

CLAIMS:

1. An isolated or purified T-cell receptor (TCR) comprising the amino acid sequences of
 - (a) all of SEQ ID NOs: 1-3,
 - (b) all of SEQ ID NOs: 4-6,
 - (c) all of SEQ ID NOs: 31-33,
 - (d) all of SEQ ID NOs: 34-36,
 - (e) all of SEQ ID NOs: 64-66,
 - (f) all of SEQ ID NOs: 67-69,
 - (g) all of SEQ ID NOs: 1-6,
 - (h) all of SEQ ID NOs: 31-36, or
 - (i) all of SEQ ID NOs: 64-69,wherein the TCR has antigenic specificity for a mutated human RAS amino acid sequence presented by a human leukocyte antigen (HLA) Class I molecule, and
wherein the mutated human RAS amino acid sequence is a mutated human Kirsten rat sarcoma viral oncogene homolog (KRAS), a mutated human Harvey rat sarcoma viral oncogene homolog (HRAS), or a mutated human Neuroblastoma rat sarcoma viral oncogene homolog (NRAS) amino acid sequence.
2. The isolated or purified TCR according to claim 1, wherein the mutated human RAS amino acid sequence is SEQ ID NO: 29 or SEQ ID NO: 30.
3. The isolated or purified TCR according to claim 1 or 2, wherein the TCR does not have antigenic specificity for the wild-type human RAS amino acid sequence of one or both of SEQ ID NO: 26 and SEQ ID NO: 27.
4. The isolated or purified TCR according to any one of claims 1-3, wherein the HLA Class I molecule is an HLA-C molecule.

5. The isolated or purified TCR according to any one of claims 1-4, wherein the HLA Class I molecule is an HLA-C*01 molecule.

6. The isolated or purified TCR according to any one of claims 1-5, wherein the HLA Class I molecule is an HLA-C*01:02 molecule.

7. The isolated or purified TCR according to any one of claims 1-6, comprising:

(i) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 7;

(ii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 8;

(iii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 90;

(iv) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 91;

(v) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 37;

(vi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 38;

(vii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 92;

(viii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 93;

(ix) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 70;

(x) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 71;

(xi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 132;

(xii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 133;

- (xiii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 47;
- (xiv) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 48;
- (xv) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 94;
- (xvi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 85;
- (xvii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 95;
- (xviii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 49;
- (xix) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 50;
- (xx) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 96;
- (xxi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 87;
- (xxii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 97;
- (xxiii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 72;
- (xxvi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 73;
- (xxv) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 88;
- (xxvi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 89;
- (xxvii) both (i) and (ii), both (i) and (iv), both (ii) and (iii), both (iii) and (iv), both (v) and (vi), both (v) and (viii), both (vi) and (vii), both (vii) and (viii), both (ix) and (x), both (ix) and (xii), both (x) and (xi), both (xi) and (xii), both (xiii) and (xiv), both (xiii) and (xvi),

both (xiii) and (xvii), both (xiv) and (xv), both (xv) and (xvi), both (xv) and (xvii), both (xviii) and (xix), both (xviii) and (xxi), both (xviii) and (xxii), both (xix) and (xx), both (xx) and (xxi), both (xx) and (xxii), both (xxiii) and (xxiv), both (xxiii) and (xxvi), both (xxiv) and (xxv), or both (xxv) and (xxvi).

8. The isolated or purified TCR according to any one of claims 1-7, comprising:

- (i) the amino acid sequence of SEQ ID NO: 7;
- (ii) the amino acid sequence of SEQ ID NO: 8;
- (iii) the amino acid sequence of SEQ ID NO: 90;
- (iv) the amino acid sequence of SEQ ID NO: 91;
- (v) the amino acid sequence of SEQ ID NO: 37;
- (vi) the amino acid sequence of SEQ ID NO: 38;
- (vii) the amino acid sequence of SEQ ID NO: 92;
- (viii) the amino acid sequence of SEQ ID NO: 93;
- (ix) the amino acid sequence of SEQ ID NO: 70;
- (x) the amino acid sequence of SEQ ID NO: 71;
- (xi) the amino acid sequence of SEQ ID NO: 132;
- (xii) the amino acid sequence of SEQ ID NO: 133;
- (xiii) the amino acid sequence of SEQ ID NO: 47;
- (xiv) the amino acid sequence of SEQ ID NO: 48;
- (xv) the amino acid sequence of SEQ ID NO: 94;
- (xvi) the amino acid sequence of SEQ ID NO: 85;
- (xvii) the amino acid sequence of SEQ ID NO: 95;
- (xviii) the amino acid sequence of SEQ ID NO: 49;
- (xix) the amino acid sequence of SEQ ID NO: 50;
- (xx) the amino acid sequence of SEQ ID NO: 96;
- (xxi) the amino acid sequence of SEQ ID NO: 87;
- (xxii) the amino acid sequence of SEQ ID NO: 97;
- (xxiii) the amino acid sequence of SEQ ID NO: 72;
- (xxvi) the amino acid sequence of SEQ ID NO: 73;

(xxv) the amino acid sequence of SEQ ID NO: 88;

(xxvi) the amino acid sequence of SEQ ID NO: 89;

(xxvii) both (i) and (ii), both (i) and (iv), both (ii) and (iii), both (iii) and (iv), both (v) and (vi), both (v) and (viii), both (vi) and (vii), both (vii) and (viii), both (ix) and (x), both (ix) and (xii), both (x) and (xi), both (xi) and (xii), both (xiii) and (xiv), both (xiii) and (xvi), both (xiii) and (xvii), both (xiv) and (xv), both (xv) and (xvi), both (xv) and (xvii), both (xviii) and (xix), both (xviii) and (xxi), both (xviii) and (xxii), both (xix) and (xx), both (xx) and (xxi), both (xx) and (xxii), both (xxiii) and (xxiv), both (xxiii) and (xxvi), both (xxiv) and (xxv), or both (xxv) and (xxvi).

9. The isolated or purified TCR according to any one of claims 1-8, further comprising:

(a) an α chain constant region comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 17, wherein:

(i) X at position 48 of SEQ ID NO: 17 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 17 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 17 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 17 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a β chain constant region comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 18, wherein X at position 57 of SEQ ID NO: 18 is Ser or Cys; or

(c) both (a) and (b) SEQ ID NO

10. The isolated or purified TCR according to any one of claims 1-9, further comprising:

(a) an α chain constant region comprising the amino acid sequence of SEQ ID NO: 17, wherein:

(i) X at position 48 of SEQ ID NO: 17 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 17 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 17 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 17 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a β chain constant region comprising the amino acid sequence of SEQ ID NO: 18, wherein X at position 57 of SEQ ID NO: 18 is Ser or Cys; or

(c) both (a) and (b) SEQ ID NO

11. The isolated or purified TCR according to any one of claims 1-10, comprising:

(a) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 21, wherein:

(i) X at position 180 of SEQ ID NO: 21 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 21 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 21 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 21 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 22, wherein X at position 190 of SEQ ID NO: 22 is Ser or Cys;

(c) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 100, wherein:

(i) X at position 180 of SEQ ID NO: 100 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 100 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 100 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 100 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(d) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 101, wherein X at position 190 of SEQ ID NO: 101 is Ser or Cys;

(e) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 41, wherein:

(i) X at position 181 of SEQ ID NO: 41 is Thr or Cys;

(ii) X at position 245 of SEQ ID NO: 41 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 247 of SEQ ID NO: 41 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 248 of SEQ ID NO: 41 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(f) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 42, wherein X at position 195 of SEQ ID NO: 42 is Ser or Cys;

(g) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 106, wherein:

(i) X at position 181 of SEQ ID NO: 106 is Thr or Cys;

(ii) X at position 245 of SEQ ID NO: 106 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 247 of SEQ ID NO: 106 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 248 of SEQ ID NO: 106 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(h) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 107, wherein X at position 195 of SEQ ID NO: 107 is Ser or Cys;

(i) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 74, wherein:

- (i) X at position 180 of SEQ ID NO: 74 is Thr or Cys;
- (ii) X at position 244 of SEQ ID NO: 74 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (iii) X at position 246 of SEQ ID NO: 74 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
- (iv) X at position 247 of SEQ ID NO: 74 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (j) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 75, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;
- (k) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 136, wherein:
 - (i) X at position 180 of SEQ ID NO: 136 is Thr or Cys;
 - (ii) X at position 244 of SEQ ID NO: 136 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 246 of SEQ ID NO: 136 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 247 of SEQ ID NO: 136 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (l) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 137, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;
- (m) both (a) and (b); both (a) and (d); both (b) and (c); or both (c) and (d);
- (n) both (e) and (f); both (e) and h); both (f) and (g); or both (g) and (h);
- (n) both (i) and (j); both (i) and l); both (j) and (k); or both (k) and (l);
- (o) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 55, wherein:
 - (i) X at position 160 of SEQ ID NO: 55 is Thr or Cys;
 - (ii) X at position 224 of SEQ ID NO: 55 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

- (iii) X at position 226 of SEQ ID NO: 55 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
- (iv) X at position 227 of SEQ ID NO: 55 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (p) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 56, wherein X at position 168 of SEQ ID NO: 56 is Ser or Cys;
- (q) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 112, wherein:
 - (i) X at position 159 of SEQ ID NO: 112 is Thr or Cys;
 - (ii) X at position 223 of SEQ ID NO: 112 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 225 of SEQ ID NO: 112 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 226 of SEQ ID NO: 112 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (r) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 113, wherein X at position 173 of SEQ ID NO: 113 is Ser or Cys;
- (s) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 57, wherein:
 - (i) X at position 160 of SEQ ID NO: 57 is Thr or Cys;
 - (ii) X at position 224 of SEQ ID NO: 57 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 226 of SEQ ID NO: 57 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 227 of SEQ ID NO: 57 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (t) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 58, wherein X at position 173 of SEQ ID NO: 58 is Ser or Cys;

(u) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 118, wherein:

(i) X at position 161 of SEQ ID NO: 118 is Thr or Cys;

(ii) X at position 225 of SEQ ID NO: 118 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 227 of SEQ ID NO: 118 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 228 of SEQ ID NO: 118 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(v) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 119, wherein X at position 103178 of SEQ ID NO: 119 is Ser or Cys;

(w) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 76, wherein:

(i) X at position 159 of SEQ ID NO: 76 is Thr or Cys;

(ii) X at position 223 of SEQ ID NO: 76 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 225 of SEQ ID NO: 76 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 226 of SEQ ID NO: 76 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(x) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 77, wherein X at position 168 of SEQ ID NO: 77 is Ser or Cys;

(y) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 144, wherein:

(i) X at position 160 of SEQ ID NO: 144 is Thr or Cys;

(ii) X at position 224 of SEQ ID NO: 144 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 226 of SEQ ID NO: 144 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 227 of SEQ ID NO: 144 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(z) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 145, wherein X at position 166 of SEQ ID NO: 145 is Ser or Cys;

(aa) both (o) and (p); or both (q) and (r);

(bb) both (s) and (t); or both (u) and (v);

(cc) both (w) and (x); or both (y) and (z);

(dd) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 51;

(ee) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 52;

(ff) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 114;

(gg) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 115;

(hh) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 128;

(ii) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 129;

(jj) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 116;

(kk) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 117;

(ll) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 53;

(mm) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 54;

(nn) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 120;

(oo) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 121;

(pp) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 130;

(qq) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 131;

(rr) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 122;

(ss) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 123;

(tt) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 80;

(uu) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 81;

(vv) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 146;

(ww) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 146;

(xx) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 142;

(yy) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 143;

(zz) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 148;

(aaa) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 149;

(bbb) both (dd) and (ee); both (ff) and (gg); both (hh) and (ii); or both (jj) and (kk);

(ccc) both (ll) and (mm); both (nn) and (oo); both (pp) and (qq); or both (rr) and (ss);

(ddd) both (tt) and (uu); both (vv) and (ww); both (xx) and (yy); or both (zz) and

(aaa);

(eee) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 23;

(fff) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 24;

(ggg) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 102;

(hhh) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 103;

(iii) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 124;

(jjj) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 125;

(kkk) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 104;

(lll) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 105;

(mmm) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 39;

(nnn) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 40;

(ooo) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 108;

(ppp) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 109;

(qqq) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 126;

(rrr) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 127;

(sss) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 110;

(ttt) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 111;

(uuu) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 78;

(vvv) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 79;

(www) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 138;

(xxx) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 139;

(yyy) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 134;

(zzz) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 135;

(aaaa) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 140;

(bbbb) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 141;

(dddd) both (eee) and (fff); both (eee) and (hhh); both (fff) and (ggg); both (ggg) and (hhh); both (iii) and (jjj); both (iii) and (lll); both (jjj) and (kkk); or both (kkk) and (lll);

(eeee) both (mmm) and (nnn); both (mmm) and (ppp); both (nnn) and (ooo); both (ooo) and (ppp); both (qqq) and (rrr); both (qqq) and (ttt); both (rrr) and (sss); or both (sss) and (ttt); or

(ffff) both (uuu) and (vvv); both (uuu) and (xxx); both (vvv) and (www); both (www) and (xxx); both (yyy) and (zzz); both (yyy) and (bbbb); both (yyy) and (aaaa); or both (aaaa) and (bbbb).

12. The isolated or purified TCR

according to any one of claims 1-11, comprising:

(a) an α chain comprising the amino acid sequence of SEQ ID NO: 21, wherein:

(i) X at position 180 of SEQ ID NO: 21 is Thr or Cys;

- (ii) X at position 244 of SEQ ID NO: 21 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (iii) X at position 246 of SEQ ID NO: 21 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
- (iv) X at position 247 of SEQ ID NO: 21 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (b) a β chain comprising the amino acid sequence of SEQ ID NO: 22, wherein X at position 190 of SEQ ID NO: 22 is Ser or Cys;
- (c) an α chain comprising the amino acid sequence of SEQ ID NO: 100, wherein:
 - (i) X at position 180 of SEQ ID NO: 100 is Thr or Cys;
 - (ii) X at position 244 of SEQ ID NO: 100 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 246 of SEQ ID NO: 100 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 247 of SEQ ID NO: 100 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (d) a β chain comprising the amino acid sequence of SEQ ID NO: 101, wherein X at position 190 of SEQ ID NO: 101 is Ser or Cys;
- (e) an α chain comprising the amino acid sequence of SEQ ID NO: 41, wherein:
 - (i) X at position 181 of SEQ ID NO: 41 is Thr or Cys;
 - (ii) X at position 245 of SEQ ID NO: 41 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 247 of SEQ ID NO: 41 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 248 of SEQ ID NO: 41 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (f) a β chain comprising the amino acid sequence of SEQ ID NO: 42, wherein X at position 195 of SEQ ID NO: 42 is Ser or Cys;
- (g) an α chain comprising the amino acid sequence of SEQ ID NO: 106, wherein:
 - (i) X at position 181 of SEQ ID NO: 106 is Thr or Cys;

- (ii) X at position 245 of SEQ ID NO: 106 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (iii) X at position 247 of SEQ ID NO: 106 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
- (iv) X at position 248 of SEQ ID NO: 106 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (h) a β chain comprising the amino acid sequence of SEQ ID NO: 107, wherein X at position 195 of SEQ ID NO: 107 is Ser or Cys;
- (i) an α chain comprising the amino acid sequence of SEQ ID NO: 74, wherein:
 - (i) X at position 180 of SEQ ID NO: 74 is Thr or Cys;
 - (ii) X at position 244 of SEQ ID NO: 74 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 246 of SEQ ID NO: 74 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 247 of SEQ ID NO: 74 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (j) a β chain comprising the amino acid sequence of SEQ ID NO: 75, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;
- (k) an α chain comprising the amino acid sequence of SEQ ID NO: 136, wherein:
 - (i) X at position 180 of SEQ ID NO: 136 is Thr or Cys;
 - (ii) X at position 244 of SEQ ID NO: 136 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 246 of SEQ ID NO: 136 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 247 of SEQ ID NO: 136 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (l) a β chain comprising the amino acid sequence of SEQ ID NO: 137, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;
- (m) both (a) and (b); both (a) and (d); both (b) and (c); or both (c) and (d);
- (n) both (e) and (f); both (e) and h); both (f) and (g); or both (g) and (h);
- (n) both (i) and (j); both (i) and l); both (j) and (k); or both (k) and (l);

- (o) an α chain comprising the amino acid sequence of SEQ ID NO: 55, wherein:
 - (i) X at position 160 of SEQ ID NO: 55 is Thr or Cys;
 - (ii) X at position 224 of SEQ ID NO: 55 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 226 of SEQ ID NO: 55 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 227 of SEQ ID NO: 55 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (p) a β chain comprising the amino acid sequence of SEQ ID NO: 56, wherein X at position 168 of SEQ ID NO: 56 is Ser or Cys;
- (q) an α chain comprising the amino acid sequence of SEQ ID NO: 112, wherein:
 - (i) X at position 159 of SEQ ID NO: 112 is Thr or Cys;
 - (ii) X at position 223 of SEQ ID NO: 112 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 225 of SEQ ID NO: 112 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 226 of SEQ ID NO: 112 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (r) a β chain comprising the amino acid sequence of SEQ ID NO: 113, wherein X at position 173 of SEQ ID NO: 113 is Ser or Cys;
- (s) an α chain comprising the amino acid sequence of SEQ ID NO: 57, wherein:
 - (i) X at position 160 of SEQ ID NO: 57 is Thr or Cys;
 - (ii) X at position 224 of SEQ ID NO: 57 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 226 of SEQ ID NO: 57 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 227 of SEQ ID NO: 57 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (t) a β chain comprising the amino acid sequence of SEQ ID NO: 58, wherein X at position 173 of SEQ ID NO: 58 is Ser or Cys;
- (u) an α chain comprising the amino acid sequence of SEQ ID NO: 118, wherein:

- (i) X at position 161 of SEQ ID NO: 118 is Thr or Cys;
- (ii) X at position 225 of SEQ ID NO: 118 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (iii) X at position 227 of SEQ ID NO: 118 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
- (iv) X at position 228 of SEQ ID NO: 118 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (v) a β chain comprising the amino acid sequence of SEQ ID NO: 119, wherein X at position 103178 of SEQ ID NO: 119 is Ser or Cys;
- (w) an α chain comprising the amino acid sequence of SEQ ID NO: 76, wherein:
 - (i) X at position 159 of SEQ ID NO: 76 is Thr or Cys;
 - (ii) X at position 223 of SEQ ID NO: 76 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 225 of SEQ ID NO: 76 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 226 of SEQ ID NO: 76 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (x) a β chain comprising the amino acid sequence of SEQ ID NO: 77, wherein X at position 168 of SEQ ID NO: 77 is Ser or Cys;
- (y) an α chain comprising the amino acid sequence of SEQ ID NO: 144, wherein:
 - (i) X at position 160 of SEQ ID NO: 144 is Thr or Cys;
 - (ii) X at position 224 of SEQ ID NO: 144 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 226 of SEQ ID NO: 144 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 227 of SEQ ID NO: 144 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (z) a β chain comprising the amino acid sequence of SEQ ID NO: 145, wherein X at position 166 of SEQ ID NO: 145 is Ser or Cys;
- (aa) both (o) and (p); or both (q) and (r);
- (bb) both (s) and (t); or both (u) and (v);

- (cc) both (w) and (x); or both (y) and (z);
- (dd) an α chain comprising the amino acid sequence of SEQ ID NO: 51;
- (ee) a β chain comprising the amino acid sequence of SEQ ID NO: 52;
- (ff) an α chain comprising the amino acid sequence of SEQ ID NO: 114;
- (gg) a β chain comprising the amino acid sequence of SEQ ID NO: 115;
- (hh) an α chain comprising the amino acid sequence of SEQ ID NO: 128;
- (ii) a β chain comprising the amino acid sequence of SEQ ID NO: 129;
- (jj) an α chain comprising the amino acid sequence of SEQ ID NO: 116;
- (kk) a β chain comprising the amino acid sequence of SEQ ID NO: 117;
- (ll) an α chain comprising the amino acid sequence of SEQ ID NO: 53;
- (mm) a β chain comprising the amino acid sequence of SEQ ID NO: 54;
- (nn) an α chain comprising the amino acid sequence of SEQ ID NO: 120;
- (oo) a β chain comprising the amino acid sequence of SEQ ID NO: 121;
- (pp) an α chain comprising the amino acid sequence of SEQ ID NO: 130;
- (qq) a β chain comprising the amino acid sequence of SEQ ID NO: 131;
- (rr) an α chain comprising the amino acid sequence of SEQ ID NO: 122;
- (ss) a β chain comprising the amino acid sequence of SEQ ID NO: 123;
- (tt) an α chain comprising the amino acid sequence of SEQ ID NO: 80;
- (uu) a β chain comprising the amino acid sequence of SEQ ID NO: 81;
- (vv) an α chain comprising the amino acid sequence of SEQ ID NO: 146;
- (ww) a β chain comprising the amino acid sequence of SEQ ID NO: 146;
- (xx) an α chain comprising the amino acid sequence of SEQ ID NO: 142;
- (yy) a β chain comprising the amino acid sequence of SEQ ID NO: 143;
- (zz) an α chain comprising the amino acid sequence of SEQ ID NO: 148;
- (aaa) a β chain comprising the amino acid sequence of SEQ ID NO: 149;
- (bbb) both (dd) and (ee); both (ff) and (gg); both (hh) and (ii); or both (jj) and (kk);
- (ccc) both (ll) and (mm); both (nn) and (oo); both (pp) and (qq); or both (rr) and (ss);
- (ddd) both (tt) and (uu); both (vv) and (ww); both (xx) and (yy); or both (zz) and (aaa);
- (eee) an α chain comprising the amino acid sequence of SEQ ID NO: 23;
- (fff) a β chain comprising the amino acid sequence of SEQ ID NO: 24;

(ggg) an α chain comprising the amino acid sequence of SEQ ID NO: 102;
 (hhh) a β chain comprising the amino acid sequence of SEQ ID NO: 103;
 (iii) an α chain comprising the amino acid sequence of SEQ ID NO: 124;
 (jjj) a β chain comprising the amino acid sequence of SEQ ID NO: 125;
 (kkk) an α chain comprising the amino acid sequence of SEQ ID NO: 104;
 (lll) a β chain comprising the amino acid sequence of SEQ ID NO: 105;
 (mmm) an α chain comprising the amino acid sequence of SEQ ID NO: 39;
 (nnn) a β chain comprising the amino acid sequence of SEQ ID NO: 40;
 (ooo) an α chain comprising the amino acid sequence of SEQ ID NO: 108;
 (ppp) a β chain comprising the amino acid sequence of SEQ ID NO: 109;
 (qqq) an α chain comprising the amino acid sequence of SEQ ID NO: 126;
 (rrr) a β chain comprising the amino acid sequence of SEQ ID NO: 127;
 (sss) an α chain comprising the amino acid sequence of SEQ ID NO: 110;
 (ttt) a β chain comprising the amino acid sequence of SEQ ID NO: 111;
 (uuu) an α chain comprising the amino acid sequence of SEQ ID NO: 78;
 (vvv) a β chain comprising the amino acid sequence of SEQ ID NO: 79;
 (www) an α chain comprising the amino acid sequence of SEQ ID NO: 138;
 (xxx) a β chain comprising the amino acid sequence of SEQ ID NO: 139;
 (yyy) an α chain comprising the amino acid sequence of SEQ ID NO: 134;
 (zzz) a β chain comprising the amino acid sequence of SEQ ID NO: 135;
 (aaaa) an α chain comprising the amino acid sequence of SEQ ID NO: 140;
 (bbbb) a β chain comprising the amino acid sequence of SEQ ID NO: 141;
 (dddd) both (eee) and (fff); both (eee) and (hhh); both (fff) and (ggg); both (ggg) and (hhh); both (iii) and (jjj); both (iii) and (lll); both (jjj) and (kkk); or both (kkk) and (lll);
 (eeee) both (mmm) and (nnn); both (mmm) and (ppp); both (nnn) and (ooo); both (ooo) and (ppp); both (qqq) and (rrr); both (qqq) and (ttt); both (rrr) and (sss); or both (sss) and (ttt); or
 (ffff) both (uuu) and (vvv); both (uuu) and (xxx); both (vvv) and (www); both (www) and (xxx); both (yyy) and (zzz); both (yyy) and (bbbb); both (yyy) and (aaaa); or both (aaaa) and (bbbb).

13. An isolated or purified polypeptide comprising a functional portion of the TCR according to any one of claims 1-12, wherein the functional portion comprises the amino acid sequences of:

- (a) all of SEQ ID NOs: 1-3,
- (b) all of SEQ ID NOs: 4-6,
- (c) all of SEQ ID NOs: 31-33,
- (d) all of SEQ ID NOs: 34-36,
- (e) all of SEQ ID NOs: 64-66,
- (f) all of SEQ ID NOs: 67-69
- (g) all of SEQ ID NOs: 1-6,
- (h) all of SEQ ID NOs: 31-36, or
- (i) all of SEQ ID NOs: 64-69.

14. The isolated or purified polypeptide according to claim 13, wherein the functional portion comprises:

- (i) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 7;
- (ii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 8;
- (iii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 90;
- (iv) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 91;
- (v) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 37;
- (vi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 38;
- (vii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 92;
- (viii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 93;

- (ix) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 70;
- (x) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 71;
- (xi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 132;
- (xii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 133;
- (xiii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 47;
- (xiv) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 48;
- (xv) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 94;
- (xvi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 85;
- (xvii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 95;
- (xviii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 49;
- (xix) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 50;
- (xx) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 96;
- (xxi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 87;
- (xxii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 97;
- (xxiii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 72;

(xxvi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 73;

(xxv) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 88;

(xxvi) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 89;

(xxvii) both (i) and (ii), both (i) and (iv), both (ii) and (iii), both (iii) and (iv), both (v) and (vi), both (v) and (viii), both (vi) and (vii), both (vii) and (viii), both (ix) and (x), both (ix) and (xii), both (x) and (xi), both (xi) and (xii), both (xiii) and (xiv), both (xiii) and (xvi), both (xiii) and (xvii), both (xiv) and (xv), both (xv) and (xvi), both (xv) and (xvii), both (xviii) and (xix), both (xviii) and (xxi), both (xviii) and (xxii), both (xix) and (xx), both (xx) and (xxi), both (xx) and (xxii), both (xxiii) and (xxiv), both (xxiii) and (xxvi), both (xxiv) and (xxv), or both (xxv) and (xxvi).

15. The isolated or purified polypeptide according to claim 13 or 14, wherein the functional portion comprises:

- (i) the amino acid sequence of SEQ ID NO: 7;
- (ii) the amino acid sequence of SEQ ID NO: 8;
- (iii) the amino acid sequence of SEQ ID NO: 90;
- (iv) the amino acid sequence of SEQ ID NO: 91;
- (v) the amino acid sequence of SEQ ID NO: 37;
- (vi) the amino acid sequence of SEQ ID NO: 38;
- (vii) the amino acid sequence of SEQ ID NO: 92;
- (viii) the amino acid sequence of SEQ ID NO: 93;
- (ix) the amino acid sequence of SEQ ID NO: 70;
- (x) the amino acid sequence of SEQ ID NO: 71;
- (xi) the amino acid sequence of SEQ ID NO: 132;
- (xii) the amino acid sequence of SEQ ID NO: 133;
- (xiii) the amino acid sequence of SEQ ID NO: 47;
- (xiv) the amino acid sequence of SEQ ID NO: 48;
- (xv) the amino acid sequence of SEQ ID NO: 94;

- (xvi) the amino acid sequence of SEQ ID NO: 85;
- (xvii) the amino acid sequence of SEQ ID NO: 95;
- (xviii) the amino acid sequence of SEQ ID NO: 49;
- (xix) the amino acid sequence of SEQ ID NO: 50;
- (xx) the amino acid sequence of SEQ ID NO: 96;
- (xxi) the amino acid sequence of SEQ ID NO: 87;
- (xxii) the amino acid sequence of SEQ ID NO: 97;
- (xxiii) the amino acid sequence of SEQ ID NO: 72;
- (xxvi) the amino acid sequence of SEQ ID NO: 73;
- (xxv) the amino acid sequence of SEQ ID NO: 88;
- (xxvi) the amino acid sequence of SEQ ID NO: 89;

(xxvii) both (i) and (ii), both (i) and (iv), both (ii) and (iii), both (iii) and (iv), both (v) and (vi), both (v) and (viii), both (vi) and (vii), both (vii) and (viii), both (ix) and (x), both (ix) and (xii), both (x) and (xi), both (xi) and (xii), both (xiii) and (xiv), both (xiii) and (xvi), both (xiii) and (xvii), both (xiv) and (xv), both (xv) and (xvi), both (xv) and (xvii), both (xviii) and (xix), both (xviii) and (xxi), both (xviii) and (xxii), both (xix) and (xx), both (xx) and (xxi), both (xx) and (xxii), both (xxiii) and (xxiv), both (xxiii) and (xxvi), both (xxiv) and (xxv), or both (xxv) and (xxvi).

16. The isolated or purified polypeptide according to any one of claims 13-15, further comprising:

(a) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 17, wherein:

- (i) X at position 48 of SEQ ID NO: 17 is Thr or Cys;
- (ii) X at position 112 of SEQ ID NO: 17 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (iii) X at position 114 of SEQ ID NO: 17 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
- (iv) X at position 115 of SEQ ID NO: 17 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 18, wherein X at position 57 of SEQ ID NO: 18 is Ser or Cys; or

(c) both (a) and (b).

17. The isolated or purified polypeptide according to any one of claims 13-16, further comprising:

(a) the amino acid sequence of SEQ ID NO: 17, wherein:

(i) X at position 48 of SEQ ID NO: 17 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 17 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 17 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 17 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) the amino acid sequence of SEQ ID NO: 18, wherein X at position 57 of SEQ ID NO: 18 is Ser or Cys; or

(c) both (a) and (b).

18. The isolated or purified polypeptide according to any one of claims 13-17, comprising:

(a) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 21, wherein:

(i) X at position 180 of SEQ ID NO: 21 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 21 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 21 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 21 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 22, wherein X at position 190 of SEQ ID NO: 22 is Ser or Cys;

(c) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 100, wherein:

(i) X at position 180 of SEQ ID NO: 100 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 100 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 100 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 100 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(d) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 101, wherein X at position 190 of SEQ ID NO: 101 is Ser or Cys;

(e) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 41, wherein:

(i) X at position 181 of SEQ ID NO: 41 is Thr or Cys;

(ii) X at position 245 of SEQ ID NO: 41 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 247 of SEQ ID NO: 41 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 248 of SEQ ID NO: 41 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(f) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 42, wherein X at position 195 of SEQ ID NO: 42 is Ser or Cys;

(g) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 106, wherein:

(i) X at position 181 of SEQ ID NO: 106 is Thr or Cys;

(ii) X at position 245 of SEQ ID NO: 106 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 247 of SEQ ID NO: 106 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 248 of SEQ ID NO: 106 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(h) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 107, wherein X at position 195 of SEQ ID NO: 107 is Ser or Cys;

(i) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 74, wherein:

(i) X at position 180 of SEQ ID NO: 74 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 74 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 74 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 74 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(j) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 75, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;

(k) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 136, wherein:

(i) X at position 180 of SEQ ID NO: 136 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 136 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 136 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 136 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(l) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 137, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;

(m) both (a) and (b); both (a) and (d); both (b) and (c); or both (c) and (d);

(n) both (e) and (f); both (e) and h); both (f) and (g); or both (g) and (h);

(n) both (i) and (j); both (i) and l); both (j) and (k); or both (k) and (l);

(o) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 55, wherein:

(i) X at position 160 of SEQ ID NO: 55 is Thr or Cys;

(ii) X at position 224 of SEQ ID NO: 55 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 226 of SEQ ID NO: 55 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 227 of SEQ ID NO: 55 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(p) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 56, wherein X at position 168 of SEQ ID NO: 56 is Ser or Cys;

(q) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 112, wherein:

(i) X at position 159 of SEQ ID NO: 112 is Thr or Cys;

(ii) X at position 223 of SEQ ID NO: 112 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 225 of SEQ ID NO: 112 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 226 of SEQ ID NO: 112 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(r) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 113, wherein X at position 173 of SEQ ID NO: 113 is Ser or Cys;

(s) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 57, wherein:

(i) X at position 160 of SEQ ID NO: 57 is Thr or Cys;

(ii) X at position 224 of SEQ ID NO: 57 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 226 of SEQ ID NO: 57 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 227 of SEQ ID NO: 57 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(t) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 58, wherein X at position 173 of SEQ ID NO: 58 is Ser or Cys;

(u) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 118, wherein:

(i) X at position 161 of SEQ ID NO: 118 is Thr or Cys;

(ii) X at position 225 of SEQ ID NO: 118 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 227 of SEQ ID NO: 118 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 228 of SEQ ID NO: 118 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(v) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 119, wherein X at position 103178 of SEQ ID NO: 119 is Ser or Cys;

(w) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 76, wherein:

(i) X at position 159 of SEQ ID NO: 76 is Thr or Cys;

(ii) X at position 223 of SEQ ID NO: 76 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 225 of SEQ ID NO: 76 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

- (iv) X at position 226 of SEQ ID NO: 76 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (x) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 77, wherein X at position 168 of SEQ ID NO: 77 is Ser or Cys;
- (y) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 144, wherein:
 - (i) X at position 160 of SEQ ID NO: 144 is Thr or Cys;
 - (ii) X at position 224 of SEQ ID NO: 144 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 226 of SEQ ID NO: 144 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 227 of SEQ ID NO: 144 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (z) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 145, wherein X at position 166 of SEQ ID NO: 145 is Ser or Cys;
- (aa) both (o) and (p); or both (q) and (r);
- (bb) both (s) and (t); or both (u) and (v);
- (cc) both (w) and (x); or both (y) and (z);
- (dd) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 51;
- (ee) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 52;
- (ff) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 114;
- (gg) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 115;
- (hh) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 128;

(ii) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 129;

(jj) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 116;

(kk) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 117;

(ll) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 53;

(mm) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 54;

(nn) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 120;

(oo) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 121;

(pp) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 130;

(qq) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 131;

(rr) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 122;

(ss) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 123;

(tt) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 80;

(uu) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 81;

(vv) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 146;

(ww) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 146;

(xx) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 142;

(yy) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 143;

(zz) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 148;

(aaa) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 149;

(bbb) both (dd) and (ee); both (ff) and (gg); both (hh) and (ii); or both (jj) and (kk);

(ccc) both (ll) and (mm); both (nn) and (oo); both (pp) and (qq); or both (rr) and (ss);

(ddd) both (tt) and (uu); both (vv) and (ww); both (xx) and (yy); or both (zz) and (aaa);

(eee) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 23;

(fff) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 24;

(ggg) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 102;

(hhh) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 103;

(iii) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 124;

(jjj) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 125;

(kkk) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 104;

(lll) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 105;

(mmm) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 39;

(nnn) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 40;

(ooo) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 108;

(ppp) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 109;

(qqq) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 126;

(rrr) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 127;

(sss) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 110;

(ttt) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 111;

(uuu) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 78;

(vvv) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 79;

(www) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 138;

(xxx) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 139;

(yyy) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 134;

(zzz) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 135;

(aaaa) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 140;

(bbbb) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 141;

(dddd) both (eee) and (fff); both (eee) and (hhh); both (fff) and (ggg); both (ggg) and (hhh); both (iii) and (jjj); both (iii) and (lll); both (jjj) and (kkk); or both (kkk) and (lll);

(eeee) both (mmm) and (nnn); both (mmm) and (ppp); both (nnn) and (ooo); both (ooo) and (ppp); both (qqq) and (rrr); both (qqq) and (ttt); both (rrr) and (sss); or both (sss) and (ttt); or

(ffff) both (uuu) and (vvv); both (uuu) and (xxx); both (vvv) and (www); both (www) and (xxx); both (yyy) and (zzz); both (yyy) and (bbbb); both (yyy) and (aaaa); or both (aaaa) and (bbbb).

19. The isolated or purified polypeptide according to any one of claims 13-18, comprising:

(a) an α chain comprising the amino acid sequence of SEQ ID NO: 21, wherein:

(i) X at position 180 of SEQ ID NO: 21 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 21 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 21 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 21 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a β chain comprising the amino acid sequence of SEQ ID NO: 22, wherein X at position 190 of SEQ ID NO: 22 is Ser or Cys;

(c) an α chain comprising the amino acid sequence of SEQ ID NO: 100, wherein:

(i) X at position 180 of SEQ ID NO: 100 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 100 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 100 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 100 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(d) a β chain comprising the amino acid sequence of SEQ ID NO: 101, wherein X at position 190 of SEQ ID NO: 101 is Ser or Cys;

- (e) an α chain comprising the amino acid sequence of SEQ ID NO: 41, wherein:
 - (i) X at position 181 of SEQ ID NO: 41 is Thr or Cys;
 - (ii) X at position 245 of SEQ ID NO: 41 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 247 of SEQ ID NO: 41 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 248 of SEQ ID NO: 41 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (f) a β chain comprising the amino acid sequence of SEQ ID NO: 42, wherein X at position 195 of SEQ ID NO: 42 is Ser or Cys;
- (g) an α chain comprising the amino acid sequence of SEQ ID NO: 106, wherein:
 - (i) X at position 181 of SEQ ID NO: 106 is Thr or Cys;
 - (ii) X at position 245 of SEQ ID NO: 106 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 247 of SEQ ID NO: 106 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 248 of SEQ ID NO: 106 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (h) a β chain comprising the amino acid sequence of SEQ ID NO: 107, wherein X at position 195 of SEQ ID NO: 107 is Ser or Cys;
- (i) an α chain comprising the amino acid sequence of SEQ ID NO: 74, wherein:
 - (i) X at position 180 of SEQ ID NO: 74 is Thr or Cys;
 - (ii) X at position 244 of SEQ ID NO: 74 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 246 of SEQ ID NO: 74 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 247 of SEQ ID NO: 74 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (j) a β chain comprising the amino acid sequence of SEQ ID NO: 75, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;
- (k) an α chain comprising the amino acid sequence of SEQ ID NO: 136, wherein:

- (i) X at position 180 of SEQ ID NO: 136 is Thr or Cys;
- (ii) X at position 244 of SEQ ID NO: 136 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (iii) X at position 246 of SEQ ID NO: 136 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
- (iv) X at position 247 of SEQ ID NO: 136 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (l) a β chain comprising the amino acid sequence of SEQ ID NO: 137, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;
- (m) both (a) and (b); both (a) and (d); both (b) and (c); or both (c) and (d);
- (n) both (e) and (f); both (e) and h); both (f) and (g); or both (g) and (h);
- (n) both (i) and (j); both (i) and l); both (j) and (k); or both (k) and (l);
- (o) an α chain comprising the amino acid sequence of SEQ ID NO: 55, wherein:
 - (i) X at position 160 of SEQ ID NO: 55 is Thr or Cys;
 - (ii) X at position 224 of SEQ ID NO: 55 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 226 of SEQ ID NO: 55 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 227 of SEQ ID NO: 55 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (p) a β chain comprising the amino acid sequence of SEQ ID NO: 56, wherein X at position 168 of SEQ ID NO: 56 is Ser or Cys;
- (q) an α chain comprising the amino acid sequence of SEQ ID NO: 112, wherein:
 - (i) X at position 159 of SEQ ID NO: 112 is Thr or Cys;
 - (ii) X at position 223 of SEQ ID NO: 112 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 225 of SEQ ID NO: 112 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 226 of SEQ ID NO: 112 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(r) a β chain comprising the amino acid sequence of SEQ ID NO: 113, wherein X at position 173 of SEQ ID NO: 113 is Ser or Cys;

(s) an α chain comprising the amino acid sequence of SEQ ID NO: 57, wherein:

(i) X at position 160 of SEQ ID NO: 57 is Thr or Cys;

(ii) X at position 224 of SEQ ID NO: 57 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 226 of SEQ ID NO: 57 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 227 of SEQ ID NO: 57 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(t) a β chain comprising the amino acid sequence of SEQ ID NO: 58, wherein X at position 173 of SEQ ID NO: 58 is Ser or Cys;

(u) an α chain comprising the amino acid sequence of SEQ ID NO: 118, wherein:

(i) X at position 161 of SEQ ID NO: 118 is Thr or Cys;

(ii) X at position 225 of SEQ ID NO: 118 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 227 of SEQ ID NO: 118 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 228 of SEQ ID NO: 118 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(v) a β chain comprising the amino acid sequence of SEQ ID NO: 119, wherein X at position 103178 of SEQ ID NO: 119 is Ser or Cys;

(w) an α chain comprising the amino acid sequence of SEQ ID NO: 76, wherein:

(i) X at position 159 of SEQ ID NO: 76 is Thr or Cys;

(ii) X at position 223 of SEQ ID NO: 76 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 225 of SEQ ID NO: 76 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 226 of SEQ ID NO: 76 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

- (x) a β chain comprising the amino acid sequence of SEQ ID NO: 77, wherein X at position 168 of SEQ ID NO: 77 is Ser or Cys;
- (y) an α chain comprising the amino acid sequence of SEQ ID NO: 144, wherein:
 - (i) X at position 160 of SEQ ID NO: 144 is Thr or Cys;
 - (ii) X at position 224 of SEQ ID NO: 144 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 226 of SEQ ID NO: 144 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 227 of SEQ ID NO: 144 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (z) a β chain comprising the amino acid sequence of SEQ ID NO: 145, wherein X at position 166 of SEQ ID NO: 145 is Ser or Cys;
- (aa) both (o) and (p); or both (q) and (r);
- (bb) both (s) and (t); or both (u) and (v);
- (cc) both (w) and (x); or both (y) and (z);
- (dd) an α chain comprising the amino acid sequence of SEQ ID NO: 51;
- (ee) a β chain comprising the amino acid sequence of SEQ ID NO: 52;
- (ff) an α chain comprising the amino acid sequence of SEQ ID NO: 114;
- (gg) a β chain comprising the amino acid sequence of SEQ ID NO: 115;
- (hh) an α chain comprising the amino acid sequence of SEQ ID NO: 128;
- (ii) a β chain comprising the amino acid sequence of SEQ ID NO: 129;
- (jj) an α chain comprising the amino acid sequence of SEQ ID NO: 116;
- (kk) a β chain comprising the amino acid sequence of SEQ ID NO: 117;
- (ll) an α chain comprising the amino acid sequence of SEQ ID NO: 53;
- (mm) a β chain comprising the amino acid sequence of SEQ ID NO: 54;
- (nn) an α chain comprising the amino acid sequence of SEQ ID NO: 120;
- (oo) a β chain comprising the amino acid sequence of SEQ ID NO: 121;
- (pp) an α chain comprising the amino acid sequence of SEQ ID NO: 130;
- (qq) a β chain comprising the amino acid sequence of SEQ ID NO: 131;
- (rr) an α chain comprising the amino acid sequence of SEQ ID NO: 122;
- (ss) a β chain comprising the amino acid sequence of SEQ ID NO: 123;

(tt) an α chain comprising the amino acid sequence of SEQ ID NO: 80;
(uu) a β chain comprising the amino acid sequence of SEQ ID NO: 81;
(vv) an α chain comprising the amino acid sequence of SEQ ID NO: 146;
(ww) a β chain comprising the amino acid sequence of SEQ ID NO: 146;
(xx) an α chain comprising the amino acid sequence of SEQ ID NO: 142;
(yy) a β chain comprising the amino acid sequence of SEQ ID NO: 143;
(zz) an α chain comprising the amino acid sequence of SEQ ID NO: 148;
(aaa) a β chain comprising the amino acid sequence of SEQ ID NO: 149;
(bbb) both (dd) and (ee); both (ff) and (gg); both (hh) and (ii); or both (jj) and (kk);
(ccc) both (ll) and (mm); both (nn) and (oo); both (pp) and (qq); or both (rr) and (ss);
(ddd) both (tt) and (uu); both (vv) and (ww); both (xx) and (yy); or both (zz) and (aaa);
(eee) an α chain comprising the amino acid sequence of SEQ ID NO: 23;
(fff) a β chain comprising the amino acid sequence of SEQ ID NO: 24;
(ggg) an α chain comprising the amino acid sequence of SEQ ID NO: 102;
(hhh) a β chain comprising the amino acid sequence of SEQ ID NO: 103;
(iii) an α chain comprising the amino acid sequence of SEQ ID NO: 124;
(jjj) a β chain comprising the amino acid sequence of SEQ ID NO: 125;
(kkk) an α chain comprising the amino acid sequence of SEQ ID NO: 104;
(lll) a β chain comprising the amino acid sequence of SEQ ID NO: 105;
(mmm) an α chain comprising the amino acid sequence of SEQ ID NO: 39;
(nnn) a β chain comprising the amino acid sequence of SEQ ID NO: 40;
(ooo) an α chain comprising the amino acid sequence of SEQ ID NO: 108;
(ppp) a β chain comprising the amino acid sequence of SEQ ID NO: 109;
(qqq) an α chain comprising the amino acid sequence of SEQ ID NO: 126;
(rrr) a β chain comprising the amino acid sequence of SEQ ID NO: 127;
(sss) an α chain comprising the amino acid sequence of SEQ ID NO: 110;
(ttt) a β chain comprising the amino acid sequence of SEQ ID NO: 111;
(uuu) an α chain comprising the amino acid sequence of SEQ ID NO: 78;
(vvv) a β chain comprising the amino acid sequence of SEQ ID NO: 79;
(www) an α chain comprising the amino acid sequence of SEQ ID NO: 138;

(xxx) a β chain comprising the amino acid sequence of SEQ ID NO: 139;
(yyy) an α chain comprising the amino acid sequence of SEQ ID NO: 134;
(zzz) a β chain comprising the amino acid sequence of SEQ ID NO: 135;
(aaaa) an α chain comprising the amino acid sequence of SEQ ID NO: 140;
(bbbb) a β chain comprising the amino acid sequence of SEQ ID NO: 141;
(dddd) both (eee) and (fff); both (eee) and (hhh); both (fff) and (ggg); both (ggg) and (hhh); both (iii) and (jjj); both (iii) and (lll); both (jjj) and (kkk); or both (kkk) and (lll);
(eeee) both (mmm) and (nnn); both (mmm) and (ppp); both (nnn) and (ooo); both (ooo) and (ppp); both (qqq) and (rrr); both (qqq) and (ttt); both (rrr) and (sss); or both (sss) and (ttt); or
(ffff) both (uuu) and (vvv); both (uuu) and (xxx); both (vvv) and (www); both (www) and (xxx); both (yyy) and (zzz); both (yyy) and (bbbb); both (yyy) and (aaaa); or both (aaaa) and (bbbb).

20. An isolated or purified protein comprising at least one of the polypeptides according to any one of claims 13-19.

21. The isolated or purified protein according to claim 20, comprising:

(a) a first polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 1-3 and a second polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 4-6;

(b) a first polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 31-33 and a second polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 34-36; or

(c) a first polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 64-66 and a second polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 67-69.

22. The isolated or purified protein according to claim 20 or 21, comprising:

(i) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 7;

- (ii) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 8;
- (iii) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 90;
- (iv) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 91;
- (v) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 37;
- (vi) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 38;
- (vii) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 92;
- (viii) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 93;
- (ix) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 70;
- (x) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 71;
- (xi) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 132;
- (xii) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 133;
- (xiii) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 47;
- (xiv) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 48;
- (xv) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 94;
- (xvi) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 85;

(xvii) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 95;

(xviii) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 49;

(xix) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 50;

(xx) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 96;

(xxi) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 87;

(xxii) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 97;

(xxiii) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 72;

(xxvi) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 73;

(xxv) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 88;

(xxvi) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 89;

(xxvii) both (i) and (ii), both (i) and (iv), both (ii) and (iii), both (iii) and (iv), both (v) and (vi), both (v) and (viii), both (vi) and (vii), both (vii) and (viii), both (ix) and (x), both (ix) and (xii), both (x) and (xi), both (xi) and (xii), both (xiii) and (xiv), both (xiii) and (xvi), both (xiii) and (xvii), both (xiv) and (xv), both (xv) and (xvi), both (xv) and (xvii), both (xviii) and (xix), both (xviii) and (xxi), both (xviii) and (xxii), both (xix) and (xx), both (xx) and (xxi), both (xx) and (xxii), both (xxiii) and (xxiv), both (xxiii) and (xxvi), both (xxiv) and (xxv), or both (xxv) and (xxvi).

23. The isolated or purified protein according to any one of claims 20-22, comprising:

(i) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 7;

- (ii) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 8;
- (iii) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 90;
- (iv) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 91;
- (v) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 37;
- (vi) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 38;
- (vii) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 92;
- (viii) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 93;
- (ix) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 70;
- (x) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 71;
- (xi) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 132;
- (xii) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 133;
- (xiii) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 47;
- (xiv) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 48;
- (xv) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 94;
- (xvi) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 85;
- (xvii) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 95;
- (xviii) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 49;
- (xix) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 50;

- (xx) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 96;
(xxi) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 87;
(xxii) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 97;
(xxiii) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 72;
(xxvi) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 73;
(xxv) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 88;
(xxvi) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 89;
(xxvii) both (i) and (ii), both (i) and (iv), both (ii) and (iii), both (iii) and (iv), both (v) and (vi), both (v) and (viii), both (vi) and (vii), both (vii) and (viii), both (ix) and (x), both (ix) and (xii), both (x) and (xi), both (xi) and (xii), both (xiii) and (xiv), both (xiii) and (xvi), both (xiii) and (xvii), both (xiv) and (xv), both (xv) and (xvi), both (xv) and (xvii), both (xviii) and (xix), both (xviii) and (xxi), both (xviii) and (xxii), both (xix) and (xx), both (xx) and (xxi), both (xx) and (xxii), both (xxiii) and (xxiv), both (xxiii) and (xxvi), both (xxiv) and (xxv), or both (xxv) and (xxvi).

24. The isolated or purified protein according to any one of claims 20-23, further comprising:

(a) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 17, wherein:

- (i) X at position 48 of SEQ ID NO: 17 is Thr or Cys;
(ii) X at position 112 of SEQ ID NO: 17 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
(iii) X at position 114 of SEQ ID NO: 17 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 17 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 18, wherein X at position 57 of SEQ ID NO: 18 is Ser or Cys; or

(c) both (a) and (b).

25. The isolated or purified protein according to any one of claims 20-24, further comprising:

(a) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 17, wherein:

(i) X at position 48 of SEQ ID NO: 17 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 17 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 17 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 17 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 18, wherein X at position 57 of SEQ ID NO: 18 is Ser or Cys; or

(c) both (a) and (b).

26. The isolated or purified protein according to any one of claims 20-25, comprising:

(a) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 21, wherein:

(i) X at position 180 of SEQ ID NO: 21 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 21 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 21 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

- (iv) X at position 247 of SEQ ID NO: 21 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (b) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 22, wherein X at position 190 of SEQ ID NO: 22 is Ser or Cys;
- (c) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 100, wherein:
 - (i) X at position 180 of SEQ ID NO: 100 is Thr or Cys;
 - (ii) X at position 244 of SEQ ID NO: 100 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 246 of SEQ ID NO: 100 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 247 of SEQ ID NO: 100 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (d) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 101, wherein X at position 190 of SEQ ID NO: 101 is Ser or Cys;
- (e) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 41, wherein:
 - (i) X at position 181 of SEQ ID NO: 41 is Thr or Cys;
 - (ii) X at position 245 of SEQ ID NO: 41 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 247 of SEQ ID NO: 41 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 248 of SEQ ID NO: 41 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (f) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 42, wherein X at position 195 of SEQ ID NO: 42 is Ser or Cys;
- (g) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 106, wherein:

- (i) X at position 181 of SEQ ID NO: 106 is Thr or Cys;
- (ii) X at position 245 of SEQ ID NO: 106 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (iii) X at position 247 of SEQ ID NO: 106 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
- (iv) X at position 248 of SEQ ID NO: 106 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (h) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 107, wherein X at position 195 of SEQ ID NO: 107 is Ser or Cys;
- (i) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 74, wherein:
 - (i) X at position 180 of SEQ ID NO: 74 is Thr or Cys;
 - (ii) X at position 244 of SEQ ID NO: 74 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 246 of SEQ ID NO: 74 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 247 of SEQ ID NO: 74 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (j) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 75, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;
- (k) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 136, wherein:
 - (i) X at position 180 of SEQ ID NO: 136 is Thr or Cys;
 - (ii) X at position 244 of SEQ ID NO: 136 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 246 of SEQ ID NO: 136 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 247 of SEQ ID NO: 136 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(l) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 137, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;

(m) both (a) and (b); both (a) and (d); both (b) and (c); or both (c) and (d);

(n) both (e) and (f); both (e) and h); both (f) and (g); or both (g) and (h);

(n) both (i) and (j); both (i) and l); both (j) and (k); or both (k) and (l);

(o) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 55, wherein:

(i) X at position 160 of SEQ ID NO: 55 is Thr or Cys;

(ii) X at position 224 of SEQ ID NO: 55 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 226 of SEQ ID NO: 55 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 227 of SEQ ID NO: 55 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(p) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 56, wherein X at position 168 of SEQ ID NO: 56 is Ser or Cys;

(q) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 112, wherein:

(i) X at position 159 of SEQ ID NO: 112 is Thr or Cys;

(ii) X at position 223 of SEQ ID NO: 112 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 225 of SEQ ID NO: 112 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 226 of SEQ ID NO: 112 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(r) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 113, wherein X at position 173 of SEQ ID NO: 113 is Ser or Cys;

(s) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 57, wherein:

(i) X at position 160 of SEQ ID NO: 57 is Thr or Cys;

(ii) X at position 224 of SEQ ID NO: 57 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 226 of SEQ ID NO: 57 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 227 of SEQ ID NO: 57 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(t) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 58, wherein X at position 173 of SEQ ID NO: 58 is Ser or Cys;

(u) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 118, wherein:

(i) X at position 161 of SEQ ID NO: 118 is Thr or Cys;

(ii) X at position 225 of SEQ ID NO: 118 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 227 of SEQ ID NO: 118 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 228 of SEQ ID NO: 118 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(v) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 119, wherein X at position 103178 of SEQ ID NO: 119 is Ser or Cys;

(w) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 76, wherein:

(i) X at position 159 of SEQ ID NO: 76 is Thr or Cys;

(ii) X at position 223 of SEQ ID NO: 76 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 225 of SEQ ID NO: 76 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

- (iv) X at position 226 of SEQ ID NO: 76 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (x) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 77, wherein X at position 168 of SEQ ID NO: 77 is Ser or Cys;
- (y) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 144, wherein:
 - (i) X at position 160 of SEQ ID NO: 144 is Thr or Cys;
 - (ii) X at position 224 of SEQ ID NO: 144 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 226 of SEQ ID NO: 144 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 227 of SEQ ID NO: 144 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (z) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 145, wherein X at position 166 of SEQ ID NO: 145 is Ser or Cys;
- (aa) both (o) and (p); or both (q) and (r);
- (bb) both (s) and (t); or both (u) and (v);
- (cc) both (w) and (x); or both (y) and (z);
- (dd) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 51;
- (ee) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 52;
- (ff) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 114;
- (gg) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 115;
- (hh) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 128;

- (ii) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 129;
- (jj) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 116;
- (kk) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 117;
- (ll) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 53;
- (mm) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 54;
- (nn) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 120;
- (oo) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 121;
- (pp) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 130;
- (qq) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 131;
- (rr) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 122;
- (ss) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 123;
- (tt) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 80;
- (uu) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 81;
- (vv) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 146;
- (ww) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 146;

(xx) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 142;

(yy) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 143;

(zz) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 148;

(aaa) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 149;

(bbb) both (dd) and (ee); both (ff) and (gg); both (hh) and (ii); or both (jj) and (kk);

(ccc) both (ll) and (mm); both (nn) and (oo); both (pp) and (qq); or both (rr) and (ss);

(ddd) both (tt) and (uu); both (vv) and (ww); both (xx) and (yy); or both (zz) and (aaa);

(eee) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 23;

(fff) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 24;

(ggg) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 102;

(hhh) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 103;

(iii) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 124;

(jjj) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 125;

(kkk) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 104;

(lll) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 105;

(mmm) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 39;

(nnn) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 40;

(ooo) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 108;

(ppp) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 109;

(qqq) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 126;

(rrr) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 127;

(sss) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 110;

(ttt) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 111;

(uuu) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 78;

(vvv) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 79;

(www) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 138;

(xxx) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 139;

(yyy) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 134;

(zzz) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 135;

(aaaa) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 140;

(bbbb) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 141;

(dddd) both (eee) and (fff); both (eee) and (hhh); both (fff) and (ggg); both (ggg) and (hhh); both (iii) and (jjj); both (iii) and (lll); both (jjj) and (kkk); or both (kkk) and (lll);

(eeee) both (mmm) and (nnn); both (mmm) and (ppp); both (nnn) and (ooo); both (ooo) and (ppp); both (qqq) and (rrr); both (qqq) and (ttt); both (rrr) and (sss); or both (sss) and (ttt); or

(ffff) both (uuu) and (vvv); both (uuu) and (xxx); both (vvv) and (www); both (www) and (xxx); both (yyy) and (zzz); both (yyy) and (bbbb); both (yyy) and (aaaa); or both (aaaa) and (bbbb).

27. The isolated or purified protein according to any one of claims 20-26, comprising:

(a) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 21, wherein:

(i) X at position 180 of SEQ ID NO: 21 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 21 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 21 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 21 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 22, wherein X at position 190 of SEQ ID NO: 22 is Ser or Cys;

(c) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 100, wherein:

(i) X at position 180 of SEQ ID NO: 100 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 100 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 100 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 100 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(d) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 101, wherein X at position 190 of SEQ ID NO: 101 is Ser or Cys;

(e) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 41, wherein:

(i) X at position 181 of SEQ ID NO: 41 is Thr or Cys;

(ii) X at position 245 of SEQ ID NO: 41 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 247 of SEQ ID NO: 41 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 248 of SEQ ID NO: 41 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(f) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 42, wherein X at position 195 of SEQ ID NO: 42 is Ser or Cys;

(g) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 106, wherein:

(i) X at position 181 of SEQ ID NO: 106 is Thr or Cys;

(ii) X at position 245 of SEQ ID NO: 106 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 247 of SEQ ID NO: 106 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 248 of SEQ ID NO: 106 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(h) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 107, wherein X at position 195 of SEQ ID NO: 107 is Ser or Cys;

(i) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 74, wherein:

(i) X at position 180 of SEQ ID NO: 74 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 74 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 74 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 74 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(j) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 75, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;

(k) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 136, wherein:

(i) X at position 180 of SEQ ID NO: 136 is Thr or Cys;

(ii) X at position 244 of SEQ ID NO: 136 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 246 of SEQ ID NO: 136 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 247 of SEQ ID NO: 136 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(l) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 137, wherein X at position 187 of SEQ ID NO: 75 is Ser or Cys;

(m) both (a) and (b); both (a) and (d); both (b) and (c); or both (c) and (d);

(n) both (e) and (f); both (e) and h); both (f) and (g); or both (g) and (h);

(n) both (i) and (j); both (i) and l); both (j) and (k); or both (k) and (l);

(o) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 55, wherein:

(i) X at position 160 of SEQ ID NO: 55 is Thr or Cys;

(ii) X at position 224 of SEQ ID NO: 55 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 226 of SEQ ID NO: 55 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 227 of SEQ ID NO: 55 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(p) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 56, wherein X at position 168 of SEQ ID NO: 56 is Ser or Cys;

(q) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 112, wherein:

- (i) X at position 159 of SEQ ID NO: 112 is Thr or Cys;
- (ii) X at position 223 of SEQ ID NO: 112 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (iii) X at position 225 of SEQ ID NO: 112 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
- (iv) X at position 226 of SEQ ID NO: 112 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (r) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 113, wherein X at position 173 of SEQ ID NO: 113 is Ser or Cys;
- (s) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 57, wherein:
 - (i) X at position 160 of SEQ ID NO: 57 is Thr or Cys;
 - (ii) X at position 224 of SEQ ID NO: 57 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 226 of SEQ ID NO: 57 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 227 of SEQ ID NO: 57 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (t) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 58, wherein X at position 173 of SEQ ID NO: 58 is Ser or Cys;
- (u) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 118, wherein:
 - (i) X at position 161 of SEQ ID NO: 118 is Thr or Cys;
 - (ii) X at position 225 of SEQ ID NO: 118 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
 - (iii) X at position 227 of SEQ ID NO: 118 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and
 - (iv) X at position 228 of SEQ ID NO: 118 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;
- (v) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 119, wherein X at position 103178 of SEQ ID NO: 119 is Ser or Cys;

(w) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 76, wherein:

(i) X at position 159 of SEQ ID NO: 76 is Thr or Cys;

(ii) X at position 223 of SEQ ID NO: 76 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 225 of SEQ ID NO: 76 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 226 of SEQ ID NO: 76 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(x) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 77, wherein X at position 168 of SEQ ID NO: 77 is Ser or Cys;

(y) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 144, wherein:

(i) X at position 160 of SEQ ID NO: 144 is Thr or Cys;

(ii) X at position 224 of SEQ ID NO: 144 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 226 of SEQ ID NO: 144 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 227 of SEQ ID NO: 144 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(z) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 145, wherein X at position 166 of SEQ ID NO: 145 is Ser or Cys;

(aa) both (o) and (p); or both (q) and (r);

(bb) both (s) and (t); or both (u) and (v);

(cc) both (w) and (x); or both (y) and (z);

(dd) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 51;

(ee) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 52;

(ff) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 114;

(gg) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 115;

- (hh) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
128;
- (ii) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
129;
- (jj) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 116;
(kk) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
117;
- (ll) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 53;
(mm) a second polypeptide chain comprising the amino acid sequence of SEQ ID
NO: 54;
- (nn) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
120;
- (oo) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
121;
- (pp) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
130;
- (qq) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
131;
- (rr) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 122;
(ss) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
123;
- (tt) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 80;
(uu) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
81;
- (vv) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
146;
- (ww) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
146;
- (xx) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
142;

(yy) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
143;
(zz) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
148;
(aaa) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
149;
(bbb) both (dd) and (ee); both (ff) and (gg); both (hh) and (ii); or both (jj) and (kk);
(ccc) both (ll) and (mm); both (nn) and (oo); both (pp) and (qq); or both (rr) and (ss);
(ddd) both (tt) and (uu); both (vv) and (ww); both (xx) and (yy); or both (zz) and
(aaa);
(eee) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
23;
(fff) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
24;
(ggg) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
102;
(hhh) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
103;
(iii) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
124;
(jjj) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
125;
(kkk) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
104;
(lll) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
105;
(mmm) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
39;
(nnn) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
40;

(ooo) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
108;
(ppp) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
109;
(qqq) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
126;
(rrr) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
127;
(sss) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
110;
(ttt) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
111;
(uuu) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
78;
(vvv) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
79;
(www) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
138;
(xxx) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
139;
(yyy) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
134;
(zzz) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO:
135;
(aaaa) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO:
140;
(bbbb) a second polypeptide chain comprising the amino acid sequence of SEQ ID
NO: 141;
(dddd) both (eee) and (fff); both (eee) and (hhh); both (fff) and (ggg); both (ggg) and
(hhh); both (iii) and (jjj); both (iii) and (lll); both (jjj) and (kkk); or both (kkk) and (lll);

(eeee) both (mmm) and (nnn); both (mmm) and (ppp); both (nnn) and (ooo); both (ooo) and (ppp); both (qqq) and (rrr); both (qqq) and (ttt); both (rrr) and (sss); or both (sss) and (ttt); or

(ffff) both (uuu) and (vvv); both (uuu) and (xxx); both (vvv) and (www); both (www) and (xxx); both (yyy) and (zzz); both (yyy) and (bbbb); both (yyy) and (aaaa); or both (aaaa) and (bbbb).

28. An isolated or purified nucleic acid comprising a nucleotide sequence encoding the TCR according to any one of claims 1-12, the polypeptide according to any one of claims 13-19, or the protein according to any one of claims 20-27.

29. An isolated or purified nucleic acid comprising, from 5' to 3', a first nucleic acid sequence and a second nucleotide sequence, wherein the first and second nucleotide sequence, respectively, encode the amino sequences of SEQ ID NOs: 7 and 8; 7 and 91; 90 and 8; 90 and 91; 8 and 7; 91 and 7; 8 and 90; 91 and 90; 37 and 38; 37 and 93; 92 and 38; 92 and 93; 38 and 37; 93 and 37; 38 and 92; 93 and 92; 70 and 71; 70 and 133; 132 and 71; 132 and 133; 71 and 70; 133 and 70; 71 and 132; 133 and 132; 23 and 24; 23 and 103; 102 and 24; 102 and 103; 24 and 23; 103 and 23; 24 and 102; 103 and 102; 39 and 40; 39 and 109; 108 and 40; 108 and 109; 40 and 39; 109 and 39; 40 and 108; 109 and 108; 78 and 79; 78 and 139; 138 and 79; 138 and 139; 79 and 78; 139 and 78; 79 and 138; 139 and 138; 21 and 22; 21 and 101; 100 and 22; 100 and 101; 22 and 21; 101 and 21; 22 and 100; 101 and 100; 41 and 42; 41 and 107; 106 and 42; 106 and 107; 42 and 41; 107 and 41; 42 and 106; 107 and 106; 74 and 75; 74 and 101; 100 and 75; 100 and 101; 75 and 74; 101 and 74; 75 and 100; 101 and 100; 124 and 125; 124 and 105; 104 and 125; 104 and 105; 125 and 124; 105 and 124; 125 and 104; 105 and 104; 126 and 127; 126 and 111; 110 and 127; 110 and 111; 127 and 126; 111 and 126; 127 and 110; 111 and 110; 134 and 135; 140 and 135; 134 and 141; 140 and 141; 135 and 134; 135 and 140; 141 and 134; 141 and 140; 47 and 48; 48 and 47; 49 and 50; 50 and 49; 72 and 73; 73 and 72; 94 and 95; 95 and 94; 94 and 85; 85 and 94; 96 and 97; 97 and 96; 96 and 87; 87 and 96; 88 and 89; 89 and 88; 51 and 52; 52 and 51; 53 and 54; 54 and 53; 80 and 81; 81 and 80; 55 and 56; 56 and 55; 57 and 58; 58 and 57; 76 and 77; 77 and 76; 128 and 129; 129 and 128; 130 and 131; 131 and 130; 142 and 143; 143 and 142; 112

and 113; 113 and 112; 118 and 119; 119 and 118; 144 and 145; 145 and 144; 114 and 115; 115 and 114; 120 and 121; 121 and 120; 146 and 147; 147 and 146; 116 and 117; 117 and 116; 122 and 123; 123 and 122; 148 and 149; 149 and 148; 150 and 151; 151 and 150; 154 and 155; 155 and 154; 152 and 153; 153 and 152; 156 and 157; 157 and 156; 160 and 161; 161 and 160; 158 and 159; or 159 and 158.

30. The isolated or purified nucleic acid according to claim 29, further comprising a third nucleotide sequence interposed between the first and second nucleotide sequence, wherein the third nucleotide sequence encodes a cleavable linker peptide.

31. The isolated or purified nucleic acid according to claim 30, wherein the cleavable linker peptide comprises the amino acid sequence of SEQ ID NO: 25.

32. A recombinant expression vector comprising the nucleic acid according to any one of claims 28-31.

33. The recombinant expression vector according to claim 32, which is a transposon or a lentiviral vector.

34. An isolated or purified TCR, polypeptide, or protein encoded by the nucleic acid according to any one of claims 28-31 or the vector according to claim 32 or 33.

35. An isolated or purified TCR, polypeptide, or protein that results from expression of the nucleic acid according to any one of claims 28-31 or the vector according to claim 32 or 33 in a cell.

36. A method of producing a host cell expressing a TCR that has antigenic specificity for the peptide of SEQ ID NO: 30, the method comprising contacting a cell with the vector according to claim 32 or 33 under conditions that allow introduction of the vector into the cell.

37. An isolated or purified host cell comprising the nucleic acid according to any one of claims 28-31 or the recombinant expression vector according to claim 32 or 33.

38. The host cell according to claim 37 wherein the cell is a human lymphocyte.

39. The host cell according to claim 37 or 38, wherein the cell is selected from the group consisting of a T cell, a natural killer T (NKT) cell, an invariant natural killer T (iNKT) cell, and a natural killer (NK) cell.

40. An isolated or purified population of cells comprising the host cell according to any one of claims 37-39.

41. A method of producing the TCR according to any one of claims 1-12, 34, or 35, the polypeptide according to any one of claims 13-19, 34, or 35, or the protein according to any one of claims 20-27, 34, or 35, the method comprising culturing the host cell according to any one of claims 37-39, or the population of host cells according to claim 40, so that the TCR, polypeptide, or protein is produced.

42. A pharmaceutical composition comprising (a) the TCR according to any one of claims 1-12, 34, or 35, the polypeptide according to any one of claims 13-19, 34, or 35, or the protein according to any one of claims 20-27, 34, or 35, the nucleic acid according to any one of claims 28-31, the recombinant expression vector according to claim 32 or 33, the host cell according to any one of claims 37-39, or the population of cells according to claim 40 and (b) a pharmaceutically acceptable carrier.

43. A method of detecting the presence of cancer in mammal, the method comprising:

(a) contacting a sample comprising cells of the cancer with the TCR according to any one of claims 1-12, 34, or 35, the polypeptide according to any one of claims 13-19, 34, or 35, or the protein according to any one of claims 20-27, 34, or 35, the nucleic acid according to any one of claims 28-31, the recombinant expression vector according to claim 32 or 33,

the host cell according to any one of claims 37-39, the population of cells according to claim 40, or the pharmaceutical composition of claim 42, thereby forming a complex; and

(b) detecting the complex,

wherein detection of the complex is indicative of the presence of cancer in the mammal.

44. The TCR according to any one of claims 1-12, 34, or 35, the polypeptide according to any one of claims 13-19, 34 or 35, or the protein according to any one of claims 20-27, 34, or 35, the nucleic acid according to any one of claims 28-31, the recombinant expression vector according to claim 32 or 33, the host cell according to any one of claims 37-39, the population of cells according to claim 40, or the pharmaceutical composition according to claim 42, for use in inducing an immune response against a cancer in a mammal.

45. The TCR according to any one of claims 1-12, 34, or 35, the polypeptide according to any one of claims 13-19, 34, or 35, or the protein according to any one of claims 20-27, 34, or 35, the nucleic acid according to any one of claims 28-31, the recombinant expression vector according to claim 32 or 33, the host cell according to any one of claims 37-39, the population of cells according to claim 40, or the pharmaceutical composition of claim 42, for use in treating or preventing cancer in a mammal.

46. The method according to claim 43 or the TCR, polypeptide, protein, nucleic acid, recombinant expression vector, host cell, population of cells, or pharmaceutical composition for the use of claim 44 or 45, wherein the cancer expresses a mutated human RAS amino acid sequence with a substitution of glycine at position 12 with valine,

wherein the mutated human RAS amino acid sequence is a mutated human Kirsten rat sarcoma viral oncogene homolog (KRAS), a mutated human Harvey rat sarcoma viral oncogene homolog (HRAS), or a mutated human Neuroblastoma rat sarcoma viral oncogene homolog (NRAS) amino acid sequence, and

wherein position 12 is defined by reference to the wild-type human KRAS, wild-type human HRAS, or wild-type human NRAS protein, respectively.

47. The method according to claim 43 or 46, or the TCR, polypeptide, protein, nucleic acid, recombinant expression vector, host cell, population of cells, or pharmaceutical composition for the use according to any one of claims 44-46, wherein the mutated human RAS amino acid sequence is a mutated human Kirsten rat sarcoma viral oncogene homolog (KRAS) amino acid sequence.

48. The method according to claim 43 or 46 or the TCR, polypeptide, protein, nucleic acid, recombinant expression vector, host cell, population of cells, or pharmaceutical composition for the use according to any one of claims 44-46, wherein the mutated human RAS amino acid sequence is a mutated human neuroblastoma rat sarcoma viral oncogene homolog (NRAS) amino acid sequence.

49. The method according to claim 43 or 46 or the TCR, polypeptide, protein, nucleic acid, recombinant expression vector, host cell, population of cells, or pharmaceutical composition for the use according to any one of claims 44-46, wherein the mutated human RAS amino acid sequence is a mutated human Harvey rat sarcoma viral oncogene homolog (HRAS) amino acid sequence.

50. The method according to any one of claims 43 and 46-49 or the TCR, polypeptide, protein, nucleic acid, recombinant expression vector, host cell, population of cells, or pharmaceutical composition for the use according to any one of claims 44-49, wherein the cancer is pancreatic, colorectal, lung, endometrial, ovarian, or prostate cancer.