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(54) **NUCLEIC ACID AND CORRESPONDING
PROTEIN ENTITLED STEAP-1 USEFUL IN
TREATMENT AND DETECTION OF
CANCER**

Related U.S. Application Data

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(57) **ABSTRACT**

A novel gene 08P1D4 (also designated STEAP-1) and its encoded protein, and variants thereof, are described wherein STEAP-1 exhibits tissue specific expression in normal adult tissue, and is aberrantly expressed in the cancers listed in Table I. Consequently, STEAP-1 provides a diagnostic, prognostic, prophylactic and/or therapeutic target for cancer. The STEAP-1 gene or fragment thereof, or its encoded protein, or variants thereof, or a fragment thereof, can be used to elicit a humoral or cellular immune response; antibodies or T cells reactive with STEAP-1 can be used in active or passive immunization.

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The cDNA (SEQ ID NO: 2) and amino acid sequence (SEQ ID NO: 3) of STEAP-1 v.1. The start methionine is underlined. The open reading frame extends from nucleic acid 66-1085 including the stop codon.

```
1 ccgagactcacggtcaagctcaaggcgaagagtgggtggctgaagccatactattttatag
1 M E S R K D I T N Q E E L W K M K P R
61 aattaATGGAAAGCAGAAAAGACATCACAACCAAGAACTTTGGAAAATGAAGCCTA
20 R N L E E D D Y L H K D T G E T S M L K
121 GGAGAAATTTAGAAGAAGACGATTATTGTCATAAGGACACGGGAGAGACCAGCATGCTAA
40 R P V L L H L H Q T A H A D E F D C P S
181 AAAGACCTGTGCTTTTGCAATTTGCACCAAACAGCCCATGCTGATGAATTTGACTGCCCTT
60 E L Q H T Q E L F P Q W H L P I K I A A
241 CAGAACTTCAGCACACACAGGAACCTTTCCACAGTGGCACTTGCCAATTAATAAGCTG
80 I I A S L T F L Y T L L R E V I H P L A
301 CTATTATAGCATCTCTGACTTTTCTTTACACTCTTCTGAGGGAAAGTAATTCACCTTTAG
100 T S H Q Q Y F Y K I P I L V I N K V L P
361 CAACTTCCCATCAACATATTTTATAAAATTCAACTCTGTCATCAACAAAGCTTTCG
120 M V S I T L L A L V Y L P G V I A A I V
421 CAATGGTTTCCATCACTCTCTTGGCAATTTTACCTGCCAGGTGTGATAGCAGCAATIG
140 Q L H N G T K Y K K P P H W L D K W M L
481 TCCAACTTCATAATGGAACCAAGTATAAGAAGTTCCACATTTGGTTGGATAAGTGGATGT
160 T R K Q F G L L S F F F A V L H A I Y S
541 TAACAAGAAAGCAGTTTGGGCTTCTCAGTTTCITTTTTTGTGTACTGTCATGCAATTTATA
180 L S Y P M R R S Y R Y K L L N W A Y Q Q
601 GTCTGTCTTACCAATGAGGCGATCCTACAGATACAAGTTGCTAAACTGGGCATATCAAC
200 V Q Q N K E D A W I E H D V W R M E I Y
661 AGGTCCAACAAAATAAAGAAGATGCCTGGATTGAGCATGATGTTTGGAGAATGGAGATT
220 V S L G I V G L A I L A L L A V T S I P
721 ATGTGTCTCTGGGAATTTGTGGATTGGCAATACTGGCTCTGTTGGCTGTGACATCTATTC
240 S V S D S L T W R E F H Y I Q S K L G I
781 CATCTGTGAGTGACTCTTTGACATGGAGAGAATTTCACTATATTCAGAGCAAGCTAGGAA
260 V S L L L G T I H A L I F A W N K W I D
841 TTGTTTCCCTTCTACTGGGCACAATACAGCATTGATTTTGGCTGGAATAAGTGGATAG
280 I K Q F V W Y T P P T F M I A V F L P I
901 ATATAAAACAATTTGTATGTATACACCTCCAACCTTTTATGATAGCTGTTTTCCTTCCAA
300 V V L I F K S I L F L P C L R K K I L K
961 TTGTTGTCTGATATTTAAAGCATACTATTTCTGCCATGCTTGAGGAAGAAGATACTGA
320 I R H G W E D V T K I N K T E I C S Q L
1021 AGATTAGACATGGTTGGGAAGACGTCAACAAAATTAACAAAACAGATATGTTCCCACT
340 *
1081 TGTAGaattactgtttacacacattttgttcaattatgatatttttatcaccaacatt
1141 tcaagtttgatttgttaataaaatgattacaaggaagaaaaa
```

Figure 1: STEAP-1 SSH sequence of 436 nucleotides. (SEQ ID NO: 1)

1 GTACAGCAAA AAAGAACTG AGAAGCCCAA ACTGCTTCT TGTAAACATC CACTTATCCA
61 ACCAATGTGG AAAGTTCTTA TACTTGGTTC CATTATGAAG TTGGACAATT GCTGCTATCA
121 CACCTGGCAG GTAAACCAAT GCCAAGAGAG TGATGGAAAC CATTGGCAAG ACTTTGTTGA
181 TGACCAGGAT TGGAAATTTA TAAAAATATT GTTGATGGGA AGTTGCTAAA GGGTGAATTA
241 CTTCCCTCAG AAGAGTGTA AGAAAAGTCA GAGATGCTAT AATAGCAGCT ATTTTAATTG
301 GCAAGTGCCA CTGTGGAAAG AGTTCCTGTG TGTGCTGAAG TTCTGAAGGG CAGTCAAATT
361 CATCAGCATG GGCTATTTGG TGCAAATGCA AAAGCACAGG TCTTTTTCAGC ATGCTGGTCT
421 CTCCCGTGTC CTTATG

Figure 2:

Figure 2A. The cDNA (SEQ ID NO: 2) and amino acid sequence (SEQ ID NO: 3) of STEAP-1 v.1. The start methionine is underlined. The open reading frame extends from nucleic acid 66-1085 including the stop codon.

```
1 ccgagactcacggtcaagctaaggcgaagagtgggtggctgaagccatactattttatag
1      M E S R K D I T N Q E E L W K M K P R
61 aattaATGGAAGCAGAAAAGACATCACAAACCAAGAAGAACTTTGGAATGAAGCCTA
20      R N L E E D D Y L H K D T G E T S M L K
121 GGAGAAATTTAGAAGAAGACGATTATTTGCATAAGGACACGGGAGAGACCAGCATGCTAA
40      R P V L L H L H Q T A H A D E F D C P S
181 AAAGACCTGTGCTTTTGCATTTGCACCAACAGCCCATGCTGATGAATTTGACTGCCCTT
60      F L Q H T Q E L F P Q W H L P I K I A A
241 CAGAACTTCAGCACACAGGAACCTCTTCCACAGTGGCACTTGCCAATTTAAATAGCTG
80      I I A S L T F L Y T L L R E V I H P L A
301 CTATTATAGCATCTCTGACTTTTCTTTTACACTCTTCTGAGGGAAGTAATTCACCCTTAG
100     T S H Q Q Y F Y K I P I L V I N K V L P
361 CAACTTCCCATCAACAATATTTTATAAAATTCCAATCCTGGTCATCAACAAAGTCTTGC
120     M V S I T L L A L V Y L P G V I A A I V
421 CAATGGTTTTCCATCACTCTCTTGGCATTGGTTTACCTGCCAGGTGTGATAGCAGCAATTG
140     Q L H N G T K Y K K F P H W L D K W M L
481 TCCAACCTTCATAATGGAACCAAGTATAAGAAGTTCCACATTGGTTGGATAAGTGGATGT
160     T R K Q F G L L S F F F A V L H A I Y S
541 TAACAAGAAAGCAGTTTGGGCTTCTCAGTTTCTTTTTTGTGCTGCTGCTGCAATTTATA
180     L S Y P M R R S Y R Y K L L N W A Y Q Q
601 GTCTGTCTTACCCAATGAGGCGATCCTACAGATACAAGTTGCTAAACTGGGCATATCAAC
200     V Q Q N K E D A W I E H D V W R M E I Y
661 AGGTCCAACAAAATAAAGAAGATGCCTGGATTGAGCATGATGTTTGGAGAATGGAGATTT
220     V S L G I V G L A I L A L L A V T S I P
721 ATGTGTCTCTGGGAATTGTGGGATTGGCAATACTGGCTCTGTTGGCTGTGACATCTATTC
240     S V S D S L T W R E F H Y I Q S K L G I
781 CATCTGTGAGTGACTCTTTGACATGGAGAGAATTTCACTATATTCAGAGCAAGCTAGGAA
260     V S L L L G T I H A L I F A W N K W I D
841 TTGTTTCCCTTCTACTGGGCACAATACACGCATTGATTTTGCCTGGAATAAGTGGATAG
280     I K Q F V W Y T P P T F M I A V F L P I
901 ATATAAAACAATTTGTATGGTATACACCTCCAACCTTTTATGATAGCTGTTTTCCTTCCAA
300     V V L I F K S I L F L P C L R K K I L K
961 TTGTTGTCTGATATTTAAAGCATACTATTCCTGCCATGCTTGAGGAAGAAGATACTGA
320     I R H G W E D V T K I N K T E I C S Q L
1021 AGATTAGACATGGTTGGGAAGACGTCACCAAAATTAACAAAACCTGAGATATGTTCCAGT
340     *
1081 TGTAGaattactgtttacacacatttttgttcaatattgatataatcaccacacatt
1141 tcaagtttgtatttgttaataaaatgattacaaggaaaaaaaaaaaaaaaaaaaaa
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Figure 2B. The cDNA (SEQ ID NO: 4) and amino acid sequence (SEQ ID NO: 5) of STEAP-1 v.2. The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

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1 ggggcccgcacctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61 gtgggtgggtgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10  Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30  K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTGCACCAAA
50  A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTTTTC
70  Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAATAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90  L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110 P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130 Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGCCAACCTCATAATGGAACCAAGTATAAGA
150 F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170 F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTGTGCTGACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190 Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210 E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTTATGTGTCTCTGGAATTGTGGGATTGGCAA
230 L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250 F H Y I Q V N N I *
841 AATTTCACTATATTACAGGTAAATAATATATAAaataaccctaagaggtaaatacttctttt
901 tgtgtttatgatatagaatatgttgactttacccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttatacttgttccaattaataatgtgctctcctgttgttttccctattg
1021 cttctaattaggacaagtgtttcctagacataaataaaaggcattaaatattctttggtt
1081 tttttttttttgtttgtttgtttttgtttgtttgttttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtggcacgatctcggctcactgcaacctgcgcctcc
1201 tgggttcaggcgattctcttgccctcagcctcctgagtagctgggattacaggcaccatc
1261 accatgtccagctaatttttgtattttttagtagagacagggttttcccatgttggccagg
1321 ctggtctcgatctcctgacctcaaatgatccgcccacctcggcctcccaaagtgtggga
1381 tgacagttgtgagccaccacactcagcctgctcttttctaataatttgaaactgttagaca
1441 atttgctacccatctaattgtgatatttttaggaatccaatatgcatggtttattatttctt
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1501 aaaaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaaag
1621 atatgctagtgtctcatttcaaaggctgctttttccagcttacattttatatacttactc
1681 acttgaagtttctaaatattcttgtaattttaaaactatctcagatttactgaggtttat
1741 cttctgggtggtagattatccataagaagagtgtgtgccagaatcactctggggtccttg
1801 tctgacaagattcaaaggactaaatttaatttcagtcatgaacactgccaaattaccgttta
1861 tgggtagacatcttttgaaatttccacaaggctcagacattcgcaactatcccttctacat
1921 gtccacacgtatactccaacactttattaggtctctgattagtttggaagtatgcctcc
1981 atctgaatttagtccagtgtggcttagagttggtacaacattctcacagaatttcctaatt
2041 ttgtaggttcagcctgataaccactggagttctttggctcctcattaaatagctttcttca
2101 cacattgctctgctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcacttaaaatctgagaactggttacactacaagttaccttg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttgttctggcaggctaataccatttccagtaaag
2461 tgaatagaggtcagaagtcgtataaaagaggtgtgtgcagaacaccgttgagattacata
2521 ggtgaacaactatttttaagcaactttatttgtgtagtgcacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattgtt
2641 catattatttccatgttatcagaatatttgatttttttaaaacataggccaagttcatte
2701 acttcattattcatttatcaaaatcagagtgaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtcaaattgatttttgcataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacagagacaa
2941 agcacaaaaataaatatcataaggggatgaacaaaatggaggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttgag
3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgctggaataagtggtatagatataaaacaatttgatggtatacacctcc
3361 aacttttatgatagctgttttccctccaattgttgtcctgatatttaaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatggttgggaagacgtcaccaa
3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacatttttgtt
3541 caatattgatataattttatcaccaacatttcaagtttgtatttgttaataaaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2C. The cDNA (SEQ ID NO: 6) and amino acid sequence (SEQ ID NO: 7) of STEAP-1 v.3. The start methionine is underlined. The open reading frame extends from nucleic acid 96-944 including the stop codon.

```
1  ggggcccgcacctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61  gtgggtggctgaagccatactattttatagaattaATGGAAGCAGAAAAGACATCACAA
10  Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30  K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTCACCAAA
50  A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACTCTTTC
70  Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAAAAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90  L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTTAGCAACTTCCCATCAACAATATTTTATAAAA
110 P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130 Y L P G V I A A I V Q L H N G T K Y K K
481 TTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTCATAATGGAACCAAGTATAAGA
150 F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170 F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTGTGCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190 Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAGAAGATGCCTGGA
210 E H D V W R M E I Y V S L G I V G L A I
721 TTGACCATGATGTTTGGAGAATGGAGATTTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230 L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250 F H Y I Q I I H K K S D V P E S L W D P
841 AATTTCACTATATTCAGATTATCCATAAGAAGAGTGATGTGCCAGAATCACTCTGGGATC
270 C L T R F K G L N L I Q S *
901 CTTGTCTGACAAGATTCAAAGGACTAAATTTAATTCAGTCATGAacactgccattaccg
961 tttatgggtagacatctttggaaatttcacaagagcaagctaggaattgtttcccttct
1021 actgggcacaatacacgcattgatttttgctggaataagtggaatagatataaaacaatt
1081 tgtatggtatacacctccaacttttatgatagctgttttccttccaattgttgtcctgat
1141 atttaaaagcatactatttctgccatgcttgaggaagaagatactgaagattagacatgg
1201 ttgggaagacgtcaccaaaattaacaaaactgagatatgttcccagttgtagaattactg
1261 ttacacacattttttgttcaatattgatataattttatcaccaacatttcaagtttgtatt
1321 tggtaataaaatgattattcaaggaaaaaaaaaaaaaaaaaaaaa
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Figure 2D. The cDNA (SEQ ID NO: 8) and amino acid sequence (SEQ ID NO: 9) of STEAP-1 v.4. The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1  ggggcccgcacctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61  gtgggtggctgaagccatactattttatagaattaATGGAAGCAGAAAAGACATCACAA
10   Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30   K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTCACCAAA
50   A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTTTTC
70   Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAAAAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90   L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110  P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130  Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTTCATAATGGAACCAAGTATAAGA
150  F P H W L D K W M L T R K Q F G L L S L
541 AGTTTCCACATGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170  F F A V L H A I Y S L S Y P M R R S Y R
601 TGTTTTTTGTCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190  Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210  E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230  L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250  F H Y I Q V N N I *
841 AATTTCACTATATTCAGGTAAATAATATATAAaataaccctaagaggtaaatacttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttataacttggtccaattaataatgtgctctcctgttggtttccctattg
1021 cttctaattaggacaagtgtttcctagacataaataaaaggcattaaaatattctttgtt
1081 tttttttttttgtttgtttgtttttgtttgtttgttttttttgagatgaagtctctg
1141 ctctgttgcccatgctggagtacagtggcagatctcggctcactgcaacctgcgcctcc
1201 tgggttcaggcgattctcttgccctcagcctcctgagtagctgggattacaggcaccatc
1261 accatgtccagctaatttttgtattttttagtagagacagggttttcccatgttgggcagg
1321 ctggtctcgatctcctgacctcaaatgatccgccacctcggcctcccaaagtgtctggga
1381 tgacagttgtgagccaccacactcagcctgctcttttctaataatttgaaactgttagaca
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1441 atttgctacccatctaattgtgatatttttaggaatccaatatgcatgggtttattatttctt
1501 aaaaaaaatattctttttacctgtcacctgaatttagtaatgccttttatgttacacaact
1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaaaag
1621 atatgctagtgtctcatttcaaaggctgctttttccagcttacattttatatacttactc
1681 acttgaagtttctaaatattcttgtaattttaaaactatctcagatttactgaggtttat
1741 cttctgggtggttagattatccataagaagagtgtgtgccagaatcactctgggatccttg
1801 tctgacaagattcaaaggactaaatttaattcagtcacgaacactgccaattaccgttta
1861 tgggttagacatctttggaaatttccacaaggctcagacattcgcaactatcccttctacat
1921 gtccacacgtatactccaacactttattagggcatctgattagtttggaagtatgcctcc
1981 atctgaatttagtccagtgtggcttagagttggtacaacattctcacagaatttcctaatt
2041 ttgtaggttcagcctgataaccactggagttccttggctcctcattaaatagctttcttca
2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggaactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcacttaaaatctgagaactgggtacactacaagttaccttgg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttgttctggcaggctaataaccatttccagtaaag
2461 tgaatagagggtcagaagtcgtataaaagagggtgtgtcagaacaccgttgagattacata
2521 ggtgaacaactatttttaagcaactttatttgtgtagtgacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattgtt
2641 catattatttccatgttatcagaatatttgattttttaaaaacataggccaagttcatct
2701 acttcattattcatttatcaaaatcagagtgaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtcaaattgatttttgcataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtccctgatttttaggtatcctgtgaaaagcagaattaagacaaatacacagagacaa
2941 agcacaaaaaataaatatcataaggggatgaacaaaatgggtggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttggag
3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgcctggaataagtggatagatataaaacaatttgtatggtatacacctcc
3361 aacttttatgatagctgttttccctccaattgttgtcctgatattttaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatgggttggaagacgtcaccaa
3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacatttttgtt
3541 caatattgatataattttatcaccaacatttcaagtttgtatttgttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2E. The cDNA (SEQ ID NO: 10) and amino acid sequence (SEQ ID NO: 11) of STEAP-1 v.5. The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1  ggggcccgcacctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61  gtgggtggetgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10   Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30   K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTGCACCAAA
50   A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTCTTTC
70   Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAAAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90   L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTTAGCAACTTCCCATCAACAATATTTTATAAAA
110  P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130  Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTCATAATGGAACCAAGTATAAGA
150  F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170  F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTTTGCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190  Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAGAAGATGCCCTGGA
210  E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230  L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250  F H Y I Q V N N I *
841 AATTTCACTATATTCAGGTAAATAATATATAAaataaccctaagaggtaaatcttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttatacttgttccaattaataatgtgctctcctgttgtttccctattg
1021 cttctaattaggacaagtgtttcctagacataaaataaaaggcattaaaatattctttgtt
1081 tttttttttttgtttgtttgtttttgtttgtttgtttgttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtggcacgatctcggtcactgcaacctgcgcctcc
1201 tgggttcaggcgattctcttgcctcagcctcctgagtagctgggattacaggcaccatc
1261 accatgtccagctaatttttgtattttttagtagagacagggttttcccatgttggccagg
1321 ctgggtctcgatctcctgacctcaaatgatccgcccacctcggcctcccaaagtgtgagga
1381 tgacagttgtgagccaccacactcagcctgctctttctaataatttgaaactgttagaca
1441 atttgctaaccatctaattgtgatatttttaggaatccaatatgcatggtttattatttctt
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1501 aaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaaag
1621 atatgctagtgtctcatttcaaaggctgctttttccagcttacattttatatacttactc
1681 acttgaagtttctaaatattcttgttaattttaaaactatctcagatttactgaggtttat
1741 cttctgggtggtagattatccataagaagagtgatgtgccagaatcactctgggatccttg
1801 tctgacaagattcaaaggactaaattttaattcagtcatgaacactgccattaccgttta
1861 tgggtagacatctttggaaattttccacaaggctcagacattcgcaactatcccttctacat
1921 gtccacacgtataactccaacactttattaggtcctgattagtttggaagtagtcctcc
1981 atctgaatttagtccagtgtggcttagagttggtacaacattctcacagaatttccctaatt
2041 ttgtaggttcagcctgataaccactggagttcttttggtcctcattaaatagctttcttca
2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacattttggtaaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcactttaaactctgagaactggttacactacaagttaccttgg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttgttctggcaggctaatagaccatttccagtaaag
2461 tgaatagaggtcagaagtcgtataaaagagggtgtgtcagaacaccgttgagattacata
2521 ggtgaacaactatttttaagcaactttatttgtgtagtgacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattgtt
2641 catattatttccatgttatcagaatatttgatttttttaaaacataggccaagttcatte
2701 acttcattattcatttatcaaaatcagagtgaaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtc aaattgatttttgctataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacagagacaa
2941 agcacaaaaataaatatcataaggggatgaacaaaatggaggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttgag
3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgctggaataagtggatagatataaaacaatttgtatggtatacacctcc
3361 aacttttatgatagctgttttcctccaattgttgtcctgatatttaaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatgggtgggaagacgtcaccaa
3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacatttttgtt
3541 caatattgatataattttatcaccaacatttcaagtttgtattttgttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2F. The cDNA (SEQ ID. NO. : 12) and amino acid sequence (SEQ ID NO: 13) of STEAP-1 v.6.

The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1  ggggcccgcacctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61  gtgggtggctgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10  Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTGCG
30  K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTGCACCAAA
50  A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTTTTC
70  Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAATAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90  L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110 P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130 Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTCATAATGGAACCAAGTATAAGA
150 F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170 F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTGTGCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190 Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210 E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230 L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250 F H Y I Q V N N I *
841 AATTTCACTATATTACAGGTAAATAATATATAAaataaccctaagaggtaaatcttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttatacttgttccaattaataatgtgctctcctgttgttttccctattg
1021 cttctaattaggacaagtgtttcctagacataaataaaaggcattaaatattctttgtt
1081 ttttttgttttgtttgtttgttttgtttgtttgttttggagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtgggcagatctcggtcactgcaacctgcgectcc
1201 tgggttcaggcgattctcttgccctcagcctcctgagtagctgggattacaggcaccctac
1261 accatgtccagctaatttttgtatttttagtagagacagggtttcccatgttggccagg
1321 ctgggtctcgatctcctgacctcaaatgatccgccacctcggcctcccaaagtgtctggga
1381 tgacagttgtgagccaccacactcagcctgctcttttctaataatttgaaacttgttagaca
1441 atttgctacccatctaattgtgatatttttaggaatccaatatgcatggtttattattctt
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1501 aaaaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaaaag
1621 atatgctagtgctctcatttcaaaggctgctttttccagcttacattttatatacttactc
1681 acttgaagtttctaaatattcttgtaattttaaaactatctcagatttactgaggtttat
1741 cttctggtaggttagattatccataagaagagtgatgtgccagaatcactctgggatccttg
1801 tctgacaagattcaaaggactaaatttaattcagtcacgaacactgccaaattaccgttta
1861 tgggtagacatctttggaaatttccacaaggctcagacattcgcaactatcccttctacat
1921 gtccacacgtatactccaacactttattaggtctgattagtttggaaagtatgcctcc
1981 atctgaatttagtccagtggtggttagagttggtacaacattctcacagaatttcctaatt
2041 ttgtaggttcagcctgataaccactggagttctttggtcctcattaaatagctttcttca
2101 cacattgctctgctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggactgcattcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcacttaaaatctgagaactgggtacactacaagttaccttg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttggtctggcaggctaataccatttccagtaaaag
2461 tgaatagaggtcagaagtcgtataaaaagaggtgtgtgcagaacaccgttgagattacata
2521 ggtgaacaactatttttaagcaactttatttggtgtagtgacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattgtt
2641 catattatttccatgttatcagaatatttgattttttaaaaacataggccaagtctatc
2701 acttcattattcatttatcaaaatcagagtgaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtc aaattgatttttgctataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacaaagagacaa
2941 agcacaaaaataaataatcataaggggatgaacaaaatgggtggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttccacttagacagcttgag
3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgcagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgctggaataagtggatagatataaaacaatttgatggtatacacctcc
3361 aacttttatgatagctgttttccctccaattgtgtcctgatattttaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatgggtgggaagacgtcaccaa
3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacatttttgtt
3541 caatattgatataattttatcaccaacatttcaagtttgattttgttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2G. The cDNA (SEQ ID NO: 14) and amino acid sequence (SEQ ID NO: 15) of STEAP-1 v.7.

The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

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1  ggggcccgcacctctgggcagcagcggcagccgagactcacggtcaagctaaggcgaaga
1                               M E S R K D I T N
61  gtgggtggctgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10   Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAAGCTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30   K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTGCACCAA
50   A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAAGCTTTTC
70   Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAATAAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90   L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110  P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTCCCATCACTCTCTTGGCATTGG
130  Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTCATAATGGAACCAAGTATAAGA
150  F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170  F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTTTGTCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190  Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210  E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230  L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250  F H Y I Q V N N I *
841 AATTTCACTATATTCAGGTAAATAATATATAAaataaccctaagaggtaaattcttctttt
901 tgtgttttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttataacttggtccaattaataatgtgctctcctgttgttttccctattg
1021 cttctaattaggacaagtggtttcctagacataaataaaaggcattaaaaatattctttgtt
1081 tttttttttttgtttgtttgtttttgtttgtttgtttgttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtggcagatctcggctcactgcaacctgcccctcc
1201 tgggttcaggcgattctcttgccctcagcctcctgagtagctgggattacaggcaccatc
1261 accatgtccagctaatttttgtatttttagtagagacagggttttcccatgttgggcagg
1321 ctggtctcgatctcctgacctcaaatgatccgcccacctcggcctcccaaagtgtctggga
1381 tgacagttgtgagccaccacactcagcctgctctttctaataatttgaaacttgtagaca
1441 atttgccacccatctaattgtgatatttttaggaatccaatatgcatggtttattattctt

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1501 aaaaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
 1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaaag
 1621 atatgctagtgtctcatttcaaaggctgctttttccagcttacattttatatacttactc
 1681 acttgaagttttctaaatattcttgtaattttaaaactatctcagatttactgaggtttat
 1741 cttctgggtggtagattatccataagaagagtgatgtgccagaatcactctgggatccttg
 1801 tctgacaagattcaaaggactaaatttaattcagtcatgaacactgccaattaccgttta
 1861 tgggtagacatctttggaaatttcacaaaggtcagacattcgcaactatcccttctacat
 1921 gtccacacgtatactccaacactttattagggcatctgattagtttggaagtatgcctcc
 1981 atctgaattagtcagtggtgcttagagttggtacaacattctcacagaatttcctaatt
 2041 ttgtaggttcagcctgataaccactggagttctttggctcctcattaaatagctttcttca
 2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
 2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
 2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtatttttcaact
 2281 agtaacctagaaaatgtttcacttaaaatctgagaactggttacactacaagttaccttgg
 2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
 2401 gcgcctgaataattgtgagttcgatttgttctggcaggctaatagaccatttccagtaaag
 2461 tgaatagaggtcagaagtcgtataaaagagggtgtgtcagaacaccgttgagattacata
 2521 ggtgaacaactatttttaagcaactttatttgtgtagtgcacaaagcatcccaatgcaggc
 2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattggt
 2641 catattatttccatgttatcagaatatttgatttttttaaaaacataggccaagttcatc
 2701 acttcattattcatttatcaaaatcagagtgaaatcacattagtcgccttcacaactgata
 2761 aagatcactgaagtcaaattgatttttgcctataatcttcaatctacctatatttaattga
 2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
 2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacaaagagacaa
 2941 agcacaaaaaataaataatcataaggggatgaacaaaatggtggagaaagagtagacaaag
 3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttggag
 3061 acaagaaattaccctaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
 3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
 3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
 3241 tgtttttcttttgcagagcaagctaggaattgtttcccttctactgggcacaatacacgc
 3301 attgatttttgcctggaataagtggatagatataaaacaatttgatgggtatacacctcc
 3361 aacttttatgatagctgttttccctccaattgttgtcctgatatttaaaagcatactatt
 3421 cctgccatgcttgaggaagaagatactgaagattagacatggttggaagacgtcaccaa
 3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacatttttgtt
 3541 caatattgatataattttatcaccaacatttcaagtttgtatttgttaataaaatgattat
 3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2H. The cDNA (SEQ ID NO: 16) and amino acid sequence (SEQ ID NO: 17) of STEAP-1 v.8.

The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1  gggggccgcacctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61  gtgggtggctgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10  Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30  K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTGCACCAAA
50  A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTTTTC
70  Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAAAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90  L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110 P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130 Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTTCATAATGGAACCAAGTATAAGA
150 F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170 F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTTTGTCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190 Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210 E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230 L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATCCATCTGTGAGTGACTCTTTGACATGGAGAG
250 F H Y I Q V N N I *
841 AATTTCATATATTTCAGGTAAATAATATATAAaataaccctaagaggtaaatacttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttatacttggtccaattaataatgtgctctcctgttgtttccctattg
1021 cttctaattaggacaagtgtttcctagacataaataaaaggcattaaaaatattctttgtt
1081 ttttttttttgtttgtttgtttttgtttgtttgtttgttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtggcacgatctcggtcactgcaacctgcgcctcc
1201 tgggttcaggcgattctcttgccctcagcctcctgagtagctgggattacaggcacccatc
1261 accatgtccagctaatttttgtatttttagtagagacagggttttcccatgttggccagg
1321 ctggtctcgatctcctgacctcaaatgatccgcccacctcggtcccaagtgtggga
1381 tgacagttgtgagccaccacactcagcctgctctttctaataatttgaaactgttagaca
1441 atttgctacccatctaattgtgatatttttaggaatccaatatgcatgggtttattattctt
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1501 aaaaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaag
1621 ttatgctagtgtctcatttcaaaggctgcttttccagcttacattttatatacttactc
1681 acttgaagtttctaaatattcttgtaattttaaaactatctcagatttactgaggtttat
1741 cttctggtggttagattatccataagaagagtgatgtgccagaatcactctgggatccttg
1801 tctgacaagattcaaaggactaaatttaattcagtcataaacactgccaataccgttta
1861 tgggtagacatctttggaaatttccacaagggtcagacattcgcaactatcccttctacat
1921 gtccacacgtatactccaacactttattaggtctctgattagtttggaaagtatgcctcc
1981 atctgaattagtccagtgtggcttagagttggtacaacattctcacagaatttcctaatt
2041 ttgtaggttcagcctgataaccactggagttctttggtcctcattaaatagctttcttca
2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcacttaaaatctgagaactggttacactacaagttaccttgg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttgttctggcaggctaataccatttccagtaaaag
2461 tgaatagaggtcagaagtcgtataaaaagaggtgttgtcagaacaccgttgagattacata
2521 ggtgaacaactatttttaagcaactttatttgtgtagtgacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattggt
2641 catattatttccatgttatcagaatatttgattttttaaaaacataggccaagttcatte
2701 acttcattattcatttatcaaaatcagagtgaaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtcaaattgatttttgctataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacagagacaa
2941 agcacaaaaataaatatcataaggggatgaacaaatggtggagaaagagttagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttggag
3061 acaagaaattaccctaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgcagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgctggaataagtggatagatataaaacaatttgatgggtatacacctcc
3361 aacttttatgatagctgttttccctccaattgttgtcctgatatttaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatggttgggaagacgtcaccaa
3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacatttttgtt
3541 caatattgatataattttatcaccaacatttcaagtttgtatttgttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2I. The cDNA (SEQ ID NO: 18) and amino acid sequence (SEQ ID NO: 19) of STEAP-1 v.9.

The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1  ggggcccgcacctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61  gtgggtggctgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10   Q E E L W K M K P R R N L E E D D Y L H
121 AC CAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30   K D T C E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTCACCAAA
50   A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTCTTTC
70   Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAAAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90   L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110  P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTGGCATTGG
130  Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTCATAATGGAACCAAGTATAAGA
150  F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170  F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTTTGCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190  Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210  E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTTATGTGTCTCTGGAATTGTGGGATTGGCAA
230  L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250  F H Y I Q V N N I *
841 AATTTCACTATATTCAGGTAAATAATATATAAaataaccctaagaggtaaactcttctttt
901 tgtgttttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttataacttgttccaattaataatgtgctctcctgttgttttcctattg
1021 cttctaattaggacaagtgtttcctagacataaataaaaggcattaaaatattctttgtt
1081 tttttttttttgtttgtttgtttttgtttgtttgttttttttgagatgaagtcctcg
1141 ctctgttgcccatgctggagtacagtggcacgatctcggtcactgcaacctgcgcctcc
1201 tgggttcaggcgattctcttgccctcagcctcctgagtagctgggattacaggcaccctcc
1261 accatgtccagctaatttttgtattttttagtagagacagggttttcccatgttggccagg
1321 ctggtctcgatctcctgacctcaaatgatccgcccacctcggcctcccaaagtgtctggga
1381 tgacagttgtgagccaccacactcagcctgctcttttetaatatgtgaaacttgtagaca
1441 atttgctacccatctaattgtgatatttttaggaatccaatatgcatgggtttattatttctt
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1501 aaaaaaaaaatattctttttacctgtcacctgaatttagtaatgccttttatgttacacaact
 1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaag
 1621 atattctagtgtctcatttcaaaggctgctttttccagcttacattttatatacttactc
 1681 acttgaagttttctaaatattcttgttaattttaaaactatctcagatttactgaggtttat
 1741 cttctggtggtagattatccataagaagagtgtgtgccagaatcactctgggatccttg
 1801 tctgacaagattcacaaggactaaatttaattcagtcataaacactgccaaattaccgttta
 1861 tgggttagacatctttggaaattttccacaaggctcagacattcgcaactatcccttctacat
 1921 gtccacacgtatactccaacacttttattaggcatctgattagtttggaaggtatgcctcc
 1981 atctgaattagtcagtggtgcttagagttggtacaacattctcacagaatttcctaatt
 2041 ttgtaggttcagcctgataaccactggagttctttggctctcattaaatagctttcttca
 2101 cacattgctctgctgttacacatatgatgaacactgcttttttagacttcattaggaatt
 2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
 2221 aggtatacaatacacatttggtaaaaactaattttcaaccaatgacatgtatttttcaact
 2281 agtaacctagaaatgtttcacttaaaaatctgagaactggttacactacaagttaccttg
 2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
 2401 gcgcctgaataattgtgagttcgatttggtctggcaggctaatagaccatttccagtaaag
 2461 tgaatagaggtcagaagtcgtataaaagaggtgtgtgcagaacaccgttgagattacata
 2521 ggtgaacaactattttttaagcaactttatttgtgtagtgcagaaagcatcccaatgcaggc
 2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattggt
 2641 catattatttccatgttatcagaatatttgatttttttaaaaacataggccaagttcatc
 2701 acttcattattcatttatcaaaatcagagtgaatcacattagtcgccttcacaactgata
 2761 aagatcactgaagtcaaattgatttttgctataatcttcaatctacctatatttaattga
 2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
 2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacagagacaa
 2941 agcacaaaaaataaatatcataaggggatgaacaaaatggtggagaaagagtagacaaag
 3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttgag
 3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
 3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
 3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
 3241 tgtttttcttttgcagagcaagctaggaattgtttcccttctactgggcacaatacacgc
 3301 attgatttttgctggaataagtggatagatataaaacaatttgatggtatacacctcc
 3361 aacttttatgatagctgttttccctccaattgttgctcctgatattttaaagcatactatt
 3421 cctgccatgcttgaggaagaagatactgaagattagacatgggttggaagacgtcaccaa
 3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacatttttgtt
 3541 caatattgatataattttatcaccaacatttcaagtttgatttggttaataaaatgattat
 3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2J. The cDNA (SEQ ID NO: 20) and amino acid sequence (SEQ ID NO.: 21) of STEAP-1 v.10.

The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1 ggggcccgcacctctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61 gtgggtggctgaagccatactatctttatagaattaATGGAAAGCAGAAAAGACATCACAA
10  Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAAATTTAGAAGAAGACGATTATTTGC
30  K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTGCACCAAA
50  A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTTTTC
70  Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAATAAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90  L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCAACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110 P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130 Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATGTCCAACCTTCATAATGGAACCAAGTATAAGA
150 F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170 F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTTTGTCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCTTACA
190 Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210 E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230 L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATCCATCTGTGAGTGACTCTTTGACATGGAGAG
250 F H Y I Q V N N I *
841 AATTTCACTATATTACAGGTAAATAATATATAAaataaccctaagaggtaaattcttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttatacttggttccaattaataatgtgctctcctgttggtttccctattg
1021 cttctaattaggacaagtgtttcctagacataaataaaaggcattaaaatattctttgtt
1081 tttttttttttgtttgtttgtttttgtttgtttgtttgttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtggcacgatctcggtcactgcaacctgagcctcc
1201 tgggttcaggcgattctcttgccctcagcctcctgagtagctgggattacaggcaccctac
1261 accatgtccagctaatttttgtattttttagtagagacagggttttcccatgttgccagg
1321 ctggtctcgatctcctgacctcaaatgatccgcccacctcggtctcccaaagtgtgga
1381 tgacagttgtgagccaccacactcagcctgctctttctaataatttgaaactgttagaca
1441 atttgctacccatctaattgtgatatttttaggaatccaatatgcatgggtttattattctt
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1501 aaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
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1681 acttgaagtttctaaatattcttgtaattttaaaaaatatctcagatttactgaggtttat
1741 cttctggtggttagattatccataagaagagtgatgtgccagaatcactctgggatccttg
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1861 tgggtagacatctttggaaatttccacaaggctcagacattcgcaactatcccttctacat
1921 gtccacacgtatactccaacactttattagggcatctgattagtttggaaagtatgcctcc
1981 atctgaattagtcagtggtggttagagttggtacaacattctcacagaatttcctaatt
2041 ttgtaggttcagcctgataaccactggagttctttggteectcattaaatagctttcttca
2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcacttaaaatctgagaactggttacactacaagttaccttgg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttgttctggcaggctaataccatttccagtaaag
2461 tgaatagaggtcagaagtcgtataaaagagggtgttgtcagaacaccgttgagattacata
2521 ggtgaacaactatttttaagcaactttatttgtgtagtgacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattggt
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2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacagagacaa
2941 agcacaaaaataaataatcataaggggatgaacaaaatggtggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttggag
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3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgcagagcaagctaggaattgtttcccttctactgggcacaatacacgc
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3541 caatattgatataattttatcaccaacatttcaagtttgtatttgttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2K. The cDNA (SEQ ID NO: 22) and amino acid sequence (SEQ ID NO: 23) of STEAP-1 v.11.

The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1  ggggcccgcacctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                                     M E S R K D I T N
61  gtgggtggctgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10   Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30   K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTGCACCAAA
50   A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACTCTTTC
70   Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAAAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90   L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110  P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130  Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTTCATAATGGAACCAAGTATAAGA
150  F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170  F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTTTGTGCTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190  Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210  E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTTATGTGTCTCTGGAATGTGGGATTGGCAA
230  L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250  F H Y I Q V N N I *
841 AATTTCACTATATTCAGGTAAATAATATATAAaataaccctaagaggtaaattcttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttatacttgttccaattaataatgtgctctcctgttgttttccctattg
1021 cttctaattaggacaagtgtttcctagacataaataaaaaggcattaaaatattctttgtt
1081 tttttttttttgtttgtttgtttttgtttgtttgtttgttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtggcacgatctcggtcactgcaacctgcgctcc
1201 tgggttcaggcgattctcttgctcagcctcctgagtagctgggattacaggcaccctac
1261 accatgtccagctaatttttgtattttttagtagagacagggttttcccatgttggccagg
1321 ctgggtctcgatctcctgacctcaaatgatccgcccacctcggcctcccaaagtgtggga
1381 tgacagttgtgagccaccacactcagcctgctcttttctaataatttgaaacttgtagaca
1441 atttgctacctatctaattgtgatatttttaggaatccaatatgcatgggtttattatttctt
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1741 cttctgggtggtagattatccataagaagagtgtgtgccagaatcactctgggatccttg
1801 tctgacaagattcaaaggactaaatttaattcagtcataaacactgccaataccgttta
1861 tgggtagacatctttggaaatttccacaagggtcagacattcgcaactatcccttctacat
1921 gtccacacgtatactccaacactttattagggcatctgattagtttggaagtatgcctcc
1981 atctgaattagtcacagtgtggcttagagttggtacaacattctcacagaatttcttaatt
2041 ttgtaggttcagcctgataaccactggagttctttggtcctcattaaatagctttcttca
2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtattttcaact
2281 agtaacctagaaatgtttcacttaaaatctgagaactgggttacactacaagttaccttgg
2341 agattcatatatgaaaatgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttgttctggcaggctaatagaccatttccagtaag
2461 tgaatagaggtcagaagtcgtataaaagagggtgtgtcagaacaccgttgagattacata
2521 ggtgaacaactattttttaagcaactttatttgtgtagtgacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaattgtt
2641 catattatttccatgttatcagaatatttgattttttaaaaacataggccaagttcatte
2701 acttcattattcattttatcaaaatcagagtgaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtcaaattgatttttgcctataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacagagacaa
2941 agcacaaaaaataaataatcataaggggatgaacaaaatgggtggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttccacttagacagcttggag
3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgcagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgcctggaataagtggatagatataaaacaatttgtatggtatacacctcc
3361 aacttttatgatagctgttttccctccaattgttgcctgatattttaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatgggttggaagacgtcaccaa
3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacatttttgtt
3541 caatattgatataattttatcaccaacatttcaagtttgattttgttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2L. The cDNA (SEQ ID NO: 24) and amino acid sequence (SEQ ID NO: 25) of STEAP-1 v.12.

The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1  ggggcccgcacctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61  gtgggtggctgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10  Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30  K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTCACCAAA
50  A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTTTTC
70  Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90  L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTTATAAAA
110 P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130 Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTTCATAATGGAACCAAGTATAAGA
150 F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170 F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTGTGCTGACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190 Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210 E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230 L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250 F H Y I Q V N N I *
841 AATTTCACTATATTACAGGTAAATAATATATAAaataaccctaagaggtaaattcttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttatacttgttccaattaataatgtgctctcctgttgttttccctattg
1021 cttctaattaggacaagtgtttcctagacataaataaaaggcattaaaaatattctttgtt
1081 tttttttttttgtttgtttgtttttgtttgtttgttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtggcacgatctcggtcactgcaacctgcgccctcc
1201 tgggttcaggcgattctcttgcctcagcctcctgagtagctgggattacaggcacccatc
1261 accatgtccagctaatttttgtatttttagtagagacagggttttcccatgttgccagg
1321 ctggtctcgatctcctgacctcaaatgatccgcccacctcggcctcccaaagtgtggga
1381 tgacagttgtgagccaccacactcagcctgctctttctaataatttgaaactgttagaca
1441 atttgctacccatctaattgtgatatttttaggaatccaatatgcatgggtttattattctt
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1501 aaaaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaag
1621 atatgctagtgtctcatttcaaaggctgctttttccagcttacattttatatacttactc
1681 acttgaagtttctaaatattcttgttaattttaaaactatctcagatttactgaggtttat
1741 cttctggtggttagattatccataagaagagtgatgtgccagaatcactctgggatccttg
1801 tctgacaagattcaaaggactaaattttaattcagtcataaacactgccaattaccgttta
1861 tgggtagacatcttttgaaatttccacaaggctcagacattcgcaactatcccttctacat
1921\gtccacacgtatactccaacactttattaggtctgatttagtttggaagtatgcctcc
1981 atctgaattagtcagtggtggttagagttggtacaacattctcacagaatttccctaatt
2041 ttgtagggttcagcctgataaccactggagttcttttggtcctcattaaatagctttcttca
2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcacttaaaatctgagaactggttacactacaagttaccttgg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttgttctggcaggctaataccatttccagtaaag
2461 tgaatagaggtcagaagtcgtataaaaagaggtgttgcagaacaccgttgagattacata
2521 ggtgaacaactatttttaagcaactttatttgtgtagtgacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaatgtt
2641 catatgatttccatgttatcagaatatttgatttttttaaaaacataggccaagttcatte
2701 acttcattattcatttatcaaaatcagagtgaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtcaaattgatttttgcctataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtcctgatttttaggtatcctgtgaaaagcagaattaagacaaatacacaaagagacaa
2941 agcacaaaaataaatatcataaggggatgaacaaaatggtggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttccacttagacagcttggag
3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgcagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgcctggaataagtggatagatataaaacaatttgtatggtatacacctcc
3361 aacttttatgatagctgttttccctccaattgttgcctgatatttaaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatggttgggaagacgtcaccaa
3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacatttttgtt
3541 caatattgatataattttatcaccaacatttcaagtttgtatttgttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2M. The cDNA (SEQ ID NO: 26) and amino acid sequence (SEQ ID NO: 27) of STEAP-1

v.13. The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1  ggggccccgcacctctgggagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61  gtgggtggtgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10   Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30   K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTGCACCAAA
50   A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTTTTC
70   Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTTAAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90   L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110  P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATGG
130  Y L P G V I A A I V Q L H N G T K Y K K
481 TTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTCATAATGGAACCAAGTATAAGA
150  F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170  F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTTTGTCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCTTACA
190  Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210  E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230  L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250  F H Y I Q V N N I *
841 AATTTCACTATATTTCAGGTAAATAATATATAAataaacccctaagaggtaaatcttctttt
901 tgtgtttatgatatagaatatgttgactttacccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttataacttgttccaattaataatgtgctctcctgttgttttccctattg
1021 cttctaattaggacaagtgtttcctagacataaataaaaggcattaaaaatattctttgtt
1081 tttttttttttgtttgtttgtttttgtttgtttgtttttgtttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtggcacgatctcggtcactgcaacctgcgcctcc
1201 tgggttcaggcgattctcttgccctcagcctcctgagtagctgggattacaggcacccatc
1261 accatgtccagctaatttttgtattttttagtagagacagggttttcccatgttggccagg
1321 ctggtctcgatctcctgacctcaaatgatccgcccacctcggtcctcccaaagtgtggtgga
1381 tgacagttgtgagccaccacactcagcctgctcttttctaataatttgaaactgttagaca
1441 atttgctacccatctaataatgtgatatttttaggaatccaatatgcatggtttattatttctt
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1501 aaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaaag
1621 atatgctagtgtctcatttcaaaggctgctttttccagcttacattttatatacttactc
1681 acttgaagtttctaaatattcttgtaattttaaaactatctcagatttactgaggtttat
1741 cttctggtggttagattatccataagaagagtgatgtgccagaatcactctgggaccttg
1801 tctgacaagattcaaaggactaaatttaattcagtcacgaacactgccattaccgttta
1861 tgggtagacatctttggaaatttccacaaggctcagacattcgcaactatcccttctacat
1921 gtccacacgtatactccaacactttattagggcatctgattagtttggaagtatgcctcc
1981 atctgaatttagtccagtggtggttagagttggtacaacattctcacagaatttcctaatt
2041 ttgtaggttcagcctgataaaccactggagttctttggctcctcattaaatagctttcttca
2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcacttaaaatctgagaactggttacactacaagttaccttgg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttggtctggcaggctaataccatttccagtaaag
2461 tgaatagaggtcagaagtcgtataaaagaggtgtgtcagaacaccgttgagattacata
2521 ggtgaacaactatttttaagcaactttatttggtgtagtgacaaagcatccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaattgtt
2641 catattatttccatgttatcagaatatttgattttttaaaaacataggccaagttcattc
2701 acttcattatttcatttatcaaaatcagagtgaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtc aaattgatttttgcataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagggatcctgctataagtaagact
2881 cagtcctgatttttaggtatcctgtgaaaagcagaattaagacaaatacacaaagagacaa
2941 agcacaaaaaataaatatcataaggggatgaacaaatgggtggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttggag
3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgctggaataagtggatagatataaaacaatttgatggtatacacctcc
3361 aacttttatgatagctgttttccctccaattgttgctcctgatatttaaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatgggttggaagacgtcaccaa
3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacattttgtt
3541 caatattgatatattttatccacaacatttcaagtttgattttgttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2N. The cDNA (SEQ ID NO: 28) and amino acid sequence (SEQ ID NO: 29) of STEAP-1 v.14.

The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1 ggggcccgcacctctgggcagcagcggcagccgagactcacgggtcaagctaaggcgaaga
1 M E S R K D I T N
61 gtgggtggctgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10 Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30 K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTCACCAAA
50 A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTCTTC
70 Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAAAATAGCTGCTATTATAGCATCTCTGACTTTCTTTTACA
90 L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110 P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGTTTCCATCACTCTCTTGGCATTGG
130 Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTTCATAATGGAACCAAGTATAAGA
150 F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170 F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTGTGCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190 Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210 E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTATGTGTCTCTGGGAATGTGGGATTGGCAA
230 L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250 F H Y I Q V N N I *
841 AATTTCACTATATTCAGGTAAATAATATATAAaataaccctaagaggtaaatcttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttatacttgttccaattaataatgtgctctcctgtgttttccctattg
1021 cttctaattaggacaagtggtttcctagacataaataaaaggcattaaaatattctttggt
1081 tttttttttttgtttgtttgtttttgtttgtttgtttgttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtagcagtggcacgatctcggctcactgcaacctgcgccctcc
1201 tgggttcaggcgattctcttgccctcagcctcctgagtagctgggattacaggcaccctac
1261 accatgtccagctaatttttgtatttttagtagagacagggttttcccatgttggccagg
1321 ctggtctcgatctcctgacctcaaatgatccgccacctcggcctcccaaagtgtctggga
1381 tgacagttgtgagccaccacactcagcctgctcttttctaataatttgaaactgttagaca
1441 atttgctaccatctaattgtgatatttttaggaatccaatatgcatgggtttattatttctt
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1501 aaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaag
1621 atatgctagtgtctcatttcaaaggctgctttttccagcttacattttatatacttactc
1681 acttgaagtttctaaatattcttgtaatttttaaaactatctcagatttactgaggtttat
1741 cttctggtggtagattatccataagaagagtgtgtgccagaatcactctgggatccttg
1801 tctgacaagattcaaaggactaaatttaattcagtcacgaacactgccaaattaccgttta
1861 tgggtagacatctttggaaatttccacaagggtcagacattcgcaactatcccttctacat
1921 gtccacacgtatactccaacactttattaggtctgtattagtttggaaggtatgcctcc
1981 atctgaattagtcagtggtggttagagttggtacaacattctcacagaatttccctaatt
2041 ttgtagggttcagcctgataaccactggagttctttggtcctcattaaatagctttcttca
2101 cacattgctctgctgttacacatatgatgaacactgctttttagacttcattaggaatt
2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcacttaaaatctgagaactggttacactacaagttaccttg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttggtctggtcaggctaataccatttccagtaaag
2461 tgaatagaggtcagaagtcgtataaaagaggtgtgtgcagaacaccgttgagattacata
2521 ggtgaacaactatttttaagcaactttatttggtgtagtgcacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattggt
2641 catattatttccatgttatcagaatatttgattttttaaaaacataggccaagttcatcc
2701 acttcattattcatttatcaaaatcagagtgaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtcaaattgatttttgcataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtccttgatttttaggtatcctgtgataagcagaattaagacaaatacacagagacaa
2941 agcacaaaaataaatatcataaggggatgaacaaaatggtggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttgga
3061 acaagaaattaccctaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgcagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgcctggaataagtggtatagatataaaacaatttgatggtatcacctcc
3361 aacttttatgatagctgttttccctccaattgtgtgctgatattttaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatgggtgggaagacgtcaccaa
3481 aattaacaaaactgagatatgttccagttgtagaattactgtttacacacatttttgtt
3541 caatattgatataattttatcaccaacatttcaagtttgtatttgttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2 (O). The cDNA (SEQ ID NO: 30) and amino acid sequence (SEQ ID NO: 31) of STEAP-1 v.15. The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1 ggggcccgcacctctgggcagcagcggcagccgagactcacggtcaagctaaggcgaaga
1                               M E S R K D I T N
61 gtgggtggctgaagccatactatatttatagaattaATGGAAAGCAGAAAAGACATCACAA
10  Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAAATTTAGAAGAAGACGATTATTGTC
30  K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTGACACAAA
50  A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTTTTC
70  Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAATAAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90  L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110 P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130 Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTCATAATGGAACCAAGTATAAGA
150 F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTIGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170 F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTTTGTCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190 Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210 E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230 L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250 F H Y I Q V N N I *
841 AATTTCACTATATTCAGGTAAATAATATATAAataaccctaagaggtaaatcttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttataacttggtccaattaataatgtgctctcctgtgttttccctattg
1021 cttctaatttaggacaagtggttccctagacataaataaaaggcattaaaaatattctttgtt
1081 tttttttttttgtttgtttgtttttgtttgtttgtttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtggcacgatctcggctcactgcaacctgcgcctcc
1201 tgggttcaggcgattctcttgcctcagcctcctgagtagctgggattacaggcaccctac
1261 accatgtccagctaatttttgtatttttagtagagacagggttttcccatgttggccagg
1321 ctgggtctcgatctcctgacctcaaatgatccgccacctcggcctcccaaagtgtggga
1381 tgacagttgtgagccaccacactcagcctgctcttttctaataatttgaaacttgtagaca
1441 atttgctacccatctaattgtgatatttttaggaatccaatatgcatgggtttattatttctt
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1501 aaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
 1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaaaag
 1621 atatgctagtgtctcatttcaaaggctgctttttccagcttacattttatatacttactc
 1681 acttgaagtttctaaatattcttgttaattttaaaactatctcagatttactgaggtttat
 1741 cttctggtaggttagattatccataagaagagtgatgtgccagaatcactctgggatccttg
 1801 tctgacaagattcaaaggactaaattttaattcagtcataaacactgccattaccggttta
 1861 tgggtagacatctttggaaatttcacaaggctcagacattcgcaactatcccttctacat
 1921 gtccacacgtataactccaacactttattaggtcctgatttagtttggaagtagtgcctcc
 1981 atctgaatttagtccagtggtggttagagttggtacaacattctcacagaatttcctaatt
 2041 ttgtaggttcagcctgataaccactggagttctttggctcctcattaaatagctttcttca
 2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
 2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
 2221 aggtatacaatacacattttggtaaaactaattttcaaccaatgacatgtatttttcaact
 2281 agtaacctagaaatgtttcacttaaaatctgagaactggttacactacaagttaccttgg
 2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
 2401 gcgcctgaataattgtgagttcgatttgttctggcaggctaataccatttccagtaaag
 2461 tgaatagaggtcagaagtcgtataaaaagaggtgtgtgcagaacaccgttgagattacata
 2521 ggtgaacaactatttttaagcaactttatttgtgtagtgcacaaagcatcccaatgcaggc
 2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattggt
 2641 catattatttccatgttatcagaatatattgatttttttaaaaacataggccaagtccattc
 2701 acttcattattcatttatcaaaatcagagtgaaatcacattagtcgccttcacaactgata
 2761 aagatcactgaagtc aaattgatttttgcctataatcttcaatctacctatatttaattga
 2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
 2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacagagacaa
 2941 agcacaaaaaataaatatcataaggggatgaacaaaatggtggagaaagagtagacaaag
 3001 tttttcatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttggag
 3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
 3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
 3181 gagcatatccagatgaggtaggatgggataaactcttattgaaccaatcttcaccaattt
 3241 tgtttttcttttgcagagcaagctaggaattgtttcccttctactgggcacaatacacgc
 3301 attgatttttgcctggaataagtggatagatataaaacaatttgtatggtatacacctcc
 3361 aacttttatgatagctgttttccctccaattgttgtcctgatattttaaagcatactatt
 3421 cctgccatgcttgaggaagaagatactgaagattagacatggttggaagacgtcaccaa
 3481 aattaacaaaactgagatatgttcccagttgttagaattactgtttacacacatttttgtt
 3541 caatattgatataattttatcaccaacatttcaagtttgtatttgttaataaaatgattat
 3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2P. The cDNA (SEQ ID NO: 32) and amino acid sequence (SEQ ID NO: 33) of STEAP-1 v.16.

The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1 ggggccccgcacctctgggcagcagcgagcagcgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61 gtgggtggctgaagccatactatatttatagaattaATGGAAAGCAGAAAAGACATCACAA
10  Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAATTTAGAAGAAGACGATTATTTGC
30  K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACCGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTGACACAAA
50  A H A D E F D C P S E L Q H T Q R L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTTTTC
70  Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTACA
90  L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110 P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTTCCATCACTCTCTTGGCATTGG
130 Y L P G V I A A I V Q L H N G T K Y K K
481 TTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACTTCATAATGGAACCAAGTATAAGA
150 F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCACTTTGGGCTTCTCAGTT
170 F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTTTGTCTGTACTGCATGCAATTATAGTCTGTCTTACCCAATGAGGCGATCTTACA
190 Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210 E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTTATGTGTCTCTGGGAATTGTGGGATTGGCAA
230 L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTTGGCTGTGACATCTATTCCATCTGTGAGTGACTCTTTGACATGGAGAG
250 F H Y I Q V N N I *
841 AATTTCACTATATTCAGGTAAATAATATATAAaataaccctaagaggtaaattcttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttatacttgttccaattaataatgtgctctcctgttgttttccctattg
1021 cttctaaattaggacaagtgtttccttagacataaataaaaggcattaaaaatattctttggtt
1081 tttttttttttgtttgtttgtttttgtttgtttgtttgttttttgagatgaagtctctg
1141 ctctgttgcccatgctggagtacagtggcacgatctcggtcactgcaacctgcgccctcc
1201 tgggttcaggcgattctcttgcctcagcctcctgagtagctgggattacaggcaccctac
1261 accatgtccagctaatttttgtatttttagtagagacagggttttcccatgttgccagg
1321 ctggtctcgatctcctgacctcaaatgatccgccacctcggcctcccaaagtgtggtgga
1381 tgacagttgtgagccaccacactcagcctgctctttctaataatttgaaacttgtagaca
1441 atttgctacccatctaattgtgatatttttaggaatccaatatgcatgggtttattattctt
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1501 aaaaaaaaaatattcttttacctgtcacctgaatttagtaatgccttttatgttacacaact
1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaaag
1621 atatgctagtgctctcatttcaaaggctgcttttccagcttacattttatatacttactc
1681 acttgaagtttctaaatattcttgtaattttaaaactatctcagatttactgaggtttat
1741 cttctggtaggttagattatccataagaagagtgatgtgccagaatcactctgggatccttg
1801 tctgacaagattcaaaggactaaatttaattcagtcataaacactgccaattaccgttta
1861 tgggtagacatctttggaaatttccacaaggctcagacattcgcaactatcccttctacat
1921 gtccacacgtatactccaacactttattagggcatctgattagtttggaagtatgcctcc
1981 atctgaattagtcagtggtggttagagttggtacaacattctcacagaatttctctaatt
2041 ttgtaggttcagcctgataaccactggagttctttggtcctcattaaatagctttcttca
2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcactttaaactctgagaactggttacactacaagttaccttgg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttggtctggcaggctaataccatttccagtaaaag
2461 tgaatagaggtcagaagtcgtataaaagagggtgtgtgcagaacaccggttgagattacata
2521 ggtgaacaactatttttaagcaactttatttggtgtagtgacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattggt
2641 catattatttccatgttatcagaatatttgattttttaaaaacataggccaagttcatte
2701 acttcattattcatttatcaaaatcagagtgaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtc aaattgatttttgctataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacagagacaa
2941 agcacaaaaaataaatatcataaggggatgaacaaaatgggtggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttgagg
3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagtagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaaca
3181 gagcatatccagatgaggtaggatgggataaaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgcagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgctggaataagtggatagatataaaacaatttgatgggtatacacctcc
3361 aacttttatgatagctgttttccctccaattgtgtgctctgatattttaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatgggtgggaagacgtcaccaa
3481 aattaacaaaactgagatatgttcccagttgtagaattactgtttacacacatttttgtt
3541 caatattgatataattttatcaccaacatttcaagtttgtatttggttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 2Q. The cDNA (SEQ ID NO: 34) and amino acid sequence (SEQ ID NO: 35) of STEAP-1 v.17.

The start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon.

```
1  ggggcccgcacctctgggcagcagcgccagccgagactcacgggtcaagctaaggcgaaga
1                               M E S R K D I T N
61  gtgggtggctgaagccatactattttatagaattaATGGAAAGCAGAAAAGACATCACAA
10  Q E E L W K M K P R R N L E E D D Y L H
121 ACCAAGAAGAACTTTGGAAAATGAAGCCTAGGAGAAAATTTAGAAGAAGACGATTATTTGC
30  K D T G E T S M L K R P V L L H L H Q T
181 ATAAGGACACGGGAGAGACCAGCATGCTAAAAAGACCTGTGCTTTTGCATTTGCACCAAA
50  A H A D E F D C P S E L Q H T Q E L F P
241 CAGCCCATGCTGATGAATTTGACTGCCCTTCAGAACTTCAGCACACACAGGAACCTTTTC
70  Q W H L P I K I A A I I A S L T F L Y T
301 CACAGTGGCACTTGCCAATTAAATAGCTGCTATTATAGCATCTCTGACTTTTCTTTTACA
90  L L R E V I H P L A T S H Q Q Y F Y K I
361 CTCTTCTGAGGGAAGTAATTCACCCCTTAGCAACTTCCCATCAACAATATTTTATAAAA
110 P I L V I N K V L P M V S I T L L A L V
421 TTCCAATCCTGGTCATCAACAAAGTCTTGCCAATGGTTCCATCACTCTCTTGGCATTGG
130 Y L P G V I A A I V Q L H N G T K Y K K
481 TTTACCTGCCAGGTGTGATAGCAGCAATTGTCCAACCTCATAATGGAACCAAGTATAAGA
150 F P H W L D K W M L T R K Q F G L L S F
541 AGTTTCCACATTGGTTGGATAAGTGGATGTTAACAAGAAAGCAGTTTGGGCTTCTCAGTT
170 F F A V L H A I Y S L S Y P M R R S Y R
601 TCTTTTTTGTCTGTACTGCATGCAATTTATAGTCTGTCTTACCCAATGAGGCGATCCTACA
190 Y K L L N W A Y Q Q V Q Q N K E D A W I
661 GATACAAGTTGTCTAAACTGGGCATATCAACAGGTCCAACAAAATAAAGAAGATGCCTGGA
210 E H D V W R M E I Y V S L G I V G L A I
721 TTGAGCATGATGTTTGGAGAATGGAGATTTATGTGTCTCTGGGAATGTGGGATTGGCAA
230 L A L L A V T S I P S V S D S L T W R E
781 TACTGGCTCTGTGGCTGTGACATCTATTCCATCTGTGAGTGAAGCTTTGACATGGAGAG
250 F H Y I Q V N N I *
841 AATTTCACTATATTCAGGTAAATAATATATAAaataaccctaagaggtaaatcttctttt
901 tgtgtttatgatatagaatatgttgactttaccccataaaaaataacaaatgtttttcaa
961 cagcaaagatcttataacttgttccaattaataatgtgctctcctgtgtgttttccctattg
1021 cttctaattaggacaagtgttttcttagacataaataaaaggcattaaaaatattctttgtt
1081 tttttttttttgtttgtttgtttttttgtttgtttgttttttttgagatgaagtctcg
1141 ctctgttgcccatgctggagtacagtgggcagcatctcggtcactgcaacctgcgctcc
1201 tgggttcaggcgattctcttgcctcagcctcctgagtagctgggattacaggcaccctc
1261 accatgtccagctaattttttagtatttttagtagagacagggttttcccatgttggccagg
1321 ctggtctcgatctcctgacctcaaagatccgcccacctcggtctccaaagtgtctggga
1381 tgacagttgtgagccaccacactcagcctgctcttttctaataatttgaaacttgtagaca
1441 atttgctacccatctaataatgtgatatttttaggaatccaatatgcatggtttattatttctt
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1501 aaaaaaaaaatattctttttacctgtcacctgaatttagtaatgccttttatgttacacaact
1561 tagcactttccagaaacaaaaactctctccttgaaataatagagtttttatctaccaaag
1621 atatgctagtgtctcatttcaaaggctgctttttccagcttacattttatatacttactc
1681 acttgaagtttctaaatattcttgtaattttaaaaactatctcagatttactgaggtttat
1741 cttctggtggttagattatccataagaagagtgatgtgccagaatcactctgggatccttg
1801 tctgacaagattcaaaggactaaatttaattcagtcacatgaacactgccaattaccgttta
1861 tgggtagacatctttggaaatttccacaagggtcagacattcgcaactatcccttctacat
1921 gtccacacgtatactccaacactttattaggtcctgatttagtttggaagtatgcctcc
1981 atctgaatttagtccagtggtgcttagagttggtacaacattctcacagaatttcctaatt
2041 ttgtaggttcagcctgataaccactggagttctttggctcctcattaaatagctttcttca
2101 cacattgctctgcctgttacacatatgatgaacactgcttttttagacttcattaggaatt
2161 taggactgcatcttgacaactgagcctattctactatatgtacaatacctagcccataat
2221 aggtatacaatacacatttggtaaaactaattttcaaccaatgacatgtatttttcaact
2281 agtaacctagaaatgtttcacttaaaatctgagaactggttacactacaagttaccttg
2341 agattcatatatgaaaacgcaaacttagctatttgattgtattcactgggacttaagaat
2401 gcgcctgaataattgtgagttcgatttggtctctggcaggctaataccatttccagtaaag
2461 tgaatagaggtcagaagtcgtataaaagaggtgtgtcagaacaccggtgagattacata
2521 ggtgaacaactatttttaagcaactttatttggtgtagtgacaaagcatcccaatgcaggc
2581 tgaaatgtttcatcacatctctggatctctctattttgtgcagacattgaaaaaattggt
2641 catattatttccatgttatcagaatatttgattttttaaaaacataggccaagttcattc
2701 acttcattattcatttatcaaaatcagagtgaatcacattagtcgccttcacaactgata
2761 aagatcactgaagtcaaattgatttttgcctataatcttcaatctacctatatttaattga
2821 gaatctaaaatgtacaaatcattgtgttgattctgcagtgatcctgctataagtaagact
2881 cagtccttgatttttaggtatcctgtgaaaagcagaattaagacaaatacacagagacaa
2941 agcacaaaaataaatatcataaggggatgaacaaaatggtggagaaagagtagacaaag
3001 tttttgatcacctgccttcaaagaaaggctgtgaattttgttcacttagacagcttgag
3061 acaagaaattacccaaaagtaagggtgaggaggataggcaaaaagagcagaaagatgtgaa
3121 tggacattgttgagaaatgtgataggaaaacaatcatagataaaggatttccaagcaact
3181 gagcatatccagatgaggtaggatgggataaaactcttattgaaccaatcttcaccaattt
3241 tgtttttcttttgagagcaagctaggaattgtttcccttctactgggcacaatacacgc
3301 attgatttttgctggaataagtggtatagatataaaacaatttgatggtatacacctcc
3361 aacttttatgatagctgttttccctccaattgtgtcctgatattttaaaagcatactatt
3421 cctgccatgcttgaggaagaagatactgaagattagacatggttggaagacgtcaccaa
3481 aattaacaaaactgagatatgttccagttgtagaattactgtttacacacatttttgtt
3541 caatattgatataattttatcaccaacatttcaagtttgattttgttaataaaatgattat
3601 tcaaggaaaaaaaaaaaaaaaaaaaaa

Figure 3:

Figure 3A. Amino acid sequence of STEAP-1 v.1 (SEQ ID NO: 36). The STEAP-1 v.1 protein has 339 amino acids.

```

1 MESRKDITNQ EELWKMKPRR NLEEDDYLHK DTGETSMLKR PVLLHLHQTA HADEFDCPSE
61 LQHTQELFPQ WHLPIKIAAI IASLTFLYTL LREVIHPLAT SHQQYFYKIP ILVINKVLPM
121 VSITLLALVY LPGVIAAIVQ LHNGTKYKKF PHWLDKWMLT RKQFGLLSFF FAVLHAIYSL
181 SYPMRRSYRY KLLNWAYQQV QQNKEDAWIE HDVWRMEIYV SLGIVGLAIL ALLAVTSIPS
241 VSDSLTWREF HYIQSKLGIV SLLLGTHIAL IFAWNKWIDI KQFVWYTPPT FMIAVFLPIV
301 VLIFKSILFL PCLRKKILKI RHGWEDVTKI NKTEICSQL

```

Figure 3B. Amino acid sequence of STEAP-1 v.2 (SEQ ID NO: 37). The STEAP-1 v.2 protein has 258 amino acids.

```

1 MESRKDITNQ EELWKMKPRR NLEEDDYLHK DTGETSMLKR PVLLHLHQTA HADEFDCPSE
61 LQHTQELFPQ WHLPIKIAAI IASLTFLYTL LREVIHPLAT SHQQYFYKIP ILVINKVLPM
121 VSITLLALVY LPGVIAAIVQ LHNGTKYKKF PHWLDKWMLT RKQFGLLSFF FAVLHAIYSL
181 SYPMRRSYRY KLLNWAYQQV QQNKEDAWIE HDVWRMEIYV SLGIVGLAIL ALLAVTSIPS
241 VSDSLTWREF HYIQVNNI

```

Figure 3C. Amino acid sequence of STEAP-1 v.3 (SEQ ID NO: 38). The STEAP-1 v.3 protein has 282 amino acids.

```

1 MESRKDITNQ EELWKMKPRR NLEEDDYLHK DTGETSMLKR PVLLHLHQTA HADEFDCPSE
61 LQHTQELFPQ WHLPIKIAAI IASLTFLYTL LREVIHPLAT SHQQYFYKIP ILVINKVLPM
121 VSITLLALVY LPGVIAAIVQ LHNGTKYKKF PHWLDKWMLT RKQFGLLSFF FAVLHAIYSL
181 SYPMRRSYRY KLLNWAYQQV QQNKEDAWIE HDVWRMEIYV SLGIVGLAIL ALLAVTSIPS
241 VSDSLTWREF HYIQIIHKKS DVPESLWDPC LTRFKGLNLI QS

```

Figure 3D. Amino acid sequence of STEAP-1 v.4 (SEQ ID NO: 39). The STEAP-1 v.4 protein has 258 amino acids.

```

1 MESRKDITNQ EELWKMKPRR NLEEDDYLHK DTGETSMLKR PVLLHLHQTA HADEFDCPSE
61 LQHTQELFPQ WHLPIKIAAI IASLTFLYTL LREVIHPLAT SHQQYFYKIP ILVINKVLPM
121 VSITLLALVY LPGVIAAIVQ LHNGTKYKKF PHWLDKWMLT RKQFGLLSLF FAVLHAIYSL
181 SYPMRRSYRY KLLNWAYQQV QQNKEDAWIE HDVWRMEIYV SLGIVGLAIL ALLAVTSIPS
241 VSDSLTWREF HYIQVNNI

```

Figure 4A-Homology of STEAP-1 (SEQ ID NO: 40) to mouse TNF α -induced adipose-related protein (gi|16905133). (SEQ ID NO: 41)

Score = 224 bits (570), Expect = 2e-57
Identities = 110/270 (40%), Positives = 174/270 (63%)

Query: 66 ELFPQWHLPIKIAAIIASLTFLYTLREVIHPLATSHQQYFYKIPILVINKVLPVMSITL 125
+LFP W P +++++ F+Y +REVI+P Y++ I + N+V P+ ++ L
Sbjct: 195 QLFPWRFPPFLSSVLCIFFFVYCAIREVIYPYVNGKTDATYRLAISIPNRVFPITALIL 254

Query: 126 LALVYLPGVIAAIVQLHNGTKYKKFPHWLDKWMLTRKQFGLLSFFFVAVLHAIYSLSYPMR 185
LALVYLPGV++AAI+QL+ GTKY++FP+WLD WML RKQ GL++ FA LH IY+L P+R
Sbjct: 255 LALVYLPGILAAILQLYRGTKYRRFPNLDHWMLCRKQLGLVALGFAFLHVIYTLVPIR 314

Query: 186 RSYRYKLLNWAYQQVQONKEDAWIEHDVWRMEIYVSLGIVGLAILALLAVTSIPSVSDSL 245
R++L N Q NK+ +I W + Y++LGI+G + LL +TS+PSVS+ +
Sbjct: 315 YYVRWRLRNATITQALTNKDSPFITSYAWINDSYLALGILGFFLFLLLGITSLSVSNMV 374

Query: 246 TWREFHYIQSKLGIVSLLGTIHALIFAWNKWIDIKQFVWYTPPTFMIAVFLPIVVLIK 305
WREF ++QSKLG ++L+L T H L++ +++ W P +++A+ +P VL+ K
Sbjct: 375 NWREFRVQSKLGYLTLVLCTAHTLVYGGKRFSLPSILRWSLPSAYILALIIPCAVLVLK 434

Query: 306 SILFLPCLRKILKIRHGVEDVTKINKTEI 335
IL +PC+ K + +IR GWE +K ++ +
Sbjct: 435 CILIMPCIDKTLTRIRQGWERNISKYTQSAL 464

Figure 4B-Homology of STEAP-1 (SEQ ID NO: 42) to rat pHyde protein (gi|21717655). (SEQ ID NO: 43)

Score = 283 bits (724), Expect = 2e-75
Identities = 127/259 (49%), Positives = 184/259 (71%)

Query: 67 LFPQWHLPIKIAAIIASLTFLYTLREVIHPLATSHQQYFYKIPILVINKVLPVMSITLL 126
L P W +P +A +++ ++ Y +R+V+ P + FYK+P+ V+N +P V+ LL
Sbjct: 208 LLPSWKVPTLLALGLSTQSYAYNFIRDVLQPYIRKDEKFKMPLSVVNTTIPCVAYVLL 267

Query: 127 ALVYLPGVIAAIVQLHNGTKYKKFPHWLDKWMLTRKQFGLLSFFFVAVLHAIYSLSYPMR 186
+LVYLPGV+AA +QL GTKY++FP WLD W+ RKQ GLLSFFFA+LHA+YS P+RR
Sbjct: 268 SLVYLPGVLAALQLRRGTKYQRFDPDLDHWLQHRKQIGLLSFFFAMLHALYSFCLPLRR 327

Query: 187 SYRYKLLNWAYQQVQONKEDAWIEHDVWRMEIYVSLGIVGLAILALLAVTSIPSVSDSLT 246
S+RY L+N A +QV NK W+E +VWRMEIY+SLG++ L +L+LLAVTSIPS+++SL
Sbjct: 328 SHRYDLVNLAVKQVLANKSRLWVBEVWRMEIYLSLGVLAGMLSLAVTSIPSTIANSLN 387

Query: 247 WREFHYIQSKLGIVSLLGTIHALIFAWNKWIDIKQFVWYTPPTFMIAVFLPIVVLIK 306
W+EF ++QS LG V+L+L T+H L + W + + + +Y PPTF + + LP V+++ K
Sbjct: 388 WKEFSFVQSTLGFVALMLSTMHTLTYGWTRAFENHYKFLPPTFTLTLLPCVILAKG 447

Query: 307 ILFLPCLRKILKIRHGWE 325
+ LPCL ++ KIR GWE
Sbjct: 448 LFLPCLSHRLTKIRRGWE 466

Figure 4C-Homology of STEAP-1 SEQ ID NO: 99) to mouse six transmembrane epithelial antigen of the prostate (gi|20820492)). (SEQ ID NO: 100)

Score = 488 bits (1256), Expect = e-137
Identities = 255/303 (84%), Positives = 277/303 (91%)

```

Query: 1   MLKRPVLLHLHQTAAHADEFDCPSELQHTQELFPQWHLPIKIAAIIASLTFLYTLLREVIH 60
          MLKRP L HL   H D FDCPSELQHTQE FP W LP+K+AAII+SLTFLYTLLRE+I+
Sbjct: 37  MLKRPGLSHLQHAVHVDAFDCPSELQHTQEFFPNWRLPVKVAAIISSLTFLYTLLREIIY 96

Query: 61  PLATSHQQYFYKIPILVINKVLPVMSITLLALVYLPGVIAAIVQLHNGTKYKKFPHWLDK 120
          PL TS +QYFYKIPILVINKVLPV+ITLLALVYLPG +AA+VQL NGTKYKKFP WLD+
Sbjct: 97  PLVTSREQYFYKIPILVINKVLPVVAITLLALVYLPGELAAVVQLRNGTKYKKFPPWLDL 156

Query: 121  WMLTRKQFGLLSFFFVAVLHAIYSLSPMRRSYRYKLLNWAYQQVQQNKEDAWIEHDVWRM 180
          WML RKQFGLLSFFFVAVLHA+YSLSPMRRSYRYKLLNWAY+QVQQNKEDAW+EHDVWRM
Sbjct: 157  WMLARKQFGLLSFFFVAVLHAVYSLSPMRRSYRYKLLNWAYQVQQNKEDAWVEHDVWRM 216

Query: 181  EIVVSLGIVGLAILALLAVTSIPSVSDSLTWREFHYIQSKLGIVSLLLGTIHALIFAWN 240
          EIVVSLGIVGLAILALLAVTSIPSVSDSLTWREFHYIQSKLGIVSLLLGT+HAL+FAWNK
Sbjct: 217  EIVVSLGIVGLAILALLAVTSIPSVSDSLTWREFHYIQSKLGIVSLLLGTVHALVFAWNK 276

Query: 241  WIDIKQFVWYTPPTFMIAVFLPIVVLIKFSLFLPCLRKKILKIRHWEDVTKINKTEIC 300
          W+D+ QFVWY PPTFMIAVFLP +VLI K L LPCLRKKILKIR GWEDV+KIN+TE+
Sbjct: 277  WVDVSQFVWYMPPTFMIAVFLPTLVLICKIALCLPCLRKKILKIRCGWEDVSKINRTEMA 336

Query: 301  SQL 303
          S+L
Sbjct: 337  SRL 339

```

Figure 5 8P1D4 variant 1 Hydrophilicity profile
(Hopp T.P., Woods K.R., 1981. Proc. Natl. Acad. Sci. U.S.A. 78:3824-3828)

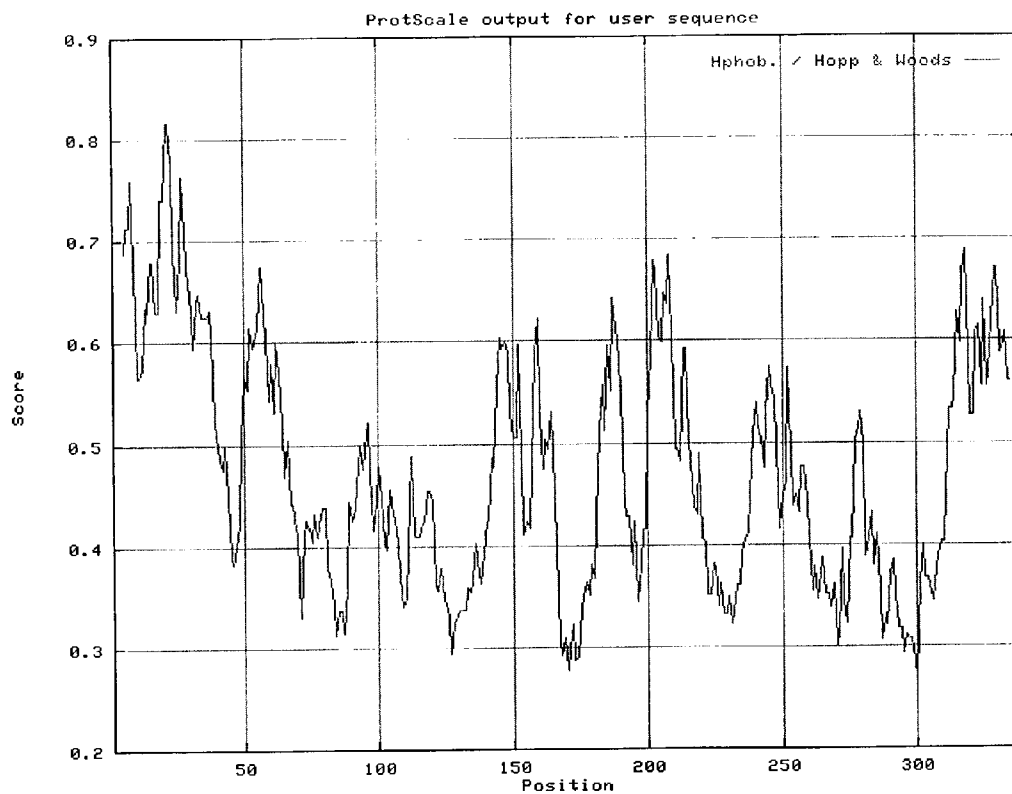


Figure 5a 8P1D4 variant 3 Hydrophilicity profile
(Hopp T.P., Woods K.R., 1981. Proc. Natl. Acad. Sci. U.S.A. 78:3824-3828)

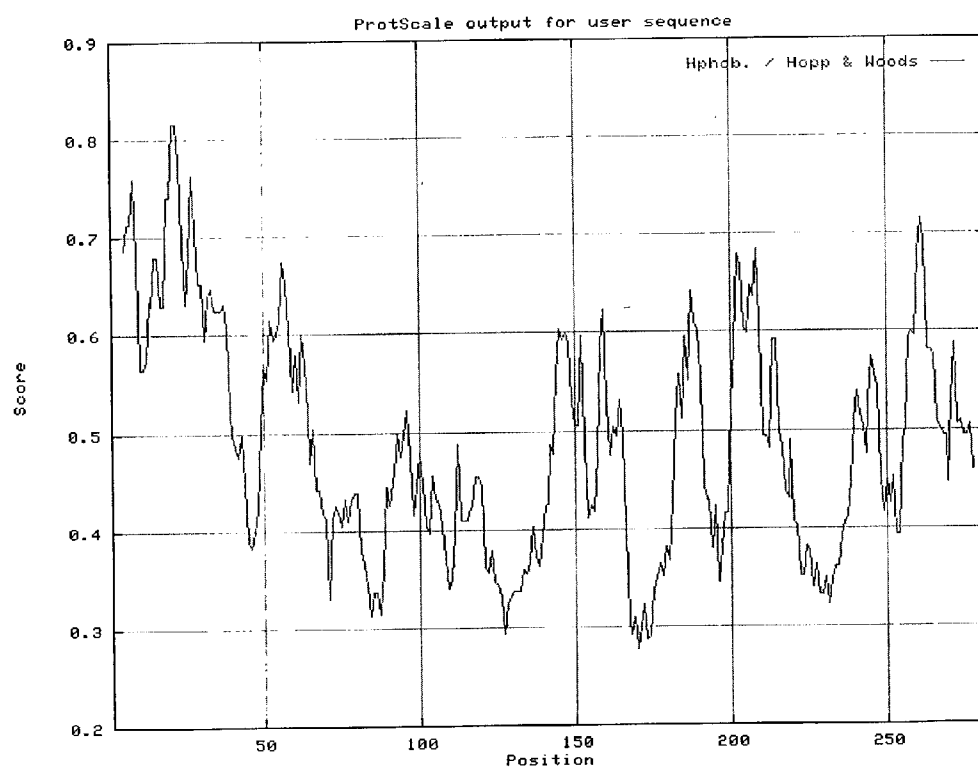


Figure 6 8P1D4 variant 1 Hydropathicity Profile
(Kyte J., Doolittle R.F., 1982. J. Mol. Biol. 157:105-132)

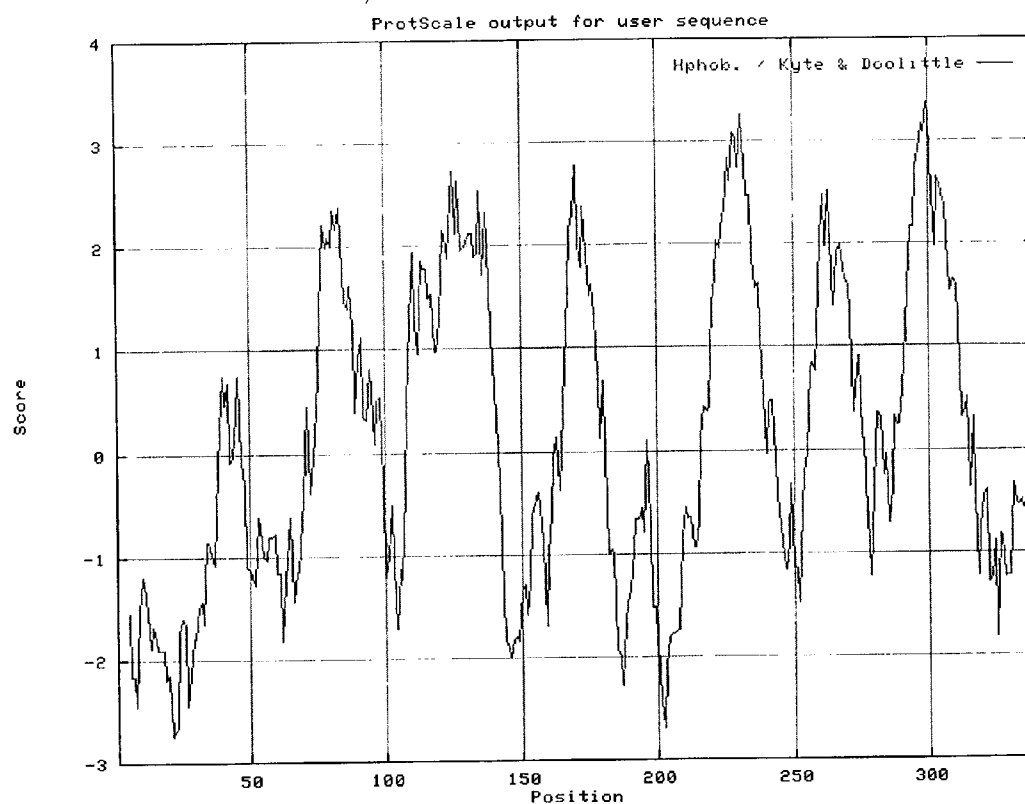


Figure 6a 8P1D4 variant 3 Hydropathicity Profile
(Kyte J., Doolittle R.F., 1982. J. Mol. Biol. 157:105-132)

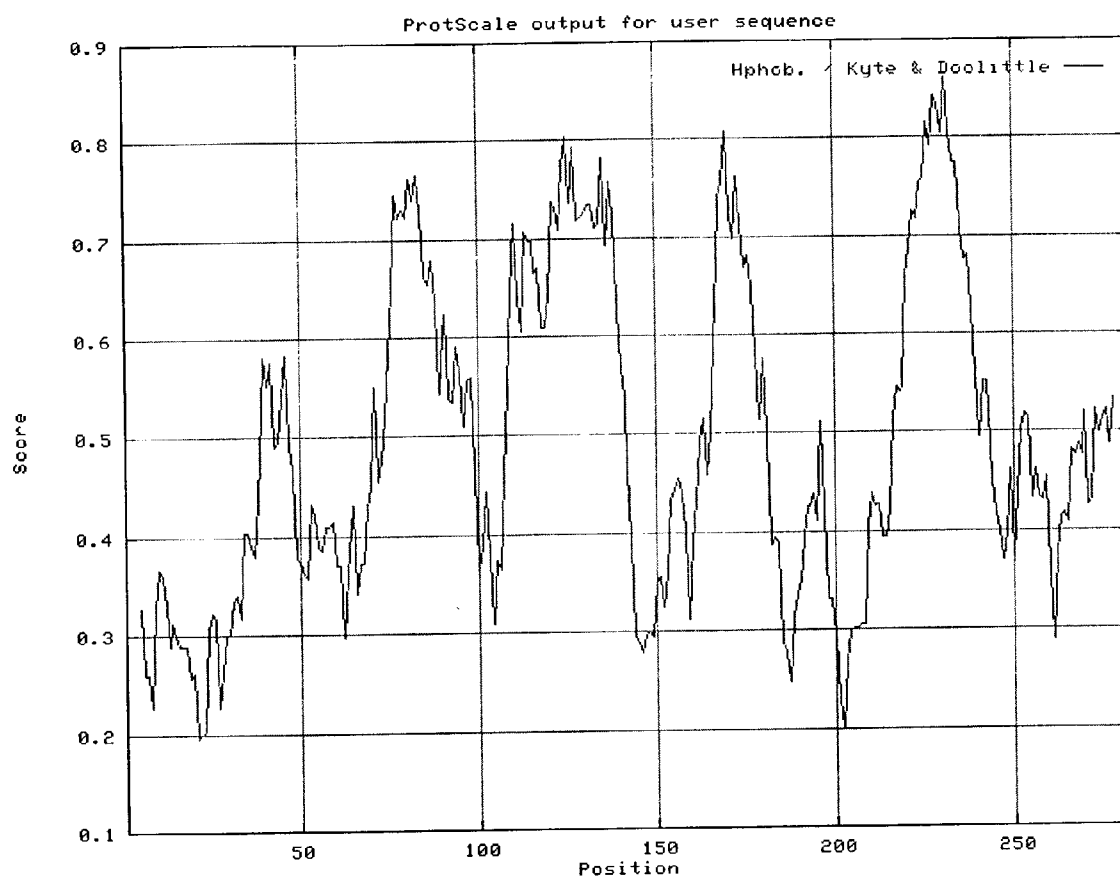


Figure 7 8P1D4 variant 1 % Accessible Residues Profile
(Janin J., 1979. Nature 277:491-492)

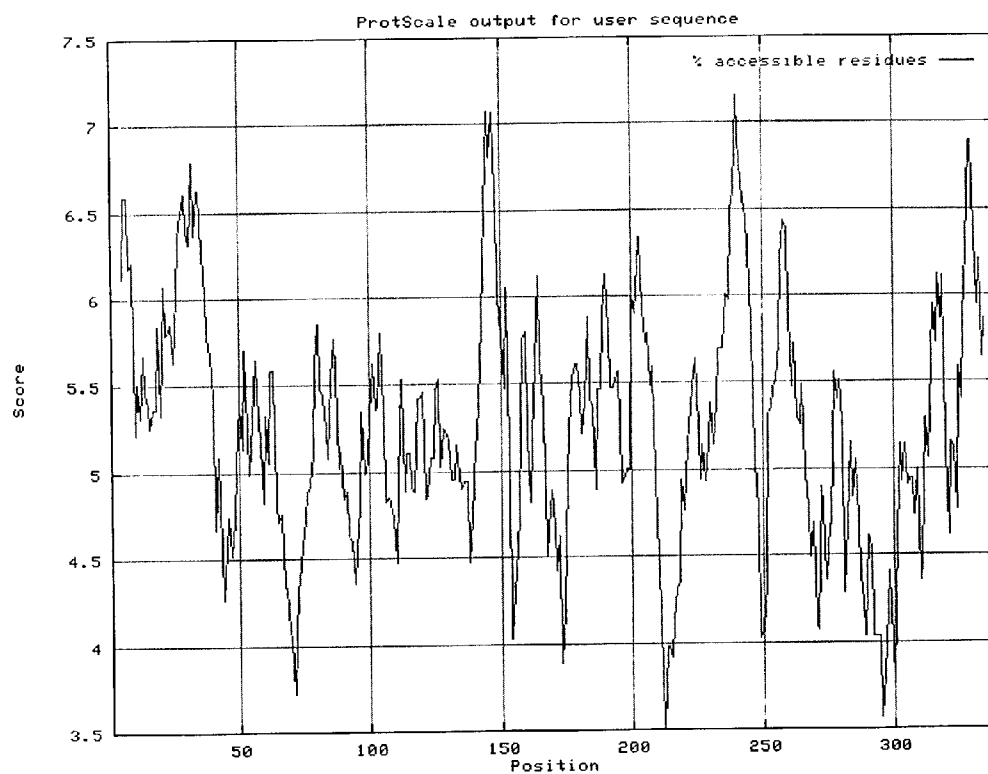


Figure 7a 8P1D4 variant 3 % Accessible Residues Profile
(Janin J., 1979. Nature 277:491-492)

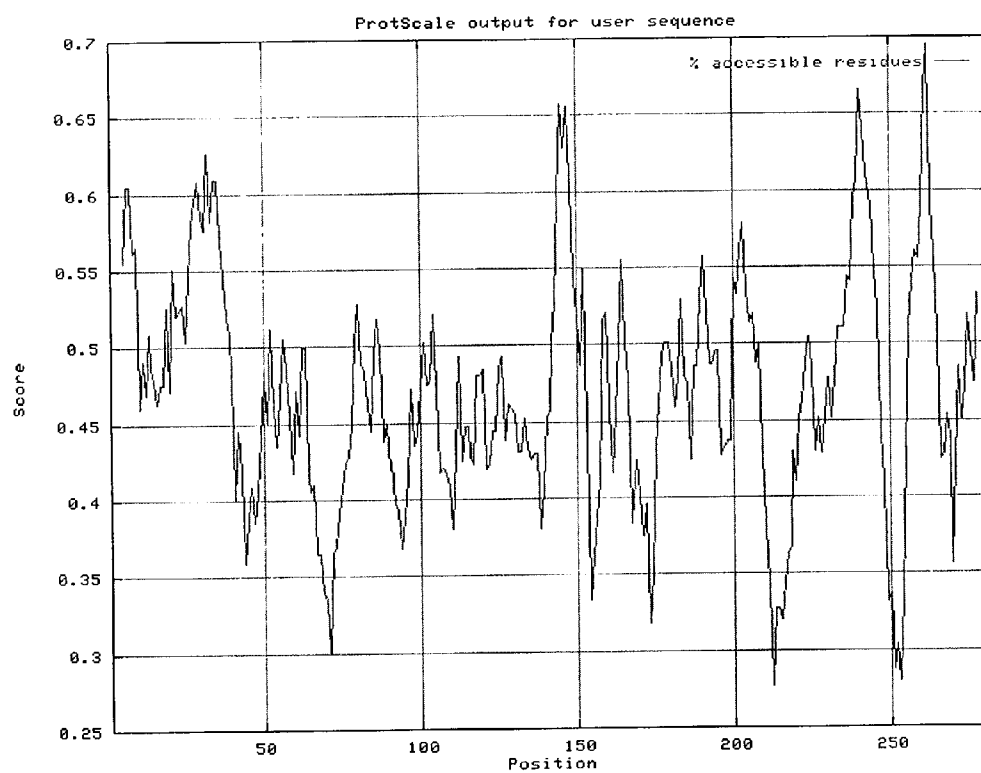


Figure 8 8P1D4 variant 1 Average Flexibility Profile

(Bhaskaran R., Ponnuswamy P.K., 1988.

Int. J. Pept. Protein Res. 32:242-255)

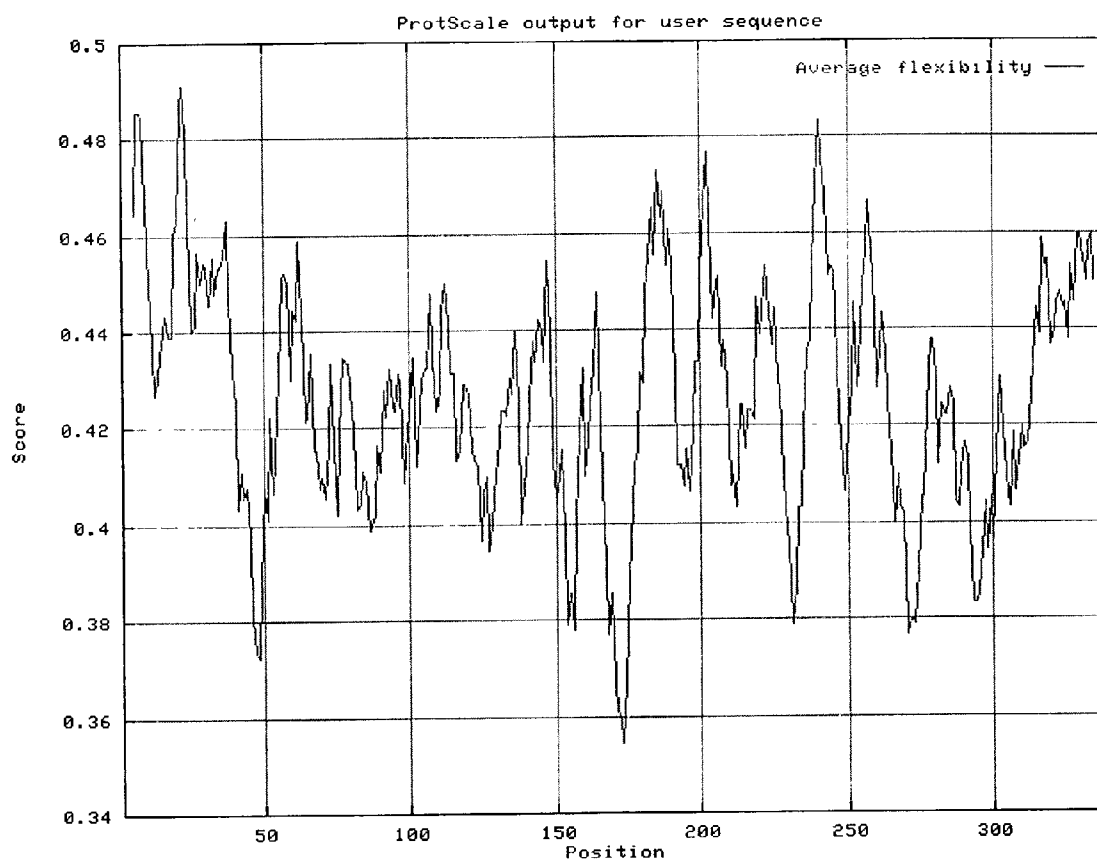


Figure 8a 8P1D4 variant 3 Average Flexibility Profile

(Bhaskaran R., Ponnuswamy P.K., 1988.

Int. J. Pept. Protein Res. 32:242-255)

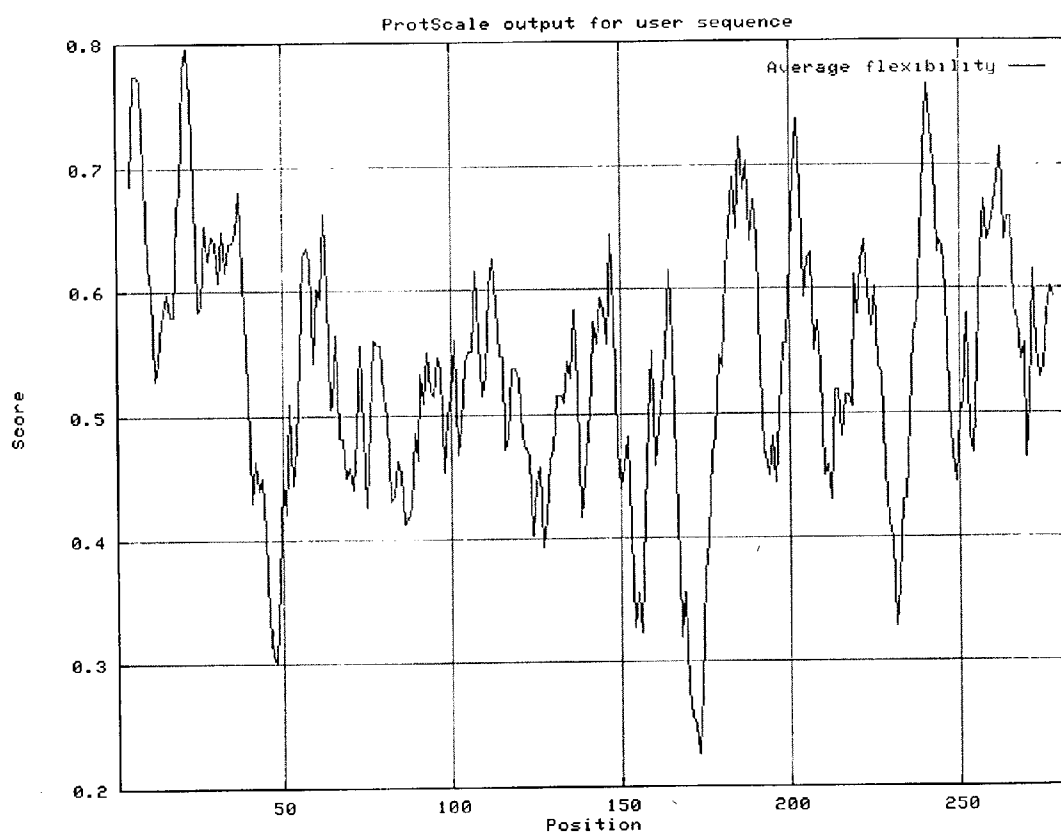


Figure 9 8P1D4 variant 1 Beta-turn Profile
(Deleage, G., Roux B. 1987. Protein Engineering 1:289-294)

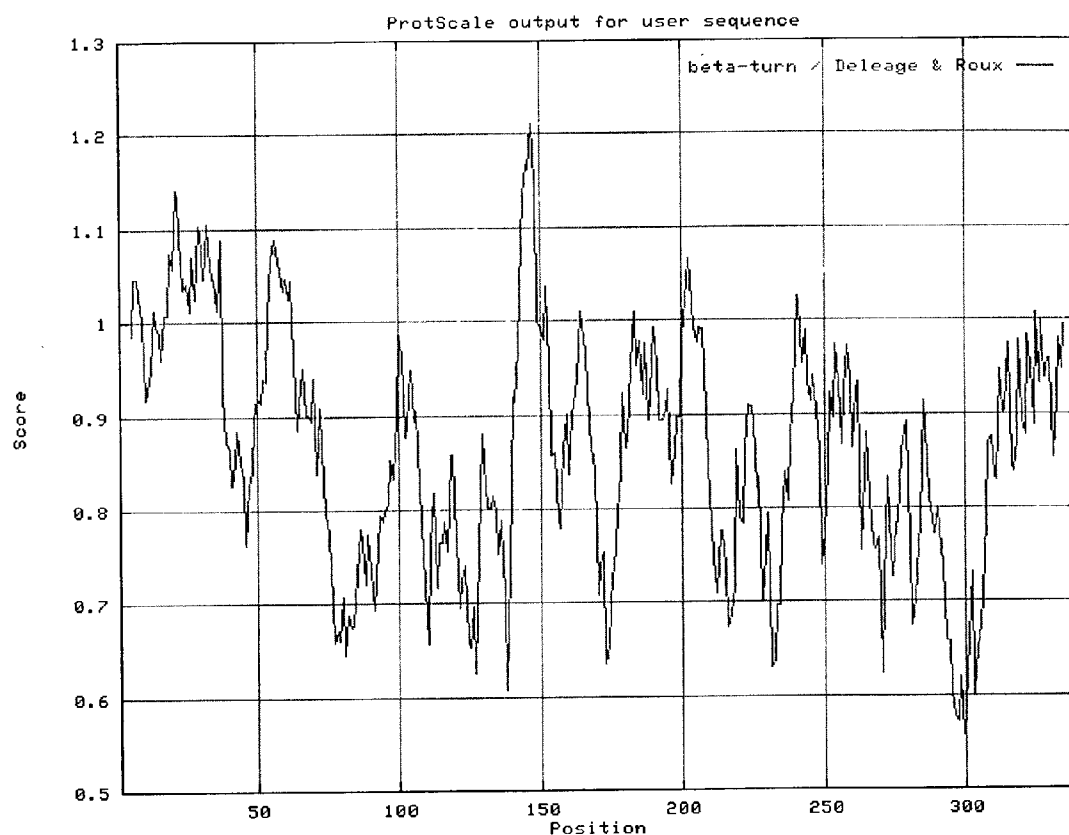


Figure 9a 8P1D4 variant 3 Beta-turn Profile
(Deleage, G., Roux B. 1987. Protein Engineering 1:289-294)

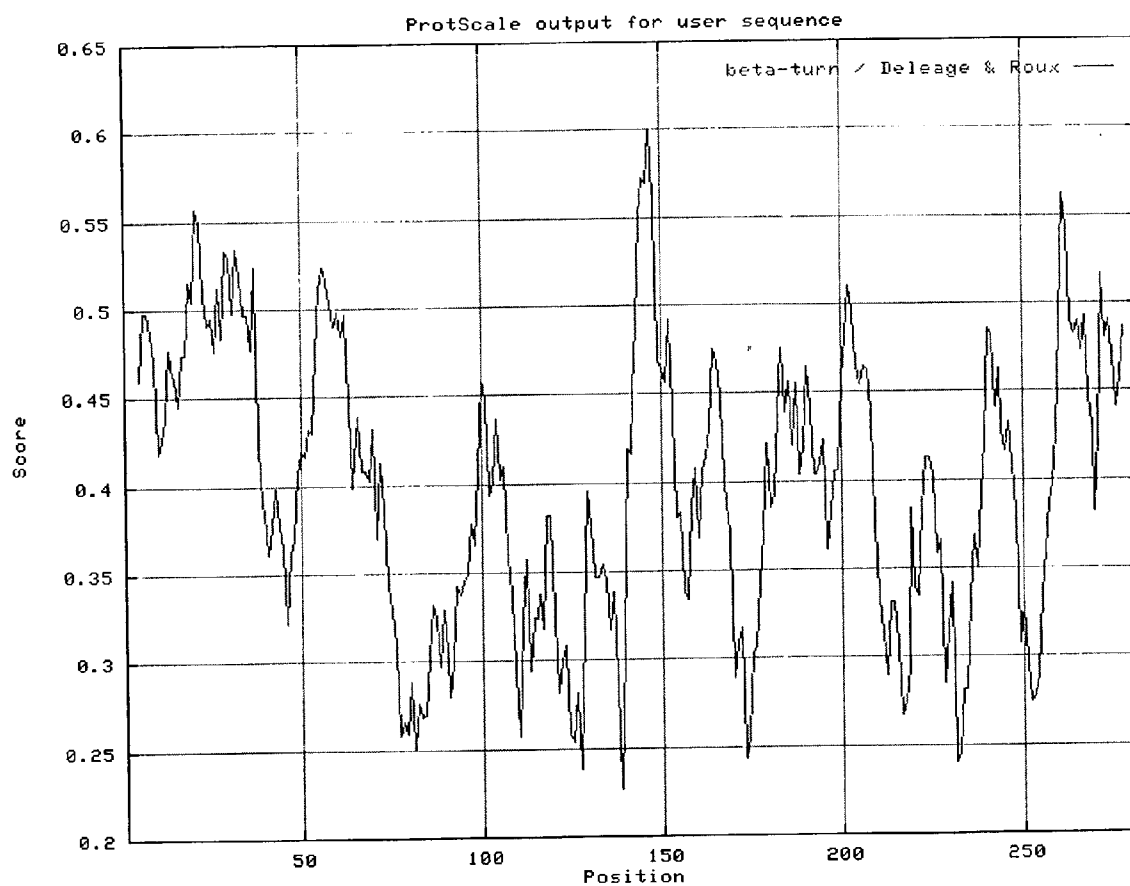


Figure 10

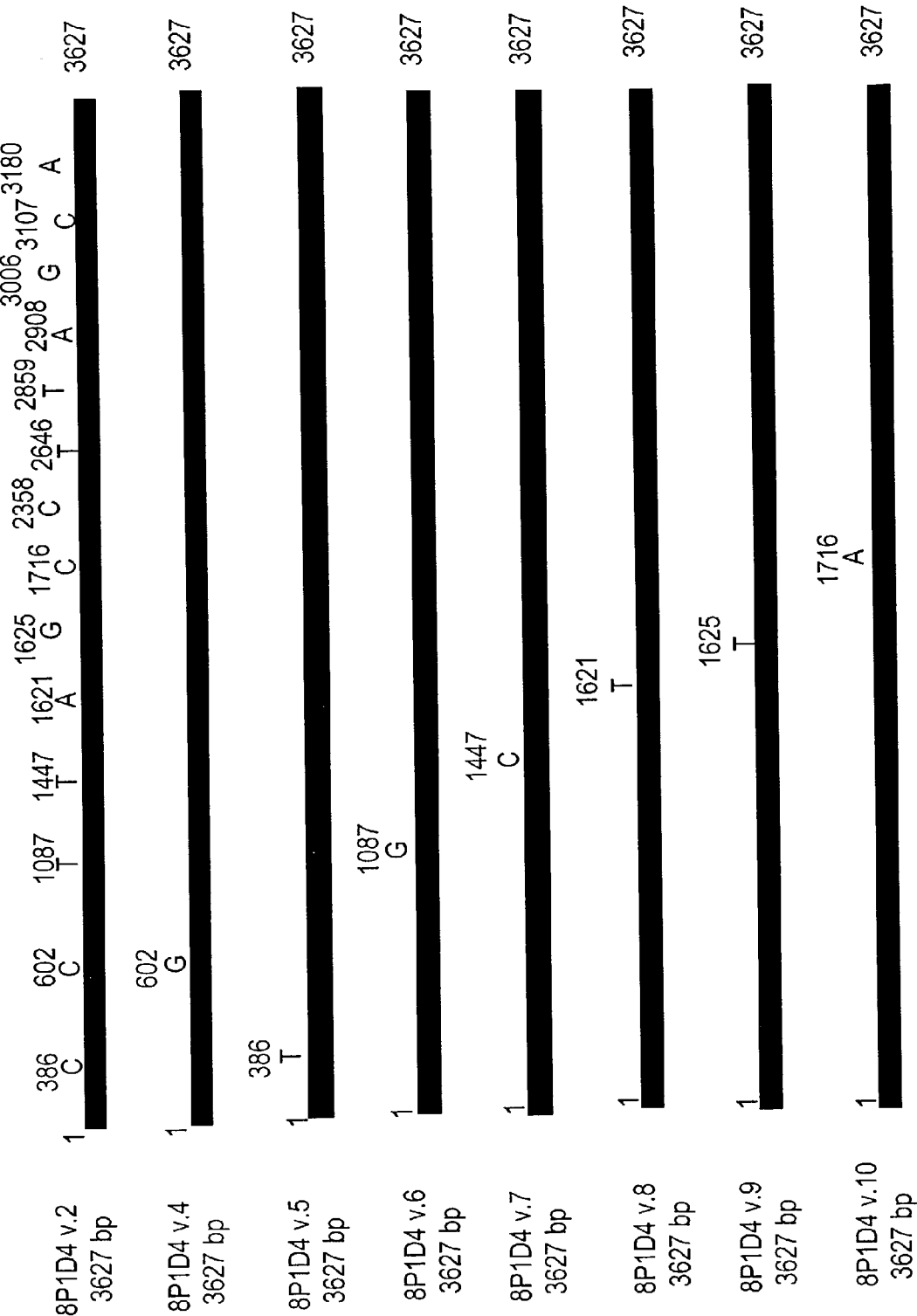


Figure 10 (con'd)

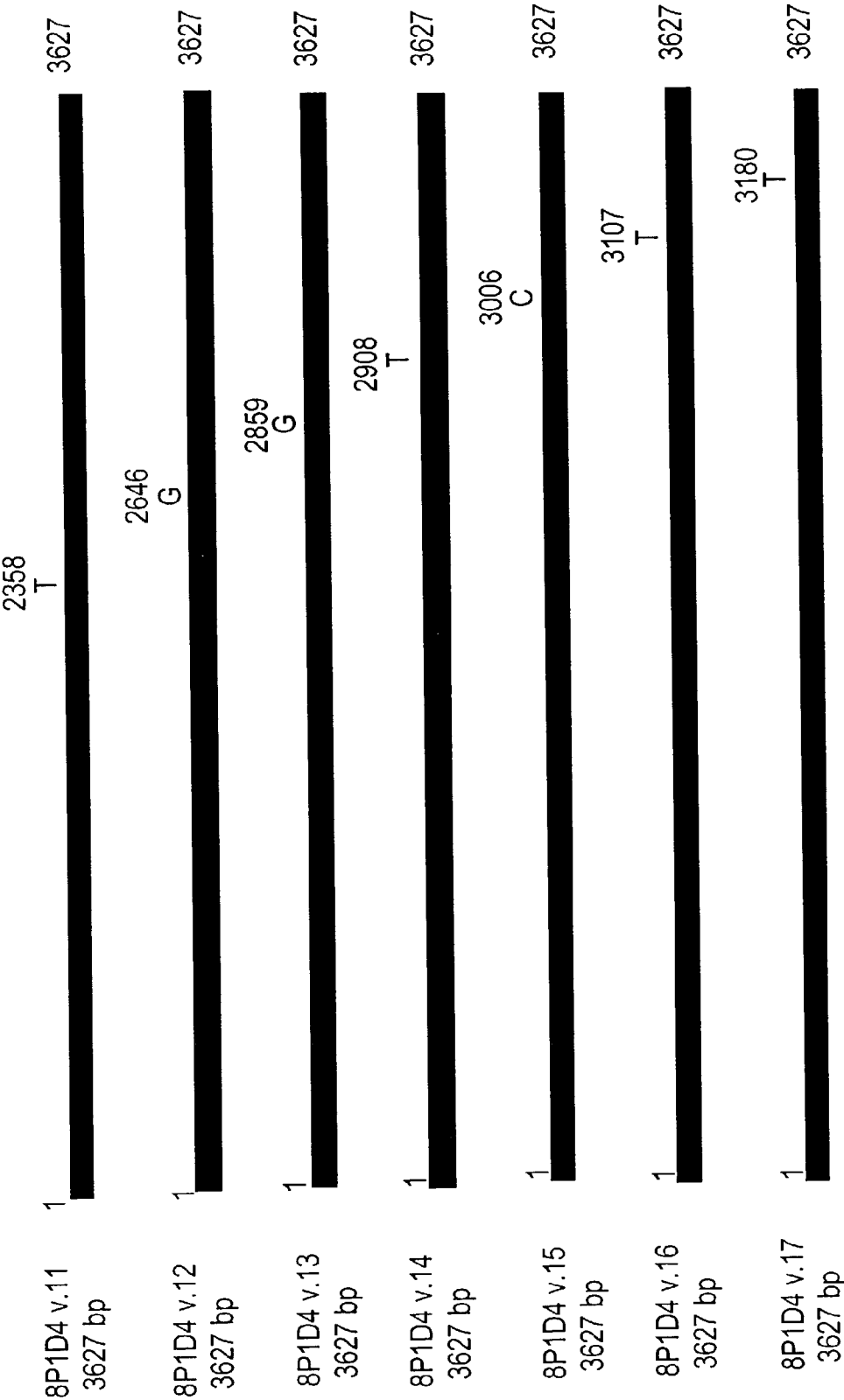


Figure 11

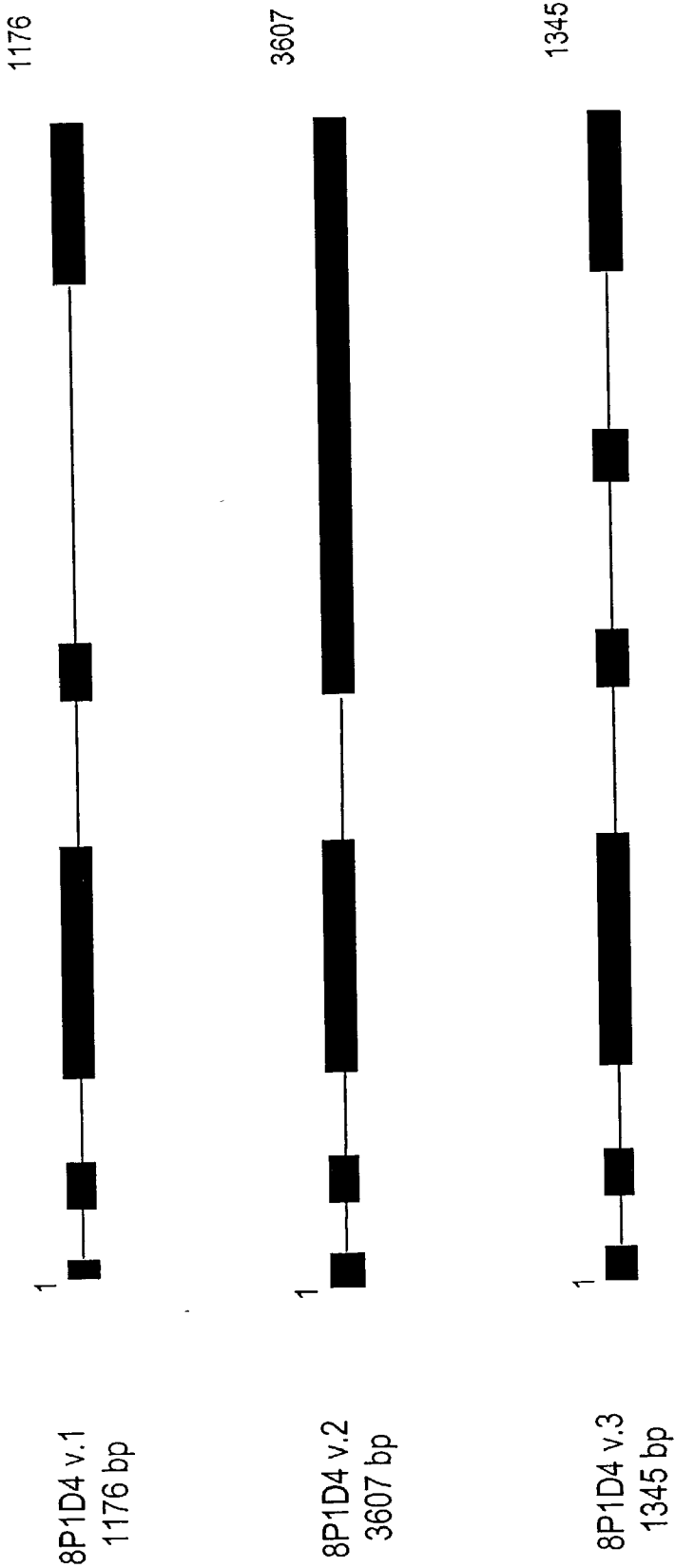
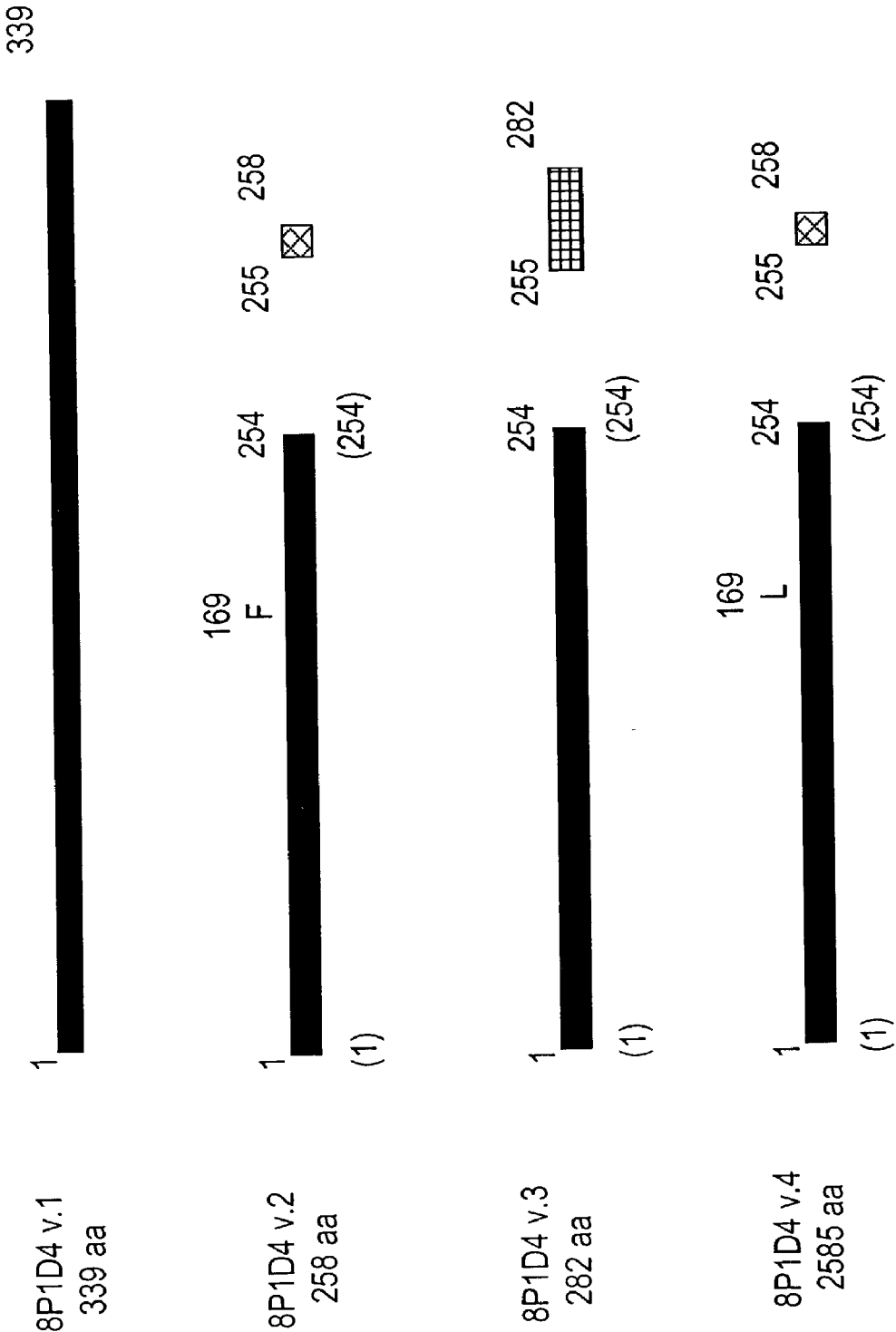


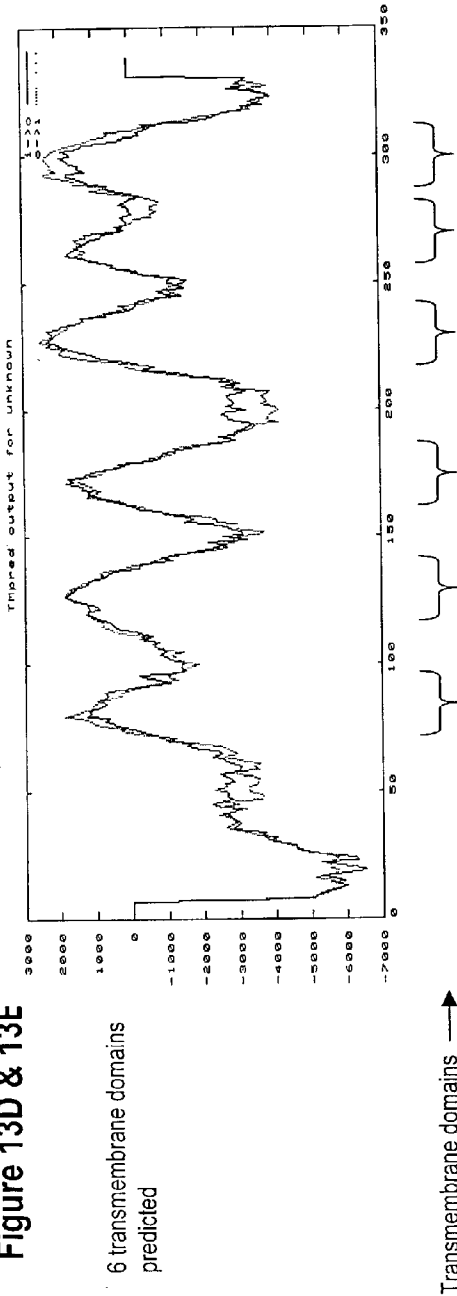
Figure 12



Transmembrane prediction for 8P1D4 variant 1

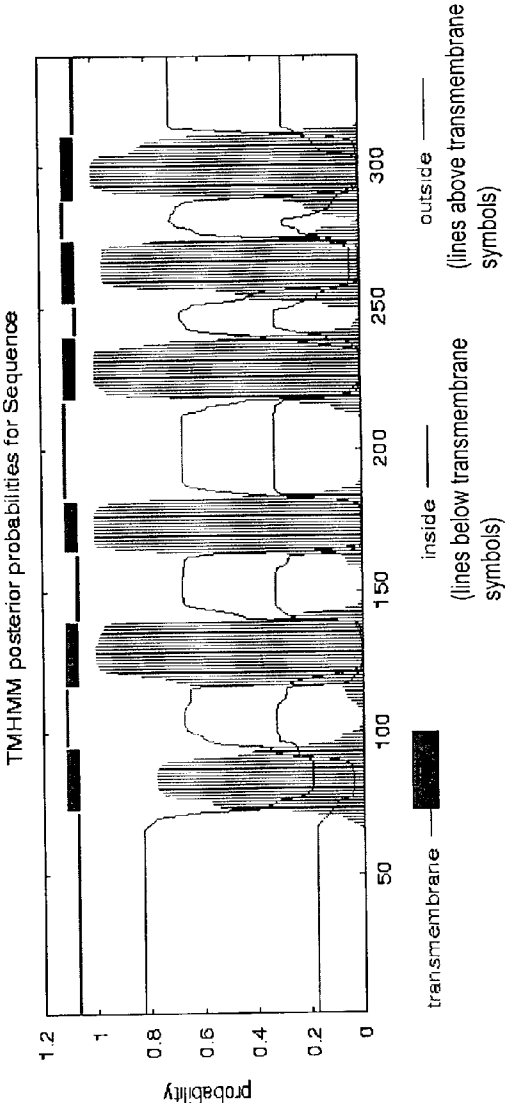
Figure 13D & 13E

6 transmembrane domains
predicted

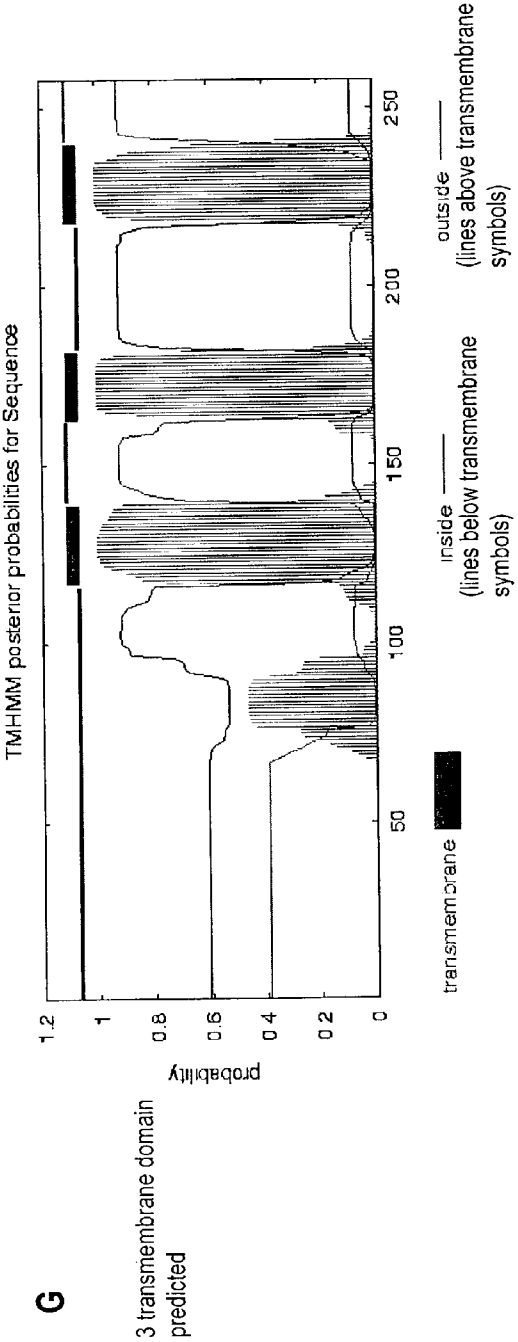
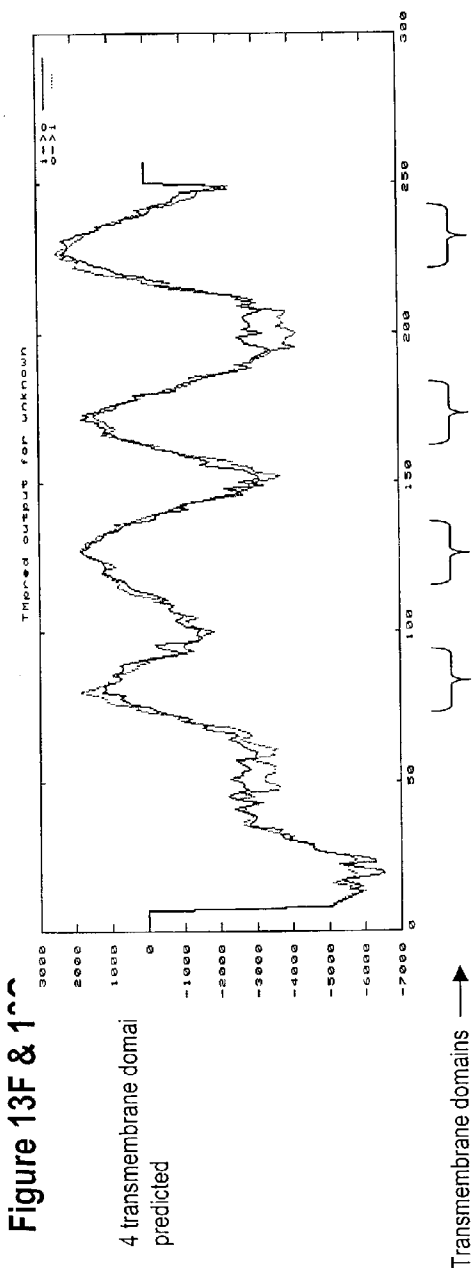


E

6 transmembrane domain
predicted



Transmembrane prediction for 8P1D4 variant 2



Transmembrane prediction for 8P1D4 variant 3

Figure 13H & 13I

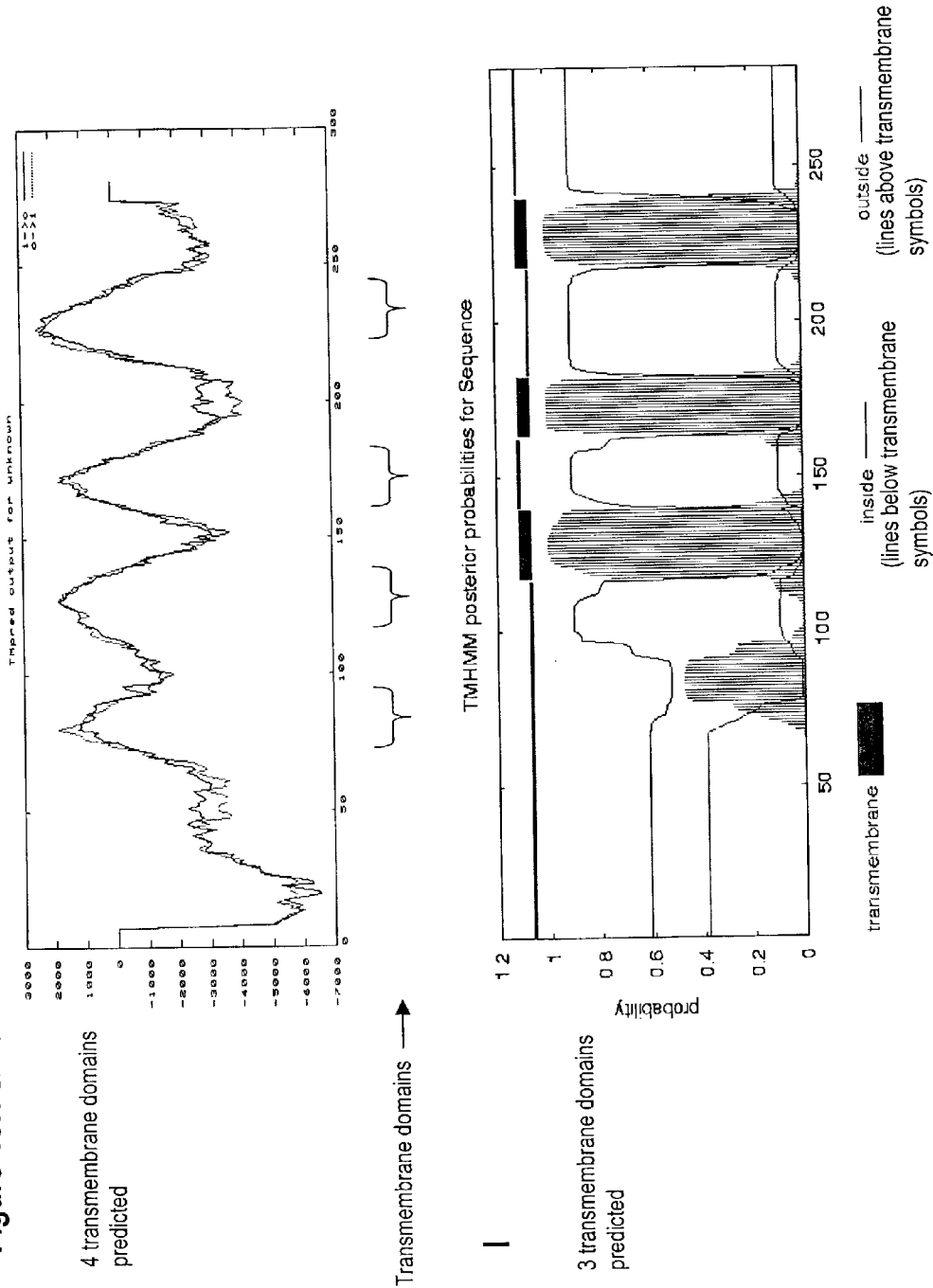


Figure 14 **STEAP-1 Expression in Stomach Cancer Patient Specimens**

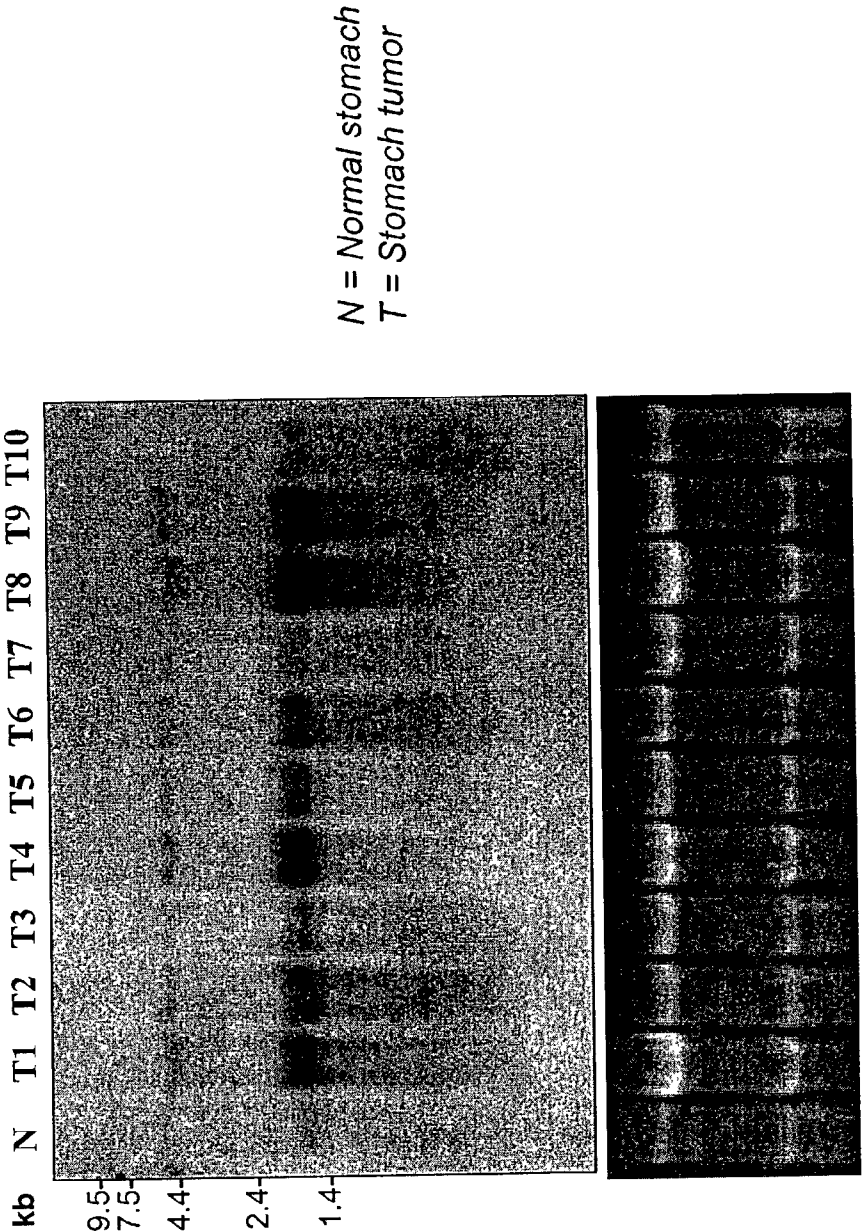


Figure 15 STEAP-1 Expression in Rectum Cancer
Patient Specimens

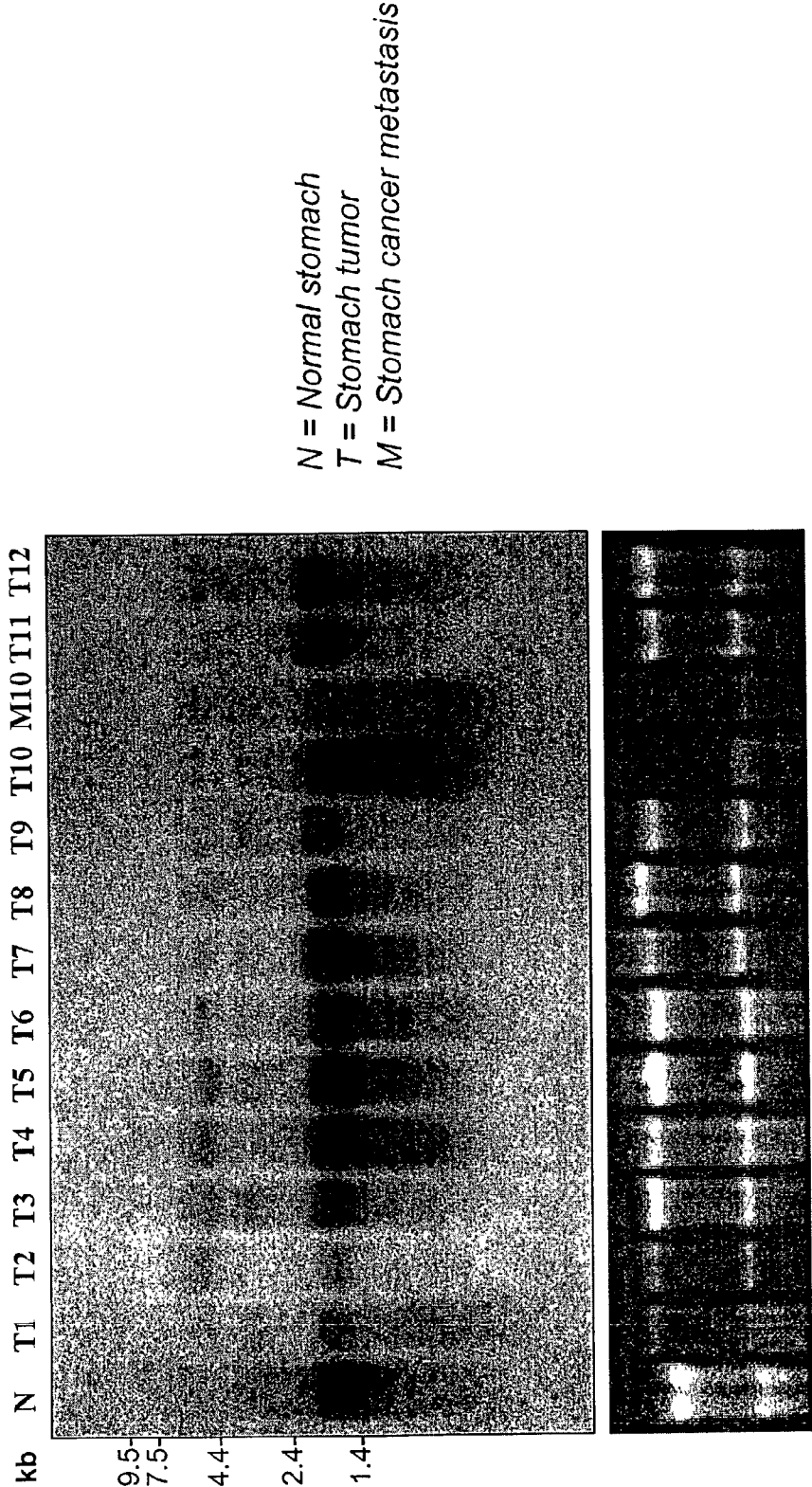


Figure 16 STEAP-1 Expression in HUVEC by RT-PCR

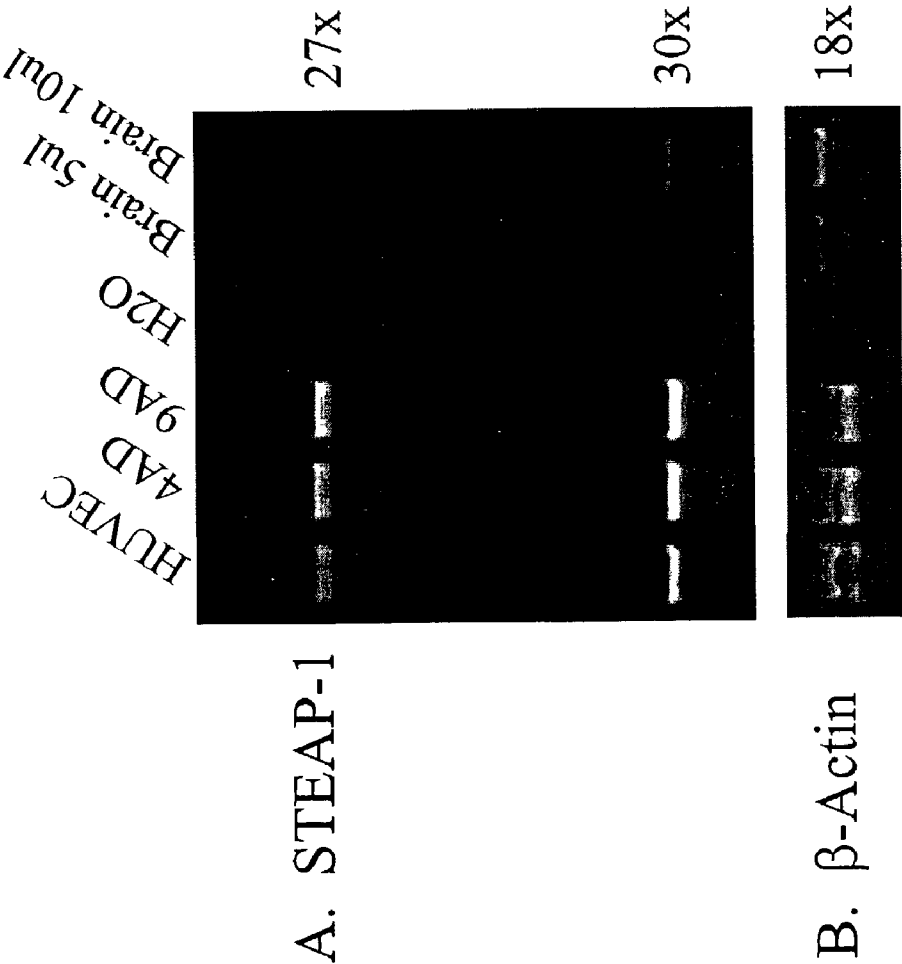
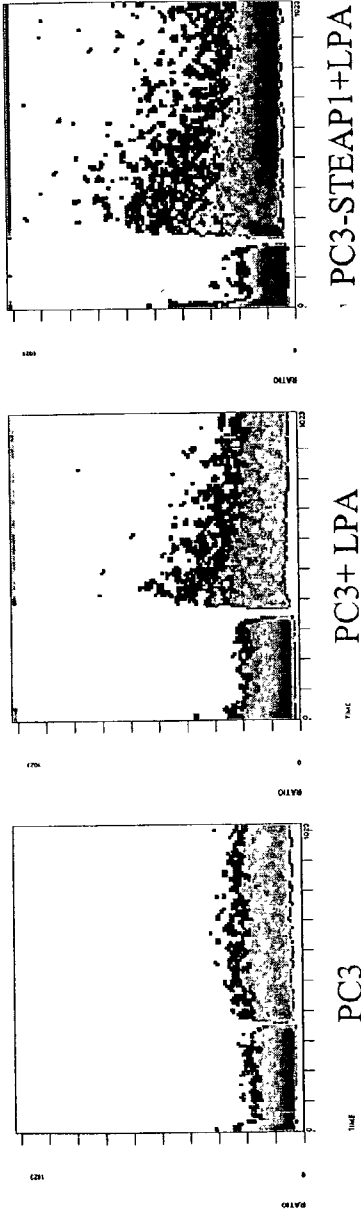


Figure 17: STEAP-1 Mediates Calcium Flux in Response to LPA



Cells	Fold Increase after LPA
PC3 Parental	1.4
PC3 STEAP-1	3.0
PC3 control gene	1.9

Figure 18: Inhibition of PC3-STEAP-1 Proliferation by a Ca^{++} Channel Inhibitor

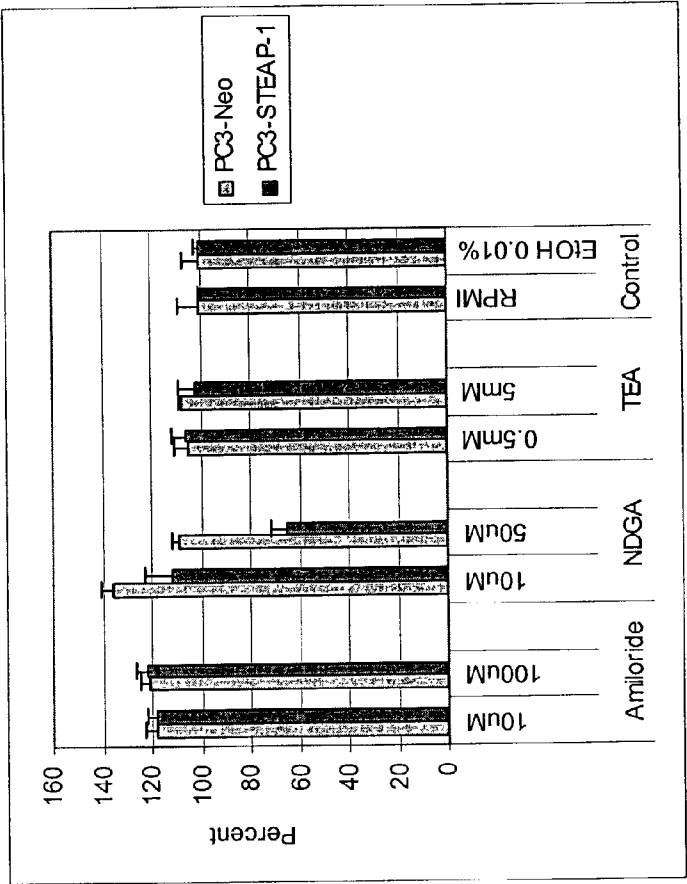
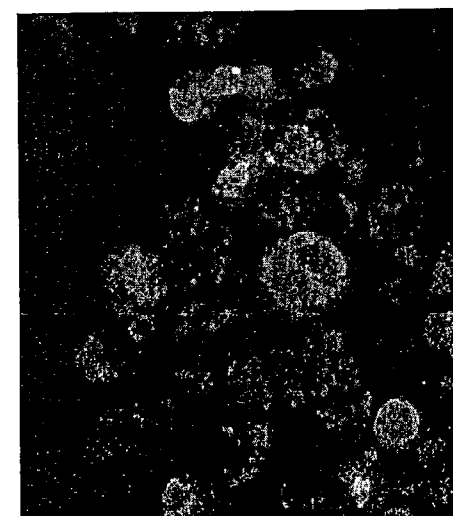
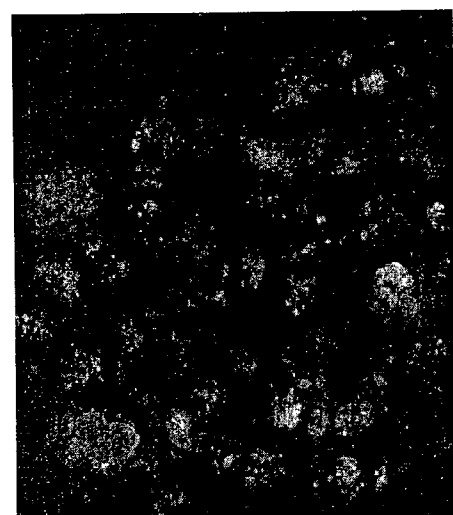


Figure 19: STEAP-1 Mediates Cell-Cell Communication



PC3-Neo



PC3-STEAP-1



PC3-Control Gene
(negative control)

Figure 20: Time Dependent STEAP-1-Mediated Cell Communication

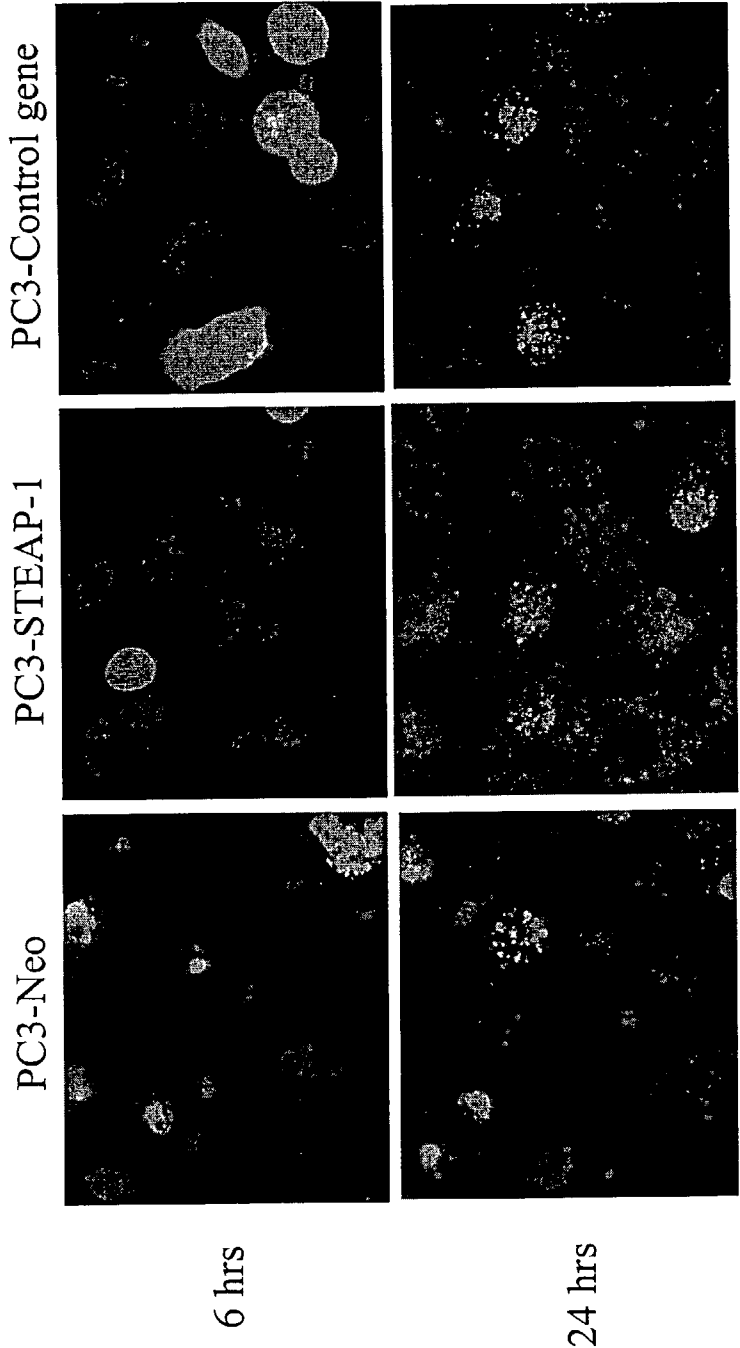


Figure 21

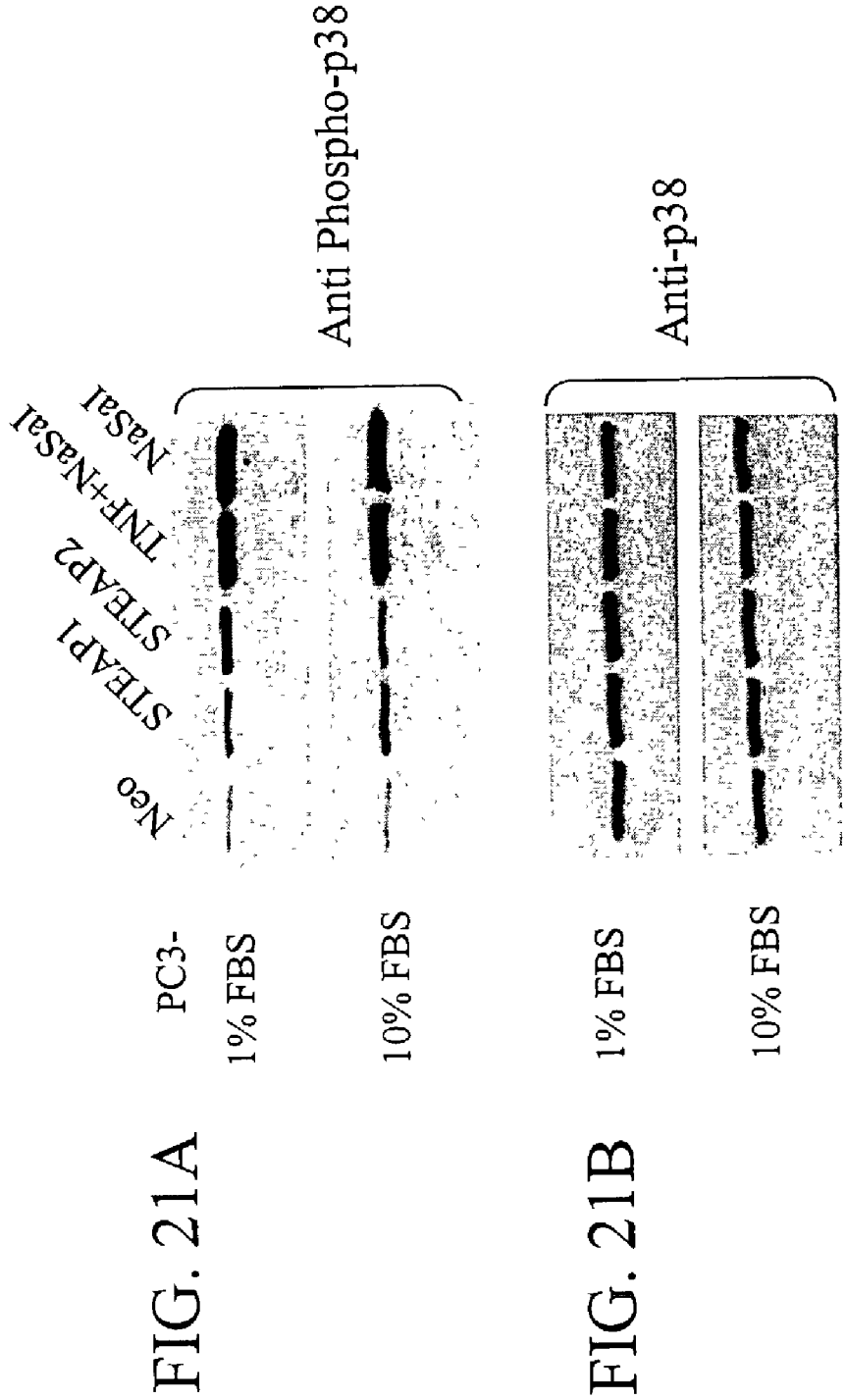


Figure 22

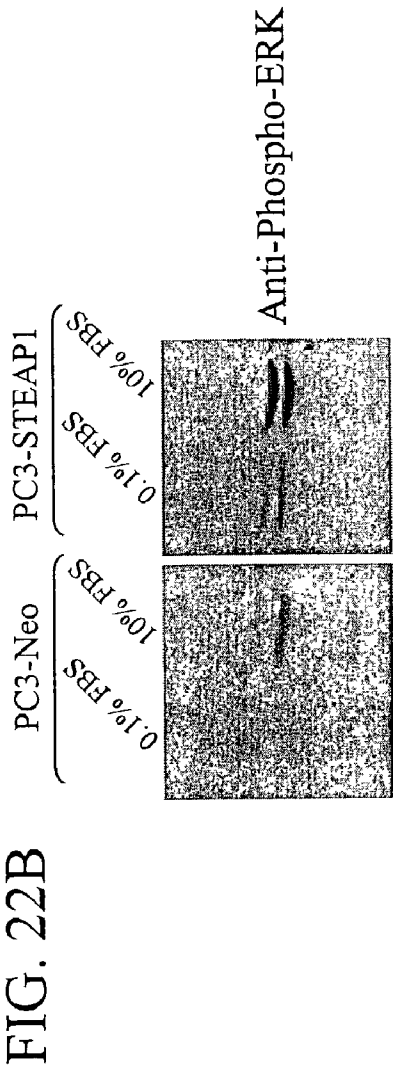
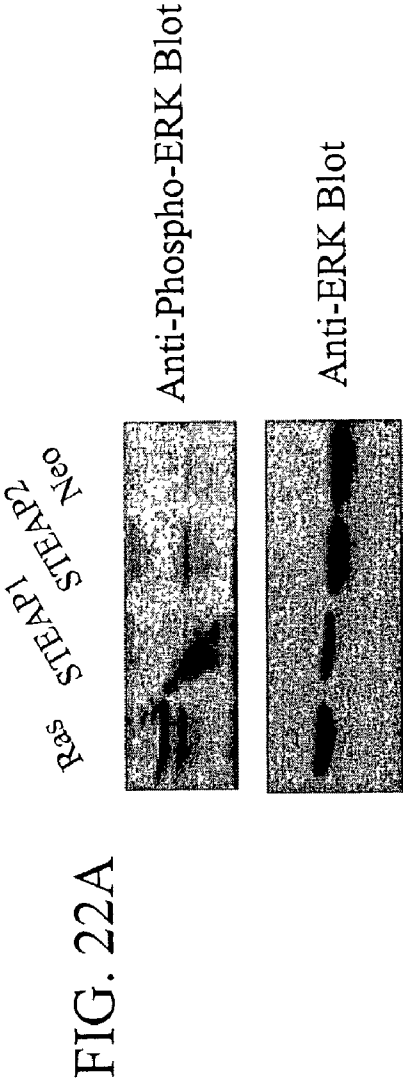


Figure 23:
Necessary Expression of STEAP-1 on Donor and Recipient Cells

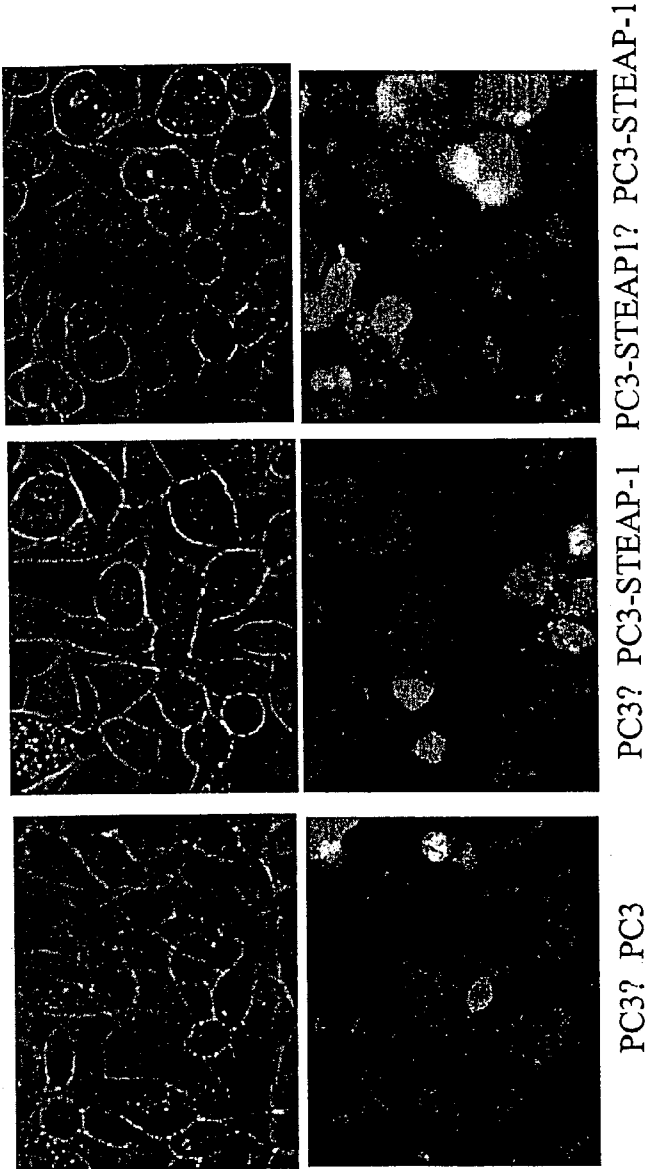


Figure 24:
RNAi Reduces STEAP-1 Expression in Recombinant Cells

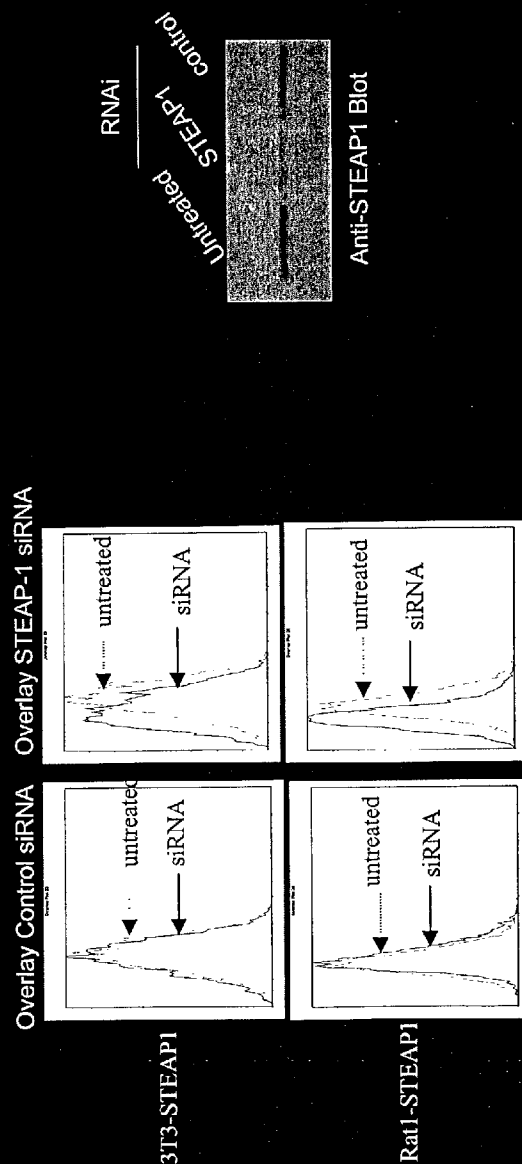
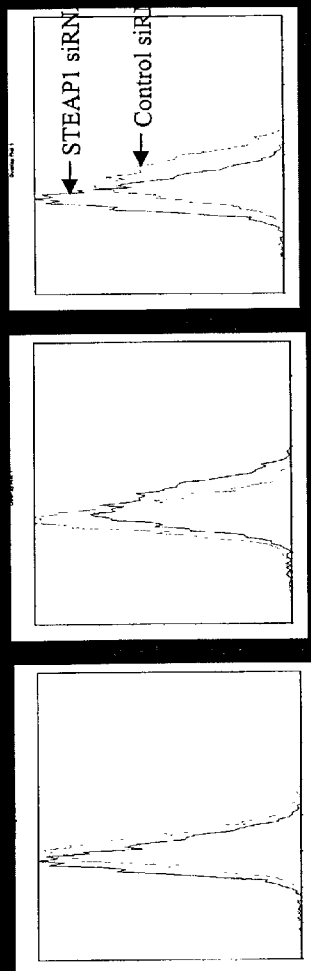


Figure 25:
Effect of RNAi on Protein Expression in LNCaP Cells

STEAP1 siRNA - treated LNCaP
Overlaid with untreated cells



NUCLEIC ACID AND CORRESPONDING PROTEIN ENTITLED STEAP-1 USEFUL IN TREATMENT AND DETECTION OF CANCER

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority from U.S. provisional patent application No. 60/317,840, filed Sep. 6, 2001 and U.S. provisional patent application No. 60/370,387 filed Apr. 5, 2002. This application relates to U.S. patent application No. 60/087,520, filed Jun. 1, 1998 and U.S. patent application No. 60/091,183, filed Jun. 30, 1998 and U.S. patent application Ser. No. 09/323,873, filed Jun. 1, 1999 and U.S. patent application Ser. No. 10/011,095, filed Dec. 6, 2001 and U.S. patent application Ser. No. 10/010,667, filed Dec. 6, 2001 and U.S. patent application Ser. No. 09/455,486, filed Dec. 6, 1999 and U.S. patent application No. 60/296,656, filed Jun. 6, 2001, and U.S. patent application Ser. No. 10/165,044, filed Jun. 6, 2002. The contents of each application listed in this paragraph are fully incorporated by reference herein.

STATEMENT OF RIGHTS TO INVENTIONS MADE UNDER FEDERALLY SPONSORED RESEARCH

[0002] Not applicable.

FIELD OF THE INVENTION

[0003] The invention described herein relates to a gene and its encoded protein, termed 08P1D4 or STEAP-1, expressed in certain cancers, and to diagnostic and therapeutic methods and compositions useful in the management of cancers that express STEAP-1.

BACKGROUND OF THE INVENTION

[0004] Cancer is the second leading cause of human death next to coronary disease. Worldwide, millions of people die from cancer every year. In the United States alone, as reported by the American Cancer Society, cancer causes the death of well over a half-million people annually, with over 1.2 million new cases diagnosed per year. While deaths from heart disease have been declining significantly, those resulting from cancer generally are on the rise. In the early part of the next century, cancer is predicted to become the leading cause of death.

[0005] Worldwide, several cancers stand out as the leading killers. In particular, carcinomas of the lung, prostate, breast, colon, pancreas, and ovary represent the primary causes of cancer death. These and virtually all other carcinomas share a common lethal feature. With very few exceptions, metastatic disease from a carcinoma is fatal. Moreover, even for those cancer patients who initially survive their primary cancers, common experience has shown that their lives are dramatically altered. Many cancer patients experience strong anxieties driven by the awareness of the potential for recurrence or treatment failure. Many cancer patients experience physical debilitations following treatment. Furthermore, many cancer patients experience a recurrence.

[0006] Worldwide, prostate cancer is the fourth most prevalent cancer in men. In North America and Northern Europe, it is by far the most common cancer in males and is the second leading cause of cancer death in men. In the

United States alone, well over 30,000 men die annually of this disease—second only to lung cancer. Despite the magnitude of these figures, there is still no effective treatment for metastatic prostate cancer. Surgical prostatectomy, radiation therapy, hormone ablation therapy, surgical castration and chemotherapy continue to be the main treatment modalities. Unfortunately, these treatments are ineffective for many and are often associated with undesirable consequences.

[0007] On the diagnostic front, the lack of a prostate tumor marker that can accurately detect early-stage, localized tumors remains a significant limitation in the diagnosis and management of this disease. Although the serum prostate specific antigen (PSA) assay has been a very useful tool, however its specificity and general utility is widely regarded as lacking in several important respects.

[0008] Progress in identifying additional specific markers for prostate cancer has been improved by the generation of prostate cancer xenografts that can recapitulate different stages of the disease in mice. The LAPC (Los Angeles Prostate Cancer) xenografts are prostate cancer xenografts that have survived passage in severe combined immune deficient (SCID) mice and have exhibited the capacity to mimic the transition from androgen dependence to androgen independence (Klein et al., 1997, Nat. Med. 3:402). More recently identified prostate cancer markers include PCTA-1 (Su et al., 1996, Proc. Natl. Acad. Sci. USA 93: 7252), prostate-specific membrane (PSM) antigen (Pinto et al., Clin Cancer Res 1996 September 2 (9): 1445-51), STEAP (Hubert, et al., Proc Natl Acad Sci USA. 1999 Dec. 7; 96(25): 14523-8) and prostate stem cell antigen (PSCA) (Reiter et al., 1998, Proc. Natl. Acad. Sci. USA 95: 1735).

[0009] While previously identified markers such as PSA, PSM, PCTA and PSCA have facilitated efforts to diagnose and treat prostate cancer, there is need for the identification of additional markers and therapeutic targets for prostate and related cancers in order to further improve diagnosis and therapy.

[0010] Renal cell carcinoma (RCC) accounts for approximately 3 percent of adult malignancies. Once adenomas reach a diameter of 2 to 3 cm, malignant potential exists. In the adult, the two principal malignant renal tumors are renal cell adenocarcinoma and transitional cell carcinoma of the renal pelvis or ureter. The incidence of renal cell adenocarcinoma is estimated at more than 29,000 cases in the United States, and more than 11,600 patients died of this disease in 1998. Transitional cell carcinoma is less frequent, with an incidence of approximately 500 cases per year in the United States.

[0011] Surgery has been the primary therapy for renal cell adenocarcinoma for many decades. Until recently, metastatic disease has been refractory to any systemic therapy. With recent developments in systemic therapies, particularly immunotherapies, metastatic renal cell carcinoma may be approached aggressively in appropriate patients with a possibility of durable responses. Nevertheless, there is a remaining need for effective therapies for these patients.

[0012] Of all new cases of cancer in the United States, bladder cancer represents approximately 5 percent in men (fifth most common neoplasm) and 3 percent in women (eighth most common neoplasm). The incidence is increasing slowly, concurrent with an increasing older population.

In 1998, there was an estimated 54,500 cases, including 39,500 in men and 15,000 in women. The age-adjusted incidence in the United States is 32 per 100,000 for men and eight per 100,000 in women. The historic male/female ratio of 3:1 may be decreasing related to smoking patterns in women. There were an estimated 11,000 deaths from bladder cancer in 1998 (7,800 in men and 3,900 in women). Bladder cancer incidence and mortality strongly increase with age and will be an increasing problem as the population becomes more elderly.

[0013] Most bladder cancers recur in the bladder. Bladder cancer is managed with a combination of transurethral resection of the bladder (TUR) and intravesical chemotherapy or immunotherapy. The multifocal and recurrent nature of bladder cancer points out the limitations of TUR. Most muscle-invasive cancers are not cured by TUR alone. Radical cystectomy and urinary diversion is the most effective means to eliminate the cancer but carry an undeniable impact on urinary and sexual function. There continues to be a significant need for treatment modalities that are beneficial for bladder cancer patients.

[0014] An estimated 130,200 cases of colorectal cancer occurred in 2000 in the United States, including 93,800 cases of colon cancer and 36,400 of rectal cancer. Colorectal cancers are the third most common cancers in men and women. Incidence rates declined significantly during 1992-1996 (-2.1% per year). Research suggests that these declines have been due to increased screening and polyp removal, preventing progression of polyps to invasive cancers. There were an estimated 56,300 deaths (47,700 from colon cancer, 8,600 from rectal cancer) in 2000, accounting for about 11% of all U.S. cancer deaths.

[0015] At present, surgery is the most common form of therapy for colorectal cancer, and for cancers that have not spread, it is frequently curative. Chemotherapy, or chemotherapy plus radiation, is given before or after surgery to most patients whose cancer has deeply perforated the bowel wall or has spread to the lymph nodes. A permanent colostomy (creation of an abdominal opening for elimination of body wastes) is occasionally needed for colon cancer and is infrequently required for rectal cancer. There continues to be a need for effective diagnostic and treatment modalities for colorectal cancer.

[0016] There were an estimated 164,100 new cases of lung and bronchial cancer in 2000, accounting for 14% of all U.S. cancer diagnoses. The incidence rate of lung and bronchial cancer is declining significantly in men, from a high of 86.5 per 100,000 in 1984 to 70.0 in 1996. In the 1990s, the rate of increase among women began to slow. In 1996, the incidence rate in women was 42.3 per 100,000.

[0017] Lung and bronchial cancer caused an estimated 156,900 deaths in 2000, accounting for 28% of all cancer deaths. During 1992-1996, mortality from lung cancer declined significantly among men (-1.7% per year) while rates for women were still significantly increasing (0.9% per year). Since 1987, more women have died each year of lung cancer than breast cancer, which, for over 40 years, was the major cause of cancer death in women. Decreasing lung cancer incidence and mortality rates most likely resulted from decreased smoking rates over the previous 30 years; however, decreasing smoking patterns among women lag

behind those of men. Of concern, although the declines in adult tobacco use have slowed, tobacco use in youth is increasing again.

[0018] Treatment options for lung and bronchial cancer are determined by the type and stage of the cancer and include surgery, radiation therapy, and chemotherapy. For many localized cancers, surgery is usually the treatment of choice. Because the disease has usually spread by the time it is discovered, radiation therapy and chemotherapy are often needed in combination with surgery. Chemotherapy alone or combined with radiation is the treatment of choice for small cell lung cancer; on this regimen, a large percentage of patients experience remission, which in some cases is long lasting. There is however, an ongoing need for effective treatment and diagnostic approaches for lung and bronchial cancers.

[0019] An estimated 182,800 new invasive cases of breast cancer were expected to occur among women in the United States during 2000. Additionally, about 1,400 new cases of breast cancer were expected to be diagnosed in men in 2000. After increasing about 4% per year in the 1980s, breast cancer incidence rates in women have leveled off in the 1990s to about 110.6 cases per 100,000.

[0020] In the U.S. alone, there were an estimated 41,200 deaths (40,800 women, 400 men) in 2000 due to breast cancer. Breast cancer ranks second among cancer deaths in women. According to the most recent data, mortality rates declined significantly during 1992-1996 with the largest decreases in younger women, both white and black. These decreases were probably the result of earlier detection and improved treatment.

[0021] Taking into account the medical circumstances and the patient's preferences, treatment of breast cancer may involve lumpectomy (local removal of the tumor) and removal of the lymph nodes under the arm; mastectomy (surgical removal of the breast) and removal of the lymph nodes under the arm; radiation therapy; chemotherapy; or hormone therapy. Often, two or more methods are used in combination. Numerous studies have shown that, for early stage disease, long-term survival rates after lumpectomy plus radiotherapy are similar to survival rates after modified radical mastectomy. Significant advances in reconstruction techniques provide several options for breast reconstruction after mastectomy. Recently, such reconstruction has been done at the same time as the mastectomy.

[0022] Local excision of ductal carcinoma in situ (DCIS) with adequate amounts of surrounding normal breast tissue may prevent the local recurrence of the DCIS. Radiation to the breast and/or tamoxifen may reduce the chance of DCIS occurring in the remaining breast tissue. This is important because DCIS, if left untreated, may develop into invasive breast cancer. Nevertheless, there are serious side effects or sequelae to these treatments. There is, therefore, a need for efficacious breast cancer treatments.

[0023] There were an estimated 23,100 new cases of ovarian cancer in the United States in 2000. It accounts for 4% of all cancers among women and ranks second among gynecologic cancers. During 1992-1996, ovarian cancer incidence rates were significantly declining. Consequent to ovarian cancer, there were an estimated 14,000 deaths in 2000. Ovarian cancer causes more deaths than any other cancer of the female reproductive system.

[0024] Surgery, radiation therapy, and chemotherapy are treatment options for ovarian cancer. Surgery usually includes the removal of one or both ovaries, the fallopian tubes (salpingo-oophorectomy), and the uterus (hysterectomy). In some very early tumors, only the involved ovary will be removed, especially in young women who wish to have children. In advanced disease, an attempt is made to remove all intra-abdominal disease to enhance the effect of chemotherapy. There continues to be an important need for effective treatment options for ovarian cancer.

[0025] There were an estimated 28,300 new cases of pancreatic cancer in the United States in 2000. Over the past 20 years, rates of pancreatic cancer have declined in men. Rates among women have remained approximately constant but may be beginning to decline. Pancreatic cancer caused an estimated 28,200 deaths in 2000 in the United States. Over the past 20 years, there has been a slight but significant decrease in mortality rates among men (about -0.9% per year) while rates have increased slightly among women.

[0026] Surgery, radiation therapy, and chemotherapy are treatment options for pancreatic cancer. These treatment options can extend survival and/or relieve symptoms in many patients but are not likely to produce a cure for most. There is a significant need for additional therapeutic and diagnostic options for pancreatic cancer.

SUMMARY OF THE INVENTION

[0027] The present invention relates to a gene, designated STEAP-1, that has now been found to be over-expressed in the cancer(s) listed in Table I. Northern blot expression analysis of STEAP-1 gene expression in normal tissues shows a restricted expression pattern in adult tissues. The nucleotide (FIG. 2) and amino acid (FIG. 2, and FIG. 3) sequences of STEAP-1 are provided. The tissue-related profile of STEAP-1 in normal adult tissues, combined with the over-expression observed in the tissues listed in Table I, shows that STEAP-1 is aberrantly over-expressed in at least some cancers, and thus serves as a useful diagnostic, prophylactic, prognostic, and/or therapeutic target for cancers of the tissue(s) such as those listed in Table I.

[0028] The invention provides polynucleotides corresponding or complementary to all or part of the STEAP-1 genes, mRNAs, and/or coding sequences, preferably in isolated form, including polynucleotides encoding STEAP-1-related proteins and fragments of 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more than 25 contiguous amino acids; at least 30, 35, 40, 45, 50, 55, 60, 65, 70, 80, 85, 90, 95, 100 or more than 100 contiguous amino acids of a STEAP-1-related protein, as well as the peptides/proteins themselves; DNA, RNA, DNA/RNA hybrids, and related molecules, polynucleotides or oligonucleotides complementary or having at least a 90% homology to the STEAP-1 genes or mRNA sequences or parts thereof, and polynucleotides or oligonucleotides that hybridize to the STEAP-1 genes, mRNAs, or to STEAP-1-encoding polynucleotides. Also provided are means for isolating cDNAs and the genes encoding STEAP-1. Recombinant DNA molecules containing STEAP-1 polynucleotides, cells transformed or transduced with such molecules, and host-vector systems for the expression of STEAP-1 gene products are also provided. The invention further provides antibodies that bind to STEAP-1 proteins and polypeptide

fragments thereof, including polyclonal and monoclonal antibodies, murine and other mammalian antibodies, chimeric antibodies, humanized and fully human antibodies, and antibodies labeled with a detectable marker or therapeutic agent. In certain embodiments there is a proviso that the entire nucleic acid sequence of FIG. 2 is not encoded and/or the entire amino acid sequence of FIG. 2 is not prepared. In certain embodiments, the entire nucleic acid sequence of FIG. 2 is encoded and/or the entire amino acid sequence of FIG. 2 is prepared, either of which are in respective human unit dose forms.

[0029] The invention further provides methods for detecting the presence and status of STEAP-1 polynucleotides and proteins in various biological samples, as well as methods for identifying cells that express STEAP-1. A typical embodiment of this invention provides methods for monitoring STEAP-1 gene products in a tissue or hematology sample having or suspected of having some form of growth dysregulation such as cancer.

[0030] The invention further provides various immunogenic or therapeutic compositions and strategies for treating cancers that express STEAP-1 such as cancers of tissues listed in Table I, including therapies aimed at inhibiting the transcription, translation, processing or function of STEAP-1 as well as cancer vaccines. In one aspect, the invention provides compositions, and methods comprising them, for treating a cancer that expresses STEAP-1 in a human subject wherein the composition comprises a carrier suitable for human use and a human unit dose of one or more than one agent that inhibits the production or function of STEAP-1. Preferably, the carrier is a uniquely human carrier. In another aspect of the invention, the agent is a moiety that is immunoreactive with STEAP-1 protein. Non-limiting examples of such moieties include, but are not limited to, antibodies (such as single chain, monoclonal, polyclonal, humanized, chimeric, or human antibodies), functional equivalents thereof (whether naturally occurring or synthetic), and combinations thereof. The antibodies can be conjugated to a diagnostic or therapeutic moiety. In another aspect, the agent is a small molecule as defined herein.

[0031] In another aspect, the agent comprises one or more than one peptide which comprises a cytotoxic T lymphocyte (CTL) epitope that binds an HLA class I molecule in a human to elicit a CTL response to STEAP-1 and/or one or more than one peptide which comprises a helper T lymphocyte (HTL) epitope which binds an HLA class II molecule in a human to elicit an HTL response. The peptides of the invention may be on the same or on one or more separate polypeptide molecules. In a further aspect of the invention, the agent comprises one or more than one nucleic acid molecule that expresses one or more than one of the CTL or HTL response stimulating peptides as described above. In yet another aspect of the invention, the one or more than one nucleic acid molecule may express a moiety that is immunologically reactive with STEAP-1 as described above. The one or more than one nucleic acid molecule may also be, or encode, a molecule that inhibits production of STEAP-1. Non-limiting examples of such molecules include, but are not limited to, those complementary to a nucleotide sequence essential for production of STEAP-1 (e.g. antisense sequences or molecules that form a triple helix with a nucleotide double helix essential for STEAP-1 production) or a ribozyme effective to lyse STEAP-1 mRNA.

[0032] Note that to determine the starting position of any peptide set forth in Tables V-XVIII and XXII to LI (collectively HLA Peptide Tables) relative to its parental protein, e.g., variant 1, variant 2, etc., reference is made to three factors: the particular variant, the length of the peptide in an HLA Peptide Table, and the Search Peptides in Table LXI. Generally, a unique Search Peptide is used to obtain HLA peptides of a particular for a particular variant. The position of each Search Peptide relative to its respective parent molecule is listed in Table LXI. Accordingly, if a Search Peptide begins at position "X", one must add the value "X-1" to each position in Tables V-XVIII and XXII to LI to obtain the actual position of the HLA peptides in their parental molecule. For example, if a particular Search Peptide begins at position 150 of its parental molecule, one must add 150-1, i.e., 149 to each HLA peptide amino acid position to calculate the position of that amino acid in the parent molecule.

[0033] One embodiment of the invention comprises an HLA peptide, that occurs at least twice in Tables V-XVIII and XXII to LI collectively, or an oligonucleotide that encodes the HLA peptide. Another embodiment of the invention comprises an HLA peptide that occurs at least once in Tables V-XVIII and at least once in tables XXII to LI, or an oligonucleotide that encodes the HLA peptide.

[0034] Another embodiment of the invention is antibody epitopes, which comprise a peptide regions, or an oligonucleotide encoding the peptide region, that has one two, three, four, or five of the following characteristics:

[0035] i) a peptide region of at least 5 amino acids of a particular peptide of FIG. 3, in any whole number increment up to the full length of that protein in FIG. 3, that includes an amino acid position having a value equal to or greater than 0.5, 0.6, 0.7, 0.8, 0.9, or having a value equal to 1.0, in the Hydrophilicity profile of FIG. 5;

[0036] ii) a peptide region of at least 5 amino acids of a particular peptide of FIG. 3, in any whole number increment up to the full length of that protein in FIG. 3, that includes an amino acid position having a value equal to or less than 0.5, 0.4, 0.3, 0.2, 0.1, or having a value equal to 0.0, in the Hydrophobicity profile of FIG. 6;

[0037] iii) a peptide region of at least 5 amino acids of a particular peptide of FIG. 3, in any whole number increment up to the full length of that protein in FIG. 3, that includes an amino acid position having a value equal to or greater than 0.5, 0.6, 0.7, 0.8, 0.9, or having a value equal to 1.0, in the Percent Accessible Residues profile of FIG. 7;

[0038] iv) a peptide region of at least 5 amino acids of a particular peptide of FIG. 3, in any whole number increment up to the full length of that protein in FIG. 3, that includes an amino acid position having a value equal to or greater than 0.5, 0.6, 0.7, 0.8, 0.9, or having a value equal to 1.0, in the Average Flexibility profile of FIG. 8; or

[0039] v) a peptide region of at least 5 amino acids of a particular peptide of FIG. 3, in any whole number increment up to the full length of that protein in FIG. 3, that includes an amino acid position having a value equal to or greater than 0.5, 0.6, 0.7, 0.8, 0.9, or having a value equal to 1.0, in the Beta-turn profile of FIG. 9.

BRIEF DESCRIPTION OF THE FIGURES

[0040] FIG. 1. The STEAP-1 SSH sequence of 436 nucleotides.

[0041] FIG. 2. The cDNA and amino acid sequence of STEAP-1 variant 1 (also called "STEAP-1 v.1" or "STEAP-1 variant 1") is shown in FIG. 2A. The start methionine is underlined. The open reading frame extends from nucleic acid 66-1085 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 2 (also called "STEAP-1 v.2") is shown in FIG. 2B. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 3 (also called "STEAP-1 v.3") is shown in FIG. 2C. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-944 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 4 (also called "STEAP-1 v.4") is shown in FIG. 2D. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 5 (also called "STEAP-1 v.5") is shown in FIG. 2E. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 6 (also called "STEAP-1 v.6") is shown in FIG. 2F. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 7 (also called "STEAP-1 v.7") is shown in FIG. 2G. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 8 (also called "STEAP-1 v.8") is shown in FIG. 2H. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 9 (also called "STEAP-1 v.9") is shown in FIG. 2I. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 10 (also called "STEAP-1 v.10") is shown in FIG. 2J. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 11 (also called "STEAP-1 v.11") is shown in FIG. 2K. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 12 (also called "STEAP-1 v.12") is shown in FIG. 2L. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 13 (also called "STEAP-1 v.13") is shown in FIG. 2M. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 14 (also called "STEAP-1 v.14") is shown in FIG. 2N. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 15 (also called "STEAP-1 v.15") is shown in FIG. 2O. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including

the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 16 (also called "STEAP-1 v.16") is shown in **FIG. 2P**. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. The cDNA and amino acid sequence of STEAP-1 variant 17 (also called "STEAP-1 v.17") is shown in **FIG. 2Q**. The codon for the start methionine is underlined. The open reading frame extends from nucleic acid 96-872 including the stop codon. As used herein, a reference to STEAP-1 includes all variants thereof, including those shown in **FIGS. 10 and 12**.

[0042] FIG. 3. Amino acid sequence of STEAP-1 v.1 is shown in **FIG. 3A**; it has 339 amino acids. The amino acid sequence of STEAP-1 v.2 is shown in **FIG. 3B**; it has 258 amino acids. The amino acid sequence of STEAP-1 v.3 is shown in **FIG. 3C**; it has 282 amino acids. The amino acid sequence of STEAP-1 v.4 is shown in **FIG. 3D**; it has 258 amino acids. As used herein, a reference to STEAP-1 includes all variants thereof, including those shown in **FIG. 11**.

[0043] FIG. 4. The amino acid sequence alignment of STEAP-1 v.1 with mouse TNF α -induced adipose-related protein (gi/16905133) is shown in **FIG. 4A**. The amino acid sequence alignment of STEAP-1 v.1 with rat pHyd protein (gi/21717665) is shown in **FIG. 4B**. **FIG. 4C** shows Homology of STEAP-1 to mouse six transmembrane epithelial antigen of the prostate (gi/20820492).

[0044] FIG. 5. (5) Hydrophilicity amino acid profile of STEAP-1 variant 1. (5A) Hydrophilicity amino acid profile of STEAP-1 variant 3, determined by computer algorithm sequence analysis using the method of Hopp and Woods (Hopp T. P., Woods K. R., 1981. Proc. Natl. Acad. Sci. U.S.A. 78:3824-3828) accessed on the ProtScale website located on the world wide web URL <http://expasy.ch/cgi-bin/protscale.pl> through the ExPasy molecular biology server.

[0045] FIG. 6. (6) Hydropathicity amino acid profile of STEAP-1 variant 1. (6A) Hydropathicity amino acid profile of STEAP-1 variant 3, determined by computer algorithm sequence analysis using the method of Kyte and Doolittle (Kyte J., Doolittle R. F., 1982. J. Mol. Biol. 157:105-132) accessed on the ProtScale website located on the world wide web URL <http://expasy.ch/cgi-bin/protscale.pl> through the ExPasy molecular biology server.

[0046] FIG. 7. (7) Percent accessible residues amino acid profile of STEAP-1 variant 1. (7A) Percent accessible residues amino acid profile of STEAP-1 variant 3, determined by computer algorithm sequence analysis using the method of Janin (Janin J., 1979 Nature 277:491-492) accessed on the ProtScale website located on the world wide web URL <http://expasy.ch/cgi-bin/protscale.pl> through the ExPasy molecular biology server.

[0047] FIG. 8. (8) Average flexibility amino acid profile of STEAP-1 variant 1. (8A) Average flexibility amino acid profile of STEAP-1 variant 3, determined by computer algorithm sequence analysis using the method of Bhaskaran and Ponnuswamy (Bhaskaran R., and Ponnuswamy P. K., 1988. Int. J. Pept. Protein Res. 32:242-255) accessed on the ProtScale website located on the world wide web URL <http://expasy.ch/cgi-bin/protscale.pl> through the ExPasy molecular biology server.

[0048] FIG. 9. (9) Beta-turn amino acid profile of STEAP-1 variant 1. (9A) Beta-turn amino acid profile of

STEAP-1 variant 3, determined by computer algorithm sequence analysis using the method of Deleage and Roux (Deleage, G., Roux B. 1987 Protein Engineering 1:289-294) accessed on the ProtScale website located on the world wide web URL <http://expasy.ch/cgi-bin/protscale.pl> through the ExPasy molecular biology server.

[0049] FIG. 10. Schematic alignment of SNP variants of 8P1D4. Variants 8P1D4 v.4 through v.17 are variants with single nucleotide differences as compared to 8P1D4 v.2. Though these SNP variants are shown separately, they could also occur in any combinations and in any transcript variants that contains the base pairs, e.g., 8P1D4 v.1 and v.3. Numbers correspond to those of 8P1D4 v.2. Black box shows the same sequence as 8P1D4 v.2. SNPs are indicated above the box.

[0050] FIG. 11. Exon compositions of transcript variants of 8P1D4. This figure shows the structure of the transcript variants without poly A tail. Variants 8P1D4 v.1, v.2 and v.3 are transcript variants that share the same exons 2 and 3. The first exon of 8P1D4 v.1 is 30 bases shorter at 5' end than the first exons of the other two transcript variants. The fourth exon of 8P1D4 v.2 is the same as the combined exon 4, intron 4 and exon 5 of 8P1D4 v.1. Compared with 8P1D4 v.1, variant 8P1D4 v.3 has an additional exon spliced out from intron 4 of 8P1D4 v.1. Lengths of introns and exons are not proportional.

[0051] FIG. 12. Schematic alignment of protein variants of 8P1D4. Protein variants correspond to nucleotide variants. Nucleotide variants 8P1D4 v.5 through v.17 in **FIG. 10** code for the same protein as 8P1D4 v.2. Proteins translated from transcript variants 8P1D4 v.1 and v.3 as shown in **FIG. 11** may contain amino acid F (Phe) or L (Leu) at position 169. Single amino acid differences were indicated above the boxes. Black boxes represent the same sequence as 8P1D4 v.1. Boxes with different patterns of filling show different sequences. Numbers underneath the box correspond to 8P1D4 v.1

[0052] FIG. 13. **FIGS. 13(a)-(c).** Secondary structure and transmembrane domains prediction for 8P1D4 protein variants. The secondary structure of 8P1D4 protein variants 1 (SEQ ID NO: 93), 2 (SEQ ID NO: 94), and 3 (SEQ ID NO: 95); (**FIGS. 13a-13c**, respectively) were predicted using the HNN—Hierarchical Neural Network method (Guermeur, 1997, http://pbil.ibcp.fr/cgi-bin/npsa_automat.pl?page=npsa_nn.html), accessed from the ExPasy molecular biology server located on the World Wide Web at (<http://expasy.ch/tools/>). This method predicts the presence and location of alpha helices, extended strands, and random coils from the primary protein sequence. The percent of the protein in a given secondary structure is also listed. **FIGS. 13(d), 13(f), and 13(h).** Schematic representations of the probability of existence of transmembrane regions and orientation of 8P1D4 variant 1-3, (**FIGS. 13(d), 13(f) and 13(h)** respectively, based on the TMpred algorithm of Hofmann and Stoffel which utilizes TMBASE (K. Hofmann, W. Stoffel. TMBASE—A database of membrane spanning protein segments Biol. Chem. Hoppe-Seyler 374:166, 1993). **FIGS. 13(e), 13(g), and 13(i).** Schematic representations of the probability of the existence of transmembrane regions and the extracellular and intracellular orientation of 8P1D4 variants 1-3, **FIGS. 13(e), 13(g), and 13(i)** respectively, based on the TMHMM algorithm of Sonnhammer, von Heijne, and Krogh (Erik L.

L. Sonnhammer, Gunnar von Heijne, and Anders Krogh: A hidden Markov model for predicting transmembrane helices in protein sequences. In Proc. of Sixth Int. Conf. on Intelligent Systems for Molecular Biology, p 175-182 Ed J. Glasgow, T. Littlejohn, F. Major, R. Lathrop, D. Sankoff, and C. Sensen Menlo Park, Calif.: AAAI Press, 1998). The TMpred and TMHMM algorithms are accessed from the ExPasy molecular biology server located on the World Wide Web at (.expasy.ch/tools/).

[0053] **FIG. 14.** Expression of STEAP-1 in stomach cancer patient specimen. RNA was extracted from normal stomach (N) and from 10 different stomach cancer patient specimens (T). Northern blot with 10 µg of total RNA/lane was probed with STEAP-1 sequence. Results show strong expression of an approximately 1.6 kb STEAP-1 in the stomach tumor tissues. The lower panel represents ethidium bromide staining of the blot showing quality of the RNA samples.

[0054] **FIG. 15** STEAP-1 expression in rectum cancer patient tissues. RNA was extracted from normal rectum (N), rectum cancer patient tumors (T), and rectum cancer metastasis (M). Northern blots with 10 µg of total RNA were probed with the STEAP-1 sequence. Results show strong expression of STEAP-1 in the rectum cancer patient tissues. The lower panel represents ethidium bromide staining of the blot showing quality of the RNA samples.

[0055] **FIG. 16.** Expression of STEAP-1 in human umbilical vein endothelial cells (HUVEC). First strand cDNA was prepared from HUVEC cells, LAPC-4AD and LAPC-9AD prostate cancer xenografts, as well as from human brain tissues. Normalization was performed by PCR using primers to actin and GAPDH. Semi-quantitative PCR, using primers to STEAP-1, was performed at 27 and 30 cycles of amplification (A). As a control, PCR using primers to actin is shown in (B). Results show strong expression of STEAP-1 in HUVEC cells similar to the expression detected in prostate cancer xenograft tissues. Expression of STEAP-1 in HUVEC cells indicates that targeting STEAP-1 may also target endothelial cells of the neovasculature of the tumors.

[0056] **FIG. 17.** Shows that STEAP-1 increased calcium flux in response to LPA.

[0057] **FIG. 18.** Shows that STEAP-1-mediated calcium transport regulates prostate cancer growth by regulating intracellular levels of calcium.

[0058] **FIG. 19.** The figure demonstrates that STEAP-1 mediates the transfer of the small molecule calcein between adjacent cells, and thereby regulates cell-cell communication in prostate cancer cells. The results demonstrated that while PC3 control cells (no detectable STEAP-1 protein expression) exhibit little calcein transfer, the expression of STEAP-1 allows the transfer of small molecules between cells, whereby the initially red recipient cells take on a brownish color, and co-localize the red and green molecules.

[0059] **FIG. 20.** The figure demonstrates that STEAP-1 mediates the transfer of the small molecule calcein between adjacent cells, and thereby regulates cell-cell communication in prostate cancer cells. The figure shows the time-dependent manner of cell-cell communication mediated by STEAP-1, where little transfer in PC3-STEAP-1 cells is seen at 6 hours, and much transfer is seen at 24 hours.

[0060] **FIG. 21.** This figure shows whether expression of STEAP-1 is sufficient to regulate specific signaling pathways not otherwise active in resting PC3 cells, the effect of these genes on the activation of the p38 MAPK cascade was investigated in the prostate cancer cell line PC3. **FIG. 21A** shows that while expression of the control neo gene has no effect on p38 phosphorylation, expression of STEAP-1 in PC3 cells is sufficient to induce the activation of the p38 pathway. **FIG. 21B** shows the results were verified using western blotting with an anti-p38 Ab, which shows equal protein loading on the gels.

[0061] **FIG. 22.** This figure shows the sufficiency of expression of STEAP-1 in the prostate cancer cell line PC3 to activate the mitogenic MAPK pathway, namely the ERK cascade. **FIG. 22A** shows that while expression of the control neo gene has no effect on ERK phosphorylation, expression of STEAP-1 in PC3 cells is sufficient to induce an increase in ERK phosphorylation. **FIG. 22B** shows these results were verified using anti-ERK western blotting and confirm the activation of the ERK pathway by STEAP-1 and STEAP-2.

[0062] **FIG. 23.** Shows necessary expression of STEAP-1 on Donor and Recipient Cells.

[0063] **FIG. 24.** Shows that the introduction of STEAP-1 specific RNAi reduces the expression of STEAP-1 in recombinant 3T3 and Rat-1 cells. Whole cell immunostaining revealed that the STEAP-1 RNAi reduced STEAP-1 expression in Rat-1 and 3T3 cells. This reduction was confirmed by Western blot analysis where STEAP-1 protein was substantially reduced in STEAP-1 RNAi treated cells relative to control and untreated cells.

[0064] **FIG. 25.** Shows that RNAi reduces the endogenous expression of STEAP-1 in the prostate cancer and LNCaP cell line.

DETAILED DESCRIPTION OF THE INVENTION

[0065] Outline of Sections

[0066] I.) Definitions

[0067] II.) STEAP-1 Polynucleotides

[0068] II.A.) Uses of STEAP-1 Polynucleotides

[0069] II.A.1.) Monitoring of Genetic Abnormalities

[0070] II.A.2.) Antisense Embodiments

[0071] II.A.3.) Primers and Primer Pairs

[0072] II.A.4.) Isolation of STEAP-1-Encoding Nucleic Acid Molecules

[0073] II.A.5.) Recombinant Nucleic Acid Molecules and Host-Vector Systems

[0074] III.) STEAP-1-related Proteins

[0075] III.A.) Motif-bearing Protein Embodiments

[0076] III.B.) Expression of STEAP-1-related Proteins

[0077] III.C.) Modifications of STEAP-1-related Proteins

[0078] III.D.) Uses of STEAP-1-related Proteins

[0079] IV.) STEAP-1 Antibodies

- [0080] V.) STEAP-1 Cellular Immune Responses
- [0081] VI.) STEAP-1 Transgenic Animals
- [0082] VII.) Methods for the Detection of STEAP-1
- [0083] VIII.) Methods for Monitoring the Status of STEAP-1-related Genes and Their Products
- [0084] IX.) Identification of Molecules That Interact With STEAP-1
- [0085] X.) Therapeutic Methods and Compositions
 - [0086] X.A.) Anti-Cancer Vaccines
- [0087] X.B.) STEAP-1 as a Target for Antibody-Based Therapy
- [0088] X.C.) STEAP-1 as a Target for Cellular Immune Responses
 - [0089] X.C.1. Minigene Vaccines
 - [0090] X.C.2. Combinations of CTL Peptides with Helper Peptides
 - [0091] X.C.3. Combinations of CTL Peptides with T Cell Priming Agents
 - [0092] X.C.4. Vaccine Compositions Comprising DC Pulsed with CTL and/or HTL Peptides
 - [0093] X.D.) Adoptive Immunotherapy
 - [0094] X.E.) Administration of Vaccines for Therapeutic or Prophylactic Purposes
- [0095] XI.) Diagnostic and Prognostic Embodiments of STEAP-1.
- [0096] XII.) Inhibition of STEAP-1 Protein Function
 - [0097] XII.A.) Inhibition of STEAP-1 With Intracellular Antibodies
 - [0098] XII.B.) Inhibition of STEAP-1 with Recombinant Proteins
 - [0099] XII.C.) Inhibition of STEAP-1 Transcription or Translation
- [0100] XII.D.) General Considerations for Therapeutic Strategies
- [0101] XIII.) KITS/Articles of Manufacture
- [0102] I.) Definitions:
 - [0103] Unless otherwise defined, all terms of art, notations and other scientific terms or terminology used herein are intended to have the meanings commonly understood by those of skill in the art to which this invention pertains. In some cases, terms with commonly understood meanings are defined herein for clarity and/or for ready reference, and the inclusion of such definitions herein should not necessarily be construed to represent a substantial difference over what is generally understood in the art. Many of the techniques and procedures described or referenced herein are well understood and commonly employed using conventional methodology by those skilled in the art, such as, for example, the widely utilized molecular cloning methodologies described in Sambrook et al., *Molecular Cloning: A Laboratory Manual* 2nd. edition (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. As appropriate, procedures involving the use of commercially available kits and

reagents are generally carried out in accordance with manufacturer defined protocols and/or parameters unless otherwise noted.

[0104] The terms “advanced prostate cancer”, “locally advanced prostate cancer”, “advanced disease” and “locally advanced disease” mean prostate cancers that have extended through the prostate capsule, and are meant to include stage C disease under the American Urological Association (AUA) system, stage C₁-C₂ disease under the Whitmore-Jewett system, and stage T3-T4 and N+ disease under the TNM (tumor, node, metastasis) system. In general, surgery is not recommended for patients with locally advanced disease, and these patients have substantially less favorable outcomes compared to patients having clinically localized (organ-confined) prostate cancer. Locally advanced disease is clinically identified by palpable evidence of induration beyond the lateral border of the prostate, or asymmetry or induration above the prostate base. Locally advanced prostate cancer is presently diagnosed pathologically following radical prostatectomy if the tumor invades or penetrates the prostatic capsule, extends into the surgical margin, or invades the seminal vesicles.

[0105] “Altering the native glycosylation pattern” is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence STEAP-1 (either by removing the underlying glycosylation site or by deleting the glycosylation by chemical and/or enzymatic means), and/or adding one or more glycosylation sites that are not present in the native sequence STEAP-1. In addition, the phrase includes qualitative changes in the glycosylation of the native proteins, involving a change in the nature and proportions of the various carbohydrate moieties present.

[0106] The term “analog” refers to a molecule which is structurally similar or shares similar or corresponding attributes with another molecule (e.g. a STEAP-1-related protein). For example, an analog of a STEAP-1 protein can be specifically bound by an antibody or T cell that specifically binds to STEAP-1.

[0107] The term “antibody” is used in the broadest sense. Therefore, an “antibody” can be naturally occurring or man-made such as monoclonal antibodies produced by conventional hybridoma technology. Anti-STEAP-1 antibodies comprise monoclonal and polyclonal antibodies as well as fragments containing the antigen-binding domain and/or one or more complementarity determining regions of these antibodies.

[0108] An “antibody fragment” is defined as at least a portion of the variable region of the immunoglobulin molecule that binds to its target, i.e., the antigen-binding region. In one embodiment it specifically covers single anti-STEAP-1 antibodies and clones thereof (including agonist, antagonist and neutralizing antibodies) and anti-STEAP-1 antibody compositions with polyepitopic specificity.

[0109] The term “codon optimized sequences” refers to nucleotide sequences that have been optimized for a particular host species by replacing any codons having a usage frequency of less than about 20%. Nucleotide sequences that have been optimized for expression in a given host species by elimination of spurious polyadenylation sequences, elimination of exon/intron splicing signals, elimination of transposon-like repeats and/or optimization of GC content in

addition to codon optimization are referred to herein as an "expression enhanced sequences."

[0110] The term "cytotoxic agent" refers to a substance that inhibits or prevents the expression activity of cells, function of cells and/or causes destruction of cells. The term is intended to include radioactive isotopes chemotherapeutic agents, and toxins such as small molecule toxins or enzymatically active toxins of bacterial, fungal, plant or animal origin, including fragments and/or variants thereof. Examples of cytotoxic agents include, but are not limited to auristatins, auromycins, maytansinoids, yttrium, bismuth, ricin, ricin A-chain, combrestatin, duocarmycins, dolostatins, doxorubicin, daunorubicin, taxol, cisplatin, cc1065, ethidium bromide, mitomycin, etoposide, teniposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin, diphtheria toxin, *Pseudomonas exotoxin* (PE) A, PE40, abrin, abrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, *Saponaire officinalis* inhibitor, and glucocorticoid and other chemotherapeutic agents, as well as radioisotopes such as At^{211} , I^{131} , I^{125} , Y^{90} , Re^{186} , Re^{188} , Sm^{153} , Bi^{212} or Bi^{213} , P^{32} and radioactive isotopes of Lu including Lu^{177} . Antibodies may also be conjugated to an anti-cancer pro-drug activating enzyme capable of converting the pro-drug to its active form.

[0111] The term "homolog" refers to a molecule which exhibits homology to another molecule, by for example, having sequences of chemical residues that are the same or similar at corresponding positions.

[0112] "Human Leukocyte Antigen" or "HLA" is a human class I or class II Major Histocompatibility Complex (MHC) protein (see, e.g., Stites, et al., IMMUNOLOGY, 8th ED., Lange Publishing, Los Altos, Calif. (1994)).

[0113] The terms "hybridize", "hybridizing", "hybridizes" and the like, used in the context of polynucleotides, are meant to refer to conventional hybridization conditions, preferably such as hybridization in 50% formamide/6×SSC/0.1% SDS/100 µg/ml ssDNA, in which temperatures for hybridization are above 37 degrees C. and temperatures for washing in 0.1×SSC/0.1% SDS are above 55 degrees C.

[0114] The phrases "isolated" or "biologically pure" refer to material which is substantially or essentially free from components which normally accompany the material as it is found in its native state. Thus, isolated peptides in accordance with the invention preferably do not contain materials normally associated with the peptides in their in situ environment. For example, a polynucleotide is said to be "isolated" when it is substantially separated from contaminant polynucleotides that correspond or are complementary to genes other than the STEAP-1 genes or that encode polypeptides other than STEAP-1 gene product or fragments thereof. A skilled artisan can readily employ nucleic acid isolation procedures to obtain an isolated STEAP-1 polynucleotide. A protein is said to be "isolated," for example, when physical, mechanical or chemical methods are employed to remove the STEAP-1 proteins from cellular constituents that are normally associated with the protein. A skilled artisan can readily employ standard purification methods to obtain an isolated STEAP-1 protein. Alternatively, an isolated protein can be prepared by chemical means.

[0115] The term "mammal" refers to any organism classified as a mammal, including mice, rats, rabbits, dogs, cats,

cows, horses and humans. In one embodiment of the invention, the mammal is a mouse. In another embodiment of the invention, the mammal is a human.

[0116] The terms "metastatic prostate cancer" and "metastatic disease" mean prostate cancers that have spread to regional lymph nodes or to distant sites, and are meant to include stage D disease under the AUA system and stage T×N×M+ under the TNM system. As is the case with locally advanced prostate cancer, surgery is generally not indicated for patients with metastatic disease, and hormonal (androgen ablation) therapy is a preferred treatment modality. Patients with metastatic prostate cancer eventually develop an androgen-refractory state within 12 to 18 months of treatment initiation. Approximately half of these androgen-refractory patients die within 6 months after developing that status. The most common site for prostate cancer metastasis is bone. Prostate cancer bone metastases are often osteoblastic rather than osteolytic (i.e., resulting in net bone formation). Bone metastases are found most frequently in the spine, followed by the femur, pelvis, rib cage, skull and humerus. Other common sites for metastasis include lymph nodes, lung, liver and brain. Metastatic prostate cancer is typically diagnosed by open or laparoscopic pelvic lymphadenectomy, whole body radionuclide scans, skeletal radiography, and/or bone lesion biopsy.

[0117] The term "monoclonal antibody" refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the antibodies comprising the population are identical except for possible naturally occurring mutations that are present in minor amounts.

[0118] A "motif", as in biological motif of a STEAP-1-related protein, refers to any pattern of amino acids forming part of the primary sequence of a protein, that is associated with a particular function (e.g. protein-protein interaction, protein-DNA interaction, etc) or modification (e.g. that is phosphorylated, glycosylated or amidated), or localization (e.g. secretory sequence, nuclear localization sequence, etc.) or a sequence that is correlated with being immunogenic, either humorally or cellularly. A motif can be either contiguous or capable of being aligned to certain positions that are generally correlated with a certain function or property. In the context of HLA motifs, "motif" refers to the pattern of residues in a peptide of defined length, usually a peptide of from about 8 to about 13 amino acids for a class I HLA motif and from about 6 to about 25 amino acids for a class II HLA motif, which is recognized by a particular HLA molecule. Peptide motifs for HLA binding are typically different for each protein encoded by each human HLA allele and differ in the pattern of the primary and secondary anchor residues.

[0119] A "pharmaceutical excipient" comprises a material such as an adjuvant, a carrier, pH-adjusting and buffering agents, tonicity adjusting agents, wetting agents, preservative, and the like.

[0120] "Pharmaceutically acceptable" refers to a non-toxic, inert, and/or composition that is physiologically compatible with humans or other mammals.

[0121] The term "polynucleotide" means a polymeric form of nucleotides of at least 10 bases or base pairs in length, either ribonucleotides or deoxynucleotides or a modified form of either type of nucleotide, and is meant to

include single and double stranded forms of DNA and/or RNA. In the art, this term is often used interchangeably with “oligonucleotide”. A polynucleotide can comprise a nucleotide sequence disclosed herein wherein thymidine (T), as shown for example in **FIG. 2**, can also be uracil (U); this definition pertains to the differences between the chemical structures of DNA and RNA, in particular the observation that one of the four major bases in RNA is uracil (U) instead of thymidine (T).

[0122] The term “polypeptide” means a polymer of at least about 4, 5, 6, 7, or 8 amino acids. Throughout the specification, standard three letter or single letter designations for amino acids are used. In the art, this term is often used interchangeably with “peptide” or “protein”.

[0123] An HLA “primary anchor residue” is an amino acid at a specific position along a peptide sequence which is understood to provide a contact point between the immunogenic peptide and the HLA molecule. One to three, usually two, primary anchor residues within a peptide of defined length generally defines a “motif” for an immunogenic peptide. These residues are understood to fit in close

contact with peptide binding groove of an HLA molecule, with their side chains buried in specific pockets of the binding groove. In one embodiment, for example, the primary anchor residues for an HLA class I molecule are located at position 2 (from the amino terminal position) and at the carboxyl terminal position of a 8, 9, 10, 11, or 12 residue peptide epitope in accordance with the invention. In another embodiment, for example, the primary anchor residues of a peptide that will bind an HLA class II molecule are spaced relative to each other, rather than to the termini of a peptide, where the peptide is generally of at least 9 amino acids in length. The primary anchor positions for each motif and supermotif are set forth in Table IV. For example, analog peptides can be created by altering the presence or absence of particular residues in the primary and/or secondary anchor positions shown in Table IV. Such analogs are used to modulate the binding affinity and/or population coverage of a peptide comprising a particular HLA motif or supermotif.

[0124] “Radioisotopes” include, but are not limited to the following (non-limiting exemplary uses are also set forth):

Examples of Medical Isotopes:

Isotope	Description of use
Actinium-225 (Ac-225)	See Thorium-229 (Th-229)
Actinium-227 (Ac-227)	Parent of Radium-223 (Ra-223) which is an alpha emitter used to treat metastases in the skeleton resulting from cancer (i.e., breast and prostate cancers), and cancer radioimmunotherapy
Bismuth-212 (Bi-212)	See Thorium-228 (Th-228)
Bismuth-213 (Bi-213)	See Thorium-229 (Th-229)
Cadmium-109 (Cd-109)	Cancer detection
Cobalt-60 (Co-60)	Radiation source for radiotherapy of cancer, for food irradiators, and for sterilization of medical supplies
Copper-64 (Cu-64)	A positron emitter used for cancer therapy and SPECT imaging
Copper-67 (Cu-67)	Beta/gamma emitter used in cancer radioimmunotherapy and diagnostic studies (i.e., breast and colon cancers, and lymphoma)
Dysprosium-166 (Dy-166)	Cancer radioimmunotherapy
Erbium-169 (Er-169)	Rheumatoid arthritis treatment, particularly for the small joints associated with fingers and toes
Europium-152 (Eu-152)	Radiation source for food irradiation and for sterilization of medical supplies
Europium-154 (Eu-154)	Radiation source for food irradiation and for sterilization of medical supplies
Gadolinium-153 (Gd-153)	Osteoporosis detection and nuclear medical quality assurance devices
Gold-198 (Au-198)	Implant and intracavity therapy of ovarian, prostate, and brain cancers
Holmium-166 (Ho-166)	Multiple myeloma treatment in targeted skeletal therapy, cancer radioimmunotherapy, bone marrow ablation, and rheumatoid arthritis treatment
Iodine-125 (I-125)	Osteoporosis detection, diagnostic imaging, tracer drugs, brain cancer treatment, radiolabeling, tumor imaging, mapping of receptors in the brain, interstitial radiation therapy, brachytherapy for treatment of prostate cancer, determination of glomerular filtration rate (GFR), determination of plasma volume, detection of deep vein thrombosis of the legs
Iodine-131 (I-131)	Thyroid function evaluation, thyroid disease detection, treatment of thyroid cancer as well as other non-malignant thyroid diseases (i.e., Graves disease, goiters, and hyperthyroidism), treatment of leukemia, lymphoma, and other forms of cancer (e.g., breast cancer) using radioimmunotherapy
Iridium-192 (Ir-192)	Brachytherapy, brain and spinal cord tumor treatment, treatment of blocked arteries (i.e., arteriosclerosis and restenosis), and implants for breast and prostate tumors
Lutetium-177 (Lu-177)	Cancer radioimmunotherapy and treatment of blocked arteries (i.e., arteriosclerosis and restenosis)

-continued

Examples of Medical Isotopes:

Isotope	Description of use
Molybdenum-99 (Mo-99)	Parent of Technetium-99m (Tc-99m) which is used for imaging the brain, liver, lungs, heart, and other organs. Currently, Tc-99m is the most widely used radioisotope used for diagnostic imaging of various cancers and diseases involving the brain, heart, liver, lungs; also used in detection of deep vein thrombosis of the legs
Osmium-194 (Os-194)	Cancer radioimmunotherapy
Palladium-103 (Pd-103)	Prostate cancer treatment
Platinum-195m (Pt-195m)	Studies on biodistribution and metabolism of cisplatin, a chemotherapeutic drug
Phosphorus-32 (P-32)	Polycythemia rubra vera (blood cell disease) and leukemia treatment, bone cancer diagnosis/treatment; colon, pancreatic, and liver cancer treatment; radiolabeling nucleic acids for in vitro research, diagnosis of superficial tumors, treatment of blocked arteries (i.e., arteriosclerosis and restenosis), and intracavity therapy
Phosphorus-33 (P-33)	Leukemia treatment, bone disease diagnosis/treatment, radiolabeling, and treatment of blocked arteries (i.e., arteriosclerosis and restenosis)
Radium-223 (Ra-223)	See Actinium-227 (Ac-227)
Rhenium-186 (Re-186)	Bone cancer pain relief, rheumatoid arthritis treatment, and diagnosis and treatment of lymphoma and bone, breast, colon, and liver cancers using radioimmunotherapy
Rhenium-188 (Re-188)	Cancer diagnosis and treatment using radioimmunotherapy, bone cancer pain relief, treatment of rheumatoid arthritis, and treatment of prostate cancer
Rhodium-105 (Rh-105)	Cancer radioimmunotherapy
Samarium-145 (Sm-145)	Ocular cancer treatment
Samarium-153 (Sm-153)	Cancer radioimmunotherapy and bone cancer pain relief
Scandium-47 (Sc-47)	Cancer radioimmunotherapy and bone cancer pain relief
Selenium-75 (Se-75)	Radiotracer used in brain studies, imaging of adrenal cortex by gamma-scintigraphy, lateral locations of steroid secreting tumors, pancreatic scanning, detection of hyperactive parathyroid glands, measure rate of bile acid loss from the endogenous pool
Strontium-85 (Sr-85)	Bone cancer detection and brain scans
Strontium-89 (Sr-89)	Bone cancer pain relief, multiple myeloma treatment, and osteoblastic therapy
Technetium-99m (Tc-99m)	See Molybdenum-99 (Mo-99)
Thorium-228 (Th-228)	Parent of Bismuth-212 (Bi-212) which is an alpha emitter used in cancer radioimmunotherapy
Thorium-229 (Th-229)	Parent of Actinium-225 (Ac-225) and grandparent of Bismuth-213 (Bi-213) which are alpha emitters used in cancer radioimmunotherapy
Thulium-170 (Tm-170)	Gamma source for blood irradiators, energy source for implanted medical devices
Tin-117m (Sn-117m)	Cancer immunotherapy and bone cancer pain relief
Tungsten-188 (W-188)	Parent for Rhenium-188 (Re-188) which is used for cancer diagnostics/treatment, bone cancer pain relief, rheumatoid arthritis treatment, and treatment of blocked arteries (i.e., arteriosclerosis and restenosis)
Xenon-127 (Xe-127)	Neuroimaging of brain disorders, high resolution SPECT studies, pulmonary function tests, and cerebral blood flow studies
Ytterbium-175 (Yb-175)	Cancer radioimmunotherapy
Yttrium-90 (Y-90)	Microseeds obtained from irradiating Yttrium-89 (Y-89) for liver cancer treatment
Yttrium-91 (Y-91)	A gamma-emitting label for Yttrium-90 (Y-90) which is used for cancer radioimmunotherapy (i.e., lymphoma, breast, colon, kidney, lung, ovarian, prostate, pancreatic, and inoperable liver cancers)

[0125] A “recombinant” DNA or RNA molecule is a DNA or RNA molecule that has been subjected to molecular manipulation in vitro.

[0126] Non-limiting examples of small molecules include compounds that bind or interact with STEAP-1, ligands including hormones, neuropeptides, chemokines, odorants, phospholipids, and functional equivalents thereof that bind and preferably inhibit STEAP-1 protein function. Such non-limiting small molecules preferably have a molecular

weight of less than about 10 kDa, more preferably below about 9, about 8, about 7, about 6, about 5 or about 4 kDa. In certain embodiments, small molecules physically associate with, or bind, STEAP-1 protein; are not found in naturally occurring metabolic pathways; and/or are more soluble in aqueous than non-aqueous solutions.

[0127] “Stringency” of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe

length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured nucleic acid sequences to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature that can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of hybridization reactions, see Ausubel et al., *Current Protocols in Molecular Biology*, Wiley Interscience Publishers, (1995).

[0128] “Stringent conditions” or “high stringency conditions”, as defined herein, are identified by, but not limited to, those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50° C.; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50 mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42° C.; or (3) employ 50% formamide, 5×SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5× Denhardt’s solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% SDS, and 10% dextran sulfate at 42° C., with washes at 42° C. in 0.2×SSC (sodium chloride/sodium citrate) and 50% formamide at 55° C., followed by a high-stringency wash consisting of 0.1×SSC containing EDTA at 55° C. “Moderately stringent conditions” are described by, but not limited to, those in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and % SDS) less stringent than those described above. An example of moderately stringent conditions is overnight incubation at 37° C. in a solution comprising: 20% formamide, 5×SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5× Denhardt’s solution, 10% dextran sulfate, and 20 mg/mL denatured sheared salmon sperm DNA, followed by washing the filters in 1×SSC at about 37-50° C. The skilled artisan will recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

[0129] An HLA “supermotif” is a peptide binding specificity shared by HLA molecules encoded by two or more HLA alleles.

[0130] As used herein “to treat” or “therapeutic” and grammatically related terms, refer to any improvement of any consequence of disease, such as prolonged survival, less morbidity, and/or a lessening of side effects which are the byproducts of an alternative therapeutic modality; full eradication of disease is not required.

[0131] A “transgenic animal” (e.g., a mouse or rat) is an animal having cells that contain a transgene, which transgene was introduced into the animal or an ancestor of the animal at a prenatal, e.g., an embryonic stage. A “transgene” is a DNA that is integrated into the genome of a cell from which a transgenic animal develops.

[0132] As used herein, an HLA or cellular immune response “vaccine” is a composition that contains or encodes one or more peptides of the invention. There are numerous embodiments of such vaccines, such as a cocktail of one or more individual peptides; one or more peptides of the invention comprised by a polyepitopic peptide; or nucleic acids that encode such individual peptides or polypeptides, e.g., a minigene that encodes a polyepitopic peptide. The “one or more peptides” can include any whole unit integer from 1-150 or more, e.g., at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, or 150 or more peptides of the invention. The peptides or polypeptides can optionally be modified, such as by lipidation, addition of targeting or other sequences. HLA class I peptides of the invention can be admixed with, or linked to, HLA class II peptides, to facilitate activation of both cytotoxic T lymphocytes and helper T lymphocytes. HLA vaccines can also comprise peptide-pulsed antigen presenting cells, e.g., dendritic cells.

[0133] The term “variant” refers to a molecule that exhibits a variation from a described type or norm, such as a protein that has one or more different amino acid residues in the corresponding position(s) of a specifically described protein (e.g. the STEAP-1 protein shown in FIG. 2 or FIG. 3. An analog is an example of a variant protein. Splice isoforms and single nucleotides polymorphisms (SNPs) are further examples of variants.

[0134] The “STEAP-1-related proteins” of the invention include those specifically identified herein, as well as allelic variants, conservative substitution variants, analogs and homologs that can be isolated/generated and characterized without undue experimentation following the methods outlined herein or readily available in the art. Fusion proteins that combine parts of different STEAP-1 proteins or fragments thereof, as well as fusion proteins of a STEAP-1 protein and a heterologous polypeptide are also included. Such STEAP-1 proteins are collectively referred to as the STEAP-1-related proteins, the proteins of the invention, or STEAP-1. The term “STEAP-1-related protein” refers to a polypeptide fragment or a STEAP-1 protein sequence of 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more than 25 amino acids; or, at least 30, 35, 40, 45, 50, 55, 60, 65, 70, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475, 500, 525, 550, 575, 600, 625, 650, or 664 or more amino acids.

[0135] II.) STEAP-1 Polynucleotides

[0136] One aspect of the invention provides polynucleotides corresponding or complementary to all or part of a STEAP-1 gene, mRNA, and/or coding sequence, preferably in isolated form, including polynucleotides encoding a STEAP-1-related protein and fragments thereof, DNA, RNA, DNA/RNA hybrid, and related molecules, polynucleotides or oligonucleotides complementary to a STEAP-1 gene or mRNA sequence or a part thereof, and polynucleotides or oligonucleotides that hybridize to a STEAP-1 gene, mRNA, or to a STEAP-1 encoding polynucleotide (collectively, “STEAP-1 polynucleotides”). In all instances when referred to in this section, T can also be U in FIG. 2.

[0137] Embodiments of a STEAP-1 polynucleotide include: a STEAP-1 polynucleotide having the sequence shown in **FIG. 2**, the nucleotide sequence of STEAP-1 as shown in **FIG. 2** wherein T is U; at least 10 contiguous nucleotides of a polynucleotide having the sequence as shown in **FIG. 2**; or, at least 10 contiguous nucleotides of a polynucleotide having the sequence as shown in **FIG. 2** where T is U. For example, embodiments of STEAP-1 nucleotides comprise, without limitation:

[0138] (I) a polynucleotide comprising, consisting essentially of, or consisting of a sequence as shown in **FIG. 2A**, wherein T can also be U;

[0139] (II) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2A**, from nucleotide residue number 66 through nucleotide residue number 1085, including the stop codon, wherein T can also be U;

[0140] (III) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2B**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0141] (IV) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2C**, from nucleotide residue number 96 through nucleotide residue number 944, including the stop codon, wherein T can also be U;

[0142] (V) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2D**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0143] (VI) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2E**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0144] (VII) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2F**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0145] (VIII) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2G**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0146] (IX) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2H**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0147] (X) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2I**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0148] (XII) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown

in **FIG. 2J**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0149] (XIII) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2K**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0150] (XIV) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2L**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0151] (XV) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2M**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0152] (XVI) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2N**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0153] (XVII) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2O**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0154] (XVIII) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2P**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0155] (XIX) a polynucleotide comprising, consisting essentially of, or consisting of the sequence as shown in **FIG. 2Q**, from nucleotide residue number 96 through nucleotide residue number 872, including the stop codon, wherein T can also be U;

[0156] (XX) a polynucleotide that encodes a STEAP-1-related protein that is at least 90% homologous to an entire amino acid sequence shown in **FIG. 2A-Q**;

[0157] (XXI) a polynucleotide that encodes a STEAP-1-related protein that is at least 90% identical to an entire amino acid sequence shown in **FIG. 2A-Q**;

[0158] (XXII) a polynucleotide that encodes at least one peptide set forth in Tables V-XVIII and XXII-LI;

[0159] (XXIII) a polynucleotide that encodes a peptide region of at least 5 amino acids of a peptide of **FIG. 3A** in any whole number increment up to 339 that includes an amino acid position having a value greater than 0.5 in the Hydrophilicity profile of **FIG. 5**;

[0160] (XXIV) a polynucleotide that encodes a peptide region of at least 5 amino acids of a peptide of **FIG. 3A** in any whole number increment up to 339 that includes an amino acid position having a value less than 0.5 in the Hydrophobicity profile of **FIG. 6**;

[0161] (XV) a polynucleotide that encodes a peptide region of at least 5 amino acids of a peptide of **FIG. 3A**

in any whole number increment up to 339 that includes an amino acid position having a value greater than 0.5 in the Percent Accessible Residues profile of **FIG. 7**;

[0162] (XVI) a polynucleotide that encodes a peptide region of at least 5 amino acids of a peptide of **FIG. 3A** in any whole number increment up to 339 that includes an amino acid position having a value greater than 0.5 in the Average Flexibility profile of **FIG. 8**;

[0163] (XXVII) a polynucleotide that encodes a peptide region of at least 5 amino acids of a peptide of **FIG. 3A** in any whole number increment up to 339 that includes an amino acid position having a value greater than 0.5 in the Beta-turn profile of **FIG. 9**;

[0164] (XXVIII) a polynucleotide that is fully complementary to a polynucleotide of any one of (I)-(XIX).

[0165] (XXIX) a peptide that is encoded by any of (I)-(XIX); and

[0166] (XXX) a polynucleotide of any of (I)-(XIX) or peptide of (XXIII-XXVII) together with a pharmaceutical excipient and/or in a human unit dose form.

[0167] As used herein, a range is understood to disclose specifically all whole unit positions thereof.

[0168] Typical embodiments of the invention disclosed herein include STEAP-1 polynucleotides that encode specific portions of STEAP-1 mRNA sequences (and those which are complementary to such sequences) such as those that encode the proteins and/or fragments thereof, for example:

[0169] (a) 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 225, 250, 275, 300, 325, 330, 339 or more contiguous amino acids of STEAP-1 variant 1; the maximal lengths relevant for other variants are: variant 2, 258 amino acids; variant 3, 282 amino acids, and variant 4, 258 amino acids.

[0170] For example, representative embodiments of the invention disclosed herein include: polynucleotides and their encoded peptides themselves encoding about amino acid 1 to about amino acid 10 of the STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polynucleotides encoding about amino acid 10 to about amino acid 20 of the STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polynucleotides encoding about amino acid 20 to about amino acid 30 of the STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polynucleotides encoding about amino acid 30 to about amino acid 40 of the STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polynucleotides encoding about amino acid 40 to about amino acid 50 of the STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polynucleotides encoding about amino acid 50 to about amino acid 60 of the STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polynucleotides encoding about amino acid 60 to about amino acid 70 of the STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polynucleotides encoding about amino acid 70 to about amino acid 80 of the STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polynucleotides encoding about amino acid 80 to about amino acid 90 of the STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polynucleotides encoding about amino acid 90 to about amino acid 100 of the STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, in increments of about

10 amino acids, ending at the carboxyl terminal amino acid set forth in **FIG. 2** or **FIG. 3**. Accordingly, polynucleotides encoding portions of the amino acid sequence (of about 10 amino acids), of amino acids, 100 through the carboxyl terminal amino acid of the STEAP-1 protein are embodiments of the invention. Wherein it is understood that each particular amino acid position discloses that position plus or minus five amino acid residues.

[0171] Polynucleotides encoding relatively long portions of a STEAP-1 protein are also within the scope of the invention. For example, polynucleotides encoding from about amino acid 1 (or 20 or 30 or 40 etc.) to about amino acid 20, (or 30, or 40 or 50 etc.) of the STEAP-1 protein "or variant" shown in **FIG. 2** or **FIG. 3** can be generated by a variety of techniques well known in the art. These polynucleotide fragments can include any portion of the STEAP-1 sequence as shown in **FIG. 2**.

[0172] Additional illustrative embodiments of the invention disclosed herein include STEAP-1 polynucleotide fragments encoding one or more of the biological motifs contained within a STEAP-1 protein "or variant" sequence, including one or more of the motif-bearing subsequences of a STEAP-1 protein "or variant" set forth in Tables V-XVIII and XXII-LI. In another embodiment, typical polynucleotide fragments of the invention encode one or more of the regions of STEAP-1 protein or variant that exhibit homology to a known molecule. In another embodiment of the invention, typical polynucleotide fragments can encode one or more of the STEAP-1 protein or variant N-glycosylation sites, cAMP and cGMP-dependent protein kinase phosphorylation sites, casein kinase II phosphorylation sites or N-myristoylation site and amidation sites.

[0173] Note that to determine the starting position of any peptide set forth in Tables V-XVIII and Tables XXII to LI (collectively HLA Peptide Tables) respective to its parental protein, e.g., variant 1, variant 2, etc., reference is made to three factors: the particular variant, the length of the peptide in an HLA Peptide Table, and the Search Peptides listed in Table LVII. Generally, a unique Search Peptide is used to obtain HLA peptides for a particular variant. The position of each Search Peptide relative to its respective parent molecule is listed in Table LXI. Accordingly, if a Search Peptide begins at position "X", one must add the value "X minus 1" to each position in Tables V-XVIII and Tables XXII-LI to obtain the actual position of the HLA peptides in their parental molecule. For example if a particular Search Peptide begins at position 150 of its parental molecule, one must add 150-1, i.e., 149 to each HLA peptide amino acid position to calculate the position of that amino acid in the parent molecule.

[0174] II.A.) Uses of STEAP-1 Polynucleotides

[0175] II.A.1.) Monitoring of Genetic Abnormalities

[0176] The polynucleotides of the preceding paragraphs have a number of different specific uses. The human STEAP-1 gene maps to the chromosomal location set forth in the Example entitled "Chromosomal Mapping of STEAP-1." For example, because the STEAP-1 gene maps to this chromosome, polynucleotides that encode different regions of the STEAP-1 proteins are used to characterize cytogenetic abnormalities of this chromosomal locale, such as abnormalities that are identified as being associated with

various cancers. In certain genes, a variety of chromosomal abnormalities including rearrangements have been identified as frequent cytogenetic abnormalities in a number of different cancers (see e.g. Krajcinovic et al., *Mutat. Res.* 382(34): 81-83 (1998); Johansson et al., *Blood* 86(10): 3905-3914 (1995) and Finger et al., *P.N.A.S.* 85(23): 9158-9162 (1988)). Thus, polynucleotides encoding specific regions of the STEAP-1 proteins provide new tools that can be used to delineate, with greater precision than previously possible, cytogenetic abnormalities in the chromosomal region that encodes STEAP-1 that may contribute to the malignant phenotype. In this context, these polynucleotides satisfy a need in the art for expanding the sensitivity of chromosomal screening in order to identify more subtle and less common chromosomal abnormalities (see e.g. Evans et al., *Am. J. Obstet. Gynecol* 171(4): 1055-1057 (1994)).

[0177] Furthermore, as STEAP-1 was shown to be highly expressed in bladder and other cancers, STEAP-1 polynucleotides are used in methods assessing the status of STEAP-1 gene products in normal versus cancerous tissues. Typically, polynucleotides that encode specific regions of the STEAP-1 proteins are used to assess the presence of perturbations (such as deletions, insertions, point mutations, or alterations resulting in a loss of an antigen etc.) in specific regions of the STEAP-1 gene, such as regions containing one or more motifs. Exemplary assays include both RT-PCR assays as well as single-strand conformation polymorphism (SSCP) analysis (see, e.g., Marrogi et al., *J. Cutan. Pathol.* 26(8): 369-378 (1999), both of which utilize polynucleotides encoding specific regions of a protein to examine these regions within the protein.

[0178] II.A.2.) Antisense Embodiments

[0179] Other specifically contemplated nucleic acid related embodiments of the invention disclosed herein are genomic DNA, cDNAs, ribozymes, and antisense molecules, as well as nucleic acid molecules based on an alternative backbone, or including alternative bases, whether derived from natural sources or synthesized, and include molecules capable of inhibiting the RNA or protein expression of STEAP-1. For example, antisense molecules can be RNAs or other molecules, including peptide nucleic acids (PNAs) or non-nucleic acid molecules such as phosphorothioate derivatives that specifically bind DNA or RNA in a base pair-dependent manner. A skilled artisan can readily obtain these classes of nucleic acid molecules using the STEAP-1 polynucleotides and polynucleotide sequences disclosed herein.

[0180] Antisense technology entails the administration of exogenous oligonucleotides that bind to a target polynucleotide located within the cells. The term "antisense" refers to the fact that such oligonucleotides are complementary to their intracellular targets, e.g., STEAP-1. See for example, Jack Cohen, *Oligodeoxynucleotides, Antisense Inhibitors of Gene Expression*, CRC Press, 1989; and *Synthesis* 1:1-5 (1988). The STEAP-1 antisense oligonucleotides of the present invention include derivatives such as S-oligonucleotides (phosphorothioate derivatives or S-oligos, see, Jack Cohen, supra), which exhibit enhanced cancer cell growth inhibitory action. S-oligos (nucleoside phosphorothioates) are isoelectronic analogs of an oligonucleotide (O-oligo) in which a nonbridging oxygen atom of the phosphate group is replaced by a sulfur atom. The S-oligos of the present

invention can be prepared by treatment of the corresponding O-oligos with 3H-1,2-benzodithiol-3-one-1,1-dioxide, which is a sulfur transfer reagent. See, e.g., Iyer, R. P. et al., *J. Org. Chem.* 55:4693-4698 (1990); and Iyer, R. P. et al., *J. Am. Chem. Soc.* 112:1253-1254 (1990). Additional STEAP-1 antisense oligonucleotides of the present invention include morpholino antisense oligonucleotides known in the art (see, e.g., Partridge et al., 1996, *Antisense & Nucleic Acid Drug Development* 6: 169-175).

[0181] The STEAP-1 antisense oligonucleotides of the present invention typically can be RNA or DNA that is complementary to and stably hybridizes with the first 100 5' codons or last 100 3' codons of a STEAP-1 genomic sequence or the corresponding mRNA. Absolute complementarity is not required, although high degrees of complementarity are preferred. Use of an oligonucleotide complementary to this region allows for the selective hybridization to STEAP-1 mRNA and not to mRNA specifying other regulatory subunits of protein kinase. In one embodiment, STEAP-1 antisense oligonucleotides of the present invention are 15 to 30-mer fragments of the antisense DNA molecule that have a sequence that hybridizes to STEAP-1 mRNA. Optionally, STEAP-1 antisense oligonucleotide is a 30-mer oligonucleotide that is complementary to a region in the first 10 5' codons or last 10 3' codons of STEAP-1. Alternatively, the antisense molecules are modified to employ ribozymes in the inhibition of STEAP-1 expression, see, e.g., L. A. Couture & D. T. Stinchcomb; *Trends Genet* 12: 510-515 (1996).

[0182] II.A.3.) Primers and Primer Pairs

[0183] Further specific embodiments of these nucleotides of the invention include primers and primer pairs, which allow the specific amplification of polynucleotides of the invention or of any specific parts thereof, and probes that selectively or specifically hybridize to nucleic acid molecules of the invention or to any part thereof. Probes can be labeled with a detectable marker, such as, for example, a radioisotope, fluorescent compound, bioluminescent compound, a chemiluminescent compound, metal chelator or enzyme. Such probes and primers are used to detect the presence of a STEAP-1 polynucleotide in a sample and as a means for detecting a cell expressing a STEAP-1 protein.

[0184] Examples of such probes include polypeptides comprising all or part of the human STEAP-1 cDNA sequence shown in **FIG. 2**. Examples of primer pairs capable of specifically amplifying STEAP-1 mRNAs are also described in the Examples. As will be understood by the skilled artisan, a great many different primers and probes can be prepared based on the sequences provided herein and used effectively to amplify and/or detect a STEAP-1 mRNA.

[0185] The STEAP-1 polynucleotides of the invention are useful for a variety of purposes, including but not limited to their use as probes and primers for the amplification and/or detection of the STEAP-1 gene(s), mRNA(s), or fragments thereof; as reagents for the diagnosis and/or prognosis of prostate cancer and other cancers; as coding sequences capable of directing the expression of STEAP-1 polypeptides; as tools for modulating or inhibiting the expression of the STEAP-1 gene(s) and/or translation of the STEAP-1 transcript(s); and as therapeutic agents.

[0186] The present invention includes the use of any probe as described herein to identify and isolate a STEAP-1 or

STEAP-1 related nucleic acid sequence from a naturally occurring source, such as humans or other mammals, as well as the isolated nucleic acid sequence per se, which would comprise all or most of the sequences found in the probe used.

[0187] II.A.4.) Isolation of STEAP-1-Encoding Nucleic Acid Molecules

[0188] The STEAP-1 cDNA sequences described herein enable the isolation of other polynucleotides encoding STEAP-1 gene product(s), as well as the isolation of polynucleotides encoding STEAP-1 gene product homologs, alternatively spliced isoforms, allelic variants, and mutant forms of a STEAP-1 gene product as well as polynucleotides that encode analogs of STEAP-1-related proteins. Various molecular cloning methods that can be employed to isolate full length cDNAs encoding a STEAP-1 gene are well known (see, for example, Sambrook, J. et al., *Molecular Cloning: A Laboratory Manual*, 2d edition, Cold Spring Harbor Press, New York, 1989; *Current Protocols in Molecular Biology*, Ausubel et al., Eds., Wiley and Sons, 1995). For example, lambda phage cloning methodologies can be conveniently employed, using commercially available cloning systems (e.g., Lambda ZAP Express, Stratagene). Phage clones containing STEAP-1 gene cDNAs can be identified by probing with a labeled STEAP-1 cDNA or a fragment thereof. For example, in one embodiment, a STEAP-1 cDNA (e.g., **FIG. 2**) or a portion thereof can be synthesized and used as a probe to retrieve overlapping and full-length cDNAs corresponding to a STEAP-1 gene. A STEAP-1 gene itself can be isolated by screening genomic DNA libraries, bacterial artificial chromosome libraries (BACs), yeast artificial chromosome libraries (YACs), and the like, with STEAP-1 DNA probes or primers.

[0189] II.A.5.) Recombinant Nucleic Acid Molecules and Host-Vector Systems

[0190] The invention also provides recombinant DNA or RNA molecules containing a STEAP-1 polynucleotide, a fragment, analog or homologue thereof, including but not limited to phages, plasmids, phagemids, cosmids, YACs, BACs, as well as various viral and non-viral vectors well known in the art, and cells transformed or transfected with such recombinant DNA or RNA molecules. Methods for generating such molecules are well known (see, for example, Sambrook et al., 1989, *supra*).

[0191] The invention further provides a host-vector system comprising a recombinant DNA molecule containing a STEAP-1 polynucleotide, fragment, analog or homologue thereof within a suitable prokaryotic or eukaryotic host cell. Examples of suitable eukaryotic host cells include a yeast cell, a plant cell, or an animal cell, such as a mammalian cell or an insect cell (e.g., a baculovirus-infectible cell such as an Sf9 or HighFive cell). Examples of suitable mammalian cells include various prostate cancer cell lines such as DU145 and TsuPr1, other transfectable or transducible prostate cancer cell lines, primary cells (PrEC), as well as a number of mammalian cells routinely used for the expression of recombinant proteins (e.g., COS, CHO, 293, 293T cells). More particularly, a polynucleotide comprising the coding sequence of STEAP-1 or a fragment, analog or homolog thereof can be used to generate STEAP-1 proteins or fragments thereof using any number of host-vector systems routinely used and widely known in the art.

[0192] A wide range of host-vector systems suitable for the expression of STEAP-1 proteins or fragments thereof are available, see for example, Sambrook et al., 1989, *supra*; *Current Protocols in Molecular Biology*, 1995, *supra*). Preferred vectors for mammalian expression include but are not limited to pcDNA 3.1 myc-His-tag (Invitrogen) and the retroviral vector pSR α tkneo (Muller et al., 1991, MCB 11: 1785). Using these expression vectors, STEAP-1 can be expressed in several prostate cancer and non-prostate cell lines, including for example 293, 293T, rat-1, NIH 3T3 and TsuPr1. The host-vector systems of the invention are useful for the production of a STEAP-1 protein or fragment thereof. Such host-vector systems can be employed to study the functional properties of STEAP-1 and STEAP-1 mutations or analogs.

[0193] Recombinant human STEAP-1 protein or an analog or homolog or fragment thereof can be produced by mammalian cells transfected with a construct encoding a STEAP-1-related nucleotide. For example, 293T cells can be transfected with an expression plasmid encoding STEAP-1 or fragment, analog or homolog thereof, a STEAP-1-related protein is expressed in the 293T cells, and the recombinant STEAP-1 protein is isolated using standard purification methods (e.g., affinity purification using anti-STEAP-1 antibodies). In another embodiment, a STEAP-1 coding sequence is subcloned into the retroviral vector pSR α MSVtkneo and used to infect various mammalian cell lines, such as NIH 3T3, TsuPr1, 293 and rat-1 in order to establish STEAP-1 expressing cell lines. Various other expression systems well known in the art can also be employed. Expression constructs encoding a leader peptide joined in frame to a STEAP-1 coding sequence can be used for the generation of a secreted form of recombinant STEAP-1 protein.

[0194] As discussed herein, redundancy in the genetic code permits variation in STEAP-1 gene sequences. In particular, it is known in the art that specific host species often have specific codon preferences, and thus one can adapt the disclosed sequence as preferred for a desired host. For example, preferred analog codon sequences typically have rare codons (i.e., codons having a usage frequency of less than about 20% in known sequences of the desired host) replaced with higher frequency codons. Codon preferences for a specific species are calculated, for example, by utilizing codon usage tables available on the INTERNET such as at URL dna.affrc.go.jp/~nakamura/codon.html.

[0195] Additional sequence modifications are known to enhance protein expression in a cellular host. These include elimination of sequences encoding spurious polyadenylation signals, exon/intron splice site signals, transposon-like repeats, and/or other such well-characterized sequences that are deleterious to gene expression. The GC content of the sequence is adjusted to levels average for a given cellular host, as calculated by reference to known genes expressed in the host cell. Where possible, the sequence is modified to avoid predicted hairpin secondary mRNA structures. Other useful modifications include the addition of a translational initiation consensus sequence at the start of the open reading frame, as described in Kozak, *Mol. Cell Biol.*, 9:5073-5080 (1989). Skilled artisans understand that the general rule that eukaryotic ribosomes initiate translation exclusively at the 5' proximal AUG codon is abrogated only under rare condi-

tions (see, e.g., Kozak PNAS 92(7): 2662-2666, (1995) and Kozak NAR 15(20): 8125-8148 (1987)).

[0196] III.) STEAP-1-Related Proteins

[0197] Another aspect of the present invention provides STEAP-1-related proteins. Specific embodiments of STEAP-1 proteins comprise a polypeptide having all or part of the amino acid sequence of human STEAP-1 as shown in **FIG. 2** or **FIG. 3**. Alternatively, embodiments of STEAP-1 proteins comprise variant, homolog or analog polypeptides that have alterations in the amino acid sequence of STEAP-1 shown in **FIG. 2** or **FIG. 3**.

[0198] Embodiments of a STEAP-1 polypeptide include: a STEAP-1 polypeptide having a sequence shown in **FIG. 2**, a peptide sequence of a STEAP-1 as shown in **FIG. 2** wherein T is U; at least 10 contiguous nucleotides of a polypeptide having the sequence as shown in **FIG. 2**; or, at least 10 contiguous peptides of a polypeptide having the sequence as shown in **FIG. 2** where T is U. For example, embodiments of STEAP-1 peptides comprise, without limitation:

[0199] (I) an protein comprising, consisting essentially of, or consisting of an amino acid sequence as shown in **FIG. 2A-Q** or **FIG. 3A-D**;

[0200] (II) a 101P3A11-related protein that is at least 90% homologous to an entire amino acid sequence shown in **FIG. 2A-Q**;

[0201] (III) a 101P3A11-related protein that is at least 90% identical to an entire amino acid sequence shown in **FIG. 2A-Q** or **3A-D**;

[0202] (IV) a protein that comprises at least one peptide set forth in Tables V-XVIII or Tables XXII to LI, optionally with a proviso that it is not an entire protein of **FIG. 2**;

[0203] (V) a protein that comprises at least one peptide set forth in Tables V-XVIII, collectively, which peptide is also set forth in Tables XXII to LI, collectively, optionally with a proviso that it is not an entire protein of **FIG. 2**;

[0204] (VI) a protein that comprises at least two peptides selected from the peptides set forth in Tables V-XVIII and XXII to LI collectively, optionally with a proviso that it is not an entire protein of **FIG. 2**;

[0205] (VII) a protein that comprises at least two peptides selected from the peptides set forth in Tables V-XVIII and XXII to LI collectively, with a proviso that the protein is not a contiguous sequence from an amino acid sequence of **FIG. 2**;

[0206] (VIII) a protein that comprises at least one peptide selected from the peptides set forth in Tables V-XVIII; and at least one peptide set forth in Tables XXII to LI, with a proviso that the protein is not a contiguous sequence from an amino acid sequence of **FIG. 2**;

[0207] (IX) a polypeptide comprising at least 5 amino acids of a protein of **FIG. 3A, 3B, 3C**, or **3D** in any whole number increment up to 339, 258, 282, or 258 respectively that includes an amino acid position having a value greater than 0.5 in the Hydrophilicity profile of **FIG. 5**;

[0208] (X) a polypeptide comprising at least 5 amino acids of a protein of **FIG. 3A, 3B, 3C**, or **3D** in any whole number increment up to 339, 258, 282, or 258, respectively, that includes an amino acid position having a value less than 0.5 in the Hydropathicity profile of **FIG. 6**;

[0209] (XI) a polypeptide comprising at least 5 amino acids of a protein of **FIG. 3A, 3B, 3C**, or **3D** in any whole number increment up to 339, 258, 282, or 258, respectively, that includes an amino acid position having a value greater than 0.5 in the Percent Accessible Residues profile of **FIG. 7**;

[0210] (XII) a polypeptide comprising at least 5 amino acids of a protein of **FIG. 3A, 3B, 3C**, or **3D** in any whole number increment up to 339, 258, 282, or 258, respectively, that includes an amino acid position having a value greater than 0.5 in the Average Flexibility profile of **FIG. 8**;

[0211] (XIII) a polypeptide comprising at least 5 amino acids of a protein of **FIG. 3A, 3B, 3C**, or **3D** in any whole number increment up to 339, 258, 282, or 258, respectively, that includes an amino acid position having a value greater than 0.5 in the Beta-turn profile of **FIG. 9**;

[0212] (XIV) a peptide that occurs at least twice in Tables V-XVIII and XXII to LI, collectively;

[0213] (XV) a peptide that occurs at least three times in Tables V-XVIII and XXII to LI, collectively;

[0214] (XVI) a peptide that occurs at least four times in Tables V-XVIII and XXII to LI, collectively;

[0215] (XVII) a peptide that occurs at least five times in Tables V-XVIII and XXII to LI, collectively;

[0216] (XVIII) a peptide that occurs at least once in Tables V-XVIII, and at least once in tables XXII to LI;

[0217] (XIX) a peptide which comprises one two, three, four, or five of the following characteristics, or an oligonucleotide encoding such peptide:

[0218] i) a region of at least 5 amino acids of a particular peptide of **FIG. 3**, in any whole number increment up to the full length of that protein in **FIG. 3**, that includes an amino acid position having a value equal to or greater than 0.5, 0.6, 0.7, 0.8, 0.9, or having a value equal to 1.0, in the Hydrophilicity profile of **FIG. 5**;

[0219] ii) a region of at least S amino acids of a particular peptide of **FIG. 3**, in any whole number increment up to the full length of that protein in **FIG. 3**, that includes an amino acid position having a value equal to or less than 0.5, 0.4, 0.3, 0.2, 0.1, or having a value equal to 0.0, in the Hydropathicity profile of **FIG. 6**;

[0220] iii) a region of at least 5 amino acids of a particular peptide of **FIG. 3**, in any whole number increment up to the full length of that protein in **FIG. 3**, that includes an amino acid position having a value equal to or greater than 0.5, 0.6, 0.7, 0.8, 0.9, or having a value equal to 1.0, in the Percent Accessible Residues profile of **FIG. 7**;

- [0221] iv) a region of at least 5 amino acids of a particular peptide of **FIG. 3**, in any whole number increment up to the full length of that protein in **FIG. 3**, that includes an amino acid position having a value equal to or greater than 0.5, 0.6, 0.7, 0.8, 0.9, or having a value equal to 1.0, in the Average Flexibility profile of **FIG. 8**; or,
- [0222] v) a region of at least 5 amino acids of a particular peptide of **FIG. 3**, in any whole number increment up to the full length of that protein in **FIG. 3**, that includes an amino acid position having a value equal to or greater than 0.5, 0.6, 0.7, 0.8, 0.9, or having a value equal to 1.0, in the Beta-turn profile of **FIG. 9**;
- [0223] (XX) a peptide of (I)-(XIX) together with a pharmaceutical excipient and/or in a human unit dose form.
- [0224] As used herein, a range is understood to specifically disclose all whole unit positions thereof.
- [0225] Typical embodiments of the invention disclosed herein include 101P3A11 polynucleotides that encode specific portions of 101P3A11 mRNA sequences (and those which are complementary to such sequences) such as those that encode the proteins and/or fragments thereof, for example:
- [0226] (a) 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 225, 250, 275, 300, 325, 330, 339 or more contiguous amino acids of STEAP-1 variant 1; the maximal lengths relevant for other variants are: variant 2, 258 amino acids; variant 3, 282 amino acids, and variant 4, 258 amino acids.
- [0227] In general, naturally occurring allelic variants of human STEAP-1 share a high degree of structural identity and homology (e.g., 90% or more homology). Typically, allelic variants of a STEAP-1 protein contain conservative amino acid substitutions within the STEAP-1 sequences described herein or contain a substitution of an amino acid from a corresponding position in a homologue of STEAP-1. One class of STEAP-1 allelic variants are proteins that share a high degree of homology with at least a small region of a particular STEAP-1 amino acid sequence, but further contain a radical departure from the sequence, such as a non-conservative substitution, truncation, insertion or frame shift. In comparisons of protein sequences, the terms, similarity, identity, and homology each have a distinct meaning as appreciated in the field of genetics. Moreover, orthology and paralogy can be important concepts describing the relationship of members of a given protein family in one organism to the members of the same family in other organisms.
- [0228] Amino acid abbreviations are provided in Table II. Conservative amino acid substitutions can frequently be made in a protein without altering either the conformation or the function of the protein. Proteins of the invention can comprise 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 conservative substitutions. Such changes include substituting any of isoleucine (I), valine (V), and leucine (L) for any other of these hydrophobic amino acids; aspartic acid (D) for glutamic acid (E) and vice versa; glutamine (Q) for asparagine (N) and vice versa; and serine (S) for threonine (T) and vice versa. Other substitutions can also be considered conservative, depending on the environment of the particular amino acid and its role in the three-dimensional structure of the protein. For example, glycine (G) and alanine (A) can frequently be interchangeable, as can alanine (A) and valine (V). Methionine (M), which is relatively hydrophobic, can frequently be interchanged with leucine and isoleucine, and sometimes with valine. Lysine (K) and arginine (R) are frequently interchangeable in locations in which the significant feature of the amino acid residue is its charge and the differing pK's of these two amino acid residues are not significant. Still other changes can be considered "conservative" in particular environments (see, e.g. Table III herein; pages 13-15 "Biochemistry" 2nd ED. Lubert Stryer ed (Stanford University); Henikoff et al., PNAS 1992 Vol 89 10915-10919; Lei et al., J. Biol Chem 1995 May 19; 270(20):11882-6).
- [0229] Embodiments of the invention disclosed herein include a wide variety of art-accepted variants or analogs of STEAP-1 proteins such as polypeptides having amino acid insertions, deletions and substitutions. STEAP-1 variants can be made using methods known in the art such as site-directed mutagenesis, alanine scanning, and PCR mutagenesis. Site-directed mutagenesis (Carter et al., *Nucl. Acids Res.*, 13:4331 (1986); Zoller et al., *Nucl. Acids Res.*, 10:6487 (1987)), cassette mutagenesis (Wells et al., *Gene*, 34:315 (1985)), restriction selection mutagenesis (Wells et al., *Philos. Trans. R. Soc. London SerA*, 317:415 (1986)) or other known techniques can be performed on the cloned DNA to produce the STEAP-1 variant DNA.
- [0230] Scanning amino acid analysis can also be employed to identify one or more amino acids along a contiguous sequence that is involved in a specific biological activity such as a protein-protein interaction. Among the preferred scanning amino acids are relatively small, neutral amino acids. Such amino acids include alanine, glycine, serine, and cysteine. Alanine is typically a preferred scanning amino acid among this group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the main-chain conformation of the variant. Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently found in both buried and exposed positions (Creighton, *The Proteins*, (W.H. Freeman & Co., N.Y.); Chothia, *J. Mol. Biol.*, 150:1 (1976)). If alanine substitution does not yield adequate amounts of variant, an isosteric amino acid can be used.
- [0231] As defined herein, STEAP-1 variants, analogs or homologs, have the distinguishing attribute of having at least one epitope that is "cross reactive" with a STEAP-1 protein having an amino acid sequence of **FIG. 3**. As used in this sentence, "cross reactive" means that an antibody or T cell that specifically binds to a STEAP-1 variant also specifically binds to a STEAP-1 protein having an amino acid sequence set forth in **FIG. 3**. A polypeptide ceases to be a variant of a protein shown in **FIG. 3**, when it no longer contains any epitope capable of being recognized by an antibody or T cell that specifically binds to the starting STEAP-1 protein. Those skilled in the art understand that antibodies that recognize proteins bind to epitopes of varying size, and a grouping of the order of about four or five amino acids, contiguous or not, is regarded as a typical number of amino acids in a minimal epitope. See, e.g., Nair

et al., *J. Immunol* 2000 165(12): 6949-6955; Hebbes et al., *Mol Immunol* (1989) 26(9):865-73; Schwartz et al., *J Immunol* (1985) 135(4):2598-608.

[0232] Other classes of STEAP-1-related protein variants share 70%, 75%, 80%, 85% or 90% or more similarity with an amino acid sequence of **FIG. 3**, or a fragment thereof. Another specific class of STEAP-1 protein variants or analogs comprises one or more of the STEAP-1 biological motifs described herein or presently known in the art. Thus, encompassed by the present invention are analogs of STEAP-1 fragments (nucleic or amino acid) that have altered functional (e.g. immunogenic) properties relative to the starting fragment. It is to be appreciated that motifs now or which become part of the art are to be applied to the nucleic or amino acid sequences of **FIG. 2** or **FIG. 3**.

[0233] As discussed herein, embodiments of the claimed invention include polypeptides containing less than the full amino acid sequence of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**. For example, representative embodiments of the invention comprise peptides/proteins having any 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more contiguous amino acids of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**.

[0234] Moreover, representative embodiments of the invention disclosed herein include polypeptides consisting of about amino acid 1 to about amino acid 10 of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polypeptides consisting of about amino acid 10 to about amino acid 20 of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polypeptides consisting of about amino acid 20 to about amino acid 30 of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polypeptides consisting of about amino acid 30 to about amino acid 40 of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polypeptides consisting of about amino acid 40 to about amino acid 50 of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polypeptides consisting of about amino acid 50 to about amino acid 60 of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polypeptides consisting of about amino acid 60 to about amino acid 70 of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polypeptides consisting of about amino acid 70 to about amino acid 80 of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polypeptides consisting of about amino acid 80 to about amino acid 90 of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, polypeptides consisting of about amino acid 90 to about amino acid 100 of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3**, etc. throughout the entirety of a STEAP-1 amino acid sequence. Moreover, polypeptides consisting of about amino acid 1 (or 20 or 30 or 40 etc.) to about amino acid 20, (or 130, or 140 or 150 etc.) of a STEAP-1 protein shown in **FIG. 2** or **FIG. 3** are embodiments of the invention. It is to be appreciated that the starting and stopping positions in this paragraph refer to the specified position as well as that position plus or minus 5 residues.

[0235] STEAP-1-related proteins are generated using standard peptide synthesis technology or using chemical cleavage methods well known in the art. Alternatively, recombinant methods can be used to generate nucleic acid molecules that encode a STEAP-1-related protein. In one embodiment, nucleic acid molecules provide a means to generate defined fragments of a STEAP-1 protein (or variants, homologs or analogs thereof).

[0236] III.A.) Motif-Bearing Protein Embodiments

[0237] Additional illustrative embodiments of the invention disclosed herein include STEAP-1 polypeptides com-

prising the amino acid residues of one or more of the biological motifs contained within a STEAP-1 polypeptide sequence set forth in **FIG. 2** or **FIG. 3**. Various motifs are known in the art, and a protein can be evaluated for the presence of such motifs by a number of publicly available Internet sites (see, e.g., URL addresses: pfam.wustl.edu/; <http://searchlauncher.bcm.tmc.edu/seq-search/struc-predict.html>; psort.ims.u-tokyo.ac.jp/; cbs.dtu.dk/; ebi.ac.uk/interpro/scan.html; expasy.ch/tools/scnpsit1.html; Epimatrix™ and Epimer™, Brown University, brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html; and BIMAS, bimas.dcrf.nih.gov/).

[0238] Motif bearing subsequences of all STEAP-1 variant proteins are set forth and identified in Tables V-XVIII and XXII-LI.

[0239] Table XIX sets forth several frequently occurring motifs based on pfam searches (see URL address pfam.wustl.edu/). The columns of Table XIX list (1) motif name abbreviation, (2) percent identity found amongst the different member of the motif family, (3) motif name or description and (4) most common function; location information is included if the motif is relevant for location.

[0240] Polypeptides comprising one or more of the STEAP-1 motifs discussed above are useful in elucidating the specific characteristics of a malignant phenotype in view of the observation that the STEAP-1 motifs discussed above are associated with growth dysregulation and because STEAP-1 is overexpressed in certain cancers (See, e.g., Table I). Casein kinase II, cAMP and camp-dependent protein kinase, and Protein Kinase C, for example, are enzymes known to be associated with the development of the malignant phenotype (see e.g. Chen et al., *Lab Invest.*, 78(2): 165-174 (1998); Gaiddon et al., *Endocrinology* 136(10): 4331-4338 (1995); Hall et al., *Nucleic Acids Research* 24(6): 1119-1126 (1996); Peterziel et al., *Oncogene* 18(46): 6322-6329 (1999) and O'Brian, *Oncol. Rep.* 5(2): 305-309 (1998)). Moreover, both glycosylation and myristoylation are protein modifications also associated with cancer and cancer progression (see e.g. Dennis et al., *Biochem. Biophys. Acta* 1473(1):21-34 (1999); Raju et al., *Exp. Cell Res.* 235(1): 145-154 (1997)). Amidation is another protein modification also associated with cancer and cancer progression (see e.g. Treston et al., *J. Natl. Cancer Inst. Monogr.* (13): 169-175 (1992)).

[0241] In another embodiment, proteins of the invention comprise one or more of the immunoreactive epitopes identified in accordance with art-accepted methods, such as the peptides set forth in Tables V-XVIII and XXII-LI. CTL epitopes can be determined using specific algorithms to identify peptides within a STEAP-1 protein that are capable of optimally binding to specified HLA alleles (e.g., Table IV; Epimatrix™ and Epimer™, Brown University, brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html; and BIMAS, bimas.dcrf.nih.gov/). Moreover, processes for identifying peptides that have sufficient binding affinity for HLA molecules and which are correlated with being immunogenic epitopes, are well known in the art, and are carried out without undue experimentation. In addition, processes for identifying peptides that are immunogenic epitopes, are well known in the art, and are carried out without undue experimentation either in vitro or in vivo.

[0242] Also known in the art are principles for creating analogs of such epitopes in order to modulate immunoge-

nicity. For example, one begins with an epitope that bears a CTL or HTL motif (see, e.g., the HLA Class I and HLA Class II motifs/supermotifs of Table IV). The epitope is analogized by substituting out an amino acid at one of the specified positions, and replacing it with another amino acid specified for that position. For example, one can substitute out a deleterious residue in favor of any other residue, such as a preferred residue as defined in Table IV; substitute a less-preferred residue with a preferred residue as defined in Table IV; or substitute an originally-occurring preferred residue with another preferred residue as defined in Table IV. Substitutions can occur at primary anchor positions or at other positions in a peptide; see, e.g., Table IV.

[0243] A variety of references reflect the art regarding the identification and generation of epitopes in a protein of interest as well as analogs thereof. See, for example, WO 97/33602 to Chesnut et al.; Sette, *Immunogenetics* 1999 50(3-4): 201-212; Sette et al., *J. Immunol.* 2001 166(2): 1389-1397; Sidney et al., *Hum. Immunol.* 1997 58(1): 12-20; Kondo et al., *Immunogenetics* 1997 45(4): 249-258; Sidney et al., *J. Immunol.* 1996 157(8): 3480-90; and Falk et al., *Nature* 351: 290-6 (1991); Hunt et al., *Science* 255:1261-3 (1992); Parker et al., *J. Immunol.* 149:3580-7 (1992); Parker et al., *J. Immunol.* 152:163-75 (1994); Kast et al., 1994 152(8): 3904-12; Borrás-Cuesta et al., *Hum. Immunol.* 2000 61(3): 266-278; Alexander et al., *J. Immunol.* 2000 164(3): 1625-1633; Alexander et al., PMID: 7895164, UI: 95202582; O'Sullivan et al., *J. Immunol.* 1991 147(8): 2663-2669; Alexander et al., *Immunity* 1994 1(9): 751-761 and Alexander et al., *Immunol. Res.* 1998 18(2): 79-92.

[0244] Related embodiments of the invention include polypeptides comprising combinations of the different motifs set forth in Table XX, and/or, one or more of the predicted CTL epitopes of Tables V-XVII and XXII-XLVII, and/or, one or more of the predicted HTL epitopes of Tables XLVIII-LI, and/or, one or more of the T cell binding motifs known in the art. Preferred embodiments contain no insertions, deletions or substitutions either within the motifs or within the intervening sequences of the polypeptides. In addition, embodiments which include a number of either N-terminal and/or C-terminal amino acid residues on either side of these motifs may be desirable (to, for example, include a greater portion of the polypeptide architecture in which the motif is located). Typically, the number of N-terminal and/or C-terminal amino acid residues on either side of a motif is between about 1 to about 100 amino acid residues, preferably 5 to about 50 amino acid residues.

[0245] STEAP-1-related proteins are embodied in many forms, preferably in isolated form. A purified STEAP-1 protein molecule will be substantially free of other proteins or molecules that impair the binding of STEAP-1 to antibody, T cell or other ligand. The nature and degree of isolation and purification will depend on the intended use. Embodiments of a STEAP-1-related proteins include purified STEAP-1-related proteins and functional, soluble STEAP-1-related proteins. In one embodiment, a functional, soluble STEAP-1 protein or fragment thereof retains the ability to be bound by antibody, T cell or other ligand.

[0246] The invention also provides STEAP-1 proteins comprising biologically active fragments of a STEAP-1 amino acid sequence shown in FIG. 2 or FIG. 3. Such

proteins exhibit properties of the starting STEAP-1 protein, such as the ability to elicit the generation of antibodies that specifically bind an epitope associated with the starting STEAP-1 protein; to be bound by such antibodies; to elicit the activation of HTL or CTL; and/or, to be recognized by HTL or CTL that also specifically bind to the starting protein.

[0247] STEAP-1-related polypeptides that contain particularly interesting structures can be predicted and/or identified using various analytical techniques well known in the art, including, for example, the methods of Chou-Fasman, Garnier-Robson, Kyte-Doolittle, Eisenberg, Karplus-Schultz or Jameson-Wolf analysis, or based on immunogenicity. Fragments that contain such structures are particularly useful in generating subunit-specific anti-STEAP-1 antibodies or T cells or in identifying cellular factors that bind to STEAP-1. For example, hydrophilicity profiles can be generated, and immunogenic peptide fragments identified, using the method of Hopp, T. P. and Woods, K. R., 1981, *Proc. Natl. Acad. Sci. U.S.A.* 78:3824-3828. Hydrophobicity profiles can be generated, and immunogenic peptide fragments identified, using the method of Kyte, J. and Doolittle, R. F., 1982, *J. Mol. Biol.* 157:105-132. Percent (%) Accessible Residues profiles can be generated, and immunogenic peptide fragments identified, using the method of Janin J., 1979, *Nature* 277:491-492. Average Flexibility profiles can be generated, and immunogenic peptide fragments identified, using the method of Bhaskaran R., Ponnuswamy P. K., 1988, *Int. J. Pept. Protein Res.* 32:242-255. Beta-turn profiles can be generated, and immunogenic peptide fragments identified, using the method of Deleage, G., Roux B., 1987, *Protein Engineering* 1:289-294.

[0248] CTL epitopes can be determined using specific algorithms to identify peptides within a STEAP-1 protein that are capable of optimally binding to specified HLA alleles (e.g., by using the SYFPEITHI site at World Wide Web URL syfpeithi.bmi-heidelberg.com/; the listings in Table IV(A)-(E); Epimatrix™ and Epimer™, Brown University, URL (brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html); and BIMAS, URL bimas.dcrt.nih.gov/). Illustrating this, peptide epitopes from STEAP-1 that are presented in the context of human MHC Class I molecules, e.g., HLA-A1, A2, A3, A11, A24, B7 and B35 were predicted (see, e.g., Tables V-XVIII, XXII-LI). Specifically, the complete amino acid sequence of the STEAP-1 protein and relevant portions of other variants, i.e., for HLA Class I predictions 9 flanking residues on either side of a point mutation, and for HLA Class II predictions 14 flanking residues on either side of a point mutation, were entered into the HLA Peptide Motif Search algorithm found in the Bioinformatics and Molecular Analysis Section (BIMAS) web site listed above; in addition to the site SYFPEITHI, at URL syfpeithi.bmi-heidelberg.com/.

[0249] The HLA peptide motif search algorithm was developed by Dr. Ken Parker based on binding of specific peptide sequences in the groove of HLA Class I molecules, in particular HLA-A2 (see, e.g., Falk et al., *Nature* 351: 290-6 (1991); Hunt et al., *Science* 255:1261-3 (1992); Parker et al., *J. Immunol.* 149:3580-7 (1992); Parker et al., *J. Immunol.* 152:163-75 (1994)). This algorithm allows location and ranking of 8-mer, 9-mer, and 10-mer peptides from a complete protein sequence for predicted binding to HLA-A2 as well as numerous other HLA Class I molecules. Many

HLA class I binding peptides are 8-, 9-, 10 or 11-mers. For example, for Class I HLA-A2, the epitopes preferably contain a leucine (L) or methionine (M) at position 2 and a valine (V) or leucine (L) at the C-terminus (see, e.g., Parker et al., *J. Immunol.* 149:3580-7 (1992)). Selected results of STEAP-1 predicted binding peptides are shown in Tables V-XVIII and XXII-LI herein. In Tables V-XVIII and XXII-XLVII, selected candidates, 9-mers and 10-mers, for each family member are shown along with their location, the amino acid sequence of each specific peptide, and an estimated binding score. In Tables XLVIII-LI, selected candidates, 15-mers, for each family member are shown along with their location, the amino acid sequence of each specific peptide, and an estimated binding score. The binding score corresponds to the estimated half time of dissociation of complexes containing the peptide at 37° C. at pH 6.5. Peptides with the highest binding score are predicted to be the most tightly bound to HLA Class I on the cell surface for the greatest period of time and thus represent the best immunogenic targets for T-cell recognition.

[0250] Actual binding of peptides to an HLA allele can be evaluated by stabilization of HLA expression on the antigen-processing defective cell line T2 (see, e.g., Xue et al., *Prostate* 30:73-8 (1997) and Peshwa et al., *Prostate* 36:129-38 (1998)). Immunogenicity of specific peptides can be evaluated in vitro by stimulation of CD8+ cytotoxic T lymphocytes (CTL) in the presence of antigen presenting cells such as dendritic cells.

[0251] It is to be appreciated that every epitope predicted by the BIMAS site, Epimer™ and Epimatrix™ sites, or specified by the HLA class I or class II motifs available in the art or which become part of the art such as set forth in Table IV (or determined using World Wide Web site URL syfpeithi.bmi-heidelberg.com/, or BIMAS, bimas.dcrf.nih.gov/) are to be “applied” to a STEAP-1 protein in accordance with the invention. As used in this context “applied” means that a STEAP-1 protein is evaluated, e.g., visually or by computer-based patterns finding methods, as appreciated by those of skill in the relevant art. Every subsequence of a STEAP-1 protein of 8, 9, 10, or 11 amino acid residues that bears an HLA Class I motif, or a subsequence of 9 or more amino acid residues that bear an HLA Class II motif are within the scope of the invention.

[0252] III.B.) Expression of STEAP-1-Related Proteins

[0253] In an embodiment described in the examples that follow, STEAP-1 can be conveniently expressed in cells (such as 293T cells) transfected with a commercially available expression vector such as a CMV-driven expression vector encoding STEAP-1 with a C-terminal 6xHis and MYC tag (pcDNA3.1/mycHis, Invitrogen or Tag5, GenHunter Corporation, Nashville, Tenn.). The Tag5 vector provides an IgGK secretion signal that can be used to facilitate the production of a secreted STEAP-1 protein in transfected cells. The secreted HIS-tagged STEAP-1 in the culture media can be purified, e.g., using a nickel column using standard techniques.

[0254] III.C.) Modifications of STEAP-1-Related Proteins

[0255] Modifications of STEAP-1-related proteins such as covalent modifications are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a STEAP-1 polypeptide

with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C-terminal residues of a STEAP-1 protein. Another type of covalent modification of a STEAP-1 polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of a protein of the invention. Another type of covalent modification of STEAP-1 comprises linking a STEAP-1 polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol (PEG), polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Pat. No. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

[0256] The STEAP-1-related proteins of the present invention can also be modified to form a chimeric molecule comprising STEAP-1 fused to another, heterologous polypeptide or amino acid sequence. Such a chimeric molecule can be synthesized chemically or recombinantly. A chimeric molecule can have a protein of the invention fused to another tumor-associated antigen or fragment thereof. Alternatively, a protein in accordance with the invention can comprise a fusion of fragments of a STEAP-1 sequence (amino or nucleic acid) such that a molecule is created that is not, through its length, directly homologous to the amino or nucleic acid sequences shown in **FIG. 2** or **FIG. 3**. Such a chimeric molecule can comprise multiples of the same subsequence of STEAP-1. A chimeric molecule can comprise a fusion of a STEAP-1-related protein with a polyhistidine epitope tag, which provides an epitope to which immobilized nickel can selectively bind, with cytokines or with growth factors. The epitope tag is generally placed at the amino- or carboxyl-terminus of a STEAP-1 protein. In an alternative embodiment, the chimeric molecule can comprise a fusion of a STEAP-1-related protein with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule (also referred to as an “immunoadhesin”), such a fusion could be to the Fc region of an IgG molecule. The Ig fusions preferably include the substitution of a soluble (transmembrane domain deleted or inactivated) form of a STEAP-1 polypeptide in place of at least one variable region within an Ig molecule. In a preferred embodiment, the immunoglobulin fusion includes the hinge, CH2 and CH3, or the hinge, CH1, CH2 and CH3 regions of an IgG1 molecule. For the production of immunoglobulin fusions see, e.g., U.S. Pat. No. 5,428,130 issued Jun. 27, 1995.

[0257] III.D.) Uses of STEAP-1-Related Proteins

[0258] The proteins of the invention have a number of different specific uses. As STEAP-1 is highly expressed in prostate and other cancers, STEAP-1-related proteins are used in methods that assess the status of STEAP-1 gene products in normal versus cancerous tissues, thereby elucidating the malignant phenotype. Typically, polypeptides from specific regions of a STEAP-1 protein are used to assess the presence of perturbations (such as deletions, insertions, point mutations etc.) in those regions (such as regions containing one or more motifs). Exemplary assays utilize antibodies or T cells targeting STEAP-1-related proteins comprising the amino acid residues of one or more of the biological motifs contained within a STEAP-1 polypeptide sequence in order to evaluate the characteristics of this region in normal versus cancerous tissues or to elicit an immune response to the epitope. Alternatively, STEAP-1-related proteins that contain the amino acid residues of one

or more of the biological motifs in a STEAP-1 protein are used to screen for factors that interact with that region of STEAP-1.

[0259] STEAP-1 protein fragments/subsequences are particularly useful in generating and characterizing domain-specific antibodies (e.g., antibodies recognizing an extracellular or intracellular epitope of a STEAP-1 protein), for identifying agents or cellular factors that bind to STEAP-1 or a particular structural domain thereof, and in various therapeutic and diagnostic contexts, including but not limited to diagnostic assays, cancer vaccines and methods of preparing such vaccines.

[0260] Proteins encoded by the STEAP-1 genes, or by analogs, homologs or fragments thereof, have a variety of uses, including but not limited to generating antibodies and in methods for identifying ligands and other agents and cellular constituents that bind to a STEAP-1 gene product. Antibodies raised against a STEAP-1 protein or fragment thereof are useful in diagnostic and prognostic assays, and imaging methodologies in the management of human cancers characterized by expression of STEAP-1 protein, such as those listed in Table I. Such antibodies can be expressed intracellularly and used in methods of treating patients with such cancers. STEAP-1-related nucleic acids or proteins are also used in generating HTL or CTL responses.

[0261] Various immunological assays useful for the detection of STEAP-1 proteins are used, including but not limited to various types of radioimmunoassays, enzyme-linked immunosorbent assays (ELISA), enzyme-linked immunofluorescent assays (ELIFA), immunocytochemical methods, and the like. Antibodies can be labeled and used as immunological imaging reagents capable of detecting STEAP-1-expressing cells (e.g., in radioscintigraphic imaging methods). STEAP-1 proteins are also particularly useful in generating cancer vaccines, as further described herein.

[0262] IV.) STEAP-1 Antibodies

[0263] Another aspect of the invention provides antibodies that bind to STEAP-1-related proteins. Preferred antibodies specifically bind to a STEAP-1-related protein and do not bind (or bind weakly) to peptides or proteins that are not STEAP-1-related proteins. For example, antibodies that bind STEAP-1 can bind STEAP-1-related proteins such as the homologs or analogs thereof.

[0264] STEAP-1 antibodies of the invention are particularly useful in cancer (see, e.g., Table I) diagnostic and prognostic assays, and imaging methodologies. Similarly, such antibodies are useful in the treatment, diagnosis, and/or prognosis of other cancers, to the extent STEAP-1 is also expressed or overexpressed in these other cancers. Moreover, intracellularly expressed antibodies (e.g., single chain antibodies) are therapeutically useful in treating cancers in which the expression of STEAP-1 is involved, such as advanced or metastatic prostate cancers.

[0265] The invention also provides various immunological assays useful for the detection and quantification of STEAP-1 and mutant STEAP-1-related proteins. Such assays can comprise one or more STEAP-1 antibodies capable of recognizing and binding a STEAP-1-related protein, as appropriate. These assays are performed within various immunological assay formats well known in the art, including but not limited to various types of radioimmuno-

assays, enzyme-linked immunosorbent assays (ELISA), enzyme-linked immunofluorescent assays (ELIFA), and the like.

[0266] Immunological non-antibody assays of the invention also comprise T cell immunogenicity assays (inhibitory or stimulatory) as well as major histocompatibility complex (MHC) binding assays.

[0267] In addition, immunological imaging methods capable of detecting prostate cancer and other cancers expressing STEAP-1 are also provided by the invention, including but not limited to radioscintigraphic imaging methods using labeled STEAP-1 antibodies. Such assays are clinically useful in the detection, monitoring, and prognosis of STEAP-1 expressing cancers such as prostate cancer.

[0268] STEAP-1 antibodies are also used in methods for purifying a STEAP-1-related protein and for isolating STEAP-1 homologues and related molecules. For example, a method of purifying a STEAP-1-related protein comprises incubating a STEAP-1 antibody, which has been coupled to a solid matrix, with a lysate or other solution containing a STEAP-1-related protein under conditions that permit the STEAP-1 antibody to bind to the STEAP-1-related protein; washing the solid matrix to eliminate impurities; and eluting the STEAP-1-related protein from the coupled antibody. Other uses of STEAP-1 antibodies in accordance with the invention include generating anti-idiotypic antibodies that mimic a STEAP-1 protein.

[0269] Various methods for the preparation of antibodies are well known in the art. For example, antibodies can be prepared by immunizing a suitable mammalian host using a STEAP-1-related protein, peptide, or fragment, in isolated or immunoconjugated form (Antibodies: A Laboratory Manual, CSH Press, Eds., Harlow, and Lane (1988); Harlow, Antibodies, Cold Spring Harbor Press, NY (1989)). In addition, fusion proteins of STEAP-1 can also be used, such as a STEAP-1 GST-fusion protein. In a particular embodiment, a GST fusion protein comprising all or most of the amino acid sequence of FIG. 2 or FIG. 3 is produced, then used as an immunogen to generate appropriate antibodies. In another embodiment, a STEAP-1-related protein is synthesized and used as an immunogen.

[0270] In addition, naked DNA immunization techniques known in the art are used (with or without purified STEAP-1-related protein or STEAP-1 expressing cells) to generate an immune response to the encoded immunogen (for review, see Donnelly et al., 1997, Ann. Rev. Immunol. 15: 617-648).

[0271] The amino acid sequence of a STEAP-1 protein as shown in FIG. 2 or FIG. 3 can be analyzed to select specific regions of the STEAP-1 protein for generating antibodies. For example, hydrophobicity and hydrophilicity analyses of a STEAP-1 amino acid sequence are used to identify hydrophilic regions in the STEAP-1 structure. Regions of a STEAP-1 protein that show immunogenic structure, as well as other regions and domains, can readily be identified using various other methods known in the art, such as Chou-Fasman, Garnier-Robson, Kyte-Doolittle, Eisenberg, Karplus-Schultz or Jameson-Wolf analysis. Hydrophilicity profiles can be generated using the method of Hopp, T. P. and Woods, K. R., 1981, Proc. Natl. Acad. Sci. U.S.A. 78:3824-3828. Hydrophobicity profiles can be generated using the method of Kyte, J. and Doolittle, R. F., 1982, J. Mol. Biol.

157:105-132. Percent (%) Accessible Residues profiles can be generated using the method of Janin J., 1979, *Nature* 277:491-A92. Average Flexibility profiles can be generated using the method of Bhaskaran R., Ponnuswamy P. K., 1988, *Int. J. Pept. Protein Res.* 32:242-255. Beta-turn profiles can be generated using the method of Deleage, G., Roux B., 1987, *Protein Engineering* 1:289-294. Thus, each region identified by any of these programs or methods is within the scope of the present invention. Methods for the generation of STEAP-1 antibodies are further illustrated by way of the examples provided herein. Methods for preparing a protein or polypeptide for use as an immunogen are well known in the art. Also well known in the art are methods for preparing immunogenic conjugates of a protein with a carrier, such as BSA, KLH or other carrier protein. In some circumstances, direct conjugation using, for example, carbodiimide reagents are used; in other instances linking reagents such as those supplied by Pierce Chemical Co., Rockford, Ill., are effective. Administration of a STEAP-1 immunogen is often conducted by injection over a suitable time period and with use of a suitable adjuvant, as is understood in the art. During the immunization schedule, titers of antibodies can be taken to determine adequacy of antibody formation.

[0272] STEAP-1 monoclonal antibodies can be produced by various means well known in the art. For example, immortalized cell lines that secrete a desired monoclonal antibody are prepared using the standard hybridoma technology of Kohler and Milstein or modifications that immortalize antibody-producing B cells, as is generally known. Immortalized cell lines that secrete the desired antibodies are screened by immunoassay in which the antigen is a STEAP-1-related protein. When the appropriate immortalized cell culture is identified, the cells can be expanded and antibodies produced either from *in vitro* cultures or from ascites fluid.

[0273] The antibodies or fragments of the invention can also be produced, by recombinant means. Regions that bind specifically to the desired regions of a STEAP-1 protein can also be produced in the context of chimeric or complementarity-determining region (CDR) grafted antibodies of multiple species origin. Humanized or human STEAP-1 antibodies can also be produced, and are preferred for use in therapeutic contexts. Methods for humanizing murine and other non-human antibodies, by substituting one or more of the non-human antibody CDRs for corresponding human antibody sequences, are well known (see for example, Jones et al., 1986, *Nature* 321: 522-525; Riechmann et al., 1988, *Nature* 332: 323-327; Verhoeyen et al., 1988, *Science* 239: 1534-1536). See also, Carter et al., 1993, *Proc. Natl. Acad. Sci. USA* 89: 4285 and Sims et al., 1993, *J. Immunol.* 151: 2296.

[0274] Methods for producing fully human monoclonal antibodies include phage display and transgenic methods (for review, see Vaughan et al., 1998, *Nature Biotechnology* 16: 535-539). Fully human STEAP-1 monoclonal antibodies can be generated using cloning technologies employing large human Ig gene combinatorial libraries (i.e., phage display) (Griffiths and Hoogenboom, Building an *in vitro* immune system: human antibodies from phage display libraries. In: *Protein Engineering of Antibody Molecules for Prophylactic and Therapeutic Applications in Man*, Clark, M. (Ed.), Nottingham Academic, pp 45-64 (1993); Burton and Barbas, *Human Antibodies from combinatorial libraries*.

Id., pp 65-82). Fully human STEAP-1 monoclonal antibodies can also be produced using transgenic mice engineered to contain human immunoglobulin gene loci as described in PCT Patent Application WO98/24893, Kucherlapati and Jakobovits et al., published Dec. 3, 1997 (see also, Jakobovits, 1998, *Exp. Opin. Invest. Drugs* 7(4): 607-614; U.S. Pat. No. 6,162,963 issued 19 Dec. 2000; U.S. Pat. No. 6,150,584 issued 12 Nov. 2000; and, U.S. Pat. No. 6,114,598 issued 5 Sep. 2000). This method avoids the *in vitro* manipulation required with phage display technology and efficiently produces high affinity authentic human antibodies.

[0275] Reactivity of STEAP-1 antibodies with a STEAP-1-related protein can be established by a number of well known means, including Western blot, immunoprecipitation, ELISA, and FACS analyses using, as appropriate, STEAP-1-related proteins, STEAP-1-expressing cells or extracts thereof. A STEAP-1 antibody or fragment thereof can be labeled with a detectable marker or conjugated to a second molecule. Suitable detectable markers include, but are not limited to, a radioisotope, a fluorescent compound, a bioluminescent compound, chemiluminescent compound, a metal chelator or an enzyme. Further, bi-specific antibodies specific for two or more STEAP-1 epitopes are generated using methods generally known in the art. Homodimeric antibodies can also be generated by cross-linking techniques known in the art (e.g., Wolff et al., *Cancer Res.* 53: 2560-2565).

[0276] V. STEAP-1 Cellular Immune Responses

[0277] The mechanism by which T cells recognize antigens has been delineated. Efficacious peptide epitope vaccine compositions of the invention induce a therapeutic or prophylactic immune responses in very broad segments of the world-wide population. For an understanding of the value and efficacy of compositions of the invention that induce cellular immune responses, a brief review of immunology-related technology is provided.

[0278] A complex of an HLA molecule and a peptidic antigen acts as the ligand recognized by HLA-restricted T cells (Buus, S. et al., *Cell* 47:1071, 1986; Babbitt, B. P. et al., *Nature* 317:359, 1985; Townsend, A. and Bodmer, H., *Annu. Rev. Immunol.* 7:601, 1989; Germain, R. N., *Annu. Rev. Immunol.* 11:403, 1993). Through the study of single amino acid substituted antigen analogs and the sequencing of endogenously bound, naturally processed peptides, critical residues that correspond to motifs required for specific binding to HLA antigen molecules have been identified and are set forth in Table IV (see also, e.g., Southwood, et al., *J. Immunol.* 160:3363, 1998; Rammensee, et al., *Immunogenetics* 41:178, 1995; Rammensee et al, SYFPEITHI, access via World Wide Web at URL syfpeithi.bmi-heidelberg.com/; Sette, A. and Sidney, J. *Curr. Opin. Immunol.* 10:478, 1998; Engelhard, V. H., *Curr. Opin. Immunol.* 6:13, 1994; Sette, A. and Grey, H. M., *Curr. Opin. Immunol.* 4:79, 1992; Sinigaglia, F. and Hammer, J. *Curr. Biol.* 6:52, 1994; Ruppert et al., *Cell* 74:929-937, 1993; Kondo et al, *J. Immunol.* 155:4307-4312, 1995; Sidney et al., *J. Immunol.* 157:3480-3490, 1996; Sidney et al., *Human Immunol.* 45:79-93, 1996; Sette, A. and Sidney, *J. Immunogenetics* 1999 November; 50(3-4):201-12, Review).

[0279] Furthermore, x-ray crystallographic analyses of HLA-peptide complexes have revealed pockets within the peptide binding cleft/groove of HLA molecules which accommodate, in an allele-specific mode, residues borne by

peptide ligands; these residues in turn determine the HLA binding capacity of the peptides in which they are present. (See, e.g., Madden, D. R. *Annu. Rev. Immunol.* 13:587, 1995; Smith, et al., *Immunity* 4:203, 1996; Fremont et al., *Immunity* 8:305, 1998; Stern et al., *Structure* 2:245, 1994; Jones, E. Y. *Curr. Opin. Immunol.* 9:75, 1997; Brown, J. H. et al., *Nature* 364:33, 1993; Guo, H. C. et al., *Proc. Natl. Acad. Sci. USA* 90:8053, 1993; Guo, H. C. et al., *Nature* 360:364, 1992; Silver, M. L. et al., *Nature* 360:367, 1992; Matsumura, M. et al., *Science* 257:927, 1992; Madden et al., *Cell* 70:1035, 1992; Fremont, D. H. et al., *Science* 257:919, 1992; Saper, M. A., Bjorkman, P. J. and Wiley, D. C., *J. Mol. Biol.* 219:277, 1991.)

[0280] Accordingly, the definition of class I and class II allele-specific HLA binding motifs, or class I or class II supermotifs allows identification of regions within a protein that are correlated with binding to particular HLA antigen(s).

[0281] Thus, by a process of HLA motif identification, candidates for epitope-based vaccines have been identified; such candidates can be further evaluated by HLA-peptide binding assays to determine binding affinity and/or the time period of association of the epitope and its corresponding HLA molecule. Additional confirmatory work can be performed to select, amongst these vaccine candidates, epitopes with preferred characteristics in terms of population coverage, and/or immunogenicity.

[0282] Various strategies can be utilized to evaluate cellular immunogenicity, including:

[0283] 1) Evaluation of primary T cell cultures from normal individuals (see, e.g., Wentworth, P. A. et al., *Mol. Immunol.* 32:603, 1995; Celis, E. et al., *Proc. Natl. Acad. Sci. USA* 91:2105, 1994; Tsai, V. et al., *J. Immunol.* 158:1796, 1997; Kawashima, I. et al., *Human Immunol.* 59:1, 1998). This procedure involves the stimulation of peripheral blood lymphocytes (PBL) from normal subjects with a test peptide in the presence of antigen presenting cells in vitro over a period of several weeks. T cells specific for the peptide become activated during this time and are detected using, e.g., a lymphokine- or ⁵¹Cr-release assay involving peptide sensitized target cells.

[0284] 2) Immunization of HLA transgenic mice (see, e.g., Wentworth, P. A. et al., *J. Immunol.* 26:97, 1996; Wentworth, P. A. et al., *Int. Immunol.* 8:651, 1996; Alexander, J. et al., *J. Immunol.* 159:4753, 1997). For example, in such methods peptides in incomplete Freund's adjuvant are administered subcutaneously to HLA transgenic mice. Several weeks following immunization, splenocytes are removed and cultured in vitro in the presence of test peptide for approximately one week. Peptide-specific T cells are detected using, e.g., a ⁵¹Cr-release assay involving peptide sensitized target cells and target cells expressing endogenously generated antigen.

[0285] 3) Demonstration of recall T cell responses from immune individuals who have been either effectively vaccinated and/or from chronically ill patients (see, e.g., Rehermann, B. et al., *J. Exp. Med.* 181:1047, 1995; Doolan, D. L. et al., *Immunity* 7:97, 1997; Berton, R. et al., *J. Clin. Invest.* 100:503, 1997; Threlkeld, S. C. et al., *J. Immunol.* 159:1648, 1997; Diepolder, H. M. et al., *J. Virol.* 71:6011, 1997). Accordingly, recall responses are detected by culturing PBL from subjects that have been exposed to the antigen due to

disease and thus have generated an immune response "naturally", or from patients who were vaccinated against the antigen. PBL from subjects are cultured in vitro for 1-2 weeks in the presence of test peptide plus antigen presenting cells (APC) to allow activation of "memory" T cells, as compared to "naive" T cells. At the end of the culture period, T cell activity is detected using assays including ⁵¹Cr release involving peptide-sensitized targets, T cell proliferation, or lymphokine release.

[0286] VI.) STEAP-1 Transgenic Animals

[0287] Nucleic acids that encode a STEAP-1-related protein can also be used to generate either transgenic animals or "knock out" animals that, in turn, are useful in the development and screening of therapeutically useful reagents. In accordance with established techniques, cDNA encoding STEAP-1 can be used to clone genomic DNA that encodes STEAP-1. The cloned genomic sequences can then be used to generate transgenic animals containing cells that express DNA that encode STEAP-1. Methods for generating transgenic animals, particularly animals such as mice or rats, have become conventional in the art and are described, for example, in U.S. Pat. No. 4,736,866 issued 12 Apr. 1988, and U.S. Pat. No. 4,870,009 issued 26 Sep. 1989. Typically, particular cells would be targeted for STEAP-1 transgene incorporation with tissue-specific enhancers.

[0288] Transgenic animals that include a copy of a transgene encoding STEAP-1 can be used to examine the effect of increased expression of DNA that encodes STEAP-1. Such animals can be used as tester animals for reagents thought to confer protection from, for example, pathological conditions associated with its overexpression. In accordance with this aspect of the invention, an animal is treated with a reagent and a reduced incidence of a pathological condition, compared to untreated animals that bear the transgene, would indicate a potential therapeutic intervention for the pathological condition.

[0289] Alternatively, non-human homologues of STEAP-1 can be used to construct a STEAP-1 "knock out" animal that has a defective or altered gene encoding STEAP-1 as a result of homologous recombination between the endogenous gene encoding STEAP-1 and altered genomic DNA encoding STEAP-1 introduced into an embryonic cell of the animal. For example, cDNA that encodes STEAP-1 can be used to clone genomic DNA encoding STEAP-1 in accordance with established techniques. A portion of the genomic DNA encoding STEAP-1 can be deleted or replaced with another gene, such as a gene encoding a selectable marker that can be used to monitor integration. Typically, several kilobases of unaltered flanking DNA (both at the 5' and 3' ends) are included in the vector (see, e.g., Thomas and Capecchi, *Cell*, 51:503 (1987) for a description of homologous recombination vectors). The vector is introduced into an embryonic stem cell line (e.g., by electroporation) and cells in which the introduced DNA has homologously recombined with the endogenous DNA are selected (see, e.g., Li et al., *Cell*, 69:915 (1992)). The selected cells are then injected into a blastocyst of an animal (e.g., a mouse or rat) to form aggregation chimeras (see, e.g., Bradley, in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, E. J. Robertson, ed. (IRL, Oxford, 1987), pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster

animal, and the embryo brought to term to create a “knock out” animal. Progeny harboring the homologously recombined DNA in their germ cells can be identified by standard techniques and used to breed animals in which all cells of the animal contain the homologously recombined DNA. Knock out animals can be characterized, for example, for their ability to defend against certain pathological conditions or for their development of pathological conditions due to absence of a STEAP-1 polypeptide.

[0290] VII.) Methods for the Detection of STEAP-1

[0291] Another aspect of the present invention relates to methods for detecting STEAP-1 polynucleotides and STEAP-1-related proteins, as well as methods for identifying a cell that expresses STEAP-1. The expression profile of STEAP-1 makes it a diagnostic marker for metastasized disease. Accordingly, the status of STEAP-1 gene products provides information useful for predicting a variety of factors including susceptibility to advanced stage disease, rate of progression, and/or tumor aggressiveness. As discussed in detail herein, the status of STEAP-1 gene products in patient samples can be analyzed by a variety of protocols that are well known in the art including immunohistochemical analysis, the variety of Northern blotting techniques including in situ hybridization, RT-PCR analysis (for example on laser capture micro-dissected samples), Western blot analysis and tissue array analysis.

[0292] More particularly, the invention provides assays for the detection of STEAP-1 polynucleotides in a biological sample, such as serum, bone, prostate, and other tissues, urine, semen, cell preparations, and the like. Detectable STEAP-1 polynucleotides include, for example, a STEAP-1 gene or fragment thereof, STEAP-1 mRNA, alternative splice variant STEAP-1 mRNAs, and recombinant DNA or RNA molecules that contain a STEAP-1 polynucleotide. A number of methods for amplifying and/or detecting the presence of STEAP-1 polynucleotides are well known in the art and can be employed in the practice of this aspect of the invention.

[0293] In one embodiment, a method for detecting a STEAP-1 mRNA in a biological sample comprises producing cDNA from the sample by reverse transcription using at least one primer; amplifying the cDNA so produced using a STEAP-1 polynucleotides as sense and antisense primers to amplify STEAP-1 cDNAs therein; and detecting the presence of the amplified STEAP-1 cDNA. Optionally, the sequence of the amplified STEAP-1 cDNA can be determined.

[0294] In another embodiment, a method of detecting a STEAP-1 gene in a biological sample comprises first isolating genomic DNA from the sample; amplifying the isolated genomic DNA using STEAP-1 polynucleotides as sense and antisense primers; and detecting the presence of the amplified STEAP-1 gene. Any number of appropriate sense and antisense probe combinations can be designed from a STEAP-1 nucleotide sequence (see, e.g., **FIG. 2**) and used for this purpose.

[0295] The invention also provides assays for detecting the presence of a STEAP-1 protein in a tissue or other biological sample such as serum, semen, bone, prostate, urine, cell preparations, and the like. Methods for detecting a STEAP-1-related protein are also well known and include,

for example, immunoprecipitation, immunohistochemical analysis, Western blot analysis, molecular binding assays, ELISA, ELIFA and the like. For example, a method of detecting the presence of a STEAP-1-related protein in a biological sample comprises first contacting the sample with a STEAP-1 antibody, a STEAP-1-reactive fragment thereof, or a recombinant protein containing an antigen-binding region of a STEAP-1 antibody; and then detecting the binding of STEAP-1-related protein in the sample.

[0296] Methods for identifying a cell that expresses STEAP-1 are also within the scope of the invention. In one embodiment, an assay for identifying a cell that expresses a STEAP-1 gene comprises detecting the presence of STEAP-1 mRNA in the cell. Methods for the detection of particular mRNAs in cells are well known and include, for example, hybridization assays using complementary DNA probes (such as in situ hybridization using labeled STEAP-1 riboprobes, Northern blot and related techniques) and various nucleic acid amplification assays (such as RT-PCR using complementary primers specific for STEAP-1, and other amplification type detection methods, such as, for example, branched DNA, SISBA, TMA and the like). Alternatively, an assay for identifying a cell that expresses a STEAP-1 gene comprises detecting the presence of STEAP-1-related protein in the cell or secreted by the cell. Various methods for the detection of proteins are well known in the art and are employed for the detection of STEAP-1-related proteins and cells that express STEAP-1-related proteins.

[0297] STEAP-1 expression analysis is also useful as a tool for identifying and evaluating agents that modulate STEAP-1 gene expression. For example, STEAP-1 expression is significantly upregulated in prostate cancer, and is expressed in cancers of the tissues listed in Table I. Identification of a molecule or biological agent that inhibits STEAP-1 expression or over-expression in cancer cells is of therapeutic value. For example, such an agent can be identified by using a screen that quantifies STEAP-1 expression by RT-PCR, nucleic acid hybridization or antibody binding.

[0298] VIII.) Methods for Monitoring the Status of STEAP-1-Related Genes and Their Products

[0299] Oncogenesis is known to be a multistep process where cellular growth becomes progressively dysregulated and cells progress from a normal physiological state to precancerous and then cancerous states (see, e.g., Alers et al., *Lab Invest.* 77(5): 437-438 (1997) and Isaacs et al., *Cancer Surv.* 23: 19-32 (1995)). In this context, examining a biological sample for evidence of dysregulated cell growth (such as aberrant STEAP-1 expression in cancers) allows for early detection of such aberrant physiology, before a pathologic state such as cancer has progressed to a stage that therapeutic options are more limited and/or the prognosis is worse. In such examinations, the status of STEAP-1 in a biological sample of interest can be compared, for example, to the status of STEAP-1 in a corresponding normal sample (e.g. a sample from that individual or alternatively another individual that is not affected by a pathology). An alteration in the status of STEAP-1 in the biological sample (as compared to the normal sample) provides evidence of dysregulated cellular growth. In addition to using a biological sample that is not affected by a pathology as a normal sample, one can also use a predetermined normative value such as a predetermined normal level of mRNA expression

(see, e.g., Grever et al., J. Comp. Neurol. 1996 Dec. 9; 376(2): 306-14 and U.S. Pat. No. 5,837,501) to compare STEAP-1 status in a sample.

[0300] The term "status" in this context is used according to its art accepted meaning and refers to the condition or state of a gene and its products. Typically, skilled artisans use a number of parameters to evaluate the condition or state of a gene and its products. These include, but are not limited to the location of expressed gene products (including the location of STEAP-1 expressing cells) as well as the level, and biological activity of expressed gene products (such as STEAP-1 mRNA, polynucleotides and polypeptides). Typically, an alteration in the status of STEAP-1 comprises a change in the location of STEAP-1 and/or STEAP-1 expressing cells and/or an increase in STEAP-1 mRNA and/or protein expression.

[0301] STEAP-1 status in a sample can be analyzed by a number of means well known in the art, including without limitation, immunohistochemical analysis, in situ hybridization, RT-PCR analysis on laser capture micro-dissected samples, Western blot analysis, and tissue array analysis. Typical protocols for evaluating the status of a STEAP-1 gene and gene products are found, for example in Ausubel et al. eds., 1995, Current Protocols In Molecular Biology, Units 2 (Northern Blotting), 4 (Southern Blotting), 15 (Immunoblotting) and 18 (PCR Analysis). Thus, the status of STEAP-1 in a biological sample is evaluated by various methods utilized by skilled artisans including, but not limited to genomic Southern analysis (to examine, for example perturbations in a STEAP-1 gene), Northern analysis and/or PCR analysis of STEAP-1 mRNA (to examine, for example alterations in the polynucleotide sequences or expression levels of STEAP-1 mRNAs), and, Western and/or immunohistochemical analysis (to examine, for example alterations in polypeptide sequences, alterations in polypeptide localization within a sample, alterations in expression levels of STEAP-1 proteins and/or associations of STEAP-1 proteins with polypeptide binding partners). Detectable STEAP-1 polynucleotides include, for example, a STEAP-1 gene or fragment thereof, STEAP-1 mRNA, alternative splice variants, STEAP-1 mRNAs, and recombinant DNA or RNA molecules containing a STEAP-1 polynucleotide.

[0302] The expression profile of STEAP-1 makes it a diagnostic marker for local and/or metastasized disease, and provides information on the growth or oncogenic potential of a biological sample. In particular, the status of STEAP-1 provides information useful for predicting susceptibility to particular disease stages, progression, and/or tumor aggressiveness. The invention provides methods and assays for determining STEAP-1 status and diagnosing cancers that express STEAP-1, such as cancers of the tissues listed in Table I. For example, because STEAP-1 mRNA is so highly expressed in prostate and other cancers relative to normal prostate tissue, assays that evaluate the levels of STEAP-1 mRNA transcripts or proteins in a biological sample can be used to diagnose a disease associated with STEAP-1 dysregulation, and can provide prognostic information useful in defining appropriate therapeutic options.

[0303] The expression status of STEAP-1 provides information including the presence, stage and location of dysplastic, precancerous and cancerous cells, predicting susceptibility to various stages of disease, and/or for gauging

tumor aggressiveness. Moreover, the expression profile makes it useful as an imaging reagent for metastasized disease. Consequently, an aspect of the invention is directed to the various molecular prognostic and diagnostic methods for examining the status of STEAP-1 in biological samples such as those from individuals suffering from, or suspected of suffering from a pathology characterized by dysregulated cellular growth, such as cancer.

[0304] As described above, the status of STEAP-1 in a biological sample can be examined by a number of well-known procedures in the art. For example, the status of STEAP-1 in a biological sample taken from a specific location in the body can be examined by evaluating the sample for the presence or absence of STEAP-1 expressing cells (e.g. those that express STEAP-1 mRNAs or proteins). This examination can provide evidence of dysregulated cellular growth, for example, when STEAP-1-expressing cells are found in a biological sample that does not normally contain such cells (such as a lymph node), because such alterations in the status of STEAP-1 in a biological sample are often associated with dysregulated cellular growth. Specifically, one indicator of dysregulated cellular growth is the metastases of cancer cells from an organ of origin (such as the prostate) to a different area of the body (such as a lymph node). In this context, evidence of dysregulated cellular growth is important for example because occult lymph node metastases can be detected in a substantial proportion of patients with prostate cancer, and such metastases are associated with known predictors of disease progression (see, e.g., Murphy et al., Prostate 42(4): 315-317 (2000); Su et al., Semin. Surg. Oncol. 18(1): 17-28 (2000) and Freeman et al., J. Urol 1995 August 154(2 Pt 1):474-8).

[0305] In one aspect, the invention provides methods for monitoring STEAP-1 gene products by determining the status of STEAP-1 gene products expressed by cells from an individual suspected of having a disease associated with dysregulated cell growth (such as hyperplasia or cancer) and then comparing the status so determined to the status of STEAP-1 gene products in a corresponding normal sample. The presence of aberrant STEAP-1 gene products in the test sample relative to the normal sample provides an indication of the presence of dysregulated cell growth within the cells of the individual.

[0306] In another aspect, the invention provides assays useful in determining the presence of cancer in an individual, comprising detecting a significant increase in STEAP-1 mRNA or protein expression in a test cell or tissue sample relative to expression levels in the corresponding normal cell or tissue. The presence of STEAP-1 mRNA can, for example, be evaluated in tissues including but not limited to those listed in Table I. The presence of significant STEAP-1 expression in any of these tissues is useful to indicate the emergence, presence and/or severity of a cancer, since the corresponding normal tissues do not express STEAP-1 mRNA or express it at lower levels.

[0307] In a related embodiment, STEAP-1 status is determined at the protein level rather than at the nucleic acid level. For example, such a method comprises determining the level of STEAP-1 protein expressed by cells in a test tissue sample and comparing the level so determined to the level of STEAP-1 expressed in a corresponding normal sample. In one embodiment, the presence of STEAP-1

protein is evaluated, for example, using immunohistochemical methods. STEAP-1 antibodies or binding partners capable of detecting STEAP-1 protein expression are used in a variety of assay formats well known in the art for this purpose.

[0308] In a further embodiment, one can evaluate the status of STEAP-1 nucleotide and amino acid sequences in a biological sample in order to identify perturbations in the structure of these molecules. These perturbations can include insertions, deletions, substitutions and the like. Such evaluations are useful because perturbations in the nucleotide and amino acid sequences are observed in a large number of proteins associated with a growth dysregulated phenotype (see, e.g., Marrogi et al., 1999, *J. Cutan. Pathol.* 26(8):369-378). For example, a mutation in the sequence of STEAP-1 may be indicative of the presence or promotion of a tumor. Such assays therefore have diagnostic and predictive value where a mutation in STEAP-1 indicates a potential loss of function or increase in tumor growth.

[0309] A wide variety of assays for observing perturbations in nucleotide and amino acid sequences are well known in the art. For example, the size and structure of nucleic acid or amino acid sequences of STEAP-1 gene products are observed by the Northern, Southern, Western, PCR and DNA sequencing protocols discussed herein. In addition, other methods for observing perturbations in nucleotide and amino acid sequences such as single strand conformation polymorphism analysis are well known in the art (see, e.g., U.S. Pat. No. 5,382,510 issued 7 Sep. 1999, and U.S. Pat. No. 5,952,170 issued 17 Jan. 1995).

[0310] Additionally, one can examine the methylation status of a STEAP-1 gene in a biological sample. Aberrant demethylation and/or hypermethylation of CpG islands in gene 5' regulatory regions frequently occurs in immortalized and transformed cells, and can result in altered expression of various genes. For example, promoter hypermethylation of the pi-class glutathione S-transferase (a protein expressed in normal prostate but not expressed in >90% of prostate carcinomas) appears to permanently silence transcription of this gene and is the most frequently detected genomic alteration in prostate carcinomas (De Marzo et al., *Am. J. Pathol.* 155(6): 1985-1992 (1999)). In addition, this alteration is present in at least 70% of cases of high-grade prostatic intraepithelial neoplasia (PIN) (Brooks et al., *Cancer Epidemiol. Biomarkers Prev.*, 1998, 7:531-536). In another example, expression of the LAGE-1 tumor specific gene (which is not expressed in normal prostate but is expressed in 25-50% of prostate cancers) is induced by deoxy-azacytidine in lymphoblastoid cells, suggesting that tumoral expression is due to demethylation (Lethe et al., *Int. J. Cancer* 76(6): 903-908 (1998)). A variety of assays for examining methylation status of a gene are well known in the art. For example, one can utilize, in Southern hybridization approaches, methylation-sensitive restriction enzymes that cannot cleave sequences that contain methylated CpG sites to assess the methylation status of CpG islands. In addition, MSP (methylation specific PCR) can rapidly profile the methylation status of all the CpG sites present in a CpG island of a given gene. This procedure involves initial modification of DNA by sodium bisulfite (which will convert all unmethylated cytosines to uracil) followed by amplification using primers specific for methylated versus unmethylated DNA. Protocols involving methy-

lation interference can also be found for example in *Current Protocols In Molecular Biology*, Unit 12, Frederick M. Ausubel et al. eds., 1995.

[0311] Gene amplification is an additional method for assessing the status of STEAP-1. Gene amplification is measured in a sample directly, for example, by conventional Southern blotting or Northern blotting to quantitate the transcription of mRNA (Thomas, 1980, *Proc. Natl. Acad. Sci. USA*, 77:5201-5205), dot blotting (DNA analysis), or in situ hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies are employed that recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. The antibodies in turn are labeled and the assay carried out where the duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound to the duplex can be detected.

[0312] Biopsied tissue or peripheral blood can be conveniently assayed for the presence of cancer cells using for example, Northern, dot blot or RT-PCR analysis to detect STEAP-1 expression. The presence of RT-PCR amplifiable STEAP-1 mRNA provides an indication of the presence of cancer. RT-PCR assays are well known in the art. RT-PCR detection assays for tumor cells in peripheral blood are currently being evaluated for use in the diagnosis and management of a number of human solid tumors. In the prostate cancer field, these include RT-PCR assays for the detection of cells expressing PSA and PSM (Verkaik et al., 1997, *Urol. Res.* 25:373-384; Ghossein et al., 1995, *J. Clin. Oncol.* 13:1195-2000; Heston et al., 1995, *Clin. Chem.* 41:1687-1688).

[0313] A further aspect of the invention is an assessment of the susceptibility that an individual has for developing cancer. In one embodiment, a method for predicting susceptibility to cancer comprises detecting STEAP-1 mRNA or STEAP-1 protein in a tissue sample, its presence indicating susceptibility to cancer, wherein the degree of STEAP-1 mRNA expression correlates to the degree of susceptibility. In a specific embodiment, the presence of STEAP-1 in prostate or other tissue is examined, with the presence of STEAP-1 in the sample providing an indication of prostate cancer susceptibility (or the emergence or existence of a prostate tumor). Similarly, one can evaluate the integrity STEAP-1 nucleotide and amino acid sequences in a biological sample, in order to identify perturbations in the structure of these molecules such as insertions, deletions, substitutions and the like. The presence of one or more perturbations in STEAP-1 gene products in the sample is an indication of cancer susceptibility (or the emergence or existence of a tumor).

[0314] The invention also comprises methods for gauging tumor aggressiveness. In one embodiment, a method for gauging aggressiveness of a tumor comprises determining the level of STEAP-1 mRNA or STEAP-1 protein expressed by tumor cells, comparing the level so determined to the level of STEAP-1 mRNA or STEAP-1 protein expressed in a corresponding normal tissue taken from the same individual or a normal tissue reference sample, wherein the degree of STEAP-1 mRNA or STEAP-1 protein expression in the tumor sample relative to the normal sample indicates the degree of aggressiveness. In a specific embodiment,

aggressiveness of a tumor is evaluated by determining the extent to which STEAP-1 is expressed in the tumor cells, with higher expression levels indicating more aggressive tumors. Another embodiment is the evaluation of the integrity of STEAP-1 nucleotide and amino acid sequences in a biological sample, in order to identify perturbations in the structure of these molecules such as insertions, deletions, substitutions and the like. The presence of one or more perturbations indicates more aggressive tumors.

[0315] Another embodiment of the invention is directed to methods for observing the progression of a malignancy in an individual over time. In one embodiment, methods for observing the progression of a malignancy in an individual over time comprise determining the level of STEAP-1 mRNA or STEAP-1 protein expressed by cells in a sample of the tumor, comparing the level so determined to the level of STEAP-1 mRNA or STEAP-1 protein expressed in an equivalent tissue sample taken from the same individual at a different time, wherein the degree of STEAP-1 mRNA or STEAP-1 protein expression in the tumor sample over time provides information on the progression of the cancer. In a specific embodiment, the progression of a cancer is evaluated by determining STEAP-1 expression in the tumor cells over time, where increased expression over time indicates a progression of the cancer. Also, one can evaluate the integrity STEAP-1 nucleotide and amino acid sequences in a biological sample in order to identify perturbations in the structure of these molecules such as insertions, deletions, substitutions and the like, where the presence of one or more perturbations indicates a progression of the cancer.

[0316] The above diagnostic approaches can be combined with any one of a wide variety of prognostic and diagnostic protocols known in the art. For example, another embodiment of the invention is directed to methods for observing a coincidence between the expression of STEAP-1 gene and STEAP-1 gene products (or perturbations in STEAP-1 gene and STEAP-1 gene products) and a factor that is associated with malignancy, as a means for diagnosing and prognosticating the status of a tissue sample. A wide variety of factors associated with malignancy can be utilized, such as the expression of genes associated with malignancy (e.g. PSA, PSCA and PSM expression for prostate cancer etc.) as well as gross cytological observations (see, e.g., Bocking et al., 1984, *Anal. Quant. Cytol.* 6(2):74-88; Epstein, 1995, *Hum. Pathol.* 26(2):223-9; Thorson et al., 1998, *Mod. Pathol.* 11(6):543-51; Baisden et al., 1999, *Am. J. Surg. Pathol.* 23(8):918-24). Methods for observing a coincidence between the expression of STEAP-1 gene and STEAP-1 gene products (or perturbations in STEAP-1 gene and STEAP-1 gene products) and another factor that is associated with malignancy are useful, for example, because the presence of a set of specific factors that coincide with disease provides information crucial for diagnosing and prognosticating the status of a tissue sample.

[0317] In one embodiment, methods for observing a coincidence between the expression of STEAP-1 gene and STEAP-1 gene products (or perturbations in STEAP-1 gene and STEAP-1 gene products) and another factor associated with malignancy entails detecting the overexpression of STEAP-1 mRNA or protein in a tissue sample, detecting the overexpression of PSA mRNA or protein in a tissue sample (or PSCA or PSM expression), and observing a coincidence of STEAP-1 mRNA or protein and PSA mRNA or protein

overexpression (or PSCA or PSM expression). In a specific embodiment, the expression of STEAP-1 and PSA mRNA in prostate tissue is examined, where the coincidence of STEAP-1 and PSA mRNA overexpression in the sample indicates the existence of prostate cancer, prostate cancer susceptibility or the emergence or status of a prostate tumor.

[0318] Methods for detecting and quantifying the expression of STEAP-1 mRNA or protein are described herein, and standard nucleic acid and protein detection and quantification technologies are well known in the art. Standard methods for the detection and quantification of STEAP-1 mRNA include *in situ* hybridization using labeled STEAP-1 riboprobes, Northern blot and related techniques using STEAP-1 polynucleotide probes, RT-PCR analysis using primers specific for STEAP-1, and other amplification type detection methods, such as, for example, branched DNA, SISBA, TMA and the like. In a specific embodiment, semi-quantitative RT-PCR is used to detect and quantify STEAP-1 mRNA expression. Any number of primers capable of amplifying STEAP-1 can be used for this purpose, including but not limited to the various primer sets specifically described herein. In a specific embodiment, polyclonal or monoclonal antibodies specifically reactive with the wild-type STEAP-1 protein can be used in an immunohistochemical assay of biopsied tissue.

[0319] IX.) Identification of Molecules that Interact with STEAP-1

[0320] The STEAP-1 protein and nucleic acid sequences disclosed herein allow a skilled artisan to identify proteins, small molecules and other agents that interact with STEAP-1, as well as pathways activated by STEAP-1 via any one of a variety of art accepted protocols. For example, one can utilize one of the so-called interaction trap systems (also referred to as the "two-hybrid assay"). In such systems, molecules interact and reconstitute a transcription factor which directs expression of a reporter gene, whereupon the expression of the reporter gene is assayed. Other systems identify protein-protein interactions *in vivo* through reconstitution of a eukaryotic transcriptional activator, see, e.g., U.S. Pat. No. 5,955,280 issued 21 Sep. 1999, U.S. Pat. No. 5,925,523 issued 20 Jul. 1999, U.S. Pat. No. 5,846,722 issued 8 Dec. 1998 and U.S. Pat. No. 6,004,746 issued 21 Dec. 1999. Algorithms are also available in the art for genome-based predictions of protein function (see, e.g., Marcotte, et al., *Nature* 402: 4 Nov. 1999, 83-86).

[0321] Alternatively one can screen peptide libraries to identify molecules that interact with STEAP-1 protein sequences. In such methods, peptides that bind to STEAP-1 are identified by screening libraries that encode a random or controlled collection of amino acids. Peptides encoded by the libraries are expressed as fusion proteins of bacteriophage coat proteins, the bacteriophage particles are then screened against the STEAP-1 protein(s).

[0322] Accordingly, peptides having a wide variety of uses, such as therapeutic, prognostic or diagnostic reagents, are thus identified without any prior information on the structure of the expected ligand or receptor molecule. Typical peptide libraries and screening methods that can be used to identify molecules that interact with STEAP-1 protein sequences are disclosed for example in U.S. Pat. No. 5,723,286 issued 3 Mar. 1998 and U.S. Pat. No. 5,733,731 issued 31 Mar. 1998.

[0323] Alternatively, cell lines that express STEAP-1 are used to identify protein-protein interactions mediated by STEAP-1. Such interactions can be examined using immunoprecipitation techniques (see, e.g., Hamilton B. J., et al. *Biochem. Biophys. Res. Commun.* 1999, 261:646-51). STEAP-1 protein can be immunoprecipitated from STEAP-1-expressing cell lines using anti-STEAP-1 antibodies. Alternatively, antibodies against His-tag can be used in a cell line engineered to express fusions of STEAP-1 and a His-tag (vectors mentioned above). The immunoprecipitated complex can be examined for protein association by procedures such as Western blotting, ³⁵S-methionine labeling of proteins, protein microsequencing, silver staining and two-dimensional gel electrophoresis.

[0324] Small molecules and ligands that interact with STEAP-1 can be identified through related embodiments of such screening assays. For example, small molecules can be identified that interfere with protein function, including molecules that interfere with STEAP-1's ability to mediate phosphorylation and de-phosphorylation, interaction with DNA or RNA molecules as an indication of regulation of cell cycles, second messenger signaling or tumorigenesis. Similarly, small molecules that modulate STEAP-1-related ion channel, protein pump, or cell communication functions are identified and used to treat patients that have a cancer that expresses STEAP-1 (see, e.g., Hille, B., *Ionic Channels of Excitable Membranes* 2nd Ed., Sinauer Assoc., Sunderland, Mass., 1992). Moreover, ligands that regulate STEAP-1 function can be identified based on their ability to bind STEAP-1 and activate a reporter construct. Typical methods are discussed for example in U.S. Pat. No. 5,928,868 issued 27 Jul. 1999, and include methods for forming hybrid ligands in which at least one ligand is a small molecule. In an illustrative embodiment, cells engineered to express a fusion protein of STEAP-1 and a DNA-binding protein are used to co-express a fusion protein of a hybrid ligand/small molecule and a cDNA library transcriptional activator protein. The cells further contain a reporter gene, the expression of which is conditioned on the proximity of the first and second fusion proteins to each other, an event that occurs only if the hybrid ligand binds to target sites on both hybrid proteins. Those cells that express the reporter gene are selected and the unknown small molecule or the unknown ligand is identified. This method provides a means of identifying modulators, which activate or inhibit STEAP-1.

[0325] An embodiment of this invention comprises a method of screening for a molecule that interacts with a STEAP-1 amino acid sequence shown in FIG. 2 or FIG. 3, comprising the steps of contacting a population of molecules with a STEAP-1 amino acid sequence, allowing the population of molecules and the STEAP-1 amino acid sequence to interact under conditions that facilitate an interaction, determining the presence of a molecule that interacts with the STEAP-1 amino acid sequence, and then separating molecules that do not interact with the STEAP-1 amino acid sequence from molecules that do. In a specific embodiment, the method further comprises purifying, characterizing and identifying a molecule that interacts with the STEAP-1 amino acid sequence. The identified molecule can be used to modulate a function performed by STEAP-1. In a preferred embodiment, the STEAP-1 amino acid sequence is contacted with a library of peptides.

[0326] X.) Therapeutic Methods and Compositions

[0327] The identification of STEAP-1 as a protein that is normally expressed in a restricted set of tissues, but which

is also expressed in prostate and other cancers, opens a number of therapeutic approaches to the treatment of such cancers. As contemplated herein, STEAP-1 functions as a transcription factor involved in activating tumor-promoting genes or repressing genes that block tumorigenesis.

[0328] Accordingly, therapeutic approaches that inhibit the activity of a STEAP-1 protein are useful for patients suffering from a cancer that expresses STEAP-1. These therapeutic approaches generally fall into two classes. One class comprises various methods for inhibiting the binding or association of a STEAP-1 protein with its binding partner or with other proteins. Another class comprises a variety of methods for inhibiting the transcription of a STEAP-1 gene or translation of STEAP-1 mRNA.

[0329] X.A.) Anti-Cancer Vaccines

[0330] The invention provides cancer vaccines comprising a STEAP-1-related protein or STEAP-1-related nucleic acid. In view of the expression of STEAP-1, cancer vaccines prevent and/or treat STEAP-1-expressing cancers with minimal or no effects on non-target tissues. The use of a tumor antigen in a vaccine that generates humoral and/or cell-mediated immune responses as anti-cancer therapy is well known in the art and has been employed in prostate cancer using human PSMA and rodent PAP immunogens (Hodge et al., 1995, *Int. J. Cancer* 63:231-237; Fong et al., 1997, *J. Immunol.* 159:3113-3117).

[0331] Such methods can be readily practiced by employing a STEAP-1-related protein, or a STEAP-1-encoding nucleic acid molecule and recombinant vectors capable of expressing and presenting the STEAP-1 immunogen (which typically comprises a number of antibody or T cell epitopes). Skilled artisans understand that a wide variety of vaccine systems for delivery of immunoreactive epitopes are known in the art (see, e.g., Heryln et al., *Ann Med* 1999 Feb. 31(1):66-78; Maruyama et al., *Cancer Immunol Immunother* 2000 June 49(3):123-32). Briefly, such methods of generating an immune response (e.g. humoral and/or cell-mediated) in a mammal, comprise the steps of: exposing the mammal's immune system to an immunoreactive epitope (e.g. an epitope present in a STEAP-1 protein shown in FIG. 3 or analog or homolog thereof) so that the mammal generates an immune response that is specific for that epitope (e.g. generates antibodies that specifically recognize that epitope). In a preferred method, a STEAP-1 immunogen contains a biological motif, see e.g., Tables V-XVIII and XXII-LI, or a peptide of a size range from STEAP-1 indicated in FIG. 5, FIG. 6, FIG. 7, FIG. 8, and FIG. 9.

[0332] The entire STEAP-1 protein, immunogenic regions or epitopes thereof can be combined and delivered by various means. Such vaccine compositions can include, for example, lipopeptides (e.g., Vitiello, A. et al., *J. Clin. Invest.* 95:341, 1995), peptide compositions encapsulated in poly(DL-lactide-co-glycolide) ("PLG") microspheres (see, e.g., Eldridge, et al., *Molec. Immunol.* 28:287-294, 1991; Alonso et al., *Vaccine* 12:299-306, 1994; Jones et al., *Vaccine* 13:675-681, 1995), peptide compositions contained in immune stimulating complexes (ISCOMS) (see, e.g., Takahashi et al., *Nature* 344:873-875, 1990; Hu et al., *Clin Exp Immunol.* 113:235-243, 1998), multiple antigen peptide systems (MAPs) (see e.g., Tam, J. P., *Proc. Natl. Acad. Sci. U.S.A.* 85:5409-5413, 1988; Tam, J. P., *J. Immunol. Methods* 196:17-32, 1996), peptides formulated as multivalent pep-

tides; peptides for use in ballistic delivery systems, typically crystallized peptides, viral delivery vectors (Perkus, M. E. et al., In: *Concepts in vaccine development*, Kaufmann, S. H. E., ed., p. 379, 1996; Chakrabarti, S. et al., *Nature* 320:535, 1986; Hu, S. L. et al., *Nature* 320:537, 1986; Kieny, M.-P. et al., *AIDS Bio/Technology* 4:790, 1986; Top, F. H. et al., *J. Infect. Dis.* 124:148, 1971; Chanda, P. K. et al., *Virology* 175:535, 1990), particles of viral or synthetic origin (e.g., Kofler, N. et al., *J. Immunol. Methods* 192:25, 1996; Eldridge, J. H. et al., *Sem. Hematol.* 30:16, 1993; Falo, L. D., Jr. et al., *Nature Med.* 7:649, 1995), adjuvants (Warren, H. S., Vogel, F. R., and Chedid, L. A. *Annu. Rev. Immunol.* 4:369, 1986; Gupta, R. K. et al., *Vaccine* 11:293, 1993), liposomes (Reddy, R. et al., *J. Immunol.* 148:1585, 1992; Rock, K. L., *Immunol. Today* 17:131, 1996), or, naked or particle absorbed cDNA (Ulmer, J. B. et al., *Science* 259:1745, 1993; Robinson, H. L., Hunt, L. A., and Webster, R. G., *Vaccine* 11:957, 1993; Shiver, J. W. et al., In: *Concepts in vaccine development*, Kaufmann, S. H. E., ed., p. 423, 1996; Cease, K. B., and Berzofsky, J. A., *Annu. Rev. Immunol.* 12:923, 1994 and Eldridge, J. H. et al., *Sem. Hematol.* 30:16, 1993). Toxin-targeted delivery technologies, also known as receptor mediated targeting, such as those of Avant Immunotherapeutics, Inc. (Needham, Mass.) may also be used.

[0333] In patients with STEAP-1-associated cancer, the vaccine compositions of the invention can also be used in conjunction with other treatments used for cancer, e.g., surgery, chemotherapy, drug therapies, radiation therapies, etc. including use in combination with immune adjuvants such as IL-2, IL-12, GM-CSF, and the like.

[0334] Cellular Vaccines:

[0335] CTL epitopes can be determined using specific algorithms to identify peptides within STEAP-1 protein that bind corresponding HLA alleles (see e.g., Table IV; Epimer™ and Epimatrix™, Brown University (URL brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html); and, BIMAS, (URL bimas.dcrf.nih.gov/; SYFPEITHI at URL syfpeithi.bmi-heidelberg.coni/). In a preferred embodiment, a STEAP-1 immunogen contains one or more amino acid sequences identified using techniques well known in the art, such as the sequences shown in Tables V-XVIII and XXII-LI or a peptide of 8, 9, 10 or 11 amino acids specified by an HLA Class I motif/supermotif (e.g., Table IV (A), Table IV (D), or Table IV (E)) and/or a peptide of at least 9 amino acids that comprises an HLA Class II motif/supermotif (e.g., Table IV (B) or Table IV (C)). As is appreciated in the art, the HLA Class I binding groove is essentially closed ended so that peptides of only a particular size range can fit into the groove and be bound, generally HLA Class I epitopes are 8, 9, 10, or 11 amino acids long. In contrast, the HLA Class II binding groove is essentially open ended; therefore a peptide of about 9 or more amino acids can be bound by an HLA Class II molecule. Due to the binding groove differences between HLA Class I and II, HLA Class I motifs are length specific, i.e., position two of a Class I motif is the second amino acid in an amino to carboxyl direction of the peptide. The amino acid positions in a Class II motif are relative only to each other, not the overall peptide, i.e., additional amino acids can be attached to the amino and/or carboxyl termini of a motif-bearing sequence.

HLA Class II epitopes are often 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids long, or longer than 25 amino acids.

[0336] Antibody-Based Vaccines

[0337] A wide variety of methods for generating an immune response in a mammal are known in the art (for example as the first step in the generation of hybridomas). Methods of generating an immune response in a mammal comprise exposing the mammal's immune system to an immunogenic epitope on a protein (e.g. a STEAP-1 protein) so that an immune response is generated. A typical embodiment consists of a method for generating an immune response to STEAP-1 in a host, by contacting the host with a sufficient amount of at least one STEAP-1 B cell or cytotoxic T-cell epitope or analog thereof; and at least one periodic interval thereafter re-contacting the host with the STEAP-1 B cell or cytotoxic T-cell epitope or analog thereof. A specific embodiment consists of a method of generating an immune response against a STEAP-1-related protein or a man-made multiepitopic peptide comprising: administering STEAP-1 immunogen (e.g. a STEAP-1 protein or a peptide fragment thereof, a STEAP-1 fusion protein or analog etc.) in a vaccine preparation to a human or another mammal. Typically, such vaccine preparations further contain a suitable adjuvant (see, e.g., U.S. Pat. No. 6,146,635) or a universal helper epitope such as a PADRE™ peptide (Epimmune Inc., San Diego, Calif.; see, e.g., Alexander et al., *J. Immunol.* 2000 164(3); 164(3): 1625-1633; Alexander et al., *Immunity* 1994 1(9): 751-761 and Alexander et al., *Immunol. Res.* 1998 18(2): 79-92). An alternative method comprises generating an immune response in an individual against a STEAP-1 immunogen by: administering in vivo to muscle or skin of the individual's body a DNA molecule that comprises a DNA sequence that encodes a STEAP-1 immunogen, the DNA sequence operatively linked to regulatory sequences which control the expression of the DNA sequence; wherein the DNA molecule is taken up by cells, the DNA sequence is expressed in the cells and an immune response is generated against the immunogen (see, e.g., U.S. Pat. No. 5,962,428). Optionally a genetic vaccine facilitator such as anionic lipids; saponins; lectins; estrogenic compounds; hydroxylated lower alkyls; dimethyl sulfoxide; and urea is also administered. In addition, an antiidiotypic antibody can be administered that mimics STEAP-1, in order to generate a response to the target antigen.

[0338] Nucleic Acid Vaccines:

[0339] Vaccine compositions of the invention include nucleic acid-mediated modalities. DNA or RNA that encode protein(s) of the invention can be administered to a patient. Genetic immunization methods can be employed to generate prophylactic or therapeutic humoral and cellular immune responses directed against cancer cells expressing STEAP-1. Constructs comprising DNA encoding a STEAP-1-related protein/immunogen and appropriate regulatory sequences can be injected directly into muscle or skin of an individual, such that the cells of the muscle or skin take-up the construct and express the encoded STEAP-1 protein/immunogen. Alternatively, a vaccine comprises a STEAP-1-related protein. Expression of the STEAP-1-related protein immunogen results in the generation of prophylactic or therapeutic humoral and cellular immunity against cells that bear a

STEAP-1 protein. Various prophylactic and therapeutic genetic immunization techniques known in the art can be used (for review, see information and references published at Internet address genweb.com). Nucleic acid-based delivery is described, for instance, in Wolff et al., *Science* 247:1465 (1990) as well as U.S. Pat. Nos. 5,580,859; 5,589,466; 5,804,566; 5,739,118; 5,736,524; 5,679,647; WO 98/04720. Examples of DNA-based delivery technologies include "naked DNA", facilitated (bupivacaine, polymers, peptide-mediated) delivery, cationic lipid complexes, and particle-mediated ("gene gun") or pressure-mediated delivery (see, e.g., U.S. Pat. No. 5,922,687).

[0340] For therapeutic or prophylactic immunization purposes, proteins of the invention can be expressed via viral or bacterial vectors. Various viral gene delivery systems that can be used in the practice of the invention include, but are not limited to, vaccinia, fowlpox, canarypox, adenovirus, influenza, poliovirus, adeno-associated virus, lentivirus, and sindbis virus (see, e.g., Restifo, 1996, *Curr. Opin. Immunol.* 8:658-663; Tsang et al. *J. Natl. Cancer Inst.* 87:982-990 (1995)). Non-viral delivery systems can also be employed by introducing naked DNA encoding a STEAP-1-related protein into the patient (e.g., intramuscularly or intradermally) to induce an anti-tumor response.

[0341] Vaccinia virus is used, for example, as a vector to express nucleotide sequences that encode the peptides of the invention. Upon introduction into a host, the recombinant vaccinia virus expresses the protein immunogenic peptide, and thereby elicits a host immune response. Vaccinia vectors and methods useful in immunization protocols are described in, e.g., U.S. Pat. No. 4,722,848. Another vector is BCG (Bacille Calmette Guérin). BCG vectors are described in Stover et al., *Nature* 351:456-460(1991). A wide variety of other vectors useful for therapeutic administration or immunization of the peptides of the invention, e.g. adeno and adeno-associated virus vectors, retroviral vectors, *Salmonella typhi* vectors, detoxified anthrax toxin vectors, and the like, will be apparent to those skilled in the art from the description herein.

[0342] Thus, gene delivery systems are used to deliver a STEAP-1-related nucleic acid molecule. In one embodiment, the full-length human STEAP-1 cDNA is employed. In another embodiment, STEAP-1 nucleic acid molecules encoding specific cytotoxic T lymphocyte (CTL) and/or antibody epitopes are employed.

[0343] Ex Vivo Vaccines

[0344] Various ex vivo strategies can also be employed to generate an immune response. One approach involves the use of antigen presenting cells (APCs) such as dendritic cells (DC) to present STEAP-1 antigen to a patient's immune system. Dendritic cells express MHC class I and II molecules, B7 co-stimulator, and IL-12, and are thus highly specialized antigen presenting cells. In prostate cancer, autologous dendritic cells pulsed with peptides of the prostate-specific membrane antigen (PSMA) are being used in a Phase I clinical trial to stimulate prostate cancer patients' immune systems (Tjoa et al., 1996, *Prostate* 28:65-69; Murphy et al., 1996, *Prostate* 29:371-380). Thus, dendritic cells can be used to present STEAP-1 peptides to T cells in the context of MHC class I or II molecules. In one embodiment, autologous dendritic cells are pulsed with STEAP-1 peptides capable of binding to MHC class I and/or class II

molecules. In another embodiment, dendritic cells are pulsed with the complete STEAP-1 protein. Yet another embodiment involves engineering the overexpression of a STEAP-1 gene in dendritic cells using various implementing vectors known in the art, such as adenovirus (Arthur et al., 1997, *Cancer Gene Ther.* 4:17-25), retrovirus (Henderson et al., 1996, *Cancer Res.* 56:3763-3770), lentivirus, adeno-associated virus, DNA transfection (Ribas et al., 1997, *Cancer Res.* 57:2865-2869), or tumor-derived RNA transfection (Ashley et al., 1997, *J. Exp. Med.* 186:1177-1182). Cells that express STEAP-1 can also be engineered to express immune modulators, such as GM-CSF, and used as immunizing agents.

[0345] X.B.) STEAP-1 as a Target for Antibody-Based Therapy

[0346] STEAP-1 is an attractive target for antibody-based therapeutic strategies. A number of antibody strategies are known in the art for targeting both extracellular and intracellular molecules (see, e.g., complement and ADCC mediated killing as well as the use of intrabodies). Because STEAP-1 is expressed by cancer cells of various lineages relative to corresponding normal cells, systemic administration of STEAP-1-immunoreactive compositions are prepared that exhibit excellent sensitivity without toxic, non-specific and/or non-target effects caused by binding of the immunoreactive composition to non-target organs and tissues. Antibodies specifically reactive with domains of STEAP-1 are useful to treat STEAP-1-expressing cancers systemically, either as conjugates with a toxin or therapeutic agent, or as naked antibodies capable of inhibiting cell proliferation or function.

[0347] STEAP-1 antibodies can be introduced into a patient such that the antibody binds to STEAP-1 and modulates a function, such as an interaction with a binding partner, and consequently mediates destruction of the tumor cells and/or inhibits the growth of the tumor cells. Mechanisms by which such antibodies exert a therapeutic effect can include complement-mediated cytotoxicity, antibody-dependent cellular cytotoxicity, modulation of the physiological function of STEAP-1, inhibition of ligand binding or signal transduction pathways, modulation of tumor cell differentiation, alteration of tumor angiogenesis factor profiles, and/or apoptosis.

[0348] Those skilled in the art understand that antibodies can be used to specifically target and bind immunogenic molecules such as an immunogenic region of a STEAP-1 sequence shown in **FIG. 2** or **FIG. 3**. In addition, skilled artisans understand that it is routine to conjugate antibodies to cytotoxic agents (see, e.g., Slevers et al. *Blood* 93:113678-113684 (Jun. 1, 1999)). When cytotoxic and/or therapeutic agents are delivered directly to cells, such as by conjugating them to antibodies specific for a molecule expressed by that cell (e.g. STEAP-1), the cytotoxic agent will exert its known biological effect (i.e. cytotoxicity) on those cells.

[0349] A wide variety of compositions and methods for using antibody-cytotoxic agent conjugates to kill cells are known in the art. In the context of cancers, typical methods entail administering to an animal having a tumor a biologically effective amount of a conjugate comprising a selected cytotoxic and/or therapeutic agent linked to a targeting agent (e.g. an anti-STEAP-1 antibody) that binds to a marker (e.g. STEAP-1) expressed, accessible to binding or localized on

the cell surfaces. A typical embodiment is a method of delivering a cytotoxic and/or therapeutic agent to a cell expressing STEAP-1, comprising conjugating the cytotoxic agent to an antibody that immunospecifically binds to a STEAP-1 epitope, and, exposing the cell to the antibody-agent conjugate. Another illustrative embodiment is a method of treating an individual suspected of suffering from metastasized cancer, comprising a step of administering parenterally to said individual a pharmaceutical composition comprising a therapeutically effective amount of an antibody conjugated to a cytotoxic and/or therapeutic agent.

[0350] Cancer immunotherapy using anti-STEAP-1 antibodies can be done in accordance with various approaches that have been successfully employed in the treatment of other types of cancer, including but not limited to colon cancer (Arlen et al., 1998, *Crit. Rev. Immunol.* 18:133-138), multiple myeloma (Ozaki et al., 1997, *Blood* 90:3179-3186, Tsunenari et al., 1997, *Blood* 90:2437-2444), gastric cancer (Kasprzyk et al., 1992, *Cancer Res.* 52:2771-2776), B-cell lymphoma (Funakoshi et al., 1996, *J. Immunother. Emphasis Tumor Immunol.* 19:93-101), leukemia (Zhong et al., 1996, *Leuk. Res.* 20:581-589), colorectal cancer (Moun et al., 1994, *Cancer Res.* 54:6160-6166; Velders et al., 1995, *Cancer Res.* 55:4398-4403), and breast cancer (Shepard et al., 1991, *J. Clin. Immunol.* 11:117-127). Some therapeutic approaches involve conjugation of naked antibody to a toxin or radioisotope, such as the conjugation of Y^{91} or I^{131} to anti-CD20 antibodies (e.g., ZevalinTM, IDEC Pharmaceuticals Corp. or BexxarTM, Coulter Pharmaceuticals), while others involve co-administration of antibodies and other therapeutic agents, such as HerceptinTM (trastuzumab) with paclitaxel (Genentech, Inc.). The antibodies can be conjugated to a therapeutic agent. To treat prostate cancer, for example, STEAP-1 antibodies can be administered in conjunction with radiation, chemotherapy or hormone ablation. Also, antibodies can be conjugated to a toxin such as calicheamicin (e.g., MylotargTM, Wyeth-Ayerst, Madison, N.J., a recombinant humanized IgG₄ kappa antibody conjugated to antitumor antibiotic calicheamicin) or a maytansinoid (e.g., taxane-based Tumor-Activated Prodrug, TAP, platform, ImmunoGen, Cambridge, Mass., also see e.g., U.S. Pat. No. 5,416,064).

[0351] Although STEAP-1 antibody therapy is useful for all stages of cancer, antibody therapy can be particularly appropriate in advanced or metastatic cancers. Treatment with the antibody therapy of the invention is indicated for patients who have received one or more rounds of chemotherapy. Alternatively, antibody therapy of the invention is combined with a chemotherapeutic or radiation regimen for patients who have not received chemotherapeutic treatment. Additionally, antibody therapy can enable the use of reduced dosages of concomitant chemotherapy, particularly for patients who do not tolerate the toxicity of the chemotherapeutic agent very well. Fan et al. (*Cancer Res.* 53:4637-4642, 1993), Prewett et al. (*International J. of Onco.* 9:217-224, 1996), and Hancock et al. (*Cancer Res.* 51:4575-4580, 1991) describe the use of various antibodies together with chemotherapeutic agents.

[0352] Although STEAP-1 antibody therapy is useful for all stages of cancer, antibody therapy can be particularly appropriate in advanced or metastatic cancers. Treatment with the antibody therapy of the invention is indicated for patients who have received one or more rounds of chemo-

therapy. Alternatively, antibody therapy of the invention is combined with a chemotherapeutic or radiation regimen for patients who have not received chemotherapeutic treatment. Additionally, antibody therapy can enable the use of reduced dosages of concomitant chemotherapy, particularly for patients who do not tolerate the toxicity of the chemotherapeutic agent very well.

[0353] Cancer patients can be evaluated for the presence and level of STEAP-1 expression, preferably using immunohistochemical assessments of tumor tissue, quantitative STEAP-1 imaging, or other techniques that reliably indicate the presence and degree of STEAP-1 expression. Immunohistochemical analysis of tumor biopsies or surgical specimens is preferred for this purpose. Methods for immunohistochemical analysis of tumor tissues are well known in the art.

[0354] Anti-STEAP-1 monoclonal antibodies that treat prostate and other cancers include those that initiate a potent immune response against the tumor or those that are directly cytotoxic. In this regard, anti-STEAP-1 monoclonal antibodies (mAbs) can elicit tumor cell lysis by either complement-mediated or antibody-dependent cell cytotoxicity (ADCC) mechanisms, both of which require an intact Fc portion of the immunoglobulin molecule for interaction with effector cell Fc receptor sites on complement proteins. In addition, anti-STEAP-1 mAbs that exert a direct biological effect on tumor growth are useful to treat cancers that express STEAP-1. Mechanisms by which directly cytotoxic mAbs act include: inhibition of cell growth, modulation of cellular differentiation, modulation of tumor angiogenesis factor profiles, and the induction of apoptosis. The mechanism(s) by which a particular anti-STEAP-1 mAb exerts an anti-tumor effect is evaluated using any number of in vitro assays that evaluate cell death such as ADCC, ADMMC, complement-mediated cell lysis, and so forth, as is generally known in the art.

[0355] In some patients, the use of murine or other non-human monoclonal antibodies, or human/mouse chimeric mAbs can induce moderate to strong immune responses against the non-human antibody. This can result in clearance of the antibody from circulation and reduced efficacy. In the most severe cases, such an immune response can lead to the extensive formation of immune complexes which, potentially, can cause renal failure. Accordingly, preferred monoclonal antibodies used in the therapeutic methods of the invention are those that are either fully human or humanized and that bind specifically to the target STEAP-1 antigen with high affinity but exhibit low or no antigenicity in the patient.

[0356] Therapeutic methods of the invention contemplate the administration of single anti-STEAP-1 mAbs as well as combinations, or cocktails, of different mAbs. Such mAb cocktails can have certain advantages inasmuch as they contain mAbs that target different epitopes, exploit different effector mechanisms or combine directly cytotoxic mAbs with mAbs that rely on immune effector functionality. Such mAbs in combination can exhibit synergistic therapeutic effects. In addition, anti-STEAP-1 mAbs can be administered concomitantly with other therapeutic modalities, including but not limited to various chemotherapeutic agents, androgen-blockers, immune modulators (e.g., IL-2, GM-CSF), surgery or radiation. The anti-STEAP-1 mAbs are administered in their "naked" or unconjugated form, or can have a therapeutic agent(s) conjugated to them.

[0357] Anti-STEAP-1 antibody formulations are administered via any route capable of delivering the antibodies to a tumor cell. Routes of administration include, but are not limited to, intravenous, intraperitoneal, intramuscular, intratumor, intradermal, and the like. Treatment generally involves repeated administration of the anti-STEAP-1 antibody preparation, via an acceptable route of administration such as intravenous injection (IV), typically at a dose in the range of about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, or 25 mg/kg body weight. In general, doses in the range of 10-1000 mg mAb per week are effective and well tolerated.

[0358] Based on clinical experience with the Herceptin™ mAb in the treatment of metastatic breast cancer, an initial loading dose of approximately 4 mg/kg patient body weight IV, followed by weekly doses of about 2 mg/kg IV of the anti-STEAP-1 mAb preparation represents an acceptable dosing regimen. Preferably, the initial loading dose is administered as a 90-minute or longer infusion. The periodic maintenance dose is administered as a 30 minute or longer infusion, provided the initial dose was well tolerated. As appreciated by those of skill in the art, various factors can influence the ideal dose regimen in a particular case. Such factors include, for example, the binding affinity and half life of the Ab or mAbs used, the degree of STEAP-1 expression in the patient, the extent of circulating shed STEAP-1 antigen, the desired steady-state antibody concentration level, frequency of treatment, and the influence of chemotherapeutic or other agents used in combination with the treatment method of the invention, as well as the health status of a particular patient.

[0359] Optionally, patients should be evaluated for the levels of STEAP-1 in a given sample (e.g. the levels of circulating STEAP-1 antigen and/or STEAP-1 expressing cells) in order to assist in the determination of the most effective dosing regimen, etc. Such evaluations are also used for monitoring purposes throughout therapy, and are useful to gauge therapeutic success in combination with the evaluation of other parameters (for example, urine cytology and/or ImmunoCyt levels in bladder cancer therapy, or by analogy, serum PSA levels in prostate cancer therapy).

[0360] Anti-idiotypic anti-STEAP-1 antibodies can also be used in anti-cancer therapy as a vaccine for inducing an immune response to cells expressing a STEAP-1-related protein. In particular, the generation of anti-idiotypic antibodies is well known in the art; this methodology can readily be adapted to generate anti-idiotypic anti-STEAP-1 antibodies that mimic an epitope on a STEAP-1-related protein (see, for example, Wagner et al., 1997, Hybridoma 16: 33-40; Foon et al., 1995, J. Clin. Invest. 96:334-342; Herlyn et al., 1996, Cancer Immunol. Immunother. 43:65-76). Such an anti-idiotypic antibody can be used in cancer vaccine strategies.

[0361] X.C.) STEAP-1 as a Target for Cellular Immune Responses

[0362] Vaccines and methods of preparing vaccines that contain an immunogenically effective amount of one or more HLA-binding peptides as described herein are further embodiments of the invention. Furthermore, vaccines in accordance with the invention encompass compositions of one or more of the claimed peptides. A peptide can be present in a vaccine individually. Alternatively, the peptide

can exist as a homopolymer comprising multiple copies of the same peptide, or as a heteropolymer of various peptides. Polymers have the advantage of increased immunological reaction and, where different peptide epitopes are used to make up the polymer, the additional ability to induce antibodies and/or CTLs that react with different antigenic determinants of the pathogenic organism or tumor-related peptide targeted for an immune response. The composition can be a naturally occurring region of an antigen or can be prepared, e.g., recombinantly or by chemical synthesis.

[0363] Carriers that can be used with vaccines of the invention are well known in the art, and include, e.g., thyroglobulin, albumins such as human serum albumin, tetanus toxoid, polyamino acids such as poly L-lysine, poly L-glutamic acid, influenza, hepatitis B virus core protein, and the like. The vaccines can contain a physiologically tolerable (i.e., acceptable) diluent such as water, or saline, preferably phosphate buffered saline. The vaccines also typically include an adjuvant. Adjuvants such as incomplete Freund's adjuvant, aluminum phosphate, aluminum hydroxide, or alum are examples of materials well known in the art. Additionally, as disclosed herein, CTL responses can be primed by conjugating peptides of the invention to lipids, such as tripalmitoyl-S-glycerylcysteinylserine (P₃CSS). Moreover, an adjuvant such as a synthetic cytosine-phosphorothiolated-guanine-containing (CpG) oligonucleotides has been found to increase CTL responses 10- to 100-fold. (see, e.g. Davila and Celis, J. Immunol. 165:539-547 (2000)).

[0364] Upon immunization with a peptide composition in accordance with the invention, via injection, aerosol, oral, transdermal, transmucosal, intrapleural, intrathecal, or other suitable routes, the immune system of the host responds to the vaccine by producing large amounts of CTLs and/or HTLs specific for the desired antigen. Consequently, the host becomes at least partially immune to later development of cells that express or overexpress STEAP-1 antigen, or derives at least some therapeutic benefit when the antigen was tumor-associated.

[0365] In some embodiments, it may be desirable to combine the class I peptide components with components that induce or facilitate neutralizing antibody and/or helper T cell responses directed to the target antigen. A preferred embodiment of such a composition comprises class I and class II epitopes in accordance with the invention. An alternative embodiment of such a composition comprises a class I and/or class II epitope in accordance with the invention, along with a cross reactive HTL epitope such as PADRE™ (Epimmune, San Diego, Calif.) molecule (described e.g., in U.S. Pat. No. 5,736,142).

[0366] A vaccine of the invention can also include antigen-presenting cells (APC), such as dendritic cells (DC), as a vehicle to present peptides of the invention. Vaccine compositions can be created in vitro, following dendritic cell mobilization and harvesting, whereby loading of dendritic cells occurs in vitro. For example, dendritic cells are transfected, e.g., with a minigene in accordance with the invention, or are pulsed with peptides. The dendritic cell can then be administered to a patient to elicit immune responses in vivo. Vaccine compositions, either DNA- or peptide-based, can also be administered in vivo in combination with dendritic cell mobilization whereby loading of dendritic cells occurs in vivo.

[0367] Preferably, the following principles are utilized when selecting an array of epitopes for inclusion in a polyepitopic composition for use in a vaccine, or for selecting discrete epitopes to be included in a vaccine and/or to be encoded by nucleic acids such as a minigene. It is preferred that each of the following principles be balanced in order to make the selection. The multiple epitopes to be incorporated in a given vaccine composition may be, but need not be, contiguous in sequence in the native antigen from which the epitopes are derived.

[0368] 1.) Epitopes are selected which, upon administration, mimic immune responses that have been observed to be correlated with tumor clearance. For HLA Class I this includes 3-4 epitopes that come from at least one tumor associated antigen (TAA). For HLA Class II a similar rationale is employed; again 3-4 epitopes are selected from at least one TAA (see, e.g., Rosenberg et al., *Science* 278:1447-1450). Epitopes from one TAA may be used in combination with epitopes from one or more additional TAAs to produce a vaccine that targets tumors with varying expression patterns of frequently-expressed TAAs.

[0369] 2.) Epitopes are selected that have the requisite binding affinity established to be correlated with immunogenicity: for HLA Class I an IC_{50} of 500 nM or less, often 200 nM or less; and for Class II an IC_{50} of 1000 nM or less.

[0370] 3.) Sufficient supermotif bearing-peptides, or a sufficient array of allele-specific motif-bearing peptides, are selected to give broad population coverage. For example, it is preferable to have at least 80% population coverage. A Monte Carlo analysis, a statistical evaluation known in the art, can be employed to assess the breadth, or redundancy of, population coverage.

[0371] 4.) When selecting epitopes from cancer-related antigens it is often useful to select analogs because the patient may have developed tolerance to the native epitope.

[0372] 5.) Of particular relevance are epitopes referred to as "nested epitopes." Nested epitopes occur where at least two epitopes overlap in a given peptide sequence. A nested peptide sequence can comprise B cell, HLA class I and/or HLA class II epitopes. When providing nested epitopes, a general objective is to provide the greatest number of epitopes per sequence. Thus, an aspect is to avoid providing a peptide that is any longer than the amino terminus of the amino terminal epitope and the carboxyl terminus of the carboxyl terminal epitope in the peptide. When providing a multi-epitopic sequence, such as a sequence comprising nested epitopes, it is generally important to screen the sequence in order to insure that it does not have pathological or other deleterious biological properties.

[0373] 6.) If a polyepitopic protein is created, or when creating a minigene, an objective is to generate the smallest peptide that encompasses the epitopes of interest. This principle is similar, if not the same as that employed when selecting a peptide comprising nested epitopes. However, with an artificial polyepitopic peptide, the size minimization objective is balanced against the need to integrate any spacer sequences between epitopes in the polyepitopic protein. Spacer amino acid residues can, for example, be introduced to avoid junctional epitopes (an epitope recognized by the immune system, not present in the target antigen, and only created by the man-made juxtaposition of epitopes), or to

facilitate cleavage between epitopes and thereby enhance epitope presentation. Junctional epitopes are generally to be avoided because the recipient may generate an immune response to that non-native epitope. Of particular concern is a junctional epitope that is a "dominant epitope." A dominant epitope may lead to such a zealous response that immune responses to other epitopes are diminished or suppressed.

[0374] 7.) Where the sequences of multiple variants of the same target protein are present, potential peptide epitopes can also be selected on the basis of their conservancy. For example, a criterion for conservancy may define that the entire sequence of an HLA class I binding peptide or the entire 9-mer core of a class II binding peptide be conserved in a designated percentage of the sequences evaluated for a specific protein antigen.

[0375] X.C.1. Minigene Vaccines

[0376] A number of different approaches are available which allow simultaneous delivery of multiple epitopes. Nucleic acids encoding the peptides of the invention are a particularly useful embodiment of the invention. Epitopes for inclusion in a minigene are preferably selected according to the guidelines set forth in the previous section. A preferred means of administering nucleic acids encoding the peptides of the invention uses minigene constructs encoding a peptide comprising one or multiple epitopes of the invention.

[0377] The use of multi-epitope minigenes is described below and in, Ishioka et al., *J. Immunol.* 162:3915-3925, 1999; An, L. and Whitton, J. L., *J. Virol.* 71:2292, 1997; Thomson, S. A. et al., *J. Immunol.* 157:822, 1996; Whitton, J. L. et al., *J. Virol.* 67:348, 1993; Hanke, R. et al., *Vaccine* 16:426, 1998. For example, a multi-epitope DNA plasmid encoding supermotif- and/or motif-bearing epitopes derived STEAP-1, the PADRE® universal helper T cell epitope or multiple HTL epitopes from STEAP-1 (see e.g., Tables V-XVIII and XXII to LI), and an endoplasmic reticulum-translocating signal sequence can be engineered. A vaccine may also comprise epitopes that are derived from other TAAs.

[0378] The immunogenicity of a multi-epitopic minigene can be confirmed in transgenic mice to evaluate the magnitude of CTL induction responses against the epitopes tested. Further, the immunogenicity of DNA-encoded epitopes in vivo can be correlated with the in vitro responses of specific CTL lines against target cells transfected with the DNA plasmid. Thus, these experiments can show that the minigene serves to both: 1.) generate a CTL response and 2.) that the induced CTLs recognized cells expressing the encoded epitopes.

[0379] For example, to create a DNA sequence encoding the selected epitopes (minigene) for expression in human cells, the amino acid sequences of the epitopes may be reverse translated. A human codon usage table can be used to guide the codon choice for each amino acid. These epitope-encoding DNA sequences may be directly adjoined, so that when translated, a continuous polypeptide sequence is created. To optimize expression and/or immunogenicity, additional elements can be incorporated into the minigene design. Examples of amino acid sequences that can be reverse translated and included in the minigene sequence include: HLA class I epitopes, HLA class II epitopes,

antibody epitopes, a ubiquitination signal sequence, and/or an endoplasmic reticulum targeting signal. In addition, HLA presentation of CTL and HTL epitopes may be improved by including synthetic (e.g. poly-alanine) or naturally-occurring flanking sequences adjacent to the CTL or HTL epitopes; these larger peptides comprising the epitope(s) are within the scope of the invention.

[0380] The minigene sequence may be converted to DNA by assembling oligonucleotides that encode the plus and minus strands of the minigene. Overlapping oligonucleotides (30-100 bases long) may be synthesized, phosphorylated, purified and annealed under appropriate conditions using well known techniques. The ends of the oligonucleotides can be joined, for example, using T4 DNA ligase. This synthetic minigene, encoding the epitope polypeptide, can then be cloned into a desired expression vector.

[0381] Standard regulatory sequences well known to those of skill in the art are preferably included in the vector to ensure expression in the target cells. Several vector elements are desirable: a promoter with a down-stream cloning site for minigene insertion; a polyadenylation signal for efficient transcription termination; an *E. coli* origin of replication; and an *E. coli* selectable marker (e.g. ampicillin or kanamycin resistance). Numerous promoters can be used for this purpose, e.g., the human cytomegalovirus (hCMV) promoter. See, e.g., U.S. Pat. Nos. 5,580,859 and 5,589,466 for other suitable promoter sequences.

[0382] Additional vector modifications may be desired to optimize minigene expression and immunogenicity. In some cases, introns are required for efficient gene expression, and one or more synthetic or naturally-occurring introns could be incorporated into the transcribed region of the minigene. The inclusion of mRNA stabilization sequences and sequences for replication in mammalian cells may also be considered for increasing minigene expression.

[0383] Once an expression vector is selected, the minigene is cloned into the polylinker region downstream of the promoter. This plasmid is transformed into an appropriate *E. coli* strain, and DNA is prepared using standard techniques. The orientation and DNA sequence of the minigene, as well as all other elements included in the vector, are confirmed using restriction mapping and DNA sequence analysis. Bacterial cells harboring the correct plasmid can be stored as a master cell bank and a working cell bank.

[0384] In addition, immunostimulatory sequences (ISSs or CpGs) appear to play a role in the immunogenicity of DNA vaccines. These sequences may be included in the vector, outside the minigene coding sequence, if desired to enhance immunogenicity.

[0385] In some embodiments, a bi-cistronic expression vector which allows production of both the minigene-encoded epitopes and a second protein (included to enhance or decrease immunogenicity) can be used. Examples of proteins or polypeptides that could beneficially enhance the immune response if co-expressed include cytokines (e.g., IL-2, IL-12, GM-CSF), cytokine-inducing molecules (e.g., LelF), costimulatory molecules, or for HTL responses, pan-DR binding proteins (PADRE™, Epimmune, San Diego, Calif.). Helper (HTL) epitopes can be joined to intracellular targeting signals and expressed separately from expressed CTL epitopes; this allows direction of the HTL epitopes to

a cell compartment different than that of the CTL epitopes. If required, this could facilitate more efficient entry of HTL epitopes into the HLA class II pathway, thereby improving HTL induction. In contrast to HTL or CTL induction, specifically decreasing the immune response by co-expression of immunosuppressive molecules (e.g. TGF- β) may be beneficial in certain diseases.

[0386] Therapeutic quantities of plasmid DNA can be produced for example, by fermentation in *E. coli*, followed by purification. Aliquots from the working cell bank are used to inoculate growth medium, and grown to saturation in shaker flasks or a bioreactor according to well-known techniques. Plasmid DNA can be purified using standard bio-separation technologies such as solid phase anion-exchange resins supplied by QIAGEN, Inc. (Valencia, Calif.). If required, supercoiled DNA can be isolated from the open circular and linear forms using gel electrophoresis or other methods.

[0387] Purified plasmid DNA can be prepared for injection using a variety of formulations. The simplest of these is reconstitution of lyophilized DNA in sterile phosphate-buffer saline (PBS). This approach, known as "naked DNA," is currently being used for intramuscular (IM) administration in clinical trials. To maximize the immunotherapeutic effects of minigene DNA vaccines, an alternative method for formulating purified plasmid DNA may be desirable. A variety of methods have been described, and new techniques may become available. Cationic lipids, glycolipids, and fusogenic liposomes can also be used in the formulation (see, e.g., as described by WO 93/24640; Mannino & Gould-Fogerite, *BioTechniques* 6(7): 682 (1988); U.S. Pat. No. 5,279,833; WO 91/06309; and Felgner, et al., *Proc. Nat'l Acad. Sci. USA* 84:7413 (1987). In addition, peptides and compounds referred to collectively as protective, interactive, non-condensing compounds (PINC) could also be complexed to purified plasmid DNA to influence variables such as stability, intramuscular dispersion, or trafficking to specific organs or cell types.

[0388] Target cell sensitization can be used as a functional assay for expression and HLA class I presentation of minigene-encoded CTL epitopes. For example, the plasmid DNA is introduced into a mammalian cell line that is suitable as a target for standard CTL chromium release assays. The transfection method used will be dependent on the final formulation. Electroporation can be used for "naked" DNA, whereas cationic lipids allow direct in vitro transfection. A plasmid expressing green fluorescent protein (GFP) can be co-transfected to allow enrichment of transfected cells using fluorescence activated cell sorting (FACS). These cells are then chromium-51 (^{51}Cr) labeled and used as target cells for epitope-specific CTL lines; cytotoxicity, detected by ^{51}Cr release, indicates both production of, and HLA presentation of, minigene-encoded CTL epitopes. Expression of HTL epitopes may be evaluated in an analogous manner using assays to assess HTL activity.

[0389] In vivo immunogenicity is a second approach for functional testing of minigene DNA formulations. Transgenic mice expressing appropriate human HLA proteins are immunized with the DNA product. The dose and route of administration are formulation dependent (e.g., IM for DNA in PBS, intraperitoneal (i.p.) for lipid-complexed DNA). Twenty-one days after immunization, splenocytes are har-

vested and restimulated for one week in the presence of peptides encoding each epitope being tested. Thereafter, for CTL effector cells, assays are conducted for cytolysis of peptide-loaded, ^{51}Cr -labeled target cells using standard techniques. Lysis of target cells that were sensitized by HLA loaded with peptide epitopes, corresponding to minigene-encoded epitopes, demonstrates DNA vaccine function for in vivo induction of CTLs. Immunogenicity of HTL epitopes is confirmed in transgenic mice in an analogous manner.

[0390] Alternatively, the nucleic acids can be administered using ballistic delivery as described, for instance, in U.S. Pat. No. 5,204,253. Using this technique, particles comprised solely of DNA are administered. In a further alternative embodiment, DNA can be adhered to particles, such as gold particles.

[0391] Minigenes can also be delivered using other bacterial or viral delivery systems well known in the art, e.g., an expression construct encoding epitopes of the invention can be incorporated into a viral vector such as vaccinia.

[0392] X.C.2. Combinations of CTL Peptides with Helper Peptides

[0393] Vaccine compositions comprising CTL peptides of the invention can be modified, e.g., analoged, to provide desired attributes, such as improved serum half life, broadened population coverage or enhanced immunogenicity.

[0394] For instance, the ability of a peptide to induce CTL activity can be enhanced by linking the peptide to a sequence which contains at least one epitope that is capable of inducing a T helper cell response. Although a CTL peptide can be directly linked to a T helper peptide, often CTL epitope/HTL epitope conjugates are linked by a spacer molecule. The spacer is typically comprised of relatively small, neutral molecules, such as amino acids or amino acid mimetics, which are substantially uncharged under physiological conditions. The spacers are typically selected from, e.g., Ala, Gly, or other neutral spacers of nonpolar amino acids or neutral polar amino acids. It will be understood that the optionally present spacer need not be comprised of the same residues and thus may be a hetero- or homo-oligomer. When present, the spacer will usually be at least one or two residues, more usually three to six residues and sometimes 10 or more residues. The CTL peptide epitope can be linked to the T helper peptide epitope either directly or via a spacer either at the amino or carboxy terminus of the CTL peptide. The amino terminus of either the immunogenic peptide or the T helper peptide may be acylated.

[0395] In certain embodiments, the T helper peptide is one that is recognized by T helper cells present in a majority of a genetically diverse population. This can be accomplished by selecting peptides that bind to many, most, or all of the HLA class II molecules. Examples of such amino acid bind many HLA Class II molecules include sequences from antigens such as tetanus toxoid at positions 830-843 (QYI-KANSKFIGITE; SEQ ID NO: 44), *Plasmodium falciparum* circumsporozoite (CS) protein at positions 378-398 (DIEK-KIAKMEKASSVFNVVNS; SEQ ID NO: 45), and *Streptococcus* 18 kD protein at positions 116-131 (GAVDSILG-GVATYGAA; SEQ ID NO: 46). Other examples include peptides bearing a DR 14-7 supermotif, or either of the DR3 motifs.

[0396] Alternatively, it is possible to prepare synthetic peptides capable of stimulating T helper lymphocytes, in a

loosely HLA-restricted fashion, using amino acid sequences not found in nature (see, e.g., PCT publication WO 95/07707). These synthetic compounds called Pan-DR-binding epitopes (e.g., PADRE™, Epimmune, Inc., San Diego, Calif.) are designed, most preferably, to bind most HLA-DR (human HLA class II) molecules. For instance, a pan-DR-binding epitope peptide having the formula: aKXVAAW-TLKAAa (SEQ ID NO: 47), where "X" is either cyclohexylalanine, phenylalanine, or tyrosine, and a is either D-alanine or L-alanine, has been found to bind to most HLA-DR alleles, and to stimulate the response of T helper lymphocytes from most individuals, regardless of their HLA type. An alternative of a pan-DR binding epitope comprises all "L" natural amino acids and can be provided in the form of nucleic acids that encode the epitope.

[0397] HTL peptide epitopes can also be modified to alter their biological properties. For example, they can be modified to include D-amino acids to increase their resistance to proteases and thus extend their serum half life, or they can be conjugated to other molecules such as lipids, proteins, carbohydrates, and the like to increase their biological activity. For example, a T helper peptide can be conjugated to one or more palmitic acid chains at either the amino or carboxyl termini.

[0398] X.C.3. Combinations of CTL Peptides with T Cell Priming Agents

[0399] In some embodiments it may be desirable to include in the pharmaceutical compositions of the invention at least one component which primes B lymphocytes or T lymphocytes. Lipids have been identified as agents capable of priming CTL in vivo. For example, palmitic acid residues can be attached to the ϵ - and α -amino groups of a lysine residue and then linked, e.g., via one or more linking residues such as Gly, Gly-Gly-, Ser, Ser-Ser, or the like, to an immunogenic peptide. The lipidated peptide can then be administered either directly in a micelle or particle, incorporated into a liposome, or emulsified in an adjuvant, e.g. incomplete Freund's adjuvant. In a preferred embodiment, a particularly effective immunogenic composition comprises palmitic acid attached to ϵ - and α -amino groups of Lys, which is attached via linkage, e.g., Ser-Ser, to the amino terminus of the immunogenic peptide.

[0400] As another example of lipid priming of CTL responses, *E. coli* lipoproteins, such as tripalmitoyl-S-glycerylcysteinylserine (P_3CSS) can be used to prime virus specific CTL when covalently attached to an appropriate peptide (see, e.g., Deres, et al., *Nature* 342:561, 1989). Peptides of the invention can be coupled to P_3CSS , for example, and the lipopeptide administered to an individual to prime specifically an immune response to the target antigen. Moreover, because the induction of neutralizing antibodies can also be primed with P_3CSS -conjugated epitopes, two such compositions can be combined to more effectively elicit both humoral and cell-mediated responses.

[0401] X.C.4. Vaccine Compositions Comprising DC Pulsed with CTL and/or HTL Peptides

[0402] An embodiment of a vaccine composition in accordance with the invention comprises ex vivo administration of a cocktail of epitope-bearing peptides to PBMC, or isolated DC therefrom, from the patient's blood. A pharma-

ceutical to facilitate harvesting of DC can be used, such as Progenipoietin™ (Pharmacia-Monsanto, St. Louis, Mo.) or GM-CSF/IL-4. After pulsing the DC with peptides and prior to reinfusion into patients, the DC are washed to remove unbound peptides. In this embodiment, a vaccine comprises peptide-pulsed DCs which present the pulsed peptide epitopes complexed with HLA molecules on their surfaces.

[0403] The DC can be pulsed *ex vivo* with a cocktail of peptides, some of which stimulate CTL responses to STEAP-1. Optionally, a helper T cell (HTL) peptide, such as a natural or artificial loosely restricted HLA Class II peptide, can be included to facilitate the CTL response. Thus, a vaccine in accordance with the invention is used to treat a cancer which expresses or overexpresses STEAP-1.

[0404] X.D. Adoptive Immunotherapy

[0405] Antigenic STEAP-1-related peptides are used to elicit a CTL and/or HTL response *ex vivo*, as well. The resulting CTL or HTL cells, can be used to treat tumors in patients that do not respond to other conventional forms of therapy, or will not respond to a therapeutic vaccine peptide or nucleic acid in accordance with the invention. *Ex vivo* CTL or HTL responses to a particular antigen are induced by incubating in tissue culture the patient's, or genetically compatible, CTL or HTL precursor cells together with a source of antigen-presenting cells (APC), such as dendritic cells, and the appropriate immunogenic peptide. After an appropriate incubation time (typically about 7-28 days), in which the precursor cells are activated and expanded into effector cells, the cells are infused back into the patient, where they will destroy (CTL) or facilitate destruction (HTL) of their specific target cell (e.g., a tumor cell). Transfected dendritic cells may also be used as antigen presenting cells.

[0406] X.E. Administration of Vaccines for Therapeutic or Prophylactic Purposes

[0407] Pharmaceutical and vaccine compositions of the invention are typically used to treat and/or prevent a cancer that expresses or overexpresses STEAP-1. In therapeutic applications, peptide and/or nucleic acid compositions are administered to a patient in an amount sufficient to elicit an effective B cell, CTL and/or HTL response to the antigen and to cure or at least partially arrest or slow symptoms and/or complications. An amount adequate to accomplish this is defined as "therapeutically effective dose." Amounts effective for this use will depend on, e.g., the particular composition administered, the manner of administration, the stage and severity of the disease being treated, the weight and general state of health of the patient, and the judgment of the prescribing physician.

[0408] For pharmaceutical compositions, the immunogenic peptides of the invention, or DNA encoding them, are generally administered to an individual already bearing a tumor that expresses STEAP-1. The peptides or DNA encoding them can be administered individually or as fusions of one or more peptide sequences. Patients can be treated with the immunogenic peptides separately or in conjunction with other treatments, such as surgery, as appropriate.

[0409] For therapeutic use, administration should generally begin at the first diagnosis of STEAP-1-associated cancer. This is followed by boosting doses until at least symptoms are substantially abated and for a period thereof.

The embodiment of the vaccine composition (i.e., including, but not limited to embodiments such as peptide cocktails, polyepitopic polypeptides, minigenes, or TAA-specific CTLs or pulsed dendritic cells) delivered to the patient may vary according to the stage of the disease or the patient's health status. For example, in a patient with a tumor that expresses STEAP-1, a vaccine comprising STEAP-1-specific CTL may be more efficacious in killing tumor cells in patient with advanced disease than alternative embodiments.

[0410] It is generally important to provide an amount of the peptide epitope delivered by a mode of administration sufficient to stimulate effectively a cytotoxic T cell response; compositions which stimulate helper T cell responses can also be given in accordance with this embodiment of the invention.

[0411] The dosage for an initial therapeutic immunization generally occurs in a unit dosage range where the lower value is about 1, 5, 50, 500, or 1,000 µg and the higher value is about 10,000; 20,000; 30,000; or 50,000 µg. Dosage values for a human typically range from about 500 µg to about 50,000 µg per 70 kilogram patient. Boosting dosages of between about 1.0 µg to about 50,000 µg of peptide pursuant to a boosting regimen over weeks to months may be administered depending upon the patient's response and condition as determined by measuring the specific activity of CTL and HTL obtained from the patient's blood. Administration should continue until at least clinical symptoms or laboratory tests indicate that the neoplasia, has been eliminated or reduced and for a period thereafter. The dosages, routes of administration, and dose schedules are adjusted in accordance with methodologies known in the art.

[0412] In certain embodiments, the peptides and compositions of the present invention are employed in serious disease states, that is, life-threatening or potentially life threatening situations. In such cases, as a result of the minimal amounts of extraneous substances and the relative nontoxic nature of the peptides in preferred compositions of the invention, it is possible and may be felt desirable by the treating physician to administer substantial excesses of these peptide compositions relative to these stated dosage amounts.

[0413] The vaccine compositions of the invention can also be used purely as prophylactic agents. Generally the dosage for an initial prophylactic immunization generally occurs in a unit dosage range where the lower value is about 1, 5, 50, 500, or 1000 µg and the higher value is about 10,000; 20,000; 30,000; or 50,000 µg. Dosage values for a human typically range from about 500 µg to about 50,000 µg per 70 kilogram patient. This is followed by boosting dosages of between about 1.0 µg to about 50,000 µg of peptide administered at defined intervals from about four weeks to six months after the initial administration of vaccine. The immunogenicity of the vaccine can be assessed by measuring the specific activity of CTL and HTL obtained from a sample of the patient's blood.

[0414] The pharmaceutical compositions for therapeutic treatment are intended for parenteral, topical, oral, nasal, intrathecal, or local (e.g. as a cream or topical ointment) administration. Preferably, the pharmaceutical compositions are administered parentally, e.g., intravenously, subcutaneously, intradermally, or intramuscularly. Thus, the invention

provides compositions for parenteral administration which comprise a solution of the immunogenic peptides dissolved or suspended in an acceptable carrier, preferably an aqueous carrier.

[0415] A variety of aqueous carriers may be used, e.g., water, buffered water, 0.8% saline, 0.3% glycine, hyaluronic acid and the like. These compositions may be sterilized by conventional, well-known sterilization techniques, or may be sterile filtered. The resulting aqueous solutions may be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile solution prior to administration.

[0416] The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions, such as pH-adjusting and buffering agents, tonicity adjusting agents, wetting agents, preservatives, and the like, for example, sodium acetate, sodium lactate, sodium chloride, potassium chloride, calcium chloride, sorbitan monolaurate, triethanolamine oleate, etc.

[0417] The concentration of peptides of the invention in the pharmaceutical formulations can vary widely, i.e., from less than about 0.1%, usually at or at least about 2% to as much as 20% to 50% or more by weight, and will be selected primarily by fluid volumes, viscosities, etc., in accordance with the particular mode of administration selected.

[0418] A human unit dose form of a composition is typically included in a pharmaceutical composition that comprises a human unit dose of an acceptable carrier, in one embodiment an aqueous carrier, and is administered in a volume/quantity that is known by those of skill in the art to be used for administration of such compositions to humans (see, e.g., Remington's Pharmaceutical Sciences, 17th Edition, A. Gennaro, Editor, Mack Publishing Co., Easton, Pa., 1985). For example a peptide dose for initial immunization can be from about 1 to about 50,000 μ g, generally 100-5,000 μ g, for a 70 kg patient. For example, for nucleic acids an initial immunization may be performed using an expression vector in the form of naked nucleic acid administered IM (or SC or ID) in the amounts of 0.5-5 mg at multiple sites. The nucleic acid (0.1 to 1000 μ g) can also be administered using a gene gun. Following an incubation period of 3-4 weeks, a booster dose is then administered. The booster can be recombinant fowlpox virus administered at a dose of $5-10^7$ to 5×10^9 pfu.

[0419] For antibodies, a treatment generally involves repeated administration of the anti-STEAP-1 antibody preparation, via an acceptable route of administration such as intravenous injection (IV), typically at a dose in the range of about 0.1 to about 10 mg/kg body weight. In general, doses in the range of 10-500 mg mAb per week are effective and well tolerated. Moreover, an initial loading dose of approximately 4 mg/kg patient body weight IV, followed by weekly doses of about 2 mg/kg IV of the anti-STEAP-1 mAb preparation represents an acceptable dosing regimen. As appreciated by those of skill in the art, various factors can influence the ideal dose in a particular case. Such factors include, for example, half life of a composition, the binding affinity of an Ab, the immunogenicity of a substance, the degree of STEAP-1 expression in the patient, the extent of circulating shed STEAP-1 antigen, the desired steady-state concentration level, frequency of treatment, and the influence of chemotherapeutic or other agents used in combina-

tion with the treatment method of the invention, as well as the health status of a particular patient. Non-limiting preferred human unit doses are, for example, 500 μ g-1 mg, 1 mg-50 mg, 50 mg-100 mg, 100 mg-200 mg, 200 mg-300 mg, 400 mg-500 mg, 500 mg-600 mg, 600 mg-700 mg, 700 mg-800 mg, 800 mg-900 mg, 900 mg-1g, or 1 mg-700 mg. In certain embodiments, the dose is in a range of 2-5 mg/kg body weight, e.g., with follow on weekly doses of 1-3 mg/kg; 0.5 mg, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 mg/kg body weight followed, e.g., in two, three or four weeks by weekly doses; 0.5-10 mg/kg body weight, e.g., followed in two, three or four weeks by weekly doses; 225, 250, 275, 300, 325, 350, 375, 400 mg m² of body area weekly; 1-600 mg m² of body area weekly; 225-400 mg m² of body area weekly; these doses can be followed by weekly doses for 2, 3, 4, 5, 6, 7, 8, 9, 19, 11, 12 or more weeks.

[0420] In one embodiment, human unit dose forms of polynucleotides comprise a suitable dosage range or effective amount that provides any therapeutic effect. As appreciated by one of ordinary skill in the art a therapeutic effect depends on a number of factors, including the sequence of the polynucleotide, molecular weight of the polynucleotide and route of administration. Dosages are generally selected by the physician or other health care professional in accordance with a variety of parameters known in the art, such as severity of symptoms, history of the patient and the like. Generally, for a polynucleotide of about 20 bases, a dosage range may be selected from, for example, an independently selected lower limit such as about 0.1, 0.25, 0.5, 1, 2, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400 or 500 mg/kg up to an independently selected upper limit, greater than the lower limit, of about 60, 80, 100, 200, 300, 400, 500, 750, 1000, 1500, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000 or 10,000 mg/kg. For example, a dose may be about any of the following: 0.1 to 100 mg/kg, 0.1 to 50 mg/kg, 0.1 to 25 mg/kg, 0.1 to 10 mg/kg, 1 to 500 mg/kg, 100 to 400 mg/kg, 200 to 300 mg/kg, 1 to 100 mg/kg, 100 to 200 mg/kg, 300 to 400 mg/kg, 400 to 500 mg/kg, 500 to 1000 mg/kg, 500 to 5000 mg/kg, or 500 to 10,000 mg/kg. Generally, parenteral routes of administration may require higher doses of polynucleotide compared to more direct application to the nucleotide to diseased tissue, as do polynucleotides of increasing length.

[0421] In one embodiment, human unit dose forms of T-cells comprise a suitable dosage range or effective amount that provides any therapeutic effect. As appreciated by one of ordinary skill in the art, a therapeutic effect depends on a number of factors. Dosages are generally selected by the physician or other health care professional in accordance with a variety of parameters known in the art, such as severity of symptoms, history of the patient and the like. A dose may be about 10^4 cells to about 10^6 cells, about 10^6 cells to about 10^8 cells, about 10^8 to about 10^{11} cells, or about 10^1 to about 5×10^{10} cells. A dose may also about 10^6 cells/m² to about 10^{10} cells/m², or about 10^6 cells/m² to about 10^6 cells/m².

[0422] Proteins(s) of the invention, and/or nucleic acids encoding the protein(s), can also be administered via liposomes, which may also serve to: 1) target the proteins(s) to a particular tissue, such as lymphoid tissue; 2) to target selectively to diseases cells; or, 3) to increase the half-life of the peptide composition. Liposomes include emulsions, foams, micelles, insoluble monolayers, liquid crystals, phos-

pholipid dispersions, lamellar layers and the like. In these preparations, the peptide to be delivered is incorporated as part of a liposome, alone or in conjunction with a molecule which binds to a receptor prevalent among lymphoid cells, such as monoclonal antibodies which bind to the CD45 antigen, or with other therapeutic or immunogenic compositions. Thus, liposomes either filled or decorated with a desired peptide of the invention can be directed to the site of lymphoid cells, where the liposomes then deliver the peptide compositions. Liposomes for use in accordance with the invention are formed from standard vesicle-forming lipids, which generally include neutral and negatively charged phospholipids and a sterol, such as cholesterol. The selection of lipids is generally guided by consideration of, e.g., liposome size, acid lability and stability of the liposomes in the blood stream. A variety of methods are available for preparing liposomes, as described in, e.g., Szoka, et al., *Ann. Rev. Biophys. Bioeng.* 9:467 (1980), and U.S. Pat. Nos. 4,235,871, 4,501,728, 4,837,028, and 5,019,369.

[0423] For targeting cells of the immune system, a ligand to be incorporated into the liposome can include, e.g., antibodies or fragments thereof specific for cell surface determinants of the desired immune system cells. A liposome suspension containing a peptide may be administered intravenously, locally, topically, etc. in a dose which varies according to, inter alia, the manner of administration, the peptide being delivered, and the stage of the disease being treated.

[0424] For solid compositions, conventional nontoxic solid carriers may be used which include, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharin, talcum, cellulose, glucose, sucrose, magnesium carbonate, and the like. For oral administration, a pharmaceutically acceptable nontoxic composition is formed by incorporating any of the normally employed excipients, such as those carriers previously listed, and generally 10-95% of active ingredient, that is, one or more peptides of the invention, and more preferably at a concentration of 25%-75%.

[0425] For aerosol administration, immunogenic peptides are preferably supplied in finely divided form along with a surfactant and propellant. Typical percentages of peptides are about 0.01%-20% by weight, preferably about 1%-10%. The surfactant must, of course, be nontoxic, and preferably soluble in the propellant. Representative of such agents are the esters or partial esters of fatty acids containing from about 6 to 22 carbon atoms, such as caproic, octanoic, lauric, palmitic, stearic, linoleic, linolenic, olesteric and oleic acids with an aliphatic polyhydric alcohol or its cyclic anhydride. Mixed esters, such as mixed or natural glycerides may be employed. The surfactant may constitute about 0.1%-20% by weight of the composition, preferably about 0.25-5%. The balance of the composition is ordinarily propellant. A carrier can also be included, as desired, as with, e.g., lecithin for intranasal delivery.

[0426] XI.) Diagnostic and Prognostic Embodiments of STEAP-1.

[0427] As disclosed herein, STEAP-1 polynucleotides, polypeptides, reactive cytotoxic T cells (CTL), reactive helper T cells (HTL) and anti-polypeptide antibodies are used in well known diagnostic, prognostic and therapeutic assays that examine conditions associated with dysregulated

cell growth such as cancer, in particular the cancers listed in Table I (see, e.g., both its specific pattern of tissue expression as well as its overexpression in certain cancers as described for example in the Example entitled "Expression analysis of STEAP-1 in normal tissues, and patient specimens").

[0428] STEAP-1 can be analogized to a prostate associated antigen PSA, the archetypal marker that has been used by medical practitioners for years to identify and monitor the presence of prostate cancer (see, e.g., Merrill et al., *J. Urol.* 163(2): 503-5120 (2000); Polascik et al., *J. Urol.* August; 162(2):293-306 (1999) and Fortier et al., *J. Nat. Cancer Inst.* 91(19): 1635-1640(1999)). A variety of other diagnostic markers are also used in similar contexts including p53 and K-ras (see, e.g., Tulchinsky et al., *Int J Mol Med* 1999 July 4(1):99-102 and Minimoto et al., *Cancer Detect Prev* 2000; 24(1):1-12). Therefore, this disclosure of STEAP-1 polynucleotides and polypeptides (as well as STEAP-1 polynucleotide probes and anti-STEAP-1 antibodies used to identify the presence of these molecules) and their properties allows skilled artisans to utilize these molecules in methods that are analogous to those used, for example, in a variety of diagnostic assays directed to examining conditions associated with cancer.

[0429] Typical embodiments of diagnostic methods which utilize the STEAP-1 polynucleotides, polypeptides, reactive T cells and antibodies are analogous to those methods from well-established diagnostic assays, which employ, e.g., PSA polynucleotides, polypeptides, reactive T cells and antibodies. For example, just as PSA polynucleotides are used as probes (for example in Northern analysis, see, e.g., Sharief et al., *Biochem. Mol. Biol. Int.* 33(3):567-74(1994)) and primers (for example in PCR analysis, see, e.g., Okegawa et al., *J. Urol.* 163(4): 1189-1190 (2000)) to observe the presence and/or the level of PSA mRNAs in methods of monitoring PSA overexpression or the metastasis of prostate cancers, the STEAP-1 polynucleotides described herein can be utilized in the same way to detect STEAP-1 overexpression or the metastasis of prostate and other cancers expressing this gene. Alternatively, just as PSA polypeptides are used to generate antibodies specific for PSA which can then be used to observe the presence and/or the level of PSA proteins in methods to monitor PSA protein overexpression (see, e.g., Stephan et al., *Urology* 55(4):560-3 (2000)) or the metastasis of prostate cells (see, e.g., Alanen et al., *Pathol. Res. Pract.* 192(3):233-7 (1996)), the STEAP-1 polypeptides described herein can be utilized to generate antibodies for use in detecting STEAP-1 overexpression or the metastasis of prostate cells and cells of other cancers expressing this gene.

[0430] Specifically, because metastases involves the movement of cancer cells from an organ of origin (such as the lung or prostate gland etc.) to a different area of the body (such as a lymph node), assays which examine a biological sample for the presence of cells expressing STEAP-1 polynucleotides and/or polypeptides can be used to provide evidence of metastasis. For example, when a biological sample from tissue that does not normally contain STEAP-1-expressing cells (lymph node) is found to contain STEAP-1-expressing cells such as the STEAP-1 expression seen in LAPC4 and LAPC9, xenografts isolated from lymph node and bone metastasis, respectively, this finding is indicative of metastasis.

[0431] Alternatively STEAP-1 polynucleotides and/or polypeptides can be used to provide evidence of cancer, for example, when cells in a biological sample that do not normally express STEAP-1 or express STEAP-1 at a different level are found to express STEAP-1 or have an increased expression of STEAP-1 (see, e.g., the STEAP-1 expression in the cancers listed in Table I and in patient samples etc. shown in the accompanying Figures). In such assays, artisans may further wish to generate supplementary evidence of metastasis by testing the biological sample for the presence of a second tissue restricted marker (in addition to STEAP-1) such as PSA, PSCA etc. (see, e.g., Alanen et al., *Pathol. Res. Pract.* 192(3): 233-237 (1996)).

[0432] Just as PSA polynucleotide fragments and polynucleotide variants are employed by skilled artisans for use in methods of monitoring PSA, STEAP-1 polynucleotide fragments and polynucleotide variants are used in an analogous manner. In particular, typical PSA polynucleotides used in methods of monitoring PSA are probes or primers which consist of fragments of the PSA cDNA sequence. Illustrating this, primers used to PCR amplify a PSA polynucleotide must include less than the whole PSA sequence to function in the polymerase chain reaction. In the context of such PCR reactions, skilled artisans generally create a variety of different polynucleotide fragments that can be used as primers in order to amplify different portions of a polynucleotide of interest or to optimize amplification reactions (see, e.g., Caetano-Anolles, G. *Biotechniques* 25(3): 472-476, 478-480 (1998); Robertson et al., *Methods Mol. Biol.* 98:121-154 (1998)). An additional illustration of the use of such fragments is provided in the Example entitled "Expression analysis of STEAP-1 in normal tissues, and patient specimens," where a STEAP-1 polynucleotide fragment is used as a probe to show the expression of STEAP-1 RNAs in cancer cells. In addition, variant polynucleotide sequences are typically used as primers and probes for the corresponding mRNAs in PCR and Northern analyses (see, e.g., Sawai et al., *Fetal Diagn. Ther.* 1996 November-December 11(6):407-13 and *Current Protocols In Molecular Biology*, Volume 2, Unit 2, Frederick M. Ausubel et al. eds., 1995). Polynucleotide fragments and variants are useful in this context where they are capable of binding to a target polynucleotide sequence (e.g., a STEAP-1 polynucleotide shown in FIG. 2 or variant thereof) under conditions of high stringency.

[0433] Furthermore, PSA polypeptides which contain an epitope that can be recognized by an antibody or T cell that specifically binds to that epitope are used in methods of monitoring PSA. STEAP-1 polypeptide fragments and polypeptide analogs or variants can also be used in an analogous manner. This practice of using polypeptide fragments or polypeptide variants to generate antibodies (such as anti-PSA antibodies or T cells) is typical in the art with a wide variety of systems such as fusion proteins being used by practitioners (see, e.g., *Current Protocols In Molecular Biology*, Volume 2, Unit 16, Frederick M. Ausubel et al. eds., 1995). In this context, each epitope(s) functions to provide the architecture with which an antibody or T cell is reactive. Typically, skilled artisans create a variety of different polypeptide fragments that can be used in order to generate immune responses specific for different portions of a polypeptide of interest (see, e.g., U.S. Pat. No. 5,840,501 and U.S. Pat. No. 5,939,533). For example it may be preferable to utilize a polypeptide comprising one of the

STEAP-1 biological motifs discussed herein or a motif-bearing subsequence which is readily identified by one of skill in the art based on motifs available in the art. Polypeptide fragments, variants or analogs are typically useful in this context as long as they comprise an epitope capable of generating an antibody or T cell specific for a target polypeptide sequence (e.g. a STEAP-1 polypeptide shown in FIG. 3).

[0434] As shown herein, the STEAP-1 polynucleotides and polypeptides (as well as the STEAP-1 polynucleotide probes and anti-STEAP-1 antibodies or T cells used to identify the presence of these molecules) exhibit specific properties that make them useful in diagnosing cancers such as those listed in Table 1. Diagnostic assays that measure the presence of STEAP-1 gene products, in order to evaluate the presence or onset of a disease condition described herein, such as prostate cancer, are used to identify patients for preventive measures or further monitoring, as has been done so successfully with PSA. Moreover, these materials satisfy a need in the art for molecules having similar or complementary characteristics to PSA in situations where, for example, a definite diagnosis of metastasis of prostatic origin cannot be made on the basis of a test for PSA alone (see, e.g., Alanen et al., *Pathol. Res. Pract.* 192(3): 233-237 (1996)), and consequently, materials such as STEAP-1 polynucleotides and polypeptides (as well as the STEAP-1 polynucleotide probes and anti-STEAP-1 antibodies used to identify the presence of these molecules) need to be employed to confirm a metastases of prostatic origin.

[0435] Finally, in addition to their use in diagnostic assays, the STEAP-1 polynucleotides disclosed herein have a number of other utilities such as their use in the identification of oncogenetic associated chromosomal abnormalities in the chromosomal region to which the STEAP-1 gene maps (see the Example entitled "Chromosomal Mapping of STEAP-1" below). Moreover, in addition to their use in diagnostic assays, the STEAP-1-related proteins and polynucleotides disclosed herein have other utilities such as their use in the forensic analysis of tissues of unknown origin (see, e.g., Takahama K *Forensic Sci Int* 1996 Jun. 28; 80(1-2): 63-9).

[0436] Additionally, STEAP-1-related proteins or polynucleotides of the invention can be used to treat a pathologic condition characterized by the over-expression of STEAP-1. For example, the amino acid or nucleic acid sequence of FIG. 2 or FIG. 3, or fragments of either, can be used to generate an immune response to a STEAP-1 antigen. Antibodies or other molecules that react with STEAP-1 can be used to modulate the function of this molecule, and thereby provide a therapeutic benefit.

[0437] XII.) Inhibition of STEAP-1 Protein Function

[0438] The invention includes various methods and compositions for inhibiting the binding of STEAP-1 to its binding partner or its association with other protein(s) as well as methods for inhibiting STEAP-1 function.

[0439] XII.A.) Inhibition of STEAP-1 with Intracellular Antibodies

[0440] In one approach, a recombinant vector that encodes single chain antibodies that specifically bind to STEAP-1 are introduced into STEAP-1 expressing cells via gene transfer technologies. Accordingly, the encoded single chain anti-STEAP-1 antibody is expressed intracellularly, binds to

STEAP-1 protein, and thereby inhibits its function. Methods for engineering such intracellular single chain antibodies are well known. Such intracellular antibodies, also known as "intrabodies", are specifically targeted to a particular compartment within the cell, providing control over where the inhibitory activity of the treatment is focused. This technology has been successfully applied in the art (for review, see Richardson and Marasco, 1995, TIBTECH vol. 13). Intrabodies have been shown to virtually eliminate the expression of otherwise abundant cell surface receptors (see, e.g., Richardson et al., 1995, Proc. Natl. Acad. Sci. USA 92: 3137-3141; Beerli et al., 1994, J. Biol. Chem. 269: 23931-23936; Deshane et al., 1994, Gene Ther. 1: 332-337).

[0441] Single chain antibodies comprise the variable domains of the heavy and light chain joined by a flexible linker polypeptide, and are expressed as a single polypeptide. Optionally, single chain antibodies are expressed as a single chain variable region fragment joined to the light chain constant region. Well-known intracellular trafficking signals are engineered into recombinant polynucleotide vectors encoding such single chain antibodies in order to target precisely the intrabody to the desired intracellular compartment. For example, intrabodies targeted to the endoplasmic reticulum (ER) are engineered to incorporate a leader peptide and, optionally, a C-terminal ER retention signal, such as the KDEL amino acid motif. Intrabodies intended to exert activity in the nucleus are engineered to include a nuclear localization signal. Lipid moieties are joined to intrabodies in order to tether the intrabody to the cytosolic side of the plasma membrane. Intrabodies can also be targeted to exert function in the cytosol. For example, cytosolic intrabodies are used to sequester factors within the cytosol, thereby preventing them from being transported to their natural cellular destination.

[0442] In one embodiment, intrabodies are used to capture STEAP-1 in the nucleus, thereby preventing its activity within the nucleus. Nuclear targeting signals are engineered into such STEAP-1 intrabodies in order to achieve the desired targeting. Such STEAP-1 intrabodies are designed to bind specifically to a particular STEAP-1 domain. In another embodiment, cytosolic intrabodies that specifically bind to a STEAP-1 protein are used to prevent STEAP-1 from gaining access to the nucleus, thereby preventing it from exerting any biological activity within the nucleus (e.g., preventing STEAP-1 from forming transcription complexes with other factors).

[0443] In order to specifically direct the expression of such intrabodies to particular cells, the transcription of the intrabody is placed under the regulatory control of an appropriate tumor-specific promoter and/or enhancer. In order to target intrabody expression specifically to prostate, for example, the PSA promoter and/or promoter/enhancer can be utilized (See, for example, U.S. Pat. No. 5,919,652 issued 6 Jul. 1999).

[0444] XII.B.) Inhibition of STEAP-1 with Recombinant Proteins

[0445] In another approach, recombinant molecules bind to STEAP-1 and thereby inhibit STEAP-1 function. For example, these recombinant molecules prevent or inhibit STEAP-1 from accessing/binding to its binding partner(s) or associating with other protein(s). Such recombinant molecules can, for example, contain the reactive part(s) of a

STEAP-1 specific antibody molecule. In a particular embodiment, the STEAP-1 binding domain of a STEAP-1 binding partner is engineered into a dimeric fusion protein, whereby the fusion protein comprises two STEAP-1 ligand binding domains linked to the Fc portion of a human IgG, such as human IgG1. Such IgG portion can contain, for example, the C_H2 and C_H3 domains and the hinge region, but not the C_H1 domain. Such dimeric fusion proteins are administered in soluble form to patients suffering from a cancer associated with the expression of STEAP-1, whereby the dimeric fusion protein specifically binds to STEAP-1 and blocks STEAP-1 interaction with a binding partner. Such dimeric fusion proteins are further combined into multimeric proteins using known antibody linking technologies.

[0446] XII.C.) Inhibition of STEAP-1 Transcription or Translation

[0447] The present invention also comprises various methods and compositions for inhibiting the transcription of the STEAP-1 gene. Similarly, the invention also provides methods and compositions for inhibiting the translation of STEAP-1 mRNA into protein.

[0448] In one approach, a method of inhibiting the transcription of the STEAP-1 gene comprises contacting the STEAP-1 gene with a STEAP-1 antisense polynucleotide. In another approach, a method of inhibiting STEAP-1 mRNA translation comprises contacting a STEAP-1 mRNA with an antisense polynucleotide. In another approach, a STEAP-1 specific ribozyme is used to cleave a STEAP-1 message, thereby inhibiting translation. Such antisense and ribozyme based methods can also be directed to the regulatory regions of the STEAP-1 gene, such as STEAP-1 promoter and/or enhancer elements. Similarly, proteins capable of inhibiting a STEAP-1 gene transcription factor are used to inhibit STEAP-1 mRNA transcription. The various polynucleotides and compositions useful in the aforementioned methods have been described above. The use of antisense and ribozyme molecules to inhibit transcription and translation is well known in the art.

[0449] Other factors that inhibit the transcription of STEAP-1 by interfering with STEAP-1 transcriptional activation are also useful to treat cancers expressing STEAP-1. Similarly, factors that interfere with STEAP-1 processing are useful to treat cancers that express STEAP-1. Cancer treatment methods utilizing such factors are also within the scope of the invention.

[0450] XII.D.) General Considerations for Therapeutic Strategies

[0451] Gene transfer and gene therapy technologies can be used to deliver therapeutic polynucleotide molecules to tumor cells synthesizing STEAP-1 (i.e., antisense, ribozyme, polynucleotides encoding intrabodies and other STEAP-1 inhibitory molecules). A number of gene therapy approaches are known in the art. Recombinant vectors encoding STEAP-1 antisense polynucleotides, ribozymes, factors capable of interfering with STEAP-1 transcription, and so forth, can be delivered to target tumor cells using such gene therapy approaches.

[0452] The above therapeutic approaches can be combined with any one of a wide variety of surgical, chemotherapy or radiation therapy regimens. The therapeutic

approaches of the invention can enable the use of reduced dosages of chemotherapy (or other therapies) and/or less frequent administration, an advantage for all patients and particularly for those that do not tolerate the toxicity of the chemotherapeutic agent well.

[0453] The anti-tumor activity of a particular composition (e.g., antisense, ribozyme, intrabody), or a combination of such compositions, can be evaluated using various in vitro and in vivo assay systems. In vitro assays that evaluate therapeutic activity include cell growth assays, soft agar assays and other assays indicative of tumor promoting activity, binding assays capable of determining the extent to which a therapeutic composition will inhibit the binding of STEAP-1 to a binding partner, etc.

[0454] In vivo, the effect of a STEAP-1 therapeutic composition can be evaluated in a suitable animal model. For example, xenogenic prostate cancer models can be used, wherein human prostate cancer explants or passaged xenograft tissues are introduced into immune compromised animals, such as nude or SCID mice (Klein et al., 1997, *Nature Medicine* 3: 402-408). For example, PCT Patent Application WO98/16628 and U.S. Pat. No. 6,107,540 describe various xenograft models of human prostate cancer capable of recapitulating the development of primary tumors, micrometastasis, and the formation of osteoblastic metastases characteristic of late stage disease. Efficacy can be predicted using assays that measure inhibition of tumor formation, tumor regression or metastasis, and the like.

[0455] In vivo assays that evaluate the promotion of apoptosis are useful in evaluating therapeutic compositions. In one embodiment, xenografts from tumor bearing mice treated with the therapeutic composition can be examined for the presence of apoptotic foci and compared to untreated control xenograft-bearing mice. The extent to which apoptotic foci are found in the tumors of the treated mice provides an indication of the therapeutic efficacy of the composition.

[0456] The therapeutic compositions used in the practice of the foregoing methods can be formulated into pharmaceutical compositions comprising a carrier suitable for the desired delivery method. Suitable carriers include any material that when combined with the therapeutic composition retains the anti-tumor function of the therapeutic composition and is generally non-reactive with the patient's immune system. Examples include, but are not limited to, any of a number of standard pharmaceutical carriers such as sterile phosphate buffered saline solutions, bacteriostatic water, and the like (see, generally, Remington's *Pharmaceutical Sciences* 16th Edition, A. Osal., Ed., 1980).

[0457] Therapeutic formulations can be solubilized and administered via any route capable of delivering the therapeutic composition to the tumor site. Potentially effective routes of administration include, but are not limited to, intravenous, parenteral, intraperitoneal, intramuscular, intratumor, intradermal, intraorgan, orthotopic, and the like. A preferred formulation for intravenous injection comprises the therapeutic composition in a solution of preserved bacteriostatic water, sterile unpreserved water, and/or diluted in polyvinylchloride or polyethylene bags containing 0.9% sterile Sodium Chloride for Injection, USP. Therapeutic protein preparations can be lyophilized and stored as sterile powders, preferably under vacuum, and then reconstituted in

bacteriostatic water (containing for example, benzyl alcohol preservative) or in sterile water prior to injection.

[0458] Dosages and administration protocols for the treatment of cancers using the foregoing methods will vary with the method and the target cancer, and will generally depend on a number of other factors appreciated in the art.

[0459] XIII.) Kits/Articles of Manufacture

[0460] For use in the diagnostic and therapeutic applications described herein, kits are also within the scope of the invention. Such kits can comprise a carrier, package or container that is compartmentalized to receive one or more containers such as vials, tubes, and the like, each of the container(s) comprising one of the separate elements to be used in the method. For example, the container(s) can comprise a probe that is or can be detectably labeled. Such probe can be an antibody or polynucleotide specific for a FIG. 2-related protein or a FIG. 2 gene or message, respectively. Where the method utilizes nucleic acid hybridization to detect the target nucleic acid, the kit can also have containers containing nucleotide(s) for amplification of the target nucleic acid sequence and/or a container comprising a reporter-means, such as a biotin-binding protein, such as avidin or streptavidin, bound to a reporter molecule, such as an enzymatic, florescent, or radioisotope label. The kit can include all or part of the amino acid sequences in FIG. 2 or FIG. 3 or analogs thereof, or a nucleic acid molecules that encodes such amino acid sequences.

[0461] The kit of the invention will typically comprise the container described above and one or more other containers comprising materials desirable from a commercial and user standpoint, including buffers, diluents, filters, needles, syringes; carrier, package, container, vial and/or tube labels listing contents and/or instructions for use, and package inserts with instructions for use.

[0462] A label can be present on the container to indicate that the composition is used for a specific therapy or non-therapeutic application, such as a diagnostic or laboratory application, and can also indicate directions for either in vivo or in vitro use, such as those described herein. Directions and other information can also be included on an insert(s) or label(s) which is included with or on the kit.

[0463] The terms "kit" and "article of manufacture" can be used as synonyms.

[0464] In another embodiment of the invention, an article(s) of manufacture containing compositions, such as amino acid sequence(s), small molecule(s), nucleic acid sequence(s), and/or antibody(s), e.g., materials useful for the diagnosis, prognosis, prophylaxis and/or treatment of neoplasias of tissues such as those set forth in Table I is provided. The article of manufacture typically comprises at least one container and at least one label. Suitable containers include, for example, bottles, vials, syringes, and test tubes. The containers can be formed from a variety of materials such as glass or plastic. The container can hold amino acid sequence(s), small molecule(s), nucleic acid sequence(s), and/or antibody(s), in one embodiment the container holds a polynucleotide for use in examining the mRNA expression profile of a cell, together with reagents used for this purpose.

[0465] The container can alternatively hold a composition which is effective for treating, diagnosis, prognosing or

prophylaxing a condition and can have a sterile access port (for example the container can be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). The active agents in the composition can be an antibody capable of specifically binding STEAP-1 and modulating the function of STEAP-1.

[0466] The label can be on or associated with the container. A label can be on a container when letters, numbers or other characters forming the label are molded or etched into the container itself; a label can be associated with a container when it is present within a receptacle or carrier that also holds the container, e.g., as a package insert. The label can indicate that the composition is used for diagnosing, treating, prophylaxing or prognosing a condition, such as a neoplasia of a tissue set forth in Table I. The article of manufacture can further comprise a second container comprising a pharmaceutically-acceptable buffer, such as phosphate-buffered saline, Ringer's solution and/or dextrose solution. It can further include other materials desirable from a commercial and user standpoint, including other buffers, diluents, filters, stirrers, needles, syringes, and/or package inserts with indications and/or instructions for use.

EXAMPLES

[0467] Various aspects of the invention are further described and illustrated by way of the several examples that follow, none of which are intended to limit the scope of the invention.

Example 1

SSH-Generated Isolation of cDNA Fragment of the STEAP Gene

Materials and Methods

LAPC Xenografts:

[0468] LAPC xenografts were obtained from Dr. Charles Sawyers (UCLA) and generated as described (Klein et al, 1997, Nature Med. 3: 402-408; Craft et al., 1999, Cancer Res. 59: 5030-5036). Androgen dependent and independent LAPC-4 xenografts (LAPC-4 AD and AI, respectively) and LAPC-9 xenografts (LAPC-9 AD and AI, respectively) were grown in intact male SCID mice or in castrated males, respectively, and were passaged as small tissue chunks in recipient males. LAPC-4 AI xenografts were derived from LAPC-4 AD tumors and LAPC-9 AI xenografts were derived from LAPC-9 AD tumors. To generate the AI xenografts, male mice bearing LAPC AD tumors were castrated and maintained for 2-3 months. After the LAPC tumors re-grew, the tumors were harvested and passaged in castrated males or in female SCID mice.

[0469] LAPC-4 AD xenografts were grown intratibially as follows. LAPC-4 AD xenograft tumor tissue grown subcutaneously was minced into 1-2 mm³ sections while the tissue was bathed in 1× Iscoves medium, minced tissue was then centrifuged at 1.3K rpm for 4 minutes, the supernatant was resuspended in 10 ml ice cold 1× Iscoves medium and centrifuged at 1.3K rpm for 4 minutes. The pellet was then resuspended in 1× Iscoves with 1% pronase E and incubated for 20 minutes at room temperature with mild rocking agitation followed by incubation on ice for 24 minutes. Filtrate was centrifuged at 1.3K rpm for 4 minutes, and the

pronase was removed from the aspirated pellet by resuspending in 10 ml Iscoves and re-centrifuging. Clumps of cells were then plated in PrEGM medium and grown overnight. The cells were then harvested, filtered, washed 2× RPMI, and counted. Approximately 50,000 cells were mixed with an equal volume of ice-cold Matrigel on ice, and surgically injected into the proximal tibial metaphyses of SCID mice via a 27 gauge needle. After 10-12 weeks, LAPC-4 tumors growing in bone marrow were recovered.

Cell Lines and Tissues:

[0470] Human cell lines (e.g., HeLa) were obtained from the ATCC and were maintained in DMEM with 5% fetal calf serum. Human tissues for RNA and protein analyses were obtained from the Human Tissue Resource Center (HTRC) at the UCLA (Los Angeles, Calif.) and from QualTek, Inc. (Santa Barbara, Calif.).

RNA Isolation:

[0471] Tumor tissue and cell lines were homogenized in Trizol reagent (Life Technologies, Gibco BRL) using 10 ml/g tissue or 10 ml/10⁸ cells to isolate total RNA. Poly A RNA was purified from total RNA using Qiagen's Oligotex mRNA Mini and Midi kits. Total and mRNA were quantified by spectrophotometric analysis (O.D. 260/280 nm) and analyzed by gel electrophoresis.

Oligonucleotides:

[0472] The following HPLC purified oligonucleotides were used.

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DPNCDN (cDNA synthesis primer):
5'TTTTGATCAAGCTT303' (SEQ ID NO: 48)

Adaptor 1:
5'CTAATACGACTCACTATAGGGCTCGAGCGGCCCGCCGGGAG3' (SEQ ID NO: 49)
3'GGCCCGTCCTAG5' (SEQ ID NO: 50)

Adaptor 2:
5'GTAATACGACTCACTATAGGGCAGCGTGGTCGCGGCCGAG3' (SEQ ID NO: 51)
3'CGGCTCCTAG5' (SEQ ID NO: 52)

PCR primer 1:
5'CTAATACGACTCACTATAGGGC3' (SEQ ID NO: 53)

Nested primer (NP)1:
5'TCGAGCGGCCCGCCGGGAGGA3' (SEQ ID NO: 54)

Nested primer (NP)2:
5'AGCGTGGTCGCGGCCGAGGA3' (SEQ ID NO: 55)

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Suppression Subtractive Hybridization:

[0473] Suppression Subtractive Hybridization (SSH) was used to identify cDNAs corresponding to genes, which may be up-regulated in androgen dependent prostate cancer compared to benign prostatic hyperplasia (BPH).

[0474] Double stranded cDNAs corresponding to the LAPC-4 AD xenograft (tester) and the BPH tissue (driver) were synthesized from 2 µg of poly(A)+ RNA isolated from

xenograft and BPH tissue, as described above, using CLONTECH's PCR-Select cDNA Subtraction Kit and 1 ng of oligonucleotide RSACDN as primer. First- and second-strand synthesis were carried out as described in the Kit's user manual protocol (CLONTECH Protocol No. PT1117-1, Catalog No. K1804-1). The resulting cDNA was digested with Rsa I for 3 hrs. at 37° C. Digested cDNA was extracted with phenol/chloroform (1:1) and ethanol precipitated.

[0475] Driver cDNA (BPH) was generated by combining in a 4 to 1 ratio Rsa I digested BPH cDNA with digested cDNA from mouse liver, in order to ensure that murine genes were subtracted from the tester cDNA (LAPC-4 AD).

[0476] Tester cDNA (LAPC-4 AD) was generated by diluting 1 µl of Rsa I digested LAPC-4 AD cDNA (400 ng) in 5 µl of water. The diluted cDNA (2 µl, 160 ng) was then ligated to 2 µl of adaptor 1 and adaptor 2 (10 µM), in separate ligation reactions, in a total volume of 10 µl at 16° C. overnight, using 400 u of T4 DNA ligase (CLONTECH). Ligation was terminated with 1 µl of 0.2 M EDTA and heating at 72° C. for 5 min.

[0477] The first hybridization was performed by adding 1.5 µl (600 ng) of driver cDNA to each of two tubes containing 1.5 µl (20 ng) adaptor 1- and adaptor 2-ligated tester cDNA. In a final volume of 4 µl, the samples were overlaid with mineral oil, denatured in an MJ Research thermal cycler at 98° C. for 1.5 minutes, and then were allowed to hybridize for 8 hrs at 68° C. The two hybridizations were then mixed together with an additional 1 µl of fresh denatured driver cDNA and were allowed to hybridize overnight at 68° C. The second hybridization was then diluted in 200 µl of 20 mM Hepes, pH 8.3, 50 mM NaCl, 0.2 mM EDTA, heated at 70° C. for 7 min. and stored at -20° C.

PCR Amplification, Cloning and Sequencing of Gene Fragments Generated from SSH:

[0478] To amplify gene fragments resulting from SSH reactions, two PCR amplifications were performed. In the primary PCR reaction 1 µl of the diluted final hybridization mix was added to 1 µl of PCR primer 1 (10 µM), 0.5 µl dNTP mix (10 µM), 2.5 µl 10× reaction buffer (CLONTECH) and 0.5 µl 50× Advantage cDNA polymerase Mix (CLONTECH) in a final volume of 25 µl. PCR 1 was conducted using the following conditions: 75° C. for 5 min., 94° C. for 25 sec., then 27 cycles of 94° C. for 10 sec, 66° C. for 30 sec, 72° C. for 1.5 min. Five separate primary PCR reactions were performed for each experiment. The products were pooled and diluted 1:10 with water. For the secondary PCR reaction, 1 µl from the pooled and diluted primary PCR reaction was added to the same reaction mix as used for PCR 1, except that primers NP1 and NP2 (10 µM) were used instead of PCR primer 1. PCR 2 was performed using 10-12 cycles of 94° C. for 10 sec, 68° C. for 30 sec, 72° C. for 1.5 minutes. The PCR products were analyzed using 2% agarose gel electrophoresis.

[0479] The PCR products were inserted into pCR2.1 using the T/A vector cloning kit (Invitrogen). Transformed *E. coli* were subjected to blue/white and ampicillin selection. White colonies were picked and arrayed into 96 well plates and were grown in liquid culture overnight. To identify inserts, PCR amplification was performed on 1 ml of bacterial culture using the conditions of PCR1 and NP 1 and NP2 as primers. PCR products were analyzed using 2% agarose gel electrophoresis.

[0480] Bacterial clones were stored in 20% glycerol in a 96 well format. Plasmid DNA was prepared, sequenced, and subjected to nucleic acid homology searches of the GenBank, dbEST, and NCI-CGAP databases.

RT-PCR Expression Analysis:

[0481] First strand cDNAs were generated from 1 µg of mRNA with oligo (dT) 12-18 priming using the Gibco-BRL Superscript Preamplification system. The manufacturer's protocol was used and included an incubation for 50 min at 42° C. with reverse transcriptase followed by RNase H treatment at 37° C. for 20 min. After completing the reaction, the volume was increased to 200 µl with water prior to normalization. First strand cDNAs from 16 different normal human tissues were obtained from Clontech.

[0482] Normalization of the first strand cDNAs from multiple tissues was performed by using the primers 5'atategccgcgtcgtcgtcgacaa3' (SEQ ID NO: 56) and 5'agc-cacacgcagctcattgtagaagg 3' (SEQ ID NO: 57) to amplify β-actin. First strand cDNA (5 µl) was amplified in a total volume of 50 µl containing 0.4 µM primers, 0.2 µM each dNTPs, 1×PCR buffer (Clontech, 10 mM Tris-HCL, 1.5 mM MgCl₂, 50 mM KCl, pH8.3) and 1× KlenTaq DNA polymerase (Clontech). Five µl of the PCR reaction was removed at 18, 20, and 22 cycles and used for agarose gel electrophoresis. PCR was performed using an MJ Research thermal cycler under the following conditions: initial denaturation was at 94° C. for 15 sec, followed by a 18, 20, and 22 cycles of 94° C. for 15, 65° C. for 2 min, 72° C. for 5 sec. A final extension at 72° C. was carried out for 2 min. After agarose gel electrophoresis, the band intensities of the 283 bp β-actin bands from multiple tissues were compared by visual inspection. Dilution factors for the first strand cDNAs were calculated to result in equal β-actin band intensities in all tissues after 22 cycles of PCR. Three rounds of normalization were required to achieve equal band intensities in all tissues after 22 cycles of PCR.

[0483] To determine expression levels of the 8P1D4 gene, 5 µl of normalized first strand cDNA was analyzed by PCR using 25, 30, and 35 cycles of amplification using the following primer pairs:

(SEQ ID NO: 58)
5' ACT TTG TTG ATG ACG AGG ATT GGA 3'

(SEQ ID NO: 59)
5' CAG AAC TTC AGC ACA GAG AGG AAC 3'

Semi quantitative expression analysis was achieved by comparing the PCR products at cycle numbers that give light band intensities.

Results

[0484] Several SSH experiments were conducted as described in the Materials and Methods, supra, and led to the isolation of numerous candidate gene fragment clones. All candidate clones were sequenced and subjected to homology analysis against all sequences in the major public gene and EST databases in order to provide information on the identity of the corresponding gene and to help guide the decision to analyze a particular gene for differential expression. In general, gene fragments which had no homology to any known sequence in any of the searched databases, and

thus considered to represent novel genes, as well as gene fragments showing homology to previously sequenced expressed sequence tags (ESTs), were subjected to differential expression analysis by RT-PCR and/or Northern analysis.

[0485] One of the cDNA clones, designated 8P1D4, was 436 bp in length and showed homology to an EST sequence in the NCI-CGAP tumor gene database. The full length cDNA encoding the 8P1D4 gene was subsequently isolated using this cDNA and re-named STEAP-1. The 8P1D4 cDNA nucleotide sequence corresponds to nucleotide residues 150 through 585 in the STEAP-1 cDNA sequence as shown in **FIG. 1A-B**. Another clone, designated 28P3EI, 561 bp in length showed homology to a number of EST sequences in the NCI-CGAP tumor gene database or in other databases. Part of the 28P3 μ l sequence (356 bp) is identical to an EST derived from human fetal tissue. After the full-length STEAP-1 cDNA was obtained and sequenced, it became apparent that this clone also corresponds to STEAP-1 (more specifically, to residues 622 through the 3' end of the STEAP-1 nucleotide sequence as shown in **FIG. 1**).

[0486] Differential expression analysis by RT-PCR using primers derived from the 8P1D4 cDNA clone showed that the 8P1D4 (STEAP-1) gene is expressed at approximately equal levels in normal prostate and the LAPC-4 and LAPC-9 xenografts. Further RT-PCR expression analysis of first strand cDNAs from 16 normal tissues showed greatest levels of 8P1D4 expression in prostate. Substantially lower level expression in several other normal tissues (i.e., colon, ovary, small intestine, spleen and testis) was detectable only at 30 cycles of amplification in brain, pancreas, colon and small intestine.

Example 2

Isolation of Full Length STEAP-1 Encoding cDNA

[0487] The 436 bp 8P1D4 gene fragment (Example 1) was used to isolate additional cDNAs encoding the 8P1D4/STEAP-1 gene. Briefly, a normal human prostate cDNA library (Clontech) was screened with a labeled probe generated from the 436 bp 8P1D4 cDNA. One of the positive clones, clone 10, is 1195 bp in length and encodes a 339 amino acid protein having nucleotide and encoded amino acid sequences bearing no significant homology to any known human genes or proteins (homology to a rat Kidney Injury Protein recently described in International Application WO98/53071). The encoded protein contains at least 6 predicted transmembrane motifs implying a cell surface orientation (see **FIG. 1A-B**, predicted transmembrane motifs underlined). These structural features led to the designation "STEAP", for "Six Transmembrane Epithelial Antigen of the Prostate".

[0488] Subsequent identification of additional "STEAP" proteins led to the re-designation of the 8P1D4 gene product as "STEAP-1". The STEAP-1 cDNA and encoded amino acid sequences are shown in **FIG. 2A-Q**. STEAP-1 cDNA clone 10 was deposited with the American Type Culture Collection ("ATCC") (10801 University Blvd., Manassas, Va. 20110-2209 USA) as plasmid 8P1D4 clone 10.1 on Aug. 26, 1998 as ATCC Accession Number 98849. The STEAP-1 cDNA clone can be excised therefrom using EcoRI/XbaI double digest (EcoRI at the 5'end, XbaI at the 3'end).

Example 3

Chromosomal Mapping of STEAP-1

[0489] Chromosomal localization can implicate genes in disease pathogenesis. Several chromosome mapping approaches are available including fluorescent in situ hybridization (FISH), human/hamster radiation hybrid (RH) panels (Walter et al., 1994; Nature Genetics 7:22; Research Genetics, Huntsville, Ala.), human-rodent somatic cell hybrid panels such as is available from the Coriell Institute (Camden, N.J.), and genomic viewers utilizing BLAST homologies to sequenced and mapped genomic clones (NCBI, Bethesda, Md.).

[0490] STEAP-1 maps to chromosome 7q2¹ using STEAP-1 sequence and the NCBI BLAST tool: (located on the World Wide Web at (ncbi.nlm.nih.gov/genome/seq/page.cgi?F=HsBlast.html&&ORG=Hs)).

Example 4

Expression Analysis of STEAP-1

[0491] Expression of STEAP-1 in stomach cancer patient specimens is shown in **FIG. 14**. RNA was extracted from normal stomach (N) and from 10 different stomach cancer patient specimens (T). Northern blot with 10 μ g of total RNA/lane was probed with STEAP-1 sequence. Results show strong expression of an approximately 1.6 kb STEAP-1 in the stomach tumor tissues. The lower panel represents ethidium bromide staining of the blot showing quality of the RNA samples.

[0492] **FIG. 15** shows that STEAP-1 was expressed in rectum cancer patient tissues. RNA was extracted from normal rectum (N), rectum cancer patient tumors (T), and rectum cancer metastasis (M). Northern blots with 10 μ g of total RNA were probed with the STEAP-1 sequence. Results show strong expression of STEAP-1 in the rectum cancer patient tissues. The lower panel represents ethidium bromide staining of the blot showing quality of the RNA samples.

[0493] Expression of STEAP-1 by RT-PCR demonstrated that STEAP-1 is strongly expressed in human umbilical vein endothelial cells (HUVEC) (**FIG. 16**). First strand cDNA was prepared from HUVEC cells, LAPC-4AD and LAPC-9AD prostate cancer xenografts, as well as from human brain tissues. Normalization was performed by PCR using primers to actin and GAPDH. Semi-quantitative PCR, using primers to STEAP-1, was performed at 27 and 30 cycles of amplification (**FIG. 16A**). As a control, PCR using primers to actin is shown in **FIG. 16B**. Results show strong expression of STEAP-1 in HUVEC cells similar to the expression detected in prostate cancer xenograft tissues. Expression of STEAP-1 in HUVEC cells indicates that targeting STEAP-1 may also target endothelial cells of the neovasculature of the tumors.

Example 5

Transcript Variants of 8P1D4

[0494] Transcript variants are variants of mature mRNA from the same gene which arise by alternative transcription or alternative splicing. Alternative transcripts are transcripts from the same gene but start transcription at different points. Splice variants are mRNA variants spliced differently from

the same transcript. In eukaryotes, when a multi-exon gene is transcribed from genomic DNA, the initial RNA is spliced to produce functional mRNA, which has only exons and is used for translation into an amino acid sequence. Accordingly, a given gene can have zero to many alternative transcripts and each transcript can have zero to many splice variants. Each transcript variant has a unique exon makeup, and can have different coding and/or non-coding (5' or 3' end) portions, from the original transcript. Transcript variants can code for similar or different proteins with the same or a similar function or can encode proteins with different functions, and can be expressed in the same tissue at the same time, or in different tissues at the same time, or in the same tissue at different times, or in different tissues at different times. Proteins encoded by transcript variants can have similar or different cellular or extracellular localizations, e.g., secreted versus intracellular.

[0495] Transcript variants are identified by a variety of art-accepted methods. For example, alternative transcripts and splice variants are identified by full-length cloning experiment, or by use of full-length transcript and EST sequences. First, all human ESTs were grouped into clusters which show direct or indirect identity with each other. Second, ESTs in the same cluster were further grouped into sub-clusters and assembled into a consensus sequence. The original gene sequence is compared to the consensus sequence(s) or other full-length sequences. Each consensus sequence is a potential splice variant for that gene (see, e.g., Kan, Z., et al., Gene structure prediction and alternative splicing analysis using genomically aligned ESTs, *Genome Research*, 2001 May, 11(5):889-900.) Even when a variant is identified that is not a full-length clone, that portion of the variant is very useful for antigen generation and for further cloning of the full-length splice variant, using techniques known in the art.

[0496] Moreover, computer programs are available in the art that identify transcript variants based on genomic sequences. Genomic-based transcript variant identification programs include FgenesH (A. Salamov and V. Solovyev, "Ab initio gene finding in *Drosophila* genomic DNA," *Genome Research*, 2000 April; 10(4):516-22); Grail (URL compbio.ornl.gov/Grail-bin/EmptyGrailForm) and GenScan (URL genes.mit.edu/GENSCAN.html). For a general discussion of splice variant identification protocols see, e.g., Southan, C., A genomic perspective on human proteases, *FEBS Lett.* 2001 Jun. 8; 498(2-3):214-8; de Souza, S. J., et al., Identification of human chromosome 22 transcribed sequences with ORF expressed sequence tags, *Proc. Natl. Acad. Sci. USA*, 2000 Nov. 7; 97(23):12690-3.

[0497] To further confirm the parameters of a transcript variant, a variety of techniques are available in the art, such as full-length cloning, proteomic validation, PCR-based validation, and 5' RACE validation, etc. (see e.g., Proteomic Validation: Brennan, S. O., et al., Albumin banks peninsula: a new termination variant characterized by electrospray mass spectrometry, *Biochem Biophys. Acta.* 1999 Aug. 17; 1433(1-2):321-6; Ferranti P, et al., Differential splicing of pre-messenger RNA produces multiple forms of mature caprine alpha(s1)-casein, *Eur. J. Biochem.* 1997 Oct. 1; 249(1):1-7. For PCR-based Validation: Wellmann S, et al., Specific reverse transcription-PCR quantification of vascular endothelial growth factor (VEGF) splice variants by LightCycler technology, *Clin. Chem.* 2001 April; 47(4):654-

60; Jia, H. P., et al., Discovery of new human beta-defensins using a genomics-based approach, *Gene*, 2001 Jan. 24; 263(1-2):211-8. For PCR-based and 5' RACE Validation: Brigle, K. E., et al., Organization of the murine reduced folate carrier gene and identification of variant splice forms, *Biochem. Biophys. Acta.* 1997 Aug. 7; 1353(2): 191-8).

[0498] It is known in the art that genomic regions are modulated in cancers. When the genomic region to which a gene maps is modulated in a particular cancer, the alternative transcripts or splice variants of the gene are modulated as well. Disclosed herein is that 8P1D4 has a particular expression profile related to cancer. Alternative transcripts and splice variants of 8P1D4 may also be involved in cancers in the same or different tissues, thus serving as tumor-associated markers/antigens.

[0499] The exon composition of the original transcript, designated as 8P1D4 v.1, is shown in Table LXI. Using the full-length gene and EST sequences, two transcript variants were identified, designated as 8P1D4 v.2 and v.3. Compared with 8P1D4 v.1, transcript variant 8P1D4 v.2 did not splice out intron 4 of 8P1D4 v.1 and variant 8P1D4 v.3 spliced out one additional exon from intron 4 of 8P1D4 v.1, as shown in FIG. 11. Theoretically, each different combination of exons in spatial order, e.g. exons 2 and 3, is a potential splice variant. FIG. 11 shows the schematic alignment of exons of the transcript variants.

[0500] Tables LIII through LX are set forth on a variant by variant bases. Tables LIII and LVII show the nucleotide sequence of the transcript variants. Table LIV shows the alignment of the transcript variant with the nucleic acid sequence of 8P1D4 v.1. Table LVIII shows the alignment of the transcript variant with the nucleic acid sequence of 8P1D4 v.2. Tables LV and LIX lay out amino acid translation of the transcript variant for the identified reading frame orientation. Table LVI displays the alignment of the amino acid sequence encoded by the splice variant with that of 8P1D4 v.1. Table LX displays the alignment of the amino acid sequence encoded by the splice variant with that of 8P1D4 v.2.

Example 6

Single Nucleotide Polymorphisms of 8P1D4

[0501] A Single Nucleotide Polymorphism (SNP) is a single base pair variation in a nucleotide sequence at a specific location. At any given point of the genome, there are four possible nucleotide base pairs: A/T, C/G, G/C and T/A. Genotype refers to the specific base pair sequence of one or more locations in the genome of an individual. Haplotype refers to the base pair sequence of more than one location on the same DNA molecule (or the same chromosome in higher organisms), often in the context of one gene or in the context of several tightly linked genes. SNPs that occur on a cDNA are called cSNPs. These cSNPs may change amino acids of the protein encoded by the gene and thus change the functions of the protein. Some SNPs cause inherited diseases; others contribute to quantitative variations in phenotype and reactions to environmental factors including diet and drugs among individuals. Therefore, SNPs and/or combinations of alleles (called haplotypes) have many applications, including diagnosis of inherited diseases, determination of drug reactions and dosage, identification of genes

responsible for diseases, and analysis of the genetic relationship between individuals (P. Nowotny, J. M. Kwon and A. M. Goate, "SNP analysis to dissect human traits," *Curr. Opin. Neurobiol.* 2001 October; 11(5):637-641; M. Pirmohamed and B. K. Park, "Genetic susceptibility to adverse drug reactions," *Trends Pharmacol. Sci.* 2001 June; 22(6):298-305; J. H. Riley, C. J. Allan, E. Lai and A. Roses, "The use of single nucleotide polymorphisms in the isolation of common disease genes," *Pharmacogenomics*. 2000 February; 1(1):39-47; R. Judson, J. C. Stephens and A. Windemuth, "The predictive power of haplotypes in clinical response," *Pharmacogenomics*. 2000 February; 1(1):15-26).

[0502] SNPs are identified by a variety of art-accepted methods (P. Bean, "The promising voyage of SNP target discovery," *Am. Clin. Lab.* 2001 October-November; 20(9):18-20; K. M. Weiss, "In search of human variation," *Genome Res.* 1998 July; 8(7):691-697; M. M. She, "Enabling large-scale pharmacogenetic studies by high-throughput mutation detection and genotyping technologies," *Clin. Chem.* 2001 February; 47(2):164-172). For example, SNPs are identified by sequencing DNA fragments that show polymorphism by gel-based methods such as restriction fragment length polymorphism (RFLP) and denaturing gradient gel electrophoresis (DGGE). They can also be discovered by direct sequencing of DNA samples pooled from different individuals or by comparing sequences from different DNA samples. With the rapid accumulation of sequence data in public and private databases, one can discover SNPs by comparing sequences using computer programs (Z. Gu, L. Hillier and P. Y. Kwok, "Single nucleotide polymorphism hunting in cyberspace," *Hum. Mutat.* 1998; 12(4):221-225). SNPs can be verified and genotype or haplotype of an individual can be determined by a variety of methods including direct sequencing and high throughput microarrays (P. Y. Kwok, "Methods for genotyping single nucleotide polymorphisms," *Annu. Rev. Genomics Hum. Genet.* 2001; 2:235-258; M. Kokoris, K. Dix, K. Moynihan, J. Mathis, B. Erwin, P. Grass, B. Hines and A. Dueterhoeft, "High-throughput SNP genotyping with the Masscode system," *Mol. Diagn.* 2000 December; 5(4):329-340).

[0503] Using the methods described above, fourteen SNPs were identified in the transcript from clone GTH9, designated as 8P1D4 v.2, at positions 602 (C/G), 386 (C/T), 1087 (T/G), 1447 (T/C), 1621 (A/T), 1625 (G/T), 1716 (C/A), 2358 (C/T), 2646 (T/G), 2859 (T/G), 2908 (A/T), 3006 (G/C), 3107 (C/T), and 3180 (A/T). The transcripts or proteins with alternative alleles were designated as variants 8P1D4 v.4, v.5, v.6, v.7, v.8, v.9, v.10, v.11, v.12, v.13, v.14, v.15, v.16 and v.17, respectively. **FIG. 10** shows the schematic alignment of the SNP variants. **FIG. 12** shows the schematic alignment of protein variants, corresponding to nucleotide variants. These alleles of the SNPs, though shown separately here, can occur in different combinations (haplotypes) and in any one of the transcript variants (such as 8P1D4 v.1 and v.3) that contains the sequence context of the SNPs. E.g., the first two SNPs were also on 8P1D4 v.3 at the same positions, but at 572 and 356, respectively, on 8P1D4 v.1.

Example 7

Production of Recombinant 8P1D4 in Prokaryotic Systems

[0504] To express recombinant 8P1D4 and 8P1D4 variants in prokaryotic cells, the full or partial length 8P1D4 and 8P1D4 variant cDNA sequences are cloned into any one of a variety of expression vectors known in the art. The full length cDNA, or any 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 or more contiguous amino acids from 8P1D4, variants, or analogs thereof are used.

[0505] A. In Vitro Transcription and Translation Constructs:

[0506] pCRII: To generate 8P1D4 sense and anti-sense RNA probes for RNA in situ investigations, pCRII constructs (Invitrogen, Carlsbad Calif.) are generated encoding either all or fragments of the 8P1D4 cDNA. The pCRII vector has Sp6 and T7 promoters flanking the insert to drive the transcription of 8P1D4 RNA for use as probes in RNA in situ hybridization experiments. These probes are used to analyze the cell and tissue expression of 8P1D4 at the RNA level. Transcribed 8P1D4 RNA representing the cDNA amino acid coding region of the 8P1D4 gene is used in in vitro translation systems such as the TnT™ Coupled Reticulolysate System (Promega, Corp., Madison, Wis.) to synthesize 8P1D4 protein.

[0507] B. Bacterial Constructs:

[0508] pGEX Constructs: To generate recombinant 8P1D4 proteins in bacteria that are fused to the Glutathione S-transferase (GST) protein, all or parts of the 8P1D4 cDNA or variants are cloned into the GST-fusion vector of the pGEX family (Amersham Pharmacia Biotech, Piscataway, N.J.). These constructs allow controlled expression of recombinant 8P1D4 protein sequences with GST fused at the amino-terminus and a six histidine epitope (6xHis) at the carboxyl-terminus. The GST and 6xHis tags permit purification of the recombinant fusion protein from induced bacteria with the appropriate affinity matrix and allow recognition of the fusion protein with anti-GST and anti-His antibodies. The 6xHis tag is generated by adding 6 histidine codons to the cloning primer at the 3' end, e.g., of the open reading frame (ORF). A proteolytic cleavage site, such as the PreScission™ recognition site in pGEX-6P-1, may be employed such that it permits cleavage of the GST tag from 8P1D4-related protein. The ampicillin resistance gene and pBR322 origin permits selection and maintenance of the pGEX plasmids in *E. coli*.

[0509] pMAL Constructs: To generate, in bacteria, recombinant 8P1D4 proteins that are fused to maltose-binding protein (MBP), all or parts of the 8P1D4 cDNA protein coding sequence are fused to the MBP gene by cloning into the pMAL-c2X and pMAL-p2X vectors (New England Biolabs, Beverly, Mass.). These constructs allow controlled expression of recombinant 8P1D4 protein sequences with MBP fused at the amino-terminus and a 6xHis epitope tag at the carboxyl-terminus. The MBP and 6xHis tags permit purification of the recombinant protein from induced bacteria with the appropriate affinity matrix and allow recognition of the fusion protein with anti-MBP and anti-His antibodies. The 6xHis epitope tag is generated by adding 6

histidine codons to the 3' cloning primer. A Factor Xa recognition site permits cleavage of the pMAL tag from 8P1D4. The pMAL-c2X and pMAL-p2X vectors are optimized to express the recombinant protein in the cytoplasm or periplasm respectively. Periplasm expression enhances folding of proteins with disulfide bonds.

[0510] pET Constructs: To express 8P1D4 in bacterial cells, all or parts of the 8P1D4 cDNA protein coding sequence are cloned into the pET family of vectors (Novagen, Madison, Wis.). These vectors allow tightly controlled expression of recombinant 8P1D4 protein in bacteria with and without fusion to proteins that enhance solubility, such as NusA and thioredoxin (Trx), and epitope tags, such as 6xHis and S-Tag™ that aid purification and detection of the recombinant protein. For example, constructs are made utilizing pET NusA fusion system 43.1 such that regions of the 8P1D4 protein are expressed as amino-terminal fusions to NusA.

[0511] C. Yeast Constructs:

[0512] pESC Constructs: To express 8P1D4 in the yeast species *Saccharomyces cerevisiae* for generation of recombinant protein and functional studies, all or parts of the 8P1D4 cDNA protein coding sequence are cloned into the pESC family of vectors each of which contain 1 of 4 selectable markers, HIS3, TRP1, LEU2, and URA3 (Stratagene, La Jolla, Calif.). These vectors allow controlled expression from the same plasmid of up to 2 different genes or cloned sequences containing either Flag™ or Myc epitope tags in the same yeast cell. This system is useful to confirm protein-protein interactions of 8P1D4. In addition, expression in yeast yields similar post-translational modifications, such as glycosylations and phosphorylations, that are found when expressed in eukaryotic cells.

[0513] pESP Constructs: To express 8P1D4 in the yeast species *Saccharomyces pombe*, all or parts of the 8P1D4 cDNA protein coding sequence are cloned into the pESP family of vectors. These vectors allow controlled high level of expression of a 8P1D4 protein sequence that is fused at either the amino terminus or at the carboxyl terminus to GST which aids purification of the recombinant protein. A Flag™ epitope tag allows detection of the recombinant protein with anti-Flag™ antibody.

Example 8

Production of Recombinant STEAP-1 in Eukaryotic Systems

[0514] A. Mammalian Constructs:

[0515] To express recombinant STEAP-1 in eukaryotic cells, the full or partial length STEAP-1 cDNA sequences can be cloned into any one of a variety of expression vectors known in the art. One or more of the following regions of STEAP-1 are expressed in these constructs, amino acids 1 to 339 of STEAP-1 v.1, v.4, amino acids 1 to 258 of v.2, amino acids 1 to 282 of v.3, or any 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50 or more contiguous amino acids from STEAP-1, variants, or analogs thereof. In certain embodiments a region of a specific variant of STEAP-1 is expressed that encodes an amino acid at a specific position which differs from the

amino acid of any other variant found at that position. In other embodiments, a region of a variant of STEAP-1 is expressed that lies partly or entirely within a sequence that is unique to that variant.

[0516] The constructs can be transfected into any one of a wide variety of mammalian cells such as 293T cells. Transfected 293T cell lysates can be probed with the anti-STEAP-1 polyclonal serum, described herein.

[0517] pcDNA4/HisMax Constructs: To express STEAP-1 in mammalian cells, a STEAP-1 ORF, or portions thereof, of STEAP-1 are cloned into pcDNA4/HisMax Version A (Invitrogen, Carlsbad, Calif.). Protein expression is driven from the cytomegalovirus (CMV) promoter and the SP 16 translational enhancer. The recombinant protein has Xpress™ and six histidine (6xHis) epitopes fused to the amino-terminus. The pcDNA4/HisMax vector also contains the bovine growth hormone (BGH) polyadenylation signal and transcription termination sequence to enhance mRNA stability along with the SV40 origin for episomal replication and simple vector rescue in cell lines expressing the large T antigen. The Zeocin resistance gene allows for selection of mammalian cells expressing the protein and the ampicillin resistance gene and ColE1 origin permits selection and maintenance of the plasmid in *E. coli*.

[0518] pcDNA3.1/MycHis Constructs: To express STEAP-1 in mammalian cells, a STEAP-1 ORF, or portions thereof, of STEAP-1 with a consensus Kozak translation initiation site was cloned into pcDNA3.1/MycHis Version A (Invitrogen, Carlsbad, Calif.). Protein expression is driven from the cytomegalovirus (CMV) promoter. The recombinant proteins have the myc epitope and 6xHis epitope fused to the carboxyl-terminus. The pcDNA3.1/MycHis vector also contains the bovine growth hormone (BGH) polyadenylation signal and transcription termination sequence to enhance mRNA stability, along with the SV40 origin for episomal replication and simple vector rescue in cell lines expressing the large T antigen. The Neomycin resistance gene was used, as it allows for selection of mammalian cells expressing the protein and the ampicillin resistance gene and ColE1 origin permits selection and maintenance of the plasmid in *E. coli*.

[0519] pcDNA3.1/CT-GFP-TOPO Construct: To express STEAP-1 in mammalian cells and to allow detection of the recombinant proteins using fluorescence, a STEAP-1 ORF, or portions thereof, with a consensus Kozak translation initiation site are cloned into pcDNA3.1/CT-GFP-TOPO (Invitrogen, Calif.). Protein expression is driven from the cytomegalovirus (CMV) promoter. The recombinant proteins have the Green Fluorescent Protein (GFP) fused to the carboxyl-terminus facilitating non-invasive, in vivo detection and cell biology studies. The pcDNA3.1/CT-GFP-TOPO vector also contains the bovine growth hormone (BGH) polyadenylation signal and transcription termination sequence to enhance mRNA stability along with the SV40 origin for episomal replication and simple vector rescue in cell lines expressing the large T antigen. The Neomycin resistance gene allows for selection of mammalian cells that express the protein, and the ampicillin resistance gene and ColE1 origin permits selection and maintenance of the plasmid in *E. coli*. Additional constructs with an amino-terminal GFP fusion are made in pcDNA3.1/NT-GFP-TOPO spanning the entire length of a STEAP-1 protein.

[0520] PAPTAg: A STEAP-1 ORF, or portions thereof, is cloned into pAPTAg-5 (GenHunter Corp. Nashville, Tenn.). This construct generates an alkaline phosphatase fusion at the carboxyl-terminus of a STEAP-1 protein while fusing the IgGK signal sequence to the amino-terminus. Constructs are also generated in which alkaline phosphatase with an amino-terminal IgGK signal sequence is fused to the amino-terminus of a STEAP-1 protein. The resulting recombinant STEAP-1 proteins are optimized for secretion into the media of transfected mammalian cells and can be used to identify proteins such as ligands or receptors that interact with STEAP-1 proteins. Protein expression is driven from the CMV promoter and the recombinant proteins also contain myc and 6×His epitopes fused at the carboxyl-terminus that facilitates detection and purification. The Zeocin resistance gene present in the vector allows for selection of mammalian cells expressing the recombinant protein and the ampicillin resistance gene permits selection of the plasmid in *E. coli*.

[0521] pTag5: A STEAP-1 ORF, or portions thereof, was cloned into pTag-5. This vector is similar to pAPTAg but without the alkaline phosphatase fusion. This construct generated STEAP-1 protein with an amino-terminal IgGK signal sequence and myc and 6×His epitope tags at the carboxyl-terminus that facilitate detection and affinity purification. The resulting recombinant STEAP-1 protein was optimized for secretion into the media of transfected mammalian cells, and is used as immunogen or ligand to identify proteins such as ligands or receptors that interact with the STEAP-1 proteins. Protein expression was driven from the CMV promoter. The Zeocin resistance gene present in the vector allowed for selection of mammalian cells expressing the protein, and the ampicillin resistance gene permits selection of the plasmid in *E. coli*.

[0522] PsecFc: A STEAP-1 ORF, or portions thereof, was also cloned into psecFc. The psecFc vector was assembled by cloning the human immunoglobulin G1 (IgG) Fc (hinge, CH2, CH3 regions) into pSecTag2 (Invitrogen, California). This construct generated an IgG1 Fc fusion at the carboxyl-terminus of the STEAP-1 proteins, while fusing the IgGK signal sequence to N-terminus. STEAP-1 fusions utilizing the murine IgG1 Fc region are also used. The resulting recombinant STEAP-1 proteins were optimized for secretion into the media of transfected mammalian cells, and can be used as immunogens or to identify proteins such as ligands or receptors that interact with STEAP-1 protein. Protein expression is driven from the CMV promoter. The hygromycin resistance gene present in the vector allowed for selection of mammalian cells that express the recombinant protein, and the ampicillin resistance gene permits selection of the plasmid in *E. coli*.

[0523] pSRα Constructs: To generate mammalian cell lines that express STEAP-1 constitutively, STEAP-1 ORF, or portions thereof, of STEAP-1 were cloned into pSRα constructs. Amphotropic and ecotropic retroviruses were generated by transfection of pSRα constructs into the 293T-10A1 packaging line or co-transfection of pSRα and a helper plasmid (containing deleted packaging sequences) into the 293 cells, respectively. The retrovirus was used to infect a variety of mammalian cell lines, resulting in the integration of the cloned gene, STEAP-1, into the host cell-lines. Protein expression was driven from a long terminal repeat (LTR). The Neomycin resistance gene present in the vector allowed for selection of mammalian cells that

express the protein, and the ampicillin resistance gene and ColE1 origin permit selection and maintenance of the plasmid in *E. coli*. The retroviral vectors were thereafter be used for infection and generation of various cell lines using, for example, PC3, NIH 3T3, TsuPr1, 293 or rat-1 cells.

[0524] Additional pSRα constructs are made that fuse an epitope tag such as the FLAG™ tag to the carboxyl-terminus of STEAP-1 sequences to allow detection using anti-Flag antibodies. For example, the FLAG™ sequence 5' gat tac aag gat gac gac gat aag 3' (SEQ ID NO: 60) is added to cloning primer at the 3' end of the ORF. Additional pSRα constructs were made to produce both amino-terminal and carboxyl-terminal GFP and myc/6×His fusion proteins of the full-length STEAP-1 proteins.

[0525] Additional Viral Vectors: Additional constructs are made for viral-mediated delivery and expression of STEAP-1. High virus titer leading to high level expression of STEAP-1 is achieved in viral delivery systems such as adenoviral vectors and herpes amplicon vectors. A STEAP-1 coding sequences or fragments thereof are amplified by PCR and subcloned into the AdEasy shuttle vector (Stratagene). Recombination and virus packaging are performed according to the manufacturer's instructions to generate adenoviral vectors. Alternatively, STEAP-1 coding sequences or fragments thereof are cloned into the HSV-1 vector (Imgenex) to generate herpes viral vectors. The viral vectors are thereafter used for infection of various cell lines such as PC3, NIH 3T3, 293 or rat-1 cells.

[0526] Regulated Expression Systems: To control expression of STEAP-1 in mammalian cells, coding sequences of STEAP-1, or portions thereof, are cloned into regulated mammalian expression systems such as the T-Rex System (Invitrogen), the GeneSwitch System (Invitrogen) and the tightly-regulated Ecdysone System (Stratagene). These systems allow the study of the temporal and concentration dependent effects of recombinant STEAP-1. These vectors are thereafter used to control expression of STEAP-1 in various cell lines such as PC3, NIH 3T3, 293 or rat-1 cells.

[0527] B. Baculovirus Expression Systems

[0528] To generate recombinant STEAP-1 proteins in a baculovirus expression system, STEAP-1 ORF, or portions thereof, are cloned into the baculovirus transfer vector pBlueBac 4.5 (Invitrogen), which provides a His-tag at the N-terminus. Specifically, pBlueBac-STEAP-1 is co-transfected with helper plasmid pBac-N-Blue (Invitrogen) into SF9 (*Spodoptera frugiperda*) insect cells to generate recombinant baculovirus (see Invitrogen instruction manual for details). Baculovirus is then collected from cell supernatant and purified by plaque assay. Recombinant STEAP-1 protein is then generated by infection of HighFive insect cells (Invitrogen) with purified baculovirus. Recombinant STEAP-1 protein can be detected using anti-STEAP-1 or anti-His-tag antibody. STEAP-1 protein can be purified and used in various cell-based assays or as immunogen to generate polyclonal and monoclonal antibodies specific for STEAP-1.

Example 9

Antigenicity Profiles and Secondary Structure

[0529] FIGS. 5-9 and FIGS. 5a-9a depict graphically five amino acid profiles of the 8P1D4 variants 1 and 3 respec-

tively, each assessment available by accessing the ProtScale website (URL www.expasy.ch/cgi-bin/protscale.pl) on the ExPasy molecular biology server.

[0530] These profiles: **FIG. 5**, Hydrophilicity, (Hopp T. P., Woods K. R., 1981. *Proc. Natl. Acad. Sci. U.S.A.* 78:3824-3828); **FIG. 6**, Hydropathicity, (Kyte J., Doolittle R. F., 1982. *J. Mol. Biol.* 157:105-132); **FIG. 7**, Percentage Accessible Residues (Janin J., 1979 *Nature* 277:491-492); **FIG. 8**, Average Flexibility, (Bhaskaran R., and Ponnuswamy P. K., 1988. *Int. J. Pept. Protein Res.* 32:242-255); **FIG. 9**, Beta-turn (Deleage, G., Roux B. 1987 *Protein Engineering* 1:289-294); and optionally others available in the art, such as on the ProtScale website, were used to identify antigenic regions of the 8P1D4 protein. Each of the above amino acid profiles of 8P1D4 were generated using the following ProtScale parameters for analysis: 1) A window size of 9; 2) 100% weight of the window edges compared to the window center; and, 3) amino acid profile values normalized to lie between 0 and 1.

[0531] Hydrophilicity (**FIG. 5**), Hydropathicity (**FIG. 6**) and Percentage Accessible Residues (**FIG. 7**) profiles were used to determine stretches of hydrophilic amino acids (i.e., values greater than 0.5 on the Hydrophilicity and Percentage Accessible Residues profile, and values less than 0.5 on the Hydropathicity profile). Such regions are likely to be exposed to the aqueous environment, be present on the surface of the protein, and thus available for immune recognition, such as by antibodies.

[0532] Average Flexibility (**FIG. 8**) and Beta-turn (**FIG. 9**) profiles determine stretches of amino acids (i.e., values greater than 0.5 on the Beta-turn profile and the Average Flexibility profile) that are not constrained in secondary structures such as beta sheets and alpha helices. Such regions are also more likely to be exposed on the protein and thus accessible to immune recognition, such as by antibodies.

[0533] Antigenic sequences of the 8P1D4 protein and of the variant proteins indicated, e.g., by the profiles set forth in **FIG. 5**, **FIG. 6**, **FIG. 7**, **FIG. 8**, and/or **FIG. 9** are used to prepare immunogens, either peptides or nucleic acids that encode them, to generate therapeutic and diagnostic anti-8P1D4 antibodies. The immunogen can be any 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50 or more than 50 contiguous amino acids, or the corresponding nucleic acids that encode them, from the 8P1D4 protein variants listed in **FIGS. 2 and 3**. In particular, peptide immunogens of the invention can comprise, a peptide region of at least 5 amino acids of **FIGS. 2 and 3** in any whole number increment that includes an amino acid position having a value greater than 0.5 in the Hydrophilicity profile of **FIG. 5**; a peptide region of at least 5 amino acids of **FIGS. 2 and 3** in any whole number increment that includes an amino acid position having a value less than 0.5 in the Hydropathicity profile of **FIG. 6**; a peptide region of at least 5 amino acids of **FIGS. 2 and 3** in any whole number increment that includes an amino acid position having a value greater than 0.5 in the Percent Accessible Residues profile of **FIG. 7**; a peptide region of at least 5 amino acids of **FIGS. 2 and 3** in any whole number increment that includes an amino acid position having a value greater than 0.5 in the Average Flexibility profile on **FIG. 8**; and, a peptide region of at least 5 amino acids of

FIGS. 2 and 3 in any whole number increment that includes an amino acid position having a value greater than 0.5 in the Beta-turn profile of **FIG. 9**. Peptide immunogens of the invention can also comprise nucleic acids that encode any of the forgoing.

[0534] All immunogens of the invention, peptide or nucleic acid, can be embodied in human unit dose form, or comprised by a composition that includes a pharmaceutical excipient compatible with human physiology.

[0535] The secondary structures of 8P1D4 variant 1 and variant 3, namely the predicted presence and location of alpha helices, extended strands, and random coils, are predicted from the respective primary amino acid sequences using the HNN—Hierarchical Neural Network method (Guermeur, 1997, http://pbil.ibcp.fr/cgi-bin/npsa_automat.pl?page=npsa_nn.html), accessed from the ExPasy molecular biology server (<http://www.expasy.ch/tools/>). The analysis indicates that 8P1D4 variant 1 is composed of 64.60% alpha helix, 4.72% extended strand, and 30.68% random coil (**FIG. 13a**). 8P1D4 variant 2 is composed of 62.79% alpha helix, 3.10% extended strand, and 34.11% random coil (**FIG. 13b**). 8P1D4 variant 3 is composed of 58.87% alpha helix, 5.32% extended strand, and 35.82% random coil (**FIG. 13c**).

[0536] Analysis for the potential presence of transmembrane domains in 8P1D4 variants were carried out using a variety of transmembrane prediction algorithms accessed from the ExPasy molecular biology server (<http://www.expasy.ch/tools/>). Shown graphically are the results of analysis of variant 1 depicting the presence and location of 6 transmembrane domains using the TMpred program (**FIG. 13d**) and TMHMM program (**FIG. 13e**). Also shown are the results of analysis of variant 2 depicting the presence and location of 4 transmembrane domains using TMpred (**FIG. 13f**) and 3 transmembrane domains using TMHMM (**FIG. 13g**). Analysis of variant 3 predicts the presence of 4 transmembrane domains using the TMpred (Figure h) and 3 transmembrane domains with TMHMM (**FIG. 13i**). The results of each program, namely the amino acids encoding the transmembrane domains are summarized in Table XX.

Example 10

Generation of 8P1D4 Polyclonal Antibodies

[0537] Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. In addition to immunizing with the full length 8P1D4 protein, computer algorithms are employed in design of immunogens that, based on amino acid sequence analysis contain characteristics of being antigenic and available for recognition by the immune system of the immunized host (see the Example entitled "Antigenicity Profiles"). Such regions would be predicted to be hydrophilic, flexible, in beta-turn conformations, and be exposed on the surface of the protein (see, e.g., **FIG. 5**, **FIG. 6**, **FIG. 7**, **FIG. 8**, or **FIG. 9** for amino acid profiles that indicate such regions of 8P1D4 and variants).

[0538] For example, 8P1D4 recombinant bacterial fusion proteins or peptides containing hydrophilic, flexible, beta-

turn regions of 8P1D4 variant proteins are used as antigens to generate polyclonal antibodies in New Zealand White rabbits. For example, such regions include, but are not limited to, amino acids 1-40, amino acids 143-165, amino acids 180-220, of 8P1D4 variants 1, 2, and 3, amino acids 312-339 of 8P1D4 variant 1, and amino acids 250-282 of 8P1D4 variant 3. It is useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include, but are not limited to, keyhole limpet hemocyanin (KLH), serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. In one embodiment, a peptide encoding amino acids 250-282 of 8P1D4 variant 3 is conjugated to KLH and used to immunize a rabbit. Alternatively the immunizing agent may include all or portions of the 8P1D4 variant proteins, analogs or fusion proteins thereof. For example, the 8P1D4 variant 1 amino acid sequence can be fused using recombinant DNA techniques to any one of a variety of fusion protein partners that are well known in the art, such as glutathione-S-transferase (GST) and HIS tagged fusion proteins. Such fusion proteins are purified from induced bacteria using the appropriate affinity matrix.

[0539] In one embodiment, a GST-fusion protein encoding amino acids 250-282, encompassing the second predicted extracellular loop, is produced, purified, and used as immunogen. Other recombinant bacterial fusion proteins that may be employed include maltose binding protein, LacZ, thioredoxin, NusA, or an immunoglobulin constant region (see the section entitled "Production of 8P1D4 in Prokaryotic Systems" and Current Protocols In Molecular Biology, Volume 2, Unit 16, Frederick M. Ausubul et al. eds., 1995; Linsley, P. S., Brady, W., Urnes, M., Grosmaire, L., Damle, N., and Ledbetter, L. (1991) J. Exp. Med. 174, 561-566).

[0540] In addition to bacterial derived fusion proteins, mammalian expressed protein antigens are also used. These antigens are expressed from mammalian expression vectors such as the Tag5 and Fc-fusion vectors (see the Example entitled "Production of Recombinant 8P1D4 in Eukaryotic Systems"), and retain post-translational modifications such as glycosylations found in native protein. In one embodiment, the predicted extracellular loop of variant 1, amino acids 185-218, is cloned into the Tag5 mammalian secretion vector. The recombinant protein is purified by metal chelate chromatography from tissue culture supernatants of 293T cells stably expressing the recombinant vector. The purified Tag5 8P1D4 protein is then used as immunogen.

[0541] During the immunization protocol, it is useful to mix or emulsify the antigen in adjuvants that enhance the immune response of the host animal. Examples of adjuvants include, but are not limited to, complete Freund's adjuvant (CFA) and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).

[0542] In a typical protocol, rabbits are initially immunized subcutaneously with up to 200 µg, typically 100-200 µg, of fusion protein or peptide conjugated to KLH mixed in complete Freund's adjuvant (CFA). Rabbits are then injected subcutaneously every two weeks with up to 200 µg, typically 100-200 µg, of the immunogen in incomplete Freund's adjuvant (IFA). Test bleeds are taken approximately 7-10 days following each immunization and used to monitor the titer of the antiserum by ELISA.

[0543] To test reactivity and specificity of immune serum, such as the rabbit serum derived from immunization with a

KLH-conjugated peptide encoding amino acids 250-282 of variant 3, the full-length 8P1D4 variant 1 cDNA is cloned into pcDNA 3.1 myc-his expression vector (Invitrogen, see the Example entitled "Production of Recombinant 8P1D4 in Eukaryotic Systems"). After transfection of the constructs into 293T cells, cell lysates are probed with the anti-8P1D4 serum and with anti-His antibody (Santa Cruz Biotechnologies, Santa Cruz, Calif.) to determine specific reactivity to denatured 8P1D4 protein using the Western blot technique. The immune serum is then tested by the Western blot technique against 293T-8P1D4 cells. In addition, the immune serum is tested by fluorescence microscopy, flow cytometry and immunoprecipitation against 293T and other recombinant 8P1D4-expressing cells to determine specific recognition of native protein. Western blot, immunoprecipitation, fluorescent microscopy, and flow cytometric techniques using cells that endogenously express 8P1D4 are also carried out to test reactivity and specificity.

[0544] Anti-serum from rabbits immunized with 8P1D4 variant fusion proteins, such as GST and MBP fusion proteins, are purified by depletion of antibodies reactive to the fusion partner sequence by passage over an affinity column containing the fusion partner either alone or in the context of an irrelevant fusion protein. For example, antiserum derived from a GST-8P1D4 fusion protein encoding amino acids 250-282 of variant 3 is first purified by passage over a column of GST protein covalently coupled to AffiGel matrix (BioRad, Hercules, Calif.). The antiserum is then affinity purified by passage over a column composed of a MBP-fusion protein also encoding amino acids 250-282 covalently coupled to AffiGel matrix. The serum is then further purified by protein G affinity chromatography to isolate the IgG fraction. Sera from other His-tagged antigens and peptide immunized rabbits as well as fusion partner depleted sera are affinity purified by passage over a column matrix composed of the original protein immunogen or free peptide.

Example 11

Generation of 8P1D4 Monoclonal Antibodies (mAbs)

[0545] In one embodiment, therapeutic mAbs to 8P1D4 variants comprise those that react with epitopes specific for each variant protein or specific to sequences in common between the variants that would disrupt or modulate the biological function of the 8P1D4 variants, for example those that would disrupt the interaction with ligands and substrates or disrupt its biological activity. Immunogens for generation of such mAbs include those designed to encode or contain the entire 8P1D4 protein variant sequence, regions of the 8P1D4 protein variants predicted to be antigenic from computer analysis of the amino acid sequence (see, e.g., FIG. 5, FIG. 6, FIG. 7, FIG. 8, or FIG. 9, and the Example entitled "Antigenicity Profiles"). Immunogens include peptides, recombinant bacterial proteins, and mammalian expressed Tag 5 proteins and human and murine IgG FC fusion proteins. In addition, cells engineered to express high levels of a respective 8P1D4 variant, such as 293T-8P1D4 variant 1 or 300.19-8P1D4 variant 1 murine Pre-B cells, are used to immunize mice.

[0546] To generate mAbs to an 8P1D4 variant, mice are first immunized intraperitoneally (IP) with, typically, 10-50

μg of protein immunogen or 10⁷ 8P1D4-expressing cells mixed in complete Freund's adjuvant. Mice are then subsequently immunized IP every 2-4 weeks with, typically, 10-50 μg of protein immunogen or 10⁷ cells mixed in incomplete Freund's adjuvant. Alternatively, MPL-TDM adjuvant is used in immunizations. In addition to the above protein and cell-based immunization strategies, a DNA-based immunization protocol is employed in which a mammalian expression vector encoding an 8P1D4 variant sequence is used to immunize mice by direct injection of the plasmid DNA. For example amino acids 185-218, is cloned into the Tag5 mammalian secretion vector and the recombinant vector is used as immunogen. In another example the same amino acids are cloned into an Fc-fusion secretion vector in which the 8P1D4 variant 1 sequence is fused at the amino-terminus to an IgK leader sequence and at the carboxyl-terminus to the coding sequence of the human or murine IgG Fc region. This recombinant vector is then used as immunogen. The plasmid immunization protocols are used in combination with purified proteins expressed from the same vector and with cells expressing the respective 8P1D4 variant.

[0547] During the immunization protocol, test bleeds are taken 7-10 days following an injection to monitor titer and specificity of the immune response. Once appropriate reactivity and specificity is obtained as determined by ELISA, Western blotting, immunoprecipitation, fluorescence microscopy, and flow cytometric analyses, fusion and hybridoma generation is then carried out with established procedures well known in the art (see, e.g., Harlow and Lane, 1988).

[0548] In one embodiment for generating 8P1D4 variant 3 specific monoclonal antibodies, a GST-8P1D4 variant 3 antigen encoding amino acids 250-282, is expressed and purified from bacteria. Balb C mice are initially immunized intraperitoneally with 25 μg of the GST-8P1D4 variant 3 protein mixed in complete Freund's adjuvant. Mice are subsequently immunized every two weeks with 25 μg of the antigen mixed in incomplete Freund's adjuvant for a total of three immunizations. ELISA using an MBP-fusion protein encoding amino acids 250-282 determines the titer of serum from immunized mice. Reactivity and specificity of serum to full length 8P1D4 variant 3 protein is monitored by Western blotting, immunoprecipitation and flow cytometry using 293T cells transfected with an expression vector encoding the 8P1D4 variant 3 cDNA compared to cells transfected with variant 1 and 2 cDNA (see e.g., the Example entitled "Production of Recombinant 8P1D4 in Eukaryotic Systems"). Other recombinant 8P1D4 variant 3-expressing cells or cells endogenously expressing 8P1D4 variant 3 are also used. Mice showing the strongest specific reactivity to 8P1D4 variant 3 are rested and given a final injection of GST-antigen in PBS and then sacrificed four days later. The spleens of the sacrificed mice are harvested and fused to SPO/2 myeloma cells using standard procedures (Harlow and Lane, 1988). Supernatants from HAT selected growth wells are screened by ELISA, Western blot, immunoprecipitation, fluorescent microscopy, and flow cytometry to identify 8P1D4 specific antibody-producing clones. The binding affinity of a 8P1D4 monoclonal antibody is determined using standard technologies. Affinity measurements quantify the strength of antibody to epitope binding and are used to help define which 8P1D4 monoclonal antibodies preferred for diagnostic or therapeutic use, as appreciated by one of

skill in the art. The BIAcore system (Uppsala, Sweden) is a preferred method for determining binding affinity. The BIAcore system uses surface plasmon resonance (SPR, Welford K. 1991, Opt. Quant. Elect. 23:1; Morton and Myszk, 1998, Methods in Enzymology 295: 268) to monitor biomolecular interactions in real time. BIAcore analysis conveniently generates association rate constants, dissociation rate constants, equilibrium dissociation constants, and affinity constants.

Example 12

HLA Class I and Class II Binding Assays

[0549] HLA class I and class II binding assays using purified HLA molecules are performed in accordance with disclosed protocols (e.g., PCT publications WO 94/20127 and WO 94/03205; Sidney et al., *Current Protocols in Immunology* 18.3.1 (1998); Sidney, et al., *J. Immunol.* 154:247 (1995); Sette, et al., *Mol. Immunol.* 31:813 (1994)). Briefly, purified MHC molecules (5 to 500 nM) are incubated with various unlabeled peptide inhibitors and 1-10 nM ¹²⁵I-radiolabeled probe peptides as described. Following incubation, MHC-peptide complexes are separated from free peptide by gel filtration and the fraction of peptide bound is determined. Typically, in preliminary experiments, each MHC preparation is titrated in the presence of fixed amounts of radiolabeled peptides to determine the concentration of HLA molecules necessary to bind 10-20% of the total radioactivity. All subsequent inhibition and direct binding assays are performed using these HLA concentrations.

[0550] Since under these conditions [label]<[HLA] and IC₅₀≅[HLA], the measured IC₅₀ values are reasonable approximations of the true K_D values. Peptide inhibitors are typically tested at concentrations ranging from 120 μg/ml to 1.2 ng/ml, and are tested in two to four completely independent experiments. To allow comparison of the data obtained in different experiments, a relative binding figure is calculated for each peptide by dividing the IC₅₀ of a positive control for inhibition by the IC₅₀ for each tested peptide (typically unlabeled versions of the radiolabeled probe peptide). For database purposes, and inter-experiment comparisons, relative binding values are compiled. These values can subsequently be converted back into IC₅₀ nM values by dividing the IC₅₀ nM of the positive controls for inhibition by the relative binding of the peptide of interest. This method of data compilation is accurate and consistent for comparing peptides that have been tested on different days, or with different lots of purified MHC.

[0551] Binding assays as outlined above may be used to analyze HLA supermotif and/or HLA motif-bearing peptides (see Table IV).

Example 13

Identification of HLA Supermotif- and Motif-Bearing CTL Candidate Epitopes

[0552] HLA vaccine compositions of the invention can include multiple epitopes. The multiple epitopes can comprise multiple HLA supermotifs or motifs to achieve broad population coverage. This example illustrates the identification and confirmation of supermotif- and motif-bearing epitopes for the inclusion in such a vaccine composition. Calculation of population coverage is performed using the strategy described below.

[0553] Computer Searches and Algorithms for Identification of Supermotif and/or Motif-Bearing Epitopes

[0554] The searches performed to identify the motif-bearing peptide sequences in the Example entitled "Antigenicity Profiles" and Tables V-XVIII and XXII-LI employ the protein sequence data from the gene product of STEAP-1 set forth in FIGS. 2 and 3, the specific peptides used to generate the tables are listed in Table LXI.

[0555] Computer searches for epitopes bearing HLA Class I or Class II supermotifs or motifs are performed as follows. All translated STEAP-1 protein sequences are analyzed using a text string search software program to identify potential peptide sequences containing appropriate HLA binding motifs; such programs are readily produced in accordance with information in the art in view of known motif/supermotif disclosures. Furthermore, such calculations can be made mentally.

[0556] Identified A2-, A3-, and DR-supermotif sequences are scored using polynomial algorithms to predict their capacity to bind to specific HLA-Class I or Class II molecules. These polynomial algorithms account for the impact of different amino acids at different positions, and are essentially based on the premise that the overall affinity (or ΔG) of peptide-HLA molecule interactions can be approximated as a linear polynomial function of the type:

$$^{\circ}\Delta G = a_{1i} \times a_{2j} \times a_{3i} \dots \times a_{ni}$$

[0557] where a_{ji} is a coefficient which represents the effect of the presence of a given amino acid (i) at a given position (j) along the sequence of a peptide of n amino acids. The crucial assumption of this method is that the effects at each position are essentially independent of each other (i.e., independent binding of individual side-chains). When residue j occurs at position i in the peptide, it is assumed to contribute a constant amount j to the free energy of binding of the peptide irrespective of the sequence of the rest of the peptide.

[0558] The method of derivation of specific algorithm coefficients has been described in Gulukota et al., *J. Mol. Biol.* 267:1258-126, 1997; (see also Sidney et al., *Human Immunol.* 45:79-93, 1996; and Southwood et al., *J. Immunol.* 160:3363-3373, 1998). Briefly, for all i positions, anchor and non-anchor alike, the geometric mean of the average relative binding (ARB) of all peptides carrying j is calculated relative to the remainder of the group, and used as the estimate of j_i . For Class II peptides, if multiple alignments are possible, only the highest scoring alignment is utilized, following an iterative procedure. To calculate an algorithm score of a given peptide in a test set, the ARB values corresponding to the sequence of the peptide are multiplied. If this product exceeds a chosen threshold, the peptide is predicted to bind. Appropriate thresholds are chosen as a function of the degree of stringency of prediction desired.

[0559] Selection of HLA-A2 Supertype Cross-Reactive Peptides

[0560] Protein sequences from STEAP-1 are scanned utilizing motif identification software, to identify 8-, 9-10- and 11-mer sequences containing the HLA-A2-supermotif main anchor specificity. Typically, these sequences are then scored using the protocol described above and the peptides corresponding to the positive-scoring sequences are synthesized

and tested for their capacity to bind purified HLA-A*0201 molecules in vitro (HLA-A*0201 is considered a prototype A2 supertype molecule).

[0561] These peptides are then tested for the capacity to bind to additional A2-supertype molecules (A*0202, A*0203, A*0206, and A*6802). Peptides that bind to at least three of the five A2-supertype alleles tested are typically deemed A2-supertype cross-reactive binders. Preferred peptides bind at an affinity equal to or less than 500 nM to three or more HLA-A2 supertype molecules.

[0562] Selection of HLA-A3 Supermotif-Bearing Epitopes

[0563] The STEAP-1 protein sequence(s) scanned above is also examined for the presence of peptides with the HLA-A3-supermotif primary anchors. Peptides corresponding to the HLA A3 supermotif-bearing sequences are then synthesized and tested for binding to HLA-A*0301 and HLA-A*1101 molecules, the molecules encoded by the two most prevalent A3-supertype alleles. The peptides that bind at least one of the two alleles with binding affinities of ≤ 500 nM, often ≤ 200 nM, are then tested for binding cross-reactivity to the other common A3-supertype alleles (e.g., A*3101, A*3301, and A*6801) to identify those that can bind at least three of the five HLA-A3-supertype molecules tested.

[0564] Selection of HLA-B7 Supermotif Bearing Epitopes

[0565] The STEAP-1 protein(s) scanned above is also analyzed for the presence of 8-, 9-10-, or 11-mer peptides with the HLA-B7-supermotif. Corresponding peptides are synthesized and tested for binding to HLA-B*0702, the molecule encoded by the most common B7-supertype allele (i.e., the prototype B7 supertype allele). Peptides binding B*0702 with IC_{50} of ≤ 500 nM are identified using standard methods. These peptides are then tested for binding to other common B7-supertype molecules (e.g., B*3501, B*5101, B*5301, and B*5401). Peptides capable of binding to three or more of the five B7-supertype alleles tested are thereby identified.

[0566] Selection of A1 and A24 Motif-Bearing Epitopes

[0567] To further increase population coverage, HLA-A1 and -A24 epitopes can also be incorporated into vaccine compositions. An analysis of the STEAP-1 protein can also be performed to identify HLA-A1- and A24-motif-containing sequences.

[0568] High affinity and/or cross-reactive binding epitopes that bear other motif and/or supermotifs are identified using analogous methodology.

Example 14

Confirmation of Immunogenicity

[0569] Cross-reactive candidate CTL A2-supermotif-bearing peptides that are identified as described herein are selected to confirm in vitro immunogenicity. Confirmation is performed using the following methodology:

[0570] Target Cell Lines for Cellular Screening:

[0571] The 0.221A2.1 cell line, produced by transferring the HLA-A2.1 gene into the HLA-A, -B, -C null mutant human B-lymphoblastoid cell line 721.221, is used as the

peptide-loaded target to measure activity of HLA-A2.1-restricted CTL. This cell line is grown in RPMI-1640 medium supplemented with antibiotics, sodium pyruvate, nonessential amino acids and 10% (v/v) heat inactivated FCS. Cells that express an antigen of interest, or transfectants comprising the gene encoding the antigen of interest, can be used as target cells to confirm the ability of peptide-specific CTLs to recognize endogenous antigen.

[0572] Primary CTL Induction Cultures:

[0573] Generation of Dendritic Cells (DC): PBMCs are thawed in RPMI with 30 µg/ml DNase, washed twice and resuspended in complete medium (RPMI-1640 plus 5% AB human serum, non-essential amino acids, sodium pyruvate, L-glutamine and penicillin/streptomycin). The monocytes are purified by plating 10×10^6 PBMC/well in a 6-well plate. After 2 hours at 37° C., the non-adherent cells are removed by gently shaking the plates and aspirating the supernatants. The wells are washed a total of three times with 3 ml RPMI to remove most of the non-adherent and loosely adherent cells. Three ml of complete medium containing 50 ng/ml of GM-CSF and 1,000 U/ml of IL-4 are then added to each well. TNFα is added to the DCs on day 6 at 75 ng/ml and the cells are used for CTL induction cultures on day 7.

[0574] Induction of CTL with DC and Peptide: CD8+ T-cells are isolated by positive selection with Dynal immunomagnetic beads (Dynabeads® M-450) and the detachabead® reagent. Typically about $200\text{--}250 \times 10^6$ PBMC are processed to obtain 24×10^6 CD8+ T-cells (enough for a 48-well plate culture). Briefly, the PBMCs are thawed in RPMI with 30 µg/ml DNase, washed once with PBS containing 1% human AB serum and resuspended in PBS/1% AB serum at a concentration of 20×10^6 cells/ml. The magnetic beads are washed 3 times with PBS/AB serum, added to the cells (140 µl beads/ 20×10^6 cells) and incubated for 1 hour at 4° C. with continuous mixing. The beads and cells are washed 4x with PBS/AB serum to remove the nonadherent cells and resuspended at 100×10^6 cells/ml (based on the original cell number) in PBS/AB serum containing 100 µl/ml detachabead® reagent and 30 µg/ml DNase. The mixture is incubated for 1 hour at room temperature with continuous mixing. The beads are washed again with PBS/AB/DNase to collect the CD8+ T-cells. The DC are collected and centrifuged at 1300 rpm for 5-7 minutes, washed once with PBS with 1% BSA, counted and pulsed with 40 µg/ml of peptide at a cell concentration of $1\text{--}2 \times 10^6$ /ml in the presence of 3 µg/ml β₂-microglobulin for 4 hours at 20° C. The DC are then irradiated (4,200 rads), washed 1 time with medium and counted again.

[0575] Setting up induction cultures: 0.25 ml cytokine-generated DC (at 1×10^5 cells/ml) are co-cultured with 0.25 ml of CD8+ T-cells (at 2×10^6 cell/ml) in each well of a 48-well plate in the presence of 10 ng/ml of IL-7. Recombinant human IL-10 is added the next day at a final concentration of 10 ng/ml and rhuman IL-2 is added 48 hours later at 10 IU/ml.

[0576] Restimulation of the induction cultures with peptide-pulsed adherent cells: Seven and fourteen days after the primary induction, the cells are restimulated with peptide-pulsed adherent cells. The PBMCs are thawed and washed twice with RPMI and DNase. The cells are resuspended at 5×10^6 cells/ml and irradiated at ~4200 rads. The PBMCs are plated at 2×10^6 in 0.5 ml complete medium per well and

incubated for 2 hours at 37° C. The plates are washed twice with RPMI by tapping the plate gently to remove the nonadherent cells and the adherent cells pulsed with 101 g/ml of peptide in the presence of 3 µg/ml β₂ microglobulin in 0.25 ml RPMI/5% AB per well for 2 hours at 37° C. Peptide solution from each well is aspirated and the wells are washed once with RPMI. Most of the media is aspirated from the induction cultures (CD8+ cells) and brought to 0.5 ml with fresh media. The cells are then transferred to the wells containing the peptide-pulsed adherent cells. Twenty four hours later recombinant human IL-10 is added at a final concentration of 10 ng/ml and recombinant human IL2 is added the next day and again 2-3 days later at 50 IU/ml (Tsai et al., *Critical Reviews in Immunology* 18(1-2):65-75, 1998). Seven days later, the cultures are assayed for CTL activity in a ⁵¹Cr release assay. In some experiments the cultures are assayed for peptide-specific recognition in the in situ IFNγ ELISA at the time of the second restimulation followed by assay of endogenous recognition 7 days later. After expansion, activity is measured in both assays for a side-by-side comparison.

[0577] Measurement of CTL Lytic Activity by ⁵¹Cr Release.

[0578] Seven days after the second restimulation, cytotoxicity is determined in a standard (5 hr) ⁵¹Cr release assay by assaying individual wells at a single E:T. Peptide-pulsed targets are prepared by incubating the cells with 10 µg/ml peptide overnight at 37° C.

[0579] Adherent target cells are removed from culture flasks with trypsin-EDTA. Target cells are labeled with 200 µCi of ⁵¹Cr sodium chromate (Dupont, Wilmington, Del.) for 1 hour at 37° C. Labeled target cells are resuspended at 10^6 per ml and diluted 1:10 with K562 cells at a concentration of 3.3×10^6 /mm (an NK-sensitive erythroblastoma cell line used to reduce non-specific lysis). Target cells (100 µl) and effectors (100 µl) are plated in 96 well round-bottom plates and incubated for 5 hours at 37° C. At that time, 100 µl of supernatant are collected from each well and percent lysis is determined according to the formula:

$$\left[\frac{\text{cpm of the test sample} - \text{cpm of the spontaneous } ^{51}\text{Cr release sample}}{\text{cpm of the maximal } ^{51}\text{Cr release sample} - \text{cpm of the spontaneous } ^{51}\text{Cr release sample}} \right] \times 100.$$

[0580] Maximum and spontaneous release are determined by incubating the labeled targets with 1% Triton X-100 and media alone, respectively. A positive culture is defined as one in which the specific lysis (sample-background) is 10% or higher in the case of individual wells and is 15% or more at the two highest E:T ratios when expanded cultures are assayed.

[0581] In situ Measurement of Human IFNγ Production as an Indicator of Peptide-Specific and Endogenous Recognition

[0582] Immulon 2 plates are coated with mouse anti-human IFNγ monoclonal antibody (4 µg/ml 0.1M NaHCO₃, pH8.2) overnight at 4° C. The plates are washed with Ca²⁺, Mg²⁺-free PBS/0.05% Tween 20 and blocked with PBS/10% FCS for two hours, after which the CTLs (100 µl/well) and targets (1001 µl/well) are added to each well, leaving empty wells for the standards and blanks (which received media only). The target cells, either peptide-pulsed or

endogenous targets, are used at a concentration of 1×10^6 cells/ml. The plates are incubated for 48 hours at 37°C . with 5% CO_2 .

[0583] Recombinant human IFN-gamma is added to the standard wells starting at 400 pg or 1200 pg/100 microliter/well and the plate incubated for two hours at 37°C . The plates are washed and 100 μl of biotinylated mouse anti-human IFN-gamma monoclonal antibody (2 microgram/ml in PBS/3% FCS/0.05% Tween 20) are added and incubated for 2 hours at room temperature. After washing again, 100 microliter HRP-streptavidin (1:4000) are added and the plates incubated for one hour at room temperature. The plates are then washed 6 \times with wash buffer, 100 microliter/well developing solution (TMB 1:1) are added, and the plates allowed to develop for 5-15 minutes. The reaction is stopped with 50 microliter/well 1M H_3PO_4 and read at OD450. A culture is considered positive if it measured at least 50 pg of IFN-gamma/well above background and is twice the background level of expression.

[0584] CTL Expansion.

[0585] Those cultures that demonstrate specific lytic activity against peptide-pulsed targets and/or tumor targets are expanded over a two week period with anti-CD3. Briefly, 5×10^4 CD8 $^+$ cells are added to a T25 flask containing the following: 1×10^6 irradiated (4,200 rad) PBMC (autologous or allogeneic) per ml, 2×10^5 irradiated (8,000 rad) EBV-transformed cells per ml, and OKT3 (anti-CD3) at 30 ng per ml in RPMI-1640 containing 10% (v/v) human AB serum, non-essential amino acids, sodium pyruvate, 25 μM 2-mercaptoethanol, L-glutamine and penicillin/streptomycin. Recombinant human IL2 is added 24 hours later at a final concentration of 200 IU/ml and every three days thereafter with fresh media at 50 IU/ml. The cells are split if the cell concentration exceeds 1×10^6 /ml and the cultures are assayed between days 13 and 15 at E:T ratios of 30, 10, 3 and 1:1 in the ^{51}Cr release assay or at 1×10^6 /ml in the in situ IFN γ assay using the same targets as before the expansion.

[0586] Cultures are expanded in the absence of anti-CD3+ as follows. Those cultures that demonstrate specific lytic activity against peptide and endogenous targets are selected and 5×10^4 CD8 $^+$ cells are added to a T25 flask containing the following: 1×10^6 autologous PBMC per ml which have been peptide-pulsed with 10 μg /ml peptide for two hours at 37°C . and irradiated (4,200 rad); 2×10^5 irradiated (8,000 rad) EBV-transformed cells per ml RPMI-1640 containing 10% (v/v) human AB serum, non-essential AA, sodium pyruvate, 25 mM 2-ME, L-glutamine and gentamicin.

[0587] Immunogenicity of A2 Supermotif-Bearing Peptides

[0588] A2-supermotif cross-reactive binding peptides are tested in the cellular assay for the ability to induce peptide-specific CTL in normal individuals. In this analysis, a peptide is typically considered to be an epitope if it induces peptide-specific CTLs in at least individuals, and preferably, also recognizes the endogenously expressed peptide.

[0589] Immunogenicity can also be confirmed using PBMCs isolated from patients bearing a tumor that expresses STEAP-1. Briefly, PBMCs are isolated from patients, re-stimulated with peptide-pulsed monocytes and assayed for the ability to recognize peptide-pulsed target cells as well as transfected cells endogenously expressing the antigen.

[0590] Evaluation of A*03/A11 Immunogenicity

[0591] HLA-A3 supermotif-bearing cross-reactive binding peptides are also evaluated for immunogenicity using methodology analogous for that used to evaluate the immunogenicity of the HLA-A2 supermotif peptides.

[0592] Evaluation of B7 Immunogenicity

[0593] Immunogenicity screening of the B7-supertype cross-reactive binding peptides identified as set forth herein are confirmed in a manner analogous to the confirmation of A2- and A3-supermotif-bearing peptides.

[0594] Peptides bearing other supermotifs/motifs, e.g., HLA-A1, HLA-A24 etc. are also confirmed using similar methodology

Example 15

Implementation of the Extended Supermotif to Improve the Binding Capacity of Native Epitopes by Creating Analogs

[0595] HLA motifs and supermotifs (comprising primary and/or secondary residues) are useful in the identification and preparation of highly cross-reactive native peptides, as demonstrated herein. Moreover, the definition of HLA motifs and supermotifs also allows one to engineer highly cross-reactive epitopes by identifying residues within a native peptide sequence which can be analoged to confer upon the peptide certain characteristics, e.g. greater cross-reactivity within the group of HLA molecules that comprise a supertype, and/or greater binding affinity for some or all of those HLA molecules. Examples of analoging peptides to exhibit modulated binding affinity are set forth in this example.

[0596] Analoging at Primary Anchor Residues

[0597] Peptide engineering strategies are implemented to further increase the cross-reactivity of the epitopes. For example, the main anchors of A2-supermotif-bearing peptides are altered, for example, to introduce a preferred L, I, V, or M at position 2, and I or V at the C-terminus.

[0598] To analyze the cross-reactivity of the analog peptides, each engineered analog is initially tested for binding to the prototype A2 supertype allele A*0201, then, if A*0201 binding capacity is maintained, for A2-supertype cross-reactivity.

[0599] Alternatively, a peptide is confirmed as binding one or all supertype members and then analoged to modulate binding affinity to any one (or more) of the supertype members to add population coverage.

[0600] The selection of analogs for immunogenicity in a cellular screening analysis is typically further restricted by the capacity of the parent wild type (WT) peptide to bind at least weakly, i.e., bind at an IC_{50} of 5000 nM or less, to three or more A2 supertype alleles. The rationale for this requirement is that the WT peptides must be present endogenously in sufficient quantity to be biologically relevant. Analoged peptides have been shown to have increased immunogenicity and cross-reactivity by T cells specific for the parent epitope (see, e.g., Parkhurst et al., *J. Immunol.* 157:2539, 1996; and Pogue et al., *Proc. Natl. Acad. Sci. USA* 92:8166, 1995).

[0601] In the cellular screening of these peptide analogs, it is important to confirm that analog-specific CTLs are also able to recognize the wild-type peptide and, when possible, target cells that endogenously express the epitope.

[0602] Analoging of HLA-A3 and B7-Supermotif-Bearing Peptides

[0603] Analogs of HLA-A3 supermotif-bearing epitopes are generated using strategies similar to those employed in analoging HLA-A2 supermotif-bearing peptides. For example, peptides binding to $\frac{3}{5}$ of the A3-supertype molecules are engineered at primary anchor residues to possess a preferred residue (V, S, M, or A) at position 2.

[0604] The analog peptides are then tested for the ability to bind A*03 and A*11 (prototype A3 supertype alleles). Those peptides that demonstrate ≤ 500 nM binding capacity are then confirmed as having A3-supertype cross-reactivity.

[0605] Similarly to the A2- and A3-motif bearing peptides, peptides binding 3 or more B7-supertype alleles can be improved, where possible, to achieve increased cross-reactive binding or greater binding affinity or binding half life. B7 supermotif-bearing peptides are, for example, engineered to possess a preferred residue (V, I, L, or F) at the C-terminal primary anchor position, as demonstrated by Sidney et al. (*J. Immunol.* 157:3480-3490, 1996).

[0606] Analoging at primary anchor residues of other motif and/or supermotif-bearing epitopes is performed in a like manner.

[0607] The analog peptides are then be confirmed for immunogenicity, typically in a cellular screening assay. Again, it is generally important to demonstrate that analog-specific CTLs are also able to recognize the wild-type peptide and, when possible, targets that endogenously express the epitope.

[0608] Analoging at Secondary Anchor Residues

[0609] Moreover, HLA supermotifs are of value in engineering highly cross-reactive peptides and/or peptides that bind HLA molecules with increased affinity by identifying particular residues at secondary anchor positions that are associated with such properties. For example, the binding capacity of a B7 supermotif-bearing peptide with an F residue at position 1 is analyzed. The peptide is then analoged to, for example, substitute L for F at position 1. The analoged peptide is evaluated for increased binding affinity, binding half life and/or increased cross-reactivity. Such a procedure identifies analoged peptides with enhanced properties.

[0610] Engineered analogs with sufficiently improved binding capacity or cross-reactivity can also be tested for immunogenicity in HLA-B7-transgenic mice, following for example, IFA immunization or lipopeptide immunization. Analoged peptides are additionally tested for the ability to stimulate a recall response using PBMC from patients with STEAP-1-expressing tumors.

[0611] Other Analoging Strategies

[0612] Another form of peptide analoging, unrelated to anchor positions, involves the substitution of a cysteine with α -amino butyric acid. Due to its chemical nature, cysteine has the propensity to form disulfide bridges and sufficiently alter the peptide structurally so as to reduce binding capac-

ity. Substitution of α -amino butyric acid for cysteine not only alleviates this problem, but has been shown to improve binding and crossbinding capabilities in some instances (see, e.g., the review by Sette et al., In: *Persistent Viral Infections*, Eds. R. Ahmed and I. Chen, John Wiley & Sons, England, 1999).

[0613] Thus, by the use of single amino acid substitutions, the binding properties and/or cross-reactivity of peptide ligands for HLA supertype molecules can be modulated.

Example 16

Identification and Confirmation of STEAP-1-Derived Sequences with HLA-DR Binding Motifs

[0614] Peptide epitopes bearing an HLA class II supermotif or motif are identified and confirmed as outlined below using methodology similar to that described for HLA Class I peptides.

[0615] Selection of HLA-DR-Supermotif-Bearing Epitopes.

[0616] To identify STEAP-1-derived, HLA class II HTL epitopes, a STEAP-1 antigen is analyzed for the presence of sequences bearing an HLA-DR-motif or supermotif. Specifically, 15-mer sequences are selected comprising a DR-supermotif, comprising a 9-mer core, and three-residue N- and C-terminal flanking regions (15 amino acids total).

[0617] Protocols for predicting peptide binding to DR molecules have been developed (Southwood et al., *J. Immunol.* 160:3363-3373, 1998). These protocols, specific for individual DR molecules, allow the scoring, and ranking, of 9-mer core regions. Each protocol not only scores peptide sequences for the presence of DR-supermotif primary anchors (i.e., at position 1 and position 6) within a 9-mer core, but additionally evaluates sequences for the presence of secondary anchors. Using allele-specific selection tables (see, e.g., Southwood et al., *ibid.*), it has been found that these protocols efficiently select peptide sequences with a high probability of binding a particular DR molecule. Additionally, it has been found that performing these protocols in tandem, specifically those for DR1, DR4w4, and DR7, can efficiently select DR cross-reactive peptides.

[0618] The STEAP-1-derived peptides identified above are tested for their binding capacity for various common HLA-DR molecules. All peptides are initially tested for binding to the DR molecules in the primary panel: DR1, DR4w4, and DR7. Peptides binding at least two of these three DR molecules are then tested for binding to DR2w2 β 1, DR2w2 β 2, DR6w19, and DR9 molecules in secondary assays. Finally, peptides binding at least two of the four secondary panel DR molecules, and thus cumulatively at least four of seven different DR molecules, are screened for binding to DR4w15, DR5w11, and DR8w2 molecules in tertiary assays. Peptides binding at least seven of the ten DR molecules comprising the primary, secondary, and tertiary screening assays are considered cross-reactive DR binders. STEAP-1-derived peptides found to bind common HLA-DR alleles are of particular interest.

[0619] Selection of DR3 Motif Peptides

[0620] Because HLA-DR3 is an allele that is prevalent in Caucasian, Black, and Hispanic populations, DR3 binding

capacity is a relevant criterion in the selection of HTL epitopes. Thus, peptides shown to be candidates may also be assayed for their DR3 binding capacity. However, in view of the binding specificity of the DR3 motif, peptides binding only to DR3 can also be considered as candidates for inclusion in a vaccine formulation.

[0621] To efficiently identify peptides that bind DR3, target STEAP-1 antigens are analyzed for sequences carrying one of the two DR3-specific binding motifs reported by Geluk et al. (*J. Immunol.* 152:5742-5748, 1994). The corresponding peptides are then synthesized and confirmed as having the ability to bind DR3 with an affinity of 1 μ M or better, i.e., less than 1 μ M. Peptides are found that meet this binding criterion and qualify as HLA class II high affinity binders.

[0622] DR3 binding epitopes identified in this manner are included in vaccine compositions with DR supermotif-bearing peptide epitopes.

[0623] Similarly to the case of HLA class I motif-bearing peptides, the class II motif-bearing peptides are analogized to improve affinity or cross-reactivity. For example, aspartic acid at position 4 of the 9-mer core sequence is an optimal residue for DR3 binding, and substitution for that residue often improves DR 3 binding.

Example 17

Immunogenicity of STEAP-1-Derived HTL Epitopes

[0624] This example determines immunogenic DR supermotif- and DR3 motif-bearing epitopes among those identified using the methodology set forth herein.

[0625] Immunogenicity of HTL epitopes are confirmed in a manner analogous to the determination of immunogenicity of CTL epitopes, by assessing the ability to stimulate HTL responses and/or by using appropriate transgenic mouse models. Immunogenicity is determined by screening for: 1.) in vitro primary induction using normal PBMC or 2.) recall responses from patients who have STEAP-1-expressing tumors.

Example 18

Calculation of Phenotypic Frequencies of HLA-Supertypes in Various Ethnic Backgrounds to Determine Breadth of Population Coverage

[0626] This example illustrates the assessment of the breadth of population coverage of a vaccine composition comprised of multiple epitopes comprising multiple supermotifs and/or motifs.

[0627] In order to analyze population coverage, gene frequencies of HLA alleles are determined. Gene frequencies for each HLA allele are calculated from antigen or allele frequencies utilizing the binomial distribution formulae $g f \cdot 1 - (\text{SQRT}(1 - af))$ (see, e.g., Sidney et al., *Human Immunol.* 45:79-93, 1996). To obtain overall phenotypic frequencies, cumulative gene frequencies are calculated, and the cumulative antigen frequencies derived by the use of the inverse formula $[af = 1 - (1 - Cgf)^2]$.

[0628] Where frequency data is not available at the level of DNA typing, correspondence to the serologically defined

antigen frequencies is assumed. To obtain total potential supertype population coverage no linkage disequilibrium is assumed, and only alleles confirmed to belong to each of the supertypes are included (minimal estimates). Estimates of total potential coverage achieved by inter-loci combinations are made by adding to the A coverage the proportion of the non-A covered population that could be expected to be covered by the B alleles considered (e.g., $\text{total} = A + B \cdot (1 - A)$). Confirmed members of the A3-like supertype are A3, A11, A31, A*3301, and A*6801. Although the A3-like supertype may also include A34, A66, and A*7401, these alleles were not included in overall frequency calculations. Likewise, confirmed members of the A2-like supertype family are A*0201, A*0202, A*0203, A*0204, A*0205, A*0206, A*0207, A*6802, and A*6901. Finally, the B7-like supertype-confirmed alleles are: B7, B*3501-03, B51, B*5301, B*5401, B*5501-2, B*5601, B*6701, and B*7801 (potentially also B*1401, B*3504-06, B*4201, and B*5602).

[0629] Population coverage achieved by combining the A2-, A3- and B7-supertypes is approximately 86% in five major ethnic groups. Coverage may be extended by including peptides bearing the A1 and A24 motifs. On average, A1 is present in 12% and A24 in 29% of the population across five different major ethnic groups (Caucasian, North American Black, Chinese, Japanese, and Hispanic). Together, these alleles are represented with an average frequency of 39% in these same ethnic populations. The total coverage across the major ethnicities when A1 and A24 are combined with the coverage of the A2-, A3- and B7-supertype alleles is >95%. An analogous approach can be used to estimate population coverage achieved with combinations of class II motif-bearing epitopes.

[0630] Immunogenicity studies in humans (e.g., Bertoni et al., *J. Clin. Invest.* 100:503, 1997; Doolan et al., *Immunity* 7:97, 1997; and Threlkeld et al., *J. Immunol.* 159:1648, 1997) have shown that highly cross-reactive binding peptides are almost always recognized as epitopes. The use of highly cross-reactive binding peptides is an important selection criterion in identifying candidate epitopes for inclusion in a vaccine that is immunogenic in a diverse population.

[0631] With a sufficient number of epitopes (as disclosed herein and from the art), an average population coverage is predicted to be greater than 95% in each of five major ethnic populations. The game theory Monte Carlo simulation analysis, which is known in the art (see e.g., Osborne, M. J. and Rubinstein, A. "A course in game theory" MIT Press, 1994), can be used to estimate what percentage of the individuals in a population comprised of the Caucasian, North American Black, Japanese, Chinese, and Hispanic ethnic groups would recognize the vaccine epitopes described herein. A preferred percentage is 90%. A more preferred percentage is 95%.

Example 19

CTL Recognition of Endogenously Processed Antigens after Priming

[0632] This example confirms that CTL induced by native or analogized peptide epitopes identified and selected as described herein recognize endogenously synthesized, i.e., native antigens.

[0633] Effector cells isolated from transgenic mice that are immunized with peptide epitopes, for example HLA-A2 supermotif-bearing epitopes, are re-stimulated in vitro using peptide-coated stimulator cells. Six days later, effector cells are assayed for cytotoxicity and the cell lines that contain peptide-specific cytotoxic activity are further re-stimulated. An additional six days later, these cell lines are tested for cytotoxic activity on ^{51}Cr labeled Jurkat-A2.1/ K^b target cells in the absence or presence of peptide, and also tested on ^{51}Cr labeled target cells bearing the endogenously synthesized antigen, i.e. cells that are stably transfected with STEAP-1 expression vectors.

[0634] The results demonstrate that CTL lines obtained from animals primed with peptide epitope recognize endogenously synthesized STEAP-1 antigen. The choice of transgenic mouse model to be used for such an analysis depends upon the epitope(s) that are being evaluated. In addition to HLA-A*0201/ K^b transgenic mice, several other transgenic mouse models including mice with human A11, which may also be used to evaluate A3 epitopes, and B7 alleles have been characterized and others (e.g., transgenic mice for HLA-A 1 and A24) are being developed. HLA-DR1 and HLA-DR3 mouse models have also been developed, which may be used to evaluate HTL epitopes.

Example 20

Activity of CTL-HTL Conjugated Epitopes in Transgenic Mice

[0635] This example illustrates the induction of CTLs and HTLs in transgenic mice, by use of a STEAP-1-derived CTL and HTL peptide vaccine compositions. The vaccine composition used herein comprise peptides to be administered to a patient with a STEAP-1-expressing tumor. The peptide composition can comprise multiple CTL and/or HTL epitopes. The epitopes are identified using methodology as described herein. This example also illustrates that enhanced immunogenicity can be achieved by inclusion of one or more HTL epitopes in a CTL vaccine composition; such a peptide composition can comprise an HTL epitope conjugated to a CTL epitope. The CTL epitope can be one that binds to multiple HLA family members at an affinity of 500 nM or less, or analogs of that epitope. The peptides may be lipidated, if desired.

[0636] Immunization procedures: Immunization of transgenic mice is performed as described (Alexander et al., *J. Immunol.* 159:4753-4761, 1997). For example, A2/ K^b mice, which are transgenic for the human HLA A2.1 allele and are used to confirm the immunogenicity of HLA-A*0201 motif- or HLA-A2 supermotif-bearing epitopes, and are primed subcutaneously (base of the tail) with a 0.1 ml of peptide in Incomplete Freund's Adjuvant, or if the peptide composition is a lipidated CTL/HTL conjugate, in DMSO/saline, or if the peptide composition is a polypeptide, in PBS or Incomplete Freund's Adjuvant. Seven days after priming, splenocytes obtained from these animals are restimulated with syngenic irradiated LPS-activated lymphoblasts coated with peptide.

[0637] Cell lines. Target cells for peptide-specific cytotoxicity assays are Jurkat cells transfected with the HLA-A2.1/ K^b chimeric gene (e.g., Vitiello et al., *J. Exp. Med.* 173:1007, 1991).

[0638] In vitro CTL activation: One week after priming, spleen cells (30×10^6 cells/flask) are co-cultured at 37°C .

with syngenic, irradiated (3000 rads), peptide coated lymphoblasts (10×10^6 cells/flask) in 10 ml of culture medium/T25 flask. After six days, effector cells are harvested and assayed for cytotoxic activity.

[0639] Assay for cytotoxic activity: Target cells (1.0 to 1.5×10^6) are incubated at 37°C . in the presence of $200 \mu\text{l}$ of ^{51}Cr . After 60 minutes, cells are washed three times and resuspended in R10 medium. Peptide is added where required at a concentration of $1 \mu\text{g/ml}$. For the assay, 10^4 ^{51}Cr -labeled target cells are added to different concentrations of effector cells (final volume of $200 \mu\text{l}$) in U-bottom 96-well plates. After a six hour incubation period at 37°C ., a 0.1 ml aliquot of supernatant is removed from each well and radioactivity is determined in a Micromedic automatic gamma counter. The percent specific lysis is determined by the formula: percent specific release = $100 \times (\text{experimental release} - \text{spontaneous release}) / (\text{maximum release} - \text{spontaneous release})$. To facilitate comparison between separate CTL assays run under the same conditions, % ^{51}Cr release data is expressed as lytic units/ 10^6 cells. One lytic unit is arbitrarily defined as the number of effector cells required to achieve 30% lysis of 10,000 target cells in a six hour ^{51}Cr release assay. To obtain specific lytic units/ 10^6 , the lytic units/ 10^6 obtained in the absence of peptide is subtracted from the lytic units/ 10^6 obtained in the presence of peptide. For example, if 30% ^{51}Cr release is obtained at the effector (E): target (T) ratio of 50:1 (i.e., 5×10^5 effector cells for 10,000 targets) in the absence of peptide and 5:1 (i.e., 5×10^4 effector cells for 10,000 targets) in the presence of peptide, the specific lytic units would be: $[(1/50,000) - (1/500,000)] \times 10^6 = 18 \text{ LU}$.

[0640] The results are analyzed to assess the magnitude of the CTL responses of animals injected with the immunogenic CTL/HTL conjugate vaccine preparation and are compared to the magnitude of the CTL response achieved using, for example, CTL epitopes as outlined above in the Example entitled "Confirmation of Immunogenicity." Analyses similar to this may be performed to confirm the immunogenicity of peptide conjugates containing multiple CTL epitopes and/or multiple HTL epitopes. In accordance with these procedures, it is found that a CTL response is induced, and concomitantly that an HTL response is induced upon administration of such compositions.

Example 21

Selection of CTL and HTL Epitopes for Inclusion in a STEAP-1-Specific Vaccine

[0641] This example illustrates a procedure for selecting peptide epitopes for vaccine compositions of the invention. The peptides in the composition can be in the form of a nucleic acid sequence, either single or one or more sequences (i.e., minigene) that encodes peptide(s), or can be single and/or polyepitopic peptides.

[0642] The following principles are utilized when selecting a plurality of epitopes for inclusion in a vaccine composition. Each of the following principles is balanced in order to make the selection.

[0643] Epitopes are selected which, upon administration, mimic immune responses that are correlated with STEAP-1 clearance. The number of epitopes used depends on observations of patients who spontaneously clear STEAP-1. For

example, if it has been observed that patients who spontaneously clear STEAP-1-expressing cells generate an immune response to at least three (3) epitopes from STEAP-1 antigen, then at least three epitopes should be included for HLA class I. A similar rationale is used to determine HLA class II epitopes.

[0644] Epitopes are often selected that have a binding affinity of an IC_{50} of 500 nM or less for an HLA class I molecule, or for class II, an IC_{50} of 1000 nM or less; or HLA Class I peptides with high binding scores from the BIMAS web site, at URL bimas.dcrt.nih.gov/.

[0645] In order to achieve broad coverage of the vaccine through out a diverse population, sufficient supermotif bearing peptides, or a sufficient array of allele-specific motif bearing peptides, are selected to give broad population coverage. In one embodiment, epitopes are selected to provide at least 80% population coverage. A Monte Carlo analysis, a statistical evaluation known in the art, can be employed to assess breadth, or redundancy, of population coverage.

[0646] When creating polyepitopic compositions, or a minigene that encodes same, it is typically desirable to generate the smallest peptide possible that encompasses the epitopes of interest. The principles employed are similar, if not the same, as those employed when selecting a peptide comprising nested epitopes. For example, a protein sequence for the vaccine composition is selected because it has maximal number of epitopes contained within the sequence, i.e., it has a high concentration of epitopes. Epitopes may be nested or overlapping (i.e., frame shifted relative to one another). For example, with overlapping epitopes, two 9-mer epitopes and one 10-mer epitope can be present in a 10 amino acid peptide. Each epitope can be exposed and bound by an HLA molecule upon administration of such a peptide. A multi-epitopic, peptide can be generated synthetically, recombinantly, or via cleavage from the native source. Alternatively, an analog can be made of this native sequence, whereby one or more of the epitopes comprise substitutions that alter the cross-reactivity and/or binding affinity properties of the polyepitopic peptide. Such a vaccine composition is administered for therapeutic or prophylactic purposes. This embodiment provides for the possibility that an as yet undiscovered aspect of immune system processing will apply to the native nested sequence and thereby facilitate the production of therapeutic or prophylactic immune response-inducing vaccine compositions. Additionally such an embodiment provides for the possibility of motif-bearing epitopes for an HLA makeup that is presently unknown. Furthermore, this embodiment (absent the creating of any analogs) directs the immune response to multiple peptide sequences that are actually present in STEAP-1, thus avoiding the need to evaluate any junctional epitopes. Lastly, the embodiment provides an economy of scale when producing nucleic acid vaccine compositions. Related to this embodiment, computer programs can be derived in accordance with principles in the art, which identify in a target sequence, the greatest number of epitopes per sequence length.

[0647] A vaccine composition comprised of selected peptides, when administered, is safe, efficacious, and elicits an immune response similar in magnitude to an immune response that controls or clears cells that bear or overexpress STEAP-1.

Example 22

Construction of "Minigene" Multi-Epitope DNA Plasmids

[0648] This example discusses the construction of a minigene expression plasmid. Minigene plasmids may, of course, contain various configurations of B cell, CTL and/or HTL epitopes or epitope analogs as described herein.

[0649] A minigene expression plasmid typically includes multiple CTL and HTL peptide epitopes. In the present example, HLA-A2, -A3, -B7 supermotif-bearing peptide epitopes and HLA-A1 and -A24 motif-bearing peptide epitopes are used in conjunction with DR supermotif-bearing epitopes and/or DR3 epitopes. HLA class I supermotif or motif-bearing peptide epitopes derived STEAP-1, are selected such that multiple supermotifs/motifs are represented to ensure broad population coverage. Similarly, HLA class II epitopes are selected from STEAP-1 to provide broad population coverage, i.e. both HLA DR-1-4-7 supermotif-bearing epitopes and HLA DR-3 motif-bearing epitopes are selected for inclusion in the minigene construct. The selected CTL and HTL epitopes are then incorporated into a minigene for expression in an expression vector.

[0650] Such a construct may additionally include sequences that direct the HTL epitopes to the endoplasmic reticulum. For example, the Ii protein may be fused to one or more HTL epitopes as described in the art, wherein the CLIP sequence of the Ii protein is removed and replaced with an HLA class II epitope sequence so that HLA class II epitope is directed to the endoplasmic reticulum, where the epitope binds to an HLA class II molecules.

[0651] This example illustrates the methods to be used for construction of a minigene-bearing expression plasmid. Other expression vectors that may be used for minigene compositions are available and known to those of skill in the art.

[0652] The minigene DNA plasmid of this example contains a consensus Kozak sequence and a consensus murine kappa Ig-light chain signal sequence followed by CTL and/or HTL epitopes selected in accordance with principles disclosed herein. The sequence encodes an open reading frame fused to the Myc and His antibody epitope tag coded for by the pcDNA 3.1 Myc-His vector.

[0653] Overlapping oligonucleotides that can, for example, average about 70 nucleotides in length with 15 nucleotide overlaps, are synthesized and HPLC-purified. The oligonucleotides encode the selected peptide epitopes as well as appropriate linker nucleotides, Kozak sequence, and signal sequence. The final multi-epitope minigene is assembled by extending the overlapping oligonucleotides in three sets of reactions using PCR. A Perkin/Elmer 9600 PCR machine is used and a total of 30 cycles are performed using the following conditions: 95° C. for 15 sec, annealing temperature (5° below the lowest calculated T_m of each primer pair) for 30 sec, and 72° C. for 1 min.

[0654] For example, a minigene is prepared as follows. For a first PCR reaction, 5 μ g of each of two oligonucleotides are annealed and extended: In an example using eight oligonucleotides, i.e., four pairs of primers, oligonucleotides 1+2, 3+4, 5+6, and 7+8 are combined in 100 μ l reactions containing Pfu polymerase buffer (1x=10 mM KCL, 10 mM

(NH₄)₂SO₄, 20 mM Tris-chloride, pH 8.75, 2 mM MgSO₄, 0.1% Triton X-100, 100 µg/ml BSA), 0.25 mM each dNTP, and 2.5 U of Pfu polymerase. The full-length dimer products are gel-purified, and two reactions containing the product of 1+2 and 3+4, and the product of 5+6 and 7+8 are mixed, annealed, and extended for 10 cycles. Half of the two reactions are then mixed, and 5 cycles of annealing and extension carried out before flanking primers are added to amplify the full length product. The full-length product is gel-purified and cloned into pCR-blunt (Invitrogen) and individual clones are screened by sequencing.

Example 23

The Plasmid Construct and the Decree to which it Induces Immunogenicity

[0655] The degree to which a plasmid construct, for example a plasmid constructed in accordance with the previous Example, is able to induce immunogenicity is confirmed in vitro by determining epitope presentation by APC following transduction or transfection of the APC with an epitope-expressing nucleic acid construct. Such a study determines “antigenicity” and allows the use of human APC. The assay determines the ability of the epitope to be presented by the APC in a context that is recognized by a T cell by quantifying the density of epitope-HLA class I complexes on the cell surface. Quantitation can be performed by directly measuring the amount of peptide eluted from the APC (see, e.g., Sijts et al., *J. Immunol.* 156:683-692, 1996; Demotz et al., *Nature* 342:682-684, 1989); or the number of peptide-HLA class I complexes can be estimated by measuring the amount of lysis or lymphokine release induced by diseased or transfected target cells, and then determining the concentration of peptide necessary to obtain equivalent levels of lysis or lymphokine release (see, e.g., Kageyama et al., *J. Immunol.* 154:567-576, 1995).

[0656] Alternatively, immunogenicity is confirmed through in vivo injections into mice and subsequent in vitro assessment of CTL and HTL activity, which are analyzed using cytotoxicity and proliferation assays, respectively, as detailed e.g., in Alexander et al., *Immunity* 1:751-761, 1994.

[0657] For example, to confirm the capacity of a DNA minigene construct containing at least one HLA-A2 supermotif peptide to induce CTLs in vivo, HLA-A2.1/K^b transgenic mice, for example, are immunized intramuscularly with 100 µg of naked cDNA. As a means of comparing the level of CTLs induced by cDNA immunization, a control group of animals is also immunized with an actual peptide composition that comprises multiple epitopes synthesized as a single polypeptide as they would be encoded by the minigene.

[0658] Splenocytes from immunized animals are stimulated twice with each of the respective compositions (peptide epitopes encoded in the minigene or the polypeptidic peptide), then assayed for peptide-specific cytotoxic activity in a ⁵¹Cr release assay. The results indicate the magnitude of the CTL response directed against the A2-restricted epitope, thus indicating the in vivo immunogenicity of the minigene vaccine and polypeptidic vaccine.

[0659] It is, therefore, found that the minigene elicits immune responses directed toward the HLA-A2 supermotif peptide epitopes as does the polypeptidic peptide vaccine. A

similar analysis is also performed using other HLA-A3 and HLA-B7 transgenic mouse models to assess CTL induction by HLA-A3 and HLA-B7 motif or supermotif epitopes, whereby it is also found that the minigene elicits appropriate immune responses directed toward the provided epitopes.

[0660] To confirm the capacity of a class II epitope-encoding minigene to induce HTLs in vivo, DR transgenic mice, or for those epitopes that cross react with the appropriate mouse MHC molecule, I-A^b-restricted mice, for example, are immunized intramuscularly with 100 µg of plasmid DNA. As a means of comparing the level of HTLs induced by DNA immunization, a group of control animals is also immunized with an actual peptide composition emulsified in complete Freund's adjuvant. CD4⁺ T cells, i.e. HTLs, are purified from splenocytes of immunized animals and stimulated with each of the respective compositions (peptides encoded in the minigene). The HTL response is measured using a ³H-thymidine incorporation proliferation assay, (see, e.g., Alexander et al. *Immunity* 1:751-761, 1994). The results indicate the magnitude of the HTL response, thus demonstrating the in vivo immunogenicity of the minigene.

[0661] DNA minigenes, constructed as described in the previous Example, can also be confirmed as a vaccine in combination with a boosting agent using a prime boost protocol. The boosting agent can consist of recombinant protein (e.g., Barnett et al., *Aids Res. and Human Retroviruses* 14, Supplement 3:S299-S309, 1998) or recombinant vaccinia, for example, expressing a minigene or DNA encoding the complete protein of interest (see, e.g., Hanke et al., *Vaccine* 16:439-445, 1998; Sedegah et al., *Proc. Natl. Acad. Sci USA* 95:7648-53, 1998; Hanke and McMichael, *Immunol. Letters* 66:177-181, 1999; and Robinson et al., *Nature Med.* 5:526-34, 1999).

[0662] For example, the efficacy of the DNA minigene used in a prime boost protocol is initially evaluated in transgenic mice. In this example, A2.1/K^b transgenic mice are immunized IM with 100 µg of a DNA minigene encoding the immunogenic peptides including at least one HLA-A2 supermotif-bearing peptide. After an incubation period (ranging from 3-9 weeks), the mice are boosted IP with 10⁷ pfu/mouse of a recombinant vaccinia virus expressing the same sequence encoded by the DNA minigene. Control mice are immunized with 100 µg of DNA or recombinant vaccinia without the minigene sequence, or with DNA encoding the minigene, but without the vaccinia boost. After an additional incubation period of two weeks, splenocytes from the mice are immediately assayed for peptide-specific activity in an ELISPOT assay. Additionally, splenocytes are stimulated in vitro with the A2-restricted peptide epitopes encoded in the minigene and recombinant vaccinia, then assayed for peptide-specific activity in an alpha, beta and/or gamma IFN ELISA.

[0663] It is found that the minigene utilized in a prime-boost protocol elicits greater immune responses toward the HLA-A2 supermotif peptides than with DNA alone. Such an analysis can also be performed using HLA-A11 or HLA-B7 transgenic mouse models to assess CTL induction by HLA-A3 or HLA-B7 motif or supermotif epitopes. The use of prime boost protocols in humans is described below in the Example entitled “Induction of CTL Responses Using a Prime Boost Protocol.”

Example 24

Peptide Compositions for Prophylactic Uses

[0664] Vaccine compositions of the present invention can be used to prevent STEAP-1 expression in persons who are at risk for tumors that bear this antigen. For example, a polyepitopic peptide epitope composition (or a nucleic acid comprising the same) containing multiple CTL and HTL epitopes such as those selected in the above Examples, which are also selected to target greater than 80% of the population, is administered to individuals at risk for a STEAP-1-associated tumor.

[0665] For example, a peptide-based composition is provided as a single polypeptide that encompasses multiple epitopes. The vaccine is typically administered in a physiological solution that comprises an adjuvant, such as Incomplete Freund's Adjuvant. The dose of peptide for the initial immunization is from about 1 to about 50,000 µg, generally 100-5,000 µg, for a 70 kg patient. The initial administration of vaccine is followed by booster dosages at 4 weeks followed by evaluation of the magnitude of the immune response in the patient, by techniques that determine the presence of epitope-specific CTL populations in a PBMC sample. Additional booster doses are administered as required. The composition is found to be both safe and efficacious as a prophylaxis against STEAP-1-associated disease.

[0666] Alternatively, a composition typically comprising transfecting agents is used for the administration of a nucleic acid-based vaccine in accordance with methodologies known in the art and disclosed herein.

Example 25

Polyepitopic Vaccine Compositions Derived from Native STEAP-1 Sequences

[0667] A native STEAP-1 polypeptide sequence is analyzed, preferably using computer algorithms defined for each class I and/or class II supermotif or motif, to identify "relatively short" regions of the polypeptide that comprise multiple epitopes. The "relatively short" regions are preferably less in length than an entire native antigen. This relatively short sequence that contains multiple distinct or overlapping, "nested" epitopes can be used to generate a minigene construct. The construct is engineered to express the peptide, which corresponds to the native protein sequence. The "relatively short" peptide is generally less than 250 amino acids in length, often less than 100 amino acids in length, preferably less than 75 amino acids in length, and more preferably less than 50 amino acids in length. The protein sequence of the vaccine composition is selected because it has maximal number of epitopes contained within the sequence, i.e., it has a high concentration of epitopes. As noted herein, epitope motifs may be nested or overlapping (i.e., frame shifted relative to one another). For example, with overlapping epitopes, two 9-mer epitopes and one 10-mer epitope can be present in a 10 amino acid peptide. Such a vaccine composition is administered for therapeutic or prophylactic purposes.

[0668] The vaccine composition will include, for example, multiple CTL epitopes from STEAP-1 antigen and at least one HTL epitope. This polyepitopic native sequence is

administered either as a peptide or as a nucleic acid sequence which encodes the peptide. Alternatively, an analog can be made of this native sequence, whereby one or more of the epitopes comprise substitutions that alter the cross-reactivity and/or binding affinity properties of the polyepitopic peptide.

[0669] The embodiment of this example provides for the possibility that an as yet undiscovered aspect of immune system processing will apply to the native nested sequence and thereby facilitate the production of therapeutic or prophylactic immune response-inducing vaccine compositions. Additionally, such an embodiment provides for the possibility of motif-bearing epitopes for an HLA makeup(s) that is presently unknown. Furthermore, this embodiment (excluding an analoged embodiment) directs the immune response to multiple peptide sequences that are actually present in native STEAP-1, thus avoiding the need to evaluate any junctional epitopes. Lastly, the embodiment provides an economy of scale when producing peptide or nucleic acid vaccine compositions.

[0670] Related to this embodiment, computer programs are available in the art which can be used to identify in a target sequence, the greatest number of epitopes per sequence length.

Example 26

Polyepitopic Vaccine Compositions from Multiple Antigens

[0671] The STEAP-1 peptide epitopes of the present invention are used in conjunction with epitopes from other target tumor-associated antigens, to create a vaccine composition that is useful for the prevention or treatment of cancer that expresses STEAP-1 and such other antigens. For example, a vaccine composition can be provided as a single polypeptide that incorporates multiple epitopes from STEAP-1 as well as tumor-associated antigens that are often expressed with a target cancer associated with STEAP-1 expression, or can be administered as a composition comprising a cocktail of one or more discrete epitopes. Alternatively, the vaccine can be administered as a minigene construct or as dendritic cells which have been loaded with the peptide epitopes in vitro.

Example 27

Use of Peptides to Evaluate an Immune Response

[0672] Peptides of the invention may be used to analyze an immune response for the presence of specific antibodies, CTL or HTL directed to STEAP-1. Such an analysis can be performed in a manner described by Ogg et al., *Science* 279:2103-2106, 1998. In this Example, peptides in accordance with the invention are used as a reagent for diagnostic or prognostic purposes, not as an immunogen.

[0673] In this example highly sensitive human leukocyte antigen tetrameric complexes ("tetramers") are used for a cross-sectional analysis of, for example, STEAP-1 HLA-A*0201-specific CTL frequencies from HLA A*0201-positive individuals at different stages of disease or following immunization comprising a STEAP-1 peptide containing an A*0201 motif. Tetrameric complexes are synthesized as described (Musey et al., *N. Engl. J. Med.* 337:1267, 1997).

Briefly, purified HLA heavy chain (A*0201 in this example) and β 2-microglobulin are synthesized by means of a prokaryotic expression system. The heavy chain is modified by deletion of the transmembrane-cytosolic tail and COOH-terminal addition of a sequence containing a BirA enzymatic biotinylation site. The heavy chain, β 2-microglobulin, and peptide are refolded by dilution. The 45-kD refolded product is isolated by fast protein liquid chromatography and then biotinylated by BirA in the presence of biotin (Sigma, St. Louis, Mo.), adenosine 5' triphosphate and magnesium. Streptavidin-phycoerythrin conjugate is added in a 1:4 molar ratio, and the tetrameric product is concentrated to 1 mg/ml. The resulting product is referred to as tetramer-phycoerythrin.

[0674] For the analysis of patient blood samples, approximately one million PBMCs are centrifuged at 300 g for 5 minutes and resuspended in 50 μ l of cold phosphate-buffered saline. Tri-color analysis is performed with the tetramer-phycoerythrin, along with anti-CD8-Tricolor, and anti-CD38. The PBMCs are incubated with tetramer and antibodies on ice for 30 to 60 min and then washed twice before formaldehyde fixation. Gates are applied to contain >99.98% of control samples. Controls for the tetramers include both A*0201-negative individuals and A*0201-positive non-diseased donors. The percentage of cells stained with the tetramer is then determined by flow cytometry. The results indicate the number of cells in the PBMC sample that contain epitope-restricted CTLs, thereby readily indicating the extent of immune response to the STEAP-1 epitope, and thus the status of exposure to STEAP-1, or exposure to a vaccine that elicits a protective or therapeutic response.

Example 28

Use of Peptide Epitopes to Evaluate Recall Responses

[0675] The peptide epitopes of the invention are used as reagents to evaluate T cell responses, such as acute or recall responses, in patients. Such an analysis may be performed on patients who have recovered from STEAP-1-associated disease or who have been vaccinated with a STEAP-1 vaccine.

[0676] For example, the class I restricted CTL response of persons who have been vaccinated may be analyzed. The vaccine may be any STEAP-1 vaccine. PBMC are collected from vaccinated individuals and HLA typed. Appropriate peptide epitopes of the invention that, optimally, bear supermotifs to provide cross-reactivity with multiple HLA super-type family members, are then used for analysis of samples derived from individuals who bear that HLA type.

[0677] PBMC from vaccinated individuals are separated on Ficoll-Histopaque density gradients (Sigma Chemical Co., St. Louis, Mo.), washed three times in HBSS (GIBCO Laboratories), resuspended in RPMI-1640 (GIBCO Laboratories) supplemented with L-glutamine (2 mM), penicillin (50 U/ml), streptomycin (50 μ g/ml), and Hepes (10 mM) containing 10% heat-inactivated human AB serum (complete RPMI) and plated using microculture formats. A synthetic peptide comprising an epitope of the invention is added at 10 μ g/ml to each well and HBV core 128-140 epitope is added at 1 μ g/ml to each well as a source of T cell help during the first week of stimulation.

[0678] In the microculture format, 4×10^5 PBMC are stimulated with peptide in 8 replicate cultures in 96-well round bottom plate in 100 μ l/well of complete RPMI. On days 3 and 10, 100 μ l of complete RPMI and 20 U/ml final concentration of rIL-2 are added to each well. On day 7 the cultures are transferred into a 96-well flat-bottom plate and restimulated with peptide, rIL-2 and 10^5 irradiated (3,000 rad) autologous feeder cells. The cultures are tested for cytotoxic activity on day 14. A positive CTL response requires two or more of the eight replicate cultures to display greater than 10% specific ^{51}Cr release, based on comparison with non-diseased control subjects as previously described (Rehermann, et al., *Nature Med.* 2:1104, 1108, 1996; Rehermann et al., *J. Clin. Invest.* 97:1655-1665, 1996; and Rehermann et al. *J. Clin. Invest.* 98:1432-1440, 1996).

[0679] Target cell lines are autologous and allogeneic EBV-transformed B-LCL that are either purchased from the American Society for Histocompatibility and Immunogenetics (ASHI, Boston, Mass.) or established from the pool of patients as described (Guilhot, et al. *J. Virol.* 66:2670-2678, 1992).

[0680] Cytotoxicity assays are performed in the following manner. Target cells consist of either allogeneic HLA-matched or autologous EBV-transformed B lymphoblastoid cell line that are incubated overnight with the synthetic peptide epitope of the invention at 10 μ M, and labeled with 100 μ Ci of ^{51}Cr (Amersham Corp., Arlington Heights, Ill.) for 1 hour after which they are washed four times with HBSS.

[0681] Cytolytic activity is determined in a standard 4-h, split well ^{51}Cr release assay using U-bottomed 96 well plates containing 3,000 targets/well. Stimulated PBMC are tested at effector/target (E/T) ratios of 20:50:1 on day 14. Percent cytotoxicity is determined from the formula: $100 \times [(\text{experimental release} - \text{spontaneous release}) / \text{maximum release} - \text{spontaneous release}]$. Maximum release is determined by lysis of targets by detergent (2% Triton X-100; Sigma Chemical Co., St. Louis, Mo.). Spontaneous release is <25% of maximum release for all experiments.

[0682] The results of such an analysis indicate the extent to which HLA-restricted CTL populations have been stimulated by previous exposure to STEAP-1 or a STEAP-1 vaccine.

[0683] Similarly, Class II restricted HTL responses may also be analyzed. Purified PBMC are cultured in a 96-well flat bottom plate at a density of 1.5×10^5 cells/well and are stimulated with 10 μ g/ml synthetic peptide of the invention, whole STEAP-1 antigen, or PHA. Cells are routinely plated in replicates of 4-6 wells for each condition. After seven days of culture, the medium is removed and replaced with fresh medium containing 10 U/ml IL-2. Two days later, 1 μ Ci ^3H -thymidine is added to each well and incubation is continued for an additional 18 hours. Cellular DNA is then harvested on glass fiber mats and analyzed for ^3H -thymidine incorporation. Antigen-specific T cell proliferation is calculated as the ratio of ^3H -thymidine incorporation in the presence of antigen divided by the ^3H -thymidine incorporation in the absence of antigen.

Example 29

Induction Of Specific CTL Response in Humans

[0684] A human clinical trial for an immunogenic composition comprising CTL and HTL epitopes of the invention

is set up as an IND Phase I, dose escalation study and carried out as a randomized, double-blind, placebo-controlled trial. Such a trial is designed, for example, as follows:

[0685] A total of about 27 individuals are enrolled and divided into 3 groups:

[0686] Group I: 3 subjects are injected with placebo and 6 subjects are injected with 5 μ g of peptide composition;

[0687] Group II: 3 subjects are injected with placebo and 6 subjects are injected with 50 μ g peptide composition;

[0688] Group III: 3 subjects are injected with placebo and 6 subjects are injected with 500 μ g of peptide composition.

[0689] After 4 weeks following the first injection, all subjects receive a booster inoculation at the same dosage.

[0690] The endpoints measured in this study relate to the safety and tolerability of the peptide composition as well as its immunogenicity. Cellular immune responses to the peptide composition are an index of the intrinsic activity of this the peptide composition, and can therefore be viewed as a measure of biological efficacy. The following summarize the clinical and laboratory data that relate to safety and efficacy endpoints.

[0691] Safety: The incidence of adverse events is monitored in the placebo and drug treatment group and assessed in terms of degree and reversibility.

[0692] Evaluation of Vaccine Efficacy: For evaluation of vaccine efficacy, subjects are bled before and after injection. Peripheral blood mononuclear cells are isolated from fresh heparinized blood by Ficoll-Hypaque density gradient centrifugation, aliquoted in freezing media and stored frozen. Samples are assayed for CTL and HTL activity.

[0693] The vaccine is found to be both safe and efficacious.

Example 30

Phase II Trials in Patients Expressing STEAP-1

[0694] Phase II trials are performed to study the effect of administering the CTL-HTL peptide compositions to patients having cancer that expresses STEAP-1. The main objectives of the trial are to determine an effective dose and regimen for inducing CTLs in cancer patients that express STEAP-1, to establish the safety of inducing a CTL and HTL response in these patients, and to see to what extent activation of CTLs improves the clinical picture of these patients, as manifested, e.g., by the reduction and/or shrinking of lesions. Such a study is designed, for example, as follows:

[0695] The studies are performed in multiple centers. The trial design is an open-label, uncontrolled, dose escalation protocol wherein the peptide composition is administered as a single dose followed six weeks later by a single booster shot of the same dose. The dosages are 50, 500 and 5,000 micrograms per injection. Drug-associated adverse effects (severity and reversibility) are recorded.

[0696] There are three patient groupings. The first group is injected with 50 micrograms of the peptide composition and the second and third groups with 500 and 5,000 micrograms of peptide composition, respectively. The patients within

each group range in age from 21-65 and represent diverse ethnic backgrounds. All of them have a tumor that expresses STEAP-1.

[0697] Clinical manifestations or antigen-specific T-cell responses are monitored to assess the effects of administering the peptide compositions. The vaccine composition is found to be both safe and efficacious in the treatment of STEAP-1-associated disease.

Example 31

Induction of CTL Responses Using a Prime Boost Protocol

[0698] A prime boost protocol similar in its underlying principle to that used to confirm the efficacy of a DNA vaccine in transgenic mice, such as described above in the Example entitled "The Plasmid Construct and the Degree to Which It Induces Immunogenicity," can also be used for the administration of the vaccine to humans. Such a vaccine regimen can include an initial administration of, for example, naked DNA followed by a boost using recombinant virus encoding the vaccine, or recombinant protein/polypeptide or a peptide mixture administered in an adjuvant.

[0699] For example, the initial immunization may be performed using an expression vector, such as that constructed in the Example entitled "Construction of "Mini-gene" Multi-Epitope DNA Plasmids" in the form of naked nucleic acid administered IM (or SC or ID) in the amounts of 0.5-5 mg at multiple sites. The nucleic acid (0.1 to 1000 μ g) can also be administered using a gene gun. Following an incubation period of 34 weeks, a booster dose is then administered. The booster can be recombinant fowlpox virus administered at a dose of $5-10^7$ to 5×10^9 pfu. An alternative recombinant virus, such as an MVA, canarypox, adenovirus, or adeno-associated virus, can also be used for the booster, or the polypeptidic protein or a mixture of the peptides can be administered. For evaluation of vaccine efficacy, patient blood samples are obtained before immunization as well as at intervals following administration of the initial vaccine and booster doses of the vaccine. Peripheral blood mononuclear cells are isolated from fresh heparinized blood by Ficoll-Hypaque density gradient centrifugation, aliquoted in freezing media and stored frozen. Samples are assayed for CTL and HTL activity.

[0700] Analysis of the results indicates that a magnitude of response sufficient to achieve a therapeutic or protective immunity against STEAP-1 is generated.

Example 32

Administration of Vaccine Compositions Using Dendritic Cells (DC)

[0701] Vaccines comprising peptide epitopes of the invention can be administered using APCs, or "professional" APCs such as DC. In this example, peptide-pulsed DC are administered to a patient to stimulate a CTL response in vivo. In this method, dendritic cells are isolated, expanded, and pulsed with a vaccine comprising peptide CTL and HTL epitopes of the invention. The dendritic cells are infused back into the patient to elicit CTL and HTL responses in vivo. The induced CTL and HTL then destroy or facilitate

destruction, respectively, of the target cells that bear the STEAP-1 protein from which the epitopes in the vaccine are derived.

[0702] For example, a cocktail of epitope-comprising peptides is administered ex vivo to PBMC, or isolated DC therefrom. A pharmaceutical to facilitate harvesting of DC can be used, such as Progenipoiectin™ (Monsanto, St. Louis, Mo.) or GM-CSF/IL4. After pulsing the DC with peptides, and prior to reinfusion into patients, the DC are washed to remove unbound peptides.

[0703] As appreciated clinically, and readily determined by one of skill based on clinical outcomes, the number of DC reinfused into the patient can vary (see, e.g., *Nature Med.* 4:328, 1998; *Nature Med.* 2:52, 1996 and *Prostate* 32:272, 1997). Although $2\text{-}50 \times 10^6$ DC per patient are typically administered, larger number of DC, such as 10^7 or 10^8 can also be provided. Such cell populations typically contain between 50-90% DC.

[0704] In some embodiments, peptide-loaded PBMC are injected into patients without purification of the DC. For example, PBMC generated after treatment with an agent such as Progenipoiectin™ are injected into patients without purification of the DC. The total number of PBMC that are administered often ranges from 10^8 to 10^{10} . Generally, the cell doses injected into patients is based on the percentage of DC in the blood of each patient, as determined, for example, by immunofluorescence analysis with specific anti-DC antibodies. Thus, for example, if Progenipoiectin™ mobilizes 2% DC in the peripheral blood of a given patient, and that patient is to receive 5×10^6 DC, then the patient will be injected with a total of 2.5×10^8 peptide-loaded PBMC. The percent DC mobilized by an agent such as Progenipoiectin™ is typically estimated to be between 2-10%, but can vary as appreciated by one of skill in the art.

[0705] Ex Vivo Activation of CTL/HTL Responses

[0706] Alternatively, ex vivo CTL or HTL responses to STEAP-1 antigens can be induced by incubating, in tissue culture, the patient's, or genetically compatible, CTL or HTL precursor cells together with a source of APC, such as DC, and immunogenic peptides. After an appropriate incubation time (typically about 7-28 days), in which the precursor cells are activated and expanded into effector cells, the cells are infused into the patient, where they will destroy (CTL) or facilitate destruction (HTL) of their specific target cells, i.e., tumor cells.

Example 33

An Alternative Method of Identifying and Confirming Motif-Bearing Peptides

[0707] Another method of identifying and confirming motif-bearing peptides is to elute them from cells bearing defined MHC molecules. For example, EBV transformed B cell lines used for tissue typing have been extensively characterized to determine which HLA molecules they express. In certain cases these cells express only a single type of HLA molecule. These cells can be transfected with nucleic acids that express the antigen of interest, e.g. STEAP-1. Peptides produced by endogenous antigen processing of peptides produced as a result of transfection will then bind to HLA molecules within the cell and be trans-

ported and displayed on the cell's surface. Peptides are then eluted from the HLA molecules by exposure to mild acid conditions and their amino acid sequence determined, e.g., by mass spectral analysis (e.g., Kubo et al., *J. Immunol.* 152:3913, 1994). Because the majority of peptides that bind a particular HLA molecule are motif-bearing, this is an alternative modality for obtaining the motif-bearing peptides correlated with the particular HLA molecule expressed on the cell.

[0708] Alternatively, cell lines that do not express endogenous HLA molecules can be transfected with an expression construct encoding a single HLA allele. These cells can then be used as described, i.e., they can then be transfected with nucleic acids that encode STEAP-1 to isolate peptides corresponding to STEAP-1 that have been presented on the cell surface. Peptides obtained from such an analysis will bear motif(s) that correspond to binding to the single HLA allele that is expressed in the cell.

[0709] As appreciated by one in the art, one can perform a similar analysis on a cell bearing more than one HLA allele and subsequently determine peptides specific for each HLA allele expressed. Moreover, one of skill would also recognize that means other than transfection, such as loading with a protein antigen, can be used to provide a source of antigen to the cell.

Example 34

Complementary Polynucleotides

[0710] Sequences complementary to the STEAP-1-encoding sequences, or any parts thereof, are used to detect, decrease, or inhibit expression of naturally occurring STEAP-1. Although use of oligonucleotides comprising from about 15 to 30 base pairs is described, essentially the same procedure is used with smaller or with larger sequence fragments. Appropriate oligonucleotides are designed using, e.g., OLIGO 4.06 software (National Biosciences) and the coding sequence of STEAP-1. To inhibit transcription, a complementary oligonucleotide is designed from the most unique 5' sequence and used to prevent promoter binding to the coding sequence. To inhibit translation, a complementary oligonucleotide is designed to prevent ribosomal binding to a STEAP-1-encoding transcript.

Example 35

Purification of Naturally-Occurring or Recombinant STEAP-1 Using STEAP-1-Specific Antibodies

[0711] Naturally occurring or recombinant STEAP-1 is substantially purified by immunoaffinity chromatography using antibodies specific for STEAP-1. An immunoaffinity column is constructed by covalently coupling anti-STEAP-1 antibody to an activated chromatographic resin, such as CNBr-activated SEPHAROSE (Amersham Pharmacia Biotech). After the coupling, the resin is blocked and washed according to the manufacturer's instructions.

[0712] Media containing STEAP-1 are passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of STEAP-1 (e.g., high ionic strength buffers in the presence of detergent). The column is eluted under conditions that disrupt antibody/STEAP-1 binding (e.g., a buffer of pH 2 to

pH 3, or a high concentration of a chaotrope, such as urea or thiocyanate ion), and GCR.P is collected.

Example 36

Identification of Molecules Which Interact with STEAP-1

[0713] STEAP-1, or biologically active fragments thereof, are labeled with 121 I Bolton-Hunter reagent. (See, e.g., Bolton et al. (1973) *Biochem. J.* 133:529.) Candidate molecules previously arrayed in the wells of a multi-well plate are incubated with the labeled STEAP-1, washed, and any wells with labeled STEAP-1 complex are assayed. Data obtained using different concentrations of STEAP-1 are used to calculate values for the number, affinity, and association of STEAP-1 with the candidate molecules.

Example 37

In Vivo Assay for STEAP-1 Tumor Growth Promotion

[0714] The effect of the STEAP-1 protein on tumor cell growth is evaluated in vivo by evaluating tumor development and growth of cells expressing or lacking STEAP-1. For example, SCID mice are injected subcutaneously on each flank with 1×10^6 of either 3T3, or prostate cancer cell lines (e.g. PC3 cells) containing tkNeo empty vector or STEAP-1. At least two strategies may be used: (1) Constitutive STEAP-1 expression under regulation of a promoter such as a constitutive promoter obtained from the genomes of viruses such as polyoma virus, fowlpox virus (UK 2,211, 504 published 5 Jul. 1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), or from heterologous mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, provided such promoters are compatible with the host cell systems, and (2) Regulated expression under control of an inducible vector system, such as ecdysone, tetracycline, etc., provided such promoters are compatible with the host cell systems. Tumor volume is then monitored by caliper measurement at the appearance of palpable tumors and followed over time to determine if STEAP-1-expressing cells grow at a faster rate and whether tumors produced by STEAP-1-expressing cells demonstrate characteristics of altered aggressiveness (e.g. enhanced metastasis, vascularization, reduced responsiveness to chemotherapeutic drugs).

[0715] Additionally, mice can be implanted with 1×10^5 of the same cells orthotopically to determine if STEAP-1 has an effect on local growth in the prostate, and whether STEAP-1 affects the ability of the cells to metastasize, specifically to lymph nodes, and bone (Miki T et al, *Oncol Res.* 2001; 12:209; Fu X et al, *Int J Cancer.* 1991, 49:938). The effect of STEAP on bone tumor formation and growth may be assessed by injecting prostate tumor cells intratibially.

[0716] The assay is also useful to determine the STEAP-1 inhibitory effect of candidate therapeutic compositions, such as for example, STEAP-1 intrabodies, STEAP-1 antisense molecules and ribozymes.

Example 38

STEAP-1 Monoclonal Antibody-Mediated Inhibition of Prostate Tumors In Vivo

[0717] The significant expression of STEAP-1 in cancer tissues and surface localization, together with its restrictive expression in normal tissues makes STEAP-1 a good target for antibody therapy. Similarly, STEAP-1 is a target for T cell-based immunotherapy. Thus, the therapeutic efficacy of anti-STEAP-1 mAbs in human prostate cancer xenograft mouse models is evaluated by using recombinant cell lines such as PC3-STEAP-1, and 3T3-STEAP-1 (see, e.g., Kaighn, M. E., et al., *Invest Urol*, 1979, 17(1): 16-23), as well as human prostate xenograft models such as LAPC 9AD (Saffran et al *PNAS* 1999, 10:1073-1078).

[0718] Antibody efficacy on tumor growth and metastasis formation is studied, e.g., in a mouse orthotopic prostate cancer xenograft models. The antibodies can be unconjugated, as discussed in this Example, or can be conjugated to a therapeutic modality, as appreciated in the art. Anti-STEAP-1 mAbs inhibit formation of both lung and prostate xenografts. Anti-STEAP-1 mAbs also retard the growth of established orthotopic tumors and prolonged survival of tumor-bearing mice. These results indicate the utility of anti-STEAP-1 mAbs in the treatment of local and advanced stages prostate cancer. (See, e.g., Saffran, D., et al., *PNAS* 10:1073-1078 or world wide web URL pnas.org/cgi/doi/10.1073/pnas.051624698).

[0719] Administration of the anti-STEAP-1 mAbs led to retardation of established orthotopic tumor growth and inhibition of metastasis to distant sites, resulting in a significant prolongation in the survival of tumor-bearing mice. These studies indicate that STEAP-1 as an attractive target for immunotherapy and demonstrate the therapeutic potential of anti-STEAP-1 mAbs for the treatment of local and metastatic prostate cancer. This example demonstrates that unconjugated STEAP-1 monoclonal antibodies are effective to inhibit the growth of human prostate tumor xenografts grown in SCID mice; accordingly a combination of such efficacious monoclonal antibodies is also effective.

[0720] Tumor Inhibition Using Multiple Unconjugated STEAP-1 mAbs

[0721] Materials and Methods

[0722] STEAP-1 Monoclonal Antibodies:

[0723] Monoclonal antibodies are raised against STEAP-1 as described in the Example entitled "Generation of STEAP-1 Monoclonal Antibodies (mAbs)." The antibodies are characterized by ELISA, Western blot, FACS, and immunoprecipitation for their capacity to bind STEAP-1. Epitope mapping data for the anti-STEAP-1 mAbs, as determined by ELISA and Western analysis, recognize epitopes on the STEAP-1 protein. Immunohistochemical analysis of prostate cancer tissues and cells with these antibodies is performed.

[0724] The monoclonal antibodies are purified from ascites or hybridoma tissue culture supernatants by Protein-G Sepharose chromatography, dialyzed against PBS, filter sterilized, and stored at -20°C . Protein determinations are performed by a Bradford assay (Bio-Rad, Hercules, Calif.). A therapeutic monoclonal antibody or a cocktail

comprising a mixture of individual monoclonal antibodies is prepared and used for the treatment of mice receiving subcutaneous or orthotopic injections of UM-UC3 and CaLul tumor xenografts.

[0725] Cell Lines and Xenografts

[0726] The prostate cancer cell lines, PC3 and LNCaP cell line as well as the fibroblast line NIH 3T3 (American Type Culture Collection) are maintained in RPMI and DMEM respectively, supplemented with L-glutamine and 10% FBS.

[0727] PC3-STEAP-1 and 3T3-STEAP-1 cell populations are generated by retroviral gene transfer as described in Hubert, R. S., et al., *Proc Natl Acad Sci USA*, 1999, 96(25): 14523.

[0728] The LAPC-9 xenograft, which expresses a wild-type androgen receptor and produces prostate-specific antigen (PSA), is passaged in 6- to 8-week-old male ICR-severe combined immunodeficient (SCID) mice (Taconic Farms) by s.c. trocar implant (Craft, N., et al., *Nat Med*, 1999, 5:280). Single-cell suspensions of LAPC-9 tumor cells are prepared as described in Craft, et al.

[0729] Xenograft Mouse Models.

[0730] Subcutaneous (s.c.) tumors are generated by injection of 1×10^6 cancer cells mixed at a 1:1 dilution with Matrigel (Collaborative Research) in the right flank of male SCID mice. To test antibody efficacy on tumor formation, i.e. antibody injections are started on the same day as tumor-cell injections. As a control, mice are injected with either purified mouse IgG (ICN) or PBS; or a purified monoclonal antibody that recognizes an irrelevant antigen not expressed in human cells. In preliminary studies, no difference is found between mouse IgG or PBS on tumor growth. Tumor sizes are determined by caliper measurements, and the tumor volume is calculated as length \times width \times height. Mice with Subcutaneous tumors greater than 1.5 cm in diameter are sacrificed.

[0731] Orthotopic injections are performed under anesthesia by using ketamine/xylazine. For prostate orthotopic studies, an incision is made through the abdomen to expose the prostate and LAPC or PC3 tumor cells (5×10^5) mixed with Matrigel are injected into the prostate capsule in a 10- μ l volume. To monitor tumor growth, mice are palpated and blood is collected on a weekly basis to measure PSA levels. The mice are segregated into groups for the appropriate treatments, with anti-STEAP-1 or control mAbs being injected i.p.

[0732] Anti-STEAP-1 mAbs Inhibit Growth of STEAP-1-Expressing Xenograft-Cancer Tumors

[0733] The effect of anti-STEAP-1 mAbs on tumor formation is tested by using LNCaP and LAPC9 orthotopic models. As compared with the s.c. tumor model, the orthotopic model, which requires injection of tumor cells directly in the mouse prostate, respectively, results in a local tumor growth, development of metastasis in distal sites, deterioration of mouse health, and subsequent death (Saffran, D., et al., *PNAS* supra). The features make the orthotopic model more representative of human disease progression and allowed us to follow the therapeutic effect of mAbs on clinically relevant end points.

[0734] Accordingly, tumor cells are injected into the mouse prostate, and 2 days later, the mice are segregated into

two groups and treated with either: a) 200-500 μ g, of anti-STEAP-1 Ab, or b) PBS three times per week for two to five weeks.

[0735] A major advantage of the orthotopic cancer models is the ability to study the development of metastases. Formation of metastasis in mice bearing established orthotopic tumors is studied by IHC analysis on lung sections using an antibody against a tumor-specific cell-surface protein such as anti-CK20 for prostate cancer (Lin S et al, *Cancer Detect Prev*, 2001; 25:202).

[0736] Another advantage of xenograft cancer models is the ability to study neovascularization and angiogenesis. Tumor growth is partly dependent on new blood vessel development. Although the capillary system and developing blood network is of host origin, the initiation and architecture of the neovasculature is regulated by the xenograft tumor (Davidoff A M et al, *Clin Cancer Res*, 2001; 7:2870; Solesvik O et al, *Eur J Cancer Clin Oncol*, 1984, 20:1295). The effect of antibody and small molecule on neovascularization is studied in accordance with procedures known in the art, such as by IHC analysis of tumor tissues and their surrounding microenvironment.

[0737] Mice bearing established orthotopic tumors are administered 1000 μ g injections of either anti-STEAP-1 mAb or PBS over a 4-week period. Mice in both groups are allowed to establish a high tumor burden, to ensure a high frequency of metastasis formation in mouse lungs. Mice then are killed and their bladders, livers, bone and lungs are analyzed for the presence of tumor cells by IHC analysis. These studies demonstrate a broad anti-tumor efficacy of anti-STEAP-1 antibodies on initiation and progression of prostate cancer in xenograft mouse models. Anti-STEAP-1 antibodies inhibit tumor formation of tumors as well as retarding the growth of already established tumors and prolong the survival of treated mice. Moreover, anti-STEAP-1 mAbs demonstrate a dramatic inhibitory effect on the spread of local prostate tumor to distal sites, even in the presence of a large tumor burden. Thus, anti-STEAP-1 mAbs are efficacious on major clinically relevant end points (tumor growth), prolongation of survival, and health.

Example 39

Therapeutic and Diagnostic Use of Anti-STEAP-1 Antibodies in Humans

[0738] Anti-STEAP-1 monoclonal antibodies are safely and effectively used for diagnostic, prophylactic, prognostic and/or therapeutic purposes in humans. Western blot and immunohistochemical analysis of cancer tissues and cancer xenografts with anti-STEAP-1 mAb show strong extensive staining in carcinoma but significantly lower or undetectable levels in normal tissues. Detection of STEAP-1 in carcinoma and in metastatic disease demonstrates the usefulness of the mAb as a diagnostic and/or prognostic indicator. Anti-STEAP-1 antibodies are therefore used in diagnostic applications such as immunohistochemistry of kidney biopsy specimens to detect cancer from suspect patients.

[0739] As determined by flow cytometry, anti-STEAP-1 mAb specifically binds to carcinoma cells. Thus, anti-STEAP-1 antibodies are used in diagnostic whole body imaging applications, such as radioimmunoscinigraphy and radioimmunotherapy, (see, e.g., Potamianos S., et. al. Anti-

cancer Res 20(2A):925-948 (2000)) for the detection of localized and metastatic cancers that exhibit expression of STEAP-1. Shedding or release of an extracellular domain of STEAP-1 into the extracellular milieu, such as that seen for alkaline phosphodiesterase B10 (Meerson, N. R., *Hepatology* 27:563-568 (1998)), allows diagnostic detection of STEAP-1 by anti-STEAP-1 antibodies in serum and/or urine samples from suspect patients.

[0740] Anti-STEAP-1 antibodies that specifically bind STEAP-1 are used in therapeutic applications for the treatment of cancers that express STEAP-1. Anti-STEAP-1 antibodies are used as an unconjugated modality and as conjugated form in which the antibodies are attached to one of various therapeutic or imaging modalities well known in the art, such as a prodrugs, enzymes or radioisotopes. In preclinical studies, unconjugated and conjugated anti-STEAP-1 antibodies are tested for efficacy of tumor prevention and growth inhibition in the SCID mouse cancer xenograft models, e.g., kidney cancer models AGS-K3 and AGS-K6, (see, e.g., the Example entitled "STEAP-1 Monoclonal Antibody-mediated Inhibition of Bladder and Lung Tumors In Vivo"). Either conjugated and unconjugated anti-STEAP-1 antibodies are used as a therapeutic modality in human clinical trials either alone or in combination with other treatments as described in following Examples.

Example 40

Human Clinical Trials for the Treatment and Diagnosis of Human Carcinomas Through Use of Human Anti-STEAP-1 Antibodies In Vivo

[0741] Antibodies are used in accordance with the present invention which recognize an epitope on STEAP-1, and are used in the treatment of certain tumors such as those listed in Table I. Based upon a number of factors, including STEAP-1 expression levels, tumors such as those listed in Table I are presently preferred indications. In connection with each of these indications, three clinical approaches are successfully pursued

[0742] I.) Adjunctive therapy: In adjunctive therapy, patients are treated with anti-STEAP-1 antibodies in combination with a chemotherapeutic or antineoplastic agent and/or radiation therapy. Primary cancer targets, such as those listed in Table I, are treated under standard protocols by the addition anti-STEAP-1 antibodies to standard first and second line therapy. Protocol designs address effectiveness as assessed by reduction in tumor mass as well as the ability to reduce usual doses of standard chemotherapy. These dosage reductions allow additional and/or prolonged therapy by reducing dose-related toxicity of the chemotherapeutic agent. Anti-STEAP-1 antibodies are utilized in several adjunctive clinical trials in combination with the chemotherapeutic or antineoplastic agents adriamycin (advanced prostate carcinoma), cisplatin (advanced head and neck and lung carcinomas), taxol (breast cancer), and doxorubicin (preclinical).

[0743] II.) Monotherapy: In connection with the use of the anti-STEAP-1 antibodies in monotherapy of tumors, the antibodies are administered to patients without a chemotherapeutic or antineoplastic agent. In one embodiment, monotherapy is conducted clinically in end stage cancer patients with extensive metastatic disease. Patients show

some disease stabilization. Trials demonstrate an effect in refractory patients with cancerous tumors.

[0744] III.) Imaging Agent: Through binding a radionuclide (e.g., iodine or yttrium (I^{131} , Y^{90}) to anti-STEAP-1 antibodies, the radiolabeled antibodies are utilized as a diagnostic and/or imaging agent. In such a role, the labeled antibodies localize to both solid tumors, as well as, metastatic lesions of cells expressing STEAP-1. In connection with the use of the anti-STEAP-1 antibodies as imaging agents, the antibodies are used as an adjunct to surgical treatment of solid tumors, as both a pre-surgical screen as well as a post-operative follow-up to determine what tumor remains and/or returns. In one embodiment, a (^{111}In)-STEAP-1 antibody is used as an imaging agent in a Phase I human clinical trial in patients having a carcinoma that expresses STEAP-1 (by analogy see, e.g., Divgi et al. *J. Natl. Cancer Inst.* 83:97-104 (1991)). Patients are followed with standard anterior and posterior gamma camera. The results indicate that primary lesions and metastatic lesions are identified

[0745] Dose and Route of Administration

[0746] As appreciated by those of ordinary skill in the art, dosing considerations can be determined through comparison with the analogous products that are in the clinic. Thus, anti-STEAP-1 antibodies can be administered with doses in the range of 5 to 400 mg/m², with the lower doses used, e.g., in connection with safety studies. The affinity of anti-STEAP-1 antibodies relative to the affinity of a known antibody for its target is one parameter used by those of skill in the art for determining analogous dose regimens. Further, anti-STEAP-1 antibodies that are fully human antibodies, as compared to the chimeric antibody, have slower clearance; accordingly, dosing in patients with such fully human anti-STEAP-1 antibodies can be lower, perhaps in the range of 50 to 300 mg/m², and still remain efficacious. Dosing in mg/m², as opposed to the conventional measurement of dose in mg/kg, is a measurement based on surface area and is a convenient dosing measurement that is designed to include patients of all sizes from infants to adults.

[0747] Three distinct delivery approaches are useful for delivery of anti-STEAP-1 antibodies. Conventional intravenous delivery is one standard delivery technique for many tumors. However, in connection with tumors in the peritoneal cavity, such as tumors of the ovaries, biliary duct, other ducts, and the like, intraperitoneal administration may prove favorable for obtaining high dose of antibody at the tumor and to also minimize antibody clearance. In a similar manner, certain solid tumors possess vasculature that is appropriate for regional perfusion. Regional perfusion allows for a high dose of antibody at the site of a tumor and minimizes short term clearance of the antibody.

[0748] Clinical Development Plan (CDP)

[0749] Overview: The CDP follows and develops treatments of anti-STEAP-1 antibodies in connection with adjunctive therapy, monotherapy, and as an imaging agent. Trials initially demonstrate safety and thereafter confirm efficacy in repeat doses. Trials are open label comparing standard chemotherapy with standard therapy plus anti-STEAP-1 antibodies. As will be appreciated, one criteria that can be utilized in connection with enrollment of patients is STEAP-1 expression levels in their tumors as determined by biopsy.

[0750] As with any protein or antibody infusion-based therapeutic, safety concerns are related primarily to (i) cytokine release syndrome, i.e., hypotension, fever, shaking, chills; (ii) the development of an immunogenic response to the material (i.e., development of human antibodies by the patient to the antibody therapeutic, or HAHA response); and, (iii) toxicity to normal cells that express STEAP-1. Standard tests and follow-up are utilized to monitor each of these safety concerns. Anti-STEAP-1 antibodies are found to be safe upon human administration.

Example 41

Human Clinical Trial Adjunctive Therapy with Human Anti-STEAP-1 Antibody and Chemotherapeutic Agent

[0751] A phase I human clinical trial is initiated to assess the safety of six intravenous doses of a human anti-STEAP-1 antibody in connection with the treatment of a solid tumor, e.g., a cancer of a tissue listed in Table I. In the study, the safety of single doses of anti-STEAP-1 antibodies when utilized as an adjunctive therapy to an antineoplastic or chemotherapeutic agent as defined herein, such as, without limitation: cisplatin, topotecan, doxorubicin, adriamycin, taxol, or the like, is assessed. The trial design includes delivery of six single doses of an anti-STEAP-1 antibody with dosage of antibody escalating from approximately about 25 mg/m² to about 275 mg/m² over the course of the treatment in accordance with the following schedule:

	Day 0	Day 7	Day 14	Day 21	Day 28	Day 35
mAb Dose	25 mg/m ²	75 mg/m ²	125 mg/m ²	175 mg/m ²	225 mg/m ²	275 mg/m ²
Chemotherapy (standard dose)	+	+	+	+	+	+

[0752] Patients are closely followed for one-week following each administration of antibody and chemotherapy. In particular, patients are assessed for the safety concerns mentioned above: (i) cytokine release syndrome, i.e., hypotension, fever, shaking, chills; (ii) the development of an immunogenic response to the material (i.e., development of human antibodies by the patient to the human antibody therapeutic, or HAHA response); and, (iii) toxicity to normal cells that express STEAP-1. Standard tests and follow-up are utilized to monitor each of these safety concerns. Patients are also assessed for clinical outcome, and particularly reduction in tumor mass as evidenced by MRI or other imaging.

[0753] The anti-STEAP-1 antibodies are demonstrated to be safe and efficacious, Phase II trials confirm the efficacy and refine optimum dosing.

Example 42

Human Clinical Trial: Monotherapy with Human Anti-STEAP-1 Antibody

[0754] Anti-STEAP-1 antibodies are safe in connection with the above-discussed adjunctive trial, a Phase II human clinical trial confirms the efficacy and optimum dosing for monotherapy. Such trial is accomplished, and entails the

same safety and outcome analyses, to the above-described adjunctive trial with the exception being that patients do not receive chemotherapy concurrently with the receipt of doses of anti-STEAP-1 antibodies.

Example 43

Human Clinical Trial: Diagnostic Imaging with Anti-STEAP-1 Antibody

[0755] Once again, as the adjunctive therapy discussed above is safe within the safety criteria discussed above, a human clinical trial is conducted concerning the use of anti-STEAP-1 antibodies as a diagnostic imaging agent. The protocol is designed in a substantially similar manner to those described in the art, such as in Divgi et al. *J. Natl. Cancer Inst.* 83:97-104 (1991). The antibodies are found to be both safe and efficacious when used as a diagnostic modality.

Example 44

Homology Comparison of STEAP-1 to Known Sequences

[0756] The human STEAP protein does not exhibit a high degree of homology to any known human proteins. The prototype member of the STEAP family, STEAP-1v.1, is a type IIIa membrane protein consisting of 339 amino acids. STEAP-1 is a six transmembrane domain protein, with intracellular N- and C-termini.

[0757] The STEAP-1 gene is somewhat homologous to a previously cloned gene, namely mouse TNF α -induced adipose-related protein (gi|16905133). STEAP-1v.1 shares 40% identities and 63% homology with TIARP. In addition, STEAP-1 shows homology to rat pHye protein, with 49% identity and 71% homology to that protein. The TIARP protein is a 6 transmembrane protein of unknown function which localizes to the cell surface (Moldes M et al, *J. Biol. Chem* 2001, 276:33938). Rat pHye is a protein expressed in Dunning rats prostate cancer lines. Overexpression of pHye in DU145 cells reduces their tumor growth properties (Steiner M et al, *Cancer Res* 2000, 60:4419). In addition, STEAP1 shows significant homology to mouse six transmembrane epithelial antigen of the prostate (gi 20820492).

[0758] Motif analysis revealed the presence of several protein functional motifs (Table XXI). Prints prediction identified a Transforming protein P21 ras signature, and Fibronectin type III repeat signature, while Blocks prediction identified a Half-A-TPR repeat, and an arsenical pump membrane protein signature. The fibronectin type III repeat region is a 100 amino acid domain, which mediated binding to DNA, heparin, basement membrane and the cell surface. The predominant role of these repeats is binding to the cell surface, allowing cell adhesion and mediating signaling event. Half-A-TPR repeat is a motif found in several RNA

processing proteins. The arsenical pump functions in the efflux of ion and small molecules (Walmsley A R et al. *J Biol Chem* 2001, 276:6378-91). The motifs can participate in tumor growth and progression by enhancing the initial stages of tumorigenesis, such as tumor take or establishment of a tumor, by allowing adhesion to basement membranes and surrounding cells, by mediating cell communication and transport of ions.

[0759] Accordingly, when STEAP-1 functions as a regulator of tumor establishment, tumor formation, tumor growth, cell signaling or as a modulator of transcription involved in activating genes associated with survival, invasion, tumorigenesis or proliferation, STEAP-1 is used for therapeutic, diagnostic, prognostic and/or preventative purposes. In addition, when a molecule, such as a variant or SNP of STEAP-1 is expressed in cancerous tissues, such as those listed in Table I, they are used for therapeutic, diagnostic, prognostic and/or preventative purposes.

Example 45

Regulation of Transcription

[0760] The localization of STEAP-1 coupled to the presence of RNA processing motifs within its sequence indicate that STEAP-1 modulates the transcriptional regulation of eukaryotic genes. Regulation of gene expression is confirmed, e.g., by studying gene expression in cells expressing or lacking STEAP-1. For this purpose, two types of experiments are performed.

[0761] In the first set of experiments, RNA from parental and STEAP-1-expressing cells are extracted and hybridized to commercially available gene arrays (Clontech) (Smid-Koopman E et al. *Br J Cancer*. 2000. 83:246). Resting cells as well as cells treated with FBS, androgen or growth factors are compared. Differentially expressed genes are identified in accordance with procedures known in the art. The differentially expressed genes are then mapped to biological pathways (Chen K et al. *Thyroid*. 2001. 11:41.).

[0762] In the second set of experiments, specific transcriptional pathway activation is evaluated using commercially available (Stratagene) luciferase reporter constructs including: NFkB-luc, SRE-luc, ELK1-luc, ARE-luc, p53-luc, and CRE-luc. These transcriptional reporters contain consensus binding sites for known transcription factors that lie downstream of well-characterized signal transduction pathways, and represent a good tool to ascertain pathway activation and screen for positive and negative modulators of pathway activation.

[0763] Thus, STEAP-1 plays a role in gene regulation, and it is used as a target for diagnostic, prognostic, preventative and/or therapeutic purposes.

Example 46

Identification and Confirmation of Potential Signal Transduction Pathways

[0764] Many mammalian proteins have been reported to interact with signaling molecules and to participate in regulating signaling pathways. (J. *Neurochem*. 2001; 76:217-223). Fibronectin in particular has been associated with the MAPK signaling cascade that control cell mitogenesis (Jiang F, Jia Y, Cohen I. *Blood*. 2002, 99:3579). In addition,

the STEAP-1 protein contains several phosphorylation sites (see Table XXI) indicating an association with specific signaling cascades. Using immunoprecipitation and Western blotting techniques, proteins are identified that associate with STEAP-1 and mediate signaling events. Several pathways known to play a role in cancer biology can be regulated by STEAP-1, including phospholipid pathways such as PI3K, AKT, etc, adhesion and migration pathways, including FAK, Rho, Rac-1, β -catenin, etc, as well as mitogenic/survival cascades such as ERK, p38, etc (Cell Growth Differ. 2000, 11:279; *J Biol. Chem.* 1999, 274:801; *Oncogene*. 2000, 19:3003, *J. Cell Biol.* 1997, 138:913.). In order to determine whether expression of STEAP-1 is sufficient to regulate specific signaling pathways not otherwise active in resting PC3 cells, the effect of these genes on the activation of the p38 MAPK cascade was investigated in the prostate cancer cell line PC3 (**FIG. 21A-B**). Activation of the p38 kinase is dependent on its phosphorylation on tyrosine and serine residues. Phosphorylated p38 can be distinguished from the non-phosphorylated state by a Phospho-p38 mAb. This phospho-specific Ab was used to study the phosphorylation state of p38 in engineered PC3 cell lines.

[0765] PC3 cells stably expressing STEAP-1 neo were grown overnight in either 1% or 10% FBS. Whole cell lysates were analyzed by western blotting. PC3 cells treated with the known p38 activators, NaSaI or TNF, were used as a positive control. The results show that while expression of the control neo gene has no effect on p38 phosphorylation, expression of STEAP-1 in PC3 cells is sufficient to induce the activation of the p38 pathway (**FIG. 21A**). The results were verified using western blotting with an anti-p38 Ab, which shows equal protein loading on the gels (**FIG. 21B**).

[0766] In another set of experiments, the sufficiency of expression of STEAP-1 in the prostate cancer cell line PC3 to activate the mitogenic MAPK pathway, namely the ERK cascade, was examined (**FIG. 22A-B**). Activation of ERK is dependent on its phosphorylation on tyrosine and serine residues. Phosphorylated ERK can be distinguished from the non-phosphorylated state by a Phospho-ERK mAb. This phospho-specific Ab was used to study the phosphorylation state of ERK in engineered PC3 cell lines. PC3 cells, expressing an activated form of Ras, were used as a positive control.

[0767] The results show that while expression of the control neo gene has no effect on ERK phosphorylation, expression of STEAP-1 in PC3 cells is sufficient to induce an increase in ERK phosphorylation (**FIG. 22A**). These results were verified using anti-ERK western blotting (**FIG. 22B**) and confirm the activation of the ERK pathway by STEAP-1 and STEAP-2.

[0768] Since FBS contains several components that may contribute to receptor-mediated ERK activation, we examined the effect of STEAP-1 in low and optimal levels of FBS. PC3 cells expressing neo or STEAP-1 were grown in either 0.1% or 10% FBS overnight. The cells were analyzed by anti-Phospho-ERK western blotting. This experiment shows that STEAP-1 induces the phosphorylation of ERK in 0.1% FBS, and confirms that expression of STEAP-1 is sufficient to induce activation of the ERK signaling cascade in the absence of additional stimuli.

[0769] To confirm that STEAP-1 directly or indirectly activates known signal transduction pathways in cells,

luciferase (luc) based transcriptional reporter assays are carried out in cells expressing individual genes. These transcriptional reporters contain consensus-binding sites for known transcription factors that lie downstream of well-characterized signal transduction pathways. The reporters and examples of these associated transcription factors, signal transduction pathways, and activation stimuli are listed below.

- [0770] 1. NFkB-luc, NFkB/Rel; Ik-kinase/SAPK; growth/apoptosis/stress
- [0771] 2. SRE-luc, SRF/TCF/ELK1; MAPK/SAPK; growth/differentiation
- [0772] 3. AP-1-luc, FOS/JUN; MAPK/SAPK/PKC; growth/apoptosis/stress
- [0773] 4. ARE-luc, androgen receptor; steroids/MAPK; growth/differentiation/apoptosis
- [0774] 5. p53-luc, p53; SAPK; growth/differentiation/apoptosis
- [0775] 6. CRE-luc, CREB/ATF2; PKA/p38; growth/apoptosis/stress
- [0776] 7. TCF-luc, TCF/Lef; β -catenin, Adhesion/invasion

[0777] Gene-mediated effects can be assayed in cells showing mRNA expression. Luciferase reporter plasmids can be introduced by lipid-mediated transfection (TFX-50, Promega). Luciferase activity, an indicator of relative transcriptional activity, is measured by incubation of cell extracts with luciferin substrate and luminescence of the reaction is monitored in a luminometer.

[0778] Signaling pathways activated by STEAP-1 are mapped and used for the identification and validation of therapeutic targets. When STEAP-1 is involved in cell signaling, it is used as target for diagnostic, prognostic, preventative and/or therapeutic purposes.

Example 47

Involvement in Tumor Progression

[0779] Based on the documented role of transforming protein in transformation, and progression, the STEAP-1 gene can contribute to the growth and transformation of cancer cells. The role of STEAP-1 in tumor growth is confirmed in a variety of primary and transfected cell lines including prostate cell lines, as well as NIH 3T3 cells engineered to stably express STEAP-1. Parental cells lacking STEAP-1 and cells expressing STEAP-1 are evaluated for cell growth using a well-documented proliferation assay (Fraser S P, Grimes J A, Djamgoz M B. Prostate. 2000; 44:61, Johnson D E, Ochieng J, Evans S L. Anticancer Drugs. 1996, 7:288).

[0780] To confirm the role of STEAP-1 in the transformation process, its effect in colony forming assays is investigated. Parental NIH-3T3 cells lacking STEAP-1 are compared to NIH-3T3 cells expressing STEAP-1, using a soft agar assay under stringent and more permissive conditions (Song Z. et al. Cancer Res. 2000; 60:6730).

[0781] To confirm the role of STEAP-1 in invasion and metastasis of cancer cells, a well-established assay is used,

e.g., a Transwell Insert System assay (Becton Dickinson) (Cancer Res. 1999; 59:6010). Control cells, including prostate, breast and kidney cell lines lacking STEAP-1 are compared to cells expressing STEAP-1. Cells are loaded with the fluorescent dye, calcein, and plated in the top well of the Transwell insert coated with a basement membrane analog. Invasion is determined by fluorescence of cells in the lower chamber relative to the fluorescence of the entire cell population.

[0782] STEAP-1 can also play a role in cell cycle and apoptosis. Parental cells and cells expressing STEAP-1 are compared for differences in cell cycle regulation using a well-established BrdU assay (Abdel-Malek Z A. J Cell Physiol. 1988, 136:247). In short, cells are grown under both optimal (full serum) and limiting (low serum) conditions are labeled with BrdU and stained with anti-BrdU Ab and propidium iodide. Cells are analyzed for entry into the G1, S, and G2M phases of the cell cycle. Alternatively, the effect of stress on apoptosis is evaluated in control parental cells and cells expressing STEAP-1, including normal and tumor prostate cells. Engineered and parental cells are treated with various chemotherapeutic agents, such as etoposide, taxol, etc, and protein synthesis inhibitors, such as cycloheximide. Cells are stained with annexin V-FITC and cell death is measured by FACS analysis. The modulation of cell death by STEAP-1 can play a critical role in regulating tumor progression and tumor load.

[0783] When STEAP-1 plays a role in cell growth, transformation, invasion or apoptosis, it is used as a target for diagnostic, prognostic, preventative and/or therapeutic purposes.

Example 48

Involvement in Angiogenesis

[0784] Angiogenesis or new capillary blood vessel formation is necessary for tumor growth (Hanahan D, Folkman J. Cell. 1996, 86:353; Folkman J. Endocrinology. 1998 139:441). Based on the effect of phosphodiesterase inhibitors on endothelial cells, STEAP-1 plays a role in angiogenesis (DeFouw L et al, Microvasc Res 2001, 62:263). Several assays have been developed to measure angiogenesis in vitro and in vivo, such as the tissue culture assays endothelial cell tube formation and endothelial cell proliferation. Using these assays as well as in vitro neo-vascularization, the role of STEAP-1 in angiogenesis, enhancement or inhibition, is confirmed.

[0785] For example, endothelial cells engineered to express STEAP-1 are evaluated using tube formation and proliferation assays. The effect of STEAP-1 is also confirmed in animal models in vivo. For example, cells either expressing or lacking STEAP-1 are implanted subcutaneously in immunocompromised mice. Endothelial cell migration and angiogenesis are evaluated 5-15 days later using immunohistochemistry techniques. STEAP-1 affects angiogenesis, and it is used as a target for diagnostic, prognostic, preventative and/or therapeutic purposes

Example 49

Involvement in Protein-Protein Interactions

[0786] Fibronectin motifs have been shown to mediate interaction with other proteins, including cell surface pro-

tein. Using immunoprecipitation techniques as well as two yeast hybrid systems, proteins are identified that associate with STEAP-1. Immunoprecipitates from cells expressing STEAP-1 and cells lacking STEAP-1 are compared for specific protein-protein associations.

[0787] Studies are performed to confirm the extent of association of STEAP-1 with effector molecules, such as nuclear proteins, transcription factors, kinases, phosphates etc. Studies comparing STEAP-1 positive and STEAP-1 negative cells as well as studies comparing unstimulated/resting cells and cells treated with epithelial cell activators, such as cytokines, growth factors, androgen and anti-integrin Ab reveal unique interactions.

[0788] In addition, protein-protein interactions are confirmed using two yeast hybrid methodology (Curr Opin Chem Biol. 1999, 3:64). A vector carrying a library of proteins fused to the activation domain of a transcription factor is introduced into yeast expressing a STEAP-1-DNA-binding domain fusion protein and a reporter construct. Protein-protein interaction is detected by calorimetric reporter activity. Specific association with effector molecules and transcription factors directs one of skill to the mode of action of STEAP-1, and thus identifies therapeutic, prognostic, preventative and/or diagnostic targets for cancer. This and similar assays are also used to identify and screen for small molecules that interact with STEAP-1.

[0789] Thus it is found that STEAP-1 associates with proteins and small molecules. Accordingly, STEAP-1 and these proteins and small molecules are used for diagnostic, prognostic, preventative and/or therapeutic purposes.

Example 50

Involvement of STEAP-1 in Small Molecule Transport and Cell-Cell Communication

[0790] Cell-cell communication is essential in maintaining organ integrity and homeostasis, both of which become deregulated during tumor formation and progression. Inter-cellular communications can be measured using two types of assays (J. Biol. Chem. 2000, 275:25207). In the first assay, cells loaded with a fluorescent dye are incubated in the presence of unlabeled recipient cells and the cell populations are examined under fluorescent microscopy. This qualitative assay measures the exchange of dye between adjacent cells. In the second assay system, donor and recipient cell populations are treated as above and quantitative measurements of the recipient cell population are performed by FACS analysis. Using these two assay systems, cells expressing STEAP-1 are compared to controls that do not express STEAP-1, and it is found that STEAP-1 enhances cell communications. FIG. 19 and FIG. 20 demonstrate that STEAP-1 mediates the transfer of the small molecule calcein between adjacent cells, and thereby regulates cell-cell communication in prostate cancer cells. In this experiment, recipient PC3 cells were labeled with dextran-Texas Red and donor PC3 cells were labeled with calcein AM (green). The donor (green) and recipient (red) cells were co-cultured at 37° C. and analyzed by microscopy for the co-localization of Texas red and calcein. The results demonstrated that while PC3 control cells (no detectable STEAP-1 protein expression) exhibit little calcein transfer, the expression of STEAP-1 allows the transfer of small molecules between

cells (FIG. 19), whereby the initially red recipient cells take on a brownish color, and co-localize the red and green molecules. Small molecules and/or antibodies that modulate cell-cell communication mediated by STEAP-1 are used as therapeutics for cancers that express STEAP-1. FIG. 20 shows the time-dependent manner of cell-cell communication mediated by STEAP-1, where little transfer in PC3-STEAP-1 cells is seen at 6 hours, and much transfer is seen at 24 hours. FIG. 23 demonstrates that expression of STEAP-1 is necessary on both donor and recipient populations for the transfer of small molecules to take place. In this experiment, donor cells labeled with dextran red were incubated with recipient cells labeled with calcein (green). However, the donor and recipient populations were alternated, such that a PC3 donor population was incubated with PC3 recipient, or with PC3-STEAP-1 recipient populations. Similarly, a PC3-STEAP-1 donor population was co-cultured with a PC3 or a PC3-STEAP-1 recipient population. The results show that co-culturing of control PC3 and PC3 cells fail to mediate calcein transfer. Similarly, co-incubation of control PC3 and PC3-STEAP-1 does not allow the transfer of calcein. However, co-culturing PC3-STEAP-1 donor and PC3-STEAP-1 recipient cells mediates small molecule transfer as depicted by co-localization of green and red pigments in the same cells. Taken together, the data shown in FIGS. 19, 20 and 23 demonstrate that STEAP-1 mediates small molecule transfer and regulates cell-cell communication by forming inter-cellular communication channels that are similar in function to gap junctions.

[0791] Thus, because STEAP-1 functions in cell-cell communication and small molecule transport, it is used as a target or marker for diagnostic, prognostic, preventative and/or therapeutic purposes.

Example 51

Involvement of STEAP-1 in Ion Transport

[0792] The localization and topology of STEAP-1 supports its function as a transporter. To confirm that STEAP-1 functions as an ion channel, FACS analysis and fluorescent microscopy techniques were used (Gergely L, et al., Clin Diagn Lab Immunol. 1997; 4:70; Skryma R, et al., J. Physiol. 2000, 527: 71). Using FACS analysis and commercially available indicators (Molecular Probes), parental cells and cells expressing STEAP-1 were compared for their ability to transport calcium; prostate cancer PC3 cell lines were used in these studies. PC3 and PC3-STEAP-1 cells were loaded with calcium responsive indicators Fluo4 and Fura red, incubated in the presence or absence of calcium and lipophosphatidic acid (LPA), and analyzed by flow cytometry. FIG. 17 shows that STEAP-1 increased calcium flux in response to LPA. This data validates an important mechanism by which cancer cells are regulated. This is particularly true in the case of calcium, as calcium channel inhibitors have been reported to induce the death of certain cancer cells, including prostate cancer cell lines (Batra S, Popper L D, Hartley-Asp B. Prostate. 1991, 19: 299).

[0793] Furthermore, FIG. 18 shows that STEAP-1-mediated calcium transport regulates prostate cancer growth by regulating intracellular levels of calcium. In this study, control PC3 and PC3-STEAP-1 cells were grown in the presence or absence of ion channel inhibitors, namely amiloride, NDGA and TEA, which inhibit the transport of

sodium, calcium and potassium, respectively. STEAP-1 expression rendered PC3 cells sensitive to treatment with the Ca⁺⁺ channel inhibitor NDGA. While PC3 control cells demonstrated 100% growth in the presence of the inhibitor, NDGA, at 50 μ M inhibited the proliferation of PC3-STEAP-1 cells by 42% and 10 example 51 μ M NDGA inhibited proliferation 20%. These findings confirm the importance of STEAP-1 as regulator of calcium transport in the proliferation of cancer cells that express this protein. Thus, STEAP-1 is used in therapeutic modalities that control the proliferation of prostate cancer cells. Because STEAP-1 functions in ion transport, it is used as a target or marker for diagnostic, prognostic, preventative and therapeutic purposes.

Example 52

RNA Interference (RNAi)

[0794] RNA interference (RNAi) makes use of sequence specific double stranded RNA to prevent gene expression. Small interfering RNA (siRNA) are transfected into mammalian cells and thereby mediate sequence specific mRNA degradation. (Elbashir, et al, Nature, 2001; vol. 411: 494-498). The following siRNA oligonucleotide sequences were used:

(SEQ ID NO: 96)
STEAP-1 (1) target: GACAUCACAAACCAAGAAG
(corresponding to nucleotides 16-34 of STEAP-1 ORF)

(SEQ ID NO: 97)
STEAP-1 (2) target: GUGGAUAGAUAAAACAA
(corresponding to nucleotides 893-911 of STEAP-1 ORF)

[0795] The sense strand of STEAP-1 (1) is labeled at 3' with fluorescein, 6-FAM (ABS 494 nm, EMM 525 nm, green). The siRNA is dissolved in RNA-free sterile buffer (100 mM KOAc, 30 mM HEPES KOH, 2 mM MOAc, at pH 7.4) to make 20 μ M stock (200 \times). The siRNA is transfected into LNCaP, 3T3-STEAP-1, and Rat-1-STEAP-1 cells seeded on 6-well plates with oligofectamine reagent (Invitrogen). The final concentration of siRNA was 100nM. The following oligonucleotide was used as a control to rule out any non-specific effect of STEAP-1 siRNA oligonucleotides:

(SEQ ID NO: 98)
Control: GCCUCCCCAUUGGUCUCCC
(corresponding to nucleotides 91-109 of ORF)

[0796] Protein expression was detected 24 hours after transfection by immunostaining followed by flow cytometry. In addition, confirmation of altered gene expression was performed by Western blotting. The results (FIG. 24) show that the introduction of STEAP-1 specific RNAi reduced the expression of STEAP-1 in recombinant 3T3 and Rat-1 cells. 3T3 and Rat-1 cells were permeabilized and stained with anti-STEAP-1 polyclonal antibodies. Whole cell immunostaining revealed that the STEAP-1 RNAi reduced STEAP-1 expression in Rat-1 and 3T3 cells. This reduction was confirmed by Western blot analysis where STEAP-1 protein was substantially reduced in STEAP-1 RNAi treated

cells relative to control and untreated cells. Additionally, RNAi reduces the endogenous expression of STEAP-1 in the prostate cancer and LNCaP cell line as shown in FIG. 25.

[0797] Accordingly, the RNA oligonucleotide sequences are used in therapeutic and prophylactic applications. Moreover, the RNA oligonucleotide sequences are used to assess how modulating the expression of a STEAP-1 gene affects function of cancer cells and/or tissues.

Example 53

Modulation of STEAP-1 Function

[0798] Ion transport plays an important role regulating cell growth intracellular permeability, molecular trafficking and signal transduction (Minke B. Cell Mol Neurobiol. 2001, 21:629; Golovina et al, Am J Physiol Heart Circ Physiol. 2001, 280:H746) these are functions that are especially relevant to the neoplastic condition. Cell-cell communication regulates homeostasis, cell proliferation and cell death (Evans W H, Martin P E. Mol Membr Biol. 2002 19:121; Carruba G, et al, Ann N Y Acad. Sci. 2002, 963:156) these functions too are especially relevant to the neoplastic condition.

[0799] Using control cell lines and cell lines expressing STEAP-1, inhibitors of STEAP-1 function are identified. For example, PC3 and PC3-STEAP-1 cells can be incubated in the presence and absence of mAb or small molecule inhibitors. The effect of these mAb or small molecule inhibitors are investigated using the ion flux, cell communication, proliferation and signaling assays described above.

[0800] Signal transduction and biological output mediated by transporters can be modulated through various mechanisms, including inhibition of receptor and ligand binding, ion antagonists, protein interactions, regulation of ion and small molecule transport, etc (Tang W et al, Front Biosci 2002, 7:1583). Using control cell lines and cell lines expressing STEAP-1, modulators (inhibitors or enhancers) of STEAP-1 function are identified. For example, PC3 and PC3-STEAP-1 cells are incubated in the presence and absence of mAb or small molecule modulators. In view of the functions of STEAP-1 disclosed herein, modulators that are ion channel blockers used in the context of the present invention include such compounds as amlodipine, azulene, dihydropyridines, thianines, nifedine, verapamil and their derivatives (Tanaka Y, Shigenobu K. Cardiovasc Drug Rev. 2001, 19:297; Djuric D, Mitrovic V, Jakovljevic V. Arzneimittelforschung. 2002, 52:365; Kourie J I, Wood H B. Prog Biophys Mol. Biol. 2000; 73:91); and, modulators that are inhibitors of cell communication used in the context of the present invention include such compounds as beta-glycyrhethinic acid, retinoids, TPA (Krutovskikh V A et al, Oncogene. 2002, 21:1989; Rudkin et al, J Surg Res. 2002, 103:183; Ruch J et al, J Cell Biochem. 2001, 83:163). Accordingly, the effect(s) of mAb or small molecule inhibitors are investigated using the ion flux, cell communication, proliferation and signaling assays described Examples above.

[0801] When mAb and small molecules modulate, e.g., inhibit, the transport and tumorigenic function of STEAP-1, they are used for preventative, prognostic, diagnostic and/or therapeutic purposes.

[0803] The present invention is not to be limited in scope by the embodiments disclosed herein, which are intended as single illustrations of individual aspects of the invention, and any that are functionally equivalent are within the scope of the invention. Various modifications to the models and methods of the invention, in addition to those described herein, will become apparent to those skilled in the art from the foregoing description and teachings, and are similarly intended to fall within the scope of the invention. Such modifications or other embodiments can be practiced without departing from the true scope and spirit of the invention.

[0804] Tables:

TABLE I

Tissues that Express STEAP-1 When Malignant
Stomach
Rectum

[0805]

TABLE II

<u>Amino Acid Abbreviations</u>		
SINGLE LETTER	THREE LETTER	FULL NAME
F	Phe	phenylalanine
L	Leu	leucine
S	Ser	serine
Y	Tyr	tyrosine
C	Cys	cysteine
W	Trp	tryptophan
P	Pro	proline
H	His	histidine
Q	Gln	glutamine
R	Arg	arginine
I	Ile	isoleucine
M	Met	methionine
T	Thr	threonine
N	Asn	asparagine
K	Lys	lysine
V	Val	valine
A	Ala	alanine
D	Asp	aspartic acid
E	Glu	glutamic acid
G	Gly	glycine

[0806]

TABLE III

[illegible]

[0807]

TABLE IV

HLA Class I/II Motifs/Supernotifs			
(A): HLA Class I Supernotifs/Motifs			
SUPERMOTIFS	POSITION	POSITION	POSITION
	2 (Primary Anchor)	3 (Primary Anchor)	C Terminus (Primary Anchor)
A1	TILVMS		FWY
A2	LIVMATQ		IVMATL
A3	VSMATLI		RK
A24	YFWIVLMT		FIYWLM
B7	P		VILFMWYA
B27	RHK		FYLWMIVA
B44	ED		FWYLIMVA
B58	ATS		FWYLIVMA
B62	QLIVMP		FWYMIVLA
MOTIFS			
A1	TSM		Y
A1		DEAS	Y
A2.1	LMVQLAT		VLIMAT
A3	LMVISATFCGD		KYRHEA
A11	VTMLISAGNCDF		KRYH
A24	YFWM		FLIW
A*3101	MVTALIS		RK
A*3301	MVALFIST		RK
A*6801	AVTMSLI		RK
B*0702	P		LMFWYAIIV
B*3501	P		LMFWYIVA
B51	P		LIVFWYAM
B*5301	P		IMFWYALV
B*5401	P		ATIVLMFWY

Bolded residues are preferred, italicized residues are less preferred: A peptide is considered motif-bearing if it has primary anchors at each primary anchor position for a motif or supernotif as specified in the above table.

(B): HLA Class II Supernotif

1	6	9
W, F, Y, V, J, L	A, V, I, L, P, C, S, T	A, V, I, L, C, S, T, M, Y

(C): HLA Class II Motifs

MOTIFS	1° anchor 1	2	3	4	5	1° anchor 6	7	8	9
DR4	preferred	FMYLIVW	M	T		I	VSTCPALIM	MH	MH
	deleterious				W			R	WDE
DR1	preferred	MFLIVWY			PAMQ		VMATSPILIC	M	AVM
	deleterious		C	CH	FD	CWD		GDE	D
DR7	preferred	MFLIVWY	M	W	A		IVMSACTPL	M	IV
	deleterious		C		G			GRD	N
DR3	MOTIFS		2	3	1° anchor 4	5	1° anchor 6		
Motif a preferred		LIVMFY			D				
Motif b preferred		LIVMFAY			DNQEST		KRH		
DR Supernotif		MFLIVWY					VMSTACPLI		

Italicized residues indicate less preferred or "tolerated" residues

(D): HLA Class I Supernotifs

SUPER-	POSITION:								
MOTIFS	1	2	3	4	5	6	7	8	C-terminus
A1		<u>1° Anchor</u> TILVMS							<u>1° Anchor</u> FWY
A2		<u>1° Anchor</u> LIVMATQ							<u>1° Anchor</u> LIVMAT
A3	Preferred	<u>1° Anchor</u> VSMATLI	YFW (4/5)			YFW (3/5)	YFW (4/5)	P (4/5)	<u>1° Anchor</u> RK
	deleterious	DE (3/5); P (5/5)	DE (4/5)						
A24		<u>1° Anchor</u> YFWIVLMT							<u>1° Anchor</u> FIYWLM

TABLE IV-continued

B7	Preferred	FWY (5/5) LIVM (3/5) DE (3/5); P(5/5); G(4/5); A(3/5); QN(3/5)	<u>1° Anchor</u> P	FWY (4/5)		DE (3/5)	G (4/5)	QN (4/5)	FWY (3/5) DE (4/5)	<u>1° Anchor</u> VILFMWYA
B27			<u>1° Anchor</u> RHK							<u>1° Anchor</u> FYLWMIVA
B44			<u>1° Anchor</u> ED							<u>1° Anchor</u> FWYLIMVA
B58			<u>1° Anchor</u> ATS							<u>1° Anchor</u> FWYLIVMA
B62			<u>1° Anchor</u> QLIVMP							<u>1° Anchor</u> FWYMLVLA

Italicized residues indicate less preferred or "tolerated" residues

(E): HLA Class I Motifs

POSITION										
		1	2	3	4	5	6	7	8	9 or C-terminus
A1 9-mer	preferred	GFYW	<u>1° Anchor</u> STM	DEA	YFW		P	DEQN	YFW	<u>1° Anchor</u> Y
A1 9-mer	deleterious	DE		RHKLIVMP	A	G	A			
A1 9-mer	preferred	GRHK	ASTCLIVM	<u>1° Anchor</u> DEAS	GSTC		ASTC	LIVM	DE	<u>1° Anchor</u> Y
A1 10-mer	deleterious	A	RHKDEPYFW	DE	PQN	RHK	PG	GP		
A1 10-mer	preferred	YFW	<u>1° Anchor</u> STM	DEAQN	A	YFWQN	PASTC	GDE	P	<u>1° Anchor</u> Y
A1 10-mer	deleterious	GP		RHKGLIVM	DE	RHK	QNA	RHKYFW	RHK	A
A1 10-mer	preferred	YFW	STCLIVM	<u>1° Anchor</u> DEAS	A	YFW	PG	G	YFW	<u>1° Anchor</u> Y
A2.1 9-mer	deleterious	RHK	RHKDEPYFW			P	G		PRHK	QN
A2.1 9-mer	preferred	YFW	<u>1° Anchor</u> LMIVQAT	YFW	STC	YFW		A	P	<u>1° Anchor</u> VLIMAT
	deleterious	DEP		DERKH			RKH	DERKH		

POSITION:										C-
		1	2	3	4	5	6	7	8	terminus
A2.1 10-mer	pre-ferred	AYFW	<u>1° Anchor</u> LMIVQAT	LVIM	G		G		FYWLIVM	<u>1° Anchor</u> VLIMAT
	dele-terious	DEP		DE	RKHA	P		RKH	DERKH	RKH
A3	pre-ferred	RHK	<u>1° Anchor</u> LMVISATFCGD	YFW	PRHKYFW	A	YFW		P	<u>1° Anchor</u> KYRHFA
	dele-terious	DEP		DE						
A11	pre-ferred	A	<u>1° Anchor</u> VTLMISAGNCD	YFW	YFW	A	YFW	YFW	P	<u>1° Anchor</u> KRYH
	dele-terious	DEP	F					A	G	
A24 9-mer	pre-ferred	YFWRHK	<u>1° Anchor</u> YFWM		STC			YFW	YFW	<u>1° Anchor</u> FLIW
	dele-terious	DEG		DE	G	QNP	DERHK	G	AQN	
A24 10-mer	Pre-ferred		<u>1° Anchor</u> YFWM		P	YFWP		P		<u>1° Anchor</u> FLIW
	Dele-terious			GDE	QN	RHK	DE	A	QN	DEA
A3101	Pre-ferred	RHK	<u>1° Anchor</u> MVTALIS	YFW	P		YFW	YFW	AP	<u>1° Anchor</u> RK
	Dele-terious	DEP		DE		ADE	DE	DE	DE	

TABLE IV-continued

A3301	Pre-ferred Dele-te-rious	GP	<u>1° Anchor</u> MVALFIST	YFW DE		AYFW		<u>1° Anchor</u> RK
A6801	Pre-ferred dele-te-rious	YFWSTC GP	<u>1° Anchor</u> AVTMSLI	DEG	YFWLIV M RHK	YFW P A		<u>1° Anchor</u> RK
B0702	Pre-ferred dele-te-rious	RHKFWY P	<u>1° Anchor</u> P	RHK	RHK RHK RHK	PA		<u>1° Anchor</u> LMFWYALP
		DEQNP		DEP DE	DE GDE	QN DE		
B3501	Pre-ferred	FWYLIVM	<u>1° Anchor</u> P	FWY		FWY		<u>1° Anchor</u> LMFWYTPA
B51	Pre-ferred dele-te-rious	LIVMFWY AGPDER HKSTC	<u>1° Anchor</u> P	FWY STC	FWY DE G	G FWY DEQN GDE		<u>1° Anchor</u> LIVFWYAM
B5301	Pre-ferred dele-te-rious	LIVMFWY AGPQN	<u>1° Anchor</u> P	FWY STC	FWY G	LIVM- FWY RHKQN DE	FWY DE	<u>1° Anchor</u> IMFWYALP
B5401	Pre-ferred dele-te-rious	FWY GPQNDE	<u>1° Anchor</u> P	FWYLIVM GDESTC	LIVM RHKDE DE	ALIVM FWYAP QNDGE DE		<u>1° Anchor</u> ATIVLMFWY

Italicized residues indicate less preferred or "tolerated" residues.
The information in this Table is specific for 9-mers unless otherwise specified.

[0808]

TABLE V

-V1-HLA-A1-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each startposition is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
32	TGETSMLKR	11.250
180	LSYPMRRSY	7.500
22	LEEDDYLHK	4.500
9	NQEELWKMK	2.700
80	IIASLTFLY	2.500
122	SITLLALVY	2.500
7	ITNQEELWK	2.500
31	DTGETSMLK	2.500
277	WIDIKQFVW	2.500
324	WEDVIKINK	2.500
99	ATSHQQYFY	2.500

TABLE V-continued

-V1-HLA-A1-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each startposition is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
244	SLTWREFHY	2.500
153	WLDKWMLTR	2.500
21	NLEEDDYLH	1.800
100	TSHQQYFYK	1.500
286	YTPPTFMIA	1.250
84	LTFLYTLR	1.250
108	KIPILVINK	1.000
307	ILFLPCLRK	1.000
208	WIEHDVWRM	0.900
178	YSLSYPMRR	0.750
78	AAIIASLTF	0.500

TABLE V-continued

-V1-HLA-A1-9mers: STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each startposition is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
51	HADEFDCPS	0.500
301	VLIFKSILF	0.500
148	KKFPHWLDK	0.500
296	FLPIVVLIF	0.500
215	RMEIYVSLG	0.450
297	LPIVVLIFF	0.250
247	WREFHYIQS	0.225
203	NKEDAWIEH	0.225
138	IVQLHNGTK	0.200
140	QLHNGTKYK	0.200
268	HALIFAWNK	0.200
236	TSIPSVSDS	0.150
64	TQELFPQWH	0.135
265	GTHALIFA	0.125
174	LHAIYSLSY	0.125
264	LGTIHALIF	0.125
210	EHDVWRMEI	0.125
94	VIHPLATSH	0.100
60	ELQHTQELF	0.100
306	SILFLPCLR	0.100
240	SVSDSLTWR	0.100
68	FPQWHLPIK	0.100
116	KVLEPMVSIT	0.100
98	LATSHQQYF	0.100
308	LFLPCLRKK	0.100
91	LREVIHPLA	0.090
139	VQLHNGTKY	0.075
241	VSDSLTWRE	0.075
256	KLGIIVSLLL	0.050
125	LLALVYLPGL	0.050
227	LAILALLAV	0.050
88	YTLLEVIH	0.050

TABLE V-continued

-V1-HLA-A1-9mers: STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each startposition is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
293	IAVFLPIVV	0.050
223	GIVGLAILA	0.050
123	ITLLALVYL	0.050
224	IVGLAILAL	0.050
97	PLATSHQQY	0.050
170	FFAVLHAIY	0.050
261	SLLLGTIHA	0.050
63	HTQELFPQW	0.050
112	LVINKVLPM	0.050
258	GIVSLLLGT	0.050
171	FAVLHAIYS	0.050
81	LASLTFLYT	0.050
49	TAHADEFDC	0.050
135	IAAIVQLHN	0.050
266	TIHALIFAW	0.050
232	LLAVTSIPS	0.050
221	SLGIVGLAI	0.050
165	GLLSFFFAV	0.050
117	VLEPMVSITL	0.050
120	MVSITLLAL	0.050
226	GLAILALLA	0.050
323	GWEDVTKIN	0.045
35	TSMLKRPVL	0.030
121	VSITLLALV	0.030
167	LSFFFAVLH	0.030
82	ASLTFLYTL	0.030
305	KSILFLPCL	0.030
34	ETSMLKRPV	0.025
19	RRNLEEDDY	0.025
129	VYLPGVIAA	0.025
24	EDDYLHKDT	0.025

TABLE V-continued

-V1-HLA-A1-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each startposition is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
182	YPMRRSYRY	0.025
71	WHLPIKIAA	0.025
285	WYTPPTFMI	0.025
291	FMIAVFLPI	0.025
163	QFGLLSFFF	0.025
29	HKDTGETSM	0.025
54	EFDCPSELQ	0.025
55	FDCPSELQH	0.025
211	HDVWRMEIY	0.025
161	RKQFGLLSF	0.025
142	HNGTKYKKF	0.025
10	QEELWKMKP	0.022
172	AVLHAIYSL	0.020
321	RHWEDVTK	0.020
133	GVIAAIVQL	0.020

[0809]

TABLE V

-V2-HLA-A1-9mers: STEAP-1		
Each peptide is a portionof SEQ ID NO: 5; each startposition is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
1	WREFHYIQV	0.225
3	EFHYIQVNN	0.001
2	REFHYIQVN	0.001
4	FHYIQVNNI	0.001

[0810]

TABLE V

-V3-HLA-A1-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
20	LWDPCLTRF	2.500
13	KSDVPESLW	0.750
16	VPESLWDPC	0.225
1	WREFHYIQI	0.225
19	SLWDPCLTR	0.050
4	FHYIQIIHK	0.050
18	ESLWDPCLT	0.015
22	DPCLTREKG	0.013
25	LTRFKGLNL	0.013
8	QIIHKKSDV	0.010
6	YIQIIHKKS	0.010
5	HYIQIIHKK	0.010
21	WDPCLTRFK	0.010
14	SDVPESLWD	0.003
3	EFHYIQIIH	0.003
28	FKGLNLIQS	0.003
15	DVPESLWDP	0.001
24	CLTRFKGLN	0.001
23	PCLTRFKGL	0.001
2	REFHYIQII	0.001
12	KKSDVPESL	0.001
27	RFKGLNLIQ	0.000
7	IQIIHKKSD	0.000
17	PESLWDPCL	0.000
9	IIHKKSDVP	0.000
11	HKKSDVPES	0.000
26	TRFKGLNLI	0.000
10	LHKKSDVPE	0.000

[0811]

TABLE V

-V4-HLA-A1-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
5	GLLSLFFAV	0.050
8	SLFFAVLHA	0.050
7	LSLFFAVLH	0.030
3	QFGLLSLFF	0.025
6	LLSLFFAVL	0.020
2	KQFGLLSLF	0.015
4	FGLLSLFFA	0.013
1	RKQFGLLSL	0.003
9	LFFAVLHAI	0.001

[0812]

TABLE VI

-V1-HLA-A1-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
21	NLEEDDYLHK	90.000
277	WIDIKQFVWY	50.000
241	VSDSLTWREF	7.500
323	GWEDVTKINK	4.500
243	DSLWREFHY	3.750
121	VSITLLALVY	3.750
99	ATSHQQYFYK	2.500
173	VLHAIYSLSY	2.500
79	AIIASLTFLY	2.500
215	RMEIYVSLGI	2.250
180	LSYPMRRSYR	1.500
210	EHDVWRMEIY	1.250
286	YTPPTFMIAV	1.250
31	DTGETSMLKR	1.250

TABLE VI-continued

-V1-HLA-A1-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
296	FLPIVVLFK	1.000
153	WLDKMWLTRK	1.000
98	LATSHQQYFY	1.000
306	SILFLPCLRK	1.000
6	DITNQEELWK	1.000
247	WREFHYIQSK	0.900
77	IAAIIASLTF	0.500
138	IVQLHNGTKY	0.500
300	VVLIFKSILF	0.500
263	LLGTIHALIF	0.500
107	YKIPILVINK	0.500
116	KVLPVMSITL	0.500
83	SLTFLYTLLR	0.500
179	SLSYPMRRSY	0.500
66	ELFPQWHLPI	0.500
10	QEELWKMKPR	0.450
140	QLHNGTKYKK	0.400
310	LPCLRKKILK	0.250
295	VFLPIVVLIF	0.250
91	LREVIHPLAT	0.225
195	WAYQQVQQNK	0.200
307	ILFLPCLRKK	0.200
176	AIYSLSYPMR	0.200
137	ALVQLHNGTK	0.200
305	KSILFLPCLR	0.150
236	TSIPSVSDSL	0.150
64	TQELFPQWHL	0.135
58	PSELQHTQEL	0.135
48	QTAHADEFDC	0.125
96	HPLATSHQQY	0.125
54	EFDCPSELQH	0.125
265	GTHALIFAW	0.125
94	VIHPLATSHQ	0.100

TABLE VI-continued

-V1-HLA-A1-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
51	HADEFDCPSE	0.100
208	WIEHDVVRME	0.090
167	LSFFFAVLHA	0.075
162	KQFGLLSFFF	0.075
260	VSLLLGTIHA	0.075
220	VSLGIVGLAI	0.075
9	NQEELWKMKP	0.068
80	IIASLTFLYT	0.050
226	GLAILALLAV	0.050
292	MIAVFLPIVV	0.050
223	GIVGLAILAL	0.050
169	FFFAVLHAIY	0.050
34	ETSMLKRPVL	0.050
30	KDTGETSMLK	0.050
217	EIYVSLGIVG	0.050
124	TLLALVYLPG	0.050
8	TNQEELWKMK	0.050
252	YIQSKLGIVS	0.050
111	ILVLNKVLPM	0.050
256	KLGIIVSLLG	0.050
301	VLIFKSILFL	0.050
231	ALLAVTSLPS	0.050
134	VIAAIVQLHN	0.050
128	LVYLPGVIAA	0.050
287	TPPTFMIAVF	0.050
181	SYPMRRSYRY	0.050
52	ADEFDCPSEL	0.045
139	VQLHNGTKYK	0.030
100	TSHQQYFYKI	0.030
35	TSMLKRPVLL	0.030
7	ITNQEELWKM	0.025
4	RKDITNQEEL	0.025

TABLE VI-continued

-V1-HLA-A1-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
29	HKDTGETSML	0.025
204	KEDAWIEHDV	0.025
235	VTSIPSVSDS	0.025
23	EEDDYLHKDT	0.025
285	WYTPPTFMIA	0.025
152	HWLDKWMLTR	0.025
157	WMLTRKQFGL	0.025
24	EDDYLHKDTG	0.025
324	WEDVTKINKT	0.025
177	IYSLSYPMRR	0.025
63	HTQELFPQWH	0.025
32	TGETSMLKRP	0.022
232	LLAVTSIPSV	0.020
43	LLHLHQTAHA	0.020
227	LAILALLAVT	0.020
130	YLPGVIAAIV	0.020
262	LLLGTIHALI	0.020
294	AVFLPIVVLI	0.020
224	IVGLAILALL	0.020
166	LLSFFFAVLH	0.020
127	ALVYLPGVIA	0.020

[0813]

TABLE VI

-V2-HLA-A1-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
2	WREFHYIQVN	0.045
3	REFHYIQVNN	0.001

TABLE VI-continued

-V2-HLA-A1-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
4	EFHYIQVNNI	0.001
1	TWREFHYIQV	0.000

[0814]

TABLE VI

-V3-HLA-A1-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
21	LWDPCLTRFK	5.000
19	ESLWDPCLTR	0.750
17	VPESLWDPCL	0.450
14	KSDVPESLWD	0.375
4	EFHYIQIIHK	0.050
2	WREFHYIQII	0.045
16	DVPESLWDPC	0.010
5	FHYIQIIHKK	0.010
20	SLWDPCLTRE	0.010
25	CLTRFKGLNL	0.005
3	REFHYIQILH	0.003
22	WDPCLTRFKG	0.003
26	LTRFKGLNLI	0.003
23	DPCLTRFKGL	0.003
8	IQIIHKKSDV	0.002
24	PCLTREKGLN	0.001
9	QIIHKKSDVP	0.001
7	YIQIIHKKSD	0.001
15	SDVPESLWDP	0.001
6	HYIQIIHKK	0.001
13	KKSDVPESLW	0.001

TABLE VI-continued

-V3-HLA-A1-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
1	TWREFHYIQI	0.000
28	RFKGLNLIQS	0.000
27	TRFKGLNLIQ	0.000
10	IIHKKSDVPE	0.000
12	HKKSDVPESL	0.000
18	PESLWDPCLT	0.000
11	IHKKSDVPES	0.000

[0815]

TABLE VI

-V4-HLA-A1-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
8	LSLFFAVLHA	0.075
3	KQFGLLSLFF	0.075
10	LFFAVLHAIY	0.050
6	GLLSLFFAVL	0.020
7	LLSLFFAVLH	0.020
5	FGLLSLFFAV	0.013
9	SLFFAVLHAI	0.010
2	RKQFGLLSLF	0.005
4	QFGLLSLFFA	0.003
1	TRKQFGLLSL	0.000

[0816]

TABLE VII

-V1-HLA-A2-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
165	GLLSFFFAV	10776.470
86	FLYTLLREV	470.951
262	LLLGTIHAL	309.050
302	LIFKSILFL	233.719
158	MLTRKQFGL	210.633
192	LLNWAYQQV	177.358
130	YLPGVIAAI	110.379
166	LLSFFFAVL	107.503
256	KLGIIVSLL	74.768
291	FMIAVFLPI	65.854
292	MIAVFLPIV	58.258
36	SMLKRPVLL	57.085
270	LIFAWNKWI	49.627
309	FLPCLRKKI	47.991
113	VINKVLPMV	37.393
79	AIIASLTFL	37.157
117	VLPMVSITL	36.316
164	FGLLSFFFA	33.454
83	SLTFLYTLL	32.044
42	VLLHLHQTA	31.249
90	LLREVLHPL	26.027
76	KIAAIIASL	23.646
123	ITLLALVYL	23.608
245	LTWREFHYI	21.365
212	DVWRMEIYV	20.836
219	YVSLGIVGL	19.776
261	SLLLGTIHA	18.382
300	VVLIFKSIL	18.318
263	LLGTIHALI	17.736
172	AVLHAIYSL	15.907
126	LALVYLPGV	13.975
65	QELFPQWHL	11.527

TABLE VII-continued

-V1-HLA-A2-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
221	SLGIVGLAI	10.433
272	FAWNKWLDI	9.405
116	KVLPMSIT	7.963
120	MVSITLLAL	7.309
224	IVGLAILAL	7.309
294	AVFLPIVVL	6.522
201	QQNKEDAWI	5.818
20	RNLEEDDYL	5.701
252	YIQSKLGIV	5.393
157	WMLTRKQFG	5.038
226	GLAILALLA	4.968
82	ASLTFLYTL	4.510
27	YLHKDTGET	4.456
133	GVIAAIVQL	4.299
305	KSILFLPCL	4.266
287	TPPTFMIAV	3.968
233	LAVTSIPSV	3.777
227	LAILALLAV	3.777
228	AILALLAVT	3.575
208	WIEHDVWRM	3.469
103	QQYFYKIP	3.385
299	LVVLIFKSI	2.949
258	GIVSLLLT	2.357
8	TNQEELWKM	2.294
176	AIYSLSYPM	2.186
319	KIRHWEDV	2.119
230	LALLAVTSI	2.096
118	LPMVSITLL	2.017
225	VGLAILALL	2.017
81	IASLTFLYT	1.839
312	CLRKILKI	1.824
109	IPILVINKV	1.775

TABLE VII-continued

-V1-HLA-A2-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
121	VSITLLALV	1.775
112	LVINKVLPM	1.700
59	SELQHTQEL	1.537
237	SIPSVSDSL	1.439
162	KQFGLLSFF	1.238
137	AIVQLHNGT	1.025
279	DIKQFVWYT	0.970
128	LVYLPGVIA	0.970
265	GTIHALIFA	0.873
150	FPHWLDKWM	0.820
72	HLPIKIAAI	0.816
276	KWIDLKQFV	0.762
105	YFYKIPILV	0.711
223	GIVGLAILA	0.683
293	IAVFLPIVV	0.673
127	ALVYLPGVI	0.556
53	DEFDCPSEL	0.473
259	IVSLLLGTI	0.464
244	SLTWREFHY	0.432
49	TAHADEFDC	0.400
216	MEIYVSLGI	0.345
296	FLPIVVLIF	0.323
131	LPGVIAAIV	0.316
214	WRMEIYVSL	0.311
169	FFFAVLHAI	0.284
217	EIYVSLGIV	0.281
255	SKLGIVSLL	0.252
283	FWYTPPTF	0.249
286	YTPPTFMIA	0.247
222	LGIVGLAIL	0.224
199	QVQQNKEDA	0.213
35	TSMLKRPVL	0.212
69	PQWHLPIKI	0.193

TABLE VII-continued

-V1-HLA-A2-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
191	KLLNWAYQQ	0.193
173	VLHAIYSLS	0.190
125	LLALVYLPG	0.190

[0817]

TABLE VII

-V2-HLA-A2-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
4	FHYIQVNNI	0.245
2	REFHYIQVN	0.005
1	WREFHYIQV	0.004
3	EFHYIQVNN	0.000

[0818]

TABLE VII

-V3-HLA-A2-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
8	QIIHKKSDV	9.563
2	REFHYIQLI	0.708
19	SLWDPCLTR	0.507
12	KKSDVPESL	0.209
6	YIQIIHKKS	0.047
25	LTRFKGLNL	0.038
24	CLTRFKGLN	0.037
23	PCLTRFKGL	0.022

TABLE VII-continued

-V3-HLA-A2-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
18	ESLWDPCLT	0.013
26	TRFKGLNLI	0.012
17	PESLWDPCL	0.009
15	DVPESLWDP	0.007
16	VPESLWDPC	0.003
7	IQIIHKKSD	0.003
28	FKGLNLIQS	0.001
9	IIHKKSDVP	0.001
13	KSDVPESLW	0.001
1	WREEHYIQI	0.001
4	FHYIQIIHK	0.000
22	DPCLTRFKG	0.000
14	SDVPESLWD	0.000
21	WDPCLTRFK	0.000
20	LWDPCLTRF	0.000
3	EFHYIQIIH	0.000
10	IHKKSDVPE	0.000
11	HKKSDVPES	0.000
5	HYIQIIHKK	0.000
27	RFKGLNLIQ	0.000

[0819]

TABLE VII

-V4-HLA-A2-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
5	GLLSLFFAV	2835.913
6	LLSLFFAVL	107.503
8	SLFFAVLHA	42.278

TABLE VII-continued

-V4-HLA-A2-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
4	FGLLSLFFA	40.497
2	KQFGLLSLF	0.225
9	LFFAVLHAI	0.105
1	RKQFGLLSL	0.068
7	LSLFFAVLH	0.012
3	QFGLLSLFF	0.000

[0820]

TABLE VII

-V1-HLA-A2-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
157	WMLTRKQFGL	1523.030
191	KLLNWAYQQV	1351.048
291	FMIAVFLPIV	828.006
301	VLIFKSILFL	459.398
164	FGLLSFFFAV	323.593
125	LLALVYLPV	271.948
232	LLAVTSIPSV	271.948
165	GLLSFFFAVL	233.977
261	SLLGTIHAL	181.794
89	TLLREVIHPL	181.794
226	GLAILALLAV	159.970
130	YLPGVIAAIV	131.175
244	SLTWREFHYI	109.023
283	FVWYTPPTFM	91.283
117	VLPMSVITLL	83.527
108	KIPILVFNKV	76.985
262	LLLGTIHALI	65.622
269	ALIFAWNKWI	57.380

TABLE VII-continued

-V1-HLA-A2-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
229	ILALLAVTSI	40.792
309	FLPCLRKIL	40.289
286	YTPPTFMIAV	38.837
122	SIILLALVYL	37.157
86	FLYTLLREVI	30.852
116	KVLPMVSITL	24.206
120	MVSITLLALV	23.795
112	LVINKVLPV	23.795
221	SLGIVGLAIL	20.145
111	ILVINKVLPV	19.425
980	IIASLTFLYT	18.203
200	VQQNKEDAWI	9.890
281	KQFVWYTPPT	9.784
158	MLTRKQFGLL	8.970
253	IQSKLGIVSL	8.469
43	LLHLHQTAHA	8.446
294	AVFLPIVLI	7.769
224	IVGLAILALL	7.309
223	GIVGLAILAL	6.756
292	MIAVFLPIVV	6.666
103	QQYFYKIPIL	6.536
278	IDIKQFVWYT	6.343
128	LVYLPGVIAA	5.439
299	IVVLIFKSIL	4.951
150	FPHWLDKWML	4.811
275	NKWIDIKQFV	4.410
81	IASLTFLYTL	4.408
78	AAIIASLTFL	3.753
76	KIAAIIASLT	3.586
171	FAVLHAIYSL	3.139
162	KQFGLLSFFF	3.121
37	MLKRPVLLHL	2.923

TABLE VII-continued

-V1-HLA-A2-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
66	ELFPQWHLPI	2.895
90	LLREVIHPLA	2.632
127	ALVYLPGVIA	2.037
7	ITNQEELWKM	2.023
145	TKYKKFPHWL	1.984
204	KEDAWIEHDV	1.893
248	REFHYIQSKL	1.537
209	IEHDVWRMEI	1.414
304	FKSILFLPCL	1.193
64	TQELFPQWHL	1.040
237	SIPSVSDSLT	1.025
296	FLPIVVLIFK	0.867
119	PMVSITLLAL	0.781
82	ASLTFLYTLL	0.774
264	LGTIHALIFA	0.697
324	WEDVTKINKT	0.613
256	KLGIVSLLLG	0.600
219	YVSLGIVGLA	0.598
35	TSMLKRPVLL	0.516
215	RMEIYVSLGI	0.482
166	LLSFFFAVLH	0.481
293	IAVFLPIVVL	0.476
167	LSFFFAVLHA	0.469
42	VLLHLHQTAH	0.469
36	SMLKRPVLLH	0.458
258	GIVSLLLGTI	0.429
220	VSLGIVGLAI	0.428
124	TLLALVYLPV	0.414
48	QTAHADEFDC	0.400
68	FPQWHLPIKI	0.313
71	WHLPIKIAAI	0.284
216	MEIYVSLGIV	0.282
231	ALLAVTSIPS	0.276

TABLE VII-continued

-V1-HLA-A2-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
33	GETSMLKRPV	0.270
198	QQVQQNKEDA	0.247
163	QFGLLSFFFA	0.209
260	VSLLLGTIHA	0.204
225	VGLAILALLA	0.204
118	LPMVSITLLA	0.204
277	WIDIKQFVWY	0.197
257	LGIVSLLLGT	0.190
302	LIFKSILFLP	0.172
27	YLHKDTGETS	0.168
227	LAILALLAVT	0.166
72	HLPIKIAAII	0.145
318	LKIRHGWEDV	0.137
100	TSHQQYFYKI	0.129
173	VLHAIYSLSY	0.127
75	IKIAAIIASL	0.116
40	RPVLLHLHQT	0.112

[0821]

TABLE VIII

-V2-HLA-A2-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
3	REFHYIQVNN	0.005
1	TWREFHYIQV	0.005
4	EFHYIQVNNI	0.001
2	WREFHYLQVN	0.000

[0822]

TABLE VIII

-V3-HLA-A2-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
25	CLTRFKGLNL	21.362
8	IQIIHKKSDV	11.988
20	SLWDPCLTRF	5.833
16	DVPESLWDPC	0.111
26	LTRFKGLNLI	0.043
23	DPCLTRFKGL	0.020
17	VPESLWDPCL	0.015
7	YIQIIHKKSD	0.009
10	IIHKKSDVPE	0.003
18	PESLWDPCLT	0.003
22	WDPCLTRFKG	0.003
3	REFHYIQILH	0.002
13	ICKSDVPESLW	0.001
14	KSDVPESLWD	0.001
1	TWREFHYIQI	0.001
9	QIIHKKSDVP	0.000
2	WREFHYIQII	0.000
15	SDVPESLWDP	0.000
5	FHYIQIIHKK	0.000
19	ESLWDPCLTR	0.000
24	PCLTRFKGLN	0.000
12	HKKSDVPESL	0.000
11	IHKKSDVPES	0.000
28	RFKGLNLIQS	0.000
27	TRFKGLNLIQ	0.000
4	EFHYIQIIHK	0.000
21	LWDPCLTRFK	0.000
6	HYIQIIHKKS	0.000

[0823]

TABLE VIII

-V4-HLA-A2-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
6	GLLSLFFAVL	233.977
9	SLFFAVLHAI	88.783
5	FGLLSLFFAV	85.156
3	KQFGLLSLFF	0.538
7	LLSLFFAVLH	0.481
8	LSLFFAVLHA	0.469
4	QFGLLSLFFA	0.253
1	TRKQFGLLSL	0.000
2	RKQFGLLSLF	0.000
10	LFFAVLHAIY	0.000

[0824]

TABLE IX

-V1-A3-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
307	ILFLPCLRK	300.000
153	WLDKMWLTR	36.000
108	KIPILVINK	36.000
165	GLLSFFFAV	24.300
296	FLPIVVLIF	18.000
244	SLTWREFHY	12.000
140	QLHNGTKYK	10.000
291	FMIAVFLPI	8.100
301	VLIFKSILF	6.000
84	LTFlyTLLR	6.000
12	ELWKMKPRR	6.000
256	KLGIIVSLLL	5.400
166	LLSFFFAVL	5.400
268	HALIFAWNK	2.700

TABLE IX-continued

-V1-A3-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
90	LLREVIHPL	2.025
162	KQFGLLSFF	2.025
262	LLLGTLHAL	2.025
130	YLPGVIAAI	2.025
7	ITNQEELWK	2.000
37	MLKRPVLLH	1.800
221	SLGIVGLAI	1.800
158	MLTRKQFGL	1.800
117	VLPVMSITL	1.800
312	CLRKKILKI	1.800
248	REFHYIQSK	1.350
297	LPIVVLIFK	1.350
226	GLAILALLA	1.200
80	IIASLTFLY	1.200
283	FVWYTPPTF	1.000
148	KKFPHWLDK	0.900
31	DTGETSMLK	0.900
72	HLPKIAAI	0.900
21	NLEEDDYLH	0.900
263	LLGTIHALI	0.900
302	LIFKSILFL	0.900
36	SMLKRPVLL	0.900
191	KLLNWAYQQ	0.810
122	SITLLALVY	0.090
294	AVFLPIVVL	0.675
60	ELQHTQELF	0.600
306	SILFLPCLR	0.600
261	SLLLGTIHA	0.600
138	IVQLHNGTK	0.600
99	ATSHQQYFY	0.600
240	SVSDSLTWR	0.600
83	SLTFLYTLL	0.600
103	QQYFYKIPI	0.540

TABLE IX-continued

-V1-A3-9mers: STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
9	NQEELWKMK	0.450
270	LIFAWNKWI	0.450
245	LTWREFHYI	0.450
76	KIAAIIASL	0.405
172	AVLHAIYSL	0.405
133	GVIAAIVQL	0.405
97	PLATSHQQY	0.400
176	AIYSLSYPM	0.300
68	FPQWHLPIK	0.300
100	TSHQQYFYK	0.300
309	FLPCLRKKI	0.300
269	ALIFAWNKW	0.300
42	VLLHLHQTA	0.300
127	ALVYLPGVI	0.270
300	VVLIFKSIL	0.270
124	TLLALVYLP	0.270
223	GIVGLAILA	0.270
299	IVVLIFKSI	0.203
116	KVLPVMSIT	0.203
43	LLHLHQTAH	0.200
183	PMRRSYRYK	0.200
192	LLNWAYQQV	0.200
178	YSLSYPMRR	0.180
139	VQLHNGTKY	0.180
224	IVGLAILAL	0.180
120	MVSITLLAL	0.180
182	YPMRRSYRY	0.180
208	WIEHDVWRM	0.180
112	LVINKVLPM	0.180
89	TLLREVIHP	0.180
215	RMEIYVSLG	0.180
128	LVYLPGVIA	0.150
86	FLYTLLREV	0.150

TABLE IX-continued

-V1-A3-9mers: STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
258	GIVSLLLGT	0.135
265	GTHALIFA	0.135
316	KILKIRHGW	0.135
79	AIIASLTFL	0.135
324	WEDVTK1NK	0.120
22	LEEDDYLHK	0.120
273	AWNKWIDIK	0.090
141	LHNGTKYKK	0.090
237	SIPSVSDSL	0.090
292	MIAVFLPIV	0.090
286	YTPPTFMIA	0.090
119	PMVSITLLA	0.090
219	YVSLGIVGL	0.090
134	VIAAIVQLH	0.090
15	KMKPRRNLE	0.090
144	GTKYKKFPH	0.090
279	DIKQFVWYT	0.081
232	LLAVTSIPS	0.080
123	ITLLALVYL	0.068

[0825]

TABLE IX

-V2-HLA-A3-9mers: STEAP-1 Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
4	FHYIQVNNI	0.009
2	REFHYIQVN	0.001
1	WREFHYIQV	0.000
3	EFHYIQVNN	0.000

[0826]

TABLE IX

-V3-HLA-A3-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
19	SLWDPCLTR	60.000
4	FHYIQIIHK	0.300
5	HYIQIIHKK	0.068
25	LTRFKGLNL	0.060
2	REFHYIQII	0.041
8	QIIHKKSDV	0.030
24	CLTRFKGLN	0.018
20	LWDPCLTRF	0.005
13	KSDVPESLW	0.005
26	TRFKGLNLI	0.005
15	DVPESLWDP	0.004
6	YIQIIHKKS	0.003
12	KKSDVPESL	0.003
21	WDPCLTRFK	0.002
16	VPESLWDPC	0.002
9	IIHKSDVP	0.002
23	PCLTRFKGL	0.001
1	WREFHYIQI	0.001
17	PESLWDPCL	0.001
7	IQIIHKKSD	0.000
18	ESLWDPCLT	0.000
22	DPCLTRFKG	0.000
3	EFHYIQIIH	0.000
28	FKGLNLIQS	0.000
11	HKKSDVPES	0.000
14	SDVPESLWD	0.000
27	RFKGLNLIQ	0.000
10	IHKKSDVPE	0.000

[0827]

TABLE IX

-V4-HLA-A3-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
5	GLLSLFFAV	8.100
8	SLFFAVLHA	6.000
6	LLSLFFAVL	5.400
2	KQFGLLSLF	2.025
9	LFFAVLHAI	0.007
7	LSLFFAVLH	0.005
3	QFGLLSLFF	0.004
1	RKQFGLLSL	0.002
4	FGLLSLFFA	0.001

[0828]

TABLE X

-V1-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 aminoacids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
140	QLHNGTKYKK	60.000
21	NLEEDDYLHK	60.000
153	WLDKWLTRK	30.000
165	GLLSFFFAVL	24.300
83	SLTFLYTLLR	24.000
173	VLHAIYSLSY	24.000
307	ILFLPCLRKK	15.000
306	SILFLPCLRK	9.000
66	ELFPQWHLPI	8.100
312	CLRKKILKIR	4.500
272	FAWNKWIDIK	4.500
162	KQFGLLSFFF	4.050
263	LLGTIHALIF	4.000
99	ATSHQQYFYK	3.000

TABLE X-continued

-V1-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 aminoacids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
86	FLYTLLREVI	3.000
157	WMLTRKQFGL	2.700
37	MLKRPVLLHL	2.700
36	SMLKRPVLLH	2.700
301	VLIFKSILFL	2.700
262	LLLGTIHALI	2.025
89	TLLREVIHPL	2.025
176	AIYSLSYPMR	2.000
229	ILALLAVTSI	1.800
79	AIIASLTFLY	1.800
226	GLAILALLAV	1.800
244	SLTWREFHYI	1.800
111	ILVINKVLPM	1.800
215	RMEIYVSLGI	1.800
195	VVAYQQVQQN	1.500
247	WREFHYIQSK	0.090
261	SLLLGTIHAL	1.350
305	KSILFLPCLR	0.090
269	ALLFAWNKWI	1.350
291	FMIAVFLPIV	1.350
116	KVLPVMSITL	1.215
223	GIVGLAILAL	1.215
6	DITNQEELWK	1.200
277	WIDIKQFVWY	1.200
117	VLPMVSITLL	0.900
137	AIVQLHNGTK	0.900
72	HLPIKIAAII	0.900
221	SLGIVGLAIL	0.900
125	LLALVYLPGV	0.900
191	KLLNWAYQQV	0.900
128	LVYLPGVIAA	0.600
300	VVLIFKSILF	0.600

TABLE X-continued

-V1-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 aminoacids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
166	LLSFFFAVLH	0.600
183	PMRRSYRYKL	0.540
158	MLTRKQFGLL	0.540
130	YLPGVIAAIV	0.450
139	VQLHNGTKYK	0.450
90	LLREVIHPLA	0.450
127	ALVYLPGVIA	0.450
133	GVIAAIVQLH	0.405
138	IVQLHNGTKY	0.400
179	SLSYPMRRSY	0.400
310	LPCLRKKILK	0.400
42	VLLHLHQTAH	0.300
309	FLPCLRKKIL	0.300
232	LLAVTSLPSV	0.300
31	DTGETSMLKR	0.270
107	YKIPILVINK	0.270
119	PMVSITLLAL	0.270
299	IVVLIFKSIL	0.270
265	GTIHALLFAW	0.203
97	PLATSHQQYF	0.200
43	LLHLHQTAHA	0.200
267	IHALIFAWNK	0.180
30	KDTGETSMLK	0.180
256	KLGIIVSLLG	0.180
15	KMKPRRNLEE	0.180
283	FVWYTPPTFM	0.150
180	LSYPMRRSYR	0.150
224	IVGLAILALL	0.135
103	QQYFYKIPIL	0.135
281	KQFVWYTPPT	0.135
286	YTPPTFMIAV	0.135
108	KIPILVINKV	0.135
258	GIVSLLLGTI	0.121

TABLE X-continued

-V1-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 aminoacids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
323	GWEDVTKINK	0.120
231	ALLAVTSIPS	0.120
98	LATSHQQYFY	0.120
102	HQQYFYKIPI	0.108
319	KIRHGWEDVT	0.090
124	TLLALVYLP	0.090
122	SLILLALVYL	0.090
144	GTKYKKFPHW	0.090
64	TQELFPQWHL	0.081
81	LASLTFLYTL	0.081
100	TSHQQYFYKI	0.081
112	LVINKVLPMV	0.068
302	LIFKSILFLP	0.068
96	HPLATSHQQY	0.060
192	LLNVVAYQQV	0.060
206	DAWIEHDVWR	0.060
80	IIASLTFLYT	0.060
317	ILKIRHGWED	0.060
188	YRYKLLNWAY	0.060

[0829]

TABLE X

-V2-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
1	TWREFHYIQV	0.001
4	EFHYIQVNNI	0.001
3	REFHYIQVNN	0.000
2	WREFHYIQVN	0.000

[0830]

TABLE X

-V3-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
20	SLWDPCLTRF	15.000
25	CLTRFKGLNL	1.200
5	FHYIQILHKK	0.225
26	LTRFKGLNLI	0.045
19	ESLWDPCLTR	0.027
17	TESLVVDPCL	0.018
4	EFHYIQIIHK	0.018
8	IQIIHKKSDV	0.009
3	REFHYIQIIH	0.009
16	DVPESLWDPC	0.009
21	LWDPCLTRFK	0.003
9	QIIHKKSDVP	0.003
2	WREFHYIQII	0.003
23	DPCLTRFKGL	0.003
10	IIHKIKSDVPE	0.002
1	TWREFHYIQI	0.002
7	YIQIIHKKSD	0.001
13	KKSDVPESLW	0.001
12	HKKSDVPESL	0.001
14	KSDVPESLWD	0.001
15	SDVPESLWDP	0.000
27	TRFKGLNLIQ	0.000
28	REKGLNLIQS	0.000
11	IHKIKSDVPES	0.000
22	WDPCCLTRFKG	0.000
6	HYIQIIHKKS	0.000
18	PESLWDPCLT	0.000
24	PCLTRFKGLN	0.000

[0831]

TABLE X

-V4-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of NO:9; each start position is specified, the length of peptide is amino acids, and the endposition for each peptide is the start plus nine.		
Start	Subsequence	Score
6	GLLSLFFAVL	24.300
9	SLFFAVLHAI	6.750
3	KQFGLLSLFF	2.700
7	LLSLFFAVLH	0.600
10	LFFAVLHAIY	0.020
8	LSLFFAVLHA	0.009
2	RKQFGLLSLF	0.003
5	FGLLSLFFAV	0.003
1	TRKQFGLLSL	0.002
4	QFGLLSLFFA	0.001

[0832]

TABLE X

-V4-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
108	KIPILVINK	2.400
138	IVQLHNGTK	2.000
7	ITNQEELWK	2.000
307	ILFLPCLRK	1.600
84	LTFlyTLLR	0.800
268	HALIFAWNK	0.600
297	LPIVVLI FK	0.600
31	DTGETSMLK	0.600
196	AYQQVQQNK	0.400
240	SVSDSLTWR	0.400
248	REFHYIQSK	0.360
9	NQEELWMMK	0.300
148	KKFPHWLDK	0.240

TABLE X-continued

-V4-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
140	QLHNGTKYK	0.200
68	FPQWHLPIK	0.200
153	WLDKWMLTR	0.160
22	LEEDDYLHK	0.120
306	SILFLPCLR	0.120
324	WEDVTKINK	0.120
144	GTKYKKEPH	0.090
133	GVIAAIVQL	0.090
265	GTHALIFA	0.090
177	IYSLSYPMR	0.080
181	SYPMRRSYR	0.080
321	RHGVEDVTK	0.060
311	PCLRKILK	0.060
100	TSHQQYFYK	0.060
172	AVLHAIYSL	0.060
112	LVThKVLP	0.060
165	GLLSFFFAV	0.054
12	ELWKMKPRR	0.048
294	AVFLPIVVL	0.040
141	LHNGTKYKK	0.040
128	LVYLPGVIA	0.040
283	FVWYTPPTF	0.040
120	MVSITLLAL	0.040
224	IVGLAILAL	0.040
162	KQFGLLSFF	0.036
223	GIVGLAILA	0.036
308	LFLPCLRKK	0.030
300	VVLIFKSIL	0.030
189	RYKLLNWAY	0.024
212	DVWRMEIYV	0.024
103	QQYFYKIPI	0.024
256	KLGIIVSLLL	0.024
226	GLAILALLA	0.024

TABLE X-continued

-V4-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
219	YVSKGUVGL	0.020
154	LDKWMLTRK	0.020
273	AWNKWIDLK	0.020
259	IVSLLLGTI	0.020
99	ATSHQQYFY	0.020
286	YTPPTFMIA	0.020
199	QVQQNKEDA	0.020
245	LTWREFHYI	0.020
316	KILKIRHGW	0.018
302	LIFKSILFL	0.016
176	AIYSLSYPM	0.016
299	IVVLIFKSI	0.015
123	ITLLALVYL	0.015
88	YTLLREVIH	0.015
178	YSLSYPMRR	0.012
244	SLTWREFHY	0.012
291	FMIAVFLPI	0.012
80	IIASLTFLY	0.012
277	WIDIKQFVW	0.012
319	KIRHGWEDV	0.012
146	KYKKFPHWL	0.012
285	WYTPPTFMI	0.012
266	TIHALIFAW	0.012
261	SLLLGTIHA	0.012
301	VLIFKSILF	0.012
76	KIAAIIASL	0.012
129	VYLPGVIAA	0.012
158	MLTRKQFGL	0.012
251	HYIQSKLGI	0.012
327	VTKINKTEI	0.010
63	HTQELFPQW	0.010
159	LTRKQFGLL	0.010

TABLE X-continued

-V4-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
116	KVLPMSIT	0.009
139	VQLHNGTKY	0.009
187	SYRYKLLNW	0.008
122	SITLLALVY	0.008
106	FYKIPILVI	0.008
32	TGETSMLKR	0.008
312	CLRKKILKI	0.008
105	YFYKIPILV	0.008
208	WIEHDVWRM	0.008
37	MLKRPVLLH	0.008
182	YPMRRSYRY	0.008
117	VLPMVSITL	0.008
168	SFFFAVLHA	0.008
104	QYFYKIPIL	0.008
296	FLPIVVLIF	0.008
21	NLEEDDY LH	0.008
272	FAWNKWIDI	0.008
221	SLGIVGLAI	0.008
207	AWIEHDVWR	0.006
262	LLGTHAL	0.006
36	SMLKRPVLL	0.006
163	QFGLLSFFF	0.006

[0833]

TABLE XI

-V2-HLA-A11-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position for plus eight.		
Start	Subsequence	Score
4	FHYIQVNNI	0.000
1	WREFHYIQV	0.000

TABLE XI-continued

-V2-HLA-A11-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position for plus eight.		
Start	Subsequence	Score
2	REFHYIQVN	0.000
3	EFHYIQVNN	0.000

[0834]

TABLE XI

-V3-HLA-A11-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
5	HYIQIIHKK	0.600
19	SLWDPCLTR	0.320
4	FHYIQIIHK	0.080
25	LTRFKGLNL	0.020
8	QIIHKKSDV	0.006
2	REFHYIQII	0.004
21	WDPCLTRFK	0.002
15	DVPESLWDP	0.001
27	RFKGLNLLQ	0.001
3	EFHYIQIIH	0.001
12	KKSDVPESL	0.001
13	KSDVPESLW	0.001
7	IQIIHKKSD	0.000
26	TRFKGLNLI	0.000
24	CLTRFKGLN	0.000
9	IIHKKSDVP	0.000
1	WREFHYIQI	0.000
6	YIQIIHKKKS	0.000
20	LWDPCLTRF	0.000
16	VPESLWDPC	0.000
22	DPCLTRFKG	0.000

TABLE XI-continued

-V3-HLA-A11-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
23	PCLTRFKGL	0.000
14	SDVPESLWD	0.000
17	PESLWDPCCL	0.000
28	FKGLNLIQS	0.000
11	HKKSDVPES	0.000
10	IHKKSDVPE	0.000
18	ESLWDPCCLT	0.000

[0835]

TABLE XI

-V4-HLA-A11-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start plus eight.		
Start	Subsequence	Score
5	GLLSLFFAV	0.054
2	KQFGLLSLF	0.036
8	SLFFAVLHA	0.016
6	LLSLFFAVL	0.004
9	LFFAVLHAI	0.004
3	QFGLLSLFF	0.004
1	RKQFGLLSL	0.001
4	FGLLSLFFA	0.001
7	LSLFFAVLH	0.000

[0836]

TABLE XII

-V1-HLA-A11-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
206	DAWIEHDVWR	0.024
226	GLAILALLAV	0.024
215	RMEIYVSLGI	0.024
120	MVSITLLALV	0.020
8	TNQEELWKM	0.020
320	IRHGWEDVTK	0.020
7	ITNQEELWKM	0.020
286	YTPPTFMIAV	0.020
138	IVQLHNGTKY	0.020
199	QVQQNKEDAW	0.020
219	YVSLGIVGLA	0.020
247	WREFHYIQSK	0.020
259	IVSLLLGTH	0.020
224	IVGLAILALL	0.020
305	KSILFLPCLR	0.018
157	WMLTRKQFGL	0.018
79	AIIASLTFLY	0.018
191	KLLNWAYQQV	0.018
258	GIVSLLLGTI	0.018
165	GLLSFFFAVL	0.018
104	QYFYKIPILV	0.016
152	HWLDKWMLTR	0.012
102	HQQYFYKIP	0.012
36	SMLKRPVLLH	0.012
108	KIPILVINKV	0.012
64	TQELFPQWHL	0.012
103	QQYFYKIPIL	0.012
301	VLIFKSILFL	0.012
111	ILVINKVLPM	0.012
63	HTQELFPQWH	0.010
198	QQVQQNKEDA	0.009
93	EVIHPLATSH	0.009

TABLE XII-continued

-V1-HLA-A11-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
285	WYTPPTFMIA	0.008
181	SYPMRRSYRY	0.008
86	FLYTLLREVI	0.008
37	MLKRPVLLHL	0.008
292	MIAVFLPIVV	0.008
180	LSYPMRRSYR	0.008
173	VLHAIYSLSY	0.008
118	LPMVSITLLA	0.008
105	YFYKIPILVI	0.008
263	LLGTIHALIF	0.008
290	TFMIAVFLPI	0.008
200	VQQNKEDAWI	0.006
171	FAVLHAIYSL	0.006
73	LPIKIAAIIA	0.006
262	LLLGTIHALI	0.006
129	VYLPGVIAAI	0.006
291	FMIAVFLPIV	0.006
253	IQSKLGIVSL	0.006
42	VLLHLHQTAH	0.006
163	QFGLLSFFFA	0.006
326	DVTKINKTEI	0.006
89	TLLREVIHPL	0.006
251	HYIQSKLGIV	0.006
295	VFLPIVVLIF	0.006
10	QEELWKMKPR	0.006
127	ALVYLPGVIA	0.006
261	SLLLGTIHAL	0.006
218	IYVSLGIVGL	0.006
175	HAIYSLSYPM	0.906
11	EELWKMKPRR	0.005
66	ELFPQWHLPI	0.005

[0837]

TABLE XII

-V2-HLA-A11-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
4	EFHYIQVNNI	0.001
1	TWREFHYIQV	0.000
3	REFHYIQVNN	0.000
2	WREFHYIQVN	0.000

[0838]

TABLE XII

-V3-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start plus nine.		
Start	Subsequence	Score
4	EFHYIQIIHK	0.120
5	FHYIQIIHKK	0.040
26	LTRFKGLNLI	0.010
8	IQIIHKKSDV	0.009
25	CLTRFKGLNL	0.008
20	SLWDPCLTRF	0.008
3	REFHYIQIIH	0.007
19	ESLWDPCLTR	0.004
21	LWDPCLTRFK	0.002
17	VPESLWDPC	0.002
28	RFKGLNLIQS	0.001
9	QIIHKKSDVP	0.001
13	KKSDVPESLW	0.001
16	DVPESLWDPC	0.001
10	IIHKKSDVPE	0.000
1	TWREFHYIQI	0.000
6	HYIQIIHKKS	0.000
23	DPCLTRFKGL	0.000
2	WREFHYIQII	0.000
12	HKKSDVPESL	0.000

TABLE XII-continued

-V3-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start plus nine.		
Start	Subsequence	Score
7	YIQIIHKKSD	0.000
14	KSDVPESLWD	0.000
27	TRFKGLNLIQ	0.000
22	WDPCCLTRFKG	0.000
15	SDVPESLWDP	0.000
24	PCLTRFKGLN	0.000
11	IHKKSDVPES	0.000
18	PESLWDPCCTL	0.000

[0839]

TABLE XII

-V4-HLA-A3-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
6	GLLSLFFAVL	24.300
9	SLFFAVLHAI	6.750
3	KQFGLLSLFF	2.700
7	LLSLFFAVLH	0.600
10	LFFAVLHAIY	0.020
8	LSLFFAVLHA	0.009
2	RKQFGLLSLF	0.003
5	FGLLSLFFAV	0.003
1	TRKQFGLLSL	0.002
4	QFGLLSLFFA	0.001

[0840]

TABLE XIII

-V1-HLA-A24-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
146	KYKFPHWL	400.000
104	QYFYKIPIL	200.000
251	HYIQSKLGI	75.000
87	LYTLLREVI	60.000
285	WYTPPTFMI	60.000
106	FYKIPILVI	50.000
249	EFHYIQSKL	30.800
20	RNLEEDDYL	14.400
295	VFLPIVLI	12.600
189	RYKLLNWAY	12.000
163	QFGLLSFFF	12.000
305	KSILFLPCL	12.000
256	KLGIIVSLLL	11.200
76	KIAAIIASL	11.200
129	VYLPGVIAA	9.000
225	VGLAILALL	8.400
237	SIPSVSDSL	8.400
117	VLPVMSITL	8.400
67	LFPQWHLPI	7.500
169	FFFAVLHAI	7.000
90	LLREVIHPL	6.720
82	ASLTFLYTL	6.000
222	LGIVGLAIL	6.000
118	LPMVSIITL	6.000
35	TSMLKRPVL	6.000
262	LLLGTIHAL	6.000
79	AIIASLTFL	6.000
156	KWMLTRKQF	6.000
36	SMLKRPVLL	6.000
133	GVIAAIVQL	6.000
172	AVLHAIYSL	6.000
123	ITLLALVYL	6.000

TABLE XIII-continued

-V1-HLA-A24-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
187	SYRYKLLNW	5.000
159	LTRKQFGLL	4.800
166	LLSFFFAVL	4.800
162	KQFGLLSFF	4.800
83	SLTFLYTLL	4.800
296	FLPIVVLIF	4.200
302	LIFKSILFL	4.000
310	LPCLRKKIL	4.000
158	MLTRKQFGL	4.000
224	IVGLAILAL	4.000
294	AVFLPIVVL	4.000
120	MVSITLLAL	4.000
219	YVSLGIVGL	4.000
254	QSKLGIVSL	4.000
60	ELQHTQELF	3.000
301	VLIFKSILF	3.000
78	AAIIASLTF	3.000
299	IVVLIFKSI	2.520
291	FMIAVFLPI	2.520
98	LATSHQQYF	2.400
47	HQTAHADEF	2.200
142	HNGTKYKKF	2.200
73	LPIKIAAII	2.100
130	YLPGVIAAI	2.100
283	FVWYTPPTF	2.000
264	LGTIHALIF	2.000
309	FLPCLRKKI	1.980
127	ALVYLPGVI	1.800
149	KFPHWLDKW	1.650
230	LALLAVTSI	1.500
201	QQNKEDAWI	1.500
72	HLPIKIAAI	1.500

TABLE XIII-continued

-V1-HLA-A24-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
263	LLGTIHALI	1.400
221	SLGIVGLAI	1.400
322	HGWEDVTKI	1.320
5	KDITNQEEL	1.320
196	AYQQVQQNK	1.260
245	LTWREFHYI	1.200
259	IVSLLLGTI	1.200
327	VTKINKTEI	1.100
312	CLRKKILKI	1.100
214	WRMEIYVSL	1.008
270	LIFAWNKWI	1.000
272	FAWNKWIDI	1.000
103	QQYFYKIPi	1.000
8	TNQEELWKM	0.990
218	IYVSLGIVG	0.900
255	SKIGIVSLL	0.840
110	PILVINKVL	0.840
185	RRSYRYKLL	0.800
30	KDTGETSML	0.800
59	SELQHTQEL	0.792
208	WIEHDVWRM	0.750
282	QFVWYTPPT	0.750
181	SYPMRRSYR	0.750
112	LVINKVLPM	0.750
26	DYLHKDTGE	0.750
105	YFYKIPILV	0.700
38	LKRPVLLHL	0.672
331	NKTEICSQL	0.672
276	KWIDIKQFV	0.605
170	FFAVLHAIY	0.600
176	AIYSLSYPM	0.600
150	FPHWLDKWM	0.600
161	RKQFGLLSF	0.600

TABLE XIII-continued

-V1-HLA-A24-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
14	WKMKPRRNL	0.600
65	QELFPQWHL	0.600

[0841]

TABLE XIII

-V2-HLA-A24-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
3	EFHYIQVNN	0.700
4	FHYIQVNNI	0.120
2	REFHYIQVN	0.024
1	WREFHYIQV	0.015

[0842]

TABLE XIII

-VI-HLA-A24-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
25	LTRFKGLNL	4.000
20	LWDPCLTRF	2.400
12	KKSDVPESL	1.344
5	HYIQIIHKK	1.155
23	PCLTRFKGL	0.720
2	REFHYIQII	0.240
6	YIQIIHKKs	0.231
13	KSDVPESLW	0.200
16	VPESLWDPC	0.180

TABLE XIII-continued

-VI-HLA-A24-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
8	QIIHKKSDV	0.150
1	WREFHYIQI	0.150
18	ESLWDPCLT	0.150
27	RFKGLNLIQ	0.120
26	TRFKGLNLI	0.120
24	CLTRFKGLN	0.100
3	EFHYIQIIH	0.070
17	PESLWDPCL	0.040
15	DVPESLWDP	0.018
7	IQIIHKKSD	0.015
19	SLWDPCLTR	0.012
11	HKKSDVPES	0.011
22	DPCLTRFKG	0.011
9	ILHKKSDVP	0.010
28	FKGLNLIQS	0.010
21	WDPCLTRFK	0.002
14	SDVPESLWD	0.002
10	IHKKSDVPE	0.001
4	FHYIQIIHK	0.001

[0843]

TABLE XIII

-V4-HLA-A24-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
3	QFGLLSLFF	12.000
9	LFFAVLHAI	7.000
2	KQFGLLSLF	4.800
6	LLSLFFAVL	4.800

TABLE XIII-continued

-V4-HLA-A24-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
1	RKQFGLLSL	1.200
5	GLLSLFFAV	0.216
4	FGLLSLFFA	0.150
8	SLFFAVLHA	0.100
7	LSLFFAVLH	0.015

[0844]

TABLE XIV-

V1-HLA-A24-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
218	IYVSLGIVGL	300.000
129	VYLPGVIAAI	126.000
295	VFLPIVVLIF	25.200
116	KVLPMSITL	20.160
282	QFVWYTPPTF	15.000
290	TFMIAVFLPI	12.600
308	LFLPCLRKKI	11.880
236	TSIPSVSDSL	10.080
149	KFPHWLDKWM	9.000
89	TLLREVIHPL	8.400
109	IPILVINKVL	8.400
26	DYLHKDTGET	8.250
181	SYPMRRSYRY	7.500
251	HYIQSKLGIV	7.500
187	SYRYKLLNWA	7.200
285	WYTPPTFMIA	7.200
82	ASLTFLYTLL	7.200
165	GLLSFFFAVL	7.200
104	QYFYKIPILV	7.000

TABLE XIV--continued

V1-HLA-A24-10mers: STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
106	FYKIPILVIN	7.000
168	SFFFAVLHAI	7.000
261	SLLLGTIHAL	6.000
293	IAVFLPIVVL	6.000
299	IVVLIFKSIL	6.000
157	WMLTRKQFGL	6.000
223	GIVGLAILAL	6.000
171	FAVLHAIYSL	6.000
309	FLPCLRRKKIL	6.000
35	TSMLKRPVLL	6.000
117	VLPMVSITLL	6.000
78	AAIIASLTFL	6.000
301	VLIFKSILFL	6.000
64	TQELFPQWHL	6.000
213	VWRMEIYVSL	5.600
254	QSKLGIVSLL	5.600
37	MLKRPVLLHL	5.600
330	INKTEICSQL	5.600
224	IVGLAILALL	5.600
271	IFAWNKWIDI	5.000
105	YFYKIPILVI	5.000
158	MLTRKQFGLL	4.800
162	KQFGLLSFFF	4.800
215	RMEIYVSLGI	4.200
103	QQYFYKIPIL	4.000
253	IQSKLGIVSL	4.000
122	SITLLALVYL	4.000
81	IASLTFLYTL	4.000
34	ETSMLKRPVL	4.000
13	LWKMKPRRNL	4.000
221	SLGIVGLAIL	4.000
150	FPHWLDKWML	4.000

TABLE XIV--continued

V1-HLA-A24-10mers: STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
287	TPPTFMIAVF	3.000
300	VVLIFKSILF	3.000
241	VSDSLTWREF	2.200
262	LLLGTIHALI	2.100
72	HLPIKLAAIL	2.100
220	VSLGIVGLAI	2.100
274	WNKWIDIKQF	2.000
263	LLGTIHALIF	2.000
77	IAAIIASLTF	2.000
68	FPQWHLPIKI	1.980
258	GIVSLLLGTI	1.800
126	LALVYLPGVI	1.800
102	HQQYFYKIPI	1.500
200	VQQNKEDAWI	1.500
269	ALIFAWNKWI	1.500
294	AVFLPIVVLI	1.400
100	TSHQQYFYKI	1.320
248	REFHYIQSKL	1.232
86	FLYTLLREVI	1.200
244	SLTWREFHYI	1.200
66	ELFPQWHLPI	1.200
19	RRNLEEDDYL	1.200
326	DVTKINKTEI	1.100
146	KYKKFPHWLD	1.000
189	RYKLLNWAYQ	1.000
284	VWYTPPTFMI	1.000
114	INKVLPMVSI	1.000
229	ILALLAVTSI	1.000
196	AYQQVQQNKE	0.990
85	TFLYTLLREV	0.990
207	AWIEHDVWRM	0.900
175	HAIYSLSYPM	0.900
4	RKDITNQEEL	0.880

TABLE XIV--continued

V1-HLA-A24-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
255	SKLGIVSLLL	0.840
75	IKIAAIIASL	0.840
7	ITNQEELWKM	0.825
58	PSELQHTQEL	0.792
111	ILVINKVLPM	0.750
161	RKQFGLLSFF	0.720
303	IFKSILFLPC	0.720
52	ADEFDCPSEL	0.660
119	PMVSITLLAL	0.600
163	QFGLLSFFFA	0.600
169	FFFAVLHAIY	0.600
132	PGVIAAIVQL	0.600
288	PPTFMIAVFL	0.560
108	KIPILVINKV	0.554
170	FFAVLHAIYS	0.500
87	LYTLLREVIH	0.500

[0845]

TABLE XIV

-V2-HLA-A24-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
4	EFHYIQVNNI	6.000
1	TWREFHYIQV	0.120
3	REFHYLQVNN	0.028
2	WREFHYIQVN	0.018

[0846]

TABLE XIV

-V3-HLA-A24-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
6	HYIQIIHKKS	11.550
17	VPESLWDPCL	6.000
23	DPCLTRFKGL	4.800
25	CLTRFKGLNL	4.000
20	SLWDPCLTRF	2.400
1	TWREFHYIQI	1.200
26	LTRFKGLNLI	1.200
28	RFKGLNLIQS	1.000
12	HKKSDVPESL	0.560
16	DVPESLWDPC	0.216
2	WREFHYIQII	0.180
8	IQIIHKKSDV	0.150
4	EFHYIQILHK	0.050
13	KKSDVPESLW	0.024
14	KSDVPESLWD	0.020
19	ESLWDPCLTR	0.015
24	PCLTRFKGLN	0.015
9	QIIHKKSDVP	0.015
7	YIQIIIIKKSD	0.015
21	LWDPCLTRFK	0.014
11	IHKKSDVPES	0.011
10	IIHKKSDVPE	0.010
3	REFHYIQIIH	0.003
15	SDVPESLWDP	0.002
22	WDPCCLTRFKG	0.002
5	FHYIQIIHKK	0.002
27	TRFKGLNLIQ	0.001
18	PESLWDPCLT	0.001

[0847]

TABLE XIV

-V4-HLA-A24-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
6	GLLSLFFAVL	7.200
3	KQFGLLSLFF	4.800
9	SLFFAVLHAI	1.400
2	RKQFGLLSLF	0.720
10	LFFAVLHAIY	0.600
4	QFGLLSLFFA	0.500
1	TRKQFGLLSL	0.400
5	FGLLSLFFAV	0.216
8	LSLFFAVLHA	0.150
7	LLSLFFAVLH	0.010

[0848]

TABLE XV

-V1-HLA-B7-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
118	LPMVSITLL	240.000
294	AVFLPIVV	90.000
310	LPCLRKKIL	80.000
172	AVLHAIYSL	60.000
159	LTRKQFGLL	40.000
90	LLREVIHPL	40.000
120	MVSITLLAL	20.000
219	YVSLGIVGL	20.000
224	IVGLAALAL	20.000
150	FPHWLDKWM	20.000
133	GVIAAIVQL	20.000
300	VVLIFKSI	20.000
35	TSMLKRPVL	18.000

TABLE XV-continued

-V1-HLA-B7-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
79	AIIASLTFL	12.000
82	ASLTFLYTTL	12.000
73	LPIKIAAII	8.000
184	MRRSYRYKL	6.000
112	LVJNKVLPM	5.000
38	LKRPVLLHL	4.000
312	CLRKKILKI	4.000
305	KSILFLPCL	4.000
225	VGLAILALL	4.000
158	MLTRKQFGL	4.000
254	QSKLGIVSL	4.000
262	LLGTIHAL	4.000
123	ITLLALVYL	4.000
287	TPPTFMIAV	4.000
131	LPGVIAAIV	4.000
166	LLSFFFAVL	4.000
302	LIFKSILFL	4.000
222	LGIVGLAIL	4.000
117	VLPMVSITL	4.000
256	KLGIIVSLLL	4.000
237	SIPSVSDSL	4.000
76	KIAAIIASL	4.000
83	SLTFLYTLL	4.000
36	SMLKRPVLL	4.000
20	RNLEEDDYL	4.000
109	IPILVINKV	4.000
176	AIYSLSYPM	3.000
14	WKMXPARNL	2.700
319	KIRHWEDV	2.000
259	IVSLLLGTI	2.000
17	KPRRNLEED	2.000
299	IVVLIFKSI	2.000
238	IPSVSDSLT	2.000

TABLE XV-continued

-V1-HLA-B7-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
182	YPMRRSYRY	1.200
272	FAWNKWIDI	1.200
214	WRMEIYVSL	1.200
230	LALLAVTSI	1.200
127	ALVYLPOVI	1.200
8	TNQEELWKM	1.000
212	DVWRMEIYV	1.000
128	LVYLPGVIA	0.750
227	LAILALLAV	0.600
293	IAVFLPIVV	0.600
126	LALVYLPGV	0.600
309	FLPCLRKKI	0.600
65	QELFPQWHL	0.600
233	LAVTSIPSV	0.600
199	QVQQNKEDA	0.500
116	KVLPMSVIT	0.500
331	NKTEICSQL	0.400
291	FMIAVFLPI	0.400
146	KYKKFPHWL	0.400
322	HGWEDVTKI	0.400
263	LLGTIHALI	0.400
245	LTWREFHYI	0.400
221	SLGIVGLAI	0.400
59	SELQHTQEL	0.400
289	PTFMIAVFL	0.400
30	KDTGETSML	0.400
53	DEFDCPSEL	0.400
201	QQNKEDAWI	0.400
270	LIFAWNKI	0.400
249	EFHYIQSKL	0.400
110	PILVINKVL	0.400
104	QYFYKIPIL	0.400

TABLE XV-continued

-V1-HLA-B7-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
103	QQYFYKIPI	0.400
5	KDITNQEEL	0.400
185	RRSYRYKLL	0.400
72	HLPIKJAAI	0.400
130	YLPGVIAAI	0.400
327	VTK1NKTEI	0.400
255	SKLGIVSLL	0.400
234	AVTSIPSVS	0.300
49	TAHADEFDC	0.300
77	IAAIIASLT	0.300
228	AILALLAVT	0.300
81	IASLTFLYT	0.300
137	AIVQLHNGT	0.300
208	WIEHDVWRM	0.300
252	YIQSKLGIV	0.200
217	EIYVSLGIV	0.200
68	FPQWHLPIK	0.200
40	RPVLLHLHQ	0.200
121	VSITLLALV	0.200
292	MIAVFLPIV	0.200
57	CPSELQHTQ	0.200
192	LLNWAYQQV	0.200

[0849]

TABLE XV

-V2-HLA-B7-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
4	FHYIQVNNI	0.040
1	WREFHYIQV	0.006

TABLE XV-continued

-V2-HLA-B7-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
2	REFHYIQVN	0.002
3	EFHYIQVNN	0.002

[0850]

TABLE XV

-V1-HLA-B7-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
6	LLSLFFAVL	4.000
1	RKQFGLLSL	0.400
5	GLLSLFFAV	0.200
4	FGLLSLFFA	0.100
8	SLFFAVLHA	0.100
9	LFFAVLHAI	0.040
2	KQFGLLSLF	0.020
7	LSLFFAVLH	0.010
3	QFGLLSLFF	0.002

[0851]

TABLE XVI

-V1-HLA-B7-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
109	IPILVINKVL	80.000
150	FPHWLDKWML	80.000
78	AAIIASLTFL	36.000
116	KVLPVMSITL	20.000

TABLE XVI-continued

-V1-HLA-B7-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
299	IVVLIFKSIL	20.000
224	IVGLAILALL	20.000
293	IAVFLPIVVV	18.000
82	ASLTFLYTLL	12.000
81	IASLTFLYTLL	12.000
171	FAVLHAIYSL	12.000
35	TSMLKRPVLL	12.000
68	FPQWHLPIKI	8.000
288	PPTFMIAVFL	8.000
283	FVWYTPPTFM	7.500
183	PMRRSYRYKL	6.000
294	AVFLPIVVLI	6.000
118	LPMVSITLLA	6.000
34	ETSMKRPVVL	6.000
261	SLLGTIHAL	4.000
165	GLLSFFFAVL	4.000
117	VLPVMSITLL	4.000
213	VWRMEIYVSL	4.000
184	MRRSYRYKLL	4.000
254	QSKLGIVSLL	4.000
330	INKTEICSQL	4.000
221	SLGIVGLAIL	4.000
309	FLPCLRKKIL	4.000
236	TSIPSVSDSL	4.000
37	MLKRPVLLHL	4.000
301	VLIFKSILFL	4.000
122	SITLLALVYL	4.000
253	IQSKLGIVSL	4.000
103	QQYFYKIPIL	4.000
223	GIVGLAILAL	4.000
157	WMLTRKQFGL	4.000
89	TLLREVIHPL	4.000

TABLE XVI-continued

-V1-HLA-B7-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
158	MLTRKQFGLL	4.000
175	HAIYSLSYPM	3.000
326	DVTKINKTEI	2.000
17	KPRRNLEEDD	2.000
73	LPIKIAAIIA	2.000
40	RPVLLHLHQT	2.000
64	TQELFPQWHL	1.800
269	ALIFAWNKWI	1.200
126	LALVYLPGVI	1.200
90	LLREVIHPLA	1.000
111	ILVINKVLPM	1.000
7	ITNQEELWKM	1.000
319	KIRHGWEDVT	1.000
112	LVINKVLPMV	1.000
120	MVSITLLALV	1.000
13	LWKMKPRRNL	0.900
136	AAIVQLHNGT	0.900
114	INKVLPMVSI	0.600
182	YPMRRSYRYK	0.600
86	FLYTLLREVI	0.600
219	YVSLGIVGLA	0.500
128	LVYLPGVIAA	0.500
127	ALVYLPGVIA	0.450
220	VSLGIVGLAI	0.400
66	ELFPQWHLPI	0.400
145	TKYKKFPHWL	0.400
255	SKLGIVSLLL	0.400
304	FKSILFLPCL	0.400
200	VQQNKEDAWI	0.400
218	IYVSLGIVGL	0.400
287	TPPTFMLAVF	0.400
297	LPWVVLIFKS	0.400
258	GIVSLLLGTI	0.400

TABLE XVI-continued

-V1-HLA-B7-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
262	LLLGTIHALI	0.400
244	SLTWREFHNI	0.400
238	IPSVSDSLTW	0.400
229	ILALLAVTSI	0.400
75	IKIAAIIASL	0.400
100	TSHQQYFYKI	0.400
96	HPLATSHQQY	0.400
119	PMVSITLLAL	0.400
102	HQQYFYKIPI	0.400
248	REFHYIQSKL	0.400
19	RRNLEEDDYL	0.400
132	PGVIAAIVQL	0.400
72	HLPIKIAAII	0.400
52	ADEFDGPSEL	0.360
207	AWIEHDVWRM	0.300
172	AVLHAIYSLS	0.300
227	LAILALLAVT	0.300
234	AVTSIPSVSD	0.225
226	GLAILALLAV	0.200
130	YLPGVIAAIV	0.200
108	KIPILVINKV	0.200
291	FMAVFLPIV	0.200
164	FGLLSFFFAV	0.200
159	LTRKQFGLLS	0.200
57	CPSELQHTQE	0.200
125	LLALVYLPGV	0.200
292	MIAVFLPIVV	0.200
286	YTPPTFMIAV	0.200
310	LPCLRKKILK	0.200
191	KLLNWAYQQV	0.200

[0852]

TABLE XVI

-V2-HLA-B7-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
1	TWREFHYIQV	0.200
4	EFHYIQVNNI	0.040
3	REFHYIQVNN	0.002
2	WREFHYIQVN	0.001

[0853]

TABLE XVI

-V3-HLA-B7-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of amino acids, and the end position for eachpeptide is the start plus nine.		
Start	Subsequence	Score
23	DPCLTRFKGL	80.000
17	VPESLWDPCL	24.000
25	CLTRFKGLNL	4.000
26	LTRFKGLNLI	4.000
16	DVPESLWDPC	0.500
1	TWREFHYIQI	0.400
12	HKKSDVPESL	0.400
8	LQIIHKKSDV	0.200
20	SLWDPCLTRF	0.020
19	ESLWDPCLTR	0.015
2	WREFHYIQII	0.012
10	IIHKKSDVPE	0.010
9	QIIHKKSDVP	0.010
7	YIQIIHKKSD	0.010
13	KKSDVPESLW	0.003
14	KSDVPESLWD	0.003
11	IHKKSDVPES	0.002
24	PCLTRFKGLN	0.002
6	HYIQIIHKKS	0.002

TABLE XVI-continued

-V3-HLA-B7-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of amino acids, and the end position for eachpeptide is the start plus nine.		
Start	Subsequence	Score
28	RFKGLNLIQS	0.002
22	WDPCLTRFKG	0.002
18	PESLWDPCLT	0.001
3	REFHYIQIIH	0.001
5	FHYIQIIHKK	0.001
15	SDVPESLWDP	0.001
27	TRFKGLNLIQ	0.001
4	EFHYIQIIHK	0.001
21	LWDPCLTRFK	0.000

[0854]

TABLE XVI

-V4-HLA-B7-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
6	GLLSLFFAVL	4.000
9	SLFFAVLHAI	0.400
1	TRKQFGLLSL	0.400
5	FGLLSLFFAV	0.200
8	LSLFFAVLHA	0.100
3	KQFGLLSLFF	0.020
7	LLSLFFAVLH	0.010
4	QFGLLSLFFA	0.010
2	RKQFGLLSLF	0.002
10	LFFAVLHAIY	0.002

[0855]

TABLE XVII

-V1-HLA-B35-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
150	FPHWLDKWM	40.000
182	YPMRRSYRY	40.000
310	LPCLRKKIL	20.000
118	LPMVSITLL	20.000
254	QSKLGIVSL	15.000
305	KSILFLPCL	10.000
180	LSYPMRRSY	10.000
73	LPIKTAAL	8.000
90	LLREVIHPL	6.000
20	RNLEEDDYL	6.000
8	TNQEELWKM	6.000
82	ASLTFLYTL	5.000
35	TSMLKRPVL	5.000
131	LPGVIAAIV	4.000
109	IPILVINKV	4.000
287	TPPTFMIAV	4.000
78	AAIIASLTF	3.000
159	LTRKQFGLL	3.000
98	LATSHQQYF	3.000
206	DAWIEHDVW	2.250
122	SITLLALVY	2.000
176	AIYSLSYPM	2.000
162	KQFGLLSFF	2.000
112	LVINKVLPM	2.000
76	KIAAIIASL	2.000
139	VQLHNGTKY	2.000
80	IIASLTFLY	2.000
244	SLTWREFHY	2.000
238	IPSVSDSLT	2.000
256	KLGIIVSLLL	2.000
99	ATSHQQYFY	2.000
288	PPTFMIAVF	2.000

TABLE XVII-continued

-V1-HLA-B35-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
319	KIRHGWEDV	1.200
189	RYKLLNWAY	1.200
17	KPRRNLEED	1.200
272	FAWNKWIDI	1.200
327	VTKINKTEI	1.200
312	CLRKKILKI	1.200
230	LALLAVTSI	1.200
322	HGWEDVTKI	1.200
262	LLGTHIAL	1.000
172	AVLHAIYSL	1.000
166	LLSFFFAVL	1.000
219	YVSLGIVGL	1.000
224	IVGLAILAL	1.000
133	GVLAIAIVQL	1.000
47	HQTAHADEF	1.000
222	LGIVGLAIL	1.000
63	HTQELFPQW	1.000
294	AVFLPIVVL	1.000
186	RSYRYKLLN	1.000
60	ELQHTQELF	1.000
264	LGTIHALIF	1.000
316	KJLKIRHGW	1.000
283	FVWYTPPTF	1.000
225	VGLAILALL	1.000
158	MLTRKQFGL	1.000
121	VSITLLALV	1.000
79	AIIASLTFL	1.000
36	SMLKRPVLL	1.000
300	VVLIFKSIL	1.000
296	FLPIVVLIF	1.000
117	VLPMVSITL	1.000
301	VLIFKSILF	1.000

TABLE XVII-continued

-V1-HLA-B35-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
237	SIPSVDSL	1.000
123	ITLLALVYL	1.000
142	HNGTKYKKF	1.000
120	MVSITLLAL	1.000
302	LIFKSILFL	1.000
83	SLTFLYTLL	1.000
208	WIEHDVWRM	0.900
201	QQNKEDAWI	0.600
146	KYKKFPHWL	0.600
233	LAVTSIPSV	0.600
293	IAVFLPIVV	0.600
19	RRNLEEDDY	0.600
245	LTWREFHYI	0.600
126	LALVYLPGV	0.600
227	LAILALLAV	0.600
200	VQQNKEDAW	0.500
220	VSLGIVGLA	0.500
269	ALIFAWNKW	0.500
236	TSIPSVSDS	0.500
6	DITNQEELW	0.500
266	TIHALIFAW	0.500
49	TAHADEFDC	0.450
221	SLGIVGLAI	0.400
259	IVSLLGTI	0.400
72	HLPIKIAAI	0.400
263	LLGTIHALI	0.400
130	YLPGVIAAI	0.400
299	IVVLIFKSI	0.400
103	QQYFYKIPI	0.400
309	FLPCLRKKI	0.400
40	RPVLLHLHQ	0.400
270	LIFAWNKWI	0.400
127	ALVYLPGVI	0.400

TABLE XVII-continued

-V1-HLA-B35-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
291	FMIAVFLPI	0.400
57	CPSELQHTQ	0.400
239	PSVSDSLTW	0.375

[0856]

TABLE XVII

-V2-HLA-B35-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is for specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
4	FHYIQVNNI	0.040
2	REFHYIQVN	0.020
3	EFHYIQVNN	0.010
1	WREFHYIQV	0.006

[0857]

TABLE XVII

-V3-HLA-B35-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
25	LTRFKGLNL	3.000
13	KSDVPESLW	1.500
18	ESLWDPCLT	0.750
16	VPESLWDPC	0.600
12	KKSDVPESL	0.400
8	QIIHKKSDV	0.200
22	DPCLTRFKG	0.200
6	YIQLHKKS	0.100

TABLE XVII-continued

-V3-HLA-B35-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
24	CLTRFKGLN	0.100
23	PCLTRFKGL	0.100
2	REFHYIQII	0.080
11	HKKSDVPES	0.045
26	TRFKGLNLI	0.040
20	LWDPCLTRF	0.030
19	SLWDPCLTR	0.020
15	DVPESLWDP	0.020
1	WREFHYIQI	0.012
9	IIHKKSDVP	0.010
28	FKGLNLIQS	0.010
17	PESLWDPCCL	0.010
7	IQIIHKKSD	0.010
27	RFKGLNLIQ	0.006
10	IHKKSDVPE	0.003
14	SDVPESLWD	0.002
3	EFHYIQIIH	0.001
5	HYIQIIHKK	0.001
4	FHYIQIIHK	0.001
21	WDPCLTRFK	0.001

[0858]

TABLE XVII

-V4-HLA-B35-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
2	KQFGLLSLF	2.000
6	LLSLFFAVL	1.000
1	RKQFGLLSL	0.200

TABLE XVII-continued

-V4-HLA-B35-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Start	Subsequence	Score
5	GLLSLFFAV	0.200
8	SLFFAVLHA	0.100
4	FGLLSLFFA	0.100
3	QFGLLSLFF	0.100
7	LSLFFAVLH	0.050
9	LFFAVLHAI	0.040

[0859]

TABLE XVIII

-V1-HLA-B35-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
96	HPLATSHQQY	40.000
150	FPHWLDKWML	30.000
109	IPILVINKVL	20.000
287	TPPTFMIAVF	20.000
238	IPSVSDSLTW	15.000
254	QSKLGIVSLL	15.000
243	DSLWREFHY	10.000
121	VSITLLALVY	10.000
68	FPQWHLPIKI	8.000
175	HAIYSLSYPM	6.000
98	LATSHQQYFY	6.000
236	TSIPSVSDSL	5.000
35	TSMLKRPVLL	5.000
186	RSYRYKLLNW	5.000
82	ASLTFLYTLL	5.000
274	WNKWIDLKQF	4.500
40	RPVLLHLHQT	4.000
171	FAVLHAIYSL	3.000

TABLE XVIII-continued

-V1-HLA-B35-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
330	INKTEICSQL	3.000
81	IASLTFLYTL	3.000
78	AAIIASLTFL	3.000
37	MLKRPVLLHL	3.000
77	LAAIIASLTF	3.000
7	ITNQEELWKM	3.000
293	IAVFLPIVVL	3.000
179	SLSYPMRRSY	2.000
297	LPIVVLIFKS	2.000
73	LPIKIAAIIA	2.000
283	FWYTPPTFM	2.000
162	KQFGLLSFFF	2.000
116	KVLPVMSITL	2.000
220	VSLGIVGLAI	2.000
138	IVQLHNGTKY	2.000
118	LPMVSIITLLA	2.000
288	PPTFMIAVPL	2.000
100	TSHQQYFYKI	2.000
111	ILVINKVLPM	2.000
79	AIIASLTFLY	2.000
173	VLHAIYSLSY	2.000
241	VSDSLWREF	1.500
268	HALIFAWNKW	1.500
144	GTKYKKFPHW	1.500
114	INKVLPMVSI	1.200
17	KIPRNLEEDD	1.200
28	LHKDTGETSM	1.200
126	LALVYLPGVI	1.200
301	VLIFKSILFL	1.000
253	IQSKLGIVSL	1.000
103	QQYFYKIPIL	1.000
224	IVGLAILALL	1.000

TABLE XVIII-continued

-V1-HLA-B35-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
122	SITLLALVYL	1.000
263	LLGTIHALIF	1.000
221	SLGIVGLAIL	1.000
223	GIVGLAILAL	1.000
158	MLTRKQFGLL	1.000
89	TLLREVIHPL	1.000
157	WMLTRKQFGL	1.000
299	IVVLIFKSIL	1.000
165	GLLSFFF AVL	1.000
261	SLLLGTIHAL	1.000
309	FLPCLRKKIL	1.000
300	VVLIFKSILF	1.000
34	ETSM LKRPVL	1.000
117	VLPMVSIITLL	1.000
200	VQQNKEDAWI	0.600
277	WIDIKQFVWY	0.600
90	LLREVIHPLA	0.600
207	AWIEHDVWRM	0.600
244	SLTWREFHYI	0.600
319	KIRHGWEDVT	0.600
178	YLSYPMRRS	0.500
167	LSFFF AVLHA	0.500
265	GTHALIFAW	0.500
260	VSLLLGTIHA	0.500
199	QVQQNKEDAW	0.500
269	ALIFAWNKI	0.400
191	KLLNWAYQQV	0.400
149	KFPHWLDKWM	0.400
294	AVFLPIVVL I	0.400
86	FLYTLREVI	0.400
66	ELFPQWHLPI	0.400
258	GIVSLLGTI	0.400
262	LLGTIHALI	0.400

TABLE XVIII-continued

-V1-HLA-B35-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
326	DVTKLNKTEI	0.400
57	CPSELQHTQE	0.400
102	HQQYFYKIPi	0.400
72	HLPIKIAAII	0.400
108	KIPILVINKV	0.400
229	ILALLAVTSI	0.400
327	VTKINKTEIC	0.300
213	VWRMEIYVSL	0.300
227	LAILALLAVT	0.300
184	MRRSYRYKLL	0.300
159	LTRKQFGLLS	0.300
233	LAVTSIPSVS	0.300
136	AAIVQLHNGT	0.300
64	TQELFPQWHL	0.300
160	TRKQFGLLSF	0.300
13	LWKMKPRRNL	0.300
183	PMRRSYRYKL	0.300

[0860]

TABLE XVIII

-V2-HLA-B35-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of amino acids, and the end position for each peptide is the start plus nine.		
Start	Subsequence	Score
1	TWREFHYIQV	0.120
4	EFHYIQVNNI	0.040
3	REFHYIQVNN	0.020
2	WREFHYIQVN	0.003

[0861]

TABLE XVIII

-V3-HLA-B35-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
23	DPCLTRFKGL	20.000
17	VPESLWDPCl	6.000
20	SLWDPClTRF	2.000
26	LTRFKGLNLI	1.200
25	CLTRFKGLNL	1.000
12	HKKSDVPESL	0.300
1	TWREFHYIQI	0.240
8	IQIIHKKSDV	0.200
16	DVPESLWDPC	0.200
13	KKSDVPESLW	0.200
28	RFKGLNLIQS	0.060
19	ESLWDPClTR	0.050
11	IHKKSDVPES	0.045
14	KSDVPESLWD	0.045
2	WREFHYIQII	0.012
6	HYIQIIHKKS	0.010
9	QIIHKKSDVP	0.010
24	PCLTRFKGLN	0.010
10	IIHKKSDVPE	0.010
7	YIQIIHKKSD	0.010
3	REFHYIQIIH	0.002
18	PESLWDPClT	0.002
22	WDPClTRFKG	0.001
5	FHYIQIIHKK	0.001
27	TRFKGLNLIQ	0.001
4	EFHYIQIIHK	0.001
15	SDVPESLWDP	0.001
21	LWDPClTRFK	0.000

[0862]

TABLE XVIII

-V4-HLA-B35-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
3	KQFGLLSLFF	2.000
6	GLLSLFFAVL	1.000
8	LSLFFAVLHA	0.500
9	SLFFAVLHAI	0.400
1	TRKQFGLLSL	0.300
10	LFFAVLHAIY	0.200
2	RKQFGLLSLF	0.200

TABLE XVIII-continued

-V4-HLA-B35-10mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Start	Subsequence	Score
5	FGLLSLFFAV	0.200
4	QFGLLSLFFA	0.010
7	LLSLFFAVLH	0.010

[0863]

TABLE XIX

Frequently Occurring Motifs			
Name	avrg. % identity	Description	Potential Function
zf-C2H2	34%	Zinc finger, C2H2 type	Nucleic acid-binding protein functions as transcription factor, nuclear location probable
cytochrome_b_N	68%	Cytochrome b(N-terminal)/b6/petB	membrane bound oxidase, generate superoxide
Ig	19%	Immunoglobulin domain	domains are one hundred amino acids long and include a conserved intradomain disulfide bond.
WD40	18%	WD domain, G-beta repeat	tandem repeats of about 40 residues, each containing a Trp-Asp motif. Function in signal transduction and protein interaction
PDZ	23%	PDZ domain	may function in targeting signaling molecules to sub-membranous sites
LRR	28%	Leucine Rich Repeat	short sequence motifs involved in protein-protein interactions
Pkinase	23%	Protein kinase domain	conserved catalytic core common to both serine/threonine and tyrosine protein kinases containing an ATP binding site and a catalytic site
PH	16%	PH domain	pleckstrin homology involved in intracellular signaling or as constituents of the cytoskeleton
EGF	34%	EGF-like domain	30-40 amino-acid long found in the extracellular domain of membrane-bound proteins or in secreted proteins
Rvt	49%	Reverse transcriptase (RNA-dependent DNA polymerase)	
Ank	25%	Ank repeat	Cytoplasmic protein, associates integral membrane proteins to the cytoskeleton
Oxidored_q1	32%	NADH-Ubiquinone/plastoquinone (complex I), various chains	membrane associated. Involved in proton translocation across the membrane
Efhand	24%	EF hand	calcium-binding domain, consists of a12 residue loop flanked on both sides by a 12 residue alpha-helical domain
Rvp	79%	Retroviral aspartyl protease	Aspartyl or acid proteases, centered on a catalytic aspartyl residue

TABLE XIX-continued

<u>Frequently Occurring Motifs</u>			
Name	avrg. % identity	Description	Potential Function
Collagen	42%	Collagen triple helix repeat (20 copies)	extracellular structural proteins involved in formation of connective tissue. The sequence consists of the G-X-Y and the polypeptide chains forms a triple helix.
fn3	20%	Fibronectin type III domain	Located in the extracellular ligand-binding region of receptors and is about 200 amino acid residues long with two pairs of cysteines involved in disulfide bonds
7tm_1	19%	7 transmembrane receptor (rhodopsin family)	seven hydrophobic transmembrane regions, with the N-terminus located extracellularly while the C-terminus is cytoplasmic. Signal through G proteins

[0864]

TABLE XX

Motifs and Post-translational Modifications of STEAP-1
<u>N-glycosylation site</u>
143-146 NGTK (SEQ ID NO: 61)
331-334 NKTE (SEQ ID NO: 62)
<u>Protein kinase C phosphorylation site</u>
3-5 SrK
160-162 TrK
187-189 SyR
246-248 TwR
<u>Casein kinase II phosphorylation site</u>
3-6 SrkD (SEQ ID NO: 63)
8-11 TnqE (SEQ ID NO: 64)
240-243 SvsD (SEQ ID NO: 65)
246-249 TwrE (SEQ ID NO: 66)

TABLE XX-continued

Motifs and Post-translational Modifications of STEAP-1
<u>Tyrosine kinase phosphorylation site</u>
19-27 RRNLEEDDY (SEQ ID NO: 67)
<u>N-myristoylation site</u>
133-138 GVLAAl (SEQ ID NO: 68)
265-270 GTIHAL (SEQ ID NO: 69)
<u>Bipartite nuclear targeting sequence</u>
4-20 RKDITNQEELWKMKPRR (SEQ ID NO: 70)

[0865]

TABLE XXI

<u>Properties of STEAP-1</u>			
	Bioinformatic Program	URL (Located on the World Wide Web at)	Outcome
ORF	ORF finder		1193 bp
Protein length			339 aa
Transmembrane region	TM Pred	(.ch.embnet.org/)	6 TM at aa 73-91, 120-141, 163-181, 218-236, 253-274, 286-304
	HMMTop	(.enzim.hu/hmmtop/)	6 TM at aa 73-90, 117-139, 164-182, 220-238, 257-274, 291-309
	Sosui	(.genome.ad.jp/SOSui/)	6 TM at aa 70-92, 114-136, 163-184, 219-241, 255-273, 292-313
	TMHMM	(.cbs.dtu.dk/services/TMHMM)	6 TM at aa 73-95, 117-139, 164-182, 218-240, 252-274, 289-311
Signal Peptide	Signal P	(.cbs.dtu.dk/services/SignalP/)	potential cleavage between aa 136 and 137

TABLE XXI-continued

Properties of STEAP-1			
	Bioinformatic Program	URL (Located on the World Wide Web at)	Outcome
pI	pI/MW tool	(.expasy.ch/tools/)	9.2 pI
Molecular weight	pI/MW tool	(.expasy.ch/tools/)	39.8 kD
Localization	PSORT	http://psort.nibb.ac.jp/	60% plasma membrane, 40% golgi, 30% endoplasmic reticulum
	PSORT II	http://psort.nibb.ac.jp/	66% endoplasmic reticulum, 11% mitochondria, 11% plasma membrane
Motifs	Pfam	(.sanger.ac.uk/Pfam/)	none
	Prints	(.biochem.ucl.ac.uk/)	Transforming protein P21 ras signature, Fibronectin type III repeat signature
	Blocks	(.blocks.fhcr.org/)	Half-A-TPR repeat, Arsenical pump membrane protein signature, M protein repeat

[0866]

TABLE XXII

-V1-HLA-A1- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
99	ATSHQQYFY	24
122	SITLLALVY	24
180	LSYPMRRSY	24
174	LHAIYSLSY	22
278	IDIKQFVWY	20
139	VQLHNGTKY	19
32T	GETSMLKR	18
244	SLTWREFHY	18
80	IIASLTFLY	17
153	WLDKWLTR	17
182	YPMRRSYRY	17
22	LEEDDYLHK	16
58	PSELQHTQE	16
97	PLATSHQQY	16
170	FFAVLHAIY	16
189	RYKLLNWAY	16
19	RRNLEEDDY	15
84	LTFLYTLLR	15
211	HDVWRMEIY	15

TABLE XXII-continued

-V1-HLA-A1- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
241	VSDSLTWRE	15
286	YTPPTFMIA	15
203	NKEDAWIEH	14
215	RMEIYVSLG	14
247	WREFHYIQS	14
324	WEDVTKINK	14
21	NLEEDDYLH	13
23	EEDDYLHKD	13
54	EFDCPSELQ	13
159	LTRKQFGLL	13
186	RSYRYKLLN	13
7	ITNQEELWK	12
10	QEELWKMKP	12
29	HKDTGETSM	12
38	LKRPVLLHL	12
91	LREVIHPLA	12
129	VYLPGVIAA	12
221	SLGIVGLAI	12
291	FMIAVFLPI	12

TABLE XXII-continued

-V1-HLA-A1- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
323	GWEDVTKIN	12
4	RKDITNQEE	11
9	NQEELWKMK	11
37	MLKRPVLLH	11
52	ADEFDCPSE	11
55	FDCPSELQH	11
208	WIEHDVWRM	11
210	EHDVWRMEI	11
256	KLGIIVSLLL	11
277	WIDIQFVW	11
296	FLPIVVLIF	11

[0867]

TABLE XXII

-V1-HLA-A1- Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide start position plus eight.		
Pos	123456789	score
2	WREFHYIQV	14

[0868]

TABLE XXII

-V3-HLA-A1- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
13	KSDVPESLW	17
1	WREEHYIQI	14
20	LWDPCLTRF	14

TABLE XXII-continued

-V3-HLA-A1- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
25	LTRFKGLNL	13
14	SDVPESLWD	12
16	VPESLWDPC	11
19	SLWDPCLTR	10
27	RFKGLNLIQ	8

[0869]

TABLE XXII

-V4-HLA-A1-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
8	SLFFAVLHA	10
1	RKQFGLLSL	8
3	QFGLLSLFF	6
7	LSLFFAVLH	6
6	LLSLFFAVL	5
5	GLLSLFFAV	4

[0870]

TABLE XXIII

-V1-HLA-A0201- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
262	LLLGTIHAL	32
76	KIAAIIASL	29
86	FLYTLLREV	29
90	LLREVIHPL	29

TABLE XXIII-continued

-V1-HLA-A0201- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
130	YLPGVIAAI	29
72	HLPIKIAAI	26
79	ATIASLTFL	26
292	MIAVFLPIV	26
302	LIFKSILFL	26
312	CLRKILKI	26
113	VINKVLPV	25
126	LALVVLPGV	25
165	GLSFFFAV	25
172	AVLHAIYSL	25
219	YVSLGIVGL	25
252	YIQSKLGIV	25
36	SMLKRPVLL	24
123	ITLLALVYL	24
166	LLSFFFAVL	24
227	LAILALLAV	24
294	AVFLPIVVL	24
117	VLPVVSITL	23
133	GVIAAIVQL	23
192	LLNWAYQQV	23
228	AILALLAVT	23
233	LAVTSIPSV	23
82	ASLTFLYTL	22
221	SLGIVGLAI	22
222	LGIVGLAIL	22
224	IVGLAILAL	22
230	LALLAVTSI	22
237	SIPSVSDSL	22
256	KLGIIVSLL	22
261	SLLGTIHA	22
263	LLGTIHALI	22
83	SLTFLYTLL	21
109	IPILVINKV	21

TABLE XXIII-continued

-V1-HLA-A0201- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
158	MLTRKQFGL	21
259	IVSLLLGTI	21
309	FLPCLRKKI	21
319	KIRHGWEDV	21
27	YLHKDTGET	20
42	VLLHLHQTA	20
120	MVSITLLAL	20
121	VSITLLALV	20
127	ALVYLPGVI	20
217	EIVVSLGIV	20
255	SKLGIVSLL	20
258	GIVSLLLGT	20
291	FMIAVFLPI	20
38	LKRPVLLHL	19
225	VGLAILALL	19
226	GLAILALLA	19
229	ILALLAVTS	19
254	QSKLGIVSL	19
295	VFLPIVCLI	19
305	KSILFLPCL	19
59	SELQHTQEL	18
112	LVINKVLPM	18
124	TLLALVYLP	18
270	LIFAWNKWI	18
300	VVLIFKSIL	18
116	KVLPMVSIT	17
118	LPMVSITLL	17
137	AIVQLHNGT	17
176	AIYSLSYPM	17
214	WRMEIYVSL	17
322	HGWEDVTKI	17
89	TLLREVIHP	16

TABLE XXIII-continued

-V1-HLA-A0201- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
104	QYFYKIPIL	16
110	PILVINKVL	16
129	VYLPGVIAA	16
159	LTRKQFGLL	16
169	FFFAVLHAI	16
223	GIVGLAILA	16
231	ALLAVTSIP	16
245	LTWREFHYI	16
269	ALIFAWNKW	16
293	IAVFLPIVV	16
296	ELPIVVLIF	16
5	KDITNQEEL	15
37	MLKRPVLLH	15
80	IIASLTFLY	15
125	LLALVYLPG	15
134	VIAAIVQLH	15
208	WIEHDVWRM	15
265	GTHALIFA	15
272	FAWNKWIDI	15
279	DIKQFVVYT	15
299	IVVLIFKSI	15
307	ILFLPCLRK	15

[0871]

TABLE XXIII

-V2-HLA-A0201- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
5	FHYIQVNNI	15
2	WREFHYIQV	8

[0872]

TABLE XXII

-V3-HLA-A0201- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
8	QIIHKKSDV	21
19	SLWDPCLTR	18
25	LTRFKGLNL	17
26	TRFKGLNLI	16
2	REFHYIQII	14
12	KKSDVPESL	14
6	YIQIIHKKS	11
9	IIHKKSDVP	11
24	CLTRFKGLN	10

[0873]

TABLE XXIII

-V4-HLA-0201- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
5	GLLSLFFAV	25
6	LLSLFFAVL	25
8	SLFFAVLHA	21
1	RKQFGLLSL	18
9	LFFAVLHAI	17

[0874]

TABLE XXIV

-V2-HLA-A202- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
NoResultsfound.		

[0875]

TABLE XXIV

-V2-HLA-A0202- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
NoResultsfound.		

[0876]

TABLE XXIV

-V3-HLA-A0202- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight. Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
NoResultsfound.		

[0877]

TABLE XXIV

-V4-HLA-A0202- 9mers:STEAP-1		
specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
NoResultsfound.		

[0878]

TABLE XXV

-V1-A0203- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	Score
Noreultsfound.		

[0879]

TABLE XXV

-V2-HLA-A0203- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
NoResultsfound.		

[0880]

TABLE XXV

-V3-HLA-A0203- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
NoResultsfound.		

[0881]

TABLE XXV

-V4-HLA-A0203- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
NoResultsfound.		

[0882]

TABLE XXVI

-V1-HLA-A3- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
138	IVQLHNGTK	28
122	SITLLALVY	26
307	ILFLPCLRK	26
140	QLHNGTKYK	25
229	ILALLAVTS	25
108	KIPILVINK	22
128	LVYLPGVIA	22
133	GVIAAIVQL	22
191	KLLNWAYQQ	22
228	AILALLAVT	22
294	AVFLPIVVL	22
321	RHWEDVTK	22
37	MLKRPVLLH	21
94	VIHPLATSH	21
116	KVLPVMSIT	21
153	WLDKWMLTR	21
231	ALLAVTSIP	21
234	AVTSIPSVS	21
93	EVIHPLATS	20
97	PLATSHQQY	20
221	SLGIVGLAI	20
76	KIAAIIASL	19
127	ALVYLPGVI	19
148	KKFPHWLDK	19
244	SLTWREFHY	19
283	FVWYTPPTF	19
296	FLPIVVLIF	19
78	AAIIASLTF	18
112	LVINKVLPM	18
226	GLAILALLA	18
240	SVSDSLTWR	18
256	KLGIIVSLLL	18

TABLE XXVI-continued

-V1-HLA-A3- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
259	IVSLLLGTI	18
301	VLIFKSILF	18
317	ILKIRHGWE	18
43	LLHLHQTAH	17
79	AIIASLTFL	17
80	IIASLTFLY	17
111	ILVINKVLP	17
130	YLPGVIAAI	17
166	LLSFFFAVL	17
172	AVLHAIYSL	17
219	YVSLGIVGL	17
224	IVGLAILAL	17
312	CLRKKILKI	17
7	ITNQEELWK	16
41	PVLLHLHQT	16
42	VLLHLHQTA	16
72	HLPIKIAAI	16
125	LLALVYLP	16
180	LSYPMRRSY	16
183	PMRRSYRYK	16
207	AWIEHDVWR	16
248	REFHYIQSK	16
261	SLLLGTIHA	16
268	HALIFAWNK	16
269	ALIFAWNKW	16
278	IDIKQFVWY	16
300	VVLIFKSIL	16
306	SILFLPCLR	16
311	PCLRKKILK	16
319	KIRHWEDV	16
21	NLEDDYLH	15
89	TLLREVIHP	15

TABLE XXVI-continued

-V1-HLA-A3- 9mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
90	LLREVIHPL	15
117	VLPMSITL	15
120	MVSITLLAL	15
134	VIAAIVQLH	15
161	RKQFGLLSF	15
173	VLHAIYSLS	15
176	AIYSLSYPM	15
262	LLLGTIHAL	15
299	IVVLIFKSI	15
308	LFLPCLRKK	15
12	ELWKMKPRR	14
22	LEEDDYLHK	14
45	HLHQTAHAD	14
60	ELQHTQELF	14
86	FLYTLLREV	14
110	PILVINKVL	14
124	TLLALVYLP	14
158	MLTRKQFGL	14
186	RSYRYKLLN	14
196	AYQQVQQNK	14
277	WIDIKQFVW	14
297	LPIVVLIFK	14
316	KILKIRHGW	14
326	DVTKINKTE	14
55	FDCPSELQH	13
66	ELFPQWHLF	13
74	PIKIAAIIA	13
88	YTLLREVIH	13
165	GLLSFFFAV	13
174	LHAIYSLSY	13
189	RYKLLNWAY	13
192	LLNWAYQQV	13
212	DVWRMEIYV	13

TABLE XXVI-continued

-V1-HLA-A3- 9mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
217	EIYVSLGIV	13
223	GIVGLAILA	13
263	LLGTIHALI	13
273	AWNKWIDIK	13

[0883]

TABLE XXVI

-V2-HLA-A3- 9mers:STEAP-1 start position plus eight.		
Pos	123456789	score
3	REFHYIQVN	8
5	FHYIQVNNI	5
1	TWREFHYIQ	4
4	EFHYIQVNN	4
2	WREFHYIQV	3

[0884]

TABLE XXVI

-V3-HLA-A3-9mers: STEAP-1 Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
19	SLWDPCLTR	23
8	QIIHKKSDV	17
4	FHYIQIIHK	15
9	IIHKKSDVP	15
24	CLTRFKGLN	14
5	HYIQIIHKK	13
15	DVPESLWDP	11

[0885]

TABLE XXVI

-V4-HLA-A3- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
6	LLSLFFAVL	18
8	SLFFAVLHA	14
5	GLLSLFFAV	13
7	LSLFFAVLH	13
2	KQFGLLSLF	12
1	RKQFGLLSL	11
3	QFGLLSLFF	10

[0886]

TABLE XXVII

V1-HLA-A26- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
133	GVIAAIVQL	26
302	LIFKSILFL	26
76	KIAAIIASL	25
79	AIIASLTFL	25
112	LVINKVLPM	25
294	AVFLPIVVL	25
60	ELQHTQELF	24
159	LTRKQFGLL	24
219	YVSLGIVGL	24
80	IIASLTFLY	23
93	EVIHPLATS	23
120	MVSITLLAL	23
123	ITLLALVYL	23
172	AVLHAIYSL	23
208	WIEHDVWRM	23
224	IVGLAILAL	23

TABLE XXVII-continued

V1-HLA-A26- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
262	LLLGTHAL	23
296	FLPIVVLIF	23
90	LLREVIHPL	22
97	PLATSHQQY	22
249	EFHYIQSKL	22
279	DIKQFVWYT	22
83	SLTFLYTLL	21
99	ATSHQQYFY	21
122	SITLLALVY	21
166	LLSFFFAVL	21
217	EIYVSLGIV	21
237	SIPSVSDSL	21
283	FVWYTPPTF	21
289	PTFMIAVFL	21
301	VLIFKSILF	21
162	KQFGLLSFF	20
176	AIYSLSYPM	20
31	DTGETSMLK	19
53	DEFDCPSEL	19
63	HTQELFPQW	19
66	ELFPQWHLF	19
170	FFAVLHAIY	19
244	SLTWREFHY	19
278	IDIKQFVWY	19
300	VVLIFKSIL	19
110	PILVINKVL	18
158	MLTRKQFGL	18
286	YTPPTFMIA	18
6	DITNQEELW	17
12	ELWKMKPRR	17
34	ETSMLKRPV	17
108	KIPILVINK	17
113	VINKVLPV	17

TABLE XXVII-continued

V1-HLA-A26- 9mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
116	KVLPMVSIT	17
117	VLPMVSITL	17
130	YLPGVIAAI	17
163	QFGLLSFFF	17
258	GIVSLLLGT	17
326	DVTKINKTE	17
72	HLPIKIAAI	16
104	QYFYKIPIL	16
134	VIAAIVQLH	16
142	HNGTKYKKF	16
212	DVWRMEIYV	16
214	WRMEIYVSL	16
228	AILALLAVT	16
240	SVSDSLTWR	16
252	YIQSKLGIV	16
256	KLGIVSLLL	16
265	GTHALIFA	16
266	TIHALIFAW	16
292	MIAVFLPIV	16
298	PIVVLEIKS	16
8	TNQEELWKM	15
38	LKRPVLLHL	15
41	PVLLHLHQT	15
161	RKQFGLLSF	15
222	LGIVGLAIL	15
254	QSKLGIVSL	15
255	SKLGIVSLL	15
259	IVSLLLGTI	15
275	NKWIDIKQF	15
288	PPTFMIAVF	15
299	IVVLIFKSI	15
305	KSILFLPCL	15

TABLE XXVII-continued

V1-HLA-A26- 9mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
312	CLRKKILKI	15
56	DCPSELQHT	14
86	FLYTLLREV	14
94	VIHPLATSH	14
153	WLDKWWLTR	14
165	GLLSFFFAV	14
192	LLNWAYQQV	14
211	HDVWRMEIY	14
245	LTWREFHYI	14
23	EEDDYLHKD	13
37	MLKRPVLLH	13
54	EFDCPSELQ	13
89	TLLREVIHP	13
118	LPMVSITLL	13
124	TLLALVYLP	13
125	LLALVYLPG	13
137	AIVQLHNGT	13
168	SFFFAVLHA	13
169	FFFAVLHAI	13
173	VLHAIYSLS	13
179	SLSYPMRRS	13
180	LSYPMRRSY	13
189	RYKLLNWAY	13
223	GIVGLAILA	13
225	VGLAILALL	13
295	VFLPIVCLI	13
308	LFLPCLRKK	13
2	ESRKDITNQ	12
30	KDTGETSML	12
78	AAIIASLTF	12
82	ASLTFLYTL	12
84	LTFLYTLLR	12
98	LATSHQQYF	12

TABLE XXVII-continued

V1-HLA-A26- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
144	GTKYKKFPH	12
149	KFPHWLDKW	12
174	LHAIYLSY	12
185	RRSYRYKLL	12
234	AVTSIPSVS	12
235	VTSIPSVSD	12
270	LIFAWNKWI	12
277	WIDIKQFVW	12
303	IFKSILFLP	12
316	KILKIRHGW	12
325	EDVTKINKT	12
327	VTKINKTEI	12
331	NKTEICSQL	12

[0887]

TABLE XXVII

-V2-HLA-A26- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
4	EFHYIQVNN	14
3	REFHYIQVN	7
5	FHYIQVNNI	6

[0888]

TABLE XXVII

-V4-HLA-A26- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
15	DVPESLWDP	24
25	LTRFKGLNL	20
20	LWDPCLTRF	18
8	QIIHKKSDV	14
23	PCLTRFKGL	13
3	EFHYIQIIH	12
9	IIHKKSDVP	12
6	YIQIIHKKS	11

[0889]

TABLE XXVII

-V4-HLA-26- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
6	LLSLFFAVL	21
2	KQFGLLSLF	20
3	QFGLLSLFF	17
5	GLLSLFFAV	15
8	SLFFAVLHA	15
1	RKQFGLLSL	13
9	LFFAVLHAI	13

[0890]

TABLE XXVII

-V1-HLA-B0702- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
118	LPMVSITLL	22
310	LPCLRKKIL	20
238	IPSVSDSLT	19
73	LPIKIAAII	18
131	LPGVIAAIV	18
288	PPTFMIAVF	18
294	AVFLPIVVL	18
109	IPILVINKV	17
287	TPPTFMIAV	17
14	WKMKPRRNL	16
150	FPHWLDKWM	16
38	LKRPVLLHL	15
79	AIIASLTFL	15
120	MVSITLLAL	15
166	LLSFFFAVL	15
224	IVGLAILAL	15
30	KDTGETSML	14
35	TSMLKRPVL	14
76	KIAAIIASL	14
159	LTRKQFGLL	14
219	YVSLGIVGL	14
256	KLGIIVSLLL	14
302	LIFKSILFL	14
17	KPRRNLEED	13
36	SMLKRPVLL	13
40	RPVLLHLHQ	13
65	QELFPQWHL	13
90	LLREVIHPL	13
123	ITLLALVYL	13
133	GVIAAIVQL	13
184	MRRSYRYKL	13
185	RRSYRYKLL	13

TABLE XXVII-continued

-V1-HLA-B0702- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
214	WRMEIYVSL	13
255	SKLGIVSLL	13
262	LLLGTIHAL	13
289	PTFMIAVFL	13
57	CPSELQHTQ	12
81	IASLTFLYT	12
82	ASLTFLYTL	12
106	FYKIPILVI	12
128	LVYLPGVIA	12
146	KYKKFPHWL	12
172	AVLHAIYSL	12
225	VGLAILALL	12
254	QSKLGIVSL	12
305	KSILFLPCL	12
5	KDITNQEEL	11
20	RNLEEDDYL	11
59	SELQHTQEL	11
68	FPQWHLPIK	11
83	SLTFLYTLL	11
96	HPLATSHQQ	11
104	QYFYKIPIL	11
110	PILVINKVL	11
115	NKVLPMVSI	11
182	YPMRRSYRY	11
221	SLGIVGLAI	11
222	LGIVGLAIL	11
228	AILALLAVT	11
249	EFHYIQSKL	11
284	VWYTPPTFM	11
285	WYTPPTFMI	11
291	FMAVFLPI	11
297	LPIVVLIK	11

TABLE XXVII-continued

-V1-HLA-B0702- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
312	CLRKKILKI	11
34	ETSMKRPV	10
53	DEFDCPSEL	10
78	AAIIASLTF	10
92	REVIHPLAT	10
112	LVINKVLPM	10
117	VLPMSITL	10
130	YLPGVIAAI	10
151	PHWLDKWML	10
158	MLTRKQFGL	10
162	KQFGLLSFF	10
237	SIPSVSDSL	10
295	VELPIVVLI	10
300	VVLIFKSIL	10
320	IRHGWEDVT	10
331	NKTEICSQL	10

[0891]

TABLE XXVIII

-V2-HLA-B0702- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
5	FHYIQVNNI	7
2	WREFHYIQV	6
4	EFHYIQVNN	3

[0892]

TABLE XXVIII

-V3-HLA-B0702- mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
25	LTRFKGLNL	15
12	KKSDVPESL	13
17	PESLWDPC	13
16	VPESLWDPC	11
22	DPCLTRFKG	11
23	PCLTRFKGL	11
20	LWDPGLTRF	9
2	REFHYIQII	7
18	ESLWDPCLT	7
26	TRFKGLNLI	7

[0893]

TABLE XXVIII

-V4-HLA-B0702- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
6	LLSLFFAVL	15
1	RKQFGLLSL	13
3	QFGLLSFF	10
2	KQFGLLSLF	9
8	SLFFAVLHA	9
5	GLLSLFFAV	8
9	LFFAVLHAI	8
4	FGLLSLFFA	7

[0894]

TABLE XXIX

-V1-HLA-B08- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
312	CLRKKILKI	29
158	MLTRKQFGL	26
310	LPCLRKKIL	26
72	HLPIKIAAI	25
90	LLREVIHPL	25
317	ILKIRHGWE	25
254	QSKLGIVSL	23
301	VLIFKSILF	23
104	QYFYKIPIL	22
144	GTKYKKFPH	22
35T	SAALKRPVL	21
36	SMLKRPVLL	21
272	FAWNKWIDI	21
13	LWKMKPRRN	20
146	KYKKFPHWL	20
185	RRSYRYKLL	20
187	SYRYKLLNW	19
15	KMKPRRNLE	18
83	SLTFLYTLL	18
106	FYKIPILVI	18
118	LPMVSITLL	18
142	HNGTKYKKF	18
262	LLGTHAL	18
327	VTKINKTEI	18
37	MLKRPVLLH	17
110	PILVINKVL	17
117	VLPMSITL	17
38	LKRPVLLHL	16
159	LTRKQFGLL	16
166	LLSFFFAVL	16
184	MRRSYRYKL	16
237	SIPSVSDSL	16

TABLE XXIX-continued

-V1-HLA-B08- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
244	SLTWREFHY	16
256	KLGIVSLLL	16
76	KIAAIIASL	15
221	SLGIVGLAI	15
279	DIKQFVWYT	15
302	LIFKSILFL	15
60	ELQHTQELF	14
74	PIKIAAIIA	14
79	AIASLTFFL	14
130	YLPGVIAAI	14
182	YPMRRSYRY	14
224	IVGLAILAL	14
252	YIQSKLGIV	14
277	WIDIKQFVW	14
296	FLPIVVLIF	14
309	FLPCLRKKI	14
11	EELWKMKPR	13
17	KPRRNLEED	13
59	SELQHTQEL	13
123	ITLLALVYL	13
127	ALVYLPGVI	13
133	GVIAAIVQL	13
189	RYKLLNWAY	13
214	WRMEIYVSL	13
219	YVSLGIVGL	13
249	EFHYIQSKL	13
255	SKLGIVSLL	13
288	PPTFMIAVF	13
294	AVFLPIVVL	13
325	EDVTKINKT	13

[0895]

TABLE XXIX

-V2-HLA-B08- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
1	TWREFHYIQ	8
5	FHYIQVNNI	8
4	EFHYIQVNN	4

[0896]

TABLE XXIX

-V1-HLA-B08- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
25	LTRFKGLNL	26
23	PCLTRFKGL	19
9	IIHKKSDVP	15
8	QIIHKKSDV	14
11	HKKSDVPES	13
10	IHKKSDVPE	12

[0897]

TABLE XXIX

-V4-B08- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
6	LLSLFFAVL	17
1	RKQFGLLSL	10
8	SLFFAVLHA	9
5	GLLSLFFAV	8

[0898]

TABLE XXIX

-V1-HLA-B1510- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
151	PHWLDKWML	21
219	YVSLGIVGL	16
294	AVFLPIVVV	16
14	WKMKPRRNL	15
35	TSMLKRPVL	15
36	SMLKRPVLL	14
71	WHLPIKIAA	14
123	ITLLALVYL	14
133	GVIAAIVQL	14
210	EHDVWRMEI	14
224	IVGLAILAL	14
254	QSKLGIVSL	14
53	DEFDCPSEL	13
110	PILVINKVL	13
166	LLSFFFAVL	13
214	WRMEIYVSL	13
262	LLLGTIHAL	13
267	IHALIFAWN	13
321	RHGWEDVTK	13
5	KDITNQEEL	12
28	LHKDTGETS	12
38	LKRPVLLHL	12
50	AHADEEDOP	12
59	SELQHTQEL	12
76	KIAAIIASL	12
90	LLREVIHPL	12
95	IHPLATSHQ	12
104	QYFYKIPIIL	12
118	LPMVSITLL	12
120	MVSITLLAL	12
141	LHNGTKYKK	12
146	KYKKFPHWL	12

TABLE XXIX-continued

-V1-HLA-B1510- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
222	LGIVGLAIL	12
255	SKLGIVSLL	12
289	PTFMIAVFL	12
302	LIFKSILFL	12
20	RNLEDDYL	11
30	KDTGETSML	11
62	QHTQELFPQ	11
65	QELFPQWHL	11
82	ASLTFLYTL	11
101	SHQQYFYKI	11
117	VLPMVSITL	11
159	LTRKQFGLL	11
172	AVLHAIYSL	11
174	LHAIYSLSY	11
184	MRRSYRYKL	11
185	RRSYRYKLL	11
249	EFHYIQSKL	11
300	VVLIFKSIL	11
305	KSILFLPCL	11
310	LPCLRKKIL	11
331	NKTEICSQL	11
44	LHLHQTAAH	10
46	LHQTAAHADE	10
79	AIIASLTFL	10
83	SLTFLYTL	10
158	MLTRKQFGL	10
208	WIEHDVWRM	10
225	VGLAILALL	10
237	SIPSVSDSL	10
242	SDSLTWREF	10
250	FHYIQSKLG	10
256	KLGIIVSLLL	10

TABLE XXIX-continued

-V1-HLA-B1510- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
283	FVWYTPPTF	9
288	PPTFMIAVF	9

[0899]

TABLE XXX

9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
5	FHYIQVNNI	11

[0900]

TABLE XXX

-V4-HLA-B1510- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
6	LLSLFFAVL	13
1	RKQFGLLSL	11
2	KQFGLLSLF	7
3	QFGLLSLFF	6

[0901]

TABLE XXXI

-V1-HLA-B2705- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
19	RRNLEDDY	24
185	RRSYRYKLL	24
214	WRMEIYVSL	24
313	LRKKILKIR	24
184	MRRSYRYKL	23
39	KRPVLLHLH	22
248	REFHYIQSK	21
294	AVFLPIVVL	21
133	GVIAAIVQL	20
162	KQFGLLSFF	20
302	LIFKSILFL	20
20	RNLEDDYL	19
161	RKQFGLLSF	19
307	ILFLPCLRK	19
76	KIAAIIASL	18
104	QYFYKIPIL	18
172	AVLHAIYSL	18
196	AYQQVQQNK	18
254	QSKLGIVSL	18
321	RHWEDVTK	18
5	KDITNQEEL	17
79	AIIASLTFL	17
108	KIPILVINK	17
148	KKFPHWLDK	17
188	YRYKLLNWA	17
219	YVSLGIVGL	17
255	SKLGIVSLL	17
262	LLGTHIAL	17
305	KSILFLPCL	17
314	RKKILKIRH	17
12	ELWKMKPRR	16
30	KDTGETSML	16

TABLE XXXI-continued

-V1-HLA-B2705- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
65	QELFPQWHL	16
78	AIIASLTF	16
82	ASLTFLYTL	16
118	LPMVSITLL	16
123	ITLLALVYL	16
141	LHNGTKYKK	16
189	RYKLLNWAY	16
207	AWIEHDVWR	16
222	LGIVGLAIL	16
224	IVGLAILAL	16
249	EFHYIQSKL	16
268	HALIFAWNK	16
273	AWNKWIDIK	16
289	PTFMIAVFL	16
308	LFLPCLRKK	16
7	ITNQEELWK	15
14	WKMKPRRNL	15
36	SMLKRPVLL	15
53	DEFDCPSEL	15
59	SELQHTQEL	15
84	LTFLYTLLR	15
90	LLREVIHPL	15
110	PILVINKVL	15
154	LDKWMLTRK	15
178	YSLSYPMRR	15
225	VGLAILALL	15
256	KLGIVSLLL	15
288	PPTFMIAVF	15
297	LPIVVLIFF	15
301	VLIFKSILF	15
311	PCLRKKILK	15
312	CLRKKILKI	15

TABLE XXXI-continued

-V1-HLA-B2705- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
8	TNQEELWKM	14
32	TGETSMLKR	14
35	TSMLKRPVL	14
38	LKRPVLLHL	14
94	VIHPLATSH	14
117	VLPMVSITL	14
138	IVQLHNGTK	14
139	VQLHNGTKY	14
146	KYKKFPHWL	14
153	WLDKWMLTR	14
156	KWMLTRKQF	14
176	AIYSLSYPM	14
177	IYSLSYPMR	14
240	SVSDSLTWR	14
260	VSLLLGTIH	14
275	NKWIDIKQF	14
278	IDIKQFVWY	14
300	VVLIPKSIL	14
320	IRHGVEDVT	14
324	WEDVTKINK	14
331	NKTEICSQL	14
3	SRKDITNQE	13
11	EELWKMKPR	13
29	HKDTGETSM	13
31	DTGETSMLK	13
43	LLHLHQTAH	13
73	LPIKIAAII	13
83	SLTFLYTLL	13
112	LVINKVLPM	13
122	SITLLALVY	13
130	YLPGVIAAI	13
142	HNGTKYKKF	13
144	GTKYKKFPH	13

TABLE XXXI-continued

-V1-HLA-B2705- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
151	PHWLDKWML	13
158	MLTRKQFGL	13
160	TRKQFGLLS	13
163	QFGLLSFFF	13
167	LSFFFAVLH	13
230	LALLAVTSI	13
237	SIPSVSDSL	13
251	HYIQSKLGI	13
284	VWYTPPTFM	13
296	FLPIVVLI	13
306	SILFLPCLR	13
9	NQEELWKMK	12
47	HQTAHADEF	12
55	FDCPSELQH	12
60	ELQHTQELF	12
68	FPQWHLPIK	12
88	YTLLREVIH	12
91	LREVIHPLA	12
98	LATSHQQYF	12
99	ATSHQQYFY	12
100	TSHQQYFYK	12
106	FYKIPILVI	12
120	MVSITLLAL	12
140	QLHNGTKYK	12
159	LTRKQFGLL	12
166	LLSFFFAVL	12
180	LSYPMRRSY	12
182	YPMRRSYRY	12
208	WIEHDVWRM	12
242	SDSLTWREF	12
247	WREFHYIQS	12
264	LGTIHALIF	12

TABLE XXXI-continued

-V1-HLA-B2705- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
283	FVWYTPPTF	12
295	VFLPIVVLI	12
310	LPCLRKKIL	12
322	HGWEDVTKI	12
18	PRRNLEEDD	11
21	NLEEDDYLH	11
22	LEEDDYLHK	11
37	MLKRPVLLH	11
72	HLPIKIAAI	11
101	SHQQYFYKI	11
109	IPILVINKV	11
115	NKVLPMVSI	11
169	FFFAVLHAI	11
174	LHAIYLSY	11
181	SYPMRRSYR	11
183	PMRRSYRYK	11
201	QQNKEDAWI	11
216	MEIYVSLGI	11
259	IVSLLLGTI	11
299	IVVLIFKSI	11

[0902]

TABLE XXXI

-V2-HLA-B2705- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
2	WREFHYIQV	12
5	FHYIQVNNI	12
3	REFHYIQVN	11
4	EFHYIQVNN	6

[0903]

TABLE XXXI

-V3-HLA-B2705- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
26	TRFKGLNLI	25
5	HYIQIIHKK	20
1	WREEHYIQI	18
2	REFHYIQII	16
4	FHYIQIIHK	16
20	LWDPCLTRF	16
12	KKSDVPESL	14
25	LTRFKGLNL	14
17	PESLWDPCL	13
19	SLWDPCLTR	13
3	EFHYIQIIH	12
23	PCLTRFKGL	12

[0904]

TABLE XXXI

-V4-HLA-B2705- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
2	KQFGLLSLF	20
1	RKQFGLLSL	19
3	QFGLLSLFF	14
6	LLSLFFAVL	13
7	LSLFFAVLH	12
9	LFFAVLHAI	11

[0905]

TABLE XXXII

-V1-HLA-B2709- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
185	RRSRYKLL	24
184	MRRSRYKLL	22
214	WRMEIYVSL	22
20	RNLEEDDY	16
133	GVIAAIVQL	16
289	PTFMIAVFL	15
19	RRNLEEDDY	14
82	ASLTFLYTL	14
123	ITLLALVYL	14
165	GLLSFFFAV	14
172	AVLHAIYSL	14
255	SKLGIVSLL	14
294	AVFLPIVVL	14
295	VFLPIVVL	14
305	KSILFLPDL	14
5	KDITNQEEL	13
30	KDTGETSML	13
36	SMLKRPVLL	13
76	KIAAIIASL	13
104	QYFYKIPIL	13
110	PILVINKVL	13
161	RKQFGLLSF	13
176	AIYSLSYPM	13
225	VGLAILALL	13
256	KLGIIVSLLL	13
302	LIFKSILFL	13
331	NKTEICSQL	13
3	SRKDITNQE	12
38	LKRPVLLHL	12
39	KRPVLLHLH	12
53	DEFDCPSEL	12
59	SELQHTQEL	12

TABLE XXXII-continued

-V1-HLA-B2709- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
65	QELFPQWHL	12
79	AIIASLTFL	12
91	LREVIHPLA	12
146	KYKKFPHWL	12
162	KQFGLLSFF	12
188	YRYKLLNWA	12
224	IVGLAILAL	12
262	LLLGTIHAL	12
276	KWIDIKQFV	12
300	WLIFKSILI	2
14	WKMKPRRNL	11
35	TSMLKRPVL	11
73	LPIKIAAII	11
78	AAIIASLTF	11
83	SLTFLYTLL	11
105	YFYKIPILV	11
112	LVINKVLPM	11
120	MVSITLLAL	11
126	LALVYLPV	11
151	PHWLDKWWL	11
156	KWMLTRKQF	11
158	MLTRKQFGL	11
160	TRKQFGLLS	11
208	WIEHDVWRM	11
219	YVSLGIVGL	11
222	LGIVGLAIL	11
230	LALLAVTSI	11
237	SIPSVSDSL	11
247	WREFHYIQS	11
249	EFHYIQSKL	11
254	QSKLGIVSL	11
264	LGTIHALIF	11

TABLE XXXII-continued

-V1-HLA-B2709- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
299	IVVLIFKSI	11
313	LRKKILKIR	11
320	IRHWEDVT	11

[0906]

TABLE XXXII

-V2-HLA-B2709- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
2	WREFHYIQV	19
5	FHYIQVNNI	12

[0907]

TABLE XXXII

-V3-B2709-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
26	TRFKGLNLI	20
1	WREFHYIQI	19
2	REFHYIQII	14
12	KKSDVPESL	12
23	PCLTRFKGL	12
25	LTRFKGLNL	12
17	PESLWDPCL	11
20	LWDPCLTRF	10
8	QIIHKKSDV	9

[0908]

TABLE XXXII

-V4-HLA-B2709- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
1	RKQFGLLSL	15
5	GLLSLFFAV	14
2	KQFGLLSLF	12
6	LLSLFFAVL	10
9	LFFAVLHAI	10
3	QFGLLSLFF	9

[0909]

TABLE XXXII

-V1-HLA-B4402- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
53	DEFDCPSEL	24
59	SELQHTQEL	23
216	MEIYVSLGI	22
65	QELFPQWHL	21
294	AVFLPIVVV	21
78	AATIASLTF	18
133	GVIAAIVQL	18
262	LLLGTIHAL	18
269	ALIFAWNKW	18
23	EEDDYLHKD	17
79	AIIASLTFL	17
82	ASLTFLYTL	17
156	KWMLTRKQF	17
172	AVLHAIYSL	17
224	IVGLAILAL	17
275	NKWIDIKQF	17
5	KDITNQEEL	16

TABLE XXXII-continued

-V1-HLA-B4402- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
36	SMLKRPVLL	16
219	YVSLGIVGL	16
255	SKLGIVSLL	16
295	VFLPIVVLI	16
302	LIFKSILFL	16
305	KSILFLPCL	16
11	EELWKMKPR	15
38	LKRPVLLHL	15
76	KIAAIIASL	15
104	QYFYKIPIL	15
110	PILVINKVL	15
118	LPMVSITLL	15
120	MVSITLLAL	15
122	SITLLALVY	15
130	YLPGVIAAI	15
162	KQFGLLSFF	15
180	LSYPMRRSY	15
185	RRSYRYKLL	15
204	KEDAWIEHD	15
248	REFHYIQSK	15
254	QSKLGIVSL	15
266	TIHALIFAW	15
278	IDIKQFVWY	15
289	PTFMIAVFL	15
301	VLIFKSILF	15
316	KILKIRHGW	15
1	MESRKDITN	14
35	TSMLKRPVL	14
72	HLPIKIAAI	14
90	LLREVIHPL	14
92	REVIHPLAT	14
99	ATSHQQYFY	14
123	ITLLALVYL	14

TABLE XXXII-continued

-V1-HLA-B4402- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
142	HNGTKYKKF	14
149	KFPHWLDKW	14
169	FFFAVLHAI	14
222	LGIVGLAIL	14
225	VGLAILALL	14
242	SDSLTWREF	14
249	EFHYIQSKL	14
288	PPTFMIAVF	14
310	LPCLRKKIL	14
14	WKMKPRRNL	13
30	KDTGETSML	13
33	GETSMLKRP	13
60	ELQHTQELF	13
73	LPIKIAAII	13
106	FYKIPILVI	13
117	VLPMSITL	13
127	ALVYLPGVI	13
139	VQLHNGTKY	13
146	KYKKFPHWL	13
166	LLSFFFAVL	13
182	YPMRRSYRY	13
187	SYRYKLLNW	13
189	RYKLLNWAY	13
200	VQQNKEDAW	13
214	WRMEIYVSL	13
256	KLGIVSLLL	13
291	FMIAVFLPI	13
296	FLPIVVLIF	13
299	IVVLIFKSI	13
309	FLPCLRKKI	13
312	CLRKKILKI	13
331	NKTEICSQL	13

TABLE XXXII-continued

-V1-HLA-B4402- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
6	DITNQEELW	12
10	QEELWKMKP	12
22	LEEDDYLHK	12
63	HTQELFPQW	12
80	IIASLTFLY	12
83	SLTFLYTLL	12
97	PLATSHQQY	12
159	LTRKQFGLL	12
161	RKQFGLLSF	12
184	MRRSRYRYKL	12
209	IEHDVVRME	12
210	EHDVVRMEI	12
221	SLGIVGLAI	12
237	SIPSVDSL	12
239	PSVSDSLTW	12
244	SLTWREFHY	12
251	HYIQSKLGI	12
259	IVSLLLGTI	12
264	LGTIHALIF	12
270	LIFAWNKWI	12
277	WIDIKQFVW	12
283	FVWYTPPTF	12
285	WYTPPTFMI	12
324	WEDVTKINK	12
19	RRNLEEDDY	11
20	RNLEEDDYL	11
47	HQTAHADEF	11
69	PQWHLPIKI	11
87	LYTLLREVI	11
101	SHQQYFYKI	11
115	NKVLPMVSI	11
145	TKYKKFPHW	11
151	PHWLDKWML	11

TABLE XXXII-continued

-V1-HLA-B4402- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
158	MLTRKQFGL	11
163	QFGLLSFFF	11
174	LHAIYSLSY	11
206	DAWIEHDVW	11
211	HDVVRMEIY	11
230	LALLAVTSI	11
245	LTWREFHYI	11
263	LLGTIHALI	11
300	VVLIFKSIL	11

[0910]

TABLE XXXIII

-V2-HLA-B4402- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
3	REFHYIQVN	16
5	FHYIQVNNI	10

[0911]

TABLE XXXIII

-V3-B4402- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
2	REEHYIQII	23
17	PESLWDPCCL	22
23	PCLTRFKGL	16
20	LWDPCLTRF	15

TABLE XXXIII-continued

-V3-B4402- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
12	KKSDVPESL	14
13	KSDVPESLW	13
26	TRFKGLNLI	13
25	LTRFKGLNL	11

[0912]

TABLE XXXIII

-V4-HLA-B4402- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
2	KQFGLLSLF	16
6	LLSLFFAVL	14
9	LFFAVLHAI	14
1	RKQFGLLSL	12
3	QFGLLSLFF	12

[0913]

TABLE XXXIV

-V1-B5101- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
230	LALLAVTSI	27
109	IPILVINKV	26
293	IAVFLPIVV	25
73	LPIKIAAII	24
126	LALVYLPGV	24
272	FAWNKWIDI	24

TABLE XXXIV-continued

-V1-B5101- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
322	HGWEDVTKI	24
233	LAVTSIPSV	23
227	LAILALLAV	22
287	TPPTFMIAV	22
118	LPMVSITLL	21
131	LPGVIAAIV	21
310	LPCLRKKIL	19
206	DAWIEHDVW	18
105	YFYKIPILV	17
130	YLPGVIAAI	17
225	VGLAILALL	17
86	FLYTLLREV	16
103	QQYFYKIPI	16
106	FYKIPILVI	16
135	IAAIVQLHN	16
169	FFFAVLHAI	16
195	WAYQQVQQN	16
270	LIFAWNKWI	16
291	FMIAVFLPI	16
295	VFLPIVVLI	16
297	LPIVVLIFFK	16
312	CLRKKILKI	16
69	PQWHLPIKI	15
81	IASLTFLYT	15
87	LYTLLREVI	15
212	DVWRMEIYV	15
222	LGIVGLAIL	15
259	IVSLLLGTI	15
288	PPTFMIAVF	15
309	FLPCLRKKI	15
57	CPSELQHTQ	14
67	LFPQWHLPI	14
96	HPLATSHQQ	14

TABLE XXXIV-continued

-V1-B5101- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
101	SHQQYFYKI	14
127	ALVYLPGVI	14
216	MEIYVSLGI	14
217	EIYVSLGIV	14
245	LTWREFHYI	14
299	IVVLIFKSI	14
38	LKRPVLLHL	13
53	DEFDCPSEL	13
72	HLPIKIAAI	13
77	IAAIIASLT	13
78	AAIIASLTF	13
90	LLREVIHPL	13
110	PILVINKVL	13
113	VINKVLP MV	13
117	VLP MV SITL	13
171	FAVLHAIYS	13
182	YPMRRSYRY	13
221	SLGIVGLAI	13
238	IPSVDSLTL	13
262	LLG TIHAL	13
263	LLG TIHALI	13
268	HALIFAWNK	13
302	LIFKSILFL	13

[0914]

TABLE XXXIV

-V2-HLA-B5101- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
5	FHYIQVNNI	18
2	WREFHYIQV	9

[0915]

TABLE XXXIV

-V3-HLA-B5101- 9mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
22	DPCLTRFKG	17
26	TRFKGLNLI	15
2	REFHYIQII	13
1	WREFHYIQI	11
16	VPESLWDPC	11
23	PCLTRFKGL	11
12	KKSDVPESL	10
25	LTRFKGLNL	10
8	QIIHKKSDV	9
15	DVPESLWDP	9
4	FHYIQIIHK	8

[0916]

TABLE XXXIV

-V4-B5101-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
9	LFFAVLHAI	17
6	LLSLFFAVL	12
4	FGLLSLFFA	11

TABLE XXXIV-continued

-V4-B5101-9mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 9 amino acids, and the end position for each peptide is the start position plus eight.		
Pos	123456789	score
5	GLLSLFFAV	11
1	RKQFGLLSL	8

[0917]

TABLE XXXV

-V1-HLA-A1- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
277	WIDIKQFVWY	28
121	VSITLLALVY	27
210	EHDVWRMEIY	25
173	VLHAIYSLSY	23
179	SLSYPMRRSY	19
243	DSLWTREFHY	19
79	AIIASLTFLY	18
138	IVQLHNGTKY	18
188	YRYKLLNWAY	18
21	NLEEDDYLHK	17
181	SYPMRRSYRY	17
54	EFDCPSELQH	16
91	LREVIHPLAT	16
169	FFFAVLHAIY	16
215	RMEIYVSLGI	16
286	YTPPTFMIAV	16
18	PRRNLEEDDY	15
96	HPLATSHQQY	15
98	LATSHQQYFY	15
159	LTRKQFGLLS	15
241	VSDSLTWREF	15
31	DTGETSMLKR	14

TABLE XXXV-continued

-V1-HLA-A1- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
58	PSELQHTQEL	14
323	GWEDVTKINK	14
88	YTLREVIHP	13
220	VSLGIVGLAI	13

[0918]

TABLE XXXV

-V2-HLA-A1- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
2	WREFHYIQVN	11

[0919]

TABLE XXXV

-V3-HLA-A1- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
14	KSDVPESLWD	20
21	LWDPCLTRFK	14
17	VPESLWDPCL	11
2	WREFHYIQII	10
19	ESLWDPLTR	10

[0920]

TABLE XXXV

-V4-HLA-A1- 10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
10	LFFAVLHAIY	15
8	LSLFFAVLHA	11
3	KQFGLLSLFF	7

[0921]

TABLE XXXVI

-V1-A0201- 10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
232	LLAVTSIPSV	31
125	LLALVYLPV	30
261	SLLLGTHAL	30
226	GLAILALLAV	29
221	SLGIVGLAIL	28
229	ILALLAVTSI	28
89	TLLREVIHPL	27
223	GIVGLAILAL	27
301	VLIFKSILFL	27
108	KIPILVINKV	26
130	YLPGVIAAIV	26
262	LLLGTHALI	26
291	FMIAVFLPIV	26
117	VLPMV SITLL	25
122	SITLLALVYL	25
165	GLLSFFFAVL	25
37	MLKRPVLLHL	24
81	IASLTFLYTL	23
112	LVINKVLPV	23
191	KLLNWAYQQV	23

TABLE XXXVI-continued

-V1-A0201- 10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
258	GIVSLLLGTI	23
75	IKIAAIIASL	22
78	AAIIASLTFL	22
171	FAVLHAIYSL	22
224	IVGLAILALL	22
111	ILVINKVLPM	21
116	KVLEPMVSITL	21
119	PMVSITLLAL	21
157	WMLTRKQFGL	21
293	IAVFLPIVVL	21
294	AVFLPIVVLI	21
72	HLPIKIAAII	20
86	FLYTLLREVI	20
120	MVSITLLALV	20
129	VYLPGVIAAI	20
244	SLTWREFHYI	20
253	IQSKLGIVSL	20
269	ALIFAWNKI	20
292	MIAVFLPIVV	20
309	FLPCLRKKIL	20
66	ELFPQWHLPI	19
71	WHLEPIKIAAI	19
90	LLREVIHPLA	19
158	MLTRKQFGLL	19
218	IYVSLGIVGL	19
286	YTPPTFMIAV	19
307	ILFLPCLRKK	19
43	LLHLHQTAHA	18
183	PMRRSYRYKL	18
227	LAILALLAVT	18
7	ITNQEELWKM	17
36	SMLKRPVLLH	17
80	IIASLTFLYT	17

TABLE XXXVI-continued

-V1-A0201- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
85	TFLYTLLREV	17
127	ALVYLPGVIA	17
215	RMEIYVSLGI	17
255	SKLGIVSLLL	17
105	YFYKIPILVI	16
126	LALVYLPGVI	16
128	LVYLPGVIAA	16
168	SFFFAVLHAI	16
228	AILALLAVTS	16
236	TSIPSVSDSL	16
251	HYIQSKLGIV	16
256	KLGIIVSLLG	16
299	IVVLIFKSIL	16
304	FKSILFLPCL	16
329	KINKTEICSQ	16
76	KIAAIIASLT	15
103	QQYFYKIPIL	15
213	VWRMEIYVSL	15
216	MEIYVSLGIV	15
220	VSLGIVGLAI	15
296	FLPIVVLIFFK	15
302	LIFKSILFLP	15
308	LFLPCLRKKI	15

[0922]

TABLE XXXVI

-V2-HLA-A0201- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
1	TWREFHYIQV	12
4	EFHYIQVNNI	9

[0923]

TABLE XXVI

-V3-HLA-A0201- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
25	CLTRFKGLNL	20
20	SLWDPCLTRF	18
26	LTRFKGLNLI	18
8	IQIIHKKSDV	14
10	IIHKKSDVPE	12
7	YIQIIHKKSD	11
12	HKKSDVPESL	11
17	VPESLWDPCL	11
1	TWREFHYIQI	10
2	WREFHYIQII	10
9	QIIHKKSDVP	10
5	FHYIQIIHKK	9
23	DPCLTRFKGL	9

[0924]

TABLE XXXVI

-V4-HLA-A0201- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9, each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
9	SLFFAVLHAI	26
6	GLLSLFFAVL	25
1	TRKQFGLLSL	16
5	FGLLSLFFAV	14
7	LLSLFFAVLH	14
8	LSLFFAVLHA	12

[0925]

TABLE XXXVII

-V1-HLA-A0202- 10mers:STEAP-1		
NoResultsfound.		
Pos	1234567890	score

[0926]

TABLE XXXVII

-V2-HLA-A0202- 10mers:STEAP-1		
NoResultsfound.		
Pos	1234567890	score

[0927]

TABLE XXXVII

-V3-HLA-A0202- 10mers:STEAP-1		
NoResultsfound.		
Pos	1234567890	score

[0928]

TABLE XXXVII

-V4-HLA-A0202- 10mers:STEAP-1		
NoResultsfound.		
Pos	1234567890	score

[0929]

TABLE XXXVIII

-V1-HLA-A0203- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9, each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
70	QWHLPIKIAA	19
128	LVYLPGVIAA	19
43	LLHLHQTAHA	18
71	WHLPIKIAAI	17
129	VYLPGVIAAI	17
41	PVLLHLHQTA	10
69	PQWHLPIKIA	10
73	LPIKIAAIIA	10
90	LLREVIHPLA	10
118	LPMVSITLLA	10
127	ALVYLPGVIA	10
163	QFGLLSFFFA	10
167	LSFFFAVLHA	10
187	SYRYKLLNWA	10
198	QQVQQNKEDA	10
219	YVSLGIVGLA	10
222	LGIVGLAILA	10
225	VGLAILALLA	10
260	VSLLLGTIHA	10
264	LGTIHALIFA	10
285	WYTPPTFMIA	10
42	VLLHLHQTAH	9
44	LHLHQTAHAD	9
74	PIKIAAIAS	9
91	LREVIHPLAT	9
119	PMVSITLLAL	9
164	FGLLSFFFAV	9
168	SFFFAVLHAI	9
188	YRYKLLNWAY	9
199	QVQQNKEDAW	9
220	VSLGIVGLAI	9
223	GIVGLAILAL	9

TABLE XXXVIII-continued

-V1-HLA-A0203- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
226	GLAILALLAV	9
261	SLLLGTIHAL	9
265	GTIHALIFAW	9
286	YTPPTFMIAV	9

[0930]

TABLE XXXVIII

-V2-HLA-A0203- 10mers: STEAP-1		
Pos	123456789	score
NoResultsfound.		

[0931]

TABLE XXXVIII

-V3-HLA-A0203- 10mers: STEAP-1		
Pos	123456789	score
NoResultsfound.		

[0932]

TABLE XXXVIII

-V4-HLA-A0203- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
4	QFGLLSLFFA	10
8	LSLFFAVLHA	10
5	FGLLSLFFAV	9
9	SLFFAVLHAI	9
6	GLLSLFFAVL	8
10	LFFAVLHAIY	8

[0933]

TABLE XXXVIII

-V1-HLA-A0203- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
137	AIVQLHNGTK	26
228	AILALLAVTS	26
21	NLEEDDYLHK	24
306	SILFLPCLRK	23
6	DITNQEELWK	23
93	EVIHPLATSH	23
138	IVQLHNGTKY	23
140	QLHNGTKYKK	23
173	VLHAIYSLSY	23
307	ILFLPCLRKK	23
79	AIIASLTFLY	22
116	KVLPMSITL	22
320	IRHGVEDVTK	22
153	WLDKWMLTRK	21
166	LLSFFFAVLH	21
259	IVSLLGTHI	21
296	FLPIVVLIFK	21
76	KIAAIIASLT	20
127	ALVYLPGVIA	20
176	AIYSLSYPMR	20
179	SLSYPMRRSY	20
263	LLGTIHALIF	20
277	WIDIKQFVWY	20
86	FLYTLLEVI	19
121	VSITLLALVY	19
133	GVIAAIVQLH	19
165	GLLSFFFAVL	19
191	KLLNWAYQQV	19
217	EIYVSLGIVG	19
234	AVTSIPSVSD	19
42	VLLHLHQTAAH	18
83	SLTFLYTLRL	18

TABLE XXXVIII-continued

-V1-HLA-A0203- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
130	YLPGVIAAIV	18
172	AVLHAIYSLS	18
294	AVFLPIVVLI	18
319	KIRHGWEDVT	18
27	YLHKDTGETS	17
37	MLKRPVLLHL	17
41	PVLLHLHQTA	17
72	HLPIKIAAII	17
124	TLLALVYLP	17
212	DVWRMEIYVS	17
229	ILALLAVTSI	17
231	ALLAVTSIPS	17
256	KLGIIVSLLG	17
262	LLLGTIHALI	17
267	IHALIFAWNK	17
269	ALIFAWNKWI	17
300	VVLIFKSILF	17
312	CLRKKILKIR	17
317	ILKIRHGWED	17
30	KDTGETSMLK	16
66	ELFPQWHLPI	16
107	YKIPILVINK	16
111	ILVINKVLPM	16
128	LVYLPGVIAA	16
224	IVGLAILALL	16
226	GLAILALLAV	16
299	IVVLIFKSIL	16
301	VLIFKSILFL	16
77	IAAIIASLTF	15
89	TLLREVIHPL	15
97	PLATSHQQYF	15
112	LVINKVLPMV	15

TABLE XXXVIII-continued

-V1-HLA-A0203- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
180	LSYPMRRSYR	15
221	SLGIVGLAIL	15
252	YIQSKLGIVS	15
261	SLLLGTIHAL	15
316	KILKIRHWE	15
43	LLHLHQTAHA	14
80	IIASLTFLYT	14
90	LLREVIHPLA	14
94	VIHPLATSHQ	14
110	PILVINKVLP	14
113	VINKVLPMS	14
120	MVSITLLALV	14
122	SITLLALVYL	14
134	VIAAIVQLHN	14
147	YKKFPHWLKD	14
152	HWLDKMWLTR	14
158	MLTRKQFGLL	14
186	RSYRYKLLNW	14
192	LLNWAYQQVQ	14
195	WAYQQVQQNK	14
223	GIVGLAILAL	14
266	TIHALIFAWN	14
292	MIAVFLPIVV	14
45	HLHQTAHADE	13
60	ELQHTQELFP	13
96	HPLATSHQQY	13
99	ATSHQQYFYK	13
182	YPMRRSYRYK	13
199	QVQQNKEDAW	13
232	LLAVTSIPSV	13
258	GIVSLLLGTI	13
279	DIKQFVWYTP	13
329	KINKTEICSQ	13

TABLE XXXVIII-continued

-V1-HLA-A0203- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
8	TNQEELWMMK	12
75	IKIAAIIASL	12
92	REVIHPLATS	12
108	KIPILVINKV	12
125	LLALVYLPGV	12
139	VQLHNGTKYK	12
219	YVSLGIVGLA	12
237	SIPSVSDSLT	12
240	SVSDSLTWRE	12
247	WREFHYIQSK	12
283	FVWYTPPTFM	12
295	VFLPIVVLI	12
305	KSILFLPCLR	12

[0934]

TABLE XXXIX

-V2-HLA-A3- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
3	REFHYIQVNN	8
1	TWREFHYIQV	7
2	WREFHYIQVN	4

[0935]

TABLE XXXIX

-V3-HLA-A3- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
25	CLTRFKGLNL	19
9	QIIHKKSDVP	17
20	SLWDPCLTRF	17
5	FHYIQIIHKK	15
10	IIHKKSDVPE	14
19	ESLWDPCLTR	13
21	LWDPCLTRFK	13
7	YIQIIHKKSD	11
16	DVPESLWDPC	11
4	EFHYIQIIHK	10
28	RFKGLNLIQS	10
8	IQIIHKKSDV	9

[0936]

TABLE XXXIX

-V4-A3- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
7	LLSLFFAVLH	22
6	GLLSLFFAVL	19
3	KQFGLLSLFF	12
9	SLFFAVLHAI	12
2	RKQFGLLSLF	11
10	LFFAVLHAIY	11

[0937]

TABLE XXXIX

-V1-HLA-A26- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
7	ITNQEELWKM	24
31	DTGETSMLKR	23
122	SITLLALVYL	23
224	IVGLAILALL	23
37	MLKRPVLLHL	22
79	AIIASLTFLY	22
165	GLLSFFFAVL	22
295	VFLPIVVLI	22
301	VLIFKSILFL	22
117	VLPMVSITLL	21
138	IVQLHNGTKY	21
210	EHDVWRMEIY	21
221	SLGIVGLAIL	21
261	SLLLGTHAL	21
89	TLLREVIHPL	20
97	PLATSHQQYF	20
111	ILVINKVLPM	20
116	KVLPMVSITL	20
158	MLTRKQFGLL	20
212	DVWRMEIYVS	20
300	VVLIFKSILF	20
93	EVIHPLATSH	19
169	FFFAVLHAIY	19
173	VLHAIYSLSY	19
179	SLSYPMRRSY	19
299	IVVLIFKSIL	19
66	ELFPQWHLPI	18
112	LVINKVLPMV	18
263	LLGTIHALIF	18
279	DIKQFVWYTP	18
283	FVWYTPPTFM	18
286	YTPPTFMIAV	18

TABLE XXXIX-continued

-V1-HLA-A26- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
326	DVTKINKTEI	18
84	LTFLYTLRE	17
133	GVIAAIVQLH	17
141	LHNGTKYKFF	17
144	GTKYKKFPHW	17
155	DKWMLTRKQF	17
160	TRKQFGLLSF	17
176	AIYSLSYPMR	17
207	AWIEHDVWRM	17
243	DSLWREFHY	17
265	GTHALIFAW	17
282	QFVWYTPPTF	17
294	AVFLPIVVLI	17
302	LIFKSILFLP	17
309	FLPCLRKIL	17
6	DITNQEELWK	16
12	ELWKMKPRRN	16
74	PIKIAAIIAS	16
75	IKIAAIIASL	16
80	IIASLTFLYT	16
108	KIPILVINKV	16
217	EIYVSLGIVG	16
274	WNKWIDIKQF	16
287	TPPTFMIAVF	16
289	PTFMIAVFLP	16
329	KINKTEICSQ	16
21	NLEEDDYLHK	15
88	YTLLREVIHP	15
120	MVSITLLALV	15
125	LLALVYLPV	15
128	LVYLPVIAA	15
149	KFPHWLDKWM	15

TABLE XXXIX-continued

-V1-HLA-A26- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
153	WLDKWLTRK	15
161	RKQFGLLSFF	15
172	AVLHAIYSL	15
218	IYVSLGIVGL	15
232	LLAVTSIPSV	15
235	VTSIPSVSDS	15
253	IQSKLGIVSL	15
258	GIVSLLGTTI	15
266	TIHALIFAWN	15
298	PIVVLIFKSI	15
307	ILFLPCLRKK	15
54	EFDCPSELQH	14
60	ELQHTQELFP	14
78	AAIIASLTFL	14
94	VIHPLATSHQ	14
99	ATSHQQYFYK	14
119	PMVSIITLLAL	14
123	ITLLALVYLP	14
132	PGVIAAIVQL	14
162	KQFGLLSFFF	14
191	KLLNWAYQQV	14
213	VWRMEIYVSL	14
219	YVSLGIVGLA	14
226	GLAILALLAV	14
229	ILALLAVTSI	14
254	QSKLGIVSLL	14
63	HTQELFPQWH	13
67	LFPQWHLPIK	13
103	QQYFYKIPIL	13
168	SFFFAVLHAI	13
171	FAVLHAIYSL	13
184	MRRSYRYKLL	13
234	AVTSIPSVSD	13

TABLE XXXIX-continued

-V1-HLA-A26- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
236	TSIPSVSDSL	13
237	SIPSVSDSLT	13
241	VSDSLTWREF	13
293	IAVFLPIVVL	13
296	FLPIVVLIFFK	13
304	FKSILFLPCL	13
312	CLRKKILKIR	13
76	KIAAIIASLT	12
81	IASLTFLYTL	12
82	ASLTFLYTLL	12
96	HPLATSHQQY	12
113	VINKVLPMS	12
121	VSITLLALVY	12
124	TLLALVYLP	12
130	YLPGVIAAIV	12
134	VIAAIVQLHN	12
181	SYPMRRSYRY	12
188	YRYKLLNWAY	12
199	QVQQNKEDAW	12
240	SVSDSLTWRE	12
244	SLTWREFHYI	12
248	REFHYIQSKL	12
249	EFHYIQSKLG	12
256	KLIVSLLLG	12
270	LIFAWNKWID	12
303	IFKSILFLPC	12

[0938]

TABLE XL

-V2-HLA-A26- 10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
4	EFHYIQVNNI	17
1	TWREFHYIQV	7

[0939]

TABLE XL

-V3-HLA-A26- 10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
20	SLWDPCLTRF	24
16	DVPESLWDPC	19
23	DPCLTRFKGL	19
4	EFHYIQIIHK	17
25	CLTRFKGLNL	17
26	LTRFKGLNLI	14
28	RFKGLNLIQS	14
9	QIIHKKSDVP	12
10	IIHKKSDVPE	12
7	YIQIIHKKSD	11
12	HKKSDVPESL	11

[0940]

TABLE XL

-V4-A26- 10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
6	GLLSLFFAVL	22
10	LFFAVLHAIY	19

TABLE XL-continued

-V4-A26- 10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
1	TRKQFGLLSL	15
2	RKQFGLLSLF	15
9	SLFFAVLHAI	15
3	KQFGLLSLFF	14
4	QFGLLSLFFA	10

[0941]

TABLE XLI

-V1-HLA-B0702- 10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
288	PPTFMIAVFL	23
109	IPILVINKVL	22
118	LPMVSITLLA	20
150	FPHWLDKWML	20
287	TPPTFMIAVF	18
40	RPVLLHLHQ	17
73	LPIKIAAIIA	17
34	ETSMMLKRPVL	16
68	FPQWHLPIKI	16
253	IQSKLGIVSL	16
223	GIVGLAILAL	15
238	IPSVSDSLTW	15
78	AAIIASLTFFL	14
213	VWRMEIYVSL	14
255	SKLGIVSLLL	14
293	IAVFLPIVVV	14
17	KPRRLEEDD	13
35	TSMLKRPVLL	13

TABLE XLI-continued

-V1-HLA-B0702- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
57	CPSELQHTQE	13
75	IKIAAIIASL	13
81	IASLTFlyTL	13
82	ASLTFlyTLL	13
119	PMVSIITLLAL	13
165	GLLSFFFAVL	13
183	PMRRSYRYKL	13
218	IYVSLGIVGL	13
224	IVGLAILALL	13
301	VLIFKSILFL	13
304	FKSILFLPCL	13
4	RKDITNQEEL	12
29	HKDTGETSML	12
37	MLKRPVLLHL	12
52	ADEFDCPSEL	12
116	KVLPMSITL	12
122	SITLLALVYL	12
131	LPGVIAAIVQ	12
132	PGVIAAIVQL	12
184	MRRSYRYKLL	12
221	SLGIVGLAIL	12
13	LWKMKPRRNL	11
19	RRNLEDDYL	11
58	PSELQHTQEL	11
66	ELFPQWHLPI	11
80	IIASLTFlyT	11
89	TLLREVIHPL	11
96	HPLATSHQQY	11
103	QQYFYKIPIL	11
111	ILVINKVLPM	11
117	VLPMSITLL	11
145	TKYKKFPHWL	11
158	MLTRKQFGLL	11

TABLE XLI-continued

-V1-HLA-B0702- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
182	YPMRRSYRYK	11
220	VSLGIVGLAI	11
236	TSIPSVSDSL	11
248	REFHYIQSKL	11
254	QSKLGIVSLL	11
261	SLLLGTIHAL	11
290	TFMIAVFLPI	11
294	AVELPIVVLI	11
299	IVVLIFKSIL	11
330	INKTEICSQL	11

[0942]

TABLE XLI

-V2-HLA-B0702- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
1	TWREFHYIQV	8
4	EFHYIQVNNI	8
3	REFHYIQVNN	3

[0943]

TABLE XLI

-V3-HLA-B0702- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
17	VPESLWDPCCL	21
23	DPCLTRFKGL	21

TABLE XLI-continued

-V3-HLA-B0702- 10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each pepfide is the start position plus nine.		
Pos	1234567890	score
25	CLTRFKGLNL	12
12	HKKSDVPESL	10

[0944]

TABLE XLI

-V4-HLA-B0702- 10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the position for each peptide is the start position plus nine.		
Pos	1234567890	score
6	GLLSLFFAVL	13
1	TRKQFGLLSL	12
3	KQFGLLSLFF	12
8	LSLFFAVLHA	9
4	QFGLLSLFFA	8
5	FGLLSLFFAV	8
2	RKQFGLLSLF	7
9	SLFFAVLHAI	7

[0945]

TABLE XLII

-V1-HLA-B08- 10mers:STEAP-1		
Pos	1234567890	score
NoResultsfound.		

[0946]

TABLE XLII

-V2-HLA-B08-10mers: STEAP-1		
Pos	123456789	score
NoResultsfound.		

[0947]

TABLE XLII

-V3-HLA-B08- 10mers:STEAP-1		
Pos	1234567890	score
NoResultsfound.		

[0948]

TABLE XLII

-V4-HLA-B08- 10mers:STEAP-1		
Pos	1234567890	score
NoResultsfound.		

[0949]

end

TABLE XLIII

-V1-HLA-B1510- 10mers:STEAP-1		
Pos	1234567890	score
NoResultsfound.		

[0950]

TABLE XLIII

-V2-HLA-B1510- 10mers:STEAP-1		
Pos	123456789	score
NoResultsfound.		

[0951]

TABLE XLIII

-V3-HLA-B1510- 10mers:STEAP-1		
Pos	1234567890	score
NoResultsfound.		

[0952]

TABLE XLIII

-V4-HLA-B1510- 10mers:STEAP-1		
Pos	1234567890	score
NoResultsfound.		

[0953]

TABLE XLIV		
<u>-V1-HLA-B2705-</u> <u>10mers:STEAP-1</u>		
Pos	1234567890	score
NoResultsfound.		

[0954]

TABLE XLIV		
<u>-V2-HLA-B2705-</u> <u>10mers:STEAP-1</u>		
Pos	1234567890	score
NoResultsfound.		

[0955]

TABLE XLIV		
<u>-V3-HLA-B2705-</u> <u>10mers:STEAP-1</u>		
Pos	1234567890	score
NoResultsfound.		

[0956]

TABLE XLIV		
<u>-V4-HLA-B2705-</u> <u>10mers:STEAP-1</u>		
Pos	1234567890	score
NoResultsfound.		

[0957]

TABLE XLV		
<u>-V1-HLA-B2709-</u> <u>10mers:STEAP-1</u>		
Pos	1234567890	score
NoResultsfound.		

[0958]

TABLE XLV		
<u>-V2-HLA-B2709-</u> <u>10mers:STEAP-1</u>		
Pos	1234567890	score
NoResultsfound.		

[0959]

TABLE XLV		
<u>-V3-HLA-B2709-</u> <u>10mers:STEAP-1</u>		
Pos	1234567890	score
NoResultsfound.		

[0960]

TABLE XLV		
<u>-V4-HLA-B2709-</u> <u>10mers:STEAP-1</u>		
Pos	1234567890	score
NoResultsfound.		

[0961]

TABLE XLVI		
<u>-V1-HLA-</u> <u>B4402:STEAP-1</u>		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
59	SELQHTQELF	23
248	REFHYIQSKL	23
209	IEHDVWRMEI	20
261	SLLGTIHAL	19
79	AIIASLTFLY	18
148	KKFPHWLDKW	18
265	GTHALIFAW	18
71	WHLPIKIAAI	17
78	AAIIASLTFL	17
109	IPILVINKVL	17
116	KVLPMSITL	17
121	VSITLLALVY	17
129	VYLPGVIAAI	17
223	GIVGLAILAL	17
294	AVFLPIVVLI	17
301	VLIFKSILFL	17
315	KKILKIRHGW	17
5	KDITNQEELW	16
23	EEDDYLHKDT	16

TABLE XLVI-continued

-V1-HLA- B4402:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
66	ELFPQWHLPI	16
75	IKIAAIIASL	16
82	ASLTFLYTLL	16
89	TLLREVIHPL	16
236	TSIPSVSDSL	16
269	ALIFAWNKWI	16
274	WNKWIDIKQF	16
276	KWIDIKQFVW	16
287	TPPTFMIAVF	16
295	VFLPIVVLI	16
308	LFLPCLRKKI	16
324	WEDVTKINKT	16
1	MESRKDITNQ	15
34	ETSMLKRPVL	15
35	TSMLKRPVLL	15
117	VLPMVSIITLL	15
132	PGVIAAIVQL	15
168	SFFFAVLHAI	15
253	IQSKLGIVSL	15
255	SKLGIVSLLL	15
293	IAVFLPIVVL	15
311	PCLRKKILKI	15
22	LEEDDYLHKD	14
52	ADEFDCPSEL	14
53	DEFDCPSELQ	14
81	IASLTFLYTLL	14
119	PMVSIITLLAL	14
122	SITLLALVYL	14
141	LHNGTKYKKF	14
155	DKWMLTRKQF	14
162	KQFGLLSFFF	14
171	FAVLHAIYSL	14

TABLE XLVI-continued

-V1-HLA- B4402:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
179	SLSYPMRRSY	14
216	MEIYVSLGIV	14
218	IYVSLGIVGL	14
10	QEELWKMKPR	13
11	EELWKMKPRR	13
29	HKDTGETSML	13
37	MLKRPVLLHL	13
65	QELFPQWHLPI	13
103	QQYFYKIPIL	13
105	YFYKIPILVI	13
158	MLTRKQFGLL	13
165	GLLSFFFAVL	13
183	PMRRSYRYKL	13
184	MRRSYRYKLL	13
186	RSYRYKLLNW	13
204	KEDAWIEHDV	13
205	EDAWIEHDVW	13
210	EHDVWRMEIY	13
220	VSLGIVGLAI	13
224	IVGLAILALL	13
238	PSVSDSLTVV	13
254	QSKLGIVSLL	13
263	LLGTIHALIF	13
268	HALIFAWNKW	13
277	WIDIKQFVWY	13
300	VVLIFKSILF	13
309	FLPCLRKKIL	13
13	LWKMKPRRNL	12
46	LHQTAAHDEF	12
58	PSELQHTQEL	12
62	QHTQELFPQW	12
77	IAAIIASLTFF	12
92	REVIHPLATS	12

TABLE XLVI-continued

-V1-HLA-B4402:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
96	HPLATSHQQY	12
138	IVQLHNGTKY	12
145	TKYKKFPHWL	12
157	WMLTRKQFGL	12
160	TRKQFGLLSF	12
169	FFFAVLHAIY	12
181	SYPMRRSYRY	12
188	YRYKLLNWAY	12
199	QVQQNKEDAW	12
221	SLGIVGLAIL	12
241	VSDSLTWREF	12
243	DSLWREFHY	12
282	QFVWYTPPTF	12
288	PPTFMIAVFL	12
304	FKSILFLPCL	12
330	INKTEICSQL	12
4	RKDITNQEEL	11
18	PRRNLEDDY	11
19	RRNLEDDYL	11
33	GETSMLKRPV	11
64	TQELFPQWHL	11
68	FPQWHLPIKI	11
86	FLYTLLREVI	11
97	PLATSHQQYF	11
126	LALVYLPGVI	11
144	GTYKKFPHW	11
161	RKQFGLLSFF	11
173	VLHAIYSLSY	11
213	VVRMEIYVSL	11
244	SLTWREFHYI	11
262	LLLGTIHALI	11
290	TFMIAVFLPI	11

TABLE XLVI-continued

-V1-HLA-B4402:STEAP-1 Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
298	PIVVLIFKSI	11
299	IVVLIFKSIL	11

[0962]

TABLE XLVI

-V2-HLA-B4402-10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
3	REFHYIQVNN	13
4	EFHYIQVNNI	12

[0963]

TABLE XLVI

-V3-HLA-B4402-10mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
13	KKSDVPESLW	14
18	PESLWDPCLT	14
23	DPCLTRFKGL	14
3	REFHYIQIIH	13
20	SLWDPCLTRF	13
25	CLTRFKGLNL	12
2	WREEHYIQII	11
12	HKKSDVPESL	11
26	LTRFKGLNLI	11
1	TWREFHYIQI	10
17	VPESLWDPCL	10

TABLE XLVI-continued

-V3-HLA-B4402- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
4	EFHYIQIIHK	6
6	HYIQIIHKKS	6
21	LWDPCLTRFK	6

[0964]

TABLE XLVI

-V4-B4402- 10mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 10 amino acids, and the end position for each peptide is the start position plus nine.		
Pos	1234567890	score
3	KQFGLLSLFF	15
9	SLFFAVLHAI	15
6	GLLSLFFAVL	13
1	TRKQFGLLSL	12
2	RKQFGLLSLF	12
10	LFFAVLHAIY	12
5	FGLLSLFFAV	5
7	LLSLFFAVLH	5

[0965]

TABLE XLVI

-V1-HLA-B5101- 10mers:STEAP-1		
Pos	1234567890	score
NoResultsfound.		

[0966]

TABLE XLVII

-V2-HLA-B5101- 10mers:STEAP-1		
Pos	1234567890	score
NoResultsfound.		

[0967]

TABLE XLVII

-V3-HLA-B5101- 10mers:STEAP-1		
Pos	1234567890	score
NoResultsfound.		

[0968]

TABLE XLVII

-V4-HLA-B5101- 10mers:STEAP-1		
Pos	1234567890	score
NoResultsfound.		

[0969]

TABLE XLVIII

-V1-HLA-DRB10101- 15mers:STEAP-1		
Each peptide is a portion of NO: 3; each start position specified, the length of peptide amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
168	SFFFAVLHAIYSLSY	34
125	LLALVYLPGVIAAIV	33
226	GLAILALLAVTSIPS	32
111	ILVINKVLPVMSITL	31
128	LVYLPGVIAAIVQLH	30
216	MEIYVSLGIVGLAIL	30
261	SLLGTHALIFAWN	30
106	FYKiPILVINKVLPM	28
114	INKVLPVMSITLLAL	28
229	ILALLAVTSIPSVSD	28
70	QWHLPIKIAAIIASL	27
161	RKQFGLLSFFFAVLH	27

TABLE XLVIII-continued

-V1-HLA-DRB10101- 15mers:STEAP-1 Each peptide is a portion of NO: 3; each start position specified, the length of peptide amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
213	VWRMEIYVSLGIVGL	27
224	IVGLAILALLAVTSI	27
25	DDYLHKDTGETSMLK	26
103	QQYFYKIPILVINKV	26
120	MVSITLLALVYLP	26
157	WMLTRKQFGLLSFFF	26
219	YVSLGIVGLAILALL	26
227	LAILALLAVTSIPSV	26
257	LGIVSLLLGTHALI	26
296	FLPIVVLIFFKSILFL	26
324	WEDVTKINKTEICSQ	26
123	ITLLALVYLPGVIAA	25
221	SLGIVGLAILALLAV	25
256	KLGIIVSLLLGTHAL	25
280	IKQFVVYTPPTFMIA	25
298	PIVVLIFFKSILFLPC	25
307	ILFLPCLRKKILKIR	25
71	WHLPIKIAAIIASLT	24
81	IASLTFLYTLREVI	24
84	LTFLYTLREVIHPL	24
88	YTLLREVIHPLATSH	24
102	HQQYFYKIPILVINK	24
115	NKVLPMVSITLLALV	24
250	FHYIQSKLGIVSLLL	24
258	GIVSLLLGTHALIF	24
282	QFVWYTPPTFMIAVF	24
286	YTPPTFMIAVFLPIV	24
293	IAVFLPIVVLIFFKSI	24
297	LPIVVLIFFKSILFLP	24
10	QEELWKMKPRRNLEE	23
41	PVLLHLHQTAHADEF	23
75	IKIXAIIASLTFLYT	23
117	VLPMSITLLALVYL	23

TABLE XLVIII-continued

-V1-HLA-DRB10101- 15mers:STEAP-1 Each peptide is a portion of NO: 3; each start position specified, the length of peptide amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
210	EHDVWRMEIYVSLGI	23
247	WREFHYIQSKLGIVS	23
281	KQFVWYTPPTFMIAV	23
64	TQELFPQWHLPIKIA	22
74	PIKIAAIIASLTFLY	22
92	REVIHPLATSHQQYF	22
108	KIPILVINKVLPMS	22
160	TRKQFGLLSFFFVAVL	22
218	IYVSLGIVGLAILAL	22
223	GIVGLAILALLAVTS	22
289	PTFMIAVFLPIVVLI	22
290	TFMIAVFLPIVVLI	22
11	EELWKMKPRRNLEED	21
56	DCPSELQHTQELFPQ	21
211	HDVWRMEIYVSLGIV	21
232	LLAVTSIPSVSDSLT	21
288	PPTFMIAVFLPIVVL	21
72	HLPKIAAIIASLT	20
85	TFLYTLREVIHPLA	20
109	IPILVINKVLPMSI	20
171	FAVLHAIYSLSYPMR	20
185	RRSYRYKLLNWAYQQ	20
187	SYRYKLLNWAYQQVQ	20
244	SLTWREFHYIQSKLG	20
253	IQSKLGIVSLLLGTHI	20
306	SILFLPCLRKKILKI	20
315	KKILKIRHGWEDVTK	20
68	FPQWHLPIKIAAIIA	19
83	SLTFLYTLREVIHP	19
118	LPMVSITLLALVYLP	19
136	AAIVQLHNGTKYKKF	19
147	YKKFPHWLDKMWLTR	19

TABLE XLVIII-continued

-V1-HLA-DRB10101- 15mers:STEAP-1 Each peptide is a portion of NO: 3; each start position specified, the length of peptide amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
166	LLSFFFAVLHAIYSL	19
181	SYPMRRSYRYKLLNW	19
248	REFHYIQSKLGIVSL	19
251	HYIQSKLGIVSLLLG	19
283	FVWYTPPTFMIAVFL	19
302	LIFKSILFLPCLRKK	19
126	LALVYLPGVIAAIVQ	18
127	ALVYLPGVIAAIVQL	18
153	WLDKWLTRKQFGLL	18
155	DKWMLTRKQFGLLSF	18
205	EDAWIEHDVWRMEIY	18
242	SDSLTWREFHYIQSK	18
249	EFHYIQSKLGIVSLL	18
267	IHALIFAWNKWIDIK	18
269	ALIFAWNKWIDIKQF	18
291	FAAIAVFLPIWLIFK	18
300	VVLIFKSILFLPCLR	18
7	ITNQEELWKMKPRRN	17
32	TGETSMLKRPVLLHL	17
35	TSMLKRPVLLHLHQT	17
39	KRPVLLHLHQTAHAD	17
40	RPVLLHLHQTAHADE	17
67	LFPQWHLPIKIAAII	17
91	LREVIHPLATSHQQY	17
112	LVINKVLPVMSITLL	17
135	IAAIVQLHNGTKYKK	17
156	KWMLTRKQFGLLSFF	17
164	FGLLSFFFAVLHAIY	17
175	HAIYSLSYPMRRSYR	17
179	SLSYPMRRSYRYKLL	17
194	NWAYQQVQQNKEDAW	17
217	EIYVSLGIVGLAILA	17
222	LGIVGLAILALLAVT	17

TABLE XLVIII-continued

-V1-HLA-DRB10101- 15mers:STEAP-1 Each peptide is a portion of NO: 3; each start position specified, the length of peptide amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
239	PSVSDSLTWREFHYI	17
254	QSKLGIVSLLLGTH	17
259	IVSLLLGTHALIFA	17
277	WIDIKQFVWYTPPTF	17
292	MIAVFLPIVVLIFKS	17
294	AVFLPIVVLIFKSIL	17
299	IVVLIFKSILFLPCL	17
301	VLIFKSILFLPCLRK	17
304	FKSILFLPCLRKKIL	17
4	RKDITNQEELWKMKP	16
24	EDDYLHKDTGETSML	16
31	DTGETSMLKRPVLLH	16
44	LHLHQTAAHADEFDCP	16
58	PSELQHTQELFPQWH	16
78	AAIIASLTFLYTLLR	16
87	LYTLLREVIHPLATS	16
95	IHPLATSHQQYFYKI	16
107	YKIPILVINKVLPV	16
110	PILVINKVLPVMSIT	16
119	PMVSIITLLALVVLPG	16
122	SITLLALVYLPGVIA	16
143	NGTKYKKFPHWLDKW	16
148	KKFPHWLDKWMLTRK	16
163	QFGLLSFFFAVLHAI	16
167	LSFFFAVLHAIYSL	16
170	FFAVLHAIYSLSYPM	16
174	LHAIYSLSYPMRRSY	16
189	RYKLLNWAYQQVQQN	16
192	LLNWAYQQVQQNKED	16
215	RMEIYVSLGIVGLAI	16
220	VSLGIVGLAILALLA	16
230	LALLAVTSIPSVSDS	16

TABLE XLVIII-continued

-V1-HLA-DRB10101- 15mers:STEAP-1		
Each peptide is a portion of NO: 3; each start position specified, the length of peptide amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
260	VSLLLGTIHALIFAW	16
264	LGTIHALIFAWNKWI	16
272	FAWNKWIDIKQFVWY	16
274	WNKWIDIKQFVWYTP	16
278	IDIKQFVWYTPPTFM	16
314	RKKILKIRHGWEDVT	16
321	RHGWEDVTKINKTEI	16

[0970]

TABLE XLVIII

-V2-HLA-DRB10101- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
4	SLTWREFHYIQVNNI	20
2	SDSLTWREFHYIQVN	18

[0971]

TABLE XLVIII

-V3-HLA-DRB10101- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
9	EFHYIQIIHKKSDVP	26
28	DPCLTRFKGLNLIQS	25
12	YIQIIHKKSDVPESL	22
4	SLTWREFHYIQIIHK	20
2	SDSLTWREFHYIQII	18
10	FHYIQIIHKKSDVPE	18

TABLE XLVIII-continued

-V3-HLA-DRB10101- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
23	PESLWDPCLTRFKGL	17
24	ESLWDPCLTRFKGLN	17
7	WREFHYIQIIHKKSD	16
20	SDVPESLWDPCLTRF	16
15	IIHKKSDVPESLWDP	15
26	LWDPCLTRFKGLNLI	12

[0972]

TABLE XLVIII

-V4-HLA-DRB10101- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
14	SLFFAVLHAIYSLSY	34
7	RKQFGLLSLFFAVLH	27
3	WMLTRKQFGLLSLFF	26
9	QFGLLSLFFAVLHAI	24
6	TRKQFGLLSLFFAVL	22
1	DKWMLTRKQFGLLSL	18
2	KWMLTRKQFGLLSLF	17
10	FGLLSLFFAVLHAIY	17
12	LLSLFFAVLHAIYSL	17
13	LSLFFAVLHAIYSLS	16

[0973]

TABLE XLIX

-V1-HLA-DRB10301-		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
155	DKWMLTRKQFGLLSF	27
181	SYPMRRSYRYKLLNW	26
297	LPIWLIFKSILFLP	26
95	IHPLATSHQQYFYKI	25
177	IYSLSYPMRRSYRYK	24
307	ILFLPCLRKKILKIR	24
19	RRNLEEDDYLHKDTG	22
117	VLPVMSITLLALVYL	22
163	QFGLLSFFFAVLHAI	22
259	IVSLLGTIHALIFA	22
298	PIVVLIFKSILFLPC	22
77	IAAIIASITFLYTLL	21
114	INKVLPVMSITLLAL	21
115	NKVLPVMSITLLALV	21
120	MVSITLLALVYLPV	21
221	SLGIVGLAILALLAV	21
222	LGIVGLAILALLAVT	21
299	IVVLIFKSILFLPCL	21
25	DDYLHKDTGETSMLK	20
35	TSMLKRPVLLHLHQ	20
87	LYTLLREVIHPLATS	20
108	KIPILVINKVLPVMS	20
136	AAIVQLHNGTKYKKF	20
156	KWMLTRKQFGLLSFF	20
206	DAWIEHDVWRMEIYV	20
219	YVSLGIVGLAILALL	20
293	IAVFLPIVVLIFKSI	20
4	RKDITNQEELWKMKP	19
13	LWKMKPRRNLEEDDY	19
40	RPVLLHLHQTAHADE	19
171	FAVLHAIYSLSYPMR	19
261	SLLLGTIHALIFAWN	19
275	NKWIDIKQFVWYTPP	19

TABLE XLIX-continued

-V1-HLA-DRB10301-		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
306	SILFLPCLRKKILKI	19
11	EELWKMKPRRNLEED	18
50	AHADEFDCPSELQHT	18
167	LSFFFAVLHAIYSLS	18
197	YQQVQQNKEDAWIEH	18
57	CPSELQHTQELFPQW	17
58	PSELQHTQELFPQWH	17
84	LTFLYTLLREVIHPL	17
132	PGVIAAIVQLHNGTK	17
135	IAAIVQLHNGTKYKK	17
138	IVQLHNGTKYKKFPH	17
190	YKLLNWAYQQVQQNK	17
267	IHALIFAWNKWIDIK	17
273	AWNKWIDIKQFVWYT	17
280	IKQFVWYTPPTFMIA	17
317	ILKIRHGWEDVTKIN	17
324	WEDVTKINKTEICSQ	17
16	MKPRRNLEEDDYLHK	16
32	TGETSMLKRPVLLHL	16
52	ADEFDCPSELQHTQE	16
62	QHTQELFPQWHLPIK	16
96	HPLATSHQQYFYKIP	16
107	YKIPILVINKVLPV	16
186	RSYRYKLLNWAYQQV	16
241	VSDSLTWREFHYIQS	16
268	HALIFAWNKWIDIKQ	16
34	ETSMLKRPVLLHLHQ	15
39	KRPVLLHLHQTAHAD	15
153	WLDKWMLTRKQFGLL	15
246	TWREFHYIQSKLGIV	15
2	ESRKDITNQEELWKM	14
148	KKFPHWLDKWMLTRK	14
226	GLAILALLAVTSIPS	14

TABLE XLIX-continued

-V1-HLA-DRB10301- Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
232	LLAVTSIPSVSDSLT	14
260	VSLLLGTIHALIFAW	14
304	FKSILFLPCLRKIL	14
81	IASLTFLYTLLREVI	13
88	YTLLREVIHPLATSH	13
109	IPILVINKVLPMVSI	13
118	LPMVSITLLALVYLP	13
122	SITLLALVYLPGVIA	13
125	LLALVYLPGVIAAIV	13
126	LALVYLPGVIAAIVQ	13
131	LPGVIAAIVQLHNGT	13
149	KFPHWLDKWMLTRKQ	13
170	FFAVLHAIYSLSPM	13
189	RYKLLNWAYQQVQQN	13
235	VTSIPSVSDSLTWRE	13
237	SIPSVSDSLTWREFH	13
254	QSKLGIVSLLLGTIH	13
256	KLGIIVSLLLGTIHAL	13
292	MIAVFLPIVVLIKFS	13

[0974]

TABLE XLIX

-V2-DRB1-0301- 15mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
1	VSDSLTWREFHYIQV	16
2	SDSLTWREFHYIQVN	12

[0975]

TABLE XLIX

-V3- DRB1030115mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
28	DPCLTRFKGLNLIQS	22
15	IIHKKSDVPESLWDP	20
23	PESLWDPCLTRFKGL	18
1	VSDSLTWREFHYIQI	16
10	FHYIQIIHKKSDVPE	16
22	VPESLWDPCLTRFKG	14
2	SDSLTWREFHYIQII	12
12	YIQIIHKKSDVPESL	12
13	IQIIHKKSDVPESLW	12
19	KSDVPESLWDPCLTR	12

[0976]

TABLE XLIX

-V4-HLA-0301- 15mers:STEAP-1 Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
1	DKWMLTRKQFGLLSL	27
9	QFGLLSLFFAVLHAI	22
2	KWMLTRKQFGLLSLF	20
13	LSLFFAVLHAIYSL	18
10	FGLLSLFFAVLHAIY	13

[0977]

TABLE L

-V1-HLA-DR1-0401- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
84	LTFLYTLLREVIHPL	26
88	YTLLREVIHPLATSH	26
92	REVIHPLATSHQQYF	26
132	PGVIAAIVQLHNGTK	26
135	IAAIVQLHNGTKYKK	26
190	YKLLNWAYQQVQQNK	26
229	ILALLAVTSIPSVSD	26
267	IHALIFAWNKWIDIK	26
103	QQYFYKIPILVINKV	22
144	GTKYKKFPHWLDKWM	22
161	RKQFGLLSFFFVAVLH	22
166	LLSFFFVAVLHAIYSL	22
167	LSFFFVAVLHAIYSLS	22
168	SFFFVAVLHAIYSLSY	22
187	SYRYKLLNWAYQQVQ	22
194	NWAYQQVQQNKEDAW	22
211	HDVWRMEIYVSLGIV	22
216	MEIYVSLGIVGLAIL	22
244	SLTWREFHYIQSKLG	22
247	WREFHYIQSKLGIVS	22
274	WNKWIDIKQFVWYTP	22
282	QFVWYTPPTFMIAVF	22
288	PPTFMIAVFLPIVVL	22
306	SILFLPCLRKKILKI	22
321	RHGVEDVTKINKTEI	22
19	RRNLEEDDYLHKDTG	20
25	DDYLHKDTGETSMLK	20
39	KRPVLLHLHQTAHAD	20
40	RPVLLHLHQTAHADE	20
41	PVLLHLHQTAHADEF	20
64	TQELFPQWHLPIKIA	20
72	HLPIKIAAIASLTF	20

TABLE L-continued

-V1-HLA-DR1-0401- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
74	PIKIAAIASLTFLY	20
78	AAIIASLTFLYTLR	20
81	IASLTFLYTLLREVI	20
87	LYTLLREVIHPLATS	20
106	FYKIPILVINKVLPM	20
111	ILVINKVLPVMSITL	20
114	INKVLPVMSITLLAL	20
115	NKVLPVMSITLLALV	20
117	VLPVMSITLLALVYL	20
120	MVSITLLALVYLPGV	20
123	ITLLALVYLPGVIAA	20
125	LLALVYLPGVIAAIV	20
128	LVYLPGVIAAIVQLH	20
163	QFGLLSFFFVAVLHAI	20
170	FFAVLHAIYSLSYPM	20
171	FAVLHAIYSLSYPMR	20
181	SYPMRRSYRYKLLNW	20
213	VWRMEIYVSLGIVGL	20
219	YVSLGIVGLAILALL	20
221	SLGIVGLAILALLAV	20
222	LGIVGLAILALLAVT	20
224	IVGLAILALLAVTSI	20
226	GLAILALLAVTSIPS	20
227	LAILALLAVTSIPSV	20
232	LLAVTSIPSVSDSLT	20
235	VTSIPSVSDSLTWRE	20
256	KLGIVSLLGTIHAL	20
260	VSLLGTIHALIFAW	20
264	LGTIHALIFAWNKWI	20
289	PTFMIAVFLPIVVLI	20
290	TFMIAVFLPIVVLI	20
294	AVFLPIVVLI	20

TABLE L-continued

-V1-HLA-DR1-0401- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
296	FLPIVVLFKSIILFL	20
297	LPIVVLFKSIILFLP	20
298	PIVVLFKSIILFLPC	20
304	FKSIILFLPCLRKKIL	20
307	ILFLPCLRKKILKIR	20
314	RKKILKIRHGWEDVT	20
324	WEDVTKINKTEICSQ	20
28	LHKDTGETSMLKRPV	18
32	TGETSMLKRPVLLHL	18
37	MLKRPVLLHLHQTAAH	18
54	EFDCPSELQHTQELF	18
62	QHTQELFPQWHLPIK	18
93	EVIHPLATSHQQYFY	18
107	YKIPILVINKVLPV	18
207	AWIEHDVWRMEIYVS	18
3	DSLWREFHYIQSKL	18
253	IQSKLGIVSLLGTI	18
258	GIVSLLGTIHALIF	18
320	IRHGWEDVTKINKTE	18
11	EELWKMKPRRNLEED	17
24	EDDYLHKDTGETSML	17
65	QELFPQWHLPIKIAA	16
68	FPQWHLPIKIAAIIA	16
83	SLTFLYTLLREVIHP	16
85	TFLYTLLREVIHPLA	16
104	QYFYKIPILVINKVL	16
127	ALVYLPGVIAAIVQL	16
147	YKKFPHWLDKWLTR	16
192	LLNWAYQQVQQNKED	16
205	EDAWIEHDVWRMEIY	16
249	EFHYIQSKLGIVSLL	16
269	ALIFAWNKWIDIKQF	16
271	IFAWNKWIDIKQFVW	16

TABLE L-continued

-V1-HLA-DR1-0401- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
283	FVWYTPPTFMIAVFL	16
293	IAVFLPIVVLFKSI	16
301	VLIFKSIILFLPCLRK	16
155	DKWMLTRKQFGLLSF	15
4	RKDITNQEELWKMKP	14
10	QEELWKMKPRRNLEE	14
35	TSMLKRPVLLHLHQT	14
43	LLHLHQTAAHAEFDC	14
77	IAAIIASLTFLYTLL	14
95	IHPLATSHQQYFYKI	14
108	KIPILVINKVLPVMS	14
109	IPILVINKVLPVMSI	14
118	LPMVSIITLLALVYLP	14
122	SITLLALVYLPGVIA	14
126	LALVYLPGVIAAIVQ	14
131	LPGVIAAIVQLHNGT	14
138	IVQLHNGTKYKKFPH	14
151	PHWLDKWLTRKQFG	14
164	FGLLSFFFAVLHAIY	14
174	LHAIYSLSYPMRRSY	14
177	IYSLSYPMRRSYRYK	14
189	RYKLLNWAYQQVQQN	14
206	DAWIEHDVWRMEIYV	14
210	EHDVWRMEIYVSLGI	14
217	EIYVSLGIVGLAILA	14
230	LALLAVTSIPSVSDS	14
238	IPSVSDSLTWREFHY	14
254	QSKLGIVSLLGTIHI	14
257	LGIVSLLGTIHALI	14
259	IVSLLGTIHALIFA	14
261	SLLGTIHALIFAWN	14
277	WIDIKQFVWYTPPTF	14

TABLE L-continued

-V1-HLA-DR1-0401- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
281	KQFVWYTPPTFMIAV	14
292	MIAVFLPIVVLIFFKS	14
305	KSILFLPCLRRKILK	14
317	ILKIRHWEDVTKIN	14
1	MESRKDITNQEELWK	12
2	ESRKDITNQEELWKM	12
5	KDITNQEELWKMKPR	12
6	DITNQEELWKMKPRR	12
17	KPRRNLEEDDYLHKD	12
21	NLEEDDYLHKDTGET	12
27	YLHKDTGETSMLKRP	12
38	LKRPVLLHLHQTAAH	12
48	QTAHADEFDCPSELQ	12
50	AHADEFDCPSELQHT	12
51	HADEFDCPSELQHTQ	12
55	FDCPSELQHTQELFP	12
56	DCPSELQHTQELFPQ	12
67	LFPQWHLPIKIAAII	12
69	PQWHLPIKIAAIIAS	12
71	WHLPIKIAAIIASLT	12
73	LPIKIAAIIASLTFL	12
75	IKIAAIIASLTFLYT	12
76	KIAAIIASLTFLYTL	12
80	IIASLTFLYILLREV	12
89	TLLREVIHPLATSHQ	12
100	TSHQQYFYKIPILVI	12
105	YFYKIPILVINKVLP	12
112	LVINKVLPMSITLL	12
116	KVLPMSITLLALVY	12
129	VYLPGVIAAIVQLHN	12
130	YLPGVIMIVQLHNG	12
134	VIAAIVQLHNGTKYK	12
137	AIVQLHNGTKYKFP	12

TABLE L-continued

-V1-HLA-DR1-0401- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
148	KKFPHWLDKWMLTRK	12
149	KFPHWLDKWMLTRKQ	12
152	HWLDKWMLTRKQFGL	12
153	WLDKWMLTRKQFGLL	12
160	TRKQFGLLSFFFAVL	12
165	GLLSFFFAVLHAIYS	12
173	VLHAIYSLSYPMRRS	12
186	RSYRYKLLNWAYQQV	12
191	KLLNWAYQQVQQNKE	12
193	LNWAYQQVQQNKEDA	12
203	NKEDAWIEHDVWRME	12
214	WRMEIYVSLGIVGLA	12
218	IYVSLGIVGLAILAL	12
223	GIVGLAILALLAVTS	12
225	VGLAILALLAVTSIP	12
228	AILALLAVTSIPSVS	12
234	AVTSIPSVDSLTVWR	12
246	TWREFHYIQSKLGIV	12
251	HYIQSKLGIVSLLLG	12
265	GTIHALIFAWNKWID	12
273	AWNKWIDIKQFVWYT	12
279	DIKQFVWYTPPTFMI	12
291	FMAVFLPIVVLIFFK	12
295	VFLPIVVLIFFKSILF	12
302	LIFKSILFLPCLRRK	12
319	KIRHWEDVTKINKT	12

[0978]

TABLE L

-V2-HLA-DR10401- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
4	SLTWREFHYIQVNNI	22
3	DSLTWREFHYIQVNN	18

[0979]

TABLE L

-V3-HLA-DR1-0401- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
9	EFHYIQIIHKSDVP	28
4	SLTWREFHYIQIIHK	22
7	WREFHYIQIIHKSD	22
24	ESLWDPCLTRFKGLN	22
28	DPCLTRFKGLNLIQS	20
3	DSLTWREFHYIQIIH	18
10	FHYIQIIHKSDVPE	14

[0980]

TABLE L

-V4-DR10401-15mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
7	RKQFGLLSLFFAVLH	22
13	LSLFFAVLHAIYSLS	22
14	SLFFAVLHAIYSLSY	22
9	QFGLLSLFFAVLHAI	20
12	LLSLFFAVLHAIYSL	20
1	DKWMLTRKQFGLLSL	15

TABLE L-continued

-V4-DR10401-15mers: STEAP-1		
Each peptide is a portion of SEQ ID NO: 9; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
10	FGLLSLFFAVLHAIY	14
4	MLTRKQFGLLSLFFA	12
6	TRKQFGLLSLFFAVL	12
11	GLLSLFFAVLHAIYS	12

[0981]

TABLE LI

-V1-DRB1101- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3, each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
108	KIPILVINKVLPVMS	28
88	YTLLREVIHPLATSH	27
167	LSFFFAVLHAIYSLS	26
68	FPQWHLPIKIAAIIA	24
154	LDKWWMLTRKQFGLLS	24
321	RHWEDVTKINKTEI	24
168	SFFFAVLHAIYSLSY	23
247	WREFHYIQSKLGIVS	23
161	RKQFGLLSFFFAVLH	22
324	WEDVTKINKTEICSQ	22
7	ITNQEELWKMKPRRN	21
84	LTFlyTLREVIHPL	21
297	LPIVVLIFKSILFLP	21
307	ILFLPCLRKILKIR	21
22	LEEDDYLHKDTGETS	20
39	KRPVLLHLHQTAAHAD	20
122	SITLLALVYLPGVIA	20
314	RKKILKIRHWEDVT	20
11	EELWKMKPRRNLEED	19

TABLE LI-continued

-V1-DRB1101- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3, each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
85	TFLYTLLREVIHPLA	19
111	ILVINKVLPMSITL	19
125	LLALVYLPGVIAAIV	19
144	GTKYKKFPHWLDKWM	19
210	EHDVWRMEIYVSLGI	19
254	QSKLGIVSLLGTIH	19
283	FVWYTPPTFMIAVFL	19
293	IAVFLPIVVLIFKSI	19
306	SILFLPCLRKILKI	19
226	GLAILALLAVTSIPS	18
229	ILALLAVTSIPSVSD	18
31	DTGETSMLKRPVLLH	17
103	QQYFYKIPILVINKV	17
194	NWAYQQVQQNKEDAW	17
274	WNKWIDIKQFVWYTP	17
185	RRSYRYKLLNWAYQQ	16
187	SYRYKLLNWAYQQVQ	16
216	MEIYVSLGIVGLAIL	16
244	SLTWREFHYIQSKLG	16
268	HALIFAWNKWIDIKQ	16
301	VLIFKSILFLPCLRK	16
311	PCLRKKILKIRHGWE	16
10	QEELWKMKPRRNLEE	15
32	TGETSMLKRPVLLHL	15
37	MLKRPVLLHLHQTAH	15
64	TQELFPQWHLPIKIA	15
81	IASLTFLYTLLREVI	15
106	FYKIPILVINKVLP	15
138	IVQLHNGTKYKKFPH	15
177	IYSLSPMRRSYRYK	15
181	SYPMRRSYRYKLLNW	15
203	NKEDAWIEHDVWRME	15
260	VSLLLGTHALIFAW	15

TABLE LI-continued

-V1-DRB1101- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3, each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
43	LLHLHQTAHADEFDC	14
55	FDCPSELQHTQELFP	14
114	INKVLPMSITLLAL	14
120	MVSITLLALVYLPV	14
132	PGVIAAIVQLHNGTK	14
140	QLHNGTKYKKFPHWL	14
148	KKFPHWLDKWMLTRK	14
153	WLDKWMLTRKQFGLL	14
178	YSLSPMRRSYRYKL	14
196	AYQQVQQNKEDAWIE	14
207	AWIEHDVWRMEIYVS	14
215	RMEIYVSLGIVGLAI	14
232	LLAVTSIPSVSDSLT	14
277	WIDIKQFVWYTPPTF	14
287	TPPTFMIAVFLPIVV	14
294	AVFLPIVVLIFKSIL	14
295	VFLPIVVLIFKSILF	14
300	VVLIFKSILFLPCLR	14
304	FKSILFLPCLRKIL	14
67	LFPQWHLPIKIAAII	13
71	WHLPIKIAAIIASLT	13
74	PIKIAAIIASLTFLY	13
115	NKVLPMSITLLALV	13
128	LVYLPGVIAAIVQLH	13
166	LLSFFFAVLHAIYSL	13
170	FFAVLHAIYSLSPM	13
212	DVWRMEIYVSLGIVG	13
217	EIYVSLGIVGLAILA	13
219	YVSLGIVGLAILALL	13
223	GIVGLAILALLAVTS	13
235	VTSIPSVSDSLTWRE	13
250	FHYIQSKLGIVSLLL	13

TABLE LI-continued

-V1-DRB1101- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
257	LGIVSLLGTIHALI	13
261	SLLGTIHALIFAWN	13
289	PTFMIAVFLPIVCLI	13
296	FLPIVCLIFKSLFL	13
312	CLRKKILKIRHGWD	13

[0982]

TABLE LI

-V2-HLA-DRB1-1101- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 5; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
4	SLTWREFHYIQVNNI	10
3	DSLTWREFHYIQVNN	9
2	SDSLTWREFHYIQVN	8

[0983]

TABLE LI

-V3-DRB11101- 15mers:STEAP-1		
Each peptide is a portion of SEQ ID NO: 7; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
9	EFHYIQIIHKSDVP	31
25	SLWDPCLTRFKGLNL	21
10	FHYIQIIHKSDVPE	20
7	WREFHYIQIIHKSD	16

[0984]

TABLE LI

-V4-DRB1101- 15mers:SIEAP-1		
Each peptide is a portion of SEQ ID NO: 3; each start position is specified, the length of peptide is 15 amino acids, and the end position for each peptide is the start position plus fourteen.		
Pos	123456789012345	score
13	LSLFFAVLHAIYSLS	26
14	SLFFAVLHAIYSLSY	23
7	RKQFGLLSLFFAVLH	22
9	QFGLLSLFFAVLHAI	13

[0985]

TABLE LII

Exon compositions of 8P1D4 v.1		
Exon number	Start	End
1	1	34
2	35	149
3	150	662
4	663	827
5	828	1176

[0986]

TABLE LIII

Nucleotide sequence of transcript variant 8P1D4 v.2 (SEQ ID NO: 81)	
ggggcccgca cctctgggca gcagcgccag ccgagactca cggcacaagt aaggcgaaga	60
gtgggtggct gaagccatac tattttatag aattaatgga aagcagaaaa gacatcacia	120
accaagaaga actttggaaa atgaagccta ggagaaattt agaagaagac gattatttgc	180

TABLE LIII-continued

Nucleotide sequence of transcript variant 8P1D4 v.2 (SEQ ID NO: 81)		
ataaggacac gggagagacc agcatgctaa aaagacctgt gcttttgcac ttgcacccaaa	240	
cagcccatgc tgatgaattt gactgccctt cagaacttca gcacacacag gaactctttc	300	
cacagtggca cttgccaat aaaatagctg ctattatagc atctctyact tttctttaca	360	
ctcttctgag ggaagtaatt caccctcttag caacttccca tcaacaatat tttataaaa	420	
ttccaatcct ggtcatcaac aaagtcttgc caatggtttc catcactctc ttggcatggg	480	
tttacctgcc aggtgtgata gcagcaattg tccaacttca taatggaacc aagtataaga	540	
agtttcacac ttggttggat aagtggatgt taacaagaaa gcagtttggg cttctcagtt	600	
tcttttttgc tgtactgcat gcaatttata gtctgtctta ccaatgagg cgatcctaca	660	
gatacaagtt gtaaaactgg gcatatcaac aggtccaaca aaataaagaa gatgcctgga	720	
ttgagcatga tgtttggaga atggagattt atgtgtctct gggaaattgt ggattggcaa	780	
tactggctct gttggctgtg acatctattc catctgtgag tgactctttg acatggagag	840	
aatttcacta tattcaggta aataatatat aaaataaccc taagaggtaa atcttctttt	900	
tgtgtttatg atatagaata tgttgacttt accccataaa aaataacaaa tgtttttcaa	960	
cagcaaagat cttatacttg ttccaattaa taatgtgctc tcctgttggt ttccctattg	1020	
cttctaatta ggacaagtgt ttcctagaca taaataaaag gcattaaaat attctttgtt	1080	
tttttttttt tgtttgtttg tttttgtttt qtttgtttgt ttttttgaga tyaagtctcg	1140	
ctctgttgcc catgctggag tacagtggca cgatctcggc tcact9caac ctgcgcctcc	1200	
tgggttcagc cgattctctt gcctcagcct cctgagtagc tgggattaca ggcacccatc	1260	
accatgtcca gctaattttt gtatttttag tagagacagg gttttcccat gttggccagg	1320	
ctggctcga tctcctgacc tcaaatgac cgccacctc ggccctccaa agtgctggga	1380	
tgacagttgt gagccaccac actcagcctg ctctttctaa tatttgaaac ttgttagaca	1440	
atttgctacc catctaattg gatatttttag gaatccaata tgcatggttt attatttctt	1500	
aaaaaaaata ttcttttacc tgtcacctga atttagtaat gccttttatg ttacacaact	1560	
tagcactttc cagaaacaaa aactctctcc ttgaaataat agagttttta tctaccaaag	1620	
atatgctagt gtctcatttc aaaggctgct ttttccagct tacattttat atacttactc	1680	
acttgaagtt tctaaatatt cttgtaattt taaaactatc tcagatttac tgaggtttat	1740	
cttctggtgg tagattatcc ataagaagag tgatgtgcca gaatcactct gggatccttg	1800	
tctgacaaga ttcaaaggac taaatttaac tcagtcatga aactgcca ttaccgttta	1860	
tgggtagaca tctttggaaa tttccacaag gtcagacatt cgcaactatc ccttctacat	1920	
gtccacacgt atactccaac actttattag gcatctgatt agtttggaaa gtatgcctcc	1980	
atctgaatta gtccagtgtg gcttagagtt ggtacaacat tctcacagaa tttcctaatt	2040	
ttgtagyttc agcctgataa ccaactggagt tctttggtcc tcattaaata gctttcttca	2100	
cacattgctc tgctgtttac acatatgatg aacactgctt tttagacttc attaggaatt	2160	
taggactgca tcttgacaac tgagcctatt ctactatatg tacaatacct agcccataat	2220	
aggtatacaa tacacattty gtaaaactaa ttttcaacca atgacatgta tttttcaact	2280	
agtaacctag aaatgtttca cttaaaatct gagaactggt tacactacaa gttaccttg	2340	
agattcatat atgaaaacgc aaacttagct atttgattgt attcactggg acttaagaat	2400	

TABLE LIII-continued

Nucleotide sequence of transcript variant 8P1D4 v.2 (SEQ ID NO: 81)	
qcgccctgaat aattgtgagt tcgatttggt ctggcaggct aatgaccatt tccagtaaag	2460
tgaatagagg tcagaagtcg tataaaagag gtgtgtgcag aacaccgttg agattacata	2520
ggtgaacaac tttttttaag caactttatt tgtgtagtga caaagcatcc caatgcaggc	2580
tgaatgttt catcacatct ctggatctct ctattttgtg cagacattga aaaaattgtt	2640
catattattt ccatgttatt agaattttg atttttttaa aacataggcc aagttcattc	2700
acttcattat tcatttatca aatcagagt gaatcacatt agtcgccttc acaactgata	2760
aagatcactg aagtcacatt gatttttgct ataacttca atctacctat atttaattga	2820
gaatctaaaa tgtacaaatc attgtgttga ttctgcaytg atcctgctat aagtaagact	2880
cagtccttga ttttaygtat cctgtgaaaa gcagaattaa gacaaatata caagagacaa	2940
agcacaaaaa ataaatatca taaggggatg aacaaaatgg tggagaaaga gtagacaaag	3000
tttttgatca cctgccttca aagaaaggct gtgaattttg ttcacttaga cagcttgag	3060
acaagaaatt acccaaaagt aaggtgagga ggataggcaa aaagagcaga aagatgtyaa	3120
tggacattgt tgagaaatgt gataggaaaa caatcataga taaaggattt ccaagcaaca	3180
gagcatatcc agatgaggta gyatyggata aactcttatt gaaccaatct tcaccaattt	3240
tgtttttctt ttgcagagca agctaggaat tgtttccctt ctactgggca caatacacgc	3300
attgattttt gcctggaata agtgataga tataaaacaa tttgtatggt atacacctcc	3360
aacttttatg atagctgttt tccttccaat tgttgcctg atattttaa gcatactatt	3420
cctgccatgc ttgaggaaga agatactgaa gattagacat ggttgggaag acgtcaccaa	3480
aattaacaaa actgagatat gttcccagt gtagaattac tgtttacaca catttttgtt	3540
caatattgat atattttatc accaacattt caagtttgta tttgttaata aaatgattat	3600
tcaaggaaaa aaaaaaaaaa aaaaaaa	3627

[0987]

TABLE LIV

Nucleotide sequence alignment of 8P1D4v.1 (SEQ ID NO: 82) and 8P1D4 v.2 (SEQ ID NO: 83)	
Score = 1584 bits (824), Expect = 0.0Identities 826/827 (99%) Strand Plus/Plus	
8P1D4v.1: 1 ccgagactcacggtcaagctaaggcgaagagtggtggctgaagccatactatatttatag	60
8P1D4v.2: 31 ccgagactcacggtcaagctaaggcgaagagtggtggctgaagccatactatatttatag	90
8P1D4v.1: 61 aattaatggaaagcagaaaagacatcacaaaccaagaagaactttgaaaatgaagccta	120
8P1D4v.2: 91 aattaatggaaagcagaaaagacatcacaaaccaagaagaactttgaaaatgaagccta	150
8P1D4v.1: 121 ggagaaatttagaagaagacgattatattgcataaggacacgggagagaccagcatgctaa	180
8P1D4v.2: 151 ggagaaatttagaagaagacgattatattgcataaggacacgggagagaccagcatgctaa	210
8P1D4v.1: 181 aaagacctgtgcttttgcatattgcacaaacagcccatgctgatgaatttgactgcccctt	240
8P1D4v.2: 211 aaagacctgtgcttttgcatattgcacaaacagcccatgctgatgaatttgactgcccctt	270
8P1D4v.1: 241 cagaacttcagcacacacaggaactctttccacagtggcacttgccaattaaaaatagctg	300
8P1D4v.2: 271 cagaacttcagcacacacaggaactctttccacagtggcacttgccaattaaaaatagctg	330

TABLE LIV-continued

Nucleotide sequence alignment of 8P1D4v.1 (SEQ ID NO: 82) and 8P1D4 v.2 (SEQ ID NO: 83)	
<hr/>	
8P1D4v.1: 301	ctattatagcatctctgactttttctttacactcttctgagggagtaattcaccctttag 360
8P1D4v.2: 331	ctattatagcatctctgactttttctttacactcttctgagggagtaattcaccctttag 390
8P1D4v.1: 361	caacttcccatcaacaatatattttataaaaattccaatcctggtcatcaaaaagtcttgc 420
8P1D4v.2: 391	caacttcccatcaacaatatattttataaaaattccaatcctggtcatcaaaaagtcttgc 450
8P1D4v.1: 421	caatggtttccatcactctcttggcattggtttacctgccaggtgtgatagcagcaattg 480
8P1D4v.2: 451	caatggtttccatcactctcttggcattggtttacctgccaggtgtgatagcagcaattg 510
8P1D4v.1: 481	tccaacttcataatggaaccaagtataagaagtttccacattggttgataaagtggatgt 540
8P1D4v.2: 511	tccaacttcataatggaaccaagtataagaagtttccacattggttgataaagtggatgt 570
8P1D4v.1: 541	taacaagaaagcagtttgggcttctcagtttctttttgtgtactgcatgcaatttata 600
8P1D4v.2: 571	taacaagaaagcagtttgggcttctcagtttctttttgtgtactgcatgcaatttata 630
8P1D4v.1: 601	gtctgtcttacccaatgaggcgatcctacagatacaagttgctaaactgggcatatcaac 660
8P1D4v.2: 631	gtctgtcttacccaatgaggcgatcctacagatacaagttgctaaactgggcatatcaac 690
8P1D4v.1: 661	aggtccaacaaaataaagaagatgcctggattgagcatgatgtttggagaatggagattt 720
8P1D4v.2: 691	aggtccaacaaaataaagaagatgcctggattgagcatgatgtttggagaatggagattt 750
8P1D4v.1: 721	atgtgtctctgggaattgtgggattggcaatactggctctgttggctgtgacatctattc 780
8P1D4v.2: 751	atgtgtctctgggaattgtgggattggcaatactggctctgttggctgtgacatctattc 810
8P1D4v.1: 781	catctgtgagtgactctttgacatggagagaatttcactatattcag 827
8P1D4v.2: 811	catctgtgagtgactctttgacatggagagaatttcactatattcag 857
Score = 714 bits (371), Expect = 0.0Identities = 371/371 (100%)	
Strand = Plus/Plus	
Query:	825 cagagcaagctaggaattgtttcccttctactgggcacaatacacgcattgatttttggc 884
Sbjct:	3254 cagagcaagctaggaattgtttcccttctactgggcacaatacacgcattgatttttggc 3313
Query:	885 tgggaataagtgatagatataaaacaatttgatggtatcacctccaacttttatgata 944
Sbjct:	3314 tgggaataagtgatagatataaaacaatttgatggtatcacctccaacttttatgata 3373
Query:	945 gctgttttccctccaattgttgcctgatattttaaagcatactattcctgcatgcttg 1004
Sbjct:	3374 gctgttttccctccaattgttgcctgatattttaaagcatactattcctgcatgcttg 3433
Query:	1005 aggaagaagatactgaagattagacatggttggaagacgtcacaaaattaacaaaact 1064
Sbjct:	3434 aggaagaagatactgaagattagacatggttggaagacgtcacaaaattaacaaaact 3493
Query:	1065 gagatatgttcccagttgtagaattactgtttacacacattttgttcaatattgatata 1124
Sbjct:	3494 gagatatgttcccagttgtagaattactgtttacacacattttgttcaatattgatata 3553
Query:	1125 tttttatcaccaacatttcaagtttgatttgtaataaaatgattattcaaggaaaaaaa 1184
Sbjct:	3554 tttttatcaccaacatttcaagtttgatttgtaataaaatgattattcaaggaaaaaaa 3613
Query:	1185 aaaaaaaaaa 1195
Sbjct:	3614 aaaaaaaaaa 3624

[0988]

TABLE LV

Peptide sequences of protein coded by 8P1D4 v.2 (SEQ ID NO: 84)	
MESRKDITNQ EELWKMKPRR NLEEDDYLHK DTGETSMLKR PVLLHLHQTA HADEFDCPSE	60
LQHTQELFPQ WHLPKIAAI IASLTFLYTL LREVIHPLAT SHQQYFYKIP ILVINKVLPM	120
VSITLLALVY LPGVIAAIVQ LHNGTKYKKF PHWLDKWLMT RKQFGLLSFF FAVLHAIYSL	180
SYPMRRSYRY KLLNWAYQQV QQNKEDAWIE HDVWRMEIYV SLGIVGLAIL ALLAVTSIPS	240
VSDSLTWREF HYIQVNNI	258

[0989]

TABLE LVI

Amino acid sequence alignment of 8P1D4v.1 (SEQ ID NO: 85) and 8P1D4v.2 (SEQ ID NO: 86)	
Score = 521 bits (1342) , Expect = e-147Identities = 254/254 (100%), Positives = 254/254 (100%)	
8P1D4v.1: 1MESRKDITNQEELWKMKPRRNLEEDDYLHKDTGETSMLKRPVLLHLHQTAHADEFDCPSE	60
MESRKDITNQEELWKMKPRRNLEEDDYLHKDTGETSMLKRPVLLHLHQTAHADEFDCPSE	
8P1D4v.2: 1MESRKDITNQEELWKMKPRRNLEEDDYLHKDTGETSMLKRPVLLHLHQTAHADEFDCPSE	60
8P1D4v.1: 61LQHTQELFPQWHLPIKIAAIIASLTFLYTLREVIHPLATSHQQYFYKIPILVINKVLPM	120
LQHTQELFPQWHLPIKIAAIIASLTFLYTLREVIHPLATSHQQYFYKIPILVINKVLPM	
8P1D4v.2: 61LQHTQELFPQWHLPIKIAAIIASLTFLYTLREVIHPLATSHQQYFYKIPILVINKVLPM	120
8P1D4v.1: 121VSITLLALVYLPGVIAAIVQLHNGTKYKKFPHWLDKWLMTKQFGLLSFFFVAVLHAIYSL	180
VSITLLALVYLPGVIAAIVQLHNGTKYKKFPHWLDKWLMTKQFGLLSFFFVAVLHAIYSL	
8P1D4v.2: 121VSITLLALVYLPGVIAAIVQLHNGTKYKKFPHWLDKWLMTKQFGLLSFFFVAVLHAIYSL	180
8P1D4v.1: 181SYPMRRSYRYKLLNWAYQQVQQNKEDAWIEHDVWRMEIYVSLGIVGLAILALLAVTSIPS	240
SYPMRRSYRYKLLNWAYQQVQQNKEDAWIEHDVWRMEIYVSLGIVGLAILALLAVTSIPS	
8P1D4v.2: 181SYPMRRSYRYKLLNWAYQQVQQNKEDAWIEHDVWRMEIYVSLGIVGLAILALLAVTSIPS	240
8P1D4v.1: 241VSDSLTWREFHYIQ	254
VSDSLTWREFHYIQ	
8P1D4v.2: 241VSDSLTWREFHYTQ	254

[0990]

TABLE LVII

Nucleotide sequence of transcript variant 8P1D4v.3 (SEQ ID NO: 87)	
ggggcccgca cctctgggca gcagcgccag ccgagactca cggccaagct aaggcgaaga	60
gtgggtggct gaagccatac tattttatag aattaatgga aagcagaaaa gacatcacia	120
accaagaaga actttggaaa atgaagccta ggagaaattt agaagaagac gattatttgc	180
ataaggacac gggagagacc agcatgctaa aaagacctgt gcttttgcac ttgcacaaaa	240
cagcccatgc tgatgaattt gactgccctt cagaacttca gcacacacag gaactctttc	300
cacagtggca cttgccaaatt aaaatagctg ctattatagc atctctgact tttctttaca	360
ctcttctgag ggaagtaatt cacccttttag caacttccca tcaacaatat ttttataaaa	420
ttccaatcct ggtcatcaac aaagtcttgc caatggtttc catcactctc ttggcatagg	480
tttacctgcc aggtgtgata gcagcaattg tccaacttca taatggaacc aagtataaga	540
agtttccaca ttggttggat aagtggtgtg taacaagaaa gcagtttggg cttctcaytt	600

TABLE LVII-continued

Nucleotide sequence of transcript variant 8P1D4v.3 (SEQ ID NO: 87)		
tcttttttgC tgtactgcat gcaatttata gtctgtctta cccaatgagg cgatcctaca	660	
gatacaagtt gctaaactgg gcatatcaac aggtccaaca aataaaagaa gatgcctgga	720	
ttgagcatga tgtttggaga atggagattt atgtgtctct gggaaattgtg ggattggcaa	780	
tactggctct gttggctgtg acatctattc catctgtgag tgactctttg acatggagag	840	
aatttcacta tattcagatt atccataaga agagtgatgt gccagaatca ctctgggatc	900	
cttgtctgac aagattcaaa ggactaaatt taattcagtc atgaacactg ccaattaccg	960	
tttatgggta gacatctttg gaaatttcca caagagcaag ctagggaattg tttcccttct	1020	
actgggcaca atacacgcat tgatttttgc ctggaataag tggatagata taaaacaatt	1080	
tgatagggtat acacctccaa cttttatgat agctgttttc cttccaattg ttgtcctgat	1140	
atttaaaagc atactattcc tgccatgctt gaggaagaag atactgaaga ttagacatgg	1200	
ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tcccagttgt agaattactg	1260	
tttacacaca tttttgttca atattgatat attttatcac caacatttca agtttgtatt	1320	
tgtaataaaa atgattattc aaggaaaaaa aaaaaaaaaa aaaaa	1365	

[0991]

TABLE LVIII

Nucleotide sequence alignment of 8P1D4v.2 (SEQ ID NO: 88) and 8P1D4v.3 (SEQ ID NO: 89)		
Score = 1642 bits (854), Expect 0.0Identities = 856/857 (99%) Strand Plus/Plus		
8P1D4v.2:	1	ggggcccgcacctctgggcagcagcgccgagactcagggtcaagctaaggcgaaga 60
8P1D4v.3:	1	ggggcccgcacctctgggcagcagcgccgagactcagggtcaagctgaggcgaaga 60
8P1D4v.2:	61	gtgggtggctgaagccatactattttatagaattaatggaaagcagaaaagacatcaca 120
8P1D4v.3:	61	gtgggtggctgaagccatactattttatagaattaatggaaagcagaaaagacatcaca 120
8P1D4v.2:	121	accaagaagaactttgaaaatgaagcctaggagaaatttagaagaagacgattatttgc 180
8P1D4v.3:	121	accaagaagaactttgaaaatgaagcctaggagaaatttagaagaagacgattatttgc 180
8P1D4v.2:	181	ataaggacacgggagagaccagcatgctaaaaagacctgtgcttttgcatttgcacaaa 240
8P1D4v.3:	181	ataaggacacgggagagaccagcatgctaaaaagacctgtgcttttgcatttgcacaaa 240
8P1D4v.2:	241	cagcccatgctgatgaatttgactgccccttcagaacttcagcacacacaggaactctttc 300
8P1D4v.3:	241	cagcccatgctgatgaatttgactgccccttcagaacttcagcacacacaggaactctttc 300
8P1D4v.2:	301	cacagtggcacttgccaattaaaatagctgctattatagcatctctgacttttctttaca 360
8P1D4v.3:	301	cacagtggcacttgccaattaaaatagctgctattatagcatctctgacttttctttaca 360
8P1D4v.2:	361	ctctctctgagggaagtaattcacccttagcaacttcccatcaacaatatttttataaaa 420
8P1D4v.3:	361	ctctctctgagggaagtaattcacccttagcaacttcccatcaacaatatttttataaaa 420
8P1D4v.2:	421	ttccaatcctggtcatcaacaaagtcttgccaatggtttccatcactctcttggcatttg 480
8P1D4v.3:	421	ttccaatcctggtcatcaacaaagtcttgccaatggtttccatcactctcttggcatttg 480
8P1D4v.2:	481	tttacctgccaggtgtgatagcagcaattgtccaacttcataatggaaccaagtataaga 540
8P1D4v.3:	481	tttacctgccaggtgtgatagcagcaattgtccaacttcataatggaaccaagtataaga 540

TABLE LVIII-continued

		Nucleotide sequence alignment of 8P1D4v.2 (SEQ ID NO: 88) and 8P1D4v.3 (SEQ ID NO: 89)	
8P1D4v.2:	541	agtttccacattggttgataagtggatgtaacaagaaagcagtttgggcttctcagtt	600
8P1D4v.3:	541	agtttccacattggttgataagtggatgtaacaagaaagcagtttgggcttctcagtt	600
8P1D4v.2:	601	tcttttttgcgtgactgcatgcaatttatagctgtcttacccaatgagcgatcctaca	660
8P1D4v.3:	601	tcttttttgcgtgactgcatgcaatttatagctgtcttacccaatgagcgatcctaca	660
8P1D4v.2:	661	gatacaagttgctaaactgggcatatcaacaggtccaacaaaataaagaagatgcctgga	720
8P1D4v.3:	661	gatacaagttgctaaactgggcatatcaacaggtccaacaaaataaagaagatgcctgga	720
8P1D4v.2:	721	ttgagcatgatgttttgagaatggagatttatgtgtctctgggaattgtgggattggcaa	780
8P1D4v.3:	721	ttgagcatgatgttttgagaatggagatttatgtgtctctgggaattgtgggattggcaa	780
8P1D4v.2:	781	tactggctctgttggctgtgacatctattccatctgtgagtgactctttgacatggagag	840
8P1D4v.3:	781	tactggctctgttggctgtgacatctattccatctgtgagtgactctttgacatggagag	840
8P1D4v.2:	841	aatttcactatattcag	857
8P1D4v.3:	841	aatttcactatattcag	857
Score 267 bits (139), Expect = 2e-68Identities = 139/139 (100%)			
Strand = Plus/Plus			
8P1D4v.2:	1752	agattatccataagaagagtgtgtgccagaatcactctgggaccttctgtgacaagat	1811
8P1D4v.3:	856	agattatccataagaagagtgtgtgccagaatcactctgggaccttctgtgacaagat	915
8P1D4v.2:	1812	tcaaaggactaaatttaattcagtcataaacactgccaaattaccgtttatgggtagacat	1871
8P1D4v.3:	916	tcaaaggactaaatttaattcagtcataaacactgccaaattaccgtttatgggtagacat	975
8P1D4v.2:	1872	ctttggaaatttcacaaag	1890
8P1D4v.3:	976	ctttggaaatttcacaaag	994
Score = 717 bits (373), Expect = 0.0Identities = 373/373 (100%)			
Strand = Plus/Plus			
8P1D4v.2:	3255	agagcaagctaggaattgtttcccttctactgggcacacacgcattgatttttgcct	3314
8P1D4v.3:	993	agagcaagctaggaattgtttcccttctactgggcacacacgcattgatttttgcct	1052
8P1D4v.2:	3315	ggaataagtggatagatataaaacaatttgatgtgtatatacacctccaacttttatgatag	3374
8P1D4v.3:	1053	ggaataagtggatagatataaaacaatttgatgtgtatatacacctccaacttttatgatag	1112
8P1D4v.2:	3375	ctgttttccctccaattgtgtcctgatattttaaagcatactattcctgccatgcttga	3434
8P1D4v.3:	1113	ctgttttccctccaattgtgtcctgatattttaaagcatactattcctgccatgcttga	1172
8P1D4v.2:	3435	ggaagaagatactgaagatttagacatggttgggaagacgtcaccaaaattaacaaaactg	3494
8P1D4v.3:	1173	ggaagaagatactgaagatttagacatggttgggaagacgtcaccaaaattaacaaaactg	1232
8P1D4v.2:	3495	agatatgttcccagttgtagaattactgtttacacacattttgttcaatattgatatat	3554
8P1D4v.3:	1233	agatatgttcccagttgtagaattactgtttacacacattttgttcaatattgatatat	1292
8P1D4v.2:	3555	tttatcaccaacatttcaagtttgtatttgttaataaaatgattattcaaggaaaaaaa	3614
8P1D4v.3:	1293	tttatcaccaacatttcaagtttgtatttgttaataaaatgattattcaaggaaaaaaa	1352
8P1D4v.2:	3615	aaaaaaaaaaaaa	3627
8P1D4v.3:	1353	aaaaaaaaaaaaa	1365

[0992]

TABLE LIX

Peptide sequences of protein coded by 8P1D4 v.3 (SEQ ID NO: 90)	
MESRKDITNQ EELWKMKPRR NLEEDDYLhK DTGETSMLKR PVLLHLHQTA HADEFDCPSE	60
LQHTQELFPQ WhLPKIAAI IASLTFLYTL LREVIHPLAT SHQQYFYKIP ILVINKVLPM	120
VSITLLALVY LPGVIAAIVQ LHNGTKYKKF PHWLDKWLMT RKQFGLLSFF FAVKHAIYSL	180
SYPMRRSYRY KLLNWAYQQV QQNKEDAWIE HDVWRMEIYV SLGIVGLAIL ALLAVTSIPS	240
VSDSLTWREF HYIQIIHKKS DVPESLWDPC LTRFKGLNLI QS	282

[0993]

TABLE LX

Amino acid sequence alignment of 8P1D4 v.2 (SEQ ID NO: 91) and 8P1D4 v.3 (SEQ ID NO: 92)	
Score = 522 bits (1345), Expect = e-147Identities 254/255 (99%), Positives = 255/255 (99%)	
8P1D4v.2: 1MESRKDITNQEELWKMKPRRNLEEDDYLHKDTGETSMLKRPVLLHLHQTAHADEFDCPSE	60
MESRKDITNQEELWKMKPRRNLEEDDYLHKDTGETSMLKRPVLLHLHQTAHADEFDCPSE	
8P1D4v.3: 1MESRKDITNQEELWKMKPRRNLEEDDYLHKDTGETSMLKRPVLLHLHQTAHADEFDCPSE	60
8P1D4v.2: 61LQHTQELFPQWHLPIKIAAIIASLTFLYTLREVIHPLATSHQQYFYKIPILVINKVLPM	120
LQHTQELFPQWHLPIKIAAIIASLTFLYTLREVIHPLATSHQQYFYKIPILVINKVLPM	
8P1D4v.3: 61LQHTQELFPQWHLPIKIAAIIASLTFLYTLREVIHPLATSHQQYFYKIPILVINKVLPM	120
8P1D4v.2: 121VSITLLALVYLPGVIAAIVQLHNGTKYKKFPHWLDKWLMTRKQFGLLSFFFVAVLHAIYSL	180
VSITLLALVYLPGVIAAIVQLHNGTKYKKFPHWLDKWLMTRKQFGLLSFFFVAVLHAIYSL	
8P1D4v.3: 121VSITLLALVYLPGVIAAIVQLHNGTKYKKFPHWLDKWLMTRKQFGLLSFFFVAVLHAIYSL	180
8P1D4v.2: 181SYPMRRSYRYKLLNWAYQQVQQNKEDAWIEHDVWRMEIYVSLGIVGLAILALLAVTSIPS	240
SYPMRRSYRYKLLNWAYQQVQQNKEDAWIEHDVWRMEIYVSLGIVGLAILALLAVTSIPS	
8P1D4v.3: 181SYPMRRSYRYKLLNWAYQQVQQNKEDAWIEHDVWRMEIYVSLGIVGLAILALLAVTSIPS	240
8P104v.2: 241VSDSLTWREFHYIQV 255	
VSDSLTWREFHYIQ+	
8P1D4v.3: 241VSDSLTWREFHYIQI 255	

[0994]

TABLE LXI

SEARCH Peptides	
STEAP 1 Variant 1	
nonamers, decamers and 15-mers: aa 1-339 (SEQ ID NO: 71)	
MESRKDITNQ EELWKMKPRR NLEEDDYLhK DTGETSMLKR PVLLHLHQTA HADEFDCPSE	60
LQHTQELFPQ WHLPIKIAAI IASLTFLYTL LREVIHPLAT SHQQYFYKIP ILVINKVLPM	120
VSITLLALVY LPGVIAAIVQ LHNGTKYKKF PHWLDKWLMT RKQFGLLSFF FAVLHAIYSL	180
SYPMRRSYRY KLLNWAYQQV QQNKEDAWIE HDVWRMEIYV SLGIVGLAIL ALLAVTSIPS	240
VSDSLTWREF HYJQSKLGIV SLLGTIHAL IFAWNKWIDI KQFVWYTPPT FMJAVFLPIV	300
VLIFKSILFL PCLRRKILKI RHGWEDVTKI NKTEICSQL	339
Variant 2:	
9-mers aa 247-258 (SEQ ID NO: 72)	
WREFHYIQVNNI	
10-mers aa 246-258 (SEQ ID NO: 73)	
TWREFHYIQVNNJ	
15-mers aa 241-258 (SEQ ID NO: 74)	
VSDSLTWREFHYIQVNNI	
Variant 3:	
9-mers aa 247- (SEQ ID NO: 75)	
WREFHYIQIIHKKSDVPESLWDPCLTRFKGLNLIQS	

TABLE LXI-continued

SEARCH Peptides

10-mers aa 246- (SEQ ID NO: 76)
 TWREFHYIQIIHKKSDVPESLWDPCLTRFKGLNLIQS
 15-mers aa 241- (SEQ ID NO: 77)
 VSDSLTWREFHYIQIIHKKSDVPESLWDPCLTRFKGLNLIQS

Variant 4:

9-mers aa 160-176 (SEQ ID NO: 78)
 RKQFCLLSLFFAVLHAI
 10-mers aa 159-177 (SEQ ID NO: 79)
 TRKQFGLLSLFFAVLHAIY
 15-mers aa 154-182 (SEQ ID NO: 80)
 DKWMLTRKQFGLLSLFFAVLHAIYSLSP

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 100

<210> SEQ ID NO 1

<211> LENGTH: 436

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 1

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accaatgtgg aaacttctta tacttggttc cattatgaag ttggacaatt gctgctatca      120
cacctggcag gtaaaccaat gccaagagag tgatggaaac cattggcaag actttgttga      180
tgaccaggat tggaatttta taaaaatatt gttgatggga agttgctaaa ggggaatta      240
cttccctcag aagagtgtaa agaaaagtca gagatgctat aatagcagct attttaattg      300
gcaagtgcc ctgtggaaa agttcctgtg tgtgctgaag ttctgaaggg cagtcaaatt      360
catcagcatg ggctatttgg tgcaaatgca aaagcacagg tctttttagc atgctggtct      420
ctcccggtgc cttatg                                     436
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<210> SEQ ID NO 2

<211> LENGTH: 1193

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (66)...(1085)

<400> SEQUENCE: 2

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aatta atg gaa agc aga aaa gac atc aca aac caa gaa gaa ctt tgg aaa      110
      Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Leu Trp Lys
        1             5             10             15
atg aag cct agg aga aat tta gaa gaa gac gat tat ttg cat aag gac      158
      Met Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp
        20             25             30
acg gga gag acc agc atg cta aaa aga cct gtg ctt ttg cat ttg cac      206
      Thr Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His
        35             40             45
caa aca gcc cat gct gat gaa ttt gac tgc cct tca gaa ctt cag cac      254
      Gln Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His
        50             55             60
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aca cag gaa ctc ttt cca cag tgg cac ttg cca att aaa ata gct gct Thr Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala 65 70 75	302
att ata gca tct ctg act ttt ctt tac act ctt ctg agg gaa gta att Ile Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile 80 85 90 95	350
cac cct tta gca act tcc cat caa caa tat ttt tat aaa att cca atc His Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile 100 105 110	398
ctg gtc atc aac aaa gtc ttg cca atg gtt tcc atc act ctc ttg gca Leu Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala 115 120 125	446
ttg gtt tac ctg cca ggt gtg ata gca gca att gtc caa ctt cat aat Leu Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn 130 135 140	494
gga acc aag tat aag aag ttt cca cat tgg ttg gat aag tgg atg tta Gly Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu 145 150 155	542
aca aga aag cag ttt ggg ctt ctc agt ttc ttt ttt gct gta ctg cat Thr Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His 160 165 170 175	590
gca att tat agt ctg tct tac cca atg agg cga tcc tac aga tac aag Ala Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys 180 185 190	638
ttg cta aac tgg gca tat caa cag gtc caa caa aat aaa gaa gat gcc Leu Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala 195 200 205	686
tgg att gag cat gat gtt tgg aga atg gag att tat gtg tct ctg gga Trp Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly 210 215 220	734
att gtg gga ttg gca ata ctg gct ctg ttg gct gtg aca tct att cca Ile Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro 225 230 235	782
tct gtg agt gac tct ttg aca tgg aga gaa ttt cac tat att cag agc Ser Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser 240 245 250 255	830
aag cta gga att gtt tcc ctt cta ctg ggc aca ata cac gca ttg att Lys Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile 260 265 270	878
ttt gcc tgg aat aag tgg ata gat ata aaa caa ttt gta tgg tat aca Phe Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr 275 280 285	926
cct cca act ttt atg ata gct gtt ttc ctt cca att gtt gtc ctg ata Pro Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile 290 295 300	974
ttt aaa agc ata cta ttc ctg cca tgc ttg agg aag aag ata ctg aag Phe Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys 305 310 315	1022
att aga cat ggt tgg gaa gac gtc acc aaa att aac aaa act gag ata Ile Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile 320 325 330 335	1070
tgt tcc cag ttg tag aattactgtt tacacacatt tttgttcaat attgatatat Cys Ser Gln Leu *	1125
tttatcacca acatttcaag tttgtatttg ttaataaaat gattacaagg aaaaaaaaaa	1185
aaaaaaaaa	1193

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<210> SEQ ID NO 3
<211> LENGTH: 339
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1             5             10             15

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
      20             25             30

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
      35             40             45

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
 50             55             60

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
65             70             75             80

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
      85             90             95

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
      100            105            110

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
      115            120            125

Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
      130            135            140

Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
      145            150            155            160

Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
      165            170            175

Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
      180            185            190

Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
      195            200            205

Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
      210            215            220

Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
      225            230            235            240

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys
      245            250            255

Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe
      260            265            270

Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro
      275            280            285

Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe
      290            295            300

Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile
      305            310            315            320

Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile Cys
      325            330            335

Ser Gln Leu

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<210> SEQ ID NO 4
<211> LENGTH: 3627

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<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (96)...(872)

<400> SEQUENCE: 4

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gtgggtggct gaagccatac tattttatag aatta atg gaa agc aga aaa gac      113
                               Met Glu Ser Arg Lys Asp
                               1           5

atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta      161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu
                               10           15           20

gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta      209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu
                               25           30           35

aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa      257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu
                               40           45           50

ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag      305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln
                               55           60           65           70

tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt      353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe
                               75           80           85

ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat      401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His
                               90           95           100

caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg      449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu
                               105           110           115

cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg      497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val
                               120           125           130

ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt      545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe
                               135           140           145           150

cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt      593
Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu
                               155           160           165

ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac      641
Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr
                               170           175           180

cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa      689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln
                               185           190           195

cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg      737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp
                               200           205           210

aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg      785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu
                               215           220           225           230

gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca      833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr
                               235           240           245

tgg aga gaa ttt cac tat att cag gta aat aat ata taa aataacccta      882
Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *
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250	255	
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ataacaaatg	tttttcaaca	gcaaagatct tatacttggt ccaattaata atgtgctctc 1002
ctgttggttt	ccctattgct	tctaattagg acaagtgttt cctagacata aataaaaggc 1062
attaaaaat	tctttgtttt	tttttttttg tttgtttgtt ttttgtttgt ttgtttgttt 1122
ttttgagatg	aagtctcgct	ctgttgccca tgctggagta cagtggcacg atctcggtc 1182
actgcaacct	gcgcctcctg	ggttcaggcg attctcttgc ctcagcctcc tgagtagctg 1242
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cctcccaaa	tgctgggatg	acagttgtga gccaccacac tcagcctgct ctttctaata 1422
tttgaaactt	gtagacaat	ttgctacca tctaattgta tatttttagga atccaatatg 1482
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cattttatat	acttactcac	ttgaagtttc taaatattct tgtaatttta aaactatctc 1722
agatttactg	aggtttatct	tctggtggta gattatccat aagaagagtg atgtgccaga 1782
atcactctgg	gatccttgct	tgacaagatt caaaggacta aatttaattc agtcatgaac 1842
actgccaatt	accgtttatg	ggtagacatc tttggaaatt tccacaaggc cagacattcg 1902
caactatccc	ttctacatgt	ccacacgtat actccaacac tttattaggc atctgattag 1962
tttgaaaagt	atgcctccat	ctgaattagt ccagtgtggc ttagagtggg tacaacattc 2022
tcacagaatt	tcctaatttt	gtaggttcag cctgataacc actggagtgc tttgggtctc 2082
attaaatagc	tttcttcaca	cattgctctg cctgttacac atatgatgaa cactgctttt 2142
tagacttcat	taggaattta	ggactgcacg ttgacaactg agcctattct actatatgta 2202
caatacctag	ccataaatag	gtatacaata cacatttggt aaaactaatt ttcaaccaat 2262
gacatgtatt	tttcaactag	taacctagaa atgtttcact taaaatctga gaactggtta 2322
cactacaagt	taccttgag	attcatatat gaaaacgcaa acttagctat ttgattgtat 2382
tcactgggac	ttaagaatgc	gcctgaataa ttgtgagttc gatttgttct ggcaggctaa 2442
tgaccatttc	cagtaaagt	aatagaggtc agaagtcgta taaaagaggc gttgtcagaa 2502
caccgttgag	attacatag	tgaacaacta tttttaagca actttatttg tgtagtgaca 2562
aagcatccca	atgcaggctg	aaatgtttca tcacatctct ggatctctct attttgtgca 2622
gacattgaaa	aaattgttca	tattatttcc atgttatcag aatatttgat tttttaaaaa 2682
cataggccaa	gttcattcac	ttcattattc atttatcaa atcagagtga atcacattag 2742
tcgccttcac	aactgataaa	gatcactgaa gtcaaattga tttttgctat aatcttcaat 2802
ctacctatat	ttaattgaga	atctaaaatg tacaatcat tgtgttgatt ctgcagtgat 2862
cctgctataa	gtaagactca	gtccctgatt ttaggtatcc tgtgaaaagc agaattaaga 2922
caaatacaca	agagacaaa	gacaaaaaat aaatatcata aggggatgaa caaaatggtg 2982
gagaagagt	agacaaagt	tttgatcacc tgccttcaaa gaaaggctgt gaattttgtt 3042
cacttagaca	gcttgagag	aagaaattac ccaaaagtaa ggtgaggagg ataggcaaaa 3102

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agagcagaaa gatgtgaatg gacattgttg agaaatgtga taggaaaaca atcatagata 3162
aaggatttcc aagcaacaga gcatatccag atgaggtagg atgggataaa ctcttattga 3222
accaatcttc accaattttg tttttctttt gcagagcaag ctaggaattg tttcccttct 3282
actgggcaca atacacgcat tgatttttgc ctggaataag tggatagata taaacaatt 3342
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ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tcccagttgt agaattactg 3522
tttacacaca tttttgttca atattgatat attttatcac caacatttca agtttgtatt 3582
tgtaataaaa atgattattc aaggaaaaaa aaaaaaaaaa aaaaa 3627

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<210> SEQ ID NO 5

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 5

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Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
          20             25             30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
          35             40             45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
          50             55             60
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
          65             70             75             80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
          85             90             95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
          100            105            110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
          115            120            125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
          130            135            140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
          145            150            155            160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
          165            170            175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
          180            185            190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
          195            200            205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
          210            215            220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
          225            230            235            240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn
          245            250            255
Asn Ile

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<210> SEQ ID NO 6																				
<211> LENGTH: 1365																				
<212> TYPE: DNA																				
<213> ORGANISM: Homo sapiens																				
<220> FEATURE:																				
<221> NAME/KEY: CDS																				
<222> LOCATION: (96)...(944)																				
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gtgggtggct gaagccatac tattttatag aatta atg gaa agc aga aaa gac																				113
Met Glu Ser Arg Lys Asp																				
1 5																				
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta																				161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu																				
10 15 20																				
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta																				209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu																				
25 30 35																				
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa																				257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu																				
40 45 50																				
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag																				305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln																				
55 60 65 70																				
tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt																				353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe																				
75 80 85																				
ctt tac act ctt ctg agg gaa gta att cac cct tta gca act tcc cat																				401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His																				
90 95 100																				
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg																				449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu																				
105 110 115																				
cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg																				497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val																				
120 125 130																				
ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt																				545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe																				
135 140 145 150																				
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt																				593
Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu																				
155 160 165																				
ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac																				641
Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr																				
170 175 180																				
cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa																				689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln																				
185 190 195																				
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg																				737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp																				
200 205 210																				
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg																				785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu																				
215 220 225 230																				
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca																				833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr																				
235 240 245																				

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tgg aga gaa ttt cac tat att cag att atc cat aag aag agt gat gtg      881
Trp Arg Glu Phe His Tyr Ile Gln Ile Ile His Lys Lys Ser Asp Val
      250                      255                      260

cca gaa tca ctc tgg gat cct tgt ctg aca aga ttc aaa gga cta aat      929
Pro Glu Ser Leu Trp Asp Pro Cys Leu Thr Arg Phe Lys Gly Leu Asn
      265                      270                      275

tta att cag tca tga acactgccaa ttaccgttta tgggtagaca tctttggaaa      984
Leu Ile Gln Ser *
      280

tttcacaag agcaagctag gaattgtttc ccttctactg ggcacaatac acgcattgat    1044
ttttgcctgg aataagtgga tagatataaa acaatttgta tgggtatacac ctccaacttt    1104
tatgatagct gttttccttc caattgttgt cctgatattt aaaagcatac tattcctgcc    1164
atgcttgagg aagaagatac tgaagattag acatgggttg gaagacgtca ccaaaattaa    1224
caaaactgag atatgttccc agttgtagaa ttactgttta cacacatttt tgttcaatat    1284
tgatatattt tatcaccaac atttcaagtt tgtatttggt aataaaatga ttattcaagg    1344
aaaaaaaaa aaaaaaaaaa a                                             1365

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<210> SEQ ID NO 7
<211> LENGTH: 282
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 7

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
  1              5              10              15

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
      20              25              30

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
      35              40              45

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
      50              55              60

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
      65              70              75              80

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
      85              90              95

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
      100             105             110

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
      115             120             125

Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
      130             135             140

Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
      145             150             155             160

Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
      165             170             175

Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
      180             185             190

Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
      195             200             205

Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
      210             215             220

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Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
225                230                235                240

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ile Ile
                245                250                255

His Lys Lys Ser Asp Val Pro Glu Ser Leu Trp Asp Pro Cys Leu Thr
                260                265                270

Arg Phe Lys Gly Leu Asn Leu Ile Gln Ser
                275                280

<210> SEQ ID NO 8
<211> LENGTH: 3627
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (96)...(872)

<400> SEQUENCE: 8

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gtgggtggct gaagccatac tattttatag aatta atg gaa agc aga aaa gac      113
                               Met Glu Ser Arg Lys Asp
                               1                5

atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta      161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu
                10                15                20

gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta      209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu
                25                30                35

aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa      257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu
                40                45                50

ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag      305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln
                55                60                65                70

tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt      353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe
                75                80                85

ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat      401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His
                90                95                100

caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg      449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu
                105                110                115

cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg      497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val
                120                125                130

ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt      545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe
                135                140                145                150

cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt      593
Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu
                155                160                165

ctc agt ttg ttt ttt gct gta ctg cat gca att tat agt ctg tct tac      641
Leu Ser Leu Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr
                170                175                180

cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa      689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln

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-continued

185	190	195	
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg			737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp			
200	205	210	
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg			785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu			
215	220	225	230
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca			833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr			
235	240	245	
tggaaga gaa ttt cac tat att cag gta aat aat ata taa aataacccta			882
Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *			
250	255		
agaggtaaat cttctttttg tgtttatgat atagaatatg ttgactttac ccataaaaa			942
ataacaaatg tttttcaaca gcaaagatct tatacttggt ccaattaata atgtgctctc			1002
ctgttgtttt ccctattgct tctaattagg acaagtgttt cctagacata aataaaaggc			1062
attaaaaatat tctttgtttt tttttttttg tttgtttgtt tttgtttgt ttgtttgttt			1122
ttttgagatg aagtctcgct ctgttgccca tgctggagta cagtggcacg atctcggctc			1182
actgcaacct gcgcctcctg ggttcaggcg attctcttgc ctgagcctcc tgagtagctg			1242
ggattacagg caccatcac catgtccagc taatttttgt atttttagta gagacaggt			1302
tttcccatgt tggccaggct ggtctcgatc tctgacctc aaatgatccg ccacctcgg			1362
cctcccaaag tgctgggatg acagtgtga gccaccacac tcagcctgct ctttctaata			1422
tttgaaactt gttagacaat ttgctaccca tctaattgtga tatttttagga atccaatatg			1482
catggtttat tatttcttaa aaaaaatatt cttttacctg tcacctgaat ttagtaatgc			1542
cttttatggt acacaactta gcactttcca gaaacaaaa ctctctcctt gaaataatag			1602
agtttttatc taccaaagat atgctagtgt ctcatctcaa aggtgctttt ttccagctta			1662
cattttatat acttactcac ttgaagtctc taaatattct tgtaatttta aaactatctc			1722
agatttactg aggtttatct tctggtgga gattatccat aagaagagtg atgtgccaga			1782
atcactctgg gatcctgtgc tgacaagatt caaaggacta aatttaattc agtcatgaac			1842
actgccaatt accgtttatg ggtagacatc tttggaaatt tccacaaggc cagacattcg			1902
caactatccc ttctacatgt ccacacgtat actccaacac tttattaggc atctgattag			1962
tttgaaagt atgcctccat ctgaattagt ccagtgtggc ttagagttgg tacaacattc			2022
tcacagaatt tcctaatttt gtaggttcag cctgataacc actggagtgc tttggctctc			2082
attaaatagc tttcttcaca cattgctctg cctgttacac atatgatgaa cactgctttt			2142
tagacttcat taggaattta ggactgcac ttgacaactg agcctattct actatatgta			2202
caatacctag ccataaatag gtatacaata cacatttggt aaaactaatt ttcaaccaat			2262
gacatgtatt tttcaactag taacctagaa atgttttact taaaatctga gaactggtta			2322
cactacaagt taccttgag attcatatat gaaaacgcaa acttagctat ttgattgtat			2382
tcactgggac ttaagaatgc gcctgaataa ttgtgagttc gatttgttct ggcaggctaa			2442
tgaccatttc cagtaaatg aatagaggtc agaagtcgta taaaagaggc gttgtcagaa			2502
caccgttgag attacatagg tgaacaacta tttttaagca actttatttg ttagtgaca			2562
aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca			2622

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gacattgaaa aaattgttca tattatttcc atgttatcag aatatttgat tttttaaaaa 2682
cataggccaa gttcattcac ttcattattc atttatcaaa atcagagtga atcacattag 2742
tcgccttcac aactgataaa gatcactgaa gtcaaattga tttttgctat aatcttcaat 2802
ctacctatat ttaattgaga atctaaaatg tacaaatcat tgtgttgatt ctgcagtgat 2862
cctgctataa gtaagactca gtccctgatt ttaggtatcc tgtgaaaagc agaattaaga 2922
caaatacaca agagacaaag cacaaaaaat aaatatcata aggggatgaa caaaatgggtg 2982
gagaaagagt agacaaagtt tttgatcacc tgccttcaaa gaaaggctgt gaattttgtt 3042
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aaggatttcc aagcaacaga gcatatccag atgaggtagg atgggataaa ctcttattga 3222
accaatcttc accaattttg tttttctttt gcagagcaag ctagggaattg tttcccttct 3282
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ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tcccagttgt agaattactg 3522
tttacacaca tttttgttca atattgatat attttatcac caacatttca agtttgtatt 3582
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<210> SEQ ID NO 9

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 9

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1             5             10             15

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
      20             25             30

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
      35             40             45

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
      50             55             60

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
      65             70             75             80

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
      85             90             95

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
      100            105            110

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
      115            120            125

Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
      130            135            140

Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
      145            150            155            160

Arg Lys Gln Phe Gly Leu Leu Ser Leu Phe Phe Ala Val Leu His Ala
      165            170            175

Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu

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180	185	190	
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp			
195	200	205	
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile			
210	215	220	
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser			
225	230	235	240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn			
245	250	255	
Asn Ile			
<210> SEQ ID NO 10			
<211> LENGTH: 3627			
<212> TYPE: DNA			
<213> ORGANISM: Homo sapiens			
<220> FEATURE:			
<221> NAME/KEY: CDS			
<222> LOCATION: (96)...(872)			
<400> SEQUENCE: 10			
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gtgggtggct gaagccatac tattttatag aatta atg gaa agc aga aaa gac			113
Met Glu Ser Arg Lys Asp			
1 5			
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta			161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu			
10 15 20			
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta			209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu			
25 30 35			
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa			257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu			
40 45 50			
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag			305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln			
55 60 65 70			
tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt			353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe			
75 80 85			
ctt tac act ctt ctg agg gaa gta att cac cct tta gca act tcc cat			401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His			
90 95 100			
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg			449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu			
105 110 115			
cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg			497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val			
120 125 130			
ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt			545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe			
135 140 145 150			
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt			593
Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu			
155 160 165			
ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac			641
Leu Ser Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr			
170 175 180			

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cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa	689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln	
185 190 195	
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg	737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp	
200 205 210	
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg	785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu	
215 220 225 230	
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca	833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr	
235 240 245	
tggaaga gaa ttt cac tat att cag gta aat aat ata taa aataacccta	882
Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *	
250 255	
agaggtaaat cttcttttttg tgtttatgat atagaatatg ttgactttac cccataaaaa	942
ataacaaatg tttttcaaca gcaaagatct tatacttggtt ccaattaata atgtgctctc	1002
ctgttgtttt ccctattgct tctaattagg acaagtgttt cctagacata aataaaaggc	1062
attaaaaatat tctttgtttt tttttttttg tttgtttgtt tttgtttgtt ttgtttgttt	1122
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ggattacagg caccatcac catgtccagc taatttttgt atttttagta gagacaggt	1302
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caactatccc ttctacatgt ccacacgtat actccaacac tttattaggc atctgattag	1962
tttgaaagt atgcctccat ctgaattagt ccagtgtggc ttagagttgg tacaacattc	2022
tcacagaatt tcctaatttt gtaggttcag cctgataacc actggagttc tttggtcctc	2082
attaaatagc tttcttcaca cattgctctg cctgttacac atatgatgaa cactgctttt	2142
tagacttcat taggaattta ggactgcac ttgacaactg agcctattct actatatgta	2202
caatacctag cccataatag gtatacaata cacatttggt aaaactaatt ttcaaccaat	2262
gacatgtatt tttcaactag taacctagaa atgtttcact taaaatctga gaactggtta	2322
cactacaagt taccttgag attcatatat gaaaacgcaa acttagctat ttgattgtat	2382
tcactgggac ttaagaatgc gcctgaataa ttgtgagttc gatttgttct ggcaggctaa	2442
tgaccatttc cagtaaaagt aatagaggtc agaagtcgta taaaagaggt gttgtcagaa	2502
caccgttgag attacatagg tgaacaacta tttttaagca actttatttg ttagtgaca	2562

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aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca 2622
gacattgaaa aaattgttca tattatttcc atgttatcag aatatttgat tttttaaaaa 2682
cataggccaa gttcattcac ttcattattc atttatcaaa atcagagtga atcacattag 2742
tcgccttcac aactgataaa gatcactgaa gtcaaattga tttttgctat aatcttcaat 2802
ctacctatat ttaattgaga atctaaaatg tacaaatcat tgtgttgatt ctgcagtgat 2862
cctgctataa gtaagactca gtccctgatt ttaggtatcc tgtgaaaagc agaattaaga 2922
caaatacaca agagacaaag cacaaaaaat aaatatcata aggggatgaa caaaatgggtg 2982
gagaaagagt agacaaagtt tttgatcacc tgccttcaaa gaaaggctgt gaattttgtt 3042
cacttagaca gcttggagac aagaaattac ccaaaagtaa ggtgaggagg ataggcaaaa 3102
agagcagaaa gatgtgaatg gacattgttg agaaatgtga taggaaaaca atcatagata 3162
aaggatttcc aagcaacaga gcatatccag atgaggtagg atgggataaa ctcttattga 3222
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<210> SEQ ID NO 11

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 11

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Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
          20             25             30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
          35             40             45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
          50             55             60
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
          65             70             75             80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
          85             90             95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
          100            105            110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
          115            120            125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
          130            135            140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
          145            150            155            160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala

```

[illegible]

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ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac	641
Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr	
170 175 180	
cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa	689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln	
185 190 195	
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg	737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp	
200 205 210	
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg	785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu	
215 220 225 230	
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca	833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr	
235 240 245	
tggaaga gaa ttt cac tat att cag gta aat aat ata taa aataacccta	882
Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *	
250 255	
agaggtaaat cttcttttttg tgtttatgat atagaatatg ttgactttac cccataaaaa	942
ataacaaatg tttttcaaca gcaaagatct tatacttggtt ccaattaata atgtgctctc	1002
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attaaaaatat tctttgtttt ttttgttttg tttgtttgtt ttttgtttgt ttgtttgttt	1122
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ggattacagg caccatcac catgtccagc taatttttgt atttttagta gagacaggg	1302
tttcccatgt tggccaggct ggtctcgatc tctgacctc aaatgatccg cccacctcgg	1362
cctcccaaag tgctgggatg acagttgtga gccaccacac tcagcctgct ctttctaata	1422
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caactatccc ttctacatgt ccacacgtat actccaacac tttattaggc atctgattag	1962
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tcactgggac ttaagaatgc gcctgaataa ttgtgagttc gatttgttct ggcaggctaa	2442

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caccgttgag attacatagg tgaacaacta tttttaagca actttatttg ttagtgaca	2562
aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca	2622
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ctacctatat ttaattgaga atctaaaatg tacaaatcat tgtgttgatt ctgcagtgat	2862
cctgctataa gtaagactca gtccctgatt ttaggtatcc tgtgaaaagc agaattaaga	2922
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<210> SEQ ID NO 13

<211> LENGTH: 258

<212> TYPE: PR

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 13

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Lys	Pro	Arg	Arg	Asn	Leu	Glu	Glu	Asp	Asp	Tyr	Leu	His	Lys	Asp	Thr
			20					25					30		

Gly	Glu	Thr	Ser	Met	Leu	Lys	Arg	Pro	Val	Leu	Leu	His	Leu	His	Gln
		35				40						45			

Thr	Ala	His	Ala	Asp	Glu	Phe	Asp	Cys	Pro	Ser	Glu	Leu	Gln	His	Thr
	50					55					60				

Gln	Glu	Leu	Phe	Pro	Gln	Trp	His	Leu	Pro	Ile	Lys	Ile	Ala	Ala	Ile
65					70					75				80	

Ile	Ala	Ser	Leu	Thr	Phe	Leu	Tyr	Thr	Leu	Leu	Arg	Glu	Val	Ile	His
			85					90						95	

Pro	Leu	Ala	Thr	Ser	His	Gln	Gln	Tyr	Phe	Tyr	Lys	Ile	Pro	Ile	Leu
		100						105					110		

Val	Ile	Asn	Lys	Val	Leu	Pro	Met	Val	Ser	Ile	Thr	Leu	Leu	Ala	Leu
		115				120						125			

Val	Tyr	Leu	Pro	Gly	Val	Ile	Ala	Ala	Ile	Val	Gln	Leu	His	Asn	Gly
	130					135					140				

Thr	Lys	Tyr	Lys	Lys	Phe	Pro	His	Trp	Leu	Asp	Lys	Trp	Met	Leu	Thr
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

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145	150	155	160
Arg Lys Gln Phe Gly	Leu Leu Ser Phe Phe	Phe Ala Val Leu His	Ala
	165	170	175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu		185	190
	180		
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp		200	205
	195		
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile		215	220
	210		
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser		230	235
	225		240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn		245	250
	245	250	255
Asn Ile			
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<212> TYPE: DNA			
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<220> FEATURE:			
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<222> LOCATION: (96)...(872)			
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	Met Glu Ser Arg Lys Asp		
	1	5	
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta			161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu			
	10	15	20
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta			209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu			
	25	30	35
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa			257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu			
	40	45	50
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag			305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln			
	55	60	65
tggtac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt			353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe			
	75	80	85
ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat			401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His			
	90	95	100
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg			449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu			
	105	110	115
cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg			497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val			
	120	125	130
ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt			545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe			
	135	140	145
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt			593

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Pro	His	Trp	Leu	Asp	Lys	Trp	Met	Leu	Thr	Arg	Lys	Gln	Phe	Gly	Leu	
				155					160					165		
ctc	agt	ttc	ttt	ttt	gct	gta	ctg	cat	gca	att	tat	agt	ctg	tct	tac	641
Leu	Ser	Phe	Phe	Phe	Ala	Val	Leu	His	Ala	Ile	Tyr	Ser	Leu	Ser	Tyr	
			170					175					180			
cca	atg	agg	cga	tcc	tac	aga	tac	aag	ttg	cta	aac	tggt	gca	tat	caa	689
Pro	Met	Arg	Arg	Ser	Tyr	Arg	Tyr	Lys	Leu	Leu	Asn	Trp	Ala	Tyr	Gln	
		185					190				195					
cag	gtc	caa	caa	aat	aaa	gaa	gat	gcc	tggt	att	gag	cat	gat	gtt	tggt	737
Gln	Val	Gln	Gln	Asn	Lys	Glu	Asp	Ala	Trp	Ile	Glu	His	Asp	Val	Trp	
	200					205					210					
aga	atg	gag	att	tat	gtgt	tct	ctgt	gga	att	gtgt	gga	ttgt	gca	ata	ctgt	785
Arg	Met	Glu	Ile	Tyr	Val	Ser	Leu	Gly	Ile	Val	Gly	Leu	Ala	Ile	Leu	
215					220					225					230	
gct	ctgt	ttgt	gct	gtgt	aca	tct	att	cca	tct	gtgt	agt	gac	tct	ttgt	aca	833
Ala	Leu	Leu	Ala	Val	Thr	Ser	Ile	Pro	Ser	Val	Ser	Asp	Ser	Leu	Thr	
			235					240						245		
tggt	aga	gaa	ttt	cac	tat	att	cagt	gta	aat	aat	ata	taa	aataacccta			882
Trp	Arg	Glu	Phe	His	Tyr	Ile	Gln	Val	Asn	Asn	Ile	*				
		250					255									
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ataacaaatg	tttttcaaca	gcaaagatct	tatacttgtt	ccaattaata	atgtgtctctc											1002
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agattttactg	agggtttatct	tctgggtgga	gattatccat	aagaagagtg	atgtgccaga											1782
atcactctgg	gacccctgtc	tgacaagatt	caaaggacta	aatttaattc	agtcatgaac											1842
actgccaatt	accgttttatg	ggtagacatc	tttggaatt	tcacaaagg	cagacattcg											1902
caactatccc	ttctacatgt	ccacacgtat	actccaacac	tttattaggc	atctgattag											1962
tttggaagg	atgcctccat	ctgaattagt	ccagtgtggc	ttagagtgtg	tacaacattc											

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caccgttgag attacatagg tgaacaacta tttttaagca actttatttg tgtagtgaca 2562
aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca 2622
gacattgaaa aaattgttca tattatttcc atgttatcag aatatttgat tttttaaaaa 2682
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cctgctataa gtaagactca gtccctgatt ttaggtatcc tgtgaaaagc agaattaaga 2922
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ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tcccagttgt agaattactg 3522
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<210> SEQ ID NO 15

<211> LENGTH: 258

<212> TYPE: PR

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 15

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Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
 20             25             30

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
 35             40             45

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
 50             55             60

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
 65             70             75             80

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
 85             90             95

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
100            105            110

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
115            120            125

Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly

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130	135	140	
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr			
145	150	155	160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala			
	165	170	175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu			
	180	185	190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp			
	195	200	205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile			
	210	215	220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser			
	225	230	235
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn			
	245	250	255
Asn Ile			
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Met Glu Ser Arg Lys Asp			
1 5			
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta			161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu			
10 15 20			
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta			209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu			
25 30 35			
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa			257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu			
40 45 50			
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag			305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln			
55 60 65 70			
tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt			353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe			
75 80 85			
ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat			401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His			
90 95 100			
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg			449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu			
105 110 115			
cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg			497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val			
120 125 130			
ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt			545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe			

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135	140	145	150	
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt				593
Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu				
	155	160	165	
ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac				641
Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr				
	170	175	180	
cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa				689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln				
	185	190	195	
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg				737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp				
	200	205	210	
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg				785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu				
	215	220	225	230
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca				833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr				
	235	240	245	
tggaaga gaa ttt cac tat att cag gta aat aat ata taa aataacccta				882
Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *				
	250	255		
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caactatccc ttctacatgt ccacacgtat actccaacac tttattaggc atctgattag				1962
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tagacttcat taggaattta ggactgcac ttgacaactg agcctattct actatatgta				2202
caataacctag cccataatag gtatacaata cacatttggt aaaactaatt ttcaaccaat				2262

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gacatgtatt tttcaactag taacctagaa atgtttcact taaaatctga gaactgggta 2322
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tcactgggac ttaagaatgc gcctgaataa ttgtgagttc gatttgttct ggcaggctaa 2442
tgaccatttc cagtaaatg aatagaggtc agaagtcgta taaaagaggt gttgtcagaa 2502
caccgttgag attacatagg tgaacaacta tttttaagca actttatttg tgtagtgaca 2562
aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca 2622
gacattgaaa aaattgttca tattatttcc atgttatcag aatatttgat tttttaaaaa 2682
cataggccaa gtcatctcac ttcattattc atttatcaaa atcagagtga atcacattag 2742
tcgccttcac aactgataaa gatcactgaa gtcaaattga tttttgctat aatcttcaat 2802
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atttaaaagc atactattcc tgccatgctt gaggaagaag atactgaaga ttagacatgg 3462
ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tcccagttgt agaattactg 3522
tttacacaca tttttgttca atattgatat attttatcac caacatttca agtttgtatt 3582
tgттаатааа atgattattc aaggaaaaaa aaaaaaaaaa aaaaaa 3627

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<210> SEQ ID NO 17

<211> LENGTH: 258

<212> TYPE: PR

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 17

```

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1             5             10             15

```

```

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
 20             25             30

```

```

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
 35             40             45

```

```

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
 50             55             60

```

```

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
 65             70             75             80

```

```

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
 85             90             95

```

```

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
100            105            110

```

```

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu

```

-continued

115	120	125	
Val Tyr Leu Pro Gly	Val Ile Ala Ala Ile	Val Gln Leu His Asn Gly	
130	135	140	
Thr Lys Tyr Lys Lys	Phe Pro His Trp Leu	Asp Lys Trp Met Leu Thr	
145	150	155	160
Arg Lys Gln Phe Gly	Leu Leu Ser Phe Phe	Phe Ala Val Leu His Ala	
165	170	175	
Ile Tyr Ser Leu Ser	Tyr Pro Met Arg Arg	Ser Tyr Arg Tyr Lys Leu	
180	185	190	
Leu Asn Trp Ala Tyr	Gln Gln Val Gln Gln	Asn Lys Glu Asp Ala Trp	
195	200	205	
Ile Glu His Asp Val	Trp Arg Met Glu Ile	Tyr Val Ser Leu Gly Ile	
210	215	220	
Val Gly Leu Ala Ile	Leu Ala Leu Leu Ala	Val Thr Ser Ile Pro Ser	
225	230	235	240
Val Ser Asp Ser Leu	Thr Trp Arg Glu Phe	His Tyr Ile Gln Val Asn	
245	250	255	
Asn Ile			
<210> SEQ ID NO 18			
<211> LENGTH: 3627			
<212> TYPE: DNA			
<213> ORGANISM: Homo sapiens			
<220> FEATURE:			
<221> NAME/KEY: CDS			
<222> LOCATION: (96)...(872)			
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gtgggtggct gaagccatac tattttatag aatta atg gaa agc aga aaa gac			113
Met Glu Ser Arg Lys Asp			
1 5			
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta			161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu			
10 15 20			
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta			209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu			
25 30 35			
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa			257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu			
40 45 50			
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag			305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln			
55 60 65 70			
tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt			353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe			
75 80 85			
ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat			401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His			
90 95 100			
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg			449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu			
105 110 115			
cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg			497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val			
120 125 130			

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ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe 135 140 145 150	545
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu 155 160 165	593
ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr 170 175 180	641
cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln 185 190 195	689
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp 200 205 210	737
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu 215 220 225 230	785
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr 235 240 245	833
tgga aga gaa ttt cac tat att cag gta aat aat ata taa aataacccta Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *	882
250 255	
agaggtaaat cttcttttttg tgtttatgat atagaatatg ttgactttac cccataaaaa	942
ataacaaatg tttttcaaca gcaaagatct tatacttggt ccaattaata atgtgctctc	1002
ctgttgtttt ccctattgct tctaattagg acaagtgttt cctagacata aataaaaggc	1062
attaaaaatat tctttgtttt tttttttttg tttgtttgtt ttttgtttgt ttgtttgttt	1122
ttttgagatg aagtctcgct ctgttgccca tgctggagta cagtggcacg atctcggctc	1182
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ggattacagg caccatcac catgtccagc taatttttgt atttttagta gagacaggg	1302
tttcccatgt tggccaggct ggtctcgatc tctgacctc aaatgatccg cccacctcg	1362
cctcccaaag tgctgggatg acagttgtga gccaccacac tcagcctgct ctttctaata	1422
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cattttatat acttactcac ttgaagtctc taaatattct tgtaatttta aaactatctc	1722
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actgccaaatt accgtttatg ggtagacatc tttggaaatt tccacaaggc cagacattcg	1902
caactatccc ttctacatgt ccacacgtat actccaacac tttattaggc atctgattag	1962
tttgaaagt atgcctccat ctgaattagt ccagtgtggc ttagagttgg tacaacattc	2022
tcacagaatt tcctaatttt gtaggttcag cctgataacc actggagtgc tttggctctc	2082
attaaatagc tttcttcaca cattgctctg cctgttacac atatgatgaa cactgctttt	2142
tagacttcat taggaattta ggactgcatc ttgacaactg agcctattct actatatgta	2202

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caatacctag cccataatag gtatacaata cacatttgggt aaaactaatt ttcaaccaat 2262
gacatgtatt tttcaactag taacctagaa atgtttcact taaaatctga gaactgggta 2322
cactacaagt taccttggag attcatatat gaaaacgcaa acttagctat ttgattgtat 2382
tcactgggac ttaagaatgc gcctgaataa ttgtgagttc gatttgttct ggcaggctaa 2442
tgaccatttc cagtaaagtg aatagaggtc agaagtcgta taaaagaggt gttgtcagaa 2502
caccgttgag attacatagg tgaacaacta tttttaagca actttatttg tgtagtgaca 2562
aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca 2622
gacattgaaa aaattgttca tattatttcc atgttatcag aatatttgat tttttaaaaa 2682
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tcgccttcac aactgataaa gatcactgaa gtcaaattga tttttgctat aatcttcaat 2802
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aaggatttcc aagcaacaga gcataatccag atgaggtagg atgggataaa ctcttattga 3222
accaatcttc accaattttg tttttctttt gcagagcaag ctaggaattg tttcccttct 3282
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tgtatgggat acacctccaa cttttatgat agctgttttc cttccaattg ttgtcctgat 3402
atttaaaagc atactattcc tgccatgctt gaggaagaag atactgaaga ttagacatgg 3462
ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tccagttgt agaattactg 3522
tttacacaca tttttgttca atattgatat attttatcac caacatttca agtttgtatt 3582
tgtaataaaa atgattattc aaggaaaaaa aaaaaaaaaa aaaaaa 3627

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<210> SEQ ID NO 19

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 19

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
  1             5             10             15

```

```

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
      20             25             30

```

```

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
      35             40             45

```

```

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
      50             55             60

```

```

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
      65             70             75             80

```

```

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
      85             90             95

```

```

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu

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100	105	110	
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu			
115	120	125	
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly			
130	135	140	
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr			
145	150	155	160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala			
165	170	175	
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu			
180	185	190	
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp			
195	200	205	
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile			
210	215	220	
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser			
225	230	235	240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn			
245	250	255	
Asn Ile			
<210> SEQ ID NO 20			
<211> LENGTH: 3627			
<212> TYPE: DNA			
<213> ORGANISM: Homo sapiens			
<220> FEATURE:			
<221> NAME/KEY: CDS			
<222> LOCATION: (96)...(872)			
<400> SEQUENCE: 20			
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gtgggtggct gaagccatac tattttatag aatta atg gaa agc aga aaa gac			113
Met Glu Ser Arg Lys Asp			
1 5			
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta			161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu			
10 15 20			
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta			209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu			
25 30 35			
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa			257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu			
40 45 50			
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag			305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln			
55 60 65 70			
tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt			353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe			
75 80 85			
ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat			401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His			
90 95 100			
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg			449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu			
105 110 115			

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cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val 120 125 130	497
ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe 135 140 145 150	545
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu 155 160 165	593
ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr 170 175 180	641
cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln 185 190 195	689
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp 200 205 210	737
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu 215 220 225 230	785
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr 235 240 245	833
tgga aga gaa ttt cac tat att cag gta aat aat ata taa aataacccta Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *	882
250 255	
agaggtaaat cttcttttttg tgtttatgat atagaatatg ttgactttac cccataaaaa	942
ataacaaatg tttttcaaca gcaaagatct tatacttggt ccaattaata atgtgctctc	1002
ctgttggttt ccctattgct tctaattagg acaagtgttt cctagacata aataaaaggc	1062
attaaaaat tctttgtttt tttttttttg tttgtttgtt ttttgtttgt ttgtttgttt	1122
ttttgagatg aagtctcgct ctgttgccca tgctggagta cagtggcacg atctcggctc	1182
actgcaacct gcgcctcctg ggttcaggcg attctcttgc ctgagcctcc tgagtagctg	1242
ggattacagg caccatcac catgtccagc taatttttgt atttttagta gagacagggt	1302
tttcccatgt tggccaggct ggtctcgatc tctgacctc aaatgatccg cccacctcg	1362
cctccaaaag tgctgggatg acagttgtga gccaccacac tcagcctgct ctttctaata	1422
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actgccaatt accgttttat ggtagacatc tttggaaatt tccacaaggc cagacattcg	1902
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tttgaaagt atgcctccat ctgaattagt ccagtgtggc ttagagttgg tacaacattc	2022
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attaaatagc tttcttcaca cattgctctg cctgttacac atatgatgaa cactgctttt 2142
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caatacctag ccataaatag gtatacaata cacatttggt aaaactaatt ttcaaccaat 2262
gacatgtatt ttcaactag taacctagaa atgtttcact taaaatctga gaactggtta 2322
cactacaagt taccttgag attcatatat gaaaacgcaa acttagctat ttgattgtat 2382
tcactgggac ttaagaatgc gcctgaataa ttgtgagttc gatttgttct ggcaggctaa 2442
tgaccatttc cagtaaagt aatagaggtc agaagtcgta taaaagaggt gttgtcagaa 2502
caccgttgag attacatagg tgaacaacta tttttaagca actttatttg tgtagtgaca 2562
aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca 2622
gacattgaaa aaattgttca tattatttcc atgttatcag aatatttgat tttttaaaaa 2682
cataggccaa gtctattcac ttcattattc atttatcaa atcagagtga atcacattag 2742
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cctgtataa gtaagactca gtccctgatt ttaggtatcc tgtgaaaagc agaattaaga 2922
caaatacaca agagacaaag cacaaaaaat aaatatcata aggggatgaa caaaatgggtg 2982
gagaaagagt agacaaagtt ttgatcacc tgccttcaa gaaaggctgt gaattttgtt 3042
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agagcagaaa gatgtgaatg gacattgttg agaatgtga taggaaaaca atcatagata 3162
aaggatttcc aagcaacaga gcatatccag atgaggtagg atgggataaa ctcttattga 3222
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ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tcccagttgt agaattactg 3522
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<210> SEQ ID NO 21

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 21

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1             5             10             15

```

```

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
 20             25             30

```

```

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
 35             40             45

```

```

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
 50             55             60

```

```

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
 65             70             75             80

```

```

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His

```


										85										90										95									
Pro	Leu	Ala	Thr	Ser	His	Gln	Gln	Tyr	Phe	Tyr	Lys	Ile	Pro	Ile	Leu																								
			100												105												110												
Val	Ile	Asn	Lys	Val	Leu	Pro	Met	Val	Ser	Ile	Thr	Leu	Leu	Ala	Leu																								
			115												120												125												
Val	Tyr	Leu	Pro	Gly	Val	Ile	Ala	Ala	Ile	Val	Gln	Leu	His	Asn	Gly																								
			130												135												140												
Thr	Lys	Tyr	Lys	Lys	Phe	Pro	His	Trp	Leu	Asp	Lys	Trp	Met	Leu	Thr																								
			145												150												155												
Arg	Lys	Gln	Phe	Gly	Leu	Leu	Ser	Phe	Phe	Phe	Ala	Val	Leu	His	Ala																								
			165												170												175												
Ile	Tyr	Ser	Leu	Ser	Tyr	Pro	Met	Arg	Arg	Ser	Tyr	Arg	Tyr	Lys	Leu																								
			180												185												190												
Leu	Asn	Trp	Ala	Tyr	Gln	Gln	Val	Gln	Gln	Asn	Lys	Glu	Asp	Ala	Trp																								
			195												200												205												
Ile	Glu	His	Asp	Val	Trp	Arg	Met	Glu	Ile	Tyr	Val	Ser	Leu	Gly	Ile																								
			210												215												220												
Val	Gly	Leu	Ala	Ile	Leu	Ala	Leu	Leu	Ala	Val	Thr	Ser	Ile	Pro	Ser																								
			225												230												235												
Val	Ser	Asp	Ser	Leu	Thr	Trp	Arg	Glu	Phe	His	Tyr	Ile	Gln	Val	Asn																								
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																Met Glu Ser Arg Lys Asp																							
																1 5																							
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta																161																							
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu																																							
																10 15 20																							
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta																209																							
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu																																							
																25 30 35																							
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa																257																							
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu																																							
																40 45 50																							
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag																305																							
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln																																							
																55 60 65 70																							
tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt																353																							
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe																																							
																75 80 85																							
ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat																401																							
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His																																							
																90 95 100																							
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg																44																							

Gln	Gln	Tyr	Phe	Tyr	Lys	Ile	Pro	Ile	Leu	Val	Ile	Asn	Lys	Val	Leu	
		105					110					115				
cca	atg	gtt	tcc	atc	act	ctc	ttg	gca	ttg	gtt	tac	ctg	cca	ggg	gtg	497
Pro	Met	Val	Ser	Ile	Thr	Leu	Leu	Ala	Leu	Val	Tyr	Leu	Pro	Gly	Val	
		120				125					130					
ata	gca	gca	att	gtc	caa	ctt	cat	aat	gga	acc	aag	tat	aag	aag	ttt	545
Ile	Ala	Ala	Ile	Val	Gln	Leu	His	Asn	Gly	Thr	Lys	Tyr	Lys	Lys	Phe	
135					140					145					150	
cca	cat	tgg	ttg	gat	aag	tgg	atg	tta	aca	aga	aag	cag	ttt	ggg	ctt	593
Pro	His	Trp	Leu	Asp	Lys	Trp	Met	Leu	Thr	Arg	Lys	Gln	Phe	Gly	Leu	
				155					160					165		
ctc	agt	ttc	ttt	ttt	gct	gta	ctg	cat	gca	att	tat	agt	ctg	tct	tac	641
Leu	Ser	Phe	Phe	Phe	Ala	Val	Leu	His	Ala	Ile	Tyr	Ser	Leu	Ser	Tyr	
			170				175						180			
cca	atg	agg	cga	tcc	tac	aga	tac	aag	ttg	cta	aac	tgg	gca	tat	caa	689
Pro	Met	Arg	Arg	Ser	Tyr	Arg	Tyr	Lys	Leu	Leu	Asn	Trp	Ala	Tyr	Gln	
		185					190					195				
cag	gtc	caa	caa	aat	aaa	gaa	gat	gcc	tgg	att	gag	cat	gat	gtt	tgg	737
Gln	Val	Gln	Gln	Asn	Lys	Glu	Asp	Ala	Trp	Ile	Glu	His	Asp	Val	Trp	
		200				205					210					
aga	atg	gag	att	tat	gtg	tct	ctg	gga	att	gtg	gga	ttg	gca	ata	ctg	785
Arg	Met	Glu	Ile	Tyr	Val	Ser	Leu	Gly	Ile	Val	Gly	Leu	Ala	Ile	Leu	
215					220					225					230	
gct	ctg	ttg	gct	gtg	aca	tct	att	cca	tct	gtg	agt	gac	tct	ttg	aca	833
Ala	Leu	Leu	Ala	Val	Thr	Ser	Ile	Pro	Ser	Val	Ser	Asp	Ser	Leu	Thr	
				235					240					245		
tgg	aga	gaa	ttt	cac	tat	att	cag	gta	aat	aat	ata	taa	aataacccta			882
Trp	Arg	Glu	Phe	His	Tyr	Ile	Gln	Val	Asn	Asn	Ile	*				
		250					255									
agaggtaaat	cttcctttttg	tggttatgat	atagaatatg	ttgacttttac	cccataaaaa											942
ataacaaatg	tttttcaaca	gcaaagatct	tatacttggt	ccaattaata	atgtgctctc											1002
ctgttgtttt	ccctatttgct	tctaattagg	acaagtgttt	cctagacata	aataaaaggc											1062
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atcactctgg	gatccttgtc	tgacaagatt	caaaggacta	aatttaattc	agtcatgaac											1842
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caactatccc	ttctacatgt	ccacacgtat	actccaacac	tttattaggc	atctgattag											1962
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tagacttcat taggaattta ggactgcacg ttgacaactg agcctattct actatatgta 2202
caatacctag ccataaatag gtatacaata cacatttggt aaaactaatt ttcaaccaat 2262
gacatgtatt tttcaactag taacctagaa atgtttcact taaaatctga gaactgggta 2322
cactacaagt taccttgag attcatatat gaaaatgcaa acttagctat ttgattgtat 2382
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caccgttgag attacatagg tgaacaacta tttttaagca actttatttg ttagtgaca 2562
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<210> SEQ ID NO 23

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 23

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Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
      20             25             30

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Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
      35             40             45

```

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Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
      50             55             60

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Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile

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65	70	75	80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His	85	90	95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu	100	105	110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu	115	120	125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly	130	135	140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr	145	150	155
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala	165	170	175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu	180	185	190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp	195	200	205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile	210	215	220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser	225	230	235
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn	245	250	255
Asn Ile			
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<211> LENGTH: 3627			
<212> TYPE: DNA			
<213> ORGANISM: Homo sapiens			
<220> FEATURE:			
<221> NAME/KEY: CDS			
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	Met Glu Ser Arg Lys Asp		
	1	5	
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta			161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu	10	15	20
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta			209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu	25	30	35
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa			257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu	40	45	50
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag			305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln	55	60	65
tggtcac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt			353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe	75	80	85
ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat			401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His			

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90	95	100	
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg			449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu			
105	110	115	
cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg			497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val			
120	125	130	
ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt			545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe			
135	140	145	150
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt			593
Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu			
155	160	165	
ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac			641
Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr			
170	175	180	
cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa			689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln			
185	190	195	
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg			737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp			
200	205	210	
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg			785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu			
215	220	225	230
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca			833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr			
235	240	245	
tgga aga gaa ttt cac tat att cag gta aat aat ata taa aataacccta			882
Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *			
250	255		
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ataacaaatg tttttcaaca gcaaagatct tatacttggtt ccaattaata atgtgctctc			1002
ctgttggttt ccctattgct tctaattagg acaagtgttt cctagacata aataaaaggc			1062
attaaaaatat tctttgtttt tttttttttg tttgtttgtt ttttgtttgt ttgtttgttt			1122
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tcacagaatt tcctaatttt gtaggttcag cctgataacc actggagttc tttggctctc	2082
attaaatagc tttcttcaca cattgctctg cctgttacac atatgatgaa cactgctttt	2142
tagacttcat taggaattta ggactgcac ttgacaactg agcctattct actatatgta	2202
caatacctag ccataaatag gtatacaata cacatttggt aaaactaatt ttcaaccaat	2262
gacatgtatt tttcaactag taacctagaa atgtttcact taaaaactga gaactggtta	2322
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tcactgggac ttaagaatgc gcctgaataa ttgtgagttc gatttgttct ggcaggctaa	2442
tgaccatttc cagtaaatg aatagaggtc agaagtcgta taaaagaggt gttgtcagaa	2502
caccgttgag attacatagg tgaacaacta tttttaagca actttatttg tgtagtgaca	2562
aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca	2622
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caaatacaca agagacaaag cacaaaaaat aaatatcata aggggatgaa caaaatggtg	2982
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<210> SEQ ID NO 25

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 25

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				20				25					30		

Gly	Glu	Thr	Ser	Met	Leu	Lys	Arg	Pro	Val	Leu	Leu	His	Leu	His	Gln
		35					40					45			

Thr	Ala	His	Ala	Asp	Glu	Phe	Asp	Cys	Pro	Ser	Glu	Leu	Gln	His	Thr
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Gln Glu Leu Phe Pro	Gln Trp His Leu Pro	Ile Lys Ile Ala Ala Ile	
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Ile Ala Ser Leu Thr	Phe Leu Tyr Thr	Leu Leu Arg Glu Val Ile His	
	85	90 95	
Pro Leu Ala Thr Ser	His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu		
	100	105 110	
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu			
	115	120 125	
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly			
	130	135 140	
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr			
	145	150 155 160	
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala			
	165	170 175	
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu			
	180	185 190	
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp			
	195	200 205	
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile			
	210	215 220	
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser			
	225	230 235 240	
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn			
	245	250 255	
Asn Ile			
<210> SEQ ID NO 26			
<211> LENGTH: 3627			
<212> TYPE: DNA			
<213> ORGANISM: Homo sapiens			
<220> FEATURE:			
<221> NAME/KEY: CDS			
<222> LOCATION: (96)...(872)			
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Met Glu Ser Arg Lys Asp			
1 5			
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta			161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu			
10 15 20			
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta			209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu			
25 30 35			
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa			257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu			
40 45 50			
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag			305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln			
55 60 65 70			
tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt			353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe			
75 80 85			

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ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat	401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His	
90 95 100	
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg	449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu	
105 110 115	
cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg	497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val	
120 125 130	
ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt	545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe	
135 140 145 150	
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt	593
Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu	
155 160 165	
ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac	641
Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr	
170 175 180	
cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa	689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln	
185 190 195	
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg	737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp	
200 205 210	
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg	785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu	
215 220 225 230	
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca	833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr	
235 240 245	
tggaaga gaa ttt cac tat att cag gta aat aat ata taa aataacccta	882
Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *	
250 255	
agaggtaaat cttcttttttg tgtttatgat atagaatatg ttgactttac cccataaaaa	942
ataacaaatg tttttcaaca gcaaagatct tatacttggt ccaattaata atgtgctctc	1002
ctgttgtttt ccctattgct tctaattagg acaagtgttt cctagacata aataaaaggc	1062
attaaaaatat tctttgtttt tttttttttg tttgtttgtt ttttgtttgt ttgtttgttt	1122
ttttgagatg aagtctcgct ctgttgccca tgctggagta cagtggcacg atctcggctc	1182
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cctcccaaag tgctgggatg acagttgtga gccaccacac tcagcctgct ctttctaata	1422
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catggtttat tattttctaa aaaaaatatt cttttacctg tcacctgaat ttagtaatgc	1542
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agtttttatc taccaaagat atgctagtgt ctcatittcaa aggctgcttt ttccagctta	1662
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agatttactg aggtttatct tctggtggtg gattatccat aagaagagtg atgtgccaga	1782
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tttggaaagt atgcctccat ctgaattagt ccagtgtggc ttagagttgg tacaacattc 2022
tcacagaatt tcctaatttt gtaggttcag cctgataacc actggagttc tttggtcctc 2082
attaaatagc tttcttcaca cattgctctg cctgttacac atatgatgaa cactgctttt 2142
tagacttcat taggaattta ggactgcac ttgacaactg agcctattct actatatgta 2202
caatacctag ccataaatag gtatacaata cacatttggt aaaactaatt ttcaaccaat 2262
gacatgtatt tttcaactag taacctagaa atgtttcact taaaatctga gaactggtta 2322
cactacaagt taccttggag attcatatat gaaaacgcaa acttagctat ttgattgtat 2382
tcactgggac ttaagaatgc gcctgaataa ttgtgagttc gatttgttct ggcaggctaa 2442
tgaccatttc cagtaaatg aatagaggtc agaagtcgta taaaagaggt gttgtcagaa 2502
caccgttgag attacatagg tgaacaacta tttttaagca actttatttg ttagtgaca 2562
aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca 2622
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gagaaagagt agacaaagtt tttgatcacc tgccttcaa gaaaggctgt gaattttgtt 3042
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agagcagaaa gatgtgaatg gacattgttg agaatgtga taggaaaaca atcatagata 3162
aaggatttcc aagcaacaga gcataccag atgaggtagg atgggataaa ctcttattga 3222
accaatcttc accaattttg tttttctttt gcagagcaag ctaggaattg tttcccttct 3282
actgggcaca atacacgcat tgatttttgc ctggaataag tggatagata taaaacaatt 3342
tgtatgggat acacctccaa cttttatgat agctgttttc cttccaattg ttgtcctgat 3402
atttaaaagc atactattcc tgccatgctt gaggaagaag atactgaaga ttagacatgg 3462
ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tccagttgt agaattactg 3522
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tgtaataaaa atgattattc aaggaaaaaa aaaaaaaaaa aaaaa 3627

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<210> SEQ ID NO 27

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 27

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
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Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
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Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln

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35	40	45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr 50 55 60		
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile 65 70 75 80		
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His 85 90 95		
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu 100 105 110		
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu 115 120 125		
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly 130 135 140		
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr 145 150 155 160		
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala 165 170 175		
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu 180 185 190		
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp 195 200 205		
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile 210 215 220		
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser 225 230 235 240		
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn 245 250 255		

Asn Ile

<210> SEQ ID NO 28

<211> LENGTH: 3627

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (96)...(872)

<400> SEQUENCE: 28

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gtgggtggct gaagccatac tattttatag aatta atg gaa agc aga aaa gac      113
                               Met Glu Ser Arg Lys Asp
                               1           5

atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta      161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu
      10           15           20

gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta      209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu
      25           30           35

aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa      257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu
      40           45           50

ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag      305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln
      55           60           65           70

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ttg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt	353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe	
75 80 85	
ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat	401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His	
90 95 100	
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg	449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu	
105 110 115	
cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg	497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val	
120 125 130	
ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt	545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe	
135 140 145 150	
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt	593
Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu	
155 160 165	
ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac	641
Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr	
170 175 180	
cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa	689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln	
185 190 195	
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg	737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp	
200 205 210	
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg	785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu	
215 220 225 230	
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca	833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr	
235 240 245	
ttg aga gaa ttt cac tat att cag gta aat aat ata taa aataacccta	882
Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *	
250 255	
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ataacaaatg tttttcaaca gcaaagatct tatacttggt ccaattaata atgtgctctc	1002
ctgttgtttt ccctattgct tctaattagg acaagtgttt cctagacata aataaaaggc	1062
attaaaaatat tctttgtttt tttttttttg ttgtttgttt tttgtttgt ttgtttgttt	1122
ttttgagatg aagtctcgct ctgttgccca tgctggagta cagtggcacg atctcggtc	1182
actgcaacct gcgcctcctg ggttcaggcg attctcttgc ctgagcctcc tgagtagctg	1242
ggattacagg caccatcac catgtccagc taatttttgt atttttagta gagacaggt	1302
tttcccatgt tggccaggct ggtctcgatc tctgacctc aaatgatccg cccacctcg	1362
cctccaaaag tgctgggatg acagttgtga gccaccacac tcagcctgct ctttctaata	1422
tttgaaactt gttagacaat ttgctaccca tctaattgtga tatttttagga atccaatatg	1482
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agtttttatc taccaaatg atgctagtgt ctcatittcaa aggtgcttt ttccagctta	1662
cattttatat acttactcac ttgaagtttc taaatatctt tgtaatttta aaactatctc	1722

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atcactctgg gatccttgtc tgacaagatt caaaggacta aatttaattc agtcatgaac 1842
actgccaaatt accgtttatg ggtagacatc tttggaaatt tccacaaggt cagacattcg 1902
caactatccc ttctacatgt ccacacgtat actccaacac tttattaggc atctgattag 1962
tttggaaagt atgcctccat ctgaattagt ccagtgtggc ttagagttgg tacaacattc 2022
tcacagaatt tcctaatttt gtaggttcag cctgataacc actggagtgc tttggtcctc 2082
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caatacctag ccataaatag gtatacaata cacatttggt aaaactaatt ttcaaccaat 2262
gacatgtatt tttcaactag taacctagaa atgtttcact taaaatctga gaactgggta 2322
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caccgttgag attacatagg tgaacaacta tttttaagca actttatttg ttagtgaca 2562
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gacattgaaa aaattgttca tattatttcc atgttatcag aatatttgat tttttaaaaa 2682
cataggccaa gttcattcac ttcattatcc atttatcaa atcagagtga atcacattag 2742
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agagcagaaa gatgtgaatg gacattgttg agaatgtga taggaaaaca atcatagata 3162
aaggatttcc aagcaacaga gcataatcag atgaggtagg atgggataaa ctcttattga 3222
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ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tccagttgt agaattactg 3522
tttacacaca tttttgttca atattgatat attttatcac caacatttca agtttgtatt 3582
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<210> SEQ ID NO 29

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 29

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Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr

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Thr	Ala	His	Ala	Asp	Glu	Phe	Asp	Cys	Pro	Ser	Glu	Leu	Gln	His	Thr									
50						55						60												
Gln	Glu	Leu	Phe	Pro	Gln	Trp	His	Leu	Pro	Ile	Lys	Ile	Ala	Ala	Ile									
65			70						75			80												
Ile	Ala	Ser	Leu	Thr	Phe	Leu	Tyr	Thr	Leu	Arg	Glu	Val	Ile	His										
			85						90			95												
Pro	Leu	Ala	Thr	Ser	His	Gln	Gln	Tyr	Phe	Tyr	Lys	Ile	Pro	Ile	Leu									
			100						105			110												
Val	Ile	Asn	Lys	Val	Leu	Pro	Met	Val	Ser	Ile	Thr	Leu	Leu	Ala	Leu									
115						120						125												
Val	Tyr	Leu	Pro	Gly	Val	Ile	Ala	Ala	Ile	Val	Gln	Leu	His	Asn	Gly									
130						135						140												
Thr	Lys	Tyr	Lys	Lys	Phe	Pro	His	Trp	Leu	Asp	Lys	Trp	Met	Leu	Thr									
145			150						155			160												
Arg	Lys	Gln	Phe	Gly	Leu	Leu	Ser	Phe	Phe	Phe	Ala	Val	Leu	His	Ala									
			165			170						175												
Ile	Tyr	Ser	Leu	Ser	Tyr	Pro	Met	Arg	Arg	Ser	Tyr	Arg	Tyr	Lys	Leu									
			180			185						190												
Leu	Asn	Trp	Ala	Tyr	Gln	Gln	Val	Gln	Gln	Asn	Lys	Glu	Asp	Ala	Trp									
195						200						205												
Ile	Glu	His	Asp	Val	Trp	Arg	Met	Glu	Ile	Tyr	Val	Ser	Leu	Gly	Ile									
210			215						220															
Val	Gly	Leu	Ala	Ile	Leu	Ala	Leu	Leu	Ala	Val	Thr	Ser	Ile	Pro	Ser									
225			230						235			240												
Val	Ser	Asp	Ser	Leu	Thr	Trp	Arg	Glu	Phe	His	Tyr	Ile	Gln	Val	Asn									
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Asn Ile																								
<210> SEQ ID NO 30																								
<211> LENGTH: 3627																								
<212> TYPE: DNA																								
<213> ORGANISM: Homo sapiens																								
<220> FEATURE:																								
<221> NAME/KEY: CDS																								
<222> LOCATION: (96)...(872)																								
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gtgggtggct gaagccatac tattttatag aatta atg gaa agc aga aaa gac 113																								
Met Glu Ser Arg Lys Asp 1 5																								
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta 161																								
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu 10 15 20																								
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta 209																								
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu 25 30 35																								
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa 257																								
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu 40 45 50																								
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag 30																								

Phe 55	Asp	Cys	Pro	Ser	Glu 60	Leu	Gln	His	Thr	Gln 65	Glu	Leu	Phe	Pro	Gln 70	
tgg	cac	ttg	cca	att	aaa	ata	gct	gct	att	ata	gca	tct	ctg	act	ttt	353
Trp	His	Leu	Pro	Ile	Lys	Ile	Ala	Ala	Ile	Ile	Ala	Ser	Leu	Thr	Phe	
				75					80					85		
ctt	tac	act	ctt	ctg	agg	gaa	gta	att	cac	ccc	tta	gca	act	tcc	cat	401
Leu	Tyr	Thr	Leu	Leu	Arg	Glu	Val	Ile	His	Pro	Leu	Ala	Thr	Ser	His	
				90				95					100			
caa	caa	tat	ttt	tat	aaa	att	cca	atc	ctg	gtc	atc	aac	aaa	gtc	ttg	449
Gln	Gln	Tyr	Phe	Tyr	Lys	Ile	Pro	Ile	Leu	Val	Ile	Asn	Lys	Val	Leu	
		105					110					115				
cca	atg	gtt	tcc	atc	act	ctc	ttg	gca	ttg	gtt	tac	ctg	cca	ggg	gtg	497
Pro	Met	Val	Ser	Ile	Thr	Leu	Leu	Ala	Leu	Val	Tyr	Leu	Pro	Gly	Val	
		120				125					130					
ata	gca	gca	att	gtc	caa	ctt	cat	aat	gga	acc	aag	tat	aag	aag	ttt	545
Ile	Ala	Ala	Ile	Val	Gln	Leu	His	Asn	Gly	Thr	Lys	Tyr	Lys	Lys	Phe	
					140					145					150	
cca	cat	tgg	ttg	gat	aag	tgg	atg	tta	aca	aga	aag	cag	ttt	ggg	ctt	593
Pro	His	Trp	Leu	Asp	Lys	Trp	Met	Leu	Thr	Arg	Lys	Gln	Phe	Gly	Leu	
				155					160				165			
ctc	agt	ttc	ttt	ttt	gct	gta	ctg	cat	gca	att	tat	agt	ctg	tct	tac	641
Leu	Ser	Phe	Phe	Phe	Ala	Val	Leu	His	Ala	Ile	Tyr	Ser	Leu	Ser	Tyr	
				170				175					180			
cca	atg	agg	cga	tcc	tac	aga	tac	aag	ttg	cta	aac	tgg	gca	tat	caa	689
Pro	Met	Arg	Arg	Ser	Tyr	Arg	Tyr	Lys	Leu	Leu	Asn	Trp	Ala	Tyr	Gln	
		185					190					195				
cag	gtc	caa	caa	aat	aaa	gaa	gat	gcc	tgg	att	gag	cat	gat	gtt	tgg	737
Gln	Val	Gln	Gln	Asn	Lys	Glu	Asp	Ala	Trp	Ile	Glu	His	Asp	Val	Trp	
		200				205					210					
aga	atg	gag	att	tat	gtg	tct	ctg	gga	att	gtg	gga	ttg	gca	ata	ctg	785
Arg	Met	Glu	Ile	Tyr	Val	Ser	Leu	Gly	Ile	Val	Gly	Leu	Ala	Ile	Leu	
					220					225				230		
gct	ctg	ttg	gct	gtg	aca	tct	att	cca	tct	gtg	agt	gac	tct	ttg	aca	833
Ala	Leu	Leu	Ala	Val	Thr	Ser	Ile	Pro	Ser	Val	Ser	Asp	Ser	Leu	Thr	
				235					240				245			
tgg	aga	gaa	ttt	cac	tat	att	cag	gta	aat	aat	ata	taa	aataacccta			882
Trp	Arg	Glu	Phe	His	Tyr	Ile	Gln	Val	Asn	Asn	Ile	*				
			250				255									
agaggtaaat	cttccttttttg	tggttatgat	atagaatatg	ttgacttttac	ccccataaaaa											942
ataacaaatg	tttttccaaca	gcaaagatct	tatacttgtt	ccaattaata	atgtgctctc											1002
ctgttgtttt	ccotatttgct	totaattagg	acaagtgttt	cctagacata	aataaaaaggc											1062
attaaaaatat	tctttgtttt	tttttttttg	tttgttttgt	tttgttttgt	ttgtttgttt											1122
ttttgagatg	aagtctcgct	ctgttgccca	tgctggagta	cagtggcacg	atctcggtct											1182
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ggattacagg	cacccatcac	catgtccagc	taatttttgt	atttttagta	gagacagggt											1302
tttcccatgt	tgccaggct	ggtctcgatc	tcttgacetc	aatgatccg	cccacctcg											1362
cctcccaaag	tgctgggatg	acagttgtga	gccaccacac	tcagcctgct	ctttctaata											1422
tttgaaactt	gtagacaat	ttgctaccca	tctaattgtga	tatttttagga	atccaatatg											1482
catggtttat	tattttcttaa	aaaaaatatt	cttttacctg	tcacctgaat	ttagtaaatgc											1542
cttttatgtt	acacaaacta	gcactttcca	gaacaaaaa	ctctctcctt	gaaataatag											1602
agtttttatc	taccaaagat	atgctagtgt	ctcattttcaa	aggctgcttt	ttccagctta											1662

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cattttatat	acttactcac	ttgaagtttc	taaatattct	tgtaatttta	aaactatctc	1722
agatttactg	aggtttatct	tctggtggta	gattatccat	aagaagagtg	atgtgccaga	1782
atcactctgg	gaccttgctc	tgacaagatt	caaaggacta	aatttaattc	agtcgatgaac	1842
actgccaaat	accgttttatg	ggtagacatc	tttggaatt	tccacaaggt	cagacattcg	1902
caactatccc	ttctacatgt	ccacacgtat	actccaacac	tttattaggc	atctgattag	1962
tttggaagt	atgcctccat	ctgaattagt	ccagtgtggc	ttagagttgg	tacaacattc	2022
tcacagaatt	tcctaatttt	gtaggttcag	cctgataacc	actggagtgc	tttggctctc	2082
attaaatagc	tttcttcaca	cattgctctg	cctgttacac	atatgatgaa	cactgctttt	2142
tagacttcat	taggaattta	ggactgcac	ttgacaactg	agcctattct	actatatgta	2202
caatacctag	cccataatag	gtatacaata	cacatttggt	aaaactaatt	ttcaaccaat	2262
gacatgtatt	tttcaactag	taacctagaa	atgtttcact	taaaatctga	gaactggtta	2322
cactacaagt	taccttggag	attcatatat	gaaaacgcaa	acttagctat	ttgattgtat	2382
tcactgggac	ttaagaatgc	gcctgaataa	ttgtgagttc	gatttgttct	ggcaggctaa	2442
tgaccatttc	cagtaaatg	aatagaggtc	agaagtcgta	taaaagaggt	gtgtgcagaa	2502
caccgttgag	attacatagg	tgaacaacta	tttttaagca	actttatttg	tgtagtgaca	2562
aagcatccca	atgcaggctg	aaatgtttca	tcacatctct	ggatctctct	atttttgtgc	2622
gacattgaaa	aaattgttca	tattatttcc	atgttatcag	aatatttgat	tttttaaaaa	2682
cataggccaa	gttcattcac	ttcattattc	atttatcaaa	atcagagtga	atcacattag	2742
tcgccttcac	aactgataaa	gatcactgaa	gtcaaattga	tttttgctat	aatcttcaat	2802
ctacctatat	ttaattgaga	atctaaaatg	tacaaatcat	tgtgttgatt	ctgcagtgat	2862
cctgctataa	gtaagactca	gtccctgatt	ttaggtatcc	tgtgaaaagc	agaattaaga	2922
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gagaaagagt	agacaaagtt	tttcatcacc	tgcttcaaaa	gaaaggctgt	gaattttgtt	3042
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aaggatttcc	aagcaacaga	gcataccag	atgaggtagg	atgggataaa	ctcttattga	3222
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ttgggaagac	gtcacaaaaa	ttaacaaaac	tgagatatgt	tcccagttgt	agaattactg	3522
tttacacaca	tttttgttca	atattgatat	attttatcac	caacatttca	agtttgtatt	3582
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<210> SEQ ID NO 31

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 31

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met

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1	5	10	15
Lys Pro Arg	Arg Asn Leu Glu Glu	Asp Asp Tyr Leu His	Lys Asp Thr
	20	25	30
Gly Glu Thr	Ser Met Leu Lys Arg Pro Val	Leu Leu His Leu His	Gln
	35	40	45
Thr Ala His	Ala Asp Glu Phe Asp Cys Pro Ser	Glu Leu Gln His Thr	
	50	55	60
Gln Glu Leu Phe Pro	Gln Trp His Leu Pro	Ile Lys Ile Ala Ala	Ile
	65	70	75
Ile Ala Ser Leu Thr	Phe Leu Tyr Thr	Leu Leu Arg Glu Val	Ile His
	85	90	95
Pro Leu Ala Thr Ser	His Gln Gln Tyr Phe Tyr Lys	Ile Pro Ile Leu	
	100	105	110
Val Ile Asn Lys Val Leu Pro Met Val Ser	Ile Thr Leu Leu Ala Leu		
	115	120	125
Val Tyr Leu Pro Gly Val	Ile Ala Ala Ile Val	Gln Leu His Asn Gly	
	130	135	140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp	Lys Trp Met Leu Thr		
	145	150	155
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala			
	165	170	175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu			
	180	185	190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp			
	195	200	205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile			
	210	215	220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser			
	225	230	235
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn			
	245	250	255

Asn Ile

<210> SEQ ID NO 32

<211> LENGTH: 3627

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (96)...(872)

<400> SEQUENCE: 32

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gtgggtggct gaagccatac tattttatag aatta atg gaa agc aga aaa gac      113
                               Met Glu Ser Arg Lys Asp
                               1           5
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta      161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu
          10           15           20
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta      209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu
          25           30           35
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa      257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu

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40	45	50	
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag			305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln			
55 60 65 70			
tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt			353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe			
75 80 85			
ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat			401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His			
90 95 100			
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg			449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu			
105 110 115			
cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg			497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val			
120 125 130			
ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt			545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe			
135 140 145 150			
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt			593
Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu			
155 160 165			
ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac			641
Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr			
170 175 180			
cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa			689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln			
185 190 195			
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg			737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp			
200 205 210			
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg			785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu			
215 220 225 230			
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca			833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr			
235 240 245			
tgg aga gaa ttt cac tat att cag gta aat aat ata taa aataacccta			882
Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *			
250 255			
agaggtaaat cttcttttttg tgtttatgat atagaatatg ttgactttac cccataaaaa			942
ataacaaatg tttttcaaca gcaaagatct tatacttggt ccaattaata atgtgctctc			1002
ctgttgtttt ccctattgct tctaattagg acaagtgttt cctagacata aataaaaggc			1062
attaaaaatat tctttgtttt tttttttttg tttgtttggt ttttgtttgt ttgtttgttt			1122
ttttgagatg aagtctcgct ctgttgccca tgctggagta cagtggcacg atctcggtc			1182
actgcaacct gcgcctcctg ggttcaggcg attctcttgc ctcagcctcc tgagtagctg			1242
ggattacagg caccatcac catgtccagc taatttttgt atttttagta gagacaggt			1302
tttcccatgt tggccaggct ggtctcgatc tctgacctc aaatgatccg cccacctcg			1362
cctcccaaag tgctgggatg acagttgtga gccaccacac tcagcctgct ctttctaata			1422
tttgaaactt gttagacaat ttgctaccca tctaagtga tatttttagga atccaatatg			1482
catggtttat tatttcttaa aaaaaatatt cttttacctg tcacctgaat ttagtaatgc			1542

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cttttatgtt acacaactta gcactttcca gaaacaaaaa ctctctcctt gaaataatag	1602
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cattttatat acttactcac ttgaagtttc taaatattct tgtaatttta aaactatctc	1722
agatttactg aggtttatct tctggtggtg gattatccat aagaagagtg atgtgccaga	1782
atcactctgg gatccttgct tgacaagatt caaaggacta aatttaattc agtcatgaac	1842
actgccaaatt accgttttatg ggtagacatc tttggaaatt tccacaaggt cagacattcg	1902
caactatccc ttctacatgt ccacacgtat actccaacac tttattaggc atctgattag	1962
tttggaaagt atgcctccat ctgaattagt ccagtgtggc ttagagttgg tacaacattc	2022
tcacagaatt tcctaatttt gtaggttcag cctgataacc actggagttc tttggtcctc	2082
attaaatagc tttcttcaca cattgctctg cctgttacac atatgatgaa cactgctttt	2142
tagacttcat taggaattta ggactgcac ttgacaactg agcctattct actatatgta	2202
caatacctag ccataaatag gtatacaata cacatttggt aaaactaatt ttcaaccaat	2262
gacatgtatt tttcaactag taacctagaa atgtttcact taaaatctga gaactggta	2322
cactacaagt taccttggag attcatatat gaaaacgcaa acttagctat ttgattgtat	2382
tcactgggac ttaagaatgc gcctgaataa ttgtgagttc gatttgttct ggcaggctaa	2442
tgaccatttc cagtaaatg aatagaggtc agaagtcgta taaaagaggt gttgtcagaa	2502
caccgttgag attacatagg tgaacaacta tttttaagca actttatttg ttagtgaca	2562
aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca	2622
gacattgaaa aaattgttca tattatttcc atgttatcag aatatttgat tttttaaaaa	2682
cataggccaa gtccattcac ttcattattc atttatcaa atcagagtga atcacattag	2742
tcgccttcac aactgataaa gatcactgaa gtcaaattga tttttgctat aatcttcaat	2802
ctacctatat ttaattgaga atctaaaatg tacaaatcat tgtgttgatt ctgcagtgat	2862
cctgctataa gtaagactca gtccctgatt ttaggtatcc tgtgaaaagc agaattaaga	2922
caaatacaca agagacaaag cacaaaaaat aaatatcata aggggatgaa caaaatggtg	2982
gagaaagagt agacaaagtt ttgtatcacc tgccttcaaa gaaaggctgt gaattttgtt	3042
cacttagaca gcttgagac aagaaattac ccaaaagtaa ggtgaggagg ataggcaaaa	3102
agagtagaaa gatgtgaatg gacattgttg agaaatgtga taggaaaaa atcatagata	3162
aaggatttcc aagcaacaga gcataatccag atgaggtagg atgggataaa ctcttattga	3222
accaatcttc accaattttg tttttctttt gcagagcaag ctagggaattg tttcccttct	3282
actgggcaca atacacgc atgatttttg ctggaataag tggatagata taaaacaatt	3342
tgtaggtgat acacctccaa cttttatgat agctgttttc cttccaattg ttgtcctgat	3402
atttaaaagc atactattcc tgccatgctt gaggaagaag atactgaaga ttagacatgg	3462
ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tccagttgt agaattactg	3522
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<210> SEQ ID NO 33

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 33

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1           5           10           15
Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
          20           25           30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
          35           40           45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
          50           55           60
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
          65           70           75           80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
          85           90           95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
          100          105          110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
          115          120          125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
          130          135          140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
          145          150          155          160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
          165          170          175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
          180          185          190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
          195          200          205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
          210          215          220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
          225          230          235          240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn
          245          250          255
Asn Ile

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<210> SEQ ID NO 34

<211> LENGTH: 3627

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (96)...(872)

<400> SEQUENCE: 34

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gtgggtggct gaagccatac tattttatag aatta atg gaa agc aga aaa gac      113
                               Met Glu Ser Arg Lys Asp
                               1           5
atc aca aac caa gaa gaa ctt tgg aaa atg aag cct agg aga aat tta      161
Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg Arg Asn Leu
          10           15           20
gaa gaa gac gat tat ttg cat aag gac acg gga gag acc agc atg cta      209
Glu Glu Asp Asp Tyr Leu His Lys Asp Thr Gly Glu Thr Ser Met Leu

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25	30	35	
aaa aga cct gtg ctt ttg cat ttg cac caa aca gcc cat gct gat gaa			257
Lys Arg Pro Val Leu Leu His Leu His Gln Thr Ala His Ala Asp Glu			
40	45	50	
ttt gac tgc cct tca gaa ctt cag cac aca cag gaa ctc ttt cca cag			305
Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Leu Phe Pro Gln			
55	60	65	70
tgg cac ttg cca att aaa ata gct gct att ata gca tct ctg act ttt			353
Trp His Leu Pro Ile Lys Ile Ala Ala Ile Ile Ala Ser Leu Thr Phe			
	75	80	85
ctt tac act ctt ctg agg gaa gta att cac ccc tta gca act tcc cat			401
Leu Tyr Thr Leu Leu Arg Glu Val Ile His Pro Leu Ala Thr Ser His			
	90	95	100
caa caa tat ttt tat aaa att cca atc ctg gtc atc aac aaa gtc ttg			449
Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys Val Leu			
105	110	115	
cca atg gtt tcc atc act ctc ttg gca ttg gtt tac ctg cca ggt gtg			497
Pro Met Val Ser Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro Gly Val			
120	125	130	
ata gca gca att gtc caa ctt cat aat gga acc aag tat aag aag ttt			545
Ile Ala Ala Ile Val Gln Leu His Asn Gly Thr Lys Tyr Lys Lys Phe			
135	140	145	150
cca cat tgg ttg gat aag tgg atg tta aca aga aag cag ttt ggg ctt			593
Pro His Trp Leu Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu			
	155	160	165
ctc agt ttc ttt ttt gct gta ctg cat gca att tat agt ctg tct tac			641
Leu Ser Phe Phe Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr			
	170	175	180
cca atg agg cga tcc tac aga tac aag ttg cta aac tgg gca tat caa			689
Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala Tyr Gln			
	185	190	195
cag gtc caa caa aat aaa gaa gat gcc tgg att gag cat gat gtt tgg			737
Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Ile Glu His Asp Val Trp			
200	205	210	
aga atg gag att tat gtg tct ctg gga att gtg gga ttg gca ata ctg			785
Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala Ile Leu			
215	220	225	230
gct ctg ttg gct gtg aca tct att cca tct gtg agt gac tct ttg aca			833
Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser Leu Thr			
	235	240	245
tgg aga gaa ttt cac tat att cag gta aat aat ata taa aataacccta			882
Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile *			
250	255		
agaggtaaatt cttctttttg tgtttatgat atagaatatg ttgactttac cccataaaaa			942
ataacaaatg tttttcaaca gcaaagatct tatacttggtt ccaattaata atgtgctctc			1002
ctgttggtttt ccctattgct tctaattagg acaagtgttt cctagacata aataaaaggc			1062
attaaaaatat tctttgtttt tttttttttg tttgtttgtt tttgtttgtt ttgtttgttt			1122
ttttgagatg aagtctcgct ctggtgcccc tgctggagta cagtggcacg atctcggtc			1182
actgcaacct gcgcctcctg gggtcaggcg attctcttgc ctcagcctcc tgagtagctg			1242
ggattacagg caccatcac catgtccagc taatttttgt atttttagta gagacagggt			1302
tttccatgt tggccaggct ggtctcgatc tctgacctc aaatgatccg cccacctcg			1362
cctcccaaag tgctgggatg acagttgtga gccaccacac tcagcctgct ctttctaata			1422

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tttgaaactt gttagacaat ttgctaccca tctaagtga ttttttagga atccaatatg	1482
catggtttat tttttcttaa aaaaaatatt cttttacctg tcacctgaat ttagtaatgc	1542
cttttatggt acacaactta gcactttcca gaaacaaaa ctctctcctt gaaataatag	1602
agtttttatac taccaaagat atgctagtgt ctcatittcaa aggcctgcttt tccagctta	1662
cattttatata acttactcac ttgaagtctt taaatattct tgtaatttta aaactatctc	1722
agatttactg aggtttatct tctggtgga gattatccat aagaagagtg atgtgccaga	1782
atcactctgg gatccttgct tgacaagatt caaaggacta aatttaattc agtcatgaac	1842
actgccaaatt accgtttatg ggtagacatc tttggaaatt tccacaaggc cagacattcg	1902
caactatccc ttctacatgt ccacacgtat actccaacac tttattaggc atctgattag	1962
tttggaaagt atgcctccat ctgaattagt ccagtgtggc ttagagttgg tacaacattc	2022
tcacagaatt tcctaatttt gtaggttcag cctgataacc actggagttc tttggctctc	2082
attaaatagc tttcttcaca cattgctctg cctgttacac atatgatgaa cactgctttt	2142
tagacttcat taggaattta ggactgcac ttgacaactg agcctattct actatatgta	2202
caatacctag ccataatag gtatacaata cacatttggc aaaactaatt ttcaaccaat	2262
gacatgtatt tttcaactag taacctagaa atgtttcact taaaatctga gaactggta	2322
cactacaagt taccttgag attcatatat gaaaacgcaa acttagctat ttgattgtat	2382
tcactgggac ttaagaatgc gcctgaataa ttgtgagttc gatttgttct ggcaggctaa	2442
tgaccatttc cagtaaatg aatagaggtc agaagtcga taaaagaggc gttgtcagaa	2502
caccgttgag attacatagg tgaacaacta tttttaagca actttatttg tgtagtgaca	2562
aagcatccca atgcaggctg aaatgtttca tcacatctct ggatctctct attttgtgca	2622
gacattgaaa aaattgttca tattatttcc atgttatcag aatatttgat tttttaaaaa	2682
cataggccaa gttcattcac ttcattattc atttatcaaa atcagagtga atcacattag	2742
tcgccttcac aactgataaa gatcactgaa gtcaaattga tttttgctat aatcttcaat	2802
ctacctatat ttaattgaga atctaaaatg tacaatcat tgtgttgatt ctgcagtga	2862
cctgctataa gtaagactca gtcctgatt ttaggtatcc tgtgaaaagc agaattaaga	2922
caaatacaca agagacaaag cacaaaaaat aaatatcata aggggatgaa caaaatggtg	2982
gagaaagagt agacaaagt tttgatcacc tgccttcaa gaaaggctgt gaattttgtt	3042
cacttagaca gcttgagac aagaaattac ccaaaagtaa ggtgaggagg ataggcaaaa	3102
agagcagaaa gatgtgaatg gacattgttg agaaatgtga taggaaaaca atcatagata	3162
aaggatttcc aagcaactga gcatatccag atgaggtagg atgggataaa ctcttattga	3222
accaatcttc accaattttg tttttctttt gcagagcaag ctagggaattg tttcccttct	3282
actgggcaca atacacgcat tgatttttgc ctggaataag tggatagata taaaacaatt	3342
tgtatgggat acacctccaa cttttatgat agctgttttc cttccaattg ttgtcctgat	3402
atttaaaagc atactatttc tgccatgctt gaggaagaag atactgaaga ttagacatgg	3462
ttgggaagac gtcacaaaa ttaacaaac tgagatatgt tcccagttgt agaattactg	3522
tttacacaca tttttgttca atattgatat attttatcac caacatttca agtttgtatt	3582
tgtaataaaa atgattattc aaggaaaaa aaaaaaaaa aaaaa	3627

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<210> SEQ ID NO 35
<211> LENGTH: 258
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 35
Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1             5             10             15
Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
 20             25             30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
 35             40             45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
 50             55             60
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
 65             70             75             80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
 85             90             95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
100            105            110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
115            120            125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
130            135            140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
145            150            155            160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
165            170            175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
180            185            190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
195            200            205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
210            215            220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
225            230            235            240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn
245            250            255

Asn Ile

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<210> SEQ ID NO 36
<211> LENGTH: 339
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 36

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1             5             10             15
Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
 20             25             30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
 35             40             45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
 50             55             60

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Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
 65 70 75 80
 Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
 85 90 95
 Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
 100 105 110
 Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
 115 120 125
 Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
 130 135 140
 Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
 145 150 155 160
 Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
 165 170 175
 Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
 180 185 190
 Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
 195 200 205
 Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
 210 215 220
 Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
 225 230 235 240
 Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys
 245 250 255
 Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe
 260 265 270
 Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro
 275 280 285
 Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe
 290 295 300
 Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile
 305 310 315 320
 Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile Cys
 325 330 335
 Ser Gln Leu

<210> SEQ ID NO 37

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 37

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

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Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
      85                      90                      95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
      100                    105                    110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
      115                    120                    125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
      130                    135                    140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
      145                    150                    155                    160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
      165                    170                    175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
      180                    185                    190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
      195                    200                    205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
      210                    215                    220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
      225                    230                    235                    240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn
      245                    250                    255

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Asn Ile

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<210> SEQ ID NO 38
<211> LENGTH: 282
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 38

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
  1                      5                      10                      15
Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
      20                    25                    30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
      35                    40                    45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
      50                    55                    60
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
      65                    70                    75                    80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
      85                      90                      95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
      100                    105                    110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
      115                    120                    125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
      130                    135                    140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
      145                    150                    155                    160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
      165                    170                    175

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Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
      180              185              190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
      195              200              205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
      210              215              220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
      225              230              235              240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ile Ile
      245              250              255
His Lys Lys Ser Asp Val Pro Glu Ser Leu Trp Asp Pro Cys Leu Thr
      260              265              270
Arg Phe Lys Gly Leu Asn Leu Ile Gln Ser
      275              280

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<210> SEQ ID NO 39
<211> LENGTH: 258
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 39

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```

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
  1          5          10          15
Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
      20          25          30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
      35          40          45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
      50          55          60
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
      65          70          75          80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
      85          90          95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
      100         105         110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
      115         120         125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
      130         135         140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
      145         150         155         160
Arg Lys Gln Phe Gly Leu Leu Ser Leu Phe Phe Ala Val Leu His Ala
      165         170         175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
      180              185              190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
      195              200              205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
      210              215              220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
      225              230              235              240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn

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	245	250	255
Asn Ile			
<210> SEQ ID NO 40			
<211> LENGTH: 339			
<212> TYPE: PRT			
<213> ORGANISM: Homo sapiens			
<400> SEQUENCE: 40			
Met	Glu	Ser	Arg
1			
	Lys	Asp	Ile
	5		
		Asn	Gln
		10	
			Glu
			15
			Leu
			Trp
			Lys
			Met
Lys	Pro	Arg	Arg
	20		
		Asn	Leu
		25	
			Glu
			30
			His
			Lys
			Asp
			Thr
Gly	Glu	Thr	Ser
	35		
		Met	Leu
		40	
			Lys
			45
			His
			Leu
			His
			Gln
Thr	Ala	His	Ala
	50		
		Asp	Glu
		55	
			Phe
			60
			Leu
			Gln
			His
			Thr
Gln	Glu	Leu	Phe
	65		
		Pro	Gln
		70	
			Trp
			His
			Leu
			Pro
			75
			Ile
			Lys
			Ile
			Ala
			Ala
			Ile
			80
Ile	Ala	Ser	Leu
	85		
		Thr	Phe
		90	
			Leu
			Arg
			Glu
			Val
			Ile
			His
			95
Pro	Leu	Ala	Thr
	100		
		Ser	His
		105	
			Gln
			Gln
			Tyr
			Phe
			110
			Ile
			Pro
			Ile
			Leu
Val	Ile	Asn	Lys
	115		
		Val	Leu
		120	
			Pro
			Met
			Val
			Ser
			Ile
			Thr
			Leu
			Leu
			Ala
			Leu
Val	Tyr	Leu	Pro
	130		
		Gly	Val
		135	
			Ile
			Ala
			Ala
			Ile
			Val
			Gln
			Leu
			His
			Asn
			Gly
			140
Thr	Lys	Tyr	Lys
	145		
		Lys	Lys
		150	
			Phe
			Pro
			His
			Trp
			Leu
			Asp
			155
			Lys
			Trp
			Met
			Leu
			Thr
			160
Arg	Lys	Gln	Phe
	165		
		Gly	Leu
		170	
			Leu
			Ser
			Phe
			Ala
			Val
			Leu
			His
			Ala
			175
Ile	Tyr	Ser	Leu
	180		
		Ser	Tyr
		185	
			Pro
			Met
			Arg
			Arg
			Ser
			Tyr
			Arg
			Tyr
			Lys
			Leu
			190
Leu	Asn	Trp	Ala
	195		
		Tyr	Gln
		200	
			Gln
			Gln
			Asn
			Lys
			Glu
			Asp
			Ala
			Trp
			205
Ile	Glu	His	Asp
	210		
		Val	Trp
		215	
			Arg
			Met
			Glu
			Ile
			Tyr
			Val
			Ser
			Leu
			Gly
			Ile
			220
Val	Gly	Leu	Ala
	225		
		Ile	Leu
		230	
			Ala
			Leu
			Leu
			Ala
			Val
			235
			Thr
			Ser
			Ile
			Pro
			Ser
			240
Val	Ser	Asp	Ser
	245		
		Leu	Thr
		250	
			Arg
			Glu
			Phe
			His
			Tyr
			Ile
			Gln
			Ser
			Lys
			255
Leu	Gly	Ile	Val
	260		
		Ser	Leu
		265	
			Leu
			Gly
			Thr
			Ile
			His
			Ala
			Leu
			Ile
			Phe
			270
Ala	Trp	Asn	Lys
	275		
		Trp	Ile
		280	
			Asp
			Ile
			Lys
			Gln
			Phe
			Val
			Trp
			Tyr
			Thr
			Pro
			285
Pro	Thr	Phe	Met
	290		
		Ile	Ala
		295	
			Val
			Phe
			Leu
			Pro
			Ile
			Val
			Val
			Leu
			Ile
			Phe
			300
Lys	Ser	Ile	Leu
	305		
		Phe	Leu
		310	
			Pro
			Cys
			Leu
			Arg
			Lys
			Lys
			Ile
			Leu
			Lys
			Ile
			320
Arg	His	Gly	Trp
	325		
		Asp	Val
		330	
			Thr
			Lys
			Ile
			Asn
			Lys
			Thr
			Glu
			Ile
			Cys
			335
Ser	Gln	Leu	

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<210> SEQ ID NO 41

<211> LENGTH: 270

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<400> SEQUENCE: 41

Gln Leu Phe Pro Met Trp Arg Phe Pro Phe Tyr Leu Ser Ser Val Leu
1 5 10 15
Cys Ile Phe Phe Phe Val Tyr Cys Ala Ile Arg Glu Val Ile Tyr Pro
20 25 30
Tyr Val Asn Gly Lys Thr Asp Ala Thr Tyr Arg Leu Ala Ile Ser Ile
35 40 45
Pro Asn Arg Val Phe Pro Ile Thr Ala Leu Ile Leu Leu Ala Leu Val
50 55 60
Tyr Leu Pro Gly Ile Leu Ala Ala Ile Leu Gln Leu Tyr Arg Gly Thr
65 70 75 80
Lys Tyr Arg Arg Phe Pro Asn Trp Leu Asp His Trp Met Leu Cys Arg
85 90 95
Lys Gln Leu Gly Leu Val Ala Leu Gly Phe Ala Phe Leu His Val Ile
100 105 110
Tyr Thr Leu Val Ile Pro Ile Arg Tyr Tyr Val Arg Trp Arg Leu Arg
115 120 125
Asn Ala Thr Ile Thr Gln Ala Leu Thr Asn Lys Asp Ser Pro Phe Ile
130 135 140
Thr Ser Tyr Ala Trp Ile Asn Asp Ser Tyr Leu Ala Leu Gly Ile Leu
145 150 155 160
Gly Phe Phe Leu Phe Leu Leu Leu Gly Ile Thr Ser Leu Pro Ser Val
165 170 175
Ser Asn Met Val Asn Trp Arg Glu Phe Arg Phe Val Gln Ser Lys Leu
180 185 190
Gly Tyr Leu Thr Leu Val Leu Cys Thr Ala His Thr Leu Val Tyr Gly
195 200 205
Gly Lys Arg Phe Leu Ser Pro Ser Ile Leu Arg Trp Ser Leu Pro Ser
210 215 220
Ala Tyr Ile Leu Ala Leu Ile Ile Pro Cys Ala Val Leu Val Leu Lys
225 230 235 240
Cys Ile Leu Ile Met Pro Cys Ile Asp Lys Thr Leu Thr Arg Ile Arg
245 250 255
Gln Gly Trp Glu Arg Asn Ser Lys Tyr Thr Gln Ser Ala Leu
260 265 270

<210> SEQ ID NO 42

<211> LENGTH: 339

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 42

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
1 5 10 15
Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
20 25 30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
35 40 45

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Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
 50 55 60
 Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
 65 70 75 80
 Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
 85 90 95
 Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
 100 105 110
 Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
 115 120 125
 Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
 130 135 140
 Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
 145 150 155 160
 Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
 165 170 175
 Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
 180 185 190
 Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
 195 200 205
 Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
 210 215 220
 Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
 225 230 235 240
 Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys
 245 250 255
 Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe
 260 265 270
 Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro
 275 280 285
 Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe
 290 295 300
 Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile
 305 310 315 320
 Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile Cys
 325 330 335
 Ser Gln Leu

<210> SEQ ID NO 43

<211> LENGTH: 259

<212> TYPE: PRT

<213> ORGANISM: Rattus norvegicus

<400> SEQUENCE: 43

Leu Leu Pro Ser Trp Lys Val Pro Thr Leu Leu Ala Leu Gly Leu Ser
 1 5 10 15
 Thr Gln Ser Tyr Ala Tyr Asn Phe Ile Arg Asp Val Leu Gln Pro Tyr
 20 25 30
 Ile Arg Lys Asp Glu Asn Lys Phe Tyr Lys Met Pro Leu Ser Val Val
 35 40 45
 Asn Thr Thr Ile Pro Cys Val Ala Tyr Val Leu Leu Ser Leu Val Tyr
 50 55 60

-continued

Leu Pro Gly Val Leu Ala Ala Ala Leu Gln Leu Arg Arg Gly Thr Lys
65 70 75 80

Tyr Gln Arg Phe Pro Asp Trp Leu Asp His Trp Leu Gln His Arg Lys
85 90 95

Gln Ile Gly Leu Leu Ser Phe Phe Phe Ala Met Leu His Ala Leu Tyr
100 105 110

Ser Phe Cys Leu Pro Leu Arg Arg Ser His Arg Tyr Asp Leu Val Asn
115 120 125

Leu Ala Val Lys Gln Val Leu Ala Asn Lys Ser Arg Leu Trp Val Glu
130 135 140

Glu Glu Val Trp Arg Met Glu Ile Tyr Leu Ser Leu Gly Val Leu Ala
145 150 155 160

Leu Gly Met Leu Ser Leu Leu Ala Val Thr Ser Ile Pro Ser Ile Ala
165 170 175

Asn Ser Leu Asn Trp Lys Glu Phe Ser Phe Val Gln Ser Thr Leu Gly
180 185 190

Phe Val Ala Leu Met Leu Ser Thr Met His Thr Leu Thr Tyr Gly Trp
195 200 205

Thr Arg Ala Phe Glu Glu Asn His Tyr Lys Phe Tyr Leu Pro Pro Thr
210 215 220

Phe Thr Leu Thr Leu Leu Pro Cys Val Ile Ile Leu Ala Lys Gly
225 230 235 240

Leu Phe Leu Leu Pro Cys Leu Ser His Arg Leu Thr Lys Ile Arg Arg
245 250 255

Gly Trp Glu

<210> SEQ ID NO 44
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Tetanus toxoid

<400> SEQUENCE: 44

Gln Tyr Ile Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu
1 5 10

<210> SEQ ID NO 45
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Plasmodium falciparum

<400> SEQUENCE: 45

Asp Ile Glu Lys Lys Ile Ala Lys Met Glu Lys Ala Ser Ser Val Phe
1 5 10 15

Asn Val Val Asn Ser
20

<210> SEQ ID NO 46
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Streptococcus

<400> SEQUENCE: 46

Gly Ala Val Asp Ser Ile Leu Gly Gly Val Ala Thr Tyr Gly Ala Ala
1 5 10 15

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<210> SEQ ID NO 47
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Pan-DR binding Epitope
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: 1, 13
<223> OTHER INFORMATION: Xaa = D-alanine
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: 1, 13
<223> OTHER INFORMATION: Xaa = L-alanine
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: 3
<223> OTHER INFORMATION: Xaa = cyclohexylalanine
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: 3
<223> OTHER INFORMATION: Xaa = phenylalanine
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: 3
<223> OTHER INFORMATION: Xaa = tyrosine

<400> SEQUENCE: 47

Ala Lys Xaa Val Ala Ala Trp Thr Leu Lys Ala Ala Ala
1 5 10

<210> SEQ ID NO 48
<211> LENGTH: 14
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: cDNA synthesis primer

<400> SEQUENCE: 48

ttttgatcaa gctt

14

<210> SEQ ID NO 49
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer

<400> SEQUENCE: 49

ctaatacgcac tcactatagg gctcgagcgg ccgcccgggc ag

42

<210> SEQ ID NO 50
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer

<400> SEQUENCE: 50

gatacctgccc gg

12

<210> SEQ ID NO 51
<211> LENGTH: 40
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer

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<400> SEQUENCE: 51

gtaatacgcac tcactatagg gcagcgtggt cgcggccgag

40

<210> SEQ ID NO 52

<211> LENGTH: 10

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: primer

<400> SEQUENCE: 52

gatacctcggc

10

<210> SEQ ID NO 53

<211> LENGTH: 22

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: PCR-primer

<400> SEQUENCE: 53

ctaatacgcac tcactatagg gc

22

<210> SEQ ID NO 54

<211> LENGTH: 22

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Nested primer

<400> SEQUENCE: 54

tcgagcggcc gcccgggcag ga

22

<210> SEQ ID NO 55

<211> LENGTH: 20

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Nested primer

<400> SEQUENCE: 55

agcgtggtcg cggccgagga

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<210> SEQ ID NO 56

<211> LENGTH: 25

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: primer

<400> SEQUENCE: 56

atatacgcgc gctcgtcgtc gacaa

25

<210> SEQ ID NO 57

<211> LENGTH: 26

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: primer

<400> SEQUENCE: 57

agccacacgc agtcattgt agaagg

26

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<210> SEQ ID NO 58
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer

<400> SEQUENCE: 58

actttgttga tgaccaggat tgga

24

<210> SEQ ID NO 59
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: primer

<400> SEQUENCE: 59

cagaacttca gcacacacag gaac

24

<210> SEQ ID NO 60
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Epitope Tag

<400> SEQUENCE: 60

gattacaagg atgacgacga taag

24

<210> SEQ ID NO 61
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 61

Asn Gly Thr Lys

1

<210> SEQ ID NO 62
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 62

Asn Lys Thr Glu

1

<210> SEQ ID NO 63
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 63

Ser Arg Lys Asp

1

<210> SEQ ID NO 64
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 64

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Thr Asn Gln Glu
1

<210> SEQ ID NO 65
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 65

Ser Val Ser Asp
1

<210> SEQ ID NO 66
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 66

Thr Trp Arg Glu
1

<210> SEQ ID NO 67
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 67

Arg Arg Asn Leu Glu Glu Asp Asp Tyr
1 5

<210> SEQ ID NO 68
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 68

Gly Val Ile Ala Ala Ile
1 5

<210> SEQ ID NO 69
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 69

Gly Thr Ile His Ala Leu
1 5

<210> SEQ ID NO 70
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 70

Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met Lys Pro Arg
1 5 10 15

Arg

<210> SEQ ID NO 71
<211> LENGTH: 339
<212> TYPE: PRT

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 71

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1           5           10           15
Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
          20           25           30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
          35           40           45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
          50           55           60
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
          65           70           75           80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
          85           90           95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
          100          105          110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
          115          120          125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
          130          135          140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
          145          150          155          160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
          165          170          175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
          180          185          190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
          195          200          205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
          210          215          220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
          225          230          235          240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys
          245          250          255
Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe
          260          265          270
Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro
          275          280          285
Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe
          290          295          300
Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile
          305          310          315          320
Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile Cys
          325          330          335
Ser Gln Leu

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<210> SEQ ID NO 72

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 72

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Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile
1 5 10

<210> SEQ ID NO 73
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 73

Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn Asn Ile
1 5 10

<210> SEQ ID NO 74
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 74

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn
1 5 10 15

Asn Ile

<210> SEQ ID NO 75
<211> LENGTH: 36
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 75

Trp Arg Glu Phe His Tyr Ile Gln Ile Ile His Lys Lys Ser Asp Val
1 5 10 15

Pro Glu Ser Leu Trp Asp Pro Cys Leu Thr Arg Phe Lys Gly Leu Asn
20 25 30

Leu Ile Gln Ser
35

<210> SEQ ID NO 76
<211> LENGTH: 37
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 76

Thr Trp Arg Glu Phe His Tyr Ile Gln Ile Ile His Lys Lys Ser Asp
1 5 10 15

Val Pro Glu Ser Leu Trp Asp Pro Cys Leu Thr Arg Phe Lys Gly Leu
20 25 30

Asn Leu Ile Gln Ser
35

<210> SEQ ID NO 77
<211> LENGTH: 42
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 77

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ile Ile
1 5 10 15

His Lys Lys Ser Asp Val Pro Glu Ser Leu Trp Asp Pro Cys Leu Thr
20 25 30

-continued

Arg Phe Lys Gly Leu Asn Leu Ile Gln Ser
35 40

<210> SEQ ID NO 78
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 78

Arg Lys Gln Phe Gly Leu Leu Ser Leu Phe Phe Ala Val Leu His Ala
1 5 10 15

Ile

<210> SEQ ID NO 79
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 79

Thr Arg Lys Gln Phe Gly Leu Leu Ser Leu Phe Phe Ala Val Leu His
1 5 10 15

Ala Ile Tyr

<210> SEQ ID NO 80
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 80

Asp Lys Trp Met Leu Thr Arg Lys Gln Phe Gly Leu Leu Ser Leu Phe
1 5 10 15

Phe Ala Val Leu His Ala Ile Tyr Ser Leu Ser Tyr Pro
20 25

<210> SEQ ID NO 81
<211> LENGTH: 3627
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 81

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gtgggtggct gaagccatac tattttatag aattaatgga aagcagaaaa gacatcacia 120
accaagaaga actttggaaa atgaagccta ggagaaattt agaagaagac gattatttgc 180
ataaggacac gggagagacc agcatgctaa aaagacctgt gcttttgcat ttgcaccaa 240
cagcccatgc tgatgaattt gactgccctt cagaacttca gcacacacag gaactctttc 300
cacagtggca cttgccaat aaaatagctg ctattatagc atctctgact tttctttaca 360
ctcttctgag ggaagtaatt cacccttag caacttccca tcaacaatat tttataaaa 420
ttccaatcct ggtcatcaac aaagtcttgc caatggtttc catcactctc ttggcattgg 480
tttacctgcc aggtgtgata gcagcaattg tccaacttca taatggaacc aagtataaga 540
agtttccaca ttggttggat aagtggatgt taacaagaaa gcagtttggg cttctcagtt 600
tcttttttgc tgtactgcat gcaatttata gtctgtctta cccaatgagg cgatcctaca 660
gatacaagtt gctaaactgg gcatatcaac aggtccaaca aaataaagaa gatgcctgga 720
ttgagcatga tgtttggaga atggagattt atgtgtctct gggaattgtg ggattggcaa 780

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tactggctct	gttggtgtg	acatctattc	catctgtgag	tgactctttg	acatggagag	840
aatttcacta	tattcaggta	aataatata	aaaataaccc	taagaggtaa	atcttctttt	900
tggttttatg	atatagaata	tggtgacttt	accccataaa	aaataacaaa	tgtttttcaa	960
cagcaaagat	cttatacttg	ttccaattaa	taatgtgctc	tcctgttggt	ttccctattg	1020
cttctaatta	ggacaagtgt	ttcctagaca	taaataaaag	gcattaaaat	attctttggt	1080
tttttttttt	tgtttgtttg	ttttttgttt	gtttgtttgt	ttttttgaga	tgaagtctcg	1140
ctctgttgcc	catgtcggag	tacagtggca	cgatctcggc	tcactgcaac	ctgcgcctcc	1200
tgggttcagg	cgattctctt	gcctcagcct	cctgagtagc	tgggattaca	ggcaccctac	1260
accatgtcca	gctaattttt	gtatttttag	tagagacagg	gttttcccat	gttgccagg	1320
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tgacagttgt	gagccaccac	actcagcctg	ctctttctaa	tatttgaaac	ttgttagaca	1440
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aaaaaaaata	ttctttttacc	tgtcacctga	atttagtaat	gccttttatg	ttacacaact	1560
tagcactttc	cagaacaaaa	aactctctcc	tgaaataaat	agagttttta	tctaccaaag	1620
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tctgacaaga	ttcaaaggac	taaatttaaat	tcagtcatga	acactgcaa	ttaccgttta	1860
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gtccacacgt	atactccaac	actttattag	gcctctgatt	agtttgaaa	gtatgcctcc	1980
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cacattgctc	tgctgtttac	acatatgatg	aacactgctt	tttagacttc	attaggaatt	2160
taggactgca	tcttgacaac	tgagcctatt	ctactatatg	tacaatacct	agcccataat	2220
aggtatacaa	tacacatttg	gtaaaactaa	ttttcaacca	atgacatgta	tttttcaact	2280
agtaacctag	aaatgtttca	cttaaaatct	gagaactggg	tacactacaa	gttaccttgg	2340
agattcatat	atgaaaacgc	aaacttagct	atttgattgt	attcactggg	acttaagaat	2400
gcgctgaat	aattgtgagt	tcgatttggt	ctggcaggct	aatgaccatt	tccagtaaag	2460
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tgaatgttt	catcacatct	ctggatctct	ctattttgtg	cagacattga	aaaaattggt	2640
catattat	ccatgttatc	agaatatttg	attttttaaa	aacataggcc	aagttcattc	2700
acttcattat	tcatttatca	aaatcagagt	gaatcacatt	agtcgccttc	acaactgata	2760
aagatcactg	aagtcaaatt	gatttttgct	ataatcttca	atctacctat	atttaattga	2820
gaatctaaaa	tgtacaaatc	attgtgttga	ttctgcagtg	atcctgctat	aagtaagact	2880
cagtcctga	ttttagggtat	cctgtgaaaa	gcagaattaa	gacaaataca	caagagacaa	2940
agcacaacaaa	ataaatatca	taaggggatg	aacaaaatgg	tggagaaaga	gtagacaaag	3000
tttttgatca	cctgccttca	aagaaaggct	gtgaattttg	ttcacttaga	cagcttgagg	3060

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acaagaaatt acccaaaagt aaggtagga ggataggcaa aaagagcaga aagatgtgaa	3120
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gagcatatcc agatgaggta ggatgggata aactcttatt gaaccaatct tcaccaattt	3240
tgtttttcct ttgcagagca agctaggaat tgtttccctt ctactgggca caatacacgc	3300
attgattttt gcctggaata agtggataga tataaaacaa tttgtatggt atacacctcc	3360
aacttttatg atagctgttt tccttccaat tgttgcctg atatttaaaa gcatactatt	3420
cctgccatgc ttgaggaaga agatactgaa gattagacat ggttgggaag acgtcaccaa	3480
aattaacaaa actgagatat gttcccagtt gtagaattac tgtttacaca catttttgtt	3540
caatattgat atattttatc accaacattt caagtttgta tttgttaata aaatgattat	3600
tcaaggaaaa aaaaaaaaaa aaaaaaa	3627

<210> SEQ ID NO 82

<211> LENGTH: 1193

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 82

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aattaatgga aagcagaaaa gacatcacia accaagaaga actttggaaa atgaagccta	120
ggagaaattt agaagaagac gattatttgc ataaggacac gggagagacc agcatgctaa	180
aaagacctgt gcttttgcac ttgcacaaaa cagcccatgc tgatgaattt gactgccctt	240
cagaacttca gcacacacag gaactcttcc cacagtggca cttgccaatt aaaatagctg	300
ctattatagc atctctgact tttctttaca ctcttctgag ggaagtaatt caccctttag	360
caacttccca tcaacaatat ttttataaaa ttccaatcct ggtcatcaac aaagtcttgc	420
caatggtttc catcactctc ttggcattgg ttacctgcc aggtgtgata gcagcaattg	480
tccaacttca taatggaacc aagtataaga agtttccaca ttggttggat aagtggatgt	540
taacaagaaa gcagtttggg cttctcagtt tcttttttgc tgtactgcat gcaatttata	600
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aggtccaaca aaataaagaa gatgcctgga ttgagcatga tgtttggaga atggagattt	720
atgtgtctct gggaattgtg ggattggcaa tactggctct gttggctgtg acatctattc	780
catctgtgag tgactctttg acatggagag aatttcacta tattcagagc aagctaggaa	840
ttgtttccct tctactgggc acaatacacg cattgatttt tgcttggaaat aagtggatag	900
atataaaaca atttgtatgg tatacacctc caacttttat gatagctggt ttcttccaa	960
ttgttgtcct gatatttaaa agcatactat tcctgccatg cttgaggaag aagatactga	1020
agattagaca tggttgggaa gacgtcacca aaattaacaa aactgagata tgttcccagt	1080
tgtagaatta ctgtttacac acatttttgt tcaatattga tatattttat caccaacatt	1140
tcaagtttgt atttgttaat aaaatgatta caaggaaaa aaaaaaaaaa aaa	1193

<210> SEQ ID NO 83

<211> LENGTH: 3627

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 83

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accaagaaga acttttgaaa atgaagccta ggagaaatth agaagaagac gattatttgc	180
ataaggacac gggagagacc agcatgctaa aaagacctgt gcttttgcac ttgcacaaa	240
cagcccatgc tgatgaatth gactgccctt cagaacttca gcacacacag gaactctttc	300
cacagtggca cttgccaat aaatagctg ctattatagc atctctgact tttctttaca	360
ctctctgag ggaagtaatt cacccttag caacttcca tcaacaatat tttataaaa	420
ttccaatcct ggtcatcaac aaagtcttgc caatggtttc catcactctc ttggcattgg	480
tttacctgcc aggtgtgata gcagcaattg tccaacttca taatggaacc aagtataaga	540
agtttcaca ttggttgat aagtggatgt taacaagaaa gcagtttggg cttctcagtt	600
tcttttttgc tgtactgcat gcaatttata gtctgtctta ccaatgagg cgatcctaca	660
gatacaagtt gctaaactgg gcatatcaac aggtccaaca aaataaagaa gatgcctgga	720
ttgagcatga tgtttggaga atggagatth atgtgtctct gggaattgtg ggattggcaa	780
tactggctct gttggctgtg acatctattc catctgtgag tgactctttg acatggagag	840
aatttcacta tattcaggt aataatatat aaaataacc taagaggtaa atcttctttt	900
tgtgtttatg atatagaata tgttgactth accccataaa aaataacaaa tgtttttcaa	960
cagcaaatgat cttatacttg ttccaattaa taatgtgtct tctgttgtt ttcctattg	1020
cttctaatta ggacaagtgt ttcctagaca taaataaaag gcattaaaat attctttgtt	1080
ttttttttt tgtttgttg tttttgtt gtttgttgt ttttttgaga tgaagtctcg	1140
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tgggttcagg cgattctctt gcctcagcct cctgagtagc tgggattaca ggcacccatc	1260
accatgtcca gtaattttt gtatttttag tagagacagg gttttcccat gttggccagg	1320
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tgacagtgtg gagccaccac actcagcctg ctctttctaa tatttgaaac ttgttagaca	1440
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aaaaaaaata tctttttacc tgtcacctga atttagtaat gccttttatg ttacacaact	1560
tagcactttc cagaaacaaa aactctctcc ttgaataaat agagttttta tctaccaaag	1620
atatgctagt gtctcatttc aaaggctgct tttccagct tacattttat atacttactc	1680
acttgaagtt tctaaatatt cttgtaatth taaaactatc tcagatttac tgaggtttat	1740
cttctggtgg tagattatcc ataagaagag tgatgtgcca gaatcactct gggatccttg	1800
tctgacaaga ttcaaaggac taaatttaat tcagtcatga aactgcaa ttaccgttta	1860
tgggttagaca tcttttgaaa tttccacaag gtcagacatt cgcaactatc ccttctacat	1920
gtccacacgt atactccaac actttattag gcacttgatt agtttgaaa gtatgcctcc	1980
atctgaatta gtccagtgtg gcttagagtt ggtacaacat tctcacagaa tttcctaatt	2040
ttgtagggtc agcctgataa ccaactggagt tctttgttcc tcattaaata gctttcttca	2100
cacattgctc tgcctgttac acatatgatg aacttgctt tttagacttc attaggaatt	2160
taggactgca tcttgacaac tgagcctatt ctactatatg tacaatacct agcccataat	2220
aggtatacaa tacacatttg gtaaaactaa ttttcaacca atgacatgta tttttcaact	2280

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agtaacctag aaatgtttca cttaaaatct gagaactggg tacactacaa gttaccttgg 2340
agattcatat atgaaaaacgc aaacttagct atttgattgt attcactggg acttaagaat 2400
gcgcctgaat aattgtgagt tcgatttgtt ctggcaggct aatgaccatt tccagtaaag 2460
tgaatagagg tcagaagtcg tataaaagag gtgttgctcag aacaccgttg agattacata 2520
ggtgaacaac tatttttaag caactttatt tgtgtagtga caaagcatcc caatgcaggc 2580
tgaaatgttt catcacatct ctggatctct ctattttgtg cagacattga aaaaattgtt 2640
catattatatt ccatgttatc agaataattg atttttttaa aacataggcc aagttcattc 2700
acttcattat tcatttatca aaatcagagt gaatcacatt agtcgccttc acaactgata 2760
aagatcactg aagtcaaatt gatttttgcg ataactctca atctacctat atttaattga 2820
gaatctaaaa tgtacaaatc attgtgttga ttctgcagtg atcctgctat aagtaagact 2880
cagtccctga ttttaggtat cctgtgaaaa gcagaattaa gacaaatata caagagacaa 2940
agcacaaaaa ataaatatca taaggggatg aacaaaatgg tggagaaaga gtagacaaag 3000
tttttgatca cctgccttca aagaaaggct gtgaattttg ttcacttaga cagcttgagg 3060
acaagaaatt acccaaaagt aagggtgagga ggataggcaa aaagagcaga aagatgtgaa 3120
tggacattgt tgagaaatgt gataggaaaa caatcataga taaaggattt ccaagcaaca 3180
gagcatatcc agatgaggta ggatgggata aactcttatt gaaccaatct tcaccaattt 3240
tgtttttctt ttgcagagca agctaggaat tgtttccctt ctactgggca caatacacgc 3300
attgattttt gcctggaata agtggataga tataaaacaa tttgtatggg atacacctcc 3360
aacttttatg atagctgttt tccttccaat tgttgtctg atatttaaaa gcatactatt 3420
cctgccatgc ttgaggaaga agatactgaa gattagacat ggttggaag acgtcaccaa 3480
aattaacaaa actgagatat gttcccagtt gtagaattac tgtttacaca catttttgtt 3540
caatattgat atattttatc accaaccatt caagtttgta tttgttaata aaatgattat 3600
tcaaggaaaa aaaaaaaaaa aaaaaaaa 3627

```

<210> SEQ ID NO 84

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 84

```

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1             5             10            15

```

```

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
20             25            30

```

```

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
35             40            45

```

```

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
50             55            60

```

```

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
65             70            75            80

```

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Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
85             90            95

```

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Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
100           105           110

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Val	Ile	Asn	Lys	Val	Leu	Pro	Met	Val	Ser	Ile	Thr	Leu	Leu	Ala	Leu
		115					120					125			
Val	Tyr	Leu	Pro	Gly	Val	Ile	Ala	Ala	Ile	Val	Gln	Leu	His	Asn	Gly
		130					135					140			
Thr	Lys	Tyr	Lys	Lys	Phe	Pro	His	Trp	Leu	Asp	Lys	Trp	Met	Leu	Thr
					150					155					160
Arg	Lys	Gln	Phe	Gly	Leu	Leu	Ser	Phe	Phe	Phe	Ala	Val	Leu	His	Ala
				165						170					175
Ile	Tyr	Ser	Leu	Ser	Tyr	Pro	Met	Arg	Arg	Ser	Tyr	Arg	Tyr	Lys	Leu
			180					185						190	
Leu	Asn	Trp	Ala	Tyr	Gln	Gln	Val	Gln	Gln	Asn	Lys	Glu	Asp	Ala	Trp
			195				200					205			
Ile	Glu	His	Asp	Val	Trp	Arg	Met	Glu	Ile	Tyr	Val	Ser	Leu	Gly	Ile
			210				215				220				
Val	Gly	Leu	Ala	Ile	Leu	Ala	Leu	Leu	Ala	Val	Thr	Ser	Ile	Pro	Ser
					230					235					240
Val	Ser	Asp	Ser	Leu	Thr	Trp	Arg	Glu	Phe	His	Tyr	Ile	Gln	Val	Asn
				245					250						255

Asn Ile

<210> SEQ ID NO 85

<211> LENGTH: 339

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 85

Met	Glu	Ser	Arg	Lys	Asp	Ile	Thr	Asn	Gln	Glu	Glu	Leu	Trp	Lys	Met
1				5					10					15	
Lys	Pro	Arg	Arg	Asn	Leu	Glu	Glu	Asp	Tyr	Leu	His	Lys	Asp	Thr	
			20					25				30			
Gly	Glu	Thr	Ser	Met	Leu	Lys	Arg	Pro	Val	Leu	Leu	His	Leu	His	Gln
			35				40					45			
Thr	Ala	His	Ala	Asp	Glu	Phe	Asp	Cys	Pro	Ser	Glu	Leu	Gln	His	Thr
			50			55					60				
Gln	Glu	Leu	Phe	Pro	Gln	Trp	His	Leu	Pro	Ile	Lys	Ile	Ala	Ala	Ile
					70					75					80
Ile	Ala	Ser	Leu	Thr	Phe	Leu	Tyr	Thr	Leu	Leu	Arg	Glu	Val	Ile	His
				85				90						95	
Pro	Leu	Ala	Thr	Ser	His	Gln	Gln	Tyr	Phe	Tyr	Lys	Ile	Pro	Ile	Leu
			100					105					110		
Val	Ile	Asn	Lys	Val	Leu	Pro	Met	Val	Ser	Ile	Thr	Leu	Leu	Ala	Leu
			115				120					125			
Val	Tyr	Leu	Pro	Gly	Val	Ile	Ala	Ala	Ile	Val	Gln	Leu	His	Asn	Gly
			130				135					140			
Thr	Lys	Tyr	Lys	Lys	Phe	Pro	His	Trp	Leu	Asp	Lys	Trp	Met	Leu	Thr
					150					155					160
Arg	Lys	Gln	Phe	Gly	Leu	Leu	Ser	Phe	Phe	Phe	Ala	Val	Leu	His	Ala
				165						170					175
Ile	Tyr	Ser	Leu	Ser	Tyr	Pro	Met	Arg	Arg	Ser	Tyr	Arg	Tyr	Lys	Leu
			180					185						190	
Leu	Asn	Trp	Ala	Tyr	Gln	Gln	Val	Gln	Gln	Asn	Lys	Glu	Asp	Ala	Trp
			195				200					205			

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Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
 210                215                220

Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
 225                230                235                240

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys
                245                250                255

Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe
                260                265                270

Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro
 275                280                285

Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe
 290                295                300

Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile
 305                310                315                320

Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile Cys
                325                330                335

Ser Gln Leu

```

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<210> SEQ ID NO 86
<211> LENGTH: 258
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 86

```

```

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1                5                10                15

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
 20                25                30

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
 35                40                45

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
 50                55                60

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
 65                70                75                80

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
 85                90                95

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
 100               105               110

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
 115               120               125

Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
 130               135               140

Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
 145               150               155               160

Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
 165               170               175

Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
 180               185               190

Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
 195               200               205

Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
 210               215               220

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Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
225 230 235 240

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn
245 250 255

Asn Ile

<210> SEQ ID NO 87

<211> LENGTH: 1365

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 87

```

ggggcccgca cctctgggca gcagcggcag ccgagactca cggccaagct aaggcgaaga    60
gtgggtggct gaagccatac tattttatag aattaatgga aagcagaaaa gacatcacia    120
accaagaaga actttggaaa atgaagccta ggagaaattht agaagaagac gattattttgc    180
ataaggacac gggagagacc agcatgctaa aaagacctgt gctttttgcat ttgcacaaa    240
cagcccatgc tgatgaattht gactgccctt cagaacttca gcacacacag gaactctttc    300
cacagtggca cttgccaatt aaaatagctg ctattatagc atctctgact tttctttaca    360
ctcttctgag ggaagtaatt cacccttttag caacttccca tcaacaatat tttataaaaa    420
ttccaatcct ggtcatcaac aaagtcttgc caatggtttc catcactctc ttggcattgg    480
tttacctgcc aggtgtgata gcagcaattg tccaacttca taatggaacc aagtataaga    540
agtttccaca ttggttggat aagtggatgt taacaagaaa gcagtttggg cttctcagtt    600
tcttttttgc tgtactgcat gcaatttata gtctgtctta ccaatgagg cgatcctaca    660
gatacaagtt gctaaactgg gcatatcaac aggtccaaca aaataaagaa gatgcctgga    720
ttgagcatga tgtttggaga atggagattht atgtgtctct gggaaattgt ggattggcaa    780
tactggctct gttggctgtg acatctattc catctgtgag tgactctttg acatggagag    840
aatttcacta tattcagatt atccataaga agagtgatgt gccagaatca ctctgggatc    900
cttgtctgac aagattcaaa ggactaaatt taattcagtc atgaacactg ccaattaccg    960
tttatgggta gacatctttg gaaatttcca caagagcaag ctagggaattg tttcccttct    1020
actgggcaca atacacgcat tgatttttgc ctggaataag tggatagata taaaacaatt    1080
tgtatggtat acacctccaa cttttatgat agctgttttc cttccaattg ttgtcctgat    1140
atttaaaagc atactattcc tgccatgctt gaggaagaag atactgaaga ttagacatgg    1200
ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tcccagttgt agaattactg    1260
tttacacaca tttttgttca atattgatat attttatcac caacatttca agtttgtatt    1320
tgtaataaaa atgattattc aaggaaaaaa aaaaaaaaaa aaaaaa    1365

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<210> SEQ ID NO 88

<211> LENGTH: 3627

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 88

```

ggggcccgca cctctgggca gcagcggcag ccgagactca cggccaagct aaggcgaaga    60
gtgggtggct gaagccatac tattttatag aattaatgga aagcagaaaa gacatcacia    120
accaagaaga actttggaaa atgaagccta ggagaaattht agaagaagac gattattttgc    180

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ataaggacac	gggagagacc agcatgctaa aaagacctgt gcttttgcac ttgcacccaaa	240
cagcccatgc	tgatgaattt gactgccctt cagaacttca gcacacacag gaactctttc	300
cacagtggca	cttgccaatt aaaatagctg ctattatagc atctctgact tttctttaca	360
ctcttctgag	ggaagtaatt caccctctag caacttccca tcaacaatat ttttataaaa	420
ttccaatcct	ggtcacaaac aaagtcttgc caatggtttc catcactctc ttggcattgg	480
tttacctgcc	aggtgtgata gcagcaattg tccaacttca taatggaacc aagtataaga	540
agtttccaca	ttggttggat aagtggatgt taacaagaaa gcagtttggg cttctcagtt	600
tcttttttgc	tgtactgcat gcaatttata gtctgtctta cccaatgagg cgatcctaca	660
gatacaagtt	gctaaactgg gcatatcaac aggtccaaca aaataaagaa gatgcctgga	720
ttgagcatga	tgtttggaga atggagattt atgtgtctct gggaaattgtg ggattggcaa	780
tactggctct	gttggctgtg acatctattc catctgtgag tgactctttg acatggagag	840
aatttcacta	tattcaggtt aataatatat aaaataacct taagaggtaa atcttctttt	900
tgtgtttatg	atatagaata tgttgacttt accccataaa aaataacaaa tgtttttcaa	960
cagcaaagat	cttatacttg ttccaattaa taatgtgctc tcctgttgtt ttccctattg	1020
cttctaatta	ggacaagtgt ttcctagaca taaataaaag gcattaaaat attctttgtt	1080
tttttttttt	tgtttgtttg tttttgtttt gtttgtttgt ttttttgaga tgaagtctcg	1140
ctctgttgcc	catgtctggag tacagtggca cgatctcggc tcaactgcaac ctgcgcctcc	1200
tgggttcagg	cgattctctt gcctcagcct cctgagtagc tgggattaca ggcacccatc	1260
accatgtcca	gctaattttt gtatttttag tagagacagg gttttcccat gttggccagg	1320
ctggctcga	tctcctgacc tcaaagtac cgccacctc ggccctccaa agtgctggga	1380
tgacagtgtg	gagccaccac actcagcctg ctctttctaa tatttgaaac ttgttagaca	1440
atttgctacc	catcctaagt gatattttag gaatccaata tgcatggttt attatttctt	1500
aaaaaaaata	ttcttttacc tgtcacctga atttagtaat gccttttatg ttacacaact	1560
tagcactttc	cagaaacaaa aactctctcc ttgaaataat agagttttta tctaccaaag	1620
atatgctagt	gtctcatttc aaaggctgct ttttccagct tacattttat ataactactc	1680
acttgaagtt	tctaaatatt cttgtaattt taaaactatc tcagatttac tgaggtttat	1740
cttctggtgg	tagatttatcc ataagaagag tgatgtgcca gaatcactct gggatccttg	1800
tctgacaaga	ttcaaaggac taaatttaat tcagtcatga acaactgcaa ttaccgttta	1860
tgggtagaca	tctttggaaa tttccacaag gtcagacatt cgcaactatc ccttctacat	1920
gtccacacgt	atactccaac actttattag gcactctgatt agtttgaaa gtatgcctcc	1980
atctgaatta	gtccagtgtg gcttagagtt ggtacaacat tctcacagaa tttcctaatt	2040
ttgtaggttc	agcctgataa ccaactggagt tctttgttcc tcattaaata gctttcttca	2100
cacattgctc	tgctgtttac acatatgatg aacactgctt ttttagacttc attaggaatt	2160
taggactgca	tcttgacaac tgagcctatt ctactatatg tacaatacct agcccataat	2220
aggtatacaa	tacacatttg gtaaaactaa ttttcaacca atgacatgta tttttcaact	2280
agtaacctag	aaatgtttca cttaaaatct gagaactggt tacactacaa gttaccttgg	2340
agattcatat	atgaaaacgc aaacttagct atttgattgt attcactggg acttaagaat	2400
gcgcctgaat	aattgtgagt tcgatttgtt ctggcaggct aatgaccatt tccagtaaa	2460

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tgaatagagg tcagaagtcg tataaaagag gtgttgctag aacaccgttg agattacata	2520
ggtgaacaac tatttttaag caactttatt tgtgtagtga caaagcatcc caatgcaggc	2580
tgaaatgttt catcacatct ctggatctct ctattttgtg cagacattga aaaaattgtt	2640
catattatct ccatgttatt agaataattg attttttaaa aacataggcc aagttcattc	2700
acttcattat tcatttatca aaatcagagt gaatcacatt agtcgccttc acaactgata	2760
aagatcactg aagtcaaatt gatttttgct ataactctca atctacctat atttaattga	2820
gaatctaaaa tgtacaaatc attgtgttga ttctgcagtg atcctgctat aagtaagact	2880
cagtccctga ttttaggtat cctgtgaaaa gcagaattaa gacaaatata caagagacaa	2940
agcacaaaa ataaatatca taaggggatg aacaaaatgg tggagaaaga gtagacaaag	3000
tttttgatca cctgccttca aagaaaggct gtgaattttg ttcacttaga cagcttgagg	3060
acaagaaatt acccaaaagt aaggtaggga ggataggcaa aaagagcaga aagatgtgaa	3120
tggacattgt tgagaaatgt gataggaaaa caatcataga taaaggattt ccaagcaaca	3180
gagcatatcc agatgaggta ggatgggata aactcttatt gaaccaatct tcaccaattt	3240
tgtttttctt ttgcagagca agctaggaat tgtttccctt ctactgggca caatacacgc	3300
attgattttt gcctggaata agtgataga tataaaacaa tttgtatggg atacacctcc	3360
aacttttatg atagctgttt tccttccaat tggtgtcctg atatttataa gcatactatt	3420
cctgccatgc ttgaggaaga agatactgaa gattagacat ggttgggaag acgtcaccaa	3480
aattaacaaa actgagatat gttcccagtt gtagaattac tgtttacaca catttttgtt	3540
caatattgat atattttatc accaactttt caagtttgta tttgttaata aaatgattat	3600
tcaaggaaaa aaaaaaaaaa aaaaaaa	3627

<210> SEQ ID NO 89

<211> LENGTH: 1365

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 89

ggggcccgca cctctgggca gcagcggcag ccgagactca cggtaagct aaggcgaaga	60
gtgggtggct gaagccatac tattttatag aattaatgga aagcagaaaa gacatcacia	120
accaagaaga actttggaaa atgaagccta ggagaaattt agaagaagac gattatttgc	180
ataaggacac gggagagacc agcatgctaa aaagacctgt gcttttgcac ttgcacaaaa	240
cagcccatgc tgatgaattt gactgccctt cagaacttca gcacacacag gaactctttc	300
cacagtggca ctgccaatt aaaatagctg ctattatagc atctctgact tttctttaca	360
ctctctctgag ggaagtaatt caccctttag caacttccca tcaacaatat ttttataaaa	420
ttccaatcct ggtcatcaac aaagtcttgc caatgggttc catcactctc ttggcattgg	480
tttacctgcc aggtgtgata gcagcaattg tccaacttca taatggaacc aagtataaga	540
agtttccaca ttggttgat aagtggatgt taacaagaaa gcagtttggg cttctcagtt	600
tcttttttgc tgtactgcat gcaatttata gtctgtctta ccaatgagg cgatcctaca	660
gatacaagtt gctaaactgg gcatatcaac aggtccaaca aaataaagaa gatgcctgga	720
ttgagcatga tgtttggaga atggagattt atgtgtctct gggaaattgt ggattggcaa	780
tactggctct gttggctgtg acatctattc catctgtgag tgactctttg acatggagag	840

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aatttcacta tattcagatt atccataaga agagtgatgt gccagaatca ctctgggatac 900
cttgtctgac aagattcaaa ggactaaatt taattcagtc atgaacactg ccaattaccg 960
tttatgggta gacatctttg gaaattttcca caagagcaag ctagggaattg tttcccttct 1020
actgggcaca atacacgcat tgatttttgc ctggaataag tggatagata taaaacaatt 1080
tgtatgggat acacctccaa cttttatgat agctgttttc cttccaattg ttgtcctgat 1140
atttaaaagc atactattcc tgccatgctt gaggaagaag atactgaaga ttagacatgg 1200
ttgggaagac gtcacaaaaa ttaacaaaac tgagatatgt tcccagttgt agaattactg 1260
tttacacaca tttttgttca atattgatat attttatcac caacatttca agtttgtatt 1320
tgtaataaaa atgattattc aaggaaaaaa aaaaaaaaaa aaaaa 1365

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<210> SEQ ID NO 90

<211> LENGTH: 282

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 90

```

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1             5             10             15

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
          20             25             30

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
          35             40             45

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
 50             55             60

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
65             70             75             80

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
          85             90             95

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
          100            105            110

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
          115            120            125

Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
          130            135            140

Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
          145            150            155            160

Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
          165            170            175

Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
          180            185            190

Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
          195            200            205

Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
          210            215            220

Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
          225            230            235            240

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ile Ile
          245            250            255

His Lys Lys Ser Asp Val Pro Glu Ser Leu Trp Asp Pro Cys Leu Thr
          260            265            270

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Arg Phe Lys Gly Leu Asn Leu Ile Gln Ser
275 280

<210> SEQ ID NO 91

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 91

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
1 5 10 15

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
20 25 30

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
35 40 45

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
50 55 60

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
65 70 75 80

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
85 90 95

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
100 105 110

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
115 120 125

Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
130 135 140

Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
145 150 155 160

Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
165 170 175

Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
180 185 190

Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
195 200 205

Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
210 215 220

Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
225 230 235 240

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn
245 250 255

Asn Ile

<210> SEQ ID NO 92

<211> LENGTH: 282

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 92

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
1 5 10 15

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
20 25 30

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Gly	Glu	Thr	Ser	Met	Leu	Lys	Arg	Pro	Val	Leu	Leu	His	Leu	His	Gln
	35						40					45			
Thr	Ala	His	Ala	Asp	Glu	Phe	Asp	Cys	Pro	Ser	Glu	Leu	Gln	His	Thr
	50					55					60				
Gln	Glu	Leu	Phe	Pro	Gln	Trp	His	Leu	Pro	Ile	Lys	Ile	Ala	Ala	Ile
65					70					75					80
Ile	Ala	Ser	Leu	Thr	Phe	Leu	Tyr	Thr	Leu	Leu	Arg	Glu	Val	Ile	His
			85						90					95	
Pro	Leu	Ala	Thr	Ser	His	Gln	Gln	Tyr	Phe	Tyr	Lys	Ile	Pro	Ile	Leu
		100						105					110		
Val	Ile	Asn	Lys	Val	Leu	Pro	Met	Val	Ser	Ile	Thr	Leu	Leu	Ala	Leu
		115					120					125			
Val	Tyr	Leu	Pro	Gly	Val	Ile	Ala	Ala	Ile	Val	Gln	Leu	His	Asn	Gly
	130					135					140				
Thr	Lys	Tyr	Lys	Lys	Phe	Pro	His	Trp	Leu	Asp	Lys	Trp	Met	Leu	Thr
145					150					155					160
Arg	Lys	Gln	Phe	Gly	Leu	Leu	Ser	Phe	Phe	Phe	Ala	Val	Leu	His	Ala
				165					170					175	
Ile	Tyr	Ser	Leu	Ser	Tyr	Pro	Met	Arg	Arg	Ser	Tyr	Arg	Tyr	Lys	Leu
		180						185					190		
Leu	Asn	Trp	Ala	Tyr	Gln	Gln	Val	Gln	Gln	Asn	Lys	Glu	Asp	Ala	Trp
	195						200					205			
Ile	Glu	His	Asp	Val	Trp	Arg	Met	Glu	Ile	Tyr	Val	Ser	Leu	Gly	Ile
	210					215					220				
Val	Gly	Leu	Ala	Ile	Leu	Ala	Leu	Leu	Ala	Val	Thr	Ser	Ile	Pro	Ser
225					230					235					240
Val	Ser	Asp	Ser	Leu	Thr	Trp	Arg	Glu	Phe	His	Tyr	Ile	Gln	Ile	Ile
				245					250					255	
His	Lys	Lys	Ser	Asp	Val	Pro	Glu	Ser	Leu	Trp	Asp	Pro	Cys	Leu	Thr
			260					265					270		
Arg	Phe	Lys	Gly	Leu	Asn	Leu	Ile	Gln	Ser						
	275						280								

<210> SEQ ID NO 93

<211> LENGTH: 339

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 93

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

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Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
  115                      120                      125

Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
  130                      135                      140

Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
  145                      150                      155                      160

Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
      165                      170                      175

Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
      180                      185                      190

Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
      195                      200                      205

Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
      210                      215                      220

Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
  225                      230                      235                      240

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys
      245                      250                      255

Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe
      260                      265                      270

Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro
      275                      280                      285

Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe
      290                      295                      300

Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile
  305                      310                      315                      320

Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile Cys
      325                      330                      335

Ser Gln Leu

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<210> SEQ ID NO 94

<211> LENGTH: 258

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 94

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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
  1                      5                      10                      15

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
      20                      25                      30

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
      35                      40                      45

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
      50                      55                      60

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
  65                      70                      75                      80

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
      85                      90                      95

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
      100                      105                      110

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
      115                      120                      125

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Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
 130 135 140

Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
 145 150 155 160

Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
 165 170 175

Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
 180 185 190

Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
 195 200 205

Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
 210 215 220

Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
 225 230 235 240

Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Val Asn
 245 250 255

Asn Ile

<210> SEQ ID NO 95
 <211> LENGTH: 282
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <400> SEQUENCE: 95

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
 1 5 10 15

Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
 20 25 30

Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
 35 40 45

Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
 50 55 60

Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
 65 70 75 80

Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
 85 90 95

Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
 100 105 110

Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
 115 120 125

Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly
 130 135 140

Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr
 145 150 155 160

Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala
 165 170 175

Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu
 180 185 190

Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp
 195 200 205

Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile
 210 215 220

-continued

Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser
225 230 235 240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ile Ile
245 250 255
His Lys Lys Ser Asp Val Pro Glu Ser Leu Trp Asp Pro Cys Leu Thr
260 265 270
Arg Phe Lys Gly Leu Asn Leu Ile Gln Ser
275 280

<210> SEQ ID NO 96
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 96

gacaucaaaa accaagaag

19

<210> SEQ ID NO 97
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 97

guggauagau auaaaacaa

19

<210> SEQ ID NO 98
<211> LENGTH: 19
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 98

gccuucccau ugugcuccc

19

<210> SEQ ID NO 99
<211> LENGTH: 339
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 99

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
1 5 10 15
Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr
20 25 30
Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln
35 40 45
Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr
50 55 60
Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile
65 70 75 80
Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His
85 90 95
Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu
100 105 110
Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu
115 120 125
Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly

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130	135	140
Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr		
145	150	155 160
Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala		
	165	170 175
Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu		
	180	185 190
Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp		
	195	200 205
Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile		
	210	215 220
Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser		
	225	230 235 240
Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys		
	245	250 255
Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe		
	260	265 270
Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro		
	275	280 285
Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe		
	290	295 300
Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile		
	305	310 315 320
Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile Cys		
	325	330 335
Ser Gln Leu		

<210> SEQ ID NO 100

<211> LENGTH: 303

<212> TYPE: PRT

<213> ORGANISM: Mus musculus

<400> SEQUENCE: 100

Met Leu Lys Arg Pro Gly Leu Ser His Leu Gln His Ala Val His Val		
1	5	10 15
Asp Ala Phe Asp Cys Pro Ser Glu Leu Gln His Thr Gln Glu Phe Phe		
	20	25 30
Pro Asn Trp Arg Leu Pro Val Lys Val Ala Ala Ile Ile Ser Ser Leu		
	35	40 45
Thr Phe Leu Tyr Thr Leu Leu Arg Glu Ile Ile Tyr Pro Leu Val Thr		
	50	55 60
Ser Arg Glu Gln Tyr Phe Tyr Lys Ile Pro Ile Leu Val Ile Asn Lys		
	65	70 75 80
Val Leu Pro Met Val Ala Ile Thr Leu Leu Ala Leu Val Tyr Leu Pro		
	85	90 95
Gly Glu Leu Ala Ala Val Val Gln Leu Arg Asn Gly Thr Lys Tyr Lys		
	100	105 110
Lys Phe Pro Pro Trp Leu Asp Arg Trp Met Leu Ala Arg Lys Gln Phe		
	115	120 125
Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala Val Tyr Ser Leu		
	130	135 140
Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu Leu Asn Trp Ala		

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145	150	155	160
Tyr Lys Gln Val Gln Gln Asn Lys Glu Asp Ala Trp Val Glu His Asp	165	170	175
Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile Val Gly Leu Ala	180	185	190
Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser Val Ser Asp Ser	195	200	205
Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys Leu Gly Ile Val	210	215	220
Ser Leu Leu Leu Gly Thr Val His Ala Leu Val Phe Ala Trp Asn Lys	225	230	235
Trp Val Asp Val Ser Gln Phe Val Trp Tyr Met Pro Pro Thr Phe Met	245	250	255
Ile Ala Val Phe Leu Pro Thr Leu Val Leu Ile Cys Lys Ile Ala Leu	260	265	270
Cys Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile Arg Cys Gly Trp	275	280	285
Glu Asp Val Ser Lys Ile Asn Arg Thr Glu Met Ala Ser Arg Leu	290	295	300

1.-32. (canceled)

33. A method of inhibiting growth of cancer cells that express a protein of **FIG. 2** (SEQ ID NO: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, or 35), the method comprising:

administering to the cells an effective amount of a substance that modulates the status of a protein of **FIG. 2** (SEQ ID NO: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, or 35).

34. The method of claim 52

wherein substance is an antibody or a fragment thereof that specifically binds to a polypeptide of **FIG. 2** (SEQ ID NO: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, or 35).

35. The method of claim 33

wherein said substance is a STEAP-1-related protein.

36. The method of claim 33

wherein said substance is a polynucleotide comprising a coding sequence for a STEAP-1-related protein or comprising a polynucleotide complementary to a coding sequence for a STEAP-1-related protein.

37. The method of claim 33

wherein said substance is a ribozyme that cleaves a polynucleotide that encodes a protein of **FIG. 2** (SEQ ID NO: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, or 35).

38. The method of claim 33 wherein said cancer cells express a protein of **FIG. 2** and a particular HLA molecule, and the method comprises

administering human T cells to said cancer cells, wherein said T cells specifically recognize a peptide subsequence of a protein of **FIG. 2** while the subsequence is in context of the particular HLA molecule.

39. A method of claim 33, the method comprising steps of:

administering a vector that delivers a nucleotide that encodes a single chain monoclonal antibody, whereby the encoded single chain monoclonal antibody is expressed intracellularly within cancer cells that express a protein of **FIG. 2** (SEQ ID NO: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, or 35).

40.-51. (canceled)

52. The method of claim 33 wherein said substance comprises an antibody or an antibody fragment that specifically binds to a protein of **FIG. 2** (SEQ ID NO: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, or 35).

53. The method of claim 34 wherein said substance is a monoclonal antibody or a fragment thereof.

54. The method of claim 53 wherein said substance is a human antibody, a humanized antibody or a chimeric antibody, of a fragment thereof.

55. The method of claim 53 wherein said cancer is selected from the group consisting of prostate cancer, gastric cancer colorectal cancer; multiple myeloma, B-cell lymphoma, leukemia, breast cancer, kidney cancer, bladder cancer, and lung cancer.

56. The method of claim 55 wherein said cancer is metastatic.

57. The method of claim 56 wherein said cancer is metastatic prostate cancer.

58. The method of claim 34 wherein the growth of said cancer cells is inhibited in a human patient.

59. The method of claim 58 wherein said human patient has been diagnosed with prostate cancer.

60. The method of claim 59 wherein said prostate cancer is advanced or metastatic prostate cancer.

61. The method of claim 59 wherein said human patient has received one or more rounds of chemotherapy prior to the administration of said antibody or antibody fragment.

62. The method of claim 58 wherein said antibody or antibody fragment is administered in conjunction with radiation, chemotherapy or hormone ablation.

63. The method of claim 58 wherein said antibody or antibody fragment is conjugated to a toxin, a radioisotope, or a chemotherapeutic agent.

64. The method of claim 63 wherein said chemotherapeutic agent is a maytansinoid.

65. The method of claim 58 wherein said human patient is diagnosed with breast cancer.

66. The method of claim 65 wherein said antibody or antibody fragment is co-administered with another cancer therapeutic agent.

67. The method of claim 66 wherein the other cancer therapeutic agent is trastuzumab or paclitaxel.

* * * * *