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(73) Nositelj patenta:

(72) Izumitelji:

Medarex, Inc., 707 State Road, Princeton, NJ 08540, US
Shrikant Deshpande, 5910 Remer Terrace, Fremont, CA 94555, US
Haichun Huang, 2425 Sueno Way, Fremont, CA 94539, US
Mohan Srinivasan, 21073 Red Fir Court, Cupertino, CA 95014, US
Josephine M. Cardarelli, 126 Leslie Drive, San Carlos, CA 94070, US
Changyu Wang, 3803 Darwin Drive, Apt. 203, Fremont, CA 94555, US
David Passmore, 98 Church street, Apt. 6, Mountain View, CA 94041, US
Vangipuram S. Rangan, 42 Village Square Place, Pleasant Hill, CA 94523, US
Thomas E. Lane, 76 Harvey Court, Irvine, CA 92612, US
Hans S. Keirstead, 2 Mendel Court, Irvine, CA 92612, US
Michael T. Liu, 1102 Elmhurst, Irvine, CA, US
ZMP IP d.o.o., 10000 Zagreb, HR

(74) Zastupnik:

(54) Naziv izuma: IP-10 PROTUTIJELA I NJIHOVA UPORABA

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PATENTNI ZAHTEJEVI

- 5 1. Izolirano humano monoklonsko protutijelo ili njegov dio koji veže antigen, pri čemu to protutijelo obuhvaća:
 - (a) varijabilnu regiju teškog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 43 i varijabilnu regiju lakog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 92;
 - (b) varijabilnu regiju teškog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 35 i varijabilnu regiju lakog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 84; or
 - 10 (c) varijabilnu regiju teškog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 39 i varijabilnu regiju lakog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 88.
2. Protutijelo ili dio koji veže antigen prema zahtjevu 1, gdje to protutijelo obuhvaća varijabilnu regiju teškog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 43 i varijabilnu regiju lakog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 92.
- 15 3. Protutijelo ili dio koji veže antigen prema zahtjevu 1, gdje to protutijelo obuhvaća varijabilnu regiju teškog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 35 i varijabilnu regiju lakog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 84.
4. Protutijelo ili dio koji veže antigen prema zahtjevu 1, gdje to protutijelo obuhvaća varijabilnu regiju teškog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 39 i varijabilnu regiju lakog lanca koja obuhvaća aminokiselinsku sekvencu SEQ ID NO: 88.
- 20 5. Imunokonjugat koji sadrži protutijelo ili dio koji veže antigen prema bilo kojem od zahtjeva 1 do 4 koji je vezan za terapijsko sredstvo.
6. Imunokonjugat prema zahtjevu 5, gdje je terapijsko sredstvo citotoksin ili radioaktivni izotop.
7. Bispecifična molekula koja sadrži protutijelo ili dio koji veže antigen prema bilo kojem od zahtjeva 1 do 4, koja je povezana s drugim funkcionalnim dijelom koji ima drugačiju specifičnost vezanja od tog protutijela ili dijela koji veže antigen.
- 25 8. Smjesa koja sadrži protutijelo ili dio koji veže antigen prema bilo kojem od zahtjeva 1 do 4, imunokonjugat prema zahtjevu 5 ili 6 ili bispecifičnu molekulu prema zahtjevu 7 te farmaceutski prihvatljivi nosač.
9. Molekula izolirane nukleinske kiseline koja kodira protutijelo ili dio koji veže antigen prema bilo kojem od zahtjeva 1 do 4.
- 30 10. Vektor ekspresije koji sadrži molekulu nukleinske kiseline prema zahtjevu 9.
11. Stanica domaćin koja sadrži vektor ekspresije prema zahtjevu 10.
12. Transgenični miš koji sadrži transgene za humani imunoglobulin teškog i lakog lanca, pri čemu miš eksprimira protutijelo prema bilo kojem od zahtjeva 1 do 4.
- 35 13. Hibridom pripremljen iz miša iz zahtjeva 12, gdje hibridom proizvod to protutijelo.

SLIKA 1A

Anti-IP10 1D4 VH

V segment: 3-33
D segment: 3-10
J segment: JH6b

```

1      Q V Q L V E S C G G V V Q P G R S L
      CAG GTG CAG TTG CTG GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG TCC CTG

                                CDR1
                                -----
55     R L S C A A S G F T F S S Y G H H W
      AGA CTC TCC TGT GCA GCG TCT GGA TTC ACC TTC AGT AGC TAT GGC ATG CAC TGG

                                CDR2
                                -----
109    V R Q A P G K G L E W V A V I W F E
      GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG GCA GTT ATA TGG TTT GAA

                                CDR2
                                -----
163    G S I K Y Y A D S V K G R F T I S R
      GGA AGT ATT AAA TAC TAT CCA GAC TCC GTG AAG GGC CCA TTC ACC ATC TCC AGA

217    D N S K N T L Y L Q H N S L R A E D
      GAC AAT TCC AAG AAT ACG CTG TAT CTG CAA ATG AAC AGC CTG AGA GCC GAG GAC

                                CDR3
                                -----
271    T A V Y Y C A R E Q A G S S L Y Y Y
      ACG GCT GTG TAT TAT TGT GCG AGA GAG GGT GCG GGG AGT TCT CTC TAC TAC TAC

                                CDR3
                                -----
325    Y G H D V W G Q G T T V T V S S
      TAC GGT ATG GAC GTC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCA

```

SLIKA 1B

Anti-IP10 1D4 VR

V segment: A27

J segment: JK2

```

      E I V L T Q S P G T L S L S P G E R
1  GAA ATT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
      A T L S C R A S Q S V S S G H L A W
55  GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC GGA CAC TTA GCC TGG

                                CDR2
      Y Q Q K P G Q A P R L L I Y G A S S
109 TAC CAG CAG AAA CCT GGC CAG CCT CCC AGG CTC CTC ATC TAT GGT GCA TCC AGC

      CDR3
      R A T G I P G R F S G S G S G T D F
163 AGG GCC ACT GGC ATC CCA GGC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC

      T L T I S R L E P E D F A V Y Y C Q
217 ACT CTC ACC ATC AGC AGA CTG GAG CCT GAA GAT TTT GCA GTG TAT TAC TGT CAG

      CDR3
      Q Y G S S P Y T P G Q G T K L E I K
271 CAG TAT GGT AGC TCA CCG TAC ACT TTT GCC CAG GGG ACC AAG CTG GAG ATC AAA

```

SLIKA 2A

Anti-IP10 1B1 VH

V segment: VH3-33
D segment: neuivrdeno
J segment: JH3a

```

1   Q E Q L V E S G G H V V Q P G R S L
    CAG GAG CAG CTG GTG GAG TCT GGG GGA AAC GTG GTC CAG CCT GGG AGG TCC CTC

                                CDR1
55  R L S C A A S G P T F S T Y G M H W
    AGA CTC TCC TGT GCA GCG TCT GGA TTC ACC TTT AGT ACT TAT GCG ATG CAC TGG

                                CDR2
109 V R Q A P Q K G L E W V A V I W Y D
    GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG GCA GTT ATA TGG TAT GAT

                                CDR3
163 G S D K Y Y A D S V K D R F T V S K
    GGA AGT GAT AAA TAC TAT GCA GAC TCC GTG AAG GAC CGA TTC ACG GTC TCC AAA

217 D N S K N T L Y L Q H N S L R A E D
    GAC AAT TCC AAG AAC ACG CTG TAT CTG CAA ATG AAC AGC CTG AGA GCG GAG GAC

                                CDR3
271 T A V Y Y C A E H I A V A D V A F D
    ACG GCT GTG TAT TAC TOT GCG AGA AAT ATA GCA GTG GCT GAC GTT GCT TTT GAT

                                CDR3
325 L W Q Q G T N V T V S S
    CTC TGG GCG CAG GCG ACA ATG GTC ACC GTC TCT TCA

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SLIKA 2B

Anti-IP10 1H1 VK

V segment: L6
J segment: JK4

```

      E I V L T Q S P A I L S L S P G E R
1  GAA ATT GTG TTG ACA CAG TCT CCA GCC ATC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
                                -----
      A T L S C R A S Q S V S S Y L A W Y
55  GCC ACC CTC TCC TCC AGG GCC AGT CAG AGT GTT AGC AGC TAC TTA GCC TCG TAC

                                CDR2
                                -----
      Q Q K P G Q A P R L L I Y D A S N R
109 CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GAT GCA TCC AAC AGG

      CDR2
      -----
      A T G I P A R F S G S G S G T D F T
163 GCC ACT GGC ATC CCA GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACT

                                CDR3
                                -----
      L T I S S L E P E D F A V Y Y C O Q
217 CTC ACC ATC AGC AGC CTG GAG CCT GAA GAT TTT GCA GTT TAT TAC TGT CAG CAG

      CDR3
      -----
      R S N W P P L T F G G G T K V E I K
271 CGT AGC AAC TGG CCT CCA CTC ACT TTC GGC GGA GGG ACC AAG GTG CAG ATC AAA

```

SLIKA 3A

Anti-IP10 2G1 VH

V segment: 3-33
D segment: neutvrđeno
J segment: JH6b

```

1   Q V Q L V E S G G G V V Q P G R S L
    CAG GTG CAG CTG GTG GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG TCC CTG

                                CDR1
                                -----
55  R L S C A A S G F T F S N C Q N H W
    AGA CTC TCC TOT GCA GCG TCT GGA TTC ACC TTC AGT AAC TGT GGC ATG CAC TGG

                                CDR2
                                -----
109 V R Q A P G K Q L E W V A L I G Y D
    GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG GCA CTT ATA GGG TAT GAT

                                CDR2
                                -----
163 G I N E Y Y A D S V K G R F T I S R
    GGA ATT AAT GAA TAC TAT GCA GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA

217 D N S K N T L Y L Q M N S L R A E D
    CAC AAT TCC AAG AAC ACG CTG TAT CTG CAA ATG AAC AGC CTG AGA GGC GAG GAC

                                CDR3
                                -----
271 T A V F Y C A R D W P E G Y Y N G H
    ACG GCT GTG TTT TAC TOT GCG AGA GAC TGG CCT GAG GGC TAC TAC AAC GGC ATG

                                CDR3
                                -----
325 D V W G Q G T T V T V S S
    GAC GTC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCA

```

SLIKA 3B

Anti-IP10 2G1 VK

V segment: A27

J segment: JK3

```

      E I V L T Q S P G T L S L S P G E R
1    GAA ATT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
                                -----
      A T L S C R A S Q E V S S S Y L A W
55   GCC ACC CTC TCC TGC AGG GGC AGT CAG AGT GTT AGC AGC AGC TAC TTA GCC TGG

                                CDR2
                                -----
      Y Q Q X P G Q A P R L L I Y G A S S
109  TAC CAG CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GGT GCA TCC AGC

      CDR3
      -----
      R A T G I P D R F S G S G S G T D P
163  AGG GCC ACT GGC ATC CCA GAC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC

                                CDR3
                                -----
      T L T I S R L E P E D F A V Y Y C Q
217  ACT CTC ACC ATC AGC AGA CTG GAG CCT GAA GAT TTT GCA GTG TAT TAC TGT CAG

      CDR3
      -----
      Q Y G S S P P F T F G P G T K V D I
271  CAG TAT GGT AGC TCA CCT CCA TTC ACT TTC GGC CCT GGG ACC AAA GTG GAT ATC

      X
325  AAA

```

SLIKA 4A

Anti-IP10 3C4 VH

V segment: 5-51
D segment: D2-15
J segment: JH1

```

1      E V Q L V Q S G A E V K K P G E S L
      GAG GTG CAG CTG GTG CAG TCT GGA GCA GAG GTG AAA AAG CCC GGG GAG TCT CTG

                                CDR1
                                -----
55     K I S C K G S G Y N F P S Y W I G W
      AAG ATC TCC TGT AAG GGT TCT GGA TAC AAC TTT CCC AGC TAC TGG ATC GGC TGG

                                CDR2
                                -----
109    V R Q M P G K G L E W H G V I S P G
      GTG CGC CAG ATG CCC GGG AAA GGC CTG GAG TGG ATG GGG GTC ATC TCT CCT GGT

                                CDR3
                                -----
163    D S D T R Y S F S F Q G Q V T I S A
      GAC TCT GAT ACC AGA TAC AGC CCG TCC TTC CAA GGC CAA GTC ACC ATC TCA GCC

217    D K S I S T A Y L Q W S S L K A S D
      GAC AAG TCC ATC AGC ACC GCC TAC CTG CAG TGG AGC AGC CTG AAG GCC TCG GAC

                                CDR3
                                -----
271    T A M Y Y C A R G Y C S G G S C Y P
      ACC GCC ATG TAT TAC TGT GCG AGA GGA TAT TGT AGT GGT GGT AGC TGC TAC CCA

                                CDR3
                                -----
325    F F Q Y W G Q G T L V T V S S
      TTC TTC CAG TAC TGG GGC CAG GGC ACC CTG GTC ACC GTC TCC TCC

```

SLIKA 4B

Anti-IP10 3C4 VK

V segment: L18

J segment: JK4

```

      A   I   Q   L   T   Q   S   P   S   S   L   S   A   S   V   G   D   R
1  GCC ATC CAG TTG ACC CAG TCT CCA TCC TCC CTG TCT GCA TCT GTA GGA GAC AGA

                                CDR1
      V   T   I   T   C   R   A   S   Q   G   I   S   S   A   L   A   W   Y
53  GTC ACC ATC ACT TGC CCG GCA AGT CAG GGC ATT AGC AGT GCT TTA GCC TGG TAT

                                CDR2
      Q   Q   K   P   Q   K   A   P   K   L   L   I   Y   D   A   S   S   L
109 CAG CAG AAA CCA GGG AAA GCT CCT AAG CTC CTG ATC TAT GAT GCC TCC AGT TTG

      CDR2
      E   S   G   V   P   S   R   F   S   G   S   G   S   G   T   D   F   T
163 GAA AGT GGG GTC CCA TCA AGG TTC AGC GGC AGT GCA TCT GGG ACA GAT TTC ACT

                                CDR3
      L   T   I   S   S   L   Q   F   E   D   F   A   T   Y   Y   C   Q   Q
217 CTC ACC ATC AGC AGC CTG CAG CCF GAA GAT TTT GCA ACT TAT TAC TGT CAA CAG

      CDR3
      F   D   S   P   P   H   T   F   G   G   G   T   K   V   E   I   K
271 TTT GAT AGT TTC CCF CAC ACT TTC GGC GGA GGG ACC AAG GTG GAS ATC AAA

```

SLIKA 5A

Anti-IP10 6A5 VH

V segment: 3-33
 D segment: 3-10
 J segment: JH6b

```

1   Q N Q L V E S G G G V V Q P G R S L
   CAA ATG CAG CTG GTG GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG TCC CTG

                                     CDR1
55  R L S C T A S G F T F S N N G M H W
   AGA CTC TCC TGT ACA GCG TCT GGA TTC ACC TTC AGT AAC AAT GGC ATG CAC TGG

                                     CDR2
109 V R Q A F G E G L E W V A V I W F D
   GTC CCG CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG GCA GTT ATA TGG TTT GAT

                                     CDR3
163 G N N K F Y V D S V X C R F T I S R
   GGA ATG AAT AAA TTC TAT GTA GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA

217 D N S K N T L Y L E M N S L R A E D
   GAC AAT TCC AAG AAC ACG CTG TAT CTG GAA ATG AAC AGC CTG AGA GCC GAG CAC

                                     CDR3
271 T A I Y Y C A R E G D G S G I Y Y Y
   ACG GCT ATA TAT TAC TGT GCG AGA GAA GGG GAT GGT TCG GGG ATT TAT TAC TAC

                                     CDR3
325 Y G M D V W G Q G T T V T V S S
   TAC GGT ATG GAC CTC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCA

```

SLIKA 5B

Anti-IP10 6A5 VK

V segment: A27

J segment: JK3

```

      E I V L T Q S P Q T L S L S P Q E R
1    GAA ATT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
      A T L S C R A S Q S V S S S Y L A W
55   GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC AGC TAT TTA GCC TCG

                                CDR2
      Y Q Q K P G Q A P R L L I Y G A S S
109  TAC CAG CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GGT GCA TCC AGC

      CDR2
      R A T G I P D R P S G S G S G T D P
163  AGG GCC ACT GGC ATC CCA GAC AGG TTC AGT GGC AGT GCG TCT GCG ACA GAC TTC

                                CDR 3
      T L T I S R L E P E D P A V Y Y C Q
217  ACT CTC ACC ATC AGC AGA CTG GAG CCT GAA GAT TTT GCA GTG TAT TAC TGT CAG

      CDR3
      Q Y G S S P I F T P G P G T K V D I
271  CAG TAT GGT AGC TCA CCT ATA TTC ACT TTC GGC CCT GGG ACC AAA GTG GAT ATC

      K
325  AAA

```

SLIKA 6A

Anti-IP10 6A8 VH

V segment: 3-33
D segment: neutvrđeno
J segment: JH6b

```

1   Q V Q L V E S G G G V V Q P G R S L
    CAG GTG CAG CTG GTG GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG TCC CTG

                                CDR1
55  R L S C T A S G F T F S T Y G M H W
    AGA CTC TCC TGT ACA GCG TCT GGA TTC ACC TTC AGT ACC TAT GGC ATG CAC TGG

                                CDR2
109 V R Q A P G K G L E W V A I I N F D
    GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG GCA ATT ATA TGG TTC GAT

                                CDR2
163 G S N E D Y A A S V K G R F T I S R
    GGA AGT AAT GAA GAT TAT GCA GCC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA

217 D N S K N T L Y L Q M N S L R A E D
    GAC AAT TCC AAG AAC ACG CTG TAT CTG CAA ATG AAC AGC CTG AGA GCC GAG GAC

                                CDR3
271 T A V Y Y C A R E G D G S S L Y Y Y
    ACG GCT GTG TAT TAC TGT GGG AGA GAG GGG GAT GGG ACC TCC TTA TAC TAC TAC

                                CDR3
325 Y G H D V W G Q G T T V T V S S
    TAC GGT ATG GAC GTC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCA

```

SLIKA 6B

Anti-IP10 6A8 VR

V segment: A27

J segment: JK4

```

      R V V L T Q S P G T L S L S F G E R
1  GAA GTT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
      A T L S C R A S Q S I S S G Y L A W
55  GCC ACC CTC TCC TGC ACG GCC AGT CAG AGT ATT AGC AGC GGC TAC TTA GCC TGG

                                CDR2
      Y Q Q K P G Q A F R L L I Y G A S S
109 TAC CAG CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GGT GCA TCC AGC

      CDR3
      R A T G I P D R F S G S G S G T D F
163 AGG GCC ACT GGC ATC CCA GAC ACG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC

      CDR3
      T L T I S R L E F E D F A V Y Y C Q
217 ACT CTC ACC ATC AGC AGA CTG GAG CCT GAA GAT TTT GCA CTG TAT TAC TGT CAG

      CDR3
      Q Y G S S P T F G G G T K V E I K
271 CAG TAT GGT AGC TCA CCC ACT TTC GGC GGA GGG ACC AAG GTG GAG ATC AAA

```

SLIKA 7A

Anti-IP10 6B10 VH

V segment: 3-30.3
 D segment: 5-12
 J segment: JH4b

```

      Q V Q L V E S G G G V V Q F G R S L
1  CAG GTG CAG CTG GTG GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG TCC CTG

                                     CDR1
      R L S C A A S G P T P S N S A N H W
55 AGA CTC TCC TGT GCA GCC TCT GGA TTC ACC TTC AGT AAC TCT GCT ATG CAC TGG

                                     CDR2
      V R Q A P G K G L E W V A L I P F D
109 GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG CCA CTT ATA CCA TTT GAT

      CDR2
      G Y N K Y Y A D S V K G R P T I S R
163 GGA TAC AAT AAA TAC TAC GCA GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA

      D N S K N T L Y L Q M N S L R A E D
217 GAC AAT TCC AAG AAC ACG CTG TAT CTG CAA ATG AAC AGC CTG AGA GCT GAG GAC

                                     CDR3
      T A V Y Y C A R E G G Y T G Y D G G
271 ACG GCT GTG TAT TAC TGC GCG AGA GAA GGT GGA TAT ACT GGC TAC GAT GGG GGA

      CDR3
      F D Y W G Q G I L V T V S S
325 TTT GAC TAT TGG GGC CAG GGA ATC CTG GTC ACC GTC TCC TCA

```

SLIKA 7B

Anti-IP10 5B15 VK

V segment: L6
J segment: JK2

```

      E I V L T Q S P A T L S L S P G E R
1    GAA ATT GTG TTG ACA CAG TCT CCA GCC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
                                -----
      A T L S C R A S Q S V S S Y L A W Y
55   GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC TAC TTA GCC TGG TAC

                                CDR2
                                -----
      Q Q K P G Q A P R L L I Y D A S N R
109  CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GAT GCA TCC AAC AGG

      CDR3
      -----
      A T G I P A R F S G S G S G T D F T
163  GCC ACT GGC ATC CCA GCC AGG TTC AGT GCC AGT GGG TCT GGG ACA GAC TTC ACT

                                CDR3
                                -----
      L T I S S L E P E D F A V Y Y C Q Q
217  CTC ACC ATC AGC AGC CTA GAG CCT GAA GAT TTT GCA GTT TAT TAC TGT CAG CAG

      CDR3
      -----
      R S N N P P Y T F S Q G T K L R I K
271  CGT AGC AAC TGG CCT CCG TAC ACT TTT GGC CAG GGG ACC AAG CTG GAG ATC AAA

```

SLIKA 8A

Anti-IP10 7C10 VH

V segment: 3-33

D segment: 3-10

J segment: JH4b

```

      Q V Q L V E S G G G V V Q P G R S L
1  CAG GTG CAA CTG GTG GAG TCT GGG GGA GGC GTG CTC CAG CCT GGG AGG TCC CTG

                                CDR1
                                -----
      R L S C A A S G F T F S N S G M H W
55  AGA CTC TCC TGT GCA GCG TCT GGA TTC ACC TTC AGT AAC TCT GGC ATG CAC TGG

                                CDR2
                                -----
      V R Q A P G R G L E W V A V I D Y D
109 GTG GGC CAG OCT CCA GGC AAG GGG CTG GAG TGG GTG GCA GTT ATA GAC TAT GAT

      CDR2
      -----
      G I I Q Y Y A D S V K G R P T I S R
163 GGA ATT ATT CAA TAC TAT GGC GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA

      D N S K N T L Y L Q I N S L R A E D
217 GAC AAT TCC AAG AAC ACG CTG TAT CTG CAA ATA AAC AGC CTG AGA GCC GAG GAC

                                CDR3
                                -----
      T A V V Y Y C A T E R G T H Y Y G S G
271 ACG GCT GTG TAT TAC TGT GCG ACA GAG AGG GGC ACG CAT TAC TAT GGT TCG GGG

      CDR3
      -----
      S F D Y W G Q G T L V T V S S
325 AGT TTT GAC TAC TCG GCC CAG GGA ACC CTG GTC ACC GTC TCC TCA

```

SLIKA 8B

Anti-IP10 7C10 VK

V segment: L15

J segment: JK4

```

      D I Q M T Q S P S S L S A S V G D R
1  GAC ATC CAG ATG ACC CAG TCT CCA TCC TCA CTG TCT GCA TCT GTA GGA GAC AGA

                                CDR1
      V T I T C R A S Q G I S S W L A W Y
55  GTC ACC ATC ACT TGT CCG GCG AGT CAG GGT ATT AGC AGC TGG TTA GCC TGG TAT

                                CDR2
      Q Q R P E K A P K S L I Y A A S S L
109 CAG CAG AAA CCA GAG AAA GCC CCT AAG TCC CTG ATC TAT GCT GCA TCC AGT TTG

      CDR3
      Q S G V P S R F S G S G S G T D F T
163 CAA AGT GGG GTC CCA TCA AGG TTC AGC GGC AGT GGA TCT GGG ACA GAT TTC ACT

                                CDR3
      L T I S S L Q P E D F A T Y Y C Q Q
217 CTC ACC ATC AGC AGC CTG CAG CCT GAA GAT TTT GCA ACT TAT TAC TCC CAA CAG

      CDR3
      Y N S Y P P T F G G G T K V E I K
271 TAT AAT AGT TAC CCT CCC ACT TTC GGC GGA GGG ACC AAG GTG GAG ATC AAA

```

SLIKA 9A

Anti-IP10 8F6 VH

V segment: 3-30.3
 D segment: 6-13
 J segment: JH4b

```

      Q V Q L V D S G G G V V Q F C R S L
1  CAG GTG CAA CTG GTG GAC TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG TCC CTG

                                CDR1
      R L S C A A S G F T F N T Y G M H W
55 AGA CTC TCC TGT GCA GCC TCT GGA TTC ACC TTC AAT ACC TAT GGC ATG CAC TGG

                                CDR2
      V R Q A P G K G L E W V A V I S Y D
109 GTC CGC CAG CCT CCA GGC AAG GGG CTG GAG TGG GTG GCA CTT ATA TCA TAT GAT

                                CDR2
      G I I K H V A D S V K G R F T I T R
163 GGA ATC ATT AAA CAC TAC GCC GAC TCC GTG AAG GGC CGA TTC ACC ATA ACC AGA

      D N S K N N V H L Q M N S L R A E D
217 GAC AAT TCC AAG AAC ATG GTG CAT CTG CAA ATG AAC AGC CTG AGA GCT GAG GAC

                                CDR3
      T A V Y Y C A R D S S S W V V Y F D
271 ACG GCT GTG TAT TAC TGT GCG AGA GAT AGC AGC AGC TGG TAC GTC TAC TTT GAC

                                CDR3
      Y W G Q G T L V T V S S
325 TAC TGG GGC CAG GGA ACC CTG GTC ACC GTC TCC TCA

```

SLIKA 9B

Anti-IP10 SP6 VK

V segment: L6
J segment: JK1

```

      E I V L T Q S P A T L S L S P G E N
1  GAA ATT GTG TTG ACA CAG TCT CCA GCC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
                                -----
      A T L S C R A S Q S V S S Y V A W Y
55  GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC TAC GTA GCC TGG TAC

                                CDR2
                                -----
      Q Q K P G Q A P R L L I Y D A S N R
109 CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GAT GCA TCC AAC AGG

      CDR3
      -----
      A T G I P A R F S G S G S G T D F T
163  GCC ACT GGC ATC CCA GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACT

                                CDR3
                                -----
      L T I S S L E P E D F A I Y Y C Q Q
217 CTC ACC ATC AGC AGC CTA GAG CCT GAA GAT TTT GCA ATT TAT TAC TGT CAG CAG

      CDR3
      -----
      R S N S P P W T F G Q G T K V E I R
271 CGT AGC AAC TCG CCT CCG TCG AGG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA

```

SLIKA 10A

Anti-IP10 10A12 VH

V-segment: 3-33
D-segment: neutyrdeno
J-segment: JH6b

```

1   Q V Q L V E S G G G V V Q P G R S L
    CAG GAG CAG CTG GTG GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG TCC CTG

                                CDR1
55  R L S C A A S G P T P S H C G H H W
    AGA CTC TCC TCT GCA GCG TCT GGA TTC ACC TTC AGT AAC TGT GGC ATG CAC TCG

                                CDR2
109 V R Q A P G K G L E W V A L I G F D
    GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG GCA CTT ATA GGG TTT GAT

                                CDR3
163 G I N E Y Y A D S V X G R F T I S R
    GGA ATT AAT GAA TAC TAT GCA GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA

217 D N S X N T L Y L Q H N S L R A E D
    GAC AAT TCC AAG AAC ACG CTG TAT CTG CAA ATG AAC AGC CTG AOA GGC GAG GAC

                                CDR3
271 T A V Y Y C A R D W F E G Y Y N G M
    ACG GCT GTG TAT TAT TGT GCG AGA GAC TGG CCT GAG GGC TAC TAC AAC GGC ATG

                                CDR3
325 D V W G Q G T T V T V S S
    GAC GTC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCA

```

SLIKA 10B

Anti-IP10 10A12 VK

V segment: A27

J segment: JK3

```

      E I V L T O S F G T L S L S F G E R
1  GAA AFT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
      A T L S C R A S Q S V S S S Y L A W
55  GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC AGC TAC TTA GCC TGG

                                CDR2
      Y Q Q K P G Q A P R L L I Y G A S S
109 TAC CAG CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GGT GCA TCC AGC

      CDR3
      R A T G I F D R F S G S G S G T D F
163 AGC CCC ACT GGC ATC CCA GAC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC

      CDR3
      T L T I S R L E F E D F A V Y Y C Q
217 ACT CTC ACC ATC AGC AGA CTG GAG CCT GAA GAT TTT GCA GTG TAT TAC TGT CAG

      CDR3
      Q Y G S S P P F T F G P G T K V D I
271 CAG TAT GGT AGC TCA CCT CCA TTC ACT TTC GGC CCT GGG ACC AAA GTG GAT ATC

      K
325 AAA

```

SLIKA 11A

Anti-IP10 13C4 VH

V segment: 4-61
 D segment: 3-10
 J segment: JH6b

```

1   Q V Q L Q E S G P G L V K P S E T L
    CAG CTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG

                                CDR1
55  S L T C T I S G G S V S S G D Y Y W
    TCC CTC ACC TGC ACT ATC TCT GGT GGC TCC GTC AGC AGT GGT GAT TAC TAC TGG

    CDR1                                CDR2
109 S W I R Q P P G K G L E W I G N I Y
    AGC TGG ATC CGG CAG CCC CCA GGG AAG GGA CTG CAG TGG ATT GGG AAC ATC TAT

                                CDR2
163 Y S G S T N Y N P S L K S R V T I S
    TAC AGT GGG AGC ACC AAC TAC AAC CCC TCC CTC AAG AGT CGA GTC ACC ATA TCG

217 V D T S K N Q P S L K L S S V T A A
    GTA GAC ACG TCC AAG AAC CAG TTC TCC CTG AAG CTG AGC TCT GTG ACC GCT GCG

                                CDR3
271 D T A V Y Y C A R G G G T V V R G I
    GAC ACG GCC GTG TAT TAC TOT GCG AGA GGG GGG GGT ACT GTG GTT CCG CGA ATT

                                CDR3
325 I H Y Y Y Y Y Q H D V W G Q G T T V
    ATC CAT TAC TAC TAC TAC TAC GGT ATG GAC GTC TGG GGC CAA GGG ACC ACG GTC

379 T V S S
    ACC GTC TCC TCA

```

SLIKA 11B

Anti-IP10 13C4 VK

V segment: A27

J segment: JK2

```

      E I V L T Q S P G T L S L S P G E R
1  GAA APT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
      A T L S C R A S Q S V S S S Y L A W
55  GCC ACC CTC TCC TCC AGG GCC AGT CAG AGT GTT AGC AGC AGC TAC TTA GCC TGG

                                CDR2
      Y Q Q K P G Q A P R L L I Y G A S S
109 TAC CAG CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GGT GCA TCC AGC

      CDR3
      R A T G I P D R P S G S G S G T D F
163 AGG GCC ACT GGC ATC CCA GAC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC

      CDR3
      T L T I S R L E P E D F A V Y Y C Q
217 ACT CTC ACC ATC AGC AGA CTG GAG CCT GAA GAT TTY GCA GTG TAT TAC TGT CAG

      CDR3
      Q Y G S S P E Y T F G Q G I K L E I
271 CAG TAT GGT AGC TCA CCG GAG TAC ACT TTT GGC CAG GGG ACC AAG CTG GAG ATC

      X
325 AAA

```

SLIKA 12

3 - 33 zametna linija
 6A5
 6A8
 2G1
 10A12
 1E1
 7C10
 1D4

Q V O L V E S Q G G V V Q P G R S L R L S C A A S G F T F S S Y G M H
 - N -
 -
 -
 - E - - - - N -
 -
 -
 -

CDR1

3 - 33 zametna linija
 6A5
 6A8
 2G1
 10A12
 1E1
 7C10
 1D4

W V R Q A P G K G L E W V A V I W Y D G S N K Y Y A D S V K G R F T I
 -
 -
 -
 -
 -
 -
 -
 -

CDR2

3 - 33 zametna linija
 6A5
 6A8
 2G1
 10A12
 1E1
 7C10
 1D4

S R D N S K N T L Y L Q M N S L R A E D T A V Y V C A R
 -
 -
 -
 -
 - K -
 -
 -
 -

CDR3

6A5
 6A8
 2G1
 10A12
 1E1
 7C10
 1D4

Y Y Y Y G M D V W G Q G T T V T V S S
 -
 N -
 N -
 A F D L -
 G S G S F D Y -
 -
 -

CDR3

SLIKA 13

3-30.3 zametna linija	Q V Q L V E S G G V V Q P G R S L R L S C A A S G F T F S S Y A M H W V R Q	CDR1
6B10 VH	- - - - - D - - - - -	- - - - - N S - - - - -
8F6 VH	- - - - -	- - - - - N T - G - - - - -
3-30.3 zametna linija	A P G K G L E W V A V I S Y D G S N K Y Y A D S V K G R F T I S R D N S K N T	CDR2
6B10 VH	- - - - - L - P F - - - - -	- - - - - T - - - - -
8F6 VH	- - - - - I I - H - - - - -	- - - - - M - - - - -
3-30.3 zametna linija	L Y L Q M N S L R A E D T A V Y Y C A R	CDR3
6B10 VH	- - - - -	- - - - - E G G Y T G Y D G G F D Y W G Q G I L
8F6 VH	V H - - - - -	- - - - - D S S S N Y V Y - - - - - T -
6B10 VH	V T V S S	
8F6 VH	- - - - -	

SLIKA 14

5-51 zametna linija CDR1
 EVQLVQSGAEVKKPKGESSLKISCKGSGYSPFTSYWIG
 3C4 VH - - - - - N - - - - -

5-51 zametna linija CDR2
 WVRQMPGKGL EWMGI IYPGDS DTRYSPSFQGVTI
 3C4 VH - - - - - V - S - - - - -

5-51 zametna linija CDR3
 SADKSI STAYLQWSSSLKASDTAMYYCAR
 3C4 VH - - - - - GYCSGGS

3C4 VH CDR3
 CYPFPQYNWGQGLVTVSS

SLIKA 15

4-61 zametna linija QVQLQESGGPGCLVKPSETLSLTCTVSGGSSVSSGSSYYW^{CDR1}SWIRQP
13C4 VH: - - - - - I - - - - - D - - - - -

4-61 zametna linija PGKGLSENIGYIYYSGSTN^{CDR2}YNPSSLKSRVTISVDTSKNQPSLKL
13C4 VH: - - - - - N - - - - - - - - - -

4-61 zametna linija SSVTAADTA^{CDR3}VYCAR
13C4 VH: - - - - - GGGTVVRGIIHYYYYGMDVWGQGT^{'S}TVTS

SLIKA 16

A27	zametna linija	E	I	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	R	A	S	Q	S	V	S	S	Y	L	A																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																	
1D4		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

SLIKA 17

	<u>CDR1</u>																																
L6 zametna linija	E	I	V	L	T	Q	S	P	A	T	L	S	L	S	P	G	E	R	A	T	L	S	C	R	A	S	Q	S	V	S	Y	L	A
1E1	-	-	-	-	-	-	-	-	-	I	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6B10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
8F6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	V

	<u>CDR2</u>																																	
L6 zametna linija	W	Y	Q	Q	K	P	G	Q	A	P	R	L	L	I	Y	D	A	S	N	R	A	T	G	I	P	A	R	F	S	G	S	G	S	G
1E1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
6B10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
8F6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

	<u>CDR3</u>																																	
L6 zametna linija	T	D	F	T	L	T	I	S	S	L	E	P	E	D	F	A	V	Y	C	Q	Q	R	S	N	W	P	-	P	L	T	F	G	G	G
1E1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
6B10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Q	
8F6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	I	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Q	

1E1	T	K	V	E	I	K	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6B10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
8F6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

SLIKA 18

[illegible]

CDR2

L18 zametna linija : W Y Q Q K P G K A P K L L I Y D A S S L E S G V P S R F S G S G S G - - - - -

3C4 VK: - - - - -

L18 zametna linija : T D F T L T I S S L Q P E D F A T Y Y C Q Q F N S Y P
3C4 VK: - - - - - - - - - - - D - F - H T F G G G T

304 1/2: XVA XVE XVI

SLIKA 19

	CDRI	
L15 : zanetna linija	DIQM TQSPSSLASV GDRVTITCRASQG I S S W L A	- - - - -
7C10 VK		- - - - -

L15, zamezna linija
 7C10 VK
 WYQQKPKPKSLIYAASLSQSGVPSRFSGSGSG
CDR2
 L15, zamezna linija
 7C10 VK

L15 zamezna Huij's
7C10 VK

7C10 VK KVEIK