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(54) Title: PROJECTION AGAINST MYCOBACTERIAL INFECTIONS

(57) Abstract: The present invention relates to a method of identifying mycobacterial genes which wre induced or up-regulated during *M. tuberculosis* virulence, and to isolated peptide products of said genes. Also provided, are inhibitors of said genes, and antibodies which bind to said peptide products. Further embodiments include DNA and RNA vectors encoding said products, attenuated mycobacteria in which the activity of at least one of said genes or peptide products has been modified, vaccines against mycobacterial infections, and methods of detecting a mycobacterial infection.

PROTECTION AGAINST MYCOBACTERIAL INFECTIONS

The present invention relates to a method of identifying mycobacterial genes which are induced or up-regulated during mycobacterial virulence, to isolated peptide products of said genes, to inhibitors of said genes, to antibodies which bind to said peptide products, to DNA and RNA vectors encoding said products, to attenuated mycobacteria in which the activity of at least one of said genes or peptide products has been modified, to vaccines against mycobacterial infections, and to methods of detecting a mycobacterial infection.

Many microorganisms are capable of forming intracellular infections. These include: infections caused by species of *Salmonella, Yersinia, Shigella, Campylobacter, Chlamydia* and *Mycobacteria*. Some of these infections are exclusively intracellular, others contain both intracellular and extracellular components. However, it is the intracellular survival cycle of bacterial infection which is suspected as a main supportive factor for disease progression.

Generally, these microorganisms do not circulate freely in the body, for example, in the bloodstream, and are often not amenable to drug treatment regimes. Where drugs are available, this problem has been exacerbated by the development of multiple drug resistant microorganisms.

A number of factors have contributed to the problem of microbial drug resistance. One is the accumulation of mutations over time and the subsequent horizontal and vertical transfer of the mutated genes to other organisms. Thus, for a given pathogen, entire classes of antibiotics have been rendered inactive. A further factor has been the absence of a new class of antibiotics in recent years. The emergence of multiple drug-resistant pathogenic bacteria represents a serious threat to public health and new forms of therapy are urgently required.

For similar reasons, vaccine therapies have not proved effective against such intracellular microorganisms. Also, increased systemic concentration of antibiotics to improve bioavailability within cells may result in severe side effects.

Mycobacterium tuberculosis and closely related species make up a small group of mycobacteria known as the *Mycobacterium tuberculosis* complex (MTC). This group comprises four species *M. tuberculosis, M. microti, M. bovis* and *M. africanum* which are the causative agent in the majority of tuberculosis (TB)

cases throughout the world.

M. tuberculosis is responsible for more than three million deaths a year world-wide. Other mycobacteria are also pathogenic in man and animals, for example *M. avium* subsp. *paratuberculosis* which causes Johne's disease in ruminants, *M. bovis* which causes tuberculosis in cattle, *M. avium* and *M. intracellulare* which cause tuberculosis in immunocompromised patients (eg. AIDS patients, and bone marrow transplant patients) and *M. leprae* which causes leprosy in humans.

M. tuberculosis infects macrophage cells within the body, particularly alveolar macrophages in the lung. Soon after macrophage infection, most *M. tuberculosis* bacteria enter, persist and replicate within cellular phagosome vesicles, where the bacteria are sequestered from host defences and extracellular factors.

It is the intracellular survival and multiplication or replication of bacterial infection which is suspected as a main supportive factor for mycobacterial disease progression.

A number of drug therapy regimens have been proposed for combatting *M. tuberculosis* infections, and currently combination therapy including the drug isoniazid has proved most effective. However, one problem with such treatment regimes is that they are long-term, and failure to complete such treatment can promote the development of multiple drug resistant microorganisms.

A further problem is that of providing an adequate bioavailability of the drug within the cells to be treated. Whilst it is possible to increase the systemic concentration of a drug (eg. by administering a higher dosage) this may result in severe side effects caused by the increased drug concentration.

The effectiveness of vaccine prevention against *M. tuberculosis* has varied widely. The current *M. tuberculosis* vaccine, BCG, is an attenuated strain of *M. bovis*. It is effective against severe complications of TB in children, but it varies greatly in its effectiveness in adults particularly across ethnic groups. BCG vaccination has been used to prevent tuberculous meningitis and helps prevent the spread of *M. tuberculosis* to extra-pulmonary sites, but does not prevent

infection. Furthermore, it can not be administered to immunocompromised individuals, a group particularly susceptible to TB, because of the risk of systemic disease resulting from the vaccine.

The limited efficacy of BCG and the global prevalence of TB has led to an international effort to generate new, more effective vaccines. The current paradigm is that protection will be mediated by the stimulation of a Th1 immune response.

BCG vaccination in man was given orally when originally introduced, but that route was discontinued because of loss of viable BCG during gastric passage and of frequent cervical adenopathy. In experimental animal species, aerosol or intra-tracheal delivery of BCG has been achieved without adverse effects, but has varied in efficacy from superior protection than parenteral inoculation in primates, mice and guinea pigs to no apparent advantage over the subcutaneous route in other studies.

There is therefore a need for an improved and/or alternative vaccine or therapeutic agent for combatting mycobacterial infections.

This need is addressed by the present invention.

According to a first aspect, the present invention provides a method of identifying a mycobacterial nucleic acid promoter sequence which is induced or up-regulated during mycobacterial virulence, said method comprising:-

infecting a macrophage target cell with a *Mycobacterium tuberculosis* host cell, which host cell contains a nucleic acid construct comprising a putative mycobacterial promoter sequence operably linked to a coding sequence of a reporter gene located down-stream from the promoter;

culturing the macrophage under conditions which support mycobacterial virulence; and

identifying a promoter sequence which is induced or up-regulated during virulence by detecting expression of the reporter sequence.

M. tuberculosis is a high containment pathogen, and use of this microorganism is therefore preferably conducted under Advisory Committee for Dangerous Pathogen (ACDP) 3 conditions.

M. tuberculosis pursues a route of intracellular infection, and there are several differences in the behaviour of *M. tuberculosis* compared to other pathogens. Thus, nucleic acid expression profiles of other bacteria during infection, even other mycobacteria, do not accurately reflect the series of changes which occur during *M. tuberculosis* infection.

For example, *M. tuberculosis* does not use type III secretion systems to inject effector molecules to alter host cell behaviour as do Salmonella species nor does it utilise pore forming toxins such as listeriolysin to escape the phagosomal vesicle as found in *L. monocytogenes* infection.

Pathogenic mycobacteria appear to rely upon a repertoire of gene products which are tightly regulated in response to the interaction with a host cell, many of which have yet to be identified.

In comparison with other mycobacterial pathogens, species such as *M. leprae* and *M. marinum* appear to have a thermotropism where the infection is manifested in the periphery of the body where temperatures are lower than the typical 37°C core body temperature. *M. leprae* also targets the myelin sheath of the nerve cells and the disease pathology reflects this tissue tropism.

M. marinum causes a limited infection resulting in a surface lesion on the skin which can be self-limiting.

Other pathogens such as *M. avium* and *M. intracellulare* typically cause infections in immunocompromised individuals and do not usually have the ability to cause disease in healthy subjects.

M. bovis infection is usually acquired through ingestion of contaminated milk products resulting in infection via the lymph nodes and leading to lymphoadenopathy.

Following infection, *M. tuberculosis* may enter a dormant state leading to a

latent infection. This latent infection may persist for decades before reactivation occurs leading to progressive active disease.

Other mycobacterial species may share in common with *M. tuberculosis* some components of conserved virulence mechanisms. However, with the publication of the genome sequences *for M. tuberculosis* and *M. leprae*, and the publication of other partially completed genome sequences (eg. *M. smegmatis*, and *M. bovis*), it is clear there are significant differences between the different mycobacterial pathogens that ultimately define their success as pathogens and the characteristics of the pathology of the diseases that they cause.

Thus, *M. tuberculosis* is a specialised bacterial pathogen typically spread by inhalation. *M. tuberculosis* has a complex interaction with its host, from initial contact with host macrophage onwards, which it manipulates to its own advantage leading to either progressive active disease, or a persistent latent infection or most likely a limited infection which is cleared or contained indefinitely by the host.

Mycobacterial virulence includes one or more of the events associated with infection by a mycobacterium of its natural target cell. For example, a natural target cell of *M. tuberculosis* is a macrophage, and virulence with respect to this bacterium and target cell would include any event involved during the sequence of events comprising phagocytosis by the macrophage or uptake via alternative pathways of the bacterium, formation of the phagosome, multiplication of the bacterium within the phagosome, lysis of the phagosome/host cell, and spread of the lesion to a secondary site (ie. haematogenous spread). Thus, virulence conditions are culture conditions which are conducive for a mycobacterium to express at least one gene which would be normally expressed *in vivo* during infection of the mycobacterium's natural target cell.

In one embodiment, the putative promoter sequence is selected from the species *M. phlei, M. smegmatis, M. africanum, M. caneti, M. fortuitum, M. marinum, M. ulcerans, M. tuberculosis, M. bovis, M. microti, M. avium, M. paratuberculosis, M. leprae, M. lepraemurium, M. intracellulare, M. scrofulaceum, M. xenopi, M. genavense, M. kansasii, M. simiae, M. szulgai, M. haemophilum, M. asiaticum, M. malmoense, M. vaccae and M. shimoidei*. Of

particular interest are members of the MTC, preferably *M. tuberculosis* or *M. bovis*.

In another embodiment, the reporter gene is a silent marker of gene expression, and does not require a selection pressure to be applied during the detection step. This is in contrast to other markers, for example, antibiotic resistance markers which require the presence of the antibiotic to permit selection of desirable transformants. The presence of a selection pressure may be undesirable as this pressure may itself induce or cause up-regulation of other genes, or result in the loss of transiently-expressed promoters. The induction or up-regulation of other genes, eg. growth-related genes, may result in increased growth of background mycobacteria and may cause problems in the identification of desirable transformants free of false positives.

The reporter sequences employed in the method of the present invention do not possess their own promoters, and are therefore reliant on the activity of the putative promoter sequence to effect expression thereof. Thus, by culturing mycobacterial host cells under virulence conditions, it is possible to select for those promoters which are active under virulence conditions by detecting expression of the reporter sequence.

The reporter gene is preferably a Green Fluorescent Protein (GFP). Suitable GFPs such as GFPmut 1, 2 or 3 are described in [Cormack *et al.* (1996) Gene, 173, pp.33-38]. In a preferred embodiment, the GFP is GFPmut2.

In those embodiments in which the reporter sequence encodes a fluorescent protein, the desirable mycobacterial host cell transformants are capable of fluorescence by expression of the reporter sequence.

Thus, in a preferred embodiment, promoters active during virulence are detected by differential fluorescence induction methods (DFI) as, for example, described in Valdivia, R.H. and Falkow, S. (1997) [Science, vol. 277, 26 September 1997, pp. 2007-2011], and desirable transformed host cells containing said promoters may be isolated by fluorescence activated cell sorting (FACS).

In use, the mycobacterial host cell infects a macrophage *in vitro*. Thereafter,

when recovering the mycobacteria (eg. for FACS analysis), phagosomal vesicles containing the bacteria may be recovered and the vesicles analysed (ie. sorted) whole. Alternatively, both the macrophage and phagosomal vesicles contained within are disrupted and the released bacteria are analysed by FACS.

Suitable macrophage cells include human acute-monocytic leukemic cell lines of macrophage lineage: $CD14^+$, $CD15^+$ (THP-I), murine bone marrow-derived macrophage cell lines, and murine BALB/c tumour derived macrophage-monocyte cell lines (eg. ATCC TIB-67, and ATCC TIB-71).

Example 3 of the present application describes one preferred macrophage assay of the present application. However, any one of numerous conventional macrophage infection assays may be employed in the present invention.

Suitable media for culturing mycobacteria under non-virulence conditions are described in Wayne, L.G. (1994) [*in* Tuberculosis: Pathogenesis, Protection, and Control published by the American Society for Microbiology, pp. 73-83]. These include Middlebrook 7H9 Medium [see Barker, L.P., *et al.* (1998) Molec. Microbiol., vol. 29(5), pp. 1167-1177, and WO00/52139 in the name of the present Applicant].

In use, an induced or up-regulated promoter is identified by detecting increased expression of the reporter sequence during macrophage infection when compared to expression of the reporter sequence under culture conditions which do not promote mycobacterial virulence. This minimises the risk of identifying mycobacterial host cells containing putative promoters which are constitutively expressed.

Suitable culture conditions which do not promote mycobacterial virulence (ie. conditions which support non-virulence) include mycobacterial culture conditions which are substantially free from macrophage.

In one embodiment, the non-virulence culture conditions are substantially non-limiting in terms of aerobic growth (eg. pH, temperature, and available nutrients) of the mycobacterial host cell culture. Thus, the mycobacterial host cell culture is preferably cultured under conventional conditions which permit a doubling time of 18-26 hours.

In use, the mycobacterial host cell culture may be cultured in batch, and is preferably harvested during mid- to late-exponential phase. Alternatively, this point in the growth phase may be mimicked under continuous culture conditions employing a steady state growth rate approximating μ_{max} which provides a generation time of approximately 18-24 hours.

The preferred culture method employed by the present invention is that of batch fermenter culture. This method permits careful monitoring of growth culture parameters such as pH, temperature, available nutrients, and dissolved oxygen tension (DOT). In particular, temperature and DOT may be strictly controlled.

The identification of transformed host cells containing promoters which are constitutively expressed may be performed before or after identification of promoters expressed during virulence conditions. In a preferred embodiment, constitutively expressed promoters are identified after identification of induced or up-regulated promoters expressed during virulence.

Increased expression means that the signal detected as a result of expression of the reporter sequence when the mycobacterial host cell is cultured under virulence conditions is at least 1.3 times greater than the signal detected when the host cell is cultured under non-virulence conditions. In one embodiment, the signal is at least 2 times, preferably at least 4 times greater when the host cell is cultured under virulence conditions. In another embodiment, the signal is at least 10, preferably at least 20, and particularly preferably at least 30 times greater when the host cell is cultured under virulence conditions.

Naturally, the expression profile for a given gene in a mycobacterial host cell may vary during the course of infection. For example, a gene may be induced or up-regulated most strongly during the early stages of an infection. Thus, the term "increased expression" refers to the maximum signal obtained for a given reporter gene under virulence conditions *vis-a-vis* non-virulence conditions.

In one embodiment, the "increased expression" concerns the maximum signal obtained within the first four days after macrophage infection, preferably within the first two days after macrophage infection.

In another embodiment, genes switched on or up-regulated at later stages of

infection are of interest, in which case a maximum signal 4 days after macrophage infection is preferred. For example, a maximum signal up to 11-12 days after infection may be preferred. However, due to the invasive and destructive nature of a *M. tuberculosis* infection on a macrophage, a post-infection period of between 4 and 6 days is particularly preferred.

A number of methods may be employed for obtaining putative mycobacterial promoter sequences for use in the present invention. These include:- generation of a library of putative promoter sequences by use of nucleic acid digestion enzymes (see Example 1); and identifying nucleic acid sequence homology to known virulence or previously implicated virulence sequences in other microorganisms (see Example 2).

In application of the above homology identification method, a single promoter construct (rather than a selection of constructs generated from a library) is prepared, and a promoter-reporter unit constructed. It is then possible to assess promoter activity by direct comparison (eg. by FACS) of mycobacterial host cultured under virulence conditions versus non-virulence conditions. Since only a single promoter-reporter construct is employed, there is no need for a separate screening of the host cells.

The method of the present invention permits identification of promoters which are induced or up-regulated during virulence. Once the nucleic acid sequence and orientation of a desirable promoter sequence has been determined, the exact location can be mapped by use of convention nucleic acid homology search computer software (eg. BLASTN, or BLASTX) performed on published sequences of the mycobacterial species concerned. Accordingly, the gene or operon under the control of the identified promoter may be identified.

Thus, in a second aspect of the present invention, there is provided a method of identifying a mycobacterial gene the expression of which is induced or up-regulated during mycobacterial virulence, said method comprising:-

identifying a mycobacterial promoter sequence which is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell, wherein the host cell contains a nucleic acid construct comprising said promoter sequence operably linked to a coding sequence of a

reporter gene located down-stream from the promoter;

aligning by sequence homology the nucleic acid sequence of the promoter with published nucleic acid sequence data for the same mycobacterial species; and

identifying the associated nucleic acid coding sequence under the control of said promoter.

Reference to "gene" throughout this specification embraces open reading frames (ORFs).

According to a third aspect of the present invention there is provided an isolated mycobacterial peptide or a fragment or derivative or variant thereof, wherein the peptide is encoded by a mycobacterial gene the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said mycobacterial gene.

The various embodiments described for the first and second aspect of the present invention apply equally for the third and subsequent aspects of the present invention.

The terms "isolated," "substantially pure," and "substantially homogenous" are used interchangeably to describe a peptide which has been separated from components which naturally accompany it. A peptide is substantially pure when at least about 60 to 75% of a sample exhibits a single peptide sequence. A substantially pure peptide will typically comprise about 60 to 90% w/w of a protein sample, more usually about 95%, and preferably will be over about 99% pure. Peptide purity or homogeneity may be indicated by, for example, polyacrylamide gel electrophoresis of a protein sample, followed by visualizing a single polypeptide band upon staining the gel. Alternatively, higher resolution may be provided by using, for example, HPLC.

A peptide is considered to be isolated when it is separated from the contaminants which accompany it in its natural state. Thus, a peptide which is chemically synthesized or synthesized in a cellular system different from the cell from which it naturally originates will be substantially free from its naturally

associated components.

The present invention provides peptides which may be purified from mycobacteria as well as from other types of cells transformed with recombinant nucleic acids encoding these peptides.

If desirable, the amino acid sequence of the proteins of the present invention may be determined by protein sequencing methods.

The terms "peptide", "oligopeptide", "polypeptide", and "protein" are used interchangeably and do not refer to a specific length of the product. These terms embrace post-translational modifications such as glycosylation, acetylation, and phosphorylation.

The term "fragment" means a peptide having at least five, preferably at least ten, more preferably at least twenty, and most preferably at least thirty-five amino acid residues of the peptide which is the gene product of the induced or up-regulated gene in question. The fragment preferably includes at least one epitope of the gene product in question.

The term "variant" means a peptide or peptide "fragment" having at least seventy, preferably at least eighty, more preferably at least ninety percent amino acid sequence homology with the peptide which is the gene product of the induced or up-regulated peptide in question. An example of a "variant" is a peptide or peptide fragment of an induced/up-regulated gene which contains one or more analogs of an amino acid (eg. an unnatural amino acid), or a substituted linkage. The terms "homology" and "identity" are considered synonymous in this specification. In a further embodiment, a "variant" may be a mimic of the peptide or peptide fragment, which mimic reproduces at least one epitope of the peptide or peptide fragment. The mimic may be, for example, a nucleic acid mimic, preferably a DNA mimic.

For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences may be then compared. When using a sequence comparison algorithm, test and reference sequences are input into a computer, subsequent coordinates are designated, if necessary, and sequence algorithm program parameters are designated. The sequence comparison algorithm then

calculates the percentage sequence identity for the test sequence(s) relative to the reference sequence, based on the designated program parameters.

Optimal alignment of sequences for comparison may be conducted, for example, by the local homology alignment algorithm of Smith and Waterman [Adv. Appl. Math. 2: 484 (1981)], by the algorithm of Needleman & Wunsch [J. Mol. Biol. 48: 443 (1970)] by the search for similarity method of Pearson & Lipman [Proc. Nat'l. Acad. Sci. USA 85: 2444 (1988)], by computer implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA - Sequence Analysis Software Package of the Genetics Computer Group, University of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, Wis. 53705), or by visual inspection [see Current Protocols in Molecular Biology, F.M. Ausbel et al, eds, Current Protocols, a joint venture between Greene Publishing Associates, In. And John Wiley & Sons, Inc. (1995 Supplement) Ausbubel].

Examples of algorithms suitable for determining percent sequence similarity are the BLAST and BLAST 2.0 algorithms [see Altschul (1990) J. Mol. Biol. 215: pp. 403-410; and "http://www.ncbi.nlm.nih.gov/" of the National Center for Biotechnology Information].

In a preferred homology comparison, the identity exists over a region of the sequences that is at least 10 amino acids, preferably at least 20 amino acids, more preferably at least 35 amino acids in length.

The term "derivative" means a protein comprising the peptide (or fragment, or variant thereof) which peptide is the gene product of the induced or up-regulated gene in question. Thus, a derivative may include the peptide in question, and a further peptide sequence which may introduce one or more additional epitopes. The further peptide sequence should preferably not interfere with the basic folding and thus conformational structure of the peptide in question. Examples of a "derivative" are a fusion protein, a conjugate, and a graft. Thus, two or more peptides (or fragments, or variants) may be joined together to form a derivative. Alternatively, a peptide (or fragment, or variant) may be joined to an unrelated molecule (eg. a second, unrelated peptide). Derivatives may be chemically synthesized, but will be typically prepared by recombinant nucleic acid methods. Additional components such as lipid, and/or

polysaccharide, and/or polyketide components may be included.

All of the molecules "fragment", "variant" and "derivative" have a common antigenic cross-reactivity and/or substantially the same *in vivo* biological activity as the peptide product of the induced or up-regulated gene in question from which they are derived. For example, an antibody capable of binding to a fragment, variant or derivative would be also capable of binding to the gene product of the induced or up-regulated gene in question. It is a preferred feature that the fragment, variant and derivative each possess the active site of the peptide which is the induced or up-regulated peptide in question. Alternatively, all of the above embodiments of a peptide of the present invention share a common ability to induce a "recall response" of a T-lymphocyte which has been previously exposed to an antigenic component of a mycobacterial infection.

In a preferred embodiment, the peptide is selected from the group consisting of SEQ ID NO: 2; 4; 6; 8; 10; 12; 14; 16; 19; 21; 23; 25; 27; 29; 31; 33; 35; 38; 40; 42; 44; 46; 48; 50; 52; 55; 58; 60; 62; 64; 67; 69; 72; 75; 78; 80; 82; 85; 87; 89; 92; 94; 97; 100; 103; 105; 107; 109; 111; 113; 115; and 117.

A fourth aspect of the invention provides an inhibitor of a mycobacterial peptide, wherein the peptide is encoded by a mycobacterial gene the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said mycobacterial gene, and wherein the inhibitor is capable of substantially preventing or inhibiting the mycobacterial peptide from exerting its native biological function or effect.

Inhibition of the mycobacterial peptide may be effected at the nucleic acid level (ie. DNA, or RNA), or at the peptide level.

In a further embodiment, the inhibitor may be an antibiotic capable of targeting the induced or up-regulated mycobacterial gene, or the peptide product thereof. The antibiotic is preferably specific for the gene and/or peptide product.

Inhibitors of the present invention may be prepared utilizing the sequence information provided herein. For example, this may be performed by overexpressing the peptide, purifying the peptide, and then performing X-ray

compounds are created which have similar molecular structures to all or portions of the peptide or its substrate. The compounds may be then combined with the peptide and attached thereto so as to block one or more of its biological activities.

Also included within the invention are isolated or recombinant polynucleotides that bind to the regions of the mycobacterial chromosome (eg. promoter, or coding region), or transcription products thereof, containing sequences that are associated with induction/up-regulation of a mycobacterial gene during macrophage infection by *M. tuberculosis*, including antisense and triplex forming polynucleotides. As used herein, the term "binding" refers to an interaction or complexation between an oligonucleotide and a target nucleotide sequence, mediated through hydrogen bonding or other molecular forces. The term "binding" more specifically refers to two types of internucleotide binding mediated through base-base hydrogen bonding. The first type of binding is "Watson-Crick-type" binding interactions in which adenine-thymine (or adenine-uracil) and guanine-cytosine base-pairs are formed through hydrogen bonding between the bases. An example of this type of binding is the binding traditionally associated with the DNA double helix and in RNA-DNA hybrids; this type of binding is normally detected by hybridization procedures.

A second type of binding is "triplex binding". In general, triplex binding refers to any type of base-base hydrogen bonding of a third polynucleotide strand with a duplex DNA (or DNA-RNA hybrid) that is already paired in a Watson-Crick manner.

In a preferred embodiment, the inhibitor may be an antisense nucleic acid sequence which is complementary to at least part of the inducible or up-regulatable gene.

The inhibitor, when in the form of a nucleic acid sequence, comprises, in use, at least 15 nucleotides, preferably at least 20 nucleotides, more preferably at least 30 nucleotides, and most preferably at least 50 nucleotides.

In a fifth aspect there is provided an antibody which binds to a peptide encoded by a gene, or to a fragment or variant or derivative of said peptide, the expression of which gene is induced or up-regulated during infection of a

macrophage by a *M. tuberculosis* host cell containing said gene,

The antibody preferably has specificity for the peptide in question, and following binding thereto may initiate coating of a mycobacterium expressing said peptide. Coating of the bacterium preferably leads to opsonization thereof. This, in turn, leads to the bacterium being destroyed. It is preferred that the antibody is specific for the mycobacterium (eg. species and/or strain) which is to be targeted.

Opsonization by antibodies may influence cellular entry and spread of mycobacteria in phagocytic and non-phagocytic cells by preventing or modulating receptor-mediated entry and replication in macrophages.

The peptides, fragments, variants or derivatives of the present invention may be used to produce antibodies, including polyclonal and monoclonal. If polyclonal antibodies are desired, a selected mammal (eg. mouse, rabbit, goat, horse, etc.) is immunized with an immunogenic polypeptide. Serum from the immunized animal is collected and treated according to known procedures. If serum containing polyclonal antibodies to a desired mycobacterial epitope contains antibodies to other antigens, the polyclonal antibodies may be purified by immunoaffinity chromatography.

Alternatively, general methodology for making monoclonal antibodies by hybridomas involving, for example, preparation of immortal antibody-producing cell lines by cell fusion, or other techniques such as direct transformation of B lymphocytes with oncogenic DNA, or transfection with Epstein-Barr virus may be employed.

The antibody employed in this aspect of the invention may belong to any antibody isotype family, or may be a derivative or mimic thereof. Reference to antibody throughout this specification embraces recombinantly produced antibody, and any part of an antibody which is capable of binding to a mycobacterial antigen.

In one embodiment the antibody belongs to the IgG, IgM or IgA isotype families.

In a preferred embodiment, the antibody belongs to the IgA isotype family. Reference to the IgA isotype throughout this specification includes the secretory form of this antibody (ie. sIgA). The secretory component (SC) of sIgA may be added *in vitro* or *in vivo*. In the latter case, the use of a patient's natural SC labelling machinery may be employed.

In one embodiment, the antibody may be raised against a peptide from a member of the MTC, preferably against *M. tuberculosis*.

In a preferred embodiment, the antibody is capable of binding to a peptide selected from the group consisting of SEQ ID NO: 2; 4; 6; 8; 10; 12; 14; 16; 19; 21; 23; 25; 27; 29; 31; 33; 35; 38; 40; 42; 44; 46; 48; 50; 52; 55; 58; 60; 62; 64; 67; 69; 72; 75; 78; 80; 82; 85; 87; 89; 92; 94; 97; 100; 103; 105; 107; 109; 111; 113; 115; and 117 (or fragment, variant, of derivative thereof). The antibodies of the present invention are preferably employed in an isolated form.

In a further embodiment, the antigen is an exposed component of a mycobacterial bacillus. In another embodiment, the antigen is a cell surface component of a mycobacterial bacillus.

The antibody of the present invention may be polyclonal, but is preferably monoclonal.

Without being bound by any theory, it is possible that following mycobacterial infection of a macrophage, the macrophage is killed and the bacilli are released. It is at this stage that the mycobacteria are considered to be most vulnerable to antibody attack. Thus, it is possible that the antibodies of the present invention act on released bacilli following macrophage death, and thereby exert a post-infection effect.

It is possible that the passive protection aspect (ie. delivery of antibodies) of the present invention is facilitated by enhanced accessibility of the antibodies of the present invention to antigens on mycobacterial bacilli. It is possible that antibody binding may block macrophage infection by steric hindrance or disruption of its oligomeric structure. Thus, antibodies acting on mycobacterial bacilli released from killed, infected macrophages may interfere with the spread

of re-infection to fresh macrophages. This hypothesis involves a synergistic action between antibodies and cytotoxic T cells, acting early after infection, eg. γδ and NK T cells, but could later involve also CD8 and CD4 cytotoxic T cells.

According to a sixth aspect of the invention there is provided an attenuated mycobacterium in which a gene has been modified, the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said mycobacterial gene, thereby rendering the mycobacterium substantially non-pathogenic.

The term "modified" refers to any genetic manipulation such as a nucleic acid or nucleic acid sequence replacement, a deletion, or an insertion which renders the mycobacterium substantially non-pathogenic or substantially incapable of macrophage infection. In one embodiment the entire inducible or up-regulatable gene may be deleted.

In one embodiment, the modification may be effected by a nucleic acid sequence encoding an anti-sense nucleic acid sequence to the induced or up-regulated gene, or a transcription product thereof. Thus, by including such a nucleic acid sequence in a mycobacterium, for example in the form of a plasmid, expression of the peptide product of the induced or up-regulated gene may be reduced or substantially inhibited.

In a preferred embodiment, the gene to be modified has a wild-type coding sequence corresponding to one of the group consisting of SEQ ID NO: 3; 5; 7; 9; 11; 13; 15; 17; 20; 22; 24; 26; 28; 30; 32; 34; 36; 39; 41; 43; 45; 47; 49; 51; 53; 56; 59; 61; 63; 65; 68; 70; 73; 76; 79; 81; 83; 86; 88; 90; 93; 95; 98; 101; 104; 106; 108; 110; 112; 114; 116; and 118.

It will be appreciated that the wild-type sequences may include minor variations depending on the Database employed. Reference to wild-type simply means that the sequence in question occurs in nature.

A seventh aspect of the present invention provides an attenuated microbial carrier, comprising a peptide encoded by a gene, or a fragment or variant or derivative of said peptide, the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell

containing said gene.

In use, the peptide (or fragment, variant or derivative) is either at least partially exposed at the surface of the carrier, or the carrier becomes degraded *in vivo* so that at least part of the peptide (or fragment, variant or derivative) is otherwise exposed to a host's immune system.

In a preferred embodiment, the peptide is selected from the group consisting of SEQ ID NO: 2; 4; 6; 8; 10; 12; 14; 16; 19; 21; 23; 25; 27; 29; 31; 33; 35; 38; 40; 42; 44; 46; 48; 50; 52; 55; 58; 60; 62; 64; 67; 69; 72; 75; 78; 80; 82; 85; 87; 89; 92; 94; 97; 100; 103; 105; 107; 109; 111; 113; 115; and 117.

In one embodiment, the attenuated microbial carrier is selected from the group consisting of attenuated salmonella, attenuated vaccinia virus, attenuated fowlpox virus, or attenuated *M. bovis* (eg. BCG strain).

According to an eighth aspect of the invention there is provided a DNA plasmid comprising a promoter, a polyadenylation signal, and a DNA sequence which corresponds to the coding sequence of a mycobacterial gene, or a fragment or variant or derivative of said DNA sequence, the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said mycobacterial gene, wherein the promoter and polyadenylation signal are operably linked to the DNA sequence.

The term DNA "fragment" used in this invention will usually comprise at least about 5 codons (15 nucleotides), more usually at least about 7 to 15 codons, and preferably at least about 35 codons. This number of nucleotides is usually about the minimal length required for a successful probe that would hybridize specifically with such a sequence.

In preferred embodiments, the DNA "fragment" has a nucleotide length which is at least 50%, preferably at least 70%, and more preferably at least 80% that of the coding sequence of the corresponding induced/up-regulated gene.

The term DNA "variant" means a DNA sequence which has substantial homology or substantial similarity to the coding sequence (or a fragment

"substantially homologous" (or "substantially similar") to another if, when optimally aligned (with appropriate nucleotide insertions or deletions) with the other nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 60% of the nucleotide bases, usually at least about 70%, more usually at least about 80%, preferably at least about 90%, and more preferably at least about 95 to 98% of the nucleotide bases. Homology determination is performed as described *supra* for peptides.

Alternatively, a DNA "variant" is substantially homologous (or substantially similar) with the coding sequence (or a fragment thereof) of an induced/up-regulated gene when they are capable of hybridizing under selective hybridization conditions. Selectivity of hybridization exists when hybridization occurs which is substantially more selective than total lack of specificity. Typically, selective hybridization will occur when there is at least about 65% homology over a stretch of at least about 14 nucleotides, preferably at least about 70%, more preferably at least about 75%, and most preferably at least about 90%. See, Kanehisa (1984) Nuc. Acids Res. 12:203-213. The length of homology comparison, as described, may be over longer stretches, and in certain embodiments will often be over a stretch of at least about 17 nucleotides, usually at least about 20 nucleotides, more usually at least about 24 nucleotides, typically at least about 28 nucleotides, more typically at least about 32 nucleotides, and preferably at least about 36 or more nucleotides.

Nucleic acid hybridization will be affected by such conditions as salt concentration (eg. NaCl), temperature, or organic solvents, in addition to the base composition, length of the complementary strands, and the number of nucleotide base mismatches between the hybridizing nucleic acids, as will be readily appreciated by those skilled in the art. Stringent temperature conditions are preferably employed, and generally include temperatures in excess of 30°C, typically in excess of 37°C and preferably in excess of 45°C. Stringent salt conditions will ordinarily be less than 1000 mM, typically less than 500 mM, and preferably less than 200 mM. The pH is typically between 7.0 and 8.3. However, the combination of parameters is much more important than the measure of any single parameter. See, eg., Wetmur and Davidson (1968) J. Mol. Biol. 31:349-370.

The term DNA "derivative" means a DNA polynucleotide which comprises a

DNA sequence (or a fragment, or variant thereof) corresponding to the coding sequence of the induced/up-regulated gene and an additional DNA sequence which is not naturally associated with the DNA sequence corresponding to the coding sequence. The comments on peptide derivative *supra* also apply to DNA "derivative". A "derivative" may, for example, include two or more coding sequences of a mycobacterial operon which is induced during macrophage infection. Thus, depending on the presence or absence of a non-coding region between the coding sequences, the expression product/s of such a "derivative" may be a fusion protein, or separate peptide products encoded by the individual coding regions.

The above terms DNA "fragment", "variant", and "derivative" have in common with each other that the resulting peptide products have cross-reactive antigenic properties which are substantially the same as those of the corresponding wild-type peptide. Preferably all of the peptide products of the above DNA molecule embodiments of the present invention bind to an antibody which also binds to the wild-type peptide. Alternatively, all of the above peptide products are capable of inducing a "recall response" of a T lymphocyte which has been previously exposed to an antigenic component of a mycobacterial infection.

The promoter and polyadenylation signal are preferably selected so as to ensure that the gene is expressed in a eukaryotic cell. Strong promoters and polyadenylation signals are preferred.

In a related aspect, the present invention provides an isolated RNA molecule which is encoded by a DNA sequence of the present invention, or a fragment or variant or derivative of said DNA sequence.

An "isolated" RNA is an RNA which is substantially separated from other mycobacterial components that naturally accompany the sequences of interest, eg., ribosomes, polymerases, and other mycobacterial polynucleotides such as DNA and other chromosomal sequences.

The above RNA molecule may be introduced directly into a host cell as, for example, a component of a vaccine.

Alternatively the RNA molecule may be incorporated into an RNA vector prior to administration.

The polynucleotide sequences (DNA and RNA) of the present invention include a nucleic acid sequence which has been removed from its naturally occurring environment, and recombinant or cloned DNA isolates and chemically synthesized analogues or analogues biologically synthesized by heterologous systems.

The term "recombinant" as used herein intends a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which, by virtue of its origin or manipulation: (1) is not associated with all or a portion of a polynucleotide with which it is associated in nature; or (2) is linked to a polynucleotide other than that to which it is linked in nature; and (3) does not occur in nature. This artificial combination is often accomplished by either chemical synthesis means, or by the artificial manipulation of isolated segments of nucleic acids, eg., by genetic engineering techniques. Such is usually done to replace a codon with a redundant codon encoding the same or a conservative amino acid, while typically introducing or removing a sequence recognition site. Alternatively, it is performed to join together nucleic acid segments of desired functions to generate a desired combination of functions.

In embodiments of the invention the polynucleotides may encode a peptide which is induced or up-regulated during macrophage infection. A nucleic acid is said to "encode" a peptide if, in its native state or when manipulated, it can be transcribed and/or translated to produce the peptide or a fragment or variant or derivative thereof. The anti-sense strand of such a nucleic acid is also said to encode the sequence.

Also contemplated within the invention are expression vectors comprising the polynucleotide of interest. Expression vectors generally are replicable polynucleotide constructs that encode a peptide operably linked to suitable transcriptional and translational regulatory elements. Examples of regulatory elements usually included in expression vectors are promoters, enhancers, ribosomal binding sites, and transcription and translation initiation and termination sequences. These regulatory elements are operably linked to the sequence to be translated. A nucleic acid sequence is operably linked when it

is placed into a functional relationship with another nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects its transcription or expression. Generally, operably linked means that the DNA sequences being linked are contiguous and, where necessary to join two protein coding regions, contiguous and in reading frame. The regulatory elements employed in the expression vectors containing a polynucleotide encoding a virulence factor are functional in the host cell used for expression.

The polynucleotides of the present invention may be prepared by any means known in the art. For example, large amounts of the polynucleotides may be produced by replication in a suitable host cell. The natural or synthetic DNA fragments coding for a desired fragment will be incorporated into recombinant nucleic acid constructs, typically DNA constructs, capable of introduction into and replication in a prokaryotic or eukaryotic cell. Usually the DNA constructs will be suitable for autonomous replication in a unicellular host, such as yeast or bacteria, but may also be intended for introduction to and integration within the genome of a cultured insect, mammalian, plant or other eukaryotic cell lines.

The polynucleotides of the present invention may also be produced by chemical synthesis, eg. by the phosphoramidite method or the triester method, and may be performed on commercial automated oligonucleotide synthesizers. A double-stranded fragment may be obtained from the single stranded product of chemical synthesis either by synthesizing the complementary strand and annealing the strand together under appropriate conditions or by adding the complementary strand using DNA polymerase with an appropriate primer sequence.

DNA constructs prepared for introduction into a prokaryotic or eukaryotic host will typically comprise a replication system recognized by the host, including the intended DNA fragment encoding the desired peptide, and will preferably also include transcription and translational initiation regulatory sequences operably linked to the polypeptide encoding segment. Expression vectors may include, for example, an origin of replication or autonomously replicating sequence (ARS) and expression control sequences, a promoter, an enhancer and necessary processing information sites, such as ribosome-binding sites, RNA splice sites, polyadenylation sites, transcriptional terminator sequences,

and mRNA stabilizing sequences. Secretion signals from polypeptides secreted from the host cell of choice may also be included where appropriate, thus allowing the protein to cross and/or lodge in cell membranes, and thus attain its functional topology or be secreted from the cell.

An appropriate promoter and other necessary vector sequences will be selected so as to be functional in the host, and may, when appropriate, include those naturally associated with mycobacterial genes. Promoters such as the trp, lac and phage promoters, tRNA promoters and glycolytic enzyme promoters may be used in prokaryotic hosts. Useful yeast promoters include the promoter regions for metallothionein, 3-phosphoglycerate kinase or other glycolytic enzymes such as enolase or glyceraldehyde-3-phosphate dehydrogenase, enzymes responsible for maltose and galactose utilization, and others.

Appropriate non-native mammalian promoters might include the early and late promoters from SV40 or promoters derived from human cytomegalovirus, murine moloney leukemia virus, mouse mammary tumour virus, avian sarcoma viruses, adenovirus II, bovine papilloma virus or polyoma. In addition, the construct may be joined to an amplifiable gene (e.g., DHFR) so that multiple copies of the gene may be made.

While such expression vectors may replicate autonomously, they may less preferably replicate by being inserted into the genome of the host cell.

Expression and cloning vectors will likely contain a selectable marker, a gene encoding a protein necessary for the survival or growth of a host cell transformed with the vector. The presence of this gene ensures the growth of only those host cells which express the inserts. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxic substances, e.g. ampicillin, kanamycin, neomycin, methotrexate, etc.; (b) complement auxotrophic deficiencies; or (c) supply critical nutrients not available from complex media, e.g. the gene encoding D-alanine racemase for Bacilli. The choice of appropriate selectable marker will depend on the host cell.

The vectors containing the nucleic acids of interest can be transcribed *in vitro* and the resulting RNA introduced into the host cell (e.g., by injection), or the vectors can be introduced directly into host cells by methods which vary

depending on the type of cellular host, including electroporation; transfection employing calcium chloride, rubidium chloride calcium phosphate, DEAE-dextran, or other substances; microprojectile bombardment; lipofection; infection (where the vector is an infectious agent, such as a retroviral genome). The cells into which have been introduced nucleic acids described above are meant to also include the progeny of such cells.

Large quantities of the nucleic acids and peptides of the present invention may be prepared by expressing the nucleic acids or portions thereof in vectors or other expression vehicles in compatible prokaryotic or eukaryotic host cells. The most commonly used prokaryotic hosts are strains of *Escherichia coli*, although other prokaryotes, such as *Bacillus subtilis* or Pseudomonas may also be used.

Mammalian or other eukaryotic host cells, such as those of yeast, filamentous fungi, plant, insect, amphibian or avian species, may also be useful for production of the proteins of the present invention. Propagation of mammalian cells in culture is *per se* well known. Examples of commonly used mammalian host cell lines are VERO and HeLa cells, Chinese hamster ovary (CHO) cells, and WI38, BHK, and COS cell lines, although other cell lines may be appropriate, e.g., to provide higher expression, desirable glycosylation patterns.

Clones are selected by using markers depending on the mode of the vector construction. The marker may be on the same or a different DNA molecule, preferably the same DNA molecule. The transformant may be screened or, preferably, selected by any of the means well known in the art, e.g., by resistance to such antibiotics as ampicillin, tetracycline.

The polynucleotides of the invention may be inserted into the host cell by any means known in the art, including for example, transformation, transduction, and electroporation. As used herein, "recombinant host cells", "host cells", "cells", "cell lines", "cell cultures", and other such terms denoting microorganisms or higher eukaryotic cell lines cultured as unicellular entities refer to cells which can be, or have been, used as recipients for recombinant vector or other transfer DNA, and include the progeny of the original cell which has been transformed. It is understood that the progeny of a single parental cell may not necessarily be completely identical in morphology or in genomic or total DNA complement as the original parent, due to natural, accidental, or

deliberate mutation. "Transformation", as used herein, refers to the insertion of an exogenous polynucleotide into a host cell, irrespective of the method used for the insertion, for example, direct uptake, transduction, f-mating or electroporation. The exogenous polynucleotide may be maintained as a non-integrated vector, for example, a plasmid, or alternatively, may be integrated into the host cell genome.

In one embodiment, a DNA plasmid or RNA vector may encode a component of the immune system which is specific to an immune response following challenge with a peptide, wherein said peptide is encoded by a mycobacterial gene which is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said mycobacterial gene.

An example of such a component is an antibody to the peptide product of an induced or up-regulated gene. Thus, in this embodiment, the nucleic acid sequence (eg. DNA plasmid or RNA vector) encodes the antibody in question.

A ninth aspect provides use of a peptide, an inhibitor, an antibody, an attenuated mycobacterium, an attenuated microbial carrier, a DNA sequence corresponding to the coding sequence of an induced or up-regulated gene or a fragment or variant or derivative of said DNA sequence, a DNA plasmid comprising said DNA sequence or said fragment or variant or derivative, an RNA sequence encoded by said DNA sequence or said fragment or variant or derivative, and/or an RNA vector comprising said RNA sequence, according to the present invention, in the manufacture of a medicament for treating or preventing a mycobacterial infection.

The term "treating" includes post-infection therapy and amelioration of a mycobacterial infection.

The term "preventing" includes reducing the severity/intensity of, or initiation of, a mycobacterial infection.

In a related aspect, there is provided a method of treating or preventing a mycobacterial infection, comprising administration of a medicament selected from the group consisting of a peptide, an inhibitor, an antibody, an attenuated mycobacterium, an attenuated microbial carrier, a DNA sequence corresponding

to the coding sequence of an induced or up-regulated gene or a fragment or variant or derivative of said DNA sequence, a DNA plasmid comprising said DNA sequence or said fragment or variant or derivative, an RNA sequence encoded by said DNA sequence or said fragment or variant or derivative, and/or an RNA vector comprising said RNA sequence, according to the present invention, to a patient.

The medicament may be administered by conventional routes, eg. intravenous, intraperitoneal, intranasal routes.

The immunogenicity of the epitopes of the peptides of the invention may be enhanced by preparing them in mammalian or yeast systems fused with or assembled with particle-forming proteins such as, for example, that associated with hepatitis B surface antigen. Vaccines may be prepared from one or more immunogenic peptides of the present invention.

Typically, such vaccines are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid prior to injection may also be prepared. The preparation may also be emulsified, or the peptide encapsulated in liposomes. The active immunogenic ingredients are often mixed with excipients which are pharmaceutically acceptable and compatible with the active ingredient. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol, or the like and combinations thereof. In addition, if desired, the vaccine may contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, and/or adjuvants which enhance the effectiveness of the vaccine. Examples of adjuvants which may be effective include but are not limited to: aluminum hydroxide, N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-nor-muramyl-L-alanyl-D-isoglutamine (CGP 11637, referred to as nor-MDP), N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalm itoyl-sn -glycero-3-hydroxyphosphoryloxy)-ethylamine (CGP 19835A, referred to as MTP-PE), and RIBI, which contains three components extracted from bacteria, monophosphoryl lipid A, trehalose dimycolate and cell wall skeleton (MPL+TDM+CWS) in a 2 % squalene/Tween 80 emulsion.

The vaccines are conventionally administered parenterally, by injection, for example, either subcutaneously or intramuscularly. Additional formulations

which are suitable for other modes of administration include suppositories and, in some cases, oral formulations or formulations suitable for distribution as aerosols. For suppositories, traditional binders and carriers may include, for example, polyalkylene glycols or triglycerides; such suppositories may be formed from mixtures containing the active ingredient in the range of 0.5 % to 10 %, preferably 1 %-2 %. Oral formulations include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, and the like. These compositions take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain 10 % - 95 % of active ingredient, preferably 25 % - 70 %.

The peptides may be formulated into the vaccine as neutral or salt forms. Pharmaceutically acceptable salts include the acid addition salts (formed with free amino groups of the peptide) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or with organic acids such as acetic, oxalic, tartaric, maleic, and the like. Salts formed with the free carboxyl groups may also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

The vaccines are administered in a manner compatible with the dosage formulation, and in such amount as will be prophylactically and/or therapeutically effective. The quantity to be administered, which is generally in the range of 5 micrograms to 250 micrograms of antigen per dose, depends on the subject to be treated, capacity of the subject's immune system to synthesize antibodies, and the degree of protection desired. Precise amounts of active ingredient required to be administered may depend on the judgment of the practitioner and may be peculiar to each subject.

The vaccine may be given in a single dose schedule, or preferably in a multiple dose schedule. A multiple dose schedule is one in which a primary course of vaccination may be with 1-10 separate doses, followed by other doses given at subsequent time intervals required to maintain and or reenforce the immune response, for example, at 1-4 months for a second dose, and if needed, a subsequent dose(s) after several months. The dosage regimen will also, at least

in part, be determined by the need of the individual and be dependent upon the judgment of the practitioner.

In addition, the vaccine containing the immunogenic mycobacterial antigen(s) may be administered in conjunction with other immunoregulatory agents, for example, immune globulins or cytokines, as well as antibiotics.

The outcome of administering antibody-containing compositions may depend on the efficiency of transmission of antibodies to the site of infection. In the case of a mycobacterial respiratory infection (eg. a *M. tuberculosis* infection), this may be facilitated by efficient transmission of antibodies to the lungs.

In one embodiment the medicament may be administered intranasally (i.n.). This mode of delivery corresponds to the route of delivery of a *M. tuberculosis* infection and, in the case of antibody delivery, ensures that antibodies are present at the site of infection to combat the bacterium before it becomes intracellular and also during the period when it spreads between cells.

An intranasal composition may be administered in droplet form having approximate diameters in the range of 100-5000 µm, preferably 500-4000 µm, more preferably 1000-3000 µm. Alternatively, in terms of volume, the droplets would be in the approximate range of 0.001-100 µl, preferably 0.1-50 µl, more preferably 1.0-25 µl.

Intranasal administration may be achieved by way of applying nasal droplets or via a nasal spray.

In the case of nasal droplets, the droplets may typically have a diameter of approximately 1000-3000 μm and/or a volume of 1-25 μl.

In the case of a nasal spray, the droplets may typically have a diameter of approximately 100-1000 μm and/or a volume of 0.001-1 μl.

It is possible that, following i.n. delivery of antibodies, their passage to the lungs is facilitated by a reverse flow of mucosal secretions, although mucociliary action in the respiratory tract is thought to take particles within the mucus out of the lungs. The relatively long persistence in the lungs, fast

clearance from the bile and lack of transport to the saliva of some antibodies suggest the role of mucosal site specific mechanisms.

In a different embodiment, the medicament may be delivered in an aerosol formulation. The aerosol formulation may take the form of a powder, suspension or solution.

The size of aerosol particles is one factor relevant to the delivery capability of an aerosol. Thus, smaller particles may travel further down the respiratory airway towards the alveoli than would larger particles. In one embodiment, the aerosol particles have a diameter distribution to facilitate delivery along the entire length of the bronchi, bronchioles, and alveoli. Alternatively, the particle size distribution may be selected to target a particular section of the respiratory airway, for example the alveoli.

The aerosol particles may be delivered by way of a nebulizer or nasal spray.

In the case of aerosol delivery of the medicament, the particles may have diameters in the approximate range of 0.1-50 μm, preferably 1-25 μm, more preferably 1-5 μm.

The aerosol formulation of the medicament of the present invention may optionally contain a propellant and/or surfactant.

By controlling the size of the droplets which are to be administered to a patient to within the defined range of the present invention, it is possible to avoid/minimise inadvertent antigen delivery to the alveoli and thus avoid alveoli-associated pathological problems such as inflammation and fibrotic scarring of the lungs.

I.n. vaccination engages both T and B cell mediated effector mechanisms in nasal and bronchus associated mucosal tissues, which differ from other mucosae-associated lymphoid tissues.

The protective mechanisms invoked by the intranasal route of administration may include: the activation of T lymphocytes with preferential lung homing; upregulation of co-stimulatory molecules, eg. B7.2; and/or activation of

macrophages or secretory IgA antibodies.

Intranasal delivery of antigens may facilitate a mucosal antibody response which is favoured by a shift in the T cell response toward the Th2 phenotype which helps antibody production. A mucosal response is characterised by enhanced IgA production, and a Th2 response is characterised by enhanced IL-4 production.

Intranasal delivery of mycobacterial antigens allows targeting of the antigens to submucosal B cells of the respiratory system. These B cells are the major local IgA-producing cells in mammals and intranasal delivery facilitates a rapid increase in IgA production by these cells against the mycobacterial antigens.

In one embodiment administration of the medicament comprising a mycobacterial antigen stimulates IgA antibody production, and the IgA antibody binds to the mycobacterial antigen. In another embodiment, a mucosal and/or Th2 immune response is stimulated.

In another embodiment monoclonal antibodies, in particular, may be used to raise anti-idiotype antibodies. Anti-idiotype antibodies are immunoglobulins which carry an "internal image" of the antigen of the infectious agent against which protection is desired. These anti-idiotype antibodies may also be useful for treatment, vaccination and/or diagnosis of mycobacterial infections.

According to a tenth aspect, the peptides (including fragments, derivatives, and variants thereof) of the present invention and antibodies to them are useful in immunoassays to detect the presence of antibodies to mycobacteria or the presence of the virulence associated antigens in biological samples.

Design of the immunoassays is subject to a great deal of variation, and many formats are known in the art. The immunoassay may utilize at least one epitope derived from a peptide of the present invention. In one embodiment, the immunoassay uses a combination of such epitopes. These epitopes may be derived from the same or from different bacterial peptides, and may be in separate recombinant or natural peptides, or together in the same recombinant peptides.

An immunoassay may use, for example, a monoclonal antibody directed towards a virulence associated peptide epitope(s), a combination of monoclonal antibodies directed towards epitopes of one mycobacterial antigen, monoclonal antibodies directed towards epitopes of different mycobacterial antigens, polyclonal antibodies directed towards the same antigen, or polyclonal antibodies directed towards different antigens.

Protocols may be based, for example, upon competition, or direct reaction, or sandwich type assays. Protocols may also, for example, use solid supports, or may be by immunoprecipitation. Most assays involve the use of labelled antibody or polypeptide; the labels may be, for example, enzymatic, fluorescent, chemiluminescent, radioactive, or dye molecules. Assays which amplify the signals from the probe are also known; examples of which are assays which utilize biotin and avidin, and enzyme-labeled and mediated immunoassays, such as ELISA assays.

Typically, an immunoassay for an antibody(s) to a peptide, will involve selecting and preparing the test sample suspected of containing the antibodies, such as a biological sample, then incubating it with an antigenic (i.e., epitope-containing) peptide(s) under conditions that allow antigen-antibody complexes to form, and then detecting the formation of such complexes. The immunoassay may be of a standard or competitive type.

The peptide is typically bound to a solid support to facilitate separation of the sample from the peptide after incubation. Examples of solid supports that can be used are nitrocellulose (eg. in membrane or microtiter well form), polyvinyl chloride (eg. in sheets or microtiter wells), polystyrene latex (eg. in beads or microtiter plates, polyvinylidine fluoride (known as Immulon), diazotized paper, nylon membranes, activated beads, and Protein A beads. For example, Dynatech Immulon microtiter plates or 60 mm diameter polystyrene beads (Precision Plastic Ball) may be used. The solid support containing the antigenic peptide is typically washed after separating it from the test sample, and prior to detection of bound antibodies.

Complexes formed comprising antibody (or, in the case of competitive assays, the amount of competing antibody) are detected by any of a number of known techniques, depending on the format. For example, unlabeled antibodies in the

complex may be detected using a conjugate of antixenogeneic Ig complexed with a label (eg. an enzyme label).

In immunoassays where the peptides are the analyte, the test sample, typically a biological sample, is incubated with antibodies directed against the peptide under conditions that allow the formation of antigen-antibody complexes. It may be desirable to treat the biological sample to release putative bacterial components prior to testing. Various formats can be employed. For example, a "sandwich assay" may be employed, where antibody bound to a solid support is incubated with the test sample; washed; incubated with a second, labeled antibody to the analyte, and the support is washed again. Analyte is detected by determining if the second antibody is bound to the support. In a competitive format, a test sample is usually incubated with antibody and a labeled, competing antigen is also incubated, either sequentially or simultaneously.

Also included as an embodiment of the invention is an immunoassay kit comprised of one or more peptides of the invention, or one or more antibodies to said peptides, and a buffer, packaged in suitable containers.

As used herein, a "biological sample" refers to a sample of tissue or fluid isolated from an individual, including but not limited to, for example, plasma, serum, spinal fluid, lymph fluid, the external sections of the skin, respiratory, intestinal, and genitourinary tracts, tears, saliva, milk, blood cells, tumours, organs, and also samples of in vitro cell culture constituents (including but not limited to conditioned medium resulting from the growth of cells in cell culture medium, putatively virally infected cells, recombinant cells, and cell components).

In a related diagnostic assay, the present invention provides nucleic acid probes for detecting a mycobacterial infection.

Using the polynucleotides of the present invention as a basis, oligomers of approximately 8 nucleotides or more can be prepared, either by excision from recombinant polynucleotides or synthetically, which hybridize with the mycobacterial sequences, and are useful in identification of mycobacteria.

The probes are a length which allows the detection of the induced or up-

regulated sequences by hybridization. While 6-8 nucleotides may be a workable length, sequences of 10-12 nucleotides are preferred, and at least about 20 nucleotides appears optimal. These probes can be prepared using routine methods, including automated oligonucleotide synthetic methods. For use as probes, complete complementarity is desirable, though it may be unnecessary as the length of the fragment is increased.

For use of such probes as diagnostics, the biological sample to be analyzed, such as blood or serum, may be treated, if desired, to extract the nucleic acids contained therein. The resulting nucleic acid from the sample may be subjected to gel electrophoresis or other size separation techniques; alternatively, the nucleic acid sample may be dot blotted without size separation. The probes are usually labeled. Suitable labels, and methods for labeling probes are known in the art, and include, for example, radioactive labels incorporated by nick translation or kinasing, biotin, fluorescent probes, and chemiluminescent probes. The nucleic acids extracted from the sample are then treated with the labeled probe under hybridization conditions of suitable stringencies.

The probes may be made completely complementary to the virulence encoding polynucleotide. Therefore, usually high stringency conditions are desirable in order to prevent false positives. The stringency of hybridization is determined by a number of factors during hybridization and during the washing procedure, including temperature, ionic strength, length of time, and concentration of formamide.

It may be desirable to use amplification techniques in hybridization assays. Such techniques are known in the art and include, for example, the polymerase chain reaction (PCR) technique.

The probes may be packaged into diagnostic kits. Diagnostic kits include the probe DNA, which may be labeled; alternatively, the probe DNA may be unlabeled and the ingredients for labeling may be included in the kit in separate containers. The kit may also contain other suitably packaged reagents and materials needed for the particular hybridization protocol, for example, standards, as well as instructions for conducting the test.

In a preferred embodiment, a peptide (or fragment or variant or derivative) of the present invention is used in a diagnostic assay to detect the presence of a

T-lymphocyte, which T-lymphocyte has been previously exposed to an antigenic component of a mycobacterial infection in a patient.

In more detail, a T-lymphocyte which has been previously exposed to a particular antigen will be activated on subsequent challenge by the same antigen. This activation provides a means for identifying a positive diagnosis of mycobacterial infection. In contrast, the same activation is not achieved by a T-lymphocyte which has not been previously exposed to the particular antigen.

The above "activation" of a T-lymphocyte is sometimes referred to as a "recall response" and may be measured, for example, by determining the release of interferon (eg. IFN-γ) from the activated T-lymphocyte. Thus, the presence of a mycobacterial infection in a patient may be determined by the release of a minimum concentration of interferon from a T-lymphocyte after a defined time period following *in vitro* challenge of the T-lymphocyte with a peptide (or fragment or variant or derivative) of the present invention.

In use, a biological sample containing T-lymphocytes is taken from a patient, and then challenged with a peptide (or fragment, variant, or derivative thereof) of the present invention.

The above T-lymphocyte diagnostic assay may include an antigen presenting cell (APC) expressing at least one major histocompatibility complex (MHC) class II molecule expressed by the patient in question. The APC may be inherently provided in the biological sample, or may be added exogenously. In one embodiment, the T-lymphocyte is a CD4 T-lymphocyte.

Example 1 - generation of putative promoter library

The routine molecular biology methods employed were as described in the standard reference protocols (Ausubel F.M., Brent R., Kingston R.E., Moore D.D., Seidman J.G., Smith J.A. and Struhl K. (1992). "Current protocols in molecular biology". John Wiley & Sons, Chichester).

The promoter library was prepared by partial restriction endonuclease digestion (Sau 3A1) of *M. tuberculosis* H37Rv chromosomal DNA. Digested DNA was size fractionated and fragments of 1-2 kb in size recovered using the Qiaex II Gel Extraction Kit (Qiagen Ltd).

Recovered fragments were ligated into the vector pCREP8GFPTTL which had been linearised with Bgl II and dephosphorylated. The vector PCREP8GFPTTL is based upon the vector pCREP8 provided by Dr P O'Gaora, ICSM, London which is itself based upon the pNG2 replicon (Radford and Hodgson, 1991, Plasmid 25: 149-153).

Modifications of pCREP8 to create pCREP8GFPTTL include replacement of the region encoding Cre recombinase with the gene encoding GFPmut2 (Cormack, Valdivia and Falkow. Gene. 1996, 173: 33-38). In addition transcriptional terminators from CelA (from *C. thermocelum*) and Ferredoxin (from *C. pasteurianum*) genes were inserted upstream and downstream of the GFPmut2 gene respectively. Finally translational stops were introduced in all three reading frames by insertion of a linker between the Bgl II cloning site and the ribosome binding site immediately preceding the ATG start codon of the GFPmut2 gene.

The ligation mixture was transformed into *E. coli* and resulting transformants banked into 96 well plates to give 23,040 individual clones. Large scale plasmid isolation was performed on pools of 480 clones using Qiagen Maxi plasmid preps (Qiagen Ltd).

Example 2 - putative promoters identified by sequence homology

Promoter regions for targeted fusions were selected by screening the annotated M.tuberculosis genome (http://www.sanger.ac.uk/Projects/M_tuberculosis/ or http://pedant.mips.biochem.mpg.de/) for secreted proteins, surface exposed

proteins and those with homology to known virulence factors or implicated previously in mycobacterial virulence using text searches.

In this way a number of candidates for targeted fusions may be isolated. Having identified a promoter, the organisation of the surrounding gene structure was examined and, where possible, a promoter was identified.

Mycobacterial promoters lack typical -35 and -10 sequences [Das Gupta SK, Bashyam MD and Tyagi AK (1993). J. Bacteriol., 175: 5186-5192].

In this instance the region immediately upstream of the gene or operon of interest was amplified by PCR using tailed primers and cloned directly into the *Bgl* II site of pCREP8GFPTTL. The GFPmut2 vector was used as described above using macrophage cell line J774.1, *in vitro* culture grown in Middlebrook 7H9 supplemented with 10 % OADC and 0.25 % Triton WR1339 (synthetic mycobacterial culture medium), or DMEM.

Table 1 lists a number of such promoters.

Table 1 FACS analysis of Targeted Promoter-GFP Fusions in Macrophage Infection Assays

Promoter	Identity/Predicted function Gene arrangement[+]	Net change[**] in % population > 10^3
TF m1	Invasion loci mce1 operon Rv0167-0174	3.3
TF h	sigE operon Rv1221-1224	21.7
TF m2	mce2 operon	1.46
TF t	Rv2462c trigger factor	4.41
TF2	mce3 operon Rv1964-1971	12.6
TF3	probable secreted protein Rv1910c	2.9
TF7	Weak similarity to pollen antigens Rv1919c	6
TF10	Putative exported protein Rv1477 -1478	40
TF11	putative exported protease Rv2671/2672/2673	5.42
TF13	proteolytic subunit Rv2461c	3.7
TF15	single gene heat shock protein Rv0384c	11.5
H37Rv	Non-fluorescing control Control	-0.1

[+] as annotated in the genome sequence (www.sanger.ac.uk/Projects/M_tuberc)
[**] increase or decrease over DMEM control in gated population with greater than 10^3 fluorescence

Example 3 - Protocol for macrophage infection, harvesting, FACS analysis and sorting, and recovery of *M. tuberculosis*

Macrophage infection with batch culture samples of *M. tuberculosis*. Wells were harvested at intervals of 24hr, 48hr and 72hrs post infection.

Materials

Mouse macrophage cell line J774A.1 (obtainable from, for example, the ECACC) in 6 well plates were seeded at $5x10^5$ cells per well.

Tissue culture medium - Dulbecco's Modified Eagle Medium supplemented with 200 mM L-glutamate,10 % foetal bovine serum (gamma-irradiated) and 10 mM HEPES.

Batch culture sample of *M. tuberculosis* was grown to mid-late exponential log ($O.D_{600}$ 0.6-0,8).

Liquid Middlebrook 7H9 medium (Difco) supplemented with 10 % OADC enrichment (Difco) and 0.25 % Triton WR1339, or organisms were cultured on solid Middlebrook 7H10 medium (Difco) supplemented with 10 % OADC enrichment (Difco) for growth of *M. tuberculosis* outside of macrophage.

Procedure

1. Macrophage were grown until confluent ($4x10^6$ cells per well).

2. Bacterial samples were prepared using the following procedure:

2-3 week old colonies were scraped from 7H10 + OADC agar plates and resuspended in 10 mls of 7H9 +OADC+Triton WR1339. A universal tube (22 mm diameter x 90 mm height) containing 10 mls of 7H9 +OADC+Triton WR1339 was inoculated with 500 µl of the bacterial suspension. Bacteria were grown on an orbital shaker (200rpm) at 37 °C for 7 days

500 µls of bacterial culture was inoculated into a universal tube (22 mm

diameter x 90mm height) containing 10 mls of 7H9 +OADC+Triton WR1339 1ml. Bacteria were grown on an orbital shaker (200 rpm) at 37 °C for 5 days ($O.D_{600}$ 0.6-0.8).

Bacterial samples were diluted in DMEM to a cell density of $1x10^7$/ml - a multiplicity of approximately 2:1 (bacteria to cells) or less is preferred.

3. Tissue culture medium was removed from each tissue culture well

4. 1 ml of bacterial suspension was added to each well and incubated at 37 °C for 3 hours in an atmosphere of 5 % CO_2 in air.

5. The inoculum suspension and was removed and each well washed 4 times with 1x phosphate buffered saline (PBS) pre-warmed to 37 °C.

6. 3 ml fresh pre-warmed DMEM was added to each well.

7. Infected monolayers were incubated at 37 °C in an atmosphere of 5 % CO_2 in air, for a period of 1, 2 or 3 days.

8. Wells for each sample were harvested at appropriate time points as follows:

i) Culture medium was removed by aspiration and monolayers washed with pre-warmed PBS to remove any external bacteria.

ii) The PBS buffer was removed and replaced with 1 ml of 0.25 % Triton X-100 in water.

iii) The monolayers were Incubated for 25 mins before disruption of the monolayer with a pastette to release bacteria from the macrophage.

iv) Samples were transferred to a FACS tube and examined using a FACS scanner/sorter at Cat III collecting highly fluorescent bacteria (typically greater than 10^3 logs of fluorescence).

9. Bacteria were recovered by passing the sorted suspensions through a 0.2 μM filter.

10. Recovered bacteria on the filter membrane were cultured on Middlebrook 7H10 +OADC agar plates and grown at 37 °C for 2 weeks.

11. Bacteria were scraped from the filter membrane into 10 mls of 7H9 + ADC medium and grow for 5-7 days (37 °C, 200 rpm).

Notes:

i) The macrophage infection assay and sorting were repeated until the desired level of enrichment of fluorescent bacteria was attained

ii) Bacteria carrying *M. tuberculosis* promoters that were highly active outside of the macrophage environment were removed by culturing bacteria in Middlebrook 7H9+ ADC medium then FACS sorting to collect the non-fluorescent bacteria. (This selection procedure was carried out between passage 1 and passage 2 of the repeat macrophage infection rounds).

Example 4 - Alternative macrophage assay procedures

1). Triccas, J.A. *et al.* (1999). Microbiology 145, 2923-2930.

Procedure

Macrophage cells were seeded at $2x10^5$ per well in 24-well plates and incubated at 37 °C in 5 % CO_2 for 7 days. Macrophage monolayers were infected with bacteria at a multiplicity of infection (m.o.i) of 1:1. After 4 hours of infection extracellular bacteria were removed by washing 4x with PBS and incubation continued in 5 % CO_2.

After 5-6 days of infection, infected macrophages were washed 3x in PBS, scraped into 1 ml PBS and analysed by FACS. To recover bacteria, sorted macrophages were centrifuged and lysed in water plus 0.1 % Tween 80. Recovered bacteria were grown in 7H9 medium for 7days and macrophage infection and sorting repeated until the desired level of enrichment of macrophage/fluorescent bacteria was attained.

To select clones with enhanced intracellular expression the macrophage infection was performed as above, however the macrophage were then lysed with Tween 80 to release the bacteria prior to FACS sorting.

2). Kremer, L. *et al.* (1995). Mol Microbiol. 17, 913-922.

Procedure (macrophage infection only)

J774A.1 macrophages were seeded in eight-chamber culture slides and incubated overnight at 37 °C in 5 % CO_2. Just prior to infection, the monolayer was washed with RPM I1640. Recombinant BCG was added at a m.o.i. of 1-5 bacteria per macrophage.

After an overnight infection at 37 °C in the presence of 5 % CO_2, the cells were washed 3x with RPMI to remove possible extracellular bacteria. The macrophage were then examined using a fluorescence microscope.

3). Dhandayuthapani, S. *et al.* (1995). Mol. Microbiol. 17, 901-912.

Procedure

Macrophages were seeded in 100 mm tissue-culture petri dishes ($5x10^6$). After overnight attachment at 37 °C in the presence of 5 % CO_2 the macrophage were infected at a m.o.i of 1 bacteria per macrophage. One hour after infection, the monolayers were washed 3x with prewarmed PBS to remove non-ingested bacteria and the DMEM replaced.

The macrophages were harvested 6 days post-infection by washing with PBS and then scraped from the dish. The macrophages were collected by centrifugation and broken by 20-30 passages through a 23-gauge needle: intact cells and nuclei were pelleted and the supernatant containing bacteria collected. The bacteria were then pelleted, washed with PBS and centrifuged again. The final bacterial pellet was suspended in PBS for FACS analysis.

4). Via, L. E. *et al.* (1996). J. Bacteriol. 178, 3314-3321.

Procedure

J774 macrophage monolayers were seeded at a density of $7.5x10^6$ cells per 100mm-diameter tissue culture petri dish. After overnight attachment at 37 °C in the presence of 5 % CO_2, macrophages were infected at a m.o.i of 10-20 bacteria per macrophage. One hour after infection any extracellular bacteria were removed by washing 3x with prewarmed PBS, then fresh DMEM + 5%FBS added.

The medium was replaced every 3-4 days of culture. The infected macrophages were incubated for 10 mins, 3 days, 7 days and 11days (FACS analysis was performed on the 10 min, 7 day and 11 day samples) before harvesting. At harvest the monolayers were washed 3x with PBS, scraped from the dish, centrifuged then homogenised in 20 mM HEPES (pH 7.2) - 250mM sucrose. For FACS the homogenate was then subjected to three rounds of centrifugation to remove unbroken macrophage and macrophage debris, the final bacterial pellet was suspended in PBS. FACS analysis and sorting were carried out as described above in reference 3.

5). Barker L. P. *et al.* (1998). Mol. Microbiol. 29, 1167-1177.

Procedure

Macrophages were seeded into tissue culture dishes at a concentration of $2x10^5$ cells/ml total volume. Macrophages were grown to semi-confluency before bacteria were added at a m.o.i. of 1-5 bacteria per macrophage. After 4 hours growth at 37 °C in the presence of 5 % CO_2 the medium was removed and fresh DMEM supplemented with amikacin 100 µg/ml was added to kill extracellular organisms.

After 24 hours at 32 °C the concentration of amikacin was reduced to 20 µg/ml. At three days after infection (the point at which most phagocytic vesicles contain only one organism) the macrophages are washed in PBS, scraped from the dish and subjected to a very gentle and controlled lysis that disrupts the cell membrane without compromising the nuclear membrane.

Vesicles containing bacteria are then isolated by centrifugation, the supernatant removed and diluted with PBS for FACS analysis. Fluorescent bacterial clones

that were sorted away from non-fluorescent vesicles and vesicles containing non-fluorescent organisms were screened further using a confocal microscope.

Those clones that appeared to fluoresce intracellularly but not on 7H10 agar or in tissue culture media were passaged through macrophage again. After 3-4 days of growth the bacteria were harvested from the macrophage by lysing the macrophage with 0.1 % Triton-X in PBS for 5 min, after which the detergent was diluted with 9 volumes of PBS ready for FACS analysis.

Example 5 - elucidation of mycobacterial nucleic acid coding sequences under the transcriptional control of identified promoters

DFI allows identification of a promoter which is induced or up-regulated during infection of macrophage, a key step in the pathogenesis of tuberculosis.

Once the DNA sequence and orientation of a promoter region has been determined the exact location can be mapped by doing a DNA homology search (e.g BLASTN or BLASTX, see http://www.sanger.ac.uk/) on the published *M. tuberculosis* H37Rv genome to reveal the gene or operon under control of the identified promoter region.

Knockout mutants of the gene(s) under control of the identified promoter may then be prepared to see if they are essential for virulence. The fact that the genes are expressed or up-regulated during the infection means they may be essential for virulence of the organism (as demonstrated by testing a knockout mutant in a suitable model).

These data help identify a) a potential vaccine candidate which the host immune response can be targeted to; b) a gene which when inactivated sufficiently attenuates the organism that it could be considered suitable as a live vaccine; c) a target for the development of a new antibiotic.

A suitable plasmid DNA vector (Tascon RE *et al.*, 1996 Nat. Med. 2:8 888-892; Huygen K *et al.*, 1996 Nat. Med. 2:8 893-898) containing the DNA sequence corresponding to one or more of the genes in an identified operon may be tested as a DNA vaccine in comparison with pre-existing TB vaccines. Similarly, gene products thereof may be tested as a vaccine in a guinea pig protection model.

Example 6 - Delete one or more of the genes from *M. tuberculosis* in order to attenuate its virulence while retaining immunogenicity

One or more genes that are identified may be disrupted using allelic exchange. In brief, the gene of interest is cloned with 1-2 kb of flanking DNA either side and is inactivated by deletion of part of the coding region and insertion of an antibiotic resistance marker, such as hygromycin.

The manipulated fragment is then transferred to a suitable suicide vector eg. pPR23 and is transformed into the wild-type parent strain of *M. tuberculosis*. Mutants are recovered by selecting for antibiotic resistant strains. Genotypic analysis (Southern Blotting with a fragment specific to the gene of interest) is performed on the selected strains to confirm that the gene has been disrupted.

The mutant strain is then studied to determine the effect of the gene disruption on the phenotype. In order to use it as a vaccine candidate it would be necessary to demonstrate attenuated virulence. This can be done using either a guinea pig or mouse model of infection. Animals are infected with the mutant strain and the progression of disease is monitored by determining the bacterial load in different organs, in particular the lung and spleen, at specific time points post infection, typically up to 16 weeks.

Comparison is made to animals infected with the wild-type strain which should have a significantly higher bacterial load in the different organs. Long-term survival studies and histopathology can also be used to assess virulence and pathogenicity.

Once attenuated virulence has been established, protection and immunogenicity studies can be performed to assess the potential of the strain as a vaccine. Suitable references for allelic exchange and preparation of TB mutants are McKinney et al., 2000 and Pelicic et al., 1997, [1, 2].

Example 7 - Select one or more of our genes, which encode proteins that are immunogenic, and put them into BCG or an attenuated strain of *M. tuberculosis* to enhance its overall immunogenicity

The gene of interest is amplified from the *M. tuberculosis* genome by PCR. The amplified product is purified and cloned into a plasmid (pMV306) that integrates site specifically into the mycobacterial genome at the attachment site (attB) for mycobacteriophage L5 [3].

BCG is transformed with the plasmid by electroporation, which involves damaging the cell envelope with high voltage electrical pulses, resulting in uptake of the DNA. The plasmid integrates into the BCG chromosome at the attB site generating stable recombinants. Recombinants are selected and are checked by PCR or Southern blotting to ensure that the gene has been integrated. The recombinant strain is then used for protection studies.

Example 8 - Use recombinant carriers such as attenuated salmonella and the Vaccinia virus to express and present TB genes.

One of the best examples of this type of approach is the use of Modified Vaccinia virus Ankara (MVA) [4]. The gene of interest is cloned into a vaccinia virus shuttle vector, e.g. pSC11. Baby Hamster Kidney (BHK) cells are then infected with wild-type MVA and are transfected with the recombinant shuttle vector. Recombinant virus is then selected using a suitable selection marker and viral plaques, selected and purified.

Recombinant virus is normally delivered as part of a prime-boost regime where animals are vaccinated initially with a DNA vaccine encoding the TB genes of interest under the control of a constitutive promoter. The immune response is boosted by administering recombinant MVA carrying the genes of interest to the animals at least 2 weeks later.

Example 9 - Sub-unit vaccines containing a single peptide/protein or a combination of proteins

To prepare sub-unit vaccines with one or more peptides or proteins it is first of all necessary to obtain a supply of protein or peptide to prepare the vaccine. Up to now, this has mainly been achieved in mycobacterial studies by purifying proteins of interest from TB culture. However, it is becoming more common to clone the gene of interest and produce a recombinant protein.

The coding sequence for the gene of interest is amplified by PCR with restriction sites inserted at the N terminus and C terminus to permit cloning in-frame into a protein expression vector such as pET-15b. The gene is inserted behind an inducible promoter such as lacZ. The vector is then transformed into *E. coli* which is grown in culture. The recombinant protein is over-expressed and is purified.

One of the common purification methods is to produce a recombinant protein with an N-terminal His-tag. The protein can then be purified on the basis of the affinity of the His-tag for metal ions on a Ni-NTA column after which the His-tag is cleaved. The purified protein is then administered to animals in a suitable adjuvant [5].

Example 10 - Plasmid DNA vaccines carrying one or more of the identified genes

DNA encoding a specific gene is amplified by PCR, purified and inserted into specialised vectors developed for vaccine development, such as pVAX1. These vectors contain promoter sequences, which direct strong expression of the introduced DNA (encoding candidate antigens) in eukaryotic cells (eg. CMV or SV40 promoters), and polyadenlyation signals (eg. SV40 or bovine growth hormone) to stabilise the mRNA transcript.

The vector is transformed into *E. coli* and transformants are selected using a marker, such as kanamycin resistance, encoded by the plasmid. The plasmid is then recovered from transformed colonies and is sequenced to check that the gene of interest is present and encoded properly without PCR generated mutations.

Large quantities of the plasmid is then produced in *E. coli* and the plasmid is recovered and purified using commercially available kits (eg. Qiagen Endofree-plasmid preparation). The vaccine is then administered to animals for example by intramuscular injection in the presence or absence of an adjuvant.

Example 11 - Preparation of DNA expression vectors

DNA vaccines consist of a nucleic acid sequence of the present invention cloned into a bacterial plasmid. The plasmid vector pVAX1 is commonly used in the preparation of DNA vaccines. The vector is designed to facilitate high copy number replication in *E. coli* and high level transient expression of the peptide of interest in most mammalian cells (for details see manufacturers protocol for pVAX1(catalog no. V260-20 www.invitrogen.com).

The vector contains the following elements

* Human cytomegalovirus immediate-early (CMV) promoter for high-level expression in a variety of mammalian cells
* T7 promoter/priming site to allow in vitro transcription in the sense orientation and sequencing through the insert
* Bovine growth hormone (BGH) polyadenylation signal for efficient transcription termination and polyadenylation of mRNA
* Kanamycin resistance gene for selection in *E. coli*
* A multiple cloning site
* pUC origin for high-copy number replication and growth in *E. coli*
* BGH reverse priming site to permit sequencing through the insert

Vectors may be prepared by means of standard recombinant techniques which are known in the art, for example Sambrook et al., (1989). Key stages in preparing the vaccine are as follows:

* The gene of interest is ligated into pVAX1 via one of the multiple cloning sites
* The ligation mixture is then transformed into a competent *E. coli* strain (eg. TOP10) and LB plates containing 50 µg/ml kanamycin are used to select transformants.
* Clones are selected and may be sequenced to confirm the presence and orientation of the gene of interest.
* Once the presence of the gene has been verified, the vector can be used to transfect a mammalian cell line to check for protein expression. Methods for transfection are known in the art and include, for example, electroporation, calcium phosphate, and lipofection.
* Once peptide expression has been confirmed, large quantities of the vector can be produced and purified from the appropriate cell host, e.g. *E. coli*.

pVAX1 does not integrate into the host chromosome. All non-essential sequences have been removed to minimise the possibility of integration. When constructing a specific vector, a leader sequence may be included to direct secretion of the encoded protein when expressed inside the eukaryotic cell.

Other examples of vectors that have been used are V1Jns.tPA and pCMV4 (Lefevre *et al.*, 2000; and Vordermeier *et al.*, 2000).

Expression vectors may be used that integrate into the genome of the host, however, it is more common and more preferable to use a vector that does not integrate. The example provided, pVAX1, does not integrate. Integration would lead to the generation of a genetically modified host which raises other issues.

Example 12 - RNA vaccine

As discussed on page 15 of US patent US 5,783,386, one approach is to introduce RNA directly into the host.

Thus, the vector construct (Example 11) may be used to generate RNA *in vitro* and the purified RNA then injected into the host. The RNA would then serve as a template for translation in the host cell. In this embodiment. In this embodiment, integration would not occur.

Another option is to use an infectious agent such as the retroviral genome carrying RNA corresponding to the gene of interest. In this embodiment, integration into the host genome will occur.

Another option is the use of RNA replicon vaccines which can be derived from virus vectors such as Sindbis virus or Semliki Forest virus. These vaccines are self-replicating and self-limiting and may be administered as either RNA or DNA which is then transcribed into RNA replicons *in vivo*. The vector eventually causes lysis of the transfected cells thereby reducing concerns about integration into the host genome. Protocols for RNA vaccine construction are detailed in Cheng, *et al.* (2001).

Example 13 - Diagnostic assays based on assessing T cell responses

For a diagnostic assay based on assessing T cell responses it would be sufficient to obtain a sample of blood from the patient. Mononuclear cells (monocytes, T and B lymphocytes) can be separated from the blood using density gradients such as Ficoll gradients.

Both monocytes and B-lymphocytes are both able to present antigen, although less efficiently than professional antigen presenting cells (APCs) such as dendritic cells. The latter are more localised in lymphoid tissue.

The simplest approach would be to add antigen to the separated mononuclear cells and incubate for a week and then assess the amount of proliferation. If the individual had been exposed to the antigen previously through infection, then T-cell closes specific to the antigen should be more prevalent in the sample and should respond.

It is also possible to separate the different cellular populations should it be desired to control the ratio of T cells to APC's.

Another variation of this type of assay is to measure cytokine production by the responding lymphocytes as a measure of response. The ELISPOT assay described below in Example 14 is a suitable example of this variation.

Example 14 - detection of latent mycobacteria

A major problem for the control of tuberculosis is the presence of a large reservoir of asymptomatic individuals infected with tubercle bacilli. Dormant bacilli are more resistant to front-line drugs.

The presence of latent mycobacteria-associated antigen may be detected indirectly either by detecting antigen specific antibody or T-cells in blood samples.

The following method is based on the method described in Lalvani *et al.* (2001) in which a secreted antigen, ESAT-6, was identified as being expressed by members of the *M. tuberculosis* complex but is absent from *M. bovis* BCG vaccine strains and most environmental mycobacteria. 60 - 80% of patients also

have a strong cellular immune response to ESAT-6. An *ex-vivo* ELISPOT assay was used to detect ESAT-6 specific T cells.

As applied to the present invention:

A 96 well plate is coated with cytokine (eg. interferon-(, IL-2) -specific antibody. Peripheral blood monocytes are then isolated from patient whole blood and are applied to the wells.

Antigen (ie. one of the peptides, fragments, derivatives or variants of the present invention) is added to stimulate specific T cells that may be present and the plates are incubated for 24h. The antigen stimulates cytokine production which then binds to the specific antibody.

The plates are washed leaving a footprint where antigen-specific T cells were present.

A second antibody coupled with a suitable detection system, eg. enzyme, is then added and the number of spots are enumerated after the appropriate substrate has been added.

The number of spots, each corresponding to a single antigen-specific T cell, is related to the total number of cells originally added.

The above Example also describes use of an antigen that may be used to distinguish TB infected individuals from BCG vaccinated individuals. This could be used in a more discriminative diagnostic assay.

The following Table 2 lists the preferred promoters, peptides, and corresponding DNA coding sequences of the present invention.

Table 2

name	amino acid sequence	nucleic acid sequence
Mce1 operon promoter		1
Rv0167	2	3
Rv0168	4	5
Rv0169	6	7
Rv0170	8	9
Rv0171	10	11
Rv0172	12	13
Rv0173	14	15
Rv0174	16	17
Rv0175	117	118
Mce2 operon promoter		18
Rv0586	19	20
Rv0587	21	22
Rv0588	23	24
Rv0589	25	26
Rv0590	27	28
Rv0591	29	30
Rv0592	31	32
Rv0593	33	34
Rv0594	35	36

name	amino acid sequence	nucleic acid sequence
Mce3 operon promoter		37
Rv1964	38	39
Rv1965	40	41
Rv1966	42	43
Rv1967	44	45
Rv1968	46	47
Rv1969	48	49
Rv1970	50	51
Rv1971	52	53
Rv2462c promoter		54
Rv2462c	55	56
SigE/htrA operon promoter		57
Rv1221	58	59
Rv1222	60	61
Rv1223	62	63
Rv1224	64	65
Rv1477/1478 operon promoter		66
Rv1477	67	68
Rv1478	69	70
Rv1919c promoter		71
Rv1919c	72	73
Rv0384c promoter		74
Rv0384c	75	76
Rv2671-2672-2673 promoter		77
Rv2671	78	79
Rv2672	80	81
Rv2673	82	83
Rv1909/1910/1912c promoter		84
Rv1910c	85	86
Rv1911c	87	88
Rv1912c	89	90

name	amino acid sequence	nucleic acid sequence
Rv2461c/2460c promoter		91
Rv2461c	92	93
Rv2460c	94	95
Rv1179c promoter		96
Rv1179c	97	98
Rv1646 promoter		99
Rv1646	100	101
Rv2042c (Rv2043-2037c) promoter		102
Rv2037c	103	104
Rv2038c	105	106
Rv2039c	107	108
Rv2040c	109	110
Rv2041c	111	112
Rv2042c	113	114
Rv2043c	115	116

References:

1. McKinney, J.D., et al., Persistence of Mycobacterium tuberculosis in macrophages and mice requires the glyoxylate shunt enzyme isocitrate lyase [see comments]. Nature, 2000. 406(6797): p. 735-8.

2. Pelicic, V., et al., Efficient allelic exchange and transposon mutagenesis in Mycobacterium tuberculosis. Proc Natl Acad Sci U S A, 1997. 94(20): p. 10955-60.

3. Lee, M.H., et al., Site-specific integration of mycobacteriophage L5: integration- proficient vectors for Mycobacterium smegmatis, Mycobacterium tuberculosis, and bacille Calmette-Guerin. Proc Natl Acad Sci U S A, 1991. 88(8): p. 3111-5.

4. McShane, H., et al., Enhanced immunogenicity of CD4(+) t-cell responses and protective efficacy of a DNA-modified vaccinia virus Ankara prime-boost vaccination regimen for murine tuberculosis. Infect Immun, 2001. 69(2): p. 681-6.

5. Movahedzadeh, F., M.J. Colston, and E.O. Davis, Characterization of *Mycobacterium tuberculosis* LexA: recognition of a Cheo (Bacillus-type SOS) box. Microbiology, 1997. 143(Pt 3): p. 929-36.

Additional References:

Sambrook, J., E. F. Fritsch, and T. Maniatis. 1989. Molecular cloning: a laboratory manual, 2nd ed. Cold Spring Harbour Laboratory Press, Cold Spring Harbour, N. Y.

Lefever, P., O. Denis, L. De Wit, A. Tanghe, P. Vandenbussche, J. Content, and K. Huygen. 2000. Cloning of the gene encoding a 22-kilodalton cell surface antigen of *Mycobacterium bovis* BCG and analysis of its potential for DNA vaccination against tuberculosis. Infection and Immunity. 68:1040-1047.

Vordermeier, H. M., P. J. Cockle, A. O. Whelan, S. Rhodes, M. A. Chambers, D. Clifford, K. Huygen, R. Tascon, D. Lowrie, M. J. Colston, and R. G.

Hewinson. 2000. Effective DNA vaccination of cattle with the mycobacterial antigens MPB83 and MPB70 does not compromise the specificity of the comparative intradermal tuberculin skin test. Vaccine. 19:1246-1255.

Cheng, W., C. Hung, C. Chai, K. Hsu, L. He, C. Rice, M. Ling, and T. Wu. 2001. Enhancement of Sindbis virus self-replicating RNA vaccine potency by linkage of *Mycobacterium tuberculosis* heat shock protein 70 gene to an antigen. J. Immunol. 166:6218-6226.

Lalvani, A. *et al.*, 2001. Enhanced contact tracing and spatial tracking of *Mycobacterium tuberculosis* infection by enumeration of antigen-specific T cells. The Lancet 357:2017-2021.

Claims

1. A method of identifying a mycobacterial nucleic acid promoter sequence which is induced or up-regulated during mycobacterial virulence, said method comprising:-

infecting a macrophage target cell with a *Mycobacterium tuberculosis* host cell, which host cell contains a nucleic acid construct comprising a putative mycobacterial promoter sequence operably linked to a coding sequence of a reporter gene located down-stream from the promoter;

culturing the macrophage under conditions which support mycobacterial virulence; and

identifying a promoter sequence which is induced or up-regulated during virulence by detecting expression of the reporter sequence.

2. A method according to Claim 1, wherein the induced or up-regulated promoter sequence is detected by increased expression of the reporter gene under conditions which support mycobacterial virulence when compared with the corresponding level of expression when cultured under conditions which do not promote mycobacterial virulence.

3. A method according to Claim 1 or 2, wherein the putative promoter sequence is derived from *M. tuberculosis* or *M. bovis*.

4. A method according to any preceding claim, wherein the reporter sequence encodes a green fluorescence protein.

5. A method according to Claim 4, wherein a mycobacterial host cell having a promoter induced or up-regulated during mycobacterial virulence is separated from other host cells by fluorescence activated cell sorting.

6. A method of identifying a mycobacterial gene the expression of which is induced or up-regulated during mycobacterial virulence, said method comprising:-

identifying a mycobacterial promoter sequence which is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell, wherein the host cell contains a nucleic acid construct comprising said promoter sequence operably linked to a coding sequence of a reporter gene located down-stream from the promoter;

aligning by sequence homology the nucleic acid sequence of the promoter with published nucleic acid sequence data for the same mycobacterial species; and

identifying the associated nucleic acid coding sequence under the control of said promoter.

7. An isolated mycobacterial promoter obtainable by a method according to any of Claims 1-5, wherein the promoter preferably has the nucleic acid sequence of SEQ ID NO: 1; 18; 37; 54; 57; 66; 71; 74; 77; 84; 91; 96; 99; or 102.

8. An isolated nucleic acid coding sequence obtainable by a method according to Claim 6, wherein the coding sequence preferably has the nucleic acid sequence of SEQ ID NO: 3; 5; 7; 9; 11; 13; 15; 17; 20; 22; 24; 26; 28; 30; 32; 34; 36; 39; 41; 43; 45; 47; 49; 51; 53; 56; 59; 61; 63; 65; 68; 70; 73; 76; 79; 81; 83; 86; 88; 90; 93; 95; 98; 101; 104; 106; 108; 110; 112; 114; 116; or 118.

9. An isolated mycobacterial peptide or a fragment or derivative or variant thereof, wherein the peptide is encoded by a mycobacterial gene the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene.

10. A pharmaceutical composition comprising a peptide, or a fragment or variant or derivative thereof, wherein the peptide is selected from the group consisting of SEQ ID NO: 2; 4; 6; 8; 10; 12; 14; 16; 19; 21; 23; 25; 27; 29; 31; 33; 35; 38; 40; 42; 44; 46; 48; 50; 52; 55; 58; 60; 62; 64; 67; 69; 72; 75; 78; 80; 82; 85; 87; 89; 92; 94; 97; 100; 103; 105; 107; 109; 111; 113; 115; and 117.

11. An inhibitor of a mycobacterial peptide, wherein the peptide is encoded by a mycobacterial gene the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene, and wherein the inhibitor is capable of substantially preventing or inhibiting the mycobacterial peptide from exerting its native biological function or effect.

12. An inhibitor according to Claim 11, selected from the group consisting of:- an antibiotic capable of targeting the induced or up-regulated mycobacterial gene, or the gene product thereof; and an antisense or triplex-forming nucleic acid sequence which is complementary to at least part of the inducible or up-regulatable gene.

13. An antibody which binds to a peptide encoded by a gene, or to a fragment or variant or derivative of said peptide, the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene.

14. An antibody according to Claim 13, wherein the peptide is selected from the group consisting of SEQ ID NO: 2; 4; 6; 8; 10; 12; 14; 16; 19; 21; 23; 25; 27; 29; 31; 33; 35; 38; 40; 42; 44; 46; 48; 50; 52; 55; 58; 60; 62; 64; 67; 69; 72; 75; 78; 80; 82; 85; 87; 89; 92; 94; 97; 100; 103; 105; 107; 109; 111; 113; 115; and 117.

15. An attenuated mycobacterium in which a gene has been modified, the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene, thereby rendering the mycobacterium substantially non-pathogenic.

16. An attenuated mycobacterium according to Claim 15, wherein the gene to be modified has a wild-type coding sequence corresponding to one of the group consisting of SEQ ID NO: 3; 5; 7; 9; 11; 13; 15; 17; 20; 22; 24; 26; 28; 30; 32; 34; 36; 39; 41; 43; 45; 47; 49; 51; 53; 56; 59; 61; 63; 65; 68; 70; 73; 76; 79; 81; 83; 86; 88; 90; 93; 95; 98; 101; 104; 106; 108; 110; 112; 114; 116; and 118.

17. An attenuated microbial carrier, comprising a peptide encoded by a gene, or a fragment or variant or derivative of said peptide, the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene.

18. An attenuated microbial carrier according to Claim 17, wherein the peptide is selected from the group consisting of SEQ ID NO: 2; 4; 6; 8; 10; 12; 14; 16; 19; 21; 23; 25; 27; 29; 31; 33; 35; 38; 40; 42; 44; 46; 48; 50; 52; 55; 58; 60; 62; 64; 67; 69; 72; 75; 78; 80; 82; 85; 87; 89; 92; 94; 97; 100; 103; 105; 107; 109; 111; 113; 115; and 117.

19. An attenuated microbial carrier according to Claim 17 or 18, wherein the attenuated microbial carrier is attenuated salmonella, attenuated vaccinia virus, attenuated fowlpox virus, or attenuated *M. bovis* (eg. BCG strain).

20. A DNA plasmid comprising a promoter, a polyadenylation signal, and a DNA sequence which corresponds to the coding sequence of a mycobacterial gene, or a fragment or variant or derivative of said DNA sequence, the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene, wherein the promoter and polyadenylation signal are operably linked to the DNA sequence.

21. A DNA plasmid according to Claim 20, wherein the coding sequence of said gene is selected from the group consisting of SEQ ID NO: 3; 5; 7; 9; 11; 13; 15; 17; 20; 22; 24; 26; 28; 30; 32; 34; 36; 39; 41; 43; 45; 47; 49; 51; 53; 56; 59; 61; 63; 65; 68; 70; 73; 76; 79; 81; 83; 86; 88; 90; 93; 95; 98; 101; 104; 106; 108; 110; 112; 114; 116; and 118.

22. A DNA plasmid according to Claim 20 or 21, wherein the promoter is selected from the group consisting of:- CMV; and SV40 promoters; and the polyadenylation signal is selected from the group consisting of:- SV40; and bovine growth hormone polyadenylation signals.

23. An isolated RNA sequence which is encoded by the coding sequence of a mycobacterial gene, or a fragment or variant or derivative of said coding sequence, the expression of which gene is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene.

24. An RNA vector comprising the RNA sequence of Claim 23 and an integration site for a chromosome of a host cell.

25. Use of a peptide or fragment or variant or derivative according to Claim 9 or Claim 10, an inhibitor according to Claim 11 or Claim 12, an antibody according to Claim 13 or Claim 14, an attenuated mycobacterium according to Claim 15 or Claim 16, an attenuated microbial carrier according to any of Claims 17-19, a DNA sequence corresponding to the coding sequence of a gene which is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene, or a fragment or variant or derivative of said DNA sequence, a DNA plasmid according to any of Claims 20-22, an RNA sequence according to Claim 23, and/or an RNA vector according to Claim 24, in the manufacture of a medicament for treating or preventing a mycobacterial infection.

26. A method of treating or preventing a mycobacterial infection, by administering to a patient a peptide or fragment or variant or derivative according to Claim 9 or Claim 10, an inhibitor according to Claim 11 or Claim 12, an antibody according to Claim 13 or Claim 14, an attenuated mycobacterium according to Claim 15 or Claim 16, an attenuated microbial carrier according to any of Claims 17-19, a DNA sequence corresponding to the coding sequence of a gene which is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene, or a fragment or variant or derivative of said DNA sequence, a DNA plasmid according to any of Claims 20-22, an RNA sequence according to Claim 23, and/or an RNA vector according to Claim 24.

27. Use of a peptide or fragment or variant or derivative according to Claim 9 or Claim 10, or an antibody according to Claim 13 or Claim 14, or a polynucleotide probe comprising at least 8 nucleotides wherein said probe binds to at least part of a gene which is induced or up-regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene, in the manufacture of a diagnostic reagent for identifying a mycobacterial infection.

28. A recombinant method of preparing a mycobacterial peptide, or a fragment or derivative or a variant of said peptide, wherein the peptide is encoded by a mycobacterial gene the expression of which is induced or up-

regulated during infection of a macrophage by a *M. tuberculosis* host cell containing said gene, comprising expressing a nucleic acid sequence corresponding to the coding sequence of said gene, or a fragment or variant or derivative of said nucleic acid sequence, in a host cell.

5

29. An isolated peptide, an inhibitor, an antibody, an attenuated mycobacterium, an attenuated microbial carrier, an isolated RNA molecule, an RNA vector, or a DNA plasmid substantially as hereinbefore described with reference to the Examples.

SEQUENCE LISTING

<110> Microbiological Research Authority

Vipond, Richard

Shuttleworth, Helen

Ambrose, Emma

Minton, Nigel Peter

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cagcgcgtcg agttggacga cctgctccac aagacgccga ccgcgttgac ggcgctcgga 900

cgcgccaacg gaacctacgg cgatttccag aacttctacc tctgcgacct ccagatcaag 960

tggaacggat tccaagccgg agggccggtc cgcacggtga agctctttag ccagccgacg 1020

ggtaggtgca cgccgcaa 1038

<210> 10

<211> 515

<212> PRT

<213> Mycobacterium tuberculosis

<400> 10

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

Ile Val Val Ala Leu Leu Val Val Ala Val Gly Gln Ser Phe Thr Ser
20 25 30

Val Pro Met Leu Phe Ala Lys Pro Ser Tyr Tyr Gly Gln Phe Thr Asp
35 40 45

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

Val Gly Thr Val Glu Gly Leu Lys Ile Asp Gly Asp His Ile Val Val
65 70 75 80

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

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

Arg Gly Ala Gln Ala Leu Pro Pro Gly Gly Val Leu Pro Val Gly Gln
115 120 125

Ser Thr Thr Pro Tyr Gln Ile Tyr Asp Ala Phe Phe Asp Val Thr Lys
130 135 140

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

Leu Ser Glu Thr Val Asp Gln Thr Tyr Pro His Leu Ser Ala Ala Leu
165 170 175

Asp Gly Val Ala Lys Phe Ser Asp Thr Ile Gly Lys Arg Asp Glu Gln

180 185 190

Ile Thr His Leu Leu Ala Gln Ala Asn Gln Val Ala Ser Ile Leu Gly
195 200 205

Asp Arg Ser Glu Gln Val Asp Arg Leu Leu Val Asn Ala Lys Thr Leu
210 215 220

Ile Ala Ala Phe Asn Glu Arg Gly Arg Ala Val Asp Ala Leu Leu Gly
225 230 235 240

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

Pro Asn Leu Asn His Val Leu Glu Gln Leu Arg Ile Leu Thr Asp Leu
260 265 270

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

Arg Phe Ser Ala Ser Phe Gly Glu Thr Phe Ala Ser Gly Pro Tyr Phe
290 295 300

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

Val Asp Ala Ala Phe Lys Lys Arg Gly Ile Ser Pro Glu Asp Phe Trp
325 330 335

Arg Ser Ala Gly Leu Pro Ala Tyr Arg Trp Pro Asp Pro Asn Gly Thr
340 345 350

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

Thr Pro Glu His Pro Gly Pro Ala Val Pro Pro Gly Ser Pro Cys Ser
370 375 380

Tyr Thr Pro Pro Ala Asp Gly Leu Pro Arg Pro Trp Asp Pro Leu Pro
385 390 395 400

Cys Ala Asn Leu Thr Gln Gly Pro Phe Gly Gly Pro Asp Phe Pro Ala
405 410 415

Pro Leu Asp Val Ala Thr Ser Pro Pro Asn Pro Asp Gly Pro Pro Pro
420 425 430

Ala Pro Gly Leu Pro Ile Ala Gly Arg Pro Gly Glu Val Pro Pro Asn
435 440 445

Val Pro Gly Thr Pro Val Pro Ile Pro Gln Glu Ala Pro Pro Gly Ala
450 455 460

Arg Thr Leu Pro Leu Gly Pro Ala Pro Gly Pro Ala Pro Pro Pro Ala
465 470 475 480

Ala Pro Gly Pro Pro Ala Pro Pro Gly Pro Gly Pro Gln Leu Pro Ala
485 490 495

Pro Phe Ile Asn Pro Gly Gly Thr Gly Gly Ser Gly Val Thr Gly Gly
500 505 510

Ser Glu Asn
515

<210> 11

<211> 1545

<212> DNA

<213> Mycobacterium tuberculosis

<400> 11

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agctactacg gccagttcac cgactccggc ggactgcaca agggcgacag ggtacgcatc 180

gccggcttgg gagtgggcac cgtggagggg ctcaagatcg acggcgacca catcgtggtc 240

aagttctcca tcggcaccaa caccatcggc accgagagcc gcctagccat ccgcaccgac 300

accatcctgg gtaggaaagt gctcgagatc gagccgcgcg gcgcccaagc gttgccgccc 360

gggggcgttt tgccggttgg gcaaagcacc accccgtacc agatttacga cgcgttcttc 420

gacgtcacca aggccgcatc cggctgggac atcgagacgg tcaagcggtc gctgaatgtg 480

ttgtcggaga ccgttgatca gacctatccg cacctgagcg ccgccctcga cggggtggct 540

aagttctccg acaccatcgg caagcgcgac gagcagatca cgcacctact agcccaggcc 600

aaccaggtgg ccagcatcct gggtgatcgc agtgagcagg tcgaccgcct attggtcaac 660

gctaagaccc tgatcgccgc gttcaacgag cgcggccgcg cggtcgacgc cctgctgggg 720

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catgtgctcg agcagctgcg catcctcacc gacctgttgg tcgaccgcaa ggaggatttg 840

gctgaaaccc tgacgatctt gggcagattc agcgcgtcgt tcggtgagac gtttgcctct 900

gggccctact tcaaagtgct gctggccaac ctggtgccgg gtcagatctt gcagccgttt 960

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ccaccaccgc cggtgttgga gggcacgccc gagcatcccg ggccggcggt gccgccggga 1140

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ccccccgggg cacgcacgct gcccctcggg ccggcgcctg gtccggctcc gccccggcg 1440

gcgccaggcc cgccggcacc accgggcccc gggccgcagt tgccggcccc gttcatcaac 1500

cccggcggca ccggcggtag tggcgtgacg ggaggtagcg agaat 1545

<210> 12

<211> 530

<212> PRT

<213> Mycobacterium tuberculosis

<400> 12

Leu Ser Thr Ile Phe Asp Ile Arg Asn Leu Arg Leu Pro Gln Leu Ser
1 5 10 15

Arg Ala Ser Val Val Ile Gly Ser Leu Val Val Val Leu Ala Leu Ala
20 25 30

Ala Gly Ile Val Gly Val Arg Leu Tyr Gln Lys Leu Thr Asn Asn Thr
35 40 45

Val Val Ala Tyr Phe Thr Gln Ala Asn Ala Leu Tyr Val Gly Asp Lys

```
    50                  55                  60

Val Gln Ile Met Gly Leu Pro Val Gly Ser Ile Asp Lys Ile Glu Pro
65                  70                  75                  80

Ala Gly Asp Lys Met Lys Val Thr Phe His Tyr Gln Asn Lys Tyr Lys
                85                  90                  95

Val Pro Ala Asn Ala Ser Ala Val Ile Leu Asn Pro Thr Leu Val Ala
            100                 105                 110

Ser Arg Asn Ile Gln Leu Glu Pro Pro Tyr Arg Gly Gly Pro Val Leu
        115                 120                 125

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

Trp Asp Glu Leu Arg Asp Ser Val Ser His Ile Ile Asp Glu Leu Gly
145                 150                 155                 160

Pro Thr Pro Glu Gln Pro Lys Gly Pro Phe Gly Glu Val Ile Glu Ala
                165                 170                 175

Phe Ala Asp Gly Leu Ala Gly Lys Gly Lys Gln Ile Asn Thr Thr Leu
            180                 185                 190

Asn Ser Leu Ser Gln Ala Leu Asn Ala Leu Asn Glu Gly Arg Gly Asp
        195                 200                 205

Phe Phe Ala Val Val Arg Ser Leu Ala Leu Phe Val Asn Ala Leu His
    210                 215                 220

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

Thr Asp Arg Leu Thr His Ser Asp Ala Asp Leu Ser Asn Ala Ile Gln
                245                 250                 255

Gln Phe Asp Ser Leu Leu Ala Val Ala Arg Pro Phe Phe Ala Lys Asn
            260                 265                 270

Arg Glu Val Leu Thr His Asp Val Asn Asn Leu Ala Thr Val Thr Thr
        275                 280                 285
```

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Thr Leu Leu Gln Pro Asp Pro Leu Asp Gly Leu Glu Thr Val Leu His
    290                 295                 300

Ile Phe Pro Thr Leu Ala Ala Asn Ile Asn Gln Leu Tyr His Pro Thr
305                 310                 315                 320

His Gly Gly Val Val Ser Leu Ser Ala Phe Thr Asn Phe Ala Asn Pro
                325                 330                 335

Met Glu Phe Ile Cys Ser Ser Ile Gln Ala Gly Ser Arg Leu Gly Tyr
            340                 345                 350

Gln Glu Ser Ala Glu Leu Cys Ala Gln Tyr Leu Ala Pro Val Leu Asp
        355                 360                 365

Ala Ile Lys Phe Asn Tyr Phe Pro Phe Gly Leu Asn Val Ala Ser Thr
    370                 375                 380

Ala Ser Thr Leu Pro Lys Glu Ile Ala Tyr Ser Glu Pro Arg Leu Gln
385                 390                 395                 400

Pro Pro Asn Gly Tyr Lys Asp Thr Thr Val Pro Gly Ile Trp Val Pro
                405                 410                 415

Asp Thr Pro Leu Ser His Arg Asn Thr Gln Pro Gly Trp Val Val Ala
            420                 425                 430

Pro Gly Met Gln Gly Val Gln Val Gly Pro Ile Thr Gln Gly Leu Leu
        435                 440                 445

Thr Pro Glu Ser Leu Ala Glu Leu Met Gly Gly Pro Asp Ile Ala Pro
    450                 455                 460

Pro Ser Ser Gly Leu Gln Thr Pro Pro Gly Pro Pro Asn Ala Tyr Asp
465                 470                 475                 480

Glu Tyr Pro Val Leu Pro Pro Ile Gly Leu Gln Ala Pro Gln Val Pro
                485                 490                 495

Ile Pro Pro Pro Pro Pro Gly Pro Asp Val Ile Pro Gly Pro Val Pro
            500                 505                 510

Pro Thr Pro Ala Pro Val Gly Ala Pro Leu Pro Ala Glu Ala Gly Gly
        515                 520                 525
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Gly Gln
530

<210> 13

<211> 1590

<212> DNA

<213> Mycobacterium tuberculosis

<400> 13
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tatcaaaaac tgacgaacaa cacggtggtc gcctacttca cccaagccaa tgcgctgtat 180

gtcggagaca aggtccagat tatgggcctc ccggtcggtt cgatcgacaa gatcgaacca 240

gccggcgaca aaatgaaggt gactttccac taccagaaca agtacaaggt gcctgccaat 300

gcctccgcgg tgatcctcaa ccccaccttg gtggcgtcgc ggaacattca gttggagcca 360

ccctacagag gtggtccagt gctggccgat aatgcggtga tcccggtcga gcgcacccag 420

gtaccgacgg agtgggacga gctgcgggac agcgtttcgc atattatcga cgagctcggc 480

ccgacacctg agcagcccaa ggggccgttc ggcgaagtca tcgaggcatt cgccgacggg 540

ctggccggca agggtaagca aatcaacacc acgctgaaca gcctgtcgca ggcgttgaac 600

gccttgaatg agggccgcgg cgacttcttc gcggtggtac gcagcctggc gctattcgtc 660

aacgcgctac atcaggacga ccaacagttc gtcgcgttga acaagaacct tgcggagttc 720

accgacaggt tgacccactc cgatgcggac ctgtcgaacg ccatccagca attcgacagc 780

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gagtaccccg tgctgccgcc gatcggttta caggccccac aggtgccgat accaccgccg 1500

cctcctgggc ccgacgtaat cccgggtccg gtgccaccga cgccggcacc ggtgggggcg 1560

ccgttgcccg ctgaggcagg agggggtcaa 1590

<210> 14

<211> 390

<212> PRT

<213> Mycobacterium tuberculosis

<400> 14

Met Met Ser Val Leu Ala Arg Met Arg Val Met Arg His Arg Ala Trp
1 5 10 15

Gln Gly Leu Val Leu Leu Val Leu Ala Leu Leu Leu Ser Ser Cys Gly
20 25 30

Trp Arg Gly Ile Ser Asn Val Ala Ile Pro Gly Gly Pro Gly Thr Gly
35 40 45

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

Asn Gly Asn Ser Arg Val Met Val Ala Asp Val Trp Val Gly Ser Ile
65 70 75 80

Arg Ala Ile Lys Leu Lys Asn Trp Val Ala Thr Leu Thr Leu Ser Leu
85 90 95

Lys Lys Asp Val Thr Leu Pro Lys Asn Ala Thr Ala Lys Ile Gly Gln
100 105 110

Thr Ser Leu Leu Gly Ser Gln His Val Glu Leu Ala Ala Pro Pro Asp
115 120 125

Pro Ser Pro Val Pro Leu Lys Asp Gly Asp Thr Ile Pro Leu Lys Arg

130 135 140

Ser Ser Ala Tyr Pro Thr Thr Glu Gln Thr Leu Ala Ser Ile Ala Thr
145 150 155 160

Leu Leu Arg Gly Gly Gly Leu Val Asn Leu Glu Gly Ile Gln Gln Glu
165 170 175

Ile Asn Ala Ile Val Thr Gly Arg Ala Asp Gln Ile Arg Ala Phe Leu
180 185 190

Gly Lys Leu Asp Thr Phe Thr Asp Glu Leu Asn Gln Gln Arg Asp Asp
195 200 205

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

Gly Arg Ser Glu Val Leu Asn Arg Val Leu Thr Asp Leu Pro Pro Leu
225 230 235 240

Ile Lys His Phe Ala Asp Lys Gln Glu Leu Leu Ile Asn Ala Ser Asp
245 250 255

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

Arg Gly Asp Leu His Gln Asp Leu Gln Ala Leu Gln Cys Pro Leu Lys
275 280 285

Glu Leu Arg Arg Ala Ala Pro Tyr Leu Val Gly Ala Leu Lys Leu Ile
290 295 300

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

Asp Tyr Met Asn Leu Ser Leu Thr Leu Asp Leu Thr Tyr Ser Ala Ile
325 330 335

Asp Asn Ala Phe Leu Thr Gly Thr Gly Phe Ser Gly Ala Leu Arg Ala
340 345 350

Leu Glu Gln Ser Phe Gly Arg Asp Pro Glu Thr Met Ile Pro Asp Ile
355 360 365

Arg Tyr Thr Pro Asn Pro Asn Asp Ala Pro Gly Gly Pro Leu Val Glu
370 375 380

Arg Gly Asn Arg Gln Cys
385 390

<210> 15

<211> 1170

<212> DNA

<213> Mycobacterium tuberculosis

<400> 15

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atccccggcg gcccgggcac cggcccgggc tcctacacca tctacgtgca gatgccggac 180

acgttggcga tcaacggcaa cagtcgggtc atggtggccg acgtctgggt cggatcgatc 240

cgcgcgatca agttgaagaa ctgggtggcc acgctgacgc tgagcctgaa gaaggacgtc 300

acgctaccga aaaatgccac cgccaagatc gggcagacca gcctgctggg ttcgcagcac 360

gtcgagctgg ccgcgccgcc agatccgtcg ccggtgccgc tgaaggatgg tgacaccatc 420

ccgttgaagc gctcctcggc ctatcccacc accgagcaga cgctggccag catcgccacc 480

ttgttgcgcg gcggcggcct ggtgaacctc gaagggattc agcaagagat caacgccatc 540

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gagctcaacc agcaacgcga tgacattacc cgcgccattg attccaccaa tcggttgttg 660

gcttatgtgg gcggtcgttc ggaagtcctc aatcgggtgc tcaccgacct accgccattg 720

atcaagcact ttgcggataa gcaggaactg ttgatcaacg cttccgatgc ggtaggccgg 780

ctcagccagt ccgccgacca gtatctttcg gctgcccggg gcgatctgca ccaggacctg 840

caggcgctgc aatgcccgct caaggaactg cgtcgagccg ctccgtatct ggtgggtgcg 900

ctcaaattga tcctcaccca gccctttgac gtcgacaccg tgccgcagct ggtgcggggc 960

gactacatga acttgtcgct gacgctggac ctgacctaca gcgccatcga caatgcgttc 1020

cttaccggga ccggattctc cggtgcgttg cgcgccctcg agcagtcttt tggccgcgat 1080

cccgagacaa tgattcccga catccggtac acaccgaacc ccaacgatgc gccgggcggc 1140

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<210> 16

<211> 515

<212> PRT

<213> Mycobacterium tuberculosis

<400> 16

Val Leu Thr Arg Phe Ile Arg Arg Gln Leu Ile Leu Phe Ala Ile Val
1 5 10 15

Ser Val Val Ala Ile Val Val Leu Gly Trp Tyr Tyr Leu Arg Ile Pro
20 25 30

Ser Leu Val Gly Ile Gly Gln Tyr Thr Leu Lys Ala Asp Leu Pro Ala
35 40 45

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

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

Thr Met Ser Ile Ala Ser Asn Tyr Lys Ile Pro Val Asp Ala Ser Ala
85 90 95

Asn Val His Ser Val Ser Ala Val Gly Glu Gln Tyr Ile Asp Leu Val
100 105 110

Ser Thr Gly Ala Pro Gly Lys Tyr Phe Ser Ser Gly Gln Thr Ile Thr
115 120 125

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

Arg Gly Leu Ala Ala Leu Pro Thr Glu Lys Ile Gly Leu Leu Leu Asp
145 150 155 160

Glu Thr Ala Gln Ala Val Gly Gly Leu Gly Pro Ala Leu Gln Arg Leu
165 170 175

Val Asp Ser Thr Gln Ala Ile Val Gly Asp Phe Lys Thr Asn Ile Gly

180 185 190

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

Val Asn Thr Gly Asp Gln Ile Glu Arg Trp Ala Arg Lys Leu Asn Asn
210 215 220

Leu Ala Ala Gln Thr Ala Thr Arg Asp Gln Asn Val Arg Ser Ile Leu
225 230 235 240

Ser Gln Ala Ala Pro Thr Ala Asp Glu Val Asn Ala Val Phe Ser Gly
245 250 255

Val Arg Asp Ser Leu Pro Gln Thr Leu Ala Asn Leu Glu Val Val Phe
260 265 270

Asp Met Leu Lys Arg Tyr His Ala Gly Val Glu Gln Leu Leu Val Phe
275 280 285

Leu Pro Gln Gly Ala Ala Ile Ala Gln Thr Val Leu Thr Pro Thr Pro
290 295 300

Gly Ala Ala Gln Leu Pro Leu Ala Pro Ala Ile Asn Tyr Pro Pro Pro
305 310 315 320

Cys Leu Thr Gly Phe Leu Pro Ala Ser Glu Trp Arg Ser Pro Ala Asp
325 330 335

Thr Ser Pro Arg Pro Leu Pro Ser Gly Thr Tyr Cys Lys Ile Pro Gln
340 345 350

Asp Ala Gln Leu Gln Val Arg Gly Ala Arg Asn Ile Pro Cys Val Asp
355 360 365

Val Leu Gly Lys Arg Ala Ala Thr Pro Lys Glu Cys Arg Ser Lys Asp
370 375 380

Pro Tyr Val Pro Leu Gly Thr Asn Pro Trp Phe Gly Asp Pro Asn Gln
385 390 395 400

Ile Leu Thr Cys Pro Ala Pro Gly Ala Arg Cys Asp Gln Pro Val Lys
405 410 415

Pro Gly Leu Val Ile Pro Ala Pro Ser Ile Asn Thr Gly Leu Asn Pro
420 425 430

Ala Pro Ala Asp Gln Val Gln Gly Thr Pro Pro Pro Val Ser Asp Pro
435 440 445

Leu Gln Arg Pro Gly Ser Gly Thr Val Gln Cys Asn Gly Gln Gln Pro
450 455 460

Asn Pro Cys Val Tyr Thr Pro Thr Ser Gly Pro Ser Ala Val Tyr Ser
465 470 475 480

Pro Ala Ser Gly Glu Leu Val Gly Pro Asp Gly Val Lys Tyr Ala Val
485 490 495

Ala Asn Ser Ser Thr Thr Gly Asp Asp Gly Trp Lys Glu Met Leu Ala
500 505 510

Pro Ala Ser
515

<210> 17

<211> 1545

<212> DNA

<213> Mycobacterium tuberculosis

<400> 17
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accttgaagg ccgacttgcc cgcatcgggt ggcctgtatc cgacggccaa tgtgacctac 180

cgcggtatca ccattggcaa ggttactgcc gtcgagccca ccgaccaggg cgcacgagtg 240

acgatgagca tcgccagcaa ctacaaaatc cccgtcgatg cctcggcgaa cgtgcattcg 300

gtgtcagcgg tgggcgagca gtacatcgac ctggtgtcca ccggtgctcc gggtaaatac 360

ttctcctccg gacagaccat caccaagggc accgttccca gtgagatcgg gccggcgctg 420

gacaattcca atcgcgggtt ggccgcattg cccacggaga agatcggctt gctgctcgac 480

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caagcgatcg tcggtgactt caaaaccaac attggcgacg tcaacgacat catcgagaac 600

tccgggccga ttttggacag ccaggtcaac acgggtgatc agatcgagcg ctgggcgcgc 660

aaattgaaca atctggccgc acagaccgcg accagggatc agaacgtgcg aagcatcctg 720

tcccaggcgg cccccaccgc cgatgaggtt aacgcggtat tcagcggtgt tcgcgattcg 780

ctgccacaga ccctggccaa tcttgaggtt gtgttcgata tgctcaagcg ctaccacgcc 840

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acgcccccgc cggtcagtga cccgttgcaa agaccgggtt cgggtactgt gcagtgcaac 1380

gggcagcagc ctaacccgtg cgtctacact ccaacatcgg gcccgtcggc ggtctatagc 1440

ccggccagcg gtgaactggt ggggccggat ggtgtcaagt acgccgtcgc aaactcgagc 1500

acaacaggag acgacggatg gaaggagatg ctggcgccgg ccagc 1545

<210> 18

<211> 1420

<212> DNA

<213> Mycobacterium tuberculosis

<400> 18

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gttggccatg cctagatcgc cgaaggcaat ggccatcagc gcgcgatgct cgaccgcacg 240

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ttggcgcagc gcgccgccgc cactttggtg cgggccgtac aactcgatca atgcctcgct 360

gcacgccccg gcgttgggct gctcgcaagc ggccgacagt accagtggcc cgggcccggc 420

cggccgcaca accgcgagcc cggacaccgc gaatccgcgt tttgccaacg cgcgaatggc 480

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caaccacccc accgccagcc ccaacaatga gcgggccggc acaatcgcgc tgacaaccag 600

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aaactgggcc agcaatgtgg cgagccggtc ggaaaggtca aagtgccatc ggggtgccgc 780

gatgcggcta ctgctgatcg acaacgggag aacggccata agtccggcgg ccgcatacgc 840

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caaaatcgcc aggccgtacc ccaggtacac cagatcggat tgcgacgggg acagcacccc 960

gacgatctcc gagatggatt tctccagcgc cacccactgc gggcgggtga tcagcgaact 1020

cgtgatcacc gccacgaggt agatcgccgc cagcaccgcc cggatgatgt cgttggtgcg 1080

ccgggtcagt ggttgcagca agttaccgga aacgccgatg tcgcgtccgt caactcgcat 1140

gttctaacga tcttccgaat cagggcccgc ggtgtctggt gccgtttcgc ggctccgcgg 1200

acaacttagc ccgataactg cgtggggtgt cggtctgacc acttgacgtc ttaccaatct 1260

tcattcacac tgggcgcatg gcgctgcagc cggtgactcg ccgatcggtg cccgaagagg 1320

tcttcgagca gatcgctacc gatgtgctca ccggcgagat gccgcccggc gaggcgttgc 1380

ccagcgagcg tcggttggct gagttgctcg gagtgtcgcg 1420

<210> 19

<211> 240

<212> PRT

<213> Mycobacterium tuberculosis

<400> 19

Met Ala Leu Gln Pro Val Thr Arg Arg Ser Val Pro Glu Glu Val Phe
1 5 10 15

Glu Gln Ile Ala Thr Asp Val Leu Thr Gly Glu Met Pro Pro Gly Glu
20 25 30

Ala Leu Pro Ser Glu Arg Arg Leu Ala Glu Leu Leu Gly Val Ser Arg
35 40 45

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

Glu Val Arg Gln Gly Asp Val Thr Thr Val Arg Asp Phe Arg Arg His
65                  70                  75                  80

Ala Gly Leu Asp Leu Leu Pro Arg Leu Leu Phe Arg Asn Gly Glu Leu
                85                  90                  95

Asp Ile Ser Val Val Arg Ser Ile Leu Glu Ala Arg Leu Arg Asn Phe
            100                 105                 110

Pro Lys Val Ala Glu Leu Ala Ala Glu Arg Asn Glu Pro Glu Leu Ala
        115                 120                 125

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

Ile Val Trp Gln Arg His Thr Leu Asp Phe Trp Asp His Val Val Asp
145                 150                 155                 160

Ser Ala Gly Ser Ile Val Asp Arg Leu Met Tyr Asn Ala Phe Arg Ala
                165                 170                 175

Ala Tyr Glu Pro Thr Leu Ala Ala Leu Thr Thr Thr Met Thr Ala Ala
            180                 185                 190

Ala Lys Arg Pro Ser Asp Tyr Arg Lys Leu Ala Asp Ala Ile Cys Ser
        195                 200                 205

Gly Asp Pro Thr Gly Ala Lys Lys Ala Ala Gln Asp Leu Leu Glu Leu
    210                 215                 220

Ala Asn Thr Ser Leu Met Ala Val Leu Val Ser Gln Ala Ser Arg Gln
225                 230                 235                 240
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<210> 20

<211> 720

<212> DNA

<213> Mycobacterium tuberculosis

<400> 20
atggcgctgc agccggtgac tcgccgatcg gtgcccgaag aggtcttcga gcagatcgct 60

accgatgtgc tcaccggcga gatgccgccc ggcgaggcgt tgcccagcga gcgtcggttg 120

gctgagttgc tcggagtgtc gcgacccgcg gtccgcgagg cgctcaaacg gctgtcggcc 180

gcaggtctgg tcgaggtgcg tcagggcgac gtcaccaccg tgcgtgactt ccggcggcac 240

gccggcctgg atctgttgcc ccgattgttg tttcgcaacg gtgagctgga tatctccgtc 300

gtccgcagca tcctcgaggc ccggctgcgc aattttccga aggtcgcgga actagcggcc 360

gaacggaacg agcccgagtt ggcggaattg ctgcaggatt cgctgcgtgc gctggacact 420

gaggaagatc cgatcgtgtg gcaacgccac acgctcgact tttgggatca tgtggtcgac 480

agcgccggtt cgatcgtaga tcgattgatg tacaacgcat ttcgtgctgc ttacgagccg 540

acgctagctg ctctgaccac cacgatgacc gctgcggcta agcgtccgtc ggactaccgg 600

aaactcgcgg atgcgatctg ctcaggtgat cccaccggag cgaagaaagc cgcccaagac 660

ctactcgaac ttgcgaacac atcgttgatg gccgtactcg ttagccaggc gagtcggcaa 720

<210> 21

<211> 265

<212> PRT

<213> Mycobacterium tuberculosis

<400> 21

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

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

Gly Lys Ala Leu Val Arg Arg Pro Phe His Trp Arg Glu Ala Ile Glu
35 40 45

Gln Gly Trp Phe Ile Thr Ser Val Ser Leu Leu Pro Thr Leu Ala Val
50 55 60

Ser Ile Pro Leu Thr Val Leu Ile Ile Phe Thr Leu Asn Ile Leu Leu
65 70 75 80

Ala Glu Phe Gly Ala Ala Asp Ile Ser Gly Ala Gly Ala Ala Leu Gly
85 90 95

Ala Val Thr Gln Leu Gly Pro Leu Thr Thr Val Leu Val Ile Ala Gly
100 105 110

Ala Gly Ala Thr Ala Ile Cys Ala Asp Leu Gly Ala Arg Thr Ile Arg
115 120 125

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

Leu Val Val Pro Arg Val Val Ala Ala Thr Ile Val Ala Ala Leu Leu
145 150 155 160

Asn Gly Ala Val Ile Thr Ile Gly Leu Val Gly Gly Phe Val Phe Ser
165 170 175

Val Phe Ile Gln His Val Ser Ala Gly Ala Tyr Val Gly Thr Leu Thr
180 185 190

Leu Val Thr Gly Leu Pro Glu Val Ile Ile Ser Val Val Lys Ser Ala
195 200 205

Thr Phe Gly Leu Ile Ala Gly Leu Val Gly Cys Tyr Arg Gly Leu Thr
210 215 220

Thr Lys Gly Gly Pro Lys Gly Val Gly Thr Ala Val Asn Glu Thr Leu
225 230 235 240

Val Leu Cys Val Ile Ala Leu Phe Ala Thr Asn Val Val Leu Thr Thr
245 250 255

Ile Gly Val Arg Phe Gly Thr Gly His
260 265

<210> 22

<211> 795

<212> DNA

<213> Mycobacterium tuberculosis

<400> 22
atgaccaccc acgccgtgat catcacctat ctccgcgacc agacgcagcc cgccgtcgat 60

gcgatcggcg ggttctaccg gacatgcgta ctgactggca aggcgctggt tcggcggccc 120

ttccattggc gtgaggcgat cgagcagggc tggttcatta ccagcgtctc gttgctgcca 180

accctggcgg tgtcgattcc gttgaccgtg ttgatcatct tcacgctcaa tatcctgctg 240

gccgagttcg gcgccgccga catctccggc gccggcgcgg cgctaggcgc ggtcacccag 300

ctgggcccgc tgaccaccgt gttggtgatt gccggcgctg gagccacagc gatctgcgcc 360

gacctgggtg cccgcaccat ccgggaagag atcgatgcga tggaggtgct gggcatcgac 420

cccatccacc ggctggtggt gcctcgggtc gttgccgcga ccatcgtcgc cgcactgctt 480

aacggcgcgg tgataaccat tggcctggtt ggtggtttcg tcttcagtgt cttcatccaa 540

cacgtctcgg ccggcgccta cgtgggcacg ctcaccttgg tcaccggtct acccgaggtg 600

atcatctcgg tggtcaagtc ggcgacgttc ggcctgatcg ctggcctagt cggctgttac 660

cgcgggctga ccacgaaagg cggccccaag ggagttggaa ccgccgtcaa cgaaaccctg 720

gtgctgtgcg tgatcgcgct gttcgcgacc aatgtggtgt tgaccacgat cggcgtgcgg 780

ttcgggacgg gacac 795

<210> 23

<211> 295

<212> PRT

<213> Mycobacterium tuberculosis

<400> 23

Met Val Glu Ser Ser Thr Ala Ser Ala Ala Ala Val Leu Arg Ala Arg
1 5 10 15

Tyr Pro Arg Thr Ala Ala Ser Leu Asp Arg Tyr Gly Gly Gly Thr Ala
20 25 30

Arg Arg Leu Glu Arg Thr Gly Thr Phe Ala Arg Phe Thr Arg Ile Ser
35 40 45

Val Val Gln Ile Gly Trp Ala Leu Arg Arg Tyr Arg Arg Glu Thr Leu
50 55 60

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Arg Leu Val Ala Glu Ile Gly Met Gly Thr Gly Ala Met Ala Val Val
65                  70                  75                  80

Gly Gly Thr Val Ala Ile Ile Gly Phe Val Thr Leu Ser Gly Gly Ser
                85                  90                  95

Leu Ile Ala Ile Gln Gly Phe Ala Ser Leu Gly Asn Ile Gly Val Glu
            100                 105                 110

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

Pro Ile Val Ser Gly Val Ala Leu Ala Ala Thr Val Gly Ala Gly Ala
    130                 135                 140

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

Glu Val Met Gly Ile Lys Ser Ile Ser Phe Leu Val Ser Thr Arg Ile
                165                 170                 175

Leu Gly Gly Leu Val Val Ile Met Pro Leu Tyr Ala Leu Ala Leu Asp
            180                 185                 190

Met Ala Phe Thr Ser Gly Gln Val Val Thr Thr Val Phe Tyr Gly Gln
        195                 200                 205

Ser Asn Gly Thr Tyr Glu His Tyr Phe Arg Thr Phe Leu Arg Pro Glu
    210                 215                 220

Asp Val Gly Trp Ser Val Val Glu Val Val Ile Ile Ala Val Val Val
225                 230                 235                 240

Met Ile Thr His Cys Tyr Tyr Gly Tyr Thr Ala Ser Gly Gly Pro Val
                245                 250                 255

Gly Val Gly Gln Ala Val Gly Arg Ser Met Arg Phe Ser Leu Val Ser
            260                 265                 270

Val Val Val Val Val Leu Leu Ala Glu Leu Ala Leu Tyr Gly Val Asp
        275                 280                 285

Pro Asn Phe Asn Leu Thr Val
    290                 295
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<210> 24

<211> 885

<212> DNA

<213> Mycobacterium tuberculosis

<400> 24
atggtggagt cttcaacggc atcagcggca gccgtattgc gggcccgcta cccacgcaca 60

gccgccagcc ttgaccgcta cggcggcggc acggcccgaa gacttgagcg gacagggact 120

ttcgcgagat tcacccggat cagcgtcgtg cagatcggct gggcactgcg tcgctatcgc 180

cgggagacgc tgcgcctggt cgccgagatc gggatgggca ccggcgcgat ggccgtcgtc 240

ggcggcacgg tcgcgatcat cggttttgtg acgctgtccg gcggctcgct gatcgccatc 300

cagggcttcg cgtcgctggg caacatcggt gtcgaggcgt ttaccggatt ctttgccgca 360

ctggccaaca cacgcgtcgc tgcgcccatt gtctccggtg tcgcgctggc cgcgacggtg 420

ggcgccggcg ccaccgcaca gttaggtgcc atgcggatca gtgaggagat cgacgcgctg 480

gaagtgatgg gcatcaagtc gatttcgttt ctggtctcca ctcggattct aggagggctg 540

gtggtgatca tgccgctgta cgcgctcgct ctcgacatgg ctttcacctc tggtcaggtg 600

gtcacaaccg tgttctacgg ccagtccaac ggcacctatg agcactactt ccgcaccttc 660

ctgcgcccag aggatgtggg ttggtcggtc gtggaggtgg tgatcatcgc ggtggtggtg 720

atgatcaccc attgctacta cgggtacacc gccagcggtg gcccggttgg ggtcggccag 780

gcggttggtc gatcgatgcg tttctcgctg gtctcggtgg tggtcgttgt cctgctggcc 840

gagttggcgc tctacggcgt cgacccgaac ttcaatctca cggtg 885

<210> 25

<211> 404

<212> PRT

<213> Mycobacterium tuberculosis

<400> 25

Val Pro Thr Leu Val Thr Arg Lys Asn Arg Arg Ala Trp Leu Tyr Val
1 5 10 15

Glu Gly Val Val Leu Leu Leu Val Gly Ala Leu Val Leu Val Leu Val
20 25 30

Tyr Lys Gln Phe Arg Gly Glu Phe Thr Pro Lys Thr Glu Leu Thr Met
35 40 45

Val Ala Phe Arg Ala Gly Leu Val Met Glu Ala Gly Ser Lys Val Thr
50 55 60

Tyr Asn Gly Val Glu Ile Gly Arg Val Gly Ser Ile Ser Glu Ile Glu
65 70 75 80

Arg Asp Gly Arg Pro Ala Ala Lys Leu Val Leu Asp Val Asn Pro Arg
85 90 95

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

Thr Leu Phe Gly Asn Lys Tyr Val Ala Leu Ser Ala Pro Lys Ile Pro
115 120 125

Gln Gln Gln Arg Ile Ser Ser His Asp Val Ile Asp Val Gly Ser Val
130 135 140

Thr Thr Glu Phe Asn Thr Leu Phe Glu Thr Ile Thr Ser Ile Ala Glu
145 150 155 160

Lys Val Asp Pro Ile Glu Leu Asn Ala Thr Leu Ser Ala Val Ala Gln
165 170 175

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

Asn Gln Ile Leu Ala Gln Leu Asn Pro Arg Leu Pro Gln Leu Gly Tyr
195 200 205

Asp Val Arg Arg Leu Ala Asp Leu Gly Glu Val Tyr Val Asp Ala Ser
210 215 220

Pro Asp Leu Trp Ser Phe Leu Gln Asn Ala Leu Thr Thr Ala Arg Thr
225 230 235 240

Leu Thr Ser Gln Gln Arg Asp Leu Asp Ala Ala Leu Leu Ala Ala Thr
245 250 255

Gly Ala Gly Asn Thr Gly Glu Asp Val Phe Ala Arg Gly Gly Pro Tyr
260 265 270

Leu Ala Arg Ala Ala Ala Asp Leu Val Pro Thr Ala Thr Leu Leu Asp
275 280 285

Thr Tyr Ser Pro Glu Leu Phe Cys Met Ile Arg Asn Phe His Asp Ala
290 295 300

Ala Pro Lys Val Ala Asp Ala Val Gly Gly Asn Gly Tyr Ser Leu Ala
305 310 315 320

Ala Ala Gly Thr Ile Leu Gly Ala Pro Asn Pro Tyr Val Tyr Pro Asp
325 330 335

Asn Leu Pro Arg Val Asn Ala His Gly Gly Pro Gly Gly Arg Pro Gly
340 345 350

Cys Trp Gln Thr Ile Thr Arg Glu Leu Trp Pro Ala Pro Tyr Leu Val
355 360 365

Met Asp Thr Gly Ala Ser Leu Ala Pro Tyr Asn His Val Glu Leu Gly
370 375 380

Gln Pro Met Phe Thr Glu Tyr Val Trp Gly Arg Gln Tyr Gly Glu Asn
385 390 395 400

Thr Ile Asn Pro

<210> 26

<211> 1212

<212> DNA

<213> Mycobacterium tuberculosis

<400> 26
gtgccaacgc tggtgacgag gaagaaccga cgtgcgtggc tgtatgtgga gggtgttgtc 60

ctgctgttgg tgggcgcgtt ggtgctcgta ttggtgtaca agcagtttcg tggggaattc 120

acgccgaaga ccgagctgac tatggtcgcc ttccgggctg ggctggttat ggaagctgga 180

tccaaagtca cctacaacgg ggtggagatc ggccgggtgg gcagcatttc ggagattgag 240

cgtgacggcc ggccggcggc gaagctggtt ttggacgtga atcctcgcta catcagcctg 300

attccggtca atgtggtggc cgatatcgag gcggccaccc tgttcggcaa caagtatgtt 360

gcgctgtccg cgccgaaaat tcctcaacag cagcggattt cctcacatga cgtgattgat 420

gtggggtcgg tgaccaccga attcaacacg ttgttcgaga cgatcacctc gatcgccgag 480

aaggtggatc cgatcgagct gaacgcgacg ctgtccgcgg tagcacaggc gctggatggg 540

ctgggcggca agttcggtga gtcgatcgtt aatggcaatc agattctggc gcaattaaat 600

ccgcggctgc cgcagctcgg ctatgatgtt cggcggttgg cggatctcgg tgaggtctat 660

gtcgatgctt cgccggatct gtggtccttt ctgcagaacg cactgaccac tgcgcgcaca 720

ttgaccagcc aacagcgcga tctggatgcc gcgttgttgg cggctacggg tgcgggcaac 780

accggtgaag acgtttttgc tcgaggcggg ccgtatcttg cgcgcgcagc cgccgatctg 840

gtgcccaccg ctacgctgct ggacacctac agtcccgaac tgttctgcat gatccgcaac 900

tttcacgacg ctgcgcccaa agtcgcggac gcggtgggcg gcaacggcta ttcgctagcg 960

gccgccggaa cgattttggg agcacccaat ccctatgtct atccggacaa tctgccgcgg 1020

gtgaatgccc acggtggacc cgggggccga ccgggctgct ggcagacgat cacccgggag 1080

ctgtggccgg caccctatct ggtgatggac accggtgcca gcctcgcacc gtacaaccac 1140

gtcgagctcg gccaaccgat gttcactgaa tacgtatggg gacgccaata cggagagaac 1200

acgatcaacc ca 1212

<210> 27

<211> 275

<212> PRT

<213> Mycobacterium tuberculosis

<400> 27

Met Lys Thr Thr Gly Thr Thr Ile Lys Leu Gly Ile Val Trp Leu Val
1 5 10 15

Leu Ser Val Phe Thr Val Met Ile Ile Val Val Phe Gly Gln Val Arg
20 25 30

Phe His His Thr Thr Gly Tyr Ser Ala Val Phe Thr His Val Ser Gly

35 40 45

Leu Arg Ala Gly Gln Phe Val Arg Ala Ala Gly Val Glu Val Gly Lys
50 55 60

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

Phe Thr Val Asp Arg Ser Leu Ser Leu Asp Gln Ala Thr Thr Ala Ser
85 90 95

Ile Arg Tyr Leu Asn Leu Ile Gly Asp Arg Tyr Leu Glu Leu Gly Arg
100 105 110

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

His Thr His Pro Ala Leu Asp Leu Asp Ala Leu Leu Gly Gly Phe Arg
130 135 140

Pro Leu Phe Gln Thr Leu Asp Pro Asp Lys Val Asn Ser Ile Ala Ser
145 150 155 160

Ser Ile Ile Thr Val Phe Gln Gly Gln Gly Ala Thr Ile Asn Asp Ile
165 170 175

Leu Asp Gln Thr Ala Ser Leu Thr Ala Thr Leu Ala Asp Arg Asp His
180 185 190

Ala Ile Gly Glu Val Val Asn Asn Leu Asn Thr Val Leu Ala Thr Thr
195 200 205

Val Lys His Gln Thr Glu Phe Asp Arg Thr Val Asp Lys Leu Glu Val
210 215 220

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

Ala His Ile Ser Ser Ala Ala Gly Thr Leu Ala Asp Leu Leu Gly Arg
245 250 255

Ile Val His Cys Cys Thr Ala Ala Ser Gly Thr Ser Arg Ala Ser Ser
260 265 270

Ser Arg Ser
275

<210> 28

<211> 825

<212> DNA

<213> Mycobacterium tuberculosis

<400> 28
atgaaaacca caggcacaac tatcaaactc ggcatcgtct ggttggtgct gtcggtgttc 60

accgtgatga tcatcgtggt gttcgggcag gtgcggttcc atcacaccac cgggtactcc 120

gcggtgttca cccatgtcag cgggctgcgg gccgggcaat ttgtccgcgc tgcgggcgta 180

gaggtcggca aggtcgccaa ggtaacgctg atcgacgggg acaagcaagt attggtggac 240

ttcaccgtgg atcgctcgct gtcactggat caggcgacga ccgcctcgat ccgctacctc 300

aacctgatcg gcgaccggta ccttgagctc ggccgcggtc acagcggtca gcggctggcg 360

ccgggtgcca cgatcccgct cgagcacacc catccggcct tggatctcga cgctctgctc 420

ggcgggtttc gcccactctt ccaaacgttg gacccagaca aggtcaacag catcgcctcc 480

tcgatcatca ccgtgttcca agggcaaggc gccaccatca acgacatcct cgaccagacc 540

gcctcgctga cggcaacgct ggccgaccgg gaccatgcga taggtgaggt cgtcaacaac 600

ttgaacaccg tgctggccac caccgtcaag catcaaacgg aattcgaccg cacggtcgac 660

aagctagagg tgctgatcac tggactgaag aacagggcgg acccgctggc cgcggcggcg 720

gcacacatca gcagcgccgc gggaacccta gccgacctgc tggggcggat cgtccattgc 780

tgcacagcag cttcgggcac ctcgagggca tccagcagcc gctca 825

<210> 29

<211> 481

<212> PRT

<213> Mycobacterium tuberculosis

<400> 29

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

Ala Val Val Thr Val Leu Val Val Gly Val Ala Gln Ser Phe Thr Ser
20 25 30

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

Thr Gly Gly Ile Asn Thr Gly Asp Lys Val Glu Ile Ala Gly Val Asn
50 55 60

Val Gly Leu Val Arg Ser Leu Ala Ile Arg Gly Asn Arg Val Leu Ile
65 70 75 80

Gly Phe Ser Leu Pro Gly Lys Thr Ile Gly Met Gln Ser Arg Ala Ala
85 90 95

Ile Arg Thr Asp Thr Ile Leu Gly Arg Lys Asn Leu Glu Ile Glu Pro
100 105 110

Arg Gly Ser Glu Pro Leu Lys Pro Asn Gly Phe Leu Pro Leu Ala Gln
115 120 125

Thr Thr Thr Pro Tyr Gln Ile Tyr Asp Ala Phe Val Asp Val Thr Lys
130 135 140

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

Leu Ser Glu Thr Phe Asp Gln Thr Ala Pro His Leu Ser Ala Ala Leu
165 170 175

Glu Gly Val Lys Ala Phe Ser Asp Thr Val Gly Arg Arg Gly Glu Gln
180 185 190

Ile Glu Gln Leu Leu Ala Asn Ala Asn Arg Ile Ala Arg Val Leu Gly
195 200 205

Asp Arg Ser Glu Gln Val Asn Gly Leu Leu Val Asn Ala Lys Thr Leu
210 215 220

Leu Ala Ala Phe Lys Gln Arg Ser Gln Ala Leu Arg Ile Leu Leu Thr
225 230 235 240

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

245 250 255

Pro Asn Leu Asn His Val Leu Ala Gln Leu Arg Thr Val Ser Glu Glu
260 265 270

Leu Val Lys Arg Lys Asn Glu Leu Ala Asp Val Ala Val Leu Leu Gly
275 280 285

Arg Tyr Thr Ala Ala Leu Thr Glu Ala Val Gly Ser Gly Pro Phe Phe
290 295 300

Lys Ala Met Val Val Asn Leu Leu Pro Tyr Gln Ile Leu Gln Pro Trp
305 310 315 320

Val Asp Ala Ala Phe Lys Lys Arg Gly Ile Asp Pro Glu Asn Phe Trp
325 330 335

Arg Ser Ala Gly Leu Pro Glu Phe Arg Trp Pro Asp Pro Asn Gly Thr
340 345 350

Arg Phe Pro Asn Gly Ala Pro Pro Ala Ala Pro Pro Val Arg Glu Gly
355 360 365

Thr Pro Lys His Pro Gly Pro Ala Val Pro Pro Gly Thr Pro Cys Ser
370 375 380

Tyr Thr Pro Ala Ala Gly Ala Leu Pro Arg Pro Asp Thr Pro Leu Pro
385 390 395 400

Cys Ala Gly Ala Thr Val Gly Pro Phe Gly Gly Pro Asp Phe Pro Ala
405 410 415

Pro Leu Asp Val Gln Pro Ser Pro Pro Asn Pro Asp Gly Pro Pro Pro
420 425 430

Thr Pro Gly Ile Leu Ser Ala Gly Arg Pro Gly Glu Pro Ala Pro Ala
435 440 445

Val Pro Gly Ile Pro Met Pro Leu Pro Pro Asn Ala Pro Pro Gly Ala
450 455 460

Arg Thr Gln Pro Leu Glu Pro Phe Pro Asp Gly Thr Gly Gly Ser Asn
465 470 475 480

Gln

<210> 30

<211> 1443

<212> DNA

<213> Mycobacterium tuberculosis

<400> 30

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gtgctcgtcg ttggtgttgc gcaaagcttc accagcgtgc cgatgctgtt cgccacacct 120

acctactatg cgcaattcgc cgacacgggt ggcatcaaca cgggcgataa ggtggaaatc 180

gctggggtga acgtcgggct ggtgcgctcg ctggcaatcc gcggcaaccg cgtgttgatc 240

ggattctcgt tgcccggcaa gacaatcggg atgcaaagcc gggcagcaat tcgcaccgac 300

accattcttg gccgtaagaa cctggagatc gaaccccgcg gttcggagcc gttgaaaccc 360

aacggtttcc tgccgttggc gcagaccact acgccatacc aaatctatga cgcgttcgtc 420

gatgtcacga aggcggcgac gggctgggac atcgatgccg tcaaacgctc gctaaacgtg 480

ttgtcggaga cattcgatca gaccgccccg catctaagtg ccgccctcga gggtgtcaag 540

gcattctccg acaccgtcgg ccggcgcggc gagcagatcg agcaactgct ggcgaacgcc 600

aacaggatcg cgcgcgtgct cggcgaccgc agcgagcagg tcaacgggct gctggtgaat 660

gccaagacgc tgctggccgc gttcaagcaa cgcagccagg cactgcgcat tctgctaacc 720

aacgtgtcgg aggcatcagc ccaggtatct ggcctgatca cagacaaccc caacctcaac 780

catgtgctgg cccagttgcg cacggtcagc gaggagctgg tgaagcgcaa gaacgaattg 840

gccgatgtag ccgtcttgct cggcagatac accgcggccc tgacagaggc cgtcggttcc 900

ggaccgttct tcaaggcgat ggtggtcaat ctgctgccct accagattct tcagccctgg 960

gttgacgcgg cgttcaaaaa gcggggcatc gacccggaga acttctggcg cagtgcgggt 1020

ctgccggaat tccgctggcc cgaccccaac ggcacccggt tccccaacgg cgcgccgccg 1080

gcggcgccac cggtgcggga gggtacaccc aagcatccgg gaccggccgt cccgccggga 1140

acgccgtgct cctacacacc ggcggcgggc gcgttgccac ggcccgacac cccactaccc 1200

tgcgcgggcg ccaccgttgg cccgttcggt ggacccgact tcccggcacc gctcgatgtc 1260

cagccgtcgc cgcctaatcc cgatgggccg ccgccgacgc cgggcatcct aagtgctggg 1320

cggccgggcg agccggctcc ggctgttccg ggcataccga tgccgctgcc gccgaacgcg 1380

ccgccgggtg cacgcaccca accgcttgag ccgtttcctg acgggacggg aggtagcaac 1440

caa 1443

<210> 31

<211> 508

<212> PRT

<213> Mycobacterium tuberculosis

<400> 31

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

Ala Lys Val Val Val Val Gly Gly Leu Val Val Val Leu Ala Val Val
20 25 30

Ala Ala Ala Ala Gly Ala Arg Leu Tyr Arg Lys Leu Thr Thr Thr Thr
35 40 45

Val Val Ala Tyr Phe Ser Glu Ala Leu Ala Leu Tyr Pro Gly Asp Lys
50 55 60

Val Gln Ile Met Gly Val Arg Val Gly Ser Ile Asp Lys Ile Glu Pro
65 70 75 80

Ala Gly Asp Lys Met Arg Val Thr Leu His Tyr Ser Asn Lys Tyr Gln
85 90 95

Val Pro Ala Thr Ala Thr Ala Ser Ile Leu Asn Pro Ser Leu Val Ala
100 105 110

Ser Arg Thr Ile Gln Leu Ser Pro Pro Tyr Thr Gly Gly Pro Val Leu
115 120 125

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

Trp Asp Gln Leu Arg Asp Ser Ile Asn Gly Ile Leu Arg Gln Leu Gly
145 150 155 160

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Pro Thr Glu Arg Gln Pro Lys Gly Pro Phe Gly Asp Leu Ile Glu Ser
                165                 170                 175

Ala Ala Asp Asn Leu Ala Gly Lys Gly Arg Gln Leu Asn Glu Thr Leu
            180                 185                 190

Asn Ser Leu Ser Gln Ala Leu Thr Ala Leu Asn Glu Gly Arg Gly Asp
        195                 200                 205

Phe Val Ala Ile Thr Arg Ser Leu Ala Leu Phe Val Ser Ala Leu Tyr
    210                 215                 220

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

Thr Asp Trp Phe Thr Lys Ser Asp His Asp Leu Ala Asp Thr Val Glu
                245                 250                 255

Arg Ile Asp Asp Val Leu Gly Thr Val Arg Lys Phe Val Ser Asp Asn
            260                 265                 270

Arg Ser Val Leu Ala Ala Asp Val Asn Asn Leu Ala Asp Ala Thr Thr
        275                 280                 285

Thr Leu Val Gln Pro Glu Pro Arg Asp Gly Leu Glu Thr Ala Leu His
    290                 295                 300

Val Leu Pro Thr Tyr Ala Ser Asn Phe Asn Asn Leu Tyr Tyr Pro Leu
305                 310                 315                 320

His Ser Ser Leu Val Gly Gln Phe Val Phe Pro Asn Phe Ala Asn Pro
                325                 330                 335

Ile Gln Leu Ile Cys Ser Ala Ile Gln Ala Gly Ser Arg Leu Gly Tyr
            340                 345                 350

Gln Glu Ser Ala Glu Leu Cys Ala Gln Tyr Leu Ala Pro Val Leu Asp
        355                 360                 365

Ala Leu Lys Phe Asn Tyr Leu Pro Phe Gly Ser Asn Pro Phe Ser Ser
    370                 375                 380

Ala Ala Thr Leu Pro Lys Glu Val Ala Tyr Ser Glu Glu Arg Leu Arg
385                 390                 395                 400
```

Pro Pro Pro Gly Tyr Lys Asp Thr Thr Val Pro Gly Ile Phe Ser Arg
405 410 415

Asp Thr Pro Phe Ser His Gly Asn His Glu Pro Gly Trp Val Val Ala
420 425 430

Pro Gly Met Gln Gly Met Gln Val Gln Pro Phe Thr Ala Asn Met Leu
435 440 445

Thr Pro Glu Ser Leu Ala Glu Leu Leu Gly Gly Pro Asp Ile Ala Pro
450 455 460

Pro Pro Pro Gly Thr Asn Leu Pro Gly Pro Pro Asn Ala Tyr Asp Glu
465 470 475 480

Ser Asn Pro Leu Pro Pro Pro Trp Tyr Pro Gln Pro Ala Ser Leu Pro
485 490 495

Ala Ala Gly Ala Thr Gly Gln Pro Gly Pro Gly Gln
500 505

<210> 32

<211> 1524

<212> DNA

<213> Mycobacterium tuberculosis

<400> 32
atgagcacca tcttcgacat ccgcagcctg cgactgccga aactgtctgc aaaggtagtg 60

gtcgtcggcg ggttggtggt ggtcttggcg gtcgtggccg ctgcggccgg cgcgcggctc 120

taccggaaac tgactaccac taccgtggtc gcgtatttct ctgaggcgct cgcgctgtac 180

ccaggagaca aagtccagat catgggtgtg cgggtcggtt ctatcgacaa gatcgagccg 240

gccggcgaca agatgcgagt cacgttgcac tacagcaaca aataccaggt gccggccacg 300

gctaccgcgt cgatcctcaa ccccagcctg gtggcctcgc gcaccatcca gctgtcaccg 360

ccgtacaccg gcggcccggt cttgcaagac ggcgcggtga tcccaatcga gcgcacccag 420

gtgcccgtcg agtgggatca gttgcgcgat tccatcaatg ggatcctccg ccagctcggc 480

ccgacggagc ggcagccgaa ggggccgttc ggcgacctca tcgaatcggc cgcggacaac 540

ctggccggca agggcaggca gctcaacgaa acgctgaaca gtttgtcgca ggcgttgacc 600

gcgctgaacg agggccgggg agacttcgtt gcgatcacgc gaagcctggc gctatttgtc 660

agcgcgctct accagaatga tcaacagttc gttgcgctca acgaaaacct tgccgagttc 720

accgactggt tcaccaaatc cgaccatgac ttggccgaca cggtggaacg gatcgacgac 780

gttctcggca ccgtccgaaa gttcgtgagc gacaacagat ccgtgctggc tgccgatgtc 840

aacaacctcg ccgacgcgac cactacacta gtgcaacccg agccgcggga cggtctggaa 900

accgcgttgc acgtgttgcc gacctacgcc agcaacttca acaaccttta ctatccactg 960

cacagctctc tggtgggcca gttcgtgttc cccaacttcg cgaacccaat tcagctcatt 1020

tgcagcgcta ttcaggccgg cagccgactc ggctatcagg aatccgccga gctgtgcgcg 1080

cagtacttgg caccggttct ggacgctctc aagttcaatt acttgccgtt cggctcaaac 1140

ccgttcagtt cggcggccac tttgcccaag gaggtggctt actccgagga gcggctccgc 1200

ccgccgcccg ggtacaagga caccactgtc ccagggatct tctcgcggga cacaccgttt 1260

tcacacggca accatgaacc gggctgggtc gttgcgcccg ggatgcaggg tatgcaggtt 1320

cagccgttta ccgcgaacat gctcaccccg gaatcgctgg cagagctgct gggtggtccg 1380

gatattgccc ccccgccgcc gggaaccaac ttgcccggac cgccgaatgc gtatgacgag 1440

tccaatccgt tgccgccgcc gtggtacccg cagcccgcgt ccctcccggc tgcgggcgcc 1500

acaggacagc caggcccggg ccag 1524

<210> 33

<211> 402

<212> PRT

<213> Mycobacterium tuberculosis

<400> 33

Val Arg Cys Gly Val Ser Ala Gly Ser Ala Asn Gly Lys Pro Asn Arg
1 5 10 15

Trp Thr Leu Arg Cys Gly Val Ser Ala Gly His Arg Gly Ser Val Phe
20 25 30

Leu Leu Ala Val Leu Leu Ala Pro Val Val Leu Thr Ser Cys Thr Trp
35 40 45

```
Arg Gly Ile Ala Asn Val Pro Leu Pro Val Gly Arg Gly Met Gly Pro
    50                  55                  60

Asp Arg Met Thr Ile Tyr Val Gln Met Pro Asp Thr Leu Ala Leu Asn
65                  70                  75                  80

Thr Asn Ser Arg Val Arg Val Ala Asp Val Trp Val Gly Thr Val Arg
                85                  90                  95

Asp Ile Ser Leu Arg Asn Trp Ile Ala Thr Leu Thr Leu Glu Leu Glu
            100                 105                 110

Pro Thr Val Arg Leu Pro Ala Asn Ala Thr Ala Lys Ile Gly Gln Thr
        115                 120                 125

Ser Leu Leu Gly Thr Gln His Val Glu Leu Ala Ala Pro Pro Ile Pro
    130                 135                 140

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

Ser Ala Tyr Pro Thr Val Glu Arg Thr Leu Ala Ser Val Ala Leu Ile
                165                 170                 175

Leu Thr Gly Gly Gly Ile Val Asn Leu Asp Val Ile Gln Thr Glu Ile
            180                 185                 190

Leu Asn Ile Leu Asp Gly His Ala Gly Gln Ile Arg Glu Phe Leu Glu
        195                 200                 205

Arg Leu Ala Thr Phe Thr Ala Glu Leu Asn Asn Gln Arg Gly Asp Leu
    210                 215                 220

Thr Arg Ala Ile Asp Ser Thr Asn Gln Leu Leu Thr Ile Ile Ala Asn
225                 230                 235                 240

Arg Asn Asp Thr Leu Asp Arg Val Leu Thr Asp Val Pro Pro Leu Ile
                245                 250                 255

Glu His Phe Ala Asp Thr Gly Gln Leu Phe Ala Asp Ala Thr Glu Ser
            260                 265                 270

Leu Gly Arg Phe Ser Glu Val Ala Asn Arg Ala Leu Ala Ala Thr Arg
        275                 280                 285
```

Pro Asn Leu His Gln Thr Leu Gln Ser Leu Gln Arg Pro Leu Arg Gln
290 295 300

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

Thr Ala Pro Phe Asn Ile Asp Glu Val Pro Asn Val Ile Arg Gly Asp
325 330 335

Tyr Val Asn Val Ser Ala Thr Phe Asp Val Thr Leu Ser Ala Leu Asp
340 345 350

Asn Ala Leu Leu Ser Gly Thr Gly Ile Ser Gly Met Leu Arg Ala Leu
355 360 365

Glu Gln Ala Trp Gly Arg Asp Pro Asp Thr Met Ile Pro Asp Val Arg
370 375 380

Tyr Thr Pro Asn Pro Asn Asp Ala Pro Gly Gly Pro Leu Val Glu Arg
385 390 395 400

Ala Glu

<210> 34

<211> 1206

<212> DNA

<213> Mycobacterium tuberculosis

<400> 34
gtgaggtgcg gcgtgagcgc gggtagcgcg aacggcaagc cgaaccgttg gaccctgagg 60

tgcggcgtga gcgcgggtca ccgtggatcg gtgttcttgc tggcggtctt gctggccccg 120

gtggttttga cttcgtgtac ctggcgtggc atcgccaatg tgccgctgcc ggtcggccgg 180

ggtatgggtc cggatcgcat gacgatctac gtgcagatgc ctgacacgct ggcgctgaac 240

actaacagcc gggtcagggt tgccgacgtc tgggtcggta cggtgcgtga catcagcctg 300

aggaactgga tcgcgaccct gacgctggag ctcgagccga ccgtgcggct accggcaaat 360

gcgaccgcga agatcggcca gaccagcctg ttaggcacac aacatgtcga gctggccgca 420

ccgccaatcc cgtcaccgca gccgctgaaa agcggcgaca ccatcggcct gaagaactcc 480

tcggcctacc ctaccgtcga acggaccttg gccagcgtcg cgttgatcct caccggcggc 540

ggcatcgtca acctcgacgt gattcaaacc gagatcctca acatccttga cggccatgcc 600

ggtcagattc gcgaattcct cgagcggcta gccactttca ccgccgagct gaacaaccaa 660

cgcggcgatc tgactcgcgc aatcgactca accaaccaac tcctgaccat catcgccaac 720

cgcaacgaca cgctggatcg ggtgctcact gacgtcccac cgctgatcga gcatttcgcc 780

gacaccggtc agctgttcgc tgacgccacc gaatccttgg ggcggttcag cgaagtcgcc 840

aaccgggcgc tggcggctac ccggcctaac cttcaccaga cgctgcagtc gttgcagcgg 900

ccgttaaggc aattggaacg ggcttcgccg tatgtggtcg gcgcgttgaa gctaggcctc 960

accgctccgt tcaacatcga cgaggtgcca aacgttatcc gcggcgacta cgtcaacgtg 1020

tccgcgacgt tcgacgtgac gctttctgca ctcgacaacg cactgctgag cggaacgggc 1080

atctcgggaa tgttgcgtgc gctcgagcag gcgtggggac gggatccgga caccatgatc 1140

ccggatgtcc gctacacgcc gaacccgaat gacgcgccgg gcggaccgct ggtggaaagg 1200

gctgag 1206

<210> 35

<211> 516

<212> PRT

<213> Mycobacterium tuberculosis

<400> 35

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

Ala Val Ile Ala Val Val Val Leu Gly Trp Tyr Phe Leu Arg Ile Pro
20 25 30

Ser Leu Val Gly Ile Gly Arg Tyr Thr Leu Tyr Ala Glu Leu Pro Arg
35 40 45

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

Ile Gly Lys Val Thr Gly Val Glu Pro Thr Glu Arg Gly Ala Arg Ala

65 70 75 80

Thr Met Ser Ile Asp Asn Gly Tyr Gln Ile Pro Thr Asp Ala Ser Ala
85 90 95

Asn Val His Ser Val Ser Ala Val Gly Glu Gln Phe Val Asp Leu Val
100 105 110

Ser Thr Arg Thr Ser Gly Pro Tyr Leu Arg His Gly Gln Thr Ile Thr
115 120 125

Thr Thr Thr Val Pro Ser Gln Ile Gly Pro Ala Leu Asp Ala Ala Asn
130 135 140

Arg Gly Leu Ala Val Leu Pro Lys Asp Arg Val Ala Ser Val Leu His
145 150 155 160

Glu Ala Ser Glu Ala Val Gly Gly Leu Gly Ser Ser Leu Asn Arg Leu
165 170 175

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

Asp Ile Asp Asp Ile Ile Glu Arg Ser Ala Pro Ile Ile Asp Ser Gln
195 200 205

Val Asn Ser Gly Asn Glu Ile Ala Arg Trp Ala Ala Asn Leu Asn Thr
210 215 220

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

Ala Asn Ala Ala Pro Thr Ala Asp Gln Val Asn Ala Thr Phe Ser Asp
245 250 255

Val Arg Glu Ser Leu Pro Gln Thr Leu Ala Asn Leu Glu Val Val Ile
260 265 270

Asp Met Leu Lys Arg Tyr His Asn Gly Val Glu Gln Ala Leu Val Phe
275 280 285

Leu Pro Gln Ser Gly Ala Ile Ala Gln Ser Val Thr Thr Glu Phe Pro
290 295 300

Gly Gln Ala Gly Leu Gly Val Gly Gly Leu Ala Leu Asn Gln Pro Pro
305 310 315 320

Pro Cys Leu Thr Gly Phe Leu Pro Ala Ser Glu Trp Arg Ser Pro Ala
325 330 335

Asp Thr Ser Thr Ala Pro Leu Pro Lys Gly Thr Tyr Cys Arg Ile Pro
340 345 350

Met Asp Ala Ser Asn Val Val Arg Gly Ala Arg Asn Asn Pro Cys Val
355 360 365

Asp Val Pro Gly Lys Arg Ala Ala Thr Pro Arg Glu Cys Arg Ser Asn
370 375 380

Glu Ala Tyr Val Pro Gly Gly Thr Asn Pro Trp Tyr Gly Asp Pro Asn
385 390 395 400

Gln Met Leu Ser Cys Pro Ala Pro Ala Ala Arg Cys Asp Gln Pro Val
405 410 415

Lys Pro Gly Gln Val Ile Pro Ala Pro Ser Val Asn Asn Gly Ile Asn
420 425 430

Pro Leu Pro Ala Asp Gln Leu Pro Gly Thr Pro Pro Pro Val Asn Asp
435 440 445

Pro Leu Gln Arg Pro Gly Ser Gly Thr Val Gln Cys Asn Gly Gln Gln
450 455 460

Pro Asn Pro Cys Val Tyr Thr Pro Ser Thr Phe Pro Thr Thr Ile Tyr
465 470 475 480

Asp Val Gln Ser Gly Lys Val Val Ala Pro Asp Gly Val Val Tyr Ser
485 490 495

Val Glu Ala Ser Thr His Ala Gly Ala Asp Gly Trp Lys Val Met Leu
500 505 510

Ala Pro Thr Gly
515

<210> 36

<211> 1548

<212> DNA

<213> Mycobacterium tuberculosis

<400> 36

atgctgactc gcgctatcaa gacccagctg gtgttgttga cggtgttggc ggtcatcgcg 60

gtggtggtcc ttggttggta tttcctgcgg atacccagcc tggtcggcat cggtcgatac 120

acgctttatg ccgaattgcc tcggtccggg ggtctatacc gaacagccaa cgtcacatat 180

cggggcatca ccatagggaa ggtcaccggc gtcgaaccaa ccgagcgggg cgcgcgagca 240

accatgagca tcgacaatgg ctaccagatc cccaccgacg cctcggccaa tgtgcactca 300

gtgtcggcgg tcggcgagca gttcgttgac ctggtgtcga cccgcaccag cggtccgtat 360

ctgcggcatg ggcagacgat caccacgact acggtcccca gccagattgg cccggcgctg 420

gacgccgcca accgtggatt ggcagtgctg cccaaagacc gggtcgcgtc ggtgctgcac 480

gaggcgtcgg aggccgtggg cgggctggga tcctcactga atcgcctcat cgaagccacc 540

caggcaatcg cccacgatgt caggggcagc ctcgaggaca tcgacgacat catcgagcgt 600

tcggcgccta tcatcgatag ccaggtcaat tccggcaacg agatcgcccg ctgggccgcc 660

aacctcaaca cgctggccgc tcagaccgcg cagaccgatc cggcggtgcg aagcattctg 720

gccaacgcgg caccgactgc cgatcaggtc aacgccacgt tcagcgacgt gcgggagtcg 780

ttgccgcaga cgctggccaa tctcgaggtc gtaatcgata tgctcaagcg ctaccacaac 840

ggcgtcgagc aggcgttggt gttcttgccg cagtccggcg cgatcgccca gtcggttact 900

acagagttcc ccggccaggc cggactgggt gtcggcggcc tggcgctcaa ccaaccaccg 960

ccgtgcctga ccggcttcct gccggcgtcg gagtggcggt cacctgctga caccagcacc 1020

gcaccgctac ccaagggcac ctactgcagg attccgatgg acgcgagcaa tgtggttcgt 1080

ggagcacgca acaacccgtg tgtagacgtg cccggcaagc gggcggcgac cccgcgggaa 1140

tgccgcagca atgaagctta tgtgcccggg ggcaccaatc cctggtatgg ggaccccaac 1200

cagatgctca gctgtcccgc gccggccgcg cgttgtgacc agccggtgaa gccaggccag 1260

gtgatcccgg cgccgtcagt taacaatggc atcaacccgc tgcccgccga tcagctgcca 1320

ggcacacctc caccggtcaa cgatcctttg cagcgacctg ggtcaggcac cgtccagtgc 1380

aatgggcaac aacccaaccc gtgcgtctac accccgagca catttcctac aaccatttac 1440

gacgtgcaga gcggcaaagt cgtagcaccc gacggtgtgg tgtattccgt tgaggcttcg 1500

actcatgccg gagccgacgg atggaaggtg atgctggcac caaccggc 1548

<210> 37

<211> 790

<212> DNA

<213> Mycobacterium tuberculosis

<400> 37
ggtgacgttt cgaggctgtg ctgctgccaa gaccccagga agtctcggac gagagactcg 60

ctagcctccg tggtatcggg catccctatc acccctgctc gatcctcaat atcggactaa 120

caaaatacat catcgcgcct gtatacgcga ttacattgca atttatcctt atcacccttc 180

ttagagtgca tatcagtaat agacatatcg cgctcctcgc gccccaggag gcggtcgacg 240

aattcgccgt gcgcaacgac atgagccgtc gctgagcctg aaaacctgca gacaaagcgc 300

gagtgggggc tggcaaaact acaggctcgt tagcagcaag ttgcttcgac gaccatggtg 360

gcaacctcgc cggtcgcgaa ggctctggtc ggcgggcccg aatcgaggcg gtcaggatgc 420

ggcatccgat caccgcccgt cgggcgcgct gttgatgcct gatcgtggtg cctcgccagc 480

gtgactcgag ccaacggctt gaccggtgat gcgcctgtcg gccgccaagg cagcagagca 540

catcgccccg cgctatagga tactagcaag atacatcata gccaatatat gccagtttgc 600

attgctattt accgatcagt tgtccaagca atcgcgtatt ggctatggac atcagcggtt 660

ctgccgcgta cgctcaccaa tgtcaccgat cgtcgacctg tccgggggggc cagcgtgcgc 720

cacctcaccc aacggcccag catcgaatcc agctggtgcg ccgcgccatg gtaatcgtgg 780

ccgacaaggc 790

<210> 38

<211> 265

<212> PRT

<213> Mycobacterium tuberculosis

<400> 38

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

```
Leu Arg Pro Val Gly Ala Leu Gly Asp Phe Phe Ala Met Thr Leu Asp
            20                  25                  30

Thr Ser Val Cys Met Phe Lys Pro Pro Phe Ala Trp Arg Glu Tyr Leu
        35                  40                  45

Leu Gln Cys Trp Phe Val Ala Arg Val Ser Thr Leu Pro Gly Val Leu
    50                  55                  60

Met Thr Ile Pro Trp Ala Val Ile Ser Gly Phe Leu Phe Asn Val Leu
65                  70                  75                  80

Leu Thr Asp Ile Gly Ala Ala Asp Phe Ser Gly Thr Gly Cys Ala Ile
                85                  90                  95

Phe Thr Val Asn Gln Ser Ala Pro Ile Val Thr Val Leu Val Val Ala
            100                 105                 110

Gly Ala Gly Ala Thr Ala Met Cys Ala Asp Leu Gly Ala Arg Thr Ile
        115                 120                 125

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

Ala Leu Ala Ala Pro Arg Val Leu Ala Ala Thr Thr Val Ser Leu Ala
145                 150                 155                 160

Leu Asn Ser Val Val Thr Ala Thr Gly Leu Ile Gly Ala Phe Phe Cys
                165                 170                 175

Ser Val Phe Leu Met His Val Ser Ala Gly Ala Trp Val Thr Gly Leu
            180                 185                 190

Thr Thr Leu Thr His Thr Val Asp Val Val Ile Ser Met Ile Lys Ala
        195                 200                 205

Thr Leu Phe Gly Leu Met Ala Gly Leu Ile Ala Cys Tyr Lys Gly Met
    210                 215                 220

Ser Val Gly Gly Gly Pro Ala Gly Val Gly Arg Ala Val Asn Glu Thr
225                 230                 235                 240

Val Val Phe Ala Phe Ile Val Leu Phe Val Ile Asn Ile Val Val Thr
                245                 250                 255
```

Ala Val Gly Ile Pro Phe Met Val Ser
260 265

<210> 39

<211> 795

<212> DNA

<213> Mycobacterium tuberculosis

<400> 39
atggtaatcg tggccgacaa ggcggccggt cgggtcgctg atccggtctt gcggccggtg 60

ggcgcgctgg gcgatttctt cgcgatgacg ctcgacacgt ccgtgtgcat gttcaagccg 120

cctttcgcgt ggcgtgaata cctacttcag tgctggttcg tggcgcgggt gtcgacgctg 180

cctggggtgt tgatgacgat cccatgggcg gtgatctcgg ggtttctctt caacgtcttg 240

ctgaccgaca tcggtgccgc ggacttttcc ggcaccggct gtgcgatctt caccgtgaac 300

caaagcgccc cgatcgtcac ggtcttggtg gtcgcgggcg cgggcgccac cgccatgtgc 360

gccgatctgg gtgcgcgcac catccgtgag gaactcgacg cactgcgggt gatgggcatc 420

aacccgatcc aagcgctagc ggctccgcgc gtgctggcgg ccaccacggt gtcgttggcg 480

ctgaattcgg tggtgaccgc gacggggctg atcggcgcgt tcttttgctc ggtgtttctc 540

atgcacgtct cggcgggggc atgggtgacc gggcttacca cgctgaccca caccgtggac 600

gtcgtcattt cgatgatcaa ggcgacgttg ttcgggctga tggccggact gatcgcctgc 660

tataagggca tgtcggtcgg tggcggcccg gccggagtcg gccgggcggt gaacgaaacc 720

gtggtgtttg ccttcatcgt cttgttcgtg atcaacatcg tcgtcaccgc ggtcggcatc 780

ccattcatgg tgtcc 795

<210> 40

<211> 271

<212> PRT

<213> Mycobacterium tuberculosis

<400> 40

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

```
1               5                   10                  15

Gln Met Arg Phe Phe Val Gly Thr Leu Ala Gly Ile Pro Asp Ala Leu
            20                  25                  30

Met His Tyr Arg Gly Glu Leu Leu Arg Val Ile Ala Gln Met Gly Leu
        35                  40                  45

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

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

Gln Phe Ala Ser Val Gly Val Glu Ala Leu Thr Gly Phe Ala Ser Ala
                85                  90                  95

Phe Phe Asn Thr Arg Glu Ile Gln Pro Gly Thr Val Met Val Ala Leu
            100                 105                 110

Ala Ala Thr Val Gly Ala Gly Thr Thr Ala Ala Leu Gly Ala Met Arg
        115                 120                 125

Ile Asn Glu Glu Ile Asp Ala Leu Glu Val Ile Gly Ile Arg Ser Ile
    130                 135                 140

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

Pro Leu Phe Cys Val Gly Leu Met Thr Ala Tyr Leu Ala Ala Arg Val
                165                 170                 175

Gly Thr Thr Ala Ile Tyr Gly Gln Gly Ser Gly Val Tyr Asp His Tyr
            180                 185                 190

Phe Asn Thr Phe Leu Arg Pro Thr Asp Val Leu Trp Ser Ser Val Glu
        195                 200                 205

Val Val Val Val Ala Leu Met Ile Met Leu Val Cys Thr Tyr Tyr Gly
    210                 215                 220

Tyr Ala Ala His Gly Gly Pro Ala Gly Val Gly Glu Ala Val Gly Arg
225                 230                 235                 240
```

Ala Val Arg Ala Ser Met Val Val Ala Ser Ile Ala Ile Leu Val Met
245 250 255

Thr Leu Ala Ile Tyr Gly Gln Ser Pro Asn Phe His Leu Ala Thr
260 265 270

<210> 41

<211> 813

<212> DNA

<213> Mycobacterium tuberculosis

<400> 41
atgacggcag cgaaagccct tgtaagcgaa tggaatcgga tgggatcgca gatgcggttc 60

ttcgtcggca cgctggccgg gattcccgac gccctcatgc actaccgcgg cgagctgctg 120

cgggtgatcg cgcaaatggg gttggggacc ggggttcttg cggtgatcgg tggaacggtc 180

gcgatcgtcg ggttcttggc gatgaccacc ggcgcgatcg tggccgtgca gggctacaac 240

cagttcgctt cggtgggtgt ggaggcgctg accggcttcg cgtcggcctt cttcaacacc 300

cgcgagattc agcccggaac cgtgatggtc gcgctagcgg ccaccgtcgg tgccggtacc 360

accgctgcgc tgggggcgat gcggataaac gaggagatcg acgcgctcga ggtgatcggc 420

atccgcagca tcagctacct ggcgagcacc cgggtgctgg ccggagtggt cgtggccgtc 480

cctctgttct gtgtgggact gatgacggcc tacctggccg cgcgcgtcgg caccaccgcc 540

atctatggcc aggggtcggg cgtgtacgac cactacttca acacgttcct gcgcccgacc 600

gacgtgctct ggtcgtcggt tgaagtcgtc gtggtcgctc tgatgatcat gctggtgtgc 660

acctattacg gctacgccgc acatggcggg ccggccgggg ttggcgaggc ggtcggccgg 720

gccgtgcgtg cctcgatggt cgtcgcgtcg atcgcaatcc ttgtcatgac gctggccatc 780

tacggccagt cgcccaactt tcacctggcg acc 813

<210> 42

<211> 425

<212> PRT

<213> Mycobacterium tuberculosis

<400> 42

```
Met Arg Arg Gly Pro Gly Arg His Arg Leu His Asp Ala Trp Trp Thr
1               5                  10                  15

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

Ser Phe Thr Gly Ser Leu Arg Ser Thr Val Pro Val Thr Leu Ala Ala
        35                  40                  45

Asp Arg Ser Gly Leu Val Met Asp Ser Gly Ala Lys Val Met Met Arg
    50                  55                  60

Gly Val Gln Val Gly Arg Val Ala Gln Ile Gly Arg Ile Glu Trp Ala
65                  70                  75                  80

Gln Asn Gly Ala Ser Leu Arg Leu Glu Ile Asp Pro Asp Gln Ile Arg
                85                  90                  95

Tyr Ile Pro Ala Asn Val Glu Ala Gln Ile Ser Ala Thr Thr Ala Phe
            100                 105                 110

Gly Ala Lys Phe Val Asp Leu Val Met Pro Gln Asn Pro Ser Arg Ala
        115                 120                 125

Arg Leu Ser Ala Gly Ala Val Leu His Ser Lys Asn Val Ser Thr Glu
    130                 135                 140

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

Pro Leu Lys Leu Asn Ala Val Leu Thr Ala Val Ala Asp Ala Val Arg
                165                 170                 175

Gly Gln Gly Glu Arg Ile Gly Gln Ala Thr Thr Asp Leu Asn Glu Val
            180                 185                 190

Leu Glu Ala Leu Asn Ala Arg Gly Asp Thr Ile Gly Gly Asn Trp Arg
        195                 200                 205

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

Leu Thr Ile Leu Asn Ala Ala Ser Thr Thr Ser Ala Thr Val Val Asn
225 230 235 240

His Ser Thr Gln Leu Asp Ala Leu Leu Leu Asn Ala Ile Gly Leu Ser
245 250 255

Asn Ala Gly Thr Asn Leu Leu Gly Ser Ser Arg Asp Asn Leu Val Gly
260 265 270

Ala Ala Asp Ile Leu Ala Pro Thr Thr Ser Leu Leu Phe Lys Tyr Asn
275 280 285

Pro Glu Tyr Thr Cys Phe Leu Gln Gly Ala Lys Trp Tyr Leu Asp Asn
290 295 300

Gly Gly Tyr Ala Ala Trp Gly Gly Ala Asp Gly Arg Thr Leu Gln Leu
305 310 315 320

Asp Val Ala Leu Leu Phe Gly Asn Asp Pro Tyr Val Tyr Pro Asp Asn
325 330 335

Leu Pro Val Val Ala Ala Lys Gly Gly Pro Gly Gly Arg Pro Gly Cys
340 345 350

Gly Pro Leu Pro Asp Ala Thr His Asn Phe Pro Val Arg Gln Leu Val
355 360 365

Thr Asn Thr Gly Trp Gly Thr Gly Leu Asp Ile Arg Pro Asn Pro Gly
370 375 380

Ile Gly His Pro Cys Trp Ala Asn Tyr Phe Pro Val Thr Arg Ala Val
385 390 395 400

Pro Glu Pro Pro Ser Ile Arg Gln Cys Ile Pro Gly Pro Ala Ile Gly
405 410 415

Pro Asn Pro Ala Ala Gly Glu Gln Pro
420 425

<210> 43

<211> 1275

<212> DNA

<213> Mycobacterium tuberculosis

<400> 43
atgagacgcg ggccgggtcg acaccgtttg cacgacgcgt ggtggacgct gatcctgttc 60

gcggtgatcg gggtggctgt cctggtgacg gcggtgtcct tcacgggcag cttgcggtcg 120

actgtgccgg tgacgctggc ggccgaccgc tccgggctgg tgatggactc cggcgccaag 180

gtcatgatgc gcggtgtgca ggtcggccgg gtcgcccaga tcggtcggat cgagtgggcc 240

cagaacgggg cgagcctcag actggagatc gaccccgacc agatccggta catcccggcc 300

aatgtcgagg cacagatcag cgccaccacc gcattcggtg ccaagttcgt cgacctggtg 360

atgccgcaaa acccaagtcg tgcacggctg tccgctgggg cggtactgca ttcgaagaac 420

gtcagcacgg aaatcaacac cgtcttcgaa aacgtcgtcg acctgctcaa catgatcgac 480

ccgctgaaac tgaacgccgt gctgaccgcg gtcgccgacg ccgttcgcgg gcaaggtgaa 540

cggataggcc aggccaccac cgacctcaac gaggtgctgg aggcactcaa cgcacgcggc 600

gacaccatcg gcggcaactg gcgatcgctc aagaacttca ccgacaccta tgacgcggcc 660

gcccaagaca tcctgacgat cctgaacgcc gccagcacca ccagtgcgac cgtcgtgaat 720

cattcgacgc agctggatgc cttgctactc aacgccatcg gactatccaa cgctggcacc 780

aacctgcttg gcagcagccg agacaatctc gtcggcgcgg ccgacatcct ggcgccgacc 840

acgagcctgc tgttcaagta caaccccgaa tacacctgct tcctgcaggg cgccaagtgg 900

tatctcgaca acggcggcta tgcggcctgg ggcggggccg acgggcgcac gctacaactc 960

gatgtggcgc tactgttcgg caacgacccc tatgtctatc cggacaacct gccggttgtc 1020

gcggccaagg ggggtcccgg cggaaggccg ggatgcgggc cattgccgga tgccacccac 1080

aacttcccgg tgcgccagct ggtcaccaac accggatggg gaaccgggct ggacatccgg 1140

cccaaccccg gcatcgggca tccctgctgg gccaactact tcccggtgac ccgcgcggtg 1200

cccgagccgc cgtcgatccg tcagtgcatc cccgggccgg cgatcgggcc caaccccgcg 1260

gcgggggagc agcca 1275

<210> 44

<211> 342

<212> PRT

<213> Mycobacterium tuberculosis

<400> 44

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

Ala Val Cys Leu Leu Thr Ala Phe Leu Leu Ile Ala Val Phe Gly Glu
20 25 30

Val Arg Phe Gly Asp Gly Lys Thr Tyr Tyr Ala Glu Phe Ala Asn Val
35 40 45

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

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

Gln Phe Thr Ala Asp Asn Ser Val Thr Leu Thr Arg Gly Thr Arg Ala
85 90 95

Val Ile Arg Tyr Asp Asn Leu Phe Gly Asp Arg Tyr Leu Ala Leu Glu
100 105 110

Glu Gly Ala Gly Gly Leu Ala Val Leu Arg Pro Gly His Thr Ile Pro
115 120 125

Leu Ala Arg Thr Gln Pro Ala Leu Asp Leu Asp Ala Leu Ile Gly Gly
130 135 140

Phe Lys Pro Leu Phe Arg Ala Leu Asn Pro Glu Gln Val Asn Ala Leu
145 150 155 160

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

Ser Leu Leu Ala Gln Ser Ala Ala Val Thr Asn Thr Leu Ala Asp Arg
180 185 190

Asp Arg Leu Ile Gly Gln Val Ile Thr Asn Leu Asn Val Val Leu Gly
195 200 205

Ser Leu Gly Ala His Thr Asp Arg Leu Asp Gln Ala Val Thr Ser Leu
210 215 220

Ser Ala Leu Ile His Arg Leu Ala Gln Arg Lys Thr Asp Ile Ser Asn
225 230 235 240

Ala Val Ala Tyr Thr Asn Ala Ala Ala Gly Ser Val Ala Asp Leu Leu
245 250 255

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

Val Ala Gly Ile Ala Ala Ala Asp His Asp Tyr Leu Asp Asn Leu Leu
275 280 285

Asn Thr Leu Pro Asp Lys Tyr Gln Ala Leu Val Arg Gln Gly Met Tyr
290 295 300

Gly Asp Phe Phe Ala Phe Tyr Leu Cys Asp Val Val Leu Lys Val Asn
305 310 315 320

Gly Lys Gly Gly Gln Pro Val Tyr Ile Lys Leu Ala Gly Gln Asp Ser
325 330 335

Gly Arg Cys Ala Pro Lys
340

<210> 45

<211> 1026

<212> DNA

<213> Mycobacterium tuberculosis

<400> 45
atgagggaga acctgggggg cgtcgtggtg cgcctcggcg tcttcctggc ggtatgcctg 60

ctgacggcgt tcctgctgat tgccgtcttc ggggaggtgc gcttcggcga cggcaagacc 120

tactacgccg agttcgccaa cgtgtccaat ctgcgaacgg gcaagctggt gcgcatcgcc 180

ggcgtcgagg tcggcaaggt caccaggatc tccatcaacc ccgacgcgac ggtgcgggtg 240

cagttcaccg ccgacaactc ggtcaccctc acgcggggca cccgggcggt gatccgctac 300

gacaacctgt tcggtgaccg ctatttggcg ctggaggaag gggccggcgg actcgccgtt 360

cttcgtcccg gtcacacgat tccgttggcg cgcacccaac cggcgttgga tctggatgcc 420

ctgatcggtg gattcaagcc gctgtttcgt gcgctgaacc ccgagcaggt caacgcgctg 480

agcgaacagt tgctgcacgc gtttgccgga caggggccca cgatcgggtc attgctggcc 540

cagtccgcgg ccgtgaccaa caccctggcc gaccgtgatc ggctgatcgg gcaggtgatc 600

accaacctca acgtggtgct gggctcgctg ggcgctcaca ccgatcggtt ggaccaggcg 660

gtgacgtcgc tatcagcgtt gattcaccgg ctcgcgcaac gcaagaccga catctccaac 720

gccgtggcct acaccaacgc cgccgccggc tcggtcgccg atctgctgtc gcaggctcgc 780

gcgccgttgg cgaaggtggt tcgcgagacc gatcgggtgg ccggcatcgc ggccgccgac 840

cacgactacc tcgacaatct gctcaacacg ctgccggaca aataccaggc gctggtccgc 900

cagggtatgt acggcgactt cttcgccttc tacctgtgcg acgtcgtgct caaggtcaac 960

ggcaagggcg gccagccggt gtacatcaag ctggccggtc aggacagcgg gcggtgcgcg 1020

ccgaaa 1026

<210> 46

<211> 410

<212> PRT

<213> Mycobacterium tuberculosis

<400> 46

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

Ile Val Val Val Ala Ala Val Ala Leu Ala Ala Leu Gln Tyr Gln Arg
20 25 30

Leu Pro Phe Phe Asn Gln Gly Thr Arg Val Ser Ala Tyr Phe Ala Asp
35 40 45

Ala Gly Gly Leu Arg Thr Gly Asn Thr Val Glu Val Ser Gly Tyr Pro
50 55 60

Val Gly Lys Val Ser Ser Ile Ser Leu Asp Gly Pro Gly Val Leu Val
65 70 75 80

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

Ala Ile Lys Thr Lys Gly Leu Leu Gly Ser Lys Phe Leu Asp Val Thr

```
            100                 105                 110

Pro Arg Gly Asp Gly Arg Leu Asp Ser Pro Ile Pro Ile Glu Arg Thr
        115                 120                 125

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

Ile Ser Gly Leu His Thr Glu Arg Leu Ser Glu Ser Leu Ala Thr Leu
145                 150                 155                 160

Ala Gln Thr Phe Ala Asp Thr Pro Ala His Phe Arg Asn Ala Ile His
                165                 170                 175

Gly Val Ala Arg Leu Ala Gln Thr Leu Asp Glu Arg Asp Asn Gln Leu
            180                 185                 190

Arg Ser Leu Leu Ala Asn Ala Ala Lys Ala Thr Gly Val Leu Ala Asn
        195                 200                 205

Arg Thr Asp Gln Ile Val Gly Leu Val Arg Asp Thr Asn Val Val Leu
    210                 215                 220

Ala Gln Leu Arg Thr Gln Ser Ala Ala Leu Asp Arg Ile Trp Ala Asn
225                 230                 235                 240

Ile Ser Ala Val Ala Glu Gln Leu Arg Gly Phe Ile Ala Glu Asn Arg
                245                 250                 255

Gln Gln Leu Arg Pro Ala Leu Asp Lys Leu Asn Gly Val Leu Ala Ile
            260                 265                 270

Val Glu Asn Arg Lys Glu Arg Val Arg Gln Ala Ile Pro Leu Ile Asn
        275                 280                 285

Thr Tyr Val Met Ser Leu Gly Glu Ser Leu Ser Ser Gly Pro Phe Phe
    290                 295                 300

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

Ile Ser Ala Ala Phe Ser Asp Leu Gly Leu Asp Pro Ala Thr Leu Leu
                325                 330                 335
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Pro Ser Gln Leu Thr Asp Pro Pro Thr Gly Gln Pro Gly Thr Pro Pro
340 345 350

Leu Pro Met Pro Tyr Pro Arg Thr Gly Gln Gly Gly Glu Pro Arg Leu
355 360 365

Thr Leu Pro Asp Ala Ile Thr Gly Asn Pro Gly Asp Pro Arg Tyr Pro
370 375 380

Tyr Arg Pro Glu Pro Pro Ala Pro Pro Pro Gly Gly Pro Pro Pro Gly
385 390 395 400

Pro Pro Ala Gln Gln Pro Gly Asp Gln Pro
405 410

<210> 47

<211> 1230

<212> DNA

<213> Mycobacterium tuberculosis

<400> 47
atgaaatcct tcgccgaacg caaccgtctg gccatcggca cagtcggcat cgtcgtcgtc 60

gccgccgttg cgctggccgc gctgcaatac cagcggctgc cgtttttcaa ccagggcacc 120

agggtctccg cctatttcgc cgacgccggc gggctgcgca ccggcaacac cgtcgaggtc 180

tccggctatc cggtgggaaa agtgtccagc atctcgctcg acggaccggg cgtgctggtg 240

gagttcaagg tcgacaccga cgtccgactc ggaaaccgca ccgaagtggc aatcaaaacc 300

aagggcttgt tgggcagcaa gttcctcgac gtcacccccc gcggggacgg ccgactcgat 360

tctccgatcc cgatcgagcg gaccacgtcg ccctaccaac tgcccgacgc ccttggcgat 420

ttggccgcca cgatcagcgg gttgcacacc gagcggctgt ccgaatcgct ggccaccctg 480

gcgcagacct ttgccgatac gccggcgcac ttccgcaacg ccatacacgg ggtggcccgg 540

ctcgcccaaa ccctcgatga gcgcgacaac caactgcgca gcctgctggc caacgcggcc 600

aaagccaccg gggtgctggc caaccgcacc gaccagatcg tcggcctggt gcgcgacacg 660

aatgtggtct tggcgcagct gcgcacccaa agcgccgccc tggaccggat ctgggcgaac 720

atctcggcgg tggccgaaca actgcggggc ttcatcgctg agaaccgcca gcagctgcgc 780

ccggcgctgg acaagctcaa cggggtgctg gctatcgtcg aaaaccgcaa agagcgtgtg 840

cggcaggcca tcccgctgat caacacctat gtcatgtcgc tgggtgagtc gctgtcgtcg 900

ggcccgttct tcaaggcata cgtggtgaac ctgctgccgg gtcagttcgt gcaaccgttc 960

atcagcgccg cgttctccga cctggggctc gacccggcca cgttgctgcc gtcgcagctg 1020

accgacccac cgaccggtca acccggaacc ccgccgttgc cgatgcccta cccgcgcacg 1080

ggccagggcg gtgagccgcg gctgacgctg cccgacgcga tcaccggcaa tcccggcgat 1140

ccgcgctatc cgtaccggcc ggagccgccc gcgccgccgc ccggcgggcc gccgcccggc 1200

ccgcccgcgc agcagccggg agaccaaccg 1230

<210> 48

<211> 423

<212> PRT

<213> Mycobacterium tuberculosis

<400> 48

Val Thr Thr Lys Leu Arg Arg Ala Arg Ser Val Leu Ala Thr Ala Leu
1 5 10 15

Val Leu Val Ala Gly Val Ile Leu Ala Met Arg Thr Ala Asp Ala Ala
20 25 30

Ala Arg Thr Thr Val Val Ala Tyr Phe Asp Asn Ser Asn Gly Val Phe
35 40 45

Ala Gly Asp Asp Val Leu Ile Arg Gly Val Pro Val Gly Lys Ile Val
50 55 60

Lys Ile Glu Pro Gln Pro Leu Arg Ala Lys Ile Ser Phe Trp Phe Asp
65 70 75 80

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

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

Gly Pro Thr Met Ala Asp Gly Thr Val Ile Pro Gln Glu Arg Thr Val
115 120 125

Val Pro Val Glu Trp Asp Asp Leu Arg Ala Gln Leu Gln Arg Leu Thr
130 135 140

Ala Leu Leu Gln Pro Thr Arg Pro Gly Gly Val Ser Thr Leu Gly Ala
145 150 155 160

Leu Ile Asn Thr Ala Ala Asp Asn Leu Arg Gly Gln Gly Ala Thr Ile
165 170 175

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

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

Thr Ala Leu His Asp Ser Ala Asp Leu Leu Glu Arg Leu Asn His Asn
210 215 220

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

Gln Ala Ala Glu Asp Leu Asn Ala Val Val Ala Asp Val Gly Ser Phe
245 250 255

Ala Ala Glu His Arg Glu Ala Ile Gly Thr Ala Ser Asp Lys Leu Ala
260 265 270

Ser Ile Thr Thr Ala Leu Val Asp Ser Leu Asp Asp Ile Lys Gln Thr
275 280 285

Leu His Ile Ser Pro Thr Val Leu Gln Asn Phe Asn Asn Ile Phe Glu
290 295 300

Pro Ala Asn Gly Ala Leu Thr Gly Ala Leu Ala Gly Asn Asn Met Ala
305 310 315 320

Asn Pro Ile Ala Phe Leu Cys Gly Ala Ile Gln Ala Ala Ser Arg Leu
325 330 335

Gly Gly Glu Gln Ala Ala Lys Leu Cys Val Gln Tyr Leu Ala Pro Ile
340 345 350

Val Lys Asn Arg Gln Tyr Asn Tyr Pro Pro Leu Gly Ala Asn Leu Phe
355 360 365

Val Gly Ala Gln Ala Arg Pro Asn Glu Val Thr Tyr Ser Glu Asp Trp
370 375 380

Leu Arg Pro Asp Tyr Val Ala Pro Val Ala Asp Thr Pro Pro Asp Pro
385 390 395 400

Ala Ala Ala Val Thr Val Asp Pro Ala Thr Gly Leu Arg Gly Met Met
405 410 415

Met Pro Pro Gly Gly Gly Ser
420

<210> 49

<211> 1269

<212> DNA

<213> Mycobacterium tuberculosis

<400> 49
gtgacaacga aactcagacg tgcccgctcg gtgttggcga ccgccctggt gctggtcgcg 60

ggcgtgatcc tggccatgcg caccgccgac gccgccgccc gcacgaccgt ggtcgcctac 120

ttcgacaaca gcaacggtgt gttcgccggt gacgacgtgc tcattcgggg cgtgccggtg 180

ggcaagatcg tcaagatcga accgcaaccg ctgcgcgcca agatttcgtt ctggttcgac 240

cgcaaatacc gagtccccgc cgatgccgcc gcggcgatcc tgtcgccgca actggtgacc 300

ggccgggcca tccagctgac accgccgtat gccggcgggc cgaccatggc cgacggcaca 360

gtaatcccgc aagagcgcac cgtggtgccg gtggagtggg acgacttgcg ggcgcaactt 420

cagcggctga ccgcattgct gcagcccacc cggccgggcg gcgtcagcac gctgggtgcg 480

ctcatcaata ctgccgccga caacctgcgc gggcaaggcg ccaccatccg cgacaccatc 540

atcaaactgt cacaagcgat ttcggctctc ggtgaccaca gcaaagacat cttctccacc 600

gtgacgaacc tgtcgacgct ggtcacggcg ctgcatgaca gcgctgacct gctcgaacgg 660

ctcaaccaca acctggccgc ggtgacctcg ctgctggccg atggcccgga caagatcggt 720

caggcagccg aggacctcaa cgcggtcgta gccgacgtcg gcagcttcgc cgccgagcac 780

cgcgaggcga tcggcaccgc atcagacaag ctcgcgtcaa tcaccaccgc gctggtcgac 840

agcctcgacg acatcaagca gacgctgcat atcagcccga cggtgttgca gaacttcaac 900

aacatcttcg aaccggccaa cggcgcgctg accggcgcgc tggcgggcaa caacatggcc 960

aacccaatcg ccttcctgtg cggcgcgatc caggctgcct cccggctggg cggcgagcaa 1020

gcggccaaat tgtgcgtgca atacctggcg ccgatcgtga agaaccgcca gtacaactac 1080

ccgccgctgg gggcgaacct gttcgtcggg gcgcaggcca ggcctaacga ggtcacctac 1140

agcgaggact ggctgcggcc cgattacgtt gcaccagttg cggacacgcc gccagatccg 1200

gccgcggccg tgaccgtcga tcccgcgacc ggcctgcgcg gcatgatgat gccgccgggg 1260

ggtggctcg 1269

<210> 50

<211> 377

<212> PRT

<213> Mycobacterium tuberculosis

<400> 50

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

Cys Gly Trp Arg Gly Leu Asn Ser Leu Pro Leu Pro Gly Thr Gln Gly
20 25 30

Asn Gly Pro Gly Ser Phe Ala Val Gln Ala Gln Leu Pro Asp Val Asn
35 40 45

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

His Val Thr Lys Ile Glu Arg Gln Gly Trp His Ala Leu Val Thr Met
65 70 75 80

Arg Leu Asp Gly Asp Val Asp Leu Pro Ala Asn Ala Thr Ala Lys Ile
85 90 95

Gly Thr Thr Ser Leu Leu Gly Ser Tyr His Ile Glu Leu Ala Pro Pro
100 105 110

Lys Gly Glu Ala Arg Gln Gly Lys Leu Arg Asp Gly Ser Leu Ile Ala
115 120 125

```
Leu Ser His Gly Ser Ala Tyr Pro Ser Thr Glu Gln Thr Leu Ala Ala
    130                 135                 140

Leu Ser Leu Val Leu Asn Gly Gly Gly Leu Gly Gln Val Gln Asp Ile
145                 150                 155                 160

Thr Glu Ala Leu Ser Thr Ala Phe Ala Gly Arg Glu His Asp Leu Arg
                165                 170                 175

Gly Leu Ile Gly Gln Leu Asp Thr Phe Thr Ala Tyr Leu Asn Asn Gln
            180                 185                 190

Ser Gly Asp Ile Ile Ala Ala Thr Asp Ser Leu Asn Arg Leu Val Gly
        195                 200                 205

Lys Phe Ala Asp Gln Gln Pro Val Phe Asp Arg Ala Leu Ala Thr Ile
    210                 215                 220

Pro Asp Ala Leu Ala Val Leu Ala Asp Glu Arg Asp Thr Leu Val Glu
225                 230                 235                 240

Ala Ala Glu Gln Leu Ser Lys Phe Ser Ala Leu Thr Val Asp Ser Val
                245                 250                 255

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

Val Leu Glu Ser Leu Ala Asn Ser Gly Pro Ala Leu Thr Arg Ser Leu
        275                 280                 285

Ser Leu Leu Ala Thr Phe Pro Phe Pro Asn Glu Thr Phe Gln Asn Phe
    290                 295                 300

Gln Arg Gly Glu Tyr Ala Asn Leu Thr Ala Ile Val Asp Leu Thr Leu
305                 310                 315                 320

Ser Arg Ile Asp Gln Gly Leu Leu Thr Gly Thr Arg Trp Glu Cys His
                325                 330                 335

Leu Thr Gln Leu Glu Leu Gln Trp Gly Arg Thr Ile Gly Gln Phe Pro
            340                 345                 350

Ser Pro Cys Thr Ala Gly Tyr Arg Gly Thr Pro Gly Asn Pro Leu Thr
        355                 360                 365
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Ile Ala Tyr Arg Trp Asp Gln Gly Pro
370 375

<210> 51

<211> 1131

<212> DNA

<213> Mycobacterium tuberculosis

<400> 51
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caggcgcagc tgccggatgt caacaacatc cagccgaact cgcgggtgcg ggttgccgac 180

gtgacggtcg gccacgtcac gaaaatcgag cgccaaggct ggcacgcgtt ggtgaccatg 240

cggctggatg gcgacgtcga tttgcccgcc aacgcaacgg ccaagatcgg caccaccagc 300

ctgctgggtt cctaccacat cgagctggcg ccaccgaaag gcgaagcgcg gcaaggcaag 360

ctgcgcgacg gttcactcat tgcgctgtca cacggtagcg cctacccaag caccgagcag 420

acgctggcag cgctgtcgct ggtgctcaac ggcggcggac tgggccaggt tcaagacatc 480

accgaggcgt tgagcaccgc gtttgccggc cgtgagcacg atctgcgcgg gctgattggg 540

cagctggaca ccttcaccgc atacctcaac aaccagtccg gtgacatcat cgcggccacc 600

gacagcctca accgcctcgt cggcaagttc gccgaccagc aacccgtctt cgatcgggcc 660

ctggccacca tccccgacgc gctcgcggtg ctggccgatg agcgggacac gctcgtcgag 720

gctgccgagc agctgagcaa gttcagcgcc ctgaccgtcg actcggtcaa caagaccacc 780

gcgaacctgg tcaccgaact gcggcaactc ggaccggtgt tggagtcgct ggccaattcc 840

ggtccggcgc tgacccgatc gctgtccctg ctggccacgt tcccgttccc gaacgagacg 900

ttccaaaatt tccagcgcgg cgaatacgcc aacctgaccg cgatcgtcga cctcacgctc 960

agccgcatcg accagggcct gttgaccggc acccgctggg agtgtcatct gacccagctc 1020

gagctgcagt ggggtcgcac cattgggcag ttccccagcc cgtgtaccgc gggctatcgg 1080

ggtaccccgg gcaatccgct gacgatcgcc taccgctggg atcaggggcc c 1131

<210> 52

<211> 437

<212> PRT

<213> Mycobacterium tuberculosis

<400> 52

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

Val Ile Ala Val Gly Val Leu Ala Ile Thr Phe Leu His Phe Val Arg
20 25 30

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

Leu Val Glu Ala Gly Gly Leu Tyr Arg Thr Gly Asn Val Thr Tyr Arg
50 55 60

Gly Phe Glu Val Gly Arg Val Ala Ala Val Arg Leu Thr Asp Thr Gly
65 70 75 80

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

Leu Lys Ala Glu Val His Ser His Thr Ala Ile Gly Glu Thr Tyr Val
100 105 110

Glu Leu Leu Pro Arg Asn Ala Ala Ser Pro Pro Leu Lys Asn Gly Asp
115 120 125

Val Ile Ala Leu Ala Asp Thr Ser Val Pro Pro Asp Ile Asn Asp Leu
130 135 140

Leu Ser Ala Ala Asn Thr Ala Leu Glu Ala Ile Pro His Glu Asn Leu
145 150 155 160

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

Glu Leu Ser Arg Leu Ile Lys Gly Ser Ala Glu Leu Ala Ile Asp Ala
180 185 190

Arg Ala Asn Leu Asp Pro Leu Val Ala Leu Ile Asp Arg Ala Gly Pro
195 200 205

```
Val Leu Asp Ser Gln Thr His Thr Ser Asp Ala Ile Ala Ala Trp Ala
    210                 215                 220

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

Val Gly Asp Leu Ile Asp Arg Gly Gly Pro Ala Leu Gly Glu Thr Arg
            245                 250                 255

Gln Leu Leu Glu Arg Leu Gln Pro Thr Val Pro Ile Leu Leu Ala Asn
        260                 265                 270

Leu Val Ser Val Gly Gln Val Ala Leu Thr Tyr His Asn Asp Ile Glu
    275                 280                 285

Gln Leu Leu Val Val Phe Pro Met Ala Ile Ala Ala Glu Gln Ala Gly
290                 295                 300

Ile Leu Ala Asn Leu Asn Thr Lys Gln Ala Tyr Arg Gly Gln Tyr Leu
305                 310                 315                 320

Ser Phe Asn Leu Asn Leu Asn Leu Pro Pro Pro Cys Thr Thr Gly Phe
                325                 330                 335

Leu Pro Ala Gln Gln Arg Arg Ile Pro Thr Phe Glu Asp Tyr Pro Asp
            340                 345                 350

Arg Pro Ala Gly Asp Leu Tyr Cys Arg Val Pro Gln Asp Ser Pro Phe
        355                 360                 365

Asn Val Arg Gly Ala Arg Asn Ile Pro Cys Glu Thr Val Pro Gly Lys
    370                 375                 380

Arg Ala Pro Thr Val Lys Leu Cys Glu Ser Asp Ala Pro Tyr Leu Pro
385                 390                 395                 400

Leu Asn Asp Gly Tyr Asn Trp Lys Gly Asp Pro Asn Ala Thr Val Pro
                405                 410                 415

Gly Leu Gly Ser Gly Gln Asp Ile Pro Gln Thr Trp Gln Thr Met Leu
            420                 425                 430

Leu Pro Pro Gly Ser
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435

<210> 53

<211> 1311

<212> DNA

<213> Mycobacterium tuberculosis

<400> 53

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ggccgctaca cggtgacgat ggagctggtc gaagccggtg ggctgtatcg caccggcaat 180

gtcacctacc gcggctttga ggtgggccgg gtggcagcgg tgcggctcac cgacaccggg 240

gtgcaagcgg tgctggccct gaaatcgggc atcgatatcc cgtcggacct caaggccgag 300

gtgcacagcc acaccgcgat cggcgaaacc tacgtcgagt tgttgccgcg caacgccgcc 360

tcgccgccac tgaagaacgg cgatgtcatt gcgctggccg acacctcggt gccgcccgac 420

atcaacgacc tgctcagcgc ggccaacacc gcattggagg caatacctca cgagaacctg 480

cagaccgtca tcgacgagtc gtacaccgcg gtggccgggt tagggctcga actttcccgg 540

ctgatcaagg gctcggcgga actggcgatc gatgctcgcg cgaatctcga tccgctggtg 600

gcgctgatcg accgggcagg accggtgctg gattcgcaga cccacacctc ggatgcgatc 660

gcggcctggg cggcacagct ggccgcagtc accggccaat tgcagacaca cgactcggcg 720

gtcggcgatc tcatcgaccg gggcggtccg gcgttggggg agacgcgcca actgctcgag 780

cggctacaac ccaccgtgcc catcctgctg gccaacctgg tcagcgtcgg ccaggtcgca 840

ctcacctatc acaacgacat cgaacagctg ctggtggtgt tccccatggc catcgccgcc 900

gaacaggccg gcatcctggc caacctcaac accaagcagg cctaccgggg ccagtatctg 960

agcttcaacc tcaacctgaa cctgccgccg ccgtgcacca ccggctttct gccggcccag 1020

cagcggcgca ttcccacgtt cgaggactac ccggatcgcc cggccggtga tctgtactgc 1080

cgggtgcccc aggattcgcc gtttaacgtg cgcggcgccc gcaacatccc ctgtgaaacc 1140

gtgccgggca agcgcgcacc caccgtgaag ttatgcgaga gcgacgcgcc atacctgccg 1200

ctgaacgacg gctacaactg gaagggcgac cccaacgcca cggtgccggg tttggggtcc 1260

ggccaggaca tcccgcagac atggcaaacg atgctgctgc cgccgggcag c 1311

<210> 54

<211> 380

<212> DNA

<213> Mycobacterium tuberculosis

<400> 54
ttgatgtcag gctgattcat gggtcgcgca tggcgccttt ctgccgaaca aacgcatggc 60

ccgagcgggc gacgggaatc gaacccgcgt cgctagtttg gaagactagg gctctaccat 120

tgagctacgc ccgcatgtat ttagtcgagc gcgactgtac gtggtgacag acatcaaatc 180

taatcggagt cgttttgaga ccttcccgtg aggtctcaag aggtcattgc ggtgccggtg 240

tcgccgggcc gtaggatcgc gaggtcagcg cggggtgtag cgcagcttgg tagcgcatcc 300

gctttgggag cggaaggccg caggttcaaa tcctgtcacc ccgaccagcc gaccgccgtt 360

atcgactacc aaggagcaca 380

<210> 55

<211> 466

<212> PRT

<213> Mycobacterium tuberculosis

<400> 55

Val Lys Ser Thr Val Glu Gln Leu Ser Pro Thr Arg Val Arg Ile Asn
1 5 10 15

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

Lys Glu Leu Ala Lys Gln Val Arg Leu Pro Gly Phe Arg Pro Gly Lys
35 40 45

Ala Pro Ala Lys Leu Leu Glu Ala Arg Ile Gly Arg Glu Ala Met Leu
50 55 60

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

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

Lys Lys Glu Tyr Gly Gln Asp Leu Gln Phe Thr Ala Glu Val Asp Ile
100 105 110

Arg Pro Lys Ile Ser Pro Pro Asp Leu Ser Ala Leu Thr Val Ser Val
115 120 125

Asp Pro Ile Glu Ile Gly Glu Asp Asp Val Asp Ala Glu Leu Gln Ser
130 135 140

Leu Arg Thr Arg Phe Gly Thr Leu Thr Ala Val Asp Arg Pro Val Ala
145 150 155 160

Val Gly Asp Val Val Ser Ile Asp Leu Ser Ala Thr Val Asp Gly Glu
165 170 175

Asp Ile Pro Asn Ala Ala Ala Glu Gly Leu Ser His Glu Val Gly Ser
180 185 190

Gly Arg Leu Ile Ala Gly Leu Asp Asp Ala Val Val Gly Leu Ser Ala
195 200 205

Asp Glu Ser Arg Val Phe Thr Ala Lys Leu Ala Ala Gly Glu His Ala
210 215 220

Gly Gln Glu Ala Gln Val Thr Val Thr Val Arg Ser Val Lys Glu Arg
225 230 235 240

Glu Leu Pro Glu Pro Asp Asp Glu Phe Ala Gln Leu Ala Ser Glu Phe
245 250 255

Asp Ser Ile Asp Glu Leu Arg Ala Ser Leu Ser Asp Gln Val Arg Gln
260 265 270

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

Ala Leu Leu Glu Gln Val Asp Val Pro Leu Pro Glu Ser Tyr Val Gln
290 295 300

Ala Gln Phe Asp Ser Val Leu His Ser Ala Leu Ser Gly Leu Asn His
305 310 315 320

Asp Glu Ala Arg Phe Asn Glu Leu Leu Val Glu Gln Gly Ser Ser Arg
325 330 335

Ala Ala Phe Asp Ala Glu Ala Arg Thr Ala Ser Glu Lys Asp Val Lys
340 345 350

Arg Gln Leu Leu Leu Asp Ala Leu Ala Asp Glu Leu Gln Val Gln Val
355 360 365

Gly Gln Asp Asp Leu Thr Glu Arg Leu Val Thr Thr Ser Arg Gln Tyr
370 375 380

Gly Ile Glu Pro Gln Gln Leu Phe Gly Tyr Leu Gln Glu Arg Asn Gln
385 390 395 400

Leu Pro Thr Met Phe Ala Asp Val Arg Arg Glu Leu Ala Ile Arg Ala
405 410 415

Ala Val Glu Ala Ala Thr Val Thr Asp Ser Asp Gly Asn Thr Ile Asp
420 425 430

Thr Ser Glu Phe Phe Gly Lys Arg Val Ser Ala Gly Glu Ala Glu Glu
435 440 445

Ala Glu Pro Ala Asp Glu Gly Ala Ala Arg Ala Ala Ser Asp Glu Ala
450 455 460

Thr Thr
465

<210> 56

<211> 1398

<212> DNA

<213> Mycobacterium tuberculosis

<400> 56
gtgaagagca ccgtcgagca gttgagcccc acccgggttc gtatcaacgt ggaggtgcca 60

ttcgccgagc ttgagccgga tttccagcgg gcctacaaag agctggccaa acaggtgcgg 120

ctgcccggct tccggcccgg gaaggcgccg gccaaactac tcgaagcccg catcggccgg 180

gaggccatgc tggatcaaat cgtcaacgat gcgctgccca gccggtacgg acaggcggtg 240

gccgagtcgg atgtccaacc gctcggccgg cccaacatcg aggtgaccaa gaaggagtac 300

ggccaggacc tgcaattcac cgccgaggtc gacatccgcc cgaagatcag tcccccggac 360

ctgagcgcgc tgacggtctc ggtggatccg atcgaaatcg gtgaggacga cgtcgacgcc 420

gaactgcagt cgttacgtac ccggttcggc accctgaccg cggtggaccg gccggtggcc 480

gtcggcgacg tcgtctcgat cgacttgtct gccacggtcg acggagagga cataccgaac 540

gcagccgctg agggactctc ccacgaggtc ggctccggcc ggctcatcgc aggtctcgac 600

gacgcggttg ttggtctgtc cgccgacgag tcccgggtct tcaccgccaa gctggcagcc 660

ggcgagcacg ccgggcagga agctcaggtt accgtcacgg tcaggtcggt taaggagcgc 720

gaactaccag agcccgacga cgaattcgcg cagttagcca gcgagttcga cagcatcgac 780

gaattgcggg ccagcctcag cgaccaggtg cgccaggcca agcgcgccca gcaggccgag 840

cagattcgaa acgccaccat cgatgcgcta ctcgaacagg tcgacgtgcc gttgccggag 900

tcgtatgtgc aggcccaatt cgacagcgtg ctgcacagcg cgctcagcgg tcttaatcac 960

gacgaagccc ggttcaatga gttgctcgtc gagcaaggct cgtcacgcgc ggcgttcgat 1020

gccgaggcgc gcaccgcctc agaaaaggac gtcaagaggc agctgttgct agacgccctg 1080

gccgatgagc tgcaggtcca agttggccag gatgatctga ccgaacgact ggtgacgacg 1140

tctcggcaat acggcatcga gccgcagcag ctgttcggct acctccaaga gcgcaaccag 1200

ctgccgacca tgttcgctga cgtgcggcgc gagctggcga tcagggccgc agtggaggcg 1260

gcgacggtca ccgacagtga cggaaacacg atcgatacca gtgagttctt cggcaagcgt 1320

gtgtcggccg gtgaggctga ggaggccgaa ccggcagacg agggtgccgc gcgggcggcg 1380

tccgacgaag cgacaacg 1398

<210> 57

<211> 313

<212> DNA

<213> Mycobacterium tuberculosis

<400> 57

ccagagtgat tcgcctcggc tgggggccgg ctggccaggc atgtcgtcgt gtccgggggt 60

gccgtccatg cccgcagcgt atgtccaatt ggcgacgccg tcgggcaggc gcgcctggtt 120

cgaacgccgg ccgagcaccg agctggacgc ttgcggctgt acccgacacg cccggcgtgc 180

cggacgcgac gaaggtcact ttgactcgat attccctgga cagcgcaggt aacggtatgg 240

tttctaagcc aaagctcaga ttgctcatat atggcccata cgccggtacg cgacggtaat 300

tcccatggaa ctc 313

<210> 58

<211> 257

<212> PRT

<213> Mycobacterium tuberculosis

<400> 58

Met Glu Leu Leu Gly Gly Pro Arg Val Gly Asn Thr Glu Ser Gln Leu
1 5 10 15

Cys Val Ala Asp Gly Asp Asp Leu Pro Thr Tyr Cys Ser Ala Asn Ser
20 25 30

Glu Asp Leu Asn Ile Thr Thr Ile Thr Thr Leu Ser Pro Thr Ser Met
35 40 45

Ser His Pro Gln Gln Val Arg Asp Asp Gln Trp Val Glu Pro Ser Asp
50 55 60

Gln Leu Gln Gly Thr Ala Val Phe Asp Ala Thr Gly Asp Lys Ala Thr
65 70 75 80

Met Pro Ser Trp Asp Glu Leu Val Arg Gln His Ala Asp Arg Val Tyr
85 90 95

Arg Leu Ala Tyr Arg Leu Ser Gly Asn Gln His Asp Ala Glu Asp Leu
100 105 110

Thr Gln Glu Thr Phe Ile Arg Val Phe Arg Ser Val Gln Asn Tyr Gln
115 120 125

Pro Gly Thr Phe Glu Gly Trp Leu His Arg Ile Thr Thr Asn Leu Phe
130 135 140

Leu Asp Met Val Arg Arg Arg Ala Arg Ile Arg Met Glu Ala Leu Pro

145 150 155 160

Glu Asp Tyr Asp Arg Val Pro Ala Asp Glu Pro Asn Pro Glu Gln Ile
165 170 175

Tyr His Asp Ala Arg Leu Gly Pro Asp Leu Gln Ala Ala Leu Ala Ser
180 185 190

Leu Pro Pro Glu Phe Arg Ala Ala Val Val Leu Cys Asp Ile Glu Gly
195 200 205

Leu Ser Tyr Glu Glu Ile Gly Ala Thr Leu Gly Val Lys Leu Gly Thr
210 215 220

Val Arg Ser Arg Ile His Arg Gly Arg Gln Ala Leu Arg Asp Tyr Leu
225 230 235 240

Ala Ala His Pro Glu His Gly Glu Cys Ala Val His Val Asn Pro Val
245 250 255

Arg

<210> 59

<211> 771

<212> DNA

<213> Mycobacterium tuberculosis

<400> 59
atggaactcc tcggcggacc ccgggttggg aatacggaat cgcaactttg cgttgccgac 60

ggtgacgact tgccaactta ttgcagtgca aattcggagg atctcaatat cacgaccatc 120

acgaccttga gtccgaccag catgtctcat ccccaacagg tccgcgatga ccagtgggtg 180

gagccgtctg accaattgca gggcaccgcc gtattcgacg ccaccgggga caaggccacc 240

atgccgtcct gggatgagct ggtccgtcag cacgccgatc gggtgtaccg gctggcttat 300

cggctctccg gcaaccagca cgatgccgaa gacctgaccc aggagacctt tatcagggtg 360

ttccggtcgg tccagaatta ccagccgggc accttcgaag gctggctaca ccgcatcacc 420

accaacttgt tcctggacat ggtccgccgc cgggctcgca tccggatgga ggcgttaccc 480

gaggactacg accgggtgcc cgccgatgag cccaaccccg agcagatcta ccacgacgca 540

cggctgggac ctgacctgca ggctgccttg gcctcgctgc cgccggagtt tcgtgccgcg 600

gtggtgctgt gtgacatcga gggtctgtcg tacgaggaga tcggcgccac actgggcgtg 660

aagctcggga cggtacgtag ccggatacac cgcggacgcc aggcactgcg ggactacctg 720

gcagcgcacc ccgaacatgg cgagtgcgca gttcacgtca acccagttcg c 771

<210> 60

<211> 154

<212> PRT

<213> Mycobacterium tuberculosis

<400> 60

Met Ala Asp Pro Gly Ser Val Gly His Val Phe Arg Arg Ala Phe Ser
1 5 10 15

Trp Leu Pro Ala Gln Phe Ala Ser Gln Ser Asp Ala Pro Val Gly Ala
20 25 30

Pro Arg Gln Phe Arg Ser Thr Glu His Leu Ser Ile Glu Ala Ile Ala
35 40 45

Ala Phe Val Asp Gly Glu Leu Arg Met Asn Ala His Leu Arg Ala Ala
50 55 60

His His Leu Ser Leu Cys Ala Gln Cys Ala Ala Glu Val Asp Asp Gln
65 70 75 80

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

Ser Thr Leu Leu Gly Leu Leu Ser Glu Ile Pro Arg Cys Pro Pro Glu
100 105 110

Gly Pro Ser Lys Gly Ser Ser Gly Gly Ser Ser Gln Gly Pro Pro Asp
115 120 125

Gly Ala Ala Ala Gly Phe Gly Asp Arg Phe Ala Asp Gly Asp Gly Gly
130 135 140

Asn Arg Gly Arg Gln Ser Arg Val Arg Arg
145 150

<210> 61

<211> 462

<212> DNA

<213> Mycobacterium tuberculosis

<400> 61
atggccgacc ccggaagcgt gggacatgtg ttccggcgcg cgttttcctg gctcccggcg 60

cagttcgcct cccagagtga cgcgccggtc ggcgcgccgc ggcagttccg ttccaccgag 120

cacctgtcaa tcgaggccat cgcggctttc gtcgacggcg agctgcggat gaacgcgcac 180

ttgcgggccg cgcatcacct ttcgctgtgt gcccaatgcg cggccgaagt ggacgaccaa 240

agtcgtgccc gcgccgctct gcgcgattcc cacccgatcc gcatccccag cacgttgctc 300

ggattactgt ccgagatccc gcgttgtcca cctgaaggtc catctaaagg ttcgtctgga 360

ggttcatccc agggcccgcc cgacggggct gcggcaggct tcggcgaccg cttcgctgac 420

ggcgatggcg ggaatcgggg ccggcaatcg cgggtgcgtc gc 462

<210> 62

<211> 549

<212> PRT

<213> Mycobacterium tuberculosis

<400> 62

Val Ser His Leu Ser Gln Arg Met Ala Gly Leu Leu Arg Val His Gly
1 5 10 15

Glu Trp Ser Arg Ser Val Asp Thr Arg Val Asp Thr Asp Asn Ala Met
20 25 30

Pro Ala Arg Phe Ser Ala Gln Ile Gln Asn Glu Asp Glu Val Thr Ser
35 40 45

Asp Gln Gly Asn Asn Gly Gly Pro Asn Gly Gly Gly Arg Leu Ala Pro
50 55 60

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Arg Pro Val Phe Arg Pro Pro Val Asp Pro Ala Ser Arg Gln Ala Phe
65                  70                  75                  80

Gly Arg Pro Ser Gly Val Gln Gly Ser Phe Val Ala Glu Arg Val Arg
                85                  90                  95

Pro Gln Lys Tyr Gln Asp Gln Ser Asp Phe Thr Pro Asn Asp Gln Leu
            100                 105                 110

Ala Asp Pro Val Leu Gln Glu Ala Phe Gly Arg Pro Phe Ala Gly Ala
        115                 120                 125

Glu Ser Leu Gln Arg His Pro Ile Asp Ala Gly Ala Leu Ala Ala Glu
    130                 135                 140

Lys Asp Gly Ala Gly Pro Asp Glu Pro Asp Asp Pro Trp Arg Asp Pro
145                 150                 155                 160

Ala Ala Ala Ala Ala Leu Gly Thr Pro Ala Leu Ala Ala Pro Ala Pro
                165                 170                 175

His Gly Ala Leu Ala Gly Ser Gly Lys Leu Gly Val Arg Asp Val Leu
            180                 185                 190

Phe Gly Gly Lys Val Ser Tyr Leu Ala Leu Gly Ile Leu Val Ala Ile
        195                 200                 205

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

Glu Val Val Asp Ala Phe Thr Thr Ser Lys Val Thr Leu Ser Thr Thr
225                 230                 235                 240

Gly Asn Ala Gln Glu Pro Ala Gly Arg Phe Thr Lys Val Ala Ala Ala
                245                 250                 255

Val Ala Asp Ser Val Val Thr Ile Glu Ser Val Ser Asp Gln Glu Gly
            260                 265                 270

Met Gln Gly Ser Gly Val Ile Val Asp Gly Arg Gly Tyr Ile Val Thr
        275                 280                 285

Asn Asn His Val Ile Ser Glu Ala Ala Asn Asn Pro Ser Gln Phe Lys
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290 295 300

Thr Thr Val Val Phe Asn Asp Gly Lys Glu Val Pro Ala Asn Leu Val
305 310 315 320

Gly Arg Asp Pro Lys Thr Asp Leu Ala Val Leu Lys Val Asp Asn Val
325 330 335

Asp Asn Leu Thr Val Ala Arg Leu Gly Asp Ser Ser Lys Val Arg Val
340 345 350

Gly Asp Glu Val Leu Ala Val Gly Ala Pro Leu Gly Leu Arg Ser Thr
355 360 365

Val Thr Gln Gly Ile Val Ser Ala Leu His Arg Pro Val Pro Leu Ser
370 375 380

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

Ala Ser Ile Asn His Gly Asn Ser Gly Gly Pro Leu Ile Asp Met Asp
405 410 415

Ala Gln Val Ile Gly Ile Asn Thr Ala Gly Lys Ser Leu Ser Asp Ser
420 425 430

Ala Ser Gly Leu Gly Phe Ala Ile Pro Val Asn Glu Met Lys Leu Val
435 440 445

Ala Asn Ser Leu Ile Lys Asp Gly Lys Ile Val His Pro Thr Leu Gly
450 455 460

Ile Ser Thr Arg Ser Val Ser Asn Ala Ile Ala Ser Gly Ala Gln Val
465 470 475 480

Ala Asn Val Lys Ala Gly Ser Pro Ala Gln Lys Gly Gly Ile Leu Glu
485 490 495

Asn Asp Val Ile Val Lys Val Gly Asn Arg Ala Val Ala Asp Ser Asp
500 505 510

Glu Phe Val Val Ala Val Arg Gln Leu Ala Ile Gly Gln Asp Ala Pro
515 520 525

Ile Glu Val Val Arg Glu Gly Arg His Val Thr Leu Thr Val Lys Pro
530 535 540

Asp Pro Asp Ser Thr
545

<210> 63

<211> 1647

<212> DNA

<213> Mycobacterium tuberculosis

<400> 63
gtgagccact tgtcgcagcg catggcgggg ttgctgcgag ttcatggcga gtggtcgcga 60

tccgtggata ctagggtgga cacggacaac gcgatgcctg cacgttttag cgcccagatt 120

cagaatgagg atgaggtgac ctccgaccaa ggcaacaacg gcggcccgaa cggcggaggc 180

cgcctggcgc cgcgcccggt ttttcggcca ccggtcgacc cggcgtcgcg tcaagcgttc 240

gggcgtccgt ccggggtcca agggtccttt gtggccgagc gtgtgcgccc gcagaagtac 300

caggaccagt ctgacttcac accgaacgat cagcttgctg acccggtgct tcaggaggcg 360

ttcggtcgtc cgttcgcggg cgccgaatcg ctgcagcgcc atcccatcga tgccggagcg 420

ctggcagctg agaaagacgg tgccggcccc gacgagcccg acgatccgtg gcgcgacccc 480

gcggccgcgg ccgcgctggg gacgccagcg ctagccgcgc cggcaccgca cggtgcgctg 540

gccggcagcg gcaagctggg tgtgcgcgac gtgctgtttg gcggcaaggt gtcctacttg 600

gcgctgggca tcttggtcgc tatcgcactg gtgatcggcg gcatcggcgg tgtcatcggc 660

cgcaagaccg cggaagtagt cgatgcgttc accacgtcga aggtgaccct gtcgaccact 720

ggcaatgccc aggaaccggc cggccggttc accaaggtgg cggccgccgt ggccgattcg 780

gtggtgacca ttgagtcggt cagcgaccag gagggcatgc aaggttccgg cgtcatcgtc 840

gatggccgcg gctacatcgt caccaacaat cacgtgatct ctgaggcggc caacaatccc 900

agccagttca agacgaccgt ggtgttcaac gacggcaagg aggtgcccgc caatctggtg 960

ggtcgtgacc ccaagaccga cttggccgtc ctcaaggtcg acaacgtcga caatctgacc 1020

gtggcccggc tcggtgattc cagcaaggta cgggtcggtg acgaagtcct cgcggtcggc 1080

gcgcccctgg ggctgcgcag tacggtgacc cagggcattg tcagcgcgct acaccgcccc 1140

gttccgttgt cgggcgaggg ctctgacacc gacaccgtca ttgacgcaat tcagaccgac 1200

gcctcgatca accacggtaa ctccggcggt ccgctaatcg acatggatgc ccaggtgatt 1260

ggcatcaaca ccgccggtaa gtcactgtcg gatagcgcca gcgggctggg ctttgcgatc 1320

ccggtcaacg agatgaaatt ggtggcaaat tctctgatca aagacggaaa gatcgtgcat 1380

ccgacgttgg gcatcagcac ccggtcagta agcaacgcga tcgcgtcggg cgcgcaggtg 1440

gccaatgtaa aggcgggaag tcccgcgcag aagggcggga tcttggagaa cgatgtgatc 1500

gtcaaggtcg gtaaccgcgc ggtcgccgac tccgacgagt tcgtcgtcgc cgtgcgccag 1560

ttggctatcg gccaggacgc tccgatagag gtggtccgcg agggtcggca tgtgacgctg 1620

acggtgaaac cggaccccga tagcacc 1647

<210> 64

<211> 131

<212> PRT

<213> Mycobacterium tuberculosis

<400> 64

Val Phe Ala Asn Ile Gly Trp Trp Glu Met Leu Val Leu Val Met Val
1 5 10 15

Gly Leu Val Val Leu Gly Pro Glu Arg Leu Pro Gly Ala Ile Arg Trp
20 25 30

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

Ser Gln Leu Arg Glu Asp Ile Gly Pro Glu Phe Asp Asp Leu Arg Gly
50 55 60

His Leu Gly Glu Leu Gln Lys Leu Arg Gly Met Thr Pro Arg Ala Ala
65 70 75 80

Leu Thr Lys His Leu Leu Asp Gly Asp Asp Ser Leu Phe Thr Gly Asp
85 90 95

Phe Asp Arg Pro Thr Pro Lys Lys Pro Asp Ala Ala Gly Ser Ala Gly
100 105 110

Pro Asp Ala Thr Glu Gln Ile Gly Ala Gly Pro Ile Pro Phe Asp Ser

115 120 125

Asp Ala Thr
130

<210> 65

<211> 393

<212> DNA

<213> Mycobacterium tuberculosis

<400> 65
gtgttcgcca acatcggttg gtgggaaatg ctcgtcctcg tcatggtcgg gctggtggtg 60

cttggcccgg agcggctccc gggtgccatc cgctgggcgg caagcgctct gcggcaggcg 120

cgcgactatc tcagcggtgt gaccagccag ctacgtgagg acattggacc cgaattcgat 180

gatctgcggg gacatctcgg tgagctgcag aagctacggg gaatgactcc gcgggctgcg 240

ttgaccaagc acctactgga tggcgatgat tccctgttca ccggagactt cgaccgaccg 300

acgccgaaga aaccggatgc ggcgggctcg gcggggccgg acgctactga gcagatcggt 360

gcggggccca tcccgtttga cagcgatgcc acc 393

<210> 66

<211> 185

<212> DNA

<213> Mycobacterium tuberculosis

<400> 66
gccagccaca tctatctctt ctcgtgttgc cgcgctaacc gggcggttgt ttgcggcaaa 60

cgcgcgaggt caccgttggg tcacattagt cgcacgtacc gggggcagtt tgtgacttac 120

gtttccatag cgtcagatgt gacgtacggt gcaaatgatg cttgtggtgt cgttggcgtt 180

gacct 185

<210> 67

<211> 472

<212> PRT

<213> Mycobacterium tuberculosis

<400> 67

Met Arg Arg Asn Arg Arg Gly Ser Pro Ala Arg Pro Ala Ala Arg Phe
1 5 10 15

Val Arg Pro Ala Ile Pro Ser Ala Leu Ser Val Ala Leu Leu Val Cys
20 25 30

Thr Pro Gly Leu Ala Thr Ala Asp Pro Gln Thr Asp Thr Ile Ala Ala
35 40 45

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

Asp Glu Val Gln Ala Glu Gln Glu Ser Val Asn Lys Ala Met Val Asp
65 70 75 80

Val Glu Thr Ala Arg Asp Asn Ala Ala Ala Ala Glu Asp Asp Leu Glu
85 90 95

Val Ser Gln Arg Ala Val Lys Asp Ala Asn Ala Ala Ile Ala Ala Ala
100 105 110

Gln His Arg Phe Asp Thr Phe Ala Ala Ala Thr Tyr Met Asn Gly Pro
115 120 125

Ser Val Ser Tyr Leu Ser Ala Ser Ser Pro Asp Glu Ile Ile Ala Thr
130 135 140

Val Thr Ala Ala Lys Thr Leu Ser Ala Ser Ser Gln Ala Val Met Ala
145 150 155 160

Asn Leu Gln Arg Ala Arg Thr Glu Arg Val Asn Thr Glu Ser Ala Ala
165 170 175

Arg Leu Ala Lys Gln Lys Ala Asp Lys Ala Ala Ala Asp Ala Lys Ala
180 185 190

Ser Gln Asp Ala Ala Val Ala Ala Leu Thr Glu Thr Arg Arg Lys Phe
195 200 205

```
Asp Glu Gln Arg Glu Glu Val Gln Arg Leu Ala Ala Glu Arg Asp Ala
    210                 215                 220

Ala Gln Ala Arg Leu Gln Ala Ala Arg Leu Val Ala Trp Ser Ser Glu
225                 230                 235                 240

Gly Gly Gln Gly Ala Pro Pro Phe Arg Met Trp Asp Pro Gly Ser Gly
                245                 250                 255

Pro Ala Gly Gly Arg Ala Trp Asp Gly Leu Trp Asp Pro Thr Leu Pro
            260                 265                 270

Met Ile Pro Ser Ala Asn Ile Pro Gly Asp Pro Ile Ala Val Val Asn
        275                 280                 285

Gln Val Leu Gly Ile Ser Ala Thr Ser Ala Gln Val Thr Ala Asn Met
    290                 295                 300

Gly Arg Lys Phe Leu Glu Gln Leu Gly Ile Leu Gln Pro Thr Asp Thr
305                 310                 315                 320

Gly Ile Thr Asn Ala Pro Ala Gly Ser Ala Gln Gly Arg Ile Pro Arg
                325                 330                 335

Val Tyr Gly Arg Gln Ala Ser Glu Tyr Val Ile Arg Arg Gly Met Ser
            340                 345                 350

Gln Ile Gly Val Pro Tyr Ser Trp Gly Gly Gly Asn Ala Ala Gly Pro
        355                 360                 365

Ser Lys Gly Ile Asp Ser Gly Ala Gly Thr Val Gly Phe Asp Cys Ser
    370                 375                 380

Gly Leu Val Leu Tyr Ser Phe Ala Gly Val Gly Ile Lys Leu Pro His
385                 390                 395                 400

Tyr Ser Gly Ser Gln Tyr Asn Leu Gly Arg Lys Ile Pro Ser Ser Gln
                405                 410                 415

Met Arg Arg Gly Asp Val Ile Phe Tyr Gly Pro Asn Gly Ser Gln His
            420                 425                 430

Val Thr Ile Tyr Leu Gly Asn Gly Gln Met Leu Glu Ala Pro Asp Val
        435                 440                 445
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Gly Leu Lys Val Arg Val Ala Pro Val Arg Thr Ala Gly Met Thr Pro
450 455 460

Tyr Val Val Arg Tyr Ile Glu Tyr
465 470

<210> 68

<211> 1416

<212> DNA

<213> Mycobacterium tuberculosis

<400> 68
atgagacgga atcgccgtgg ctcgccagcg cgaccggccg cacggtttgt ccgtccggca 60

attccgtcgg ctttgagtgt ggccctgctg gtatgcacac cggggctggc taccgccgat 120

ccacagacgg acaccatcgc cgcgctgatt gccgacgtcg ccaaggccaa ccagcgcctg 180

caagacctga gcgacgaggt tcaggccgaa caggaaagcg ttaacaaggc gatggtcgac 240

gtggaaaccg ctcgggacaa cgctgccgcg gccgaagacg acctggaggt cagccagcgc 300

gcggttaagg acgccaacgc ggcgatcgcc gcggctcagc accggttcga caccttcgcg 360

gcggccacct acatgaacgg tccctcggtc agctacctca gcgcgagcag ccccgacgag 420

atcattgcca ctgtgaccgc cgccaagacc cttagcgcca gttcccaagc ggtgatggcc 480

aacctgcagc gggcccggac cgagcgggtg aacacggagt cggcggcgcg gctagccaag 540

cagaaggctg ataaggccgc cgccgacgca aaggccagcc aggatgccgc ggtggcggcg 600

ctcaccgaga cccggcggaa gttcgatgaa cagcgcgagg aggtccaacg cctggccgcc 660

gagcgcgatg cggctcaagc ccgactgcag gcggccaggt tggttgcctg gtcctcggag 720

ggtggtcagg gtgcgccgcc gttccggatg tgggatcccg gatcgggccc tgccggtggg 780

cgtgcatggg atggcttgtg ggaccccacg ctgcccatga tccccagcgc caacatcccc 840

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accgccaata tggggcgcaa gttcctggag cagctgggca tcttgcagcc caccgatacc 960

ggcatcacca acgctccggc gggctcggcc cagggccgga ttccgcgagt ttatgggcgc 1020

caggcttctg aatacgtgat ccgccgcggc atgtcacaga tcggggtgcc ctattcctgg 1080

ggcggcggca atgccgcggg cccgagcaag ggcatcgact ccggggccgg caccgtcggc 1140

ttcgactgct caggcctggt gttgtactcg tttgctgggg tgggcatcaa gctgccgcac 1200

tactcgggtt cgcagtacaa cctgggccgc aagatcccgt cctcgcagat gcgccgcggc 1260

gacgtcatct tctacggccc gaacggtagc cagcacgtga cgatctacct cggcaacggc 1320

cagatgctcg aggcgcccga cgtcggtttg aaggtgcggg ttgcgcccgt gcgcacggct 1380

ggcatgaccc cgtatgtggt ccgatacatc gagtac 1416

<210> 69

<211> 241

<212> PRT

<213> Mycobacterium tuberculosis

<400> 69

Met Arg His Thr Arg Phe His Pro Ile Lys Leu Ala Trp Ile Thr Ala
1 5 10 15

Val Val Ala Gly Leu Met Val Gly Val Ala Thr Pro Ala Asp Ala Glu
20 25 30

Pro Gly Gln Trp Asp Pro Thr Leu Pro Ala Leu Val Ser Ala Gly Ala
35 40 45

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

Gln Ala Thr Gln Thr Thr Leu Asp Leu Gly Arg Gln Phe Leu Gly Gly
65 70 75 80

Leu Gly Ile Asn Leu Gly Gly Pro Ala Ala Ser Ala Pro Ser Ala Ala
85 90 95

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

Glu Tyr Val Ile Arg Arg Ala Gly Ser Gln Met Gly Val Pro Tyr Ser
115 120 125

Trp Gly Gly Gly Ser Leu Gln Gly Pro Ser Lys Gly Val Asp Ser Gly
130 135 140

Ala Asn Thr Val Gly Phe Asp Cys Ser Gly Leu Val Arg Tyr Ala Phe
145 150 155 160

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

Ala Gly Arg His Val Pro Pro Ala Glu Ala Lys Arg Gly Asp Leu Ile
180 185 190

Phe Tyr Gly Pro Gly Gly Gly Gln His Val Thr Leu Tyr Leu Gly Asn
195 200 205

Gly Gln Met Leu Glu Ala Ser Gly Ser Ala Gly Lys Val Thr Val Ser
210 215 220

Pro Val Arg Lys Ala Gly Met Thr Pro Phe Val Thr Arg Ile Ile Glu
225 230 235 240

Tyr

<210> 70

<211> 723

<212> DNA

<213> Mycobacterium tuberculosis

<400> 70
atgcgccaca cgcgttttca cccgatcaaa ctggcctgga tcaccgcggt ggttgccggc 60

ctgatggtcg gtgtggcaac gcccgccgat gccgaacccg gacaatggga tcccacgctg 120

ccggcattgg tcagtgcggg ggcgcccgga gatccgctgg cggtagccaa cgcgtcgttg 180

caggccaccg cccaggccac ccagaccacg ctggatttgg gcaggcagtt cctcggtggg 240

ttgggaatca acctcggcgg ccctgctgcc agcgctccca gcgccgccac aaccggcgcg 300

agccggattc cgcgggccaa cgcccgtcag gccgtcgaat atgtgattcg ccgggccggg 360

tcgcagatgg gggtgcccta ttcgtggggt ggtggctcgc ttcagggccc cagcaagggc 420

gtggactcgg gggccaacac tgtcggcttc gactgctcag gtctggtgcg gtatgccttc 480

gccggggtcg gcgtgctgat cccgcggttc tccggtgatc agtacaacgc cggtcgccac 540

gttccgcccg ctgaggccaa gcgcggcgac ctgatctttt acggcccagg cggcggccag 600

cacgtcaccc tgtatctggg caacggccaa atgctggagg catccggaag cgccggcaaa 660

gtcacggtga gcccggtgcg aaaggccgga atgacgccgt tcgtgactag gatcatcgaa 720

tac 723

<210> 71

<211> 180

<212> DNA

<213> Mycobacterium tuberculosis

<400> 71
ggacacctcg tgattatgcg cctgctgcgg ccagcgcggg aacaccttgg ctggtccact 60

acggccggca cggacggctg cgcggtaggg tacgcggcag caccatatcg ggccgcttca 120

gttgtcgttt cgggagtcgc gcatgtcggg tcggaaattt tcgttcgagg tcaccaagac 180

<210> 72

<211> 154

<212> PRT

<213> Mycobacterium tuberculosis

<400> 72

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

Pro Ala Ala Thr Leu Phe Arg Leu Val Thr Asp Gly Gly Asn Trp Ala
20 25 30

Thr Trp Ala Lys Pro Ile Val Ala Gln Ser Ser Trp Ala Arg Arg Gly
35 40 45

Asp Pro Ala Pro Gly Gly Ile Gly Ala Ile Arg Lys Leu Gly Met Trp
50 55 60

Pro Val Phe Val Gln Glu Glu Thr Val Glu Tyr Glu Gln Asp Arg Arg
65 70 75 80

His Val Tyr Lys Leu Val Gly Ala Arg Thr Pro Val Gln Asp Tyr Phe

85 90 95

Gly Glu Val Val Leu Thr Pro Asn Ala Ser Gly Gly Thr Asp Leu Arg
100 105 110

Trp Ser Gly Ser Phe Thr Glu Lys Val Arg Gly Thr Gly Pro Val Met
115 120 125

Arg Ala Ala Leu Gly Gly Ala Val Arg Phe Phe Ala Gly Gln Leu Val
130 135 140

Lys Ala Ala Glu Arg Glu Ala Val Arg Arg
145 150

<210> 73

<211> 462

<212> DNA

<213> Mycobacterium tuberculosis

<400> 73
atgtcgggtc ggaaattttc gttcgaggtc accaagacca gcagcgcgcc ggctgcaacc 60

ttgtttcggc tcgtgacaga cggtggcaac tgggcgacct gggccaagcc catcgttgct 120

caatcgagtt gggcgcgacg cggtgatccc gcgcccggcg gcatcggggc catccgcaaa 180

ctaggcatgt ggccggtgtt cgtgcaggaa gagaccgtcg agtatgagca ggaccgtcgc 240

cacgtctaca agctggttgg cgcgaggaca cccgtccagg actacttcgg cgaggtggtc 300

cttacaccaa atgcgtcggg cggtaccgat ctccgctgga gtggctcgtt taccgaaaag 360

gttcgtggga cggggccggt gatgcgggcg gcgctgggtg gcgcggtcag gttcttcgcg 420

ggtcaactgg tgaaggcggc cgagcgggag gcggtgcgcc gg 462

<210> 74

<211> 140

<212> DNA

<213> Mycobacterium tuberculosis

<400> 74

cacggacctc gattctaagc tcgcggcgaa acggcggcgg atgcacaagt gggtaaaatt 60

gagcggaaca gactcaacat tgacggcgtt gaacaacccg acaagcattt cgaacggacc 120

ccgaatggag gtgtcgtgga 140

<210> 75

<211> 848

<212> PRT

<213> Mycobacterium tuberculosis

<400> 75

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

Ala Leu Gln Ala Ala Ser Thr Ala Gly Asn Pro Glu Ile Arg Pro Ala
20 25 30

His Leu Leu Met Ala Leu Leu Thr Gln Asn Asp Gly Ile Ala Ala Pro
35 40 45

Leu Leu Glu Ala Val Gly Val Glu Pro Ala Thr Val Arg Ala Glu Thr
50 55 60

Gln Arg Leu Leu Asp Arg Leu Pro Gln Ala Thr Gly Ala Ser Thr Gln
65 70 75 80

Pro Gln Leu Ser Arg Glu Ser Leu Ala Ala Ile Thr Thr Ala Gln Gln
85 90 95

Leu Ala Thr Glu Leu Asp Asp Glu Tyr Val Ser Thr Glu His Val Met
100 105 110

Val Gly Leu Ala Thr Gly Asp Ser Asp Val Ala Lys Leu Leu Thr Gly
115 120 125

His Gly Ala Ser Pro Gln Ala Leu Arg Glu Ala Phe Val Lys Val Arg
130 135 140

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

```
Leu Gln Lys Tyr Ser Thr Asp Leu Thr Ala Arg Ala Arg Glu Gly Lys
                165                 170                 175

Leu Asp Pro Val Ile Gly Arg Asp Asn Glu Ile Arg Arg Val Val Gln
            180                 185                 190

Val Leu Ser Arg Arg Thr Lys Asn Asn Pro Val Leu Ile Gly Glu Pro
        195                 200                 205

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

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

Asp Leu Gly Ser Met Val Ala Gly Ser Lys Tyr Arg Gly Glu Phe Glu
                245                 250                 255

Glu Arg Leu Lys Ala Val Leu Asp Asp Ile Lys Asn Ser Ala Gly Gln
            260                 265                 270

Ile Ile Thr Phe Ile Asp Glu Leu His Thr Ile Val Gly Ala Gly Ala
        275                 280                 285

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

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

Arg Lys His Ile Glu Lys Asp Ala Ala Leu Glu Arg Arg Phe Gln Gln
                325                 330                 335

Val Tyr Val Gly Glu Pro Ser Val Glu Asp Thr Ile Gly Ile Leu Arg
            340                 345                 350

Gly Leu Lys Asp Arg Tyr Glu Val His His Gly Val Arg Ile Thr Asp
        355                 360                 365

Ser Ala Leu Val Ala Ala Ala Thr Leu Ser Asp Arg Tyr Ile Thr Ala
    370                 375                 380

Arg Phe Leu Pro Asp Lys Ala Ile Asp Leu Val Asp Glu Ala Ala Ser
385                 390                 395                 400
```

Arg Leu Arg Met Glu Ile Asp Ser Arg Pro Val Glu Ile Asp Glu Val
405 410 415

Glu Arg Leu Val Arg Arg Leu Glu Ile Glu Glu Met Ala Leu Ser Lys
420 425 430

Glu Glu Asp Glu Ala Ser Ala Glu Arg Leu Ala Lys Leu Arg Ser Glu
435 440 445

Leu Ala Asp Gln Lys Glu Lys Leu Ala Glu Leu Thr Thr Arg Trp Gln
450 455 460

Asn Glu Lys Asn Ala Ile Glu Ile Val Arg Asp Leu Lys Glu Gln Leu
465 470 475 480

Glu Ala Leu Arg Gly Glu Ser Glu Arg Ala Glu Arg Asp Gly Asp Leu
485 490 495

Ala Lys Ala Ala Glu Leu Arg Tyr Gly Arg Ile Pro Glu Val Glu Lys
500 505 510

Lys Leu Asp Ala Ala Leu Pro Gln Ala Gln Ala Arg Glu Gln Val Met
515 520 525

Leu Lys Glu Glu Val Gly Pro Asp Asp Ile Ala Asp Val Val Ser Ala
530 535 540

Trp Thr Gly Ile Pro Ala Gly Arg Leu Leu Glu Gly Glu Thr Ala Lys
545 550 555 560

Leu Leu Arg Met Glu Asp Glu Leu Gly Lys Arg Val Ile Gly Gln Lys
565 570 575

Ala Ala Val Thr Ala Val Ser Asp Ala Val Arg Arg Ser Arg Ala Gly
580 585 590

Val Ser Asp Pro Asn Arg Pro Thr Gly Ala Phe Met Phe Leu Gly Pro
595 600 605

Thr Gly Val Gly Lys Thr Glu Leu Ala Lys Ala Leu Ala Asp Phe Leu
610 615 620

Phe Asp Asp Glu Arg Ala Met Val Arg Ile Asp Met Ser Glu Tyr Gly

625 630 635 640

Glu Lys His Thr Val Ala Arg Leu Ile Gly Ala Pro Pro Gly Tyr Val
645 650 655

Gly Tyr Glu Ala Gly Gly Gln Leu Thr Glu Ala Val Arg Arg Arg Pro
660 665 670

Tyr Thr Val Val Leu Phe Asp Glu Ile Glu Lys Ala His Pro Asp Val
675 680 685

Phe Asp Val Leu Leu Gln Val Leu Asp Glu Gly Arg Leu Thr Asp Gly
690 695 700

His Gly Arg Thr Val Asp Phe Arg Asn Thr Ile Leu Ile Leu Thr Ser
705 710 715 720

Asn Leu Gly Ser Gly Gly Ser Ala Glu Gln Val Leu Ala Ala Val Arg
725 730 735

Ala Thr Phe Lys Pro Glu Phe Ile Asn Arg Leu Asp Asp Val Leu Ile
740 745 750

Phe Glu Gly Leu Asn Pro Glu Glu Leu Val Arg Ile Val Asp Ile Gln
755 760 765

Leu Ala Gln Leu Gly Lys Arg Leu Ala Gln Arg Arg Leu Gln Leu Gln
770 775 780

Val Ser Leu Pro Ala Lys Arg Trp Leu Ala Gln Arg Gly Phe Asp Pro
785 790 795 800

Val Tyr Gly Ala Arg Pro Leu Arg Arg Leu Val Gln Gln Ala Ile Gly
805 810 815

Asp Gln Leu Ala Lys Met Leu Leu Ala Gly Gln Val His Asp Gly Asp
820 825 830

Thr Val Pro Val Asn Val Ser Pro Asp Ala Asp Ser Leu Ile Leu Gly
835 840 845

<210> 76

<211> 2544

<212> DNA

<213> Mycobacterium tuberculosis

<400> 76

gtggactcgt ttaacccgac gaccaagacg caggcggcgc taaccgcggc gttacaggcg 60

gcttcgaccg ccggcaatcc cgagatccgg cccgctcacc tgctgatggc gctgctgacc 120

caaaacgacg gtatcgccgc accgctactg gaggctgtcg gtgtcgagcc cgccaccgtc 180

cgcgccgaaa cccagcgcct gctcgaccgt ttgccgcagg cgactggagc cagcacgcag 240

ccgcagctgt cccgcgagtc gttagcggcg atcaccaccg cgcagcagct ggccaccgag 300

ctggacgacg agtacgtctc caccgagcac gtgatggtcg ggctggccac cggtgactcc 360

gacgtcgcca agctgttgac cggccacggc gcctcgccgc aggcgctgcg ggaggcgttc 420

gtcaaggtgc gcggcagcgc ccgggtcacc agccccgaac cggaggcgac ctatcaggcg 480

ctgcagaagt actccaccga cctgaccgcc cgcgcccgcg aaggcaaact cgacccggtc 540

atcggccgcg acaacgagat ccgccgcgtg gtgcaggtgc tgtcccgtcg caccaagaac 600

aacccggtgc tgatcggtga gcccggcgtc ggcaagaccg cgatcgtgga gggcctggcg 660

cagcgcatcg tggccggcga cgtgccggag agcttgcgcg acaagaccat cgtcgcgctc 720

gatctcggct cgatggtcgc cggctccaaa taccgcggcg aattcgagga acggctcaag 780

gccgtcctcg acgacatcaa gaactcggcc ggccaaatca tcacgttcat cgacgagctg 840

cacaccatcg tcggcgccgg cgccaccggc gaggggggcga tggacgccgg caacatgatc 900

aagccgatgc tggcccgcgg cgagttacgg ctggtcgggg cgaccacgct ggacgaatac 960

cgcaagcaca tcgagaagga cgccgcgctc gagcgccgtt tccaacaggt gtacgtcggc 1020

gagccgtcgg tggaggacac catcggcatc ctgcgcgggc tcaaagaccg ctacgaggtg 1080

caccacgggg tgcgcatcac cgactcggcg ctggtggcag ctgccacttt gagcgaccgg 1140

tatatcaccg cccgcttcct gcccgacaag gccatcgacc tggtcgacga ggcggccagc 1200

cggctgcgga tggagatcga ctcgcggccc gtcgagatcg acgaggtcga gcggctggtg 1260

cgccggctgg agatcgaaga gatggcgctg tccaaagaag aagacgaggc gtcggcggag 1320

cggttggcca agctgcgctc cgagctggcc gaccagaaag agaagttggc cgagctcacc 1380

acccgctggc agaacgagaa gaacgcgatc gaaatcgtcc gcgacctcaa ggagcagctg 1440

gaagccctgc gcggggaatc cgagcgggcc gaacgcgacg gcgacctggc caaggccgcc 1500

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gcgcaggccc gggagcaggt gatgctcaag gaggaggtcg gtcccgacga catcgccgac 1620

gtggtgtcgg cgtggaccgg catcccggcc ggtcggctgc tggaaggcga gaccgccaag 1680

ctgctgcgca tggaagacga gctgggcaag cgggtcatcg ggcagaaggc cgcggttacc 1740

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gccgacttcc tgttcgacga cgagcgggcg atggtccgca tcgacatgag cgagtacggc 1920

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ctcaccgacg ggcacggccg cacggtcgac ttccgcaaca ccatcttgat cctgacgtcc 2160

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ccggagttca tcaaccggct cgacgacgtg ctcatctttg agggtctcaa ccccgaagag 2280

ctggtgcgca tcgtcgacat ccagctggcg cagctgggca agcggctggc gcagcggcgg 2340

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gtgtacgggg cgcggccgtt gcgccggctg gtgcagcagg ccatcggtga ccagctggcc 2460

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gacgccgact cgctgatcct gggc 2544

<210> 77

<211> 182

<212> DNA

<213> Mycobacterium tuberculosis

<400> 77

gtcctggcac gccacgacgg cggccgcctg ggtgggttca accgggtcag gtcgatacgt 60

cgcgaagctc acctcggcga acgtcggagg cggccgcagt tgggcgatca gccgcaccgg 120

agacacggtc ggatgcctgt ccaccaggtg gtccaccgaa ccgcaagctt cggaggcaga 180

cc 182

<210> 78

<211> 258

<212> PRT

<213> Mycobacterium tuberculosis

<400> 78

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

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

Asp Tyr Pro Asp Asp Gly Thr Trp Leu Arg Ala Asn Phe Ile Ser Ser
        35                  40                  45

Leu Asp Gly Gly Ala Thr Val Asp Gly Thr Ser Gly Ala Met Ala Gly
    50                  55                  60

Pro Gly Asp Arg Phe Val Phe Asn Leu Leu Arg Glu Leu Ala Asp Val
65                  70                  75                  80

Ile Val Val Gly Val Gly Thr Val Arg Ile Glu Gly Tyr Ser Gly Val
                85                  90                  95

Arg Met Gly Val Val Gln Arg Gln His Arg Gln Ala Arg Gly Gln Ser
            100                 105                 110

Glu Val Pro Gln Leu Ala Ile Val Thr Arg Ser Gly Arg Leu Asp Arg
        115                 120                 125

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

Thr Thr Ala Val Ala Asp Asp Thr Arg Gln Arg Leu Ala Gly Leu Ala
145                 150                 155                 160

Glu Val Ile Ala Cys Ser Gly Asp Asp Pro Gly Thr Val Asp Glu Ala
                165                 170                 175

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

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

Arg Arg Ile Val Thr Gly Pro Gly Gln Val Leu Thr Arg Met Arg Cys
225 230 235 240

Ala His Val Leu Thr Asp Asp Ser Gly Tyr Leu Tyr Thr Arg Tyr Val
245 250 255

Lys Thr

<210> 79

<211> 774

<212> DNA

<213> Mycobacterium tuberculosis

<400> 79
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cattacctca ccgacggcga actcccccag ctttacgact atccggatga cggcacctgg 120

ttgcgggcga acttcatcag cagcttggac ggcggcgcta ccgtcgatgg caccagcggg 180

gcgatggccg ggcccggcga ccgattcgtc ttcaacctgt tgcgtgaact tgccgacgtc 240

atcgtggtcg gcgtgggcac cgtgcgcatt gagggctact ccggcgtccg gatgggtgtc 300

gtccagcgcc agcaccggca ggcccgaggc caaagcgaag ttccgcaact ggcaatcgtc 360

accaggtccg gtcgccttga ccgtgacatg gcggtattca cccggaccga gatggcaccg 420

ttggtgctca ccaccacggc ggtcgccgat gacacgcgcc agcggctcgc gggcctcgcc 480

gaggtgatcg cgtgctccgg cgacgatccg ggcacggtcg atgaggcagt gctcgtgtcc 540

cagctcgcgg ctcgcggtct gcgccggatc cttaccgaag gcgggccgac gttgctcggg 600

acattcgtcg agcgtgacgt gctcgacgag ctgtgtctga cgatcgcccc ctacgtcgtc 660

ggcggcctgg cgcgccgcat agtgacggga cccgggcagg tgctgacccg gatgcgctgt 720

gcccatgtcc tcaccgacga ctccggctac ctgtacaccc gctacgtcaa gacc 774

<210> 80

<211> 528

<212> PRT

<213> Mycobacterium tuberculosis

<400> 80

Met Ala Thr Val Val Gly Met Ser Arg Pro Met Thr Ser Thr Ala Met
1 5 10 15

Leu Val Ala Leu Thr Cys Ser Ala Thr Val Leu Ala Ala Cys Val Pro
20 25 30

Ala Phe Gly Ala Asp Pro Arg Phe Ala Thr Tyr Ser Gly Ala Gly Pro
35 40 45

Gln Gly Ala Ala Thr Thr Thr Pro Pro Pro Ala Gly Pro Pro Pro Leu
50 55 60

Ala Ala Pro Lys Asn Asp Leu Ser Trp His Asp Cys Thr Ser Arg Val
65 70 75 80

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

Ala Ser Tyr Asp Thr Asp Leu Asp Pro Leu Val Gly Gly Ser Thr Ala
100 105 110

Val Ser Ile Gly Val Val Arg Ala Arg Ser Asn Gln Thr Pro Ser Asp
115 120 125

Ala Gly Pro Leu Val Phe Thr Thr Gly Ser Asp Leu Pro Ser Ser Thr
130 135 140

Gln Leu Pro Val Trp Leu Ala His Ala Gly Ile Asp Val Leu Arg Ser
145 150 155 160

His Pro Ile Val Ala Val Asp Arg Arg Gly Met Gly Met Ser Ser Pro
165 170 175

Ile Asp Cys Arg Asp His Phe Asp Arg Asp Glu Met Arg Asp Gln Ala
180 185 190

Gln Phe Gln Ala Gly Asp Asp Pro Val Ala Asn Leu Ser Asp Ile Ser
195 200 205

```
Asn Thr Ala Thr Thr Asp Cys Thr Asp Ala Ile Ala Pro Gly Glu Ser
    210                 215                 220

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

Leu Trp Asp Val Pro Ala Leu Ala Phe Val Gly Ile Gly Asn Gly Thr
                245                 250                 255

Gln Val Ala Leu Ala Tyr Ala Ala Ser Arg Pro Asp Asn Val Ala Arg
            260                 265                 270

Leu Ile Leu Asp Ser Pro Ile Ala Leu Gly Val Ser Ala Glu Ala Ala
        275                 280                 285

Ala Glu Gln Gln Val Gln Gly Gln Gln Ala Ala Leu Asp Ala Phe Ala
    290                 295                 300

Ala Gln Cys Val Ala Val Asn Cys Ala Leu Gly Ser His Pro Lys Gly
305                 310                 315                 320

Ala Val Ser Ala Leu Leu Ser Ala Ala Arg Ser Gly Asp Gly Pro Gly
                325                 330                 335

Gly Ala Ser Val Ala Ala Val Ala Asn Ala Val Ala Thr Ala Leu Gly
            340                 345                 350

Phe Pro Asp Ser Gly Arg Val Asp Ser Thr Thr Lys Leu Ala Asp Ala
        355                 360                 365

Leu Ala Ala Ala Arg Ser Gly Asp Met Asn Leu Leu Ser Ala Leu Ile
    370                 375                 380

Asn Arg Ala Asp Thr Thr Arg Asp Thr Asp Gly Gln Phe Ile Ser Ser
385                 390                 395                 400

Cys Ser Asp Ala Val Asn Arg Pro Thr Pro Asp Arg Val Arg Glu Leu
                405                 410                 415

Val Val Ala Trp Gly Lys Leu Tyr Pro Gln Phe Gly Ala Val Ala Ala
            420                 425                 430

Leu Asn Leu Val Lys Cys Val His Trp Pro Ser Ser Ser Pro Pro Gln
```

435 440 445

Pro Pro Lys Asp Leu Lys Val Asp Val Leu Leu Leu Gly Val Gln Asn
450 455 460

Asp Pro Ile Val Gly Asn Glu Gly Val Ala Ala Thr Ala Ala Thr Ala
465 470 475 480

Ile Asn Ala Asn Ala Ala Ser Lys Arg Val Met Trp Gln Gly Ile Gly
485 490 495

His Gly Ala Ser Ile Tyr Ser Ser Cys Ala Val Pro Pro Leu Val Ala
500 505 510

Tyr Leu Asp Thr Gly Lys Leu Pro Asp Thr Asp Thr Tyr Cys Pro Ala
515 520 525

<210> 81

<211> 1584

<212> DNA

<213> Mycobacterium tuberculosis

<400> 81
atggctactg tggtcggcat gagtcggccc atgacgtcaa ccgcgatgtt ggtcgcgctg 60

acctgctcgg cgacagtgct ggccgcatgc gtcccggcgt tcggcgccga cccgcggttc 120

gcgacctact cgggcgcagg accgcaaggc gcagccacca cgacaccacc gccggctggc 180

ccaccaccgc tcgccgcacc caagaacgac ttgtcgtggc acgactgcac gtcacgggtg 240

tactcgaatg ctgggatccc agcagcgccc ggcgtcaagc tggaatgcgc aagctatgac 300

accgacctcg acccgctcgt cggcgggtcc acagcggtaa gcatcggcgt agtgcgcgcg 360

cgctccaacc agaccccgag cgacgcagga cccctggtgt tcaccaccgg ctccgaccta 420

ccctcgtcga cgcagttgcc ggtctggctg gcacacgcgg gcatcgatgt gctccgcagc 480

caccccattg tcgccgtcga ccgccgcggc atgggcatgt cgagcccaat cgactgccgc 540

gatcactttg accgcgacga gatgcgtgat caggcgcaat tccaggctgg cgacgatccg 600

gtggccaacc tttccgacat ctccaacacc gccaccaccg actgcaccga cgccatcgcg 660

ccaggcgagt ccgcctacga caacacccac gccgcctcgg atatcgagcg cttacgcaaa 720

ctctgggacg tccctgccct cgccttcgtc ggcattggca acggcaccca agtggcgctg 780

gcctacgcag catcgcgtcc cgacaacgtc gccagactga tcctcgactc cccaatcgcg 840

ttgggggtct ctgccgaagc cgccgccgag caacaggtcc agggccaaca ggcggcgctg 900

gacgcattcg ctgcgcaatg tgtcgcggtg aactgcgcgc tgggctccca tccgaaaggc 960

gcggtcagcg cgctgctgtc ggccgcccgg tccggtgatg ggcccggcgg cgcgtcggtg 1020

gcggctgtcg ccaacgccgt cgccaccgcg ttgggcttcc ccgacagtgg ccgggtcgat 1080

agcaccacga aattggccga cgcgctggcc gcggcccgct ccggggacat gaacttgctg 1140

tccgccctga tcaaccgcgc cgataccacc cgggatacgg acggtcagtt catcagctcg 1200

tgcagcgatg cggtcaaccg cccgacaccg gaccgggtgc gcgagctggt ggtggcttgg 1260

gggaagctct acccgcagtt cggcgccgtc gcggcgctca acctggtgaa atgcgtgcac 1320

tggcccagca gttcgccgcc gcagccaccg aaagacctca aggtcgacgt gctgttgctc 1380

ggtgtgcaaa acgacccgat cgtgggcaac gaaggggtcg ccgcgaccgc cgccacggcc 1440

atcaacgcca acgccgccag caagcgggtg atgtggcaag gtattggcca cggcgccagc 1500

atctactcgt cctgcgcggt gccgccactc gtcgcctacc tggacactgg caagctgcct 1560

gacaccgaca cctattgccc cgcc 1584

<210> 82

<211> 433

<212> PRT

<213> Mycobacterium tuberculosis

<400> 82

Val Tyr Gly Ala Leu Val Thr Ala Ala Asp Ser Ile Arg Thr Gly Leu
1 5 10 15

Gly Ala Ser Leu Leu Ala Gly Phe Arg Pro Arg Thr Gly Ala Pro Ser
20 25 30

Thr Ala Thr Ile Leu Arg Ser Ala Leu Trp Pro Ala Ala Val Leu Ser
35 40 45

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

Asp Phe Lys Pro Val Tyr Arg Ala Val Leu Asn Phe Arg Arg Gly Trp
65 70 75 80

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

Pro Pro Gly Gly Thr Leu Leu Met Ala Pro Phe Gly Tyr Leu Pro Phe
100 105 110

Ala Pro Ser Arg Tyr Leu Phe Ile Ser Ile Asn Thr Ala Ala Ile Leu
115 120 125

Val Ala Ala Tyr Leu Leu Leu Arg Met Phe Asn Phe Thr Leu Thr Ser
130 135 140

Val Ala Ala Pro Ala Leu Ile Leu Ala Met Phe Ala Thr Glu Thr Val
145 150 155 160

Thr Asn Thr Leu Val Phe Thr Asn Ile Asn Gly Cys Ile Leu Leu Leu
165 170 175

Glu Val Leu Phe Leu Arg Trp Leu Leu Asp Gly Arg Ala Ser Arg Gln
180 185 190

Trp Cys Gly Gly Leu Ala Ile Gly Leu Thr Leu Val Leu Lys Pro Leu
195 200 205

Leu Gly Pro Leu Leu Leu Leu Pro Leu Leu Asn Arg Gln Trp Arg Ala
210 215 220

Leu Val Ala Ala Val Val Val Pro Val Val Val Asn Val Ala Ala Leu
225 230 235 240

Pro Leu Val Ser Asp Pro Met Ser Phe Phe Thr Arg Thr Leu Pro Tyr
245 250 255

Ile Leu Gly Thr Arg Asp Tyr Phe Asn Ser Ser Ile Leu Gly Asn Gly
260 265 270

Val Tyr Phe Gly Leu Pro Thr Trp Leu Ile Leu Phe Leu Arg Ile Leu
275 280 285

Phe Thr Ala Ile Thr Phe Gly Ala Leu Trp Leu Leu Tyr Arg Tyr Tyr
290 295 300

Arg Thr Gly Asp Pro Leu Phe Trp Phe Thr Thr Ser Ser Gly Val Leu
305 310 315 320

Leu Leu Trp Ser Trp Leu Val Met Ser Leu Ala Gln Gly Tyr Tyr Ser
325 330 335

Met Met Leu Phe Pro Phe Leu Met Thr Val Val Leu Pro Asn Ser Val
340 345 350

Ile Arg Asn Trp Pro Ala Trp Leu Gly Val Tyr Gly Phe Met Thr Leu
355 360 365

Asp Arg Trp Leu Leu Phe Asn Trp Met Arg Trp Gly Arg Ala Leu Glu
370 375 380

Tyr Leu Lys Ile Thr Tyr Gly Trp Ser Leu Leu Leu Ile Val Thr Phe
385 390 395 400

Thr Val Leu Tyr Phe Arg Tyr Leu Asp Ala Lys Ala Asp Asn Arg Leu
405 410 415

Asp Gly Gly Ile Asp Pro Ala Trp Leu Thr Pro Glu Arg Glu Gly Gln
420 425 430

Arg

<210> 83

<211> 1299

<212> DNA

<213> Mycobacterium tuberculosis

<400> 83
gtgtacggtg cgctggtgac ggcagctgac tccatccgaa ccggcctagg cgcatccttg 60

ttggccggat tccgtccgcg caccggcgcc ccgagcaccg cgacgatcct gcggtcggcg 120

ctctggccgg ccgccgtcct gtcggtgctg caccgcagca tcgtattgac gaccaacggc 180

aacatcaccg acgatttcaa gccggtctac cgcgcggtgc tgaacttccg gcgcggatgg 240

gacatctata acgagcactt cgactacgtc gacccgcact acctgtatcc ccccggtggc 300

accctgctga tggcgccgtt cggctacctg cccttcgccc cgtcgcgcta tctgtttatc 360

tcgatcaaca ccgcggccat cctggtcgcc gcctacctgc tgctgcggat gttcaacttc 420

acgctgacct cggtggccgc acccgccctg attctggcca tgtttgctac cgagaccgtg 480

accaacacgc tggtgttcac caacatcaac ggctgcatcc tgctgttgga ggtgctcttt 540

ctgagatggc tgttggacgg ccgagccagt cgtcagtggt gcggcggcct ggcgatcggg 600

ctgaccctgg ttctcaaacc cctgctcggt ccgctgttgt tgctgccgct gctgaaccgc 660

cagtggcggg ctctggtggc cgccgtcgtc gttcccgtcg tcgtcaacgt ggccgcgctg 720

ccgctggtca gtgacccgat gagcttcttc acccgcacgc tgccctacat cttgggcacc 780

cgggactact tcaacagctc gatcttgggc aacggcgtct acttcgggct gcccacctgg 840

ctgatcctgt tcctgcggat cctgttcacc gcgatcacct tcggcgcatt gtggctgttg 900

taccgctact accgcaccgg tgacccgctg ttttggttca ccacctcgtc gggtgtgctg 960

ctgctgtggt cgtggctggt gatgtcgctg gcccagggct actactcgat gatgctgttc 1020

ccgttcctga tgaccgttgt gctgcccaac tcggtgatcc gcaactggcc ggcgtggctg 1080

ggagtctacg gcttcatgac gttggatcgc tggctgctgt tcaactggat gagatggggc 1140

cgcgcgctgg aatacctcaa gatcacctac ggttggtcgt tgctgttgat cgtgacgttt 1200

accgtgctct atttccgcta tctggacgcc aaggcggaca accggctgga cggcggtatc 1260

gatccagcct ggctgacgcc cgagcgggag ggccagcgg 1299

<210> 84

<211> 314

<212> DNA

<213> Mycobacterium tuberculosis

<400> 84

tctccttgtc aggcttgacg ggtcgcaccc gcgaacaccc ctctgtgata gcacgagtta 60

tcaggaggtt cggcggggcg ttacctttgc ggttgtgcac ttcgactggg agcgcctgac 120

cgacagcgtg catcgctgcc ggctgccgtt ctgtgacgtc accgttgggc tggtccgggg 180

ccgcaccgga atactgctcg tcgacaccgg gaccaccctc ggcgaagcaa cagcaatcgc 240

ggccgacgtc aagcagatcg ctggttgcca ggtaacgcat gttgtgttga cacacaagca 300

tttcgaccat gtgc 314

<210> 85

<211> 197

<212> PRT

<213> Mycobacterium tuberculosis

<400> 85

Val Ala His Ala Phe His Arg Phe Ala Leu Ala Ile Leu Gly Leu Ala
1 5 10 15

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

Ala Ala Pro Leu Ala Pro Lys Ala Ala Ala Leu Gly Arg Ser Met Pro
35 40 45

Glu Thr Pro Thr Gly Asp Val Leu Thr Ile Ser Ser Pro Ala Phe Ala
50 55 60

Asp Gly Ala Pro Ile Pro Glu Gln Tyr Thr Cys Lys Gly Ala Asn Ile
65 70 75 80

Ala Pro Pro Leu Thr Trp Ser Ala Pro Phe Gly Gly Ala Leu Val Val
85 90 95

Asp Asp Pro Asp Ala Pro Arg Glu Pro Tyr Val His Trp Ile Val Ile
100 105 110

Gly Ile Ala Pro Gly Ala Gly Ser Thr Ala Asp Gly Glu Thr Pro Gly
115 120 125

Gly Gly Ile Ser Leu Pro Asn Ser Ser Gly Gln Pro Ala Tyr Thr Gly
130 135 140

Pro Cys Pro Pro Ala Gly Thr Gly Thr His His Tyr Arg Phe Thr Leu
145 150 155 160

Tyr His Leu Pro Ala Val Pro Pro Leu Ala Gly Leu Ala Gly Thr Gln
165 170 175

Ala Ala Arg Val Ile Ala Gln Ala Ala Thr Met Gln Ala Arg Leu Ile
180 185 190

Gly Thr Tyr Glu Gly
195

<210> 86

<211> 591

<212> DNA

<213> Mycobacterium tuberculosis

<400> 86
gtggcgcacg catttcaccg gttcgcactg gccatcttgg ggctggcgct ccccgtggcg 60

ctagttgcct acggtggcaa cggtgacagt cgaaaggcgg cgccgctggc gccgaaagca 120

gcagcgctcg gtcggagtat gcccgaaacg cctaccggcg atgtactgac aatcagcagt 180

ccggcattcg ccgacggtgc gccgatcccg gaacagtaca cctgcaaagg agccaatatc 240

gcgcctccgt tgacctggtc ggcgccgttt ggcggcgcac tcgttgtcga tgatccggac 300

gcacctcgcg aaccttacgt ccattggatc gtgatcggga tcgcccctgg tgctggcagc 360

accgccgatg gtgagactcc cggtggcgga atcagcctgc cgaactccag cggtcagccc 420

gcatacaccg gcccctgccc gccggcgggc accgggacac accactaccg gtttaccctc 480

taccaccttc ctgccgtgcc tccactcgcg ggactggctg ggacacaagc ggcgcgggtg 540

atcgcgcagg ccgccaccat gcaggcccgg ctcatcggaa catacgaagg c 591

<210> 87

<211> 201

<212> PRT

<213> Mycobacterium tuberculosis

<400> 87

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

Leu Val Val Ala Leu Gly Gly Cys Gly Gly Gly Gly Gly Asp Ser Arg
20 25 30

Glu Thr Pro Pro Tyr Val Pro Lys Ala Thr Thr Val Asp Ala Thr Thr

35 40 45

Pro Ala Pro Ala Ala Glu Pro Leu Thr Ile Ala Ser Pro Met Phe Ala
50 55 60

Asp Gly Ala Pro Ile Pro Val Gln Phe Ser Cys Lys Gly Ala Asn Val
65 70 75 80

Ala Pro Pro Leu Thr Trp Ser Ser Pro Ala Gly Ala Ala Glu Leu Ala
85 90 95

Leu Val Val Asp Asp Pro Asp Ala Val Gly Gly Leu Tyr Val His Trp
100 105 110

Ile Val Thr Gly Ile Ala Pro Gly Ser Gly Ser Thr Ala Asp Gly Gln
115 120 125

Thr Pro Ala Gly Gly His Ser Val Pro Asn Ser Gly Gly Arg Gln Gly
130 135 140

Tyr Phe Gly Pro Cys Pro Pro Ala Gly Thr Gly Thr His His Tyr Arg
145 150 155 160

Phe Thr Leu Tyr His Leu Pro Val Ala Leu Gln Leu Pro Pro Gly Ala
165 170 175

Thr Gly Val Gln Ala Ala Gln Ala Ile Ala Gln Ala Ala Ser Gly Gln
180 185 190

Ala Arg Leu Val Gly Thr Phe Glu Gly
195 200

<210> 88

<211> 603

<212> DNA

<213> Mycobacterium tuberculosis

<400> 88
atgacgagca cacttcaccg aaccccatta gccaccgcgg ggctggcgct cgtagtggcg 60

ctgggtggct gcgggggcgg gggcggtgac agtcgagaga caccgccata cgtgccgaaa 120

gcgacgaccg tcgacgcaac aacgccggcg ccggccgccg agccactgac gatcgccagt 180

cccatgttcg ccgacggcgc cccgatcccg gtgcaattca gctgcaaggg ggccaacgtg 240

gcgccaccgt tgacgtggtc gtcgcccgcg ggcgcagccg aactggcact cgtcgtcgat 300

gaccccgacg cggtcggcgg actgtacgtg cactggatcg tgaccggaat cgcccctggc 360

tctggcagca cggcggatgg tcagactcct gctggtgggc acagcgtgcc gaattctggt 420

ggtcggcaag gatacttcgg tccatgcccg ccggcgggca ccgggacaca ccactaccgg 480

tttaccctct accaccttcc tgtcgcgctc cagctgccac cgggagccac gggagtccaa 540

gcggcacagg cgatagcaca ggccgccagc ggacaggccc ggctcgtcgg cacattcgaa 600

ggc 603

<210> 89

<211> 334

<212> PRT

<213> Mycobacterium tuberculosis

<400> 89

Met Arg Ala Val Val Ile Thr Lys His Gly Asp Pro Ser Val Leu Gln
1 5 10 15

Val Arg Gln Arg Pro Asp Pro Pro Pro Pro Gly Pro Gly Gln Leu Arg
20 25 30

Val Ala Val Arg Ala Ala Gly Val Asn Phe Ala Asp His Leu Ala Arg
35 40 45

Val Gly Leu Tyr Pro Asp Ala Pro Lys Leu Pro Ala Val Val Gly Tyr
50 55 60

Glu Val Ala Gly Thr Val Glu Ala Val Gly Asp Gly Val Asp Pro Asn
65 70 75 80

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

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

```
Leu Ser Phe Glu Gln Gly Ala Ala Val Pro Val Asn Tyr Ala Thr Ala
        115                 120                 125

Trp Ala Ala Leu His Gly Tyr Gly Ser Leu Arg Ala Gly Glu Arg Val
    130                 135                 140

Leu Ile His Ala Ala Ala Gly Gly Val Gly Ile Ala Ala Val Gln Phe
145                 150                 155                 160

Ala Lys Ala Ala Lys Ala Glu Val His Gly Thr Ala Ser Pro Gln Lys
                165                 170                 175

His Gln Lys Leu Ala Glu Phe Gly Val Asp Arg Ala Ile Asp Tyr Arg
            180                 185                 190

Arg Asp Gly Trp Trp Gln Gly Leu Gly Pro Tyr Asp Val Val Leu Asp
        195                 200                 205

Ala Leu Gly Gly Thr Ser Leu Arg Arg Ser Tyr Thr Leu Leu Arg Pro
    210                 215                 220

Gly Gly Arg Leu Val Gly Tyr Gly Ile Ser Asn Met Gln His Gly Glu
225                 230                 235                 240

Lys Arg Ser Met Arg Arg Val Ala Pro His Ala Leu Ser Met Leu Arg
                245                 250                 255

Gly Phe Asn Leu Met Lys Gln Leu Glu Glu Ser Lys Thr Val Ile Gly
            260                 265                 270

Leu Asn Met Leu Arg Leu Trp Asp Asp Arg Arg Thr Leu Glu Pro Trp
        275                 280                 285

Ile Ala Pro Leu Thr Lys Ala Leu Asn Asp Gly Thr Ile Leu Pro Ile
    290                 295                 300

Val His Ala Ile Val Pro Phe Ala Glu Ala Pro Glu Ala His Arg Ile
305                 310                 315                 320

Leu Ala Ala Arg Glu Asn Val Asp Lys Val Val Leu Val Pro
                325                 330
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<210> 90

<211> 1002

<212> DNA

<213> Mycobacterium tuberculosis

<400> 90
atgcgagcag tggtcatcac caaacatggc gacccatcgg tcttgcaggt gcggcagcga 60

ccggacccgc cgccaccggg cccgggccag ctgcgggtcg ccgtccgcgc agcaggggtg 120

aacttcgctg accatctcgc ccgcgtcggc ctgtacccag acgcgccgaa acttccggcg 180

gtggtcggat acgaagtcgc tgggacggtc gaggctgtcg gtgatggggt cgacccgaac 240

cgggtcggcg aacgagtcct ggccggtaca cgatttggtg gctactgcga gatcgtcaac 300

gttgcggcca ccgactcggt tgtgctcccc gatgcgctga gcttcgaaca gggtgccgcg 360

gtcccggtga attacgcgac cgcctgggcg gcgctgcacg gctacggatc gttgcgcgcc 420

ggtgagcggg tgctgattca cgccgcggcc ggtggagtcg gcatcgcggc ggtccaattc 480

gcgaaagcag ccaaggccga agtgcacggc accgcatcac cccaaaaaca tcagaagctg 540

gccgagttcg gtgtggaccg cgcgatcgac taccgccggg acggctggtg gcagggattg 600

ggcccgtatg acgtcgtgct tgacgcgctc ggcggcacct cgctgcggcg gtcctacact 660

ctgctgcgcc cgggtggaag gctggttggc tacgggattt cgaatatgca gcacggcgag 720

aaacgatcga tgcgcagggt ggcgccccac gcgttgtcaa tgctgcgcgg ctttaacctg 780

atgaaacaac tcgaggagtc gaaaaccgtg atcggtctta acatgctgcg gttgtgggac 840

gatcgccgca cccttgaacc ctggatcgcg ccgctgacca aggcgctcaa cgacggaacg 900

atcctgccga tcgttcatgc aatcgtgccg ttcgccgaag ctcctgaagc acatcggatt 960

ctggccgcac gggagaacgt cgacaaggtg gtgctggtac cg 1002

<210> 91

<211> 145

<212> DNA

<213> Mycobacterium tuberculosis

<400> 91
gtcagtcact tggctcacag tggggcacct gctttcctcg agttcttcta tgctccgaca 60

ctaaccaacc aggctggctg tttcgcggtc acgcaccccc tgaaaccggc gcgttcgctt 120

acagcgtcat acggtcacgt tgtcg 145

<210> 92

<211> 200

<212> PRT

<213> Mycobacterium tuberculosis

<400> 92

Val Ser Gln Val Thr Asp Met Arg Ser Asn Ser Gln Gly Leu Ser Leu
1 5 10 15

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

Gly Ser Glu Val Asn Asp Glu Ile Ala Asn Arg Leu Cys Ala Gln Ile
35 40 45

Leu Leu Leu Ala Ala Glu Asp Ala Ser Lys Asp Ile Ser Leu Tyr Ile
50 55 60

Asn Ser Pro Gly Gly Ser Ile Ser Ala Gly Met Ala Ile Tyr Asp Thr
65 70 75 80

Met Val Leu Ala Pro Cys Asp Ile Ala Thr Tyr Ala Met Gly Met Ala
85 90 95

Ala Ser Met Gly Glu Phe Leu Leu Ala Ala Gly Thr Lys Gly Lys Arg
100 105 110

Tyr Ala Leu Pro His Ala Arg Ile Leu Met His Gln Pro Leu Gly Gly
115 120 125

Val Thr Gly Ser Ala Ala Asp Ile Ala Ile Gln Ala Glu Gln Phe Ala
130 135 140

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

Pro Ile Glu Arg Ile Glu Ala Asp Ser Asp Arg Asp Arg Trp Phe Thr
165 170 175

Ala Ala Glu Ala Leu Glu Tyr Gly Phe Val Asp His Ile Ile Thr Arg
180 185 190

Ala His Val Asn Gly Glu Ala Gln
195 200

<210> 93

<211> 600

<212> DNA

<213> Mycobacterium tuberculosis

<400> 93
gtgagccaag tgactgacat gcgttcgaac tcgcagggtc ttagcctcac ggattcggtc 60

tacgagcgct tgctctccga gcgcatcatc ttcctgggct cggaggtgaa cgacgagatc 120

gccaaccggt tatgcgctca gattctgctg ctggccgccg aagacgccag caaggacatc 180

agcctctaca tcaattcgcc gggtggatcg atcagcgccg gcatggcgat ctacgacacc 240

atggtgctgg cgccctgtga catcgccacc tacgcgatgg gcatggccgc ctcgatgggc 300

gagttcctgc tggcggcagg taccaagggc aagcgctacg cgctgccgca tgctcgcatc 360

ctgatgcacc agccgttggg cggggtgacc ggcagcgcgg ccgatatcgc catccaggcc 420

gagcagttcg ccgtgatcaa gaaagaaatg ttccggctca acgccgaatt caccggccag 480

ccgatcgagc gcattgaggc ggattccgat cgcgaccgct ggttcaccgc cgccgaagcc 540

ctggaatacg gtttcgtcga tcacatcatc acccgcgccc acgtcaatgg agaagcacag 600

<210> 94

<211> 214

<212> PRT

<213> Mycobacterium tuberculosis

<400> 94

Val Asn Ser Gln Asn Ser Gln Ile Gln Pro Gln Ala Arg Tyr Ile Leu
1 5 10 15

Pro Ser Phe Ile Glu His Ser Ser Phe Gly Val Lys Glu Ser Asn Pro
20 25 30

Tyr Asn Lys Leu Phe Glu Glu Arg Ile Ile Phe Leu Gly Val Gln Val
35 40 45

Asp Asp Ala Ser Ala Asn Asp Ile Met Ala Gln Leu Leu Val Leu Glu
50 55 60

Ser Leu Asp Pro Asp Arg Asp Ile Thr Met Tyr Ile Asn Ser Pro Gly
65 70 75 80

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

Arg Ala Asp Ile Gln Thr Val Cys Leu Gly Gln Ala Ala Ser Ala Ala
100 105 110

Ala Val Leu Leu Ala Ala Gly Thr Pro Gly Lys Arg Met Ala Leu Pro
115 120 125

Asn Ala Arg Val Leu Ile His Gln Pro Ser Leu Ser Gly Val Ile Gln
130 135 140

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

Arg Thr Leu Met Glu Thr Thr Leu Ala Arg His Thr Gly Lys Asp Ala
165 170 175

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

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

Leu Ser Ala Gln Thr Ala
210

<210> 95

<211> 642

<212> DNA

<213> Mycobacterium tuberculosis

<400> 95
gtgaattccc aaaattctca gatccagccc caggcgcgct acatcctgcc gtcgttcatc 60

gagcactcca gcttcggggt caaggagtcc aatccataca acaagctgtt cgaggaacgc 120

atcatcttcc tcggcgtcca ggtcgacgac gcgtcggcga acgacatcat ggcacagttg 180

ctggtgttgg agtcgttgga tcccgaccgc gatatcacca tgtacatcaa ctcgccgggc 240

ggtgggttca cctcgctgat ggcgatctac gacaccatgc aatacgtgcg ggccgatatc 300

cagacggtgt gtctgggcca ggccgcctcg gcggctgcgg tgctgctggc cgccggaaca 360

ccgggcaagc gcatggcgct gccgaatgcg cgggtgttga tccatcagcc gtcgttgtcg 420

ggcgtgatcc agggacagtt ctccgatctg gagatccagg ccgccgagat cgagcggatg 480

cgcaccctga tggaaaccac gctggcccgc cacaccggca aggacgccgg agtgatccgc 540

aaagacactg accgggacaa gatcttgacc gcggaagagg ctaaggacta cggcatcatc 600

gacacggtgc tcgagtaccg gaagctctcc gcgcaaaccg cc 642

<210> 96

<211> 381

<212> DNA

<213> Mycobacterium tuberculosis

<400> 96
ccatttacca acacattcgg gctcaggatt gtttagcgta ctaacttcat ggtagtggct 60

caagacgaaa gcatcgcatg ctgcaaggtc cgatacaacg ggaaaactgt tgtgggactt 120

gttaatctgc aggccacagc acgacgaaga acacattatc cagccaactc acaggccgtt 180

gccatgccgc taccagacgt cgtaggcctg ggaaagttaa ggtagcaaca ctgctcgaca 240

gccacagcag catgcaccgc gcgtgtgatc cgcacgagcc gcacgggcgc gagcagacgc 300

aaaaggcccc gaaatccgtt ggattcgggg ccttttgcgt ctttcgcgcc caacgtgggt 360

gcttggctag ggtgaatcct t 381

<210> 97

<211> 939

<212> PRT

<213> Mycobacterium tuberculosis

<400> 97

Val Asp Pro His Arg Asp Leu Glu Ser Arg Ala Phe Ala Gly Asn Trp
1 5 10 15

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

Ala Gly Asp Asn Arg Ala Tyr Leu Val Leu Pro Pro Gly Ala Gly Lys
35 40 45

Thr Met Ile Gly Leu Glu Ala Ala Arg Arg Leu Gly Arg Arg Ser Leu
50 55 60

Val Leu Val Pro Asn Thr Ala Val Gln Ala Gln Trp Ala Ala Ala Trp
65 70 75 80

Asp Asn Ser Phe Pro Ser Ser Asp Arg Ser Ala Ser Lys Cys Gly Thr
85 90 95

Glu Arg Gly Leu Ala Ser Ala Met Asn Val Leu Thr Tyr Gln Ser Leu
100 105 110

Ala Val Ile Asp Ala Glu Thr Asp Ser Thr Val Arg Arg Glu Val Leu
115 120 125

Arg Asn Arg Asp Gln Gln Ala Leu Leu Asp Leu Leu His Pro Asn Gly
130 135 140

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

Leu Asp Glu Cys His His Leu Leu Ala Thr Trp Gly Ala Leu Val Ser
165 170 175

Ala Leu Ala Ser Val Leu Gly Ala Gln Thr Ala Leu Ile Gly Leu Thr
180 185 190

Ala Thr Pro Ala Thr Glu Leu Thr Ala Trp Gln His Thr Leu His Asp
195 200 205

Glu Leu Phe Gly Thr Ala Asp Phe Val Ile Pro Thr Pro Ala Leu Val
210 215 220

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Arg Glu Gly Asp Leu Ala Pro Tyr Gln Glu Leu Val Tyr Leu Thr Gln
225                 230                 235                 240

Pro Thr Pro Glu Glu Gln Ala Trp Ile Gly Thr His Arg Ala Arg Phe
                245                 250                 255

Ala Asp Leu Met Leu Ala Leu Ile Asp Gln Lys Val Gly Ser Met Ser
            260                 265                 270

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

Gly Asn Gln Ile Ala Trp Ser Thr Phe Glu Arg Ala Glu Pro Asp Leu
    290                 295                 300

Ala Cys Ser Gly Leu Arg Phe Ala Tyr Asp Gly Leu Ile Pro Leu Pro
305                 310                 315                 320

Asp Gly Val Arg Leu Arg Glu Gln His Arg Ile Ala Pro Asp Ala Gln
                325                 330                 335

Asp Trp Val Asn Val Leu Thr Asp Phe Ser Val Gly His Leu Gln Gln
            340                 345                 350

Ser Ala Asp Pro Arg Asp Ala His Ala Leu Thr Ala Ile Lys Arg Val
        355                 360                 365

Leu Pro Gly Leu Gly Tyr Arg Leu Thr Ser Arg Gly Val Arg Val Ala
    370                 375                 380

Thr Ser Pro Val Asp Arg Leu Cys Ala Leu Ser Glu Ser Lys Ile Ala
385                 390                 395                 400

Ala Thr Ala His Ile Leu Asp Thr Glu Asp Ala Val Leu Gly Ala Arg
                405                 410                 415

Leu Arg Ala Leu Val Leu Cys Asp Phe Glu Ser Met Thr Gly Ala Leu
            420                 425                 430

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

Gln Leu Val Ala Ala Met Leu Ala Ala Ser Asp His Arg Arg Arg Thr
    450                 455                 460
```

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Pro Leu His Ala Leu Leu Val Thr Gly Gln Thr Phe Ala Cys Pro Ala
465                 470                 475                 480

Ala Ile Glu Asp Asp Leu Ile Ala Phe Cys Ala Glu Arg Gly Ala Leu
                485                 490                 495

Val Thr Ala Glu Pro Leu Asp Ala His Pro Ser Leu Arg Val Met Arg
            500                 505                 510

Gly Thr Gly Gly Phe Thr Pro Arg Thr Trp Val Ala Leu Ala Thr Glu
        515                 520                 525

Tyr Phe Leu Ala Gly Arg Ala Arg Val Leu Val Gly Thr Arg Ser Leu
    530                 535                 540

Leu Gly Glu Gly Trp Asp Cys Ala Ala Val Asn Val Asn Ile Asp Leu
545                 550                 555                 560

Thr Ser Ala Thr Thr Gln Ala Ala Ile Thr Gln Met Arg Gly Arg Ala
                565                 570                 575

Ile Arg Asn Asp Pro Ser Asp Gly His Lys Val Ala Asp Asn Trp Ser
            580                 585                 590

Val Cys Cys Ile Ala Thr Glu His Pro Arg Gly Asp Ala Asp Tyr Leu
        595                 600                 605

Arg Leu Val Arg Lys His Asp Gly Tyr Tyr Ala Ala Thr Pro Gln Gly
    610                 615                 620

Leu Ile Glu Ser Gly Val Thr His Cys Asp Pro Ser Leu Ser Pro Tyr
625                 630                 635                 640

Gly Pro Pro Val Thr Asp Thr His Ala Ile Thr Ala Arg Ala Leu Gln
                645                 650                 655

Arg Val Ala Glu Arg Ala Gln Ala Arg Ser Trp Trp Arg Ile Gly Glu
            660                 665                 670

Pro Tyr Glu Gly Val Asp Val Ala Thr Ile Arg Val Arg Ser Arg Gln
        675                 680                 685

Pro Leu Gly Val Ala Ala Pro Arg Ile Pro Ala Ser Ala Leu Thr Pro
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690 695 700

Pro Val Pro Gly Gln Phe Ser Pro Val Arg Leu Ala Arg Gly Ala Val
705 710 715 720

Ala Ala Val Ser Val Val Gly Ala Ser Thr Ala Thr Ala Val Ala Ser
725 730 735

Ala Asn Leu Gly Met Leu Ala Gly Ala Gly Thr Ala Gly Ala Ile Val
740 745 750

Ala Ala Gly Val Gly Leu Val Ala Thr Ala Ala Ala Ala Glu Ser Arg
755 760 765

Arg Leu Asp His Ala Pro Asn Ala Leu Glu Gln Leu Ala Ala Val Val
770 775 780

Ala Asp Ala Leu Tyr Ala Ala Gly Gly Ala Gln Arg Gly Ser Ala Ala
785 790 795 800

Leu Arg Leu Ala Ser Asp Pro Glu Gly Trp Ile Arg Cys Gln Leu Asp
805 810 815

Gly Val Pro Thr Glu Gln Ser Leu Arg Phe Thr Ala Ala Leu Asp Glu
820 825 830

Leu Leu Ala Pro Leu Ala Glu Pro Arg Tyr Leu Ile Gly Arg Lys Ile
835 840 845

Leu Thr Pro Pro Ala Arg Pro Val Ala Arg Arg Leu Phe Ala Val Arg
850 855 860

Ala Val Val Gly Leu Ser Leu Pro Gly Thr Val Ala Trp His Ala Val
865 870 875 880

Pro Arg Trp Phe Ala Arg Asn Lys Asp Arg Arg Gln His Leu Ala Gln
885 890 895

Ala Trp Arg Lys His Ile Gly Pro Pro Arg Gln Leu Pro Ala Asp Ser
900 905 910

Pro Gln Gly Gln Ala Ile Leu Asp Leu Phe Arg Gly Asp Asn Pro Leu
915 920 925

Ser Val Thr Thr Gln Leu Arg Thr Thr Trp Arg
930 935

<210> 98

<211> 2817

<212> DNA

<213> Mycobacterium tuberculosis

<400> 98
gtggatcctc accgcgacct ggaatcgcgg gcctttgccg gcaactggcg ggtataccaa 60

cagcaagcgt tggacgcgtt cgacgccgac gtcgctgccg gcgacaaccg tgcctatctg 120

gtgctgccgc cgggtgcggg caagacgatg atcggcctgg aagcagcgcg ccggctgggg 180

cgccggagtt tggtgttggt tcccaacacg gcggtgcagg cgcagtgggc cgccgcgtgg 240

gataacagtt ttccgtcgtc ggaccggtcg gcatcgaagt gtggaaccga gcgtggcctt 300

gcctcggcga tgaacgtcct gacgtatcag tcgcttgccg tcatcgacgc cgaaaccgat 360

tcgacagtcc ggcgggaagt cctgcgcaac cgcgaccagc aagcgttgct ggatctcctg 420

caccccaacg ggagggcggt gatcgagcgg gcggcgacgc taggcccgtg gacgctggtg 480

ctcgatgagt gccaccatct gctagctacg tggggcgccc tggtcagtgc gttggcgtcg 540

gtcctcggag cgcagaccgc gctgatcggt ctaacggcga ccccggccac agagctcacc 600

gcgtggcagc acaccctgca tgatgagctg ttcggcaccg ccgacttcgt gatcccgaca 660

cccgctctgg ttagggaagg cgacctggct ccctaccaag agttggtcta tctgacccaa 720

ccgacgcccg aagagcaggc ctggatcggc acccaccggg cgcgcttcgc cgacctcatg 780

ctggccctca tcgaccaaaa ggtgggcagc atgtcgttgg ccgcgtggct gcacacccgg 840

atcgtggatc gagcgacgcg cgagggcaat cagatcgcct ggtcgacgtt cgagcgtgcc 900

gaacccgacc tcgcgtgcag cggcctgcgc ttcgcctacg acggcctgat tccactaccc 960

gacggcgtgc gcctgcgcga gcagcaccga attgcgcccg atgcccagga ctgggttaac 1020

gtattgaccg acttcagcgt cgggcacctg caacaaagcg cggatccgcg cgacgcgcac 1080

gcgctgaccg cgatcaagcg ggtgctaccc ggcctgggct accggctgac cagtcgcggc 1140

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gcgaccgcgc acatcctcga caccgaggac gccgtcttgg gggcgcggtt gcgggcgctg 1260

gtgctctgcg atttcgaatc gatgaccggc gcccttccca catcgctgaa gggcgcaccc 1320

gtcagcgagc agtcgggttc ggcccagctg gttgccgcca tgctcgccgc gtcggatcac 1380

cgccgccgca ccccactgca cgcccttctg gtaacaggtc aaaccttcgc ctgcccggcc 1440

gcgatcgaag atgacctgat cgccttctgc gccgagcgcg gcgcgctcgt caccgccgag 1500

ccgcttgacg cccaccctag tctgcgggtc atgcgcggca ccggcggctt cacgccacgt 1560

acgtgggtcg cgctggctac cgaatacttc ctggccggcc gcgcccgcgt cctggtcggc 1620

acccgttcgc tactaggtga agggtgggac tgcgcggcgg tcaacgtcaa tatcgacctg 1680

acgagcgcaa ccacccaggc agcgatcact cagatgcgcg gccgcgccat ccgcaacgac 1740

ccctcggacg gtcacaaggt ggcggacaac tggtcggtct gctgtatcgc cacagaacac 1800

ccgcgcggtg atgccgacta cctgcgcctg gtgcgcaaac atgacgggta ctacgcggca 1860

accccgcagg ggctcatcga atcgggtgtg acgcactgcg atccgtcgct gtcgccgtac 1920

ggtcctccgg tcaccgatac ccacgccatc acggcgcgag cgctgcagcg cgtcgccgaa 1980

cgcgcccagg cgagatcctg gtggcgaatc ggcgagccct acgaaggagt cgacgtcgca 2040

accatccgcg tgcgctcccg ccagccgctc ggggtcgccg caccccgcat ccccgcctcg 2100

gcattgaccc caccggtgcc gggacagttc agtccggtcc gcctggcaag gggtgccgtg 2160

gccgccgttt ccgtggtcgg cgccagcacc gccaccgcag ttgcctccgc caatctcggc 2220

atgctggcgg gtgccggcac ggccggcgcc atcgtcgcgg cgggtgttgg cctggtggca 2280

accgctgcgg cggccgaaag ccgccgcctg gaccacgcgc ccaacgcgct cgagcaactg 2340

gccgccgtcg tcgcggatgc gctgtacgcc gcgggcggcg cacagcgagg atccgcggca 2400

ctacggttgg cctccgaccc cgaaggctgg atccggtgtc aactcgacgg cgtgcccacc 2460

gagcagtccc tgcggttcac cgcggccctc gacgagctac tggcgccgct tgccgaaccg 2520

cgctacctca tcggacgcaa gatcctcacg ccgcccgccc ggcccgttgc ccggaggctg 2580

ttcgcggttc gtgccgtcgt cgggctatcg ctgcccggca cggttgcctg gcacgccgtg 2640

ccccgctggt tcgcacgaaa caaggatcgg cggcaacatc tggcacaggc atggcgaaag 2700

cacatcggcc caccccgaca actgccagca gactccccac aagggcaagc catcctcgat 2760

ctgttccgcg gcgataaccc gctctcggtg acaacccagc tgcgcacgac ctggcgg 2817

<210> 99

<211> 309

<212> DNA

<213> Mycobacterium tuberculosis

<400> 99
gactgcctcc gtgccaggtt agtctgcgcc cacgataggc attgacaacg cgcgttgtcc 60

acgatttggt ccgccgatat cgcgccgtgt cacccagtgc ctcctccggg tggcaacgag 120

cgtggacgag gactgcagct gcatagcttg gcccgcggtg cgtgcggggg cagggagtcc 180

aatgaaaaat gttgcttaga acgccagaaa gtttttaact agatcaggat tgcttagctg 240

tagactttat ttctcaatga ccacgtaagg attgctgcgg ccagtacaac gtgtacaagg 300

agtcgggct 309

<210> 100

<211> 310

<212> PRT

<213> Mycobacterium tuberculosis

<400> 100

Met Ser Phe Leu Thr Val Ala Pro Asp Met Val Thr Ala Ala Ala Gly
1 5 10 15

Asn Leu Glu Ser Val Gly Ser Ala Leu Asn Glu Ala Ala Ala Ala Ala
20 25 30

Ala Pro Ala Thr Val Gly Leu Ala Ala Pro Ala Ala Asp Arg Val Ser
35 40 45

Ala Val Val Ala Ala Met Leu Gly Ala Tyr Ala Arg Asp Phe Gln Gly
50 55 60

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

Arg Gly Gly Ala Ala Ala Tyr Ala Ser Ala Glu Ala Ala Asn Val Gln
85 90 95

Gln Thr Val Val Asn Ala Val Asn Ala Pro Ala Gln Ala Leu Leu Gly
100 105 110

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

Ser Phe Gly Phe Gly Pro Leu Leu Leu Ala Gly Ser Asp Pro Leu Leu
130 135 140

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

Val Thr Met Thr Leu Asn Gly Ser Phe Asp Pro Leu Thr Gln Gln Val
165 170 175

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

Leu Gly Ala Val Gly Pro Ala Leu Thr Thr Met Thr Ala Leu Gln Asn
195 200 205

Ser Gly Thr Ala Phe Ser Gly Ala Val Gln Ser Gly Asn Leu Leu Gly
210 215 220

Ala Ala Gly Ala Leu Leu Gln Ala Pro Gly Asn Ala Val Thr Gly Phe
225 230 235 240

Leu Phe Gly Gln Thr Ala Ile Ser Gln Ser Ile Pro Gly Pro Ser Asn
245 250 255

Leu Gly Tyr Glu Ser Val Gly Ile Ser Val Pro Val Gly Gly Leu Leu
260 265 270

Ala Pro Leu Gln Pro Val Thr Val Thr Leu Thr Pro Thr Ser Gly Met
275 280 285

Pro Thr Ala Ile Gln Leu Ser Gly Thr Gln Phe Gly Gly Leu Leu Pro
290 295 300

Ala Leu Leu Asn Gly Phe
305 310

<210> 101

<211> 930

<212> DNA

<213> Mycobacterium tuberculosis

<400> 101
atgtcgtttc tcaccgtggc gccggacatg gtaacggcgg ccgccgggaa tttggaaagc 60

gttggctcgg cactgaatga ggccgctgcg gcggcggcgc cagccacggt tgggctggcg 120

gccccggccg cggatcgggt gtcggcggtc gtcgcggcga tgttgggggc atatgcccgg 180

gattttcaag gcatcagtgc tcagatcgcg ggttttcata accagttcgt gggcgcgttg 240

cggggcggtg cggccgccta cgccagcgcc gaagccgcca acgtccagca gaccgtggtg 300

aacgccgtga atgcgcccgc ccaggcgctg ttggggcacc cgttgatcgg gcccgagacg 360

gtcggctcca gcgccgccgc ggtctccttc ggcttcggcc cgttgctcct cgctggtagc 420

gatccgctgc tggccgtgcc attcagctat ccggccagtc tgcccacccc attcggtcca 480

gtaacgatga cgctcaacgg gtcgtttgat ccgcttaccc aacaggttgt tttcgactcg 540

ggatcactca ccgcgcccgc tccgttcgtg tacggtcttg gtgcggtagg tccagctctc 600

accaccatga ccgcgctgca aaacagcggc acagcatttt ccggcgcggt gcaaagcggg 660

aacctgctag gggccgcggg cgcgcttctg caagctcccg gcaacgcggt gaccggcttc 720

ctgtttggcc aaacagcgat atcgcagtcg ataccggggc catcgaatct gggctacgag 780

tcggtgggta tcagcgttcc ggtcgggggg ctcttggctc cgctgcagcc cgtgacggtc 840

acgttgacgc ccacatctgg tatgccgact gccattcaat tgagtggtac gcagtttggc 900

ggccttcttc ccgccctact caacggtttc 930

<210> 102

<211> 490

<212> DNA

<213> Mycobacterium tuberculosis

<400> 102
cgcccgcata cgtccaccat acgttcgggc gactgcccgg gcagtttgcc taccgacgcg 60

gcagccacag atatagggtc catgacgccg cgacgatcgc gaacatgacc agctgagcgg 120

cggccaccca accggcggga tagatcacgc cggtgatgta gtgagcgaca aatccgtccg 180

gtgacagagg tgtcatcgcg gccttggtgc gagcccagcg ctccacccag gtcagcgggc 240

agtcgacccg cttagcggcg atgccgatcc cccatatcac cgccggaaca tgcagccaca 300

tcgtgcgtcg ccaccgcagg gcaaggaaac cgccggcaag gacgtaagcg atgaaagcga 360

agtgcattac caccgttgat acaacgacgg tttcgtacat ctctcgggtt gcctttccag 420

gtcgcggcgc tccggccact gacagaaaag gttcaattcg ccagcgaaaa cccgtcccat 480

gcgatccggc 490

<210> 103

<211> 324

<212> PRT

<213> Mycobacterium tuberculosis

<400> 103

Val Ala Leu Val Ser Thr Ala Arg Val Asp Leu Val Cys Glu Gly Gly
1 5 10 15

Gly Val Arg Gly Ile Gly Leu Val Gly Ala Val Asp Ala Leu Ala Asp
20 25 30

Ala Gly Tyr Arg Phe Pro Arg Val Ala Gly Ser Ser Ala Gly Ala Ile
35 40 45

Val Ala Ser Leu Val Ala Ala Leu Gln Thr Ala Gly Glu Pro Val Thr
50 55 60

Arg Leu Ala Glu Met Met Arg Ser Ile Asp Tyr Pro Lys Phe Leu Asp
65 70 75 80

Arg Asn Leu Ile Gly His Val Pro Leu Ile Gly Gly Gly Leu Ser Leu
85 90 95

Leu Leu Ser Asp Gly Val Tyr Arg Gly Ala Tyr Leu Glu Gln Leu Leu
100 105 110

Gly Gly Leu Leu Ala Asp Leu Gly Val His Thr Phe Gly Asp Leu Arg
115 120 125

Thr Gly Glu Ala Pro Glu Gln Phe Ala Trp Ser Leu Val Val Thr Ala
130 135 140

Ser Asp Leu Ser Arg Arg Arg Leu Val Arg Ile Pro Trp Asp Leu Asp
145 150 155 160

Ser Tyr Gly Ile His Pro Asp Asp Phe Ser Val Ala Arg Ala Val His

165 170 175

Ala Ser Ser Ala Ile Pro Phe Val Phe Glu Pro Val Arg Val Arg Gly
180 185 190

Ala Thr Trp Val Asp Gly Gly Leu Leu Ser Asn Phe Pro Val Ala Leu
195 200 205

Phe Asp Arg Thr Asp Ala Glu Pro Arg Trp Pro Thr Phe Gly Ile Arg
210 215 220

Leu Ser Ala Arg Pro Gly Ile Pro Pro Thr Arg Pro Val Gln Gly Pro
225 230 235 240

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

Asn Ala Tyr Ile Asp Asp Pro Cys Thr Val Arg Arg Thr Ile Phe Val
260 265 270

Pro Ala His Asp Val Ser Pro Ile Asp Phe Asp Ile Thr Ala Glu Gln
275 280 285

Arg Glu Ala Leu Tyr Gln Arg Gly Phe Gln Ala Gly Gln Lys Phe Leu
290 295 300

Ala Asn Trp Asn Tyr Ala Asp Cys Leu Ala Asp Cys Gly Gly Pro Phe
305 310 315 320

Thr Pro Ser Leu

<210> 104

<211> 972

<212> DNA

<213> Mycobacterium tuberculosis

<400> 104
gtggcgctgg tgagcacagc acgcgtcgac ctggtgtgtg aaggcggcgg ggtccggggg 60

atagggttgg ttggagcggt ggacgcgctg gccgatgccg gttaccgatt tcccagggtg 120

gcgggcagca gcgcgggtgc gatcgtcgcg tcgctggtcg cggccctaca aacggccggt 180

gagccggtga cgcggcttgc cgagatgatg cgcagcatcg actacccgaa gttcctcgac 240

cgcaatctga taggacacgt gccgttgatc ggcgggggac tttctctgct gttgtcggac 300

ggcgtttacc gcggggccta tctggaacag ctgctcggcg gtttgctcgc tgacctaggc 360

gtgcacacct ttggcgactt gcgcaccggc gaggcacccg aacagttcgc ctggtcgctg 420

gtggtcaccg ccagcgacct atcccgtcgc cgactcgttc gcatcccgtg ggacctggac 480

tcctacggca tccacccgga cgacttctcg gtggcgcgtg cggtgcacgc ctcatcggcg 540

atcccgtttg tgttcgagcc tgttcgggtg cgcggcgcta cctgggtcga cggtggcttg 600

ctgtcgaact ttccggtggc gctgttcgac cgaaccgacg ctgaaccgcg atggcccacg 660

ttcgggatca ggttgtcagc gcgtccgggc attccaccta cccggccggt ccaagggcca 720

gtgtcgttgg gcatcgcggc gatcgaaaca ctggtgagca atcaggacaa cgcctacatc 780

gacgatccgt gtaccgttcg gcgcaccatc ttcgtgcccg cccacgacgt gagtccgatc 840

gacttcgaca tcaccgccga acaacgcgag gctctttacc aacgcggatt tcaggcgggt 900

caaaagttct tggcgaactg gaattacgcc gattgtctgg ctgactgcgg cggcccgttc 960

acgccgtcgc tg 972

<210> 105

<211> 357

<212> PRT

<213> Mycobacterium tuberculosis

<400> 105

Met Ala Ser Val Ser Phe Glu Gln Ala Thr Arg Arg Tyr Pro Gly Thr
1 5 10 15

Asp Arg Pro Ala Leu Asp Arg Leu Asp Leu Ile Val Gly Asp Gly Glu
20 25 30

Phe Val Val Leu Val Gly Pro Ser Gly Cys Gly Lys Thr Thr Ser Leu
35 40 45

Arg Met Val Ala Gly Leu Glu Thr Leu Asp Cys Gly Arg Ile Arg Ile
50 55 60

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

Met Val Phe Gln Asn Tyr Ala Leu Tyr Pro His Met Thr Val Ala Gln
                85                  90                  95

Asn Met Gly Phe Ala Leu Lys Val Ala Lys Ile Gly Lys Ala Glu Ile
            100                 105                 110

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

Leu Asp Arg Lys Pro Lys Asp Leu Ser Gly Gly Gln Arg Gln Arg Val
    130                 135                 140

Ala Met Gly Arg Ala Ile Val Arg Arg Pro Gln Val Phe Leu Met Asp
145                 150                 155                 160

Glu Pro Leu Ser Asn Leu Asp Ala Lys Leu Arg Gly Gln Thr Arg Asn
                165                 170                 175

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

Thr His Asp Gln Val Glu Ala Met Thr Met Gly Asp Arg Val Ala Val
        195                 200                 205

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

Arg Asn Pro Gly Asn Val Phe Val Ala Gly Phe Ile Gly Ser Pro Ala
225                 230                 235                 240

Met Asn Leu Phe Arg Leu Ser Ile Ala Asp Ser Thr Val Ser Leu Gly
                245                 250                 255

Asp Trp Gln Ile Leu Leu Pro Arg Ala Val Val Gly Thr Ala Ala Glu
            260                 265                 270

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

Ile Glu Met Asp Val Asp Met Val Glu Glu Leu Gly Ala Asp Ala Tyr
    290                 295                 300
```

Leu Tyr Gly Arg Ile Val Ser Gly Gly Cys Glu Met Asp Gln Ser Ile
305 310 315 320

Val Ala Arg Val Asp Gly Arg Gly Pro Pro Glu Arg Gly Ser Arg Val
325 330 335

Arg Leu Cys Pro Thr Pro Gly His Leu His Phe Phe Ala Val Asp Gly
340 345 350

Arg Arg Ile Pro Gly
355

<210> 106

<211> 1071

<212> DNA

<213> Mycobacterium tuberculosis

<400> 106
atggcttcgg tgagttttga gcaggcaacc cggcgctatc ccggcacgga ccgaccggcc 60

ctggatcggc tcgacctgat cgtcggcgat ggcgagttcg ttgtcctggt ggggccgtcc 120

ggatgtggca agacgacgtc gttacggatg gtggctggct tggagacgct ggactgtggg 180

cgtatccgga tcggcgagcg cgacgtcacc gaggtcgatc ccaaggatcg tgatgtcgcc 240

atggtgttcc agaactacgc cctctacccg cacatgacgg tggcgcagaa catgggcttc 300

gcgttgaagg tcgccaagat cggcaaggcc gagatccgcg agcgggtgct tgccgcagcg 360

aaattgcttg atctgcaatc ttatctggat cgcaagccga aagatctctc cggcggccaa 420

cggcaacggg tggcgatggg tcgtgcgatc gtgcggcgcc cacaggtatt cctgatggac 480

gaaccgctgt ccaatcttga cgccaaactt cgcgggcaaa cccgcaatca gatcgccgcg 540

ttacaacggc aactgggtac gaccaccgtg tatgtcactc acgaccaggt cgaggccatg 600

acgatgggtg accgcgtcgc ggtgctgtct gacggtgtgc tgcaacagtg tgcttcgcct 660

cgagagctct accgcaaccc gggcaacgtg ttcgtcgcgg ggttcatcgg ttccccggcg 720

atgaacctgt tcaggctttc catcgccgat tccacggtgt cactgggtga ttggcagatc 780

ctgctgccgc gtgcggtcgt cggtacggca gccgaggtca ttatcggtgt tcgccccgaa 840

catttggagc tgggcggcgc cggcatcgag atggacgtcg acatggtcga agaacttgga 900

gcggacgcct acttgtatgg ccgaatcgtg tcgggcggct gcgaaatgga ccagtcaatc 960

gtcgctcgag tggacggccg cggcccgccc gagcggggta gtcgcgtgcg gctatgtccc 1020

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<210> 107

<211> 280

<212> PRT

<213> Mycobacterium tuberculosis

<400> 107

Val Gly Trp Ala Asp Arg Ile Val His Arg His Phe Ile Arg Gly Leu
1 5 10 15

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

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

Glu Pro Thr Leu Phe Pro Ser His Pro Gln Trp Ser Asn Tyr Arg Glu
50 55 60

Val Phe Ala Leu Met Pro Phe Trp Arg Met Phe Phe Asn Thr Val Leu
65 70 75 80

Tyr Ala Gly Cys Val Thr Ala Gly Gln Val Phe Phe Cys Ser Leu Ala
85 90 95

Gly Tyr Ala Phe Ala Arg Leu Gln Phe Arg Gly Arg Asp Thr Leu Phe
100 105 110

Val Leu Tyr Leu Ser Thr Leu Met Val Pro Leu Thr Val Thr Val Ile
115 120 125

Pro Gln Val Ile Leu Met Arg Ile Val Gly Trp Val Asp Thr Pro Trp
130 135 140

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

Met Arg Gln Phe Phe Arg Thr Leu Pro Thr Asp Leu Glu Glu Ala Ala
165 170 175

Ile Leu Asp Gly Cys Ser Pro Trp Gln Ile Tyr Trp Arg Ile Leu Leu
180 185 190

Pro His Ser Arg Pro Ala Val Leu Val Leu Gly Val Leu Thr Trp Val
195 200 205

Asn Val Trp Asn Asp Phe Leu Trp Pro Leu Leu Met Ile Gln Arg Asn
210 215 220

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

Val Ala Arg Trp Pro Val Leu Met Ala Ala Ser Met Leu Met Leu Val
245 250 255

Pro Leu Val Ile Leu Tyr Ala Val Ala Gln Arg Ser Phe Val Arg Gly
260 265 270

Ile Ala Val Thr Gly Leu Gly Gly
275 280

<210> 108

<211> 840

<212> DNA

<213> Mycobacterium tuberculosis

<400> 108
gtgggctggg ctgatcgaat agtccaccgc cacttcattc gtgggcttgc cctgtacgcg 60

ggactgatcg ggatcgcttg gtgcgcgctg ttccctatca tctgggcgct gtcgggctcc 120

ctgaaggcgg acggcgaggt gaccgagccg acgctgttcc cgtcgcatcc gcaatggtcc 180

aactaccgcg aggtgttcgc gttgatgccg ttctggcgga tgttcttcaa caccgtgctg 240

tatgccggat gtgtcaccgc cgggcaggtc ttcttctgct cgttggccgg ttatgccttc 300

gcgcgactgc agttccgggg ccgcgatacg ttgttcgtct tgtacttgag cactttgatg 360

gtgccgttga cggtgaccgt catcccacag gtcattctca tgcggatcgt ggggtgggtg 420

gatacgccgt gggcgatgat cgtgccggga ttgttcggta gcgcgttcgg tacctacctg 480

atgcggcagt tcttccgcac gctgccgacc gatctcgagg aagccgcgat tctcgacggt 540

tgctcgccgt ggcagatcta ctggcggatt ctgctgccgc attcacgtcc cgcggtgctg 600

gtgctgggtg tgctcacctg ggtcaacgtg tggaacgact ttctgtggcc gctgctgatg 660

atccagcgaa acagcctggc gacgctcacc cttggcctgg tccgattgcg gggcgaatac 720

gtcgcccggt ggccggtgct gatggcggcg tcgatgctga tgctggtgcc gttggtcatc 780

ctttatgcgg tcgcacaacg ttcctttgtc cgtggtatcg cggtgactgg gctcggcggg 840

<210> 109

<211> 300

<212> PRT

<213> Mycobacterium tuberculosis

<400> 109

Met Thr Arg Arg Arg Gly Arg Arg Ala Trp Ala Gly Arg Met Phe Val
1 5 10 15

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

Phe Ser Leu Tyr Met Ser Phe Gln Lys Trp Asp Leu Phe Thr His Ala
35 40 45

Thr Phe Val Arg Leu Asp Asn Phe Arg Asn Leu Phe Thr Ser Asp Pro
50 55 60

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

Val Val Pro Thr Val Ile Val Ser Leu Val Val Ala Ala Phe Leu Asn
85 90 95

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

Leu Ala Ile Ser Ser Val Val Met Ala Val Val Trp Gln Phe Val Phe
115 120 125

Asn Thr Asp Asn Gly Leu Leu Asn Ile Met Leu Gly Trp Leu Gly Ile

130 135 140

Gly Pro Ile Pro Trp Leu Ile Glu Pro Arg Trp Ala Met Val Ser Leu
145 150 155 160

Cys Leu Val Ser Val Trp Arg Ser Val Pro Phe Ala Thr Val Val Leu
165 170 175

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

Ile Asp Gly Ala Gly Glu Ile Arg Gln Phe Val Ser Ile Thr Val Pro
195 200 205

Leu Ile Arg Gly Ala Leu Ser Phe Val Val Val Ile Ser Ile Ile His
210 215 220

Ala Phe Gln Ala Phe Asp Leu Val Tyr Val Leu Thr Gly Ala Asn Gly
225 230 235 240

Gly Pro Glu Thr Ala Thr Tyr Val Leu Gly Ile Met Leu Phe Gln His
245 250 255

Ala Phe Ser Phe Leu Glu Phe Gly Tyr Ala Ser Ala Leu Ala Trp Val
260 265 270

Met Phe Ala Ile Leu Leu Val Leu Thr Val Leu Gln Leu Arg Ile Thr
275 280 285

His Arg Arg Ser Trp Glu Ala Ser Arg Gly Leu Gly
290 295 300

<210> 110

<211> 900

<212> DNA

<213> Mycobacterium tuberculosis

<400> 110
atgacacggc gcaggggcg acgcgcgtgg gcggggcgta tgttcgtcgc gccgaacttg 60

gctgccgttg tggtgttcat gctgtttccg ctgggattct cgctgtacat gagctttcag 120

aagtgggact tgtttacgca tgcgacgttc gtgaggttgg acaatttcag aaacctcttc 180

acttctgatc cgctgtttct catcgccgtg gtcaacaccg cggtttacac cgtcggcacc 240

gtggtaccga ccgttatcgt cagcctcgtc gtcgccgcct ttctaaaccg gaaaatcaaa 300

ggcatcagcc tctttcggac ggtcgtcttc ttgccgttgg cgatttcctc ggtggtgatg 360

gcggtcgtct ggcagttcgt cttcaacacc gacaatggcc tactcaacat catgctcggc 420

tggctgggaa tcggccccat cccatggcta atcgaacccc gatgggccat ggtctcgctt 480

tgcctggtca gcgtctggcg cagtgtgccc ttcgccacgg tcgtcctgct ggccgcgatg 540

caggggttc cggagactgt gtacgaggcg gccaggatcg atggtgccgg cgagattcgc 600

cagttcgtgt ccatcacggt accgctgatc cgggggggcat tgtcattcgt ggttgtcata 660

tcgatcatcc acgcgttcca ggcgtttgac cttgtctacg tccttaccgg tgccaacggt 720

ggtcccgaga cggctaccta tgttttgggc atcatgctgt tccagcacgc gttttcgttc 780

ctggaattcg gctatgcgtc cgcgttggcg tgggtgatgt tcgccatctt gctggtgttg 840

accgtgctgc agttgcgaat tacgcaccgg cgctcctggg aggcgtcccg tgggctgggc 900

<210> 111

<211> 439

<212> PRT

<213> Mycobacterium tuberculosis

<400> 111

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

Ala Leu Thr Ala Ala Ser Leu Ala Pro Trp Ala Ala Gly Cys Ala Ala
20 25 30

Asp Asp Asp Asp Ala Leu Thr Phe Phe Phe Ala Ala Asn Pro Asp Glu
35 40 45

Leu Arg Pro Arg Met Arg Val Val Asn Glu Phe Gln Arg Arg Tyr Pro
50 55 60

Asp Ile Lys Val Arg Ala Leu Leu Ser Gly Pro Gly Val Met Gln Gln
65 70 75 80

```
Leu Ala Thr Phe Cys Ala Gly Gly Lys Cys Pro Asp Val Leu Met Ala
                85                  90                  95

Trp Glu Leu Thr Tyr Ala Glu Leu Ala Asp Arg Gly Val Leu Leu Asp
            100                 105                 110

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

Ser Asp Ser Ile Gly Ala Leu Tyr Glu Thr Phe Thr Phe Asn Gly Gly
    130                 135                 140

Gln Tyr Ala Phe Pro Glu Gln Trp Ser Gly Asn Phe Leu Phe Tyr Asn
145                 150                 155                 160

Lys Gln Leu Phe Asp Asp Ala Gly Val Pro Pro Pro Pro Gly Ser Trp
                165                 170                 175

Glu Arg Pro Trp Ser Phe Ala Glu Phe Leu Asp Ala Ala Gln Ala Leu
            180                 185                 190

Thr Lys Gln Gly Arg Ser Gly Arg Asp Arg Gln Trp Gly Phe Val Asn
        195                 200                 205

Ala Trp Val Ser Phe Tyr Ala Ala Gly Leu Phe Ala Met Asn Asn Gly
    210                 215                 220

Val Pro Trp Ser Val Pro Arg Met Asn Pro Thr His Leu Asn Phe Asp
225                 230                 235                 240

His Asp Gly Phe Leu Glu Ala Val Gln Phe Tyr Ala Asp Leu Thr Asn
                245                 250                 255

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

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

Trp Arg Tyr Gln Thr Phe Asp Arg Ala Asp Gly Leu Asp Phe Asp Val
    290                 295                 300

Ala Pro Leu Pro Ile Gly Pro Arg Gly Arg Ala Ala Cys Ser Asp Ile
305                 310                 315                 320
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Gly Val Thr Gly Leu Ala Ile Ala Ala Thr Ser Arg Arg Lys Asp Gln
325 330 335

Ala Trp Glu Phe Val Lys Phe Ala Thr Gly Pro Val Gly Gln Ala Leu
340 345 350

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

Ser His Gly Phe Ala Asn Ala His Arg Arg Val Gly Asn Leu Ala Val
370 375 380

Leu Ser Glu Gly Pro Ala Tyr Ser Glu Gly Leu Pro Val Thr Pro Ala
385 390 395 400

Trp Glu Lys Ile Ala Ala Leu Met Asp Arg Tyr Phe Gly Pro Val Leu
405 410 415

Arg Gly Ser Arg Pro Ala Thr Ser Leu Thr Gly Leu Ser Gln Ala Val
420 425 430

Asp Glu Val Leu Arg Asn Pro
435

<210> 112

<211> 1317

<212> DNA

<213> Mycobacterium tuberculosis

<400> 112
atggtcaata agccgttcga gcggcgcagt ctgttacggg gtgcgggcgc gcttactgcg 60

gcctcgctgg ctccctgggc cgctgggtgt gctgccgatg acgatgacgc gttgactttc 120

ttttttgcag ccaatccgga cgagctccgt ccccggatgc gcgtcgtcaa cgaattccag 180

cggcgctatc ccgatatcaa ggtacgggcc ctgttgtccg gacccggcgt catgcagcag 240

ctcgcaacgt tttgcgcggg tggcaagtgt ccggatgtgc tgatggcatg ggaactgacc 300

tatgccgaac tggccgaccg gggggtgttg cttgacctga acacgctatt ggcgcgcgac 360

caggctttcg ccgcggagct gaaatcggac agcatcgggg ccctgtatga gactttcacg 420

ttcaacggag gccagtacgc ctttccggag caatggtccg gcaacttctt gttctacaac 480

aaacagctat tcgacgacgc cggcgtgcca ccgccgcccg gtagctggga acggccatgg 540

agcttcgccg aattcctgga tgccgcccag gcgcttacca agcagggccg gtcgggacgg 600

gacaggcaat ggggcttcgt caacgcgtgg gtctcgttct acgctgccgg gttgttcgcc 660

atgaataacg gtgtaccgtg gtcggttccg cggatgaatc ccacccacct caatttcgac 720

cacgatgggt tcctcgaagc ggtgcagttc tacgccgacc tgaccaacaa gcacaaggtg 780

gcccccagcg ctgctgagca gcagtcgatg tcgacggcgg acctgttttc tgtgggcaag 840

gccgggatcg cgttggccgg gcactggcga tatcagacgt tcgaccgtgc cgacggtctg 900

gacttcgacg tcgccccact gcccatcggt ccgcgcggac gagccgcctg ttcagatatc 960

ggtgtcaccg ggctggccat tgcggcgacc agtcgacgca aggaccaggc gtgggaattc 1020

gtaaagttcg cgaccggccc ggtggggcag gcattgatcg gcgaatcccg cctgttcgtg 1080

ccggtgctga gatcggcgat caactcgcac ggattcgcca acgcccaccg cagggtaggc 1140

aatcttgccg tgctcagcga ggggccggcc tattcggaag gcttgccggt gaccccggcc 1200

tgggagaaga tcgccgccct gatggaccgc tacttcggac ccgtgctgcg tggatcccgg 1260

ccggcgacct cgctgaccgg gctatcacag gccgtcgatg aagtgctgcg caatcca 1317

<210> 113

<211> 265

<212> PRT

<213> Mycobacterium tuberculosis

<400> 113

Met Ala Pro Pro Asn Arg Asp Glu Leu Leu Ala Ala Val Glu Arg Ser
1 5 10 15

Pro Gln Ala Ala Ala Ala His Asp Arg Ala Gly Trp Val Gly Leu Phe
20 25 30

Thr Gly Asp Ala Arg Val Glu Asp Pro Val Gly Ser Gln Pro Gln Val
35 40 45

Gly His Glu Ala Ile Gly Arg Phe Tyr Asp Thr Phe Ile Gly Pro Arg
50 55 60

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Asp Ile Thr Phe His Arg Asp Leu Asp Ile Val Ser Gly Thr Val Val
65                  70                  75                  80

Leu Arg Asp Leu Glu Leu Glu Val Ala Met Asp Ser Ala Val Thr Val
                85                  90                  95

Phe Ile Pro Ala Phe Leu Arg Tyr Asp Leu Arg Pro Val Thr Gly Glu
            100                 105                 110

Trp Gln Ile Ala Ala Leu Arg Ala Tyr Trp Glu Leu Pro Ala Met Met
        115                 120                 125

Leu Gln Phe Leu Arg Thr Gly Ser Gly Ala Thr Arg Pro Ala Leu Gln
    130                 135                 140

Leu Ser Arg Ala Leu Leu Gly Asn Gln Gly Leu Gly Gly Thr Ala Gly
145                 150                 155                 160

Phe Leu Thr Gly Phe Arg Arg Ala Gly Arg Arg His Lys Lys Leu Val
                165                 170                 175

Glu Thr Phe Leu Asn Ala Ala Ser Arg Ala Asp Lys Ser Ala Ala Tyr
            180                 185                 190

His Ala Leu Ser Arg Thr Ala Thr Met Thr Leu Gly Glu Asp Glu Leu
        195                 200                 205

Leu Asp Ile Val Glu Leu Phe Glu Gln Leu Arg Gly Ala Ser Trp Thr
    210                 215                 220

Lys Val Thr Gly Ala Gly Ser Thr Val Ala Val Ser Leu Ala Ser Asp
225                 230                 235                 240

His Arg Arg Gly Ile Met Phe Ala Asp Val Pro Trp Arg Gly Asn Arg
                245                 250                 255

Ile Asn Arg Ile Arg Tyr Phe Pro Ala
            260                 265
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<210> 114

<211> 795

<212> DNA

<213> Mycobacterium tuberculosis

<400> 114
atggcaccgc cgaaccggga tgaactgttg gcggcggtgg agcgctcgcc gcaagcggcc 60

gccgcgcacg accgcgccgg ctgggtcggg ttgttcaccg gtgacgcgcg ggtcgaagac 120

ccggtgggtt cgcagccgca ggtggggcat gaggccatcg gccgcttcta cgacaccttc 180

atcgggccgc gggatatcac gttccatcgc gatctggata tcgtctccgg cacggtggtg 240

ctgcgcgatc tcgaactcga ggtcgcgatg gactcggctg tgacggtgtt cattcccgcc 300

ttcctacgct atgacctacg accggttacc ggcgagtggc agattgccgc actgcgggcg 360

tactgggagt tgccggcgat gatgctgcag tttctgcgca cgggatcggg ggccacaaga 420

cccgccctgc aactgtcgcg agcgctgcta ggcaatcaag ggttgggcgg caccgcagga 480

ttcctgaccg gctttcgccg ggcgggccgg cggcacaaga agctggtgga aacgttcctc 540

aacgccgcgt cccgggcaga caagtccgct gcgtatcacg cgttatcacg cactgccaca 600

atgactttag gcgaggatga gctactcgac attgtcgagc tgttcgagca gctgcgcggg 660

gctagctgga ccaaggtgac cggtgccgga tccaccgtcg cggtgtcgct cgcgtcggac 720

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cggtacttcc cagcc 795

<210> 115

<211> 186

<212> PRT

<213> Mycobacterium tuberculosis

<400> 115

Met Arg Ala Leu Ile Ile Val Asp Val Gln Asn Asp Phe Cys Glu Gly
1 5 10 15

Gly Ser Leu Ala Val Thr Gly Gly Ala Ala Leu Ala Arg Ala Ile Ser
20 25 30

Asp Tyr Leu Ala Glu Ala Ala Asp Tyr His His Val Val Ala Thr Lys
35 40 45

Asp Phe His Ile Asp Pro Gly Asp His Phe Ser Gly Thr Pro Asp Tyr
50 55 60

Ser Ser Ser Trp Pro Pro His Cys Val Ser Gly Thr Pro Gly Ala Asp
65 70 75 80

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

Gly Ala Tyr Thr Gly Ala Tyr Ser Gly Phe Glu Gly Val Asp Glu Asn
100 105 110

Gly Thr Pro Leu Leu Asn Trp Leu Arg Gln Arg Gly Val Asp Glu Val
115 120 125

Asp Val Val Gly Ile Ala Thr Asp His Cys Val Arg Gln Thr Ala Glu
130 135 140

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

Ala Gly Val Ser Ala Asp Thr Thr Val Ala Ala Leu Glu Glu Met Arg
165 170 175

Thr Ala Ser Val Glu Leu Val Cys Ser Ser
180 185

<210> 116

<211> 558

<212> DNA

<213> Mycobacterium tuberculosis

<400> 116
atgcgggcgt tgatcatcgt cgacgtgcag aacgacttct gcgagggtgg ctcgctggcg 60

gtaaccggtg gcgccgcgct ggcccgcgcc atcagcgact acctggccga agcggcggac 120

taccatcacg tcgtggcaac caaggacttc cacatcgacc cgggtgacca cttctccggc 180

acaccggact attcctcgtc gtggccaccg cattgcgtca gcggtactcc cggcgcggac 240

ttccatccca gtctggacac gtcggcaatc gaggcggtgt tctacaaggg tgcctacacc 300

ggagcgtaca gcggcttcga aggagtcgac gagaacggca cgccactgct gaattggctg 360

cggcaacgcg gcgtcgatga ggtcgatgtg gtcggtattg ccaccgatca ttgtgtgcgc 420

cagacggccg aggacgcggt acgcaatggc ttggccacca gggtgctggt ggacctgaca 480

gcgggtgtgt cggccgatac caccgtcgcc gcgctggagg agatgcgcac cgccagcgtc 540

gagttggttt gcagctcc 558

<210> 117

<211> 213

<212> PRT

<213> Mycobacterium tuberculosis

<400> 117

Val Lys Ala Ala Asp Ser Ala Glu Ser Asp Ala Gly Ala Asp Gln Thr
1 5 10 15

Gly Pro Gln Val Lys Ala Ala Asp Ser Ala Glu Ser Asp Ala Gly Glu
20 25 30

Leu Gly Glu Asp Ala Cys Pro Glu Gln Ala Leu Val Glu Arg Arg Pro
35 40 45

Ser Arg Leu Arg Arg Gly Trp Leu Val Gly Ile Ala Ala Thr Leu Leu
50 55 60

Ala Leu Ala Gly Gly Leu Gly Ala Ala Gly Tyr Phe Ala Leu Arg Ser
65 70 75 80

His Gln Glu Ser Gln Ser Ile Ala Arg Glu Asp Leu Ala Ala Ile Glu
85 90 95

Ala Ala Lys Asp Cys Val Ala Ala Thr Gln Ala Pro Asp Ala Gly Ala
100 105 110

Met Ser Ala Ser Met Gln Lys Ile Ile Glu Cys Gly Thr Gly Asp Phe
115 120 125

Gly Ala Gln Ala Ser Leu Tyr Thr Ser Met Leu Val Glu Ala Tyr Gln
130 135 140

Ala Ala Ser Val His Val Gln Val Thr Asp Met Arg Ala Ala Val Glu

145 150 155 160

Arg Asn Asn Asn Asp Gly Ser Val Asp Val Leu Val Ala Leu Arg Val
165 170 175

Lys Val Ser Asn Thr Asp Ser Asp Ala His Glu Val Gly Tyr Arg Leu
180 185 190

Arg Val Arg Met Ala Leu Asp Glu Gly Arg Tyr Lys Ile Ala Lys Leu
195 200 205

Asp Gln Val Thr Lys
210

<210> 118

<211> 639

<212> DNA

<213> Mycobacterium tuberculosis

<400> 118
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aaggcggcgg attcggcgga atctgacgcc ggagagctcg gcgaggacgc gtgcccagaa 120

caggccctcg tcgagcggcg cccgtcgcgg ttgcggcgag gctggcttgt tggcattgcg 180

gcgacgctgc tcgcgttggc cggtggcctt ggcgcagcgg gttattttgc gttgcgctca 240

caccaggaaa gccaatcaat cgcgcgcgag gaccttgcgg ccattgaggc cgctaaggat 300

tgcgttgcgg ccacgcaggc acccgatgct ggggcgatgt cggctagcat gcagaagatc 360

atcgagtgtg gcaccggtga tttcggtgcc caggcgtcgt tgtacaccag catgctcgtc 420

gaggcgtatc aagcggccag cgtccacgtg caagtgaccg atatgcgcgc ggcggtcgag 480

cgcaacaaca atgacgggtc ggtcgatgtt ctggtggcgc tccgggtcaa ggtgtccaac 540

accgactcgg atgcccatga agtcggctac cgtcttcggg tccggatggc actggatgag 600

ggccgctata agatcgccaa actcgaccag gtgacgaag 639