and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and the example are illustrative only and not intended to be limiting.

The details of one or more embodiments featured in the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages featured in the invention will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF DRAWINGS

FIG. 1 is a snapshot of the sequencing reads illustrating that there are RET read pairs that map on one end to 5'KIF5B and on the other end to 3'RET, and other RET read pairs that map on one end to 5'RET and on the other end to 3'KIFB.

FIGs. 2A and 2B are schematic diagrams illustrating the inversion event that brings together exon 15 of KIF5B and exon 12 of RET. FIGs 2A and 2B disclose SEQ ID NOS 6 and 7, respectively.

FIGs. 3A to 3D are the predicted cDNA sequence (SEQ ID NO:1) and protein sequence of the KIF5B-RET fusion (SEQ ID NO:2). The KIF5B portion of the cDNA sequence is equivalent to nucleotides 471-2195 of RefSeq NM_004521.2, and the KIF5B portion of the protein sequence is equivalent to amino acids 1-575 of RefSeq NP_004512. The KIF5B portions of the cDNA and protein sequences are underlined. The RET portion of the cDNA sequence is equivalent to nucleotides 2327-3535 of RefSeq NM_020975, and the RET portion of the protein sequence is equivalent to amino acids 713-1114 of RefSeq NP_066124.1. The intact tyrosine kinase domain of RET is represented by a gray box (see FIG. 3C).

FIGs. 4A to 4D are the predicted cDNA sequence (SEQ ID NO:3) and protein sequence of the RET-KIF5B fusion (SEQ ID NO:4). The cDNA sequence of the RET portion of the fusion transcript is equivalent to nucleotides 190-2326 of RefSeq NM_020975, and the protein sequence is equivalent to amino acids 1-712 of RefSeq NP_066124.1. The cDNA sequence of the KIF5B portion of the fusion transcript is equivalent to nucleotides 2196-3362 of RefSeq NM_004521.2, and the protein portion is equivalent to amino acids 576-963 of RefSeq NP_004512. The KIF5B portions of the cDNA and protein sequences are underlined.

FIG. 5 is a summary of the DNA alterations identified in colorectal cancer cells.

FIG. 6A provides a schematic representation of the 11,294,741 bp inversion in NSCLC that generates an in-frame *KIF5B-RET* gene fusion (not to scale). The inverted region of chromosome 10 starts at 32,316,377 bps (within *KIF5B* intron 15) and ends at 43,611,118 bps (within *RET* intron 11).

FIG. 6B is a schematic of the protein domain structure of the *RET-KIF5B and KIF5B-RET* gene fusions. The cadherin domain of *RET* is included in the predicted *RET-KIF5B* protein. The kinesin and coiled coil domains of *KIF5B* and the tyrosine kinase domain of *RET* are included in the *KIF5B-RET* fusion protein. RT-PCR of primer designed to *RET* exon 11 and *KIF5B* exon 16 yielded no product. RT-PCR of primer designed to KIF5B exon 15 and RET exon 12 yielded a strong product (data not shown).

FIG. 6C is a photograph depicting the distribution of RET expression in the case of NSCLC with confirmed RET fusion on DNA sequencing by NGS. Note focal moderate cytoplasmic immunoreactivity for RET protein expression (avidin-biotin perxodase X 200). High magnification detail of cytoplasmic immunostaining for RET is shown in the insert at the lower right.

FIG. 6D is a summary of the exons present or absent in the KIF5B-RET fusion.

FIG. 7A provides another schematic representation of the KIF5B-RET fusion. This variant was identified in 8 CRC cases, where KIF5B exon 15 is fused in-frame to RET exon 12. The predicted full length fusion protein is 977 amino acids in length, with amino acids 1-575 derived from KIF5B and amino acids 576-977 derived from RET (shown above). Capillary sequence confirmation of the exon junction boundaries derived from cDNA is shown below. FIG. 7A discloses SEQ ID NO: 8.

Figure 7B is another representation of the predicted KIF5B-RET variant amino acid sequence (SEQ ID NO: 9).

FIG. 8 is a graph showing the effects of different drugs on Ba/F3 cells transfected with KIF5B-RET fusion constructs.

FIG. 9 is a Western blot showing the effects of sunitinib and gefitinib on RET phosphorylation in Ba/R3 cells expressing KIF5B-RET.

The Tables are described herein.

commercial suppliers, such as Agilent Technologies, Inc., and amplified using known nucleic acid amplification methods.

Each bait sequence can include a target-specific (*e.g.*, a member-specific) bait sequence and universal tails on each end. As used herein, the term "bait sequence" can refer to the target-specific bait sequence or the entire oligonucleotide including the target-specific "bait sequence" and other nucleotides of the oligonucleotide. In one embodiment, a target-specific bait hybridizes to a nucleic acid sequence comprising a nucleic acid sequence in intron 15 of KIF5B, in intron 11 of RET, or a fusion junction joining exon 15 of KIF5B and exon 12 of RET.

In one embodiment, the bait is an oligonucleotide about 200 nucleotides in length, of which 170 nucleotides are target-specific "bait sequence". The other 30 nucleotides (*e.g.*, 15 nucleotides on each end) are universal arbitrary tails used for PCR amplification. The tails can be any sequence selected by the user. For example, the pool of synthetic oligonucleotides can include oligonucleotides of the sequence of 5'-ATCGCACCAGCGTGTN$_{170}$CACTGCGGCTCCTCA-3' (SEQ ID NO: 5) with N$_{170}$ indicating the target-specific bait sequences.

The bait sequences described herein can be used for selection of exons and short target sequences. In one embodiment, the bait is between about 100 nucleotides and 300 nucleotides in length. In another embodiment, the bait is between about 130 nucleotides and 230 nucleotides in length. In yet another embodiment, the bait is between about 150 nucleotides and 200 nucleotides in length. The target-specific sequences in the baits, *e.g.*, for selection of exons and short target sequences, are between about 40 nucleotides and 1000 nucleotides in length. In one embodiment, the target-specific sequence is between about 70 nucleotides and 300 nucleotides in length. In another embodiment, the target-specific sequence is between about 100 nucleotides and 200 nucleotides in length. In yet another embodiment, the target-specific sequence is between about 120 nucleotides and 170 nucleotides in length.

Sequencing

The invention also includes methods of sequencing nucleic acids. In one embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence at least a portion of a KIF5B-RET fusion. In one embodiment, the

SEQUENCE LISTING

<110> FOUNDATION MEDICINE, INC.

<120> NOVEL KIF5B-RET FUSION MOLECULES AND USES THEREOF

<130> F2036-7025WO

<140> PCT/US2012/051978
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cct ctc aac gag tct gaa gtg aac cgc ggc gac aag tac atc gcc aag        96
Pro Leu Asn Glu Ser Glu Val Asn Arg Gly Asp Lys Tyr Ile Ala Lys
            20                  25                  30

ttt cag gga gaa gac acg gtc gtg atc gcg tcc aag cct tat gca ttt       144
Phe Gln Gly Glu Asp Thr Val Val Ile Ala Ser Lys Pro Tyr Ala Phe
        35                  40                  45

gat cgg gtg ttc cag tca agc aca tct caa gag caa gtg tat aat gac       192
Asp Arg Val Phe Gln Ser Ser Thr Ser Gln Glu Gln Val Tyr Asn Asp
    50                  55                  60

tgt gca aag aag att gtt aaa gat gta ctt gaa gga tat aat gga aca       240
Cys Ala Lys Lys Ile Val Lys Asp Val Leu Glu Gly Tyr Asn Gly Thr
65                  70                  75                  80

ata ttt gca tat gga caa aca tcc tct ggg aag aca cac aca atg gag       288
Ile Phe Ala Tyr Gly Gln Thr Ser Ser Gly Lys Thr His Thr Met Glu
                85                  90                  95

ggt aaa ctt cat gat cca gaa ggc atg gga att att cca aga ata gtg       336
Gly Lys Leu His Asp Pro Glu Gly Met Gly Ile Ile Pro Arg Ile Val
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        115                 120                 125

cat att aag gtt tca tat ttt gaa ata tat ttg gat aag ata agg gac      432
His Ile Lys Val Ser Tyr Phe Glu Ile Tyr Leu Asp Lys Ile Arg Asp
    130                 135                 140

ctg tta gat gtt tca aag acc aac ctt tca gtt cat gaa gac aaa aac      480
Leu Leu Asp Val Ser Lys Thr Asn Leu Ser Val His Glu Asp Lys Asn
145                 150                 155                 160

cga gtt ccc tat gta aag ggg tgc aca gag cgt ttt gta tgt agt cca      528
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                165                 170                 175

gat gaa gtt atg gat acc ata gat gaa gga aaa tcc aac aga cat gta      576
Asp Glu Val Met Asp Thr Ile Asp Glu Gly Lys Ser Asn Arg His Val
            180                 185                 190

gca gtt aca aat atg aat gaa cat agc tct agg agt cac agt ata ttt      624
Ala Val Thr Asn Met Asn Glu His Ser Ser Arg Ser His Ser Ile Phe
        195                 200                 205

ctt att aat gtc aaa caa gag aac aca caa acg gaa caa aag ctg agt      672
Leu Ile Asn Val Lys Gln Glu Asn Thr Gln Thr Glu Gln Lys Leu Ser
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gga aaa ctt tat ctg gtt gat tta gct ggt agt gaa aag gtt agt aaa      720
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225                 230                 235                 240

act gga gct gaa ggt gct gtg ctg gat gaa gct aaa aac atc aac aag      768
Thr Gly Ala Glu Gly Ala Val Leu Asp Glu Ala Lys Asn Ile Asn Lys
                245                 250                 255

tca ctt tct gct ctt gga aat gtt att tct gct ttg gct gag ggt agt      816
Ser Leu Ser Ala Leu Gly Asn Val Ile Ser Ala Leu Ala Glu Gly Ser
            260                 265                 270

aca tat gtt cca tat cga gat agt aaa atg aca aga atc ctt caa gat      864
Thr Tyr Val Pro Tyr Arg Asp Ser Lys Met Thr Arg Ile Leu Gln Asp
        275                 280                 285

tca tta ggt ggc aac tgt aga acc act att gta att tgc tgc tct cca      912
Ser Leu Gly Gly Asn Cys Arg Thr Thr Ile Val Ile Cys Cys Ser Pro
    290                 295                 300

tca tca tac aat gag tct gaa aca aaa tct aca ctc tta ttt ggc caa      960
Ser Ser Tyr Asn Glu Ser Glu Thr Lys Ser Thr Leu Leu Phe Gly Gln
305                 310                 315                 320

agg gcc aaa aca att aag aac aca gtt tgt gtc aat gtg gag tta act     1008
Arg Ala Lys Thr Ile Lys Asn Thr Val Cys Val Asn Val Glu Leu Thr
                325                 330                 335

gca gaa cag tgg aaa aag aag tat gaa aaa gaa aaa gaa aaa aat aag     1056
Ala Glu Gln Trp Lys Lys Lys Tyr Glu Lys Glu Lys Glu Lys Asn Lys
            340                 345                 350

atc ctg cgg aac act att cag tgg ctt gaa aat gag ctc aac aga tgg     1104
Ile Leu Arg Asn Thr Ile Gln Trp Leu Glu Asn Glu Leu Asn Arg Trp
        355                 360                 365

cgt aat ggg gag acg gtg cct att gat gaa cag ttt gac aaa gag aaa     1152
Arg Asn Gly Glu Thr Val Pro Ile Asp Glu Gln Phe Asp Lys Glu Lys
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385                 390                 395                 400

gat aaa cca gca acc gca att gga gtt ata gga aat ttt act gat gct      1248
Asp Lys Pro Ala Thr Ala Ile Gly Val Ile Gly Asn Phe Thr Asp Ala
                405                 410                 415

gaa aga aga aag tgt gaa gaa gaa att gct aaa tta tac aaa cag ctt      1296
Glu Arg Arg Lys Cys Glu Glu Glu Ile Ala Lys Leu Tyr Lys Gln Leu
            420                 425                 430

gat gac aag gat gaa gaa att aac cag caa agt caa ctg gta gag aaa      1344
Asp Asp Lys Asp Glu Glu Ile Asn Gln Gln Ser Gln Leu Val Glu Lys
        435                 440                 445

ctg aag acg caa atg ttg gat cag gag gag ctt ttg gca tct acc aga      1392
Leu Lys Thr Gln Met Leu Asp Gln Glu Glu Leu Leu Ala Ser Thr Arg
    450                 455                 460

agg gat caa gac aat atg caa gct gag ctg aat cgc ctt caa gca gaa      1440
Arg Asp Gln Asp Asn Met Gln Ala Glu Leu Asn Arg Leu Gln Ala Glu
465                 470                 475                 480

aat gat gcc tct aaa gaa gaa gtg aaa gaa gtt tta cag gcc cta gaa      1488
Asn Asp Ala Ser Lys Glu Glu Val Lys Glu Val Leu Gln Ala Leu Glu
                485                 490                 495

gaa ctt gct gtc aat tat gat cag aag tct cag gaa gtt gaa gac aaa      1536
Glu Leu Ala Val Asn Tyr Asp Gln Lys Ser Gln Glu Val Glu Asp Lys
            500                 505                 510

act aag gaa tat gaa ttg ctt agt gat gaa ttg aat cag aaa tcg gca      1584
Thr Lys Glu Tyr Glu Leu Leu Ser Asp Glu Leu Asn Gln Lys Ser Ala
        515                 520                 525

act tta gcg agt ata gat gct gag ctt cag aaa ctt aag gaa atg acc      1632
Thr Leu Ala Ser Ile Asp Ala Glu Leu Gln Lys Leu Lys Glu Met Thr
    530                 535                 540

aac cac cag aaa aaa cga gca gct gag atg atg gca tct tta cta aaa      1680
Asn His Gln Lys Lys Arg Ala Ala Glu Met Met Ala Ser Leu Leu Lys
545                 550                 555                 560

gac ctt gca gaa ata gga att gct gtg gga aat aat gat gta aag gag      1728
Asp Leu Ala Glu Ile Gly Ile Ala Val Gly Asn Asn Asp Val Lys Glu
                565                 570                 575

gat cca aag tgg gaa ttc cct cgg aag aac ttg gtt ctt gga aaa act      1776
Asp Pro Lys Trp Glu Phe Pro Arg Lys Asn Leu Val Leu Gly Lys Thr
            580                 585                 590

cta gga gaa ggc gaa ttt gga aaa gtg gtc aag gca acg gcc ttc cat      1824
Leu Gly Glu Gly Glu Phe Gly Lys Val Val Lys Ala Thr Ala Phe His
        595                 600                 605

ctg aaa ggc aga gca ggg tac acc acg gtg gcc gtg aag atg ctg aaa      1872
Leu Lys Gly Arg Ala Gly Tyr Thr Thr Val Ala Val Lys Met Leu Lys
    610                 615                 620

gag aac gcc tcc ccg agt gag ctg cga gac ctg ctg tca gag ttc aac      1920
Glu Asn Ala Ser Pro Ser Glu Leu Arg Asp Leu Leu Ser Glu Phe Asn
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Cys Ser Gln Asp Gly Pro Leu Leu Leu Ile Val Glu Tyr Ala Lys Tyr
            660                 665                 670

ggc tcc ctg cgg ggc ttc ctc cgc gag agc cgc aaa gtg ggg cct ggc      2064
Gly Ser Leu Arg Gly Phe Leu Arg Glu Ser Arg Lys Val Gly Pro Gly
        675                 680                 685

tac ctg ggc agt gga ggc agc cgc aac tcc agc tcc ctg gac cac ccg      2112
Tyr Leu Gly Ser Gly Gly Ser Arg Asn Ser Ser Ser Leu Asp His Pro
    690                 695                 700

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Asp Glu Arg Ala Leu Thr Met Gly Asp Leu Ile Ser Phe Ala Trp Gln
705                 710                 715                 720

atc tca cag ggg atg cag tat ctg gcc gag atg aag ctc gtt cat cgg      2208
Ile Ser Gln Gly Met Gln Tyr Leu Ala Glu Met Lys Leu Val His Arg
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gac ttg gca gcc aga aac atc ctg gta gct gag ggg cgg aag atg aag      2256
Asp Leu Ala Ala Arg Asn Ile Leu Val Ala Glu Gly Arg Lys Met Lys
            740                 745                 750

att tcg gat ttc ggc ttg tcc cga gat gtt tat gaa gag gat tcc tac      2304
Ile Ser Asp Phe Gly Leu Ser Arg Asp Val Tyr Glu Glu Asp Ser Tyr
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ggg att cct cct gag cgg ctc ttc aac ctt ctg aag acc ggc cac cgg      2496
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atg gag agg cca gac aac tgc agc gag gag atg tac cgc ctg atg ctg      2544
Met Glu Arg Pro Asp Asn Cys Ser Glu Glu Met Tyr Arg Leu Met Leu
        835                 840                 845

caa tgc tgg aag cag gag ccg gac aaa agg ccg gtg ttt gcg gac atc      2592
Gln Cys Trp Lys Gln Glu Pro Asp Lys Arg Pro Val Phe Ala Asp Ile
    850                 855                 860

agc aaa gac ctg gag aag atg atg gtt aag agg aga gac tac ttg gac      2640
Ser Lys Asp Leu Glu Lys Met Met Val Lys Arg Arg Asp Tyr Leu Asp
865                 870                 875                 880

ctt gcg gcg tcc act cca tct gac tcc ctg att tat gac gac ggc ctc      2688
Leu Ala Ala Ser Thr Pro Ser Asp Ser Leu Ile Tyr Asp Asp Gly Leu
                885                 890                 895

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            900                 905                 910

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    930                 935                 940

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945                 950                 955                 960

aac tgg atg ctt tca ccc tca gcg gca aaa tta atg gac acg ttt gat       2928
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Ser
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        35                  40                  45

Asp Arg Val Phe Gln Ser Ser Thr Ser Gln Glu Gln Val Tyr Asn Asp
    50                  55                  60

Cys Ala Lys Lys Ile Val Lys Asp Val Leu Glu Gly Tyr Asn Gly Thr
65                  70                  75                  80

Ile Phe Ala Tyr Gly Gln Thr Ser Ser Gly Lys Thr His Thr Met Glu
                85                  90                  95

Gly Lys Leu His Asp Pro Glu Gly Met Gly Ile Ile Pro Arg Ile Val
            100                 105                 110

Gln Asp Ile Phe Asn Tyr Ile Tyr Ser Met Asp Glu Asn Leu Glu Phe
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Leu Leu Asp Val Ser Lys Thr Asn Leu Ser Val His Glu Asp Lys Asn
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275 280 285

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355 360 365

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370 375 380

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515 520 525

Thr Leu Ala Ser Ile Asp Ala Glu Leu Gln Lys Leu Lys Glu Met Thr
530 535 540

Asn His Gln Lys Lys Arg Ala Ala Glu Met Met Ala Ser Leu Leu Lys
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Asp Leu Ala Glu Ile Gly Ile Ala Val Gly Asn Asn Asp Val Lys Glu
565 570 575

Asp Pro Lys Trp Glu Phe Pro Arg Lys Asn Leu Val Leu Gly Lys Thr
580 585 590

Leu Gly Glu Gly Glu Phe Gly Lys Val Val Lys Ala Thr Ala Phe His
595 600 605

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Glu Asn Ala Ser Pro Ser Glu Leu Arg Asp Leu Leu Ser Glu Phe Asn
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Cys Ser Gln Asp Gly Pro Leu Leu Leu Ile Val Glu Tyr Ala Lys Tyr
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Gly Ser Leu Arg Gly Phe Leu Arg Glu Ser Arg Lys Val Gly Pro Gly
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Tyr Leu Gly Ser Gly Gly Ser Arg Asn Ser Ser Ser Leu Asp His Pro
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Ile Ser Gln Gly Met Gln Tyr Leu Ala Glu Met Lys Leu Val His Arg
725 730 735

Asp Leu Ala Ala Arg Asn Ile Leu Val Ala Glu Gly Arg Lys Met Lys
740 745 750

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755 760 765

Val Lys Arg Ser Gln Gly Arg Ile Pro Val Lys Trp Met Ala Ile Glu
770 775 780

Ser Leu Phe Asp His Ile Tyr Thr Thr Gln Ser Asp Val Trp Ser Phe
785 790 795 800

Gly Val Leu Leu Trp Glu Ile Val Thr Leu Gly Gly Asn Pro Tyr Pro
805 810 815

Gly Ile Pro Pro Glu Arg Leu Phe Asn Leu Leu Lys Thr Gly His Arg
820 825 830

Met Glu Arg Pro Asp Asn Cys Ser Glu Glu Met Tyr Arg Leu Met Leu
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Gln Cys Trp Lys Gln Glu Pro Asp Lys Arg Pro Val Phe Ala Asp Ile
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Ser Lys Asp Leu Glu Lys Met Met Val Lys Arg Arg Asp Tyr Leu Asp
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Arg Ala Leu Pro Ser Thr Trp Ile Glu Asn Lys Leu Tyr Gly Met Ser
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Asp Pro Asn Trp Pro Gly Glu Ser Pro Val Pro Leu Thr Arg Ala Asp
930 935 940

Gly Thr Asn Thr Gly Phe Pro Arg Tyr Pro Asn Asp Ser Val Tyr Ala
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Ser

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ctg ctg ctg ccg ctg cta ggc aaa gtg gca ttg ggc ctc tac ttc tcg          96
Leu Leu Leu Pro Leu Leu Gly Lys Val Ala Leu Gly Leu Tyr Phe Ser
            20                  25                  30

agg gat gct tac tgg gag aag ctg tat gtg gac cag gca gcc ggc acg         144
Arg Asp Ala Tyr Trp Glu Lys Leu Tyr Val Asp Gln Ala Ala Gly Thr
        35                  40                  45

ccc ttg ctg tac gtc cat gcc ctg cgg gac gcc cct gag gag gtg ccc         192
Pro Leu Leu Tyr Val His Ala Leu Arg Asp Ala Pro Glu Glu Val Pro
    50                  55                  60

agc ttc cgc ctg ggc cag cat ctc tac ggc acg tac cgc aca cgg ctg         240
Ser Phe Arg Leu Gly Gln His Leu Tyr Gly Thr Tyr Arg Thr Arg Leu
65                  70                  75                  80

cat gag aac aac tgg atc tgc atc cag gag gac acc ggc ctc ctc tac         288
His Glu Asn Asn Trp Ile Cys Ile Gln Glu Asp Thr Gly Leu Leu Tyr
                85                  90                  95

ctt aac cgg agc ctg gac cat agc tcc tgg gag aag ctc agt gtc cgc         336
Leu Asn Arg Ser Leu Asp His Ser Ser Trp Glu Lys Leu Ser Val Arg
            100                 105                 110

aac cgc ggc ttt ccc ctg ctc acc gtc tac ctc aag gtc ttc ctg tca         384
Asn Arg Gly Phe Pro Leu Leu Thr Val Tyr Leu Lys Val Phe Leu Ser
        115                 120                 125

ccc aca tcc ctt cgt gag ggc gag tgc cag tgg cca ggc tgt gcc cgc         432
Pro Thr Ser Leu Arg Glu Gly Glu Cys Gln Trp Pro Gly Cys Ala Arg
    130                 135                 140

gta tac ttc tcc ttc ttc aac acc tcc ttt cca gcc tgc agc tcc ctc         480
Val Tyr Phe Ser Phe Phe Asn Thr Ser Phe Pro Ala Cys Ser Ser Leu
145                 150                 155                 160

aag ccc cgg gag ctc tgc ttc cca gag aca agg ccc tcc ttc cgc att         528
Lys Pro Arg Glu Leu Cys Phe Pro Glu Thr Arg Pro Ser Phe Arg Ile
                165                 170                 175

cgg gag aac cga ccc cca ggc acc ttc cac cag ttc cgc ctg ctg cct         576
Arg Glu Asn Arg Pro Pro Gly Thr Phe His Gln Phe Arg Leu Leu Pro
            180                 185                 190
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gtg cag ttc ttg tgc ccc aac atc agc gtg gcc tac agg ctc ctg gag        624
Val Gln Phe Leu Cys Pro Asn Ile Ser Val Ala Tyr Arg Leu Leu Glu
        195                 200                 205

ggt gag ggt ctg ccc ttc cgc tgc gcc ccg gac agc ctg gag gtg agc        672
Gly Glu Gly Leu Pro Phe Arg Cys Ala Pro Asp Ser Leu Glu Val Ser
    210                 215                 220

acg cgc tgg gcc ctg gac cgc gag cag cgg gag aag tac gag ctg gtg        720
Thr Arg Trp Ala Leu Asp Arg Glu Gln Arg Glu Lys Tyr Glu Leu Val
225                 230                 235                 240

gcc gtg tgc acc gtg cac gcc ggc gcg cgc gag gag gtg gtg atg gtg        768
Ala Val Cys Thr Val His Ala Gly Ala Arg Glu Glu Val Val Met Val
                245                 250                 255

ccc ttc ccg gtg acc gtg tac gac gag gac gac tcg gcg ccc acc ttc        816
Pro Phe Pro Val Thr Val Tyr Asp Glu Asp Asp Ser Ala Pro Thr Phe
            260                 265                 270

ccc gcg ggc gtc gac acc gcc agc gcc gtg gtg gag ttc aag cgg aag        864
Pro Ala Gly Val Asp Thr Ala Ser Ala Val Val Glu Phe Lys Arg Lys
        275                 280                 285

gag gac acc gtg gtg gcc acg ctg cgt gtc ttc gat gca gac gtg gta        912
Glu Asp Thr Val Val Ala Thr Leu Arg Val Phe Asp Ala Asp Val Val
    290                 295                 300

cct gca tca ggg gag ctg gtg agg cgg tac aca agc acg ctg ctc ccc        960
Pro Ala Ser Gly Glu Leu Val Arg Arg Tyr Thr Ser Thr Leu Leu Pro
305                 310                 315                 320

ggg gac acc tgg gcc cag cag acc ttc cgg gtg gaa cac tgg ccc aac       1008
Gly Asp Thr Trp Ala Gln Gln Thr Phe Arg Val Glu His Trp Pro Asn
                325                 330                 335

gag acc tcg gtc cag gcc aac ggc agc ttc gtg cgg gcg acc gta cat       1056
Glu Thr Ser Val Gln Ala Asn Gly Ser Phe Val Arg Ala Thr Val His
            340                 345                 350

gac tat agg ctg gtt ctc aac cgg aac ctc tcc atc tcg gag aac cgc       1104
Asp Tyr Arg Leu Val Leu Asn Arg Asn Leu Ser Ile Ser Glu Asn Arg
        355                 360                 365

acc atg cag ctg gcg gtg ctg gtc aat gac tca gac ttc cag ggc cca       1152
Thr Met Gln Leu Ala Val Leu Val Asn Asp Ser Asp Phe Gln Gly Pro
    370                 375                 380

gga gcg ggc gtc ctc ttg ctc cac ttc aac gtg tcg gtg ctg ccg gtc       1200
Gly Ala Gly Val Leu Leu Leu His Phe Asn Val Ser Val Leu Pro Val
385                 390                 395                 400

agc ctg cac ctg ccc agt acc tac tcc ctc tcc gtg agc agg agg gct       1248
Ser Leu His Leu Pro Ser Thr Tyr Ser Leu Ser Val Ser Arg Arg Ala
                405                 410                 415

cgc cga ttt gcc cag atc ggg aaa gtc tgt gtg gaa aac tgc cag gca       1296
Arg Arg Phe Ala Gln Ile Gly Lys Val Cys Val Glu Asn Cys Gln Ala
            420                 425                 430

ttc agt ggc atc aac gtc cag tac aag ctg cat tcc tct ggt gcc aac       1344
Phe Ser Gly Ile Asn Val Gln Tyr Lys Leu His Ser Ser Gly Ala Asn
        435                 440                 445

tgc agc acg cta ggg gtg gtc acc tca gcc gag gac acc tcg ggg atc       1392
Cys Ser Thr Leu Gly Val Val Thr Ser Ala Glu Asp Thr Ser Gly Ile
    450                 455                 460
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ctg ttt gtg aat gac acc aag gcc ctg cgg cgg ccc aag tgt gcc gaa      1440
Leu Phe Val Asn Asp Thr Lys Ala Leu Arg Arg Pro Lys Cys Ala Glu
465                 470                 475                 480

ctt cac tac atg gtg gtg gcc acc gac cag cag acc tct agg cag gcc      1488
Leu His Tyr Met Val Val Ala Thr Asp Gln Gln Thr Ser Arg Gln Ala
                485                 490                 495

cag gcc cag ctg ctt gta aca gtg gag ggg tca tat gtg gcc gag gag      1536
Gln Ala Gln Leu Leu Val Thr Val Glu Gly Ser Tyr Val Ala Glu Glu
            500                 505                 510

gcg ggc tgc ccc ctg tcc tgt gca gtc agc aag aga cgg ctg gag tgt      1584
Ala Gly Cys Pro Leu Ser Cys Ala Val Ser Lys Arg Arg Leu Glu Cys
        515                 520                 525

gag gag tgt ggc ggc ctg ggc tcc cca aca ggc agg tgt gag tgg agg      1632
Glu Glu Cys Gly Gly Leu Gly Ser Pro Thr Gly Arg Cys Glu Trp Arg
    530                 535                 540

caa gga gat ggc aaa ggg atc acc agg aac ttc tcc acc tgc tct ccc      1680
Gln Gly Asp Gly Lys Gly Ile Thr Arg Asn Phe Ser Thr Cys Ser Pro
545                 550                 555                 560

agc acc aag acc tgc ccc gac ggc cac tgc gat gtt gtg gag acc caa      1728
Ser Thr Lys Thr Cys Pro Asp Gly His Cys Asp Val Val Glu Thr Gln
                565                 570                 575

gac atc aac att tgc cct cag gac tgc ctc cgg ggc agc att gtt ggg      1776
Asp Ile Asn Ile Cys Pro Gln Asp Cys Leu Arg Gly Ser Ile Val Gly
            580                 585                 590

gga cac gag cct ggg gag ccc cgg ggg att aaa gct ggc tat ggc acc      1824
Gly His Glu Pro Gly Glu Pro Arg Gly Ile Lys Ala Gly Tyr Gly Thr
        595                 600                 605

tgc aac tgc ttc cct gag gag gag aag tgc ttc tgc gag ccc gaa gac      1872
Cys Asn Cys Phe Pro Glu Glu Glu Lys Cys Phe Cys Glu Pro Glu Asp
    610                 615                 620

atc cag gat cca ctg tgc gac gag ctg tgc cgc acg gtg atc gca gcc      1920
Ile Gln Asp Pro Leu Cys Asp Glu Leu Cys Arg Thr Val Ile Ala Ala
625                 630                 635                 640

gct gtc ctc ttc tcc ttc atc gtc tcg gtg ctg ctg tct gcc ttc tgc      1968
Ala Val Leu Phe Ser Phe Ile Val Ser Val Leu Leu Ser Ala Phe Cys
                645                 650                 655

atc cac tgc tac cac aag ttt gcc cac aag cca ccc atc tcc tca gct      2016
Ile His Cys Tyr His Lys Phe Ala His Lys Pro Pro Ile Ser Ser Ala
            660                 665                 670

gag atg acc ttc cgg agg ccc gcc cag gcc ttc ccg gtc agc tac tcc      2064
Glu Met Thr Phe Arg Arg Pro Ala Gln Ala Phe Pro Val Ser Tyr Ser
        675                 680                 685

tct tcc ggt gcc cgc cgg ccc tcg ctg gac tcc atg gag aac cag gtc      2112
Ser Ser Gly Ala Arg Arg Pro Ser Leu Asp Ser Met Glu Asn Gln Val
    690                 695                 700

tcc gtg gat gcc ttc aag atc ctg cag cct gag gga act ggc atg ata      2160
Ser Val Asp Ala Phe Lys Ile Leu Gln Pro Glu Gly Thr Gly Met Ile
705                 710                 715                 720

gat gaa gag ttc act gtt gca aga ctc tac att agc aaa atg aag tca      2208
Asp Glu Glu Phe Thr Val Ala Arg Leu Tyr Ile Ser Lys Met Lys Ser
                725                 730                 735
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gaa gta aaa acc atg gtg aaa cgt tgc aag cag tta gaa agc aca caa       2256
Glu Val Lys Thr Met Val Lys Arg Cys Lys Gln Leu Glu Ser Thr Gln
            740                 745                 750

act gag agc aac aaa aaa atg gaa gaa aat gaa aag gag tta gca gca       2304
Thr Glu Ser Asn Lys Lys Met Glu Glu Asn Glu Lys Glu Leu Ala Ala
        755                 760                 765

tgt cag ctt cgt atc tct caa cat gaa gcc aaa atc aag tca ttg act       2352
Cys Gln Leu Arg Ile Ser Gln His Glu Ala Lys Ile Lys Ser Leu Thr
    770                 775                 780

gaa tac ctt caa aat gtg gaa caa aag aaa aga cag ttg gag gaa tct       2400
Glu Tyr Leu Gln Asn Val Glu Gln Lys Lys Arg Gln Leu Glu Glu Ser
785                 790                 795                 800

gtc gat gcc ctc agt gaa gaa cta gtc cag ctt cga gca caa gag aaa       2448
Val Asp Ala Leu Ser Glu Glu Leu Val Gln Leu Arg Ala Gln Glu Lys
                805                 810                 815

gtc cat gaa atg gaa aag gag cac tta aat aag gtt cag act gca aat       2496
Val His Glu Met Glu Lys Glu His Leu Asn Lys Val Gln Thr Ala Asn
            820                 825                 830

gaa gtt aag caa gct gtt gaa cag cag atc cag agc cat aga gaa act       2544
Glu Val Lys Gln Ala Val Glu Gln Gln Ile Gln Ser His Arg Glu Thr
        835                 840                 845

cat caa aaa cag atc agt agt ttg aga gat gaa gta gaa gca aaa gca       2592
His Gln Lys Gln Ile Ser Ser Leu Arg Asp Glu Val Glu Ala Lys Ala
    850                 855                 860

aaa ctt att act gat ctt caa gac caa aac cag aaa atg atg tta gag       2640
Lys Leu Ile Thr Asp Leu Gln Asp Gln Asn Gln Lys Met Met Leu Glu
865                 870                 875                 880

cag gaa cgt cta aga gta gaa cat gag aag ttg aaa gcc aca gat cag       2688
Gln Glu Arg Leu Arg Val Glu His Glu Lys Leu Lys Ala Thr Asp Gln
                885                 890                 895

gaa aag agc aga aaa cta cat gaa ctt acg gtt atg caa gat aga cga       2736
Glu Lys Ser Arg Lys Leu His Glu Leu Thr Val Met Gln Asp Arg Arg
            900                 905                 910

gaa caa gca aga caa gac ttg aag ggt ttg gaa gag aca gtg gca aaa       2784
Glu Gln Ala Arg Gln Asp Leu Lys Gly Leu Glu Glu Thr Val Ala Lys
        915                 920                 925

gaa ctt cag act tta cac aac ctg cgc aaa ctc ttt gtt cag gac ctg       2832
Glu Leu Gln Thr Leu His Asn Leu Arg Lys Leu Phe Val Gln Asp Leu
    930                 935                 940

gct aca aga gtt aaa aag agt gct gag att gat tct gat gac acc gga       2880
Ala Thr Arg Val Lys Lys Ser Ala Glu Ile Asp Ser Asp Asp Thr Gly
945                 950                 955                 960

ggc agc gct gct cag aag caa aaa atc tcc ttt ctt gaa aat aat ctt       2928
Gly Ser Ala Ala Gln Lys Gln Lys Ile Ser Phe Leu Glu Asn Asn Leu
                965                 970                 975

gaa cag ctc act aaa gtg cac aaa cag ttg gta cgt gat aat gca gat       2976
Glu Gln Leu Thr Lys Val His Lys Gln Leu Val Arg Asp Asn Ala Asp
            980                 985                 990

ctc cgc tgt gaa ctt cct aag ttg  gaa aag cga ctt cga  gct aca gct     3024
Leu Arg Cys Glu Leu Pro Lys Leu  Glu Lys Arg Leu Arg  Ala Thr Ala
        995                 1000                1005
```

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gag aga  gtg aaa gct ttg gaa  tca gca ctg aaa gaa  gct aaa gaa        3069
Glu Arg  Val Lys Ala Leu Glu  Ser Ala Leu Lys Glu  Ala Lys Glu
    1010                 1015                 1020

aat gca  tct cgt gat cgc aaa  cgc tat cag caa gaa  gta gat cgc        3114
Asn Ala  Ser Arg Asp Arg Lys  Arg Tyr Gln Gln Glu  Val Asp Arg
    1025                 1030                 1035

ata aag  gaa gca gtc agg tca  aag aat atg gcc aga  aga ggg cat        3159
Ile Lys  Glu Ala Val Arg Ser  Lys Asn Met Ala Arg  Arg Gly His
    1040                 1045                 1050

tct gca  cag att gct aaa cct  att cgt ccc ggg caa  cat cca gca        3204
Ser Ala  Gln Ile Ala Lys Pro  Ile Arg Pro Gly Gln  His Pro Ala
    1055                 1060                 1065

gct tct  cca act cac cca agt  gca att cgt gga gga  ggt gca ttt        3249
Ala Ser  Pro Thr His Pro Ser  Ala Ile Arg Gly Gly  Gly Ala Phe
    1070                 1075                 1080

gtt cag  aac agc cag cca gtg  gca gtg cga ggt gga  gga ggc aaa        3294
Val Gln  Asn Ser Gln Pro Val  Ala Val Arg Gly Gly  Gly Gly Lys
    1085                 1090                 1095

caa gtg  taa                                                       3303
Gln Val
    1100
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<210> 4
<211> 1100
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 4

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Met Ala Lys Ala Thr Ser Gly Ala Ala Gly Leu Arg Leu Leu Leu Leu
1               5                  10                  15

Leu Leu Leu Pro Leu Leu Gly Lys Val Ala Leu Gly Leu Tyr Phe Ser
            20                  25                  30

Arg Asp Ala Tyr Trp Glu Lys Leu Tyr Val Asp Gln Ala Ala Gly Thr
        35                  40                  45

Pro Leu Leu Tyr Val His Ala Leu Arg Asp Ala Pro Glu Glu Val Pro
    50                  55                  60

Ser Phe Arg Leu Gly Gln His Leu Tyr Gly Thr Tyr Arg Thr Arg Leu
65                  70                  75                  80

His Glu Asn Asn Trp Ile Cys Ile Gln Glu Asp Thr Gly Leu Leu Tyr
                85                  90                  95

Leu Asn Arg Ser Leu Asp His Ser Ser Trp Glu Lys Leu Ser Val Arg
            100                 105                 110

Asn Arg Gly Phe Pro Leu Leu Thr Val Tyr Leu Lys Val Phe Leu Ser
```

```
        115                 120                 125

Pro Thr Ser Leu Arg Glu Gly Glu Cys Gln Trp Pro Gly Cys Ala Arg
    130                 135                 140

Val Tyr Phe Ser Phe Phe Asn Thr Ser Phe Pro Ala Cys Ser Ser Leu
145                 150                 155                 160

Lys Pro Arg Glu Leu Cys Phe Pro Glu Thr Arg Pro Ser Phe Arg Ile
                165                 170                 175

Arg Glu Asn Arg Pro Pro Gly Thr Phe His Gln Phe Arg Leu Leu Pro
            180                 185                 190

Val Gln Phe Leu Cys Pro Asn Ile Ser Val Ala Tyr Arg Leu Leu Glu
        195                 200                 205

Gly Glu Gly Leu Pro Phe Arg Cys Ala Pro Asp Ser Leu Glu Val Ser
    210                 215                 220

Thr Arg Trp Ala Leu Asp Arg Glu Gln Arg Glu Lys Tyr Glu Leu Val
225                 230                 235                 240

Ala Val Cys Thr Val His Ala Gly Ala Arg Glu Glu Val Val Met Val
                245                 250                 255

Pro Phe Pro Val Thr Val Tyr Asp Glu Asp Asp Ser Ala Pro Thr Phe
            260                 265                 270

Pro Ala Gly Val Asp Thr Ala Ser Ala Val Val Glu Phe Lys Arg Lys
        275                 280                 285

Glu Asp Thr Val Val Ala Thr Leu Arg Val Phe Asp Ala Asp Val Val
    290                 295                 300

Pro Ala Ser Gly Glu Leu Val Arg Arg Tyr Thr Ser Thr Leu Leu Pro
305                 310                 315                 320

Gly Asp Thr Trp Ala Gln Gln Thr Phe Arg Val Glu His Trp Pro Asn
                325                 330                 335

Glu Thr Ser Val Gln Ala Asn Gly Ser Phe Val Arg Ala Thr Val His
            340                 345                 350

Asp Tyr Arg Leu Val Leu Asn Arg Asn Leu Ser Ile Ser Glu Asn Arg
        355                 360                 365

Thr Met Gln Leu Ala Val Leu Val Asn Asp Ser Asp Phe Gln Gly Pro
    370                 375                 380

Gly Ala Gly Val Leu Leu Leu His Phe Asn Val Ser Val Leu Pro Val
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385 390 395 400

Ser Leu His Leu Pro Ser Thr Tyr Ser Leu Ser Val Ser Arg Arg Ala
405 410 415

Arg Arg Phe Ala Gln Ile Gly Lys Val Cys Val Glu Asn Cys Gln Ala
420 425 430

Phe Ser Gly Ile Asn Val Gln Tyr Lys Leu His Ser Ser Gly Ala Asn
435 440 445

Cys Ser Thr Leu Gly Val Val Thr Ser Ala Glu Asp Thr Ser Gly Ile
450 455 460

Leu Phe Val Asn Asp Thr Lys Ala Leu Arg Arg Pro Lys Cys Ala Glu
465 470 475 480

Leu His Tyr Met Val Val Ala Thr Asp Gln Gln Thr Ser Arg Gln Ala
485 490 495

Gln Ala Gln Leu Leu Val Thr Val Glu Gly Ser Tyr Val Ala Glu Glu
500 505 510

Ala Gly Cys Pro Leu Ser Cys Ala Val Ser Lys Arg Arg Leu Glu Cys
515 520 525

Glu Glu Cys Gly Gly Leu Gly Ser Pro Thr Gly Arg Cys Glu Trp Arg
530 535 540

Gln Gly Asp Gly Lys Gly Ile Thr Arg Asn Phe Ser Thr Cys Ser Pro
545 550 555 560

Ser Thr Lys Thr Cys Pro Asp Gly His Cys Asp Val Val Glu Thr Gln
565 570 575

Asp Ile Asn Ile Cys Pro Gln Asp Cys Leu Arg Gly Ser Ile Val Gly
580 585 590

Gly His Glu Pro Gly Glu Pro Arg Gly Ile Lys Ala Gly Tyr Gly Thr
595 600 605

Cys Asn Cys Phe Pro Glu Glu Glu Lys Cys Phe Cys Glu Pro Glu Asp
610 615 620

Ile Gln Asp Pro Leu Cys Asp Glu Leu Cys Arg Thr Val Ile Ala Ala
625 630 635 640

Ala Val Leu Phe Ser Phe Ile Val Ser Val Leu Leu Ser Ala Phe Cys
645 650 655

Ile His Cys Tyr His Lys Phe Ala His Lys Pro Pro Ile Ser Ser Ala

660 665 670

Glu Met Thr Phe Arg Arg Pro Ala Gln Ala Phe Pro Val Ser Tyr Ser
675 680 685

Ser Ser Gly Ala Arg Arg Pro Ser Leu Asp Ser Met Glu Asn Gln Val
690 695 700

Ser Val Asp Ala Phe Lys Ile Leu Gln Pro Glu Gly Thr Gly Met Ile
705 710 715 720

Asp Glu Glu Phe Thr Val Ala Arg Leu Tyr Ile Ser Lys Met Lys Ser
725 730 735

Glu Val Lys Thr Met Val Lys Arg Cys Lys Gln Leu Glu Ser Thr Gln
740 745 750

Thr Glu Ser Asn Lys Lys Met Glu Glu Asn Glu Lys Glu Leu Ala Ala
755 760 765

Cys Gln Leu Arg Ile Ser Gln His Glu Ala Lys Ile Lys Ser Leu Thr
770 775 780

Glu Tyr Leu Gln Asn Val Glu Gln Lys Lys Arg Gln Leu Glu Glu Ser
785 790 795 800

Val Asp Ala Leu Ser Glu Glu Leu Val Gln Leu Arg Ala Gln Glu Lys
805 810 815

Val His Glu Met Glu Lys Glu His Leu Asn Lys Val Gln Thr Ala Asn
820 825 830

Glu Val Lys Gln Ala Val Glu Gln Gln Ile Gln Ser His Arg Glu Thr
835 840 845

His Gln Lys Gln Ile Ser Ser Leu Arg Asp Glu Val Glu Ala Lys Ala
850 855 860

Lys Leu Ile Thr Asp Leu Gln Asp Gln Asn Gln Lys Met Met Leu Glu
865 870 875 880

Gln Glu Arg Leu Arg Val Glu His Glu Lys Leu Lys Ala Thr Asp Gln
885 890 895

Glu Lys Ser Arg Lys Leu His Glu Leu Thr Val Met Gln Asp Arg Arg
900 905 910

Glu Gln Ala Arg Gln Asp Leu Lys Gly Leu Glu Glu Thr Val Ala Lys
915 920 925

Glu Leu Gln Thr Leu His Asn Leu Arg Lys Leu Phe Val Gln Asp Leu

930 935 940

Ala Thr Arg Val Lys Lys Ser Ala Glu Ile Asp Ser Asp Asp Thr Gly
945 950 955 960

Gly Ser Ala Ala Gln Lys Gln Lys Ile Ser Phe Leu Glu Asn Asn Leu
965 970 975

Glu Gln Leu Thr Lys Val His Lys Gln Leu Val Arg Asp Asn Ala Asp
980 985 990

Leu Arg Cys Glu Leu Pro Lys Leu Glu Lys Arg Leu Arg Ala Thr Ala
995 1000 1005

Glu Arg Val Lys Ala Leu Glu Ser Ala Leu Lys Glu Ala Lys Glu
1010 1015 1020

Asn Ala Ser Arg Asp Arg Lys Arg Tyr Gln Gln Glu Val Asp Arg
1025 1030 1035

Ile Lys Glu Ala Val Arg Ser Lys Asn Met Ala Arg Arg Gly His
1040 1045 1050

Ser Ala Gln Ile Ala Lys Pro Ile Arg Pro Gly Gln His Pro Ala
1055 1060 1065

Ala Ser Pro Thr His Pro Ser Ala Ile Arg Gly Gly Gly Ala Phe
1070 1075 1080

Val Gln Asn Ser Gln Pro Val Ala Val Arg Gly Gly Gly Gly Lys
1085 1090 1095

Gln Val
1100

<210> 5
<211> 200
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polynucleotide

<220>
<221> modified_base
<222> (16)..(185)
<223> a, c, t, g, unknown or other

<400> 5
atcgcaccag cgtgtnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 60

nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 120

nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 180

nnnnncactg cggctcctca 200

<210> 6
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 6
Lys Val Asp Asn Asn Gly Val Ala Ile Gly Ile Glu Ala Leu Asp Lys
1 5 10 15

<210> 7
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 7
Glu Asp Pro Lys Trp Glu Phe Pro Arg Lys Asn Leu Val Leu Gly Lys
1 5 10 15

Thr

<210> 8
<211> 14
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 8
tgtaaaggag gatc 14

<210> 9
<211> 976
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 9
Met Ala Asp Leu Ala Glu Cys Asn Ile Lys Val Met Cys Arg Phe Arg
1 5 10 15

Pro Leu Asn Glu Ser Glu Val Asn Arg Gly Asp Lys Tyr Ile Ala Lys
20 25 30

Phe Gln Gly Glu Asp Thr Val Val Ile Ala Ser Lys Pro Tyr Ala Phe

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        35                  40                  45

Asp Arg Val Phe Gln Ser Ser Thr Ser Gln Glu Gln Val Tyr Asn Asp
    50                  55                  60

Cys Ala Lys Lys Ile Val Lys Asp Val Leu Glu Gly Tyr Asn Gly Thr
65                  70                  75                  80

Ile Phe Ala Tyr Gly Gln Thr Ser Ser Gly Lys Thr His Thr Met Glu
                85                  90                  95

Gly Lys Leu His Asp Pro Glu Gly Met Gly Ile Ile Pro Arg Ile Val
            100                 105                 110

Gln Asp Ile Phe Asn Tyr Ile Tyr Ser Met Asp Glu Asn Leu Glu Phe
        115                 120                 125

His Ile Lys Val Ser Tyr Phe Glu Ile Tyr Leu Asp Lys Ile Arg Asp
    130                 135                 140

Leu Leu Asp Val Ser Lys Thr Asn Leu Ser Val His Glu Asp Lys Asn
145                 150                 155                 160

Arg Val Pro Tyr Val Lys Gly Cys Thr Glu Arg Phe Val Cys Ser Pro
                165                 170                 175

Asp Glu Val Met Asp Thr Ile Asp Glu Gly Lys Ser Asn Arg His Val
            180                 185                 190

Ala Val Thr Asn Met Asn Glu His Ser Ser Arg Ser His Ser Ile Phe
        195                 200                 205

Leu Ile Asn Val Lys Gln Glu Asn Thr Gln Thr Glu Gln Lys Leu Ser
    210                 215                 220

Gly Lys Leu Tyr Leu Val Asp Leu Ala Gly Ser Glu Lys Val Ser Lys
225                 230                 235                 240

Thr Gly Ala Glu Gly Ala Val Leu Asp Glu Ala Lys Asn Ile Asn Lys
                245                 250                 255

Ser Leu Ser Ala Leu Gly Asn Val Ile Ser Ala Leu Ala Glu Gly Ser
            260                 265                 270

Thr Tyr Val Pro Tyr Arg Asp Ser Lys Met Thr Arg Ile Leu Gln Asp
        275                 280                 285

Ser Leu Gly Gly Asn Cys Arg Thr Thr Ile Ile Cys Cys Ser Pro Ser
    290                 295                 300

Ser Tyr Asn Glu Ser Glu Thr Lys Ser Thr Leu Leu Phe Gly Gln Arg
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305 310 315 320

Ala Lys Thr Ile Lys Asn Thr Val Cys Val Asn Val Glu Leu Thr Ala
325 330 335

Glu Gln Trp Lys Lys Lys Tyr Glu Lys Glu Lys Glu Lys Asn Lys Ile
340 345 350

Leu Arg Asn Thr Ile Gln Trp Leu Glu Asn Glu Leu Asn Arg Trp Arg
355 360 365

Asn Gly Glu Thr Val Pro Ile Asp Glu Gln Phe Asp Lys Glu Lys Ala
370 375 380

Asn Leu Glu Ala Phe Thr Val Asp Lys Asp Ile Thr Leu Thr Asn Asp
385 390 395 400

Lys Pro Ala Thr Ala Ile Gly Val Ile Gly Asn Phe Thr Asp Ala Glu
405 410 415

Arg Arg Lys Cys Glu Glu Glu Ile Ala Lys Leu Tyr Lys Gln Leu Asp
420 425 430

Asp Lys Asp Glu Glu Ile Asn Gln Gln Ser Gln Leu Val Glu Lys Leu
435 440 445

Lys Thr Gln Met Leu Asp Gln Glu Glu Leu Leu Ala Ser Thr Arg Arg
450 455 460

Asp Gln Asp Asn Met Gln Ala Glu Leu Asn Arg Leu Gln Ala Glu Asn
465 470 475 480

Asp Ala Ser Lys Glu Glu Val Lys Glu Val Leu Gln Ala Leu Glu Glu
485 490 495

Leu Ala Val Asn Tyr Asp Gln Lys Ser Gln Glu Val Glu Asp Lys Thr
500 505 510

Lys Glu Tyr Glu Leu Leu Ser Asp Glu Leu Asn Gln Lys Ser Ala Thr
515 520 525

Leu Ala Ser Ile Asp Ala Glu Leu Gln Lys Leu Lys Glu Met Thr Asn
530 535 540

His Gln Lys Lys Arg Ala Ala Glu Met Met Ala Ser Leu Leu Lys Asp
545 550 555 560

Leu Ala Glu Ile Gly Ile Ala Val Gly Asn Asn Asp Val Lys Glu Asp
565 570 575

Pro Lys Trp Glu Phe Pro Arg Lys Asn Leu Val Leu Gly Lys Thr Leu

580 585 590

Gly Glu Gly Glu Phe Gly Lys Val Val Lys Ala Thr Ala Phe His Leu
595 600 605

Lys Gly Arg Ala Gly Tyr Thr Thr Val Ala Val Lys Met Leu Lys Glu
610 615 620

Asn Ala Ser Pro Ser Glu Leu Arg Asp Leu Leu Ser Glu Phe Asn Val
625 630 635 640

Leu Lys Gln Val Asn His Pro His Val Ile Lys Leu Tyr Gly Ala Cys
645 650 655

Ser Gln Asp Gly Pro Leu Leu Leu Ile Val Glu Tyr Ala Lys Tyr Gly
660 665 670

Ser Leu Arg Gly Phe Leu Arg Glu Ser Arg Lys Val Gly Pro Gly Tyr
675 680 685

Leu Gly Ser Gly Gly Ser Arg Asn Ser Ser Ser Leu Asp His Pro Asp
690 695 700

Glu Arg Ala Leu Thr Met Gly Asp Leu Ile Ser Phe Ala Trp Gln Ile
705 710 715 720

Ser Gln Gly Met Gln Tyr Leu Ala Glu Met Lys Leu Val His Arg Asp
725 730 735

Leu Ala Ala Arg Asn Ile Leu Val Ala Glu Gly Arg Lys Met Lys Ile
740 745 750

Ser Asp Phe Gly Leu Ser Arg Asp Val Tyr Glu Glu Asp Ser Tyr Val
755 760 765

Lys Arg Ser Gln Gly Arg Ile Pro Val Lys Trp Met Ala Ile Glu Ser
770 775 780

Leu Phe Asp His Ile Tyr Thr Thr Gln Ser Asp Val Trp Ser Phe Gly
785 790 795 800

Val Leu Leu Trp Glu Ile Val Thr Leu Gly Gly Asn Pro Tyr Pro Gly
805 810 815

Ile Pro Pro Glu Arg Leu Phe Asn Leu Leu Lys Thr Gly His Arg Met
820 825 830

Glu Arg Pro Asp Asn Cys Ser Glu Glu Met Tyr Arg Leu Met Leu Gln
835 840 845

Cys Trp Lys Gln Glu Pro Asp Lys Arg Pro Val Phe Ala Asp Ile Ser

850 855 860

Lys Asp Leu Glu Lys Met Met Val Lys Arg Arg Asp Tyr Leu Asp Leu
865 870 875 880

Ala Ala Ser Thr Pro Ser Asp Ser Leu Ile Tyr Asp Asp Gly Leu Ser
885 890 895

Glu Glu Glu Thr Pro Leu Val Asp Cys Asn Asn Ala Pro Leu Pro Arg
900 905 910

Ala Leu Pro Ser Thr Trp Ile Glu Asn Lys Leu Tyr Gly Met Ser Asp
915 920 925

Pro Asn Trp Pro Gly Glu Ser Pro Val Pro Leu Thr Arg Ala Asp Gly
930 935 940

Thr Asn Thr Gly Phe Pro Arg Tyr Pro Asn Asp Ser Val Tyr Ala Asn
945 950 955 960

Trp Met Leu Ser Pro Ser Ala Ala Lys Leu Met Asp Thr Phe Asp Ser
965 970 975