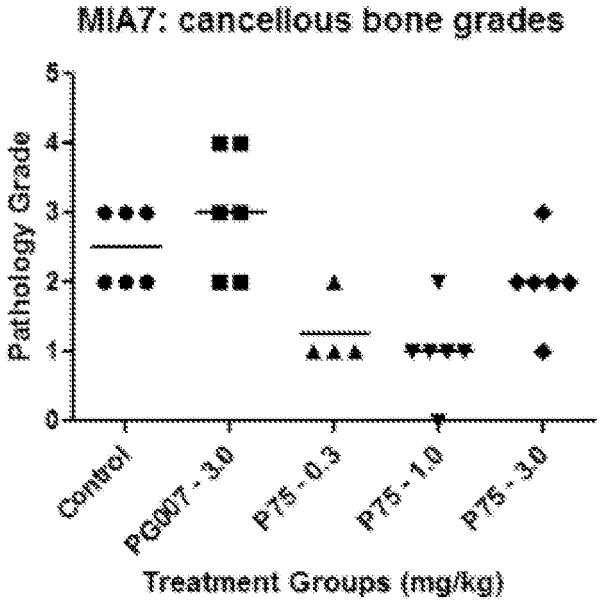


Figure 42

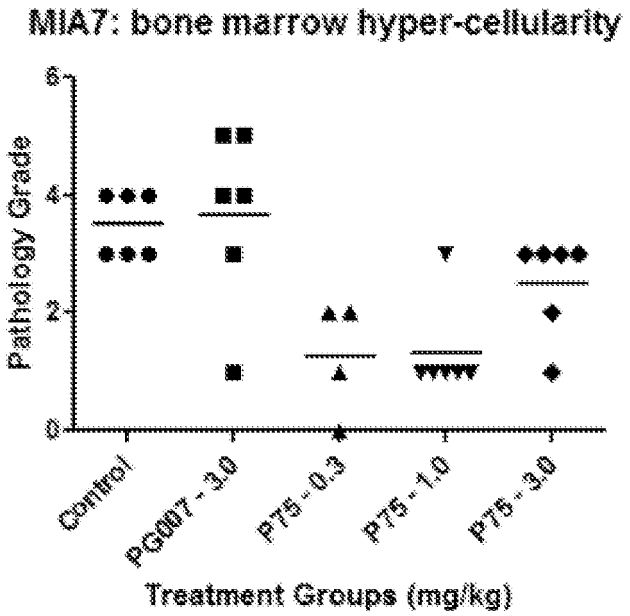


Figure 43

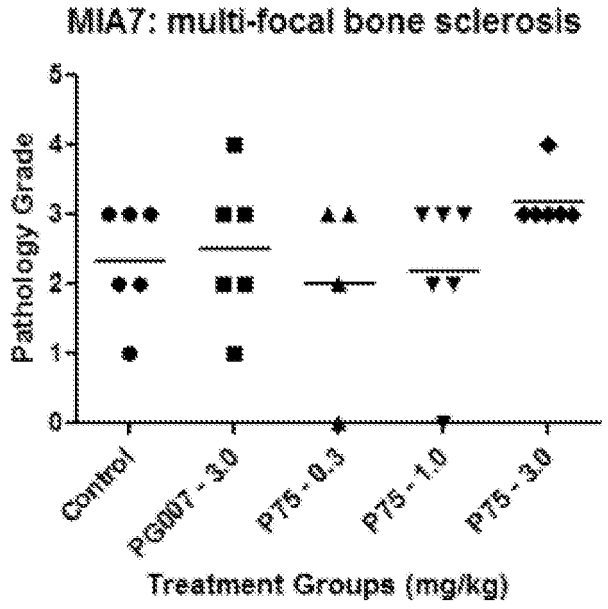


Figure 44

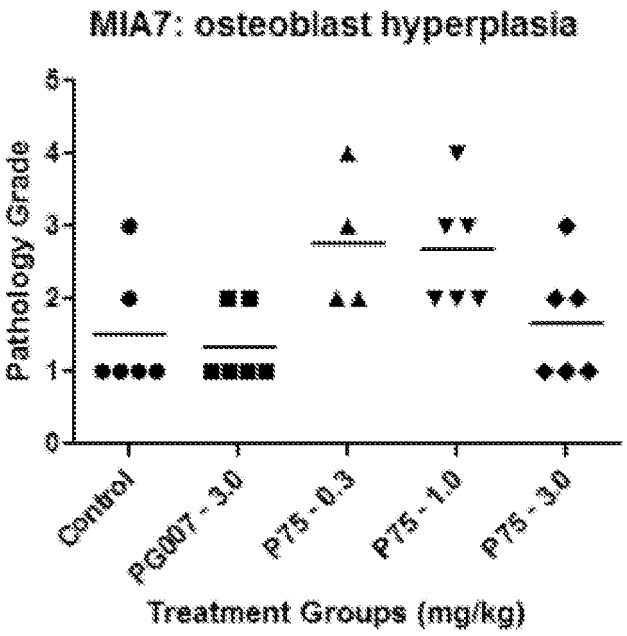

MIA7: osteoblast hyperplasia
Pathology Grade
0
1
2
3
4
5
Control
PG007 - 3.0
P75 - 0.3
P75 - 1.0
P75 - 3.0
Treatment Groups (mg/kg)

Figure 45