

IEC170038PCT-seq1 翻译
SEQUENCE LISTING

<110> AKESO BIOPHARMA, INC

<120> ANTI-CTLA4 AND ANTI-PD-1 BIFUNCTIONAL ANTIBODY, PHARMACEUTICAL
COMPOSITION THEREOF AND USE THEREOF

<130> IEC170038PCT

<160> 47

<170> PatentIn version 3.2

<210> 1

<211> 372

<212> DNA

<213> Artificial

<220>

<223> Nucleic acid sequence of 4G10 heavy chain variable region

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catggaaaga accttgaatg gattggactt attaatcctt acaataatat tactaactac      180
aaccagaagt tcatgggcaa ggccacattt actgtagaca agtcatccag cacagcctac      240
atggaactcc tcagactgac atctgaagac tctggagtct atttctgtgc aagactcgac      300
tatagggtctt attggggcca agggactctg gtcactgtct ctgcagccaa aacgacaccc      360
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<210> 2

<211> 124

<212> PRT

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<223> The amino acid sequence of 4G10 heavy chain variable region

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Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20          25          30
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Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Ile
35          40          45
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Gly Leu Ile Asn Pro Tyr Asn Asn Ile Thr Asn Tyr Asn Gln Lys Phe
50          55          60
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Met Gly Lys Ala Thr Phe Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65          70          75          80
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Met Glu Leu Leu Arg Leu Thr Ser Glu Asp Ser Gly Val Tyr Phe Cys
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Ala Arg Leu Asp Tyr Arg Ser Tyr Trp Gly Gln Gly Thr Leu Val Thr
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Val Ser Ala Ala Lys Thr Thr Pro Pro Ser Val Tyr
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<210> 3
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 aaaccagatc atttattcac tagtctaata ggtggtacca acaaccgagc tccaggtgtt 180
 cctgccagat tctcaggctc cctgattgga gacaaggctg ccctcaccat cacaggggca 240
 cagactgagg atgaggcaat atatttctgt gctctatggt acagcaacca ttgggtgttc 300
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<220>
 <223> The amino acid sequence of 4G10 light chain variable region

<400> 4

Gln Ala Val Val Thr Gln Glu Ser Ala Leu Thr Thr Ser Pro Gly Glu
 1 5 10 15

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser
 20 25 30

Asn Phe Ala Asn Trp Val Gln Glu Lys Pro Asp His Leu Phe Thr Ser
 35 40 45

Leu Ile Gly Gly Thr Asn Asn Arg Ala Pro Gly Val Pro Ala Arg Phe
 50 55 60

Ser Gly Ser Leu Ile Gly Asp Lys Ala Ala Leu Thr Ile Thr Gly Ala
 65 70 75 80

Gln Thr Glu Asp Glu Ala Ile Tyr Phe Cys Ala Leu Trp Tyr Ser Asn
 85 90 95

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His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro
 100 105 110

Lys Ser Ser Pro Ser Val Thr Leu Phe Gln Gly Gln Phe Cys
 115 120 125

<210> 5
 <211> 345
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 <223> Nucleic acid sequence of 4G10H1L1 heavy chain variable region

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 ccaggacagg gactggagtg gatcgggctg attaatcctt acaacaacat caccaactac 180
 aaccagaagt tcatgggaaa agcaaccttt acagtggaca agagcatttc cacagcctac 240
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 <212> PRT
 <213> Artificial

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 <223> The amino acid sequence of 4G10H1L1 heavy chain variable region

<400> 6
 Gln Val Gln Leu Val Glu Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
 1 5 10 15
 Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
 20 25 30
 Thr Met Asn Trp Val Lys Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Leu Ile Asn Pro Tyr Asn Asn Ile Thr Asn Tyr Asn Gln Lys Phe
 50 55 60
 Met Gly Lys Ala Thr Phe Thr Val Asp Lys Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Arg Leu Thr Ser Asp Asp Ser Gly Val Tyr Phe Cys
 85 90 95
 Ala Arg Leu Asp Tyr Arg Ser Tyr Trp Gly Gln Gly Thr Leu Val Thr
 100 105 110

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Val Ser Ala
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<210> 7
<211> 327
<212> DNA
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<223> Nucleic acid sequence of 4G10H1L1 light chain variable region

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aagccaggcc aggcatttcg atccctgac ggaggcacia acaatcgggc ttcttggggtg 180
cccgcaagat tctcaggaag cctgctgggg ggaaaagccg ctctgaccat tagtggcgct 240
cagcctgagg acgaagccga gtacttctgc gctctgtggt atagcaacca ctgggtgttt 300
ggcgggggaa caaagctgac tgtgctg 327

<210> 8
<211> 109
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<213> Artificial

<220>
<223> The amino acid sequence of 4G10H1L1 light chain variable region

<400> 8

Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Phe Ala Asn Trp Val Gln Glu Lys Pro Gly Gln Ala Phe Arg Ser
35 40 45

Leu Ile Gly Gly Thr Asn Asn Arg Ala Ser Trp Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 9
<211> 345

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<212> DNA
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<220>
<223> Nucleic acid sequence of 4G10H3L3 heavy chain variable region

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cctggccagg ggctggagtg gatcggcctg attaacctt acaacaacat cactaactac 180
gcacagaagt tccaggggag agtgacctt acagtggaca ccagcatttc cacagcctac 240
atggaactgt cccggctgag atctgacgat acaggcgtgt acttctgcgc taggctggat 300
taccgcagct attggggaca gggcacactg gtgactgtca gcgca 345

<210> 10
<211> 115
<212> PRT
<213> Artificial

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<223> The amino acid sequence of 4G10H3L3 heavy chain variable region

<400> 10
Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30
Thr Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45
Gly Leu Ile Asn Pro Tyr Asn Asn Ile Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Phe Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Gly Val Tyr Phe Cys
85 90 95
Ala Arg Leu Asp Tyr Arg Ser Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110
Val Ser Ala
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<210> 11
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<212> DNA
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<223> Nucleic acid sequence of 4G10H3L3 light chain variable region

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 aagccaggac aggctccccg gagtctgata ggaggcacca acaacaaggc cagctggaca 180
 cccgcacggg tcagcggcag cctgctgggc ggcaaggccg ctctgacaat tagcggagcc 240
 cagcctgagg acgaagccga gtactattgc gctctgtggg actccaacca ctgggtgttc 300
 ggcggcggca ccaagctgac tgtgctg 327

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 1 5 10 15
 Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
 20 25 30
 Asn Phe Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Ser
 35 40 45
 Leu Ile Gly Gly Thr Asn Asn Lys Ala Ser Trp Thr Pro Ala Arg Phe
 50 55 60
 Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
 65 70 75 80
 Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
 85 90 95
 His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105

<210> 13
 <211> 345
 <212> DNA
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 <223> Nucleic acid sequence of 4G10H4L3 heavy chain variable region

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 agctgcaagg ccagcgggta cagtttcact ggatatacca tgaactgggt ccgacaggcc 120
 cctggccagg ggctggagtg gatcggcctg attaaccctt acaacgacat cactaactac 180

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gcacagaagt tccaggggag agtgaccttt acagtggaca ccagcatttc cacagcctac 240
 atggaactgt cccggctgag atctgacgat acaggcgtgt acttctgcgc taggctggat 300
 taccgcagct attgggggaca gggcacactg gtgactgtca gcgca 345

<210> 14
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<400> 14

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 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
 20 25 30

Thr Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Leu Ile Asn Pro Tyr Asn Asp Ile Thr Asn Tyr Ala Gln Lys Phe
 50 55 60

Gln Gly Arg Val Thr Phe Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
 65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Gly Val Tyr Phe Cys
 85 90 95

Ala Arg Leu Asp Tyr Arg Ser Tyr Trp Gly Gln Gly Thr Leu Val Thr
 100 105 110

Val Ser Ala
 115

<210> 15
 <211> 354
 <212> DNA
 <213> Artificial

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 <223> Nucleic acid sequence of 14C12 heavy chain variable region

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 cctgagaagc gcctggaatg ggtcgctact atcagcggag gcgggcgata cacctactat 180
 cctgactctg tcaaaggag attcacaatt agtcgggata acgccagaaa tactctgtat 240
 ctgcagatgt ctagtctgcg gtccgaggat acagctctgt actattgtgc aaaccgggtac 300

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354

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 <223> The amino acid sequence of 14C12 heavy chain variable region
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Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Ser Ser Tyr
 20 25 30

Asp Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
 35 40 45

Ala Thr Ile Ser Gly Gly Gly Arg Tyr Thr Tyr Tyr Pro Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95

Ala Asn Arg Tyr Gly Glu Ala Trp Phe Ala Tyr Trp Gly Gln Gly Thr
 100 105 110

Leu Val Thr Val Ser Ala
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<210> 17
 <211> 318
 <212> DNA
 <213> Artificial

<220>
 <223> Nucleic acid sequence of 14C12 light chain variable region

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 ttcacatgca aagcatccca ggacatcaac acatacctgt cttggtttca gcagaagcca 120
 ggcaaaagcc ccaagaccct gatctaccgg gccaatagac tgggtggacgg ggtccccagc 180
 agattctccg gatctggcag tgggcaggat tactccctga ccatcagctc cctggagtat 240
 gaagacatgg gcatctacta ttgcctgcag tatgatgagt tccctctgac ctttgagca 300
 ggcacaaaac tggaactg 318

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<210> 18
 <211> 106
 <212> PRT
 <213> Artificial

<220>
 <223> The amino acid sequence of 14C12 light chain variable region

<400> 18

Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
 1 5 10 15

Glu Arg Val Thr Phe Thr Cys Lys Ala Ser Gln Asp Ile Asn Thr Tyr
 20 25 30

Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
 35 40 45

Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr
 65 70 75 80

Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Leu
 85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu
 100 105

<210> 19
 <211> 354
 <212> DNA
 <213> Artificial

<220>
 <223> Nucleic acid sequence of 14C12H1L1 heavy chain variable region

<400> 19

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ccaggaaagg gactggattg ggtcgctact atctcaggag gcgggagata cacctactat	180
cctgacagcg tcaagggccg gttcacaatc tctagagata acagtaagaa caatctgtat	240
ctgcagatga acagcctgag ggctgaggac accgcactgt actattgtgc caaccgctac	300
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<210> 20
 <211> 118
 <212> PRT
 <213> Artificial

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 <223> The amino acid sequence of 14C12H1L1 heavy chain variable region

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<400> 20

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Ser Ser Tyr
 20 25 30

Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Asp Trp Val
 35 40 45

Ala Thr Ile Ser Gly Gly Gly Arg Tyr Thr Tyr Tyr Pro Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Asn Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95

Ala Asn Arg Tyr Gly Glu Ala Trp Phe Ala Tyr Trp Gly Gln Gly Thr
 100 105 110

Leu Val Thr Val Ser Ser
 115

<210> 21

<211> 321

<212> DNA

<213> Artificial

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<223> Nucleic acid sequence of 14C12H1L1 light chain variable region

<400> 21

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 gggaaaagcc ccaagacact gatctaccgg gctaataagac tgggtgtctgg agtcccaagt 180
 cggttcagtg gctcaggagg cggacaggac tacactctga ccatcagctc cctgcagcct 240
 gaggacatgg caacctacta ttgcctgcag tatgatgagt tcccactgac ctttggcgcc 300
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<210> 22

<211> 107

<212> PRT

<213> Artificial

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<223> The amino acid sequence of 14C12H1L1 light chain variable region

<400> 22

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Val Gly
 1 5 10 15

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Asp Arg Val Thr Phe Thr Cys Arg Ala Ser Gln Asp Ile Asn Thr Tyr
20 25 30

Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
35 40 45

Tyr Arg Ala Asn Arg Leu Val Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Gln Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Met Ala Thr Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Leu
85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 23
<211> 15
<212> PRT
<213> Artificial

<220>
<223> Linker 1

<400> 23

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 24
<211> 20
<212> PRT
<213> Artificial

<220>
<223> Linker 2

<400> 24

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
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<210> 25
<211> 115
<212> PRT
<213> Artificial

<220>
<223> The amino acid sequence of 8D2H14L2 heavy chain variable region

<400> 25

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Ser Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Asn
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Ala
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80

Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Gly Val Tyr
85 90 95

Tyr Cys Thr Ala Gln Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

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<211> 345
<212> DNA
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<223> Nucleic acid sequence of 8D2H14L2 heavy chain variable region

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ccaggcaaag gactggagtg gctggctcag atccggaaca agccctacaa ttatgaaaca 180
tactatagcg cctccgtgaa aggccggttc actattagta gagacgattc taagaacagc 240
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cagtttgcct attggggaca gggcaccttg gtgacagtct ctagt 345

<210> 27
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<212> PRT
<213> Artificial

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<223> The amino acid sequence of 8D2H14L2 light chain variable region

<400> 27

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

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Asp Arg Val Thr Ile Thr Cys Arg Thr Ser Glu Asn Ile Tyr Gly Gly
20 25 30

Leu Asn Trp Tyr Gln Arg Lys Pro Gly Lys Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Gly Ala Thr Asn Leu Ala Ser Gly Val Ser Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Asn Val Leu Arg Ser Pro Phe
85 90 95

Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 28
<211> 321
<212> DNA
<213> Artificial

<220>
<223> Nucleic acid sequence of 8D2H14L2 light chain variable region

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atcacatgtc gcacctcca aaacatctac gggggactga attggtatca gcgcaagccc 120
ggcaaatccc ctaagctgct gatctacggc gctaccaacc tggcatctgg ggtgtcctct 180
cgattttcag ggagcggcag cggcaccgac tatactctga ccattagttc actgcagcct 240
gaggatgtgg ccacatacta ttgccagaat gtcctgagat caccattcac ttttgggagc 300
ggaaccaaac tggaaattaa g 321

<210> 29
<211> 8
<212> PRT
<213> Artificial

<220>
<223> 14C12HCDR1

<400> 29
Gly Phe Ala Phe Ser Ser Tyr Asp
1 5

<210> 30
<211> 8
<212> PRT
<213> Artificial

<220>
<223> 14C12HCDR2

<400> 30

Ile Ser Gly Gly Gly Arg Tyr Thr
1 5

<210> 31

<211> 11

<212> PRT

<213> Artificial

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<223> 14C12HCDR3

<400> 31

Ala Asn Arg Tyr Gly Glu Ala Trp Phe Ala Tyr
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<210> 32

<211> 6

<212> PRT

<213> Artificial

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<223> 14C12LCDR1

<400> 32

Gln Asp Ile Asn Thr Tyr
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<210> 33

<211> 3

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<213> Artificial

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<223> 14C12LCDR2

<400> 33

Arg Ala Asn
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<210> 34

<211> 9

<212> PRT

<213> Artificial

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<223> 14C12LCDR3

<400> 34

Leu Gln Tyr Asp Glu Phe Pro Leu Thr
1 5

<210> 35

<211> 8

<212> PRT

<213> Artificial

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<223> 4G10HCDR1

<400> 35

Gly Tyr Ser Phe Thr Gly Tyr Thr
1 5

<210> 36

<211> 8

<212> PRT

<213> Artificial

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<223> 4G10HCR2

<400> 36

Ile Asn Pro Tyr Asn Asn Ile Thr
1 5

<210> 37

<211> 8

<212> PRT

<213> Artificial

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<223> 4G10HCDR3

<400> 37

Ala Arg Leu Asp Tyr Arg Ser Tyr
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<210> 38

<211> 9

<212> PRT

<213> Artificial

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<223> 4G10LCDR1

<400> 38

Thr Gly Ala Val Thr Thr Ser Asn Phe
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<210> 39

<211> 3

<212> PRT

<213> Artificial

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<223> 4G10LCDR2

<400> 39

Gly Thr Asn
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<210> 40

<211> 9

<212> PRT

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<223> 4G10LCDR3

<400> 40

Ala Leu Trp Tyr Ser Asn His Trp Val
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<210> 41

<211> 8

<212> PRT

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<220>

<223> 4G10H4L3HCDR2

<400> 41

Ile Asn Pro Tyr Asn Asp Ile Thr
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<210> 42

<211> 8

<212> PRT

<213> Artificial

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<223> 8D2H14L2HCDR1

<400> 42

Gly Phe Thr Phe Ser Asp Asn Trp
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<210> 43

<211> 10

<212> PRT

<213> Artificial

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<223> 8D2H14L2HCDR2

<400> 43

Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr
1 5 10

<210> 44

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