CLAIMS

1. A modified Rv3616c protein, said protein comprising:
(a) the amino acid sequence of SEQ ID No: 164, 179 or 180; or
(b) a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:
(i) the first polypeptide is a sequence having at least 98% identity to residues 1-134 of SEQ ID No: 1; and
(ii) the second polypeptide is a sequence having at least 98% identity to residues 155-392 of SEQ ID No: 1;
wherein the first and second polypeptides are directly linked or indirectly linked via a third polypeptide, said third polypeptide having at least 80% identity to a sequence corresponding to residues 135-154 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted.

2. The modified Rv3616c protein according to claim 1, said protein comprising a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:
(iii) the first polypeptide is a sequence having at least 98% identity to residues 1-134 of SEQ ID No: 1; and
(iv) the second polypeptide is a sequence having at least 98% identity to residues 155-392 of SEQ ID No: 1;
wherein the first and second polypeptides are directly linked or indirectly linked via a third polypeptide, said third polypeptide having at least 80% identity to a sequence corresponding to residues 135-154 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted.

3. The modified Rv3616c protein according to claim 2, wherein the first polypeptide has 100% identity to residues 1-134 of SEQ ID No: 1.

~~2~~4. ~~A~~ The modified Rv3616c protein according to claim ~~1~~2 or 3, wherein the second polypeptide has at least 99% identity to residues 155-392 of SEQ ID No: 1.

5. The modified Rv3616c protein according to claim 4, wherein the second polypeptide has 100% identity to residues 155-392 of SEQ ID No: 1.

6. The modified Rv3616c protein according to any one of claims 2 to 5, wherein the peptide linkage is direct.

7. The modified Rv3616c protein according to any one of claims 2 to 5, wherein the peptide linkage is indirect.

8. The modified Rv3616c protein according to claim 7, wherein the third polypeptide is a sequence having at least 90% identity to a sequence corresponding to residues 135-154 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted.

~~39~~. ~~A~~ The modified Rv3616c protein according to claim 8~~either claim 1 or 2~~, wherein the third polypeptide is a sequence having at least 95% identity to a sequence corresponding to residues 135-154 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted.

10. The modified Rv3616c protein according to any one of claims 2 to 9, in which the contiguous portion deleted from the residues corresponding to 134-154 in SEQ ID No: 1 is least 4 amino acids.

11. The modified Rv3616c protein according to claim 10, in which the contiguous portion deleted from the residues corresponding to 134-154 in SEQ ID No: 1 is least 5 amino acids.

12. The modified Rv3616c protein according to any one of claims 7 to 11, in which the third polypeptide is 20 amino acids or fewer in length.

13. The modified Rv3616c protein according to any one of claims 1 to 12, said protein being fewer than 500 amino acid residues in length.

14. The modified Rv3616c protein according to claim 13, said protein being fewer than 400 amino acid residues in length.

~~4. The modified Rv3616c protein according to claim 1, comprising the amino acid sequence of SEQ ID No: 163, 165-169, 179 or 180.~~

~~5. The modified Rv3616c protein according to claim 1, comprising the amino acid sequence of SEQ ID No: 163, 165-167 or 169.~~

15. The modified Rv3616c protein according to any one of claims 1, 13 or 14, comprising the amino acid sequence of SEQ ID No: 163.

~~6~~16. The~~A~~ modified Rv3616c protein according to any one of claims 1, 13 or 14, comprising the amino acid sequence of SEQ ID No: 164.

17. The modified Rv3616c protein according to any one of claims 1, 13 or 14, comprising the amino acid sequence of SEQ ID No: 165.

18. The modified Rv3616c protein according to any one of claims 1, 13 or 14, comprising the amino acid sequence of SEQ ID No: 166.

19. The modified Rv3616c protein according to any one of claims 1, 13 or 14, comprising the amino acid sequence of SEQ ID No: 167.

20. The modified Rv3616c protein according to any one of claims 1, 13 or 14, comprising the amino acid sequence of SEQ ID No: 168.

21. The modified Rv3616c protein according to any one of claims 1, 13 or 14, comprising the amino acid sequence of SEQ ID No: 169.

22. The modified Rv3616c protein according to any one of claims 1, 13 or 14, comprising the amino acid sequence of SEQ ID No: 179.

23. The modified Rv3616c protein according to any one of claims 1, 13 or 14, comprising the amino acid sequence of SEQ ID No: 180.

24. The modified Rv3616c protein according to any one of claims 1 to 23, said protein consisting of:

(a) the amino acid sequence of SEQ ID No: 164, 179 or 180; or

(b) a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a sequence having at least 98% identity to residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a sequence having at least 98% identity to residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are directly linked or indirectly linked via a third polypeptide, said third polypeptide having at least 80% identity to a sequence corresponding to residues 135-154 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted.

~~7~~25. A polynucleotide comprising a nucleic acid sequence encoding a modified Rv3616c protein according to any one of claims 1 to ~~6~~24.

26. The polynucleotide according to claim 26, consisting of a nucleic acid sequence encoding a modified Rv3616c protein according to any one of claims 1 to 24.

~~8. The polynucleotide according to claim 7, comprising a nucleic acid sequence encoding a modified Rv3616c protein comprising the amino acid sequence of SEQ ID No: 163, 165-167 or 169.~~

27. The polynucleotide according to either claim 26 or 27, comprising a sequence encoding a polypeptide according to any one of SEQ ID Nos: 163 to 169.

28. The polynucleotide according to either claim 26 or 27, comprising a sequence encoding a polypeptide according to either of SEQ ID Nos: 179 or 180.

~~9~~29. A fusion protein comprising a modified Rv3616c protein according to any one of claims 1 to ~~6~~ 23 and an additional heterologous polypeptide.

~~10~~30. A polynucleotide encoding a fusion protein according to claim ~~9~~29.

~~11~~31. A host cell which recombinantly expresses a modified Rv3616c protein according to any one of claims 1 to ~~6~~ 23 or a fusion protein according to claim ~~10~~29.

32. Use of a modified Rv3616c protein according to any one of claims 1 to 24 in the manufacture of a medicament for the treatment, prevention or amelioration of TB.

~~12~~33. Use of a modified Rv3616c protein, or a polynucleotide comprising a nucleic acid sequence encoding it, in the manufacture of a medicament for the treatment of latent TB, wherein said modified Rv3616c protein is selected from:

(a) a modified Rv3616c protein comprising a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 175 amino acids within residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are either directly linked or indirectly linked via a third polypeptide, wherein said third polypeptide corresponds to residues 135-154 in SEQ ID No:1 in which at least 1 amino acid has been deleted; or

(b) a modified Rv3616c protein comprising a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 175 amino acids within residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are either directly linked or indirectly linked via a third polypeptide, wherein said third polypeptide corresponds to residues 135-154 in SEQ ID No:1 in which at least a contiguous portion of at least 3 amino acids has been deleted; or

(c) a modified Rv3616c protein comprising a Rv3616c sequence in which at least one amino acid has been deleted from the region corresponding to residues 134-183 in SEQ ID No:1; or

(d) a modified Rv3616c protein comprising a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-133 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 155 amino acids within residues 184-392 of SEQ ID No: 1;

wherein the first and second polypeptides are directly or indirectly linked via a third polypeptide, said third polypeptide corresponding to residues 134-183 in SEQ ID No:1 in which at least 1 amino acid has been deleted; or

(e) a modified Rv3616c protein comprising a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-133 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 155 amino acids within residues 184-392 of SEQ ID No: 1;

wherein the first and second polypeptides are directly or indirectly linked via a third polypeptide, said third polypeptide corresponding to residues 134-183 in SEQ ID No:1 in which at least a contiguous portion of at least 3 amino acids has been deleted; or

(f) a modified Rv3616c protein comprising a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 175 amino acids within residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are either directly linked or indirectly linked via a third polypeptide, wherein said third polypeptide corresponds to residues 135-154 in SEQ ID No:1 in which at least 1 amino acid has been deleted; or

(g) a modified Rv3616c protein comprising a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 175 amino acids within residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are either directly linked or indirectly linked via a third polypeptide, wherein said third polypeptide corresponds to residues 135-154 in SEQ ID No:1 in which at least a contiguous portion of at least 3 amino acids has been deleted; or

(h) a modified Rv3616c protein comprising a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a sequence having at least 90% identity to residues 1-133 of SEQ ID No: 1; and

(ii) the second polypeptide is a sequence having at least 90% identity to residues 184-392 of SEQ ID No: 1;

wherein the first and second polypeptides are directly linked or indirectly linked via a third polypeptide, said third polypeptide having at least 90% identity to a sequence corresponding to residues 134-183 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted; or

(i) a modified Rv3616c protein comprising a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a sequence having at least 90% identity to residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a sequence having at least 90% identity to residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are directly linked or indirectly linked via a third polypeptide, said third polypeptide having at least 80% identity to a sequence corresponding to residues 135-154 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted.

13. The use according to claim 12, wherein the modified Rv3616c protein comprises a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 175 amino acids within residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are either directly linked or indirectly linked via a third polypeptide, wherein said third polypeptide corresponds to residues 135-154 in SEQ ID No:1 in which at least 1 amino acid has been deleted.

14. The use according to claim 12, wherein the modified Rv3616c protein comprises a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 175 amino acids within residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are either directly linked or indirectly linked via a third polypeptide, wherein said third polypeptide corresponds to residues 135-154 in SEQ ID No:1 in which at least a contiguous portion of at least 3 amino acids has been deleted.

15. The use according to claim 12, wherein the modified Rv3616c protein comprises a Rv3616c sequence in which at least one amino acid has been deleted from the region corresponding to residues 134-183 in SEQ ID No:1.

16. The use according to claim 17, said protein comprising a Rv3616c sequence in which at least two amino acids have been deleted from the region corresponding to residues 134-183 in SEQ ID No:1.

17. The use according to claim 16, said protein comprising a Rv3616c sequence in which at least one amino acid has been deleted from the region corresponding to residues 135-154 in SEQ ID No:1.

18. The use according to claim 16, said protein comprising a Rv3616c sequence in which at least two amino acids have been deleted from the region corresponding to residues 135-154 in SEQ ID No:1.

19. The use according to claim 12, wherein the modified Rv3616c protein comprises a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-133 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 155 amino acids within residues 184-392 of SEQ ID No: 1;

wherein the first and second polypeptides are directly or indirectly linked via a third polypeptide, said third polypeptide corresponding to residues 134-183 in SEQ ID No:1 in which at least 1 amino acid has been deleted.

20. The use according to claim 12, wherein the modified Rv3616c protein comprises a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-133 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 155 amino acids within residues 184-392 of SEQ ID No: 1;

wherein the first and second polypeptides are directly or indirectly linked via a third polypeptide, said third polypeptide corresponding to residues 134-183 in SEQ ID No:1 in which at least a contiguous portion of at least 3 amino acids has been deleted.

21. The use according to claim 12, wherein the modified Rv3616c protein comprises a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 175 amino acids within residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are either directly linked or indirectly linked via a third polypeptide, wherein said third polypeptide corresponds to residues 135-154 in SEQ ID No:1 in which at least 1 amino acid has been deleted.

22. The use according to claim 12, wherein the modified Rv3616c protein comprises a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a contiguous sequence of at least 100 amino acids within residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a contiguous sequence of at least 175 amino acids within residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are either directly linked or indirectly linked via a third polypeptide, wherein said third polypeptide corresponds to residues 135-154 in SEQ ID No:1 in which at least a contiguous portion of at least 3 amino acids has been deleted.

23. The use according to claim 12, wherein the modified Rv3616c protein comprises a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a sequence having at least 90% identity to residues 1-133 of SEQ ID No: 1; and

(ii) the second polypeptide is a sequence having at least 90% identity to residues 184-392 of SEQ ID No: 1;

wherein the first and second polypeptides are directly linked or indirectly linked via a third polypeptide, said third polypeptide having at least 90% identity to a sequence corresponding to residues 134-183 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted.

24. The use according to claim 23, wherein the first polypeptide has at least 95% identity to residues 1-133 of SEQ ID No: 1.

25. The use according to either claim 23 or 24, wherein the second polypeptide has at least 95% identity to residues 184-392 of SEQ ID No: 1.

26. The use according to any one of claims 23 to 25, wherein the peptide linkage is direct.

27. The use according to any one of claims 23 to 25, wherein the peptide linkage is indirect.

28. The use according to claim 27, wherein the third polypeptide is a sequence having at least 95% identity to a sequence corresponding to residues 134-183 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted.

29. The use according to claim 12, wherein the modified Rv3616c protein comprises a first polypeptide and a second polypeptide, the first polypeptide being located towards the N-terminus relative to the second polypeptide, and wherein:

(i) the first polypeptide is a sequence having at least 90% identity to residues 1-134 of SEQ ID No: 1; and

(ii) the second polypeptide is a sequence having at least 90% identity to residues 155-392 of SEQ ID No: 1;

wherein the first and second polypeptides are directly linked or indirectly linked via a third polypeptide, said third polypeptide having at least 80% identity to a sequence corresponding to residues 135-154 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted.

30. The use according to claim 29, wherein the first polypeptide has at least 95% identity to residues 1-134 of SEQ ID No: 1.

31. The use according to claim 30, wherein the first polypeptide has at least 98% identity to residues 1-134 of SEQ ID No: 1.

32. The use according to any one of claims 29 to 31, wherein the second polypeptide has at least 95% identity to residues 155-392 of SEQ ID No: 1.

33. The use according to claim 32, wherein the second polypeptide has at least 98% identity to residues 155-392 of SEQ ID No: 1.

34. The use according to any one of claims 29 to 33, wherein the peptide linkage is direct.

35. The use according to any one of claims 29 to 33, wherein the peptide linkage is indirect.

36. The use according to claim 35, wherein the third polypeptide is a sequence having at least 95% identity to a sequence corresponding to residues 135-154 in SEQ ID No:1 in which a contiguous portion of at least 3 amino acids has been deleted.

~~37~~34. The use according to ~~any one of claims 12 to 36~~claim 33 wherein the modified Rv3616c protein is fewer than 500 amino acid residues in length.

~~38~~35. The use according to any one of claims 33 or 34~~12 to 37~~, wherein a modified Rv3616c protein is used in the manufacture of the medicament.

~~39~~36. The use according to any one of claims ~~12~~ 33 or 34~~to 37~~, wherein a polynucleotide comprising a nucleic acid sequence encoding the modified Rv3616c protein is used in the manufacture of the medicament.

~~40~~37. The use according to any one of claims ~~12~~ 33 to ~~39~~ 36 in the manufacture of a medicament for the prevention of reactivation of tuberculosis.

~~41~~38. The use according to any one of claims ~~12~~ 33 to ~~39~~36, in the manufacture of a medicament for the delay of reactivation of tuberculosis.