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.

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

3. The mammalian cell of claim 1 or 2, wherein the cell is a CHO cell.

4. The mammalian cell of any one of claims 1-3, comprising a nucleic acid sequence encoding a product of interest.

5. The mammalian cell of claim 4, wherein the product of interest comprises a protein.

6. The mammalian cell of claim 4 or 5, wherein the product of interest comprises a recombinant protein.

7. The mammalian cell of any one of claims 4-6, wherein the product of interest comprises an antibody or an antigen-binding fragment thereof.

8. The mammalian cell of claim 7, wherein the antibody is a multispecific antibody or an antigen-binding fragment thereof.

9. The mammalian cell of claim 7, wherein the antibody consists of a single heavy chain sequence and a single light chain sequence or antigen-binding fragments thereof.

10. The mammalian cell of any one of claims 7-9, wherein the antibody comprises a chimeric antibody, a human antibody or a humanized antibody.

11. The mammalian cell of any one of claims 7-10, wherein the antibody comprises a monoclonal antibody.

12. The mammalian cell of any one of claims 4-11, wherein the nucleic acid sequence is integrated in the cellular genome of the mammalian cell at a targeted location.

13. The mammalian cell of claim 12, further comprising a nucleic acid encoding the product of interest that is randomly integrated in the cellular genome of the mammalian cell.

14. The mammalian cell of any one of claims 1-13, wherein the lactogenic activity of the mammalian cells is less than about 50% of the lactogenic activity of a reference cell.

15. The mammalian cell of claim 14, wherein the lactogenic activity of the mammalian cells is less than about 20% of the lactogenic activity of a reference cell.

16. The mammalian cell of claim 14 or 15, wherein the reference cell is a cell that comprises wild-type alleles of the *PKM* gene.

17. The mammalian cell of any one of claims 1-16, wherein the lactogenic activity of the mammalian cell is determined at day 14 or day 15 of a production phase.

18. The mammalian cell of any one of claims 1-17, wherein the mammalian cell produces less than about 2.0 g/L of lactate during a production phase.

19. The mammalian cell of any one of claims 1-17, wherein the mammalian cell produces less than about 2.0 g/L of lactate during a production phase in a shake flask.

20. The mammalian cell of any one of claims 1-17, wherein the mammalian cell produces less than about 2.0 g/L of lactate during a production phase in a bioreactor.

21. A mammalian cell comprising an allele of a *PKM* gene that comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs: 39-41, or the nucleotide sequences set forth in SEQ ID NOs: 37 and 38.

22. A composition comprising a mammalian cell of any one of claims 1-21.

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

24. A method for reducing or eliminating lactogenic activity in a cell, comprising administering to the cell a genetic engineering system, wherein the genetic engineering system knocks down or knocks out the expression of a pyruvate kinase muscle (PKM) polypeptide isoform.

25. The method of claim 24, wherein the genetic engineering system is selected from the group consisting of a CRISPR/Cas system, a zinc-finger nuclease (ZFN) system, a transcription activator-like effector nuclease (TALEN) system and a combination thereof.

26. The method of claim 24 or 25, wherein the genetic engineering system is a CRISPR/Cas9 system.

27. The method of claim 26, wherein the CRISPR/Cas9 system comprises:

(a) a Cas9 molecule, and

(b) one or more guide RNAs (gRNAs) comprising a targeting sequence that is complementary to a target sequence in a *PKM* gene.

28. The method of claim 27, 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.

29. The method of claim 27 or 28, wherein the one or more gRNAs comprises:

(i) (1) a first gRNA comprising a target sequence that is complementary to a 5' intron region flanking exon 9 of the *PKM* gene; and (2) a second gRNA comprising a target domain that is complementary to a 3' intron region flanking exon 9 of the *PKM* gene; or

(ii) (1) a first gRNA comprising a target sequence that is complementary to a region within exon 2 of the *PKM* gene; and (2) a second gRNA comprising a target domain that is complementary to a region within exon 12 of the *PKM* gene.

30. The method of any one of claims 27-29, wherein the one or more gRNAs comprises a sequence selected from the group consisting of SEQ ID NOs: 33-34 and 42-43 and a combination thereof.

31. The method of any one of claims 23-30, wherein the expression of the PKM polypeptide isoform is knocked out, and the lactogenic activity in the cell is eliminated or reduced compared to the lactogenic activity of a reference cell.

32. The method of any one of claims 23-30, wherein the expression of the PKM polypeptide isoform is knocked down, and the lactogenic activity in the cell is reduced compared to the lactogenic activity of a reference cell.

33. The method of claim 31 or 32, wherein the lactogenic activity of the cell is less than about 50% of the lactogenic activity of the reference cell.

34. The method of claim 31 or 32, wherein the lactogenic activity of the cell is less than about 20% of the lactogenic activity of the reference cell.

35. The method of any one of claims 23-34, wherein the lactogenic activity of the cell is determined at day 14 or day 15 of a production phase.

36. The method of any one of claims 23-35, wherein the cell produces less than about 2.0 g/L of lactate during a production phase.

37. The method of any one of claims 23-35, wherein the cell produces less than about 2.0 g/L of lactate during a production phase in a shake flask.

38. The method of any one of claims 23-35, wherein the cell produces less than about 2.0 g/L of lactate during a production phase in a bioreactor.

39. The method of any one of claims 31-38, wherein the reference cell is a cell that comprises wild-type alleles of the *PKM* gene.

40. The method of any one of claims 23-39, wherein the PKM polypeptide isoform is the PKM-1 polypeptide isoform.

41. The method of any one of claims 23-39, wherein the PKM polypeptide isoform is the PKM-1 polypeptide isoform and the PKM-2 polypeptide isoform.

42. The method of claim 24, wherein the genetic engineering system comprises 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.

43. The method of claim 42, wherein the mRNA expressed by the *PKM* gene encodes a PKM-1 polypeptide isoform.

44. The method of claim 43, wherein the expression of the PKM-1 polypeptide isoform is knocked out or knocked down and the lactogenic activity of the cell is reduced as compared to the lactogenic activity of a reference cell.

45. The method of any one of claims 42-44, wherein the genetic engineering system further comprises a second RNA selected from the group consisting of: shRNA, an siRNA, and a microRNA miRNA, wherein the second RNA is complementary to a portion of an mRNA expressed by the *PKM* gene that encodes a PKM-2 polypeptide isoform.

46. The method of claim 45, wherein the expression of the PKM-1 and PKM-2 polypeptide isoforms are knocked out or knocked down, and the lactogenic activity of the cell is reduced.

47. The method of claim 24, wherein the genetic engineering system is a zinc-finger nuclease (ZFN) system or a transcription activator-like effector nuclease (TALEN) system.

48. The method of any one of claims 23-47, wherein the cell is a mammalian cell.

49. The method of claim 49, wherein the mammalian cell is a CHO cell.

50. The method of any one of claims 23-49, wherein the cell expresses a product of interest.

51. The method of claim 50, wherein the product of interest expressed by the cells is encoded by a nucleic acid sequence.

52. The method of claim 51, wherein the nucleic acid sequence is integrated in the cellular genome of the cell at a targeted location.

53. The method of any one of claims 50-52, wherein the product of interest expressed by the cells is further encoded by a nucleic acid sequence that is randomly integrated in the cellular genome of the mammalian cell.

54. The method of any one of claims 50-53, wherein the product of interest comprises a protein.

55. The method of claim 54, wherein the product of interest comprises a recombinant protein.

56. The method of any one of claims 50-55, wherein the product of interest comprises an antibody or an antigen-binding fragment thereof.

57. The method of claim 56, wherein the antibody is a multispecific antibody or an antigen-binding fragment thereof.

58. The method of claim 56, wherein the antibody consists of a single heavy chain sequence and a single light chain sequence or antigen-binding fragments thereof.

59. The method of any one of claims 56-58, wherein the antibody is a chimeric antibody, a human antibody or a humanized antibody.

60. The method of any one of claims 56-59, wherein the antibody is a monoclonal antibody.

61. 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.

62. A method of culturing a population of mammalian cells expressing a product of interest, wherein the mammalian cells have reduced or eliminated lactogenic activity.

63. The method of claim 61 or 62, wherein the reduction or elimination of lactogenic activity results from the knock out or knock down of the expression of a pyruvate kinase muscle (PKM) polypeptide isoform in the mammalian cells.

64. The method of claim 63, wherein the PKM polypeptide isoform is the PKM-1 polypeptide isoform.

65. The method of 63, wherein the PKM polypeptide isoform is the PKM-1 polypeptide isoform and the PKM-2 polypeptide isoform.

66. The method of any one of claims 61-65, wherein the lactogenic activity of the mammalian cells is less than about 50% of the lactogenic activity of a reference cell.

67. The method of any one of claims 61-65, wherein the lactogenic activity of the mammalian cells is less than about 20% of the lactogenic activity of a reference cell.

68. The method of any one of claims 61-67, wherein the lactogenic activity of the mammalian cells is determined at day 14 or day 15 of a production phase.

69. The method of any one of claims 61-68, wherein the mammalian cells produce less than about 2.0 g/L of lactate during a production phase.

70. The method of any one of claims 61-68, wherein the mammalian cells produce less than about 2.0 g/L of lactate during a production phase in a shake flask.

71. The method of any one of claims 61-68, wherein the mammalian cells produce less than about 2.0 g/L of lactate during a production phase in a bioreactor.

72. The method of any one of claims 66-71, wherein the reference cell is a cell that comprises at least one or both wild-type alleles of the *PKM* gene.

73. The method of any one of claims 61-72, wherein the mammalian cells are CHO cells.

74. The method of any one of claims 61-73, wherein the product of interest expressed by the mammalian cells is encoded by a nucleic acid sequence.

75. The method of claim 74, wherein the nucleic acid sequence is integrated in the cellular genome of the mammalian cells at a targeted location.

76. The method of any one of claims 61-75, wherein the product of interest expressed by the cells is further encoded by a nucleic acid sequence that is randomly integrated in the cellular genome of the mammalian cells.

77. The method of any one of claims 61-76, wherein the product of interest comprises a protein.

78. The method of any one of claims 61-77, wherein the product of interest comprises a recombinant protein.

79. The method of any one of claims 61-79, wherein the product of interest comprises an antibody or an antigen-binding fragment thereof.

80. The method of claim 79, wherein antibody is a multispecific antibody or an antigen-binding fragment thereof.

81. The method of claim 79, wherein the antibody consists of a single heavy chain sequence and a single light chain sequence or antigen-binding fragments thereof.

82. The method of any one of claims 79-81, wherein the antibody is a chimeric antibody, a human antibody or a humanized antibody.

83. The method of any one of claims 79-82, wherein the antibody is a monoclonal antibody.

84. The method of any one of claims 61-83, further comprising harvesting the product of interest.