Claims

1. A method of increasing the yield of a protein of interest in a eukaryotic host cell, comprising overexpressing in said host cell at least one polynucleotide encoding at least one protein which is involved in lipid metabolism, thereby increasing the yield of said protein of interest in comparison to a host cell which does not overexpress a polynucleotide encoding a protein which is involved in lipid metabolism,
   wherein said protein which is involved in lipid metabolism is involved in sphingolipid biosynthesis and comprises an amino acid sequence as shown in SEQ ID NO: 1 or a homologue thereof having at least 70% sequence identity to an amino acid sequence as shown in SEQ ID NO: 1.

2. A method of manufacturing a protein of interest according to claim 1 comprising:
   - providing the host cell engineered to overexpress at least one polynucleotide encoding at least one protein, wherein said protein which is involved in lipid metabolism is involved in sphingolipid biosynthesis and comprises an amino acid sequence as shown in SEQ ID NO: 1 or a homologue thereof, wherein the homologue has at least 70% sequence identity to an amino acid sequence as shown in SEQ ID NO: 1, wherein said host cell comprises a heterologous polynucleotide encoding a protein of interest;
   - culturing the host cell under suitable conditions to overexpress the protein involved in lipid metabolism or homologue thereof and to express said protein of interest; and optionally
   - isolating said protein of interest from the cell culture.

3. The method of claim 1, wherein at least one polynucleotide encoding a protein involved in lipid transport is also overexpressed, wherein said protein involved in lipid transport comprises an amino acid sequence as shown in SEQ ID NO: 11 or a homologue thereof, wherein the homologue has at least 70% sequence identity to an amino acid sequence as shown in SEQ ID NO: 11, or

   wherein at least one polynucleotide encoding a chaperone is also overexpressed, wherein said chaperone comprises an amino acid sequence as shown in SEQ ID NO: 18 or a

homologue thereof, wherein the homologue thereof comprises at least 70% sequence identity to an amino acid sequence as shown in SEQ ID NO: 18.

4. The method of claim 2, wherein at least one polynucleotide encoding a protein involved in lipid transport is also overexpressed, wherein said protein involved in lipid transport comprises an amino acid sequence as shown in SEQ ID NO: 11 or a homologue thereof, wherein the homologue has at least 70% sequence identity to an amino acid sequence as shown in SEQ ID NO: 11, or

wherein at least one polynucleotide encoding a chaperone is also overexpressed, wherein said chaperone comprises an amino acid sequence as shown in SEQ ID NO: 18 or a homologue thereof, wherein the homologue thereof comprises at least 70% sequence identity to an amino acid sequence as shown in SEQ ID NO: 18.

5. The method of claim1 wherein the host cell is selected from the group consisting of *Pichia pastoris, Hansenula polymorpha, Trichoderma reesei, Saccharomyces cerevisiae, Kluyveromyces lactis, Yarrowia lipolytica, Pichia methanolica, Candida boidinii, Komagataella sp., Aspergillus sp.* and *Schizosaccharomyces pombe*.

6. The method of claim 2 wherein the host cell is selected from the group consisting of *Pichia pastoris, Hansenula polymorpha, Trichoderma reesei, Saccharomyces cerevisiae, Kluyveromyces lactis, Yarrowia lipolytica, Pichia methanolica, Candida boidinii, Komagataella sp., Aspergillus sp.* and *Schizosaccharomyces pombe*.

7. The method of claim 1, wherein said protein of interest is a non-membrane protein of interest.

8. The method of claim 7, wherein said non-membrane protein of interest is any one of an enzyme, a therapeutic protein, a food additive or feed additive.

9. The method of claim 8, wherein said therapeutic protein comprises an antibody or an antibody fragment still having the activity of binding its antigen.

10. The method of claim 1, wherein said protein involved in sphingolipid biosynthesis or homologue thereof increases the yield of the model protein HyHEL (SEQ ID NO: 39 for

heavy chain and SEQ ID NO: 40 for light chain) compared to the host cell prior to engineering by at least 10%, at least 15%, at least 20%, at least 25%, or at least 30%.

11. The method of claim 2, wherein said protein of interest is a non-membrane protein of interest.

12. The method of claim 11, wherein said non-membrane protein of interest is any one of an enzyme, a therapeutic protein, a food additive or feed additive.

13. The method of claim 12, wherein said therapeutic protein comprises an antibody or an antibody fragment still having the activity of binding its antigen.

14. The method of claim 2, wherein said protein involved in sphingolipid biosynthesis or homologue thereof increases the yield of the model protein HyHEL (SEQ ID NO: 39 for heavy chain and SEQ ID NO: 40 for light chain) compared to the host cell prior to engineering by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%.

15. A recombinant eukaryotic host cell for manufacturing a protein of interest, wherein the host cell is engineered to overexpress at least one polynucleotide encoding at least one protein which is involved in lipid metabolism,
wherein said protein which is involved in lipid metabolism is involved in sphingolipid biosynthesis and comprises an amino acid sequence as shown in SEQ ID NO: 1 or a homologue thereof, wherein the homologue has at least 70% sequence identity to an amino acid sequence as shown in SEQ ID NO: 1.

16. The recombinant eukaryotic host cell of claim 15, wherein at least one polynucleotide encoding a protein involved in lipid transport is also overexpressed, wherein said protein involved in lipid transport comprises an amino acid sequence as shown in SEQ ID NO: 11 or a homologue thereof, wherein the homologue has at least 70% sequence identity to an amino acid sequence as shown in SEQ ID NO: 11, or

wherein at least one polynucleotide encoding a chaperone is also overexpressed, wherein said chaperone comprises an amino acid sequence as shown in SEQ ID NO: 18 or a homologue thereof, wherein the homologue thereof comprises at least 70% sequence identity to an amino acid sequence as shown in SEQ ID NO: 18.

17. The recombinant eukaryotic host cell of claim 15, wherein the host cell is selected from the group consisting of *Pichia pastoris, Hansenula polymorpha, Trichoderma reesei, Saccharomyces cerevisiae, Kluyveromyces lactis, Yarrowia lipolytica, Pichia methanolica, Candida boidinii, Komagataella sp., Aspergillus sp.* and *Schizosaccharomyces pombe*.

18. The recombinant eukaryotic host cell of claim 15, wherein said protein of interest is a non-membrane protein of interest.

19. The recombinant eukaryotic host cell of claim 18, wherein said non-membrane protein of interest is any one of an enzyme, a therapeutic protein, a food additive or feed additive.

20. The recombinant eukaryotic host cell of claim 19, wherein said therapeutic protein comprises an antibody or an antibody fragment still having the activity of binding its antigen.

21. The recombinant eukaryotic host cell of claim 15, wherein said protein involved in sphingolipid biosynthesis or homologue thereof increases the yield of the model protein HyHEL (SEQ ID NO: 39 for heavy chain and SEQ ID NO: 40 for light chain) compared to the host cell prior to engineering by at least 10%, at least 15%, at least 20%, at least 25%, or at least 30%.