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(54) Title: VIRULENCE GENES AND PROTEINS, AND THEIR USE (57) Abstract The present invention is based on the identification of a series of virulence genes in <i>E. coli</i> K1, the products of which may be implicated in the pathogenicity of the organism. The identification of the genes allows them, or their expressed products, to be used in a number of ways to treat infection.																																		

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VIRULENCE GENES AND PROTEINS, AND THEIR USE

Field of the Invention

This invention relates to the identification of virulence genes and proteins, and their use. More particularly, it relates to their use in therapy and
5 in screening for drugs.

Background to the Invention

E. coli is a member of the *Enterobacteriaceae*, or enteric bacteria, which are Gram-negative microorganisms that populate the intestinal tracts of animals. Other members of this bacterial family include *Enterobacter*,
10 *Klebsiella*, *Salmonella*, *Shigella* and *Yersinia*. Although *E. coli* is found normally in the human gastrointestinal tract, it has been implicated in human disease, including septicaemia, meningitis, urinary tract infection, wound infection, abscess formation, peritonitis and cholangitis.

The disease states caused by *E. coli* are dependent upon certain
15 virulence determinants. For example, *E. coli* has been implicated in neonatal meningitis and a major determinant of virulence has been identified as the K1 antigen, which is a homopolymer of sialic acid. The K1 antigen may have a role in avoiding the host's immunological system and preventing phagocytosis.

Summary of the Invention

20 The present invention is based on the identification of a series of virulence genes in *E. coli* K1, and also related organisms the products of which may be implicated in the pathogenicity of the organism.

According to one aspect of the present invention, a peptide is encoded by an operon including any of the genes identified herein as *mdoG*, *creC*, *recG*,
25 *yggN*, *tatA*, *tatB*, *tatC*, *tatE*, *eck1*, *iroD*, *iroC*, *iroE*, *mtd2* and *ms1* to 16, from *E. coli* K1, or a homologue thereof in a Gram-negative bacterium, or a functional fragment thereof. Such a peptide is suitable for therapeutic use, e.g. when isolated.

The term "functional fragments" is used herein to define a part of the
30 gene or peptide which retains similar therapeutic utility as the whole gene or peptide. For example, a functional fragment of the peptide may be used as an antigenic determinant, useful in a vaccine or in the production of antibodies.

A gene fragment may be used to encode the active peptide. Alternatively, the gene fragment may have utility in gene therapy, targetting the wild-type gene *in vivo* to exert a therapeutic effect.

A peptide according to the present invention may comprise any of the amino acid sequences identified herein as SEQ ID NOS. 2, 5, 7, 9, 11, 12, 13, 14, 16, 23, 24, 25, 26, 28, 31, 29, 32 and 35-48.

The identification of these peptides as virulence determinants allows them to be used in a number of ways in the treatment of infection. For example, a host may be transformed to express a peptide according to the invention or modified to disrupt expression of the gene encoding the peptide. A vaccine may also comprise a peptide according to the invention, or the means for its expression, for the treatment of infection. In addition, a vaccine may comprise a microorganism having a virulence gene deletion, wherein the gene encodes a peptide according to the invention.

According to another aspect of the invention, the peptides or genes may be used for screening potential antimicrobial drugs or for the detection of virulence.

A further aspect of this invention is the use of any of the products identified herein, for the treatment or prevention of a condition associated with infection by a Gram-negative bacterium, in particular by *E. coli*.

Description of the Invention

The present invention has made use of signature-tagged mutagenesis (STM) (Hensel *et al*, Science, 1995;269:400-403) to screen *E. coli* K1 strain RS228 (Pluschke *et al*, Infection and Immunity 39:599-608) mini-Tn5 mutant bank for attenuated mutants, to identify virulence genes (and virulence determinants) of *E. coli*.

Although *E. coli* K1 was used as the microorganism to identify the virulence genes, corresponding genes in other enteric bacteria are considered to be within the scope of the present invention. For example, corresponding genes or encoded proteins may be found, based on sequence homology, in *Enterobacter*, *Klebsiella* and other genera implicated in human intestinal disease, including *Salmonella*, *Shigella* and *Yersinia*.

The term "virulence determinant" is used herein to define a product, e.g. a peptide or protein that may have a role in the maintenance of pathogenic bacteria. In particular, a virulence determinant is a bacterial protein or peptide that is implicated in the pathogenicity of the infectious or disease-causing microorganism.

A gene that encodes a virulence determinant may be termed a "virulence gene". Disruption of a virulence gene by way of mutation, deletion or insertion, will result in a reduced level of survival of the bacteria in a host, or a general reduction in the pathogenicity of the microorganism.

Signature-tagged mutagenesis has proved a very useful technique for identifying virulence genes, and their products. The technique relies on the ability of transposons to insert randomly into the genome of a microorganism, under permissive conditions. The transposons are individually marked for easy identification, and then introduced separately into a microorganism, resulting in disruption of the genome. Mutated microorganisms with reduced virulence are then detected by negative selection and the genes where insertional inactivation has occurred are identified and characterised.

A first stage in the STM process is the preparation of suitable transposons or transposon-like elements. A library of different transposons are prepared, each being incorporated into a vector or plasmid to facilitate transfer into the microorganism. The preparation of vectors with suitable transposons will be apparent to a skilled person in the art and is further disclosed in WO-A-96/17951. For the Gram-negative bacteria, e.g. *E. coli*, suitable transposons include Tn5 and Tn10. Having prepared the transposons, mutagenesis of a bacterial strain is then carried out to create a library of individually mutated bacteria.

Pools of the mutated microorganisms are then introduced into a suitable host. After a suitable length of time, the microorganisms are recovered from the host and those microorganisms that have survived in the host are identified, thereby also identifying the mutated strains that failed to survive, i.e. avirulent strains. Corresponding avirulent strains in a stored library are then used to identify the genes where insertional inactivation occurred. Usually, the site of

transposon insertion is identified by isolating the DNA flanking the transposons insertion site, and this permits characterisation of the genes implicated in virulence.

Once an avirulent microorganism has been identified, it is possible to
5 determine more fully the potential role of the mutated gene in virulence, by infecting a suitable host animal with a lethal dose of the mutant. The survival time of the infected animal is compared with that of a control infected with the wild-type strain, and those animals surviving for longer periods than the control may be said to be infected with microorganisms having mutated virulence
10 genes.

Alternatively, the potential role in virulence can be investigated by infecting an animal host with a mixture of the wild-type and mutant bacteria. After a suitable period of time, bacteria are harvested from organs of the host animal and the ratio of wild-type and mutant bacteria determined. This ratio is
15 divided by the ratio of mutant to wild-type bacteria in the inoculum, to determine the competitive index (CI). Mutants which have a competitive index of less than 1 may be said to be avirulent.

It is possible that the gene which is inactivated by the insertion of the transposon may not be a true virulence gene, but may be having a polar effect
20 on a downstream (virulence) gene. This can be determined by further experimentation, placing non-polar mutations in more defined regions of the gene, or mutating other adjacent genes, and establishing whether or not the mutant is avirulent.

Having characterised a virulence gene in *E. coli*, it is possible to use the
25 gene sequence to establish homologies in other microorganisms. In this way it is possible to determine whether other microorganisms have similar virulence determinants. Sequence homologies may be established by searching in existing databases, e.g. EMBL or Genbank.

Virulence genes are often clustered together in distinct chromosomal
30 regions called pathogenicity islands. Pathogenicity islands can be recognised as they are usually flanked by repeat sequences, insertion elements or tRNA genes. Also the G+C content is normally different from the remainder of the

chromosome, suggesting that they were acquired by horizontal transmission from another organism. For example the G+C content of the *E. coli* K12 genome is 52%. Any pathogenicity islands found in *E. coli* strains are likely to have a G+C content that varies from this average.

5 The identified virulence genes are likely to be useful both in generating attenuated vaccine strains and as a target for antimicrobials. The same may be true for homologues in Gram-negative bacteria in general.

For the purpose of this invention, the appropriate degree of homology is typically at least 30%, preferably at least 50%, 60% or 70%, and more
10 preferably at least 80% or 90% (at the amino acid or nucleotide level).

Proteins according to the invention may be purified and isolated by methods known in the art. In particular, having identified the gene sequence, it will be possible to use recombinant techniques to express the genes in a suitable host. Active fragments and homologues can be identified and may be
15 useful in therapy. For example, the proteins or their active fragments may be used as antigenic determinants in a vaccine, to elicit an immune response. They may also be used in the preparation of antibodies, for passive immunisation, or diagnostic applications. Suitable antibodies include monoclonal antibodies, or fragments thereof, including single chain fv
20 fragments. Methods for the preparation of antibodies will be apparent to those skilled in the art.

The preparation of vaccines based on attenuated microorganisms is known to those skilled in the art. Vaccine compositions can be formulated with suitable carriers or adjuvants, e.g. alum, as necessary or desired, and used in
25 therapy, to provide effective immunisation against *E. coli* or other Gram-negative bacteria. The preparation of vaccine formulations will be apparent to the skilled person.

More generally, and as is well known to those skilled in the art, a suitable amount of an active component of the invention can be selected, for therapeutic
30 use, as can suitable carriers or excipients, and routes of administration. These factors will be chosen or determined according to known criteria such as the

nature/severity of the condition to be treated, the type or health of the subject etc.

The following Examples illustrate the invention. For the Examples, STM was used to screen an *E. coli* K1 mini-Tn5 mutant bank for attenuated mutants, using a mouse model of systemic infection. The basic procedure followed that disclosed in Hensel *et al, supra*. *E. coli* K1 containing a mini-Tn5 insertion within a virulence gene was not recovered from mice inoculated with a mixed population of mutants, and is therefore likely to be attenuated.

The DNA region flanking either side of the mini-Tn5 insertion was cloned by inverse PCR or by rescue of a kanamycin-resistance marker. In the latter case, chromosomal DNA from the STM-derived mutant was digested with restriction enzymes, ligated into the plasmid pUC19, and kanamycin-resistant clones selected after transformation into competent *E. coli* K12 cells. Subsequent cloning and sequencing was then performed and the gene sequences compared using sequences in publicly available sequence databases (EMBL) to help characterise the putative gene products.

Example 1

In a first mutant, two fragments of cloned DNA were sequenced. The nucleotide sequences are shown as SEQ ID NO. 1 and SEQ ID NO. 3 and a translated region of the DNA from SEQ ID NO. 1 is shown as SEQ ID NO. 2. SEQ ID NO. 1 shows 99.8% identity to the *mdoGH* region from *E. coli* K12 (EMBL database accession number AE000206) from nucleotides 2577 to 6908. This DNA fragment encodes the 5'-part of the *ymdD* gene, the entire *mdoG* gene and the 5'-part of the *mdoH* gene. The product of the *mdoG* gene is of unknown function, but is believed to be involved in the biosynthesis of membrane-derived oligosaccharides.

SEQ ID NO. 3 shows 98.3% identity to the 3'-part of the *mdoH* gene and downstream gene sequences from *E. coli* K12 (nucleotides 7187 to 7760). SEQ ID NO. 2 shows 99.6% identity to the *mdoG* protein from *E. coli* K12 (Swiss Prot accession number P33136) at amino acid 1 to 511.

The novel gene was tested for attenuation of virulence, using mixed infections, in a murine model of systemic infection (Achtman *et al.*, Infection and

Immunity, 1983; Vol. 39:315-335), and shown to be attenuated with a competitive index (CI) of 0.38. This confirms that the attenuation of the original transposon mutant is likely to be due to the disruption of the *mdoG* gene.

Polar and a non-polar deletion mutants of *mdoG* were constructed. The *mdoG* gene and flanking regions were amplified by PCR with oligonucleotides 5'-TGCTCTAGAGCCATTACTCAGAATGGG-3' (SEQ ID NO. 49) and 5'-CGCGAGCTCGACGACTGAATGATCCC-3' (SEQ ID NO. 50). The product was cloned into pUC19. A PCR product containing 5'- and 3'-terminal fragments of *mdoG* and the entire pUC19 sequence was then amplified by inverse PCR with the oligonucleotides 5'-TCCCCCGGGTACTGCAGCACTCAACC-3' (SEQ ID NO. 51) and 5'-GATCCCGGGACCACTGAAATGCGTGC-3' (SEQ ID NO. 52). A non-polar kanamycin resistance cassette (*aphT*) was inserted in both orientations between the *mdoG* sequences to give a polar and a non-polar construct. The *mdoG::aphT* fusions were then transferred to the suicide vector pCDV442. The chromosomal copy of the *mdoG* was mutated by allelic transfer after conjugation of the pCDV442 constructs into wild type *E. coli* K1.

The constructed mutants were tested for attenuation of virulence in a murine model of systemic infection (Achtman et al., *supra*). Both the polar and the non-polar constructs were attenuated in virulence, with competitive indices of 0.37 and 0.35, respectively (mean CI from three mice each). This confirms that the attenuation of the original transposon mutant is likely to be due to the disruption of the *mdoG* gene.

Example 2

A second mutant was identified with a virulence gene having the nucleotide sequence shown in SEQ ID NO. 4 and the translated amino acid sequence shown as SEQ ID NO. 5. The mini-Tn5 transposon inserted at nucleotide 581 (SEQ ID NO. 4) and at amino acid 187 (SEQ ID NO. 5).

These sequences show 97.9% identity to the *creC* gene of *E. coli* K12 (EMBL and Genbank accession numbers M13608, AE000510 and U14003).

The *creC* protein from *E. coli* K12 belongs to the protein family of histidine kinases as well as to a protein family consisting of proteins containing a signal domain.

The novel gene was tested for attenuation of virulence (Achtman *et al*, *supra*.), and shown to be attenuated with a competitive index of 0.09.

As the *E. coli* K12 *creC* gene is transcribed as part of an operon with the *creD* gene, it is possible that this attenuation is due to a polar effect on a presumed *E. coli* K1 *creD* gene.

Example 3

A third mutant had a nucleotide sequence shown as SEQ ID NO. 6 immediately following the mini-Tn5. A translation of this sequence is shown as SEQ ID NO. 7.

The nucleotide sequence shows 93.7% identity to the *recG* gene of *E. coli* K12, at nucleotides 5-146 (EMBL and Genbank accession numbers P24230 and M64367). This demonstrates that the disrupted gene is at least partially identical to the *recG* gene of *E. coli* K12. The *recG* gene of *E. coli* K12 encodes a 76.4kD protein which functions as ATP-dependent DNA helicase, and plays a critical role in DNA repair.

In tests for attenuation, the competitive index was shown to be 0.48. The *recG* gene is transcribed as the terminal gene of an operon, and it is therefore unlikely that this attenuation is due to a polar effect on another *E. coli* K1 gene.

Example 4

A fourth mutant had a transposon inserted within the nucleotide sequence shown as SEQ ID NO. 8, with a translation product shown as SEQ ID NO. 9.

The mini-Tn5 transposon inserted at nucleotide 359 and amino acid 80.

These sequences show 98.5% sequence identity to the *yggN* gene of *E. coli* K12 (EMBL accession number AE000378) at nucleotides 339-1054, and 99.6% identity at the amino acid level.

Although the sequence of the *yggN* gene is known, the function of its encoded protein has not yet been determined.

The novel gene was tested for attenuation of virulence, and shown to be attenuated with a competitive index of 0.43.

Example 5

Several mutants were also found with a transposon insertion within the same region. Cloning and sequencing the region revealed a nucleotide sequence shown as SEQ ID NO. 10. This sequence has homology with the *tatABCD* operon of *E. coli* K12 (EMBL and Genbank accession numbers
5 AJ005830, AE000459 and AE000167). This operon encodes proteins of predicted mass 9.6 kD, 18.4 kD, 28.9 kD and 29.5 kD, which function as components of a Sec-independent protein export pathway. The pathway permits translocation of fully folded proteins to the periplasm through a gated pore, after the attachment of co-factors in the cytoplasm.

10 Translation of the nucleotide sequence revealed a protein corresponding to *tatA* (SEQ ID NO. 11), a sequence corresponding to *tatB* (SEQ ID NO. 12), a sequence corresponding to *tatC* (SEQ ID NO. 13) and a sequence corresponding to *tatD* (SEQ ID NO. 14).

The mini-Tn5 transposons in the mutants identified by STM are located
15 at nucleotides 1429 and 2226 of SEQ ID NO. 10. These transposon insertions disrupt the *tatB* protein sequence at amino acid 50 and the *tatC* protein sequence at amino acid 143.

The *tatB* and *tatC* genes were tested for attenuation of virulence and were shown to be attenuated with competitive indices of 0.0012 and 0.0039,
20 respectively. These genes were also attenuated in virulence when tested in single infections in the same model of systemic infection.

Example 6

A further mutant was insertionally inactivated within a region corresponding to the *tatE* gene of *E. coli* K12, shown as SEQ ID NO. 15. A
25 translation of the sequence as shown as SEQ ID NO. 16. The *tatE* gene shows 98% identity to that of the *E. coli* K12 gene (accession number AE000167) at nucleotides 6719-7306.

To establish whether the *tatA*, *tatD* and *tatE* genes are required for virulence, non-polar deletion mutations were constructed in each. The regions
30 of DNA flanking either side of the *tatA*, *tatD* and *tatE* genes were amplified with the following primers:

tatA

5'-TCG TCT AGA GAT GAT GGT GAT GGA GCG-3' (SEQ ID NO. 53)

5 5'-GAA CTG CAG CCA AAT ACT GAT ACC ACC C-3' (SEQ ID NO. 54)

5'-GAA CTG CAG GCT AAA ACA GAA GAC GCG-3' (SEQ ID NO. 55)

10 5'-CAT GCA TGC ACT CCA TAT GAC AAC CGC-3' (SEQ ID NO. 56)

Primers SEQ ID NO. 53 and SEQ ID NO. 54 were used to amplify DNA sequences upstream of *tatA*, Primers SEQ ID NO. 55 and SEQ ID NO. 56 were used to amplify DNA sequences downstream of *tatA*.

15 *tatD*

5'-TCG TCT AGA ATG AAG CTG CGC ATG AGG-3' (SEQ ID NO. 57)

20 5'-CAA CTG CAG TCG CAA ATT GCG AAC TGG-3' (SEQ ID NO. 58)

5'-CAA CTG CAG ACC GCA ACT TTT CGA CGC-3' (SEQ ID NO. 59)

5'-CAT GCA TGC CAG TGA GCC ATT GTT CCC-3' (SEQ ID NO. 60)

25 Primers SEQ ID NO. 57 and SEQ ID NO. 58 were used to amplify DNA sequences upstream of *tatD*, Primers SEQ ID NO. 59 and SEQ ID NO. 60 were used to amplify DNA sequences downstream of *tatD*.

tatE

30 5'-TGC TCT AGA TAC GAC TCT GAC AGG AGG-3' (SEQ ID NO. 61)

5'-TCA GAT ATC AAC TAC CAG CAG TTT GG-3' (SEQ ID NO. 62)

35 5'-TCA GAT ATC CAT AAA GAG TGA CGT GGC-3' (SEQ ID NO. 63)

5'-TGC TCT AGA AAA CGT GGC AAC AGA GCG-3' (SEQ ID NO. 64)

40 Primers SEQ ID NO. 61 and SEQ ID NO. 62 were used to amplify DNA sequences upstream of *tatE*, Primers SEQ ID NO. 63 and SEQ ID NO. 64 were used to amplify DNA sequences downstream of *tatE*.

After cloning these flanking DNA fragments into pUC19, a non-polar *aphT* kanamycin resistance cassette (Galan *et al*, J.Bacteriol, 1992;174:4338-4349) was inserted between the flanking DNA fragments to replace the *tatA*, *tatD* and *tatE* genes. These DNA fragments were then transferred to the suicide
5 vector pCVD442 (Blomfield *et. al*, Mol. Micro., 1991;5:1447-1457). The chromosomal copies of the *E. coli* K1 *tatA*, *tatD* and *tatE* genes were then mutated by allelic transfer after conjugation of the pCVD442 constructs into wild type *E. coli* K1.

Disruptions of the *tatA*, *tatD* and *tatE* genes have been tested for
10 attenuation of virulence (Achtman *et al.*, *supra*).

None of the genes was attenuated when deleted in isolation. The genes may still play a role in virulence, and to test this, mutants were prepared with deletions in both *tatA* and *tatE* genes. The double mutant was tested for attenuation in virulence using mixed infections with the wild-type strain and
15 shown to be attenuated with a competitive index of 0.0017. It seems therefore that the *tatA*, *tatD* and *tatE* genes may be used in combination to create avirulent microorganisms.

Given the similarity of the *E. coli* K1 *tatABCD* genes to predicted *tatABCD* genes present in the *S. typhimurium* genome and *Neisseria meningitidis* genome it seemed likely that the *tat* system may also be required
20 for virulence in these, and other, organisms. A deletion in the *S. typhimurium* *tatC* gene (SEQ ID NO. 17) was constructed by amplifying the DNA flanking either side of the *tatC* gene with the following primers:

25 5'-TGC TCT AGA AGG CGT TGT CGA TCC TG-3' (SEQ ID NO. 65)

5'-GAA CTG CAG GAA AAG GCC GAG CAG ACT G-3' (SEQ ID NO. 66)

5'-GAA CTG CAG TAC AGC CAT GTT TAC GGT-3' (SEQ ID NO. 67)

30

5'-CAT GCA TGC GGT GTA CGA CAG TTT GCG-3' (SEQ ID NO. 68)

Primers SEQ ID NO. 65 and SEQ ID NO. 66 were used to amplify DNA sequences downstream of the *S. typhimurium tatC* gene, Primers SEQ ID NO. 67 and SEQ ID NO. 68 were used to amplify DNA sequences upstream of the *S. typhimurium tatC* gene.

5 The encoded amino acid sequences for two regions of the *tatC* gene are shown as SEQ ID NO. 18 and SEQ ID NO. 19.

 After cloning these flanking DNA fragments into pUC19, a non-polar kanamycin resistance cassette (*aphT*) was inserted between the flanking DNA fragments to replace the *S. typhimurium tatC* gene. This DNA fragment was
10 then transferred to the suicide vector pCVD442. The chromosomal copy of the *S. typhimurium tatC* gene was then mutated by allelic transfer after conjugation of the pCVD442 construct into wild type *S. typhimurium* strains TML and SL1344.

 The disrupted *S. typhimurium tatC* gene was tested for attenuation of
15 virulence, using mixed and single infections in a murine model of systemic infection. For mixed infections, 6-7 week old *balbC* mice were inoculated intraperitoneally with 10^4 bacterial cells. Competitive indices were calculated after comparing the numbers of mutant and wild-type bacteria present in spleens after 3 days. For single infections, mice were inoculated either
20 intraperitoneally or orally with varying doses and mouse survival monitored for 17 days. The strains were attenuated in virulence, the competitive indices of the SL1344 *tatC* and TML *tatC* deletion strains being 0.078 and 0.098, respectively.

 In single infections, mouse survival was extended compared to the wild-
25 type controls.

 Sequence homology was also demonstrated with the *tat* sequence from *Neisseria meningitidis*. The gene sequence from *N. meningitidis* is shown as SEQ ID NO. 20 and the encoded amino acid sequence for *tatC* is shown as SEQ ID NO. 21.

30 To test for virulence, a deletion mutant was created using the following primers:

5'-TGCTCTAGACACATCATGGGCACACC-3' (SEQ ID NO. 69)

5'-GAACTGCAGAACCGTCCACATCAGGCG-3' (SEQ ID NO. 70)

5 5'-GAACTGCAGACCCTGCTTGCCATTCCG-3' (SEQ ID NO. 71)

5'-GAACTGCAGACCCTGCTTGCCATTCCG-3' (SEQ ID NO. 72)

Cloning of the DNA fragments and the *aphT* kanamycin resistance
 10 cassette into pUC19 followed the procedure outlined above for *S. typhimurium*.
 The chromosomal copy of the *N. meningitidis tatC*
 gene was mutated by transformation of the pUC19-based constructs into wild-
 type *N. meningitidis* cells.

Southern analysis of the resulting transformants indicated that all the
 15 transformants were merodiploids and contained both the wild-type and mutated
 copies of the *tatC* gene. This indicates that there is some selection against the
 isolation of mutants in which the *tatC* gene has been deleted.

Further studies on polar and non-polar constructs showed that
 transformants did not grow on selective media. This suggests that the *N.*
 20 *meningitidis tatC* gene is essential for the *in vitro* growth of this organism.

Example 7

A further mutant was identified with a transposon insertion within a
 nucleotide sequence identified herein as SEQ ID NO. 22, at nucleotide 3981.
 The sequence defined herein as *eck1*, shows sequence homology to several
 25 Group 1 glycosyltransferases from a number of bacteria. Sequence homology
 was also shown to the *gnd* gene of *E. coli* K12 (at nucleotides 4197-4604 of
 SEQ ID NO. 22).

The translation of the *E. coli eck1* gene is shown as SEQ ID NO. 26.
 The gene has been tested for attenuation of virulence, as described above, and
 30 is shown to be attenuated with a competitive index of 0.025.

Several open reading frames (ORF) were also identified from the DNA
 sequence (SEQ ID NO. 22). The first of these is defined herein as MS1 and a
 translation product shown as SEQ ID NO. 25. The amino acid sequence is
 shown to have 50.3% identity to a putative glycosyl transferase from *E. coli*

serotype 0111 (TrEMBL database accession number AAD46732). The amino acid sequence also shows homology with the eck1 protein from *E. coli* K1 and also the TrsE protein from *Yersinia enterocolitica* (TrEMBL database accession number Q56917).

5 A second open reading frame identified herein as MS2 had the gene sequence shown as SEQ ID NO. 24. This shows sequence homology to the putative glycosyl transferase TrsC from *Yersinia enterocolitica* (TrRMBL database accession number Q56915), and also the glycosyl transferase WbnA from *E. coli* serotype 0113 (TrEMBL database accession number AAD50485).

10 A third open reading frame encodes a product identified herein as MS3 (SEQ ID NO. 23). The amino acid sequence shows 30.2% identity to a rhamnosyltransferase from *Streptococcus mutans*.

 The gene sequence shown as SEQ ID NO. 22 may be at least part of a pathogenicity island, with multiple virulence genes being positioned in a cluster
15 on the microorganism's genome.

Example 8

 A further mutant was identified having a transposon insertion within the *iroCDE* operon. The nucleotide sequences flanking either side of the mini-Tn5 insertion are shown as SEQ ID NO. 27 and SEQ ID NO. 30.

20 The mini-Tn5 transposon is inserted at nucleotide 1272 of SEQ ID NO. 27 and at nucleotide 1 of SEQ ID NO. 30, and interrupts the *iroD* gene. The N-terminal region of *iroD* is shown as SEQ ID NO. 29, and the C-terminal region is shown as SEQ ID NO. 31.

 In addition to *iroD*, the gene shown as SEQ ID NO. 27 encodes a partial
25 peptide with the amino acid sequence shown as SEQ ID NO. 28. This amino acid sequence shows 70.9% identity to the putative ATP binding cassette transporter *iroC* from *Salmonella typhi*.

 The gene sequence shown as SEQ ID NO. 30 includes an open reading frame that encodes a peptide with the amino acid sequence shown as SEQ ID
30 NO. 32 and this has sequence homology to the *iroE* protein from *Salmonella typhi*.

Testing the genes in a model for attenuation of virulence, as described above, showed that the *iroD* gene was attenuated with a competitive index of 0.107. The mini-Tn5 mutation in the *iroD* gene has been reintroduced into the wild-type *E. coli* K1 strain by P1 transduction. The resulting transductant is also

5 attenuated in virulence with a competitive index of 0.1. This indicates that the attenuated phenotype is linked to the insertion within *iroD*. However, it is possible that the attenuation is due to a polar effect on the *E. coli* K1 *iroE* gene.

Example 9

A further mutant was identified with a transposon insertion within the

10 nucleotide sequence shown as SEQ ID NO. 33. The transposon is inserted at nucleotide 2264 of SEQ ID NO. 33. The nucleotide sequence shows sequence homology to the *as/A* / *hemY* region of *E. coli* K12 (EMBL accession number AE000456). The *as/A* encodes an arylsulfatase homologue whereas *hemY* is involved in the biosynthesis of protoheme IX. This demonstrates that the

15 disrupted region is at least partially identical to the *as/A* / *hemY* region of *E. coli* K12.

The transposon is inserted at nucleotide 2264 of SEQ ID NO. 33. This insertion site is 216 nucleotides downstream from the stop codon of the *hemY* gene and 472 nucleotides upstream from the start codon of the *as/A* gene.

20 The novel region has been tested for attenuation of virulence, as described above, and shown to be attenuated with a competitive index of 0.033. The mini-Tn5 mutation in this region has been reintroduced into the wild-type *E. coli* K1 strain by P1 transduction. The resulting transductant is also attenuated in virulence with a competitive index of 0.008. This indicates that

25 the attenuated phenotype is linked to the transposon insertion in this region. However, polar and non-polar deletion mutants of *as/A* were constructed and tested for attenuation of virulence as described above.

Neither the polar nor the non-polar mutants were attenuated in virulence and this demonstrates that the attenuation of the original transposon mutant is

30 not due to a polar effect on the *as/A* gene. This indicates that the transposon is disrupting some other function encoded within the intergenic region between *as/A* and *hemY*. For example there could be some untranslated RNA molecule,

such as a regulatory RNA similar to oxyS (Altuvia *et al.*, Cell, 1997;90:43-53), encoded within this region. Alternatively the transposon could be disrupting some DNA structure that may, for example, be involved in DNA replication. This DNA region is also present in the pathogen *Salmonella typhimurium* suggesting that it may be important for pathogenicity in other organisms. This region (SEQ ID NO. 33) may be used as a target, to identify anti-microbial drugs.

Example 10

A further mutant was identified and the DNA region flanking either side of the mini-Tn5 insertion was cloned and had the nucleotide sequence shown as SEQ ID NO. 34. This nucleotide sequence has homology with the *mtd2* gene of *Herpetosiphon aurantiacus* (EMBL accession number P25265), with the *mtd2* gene product functioning as a cytosine-specific methyltransferase. The *mtd2* gene is not found in the *E. coli* K12 genome and may represent a pathogenicity island.

The mini-Tn5 transposon insertions were located at nucleotides 4773 and 3764 of SEQ ID NO. 34 and were shown to interrupt the *mtd2* gene.

The amino acid sequence of the *mtd2* gene is shown as SEQ ID NO. 43.

The *E. coli* K1 *mtd2* gene was tested for attenuation of virulence, as described above, and shown to be attenuated with a competitive index of 0.073.

In addition to the *mtd2* gene, a series of open reading frames were also identified with translation products identified herein as MS4 to MS16, SEQ ID NOS. 48-44 and 42-35, respectively. As the open reading frames are located in a potential pathogenicity island, mutations in these genes may also result in attenuation in virulence. Further, since it is known that *E. coli* and other bacteria may encode peptides in different forms in the nucleotide sequence, the coding regions of some of these proteins may overlap. In addition, any aminoacid sequence shown starting with Val may in fact start with Met.

CLAIMS

1. A peptide encoded by an operon including any of the genes identified herein as *tatA*, *tatB*, *tatC*, *tatE*, *mdoG*, *creC*, *recG*, *yggN*, *eck1*, *iroD*, *iroC*, *iroE*, *mtd2* and *ms1* to 16, obtainable from *E. coli* K1, or a homologue thereof in a
5 Gram-negative bacterium, or a functional fragment thereof, for therapeutic use.
2. A peptide according to claim 1, comprising any of the amino acid sequences identified herein as SEQ ID NOS. 2, 5, 7, 9, 11, 12, 13, 14, 16, 18, 19, 21, 23, 24, 25, 26, 28, 29, 31, 32 and 35-48.
3. A polynucleotide encoding a peptide according to claim 1 or claim 2, for
10 therapeutic use.
4. A host transformed to express a peptide according to claim 1 or claim 2.
5. A vaccine comprising a peptide according to claim 1 or claim 2, or the means for its expression.
6. A vaccine comprising a microorganism having a virulence gene mutation,
15 wherein the gene encodes a peptide according to claim 1 or claim 2.
7. A vaccine according to claim 6, having a virulence gene deletion in two genes, wherein one gene encodes *tatA* and the other encodes *tatE*.
8. A vaccine according to claim 6, wherein the gene lies within a pathogenicity island, wherein the island comprises a gene identified herein.
- 20 9. Use of a product according to any of claims 1 to 4, or SEQ ID NO. 33, for screening potential drugs or for the detection of virulence.
10. Use of a product according to any of claims 1 to 4, for the manufacture of a medicament for use in the treatment or prevention of a condition associated with infection by a Gram-negative bacterium.
- 25 11. Use according to claim 10, wherein the bacterium is *E. coli*.

SEQUENCE LISTING

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<120> VIRULENCE GENES AND PROTEINS, AND THEIR USE

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 Val Gln Gln Thr Arg Arg Ser Thr Gly Asp Val Lys Gln Ser Asn Leu
 405 410 415

att cgc cag cct gac ggt act atc gcc ttt gtg gtc gat ttt acc ggc 2315
 Ile Arg Gln Pro Asp Gly Thr Ile Ala Phe Val Val Asp Phe Thr Gly
 420 425 430

gct gag atg aaa aaa ctg cca gag gat acc ccg gtc aca gcg caa acc 2363
 Ala Glu Met Lys Lys Leu Pro Glu Asp Thr Pro Val Thr Ala Gln Thr
 435 440 445

agc att ggt gat aat ggt gag ata gtt gaa agc acg gtg cgt tat aac 2411
 Ser Ile Gly Asp Asn Gly Glu Ile Val Glu Ser Thr Val Arg Tyr Asn
 450 455 460 465

ccg gtt acc aaa ggc tgg cgt ctg gtg atg cgt gtg aaa gtg aaa gat 2459
 Pro Val Thr Lys Gly Trp Arg Leu Val Met Arg Val Lys Val Lys Asp
 470 475 480

gcc aag aaa acc act gaa atg cgt gct gcg ctg gtg aat gcc gat cag 2507
 Ala Lys Lys Thr Thr Glu Met Arg Ala Ala Leu Val Asn Ala Asp Gln
 485 490 495

acg ttg agt gaa acc tgg agc tac cag tta cct gcc aat gaa 2549
 Thr Leu Ser Glu Thr Trp Ser Tyr Gln Leu Pro Ala Asn Glu
 500 505 510

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<211> 511

<212> PRT

<213> Escherichia coli

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 35 40 45

Ser Val Phe Arg Asp Met Lys Tyr Ala Asp Tyr Gln Gln Ile Gln Phe
 50 55 60

Asn His Asp Lys Ala Tyr Trp Asn Asn Leu Lys Thr Pro Phe Lys Leu
 65 70 75 80

Glu Phe Tyr His Gln Gly Met Tyr Phe Asp Thr Pro Val Lys Ile Asn
 85 90 95

Glu Val Thr Ala Thr Ala Val Lys Arg Ile Lys Tyr Ser Pro Asp Tyr
 100 105 110

Phe Thr Phe Gly Asp Val Gln His Asp Lys Asp Thr Val Lys Asp Leu
 115 120 125

Gly Phe Ala Gly Phe Lys Val Leu Tyr Pro Ile Asn Ser Lys Asp Lys
 130 135 140

Asn Asp Glu Ile Val Ser Met Leu Gly Ala Ser Tyr Phe Arg Val Ile
 145 150 155 160

Gly Ala Gly Gln Val Tyr Gly Leu Ser Ala Arg Gly Leu Ala Ile Asp
 165 170 175

Thr Ala Leu Pro Ser Gly Glu Glu Phe Pro Arg Phe Lys Glu Phe Trp
 180 185 190

Ile Glu Arg Pro Lys Pro Thr Asp Lys Arg Leu Thr Ile Tyr Ala Leu
 195 200 205

Leu Asp Ser Pro Arg Ala Thr Gly Ala Tyr Lys Phe Val Val Met Pro
 210 215 220

Gly Arg Asp Thr Val Val Asp Val Gln Ser Lys Ile Tyr Leu Arg Asp
 225 230 235 240

Lys Val Gly Lys Leu Gly Val Ala Pro Leu Thr Ser Met Phe Leu Phe
 245 250 255

Gly Pro Asn Gln Pro Ser Pro Ala Asn Asn Tyr Arg Pro Glu Leu His
 260 265 270

Asp Ser Asn Gly Leu Ser Ile His Ala Gly Asn Gly Glu Trp Ile Trp
 275 280 285

Arg Pro Leu Asn Asn Pro Lys His Leu Ala Val Ser Ser Phe Ser Met
 290 295 300

Glu Asn Pro Gln Gly Phe Gly Leu Leu Gln Arg Gly Arg Asp Phe Ser
 305 310 315 320

Arg Phe Glu Asp Leu Asp Asp Arg Tyr Asp Leu Arg Pro Ser Ala Trp
 325 330 335

Val Thr Pro Lys Gly Glu Trp Gly Lys Gly Ser Val Glu Leu Val Glu
 340 345 350

Ile Pro Thr Asn Asp Glu Thr Asn Asp Asn Ile Val Ala Tyr Trp Thr
 355 360 365

Pro Asp Gln Leu Pro Glu Pro Gly Lys Glu Met Asn Phe Lys Tyr Thr
 370 375 380

Ile Thr Phe Ser Arg Asp Glu Asp Lys Leu His Ala Pro Asp Asn Ala
 385 390 395 400

Trp Val Gln Gln Thr Arg Arg Ser Thr Gly Asp Val Lys Gln Ser Asn
 405 410 415

Leu Ile Arg Gln Pro Asp Gly Thr Ile Ala Phe Val Val Asp Phe Thr
 420 425 430

Gly Ala Glu Met Lys Lys Leu Pro Glu Asp Thr Pro Val Thr Ala Gln
 435 440 445

Thr Ser Ile Gly Asp Asn Gly Glu Ile Val Glu Ser Thr Val Arg Tyr
 450 455 460

Asn Pro Val Thr Lys Gly Trp Arg Leu Val Met Arg Val Lys Val Lys
 465 470 475 480

Asp Ala Lys Lys Thr Thr Glu Met Arg Ala Ala Leu Val Asn Ala Asp
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Gln Thr Leu Ser Glu Thr Trp Ser Tyr Gln Leu Pro Ala Asn Glu
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<211> 574

<212> DNA

<213> Escherichia coli

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 tgataccgat cggttccttg agatgaatcg tcaatgctcc cttgatgatg gttttatgca 180
 cgcggtgttt aaccgctcat ttaacgctct ggcaaccgca atggcgaccg cgcgtcaccg 240
 cgccagcaag gtgctggaaa tcgcccgtga ccgccacggt gaacaggcgc tgaacgagac 300
 gccagagaag ctgaatcgcg atcgtcgccct ggtgctgcta agcgatccgg tgacgatggc 360
 ccgtctgcat ttccgctct ggaattcccc ggagagatat tcttcatggg tgagttatta 420
 cgaagggata aagctcaatc cactggcatt gcgtaaaccg gatgcggcct cgcaataaaa 480
 acgtagtgtc ctgatgcgt acgcttatca ggcctacatc gttcctgcaa tttattgatt 540
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<210> 4

<211> 1478

<212> DNA

<213> Escherichia coli

<220>

<221> CDS

<222> (25) .. (1449)

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 Met Arg Ile Gly Met Arg Leu Leu Leu

1

5

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Gly Tyr Phe Leu Leu Val Ala Val Ala Ala Trp Phe Val Leu Ala Ile
10 15 20 25

ttt gtc aaa gaa gtt aaa ccg ggc gtg cga aga gca acc gag ggg acg 147
Phe Val Lys Glu Val Lys Pro Gly Val Arg Arg Ala Thr Glu Gly Thr
30 35 40

tta atc gac acc gca acg ttg ctg gcg gag ctg gcg cgt ccc gat ttg 195
Leu Ile Asp Thr Ala Thr Leu Leu Ala Glu Leu Ala Arg Pro Asp Leu
45 50 55

ctc tct ggg gac cca acg cat ggg caa ctg gcg cag gcg ttt aat cag 243
Leu Ser Gly Asp Pro Thr His Gly Gln Leu Ala Gln Ala Phe Asn Gln
60 65 70

cta caa cat cgc ccg ttt cgc gcc aat atc ggt ggc att aac aaa gtg 291
Leu Gln His Arg Pro Phe Arg Ala Asn Ile Gly Gly Ile Asn Lys Val
75 80 85

cgc aac gaa tat cat gtc tat atg acc gat gcg cag ggc aaa gta ttg 339
Arg Asn Glu Tyr His Val Tyr Met Thr Asp Ala Gln Gly Lys Val Leu
90 95 100 105

ttc gat tcg gca aat aaa gcc gtt gga cag gat tat tcg cgc tgg aat 387
Phe Asp Ser Ala Asn Lys Ala Val Gly Gln Asp Tyr Ser Arg Trp Asn
110 115 120

gac gtc tgg cta acg ttg cgt ggt cag tat ggt gcg cgc agc acg ttg 435
Asp Val Trp Leu Thr Leu Arg Gly Gln Tyr Gly Ala Arg Ser Thr Leu
125 130 135

caa aat cct gcc gat ccc gaa agt tct gtg atg tat gtt gcc gcg ccg 483
Gln Asn Pro Ala Asp Pro Glu Ser Ser Val Met Tyr Val Ala Ala Pro
140 145 150

att atg gac ggc tcg cgg ctt att ggc gtt ttg agc gta ggc aaa ccg 531
Ile Met Asp Gly Ser Arg Leu Ile Gly Val Leu Ser Val Gly Lys Pro
155 160 165

aac gcg gcg atg gct ccg gtc att aag cgt agc gag cgg cga att tta 579
Asn Ala Ala Met Ala Pro Val Ile Lys Arg Ser Glu Arg Arg Ile Leu
170 175 180 185

tgg gcc agc gcc att ttg ttg ggg att gca ctg gtg att ggc gca ggc 627
Trp Ala Ser Ala Ile Leu Leu Gly Ile Ala Leu Val Ile Gly Ala Gly

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	190	195	200	
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Met Val Trp Trp Ile Asn Arg Ser Ile Ala Arg Leu Thr Arg Tyr Ala				
	205	210	215	
gat tcc gtc act gac aat aag ccc gtt cct ctc ccc gat ctc ggt agt				723
Asp Ser Val Thr Asp Asn Lys Pro Val Pro Leu Pro Asp Leu Gly Ser				
	220	225	230	
agc gag ttg cgt aaa ctc gcg cag gcg ctg gaa agt atg cgc gtg aag				771
Ser Glu Leu Arg Lys Leu Ala Gln Ala Leu Glu Ser Met Arg Val Lys				
	235	240	245	
ctg gaa ggg aaa aac tat att gag cag tat gtt tat gcg tta act cat				819
Leu Glu Gly Lys Asn Tyr Ile Glu Gln Tyr Val Tyr Ala Leu Thr His				
	250	255	260	265
gag cta aaa agc cca ctg gcg gcg att cgt ggc gcg gcg gaa att tta				867
Glu Leu Lys Ser Pro Leu Ala Ala Ile Arg Gly Ala Ala Glu Ile Leu				
	270	275	280	
cgc gaa ggt ccg ccg ccg gaa gtg gtg gct cgt ttt acc gac aac att				915
Arg Glu Gly Pro Pro Pro Glu Val Val Ala Arg Phe Thr Asp Asn Ile				
	285	290	295	
ctg acg caa aat gcg cga atg cag gca ctg gtg gaa acg tta cta cgc				963
Leu Thr Gln Asn Ala Arg Met Gln Ala Leu Val Glu Thr Leu Leu Arg				
	300	305	310	
cag gca aga ctg gag aat cgt cag gaa gtc gtt ctg act gct gtt gat				1011
Gln Ala Arg Leu Glu Asn Arg Gln Glu Val Val Leu Thr Ala Val Asp				
	315	320	325	
gtg gcg gca tta ttt cgc cgc gtc agc gaa gcg cgc acc gtg cag ttg				1059
Val Ala Ala Leu Phe Arg Arg Val Ser Glu Ala Arg Thr Val Gln Leu				
	330	335	340	345
gca gaa aaa aac atc act ttg cat gtt atg cct act gag gtt aac gtt				1107
Ala Glu Lys Asn Ile Thr Leu His Val Met Pro Thr Glu Val Asn Val				
	350	355	360	
gct tct gaa ccg gcg tta ctg gag cag gcg ctg ggg aat tta ctg gat				1155
Ala Ser Glu Pro Ala Leu Leu Glu Gln Ala Leu Gly Asn Leu Leu Asp				
	365	370	375	
aac gcc atc gat ttt act ccc gag agc ggt tgc ata acg cta agc gcc				1203
Asn Ala Ile Asp Phe Thr Pro Glu Ser Gly Cys Ile Thr Leu Ser Ala				

380 385 390
 gaa gtg gat cag gaa tac gtc acc ctt aag gtg ctg gat acc ggt agt 1251
 Glu Val Asp Gln Glu Tyr Val Thr Leu Lys Val Leu Asp Thr Gly Ser
 395 400 405
 ggg att cct gac tac gcg ctg tca cgt att ttt gaa cgc ttt tac tct 1299
 Gly Ile Pro Asp Tyr Ala Leu Ser Arg Ile Phe Glu Arg Phe Tyr Ser
 410 415 420 425
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 Leu Pro Arg Ala Asn Gly Gln Lys Ser Ser Gly Leu Gly Leu Ala Phe
 430 435 440
 gtc agt gag gtc gcc cgt ttg ttt aac ggc gaa gtc acg ctg cgc aac 1395
 Val Ser Glu Val Ala Arg Leu Phe Asn Gly Glu Val Thr Leu Arg Asn
 445 450 455
 gtg cag gaa ggt ggc gtg ctg gcc tcg ctt cga ctt cac cgt cac ttc 1443
 Val Gln Glu Gly Gly Val Leu Ala Ser Leu Arg Leu His Arg His Phe
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 aca tag cttcaaattc ttccacata gtcttcgta 1478
 Thr
 475
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 <213> Escherichia coli
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 Gly Val Arg Arg Ala Thr Glu Gly Thr Leu Ile Asp Thr Ala Thr Leu
 35 40 45
 Leu Ala Glu Leu Ala Arg Pro Asp Leu Leu Ser Gly Asp Pro Thr His
 50 55 60
 Gly Gln Leu Ala Gln Ala Phe Asn Gln Leu Gln His Arg Pro Phe Arg
 65 70 75 80

Ala Asn Ile Gly Gly Ile Asn Lys Val Arg Asn Glu Tyr His Val Tyr
 85 90 95

Met Thr Asp Ala Gln Gly Lys Val Leu Phe Asp Ser Ala Asn Lys Ala
 100 105 110

Val Gly Gln Asp Tyr Ser Arg Trp Asn Asp Val Trp Leu Thr Leu Arg
 115 120 125

Gly Gln Tyr Gly Ala Arg Ser Thr Leu Gln Asn Pro Ala Asp Pro Glu
 130 135 140

Ser Ser Val Met Tyr Val Ala Ala Pro Ile Met Asp Gly Ser Arg Leu
 145 150 155 160

Ile Gly Val Leu Ser Val Gly Lys Pro Asn Ala Ala Met Ala Pro Val
 165 170 175

Ile Lys Arg Ser Glu Arg Arg Ile Leu Trp Ala Ser Ala Ile Leu Leu
 180 185 190

Gly Ile Ala Leu Val Ile Gly Ala Gly Met Val Trp Trp Ile Asn Arg
 195 200 205

Ser Ile Ala Arg Leu Thr Arg Tyr Ala Asp Ser Val Thr Asp Asn Lys
 210 215 220

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

Gln Ala Leu Glu Ser Met Arg Val Lys Leu Glu Gly Lys Asn Tyr Ile
 245 250 255

Glu Gln Tyr Val Tyr Ala Leu Thr His Glu Leu Lys Ser Pro Leu Ala
 260 265 270

Ala Ile Arg Gly Ala Ala Glu Ile Leu Arg Glu Gly Pro Pro Pro Glu
 275 280 285

Val Val Ala Arg Phe Thr Asp Asn Ile Leu Thr Gln Asn Ala Arg Met
 290 295 300

Gln Ala Leu Val Glu Thr Leu Leu Arg Gln Ala Arg Leu Glu Asn Arg
 305 310 315 320

Gln Glu Val Val Leu Thr Ala Val Asp Val Ala Ala Leu Phe Arg Arg
 325 330 335

Val Ser Glu Ala Arg Thr Val Gln Leu Ala Glu Lys Asn Ile Thr Leu
340 345 350

His Val Met Pro Thr Glu Val Asn Val Ala Ser Glu Pro Ala Leu Leu
355 360 365

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

Glu Ser Gly Cys Ile Thr Leu Ser Ala Glu Val Asp Gln Glu Tyr Val
385 390 395 400

Thr Leu Lys Val Leu Asp Thr Gly Ser Gly Ile Pro Asp Tyr Ala Leu
405 410 415

Ser Arg Ile Phe Glu Arg Phe Tyr Ser Leu Pro Arg Ala Asn Gly Gln
420 425 430

Lys Ser Ser Gly Leu Gly Leu Ala Phe Val Ser Glu Val Ala Arg Leu
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Ala Ser Leu Arg Leu His Arg His Phe Thr
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<213> Escherichia coli

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<222> (1)..(126)

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gtt ggc gca gcg ctt agt aac aag ctg gcg aaa atc aac ctg cat acc 96
Val Gly Ala Ala Leu Ser Asn Lys Leu Ala Lys Ile Asn Leu His Thr
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gta cag gat tta ctc tta cac ctt cct ctg cg 128

Val Gln Asp Leu Leu Leu His Leu Pro Leu
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 20 25 30

Val Gln Asp Leu Leu Leu His Leu Pro Leu
 35 40

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 atg atg cgc aaa atg ctg ctg gcg gca gca ctt tca gtg acg gca atg 168
 Met Met Arg Lys Met Leu Leu Ala Ala Ala Leu Ser Val Thr Ala Met
 1 5 10 15

 acc gct cac gcc gac tac cag tgc agc gtc acg ccg cgt gac gat gtg 216
 Thr Ala His Ala Asp Tyr Gln Cys Ser Val Thr Pro Arg Asp Asp Val
 20 25 30

 att gtc agc ccg caa acc gtg cag gtg aag ggc gaa aac ggc aat ctg 264
 Ile Val Ser Pro Gln Thr Val Gln Val Lys Gly Glu Asn Gly Asn Leu
 35 40 45

 gtg atc acg cca gac ggc aac gtg atg tat aac ggt aag caa tat tcc 312

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ctg	aat	gcc	gcc	cag	cgc	gag	cag	gcg	aag	gat	tat	cag	gct	gaa	cta	360	
Leu	Asn	Ala	Ala	Gln	Arg	Glu	Gln	Ala	Lys	Asp	Tyr	Gln	Ala	Glu	Leu		
65					70				75					80			
cgt	agc	acc	ctg	ccg	tgg	att	gat	gga	ggc	gcg	aaa	agc	cgc	gtc	gag	408	
Arg	Ser	Thr	Leu	Pro	Trp	Ile	Asp	Gly	Gly	Ala	Lys	Ser	Arg	Val	Glu		
				85				90						95			
aaa	gct	cgt	att	gcg	ctg	gat	aaa	att	atc	gtt	cag	gag	atg	ggc	gaa	456	
Lys	Ala	Arg	Ile	Ala	Leu	Asp	Lys	Ile	Ile	Val	Gln	Glu	Met	Gly	Glu		
			100				105						110				
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Ser	Ser	Lys	Met	Arg	Ser	Arg	Leu	Thr	Lys	Leu	Asp	Ala	Gln	Leu	Lys		
		115					120					125					
gag	cag	atg	aac	cgc	att	atc	gaa	acg	cgc	agc	gat	ggc	ctg	acg	ttt	552	
Glu	Gln	Met	Asn	Arg	Ile	Ile	Glu	Thr	Arg	Ser	Asp	Gly	Leu	Thr	Phe		
	130					135						140					
cac	tat	aaa	gcc	att	gat	cag	gtt	cgt	gcc	gaa	ggc	cag	caa	tta	gtg	600	
His	Tyr	Lys	Ala	Ile	Asp	Gln	Val	Arg	Ala	Glu	Gly	Gln	Gln	Leu	Val		
145					150					155				160			
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Asn	Gln	Ala	Met	Gly	Gly	Ile	Leu	Gln	Asp	Ser	Ile	Asn	Glu	Met	Gly		
				165					170					175			
gcg	aaa	gcg	gtg	ctg	aaa	agc	ggc	ggt	aac	cca	tta	cag	aac	gtg	ctg	696	
Ala	Lys	Ala	Val	Leu	Lys	Ser	Gly	Gly	Asn	Pro	Leu	Gln	Asn	Val	Leu		
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Gly	Ser	Leu	Gly	Gly	Leu	Gln	Ser	Ser	Ile	Gln	Thr	Glu	Trp	Lys	Lys		
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Val	Thr	Leu	Glu	Asp	Ser	Arg	Lys	Ala	Leu	Val	Gly	Asn	Leu	Lys			
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<211> 239

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<213> *Escherichia coli*

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Ile Val Ser Pro Gln Thr Val Gln Val Lys Gly Glu Asn Gly Asn Leu
35 40 45

Val Ile Thr Pro Asp Gly Asn Val Met Tyr Asn Gly Lys Gln Tyr Ser
50 55 60

Leu Asn Ala Ala Gln Arg Glu Gln Ala Lys Asp Tyr Gln Ala Glu Leu
65 70 75 80

Arg Ser Thr Leu Pro Trp Ile Asp Gly Gly Ala Lys Ser Arg Val Glu
85 90 95

Lys Ala Arg Ile Ala Leu Asp Lys Ile Ile Val Gln Glu Met Gly Glu
100 105 110

Ser Ser Lys Met Arg Ser Arg Leu Thr Lys Leu Asp Ala Gln Leu Lys
115 120 125

Glu Gln Met Asn Arg Ile Ile Glu Thr Arg Ser Asp Gly Leu Thr Phe
130 135 140

His Tyr Lys Ala Ile Asp Gln Val Arg Ala Glu Gly Gln Gln Leu Val
145 150 155 160

Asn Gln Ala Met Gly Gly Ile Leu Gln Asp Ser Ile Asn Glu Met Gly
 165 170 175

Ala Lys Ala Val Leu Lys Ser Gly Gly Asn Pro Leu Gln Asn Val Leu
 180 185 190

Gly Ser Leu Gly Gly Leu Gln Ser Ser Ile Gln Thr Glu Trp Lys Lys
 195 200 205

Gln Glu Lys Asp Phe Gln Gln Phe Gly Lys Asp Val Cys Ser Arg Val
 210 215 220

Val Thr Leu Glu Asp Ser Arg Lys Ala Leu Val Gly Asn Leu Lys
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agaagataaa cgctatctgg cggaaaactt tatcgccttc tttaatcgcg actatcgcaa 300

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tataatgcgg ctttgtttaa tcatcatcta ccacagagga acatgt atg ggt ggt      1015
                                   Met Gly Gly
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atc agt att tgg cag tta ttg att att gcc gtc atc gtt gta ctg ctt      1063
Ile Ser Ile Trp Gln Leu Leu Ile Ile Ala Val Ile Val Val Leu Leu
      5              10              15

ttt ggc acc aaa aag ctc ggc tcc atc ggt tcc gat ctt ggt gcg tcg      1111
Phe Gly Thr Lys Lys Leu Gly Ser Ile Gly Ser Asp Leu Gly Ala Ser
      20              25              30              35

atc aaa ggc ttt aaa aaa gca atg agc gat gat gaa cca aag cag gat      1159
Ile Lys Gly Phe Lys Lys Ala Met Ser Asp Asp Glu Pro Lys Gln Asp
              40              45              50

aaa acc agc cag gat gct gat ttt act gcg aaa act atc gcc gat aag      1207
Lys Thr Ser Gln Asp Ala Asp Phe Thr Ala Lys Thr Ile Ala Asp Lys
              55              60              65

cag gcg gat acg aat cag gaa cag gct aaa ata gaa gac gcg aag cgc      1255
Gln Ala Asp Thr Asn Gln Glu Gln Ala Lys Ile Glu Asp Ala Lys Arg
              70              75              80

cac gat aaa gag cag gtg taa tct gtg ttt gat atc ggt ttt agc gaa      1303

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His Asp Lys Glu Gln Val	Val Phe Asp Ile Gly Phe Ser Glu	
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ctg cta ttg gtg ttc atc atc ggc ctc gtc gtt ctg ggg ccg caa cga	1351	
Leu Leu Leu Val Phe Ile Ile Gly Leu Val Val Leu Gly Pro Gln Arg		
100	105	110
ctg cct gtg gcg gta aaa acg gta gcg ggc tgg att cgc gcg ttg cgt	1399	
Leu Pro Val Ala Val Lys Thr Val Ala Gly Trp Ile Arg Ala Leu Arg		
115	120	125 130
tca ctg gcg aca acg gtg cag aac gaa ctg acc cag gag tta aaa ctc	1447	
Ser Leu Ala Thr Thr Val Gln Asn Glu Leu Thr Gln Glu Leu Lys Leu		
135	140	145
cag gag ttt cag gac agt ctg aaa aag gtt gaa aag gcg agc ctc act	1495	
Gln Glu Phe Gln Asp Ser Leu Lys Lys Val Glu Lys Ala Ser Leu Thr		
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aac ctg acg ccc gaa ctg aaa gcg tcg atg gat gaa tta cgc cag gct	1543	
Asn Leu Thr Pro Glu Leu Lys Ala Ser Met Asp Glu Leu Arg Gln Ala		
165	170	175
gcg gag tcg atg aaa cgt tcc tac gtt gca aac gat cct gaa aag gcg	1591	
Ala Glu Ser Met Lys Arg Ser Tyr Val Ala Asn Asp Pro Glu Lys Ala		
180	185	190
agc gat gaa gcg cac acc atc cat aac ccg gtg gtg aaa gac aat gaa	1639	
Ser Asp Glu Ala His Thr Ile His Asn Pro Val Val Lys Asp Asn Glu		
195	200	205 210
act gcg cat gaa ggc gta acg cct gct gct gca caa acg cag gcc agt	1687	
Thr Ala His Glu Gly Val Thr Pro Ala Ala Ala Gln Thr Gln Ala Ser		
215	220	225
tcg ccg gaa cag aag cca gaa acc acg cca gag ccg gtg gta aaa cct	1735	
Ser Pro Glu Gln Lys Pro Glu Thr Thr Pro Glu Pro Val Val Lys Pro		
230	235	240
gct gcg gac gct gaa ccg aaa acc gct gca cct tcc cct tcg tcg agt	1783	
Ala Ala Asp Ala Glu Pro Lys Thr Ala Ala Pro Ser Pro Ser Ser Ser		
245	250	255
gat aaa ccg taaac atg tct gta gaa gat act caa ccg ctt atc acg cat	1833	
Asp Lys Pro Met Ser Val Glu Asp Thr Gln Pro Leu Ile Thr His		
260	265	270
ctg att gag ctg cgt aag cgt ctg ctg aac tgc att atc tcg gtg atc	1881	

Leu Ile Glu Leu Arg Lys Arg Leu Leu Asn Cys Ile Ile Ser Val Ile	
275	280 285
gtg ata ttc ctg tgt ctg gtc tat ttc gcc aat gac atc tat cac ctg	1929
Val Ile Phe Leu Cys Leu Val Tyr Phe Ala Asn Asp Ile Tyr His Leu	
290	295 300 305
gta tcc gcg cca ctg atc aag cag ttg ccg caa ggt tca acg atg atc	1977
Val Ser Ala Pro Leu Ile Lys Gln Leu Pro Gln Gly Ser Thr Met Ile	
	310 315 320
gcc acc gac gtg gcc tcg ccg ttc ttt acg ccg atc aag ctg acc ttt	2025
Ala Thr Asp Val Ala Ser Pro Phe Phe Thr Pro Ile Lys Leu Thr Phe	
	325 330 335
atg gtg tcg ctg att ctg tca gcg ccg gtg att ctc tat cag gtg tgg	2073
Met Val Ser Leu Ile Leu Ser Ala Pro Val Ile Leu Tyr Gln Val Trp	
	340 345 350
gcg ttt atc gcc cca gcg ctg tat aag cat gaa cgt cgc ctg gtg gtg	2121
Ala Phe Ile Ala Pro Ala Leu Tyr Lys His Glu Arg Arg Leu Val Val	
	355 360 365
ccg ctg ctg gtt tcc agc tct ctg ctg ttt tat atc ggc atg gcg ttc	2169
Pro Leu Leu Val Ser Ser Ser Leu Leu Phe Tyr Ile Gly Met Ala Phe	
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gcc tac ttt gtg gtc ttt ccg ctg gca ttt ggc ttc ctt gcc aat acc	2217
Ala Tyr Phe Val Val Phe Pro Leu Ala Phe Gly Phe Leu Ala Asn Thr	
	390 395 400
gcg ccg gaa ggg gta cag gta tcc acc gac atc gcg agc tat tta agc	2265
Ala Pro Glu Gly Val Gln Val Ser Thr Asp Ile Ala Ser Tyr Leu Ser	
	405 410 415
ttc gtt atg gcg ctg ttt atg gcg ttt ggt gtc tcc ttt gaa gtg ccg	2313
Phe Val Met Ala Leu Phe Met Ala Phe Gly Val Ser Phe Glu Val Pro	
	420 425 430
gtg gca att gtg ctg ctg tgc tgg atg ggg att acc tcg cca gaa gac	2361
Val Ala Ile Val Leu Leu Cys Trp Met Gly Ile Thr Ser Pro Glu Asp	
	435 440 445
tta cgc aaa aaa cgc ccg tat gtg ctg gtt ggt gca ttc gtt gtc ggg	2409
Leu Arg Lys Lys Arg Pro Tyr Val Leu Val Gly Ala Phe Val Val Gly	
	450 455 460 465
atg ttg ctg acg ccg ccg gat gtc ttc tcg caa acg ctg ttg gcg atc	2457

Met Leu Leu Thr Pro Pro Asp Val Phe Ser Gln Thr Leu Leu Ala Ile	
470 475 480	
cct atg tac tgc ctg ttt gaa atc ggt gtc ttc ttc tca cgc ttt tac	2505
Pro Met Tyr Cys Leu Phe Glu Ile Gly Val Phe Phe Ser Arg Phe Tyr	
485 490 495	
ggt ggt aaa ggg cga aac cgg gaa gag gaa aac gac gct gaa gca gaa	2553
Val Gly Lys Gly Arg Asn Arg Glu Glu Glu Asn Asp Ala Glu Ala Glu	
500 505 510	
agc gaa aaa act gaa gaa taa attcaaccgc ccgtcagggc gggtgtcat atg	2606
Ser Glu Lys Thr Glu Glu Met	
515 520	
gag tac agg atg ttt gat atc ggc gtt aat ttg acc agt tcg caa ttt	2654
Glu Tyr Arg Met Phe Asp Ile Gly Val Asn Leu Thr Ser Ser Gln Phe	
525 530 535	
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Ala Lys Asp Arg Asp Asp Val Val Ala Arg Ala Phe Asp Ala Gly Val	
540 545 550	
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Asn Gly Leu Leu Ile Thr Gly Thr Asn Leu Arg Glu Ser Gln Gln Ala	
555 560 565	
caa aag ctg gcg cgt cag tat tcg tcc tgt tgg tca acg gcg ggc gta	2798
Gln Lys Leu Ala Arg Gln Tyr Ser Ser Cys Trp Ser Thr Ala Gly Val	
570 575 580 585	
cat cct cac gac agc agc cag tgg caa gct gtg act gaa gaa gcg att	2846
His Pro His Asp Ser Ser Gln Trp Gln Ala Val Thr Glu Glu Ala Ile	
590 595 600	
att gag ctg gcc gcg cag cca gaa gtg gtg gcg att ggt gaa tgt ggt	2894
Ile Glu Leu Ala Ala Gln Pro Glu Val Val Ala Ile Gly Glu Cys Gly	
605 610 615	
ctc gac ttt aac cgc aac ttt tcg acg ccg gaa gag cag gaa cgc gct	2942
Leu Asp Phe Asn Arg Asn Phe Ser Thr Pro Glu Glu Gln Glu Arg Ala	
620 625 630	
ttt gtt gcc cag cta cgc att gcc gca gaa tta aac atg ccg gta ttt	2990
Phe Val Ala Gln Leu Arg Ile Ala Ala Glu Leu Asn Met Pro Val Phe	
635 640 645	
atg cac tgt cgc gat gcc cac gag cgg ttt atg aca ttg ctg gag ccg	3038

Met His Cys Arg Asp Ala His Glu Arg Phe Met Thr Leu Leu Glu Pro
650 655 660 665

tgg ctg gat aaa ctg cct ggt gcg gtt ctt cat tgc ttt acc ggc aca 3086
Trp Leu Asp Lys Leu Pro Gly Ala Val Leu His Cys Phe Thr Gly Thr
670 675 680

cgc gaa gag atg cag gcg tgc gtg gcg tgt gga att tat atc ggc att 3134
Arg Glu Glu Met Gln Ala Cys Val Ala Cys Gly Ile Tyr Ile Gly Ile
685 690 695

acc ggt tgg gtt tgc gat gaa cga cgc ggg ctg gag ctg cgg gaa ttg 3182
Thr Gly Trp Val Cys Asp Glu Arg Arg Gly Leu Glu Leu Arg Glu Leu
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Leu Pro Leu Ile Pro Ala Glu Lys Leu Leu Ile Glu Thr Asp Ala Pro
715 720 725

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Tyr Leu Leu Pro Arg Asp Leu Thr Pro Lys Pro Ser Ser Arg Arg Asn
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Glu Pro Ala His Leu Pro His Ile Leu Gln Arg Ile Ala His Trp Arg
750 755 760

gga gaa gat gcc gca tgg ctg gct gcc acc acg gat gcc aat gtc aaa 3374
Gly Glu Asp Ala Ala Trp Leu Ala Ala Thr Thr Asp Ala Asn Val Lys
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aca ctg ttt ggg att gcg ttt tag agtttgcg 3406
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<213> Escherichia coli

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Gly Ala Ser Ile Lys Gly Phe Lys Lys Ala Met Ser Asp Asp Glu Pro
 35 40 45

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

Glu Leu Thr Gln Glu Leu Lys Leu Gln Glu Phe Gln Asp Ser Leu Lys
 50 55 60

Lys Val Glu Lys Ala Ser Leu Thr Asn Leu Thr Pro Glu Leu Lys Ala
 65 70 75 80

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

Val Ala Asn Asp Pro Glu Lys Ala Ser Asp Glu Ala His Thr Ile His
 100 105 110

Asn Pro Val Val Lys Asp Asn Glu Thr Ala His Glu Gly Val Thr Pro
 115 120 125

Ala Ala Ala Gln Thr Gln Ala Ser Ser Pro Glu Gln Lys Pro Glu Thr
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Thr Pro Glu Pro Val Val Lys Pro Ala Ala Asp Ala Glu Pro Lys Thr
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Ala Ala Pro Ser Pro Ser Ser Ser Asp Lys Pro
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<213> Escherichia coli

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Cys Leu Val Tyr Phe Ala Asn Asp Ile Tyr His Leu Val Ser Ala Pro
 35 40 45

Leu Ile Lys Gln Leu Pro Gln Gly Ser Thr Met Ile Ala Thr Asp Val
 50 55 60

Ala Ser Pro Phe Phe Thr Pro Ile Lys Leu Thr Phe Met Val Ser Leu
 65 70 75 80

Ile Leu Ser Ala Pro Val Ile Leu Tyr Gln Val Trp Ala Phe Ile Ala
 85 90 95

Pro Ala Leu Tyr Lys His Glu Arg Arg Leu Val Val Pro Leu Leu Val
 100 105 110

Ser Ser Ser Leu Leu Phe Tyr Ile Gly Met Ala Phe Ala Tyr Phe Val
 115 120 125

Val Phe Pro Leu Ala Phe Gly Phe Leu Ala Asn Thr Ala Pro Glu Gly
 130 135 140

Val Gln Val Ser Thr Asp Ile Ala Ser Tyr Leu Ser Phe Val Met Ala
 145 150 155 160

Leu Phe Met Ala Phe Gly Val Ser Phe Glu Val Pro Val Ala Ile Val
 165 170 175

Leu Leu Cys Trp Met Gly Ile Thr Ser Pro Glu Asp Leu Arg Lys Lys
 180 185 190

Arg Pro Tyr Val Leu Val Gly Ala Phe Val Val Gly Met Leu Leu Thr

195	200	205
Pro Pro Asp Val Phe Ser Gln Thr Leu Leu Ala Ile Pro Met Tyr Cys		
210	215	220
Leu Phe Glu Ile Gly Val Phe Phe Ser Arg Phe Tyr Val Gly Lys Gly		
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Glu Glu

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<211> 264

<212> PRT

<213> Escherichia coli

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Val Asn Gly Leu Leu Ile Thr Gly Thr Asn Leu Arg Glu Ser Gln Gln		
35	40	45
Ala Gln Lys Leu Ala Arg Gln Tyr Ser Ser Cys Trp Ser Thr Ala Gly		
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Val His Pro His Asp Ser Ser Gln Trp Gln Ala Val Thr Glu Glu Ala		
65	70	75 80
Ile Ile Glu Leu Ala Ala Gln Pro Glu Val Val Ala Ile Gly Glu Cys		
85	90	95
Gly Leu Asp Phe Asn Arg Asn Phe Ser Thr Pro Glu Glu Gln Glu Arg		
100	105	110
Ala Phe Val Ala Gln Leu Arg Ile Ala Ala Glu Leu Asn Met Pro Val		
115	120	125
Phe Met His Cys Arg Asp Ala His Glu Arg Phe Met Thr Leu Leu Glu		
130	135	140
Pro Trp Leu Asp Lys Leu Pro Gly Ala Val Leu His Cys Phe Thr Gly		

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Phe Gly Thr Lys Lys Leu Arg Thr Leu Gly Gly Asp Leu Gly Ala Ala
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 Ile Lys Gly Phe Lys Lys Ala Met Asn Asp Asp Ala Ala Ala Lys
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 aaa ggc gca gac gtt gat ctt cag gct gaa aag ctc tct cat aaa gag 370
 Lys Gly Ala Asp Val Asp Leu Gln Ala Glu Lys Leu Ser His Lys Glu
 55 60 65
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 agcggggtttt ttatcagaca gatgtaagta attattacag gattacttaa cttccatccc 490
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<211> 67

<212> PRT

<213> Escherichia coli

<400> 16

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 20 25 30
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 Ala Ala Lys Lys Gly Ala Asp Val Asp Leu Gln Ala Glu Lys Leu Ser
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 His Lys Glu
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<210> 17

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<212> DNA

<213> Salmonella typhimurium

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<222> (947) .. (1444)

<220>

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<222> (1450) .. (1722)

<400> 17

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gaa gat act caa ccg ctt atc acg cat ctg atc gag ttg cgt aag cgc 1003
Glu Asp Thr Gln Pro Leu Ile Thr His Leu Ile Glu Leu Arg Lys Arg
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 Tyr Phe Ala Asn Asp Ile Tyr His Leu Val Ala Ala Pro Leu Ile Lys
 40 45 50

 cag atg ccg caa ggg gcg aca atg att gcg acg gat gtg gcg tcg ccg 1147
 Gln Met Pro Gln Gly Ala Thr Met Ile Ala Thr Asp Val Ala Ser Pro
 55 60 65

 ttt ttt acg cct atc aaa ctc acc ttc atg gtg tct ttg atc tta tcc 1195
 Phe Phe Thr Pro Ile Lys Leu Thr Phe Met Val Ser Leu Ile Leu Ser
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 Tyr Lys His Glu Arg Arg Leu Val Val Pro Leu Leu Val Ser Ser Ser
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 ctg ctt ttc tat att ggt atg gcc ttc gcc tat ttt gtc gta ttc cct 1339
 Leu Leu Phe Tyr Ile Gly Met Ala Phe Ala Tyr Phe Val Val Phe Pro
 120 125 130

 ttg gcc ttt ggt ttc ctg acg cat acg gcg ccg gaa ggg gta cag gtt 1387
 Leu Ala Phe Gly Phe Leu Thr His Thr Ala Pro Glu Gly Val Gln Val
 135 140 145

 tcg aca gat atc gcc agc tat ctt agc ttt gtc atg gcg ctt ttt atg 1435
 Ser Thr Asp Ile Ala Ser Tyr Leu Ser Phe Val Met Ala Leu Phe Met
 150 155 160

 gcc ttt gcg tagcc ttt gaa gtg ccg gtg gcg att gtg ttg ctg tgc tgg 1485
 Ala Phe Ala Phe Glu Val Pro Val Ala Ile Val Leu Leu Cys Trp
 165 170 175

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 Met Gly Ile Thr Thr Pro Glu Asp Leu Arg Lys Lys Arg Pro Tyr Ile
 180 185 190

 ctg gtc ggg gca ttc att gtg gga atg ctg ctt acg ccg cca gat gtt 1581
 Leu Val Gly Ala Phe Ile Val Gly Met Leu Leu Thr Pro Pro Asp Val
 195 200 205 210

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ggctacaatg gacgccatga aatatcacga ttacgcgac ttctgacgc tacttgagca 3282
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 <211> 166
 <212> PRT
 <213> Salmonella typhimurium

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 Arg Lys Arg Leu Leu Asn Cys Ile Val Ala Val Leu Leu Ile Phe Leu
 20 25 30
 Ala Leu Ile Tyr Phe Ala Asn Asp Ile Tyr His Leu Val Ala Ala Pro
 35 40 45
 Leu Ile Lys Gln Met Pro Gln Gly Ala Thr Met Ile Ala Thr Asp Val
 50 55 60
 Ala Ser Pro Phe Phe Thr Pro Ile Lys Leu Thr Phe Met Val Ser Leu
 65 70 75 80
 Ile Leu Ser Ala Pro Val Ile Leu Tyr Gln Val Trp Ala Phe Ile Ala
 85 90 95
 Pro Ala Leu Tyr Lys His Glu Arg Arg Leu Val Val Pro Leu Leu Val
 100 105 110
 Ser Ser Ser Leu Leu Phe Tyr Ile Gly Met Ala Phe Ala Tyr Phe Val
 115 120 125
 Val Phe Pro Leu Ala Phe Gly Phe Leu Thr His Thr Ala Pro Glu Gly
 130 135 140
 Val Gln Val Ser Thr Asp Ile Ala Ser Tyr Leu Ser Phe Val Met Ala
 145 150 155 160
 Leu Phe Met Ala Phe Ala
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 <211> 91
 <212> PRT
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 20 25 30

Phe Ile Val Gly Met Leu Leu Thr Pro Pro Asp Val Phe Ser Gln Thr
 35 40 45

Leu Leu Ala Ile Pro Met Tyr Cys Leu Phe Glu Ile Gly Val Phe Cys
 50 55 60

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

Ala Glu Thr Glu Lys Ala Glu His Thr Glu Asp
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<210> 20

<211> 2601

<212> DNA

<213> *Neisseria meningitidis*

<220>

<221> CDS

<222> (1572)..(2339)

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 aactgtatatt tctgcaaaat cgccgcaaaa gacattccgg cgcaaaccgt ctatgaagac 360
 ggcgaaatgg tttgtttcaa agacatcaac cccgctgctc cggttcatct gctgctgatt 420
 cccaaagtcc atttcgattc gttggcacac gccgcgcccg aacatcagcc ccttttggga 480
 aaaatgatgc tgaaagttcc cgaaatcgcc aaagcggcag gactggcaga cggcttcaaa 540
 accctgatca acaccgaaa aggcggcgga caagaggtct tccacctgca tatacacatc 600

34

agc atg att gcc acc gat gtc atc gca cca ttt ttc gtg ccg gtc aaa	1802
Ser Met Ile Ala Thr Asp Val Ile Ala Pro Phe Phe Val Pro Val Lys	
65 70 75	
gtt acc ctg atg gcg gca ttt tta att tcg ctg ccg cat acg ctc tac	1850
Val Thr Leu Met Ala Ala Phe Leu Ile Ser Leu Pro His Thr Leu Tyr	
80 85 90	
caa atc tgg gca ttc gtc gcc ccc gca ctc tac caa aac gaa aaa cgc	1898
Gln Ile Trp Ala Phe Val Ala Pro Ala Leu Tyr Gln Asn Glu Lys Arg	
95 100 105	
ctg att acg ccg ctc gtc ctc tcc agc gtc agc ctg ttt ttc atc ggc	1946
Leu Ile Thr Pro Leu Val Leu Ser Ser Val Ser Leu Phe Phe Ile Gly	
110 115 120 125	
atg gca ttt gcc tac ttt ttg gtt ttc ccc gtc att ttc aaa ttc ctt	1994
Met Ala Phe Ala Tyr Phe Leu Val Phe Pro Val Ile Phe Lys Phe Leu	
130 135 140	
gcc agc gtt acc cct gtc ggt gtc aat atg gcg aca gac atc gac aaa	2042
Ala Ser Val Thr Pro Val Gly Val Asn Met Ala Thr Asp Ile Asp Lys	
145 150 155	
tac ctc tcc ttc atc ttg ggg atg ttt gtc gca ttc ggt aca acg ttt	2090
Tyr Leu Ser Phe Ile Leu Gly Met Phe Val Ala Phe Gly Thr Thr Phe	
160 165 170	
gaa gtc ccc att gtc gtt atc ctg tta acc aaa att ggt gtg gta aca	2138
Glu Val Pro Ile Val Val Ile Leu Leu Thr Lys Ile Gly Val Val Thr	
175 180 185	
acc gaa cag ctc aaa cgc gcc cgc ccc tat gtg att gtc ggc gcg ttt	2186
Thr Glu Gln Leu Lys Arg Ala Arg Pro Tyr Val Ile Val Gly Ala Phe	
190 195 200 205	
gtc att gcc gcc atc atc acg ccg ccc gat gtg att tca caa acc ctg	2234
Val Ile Ala Ala Ile Ile Thr Pro Pro Asp Val Ile Ser Gln Thr Leu	
210 215 220	
ctt gcc att ccg ctg att ctc tta tac gaa gca ggt att tgg ttc gga	2282
Leu Ala Ile Pro Leu Ile Leu Leu Tyr Glu Ala Gly Ile Trp Phe Gly	
225 230 235	
cgc ttt ttc acg cca cgt tca gaa cag gat ggc gac ata cag ccg cct	2330
Arg Phe Phe Thr Pro Arg Ser Glu Gln Asp Gly Asp Ile Gln Pro Pro	
240 245 250	

gca aca acc tgacactatg ccgtccgaac ctccgcctca taccgccaca 2379
 Ala Thr Thr
 255

gattaaggaa tacctttgaa taccctctat ttaggttcaa acagcccgcg ccgaatggaa 2439
 atcctgacac agttgggcta tcaggtcgtc aagctgcctg ccaacatcga cgaaacggtc 2499
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<210> 21

<211> 256

<212> PRT

<213> Neisseria meningitidis

<400> 21

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Leu	Ile	Glu	Leu	Arg	Arg	Arg	Leu	Met	Trp	Thr	Val	Val	Gly	Ile	Leu
			20				25						30		

Val	Cys	Phe	Phe	Gly	Leu	Met	Pro	Phe	Ala	Gln	Gln	Leu	Tyr	Thr	Phe
	35						40					45			

Ile	Ala	Asp	Pro	Leu	Met	Ala	Asn	Leu	Pro	Lys	Asp	Thr	Ser	Met	Ile
50						55				60					

Ala	Thr	Asp	Val	Ile	Ala	Pro	Phe	Phe	Val	Pro	Val	Lys	Val	Thr	Leu
65					70				75						80

Met	Ala	Ala	Phe	Leu	Ile	Ser	Leu	Pro	His	Thr	Leu	Tyr	Gln	Ile	Trp
			85					90						95	

Ala	Phe	Val	Ala	Pro	Ala	Leu	Tyr	Gln	Asn	Glu	Lys	Arg	Leu	Ile	Thr
		100				105						110			

Pro	Leu	Val	Leu	Ser	Ser	Val	Ser	Leu	Phe	Phe	Ile	Gly	Met	Ala	Phe
	115					120					125				

Ala	Tyr	Phe	Leu	Val	Phe	Pro	Val	Ile	Phe	Lys	Phe	Leu	Ala	Ser	Val
	130					135					140				

Thr	Pro	Val	Gly	Val	Asn	Met	Ala	Thr	Asp	Ile	Asp	Lys	Tyr	Leu	Ser
145					150				155					160	

Phe Ile Leu Gly Met Phe Val Ala Phe Gly Thr Thr Phe Glu Val Pro
 165 170 175

Ile Val Val Ile Leu Leu Thr Lys Ile Gly Val Val Thr Thr Glu Gln
 180 185 190

Leu Lys Arg Ala Arg Pro Tyr Val Ile Val Gly Ala Phe Val Ile Ala
 195 200 205

Ala Ile Ile Thr Pro Pro Asp Val Ile Ser Gln Thr Leu Leu Ala Ile
 210 215 220

Pro Leu Ile Leu Leu Tyr Glu Ala Gly Ile Trp Phe Gly Arg Phe Phe
 225 230 235 240

Thr Pro Arg Ser Glu Gln Asp Gly Asp Ile Gln Pro Pro Ala Thr Thr
 245 250 255

<210> 22

<211> 4604

<212> DNA

<213> Escherichia coli

<220>

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<222> (2982)..(4082)

<220>

<221> CDS

<222> (1534)..(2637)

<220>

<221> CDS

<222> (749)..(1531)

<220>

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<222> (6)..(746)

<400> 22

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tcg ctg ata aag tac agc gag aca gat tat aca att tat tgt gac caa 98

Ser	Leu	Ile	Lys	Tyr	Ser	Glu	Thr	Asp	Tyr	Thr	Ile	Tyr	Cys	Asp	Gln	
				20					25					30		
gat	gat	att	tgg	tta	gaa	aac	aaa	ata	ttt	gaa	tta	gta	aag	tat	gca	146
Asp	Asp	Ile	Trp	Leu	Glu	Asn	Lys	Ile	Phe	Glu	Leu	Val	Lys	Tyr	Ala	
			35					40					45			
aat	gaa	att	aaa	ttg	aat	gta	tca	gat	gcg	cct	tcg	cta	gtt	tat	gct	194
Asn	Glu	Ile	Lys	Leu	Asn	Val	Ser	Asp	Ala	Pro	Ser	Leu	Val	Tyr	Ala	
			50					55					60			
gat	ggc	tat	gct	tat	atg	gat	ggg	gag	ggg	aca	atc	gat	ttt	tct	ggg	242
Asp	Gly	Tyr	Ala	Tyr	Met	Asp	Gly	Glu	Gly	Thr	Ile	Asp	Phe	Ser	Gly	
			65				70					75				
ata	tct	aac	aat	cat	gct	gat	caa	tta	aag	gat	ttt	ctt	ttt	ttt	aat	290
Ile	Ser	Asn	Asn	His	Ala	Asp	Gln	Leu	Lys	Asp	Phe	Leu	Phe	Phe	Asn	
			80				85				90				95	
ggg	gga	tac	caa	gga	tgt	tct	att	atg	ttc	aat	cgt	gca	atg	acc	aaa	338
Gly	Gly	Tyr	Gln	Gly	Cys	Ser	Ile	Met	Phe	Asn	Arg	Ala	Met	Thr	Lys	
							100				105				110	
ttt	ctt	ctg	aat	tat	cga	gga	ttt	gta	tat	cta	cat	gac	gat	atc	aca	386
Phe	Leu	Leu	Asn	Tyr	Arg	Gly	Phe	Val	Tyr	Leu	His	Asp	Asp	Ile	Thr	
			115					120					125			
aca	tta	gct	gca	tac	gct	ctt	ggg	aaa	gtt	tat	ttt	ctc	ccg	aaa	tac	434
Thr	Leu	Ala	Ala	Tyr	Ala	Leu	Gly	Lys	Val	Tyr	Phe	Leu	Pro	Lys	Tyr	
			130					135					140			
ctt	atg	tta	tat	aga	cag	cac	acg	aat	gcg	gta	act	ggg	atc	aaa	aca	482
Leu	Met	Leu	Tyr	Arg	Gln	His	Thr	Asn	Ala	Val	Thr	Gly	Ile	Lys	Thr	
			145					150				155				
ttc	cgc	aat	gga	ttg	act	tct	aaa	ttt	aaa	tca	cca	gta	aac	tat	ctt	530
Phe	Arg	Asn	Gly	Leu	Thr	Ser	Lys	Phe	Lys	Ser	Pro	Val	Asn	Tyr	Leu	
							160				170				175	
tta	tca	cga	aaa	cat	tat	cag	gta	aaa	aaa	tct	ttt	ttt	gaa	tgt	aac	578
Leu	Ser	Arg	Lys	His	Tyr	Gln	Val	Lys	Lys	Ser	Phe	Phe	Glu	Cys	Asn	
							180				185				190	
agc	tct	atc	tta	tca	gag	acg	aat	aaa	aaa	gtt	ttt	ttg	gat	ttt	att	626
Ser	Ser	Ile	Leu	Ser	Glu	Thr	Asn	Lys	Lys	Val	Phe	Leu	Asp	Phe	Ile	
							195				200				205	
tca	ttt	tgt	gaa	tca	aat	aat	aaa	ttt	aca	gat	ttt	ttt	aag	tta	tgg	674

Ser Phe Cys Glu Ser Asn Asn Lys Phe Thr Asp Phe Phe Lys Leu Trp	
210	215 220
cga ggt ggg ttt aga tta aat aac agt aga act aaa tta tta tta aaa	722
Arg Gly Gly Phe Arg Leu Asn Asn Ser Arg Thr Lys Leu Leu Leu Lys	
225	230 235
ttc tta ata cgg aga aaa ttt agc ga atg att tca ata ctt aca cct	769
Phe Leu Ile Arg Arg Lys Phe Ser Met Ile Ser Ile Leu Thr Pro	
240	245 250
act ttt aat cgg caa cat act tta tca agg cta ttc aat tct ctt ata	817
Thr Phe Asn Arg Gln His Thr Leu Ser Arg Leu Phe Asn Ser Leu Ile	
255	260 265 270
tta caa act gat aaa gat ttt gag tgg ata ata att gat gat ggt agt	865
Leu Gln Thr Asp Lys Asp Phe Glu Trp Ile Ile Ile Asp Asp Gly Ser	
	275 280 285
ata gat gca aca gcg gta ctt gta gaa gat ttt aga aaa aaa tgt gat	913
Ile Asp Ala Thr Ala Val Leu Val Glu Asp Phe Arg Lys Lys Cys Asp	
	290 295 300
ttt gac ttg att tat tgc tat cag gaa aat aat ggt aag ccc atg gct	961
Phe Asp Leu Ile Tyr Cys Tyr Gln Glu Asn Asn Gly Lys Pro Met Ala	
	305 310 315
tta aac gct ggt gtt aaa gct tgt aga ggc gat tat atc ttt att gtt	1009
Leu Asn Ala Gly Val Lys Ala Cys Arg Gly Asp Tyr Ile Phe Ile Val	
	320 325 330
gac agt gat gat gca cta act ccc gat gcc ata aaa tta att aaa gaa	1057
Asp Ser Asp Asp Ala Leu Thr Pro Asp Ala Ile Lys Leu Ile Lys Glu	
	335 340 345 350
tca ata cat gat tgc tta tct gag aag gaa agt ttc agc gga gtc ggt	1105
Ser Ile His Asp Cys Leu Ser Glu Lys Glu Ser Phe Ser Gly Val Gly	
	355 360 365
ttt aga aaa gca tat ata aaa ggg ggg att att ggt aat gat tta aat	1153
Phe Arg Lys Ala Tyr Ile Lys Gly Gly Ile Ile Gly Asn Asp Leu Asn	
	370 375 380
aat tct tca gaa cat ata tac tat tta aat gcg act gag att agc aat	1201
Asn Ser Ser Glu His Ile Tyr Tyr Leu Asn Ala Thr Glu Ile Ser Asn	
	385 390 395
tta ata aat ggt gat gtt gca tat tgt ttt aaa aaa gaa agt ttg gta	1249

Leu Ile Asn Gly Asp Val Ala Tyr Cys Phe Lys Lys Glu Ser Leu Val
 400 405 410

aaa aat cca ttc ccc cgt ata gaa gat gaa aaa ttt gtt cca gaa tta 1297
 Lys Asn Pro Phe Pro Arg Ile Glu Asp Glu Lys Phe Val Pro Glu Leu
 415 420 425 430

tat att tgg aat aaa ata act gac aag gcg aag att cga ttt aac ata 1345
 Tyr Ile Trp Asn Lys Ile Thr Asp Lys Ala Lys Ile Arg Phe Asn Ile
 435 440 445

agc aaa gtt ata tat ctt tgt gag tat ctt gat gat ggt ctt tct aaa 1393
 Ser Lys Val Ile Tyr Leu Cys Glu Tyr Leu Asp Asp Gly Leu Ser Lys
 450 455 460

aat ttc cat aac cag ctt aaa aaa tac cca aag ggg ttt aag att tat 1441
 Asn Phe His Asn Gln Leu Lys Lys Tyr Pro Lys Gly Phe Lys Ile Tyr
 465 470 475

tac aaa gat caa aga aaa cga gag aaa act tat ata aaa aaa aca aag 1489
 Tyr Lys Asp Gln Arg Lys Arg Glu Lys Thr Tyr Ile Lys Lys Thr Lys
 480 485 490

atg cta att aga tat ttg caa tgt tgt tat tat gag aaa ata aa atg 1536
 Met Leu Ile Arg Tyr Leu Gln Cys Cys Tyr Tyr Glu Lys Ile Met
 495 500 505

aaa ata cta ttt gtc att aca ggt tta ggc ctt gga ggt gct gag aag 1584
 Lys Ile Leu Phe Val Ile Thr Gly Leu Gly Leu Gly Gly Ala Glu Lys
 510 515 520 525

cag gtt tgt ctt tta gct gat aaa tta agt tta agc ggg cac cat gta 1632
 Gln Val Cys Leu Leu Ala Asp Lys Leu Ser Leu Ser Gly His His Val
 530 535 540

aag att att tca ctt gga cat atg tct aat aat aaa gtc ttt cct agc 1680
 Lys Ile Ile Ser Leu Gly His Met Ser Asn Asn Lys Val Phe Pro Ser
 545 550 555

gaa aat aat gtt aat gtc att aat gta aat atg tca aaa aac att tct 1728
 Glu Asn Asn Val Asn Val Ile Asn Val Asn Met Ser Lys Asn Ile Ser
 560 565 570

gga gtt ata aaa ggt tgt gtc aga att aga gat gtt ata gct aat ttc 1776
 Gly Val Ile Lys Gly Cys Val Arg Ile Arg Asp Val Ile Ala Asn Phe
 575 580 585

aaa cca gac att gta cac agt cat atg ttt cat gca aac att atc act 1824

Lys Pro Asp Ile Val His Ser His Met Phe His Ala Asn Ile Ile Thr	
590	605
aga ttg tct gta att gga atc aaa aac aga cct ggt att ata tca act	1872
Arg Leu Ser Val Ile Gly Ile Lys Asn Arg Pro Gly Ile Ile Ser Thr	
610	620
gca cat aat aaa aat gaa ggt ggg tat ttc aga atg ctc aca tat aga	1920
Ala His Asn Lys Asn Glu Gly Gly Tyr Phe Arg Met Leu Thr Tyr Arg	
625	635
ata acc gat tgt tta agt gat tgt tgt aca aat gtt agc aaa gaa gca	1968
Ile Thr Asp Cys Leu Ser Asp Cys Cys Thr Asn Val Ser Lys Glu Ala	
640	650
gtg gat gag ttt tta cgg ata aaa gcc ttt aat ccc gct aaa gca att	2016
Val Asp Glu Phe Leu Arg Ile Lys Ala Phe Asn Pro Ala Lys Ala Ile	
655	665
act atg tat aat ggg ata gat acc aat aaa ttt aaa ttt gat tta ttg	2064
Thr Met Tyr Asn Gly Ile Asp Thr Asn Lys Phe Lys Phe Asp Leu Leu	
670	685
gca agg agg gaa att cga gac ggt att aat ata aaa aat gat gat ata	2112
Ala Arg Arg Glu Ile Arg Asp Gly Ile Asn Ile Lys Asn Asp Asp Ile	
690	700
tta tta ctt gct gca ggt cgt tta acg tta gct aaa gat tat cct aat	2160
Leu Leu Leu Ala Ala Gly Arg Leu Thr Leu Ala Lys Asp Tyr Pro Asn	
705	715
tta ttg aat gca atg act ctg ctt cct gaa cac ttt aaa ctt att att	2208
Leu Leu Asn Ala Met Thr Leu Leu Pro Glu His Phe Lys Leu Ile Ile	
720	730
att ggt gat ggt gaa ttg cgt gac gaa att aat atg ctt ata aaa aaa	2256
Ile Gly Asp Gly Glu Leu Arg Asp Glu Ile Asn Met Leu Ile Lys Lys	
735	745
ttg caa tta tct aat agg gtg tcc ttg ttg gga gtt aaa aaa aat att	2304
Leu Gln Leu Ser Asn Arg Val Ser Leu Leu Gly Val Lys Lys Asn Ile	
750	765
gct ccc tat ttt tct gca tgt gat att ttt gtt ctc tct tct cgt tgg	2352
Ala Pro Tyr Phe Ser Ala Cys Asp Ile Phe Val Leu Ser Ser Arg Trp	
770	780
gaa gga ttt gga tta gtc gtg gca gaa gct atg tca tgt gag cga att	2400

Glu Gly Phe Gly Leu Val Val Ala Glu Ala Met Ser Cys Glu Arg Ile	
785 790 795	
ggt ggt ggc acg gat tca ggg gga gta aga gaa gtt att ggt gac gat	2448
Val Val Gly Thr Asp Ser Gly Gly Val Arg Glu Val Ile Gly Asp Asp	
800 805 810	
gat ttt ctt gta ccc ata tct gat tca aca caa ctt gca agc aaa att	2496
Asp Phe Leu Val Pro Ile Ser Asp Ser Thr Gln Leu Ala Ser Lys Ile	
815 820 825	
gaa aaa ttg tct ttg agc cag ata cgt gat cac att ggt ttt cgg aat	2544
Glu Lys Leu Ser Leu Ser Gln Ile Arg Asp His Ile Gly Phe Arg Asn	
830 835 840 845	
cgt gag cgt att tta aaa aat ttc tca ata gat act att att atg cag	2592
Arg Glu Arg Ile Leu Lys Asn Phe Ser Ile Asp Thr Ile Ile Met Gln	
850 855 860	
tgg caa gaa ctc tat gga act ata att tgc tca aaa cat gaa agg	2637
Trp Gln Glu Leu Tyr Gly Thr Ile Ile Cys Ser Lys His Glu Arg	
865 870 875	
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tgtattttcaa aaataccatc atagctaacg atgattggta tttatttttaa gatgctttct	2757
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ttaattattt ataataaatc aagatttaaat gttaataaat gataatcttt tctgacactc	2937
atattaatta tgagtggtag gtttggtaaa cggtaaacta ttat atg aca gct aga	2993
Met Thr Ala Arg	
880	
aca act aaa gtt ttg cac tta caa tta ctc cca ctc tta agt ggc gtt	3041
Thr Thr Lys Val Leu His Leu Gln Leu Leu Pro Leu Leu Ser Gly Val	
885 890 895	
caa agg gta aca tta aac gaa att agt gcg tta tat act gat tat gat	3089
Gln Arg Val Thr Leu Asn Glu Ile Ser Ala Leu Tyr Thr Asp Tyr Asp	
900 905 910	
tat aca cta gtt tgc tca aaa aaa ggt cca cta aca aaa gca ttg ctg	3137
Tyr Thr Leu Val Cys Ser Lys Lys Gly Pro Leu Thr Lys Ala Leu Leu	
915 920 925	

gaa tat gat gtc gat tgt cat tgt atc ccc gaa ctt acg aga gaa att	3185
Glu Tyr Asp Val Asp Cys His Cys Ile Pro Glu Leu Thr Arg Glu Ile	
930 935 940	
acc gta aag aat gat ttt aaa gca ttg ttc aag ctt tat aag ttc ata	3233
Thr Val Lys Asn Asp Phe Lys Ala Leu Phe Lys Leu Tyr Lys Phe Ile	
945 950 955 960	
aaa aaa gaa aaa ttt gac att gtg cat aca cat tct tca aaa aca ggt	3281
Lys Lys Glu Lys Phe Asp Ile Val His Thr His Ser Ser Lys Thr Gly	
965 970 975	
att ttg ggg cga gtt gct gcc aaa tta gca cgt gtt gga aag gtg atc	3329
Ile Leu Gly Arg Val Ala Ala Lys Leu Ala Arg Val Gly Lys Val Ile	
980 985 990	
cac act gta cat ggt ttt tct ttt cca gcc gca tct agt aaa aaa agt	3377
His Thr Val His Gly Phe Ser Phe Pro Ala Ala Ser Ser Lys Lys Ser	
995 1000 1005	
tat tac ctt tat ttt ttc atg gaa tgg ata gca aag ttc ttt acg gat	3425
Tyr Tyr Leu Tyr Phe Phe Met Glu Trp Ile Ala Lys Phe Phe Thr Asp	
1010 1015 1020	
aag tta atc gtc ttg aat gta gat gat gaa tat ata gca ata aac aaa	3473
Lys Leu Ile Val Leu Asn Val Asp Asp Glu Tyr Ile Ala Ile Asn Lys	
1025 1030 1035 1040	
tta aaa ttc aag cgg gat aaa gtt ttt tta att cct aat gga gta gac	3521
Leu Lys Phe Lys Arg Asp Lys Val Phe Leu Ile Pro Asn Gly Val Asp	
1045 1050 1055	
act gat aag ttt tct cct tta gaa aat aaa att tat agt agc acc ttg	3569
Thr Asp Lys Phe Ser Pro Leu Glu Asn Lys Ile Tyr Ser Ser Thr Leu	
1060 1065 1070	
aat cta gta atg gtt ggt aga tta tcc aag caa aaa gat cct gag aca	3617
Asn Leu Val Met Val Gly Arg Leu Ser Lys Gln Lys Asp Pro Glu Thr	
1075 1080 1085	
tta ttg ctt gct gtt gaa aaa ctg ctg aat gaa aat gtt aat gtt aag	3665
Leu Leu Leu Ala Val Glu Lys Leu Leu Asn Glu Asn Val Asn Val Lys	
1090 1095 1100	
ctg aca ctt gta gga gat ggt gaa cta aaa gaa cag tta gaa agc agg	3713
Leu Thr Leu Val Gly Asp Gly Glu Leu Lys Glu Gln Leu Glu Ser Arg	
1105 1110 1115 1120	

ttc aaa cgg caa gat gga cgt ata att ttt cat gga tgg tca gat aac 3761
 Phe Lys Arg Gln Asp Gly Arg Ile Ile Phe His Gly Trp Ser Asp Asn
 1125 1130 1135

att gtt aat att tta aaa gtt aat gat ctt ttt ata tta cct tct ctt 3809
 Ile Val Asn Ile Leu Lys Val Asn Asp Leu Phe Ile Leu Pro Ser Leu
 1140 1145 1150

tgg gag ggt atg cca tta gca att tta gaa gca ttg agc tgt gga ctt 3857
 Trp Glu Gly Met Pro Leu Ala Ile Leu Glu Ala Leu Ser Cys Gly Leu
 1155 1160 1165

cca tgt ata gtc act aat att cca ggt aat aat agc tta ata gaa gat 3905
 Pro Cys Ile Val Thr Asn Ile Pro Gly Asn Asn Ser Leu Ile Glu Asp
 1170 1175 1180

ggc tat aat ggt tgt ttg ttt gaa att aga gat tgt cag tta tta tct 3953
 Gly Tyr Asn Gly Cys Leu Phe Glu Ile Arg Asp Cys Gln Leu Leu Ser
 1185 1190 1195 1200

caa aaa atc atg tca tat gtt ggt aag cca gaa ctg att gca cag caa 4001
 Gln Lys Ile Met Ser Tyr Val Gly Lys Pro Glu Leu Ile Ala Gln Gln
 1205 1210 1215

tct acc aat gca cga tca ttt att ctg aaa aat tat gga tta gtt aaa 4049
 Ser Thr Asn Ala Arg Ser Phe Ile Leu Lys Asn Tyr Gly Leu Val Lys
 1220 1225 1230

aga aat aat aag gtc aga cag cta tat gat aat taaatgaaac cgaaaagtta 4102
 Arg Asn Asn Lys Val Arg Gln Leu Tyr Asp Asn
 1235 1240

aaaaagaaca gggttttcaa agtgaaaata aaattacagt ttttttattg caatgattaa 4162

cgtaacatct gcattacatt caagccgcac aaccccgagg tgaccacccc tgacaggagt 4222

aaacaatgtc aaagcaacag atcggcgctcg tcggtatggc agtgatggga cgcaacctcg 4282

cgctcaacat cgaaagccgt gggtataccg tctctatttt caaccgttcc cgtgaaaaga 4342

cggaagaagt tattgccgaa aatccaggca agaaactggc tccttactat acggtgaaag 4402

agttcgttga atctcttgaa acgcctcgtc gcacacctgtt aatgggttaa agcaggtgca 4462

ggcacggatg ctgctattga ttccctgaaa ccatatctcg ataaaggcga tatcatcatt 4522

gatgggtggg taataccttc tttcaggaca ccattcgctg taaccgcgag ctttctgcac 4582

aaggctttac ttcacggtta cc

4604

<210> 23

<211> 247

<212> PRT

<213> Escherichia coli

<400> 23

Val	Asp	Asp	Asn	Leu	Lys	Gly	Gln	Gly	Ala	Gly	Lys	Asn	Phe	Leu	Ser
1				5					10					15	

Leu	Ile	Lys	Tyr	Ser	Glu	Thr	Asp	Tyr	Thr	Ile	Tyr	Cys	Asp	Gln	Asp
			20					25					30		

Asp	Ile	Trp	Leu	Glu	Asn	Lys	Ile	Phe	Glu	Leu	Val	Lys	Tyr	Ala	Asn
		35					40						45		

Glu	Ile	Lys	Leu	Asn	Val	Ser	Asp	Ala	Pro	Ser	Leu	Val	Tyr	Ala	Asp
	50					55						60			

Gly	Tyr	Ala	Tyr	Met	Asp	Gly	Glu	Gly	Thr	Ile	Asp	Phe	Ser	Gly	Ile
65					70					75					80

Ser	Asn	Asn	His	Ala	Asp	Gln	Leu	Lys	Asp	Phe	Leu	Phe	Phe	Asn	Gly
			85						90					95	

Gly	Tyr	Gln	Gly	Cys	Ser	Ile	Met	Phe	Asn	Arg	Ala	Met	Thr	Lys	Phe
		100						105					110		

Leu	Leu	Asn	Tyr	Arg	Gly	Phe	Val	Tyr	Leu	His	Asp	Asp	Ile	Thr	Thr
		115					120					125			

Leu	Ala	Ala	Tyr	Ala	Leu	Gly	Lys	Val	Tyr	Phe	Leu	Pro	Lys	Tyr	Leu
	130					135						140			

Met	Leu	Tyr	Arg	Gln	His	Thr	Asn	Ala	Val	Thr	Gly	Ile	Lys	Thr	Phe
145					150					155				160	

Arg	Asn	Gly	Leu	Thr	Ser	Lys	Phe	Lys	Ser	Pro	Val	Asn	Tyr	Leu	Leu
			165						170					175	

Ser	Arg	Lys	His	Tyr	Gln	Val	Lys	Lys	Ser	Phe	Phe	Glu	Cys	Asn	Ser
		180						185					190		

Ser	Ile	Leu	Ser	Glu	Thr	Asn	Lys	Lys	Val	Phe	Leu	Asp	Phe	Ile	Ser
		195					200					205			

Phe Cys Glu Ser Asn Asn Lys Phe Thr Asp Phe Phe Lys Leu Trp Arg
 210 215 220

Gly Gly Phe Arg Leu Asn Asn Ser Arg Thr Lys Leu Leu Leu Lys Phe
 225 230 235 240

Leu Ile Arg Arg Lys Phe Ser
 245

<210> 24

<211> 261

<212> PRT

<213> Escherichia coli

<400> 24

Met Ile Ser Ile Leu Thr Pro Thr Phe Asn Arg Gln His Thr Leu Ser
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Arg Leu Phe Asn Ser Leu Ile Leu Gln Thr Asp Lys Asp Phe Glu Trp
 20 25 30

Ile Ile Ile Asp Asp Gly Ser Ile Asp Ala Thr Ala Val Leu Val Glu
 35 40 45

Asp Phe Arg Lys Lys Cys Asp Phe Asp Leu Ile Tyr Cys Tyr Gln Glu
 50 55 60

Asn Asn Gly Lys Pro Met Ala Leu Asn Ala Gly Val Lys Ala Cys Arg
 65 70 75 80

Gly Asp Tyr Ile Phe Ile Val Asp Ser Asp Asp Ala Leu Thr Pro Asp
 85 90 95

Ala Ile Lys Leu Ile Lys Glu Ser Ile His Asp Cys Leu Ser Glu Lys
 100 105 110

Glu Ser Phe Ser Gly Val Gly Phe Arg Lys Ala Tyr Ile Lys Gly Gly
 115 120 125

Ile Ile Gly Asn Asp Leu Asn Asn Ser Ser Glu His Ile Tyr Tyr Leu
 130 135 140

Asn Ala Thr Glu Ile Ser Asn Leu Ile Asn Gly Asp Val Ala Tyr Cys
 145 150 155 160

Phe Lys Lys Glu Ser Leu Val Lys Asn Pro Phe Pro Arg Ile Glu Asp

165 170 175
 Glu Lys Phe Val Pro Glu Leu Tyr Ile Trp Asn Lys Ile Thr Asp Lys
 180 185 190
 Ala Lys Ile Arg Phe Asn Ile Ser Lys Val Ile Tyr Leu Cys Glu Tyr
 195 200 205
 Leu Asp Asp Gly Leu Ser Lys Asn Phe His Asn Gln Leu Lys Lys Tyr
 210 215 220
 Pro Lys Gly Phe Lys Ile Tyr Tyr Lys Asp Gln Arg Lys Arg Glu Lys
 225 230 235 240
 Thr Tyr Ile Lys Lys Thr Lys Met Leu Ile Arg Tyr Leu Gln Cys Cys
 245 250 255
 Tyr Tyr Glu Lys Ile
 260

<210> 25
 <211> 368
 <212> PRT
 <213> Escherichia coli

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

Thr	Ala	His	Asn	Lys	Asn	Glu	Gly	Gly	Tyr	Phe	Arg	Met	Leu	Thr	Tyr	115	120	125	
Arg	Ile	Thr	Asp	Cys	Leu	Ser	Asp	Cys	Cys	Thr	Asn	Val	Ser	Lys	Glu	130	135	140	
Ala	Val	Asp	Glu	Phe	Leu	Arg	Ile	Lys	Ala	Phe	Asn	Pro	Ala	Lys	Ala	145	150	155	160
Ile	Thr	Met	Tyr	Asn	Gly	Ile	Asp	Thr	Asn	Lys	Phe	Lys	Phe	Asp	Leu	165	170	175	
Leu	Ala	Arg	Arg	Glu	Ile	Arg	Asp	Gly	Ile	Asn	Ile	Lys	Asn	Asp	Asp	180	185	190	
Ile	Leu	Leu	Leu	Ala	Ala	Gly	Arg	Leu	Thr	Leu	Ala	Lys	Asp	Tyr	Pro	195	200	205	
Asn	Leu	Leu	Asn	Ala	Met	Thr	Leu	Leu	Pro	Glu	His	Phe	Lys	Leu	Ile	210	215	220	
Ile	Ile	Gly	Asp	Gly	Glu	Leu	Arg	Asp	Glu	Ile	Asn	Met	Leu	Ile	Lys	225	230	235	240
Lys	Leu	Gln	Leu	Ser	Asn	Arg	Val	Ser	Leu	Leu	Gly	Val	Lys	Lys	Asn	245	250	255	
Ile	Ala	Pro	Tyr	Phe	Ser	Ala	Cys	Asp	Ile	Phe	Val	Leu	Ser	Ser	Arg	260	265	270	
Trp	Glu	Gly	Phe	Gly	Leu	Val	Val	Ala	Glu	Ala	Met	Ser	Cys	Glu	Arg	275	280	285	
Ile	Val	Val	Gly	Thr	Asp	Ser	Gly	Gly	Val	Arg	Glu	Val	Ile	Gly	Asp	290	295	300	
Asp	Asp	Phe	Leu	Val	Pro	Ile	Ser	Asp	Ser	Thr	Gln	Leu	Ala	Ser	Lys	305	310	315	320
Ile	Glu	Lys	Leu	Ser	Leu	Ser	Gln	Ile	Arg	Asp	His	Ile	Gly	Phe	Arg	325	330	335	
Asn	Arg	Glu	Arg	Ile	Leu	Lys	Asn	Phe	Ser	Ile	Asp	Thr	Ile	Ile	Met	340	345	350	
Gln	Trp	Gln	Glu	Leu	Tyr	Gly	Thr	Ile	Ile	Cys	Ser	Lys	His	Glu	Arg	355	360	365	

<210> 26

<211> 367

<212> PRT

<213> Escherichia coli

<400> 26

Met Thr Ala Arg Thr Thr Lys Val Leu His Leu Gln Leu Leu Pro Leu
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Leu Ser Gly Val Gln Arg Val Thr Leu Asn Glu Ile Ser Ala Leu Tyr
 20 25 30

Thr Asp Tyr Asp Tyr Thr Leu Val Cys Ser Lys Lys Gly Pro Leu Thr
 35 40 45

Lys Ala Leu Leu Glu Tyr Asp Val Asp Cys His Cys Ile Pro Glu Leu
 50 55 60

Thr Arg Glu Ile Thr Val Lys Asn Asp Phe Lys Ala Leu Phe Lys Leu
 65 70 75 80

Tyr Lys Phe Ile Lys Lys Glu Lys Phe Asp Ile Val His Thr His Ser
 85 90 95

Ser Lys Thr Gly Ile Leu Gly Arg Val Ala Ala Lys Leu Ala Arg Val
 100 105 110

Gly Lys Val Ile His Thr Val His Gly Phe Ser Phe Pro Ala Ala Ser
 115 120 125

Ser Lys Lys Ser Tyr Tyr Leu Tyr Phe Phe Met Glu Trp Ile Ala Lys
 130 135 140

Phe Phe Thr Asp Lys Leu Ile Val Leu Asn Val Asp Asp Glu Tyr Ile
 145 150 155 160

Ala Ile Asn Lys Leu Lys Phe Lys Arg Asp Lys Val Phe Leu Ile Pro
 165 170 175

Asn Gly Val Asp Thr Asp Lys Phe Ser Pro Leu Glu Asn Lys Ile Tyr
 180 185 190

Ser Ser Thr Leu Asn Leu Val Met Val Gly Arg Leu Ser Lys Gln Lys
 195 200 205

Asp Pro Glu Thr Leu Leu Leu Ala Val Glu Lys Leu Leu Asn Glu Asn
 210 215 220

Val Asn Val Lys Leu Thr Leu Val Gly Asp Gly Glu Leu Lys Glu Gln
 225 230 235 240

Leu Glu Ser Arg Phe Lys Arg Gln Asp Gly Arg Ile Ile Phe His Gly
 245 250 255

Trp Ser Asp Asn Ile Val Asn Ile Leu Lys Val Asn Asp Leu Phe Ile
 260 265 270

Leu Pro Ser Leu Trp Glu Gly Met Pro Leu Ala Ile Leu Glu Ala Leu
 275 280 285

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

Leu Ile Glu Asp Gly Tyr Asn Gly Cys Leu Phe Glu Ile Arg Asp Cys
 305 310 315 320

Gln Leu Leu Ser Gln Lys Ile Met Ser Tyr Val Gly Lys Pro Glu Leu
 325 330 335

Ile Ala Gln Gln Ser Thr Asn Ala Arg Ser Phe Ile Leu Lys Asn Tyr
 340 345 350

Gly Leu Val Lys Arg Asn Asn Lys Val Arg Gln Leu Tyr Asp Asn
 355 360 365

<210> 27

<211> 1272

<212> DNA

<213> Escherichia coli

<220>

<221> CDS

<222> (319)..(1269)

<220>

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<222> (3)..(215)

<400> 27

cc ggg aag cac tcg gcg ctg att gtt gca cat cgt ctg acc acc gcg 47
 Gly Lys His Ser Ala Leu Ile Val Ala His Arg Leu Thr Thr Ala
 1 5 10 15

caa cgc tgc gat ctg att gcc gtt att gat aag ggg tta ctt gcg gaa 95
 Gln Arg Cys Asp Leu Ile Ala Val Ile Asp Lys Gly Leu Leu Ala Glu
 20 25 30

tac gga acc cac gaa cag ctg tta tct gcg ggc ggc ctc tat acc cgc 143
 Tyr Gly Thr His Glu Gln Leu Leu Ser Ala Gly Gly Leu Tyr Thr Arg
 35 40 45

tta tgg cat gac agc gtc agc agt act gct ctc cat cgc cag cac aac 191
 Leu Trp His Asp Ser Val Ser Ser Thr Ala Leu His Arg Gln His Asn
 50 55 60

atg aag gag gaa acc ccg gga tag ttactggaca cgtaatgtat taaaaacaca 245
 Met Lys Glu Glu Thr Pro Gly
 65 70

gtcagaagcgc gcggtaccgt gaatagccgc ttttaattatt tataactgaca tccttaattt 305

ttaaagagta tga atg ctg aac atg caa caa cat ctc tct gct atc gcc 354
 Met Leu Asn Met Gln Gln His Leu Ser Ala Ile Ala
 75 80

agc ctg cgc aac caa ctg gca gcg ggc cac att gct aac ctt act gac 402
 Ser Leu Arg Asn Gln Leu Ala Ala Gly His Ile Ala Asn Leu Thr Asp
 85 90 95

ttc tgg cgc gaa gct gag tcg ctg aat gtt cct ctt gtg acg cca gtc 450
 Phe Trp Arg Glu Ala Glu Ser Leu Asn Val Pro Leu Val Thr Pro Val
 100 105 110 115

gaa gga gcg gaa gat gag cga gaa gtg acc ttt ctg tgg cgc gcc cga 498
 Glu Gly Ala Glu Asp Glu Arg Glu Val Thr Phe Leu Trp Arg Ala Arg
 120 125 130

cat cct ctg cag ggc gtt tat ctg cgt ctg aac cgg gtg acg gat aaa 546
 His Pro Leu Gln Gly Val Tyr Leu Arg Leu Asn Arg Val Thr Asp Lys
 135 140 145

gag cac gta gaa aaa gga atg atg agc gcc ctt ccc gaa acg gat atc 594
 Glu His Val Glu Lys Gly Met Met Ser Ala Leu Pro Glu Thr Asp Ile
 150 155 160

tgg aca ctg aca ctg cgt tta ccc gca agt tac tgc ggc tcc tat tcg 642
 Trp Thr Leu Thr Leu Arg Leu Pro Ala Ser Tyr Cys Gly Ser Tyr Ser
 165 170 175

ctg ctg gaa atc ccc ccc ggc act acg gct gag acg att gca ctg tcc 690
 Leu Leu Glu Ile Pro Pro Gly Thr Thr Ala Glu Thr Ile Ala Leu Ser

180	185	190	195	
gga ggc cgt ttt gcc acc ctt gcc gga aag gcc gat ccg cta aac aaa				738
Gly Gly Arg Phe Ala Thr Leu Ala Gly Lys Ala Asp Pro Leu Asn Lys				
	200	205	210	
atg ccg gag atc aac gtt cgg gga aac gca aag gaa tca gtg ctg aca				786
Met Pro Glu Ile Asn Val Arg Gly Asn Ala Lys Glu Ser Val Leu Thr				
	215	220	225	
ctt gat aaa gct ccc gcc ctg tcg gaa tgg aac ggc ggc ttc cac acc				834
Leu Asp Lys Ala Pro Ala Leu Ser Glu Trp Asn Gly Gly Phe His Thr				
	230	235	240	
gga caa ctg ctt acc tcc atg cgc att atc gcc ggg aaa tct cgc cag				882
Gly Gln Leu Leu Thr Ser Met Arg Ile Ile Ala Gly Lys Ser Arg Gln				
	245	250	255	
gtt cgg ctc tat att ccg gat gtt gat att tct cag ccc ctc ggg ctg				930
Val Arg Leu Tyr Ile Pro Asp Val Asp Ile Ser Gln Pro Leu Gly Leu				
	260	265	270	275
gtc gtg ctg ccc gat ggt gaa acc tgg ttt gat cac ctt ggc gta tgc				978
Val Val Leu Pro Asp Gly Glu Thr Trp Phe Asp His Leu Gly Val Cys				
	280	285	290	
gcg gca att gac gcc gcc ata aat aat ggg cgc atc gtg ccc gtg gct				1026
Ala Ala Ile Asp Ala Ala Ile Asn Asn Gly Arg Ile Val Pro Val Ala				
	295	300	305	
gta ctg ggc att gac aac att aat gaa cat gaa cgc act gag ata ctc				1074
Val Leu Gly Ile Asp Asn Ile Asn Glu His Glu Arg Thr Glu Ile Leu				
	310	315	320	
ggc ggg cgc agc aaa ctg ata aag gat atc gcc gga cat ctg ctg ccg				1122
Gly Gly Arg Ser Lys Leu Ile Lys Asp Ile Ala Gly His Leu Leu Pro				
	325	330	335	
atg att cgc gct gaa caa ccg cag cgt cag tgg gca gac cgt tcg cgc				1170
Met Ile Arg Ala Glu Gln Pro Gln Arg Gln Trp Ala Asp Arg Ser Arg				
	340	345	350	355
aca gtg ctg gcc ggg cag agc ctc ggc ggg atc agt gcg cta atg ggg				1218
Thr Val Leu Ala Gly Gln Ser Leu Gly Gly Ile Ser Ala Leu Met Gly				
	360	365	370	
gct cgt tac gca ccg gaa acg ttc ggt ctg gtg ctc agc cac tct cct				1266
Ala Arg Tyr Ala Pro Glu Thr Phe Gly Leu Val Leu Ser His Ser Pro				

375

380

385

caa tgc

1272

Gln

<210> 28

<211> 70

<212> PRT

<213> Escherichia coli

<400> 28

Gly Lys His Ser Ala Leu Ile Val Ala His Arg Leu Thr Thr Ala Gln

1

5

10

15

Arg Cys Asp Leu Ile Ala Val Ile Asp Lys Gly Leu Leu Ala Glu Tyr

20

25

30

Gly Thr His Glu Gln Leu Leu Ser Ala Gly Gly Leu Tyr Thr Arg Leu

35

40

45

Trp His Asp Ser Val Ser Ser Thr Ala Leu His Arg Gln His Asn Met

50

55

60

Lys Glu Glu Thr Pro Gly

65

70

<210> 29

<211> 317

<212> PRT

<213> Escherichia coli

<400> 29

Met Leu Asn Met Gln Gln His Leu Ser Ala Ile Ala Ser Leu Arg Asn

1

5

10

15

Gln Leu Ala Ala Gly His Ile Ala Asn Leu Thr Asp Phe Trp Arg Glu

20

25

30

Ala Glu Ser Leu Asn Val Pro Leu Val Thr Pro Val Glu Gly Ala Glu

35

40

45

Asp Glu Arg Glu Val Thr Phe Leu Trp Arg Ala Arg His Pro Leu Gln

50

55

60

Gly Val Tyr Leu Arg Leu Asn Arg Val Thr Asp Lys Glu His Val Glu

65

70

75

80

Lys Gly Met Met Ser Ala Leu Pro Glu Thr Asp Ile Trp Thr Leu Thr
 85 90 95

Leu Arg Leu Pro Ala Ser Tyr Cys Gly Ser Tyr Ser Leu Leu Glu Ile
 100 105 110

Pro Pro Gly Thr Thr Ala Glu Thr Ile Ala Leu Ser Gly Gly Arg Phe
 115 120 125

Ala Thr Leu Ala Gly Lys Ala Asp Pro Leu Asn Lys Met Pro Glu Ile
 130 135 140

Asn Val Arg Gly Asn Ala Lys Glu Ser Val Leu Thr Leu Asp Lys Ala
 145 150 155 160

Pro Ala Leu Ser Glu Trp Asn Gly Gly Phe His Thr Gly Gln Leu Leu
 165 170 175

Thr Ser Met Arg Ile Ile Ala Gly Lys Ser Arg Gln Val Arg Leu Tyr
 180 185 190

Ile Pro Asp Val Asp Ile Ser Gln Pro Leu Gly Leu Val Val Leu Pro
 195 200 205

Asp Gly Glu Thr Trp Phe Asp His Leu Gly Val Cys Ala Ala Ile Asp
 210 215 220

Ala Ala Ile Asn Asn Gly Arg Ile Val Pro Val Ala Val Leu Gly Ile
 225 230 235 240

Asp Asn Ile Asn Glu His Glu Arg Thr Glu Ile Leu Gly Gly Arg Ser
 245 250 255

Lys Leu Ile Lys Asp Ile Ala Gly His Leu Leu Pro Met Ile Arg Ala
 260 265 270

Glu Gln Pro Gln Arg Gln Trp Ala Asp Arg Ser Arg Thr Val Leu Ala
 275 280 285

Gly Gln Ser Leu Gly Gly Ile Ser Ala Leu Met Gly Ala Arg Tyr Ala
 290 295 300

Pro Glu Thr Phe Gly Leu Val Leu Ser His Ser Pro Gln
 305 310 315

<210> 30
 <211> 4039
 <212> DNA
 <213> Escherichia coli

<220>
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 <222> (1)..(285)

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 <222> (370)..(1326)

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agc gaa acc gat acc tca tgg gtg agt gag cat ctg ctt tct gcc cca 96
 Ser Glu Thr Asp Thr Ser Trp Val Ser Glu His Leu Leu Ser Ala Pro
 20 25 30

ccg cag ggc gta cgt atc agc ctg tgc gtg gga tcg ctg gaa ggt tcg 144
 Pro Gln Gly Val Arg Ile Ser Leu Cys Val Gly Ser Leu Glu Gly Ser
 35 40 45

aca gtg cct cac gtt cag cag ctt cac cag cgg ctg att acc gct ggc 192
 Thr Val Pro His Val Gln Gln Leu His Gln Arg Leu Ile Thr Ala Gly
 50 55 60

gtc gaa agc cat tgc gca atc tac acc ggt ggt cac gat tac gca tgg 240
 Val Glu Ser His Cys Ala Ile Tyr Thr Gly Gly His Asp Tyr Ala Trp
 65 70 75 80

tgg cgc ggt gca ctg att gac ggg att ggt tta cta cag ggt tga 285
 Trp Arg Gly Ala Leu Ile Asp Gly Ile Gly Leu Leu Gln Gly
 85 90 95

gttgacccac aaacactttc aggaaacggt acagacttcc tgaataaatc aaatagtcac 345

ctgcggaaaa ggaataatca tcag atg tat gcc cgc gag tat cgc tca aca 396
 Met Tyr Ala Arg Glu Tyr Arg Ser Thr
 100

cgc ccg cat aaa gcg att ttc ttt cat ctt tct tgc ctc acc ctt atc 444
 Arg Pro His Lys Ala Ile Phe Phe His Leu Ser Cys Leu Thr Leu Ile
 105 110 115 120

tgt agt gcg caa gtt tat gcg aag ccg gat atg cgg cca ctg ggg ccg	492
Cys Ser Ala Gln Val Tyr Ala Lys Pro Asp Met Arg Pro Leu Gly Pro	
125 130 135	
aat ata gcc gat aaa ggc tcc gtg ttt tac cat ttc agc gtc acc tct	540
Asn Ile Ala Asp Lys Gly Ser Val Phe Tyr His Phe Ser Val Thr Ser	
140 145 150	
ttc gac tct gtc gat ggc aca cgc cat tat cgg gta tgg acg gcc gtg	588
Phe Asp Ser Val Asp Gly Thr Arg His Tyr Arg Val Trp Thr Ala Val	
155 160 165	
ccg aat aca acc gca ccg gca tcg ggt tac ccg att tta tat atg ctt	636
Pro Asn Thr Thr Ala Pro Ala Ser Gly Tyr Pro Ile Leu Tyr Met Leu	
170 175 180	
gac ggt aac gca gtt atg gat cgc ctg gat gac gaa ctg ctc aaa caa	684
Asp Gly Asn Ala Val Met Asp Arg Leu Asp Asp Glu Leu Leu Lys Gln	
185 190 195 200	
ttg tca gaa aaa aca ccg cca gtg atc gtg gct gtc ggg tat cag acc	732
Leu Ser Glu Lys Thr Pro Pro Val Ile Val Ala Val Gly Tyr Gln Thr	
205 210 215	
aac ctc cct ttc gat ctc aac agc agg gct tac gac tat acg cca gca	780
Asn Leu Pro Phe Asp Leu Asn Ser Arg Ala Tyr Asp Tyr Thr Pro Ala	
220 225 230	
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Ala Glu Ser Arg Lys Thr Asp Leu His Ser Gly Arg Phe Ser Arg Lys	
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Ser Gly Gly Ser Asn Asn Phe Arg Gln Leu Leu Glu Thr Arg Ile Ala	
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Pro Lys Val Glu Gln Gly Leu Asn Ile Asp Arg Gln Arg Arg Gly Leu	
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 His Glu Leu Ser His
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 35 40 45

Thr Val Pro His Val Gln Gln Leu His Gln Arg Leu Ile Thr Ala Gly
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<213> Escherichia coli

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Lys Pro Asp Met Arg Pro Leu Gly Pro Asn Ile Ala Asp Lys Gly Ser
 35 40 45

Val Phe Tyr His Phe Ser Val Thr Ser Phe Asp Ser Val Asp Gly Thr
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Arg His Tyr Arg Val Trp Thr Ala Val Pro Asn Thr Thr Ala Pro Ala
 65 70 75 80

Ser Gly Tyr Pro Ile Leu Tyr Met Leu Asp Gly Asn Ala Val Met Asp
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Arg Leu Asp Asp Glu Leu Leu Lys Gln Leu Ser Glu Lys Thr Pro Pro
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Val Ile Val Ala Val Gly Tyr Gln Thr Asn Leu Pro Phe Asp Leu Asn
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Leu His Ser Gly Arg Phe Ser Arg Lys Ser Gly Gly Ser Asn Asn Phe
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Asn Ile Asp Arg Gln Arg Arg Gly Leu Trp Gly His Ser Tyr Gly Gly
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Tyr Ser Ala Ser Pro Ser Leu Gly Arg Gly Tyr Asp Ala Leu Leu Ser
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Ile Met Glu Gly Ser Ala Thr Gln Gly Asp Asn Arg Glu Thr His Ala
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Val Gly Val Leu Ser Lys Ile His Thr Thr Leu Thr Ile Leu Lys Asp
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Lys Gly Val Asn Ala Val Phe Trp Asp Phe Pro Asn Leu Gly His Gly
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Glu Leu Ala Asn Ile Ile Gly His His Ala Gly Ile Asp Asp Asn Thr
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Ala Ala Lys Ala Ile Ala His Ala Ile Leu Gly Gly Val Thr Ala Ala
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Leu Gln Gly Asn Ser Ala Ala Ala Gly Ala Ile Gly Ala Gly Thr Gly
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Glu Val Ile Ala Ser Ala Ile Ala Lys Ser Leu Tyr Pro Gly Val Asp
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Pro Ser Lys Leu Thr Glu Asp Gln Lys Gln Thr Val Ser Thr Leu Ala
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Thr Leu Ser Ala Gly Met Ala Gly Gly Ile Ala Ser Gly Asp Val Ala
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Gly Ala Ala Ala Gly Ala Gly Ala Gly Lys Asn Val Val Glu Asn Asn
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Thr Lys Val Ala Glu Gln Leu Leu Glu Ile Gly Ala Lys Ala Gly Met
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Glu Ile Thr Thr Lys Tyr Leu Ser Ser Leu His Asp Lys Tyr Gly Ser	
210 215 220	
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Gly Ala Ala Ser Asn Pro Asn Ile Gly Lys Asp Leu Thr Asp Ala Glu	
225 230 235 240	
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Lys Val Glu Leu Gly Gly Ser Gly Ser Gly Thr Gly Thr Pro Pro Pro	
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Ser Glu Asn Asp Pro Lys Gln Gln Asn Glu Lys Thr Val Asp Lys Leu	
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cct ctt gaa aag tta aca gtg gaa gat ctt tgc cgc gct atc cga caa 1248
 Pro Leu Glu Lys Leu Thr Val Glu Asp Leu Cys Arg Ala Ile Arg Gln
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 Asn Leu Cys Ile Asp Gln Leu Met Pro Arg Val Leu Glu Val Leu Thr
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 620 625 630 635

ctg aat ccg gta tct gcc ctg agt gca ctg gat aac cct ttc cgg tca 2088
 Leu Asn Pro Val Ser Ala Leu Ser Ala Leu Asp Asn Pro Phe Arg Ser
 640 645 650

gca gat aac gcg act ggc aga att acc tcc agc ata caa cct gcg gtg 2136
 Ala Asp Asn Ala Thr Gly Arg Ile Thr Ser Ser Ile Gln Pro Ala Val
 655 660 665

cag tgc gca gct gct gca gca act gag ggt tct tgt ccc cgg caa tcc 2184
 Gln Cys Ala Ala Ala Ala Thr Glu Gly Ser Cys Pro Arg Gln Ser
 670 675 680

ccg tgt tca gga a atg gtg gat aac tgg cag aag agt gta agg agt cgt 2233
 Pro Cys Ser Gly Met Val Asp Asn Trp Gln Lys Ser Val Arg Ser Arg
 685 690 695

gcg ctc ccg gaa gag gcg atg acg ggc tgg aac gaa ggc atg atc cgc 2281
 Ala Leu Pro Glu Glu Ala Met Thr Gly Trp Asn Glu Gly Met Ile Arg
 700 705 710 715

tta cag cag ttg gct gag cgc ctg aac cgt cag gat gaa cag cgg gga 2329
 Leu Gln Gln Leu Ala Glu Arg Leu Asn Arg Gln Asp Glu Gln Arg Gly
 720 725 730

aaa tac atg acg gtc agt gaa ctg aaa acg gag gtg ttt ggc atc atg 2377

Lys Tyr Met Thr Val Ser Glu Leu Lys Thr Glu Val Phe Gly Ile Met	
735 740 745	
cag gct ttt aac cgg cat atc ccg gcg gaa gag cag tta cgt cgc tac	2425
Gln Ala Phe Asn Arg His Ile Pro Ala Glu Glu Gln Leu Arg Arg Tyr	
750 755 760	
ggt gaa gtc cgt aac cag aat ggc agt gaa cag cag caa aaa cag gct	2473
Gly Glu Val Arg Asn Gln Asn Gly Ser Glu Gln Gln Gln Lys Gln Ala	
765 770 775	
gaa atg gcg cta aat cag tta att aac cgt tat cag atg ata cgt gca	2521
Glu Met Ala Leu Asn Gln Leu Ile Asn Arg Tyr Gln Met Ile Arg Ala	
780 785 790 795	
ggc aaa caa tagtggtagc cataatgcag gagcaaagcc tgaatcagga	2570
Gly Lys Gln	
agagttattc tgactgagtt tggttttctg gcgattcttg tg atg gtg gga tgt	2624
Met Val Gly Cys	
800	
gct tgg tta gct gaa cag gcc ttt tcc gac cat gcg ctt tca cca cac	2672
Ala Trp Leu Ala Glu Gln Ala Phe Ser Asp His Ala Leu Ser Pro His	
805 810 815	
agt gct tgg ccg tac agt gca tcg cgc gat gcc ggg ctg gcc gat acg	2720
Ser Ala Trp Pro Tyr Ser Ala Ser Arg Asp Ala Gly Leu Ala Asp Thr	
820 825 830	
ggc gcg ggc ggc tat ccc act tgt aaa cag ccg tgg gcc gac gac acc	2768
Gly Ala Gly Gly Tyr Pro Thr Cys Lys Gln Arg Trp Ala Asp Asp Thr	
835 840 845 850	
gtt ggg ctg aaa gcc cgt cta ctg caa ctt cct gcc cta gat atc tgg	2816
Val Gly Leu Lys Ala Arg Leu Leu Gln Leu Pro Ala Leu Asp Ile Trp	
855 860 865	
acg gcg ttt aaa aaa atc gac cag tcg cag gta gtg tat gaa gag gcc	2864
Thr Ala Phe Lys Lys Ile Asp Gln Ser Gln Val Val Tyr Glu Glu Ala	
870 875 880	
gtg ctg cgc tcg ccg gtc agt gaa cga aat atg cag gta tcg cag aat	2912
Val Leu Arg Ser Arg Val Ser Glu Arg Asn Met Gln Val Ser Gln Asn	
885 890 895	
ggg cgc gtt tat cca agc tat ggc ggt aac gtt gat ggc acc gtc gcc	2960
Gly Arg Val Tyr Pro Ser Tyr Gly Gly Asn Val Asp Gly Thr Val Ala	

900	905	910	
aat gcc gcc acc cgg ttg gca tcc ggc gct aga aat atc ctc ggc agc			3008
Asn Ala Ala Thr Arg Leu Ala Ser Gly Ala Arg Asn Ile Leu Gly Ser			
915	920	925	930
ata gcg gca tgt acg gca ttc gac agc gtg cgt taggcactac cg atg gta			3059
Ile Ala Ala Cys Thr Ala Phe Asp Ser Val Arg			Met Val
	935	940	
cag gcg cag ctg caa ata gcg ctg gtg atc tgt att ccg ctg ata acg			3107
Gln Ala Gln Leu Gln Ile Ala Leu Val Ile Cys Ile Pro Leu Ile Thr			
945	950	955	
ctc tgt tcg gcg tgg gat gtg aaa gta gtg atg acg ctg acg ttt gtg			3155
Leu Cys Ser Ala Trp Asp Val Lys Val Val Met Thr Leu Thr Phe Val			
960	965	970	975
cag ttt gca cta ttt ttc ctc acc ttt tgg tgg gaa ctg gca cgg tgg			3203
Gln Phe Ala Leu Phe Phe Leu Thr Phe Trp Trp Glu Leu Ala Arg Trp			
	980	985	990
ctt gat agc tgg ctg ctg gat gtg ctc tac aac agc gat acc cac agt			3251
Leu Asp Ser Trp Leu Leu Asp Val Leu Tyr Asn Ser Asp Thr His Ser			
	995	1000	1005
agc tgg aat tta gcc ggg atc cag aat acg cag gat gac gtg att atc			3299
Ser Trp Asn Leu Ala Gly Ile Gln Asn Thr Gln Asp Asp Val Ile Ile			
	1010	1015	1020
aat ctg gtg atg agg ttg atg ttt ctg gtg ttg ccg aca ttc tgg ctg			3347
Asn Leu Val Met Arg Leu Met Phe Leu Val Leu Pro Thr Phe Trp Leu			
	1025	1030	1035
ggg gcg atg acg tgg gct gga gtg agg gtt ggc gtg gcg ctg aat gga			3395
Gly Ala Met Thr Trp Ala Gly Val Arg Val Gly Val Ala Leu Asn Gly			
1040	1045	1050	1055
gcg ctg gcg gga tgattgggag gtgattcgcc aatctcactt tcctatacac			3447
Ala Leu Ala Gly			
atataaaatg ta atg aaa tat ctc ttt ttt gag aat ata cat tct ata ttt			3498
	Met Lys Tyr Leu Phe Phe Glu Asn Ile His Ser Ile Phe		
	1060	1065	1070
tta aca ttc agt ctc ttc cga aca tct gtg tcg cct gat ttc cca atg			3546
Leu Thr Phe Ser Leu Phe Arg Thr Ser Val Ser Pro Asp Phe Pro Met			
	1075	1080	1085

att ttt gca ttg ccc tca atc att tta ggt caa ttt acg acc aac caa 3594
 Ile Phe Ala Leu Pro Ser Ile Ile Leu Gly Gln Phe Thr Thr Asn Gln
 1090 1095 1100

tta act aac ttt gtg ata tgt atg ggt aac acc gtt gaa cgt cgg ctg 3642
 Leu Thr Asn Phe Val Ile Cys Met Gly Asn Thr Val Glu Arg Arg Leu
 1105 1110 1115 1120

ggt gtt gtt cat aat ccc ttt aaa agg tct ggg gat ggc cat gac ctc 3690
 Gly Val Val His Asn Pro Phe Lys Arg Ser Gly Asp Gly His Asp Leu
 1125 1130 1135

agg gcg gta gcg tgaccaaagt tcatatccat accaattatt tttattttaa 3742
 Arg Ala Val Ala
 1140

atatcaactt attcgagttg ttttatttag ttcaaagaag gtatcaaa ttg ata gtt 3799
 Leu Ile Val

ata gat ttt ttt tgt ggc tgt ggt gga gcc agt gaa ggg cta cgt cag 3847
 Ile Asp Phe Phe Cys Gly Cys Gly Gly Ala Ser Glu Gly Leu Arg Gln
 1145 1150 1155

gct ggc ttt gat atc gag ctt gga tta gat att gac caa caa gca tca 3895
 Ala Gly Phe Asp Ile Glu Leu Gly Leu Asp Ile Asp Gln Gln Ala Ser
 1160 1165 1170 1175

gaa aca ttt aaa gct aat ttc cct gat gca aaa ttc atc caa gat gat 3943
 Glu Thr Phe Lys Ala Asn Phe Pro Asp Ala Lys Phe Ile Gln Asp Asp
 1180 1185 1190

att agg aaa atc gaa cct caa gat atc tcc gac atc att gat att aaa 3991
 Ile Arg Lys Ile Glu Pro Gln Asp Ile Ser Asp Ile Ile Asp Ile Lys
 1195 1200 1205

gct aaa cgg cct ttg tta ctg agt gca tgt gca cca tgt caa cca ttt 4039
 Ala Lys Arg Pro Leu Leu Leu Ser Ala Cys Ala Pro Cys Gln Pro Phe
 1210 1215 1220

tcg caa cag aat aaa aat aaa act agt gac gac tca agg aga aat cta 4087
 Ser Gln Gln Asn Lys Asn Lys Thr Ser Asp Asp Ser Arg Arg Asn Leu
 1225 1230 1235

cta aat gaa act cat cgt ttt att aga gaa ctt ctt cct gaa tat att 4135
 Leu Asn Glu Thr His Arg Phe Ile Arg Glu Leu Leu Pro Glu Tyr Ile
 1240 1245 1250 1255

atg ctt gaa aat gtt cct gga atg caa aaa att gat gaa gaa aaa gaa	4183
Met Leu Glu Asn Val Pro Gly Met Gln Lys Ile Asp Glu Glu Lys Glu	
1260 1265 1270	
ggc cca ttt cag gag ttt att aag cta ctt aaa gag tta gag tat aac	4231
Gly Pro Phe Gln Glu Phe Ile Lys Leu Leu Lys Glu Leu Glu Tyr Asn	
1275 1280 1285	
tat ata tct ttt ata gcc aat gct gag aac tat ggg att ccc caa aga	4279
Tyr Ile Ser Phe Ile Ala Asn Ala Glu Asn Tyr Gly Ile Pro Gln Arg	
1290 1295 1300	
aga aaa aga ctc gtg ctc tta gct agt cga gta ggt aaa gtt acc cta	4327
Arg Lys Arg Leu Val Leu Leu Ala Ser Arg Val Gly Lys Val Thr Leu	
1305 1310 1315	
cca gag ata acc cat ggt aaa aat aaa atc cca ttc aaa act gta cga	4375
Pro Glu Ile Thr His Gly Lys Asn Lys Ile Pro Phe Lys Thr Val Arg	
1320 1325 1330 1335	
gat tat atc cag gac ttc aca aag tta tgt tca gga gaa acc gac ccc	4423
Asp Tyr Ile Gln Asp Phe Thr Lys Leu Cys Ser Gly Glu Thr Asp Pro	
1340 1345 1350	
aaa gat cct tta cat agg gct gga aca ctg agc cct ctt aac cta aaa	4471
Lys Asp Pro Leu His Arg Ala Gly Thr Leu Ser Pro Leu Asn Leu Lys	
1355 1360 1365	
aga att atg cac act cca gaa gga ggg gat aga aga aat tgg cca gaa	4519
Arg Ile Met His Thr Pro Glu Gly Gly Asp Arg Arg Asn Trp Pro Glu	
1370 1375 1380	
gag tta gtt aat aaa tgc cat aaa aat tat gat ggc cac aca gat act	4567
Glu Leu Val Asn Lys Cys His Lys Asn Tyr Asp Gly His Thr Asp Thr	
1385 1390 1395	
tat gga aga atg agt tgg gat aag cct gcg cct aca ctt acg acg aaa	4615
Tyr Gly Arg Met Ser Trp Asp Lys Pro Ala Pro Thr Leu Thr Thr Lys	
1400 1405 1410 1415	
tgt aat agt tac tcc aat ggt cgt ttt ggg cat cct gac ccc act caa	4663
Cys Asn Ser Tyr Ser Asn Gly Arg Phe Gly His Pro Asp Pro Thr Gln	
1420 1425 1430	
cat aga gca att agc ata aga gaa gca tca aga tta caa aca ttt cct	4711
His Arg Ala Ile Ser Ile Arg Glu Ala Ser Arg Leu Gln Thr Phe Pro	
1435 1440 1445	

tta agc tat gtt ttt aaa ggt tgc ctg aat tca atg gca aag caa atc	4759
Leu Ser Tyr Val Phe Lys Gly Ser Leu Asn Ser Met Ala Lys Gln Ile	
1450 1455 1460	
ggc aat gct gta cct tgc gaa ctc gct aga cta ttt ggg cta cat ctc	4807
Gly Asn Ala Val Pro Cys Glu Leu Ala Arg Leu Phe Gly Leu His Leu	
1465 1470 1475	
ata gaa aat tgt act aat aag gat tca tagatatatg gctaaaataa	4854
Ile Glu Asn Cys Thr Asn Lys Asp Ser	
1480 1485	
gaacaaaggc tcgagctttg gac atg ctt ggc aga caa caa att gca ggt ata	4907
Met Leu Gly Arg Gln Gln Ile Ala Gly Ile	
1490 1495	
cct act gcc ttg agt gag tta ttt aaa aat gct cat gat gcc tat gct	4955
Pro Thr Ala Leu Ser Glu Leu Phe Lys Asn Ala His Asp Ala Tyr Ala	
1500 1505 1510	
gat aat gtc gaa gtt gat ttt ttt agg aaa gaa aat ctt ctt atc ttg	5003
Asp Asn Val Glu Val Asp Phe Phe Arg Lys Glu Asn Leu Leu Ile Leu	
1515 1520 1525 1530	
aga gat gat gga tta ggt atg aca acc gat gaa ttt gaa gag agg tgg	5051
Arg Asp Asp Gly Leu Gly Met Thr Thr Asp Glu Phe Glu Glu Arg Trp	
1535 1540 1545	
ttg act att gga acc tcc agc aaa tta atc gac gat gat gca att aat	5099
Leu Thr Ile Gly Thr Ser Ser Lys Leu Ile Asp Asp Asp Ala Ile Asn	
1550 1555 1560	
aaa cca gca gtg gat agt aat aaa gcc ttt cgc cct atc atg gga gag	5147
Lys Pro Ala Val Asp Ser Asn Lys Ala Phe Arg Pro Ile Met Gly Glu	
1565 1570 1575	
aaa gga ata ggc cgt tta tct atc gca gca att gga cca cag gtg ctg	5195
Lys Gly Ile Gly Arg Leu Ser Ile Ala Ala Ile Gly Pro Gln Val Leu	
1580 1585 1590	
gtt ctt act agg gcc aaa aga gac aat gag ctt aag cca tta gtt gct	5243
Val Leu Thr Arg Ala Lys Arg Asp Asn Glu Leu Lys Pro Leu Val Ala	
1595 1600 1605 1610	
gca ttt gtt aat tgg agt tta ttt gct ata cca tca ctt gat ctt gat	5291
Ala Phe Val Asn Trp Ser Leu Phe Ala Ile Pro Ser Leu Asp Leu Asp	
1615 1620 1625	

gat ata gaa ata cca att aga act att atc aac gac gaa tgc ttc act	5339
Asp Ile Glu Ile Pro Ile Arg Thr Ile Ile Asn Asp Glu Cys Phe Thr	
1630 1635 1640	
aaa aaa act ctt gat gag atg att gag caa gca aga aat aat tta gac	5387
Lys Lys Thr Leu Asp Glu Met Ile Glu Gln Ala Arg Asn Asn Leu Asp	
1645 1650 1655	
tct tta tca cac aaa ata tca aaa tca aaa gta tca caa ata aat aca	5435
Ser Leu Ser His Lys Ile Ser Lys Ser Lys Val Ser Gln Ile Asn Thr	
1660 1665 1670	
caa tta tca tct ttt gaa ttt gat cct att cta tgg gaa aaa aaa tta	5483
Gln Leu Ser Ser Phe Glu Phe Asp Pro Ile Leu Trp Glu Lys Lys Leu	
1675 1680 1685 1690	
ggg ggg cta aga cta tct gga gat ggg cat gga act cac ttc ata ata	5531
Gly Gly Leu Arg Leu Ser Gly Asp Gly His Gly Thr His Phe Ile Ile	
1695 1700 1705	
atg cct acc gaa gaa ata tta ata gat gac att tcc acg agc gat agc	5579
Met Pro Thr Glu Glu Ile Leu Ile Asp Asp Ile Ser Thr Ser Asp Ser	
1710 1715 1720	
aat aaa aca tca gag cag tct tct cgc tta gaa aaa gct tta tta ggt	5627
Asn Lys Thr Ser Glu Gln Ser Ser Arg Leu Glu Lys Ala Leu Leu Gly	
1725 1730 1735	
ttt aca aac aca atg tac agt gat tca aac cct cct att ata gct cgt	5675
Phe Thr Asn Thr Met Tyr Ser Asp Ser Asn Pro Pro Ile Ile Ala Arg	
1740 1745 1750	
ttt aga gac tat ctg gaa gat ggt gag tgc att gac aga att agc gaa	5723
Phe Arg Asp Tyr Leu Glu Asp Gly Glu Cys Ile Asp Arg Ile Ser Glu	
1755 1760 1765 1770	
tca att ttt ttt aca ccg caa gaa ttc aat ctt gca gat cac cac att	5771
Ser Ile Phe Phe Thr Pro Gln Glu Phe Asn Leu Ala Asp His His Ile	
1775 1780 1785	
gaa gga tgg ttc aat gaa ttt ggt caa ttc agt gga act gtt tct gtt	5819
Glu Gly Trp Phe Asn Glu Phe Gly Gln Phe Ser Gly Thr Val Ser Val	
1790 1795 1800	
tat ggt gaa gag cca att cat cat gtc gtg act tgg aaa aat aat aat	5867
Tyr Gly Glu Glu Pro Ile His His Val Val Thr Trp Lys Asn Asn Asn	
1805 1810 1815	

caa tta acc caa tgc ggt cca ttt aaa ata aaa tta gcg tat att cat	5915
Gln Leu Thr Gln Cys Gly Pro Phe Lys Ile Lys Leu Ala Tyr Ile His	
1820 1825 1830	
ggt cgg ctt cgt gat tca cgc tta ccc atg gag ttg tgg gcc cct ctg	5963
Gly Arg Leu Arg Asp Ser Arg Leu Pro Met Glu Leu Trp Ala Pro Leu	
1835 1840 1845 1850	
aag gag aaa aca gat aga tat ggt ggt tta tat atc tat cga gat gga	6011
Lys Glu Lys Thr Asp Arg Tyr Gly Gly Leu Tyr Ile Tyr Arg Asp Gly	
1855 1860 1865	
tta aga att ttg ccc tat gga gat tca gat acg gat ttt cta aaa ata	6059
Leu Arg Ile Leu Pro Tyr Gly Asp Ser Asp Thr Asp Phe Leu Lys Ile	
1870 1875 1880	
gaa aag aga aga acg tta tcc gct tct gaa tat ttt ttc tca tat cga	6107
Glu Lys Arg Arg Thr Leu Ser Ala Ser Glu Tyr Phe Phe Ser Tyr Arg	
1885 1890 1895	
cgt ttg ttt gga gca ata gaa tta aca aaa gaa aac aat gct tca tta	6155
Arg Leu Phe Gly Ala Ile Glu Leu Thr Lys Glu Asn Asn Ala Ser Leu	
1900 1905 1910	
gtt gaa aaa gct ggg cga gaa gga ttc att gaa aat aag cca tat aaa	6203
Val Glu Lys Ala Gly Arg Glu Gly Phe Ile Glu Asn Lys Pro Tyr Lys	
1915 1920 1925 1930	
cag ttt aaa gaa atg ctt gaa aat ttc ttc atc gaa atc gca aga gat	6251
Gln Phe Lys Glu Met Leu Glu Asn Phe Phe Ile Glu Ile Ala Arg Asp	
1935 1940 1945	
ttc ttt aag gac gat ggc gat atg tct gaa tta ttt gtt gag aca aag	6299
Phe Phe Lys Asp Asp Gly Asp Met Ser Glu Leu Phe Val Glu Thr Lys	
1950 1955 1960	
caa cgt aga aat gaa gaa cat gat ttg tta tct aaa aga tct aaa caa	6347
Gln Arg Arg Asn Glu Glu His Asp Leu Leu Ser Lys Arg Ser Lys Gln	
1965 1970 1975	
act aaa gct aaa aaa gat aga tta aag aaa gat ctg tat gat ttt ttt	6395
Thr Lys Ala Lys Lys Asp Arg Leu Lys Lys Asp Leu Tyr Asp Phe Phe	
1980 1985 1990	
gat aag tta gat aat gat tac tgg aat att gaa ata aat aag cta atc	6443
Asp Lys Leu Asp Asn Asp Tyr Trp Asn Ile Glu Ile Asn Lys Leu Ile	
1995 2000 2005 2010	

aat aaa aac gag gaa tat ttc tcc agt aca gaa ata aca gac acc aat	6491
Asn Lys Asn Glu Glu Tyr Phe Ser Ser Thr Glu Ile Thr Asp Thr Asn	
2015 2020 2025	
ata gat tat gta tac aat aaa att aaa gaa caa aat gat gct atc att	6539
Ile Asp Tyr Val Tyr Asn Lys Ile Lys Glu Gln Asn Asp Ala Ile Ile	
2030 2035 2040	
aaa aat cta cgt aat tct gtg gat ata aag aaa ccc tct gga gtt gga	6587
Lys Asn Leu Arg Asn Ser Val Asp Ile Lys Lys Pro Ser Gly Val Gly	
2045 2050 2055	
tta aca aaa gag tta tct aat tta tgg gat aga tat caa ata gaa aga	6635
Leu Thr Lys Glu Leu Ser Asn Leu Trp Asp Arg Tyr Gln Ile Glu Arg	
2060 2065 2070	
caa aaa ata ctg tta tca cta aat gag cta aaa gat aac gtt gat aga	6683
Gln Lys Ile Leu Leu Ser Leu Asn Glu Leu Lys Asp Asn Val Asp Arg	
2075 2080 2085 2090	
aag ctt ata gaa ctg gat aat aaa aat aat gat ttt ctc aac tta cgg	6731
Lys Leu Ile Glu Leu Asp Asn Lys Asn Asn Asp Phe Leu Asn Leu Arg	
2095 2100 2105	
aag aga ctt gaa gat tct ttg aat cta caa caa agt tac tat gaa aaa	6779
Lys Arg Leu Glu Asp Ser Leu Asn Leu Gln Gln Ser Tyr Tyr Glu Lys	
2110 2115 2120	
gaa cta aca aag tta tat aat gac gct aaa aat gct ttg aaa gat gtg	6827
Glu Leu Thr Lys Leu Tyr Asn Asp Ala Lys Asn Ala Leu Lys Asp Val	
2125 2130 2135	
caa tct aaa gca aat agg tta att tct gat aat aag aaa aaa cat aag	6875
Gln Ser Lys Ala Asn Arg Leu Ile Ser Asp Asn Lys Lys Lys His Lys	
2140 2145 2150	
agt gaa cta aaa aac att tct tat gaa ttc caa tca act aat ctc aat	6923
Ser Glu Leu Lys Asn Ile Ser Tyr Glu Phe Gln Ser Thr Asn Leu Asn	
2155 2160 2165 2170	
ggc aaa gat act gcg tat ata ttg gat gta aaa aga aat cta gaa agt	6971
Gly Lys Asp Thr Ala Tyr Ile Leu Asp Val Lys Arg Asn Leu Glu Ser	
2175 2180 2185	
aaa att gag aat act tca aac gaa gtg att aat gaa ata aga aaa cta	7019
Lys Ile Glu Asn Thr Ser Asn Glu Val Ile Asn Glu Ile Arg Lys Leu	
2190 2195 2200	

acc gac cag att gca ata att agt gat agt acc act tct gaa aat tta	7067
Thr Asp Gln Ile Ala Ile Ile Ser Asp Ser Thr Thr Ser Glu Asn Leu	
2205 2210 2215	
tca tcg gct caa gta act gaa gca atc gaa act gaa ctt gaa cat tta	7115
Ser Ser Ala Gln Val Thr Glu Ala Ile Glu Thr Glu Leu Glu His Leu	
2220 2225 2230	
cga gac caa caa gca aat aac gca gag tta ata cta ctt ggc atg gct	7163
Arg Asp Gln Gln Ala Asn Asn Ala Glu Leu Ile Leu Leu Gly Met Ala	
2235 2240 2245 2250	
ctt tct gta gta cat cat gaa ttt aat ggt aat att agg gca att aga	7211
Leu Ser Val Val His His Glu Phe Asn Gly Asn Ile Arg Ala Ile Arg	
2255 2260 2265	
agt gcg cta agg gaa tta aaa gca tgg gct gac aga aat cct aag ctt	7259
Ser Ala Leu Arg Glu Leu Lys Ala Trp Ala Asp Arg Asn Pro Lys Leu	
2270 2275 2280	
gat att ata tac caa aaa atc aga act agt ttt gat cac tta gat ggt	7307
Asp Ile Ile Tyr Gln Lys Ile Arg Thr Ser Phe Asp His Leu Asp Gly	
2285 2290 2295	
tat tta aaa acc ttt aca cca ttg aca aga cgt tta agt cgc tct aaa	7355
Tyr Leu Lys Thr Phe Thr Pro Leu Thr Arg Arg Leu Ser Arg Ser Lys	
2300 2305 2310	
acc aat ata act gga act gcc att tta gaa ttt atc aga gat gta ttc	7403
Thr Asn Ile Thr Gly Thr Ala Ile Leu Glu Phe Ile Arg Asp Val Phe	
2315 2320 2325 2330	
gat gat cgt ctt gag aaa gaa gga att gaa tta ttc act acc tca aag	7451
Asp Asp Arg Leu Glu Lys Glu Gly Ile Glu Leu Phe Thr Thr Ser Lys	
2335 2340 2345	
ttt gtt aat caa gaa att gta act tac aca tca acc att tac cct gtc	7499
Phe Val Asn Gln Glu Ile Val Thr Tyr Thr Ser Thr Ile Tyr Pro Val	
2350 2355 2360	
ttt ata aat cta att gat aac gca ata tac tgg ctt ggg aaa aca act	7547
Phe Ile Asn Leu Ile Asp Asn Ala Ile Tyr Trp Leu Gly Lys Thr Thr	
2365 2370 2375	
gga gaa aaa aga ctt ata ctt gat gct act gaa aca gga ttt gtt att	7595
Gly Glu Lys Arg Leu Ile Leu Asp Ala Thr Glu Thr Gly Phe Val Ile	
2380 2385 2390	

77

gat ata aca ata ctt gac tgg gat atg caa agc gat agt ggg caa ttt	8220
Asp Ile Thr Ile Leu Asp Trp Asp Met Gln Ser Asp Ser Gly Gln Phe	
2585 2590 2595	
gct att gaa ata ata aaa tcg ata atc gtt tca gat ata aat tct gga	8268
Ala Ile Glu Ile Ile Lys Ser Ile Ile Val Ser Asp Ile Asn Ser Gly	
2600 2605 2610	
gga cgt tta cgt ctt ctt tct att tat act ggt gaa cat gtt act gct	8316
Gly Arg Leu Arg Leu Leu Ser Ile Tyr Thr Gly Glu His Val Thr Ala	
2615 2620 2625 2630	
gtt ata act aag ttg aac aat gag tta aag aaa aca tac cgt agc gta	8364
Val Ile Thr Lys Leu Asn Asn Glu Leu Lys Lys Thr Tyr Arg Ser Val	
2635 2640 2645	
ata aaa aat gat gat agt att ttt att gaa gat aac tat gca ctc gaa	8412
Ile Lys Asn Asp Asp Ser Ile Phe Ile Glu Asp Asn Tyr Ala Leu Glu	
2650 2655 2660	
caa tgg tgt ata gtt gtt att agt aaa gac gtt tat gaa aaa gat ctt	8460
Gln Trp Cys Ile Val Val Ile Ser Lys Asp Val Tyr Glu Lys Asp Leu	
2665 2670 2675	
cca aat gtg tta ata aaa aaa ttc act aac ctt aca gct ggg ttg cta	8508
Pro Asn Val Leu Ile Lys Lys Phe Thr Asn Leu Thr Ala Gly Leu Leu	
2680 2685 2690	
tcc aac gcc gca ctc tct tgc att tct gaa ata aga gaa aaa acc cat	8556
Ser Asn Ala Ala Leu Ser Cys Ile Ser Glu Ile Arg Glu Lys Thr His	
2695 2700 2705 2710	
ggg ata tta aca aaa tat aat aat aaa tta gac act gca tat gtt tcc	8604
Gly Ile Leu Thr Lys Tyr Asn Asn Lys Leu Asp Thr Ala Tyr Val Ser	
2715 2720 2725	
cac atc tta aat tta ata aaa tcc aag gag tca agg gca tat gct tat	8652
His Ile Leu Asn Leu Ile Lys Ser Lys Glu Ser Arg Ala Tyr Ala Tyr	
2730 2735 2740	
gaa aat gct cat gat tat gca gta gat tta att tct gaa gaa ata aga	8700
Glu Asn Ala His Asp Tyr Ala Val Asp Leu Ile Ser Glu Glu Ile Arg	
2745 2750 2755	
tca ata ttg caa ata agt gaa aac tta aag aaa tct cta agc aaa aac	8748
Ser Ile Leu Gln Ile Ser Glu Asn Leu Lys Lys Ser Leu Ser Lys Asn	
2760 2765 2770	

79

tta ctc gtt gaa aaa ata tct act cca aaa gta ttg aaa tgg atc ggg 9372
 Leu Leu Val Glu Lys Ile Ser Thr Pro Lys Val Leu Lys Trp Ile Gly
 2970 2975 2980

gaa ata aaa aca acg tac gcg caa aaa ata aca act gat att gtt gct 9420
 Glu Ile Lys Thr Thr Tyr Ala Gln Lys Ile Thr Thr Asp Ile Val Ala
 2985 2990 2995

aat ctg tca aga ata ggt tta gat caa cat gag tgg tta cga ata aaa 9468
 Asn Leu Ser Arg Ile Gly Leu Asp Gln His Glu Trp Leu Arg Ile Lys
 3000 3005 3010

tca aaa gat ata taaatgatta tatatgccgt cgtttttataa aaactggcgg 9520
 Ser Lys Asp Ile
 3015

catgtatatc tagttagtcc atcatagaag tcaagaaatt tagtttgccc tatatcttat 9580

agaaaatata ttttatatgc ttaaaaaaca ccatctttct aagatggcat ttatgtgctt 9640

tgtttcgatc aattacaact gatataattac catattgatt aattttatgt tatttaccaa 9700

agtaacggca tcttaataata tcgtcataat atagtgcgcg ttctgactct aatactgaaa 9760

aatttatttg ttctatttta cacttactgc aaatagcatc cagtttatca tatagtgtcg 9820

catcaattgg cgcag atg tca tca cgc caa atc ctt gag cat tat aat gct 9871
 Met Ser Ser Arg Gln Ile Leu Glu His Tyr Asn Ala
 3020 3025 3030

cta aca tat ccc cta cat caa tca atc ttg ttg cag ata atg act tcg 9919
 Leu Thr Tyr Pro Leu His Gln Ser Ile Leu Leu Gln Ile Met Thr Ser
 3035 3040 3045

aat ttg tta tca gtt tgc act gga aaa tcc att tac gag gat atc tcc 9967
 Asn Leu Leu Ser Val Cys Thr Gly Lys Ser Ile Tyr Glu Asp Ile Ser
 3050 3055 3060

ggc agt tct tgg aat atc ata cac ttc aat atc cct ctc ccc atc tct 10015
 Gly Ser Ser Trp Asn Ile Ile His Phe Asn Ile Pro Leu Pro Ile Ser
 3065 3070 3075

aga gcg aga ctt tcc ata ttt tot tat tgt gtc aga att aaa cct tgg 10063
 Arg Ala Arg Leu Ser Ile Phe Ser Tyr Cys Val Arg Ile Lys Pro Trp
 3080 3085 3090

atg agt atg gat tac atg taaccggctc atttaaaccg tctgggtctgt 10111
 Met Ser Met Asp Tyr Met

3095

3100

ttcctccggt tttaaaaa ta atg tcc atc att ttt aat gga cac tat cgt 10163
Met Ser Ile Ile Phe Asn Gly His Tyr Arg

3105

3110

atg aaa cac cgg act tgg atc act gaa gct tta cgt ctt cac ttt gaa 10211
Met Lys His Arg Thr Trp Ile Thr Glu Ala Leu Arg Leu His Phe Glu

3115

3120

3125

gaa cat tta ccc cag gtt gtg gtc ggg cgt cgc ctg ggc gta cca aaa 10259
Glu His Leu Pro Gln Val Val Val Gly Arg Arg Leu Gly Val Pro Lys

3130

3135

3140

tca aca gct tgt ggt atg ttc gtg cgc ttt cgc aaa gct ggc ttt tca 10307
Ser Thr Ala Cys Gly Met Phe Val Arg Phe Arg Lys Ala Gly Phe Ser

3145

3150

3155

tgg cct ctg ccc gca ggt atg tcg gag cgg gag ctt gat ggc cgt ctt 10355
Trp Pro Leu Pro Ala Gly Met Ser Glu Arg Glu Leu Asp Gly Arg Leu

3160

3165

3170

tac ggg agt acc tcc aca gta cct gtc gta ctt tgt agt gga tcg gta 10403
Tyr Gly Ser Thr Ser Thr Val Pro Val Val Leu Cys Ser Gly Ser Val

3175

3180

3185

3190

att cag gac acc tcg aaa tcc tgt taatgttaaa acagtgaataa tgaggtgatg 10457
Ile Gln Asp Thr Ser Lys Ser Cys

3195

c atg atc aaa act cgt cgg act aaa cgt acc ttt tcc ccg gag ttc aag 10506
Met Ile Lys Thr Arg Arg Thr Lys Arg Thr Phe Ser Pro Glu Phe Lys

3200

3205

3210

ctt gaa gct ttc gag cag gtg gtg gtt aaa tac cag cgt gat gtc aga 10554
Leu Glu Ala Phe Glu Gln Val Val Val Lys Tyr Gln Arg Asp Val Arg

3215

3220

3225

3230

gaa gtc gcg cag gca ctc gag ctc aac cct gac cat ttg cgt aaa tgg 10602
Glu Val Ala Gln Ala Leu Glu Leu Asn Pro Asp His Leu Arg Lys Trp

3235

3240

3245

ata cgg ttg tat aag cag gaa ctt cag ggt att gag cca gct ggt aat 10650
Ile Arg Leu Tyr Lys Gln Glu Leu Gln Gly Ile Glu Pro Ala Gly Asn

3250

3255

3260

gct att acc cct gaa caa cgc gaa att cag cag ctt aaa gcg cag ata 10698
Ala Ile Thr Pro Glu Gln Arg Glu Ile Gln Gln Leu Lys Ala Gln Ile

3265 3270 3275
 aag cgc gtt gag atg gaa aaa gaa ata cta aag cag gct gcc gtg ctg 10746
 Lys Arg Val Glu Met Glu Lys Glu Ile Leu Lys Gln Ala Ala Val Leu
 3280 3285 3290
 atg agc gaa atc ccc ggg aag ctg tcg cgc taatcacaca gctgaaagca 10796
 Met Ser Glu Ile Pro Gly Lys Leu Ser Arg
 3295 3300
 aagtggccag tgtgggttat ttgtcattta ttcggtatta accgtagcgt ttattacgcg 10856
 caggtgaagc gtcctgttaa tgtgcaaaga attgaattac gaagccgggt gagggctttc 10916
 catgctctca gtcgtggcgc agccgggtag ccgggcaatc agtcagatgt tgcgccagag 10976
 tggcggttgat gcaggccgggt ggctggcatg acgactgatg cgggaatgag ggctgacaag 11036
 tcgacagccg gttaaaccatc acaaccgggt aaacgaagac aaaagtccgc cattgccaaa 11096
 tttactgaac cggcaatttc accccgccgc accaaactgc gtctggtgcg gcgacatcag 11156
 ttttattcg 11165

<210> 35

<211> 366

<212> PRT

<213> Escherichia coli

<400> 35

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

Leu Val Gly Gly Asn Met Ala Gly Ala Leu Ala Gly Ala Ser Ala Pro
 20 25 30

Glu Leu Ala Asn Ile Ile Gly His His Ala Gly Ile Asp Asp Asn Thr
 35 40 45

Ala Ala Lys Ala Ile Ala His Ala Ile Leu Gly Gly Val Thr Ala Ala
 50 55 60

Leu Gln Gly Asn Ser Ala Ala Ala Gly Ala Ile Gly Ala Gly Thr Gly
 65 70 75 80

Glu Val Ile Ala Ser Ala Ile Ala Lys Ser Leu Tyr Pro Gly Val Asp
 85 90 95

Pro Ser Lys Leu Thr Glu Asp Gln Lys Gln Thr Val Ser Thr Leu Ala
 100 105 110

Thr Leu Ser Ala Gly Met Ala Gly Gly Ile Ala Ser Gly Asp Val Ala
 115 120 125

Gly Ala Ala Ala Gly Ala Gly Ala Gly Lys Asn Val Val Glu Asn Asn
 130 135 140

Ala Leu Ser Leu Val Ala Arg Gly Cys Ala Val Ala Ala Pro Cys Arg
 145 150 155 160

Thr Lys Val Ala Glu Gln Leu Leu Glu Ile Gly Ala Lys Ala Gly Met
 165 170 175

Ala Gly Leu Ala Gly Ala Ala Val Lys Asp Met Ala Asp Arg Met Thr
 180 185 190

Ser Asp Glu Leu Glu His Leu Ile Thr Leu Gln Met Met Gly Asn Asp
 195 200 205

Glu Ile Thr Thr Lys Tyr Leu Ser Ser Leu His Asp Lys Tyr Gly Ser
 210 215 220

Gly Ala Ala Ser Asn Pro Asn Ile Gly Lys Asp Leu Thr Asp Ala Glu
 225 230 235 240

Lys Val Glu Leu Gly Gly Ser Gly Ser Gly Thr Gly Thr Pro Pro Pro
 245 250 255

Ser Glu Asn Asp Pro Lys Gln Gln Asn Glu Lys Thr Val Asp Lys Leu
 260 265 270

Asn Gln Lys Gln Glu Ser Ala Ile Lys Lys Ile Asp Asn Thr Ile Lys
 275 280 285

Asn Ala Leu Lys Asp His Asp Ile Ile Gly Thr Leu Lys Asp Met Asp
 290 295 300

Gly Lys Pro Val Pro Lys Glu Asn Gly Gly Tyr Trp Asp His Met Gln
 305 310 315 320

Glu Met Gln Asn Thr Leu Arg Gly Leu Arg Asn His Ala Asp Thr Leu
 325 330 335

Lys Asn Val Asn Asn Pro Glu Ala Gln Ala Ala Tyr Gly Arg Ala Thr
 340 345 350

Asp Ala Ile Asn Lys Ile Glu Ser Ala Leu Lys Gly Tyr Gly
 355 360 365

<210> 36

<211> 128

<212> PRT

<213> Escherichia coli

<400> 36

Met Ile Thr Leu Arg Lys Leu Ile Gly Asn Ile Asn Met Thr Lys Glu
 1 5 10 15

Pro Glu Gln Gln Ser Pro Leu Glu Leu Trp Phe Glu Arg Ile Ile Asp
 20 25 30

Val Pro Leu Glu Lys Leu Thr Val Glu Asp Leu Cys Arg Ala Ile Arg
 35 40 45

Gln Asn Leu Cys Ile Asp Gln Leu Met Pro Arg Val Leu Glu Val Leu
 50 55 60

Thr Lys Glu Pro Leu Ala Gly Glu Tyr Tyr Asp Gly Glu Leu Ile Ala
 65 70 75 80

Ala Leu Ser Thr Ile Lys Gly Glu Asp Leu Lys Asp Gln Lys Ser Thr
 85 90 95

Phe Thr Gln Ile Arg Gln Leu Ile Asn Gln Leu Glu Pro Ser Asp Ile
 100 105 110

Asn Asp Asp Leu Arg Lys Asp Ile Leu Lys Ile Asn Gln Ile Ile Val
 115 120 125

<210> 37

<211> 107

<212> PRT

<213> Escherichia coli

<400> 37

Met Val Ala Lys Ala Phe Ala Tyr Ala Leu Asn Gln Trp Pro Ala Leu
 1 5 10 15

Thr Tyr Tyr Ala Asn Asp Gly Trp Val Glu Ile Asp Asn Asn Ile Ala
 20 25 30

Glu Asn Ala Leu Arg Ala Val Ser Leu Gly Arg Lys Asn Phe Leu Phe
 35 40 45

Phe Gly Ser Asp His Gly Gly Glu Arg Gly Ala Leu Leu Tyr Ser Leu
 50 55 60

Ile Gly Thr Cys Lys Leu Asn Asp Val Asp Pro Glu Ser Tyr Leu Arg
 65 70 75 80

His Val Leu Ala Val Ile Ala Asp Trp Pro Val Asn Arg Val Ser Glu
 85 90 95

Leu Leu Pro Trp Arg Ile Ala Leu Pro Ala Glu
 100 105

<210> 38

<211> 86

<212> PRT

<213> Escherichia coli

<400> 38

Met Leu Met Ser Val Gln Lys Glu Lys Asn Val Ala Glu Ser Val Val
 1 5 10 15

Ser Glu Thr His Thr Gly Asp Ser Val Tyr Ala Ser Leu Phe Glu Lys
 20 25 30

Ile Asn Leu Asn Pro Val Ser Ala Leu Ser Ala Leu Asp Asn Pro Phe
 35 40 45

Arg Ser Ala Asp Asn Ala Thr Gly Arg Ile Thr Ser Ser Ile Gln Pro
 50 55 60

Ala Val Gln Cys Ala Ala Ala Ala Thr Glu Gly Ser Cys Pro Arg
 65 70 75 80

Gln Ser Pro Cys Ser Gly
 85

<210> 39

<211> 111

<212> PRT

<213> Escherichia coli

<400> 39

Met Val Asp Asn Trp Gln Lys Ser Val Arg Ser Arg Ala Leu Pro Glu

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

<210> 40

<211> 143

<212> PRT

<213> Escherichia coli

<400> 40

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

Gly Thr Val Ala Asn Ala Ala Thr Arg Leu Ala Ser Gly Ala Arg Asn
 115 120 125

Ile Leu Gly Ser Ile Ala Ala Cys Thr Ala Phe Asp Ser Val Arg
 130 135 140

<210> 41

<211> 118

<212> PRT

<213> Escherichia coli

<400> 41

Met Val Gln Ala Gln Leu Gln Ile Ala Leu Val Ile Cys Ile Pro Leu
 1 5 10 15

Ile Thr Leu Cys Ser Ala Trp Asp Val Lys Val Val Met Thr Leu Thr
 20 25 30

Phe Val Gln Phe Ala Leu Phe Phe Leu Thr Phe Trp Trp Glu Leu Ala
 35 40 45

Arg Trp Leu Asp Ser Trp Leu Leu Asp Val Leu Tyr Asn Ser Asp Thr
 50 55 60

His Ser Ser Trp Asn Leu Ala Gly Ile Gln Asn Thr Gln Asp Asp Val
 65 70 75 80

Ile Ile Asn Leu Val Met Arg Leu Met Phe Leu Val Leu Pro Thr Phe
 85 90 95

Trp Leu Gly Ala Met Thr Trp Ala Gly Val Arg Val Gly Val Ala Leu
 100 105 110

Asn Gly Ala Leu Ala Gly
 115

<210> 42

<211> 81

<212> PRT

<213> Escherichia coli

<400> 42

Met Lys Tyr Leu Phe Phe Glu Asn Ile His Ser Ile Phe Leu Thr Phe
 1 5 10 15

Ser Leu Phe Arg Thr Ser Val Ser Pro Asp Phe Pro Met Ile Phe Ala

20 25 30
 Leu Pro Ser Ile Ile Leu Gly Gln Phe Thr Thr Asn Gln Leu Thr Asn
 35 40 45
 Phe Val Ile Cys Met Gly Asn Thr Val Glu Arg Arg Leu Gly Val Val
 50 55 60
 His Asn Pro Phe Lys Arg Ser Gly Asp Gly His Asp Leu Arg Ala Val
 65 70 75 80

Ala

<210> 43
 <211> 348
 <212> PRT
 <213> Escherichia coli

<400> 43
 Leu Ile Val Ile Asp Phe Phe Cys Gly Cys Gly Gly Ala Ser Glu Gly
 1 5 10 15
 Leu Arg Gln Ala Gly Phe Asp Ile Glu Leu Gly Leu Asp Ile Asp Gln
 20 25 30
 Gln Ala Ser Glu Thr Phe Lys Ala Asn Phe Pro Asp Ala Lys Phe Ile
 35 40 45
 Gln Asp Asp Ile Arg Lys Ile Glu Pro Gln Asp Ile Ser Asp Ile Ile
 50 55 60
 Asp Ile Lys Ala Lys Arg Pro Leu Leu Leu Ser Ala Cys Ala Pro Cys
 65 70 75 80
 Gln Pro Phe Ser Gln Gln Asn Lys Asn Lys Thr Ser Asp Asp Ser Arg
 85 90 95
 Arg Asn Leu Leu Asn Glu Thr His Arg Phe Ile Arg Glu Leu Leu Pro
 100 105 110
 Glu Tyr Ile Met Leu Glu Asn Val Pro Gly Met Gln Lys Ile Asp Glu
 115 120 125
 Glu Lys Glu Gly Pro Phe Gln Glu Phe Ile Lys Leu Leu Lys Glu Leu
 130 135 140
 Glu Tyr Asn Tyr Ile Ser Phe Ile Ala Asn Ala Glu Asn Tyr Gly Ile

145	150	155	160
Pro Gln Arg Arg Lys Arg Leu Val Leu Leu Ala Ser Arg Val Gly Lys	165	170	175
Val Thr Leu Pro Glu Ile Thr His Gly Lys Asn Lys Ile Pro Phe Lys	180	185	190
Thr Val Arg Asp Tyr Ile Gln Asp Phe Thr Lys Leu Cys Ser Gly Glu	195	200	205
Thr Asp Pro Lys Asp Pro Leu His Arg Ala Gly Thr Leu Ser Pro Leu	210	215	220
Asn Leu Lys Arg Ile Met His Thr Pro Glu Gly Gly Asp Arg Arg Asn	225	230	235
Trp Pro Glu Glu Leu Val Asn Lys Cys His Lys Asn Tyr Asp Gly His	245	250	255
Thr Asp Thr Tyr Gly Arg Met Ser Trp Asp Lys Pro Ala Pro Thr Leu	260	265	270
Thr Thr Lys Cys Asn Ser Tyr Ser Asn Gly Arg Phe Gly His Pro Asp	275	280	285
Pro Thr Gln His Arg Ala Ile Ser Ile Arg Glu Ala Ser Arg Leu Gln	290	295	300
Thr Phe Pro Leu Ser Tyr Val Phe Lys Gly Ser Leu Asn Ser Met Ala	305	310	315
Lys Gln Ile Gly Asn Ala Val Pro Cys Glu Leu Ala Arg Leu Phe Gly	325	330	335
Leu His Leu Ile Glu Asn Cys Thr Asn Lys Asp Ser	340	345	

<210> 44

<211> 974

<212> PRT

<213> Escherichia coli

<400> 44

Met Leu Gly Arg Gln Gln Ile Ala Gly Ile Pro Thr Ala Leu Ser Glu
1 5 10 15

Leu Phe Lys Asn Ala His Asp Ala Tyr Ala Asp Asn Val Glu Val Asp
 20 25 30

Phe Phe Arg Lys Glu Asn Leu Leu Ile Leu Arg Asp Asp Gly Leu Gly
 35 40 45

Met Thr Thr Asp Glu Phe Glu Glu Arg Trp Leu Thr Ile Gly Thr Ser
 50 55 60

Ser Lys Leu Ile Asp Asp Asp Ala Ile Asn Lys Pro Ala Val Asp Ser
 65 70 75 80

Asn Lys Ala Phe Arg Pro Ile Met Gly Glu Lys Gly Ile Gly Arg Leu
 85 90 95

Ser Ile Ala Ala Ile Gly Pro Gln Val Leu Val Leu Thr Arg Ala Lys
 100 105 110

Arg Asp Asn Glu Leu Lys Pro Leu Val Ala Ala Phe Val Asn Trp Ser
 115 120 125

Leu Phe Ala Ile Pro Ser Leu Asp Leu Asp Asp Ile Glu Ile Pro Ile
 130 135 140

Arg Thr Ile Ile Asn Asp Glu Cys Phe Thr Lys Lys Thr Leu Asp Glu
 145 150 155 160

Met Ile Glu Gln Ala Arg Asn Asn Leu Asp Ser Leu Ser His Lys Ile
 165 170 175

Ser Lys Ser Lys Val Ser Gln Ile Asn Thr Gln Leu Ser Ser Phe Glu
 180 185 190

Phe Asp Pro Ile Leu Trp Glu Lys Lys Leu Gly Gly Leu Arg Leu Ser
 195 200 205

Gly Asp Gly His Gly Thr His Phe Ile Ile Met Pro Thr Glu Glu Ile
 210 215 220

Leu Ile Asp Asp Ile Ser Thr Ser Asp Ser Asn Lys Thr Ser Glu Gln
 225 230 235 240

Ser Ser Arg Leu Glu Lys Ala Leu Leu Gly Phe Thr Asn Thr Met Tyr
 245 250 255

Ser Asp Ser Asn Pro Pro Ile Ile Ala Arg Phe Arg Asp Tyr Leu Glu
 260 265 270

Asp Gly Glu Cys Ile Asp Arg Ile Ser Glu Ser Ile Phe Phe Thr Pro
 275 280 285
 Gln Glu Phe Asn Leu Ala Asp His His Ile Glu Gly Trp Phe Asn Glu
 290 295 300
 Phe Gly Gln Phe Ser Gly Thr Val Ser Val Tyr Gly Glu Glu Pro Ile
 305 310 315 320
 His His Val Val Thr Trp Lys Asn Asn Asn Gln Leu Thr Gln Cys Gly
 325 330 335
 Pro Phe Lys Ile Lys Leu Ala Tyr Ile His Gly Arg Leu Arg Asp Ser
 340 345 350
 Arg Leu Pro Met Glu Leu Trp Ala Pro Leu Lys Glu Lys Thr Asp Arg
 355 360 365
 Tyr Gly Gly Leu Tyr Ile Tyr Arg Asp Gly Leu Arg Ile Leu Pro Tyr
 370 375 380
 Gly Asp Ser Asp Thr Asp Phe Leu Lys Ile Glu Lys Arg Arg Thr Leu
 385 390 395 400
 Ser Ala Ser Glu Tyr Phe Phe Ser Tyr Arg Arg Leu Phe Gly Ala Ile
 405 410 415
 Glu Leu Thr Lys Glu Asn Asn Ala Ser Leu Val Glu Lys Ala Gly Arg
 420 425 430
 Glu Gly Phe Ile Glu Asn Lys Pro Tyr Lys Gln Phe Lys Glu Met Leu
 435 440 445
 Glu Asn Phe Phe Ile Glu Ile Ala Arg Asp Phe Phe Lys Asp Asp Gly
 450 455 460
 Asp Met Ser Glu Leu Phe Val Glu Thr Lys Gln Arg Arg Asn Glu Glu
 465 470 475 480
 His Asp Leu Leu Ser Lys Arg Ser Lys Gln Thr Lys Ala Lys Lys Asp
 485 490 495
 Arg Leu Lys Lys Asp Leu Tyr Asp Phe Phe Asp Lys Leu Asp Asn Asp
 500 505 510
 Tyr Trp Asn Ile Glu Ile Asn Lys Leu Ile Asn Lys Asn Glu Glu Tyr
 515 520 525

Phe Ser Ser Thr Glu Ile Thr Asp Thr Asn Ile Asp Tyr Val Tyr Asn
 530 535 540

Lys Ile Lys Glu Gln Asn Asp Ala Ile Ile Lys Asn Leu Arg Asn Ser
 545 550 555 560

Val Asp Ile Lys Lys Pro Ser Gly Val Gly Leu Thr Lys Glu Leu Ser
 565 570 575

Asn Leu Trp Asp Arg Tyr Gln Ile Glu Arg Gln Lys Ile Leu Leu Ser
 580 585 590

Leu Asn Glu Leu Lys Asp Asn Val Asp Arg Lys Leu Ile Glu Leu Asp
 595 600 605

Asn Lys Asn Asn Asp Phe Leu Asn Leu Arg Lys Arg Leu Glu Asp Ser
 610 615 620

Leu Asn Leu Gln Gln Ser Tyr Tyr Glu Lys Glu Leu Thr Lys Leu Tyr
 625 630 635 640

Asn Asp Ala Lys Asn Ala Leu Lys Asp Val Gln Ser Lys Ala Asn Arg
 645 650 655

Leu Ile Ser Asp Asn Lys Lys Lys His Lys Ser Glu Leu Lys Asn Ile
 660 665 670

Ser Tyr Glu Phe Gln Ser Thr Asn Leu Asn Gly Lys Asp Thr Ala Tyr
 675 680 685

Ile Leu Asp Val Lys Arg Asn Leu Glu Ser Lys Ile Glu Asn Thr Ser
 690 695 700

Asn Glu Val Ile Asn Glu Ile Arg Lys Leu Thr Asp Gln Ile Ala Ile
 705 710 715 720

Ile Ser Asp Ser Thr Thr Ser Glu Asn Leu Ser Ser Ala Gln Val Thr
 725 730 735

Glu Ala Ile Glu Thr Glu Leu Glu His Leu Arg Asp Gln Gln Ala Asn
 740 745 750

Asn Ala Glu Leu Ile Leu Leu Gly Met Ala Leu Ser Val Val His His
 755 760 765

Glu Phe Asn Gly Asn Ile Arg Ala Ile Arg Ser Ala Leu Arg Glu Leu
 770 775 780

Lys Ala Trp Ala Asp Arg Asn Pro Lys Leu Asp Ile Ile Tyr Gln Lys
 785 790 795 800

Ile Arg Thr Ser Phe Asp His Leu Asp Gly Tyr Leu Lys Thr Phe Thr
 805 810 815

Pro Leu Thr Arg Arg Leu Ser Arg Ser Lys Thr Asn Ile Thr Gly Thr
 820 825 830

Ala Ile Leu Glu Phe Ile Arg Asp Val Phe Asp Asp Arg Leu Glu Lys
 835 840 845

Glu Gly Ile Glu Leu Phe Thr Thr Ser Lys Phe Val Asn Gln Glu Ile
 850 855 860

Val Thr Tyr Thr Ser Thr Ile Tyr Pro Val Phe Ile Asn Leu Ile Asp
 865 870 875 880

Asn Ala Ile Tyr Trp Leu Gly Lys Thr Thr Gly Glu Lys Arg Leu Ile
 885 890 895

Leu Asp Ala Thr Glu Thr Gly Phe Val Ile Gly Asp Thr Gly Pro Gly
 900 905 910

Val Ser Thr Arg Asp Arg Asp Ile Ile Phe Asp Met Gly Phe Thr Arg
 915 920 925

Lys Thr Gly Gly Arg Gly Met Gly Leu Phe Ile Ser Lys Glu Cys Leu
 930 935 940

Ser Arg Asp Gly Phe Thr Ile Arg Leu Asp Asp Tyr Thr Pro Glu Gln
 945 950 955 960

Gly Ala Phe Phe Ile Ile Glu Pro Ser Glu Glu Thr Ser Glu
 965 970

<210> 45

<211> 555

<212> PRT

<213> Escherichia coli

<400> 45

Met Thr Ser Ser Thr Asp Phe His Lys Leu Ser Glu Asp Cys Val Arg
 1 5 10 15

Arg Phe Leu His Ser Val Val Ala Val Asp Asp Asn Met Ser Phe Gly
 20 25 30

Ala Gly Ser Asp Thr Phe Pro Thr Asp Glu Asp Ile Asn Ala Leu Val
 35 40 45
 Asp Pro Asp Asp Asp Pro Thr Pro Ile Ile Thr Ala Ser Ala Ser Pro
 50 55 60
 Arg Ile Glu Ser Thr Lys Ser Lys Ala Lys Val Lys Asn His Pro Phe
 65 70 75 80
 Asp Tyr Gln Ala Leu Ala Glu Ala Phe Ala Lys Asp Gly Ile Ala Cys
 85 90 95
 Cys Gly Leu Leu Ala Lys Ser Phe Asn Val Glu Glu Arg Asp Ile Ile
 100 105 110
 Thr Ala Ser Ser His Lys Ala Asp Ile Thr Ile Leu Asp Trp Asp Met
 115 120 125
 Gln Ser Asp Ser Gly Gln Phe Ala Ile Glu Ile Ile Lys Ser Ile Ile
 130 135 140
 Val Ser Asp Ile Asn Ser Gly Gly Arg Leu Arg Leu Leu Ser Ile Tyr
 145 150 155 160
 Thr Gly Glu His Val Thr Ala Val Ile Thr Lys Leu Asn Asn Glu Leu
 165 170 175
 Lys Lys Thr Tyr Arg Ser Val Ile Lys Asn Asp Asp Ser Ile Phe Ile
 180 185 190
 Glu Asp Asn Tyr Ala Leu Glu Gln Trp Cys Ile Val Val Ile Ser Lys
 195 200 205
 Asp Val Tyr Glu Lys Asp Leu Pro Asn Val Leu Ile Lys Lys Phe Thr
 210 215 220
 Asn Leu Thr Ala Gly Leu Leu Ser Asn Ala Ala Leu Ser Cys Ile Ser
 225 230 235 240
 Glu Ile Arg Glu Lys Thr His Gly Ile Leu Thr Lys Tyr Asn Asn Lys
 245 250 255
 Leu Asp Thr Ala Tyr Val Ser His Ile Leu Asn Leu Ile Lys Ser Lys
 260 265 270
 Glu Ser Arg Ala Tyr Ala Tyr Glu Asn Ala His Asp Tyr Ala Val Asp
 275 280 285

Leu Ile Ser Glu Glu Ile Arg Ser Ile Leu Gln Ile Ser Glu Asn Leu
 290 295 300
 Lys Lys Ser Leu Ser Lys Asn Ser Leu Ser His Trp Pro Ile Phe His
 305 310 315 320
 Tyr Ala Lys Asn Gly Cys Lys Asn Phe Leu Leu Thr Gly Lys Lys Gln
 325 330 335
 Lys Asp Leu Ser Val Glu His Leu Arg Asn Ile Leu Ser Ala Asp Ser
 340 345 350
 Leu Glu Glu Ile Gln His Ala Ile Glu His Ala Ser Leu Gly Lys Lys
 355 360 365
 Glu Tyr Leu Ser Gln Asp Gly Glu Glu Asp Lys Lys Leu Met Gln Leu
 370 375 380
 Cys Ser Leu Glu Ile Thr Arg Arg Ser Leu Arg Tyr His Ser His Ile
 385 390 395 400
 Asp Asn Val Ser Leu Lys Gln Gly Thr Leu Leu Leu Asp Ala Tyr Asn
 405 410 415
 Phe Val Tyr Leu Cys Ile Gln Pro Leu Cys Asp Ser Val Arg Leu His
 420 425 430
 Glu Lys Ala Asp Phe Leu Phe Leu Arg Gly Thr Leu Asp Asp Asn Asn
 435 440 445
 Tyr Asn Leu Leu Ile Glu Asp Glu Tyr Gly Gly Phe Tyr Lys Ile Lys
 450 455 460
 Met Pro Ala Lys Ala Ser Asn Ile Ile Ser Phe Ser Phe Gly Val Glu
 465 470 475 480
 Asn Gly Asn Gly Val Ile Ile Gly Lys Lys Asn Asn Leu Val Asn Thr
 485 490 495
 Asp Tyr Ile Ser Phe Val Pro Leu Leu Val Glu Lys Ile Ser Thr Pro
 500 505 510
 Lys Val Leu Lys Trp Ile Gly Glu Ile Lys Thr Thr Tyr Ala Gln Lys
 515 520 525
 Ile Thr Thr Asp Ile Val Ala Asn Leu Ser Arg Ile Gly Leu Asp Gln
 530 535 540

His Glu Trp Leu Arg Ile Lys Ser Lys Asp Ile
 545 550 555

<210> 46

<211> 82

<212> PRT

<213> Escherichia coli

<400> 46

Met Ser Ser Arg Gln Ile Leu Glu His Tyr Asn Ala Leu Thr Tyr Pro
 1 5 10 15

Leu His Gln Ser Ile Leu Leu Gln Ile Met Thr Ser Asn Leu Leu Ser
 20 25 30

Val Cys Thr Gly Lys Ser Ile Tyr Glu Asp Ile Ser Gly Ser Ser Trp
 35 40 45

Asn Ile Ile His Phe Asn Ile Pro Leu Pro Ile Ser Arg Ala Arg Leu
 50 55 60

Ser Ile Phe Ser Tyr Cys Val Arg Ile Lys Pro Trp Met Ser Met Asp
 65 70 75 80

Tyr Met

<210> 47

<211> 98

<212> PRT

<213> Escherichia coli

<400> 47

Met Ser Ile Ile Phe Asn Gly His Tyr Arg Met Lys His Arg Thr Trp
 1 5 10 15

Ile Thr Glu Ala Leu Arg Leu His Phe Glu Glu His Leu Pro Gln Val
 20 25 30

Val Val Gly Arg Arg Leu Gly Val Pro Lys Ser Thr Ala Cys Gly Met
 35 40 45

Phe Val Arg Phe Arg Lys Ala Gly Phe Ser Trp Pro Leu Pro Ala Gly
 50 55 60

Met Ser Glu Arg Glu Leu Asp Gly Arg Leu Tyr Gly Ser Thr Ser Thr

65 70 75 80

Val Pro Val Val Leu Cys Ser Gly Ser Val Ile Gln Asp Thr Ser Lys

 85 90 95

Ser Cys

<210> 48

<211> 106

<212> PRT

<213> Escherichia coli

<400> 48

Met Ile Lys Thr Arg Arg Thr Lys Arg Thr Phe Ser Pro Glu Phe Lys
1 5 10 15

Leu Glu Ala Phe Glu Gln Val Val Val Lys Tyr Gln Arg Asp Val Arg
20 25 30

Glu Val Ala Gln Ala Leu Glu Leu Asn Pro Asp His Leu Arg Lys Trp
35 40 45

Ile Arg Leu Tyr Lys Gln Glu Leu Gln Gly Ile Glu Pro Ala Gly Asn
50 55 60

Ala Ile Thr Pro Glu Gln Arg Glu Ile Gln Gln Leu Lys Ala Gln Ile
65 70 75 80

Lys Arg Val Glu Met Glu Lys Glu Ile Leu Lys Gln Ala Ala Val Leu
85 90 95

Met Ser Glu Ile Pro Gly Lys Leu Ser Arg
100 105

<210> 49

<211> 27

<212> DNA

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<220>

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<400> 49

tgctctagag ccattactca gaatggg

<210> 50

<211> 26

<212> DNA

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<223> Description of Artificial Sequence:Oligonucleotide

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26

<210> 51

<211> 26

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26

<210> 52

<211> 26

<212> DNA

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26

<210> 53

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<212> DNA

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27

<210> 54

<211> 28

<212> DNA

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28

<210> 55

<211> 27

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27

<210> 56

<211> 27

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27

<210> 57

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27

<210> 58

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27

<210> 59

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caactgcaga ccgcaacttt tcgacgc

27

<210> 60

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27

<210> 61

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27

<210> 62

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26

<210> 63

<211> 27

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence:Oligonucleotide

<400> 63

tcagatatcc ataaagagtg acgtggc

27

<210> 64

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<212> DNA

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27

<210> 65

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26

<210> 66

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28

<210> 67

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gaactgcagt acagccatgt ttacggt

27

<210> 68

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27

<210> 69

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26

<210> 70

<211> 27

<212> DNA

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<400> 70

gaactgcaga accgtccaca tcaggcg

27

<210> 71

<211> 27

<212> DNA

<213> Artificial Sequence

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<400> 71

gaactgcaga ccctgcttgc cattccg

27

<210> 72

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<212> DNA

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27