CLAIMS

1. A *Komagataella pfaffii* host cell engineered to produce a heterologous protein of interest (POI), which cell is genetically modified to reduce production of

an endogenous host cell protein which comprises the amino acid sequence comprising at least 90% sequence identity to SEQ ID NO:1, (HCP1).

2. The host cell of claim 1, wherein the cell is further genetically modified additionally reduce one or both of the endogenous host cell proteins which are:

a) an endogenous host cell protein comprising the amino acid sequence comprising at least 90% sequence identity to SEQ ID NO:3, (HCP2);
b) an endogenous host cell protein comprising the amino acid sequence comprising at least 90% sequence identity to SEQ ID NO:5, (HCP3).

3. The host cell of claim 1 or 2, wherein the cell is further genetically modified to additionally reduce production of an endogenous host cell protein which is

a) an endogenous host cell protein comprising the amino acid sequence comprising at least 90% sequence identity to SEQ ID NO:7, (HCP4).

4. The host cell of any of claims 1 to 3, wherein the cell is genetically modified to reduce the amount of HCP1 in the supernatant of a cell culture of the host cell by at least 10% (mol/mol) compared to the host cell without the genetic modification.

5. The host cell of any of claims 1 to 4, wherein the host cell is genetically modified to reduce the respective endogenous host cell protein by one or more genetic modifications of the host cell genome comprising a disruption, substitution, deletion or knockout of (i) one or more endogenous polynucleotides, or a part thereof; or (ii) an expression control sequence.

6. The host cell of claim 5, wherein the expression control sequence is selected from the group consisting of a promoter, a ribosomal binding site, transcriptional or translational start and stop sequences, an enhancer and activator sequence.

7. The host cell of any one of claims 1 to 6, wherein the host cell is genetically modified to reduce the respective endogenous host cell protein by one or more genetic modifications which comprise a knockout of a gene encoding the respective endogenous host cell protein.

8. The host cell of any one of claims 1 to 7, wherein the host cell is genetically modified to reduce the respective endogenous host cell protein by at least 50% (mol/mol) compared to the host cell without said modification.

9. The host cell of claim 8, wherein the host cell is genetically modified to knockout a gene encoding the respective host cell protein.

10 The host cell of any one of claims 1 to 9, which comprises an expression cassette comprising one or more regulatory nucleic acid sequences operably linked to a nucleotide sequence encoding the POI, wherein said one or more operably linked sequences are not naturally associated with the POI encoding sequence.

11. The host cell of any one of claims 1 to 10, wherein the POI is a peptide or protein selected from the group consisting of an antigen-binding protein, a therapeutic protein, an enzyme, a peptide, a protein antibiotic, a toxin fusion protein, a carbohydrate - protein conjugate, a structural protein, a regulatory protein, a vaccine antigen, a growth factor, a hormone, a cytokine, a process enzyme, and a metabolic enzyme.

12. A method for producing a protein of interest (POI) in a Komagataella host cell, comprising the steps:

a) a) genetically modifying the host cell to reduce production of an endogenous host cell protein which comprises the amino acid sequence comprising at least 90% sequence identity to SEQ ID NO:1, (HCP1); introducing into the host cell an expression cassette comprising one or more regulatory nucleic acid sequences operably linked to a nucleotide sequence encoding the POI;
b) culturing said host cell under conditions to produce said POI; and optionally
c) isolating said POI from the cell culture; and optionally

d) purifying said POI.

13. The method of claim 12, further comprising the step of genetically modifying the host cell to additionally reduce one or more of the endogenous host cell proteins which are:

a) an endogenous host cell protein comprising the amino acid sequence comprising at least 90% sequence identity to SEQ ID NO:3, (HCP2);
b) an endogenous host cell protein comprising the amino acid sequence comprising at least 90% sequence identity to SEQ ID NO:5, (HCP3);
c) an endogenous host cell protein comprising the amino acid sequence comprising at least 90% sequence identity to SEQ ID NO:7, (HCP4).

14. A method for producing a protein of interest (POI) by culturing the host cell of any one of claims 1 to 11 under conditions to produce said POI.

15. The method of any one of claims 12 to 14, wherein said genetically modifying comprises a genetic modification that reduces the amount of the respective endogenous host cell protein by at least 50% (mol/mol) compared to the host cell without said genetic modification.

16. The method of claim 15, wherein the genetic modification comprises a knockout of a gene encoding the respective endogenous host cell protein.

17. A method of reducing the risk of endogenous host cell protein contaminations of a protein of interest (POI) produced in a host cell culture, by culturing the host cell of any one of claims 1 to 11 under conditions to produce said POI and isolating the POI from said cell culture.