

(12) PATENT
(19) AUSTRALIAN PATENT OFFICE

(11) Application No. AU 200123823 B2
(10) Patent No. 775385

(54) Title
Virulence genes, proteins, and their use

(51)⁷ International Patent Classification(s)
C12N 015/31 C07K 016/12
A61K 038/16 C12Q 001/68
A61K 039/09 G01N 033/68
C07K 014/15

(21) Application No: **200123823**

(22) Application Date: **2000.12.22**

(87) WIPO No: **WO01/48208**

(30) Priority Data

(31) Number	(32) Date	(33) Country
9930462	1999.12.23	GB
9930463	1999.12.23	GB
9930464	1999.12.23	GB
9930466	1999.12.23	GB
9930467	1999.12.23	GB
9930469	1999.12.23	GB
9930471	1999.12.23	GB
9930472	1999.12.23	GB
9930473	1999.12.23	GB
9930474	1999.12.23	GB
9930475	1999.12.23	GB
9930476	1999.12.23	GB
0003735	2000.02.17	GB
0003733	2000.02.17	GB
0003732	2000.02.17	GB
0003731	2000.02.17	GB
0003736	2000.02.17	GB
0003730	2000.02.17	GB
0003729	2000.02.17	GB
0003728	2000.02.17	GB
0003727	2000.02.17	GB
0003726	2000.02.17	GB
0003725	2000.02.17	GB
0010587	2000.05.02	GB
0010585	2000.05.02	GB

(43) Publication Date : **2001.07.09**

(43) Publication Journal Date : **2001.09.20**

(44) Accepted Journal Date : **2004.07.29**

(71) Applicant(s)
Microscience Limited

(72) Inventor(s)
Enda Elizabeth Clarke; Liqing Zhou; Jacqueline Elizabeth Shea; Robert Graham Feldman; David William Holden

(74) Agent/Attorney
PIZZEYS, PO Box 291, WODEN ACT 2606

(12) PATENT
(19) AUSTRALIAN PATENT OFFICE

(11) Application No. **AU 200123823 B2**
(10) Patent No. **775385**

(56) Related Art
EP 786519
J BACTERIOL 180, 647-54
INF. IMMUNOL. 63, 2556-63

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
5 July 2001 (05.07.2001)

PCT

(10) International Publication Number
WO 01/48208 A2(51) International Patent Classification⁷: C12N 15/31,
C07K 14/15, 16/12, C12Q 1/68, G01N 33/68, A61K
38/16, 39/09

(21) International Application Number: PCT/GB00/04997

(22) International Filing Date:
22 December 2000 (22.12.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

9930462.8	23 December 1999 (23.12.1999)	GB
9930463.6	23 December 1999 (23.12.1999)	GB
9930464.4	23 December 1999 (23.12.1999)	GB
9930466.9	23 December 1999 (23.12.1999)	GB
9930467.7	23 December 1999 (23.12.1999)	GB
9930469.3	23 December 1999 (23.12.1999)	GB
9930471.9	23 December 1999 (23.12.1999)	GB
9930472.7	23 December 1999 (23.12.1999)	GB
9930473.5	23 December 1999 (23.12.1999)	GB
9930474.3	23 December 1999 (23.12.1999)	GB
9930475.0	23 December 1999 (23.12.1999)	GB
9930476.8	23 December 1999 (23.12.1999)	GB
0003735.8	17 February 2000 (17.02.2000)	GB
0003733.3	17 February 2000 (17.02.2000)	GB
0003732.5	17 February 2000 (17.02.2000)	GB
0003731.7	17 February 2000 (17.02.2000)	GB
0003736.6	17 February 2000 (17.02.2000)	GB
0003730.9	17 February 2000 (17.02.2000)	GB
0003729.1	17 February 2000 (17.02.2000)	GB
0003728.3	17 February 2000 (17.02.2000)	GB
0003727.5	17 February 2000 (17.02.2000)	GB
0003726.7	17 February 2000 (17.02.2000)	GB
0003725.9	17 February 2000 (17.02.2000)	GB
0010587.4	2 May 2000 (02.05.2000)	GB
0010585.8	2 May 2000 (02.05.2000)	GB

(71) Applicant (for all designated States except US): MICRO-
SCIENCE LIMITED [GB/GB]; 545 Eskdale Road, Win-
nersh Triangle, Wokingham, Berkshire RG41 5TU (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): CLARKE, Enda,
Elizabeth [IE/GB]; Microscience Limited, 545 Eskdale
Road, Winnersh Triangle, Wokingham, Berkshire RG41
5TU (GB). ZHOU, Liqing [CN/GB]; Microscience Lim-
ited, 545 Eskdale Road, Winnersh Triangle, Wokingham,
Berkshire RG41 5TU (GB). SHEA, Jacqueline, Eliza-
beth [GB/GB]; Microscience Limited, 545 Eskdale Road,
Winnersh Triangle, Wokingham, Berkshire RG41 5TU
(GB). FELDMAN, Robert, Graham [GB/GB]; Micro-
science Limited, 545 Eskdale Road, Winnersh Triangle,
Wokingham, Berkshire RG41 5TU (GB). HOLDEN,
David, William [GB/GB]; Dept. of Infectious Diseases,
Imperial College School of Medicine, at the Hammersmith
Campus, Du Cane Road, London W12 0NN (GB).(74) Agent: GILL JENNINGS & EVERY; Broadgate House,
7 Eldon Street, London EC2M 7LH (GB).(81) Designated States (national): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GI, GM, IIR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— Without international search report and to be republished
upon receipt of that report.For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: VIRULENCE GENES, PROTEINS, AND THEIR USE

(57) Abstract: A series of genes from *Streptococcus pyogenes* are shown to encode products which are implicated in virulence. The
identification of these genes therefore allows attenuated microorganisms to be produced. Furthermore, the genes or their encoded
products can be used in the manufacture of vaccines for therapeutic application.

WO 01/48208 A2

VIRULENCE GENES, PROTEINS, AND THEIR USE

Field of the Invention

This invention relates to virulence genes and proteins, and their use. More particularly, it relates to genes and proteins/peptides obtained from *Streptococcus pyogenes*, and their use in therapy and in screening for drugs.

Background of the Invention

Group A *Streptococcus* (GAS) is responsible for the majority of *Streptococcal* illnesses. An organism of particular interest is *S. pyogenes*, which is implicated in a wide range of non-invasive and invasive infections, such as impetigo, pharyngitis, necrotizing fasciitis, bacteraemia, streptococcal toxic shock syndrome (STSS), pneumonia and rheumatic fever.

Some GAS infections can be treated with antibiotics, including penicillin and erythromycin. However, due to the problems associated with resistance to antibiotics, and antibiotic-allergic patients, there is a need for further therapeutics which may be useful in treating or preventing GAS infection.

Summary of the Invention

The present invention is based on the discovery of virulence genes in *S. pyogenes*.

According to a first aspect of the invention, a peptide of the invention is encoded by an operon including any of the nucleotide sequences identified herein as SEQ ID NOS. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59 and 61 of *S. pyogenes* or a homologue thereof in a Gram-positive bacterium, or a functional fragment thereof, for therapeutic or diagnostic use.

The peptides may have many therapeutic uses for treating Group A *Streptococcal* infections, including use in vaccines for prophylactic application.

According to a second aspect, a polynucleotide encoding a peptide defined above, may also be useful for therapy or diagnosis.

According to a third aspect, the genes that encode the peptides may be utilised to prepare attenuated microorganisms. The attenuated microorganisms will usually have a mutation that disrupts the expression of one or more
5 of the genes identified herein, to provide a strain that lacks virulence. These microorganisms will also have use in therapy and diagnosis.

According to a fourth aspect, the peptides, genes and attenuated microorganisms according to the invention may be
10 used in the treatment or prevention of a condition associated with infection by Streptococcal or Gram-positive bacteria.

Description of the Invention

The present invention is based on the discovery of
15 genes encoding peptides which are implicated in virulence. The peptides and genes of the invention are therefore useful for the preparation of therapeutic agents to treat infection. It should be understood that references to therapy also include preventative treatments, e.g.
20 vaccination. Furthermore, while the products of the invention are intended primarily for treatment of infections in human patients, veterinary applications are also considered to be within the scope of the invention.

The present invention is described with reference to
25 *Streptococcus pyogenes*. However, all the Group A Streptococcal strains, and many other Gram-positive bacterial strains are likely to include related peptides or proteins having amino acid sequence identity or similarity to those identified herein. Organisms likely to contain the
30 peptides include, but are not limited to the genera *Lactococcus*, *Enterococcus*, *Streptococcus* and *Staphylococcus*.

Preferably, the peptides that may be useful in the various aspects of the invention have greater than a 40% similarity with the peptides identified herein. More
35 preferably, the peptides have greater than 60% sequence similarity. Most preferably, the peptides have greater than 80% sequence similarity, e.g. 95% similarity. With regard to the polynucleotide sequences identified herein, related

polynucleotides that may be useful in the various aspects of the invention may have greater than 40% identity with the sequences identified herein. More preferably, the polynucleotide sequences have greater than 60% sequence identity. Most preferably, the polynucleotide sequences have greater than 80% sequence identity, e.g. 95% identity.

The terms "similarity" and "identity" are known in the art. The use of the term "identity" refers to a sequence comparison based on identical matches between correspondingly identical positions in the sequences being compared. The term "similarity" refers to a comparison between amino acid sequences, and takes into account not only identical amino acids in corresponding positions, but also functionally similar amino acids in corresponding positions. Thus similarity between polypeptide sequences indicates functional similarity, in addition to sequence similarity.

Levels of identity between gene sequences and levels of identity or similarity between amino acid sequences can be calculated using known methods. In relation to the present invention, publicly available computer based methods for determining identity and similarity include the BLASTP, BLASTN and FASTA (Atschul et al., J. Molec. Biol., 1990; 215:403-410), the BLASTX program available from NCBI, and the Gap program from Genetics Computer Group, Madison WI. The levels of similarity and identity provided herein, were obtained using the Gap program, with a Gap penalty of 12 and a Gap length penalty of 4 for determining the amino acid sequence comparisons, and a Gap penalty of 50 and a Gap length penalty of 3 for the polynucleotide sequence comparisons.

Having characterised a gene according to the invention, it is possible to use the gene sequence to search for related genes or peptides in other microorganisms. This may be carried out by searching in existing databases, e.g. EMBL or GenBank.

Peptides or 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 related molecules can be identified and may be useful in therapy. For example, the peptides 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 fragments. Methods for the preparation of antibodies will be apparent to those skilled in the art.

Active fragments of the peptides are those that retain the biological function of the peptide. For example, when used to elicit an immune response, the fragment will be of sufficient size, such that antibodies generated from the fragment will discriminate between that peptide and other peptides on the bacterial microorganism. Typically, the fragment will be at least 30 nucleotides (10 amino acids) in size, preferably 60 nucleotides (20 amino acids) and most preferably greater than 90 nucleotides (30 amino acids) in size.

It should also be understood, that in addition to related molecules from other microorganisms, the invention encompasses modifications made to the peptides and polynucleotides identified herein which do not significantly alter the biological function. It will be apparent to the skilled person that the degeneracy of the genetic code can result in polynucleotides with minor base changes from those specified herein, but which nevertheless encode the same peptides. Complementary polynucleotides are also within the invention. Conservative replacements at the amino acid level are also envisaged, i.e. different acidic or basic amino acids may be substituted without substantial loss of function.

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, to provide effective immunisation against infection. The preparation of vaccine formulations will be apparent to the skilled person. The attenuated microorganisms may be prepared with a mutation that disrupts the expression of any of the genes identified herein. The skilled person will be aware of methods for disrupting expression of particular genes. Techniques that may be used include insertional inactivation or gene deletion techniques. Attenuated microorganisms according to the invention may also comprise additional mutations in other genes, for example in a second gene identified herein or in a separate gene required for growth of the microorganism, e.g. an *aro* mutation. Attenuated microorganisms may also be used as carrier systems for the delivery of heterologous antigens, therapeutic proteins or nucleic acids (DNA or RNA). In this embodiment, the attenuated microorganisms are used to deliver a heterologous antigen, protein or nucleic acid to a particular site *in vivo*. Introduction of a heterologous antigen, peptide or nucleic acid into an attenuated microorganism can be carried out by conventional techniques, including the use of recombinant constructs, e.g. vectors, which comprise polynucleotides that express the heterologous antigen or therapeutic protein, and also include suitable promoter sequences. Alternatively, the gene that encodes the heterologous antigen or protein may be incorporated into the genome of the organism and the endogenous promoters used to control expression.

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 use, as can suitable carriers or excipients, and routes of administration. These factors would be chosen or determined according to known criteria such as the nature/severity of the condition to be treated, the type and/or health of the subject etc.

In a separate embodiment, the products of the invention may be used in screening assays for the identification of

potential antimicrobial drugs or for the detection for virulence. Routine screening assays are known to those skilled in the art, and can be adapted using the products of the invention in the appropriate way. For example, the products of the invention may be used as the target for a potential drug, with the ability of the drug to inactivate or bind to the target indicating its potential antimicrobial activity.

The various products of the invention may also be used in veterinary applications.

The following is a brief overview of the experimental procedure used to identify the virulence genes. The virulence genes in *S. pyogenes* were identified by using signature-tagged mutagenesis (STM) to screen an *S. pyogenes* mutant bank for attenuated mutants (Hensel et al., 1995. Science 269(5222):400-3).

Mutants were generated via Tn917 transposon insertion, using a plasmid vector. In addition to a fragment of Tn917, the vector comprised a spectromycin-resistance gene, a chloramphenicol-resistance gene (CAT gene) with a synthetic promoter, a Gram-negative origin of replication (rop.ori) and a cloning site for the STM tags. After ligating the tags into the vector, *E. coli* transformation was carried out, and 96 plasmids that hybridised with the original tags were selected.

The *S. pyogenes* strain B514-SM (type M50) was transformed with each of the 96 tagged plasmids, and transformants were selected by resistance to spectinomycin and chloramphenicol. For each of the transformed *S. pyogenes* strains, 20 mutants were generated via Tn917 transposon insertion to create a mutant bank.

The mutant bank was screened in either a skin invasive lesion model of mouse infection (Schrager et al., J. Clinical Investigation 1996; 98:1954-1958) or from a throat colonisation model of mouse infection (Husmann et al., Infection and Immunity, 1997; 65 (4):935-944).

In the skin model, five CD1 mice were each inoculated intradermally with 1×10^8 cells in a volume of 50 μ l

representing the collection of 96 distinct and readily distinguishable mutants. 48 hours after inoculation, samples were taken and bacteria recovered. The skin lesions were macerated in 2xBHI medium and bacteria liberated from the lesion by treatment in a stomacher for 10 minutes. The released bacteria were plated out and a minimum of 10,000 colonies recovered from a minimum of 3 mice. DNA was isolated from these samples and used to amplify the tagged DNA present in the recovered bacteria. The DNA isolated from each recovered pool was used as a hybridisation probe to reveal those mutants in each pool that failed to be recovered from the animals and which were therefore attenuated in this animal model of infection.

In the throat colonisation model, 2×10^8 cells were inoculated intranasally into six C57BL/6 mice and samples taken after 48 hours. As with the skin model, bacteria containing a transposon Tn917 insertion within a virulence gene failed to be recovered from mice inoculated with a mixed population of mutants, and were therefore likely to be attenuated.

Additional experiments were carried out on mutants identified through the STM screen to determine the competitive index (CI). Individual mutants were tested in mixed infections with the wild-type strain in the skin lesion model of infection (Chiang, S.L. and Mekalanos, J.J. Molecular Microbiology 1998; 27(4):797-805). As for the initial screen, groups of four CD1 mice were inoculated with equal numbers of both wild-type and mutant cells, to a total number of 1×10^8 cells. Bacteria recovered after 48 hours were plated out onto selective media that allows the wild-type and mutant colonies to be distinguished. The ratio of mutant bacteria to wild-type bacteria seen in the inoculum compared with the ratio in recovered bacteria is the competitive index (ratio of mutants versus wild-type in the inoculum divided by the ratio of mutants versus wild-type bacteria recovered from the animal model).

The following Examples illustrate the invention.

Example 1

A first mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

5 The nucleotide sequence shows 100% identity at the nucleotide level to a coding sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 1, with the putative protein sequence shown as SEQ ID NO. 2.

10 The amino acid sequence of the predicted protein product shows 43% identity to the putative NAD(P)H nitroreductase of *H. influenzae* (accession number: SW: Q57431).

15 Given the similarity of the putative NAD(P)H nitroreductase gene in *S. pyogenes* to the gene in *H. influenzae*, the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may also be implicated in virulence.

In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive index (CI) of 0.644.

20 Example 2

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

25 The nucleotide sequence has 98% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 3. The putative amino acid sequence is shown as SEQ ID NO. 4.

30 The amino acid sequence shows 81% identity to a probable integrase enzyme of *S. mutans* (accession number: TREMBL: O69155).

This demonstrates that the disrupted gene is at least partially identical to a probable integrase gene of *S. mutans*. However, this gene was previously unknown in *S. pyogenes*, and has not been assigned a role in virulence.

35 Given the similarity of the *S. pyogenes* gene to the probable integrase gene of *S. mutans*, the skilled person will appreciate that similar sequences in other *Streptococci*

and Gram-positive bacteria may also be virulence determinants.

In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive
5 index (CI) of 0.229.

Example 3

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

10 The nucleotide sequence has 97% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 5. The predicted amino acid sequence is shown as SEQ ID NO. 6.

The amino acid sequence shows 37% identity at the amino
15 acid level to the GlgP protein of the unicellular cyanobacterium *Synechocystis* spp. (accession number: TREMBL: P73511).

This demonstrates that the disrupted gene is at least partially identical to the *glgP* gene of *Synechocystis* spp.

20 Given the similarity of the gene of *S. pyogenes* to the *glgP* gene of *Synechocystis* spp., the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may also be virulence determinants.

In the test for attenuation of virulence, the mutated
25 microorganism was shown to be attenuated with a competitive index (CI) of 0.011.

Example 4

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was
30 cloned.

The nucleotide sequence has 97% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 7. The predicted amino acid sequence is shown as SEQ ID NO. 8.

35 The amino acid sequence shows 35% identity at the amino acid level to the *BraB* protein of *B. subtilis* (accession number: TREMBL: O34545).

This demonstrates that the disrupted gene is at least partially identical to the *braB* gene of *B. subtilis*.

Given the similarity of the *braB* gene of *S. pyogenes* to the *braB* gene in *B. subtilis*, the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may also be implicated in virulence.

In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive index (CI) of 0.88.

10 Example 5

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence shows 99% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 9. The predicted amino acid sequence is shown as SEQ ID NO. 10.

A still further attenuated mutant was also identified with a nucleotide sequence having 98% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 11. The predicted amino acid sequence is shown as SEQ ID NO. 12.

The predicted protein of the first mutant shows 53% identity at the amino acid level to the AdcR protein of *S. pneumoniae* (accession number: TREMBL:O33703). That of the second mutant shows 79% identity at the amino acid level to the AdcC protein of *S. pneumoniae* (accession number: TREMBL: O87862).

This demonstrates that the disrupted genes are at least partially identical to the *adcR* and *adcC* genes of *S. pneumoniae*. The *adcR* and *adcC* genes are part of the *adc* operon (including *adcR*, *adcC*, *adcB*, and *adcA*) in *S. pneumoniae*. Therefore the attenuation of *S. pyogenes* *adcR* and *adcC* mutants could result from a failure to express the *adcR* and *adcC* genes, or the predicted downstream genes (*adcB* and *abcA* homologues). These genes have not previously been assigned a role in virulence in *S. pyogenes*.

Given the similarity of the *S. pyogenes* genes to the *adcR* and *adcC* genes in *S. pneumoniae*, the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may be implicated in virulence.

5 In the test for attenuation of virulence, the mutated microorganisms were shown to be attenuated with a competitive index (CI) of 0.548 (*adcR*) and 0.028 (*adcC*).

Example 6

10 A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 99% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 13. The predicted amino acid
15 sequence is shown as SEQ ID NO. 14.

The amino acid sequence shows 39% identity at the amino acid level to the DNA repair protein *radC* homologue (*orfB*) of *B. subtilis* (accession number: SW: Q02170).

20 This demonstrates that the disrupted gene is at least partially identical to the *orfB* gene of *B. subtilis*.

Given the similarity of the *orfB* gene of *S. pyogenes* to that of *B. subtilis*, the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may be implicated in virulence.

25 In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive index (CI) of 0.766.

Example 7

30 A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 98% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 15. The predicted amino acid
35 sequence is shown as SEQ ID NO. 16.

The amino acid sequence shows 54% identity at the amino acid level to the biotin carboxyl carrier protein (BCCP) in *S. mutans* (accession number: SW: P29337).

This demonstrates that the disrupted gene is at least partially identical to the gene encoding BCCP of *S. mutans*. This gene was previously unknown in *S. pyogenes* and has not been assigned a role in virulence.

5 Given the similarity of the translated *S. pyogenes* gene to the BCCP of *S. mutans*, the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may be implicated in virulence.

10 In the test for attenuation of virulence, the mutated microorganisms was shown to be attenuated with a competitive index (CI) of 0.044.

Example 8

15 A series of mutants were identified having sequence similarity to genes involved in citrate fermentation. The nucleotide sequences of eight mutants showed 100% identity to a sequence within the *S. pyogenes* genome, shown to SEQ ID NO. 17. The predicted amino acid sequence is shown as SEQ ID NO. 18.

20 The predicted protein of the *S. pyogenes* gene shows 58% identity at the amino acid level to the citF protein, citrate lyase alpha chain, of *E. coli* (accession number: SW: P75726).

25 The nucleotide sequences of three further mutants showed 99% identity to a different sequence within the *S. pyogenes* genome. The nucleotide sequence is shown as SEQ ID NO. 19, and the predicted amino acid sequence is shown as SEQ ID NO. 20.

30 The amino acid sequences show 55% identity at the amino acid level to the citE protein, citrate lyase beta chain, of *E. coli* (accession number: SW:P77770).

 The nucleotide sequences of two further mutants showed 99% identity to the *S. pyogenes* nucleotide sequence identified herein as SEQ ID NO. 21. The predicted amino acid sequence is shown as SEQ ID NO. 22.

35 The amino acid sequences show 46% identity at the amino acid level to the CitD protein, citrate lyase acyl carrier protein (citrate lyase gamma chain), of *E. coli* (accession number: SW: P77618).

Two further mutants were identified with nucleotide sequences which showed 99% identity to a nucleotide sequence from *S. pyogenes*, identified herein as SEQ ID NO. 23. The predicted amino acid sequence as SEQ ID NO. 24.

- 5 The amino acid sequences show 34% identity at the amino acid level to the CitC protein, citrate (pro-3s)-lyase (ligase), of *E. coli* (accession number: SW: P77390).

- 10 A further mutant was identified with a nucleotide sequence having 99% sequence identity to the *S. pyogenes* nucleotide sequence identified herein as SEQ ID NO. 25. The predicted amino acid sequence is shown as SEQ ID NO. 26.

The amino acid sequence shows 37% identity at the amino acid level to the CitX protein, of *E. coli* (accession number: SW: P77563).

- 15 A further three mutants were identified with nucleotide sequences showing 100% identity to the *S. pyogenes* nucleotide sequence identified herein as SEQ ID NO. 27. The predicted amino acid sequence is shown as SEQ ID NO. 28.

- 20 The amino acid sequences show 59% identity at the amino acid level to the OadA protein, oxaloacetate decarboxylase subunit alpha, of *K. pneumoniae* (accession number: SW:P13187).

- 25 All the predicted protein sequences of the above mutants show various degrees of identity to gene products of *E. coli* or *K. pneumoniae* required for citrate fermentation.

- 30 This demonstrates that the disrupted genes are at least partially identical to the *citF,E,D,C,X* and *oadA* genes of *E. coli* or *K. pneumoniae*. The genes involved in citrate fermentation are located together at a single locus on the chromosome in *E. coli* and *K. pneumoniae*. Therefore, the attenuation of *S. pyogenes* mutants could result from a failure to express its *citFEDCX* and *oadA* genes, or downstream genes. These genes have not previously been
35 assigned a role in virulence.

Given the similarity of the *S. pyogenes* genes to those present in *E. coli* or *K. pneumoniae*, the skilled person will

appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may be implicated in virulence.

Mutants for each of *citF*, *E*, *D*, *X* and *oadA* were tested for attenuation of virulence. The mutated microorganisms were
5 shown to be attenuated with a competitive index (CI) of 0.122 (*citF*), 0.064 (*citE*), 0.078 (*citD*), 0.025 (*citX*) and 0.251 (*oadA*).

Example 9

A further mutant was identified and the nucleotide
10 sequence immediately following the transposon insertion was cloned.

The nucleotide sequence showed 98% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, identified herein as SEQ ID NO. 29. The predicted
15 amino acid sequence is shown as SEQ ID NO. 30.

The amino acid sequence shows 27% identity at the amino acid level to the *femB* protein of *S. aureas* (accession number: TREMBL: Q9X9D7).

This demonstrates that the disrupted gene is at least
20 partially identical to the *femB* gene of *S. aureas*. However, this gene was previously unknown in *S. pyogenes*, and has not been assigned a role in virulence.

Given the similarity of the *S. pyogenes* gene to the *femB* gene in *S. aureas*, the skilled person will appreciate
25 that similar sequences in other *Streptococci* and Gram-positive bacteria may be implicated in virulence.

Example 10

A further mutant was identified and the nucleotide
30 sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has significant identity to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 31. The predicted amino acid sequence is shown as SEQ ID NO. 32.

35 In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive index (CI) of 0.160.

Example 11

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 100% identity to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 33. The predicted amino acid sequence is shown as SEQ ID NO. 34.

Example 12

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 98% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 35. The predicted amino acid sequence is shown as SEQ ID NO. 36.

The amino acid sequence shows 46% identity at the amino acid level to the subtilin transport ATP-binding protein of *Bacillus subtilis* (accession number: SW: P33116).

This demonstrates that the disrupted gene is at least partially identical to the *braB* gene of *B. subtilis*.

Given the similarity of the gene of *S. pyogenes* to that in *B. subtilis*, the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may be implicated in virulence.

In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive index (CI) of 0.128.

Example 13

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 98% identity to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 37. The predicted amino acid sequence is shown as SEQ ID NO. 38.

Example 14

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 98% identity to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 39. The predicted amino acid sequence is shown as SEQ ID NO. 40.

5 The amino acid sequence shows 29% identity at the amino acid level to a 36.9kDa hypothetical protein from *E. coli* (accession number SW: P33019).

This demonstrates that the disrupted gene is at least partially identical to the gene of *E. coli*. Other similar sequences may be implicated in virulence.

10 In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive index (CI) of 0.747.

Example 15

15 A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 99% identity to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 41. The predicted amino acid sequence is shown as SEQ ID NO. 42.

20 The amino acid sequence shows 29% identity at the amino acid level to a 89kDa hypothetical protein from *A. fulgidus* (accession number TREMBL: 028455).

25 This demonstrates that the disrupted gene is at least partially identical to the gene of *E. coli*. Other, similar sequences may be implicated in virulence.

In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive index (CI) of 0.588.

Example 16

30 A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 99% identity to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 43. The predicted amino acid sequence is shown as SEQ ID NO. 44.

Example 17

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 98% identity to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 45. The predicted amino acid sequence is shown as SEQ ID NO. 46.

Example 18

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 97% identity to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 47. The predicted amino acid sequence is shown as SEQ ID NO. 48.

Example 19

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 98% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 49. The predicted amino acid sequence is shown as SEQ ID NO. 50.

The amino acid sequence shows 47% identity at the amino acid level to the *ciaH* protein of *S. pneumoniae* (accession number:SW: Q54955).

This demonstrates that the disrupted gene is at least partially identical to the *ciaH* gene of *S. pneumoniae*.

Given the similarity of the *ciaH* gene of *S. pyogenes* to the *ciaH* gene of *S. pneumoniae*., the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may be implicated in virulence.

In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive index (CI) of 0.205.

Example 20

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 98% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 51. The predicted amino acid sequence is shown as SEQ ID NO. 52.

5 The amino acid sequence shows 39% identity at the amino acid level to the *muca* homologue protein of *S. pneumonia* (accession number: TREMBL: Q9ZBB1).

This demonstrates that the disrupted gene is at least partially identical to the *muca* gene of *S. pneumoniae*.

10 Given the similarity of the gene of *S. pyogenes* to the *muca* gene of *S. pneumoniae*, the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may be implicated in virulence.

In the test for attenuation of virulence, the mutated
15 microorganism was shown to be attenuated with a competitive index (CI) of 0.547.

Example 21

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was
20 cloned.

The nucleotide sequence has 98% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 53. The predicted amino acid sequence is shown as SEQ ID NO. 54.

25 The amino acid sequence shows 69% identity at the amino acid level to the *gidA* protein of *B. subtilis* (accession number: SW:P39815).

This demonstrates that the disrupted gene is at least partially identical to the gene of *B. subtilis*.

30 Given the similarity of the *S. pyogenes* to the *gidA* gene of *B. subtilis*, the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may be implicated in virulence.

In the test for attenuation of virulence, the mutated
35 microorganism was shown to be attenuated with a competitive index (CI) of 0.444.

Example 22

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

5 The nucleotide sequence has 98% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 55. The predicted amino acid sequence is shown as SEQ ID NO. 56.

10 The amino acid sequence shows 74% identity at the amino acid level to the *dlta* protein of *S. mutans* (accession number: SW:Q53526).

This demonstrates that the disrupted gene is at least partially identical to the *dlta* gene of *S. mutans*.

15 Given the similarity of the *S. pyogenes* gene to the *dlta* gene of *S. mutans*, the skilled person will appreciate that similar sequences in other Gram-positive bacteria may be implicated in virulence.

In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive index (CI) of 0.205.

20 Example 23

A further mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

25 The nucleotide sequence has 98% identity at the nucleotide level to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 57. The predicted amino acid sequence is shown as SEQ ID NO. 58.

30 The amino acid sequence shows 41% identity at the amino acid level to the *hmgA* protein of *A. fulgidus* (accession number: SW: O28538).

This demonstrates that the disrupted gene is at least partially identical to the gene of *A. fulgidus*.

35 Given the similarity of the gene of *S. pyogenes* to the *hmgA* gene of *A. fulgidus*, the skilled person will appreciate that similar sequences in other *Streptococci* and Gram-positive bacteria may be implicated in virulence.

In the test for attenuation of virulence, the mutated microorganism was shown to be attenuated with a competitive index (CI) of 0.205.

Example 24

5 A first mutant was identified and the nucleotide sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 99% identity to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 59. The
10 predicted amino acid sequence is shown as SEQ ID NO. 60.

The amino acid sequence shows 34% identity at the amino acid level to the putative JAG protein from *T. maritima* (accession number TREMBL: Q9X1H1).

This demonstrates that the disrupted gene from
15 *S. pyogenes* is at least partially identical to the gene of *T. maritima*. Similar sequences in other Gram-negative bacteria may be implicated in virulence.

Example 25

A further mutant was identified and the nucleotide
20 sequence immediately following the transposon insertion was cloned.

The nucleotide sequence has 99% identity to a sequence within the *S. pyogenes* genome, shown as SEQ ID NO. 61. The
predicted amino acid sequence is shown as SEQ ID NO. 62.

25 The amino acid sequence shows 49% identity at the amino acid level to a 49.4 kDa hypothetical protein from *S. suis* (accession number TREMBL: Q9X4U3).

This demonstrates that the disrupted gene of
30 *S. pyogenes* is at least partially identical to the gene of *S. suis*. Similar sequences in other Gram-negative bacteria may also be implicated in virulence.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

The reference to any prior art in this specification is not, and should not be taken as, an acknowledgement or any form of suggestion that the prior art forms part of the common general knowledge in Australia.

EDITORIAL NOTE

APPLICATION NUMBER - 23823/01

The following Sequence Listing pages 1 to 68 are part of the description. The claims pages follow on pages "21" to "22".

SEQUENCE LISTING

<110> Microscience Limited

<120> VIRULENCE GENES, PROTEINS, AND THEIR USE

<130> REP06309WO

<140> (not yet known)

<141> 2000-12-22

<150> 9930462.8

<151> 1999-12-23

<150> 9930463.6

<151> 1999-12-23

<150> 9930464.4

<151> 1999-12-23

<150> 9930466.9

<151> 1999-12-23

<150> 9930467.7

<151> 1999-12-23

<150> 9930469.3

<151> 1999-12-23

<150> 9930471.9

<151> 1999-12-23

<150> 9930472.7

<151> 1999-12-23

<150> 9930473.5

<151> 1999-12-23

<150> 9930474.3

<151> 1999-12-23

<150> 9930475.0

<151> 1999-12-23

<150> 9930476.8

<151> 1999-12-23

<150> 0003735.8

<151> 2000-02-17

<150> 0003733.3

<151> 2000-02-17

<150> 0003732.5

<151> 2000-02-17

<150> 0003731.7

<151> 2000-02-17

<150> 0003736.6

<151> 2000-02-17

<150> 0003730.9

<151> 2000-02-17

<150> 0003729.1

<151> 2000-02-17

<150> 0003728.3

<151> 2000-02-17

<150> 0003727.5

<151> 2000-02-17

<150> 0003726.7

<151> 2000-02-17

<150> 0003725.9

<151> 2000-02-17

<150> 0010587.4

<151> 2000-05-02

<150> 0010585.8

<151> 2000-05-02

<160> 62

<170> PatentIn Ver. 2.1

<210> 1

<211> 666

<212> DNA

<213> Streptococcus pyogenes

<400> 1

```

atggatcaaa ccattcatca ccaaatacag caagcactac actttagaac agccgttcgt 60
gtttataagg aagaaaagat ttctgatgag gatttagccc ttatccttga tgctgcttgg 120
ttaagccctt cttctattgg cttagaaggc tggcgctttg tcgtttttaga caacaagcct 180
attaaagaag aaatcaagcc ctttgcctgg ggagcccagt atcaactgga aacagctagt 240
cactttattc ttttaatagc cgaaaaacat gcaagatacg atagccctgc tatcaaaaat 300
agcctttttac ggcgtgggtat caaagaaggt gatggtctca acagccgcct aaaactctat 360
gaatctttcc aaaaagagga catggatatg gcagataatc ctcgggcact ctttgattgg 420
acagctaaac aaacctatat cgctcttggg aatatgatga tgacagctgc tcttttgggc 480
attgatactt gccctattga aggctttcat tatgataagg tcaatcatat cctagctaag 540
cataatgtga ttgattttaga aaaagaaggc attgctagca tgttatccct aggctatcgt 600
ttgcgagatc ccaaacatgc tcaagttcgt aagcctaaag aagaagtgat ttcagtcggt 660
aatga

```

<210> 2

<211> 221

<212> PRT

<213> Streptococcus pyogenes

<400> 2

```

Met Asp Gln Thr Ile His His Gln Ile Gln Gln Ala Leu His Phe Arg
  1              5              10              15

```

```

Thr Ala Val Arg Val Tyr Lys Glu Glu Lys Ile Ser Asp Glu Asp Leu
      20              25              30

```

```

Ala Leu Ile Leu Asp Ala Ala Trp Leu Ser Pro Ser Ser Ile Gly Leu
    35              40              45

```

```

Glu Gly Trp Arg Phe Val Val Leu Asp Asn Lys Pro Ile Lys Glu Glu
    50              55              60

```

```

Ile Lys Pro Phe Ala Trp Gly Ala Gln Tyr Gln Leu Glu Thr Ala Ser
   65              70              75              80

```

```

His Phe Ile Leu Leu Ile Ala Glu Lys His Ala Arg Tyr Asp Ser Pro
      85              90              95

```

```

Ala Ile Lys Asn Ser Leu Leu Arg Arg Gly Ile Lys Glu Gly Asp Gly
    100              105              110

```

```

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

```

```

Asp Met Ala Asp Asn Pro Arg Ala Leu Phe Asp Trp Thr Ala Lys Gln
    130              135              140

```

```

Thr Tyr Ile Ala Leu Gly Asn Met Met Met Thr Ala Ala Leu Leu Gly

```

145	150	155	160
Ile Asp Thr Cys Pro Ile Glu Gly Phe His Tyr Asp Lys Val Asn His			
	165	170	175
Ile Leu Ala Lys His Asn Val Ile Asp Leu Glu Lys Glu Gly Ile Ala			
	180	185	190
Ser Met Leu Ser Leu Gly Tyr Arg Leu Arg Asp Pro Lys His Ala Gln			
	195	200	205
Val Arg Lys Pro Lys Glu Glu Val Ile Ser Val Val Lys			
	210	215	220

<210> 3

<211> 1071

<212> DNA

<213> Streptococcus pyogenes

<400> 3

```

atgagacgcg aattattact agaaaaaatt gaaacctaca aggctatcat gccctgggtat 60
gttttagatt attaccaatc caaattagct gttccataca gctttaccac cttatatgag 120
tatttaaaag aatacaaacg cttttttgat tggctgatgg atgctgattt aacgcaggcg 180
ccaaagattg ctgatattga cttgagcacg cttgagcacc ttaccaagaa ggatttagag 240
gcctttgtgc tttatattgcg ggaacgacct tctctcaaca cctattccac caaagagggg 300
ctttctcaaa ccactattaa tcggaccttg tctgccttat caagccttta caagtacttg 360
actgaagagg ttgaaaatga ccaaggggag ccttattttt atcggaatgt tatgaaaaaa 420
gtgtcaacaa aaaagaaaaa agaaaccctg gcttcagag cggaaaatat taagcagaaa 480
ctgttttttag gtgatgaaac tctagctttc ttggattatg tggataagga atatgagcaa 540
aaattgtcta atcgtgccaa atcttctttc cgtaaaaaata aggagaggga tttggctatt 600
attgctctac tacttgcttc tgggtgttcgt ttgtctgaag cagtgaatct tgatttaaaa 660
gatgtcaatc taaatatgat gattatcgaa gttattcgca aaggcggaac acgtgattca 720
gtcaatgtag cagggttttg gaaaggttat ttggagtctt atttagctgt tcgtcagaga 780
cgttacaagg ctgaaaaaca ggatcttgct ttctttttaa cagaataaccg tggcgttcca 840
aatcgaatgg atgcttctag tatagaaaag atggttgga agtactctga ggatttttaa 900
attcgtgtga ctctcaciaa attgcgtcat acgctagcga caagactata tgatgctact 960
aaatctcagg tgtagtttag tcatcaatta ggccattcct ctactcaagt cacggatctt 1020
tatacccata ttgtcaatga tgagcaaaaaaatgcttttag ataaccttta a 1071

```

<210> 4

<211> 356

<212> PRT

<213> Streptococcus pyogenes

<400> 4

Met Arg Arg Glu Leu Leu Leu Glu Lys Ile Asp Glu Leu Lys Glu Leu
 1 5 10 15
 Met Pro Trp Tyr Val Leu Glu Tyr Tyr Gln Ser Lys Leu Thr Val Pro
 20 25 30
 Tyr Ser Phe Thr Thr Leu Tyr Glu Tyr Leu Lys Glu Tyr Arg Arg Phe
 35 40 45
 Phe Glu Trp Leu Ile Asp Ser Gly Val Ser Asn Ala Asn Lys Leu Ala
 50 55 60
 Asp Ile Pro Leu Glu Thr Leu Glu His Leu Ser Lys Lys Asp Met Glu
 65 70 75 80
 Ser Phe Ile Leu Tyr Leu Arg Glu Arg Thr Leu Leu Asn Thr Lys Asn
 85 90 95
 Lys Arg Gln Gly Val Ser Gln Thr Thr Ile Asn Arg Thr Leu Ser Ala
 100 105 110
 Leu Ser Ser Leu Tyr Lys Tyr Leu Thr Glu Glu Val Glu Asn Ala Asp
 115 120 125
 Gly Glu Pro Tyr Phe Tyr Arg Asn Val Met Lys Lys Val Ser Thr Lys
 130 135 140
 Lys Lys Lys Glu Thr Leu Ala Ala Arg Ala Glu Asn Ile Lys Gln Lys
 145 150 155 160
 Leu Phe Leu Gly Asn Glu Thr Met Glu Phe Leu Glu Tyr Val Asp Cys
 165 170 175
 Glu Tyr Glu Gln Lys Leu Ser Lys Arg Ala Leu Ser Ser Phe Arg Lys
 180 185 190
 Asn Lys Glu Arg Asp Leu Ala Ile Ile Ala Leu Leu Leu Ala Ser Gly
 195 200 205
 Val Arg Leu Ser Glu Ala Val Asn Leu Asp Leu Lys Asp Val Asn Leu
 210 215 220
 Asn Met Met Ile Ile Glu Val Thr Arg Lys Gly Gly Lys His Asp Ser
 225 230 235 240
 Val Asn Val Ala Gly Phe Ala Lys Pro Tyr Leu Glu Asn Tyr Ile Thr
 245 250 255

Ile Arg Arg Gly Arg Tyr Lys Ala Lys Lys Thr Asp Leu Ala Phe Phe
260 265 270

Leu Ser Glu Tyr Arg Gly Val Pro Asn Arg Met Asp Ala Ser Ser Ile
275 280 285

Glu Lys Met Val Ala Lys Tyr Ser Gln Asp Phe Lys Ile Arg Val Thr
290 295 300

Pro His Lys Leu Arg His Thr Leu Ala Thr Arg Leu Tyr Asp Ala Thr
305 310 315 320

Lys Ser Gln Val Leu Val Ser His Gln Leu Gly His Ala Ser Thr Gln
325 330 335

Val Thr Asp Leu Tyr Thr His Ile Val Asn Asp Glu Gln Lys Asn Ala
340 345 350

Leu Asp Lys Leu
355

<210> 5

<211> 2265

<212> DNA

<213> Streptococcus pyogenes

<400> 5

atgacacgct ttacagaata tgttgaaact aaactaggaa aatcacttac gcaagccagc 60
aatgaagaga tttatctatc attattaaac tttgtcaaag aagaagctag ccacaaggct 120
aaaaattctg ctaaacgcaa agtttactat atctcagcag agtttttgat tggtaaatta 180
ctatcaaaca acctgattaa cctaggaatt tacaaggaca tcaaagaaga attggcagct 240
gctggcaagt ctatcgaga agtcgaagat gttgaattag aaccatcact aggtaatggg 300
ggtttaggac gccttgcttc atgttttatt gactctattg catctcttgg gattaatggg 360
gaagggggtg gtttaaacta tcattgtggg ttgtttaagc aagtcttcaa acacaatgag 420
caagaagctg agccaaactt ctggattgaa gatgactcat gggtgggtcc aacagacatt 480
tcttacgatg tgccttttaa gaacttcacc ttgaaatctc gtcttgatcg tattgatgtt 540
ttggggttaca aacgcgacac taaaaactac cttaacttgt ttgatatcga gggcgttgat 600
tacgggttaa tcaaagacgg catttctttt gataaaacgc aaattgctaa aaacttgacc 660
ttgttctctc acccagacga ttctgacaaa aatggggaat tgctccgtat ttaccaacag 720
tactttatgg tgtcaaatgc agcgcaatta atcattgatg aagctatcga acgtgggtca 780
aaccttcatg acctgcaga ctacgcttac gtgcaaatta atgacacgca tccatcaatg 840
gtcatcccag aattaattcg tctcttgact gaaaaacatg gctttgactt tgatgaagcg 900
gtagctgttg tgaaaaatat gggtggttac actaaccaca ctattcttgc agaagccctt 960
gaaaaatggc caactgctta cttaaacgaa gtagtgccac acttggtaac catcattgaa 1020
aaattggatg ctcttggtcg ttcagaagtg tctgatccag ctgttcaaatt tattgacgaa 1080
tcaggtcgtg tgcacatggc ccatatggat attcattttg caacaagtgt caatggggta 1140

```

gcagcactcc acacagaaat cttgaaaaac agcgaattaa aagctttcta tgacctttac 1200
ccagaaaaat tcaacaacaa aaccaacggg attactttcc gtcgttggct agaatttgct 1260
aaccaagact tggctgatta cattaagaa cttattggcg atgagtactt gactgacgca 1320
acaaaattag aaaaattgat ggcctttgca gatgacaaag ctgttcatgc taaattggct 1380
gaaatcaaat tcaacaacaa attagctctt aaacgttacc ttaaagacaa taaagacatt 1440
gagcttgatg aacattctat tattgatacc caaatcaaac gtttccacga gtacaaacgt 1500
caacagatga atgctcttta cgtgattcac aaatatttgg aaattaaaaa aggcaacctt 1560
ccaaaacgta aaatcactgt tatctttgga ggtaaagcag cgcctgctta cattattgcg 1620
caagacatca ttcacttgat cctttgcttg tctgaattga ttaacaatga ccctgaagta 1680
agcccatacc ttaatgtgca tctagttgaa aattacaacg tgacagtagc agagcacttg 1740
attccagcaa ctgatatttc tgagcaaatt tcactagcat ccaaagaagc ttctggaact 1800
ggtaatatga aattcatgct taacgggtgct ttaacacttg gtacaatgga cgggtgctaac 1860
gtagaaatcg ctgagcttgc aggcattggag aatatctata cctttggtaa agattctgac 1920
accatcatca acctttatgc gactgcttct tatgtagcaa aagattacta tgataaccac 1980
cctgctatta aagcagcagt gaactttatt atcagtccag aattgctagc atttggaac 2040
gaagaacgtc ttgatcgtct ttataaagaa ttgatttcaa aagactgggt catgactttg 2100
attgaccttg aagagtacat tgaagtgaag gaaaaaatgt tagcagacta tgaagaccaa 2160
gatttatgga tgacaaaagt ggtccataac atcgcaaaag ctggattctt ctcactctgac 2220
cgtaccattg agcagtataa cgaagatatt tggcattcac gataa 2265

```

<210> 6

<211> 754

<212> PRT

<213> Streptococcus pyogenes

<400> 6

```

Met Thr Arg Phe Thr Glu Tyr Val Glu Thr Lys Leu Gly Lys Ser Leu
  1              5              10              15

```

```

Thr Gln Ala Ser Asn Glu Glu Ile Tyr Leu Ser Leu Leu Asn Phe Val
      20              25              30

```

```

Lys Glu Glu Ala Ser His Lys Ala Lys Asn Ser Ala Lys Arg Lys Val
      35              40              45

```

```

Tyr Tyr Ile Ser Ala Glu Phe Leu Ile Gly Lys Leu Leu Ser Asn Asn
      50              55              60

```

```

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

```

```

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

```

```

Leu Gly Asn Gly Gly Leu Gly Arg Leu Ala Ser Cys Phe Ile Asp Ser
      100             105             110

```

Ile Ala Ser Leu Gly Ile Asn Gly Glu Gly Val Gly Leu Asn Tyr His
 115 120 125

Cys Gly Leu Phe Lys Gln Val Phe Lys His Asn Glu Gln Glu Ala Glu
 130 135 140

Pro Asn Phe Trp Ile Glu Asp Asp Ser Trp Leu Val Pro Thr Asp Ile
 145 150 155 160

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

Arg Ile Asp Val Leu Gly Tyr Lys Arg Asp Thr Lys Asn Tyr Leu Asn
 180 185 190

Leu Phe Asp Ile Glu Gly Val Asp Tyr Gly Leu Ile Lys Asp Gly Ile
 195 200 205

Ser Phe Asp Lys Thr Gln Ile Ala Lys Asn Leu Thr Leu Phe Leu Tyr
 210 215 220

Pro Asp Asp Ser Asp Lys Asn Gly Glu Leu Leu Arg Ile Tyr Gln Gln
 225 230 235 240

Tyr Phe Met Val Ser Asn Ala Ala Gln Leu Ile Ile Asp Glu Ala Ile
 245 250 255

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

Ile Asn Asp Thr His Pro Ser Met Val Ile Pro Glu Leu Ile Arg Leu
 275 280 285

Leu Thr Glu Lys His Gly Phe Asp Phe Asp Glu Ala Val Ala Val Val
 290 295 300

Lys Asn Met Val Gly Tyr Thr Asn His Thr Ile Leu Ala Glu Ala Leu
 305 310 315 320

Glu Lys Trp Pro Thr Ala Tyr Leu Asn Glu Val Val Pro His Leu Val
 325 330 335

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

Pro Ala Val Gln Ile Ile Asp Glu Ser Gly Arg Val His Met Ala His
 355 360 365

Met Asp Ile His Phe Ala Thr Ser Val Asn Gly Val Ala Ala Leu His
 370 375 380

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

Pro Glu Lys Phe Asn Asn Lys Thr Asn Gly Ile Thr Phe Arg Arg Trp
 405 410 415

Leu Glu Phe Ala Asn Gln Asp Leu Ala Asp Tyr Ile Lys Glu Leu Ile
 420 425 430

Gly Asp Glu Tyr Leu Thr Asp Ala Thr Lys Leu Glu Lys Leu Met Ala
 435 440 445

Phe Ala Asp Asp Lys Ala Val His Ala Lys Leu Ala Glu Ile Lys Phe
 450 455 460

Asn Asn Lys Leu Ala Leu Lys Arg Tyr Leu Lys Asp Asn Lys Asp Ile
 465 470 475 480

Glu Leu Asp Glu His Ser Ile Ile Asp Thr Gln Ile Lys Arg Phe His
 485 490 495

Glu Tyr Lys Arg Gln Gln Met Asn Ala Leu Tyr Val Ile His Lys Tyr
 500 505 510

Leu Glu Ile Lys Lys Gly Asn Leu Pro Lys Arg Lys Ile Thr Val Ile
 515 520 525

Phe Gly Gly Lys Ala Ala Pro Ala Tyr Ile Ile Ala Gln Asp Ile Ile
 530 535 540

His Leu Ile Leu Cys Leu Ser Glu Leu Ile Asn Asn Asp Pro Glu Val
 545 550 555 560

Ser Pro Tyr Leu Asn Val His Leu Val Glu Asn Tyr Asn Val Thr Val
 565 570 575

Ala Glu His Leu Ile Pro Ala Thr Asp Ile Ser Glu Gln Ile Ser Leu
 580 585 590

Ala Ser Lys Glu Ala Ser Gly Thr Gly Asn Met Lys Phe Met Leu Asn
 595 600 605

Gly Ala Leu Thr Leu Gly Thr Met Asp Gly Ala Asn Val Glu Ile Ala
 610 615 620

Glu Leu Ala Gly Met Glu Asn Ile Tyr Thr Phe Gly Lys Asp Ser Asp
625 630 635 640

Thr Ile Ile Asn Leu Tyr Ala Thr Ala Ser Tyr Val Ala Lys Asp Tyr
645 650 655

Tyr Asp Asn His Pro Ala Ile Lys Ala Ala Val Asn Phe Ile Ile Ser
660 665 670

Pro Glu Leu Leu Ala Phe Gly Asn Glu Glu Arg Leu Asp Arg Leu Tyr
675 680 685

Lys Glu Leu Ile Ser Lys Asp Trp Phe Met Thr Leu Ile Asp Leu Glu
690 695 700

Glu Tyr Ile Glu Val Lys Glu Lys Met Leu Ala Asp Tyr Glu Asp Gln
705 710 715 720

Asp Leu Trp Met Thr Lys Val Val His Asn Ile Ala Lys Ala Gly Phe
725 730 735

Phe Ser Ser Asp Arg Thr Ile Glu Gln Tyr Asn Glu Asp Ile Trp His
740 745 750

Ser Arg

<210> 7

<211> 1371

<212> DNA

<213> Streptococcus pyogenes

<400> 7

atgaaacaaa aaaatgtata tatcgtcatt ggattcatgc tatttgcgct attttttgga 60
gcagcaaacc tcatttacct agctttttta ggcattctact caggatcatca gattctatgg 120
tctatcattg gtttttggtt aactgggtgc tccttgccct tactcggtgt cattgctggt 180
gctaaatctg gatcaggcga tgttgaaagt ttggcacgcc ccatctctaa atgggtatgca 240
atcttctatt ctccattttt gtatttatct attggcccat tttttgctat tccaagaaca 300
ggagccactt ctttttcagt cggtatcgct cctatcttag gagataatac aaccaataaa 360
gctatttatg ctatactatt ttttggtctg tcctacttcc ttgctatcaa acctagtaaa 420
ctagctgaaa atatcggaat atttttaacg ccaacgttgt tagttgttat ttctattttg 480
gttatcgctg cctttgtcca tcctgctgga aattacggtg atgcttttaa cgctggggtc 540
ggtgttaata atgcctttta agattttcct tttatagcag gattaattca aggttatggc 600
actatggatg cactagcttc tcttggtttt gctatttttag tcattgaggc taccaaaca 660
tttggcgcta agacggacaa agaaatgacc aaaataacac ttatttctgg ggctattgcc 720
attttgctat tagcacttgt ctatatcttt gtcggtcgta ttggagcaac atcacaatca 780

```

ttatttcctt ttattgatgg cagctttacc cttcatggta atccagttaa tggcggtcaa 840
atcttaagtc atgcttctcg tttttaccta ggtggcatcg gacaagcatt tctagctgtt 900
gtgattttcc tggcctgtct aaccacttca acaggcttaa tcacgtcaag tgctgaatac 960
ttccataaat tagtgctgc tttatctcat attgcttggg caactatctt tactttacta 1020
tcagctttct tttattttgg tggttatca gtcattatca actggtcagc tcctgtttta 1080
ttccttttat acccattaac agtcgattta attttccttg ttttggcaca aaaatgcttc 1140
aataatgata ctattgtcta tcgaactaca attggtctaa cctttattcc tgccatattt 1200
gatgcactcc taacactatc aaaaatgact ggattatttc atttaccaga agccgttgta 1260
acttttttcc aaaaaactgt tccactaggg caattctcaa tgggatggat tatctttgct 1320
gctattgggt ttttaatagg gcttatacta agtaaaacga agaaaagcta a 1371

```

<210> 8

<211> 456

<212> PRT

<213> Streptococcus pyogenes

<400> 8

```

Met Lys Gln Lys Asn Val Tyr Ile Val Ile Gly Phe Met Leu Phe Ala
  1             5             10             15

```

```

Leu Phe Phe Gly Ala Ala Asn Leu Ile Tyr Pro Ala Phe Leu Gly Ile
          20             25             30

```

```

Tyr Ser Gly His Gln Ile Leu Trp Ser Ile Ile Gly Phe Cys Leu Thr
      35             40             45

```

```

Gly Val Ser Leu Pro Leu Leu Gly Val Ile Ala Val Ala Lys Ser Gly
      50             55             60

```

```

Ser Gly Asp Val Glu Ser Leu Ala Arg Pro Ile Ser Lys Trp Tyr Ala
      65             70             75             80

```

```

Ile Phe Tyr Ser Ser Ile Leu Tyr Leu Ser Ile Gly Pro Phe Phe Ala
          85             90             95

```

```

Ile Pro Arg Thr Gly Ala Thr Ser Phe Ser Val Gly Ile Ala Pro Ile
      100             105             110

```

```

Leu Gly Asp Asn Thr Thr Asn Lys Ala Ile Tyr Ala Ile Leu Phe Phe
      115             120             125

```

```

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

```

```

Ile Gly Lys Phe Leu Thr Pro Thr Leu Leu Val Val Ile Ser Ile Leu
      145             150             155             160

```

Val Ile Ala Ser Phe Val His Pro Ala Gly Asn Tyr Gly Asp Ala Phe
 165 170 175

Asn Ala Gly Val Gly Val Asn Asn Ala Phe Lys Asp Phe Pro Phe Ile
 180 185 190

Ala Gly Leu Ile Gln Gly Tyr Gly Thr Met Asp Ala Leu Ala Ser Leu
 195 200 205

Val Phe Ala Ile Leu Val Ile Glu Ala Thr Lys Gln Phe Gly Ala Lys
 210 215 220

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

Ile Leu Leu Leu Ala Leu Val Tyr Ile Phe Val Gly Arg Ile Gly Ala
 245 250 255

Thr Ser Gln Ser Leu Phe Pro Phe Ile Asp Gly Ser Phe Thr Leu His
 260 265 270

Gly Asn Pro Val Asn Gly Gly Gln Ile Leu Ser His Ala Ser Arg Phe
 275 280 285

Tyr Leu Gly Gly Ile Gly Gln Ala Phe Leu Ala Val Val Ile Phe Leu
 290 295 300

Ala Cys Leu Thr Thr Ser Thr Gly Leu Ile Thr Ser Ser Ala Glu Tyr
 305 310 315 320

Phe His Lys Leu Val Pro Ala Leu Ser His Ile Ala Trp Ala Thr Ile
 325 330 335

Phe Thr Leu Leu Ser Ala Phe Phe Tyr Phe Gly Gly Leu Ser Val Ile
 340 345 350

Ile Asn Trp Ser Ala Pro Val Leu Phe Leu Leu Tyr Pro Leu Thr Val
 355 360 365

Asp Leu Ile Phe Leu Val Leu Ala Gln Lys Cys Phe Asn Asn Asp Pro
 370 375 380

Ile Val Tyr Arg Thr Thr Ile Gly Leu Thr Phe Ile Pro Ala Ile Phe
 385 390 395 400

Asp Ala Leu Leu Thr Leu Ser Gln Met Thr Gly Leu Phe His Leu Pro
 405 410 415

Glu Ala Val Val Thr Phe Phe Gln Lys Thr Val Pro Leu Gly Gln Phe
 420 425 430

Ser Met Gly Trp Ile Ile Phe Ala Ala Ile Gly Phe Leu Ile Gly Leu
 435 440 445

Ile Leu Ser Lys Thr Lys Lys Ser
 450 455

<210> 9

<211> 441

<212> DNA

<213> Streptococcus pyogenes

<400> 9

atggggattt tagaaaaaaa acttgataac ttagtaaata ctattttatt aaaagcagaa 60
 aatcagcatg agttattatt tggagcttgt caaagtgcg ttaagcttac taatacgcaa 120
 gaacatattt taatgttact atctcagcaa cgtctcacta atacagattt ggctaaggca 180
 ttaaataatta gtcaggcggc agtaactaag gctatcaaga gtttgggtcaa acaagacatg 240
 ttagcaggaa ctaaggatac ggttgatgct aggggtgactt attttgaatt aaccgagtta 300
 gctaagccta ttgcgtcaga acatacccat catcatgatg aaaccttaaa tgtttacaac 360
 cgtttattac aaaaattctc cgcgaaagaa ttagagattg tagataagtt tgtaacagtt 420
 tttgctgagg aattagaagg g 441

<210> 10

<211> 147

<212> PRT

<213> Streptococcus pyogenes

<400> 10

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

Leu Lys Ala Glu Asn Gln His Glu Leu Leu Phe Gly Ala Cys Gln Ser
 20 25 30

Asp Val Lys Leu Thr Asn Thr Gln Glu His Ile Leu Met Leu Leu Ser
 35 40 45

Gln Gln Arg Leu Thr Asn Thr Asp Leu Ala Lys Ala Leu Asn Ile Ser
 50 55 60

Gln Ala Ala Val Thr Lys Ala Ile Lys Ser Leu Val Lys Gln Asp Met
 65 70 75 80

Leu Ala Gly Thr Lys Asp Thr Val Asp Ala Arg Val Thr Tyr Phe Glu
85 90 95

Leu Thr Glu Leu Ala Lys Pro Ile Ala Ser Glu His Thr His His His
100 105 110

Asp Glu Thr Leu Asn Val Tyr Asn Arg Leu Leu Gln Lys Phe Ser Ala
115 120 125

Lys Glu Leu Glu Ile Val Asp Lys Phe Val Thr Val Phe Ala Glu Glu
130 135 140

Leu Glu Gly
145

<210> 11
<211> 815
<212> DNA
<213> Streptococcus pyogenes

<400> 11
atgcttgata ttttattcta tgatttcacg caacgggagg taatggcggg agttgccatt 60
agtatttttg ctccgatttt aggtattttc cttattttac gtcgtcaaag tttgatgagc 120
gataccctta gtcattgttc tttggctggg gtagcgcttg gggtagtcct tggattttca 180
ccaaccatca ctactattat tgttgtgggt ttagctgcta ttttgtaga atacctgcgt 240
gtagtttaca aacactacat ggagatttca acggcgattt tgatgtcact tggcttggcc 300
ctatctctga ttattatgag taagtcgcat agttcatcaa gcatgagttt agaacaatac 360
ctttttggat cgatcatcac gattagtagt gaacaagttg tcgccttggt tgctattgct 420
gcgattattt taatcttgac cgttctcttc attagaccga tgtacattct gacctttgat 480
gaagatactg cttttgtaga tggtttggcc gttcgcttga tgtctgttct attcaatatc 540
gtcactgggg ttgctattgc tttgaccatt ccagcagcag gagcactttt ggtttctacc 600
attatgggtc tgccagcaag tatcgcaatg agattgggta aaaactttta aacagttatc 660
ttactgggaa ttgtcatcgg ttttagcggg atgttatctg gtattttctt atcttatttc 720
tttgaaacgc cagctagtgc cactattacc atgattttca ttagtatttt cctcttagtt 780
agtctaggtg gaatgcttaa aaaacgggta ttttaa 815

<210> 12
<211> 239
<212> PRT
<213> Streptococcus pyogenes

<400> 12
Met Arg Tyr Ile Ser Val Lys Asn Leu Ser Phe Gln Tyr Glu Ser Glu
1 5 10 15

Pro Val Leu Glu Gly Ile Thr Tyr His Leu Asp Ser Gly Glu Phe Val
 20 25 30

Thr Met Thr Gly Glu Asn Gly Ala Ala Lys Ser Thr Leu Ile Lys Ala
 35 40 45

Thr Leu Gly Ile Leu Gln Pro Lys Ala Gly Arg Val Thr Ile Ala Lys
 50 55 60

Lys Asn Lys Asp Gly Lys Gln Leu Arg Ile Ala Tyr Leu Pro Gln Gln
 65 70 75 80

Val Ala Ser Phe Asn Ala Gly Phe Pro Ser Thr Val Tyr Glu Phe Val
 85 90 95

Lys Ser Gly Arg Tyr Pro Arg Ser Gly Trp Phe Arg His Leu Asn Lys
 100 105 110

His Asp Glu Glu His Val Gln Ala Ser Leu Glu Ala Val Gly Met Trp
 115 120 125

Glu Asn Arg His Lys Arg Ile Gly Ser Leu Ser Gly Gly Gln Lys Gln
 130 135 140

Arg Val Val Ile Ala Arg Met Phe Ala Ser Asp Pro Asp Ile Phe Val
 145 150 155 160

Leu Asp Glu Pro Thr Thr Gly Met Asp Ser Gly Thr Thr Asp Thr Phe
 165 170 175

Tyr Glu Leu Met His His Ser Ala His Gln His Gly Lys Ser Val Leu
 180 185 190

Met Ile Thr His Asp Pro Glu Glu Val Lys Ala Tyr Ala Asp Arg Asn
 195 200 205

Ile His Leu Val Arg Asn Gln Lys Leu Pro Trp Arg Cys Phe Asn Ile
 210 215 220

His Glu Ala Glu Thr Asp Asp Glu Lys Gly Gly His Gly His Ala
 225 230 235

<210> 13

<211> 681

<212> DNA

<213> Streptococcus pyogenes

<400> 13

```

atgtattcta taaaatgtga tgataataaa gccatgccaa gagaacgttt gatgcgacta 60
ggagcagagt ctctaagtaa tcaagaatta ttagcaattt tattacgaac aggtaataaa 120
gaaaagcatg tcttagagct gtcacacctat cttttatcgc atttagacag tctggcagat 180
tttaaaaaga tgtctttgca agaattacaa catttggcag gtataggaaa agttaaacg 240
attgaaatta aagctatgat tgagttgggt tcccgaattt tagcgacaga taagacatta 300
actgatagcg tattaaccag tggttcaggct gctgaaaaaa tgatggcagc tttaggagat 360
aaaaaacaag agcatttagt cgtattgtat ttagataatc aaaatcgtat tattgaagaa 420
aaaactatct ttattgggac tgtccgacgt tcacttgcag aaccaagaga aattttatac 480
tatgcctgta aaaatatggc gactagtctc attgttattc ataatcatcc ttcaggaaat 540
attgaacctt gttctaacga ttattgcttt actgaaaaaa taaaacgac atgtgaagat 600
ttaggcatta tctgtctaga tcacattatc gtttagctata aagattatta tagttttcga 660
gaaaaatcaa ccctttttta a 681

```

<210> 14

<211> 226

<212> PRT

<213> Streptococcus pyogenes

<400> 14

```

Met Tyr Ser Ile Lys Cys Asp Asp Asn Lys Ala Met Pro Arg Glu Arg
 1             5             10             15

Leu Met Arg Leu Gly Ala Glu Ser Leu Ser Asn Gln Glu Leu Leu Ala
      20             25             30

Ile Leu Leu Arg Thr Gly Asn Lys Glu Lys His Val Leu Glu Leu Ser
      35             40             45

Ser Tyr Leu Leu Ser His Leu Asp Ser Leu Ala Asp Phe Lys Lys Met
      50             55             60

Ser Leu Gln Glu Leu Gln His Leu Ala Gly Ile Gly Lys Val Lys Ala
      65             70             75             80

Ile Glu Ile Lys Ala Met Ile Glu Leu Val Ser Arg Ile Leu Ala Thr
      85             90             95

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

Lys Met Met Ala Ala Leu Gly Asp Lys Lys Gln Glu His Leu Val Val
      115            120            125

Leu Tyr Leu Asp Asn Gln Asn Arg Ile Ile Glu Glu Lys Thr Ile Phe
      130            135            140

```

Ile Gly Thr Val Arg Arg Ser Leu Ala Glu Pro Arg Glu Ile Leu Tyr
 145 150 155 160

Tyr Ala Cys Lys Asn Met Ala Thr Ser Leu Ile Val Ile His Asn His
 165 170 175

Pro Ser Gly Asn Ile Glu Pro Ser Ser Asn Asp Tyr Cys Phe Thr Glu
 180 185 190

Lys Ile Lys Arg Ser Cys Glu Asp Leu Gly Ile Ile Cys Leu Asp His
 195 200 205

Ile Ile Val Ser Tyr Lys Asp Tyr Tyr Ser Phe Arg Glu Lys Ser Thr
 210 215 220

Leu Phe
 225

<210> 15

<211> 410

<212> DNA

<213> Streptococcus pyogenes

<400> 15

atgatgttac gaaaatttaa aattaccatt gacggtaaag agtatcttgt agaaatggaa 60
 gaaatcggtg ctctgcca agcagctgcc cccgtcaac caatatccac tccagtacct 120
 gtccctactg aagcaagccc acaagtggag gaagcgcaag caccacagcc agtagctgca 180
 gcgggagcgg atgccattcc atcaccaatg cctggaacca tcttaaaagt cttagtagca 240
 gtgggagacc aagtaactga aaatcagcca ctattgattt tagaagccat gaagatggaa 300
 aatgagattg tggcctcacc agcaggaacc attacagcta tccacgtcgg tccaggtcaa 360
 gtggtcaatc ctggtgatgg tctcattaca attggttaat agtactataa 410

<210> 16

<211> 134

<212> PRT

<213> Streptococcus pyogenes

<400> 16

Met Met Leu Arg Lys Phe Lys Ile Thr Ile Asp Gly Lys Glu Tyr Leu
 1 5 10 15

Val Glu Met Glu Glu Ile Gly Ala Pro Ala Gln Ala Ala Ala Pro Ala
 20 25 30

Gln Pro Ile Ser Thr Pro Val Pro Val Pro Thr Glu Ala Ser Pro Gln
 35 40 45

Val Glu Glu Ala Gln Ala Pro Gln Pro Val Ala Ala Gly Ala Asp
 50 55 60

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

Val Gly Asp Gln Val Thr Glu Asn Gln Pro Leu Leu Ile Leu Glu Ala
 85 90 95

Met Lys Met Glu Asn Glu Ile Val Ala Ser Ser Ala Gly Thr Ile Thr
 100 105 110

Ala Ile His Val Gly Pro Gly Gln Val Val Asn Pro Gly Asp Gly Leu
 115 120 125

Ile Thr Ile Gly Tyr Tyr
 130

<210> 17

<211> 1533

<212> DNA

<213> Streptococcus pyogenes

<400> 17

atggttaacaa ataaactcgg tagagatatt cctcaaccat acgccgacca atacggtgtc 60
 tttgaaggag aactcgcaaa tatcaaacag tatgacgaat caagtcgccg tattaaccca 120
 gtttaagcctg gagattctaa attactagga tctgttcgtg aagcgattga aaaaacagggt 180
 ttaacagatg gcatgacccat ttctttccac caccatttcc gtgaaggggga tttcattatg 240
 aatatggtct tggaggaaat tgccaaaatg ggcattaaaa acctgtctat tgccccaagt 300
 tccatcgcta atgtacatga gcctttgatt gatcacatca aaaatggtgt ggtcactaac 360
 atcacttcat ctggtcttcg tgacaaagta ggggcagcca tctcagaagg actaatggaa 420
 aatcctgtgg ttattcgctc ccatggtggt cgcgctcgtg ccattgctag tggggatata 480
 catattgatg ttgcctttct gggcgcccca agttcagatg cttacggaaa tgtaaatggg 540
 acaaaaggga aagcaacctg tggttctttg ggctatgcca tgattgatgc caaatatgcg 600
 gatcaggtgg ttatcttgac agataatttg gttccttatc ctaatacccc aatcagcatt 660
 cctcaaacag atgttgacta tgtggttaaca gtggatgcta tcggagatcc tcaaggaatc 720
 gccaaagggg caactcgttt tacgaaaaat cctaaagaac tcttaattgc agaatacgcc 780
 gctaaagtaa tcaccaactc tccttatttt aaagaaggat tctctttcca aactggaaca 840
 ggtggcgctt ctttggcagt aaccggtttc atgctgaag ctatgattaa agaaaatata 900
 aaagctagct ttgctcttg tggattacc aatgctatgg tggagttgct cgaagaagaa 960
 ctggttgaaa aaattcttga tgtccaagac tttgatcacc catcagctgt ttctcttggg 1020
 aagcatgctg aacattatga aattgatgcc aacatgtatg cctcaccttt gagcaagggt 1080
 gctgttatca atcaattaga cacttgattt ttatcagccc ttgaagttga tactaacttc 1140

```

aatgttaatg tgatgacagg atctgacggc gtgattcgtg gcgcttcttg aggacactgc 1200
gacactgcct ttgcggctaa gatgagtttg gttatttcac cacttatccg cggacgcac 1260
ccaacttttg tagatgaggt taatacggtc attacaccag gaacaagtgt cgatgtgatc 1320
gtcacagaag tgggaattgc cattaaccca aatcgtaag acttagtaga ccatttcaaa 1380
tccctcaatg tgccacaatt tagtattgag gagctaaaag agaaggctta cgccatcggt 1440
ggcacacctg agcgtattca atatggtgat aaggttgttg ctcttattga ataccgtgac 1500
ggtagcctca tggatgtggt ttacaatgtg taa 1533

```

<210> 18
 <211> 510
 <212> PRT
 <213> Streptococcus pyogenes

```

<400> 18
Met Val Thr Asn Lys Leu Gly Arg Asp Ile Pro Gln Pro Tyr Ala Asp
  1              5              10              15

Gln Tyr Gly Val Phe Glu Gly Glu Leu Ala Asn Ile Lys Gln Tyr Asp
      20              25              30

Glu Ser Ser Arg Arg Ile Lys Pro Val Lys Pro Gly Asp Ser Lys Leu
      35              40              45

Leu Gly Ser Val Arg Glu Ala Ile Glu Lys Thr Gly Leu Thr Asp Gly
      50              55              60

Met Thr Ile Ser Phe His His His Phe Arg Glu Gly Asp Phe Ile Met
      65              70              75              80

Asn Met Val Leu Glu Glu Ile Ala Lys Met Gly Ile Lys Asn Leu Ser
      85              90              95

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

Ile Lys Asn Gly Val Val Thr Asn Ile Thr Ser Ser Gly Leu Arg Asp
      115              120              125

Lys Val Gly Ala Ala Ile Ser Glu Gly Leu Met Glu Asn Pro Val Val
      130              135              140

Ile Arg Ser His Gly Gly Arg Ala Arg Ala Ile Ala Ser Gly Asp Ile
      145              150              155              160

His Ile Asp Val Ala Phe Leu Gly Ala Pro Ser Ser Asp Ala Tyr Gly
      165              170              175

```

Asn Val Asn Gly Thr Lys Gly Lys Ala Thr Cys Gly Ser Leu Gly Tyr
 180 185 190

Ala Met Ile Asp Ala Lys Tyr Ala Asp Gln Val Val Ile Leu Thr Asp
 195 200 205

Asn Leu Val Pro Tyr Pro Asn Thr Pro Ile Ser Ile Pro Gln Thr Asp
 210 215 220

Val Asp Tyr Val Val Thr Val Asp Ala Ile Gly Asp Pro Gln Gly Ile
 225 230 235 240

Ala Lys Gly Ala Thr Arg Phe Thr Lys Asn Pro Lys Glu Leu Leu Ile
 245 250 255

Ala Glu Tyr Ala Ala Lys Val Ile Thr Asn Ser Pro Tyr Phe Lys Glu
 260 265 270

Gly Phe Ser Phe Gln Thr Gly Thr Gly Gly Ala Ser Leu Ala Val Thr
 275 280 285

Arg Phe Met Arg Glu Ala Met Ile Lys Glu Asn Ile Lys Ala Ser Phe
 290 295 300

Ala Leu Gly Gly Ile Thr Asn Ala Met Val Glu Leu Leu Glu Glu Glu
 305 310 315 320

Leu Val Glu Lys Ile Leu Asp Val Gln Asp Phe Asp His Pro Ser Ala
 325 330 335

Val Ser Leu Gly Lys His Ala Glu His Tyr Glu Ile Asp Ala Asn Met
 340 345 350

Tyr Ala Ser Pro Leu Ser Lys Gly Ala Val Ile Asn Gln Leu Asp Thr
 355 360 365

Cys Ile Leu Ser Ala Leu Glu Val Asp Thr Asn Phe Asn Val Asn Val
 370 375 380

Met Thr Gly Ser Asp Gly Val Ile Arg Gly Ala Ser Gly Gly His Cys
 385 390 395 400

Asp Thr Ala Phe Ala Ala Lys Met Ser Leu Val Ile Ser Pro Leu Ile
 405 410 415

Arg Gly Arg Ile Pro Thr Phe Val Asp Glu Val Asn Thr Val Ile Thr
 420 425 430

Pro Gly Thr Ser Val Asp Val Ile Val Thr Glu Val Gly Ile Ala Ile
435 440 445

Asn Pro Asn Arg Gln Asp Leu Val Asp His Phe Lys Ser Leu Asn Val
450 455 460

Pro Gln Phe Ser Ile Glu Glu Leu Lys Glu Lys Ala Tyr Ala Ile Val
465 470 475 480

Gly Thr Pro Glu Arg Ile Gln Tyr Gly Asp Lys Val Val Ala Leu Ile
485 490 495

Glu Tyr Arg Asp Gly Ser Leu Met Asp Val Val Tyr Asn Val
500 505 510

<210> 19

<211> 888

<212> DNA

<213> Streptococcus pyogenes

<400> 19

```

atggaacggt taagaagaac aatgatgttt gtgcctggtg ccaatgcagc catgcttcga 60
gatgctcctt tatttggcgc tgattcaatc atgtttgact tggaagattc tgtttcactc 120
aaagaaaaag acacctctag agctctcggt cattttgcgc ttaaaacttt tgattattca 180
agcgttgaaa cgggtgttcg tgtgaatggt cttgattcct gtggggcctt agacatcgaa 240
gctgttggtt tggcagggtg caacgtgatt cgtcttccaa aaacagagac tgctcaagat 300
attattgatg tggagggtgt tattgaacgt gtcgaacgcg agaacagcat tgaagttggt 360
cgcacacgta tgatggcagc cattgaatca gccgaagggt tcctaaatgc tcgtgagatt 420
gccaaagctt ctaagcgctt gatttgtatt gctcttgagc cagaagacta tgtcacgaat 480
atgaaaacgc gtcgttaccc agatggtcaa gaattattct ttgctcgtag catgatttta 540
cacgctgctc gtgctgctgg aattgctgcc attgatactg tttattctga tgtcaataat 600
accgaagggt tccaaaacga agttcgcatg atcaaacagt taggatttga tggtaaactc 660
gtcatcaacc ctgcgcaaat tcctctggtc aatgagattt ataccccaac aaaaaaagaa 720
attgaccatg ccaaacaagt catctgggca attcgtgaag ctgaaagcaa aggctctggc 780
gttatttcct taaatggaaa aatggttgat aaaccaatcg ttgaacgtgc agaacgtgtg 840
attgccctag caacagcagc aggtgtttta tctgaggagg atatttaa 888

```

<210> 20

<211> 295

<212> PRT

<213> Streptococcus pyogenes

<400> 20

Met Glu Arg Leu Arg Arg Thr Met Met Phe Val Pro Gly Ala Asn Ala
1 5 10 15

Ala Met Leu Arg Asp Ala Pro Leu Phe Gly Ala Asp Ser Ile Met Phe
 20 25 30
 Asp Leu Glu Asp Ser Val Ser Leu Lys Glu Lys Asp Thr Ser Arg Ala
 35 40 45
 Leu Val His Phe Ala Leu Lys Thr Phe Asp Tyr Ser Ser Val Glu Thr
 50 55 60
 Val Val Arg Val Asn Gly Leu Asp Ser Cys Gly Ala Leu Asp Ile Glu
 65 70 75 80
 Ala Val Val Leu Ala Gly Val Asn Val Ile Arg Leu Pro Lys Thr Glu
 85 90 95
 Thr Ala Gln Asp Ile Ile Asp Val Glu Ala Val Ile Glu Arg Val Glu
 100 105 110
 Arg Glu Asn Ser Ile Glu Val Gly Arg Thr Arg Met Met Ala Ala Ile
 115 120 125
 Glu Ser Ala Glu Gly Val Leu Asn Ala Arg Glu Ile Ala Lys Ala Ser
 130 135 140
 Lys Arg Leu Ile Gly Ile Ala Leu Gly Ala Glu Asp Tyr Val Thr Asn
 145 150 155 160
 Met Lys Thr Arg Arg Tyr Pro Asp Gly Gln Glu Leu Phe Phe Ala Arg
 165 170 175
 Ser Met Ile Leu His Ala Ala Arg Ala Ala Gly Ile Ala Ala Ile Asp
 180 185 190
 Thr Val Tyr Ser Asp Val Asn Asn Thr Glu Gly Phe Gln Asn Glu Val
 195 200 205
 Arg Met Ile Lys Gln Leu Gly Phe Asp Gly Lys Ser Val Ile Asn Pro
 210 215 220
 Arg Gln Ile Pro Leu Val Asn Glu Ile Tyr Thr Pro Thr Lys Lys Glu
 225 230 235 240
 Ile Asp His Ala Lys Gln Val Ile Trp Ala Ile Arg Glu Ala Glu Ser
 245 250 255
 Lys Gly Ser Gly Val Ile Ser Leu Asn Gly Lys Met Val Asp Lys Pro
 260 265 270

Ile Val Glu Arg Ala Glu Arg Val Ile Ala Leu Ala Thr Ala Ala Gly
 275 280 285

Val Leu Ser Glu Glu Asp Ile
 290 295

<210> 21
 <211> 309
 <212> DNA
 <213> Streptococcus pyogenes

<400> 21
 atggatatta aacaaactgc cggtgctggt tcacttgaat caagtgcct aatgattaca 60
 gtatccccta atgacgagca aaccattaca ataaccctag acagtagtgt tgaaaaacaa 120
 tttggcaatc acattcgta actcattcat caaaccctag tgaatttgaa ggtgacggct 180
 gctaaagtag aggctgttga taaagggtgca ttagattgca ccattcaagc gagaaccatc 240
 gcagctgttc atcgcgctgc tggattgac caatacgatt ggaaggagat tgactcatgg 300
 aacgtttaa 309

<210> 22
 <211> 102
 <212> PRT
 <213> Streptococcus pyogenes

<400> 22
 Met Asp Ile Lys Gln Thr Ala Val Ala Gly Ser Leu Glu Ser Ser Asp
 1 5 10 15

Leu Met Ile Thr Val Ser Pro Asn Asp Glu Gln Thr Ile Thr Ile Thr
 20 25 30

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

Ile His Gln Thr Leu Val Asn Leu Lys Val Thr Ala Ala Lys Val Glu
 50 55 60

Ala Val Asp Lys Gly Ala Leu Asp Cys Thr Ile Gln Ala Arg Thr Ile
 65 70 75 80

Ala Ala Val His Arg Ala Ala Gly Ile Asp Gln Tyr Asp Trp Lys Glu
 85 90 95

Ile Asp Ser Trp Asn Val

100

<210> 23
 <211> 1053
 <212> DNA
 <213> Streptococcus pyogenes

<400> 23
 atgccttact acactatttc aaaagtcttt ccttcagata aaacgacaat ggctagtgtgta 60
 aagaacctgc ttcatacaaga aggtattcgt ttggatgctc atttagatta tactttgtgcc 120
 atcatgaatg cgcaaaatga tgtgattgct accggttcctt actttggaaa tagcttgccgc 180
 tgtcttttgcg tatccagtgc ctatcaagggt gaaggacttc ttaataggat tgtgagtcacat 240
 ctcatatgatg aagaatatgc ccttggcaac tatcatcttt ttgtttatac gaagacctct 300
 tctgctgctt ttttcaaaga tcttggtttt actgaaattg tccatatacga caatcacatc 360
 agtttcttgg aaaataaaaa aactgggttt caagattatc tgatgacact taataagcct 420
 gagcaaacac ctggttaaagt cgctgctatt gttatcaacg ctaaccctt taccttaggg 480
 catcaatttt tagtagagaa agctgcaaga gaaaatgatt gggttcatct gtttatggtc 540
 agtgaagacc gcagtctaata tcctttttcg gtgagaaaaga gggttgattca agaaggtcta 600
 gctcatcttg ataatgtcat atatcatgaa acaggctcctt atttgattag ccaagcgact 660
 ttcccagcct atttccaaaa agaagacaat gacgtgatta agagccaagc tttgctggat 720
 actgctattt ttctaaagat tgctcaaacc ttacagatta caaaaagata cgttggagaa 780
 gagccaacca gccgagtaac tgctattttac aatgaaatta tggcagagca gttgcagcaa 840
 gctgggtatcc tcctagatat tttgccaagg aaagctatca atcagcagca agatcctatc 900
 agtgcctcaa cggtcaggca ggcatgaaa gataatgatt gggaccttct ggcaaaactc 960
 cttcccaaaa cgtcttttaga ttatttttgt tctgctaaaaag cccaacccat tattaataaag 1020
 atacaagcca cttcatctgt caaacattac taa 1053

<210> 24
 <211> 350
 <212> PRT
 <213> Streptococcus pyogenes

<400> 24
 Met Pro Tyr Tyr Thr Ile Ser Lys Val Phe Pro Ser Asp Lys Thr Thr
 1 5 10 15
 Met Ala Ser Val Lys Asn Leu Leu His Gln Glu Gly Ile Arg Leu Asp
 20 25 30
 Ala His Leu Asp Tyr Thr Cys Ala Ile Met Asn Ala Gln Asn Asp Val
 35 40 45
 Ile Ala Thr Gly Ser Tyr Phe Gly Asn Ser Leu Arg Cys Leu Cys Val
 50 55 60

Ser Ser Ala Tyr Gln Gly Glu Gly Leu Leu Asn Arg Ile Val Ser His
 65 70 75 80

Leu Ile Asp Glu Glu Tyr Ala Leu Gly Asn Tyr His Leu Phe Val Tyr
 85 90 95

Thr Lys Thr Ser Ser Ala Ala Phe Phe Lys Asp Leu Gly Phe Thr Glu
 100 105 110

Ile Val His Ile Asp Asn His Ile Ser Phe Leu Glu Asn Lys Lys Thr
 115 120 125

Gly Phe Gln Asp Tyr Leu Met Thr Leu Asn Lys Pro Glu Gln Thr Pro
 130 135 140

Gly Lys Val Ala Ala Ile Val Ile Asn Ala Asn Pro Phe Thr Leu Gly
 145 150 155 160

His Gln Phe Leu Val Glu Lys Ala Ala Arg Glu Asn Asp Trp Val His
 165 170 175

Leu Phe Met Val Ser Glu Asp Arg Ser Leu Ile Pro Phe Ser Val Arg
 180 185 190

Lys Arg Leu Ile Gln Glu Gly Leu Ala His Leu Asp Asn Val Ile Tyr
 195 200 205

His Glu Thr Gly Pro Tyr Leu Ile Ser Gln Ala Thr Phe Pro Ala Tyr
 210 215 220

Phe Gln Lys Glu Asp Asn Asp Val Ile Lys Ser Gln Ala Leu Leu Asp
 225 230 235 240

Thr Ala Ile Phe Leu Lys Ile Ala Gln Thr Leu Gln Ile Thr Lys Arg
 245 250 255

Tyr Val Gly Glu Glu Pro Thr Ser Arg Val Thr Ala Ile Tyr Asn Glu
 260 265 270

Ile Met Ala Glu Gln Leu Gln Gln Ala Gly Ile Leu Leu Asp Ile Leu
 275 280 285

Pro Arg Lys Ala Ile Asn Gln Gln Gln Asp Pro Ile Ser Ala Ser Thr
 290 295 300

Ala Arg Gln Ala Leu Lys Asp Asn Asp Trp Asp Leu Leu Ala Lys Leu
 305 310 315 320

Leu Pro Lys Thr Ser Leu Asp Tyr Phe Cys Ser Leu Lys Ala Gln Pro
 325 330 335

Ile Ile Lys Lys Ile Gln Ala Thr Ser Ser Val Lys His Tyr
 340 345 350

<210> 25

<211> 642

<212> DNA

<213> Streptococcus pyogenes

<400> 25

atggtgataa ggttggtgct cttattgaat accgtgacgg tagcctcatg gatgtggttt 60
 acaatgtgta aagacactta tttttcaggc gaagctatcc aacttagtga tatgttaaga 120
 gccgcggaag aaagagctct gcgtcagctg catttattaa aggagtaccc agaaggtagc 180
 ttattatcgg tcaccatgaa tatccctgga ccaattaaaa cctctcctaa acttcttgaa 240
 gcttttgata tagtgattaa ggccattcaa actgccttag ctgacgataa gatttggtac 300
 cagttgcatg tactgcctac aacgggttat gagtattacc tcatcacaag tctacctagc 360
 cgcgacctga agttaaaaaat gatagcctta gagacagagt tgccaatagg tcgtctcatg 420
 gatttagatg tcttggtctt gcaaaatgat ctgcctcatt caattagcag aaccgtatta 480
 ggaggctccc ctaggcaatg ttttatctgt tctaaagagg ccaaagtctg cggtcgccta 540
 cgtaagcaca gtgtcgagga gatgcagact gctatttcaa aattactcca ttcatttttc 600
 aataaagaca accaatcatc gtcacagat aagacagggt ga 642

<210> 26

<211> 213

<212> PRT

<213> Streptococcus pyogenes

<400> 26

Met Val Ile Arg Leu Leu Leu Leu Leu Asn Thr Val Thr Val Ala Ser
 1 5 10 15

Trp Met Trp Phe Thr Met Cys Lys Asp Thr Tyr Phe Ser Gly Glu Ala
 20 25 30

Ile Gln Leu Ser Asp Met Leu Arg Ala Arg Glu Glu Arg Ala Leu Arg
 35 40 45

Gln Leu His Leu Leu Lys Glu Tyr Pro Glu Gly Ser Leu Leu Ser Val
 50 55 60

Thr Met Asn Ile Pro Gly Pro Ile Lys Thr Ser Pro Lys Leu Leu Glu
 65 70 75 80

Ala Phe Asp Ile Val Ile Lys Ala Ile Gln Thr Ala Leu Ala Asp Asp
85 90 95

Lys Ile Cys Tyr Gln Leu Arg Leu Leu Pro Thr Thr Gly Tyr Glu Tyr
100 105 110

Tyr Leu Ile Thr Ser Leu Pro Ser Arg Asp Leu Lys Leu Lys Met Ile
115 120 125

Ala Leu Glu Thr Glu Leu Pro Ile Gly Arg Leu Met Asp Leu Asp Val
130 135 140

Leu Val Leu Gln Asn Asp Leu Pro His Ser Ile Ser Arg Thr Val Leu
145 150 155 160

Gly Gly Ser Pro Arg Gln Cys Phe Ile Cys Ser Lys Glu Ala Lys Val
165 170 175

Cys Gly Arg Leu Arg Lys His Ser Val Glu Glu Met Gln Thr Ala Ile
180 185 190

Ser Lys Leu Leu His Ser Phe Phe Asn Lys Asp Asn Gln Ser Ser Ser
195 200 205

Ser Asp Lys Thr Gly
210

<210> 27

<211> 1395

<212> DNA

<213> Streptococcus pyogenes

<400> 27

atgacgaaaa tccgtataac ggaaacagtt ttacgtgatg gtcaacaaaag tcagattgcc 60
acacgtatga caaccaagga aatgattcct attctcgaaa cgctagacaa tgctggttat 120
catgcccttg aaatgtgggg aggagcaacc ttgattcct gcctacgctt tttaaataaa 180
gacccttggg aacggctaag agccatccgt aaagcagtga aaaagactaa acttcagatg 240
ctcttacgcg gacaaaacct tcttgatatt cgcaattatg ctgacgatgt ggtcagatcc 300
tttattcaaa aatccattga aaatgggatt gatattgtcc gtattttcga tgctttaaac 360
gacccacgca acttgcaaac agctgtttca gcgactaaaa aatttgagg gcatgctcaa 420
gttgccattt cttacacgac aagtcggta cataccattg actactttgt tgaattggcg 480
aaagcttacc aagctatcgg agcggactcc atttgatca aagacatggc tgggtgtctta 540
actcctgaaa taggttacca attgggtcaaa tgtatcaagg agaatacaac tatccctctt 600
gagggtcata cccatgctac cagtggatt tcagaaatga cttacttaaa agtagcagaa 660
gcaggagctg atattattga tacggcgatt tcctctttt cagggggaac cagtcagcct 720
gccacagagt caatggcgat tgccttgacg gatttaggct ttgacacagg cttggatatg 780

caagaggtgg ccaaagttgc agaataatttc aacactattc gtgaccacta tcgagaaata 840
 gggatttttaa atcctaaagt caaagatact gagccaaaaa cattgattta ccaagttcca 900
 ggtggcatgc tatcaaacct attgagccaa ttaaccgagc aaggcctaac tgataaatac 960
 gaagaagtct tagcagaagt acctaaagta agggctgac ttgggtatcc gccactcgta 1020
 acgccattat cacaaatggt tggcacacag gccttgatga atatcatctc aggggaacgt 1080
 tacaaggtag ttccaaatga aatcaaagac tatgttcgag ggctatacgg tcaatcacca 1140
 gcgccattag cagaaggtat caaagagaaa atcattggtg acgaagcagt tattacttgc 1200
 agaccagccg acctaatacga gcctcaaatag atttatctac gtgacgagat tgctccatac 1260
 gctcattcag aagaagacgt gttaagctat gcaagcttcc cgcaacaagc tagagatttc 1320
 ttgggacgcc gtgaagatcc tttctatgat gttccggttc aagaagttac tgtacaactg 1380
 gacattcaag actaa 1395

<210> 28

<211> 464

<212> PRT

<213> Streptococcus pyogenes

<400> 28

Met Thr Lys Ile Arg Ile Thr Glu Thr Val Leu Arg Asp Gly Gln Gln
 1 5 10 15

Ser Gln Ile Ala Thr Arg Met Thr Thr Lys Glu Met Ile Pro Ile Leu
 20 25 30

Glu Thr Leu Asp Asn Ala Gly Tyr His Ala Leu Glu Met Trp Gly Gly
 35 40 45

Ala Thr Phe Asp Ser Cys Leu Arg Phe Leu Asn Glu Asp Pro Trp Glu
 50 55 60

Arg Leu Arg Ala Ile Arg Lys Ala Val Lys Lys Thr Lys Leu Gln Met
 65 70 75 80

Leu Leu Arg Gly Gln Asn Leu Leu Gly Tyr Arg Asn Tyr Ala Asp Asp
 85 90 95

Val Val Arg Ser Phe Ile Gln Lys Ser Ile Glu Asn Gly Ile Asp Ile
 100 105 110

Val Arg Ile Phe Asp Ala Leu Asn Asp Pro Arg Asn Leu Gln Thr Ala
 115 120 125

Val Ser Ala Thr Lys Lys Phe Gly Gly His Ala Gln Val Ala Ile Ser
 130 135 140

Tyr Thr Thr Ser Pro Val His Thr Ile Asp Tyr Phe Val Glu Leu Ala
 145 150 155 160

Lys Ala Tyr Gln Ala Ile Gly Ala Asp Ser Ile Cys Ile Lys Asp Met
 165 170 175
 Ala Gly Val Leu Thr Pro Glu Ile Gly Tyr Gln Leu Val Lys Cys Ile
 180 185 190
 Lys Glu Asn Thr Thr Ile Pro Leu Glu Val His Thr His Ala Thr Ser
 195 200 205
 Gly Ile Ser Glu Met Thr Tyr Leu Lys Val Ala Glu Ala Gly Ala Asp
 210 215 220
 Ile Ile Asp Thr Ala Ile Ser Ser Phe Ser Gly Gly Thr Ser Gln Pro
 225 230 235 240
 Ala Thr Glu Ser Met Ala Ile Ala Leu Thr Asp Leu Gly Phe Asp Thr
 245 250 255
 Gly Leu Asp Met Gln Glu Val Ala Lys Val Ala Glu Tyr Phe Asn Thr
 260 265 270
 Ile Arg Asp His Tyr Arg Glu Ile Gly Ile Leu Asn Pro Lys Val Lys
 275 280 285
 Asp Thr Glu Pro Lys Thr Leu Ile Tyr Gln Val Pro Gly Gly Met Leu
 290 295 300
 Ser Asn Leu Leu Ser Gln Leu Thr Glu Gln Gly Leu Thr Asp Lys Tyr
 305 310 315 320
 Glu Glu Val Leu Ala Glu Val Pro Lys Val Arg Ala Asp Leu Gly Tyr
 325 330 335
 Pro Pro Leu Val Thr Pro Leu Ser Gln Met Val Gly Thr Gln Ala Leu
 340 345 350
 Met Asn Ile Ile Ser Gly Glu Arg Tyr Lys Val Val Pro Asn Glu Ile
 355 360 365
 Lys Asp Tyr Val Arg Gly Leu Tyr Gly Gln Ser Pro Ala Pro Leu Ala
 370 375 380
 Glu Gly Ile Lys Glu Lys Ile Ile Gly Asp Glu Ala Val Ile Thr Cys
 385 390 395 400
 Arg Pro Ala Asp Leu Ile Glu Pro Gln Met Ile Tyr Leu Arg Asp Glu
 405 410 415

Ile Ala Pro Tyr Ala His Ser Glu Glu Asp Val Leu Ser Tyr Ala Ser
 420 425 430

Phe Pro Gln Gln Ala Arg Asp Phe Leu Gly Arg Arg Glu Asp Pro Phe
 435 440 445

Tyr Asp Val Pro Val Gln Glu Val Thr Val Gln Leu Asp Ile Gln Asp
 450 455 460

<210> 29

<211> 1224

<212> DNA

<213> Streptococcus pyogenes

<400> 29

```

atgacgaatt taacgtttta tgcaaaaatc ggtatttcag aagaagagca tgactctttt 60
gttaaagaac atcagcaaat tagcgtttta caaggtagtg attgggcaaa aatcaaaaat 120
caatggcaga atgagcgaat tggatatctat aaagaggaaa agcagggttg ctcctttatca 180
cttttgatta agctattgcc acttgggaaga agcattatct atattccaag agggccagtc 240
atggattatc ttgaccgtga tttggtggca ttaccatga aaacactaaa ggattatggt 300
aaaactaaaa aggccctctt tatcaaatat gatccagcta tcctgttaaa acaatacgca 360
ctgggacagg aagaagaaga aaaaccttta gctttagcag ctattaagaa tctccaagaa 420
gctggtgttc attggactgg tttacaatg gagattgcag atagtatcca acctcgtttc 480
caagctaata ttacactca agaaaacctt gagatgcaat ttcctaagca taccagacgt 540
ttaataaaaag atgctaagca gcgtggtgta aaaacatata gtgtcagtc atcagaactt 600
caciaatttt ccaagattgt ctccttaaca gaaaaacgta aaaatatttc tttgcgtaac 660
gaagcttact ttcaaaagtt gatgactact tatggggata aggcctactt acatctagca 720
aaagtgaata ttcctcaaaa actagatcaa taccgccagc aattaattct tattaaccaa 780
gatattactc gcacccaagc tcatcaaaag aagcgtttaa aaaaattaga agatcaaaaa 840
gcttcttttag aacgttatat aactgaattt gaaggcttta cagaccaata tcctgaggaa 900
gttggtgtag caggatatatt atctatttct tatggaaatg ttatggaaat gctttatgct 960
gggatgaatg atgattttta gaagttttat cctcagtatc tgctgtatcc taatgttttt 1020
caggatgctt atcaagatgg tattatttgg gctaacatgg gaggagtaga aggctcgctt 1080
gatgatggac ttaccaaatt taaggccaac tttgctccga caatagaaga atttatagga 1140
gaatttaatc tccctgtcag cccactttat catattgcta ataccatgta caaaatacga 1200
aaacagttaa agaataaaca ttaa
1224

```

<210> 30

<211> 407

<212> PRT

<213> Streptococcus pyogenes

<400> 30

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

His Asp Ser Phe Val Lys Glu His Gln Gln Ile Ser Val Leu Gln Gly
 20 25 30

Ser Asp Trp Ala Lys Ile Lys Asn Gln Trp Gln Asn Glu Arg Ile Gly
 35 40 45

Ile Tyr Lys Glu Glu Lys Gln Val Ala Ser Leu Ser Leu Leu Ile Lys
 50 55 60

Leu Leu Pro Leu Gly Arg Ser Ile Ile Tyr Ile Pro Arg Gly Pro Val
 65 70 75 80

Met Asp Tyr Leu Asp Arg Asp Leu Val Ala Phe Thr Met Lys Thr Leu
 85 90 95

Lys Asp Tyr Gly Lys Thr Lys Lys Ala Leu Phe Ile Lys Tyr Asp Pro
 100 105 110

Ala Ile Leu Leu Lys Gln Tyr Ala Leu Gly Gln Glu Glu Glu Glu Lys
 115 120 125

Pro Leu Ala Leu Ala Ala Ile Lys Asn Leu Gln Glu Ala Gly Val His
 130 135 140

Trp Thr Gly Leu Thr Met Glu Ile Ala Asp Ser Ile Gln Pro Arg Phe
 145 150 155 160

Gln Ala Asn Ile Tyr Thr Gln Glu Asn Leu Glu Met Gln Phe Pro Lys
 165 170 175

His Thr Arg Arg Leu Ile Lys Asp Ala Lys Gln Arg Gly Val Lys Thr
 180 185 190

Tyr Arg Val Ser Gln Ser Glu Leu His Lys Phe Ser Lys Ile Val Ser
 195 200 205

Leu Thr Glu Lys Arg Lys Asn Ile Ser Leu Arg Asn Glu Ala Tyr Phe
 210 215 220

Gln Lys Leu Met Thr Thr Tyr Gly Asp Lys Ala Tyr Leu His Leu Ala
 225 230 235 240

Lys Val Asn Ile Pro Gln Lys Leu Asp Gln Tyr Arg Gln Gln Leu Ile

245	250	255
Leu Ile Asn Gln Asp Ile Thr Arg Thr Gln Ala His Gln Lys Lys Arg		
260	265	270
Leu Lys Lys Leu Glu Asp Gln Lys Ala Ser Leu Glu Arg Tyr Ile Thr		
275	280	285
Glu Phe Glu Gly Phe Thr Asp Gln Tyr Pro Glu Glu Val Val Val Ala		
290	295	300
Gly Ile Leu Ser Ile Ser Tyr Gly Asn Val Met Glu Met Leu Tyr Ala		
305	310	315
Gly Met Asn Asp Asp Phe Lys Lys Phe Tyr Pro Gln Tyr Leu Leu Tyr		
325	330	335
Pro Asn Val Phe Gln Asp Ala Tyr Gln Asp Gly Ile Ile Trp Ala Asn		
340	345	350
Met Gly Gly Val Glu Gly Ser Leu Asp Asp Gly Leu Thr Lys Phe Lys		
355	360	365
Ala Asn Phe Ala Pro Thr Ile Glu Glu Phe Ile Gly Glu Phe Asn Leu		
370	375	380
Pro Val Ser Pro Leu Tyr His Ile Ala Asn Thr Met Tyr Lys Ile Arg		
385	390	395
Lys Gln Leu Lys Asn Lys His		
405		

<210> 31

<211> 483

<212> DNA

<213> Streptococcus pyogenes

<400> 31

```

atgccaaaga gaataagaaa agctctagga gtagttggga aactgatgtc aattgttcct 60
gacactactg aaattattgg aaaaacgatt gataacagtc gaccaattat cgaaaaacgt 120
atggaacaaa aacatgaaaa agagatgcaa ttacgcacga taaatgatgt gattaatctt 180
cctgttgatc aggcacaagc tcatttggaa caacttggct ttgtagtagc cactatacct 240
gctaagcctc ataaaaaatg gcttcatagt aatctcaatg aagtgggtgc tatgtctcca 300
aaatctggtg aatataagat aggaagcctg atcaaactct actacattac tgttgatgtt 360
ttggaaaaaa gtcaagactt attagaccaa gaaaacttgc ggactgtgga acgcaatcaa 420
aaaatcgctg atacttttga gtctgtcaaa cacattcgat ttccttttaa aaaatggcgt 480

```

taa

483

<210> 32

<211> 160

<212> PRT

<213> Streptococcus pyogenes

<400> 32

Met Pro Lys Arg Ile Arg Lys Ala Leu Gly Val Val Gly Lys Leu Met
 1 5 10 15

Ser Ile Val Pro Asp Thr Thr Glu Ile Ile Gly Lys Thr Ile Asp Asn
 20 25 30

Ser Arg Pro Ile Ile Glu Lys Arg Met Glu Gln Lys His Glu Lys Glu
 35 40 45

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

Ala Gln Ala His Leu Glu Gln Leu Gly Phe Val Val Ala Thr Ile Pro
 65 70 75 80

Ala Lys Pro His Lys Lys Trp Leu His Ser Asn Leu Asn Glu Val Val
 85 90 95

Ala Met Ser Pro Lys Ser Gly Lys Tyr Lys Ile Gly Ser Leu Ile Lys
 100 105 110

Leu Tyr Tyr Ile Thr Val Asp Val Leu Glu Lys Ser Gln Asp Leu Leu
 115 120 125

Asp Gln Glu Asn Leu Arg Thr Val Glu Arg Asn Gln Lys Ile Ala Asp
 130 135 140

Thr Phe Glu Ser Val Lys His Ile Arg Phe Pro Phe Lys Lys Trp Arg
 145 150 155 160

<210> 33

<211> 1345

<212> DNA

<213> Streptococcus pyogenes

<400> 33

```

atgatgttaa cgaaggggca acttccttat agtgcgtcctt ttacaacagg agggctcttt 60
tactttgtta tcattgcatt aagttattat ttgggatcga cactttggct agtctttgtt 120
caggtgtttt gtttttactt atctggttta tatctttata aactcattaa ttatatgaca 180
ggctttcaaa aagtggcttt aactttttca attagctact atttattatc tgtagtctt 240
ggttttgggg gattgtatcc tactcaactg gctatgccat ttatattaat atcggcttgg 300
tttttaacta agtattttgc ctgttttagtg aaagatgagg catttattct ttttggcttt 360
gtaggtgctc ttgcaatgct aattgacccg agtaccctta tcttttggtc ttttgcttgt 420
gtgacagttt tttcttataa tataagccaa aagcatcttg caagaggttt ttatcaactg 480
ctagcttcga tttttggaat gatttttagtt ttttacacag caggatattt cattttgaac 540
ttacaagtgc taaatcctta tttatcacia acgatgattt atccttttac tttttttaaa 600
tcaggaaact tatcggttgc ttttggactg gctattcagt tgttcttcgc tttggggctt 660
ggctctttga cgggaatgga gaatgtcatt aggcgattta aaaacaattc tgataggggtc 720
gtcaagtggc tatttgtcat ggtcattcta gaatctatac ttgtggctat attttcacia 780
gactatcgcc cctatcatct tttacctctt ttaccttttg gattaatttt gactgctatt 840
cctgttggct atcagtatgg tataggatta ggtcagagta gtcacgcag acgtcatggt 900
aaaaatggtg ttggtcgagt aatgatgatt tatcttaaga gacactttta ttgccaatt 960
ttaattgtag ggacaatact aatctgttct acttattgtt tcattagtag tattectctt 1020
aatcaggagc gtgatcatat tgctagtatt ttagaacaga aactaaataa aactcaatct 1080
atztatgttt gggatgatac ttctaaaatt tatttggaca gtaaagctaa atctgtttct 1140
caatttagtt ctctgacat caatacga aaagagagtc atcgaaaaat attagaagat 1200
gaactattag aaaataaggc tgcttatatc gttgttaatc gctataaaaa cctgcctaaa 1260
atcattcaaa aagtattatc tactaattac aaagtagata aacagataac gacaaaaagt 1320
tttattgttt atcagaaaaa gtaat 1345

```

<210> 34

<211> 447

<212> PRT

<213> Streptococcus pyogenes

<400> 34

```

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

Gly Gly Leu Phe Tyr Phe Val Ile Ile Ala Leu Ser Tyr Tyr Leu Gly
      20              25              30

Ser Thr Leu Trp Leu Val Phe Val Gln Val Phe Cys Phe Tyr Leu Ser
      35              40              45

Gly Leu Tyr Leu Tyr Lys Leu Ile Asn Tyr Met Thr Gly Phe Gln Lys
      50              55              60

Val Ala Leu Thr Phe Ser Ile Ser Tyr Tyr Leu Leu Ser Val Ser Leu
      65              70              75              80

```

Gly Phe Gly Gly Leu Tyr Pro Thr Gln Leu Ala Met Pro Phe Ile Leu
 85 90 95

Ile Ser Ala Trp Phe Leu Thr Lys Tyr Phe Ala Cys Leu Val Lys Asp
 100 105 110

Glu Ala Phe Ile Leu Phe Gly Phe Val Gly Ala Leu Ala Met Leu Ile
 115 120 125

Asp Pro Ser Thr Leu Ile Phe Trp Ser Phe Ala Cys Val Thr Val Phe
 130 135 140

Ser Tyr Asn Ile Ser Gln Lys His Leu Ala Arg Gly Phe Tyr Gln Leu
 145 150 155 160

Leu Ala Ser Ile Phe Gly Met Ile Leu Val Phe Tyr Thr Ala Gly Tyr
 165 170 175

Phe Ile Leu Asn Leu Gln Val Leu Asn Pro Tyr Leu Ser Gln Thr Met
 180 185 190

Ile Tyr Pro Phe Thr Phe Phe Lys Ser Gly Asn Leu Ser Leu Leu Phe
 195 200 205

Gly Leu Ala Ile Gln Leu Phe Phe Ala Leu Gly Leu Gly Leu Leu Thr
 210 215 220

Gly Met Glu Asn Val Ile Arg Arg Phe Lys Asn Asn Ser Asp Arg Val
 225 230 235 240

Val Lys Trp Leu Phe Val Met Val Ile Leu Glu Ser Ile Leu Val Ala
 245 250 255

Ile Phe Ser Gln Asp Tyr Arg Pro Tyr His Leu Leu Pro Leu Leu Pro
 260 265 270

Phe Gly Leu Ile Leu Thr Ala Ile Pro Val Gly Tyr Gln Tyr Gly Ile
 275 280 285

Gly Leu Gly Gln Ser Ser His Arg Arg Arg His Gly Lys Asn Gly Val
 290 295 300

Gly Arg Val Met Met Ile Tyr Leu Lys Arg His Phe Tyr Leu Pro Ile
 305 310 315 320

Leu Ile Val Gly Thr Ile Leu Ile Cys Ser Thr Tyr Cys Phe Ile Ser
 325 330 335

-12

Ser Ile Pro Leu Asn Gln Glu Arg Asp His Ile Ala Ser Tyr Leu Glu
 340 345 350

Gln Lys Leu Asn Lys Thr Gln Ser Ile Tyr Val Trp Asp Asp Thr Ser
 355 360 365

Lys Ile Tyr Leu Asp Ser Lys Ala Lys Ser Val Ser Gln Phe Ser Ser
 370 375 380

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

Glu Leu Leu Glu Asn Lys Ala Ala Tyr Ile Val Val Asn Arg Tyr Lys
 405 410 415

Asn Leu Pro Lys Ile Ile Gln Lys Val Leu Ser Thr Asn Tyr Lys Val
 420 425 430

Asp Lys Gln Ile Thr Thr Lys Ser Phe Ile Val Tyr Gln Lys Lys
 435 440 445

<210> 35

<211> 618

<212> DNA

<213> Streptococcus pyogenes

<400> 35

atgattaaag ctcagctaaa gaatctaata aaaacaattc atctcgtaaa agaggctggt 60
 ttctccctaa atgggttcatt gtacatggag ttattgcatg attttacgca tgatgagtta 120
 gtacataacc ctataatcga aagtacgggt gatacaattc agtcagttga atttgaaagg 180
 gtttcttttt catataatgg taaggataat gtaataaacg atataagttt ttcaattaaa 240
 gcaggagaga ggtagcaat tgttggtgga aatgggtctg gaaaaagtac gattttcaaa 300
 ttagcctgcg gtctttacga taattatgaa ggcaatatat atataaatgg tattaatctt 360
 tgttcaatac agaaaaagtc atactacaag agaatatccg cattgttcca agatttttta 420
 aagtatgaat tgacactgcg tgaaaatggt ggattgggtg aattatcaaa gttatatagt 480
 gatgagtctt ataatacttc attttttacc acatcatggg attcagagaa tgaactgcga 540
 ttggaggata tttatataag atatatgat ggtaagtttc attttacaac tatcgatgaa 600
 tcgattaaac ggatttaa 618

<210> 36

<211> 205

<212> PRT

<213> Streptococcus pyogenes

<400> 36

Met Ile Lys Ala Gln Leu Lys Asn Leu Ile Lys Thr Ile His Leu Val
 1 5 10 15

Lys Glu Ala Gly Phe Ser Leu Asn Gly Ser Leu Tyr Met Glu Leu Leu
 20 25 30

His Asp Phe Thr His Asp Glu Leu Val His Asn Pro Ile Ile Glu Ser
 35 40 45

Thr Val Asp Thr Ile Gln Ser Val Glu Phe Glu Arg Val Ser Phe Ser
 50 55 60

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

Ala Gly Glu Arg Leu Ala Ile Val Gly Gly Asn Gly Ser Gly Lys Ser
 85 90 95

Thr Ile Phe Lys Leu Ala Cys Gly Leu Tyr Asp Asn Tyr Glu Gly Asn
 100 105 110

Ile Tyr Ile Asn Gly Ile Asn Leu Cys Ser Ile Gln Lys Lys Ser Tyr
 115 120 125

Tyr Lys Arg Ile Ser Ala Leu Phe Gln Asp Phe Leu Lys Tyr Glu Leu
 130 135 140

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

Asp Glu Ser Tyr Asn Thr Ser Phe Phe Thr Thr Ser Trp Asp Ser Glu
 165 170 175

Asn Glu Leu Arg Leu Glu Asp Ile Tyr Ile Arg Tyr Ser Asp Gly Lys
 180 185 190

Phe His Phe Thr Thr Ile Asp Glu Ser Ile Lys Arg Asp
 195 200 205

<210> 37

<211> 1434

<212> DNA

<213> Streptococcus pyogenes

<400> 37

atgctaagaa aaaagagaat tttgggttta tttcgacttg ttgaattaat tttcctagga 60

```

ttattgttga gtttagttgt ttcgtacctt gcgtggacca atagttttgc aacacttcat 120
aatatattag caactgtcgg aatagtggaa cgaagcaaag atcaacagcc tcgctatcac 180
attggacaag ctattcaagt acaaaaaagt ggtccatata atcaatggat tggaaactatt 240
aataaacagg tagaagatat agccgaaaat taccgagtga gttatcatta tgaagtggta 300
tttccaatag gaaaagtcac tgtttctttg ccagaacata acctgaaaga gcctgataaa 360
ccgaggttta aaaaaggaga tatcggttaa ttatcttcat taactaaaaa gccacatata 420
aaagtatatc aaggtcaatt agcgactatt aaacaagtta aaaaatgcta tgactattcg 480
ttaggaggat atcagtacga tattaatctg aaagataatc taagattaga tggaaattca 540
gagcaagatt ttgttaaacc ttattatatt aggttcaata aaggaaattc ccctgagcaa 600
aacaatcgtc ttttgcgaaa agctttcgtc tatgcaaagc agcatccaaa tagcgttata 660
tcttttccaa aggggcaatt tcacattggc tctttgcctt cacaaaaaga ttattttgag 720
cttccatctg atacagctat tattgggtcat cagacagagt tcattattca cggtaaaatg 780
ttgtggtttg gattccctac aggaccaaag gctgaacaag gtgttcgtaa tctcgtgttg 840
actggagtgc atttcaaagc aaatgatttg aaaaaaggag accactttat gattatggct 900
gatcatggta ctgattggca tatttacgat aacaaattta ctatggttca taagcgtaat 960
agtcataatt ttgatttagg atctctacaa aattcattgt ttgagaaaaa ccaatttatt 1020
ggctatgcgc cagaattagt acaagaccaa cagctgctat caaaggctca agggcatgat 1080
tttttttcag aagtcattca gtttgatgct gctgttcata attttgcatg ggatggagggt 1140
ctacttagta atattgctcc aaactatgaa gcatttaacc aaactcgaca tctatgtcac 1200
aatattactg taagccaaaa tcaattttta ccttatatag atccgactgg ttgcctgaga 1260
gcctatagtg gttctattgg tcagcattcc tcaaaagtag gagttattag ggttttaaat 1320
aatgttttta cctcatccat tgttactaaa gcgaagctca ctagttgggt tatggaacct 1380
attcattttc caccaaattc accggttatt gtcgcaggta atatcattaa ttga 1434

```

<210> 38

<211> 477

<212> PRT

<213> Streptococcus pyogenes

<400> 38

```

Met Leu Arg Lys Lys Arg Ile Leu Gly Leu Phe Arg Leu Val Glu Leu
  1             5             10             15

```

```

Ile Phe Leu Gly Leu Leu Leu Ser Leu Val Val Ser Tyr Leu Ala Trp
      20             25             30

```

```

Thr Asn Ser Phe Ala Thr Leu His Asn Ile Leu Ala Thr Val Gly Ile
      35             40             45

```

```

Val Glu Arg Ser Lys Asp Gln Gln Pro Arg Tyr His Ile Gly Gln Ala
      50             55             60

```

```

Ile Gln Val Gln Lys Ser Gly Pro Tyr His Gln Trp Ile Gly Thr Ile
      65             70             75             80

```

```

Asn Lys Gln Val Glu Asp Ile Ala Glu Asn Tyr Arg Val Ser Tyr His
      85             90             95

```

Tyr Glu Val Val Phe Pro Ile Gly Lys Val Thr Val Ser Leu Pro Glu
 100 105 110

His Asn Leu Lys Glu Pro Asp Lys Pro Arg Phe Lys Lys Gly Asp Ile
 115 120 125

Val Lys Leu Ser Ser Leu Thr Lys Lys Pro His Ile Lys Val Tyr Gln
 130 135 140

Gly Gln Leu Ala Thr Ile Lys Gln Val Lys Lys Cys Tyr Asp Tyr Ser
 145 150 155 160

Leu Gly Gly Tyr Gln Tyr Asp Ile Asn Leu Lys Asp Asn Leu Arg Leu
 165 170 175

Asp Gly Ile Ser Glu Gln Asp Phe Val Lys Pro Tyr Tyr Ile Arg Phe
 180 185 190

Asn Lys Gly Asn Ser Pro Glu Gln Asn Asn Arg Leu Leu Arg Lys Ala
 195 200 205

Phe Ala Tyr Ala Lys Gln His Pro Asn Ser Val Ile Ser Phe Pro Lys
 210 215 220

Gly Gln Phe His Ile Gly Ser Leu Pro Ser Gln Lys Asp Tyr Phe Glu
 225 230 235 240

Leu Pro Ser Asp Thr Ala Ile Ile Gly His Gln Thr Glu Phe Ile Ile
 245 250 255

His Gly Lys Met Leu Trp Phe Gly Phe Pro Thr Gly Pro Lys Ala Glu
 260 265 270

Gln Gly Val Arg Asn Leu Val Leu Thr Gly Val His Phe Lys Ala Asn
 275 280 285

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

Asp Trp His Ile Tyr Asp Asn Lys Phe Thr Met Val His Lys Arg Asn
 305 310 315 320

Ser His Ile Phe Asp Leu Gly Ser Leu Gln Asn Ser Leu Phe Glu Lys
 325 330 335

Asn Gln Phe Ile Gly Tyr Ala Pro Glu Leu Val Gln Asp Gln Gln Leu
 340 345 350

Leu Ser Lys Ala Gln Gly His Asp Phe Phe Ser Glu Val Ile Gln Phe
 355 360 365

Asp Ala Ala Val His His Phe Ala Trp Asp Gly Gly Leu Leu Ser Asn
 370 375 380

Ile Ala Pro Asn Tyr Glu Ala Phe Asn Gln Thr Arg His Leu Cys His
 385 390 395 400

Asn Ile Thr Val Ser Gln Asn Gln Phe Leu Pro Tyr Ile Asp Pro Thr
 405 410 415

Gly Cys Leu Arg Ala Tyr Ser Gly Ser Ile Gly Gln His Ser Ser Lys
 420 425 430

Val Gly Val Ile Arg Val Leu Asn Asn Val Phe Thr Ser Ser Ile Val
 435 440 445

Thr Lys Ala Lys Leu Thr Ser Trp Phe Met Glu Pro Ile His Phe Pro
 450 455 460

Pro Asn Ser Pro Val Ile Val Ala Gly Asn Ile Ile Asn
 465 470 475

<210> 39

<211> 1020

<212> DNA

<213> Streptococcus pyogenes

<400> 39

atgtcaactc acttaagaaa acttccaggg ctgttacttt gcttattggt agctcttcca 60
 gcctgggtgt tagggcgctt atttcccatt attggagcac ctgtttttgc tattctttta 120
 ggaatgttgt tagccttggt ttatgaacat cgtgacaaga ctaaagaggg aattagtttt 180
 acatccaagt atattttaca aacagcagtg gttttgcttg gttttggatt aaacctaacc 240
 caagttatgg cagtgggcat gcagtcctta ccgattatca tttcaactat tgcgacagct 300
 cttttggtag cttatggctt acagaaatgg ctgcgcttag atgtcaatac agccaccttg 360
 gtaggtgtag gatcttccat ttgtgggggg tctgctgttg cagcgacagc tctgtcatt 420
 aaggcaaagg atgacgaggt tgctaaggca atttcagtca tttttctctt taatatgtta 480
 gcagctttgc tatttccaag tttaggacaa ttactaggct tatctaataga aggttttgct 540
 atttttgccg ggacagctgt taacgacact tcttccgtga ctgcaacggc cacggcctgg 600
 gatgcccttc accattccaa taccactagat ggagcaacca ttgttaaatt gactcgcacc 660
 ttggctattc tcccaattac tttaggttta tccctttacc gagcgaaaaa agagcacgac 720
 atcgttacag aagaaaactt tagccttagg aagtcattcc ctcgtttcat cctcttcttt 780
 ttattagctt ctctcatcac aacattgatg accagtttgg gagtttctgc cgatagtttc 840
 cattaccta aaaccttatt aaaattcttt atcgtgatgg ctatggcagc gattgggtta 900

aacacaaacc tggtaaact gattaagacg ggcggtcagg ctatcctttt aggagctatt 960
 tgctgggtag ctatcacctt tgtcagttta gccatgcaat taagtttggg catttggttaa 1020

<210> 40

<211> 339

<212> PRT

<213> Streptococcus pyogenes

<400> 40

Met Ser Thr His Leu Arg Lys Leu Pro Gly Leu Leu Leu Cys Leu Leu
 1 5 10 15

Leu Ala Leu Pro Ala Trp Cys Leu Gly Arg Leu Phe Pro Ile Ile Gly
 20 25 30

Ala Pro Val Phe Ala Ile Leu Leu Gly Met Leu Leu Ala Leu Phe Tyr
 35 40 45

Glu His Arg Asp Lys Thr Lys Glu Gly Ile Ser Phe Thr Ser Lys Tyr
 50 55 60

Ile Leu Gln Thr Ala Val Val Leu Leu Gly Phe Gly Leu Asn Leu Thr
 65 70 75 80

Gln Val Met Ala Val Gly Met Gln Ser Leu Pro Ile Ile Ile Ser Thr
 85 90 95

Ile Ala Thr Ala Leu Leu Val Ala Tyr Gly Leu Gln Lys Trp Leu Arg
 100 105 110

Leu Asp Val Asn Thr Ala Thr Leu Val Gly Val Gly Ser Ser Ile Cys
 115 120 125

Gly Gly Ser Ala Val Ala Ala Thr Ala Pro Val Ile Lys Ala Lys Asp
 130 135 140

Asp Glu Val Ala Lys Ala Ile Ser Val Ile Phe Leu Phe Asn Met Leu
 145 150 155 160

Ala Ala Leu Leu Phe Pro Ser Leu Gly Gln Leu Leu Gly Leu Ser Asn
 165 170 175

Glu Gly Phe Ala Ile Phe Ala Gly Thr Ala Val Asn Asp Thr Ser Ser
 180 185 190

Val Thr Ala Thr Ala Thr Ala Trp Asp Ala Leu His His Ser Asn Thr
 195 200 205

Leu Asp Gly Ala Thr Ile Val Lys Leu Thr Arg Thr Leu Ala Ile Leu
210 215 220

Pro Ile Thr Leu Gly Leu Ser Leu Tyr Arg Ala Lys Lys Glu His Asp
225 230 235 240

Ile Val Thr Glu Glu Asn Phe Ser Leu Arg Lys Ser Phe Pro Arg Phe
245 250 255

Ile Leu Phe Phe Leu Leu Ala Ser Leu Ile Thr Thr Leu Met Thr Ser
260 265 270

Leu Gly Val Ser Ala Asp Ser Phe His Tyr Leu Lys Thr Leu Ser Lys
275 280 285

Phe Phe Ile Val Met Ala Met Ala Ala Ile Gly Leu Asn Thr Asn Leu
290 295 300

Val Lys Leu Ile Lys Thr Gly Gly Gln Ala Ile Leu Leu Gly Ala Ile
305 310 315 320

Cys Trp Val Ala Ile Thr Leu Val Ser Leu Ala Met Gln Leu Ser Leu
325 330 335

Gly Ile Trp

<210> 41

<211> 2637

<212> DNA

<213> Streptococcus pyogenes

<400> 41

atgataaaga aaaccttatg gaaggatatt ttgagagcta tcaagaatag taaagggcga 60
ttcatttcct tatttttcct aatggcctta ggctcctttg ctttagttgg acttaaagtc 120
accggtccag atatggaacg aacagccagc cgttacctcg aaagacacca ggtgatggac 180
ctaacggtac tggcttctca tcaattttcc caagccgata aacaagagtt agatacgtta 240
aaaggggctc atttagaata tggtcattta cttgatgtca gtctaactag caaccagaaa 300
tctcttaggc tctatagcgt gccaaagaaa gtgtctaagc cagtcttggt taaagggagt 360
tgcccaaagc gagagacaga tttgggttta tcctcctcac ttgctaaaaa ctatcagatt 420
ggagatgaac tagcagtcac ctcacctatg gaaggtttgc tgacgacaac ccattttcaa 480
gtggttggtt ttgcgaattc ttcagaagtt tggccaagt ccaatttagg aagttcctca 540
accggagatg gaagtctcta cgcttatgct tttgttaatc caaacgtttt taaaagtgcc 600
tttaacctgc tgcgcatccg ttttagtcat cttcgtctga caaacgcttt ttccaaagac 660
tatcaaaaaa gggtaaccca aaaccaagct catttgata atctacttaa agataatggc 720

cagaagcgtt atgatgacct ccaaaatcag tatgaccttg ccttaaaaaa tggcagagca 780
 gcacttgcaa aggaaacagt gaaactagct gcgagtggagg agaacttaac ttttttagaa 840
 ggctctgctt tacaagaagc taagcatcag attgaacaag gcaaacaagc attagccaag 900
 gaggaaaagc agttagagca ggtgcaggct acaaaagata agctagaaaa acccagttac 960
 ctgacttata atcgctcgac cctaccagga ggagaaggat atcatactta tgcaacttca 1020
 acgacctcca tttcaaagtgt tggaaatatt tttcctggtt ttctttatct cgtagctgct 1080
 ctagtagcct ttaccaccat gacacgttat gttgatgaag aaagaacaag ctctgggtcta 1140
 ttaaaagcca ttgggttattc taacaaggat atcagtttaa agtttcttat ctatgggctt 1200
 ttagccagtt ttttagggac aacttttaggt attattgggg gaacttacct cttatctacc 1260
 ttgatttcag agatcttaac aggagctttg actattggaa agactcacct ttatagttat 1320
 tggttttata atggcatagc ttacttgctg gctatgttat ctgctgtttt accagcctac 1380
 ttaattgtca aaaaggaatt attcctcaat gcagctcagt tattgctgcc caaacctcct 1440
 agtaaggggg caaaaatctg gttggaacac cttacttttg tctggaaagc cctgtccttt 1500
 actcacaagg tgaccatacg taatatTTTT cgctataaac aaagaatgct gatgaccatt 1560
 gtaggcgttg caggctcagt agccctttta tttgcaggct tagggattca gtcgtcatta 1620
 gccaaagtag ttgagcatca atttgggtgat ttaacgactt atgatatttt ggctgtcgg 1680
 tcggccaaag cgacagcgac agagcaaact gacttagcta gctatcttaa acaagaacct 1740
 attacagggt accaaaagggt atcttatgcc agcttaacct ttctgtaaa gggattacct 1800
 gataagcaaa gtatttccat tttatcaagt tcagctactt ctcttagtcc ctattttaat 1860
 ctgctggata gtcaggagca aaagaagggt cccattccaa cctctggtgt tttgatttct 1920
 gagaaattag cctcctatta caaggtaaaa ccagggtgac agttgggtatt gactgatcgg 1980
 aaaggacagt cttataaagt gacgattaaa cagggtattg acatgacagt tggccattac 2040
 ctgataatgt ctgataccta ttttaagaat catttttaaag gattggaggc tgctcctgcc 2100
 tatctgatta aggtaaaaga caaagatagc aagcacataa aggagacagc cagtgacttg 2160
 ttaaccttaa aagcgattag agcagtttca caaacgtca atcatattaa atctgttcag 2220
 ctagtagtca cctctcttaa tcaggtcagt accctccttg tcttcttgct tattttatta 2280
 gcaatcgta tcttttataa cttacgact attaatattg ctgagcgtat tcgagaatta 2340
 tccactatta aagttctggg attttacgat caggagggtca ccttatatat ttatcgagaa 2400
 actatttcgc tatccctagt aggcattctt ttaggtatct atttaggaaa aggcctgcat 2460
 acttatatca tgacaatgat ttcaactggg gatattcaat ttggtgtaaa ggttgatgct 2520
 tatgtttatc tagtgccaat tctagtaatc cttagcttgt tagcggtatt aggtatctgg 2580
 gttaatcgcc atttaaaaaa ggttgatatg ttagaagctt tgaaatccat agattga 2637

<210> 42

<211> 878

<212> PRT

<213> Streptococcus pyogenes

<400> 42

Met Ile Lys Lys Thr Leu Trp Lys Asp Ile Leu Arg Ala Ile Lys Asn
 1 5 10 15

Ser Lys Gly Arg Phe Ile Ser Leu Phe Phe Leu Met Ala Leu Gly Ser
 20 25 30

Phe Ala Leu Val Gly Leu Lys Val Thr Gly Pro Asp Met Glu Arg Thr
 35 40 45

Ala Ser Arg Tyr Leu Glu Arg His Gln Val Met Asp Leu Thr Val Leu
 50 55 60

Ala Ser His Gln Phe Ser Gln Ala Asp Lys Gln Glu Leu Asp Thr Leu
 65 70 75 80

Lys Gly Ala His Leu Glu Tyr Gly His Leu Leu Asp Val Ser Leu Thr
 85 90 95

Ser Asn Gln Lys Ser Leu Arg Leu Tyr Ser Val Pro Lys Lys Val Ser
 100 105 110

Lys Pro Val Leu Val Lys Gly Ser Trp Pro Lys Arg Glu Thr Asp Leu
 115 120 125

Val Leu Ser Ser Ser Leu Ala Lys Asn Tyr Gln Ile Gly Asp Glu Leu
 130 135 140

Ala Val Thr Ser Pro Met Glu Gly Leu Leu Thr Thr Thr His Phe Gln
 145 150 155 160

Val Val Gly Phe Ala Asn Ser Ser Glu Val Trp Ser Lys Ser Asn Leu
 165 170 175

Gly Ser Ser Ser Thr Gly Asp Gly Ser Leu Tyr Ala Tyr Ala Phe Val
 180 185 190

Asn Pro Asn Val Phe Lys Ser Ala Phe Asn Leu Leu Arg Ile Arg Phe
 195 200 205

Ser His Leu Arg Leu Thr Asn Ala Phe Ser Lys Asp Tyr Gln Lys Arg
 210 215 220

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

Gln Lys Arg Tyr Asp Asp Leu Gln Asn Gln Tyr Asp Leu Ala Leu Lys
 245 250 255

Asn Gly Arg Ala Ala Leu Ala Lys Glu Thr Val Lys Leu Ala Ala Ser
 260 265 270

Glu Glu Asn Leu Thr Phe Leu Glu Gly Ser Ala Leu Gln Glu Ala Lys
 275 280 285

His Gln Ile Glu Gln Gly Lys Gln Ala Leu Ala Lys Glu Glu Lys Gln
 290 295 300

Leu Glu Gln Val Gln Ala Thr Lys Asp Lys Leu Glu Lys Pro Ser Tyr
 305 310 315 320
 Leu Thr Tyr Asn Arg Ser Thr Leu Pro Gly Gly Glu Gly Tyr His Thr
 325 330 335
 Tyr Ala Thr Ser Thr Thr Ser Ile Ser Asn Val Gly Asn Ile Phe Pro
 340 345 350
 Val Val Leu Tyr Leu Val Ala Ala Leu Val Ala Phe Thr Thr Met Thr
 355 360 365
 Arg Tyr Val Asp Glu Glu Arg Thr Ser Ser Gly Leu Leu Lys Ala Ile
 370 375 380
 Gly Tyr Ser Asn Lys Asp Ile Ser Leu Lys Phe Leu Ile Tyr Gly Leu
 385 390 395 400
 Leu Ala Ser Phe Leu Gly Thr Thr Leu Gly Ile Ile Gly Gly Thr Tyr
 405 410 415
 Leu Leu Ser Thr Leu Ile Ser Glu Ile Leu Thr Gly Ala Leu Thr Ile
 420 425 430
 Gly Lys Thr His Leu Tyr Ser Tyr Trp Phe Tyr Asn Gly Ile Ala Tyr
 435 440 445
 Leu Leu Ala Met Leu Ser Ala Val Leu Pro Ala Tyr Leu Ile Val Lys
 450 455 460
 Lys Glu Leu Phe Leu Asn Ala Ala Gln Leu Leu Leu Pro Lys Pro Pro
 465 470 475 480
 Ser Lys Gly Ala Lys Ile Trp Leu Glu His Leu Thr Phe Val Trp Lys
 485 490 495
 Ala Leu Ser Phe Thr His Lys Val Thr Ile Arg Asn Ile Phe Arg Tyr
 500 505 510
 Lys Gln Arg Met Leu Met Thr Ile Val Gly Val Ala Gly Ser Val Ala
 515 520 525
 Leu Leu Phe Ala Gly Leu Gly Ile Gln Ser Ser Leu Ala Lys Val Val
 530 535 540
 Glu His Gln Phe Gly Asp Leu Thr Thr Tyr Asp Ile Leu Ala Val Gly
 545 550 555 560

Ser Ala Lys Ala Thr Ala Thr Glu Gln Thr Asp Leu Ala Ser Tyr Leu
 565 570 575
 Lys Gln Glu Pro Ile Thr Gly Tyr Gln Lys Val Ser Tyr Ala Ser Leu
 580 585 590
 Thr Leu Pro Val Lys Gly Leu Pro Asp Lys Gln Ser Ile Ser Ile Leu
 595 600 605
 Ser Ser Ser Ala Thr Ser Leu Ser Pro Tyr Phe Asn Leu Leu Asp Ser
 610 615 620
 Gln Glu Gln Lys Lys Val Pro Ile Pro Thr Ser Gly Val Leu Ile Ser
 625 630 635 640
 Glu Lys Leu Ala Ser Tyr Tyr Lys Val Lys Pro Gly Asp Gln Leu Val
 645 650 655
 Leu Thr Asp Arg Lys Gly Gln Ser Tyr Lys Val Thr Ile Lys Gln Val
 660 665 670
 Ile Asp Met Thr Val Gly His Tyr Leu Ile Met Ser Asp Thr Tyr Phe
 675 680 685
 Lys Asn His Phe Lys Gly Leu Glu Ala Ala Pro Ala Tyr Leu Ile Lys
 690 695 700
 Val Lys Asp Lys Asp Ser Lys His Ile Lys Glu Thr Ala Ser Asp Leu
 705 710 715 720
 Leu Thr Leu Lys Ala Ile Arg Ala Val Ser Gln Asn Val Asn His Ile
 725 730 735
 Lys Ser Val Gln Leu Val Val Thr Ser Leu Asn Gln Val Met Thr Leu
 740 745 750
 Leu Val Phe Leu Ser Ile Leu Leu Ala Ile Val Ile Leu Tyr Asn Leu
 755 760 765
 Thr Thr Ile Asn Ile Ala Glu Arg Ile Arg Glu Leu Ser Thr Ile Lys
 770 775 780
 Val Leu Gly Phe Tyr Asp Gln Glu Val Thr Leu Tyr Ile Tyr Arg Glu
 785 790 795 800
 Thr Ile Ser Leu Ser Leu Val Gly Ile Leu Leu Gly Ile Tyr Leu Gly
 805 810 815

Lys Gly Leu His Thr Tyr Ile Met Thr Met Ile Ser Thr Gly Asp Ile
 820 825 830

Gln Phe Gly Val Lys Val Asp Ala Tyr Val Tyr Leu Val Pro Ile Leu
 835 840 845

Val Ile Leu Ser Leu Leu Ala Val Leu Gly Ile Trp Val Asn Arg His
 850 855 860

Leu Lys Lys Val Asp Met Leu Glu Ala Leu Lys Ser Ile Asp
 865 870 875

<210> 43

<211> 1344

<212> DNA

<213> Streptococcus pyogenes

<400> 43

```

atgatgttaa cgaaggggca acttccctat agtgcgtgctt ttacaacagg agggctcttt 60
tactttgtta tcattgcatt aagtattat ttgggatcga cactttggct agtctttggt 120
caggtgtttt gtttttactt atctggttta tatctttata aactcattaa ttatatgaca 180
ggctttcaaa aagtggcttt aactttttca attagctact atttattatc tgtagtctt 240
ggttttgggg gattgtatcc tactcaactg gctatgccat ttatattaat atcggttgg 300
ttttaacta agtattttgc ctggttagtg aaagatgagg catttattct ttttggcttt 360
gtaggtgctc ttgcaatgct aattgacccg agtaccctta tcttttggtc ttttgcttgt 420
gtgacagttt tttcttataa tataagccaa aagcatcttg caagagggtt ttatcaactg 480
ctagcttcga tttttggaat gattttagtt ttttacacag caggatattt cattttgaac 540
ttacaagtgc taaatcctta tttatcacia acgatgattt atccttttac tttttttaa 600
tcaggaaact tatcgttgct ttttggactg gctattcagt tgttcttcgc tttggggctt 660
ggtcttttga cgggaatgga gaatgtcatt aggcgattta aaaacaattc tgatagggtc 720
gtcaagtggc tatttgtcat ggtcattcta gaatctatac ttgtggctat attttcacia 780
gactatcgcc cctatcatct tttacctctt ttaccttttg gattaatttt gactgctatt 840
cctgttggct atcagtatgg tataggatta ggtcagagta gtcacgcag acgtcatggt 900
aaaaatggtg ttggtcgagt aatgatgatt tatcttaaga gacacttta tttgccaatt 960
ttaattgtag ggacaatact aatctgttct acttattggt tcattagtag tattcctctt 1020
aatcaggagc gtgatcatat tgctagtatt ttagaacaga aactaaataa aactcaatct 1080
atttatgttt gggatgatac ttctaaaatt tatttggaca gtaaagctaa atctgtttct 1140
caatttagtt ctcctgacat caatacgcaa aaagagagtc atcgaaaaat attagaagat 1200
gaactatlag aaaataaggc tgcttatatc gttgttaatc gctataaaaa cctgcctaaa 1260
atcattcaaa aagtattatc tactaattac aaagtagata aacagataac gacaaaaagt 1320
tttattgttt atcagaaaaa gtaa                                     1344

```

<210> 44

<211> 447

<212> PRT

<213> Streptococcus pyogenes

<400> 44

```

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

Gly Gly Leu Phe Tyr Phe Val Ile Ile Ala Leu Ser Tyr Tyr Leu Gly
      20              25              30

Ser Thr Leu Trp Leu Val Phe Val Gln Val Phe Cys Phe Tyr Leu Ser
      35              40              45

Gly Leu Tyr Leu Tyr Lys Leu Ile Asn Tyr Met Thr Gly Phe Gln Lys
      50              55              60

Val Ala Leu Thr Phe Ser Ile Ser Tyr Tyr Leu Leu Ser Val Ser Leu
      65              70              75              80

Gly Phe Gly Gly Leu Tyr Pro Thr Gln Leu Ala Met Pro Phe Ile Leu
      85              90              95

Ile Ser Ala Trp Phe Leu Thr Lys Tyr Phe Ala Cys Leu Val Lys Asp
      100              105              110

Glu Ala Phe Ile Leu Phe Gly Phe Val Gly Ala Leu Ala Met Leu Ile
      115              120              125

Asp Pro Ser Thr Leu Ile Phe Trp Ser Phe Ala Cys Val Thr Val Phe
      130              135              140

Ser Tyr Asn Ile Ser Gln Lys His Leu Ala Arg Gly Phe Tyr Gln Leu
      145              150              155              160

Leu Ala Ser Ile Phe Gly Met Ile Leu Val Phe Tyr Thr Ala Gly Tyr
      165              170              175

Phe Ile Leu Asn Leu Gln Val Leu Asn Pro Tyr Leu Ser Gln Thr Met
      180              185              190

Ile Tyr Pro Phe Thr Phe Phe Lys Ser Gly Asn Leu Ser Leu Leu Phe
      195              200              205

Gly Leu Ala Ile Gln Leu Phe Phe Ala Leu Gly Leu Gly Leu Leu Thr
      210              215              220

Gly Met Glu Asn Val Ile Arg Arg Phe Lys Asn Asn Ser Asp Arg Val
      225              230              235              240

```

Val Lys Trp Leu Phe Val Met Val Ile Leu Glu Ser Ile Leu Val Ala
 245 250 255

 Ile Phe Ser Gln Asp Tyr Arg Pro Tyr His Leu Leu Pro Leu Leu Pro
 260 265 270

 Phe Gly Leu Ile Leu Thr Ala Ile Pro Val Gly Tyr Gln Tyr Gly Ile
 275 280 285

 Gly Leu Gly Gln Ser Ser His Arg Arg Arg His Gly Lys Asn Gly Val
 290 295 300

 Gly Arg Val Met Met Ile Tyr Leu Lys Arg His Phe Tyr Leu Pro Ile
 305 310 315 320

 Leu Ile Val Gly Thr Ile Leu Ile Cys Ser Thr Tyr Cys Phe Ile Ser
 325 330 335

 Ser Ile Pro Leu Asn Gln Glu Arg Asp His Ile Ala Ser Tyr Leu Glu
 340 345 350

 Gln Lys Leu Asn Lys Thr Gln Ser Ile Tyr Val Trp Asp Asp Thr Ser
 355 360 365

 Lys Ile Tyr Leu Asp Ser Lys Ala Lys Ser Val Ser Gln Phe Ser Ser
 370 375 380

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

 Glu Leu Leu Glu Asn Lys Ala Ala Tyr Ile Val Val Asn Arg Tyr Lys
 405 410 415

 Asn Leu Pro Lys Ile Ile Gln Lys Val Leu Ser Thr Asn Tyr Lys Val
 420 425 430

 Asp Lys Gln Ile Thr Thr Lys Ser Phe Ile Val Tyr Gln Lys Lys
 435 440 445

<210> 45
 <211> 324
 <212> DNA
 <213> Streptococcus pyogenes

 <400> 45

atgcagtttt tacaaaaatg gtttaaacac tctaaaaaag agaagttgaa agaatcctcg 60
 tcccttagta cagaaataga accttctgaa aactgggcaa agattcccgc ttatatctct 120
 gcagacaaaa gtgattacaa aaagggtact ttaattacca gtgttattgc tgctgggcca 180
 tagacctaat agtcaattca aggttaaacy cattctcaag cgcaatcctg aggcaatcac 240
 tgtttcttta attgcttcaa gtatcgctgc aggtgtttac ccagaaagtc agtttcgggt 300
 gacatccatc tattgcaaaa gtaa 324

<210> 46

<211> 107

<212> PRT

<213> Streptococcus pyogenes

<400> 46

Met Gln Phe Leu Gln Lys Trp Phe Lys His Ser Lys Lys Glu Lys Leu
 1 5 10 15

Lys Glu Ser Ser Pro Leu Ser Thr Glu Ile Glu Pro Ser Glu Asn Trp
 20 25 30

Glu Lys Ile Pro Ala Tyr Ile Pro Ala Asp Lys Ser Asp Tyr Lys Lys
 35 40 45

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

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

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

Gln Phe Arg Val Thr Ser Ile Tyr Cys Lys Arg
 100 105

<210> 47

<211> 288

<212> DNA

<213> Streptococcus pyogenes

<400> 47

atgacaaaac gtaattcaaa agcctatata ttatggcaaa aaattatcaa aatttttagga 60
 attattgcac taattggtac ttttttcttc gctttttggc tgtatagact aggtatatta 120
 aacgatagta atgctcttaa agacttagtg cagcgctata gattatgggg gccgtttggt 180
 tttattgtcg tgcagatcat acagattggt tttcctgtga ttcctggagg ccttacgaca 240
 gttgcaggtt ttttaatctt tggccctgt aacaggtttt atttataa 288

<210> 48
 <211> 95
 <212> PRT
 <213> Streptococcus pyogenes

<400> 48
 Met Thr Lys Arg Asn Ser Lys Ala Tyr Ile Leu Trp Gln Lys Ile Ile
 1 5 10 15

 Lys Ile Leu Gly Ile Ile Ala Leu Ile Gly Thr Phe Phe Leu Ala Phe
 20 25 30

 Trp Leu Tyr Arg Leu Gly Ile Leu Asn Asp Ser Asn Ala Leu Lys Asp
 35 40 45

 Leu Val Gln Arg Tyr Arg Leu Trp Gly Pro Phe Val Phe Ile Val Val
 50 55 60

 Gln Ile Ile Gln Ile Val Phe Pro Val Ile Pro Gly Gly Leu Thr Thr
 65 70 75 80

 Val Ala Gly Phe Leu Ile Phe Gly Pro Cys Asn Arg Phe Tyr Leu
 85 90 95

<210> 49
 <211> 1311
 <212> DNA
 <213> Streptococcus pyogenes

<400> 49
 atgaataaat taaaaaaaga gattttatca gataactata accacttttt tcattttttt 60
 gcggttttta caggtatttt tgcattatg actattatta tcttacagat tatgcggttt 120
 ggcgttttatt cgtcagttga cagtagttta gtttctgta gtaataatgc aagtagctat 180
 gctaatacgta cgatggctag aatatcttct ttttactttg atactgaaaa taacattatt 240
 aaggcgctgc ctgattcaga tagttctaag ttattaggaa cgctgcagc taatacagat 300
 atcattttgt ttagtgctaa tggaacaatt ttaaatgctt ttgatgcgtt ttctaactat 360
 caaaattttc atttagataa acgccggttg gggagtattg aaaccaccag tttaatgaat 420
 ttttatggac aagaagaaaa ataccatacg ataactgtag gggttcatat caaaaattat 480
 cctgcagttg cctatatgat ggcagtagta aatgtggaac aattagaccg cgctaataaa 540
 cgttatgagc gcattattat tatagttatg agtggttttt ggctaatttc tatttttagca 600
 agtattttatt tagccaagtg gagcagaaaa cctatttttag aaagctatga aaaacaaaaa 660
 atgtttgttg aaaatgctag tcatgaatta aggacccctt tggcggtcct acagaatcgt 720
 ctggaatcgc tttttcgtaa gcccaacgaa acgatattag aaaatagtga gcatctcgct 780
 tctagtttag acgaggttcg caacatgcgc atcttaacaa ctaatttatt aaatttagca 840

```

agacgagatg atggcattaa tccacagtgg actcatttag atacagattt ttttaatgct 900
atTTTTgaga attatgaact agttgctaaa gaatatggaa aaatatTTta ttttcagaac 960
caagtcaata gatcgTTaag aatggataag gctttactaa aacaattaat aacgattTTa 1020
tttgacaatg ctattaaata tacagataaa aatggTatta ttgaaattat agtgaaaaca 1080
acggacaaaa atTTattaat ttctgttatt gataatggTc cagggataac agatgaagaa 1140
aagaaaaaga tttttgatcg tttttatcga gttgacaaag ctagaacacg gcaaacaggt 1200
ggatttggct tggggTtggc tttagctcag caaatcgTga tgtctTTaaa aggaaatatt 1260
acagtaaagg ataatgatcc taaaggtagt atTTTTgaag tcaaactata a 1311

```

<210> 50

<211> 436

<212> PRT

<213> Streptococcus pyogenes

<400> 50

```

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

```

```

Phe His Phe Phe Ala Val Phe Thr Gly Ile Phe Val Ile Met Thr Ile
      20              25              30

```

```

Ile Ile Leu Gln Ile Met Arg Phe Gly Val Tyr Ser Ser Val Asp Ser
    35              40              45

```

```

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

```

```

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

```

```

Lys Ala Leu Pro Asp Ser Asp Ser Ser Lys Leu Leu Gly Thr Pro Ala
      85              90              95

```

```

Ala Asn Thr Asp Ile Ile Leu Phe Ser Ala Asn Gly Thr Ile Leu Asn
    100              105              110

```

```

Ala Phe Asp Ala Phe Ser Asn Tyr Gln Asn Phe His Leu Asp Lys Arg
    115              120              125

```

```

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

```

```

Glu Glu Lys Tyr His Thr Ile Thr Val Gly Val His Ile Lys Asn Tyr
    145              150              155              160

```

```

Pro Ala Val Ala Tyr Met Met Ala Val Val Asn Val Glu Gln Leu Asp
      165              170              175

```

Arg Ala Asn Glu Arg Tyr Glu Arg Ile Ile Ile Ile Val Met Ser Val
 180 185 190

Phe Trp Leu Ile Ser Ile Leu Ala Ser Ile Tyr Leu Ala Lys Trp Ser
 195 200 205

Arg Lys Pro Ile Leu Glu Ser Tyr Glu Lys Gln Lys Met Phe Val Glu
 210 215 220

Asn Ala Ser His Glu Leu Arg Thr Pro Leu Ala Val Leu Gln Asn Arg
 225 230 235 240

Leu Glu Ser Leu Phe Arg Lys Pro Asn Glu Thr Ile Leu Glu Asn Ser
 245 250 255

Glu His Leu Ala Ser Ser Leu Asp Glu Val Arg Asn Met Arg Ile Leu
 260 265 270

Thr Thr Asn Leu Leu Asn Leu Ala Arg Arg Asp Asp Gly Ile Asn Pro
 275 280 285

Gln Trp Thr His Leu Asp Thr Asp Phe Phe Asn Ala Ile Phe Glu Asn
 290 295 300

Tyr Glu Leu Val Ala Lys Glu Tyr Gly Lys Ile Phe Tyr Phe Gln Asn
 305 310 315 320

Gln Val Asn Arg Ser Leu Arg Met Asp Lys Ala Leu Leu Lys Gln Leu
 325 330 335

Ile Thr Ile Leu Phe Asp Asn Ala Ile Lys Tyr Thr Asp Lys Asn Gly
 340 345 350

Ile Ile Glu Ile Ile Val Lys Thr Thr Asp Lys Asn Leu Leu Ile Ser
 355 360 365

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

Phe Asp Arg Phe Tyr Arg Val Asp Lys Ala Arg Thr Arg Gln Thr Gly
 385 390 395 400

Gly Phe Gly Leu Gly Leu Ala Leu Ala Gln Gln Ile Val Met Ser Leu
 405 410 415

Lys Gly Asn Ile Thr Val Lys Asp Asn Asp Pro Lys Gly Ser Ile Phe
 420 425 430

Glu Val Lys Leu
435

<210> 51
<211> 699
<212> DNA
<213> Streptococcus pyogenes

<400> 51
atgttttctg gacatcaact aaaaacagca cgattatcaa agggaataac tcaatcagaa 60
ttgggaagat tggtgcatgt caataaaatg acaatatcta attgggaaaa aggtaagaat 120
ataccaaatg aaaaacattt aaatgcctta ttgcatctat tcaatgtgac atctgattat 180
ttcgacccaa actatagatt gctaacgcct tataaccagc tgacaatata taataaagaa 240
aaagtaattg gctattcaga gcgattgtta aatcatcaaa tagacaaaaa atctaaagat 300
ctcatagata aaccatcaca attatatgct tatcggttct atgaaagttt atctgctggt 360
actggttact cctatttttg tgatggtaac tttgatgttg tcttttacga tgaacaatta 420
gaatacgatt ttgcgtcttg ggtttttgga gattctatgg agccaactta tttaaatggt 480
gaagttgttc ttataaaaca aaatagtttt gattacgatg gagcaattta tgcagtcgaa 540
tgggatgggc aaacatatat caaaaaggta tttcgtgaag atgagggatt acgtctagt 600
tccttaata aaaaatattc tgataagttt gctccctata gcgaagaacc tcgcattatt 660
ggcaaaatta tcgctaattt taggcctta gaaatttaa 699

<210> 52
<211> 232
<212> PRT
<213> Streptococcus pyogenes

<400> 52
Met Phe Ser Gly His Gln Leu Lys Thr Ala Arg Leu Ser Lys Gly Ile
1 5 10 15
Thr Gln Ser Glu Leu Gly Arg Leu Leu His Val Asn Lys Met Thr Ile
20 25 30
Ser Asn Trp Glu Lys Gly Lys Asn Ile Pro Asn Glu Lys His Leu Asn
35 40 45
Ala Leu Leu His Leu Phe Asn Val Thr Ser Asp Tyr Phe Asp Pro Asn
50 55 60
Tyr Arg Leu Leu Thr Pro Tyr Asn Gln Leu Thr Ile Ser Asn Lys Glu
65 70 75 80
Lys Val Ile Gly Tyr Ser Glu Arg Leu Leu Asn His Gln Ile Asp Lys

	85		90		95
Lys Ser Lys Asp Leu Ile Asp Lys Pro Ser Gln Leu Tyr Ala Tyr Arg					
	100		105		110
Val Tyr Glu Ser Leu Ser Ala Gly Thr Gly Tyr Ser Tyr Phe Gly Asp					
	115		120		125
Gly Asn Phe Asp Val Val Phe Tyr Asp Glu Gln Leu Glu Tyr Asp Phe					
	130		135		140
Ala Ser Trp Val Phe Gly Asp Ser Met Glu Pro Thr Tyr Leu Asn Gly					
	145		150		155
Glu Val Val Leu Ile Lys Gln Asn Ser Phe Asp Tyr Asp Gly Ala Ile					
	165		170		175
Tyr Ala Val Glu Trp Asp Gly Gln Thr Tyr Ile Lys Lys Val Phe Arg					
	180		185		190
Glu Asp Glu Gly Leu Arg Leu Val Ser Leu Asn Lys Lys Tyr Ser Asp					
	195		200		205
Lys Phe Ala Pro Tyr Ser Glu Glu Pro Arg Ile Ile Gly Lys Ile Ile					
	210		215		220
Ala Asn Phe Arg Pro Leu Glu Ile					
	225		230		

<210> 53
 <211> 1497
 <212> DNA
 <213> Streptococcus pyogenes

<400> 53
 ttgaaaaggg ttcccgtaga aagagacaaa cgcttagtct ctttcttttt ctttcttctc 60
 atttctgtta taataagtca ggtaactaca ttagaaagat ttgtgggtct gtcattctaag 120
 agatgtcatt cccgaagagg tattagtgc ttgtctcaat caactgcaac ttatattaat 180
 gttattggag ctgggctagc tgggtctgaa gctgcctatc agattgctaa gcgcgggtatc 240
 cccgttaa at tgtatgaaat gcgtgggtgc aaagcaacac cgcaacataa aaccactaat 300
 ttgcccgaat tgggtctgttc caactcattt cgtgggtgata gcttaaccaa tgcagtcggt 360
 cttctcaaag aagaaatgcg gcgattagac tccattatta tgcgtaatgg tgaagctaac 420
 cgcgtagctg ctgggggagc aatggctggt gaccgtgagg ggtatgcaga gagtgtcact 480
 gcagagttgg aaaatcatcc tctcattgag gtcattcgtg gtgaaattac agaaatccct 540
 gacgatgcta tcacggttat cgcgacggga ccgctgactt cggatgccct ggcagaaaaa 600
 attcacgcgc taaatggtgg cgacggattc tatttttacg atgcagcagc gcctatcatt 660

gataaatcta ccattgatat gagcaaggtt taccttaa at ctcgctacga taaaggcgaa 720
 gctgcttacc tcaactgccc tatgacccaa gaagaattca tggctttcca tgaagctctg 780
 acaaccgcag aagaagcccc gctgaatgcc tttgaaaaag aaaagtat tt tgaaggctgt 840
 atgccgattg aagttatggc taaacgtggc attaaaacca tgctttatgg acctatgaaa 900
 cccgttggat tggaaatatcc agatgactat acaggtcctc gcgatggaga atttaaaacg 960
 ccatatgccg tcgtgcaatt gcgtcaagat aatgcagctg gaagccttta taatatcggt 1020
 gggtttccaaa cccatctcaa atgggggtgag caaaaacgcg ttttccaaat gattccaggg 1080
 cttgaaaatg ctgagtttgt ccgctacggc gtcatgcac gcaattccta tatggattca 1140
 ccaaattctt taaccgaaac cttccaatct cggagcaatc caaacctttt ctttgcaggt 1200
 cagatgactg gagttgaagg ttatgtcgaa tcagctgctt caggtttagt agcaggaatc 1260
 aatgctgctc gtttgttcaa aagagaagaa gcacttat ttctcagac aacagctatt 1320
 gggagtttgc ctcattatgt gactcatgcc gacagtaagc atttccaacc aatgaacgtc 1380
 aactttggca tcatcaaaga gttagaaggc ccacgcattc gtgacaaaaa agaacgttat 1440
 gaagctattg ctagtctgtc tttggcagat ttagacacct gcttagcgtc gctttaa 1497

<210> 54

<211> 498

<212> PRT

<213> Streptococcus pyogenes

<400> 54

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

1

5

10

15

Phe Phe Leu Leu Ile Ser Val Ile Ile Ser Gln Val Thr Thr Leu Glu

20

25

30

Arg Phe Val Gly Leu Ser Ser Lys Arg Cys His Ser Arg Arg Gly Ile

35

40

45

Ser Asp Leu Ser Gln Ser Thr Ala Thr Tyr Ile Asn Val Ile Gly Ala

50

55

60

Gly Leu Ala Gly Ser Glu Ala Ala Tyr Gln Asn Ala Lys Arg Gly Ile

65

70

75

80

Pro Val Lys Leu Tyr Glu Met Arg Gly Val Lys Ala Thr Pro Gln His

85

90

95

Lys Thr Thr Asn Phe Ala Glu Leu Val Cys Ser Asn Ser Phe Arg Gly

100

105

110

Asp Ser Leu Thr Asn Ala Val Gly Leu Leu Lys Glu Glu Met Arg Arg

115

120

125

Leu Asp Ser Ile Ile Met Arg Asn Gly Glu Ala Asn Arg Val Pro Ala

130

135

140

Gly Gly Ala Met Ala Val Asp Arg Glu Gly Tyr Ala Glu Ser Val Thr
 145 150 155 160

Ala Glu Leu Glu Asn His Pro Leu Ile Glu Val Ile Arg Gly Glu Ile
 165 170 175

Thr Glu Ile Pro Asp Asp Ala Ile Thr Val Ile Ala Thr Gly Pro Leu
 180 185 190

Thr Ser Asp Ala Leu Ala Glu Lys Ile His Ala Leu Asn Gly Gly Asp
 195 200 205

Gly Phe Tyr Phe Tyr Asp Ala Ala Ala Pro Ile Ile Asp Lys Ser Thr
 210 215 220

Ile Asp Met Ser Lys Val Tyr Leu Lys Ser Arg Tyr Asp Lys Gly Glu
 225 230 235 240

Ala Ala Tyr Leu Asn Cys Pro Met Thr Lys Glu Glu Phe Met Ala Phe
 245 250 255

His Glu Ala Leu Thr Thr Ala Glu Glu Ala Pro Leu Asn Ala Phe Glu
 260 265 270

Lys Glu Lys Tyr Phe Glu Gly Cys Met Pro Ile Glu Val Met Ala Lys
 275 280 285

Arg Gly Ile Lys Thr Met Leu Tyr Gly Pro Met Lys Pro Val Gly Leu
 290 295 300

Glu Tyr Pro Asp Asp Tyr Thr Gly Pro Arg Asp Gly Glu Phe Lys Thr
 305 310 315 320

Pro Tyr Ala Val Val Gln Leu Arg Gln Asp Asn Ala Ala Gly Ser Leu
 325 330 335

Tyr Asn Ile Val Gly Phe Gln Thr His Leu Lys Trp Gly Glu Gln Lys
 340 345 350

Arg Val Phe Gln Met Ile Pro Gly Leu Glu Asn Ala Glu Phe Val Arg
 355 360 365

Tyr Gly Val Met His Arg Asn Ser Tyr Met Asp Ser Pro Asn Leu Leu
 370 375 380

Thr Glu Thr Phe Gln Ser Arg Ser Asn Pro Asn Leu Phe Phe Ala Gly
 385 390 395 400

Gln Met Thr Gly Val Glu Gly Tyr Val Glu Ser Ala Ala Ser Gly Leu
 405 410 415

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

Ile Phe Pro Gln Thr Thr Ala Ile Gly Ser Leu Pro His Tyr Val Thr
 435 440 445

His Ala Asp Ser Lys His Phe Gln Pro Met Asn Val Asn Phe Gly Ile
 450 455 460

Ile Lys Glu Leu Glu Gly Pro Arg Ile Arg Asp Lys Lys Glu Arg Tyr
 465 470 475 480

Glu Ala Ile Ala Ser Arg Ala Leu Ala Asp Leu Asp Thr Cys Leu Ala
 485 490 495

Ser Leu

<210> 55

<211> 1539

<212> DNA

<213> Streptococcus pyogenes

<400> 55

atgattaagg atatgattga cagtattgag cagtttgctc agacacaggc tgattttcca 60
 gtttatgatt gtttagggga acgccgcact tacggacaac tcaaaagaga ttctgatagc 120
 attgctgcat ttatagatag cttagcttta ctggcaaaat ctccagtttt gggttttggg 180
 ggcgaaaactt atgatatgtt agctactttt gtagctttta ccaaactctgg tcatgcctat 240
 atcccagtag atgtgcattc agcaccagaa cgtatttttag cgattattga gattgcaaag 300
 cccagtttaa tcattgctat tgaggaattc cctcttacta ttgaagggat ttcccttgctc 360
 tcactatcag agattgagtc agcaaaatta gcagaaatgc cctatgagcg aacacattct 420
 gttaaaggag atgataatta ttacattatt ttcacctctg gaacaacggg ccaacaaaaa 480
 ggggtgcaaa tttcacatga caatcttttg agctttacca actggatgat cgaagatgca 540
 gcatttgatg tacctaaaca gccacaaatg ctggcgcagc caccctattc ctttgacctt 600
 tctgtcatgt actgggcacc taccttggtt ttaggtggaa ccttatttgc acttccaaaa 660
 gaattggtgg cagactttaa acagttattt acaacgattg cgcaacttcc agttggcatt 720
 tggacatcga ctccctcatt tgctgatatg gccatgctta gcgatgattt ttgccaggct 780
 aagatgccag ctttaacgca tttttatttt gatggcgaag aattaaccgt ttctacggct 840
 cgaaaactct ttgaacgttt cccgagtgcc aagattatca atgcctatgg accaacagaa 900
 gcgactgtag ccttatccgc tattgaaatt accagagaaa tggaggataa ttataccgcg 960
 ttgccgattg gctaccccaa accagattct ccgacctata ttattgatga agatggtaag 1020
 gagttatctt caggggagca gggtgaaatt attgttacag ggctgctgt gtcaaaaggt 1080

```

tacctcaaca atcctgagaa aaccgcagaa gctttcttta cttttaagag acagcctgct 1140
tatcatacag gggacattgg ctactgaca gaagataata ttttggtgta tgggtgggcgt 1200
ttggattttc agattaaata tgctgggtat cgtattgaac tagaagatgt ttcccaacag 1260
ttgaatcaat caccaatggg agcatcggtt gtggctgttc caaggtacaa taaagaacat 1320
aaggttcaaa atctcttggc ctatatcggt gtcaaagatg ggggttaaaga gcgttttgat 1380
aggggaattgg agttaaccaa agctatcaaa gcctctgtta aggatcatat gatgagttat 1440
atgatgcctt ctaagtttct ttatcgagat agtctaccat taactccaaa tggtaagata 1500
gatattaaaa ctttgattaa tgaggtcaat aaccgataa 1539

```

<210> 56

<211> 512

<212> PRT

<213> Streptococcus pyogenes

<400> 56

```

Met Ile Lys Asp Met Ile Asp Ser Ile Glu Gln Phe Ala Gln Thr Gln
  1             5             10             15

```

```

Ala Asp Phe Pro Val Tyr Asp Cys Leu Gly Glu Arg Arg Thr Tyr Gly
      20             25             30

```

```

Gln Leu Lys Arg Asp Ser Asp Ser Ile Ala Ala Phe Ile Asp Ser Leu
      35             40             45

```

```

Ala Leu Leu Ala Lys Ser Pro Val Leu Val Phe Gly Ala Gln Thr Tyr
      50             55             60

```

```

Asp Met Leu Ala Thr Phe Val Ala Leu Thr Lys Ser Gly His Ala Tyr
      65             70             75             80

```

```

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

```

```

Glu Ile Ala Lys Pro Ser Leu Ile Ile Ala Ile Glu Glu Phe Pro Leu
      100            105            110

```

```

Thr Ile Glu Gly Ile Ser Leu Val Ser Leu Ser Glu Ile Glu Ser Ala
      115            120            125

```

```

Lys Leu Ala Glu Met Pro Tyr Glu Arg Thr His Ser Val Lys Gly Asp
      130            135            140

```

```

Asp Asn Tyr Tyr Ile Ile Phe Thr Ser Gly Thr Thr Gly Gln Pro Lys
      145            150            155            160

```

```

Gly Val Gln Ile Ser His Asp Asn Leu Leu Ser Phe Thr Asn Trp Met
      165            170            175

```

Ile Glu Asp Ala Ala Phe Asp Val Pro Lys Gln Pro Gln Met Leu Ala
 180 185 190

Gln Pro Pro Tyr Ser Phe Asp Leu Ser Val Met Tyr Trp Ala Pro Thr
 195 200 205

Leu Ala Leu Gly Gly Thr Leu Phe Ala Leu Pro Lys Glu Leu Val Ala
 210 215 220

Asp Phe Lys Gln Leu Phe Thr Thr Ile Ala Gln Leu Pro Val Gly Ile
 225 230 235 240

Trp Thr Ser Thr Pro Ser Phe Ala Asp Met Ala Met Leu Ser Asp Asp
 245 250 255

Phe Cys Gln Ala Lys Met Pro Ala Leu Thr His Phe Tyr Phe Asp Gly
 260 265 270

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

Ser Ala Lys Ile Ile Asn Ala Tyr Gly Pro Thr Glu Ala Thr Val Ala
 290 295 300

Leu Ser Ala Ile Glu Ile Thr Arg Glu Met Val Asp Asn Tyr Thr Arg
 305 310 315 320

Leu Pro Ile Gly Tyr Pro Lys Pro Asp Ser Pro Thr Tyr Ile Ile Asp
 325 330 335

Glu Asp Gly Lys Glu Leu Ser Ser Gly Glu Gln Gly Glu Ile Ile Val
 340 345 350

Thr Gly Pro Ala Val Ser Lys Gly Tyr Leu Asn Asn Pro Glu Lys Thr
 355 360 365

Ala Glu Ala Phe Phe Thr Phe Lys Gly Gln Pro Ala Tyr His Thr Gly
 370 375 380

Asp Ile Gly Ser Leu Thr Glu Asp Asn Ile Leu Leu Tyr Gly Gly Arg
 385 390 395 400

Leu Asp Phe Gln Ile Lys Tyr Ala Gly Tyr Arg Ile Glu Leu Glu Asp
 405 410 415

Val Ser Gln Gln Leu Asn Gln Ser Pro Met Val Ala Ser Ala Val Ala
 420 425 430

Val Pro Arg Tyr Asn Lys Glu His Lys Val Gln Asn Leu Leu Ala Tyr
 435 440 445

Ile Val Val Lys Asp Gly Val Lys Glu Arg Phe Asp Arg Glu Leu Glu
 450 455 460

Leu Thr Lys Ala Ile Lys Ala Ser Val Lys Asp His Met Met Ser Tyr
 465 470 475 480

Met Met Pro Ser Lys Phe Leu Tyr Arg Asp Ser Leu Pro Leu Thr Pro
 485 490 495

Asn Gly Lys Ile Asp Ile Lys Thr Leu Ile Asn Glu Val Asn Asn Arg
 500 505 510

<210> 57

<211> 1278

<212> DNA

<213> Streptococcus pyogenes

<400> 57

atgacaaaaa ctaatcttaa ctggagcggg ttttcaaaga aaacattcga agaacgcctc 60
 caacttatcg aaaaatttaa actacttaat gctgaaaact taaatcaact caaacagac 120
 gttcttttgc ctatccaaac agctaataca atgactgaaa atgtcttagg acgattggct 180
 ttgcccttta gcatagctcc tgattttctt gtcaacgggt caacttatca gatgcctttt 240
 gtcacggaag aaccttctgt tgttgctgca gcatctttcg cagcaaaact aatcaaacgc 300
 tcaggtgggt ttaaagctca aaccctaaac cgacaaatga ttggtcaa atgttctttac 360
 gatatcgacc aaatagataa cgctaaagcc gccatccttc ataaaaaaa aaagctaatt 420
 gcattggcaa ataaagctta tccttcatt gttaaaagag gtggaggcgc tagaaccatt 480
 catttgaag aaaaaggaga atttttgatt ttctatctga ctgttgatac ccaagaagct 540
 atgggagcaa atatggtcaa tactatgatg gaagctcttg ttctgattt aacaagactg 600
 tctaaggggc attgtctaat ggcgatttta tctaattacg caacagagtc gcttgttact 660
 actagtgtg agattcccgt gcgcctttta gatcacgata aaacaaaatc cctacagtta 720
 gctcaaaaaa tagagctagc cagccgacta gctcaagtag atccttaccg ggctactact 780
 cataataaag gtatttttaa tggcattgat gcagtggtaa tagccacagg aaatgactgg 840
 cgtgctattg aagcaggggc ccattgcttat gcctcaagaa atggtagcta tcaaggactt 900
 agtcagtggc attttgacca agataaacia gttctgcttg gccaaatgac cctccctatg 960
 cctattgcta gtaagggggg atctatcggg cttaacccta ctgtttctat cgcacatgat 1020
 cttcttaatc aacctgatgc caaacatta gcccaattga ttgcatctgt ggggttagct 1080
 caaaactttg ctgactaaa agctctgacc tcacttgcca tccaagctgg tcacatgaaa 1140
 ctacatgcga aatcattagc tcttttggcg ggggcaacc aagacgaaat tgctccttta 1200
 gttaatgctt tactagctga taaaccaata aatctagaaa aagcacattt ttacttatcc 1260

cagctaagac agtcttaa

1278

<210> 58

<211> 425

<212> PRT

<213> Streptococcus pyogenes

<400> 58

Met Thr Lys Thr Asn Leu Asn Trp Ser Gly Phe Ser Lys Lys Thr Phe
 1 5 10 15

Glu Glu Arg Leu Gln Leu Ile Glu Lys Phe Lys Leu Leu Asn Ala Glu
 20 25 30

Asn Leu Asn Gln Leu Lys Thr Asp Val Leu Leu Pro Ile Gln Thr Ala
 35 40 45

Asn Gln Met Thr Glu Asn Val Leu Gly Arg Leu Ala Leu Pro Phe Ser
 50 55 60

Ile Ala Pro Asp Phe Leu Val Asn Gly Ser Thr Tyr Gln Met Pro Phe
 65 70 75 80

Val Thr Glu Glu Pro Ser Val Val Ala Ala Ala Ser Phe Ala Ala Lys
 85 90 95

Leu Ile Lys Arg Ser Gly Gly Phe Lys Ala Gln Thr Leu Asn Arg Gln
 100 105 110

Met Ile Gly Gln Ile Val Leu Tyr Asp Ile Asp Gln Ile Asp Asn Ala
 115 120 125

Lys Ala Ala Ile Leu His Lys Thr Lys Lys Leu Ile Ala Leu Ala Asn
 130 135 140

Lys Ala Tyr Pro Ser Ile Val Lys Arg Gly Gly Gly Ala Arg Thr Ile
 145 150 155 160

His Leu Glu Glu Lys Gly Glu Phe Leu Ile Phe Tyr Leu Thr Val Asp
 165 170 175

Thr Gln Glu Ala Met Gly Ala Asn Met Val Asn Thr Met Met Glu Ala
 180 185 190

Leu Val Pro Asp Leu Thr Arg Leu Ser Lys Gly His Cys Leu Met Ala
 195 200 205

Ile Leu Ser Asn Tyr Ala Thr Glu Ser Leu Val Thr Thr Ser Cys Glu
 210 215 220

Ile Pro Val Arg Leu Leu Asp His Asp Lys Thr Lys Ser Leu Gln Leu
 225 230 235 240

Ala Gln Lys Ile Glu Leu Ala Ser Arg Leu Ala Gln Val Asp Pro Tyr
 245 250 255

Arg Ala Thr Thr His Asn Lys Gly Ile Phe Asn Gly Ile Asp Ala Val
 260 265 270

Val Ile Ala Thr Gly Asn Asp Trp Arg Ala Ile Glu Ala Gly Ala His
 275 280 285

Ala Tyr Ala Ser Arg Asn Gly Ser Tyr Gln Gly Leu Ser Gln Trp His
 290 295 300

Phe Asp Gln Asp Lys Gln Val Leu Leu Gly Gln Met Thr Leu Pro Met
 305 310 315 320

Pro Ile Ala Ser Lys Gly Gly Ser Ile Gly Leu Asn Pro Thr Val Ser
 325 330 335

Ile Ala His Asp Leu Leu Asn Gln Pro Asp Ala Lys Thr Leu Ala Gln
 340 345 350

Leu Ile Ala Ser Val Gly Leu Ala Gln Asn Phe Ala Ala Leu Lys Ala
 355 360 365

Leu Thr Ser Ser Gly Ile Gln Ala Gly His Met Lys Leu His Ala Lys
 370 375 380

Ser Leu Ala Leu Leu Ala Gly Ala Thr Gln Asp Glu Ile Ala Pro Leu
 385 390 395 400

Val Asn Ala Leu Leu Ala Asp Lys Pro Ile Asn Leu Glu Lys Ala His
 405 410 415

Phe Tyr Leu Ser Gln Leu Arg Gln Ser
 420 425

<210> 59

<211> 915

<212> DNA

<213> Streptococcus pyogenes

<400> 59

```

atgggtattat ttacaggaaa aacagtcgaa gaagctatcg aaacaggact tcaagagtta 60
gggttatcac gccttaaagc gcataatcaaa gtcatttcaa aagagaaaaa aggtttcctc 120
gggtttggta aaaagccagc ccaagttgat atcgaaggta tcagcgacaa gacggtttat 180
aaggctgata aaaaagccac tcgaggtgtt ccagaggata ttaatcgta aaatactccc 240
gcggtcaatt ctgctgatgt agaacctgaa gaaataaaaag ccaactcaaag gttagaagca 300
gaagatacca aagtgggtcc tctcatgtct gaagatagtc cagcgcaaac cccttctaata 360
cttgctgaga cagtcactga aacaaaagca caacaaccgt caatcccagt cgaagaatca 420
gaagtgtccc aagatgctgg taatgatggt ttcagcaaag atattgaaaa agctgctcag 480
gaagtgtccg attatgtgac taaaattatc tatgaaatgg atatcgaagc taccgttgaa 540
accagcaaca atcgtcgcca aatcaatttg cagattgaaa cgccagaggc gggacgtgtg 600
attggttacc atggtaaggc cttgaaatcc ttgcagttgt tagctcaaaa tttcttgca 660
gaccgtatt caaaaaattt ttcagtatcc ttgaatgtcc atgattatgt ggaacatcga 720
acagaaacct tgattgactt tacgcaaaaa gttgccaaac gcgttttgga atctggtcaa 780
gattacacca tggatcccat gagtaacagt gacgtaaaaa tcgttcataa aaccgtttca 840
tccattgaag gggttgatag ttattctgaa ggcaatgacc ctaaccgcta tgtggtagtc 900
agtcctcaac gttaa 915

```

<210> 60

<211> 304

<212> PRT

<213> Streptococcus pyogenes

<400> 60

```

Met Val Leu Phe Thr Gly Lys Thr Val Glu Glu Ala Ile Glu Thr Gly
  1             5             10             15

Leu Gln Glu Leu Gly Leu Ser Arg Leu Lys Ala His Ile Lys Val Ile
      20             25             30

Ser Lys Glu Lys Lys Gly Phe Leu Gly Phe Gly Lys Lys Pro Ala Gln
      35             40             45

Val Asp Ile Glu Gly Ile Ser Asp Lys Thr Val Tyr Lys Ala Asp Lys
      50             55             60

Lys Ala Thr Arg Gly Val Pro Glu Asp Ile Asn Arg Gln Asn Thr Pro
      65             70             75             80

Ala Val Asn Ser Ala Asp Val Glu Pro Glu Glu Ile Lys Ala Thr Gln
      85             90             95

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

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

```

115	120	125
Lys Ala Gln Gln Pro Ser Ile Pro Val Glu Glu Ser Glu Val Pro Gln		
130	135	140
Asp Ala Gly Asn Asp Gly Phe Ser Lys Asp Ile Glu Lys Ala Ala Gln		
145	150	155
Glu Val Ser Asp Tyr Val Thr Lys Ile Ile Tyr Glu Met Asp Ile Glu		
165	170	175
Ala Thr Val Glu Thr Ser Asn Asn Arg Arg Gln Ile Asn Leu Gln Ile		
180	185	190
Glu Thr Pro Glu Ala Gly Arg Val Ile Gly Tyr His Gly Lys Val Leu		
195	200	205
Lys Ser Leu Gln Leu Leu Ala Gln Asn Phe Leu His Asp Arg Tyr Ser		
210	215	220
Lys Asn Phe Ser Val Ser Leu Asn Val His Asp Tyr Val Glu His Arg		
225	230	235
Thr Glu Thr Leu Ile Asp Phe Thr Gln Lys Val Ala Lys Arg Val Leu		
245	250	255
Glu Ser Gly Gln Asp Tyr Thr Met Asp Pro Met Ser Asn Ser Glu Arg		
260	265	270
Lys Ile Val His Lys Thr Val Ser Ser Ile Glu Gly Val Asp Ser Tyr		
275	280	285
Ser Glu Gly Asn Asp Pro Asn Arg Tyr Val Val Val Ser Leu Gln Arg		
290	295	300

<210> 61

<211> 1269

<212> DNA

<213> Streptococcus pyogenes

<400> 61

atgacaacaa aatatcaaac aatcatttcc aatatcgaac aagatatcca gaaacagcga 60
ctaaaaaaag gggacaagct accttcaatt aggggtactaa gtaagggtta ttattgtagc 120

```

aaagatactg ttcagcgggc tcttttagaa ttaaaatata gtcacttaat ttatgctgtt 180
cctaaaagtg gttattatgt tttgggtaac gtaagcatgc ccgataatgt tcttaatacta 240
agtcttgaag attataataa tatggcttat gaagatttcc gactctgctt aaatgaggcc 300
ttaagtgcta aagacaaata cctctttcat tattatcaca aaaccgaagg actagaagaa 360
ctaaggggaag ctttgccttct ttacttagct gaaaatagtg ttacagtaa caaagaccaa 420
ctattaatca cctctgggac gcaacaagcg ctttataattt tatcacaaat gccttttcct 480
aatacgggca aaacaattct ccttgaaaag cctacttata atcggatgga agctattgtt 540
gctcagttag gattacccta tcaaaactata tctagacact ttaatggcct tgatttagaa 600
ctcttagaat ctttatttca aactggcgat attaaatttt ttacacgat ttcacgattt 660
tcacatcttc tgggactttc ttatagcact aaggaaaagg aagctattgt tcgtctagca 720
caacgatacc aggtttatat tttagaagat gattatttag gagattttgt gaaacttaaa 780
gagccaccaa ttcattatta tgacactcat caccgaatca tctacctaaa atctttttca 840
atgagtgttt ttcctgcact ccgatcggga gctctagtgt taccgtcagg tttaaacct 900
cattttttta cccaaaaatac attgattgat ttagacacga acttactaat gcaaaaagca 960
ttagctcttt atttagaaaa tgggatgttt caaaaaatac ttcgctttat taagcgttat 1020
ctaaaacagc gggaacgtca attggctctc tttttaaaac aaaattgcc tgatattcac 1080
tatcaactaa cccctactca tttagtgatt gattacacga catcagactc ttatagaaac 1140
tttacattag ataaatctga tagaataata ataactggaa aaaaacgcta tctctctatt 1200
actatcaatc aacaaatata aagcaaatta aactactata tcaaaaatac ttgtggaaag 1260
agcaactaa 1269

```

<210> 62

<211> 422

<212> PRT

<213> Streptococcus pyogenes

<400> 62

```

Met Thr Thr Lys Tyr Gln Thr Ile Ile Ser Asn Ile Glu Gln Asp Ile
  1             5             10             15

```

```

Gln Lys Gln Arg Leu Lys Lys Gly Asp Lys Leu Pro Ser Ile Arg Val
          20             25             30

```

```

Leu Ser Lys Val Tyr Tyr Cys Ser Lys Asp Thr Val Gln Arg Ala Leu
          35             40             45

```

```

Leu Glu Leu Lys Tyr Arg His Leu Ile Tyr Ala Val Pro Lys Ser Gly
          50             55             60

```

```

Tyr Tyr Val Leu Gly Asn Val Ser Met Pro Asp Asn Val Leu Asn Leu
          65             70             75             80

```

```

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

```

```

Leu Asn Glu Ala Leu Ser Ala Lys Asp Lys Tyr Leu Phe His Tyr Tyr
          100            105            110

```

His Lys Thr Glu Gly Leu Glu Glu Leu Arg Glu Ala Leu Leu Leu Tyr
 115 120 125

Leu Ala Glu Asn Ser Val Tyr Ser Asn Lys Asp Gln Leu Leu Ile Thr
 130 135 140

Ser Gly Thr Gln Gln Ala Leu Tyr Ile Leu Ser Gln Met Pro Phe Pro
 145 150 155 160

Asn Thr Gly Lys Thr Ile Leu Leu Glu Lys Pro Thr Tyr His Arg Met
 165 170 175

Glu Ala Ile Val Ala Gln Leu Gly Leu Pro Tyr Gln Thr Ile Ser Arg
 180 185 190

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

Gly Asp Ile Lys Phe Phe Tyr Thr Ile Ser Arg Phe Ser His Pro Leu
 210 215 220

Gly Leu Ser Tyr Ser Thr Lys Glu Lys Glu Ala Ile Val Arg Leu Ala
 225 230 235 240

Gln Arg Tyr Gln Val Tyr Ile Leu Glu Asp Asp Tyr Leu Gly Asp Phe
 245 250 255

Val Lys Leu Lys Glu Pro Pro Ile His Tyr Tyr Asp Thr His His Arg
 260 265 270

Ile Ile Tyr Leu Lys Ser Phe Ser Met Ser Val Phe Pro Ala Leu Arg
 275 280 285

Ile Gly Ala Leu Val Leu Pro Ser Gly Leu Lys Pro His Phe Leu Thr
 290 295 300

Gln Lys Ser Leu Ile Asp Leu Asp Thr Asn Leu Leu Met Gln Lys Ala
 305 310 315 320

Leu Ala Leu Tyr Leu Glu Asn Gly Met Phe Gln Lys Asn Leu Arg Phe
 325 330 335

Ile Lys Arg Tyr Leu Lys Gln Arg Glu Arg Gln Leu Ala Leu Phe Leu
 340 345 350

Lys Gln Asn Cys Pro Asp Ile His Tyr Gln Leu Thr Pro Thr His Leu
 355 360 365

Val Ile Asp Tyr Thr Thr Ser Asp Ser Tyr Arg Asn Phe Thr Leu Asp
370 375 380

Lys Ser Asp Arg Ile Ile Ile Thr Gly Lys Lys Arg Tyr Leu Ser Ile
385 390 395 400

Thr Ile Asn Gln Gln Ile Gln Ser Lys Leu Asn Ser Leu Ile Lys Asn
405 410 415

Thr Cys Gly Lys Ser Asn
420

CLAIMS

1. An isolated peptide comprising any of the amino acid sequences identified herein as SEQ ID NOS. 2, 16, 18, 20, 22, 24, 26, 28, 56 and 58 or an immunogenic portion thereof, wherein the immunogenic portion elicits a protective immune response against Group A Streptococcus, or a homologue thereof having at least 80% sequence identity, when used in therapy or diagnosis.
2. A peptide according to claim 1, wherein the sequence identity is at least 90%.
3. A polynucleotide encoding a peptide according to claim 1 or claim 2 when used in therapy or diagnosis.
4. An attenuated microorganism comprising a mutation that specifically disrupts the expression of any of the nucleotide sequences identified herein as SEQ ID NOS. 1, 15, 17, 19, 21, 23, 25, 27, 55 and 57.
5. A microorganism according to claim 4, wherein the mutation is insertional inactivation or a gene deletion.
6. A microorganism according to claim 4 or claim 5, wherein the microorganism is a Group A Streptococcus.
7. A microorganism according to any of claims 4 to 6, for therapeutic or diagnostic use.
8. A microorganism according to any of claims 4 to 7, comprising a mutation in a further nucleotide sequence.
9. A microorganism according to any of claims 4 to 8, comprising a heterologous antigen, therapeutic peptide or nucleic acid.

10. A vaccine comprising a peptide according to claim 1 or claim 2.
11. A vaccine comprising a microorganism according to any of claims 4 to 9.
12. Use of a product according to any of claims 1 to 9, for the manufacture of a medicament for use in the treatment or prevention of a condition associated with infection by *Streptococcal* or Gram-positive bacteria.
13. Use according to claim 12, wherein the condition is pneumonia.
14. Use according to claim 12, or claim 13, for veterinary treatment.
15. An antibody raised against an isolated peptide comprising any of the amino acid sequences identified herein as SEQ ID NOS. 2, 16, 18, 20, 22, 24, 26, 28, 56 and 58 or an immunogenic portion thereof, wherein the immunogenic portion elicits a protective immune response against Group A Streptococcus, or a homologue thereof having at least 80% sequence identity.
16. Use of:
 - an isolated peptide comprising any of the amino acid sequences identified herein as SEQ ID NOS. 2, 16, 18, 20, 22, 24, 26, 28, 56 and 58 or an immunogenic portion thereof, wherein the immunogenic portion elicits a protective immune response against Group A Streptococcus, or a homologue thereof having at least 80% sequence identity,
 - or
 - a polynucleotide encoding said peptide, or
 - a microorganism according to any of claims 4 to 9, in a screening assay for the identification of an antimicrobial drug.