FIGURE 1A

CA019_969 Ab sequences

CDR-L1

LASEDIYDNLA SEQ ID NO:1

CDRL2

YASSLQD SEQ ID NO:2

CDR-L3

LQDSEYPWT SEQ ID NO:3

CDR-H1

GFSLTTYGMGVG SEQ ID NO:4

CDR-H2

NIWWDDDKYYNPSLKN SEQ ID NO:5

CDR-H3

IGPIKYPTAPYRYFDF SEQ ID NO:6

FIGURE 1B

Rat Ab 969 VL region SEQ ID NO:7

DIQMTQSPAS LSASLGETVS IECLASEDIY DNLAWYQKKP GKSPHLLIYY
ASSLQDGVPS RFSGSGSGTQ YSLKINSLES EDAATYFCLQ DSEYPWTFGG
GTKLELK

Rat Ab 969 VL region SEQ ID NO:8

gacatccaga tgacacagtc tccagcttcc ctgtctgcat ctctgggaga
aactgtctcc atcgaatgtc tagcaagtga ggacatttac gataatttag
cgtggtacca gaagaagcca ggaaaatctc ctcacctcct catctattat
gcaagtagct tgcaagatgg ggtcccatca cggttcagtg gcagtggatc
tggcacacag tattctctca aaatcaacag cctggaatct gaagatgctg
cgacttattt ctgtctacag gattctgagt atccgtggac gttcggtgga
ggcaccaagc tggaattgaa a

Rat Ab 969 VL region with signal sequence underlined and italicised SEQ ID NO:9

MGVPTQLLVL LLLWITDAIC DIQMTQSPAS LSASLGETVS IECLASEDIY
DNLAWYQKKP GKSPHLLIYY ASSLQDGVPS RFSGSGSGTQ YSLKINSLES
EDAATYFCLQ DSEYPWTFGG GTKLELK

Rat Ab 969 VL region with signal sequence underlined and italicised SEQ ID NO:10

atgggtgtcc ccactcagct cttggtgttg ttgctgctgt ggattacaga
tgccatatgt gacatccaga tgacacagtc tccagcttcc ctgtctgcat
ctctgggaga aactgtctcc atcgaatgtc tagcaagtga ggacatttac
gataatttag cgtggtacca gaagaagcca ggaaaatctc ctcacctcct
catctattat gcaagtagct tgcaagatgg ggtcccatca cggttcagtg
gcagtggatc tggcacacag tattctctca aaatcaacag cctggaatct
gaagatgctg cgacttattt ctgtctacag gattctgagt atccgtggac
gttcggtgga ggcaccaagc tggaattgaa a

Rat Ab 969 VH region SEQ ID NO:11

QVTLKESGPG ILQPSQTLSL TCTFSGFSLT TYGMGVGWIR QPSGKGLEWL
ANIWWDDDKY YNPSLKNRLT ISKDTSNNQA FLKLTNVHTS DSATYYCARI
GPIKYPTAPY RYFDFWGPGT MVTVS

Rat Ab 969 VH region SEQ ID NO:12

caggttactc tgaaagagtc tggccctggg atattgcagc cctcccagac
cctcagtctg acttgcactt tctctgggtt ttcactgacc acttatggta
tgggtgtggg ctggattcgt cagccttcag ggaagggtct ggagtggctg
gcaaacattt ggtgggatga tgataagtat tacaatccat ctctgaaaaa
ccggctcaca atctccaagg acacctccaa caaccaagca ttcctcaagc

tcaccaatgt acacacttca gattctgcca catactactg tgctcggata
gggccgatta aatacccgac ggccccctac cggtactttg acttctgggg
cccaggaacc atggtcaccg tctcg

Rat Ab 969 VH region with signal sequence underlined and italicised SEQ ID NO:13

MDRLTSSFLL LIVPAYVLSQ VTLKESGPGI LQPSQTLSLT CTFSGFSLTT
YGMGVGWIRQ PSGKGLEWLA NIWWDDDKYY NPSLKNRLTI SKDTSNNQAF
LKLTNVHTSD SATYYCARIG PIKYPTAPYR YFDFWGPGTM VTVS

Rat Ab 969 VH region with signal sequence underlined and italicised SEQ ID NO:14

atggacaggc ttacttcctc attcctactg ctgattgtcc ctgcatatgt
*cctgtct*cag gttactctga aagagtctgg ccctgggata ttgcagccct
cccagaccct cagtctgact tgcactttct ctgggttttc actgaccact
tatggtatgg gtgtgggctg gattcgtcag ccttcaggga agggtctgga
gtggctggca aacatttggt gggatgatga taagtattac aatccatctc
tgaaaaaccg gctcacaatc tccaaggaca cctccaacaa ccaagcattc
ctcaagctca ccaatgtaca cacttcagat tctgccacat actactgtgc
tcggataggg ccgattaaat acccgacggc cccctaccgg tactttgact
tctggggccc aggaaccatg gtcaccgtct cg

FIBURE 1C

969 gL7 V-region SEQ ID NO:15

DIQMTQSPSS LSASVGDRVT ITCLASEDIY DNLAWYQQKP GKAPKLLIYY
ASSLQDGVPS RFSGSGSGTD YTLTISSLQP EDFATYYCLQ DSEYPWTFGG
GTKVEIK

969 gL7 V-region SEQ ID NO:16

gacatacaga tgactcagtc accctcaagc ctgagtgcca gtgtgggaga
cagggtgaca atcacctgtc tggcctccga ggatatctac gataacctgg
catggtatca gcagaaacct ggaaaggctc ccaagctcct gatttattat
gcctcctctc tccaagacgg cgttccatct cggttcagcg gaagcggctc
cgggacggat tacacactga caattagctc tctgcaaccg gaggattttg
ctacttacta ctgcctgcaa gactccgaat acccatggac cttcggtggt
ggcaccaaag tggaaatcaa g

969 gL7 V-region with signal sequence underlined and italicized SEQ ID NO:17

MSVPTQVLGL LLLWLTDARC DIQMTQSPSS LSASVGDRVT ITCLASEDIY
DNLAWYQQKP GKAPKLLIYY ASSLQDGVPS RFSGSGSGTD YTLTISSLQP
EDFATYYCLQ DSEYPWTFGG GTKVEIK

969 gL7 V-region with signal sequence underlined and italicized SEQ ID NO:18

atgagcgtgc ctactcaagt cttggggctg ctcttgcttt ggcttaccga
cgcaagatgc gacatacaga tgactcagtc accctcaagc ctgagtgcca
gtgtgggaga cagggtgaca atcacctgtc tggcctccga ggatatctac
gataacctgg catggtatca gcagaaacct ggaaaggctc ccaagctcct
gatttattat gcctcctctc tccaagacgg cgttccatct cggttcagcg
gaagcggctc cgggacggat tacacactga caattagctc tctgcaaccg
gaggattttg ctacttacta ctgcctgcaa gactccgaat acccatggac
cttcggtggt ggcaccaaag tggaaatcaa g

969 gL7 light chain (V + constant) SEQ ID NO:19

DIQMTQSPSS LSASVGDRVT ITCLASEDIY DNLAWYQQKP GKAPKLLIYY
ASSLQDGVPS RFSGSGSGTD YTLTISSLQP EDFATYYCLQ DSEYPWTFGG
GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV
DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG
LSSPVTKSFN RGEC

969 gL7 light chain (V + constant) SEQ ID NO:20

gacatacaga tgactcagtc accctcaagc ctgagtgcca gtgtgggaga
cagggtgaca atcacctgtc tggcctccga ggatatctac gataacctgg

catggtatca gcagaaacct ggaaaggctc ccaagctcct gatttattat
gcctcctctc tccaagacgg cgttccatct cggttcagcg gaagcggctc
cgggacggat tacacactga caattagctc tctgcaaccg gaggattttg
ctacttacta ctgcctgcaa gactccgaat acccatggac cttcggtggt
ggcaccaaag tggaaatcaa gcgtacggta gcggccccat ctgtcttcat
cttcccgcca tctgatgagc agttgaaatc tggaactgcc tctgttgtgt
gcctgctgaa taacttctat cccagagagg ccaaagtaca gtggaaggtg
gataacgccc tccaatcggg taactcccag gagagtgtca cagagcagga
cagcaaggac agcacctaca gcctcagcag caccctgacg ctgagcaaag
cagactacga gaaacacaaa gtctacgcct gcgaagtcac ccatcagggc
ctgagctcgc ccgtcacaaa gagcttcaac aggggagagt gt

969 gL7 light chain (V + constant) with signal sequence underlined and italicized SEQ ID NO:21

MSVPTQVLGL LLLWLTDARC DIQMTQSPSS LSASVGDRVT ITCLASEDIY
DNLAWYQQKP GKAPKLLIYY ASSLQDGVPS RFSGSGSGTD YTLTISSLQP
EDFATYYCLQ DSEYPWTFGG GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA
SVVCLLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSTLT
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEC

969 gL7 light chain (V + constant) with signal sequence underlined and italicized SEQ ID NO:22

atgagcgtgc ctactcaagt cttggggctg ctcttgcttt ggcttaccga cgcaagatgc gacatacaga tgactcagtc accctcaagc ctgagtgcca
gtgtgggaga cagggtgaca atcacctgtc tggcctccga ggatatctac
gataacctgg catggtatca gcagaaacct ggaaaggctc ccaagctcct
gatttattat gcctcctctc tccaagacgg cgttccatct cggttcagcg
gaagcggctc cgggacggat tacacactga caattagctc tctgcaaccg
gaggattttg ctacttacta ctgcctgcaa gactccgaat acccatggac
cttcggtggt ggcaccaaag tggaaatcaa gcgtacggta gcggccccat
ctgtcttcat cttcccgcca tctgatgagc agttgaaatc tggaactgcc
tctgttgtgt gcctgctgaa taacttctat cccagagagg ccaaagtaca
gtggaaggtg gataacgccc tccaatcggg taactcccag gagagtgtca
cagagcagga cagcaaggac agcacctaca gcctcagcag caccctgacg
ctgagcaaag cagactacga gaaacacaaa gtctacgcct gcgaagtcac
ccatcagggc ctgagctcgc ccgtcacaaa gagcttcaac aggggagagt
gt

FIGURE 1D

969 gH2 V-region SEQ ID NO:23

EVTLKESGPA LVKPTQTLTL TCTFSGFSLT TYGMGVGWIR QPPGKALEWL
ANIWWDDDKY YNPSLKNRLT ISKDTSKNQV VLTMTNMDPV DTATYYCARI
GPIKYPTAPY RYFDFWGQGT MVTVS

969 gH2 V-region SEQ ID NO:24

gaagtgacac tcaaggagtc tggacccgct ctggtgaaac caacccaaac
actcactttg acatgtactt ttagtggctt ctcattgact acctatggaa
tgggcgtggg atggatcaga cagccacctg gcaaggctct ggaatggctg
gccaacatct ggtgggatga cgacaagtac tataacccgt ccctgaaaaa
ccggctgacc attagcaagg atacttctaa aaatcaagtg gtgctgacca
tgacaaatat ggatcccgtt gacaccgcaa cctactactg cgcccgcatt
ggtcccataa agtaccctac ggcaccttac cgatatttcg acttttgggg
ccaagggaca atggttactg tctcg

969 gH2 V-region with signal sequence underlined and italicized SEQ ID NO:25

*MEWSWVFLFF LSVTTGVHS*E VTLKESGPAL VKPTQTLTLT CTFSGFSLTT
YGMGVGWIRQ PPGKALEWLA NIWWDDDKYY NPSLKNRLTI SKDTSKNQVV
LTMTNMDPVD TATYYCARIG PIKYPTAPYR YFDFWGQGTM VTVS

969 gH2 V-region with signal sequence underlined and italicized SEQ ID NO:26

atggagtggt cctgggtgtt tctgttcttc ctgagtgtga ccaccggggt
*ccactccg*aa gtgacactca aggagtctgg acccgctctg gtgaaaccaa
cccaaacact cactttgaca tgtactttta gtggcttctc attgactacc
tatggaatgg gcgtgggatg gatcagacag ccacctggca aggctctgga
atggctggcc aacatctggt gggatgacga caagtactat aacccgtccc
tgaaaaaccg gctgaccatt agcaaggata cttctaaaaa tcaagtggtg
ctgaccatga caaatatgga tcccgttgac accgcaacct actactgcgc
ccgcattggt cccataaagt accctacggc accttaccga tatttcgact
tttggggcca agggacaatg gttactgtct cg

969 gH2 heavy chain (V + constant – hu IgG4P) SEQ ID NO:27

EVTLKESGPA LVKPTQTLTL TCTFSGFSLT TYGMGVGWIR QPPGKALEWL
ANIWWDDDKY YNPSLKNRLT ISKDTSKNQV VLTMTNMDPV DTATYYCARI
GPIKYPTAPY RYFDFWGQGT MVTVSSASTK GPSVFPLAPC SRSTSESTAA
LGCLVKDYFP EPVTVSWNSG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS
SLGTKTYTCN VDHKPSNTKV DKRVESKYGP PCPPCPAPEF LGGPSVFLFP
PKPKDTLMIS RTPEVTCVVV DVSQEDPEVQ FNWYVDGVEV HNAKTKPREE
QFNSTYRVVS VLTVLHQDWL NGKEYKCKVS NKGLPSSIEK TISKAKGQPR

EPQVYTLPPS QEEMTKNQVS LTCLVKGFYP SDIAVEWESN GQPENNYKTT
PPVLDSDGSF FLYSRLTVDK SRWQEGNVFS CSVMHEALHN HYTQKSLSLS
LGK

969 gH2 heavy chain (V + constant – hu IgG4P, exons underlined) SEQ ID NO:28

gaagtgacac tcaaggagtc tggacccgct ctggtgaaac caacccaaac
actcactttg acatgtactt ttagtggctt ctcattgact acctatggaa
tgggcgtggg atggatcaga cagccacctg gcaaggctct ggaatggctg
gccaacatct ggtgggatga cgacaagtac tataacccgt ccctgaaaaa
ccggctgacc attagcaagg atacttctaa aaatcaagtg gtgctgacca
tgacaaatat ggatcccgtt gacaccgcaa cctactactg cgcccgcatt
ggtcccataa agtaccctac ggcaccttac cgatatttcg acttttgggg
ccaagggaca atggttactg tctcgagcgc ttctacaaag ggcccatccg
tcttcccccc ggcgccctgc tccaggagca cctccgagag cacagccgcc
ctgggctgcc tggtcaagga ctacttcccc gaaccggtga cggtgtcgtg
gaactcaggc gccctgacca gcggcgtgca caccttcccg gctgtcctac
agtcctcagg actctactcc ctcagcagcg tggtgaccgt gccctccagc
agcttgggca cgaagaccta cacctgcaac gtagatcaca agcccagcaa
caccaaggtg gacaagagag ttggtgagag gccagcacag ggagggaggg
tgtctgctgg aagccaggct cagccctcct gcctggacgc accccggctg
tgcagcccca gcccagggca gcaaggcatg ccccatctgt ctcctcaccc
ggaggcctct gaccacccca ctcatgccca gggagagggt cttctggatt
tttccaccag gctccgggca gccacaggct ggatgcccct accccaggcc
ctgcgcatac aggggcaggt gctgcgctca gacctgccaa gagccatatc
cgggaggacc ctgcccctga cctaagccca ccccaaaggc caaactctcc
actcctcag ctcagacacc ttctctcctc ccagatctga gtaactccca
atcttctctc tgcagagtcc aaatatggtc ccccatgccc accatgccca
ggtaagccaa cccaggcctc gccctccagc tcaaggcggg acaggtgccc
tagagtagcc tgcatccagg gacaggcccc agccgggtgc tgacgcatcc
acctccatct cttcctcagc acctgagttc ctgggggggac catcagtctt
cctgttcccc ccaaaaccca aggacactct catgatctcc cggacccctg
aggtcacgtg cgtggtggtg gacgtgagcc aggaagaccc cgaggtccag
ttcaactggt acgtggatgg cgtggaggtg cataatgcca agacaaagcc
gcgggaggag cagttcaaca gcacgtaccg tgtggtcagc gtcctcaccg
tcctgcacca ggactggctg aacggcaagg agtacaagtg caaggtctcc
aacaaaggcc tcccgtcctc catcgagaaa accatctcca aagccaaagg
tgggacccac ggggtgcgag ggccacatgg acagaggtca gctcggccca
ccctctgccc tgggagtgac cgctgtgcca acctctgtcc ctacagggca
gccccgagag ccacaggtgt acaccctgcc cccatcccag gaggagatga
ccaagaacca ggtcagcctg acctgcctgg tcaaaggctt ctaccccagc
gacatcgccg tggagtggga gagcaatggg cagccggaga acaactacaa
gaccacgcct cccgtgctgg actccgacgg ctccttcttc ctctacagca
ggctaaccgt ggacaagagc aggtggcagg aggggaatgt cttctcatgc
tccgtgatgc atgaggctct gcacaaccac tacacacaga agagcctctc
cctgtctctg ggtaaa

969 gH2 heavy chain (V + constant – hu IgG4P) with signal sequence underlined and italicised SEQ ID NO:29

*MEWSWVFLFF LSVTTGVHS*E VTLKESGPAL VKPTQTLTLT CTFSGFSLTT
YGMGVGWIRQ PPGKALEWLA NIWWDDDKYY NPSLKNRLTI SKDTSKNQVV
LTMTNMDPVD TATYYCARIG PIKYPTAPYR YFDFWGQGTM VTVSSASTKG
PSVFPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA
VLQSSGLYSL SSVVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP
CPPCPAPEFL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSQEDPEVQF
NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV LTVLHQDWLN GKEYKCKVSN
KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL TCLVKGFYPS
DIAVEWESNG QPENNYKTTP PVLDSDGSFF LYSRLTVDKS RWQEGNVFSC
SVMHEALHNH YTQKSLSLSL GK

969 gH2 heavy chain (V + constant – hu IgG4P, exons underlined) with signal sequence underlined and italicized SEQ ID NO:30

atggagtggt cctgggtgtt tctgttcttc ctgagtgtga ccaccggggt
ccactccgaa gtgacactca aggagtctgg acccgctctg gtgaaaccaa
cccaaaacact cactttgaca tgtactttta gtggcttctc attgactacc
tatggaatgg gcgtgggatg gatcagacag ccacctggca aggctctgga
atggctggcc aacatctggt gggatgacga caagtactat aacccgtccc
tgaaaaaccg gctgaccatt agcaaggata cttctaaaaa tcaagtggtg
ctgaccatga caaatatgga tcccgttgac accgcaacct actactgcgc
ccgcattggt cccataaagt accctacggc accttaccga tatttcgact
tttggggcca agggacaatg gttactgtct cgagcgcttc tacaaagggc
ccatccgtct tccccctggc gccctgctcc aggagcacct ccgagagcac
agccgccctg ggctgcctgg tcaaggacta cttccccgaa ccggtgacgg
tgtcgtggaa ctcaggcgcc ctgaccagcg gcgtgcacac cttcccggct
gtcctacagt cctcaggact ctactccctc agcagcgtgg tgaccgtgcc
ctccagcagc ttgggcacga agacctacac ctgcaacgta gatcacaagc
ccagcaacac caaggtggac aagagagttg gtgagaggcc agcacaggga
gggagggtgt ctgctggaag ccaggctcag ccctcctgcc tggacgcacc
ccggctgtgc agccccagcc cagggcagca aggcatgccc catctgtctc
ctcacccgga ggcctctgac caccccactc atgcccaggg agagggtctt
ctggattttt ccaccaggct ccgggcagcc acaggctgga tgcccctacc
ccaggccctg cgcatacagg ggcaggtgct gcgctcagac ctgccaagag
ccatatccgg gaggaccctg cccctgacct aagcccaccc caaaggccaa
actctccact ccctcagctc agacaccttc tctcctccca gatctgagta
actcccaatc ttctctctgc agagtccaaa tatggtcccc catgcccacc
atgcccaggt aagccaaccc aggcctcgcc ctccagctca aggcgggaca
ggtgccctag agtagcctgc atccagggac aggccccagc cgggtgctga
cgcatccacc tccatctctt cctcagcacc tgagttcctg gggggaccat
cagtcttcct gttcccccca aaacccaagg acactctcat gatctcccgg
acccctgagg tcacgtgcgt ggtggtggac gtgagccagg aagaccccga
ggtccagttc aactggtacg tggatggcgt ggaggtgcat aatgccaaga

caaagccgcg ggaggagcag ttcaacagca cgtaccgtgt ggtcagcgtc
ctcaccgtcc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa
ggtctccaac aaaggcctcc cgtcctccat cgagaaaacc atctccaaag
ccaaaggtgg gacccacggg gtgcgagggc cacatggaca gaggtcagct
cggcccaccc tctgccctgg gagtgaccgc tgtgccaacc tctgtcccta
cagggcagcc ccgagagcca caggtgtaca ccctgccccc atcccaggag
gagatgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta
ccccagcgac atcgccgtgg agtgggagag caatgggcag ccggagaaca
actacaagac cacgcctccc gtgctggact ccgacggctc cttcttcctc
tacagcaggc taaccgtgga caagagcagg tggcaggagg ggaatgtctt
ctcatgctcc gtgatgcatg aggctctgca caaccactac acacagaaga
gcctctccct gtctctgggt aaa

FIGURE 1E

Human VK1 2-1-(1) O12 JK4 acceptor framework SEQ ID NO:31

DIQMTQSPSS LSASVGDRVT ITCRASQSIS SYLNWYQQKP GKAPKLLIYA
ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ SYSTPLTFGG GTKVEIK

Human VK1 2-1-(1) O12 JK4 acceptor framework SEQ ID NO:32

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga
cagagtcacc atcacttgcc gggcaagtca gagcattagc agctatttaa
attggtatca gcagaaacca gggaaagccc ctaagctcct gatctatgct
gcatccagtt tgcaaagtgg ggtcccatca aggttcagtg gcagtggatc
tgggacagat ttcactctca ccatcagcag tctgcaacct gaagattttg
caacttacta ctgtcaacag agttacagta cccctctcac tttcggcgga
gggaccaagg tggagatcaa a

Human VH2 3-1 2-70 JH3 acceptor framework SEQ ID NO:33

QVTLKESGPA LVKPTQTLTL TCTFSGFSLS TSGMRVSWIR QPPGKALEWL
ARIDWDDDKF YSTSLKTRLT ISKDTSKNQV VLTMTNMDPV DTATYYCARI
AFDIWGQGTM VTVS

Human VH2 3-1 2-70 JH3 acceptor framework SEQ ID NO:34

caggtcacct tgaaggagtc tggtcctgcg ctggtgaaac ccacacagac
cctcacactg acctgcacct tctctgggtt ctcactcagc actagtggaa
tgcgtgtgag ctggatccgt cagccccag ggaaggccct ggagtggctt
gcacgcattg attgggatga tgataaattc tacagcacat ctctgaagac
caggctcacc atctccaagg acacctccaa aaaccaggtg gtccttacaa
tgaccaacat ggaccctgtg gacacagcca cgtattactg tgcacggata
gcttttgata tctggggcca agggacaatg gtcaccgtct ct

FIGURE 1F

Amino acid sequence for CSF-1R SEQ ID NO: 35

MGPGVLLLLL VATAWHGQGI PVIEPSVPEL VVKPGATVTL RCVGNGSVEW
DGPPSPHWTL YSDGSSSILS TNNATFQNTG TYRCTEPGDP LGGSAAIHLY
VKDPARPWNV LAQEVVVFED QDALLPCLLT DPVLEAGVSL VRVRGRPLMR
HTNYSFSPWH GFTIHRAKFI QSQDYQCSAL MGGRKVMSIS IRLKVQKVIP
GPPALTLVPA ELVRIRGEAA QIVCSASSVD VNFDVFLQHN NTKLAIPQQS
DFHNNRYQKV LTLNLDQVDF QHAGNYSCVA SNVQGKHSTS MFFRVVESAY
LNLSSEQNLI QEVTVGEGLN LKVMVEAYPG LQGFNWTYLG PFSDHQPEPK
LANATTKDTY RHTFTLSLPR LKPSEAGRYS FLARNPGGWR ALTFELTLRY
PPEVSVIWTF INGSGTLLCA ASGYPQPNVT WLQCSGHTDR CDEAQVLQVW
DDPYPEVLSQ EPFHKVTVQS LLTVETLEHN QTYECRAHNS VGSGSWAFIP
ISAGAHTHPP DEFLFTPVVV ACMSIMALLL LLLLLLLYKY KQKPKYQVRW
KIIESYEGNS YTFIDPTQLP YNEKWEFPRN NLQFGKTLGA GAFGKVVEAT
AFGLGKEDAV LKVAVKMLKS TAHADEKEAL MSELKIMSHL GQHENIVNLL
GACTHGGPVL VITEYCCYGD LLNFLRRKAE AMLGPSLSPG QDPEGGVDYK
NIHLEKKYVR RDSGFSSQGV DTYVEMRPVS TSSNDSFSEQ DLDKEDGRPL
ELRDLLHFSS QVAQGMAFLA SKNCIHRDVA ARNVLLTNGH VAKIGDFGLA
RDIMNDSNYI VKGNARLPVK WMAPESIFDC VYTVQSDVWS YGILLWEIFS
LGLNPYPGIL VNSKFYKLVK DGYQMAQPAF APKNIYSIMQ ACWALEPTHR
PTFQQICSFL QEQAQEDRRE RDYTNLPSSS RSGGSGSSSS ELEEESSSEH
LTCCEQGDIA QPLLQPNNYQ FC

Amino acid sequence for CSF-1R SEQ ID NO: 36

IPVIEPSVPELVVKPGATVTLRCVGNGSVEWDGPPSPHWTLYSDGSSSILSTNNATFQNTGTYR
CTEPGDPLGGSAAIHLYVKDPARPWNVLAQEVVVFEDQDALLPCLLTDPVLEAGVSLVRVRGRP
LMRHTNYSFSPWHGFTIHRAKFIQSQDYQCSALMGGRKVMSISIRLKVQKVIPGPPALTLVPAE
LVRIRGEAAQIVCSASSVDVNFDVFLQHNNTKLAIPQQSDFHNNRYQKVLTLNLDQVDFQHAGN
YSCVASNVQGKHSTSMFFRVV

Amino acid sequence for CSF-1R SEQ ID NO: 37

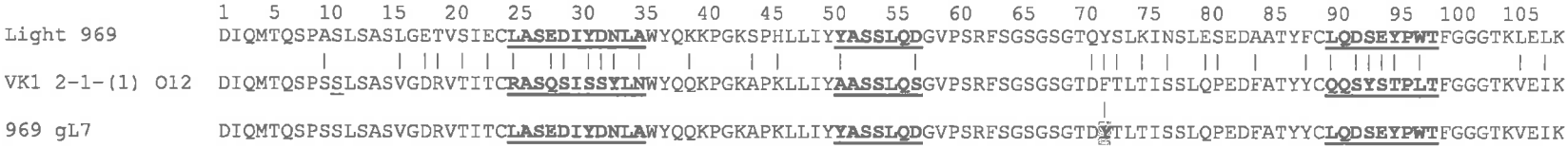
MRHTNYSFSPWHGFTIHRAKFIQSQDYQCSALMGGRKVMSISIRLKVQK

Amino acid sequence for CSF-1R SEQ ID NO:38 (SNP V32G, A245S, H247P, V279M, position underlined)

IPVIEPSVPELV**V**KPGATVTLRCVGNGSVEWDGPPSPHWTLYSDGSSSILSTNNATFQNTGTYR
CTEPGDPLGGSAAIHLYVKDPARPWNVLAQEVVVFEDQDALLPCLLTDPVLEAGVSLVRVRGRP
LMRHTNYSFSPWHGFTIHRAKFIQSQDYQCSALMGGRKVMSISIRLKVQKVIPGPPALTLVPAE
LVRIRGEAAQIVCSASSVDVNFDVFLQHNNTKL**A**I**H**QQSDFHNNRYQKVLTLNLDQVDFQHAGN
YSC**V**ASNVQGKHSTSMFFRVVESAYLNLSSEQNLIQEVTVGEGLNLKVMVEAYPGLQGFNWTYL
GPF**S**DHQPEPKLANATTKDTYRHTFTLSLPRLKPSEAGRYSFLARNPGGWRALTFELTLRYPPE
VSVIWTFINGSGTLLCAASGYPQPNVTWLQCSGHTDRCDEAQVLQVWDDPYPEVLSQEPFHKVT
VQSLLTVETLEHNQTYECRAHNSVGSGSWAFIPISAGAHTHPPDE

FIGURE 2A

LIGHT CHAIN Graft 969



Legend

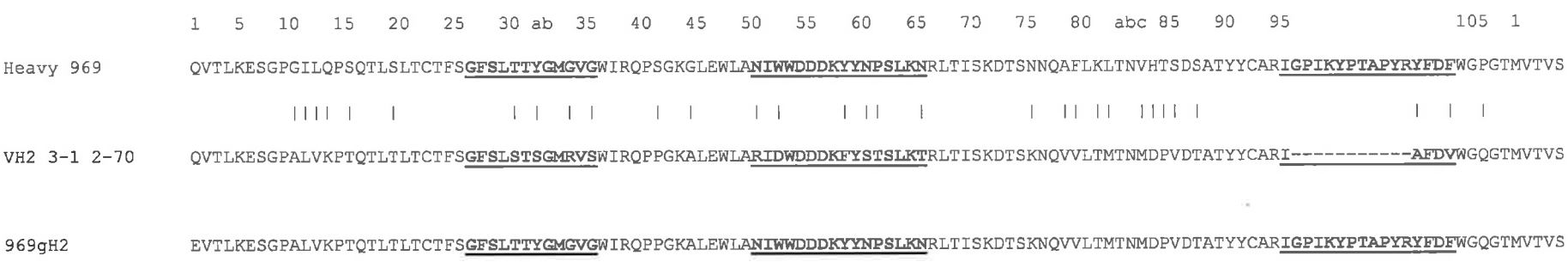
969 = Rat variable light chain sequence
969 gL7 = Humanized graft of 969 variable light chain using VK1 2-1-(1) O12 plus JK4 human germline as the acceptor framework.

CDRs are shown in bold/underlined
Donor residue is shown in bold/italic and is highlighted: Y71

WO 2015/028455 PCT/EP2014/068050

FIGURE 2B

HEAVY CHAIN Graft 969



Legend

969 = Rat variable heavy chain sequence
969gH2 = Humanized graft of 969 variable heavy chain using VH2 3-1 2-70 plus JH3 human germline as the acceptor framework.

CDRs are shown in bold/underlined

WO 2015/028455 PCT/EP2014/068050

FIGURE 3

SEQ ID NO: 39

MGPGVLLLLL VATAWHGQGI PVIEPSVPEL VVKPGATVTL RCVGNGSVEW DGPPSPHWTL YSDGSSSILS
TNNATFQNTG TYRCTEPGDP LGGSAAIHLY VKDPARPWNV LAQEVVVFED QDALLPCLLT DPVLEAGVSL
VRVRGRPLMR HTNYSFSPWH GFTIHRAKFI QSQDYQCSAL MGGRKVMSIS IRLKVQKVIP GPPALTLVPA
ELVRIRGEAA QIVCSASSVD VNFDVFLQHN NTKLAIPQQS DFHNNRYQKV LTLNLDQVDF QHAGNYSCVA
SNVQGKHSTS MFFRVVESAY LNLSSEQNLI QEVTVGEGLN LKVMVEAYPG LQGFNWTYLG PFSDHQPEPK
LANATTKDTY RHTFTLSLPR LKPSEAGRYS FLARNPGGWR ALTFELTLRY PPEVSVIWTF INGSGTLLCA
ASGYPQPNVT WLQCSGHTDR CDEAQVLQVW DDPYPEVLSQ EPFHKVTVQS LLTVETLEHN QTYECRAHNS
VGSGSWAFIP ISAGAHTHPP DE

FIGURE 4

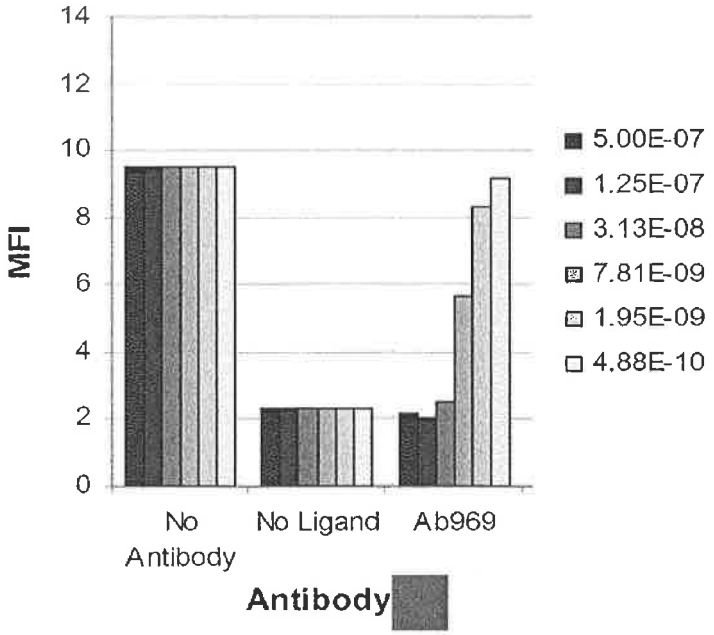


FIGURE 5a

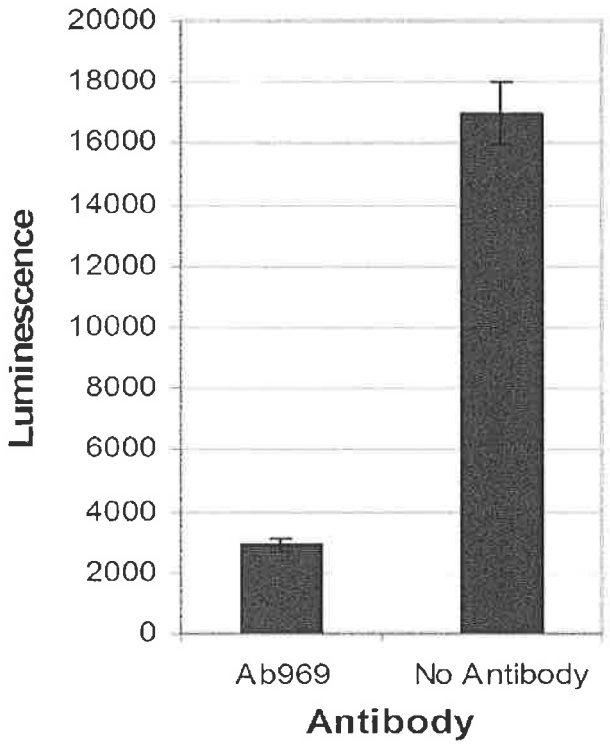


FIGURE 5b

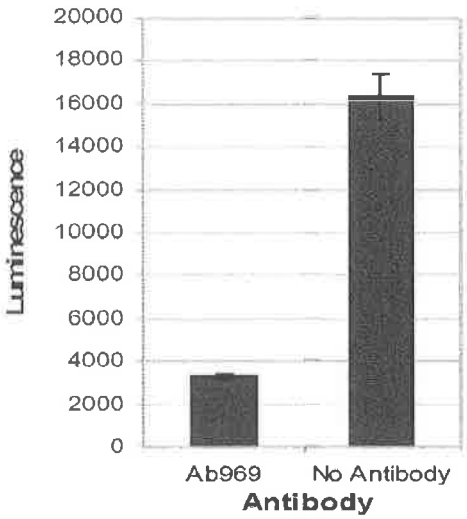


FIGURE 6

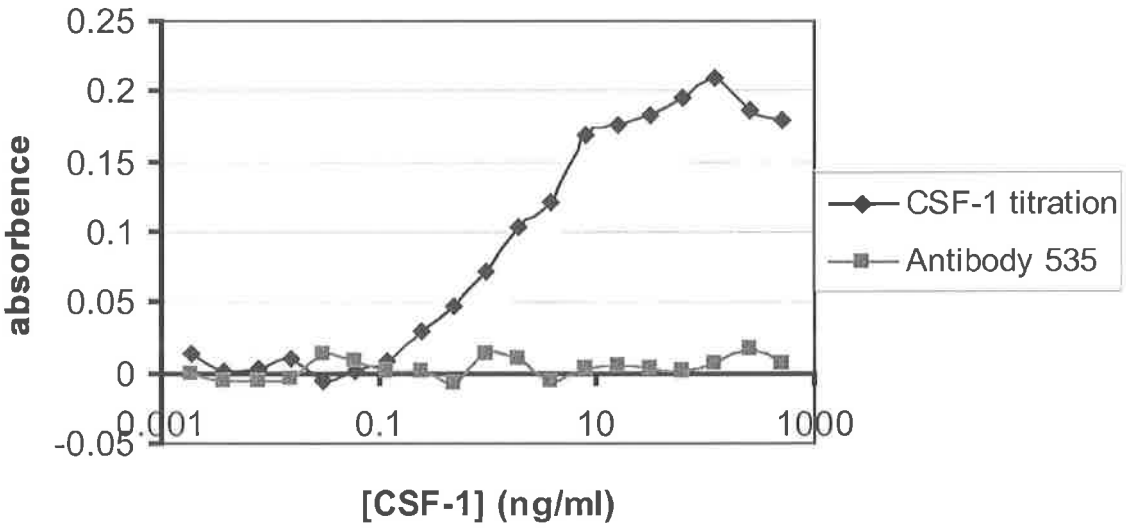


FIGURE 7

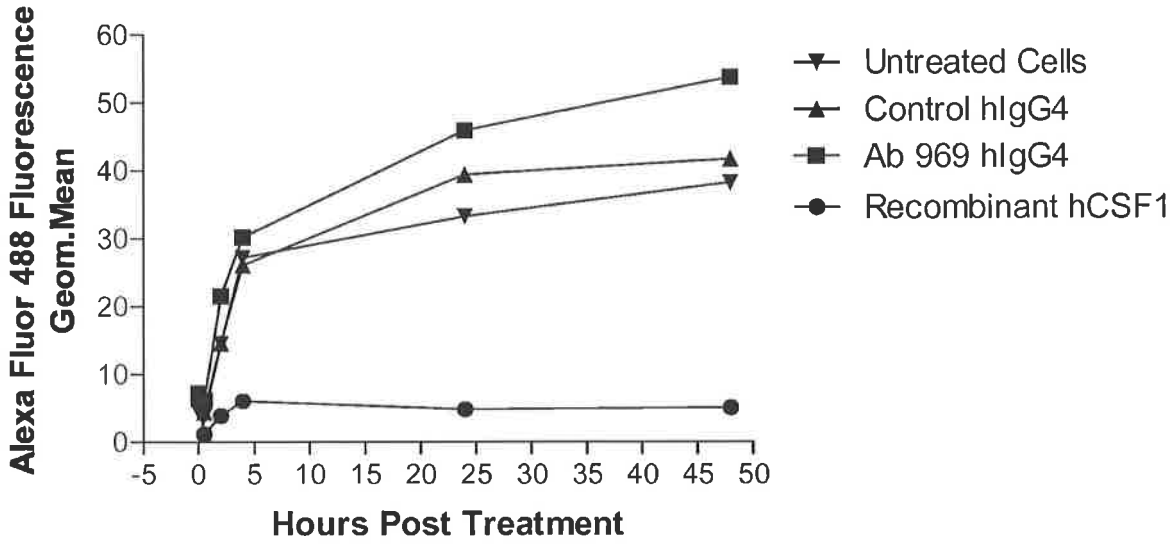

Alexa Fluor 488 Fluorescence Geom.Mean
60
50
40
30
20
10
0
-5
0
5
10
15
20
25
30
35
40
45
50
Hours Post Treatment
Untreated Cells
Control hIgG4
Ab 969 hIgG4
Recombinant hCSF1

FIGURE 8

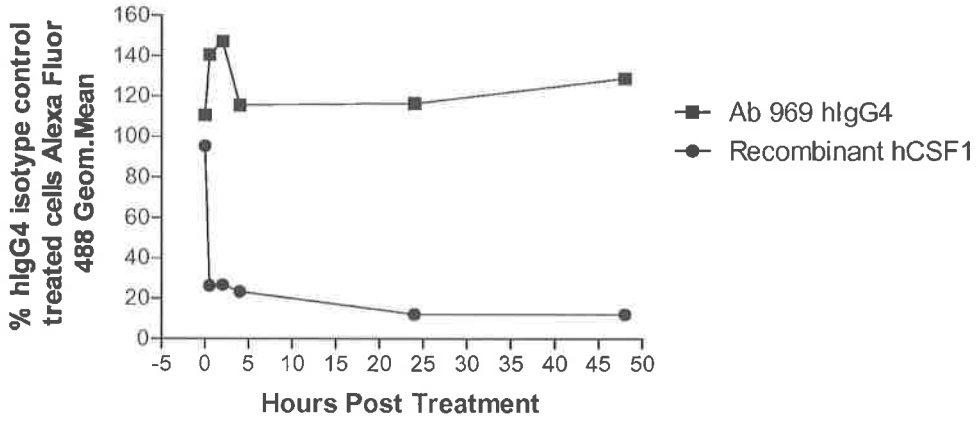


FIGURE 9

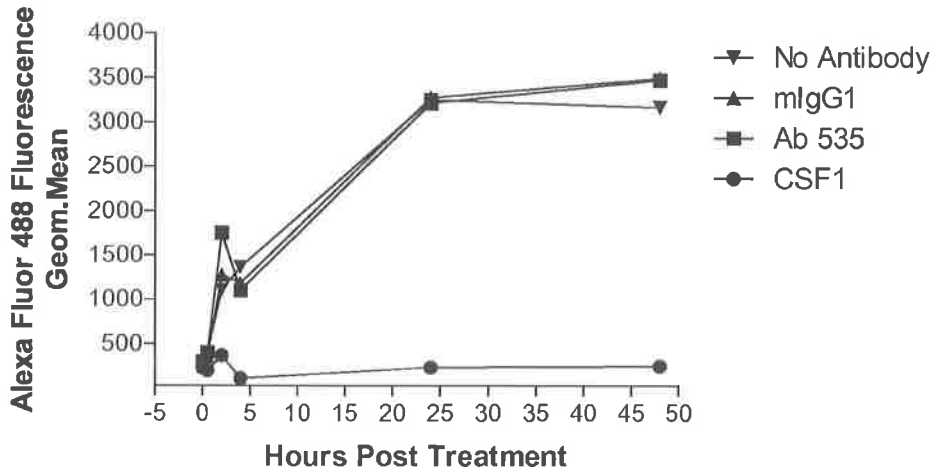


FIGURE 10

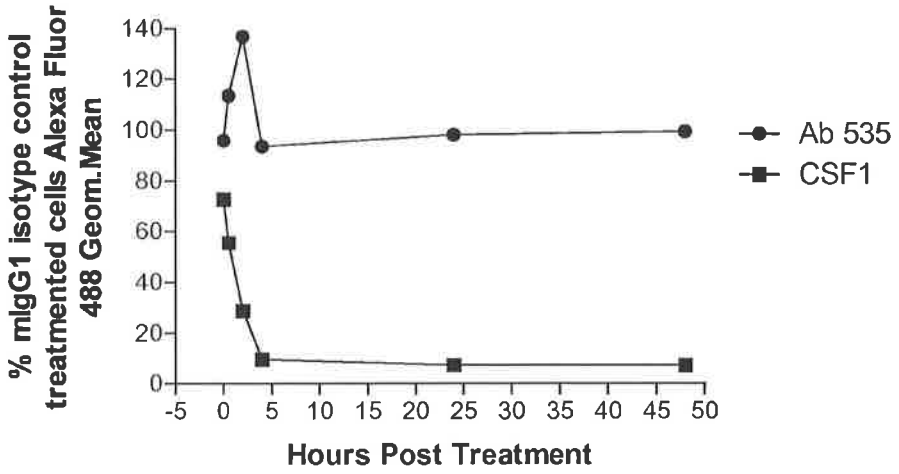
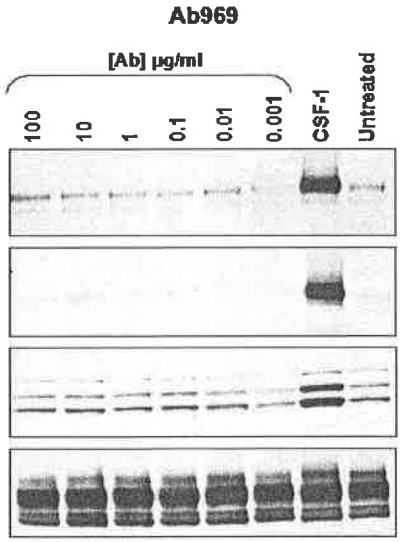


FIGURE 11



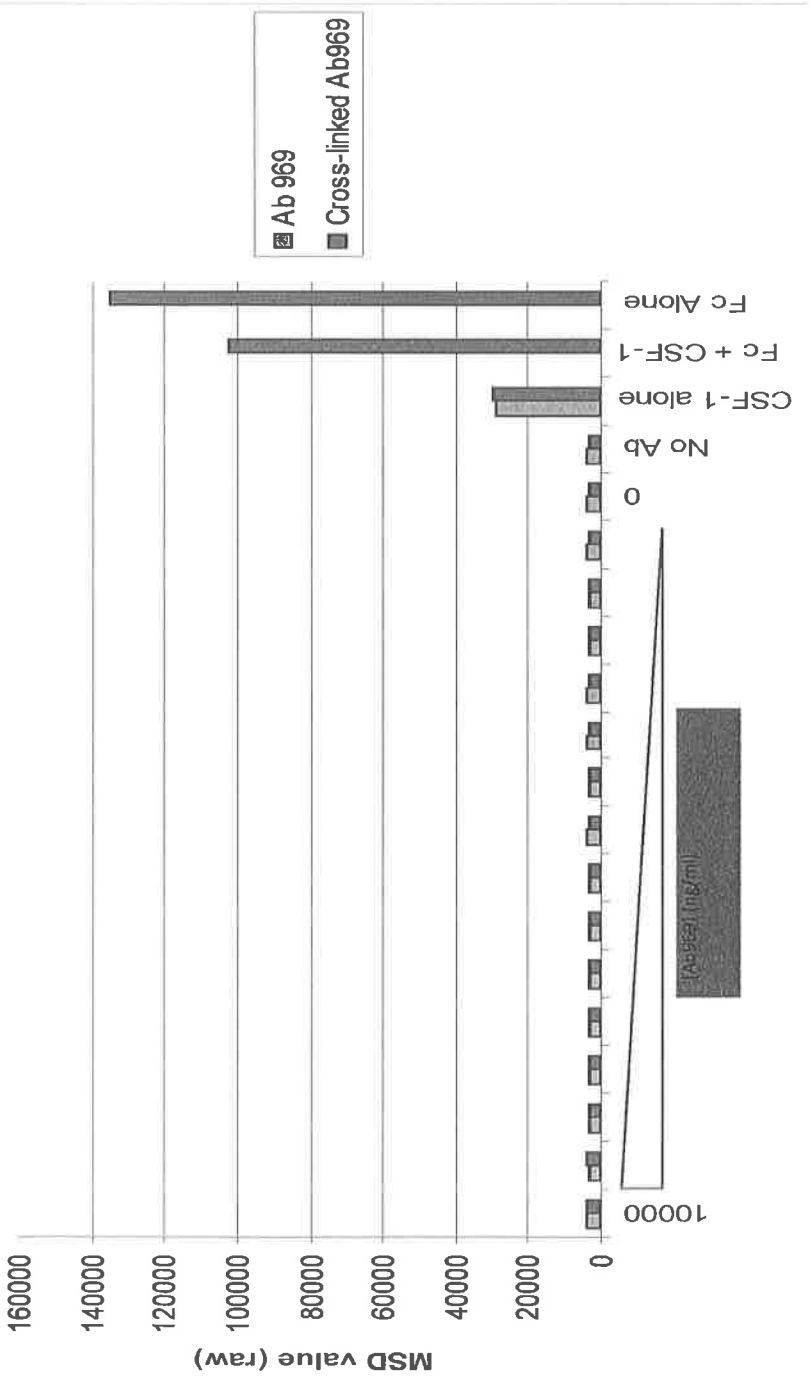

Ab 969
Cross-linked Ab969
MSD value (raw)
160000
140000
120000
100000
80000
60000
40000
20000
0
10000
0
No Ab
CSF-1 alone
Fc + CSF-1
Fc Alone

FIGURE 12

FIGURE 13

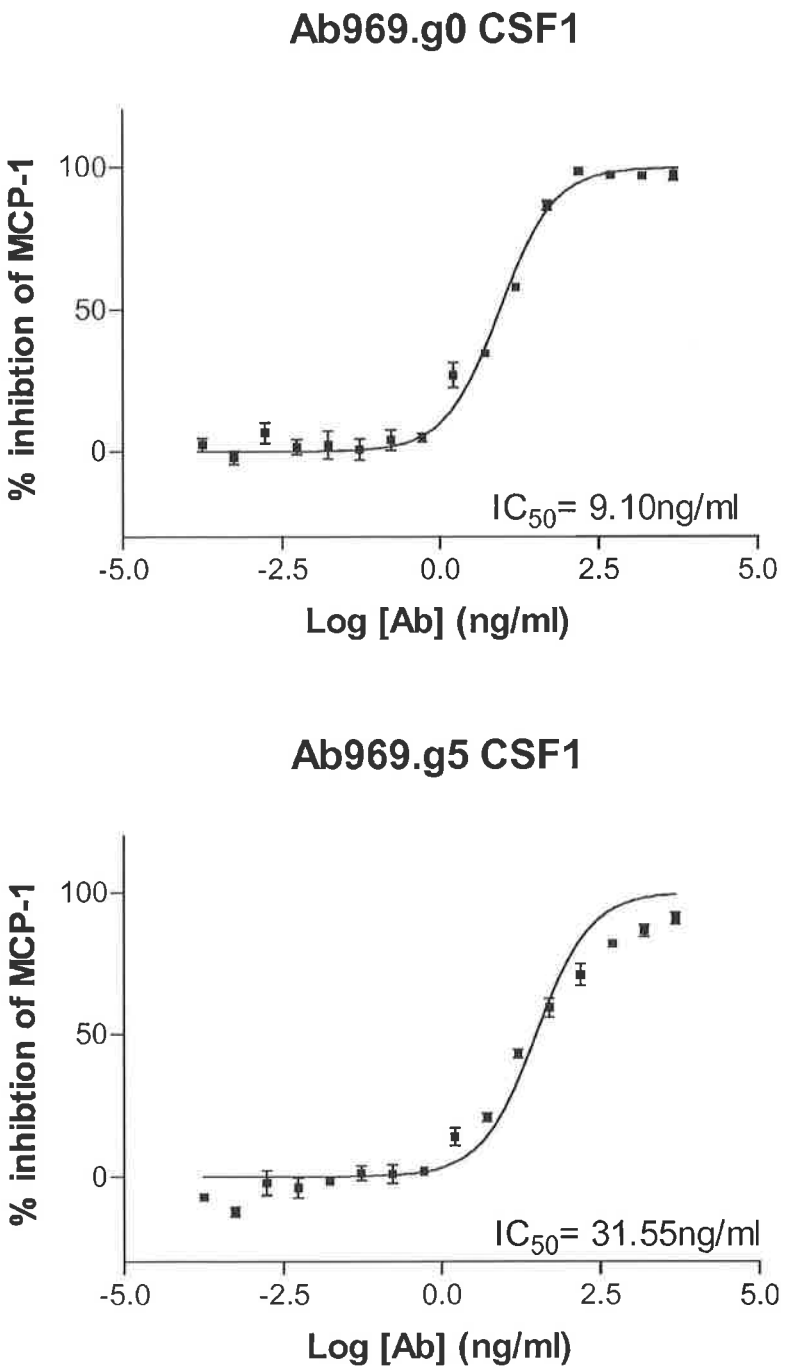

Ab969.g0 CSF1
% inhibtion of MCP-1
100
50
0
IC50= 9.10ng/ml
-5.0
-2.5
0.0
2.5
5.0
Log [Ab] (ng/ml)
Ab969.g5 CSF1
% inhibtion of MCP-1
100
50
0
IC50= 31.55ng/ml
-5.0
-2.5
0.0
2.5
5.0
Log [Ab] (ng/ml)

FIGURE 14

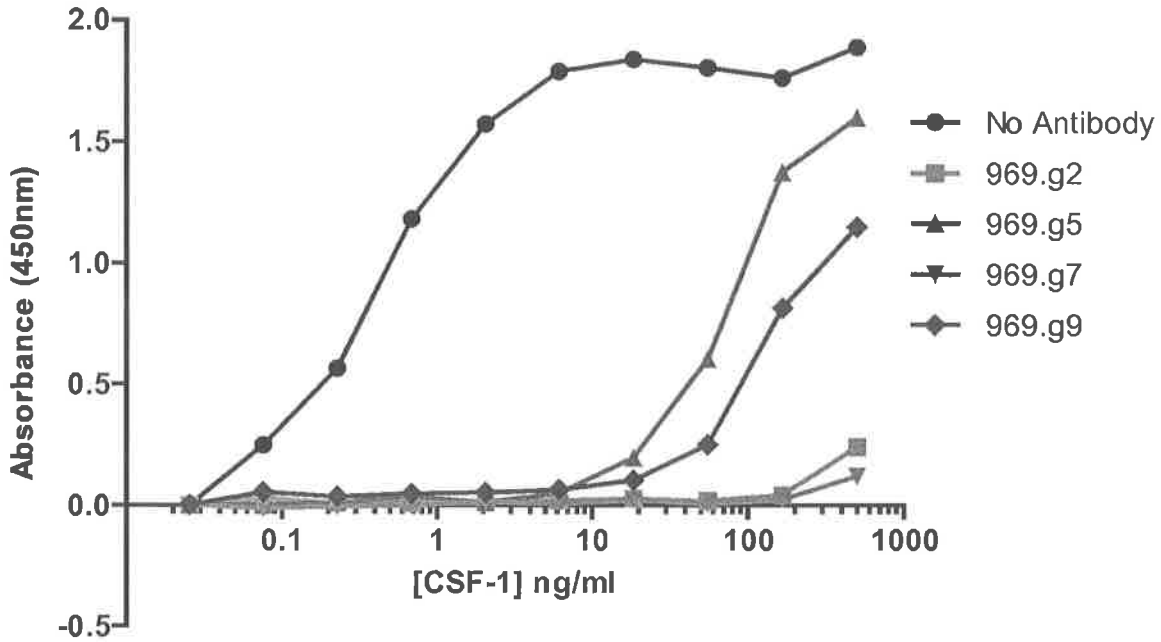

2.0
1.5
1.0
0.5
0.0
-0.5
Absorbance (450nm)
0.1
1
10
100
1000
[CSF-1] ng/ml
No Antibody
969.g2
969.g5
969.g7
969.g9

FIGURE 15a

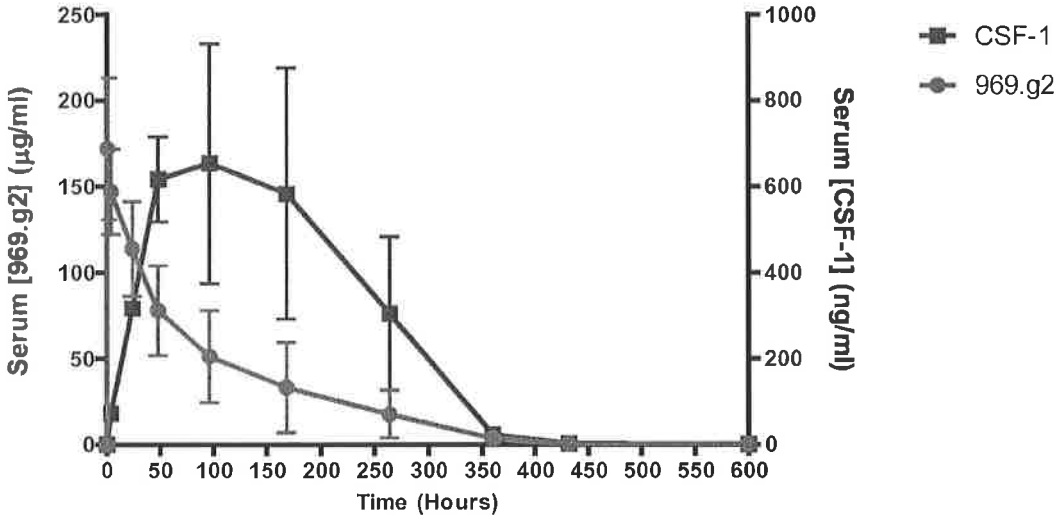


FIGURE 15b

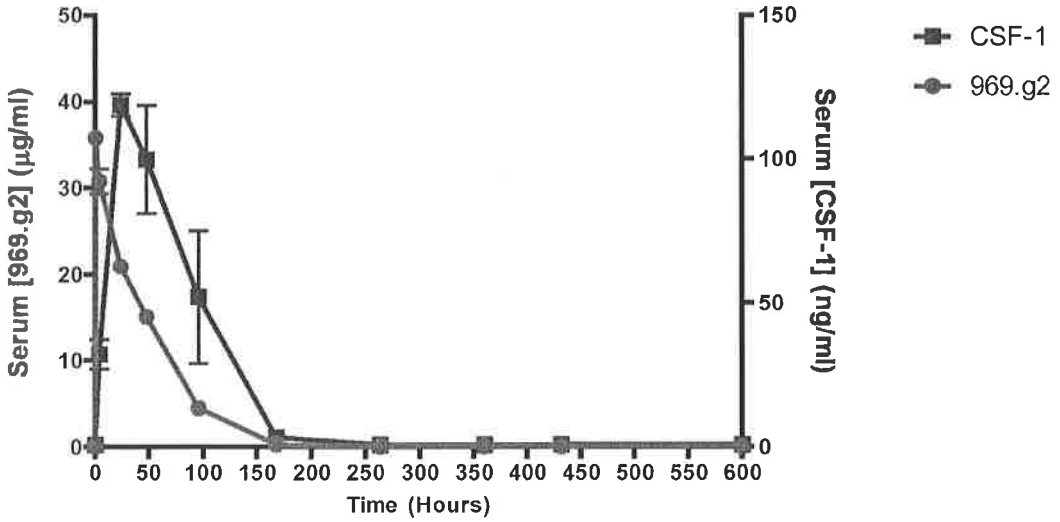


Figure 15c

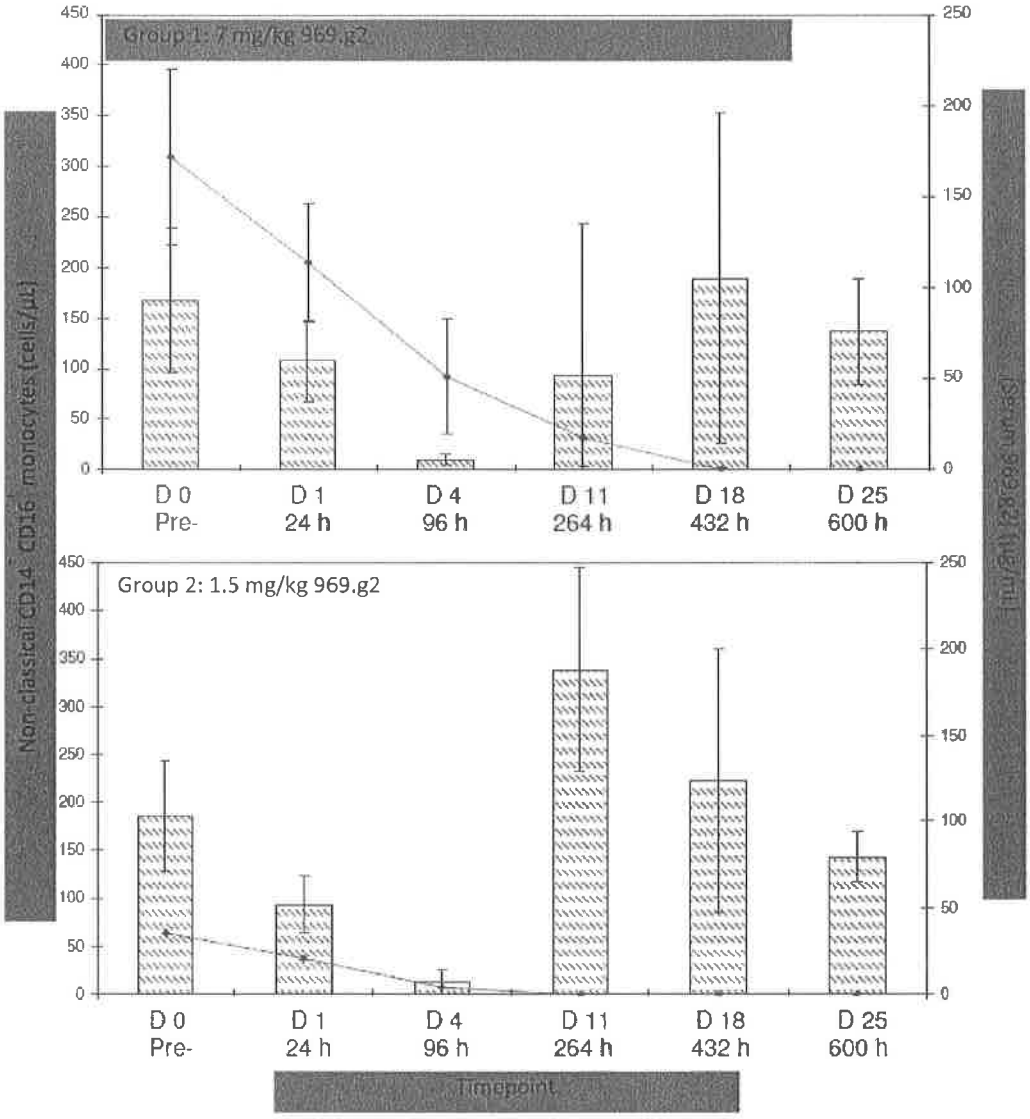

Group 1: 7 mg/kg 969.g2
Group 2: 1.5 mg/kg 969.g2
Non-classical CD14+ CD16+ monocytes [cells/µL]
TNFα [pg/mL]
D 0 Pre-
D 1 24 h
D 4 96 h
D 11 264 h
D 18 432 h
D 25 600 h
Timepoint

FIGURE 16

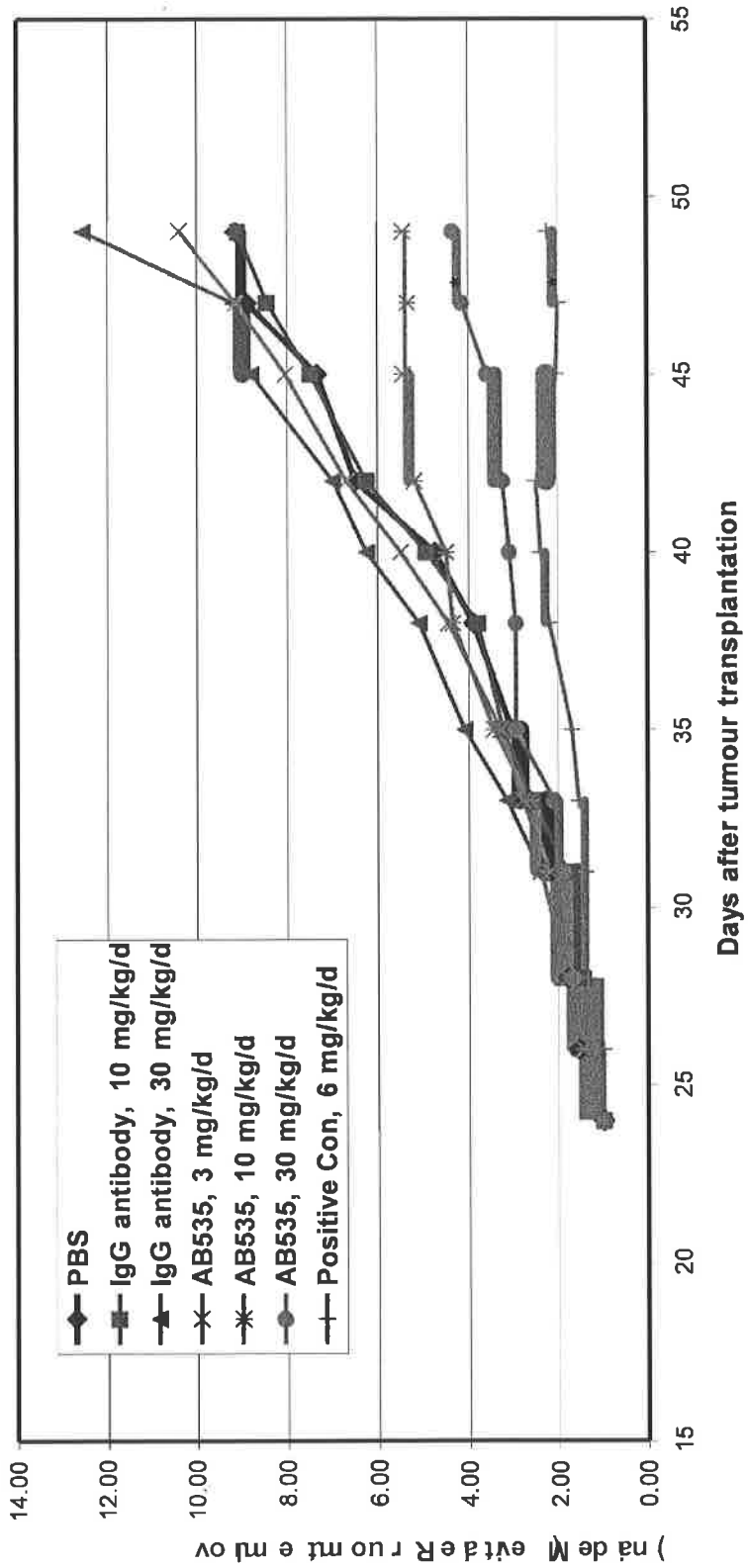

PBS
IgG antibody, 10 mg/kg/d
IgG antibody, 30 mg/kg/d
AB535, 3 mg/kg/d
AB535, 10 mg/kg/d
AB535, 30 mg/kg/d
Positive Con, 6 mg/kg/d
Days after tumour transplantation
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
15
20
25
30
35
40
45
50
55

FIGURE 17

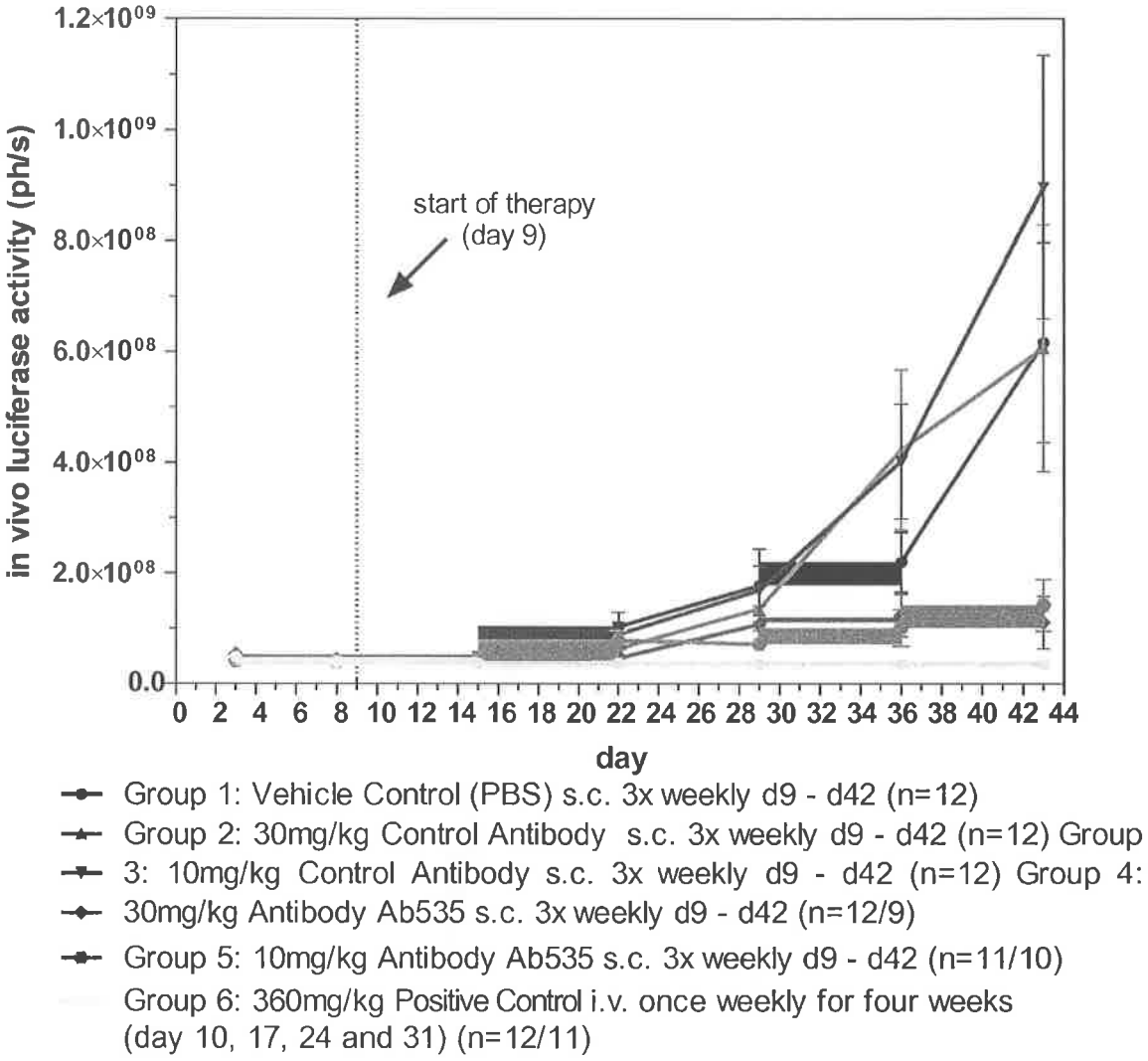

1.2×10^09
1.0×10^09
8.0×10^08
6.0×10^08
4.0×10^08
2.0×10^08
0.0
in vivo luciferase activity (ph/s)
start of therapy
(day 9)
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44
day
Group 1: Vehicle Control (PBS) s.c. 3x weekly d9 - d42 (n=12)
Group 2: 30mg/kg Control Antibody s.c. 3x weekly d9 - d42 (n=12) Group
3: 10mg/kg Control Antibody s.c. 3x weekly d9 - d42 (n=12) Group 4:
30mg/kg Antibody Ab535 s.c. 3x weekly d9 - d42 (n=12/9)
Group 5: 10mg/kg Antibody Ab535 s.c. 3x weekly d9 - d42 (n=11/10)
Group 6: 360mg/kg Positive Control i.v. once weekly for four weeks
(day 10, 17, 24 and 31) (n=12/11)

Figure 18a

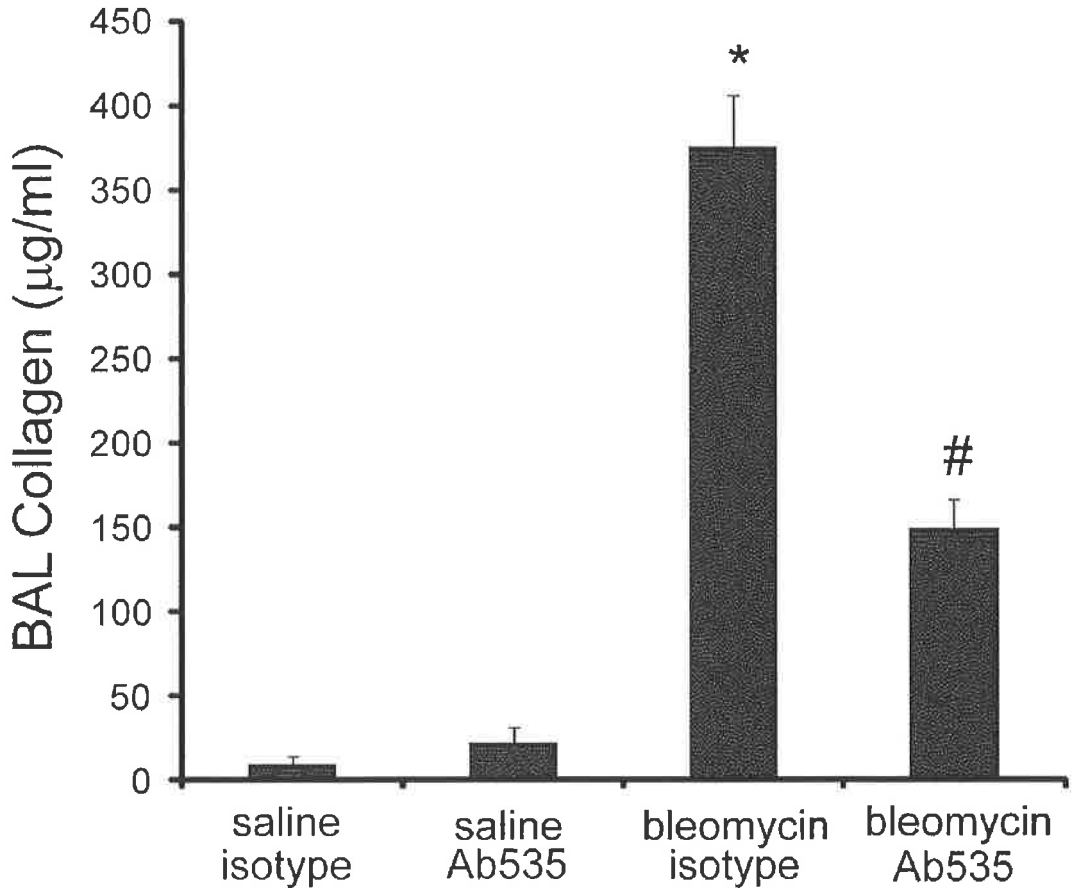

BAL Collagen (µg/ml)
450
400
350
300
250
200
150
100
50
0
*
#
saline isotype
saline Ab535
bleomycin isotype
bleomycin Ab535

Figure 18b

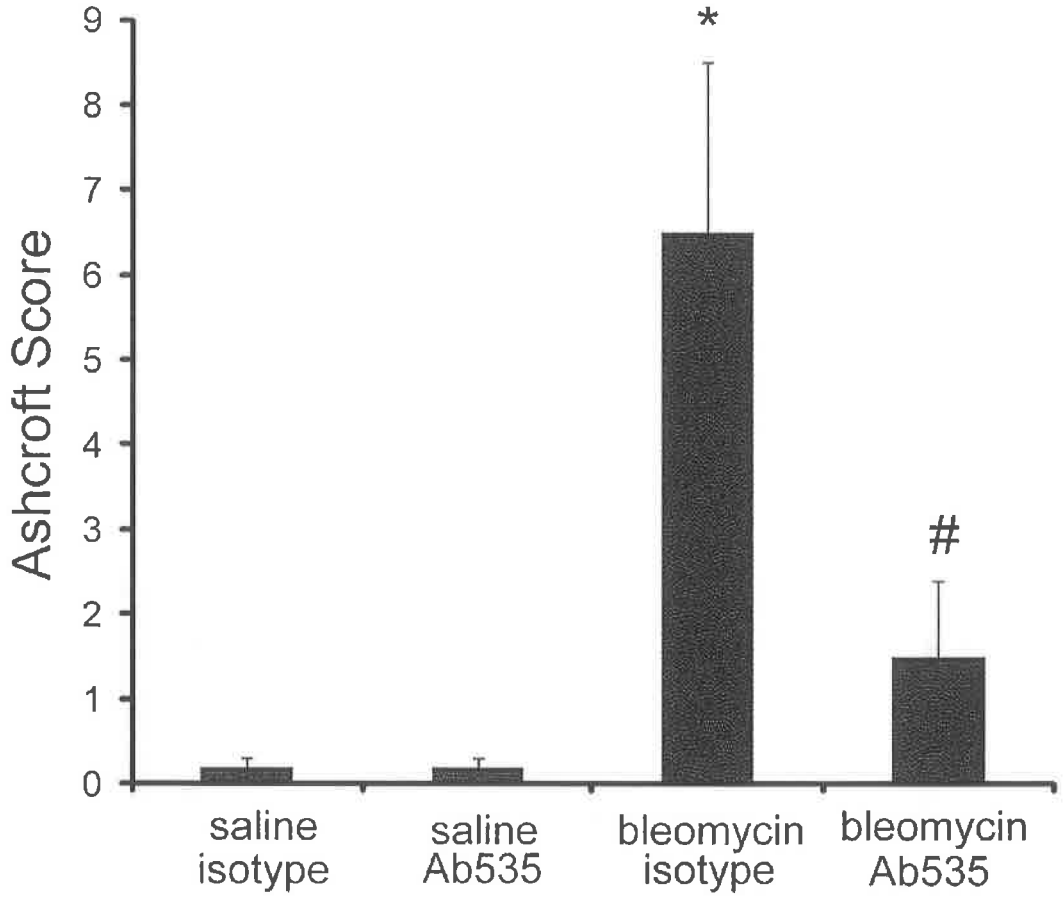

Ashcroft Score
0
1
2
3
4
5
6
7
8
9
*
#
saline isotype
saline Ab535
bleomycin isotype
bleomycin Ab535

Figure 18c

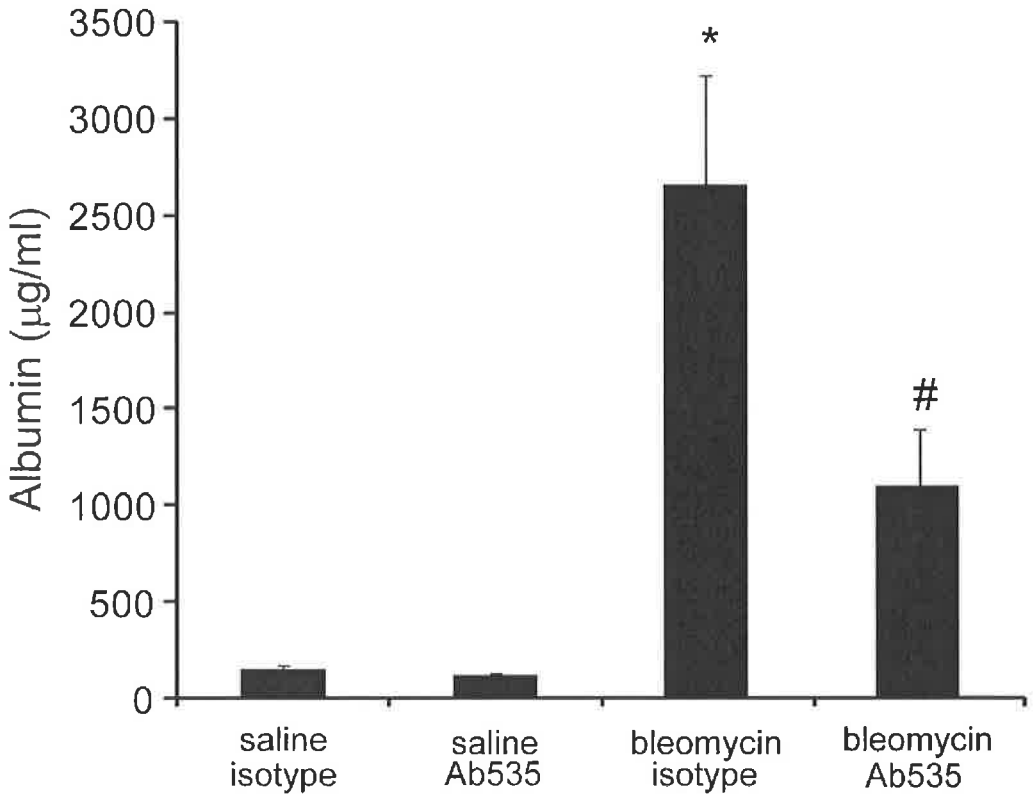
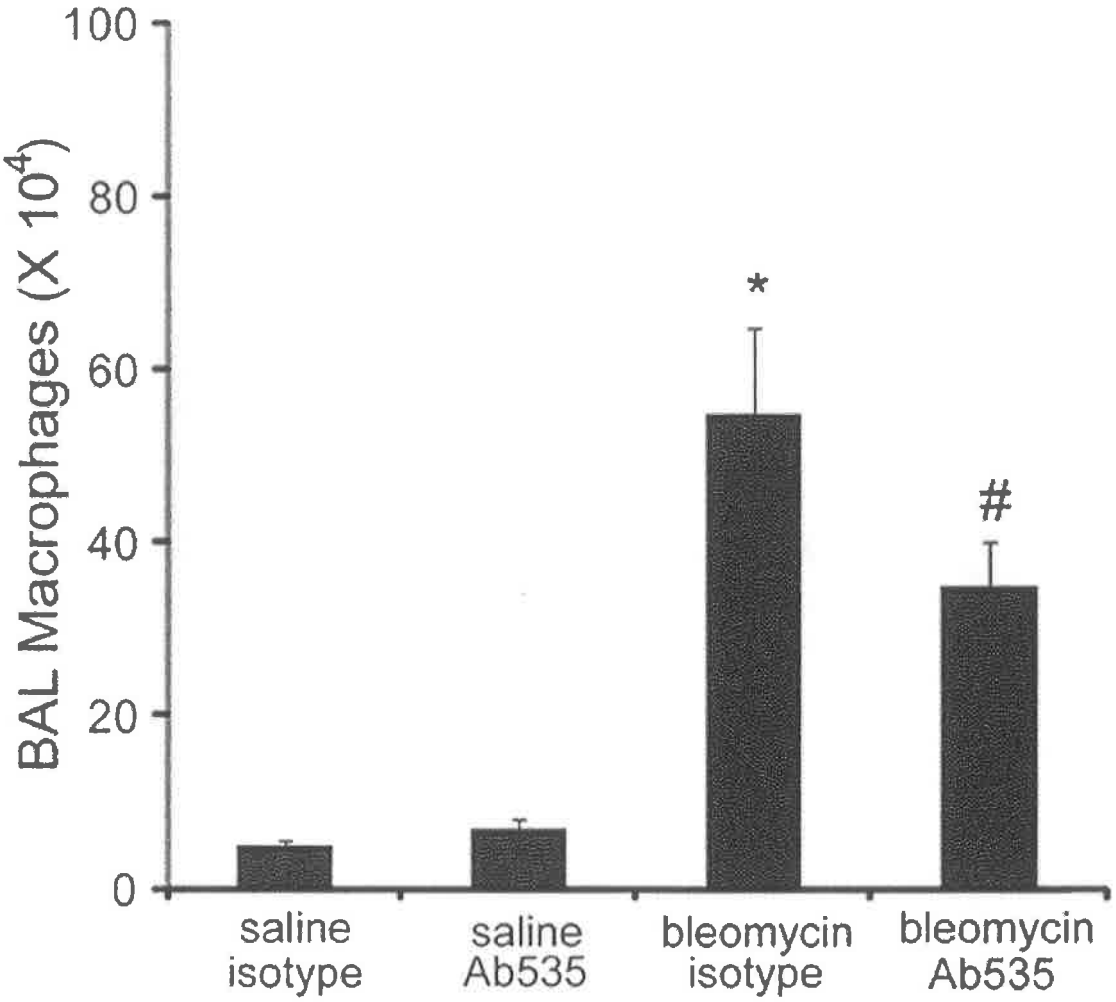

3500
3000
2500
2000
1500
1000
500
0
Albumin (µg/ml)
*
#
saline isotype
saline Ab535
bleomycin isotype
bleomycin Ab535

Fig 18d:


100
80
60
40
20
0
BAL Macrophages (X 10^4)
*
#
saline isotype
saline Ab535
bleomycin isotype
bleomycin Ab535

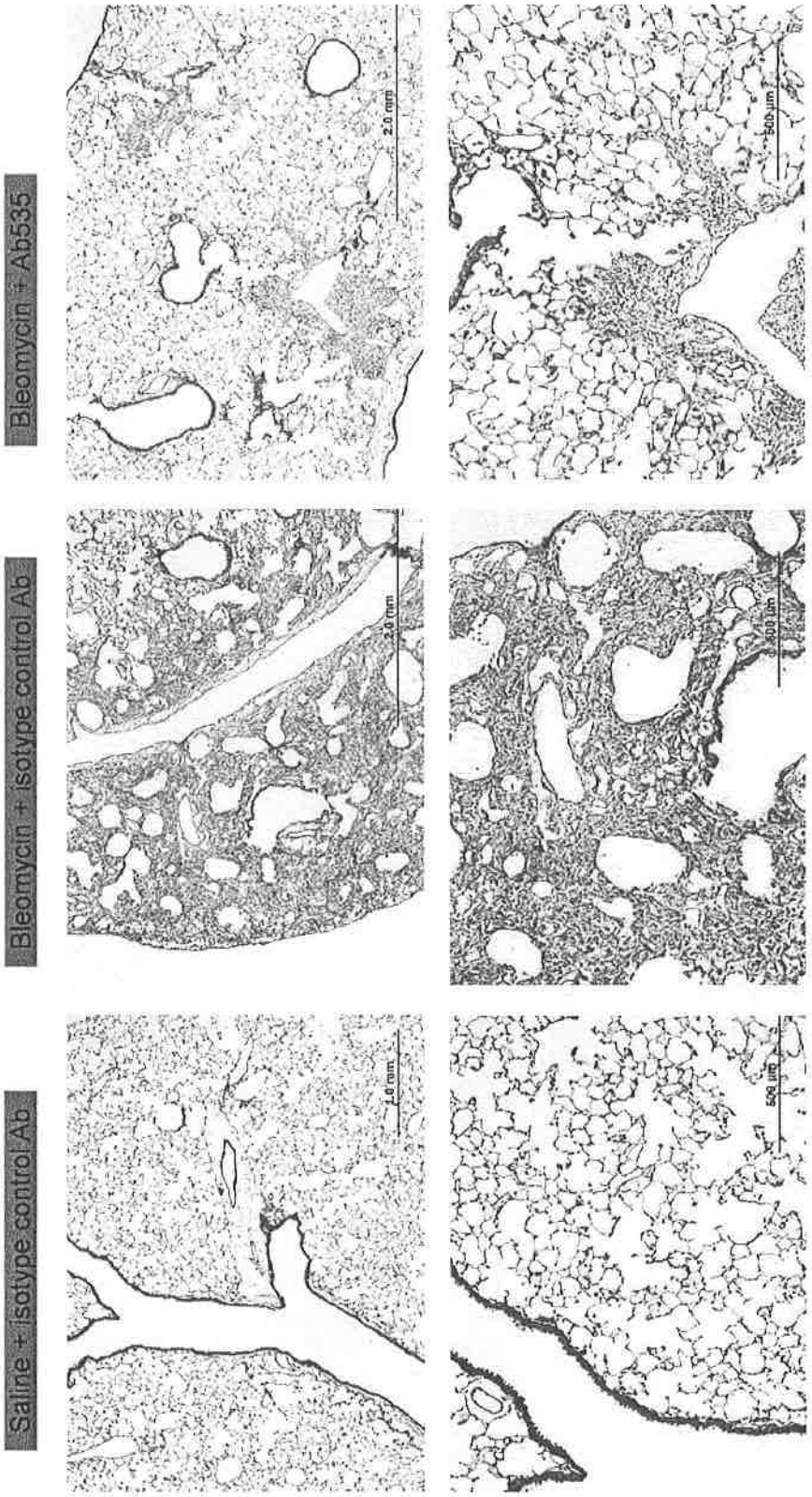

Saline + isotype control Ab
Bleomycin + isotype control Ab
Bleomycin + Ab535
1.0 mm
2.0 mm
2.0 mm
500 µm
500 µm
500 µm

Figure 19

Figure 20a

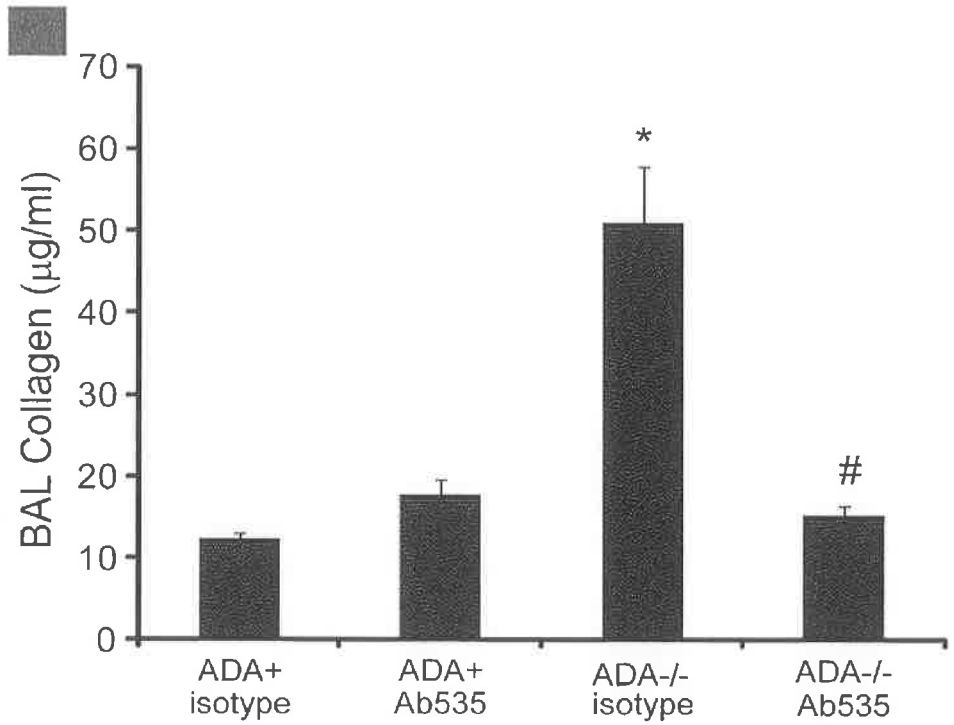

BAL Collagen (µg/ml)
70
60
50
40
30
20
10
0
*
#
ADA+ isotype
ADA+ Ab535
ADA-/- isotype
ADA-/- Ab535

Figure 20b

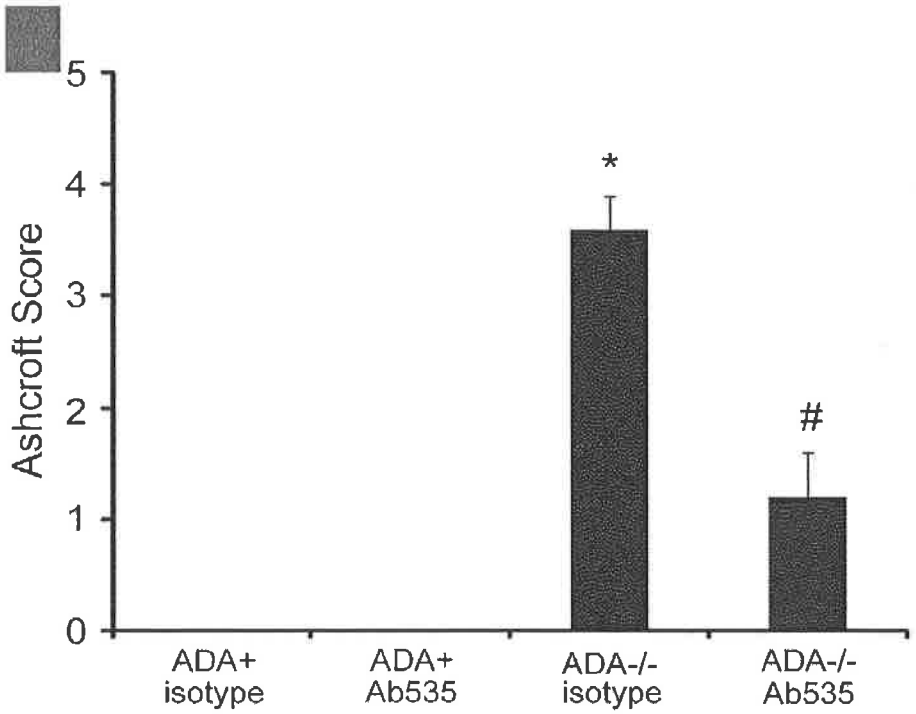

Ashcroft Score
0
1
2
3
4
5
*
#
ADA+ isotype
ADA+ Ab535
ADA-/- isotype
ADA-/- Ab535

Figure 20c

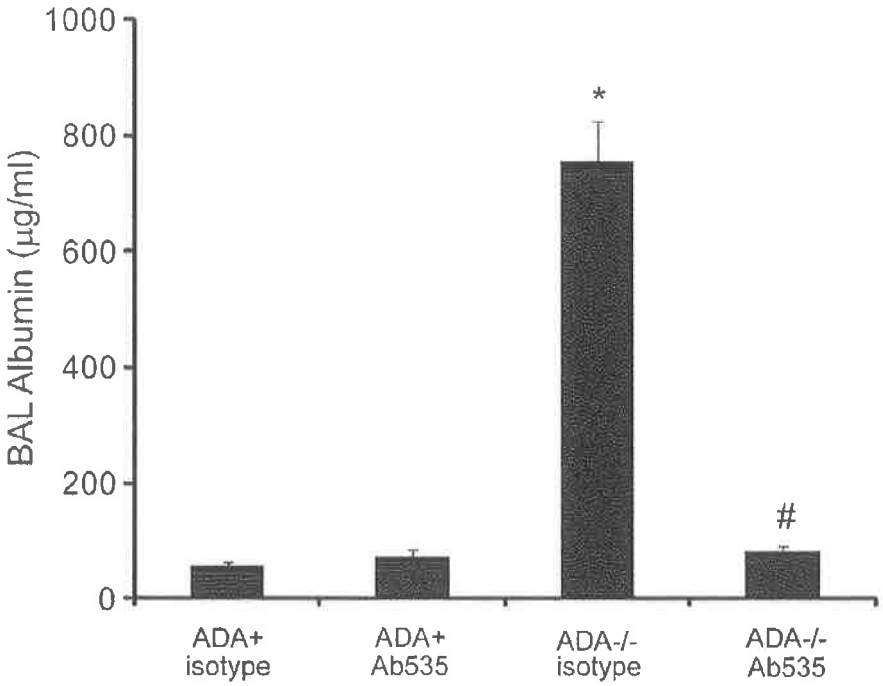
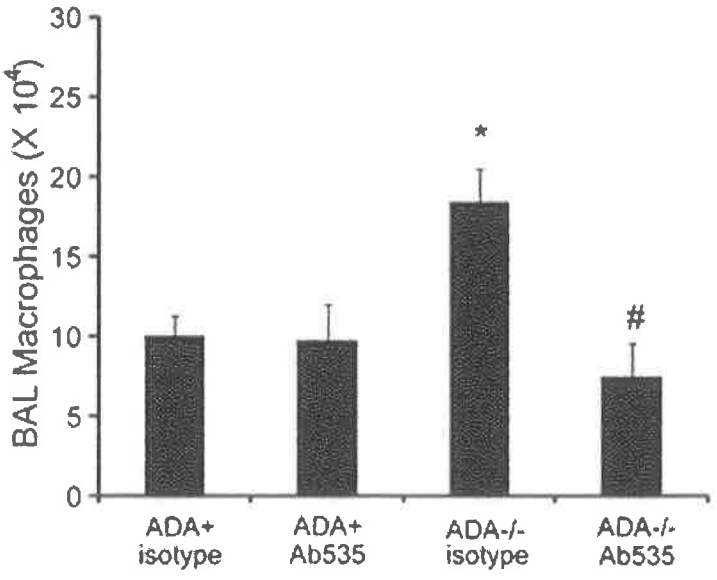


Figure 20d



* Denotes significant difference from ADA+ (wild type); # denotes significant difference from ADA-/- mice treated with isotype control antibody ($p \leq 0.05$).

Figure 21

