

Claims

1. A recombinant signal sequence comprising (a) the sequence MGRISGG (SEQ ID NO: 1) 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 MGRISGGMKKTAIAI AVALAGFATVAQA (SEQ ID NO: 55).
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 claim 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 claim 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 (a) the sequence MGRISGG (SEQ ID NO: 1) and (b) a heterologous signal sequence C-terminal to (a), 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 (a) the sequence MGRISGG (SEQ ID NO: 1) and (b) a heterologous signal sequence C-terminal to (a), and (ii) the recombinant protein.

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