Claims:

1. A recombinant gram-negative bacterial cell comprising:

   a. a mutant spr gene encoding a spr protein having a mutation at one or more amino acids selected from D133, H145, H157, N31, R62, I70, Q73, C94, S95, V98, Q99, R100, L108, Y115, V135, L136, G140, R144 and G147 and

   b. a gene capable of expressing or overexpressing one or more proteins capable of facilitating protein folding, such as FkpA, Skp, SurA, PPiA and PPiD

wherein the cell has reduced Tsp protein activity compared to a wild-type cell.

2. A cell according to claim 1, wherein the mutant spr gene encodes an spr protein having one or more mutations selected from D133A, H145A, H157A, N31Y, R62C, I70T, Q73R, C94A, S95F, V98E, Q99P, R100G, L108S, Y115F, V135D, V135G, L136P, G140C, R144C and G147C.

3. A cell according to claim 2, wherein the mutant spr gene encodes an spr protein having one or more mutations selected from S95F, V98E, Y115F, D133A, V135D, V135G and G147C.

4. A cell according to clam 3, wherein the mutant spr gene encodes a spr protein having the mutations C94 and H145A, such as C94.

5. A cell according to claim 2, wherein the mutant spr gene encodes a spr protein having a mutation selected from D133A, H145A and H157A.

6. A cell according to claim 1, wherein the mutant spr gene encodes a spr protein having a mutation selected from C94A.

7. A cell according to any preceding claim, wherein the mutant spr gene is integrated in to the genome of the cell.

8. A cell according to any preceding claim wherein a gene encoding a protein capable of facilitating protein folding are transiently transfected into the cell, for example on a plasmid.

9. A cell according to any one of claims 1 to 7 wherein a gene encoding a protein capable of facilitating protein folding is integrated in to the cells genome.

10. A cell according to any preceding claim wherein the protein capable of facilitating protein folding is FkpA, Skp or a combination of FkpA and Skp, in particular FkpA.

11. A cell according to any preceding claim, wherein the cell further comprises one or more of the following mutated genes:

a. a mutated DegP gene encoding a DegP protein having chaperone activity and reduced protease activity;

b. a mutated ptr gene, wherein the mutated ptr gene encodes a Protease III protein having reduced protease activity or is a knockout mutated ptr gene; and

c. a mutated OmpT gene, wherein the mutated OmpT gene encodes a OmpT protein having reduced protease activity or is a knockout mutated OmpT gene.

12. A cell according to any preceding claim, wherein the cell comprises a mutated Tsp gene encoding a Tsp protein having reduced protease activity or is a knockout mutated Tsp gene.

13. A cell according to claim 12, wherein the cell's genome is isogenic to a wild-type bacterial cell except for the mutated spr gene and the mutated Tsp gene.

14. A cell according to any preceding claim wherein the cell does not comprise a gene encoding DsbC.

15. A recombinant gram-negative bacterial cell having reduced Tsp protein activity compared to a wild-type cell, and a mutant spr gene encoding a spr protein capable of suppressing the phenotype of a cell comprising a mutated Tsp gene and a gene encoding FkpA, Skp or a combination of FkpA and Skp, in particular FkpA suitable for expressing a protein capable of facilitating protein folding, wherein the cell's genome is isogenic to a wild-type bacterial cell except for the modification required to reduce Tsp protein activity compared to a wild-type cell and the mutated spr gene.

16. A cell according to claim 15, wherein the mutant spr gene encodes a spr protein having one or more mutations selected from N31Y, R62C, I70T, Q73R, C94A, S95F, V98E, Q99P, R100G, L108S, Y115F, D133A, V135D, V135G, L136P, G140C, R144C, H145A, G147C, H157A and W174R.

17. A cell according to claim 15, wherein the mutant spr gene encodes a spr protein having one of more mutations as defined in any of claims 1 to 6.

18. A cell according to any preceding claim, wherein the cell has a knockout mutated Tsp gene which comprises a mutation to the gene start codon and/or one or more stop codons positioned downstream of the gene start codon and upstream of the gene stop codon.

19. A cell according to claim 18, wherein the knockout mutated Tsp gene comprises a restriction marker site created by a missense mutation to the gene start codon and optionally one or more further point mutations.

20. A cell according to claim 19, wherein the knockout mutated Tsp gene comprises SEQ ID NO:3.

21. A cell according to any preceding claim, wherein the cell is E. coli, for example wherein the E coli is strain K12 or W3110.

22. A cell according to any preceding claim, wherein the cell comprises a polynucleotide sequence encoding a protein of interest.

23. A cell according to claim 21, wherein the protein of interest is an antibody or an antigen binding fragment thereof.

24. A cell according to claim 22, wherein the antibody or antigen binding fragment thereof is specific for FcRn.

25. A recombinant gram-negative bacterial cell having reduced Tsp protein activity compared to a wild-type cell and comprising a mutant spr gene encoding a mutant spr protein and a gene encoding a gene suitable for expressing a protein capable of facilitating protein folding and a polynucleotide sequence encoding an antibody or an antigen binding fragment thereof specific for FcRn.

26. A cell according to claim 25, wherein the cell comprises a mutated Tsp gene encoding a Tsp protein having reduced protease activity or a knockout mutated Tsp gene.

27. A method for producing a protein of interest comprising culturing a recombinant gram-negative bacterial cell as defined in any of claims 1 to 26 in a culture medium under conditions effective to express the recombinant protein of interest and recovering the recombinant protein of interest from the periplasm of the recombinant gram-negative bacterial cell and/or the culture medium.

28. A method according to claim 27, wherein the method further comprises recovering the protein of interest from the cell.

29. A method according to claim 28, wherein the protein of interest is recovered from the periplasm and/or the supernatant.

Claims:

1. A recombinant gram-negative bacterial cell comprising:

   a. a mutant spr gene encoding a spr protein having a mutation at one or more amino acids selected from D133, H145, H157, N31, R62, I70, Q73, C94, S95, V98, Q99, R100, L108, Y115, V135, L136, G140, R144 and G147 and

   b. a gene capable of expressing or overexpressing one or more proteins capable of facilitating protein folding, selected from FkpA and Skp

wherein the cell has reduced Tsp protein activity compared to a wild-type cell, and

wherein the cell does not comprise a recombinant polynucleotide encoding DsbC.

2. A cell according to claim 1, wherein the mutant spr gene encodes an spr protein having one or more mutations selected from D133A, H145A, H157A, N31Y, R62C, I70T, Q73R, C94A, S95F, V98E, Q99P, R100G, L108S, Y115F, V135D, V135G, L136P, G140C, R144C and G147C.

3. A cell according to claim 2, wherein the mutant spr gene encodes an spr protein having one or more mutations selected from S95F, V98E, Y115F, D133A, V135D, V135G and G147C.

4. A cell according to clam 3, wherein the mutant spr gene encodes a spr protein having the mutations C94 and H145A, such as C94.

5. A cell according to claim 2, wherein the mutant spr gene encodes a spr protein having a mutation selected from D133A, H145A and H157A.

6. A cell according to claim 1, wherein the mutant spr gene encodes a spr protein having a mutation selected from C94A.

7. A cell according to any preceding claim, wherein the mutant spr gene is integrated in to the genome of the cell.

8. A cell according to any preceding claim wherein a gene encoding a protein capable of facilitating protein folding are transiently transfected into the cell, for example on a plasmid.

9. A cell according to any one of claims 1 to 7 wherein a gene encoding a protein capable of facilitating protein folding is integrated in to the cells genome.

10. A cell according to any preceding claim wherein the protein capable of facilitating protein folding is FkpA, Skp or a combination of FkpA and Skp, in particular FkpA.

11. A cell according to any preceding claim, wherein the cell further comprises one or more of the following mutated genes:

a. a mutated DegP gene encoding a DegP protein having chaperone activity and reduced protease activity;

b. a mutated ptr gene, wherein the mutated ptr gene encodes a Protease III protein having reduced protease activity or is a knockout mutated ptr gene; and

c. a mutated OmpT gene, wherein the mutated OmpT gene encodes a OmpT protein having reduced protease activity or is a knockout mutated OmpT gene.

12. A cell according to any preceding claim, wherein the cell comprises a mutated Tsp gene encoding a Tsp protein having reduced protease activity or is a knockout mutated Tsp gene.

13. A cell according to claim 12, wherein the cell's genome is isogenic to a wild-type bacterial cell except for the mutated spr gene and the mutated Tsp gene.

14. A recombinant gram-negative bacterial cell having reduced Tsp protein activity compared to a wild-type cell, and a mutant spr gene encoding a spr protein capable of suppressing the phenotype of a cell comprising a mutated Tsp gene and a gene encoding FkpA, Skp or a combination of FkpA and Skp, in particular FkpA suitable for expressing a protein capable of facilitating protein folding, wherein the cell's genome is isogenic to a wild-type bacterial cell except for the modification required to reduce Tsp protein activity compared to a wild-type cell and the mutated spr gene and wherein the cell does not comprise a recombinant polynucleotide encoding DsbC.

15. A cell according to claim 14, wherein the mutant spr gene encodes a spr protein having one or more mutations selected from N31Y, R62C, I70T, Q73R, C94A, S95F, V98E, Q99P, R100G, L108S, Y115F, D133A, V135D, V135G, L136P, G140C, R144C, H145A, G147C, H157A and W174R.

16. A cell according to claim 14, wherein the mutant spr gene encodes a spr protein having one of more mutations as defined in any of claims 1 to 6.

17. A cell according to any preceding claim, wherein the cell has a knockout mutated Tsp gene which comprises a mutation to the gene start codon and/or one or more stop codons positioned downstream of the gene start codon and upstream of the gene stop codon.

18. A cell according to claim 17, wherein the knockout mutated Tsp gene comprises a restriction marker site created by a missense mutation to the gene start codon and optionally one or more further point mutations.

19. A cell according to claim 18, wherein the knockout mutated Tsp gene comprises SEQ ID NO:3.

20. A cell according to any preceding claim, wherein the cell is *E. coli*, for example wherein the E coli is strain K12 or W3110.

21. A cell according to any preceding claim, wherein the cell comprises a polynucleotide sequence encoding a protein of interest.

22. A cell according to claim 21, wherein the protein of interest is an antibody or an antigen binding fragment thereof.

23. A cell according to claim 22, wherein the antibody or antigen binding fragment thereof is specific for FcRn.

24. A recombinant gram-negative bacterial cell having reduced Tsp protein activity compared to a wild-type cell and comprising a mutant spr gene encoding a mutant spr protein and a gene encoding a gene suitable for expressing a protein capable of facilitating protein folding and a polynucleotide sequence encoding an antibody or an antigen binding fragment thereof specific for FcRn, wherein the cell does not comprise a recombinant nucleotide encoding DsbC.

25. A cell according to claim 24, wherein the cell comprises a mutated Tsp gene encoding a Tsp protein having reduced protease activity or a knockout mutated Tsp gene.

26. A method for producing a protein of interest comprising culturing a recombinant gram-negative bacterial cell as defined in any of claims 1 to 25 in a culture medium under conditions effective to express the recombinant protein of interest and recovering the recombinant protein of interest from the periplasm of the recombinant gram-negative bacterial cell and/or the culture medium.

27. A method according to claim 26, wherein the method further comprises recovering the protein of interest from the cell.

28. A method according to claim 27, wherein the protein of interest is recovered from the periplasm and/or the supernatant.