

Fig. 1

Generic Sequences, Human, Mouse and Rat

L-generic-TAT(s)	:	NH ₂ -X ^b _n -RKKRRQRRR-X ^b _n -COOH
L-TAT-IB (generic) (s):		NH ₂ -X ^b _n -RKKRRQRRR-X ^b _n -X ^a _n -RPTTLXLXXXXXXXXXD-X ^b _n -COOH
L-TAT-IB (generic)	:	NH ₂ -XXXXXXXXRKKRRQRRRXXXXXXXXRRPTTLXLXXXXXXXXXQDS/TX-COOH
D-generic-TAT(s)	:	NH ₂ -X ^b _n -RRRQRRKKR-X ^b _n -COOH
D-TAT-IB (generic) (s):		NH ₂ -X ^b _n -DQXXXXXXXXXLTLTPR-X ^a _n -X ^b _n -RRRQRRKKR-X ^b _n -COOH
D-TAT-IB (generic)	:	NH ₂ -XT/SDQXXXXXXXXXLTLTPRXXXXXXXXRRRQRRKKRXXXXXXXXX-COOH

Fig. 2

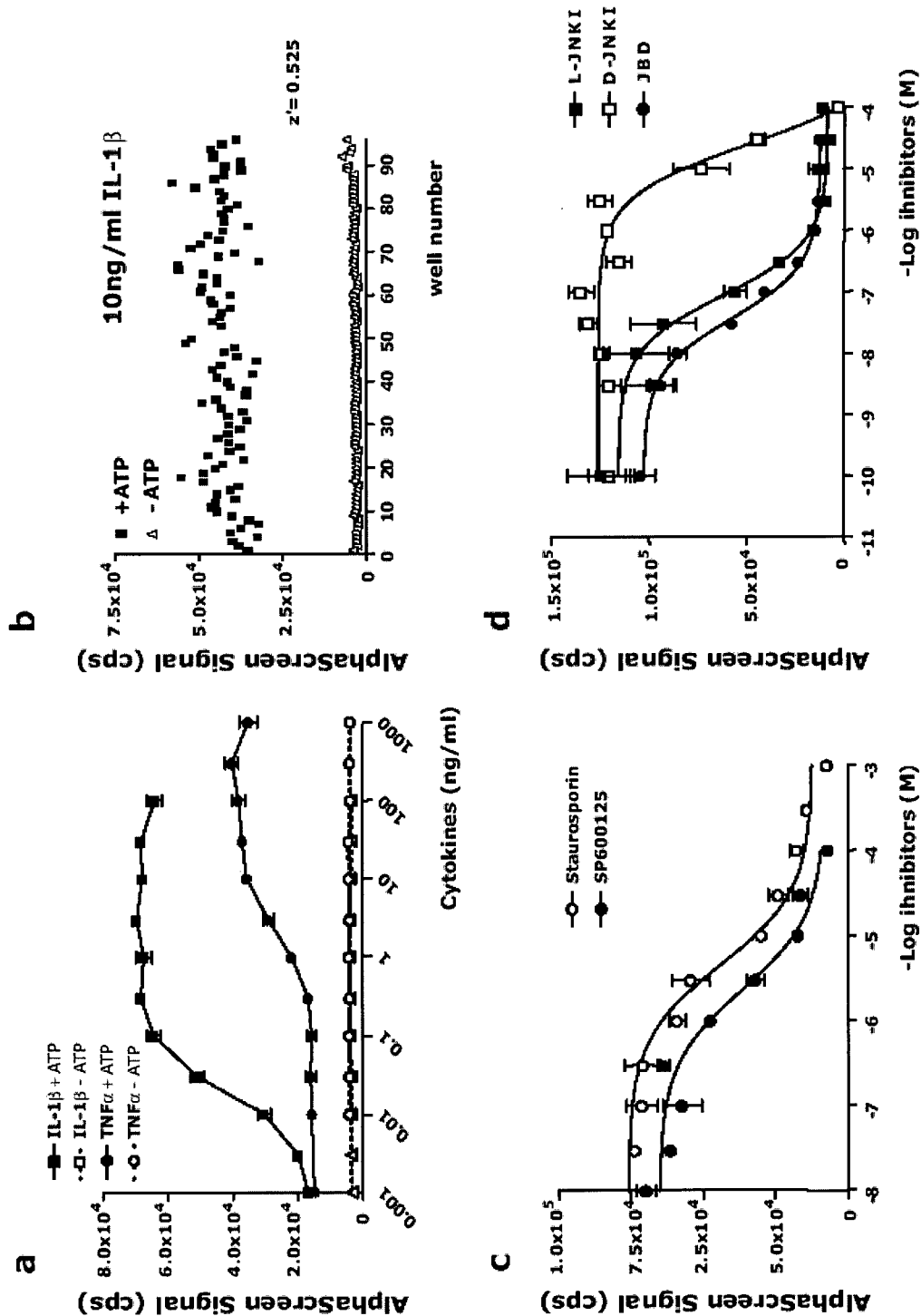


Fig. 3

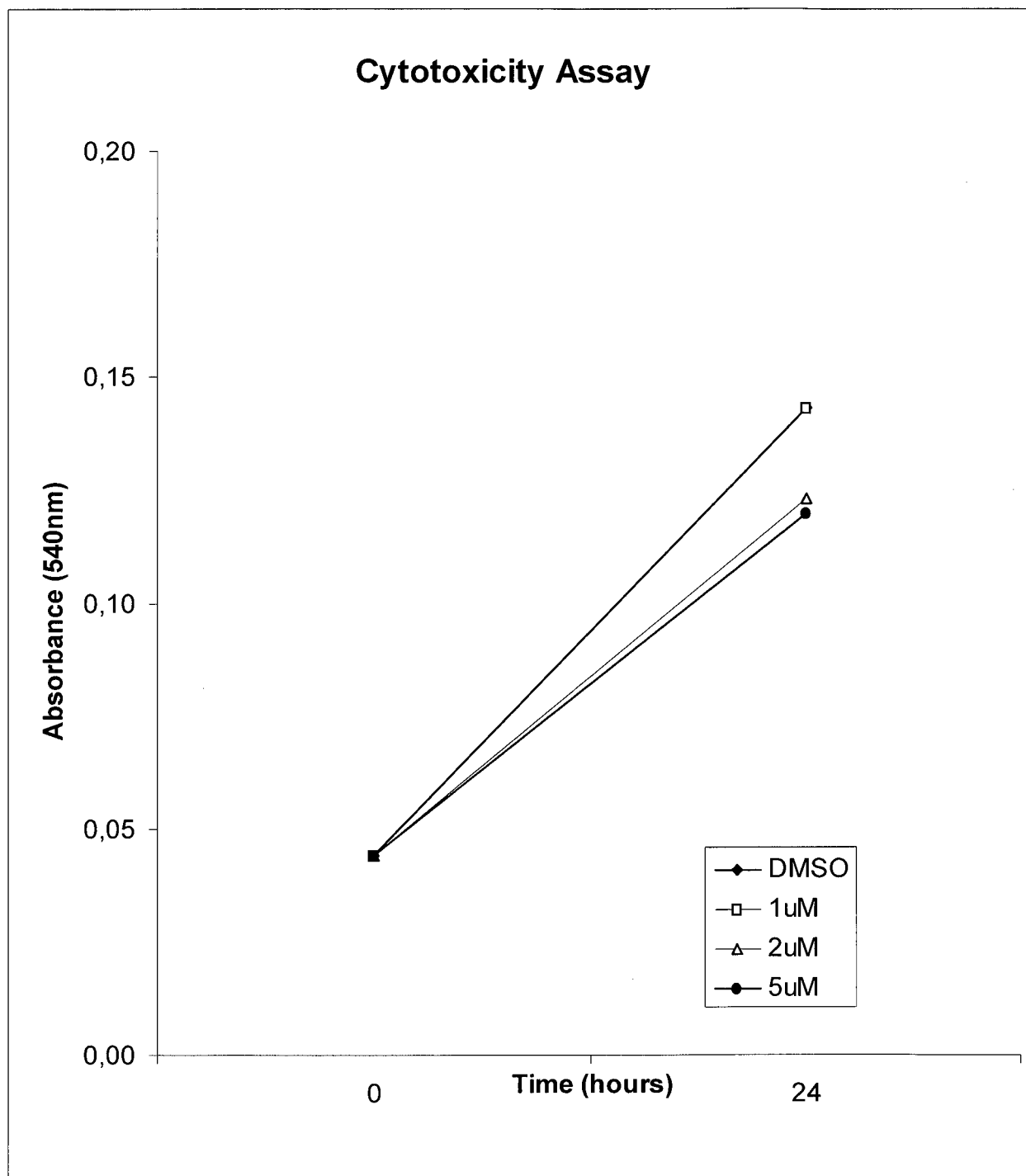


Fig. 4

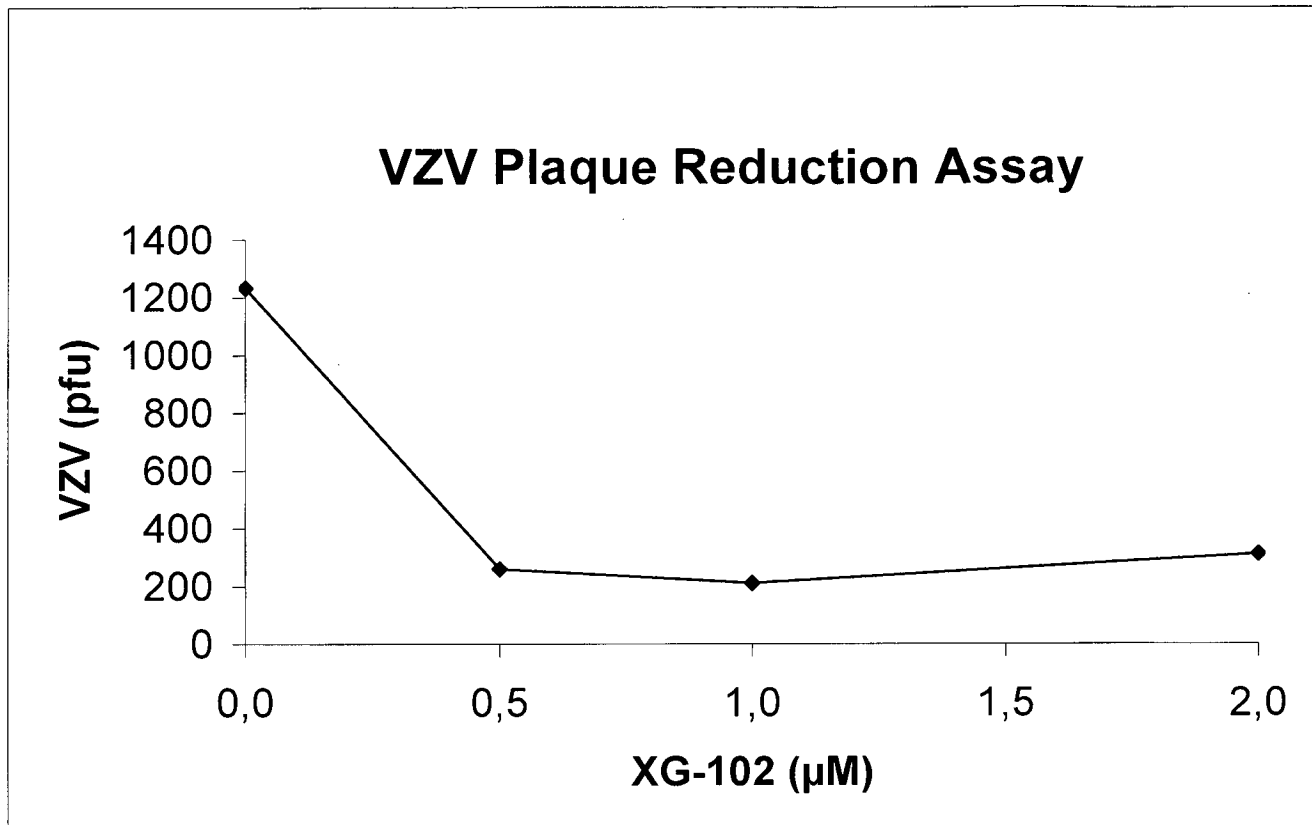


Fig. 5

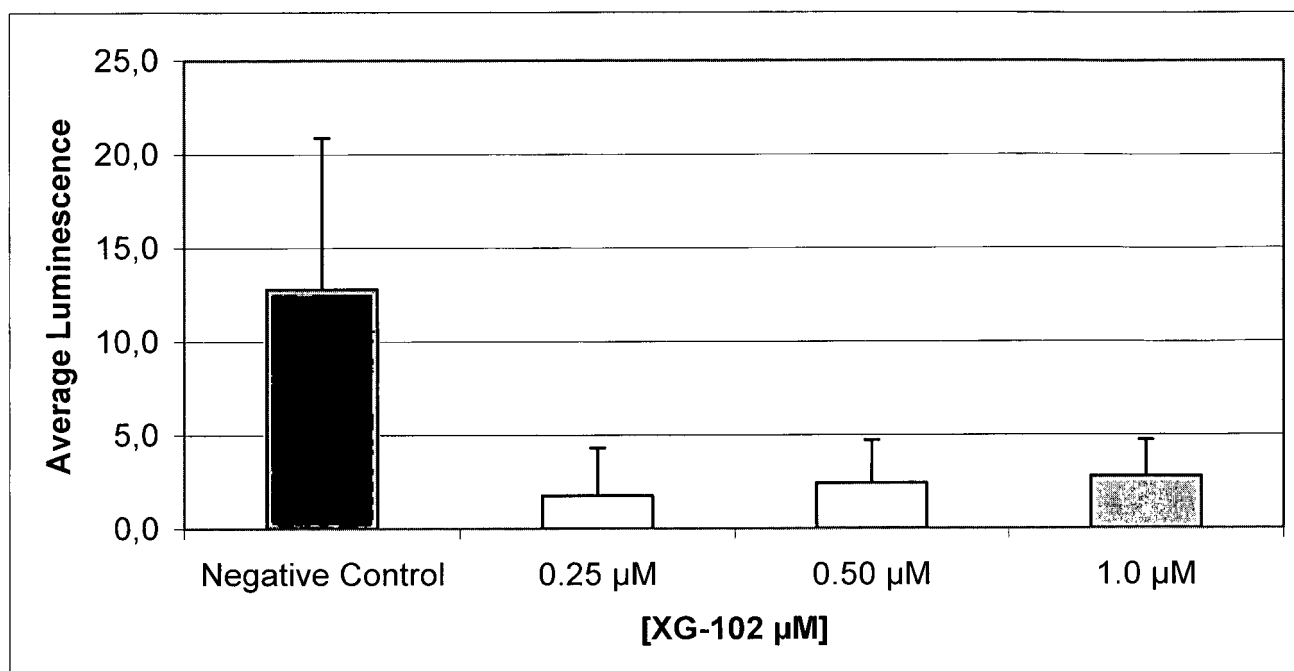


Fig. 6

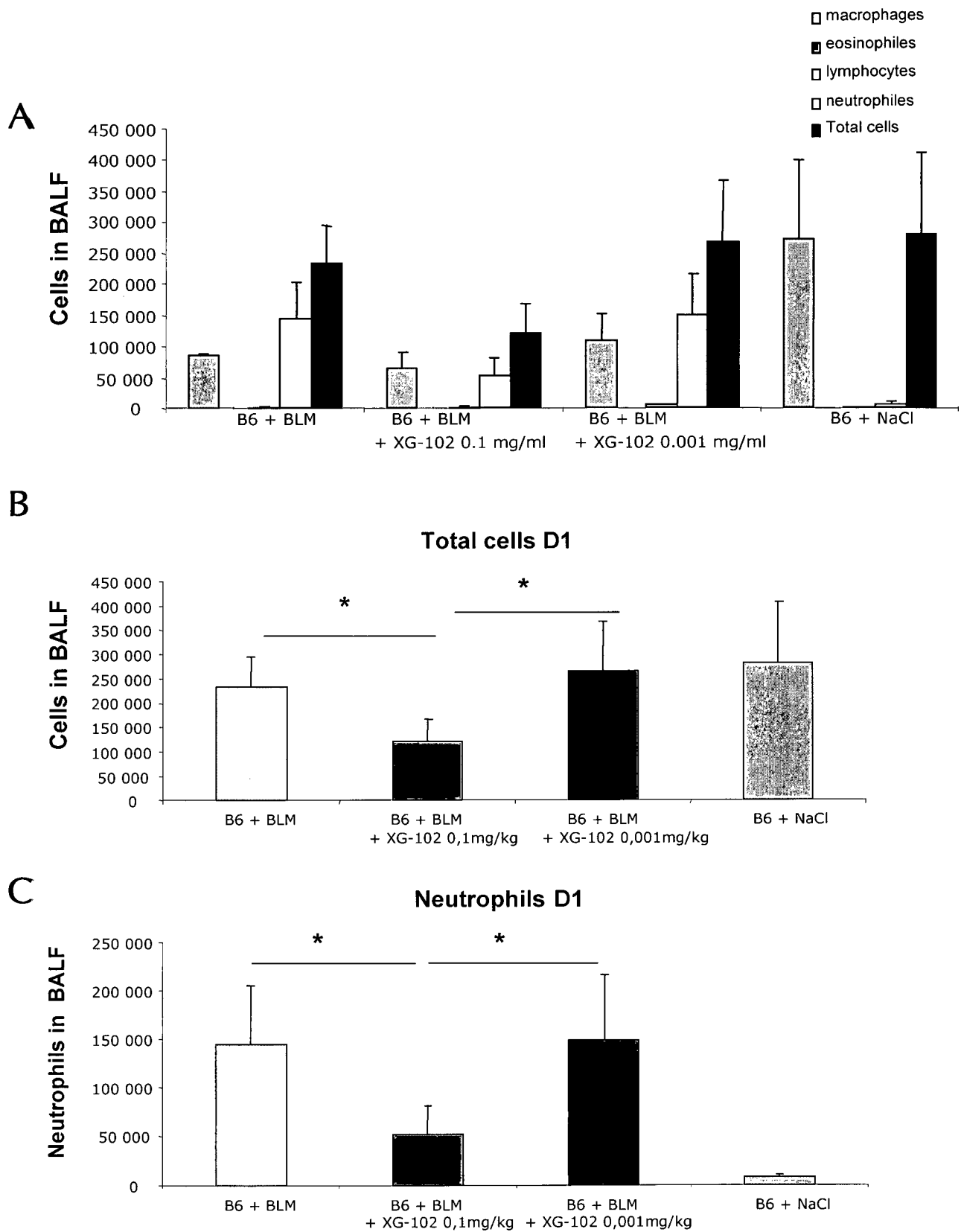


Fig. 7

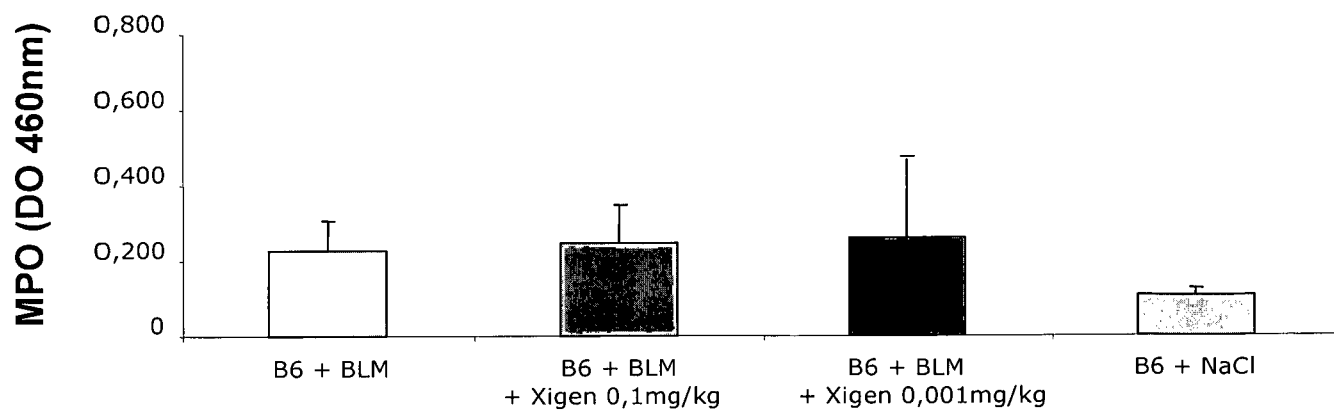


Fig. 8

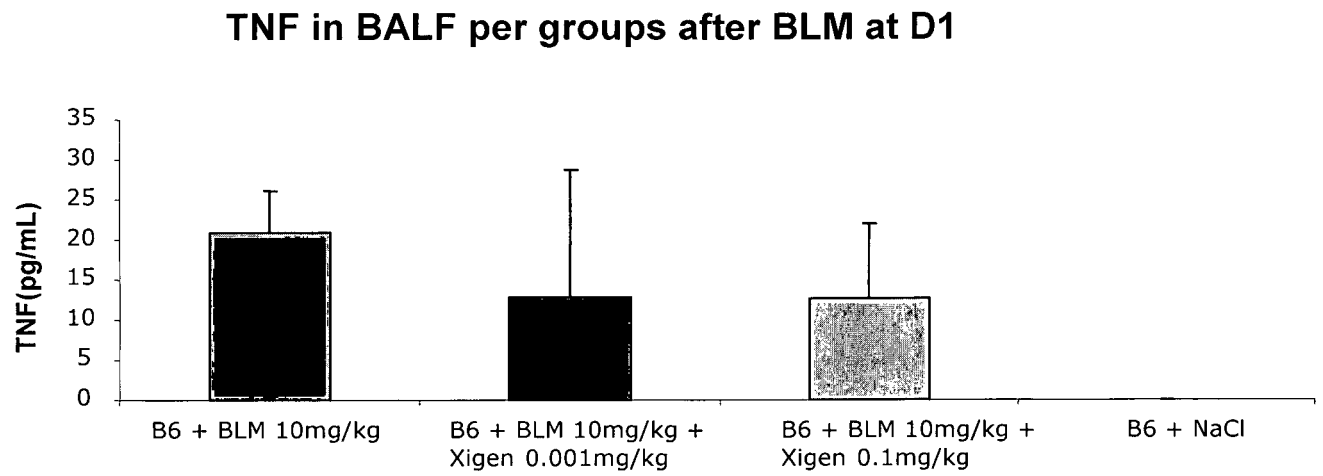
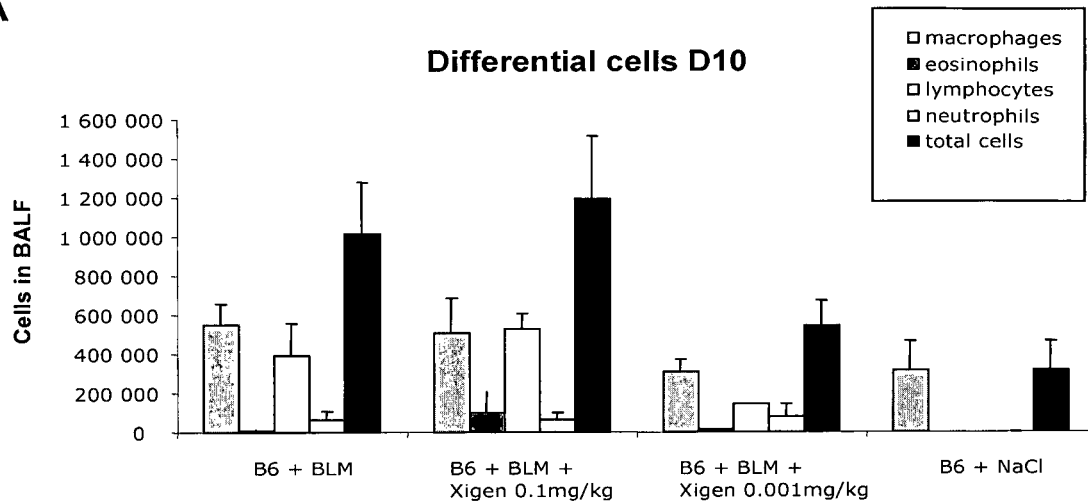
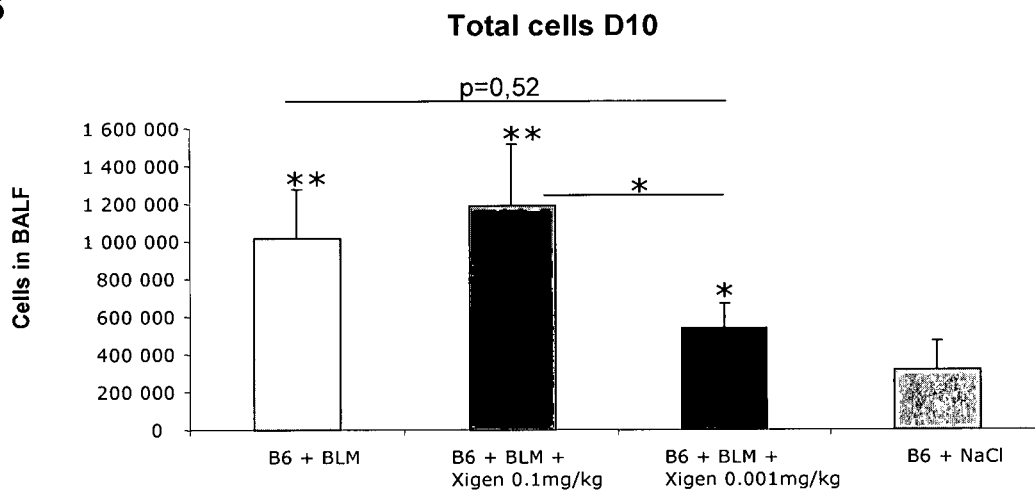
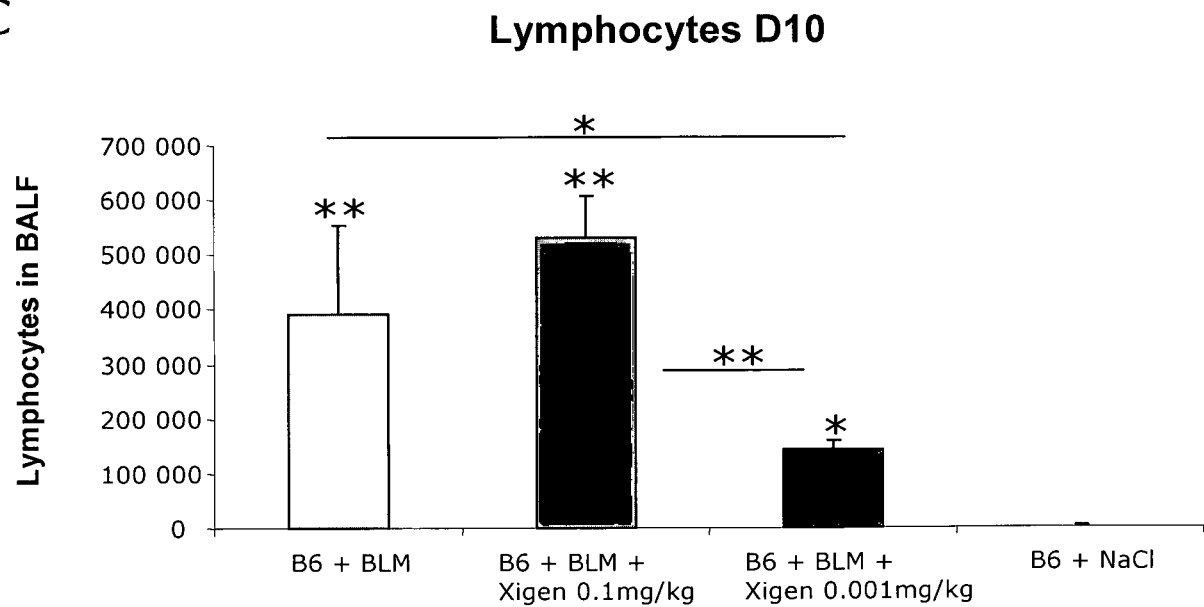


Fig. 9

A**B****C****Fig. 10**

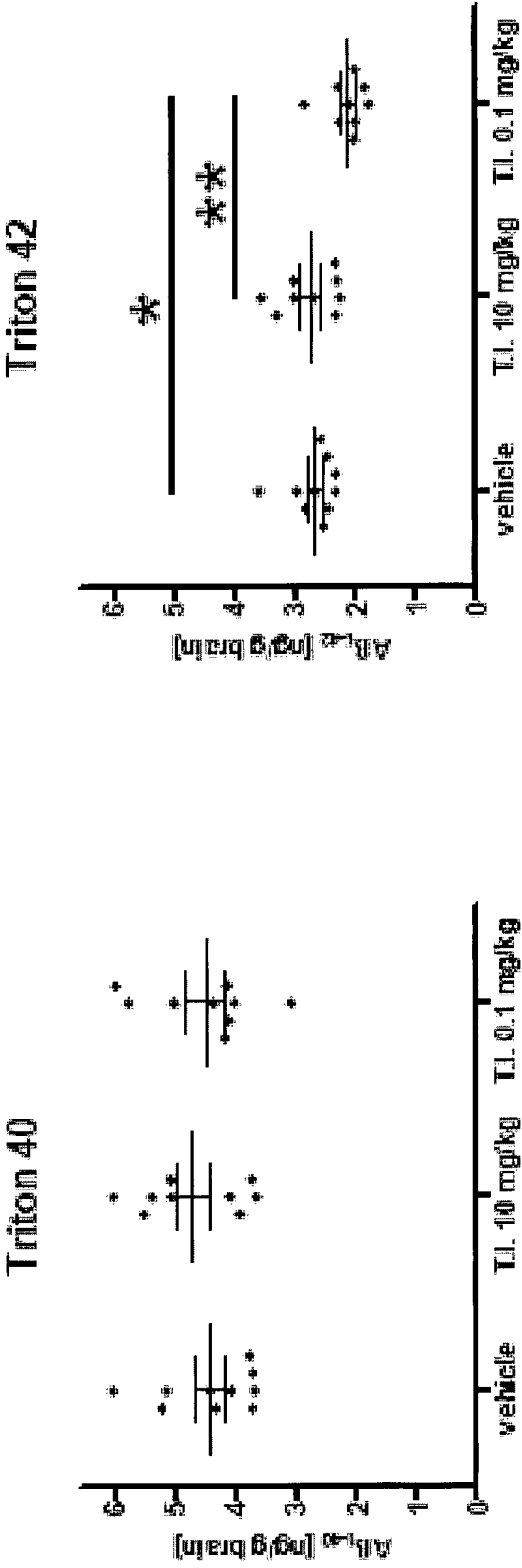


Fig. 11

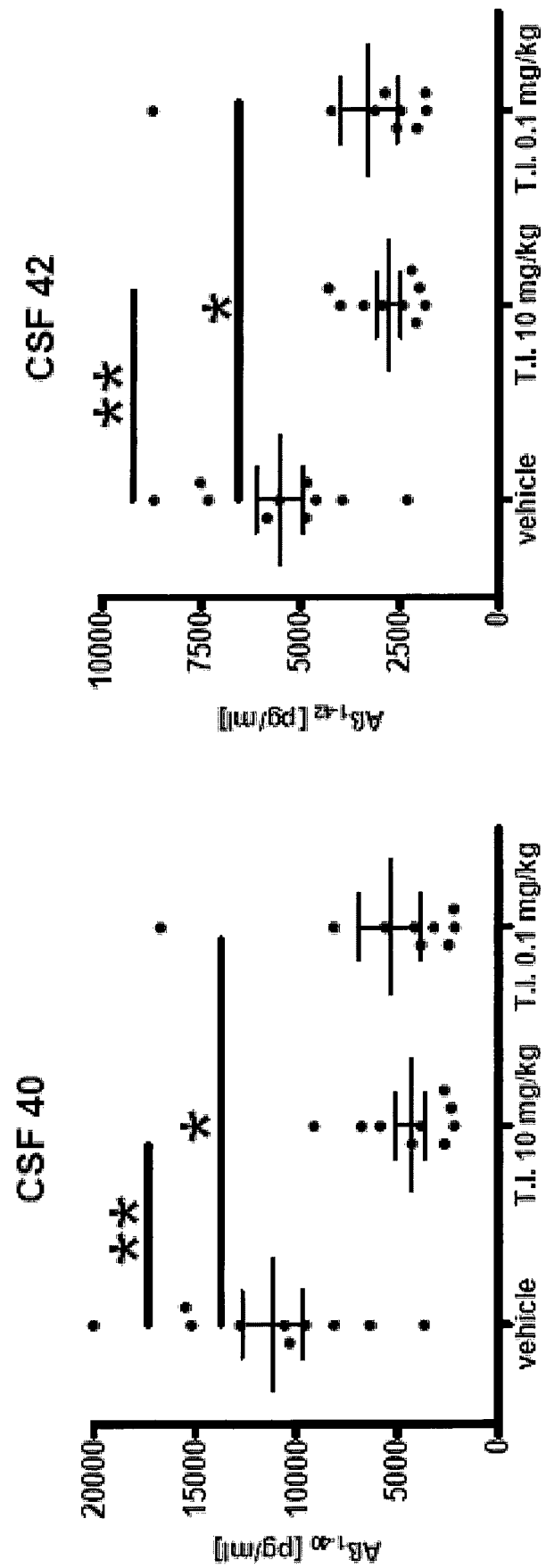


Fig. 12

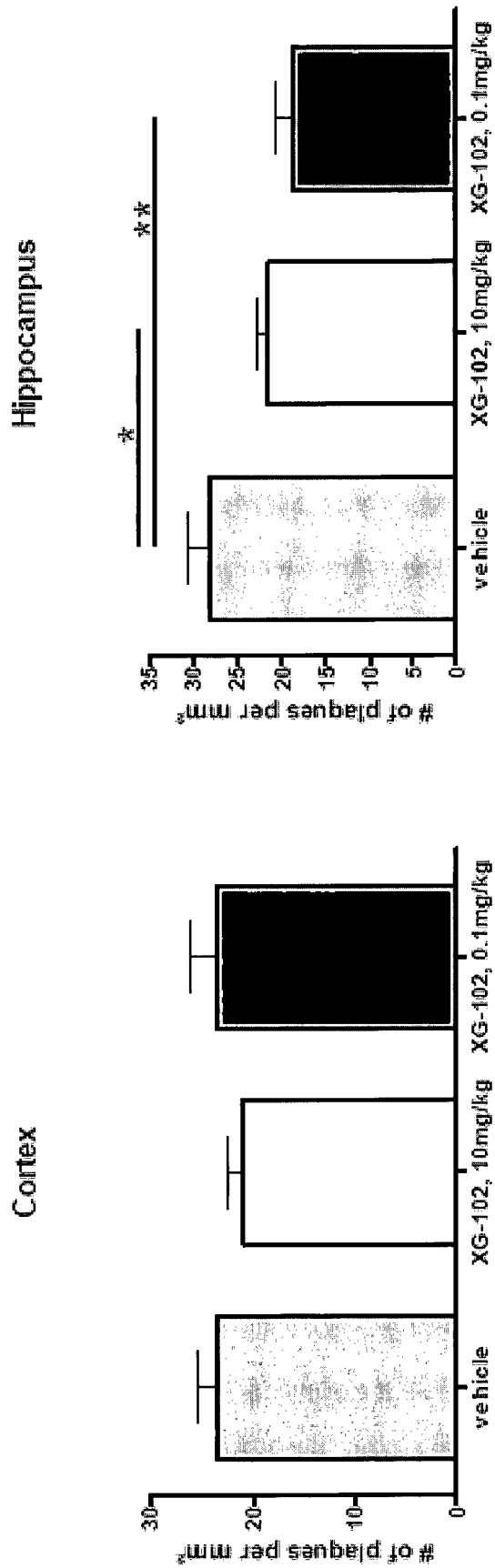


Fig. 13

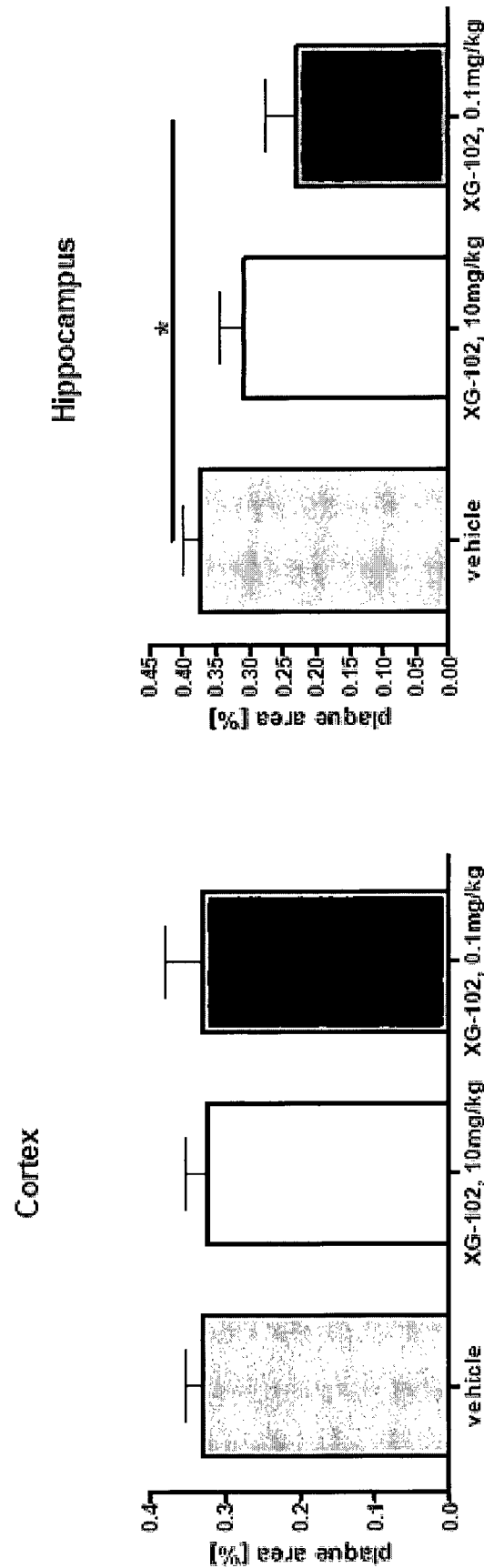


Fig. 14

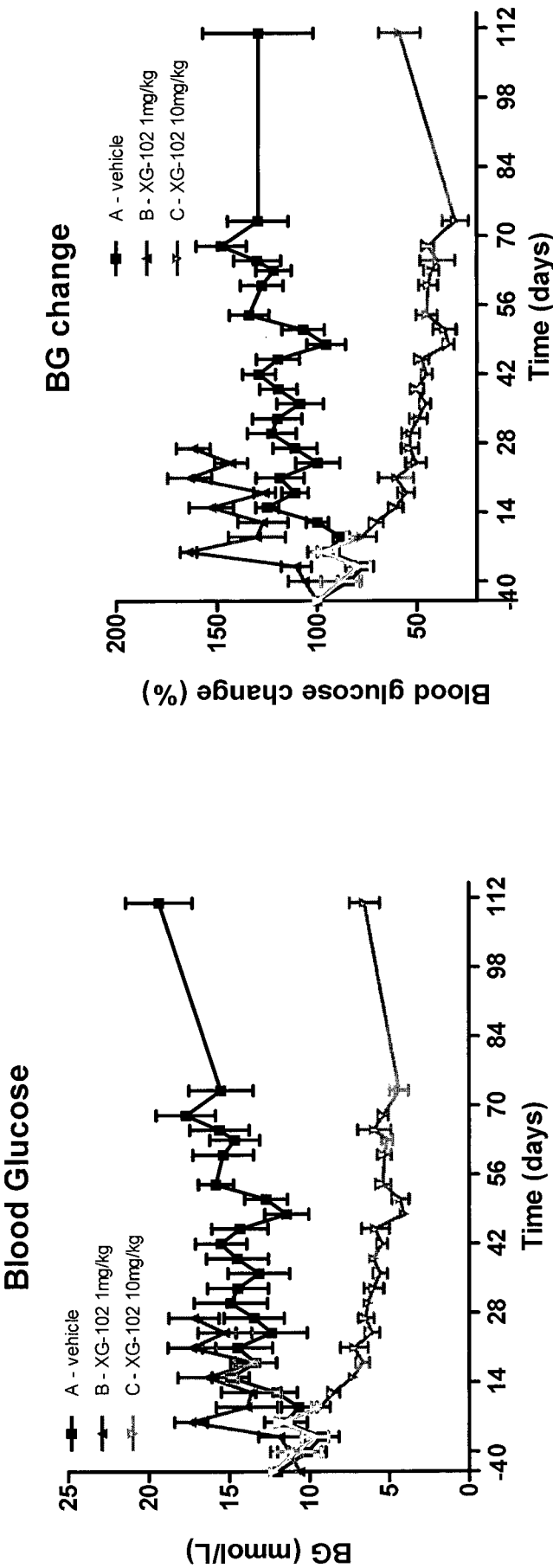


Fig. 15

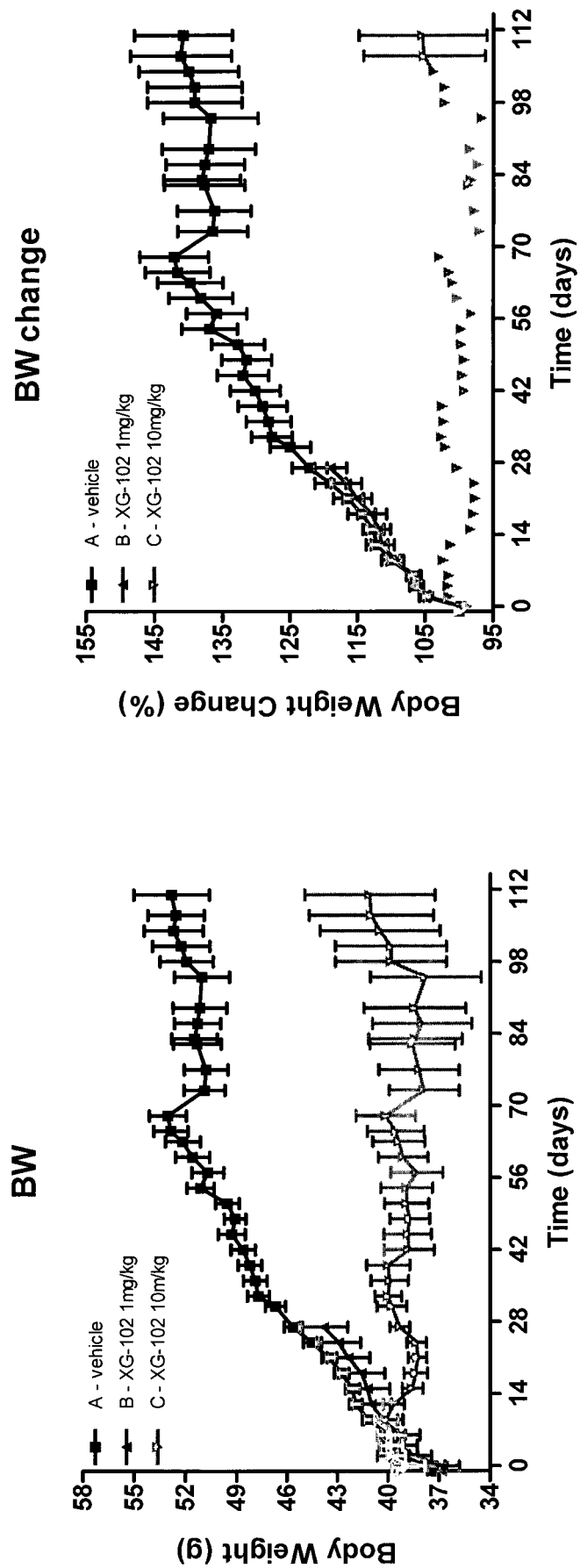


Fig. 16

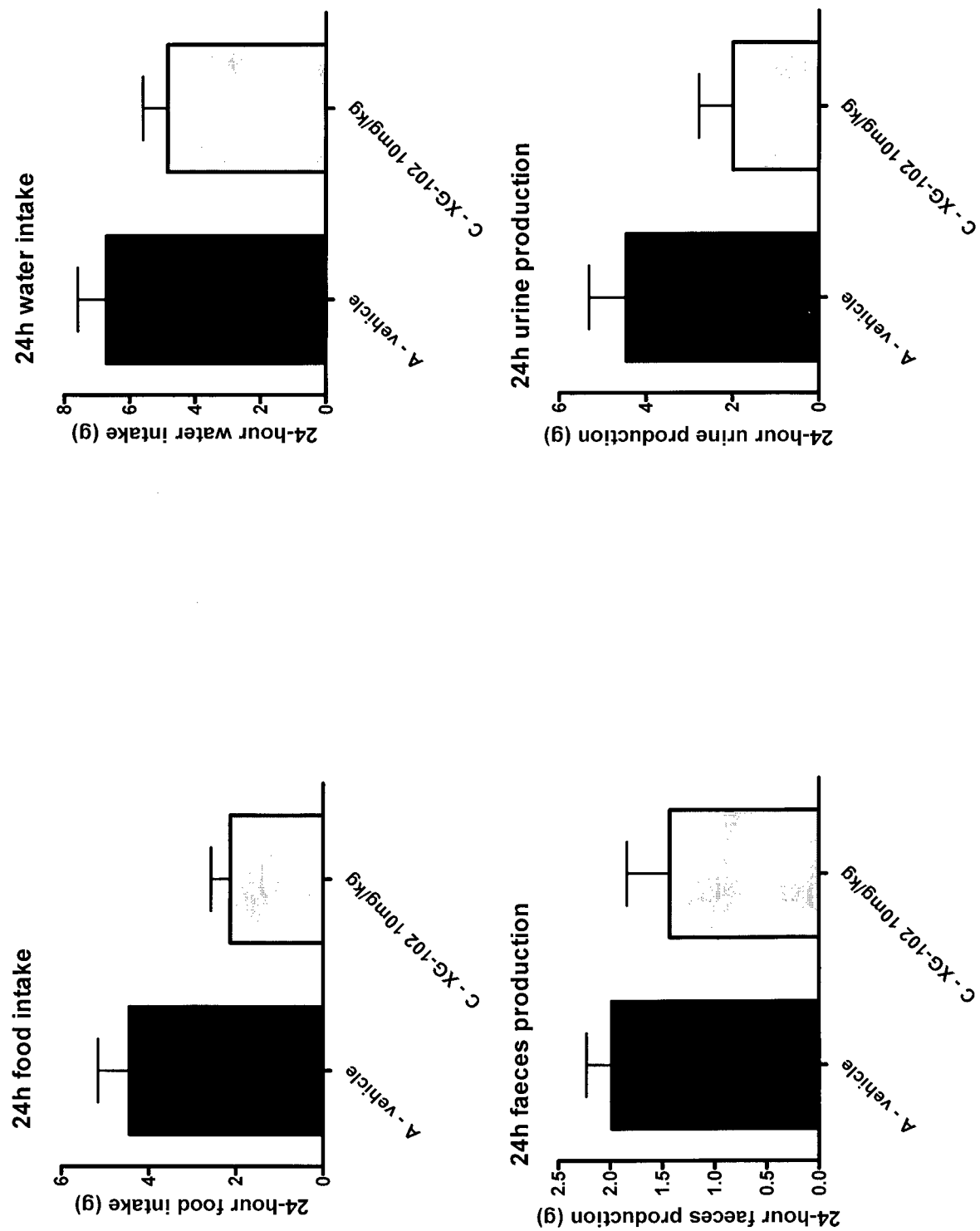


Fig. 17

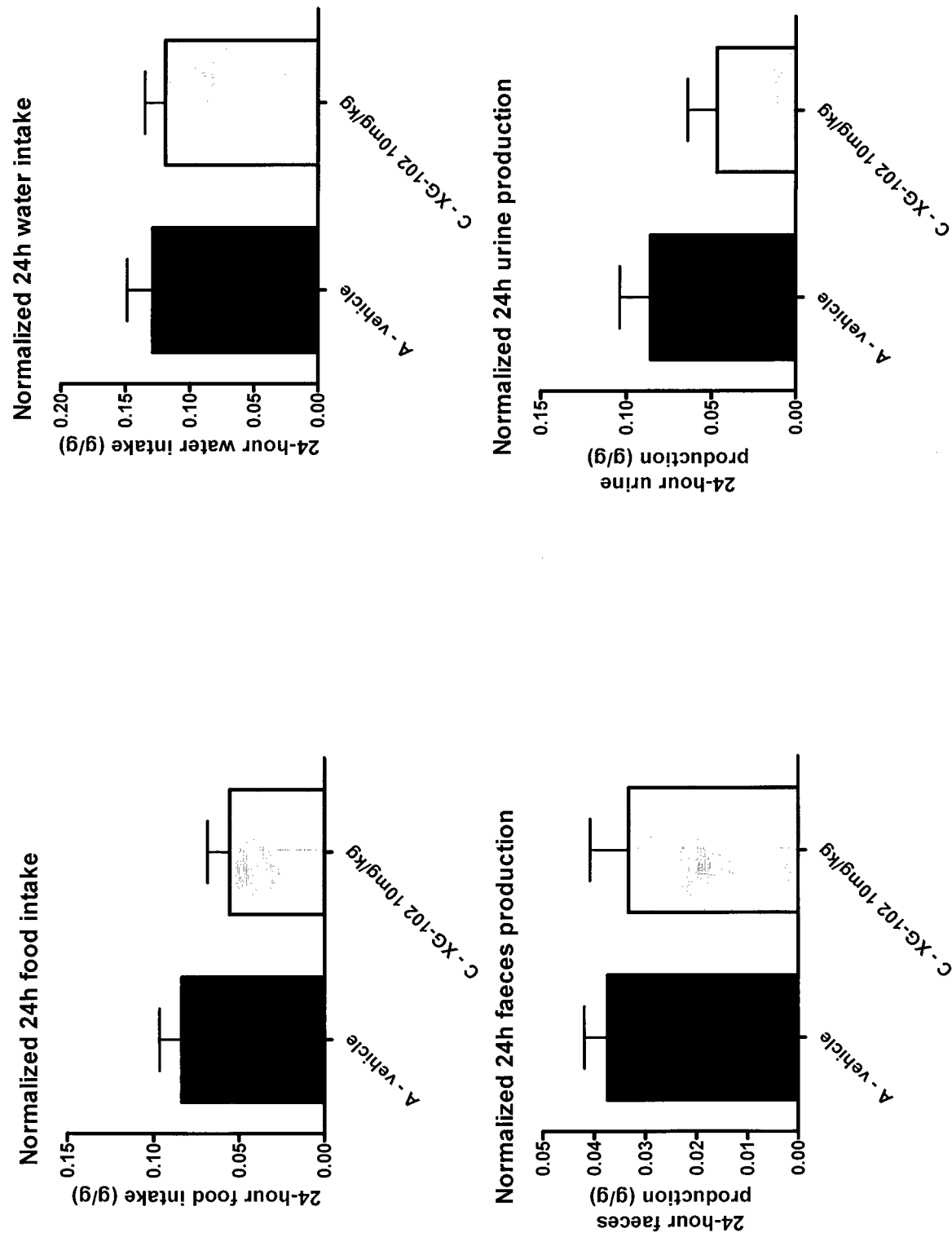


Fig. 18

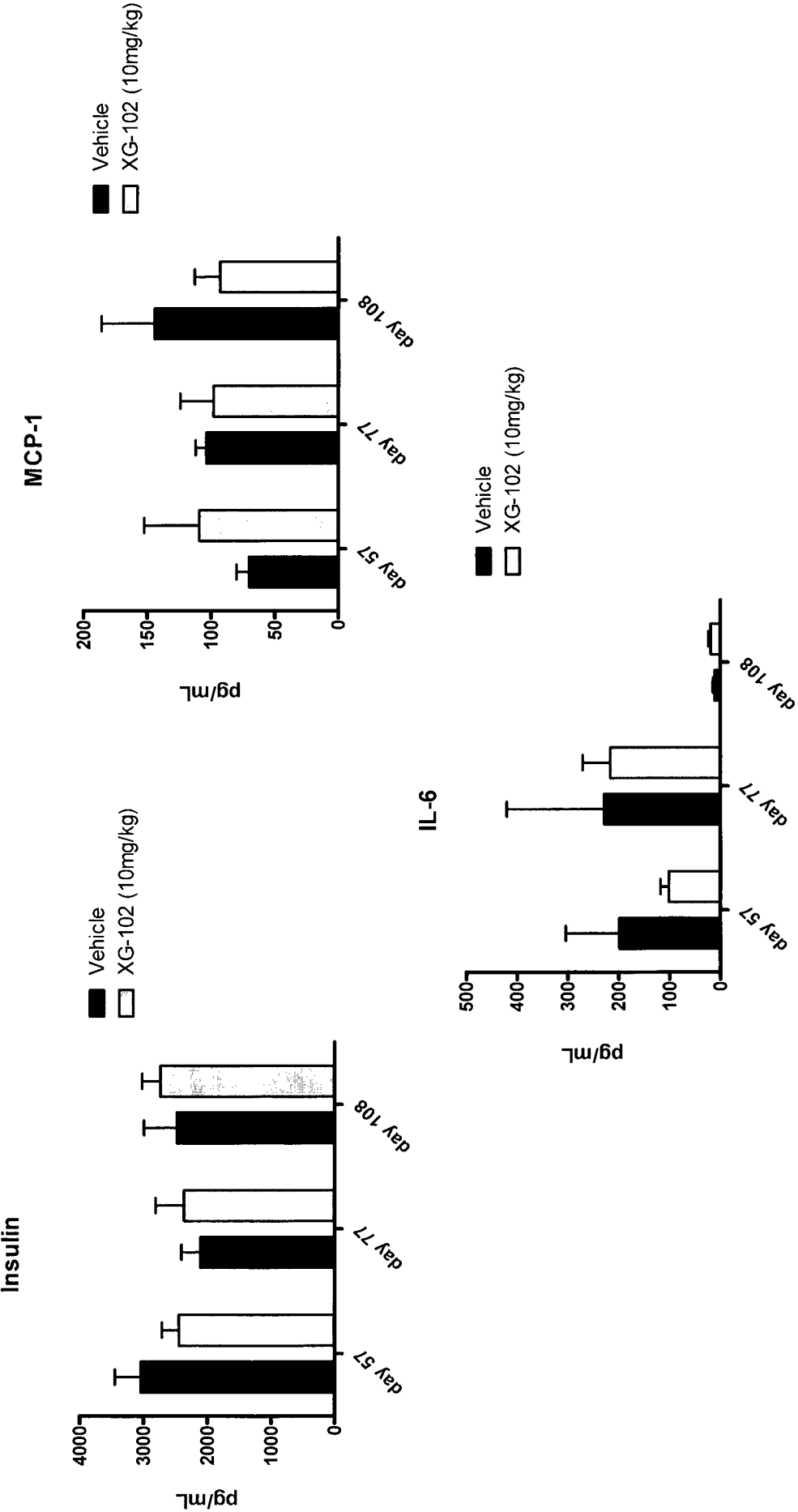


Fig. 19

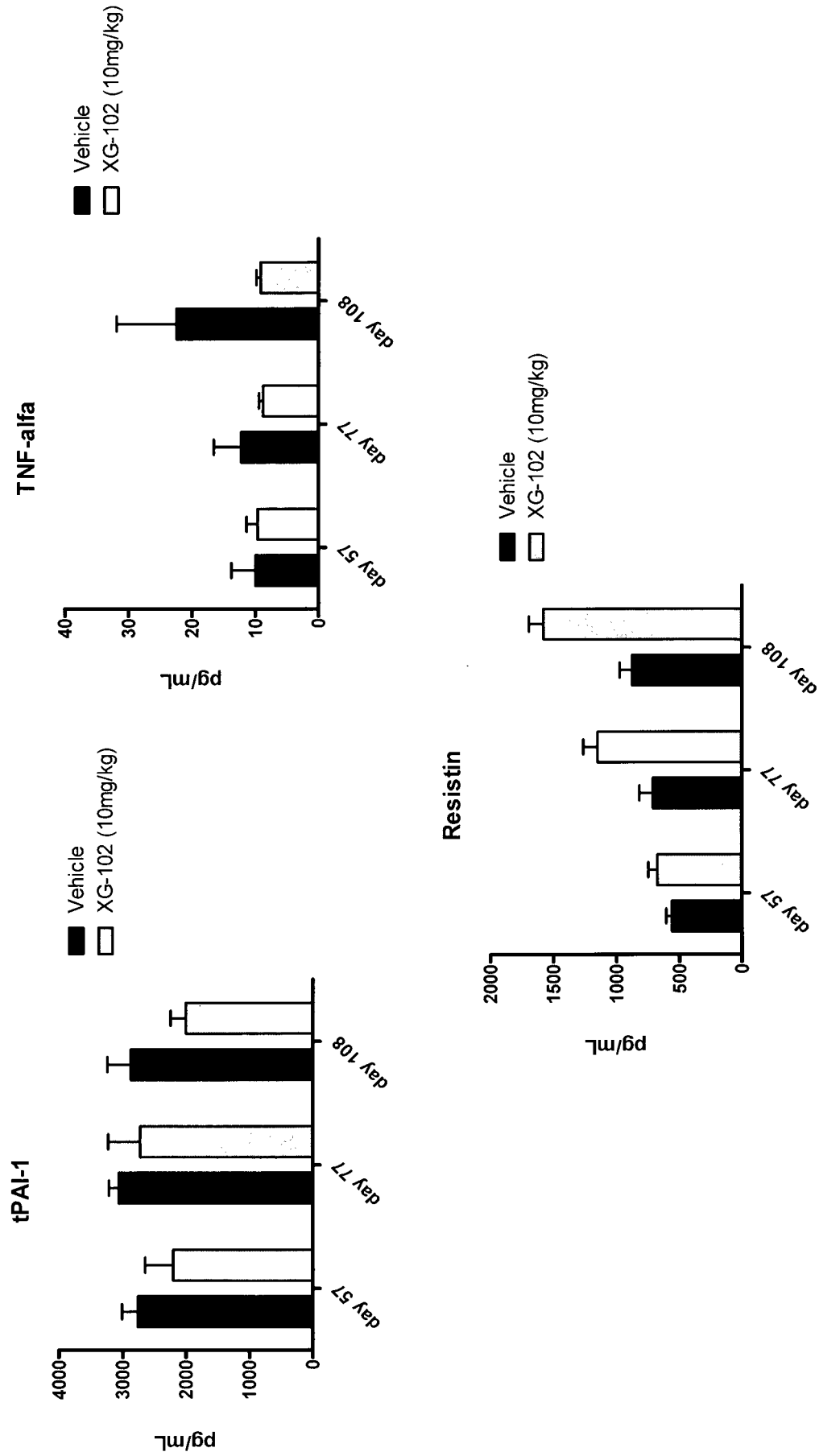


Fig. 20

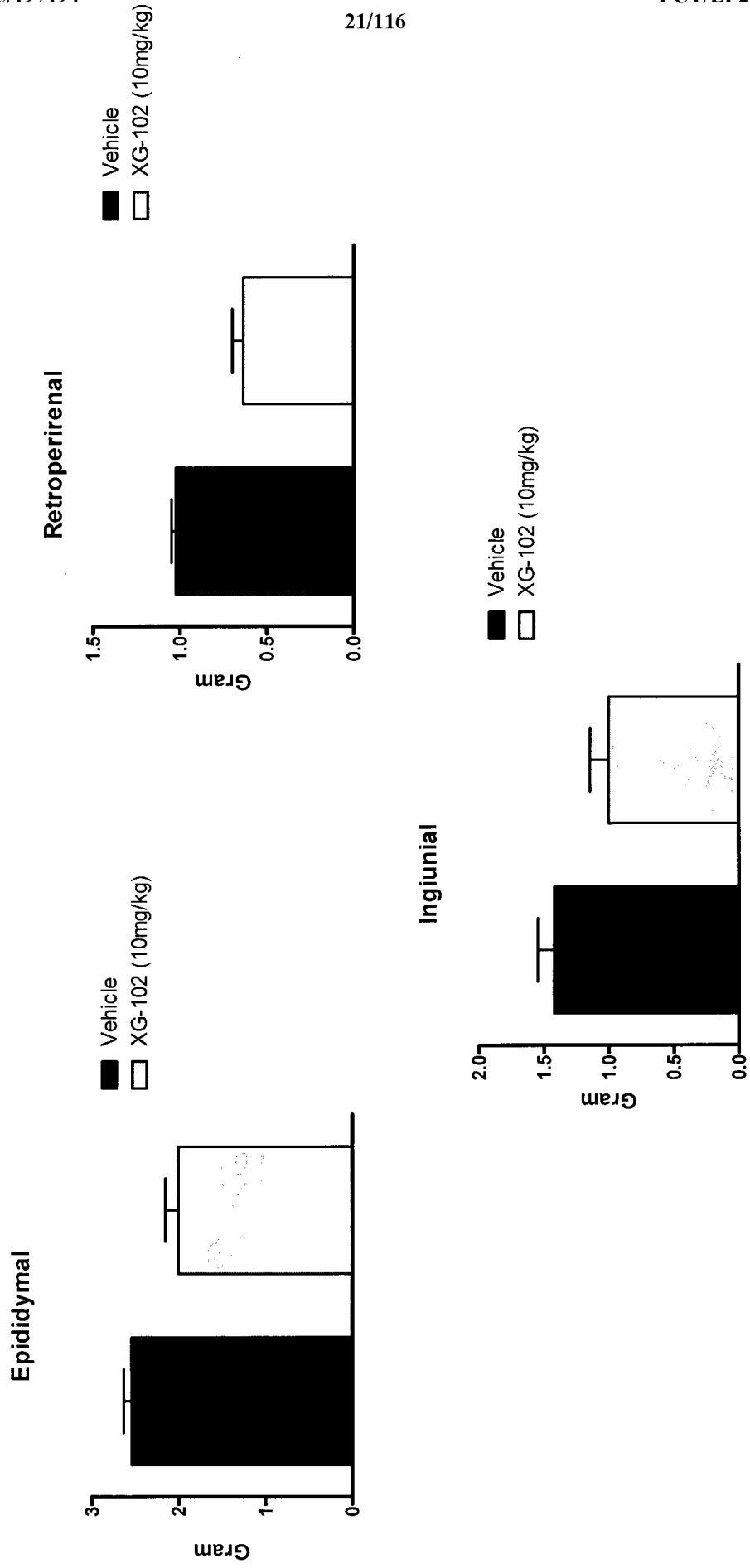


Fig. 21

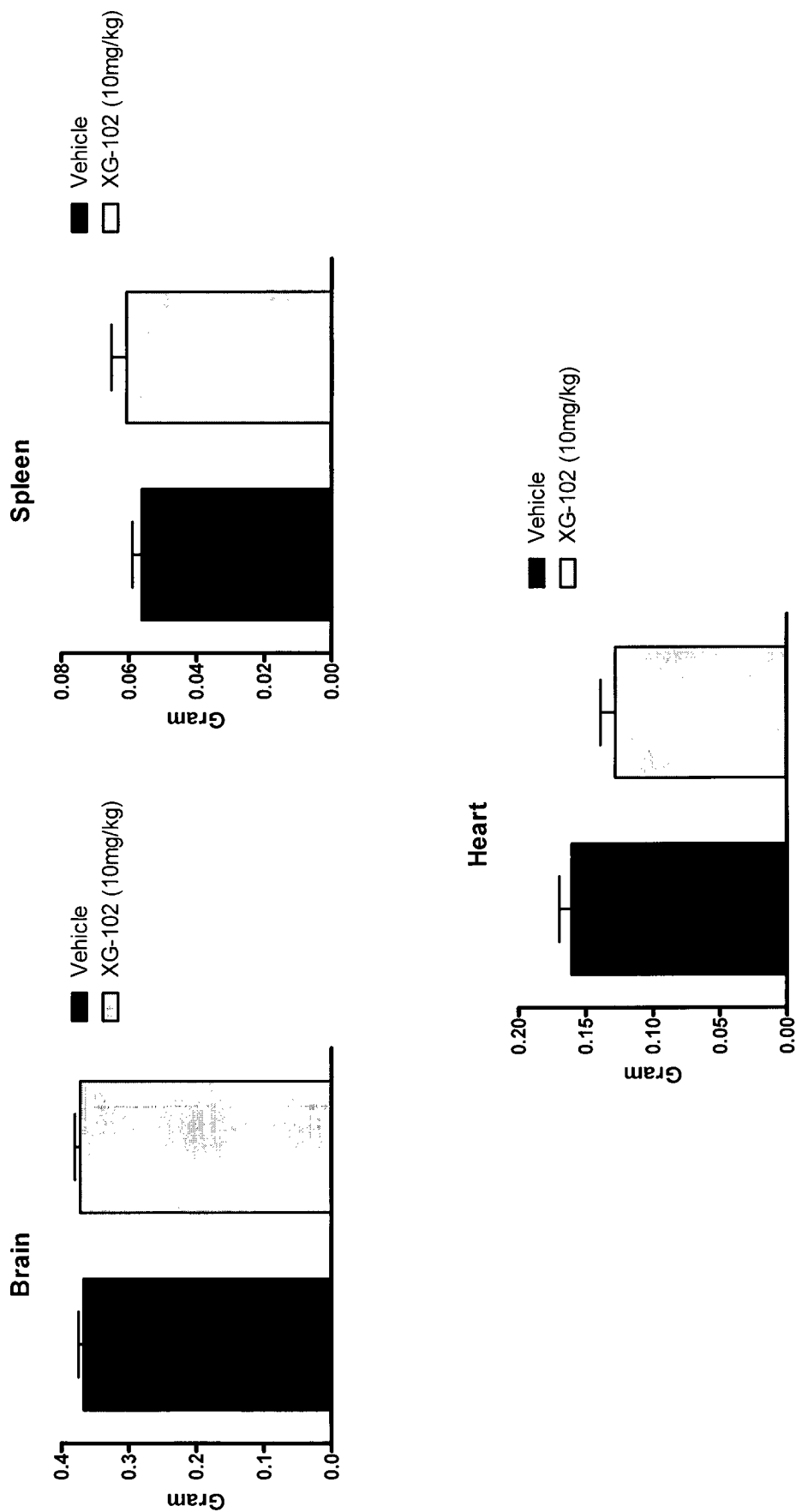


Fig. 22

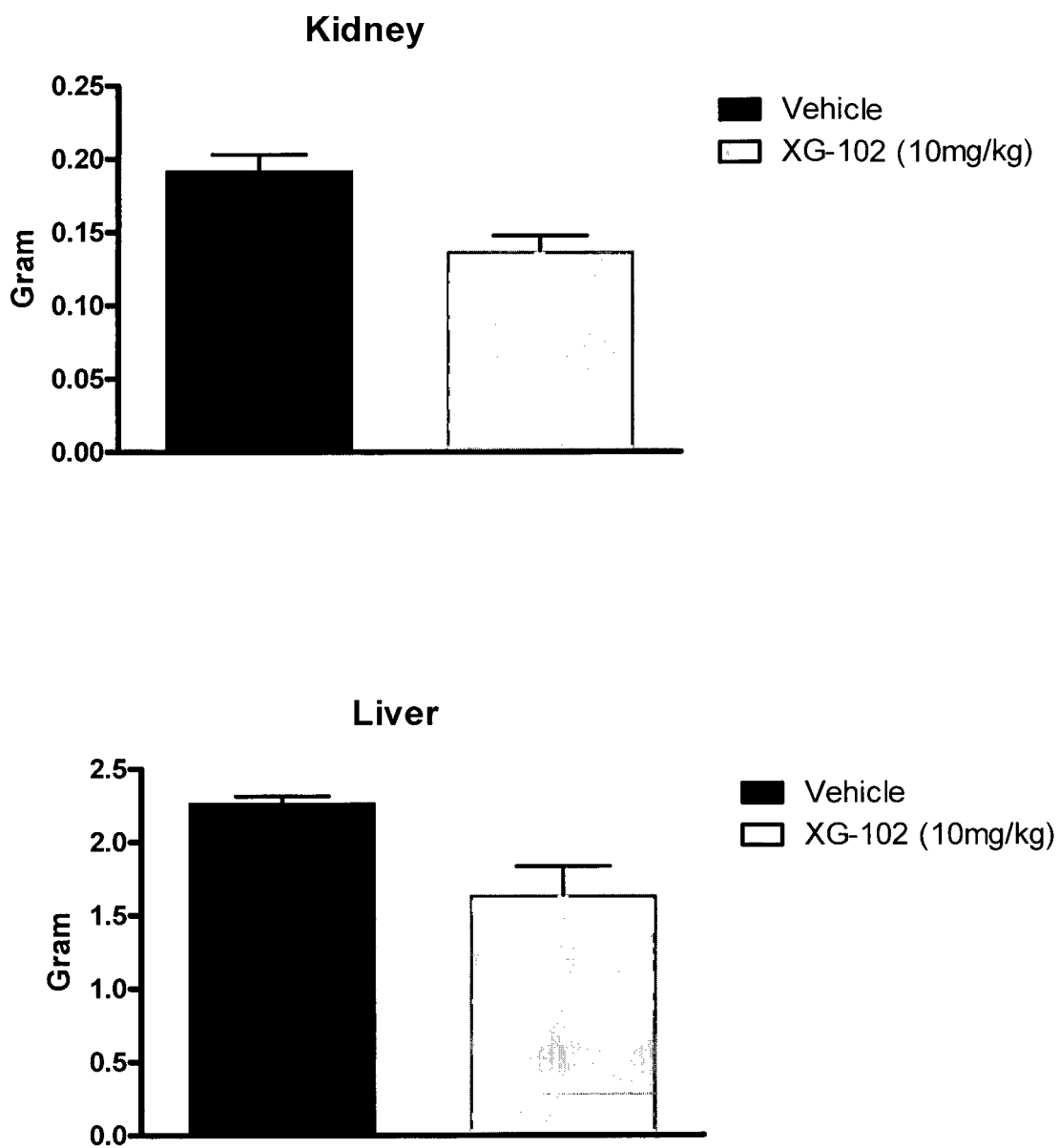
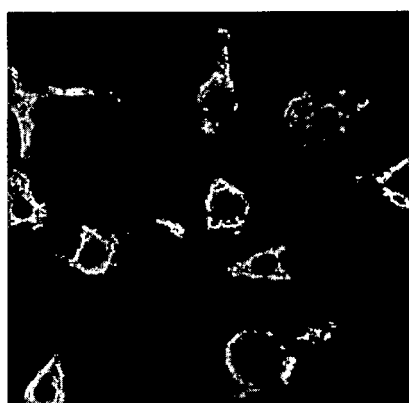


Fig. 23

Macrophage



DMEM Control



XG-102

Fig. 24

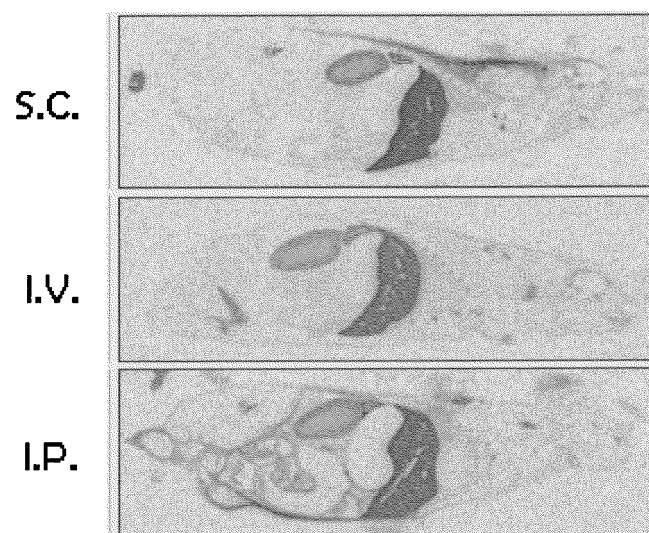
^{14}C -XG-102

Fig. 25

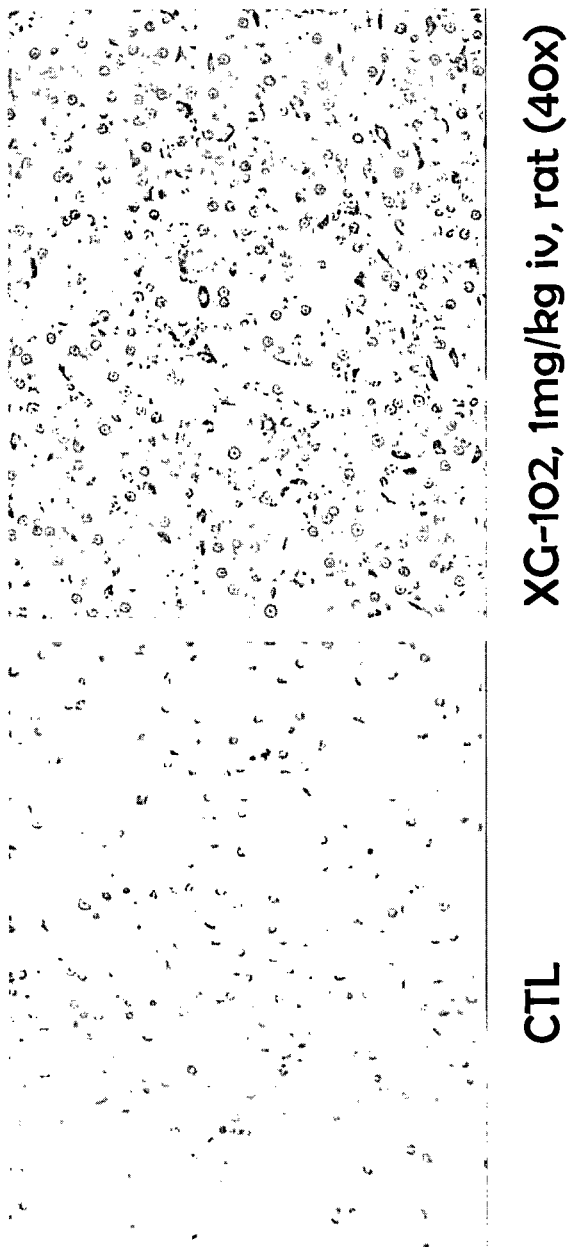


Fig. 26

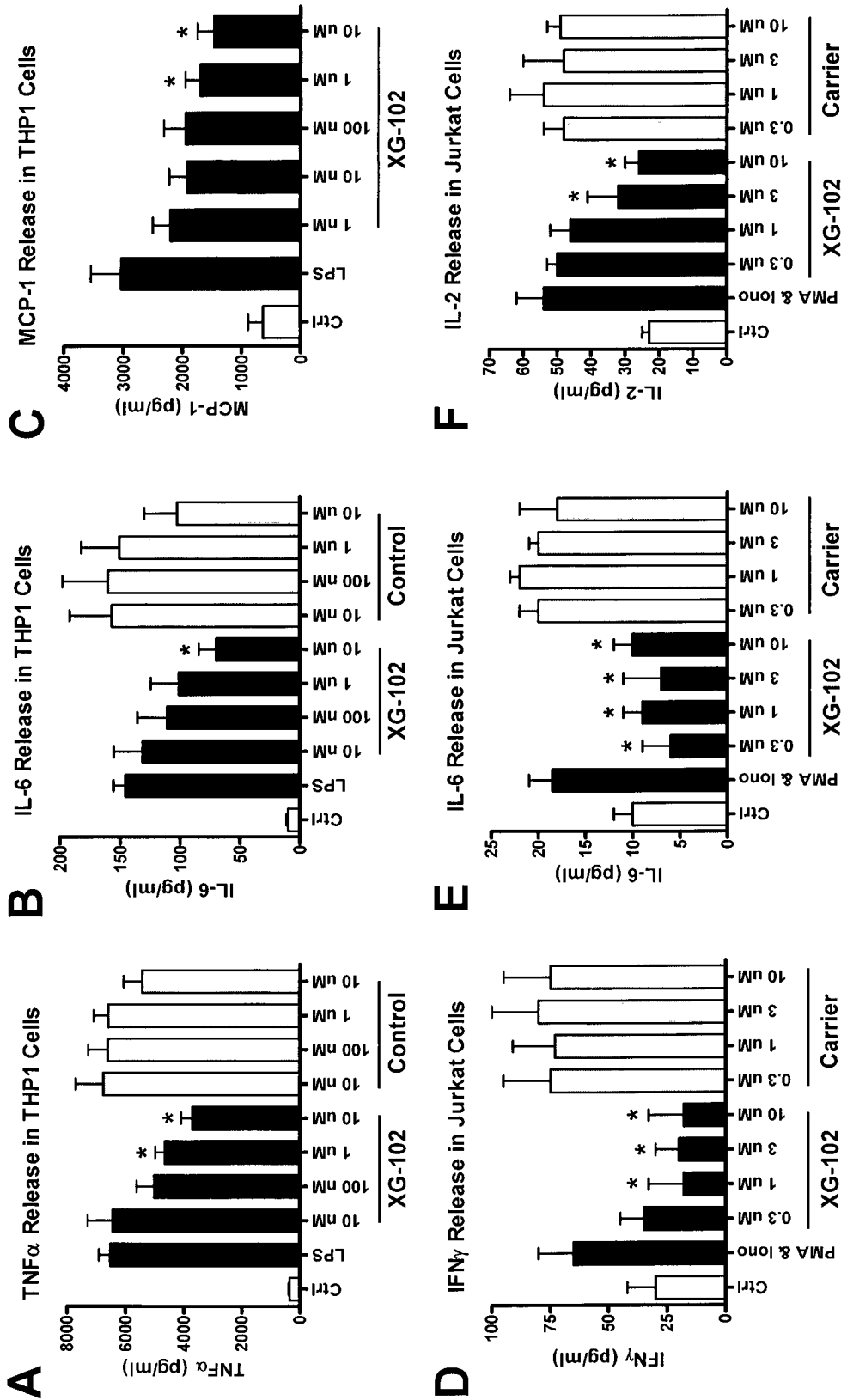


Fig. 27

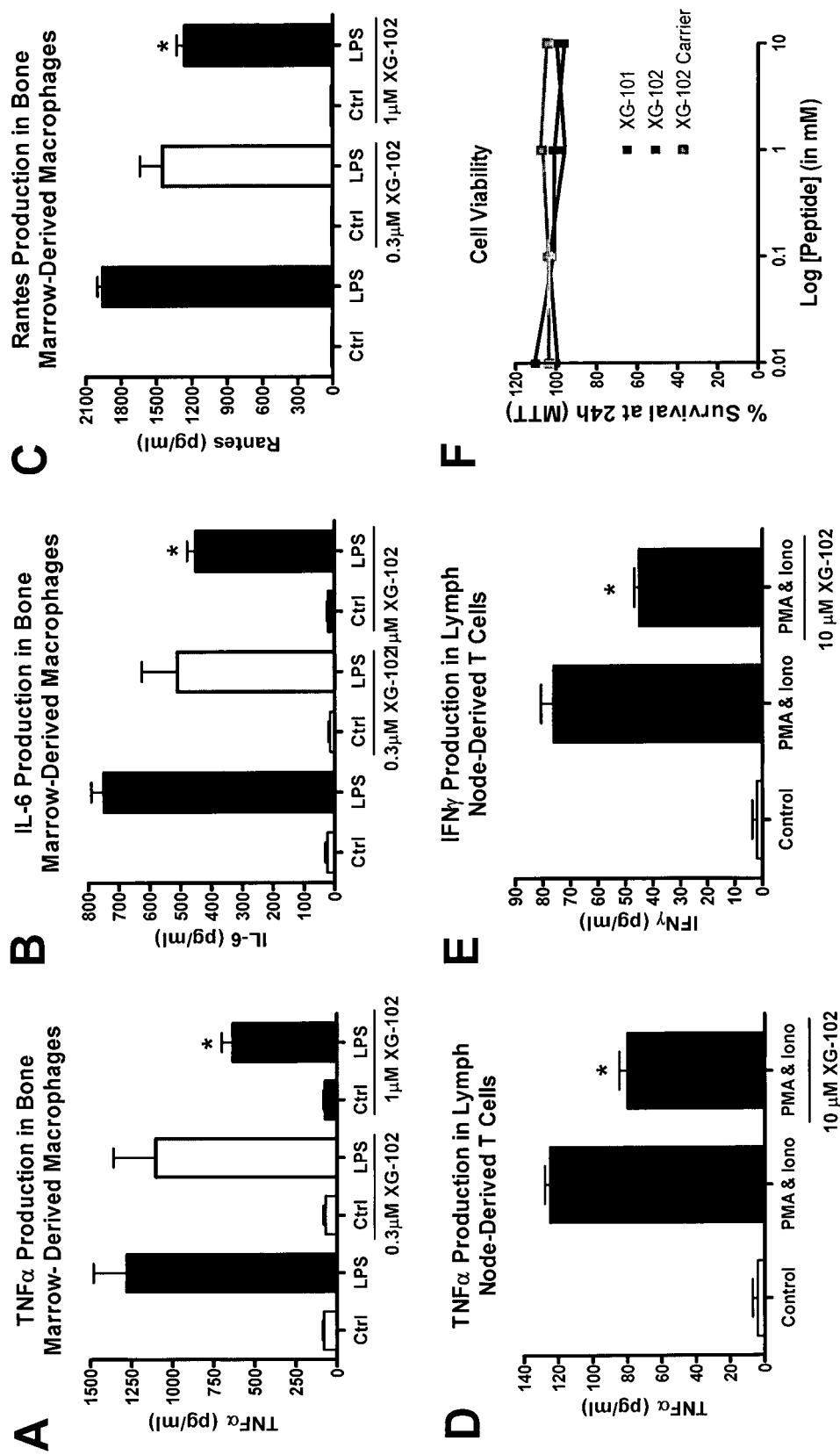


Fig. 28

ccgccccagc tcagtccgaa ccccgcgggc gcggcgggct cctccacacg cctccacctc	60
cgccgcccgc gccgcccgcg ccgcctcccc cgccgctctc cgcccggatg gccaggctga	120
gccccgggaat ggcgagcgca gagagcgggc tgagcggggg tgccgcgtcc ccaccggccg	180
cttccccatt cctgggactg cacatcgctg cgctcccaa ttccaggctc acccatgata	240
tcagcctgga ggagtttgag gatgaagacc ttccggagat cactgatgag tgtggcatca	300
gcctgcagtg caaagacacc ttgtctctcc gggccccgcg cgccgggcta ctgtctgcgg	360
gtagcagcgg tagcgcgggg agccggctgc agcgggagat gctgcagatg gacctgatcg	420
acgcggcaag tgacactccg ggcgcccagg acgacgaaga ggacgacgac gagctcgtg	480
cccaacggcc aggagtgggg ccttccaaag ccgagtctgg ccaggagccg gcgtctcgca	540
gccaggggtca gggccagggc cccggcacag gctgcggaga cacctaccgg cccaagaggc	600
ctaccacgct caaccttttc ccgcaggtgc cgcggtctca ggacacgctg aataataact	660
ctttaggcaa aaagcacagt tggcaggacc gtgtgtctcg atcatcctcc cctctgaaga	720
caggggagca gacgcctcca catgaacata tctgcctgag tgatgagctg ccgccccagg	780
gcagtcctgt tcccaccag gatcgtggca cttccaccga cagcccttgt cgccgtactg	840
cagccacca gatggcacct ccaagtggtc cccctgccac tgcacctggt ggccggggcc	900
actcccatcg agatcgggtc atatcagcag atgtgcggct cgaggcgact gaggagatct	960
acctgacccc agtgagagg cccccagacc ctgcagaacc cacctccacc ttcttgccac	1020
ccactgagag ccggatgtct gtcagctcgg atcctgacct tgccgcttac tctgtaactg	1080
cagggcgacc gcacccttcc atcagtgaag aggatgaggg cttcgactgt ctgtcatccc	1140
cagagcaagc tgagccacca ggtggagggg ggcggggaag cctcggggag ccaccaccgc	1200
ctccacgggc ctactgagc tcggacacca gcgcactgtc ctacgactct gtcaagtaca	1260
cactggtggt ggatgagcat gccagcttg agttggtgag cctgcggcca tgttttggag	1320
attacagtga cgaaagcgac tctgccactg tctatgacaa ctgtgcctct gcctcctcgc	1380
cctacgagtc agccattggt gaggaatatg aggaggcccc tcaaccccg cctccacct	1440
gcctgtcaga ggactccaca ccgatgagc ctgacgtcca cttctctaag aagtttctga	1500
atgtcttcat gaggggccgc tctcgttcct ccagtgccga gtcctttggg ctgttctcct	1560
gtgtcatcaa tggggaggag catgagcaaa cccatcgggc tatattcagg ttgtgcctc	1620
ggcatgaaga tgaacttgag ctggaagtgg acgacctct gctggtggag ctgcaggcag	1680

Fig. 29

aagactattg gtatgaggcc tataacatgc gcactggagc ccgtgggtgtc tttcctgcct	1740
actatgccat tgaggtcacc aaggagcctg agcacatggc agcccttgcc aaaaacagcg	1800
actggattga ccagttccgg gtgaagttcc tgggctctgt ccagggttcct tatcacaagg	1860
gcaatgatgt cctctgtgct gctatgcaaa agatcgccac caccgcccgg ctcaccgtgc	1920
actttaaccc gccctccagc tgtgtccttg aaatcagcgt taggggtgtc aagatagggtg	1980
tcaaagctga tgaagctcag gaggccaagg gaaataaatg tagccacttt ttccagctaa	2040
aaaacatctc tttctgtggg taccatccaa agaacaacaa gtactttggg tttatcacta	2100
agcaccctgc tgaccaccgg tttgcctgcc atgtctttgt gtctgaagat tccaccaaag	2160
ccctggcaga gtctgtgggg cgtgcatttc agcagttcta caagcaattt gtggaatata	2220
cctgtcctac agaagatata tacttggagt agcagcaacc cccctctctg cagcccccta	2280
gccccaggcc agtactagga cagctgactg ctgacaggat gttgtactgc cacgagagaa	2340
tgggggagtg agggctgttg gggctcgggg gcaggggttt ggggagaggc agatgcagtt	2400
tattgtaata tatggggtta gattaatcta tggaggacag tacaggctct ctcggggctg	2460
gggaagggca gggctggggg ggggggtcagg catctggcca caaaggggtc ccctagggac	2520
agaggcgctg caccatcctg ggcttgtttc atactagagg ccctggcttt ctggctcttg	2580
ggtcctgcct tgacaaagcc cagccacctg gaagtgtcac ctcccttgt ccacctcacc	2640
cagtgccctg agctcatgct gagcccaagc acctccgaag gactttccag taaggaaatg	2700
gcaacatgtg acagtgagac cctgttctca tctgtggggc tccggcagct ccgaccccca	2760
gcctggccag cacgtgacc ctggcaagct tgtgtgttca aagaaggaga gggccacagc	2820
aagccctgcc tgccaggga ggttccctct cagctggccc cagccaactg gtcactgtct	2880
tgtcacctgg ctactactat taaagtgcc tttcttgtct gaaaaaaaaa aaaaaaaaaa	2940
aaaaaaactc gag	2953

Fig. 29 (cont.)

Met Ala Arg Leu Ser Pro Gly Met Ala Glu Arg Glu Ser Gly Leu Ser
 1 5 10 15
 Gly Gly Ala Ala Ser Pro Pro Ala Ala Ser Pro Phe Leu Gly Leu His
 20 25 30
 Ile Ala Ser Pro Pro Asn Phe Arg Leu Thr His Asp Ile Ser Leu Glu
 35 40 45
 Glu Phe Glu Asp Glu Asp Leu Ser Glu Ile Thr Asp Glu Cys Gly Ile
 50 55 60
 Ser Leu Gln Cys Lys Asp Thr Leu Ser Leu Arg Pro Pro Arg Ala Gly
 65 70 75 80
 Leu Leu Ser Ala Gly Ser Ser Gly Ser Ala Gly Ser Arg Leu Gln Ala
 85 90 95
 Glu Met Leu Gln Met Asp Leu Ile Asp Ala Ala Ser Asp Thr Pro Gly
 100 105 110
 Ala Glu Asp Asp Glu Glu Asp Asp Asp Glu Leu Ala Ala Gln Arg Pro
 115 120 125
 Gly Val Gly Pro Ser Lys Ala Glu Ser Gly Gln Glu Pro Ala Ser Arg
 130 135 140
 Ser Gln Gly Gln Gly Gln Gly Pro Gly Thr Gly Cys Gly Asp Thr Tyr
 145 150 155 160
 Arg Pro Lys Arg Pro Thr Thr Leu Asn Leu Phe Pro Gln Val Pro Arg
 165 170 175
 Ser Gln Asp Thr Leu Asn Asn Asn Ser Leu Gly Lys Lys His Ser Trp
 180 185 190
 Gln Asp Arg Val Ser Arg Ser Ser Ser Pro Leu Lys Thr Gly Glu Gln
 195 200 205
 Thr Pro Pro His Glu His Ile Cys Leu Ser Asp Glu Leu Pro Pro Gln
 210 215 220
 Gly Ser Pro Val Pro Thr Gln Asp Arg Gly Thr Ser Thr Asp Ser Pro
 225 230 235 240
 Cys Arg Arg Thr Ala Ala Thr Gln Met Ala Pro Pro Ser Gly Pro Pro
 245 250 255

Fig. 30

Ala Thr Ala Pro Gly Gly Arg Gly His Ser His Arg Asp Arg Ser Ile
 260 265 270
 Ser Ala Asp Val Arg Leu Glu Ala Thr Glu Glu Ile Tyr Leu Thr Pro
 275 280 285
 Val Gln Arg Pro Pro Asp Pro Ala Glu Pro Thr Ser Thr Phe Leu Pro
 290 295 300
 Pro Thr Glu Ser Arg Met Ser Val Ser Ser Asp Pro Asp Pro Ala Ala
 305 310 315 320
 Tyr Ser Val Thr Ala Gly Arg Pro His Pro Ser Ile Ser Glu Glu Asp
 325 330 335
 Glu Gly Phe Asp Cys Leu Ser Ser Pro Glu Gln Ala Glu Pro Pro Gly
 340 345 350
 Gly Gly Trp Arg Gly Ser Leu Gly Glu Pro Pro Pro Pro Pro Arg Ala
 355 360 365
 Ser Leu Ser Ser Asp Thr Ser Ala Leu Ser Tyr Asp Ser Val Lys Tyr
 370 375 380
 Thr Leu Val Val Asp Glu His Ala Gln Leu Glu Leu Val Ser Leu Arg
 385 390 395 400
 Pro Cys Phe Gly Asp Tyr Ser Asp Glu Ser Asp Ser Ala Thr Val Tyr
 405 410 415
 Asp Asn Cys Ala Ser Ala Ser Ser Pro Tyr Glu Ser Ala Ile Gly Glu
 420 425 430
 Glu Tyr Glu Glu Ala Pro Gln Pro Arg Pro Pro Thr Cys Leu Ser Glu
 435 440 445
 Asp Ser Thr Pro Asp Glu Pro Asp Val His Phe Ser Lys Lys Phe Leu
 450 455 460
 Asn Val Phe Met Ser Gly Arg Ser Arg Ser Ser Ser Ala Glu Ser Phe
 465 470 475 480
 Gly Leu Phe Ser Cys Val Ile Asn Gly Glu Glu His Glu Gln Thr His
 485 490 495
 Arg Ala Ile Phe Arg Phe Val Pro Arg His Glu Asp Glu Leu Glu Leu
 500 505 510

Fig. 30 (cont.)

Glu Val Asp Asp Pro Leu Leu Val Glu Leu Gln Ala Glu Asp Tyr Trp
 515 520 525

Tyr Glu Ala Tyr Asn Met Arg Thr Gly Ala Arg Gly Val Phe Pro Ala
 530 535 540

Tyr Tyr Ala Ile Glu Val Thr Lys Glu Pro Glu His Met Ala Ala Leu
 545 550 555 560

Ala Lys Asn Ser Asp Trp Ile Asp Gln Phe Arg Val Lys Phe Leu Gly
 565 570 575

Ser Val Gln Val Pro Tyr His Lys Gly Asn Asp Val Leu Cys Ala Ala
 580 585 590

Met Gln Lys Ile Ala Thr Thr Arg Arg Leu Thr Val His Phe Asn Pro
 595 600 605

Pro Ser Ser Cys Val Leu Glu Ile Ser Val Arg Gly Val Lys Ile Gly
 610 615 620

Val Lys Ala Asp Glu Ala Gln Glu Ala Lys Gly Asn Lys Cys Ser His
 625 630 635 640

Phe Phe Gln Leu Lys Asn Ile Ser Phe Cys Gly Tyr His Pro Lys Asn
 645 650 655

Asn Lys Tyr Phe Gly Phe Ile Thr Lys His Pro Ala Asp His Arg Phe
 660 665 670

Ala Cys His Val Phe Val Ser Glu Asp Ser Thr Lys Ala Leu Ala Glu
 675 680 685

Ser Val Gly Arg Ala Phe Gln Gln Phe Tyr Lys Gln Phe Val Glu Tyr
 690 695 700

Thr Cys Pro Thr Glu Asp Ile Tyr Leu Glu
 705 710

Fig. 30 (cont.)

Met Ala Glu Arg Glu Ser Gly Gly Leu Gly Gly Gly Ala Ala Ser Pro
 1 5 10 15
 Pro Ala Ala Ser Pro Phe Leu Gly Leu His Ile Ala Ser Pro Pro Asn
 20 25 30
 Phe Arg Leu Thr His Asp Ile Ser Leu Glu Glu Phe Glu Asp Glu Asp
 35 40 45
 Leu Ser Glu Ile Thr Asp Glu Cys Gly Ile Ser Leu Gln Cys Lys Asp
 50 55 60
 Thr Leu Ser Leu Arg Pro Pro Arg Ala Gly Leu Leu Ser Ala Gly Gly
 65 70 75 80
 Gly Gly Ala Gly Ser Arg Leu Gln Ala Glu Met Leu Gln Met Asp Leu
 85 90 95
 Ile Asp Ala Thr Gly Asp Thr Pro Gly Ala Glu Asp Asp Glu Glu Asp
 100 105 110
 Asp Asp Glu Glu Arg Ala Ala Arg Arg Pro Gly Ala Gly Pro Pro Lys
 115 120 125
 Ala Glu Ser Gly Gln Glu Pro Ala Ser Arg Gly Gln Gly Gln Ser Gln
 130 135 140
 Gly Gln Ser Gln Gly Pro Gly Ser Gly Asp Thr Tyr Arg Pro Lys Arg
 145 150 155 160
 Pro Thr Thr Leu Asn Leu Phe Pro Gln Val Pro Arg Ser Gln Asp Thr
 165 170 175
 Leu Asn Asn Asn Ser Leu Gly Lys Lys His Ser Trp Gln Asp Arg Val
 180 185 190
 Ser Arg Ser Ser Ser Pro Leu Lys Thr Gly Glu Gln Thr Pro Pro His
 195 200 205
 Glu His Ile Cys Leu Ser Asp Glu Leu Pro Pro Gln Ser Gly Pro Ala
 210 215 220
 Pro Thr Thr Asp Arg Gly Thr Ser Thr Asp Ser Pro Cys Arg Arg Ser
 225 230 235 240
 Thr Ala Thr Gln Met Ala Pro Pro Gly Gly Pro Pro Ala Ala Pro Pro
 245 250 255

Fig. 31

Gly Gly Arg Gly His Ser His Arg Asp Arg Ile His Tyr Gln Ala Asp
 260 265 270
 Val Arg Leu Glu Ala Thr Glu Glu Ile Tyr Leu Thr Pro Val Gln Arg
 275 280 285
 Pro Pro Asp Ala Ala Glu Pro Thr Ser Ala Phe Leu Pro Pro Thr Glu
 290 295 300
 Ser Arg Met Ser Val Ser Ser Asp Pro Asp Pro Ala Ala Tyr Pro Ser
 305 310 315 320
 Thr Ala Gly Arg Pro His Pro Ser Ile Ser Glu Glu Glu Glu Gly Phe
 325 330 335
 Asp Cys Leu Ser Ser Pro Glu Arg Ala Glu Pro Pro Gly Gly Gly Trp
 340 345 350
 Arg Gly Ser Leu Gly Glu Pro Pro Pro Pro Pro Arg Ala Ser Leu Ser
 355 360 365
 Ser Asp Thr Ser Ala Leu Ser Tyr Asp Ser Val Lys Tyr Thr Leu Val
 370 375 380
 Val Asp Glu His Ala Gln Leu Glu Leu Val Ser Leu Arg Pro Cys Phe
 385 390 395 400
 Gly Asp Tyr Ser Asp Glu Ser Asp Ser Ala Thr Val Tyr Asp Asn Cys
 405 410 415
 Ala Ser Val Ser Ser Pro Tyr Glu Ser Ala Ile Gly Glu Glu Tyr Glu
 420 425 430
 Glu Ala Pro Arg Pro Gln Pro Pro Ala Cys Leu Ser Glu Asp Ser Thr
 435 440 445
 Pro Asp Glu Pro Asp Val His Phe Ser Lys Lys Phe Leu Asn Val Phe
 450 455 460
 Met Ser Gly Arg Ser Arg Ser Ser Ser Ala Glu Ser Phe Gly Leu Phe
 465 470 475 480
 Ser Cys Ile Ile Asn Gly Glu Glu Gln Glu Gln Thr His Arg Ala Ile
 485 490 495
 Phe Arg Phe Val Pro Arg His Glu Asp Glu Leu Glu Leu Glu Val Asp
 500 505 510

Fig. 31 (cont.)

Asp Pro Leu Leu Val Glu Leu Gln Ala Glu Asp Tyr Trp Tyr Glu Ala
 515 520 525
 Tyr Asn Met Arg Thr Gly Ala Arg Gly Val Phe Pro Ala Tyr Tyr Ala
 530 535 540
 Ile Glu Val Thr Lys Glu Pro Glu His Met Ala Ala Leu Ala Lys Asn
 545 550 555 560
 Ser Asp Trp Val Asp Gln Phe Arg Val Lys Phe Leu Gly Ser Val Gln
 565 570 575
 Val Pro Tyr His Lys Gly Asn Asp Val Leu Cys Ala Ala Met Gln Lys
 580 585 590
 Ile Ala Thr Thr Arg Arg Leu Thr Val His Phe Asn Pro Pro Ser Ser
 595 600 605
 Cys Val Leu Glu Ile Ser Val Arg Gly Val Lys Ile Gly Val Lys Ala
 610 615 620
 Asp Asp Ser Gln Glu Ala Lys Gly Asn Lys Cys Ser His Phe Phe Gln
 625 630 635 640
 Leu Lys Asn Ile Ser Phe Cys Gly Tyr His Pro Lys Asn Asn Lys Tyr
 645 650 655
 Phe Gly Phe Ile Thr Lys His Pro Ala Asp His Arg Phe Ala Cys His
 660 665 670
 Val Phe Val Ser Glu Asp Ser Thr Lys Ala Leu Ala Glu Ser Val Gly
 675 680 685
 Arg Ala Phe Gln Gln Phe Tyr Lys Gln Phe Val Glu Tyr Thr Cys Pro
 690 695 700
 Thr Glu Asp Ile Tyr Leu Glu
 705 710

Fig. 31 (cont.)

atggcggagc gagaaagcgg cggcctggga gggggggccg cgtccccgcc cgccgcctcc	60
ccgttctctgg ggctgcacat cgcttcgcct cccaatttca ggctcaccca tgacatcagc	120
ctggaggagt ttgaggatga agacctctcg gagatcactg atgagtgtgg catcagctta	180
cagtgcaaag acaccctgtc cttacggccc ccgcgcgccg ggctgctctc tgcgggcggc	240
ggcggcgccg ggagccggtt gcaggccgag atgctgcaga tggacctgat cgacgcgacg	300
ggggacactc ccggggccga ggacgacgag gaggacgacg acgaggagcg cgcgccccgg	360
cggccgggag cggggccgcc caaggccgag tccggccagg agccggcgctc ccgcggccag	420
ggccagagcc aaggccagag ccaggggccg ggcagcgggg acacgtaccg gcccagcgg	480
cccaccacgc tcaacctctt tccgcagggtg ccgcgggtctc aggacacact gaataataat	540
tctctgggca aaaagcacag ttggcaggat cgggtgtctc gatcatcctc acccctgaag	600
acaggggagc agacaccacc gcatgaacac atctgcctga gcgatgagct gccccccag	660
agcggccccc cccccaccac agatcgaggc acctccaccg acagcccttg ccgccgcagc	720
acagccaccc agatggcacc tccgggtggt ccccctgctg ccccgcttg gggtcggggc	780
cactcgcacg gagaccgaat ccactaccag gccgatgtgc gactagaggc cactgaggag	840
atctacctga cccagtgca gaggccccca gacgtgcag agcccacctc cgccttctg	900
ccgcccactg agagccggat gtcagtcagc tccgatccag accctgccgc ctaccctcc	960
acggcagggc ggccgcaccc ctccatcagt gaagaggaag agggcttcga ctgcctgtcg	1020
tccccagagc gggctgagcc cccaggcgga gggtaggggg ggagcctggg ggagccgccg	1080
ccacctccac gggcctctct gagctcggac accagcgccc tgcctatga ctctgtcaag	1140
tacacgttg tggtagatga gcatgcacag ctggagctgg tgagcctgcg gccgtgcttc	1200
ggagactaca gtgacgagag tgactctgcc accgtctatg acaactgtgc ctccgtctcc	1260
tcgccctatg agtcggccat cggagaggaa tatgaggagg ccccgcggcc ccagccccct	1320
gcctgcctct ccgaggactc cacgcctgat gaacccgacg tccatttctc caagaaattc	1380
ctgaacgtct tcatgagtgg ccgctcccgc tcctccagtg ctgagtcctt cgggctgttc	1440
tcctgcatca tcaacgggga ggagcaggag cagaccaccc gggccatatt caggtttgtg	1500
cctcgacacg aagacgaact tgagctggaa gtggatgacc ctctgctagt ggagctccag	1560
gctgaagact actggtacga ggcctacaac atgcgcaact gtgccccggg tgtctttcct	1620
gcctattacg ccatcgaggt caccaaggag cccgagcaca tggcagccct ggccaaaaac	1680
agtgactggg tggaccagtt ccgggtgaag ttcttgggct cagtccaggt tccctatcac	1740

Fig. 32

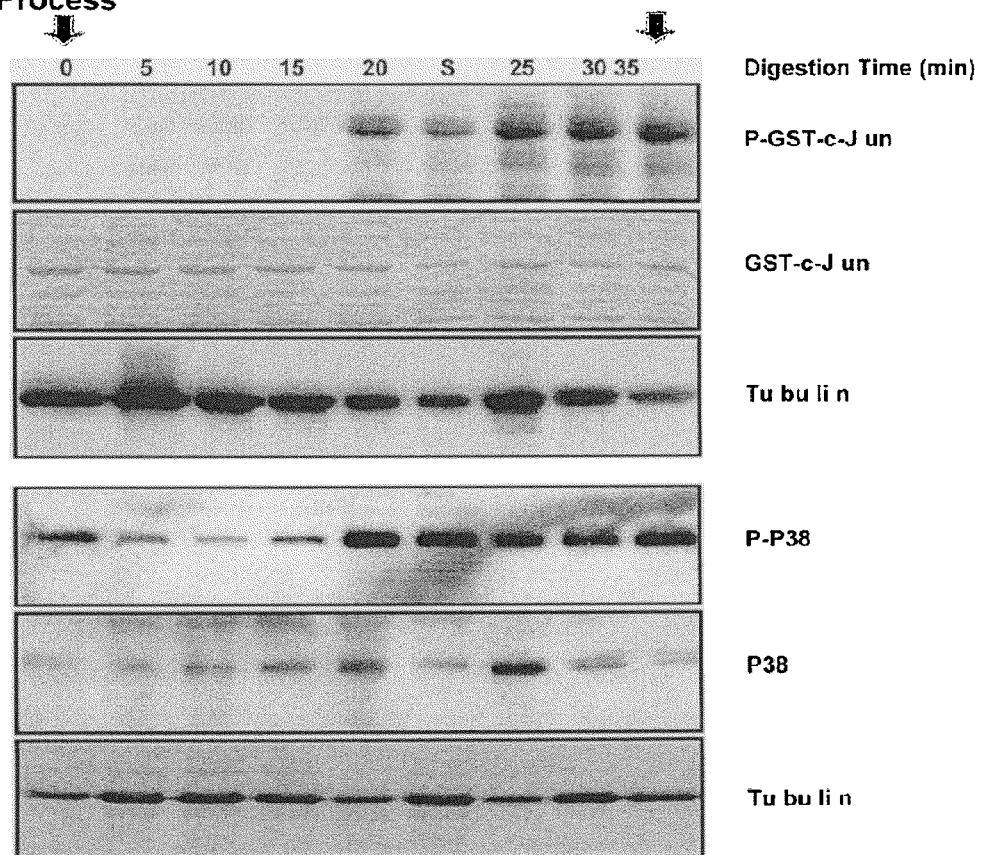
aagggcaatg acgtcctctg tgctgctatg caaaagattg ccaccacccg ccggctcacc	1800
gtgcacttta acccgccctc cagctgtgtc ctggagatca gcgtgcgggg tgtgaagata	1860
ggcgtcaagg ccgatgactc ccaggaggcc aaggggaata aatgtagcca ctttttccag	1920
ttaaaaaaca tctctttctg cggatatcat ccaaagaaca acaagtactt tgggttcac	1980
accaagcacc ccgccgacca ccggtttgcc tgccacgtct ttgtgtctga agactccacc	2040
aaagccctgg cagagtccgt ggggagagca ttccagcagt tctacaagca gtttgtggag	2100
tacacctgcc ccacagaaga tatctacctg gagtag	2136

Fig. 32 (cont.)

Effect of Islet Isolation (Pancreas enzymatic digestion) on JNK/P38 activation

Beginning of Isolation Process

End of Isolation



**Effect of XG-102 (DJNK inhibitor) on c-fos gene expression
(Measured by Realtime RTPCr)**

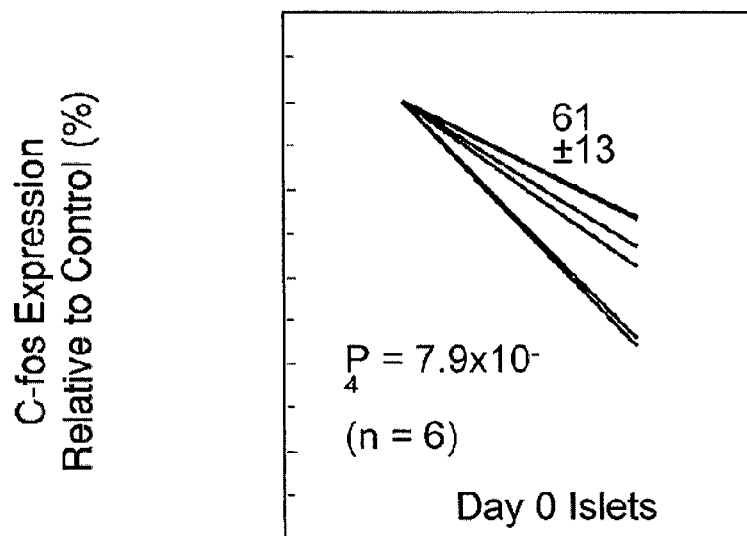


Fig. 35

Effect of XI-102 (DJNK inhibitor) on OCR/DNA

Day 0 Islets

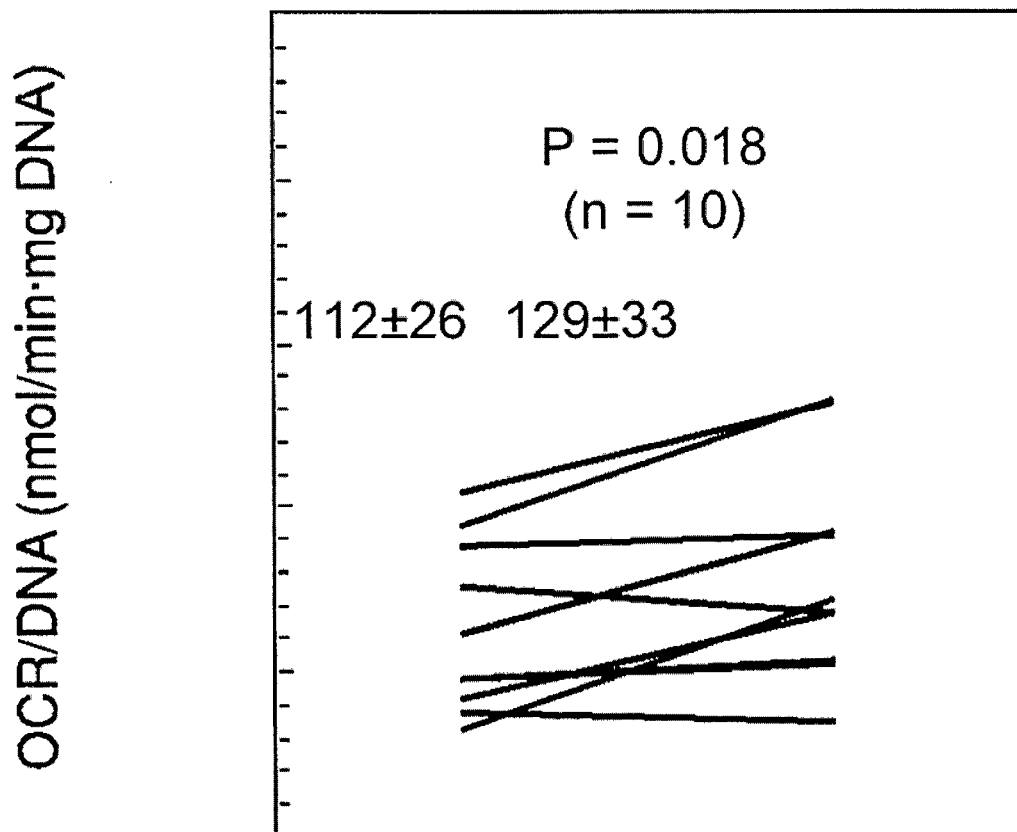


Fig. 36

Effect of XI-102 (DJNK inhibitor) on ATP/Protein

Day 0 Islets

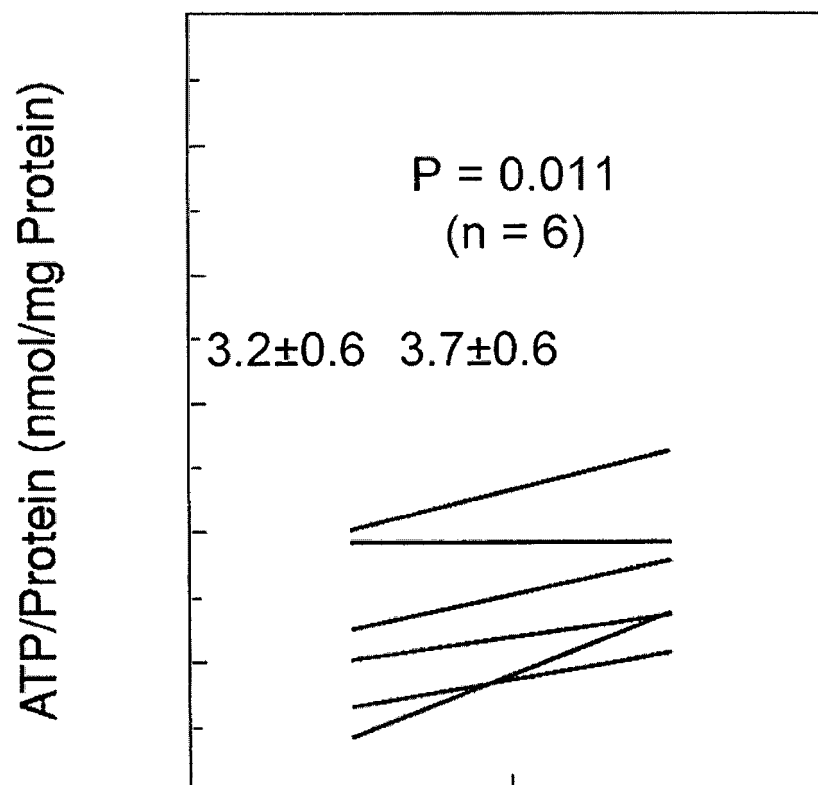
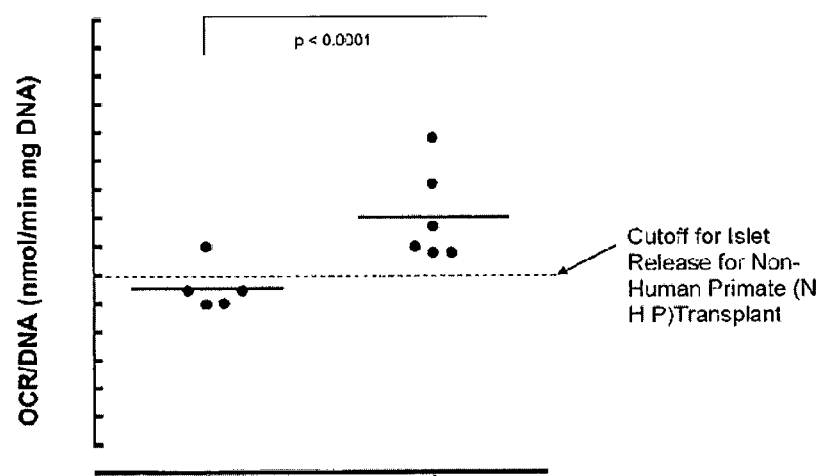


Fig. 37

XG-1 02 increases islet viability (OCR/DNA)
measured after 7 days of culture

75



**Each point represents a different isolation

***Without DJNK 1 of 5 (20%) consecutive isolations met the release criteria. With DJNKi 6/6 (100%) consecutive isolations met the release criteria and were successfully transplanted into an NHP

Fig. 38

Figure 1: Fluorescein angiography evaluation (mean score) (10 minutes after fluorescein injection)

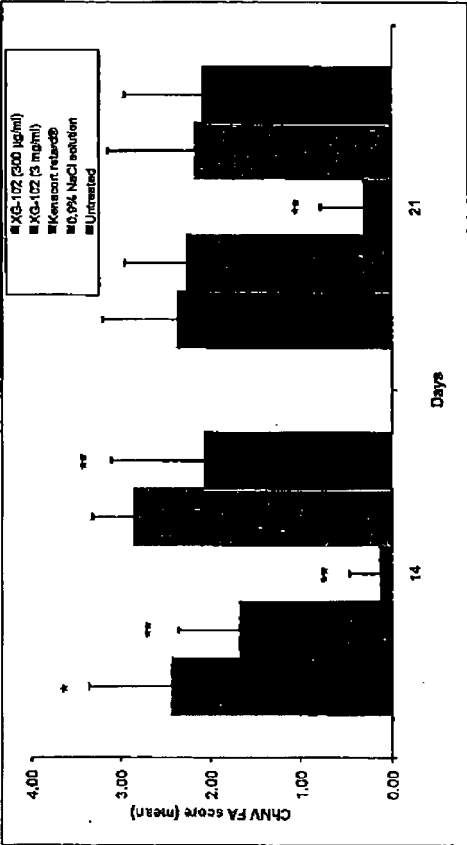


Figure 2: Proportion of fluorescein angiography score (10 minutes after fluorescein injection)

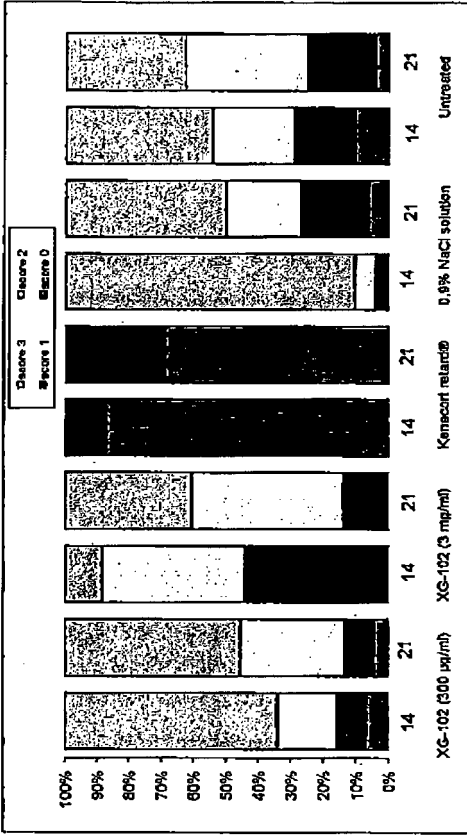


Figure 3: Incidence of CHNV formation (score > 0) (10 minutes after fluorescein injection)

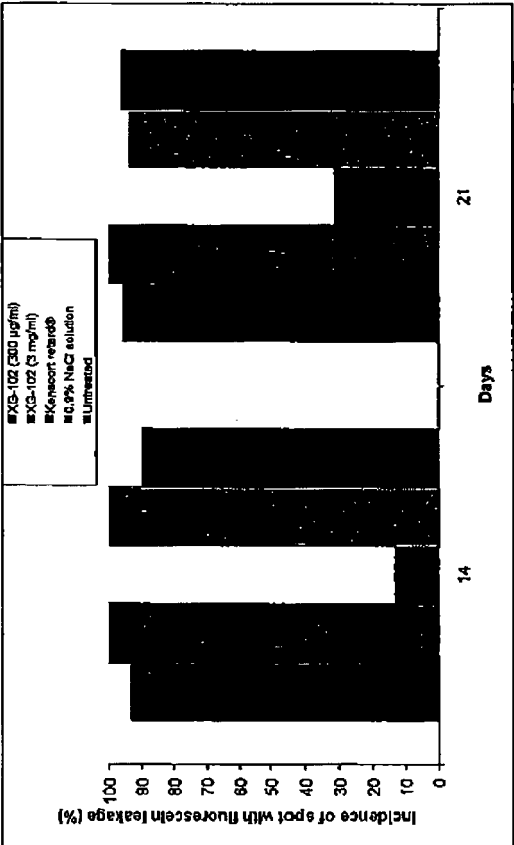
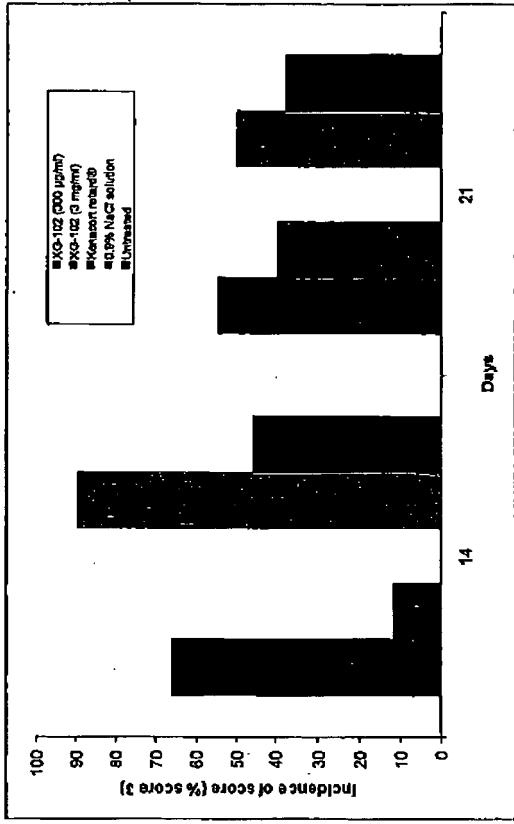


Figure 4: Incidence of fluorescein leakage extend (score 3) (10 minutes after fluorescein injection)



* p<0.05 compared to 0.9% NaCl solution group
** p<0.01 compared to 0.9% NaCl solution group

Fig. 39

Group N°	ADR (Day 0)	Treatment (Day 0)	Dose, volume / Route of administration	Dose concentration	Number of animals
1	0 mg/kg	NaCl 0.9%	0.2 mL, IV	0	10
2	10 mg/kg	XG-102 20 mg/kg	0.2 mL, IV	0.01 mg/mL	10
3	10 mg/kg	XG-102 200 mg/kg	0.2 mL, IV	0.1 mg/mL	10
4	0	NaCl 0.9%	0.2 mL, IV	0	10

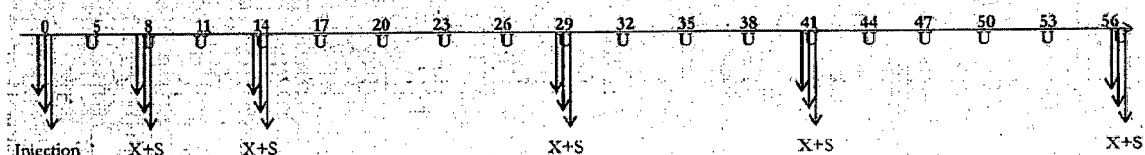


Fig. 40

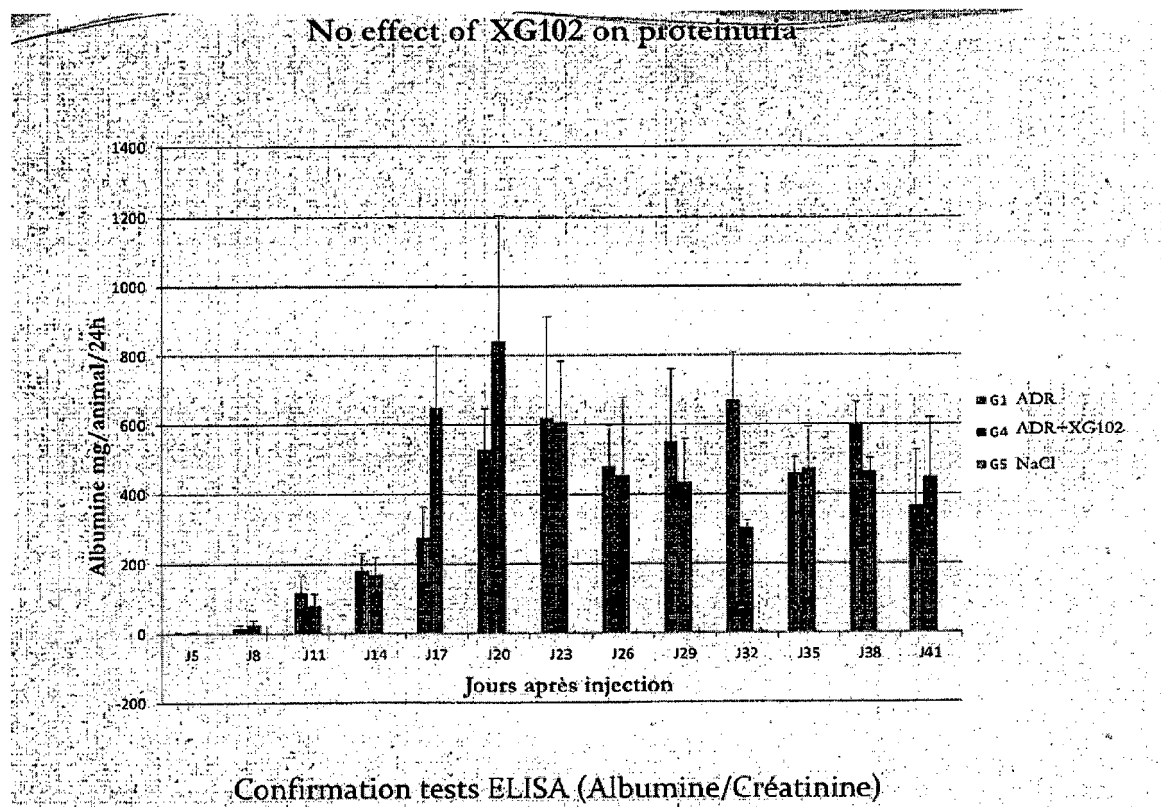


Fig. 41

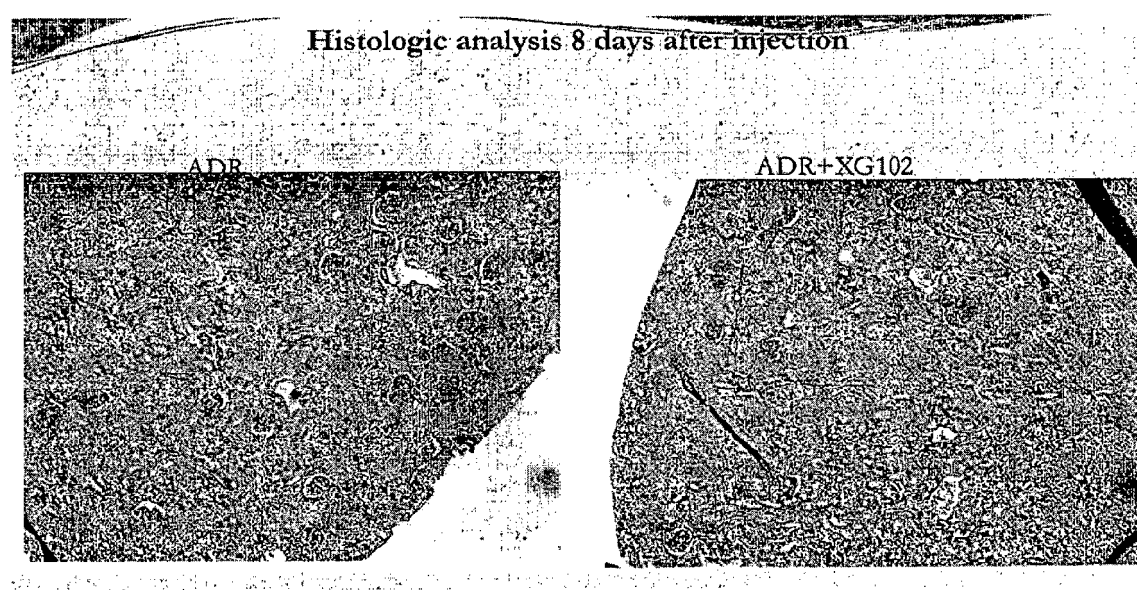


Fig. 42

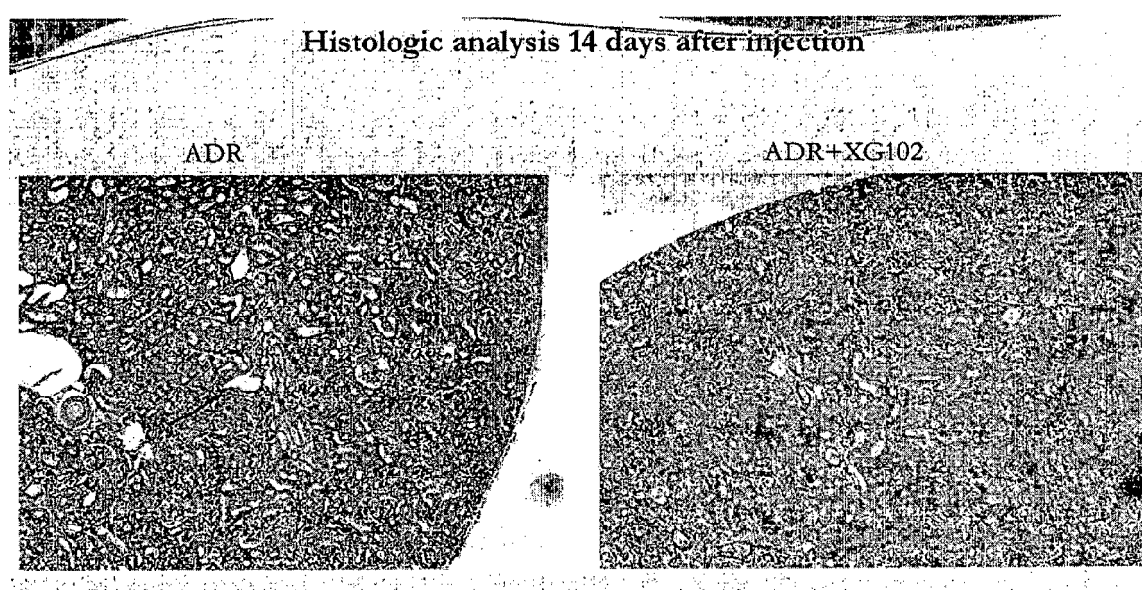


Fig. 43

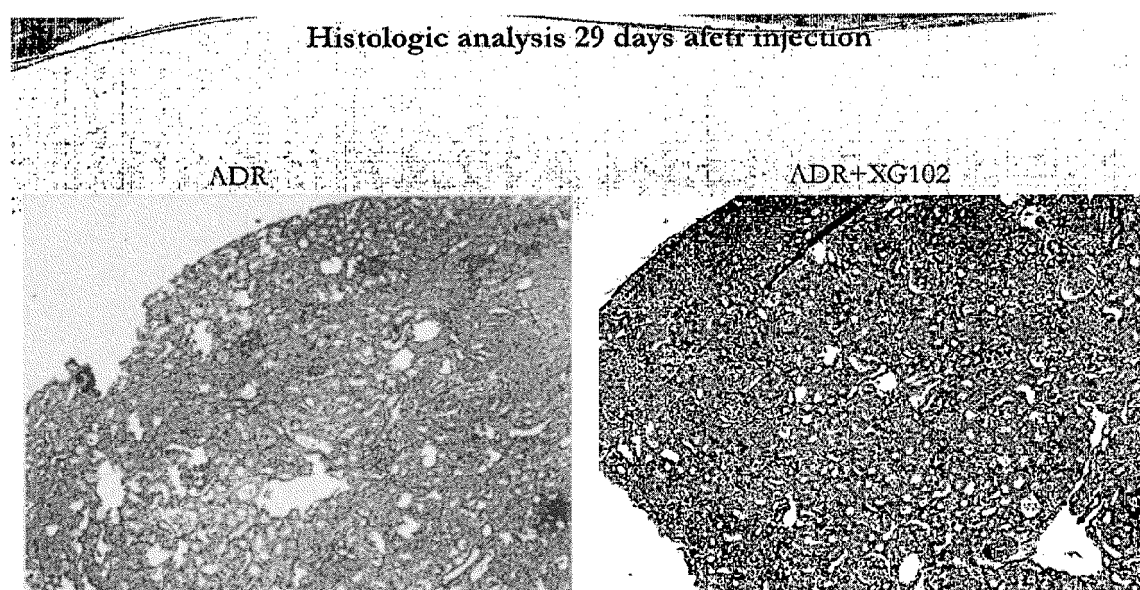


Fig. 44

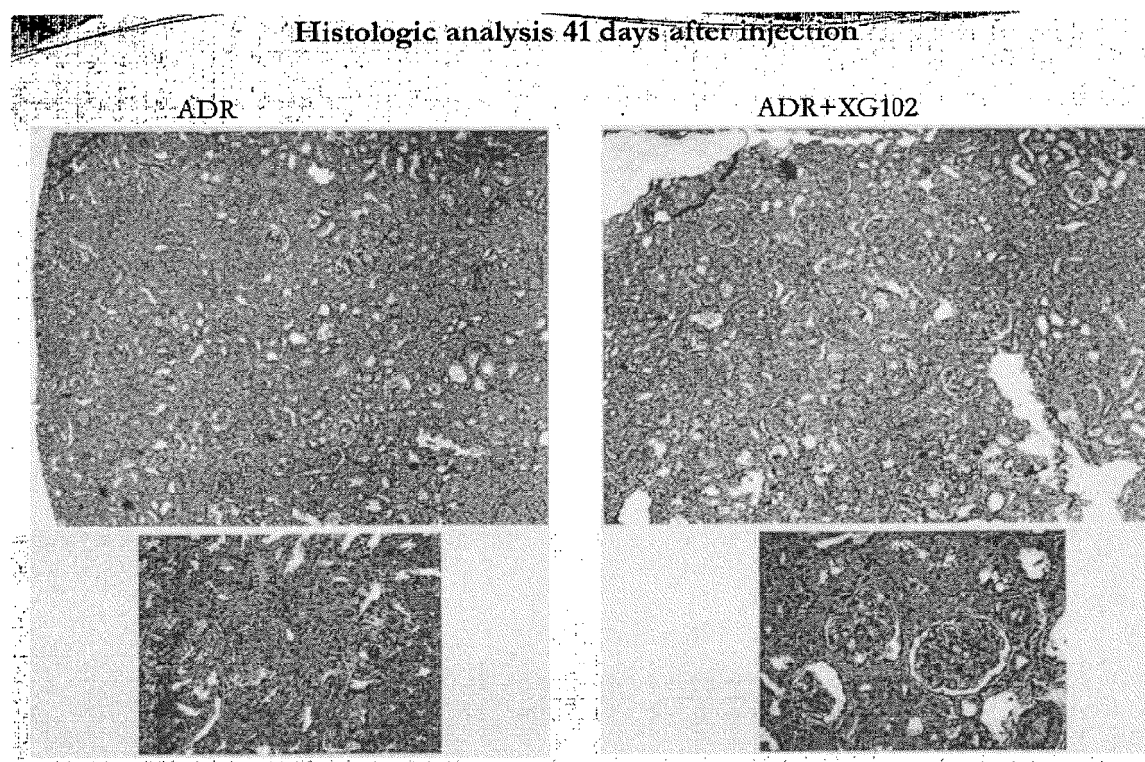


Fig. 45

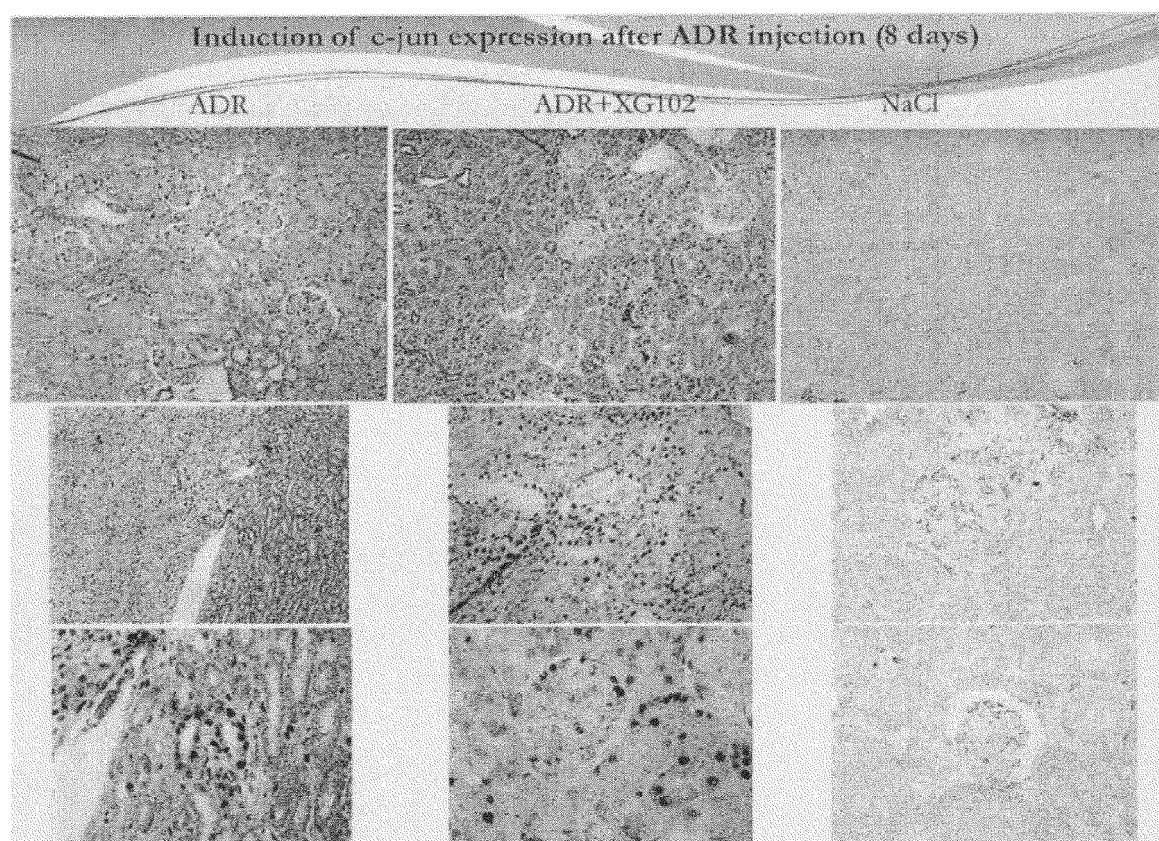


Fig. 46

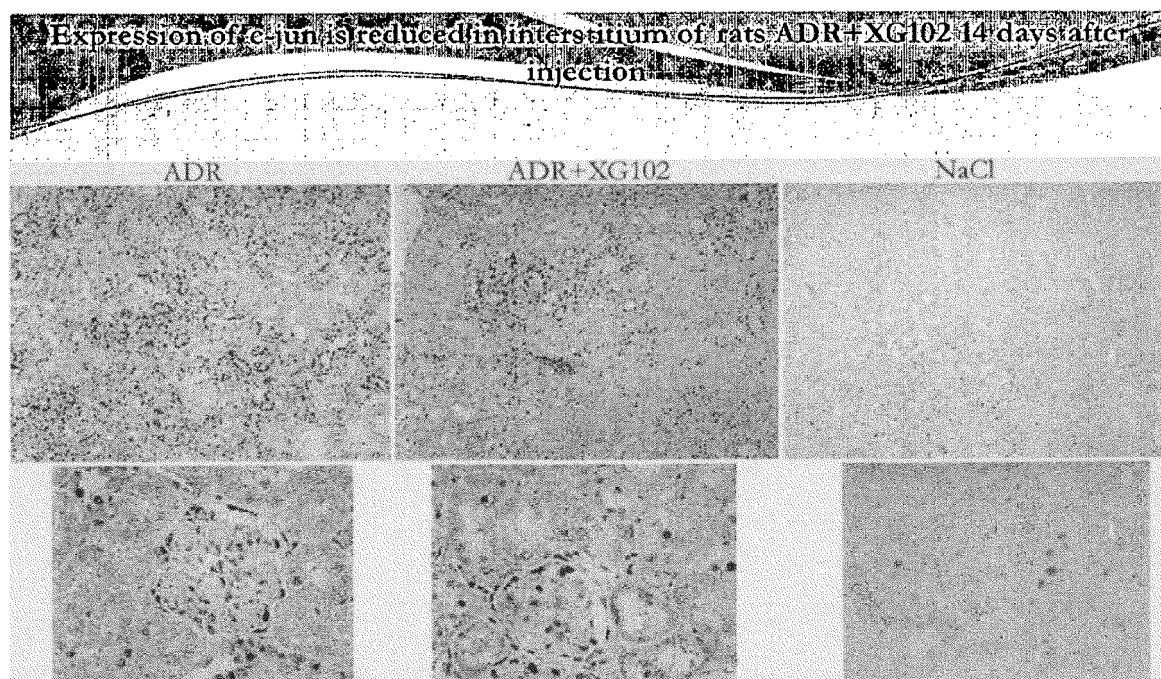
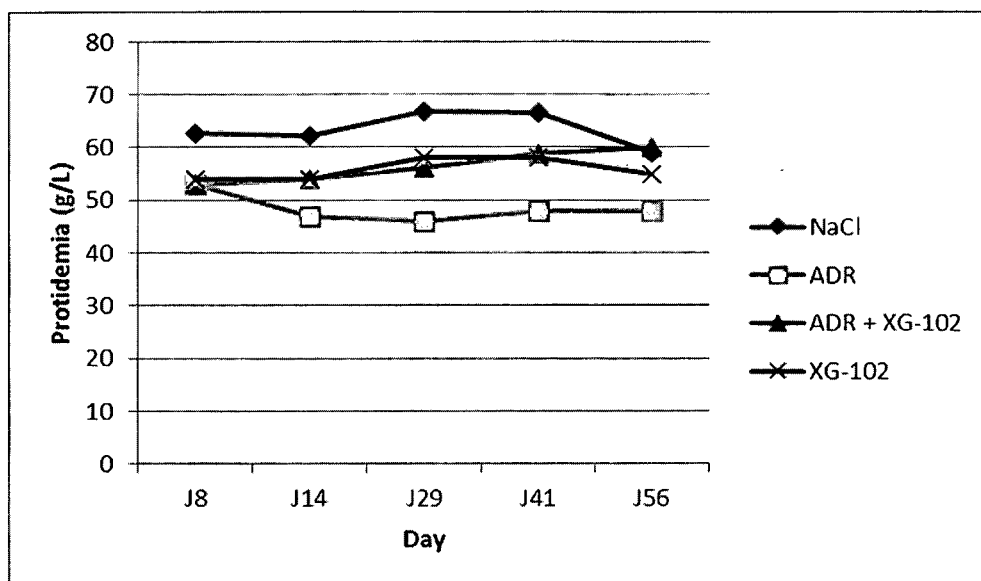
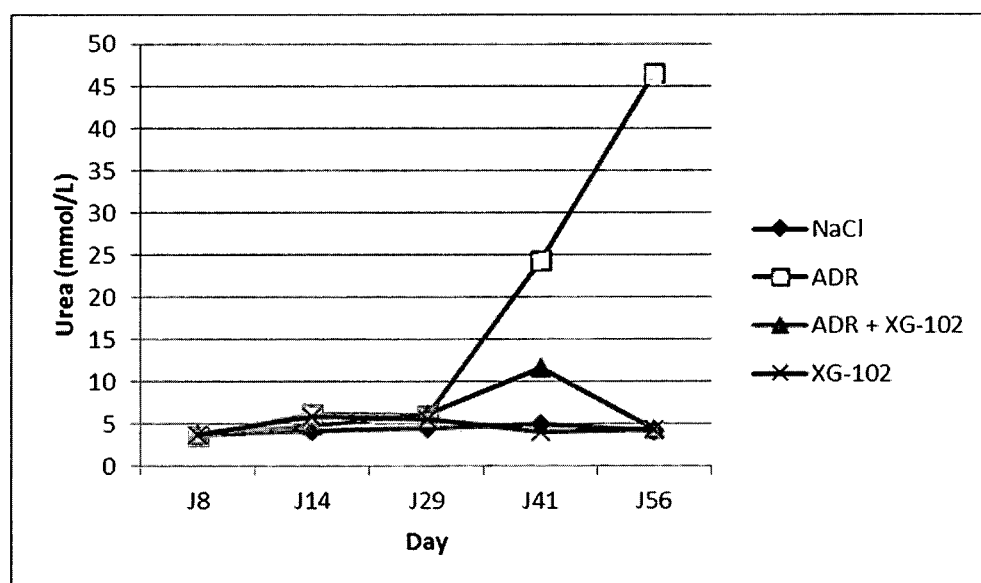


Fig. 47



A



B

Fig. 48

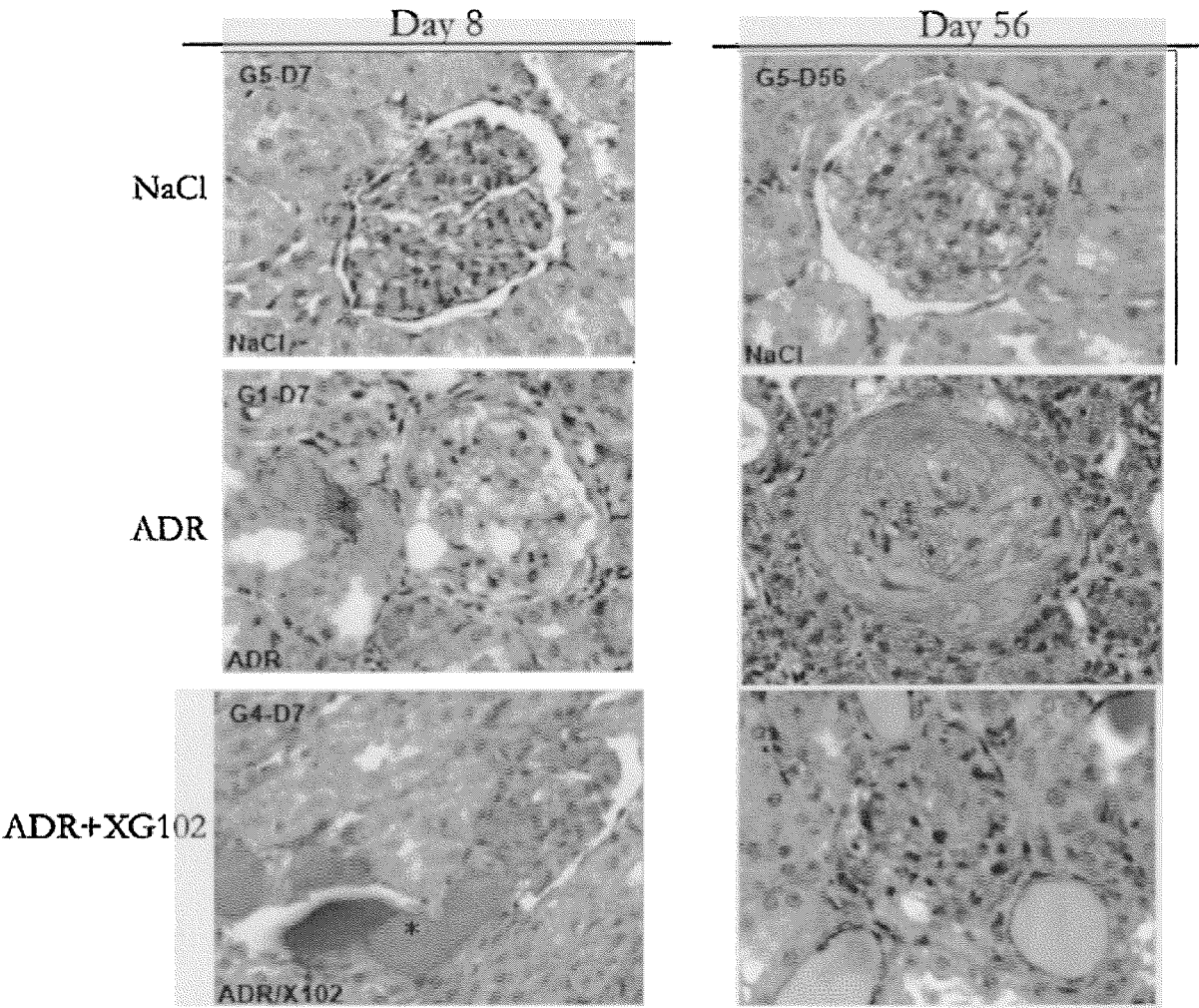


Fig. 49

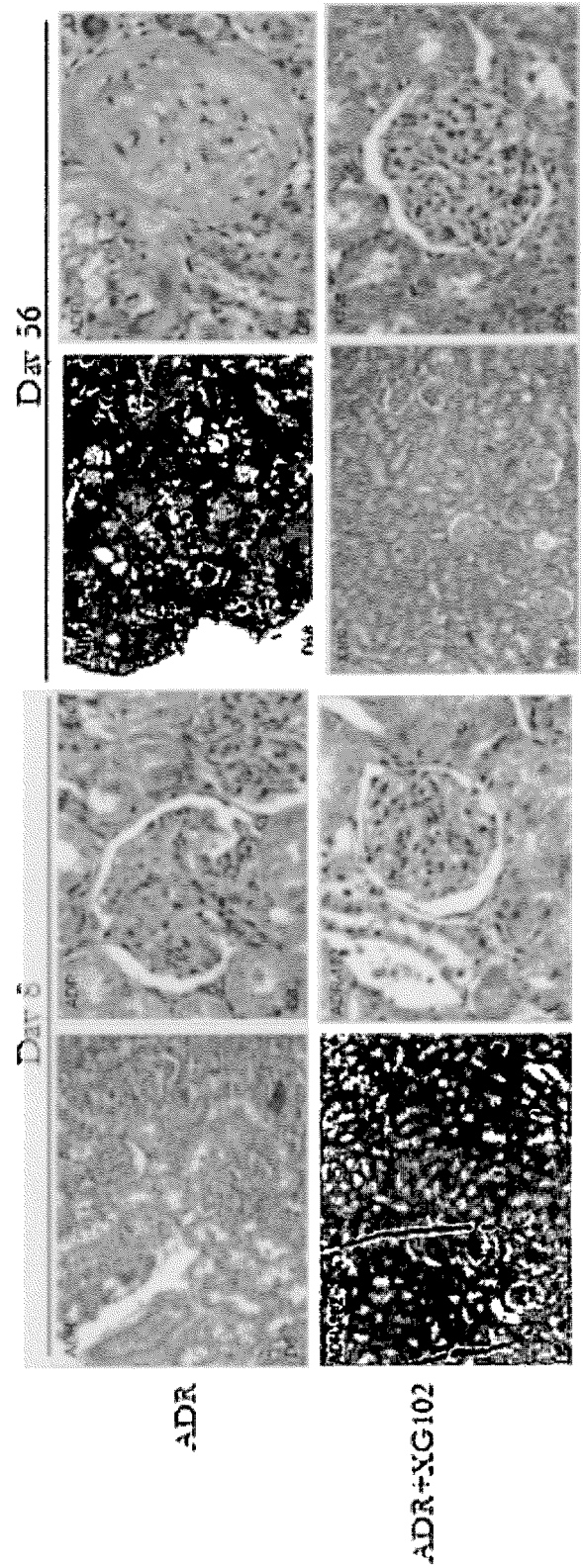


Fig. 50

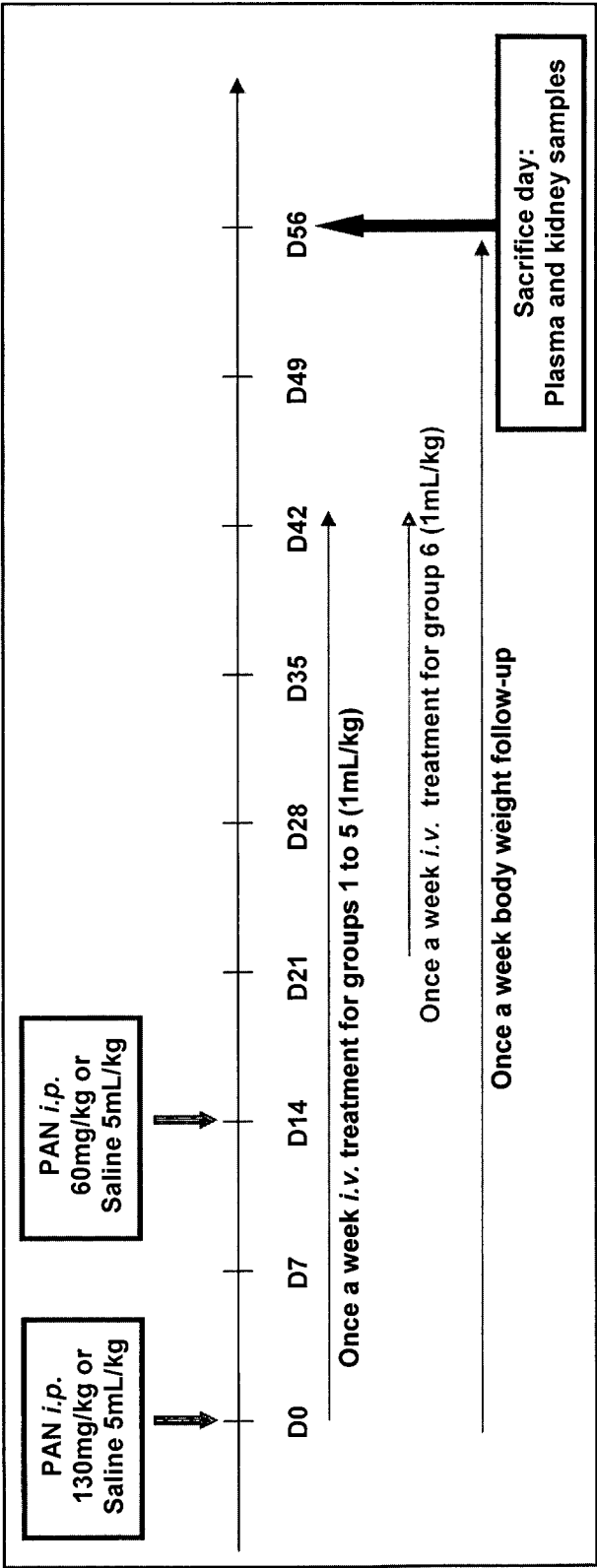


Fig. 51

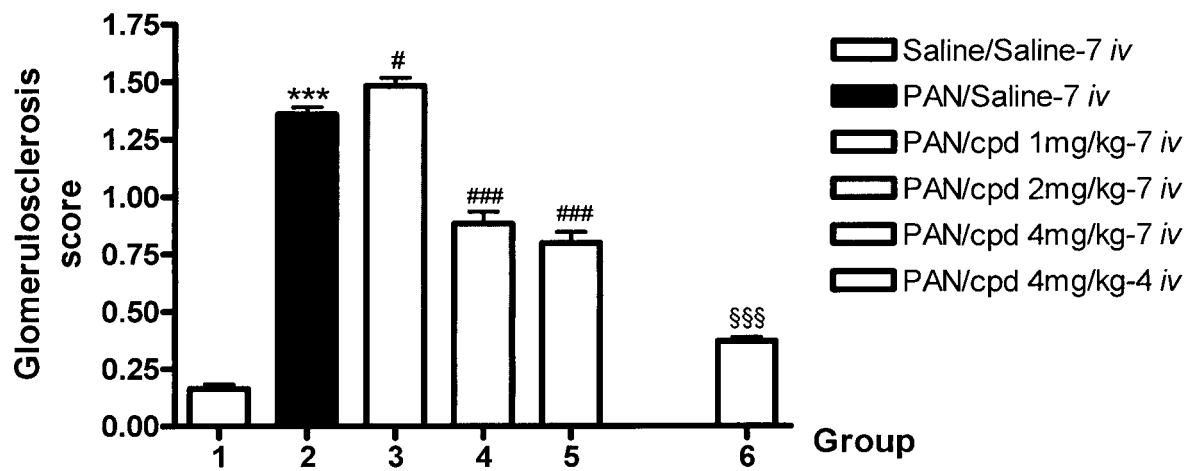
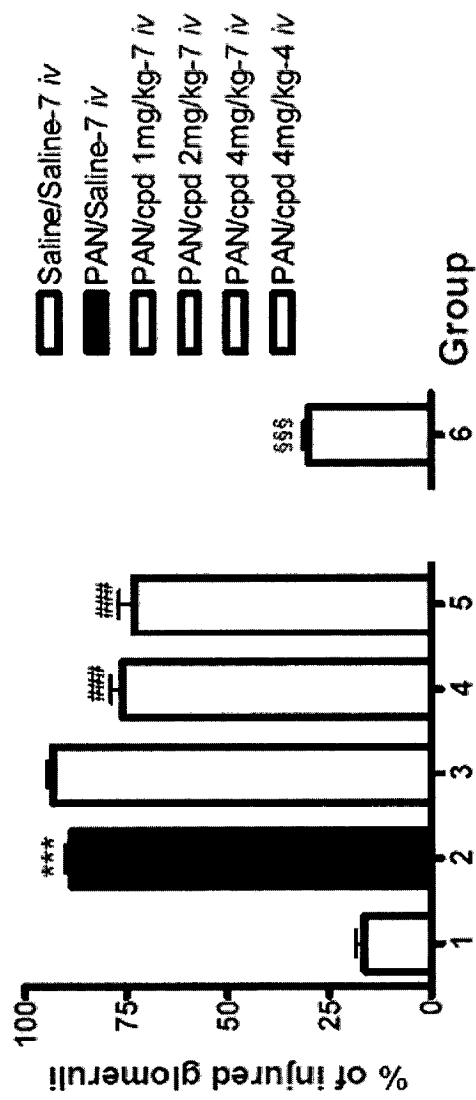


Fig. 52



***P<0.001 versus Group 1 using unpaired Student t-test
P<0.001 versus Group 2 using one-way ANOVA followed by Newman-Keuls test
\$\$\$ P<0.001 versus Group 2 using unpaired Student t-test

The Group 2 and the Group 6 are different in term of number of iv injections as stated in the Study Plan.

Fig. 53

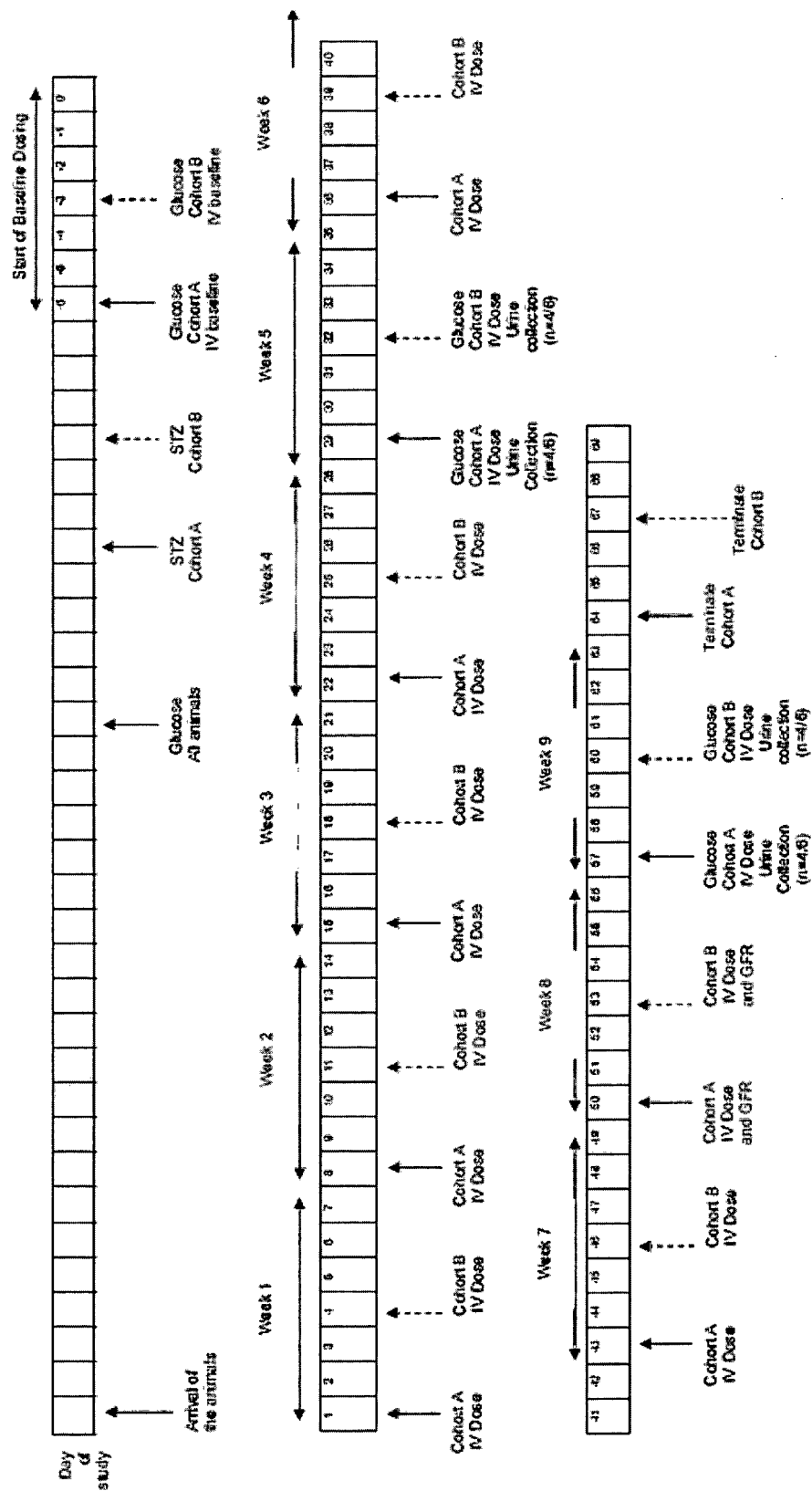


Fig. 54

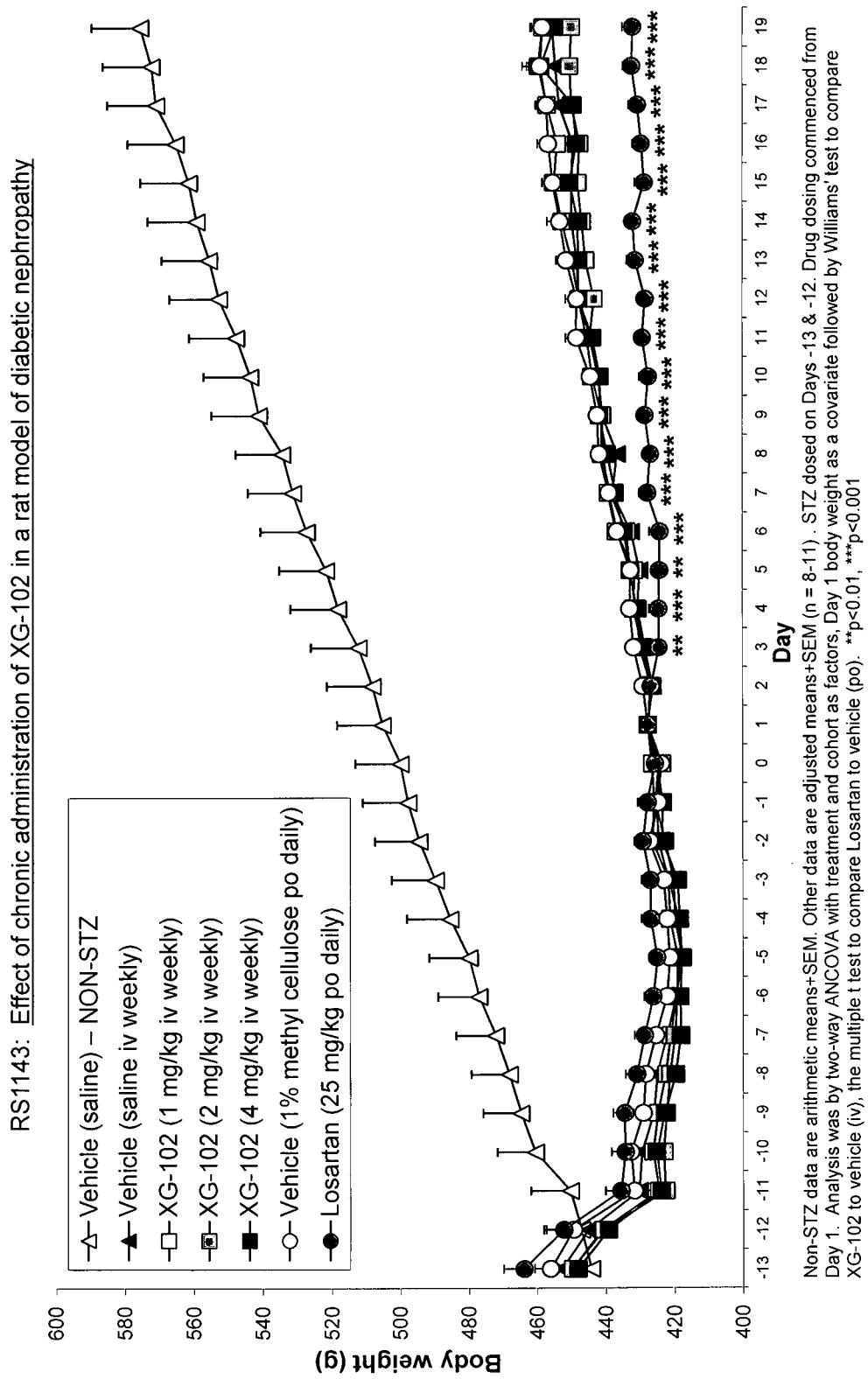
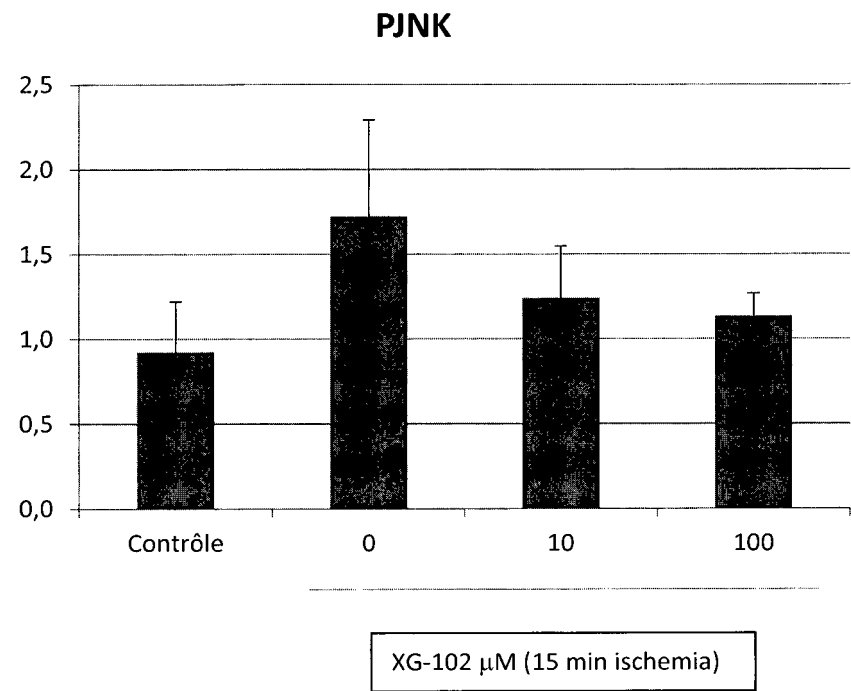
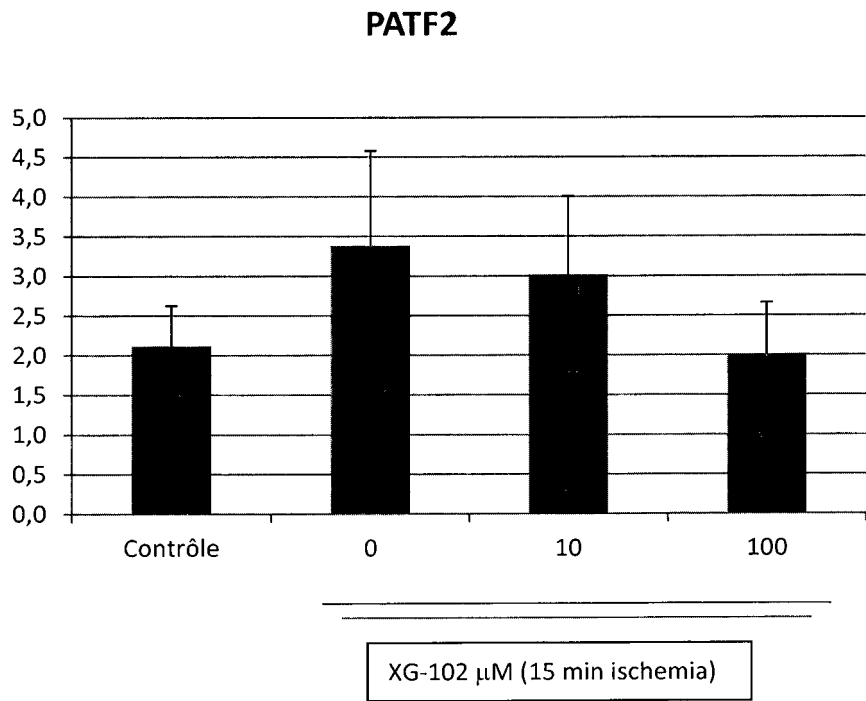


Fig. 55



A



B

Fig. 56

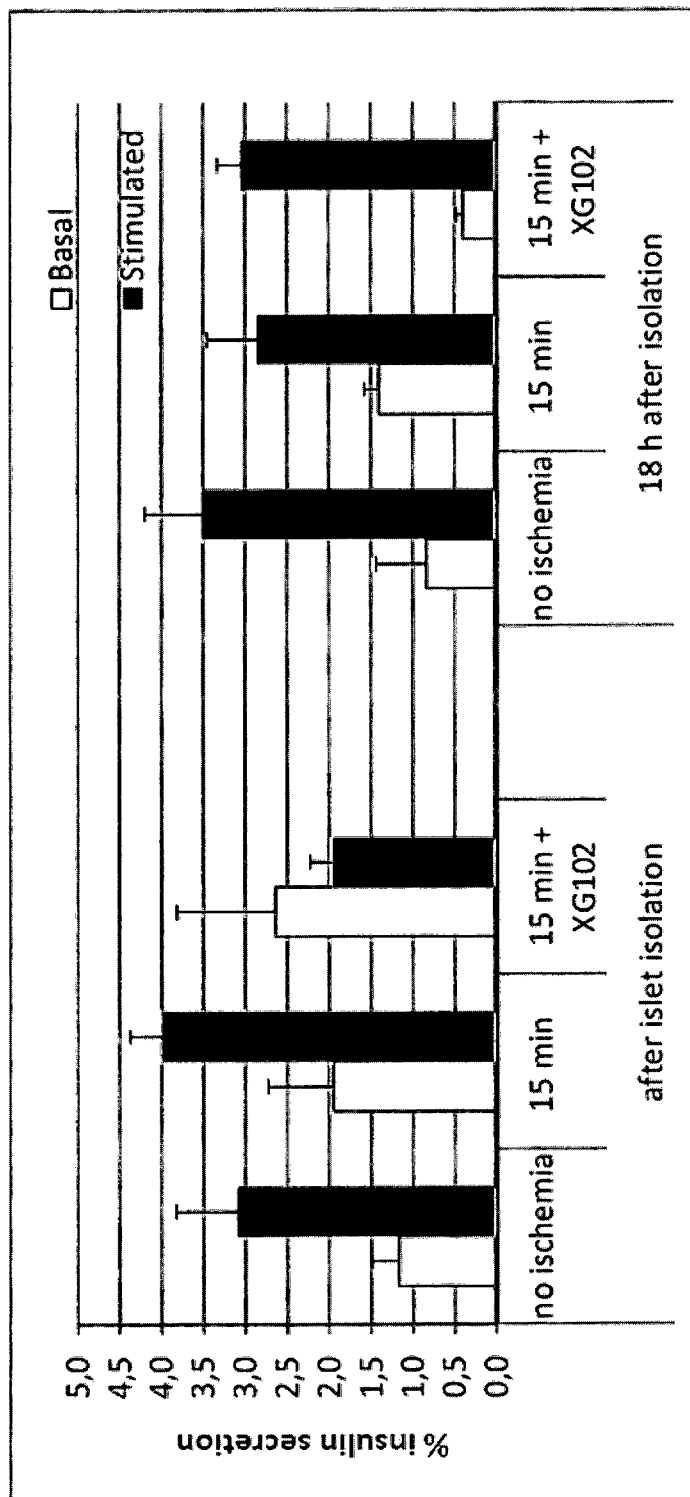


Fig. 57

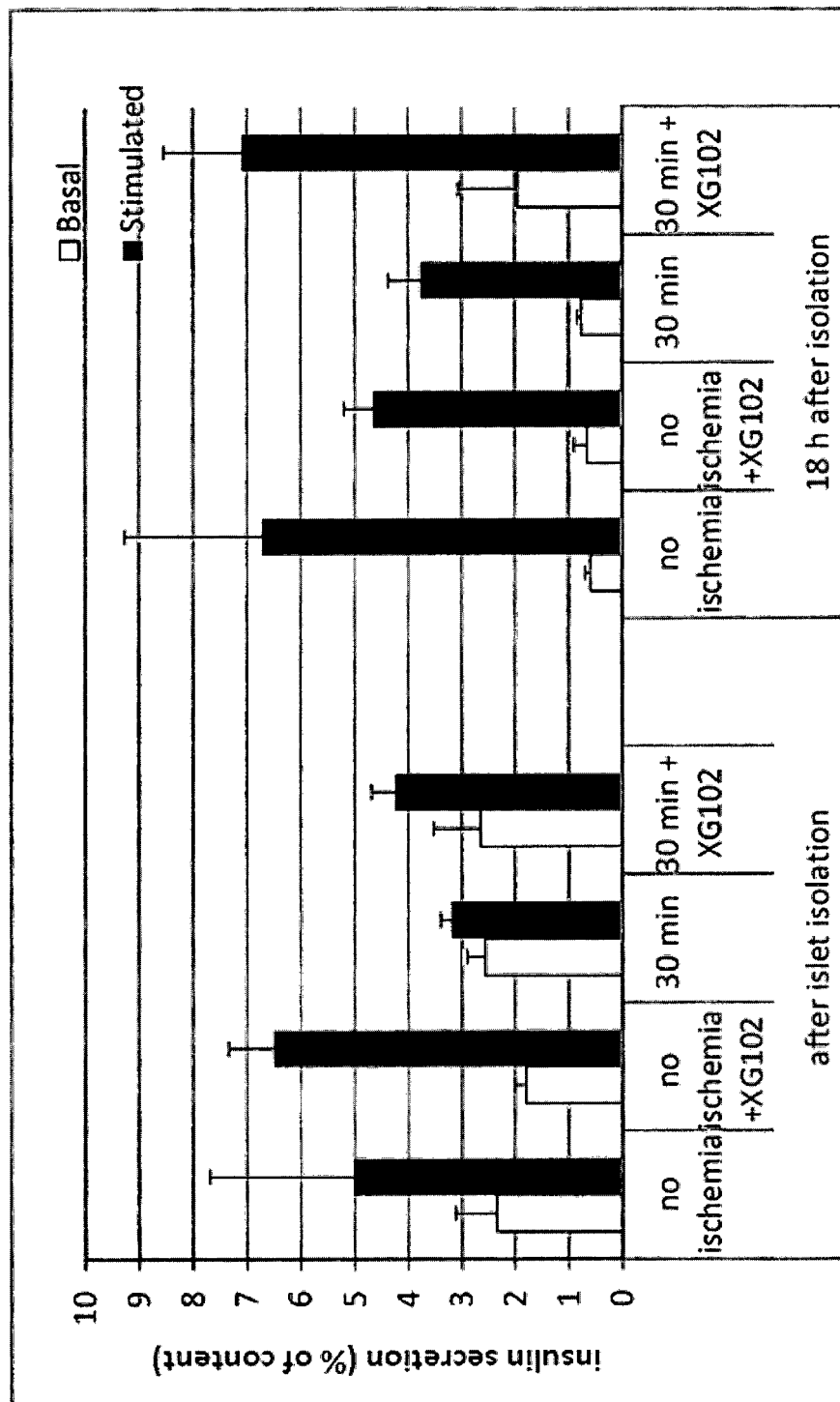


Fig. 58

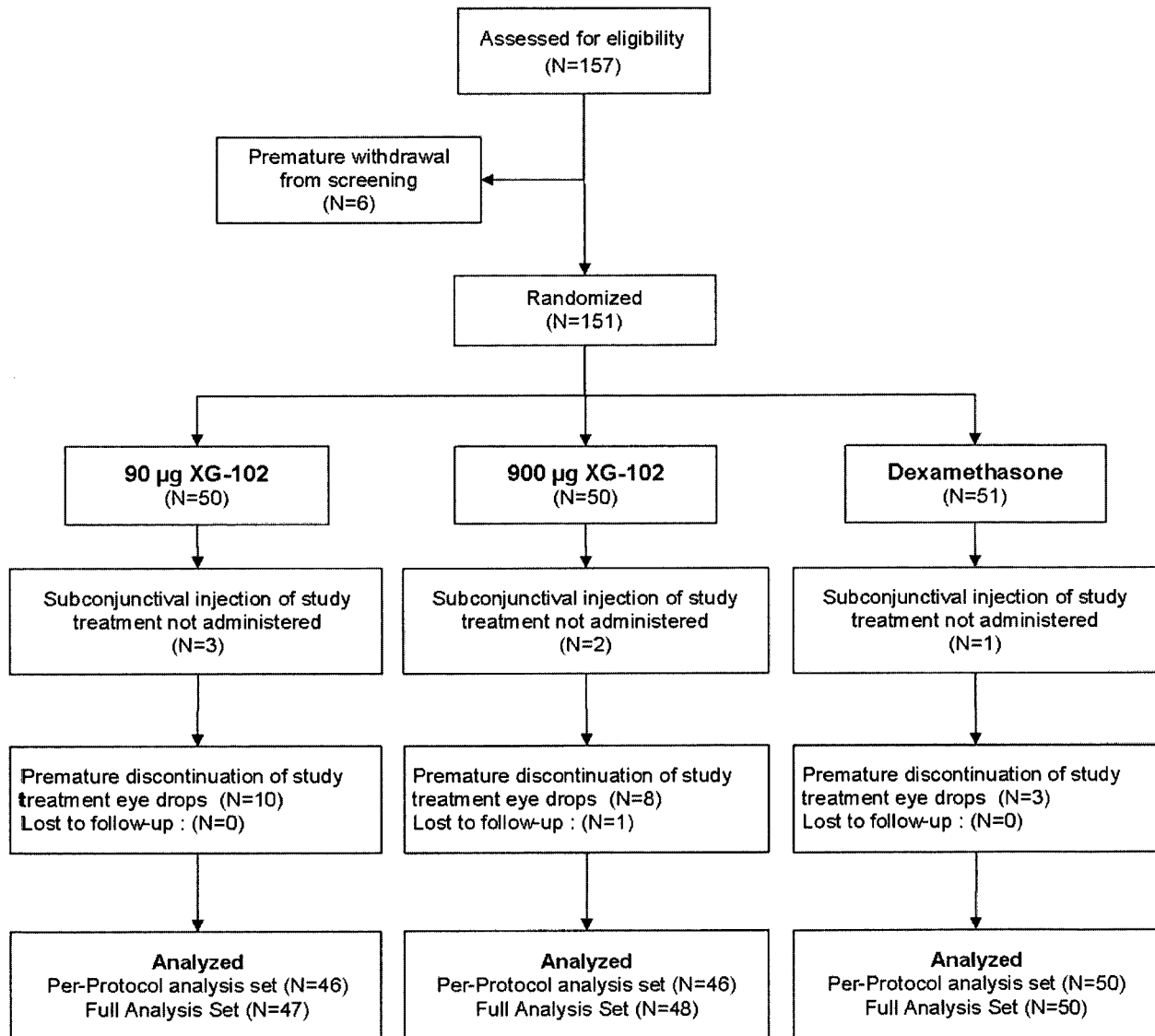


Fig. 59

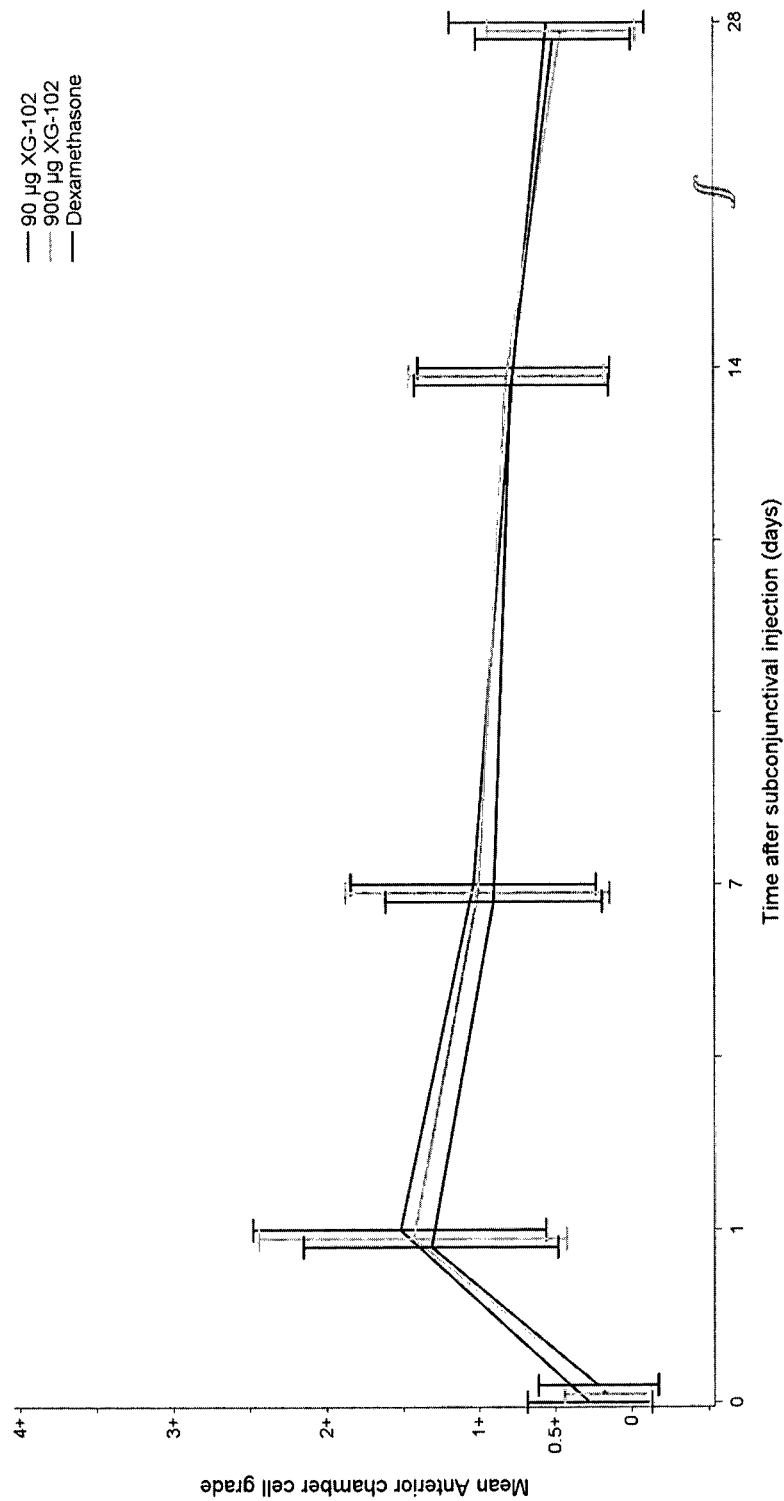


Fig. 60

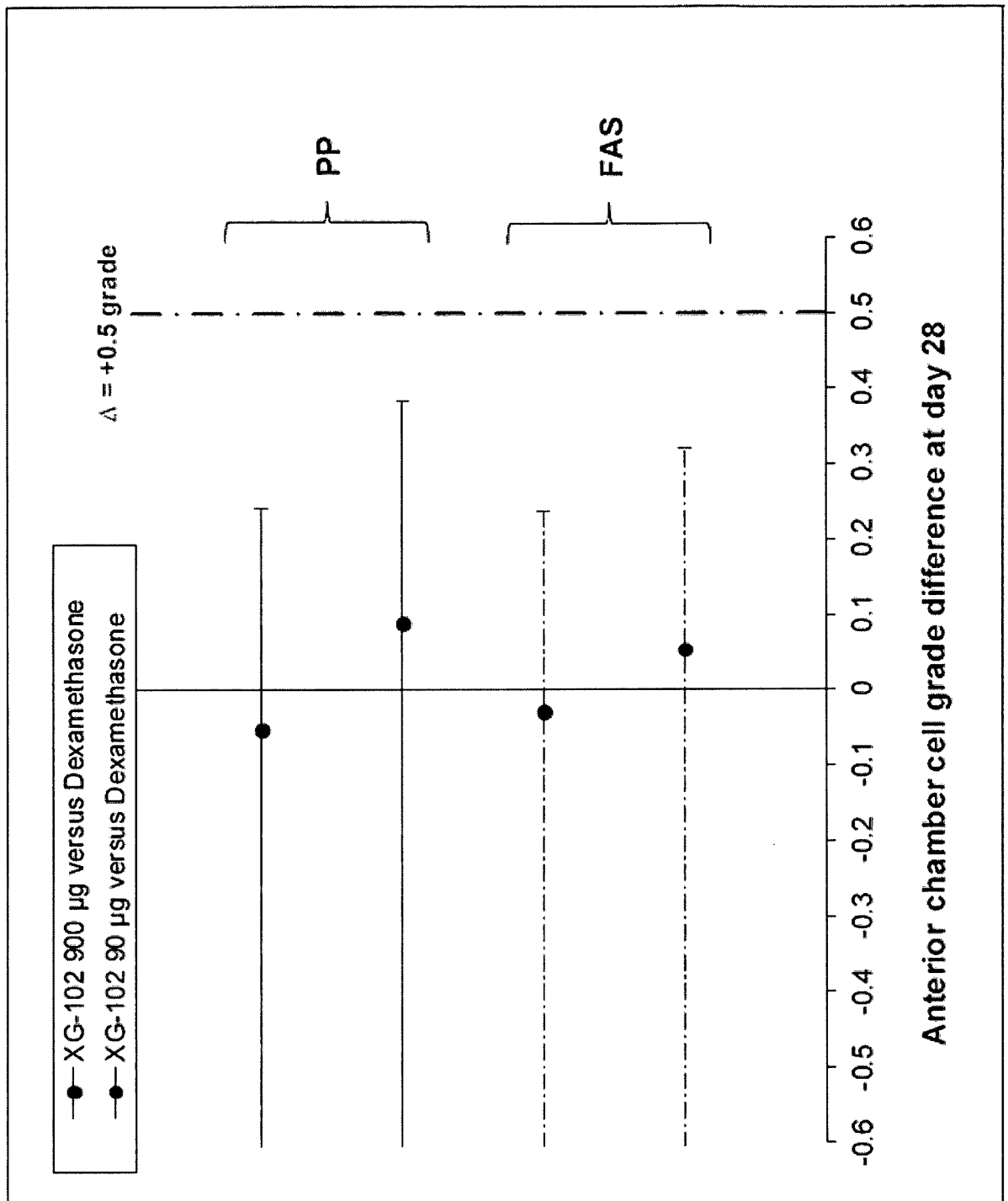


Fig. 61

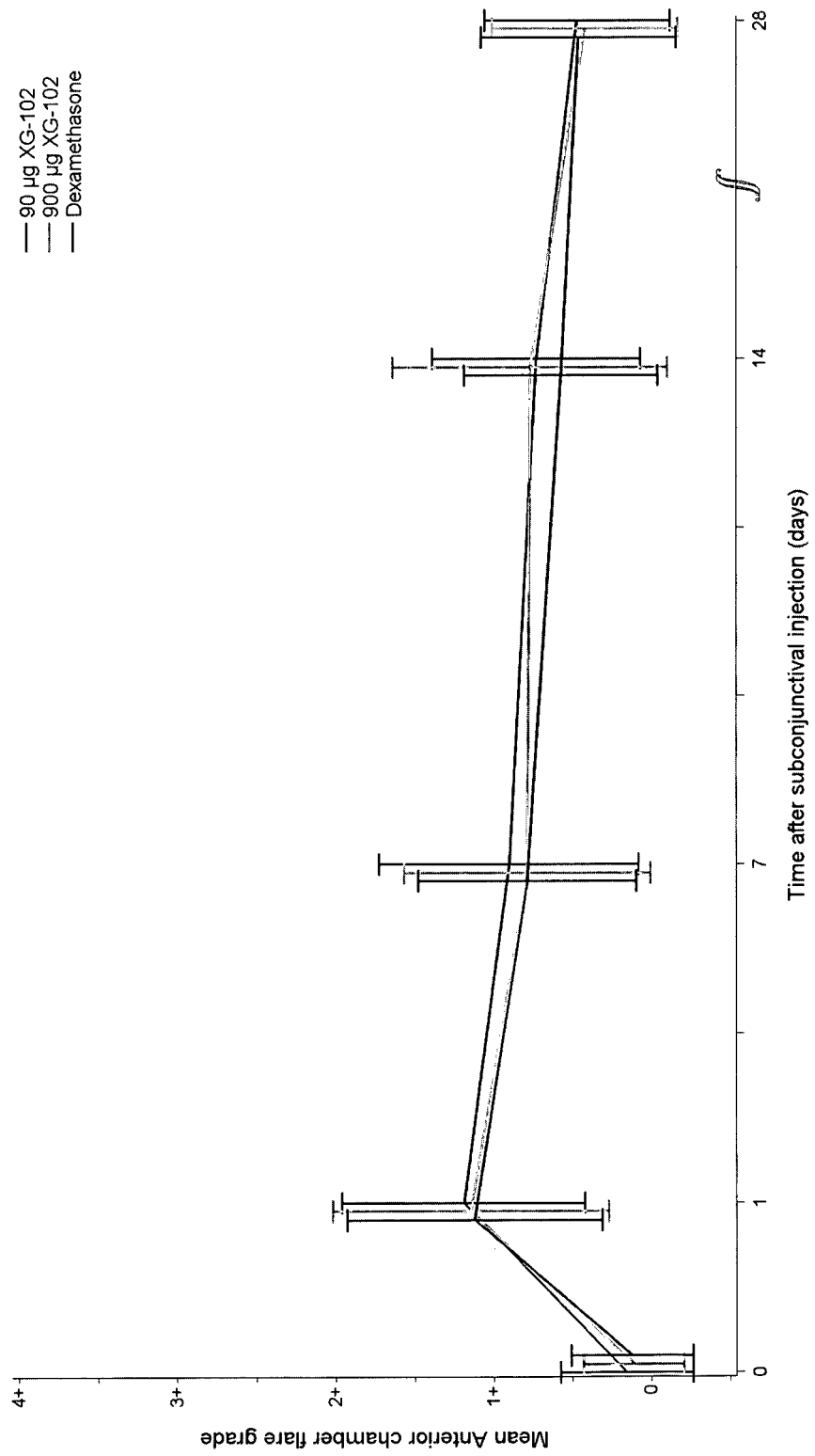


Fig. 62

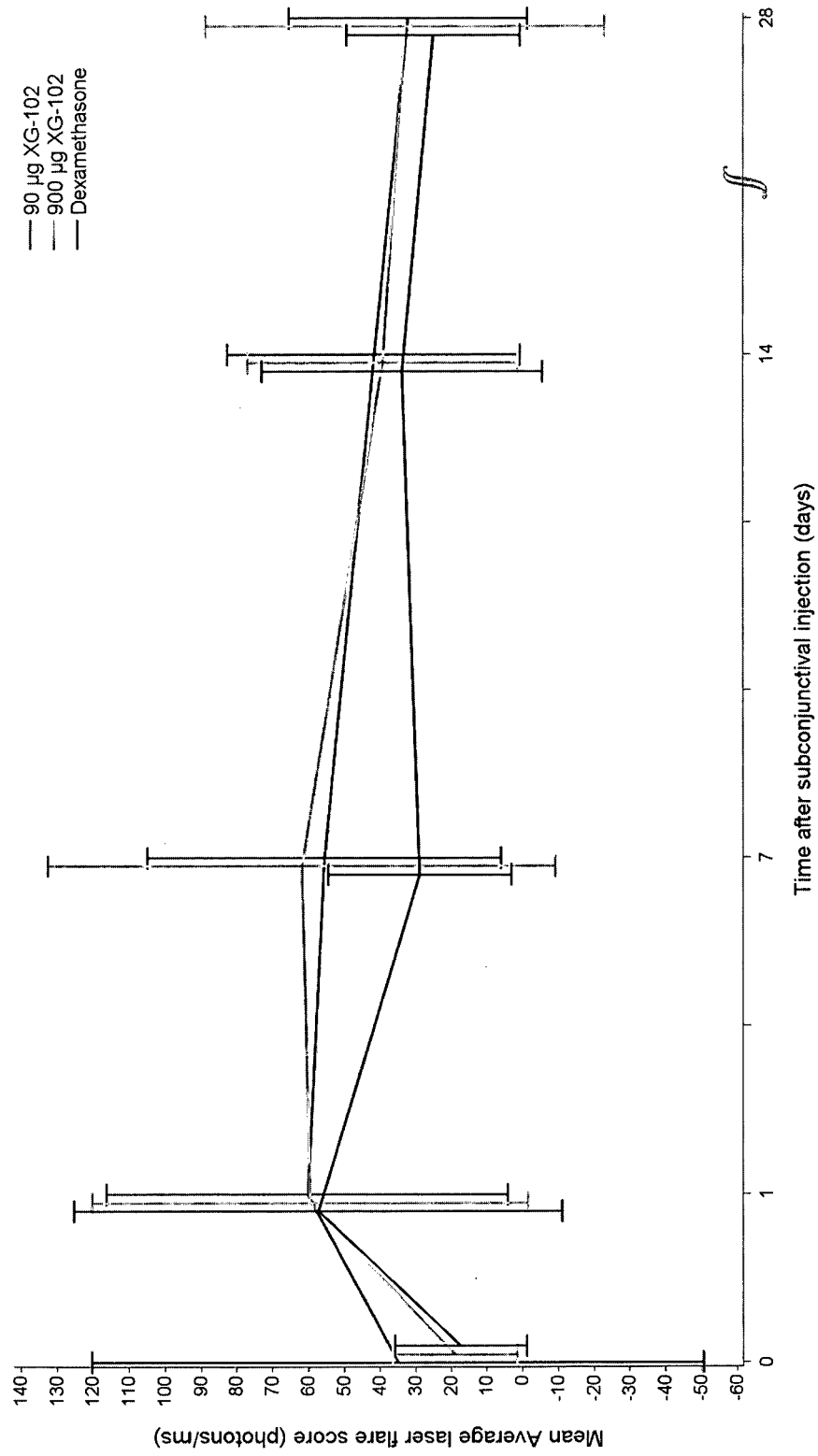


Fig. 63

	90 µg XG-102 (N=47)		900 µg XG-102 (N=48)		Dexamethasone (N=50)		Exact Chi-square test P-values	
	Total # events	# patients (%)	Total # events	# patients (%)	Total # events	# patients (%)	90 µg XG-102 vs. Dexamethasone	900 µg XG-102 vs. Dexamethasone
Adverse event summary	78	31 (66.0%)	69	32 (66.7%)	55	29 (58.0%)	0.531	0.410
Adverse event up to 24 hours after the subconjunctival injection of study treatment	31	16 (34.0%)	19	13 (27.1%)	19	15 (30.0%)	0.828	0.825
Adverse event after 24 hours after the subconjunctival injection of study treatment	47	27 (57.4%)	50	24 (50.0%)	36	19 (38.0%)	0.068	0.309
Serious adverse event summary	4	4 (8.5%)	3	3 (6.3%)	2	2 (4.0%)	0.426	0.674
Serious adverse event up to 24 hours after the subconjunctival injection of study treatment	1	1 (2.1%)	0	0 (0.0%)	0	0 (0.0%)	0.485	0.309
Serious adverse event after 24 hours after the subconjunctival injection of study treatment	3	3 (6.4%)	3	3 (6.3%)	2	2 (4.0%)	0.671	0.674

Data are number of patients (%). N=Number of patients in each group, # = number, µg = microgram, % = percentage.

Fig. 64

	90 µg XG-102 (N=47)		900 µg XG-102 (N=48)		Dexamethasone (N=50)		Exact Chi-square test P values	
	Total # events	# patients (%)	Total # events	# patients (%)	Total # events	# patients (%)	90µg XG-102 vs. Dexamethasone	900µg XG-102 vs. Dexamethasone
Cardiac disorders								
Tachycardia	2	2 (4.3%)	0	0 (0.0%)	1	1 (2.0%)	0.610	1.000
Eye disorders								
Cataract	2	2 (4.3%)	3	3 (6.3%)	4	4 (8.0%)	0.678	1.000
Conjunctival hyperaemia	1	1 (2.1%)	3	3 (6.3%)	2	2 (4.0%)	1.000	0.674
Corneal oedema	4	4 (8.5%)	2	2 (4.2%)	5	5 (10.0%)	1.000	0.436
Cyclitic membrane	3	3 (6.4%)	1	1 (2.1%)	1	1 (2.0%)	0.352	1.000
Eye inflammation	5	5 (10.6%)	2	2 (4.2%)	0	0 (0.0%)	0.024	0.237
Eye pain	3	2 (4.3%)	8	7 (14.6%)	1	1 (2.0%)	0.610	0.029
Eyelid oedema	5	5 (10.6%)	2	2 (4.2%)	1	1 (2.0%)	0.105	0.613
Hyphaema	1	1 (2.1%)	2	2 (4.2%)	1	1 (2.0%)	1.000	0.613
Macular oedema	2	2 (4.3%)	4	4 (8.3%)	3	3 (6.0%)	1.000	0.712
Punctate keratitis	3	3 (6.4%)	2	2 (4.2%)	3	3 (6.0%)	1.000	1.000
Retinal detachment	2	2 (4.3%)	3	3 (6.3%)	2	2 (4.0%)	1.000	0.674
Ulcerative keratitis	3	3 (6.4%)	2	2 (4.2%)	1	1 (2.0%)	0.352	0.613
Vitreous haemorrhage	1	1 (2.1%)	1	1 (2.1%)	1	1 (2.0%)	1.000	1.000
Investigations								
Aspartate Transaminase increased	1	1 (2.1%)	1	1 (2.1%)	1	1 (2.0%)	1.000	1.000
Blood creatine phosphokinase increased	2	2 (4.3%)	2	2 (4.2%)	4	4 (8.0%)	0.678	0.678
Blood creatinine increased	0	0 (0.0%)	2	2 (4.2%)	1	1 (2.0%)	1.000	0.613
Blood pressure increased	1	1 (2.1%)	2	2 (4.2%)	1	1 (2.0%)	1.000	0.613
Gamma-glutamyltransferase increased	0	0 (0.0%)	3	3 (6.3%)	0	0 (0.0%)	0.114	0.114
Intraocular pressure increased	12	11 (23.4%)	6	5 (10.4%)	8	7 (14.0%)	0.299	0.760
White blood cell count increased	0	0 (0.0%)	3	3 (6.3%)	0	0 (0.0%)	0.114	0.114
Nervous system disorders								
Headache	2	2 (4.3%)	1	1 (2.1%)	0	0 (0.0%)	0.232	0.490
Surgical and medical procedures								
Retinal operation	1	1 (2.1%)	2	2 (4.2%)	0	0 (0.0%)	0.485	0.237

Data are number of patients (%). N=Number of patients in each group. #=percentage. For two patients - FR-01-0001(XG-102 90 µg) and FR-01-0013 (dexamethasone), intraocular hypertension was coded as 'Ocular hypertension' - SOC - EYE.

Fig. 65

	90 µg XG-102 (N=47)		900 µg XG-102 (N=48)		Dexamethasone (N=50)		Exact Chi-square test P-values	
	Total # events	# patients (%)	Total # events	# patients (%)	Total # events	# patients (%)	90µg XG-102 vs. Dexamethasone	900µg XG-102 vs. Dexamethasone
Eye disorders	2	2 (4.3%)	1	1 (2.1%)	2	2 (4.0%)	1.000	1.000
Lens dislocation	0	0 (0.0%)	1	1 (2.1%)	0	0 (0.0%)		0.490
Retinal detachment	0	0 (0.0%)	0	0 (0.0%)	2	2 (4.0%)	0.495	0.495
Retinal oedema	1	1 (2.1%)	0	0 (0.0%)	0	0 (0.0%)	0.485	
Choroidal haematoma	1	1 (2.1%)	0	0 (0.0%)	0	0 (0.0%)	0.485	
Investigations	1	1 (2.1%)	0	0 (0.0%)	0	0 (0.0%)	0.485	
Intraocular pressure increased	1	1 (2.1%)	0	0 (0.0%)	0	0 (0.0%)	0.485	
Surgical and medical procedures	1	1 (2.1%)	2	2 (4.2%)	0	0 (0.0%)	0.485	0.237
Retinal operation	1	1 (2.1%)	2	2 (4.2%)	0	0 (0.0%)	0.485	0.237

Data are number of patients (%). N = Number of patients in each group, n = number, µg = microgram, % = percentage.

Fig. 66

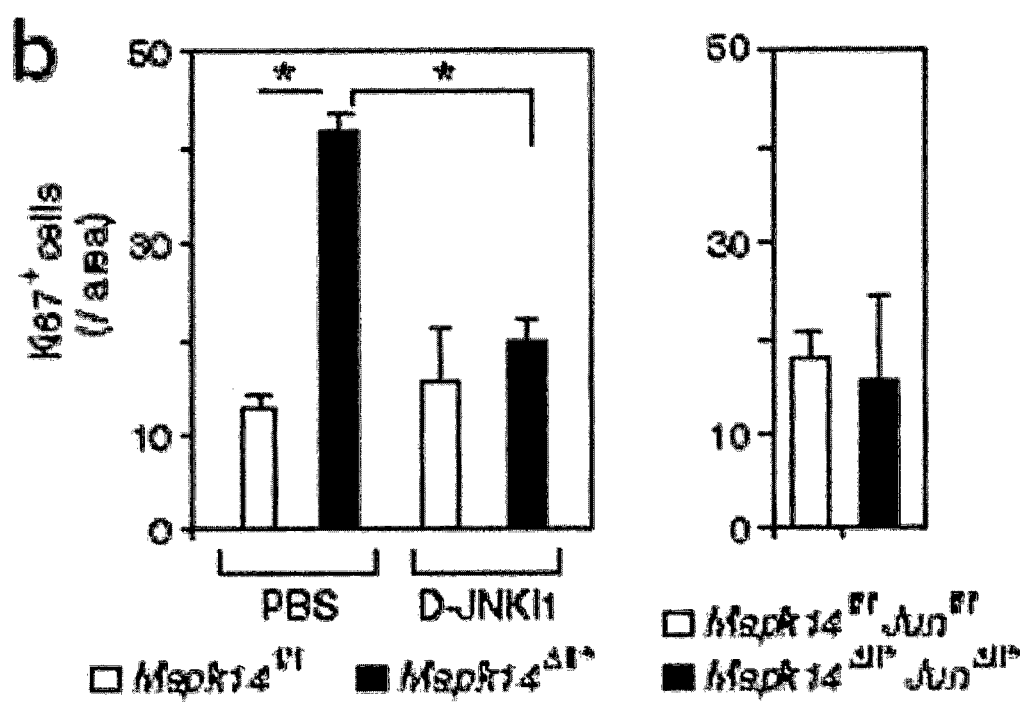


Fig. 67

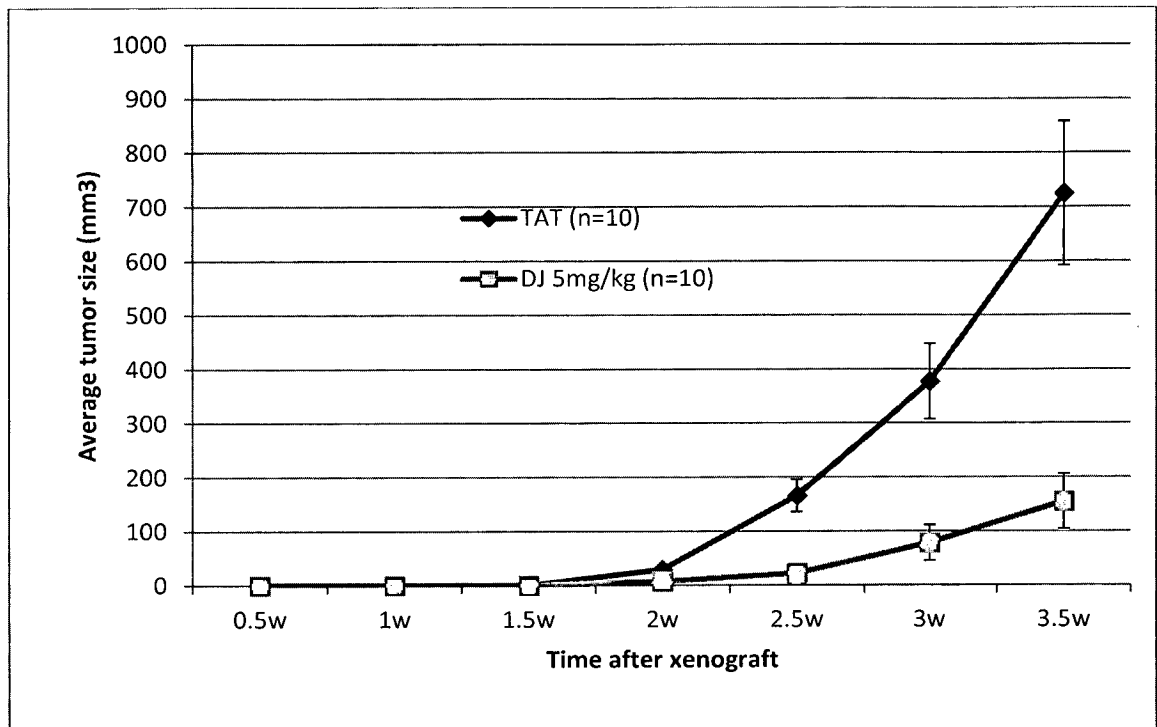


Fig. 68

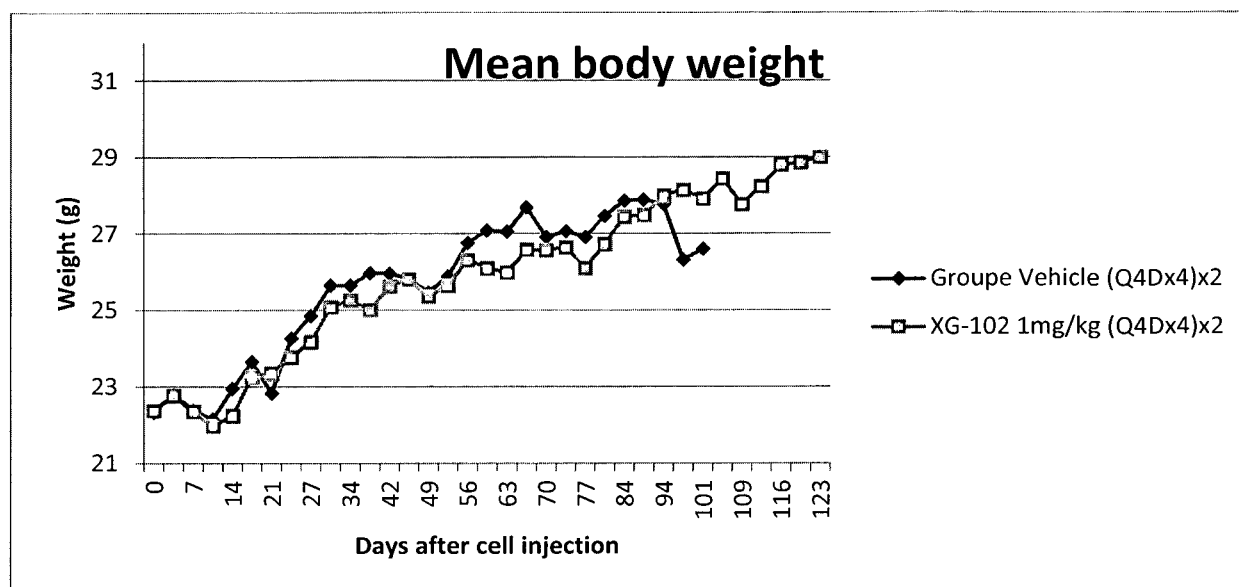


Fig. 69

Group	Treatment				Body weight $\pm$ SD (g)			MBWC $\pm$ SD (%)	
	substance	Dose (mg/kg/inj)	Route of administration	Treatment schedule	D0	D10	D42	D94	
1	Vehicle	-	IV	(Q4Dx4)x2	22.4 $\pm$ 1.2	22.1 $\pm$ 1.6	25.9 $\pm$ 1.4	27.8 $\pm$ 3.4	D10 to D42 +17.7 $\pm$ 9.7
2	XG-102	1	IV	(Q4Dx4)x2	22.4 $\pm$ 1.0	22.0 $\pm$ 1.7	25.6 $\pm$ 1.7	28.0 $\pm$ 0.9	D10 to D94 +25.7 $\pm$ 15.9
									+28.2 $\pm$ 11.9

Group	Body weight $\pm$ SD (g)				MBWC $\pm$ SD (%)	
	D0	D10	D42	D94	D10 to D42	D10 to D94
XG-102 1mg/kg	NS	NS	NS	NS	NS	NS

Fig. 70

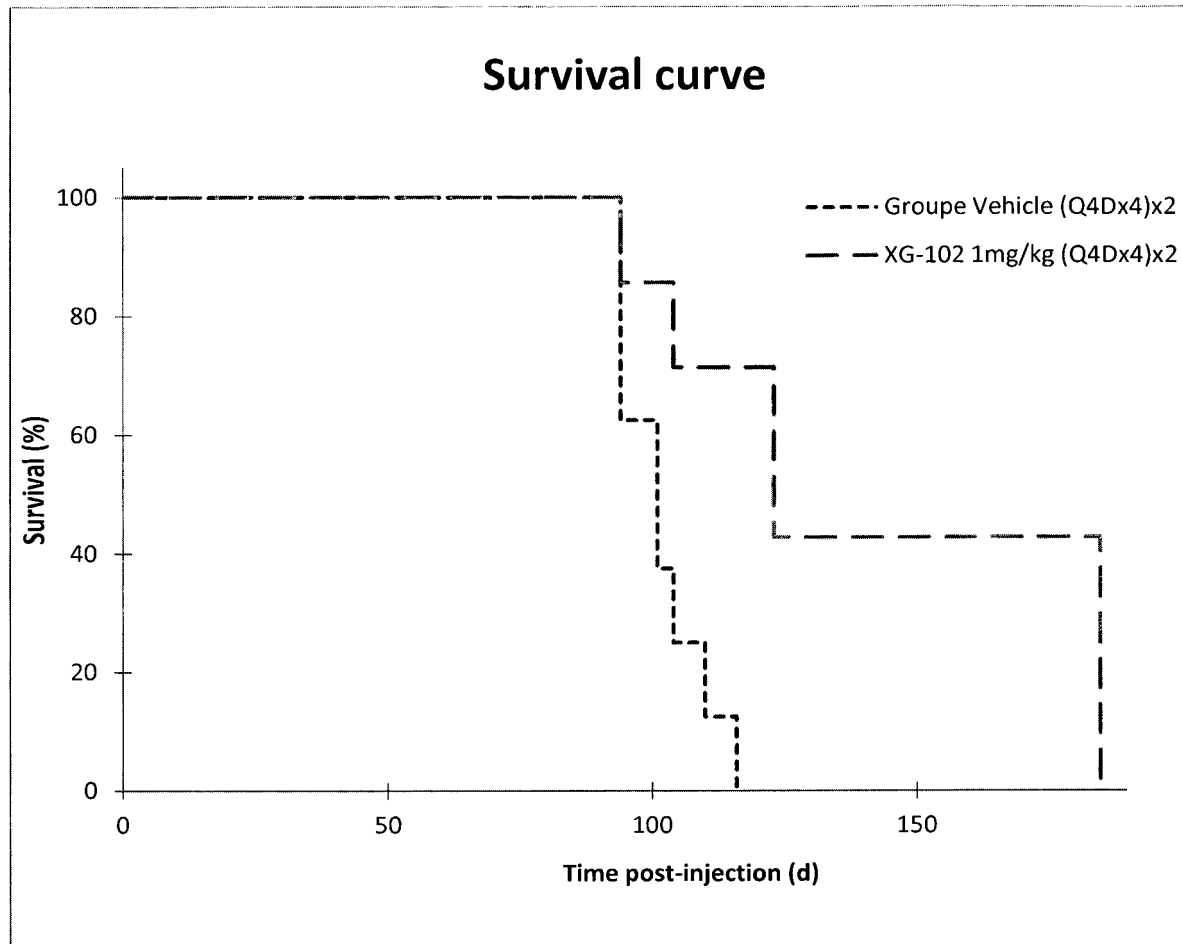


Fig. 71

Group	Treatment				Body weight $\pm$ SD (g)				MBWC $\pm$ SD (%)	
	substance	Dose (mg/kg/inj)	Route of administration	Treatment schedule	D0	D10	D41	D67	D10 to D41	D10 to D67
1	Vehicle	-	IV	(Q4Dx4)x2	19.7 $\pm$ 1.4	20.9 $\pm$ 1.5	23.4 $\pm$ 1.8	23.6 $\pm$ 1.8	+11.7 $\pm$ 3.1	+13.0 $\pm$ 5.8
2	XG-102	0.1	IV	(Q4Dx4)x2	19.4 $\pm$ 1.2	21.0 $\pm$ 1.3	23.3 $\pm$ 1.1	23.9 $\pm$ 1.1	+11.4 $\pm$ 3.9	+15.0 $\pm$ 4.1
3	XG-102	1	IV	(Q4Dx4)x2	19.4 $\pm$ 1.2	21.0 $\pm$ 1.3	23.4 $\pm$ 1.5	25.1 $\pm$ 1.7	+11.2 $\pm$ 5.0	+21.7 $\pm$ 6.8
4	XG-102	5	IV	(Q4Dx4)x2	19.6 $\pm$ 1.1	21.1 $\pm$ 1.3	23.8 $\pm$ 1.4	25.2 $\pm$ 1.4	+12.8 $\pm$ 3.2	+19.6 $\pm$ 7.4

Fig. 72

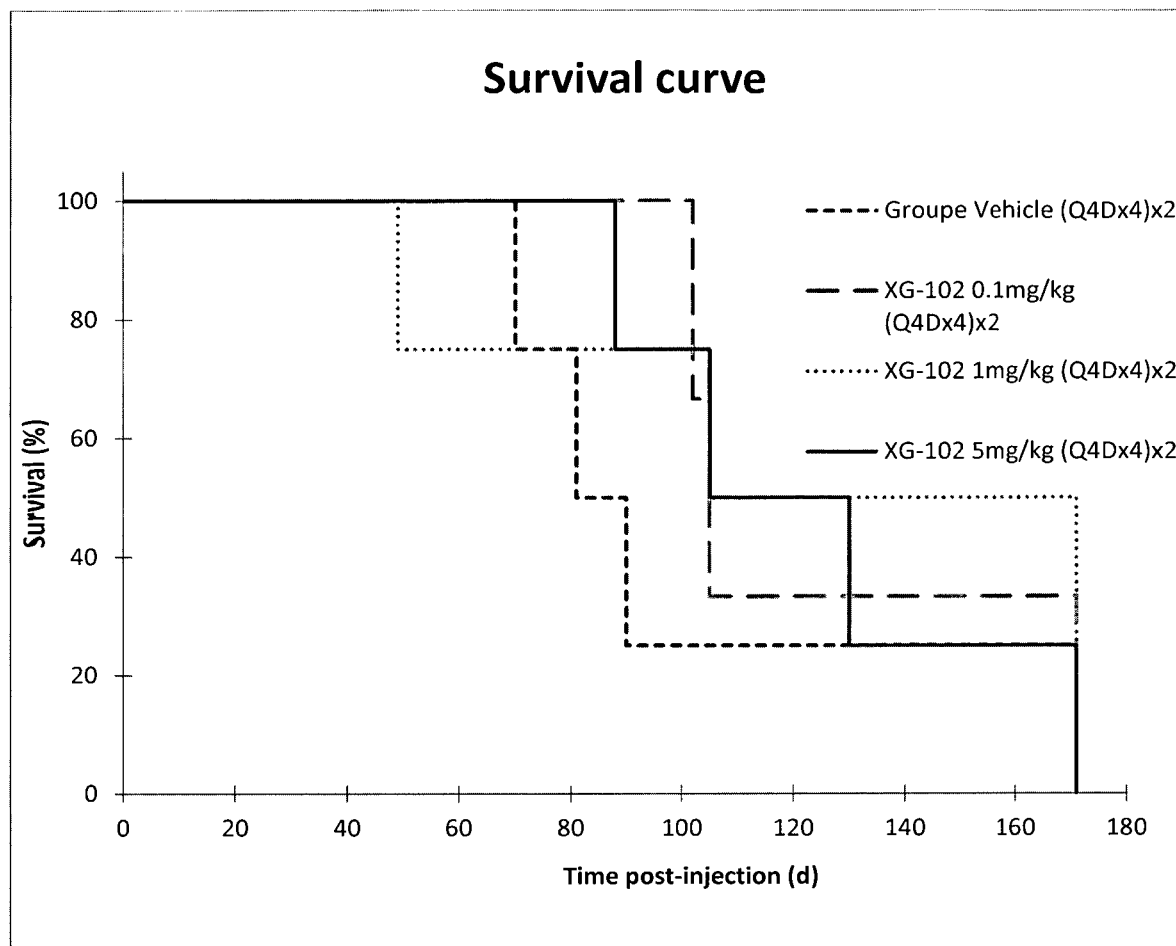


Fig. 73

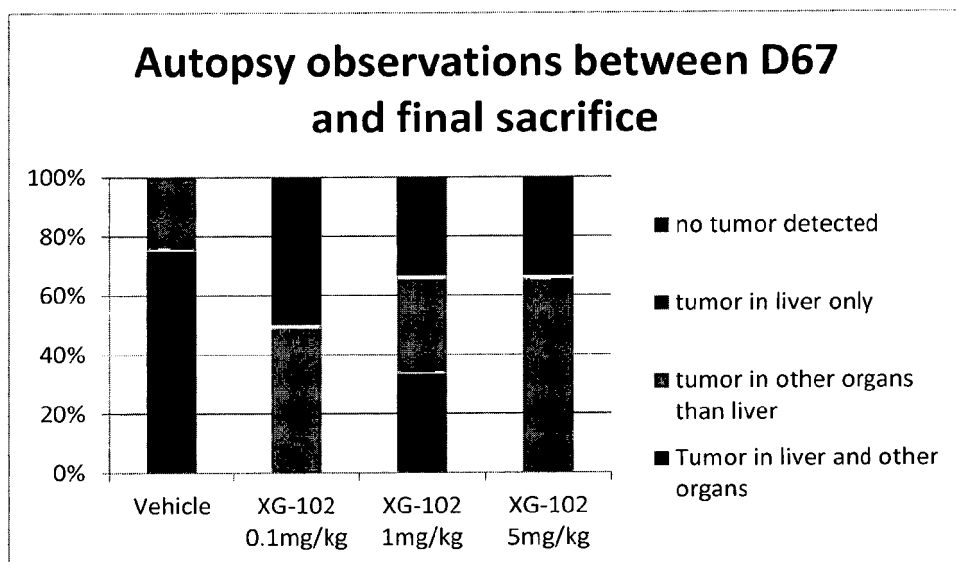
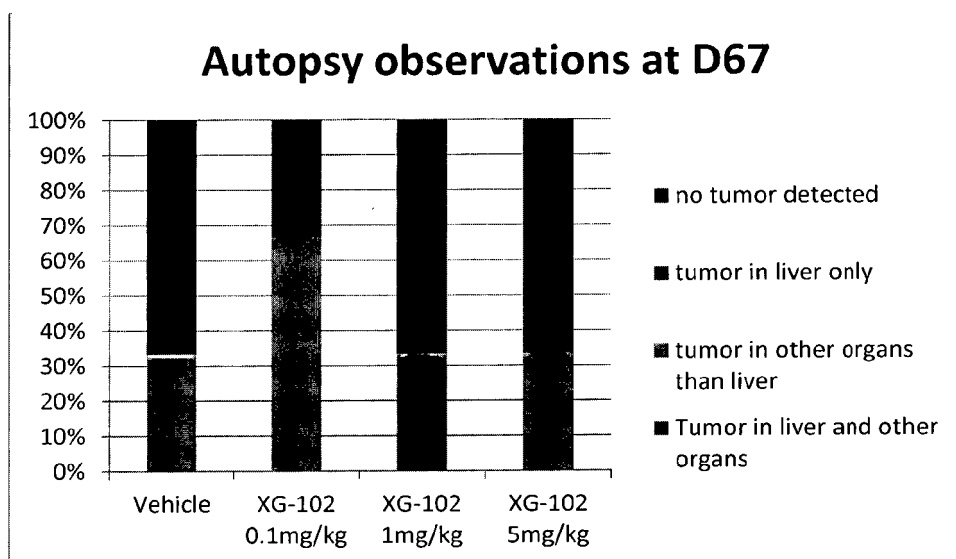


Fig. 74

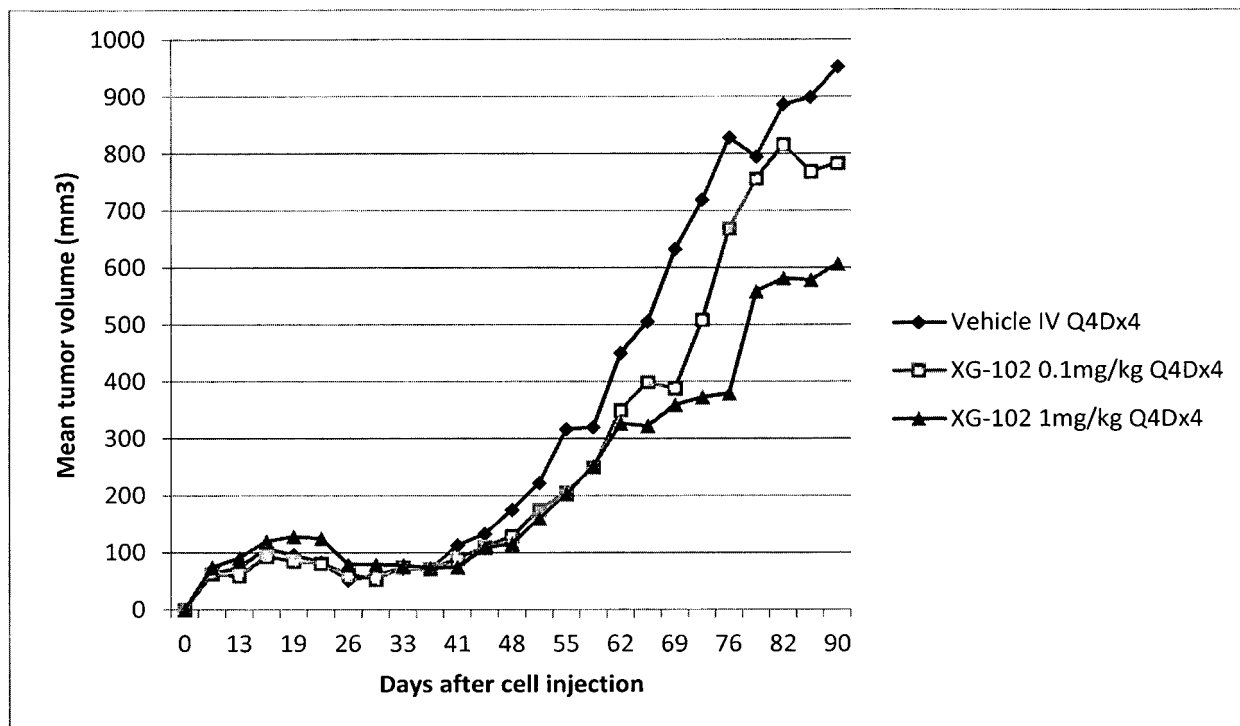


Fig. 75

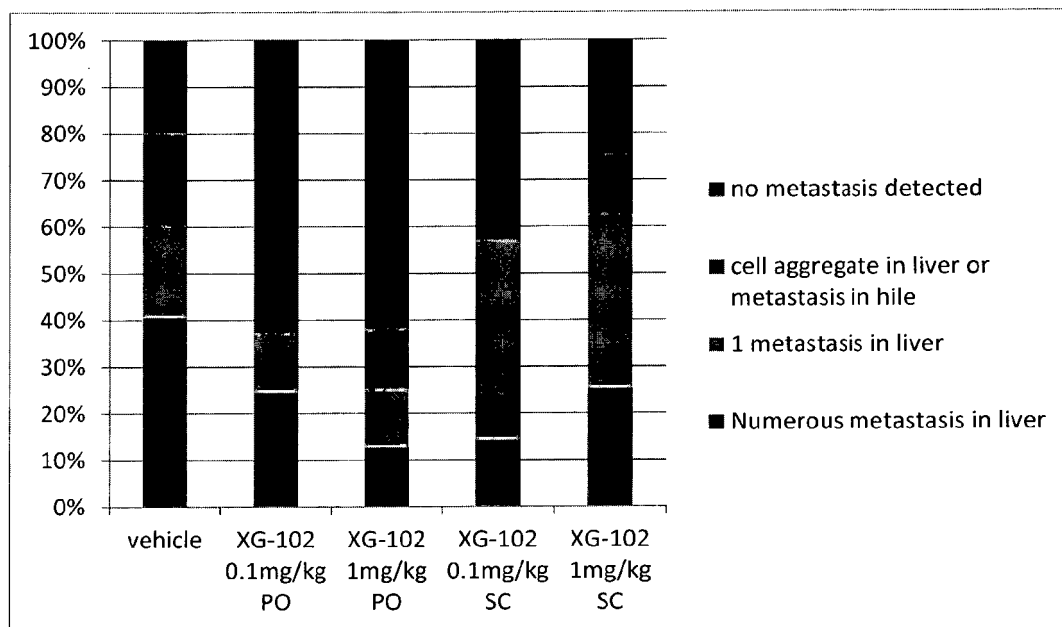


Fig. 76

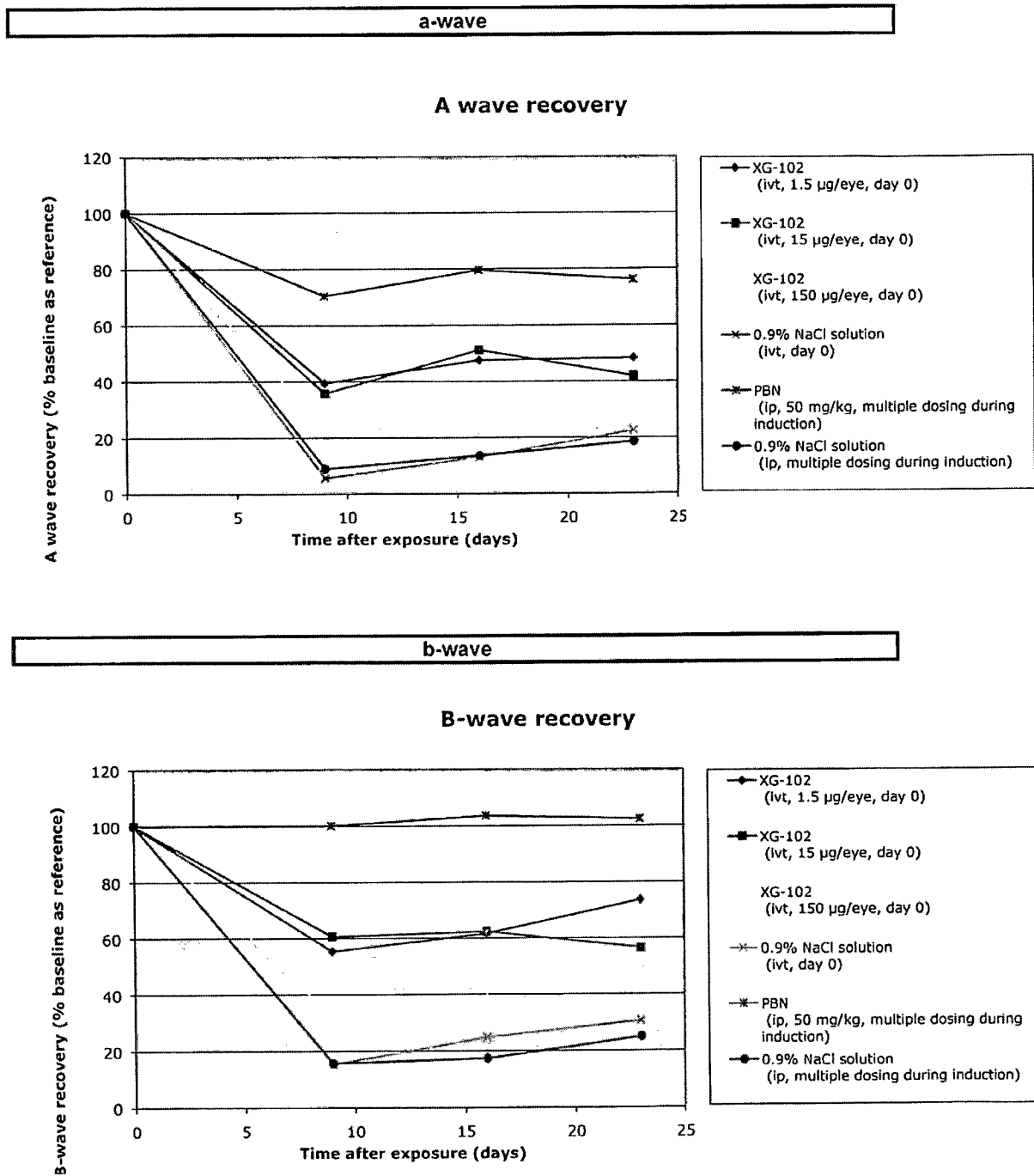


Fig. 77

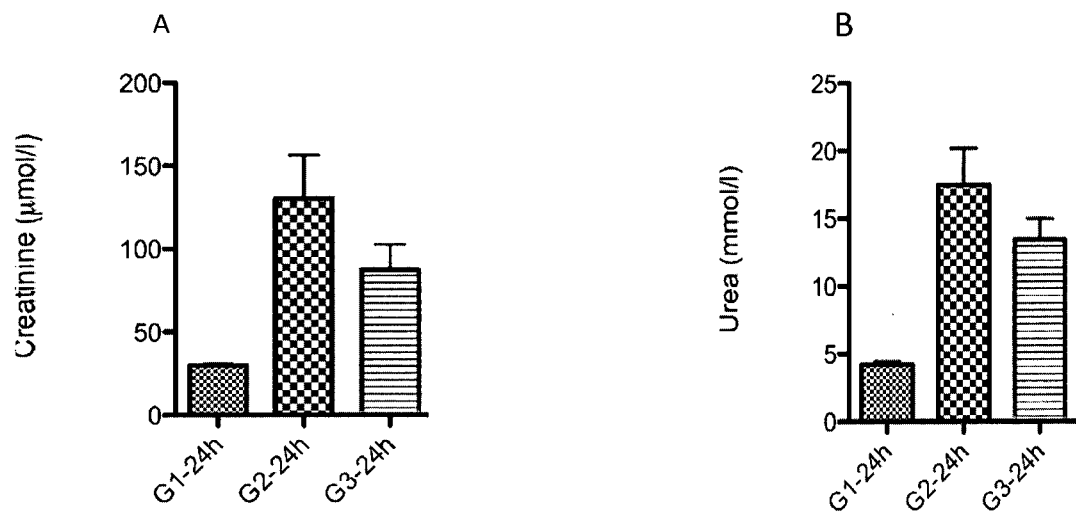


Fig. 78

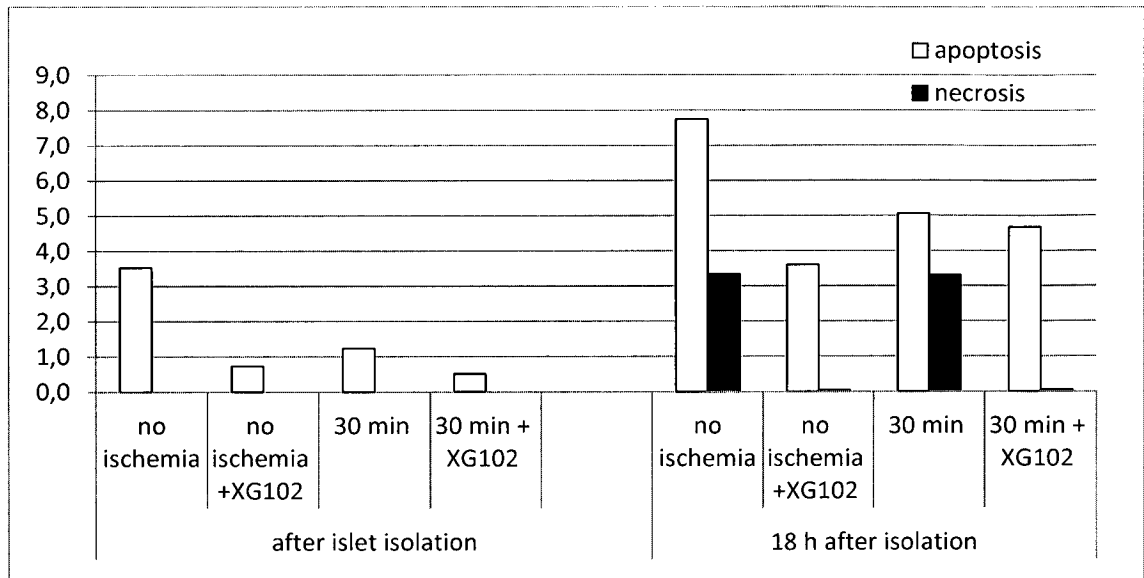


Fig. 79

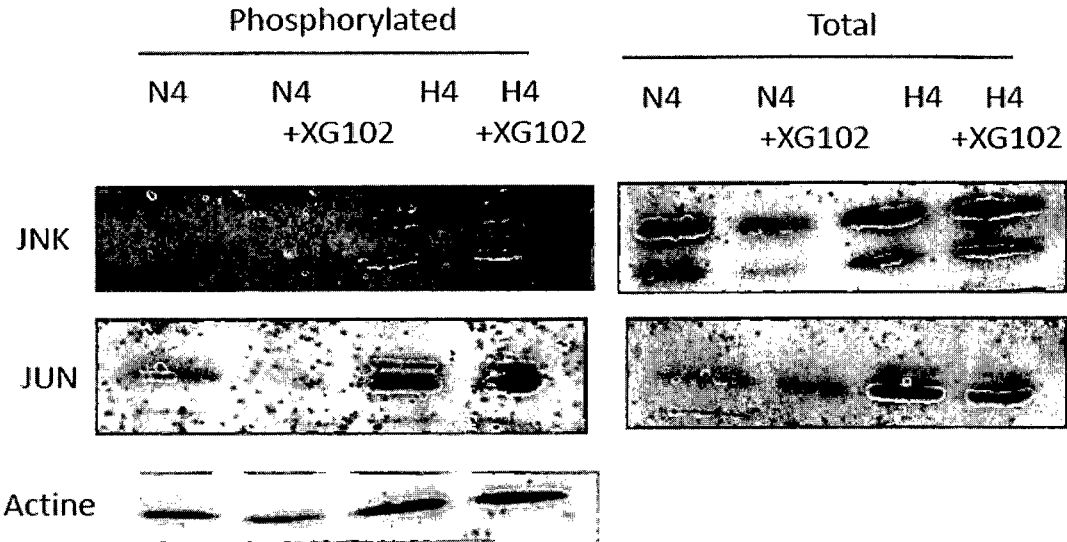


Fig. 80

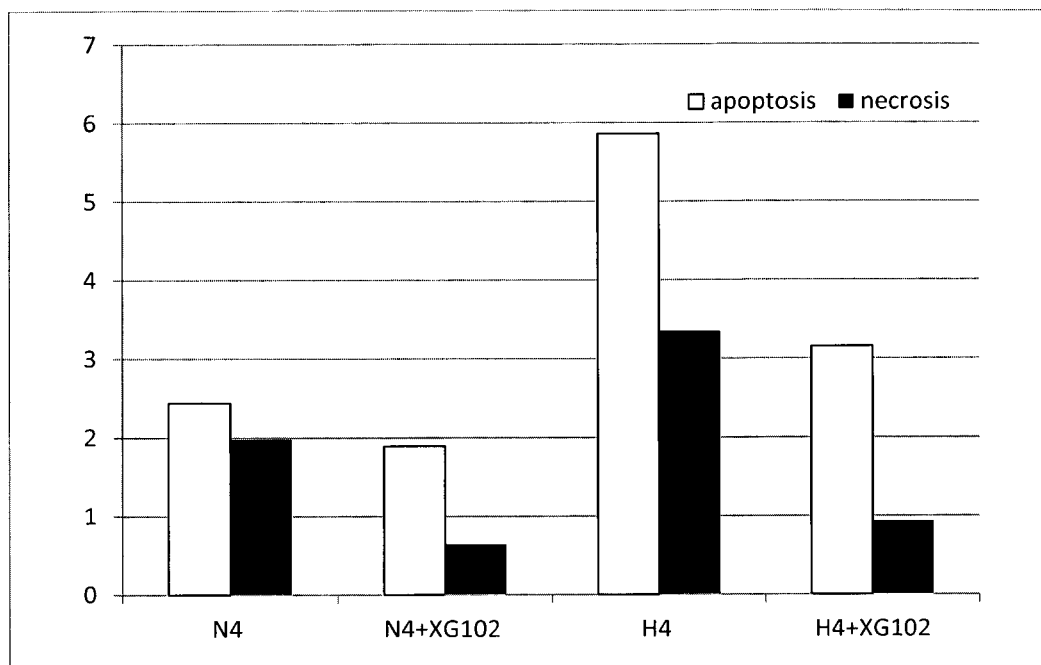


Fig. 81

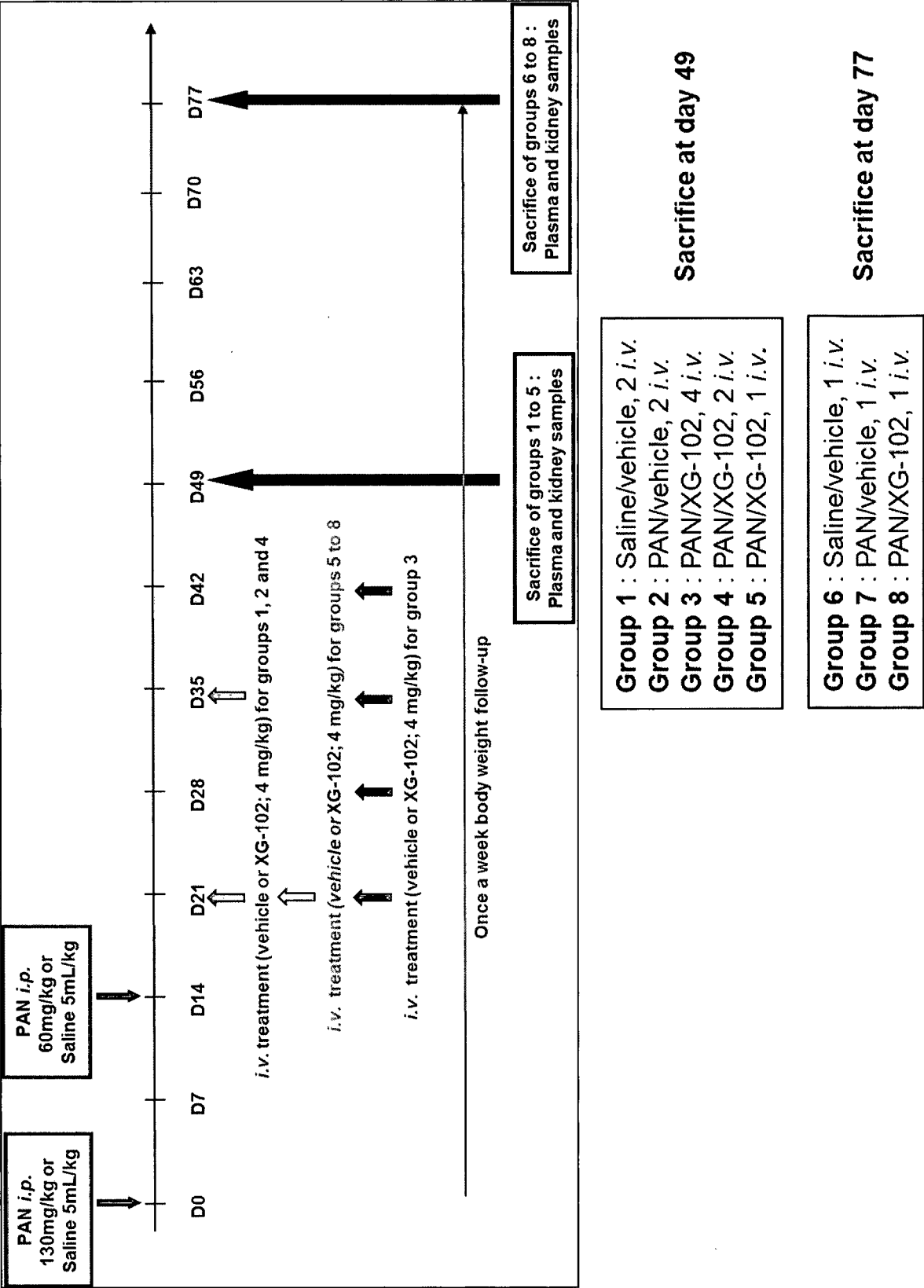


Fig. 82

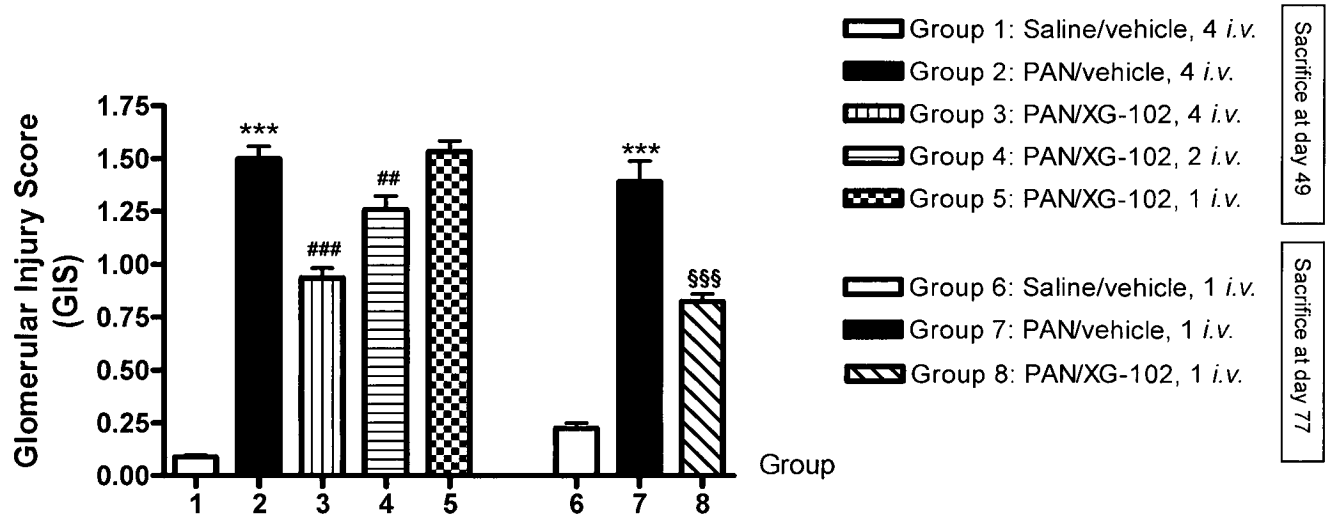


Fig. 83

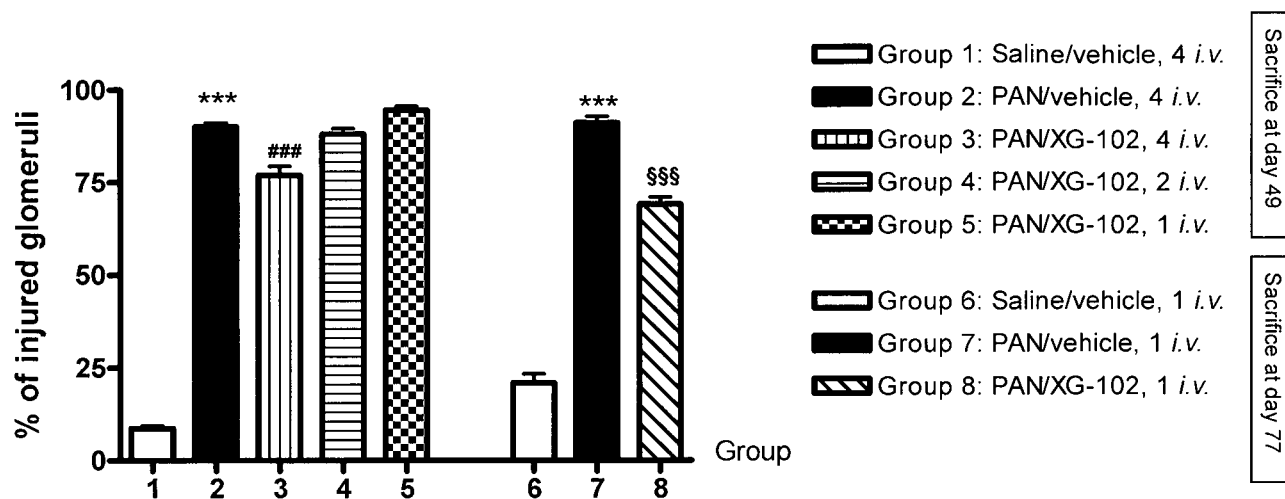


Fig. 84

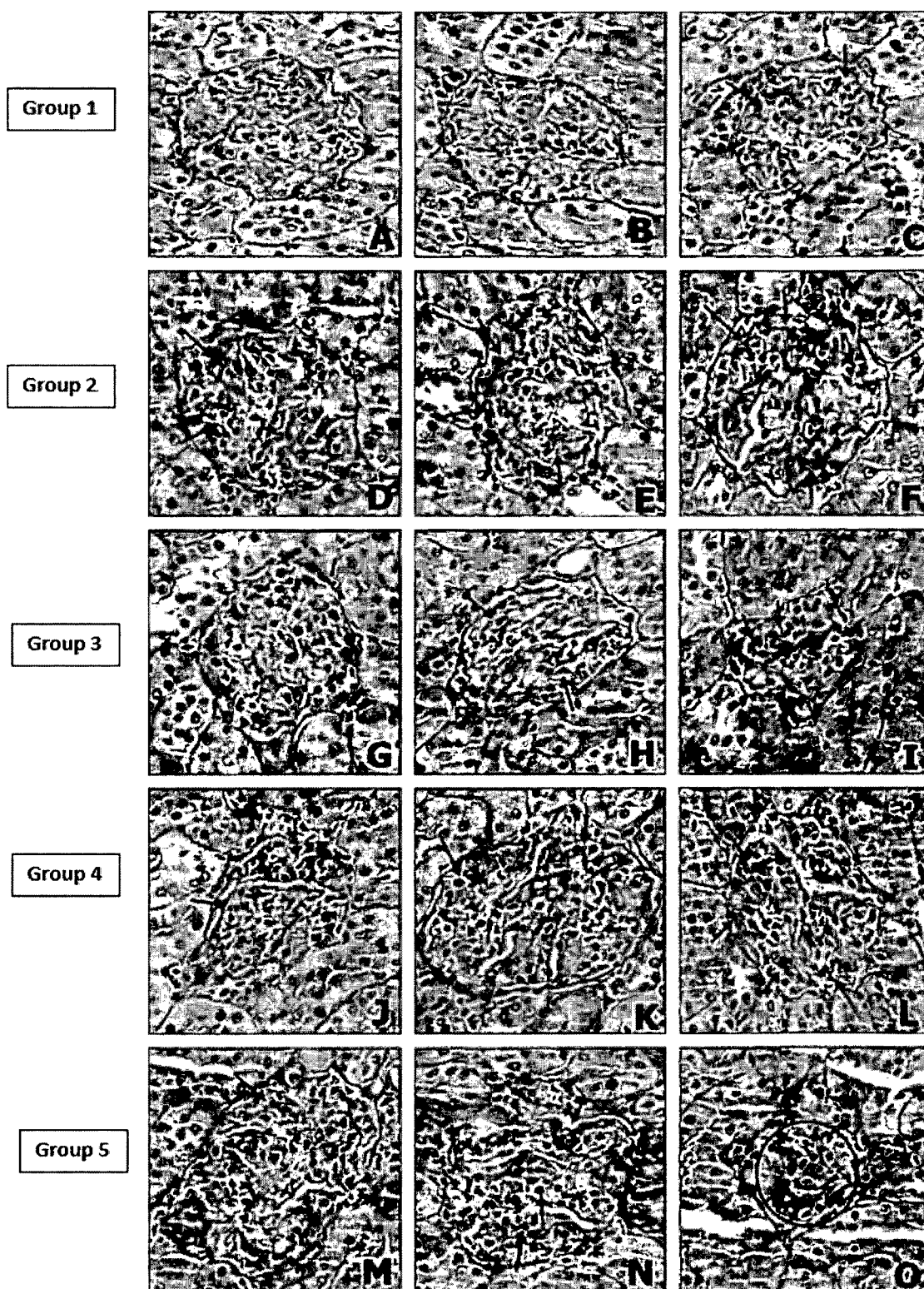


Fig. 85

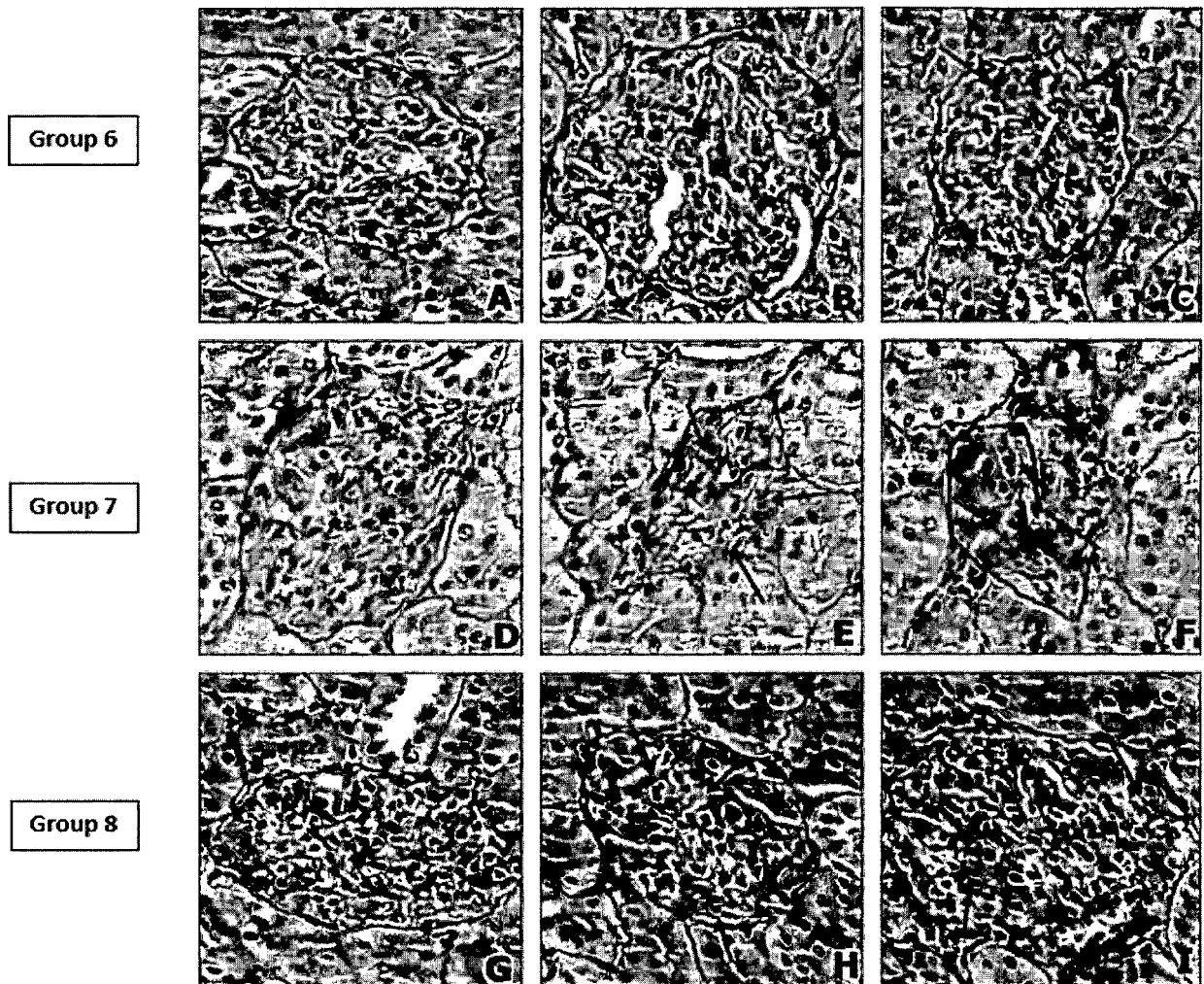
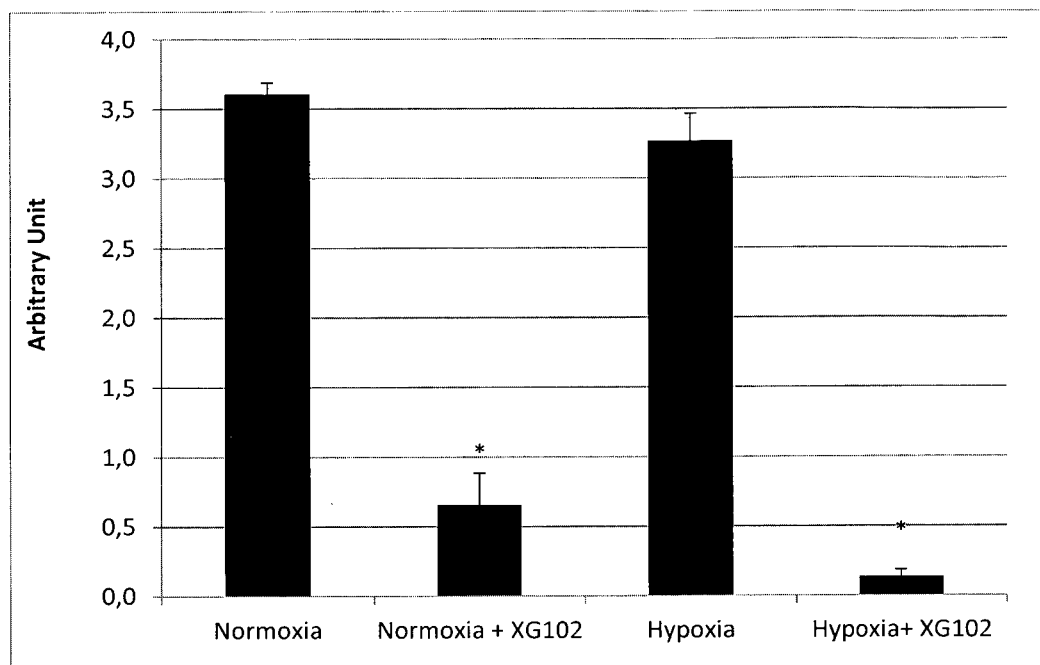
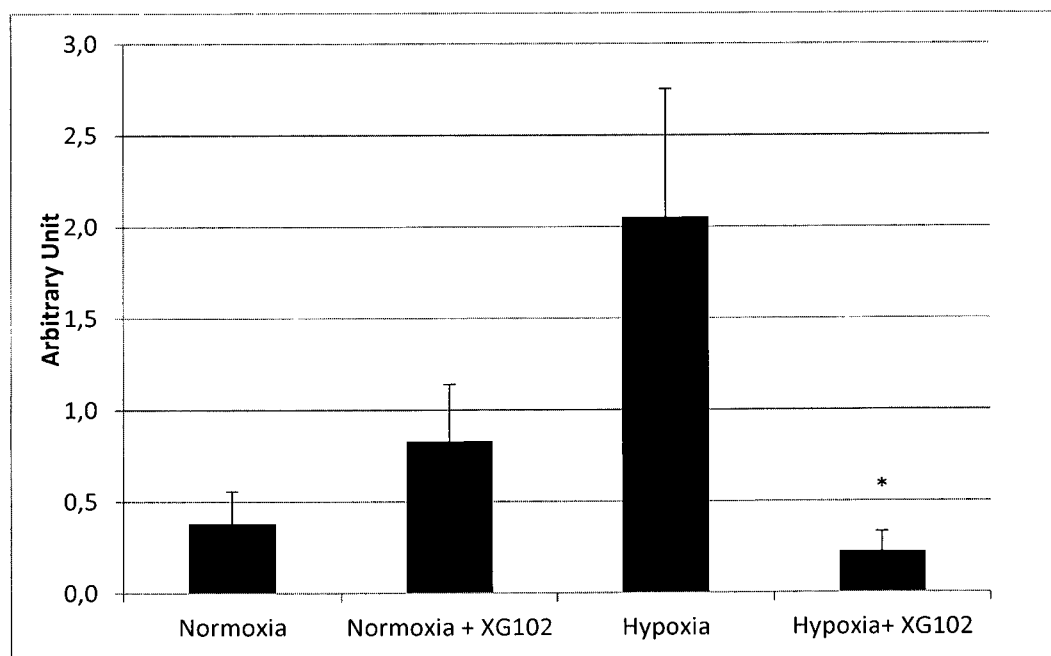


Fig. 86



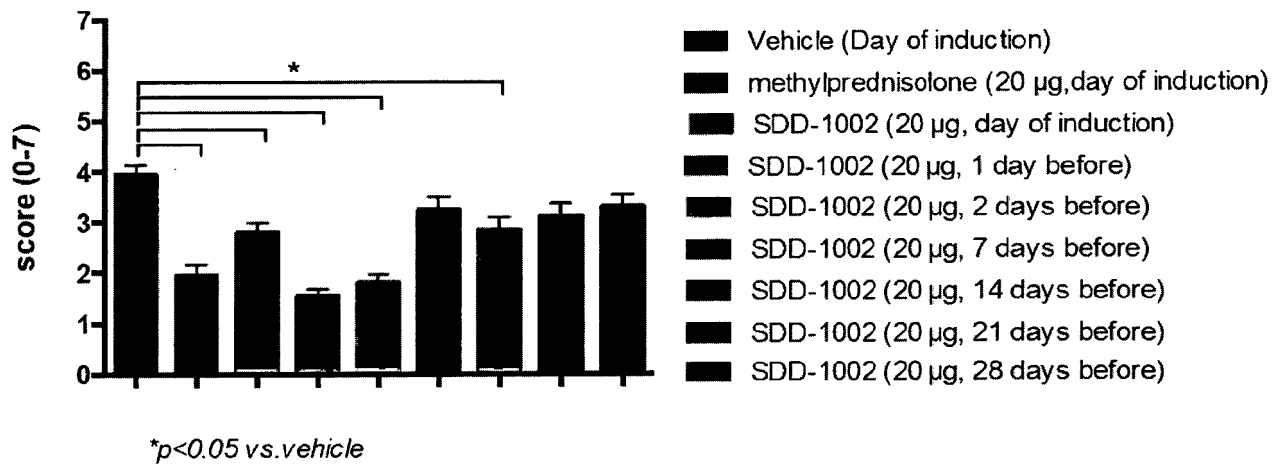
A



B

Fig. 87

A



B

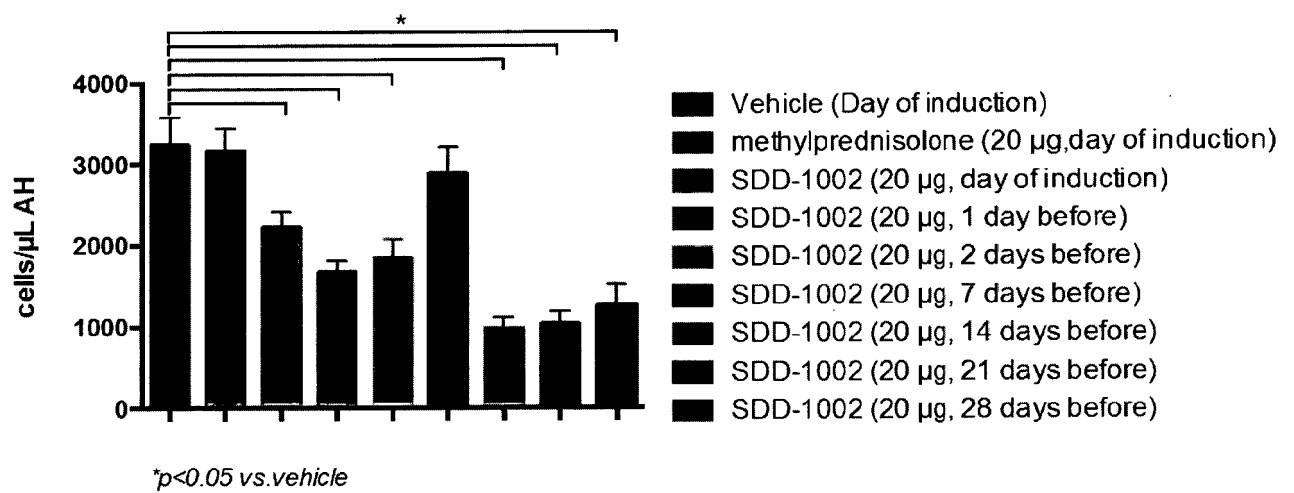
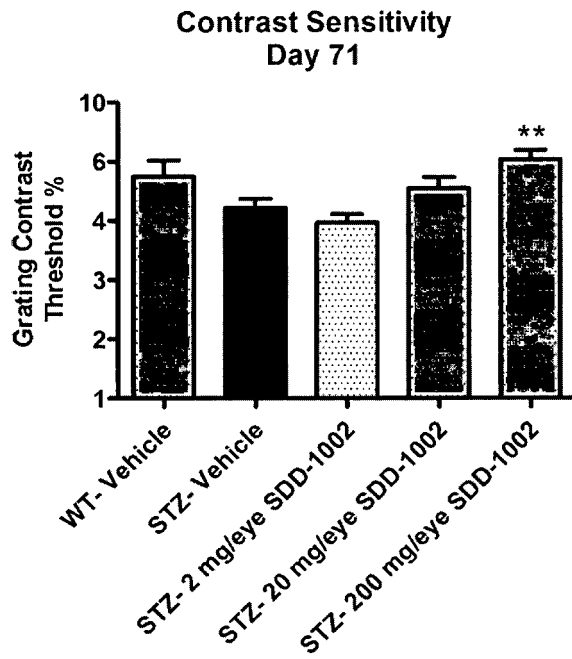
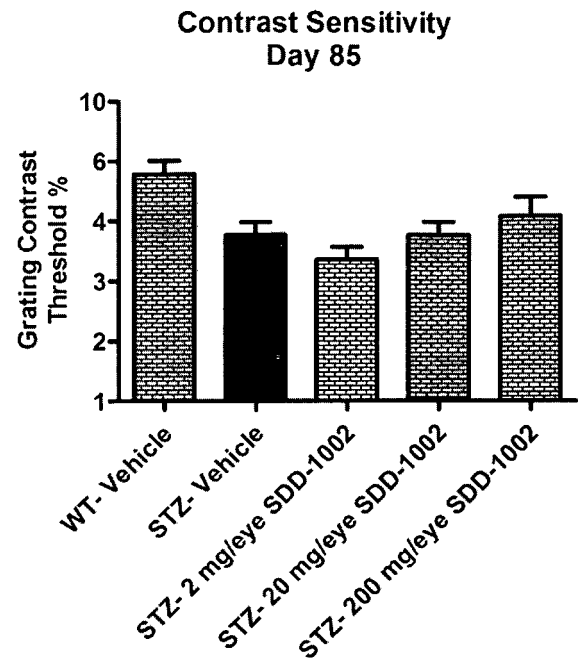


Fig. 88

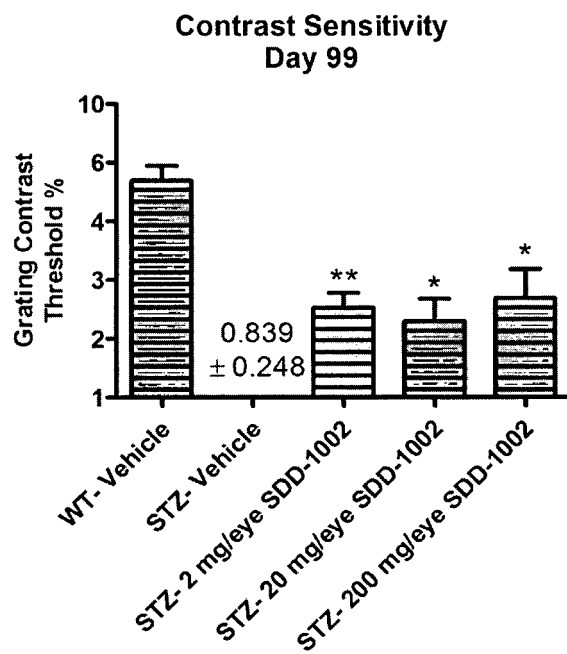
A



B



C



D

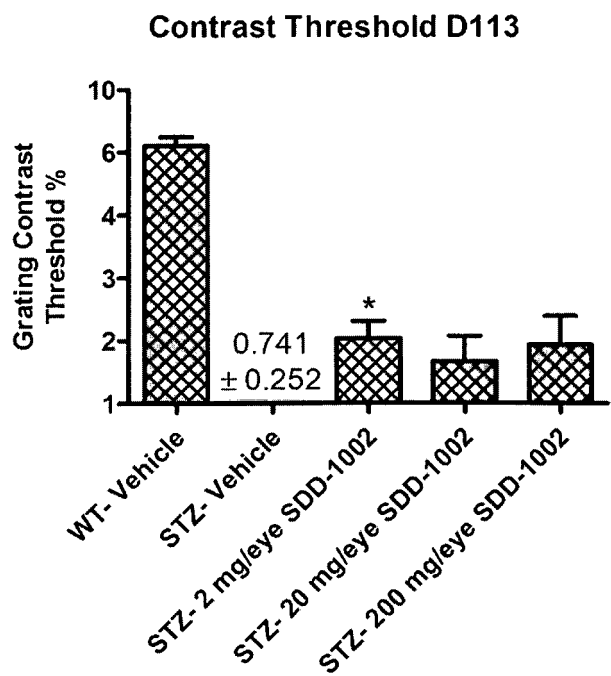


Fig. 89

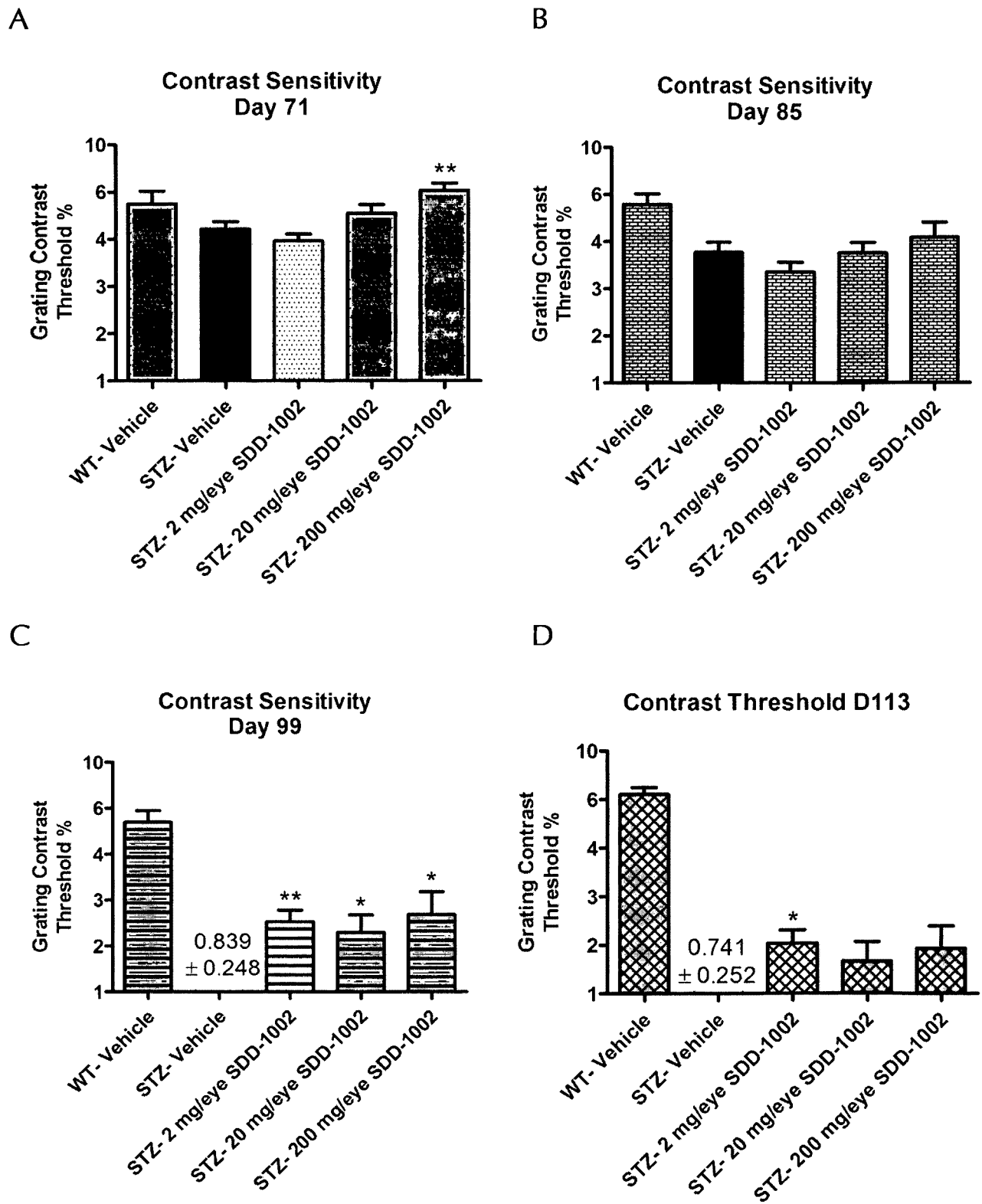


Fig. 90

Retina	Naive- Vehicle		Diabetic- Vehicle		Diabetic- SDD-1002 2 µg/eye		Diabetic- SDD-1002 20 µg/eye	Diabetic- SDD-1002 200 µg/eye
	pg/mg	SEM	pg/mg	SEM	pg/mg	SEM	pg/mg	pg/mg
Protein								
IL-1α	22.373	9.206	26.600	7.373	53.408	19.546	BLQ	BLQ
IL-4	4.487	0.975	4.893	0.664	6.723	1.944	BLQ	BLQ
IL-1β	201.160	60.753	430.250	172.016	28.220	5.511	BLQ	BLQ
IL-2	107.550	37.594	71.600	15.031	209.167	46.984	BLQ	BLQ
IL-6	94.800	23.142	29.200	0.000	133.600	7.933	BLQ	BLQ
IL-13	20.150	7.247	25.343	4.298	18.257	5.329	BLQ	BLQ
IL-10	BLQ		BLQ		BLQ		BLQ	BLQ
IL-12 (p70)	18.080	5.580	23.000	8.698	22.400	2.813	BLQ	BLQ
IFNγ	BLQ		BLQ		BLQ		BLQ	BLQ
IL-5	199.018	52.139	243.600	24.029	309.618	70.244	BLQ	BLQ
IL-17	51.286	15.669	117.000	57.714	82.175	25.046	BLQ	BLQ
IL-18	352.720	58.062	429.218	59.902	421.364	79.811	BLQ	BLQ
MCP-1	63.150	16.784	64.636	12.872	88.891	22.094	BLQ	BLQ
GRO-KC	30.644	12.046	52.520	9.446	65.556	42.157	BLQ	BLQ
VEGF	211.600	21.971	153.550	8.777	103.583	11.802	BLQ	BLQ
RANTES	216.560	38.592	245.980	26.700	219.680	38.629	BLQ	BLQ
EPO	351.700	52.901	469.300	50.835	468.785	61.099	BLQ	BLQ
IL-7	214.133	76.681	663.500	28.990	130.067	24.063	BLQ	BLQ
M-CSF	18.333	1.415	19.875	3.551	8.200	0.000	BLQ	BLQ
MIP-3α	169.360	26.829	125.127	22.776	202.422	29.856	BLQ	BLQ
G-CSF	1.597	0.346	1.450	0.179	1.253	0.244	BLQ	BLQ
GM-CSF	5.043	1.067	180.138	154.233	7.357	2.577	BLQ	BLQ
TNFα	348.444	50.983	181.800	42.499	184.920	26.576	BLQ	BLQ

*BLQ= Below Limit of Quantification

Fig. 91

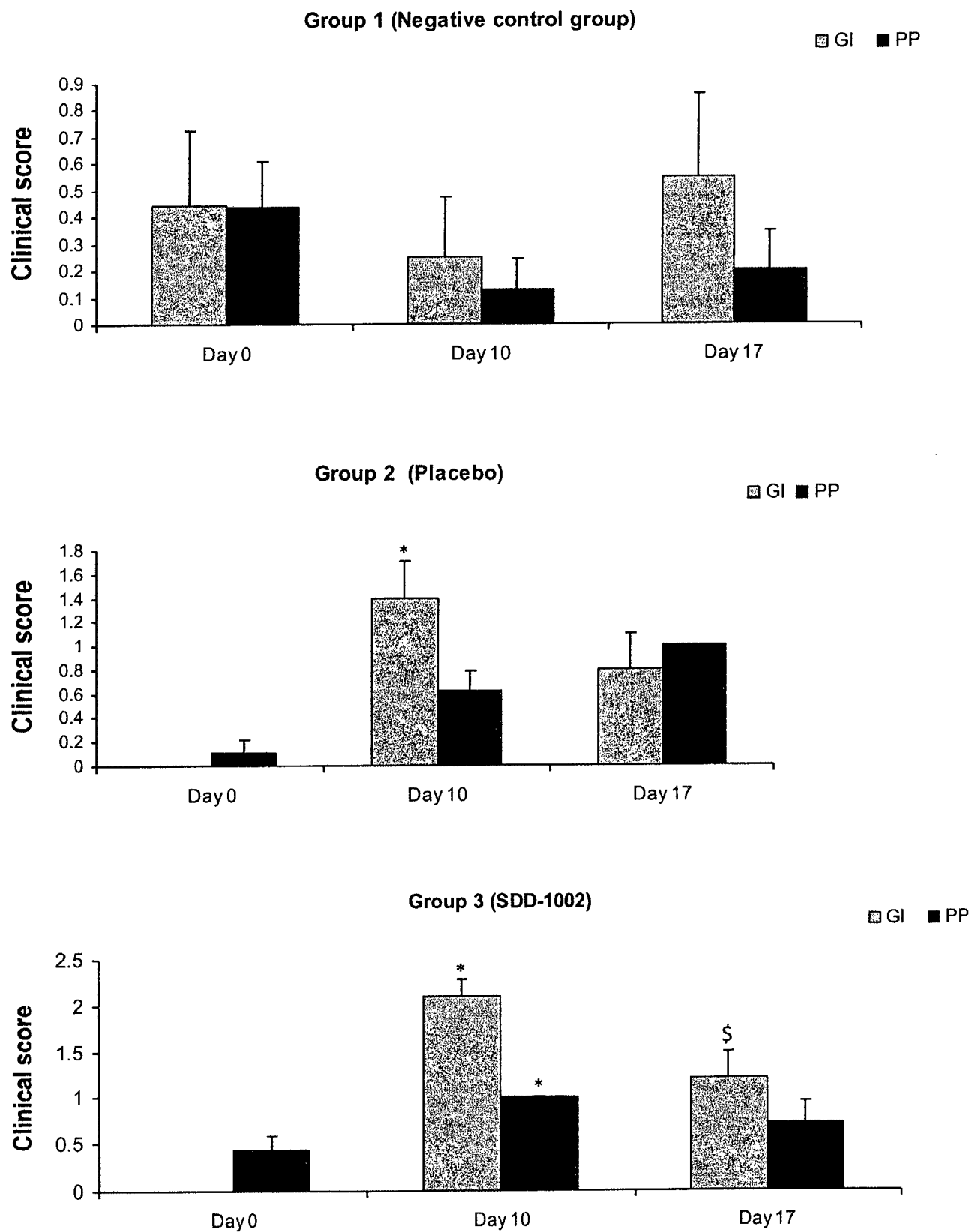


Fig. 92

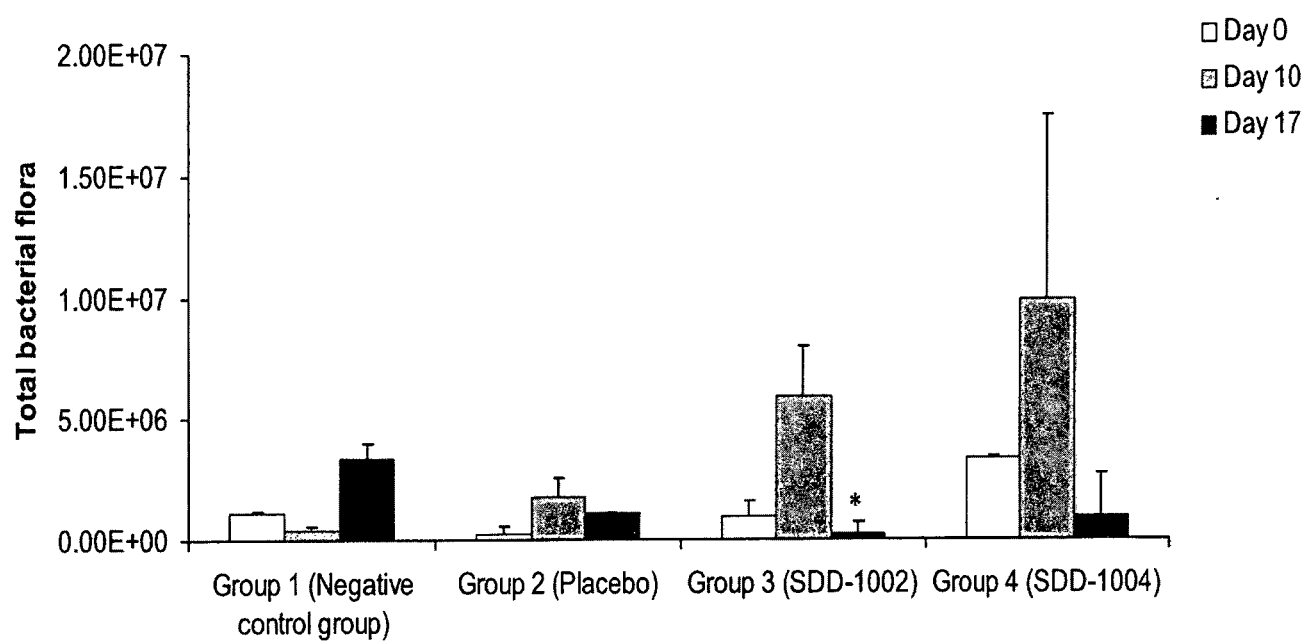


Fig. 93

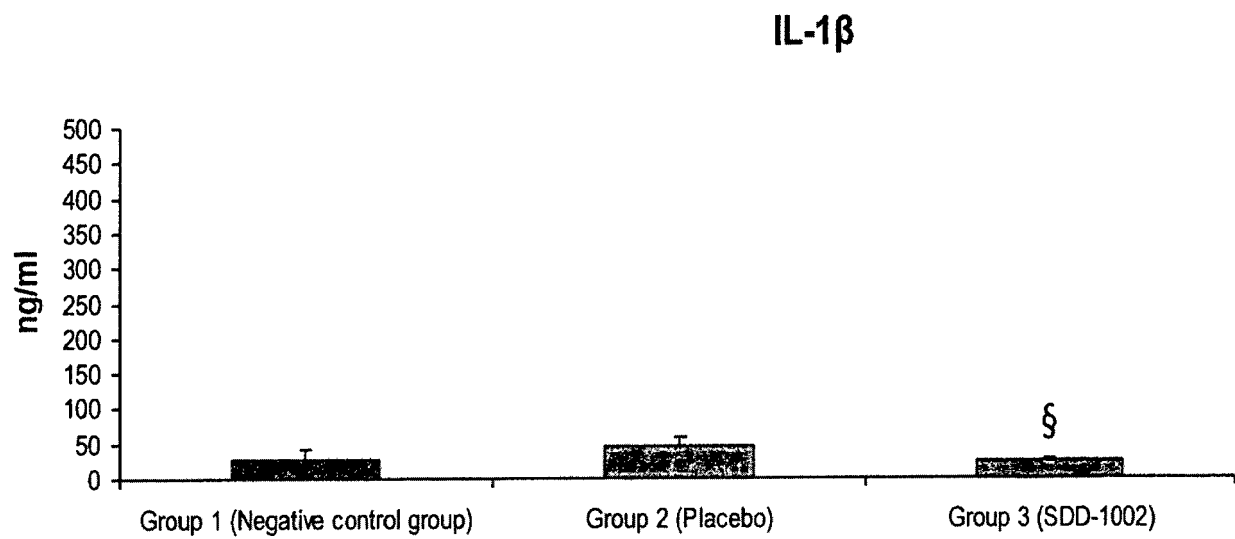


Fig. 94

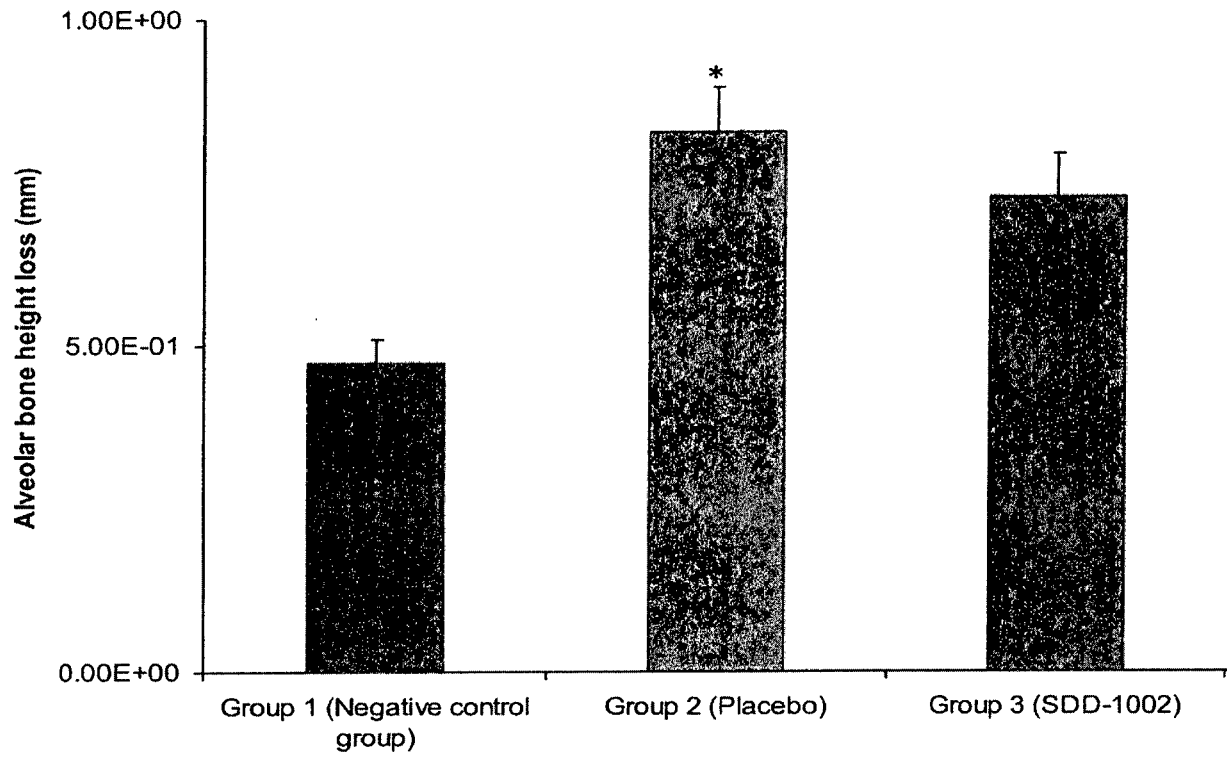


Fig. 95

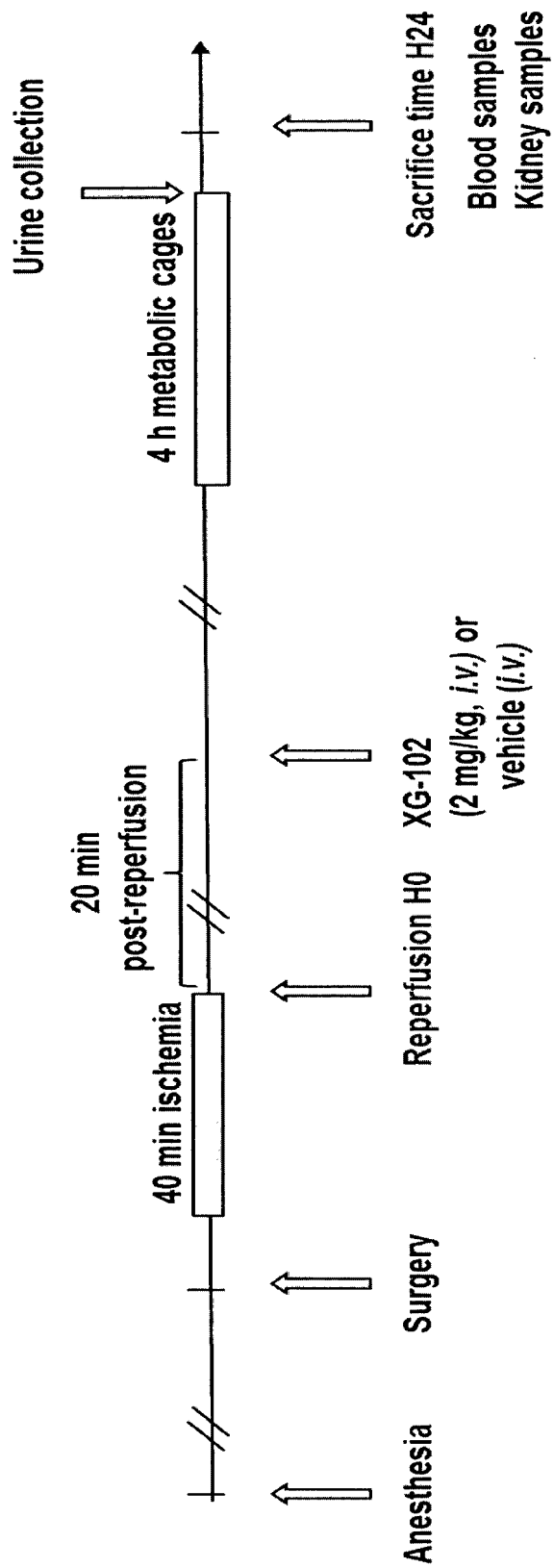


Fig. 96

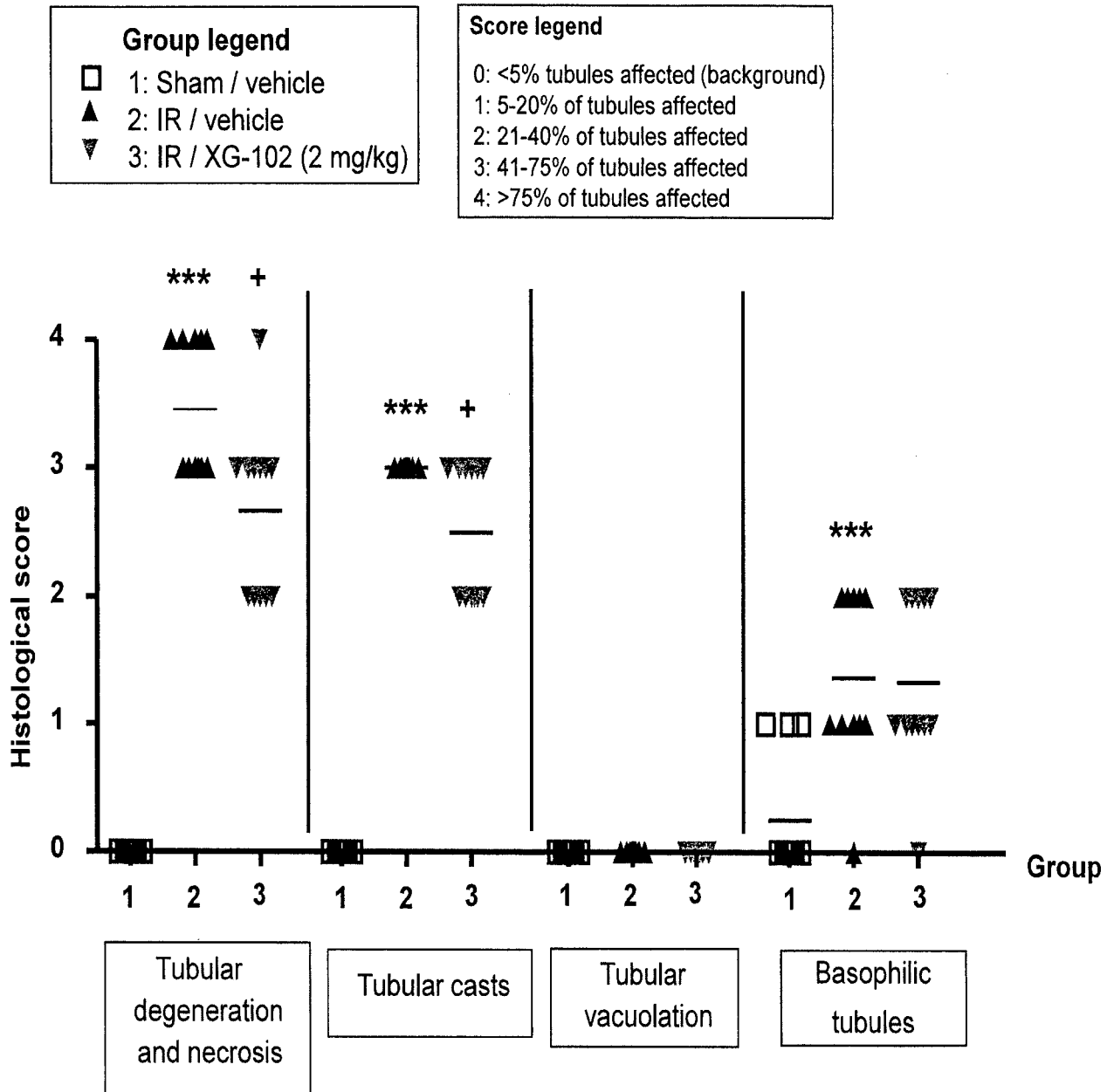


Fig. 97

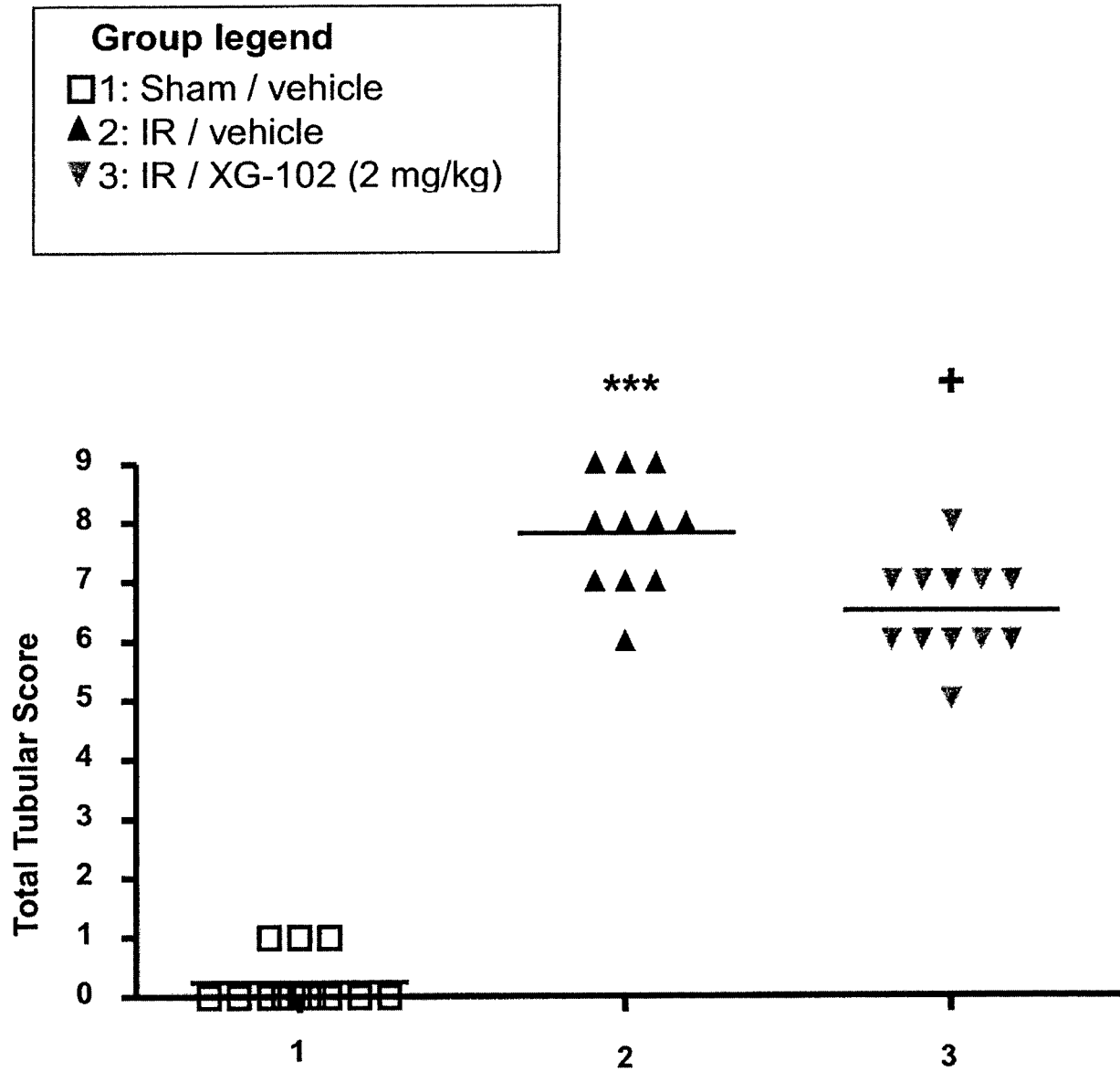


Fig. 98

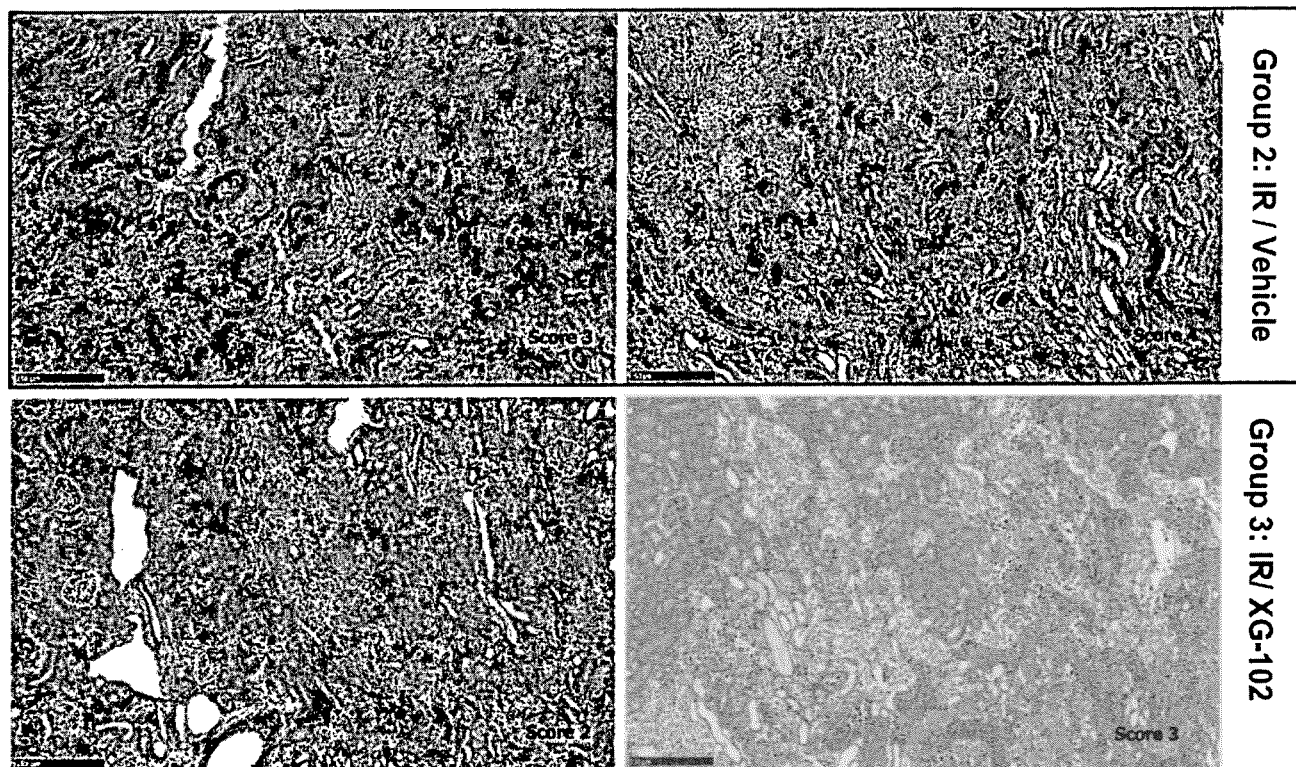
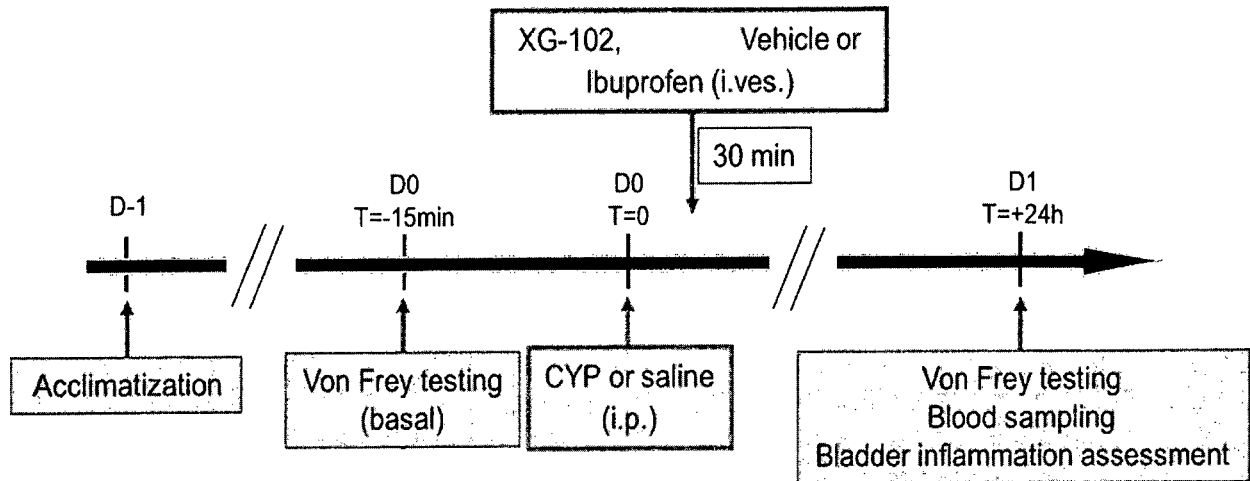


Fig. 99

A



B

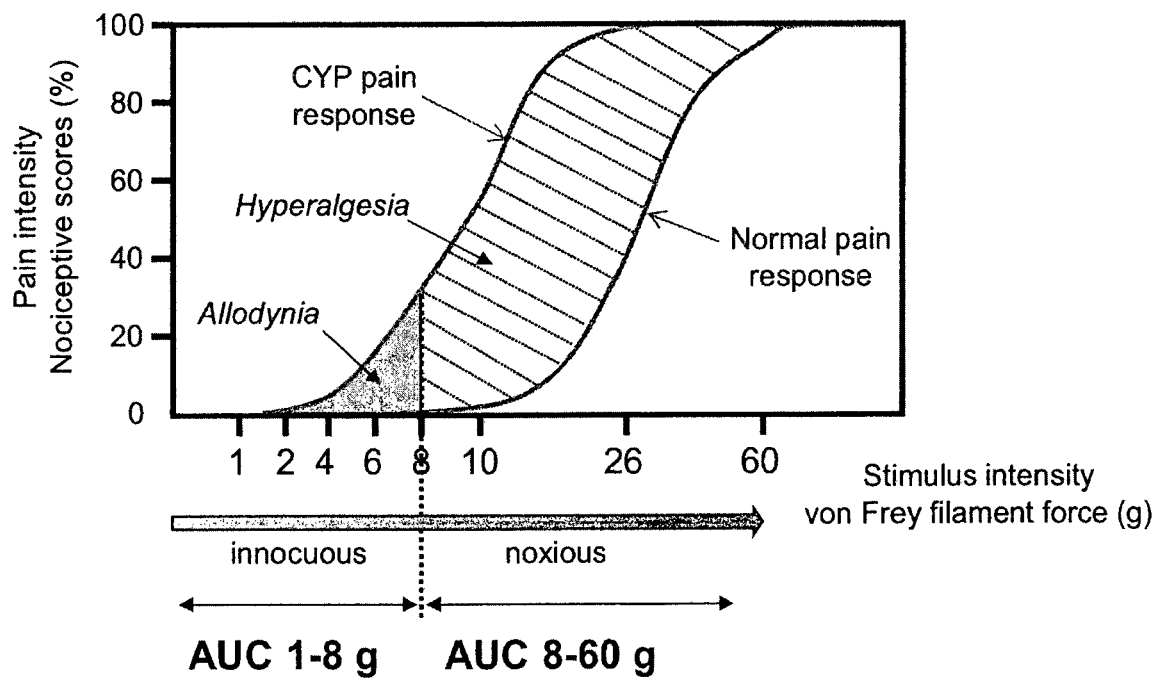
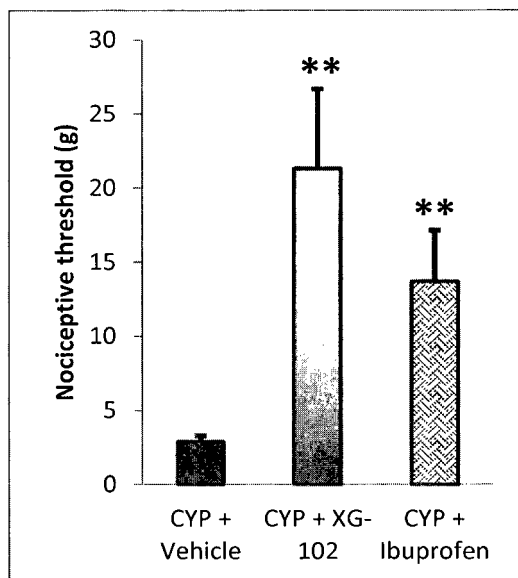
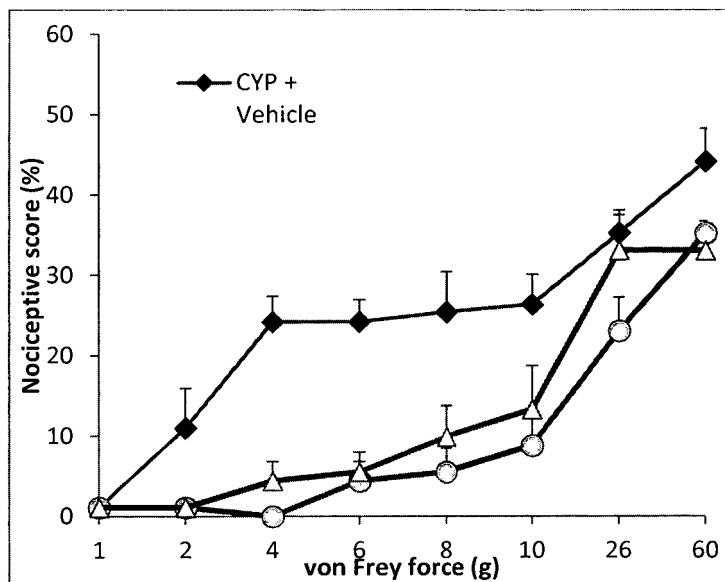


Fig. 100

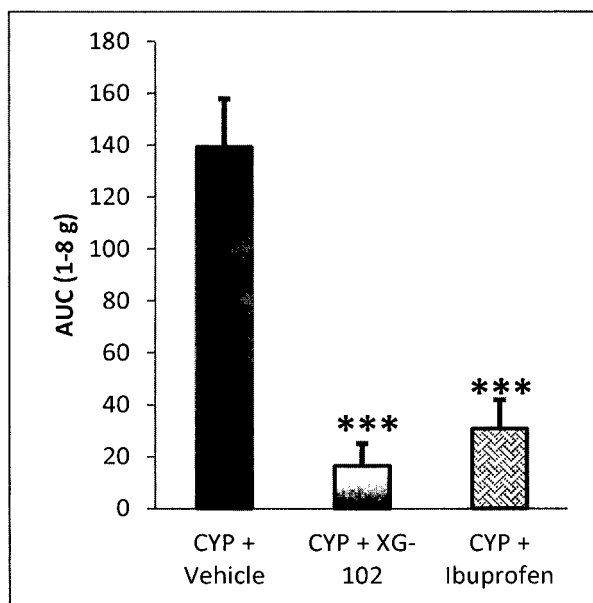
A



B



C



D

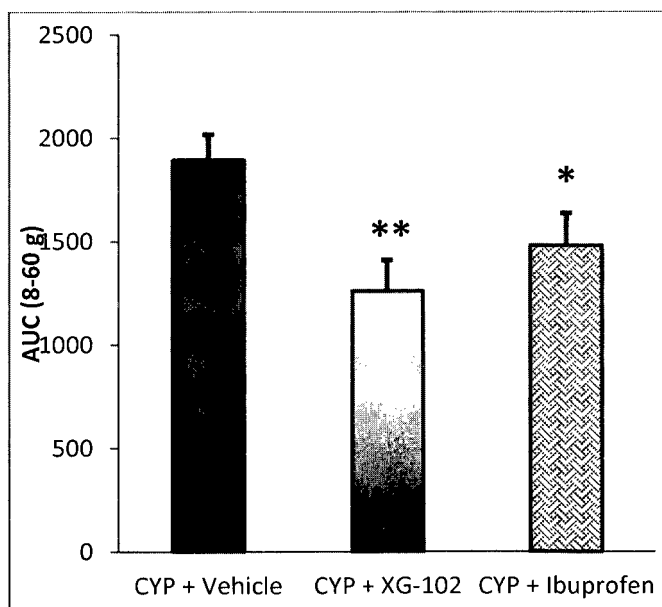
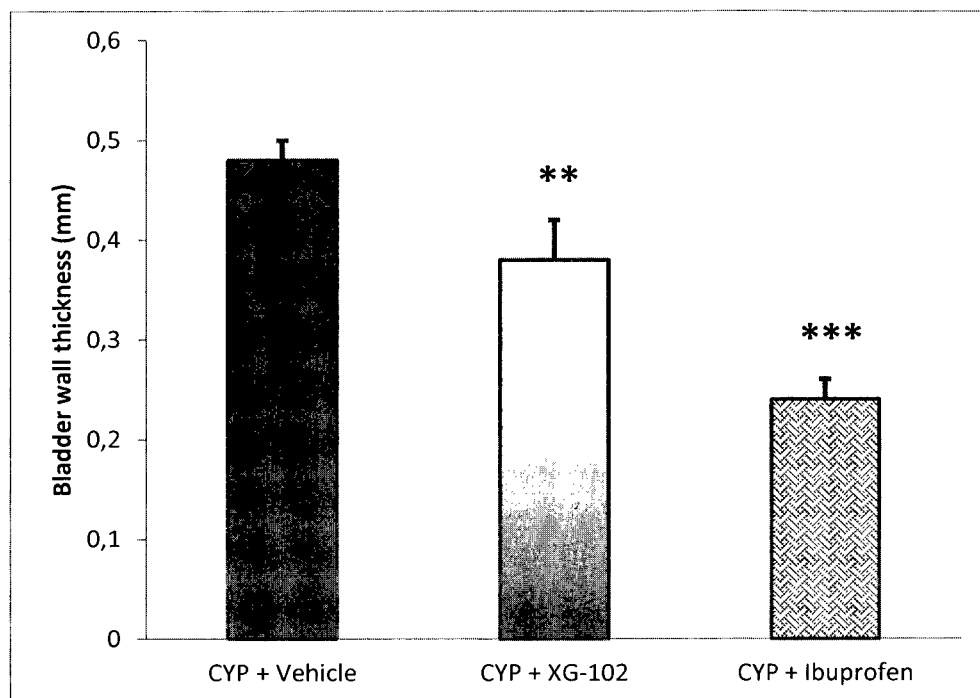


Fig. 101

A



B

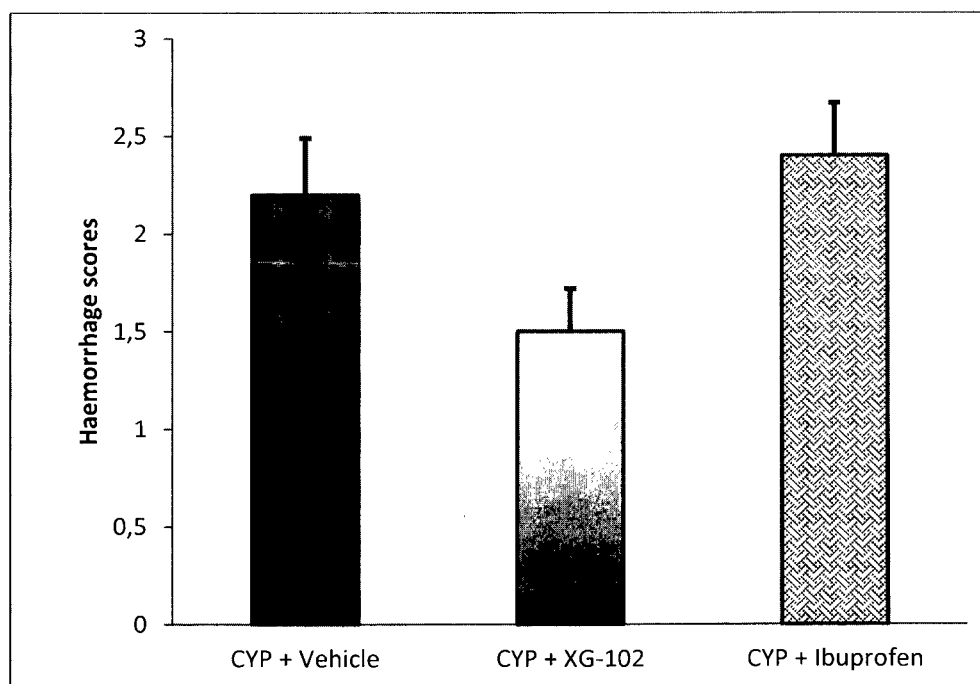


Fig. 102

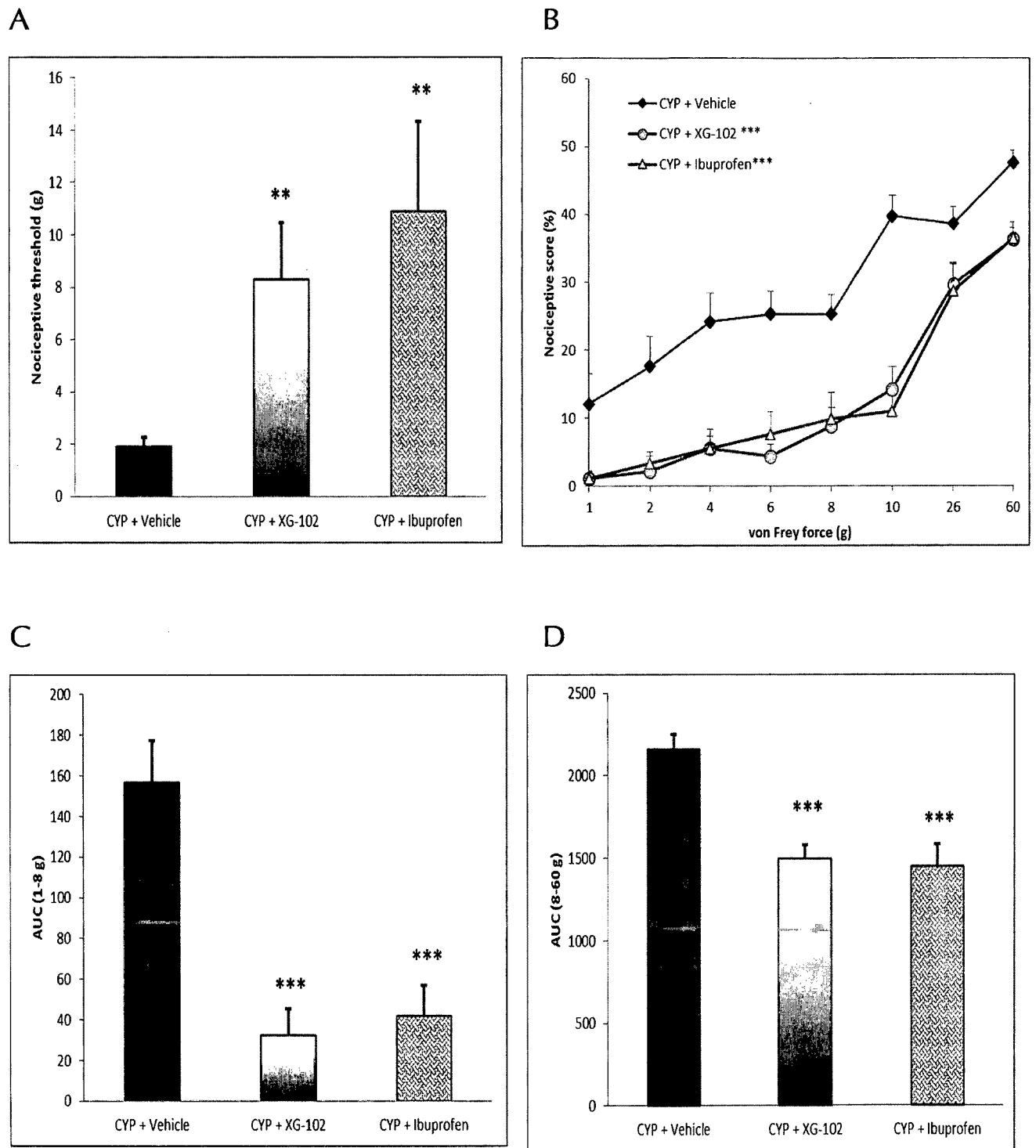
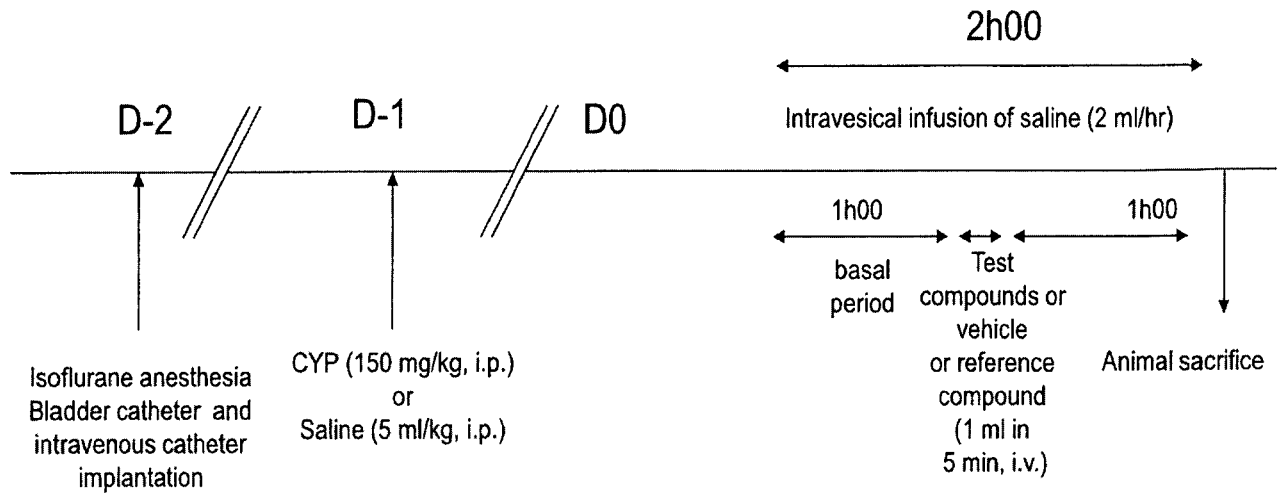


Fig. 103

A



B

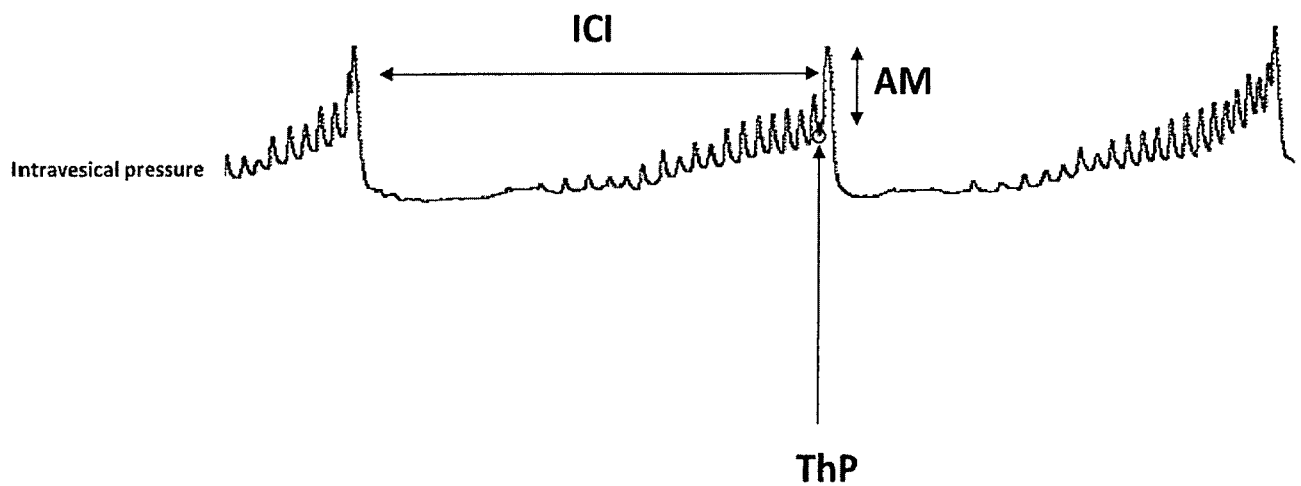


Fig. 104

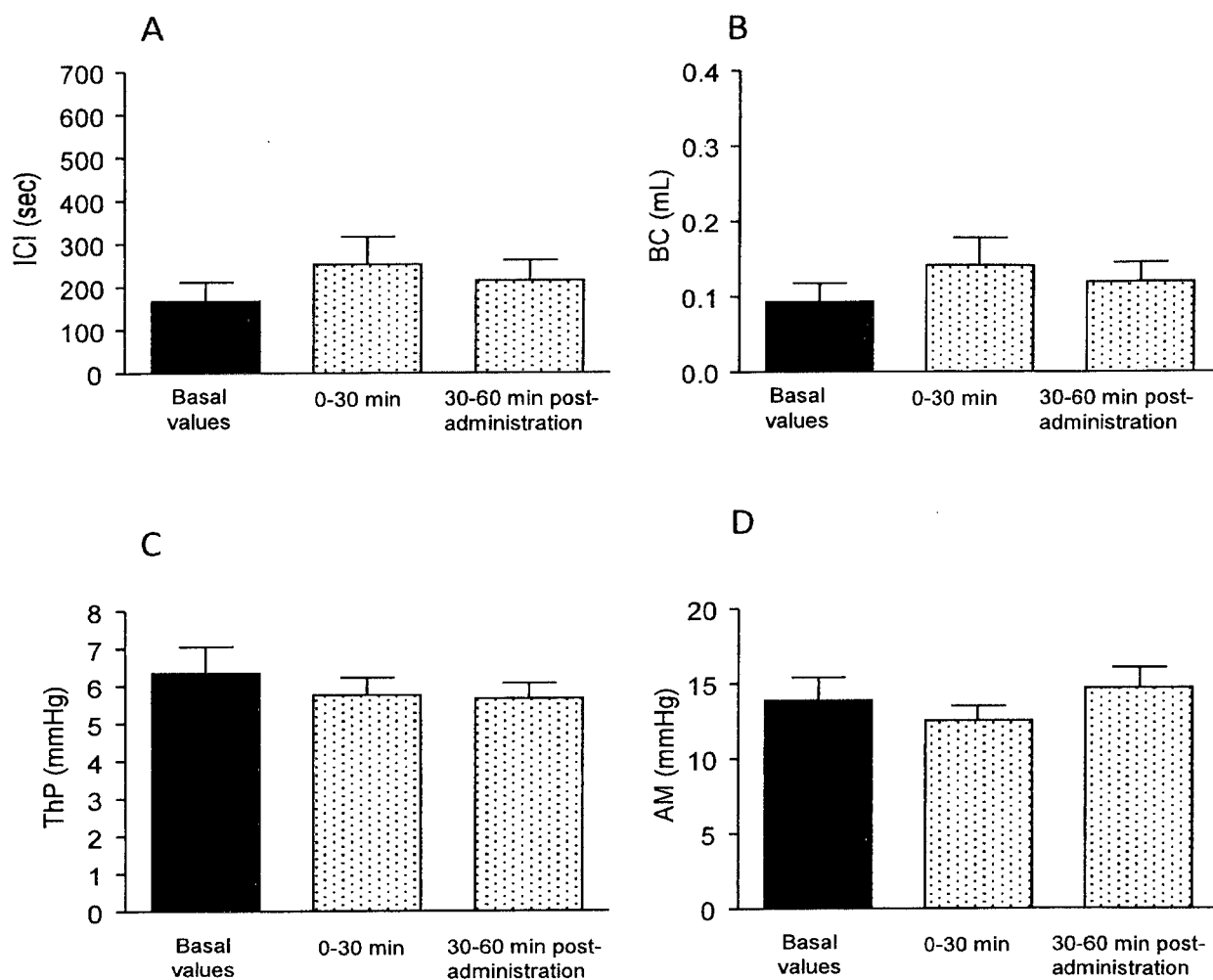


Fig. 105

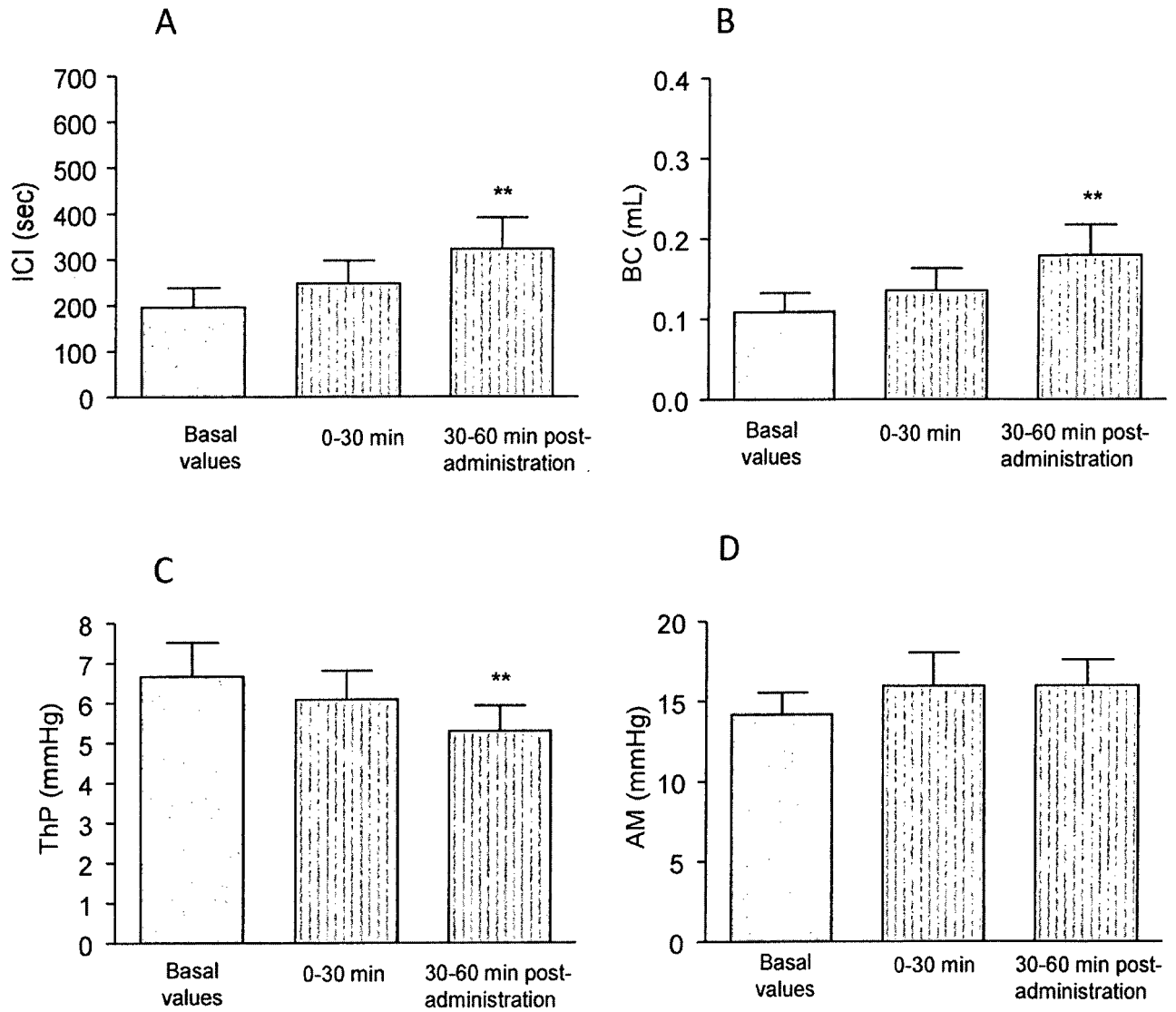
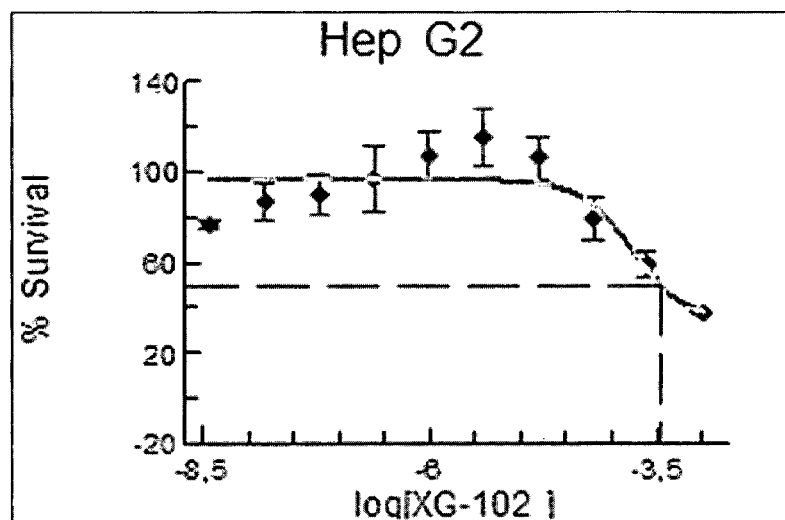


Fig. 106

A



B

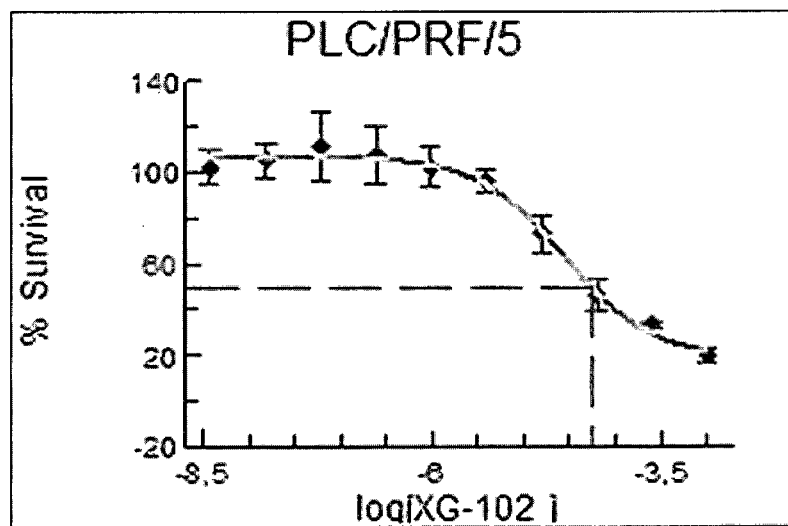


Fig. 107

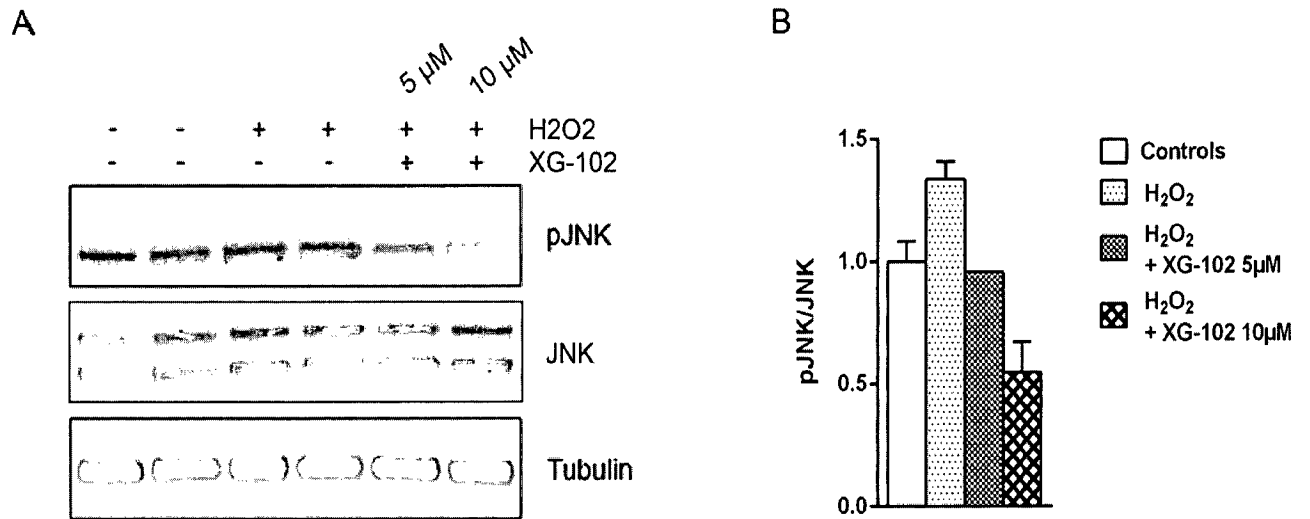


Fig. 108

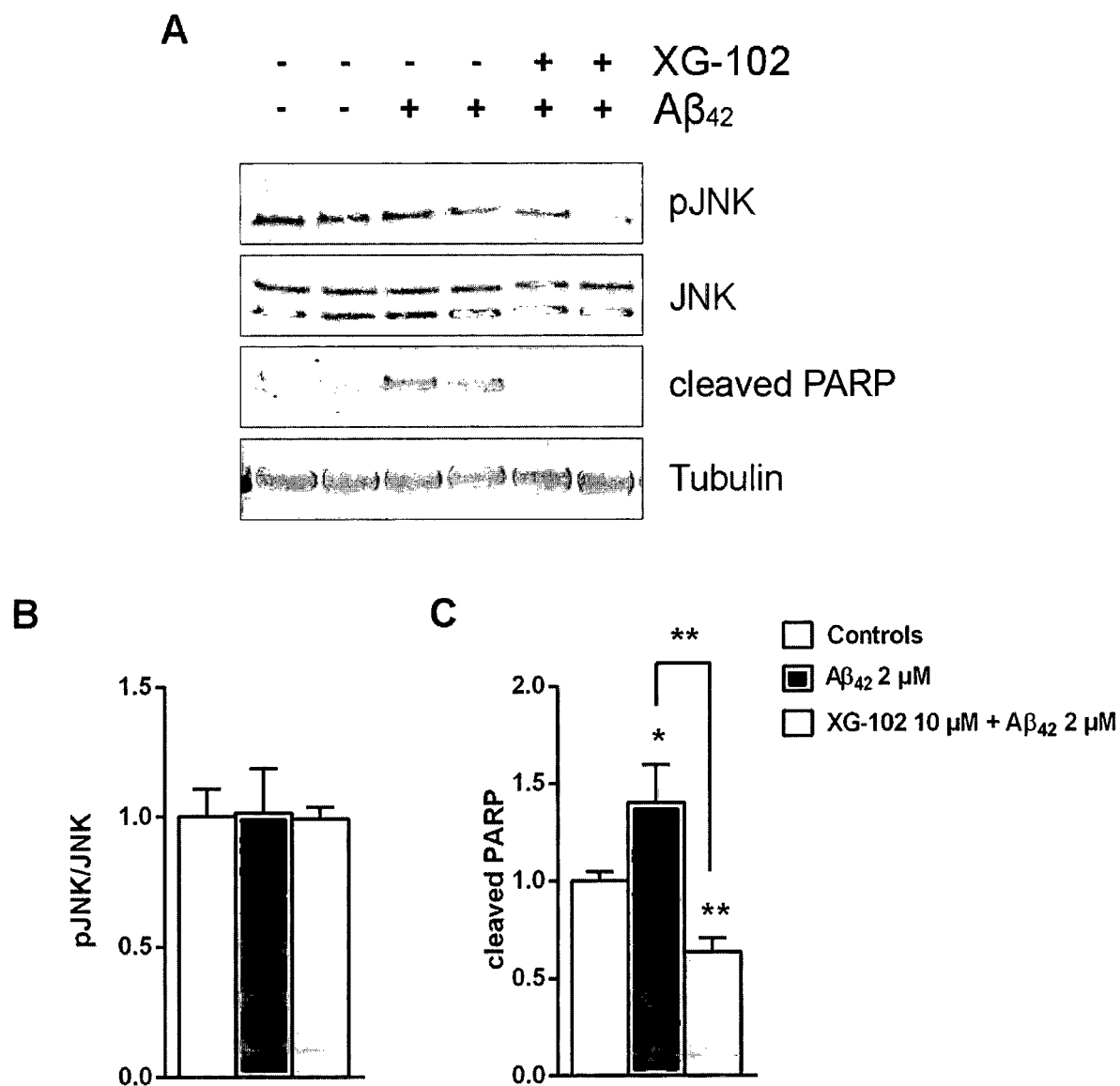


Fig. 109

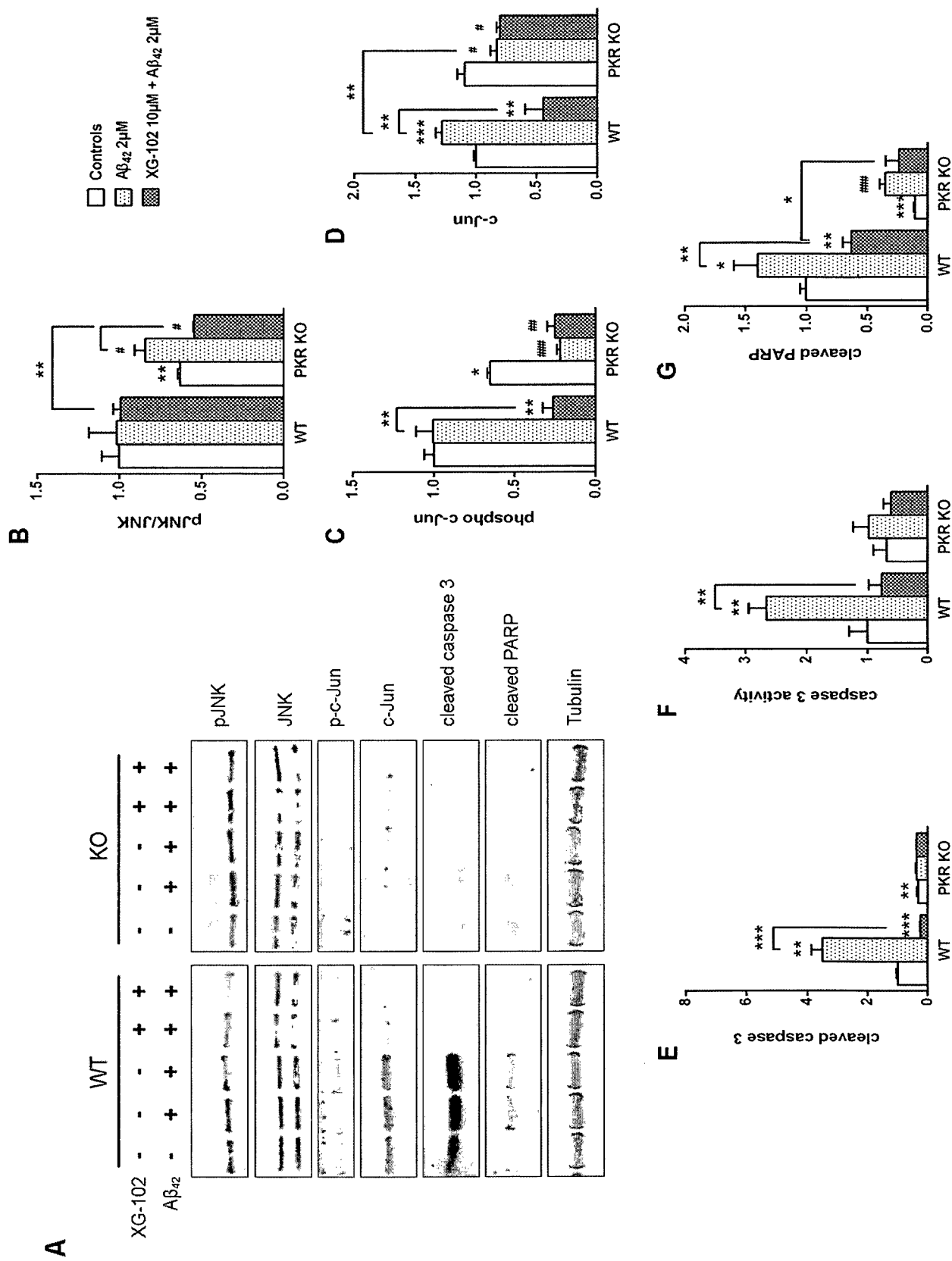


Fig. 110