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   1 CCCACGCGTC CGCCCACGCG TCCGCCCACG GGTCCGCCCA CGCGTCCGGG CCACCAGAAG TTTGAGCCTC TTTGGTAGCA GGAGGCTGGA AGAAAGGACA
     GGGTGCGCAG GCGGGTGCGC AGGCGGGTGC CCAGGCGGGT GCGCAGGCCC GGTGGTCTTC AAACTCGGAG AAACCATCGT CCTCCGACCT TCTTTCCTGT

 101 GAAGTAGCTC TGGCTGTGAT GGGGATCTTA CTGGGCCTGC TACTCCTGGG GCACCTAACA GTGGACACTT ATGGCCGTCC CATCCTGGAA GTGCCAGAGA
     CTTCATCGAG ACCGACACTA CCCCTAGAAT GACCCGGACG ATGAGGACCC CGTGGATTGT CACCTGTGAA TACCGGCAGG GTAGGACCTT CACGGTCTCT
   1           SEQ ID NO:2 M  G  I  L  L  G  L  L  L  L  G  H  L  T  V  D  T  Y  G  R  P  I  L  E  V  P  E  S
                           ^MET

 201 GTGTAACAGG ACCTTGGAAA GGGGATGTGA ATCTTCCCTG CACCTATGAC CCCCTGCAAG GCTACACCCA AGTCTTGGTG AAGTGGCTGG TACAACGTGG
     CACATTGTCC TGGAACCTTT CCCCTACACT TAGAAGGGAC GTGGATACTG GGGGACGTTC CGATGTGGGT TCAGAACCAC TTCACCGACC ATGTTGCACC
  29   V  T  G  P  W  K  G  D  V  N  L  P  C  T  Y  D  P  L  Q  G  Y  T  Q  V  L  V  K  W  L  V  Q  R  G

 301 CTCAGACCCT GTCACCATCT TTCTACGTGA CTCTTCTGGA GACCATATCC AGCAGGCAAA GTACCAGGGC CGCCTGCATG TGAGCCACAA GGTTCCAGGA
     GAGTCTGGGA CAGTGGTAGA AAGATGCACT GAGAAGACCT CTGGTATAGG TCGTCCGTTT CATGGTCCCG GCGGACGTAC ACTCGGTGTT CCAAGGTCCT
  62 S  D  P  V  T  I  F  L  R  D  S  S  G  D  H  I  Q  Q  A  K  Y  Q  G  R  L  H  V  S  H  K  V  P  G

 401 GATGTATCCC TCCAATTGAG CACCCTGGAG ATGGATGACC GGAGCCACTA CACGTGTGAA GTCACCTGGC AGACTCCTGA TGGCAACCAA GTCGTGAGAG
     CTACATAGGG AGGTTAACTC GTGGGACCTC TACCTACTGG·CCTCGGTGAT GTGCACACTT CAGTGGACCG TCTGAGGACT ACCGTTGGTT CAGCACTCTC
  95 D  V  S  L  Q  L  S  T  L  E  M  D  D  R  S  H  Y  T  C  E  V  T  W  Q  T  P  D  G  N  Q  V  V  R  D

 501 ATAAGATTAC TGAGCTCCGT GTCCAGAAAC TCTCTGTCTC CAAGCCCACA GTGACAACTG GCAGCGGTTA TGGCTTCACG GTGCCCCAGG GAATGAGGAT
     TATTCTAATG ACTCGAGGCA CAGGTCTTTG AGAGACAGAG GTTCGGGTGT CACTGTTGAC CGTCGCCAAT ACCGAAGTGC CACGGGGTCC CTTACTCCTA
 129   K  I  T  E  L  R  V  Q  K  L  S  V  S  K  P  T  V  T  T  G  S  G  Y  G  F  T  V  P  Q  G  M  R  I

 601 TAGCCTTCAA TGCCAGGCTC GGGGTTCTCC TCCCATCAGT TATATTTGGT ATAAGCAACA GACTAATAAC CAGGAACCCA TCAAAGTAGC AACCCTAAGT
     ATCGGAAGTT ACGGTCCGAG CCCCAAGAGG AGGGTAGTCA ATATAAACCA TATTCGTTGT CTGATTATTG GTCCTTGGGT AGTTTCATCG TTGGGATTCA
 162   S  L  Q  C  Q  A  R  G  S  P  P  I  S  Y  I  W  Y  K  Q  Q  T  N  N  Q  E  P  I  K  V  A  T  L  S

 701 ACCTTACTCT TCAAGCCTGC GGTGATAGCC GACTCAGGCT CCTATTTCTG CACTGCCAAG GGCCAGGTTG GCTCTGAGCA GCACAGCGAC AATGTGAAGT
     TGGAATGAGA AGTTCGGACG CCACTATCGG CTGAGTCCGA GGATAAAGAC GTGACGGTTC CCGGTCCAAC CGAGACTCGT CGTGTCGCTG TAACACTTCA
 195 T  L  L  F  K  P  A  V  I  A  D  S  G  S  Y  F  C  T  A  K  G  Q  V  G  S  E  Q  H  S  D  I  V  K  F

 801 TTGTGGTCAA AGACTCCTCA AAGCTACTCA AGACCAAGAC TGAGGCACCT ACAACCATGA CATACCCCTT GAAAGCAACA TCTACAGTGA AGCAGTCCTG
     AACACCAGTT TCTGAGGAGT TTCGATGAGT TCTGGTTCTG ACTCCGTGGA TGTTGGTACT GTATGGGGAA CTTTCGTTGT AGATGTCACT TCGTCAGGAC
 229   V  V  K  D  S  S  K  L  L  K  T  K  T  E  A  P  T  T  M  T  Y  P  L  K  A  T  S  T  V  K  Q  S  W
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Figure 1A (SEQ ID: 1,2)

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901 GGACTGGACC ACTGACATGG ATGGCTACCT TGGAGAGACC AGTGCTGGGC CAGGAAAGAG CCTGCCTGTC TTTGCCATCA TCCTCATCAT CTCCTTGTGC
    CCTGACCTGG TGACTGTACC TACCGATGGA ACCTCTCTGG TCACGACCCG GTCCTTTCTC GGACGGACAG AAACGGTAGT AGGAGTAGTA GAGGAACACG
262  D  W  T   T  D  M  D   G  Y  L   G  E  T   S  A  G  P   G  K  S   L  P  V   F  A  I  I   L  I  I   S  L  C

1001 TGTATGGTGG TTTTTACCAT GGCCTATATC ATGCTCTGTC GGAAGACATC CCAACAAGAG CATGTCTACG AAGCAGCCAG GTAAGAAAGT CTCTCCTCTT
     ACATACCACC AAAAATGGTA CCGGATATAG TACGAGACAG CCTTCTGTAG GGTTGTTCTC GTACAGATGC TTCGTCGGTC CATTCTTTCA GAGAGGAGAA
295  C  M  V  V   F  T  M   A  Y  I   M  L  C  R   K  T  S   Q  Q  E   H  V  Y  E   A  A  R   O

1101 CCATTTTTGA CCCCGTCCCT GCCCTCAATT TTGATTACTG GCAGGAAATG TGGAGGAAGG GGGGTGTGGC ACAGACCCAA TCCTAAGGCC GGAGGCCTTC
     GGTAAAAACT GGGGCAGGGA CGGGAGTTAA AACTAATGAC CGTCCTTTAC ACCTCCTTCC CCCCACACCG TGTCTGGGTT AGGATTCCGG CCTCCGGAAG

1201 AGGGTCAGGA CATAGCTGCC TTCCCTCTCT CAGGCACCTT CTGAGGTTGT TTTGGCCCTC TGAACACAAA GGATAATTTA GATCCATCTG CCTTCTGCTT
     TCCCAGTCCT GTATCGACGG AAGGGAGAGA GTCCGTGGAA GACTCCAACA AAACCGGGAG ACTTGTGTTT CCTATTAAAT CTAGGTAGAC GGAAGACGAA

1301 CCAGAATCCC TGGGTGGTAG GATCCTGATA ATTAATTGGC AAGAATTGAG GCAGAAGGGT GGGAAACCAG GACCACAGCC CCAAGTCCCT TCTTATGGGT
     GGTCTTAGGG ACCCACCATC CTAGGACTAT TAATTAACCG TTCTTAACTC CGTCTTCCCA CCCTTTGGTC CTGGTGTCGG GGTTCAGGGA AGAATACCCA

1401 GGTGGGCTCT TGGGCCATAG GGCACATGCC AGAGAGGCCA ACGACTCTGG AGAAACCATG AGGGTGGCCA TCTTCGCAAG TGGCTGCTCC AGTGATGAGC
     CCACCCGAGA ACCCGGTATC CCGTGTACGG TCTCTCCGGT TGCTGAGACC TCTTTGGTAC TCCCACCGGT AGAAGCGTTC ACCGACGAGG TCACTACTCG

1501 CAACTTCCCA GAATCTGGGC AACAACTACT CTGATGAGCC CTGCATAGGA CAGGAGTACC AGATCATCGC CCAGATCAAT GGCAACTACG CCCGCCTGCT
     GTTGAAGGGT CTTAGACCCG TTGTTGATGA GACTACTCGG GACGTATCCT GTCCTCATGG TCTAGTAGCG GGTCTAGTTA CCGTTGATGC GGGCGGACGA

1601 GGACACAGTT CCTCTGGATT ATGAGTTTCT GGCCACTGAG GGCAAAAGTG TCTGTTAAAA ATGCCCCATT AGGCCAGGAT CTGCTGACAT AATTGCCTAG
     CCTGTGTCAA GGAGACCTAA TACTCAAAGA CCGGTGACTC CCGTTTTCAC AGACAATTTT TACGGGGTAA TCCGGTCCTA GACGACTGTA TTAACGGATC

1701 TCAGTCCTTG CCTTCTGCAT GGCCTTCTTC CCTGCTACCT CTCTTCCTGG ATAGCCCAAA GTGTCCGCCT ACCAACACTG GAGCCGCTGG GAGTCACTGG
     AGTCAGGAAC GGAAGACGTA CCGGAAGAAG GGACGATGGA GAGAAGGACC TATCGGGTTT CACAGGCGGA TGGTTGTGAC CTCGGCGACC CTCAGTGACC

1801 CTTTGCCCTG GAATTTGCCA GATGCATCTC AAGTAAGCCA GCTGCTGGAT TTGGCTCTGG GCCCTTCTAG TATCTCTGCC GGGGGCTTCT GGTACTCCTC
     GAAACGGGAC CTTAAACGGT CTACGTAGAG TTCATTCGGT CGACGACCTA AACCGAGACC CGGGAAGATC ATAGAGACGG CCCCCGAAGA CCATGAGGAG

1901 TCTAAATACC AGAGGGAAGA TGCCCATAGC ACTAGGACTT GGTCATCATG CCTACAGACA CTATTCAACT TTGGCATCTT GCCACCAGAA GACCCGAGGG
     AGATTTATGG TCTCCCTTCT ACGGGTATCG TGATCCTGAA CCAGTAGTAC GGATGTCTGT GATAAGTTGA AACCGTAGAA CGGTGGTCTT CTGGGCTCCC

2001 AGGCTCAGCT CTGCCAGCTC AGAGGACCAG CTATATCCAG GATCATTTCT CTTTCTTCAG GGCCAGACAG CTTTTAATTG AAATTGTTAT TTCACAGGCC
     TCCGAGTCGA GACGGTCGAG TCTCCTGGTC GATATAGGTC CTAGTAAAGA GAAAGAAGTC CCGGTCTGTC GAAAATTAAC TTTAACAATA AAGTGTCCGG

2101 AGGGTTCAGT TCTGCTCCTC CACTATAAGT CTAATGTTCT GACTCTCTCC TGGTGCTCAA TAAATATCTA ATCATAACAG C
     TCCCAAGTCA AGACGAGGAG GTGATATTCA GATTACAAGA CTGAGAGAGG ACCACGAGTT ATTTATAGAT TAGTATTGTC G
```

Figure 1B
(SEQ ID: 1,2)

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1   CCAACTGCAC CTCGGTTCTA TCGATAGGAG GCTGGAAGAA AGGACAGAAG TAGCTCTGGC TGTGATGGGG ATCTTACTGG GCCTGCTACT CCTGGGGCAC
    GGTTGACGTG GAGCCAAGAT AGCTATCCTC CGACCTTCTT TCCTGTCTTC ATCGAGACCG ACACTACCCC TAGAATGACC CGGACGATGA GGACCCCGTC
1                                                                                   M  G  I  L  L  G  L  L  L  L  G  H
                                                                                    ^MET

101 CTAACAGTGG ACACTTATGG CCGTCCCATC CTGGAAGTGC CAGAGAGTGT AACAGGACCT TGGAAAGGGG ATGTGAATCT TCCCTGCACC TATGACCCCC
    GATTGTCACC TGTGAATACC GGCAGGGTAG GACCTTCACG GTCTCTCACA TTGTCCTGGA ACCTTTCCCC TACACTTAGA AGGGACGTGG ATACTGGGGG
13  L  T  V  D  T  Y  G  R  P  I  L  E  V  P  E  S  V  T  G  P  W  K  G  D  V  N  L  P  C  T  Y  D  P  L

201 TGCAAGGCTA CACCCAAGTC TTGGTGAAGT GGCTGGTACA ACGTGGCTCA GACCCTGTCA CCATCTTTCT ACGTGACTCT TCTGGAGACC ATATCCAGCA
    ACGTTCCGAT GTGGGTTCAG AACCACTTCA CCGACCATGT TGCACCGAGT CTGGGACAGT GGTAGAAAGA TGCACTGAGA AGACCTCTGG TATAGGTCGT
47    Q  G  Y  T  Q  V  L  V  K  W  L  V  Q  R  G  S  D  P  V  T  I  F  L  R  D  S  S  G  D  H  I  Q  Q

301 GGCAAAGTAC CAGGGCCGCC TGCATGTGAG CCACAAGGTT CCAGGAGATG TATCCCTCCA ATTGAGCACC CTGGAGATGG ATGACCGGAG CCACTACACG
    CCGTTTCATG GTCCCGGCGG ACGTACACTC GGTGTTCCAA GGTCCTCTAC ATAGGGAGGT TAACTCGTGG GACCTCTACC TACTGGCCTC GGTGATGTGC
80  A  K  Y  Q  G  R  L  H  V  S  H  K  V  P  G  D  V  S  L  Q  L  S  T  L  E  M  D  D  R  S  H  Y  T

401 TGTGAAGTCA CCTGGCAGAC TCCTGATGGC AACCAAGTCG TGAGAGATAA GATTACTGAG CTCCGTGTCC AGAAACTCTC TGTCTCCAAG CCCACAGTGA
    ACACTTCAGT GGACCGTCTG AGGACTACCG TTGGTTCAGC ACTCTCTATT CTAATGACTC GAGGCACAGG TCTTTGAGAG ACAGAGGTTC GGGTGTCACT
113 C  E  V  T  W  Q  T  P  D  G  N  Q  V  V  R  D  K  I  T  E  L  R  V  Q  K  L  S  V  S  K  P  T  V  T

501 CAACTGGCAG CGGTTATGGC TTCACGGTGC CCCAGGGAAT GAGGATTAGC CTTCAATGCC AGGCTCGGGG TTCTCCTCCC ATCAGTTATA TTTGGTATAA
    GTTGACCGTC GCCAATACCG AAGTGCCACG GGGTCCCTTA CTCCTAATCG GAAGTTACGG TCCGAGCCCC AAGAGGAGGG TAGTCAATAT AAACCATATT
147   T  G  S  G  Y  G  F  T  V  P  Q  G  M  R  I  S  L  Q  C  Q  A  R  G  S  P  P  I  S  Y  I  W  Y  K
```

Figure 2A

```
601 GCAACAGACT AATAACCAGG AACCCATCAA AGTAGCAACC CTAAGTACCT TACTCTTCAA GCCTGCGGTG ATAGCCGACT CAGGCTCCTA TATCTGCACT
    CGTTGTCTGA TTATTGGTCC TTGGGTAGTT TCATCGTTGG GATTCATGGA ATGAGAAGTT CGGACGCCAC TATCGGCTGA GTCCGAGGAT AAAGACGTGA
180  Q  Q  T  N  N  Q  E  P  I  K  V  A  T  L  S  T  L  L  F  K  P  A  V  I  A  D  S  G  S  Y  F  C  T

701 GCCAAGGGCC AGGTTGGCTC TGAGCAGCAC AGCGACATTG TGAAGTTTGT GGTCAAAGAC TCCTCAAAGC TACTCAAGAC CAAGACTGAG GCACCTACAA
    CGGTTCCCGG TCCAACCGAG ACTCGTCGTG TCGCTGTAAC ACTTCAAACA CCAGTTTCTG AGGAGTTTCG ATGAGTTCTG GTTCTGACTC CGTGGATGTT
213 A  K  G  Q  V  G  S  E  Q  H  S  D  I  V  K  F  V  V  K  D  S  S  K  L  L  K  T  K  T  E  A  P  T  T

801 CCATGACATA CCCCTTGAAA GCAACATCTA CAGTGAAGCA GTCCTGGGAC TGGACCACTG ACATGGATGG CTACCTTGGA GAGACCAGTG CTGGGCCAGG
    GGTACTGTAT GGGGAACTTT CGTTGTAGAT GTCACTTCGT CAGGACCCTG ACCTGGTGAC TGTACCTACC GATGGAACCT CTCTGGTCAC GACCCGGTCC
247  M  T  Y  P  L  K  A  T  S  T  V  K  Q  S  W  D  W  T  T  D  M  D  G  Y  L  G  E  T  S  A  G  P  G

901 AAAGAGCCTG CCTGTCTTTG CCATCATCCT CATCATCTCC TTGTGCTGTA TGGTGGTTTT TACCATGGCC TATATCATGC TCTGTCGGAA GACATCCCAA
    TTTCTCGGAC GGACAGAAAC GGTAGTAGGA GTAGTAGAGG AACACGACAT ACCACCAAAA ATGGTACCGG ATATAGTACG AGACAGCCTT CTGTAGGGTT
280  K  S  L  P  V  F  A  I  I  L  I  I  S  L  C  C  M  V  V  F  T  M  A  Y  I  M  L  C  R  K  T  S  Q

1001 CAAGAGCATG TCTACGAAGC AGCCAGGGCA CATGCCAGAG AGGCCAACGA CTCTGGAGAA ACCATGAGGG TGGCCATCTT CGCAAGTGGC TGCTCCAGTG
     GTTCTCGTAC AGATGCTTCG TCGGTCCCGT GTACGGTCTC TCCGGTTGCT GAGACCTCTT TGGTACTCCC ACCGGTAGAA GCGTTCACCG ACGAGGTCAC
313  Q  E  H  V  Y  E  A  A  R  A  H  A  R  E  A  N  D  S  G  E  T  M  R  V  A  I  F  A  S  G  C  S  S  D

1101 ATGAGCCAAC TTCCCAGAAT CTGGGCAACA ACTACTCTGA TGAGCCCTGC ATAGGACAGG AGTACCAGAT CATCGCCCAG ATCAATGGCA ACTACGCCCG
     TACTCGGTTG AAGGGTCTTA GACCCGTTGT TGATGAGACT ACTCGGGACG TATCCTGTCC TCATGGTCTA GTAGCGGGTC TAGTTACCGT TGATGCGGGC
347   E  P  T  S  Q  N  L  G  N  N  Y  S  D  E  P  C  I  G  Q  E  Y  Q  I  I  A  Q  I  N  G  N  Y  A  R

1201 CCTGCTGGAC ACAGTTCCTC TGGATTATGA GTTTCTGGCC ACTGAGGGCA AAAGTGTCTG TTAAAAATGC CCCATTAGGC CAGGATCTGC TGACATAATC
     GGACGACCTG TGTCAAGGAG ACCTAATACT CAAAGACCGG TGACTCCCGT TTTCACAGAC AATTTTTACG GGGTAATCCG GTCCTAGACG ACTGTATTAG
380  L  L  D  T  V  P  L  D  Y  E  F  L  A  T  E  G  K  S  V  C  O

1301 TAGAGTCGAC CTGCAGAAGC TTGGCCGCCA TGGCCCAACT TGTTTATTGC AGCTTATAAT GGTTACAAAT AA
     ATCTCAGCTG GACGTCTTCG AACCGGCGGT ACCGGGTTGA ACAAATAACG TCGAATATTA CCAATGTTTA TT
```

Figure 2B

```
1   GTCCAACTGC ACCTCGGTTC TATCGATAGG AGGCTGGAAG AAAGGACAGA AGTAGCTCTG GCTGTGATGG GGATCTTACT GGGCCTGCTA CTCCTGGGGC
    CAGGTTGACG TGGAGCCAAG ATAGCTATCC TCCGACCTTC TTTCCTGTCT TCATCGAGAC CGACACTACC CCTAGAATGA CCCGGACGAT GAGGACCCCG
1                                                                                  M  G  I  L  L  G  L  L  L  L  G  H
                                    ^insert begins here

101 ACCTAACAGT GGACACTTAT GGCCGTCCCA TCCTGGAAGT GCCAGAGAGT GTAACAGGAC CTTGGAAAGG GGATGTGAAT CTTCCCTGCA CCTATGACCC
    TGGATTGTCA CCTGTGAATA CCGGCAGGGT AGGACCTTCA CGGTCTCTCA CATTGTCCTG GAACCTTTCC CCTACACTTA GAAGGGACGT GGATACTGGG
13   L  T  V  D  T  Y  G  R  P  I  L  E  V  P  E  S  V  T  G  P  W  K  G  D  V  N  L  P  C  T  Y  D  P

201 CCTGCAAGGC TACACCCAAG TCTTGGTGAA GTGGCTGGTA CAACGTGGCT CAGACCCTGT CACCATCTTT CTACGTGACT CTTCTGGAGA CCATATCCAG
    GGACGTTCCG ATGTGGGTTC AGAACCACTT CACCGACCAT GTTGCACCGA GTCTGGGACA GTGGTAGAAA GATGCACTGA GAAGACCTCT GGTATAGGTC
46  L  Q  G  Y  T  Q  V  L  V  K  W  L  V  Q  R  G  S  D  P  V  T  I  F  L  R  D  S  S  G  D  H  I  Q

301 CAGGCAAAGT ACCAGGGCCG CCTGGATGTG AGCCACAAGG TTCCAGGAGA TGTATCCCTC CAATTGAGCA CCCTGGAGAT GGATGACCGG AGCCACTACA
    GTCCGTTTCA TGGTCCCGGC GGACGTACAC TCGGTGTTCC AAGGTCCTCT ACATAGGGAG GTTAACTCGT GGGACCTCTA CCTACTGGCC TCGGTGATGT
79  Q  A  K  Y  Q  G  R  L  H  V  S  H  K  V  P  G  D  V  S  L  Q  L  S  T  L  E  M  D  D  R  S  H  Y  T

401 CGTGTGAAGT CACCTGGCAG ACTCCTGATG GCAACCAAGT CGTGAGAGAT AAGATTACTG AGCTCCGTGT CCAGAAACAC TCCTCAAAGC TACTCAAGAC
    GCACACTTCA GTGGACCGTC TGAGGACTAC CGTTGGTTCA GCACTCTCTA TTCTAATGAC TCGAGGCACA GGTCTTTGTG AGGAGTTTCG ATGAGTTCTG
113  C  E  V  T  W  Q  T  P  D  G  N  Q  V  V  R  D  K  I  T  E  L  R  V  Q  K  H  S  S  K  L  L  K  T

501 CAAGACTGAG GCACCTACAA CCATGACATA CCCCTTGAAA GCAACATCTA CAGTGAAGCA GTCCTGGGAC TGGACCACTG ACATGGATGG CTACCTTGGA
    GTTCTGACTC CGTGGATGTT GGTACTGTAT GGGGAACTTT CGTTGTAGAT GTCACTTCGT CAGGACCCTG ACCTGGTGAC TGTACCTACC GATGGAACCT
146 K  T  E  A  P  T  T  M  T  Y  P  L  K  A  T  S  T  V  K  Q  S  W  D  W  T  T  D  M  D  G  Y  L  G
```

Figure 3A

```
601 GAGACCAGTG CTGGGCCAGG AAAGAGCCTG CCTGTCTTTG CCATCATCCT CATCATCTCC TTGTGCTGTA TGGTGGTTTT TACCATGGCC TATATCATGC
    CTCTGGTCAC GACCCGGTCC TTTCTCGGAC GGACAGAAAC GGTAGTAGGA GTAGTAGAGG AACACGACAT ACCACCAAAA ATGGTACCGG ATATAGTACG
179 E  T  S  A  G  P  G  K  S  L  P  V  F  A  I  I  L  I  I  S  L  C  C  M  V  V  F  T  M  A  Y  I  M  L

701 TCTGTCGGAA GACATCCCAA CAAGAGCATG TCTACGAAGC AGCCAGGGCA CATGCCAGAG AGGCCAACGA CTCTGGAGAA ACCATGAGGG TGGCCATCTT
    AGACAGCCTT CTGTAGGGTT GTTCTCGTAC AGATGCTTCG TCGGTCCCGT GTACGGTCTC TCCGGTTGCT GAGACCTCTT TGGTACTCCC ACCGGTAGAA
213   C  R  K  T  S  Q  Q  E  H  V  Y  E  A  A  R  A  H  A  R  E  A  N  D  S  G  E  T  M  R  V  A  I  F

801 CGCAAGTGGC TGCTCCAGTG ATGAGCCAAC TTCCCAGAAT CTGGGCAACA ACTACTCTGA TGAGCCCTGC ATAGGACAGG AGTACCAGAT CATCGCCCAG
    GCGTTCACCG ACGAGGTCAC TACTCGGTTG AAGGGTCTTA GACCCGTTGT TGATGAGACT ACTCGGGACG TATCCTGTCC TCATGGTCTA GTAGCGGGTC
246 A  S  G  C  S  S  D  E  P  T  S  Q  N  L  G  N  N  Y  S  D  E  P  C  I  G  Q  E  Y  Q  I  I  A  Q

901 ATCAATGGCA ACTACGCCCG CCTGCTGGAC ACAGTTCCTC TGGATTATGA GTTTCTGGCC ACTGAGGGCA AAAGTGTCTG TTAAAAATGC CCCATTAGGC
    TAGTTACCGT TGATGCGGGC GGACGACCTG TGTCAAGGAG ACCTAATACT CAAAGACCGG TGACTCCCGT TTTCACAGAC AATTTTTACG GGGTAATCCG
279 I  N  G  N  Y  A  R  L  L  D  T  V  P  L  D  Y  E  F  L  A  T  E  G  K  S  V  C  O

1001 CAGGATCTGC TGACATAATC TAGAGTCGAC CTGCAGAAGC TTGGCCGCCA TGGCCCAACT TGTTTATTGC AGCTTATAAT GGTTACAATA
     GTCCTAGACG ACTGTATTAG ATCTCAGCTG GACGTCTTCG AACCGGCGGT ACCGGGTTGA ACAAATAACG TCGAATATTA CCAATGTTAT
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Figure 3B

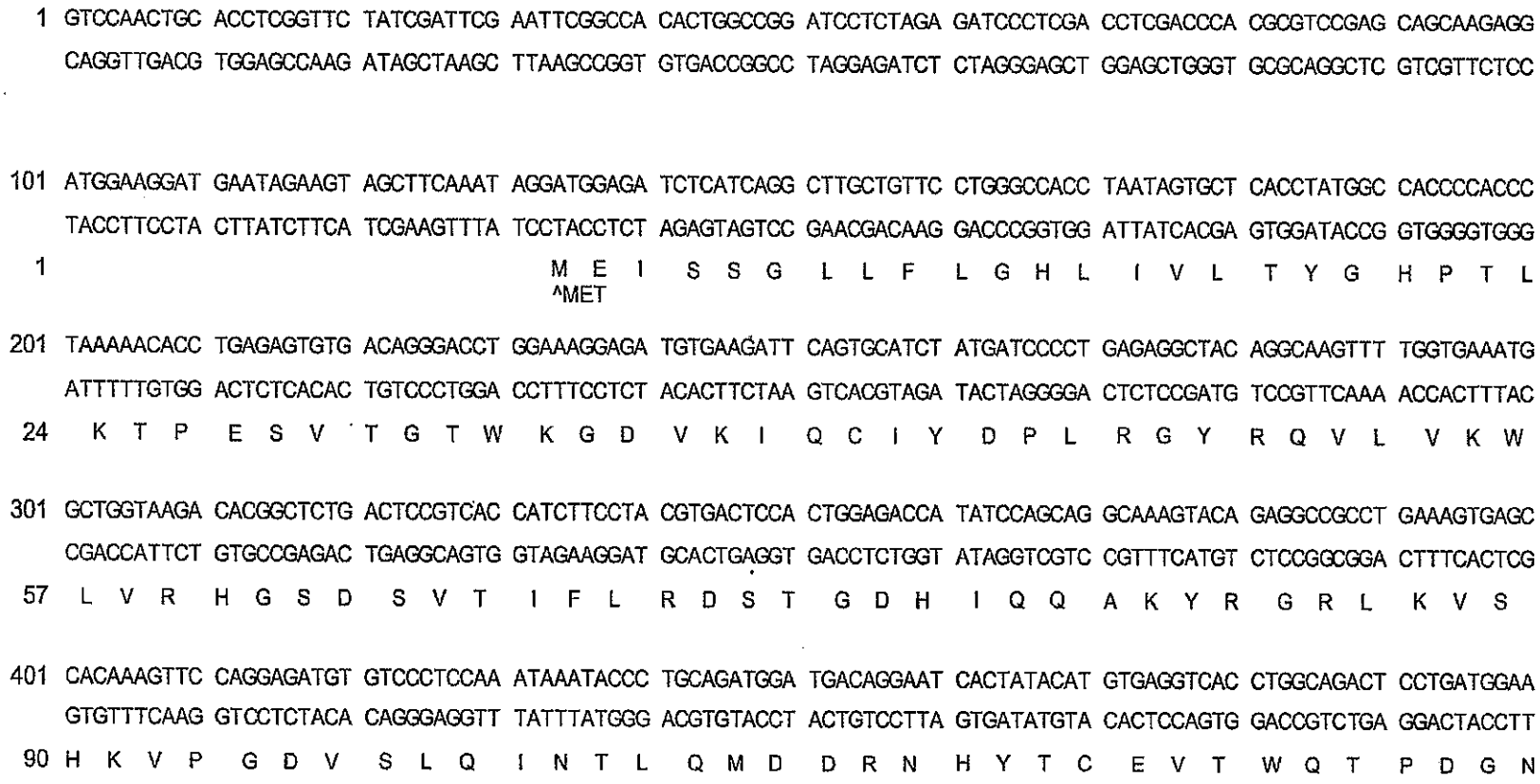

1 GTCCAACTGC ACCTCGGTTC TATCGATTCG AATTCGGCCA CACTGGCCGG ATCCTCTAGA GATCCCTCGA CCTCGACCCA CGCGTCCGAG CAGCAAGAGG
CAGGTTGACG TGGAGCCAAG ATAGCTAAGC TTAAGCCGGT GTGACCGGCC TAGGAGATCT CTAGGGAGCT GGAGCTGGGT GCGCAGGCTC GTCGTTCTCC
101 ATGGAAGGAT GAATAGAAGT AGCTTCAAAT AGGATGGAGA TCTCATCAGG CTTGCTGTTC CTGGGCCACC TAATAGTGCT CACCTATGGC CACCCCACCC
TACCTTCCTA CTTATCTTCA TCGAAGTTTA TCCTACCTCT AGAGTAGTCC GAACGACAAG GACCCGGTGG ATTATCACGA GTGGATACCG GTGGGGTGGG
1 M E I S S G L L F L G H L I V L T Y G H P T L
^MET
201 TAAAAACACC TGAGAGTGTG ACAGGGACCT GGAAAGGAGA TGTGAAGATT CAGTGCATCT ATGATCCCCT GAGAGGCTAC AGGCAAGTTT TGGTGAAATG
ATTTTTGTGG ACTCTCACAC TGTCCCTGGA CCTTTCCTCT ACACTTCTAA GTCACGTAGA TACTAGGGGA CTCTCCGATG TCCGTTCAAA ACCACTTTAC
24 K T P E S V T G T W K G D V K I Q C I Y D P L R G Y R Q V L V K W
301 GCTGGTAAGA CACGGCTCTG ACTCCGTCAC CATCTTCCTA CGTGACTCCA CTGGAGACCA TATCCAGCAG GCAAAGTACA GAGGCCGCCT GAAAGTGAGC
CGACCATTCT GTGCCGAGAC TGAGGCAGTG GTAGAAGGAT GCACTGAGGT GACCTCTGGT ATAGGTCGTC CGTTTCATGT CTCCGGCGGA CTTTCACTCG
57 L V R H G S D S V T I F L R D S T G D H I Q Q A K Y R G R L K V S
401 CACAAAGTTC CAGGAGATGT GTCCCTCCAA ATAAATACCC TGCAGATGGA TGACAGGAAT CACTATACAT GTGAGGTCAC CTGGCAGACT CCTGATGGAA
GTGTTTCAAG GTCCTCTACA CAGGGAGGTT TATTTATGGG ACGTGTACCT ACTGTCCTTA GTGATATGTA CACTCCAGTG GACCGTCTGA GGACTACCTT
90 H K V P G D V S L Q I N T L Q M D D R N H Y T C E V T W Q T P D G N

Figure 4A

```
501 ACCAAGTAAT AAGAGATAAG ATCATTGAGC TCCGTGTTCG GAAATATAAT CCACCTAGAA TCAATACTGA AGCACCTACA ACCCTGCACT CCTCTTTGGA
    TGGTTCATTA TTCTCTATTC TAGTAACTCG AGGCACAAGC CTTTATATTA GGTGGATCTT AGTTATGACT TCGTGGATGT TGGGACGTGA GGAGAAACCT
124   Q  V  I  R  D  K  I  I  E  L  R  V  R  K  Y  N  P  P  R  I  N  T  E  A  P  T  T  L  H  S  S  L  E

601 AGCAACAACT ATAATGAGTT CAACCTCTGA CTTGACCACT AATGGGACTG GAAAACTTGA GGAGACCATT GCTGGTTCAG GGAGGAACCT GCCAATCTTT
    TCGTTGTTGA TATTACTCAA GTTGGAGACT GAACTGGTGA TTACCCTGAC CTTTTGAACT CCTCTGGTAA CGACCAAGTC CCTCCTTGGA CGGTTAGAAA
157 A  T  T  I  M  S  S  T  S  D  L  T  T  N  G  T  G  K  L  E  E  T  I  A  G  S  G  R  N  L  P  I  F

701 GCCATAATCT TCATCATCTC CCTTTGCTGC ATAGTAGCTG TCACCATACC TTATATCTTG TTCCGCTGCA GGACATTCCA ACAAGAGTAT GTCTATGGAG
    CGGTATTAGA AGTAGTAGAG GGAAACGACG TATCATCGAC AGTGGTATGG AATATAGAAC AAGGCGACGT CCTGTAAGGT TGTTCTCATA CAGATACCTC
190 A  I  I  F  I  I  S  L  C  C  I  V  A  V  T  I  P  Y  I  L  F  R  C  R  T  F  Q  Q  E  Y  V  Y  G  V

801 TGAGCAGGGT GTTTGCCAGG AAGACAAGCA ACTCTGAAGA AACCACAAGG GTGACTACCA TCGCAACTGA TGAACCAGAT TCCCAGGCTC TGATTAGTGA
    ACTCGTCCCA CAAACGGTCC TTCTGTTCGT TGAGACTTCT TTGGTGTTCC CACTGATGGT AGCGTTGACT ACTTGGTCTA AGGGTCCGAG ACTAATCACT
224   S  R  V  F  A  R  K  T  S  N  S  E  E  T  T  R  V  T  T  I  A  T  D  E  P  D  S  Q  A  L  I  S  D

901 CTACTCTGAT GATCCTTGCC TCAGCCAGGA GTACCAAATA ACCATCAGAT CAACAATGTC TATTCCTGCC TGCTGAACAC AGTTTCCAGA AACTAAGAAG
    GATGAGACTA CTAGGAACGG AGTCGGTCCT CATGGTTTAT TGGTAGTCTA GTTGTTACAG ATAAGGACGG ACGACTTGTG TCAAAGGTCT TTGATTCTTC
257 Y  S  D  D  P  C  L  S  Q  E  Y  Q  I  T  I  R  S  T  M  S  I  P  A  C  O

1001 TTCTTGCTAC TGAAGAAAAT AACATCTGCT AAAATGCCCC TACTAAGTCA AGGTCTACTG GCGTAATTAC CTGTTACTTA TTTACTACTT GCCTTCAACA
     AAGAACGATG ACTTCTTTTA TTGTAGACGA TTTTACGGGG ATGATTCAGT TCCAGATGAC CGCATTAATG GACAATGAAT AAATGATGAA CGGAAGTTGT
```

Figure 4B

1101 TAGCTTTCTC CCTGGCTTCC TTTCTTCTTA GACAACCTAA AGTATCTATC TAGTCTGCCA ATTCTGGGGC CATTGAGAAA TCCTGGGTTT GGCTAAGAAT
ATCGAAAGAG GGACCGAAGG AAAGAAGAAT CTGTTGGATT TCATAGATAG ATCAGACGGT TAAGACCCCG GTAACTCTTT AGGACCCAAA CCGATTCTTA

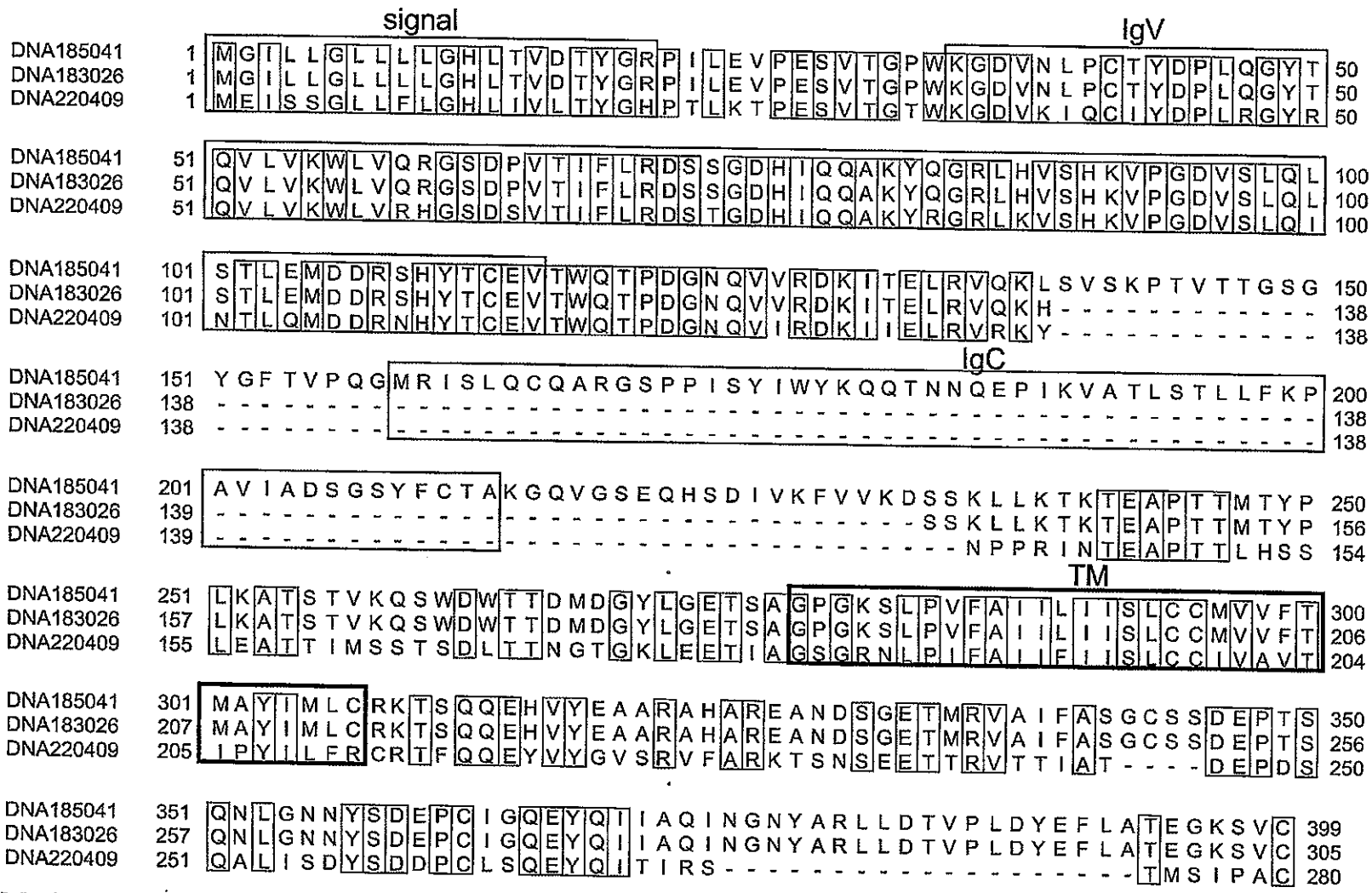
1201 ATACTACATG CACCTCAAGA AATCTAGCTT CTGGGCTTCA CCCAGAACAA TTTTCTTCCT AGGGCCTTCA CAACTCTTCT CCAAACAGCA GAGAAATTCC
TATGATGTAC GTGGAGTTCT TTAGATCGAA GACCCGAAGT GGGTCTTGTT AAAAGAAGGA TCCCGGAAGT GTTGAGAAGA GGTTTGTCGT CTCTTTAAGG

1301 ATAGCAGTAG AGGTTCTTTA TCATGCCTCC AGACAGCGTG AGTCTCAGTC CTACAAACTC AGACAAGCAC ATGGGTCTAG GATTACTCCT CTTTCTCTAG
TATCGTCATC TCCAAGAAAT AGTACGGAGG TCTGTCGCAC TCAGAGTCAG GATGTTTGAG TCTGTTCGTG TACCCAGATC CTAATGAGGA GAAAGAGATC

1401 GGCCAGATGA CTTTTAATTG ATATTACTAT TGCTACATTA TGAATCTAAT GCACATGTAT TCTTTTGTTG TTAATAAATG TTTAATCATG ACATCAAAAA
CCGGTCTACT GAAAATTAAC TATAATGATA ACGATGTAAT ACTTAGATTA CGTGTACATA AGAAAACAAC AATTATTTAC AAATTAGTAC TGTAGTTTTT

1501 AAAAAAAAAA AAGGGCGGCC GCGACTCTAG AGTCGACCTG CAGTAGGGAT AACAGGGTAA TAAGCTTGGC CGCCATGGCC CAACTTGTTT
TTTTTTTTTT TTCCCGCCGG CGCTGAGATC TCAGCTGGAC GTCATCCCTA TTGTCCCATT ATTCGAACCG GCGGTACCGG GTTGAACAAA
^pRK5 continues here

Figure 4C



Murine STIgMA on Chr 11
Human STIgMA on X-chromosome

Figure 5

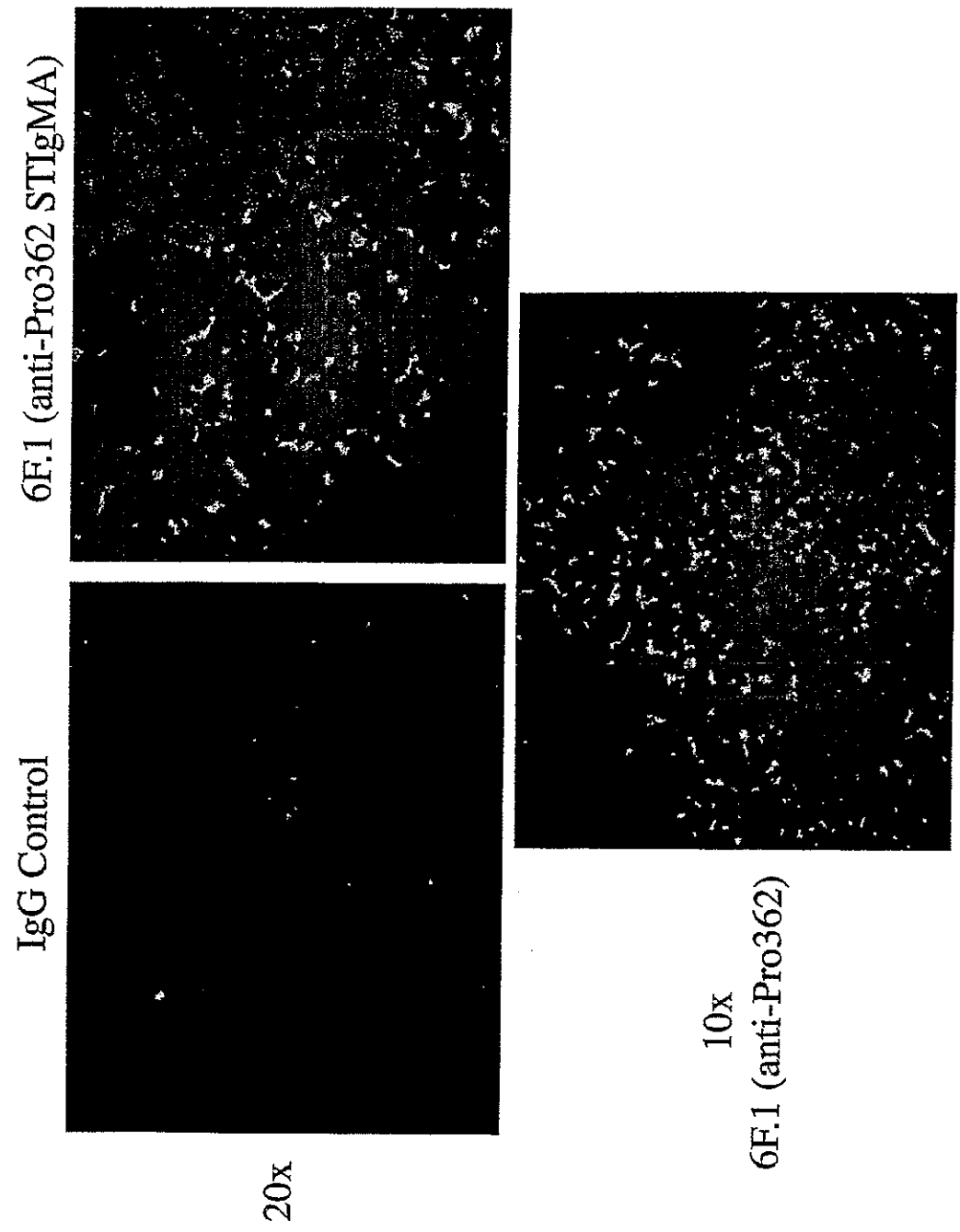


Figure 6

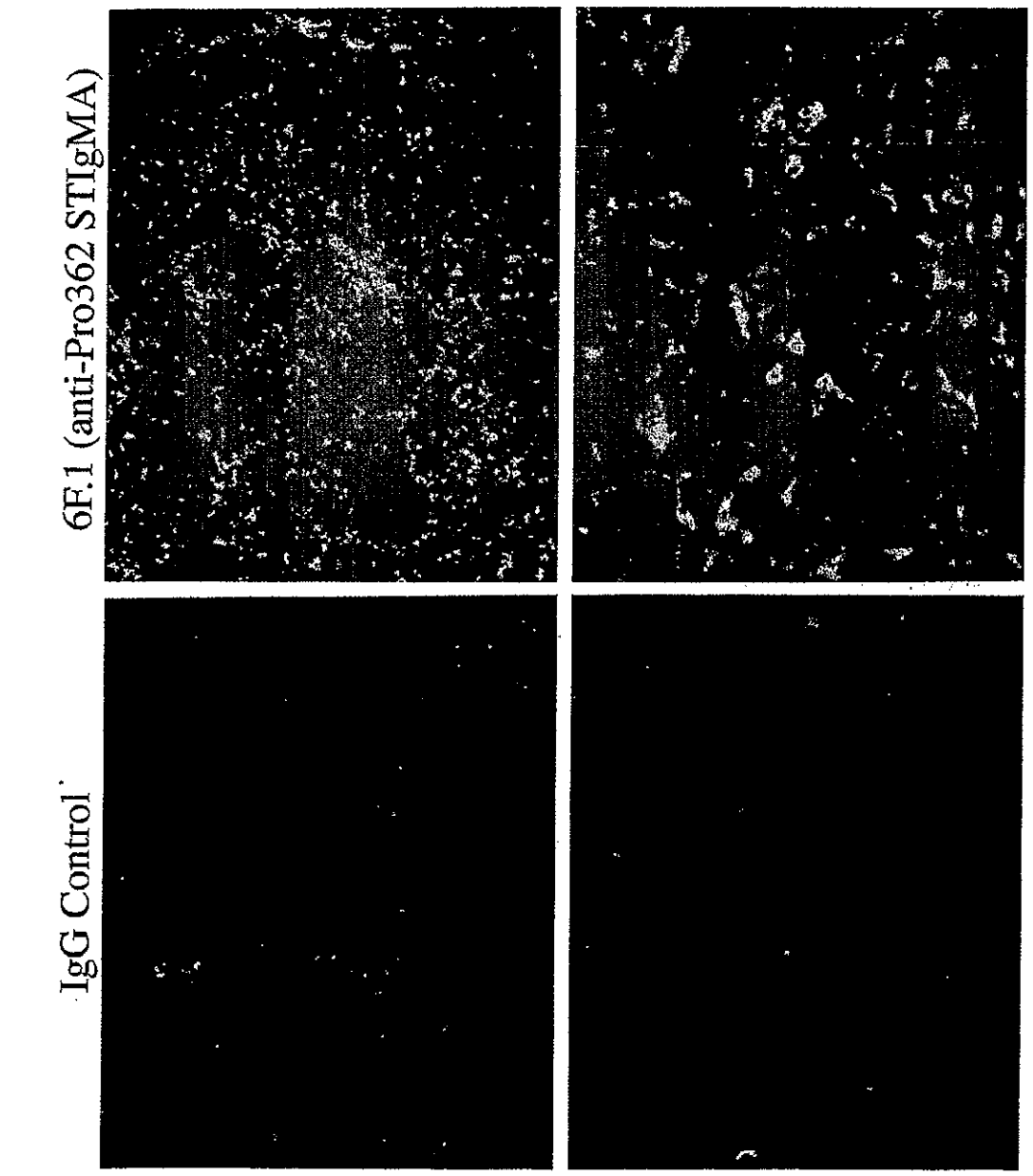


Figure 7

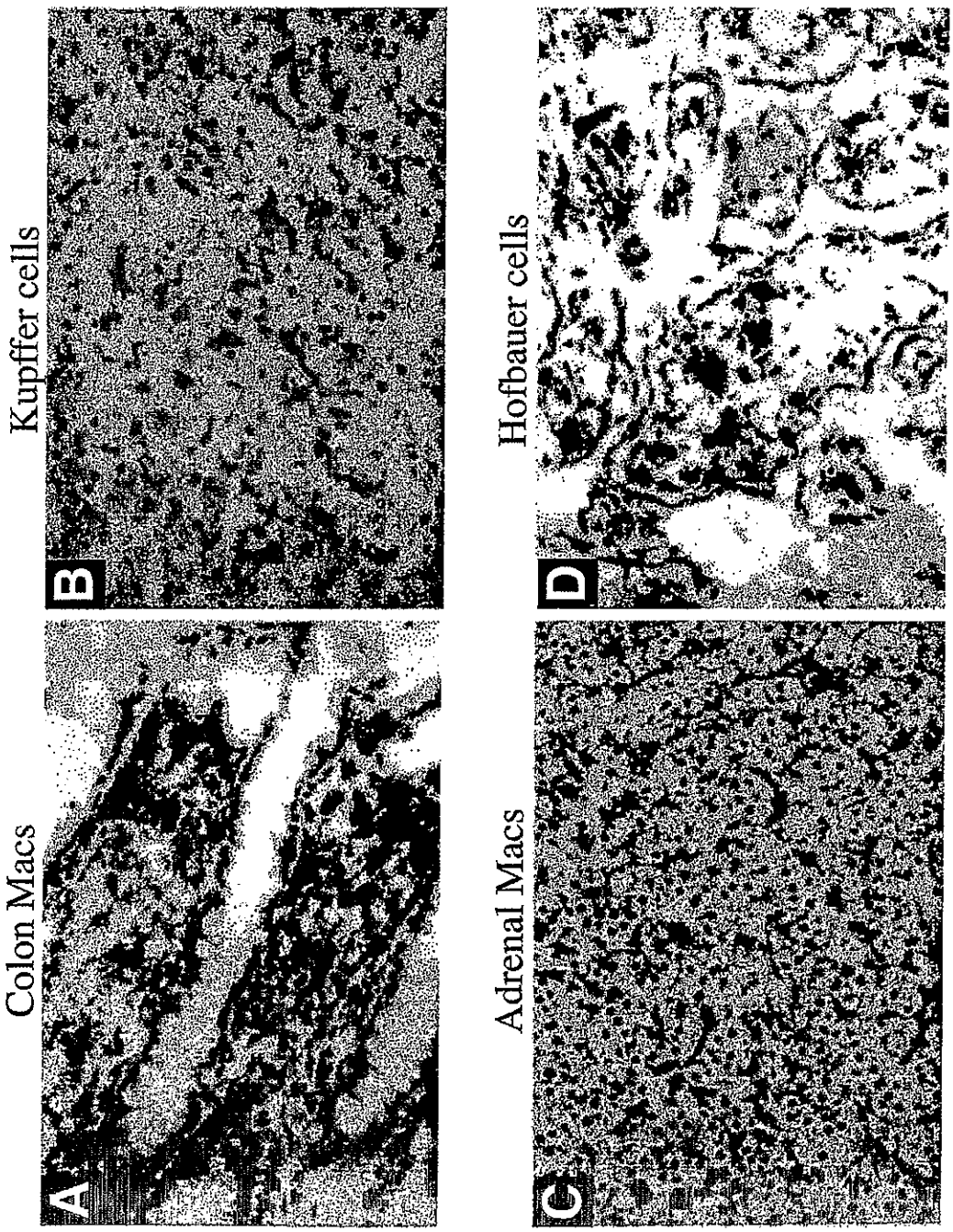


Figure 8

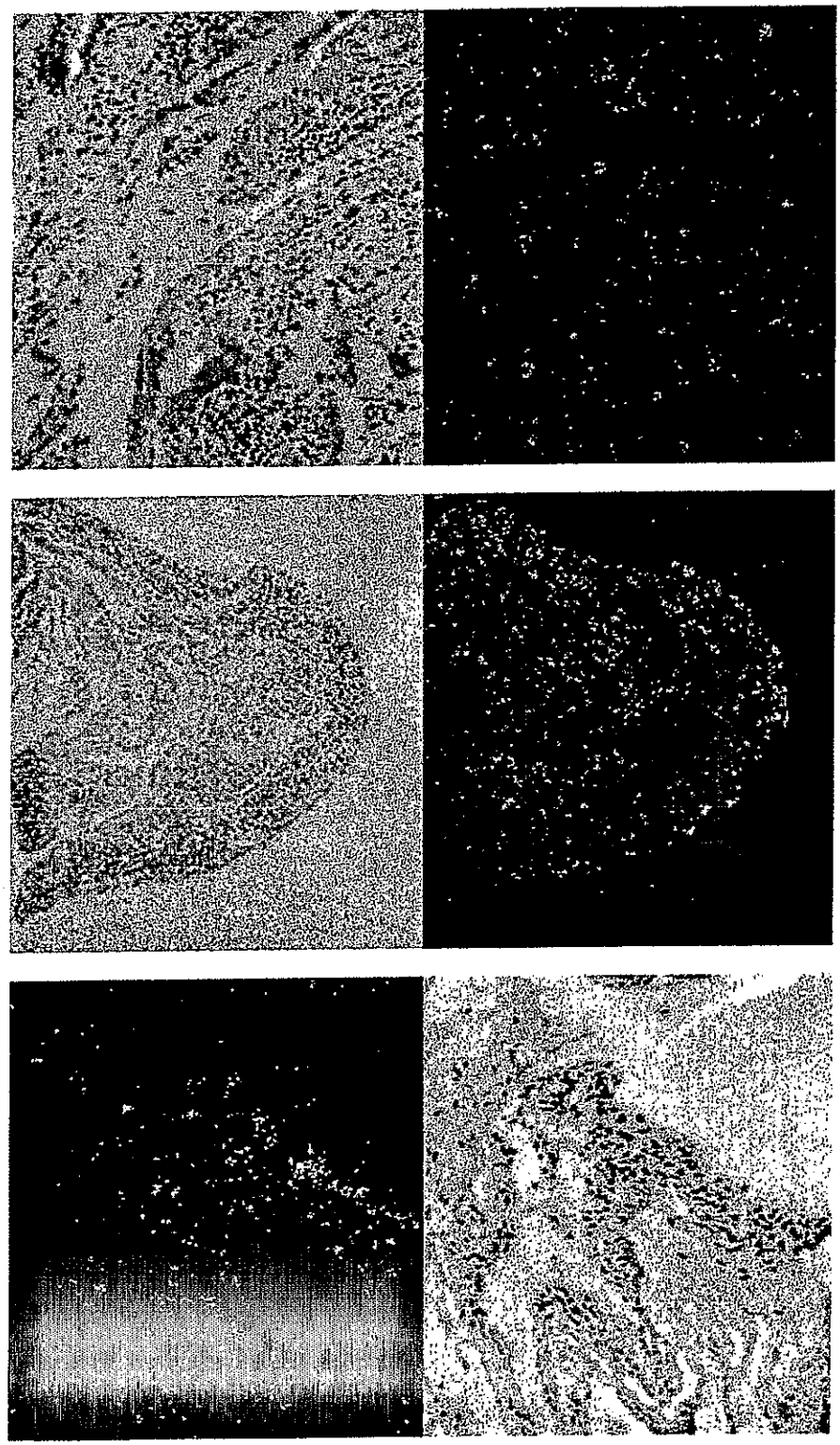


Figure 9

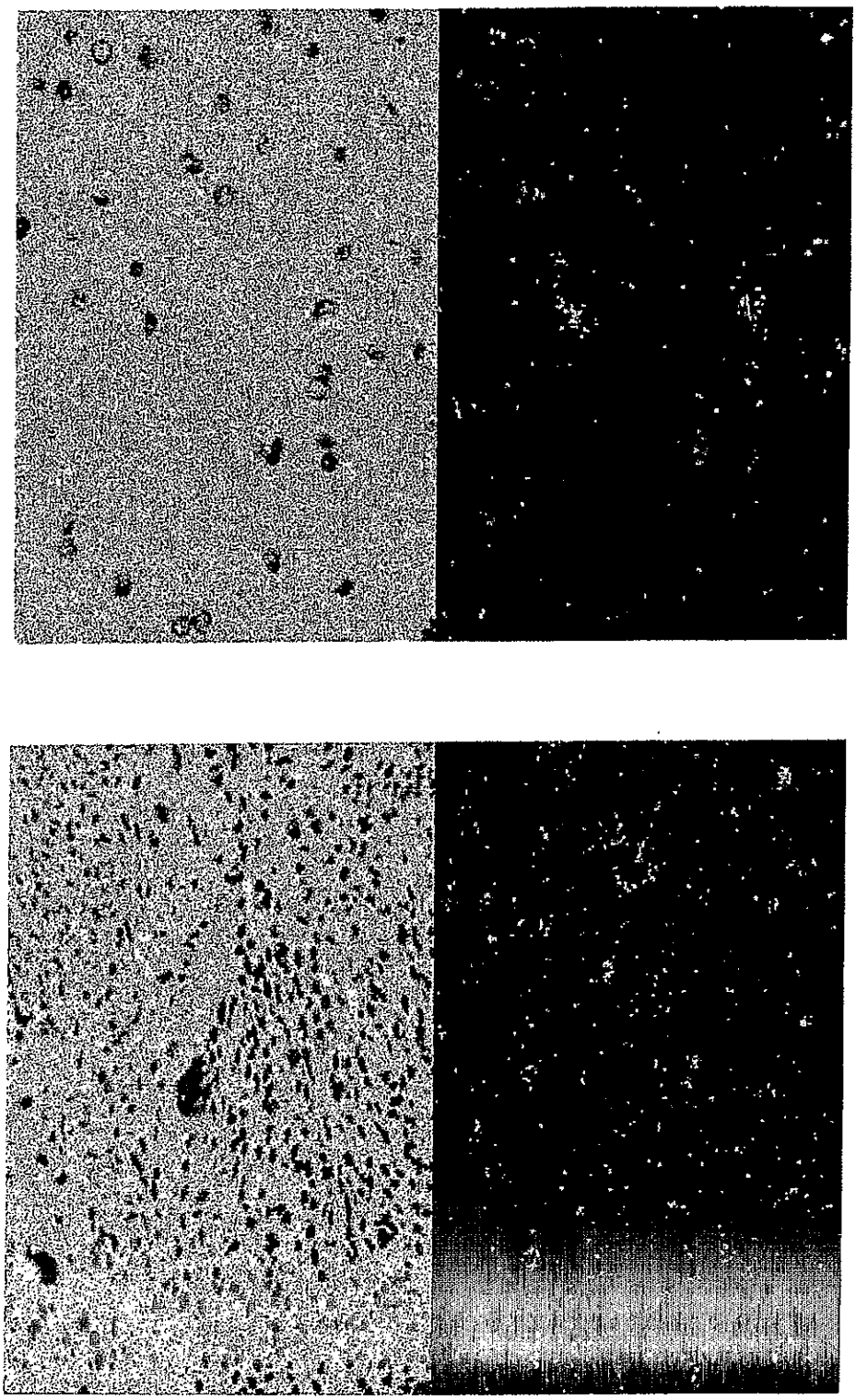


Figure 10

Aveolar Macs

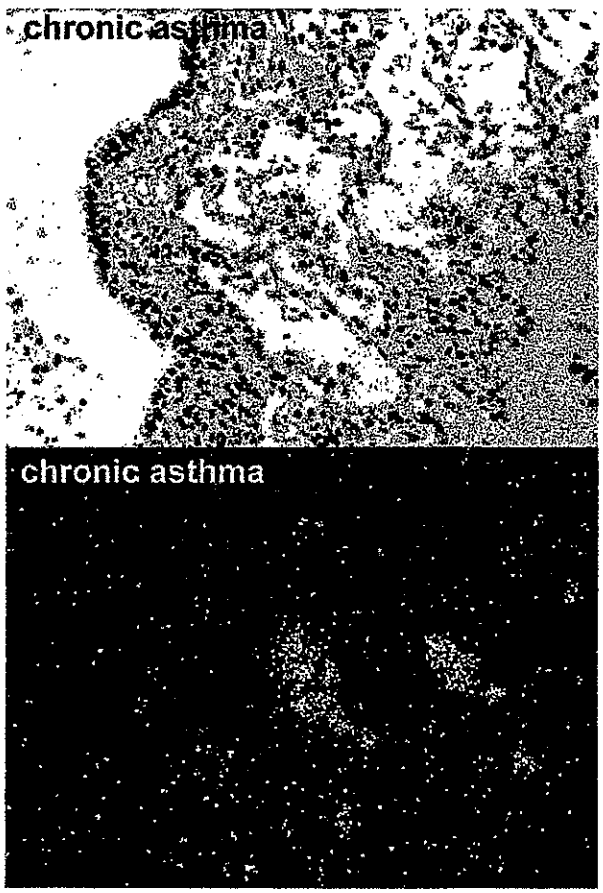


Figure 11

Liver Kupffer cells

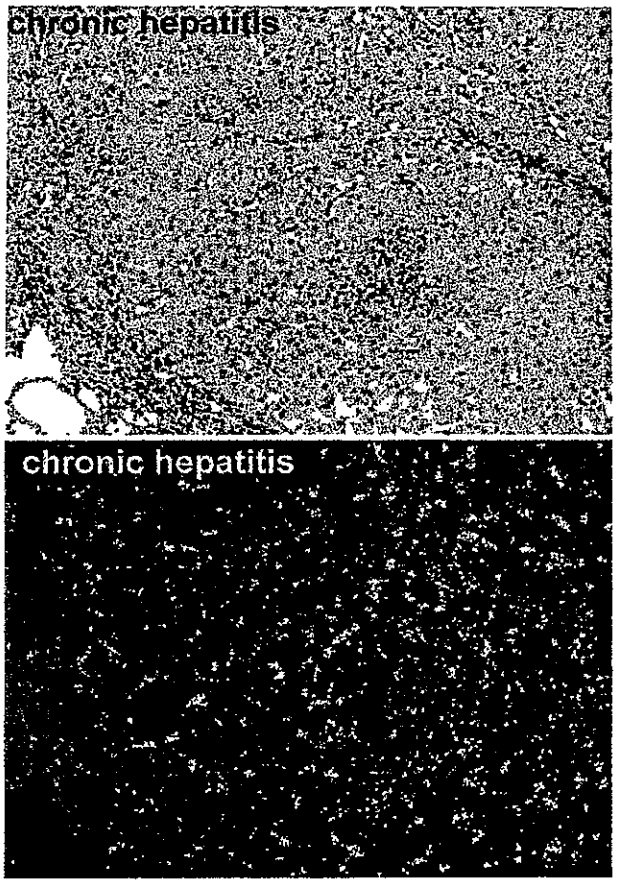
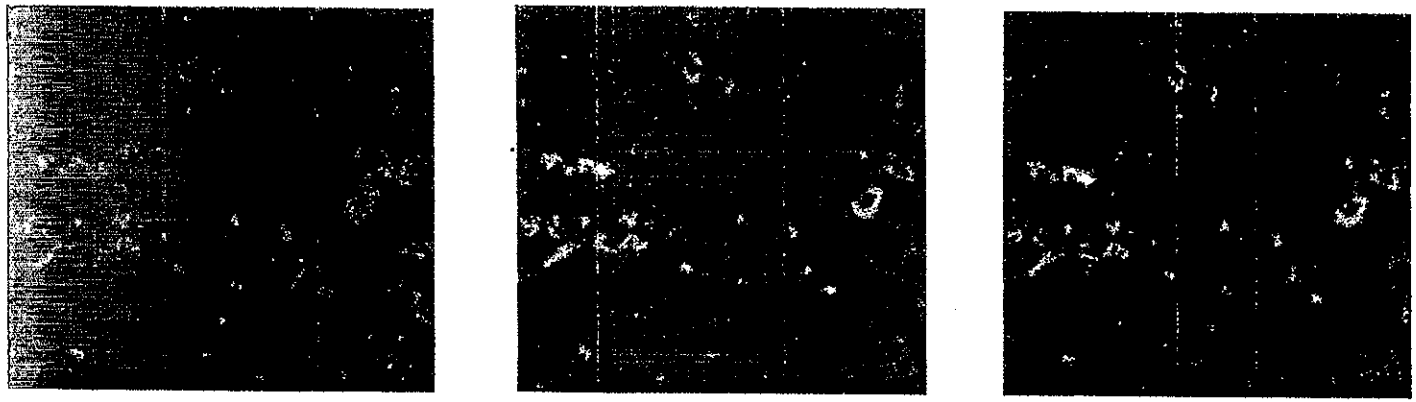


Figure 12

DUAL STIgMA-CD68 IHC

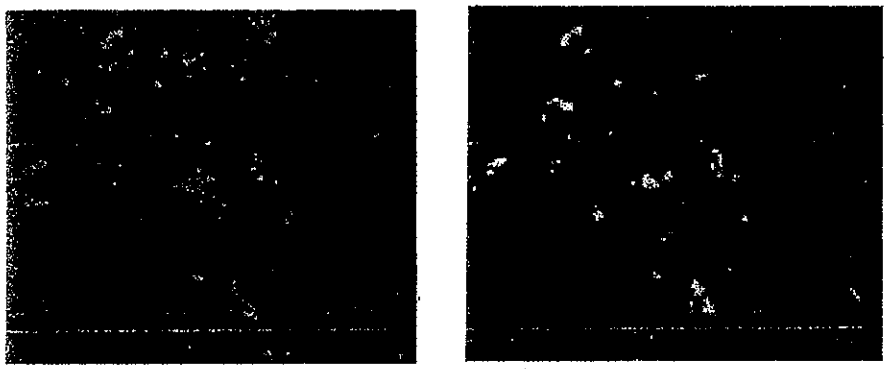
Adrenal gland macrophages



Adrenal-STIgMA | Adrenal-CD68 | Adrenal-STIgMA/CD68

Figure 13

Liver Kupffer cells



Liver-STIgMA Liver-CD68

Figure 14

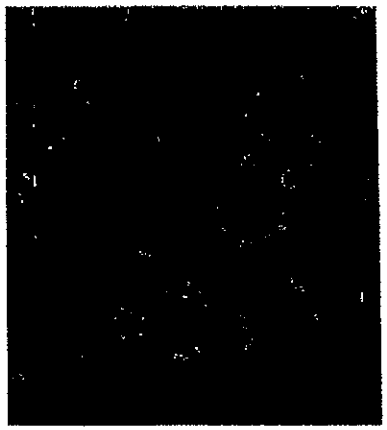
Brain Microglial cells



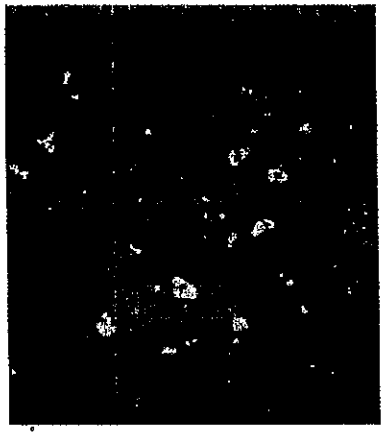
Brain-STIgMA Brain-CD68 Brain-STIgMA/CD68

Figure 15

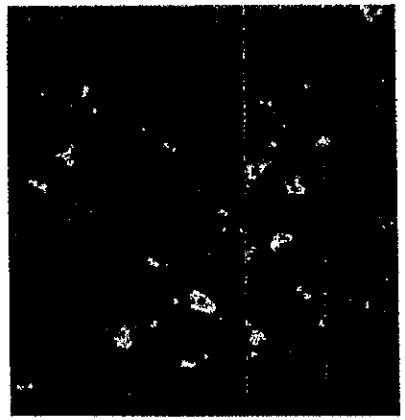
Placental Hofbauer cells



Placenta-STIgMA



Placenta-CD68



Placenta-STIgMA/CD68

Figure 16

1.8
1.5
brain
heart
sk. musc.
colon
thymus
spleen
kidney
liver
small int.
placenta
lung
PBL
adrenal gland
bladder
bone marrow
brain
lymph node
mammary gland
prostate
spinal chord
stomach
thyroid
trachea
uterus

Figure 17

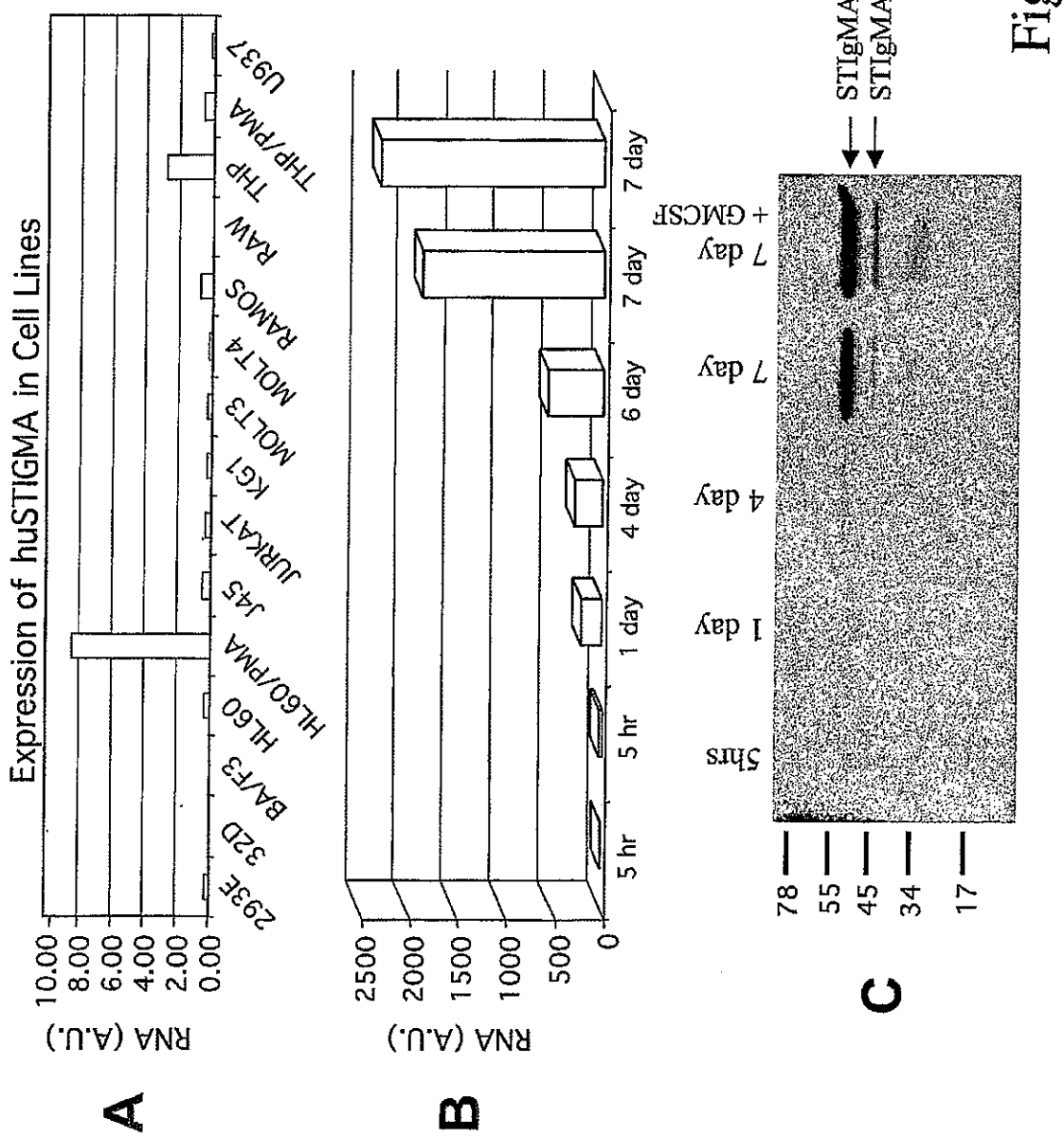

A
Expression of huSTIGMA in Cell Lines
RNA (A.U.)
10.00
8.00
6.00
4.00
2.00
0.00
293E
32D
BA/F3
HL60
HL60/PMA
J45
JURKAT
K51
MOLT3
MOLT4
RAMOS
RAW
THP
THP/PMA
U937
B
RNA (A.U.)
2500
2000
1500
1000
500
0
5 hr
1 day
4 day
6 day
7 day
7 day
C
STIgMA_long
STIgMA_short
5hrs
1 day
4 day
7 day
7 day + GMCSF
78
55
45
34
17

Figure 18

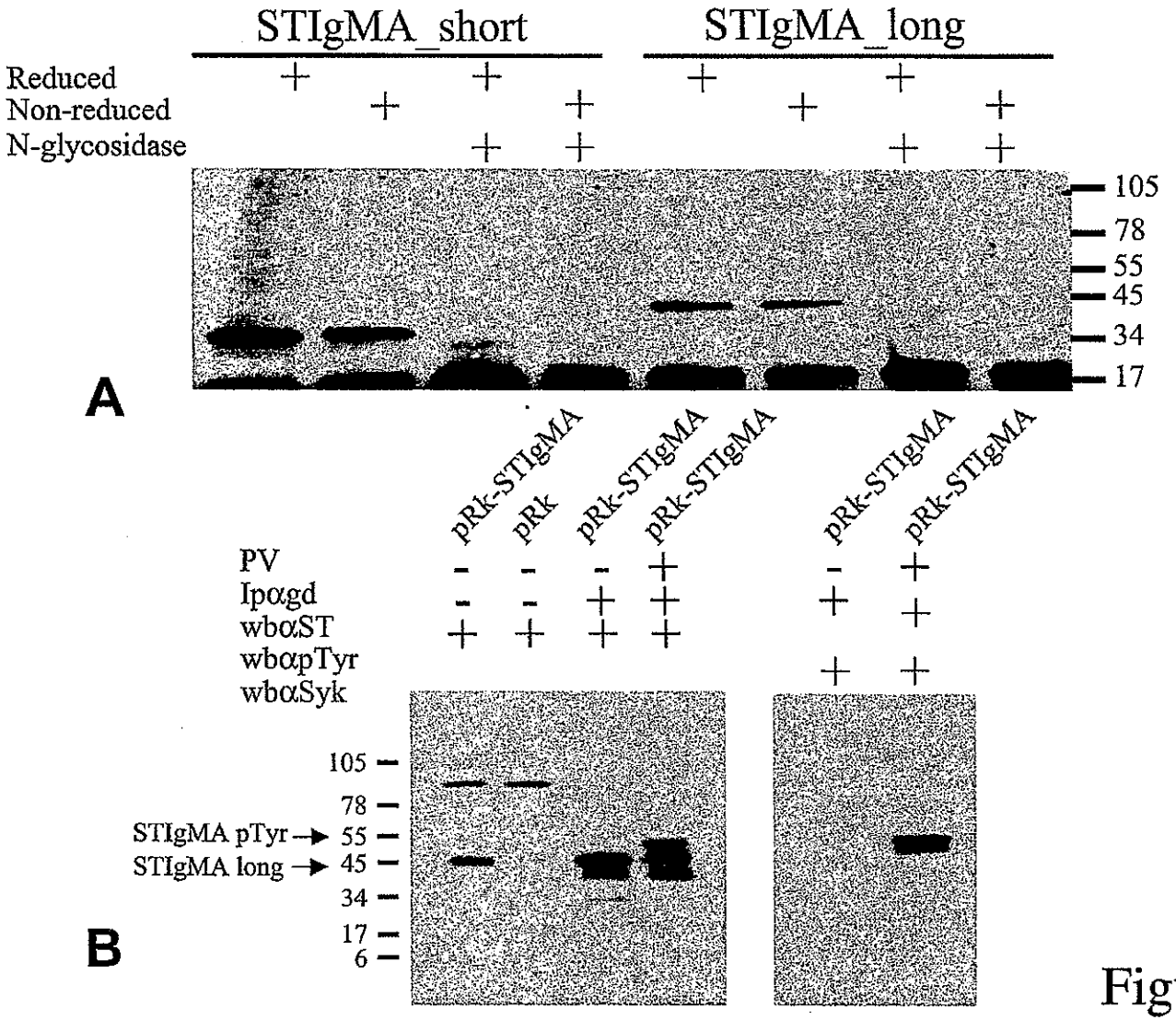

STIgMA_short
STIgMA_long
Reduced
Non-reduced
N-glycosidase
105
78
55
45
34
17
A
pRk-STIgMA
pRk
pRk-STIgMA
pRk-STIgMA
pRk-STIgMA
pRk-STIgMA
PV
Ipαgd
wbαST
wbαpTyr
wbαSyk
105
78
STIgMA pTyr
55
STIgMA long
45
34
17
6
B

Figure 19

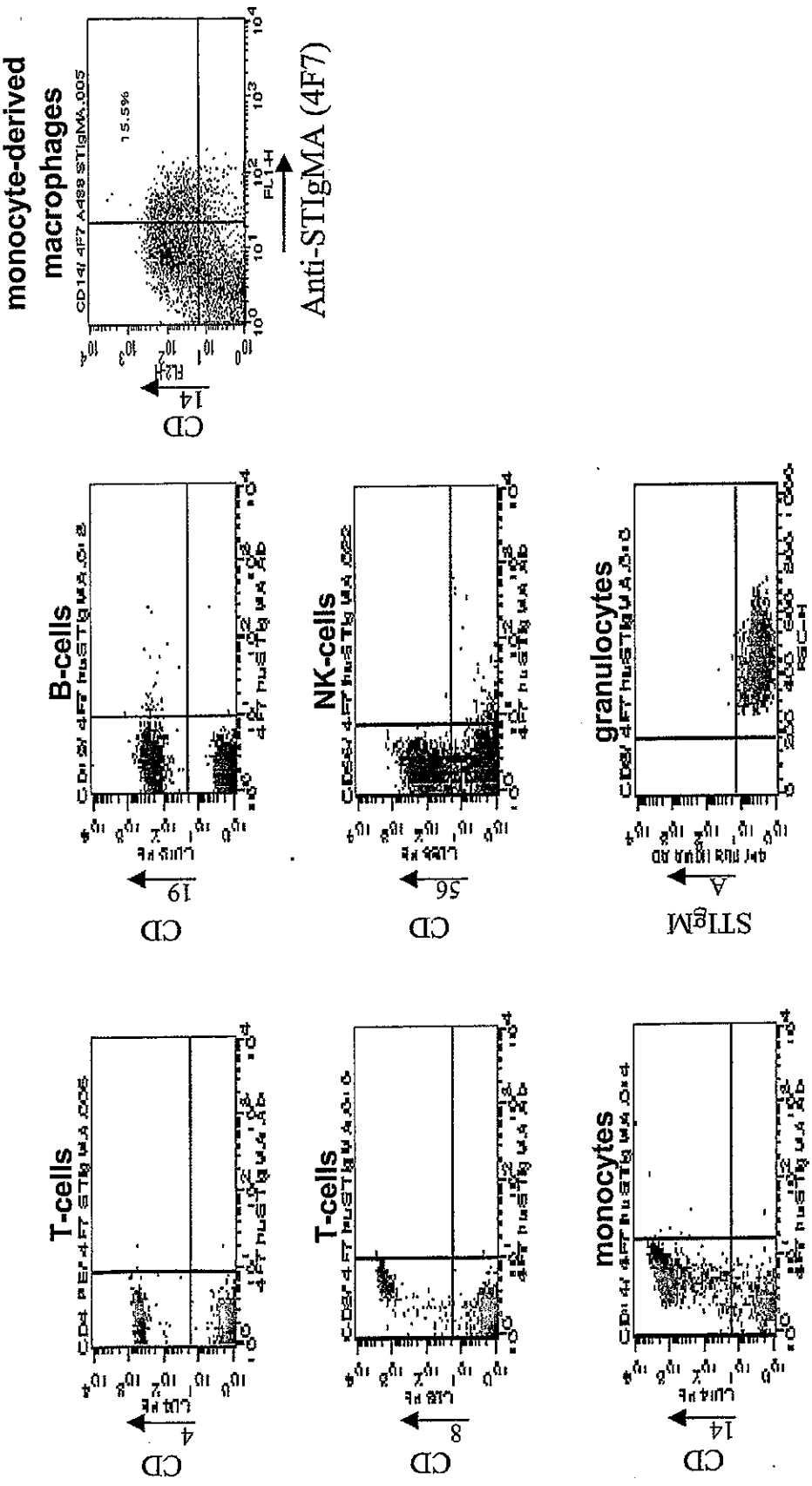

monocyte-derived macrophages
15.5%
Anti-STIgMA (4F7)
CD14
B-cells
CD19
NK-cells
CD56
granulocytes
STIgM
CD15
T-cells
CD4
T-cells
CD8
monocytes
CD14

Figure 20

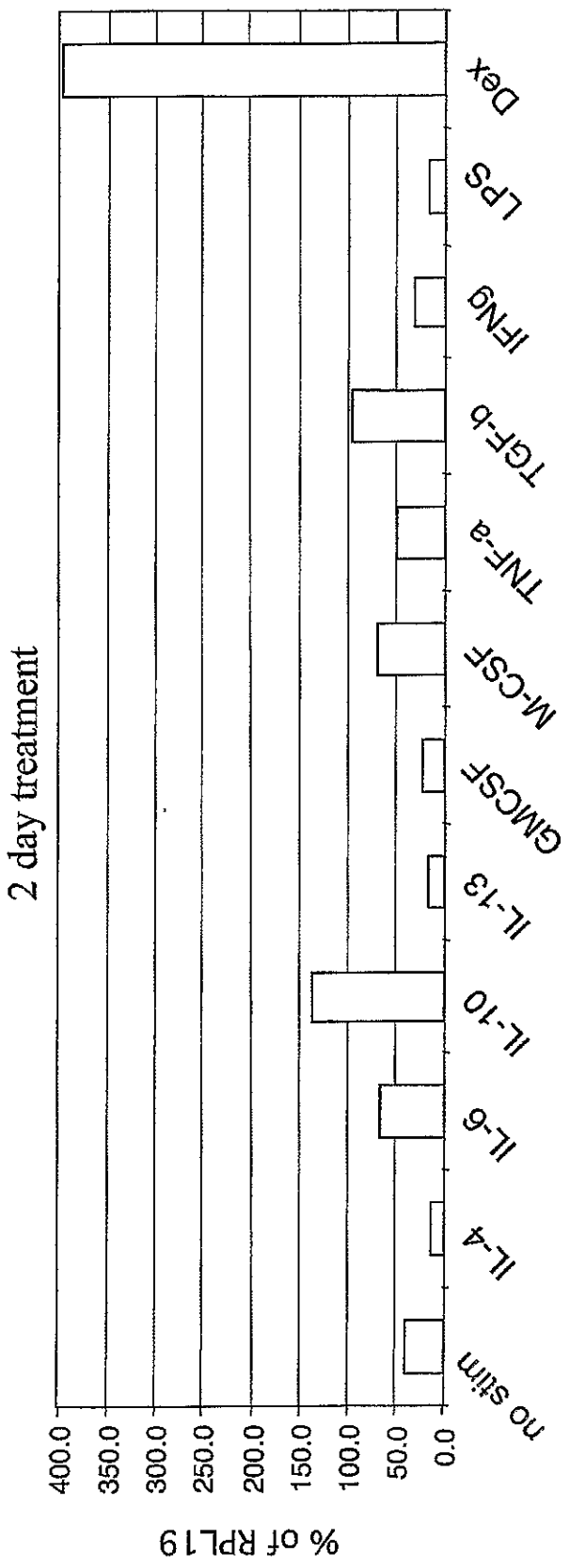

2 day treatment
% of RPL19
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
no stim
IL-4
IL-6
IL-10
IL-13
GMCSF
M-CSF
TNF-a
TGF-b
IFNg
LPS
Dex

Figure 21A

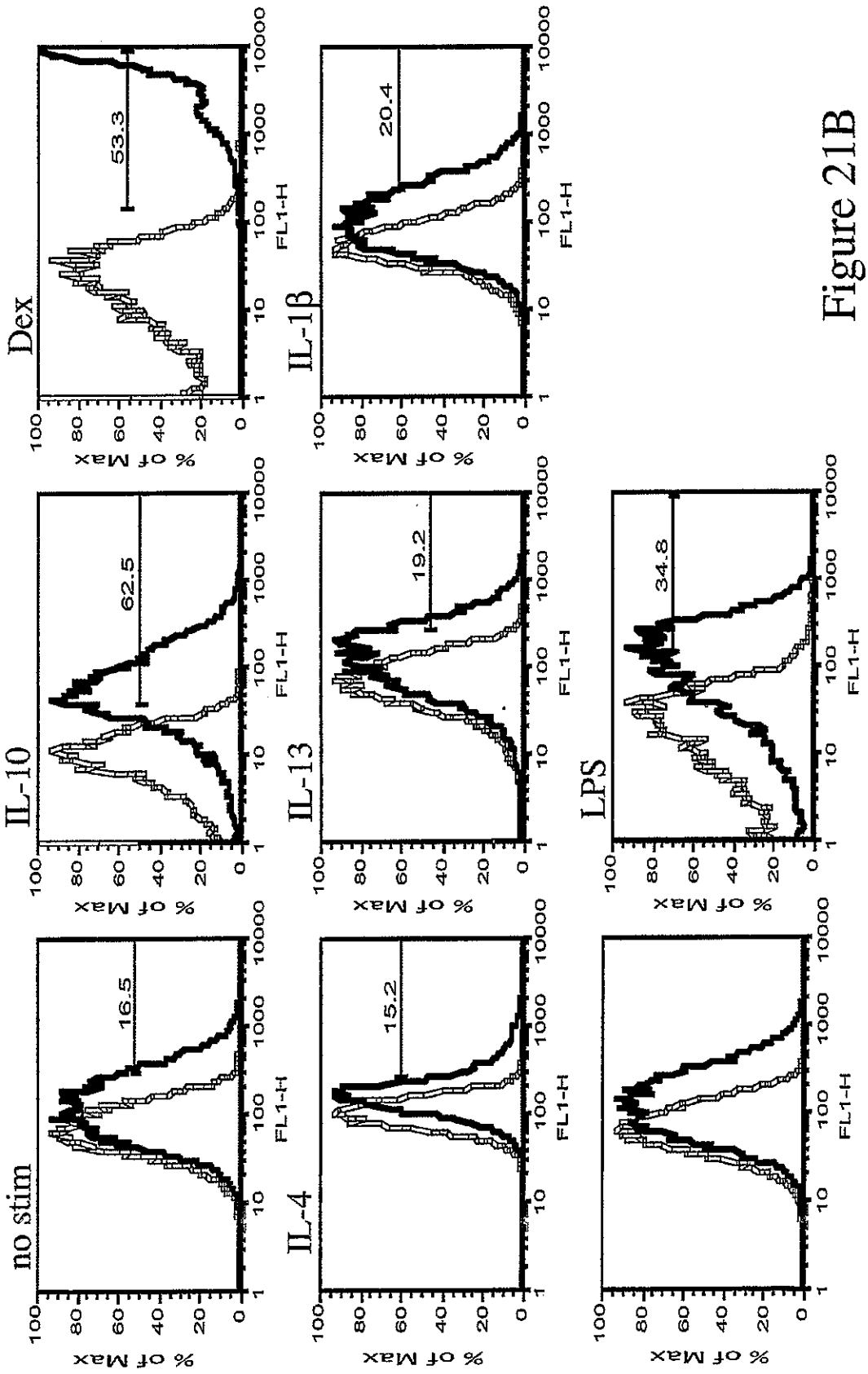
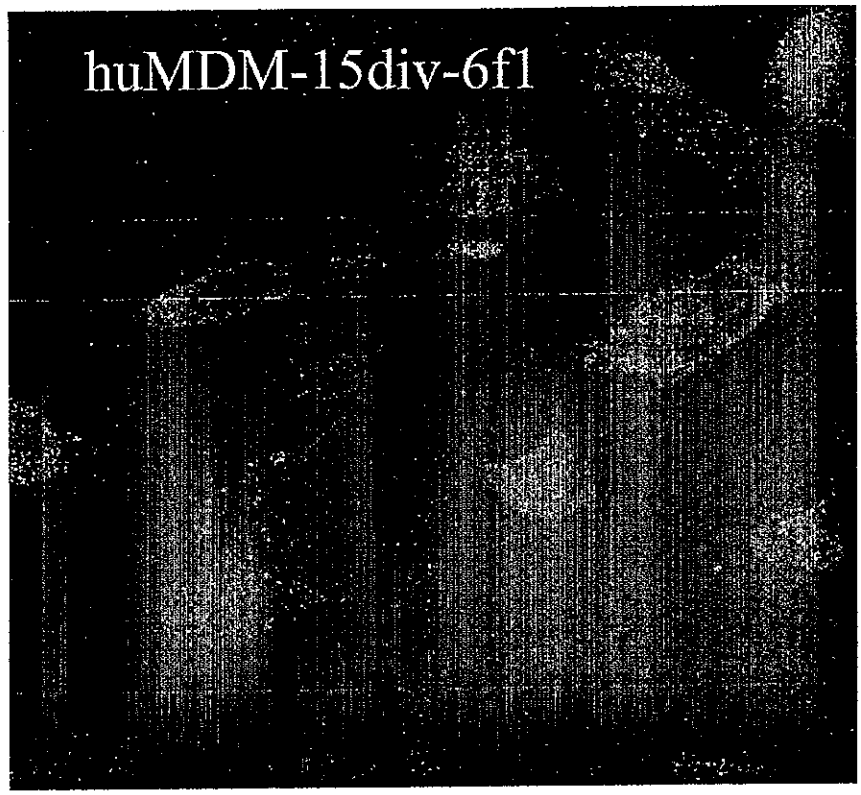

no stim
16.5
IL-10
62.5
IL-4
15.2
IL-13
19.2
LPS
34.8
Dex
53.3
IL-1β
20.4
% of Max
FL1-H
1
10
100
1000
10000
0
20
40
60
80
100

Figure 21B



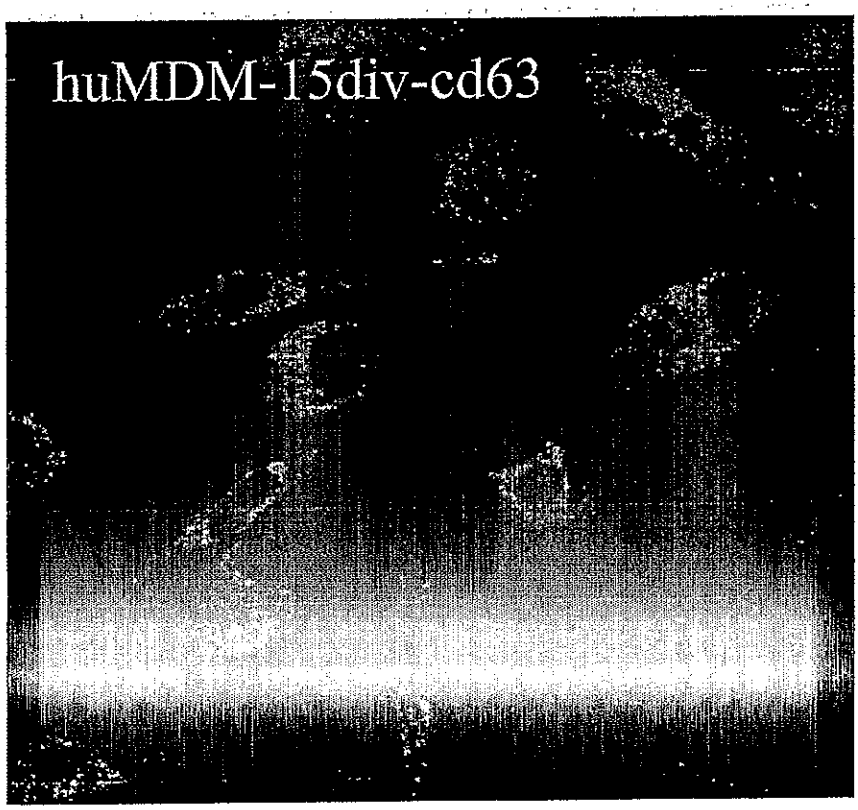


Figure 22

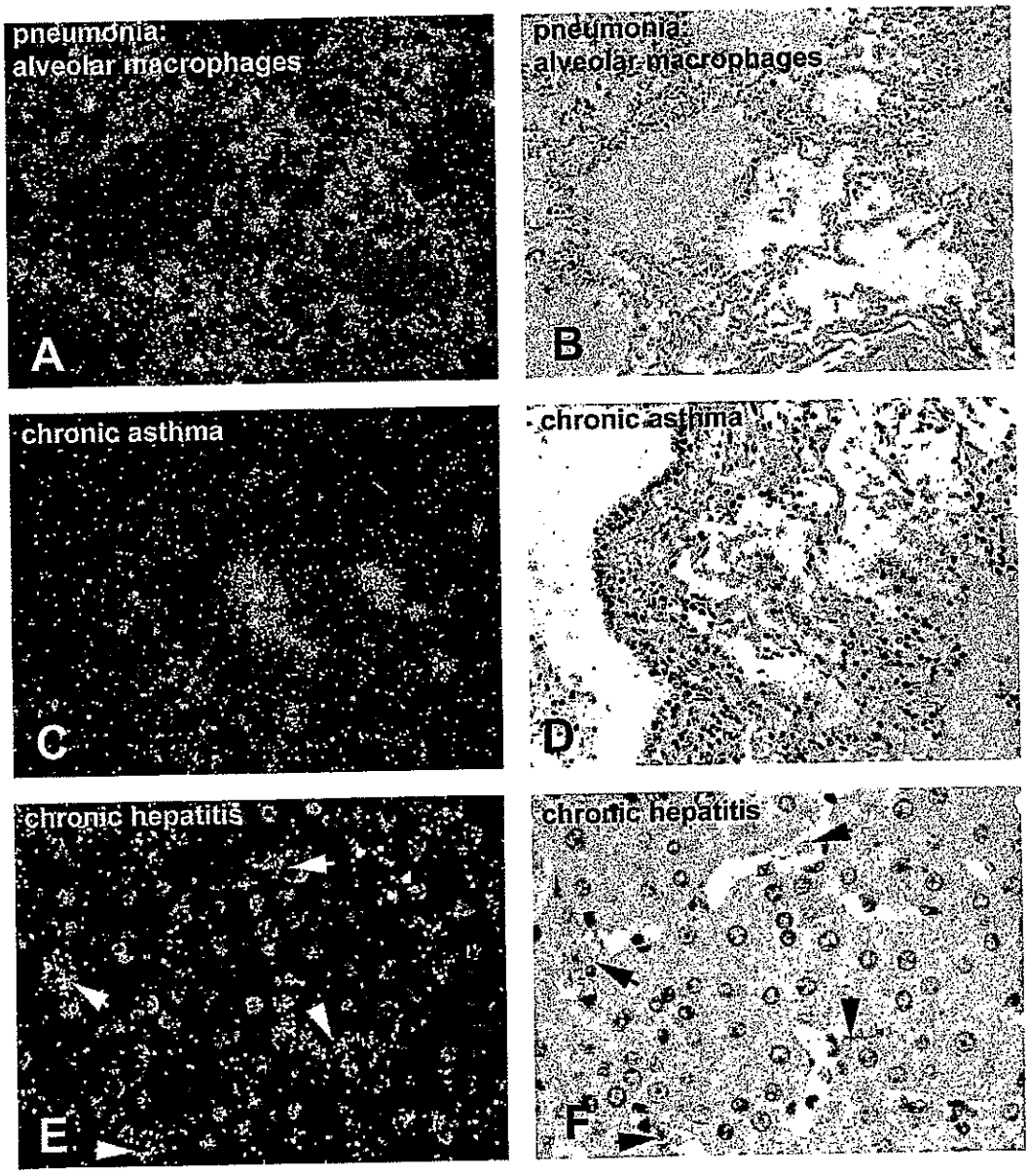

pneumonia:
alveolar macrophages
A
pneumonia:
alveolar macrophages
B
chronic asthma
C
chronic asthma
D
chronic hepatitis
E
chronic hepatitis
F

Figure 23

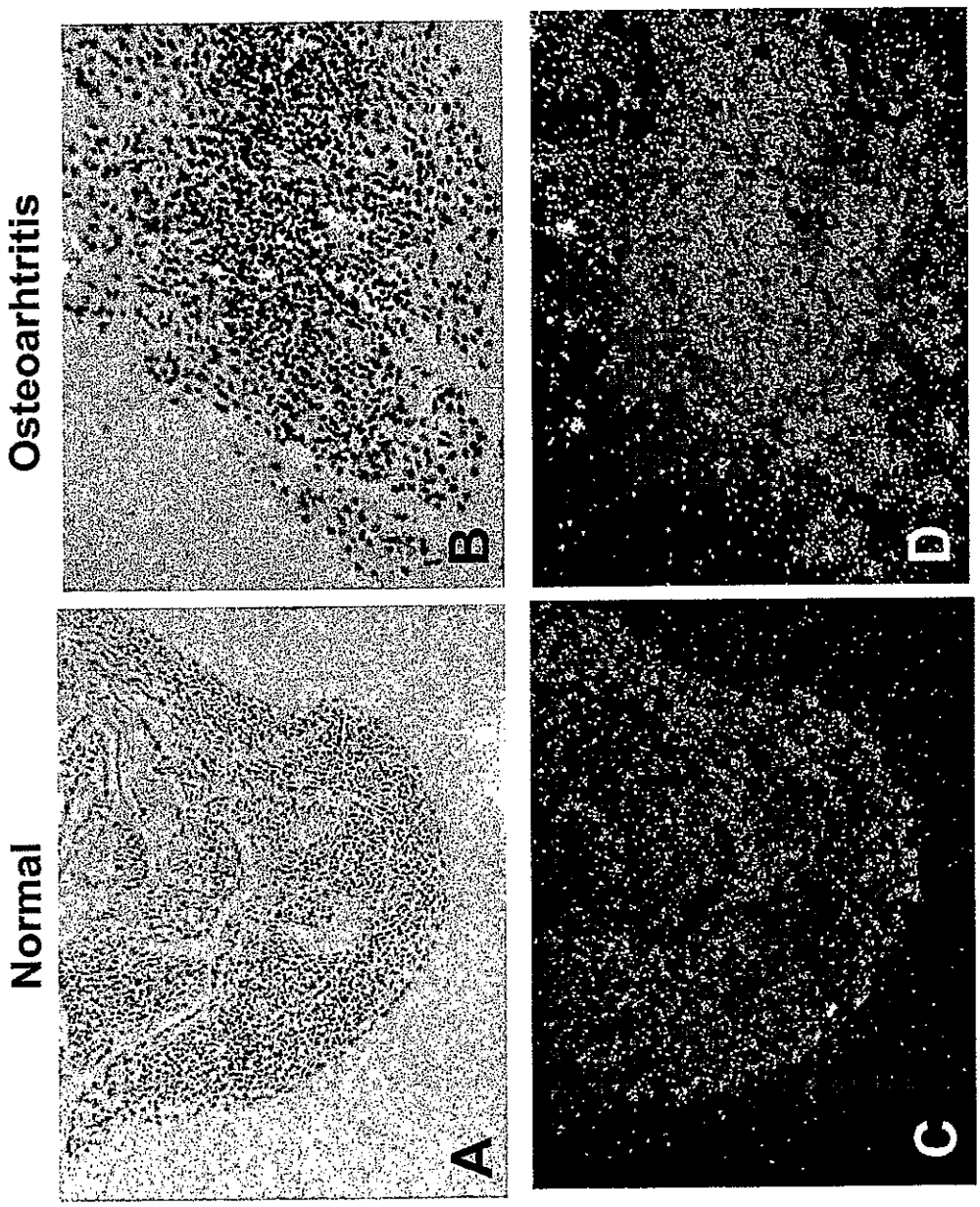


Figure 24

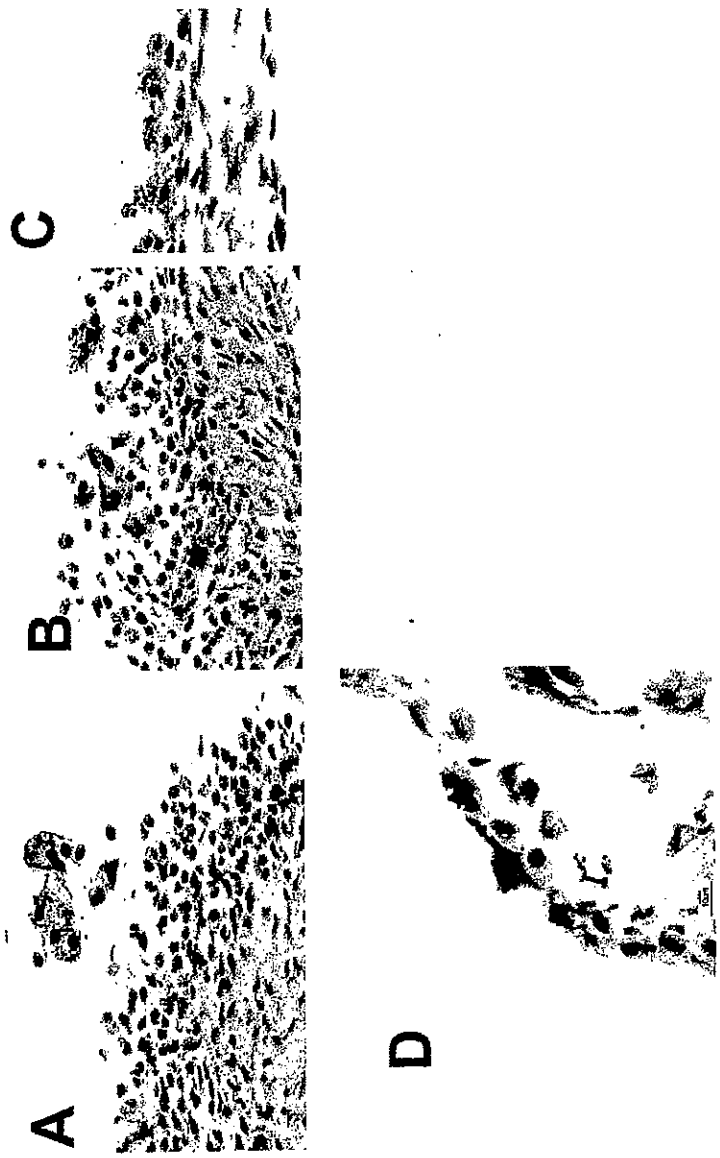


Figure 25

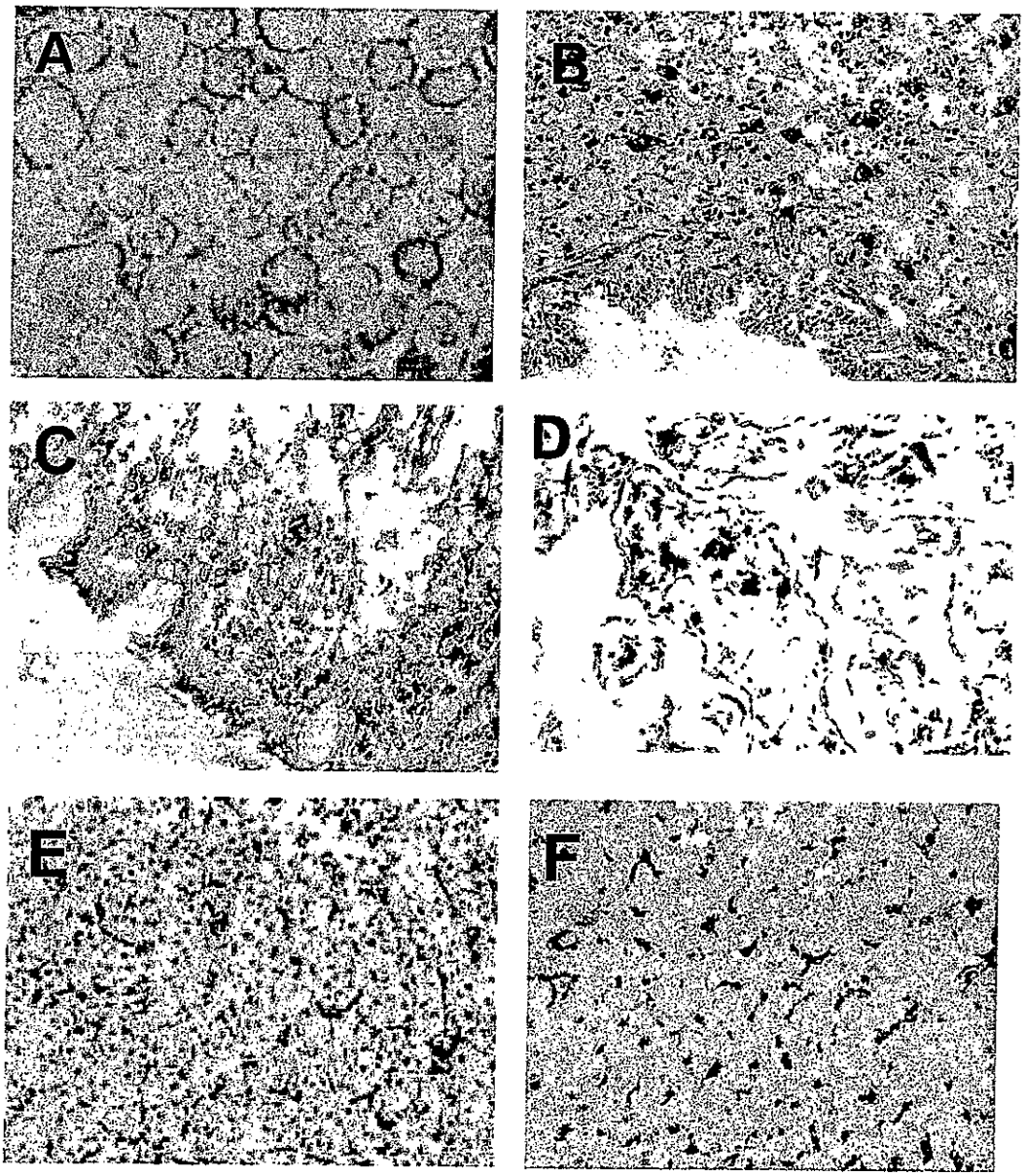


Figure 26

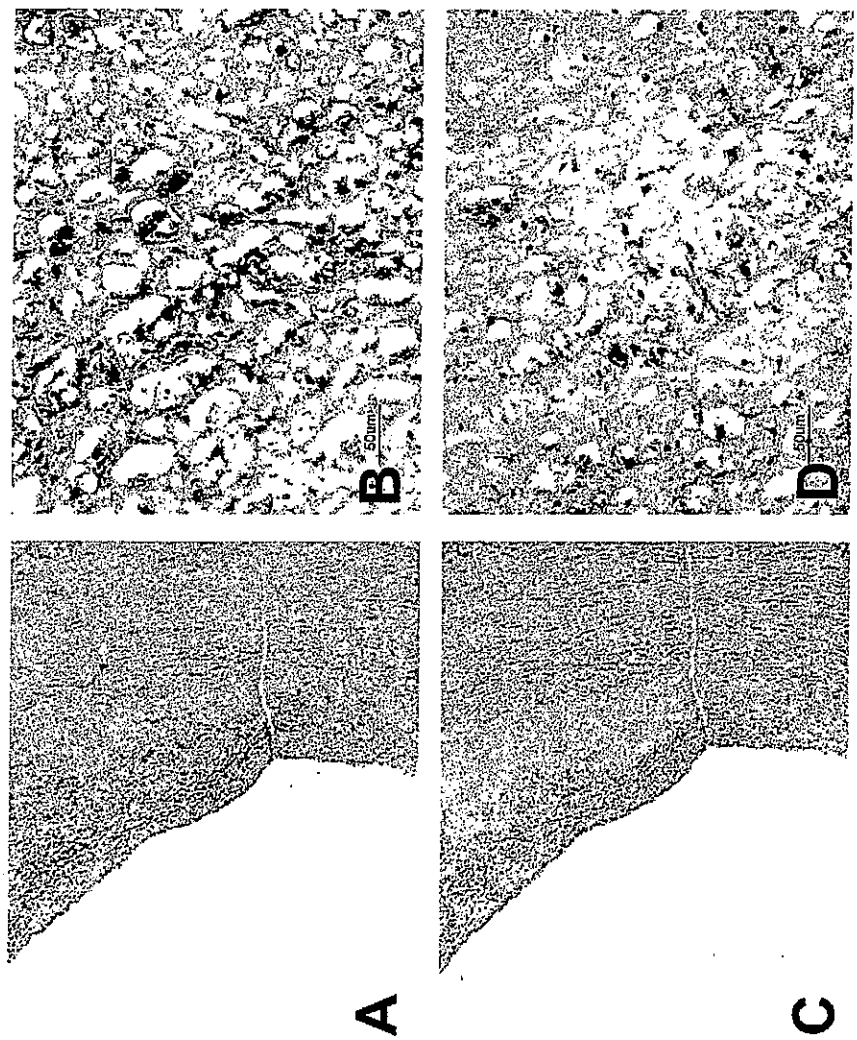


Figure 27

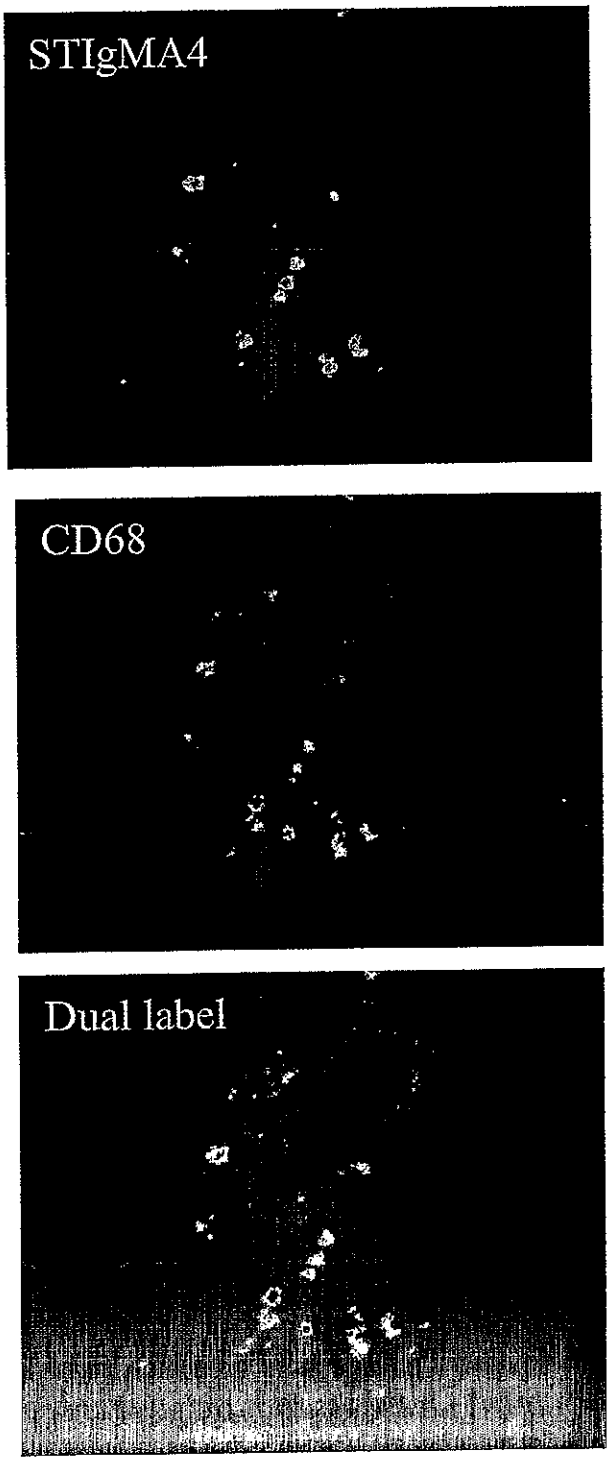


Figure 28

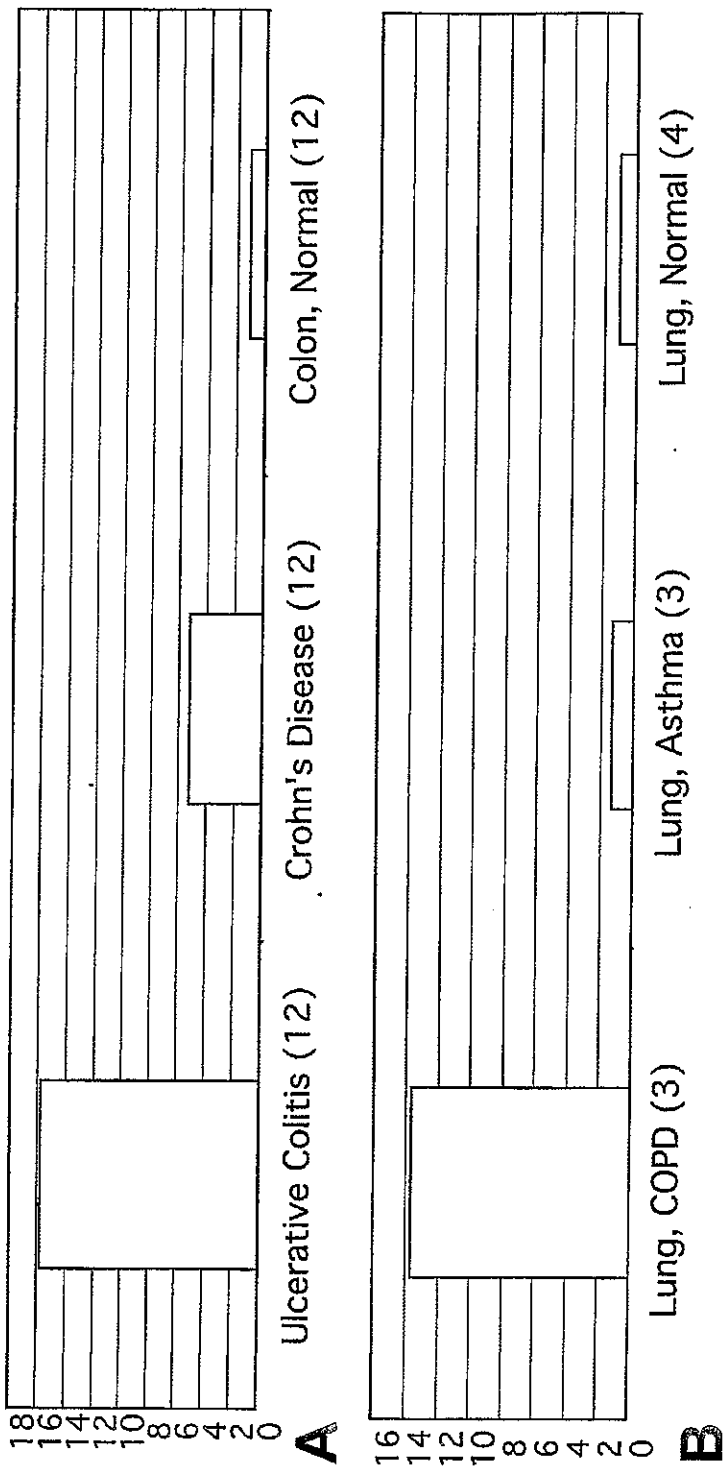
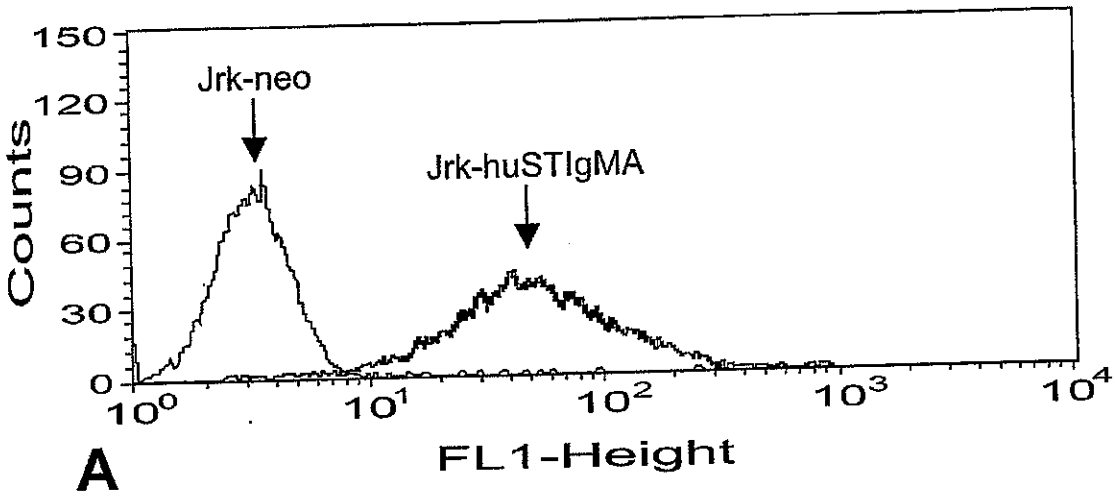

Fold Difference From Normal
18
16
14
12
10
8
6
4
2
0
A
Ulcerative Colitis (12)
Crohn's Disease (12)
Colon, Normal (12)
16
14
12
10
8
6
4
2
0
B
Lung, COPD (3)
Lung, Asthma (3)
Lung, Normal (4)

Figure 29


150
120
90
60
30
0
Counts
Jrk-neo
Jrk-huSTIgMA
10^0
10^1
10^2
10^3
10^4
FL1-Height
A

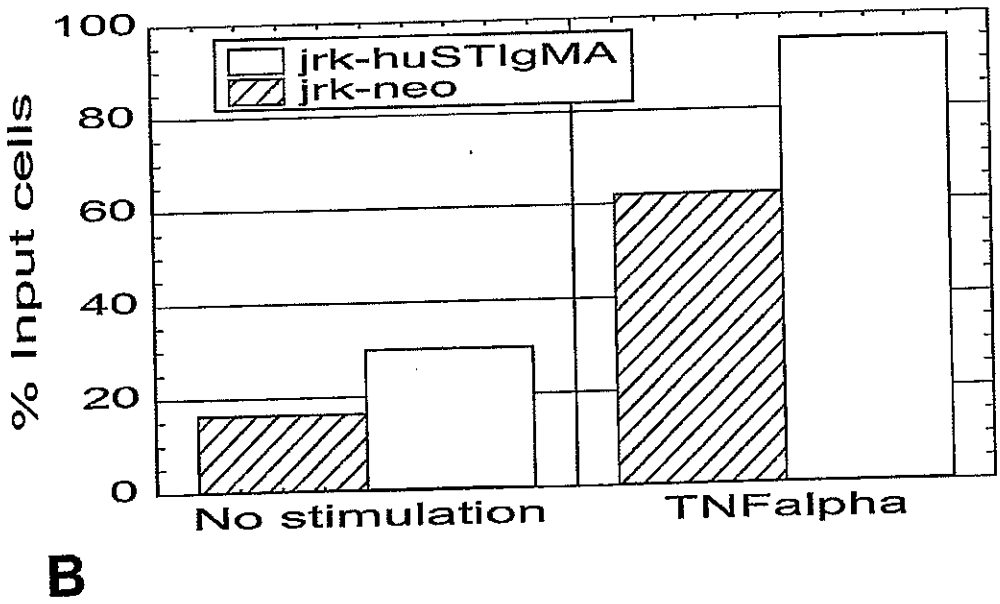
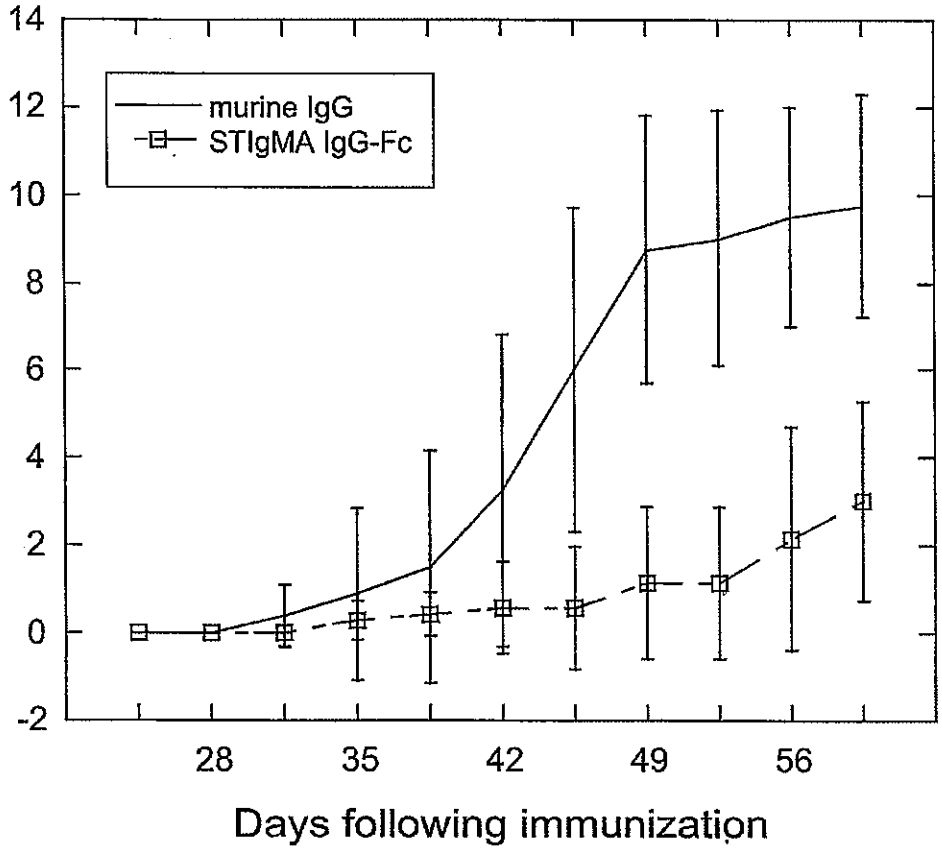

100
80
60
40
20
0
% Input cells
jrk-huSTIgMA
jrk-neo
No stimulation
TNFalpha
B

Figure 30

Effect of Systemic Injection of muSTIgMA-Fc on the Progression of CIA



t-test

p-value = .0004 for IgG1 vs. muSTIgMA

This p-value has been (very) conservatively adjusted for multiple comparisons (Bonferroni adjustment: 2*p-value since there are two comparisons being performed)

Plots indicate mean ± SD

Figure 31

consen02 (SEQ ID NO:9)

GCAGGCAAAG TACCAGGGCC GCCTGCATGT GAGCCACAAG GTTCCAGGAG 50
ATGTATCCCT CCAATTGAGC ACCCTGGAGA TGGATGACCG GAGCCACTAC 100
ACGTGTGAAG TCACCTGGCA GACTCCTGAT GGCAACCAAG TCGTGAGAGA 150
TAAGATTACT GAGCTCCGTG TCCAGAAACT CTCTGACTCC AAGCCCACAG 200
TGACAACTGG CAGCGGTTAT GGCTTCACGG TGCCCCAGGG AATGAGGATT 250
AGCCTTCAAT GCCAGGGTTC GGGGTTCTCC TCCCATCAGT TATATTTGGT 300
ATAAGCAACA GACTAATAAC GAGGGAACCC ATCAAAGTAG CAACCCTAAG 350
TACCTTACTC TTCAAGCCTG CGGTGATAGC CGACTCAGGC TCCTATTTCT 400
GCACTGCCAA GGGCCAGGTT GGCTCTGAGC AGCACAGCGA CATTGTGAAG 450
TTTGTGGTCA AAGACTCCTC AAAGCTACTC AAGACCAAGA CTGAGGCACC 500
TACAACCATG ACATACCCCT TGAAAGAAAC ATCTACAGTG AAGCAGTCCT 550
GGGACTGGAC CACTGACATG GATGGCTACC TTGGAGAGAC CAGTGCTGGG 600
CCAGGAAAGA GCCTGCCTGT CTTTGCCATC ATCCTCATCA TCTCCTTGTG 650
CTGTATGGTG GTTTTTACCC TGGCCTATAT CATGCTCTGT CGGAAGACAT 700
CCCAACAAGA GCATGTCTAC GAAGCAGCCA GGGCACATGC CAGAGAGGCC 750
AACGACTCTG GAGAAACCAT GAGGGTGGCC ATCTTCGCAA GTGGCTGCTC 800
CAGTGATGAG CCAACTTCCC AGAATCTGGG GCAACAACTA CTCTGATGAG 850
CCCTGCATAG GACAGGAGTA CCAGATCATC GCCCAGATCA ATGGCAACTA 900
CGCCCGCCTG CTGGACACAG TTCCTCTGGA TTATGAGTTT CTGGCCACTG 950
AGGGCAAAAG TGTCTGTTAA AAATGCCCCA GAGCCACAAG ATCTGCTGAC 1000
ATAATTGCCT AGTCAGTCCT TGCCTTCTGC ATGTCCTTCT TCCCTACTAC 1050
CTCTCTTCCT GGATAGCCCA AAGTGTCCGC CTACCAACAC TGGAGCCGCT 1100
GGGAGTCACT GGCTTTGCCC TGGAATTTGC CAGATGCATC TCAAGTAAGC 1150
GAGCTGCTGG ATTTGGCTCT GGGCCCTTCT AGTATCTCTG CCGGGGGCTT 1200
CTGGTACTCC TCTCTAAATA CCAGAGGGAA GATGCCCATA GCACTAGGAC 1250
TTGGTCATCA TGCCTACAGA CACTATTCAA CTTTGGCATC TTGCCAGCAG 1300
AAGACCCGAG GGGATTCTCA GCTCTGCCAG CTCAGAGGAC CAGCTATATC 1350
TATTTCACAG TCTCTTTCTT CAGGGCCAGA CAGCTTTTAA TTGAAATTGT 1400
TATTTCACAG GCCAGGGTTC AGTTCTGCTC CTCCACTATA AGTCTAATGT 1450
TCTGACTCTC TCCTGGTGCT CAATAAATAT CTAATCATAA CAGCAAAAAA 1500

AAA 1503

Figure 32

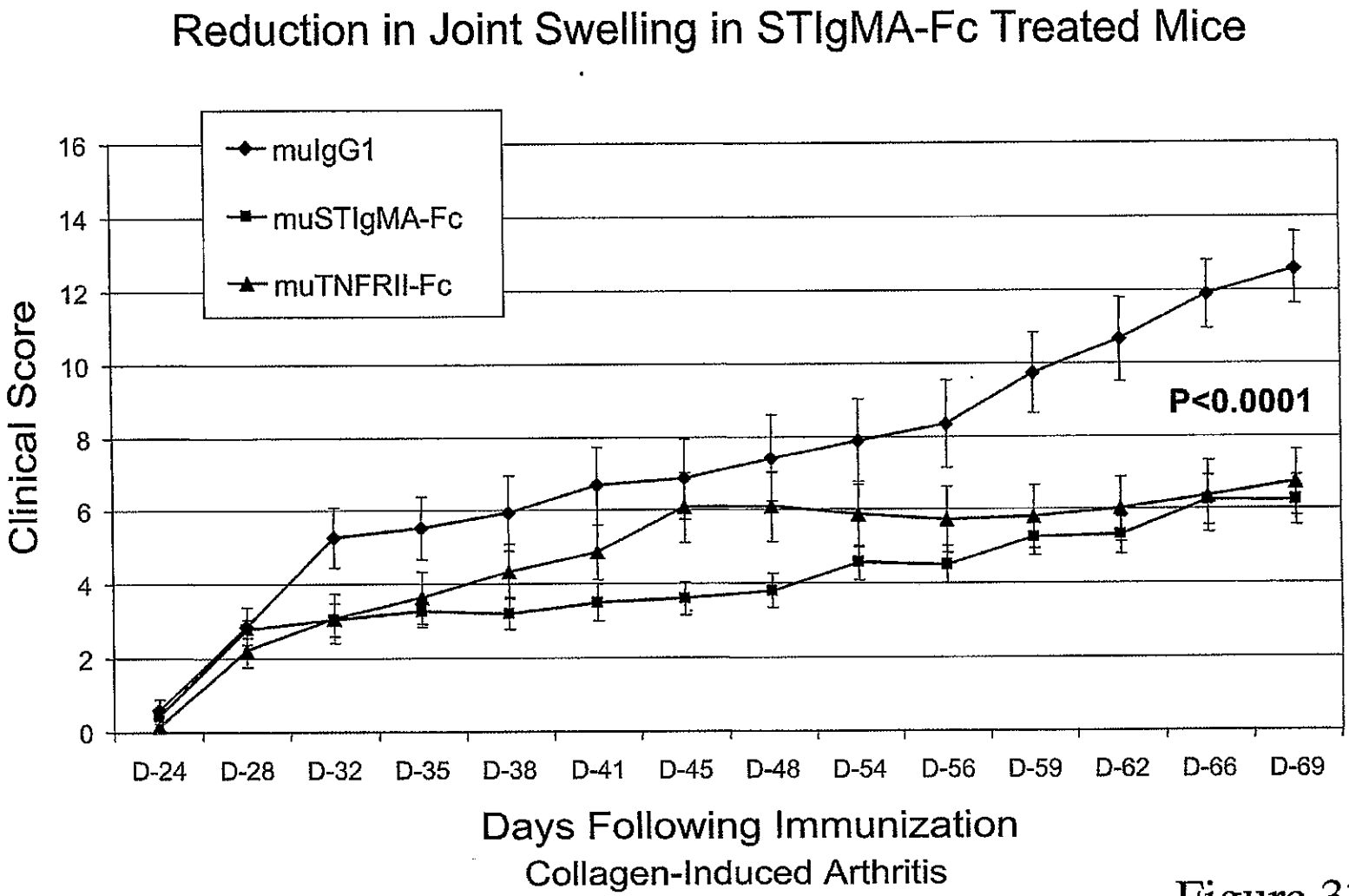
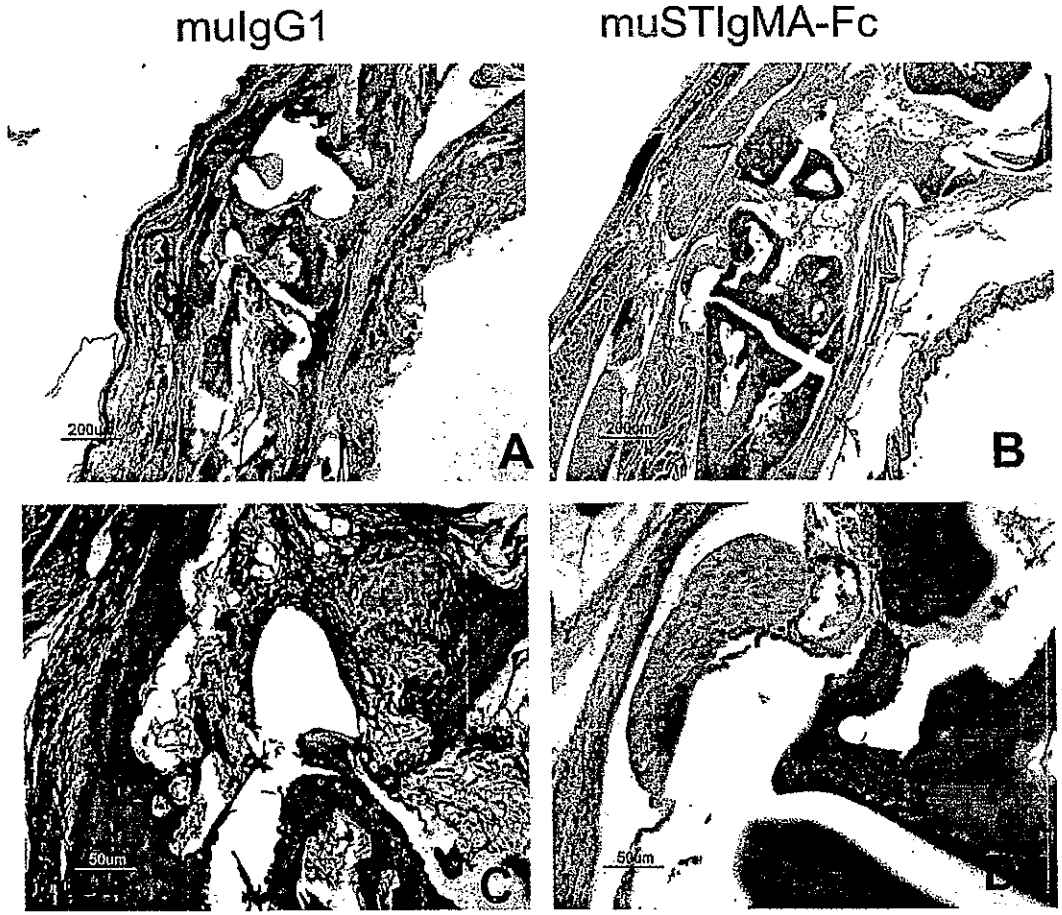

Reduction in Joint Swelling in STIgMA-Fc Treated Mice
muIgG1
muSTIgMA-Fc
muTNFRII-Fc
P<0.0001
Clinical Score
0
2
4
6
8
10
12
14
16
D-24
D-28
D-32
D-35
D-38
D-41
D-45
D-48
D-54
D-56
D-59
D-62
D-66
D-69
Days Following Immunization
Collagen-Induced Arthritis

Figure 33

muSTIgMA-Fc Inhibits Joint Inflammation

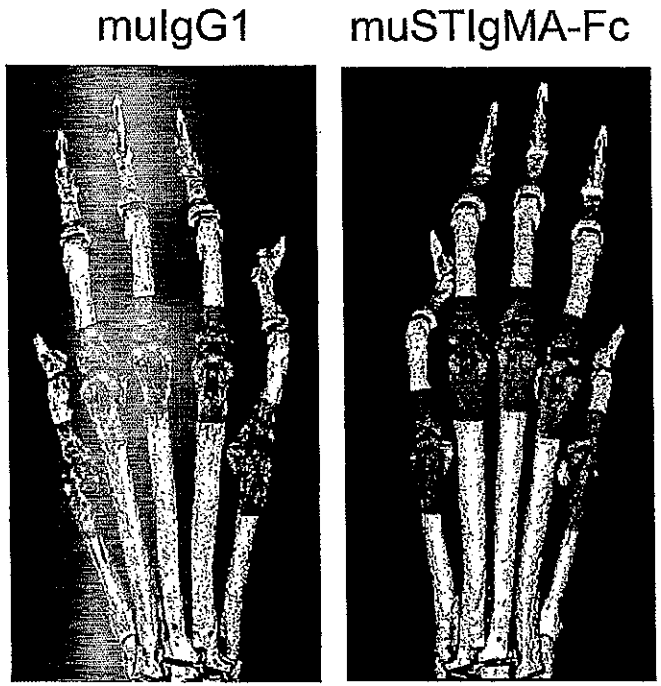


H&E staining on paraffin-embedded tissue

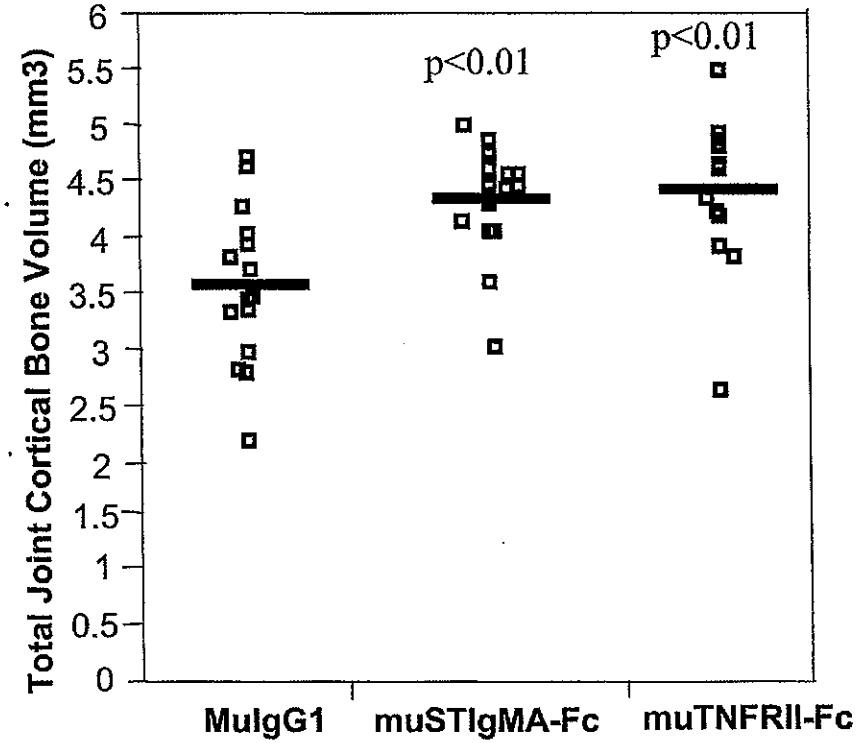
Collagen-induced arthritis day 70

Figure 34

Preservation of Cortical Bone Volume in joints of mice treated with muSTIgMA-Fc



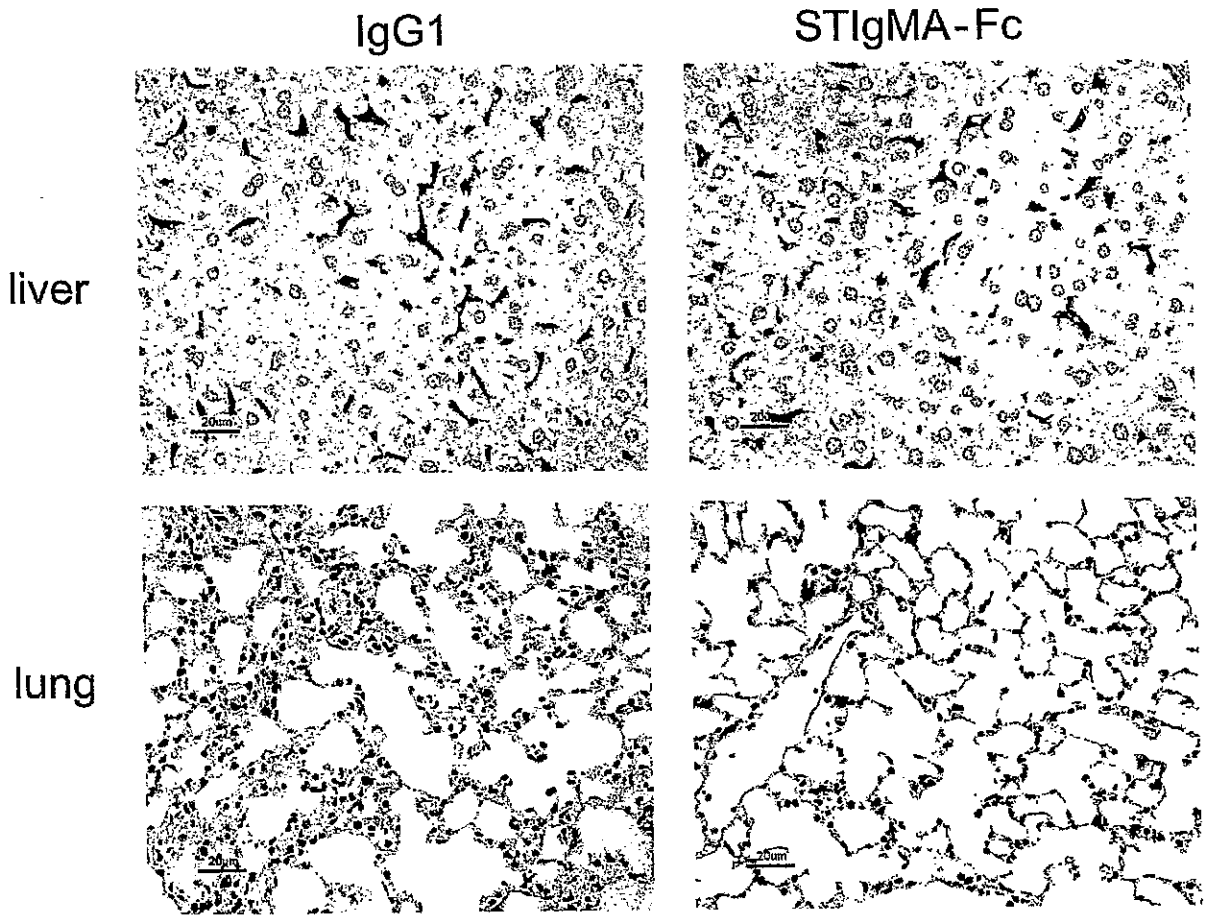
CT-Scan of Hind Paws



Collagen-induced arthritis day 70

Figure 35

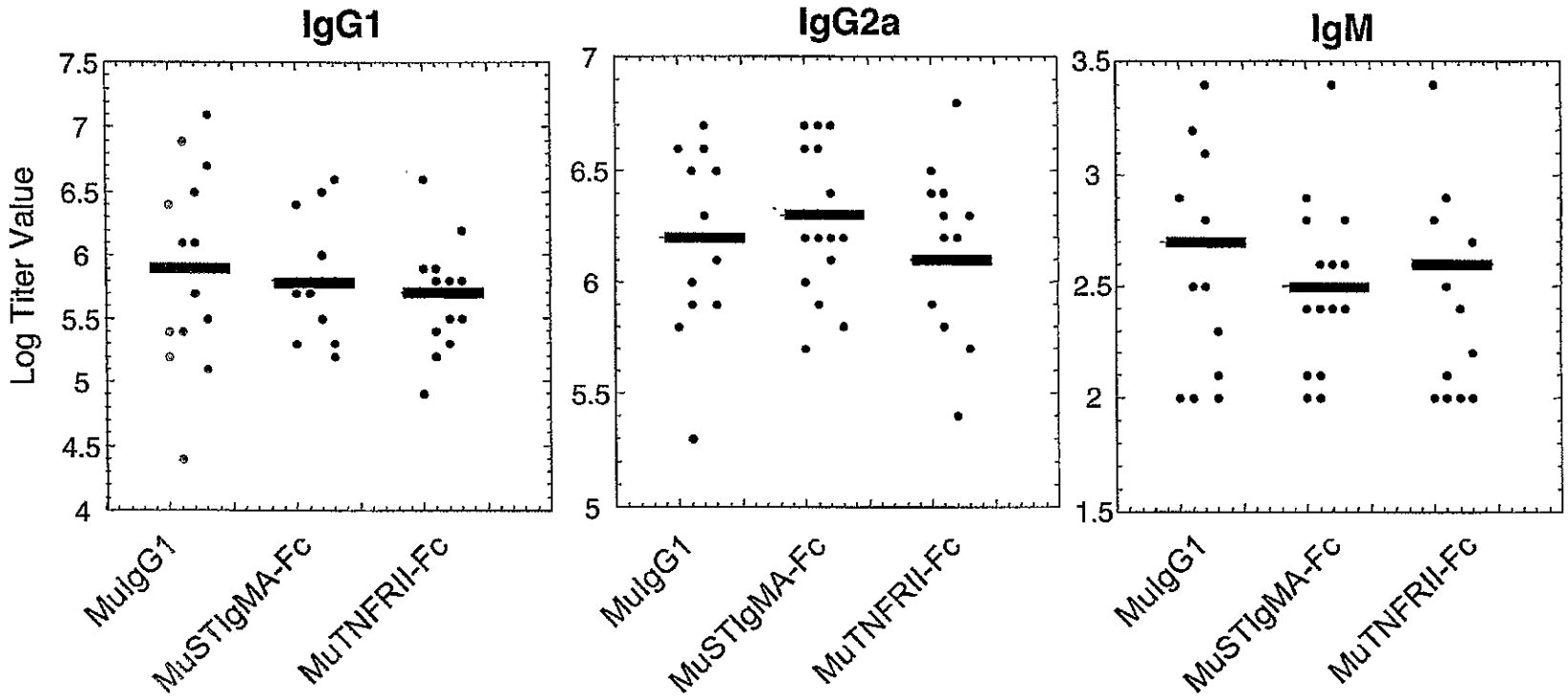
STIgMA-Fc treatment does not alter the number nor morphology of tissue resident macrophages



Collagen-induced arthritis day 70

Figure 36

muSTIgMA-Fc treatment does not affect serum anti-collagen antibody titers

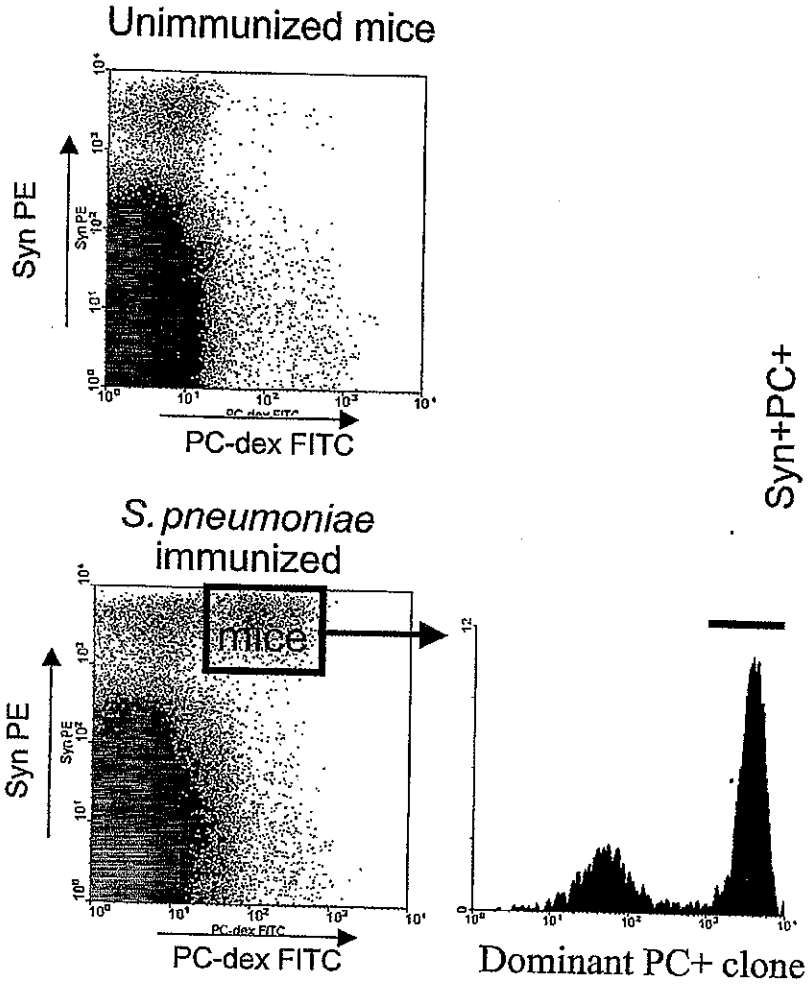


Anova test *shows no difference between groups*

Collagen-induced arthritis day 70

Figure 37

muSTIgMA-Fc does not alter T-Independent B cell responses *in vivo*



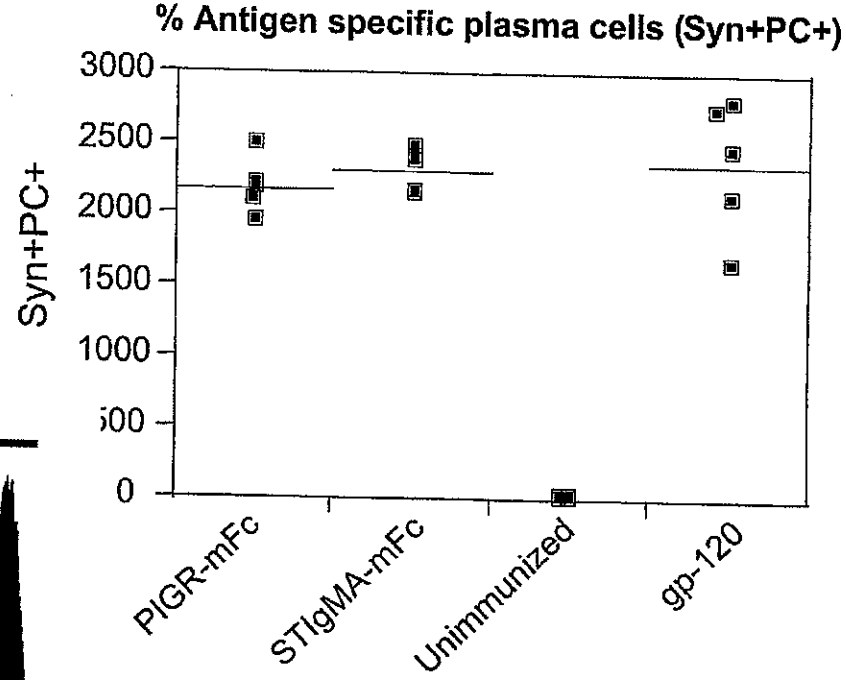
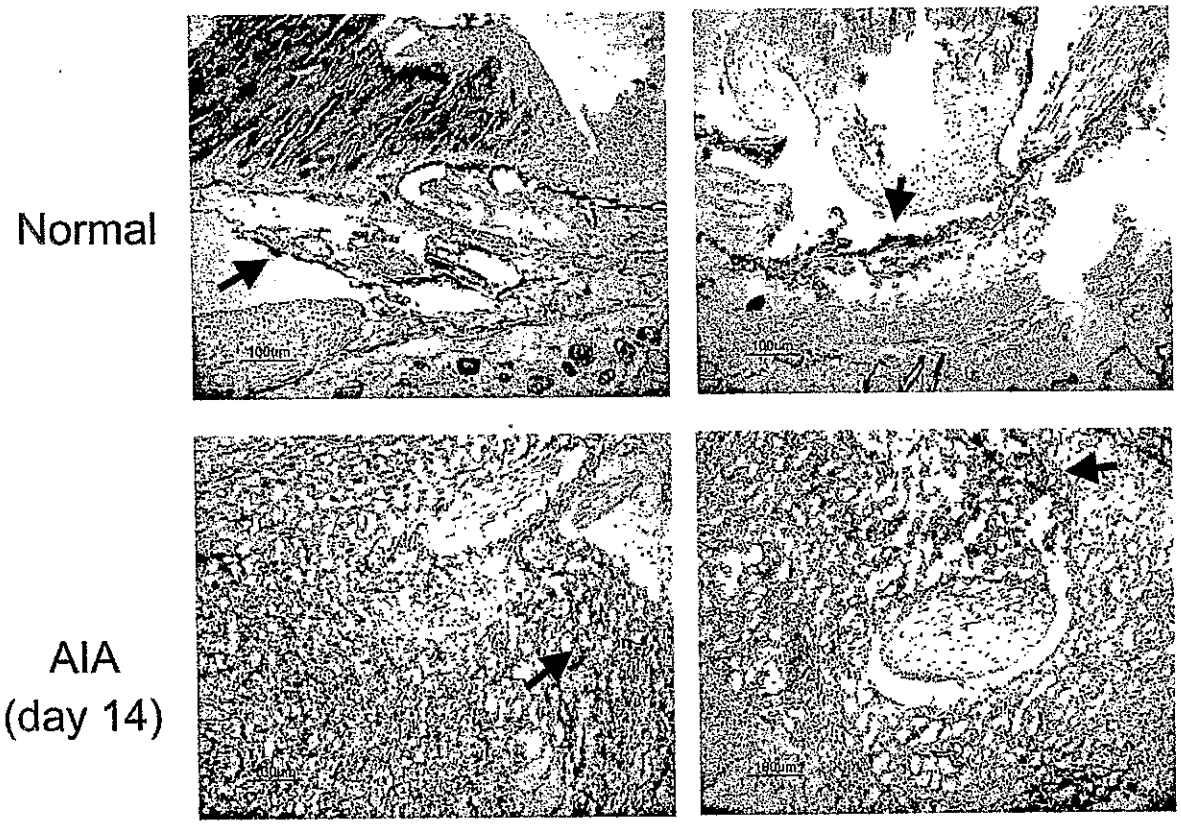


Figure 38

Macrophage infiltration in joints following antibody-induced arthritis (AIA)



F4/80 staining in undecalcified frozen joints

Figure 39

MuSTIgMA-Fc prevents joint swelling following antibody-induced arthritis in balb/c mice

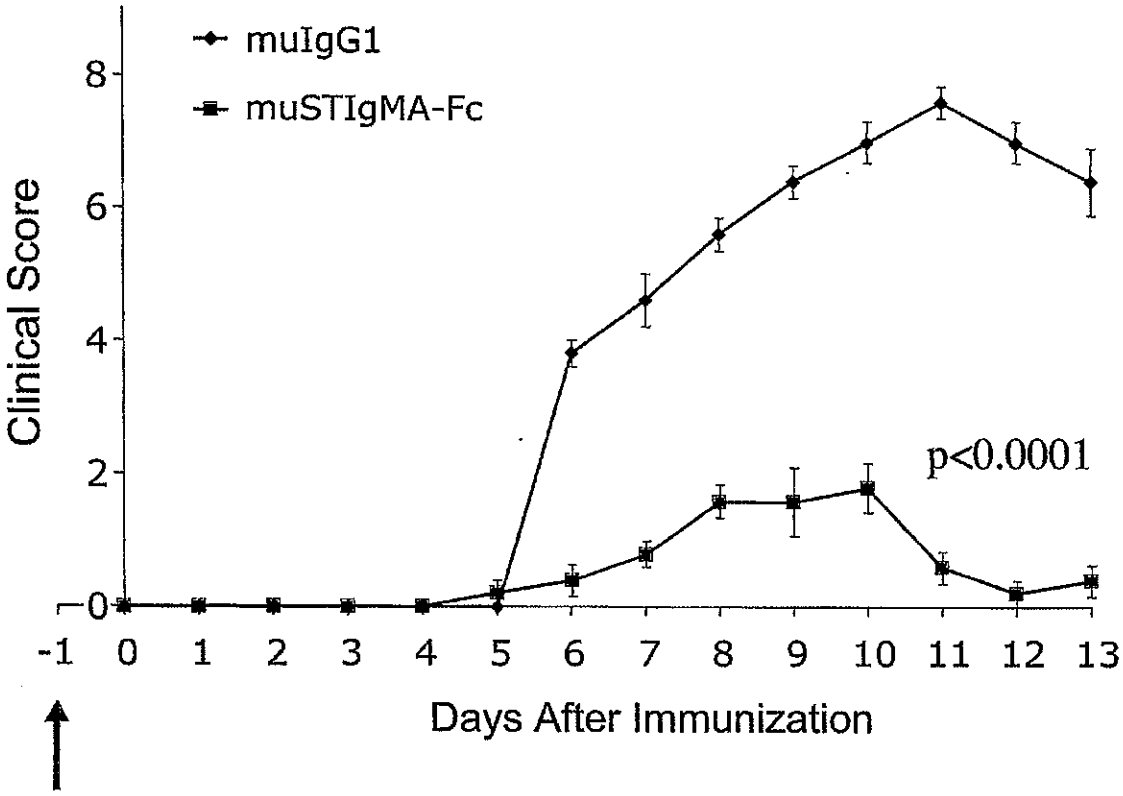
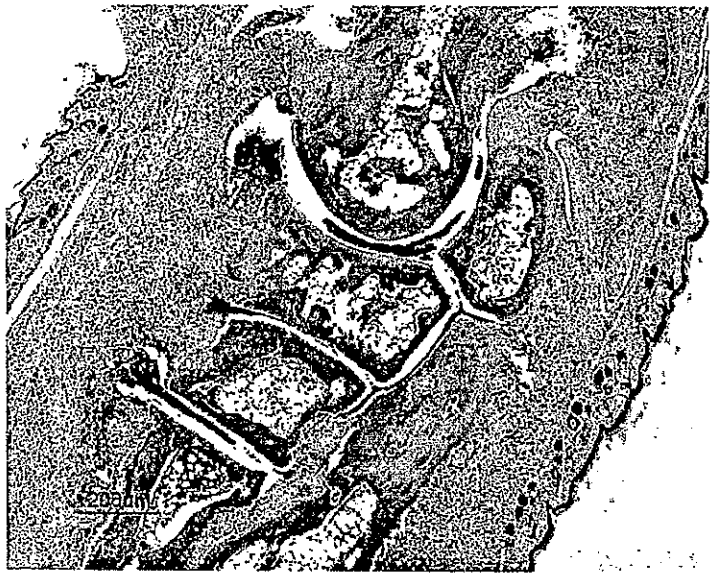


Figure 40

MuSTIgMA-Fc inhibits joint inflammation in antibody-induced arthritis

muIgG1



muSTIgMA-Fc

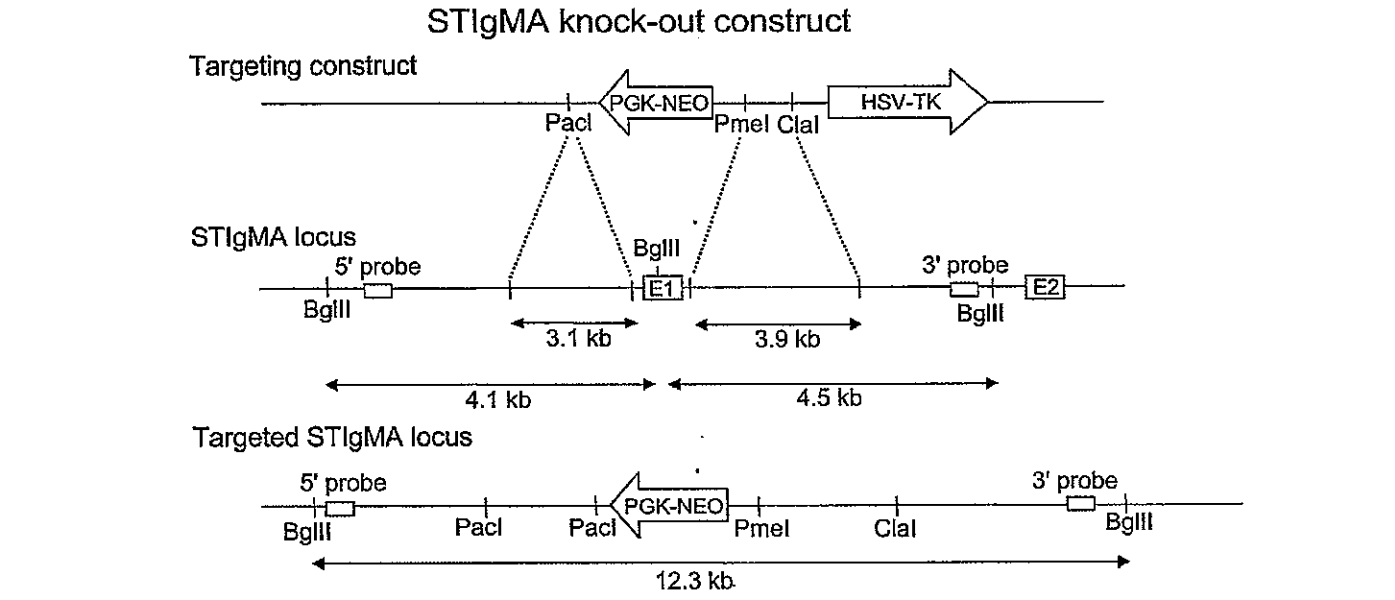


- Control treated mice (muIgG1) have moderate to severe arthritis (left)
- MuSTIgMA-Fc treated mice have minimal to no arthitis (right)

H&E staining

Figure 41

Generation of mSTIgMA knock-out mice



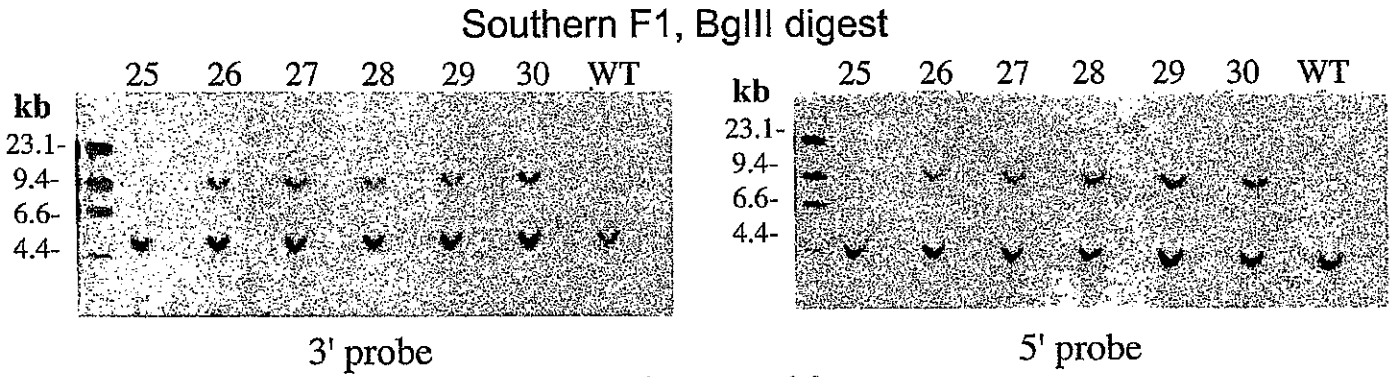
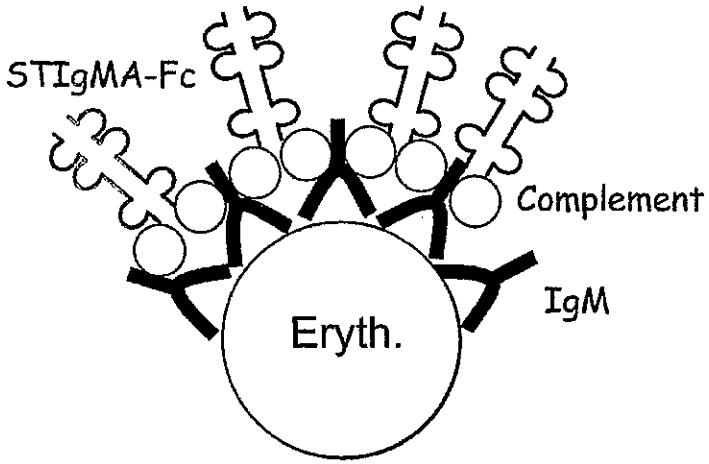
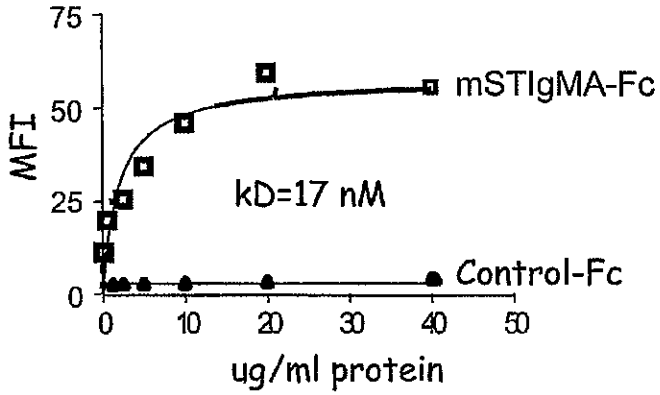


Figure 42

Murine STIgMA-Fc binds to C3-opsonized sheep red blood cells (E-IgM)





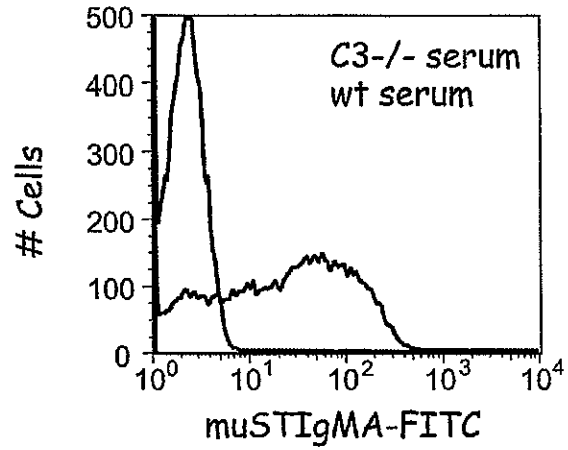
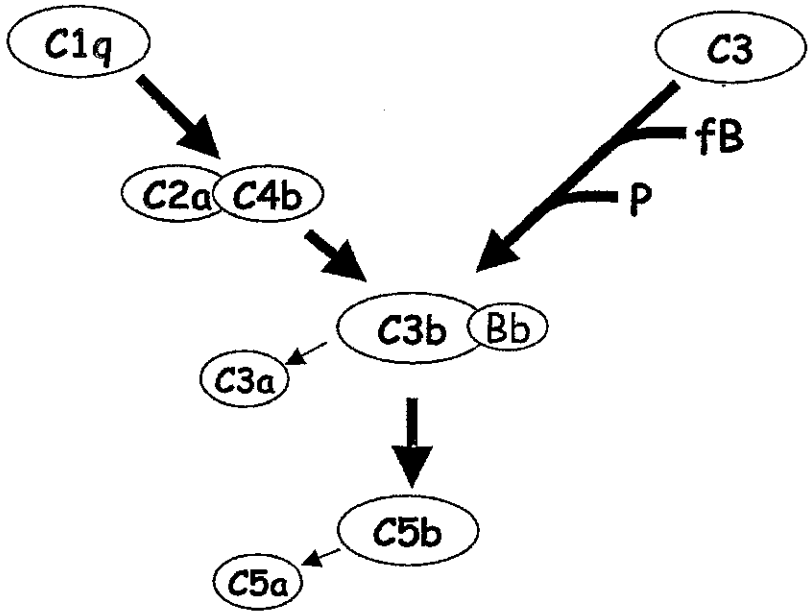
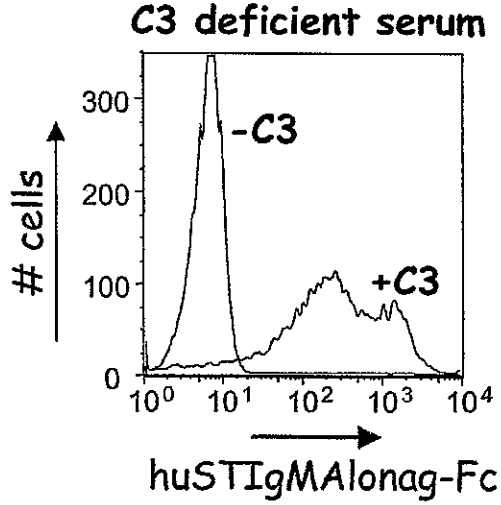
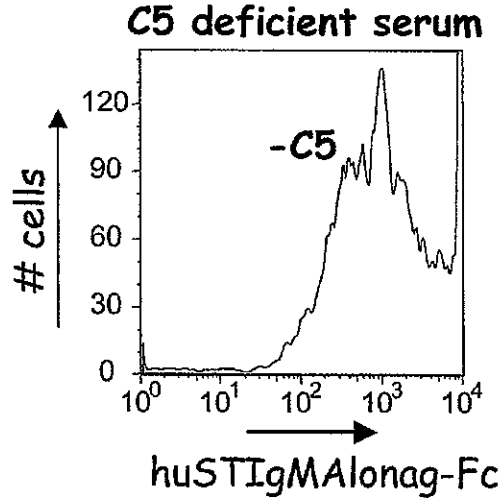


Figure 43

Binding of human STIgMA-Fc to E-IgM is C3 dependent







Similar results found with human STIgMA-ECD

Figure 44

Binding of serum-opsonized particles to STIgMA-expressing CHO cells

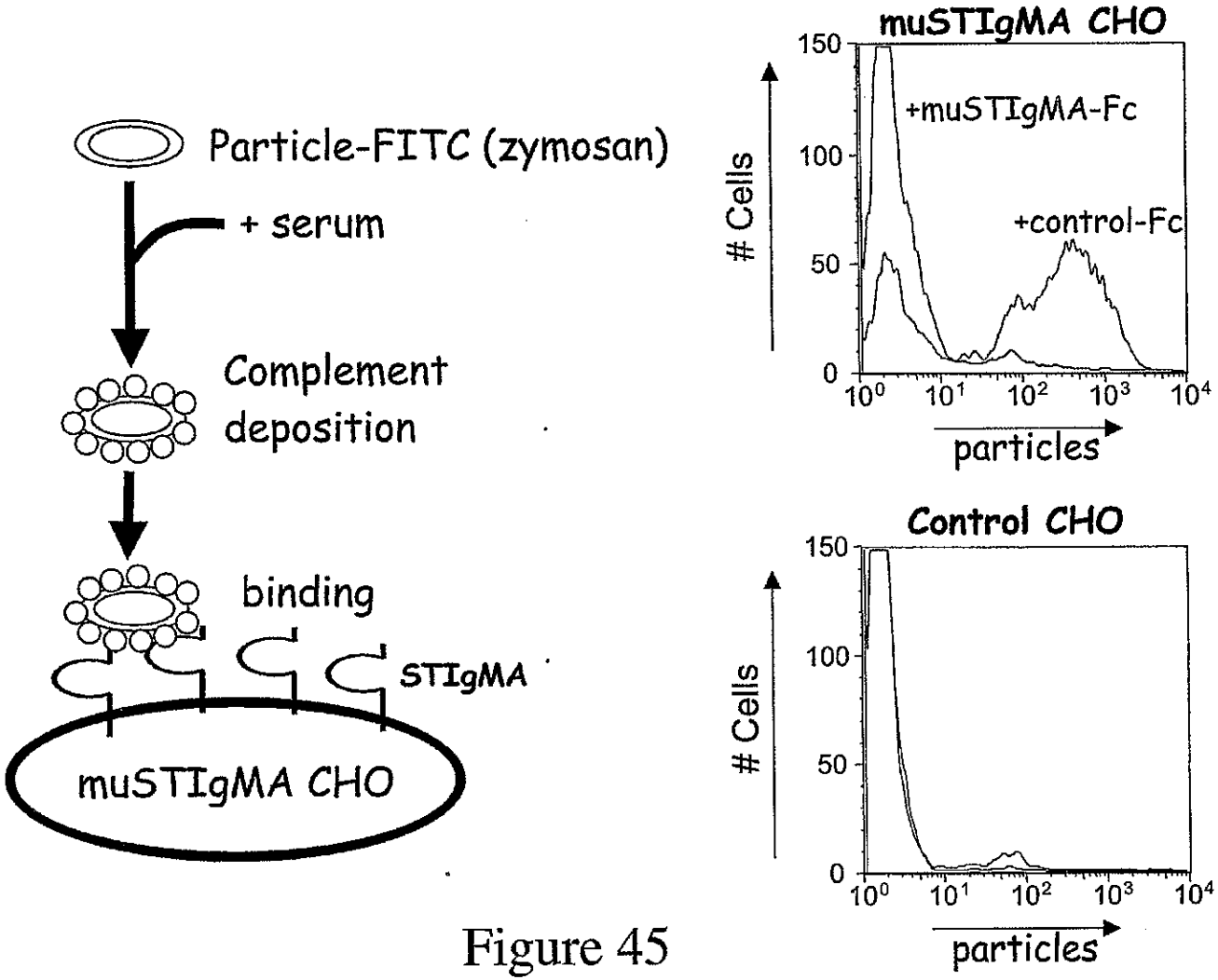
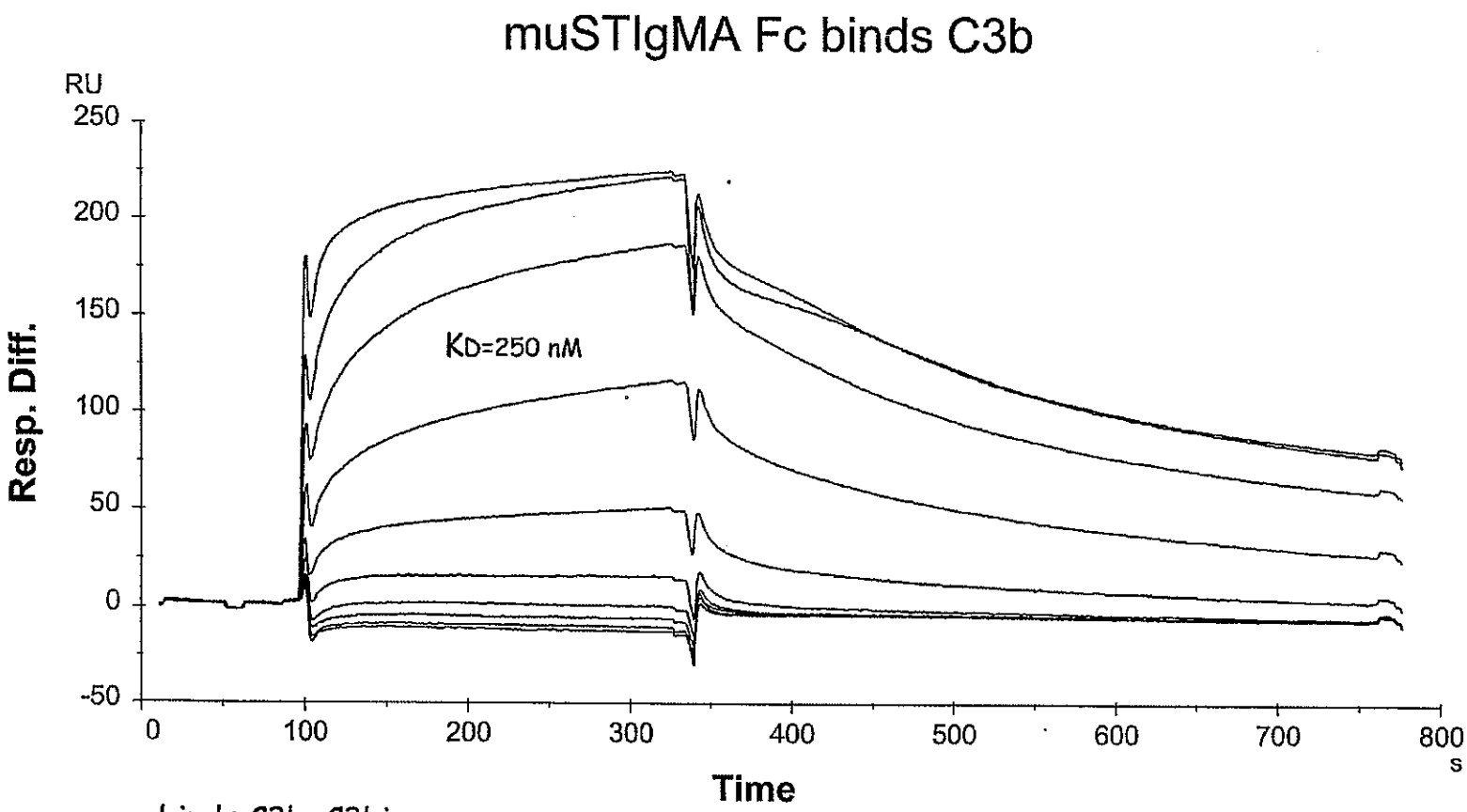


Figure 45



Biacore: 1720 RU coated C3b; increasing concentrations 4-2000 nM mSTIgMA-mFc flowed over cell

Figure 46

Mouse and human STIgMA-Fc bind complement C3b

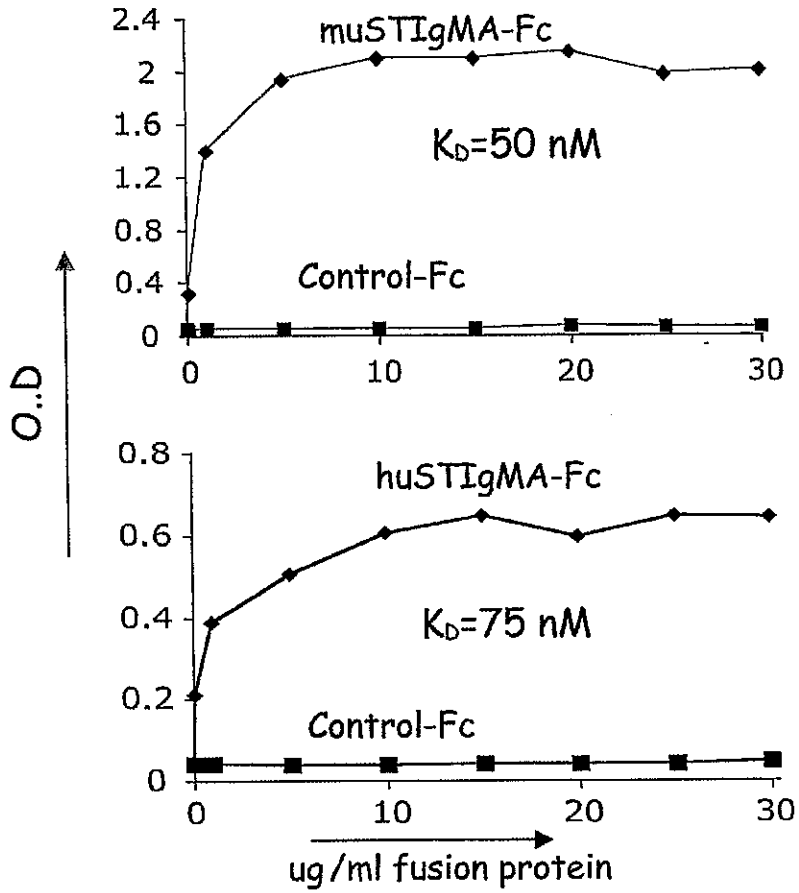


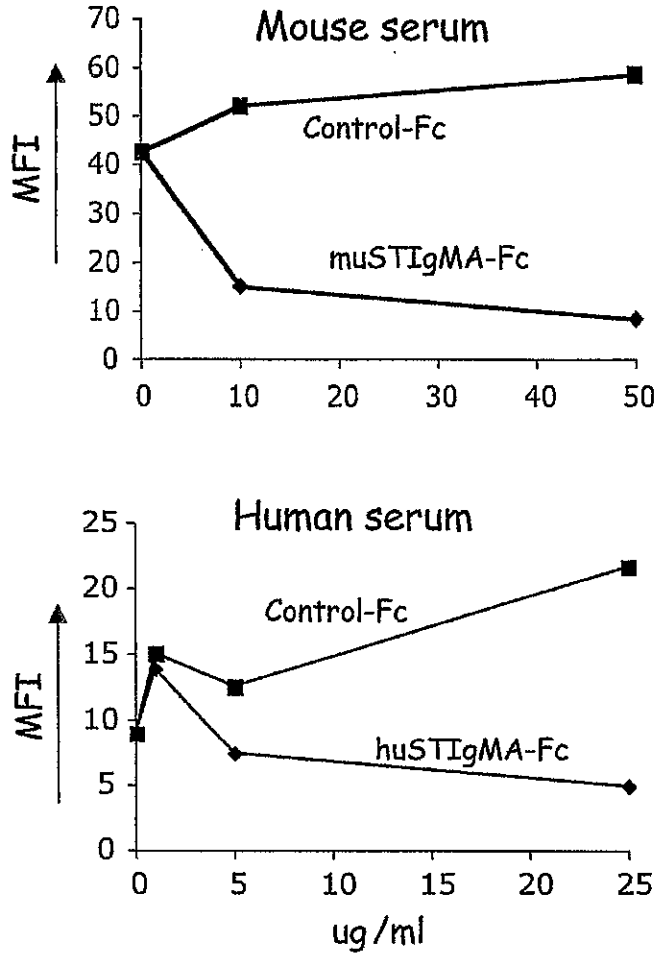
Plate-bound ELISA

-binds C3b, C3bi and C3c

-does not bind C1, C2, C4, C3a, C3d

Figure 47

Mouse and human STIgMA-Fc inhibit C3 deposition on zymosan

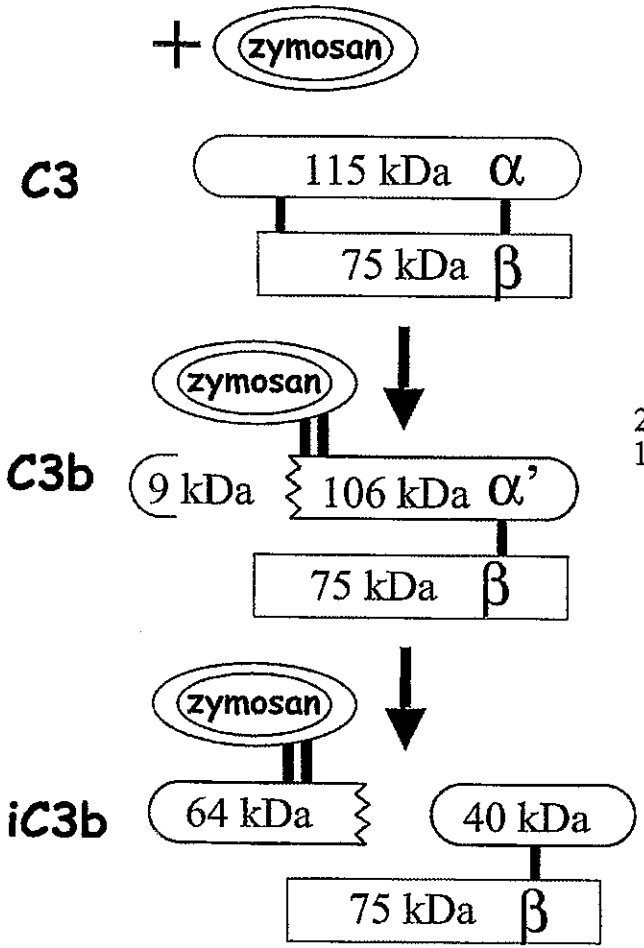


Inhibits deposition of C3 on:

- Staph. Aureus
- Listeria M.
- Immune complexes
- Collagen
- Charged surfaces (tissue culture plastic)
- All in the presence of EGTA
- (Alternative pathway-mediated deposition)

Figure 48A

muSTIgMA-Fc inhibits C3 activation in serum



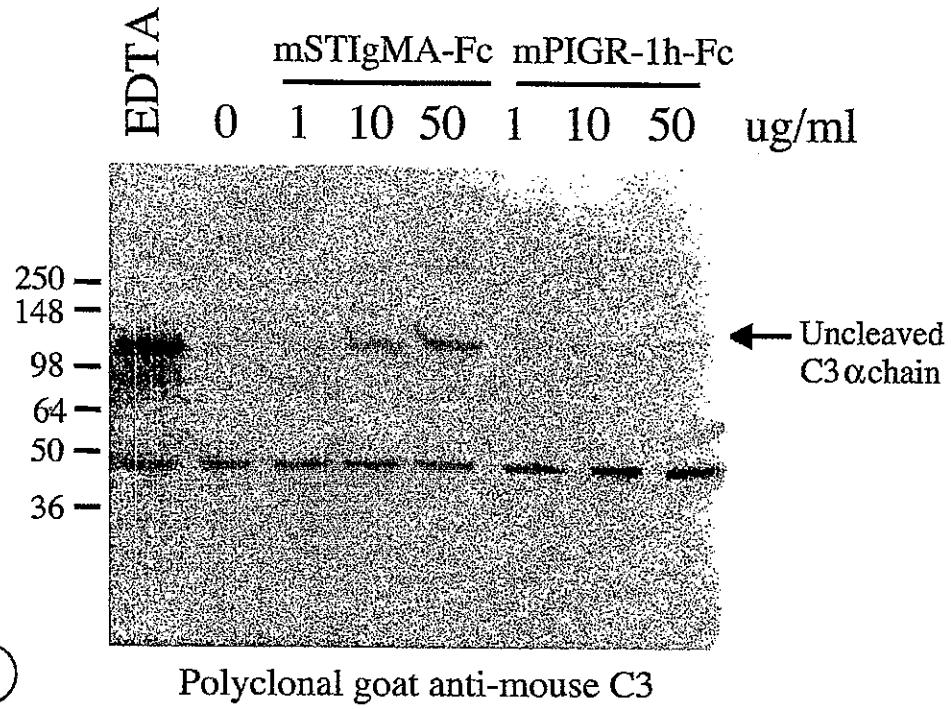
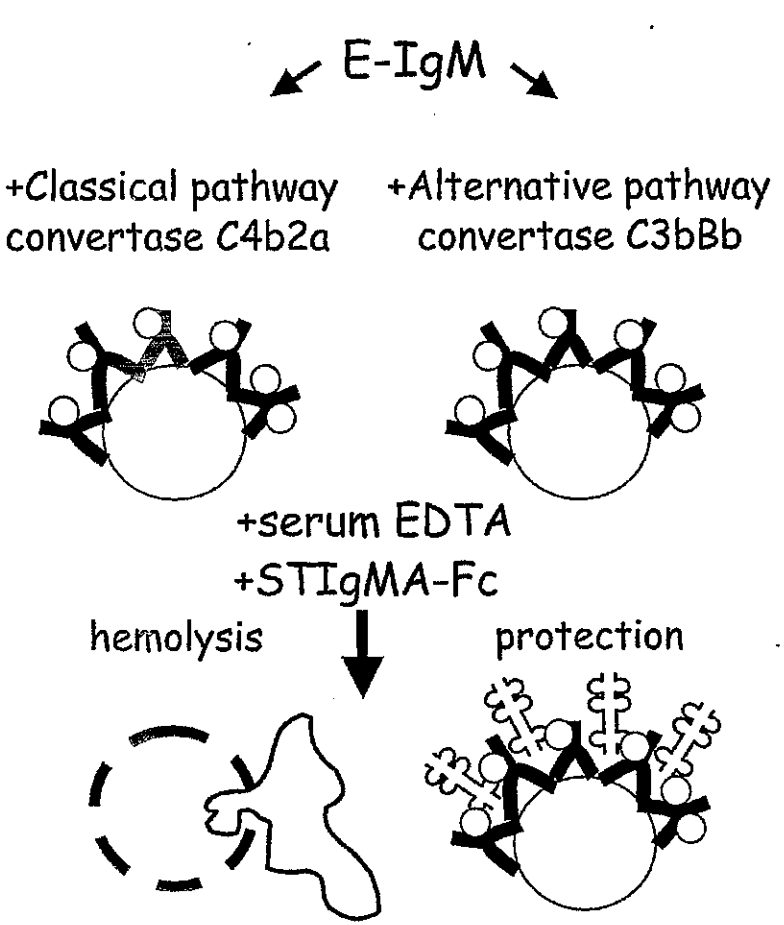
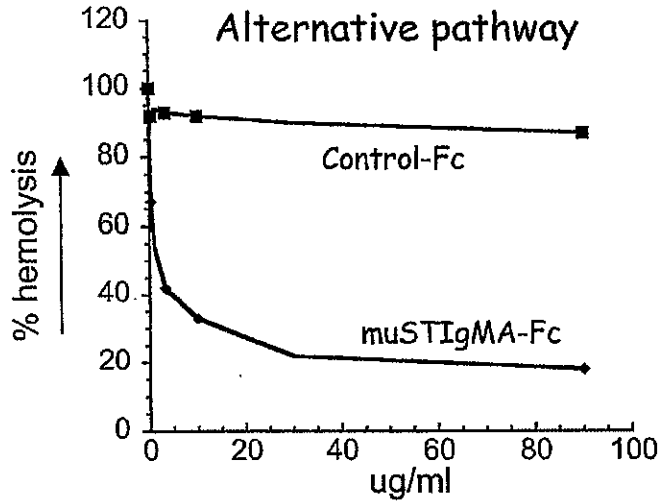


Figure 48B

STIgMA inhibits alternative pathway hemolysis of SRBC





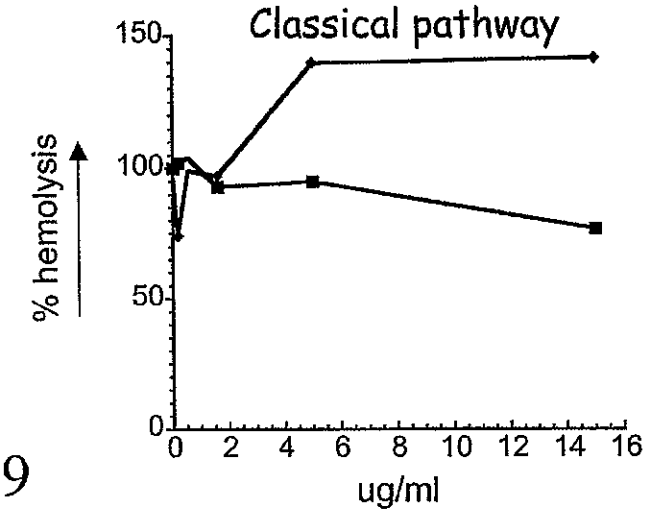


Figure 49

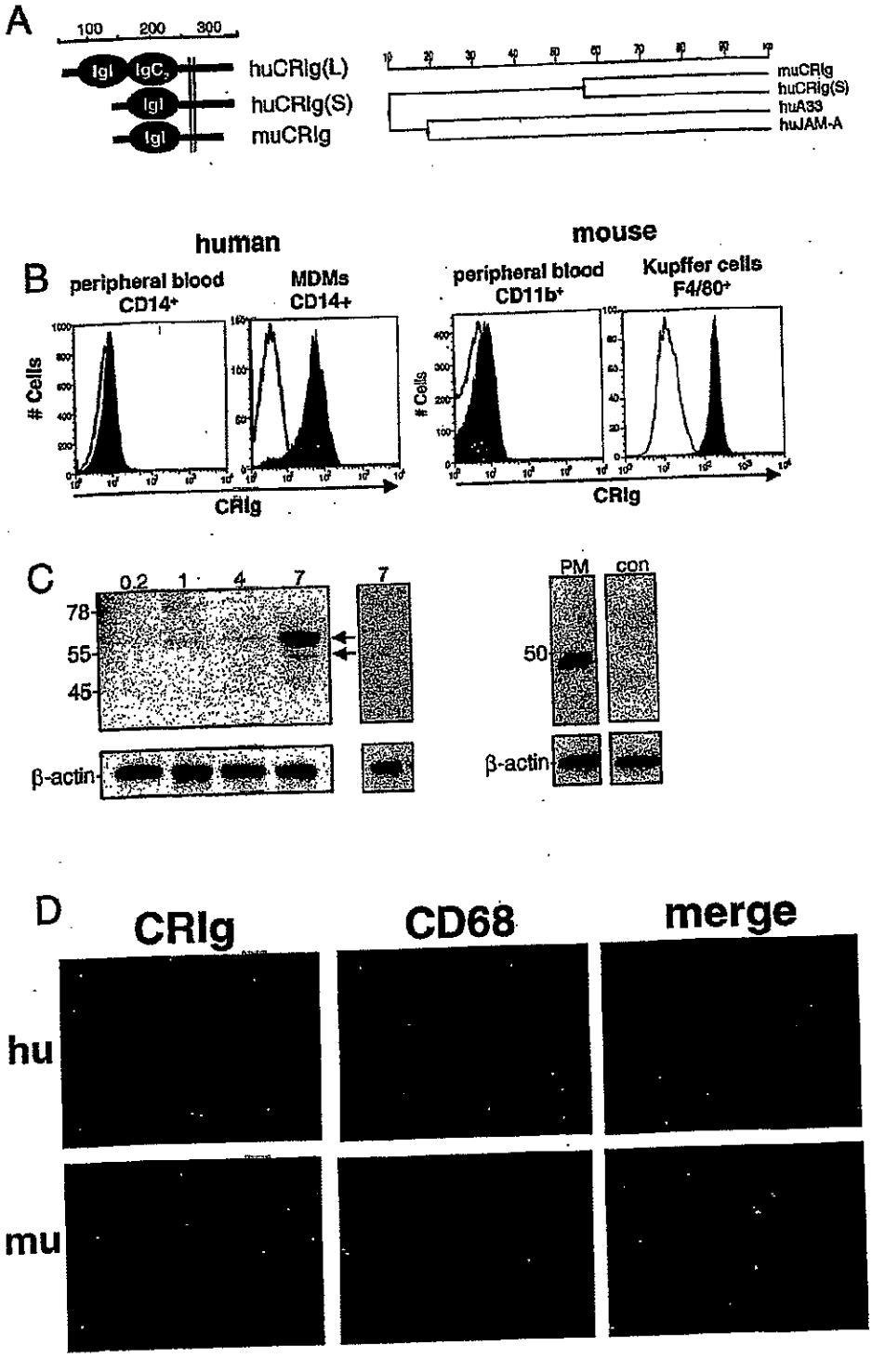

A
100
200
300
IgI
IgC2
huCRIg(L)
huCRIg(S)
muCRIg
muCRIg
huCRIg(S)
huA33
huJAM-A
B
human
mouse
peripheral blood CD14+
MDMs CD14+
peripheral blood CD11b+
Kupffer cells F4/80+
Cells
CRIg
C
0.2
1
4
7
7
78
55
45
β-actin
PM
con
50
β-actin
D
CRIg
CD68
merge
hu
mu

Figure 50

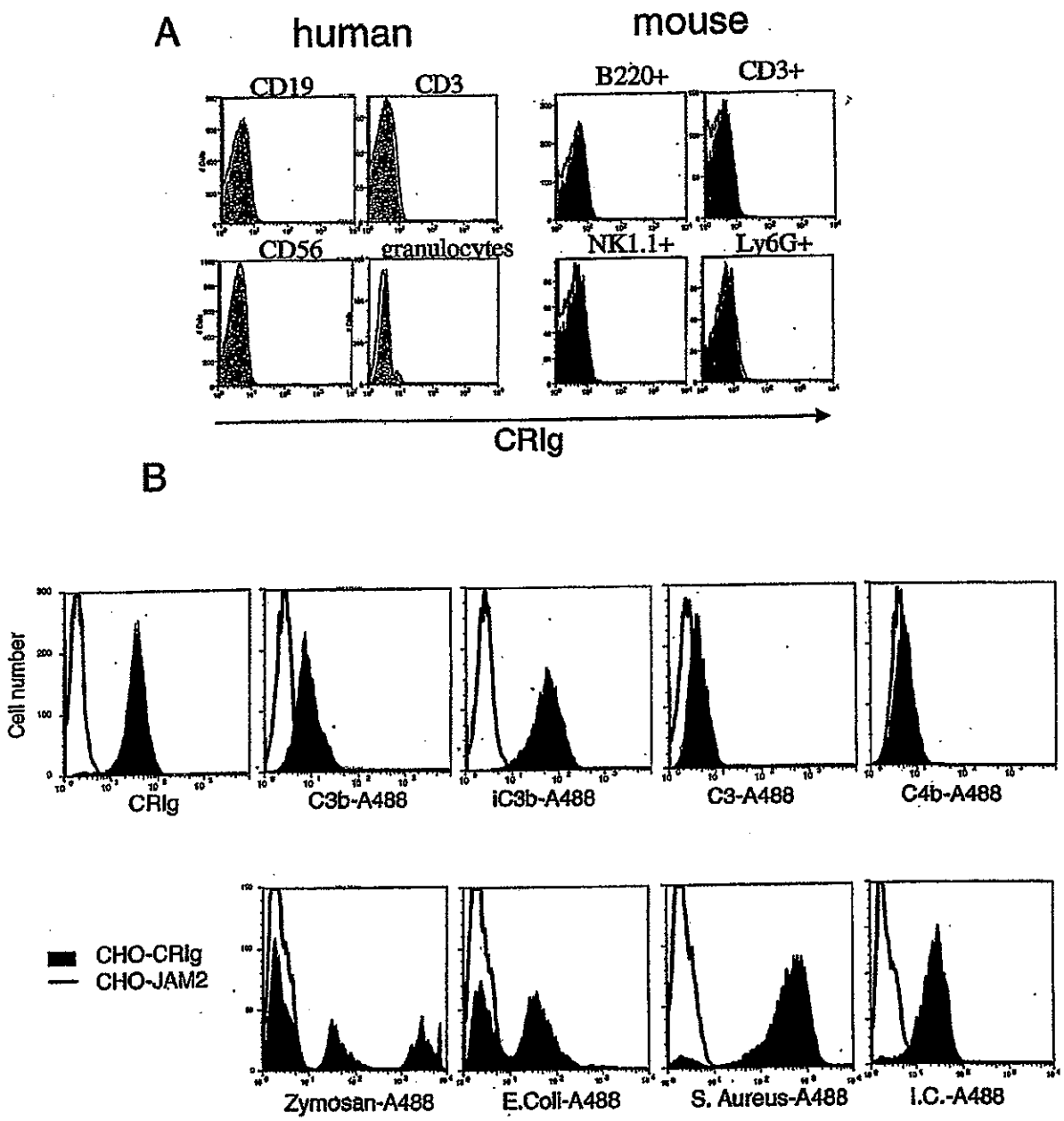

A
human
mouse
CD19
CD3
B220+
CD3+
CD56
granulocytes
NK1.1+
Ly6G+
CRIg
B
Cell number
CRIg
C3b-A488
iC3b-A488
C3-A488
C4b-A488
CHO-CRIg
CHO-JAM2
Zymosan-A488
E.Coli-A488
S. Aureus-A488
I.C.-A488

Figure 51

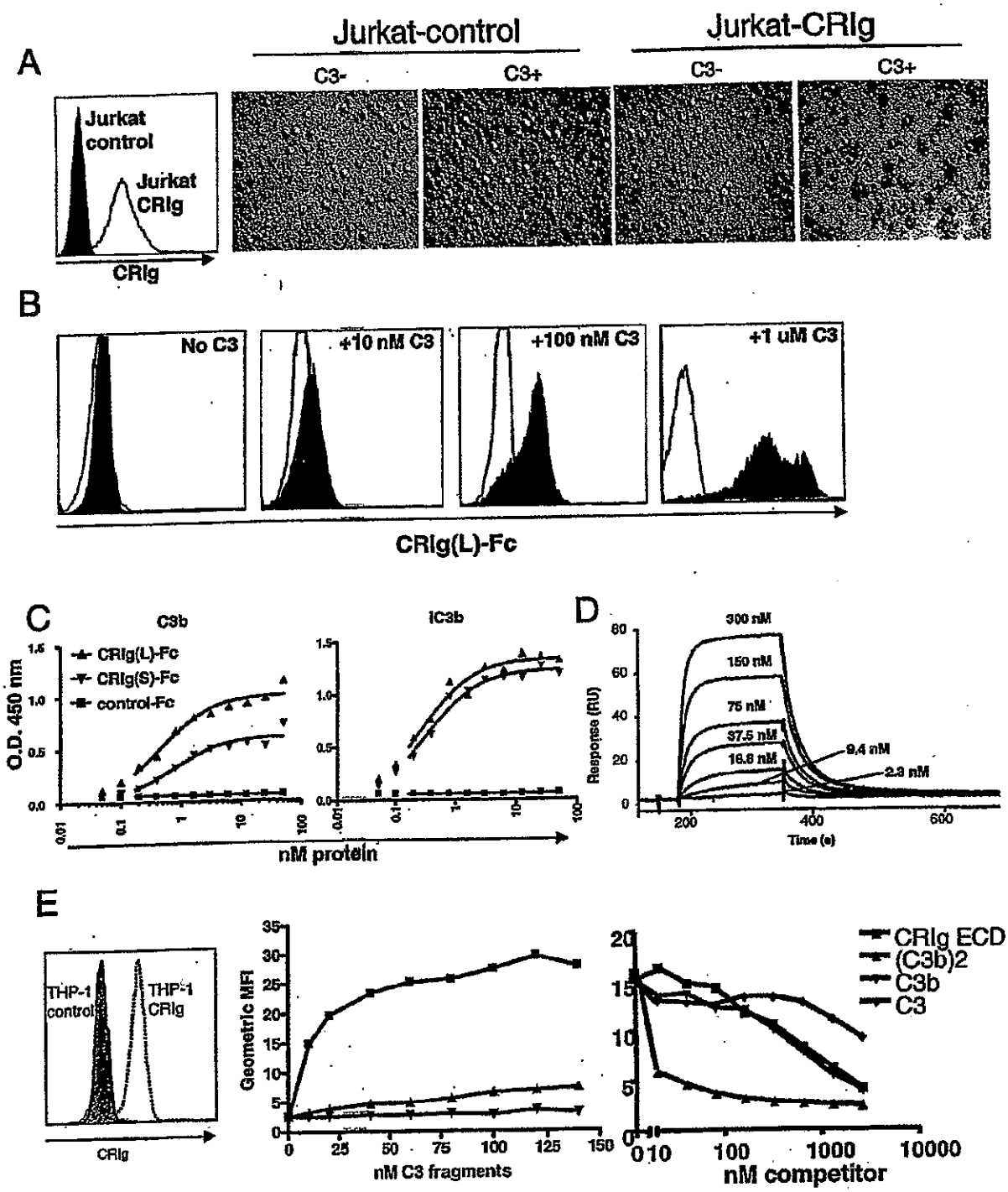

A
Jurkat-control
Jurkat-CRIg
C3-
C3+
C3-
C3+
Jurkat control
Jurkat CRIg
CRIg
B
No C3
+10 nM C3
+100 nM C3
+1 uM C3
CRIg(L)-Fc
C
C3b
iC3b
CRIg(L)-Fc
CRIg(S)-Fc
control-Fc
O.D. 450 nm
nM protein
D
300 nM
150 nM
75 nM
37.5 nM
18.8 nM
9.4 nM
2.3 nM
Response (RU)
Time (s)
E
THP-1 control
THP-1 CRIg
CRIg
Geometric MFI
nM C3 fragments
CRIg ECD
(C3b)2
C3b
C3
nM competitor

Figure 52

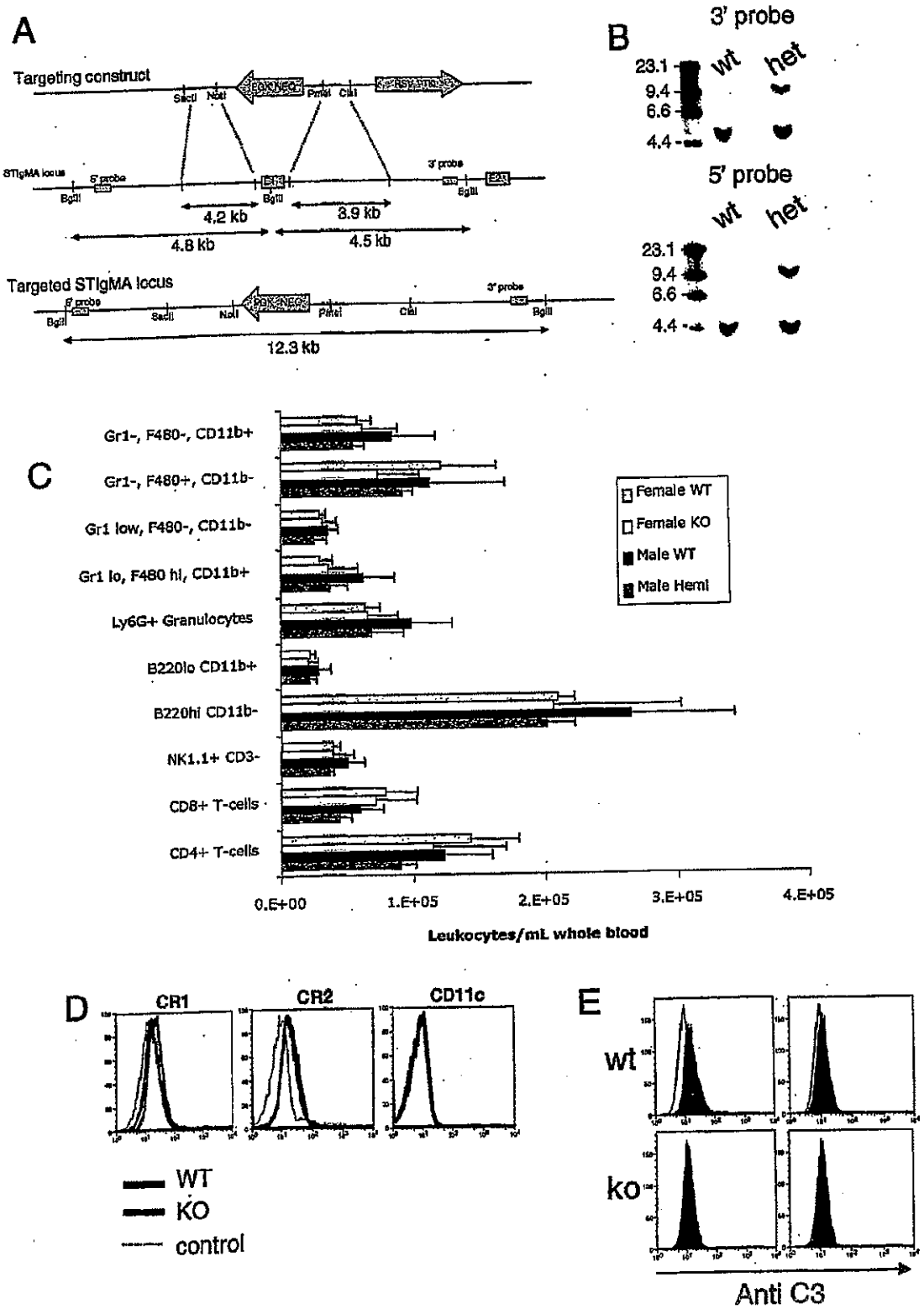

A
Targeting construct
SacII
NotI
PmeI
ClaI
STIgMA locus
5' probe
3' probe
BglII
4.2 kb
3.9 kb
4.8 kb
4.5 kb
Targeted STIgMA locus
12.3 kb
B
3' probe
wt
het
23.1
9.4
6.6
4.4
5' probe
C
Gr1-, F480-, CD11b+
Gr1-, F480+, CD11b-
Gr1 low, F480-, CD11b-
Gr1 lo, F480 hi, CD11b+
Ly6G+ Granulocytes
B220lo CD11b+
B220hi CD11b-
NK1.1+ CD3-
CD8+ T-cells
CD4+ T-cells
Female WT
Female KO
Male WT
Male Hemi
0.E+00
1.E+05
2.E+05
3.E+05
4.E+05
Leukocytes/mL whole blood
D
CR1
CR2
CD11c
WT
KO
control
E
wt
ko
Anti C3

Figure 53

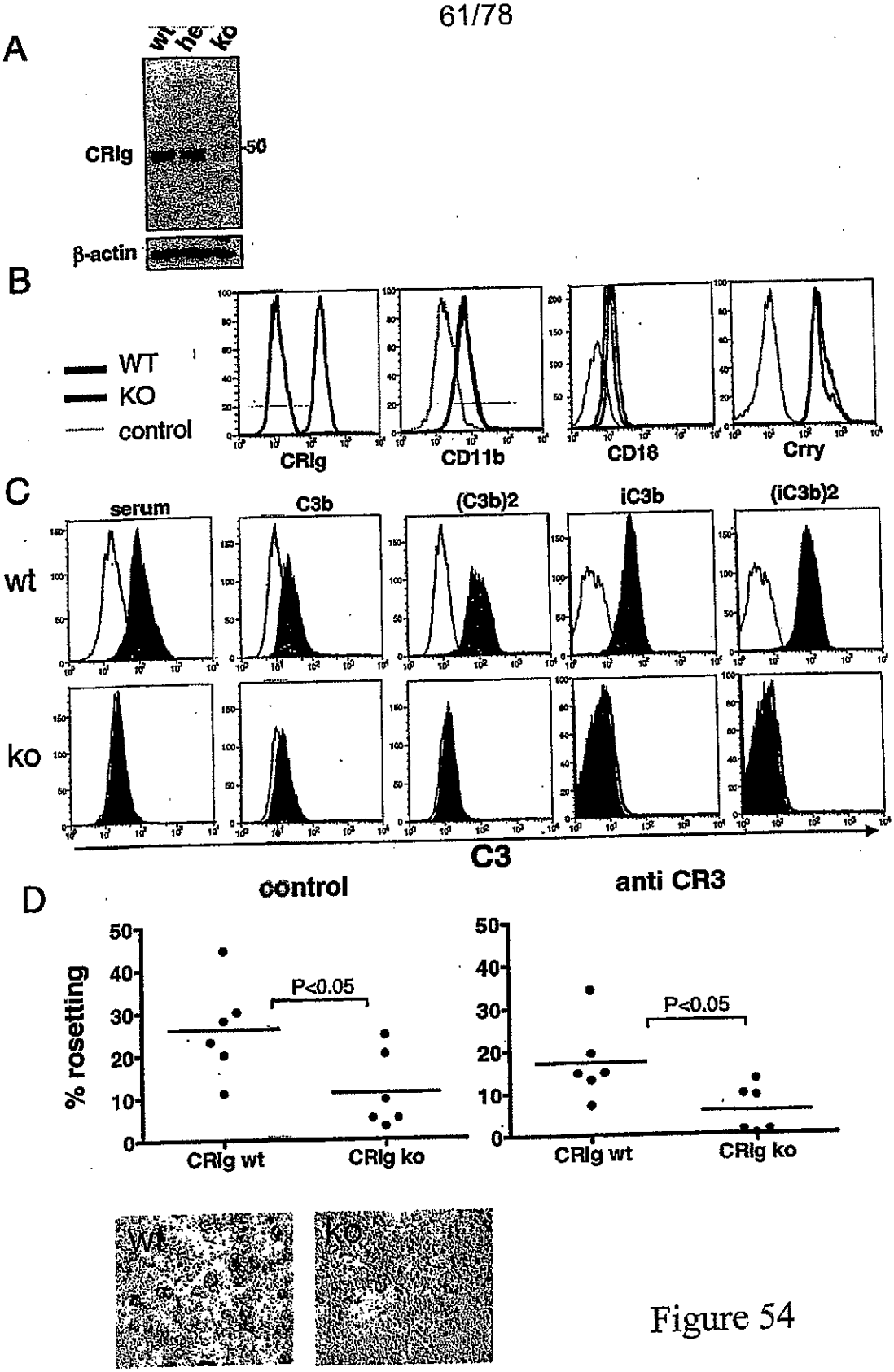

A
wt
he
ko
CRIg
50
β-actin
B
WT
KO
control
CRIg
CD11b
CD18
Crry
C
serum
C3b
(C3b)2
iC3b
(iC3b)2
wt
ko
C3
D
control
anti CR3
% rosetting
P<0.05
P<0.05
CRIg wt
CRIg ko
CRIg wt
CRIg ko
wt
KO

Figure 54

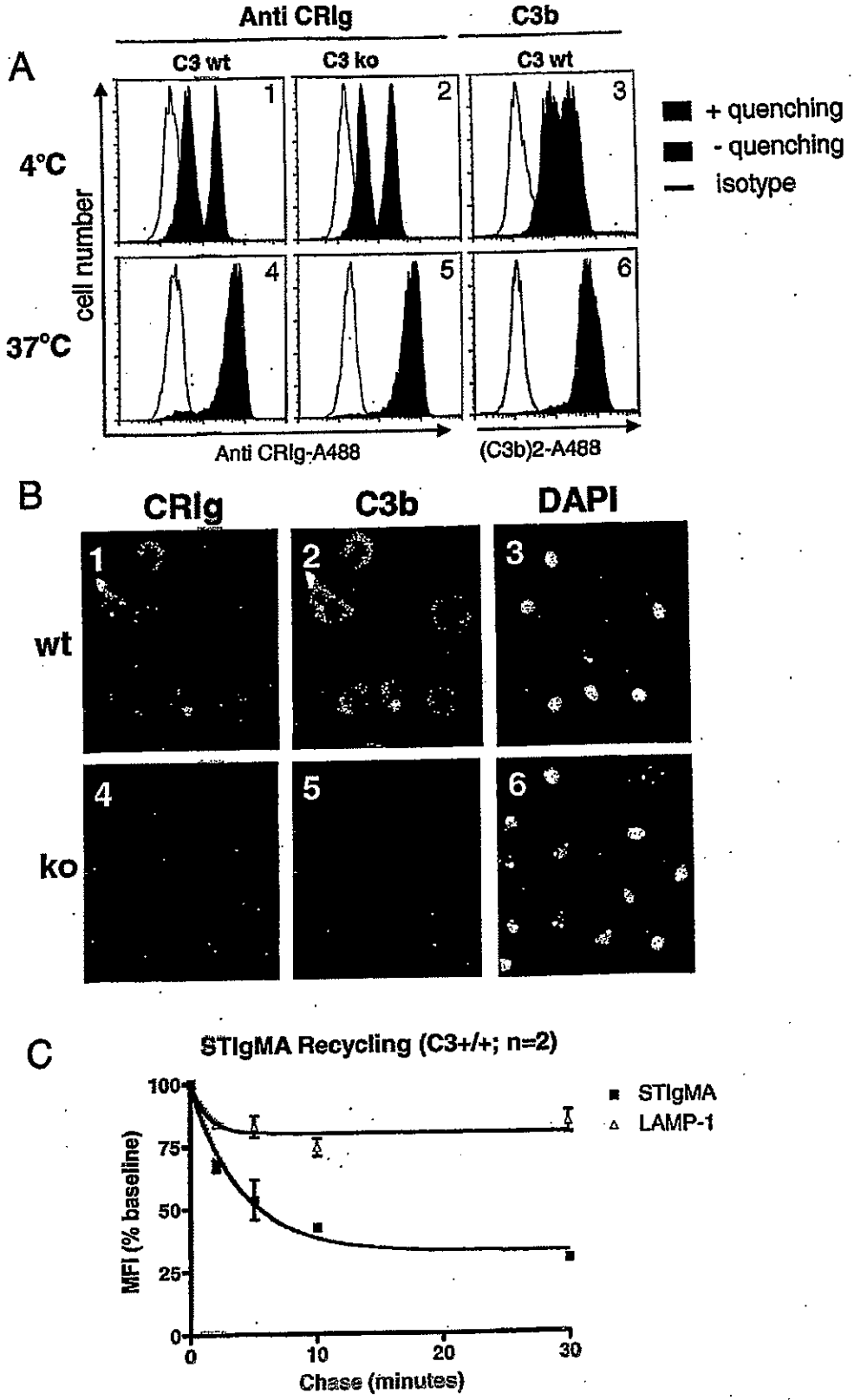

A
Anti CRIg
C3b
C3 wt
C3 ko
C3 wt
4°C
37°C
cell number
1
2
3
4
5
6
+ quenching
- quenching
isotype
Anti CRIg-A488
(C3b)2-A488
B
CRIg
C3b
DAPI
wt
ko
C
STIgMA Recycling (C3+/+; n=2)
STIgMA
LAMP-1
MFI (% baseline)
100
75
50
25
0
0
10
20
30
Chase (minutes)

Figure 55

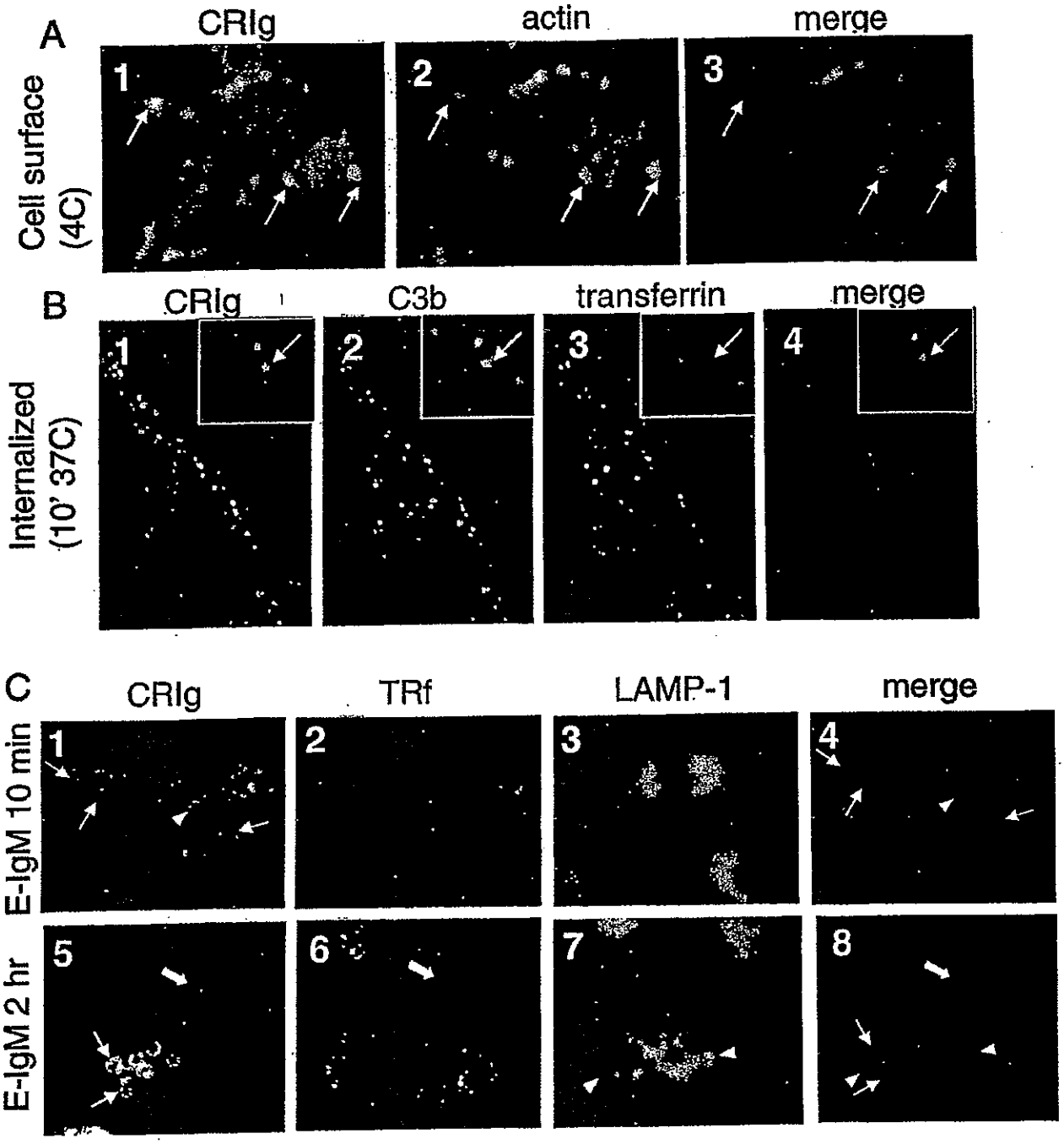

A
CRIg
actin
merge
Cell surface (4C)
1
2
3
B
CRIg
C3b
transferrin
merge
Internalized (10' 37C)
1
2
3
4
C
CRIg
TRf
LAMP-1
merge
E-IgM 10 min
E-IgM 2 hr
1
2
3
4
5
6
7
8

Figure 56

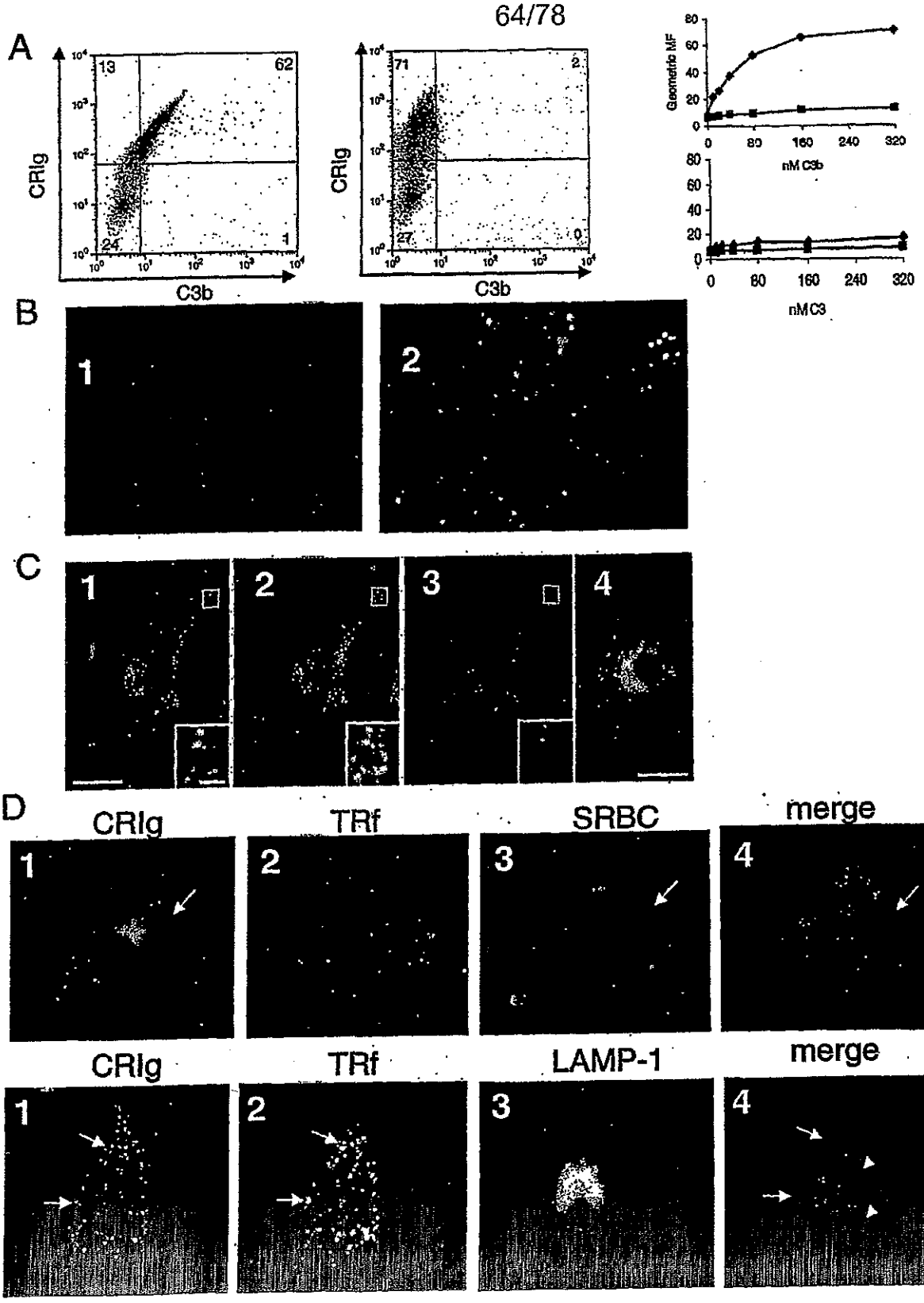

A
CRIg
C3b
13
62
24
1
71
2
27
0
Geometric MF
nM C3b
nM C3
B
1
2
C
1
2
3
4
D
CRIg
TRf
SRBC
merge
LAMP-1

Figure 57

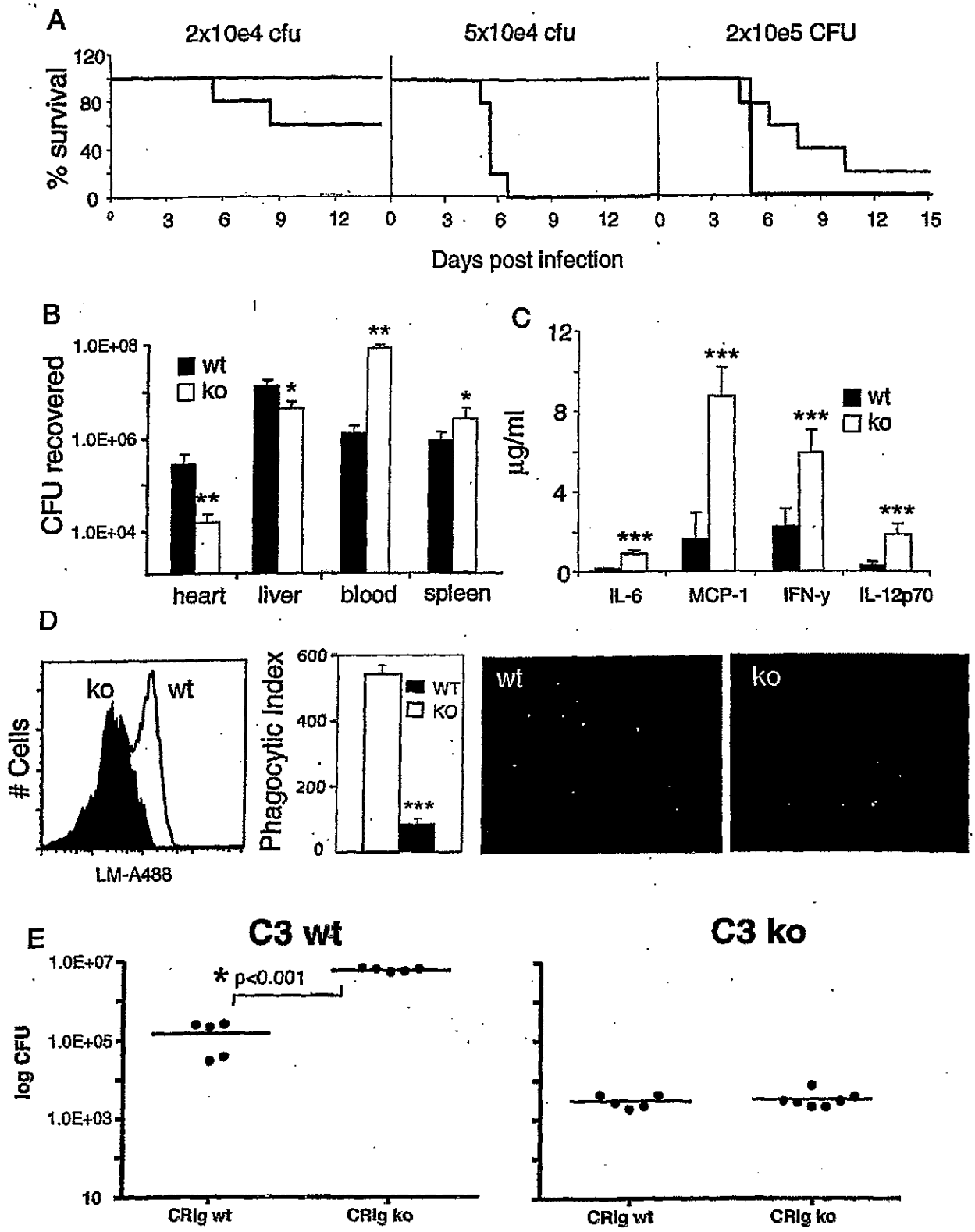

A
2x10e4 cfu
5x10e4 cfu
2x10e5 CFU
% survival
120
80
40
0
0 3 6 9 12 0 3 6 9 12 0 3 6 9 12 15
Days post infection
B
CFU recovered
1.0E+08
1.0E+06
1.0E+04
wt
ko
heart
liver
blood
spleen
C
µg/ml
12
8
4
0
wt
ko
IL-6
MCP-1
IFN-γ
IL-12p70
D
Cells
ko
wt
LM-A488
Phagocytic Index
600
400
200
0
WT
KO
wt
ko
E
C3 wt
C3 ko
log CFU
1.0E+07
1.0E+05
1.0E+03
10
* p<0.001
CRIg wt
CRIg ko
CRIg wt
CRIg ko

Figure 58

```
A
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ATCGATGCTCTCAATAAACCACC
><MET>
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GAGTGTAACAGGACCTTGGAAAGGGGATGTGAATCTTCCCTGCACCTATGACCCCCTGCAAGGCTACACCCAAGTCTTGG
TGAAGTGGCTGGTACAACGTGGCTCAGACCCTGTCACCATCTTTCTACGTGACTCTTCTGGAGACCATATCCAGCAGGCA
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GACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAA
AGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGAAGAGATGACCAAGAACCAGGTCAGCC
TGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTAC
AAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCA
GCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTC
CGGGTAAA
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><Sal {underline=1-6, dir=f, 5tag=}>
GTCGACCTGCAGAAGCT
><Xba>
TCTAGAGTCGACCTGCAGAAGCT
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Figure 59
SEQ ID:20

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CATCAAAGTAGCAACCCTAAGTACCTTACTCTTCAAGCCTGCGGTGATAGCCGACTCAGGCTCCTATTTCTGCACTGCCA
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TCTAGAGTCGACCTGCAGAAGCT
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Figure 60
SEQ ID:21

Different aa sequences in junction

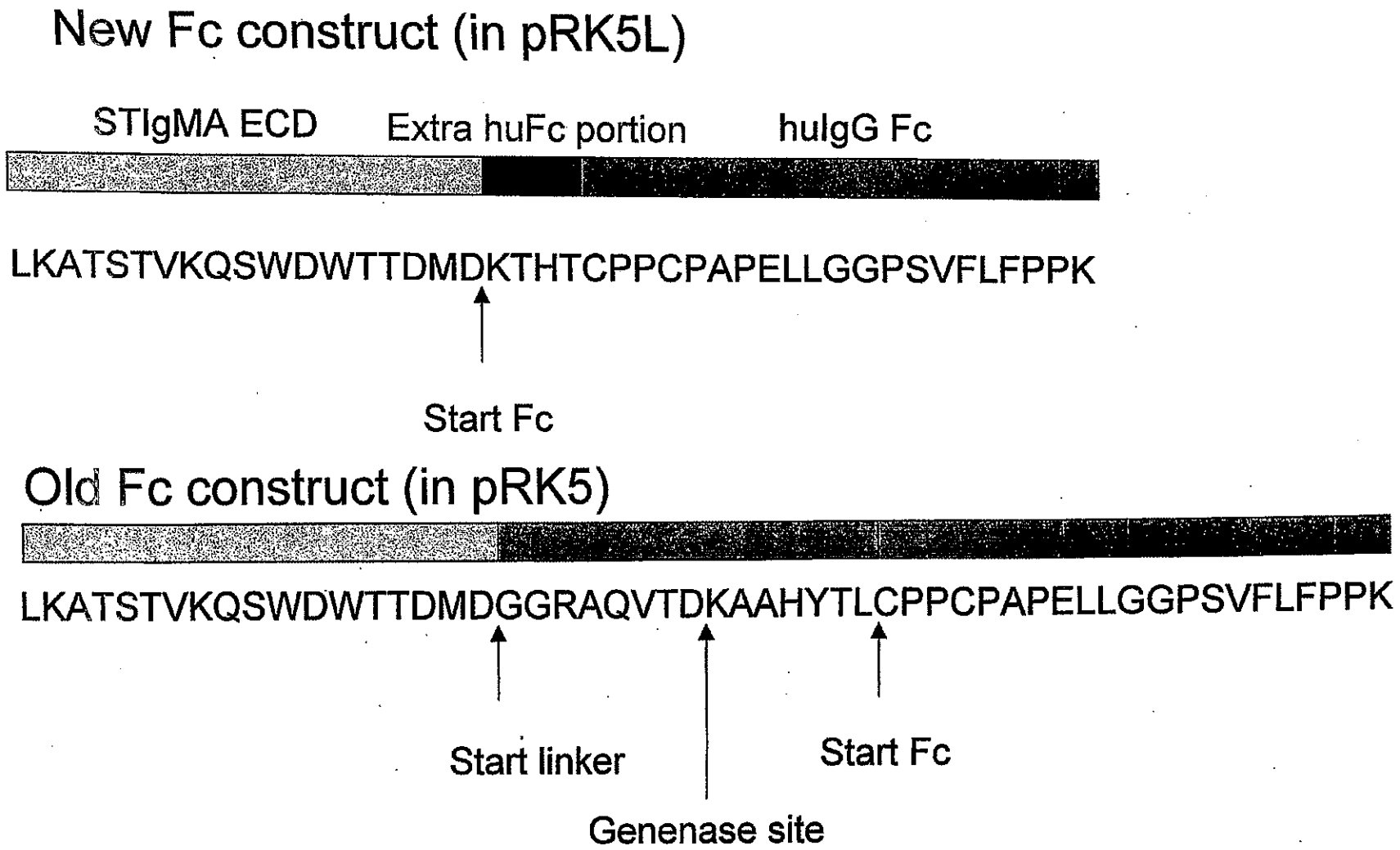


Figure 61

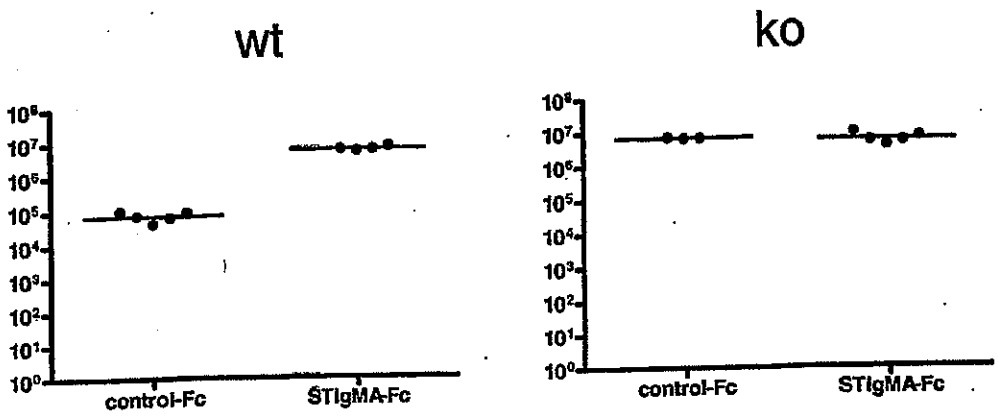


Figure 62

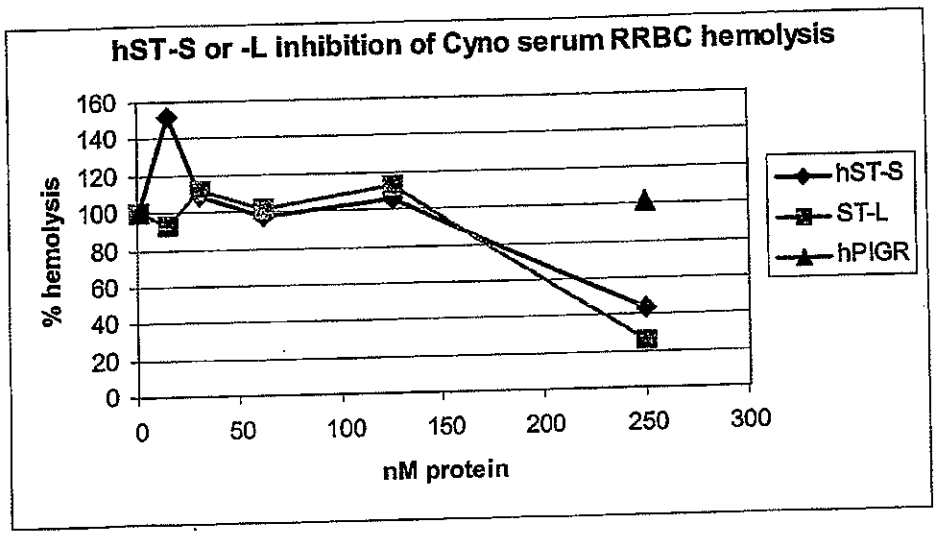


Figure 63A

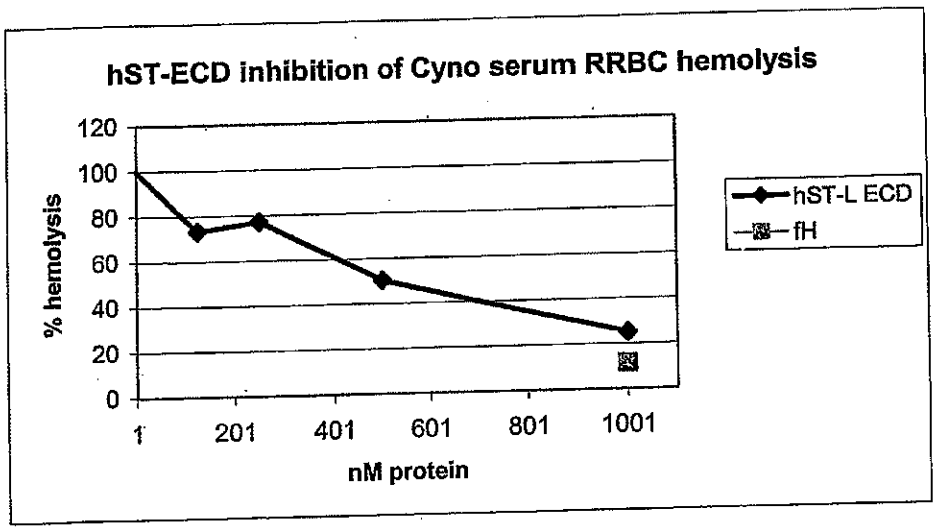


Figure 63B

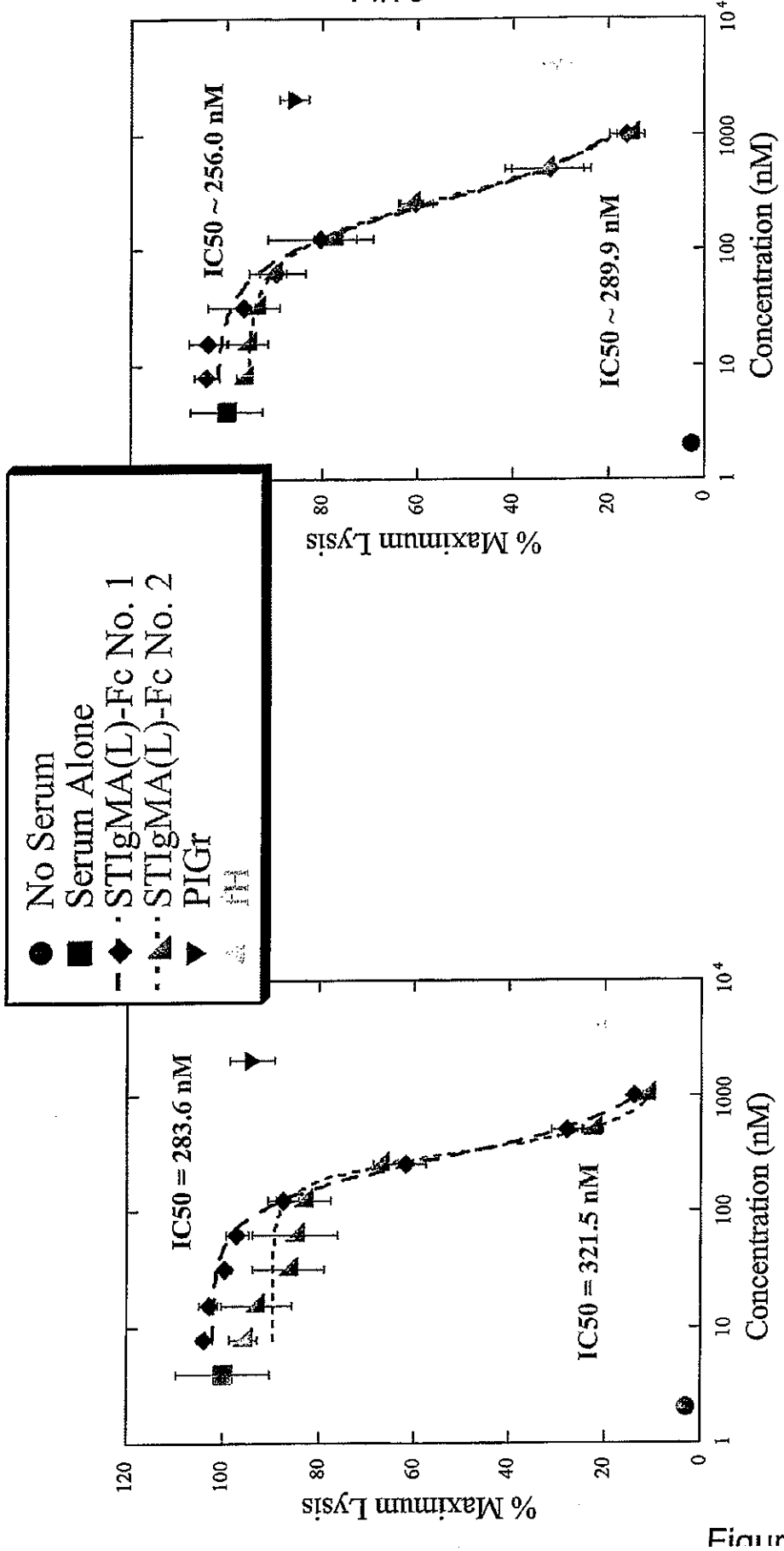

No Serum
Serum Alone
STIgMA(L)-Fc No. 1
STIgMA(L)-Fc No. 2
PIGr
% Maximum Lysis
Concentration (nM)
IC50 = 283.6 nM
IC50 = 321.5 nM
IC50 ~ 256.0 nM
IC50 ~ 289.9 nM

Figure 64

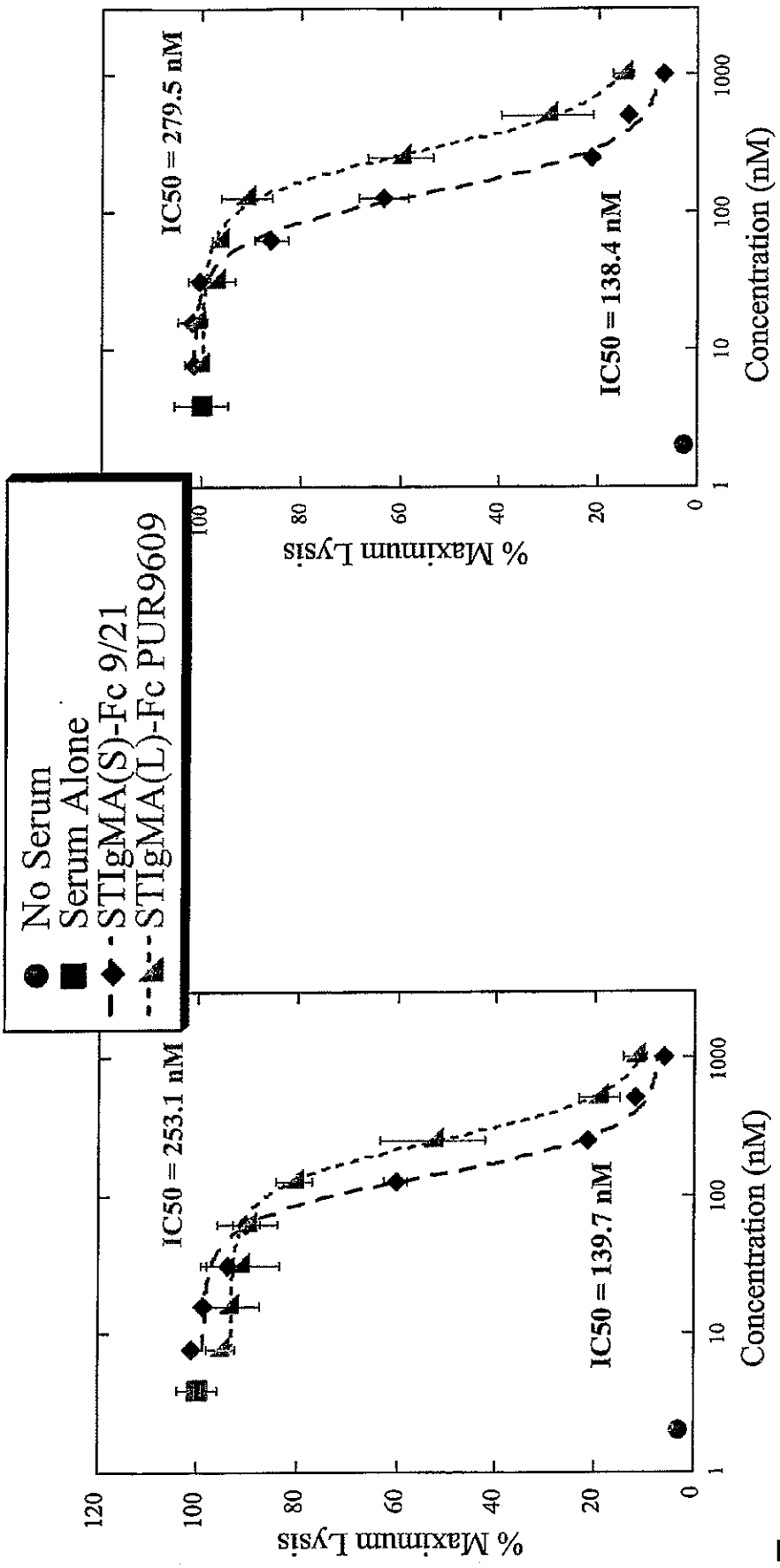

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Serum Alone
- STIgMA(S)-Fc 9/21
- STIgMA(L)-Fc PUR9609
% Maximum Lysis
Concentration (nM)
IC50 = 253.1 nM
IC50 = 139.7 nM
IC50 = 279.5 nM
IC50 = 138.4 nM

Figure 65

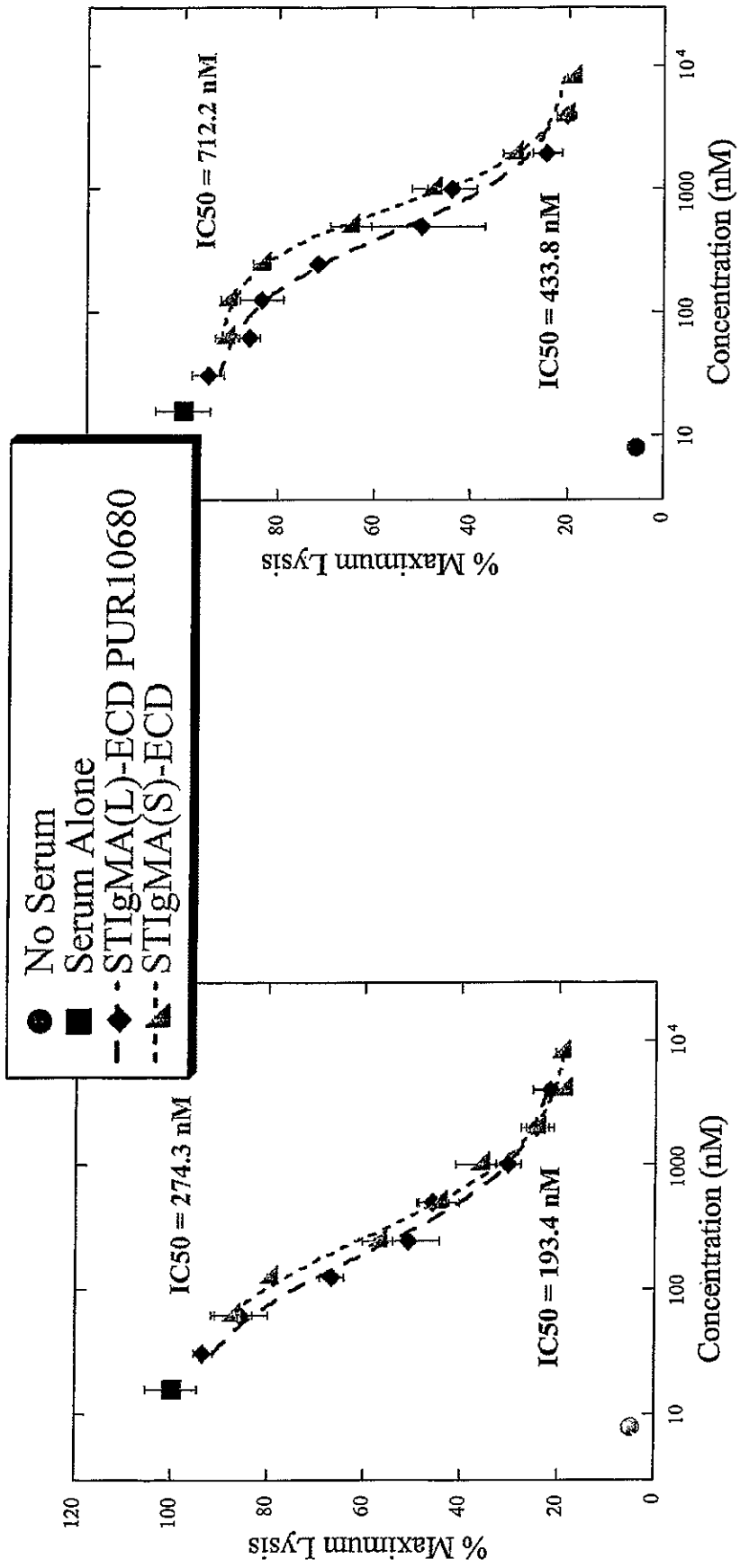

No Serum
Serum Alone
STIgMA(L)-ECD PUR10680
STIgMA(S)-ECD
% Maximum Lysis
Concentration (nM)
IC50 = 274.3 nM
IC50 = 193.4 nM
IC50 = 712.2 nM
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Figure 66

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Figure 67

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Figure 68

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TCTAGAGTCGACCTGCAGAAGCT

Figure 69

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Figure 70

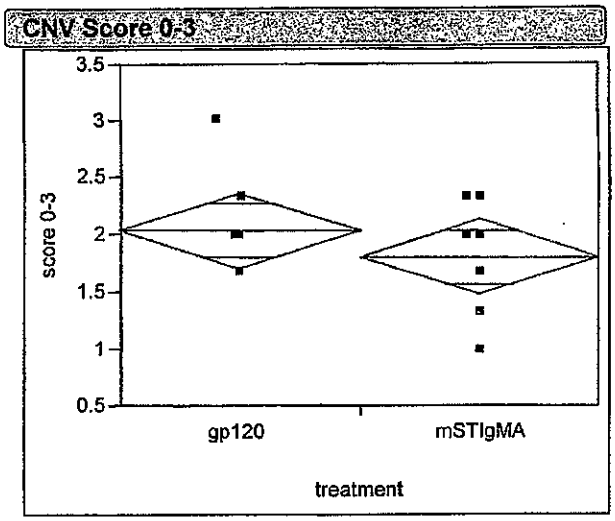


Figure 71A

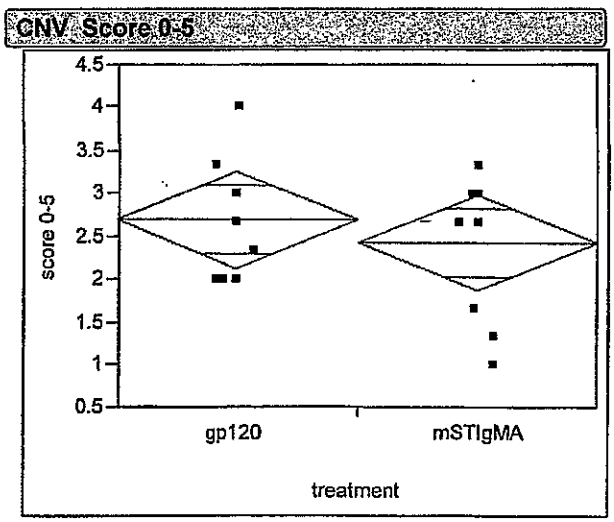


Figure 71B