In another aspect, the present disclosure provides a method of producing a product of interest, comprising culturing the mammalian cell as described herein, wherein the mammalian cell expresses the product of interest.

In another aspect, the present disclosure provides a method of culturing a population of mammalian cells having reduced or eliminated lactogenic activity, comprising culturing one or more mammalian cells as described herein.

In another aspect, the present disclosure provides a mammalian cell comprising an allele of a *PKM* gene that comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs: 37-41, wherein the cell is a CHO cell.

In another aspect, the present disclosure provides a method for reducing or eliminating lactogenic activity in a CHO cell, comprising knocking down or knocking out the expression of a pyruvate kinase muscle (PKM) polypeptide isoform, wherein the PKM polypeptide isoform is (i) a PKM-1 polypeptide isoform; or (ii) a PKM-1 polypeptide isoform and a PKM-2 polypeptide isoform.

In another aspect, the present disclosure provides a method of producing a product of interest comprising culturing mammalian cells expressing the product of interest, wherein the mammalian cells express the product of interest and have reduced or eliminated lactogenic activity, wherein the reduction or elimination of lactogenic activity results from the knockout or knockdown of the expression of a pyruvate kinase muscle (PKM) polypeptide isoform in the mammalian cells, wherein the PKM polypeptide isoform is (i) a PKM-1 polypeptide isoform; or (ii) a PKM-1 polypeptide isoform and a PKM-2 polypeptide isoform, and wherein the cells are CHO cells.

4. BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A-1F. Lactate levels of mAb-1 cell line directly correlate with the PKM-1 levels. Percent cell viability (Figure 1A), day 14 titer (Figure 1B), and lactate levels (Figure 1C) in mAb-1 cell line under low and high lactate processes. (Figure 1D) PKM-1 and PKM-2 western blot analysis of mAb-1 cell lysates at different days during production

WHAT IS CLAIMED IS:

1. A mammalian cell having reduced or eliminated lactogenic activity, wherein the expression of a pyruvate kinase muscle (PKM) polypeptide isoform is knocked down or knocked out, and wherein the PKM polypeptide isoform comprises a PKM-1 polypeptide isoform, wherein the cell is a CHO cell.

2. The mammalian cell of claim 1, wherein the expression of a PKM-2 polypeptide isoform is knocked down or knocked out.

3. The mammalian cell of claim 1, comprising a nucleic acid sequence encoding a product of interest.

4. The mammalian cell of claim 3, wherein the product of interest comprises: (i) a protein; (ii) a recombinant protein; (iii) an antibody or an antigen-binding fragment thereof; or (iv) a combination thereof.

5. The mammalian cell of claim 4, wherein (i) the antibody is a multispecific antibody or an antigen-binding fragment thereof; or (ii) the antibody consists of a single heavy chain sequence and a single light chain sequence or antigen-binding fragments thereof.

6. The mammalian cell of claim 3, wherein the nucleic acid sequence is integrated in the cellular genome of the mammalian cell at a targeted location.

7. The mammalian cell of claim 1, wherein the lactogenic activity of the mammalian cell is less than about 50% or less than about 20% of the lactogenic activity of a reference cell.

8. The mammalian cell of claim 1, wherein the mammalian cell produces less than about 2.0 g/L of lactate during a production phase.

9. A composition comprising the mammalian cell of claim 1.

10. A method of producing a product of interest, comprising culturing the mammalian cell of claim 1, wherein the mammalian cell expresses the product of interest.

11. A method of culturing a population of mammalian cells having reduced or eliminated lactogenic activity, comprising culturing one or more mammalian cells of claim 1.

12. A mammalian cell comprising an allele of a *PKM* gene that comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs: 37-41, wherein the cell is a CHO cell.

13. The mammalian cell of claim 12, comprising a nucleic acid sequence encoding a product of interest.

14. A composition comprising a mammalian cell of claim 12.

15. A method of producing a product of interest, comprising culturing the mammalian cell of claim 13, wherein the mammalian cell expresses the product of interest.

16. A method of culturing a population of mammalian cells having reduced or eliminated lactogenic activity, comprising culturing one or more mammalian cells of claim 12.

17. A method for reducing or eliminating lactogenic activity in a CHO cell, comprising knocking down or knocking out the expression of a pyruvate kinase muscle (PKM) polypeptide isoform, wherein the PKM

polypeptide isoform is (i) a PKM-1 polypeptide isoform; or (ii) a PKM-1 polypeptide isoform and a PKM-2 polypeptide isoform.

18. The method of claim 17, wherein a genetic engineering system is administered to the cell for knocking down or knocking out the expression of the pyruvate kinase muscle (PKM) polypeptide isoform.

19. The method of claim 18, wherein the genetic engineering system is: (i) a CRISPR/Cas system; (ii) a zinc-finger nuclease (ZFN) system; (iii) a transcription activator-like effector nuclease (TALEN) system; (iv) an RNA selected from the group consisting of a short hairpin RNA (shRNA), a small interference RNA (siRNA), and a microRNA (miRNA), wherein the RNA is complementary to a portion of an mRNA expressed by the *PKM* gene; or (v) a combination thereof.

20. The method of claim 19, wherein the genetic engineering system is a CRISPR/Cas9 system comprising: (i) a Cas9 molecule; and (ii) one or more guide RNAs (gRNAs) comprising a targeting sequence that is complementary to a target sequence in a *PKM* gene.

21. The method of claim 20, wherein the target sequence is selected from the group consisting of: a portion of the *PKM* gene, a 5' intron region flanking exon 9 of the *PKM* gene, a 3' intron region flanking exon 9 of the *PKM* gene, a 3' intron region flanking exon 10 of the *PKM* gene, a region within exon 1 of the *PKM* gene, a region within exon 2 of the *PKM* gene, a region within exon 12 of the *PKM* gene and combinations thereof.

22. The method of claim 17, wherein the cell expresses a product of interest.

23. A method of producing a product of interest comprising culturing mammalian cells expressing the product of interest, wherein the mammalian cells express the product of interest and have reduced or eliminated lactogenic activity, wherein the reduction or elimination of lactogenic activity results from the knockout or knockdown of the expression of a pyruvate kinase muscle (PKM) polypeptide isoform in the mammalian cells, wherein the PKM polypeptide isoform is (i) a PKM-1 polypeptide isoform; or (ii) a PKM-1 polypeptide isoform and a PKM-2 polypeptide isoform, and wherein the cells are CHO cells.