

CLAIMS

WHAT IS CLAIMED IS:

1. A method for generating an engineered cell, the method comprising:
 - (a) providing a non-mammary adult stem cell or a derivative thereof; and
 - (b) subjecting said non-mammary adult stem cell or said derivative thereof to conditions sufficient to generate said engineered cell exhibiting one or more characteristics of a cell of a mammary cell lineage (e.g., a mammary epithelial cell lineage, such as a mammary epithelial luminal cell lineage, or a mammary basal cell lineage).
2. A method for generating an engineered cell, the method comprising:
 - (a) providing a non-mammary adult stem cell or a derivative thereof; and
 - (b) subjecting said non-mammary adult stem cell or said derivative thereof to conditions sufficient to generate said engineered cell capable of lactation.
3. The method of any one of claims 1-2, wherein (b) is performed *in vitro*.
4. The method of any one of claims 1-3, wherein said engineered cell is capable of producing a milk component (e.g., comprising a fat, a protein, a carbohydrate, or a combination thereof).
5. The method of any one of claims 1-4, wherein said non-mammary adult stem cell is a mesenchymal stem cell.
6. The method of any one of claims 1-5, wherein (b) comprises: contacting said non-mammary adult stem cell or said derivative thereof with a heterologous polypeptide including a gene regulating moiety, wherein said gene regulating moiety is configured to regulate an expression of a target gene, a target transcript, or a target protein of said non-mammary adult stem cell or said derivative thereof, thereby effecting a modified expression profile (e.g., an up-regulated expression, or a down-regulated expression) of said target gene, said target transcript, or said target protein in said engineered cell as compared to a corresponding non-engineered non-mammary adult stem cell.
7. The method of claim 6, wherein said target gene, said target transcript, or said target protein is associated with production of a milk component (e.g., comprising a fat, a protein, a carbohydrate, or a combination thereof).
8. The method of claim 6 or 7, wherein said target gene, said target transcript, or said target protein is a gene or a transcript selected from the group consisting of: CIDEA, XDH, C/EBP β , HDAC, DGAT1, DGAT2, acyl-CoA: cholesterol acyltransferase, AKT1, S14, LPL, BTN/BTN1A1, ADFP, ACACA/B, FASN, ACLY, S-acyl fatty acid synthase thioesterase, ACOT, SCD, ELOVL, FADS, ACSS, ACSL, GPD1L, GK5, DGKA, GPAM, AGPAT1, LPIN1, LPIN2, SLC27A, FABP, ABCG2, FDFT1, SC4MOL, SC5DL, IDI1, MVD, CH25H, DHCR7, PLIN2, SREBP1, MUC1, MFGE8, mTORC1, CASTOR1, GATOR1, GATOR2, RRAGA/B, RHEB, TSC2, PIK3C3, EAAT3, CAT1, 4F2hc, LAT1, ASCT2, AMPK, STK11, SIRT1, ARNTL, CLOCK, NAMPT, CRY, PER1, CSN1, CSN2, CSN3, LALBA, LTF, LYZ, LPO, TC-1, SPP1, ABL, C3, C4, Galactosyltransferase, B4GALT1, B4GALT2, LGALS1, LGALS2, LGALS3, LGALS8, LGALS9, LGALS12, LGALS13, LGALS14, LGALS16, LCT, GLUT1, FUT1, FUT2, FUT3,

FUT4, FUT5, FUT6, FUT7, FUT8, FUT9, sialyltransferase, GALM, GLTP, LGALSL, N-acetylglucosaminyltransferase, glycosyltransferase, and a combination thereof.

9. The method of claim 4 or 7, wherein said milk component is a milk protein selected from the group consisting of: casein (e.g., α S1/S2 casein, β casein, κ casein, or a combination thereof), whey protein, lactoferrin, lactoperoxidase, lysozyme, haptocorrin, osteopontin, albumin (e.g., α -lactalbumin), complement component (e.g., C3, C4, or a combination thereof), and a combination thereof.

10. The method of claim 9, wherein said gene or said transcript regulating production of said milk protein is a gene or a transcript selected from the group consisting of: mTORC1, CASTOR1, GATOR1, GATOR2, RAGA/B, RHEB, TSC2, PIK3C3, EAAT3, CAT1, 4F2hc, LAT1, ASCT2, AMPK, STK11, SIRT1, ARNTL, CLOCK, NAMPT, CRY, PER1, CSN1, CSN2, CSN3, LALBA, LTF, LYZ, LPO, TC-1, SPP1, ABL, C3, C4, and a combination thereof.

11. The method of claim 4 or 7, wherein said milk component is a milk carbohydrate selected from the group consisting of: 2'-fucosyllactose, 3-fucosyllactose, difucosyllactose, difucosyllacto-N-tetrose (DFLNT), difucosyllacto-N-hexaose, fucosyllacto-N-hexaose (FLNH), lacto-N-fucopentaose (LNFP) I, LNFP II, LNFP III, 3'-sialyllactose, 6'-sialyllactose, disialyllacto-N-hexaose (DSLNH), disialyllacto-N-tetraose (DSLNT), fucodisialyllacto-N-hexaose (FDSLNH), sialyl-lacto-N-tetraose b (LSTb), and sialyl-lacto-N-tetraose c (LSTc), lacto-N-hexaose, lacto-N-neotetraose (LNnT), lacto-N-tetrose (LNT), lactose, and a combination thereof.

12. The method of claim 11, wherein said gene or said transcript regulating production of said milk carbohydrate is a gene or a transcript selected from the group consisting of: LALBA, galactosyltransferase B4GALT1, galactosyltransferase B4GALT2, LGALS1, LGALS2, LGALS3, LGALS8, LGALS9, LGALS12, LGALS13, LGALS14, LGALS16, LCT, GLUT1, FUT1, FUT2, FUT3, FUT4, FUT5, FUT6, FUT7, FUT8, FUT9, sialyltransferase, GALM, GLTP, LGALSL, N-acetylglucosaminyltransferase, glycosyltransferase, and a combination thereof.

13. The method of claim 4 or 7, wherein said modified expression profile comprises an up-regulated expression of a gene or a transcript that degrades lactose.

14. The method of claim 13, wherein said gene or said transcript that degrades said lactose is a gene or a transcript selected from the group consisting of: Lac operon, lactase, and glycosidase.

15. The method of claim 4 or 7, wherein said milk component is a milk fat.

16. The method of claim 15, wherein said gene or said transcript regulating production of said milk fat is a gene or a transcript selected from the group consisting of: CIDEA, XDH, C/EBP β , HDAC, DGAT1, DGAT2, acyl-CoA: cholesterol acyltransferase, AKT1, S14, LPL, BTN/BTN1A1, ADFP, ACACA/B, FASN, ACLY, S-acyl fatty acid synthase thioesterase, medium chain/OLAH, ACOT, SCD, ELOVL, FADS, ACSS, ACSL, GDP1L, GK5, DGKA, GPAM, AGPAT1, LPIN1, LPIN2, SLC27A, FABP, ABCG2, FDFT1, SC4MOL, SC5DL, IDI1, MVD, CH25H, DHCR7, PLIN2, SREBP1, MUC1, MFGE8, and a combination thereof.

17. The method of claim 4 or 7, wherein said milk component is a milk lipid selected from the group

consisting of: palmitic acid, myristic acid, stearic acid, butyric acid, caproic acid, oleic acid, linoleic acid, α -linoleic acid, vaccenic acid, eicosapentaenoic acid, docosahexaenoic acid, calendic acid, γ -linoleic acid, eicosadienoic acid, dihomogamma-linoleic acid, arachidonic acid, docosadienoic acid, adrenic acid, asbond acid, tetracosatetraenoic acid, tetracosapentaenoic acid, hexadecatrienoic acid, stearidonic acid, eicosatrienoic acid, eicosatetraenoic acid, heneicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid, tetracosapentaenoic acid, tetracosahexaenoic acid, rumenic acid, caprylic acid, capric acid, and a combination thereof.

18. The method of claim 17, wherein said gene or said transcript regulating production of said milk lipid is a gene or a transcript selected from the group consisting of: CIDEA, XDH, C/EBP β , HDAC, DGAT1, DGAT2, acyl-CoA: cholesterol acyltransferase, AKT1, S14, LPL, BTN/BTN1A1, ADFP, ACACA/B, FASN, ACLY, S-acyl fatty acid synthase thioesterase, medium chain/OLAH, ACOT, SCD, ELOVL, FADS, ACSS, ACSL, GDP1L, GK5, DGKA, GPAM, AGPAT1, LPIN1, LPIN2, SLC27A, FABP, ABCG2, FDFT1, SC4MOL, SC5DL, IDI1, MVD, CH25H, DHCR7, PLIN2, SREBP1, MUC1, MFGE8, and a combination thereof.

19. The method of claim 6, wherein said target gene, said target transcript, or said target protein is a gene or a transcript that regulates a cellular response to a hormone or a signaling factor.

20. The method of claim 19, wherein said gene or said transcript regulating said cellular response is a gene or a transcript selected from the group consisting of: USF, GATA-1, GATA-2, GATA-3 c-Myc:Max, ATF, USF, CREB, TATA, SREBP-1, Amt, USF, Tal-1beta, NRF-2, FOXD3, HNF-3beta, v-Myb, FOXJ2, FOXO1, Evi-1, FOXO4, ARP-1, Staf, NF-kappaB, myogenin, AML-1a, Elk-1 Oct-1, Tax/CREB, HNF-1, AP-1, Ahr, Bach1, RP58, AREB6, NKX3A, XFD-1, deltaEF1, poly A downstream element, Pax-4, Sox-5, Sox-9, Zic3, E47, LPL, AGPAT6, CD36, SCD, GPAM, BTN1A1, ACACA, ACSL1, LPIN1, FASN, FABP3, AGPAT6, SREBP1, INSR, PRLR, EGFR, and a combination thereof.

21. The method of any one of claims 6-20, wherein said modified expression profile is characteristic of a mammary cell lineage.

22. The method of claim 21, wherein said modified expression profile comprises a modified expression profile (e.g., an up-regulated expression, or a down-regulated expression) of a gene, a transcript, or a protein selected from the group consisting of: EpCAM, CD14, CD29, CD49b, CD49f, CD61, Sca1, Prolactin, ALDEFLUOR, CK14, CK18, and a combination thereof.

23. The method of claim 21 or 22, wherein said engineered cell exhibits a cellular morphology indicative of said mammary cell lineage.

24. The method of any one of claims 6-23, wherein said gene regulating moiety is a polynucleotide-guided gene regulating moiety.

25. The method of any one of claims 6-24, wherein said gene regulating moiety is an endonuclease.

26. The method of claim 25, wherein said endonuclease is a clustered regularly interspaced short palindromic repeats (CRISPR)-associated (Cas) endonuclease (e.g., selected from the group consisting of: C2C1, C2C2, C2C3, Cas1, Cas1B, Cas2, Cas3, Cas4, Cas5, Cas5e, Cas6, Cas6e, Cas6f, Cas7, Cas8a,

Cas8a1, Cas8a2, Cas8b, Cas8c, Cas9, Cas10, Cas10d, Cas10, Cas10d, Cas 11, Cas12, Cas13, Cas14, CasF, CasG, CasH, CasX, CaxY, Cpf1, Csy1, Csy2, Csy3, Cse1, Cse2, Cse3, Cse4, Csc1, Csc2, Csa5, Csn2, Csm2, Csm3, Csm4, Csm5, Csm6, Cmr1, Cmr3, Cmr4, Cmr5, Cmr6, Csb1, Csb2, Csb3, Csx17, Csx14, Csx10, Csx16, CsaX, Csx3, Csx1, Csx15, Csf1, Csf2, Csf3, Csf4, a modification thereof, and a combination thereof).

27. The method of any one of claims 6-26, wherein (b) further comprises contacting said non-mammary adult stem cell or said derivative thereof with a heterologous polynucleotide configured to bind at least a portion of said target gene or said target transcript.

28. The method of any one of claims 1-27, wherein said engineered cell is configured to generate a milk component (e.g., comprising a fat, a protein, a carbohydrate, or a combination thereof) in response to a hormone or a signaling factor.

29. The method of any one of claims 1-28, further comprising: contacting said non-mammary adult stem cell or said derivative thereof with an exogenous polynucleotide, which exogenous polynucleotide (1) comprises an inducible promoter sequence (e.g., configured for activation by a substance) and (2) encodes a hormone or a signaling factor.

30. The method of any one of claims 1-29, wherein said engineered cell has an altered (e.g., enhanced, or diminished) response to a hormone or a signaling factor as compared to a corresponding non-engineered non-mammary adult stem cell.

31. The method of any one of claims 19-20 and 28-30, wherein said hormone or said signaling factor is selected from the group consisting of: glucocorticoid, insulin, transferrin, apo transferrin, progesterone, prolactin, ethanolamine, estrogen, fibroblast growth factor (FGF), FGF receptor, T-box 3 (TBX3), NRG3/ERBB4, Wnt/LEF1, insulin-like growth factor 1 (IGF-1), epidermal growth factor (EGF), hepatocyte growth factor (HGF), nuclear factor κ B (NF- κ B), pTHrP, non-phospho β -catenin, p-p65, RELA, CTNNB1, SMAD3, and a combination thereof.

32. The method of claim 31, wherein said glucocorticoid comprises beclomethasone, betamethasone, budesonide, cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone, or a combination thereof.

33. A composition comprising an engineered non-mammary adult stem cell exhibiting a modified expression profile (e.g., an up-regulated expression, or a down-regulated expression) that is different than an expression profile of a corresponding non-engineered non-mammary adult stem cell, wherein said engineered non-mammary adult stem cell is configured to be differentiated to an engineered cell exhibiting one or more characteristics of a cell of a mammary cell lineage (e.g., a mammary epithelial cell lineage, such as a mammary epithelial luminal cell lineage, or a mammary basal cell lineage).

34. A composition comprising an engineered non-mammary adult stem cell exhibiting a modified expression profile (e.g., an up-regulated expression, or a down-regulated expression) that is different than an expression profile of a corresponding non-engineered non-mammary adult stem cell, wherein said engineered non-mammary adult stem cell is configured to be differentiated to an engineered cell capable of

lactation.

35. The composition of claim 33 or 34, wherein said engineered non-mammary adult stem cell is configured to produce a milk component (e.g., comprising a fat, a protein, a carbohydrate, or a combination thereof).

36. The composition of any one of claims 33-35, wherein said engineered non-mammary adult stem cell is an engineered mesenchymal stem cell.

37. The composition of any one of claims 33-36, wherein said corresponding non-engineered non-mammary adult stem cell is a corresponding non-engineered mesenchymal stem cell.

38. The composition of any one of claims 33-37, wherein said engineered non-mammary adult stem cell or an ancestor cell thereof has been brought in contact with a heterologous polypeptide, which heterologous polypeptide includes a gene regulating moiety.

39. The composition of claim 38, wherein said gene regulating moiety is a polynucleotide-guided gene regulating moiety.

40. The composition of claim 38 or 39, wherein said gene regulating moiety is an endonuclease.

41. The composition of claim 40, wherein said endonuclease is a clustered regularly interspaced short palindromic repeats (CRISPR)-associated (Cas) endonuclease (e.g., selected from the group consisting of: C2C1, C2C2, C2C3, Cas1, Cas1B, Cas2, Cas3, Cas4, Cas5, Cas5e, Cas6, Cas6e, Cas6f, Cas7, Cas8a, Cas8a1, Cas8a2, Cas8b, Cas8c, Cas9, Cas10, Cas10d, Cas10, Cas10d, Cas 11, Cas12, Cas13, Cas14, CasF, CasG, CasH, CasX, CaxY, Cpf1, Csy1, Csy2, Csy3, Cse1, Cse2, Cse3, Cse4, Csc1, Csc2, Csa5, Csn2, Csm2, Csm3, Csm4, Csm5, Csm6, Cmr1, Cmr3, Cmr4, Cmr5, Cmr6, Csb1, Csb2, Csb3, Csx17, Csx14, Csx10, Csx16, CsaX, Csx3, Csx1, Csx15, Csf1, Csf2, Csf3, Csf4, a modification thereof, and a combination thereof).

42. The composition of any one of claims 38-41, wherein said gene regulating moiety is configured to regulate an expression of a target gene, a target transcript, or a target protein of said engineered non-mammary adult stem cell.

43. The composition of claim 42, wherein said target gene, said target transcript, or said target protein is associated with production of a milk component (e.g., comprising a fat, a protein, a carbohydrate, or a combination thereof).

44. The composition of claim 42 or 43, wherein said target gene, said target transcript, or said target protein is selected from a gene, a transcript, or a protein selected from the group consisting of: CIDEA, XDH, C/EBP β , HDAC, DGAT1, DGAT2, acyl-CoA: cholesterol acyltransferase, AKT1, S14, LPL, BTN/BTN1A1, ADFP, ACACA/B, FASN, ACLY, S-acyl fatty acid synthase thioesterase, ACOT, SCD, ELOVL, FADS, ACSS, ACSL, GPD1L, GK5, DGKA, GPAM, AGPAT1, LPIN1, LPIN2, SLC27A, FABP, ABCG2, FDFT1, SC4MOL, SC5DL, IDI1, MVD, CH25H, DHCR7, PLIN2, SREBP1, MUC1, MFGE8, mTORC1, CASTOR1, GATOR1, GATOR2, RRAGA/B, RHEB, TSC2, PIK3C3, EAAT3, CAT1, 4F2hc, LAT1, ASCT2, AMPK, STK11, SIRT1, ARNTL, CLOCK, NAMPT, CRY, PER1, CSN1, CSN2, CSN3, LALBA, LTF, LYZ, LPO, TC-1, SPP1, ABL, C3, C4, Galactosyltransferase, B4GALT1,

B4GALT2, LGALS1, LGALS2, LGALS3, LGALS8, LGALS9, LGALS12, LGALS13, LGALS14, LGALS16, LCT, GLUT1, FUT1, FUT2, FUT3, FUT4, FUT5, FUT6, FUT7, FUT8, FUT9, sialyltransferase, GALM, GLTP, LGALSL, N-acetylglucosaminyltransferase, glycosyltransferase, and a combination thereof.

45. The composition of claim 35 or 43, wherein said milk component is a milk protein is selected from the group consisting of: casein (e.g., α S1/S2 casein, β casein, κ casein, or a combination thereof), whey protein, α -lactalbumin, lactoferrin, lactoperoxidase, lysozyme, haptocorrin, osteopontin, albumin, complement C3, complement C4, and a combination thereof.

46. The composition of claim 45, wherein said gene or said transcript regulating said production of said milk protein is a gene or a transcript selected from the group consisting of: mTORC1, CASTOR1, GATOR1, GATOR2, RAGA/B, RHEB, TSC2, PIK3C3, EAAT3, CAT1, 4F2hc, LAT1, ASCT2, AMPK, STK11, SIRT1, ARNTL, CLOCK, NAMPT, CRY, PER1, CSN1, CSN2, CSN3, LALBA, LTF, LYZ, LPO, TC-1, SPP1, ABL, C3, C4, and a combination thereof.

47. The composition of claim 35 or 43, wherein said milk component is a milk carbohydrate selected from the group consisting of: 2'-fucosyllactose, 3-fucosyllactose, difucosyllactose, difucosyllacto-N-tetrose (DFLNT), difucosyllacto-N-hexaose, fucosyllacto-N-hexaose (FLNH), lacto-N-fucopentaose (LNFP) I, LNFP II, LNFP III, 3'-sialyllactose, 6'-sialyllactose, disialyllacto-N-hexaose (DSLNH), disialyllacto-N-tetraose (DSLNT), fucodisialyllacto-N-hexaose (FDSLNH), sialyl-lacto-N-tetraose b (LSTb), and sialyl-lacto-N-tetraose c (LSTc), lacto-N-hexaose, lacto-N-neotetraose (LNnT), lacto-N-tetrose (LNT), Lactose, and a combination thereof.

48. The composition of claim 47, wherein said gene or said transcript regulating production of said milk carbohydrate is a gene or a transcript selected from the group consisting of: LALBA, Galactosyltransferase B4GALT1, Galactosyltransferase B4GALT2, LGALS1, LGALS2, LGALS3, LGALS8, LGALS9, LGALS12, LGALS13, LGALS14, LGALS16, LCT, GLUT1, FUT1, FUT2, FUT3, FUT4, FUT5, FUT6, FUT7, FUT8, FUT9, sialyltransferase, GALM, GLTP, LGALSL, N-acetylglucosaminyl transferase, glycosyltransferase, and a combination thereof.

49. The composition of claim 35 or 43, wherein said modified expression profile comprises an up-regulated expression of a gene or a transcript that degrades lactose.

50. The composition of claim 49, wherein said gene or said transcript that degrades lactose is a gene or a transcript selected from the group consisting of: Lac operon, lactase, and glycosidase.

51. The composition of claim 35 or 43, wherein said milk component is a milk fat selected from the group consisting of: palmitic acid, myristic acid, stearic acid, butyric acid, caproic acid, oleic acid, linoleic acid, α -linoleic acid, vaccenic acid, eicosapentaenoic acid, docosahexaenoic acid, calendic acid, γ -linoleic acid, eicosadienoic acid, dihomo- γ -linoleic acid, arachidonic acid, docosadienoic acid, adrenic acid, asbond acid, tetracosatetraenoic acid, tetracosapentaenoic acid, hexadecatrienoic acid, stearidonic acid, eicosatrienoic acid, eicosatetraenoic acid, heneicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid, tetracosapentaenoic acid, tetracosahexaenoic acid, rumenic acid, caprylic acid,

capric acid, and a combination thereof.

52. The composition of claim 51, wherein said gene or said transcript regulating production of said milk fat is a gene or a transcript selected from the group consisting of: CIDEA, XDH, C/EBP β , HDAC, DGAT1, DGAT2, acyl-CoA: cholesterol acyltransferase, AKT1, S14, LPL, BTN/BTN1A1, ADFP, ACACA/B, FASN, ACLY, S-acyl fatty acid synthase thioesterase, medium chain/OLAH, ACOT, SCD, ELOVL, FADS, ACSS, ACSL, GDP1L, GK5, DGKA, GPAM, AGPAT1, LPIN1, LPIN2, SLC27A, FABP, ABCG2, FDFT1, SC4MOL, SC5DL, IDI1, MVD, CH25H, DHCR7, PLIN2, SREBP1, MUC1, MFGE8, and a combination thereof.

53. The composition of claim 35 or 43, wherein said milk component is a milk lipid selected from the group consisting of: palmitic acid, myristic acid, stearic acid, butyric acid, caproic acid, oleic acid, linoleic acid, α -linoleic acid, vaccenic acid, eicosapentaenoic acid, docosahexaenoic acid, calendic acid, γ -linoleic acid, eicosadienoic acid, dihomogamma-linoleic acid, arachidonic acid, docosadienoic acid, adrenic acid, asbond acid, tetracosatetraenoic acid, tetracosapentaenoic acid, hexadecatrienoic acid, stearidonic acid, eicosatrienoic acid, eicosatetraenoic acid, heneicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid, tetracosapentaenoic acid, tetracosahexaenoic acid, rumenic acid, caprylic acid, capric acid, and a combination thereof.

54. The composition of claim 53, wherein said gene or said transcript regulating production of said milk lipid is a gene or a transcript selected from the group consisting of: CIDEA, XDH, C/EBP β , HDAC, DGAT1, DGAT2, acyl-CoA: cholesterol acyltransferase, AKT1, S14, LPL, BTN/BTN1A1, ADFP, ACACA/B, FASN, ACLY, S-acyl fatty acid synthase thioesterase, medium chain/OLAH, ACOT, SCD, ELOVL, FADS, ACSS, ACSL, GDP1L, GK5, DGKA, GPAM, AGPAT1, LPIN1, LPIN2, SLC27A, FABP, ABCG2, FDFT1, SC4MOL, SC5DL, IDI1, MVD, CH25H, DHCR7, PLIN2, SREBP1, MUC1, MFGE8, and a combination thereof.

55. The composition of claim 42, wherein said target gene, said target transcript, or said target protein is a gene or a transcript that regulates a cellular response to a hormone or a signaling factor.

56. The composition of claim 55, wherein said gene or said transcript regulating said cellular response is a gene or a transcript selected from the group consisting of: USF, GATA-1, GATA-2, GATA-3 c-Myc:Max, ATF, USF, CREB, TATA, SREBP-1, Arnt, USF, Tal-1beta, NRF-2, FOXD3, HNF-3beta, v-Myb, FOXJ2, FOXO1, Evi-1, FOXO4, ARP-1, Staf, NF-kappaB, myogenin, AML-1a, Elk-1 Oct-1, Tax/CREB, HNF-1, AP-1, Ahr, Bach1, RP58, AREB6, NKX3A, XFD-1, deltaEF1, poly A downstream element, Pax-4, Sox-5, Sox-9, Zic3, E47, LPL, AGPAT6, CD36, SCD, GPAM, BTN1A1, ACACA, ACSL1, LPIN1, FASN, FABP3, AGPAT6, SREBP1, INSR, PRLR, EGFR, and a combination thereof.

57. The composition of any one of claims 33-56, wherein said modified expression profile is characteristic of said mammary cell lineage.

58. The composition of claim 57, wherein said modified expression profile comprises a modified expression profile (e.g., an up-regulated expression, or a down-regulated expression) of a gene, a transcript, or a protein selected from the group consisting of: EpCAM, CD14, CD29, CD49b, CD49f, CD61, Sca1,

Prominin, ALDEFLUOR, CK14, CK18, and a combination thereof.

59. The composition of claim 57 or 58, wherein said engineered non-mammary adult stem cell exhibits a cellular morphology indicative of said mammary cell lineage.

60. The composition of any one of claims 33-59, wherein said engineered non-mammary adult stem cell is configured to generate a milk component in response to a hormone or a signaling factor.

61. The composition of any one of claims 33-60, wherein said engineered non-mammary adult stem cell comprises an exogenous polynucleotide that (1) comprises an inducible promoter sequence (e.g., configured for activation by a substance) and (2) encodes a hormone or a signaling factor.

62. The composition of any one of claims 33-61, wherein said engineered non-mammary adult stem cell has an altered (e.g., enhanced, or diminished) response to a hormone or a signaling factor as compared to a corresponding non-engineered non-mammary adult stem cell.

63. The composition of any one of claims 55-56 and 60-62, wherein said hormone or said signaling factor is selected from the group consisting of: glucocorticoid, insulin, transferrin, apo transferrin, progesterone, prolactin, ethanolamine, estrogen, fibroblast growth factor (FGF), FGF receptor, TBX3, NRG3/ERBB4, Wnt/LEF1, insulin-like growth factor 1 (IGF-1), epidermal growth factor (EGF), hepatocyte growth factor (HGF), nuclear factor κ B (NF- κ B), pTHrP, non-phospho β -catenin, p-p65, RELA, CTNNB1, SMAD3, and a combination thereof.

64. The composition of claim 63, wherein said glucocorticoid comprises beclomethasone, betamethasone, budesonide, cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone, or a combination thereof.

65. A method for generating a milk component, the method comprising:

(a) providing a reaction vessel including a cell culture (e.g., comprising a culture medium), which cell culture comprises an engineered mammary or mammary-like cell derived from a non-mammary adult stem cell; and

(b) subjecting said cell culture to conditions sufficient to produce said milk component *in vitro*.

66. The method of claim 65, wherein said milk component comprises whey protein, casein, a lipid, an oligosaccharide, or a combination thereof.

67. The method of claim 65 or 66, wherein said engineered mammary or mammary-like cell is an engineered milk-producing cell.

68. The method of any one of claims 65-67, wherein said non-mammary adult stem cell is a mesenchymal stem cell.

69. The method of any one of claims 65-68, wherein said engineered mammary or mammary-like cell comprises a genome that is different from a genome of a naturally occurring milk-producing cell.

70. The method of any one of claims 65-69, wherein said engineered mammary or mammary-like cell has been brought in contact with a heterologous polypeptide, which heterologous polypeptide includes a gene regulating moiety.

71. The method of claim 70, wherein said gene regulating moiety is a polynucleotide-guided gene

regulating moiety.

72. The method of claim 70 or 71, wherein said gene regulating moiety is an endonuclease.
73. The method of claim 72, wherein said endonuclease is a clustered regularly interspaced short palindromic repeats (CRISPR)-associated (Cas) endonuclease (e.g., selected from the group consisting of: C2C1, C2C2, C2C3, Cas1, Cas1B, Cas2, Cas3, Cas4, Cas5, Cas5e, Cas6, Cas6e, Cas6f, Cas7, Cas8a, Cas8a1, Cas8a2, Cas8b, Cas8c, Cas9, Cas10, Cas10d, Cas10, Cas10d, Cas 11, Cas12, Cas13, Cas14, CasF, CasG, CasH, CasX, CaxY, Cpf1, Csy1, Csy2, Csy3, Cse1, Cse2, Cse3, Cse4, Csc1, Csc2, Csa5, Csn2, Csm2, Csm3, Csm4, Csm5, Csm6, Cmr1, Cmr3, Cmr4, Cmr5, Cmr6, Csb1, Csb2, Csb3, Csx17, Csx14, Csx10, Csx16, CsaX, Csx3, Csx1, Csx15, Csf1, Csf2, Csf3, Csf4, a modification thereof, and a combination thereof).
74. The method of any one of claims 65-73, further comprising isolating said non-mammary adult stem cell from a tissue or a bodily secretion (e.g., comprising adipose tissue, muscle tissue, cord blood, bone marrow, organ tissue, mammary tissue, extra-embryonic tissue, umbilical cord blood, tendon, periodontal ligament, synovial membrane, trabecular bone, bone marrow, nervous system, skin, periosteum, muscle, peripheral blood, breastmilk, or other body fluid, or a combination thereof) of a subject (e.g., a mammal (e.g., a human, a non-human primate, a horse, a cow, a dairy cow, a buffalo, a goat, a sheep, a camel, an elephant, a snow leopard, a whale, a seal, a pig, a dog, a mouse, a rat, or a rabbit)).
75. The method of any one of claims 65-74, wherein said cell culture comprises a two-dimensional cell culture including said engineered mammary or mammary-like cell, a three-dimensional cell culture including said engineered mammary or mammary-like cell, or a high-density cell culture including said engineered mammary or mammary-like cell.
76. The method of any one of claims 65-75, wherein (b) comprises contacting said engineered mammary or mammary-like cell or a derivative thereof with a lactogenic medium under conditions sufficient to produce said milk component.
77. The method of claim 76, wherein said lactogenic medium comprises a substance capable of activating an expression of a hormone or a signaling factor in said engineered mammary or mammary-like cell or said derivative thereof.
78. The method of claim 76 or 77, wherein said lactogenic medium comprises a substance capable of regulating a cellular response to a hormone or a signaling factor of said engineered milk-producing cell or said derivative thereof.
79. The method of any one of claims 65-78, wherein (b) comprises using said cell culture to generate an aqueous medium comprising one or more particles.
80. The method of claim 79, wherein a particle of said one or more particles comprises a fat surrounded by a layer.
81. The method of claim 80, wherein said layer comprises a milk lipid or fat.
82. The method of any one of claims 65-81, wherein said milk component not comprise lactose.
83. The method of any one of claims 79-82, wherein said one or more particles are emulsified by said

layer and dispersed in said aqueous medium.

84. The method of any one of claims 65-83, wherein said milk component comprises a fat, a protein (e.g., comprising casein, whey protein, alpha-lactalbumin, lactoferrin, immunoglobulin IgA, lysozyme, and albumin, or a combination thereof), or a carbohydrate, or a combination thereof.

85. A food composition (e.g., liquid composition) comprising a milk component, wherein said milk component is produced by one or more engineered mammary or mammary-like cells derived from a non-mammary adult stem cell.

86. The composition of claim 85, wherein said milk component is produced by said one or more engineered mammary or mammary-like cells in a culture medium.

87. The composition of claim 85 or 86, wherein said food composition is a dairy composition selected from the group consisting of: milk (e.g., formulated for a subject (e.g., human) of an age), yogurt, cheese, cream, and butter.

88. The composition of any one of claims 85-87, wherein said milk component comprises a fat, a protein, a carbohydrate, or a combination thereof.

89. The composition of any one of claims 85-88, wherein said milk component comprises, by weight, from about 0.1% to about 20% (e.g., about 0.1% to about 15%, such as about 3% to about 7%, or about 1% to about 2%) protein.

90. The composition of any one of claims 85-89, wherein said milk component comprises, by weight, at most about 30% (e.g., about 0.1% to about 30%, such as about 1% to about 5%, or about 7% to about 8%) carbohydrate.

91. The composition of claim 90, wherein said milk component comprises, by weight, at most about 30% lactose.

92. The composition of any one of claims 85-91, wherein said milk component comprises, by weight, at most about 60% fat (e.g., at most 30%, such as about 3% to about 8%, or about 3% to about 5%).

93. The composition of any one of claims 85-92, wherein said milk component comprises, by weight, (i) from about 3% to about 8% fat, (ii) from about 1% to about 7% protein, and (iii) from about 1% to about 7% carbohydrate.

94. The composition of any one of claims 85-93, wherein said food composition is sterile.

95. The composition of any one of claims 85-94, wherein said food composition is lactose-free.

96. The composition of any one of claims 85-95, wherein said food composition comprises (e.g., by weight, about 0.0005% to about 3%, such as about 0.1% to about 3%, or about 0.1% to about 1%) a mineral.

97. The composition of any one of claim 85-96, wherein said food composition comprises a vitamin.

98. The composition of any one of claim 85-97, wherein said food composition comprises an amino acid.

99. The composition of any one of claim 85-98, wherein said food composition comprises one or more probiotic bacteria (e.g., selected from the group consisting of: *Bifidobacterium*, *Lactobacillus*, *Clostridium*, *Ralstonia*, *Staphylococcus*, *Streptococcus*, and a combination thereof) (e.g., selected from the group

consisting of: *Pseudomonas*, *Staphylococcus*, *Streptococcus*, *Elizabethkingia*, *Variovorax*, *Bifidobacterium*, *Flavobacterium*, *Lactobacillus*, *Stenotrophomonas*, *Brevundimonas*, *Chryseobacterium*, *Enterobacter*, and a combination thereof).

100. The composition of any one of claims 85-99, wherein said food composition comprises an antibody (e.g., immunoglobulin IgA).