```
                 |----------FRI----------|          CDRI          |----
                          10        20              30                40
2H7              QIVLSQSPAILSASPGEKVTMTC [RASSSVS-YMH] WYQQKP
                 * ***    **    * **  *
hu2H7.v16        DIQMTQSPSSLSASVGDRVTITC [RASSSVS-YMH] WYQQKP
                                         * * * * **
hum kI           DIQMTQSPSSLSASVGDRVTITC [RASQSISNYLA] WYQQKP

                 --FR2--|    CDR2    |----------FR3----------
                        50           60        70          80
2H7              GSSPKPWIY [APSNLAS] GVPARFSGSGSGTSYSLTISRVEA
                  **   *                *         ***    ****
hu2H7.v16        GKAPKPLIY [APSNLAS] GVPSRFSGSGSGTDFTLTISSLQP
                       *     * * *
hum kI           GKAPKLLIY [AASSLES] GVPSRFSGSGSGTDFTLTISSLQP

                 ---------|    CDR3    |--FR4--|
                          90           100
2H7              EDAATYYC [QQWSFNPPT] FGAGTKLELKR
                   *                   *   * *
hu2H7.v16        EDFATYYC [QQWSFNPPT] FGQGTKVEIKR
                          **** *
hum kI           EDFATYYC [QQYNSLPWT] FGQGTKVEIKR
```

FIG._1A

```
                 |----------FRI----------|          CDRI          |----
                          10        20              30                40
2H7              QAYLQQSGAELVRPGASVKMSCKAS [GYTFTSYNMH] WVKQT
                 *** **   **   *  * *** *                        * *
hu2H7.v16        EVQLVESGGGLVQPGGSLRLSCAAS [GYTFTSYNMH] WVRQA
                                           *  *  * *
hum III          EVQLVESGGGLVQPGGSLRLSCAAS [GFTFSSYAMS] WVRQA

                 --FR2--|       CDR2       |----FR3----
                        50 a        60          70        80
2H7              PRQGLEWIG [AIYPGNGDTSYNQKFKG] KATLTVDKSSSTAYM
                  **    *                     ** **    ** * *
hu2H7.v16        PGKGLEWVG [AIYPGNGDTSYNQKFKG] RFTISVDKSKNTLYL
                         *  * **** * * ****       * *
hum III          PGKGLEWVA [VISGDGGSTYYADSVKG] RFTISRDNSKNTLYL

                 ----------------|    CDR3    |--FR4--|
                   abc       90          100abcde      110
2H7              QLSSLTSEDSAVYFCAR [VVYYSNSYWYFDV] WGTGTTVTVSS
                 **  **  *   *                      *  *
hu2H7.v16        QMNSLRAEDTAVYYCAR [VVYYSNSYWYFDV] WGQGTLVTVSS
                                   ******* *** *
hum III          QMNSLRAEDTAVYYCAR [GRVGYSLY---DY] WGQGTLVTVSS
```

FIG._1B

```
   1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
     CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTTCTTCT TCTCAGCTTA

 101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
     CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC

 201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
     CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

 301 AAAAGTTAAT CTTTTCAACA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TTTGTAACTA GAATTCGAGC
     TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CTTAAGCTCG

   1                                                 M  K  K  N  I  A  F  L  L  A  S  M  F  V  F  S  I  A  T  N  A
 501 GTACGCTGAT ATCCAGATGA CCCAGTCCCC GAGCTCCCTG TCCGCCTCTG TGGGCGATAG GGTCACCATC ACCTGCAGAG CCAGTCAGAG CGTGTCGACT
     CATGCGACTA TAGGTCTACT GGGTCAGGGG CTCGAGGGAC AGGCGGAGAC ACCCGCTATC CCAGTGGTAG TGGACGTCTC GGTCAGTCTC GCACAGCTGA
  22 Y  A  D  I  Q  M  T  Q  S  P  S  S  L  S  A  S  V  G  D  R  V  T  I  T  C  R  A  S  Q  S  V  S  T

 601 AGCTCTTATA GCTATATGCA CTGGTATCAA CAGAAACCAG GAAAAGCTCC GAAACTACTG ATTTACTATG CTAGCAACCT CGAGTCTGGA GTCCCTTCTC
     TCGAGAATAT CGATATACGT GACCATAGTT GTCTTTGGTC CTTTTCGAGG CTTTGATGAC TAAATGATAC GATCGTTGGA GCTCAGACCT CAGGGAAGAG
  55 S  S  Y  S  Y  M  H  W  Y  Q  Q  K  P  G  K  A  P  K  L  L  I  Y  Y  A  S  N  L  E  S  G  V  P  S  R

 701 GCTTCTCTGG ATCCGGTTCT GGGACGGATT TCACTCTGAC CATCAGCAGT CTGCAGCCAG AAGACTTCGC AACTTATTAC TGTCAACACT CTTGGGGTAT
     CGAAGAGACC TAGGCCAAGA CCCTGCCTAA AGTGAGACTG GTAGTCGTCA GACGTCGGTC TTCTGAAGCG TTGAATAATG ACAGTTGTGA GAACCCCATA
  89 F  S  G  S  G  S  G  T  D  F  T  L  T  I  S  S  L  Q  P  E  D  F  A  T  Y  Y  C  Q  H  S  W  G  I

 801 TCCGCGCACA TTTGGACAGG GTACCAAGGT GGAGATCAAA CGAACTGTGG CTGCACCATC TGTCTTCATC TTCCCGCCAT CTGATGAGCA GTTGAAATCT
     AGGCGCGTGT AAACCTGTCC CATGGTTCCA CCTCTAGTTT GCTTGACACC GACGTGGTAG ACAGAAGTAG AAGGGCGGTA GACTACTCGT CAACTTTAGA
 122 P  R  T  F  G  Q  G  T  K  V  E  I  K  R  T  V  A  A  P  S  V  F  I  F  P  P  S  D  E  Q  L  K  S

 901 GGAACTGCTT CTGTTGTGTG CCTGCTGAAT AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACGCCCT CCAATCGGGT AACTCCCAGG
     CCTTGACGAA GACAACACAC GGACGACTTA TTGAAGATAG GGTCTCTCCG GTTTCATGTC ACCTTCCACC TATTGCGGGA GGTTAGCCCA TTGAGGGTCC
 155 G  T  A  S  V  V  C  L  L  N  N  F  Y  P  R  E  A  K  V  Q  W  K  V  D  N  A  L  Q  S  G  N  S  Q  E
```

FIG._2A

```
1001 AGAGTGTCAC AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC ACCCTGACGC TGAGCAAAGC AGACTACGAG AAACACAAAG TCTACGCCTG
     TCTCACAGTG TCTCGTCCTG TCGTTCCTGT CGTGGATGTC GGAGTCGTCG TGGGACTGCG ACTCGTTTCG TCTGATGCTC TTTGTGTTTC AGATGCGGAC
 189   S  V  T   E  Q  D   S  K  D  S   T  Y  S   L  S  S   T  L  T  L   S  K  A   D  Y  E   K  H  K  V   Y  A  C

1101 CGAAGTCACC CATCAGGGCC TGAGCTCGCC CGTCACAAAG AGCTTCAACA GGGGAGAGTG TTAAGCTGAT CCTCTACGCC GGACGCATCG TGGCCCTAGT
     GCTTCAGTGG GTAGTCCCGG ACTCGAGCGG GCAGTGTTTC TCGAAGTTGT CCCCTCTCAC AATTCGACTA GGAGATGCGG CCTGCGTAGC ACCGGGATCA
 222   E  V  T   H  Q  G  L   S  S  P   V  T  K   S  F  N  R   G  E  C   O

1201 ACGCAAGTTC ACGTAAAAAG GGTATCTAGA GGTTGAGGTG ATTTTATGAA AAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA
     TGCGTTCAAG TGCATTTTTC CCATAGATCT CCAACTCCAC TAAAATACTT TTTCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT
   1                                                 M  K   K  N  I   A  F  L  L   A  S  M   F  V  F   S  I  A  T

1301 CAAACGCGTA CGCTGAGGTT CAGCTGGTGG AGTCTGGCGG TGGCCTGGTG CAGCCAGGGG GCTCACTCCG TTTGTCCTGT GCAGCTTCTG GCTACACCTT
     GTTTGCGCAT GCGACTCCAA GTCGACCACC TCAGACCGCC ACCGGACCAC GTCGGTCCCC CGAGTGAGGC AAACAGGACA CGTCGAAGAC CGATGTGGAA
  20   N  A  Y   A  E  V   Q  L  V  E   S  G  G   G  L  V   Q  P  G  G   S  L  R   L  S  C   A  A  S  G   Y  T  F

1401 CACCGAATAT ATCATCCACT GGGTCCGTCA GGCCCCGGGT AAGGGCCTGG AATGGGTTGC ATCGATTAAT CCTGACTACG ACATCACGAA CTATAACCAG
     GTGGCTTATA TAGTAGGTGA CCCAGGCAGT CCGGGGCCCA TTCCCGGACC TTACCCAACG TAGCTAATTA GGACTGATGC TGTAGTGCTT GATATTGGTC
  53   T  E  Y   I  I  H  W   V  R  Q   A  P  G   K  G  L  E   W  V  A   S  I  N   P  D  Y  D   I  T  N   Y  N  Q

1501 CGCTTCAAGG GCCGTTTCAC TATAAGTCGC GACGATTCCA AAAACACATT ATACCTGCAG ATGAACAGCC TGCGTGCTGA GGACACTGCC GTCTATTATT
     GCGAAGTTCC CGGCAAAGTG ATATTCAGCG CTGCTAAGGT TTTTGTGTAA TATGGACGTC TACTTGTCGG ACGCACGACT CCTGTGACGG CAGATAATAA
  86 R  F  K  G   R  F  T   I  S  R   D  D  S  K   N  T  L   Y  L  Q   M  N  S  L   R  A  E   D  T  A   V  Y  Y  C

1601 GTGCTCGATG GATCAGCGAT TTCTTCGACT ACTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC CCATCGGTCT TCCCCCTGGC
     CACGAGCTAC CTAGTCGCTA AAGAAGCTGA TGACCCCAGT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG GGTAGCCAGA AGGGGGACCG
 120   A  R  W   I  S  D   F  F  D  Y   W  G  Q   G  T  L   V  T  V  S   S  A  S   T  K  G   P  S  V  F   P  L  A

1701 ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
     TGGGAGGAGG TTCTCGTGGA GACCCCCGTG TCGCCGGGAC CCGACGGACC AGTTCCTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
 153   P  S  S   K  S  T  S   G  G  T   A  A  L   G  C  L  V   K  D  Y   F  P  E   P  V  T  V   S  W  N   S  G  A

1801 CTGACCAGCG GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC
     GACTGGTCGC CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG TCGTCGCACC ACTGGCACGG GAGGTCGTCG AACCCGTGGG
 186 L  T  S  G   V  H  T   F  P  A   V  L  Q  S   S  G  L   Y  S  L   S  S  V  V   T  V  P   S  S  S   L  G  T  Q
```

FIG._2B

```
1901 AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GACCACCGCA
     TCTGGATGTA GACGTTGCAC TTAGTGTTCG GGTCGTTGTG GTTCCACCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CTGGTGGCGT
 220   T   Y   I     C   N   V     N   H   K   P     S   N   T     K   V   D     K   K   V   E     P   K   S     C   D   K     T   H   T   O

2001 TGCACCAGTA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGGCGTGCT GCTAGCGCCG CCCTATACCT TGTCTGCCTC CCCGCGTTGC GTCGCGGTGC
     ACGTGGTCAT AGCAGGTAAG GCTGTCGTAG CGGTCAGTGA TACCGCACGA CGATCGCGGC GGGATATGGA ACAGACGGAG GGGCGCAACG CAGCGCCACG

2101 ATGGAGCCGG GCCACCTCGA CCTGAATGGA AGCCGGCGGC ACCTCGCTAA CGGATTCACC ACTCCAAGAA TTGGAGCCAA TCAATTCTTG CGGAGAACTG
     TACCTCGGCC CGGTGGAGCT GGACTTACCT TCGGCCGCCG TGGAGCGATT GCCTAAGTGG TGAGGTTCTT AACCTCGGTT AGTTAAGAAC GCCTCTTGAC

2201 TGAATGCGCA AACCAACCCT TGGCAGAACA TATCCATCGC GTCCGCCATC TCCAGCAGCC GCACGCGGCG CATCTCGGGC AGCGTTGGGT CCTGGCCACG
     ACTTACGCGT TTGGTTGGGA ACCGTCTTGT ATAGGTAGCG CAGGCGGTAG AGGTCGTCGG CGTGCGCCGC GTAGAGCCCG TCGCAACCCA GGACCGGTGC

2301 GGTGCGCATG ATCGTGCTCC TGTCGTTGAG GACCCGGCTA GGCTGGCGGG GTTGCCTTAC TGGTTAGCAG AATGAATCAC CGATACGCGA GCGAACGTGA
     CCACGCGTAC TAGCACGAGG ACAGCAACTC CTGGGCCGAT CCGACCGCCC CAACGGAATG ACCAATCGTC TTACTTAGTG GCTATGCGCT CGCTTGCACT

2401 AGCGACTGCT GCTGCAAAAC GTCTGCGACC TGAGCAACAA CATGAATGGT CTTCGGTTTC CGTGTTTCGT AAAGTCTGGA AACGCGGAAG TCAGCGCCCT
     TCGCTGACGA CGACGTTTTG CAGACGCTGG ACTCGTTGTT GTACTTACCA GAAGCCAAAG GCACAAAGCA TTTCAGACCT TTGCGCCTTC AGTCGCGGGA

2501 GCACCATTAT GTTCCGGATC TGCATCGCAG GATGCTGCTG GCTACCCTGT GGAACACCTA CATCTGTATT AACGAAGCGC TGGCATTGAC CCTGAGTGAT
     CGTGGTAATA CAAGGCCTAG ACGTAGCGTC CTACGACGAC CGATGGGACA CCTTGTGGAT GTAGACATAA TTGCTTCGCG ACCGTAACTG GGACTCACTA

2601 TTTTCTCTGG TCCCGCCGCA TCCATACCGC CAGTTGTTTA CCCTCACAAC GTTCCAGTAA CCGGGCATGT TCATCATCAG TAACCCGTAT CGTGAGCATC
     AAAAGAGACC AGGGCGGCGT AGGTATGGCG GTCAACAAAT GGGAGTGTTG CAAGGTCATT GGCCCGTACA AGTAGTAGTC ATTGGGCATA GCACTCGTAG

2701 CTCTCTCGTT TCATCGGTAT CATTACCCCC ATGAACAGAA ATTCCCCCTT ACACGGAGGC ATCAAGTGAC CAAACAGGAA AAAACCGCCC TTAACATGGC
     GAGAGAGCAA AGTAGCCATA GTAATGGGGG TACTTGTCTT TAAGGGGGAA TGTGCCTCCG TAGTTCACTG GTTTGTCCTT TTTTGGCGGG AATTGTACCG

2801 CCGCTTTATC AGAAGCCAGA CATTAACGCT TCTGGAGAAA CTCAACGAGC TGGACGCGGA TGAACAGGCA GACATCTGTG AATCGCTTCA CGACCACGCT
     GGCGAAATAG TCTTCGGTCT GTAATTGCGA AGACCTCTTT GAGTTGCTCG ACCTGCGCCT ACTTGTCCGT CTGTAGACAC TTAGCGAAGT GCTGGTGCGA

2901 GATGAGCTTT ACCGCAGCAT CCGGAAATTG TAAACGTTAA TATTTTGTTA AAATTCGCGT TAAATTTTTG TTAAATCAGC TCATTTTTTA ACCAATAGGC
     CTACTCGAAA TGGCGTCGTA GGCCTTTAAC ATTTGCAATT ATAAAACAAT TTTAAGCGCA ATTTAAAAAC AATTTAGTCG AGTAAAAAAT TGGTTATCCG

3001 CGAAATCGGC AAAATCCCTT ATAAATCAAA AGAATAGACC GAGATAGGGT TGAGTGTTGT TCCAGTTTGG AACAAGAGTC CACTATTAAA GAACGTGGAC
     GCTTTAGCCG TTTTAGGGAA TATTTAGTTT TCTTATCTGG CTCTATCCCA ACTCACAACA AGGTCAAACC TTGTTCTCAG GTGATAATTT CTTGCACCTG
```

FIG._2C

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3101 TCCAACGTCA AAGGGCGAAA AACCGTCTAT CAGGGCTATG GCCCACTACG TGAACCATCA CCCTAATCAA GTTTTTTGGG GTCGAGGTGC CGTAAAGCAC
     AGGTTGCAGT TTCCCGCTTT TTGGCAGATA GTCCCGATAC CGGGTGATGC ACTTGGTAGT GGGATTAGTT CAAAAAACCC CAGCTCCACG GCATTTCGTG
3201 TAAATCGGAA CCCTAAAGGG AGCCCCCGAT TTAGAGCTTG ACGGGGAAAG CCGGCGAACG TGGCGAGAAA GGAAGGGAAG AAAGCGAAAG GAGCGGGCGC
     ATTTAGCCTT GGGATTTCCC TCGGGGGCTA AATCTCGAAC TGCCCCTTTC GGCCGCTTGC ACCGCTCTTT CCTTCCCTTC TTTCGCTTTC CTCGCCCGCG
3301 TAGGGCGCTG GCAAGTGTAG CGGTCACGCT GCGCGTAACC ACCACACCCG CCGCGCTTAA TGCGCCGCTA CAGGGCGCGT CCGCATCCTG CCTCGCGCGT
     ATCCCGCGAC CGTTCACATC GCCAGTGCGA CGCGCATTGG TGGTGTGGGC GGCGCGAATT ACGCGGCGAT GTCCCGCGCA GGCGTAGGAC GGAGCGCGCA
3401 TTCGGTGATG ACGGTGAAAA CCTCTGACAC ATGCAGCTCC CGGAGACGGT CACAGCTTGT CTGTAAGCGG ATGCCGGGAG CAGACAAGCC CGTCAGGGCG
     AAGCCACTAC TGCCACTTTT GGAGACTGTG TACGTCGAGG GCCTCTGCCA GTGTCGAACA GACATTCGCC TACGGCCCTC GTCTGTTCGG GCAGTCCCGC
3501 CGTCAGCGGG TGTTGGCGGG TGTCGGGGCG CAGCCATGAC CCAGTCACGT AGCGATAGCG GAGTGTATAC TGGCTTAACT ATGCGGCATC AGAGCAGATT
     GCAGTCGCCC ACAACCGCCC ACAGCCCCGC GTCGGTACTG GGTCAGTGCA TCGCTATCGC CTCACATATG ACCGAATTGA TACGCCGTAG TCTCGTCTAA
3601 GTACTGAGAG TGCACCATAT GCGGTGTGAA ATACCGCACA GATGCGTAAG GAGAAAATAC CGCATCAGGC GCTCTTCCGC TTCCTCGCTC ACTGACTCGC
     CATGACTCTC ACGTGGTATA CGCCACACTT TATGGCGTGT CTACGCATTC CTCTTTTATG GCGTAGTCCG CGAGAAGGCG AAGGAGCGAG TGACTGAGCG
3701 TGCGCTCGGT CGTTCGGCTG CGGCGAGCGG TATCAGCTCA CTCAAAGGCG GTAATACGGT TATCCACAGA ATCAGGGGAT AACGCAGGAA AGAACATGTG
     ACGCGAGCCA GCAAGCCGAC GCCGCTCGCC ATAGTCGAGT GAGTTTCCGC CATTATGCCA ATAGGTGTCT TAGTCCCCTA TTGCGTCCTT TCTTGTACAC
3801 AGCAAAAGGC CAGCAAAAGG CCAGGAACCG TAAAAAGGCC GCGTTGCTGG CGTTTTTCCA TAGGCTCCGC CCCCCTGACG AGCATCACAA AAATCGACGC
     TCGTTTTCCG GTCGTTTTCC GGTCCTTGGC ATTTTTCCGG CGCAACGACC GCAAAAAGGT ATCCGAGGCG GGGGGACTGC TCGTAGTGTT TTTAGCTGCG
3901 TCAAGTCAGA GGTGGCGAAA CCCGACAGGA CTATAAAGAT ACCAGGCGTT TCCCCCTGGA AGCTCCCTCG TGCGCTCTCC TGTTCCGACC CTGCCGCTTA
     AGTTCAGTCT CCACCGCTTT GGGCTGTCCT GATATTTCTA TGGTCCGCAA AGGGGGACCT TCGAGGGAGC ACGCGAGAGG ACAAGGCTGG GACGGCGAAT
4001 CCGGATACCT GTCCGCCTTT CTCCCTTCGG GAAGCGTGGC GCTTTCTCAT AGCTCACGCT GTAGGTATCT CAGTTCGGTG TAGGTCGTTC GCTCCAAGCT
     GGCCTATGGA CAGGCGGAAA GAGGGAAGCC CTTCGCACCG CGAAAGAGTA TCGAGTGCGA CATCCATAGA GTCAAGCCAC ATCCAGCAAG CGAGGTTCGA
4101 GGGCTGTGTG CACGAACCCC CCGTTCAGCC CGACCGCTGC GCCTTATCCG GTAACTATCG TCTTGAGTCC AACCCGGTAA GACACGACTT ATCGCCACTG
     CCCGACACAC GTGCTTGGGG GGCAAGTCGG GCTGGCGACG CGGAATAGGC CATTGATAGC AGAACTCAGG TTGGGCCATT CTGTGCTGAA TAGCGGTGAC
4201 GCAGCAGCCA CTGGTAACAG GATTAGCAGA GCGAGGTATG TAGGCGGTGC TACAGAGTTC TTGAAGTGGT GGCCTAACTA CGGCTACACT AGAAGGACAG
     CGTCGTCGGT GACCATTGTC CTAATCGTCT CGCTCCATAC ATCCGCCACG ATGTCTCAAG AACTTCACCA CCGGATTGAT GCCGATGTGA TCTTCCTGTC
4301 TATTTGGTAT CTGCGCTCTG CTGAAGCCAG TTACCTTCGG AAAAAGAGTT GGTAGCTCTT GATCCGGCAA ACAAACCACC GCTGGTAGCG GTGGTTTTTT
     ATAAACCATA GACGCGAGAC GACTTCGGTC AATGGAAGCC TTTTTCTCAA CCATCGAGAA CTAGGCCGTT TGTTTGGTGG CGACCATCGC CACCAAAAAA
```

FIG._2D

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4401 TGTTTGCAAG CAGCAGATTA CGCGCAGAAA AAAAGGATCT CAAGAAGATC CTTTGATCTT TTCTACGGGG TCTGACGCTC AGTGGAACGA AAACTCACGT
     ACAAACGTTC GTCGTCTAAT GCGCGTCTTT TTTTCCTAGA GTTCTTCTAG GAAACTAGAA AAGATGCCCC AGACTGCGAG TCACCTTGCT TTTGAGTGCA

4501 TAAGGGATTT TGGTCATGAG ATTATCAAAA AGGATCTTCA CCTAGATCCT TTTAAATTAA AAATGAAGTT TTAAATCAAT CTAAAGTATA TATGAGTAAA
     ATTCCCTAAA ACCAGTACTC TAATAGTTTT TCCTAGAAGT GGATCTAGGA AAATTTAATT TTTACTTCAA AATTTAGTTA GATTTCATAT ATACTCATTT

4601 CTTGGTCTGA CAGTTACCAA TGCTTAATCA GTGAGGCACC TATCTCAGCG ATCTGTCTAT TTCGTTCATC CATAGTTGCC TGACTCCCCG TCGTGTAGAT
     GAACCAGACT GTCAATGGTT ACGAATTAGT CACTCCGTGG ATAGAGTCGC TAGACAGATA AAGCAAGTAG GTATCAACGG ACTGAGGGGC AGCACATCTA

4701 AACTACGATA CGGGAGGGCT TACCATCTGG CCCCAGTGCT GCAATGATAC CGCGAGACCC ACGCTCACCG GCTCCAGATT TATCAGCAAT AAACCAGCCA
     TTGATGCTAT GCCCTCCCGA ATGGTAGACC GGGGTCACGA CGTTACTATG GCGCTCTGGG TGCGAGTGGC CGAGGTCTAA ATAGTCGTTA TTTGGTCGGT

4801 GCCGGAAGGG CCGAGCGCAG AAGTGGTCCT GCAACTTTAT CCGCCTCCAT CCAGTCTATT AATTGTTGCC GGGAAGCTAG AGTAAGTAGT TCGCCAGTTA
     CGGCCTTCCC GGCTCGCGTC TTCACCAGGA CGTTGAAATA GGCGGAGGTA GGTCAGATAA TTAACAACGG CCCTTCGATC TCATTCATCA AGCGGTCAAT

4901 ATAGTTTGCG CAACGTTGTT GCCATTGCTG CAGGCATCGT GGTGTCACGC TCGTCGTTTG GTATGGCTTC ATTCAGCTCC GGTTCCCAAC GATCAAGGCG
     TATCAAACGC GTTGCAACAA CGGTAACGAC GTCCGTAGCA CCACAGTGCG AGCAGCAAAC CATACCGAAG TAAGTCGAGG CCAAGGGTTG CTAGTTCCGC

5001 AGTTACATGA TCCCCCATGT TGTGCAAAAA AGCGGTTAGC TCCTTCGGTC CTCCGATCGT TGTCAGAAGT AAGTTGGCCG CAGTGTTATC ACTCATGGTT
     TCAATGTACT AGGGGGTACA ACACGTTTTT TCGCCAATCG AGGAAGCCAG GAGGCTAGCA ACAGTCTTCA TTCAACCGGC GTCACAATAG TGAGTACCAA

5101 ATGGCAGCAC TGCATAATTC TCTTACTGTC ATGCCATCCG TAAGATGCTT TTCTGTGACT GGTGAGTACT CAACCAAGTC ATTCTGAGAA TAGTGTATGC
     TACCGTCGTG ACGTATTAAG AGAATGACAG TACGGTAGGC ATTCTACGAA AAGACACTGA CCACTCATGA GTTGGTTCAG TAAGACTCTT ATCACATACG

5201 GGCGACCGAG TTGCTCTTGC CCGGCGTCAA CACGGGATAA TACCGCGCCA CATAGCAGAA CTTTAAAAGT GCTCATCATT GGAAAACGTT CTTCGGGGCG
     CCGCTGGCTC AACGAGAACG GGCCGCAGTT GTGCCCTATT ATGGCGCGGT GTATCGTCTT GAAATTTTCA CGAGTAGTAA CCTTTTGCAA GAAGCCCCGC

5301 AAAACTCTCA AGGATCTTAC CGCTGTTGAG ATCCAGTTCG ATGTAACCCA CTCGTGCACC CAACTGATCT TCAGCATCTT TTACTTTCAC CAGCGTTTCT
     TTTTGAGAGT TCCTAGAATG GCGACAACTC TAGGTCAAGC TACATTGGGT GAGCACGTGG GTTGACTAGA AGTCGTAGAA AATGAAAGTG GTCGCAAAGA

5401 GGGTGAGCAA AAACAGGAAG GCAAAATGCC GCAAAAAAGG GAATAAGGGC GACACGGAAA TGTTGAATAC TCATACTCTT CCTTTTTCAA TATTATTGAA
     CCCACTCGTT TTTGTCCTTC CGTTTTACGG CGTTTTTTCC CTTATTCCCG CTGTGCCTTT ACAACTTATG AGTATGAGAA GGAAAAAGTT ATAATAACTT

5501 GCATTTATCA GGGTTATTGT CTCATGAGCG GATACATATT TGAATGTATT TAGAAAAATA AACAAATAGG GGTTCCGCGC ACATTTCCCC GAAAAGTGCC
     CGTAAATAGT CCCAATAACA GAGTACTCGC CTATGTATAA ACTTACATAA ATCTTTTTAT TTGTTTATCC CCAAGGCGCG TGTAAAGGGG CTTTTCACGG

5601 ACCTGACGTC TAAGAAACCA TTATTATCAT GACATTAACC TATAAAAATA GGCGTATCAC GAGGCCCTTT CGTCTTCAA
     TGGACTGCAG ATTCTTTGGT AATAATAGTA CTGTAATTGG ATATTTTTAT CCGCATAGTG CTCCGGGAAA GCAGAAGTT
```

FIG._2E

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   1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
     CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTTCTTCT TCTCAGCTTA

 101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
     CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC

 201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
     CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

 301 AAAAGTTAAT CTTTTCAACA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TTTGTAACTA GAATTCGAGC
     TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CTTAAGCTCG

 401 TCGGTACCCG GGGATCCTCT AGAGGTTGAG GTGATTTATG AAAAAGAATA TCGCATTTCT TCTTGCATCT ATGTTCGTTT TTTCTATTGC TACAAACGCG
     AGCCATGGGC CCCTAGGAGA TCTCCAACTC CACTAAATAC TTTTTCTTAT AGCGTAAAGA AGAACGTAGA TACAAGCAAA AAAGATAACG ATGTTTGCGC
   1                                             M  K  K  N  I   A  F  L   L  A  S   M  F  V  F   S  I  A   T  N  A

 501 TACGCTCAGA TAGTACTGTC CCAGTCCCCG GCTATCCTGT CCGCCTCTCC TGGCGAGAAG GTCACTATGA CCTGCAGAGC CAGCTCTTCT GTGAGCTATA
     ATGCGAGTCT ATCATGACAG GGTCAGGGGC CGATAGGACA GGCGGAGAGG ACCGCTCTTC CAGTGATACT GGACGTCTCG GTCGAGAAGA CACTCGATAT
  22 Y  A  Q  I   V  L  S   Q  S  P   A  I  L  S   A  S  P   G  E  K   V  T  M  T   C  R  A   S  S  S   V  S  Y  M

 601 TGCATTGGTA TCAACAGAAA CCAGGAAGCT CTCCGAAACC ATGGATTTAC GCTCCATCGA ACCTCGCGTC TGGAGTCCCT GCGCGCTTCT CTGGATCCGG
     ACGTAACCAT AGTTGTCTTT GGTCCTTCGA GAGGCTTTGG TACCTAAATG CGAGGTAGCT TGGAGCGCAG ACCTCAGGGA CGCGCGAAGA GACCTAGGCC
  56   H  W  Y   Q  Q  K   P  G  S  S   P  K  P   W  I  Y   A  P  S  N   L  A  S   G  V  P   A  R  F  S   G  S  G

 701 TTCTGGGACT AGTTACTCTC TGACCATCAG CAGAGTGGAG GCAGAAGACG CCGCAACTTA TTACTGTCAA CAGTGGAGCT TCAATCCGCC CACATTTGGA
     AAGACCCTGA TCAATGAGAG ACTGGTAGTC GTCTCACCTC CGTCTTCTGC GGCGTTGAAT AATGACAGTT GTCACCTCGA AGTTAGGCGG GTGTAAACCT
  89 S  G  T   S  Y  S  L   T  I  S   R  V  E   A  E  D  A   A  T  Y   Y  C  Q   Q  W  S  F   N  P  P   T  F  G

 801 GCCGGCACCA AGCTGGAGCT CAAACGAACT GTGGCTGCAC CATCTGTCTT CATCTTCCCG CCATCTGATG AGCAGTTGAA ATCTGGAACT GCTTCTGTTG
     CGGCCGTGGT TCGACCTCGA GTTTGCTTGA CACCGACGTG GTAGACAGAA GTAGAAGGGC GGTAGACTAC TCGTCAACTT TAGACCTTGA CGAAGACAAC
 122 A  G  T  K   L  E  L   K  R  T   V  A  A  P   S  V  F   I  F  P   P  S  D  E   Q  L  K   S  G  T   A  S  V  V

 901 TGTGCCTGCT GAATAACTTC TATCCCAGAG AGGCCAAAGT ACAGTGGAAG GTGGATAACG CCCTCCAATC GGGTAACTCC CAGGAGAGTG TCACAGAGCA
     ACACGGACGA CTTATTGAAG ATAGGGTCTC TCCGGTTTCA TGTCACCTTC CACCTATTGC GGGAGGTTAG CCCATTGAGG GTCCTCTCAC AGTGTCTCGT
 156   C  L  L   N  N  F   Y  P  R  E   A  K  V   Q  W  K   V  D  N  A   L  Q  S   G  N  S   Q  E  S  V   T  E  Q
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FIG._3A

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1001 GGACAGCAAG GACAGCACCT ACAGCCTCAG CAGCACCCTG ACGCTGAGCA AAGCAGACTA CGAGAAACAC AAAGTCTACG CCTGCGAAGT CACCCATCAG
     CCTGTCGTTC CTGTCGTGGA TGTCGGAGTC GTCGTGGGAC TGCGACTCGT TTCGTCTGAT GCTCTTTGTG TTTCAGATGC GGACGCTTCA GTGGGTAGTC
 189  D  S  K   D  S  T  Y   S  L  S   S  T  L   T  L  S  K   A  D  Y   E  K  H   K  V  Y  A   C  E  V   T  H  Q

1101 GGCCTGAGCT CGCCCGTCAC AAAGAGCTTC AACAGGGGAG AGTGTTAAGC TGATCCTCTA CGCCGGACGC ATCGTGGCCC TAGTACGCAA GTTCACGTAA
     CCGGACTCGA GCGGGCAGTG TTTCTCGAAG TTGTCCCCTC TCACAATTCG ACTAGGAGAT GCGGCCTGCG TAGCACCGGG ATCATGCGTT CAAGTGCATT
 222 G  L  S  S   P  V  T   K  S  F   N  R  G  E   C  O

1201 AAAGGGTATC TAGAGGTTGA GGTGATTTTA TGAAAAAGAA TATCGCATTT CTTCTTGCAT CTATGTTCGT TTTTTCTATT GCTACAAACG CGTACGCTCA
     TTTCCCATAG ATCTCCAACT CCACTAAAAT ACTTTTTCTT ATAGCGTAAA GAAGAACGTA GATACAAGCA AAAAAGATAA CGATGTTTGC GCATGCGAGT
    1                                M   K  K  N   I  A  F   L  L  A  S   M  F  V   F  S  I   A  T  N  A   Y  A  Q

1301 GGCTTATCTG CAGCAGTCTG GCGCCGAGCT GGTGCGGCCA GGAGCTAGCG TCAAGATGTC CTGTAAAGCT TCTGGCTACA CCTTCACCAG CTATAACATG
     CCGAATAGAC GTCGTCAGAC CGCGGCTCGA CCACGCCGGT CCTCGATCGC AGTTCTACAG GACATTTCGA AGACCGATGT GGAAGTGGTC GATATTGTAC
  25  A  Y  L   Q  Q  S  G   A  E  L   V  R  P   G  A  S  V   K  M  S   C  K  A   S  G  Y  T   F  T  S   Y  N  M

1401 CATTGGGTCA AGCAGACACC GAGGCAAGGC CTGGAATGGA TTGGAGCGAT CTATCCTGGC AACGGCGACA CGAGCTATAA CCAGAAGTTC AAGGGCAAGG
     GTAACCCAGT TCGTCTGTGG CTCCGTTCCG GACCTTACCT AACCTCGCTA GATAGGACCG TTGCCGCTGT GCTCGATATT GGTCTTCAAG TTCCCGTTCC
  58 H  W  V  K   Q  T  P   R  Q  G   L  E  W  I   G  A  I   Y  P  G   N  G  D  T   S  Y  N   Q  K  F   K  G  K  A

1501 CCACTCTGAC TGTGGACAAG TCCAGCAGTA CTGCCTACAT GCAACTGAGC AGCCTGACTT CTGAGGACAG CGCTGTCTAC TTTTGTGCTC GCGTGGTCTA
     GGTGAGACTG ACACCTGTTC AGGTCGTCAT GACGGATGTA CGTTGACTCG TCGGACTGAA GACTCCTGTC GCGACAGATG AAAACACGAG CGCACCAGAT
  92   T  L  T   V  D  K   S  S  S  T   A  Y  M   Q  L  S   S  L  T  S   E  D  S   A  V  Y   F  C  A  R   V  V  Y

1601 CTATAGCAAC AGCTACTGGT ACTTCGACGT CTGGGGTACC GGAACCACAG TCACCGTCTC CTCGGCCTCC ACCAAGGGCC CATCGGTCTT CCCCCTGGCA
     GATATCGTTG TCGATGACCA TGAAGCTGCA GACCCCATGG CCTTGGTGTC AGTGGCAGAG GAGCCGGAGG TGGTTCCCGG GTAGCCAGAA GGGGGACCGT
  125  Y  S  N   S  Y  W  Y   F  D  V   W  G  T   G  T  T  V   T  V  S   S  A  S   T  K  G  P   S  V  F   P  L  A

1701 CCCTCCTCCA AGAGCACCTC TGGGGGCACA GCGGCCCTGG GCTGCCTGGT CAAGGACTAC TTCCCCGAAC CGGTGACGGT GTCGTGGAAC TCAGGCGCCC
     GGGAGGAGGT TCTCGTGGAG ACCCCCGTGT CGCCGGGACC CGACGGACCA GTTCCTGATG AAGGGGCTTG GCCACTGCCA CAGCACCTTG AGTCCGCGGG
  158 P  S  S  K   S  T  S   G  G  T   A  A  L  G   C  L  V   K  D  Y   F  P  E  P   V  T  V   S  W  N   S  G  A  L

1801 TGACCAGCGG CGTGCACACC TTCCCGGCTG TCCTACAGTC CTCAGGACTC TACTCCCTCA GCAGCGTGGT GACCGTGCCC TCCAGCAGCT TGGGCACCCA
     ACTGGTCGCC GCACGTGTGG AAGGGCCGAC AGGATGTCAG GAGTCCTGAG ATGAGGGAGT CGTCGCACCA CTGGCACGGG AGGTCGTCGA ACCCGTGGGT
  192   T  S  G   V  H  T   F  P  A  V   L  Q  S   S  G  L   Y  S  L  S   S  V  V   T  V  P   S  S  S  L   G  T  Q
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FIG._3B

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1901 GACCTACATC TGCAACGTGA ATCACAAGCC CAGCAACACC AAGGTGGACA AGAAAGTTGA GCCCAAATCT TGTGACAAAA CTCACACATG ACCACCGCAT
     CTGGATGTAG ACGTTGCACT TAGTGTTCGG GTCGTTGTGG TTCCACCTGT TCTTTCAACT CGGGTTTAGA ACACTGTTTT GAGTGTGTAC TGGTGGCGTA
 225  T  Y  I   C  N  V  N   H  K  P   S  N  T   K  V  D  K   K  V  E   P  K  S   C  D  K  T   H  T  O

2001 GCACCAGTAT CGTCCATTCC GACAGCATCG CCAGTCACTA TGGCGTGCTG CTAGCGCCGC CCTATACCTT GTCTGCCTCC CCGCGTTGCG TCGCGGTGCA
     CGTGGTCATA GCAGGTAAGG CTGTCGTAGC GGTCAGTGAT ACCGCACGAC GATCGCGGCG GGATATGGAA CAGACGGAGG GGCGCAACGC AGCGCCACGT

2101 TGGAGCCGGG CCACCTCGAC CTGAATGGAA GCCGGCGGCA CCTCGCTAAC GGATTCACCA CTCCAAGAAT TGGAGCCAAT CAATTCTTGC GGAGAACTGT
     ACCTCGGCCC GGTGGAGCTG GACTTACCTT CGGCCGCCGT GGAGCGATTG CCTAAGTGGT GAGGTTCTTA ACCTCGGTTA GTTAAGAACG CCTCTTGACA

2201 GAATGCGCAA ACCAACCCTT GGCAGAACAT ATCCATCGCG TCCGCCATCT CCAGCAGCCG CACGCGGCGC ATCTCGGGCA GCGTTGGGTC CTGGCCACGG
     CTTACGCGTT TGGTTGGGAA CCGTCTTGTA TAGGTAGCGC AGGCGGTAGA GGTCGTCGGC GTGCGCCGCG TAGAGCCCGT CGCAACCCAG GACCGGTGCC

2301 GTGCGCATGA TCGTGCTCCT GTCGTTGAGG ACCCGGCTAG GCTGGCGGGG TTGCCTTACT GGTTAGCAGA ATGAATCACC GATACGCGAG CGAACGTGAA
     CACGCGTACT AGCACGAGGA CAGCAACTCC TGGGCCGATC CGACCGCCCC AACGGAATGA CCAATCGTCT TACTTAGTGG CTATGCGCTC GCTTGCACTT

2401 GCGACTGCTG CTGCAAAACG TCTGCGACCT GAGCAACAAC ATGAATGGTC TTCGGTTTCC GTGTTTCGTA AAGTCTGGAA ACGCGGAAGT CAGCGCCCTG
     CGCTGACGAC GACGTTTTGC AGACGCTGGA CTCGTTGTTG TACTTACCAG AAGCCAAAGG CACAAAGCAT TTCAGACCTT TGCGCCTTCA GTCGCGGGAC

2501 CACCATTATG TTCCGGATCT GCATCGCAGG ATGCTGCTGG CTACCCTGTG GAACACCTAC ATCTGTATTA ACGAAGCGCT GGCATTGACC CTGAGTGATT
     GTGGTAATAC AAGGCCTAGA CGTAGCGTCC TACGACGACC GATGGGACAC CTTGTGGATG TAGACATAAT TGCTTCGCGA CCGTAACTGG GACTCACTAA

2601 TTTCTCTGGT CCCGCCGCAT CCATACCGCC AGTTGTTTAC CCTCACAACG TTCCAGTAAC CGGGCATGTT CATCATCAGT AACCCGTATC GTGAGCATCC
     AAAGAGACCA GGGCGGCGTA GGTATGGCGG TCAACAAATG GGAGTGTTGC AAGGTCATTG GCCCGTACAA GTAGTAGTCA TTGGGCATAG CACTCGTAGG

2701 TCTCTCGTTT CATCGGTATC ATTACCCCCA TGAACAGAAA TTCCCCCTTA CACGGAGGCA TCAAGTGACC AAACAGGAAA AAACCGCCCT TAACATGGCC
     AGAGAGCAAA GTAGCCATAG TAATGGGGGT ACTTGTCTTT AAGGGGGAAT GTGCCTCCGT AGTTCACTGG TTTGTCCTTT TTTGGCGGGA ATTGTACCGG

2801 CGCTTTATCA GAAGCCAGAC ATTAACGCTT CTGGAGAAAC TCAACGAGCT GGACGCGGAT GAACAGGCAG ACATCTGTGA ATCGCTTCAC GACCACGCTG
     GCGAAATAGT CTTCGGTCTG TAATTGCGAA GACCTCTTTG AGTTGCTCGA CCTGCGCCTA CTTGTCCGTC TGTAGACACT TAGCGAAGTG CTGGTGCGAC

2901 ATGAGCTTTA CCGCAGCATC CGGAAATTGT AAACGTTAAT ATTTTGTTAA AATTCGCGTT AAATTTTTGT TAAATCAGCT CATTTTTTAA CCAATAGGCC
     TACTCGAAAT GGCGTCGTAG GCCTTTAACA TTTGCAATTA TAAAACAATT TTAAGCGCAA TTTAAAAACA ATTTAGTCGA GTAAAAAATT GGTTATCCGG

3001 GAAATCGGCA AAATCCCTTA TAAATCAAAA GAATAGACCG AGATAGGGTT GAGTGTTGTT CCAGTTTGGA ACAAGAGTCC ACTATTAAAG AACGTGGACT
     CTTTAGCCGT TTTAGGGAAT ATTTAGTTTT CTTATCTGGC TCTATCCCAA CTCACAACAA GGTCAAACCT TGTTCTCAGG TGATAATTTC TTGCACCTGA
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FIG._3C

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3101 CCAACGTCAA AGGGCGAAAA ACCGTCTATC AGGGCTATGG CCCACTACGT GAACCATCAC CCTAATCAAG TTTTTTGGGG TCGAGGTGCC GTAAAGCACT
     GGTTGCAGTT TCCCGCTTTT TGGCAGATAG TCCCGATACC GGGTGATGCA CTTGGTAGTG GGATTAGTTC AAAAAACCCC AGCTCCACGG CATTTCGTGA

3201 AAATCGGAAC CCTAAAGGGA GCCCCCGATT TAGAGCTTGA CGGGGAAAGC CGGCGAACGT GGCGAGAAAG GAAGGGAAGA AAGCGAAAGG AGCGGGCGCT
     TTTAGCCTTG GGATTTCCCT CGGGGGCTAA ATCTCGAACT GCCCCTTTCG GCCGCTTGCA CCGCTCTTTC CTTCCCTTCT TTCGCTTTCC TCGCCCGCGA

3301 AGGGCGCTGG CAAGTGTAGC GGTCACGCTG CGCGTAACCA CCACACCCGC CGCGCTTAAT GCGCCGCTAC AGGGCGCGTC CGCATCCTGC CTCGCGCGTT
     TCCCGCGACC GTTCACATCG CCAGTGCGAC GCGCATTGGT GGTGTGGGCG GCGCGAATTA CGCGGCGATG TCCCGCGCAG GCGTAGGACG GAGCGCGCAA

3401 TCGGTGATGA CGGTGAAAAC CTCTGACACA TGCAGCTCCC GGAGACGGTC ACAGCTTGTC TGTAAGCGGA TGCCGGGAGC AGACAAGCCC GTCAGGGCGC
     AGCCACTACT GCCACTTTTG GAGACTGTGT ACGTCGAGGG CCTCTGCCAG TGTCGAACAG ACATTCGCCT ACGGCCCTCG TCTGTTCGGG CAGTCCCGCG

3501 GTCAGCGGGT GTTGGCGGGT GTCGGGGCGC AGCCATGACC CAGTCACGTA GCGATAGCGG AGTGTATACT GGCTTAACTA TGCGGCATCA GAGCAGATTG
     CAGTCGCCCA CAACCGCCCA CAGCCCCGCG TCGGTACTGG GTCAGTGCAT CGCTATCGCC TCACATATGA CCGAATTGAT ACGCCGTAGT CTCGTCTAAC

3601 TACTGAGAGT GCACCATATG CGGTGTGAAA TACCGCACAG ATGCGTAAGG AGAAAATACC GCATCAGGCG CTCTTCCGCT TCCTCGCTCA CTGACTCGCT
     ATGACTCTCA CGTGGTATAC GCCACACTTT ATGGCGTGTC TACGCATTCC TCTTTTATGG CGTAGTCCGC GAGAAGGCGA AGGAGCGAGT GACTGAGCGA

3701 GCGCTCGGTC GTTCGGCTGC GGCGAGCGGT ATCAGCTCAC TCAAAGGCGG TAATACGGTT ATCCACAGAA TCAGGGGATA ACGCAGGAAA GAACATGTGA
     CGCGAGCCAG CAAGCCGACG CCGCTCGCCA TAGTCGAGTG AGTTTCCGCC ATTATGCCAA TAGGTGTCTT AGTCCCCTAT TGCGTCCTTT CTTGTACACT

3801 GCAAAAGGCC AGCAAAAGGC CAGGAACCGT AAAAAGGCCG CGTTGCTGGC GTTTTTCCAT AGGCTCCGCC CCCCTGACGA GCATCACAAA AATCGACGCT
     CGTTTTCCGG TCGTTTTCCG GTCCTTGGCA TTTTTCCGGC GCAACGACCG CAAAAAGGTA TCCGAGGCGG GGGGACTGCT CGTAGTGTTT TTAGCTGCGA

3901 CAAGTCAGAG GTGGCGAAAC CCGACAGGAC TATAAAGATA CCAGGCGTTT CCCCCTGGAA GCTCCCTCGT GCGCTCTCCT GTTCCGACCC TGCCGCTTAC
     GTTCAGTCTC CACCGCTTTG GGCTGTCCTG ATATTTCTAT GGTCCGCAAA GGGGGACCTT CGAGGGAGCA CGCGAGAGGA CAAGGCTGGG ACGGCGAATG

4001 CGGATACCTG TCCGCCTTTC TCCCTTCGGG AAGCGTGGCG CTTTCTCATA GCTCACGCTG TAGGTATCTC AGTTCGGTGT AGGTCGTTCG CTCCAAGCTG
     GCCTATGGAC AGGCGGAAAG AGGGAAGCCC TTCGCACCGC GAAAGAGTAT CGAGTGCGAC ATCCATAGAG TCAAGCCACA TCCAGCAAGC GAGGTTCGAC

4101 GGCTGTGTGC ACGAACCCCC CGTTCAGCCC GACCGCTGCG CCTTATCCGG TAACTATCGT CTTGAGTCCA ACCCGGTAAG ACACGACTTA TCGCCACTGG
     CCGACACACG TGCTTGGGGG GCAAGTCGGG CTGGCGACGC GGAATAGGCC ATTGATAGCA GAACTCAGGT TGGGCCATTC TGTGCTGAAT AGCGGTGACC

4201 CAGCAGCCAC TGGTAACAGG ATTAGCAGAG CGAGGTATGT AGGCGGTGCT ACAGAGTTCT TGAAGTGGTG GCCTAACTAC GGCTACACTA GAAGGACAGT
     GTCGTCGGTG ACCATTGTCC TAATCGTCTC GCTCCATACA TCCGCCACGA TGTCTCAAGA ACTTCACCAC CGGATTGATG CCGATGTGAT CTTCCTGTCA

4301 ATTTGGTATC TGCGCTCTGC TGAAGCCAGT TACCTTCGGA AAAAGAGTTG GTAGCTCTTG ATCCGGCAAA CAAACCACCG CTGGTAGCGG TGGTTTTTTT
     TAAACCATAG ACGCGAGACG ACTTCGGTCA ATGGAAGCCT TTTTCTCAAC CATCGAGAAC TAGGCCGTTT GTTTGGTGGC GACCATCGCC ACCAAAAAAA
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FIG._3D

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4401 GTTTGCAAGC AGCAGATTAC GCGCAGAAAA AAAGGATCTC AAGAAGATCC TTTGATCTTT TCTACGGGGT CTGACGCTCA GTGGAACGAA AACTCACGTT
     CAAACGTTCG TCGTCTAATG CGCGTCTTTT TTTCCTAGAG TTCTTCTAGG AAACTAGAAA AGATGCCCCA GACTGCGAGT CACCTTGCTT TTGAGTGCAA

4501 AAGGGATTTT GGTCATGAGA TTATCAAAAA GGATCTTCAC CTAGATCCTT TTAAATTAAA AATGAAGTTT TAAATCAATC TAAAGTATAT ATGAGTAAAC
     TTCCCTAAAA CCAGTACTCT AATAGTTTTT CCTAGAAGTG GATCTAGGAA AATTTAATTT TTACTTCAAA ATTTAGTTAG ATTTCATATA TACTCATTTG

4601 TTGGTCTGAC AGTTACCAAT GCTTAATCAG TGAGGCACCT ATCTCAGCGA TCTGTCTATT TCGTTCATCC ATAGTTGCCT GACTCCCCGT CGTGTAGATA
     AACCAGACTG TCAATGGTTA CGAATTAGTC ACTCCGTGGA TAGAGTCGCT AGACAGATAA AGCAAGTAGG TATCAACGGA CTGAGGGGCA GCACATCTAT

4701 ACTACGATAC GGGAGGGCTT ACCATCTGGC CCCAGTGCTG CAATGATACC GCGAGACCCA CGCTCACCGG CTCCAGATTT ATCAGCAATA AACCAGCCAG
     TGATGCTATG CCCTCCCGAA TGGTAGACCG GGGTCACGAC GTTACTATGG CGCTCTGGGT GCGAGTGGCC GAGGTCTAAA TAGTCGTTAT TTGGTCGGTC

4801 CCGGAAGGGC CGAGCGCAGA AGTGGTCCTG CAACTTTATC CGCCTCCATC CAGTCTATTA ATTGTTGCCG GGAAGCTAGA GTAAGTAGTT CGCCAGTTAA
     GGCCTTCCCG GCTCGCGTCT TCACCAGGAC GTTGAAATAG GCGGAGGTAG GTCAGATAAT TAACAACGGC CCTTCGATCT CATTCATCAA GCGGTCAATT

4901 TAGTTTGCGC AACGTTGTTG CCATTGCTGC AGGCATCGTG GTGTCACGCT CGTCGTTTGG TATGGCTTCA TTCAGCTCCG GTTCCCAACG ATCAAGGCGA
     ATCAAACGCG TTGCAACAAC GGTAACGACG TCCGTAGCAC CACAGTGCGA GCAGCAAACC ATACCGAAGT AAGTCGAGGC CAAGGGTTGC TAGTTCCGCT

5001 GTTACATGAT CCCCCATGTT GTGCAAAAAA GCGGTTAGCT CCTTCGGTCC TCCGATCGTT GTCAGAAGTA AGTTGGCCGC AGTGTTATCA CTCATGGTTA
     CAATGTACTA GGGGGTACAA CACGTTTTTT CGCCAATCGA GGAAGCCAGG AGGCTAGCAA CAGTCTTCAT TCAACCGGCG TCACAATAGT GAGTACCAAT

5101 TGGCAGCACT GCATAATTCT CTTACTGTCA TGCCATCCGT AAGATGCTTT TCTGTGACTG GTGAGTACTC AACCAAGTCA TTCTGAGAAT AGTGTATGCG
     ACCGTCGTGA CGTATTAAGA GAATGACAGT ACGGTAGGCA TTCTACGAAA AGACACTGAC CACTCATGAG TTGGTTCAGT AAGACTCTTA TCACATACGC

5201 GCGACCGAGT TGCTCTTGCC CGGCGTCAAC ACGGGATAAT ACCGCGCCAC ATAGCAGAAC TTTAAAAGTG CTCATCATTG GAAAACGTTC TTCGGGGCGA
     CGCTGGCTCA ACGAGAACGG GCCGCAGTTG TGCCCTATTA TGGCGCGGTG TATCGTCTTG AAATTTTCAC GAGTAGTAAC CTTTTGCAAG AAGCCCCGCT

5301 AAACTCTCAA GGATCTTACC GCTGTTGAGA TCCAGTTCGA TGTAACCCAC TCGTGCACCC AACTGATCTT CAGCATCTTT TACTTTCACC AGCGTTTCTG
     TTTGAGAGTT CCTAGAATGG CGACAACTCT AGGTCAAGCT ACATTGGGTG AGCACGTGGG TTGACTAGAA GTCGTAGAAA ATGAAAGTGG TCGCAAAGAC

5401 GGTGAGCAAA AACAGGAAGG CAAAATGCCG CAAAAAAGGG AATAAGGGCG ACACGGAAAT GTTGAATACT CATACTCTTC CTTTTTCAAT ATTATTGAAG
     CCACTCGTTT TTGTCCTTCC GTTTTACGGC GTTTTTTCCC TTATTCCCGC TGTGCCTTTA CAACTTATGA GTATGAGAAG GAAAAAGTTA TAATAACTTC

5501 CATTTATCAG GGTTATTGTC TCATGAGCGG ATACATATTT GAATGTATTT AGAAAAATAA ACAAATAGGG GTTCCGCGCA CATTTCCCCG AAAAGTGCCA
     GTAAATAGTC CCAATAACAG AGTACTCGCC TATGTATAAA CTTACATAAA TCTTTTTATT TGTTTATCCC CAAGGCGCGT GTAAAGGGGC TTTTCACGGT

5601 CCTGACGTCT AAGAAACCAT TATTATCATG ACATTAACCT ATAAAAATAG GCGTATCACG AGGCCCTTTC GTCTTCAA
     GGACTGCAGA TTCTTTGGTA ATAATAGTAC TGTAATTGGA TATTTTTATC CGCATAGTGC TCCGGGAAAG CAGAAGTT
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FIG._3E

TTCGAGCTCGCCCGACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCA
TTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCT
GGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTA
ACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCAC
TTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTCAATGACGGT
AAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGCAG
TACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAAT
GGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAAT
GGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCC
CCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCGT
TTAGTGAACCGTCAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGA
CACCGGGACCGATCCAGCCTCCGCGGCCGGGAACGGTGCATTGGAACGCGGATTCCCCGT
GCCAAGAGTGACGTAAGTACCGCCTATAGAGTCTATAGGCCCACCCCCTTGGCTTCGTTA
GAACGCGGCTACAATTAATACATAACCTTATGTATCATACACATACGATTTAGGTGACAC
TATAGAATAACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGGTCCAACTGC
ACCTCGGTTCTATCGATTGAATTCCACC**ATG**GGATGGTCATGTATCATCCTTTTTCTAGT
AGCAACTGCAACTGGAGTACATTCAGATATCCAGATGACCCAGTCCCCGAGCTCCCTGTC
CGCCTCTGTGGGCGATAGGGTCACCATCACCTGCCGTGCCAGTCAGGACATCCGTAATTA
TTTGAACTGGTATCAACAGAAACCAGGAAAAGCTCCGAAACTACTGATTTACTATACCTC
CCGCCTGGAGTCTGGAGTCCCTTCTCGCTTCTCTGGTTCTGGTTCTGGGACGGATTACAC
TCTGACCATCAGTAGTCTGCAACCGGAGGACTTCGCAACTTATTACTGTCAGCAAGGTAA
TACTCTGCCGTGGACGTTCGGACAGGGCACCAAGGTGGAGATCAAACGAACTGTGGCTGC
ACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGT
TGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAA
CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCAC
CTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTA
CGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGG
AGAGTGT**TAA**GCTTGGCCGCCATGGCCCAACTTGTTTATTGCAGCTTATAATGGTTACAA
ATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTG
TGGTTTGTCCAAACTCATCAATGTATCTTATCATGTCTGGATCGATCGGGAATTAATTCG
GCGCAGCACCATGGCCTGAAATAACCTCTGAAAGAGGAACTTGGTTAGGTACCTTCTGAG
GCGGAAAGAACCAGCTGTGGAATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCC
CAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGT
CCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCA
TAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTC
CGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTG
AGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTGT
TAACAGCTTGGCACTGGCCGTCGTTTTACAACGTCGTGACTGGGAAAACCCTGGCGTTAC
CCAACTTAATCGCCTTGCAGCACATCCCCCCTTCGCCAGCTGGCGTAATAGCGAAGAGGC
CCGCACCGATCGCCCTTCCCAACAGTTGCGTAGCCTGAATGGCGAATGGCGCCTGATGCG
GTATTTTCTCCTTACGCATCTGTGCGGTATTTCACACCGCATACGTCAAAGCAACCATAG
TACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACC
GCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCC
ACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTT
AGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTTGGGTGATGGTTCACGTAGTGGG
CCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAATAGT
GGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGGCTATTCTTTTGATTTA
TAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTT
AACGCGAATTTTAACAAAATATTAACGTTTACAATTTTATGGTGCACTCTCAGTACAATC
TGCTCTGATGCCGCATAGTTAAGCCAACTCCGCTATCGCTACGTGACTGGGTCATGGCTG
CGCCCCGACACCCGCCAACACCCGCTGACGCGCCCTGACGGGCTTGTCTGCTCCCGGCAT

FIG._4A

CCGCTTACAGACAAGCTGTGACCGTCTCCGGGAGCTGCATGTGTCAGAGGTTTTCACCGT
CATCACCGAAACGCGCGAGGCAGTATTCTTGAAGACGAAAGGGCCTCGTGATACGCCTAT
TTTTATAGGTTAATGTCATGATAATAATGGTTTCTTAGACGTCAGGTGGCACTTTTCGGG
GAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAAATACATTCAAATATGTATCCGC
TCATGAGACAATAACCCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAGTATGAGTA
TTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCATTTTGCCTTCCTGTTTTTG
CTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGTGG
GTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAAC
GTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTGATG
ACGCCGGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGT
ACTCACCAGTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTG
CTGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAGGAC
CGAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAACTCGCCTTGATCGTT
GGGAACCGGAGCTGAATGAAGCCATACCAAACGACGAGCGTGACACCACGATGCCAGCAG
CAATGGCAACAACGTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTCCCGGC
AACAATTAATAGACTGGATGGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCC
TTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTA
TCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGTAGTTATCTACACGACGG
GGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAGGTGCCTCACTGA
TTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAAAC
TTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAA
TCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGAT
CTTCTTGAGATCCTTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGC
TACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTG
GCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTAGGCCACC
ACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGG
CTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGG
ATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAA
CGACCTACACCGAACTGAGATACCTACAGCGTGAGCATTGAGAAAGCGCCACGCTTCCCG
AAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGA
GGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCT
GACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCA
GCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTC
CTGCGTTATCCCCTGATTCTGTGGATAACCGTATTACCGCCTTTGAGTGAGCTGATACCG
CTCGCCGCAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCGCC
CAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATCCAGCTGGCACGACA
GGTTTCCCGACTGGAAAGCGGGCAGTGAGCGCAACGCAATTAATGTGAGTTACCTCACTC
ATTAGGCACCCCAGGCTTTACACTTTATGCTTCCGGCTCGTATGTTGTGTGGAATTGTGA
GCGGATAACAATTTCACACAGGAAACAGCTATGACCATGATTACGAATTAA

FIG._4B

ATTCGAGCTCGCCCGACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTC
ATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCC
TGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGT
AACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCA
CTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTCAATGACGG
TAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGCA
GTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACATCAA
TGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAA
TGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGC
CCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCG
TTTAGTGAACCGTCAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAG
ACACCGGGACCGATCCAGCCTCCGCGGCCGGGAACGGTGCATTGGAACGCGGATTCCCCG
TGCCAAGAGTGACGTAAGTACCGCCTATAGAGTCTATAGGCCCACCCCCTTGGCTTCGTT
AGAACGCGGCTACAATTAATACATAACCTTATGTATCATACACATACGATTTAGGTGACA
CTATAGAATAACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGGTCCAACTG
CACCTCGGTTCTATCGATTGAATTCCACC**ATG**GGATGGTCATGTATCATCCTTTTTCTAG
TAGCAACTGCAACTGGAGTACATTCAGAAGTTCAGCTGGTGGAGTCTGGCGGTGGCCTGG
TGCAGCCAGGGGGCTCACTCCGTTTGTCCTGTGCAGCTTCTGGCTACTCCTTTACCGGCT
ACACTATGAACTGGGTGCGTCAGGCCCCAGGTAAGGGCCTGGAATGGGTTGCACTGATTA
ATCCTTATAAAGGTGTTACTACCTATGCCGATAGCGTCAAGGGCCGTTTCACTATAAGCG
TAGATAAATCCAAAAACACAGCCTACCTGCAAATGAACAGCCTGCGTGCTGAGGACACTG
CCGTCTATTATTGTGCTAGAAGCGGATACTACGGCGATAGCGACTGGTATTTTGACGTCT
GGGGTCAAGGAACCCTGGTCACCGTCTCCTCGGCCTCCACCAAGGGCCCATCGGTCTTCC
CCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCA
AGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCG
TGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGA
CTGTGCCCTCTAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCA
GCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCC
CACCGTGCCCAGCACCTGAACTCCTGGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAAC
CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA
GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG
CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA
CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG
CCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC
AGGTGTACACCCTGCCCCCATCCCGGGAAGAGATGACCAAGAACCAGGTCAGCCTGACCT
GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC
CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT
ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG
TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA
AA**TGA**GTGCGACGGCCCTAGAGTCGACCTGCAGAAGCTTGGCCGCCATGGCCCAACTTGT
TTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAG
CATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAAACTCATCAATGTATCTTATCATG
TCTGGATCGATCGGGAATTAATTCGGCGCAGCACCATGGCCTGAAATAACCTCTGAAAGA
GGAACTTGGTTAGGTACCTTCTGAGGCGGAAAGAACCATCTGTGGAATGTGTGTCAGTTA
GGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAAT
TAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGC
ATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTA
ACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCA
GAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGA
GGCCTAGGCTTTTGCAAAAAGCTGTTAACAGCTTGGCACTGGCCGTCGTTTTACAACGTC
GTGACTGGGAAAACCCTGGCGTTACCCAACTTAATCGCCTTGCAGCACATCCCCCCTTCG

FIG._5A

CCAGTTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGCGTAGCC
TGAATGGCGAATGGCGCCTGATGCGGTATTTTCTCCTTACGCATCTGTGCGGTATTTCAC
ACCGCATACGTCAAAGCAACCATAGTACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGG
TGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTT
CGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCG
GGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGA
TTTGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGAC
GTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCC
TATCTCGGGCTATTCTTTTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAA
AAATGAGCTGATTTAACAAAAATTTAACGCGAATTTTAACAAAATATTAACGTTTACAAT
TTTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCCAACTCCGCTA
TCGCTACGTGACTGGGTCATGGCTGCGCCCCGACACCCGCCAACACCCGCTGACGCGCCC
TGACGGGCTTGTCTGCTCCCGGCATCCGCTTACAGACAAGCTGTGACCGTCTCCGGGAGC
TGCATGTGTCAGAGGTTTTCACCGTCATCACCGAAACGCGCGAGGCAGTATTCTTGAAGA
CGAAAGGGCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATGGTTTCT
TAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTC
TAAATACATTCAAATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAA
TATTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTT
GCGGCATTTTGCCTTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCT
GAAGATCAGTTGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATC
CTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTA
TGTGGCGCGGTATTATCCCGTGATGACGCCGGGCAAGAGCAACTCGGTCGCCGCATACAC
TATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGCATCTTACGGATGGC
ATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAAC
TTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACAACATGGGG
GATCATGTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAAACGAC
GAGCGTGACACCACGATGCCAGCAGCAATGGCAACAACGTTGCGCAAACTATTAACTGGC
GAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGATGGAGGCGGATAAAGTT
GCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGA
GCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCC
CGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAG
ATCGCTGAGATAGGTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCA
TATATACTTTAGATTGATTTAAAACTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATC
CTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCA
GACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGC
TGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCTA
CCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTT
CTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTC
GCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGG
TTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCG
TGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAG
CATTGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGC
AGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTAT
AGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGG
GGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGC
TGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATAACCGTATT
ACCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGCGAGTCA
GTGAGCGAGGAAGCGGAAGAGCGCCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCG
ATTCATTAATCCAACTGGCACGACAGGTTTCCCGACTGGAAAGCGGGCAGTGAGCGCAAC
GCAATTAATGTGAGTTACCTCACTCATTAGGCACCCCAGGCTTTACACTTTATGCTTCCG
GCTCGTATGTTGTGTGGAATTGTGAGCGGATAACAATTTCACACAGGAAACAGCTATGAC
CATGATTACGAATTA

FIG._5B

MGWSCIILFLVATATGVHSDIQMTQSPSSLSASVGDRVTITCRASSSVSYMHWYQQKPGK
APKPLIYAPSNLASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQWSFNPPTFGQGT
KVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQES
VTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIG._6

MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCAASGYTFTSYNMHWVRQAP
GKGLEWVGAIYPGNGDTSYNQKFKGRFTISVDKSKNTLYLQMNSLRAEDTAVYYCARVVY
YSNSYWYFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV
SWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP
VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG._7

MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCAASGYTFTSYNMHWVRQAP
GKGLEWVGAIYPGNGDTSYNQKFKGRFTISVDKSKNTLYLQMNSLRAEDTAVYYCARVVY
YSNSYWYFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV
SWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNATYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIAATI
SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP
VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG._8

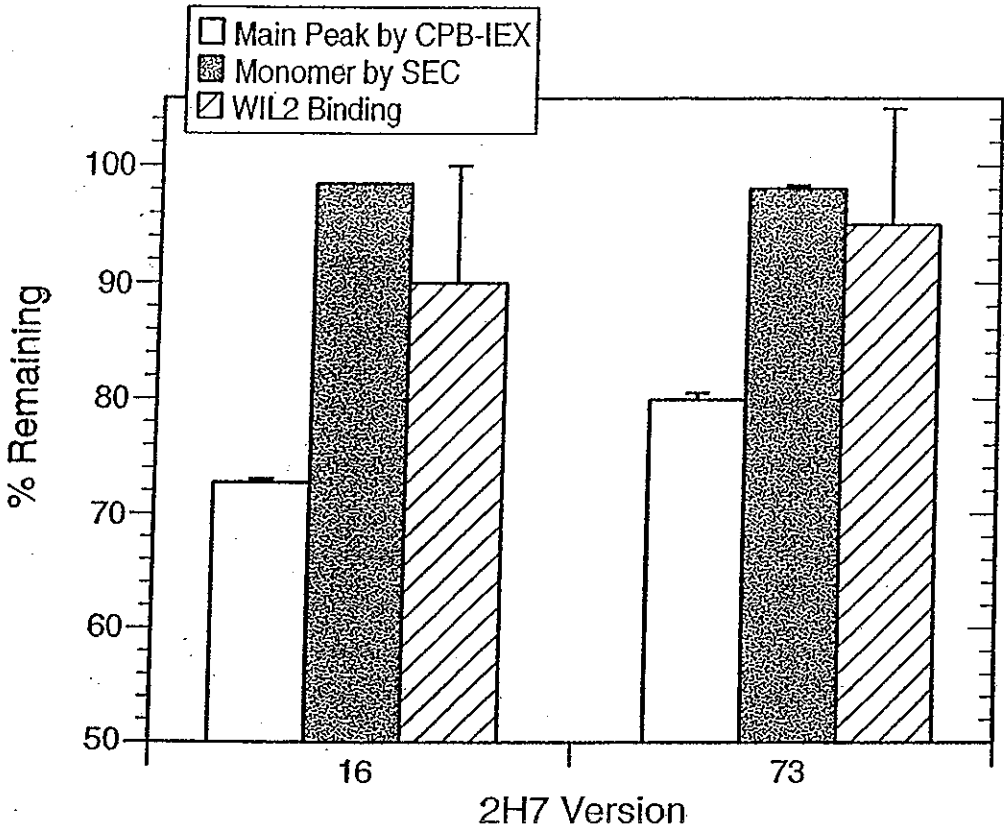

Main Peak by CPB-IEX
Monomer by SEC
WIL2 Binding
% Remaining
100
90
80
70
60
50
16
73
2H7 Version

FIG._9

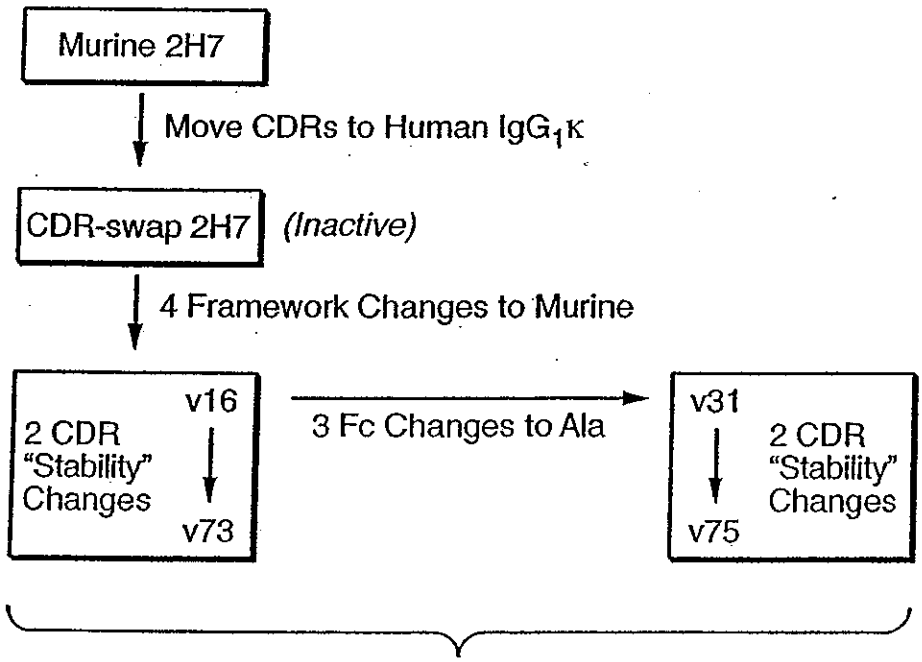

Murine 2H7
Move CDRs to Human IgG1κ
CDR-swap 2H7
(Inactive)
4 Framework Changes to Murine
2 CDR "Stability" Changes
v16
v73
3 Fc Changes to Ala
v31
v75
2 CDR "Stability" Changes

FIG._10

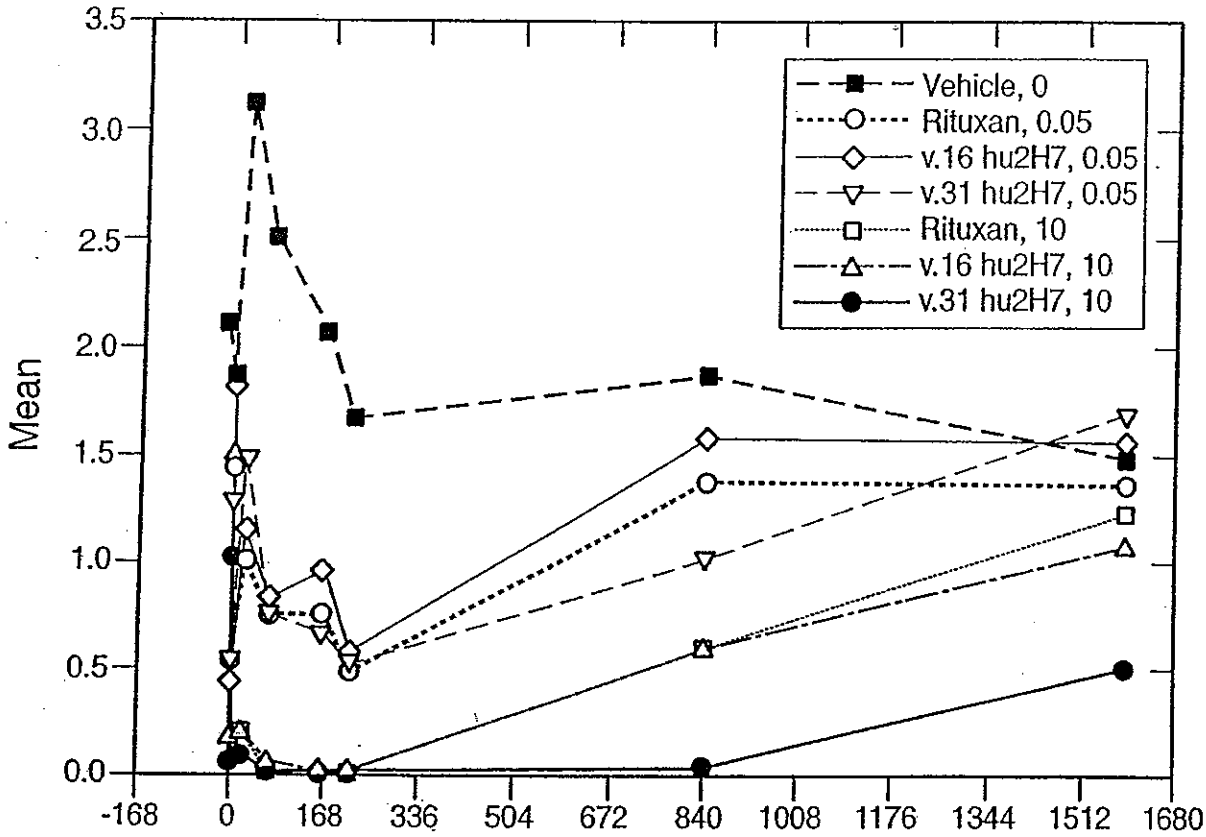

Vehicle, 0
Rituxan, 0.05
v.16 hu2H7, 0.05
v.31 hu2H7, 0.05
Rituxan, 10
v.16 hu2H7, 10
v.31 hu2H7, 10
Mean
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-168
0
168
336
504
672
840
1008
1176
1344
1512
1680
Timepoint_(Hrs)

FIG._11

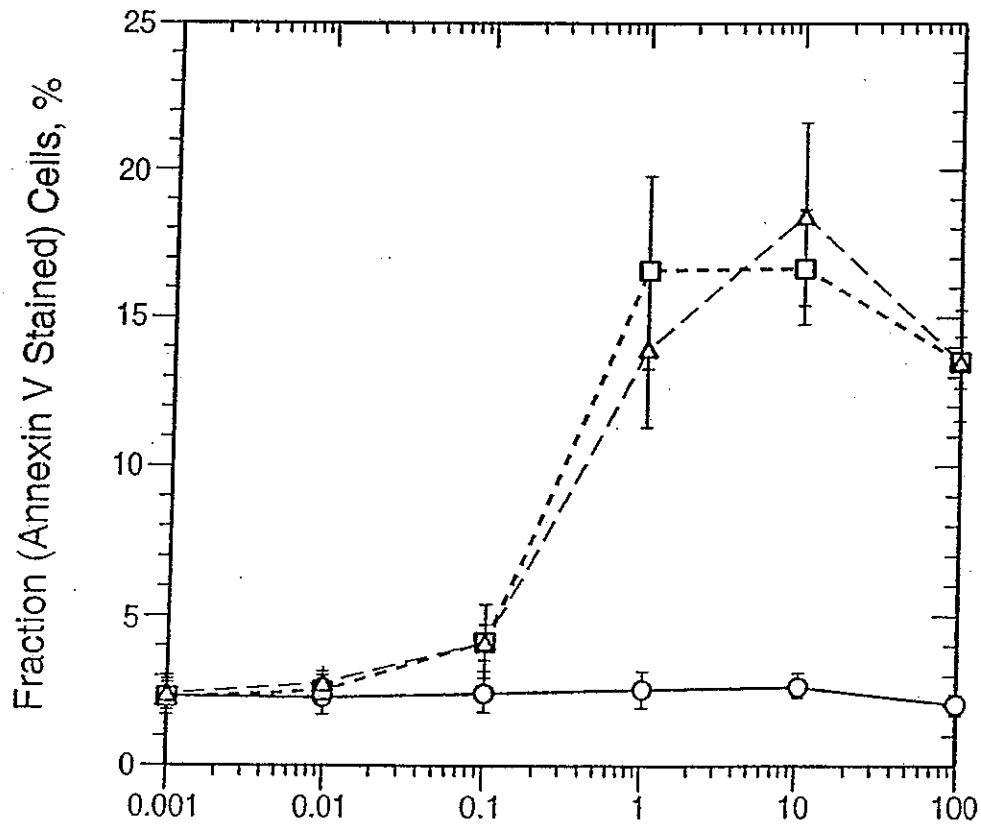

Fraction (Annexin V Stained) Cells, %
25
20
15
10
5
0
0.001
0.01
0.1
1
10
100
[IgG,], nM

FIG._13

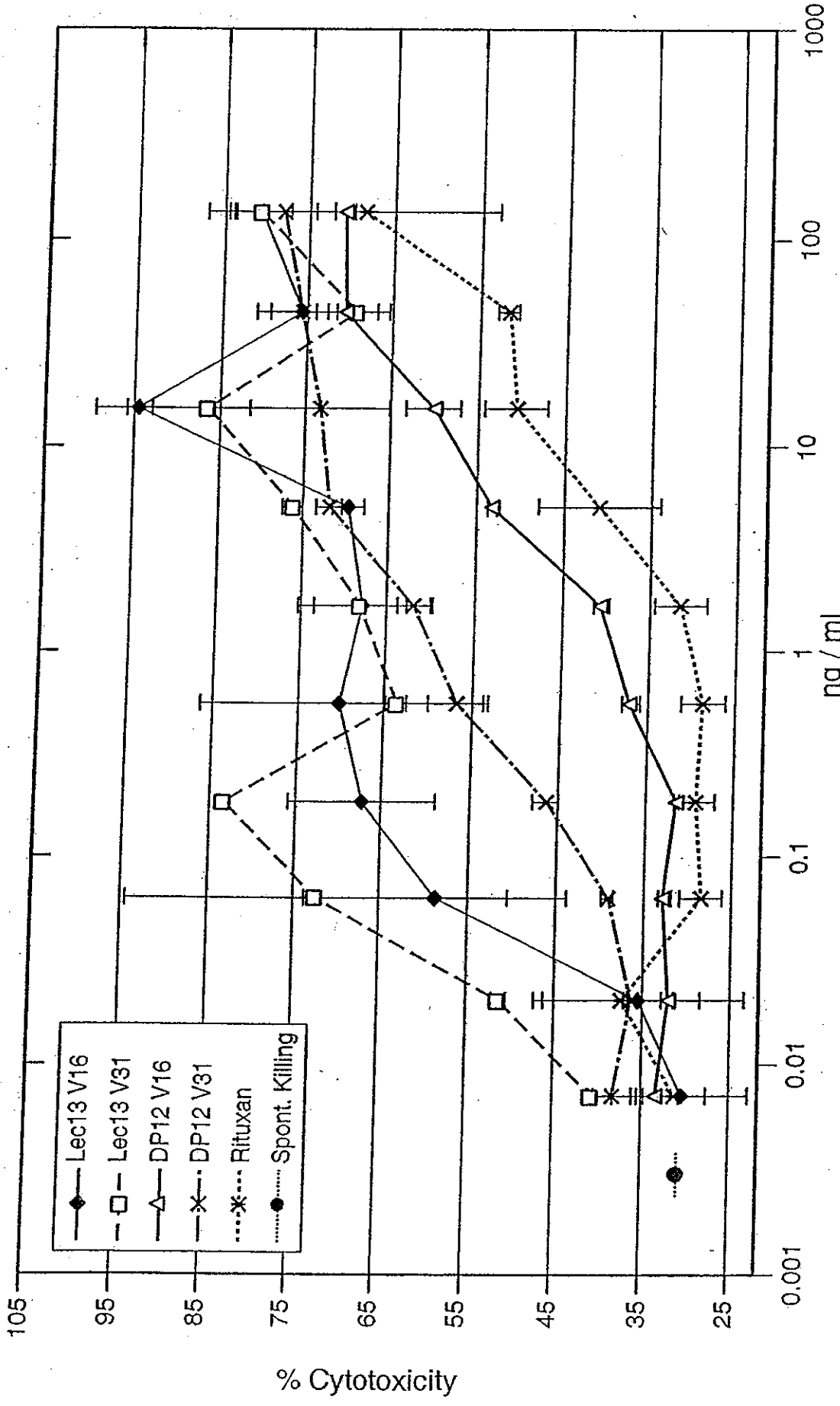

Lec13 V16
Lec13 V31
DP12 V16
DP12 V31
Rituxan
Spont. Killing
% Cytotoxicity
105
95
85
75
65
55
45
35
25
0.001
0.01
0.1
1
10
100
1000
ng / ml

FIG._12

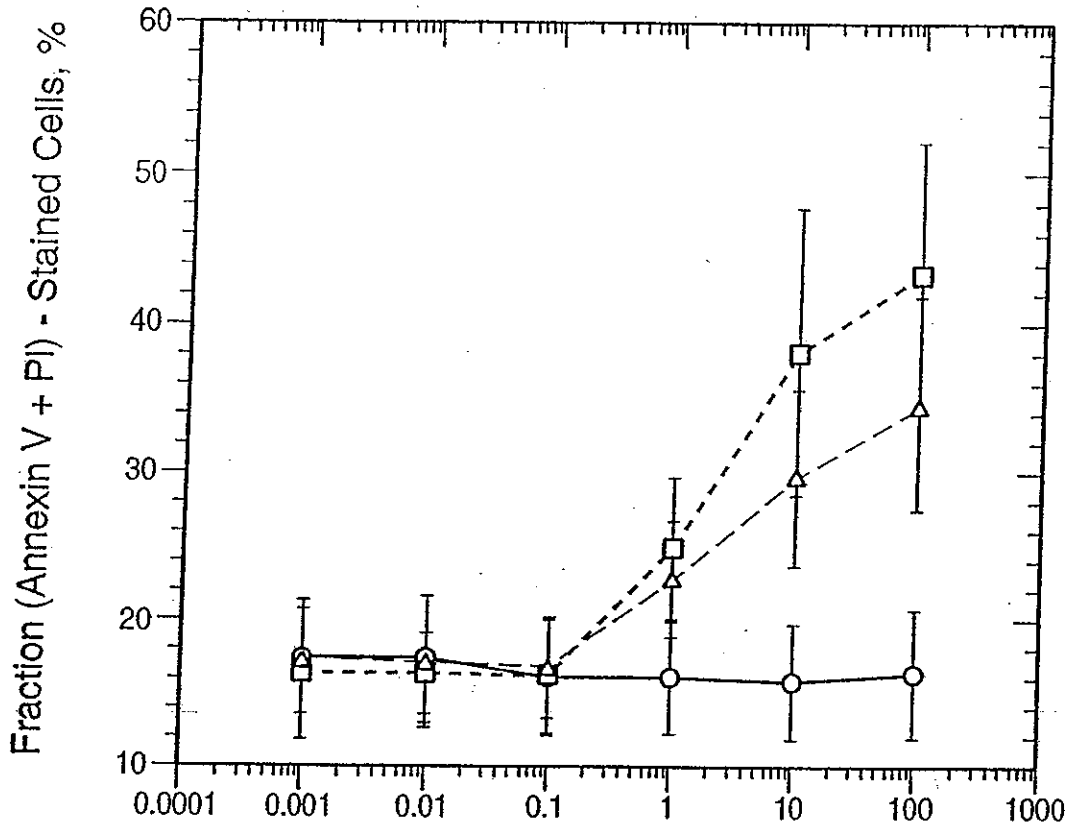

Fraction (Annexin V + PI) - Stained Cells, %
60
50
40
30
20
10
0.0001
0.001
0.01
0.1
1
10
100
1000
[IgG,], nM

FIG._14

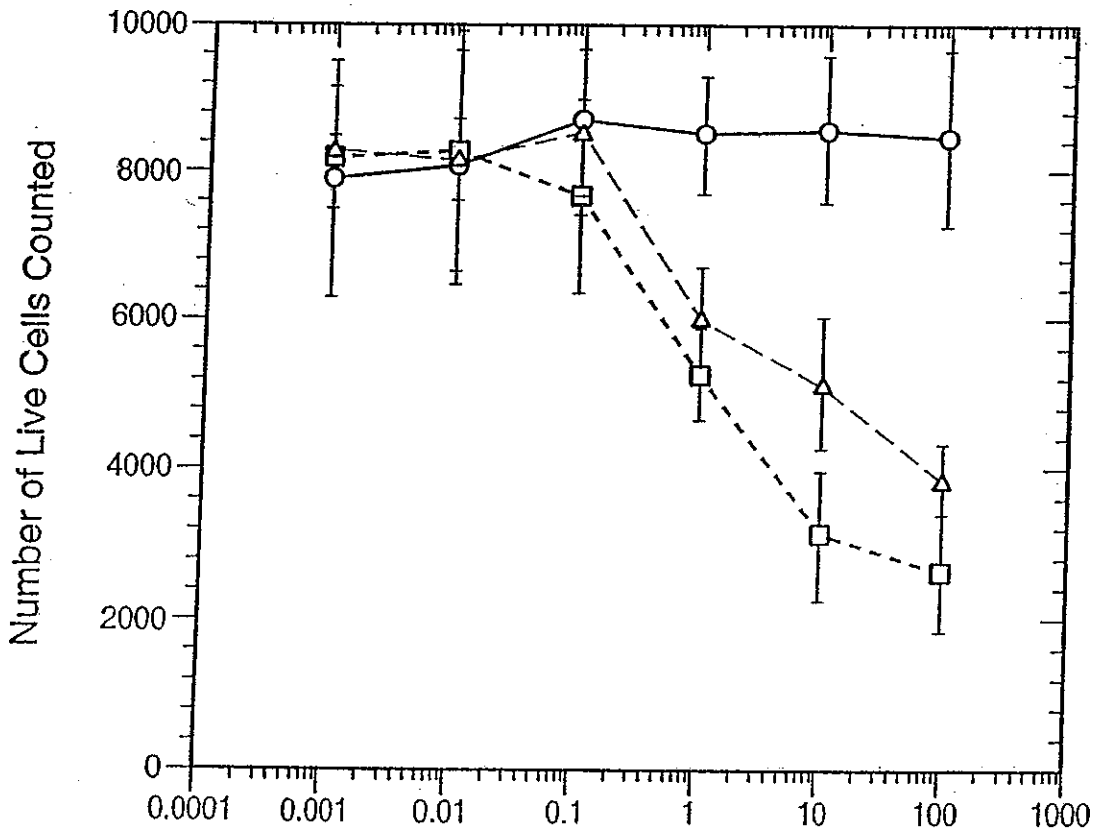

Number of Live Cells Counted
10000
8000
6000
4000
2000
0
0.0001
0.001
0.01
0.1
1
10
100
1000
[IgG,], nM

FIG._15

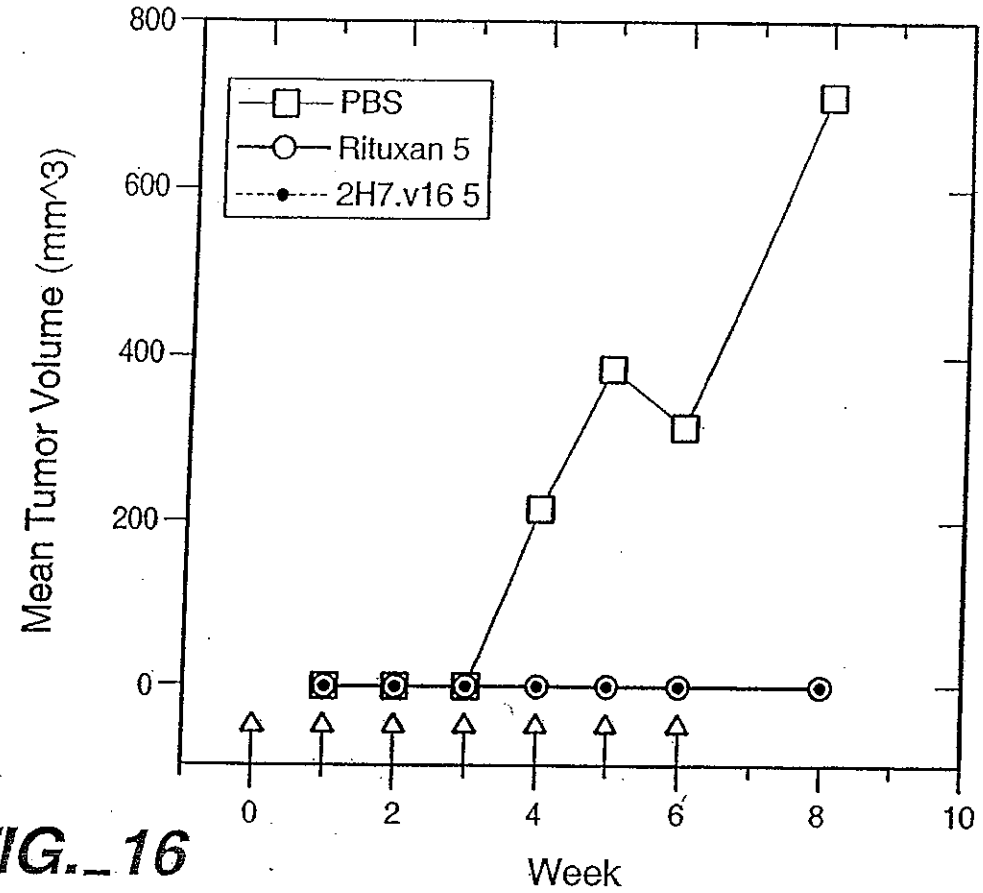

800
600
400
200
0
Mean Tumor Volume (mm^3)
PBS
Rituxan 5
2H7.v16 5
0
2
4
6
8
10
Week

FIG._16

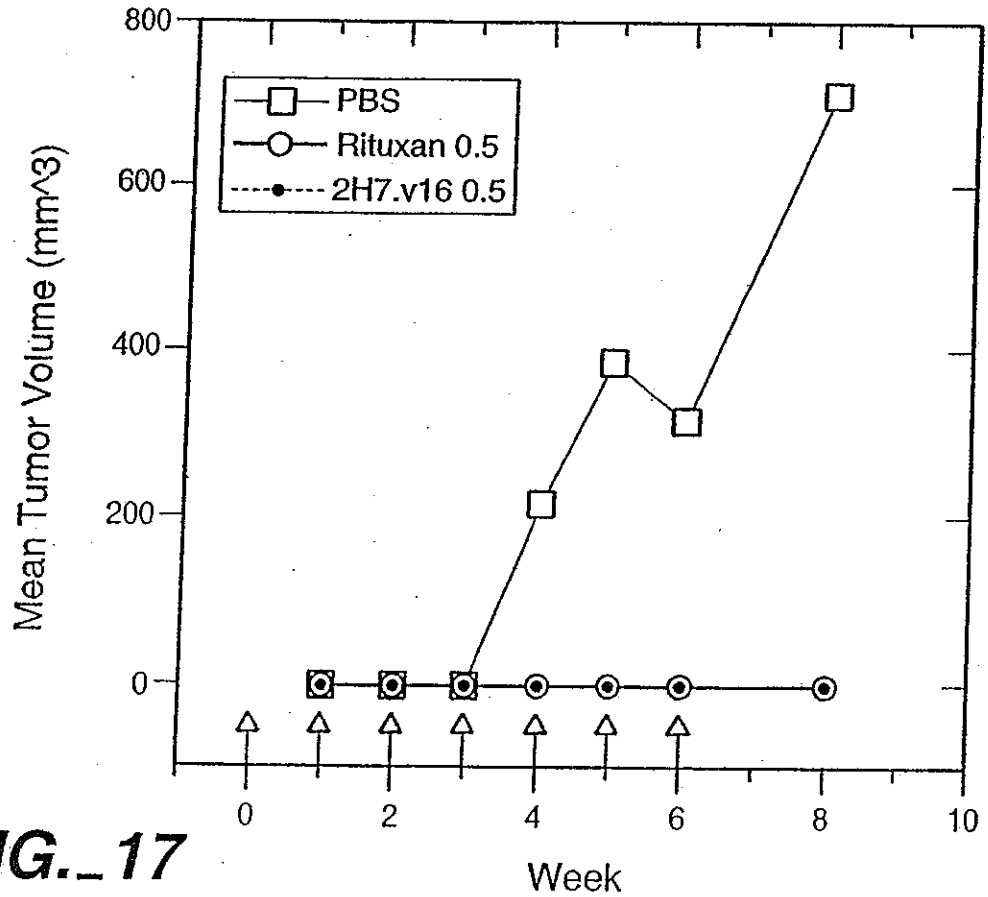

800
600
400
200
0
Mean Tumor Volume (mm^3)
PBS
Rituxan 0.5
2H7.v16 0.5
0
2
4
6
8
10
Week

FIG._17

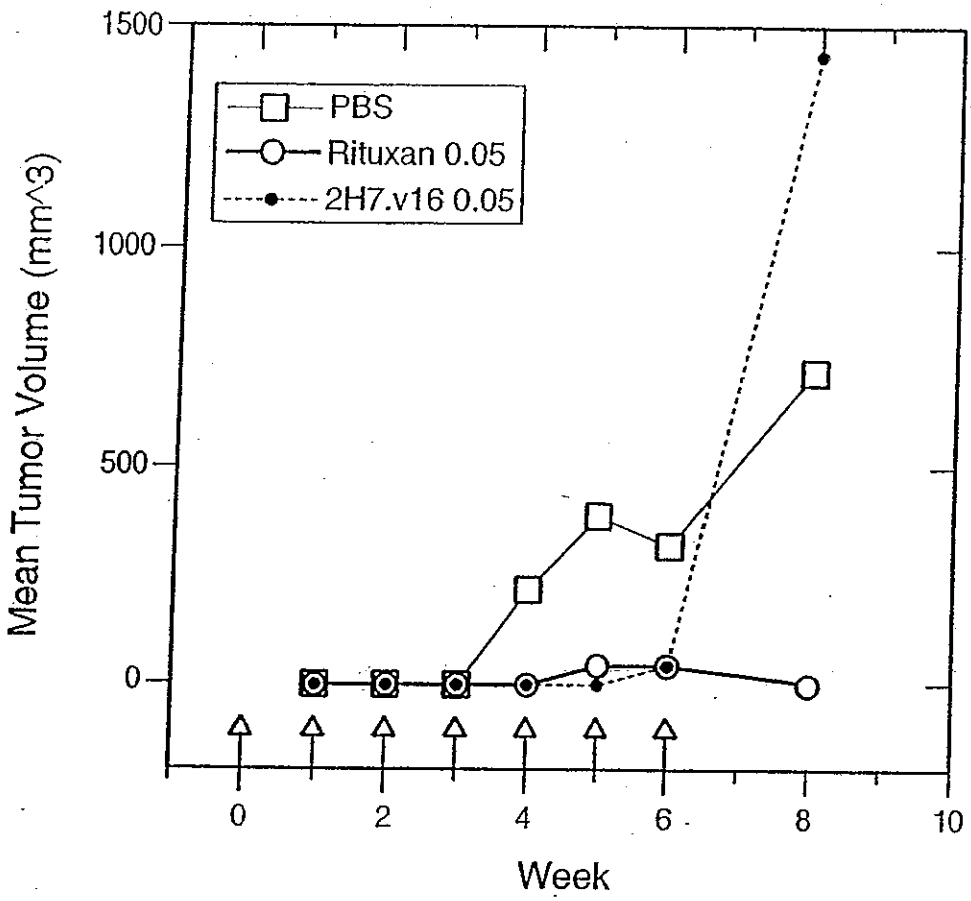


FIG._18

MTTPRNSVNGTFPAEPMKGPIAMQPGPKPLLRRMSSLVGPTQSFFMR
S F
ESKALGAVQIMNGLFHIALGGLLMIPAGIYAPICVTVWYPLWGGIMYII

SGSLLAATEKNSRKCLVKGKMIMNSLSLFAAISGMILSIMDILNI**KISH**

FLKMESLNFIRVHTPYINIYNCEPANPSEKNSPSTQYCYSIQSLFLGILS
A
VMLIFAFFQELVIAGIVENEWRRTCSRPKSSVVLLSAEEKKEQVIEIKE
K NI T
EVVGLTETSSQPKNEEAIEIIPIQEEEEEETETNFPEPPQDQESSPIENDS
D

SP

FIG._20

```
1    ATGACAACAC CCAGAAATTC AGTAAATGGG ACTTTCCCAG CAGAGCCAAT GAAAGGCCCT
     METThrThrPro ArgAsnSer ValAsnGly ThrPheProAla GluProMET LysGlyPro
61   ATTGCTATGC AACCTGGTCC AAAACCACTC CTCAGGAGGA TGTCTTCACT GGTGGGTCCC
     IleAlaMETGln ProGlyPro LysProLeu LeuArgArgMET SerSerLeu ValGlyPro
121  ACGCAAAGCT TCTTCATGAG GGAATCTAAG GCTTTGGGGG CTGTCCAGAT TATGAATGGG
     ThrGlnSerPhe PheMETArg GluSerLys AlaLeuGlyAla ValGlnIle METAsnGly
181  CTCTTCCACA TTGCCCTGGG GGGTCTTCTG ATGATCCCAG CAGGGATCTA TGCACCCATC
     LeuPheHisIle AlaLeuGly GlyLeuLeu METIleProAla GlyIleTyr AlaProIle
241  TGTGTGACTG TGTGGTACCC TCTGTGGGGA GGCATTATGT ATATTATTTC CGGATCACTC
     CysValThrVal TrpTyrPro LeuTrpGly GlyIleMETTyr IleIleSer GlySerLeu
301  CTGGCAGCAA CGGAGAAAAA CTCCAGGAAG TGTTTGGTCA AAGGAAAAAT GATAATGAAT
     LeuAlaAlaThr GluLysAsn SerArgLys CysLeuValLys GlyLysMET IleMETAsn
361  TCATTGAGCC TCTTTGCTGC CATTTCTGGA ATGATTCTTT CAATCATGGA CATACTTAAT
     SerLeuSerLeu PheAlaAla IleSerGly METIleLeuSer IleMETAsp IleLeuAsn
421  ATTAAAATTT CCCATTTTTT AAAAATGGAG AGTCTGAATT TTATCAGAGT TCACACACCA
     IleLysIleSer HisPheLeu LysMETGlu SerLeuAsnPhe IleArgVal HisThrPro
481  TATATTAACA TATACAACTG TGAACCAGCT AATCCCTCTG AGAAAAACTC TCCATCTACT
     TyrIleAsnIle TyrAsnCys GluProAla AsnProSerGlu LysAsnSer ProSerThr
541  CAATACTGTT ACAGCATACA ATCTCTGTTC CTGGGCATTT TGTCAGTGAT GCTGATCTTT
     GlnTyrCysTyr SerIleGln SerLeuPhe LeuGlyIleLeu SerValMET LeuIlePhe
601  GCCTTCTTCC AGGAACTTGT AATAGCTGGC ATCGTTGAGA ATGAATGGAG AAGAACATGC
     AlaPhePheGln GluLeuVal IleAlaGly IleValGluAsn GluTrpArg ArgThrCys
661  TCCAGACCCA AATCTAGCGT AGTTCTCCTG TCAGCTGAAG AAAAAAAAGA ACAAGTCATT
     SerArgProLys SerSerVal ValLeuLeu SerAlaGluGlu LysLysGlu GlnValIle
721  GAAATAAAAG AAGAAGTGGT TGGGCTAACT GAAACATCTT CCCAACCAAA GAATGAAGAA
     GluIleLysGlu GluValVal GlyLeuThr GluThrSerSer GlnProLys AsnGluGlu
781  GCCATTGAAA TTATTCCAAT CCAAGAAGAG GAAGAAGAAG AAACAGAGAC AAACTTTCCA
     AlaIleGluIle IleProIle GlnGluGlu GluGluGluGlu ThrGluThr AsnPhePro
841  GAACCTCCCC AAGATCAGGA ATCTTCACCA ATAGAAAATG ACAGCTCTCC T
     GluProProGln AspGlnGlu SerSerPro IleGluAsnAsp SerSerPro
```

FIG._19

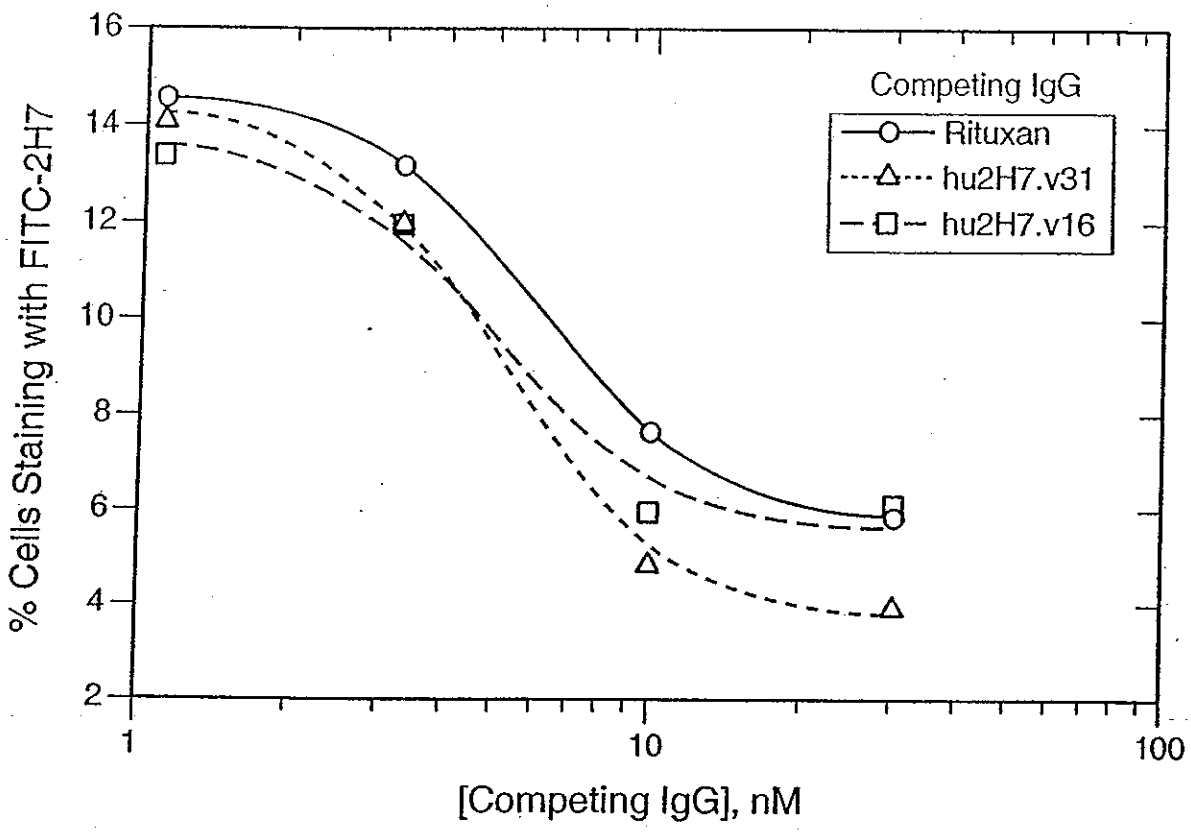

% Cells Staining with FITC-2H7
16
14
12
10
8
6
4
2
1
10
100
[Competing IgG], nM
Competing IgG
Rituxan
hu2H7.v31
hu2H7.v16

FIG._21

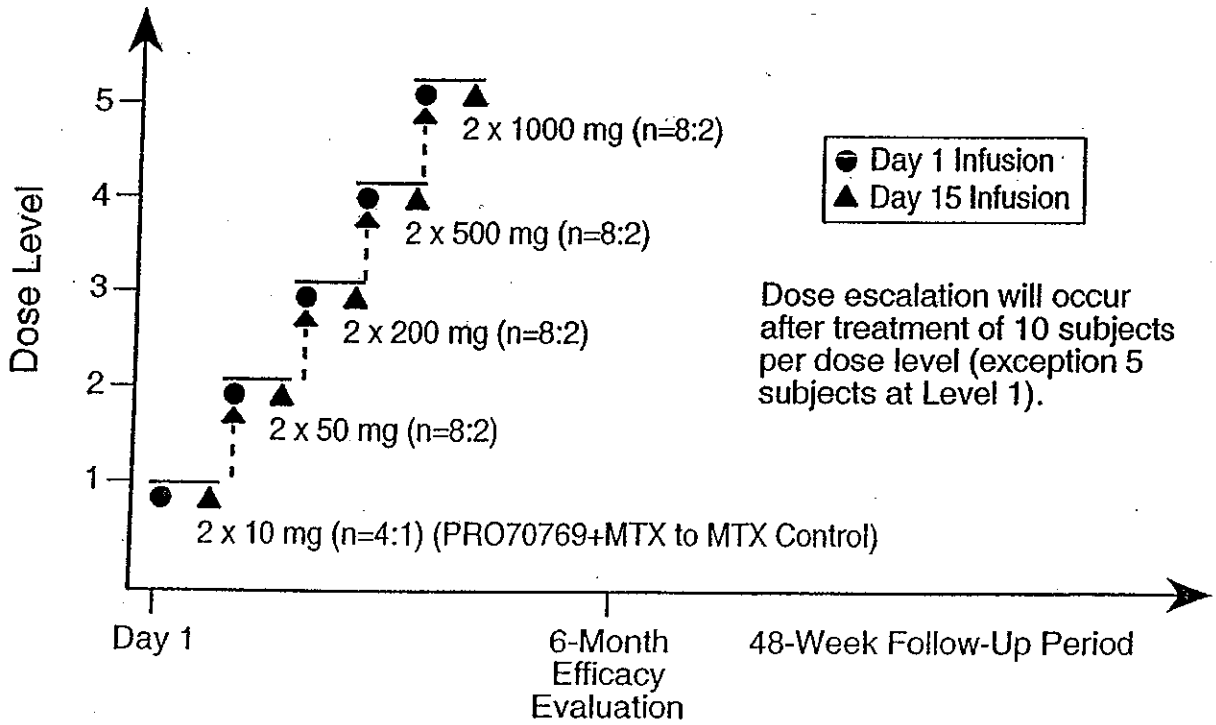

Dose Level
5
4
3
2
1
2 x 1000 mg (n=8:2)
2 x 500 mg (n=8:2)
2 x 200 mg (n=8:2)
2 x 50 mg (n=8:2)
2 x 10 mg (n=4:1) (PRO70769+MTX to MTX Control)
Day 1 Infusion
Day 15 Infusion
Dose escalation will occur after treatment of 10 subjects per dose level (exception 5 subjects at Level 1).
Day 1
6-Month Efficacy Evaluation
48-Week Follow-Up Period

FIG._22

SV40.PD.hu2H7.H16.SV.L16
8.277 kb

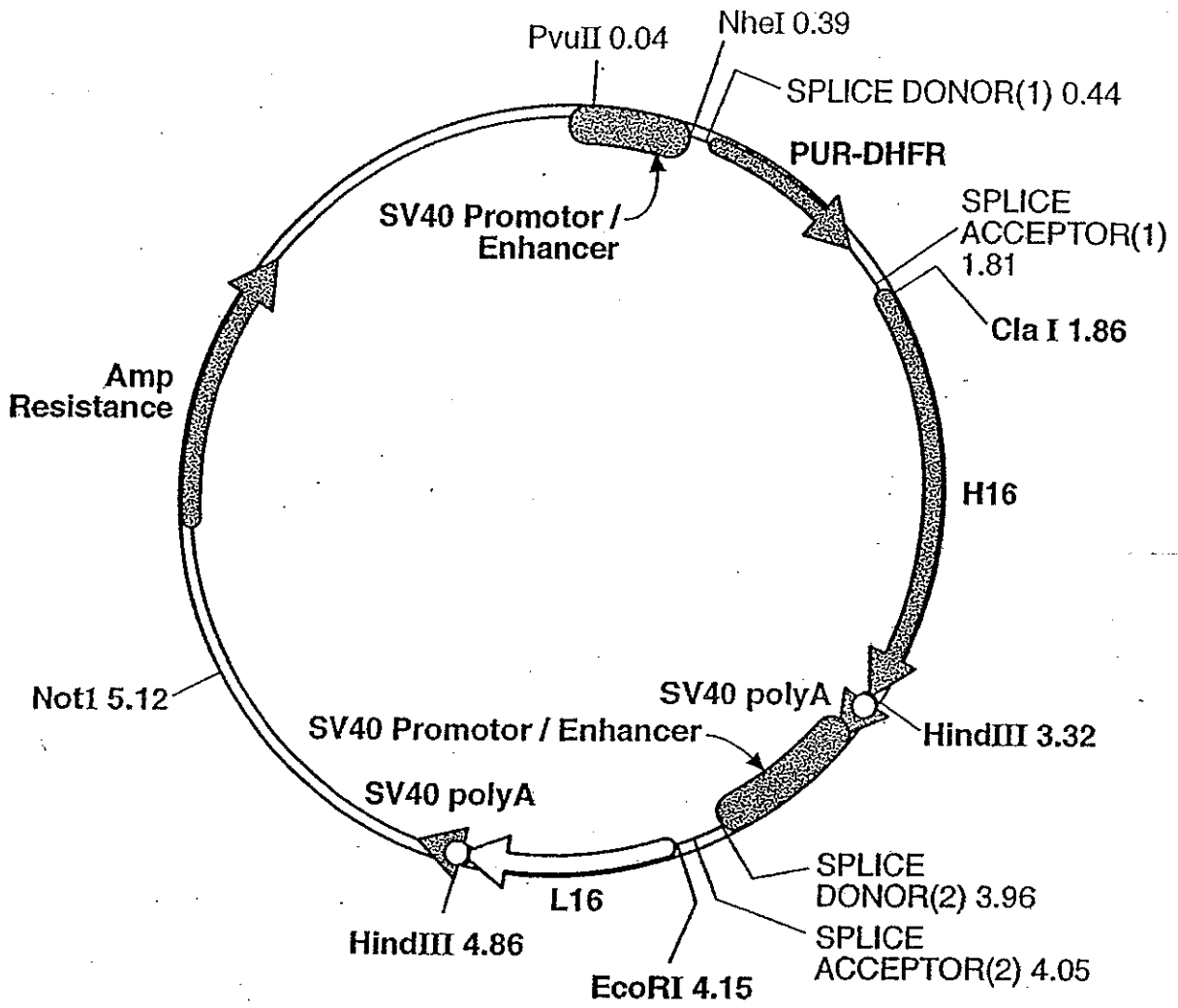


FIG._23