Claims

1. Vector expressible in a prokaryotic host cell comprising a mannose-inducible promoter of the mannose operon of *Bacillus subtilis* operably linked to a transcriptional unit comprising a heterologous nucleic acid sequence encoding a polypeptide.

2. Vector according to claim 1 wherein the vector comprises the complete or a partial sequence of the regulatory gene *manR*.

3. Vector according to claim 1 or 2 wherein said promoter is the *manP* promoter.

4. Vector according to any of claims 1 to 3, wherein the *manP* promoter comprises a sequence selected from SEQ ID NO. 1 and SEQ ID NO. 2, a sequence complementary thereto or variants thereof.

5. Vector according to claim 1 wherein said promoter is the *manR* promoter.

6. Vector according to claim 5, wherein the *manR* promoter comprises a sequence selected from of SEQ ID NO. 3, SEQ ID NO. 4, and SEQ ID NO. 5, a sequence complementary thereto or variants thereof.

7. Vector according to any one of the preceding claims, wherein the vector comprises upstream of the heterologous nucleic acid sequence a catabolite-responsive element.

8. Vector according to any one of preceding claims wherein the vector comprises a transcription termination sequence located downstream from the heterologous nucleic acid sequence.

9. Vector according to claim 8 wherein the transcription termination sequence is derived from the 3' region of the *tufA* gene of *Bacillus subtilis*.

10. Vector according to any one of the preceding claims wherein the vector is a shuttle vector replicable in *Escherichia coli* and *Bacillus subtilis*.

11. Vector according to any of the preceding claims wherein the vector comprises the replication origin of plasmid pUC18 and/or the pBS72 replicon or the *rep* gene together with the replication origin of plasmid pUB110.

12. Vector according to any one of the preceding claims wherein the heterologous nucleic acid sequence encodes an antibody or a fragment thereof.

13. Vector according to any of the preceding claims, wherein the transcription initiation region of *manP* gene or *manR* gene is replaced by the transcription inition region of another gene.

14. Vector according to claim 13, wherein the transcription initiation region of *manP* gene or *manR* gene is replaced by the transcription initiation region of *tufA* gene or *gsiB* gene.

15. An isolated and purified nucleic acid sequence of the mannose-inducible promoter region of the mannose operon of B*acillus subtilis,* sequence complementary thereto or variants thereof.

16. The isolated and purified nucleic acid sequence of claim 15, wherein the sequence comprises any of SEQ ID NOs 1 to 5, sequence complementary thereto or variants thereof.

17. Prokaryotic host cell transformed with the vector of any one of claims 1 to 14 or with a nucleic acid sequence according to any of the claims 15 or 16.

18. Prokaryotic host cell according to claim 17, wherein the prokaryotic host cell is subject to carbon catabolite repression and comprises a phosphoenole pyruvate: carbohydrate phosphortransferase system.

19. Prokaryotic host cell according to claims 17 or 18, wherein the prokaryotic host cell is Gram-positive.

20. Prokaryotic host cell according to any of the claims 18 to 19, wherein the host cell belongs to the phylum Firmicutes.

21. Method for producing a polypeptide in a prokaryotic host cell comprising the steps of constructing a vector according to any one of claims 1 to 14, transforming a prokaryotic host cell with said vector, allowing expression of said polypeptide by growing the transformed host cell in a cell culture medium under suitable conditions and recovering the polypeptide from the cells or from the cell culture.

22. Method according to claim 21 wherein the host cells are grown first in the presence of a carbon source different from the inducer, and then, in a second step, in the presence of the inducer.

23. Use of the vector of any one of claims 1 to 14 or of an isolated and purified nucleic acid sequence according to any of the claims 15 and 16, for the regulated expression of a heterologous nucleic acid sequence encoding a polypeptide in a prokaryotic host cell.

Claims

1. Vector expressible in a prokaryotic host cell comprising a mannose-inducible promoter of the mannose operon of *Bacillus subtilis* operably linked to a transcriptional unit comprising a heterologous nucleic acid sequence encoding a polypeptide, wherein the mannose-inducible promoter is selected from the *manP* promoter and *manR* promoter.

2. Vector according to claim 1 wherein the vector comprises the complete or a partial sequence of the regulatory gene *manR*.

3. Vector according to any of claims 1 or 2, wherein the *manP* promoter comprises a sequence selected from

SEQ ID NO. 1

tagggaaaaa tgcctttatt accggaacct atggtaaaaa aagcgatttt aatgagctga 60

tttcggtata cagttgagac aagatcttat tattcacact ttctagaaat aattttctta 120

agaaggagat atacatatga cac 143

and

SEQ ID NO. 2

tagggaaaaa tgcctttatt accggaacct atggtaaaaa aagcgatttt aatgagctga 60

tttcggtata cagttgagac 80,

a sequence complementary thereto or variants thereof.

4. Vector according to claim 1, wherein the *manR* promoter comprises a sequence selected from

SEQ ID NO. 3

tgaatttctg ctgaatatac attacatagc aaactcaaag agtataaaaa tcgctttttt 60

ccggaagctt cggtaaaaaa cgaaactttt gtctctatga ttttgtttta taatgtaaac 120

ggtttcttat atagtatact tatactatca atttgctcaa gtagatactg acaggcttaa 180

gaaggagata tacat 195,

SEQ ID NO. 4.

tgaatttctg ctgaatatac attacatagc aaactcaaag agtataaaaa tcgctttttt 60

ccggaagctt cggtaaaaaa cgaaactttt gtctctatga ttttgtttta taatgtaaac 120

ggtttctt 128

and

SEQ ID NO. 5

tgaatttctg ctgaatatac attacatagc aaactcaaag agtataaaaa tcgctttttt 60

ccggaagctt cggtaaaaaa cgaaactttt gtctctatga ttttgtttta taatgtaaac 120

g 121,

a sequence complementary thereto or variants thereof.

5. Vector according to any one of the preceding claims, wherein the vector comprises upstream of the heterologous nucleic acid sequence a catabolite-responsive element.

6. Vector according to any one of preceding claims wherein the vector comprises a transcription termination sequence located downstream from the heterologous nucleic acid sequence.

7. Vector according to claim 6 wherein the transcription termination sequence is derived from the 3' region of the *tufA* gene of *Bacillus subtilis*.

8. Vector according to any one of the preceding claims wherein the vector is a shuttle vector replicable in *Escherichia coli* and *Bacillus subtilis*.

9. Vector according to any of the preceding claims wherein the vector comprises the replication origin of plasmid pUC18 and/or the pBS72 replicon or the *rep* gene together with the replication origin of plasmid pUB110.

10. Vector according to any one of the preceding claims wherein the heterologous nucleic acid sequence encodes an antibody or a fragment thereof.

11. Vector according to any of the preceding claims, wherein the transcription initiation region of *manP* gene or *manR* gene is replaced by the transcription initiation region of another gene.

12. Vector according to claim 11, wherein the transcription initiation region of *manP* gene or *manR* gene is replaced by the transcription initiation region of *tufA* gene or *gsiB* gene.

13. An isolated and purified nucleic acid sequence of the mannose-inducicle promoter region of the mannose operon of *Bacillus subtilis*, sequence complementary thereto or variants thereof, wherein the mannose-inducible promoter is selected from the *manP* promoter and *manR* promoter.

14. The isolated and purified nucleic acid sequence according to claim 13, wherein the sequence comprises any of

SEQ ID NO. 1

tagggaaaaa tgcctttatt accggaacct atggtaaaaa aagcgatttt aatgagctga 60

tttcggtata cagttgagac aagatcttat tattcacact ttctagaaat aatttttcta 120

agaaggagat atacatatga cac 143,

SEQ ID NO. 2

tagggaaaaa tgcctttatt accggaacct atggtaaaaa aagcgatttt aatgagctga 60

tttcggtata cagttgagac 80,

SEQ ID NO. 3

tgaatttctg ctgaatatac attacatagc aaactcaaag agtataaaaa tcgcttttt 60

ccggaagctt cggtaaaaaa cgaaactttt gtctctatga tttgtttta taatgtaaac 120

ggtttcttat atagtatact tatactatca atttgctcaa gtagatactg acaggcttaa 180

gaaggagata tacat 195,

SEQ ID NO. 4.

tgaatttctg ctgaatatac attacatagc aaactcaaag agtataaaaa tcgcttttt 60

ccggaagctt cggtaaaaaa cgaaactttt gtctctatga tttgtttta taatgtaaac 120

ggtttctt 128

and

SEQ ID NO. 5

tgaatttctg ctgaatatac attacatagc aaactcaaag agtataaaaa tcgctttttt 60

ccggaagctt cggtaaaaaa cgaaactttt gtctctatga ttttgtttta taatgtaaac 120

g 121,

sequence complementary thereto or variants thereof.

15. Prokaryotic host cell transformed with the vector of any one of claims 1 to 12 or with a nucleic acid sequence according to claim 13 or 14.

16. Prokaryotic host cell according to claim 15, wherein the prokaryotic host cell is subject to carbon catabolite repression and comprises a phosphoenole pyruvate: carbohydrate phosphortransferase system.

17. Prokaryotic host cell according to claims 15 or 16, wherein the prokaryotic host cell is Gram-positive.

18. Prokaryotic host cell according to any of the claims 16 to 17, wherein the host cell belongs to the phylum Firmicutes.

19. Method for producing a polypeptide in a prokaryotic host cell comprising the steps of constructing a vector according to any one of claims 1 to 12, transforming a prokaryotic host cell with said vector, allowing expression of said polypeptide by growing the transformed host cell in a cell culture medium under suitable conditions and recovering the polypeptide from the cells or from the cell culture.

20. Method according to claim 19 wherein the host cells are grown first in the presence of a carbon source different from the inducer, and then, in a second step, in the presence of the inducer.

21. Use of the vector of any one of claims 1 to 12 or of an isolated and purified nucleic acid sequence according to claim 13 or 14, for the regulated expression of a heterologous nucleic acid sequence encoding a polypeptide in a prokaryotic host cell.