CLAIMS

1. A method of reducing batch-to-batch variation or increasing homogeneity between batches in the production of a recombinantly expressed polypeptide, the method comprising expressing the polypeptide in a Chinese hamster ovary (CHO) cell comprising (i) reduced UDP-galactose transporter activity and (ii) reduced GDP-fucose transporter activity, compared to a wild-type CHO cell.

2. A method according to Claim 1, in which the CHO cell comprises a loss of function mutation in a UDP-galactose transporter gene (Slc35a2), for example:

(a) comprising a T insertion at position 955 of the Slc35a2 open reading frame; or

(b) in which both alleles of a UDP-galactose transporter gene comprise a loss of function mutation.

3. A method according to Claim 1 or 2, in which the CHO cell comprises a loss of function mutation in a GDP-fucose transporter gene (Slc35c1 or Slc35c2), for example:

(a) in which both alleles of a GDP-fucose transporter gene comprise a loss of function mutation; or

(b) comprising a 3-nucleotide (GTA) insertion or a 4-nucleotide insertion at position 411 of Slc35c1.

4. A method according to Claim 1, 2 or 3, in which the CHO cell is comprised in a CHO-gmt9 cell line (deposited on 21 October 2014 at the American Type Culture Collection (ATCC), P.O. Box 1549, Manassas, Virginia 20108, United States of America under the Budapest Treaty as accession number PTA-121625).

5. A method according to any preceding claim, in which the CHO cell is capable of expressing recombinant antibodies for example tumour/cancer-targeting antibodies with enhanced antibody-dependent cellular cytotoxicity (ADCC).

6. A method according to any preceding claim, in which:

(a) homogeneity is assayed by detecting the number of peaks in a liquid chromatogram of *N*-glycans of a recombinant polypeptide expressed by a CHO cell comprising reduced UDP-galactose transporter activity and reduced GDP-fucose

transporter activity, as compared to a control comprising a liquid chromatogram of *N*-glycans of recombinant polypeptide expressed by wild type CHO-K1;

(b) a increase in homogeneity is detected as a reduction in the number of peaks as assayed in (a) above, for example to one peak compared to 3 peaks in the control;

(c) homogeneity is assayed by measuring the area under the peak of the major product (i.e., G0F) in a liquid chromatogram of *N*-glycans of a recombinantly expressed polypeptide as a percentage of the total area under the curve; or

(d) batch to batch variation is assayed by determining the ratio of the respective areas under the peaks of the products in a liquid chromatogram of *N*-glycans of a recombinantly expressed polypeptide.

7. A method according to any preceding claim, in which batch-to-batch variation is reduced and/or homogeneity is increased by 5% or more, 10% or more, 15% or more, 20% or more, 25% or more, 30% or more, 35% or more, 40% or more, 45% or more, 50% or more, 55% or more, 60% or more, 65% or more, 70% or more, 75% or more, 80% or more, 85% or more, 90% or more or 95% or more.

8. A method according to any preceding claim, in which batch-to-batch variation or homogeneity or both are measured using mass spectrometry or liquid chromatography, for example liquid chromatography mass spectrometry (LC-MS) or ultra-high performance liquid chromatography (UHPLC).

9. A method according to any preceding claim, in which the recombinantly expressed polypeptide comprises predominantly G0F, for example with low levels or no G1F or G2F N-glycans.

10. A method according to any preceding claim, in which the polypeptide comprises erythropoietin-Fc fusion polypeptide (EPO-Fc), MUC1-Fc fusion polypeptide, an antibody, anti-HER2 antibody (Herceptin), Anti-CD20 antibody (Rituxan or GA101), IgG1, IgG2, IgG3 or IgG4.

11. A method according to any preceding claim, in which the CHO cell or cell line is adapted to suspension culture in a serum-free medium.

12. A method of production of a recombinantly expressed polypeptide with reduced batch-to-batch variation or increased homogeneity between batches, the method comprising a method as set out in any preceding claim.

13. A method according to any preceding claim, in which the method further comprises allowing the polypeptide to be expressed from the CHO cell or a descendent thereof and purifying the polypeptide.

14. Use of a Chinese hamster ovary (CHO) cell which has reduced UDP-galactose transporter activity and reduced GDP-fucose transporter activity compared to a wild-type cell, in a method of expressing recombinant polypeptide with reduced batch-to-batch variation or increased homogeneity between batches, or both.

15. A method comprising expressing a recombinant polypeptide in a Chinese hamster ovary (CHO) cell which has reduced UDP-galactose transporter activity and reduced GDP-fucose transporter activity compared to a wild-type cell and detecting reduced batch-to-batch variation or increased homogeneity between batches, or both.

16. A method of producing a Chinese hamster ovary (CHO) cell suitable for recombinant polypeptide expression with reduced batch-to-batch variation or increased homogeneity, or both, the method comprising reducing UDP-galactose transporter activity and reducing GDP-fucose transporter activity in or of the cell, for example by introducing a loss of function mutation in a UDP-galactose transporter gene (Slc35a2) or a loss of function mutation in a GDP-fucose transporter gene (Slc35c1 or Slc35c2).

17. A Chinese hamster ovary (CHO) cell comprising reduced UDP-galactose transporter activity and reduced GDP-fucose transporter activity.

18. A CHO cell according to Claim 17 which is capable of expressing recombinant antibodies for example tumour/cancer-targeting antibodies with enhanced antibody-dependent cellular cytotoxicity (ADCC) and reduced batch-to-batch variation or increased homogeneity between batches.

19. A CHO cell according to Claim 17 or 18 comprising a loss of function mutation in a UDP-galactose transporter gene (Slc35a2) and a loss of function mutation in a GDP-fucose transporter gene (Slc35c1 or Slc35c2).

20. A CHO cell according to Claim 17, 18 or 19, comprising a T insertion at position 955 of the Slc35a2 open reading frame and a 3-nucleotide (GTA) insertion or a 4-nucleotide insertion at position 411 of Slc35c1.

21. A CHO cell according to any of Claims 17 to 20, in which the CHO cell is comprised in a CHO-gmt9 cell line (deposited on 21 October 2014 at the American Type Culture Collection (ATCC), P.O. Box 1549, Manassas, Virginia 20108, United States of America under the Budapest Treaty as accession number PTA-121625).

22. A CHO cell according to any of Claims 17 to 21, which is or has been adapted to suspension culture in a serum-free medium.

23. Use of a CHO cell according to any of Claims 17 to 22 in a method of expression of a recombinant polypeptide.