

Claims

1. A recombinant signal sequence comprising (a) the sequence MGRISGG (SEQ ID NO: 1) or a variant thereof that differs in sequence by 1 amino acid substitution, deletion or insertion, and (b) a heterologous signal sequence C-terminal to (a).
2. A recombinant fusion protein comprising (a) the recombinant signal sequence of claim 1; and (b) a heterologous recombinant protein C-terminal to (a).
3. A recombinant nucleic acid sequence which encodes the recombinant signal sequence of claim 1 or the recombinant fusion protein as defined in claim 2.
4. The recombinant nucleic acid sequence of claim 3 which encodes the recombinant signal sequence, wherein the nucleic acid sequence has been codon optimised for expression in a host cell.
5. The recombinant nucleic acid sequence of claim 4, wherein the codon optimised nucleic acid sequence encodes a signal sequence comprising the sequence MGRISGGMKKTAIAIAVALAGFATVAQA (SEQ ID NO: 55), or a variant thereof that differs in sequence by 1, 2, or 3 amino acid substitutions, deletions or insertions.
6. The recombinant nucleic acid sequence of any one of claims 3 to 5, wherein the nucleic acid sequence has been codon optimised for expression in a host cell and has a Codon Adaptation Index (CAI) of 0.40 or above.
7. A recombinant expression vector comprising the nucleic acid sequence of any one of claims 3 to 6.
8. The recombinant expression vector according to claim 7 comprising the recombinant nucleic acid sequence of the recombinant fusion protein of claims 3 or 6, wherein the nucleic acid sequence encoding the recombinant signal sequence is operably linked to the nucleic acid sequence encoding the recombinant fusion protein.
9. A method for producing a recombinant protein in a host cell comprising:

(a) culturing the host cell under conditions that allow expression of the recombinant protein from the recombinant expression vector according to claim 7 comprising the recombinant nucleic acid sequence of the recombinant fusion protein of claims 3 or 6, or claim 8 present in the host cell; and

(b) recovering the recombinant protein.

10. A method for lowering the viscosity of a host cell broth that expresses a recombinant protein, comprising:

culturing the host cell under conditions that allow expression of the recombinant protein, wherein the host cell comprises a recombinant nucleic acid sequence which encodes (i) a recombinant signal sequence comprising the sequence MGRISGG (SEQ ID NO: 1) or a variant thereof that differs in sequence by 1 amino acid substitution, deletion or insertion, and (ii) the recombinant protein.

11. A method for lowering basal expression of a recombinant protein expressed by a host cell broth, comprising: culturing the host cell under pre-induction conditions,

wherein the host cell comprises a recombinant nucleic acid sequence which encodes (i) a recombinant signal sequence comprising the sequence MGRISGG (SEQ ID NO: 1) or a variant thereof that differs in sequence by 1 amino acid substitution, deletion or insertion, and (ii) the recombinant protein.

12. The method according to claim 10 or 11 wherein the nucleic acid sequence is as defined in claim 3 or 6.

13. The method according to any one of claims 9 to 12, wherein the recombinant protein is recovered from the periplasm or the extracellular media.

14. The method according to any one of claims 9 to 13, wherein the signal sequence is operably linked to the recombinant protein.

15. The method according to any one of claims 9 to 14, wherein a pre-induction expression level of the recombinant protein is $\leq 0.5\text{g/L}$; and/or a post-induction expression level of the recombinant protein is $\geq 5\text{g/L}$.

16. The method according to any one of claims 9 to 15, wherein the signal sequence is cleaved from the recombinant protein.

17. The method according to any one of claims 9 to 16, wherein the recombinant protein is an antigen binding protein.

18. The method according to any one of claims 9 to 17, wherein the host cell is a microbial cell with a periplasm.