NUTRIENT COMPOSITIONS AND METHODS, KITS, AND CELL COMPOSITIONS FOR PRODUCING THE SAME

CROSS-REFERENCE

[0001] This application claims the benefit of Singapore Patent Application No. 10201909295W, filed October 3, 2019, and U.S. Provisional Application No. 63/045,677, filed June 29, 2020, both of which are incorporated herein in their entireties by reference for all purposes.

BACKGROUND

[0002] The global population is expected to surpass 9 billion by 2050. Food production may need to substantially increase to fulfill the demand of the growing population, however there are constraints on resources and arable land. Rapidly developing countries such as China, India, and Russia may increase consumption of richer food products, such as meat, dairy, and eggs leading to an increased global demand on these items. Milk is a popular source of nutrition. It comprises high-quality protein, essential minerals (such as calcium, phosphorus, zinc, magnesium), as well as vitamins (such as riboflavin, vitamin A, vitamin B12) among other components. The only dietary component of infant mammals is milk. Milk components also possess advantageous functional characteristics that permit production of a wide variety of derivative dairy products, such as yogurt, cheese, cream, ice cream, and butter, which further contribute to the industrial and cultural significance of milk.

[0003] The global dairy market volume is estimated to be 216 metric tons (of which 54% market share is taken up by liquid milk) with the global annual sale of 674 billion USD and world consumption of fresh dairy products and processed dairy products are projected to increase by 2.1% and 1.7% per year respectively over the next decade. Plant-based dairy alternatives further account for $1 billion in the US and an estimated $700 million is estimated for lactose-intolerant milk. According to the report of the Food and Agriculture Organization of the United Nations, greenhouse gas emissions from dairy activities make up a high share of total emissions in some countries and the total livestock sector is responsible for 18% of Greenhouse Gas (GHG) emissions, use 30% of earth's terrain, 70% of arable land, and 8% of global freshwater. In addition, the world's demand for dairy is expected to increase by 22% by 2027, rendering traditional dairy production systems unsustainable. Compared to several dairy sources, particularly bovine milk production, cultured dairy is may decrease energy use, GHG emissions, land use and water use while providing access to dairy products.

SUMMARY

[0003a] In one aspect, the present disclosure refers to a method for generating a milk component, the method comprising: a) providing a reaction vessel including a cell culture, 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*.

[0004] Cultured dairy products can be an emerging technology in which milk-producing mammalian cells may be produced through *in vitro* tissue culture in contrast to inefficient traditional livestock agriculture. Compositions and methods are disclosed herein for nutrient compositions (such as liquid nutrient compositions), for example, including at least one lipid, at least one protein, and at least one

oligosaccharide. The nutrient composition (such as liquid nutrient composition) can be substantially free of an immunoglobulin, substantially free of whole cells, or substantially free of bacterial microbes. The liquid compositions described herein can be used for consumption by mammals (e.g., humans) as a nutritious composition, a food composition (e.g., a food product), a food supplement, or as a component or ingredient in a food composition.

[0005] Multiple cell types may be desirable in creating a cultured dairy product (or dairy composition), as traditional dairy products generally do not solely consist of one cell type or component, but consist of, e.g., mammary epithelial and luminal cells, milk proteins, lipids, and polysaccharides among others. Stem cell differentiation may provide an efficient avenue in producing multiple cell types and components for a heterogeneous cultured dairy product. Forced, transient gene expression in cells such as stem cells and with simultaneous conditioning and expansion in a bioreactor may result in an efficient and holistic approach in developing a cultured dairy product. Provided herein are methods and systems for producing milk and resultant milk products (e.g., *in vitro*).

[0006] In some ~~aspects~~examples, the present disclosure provides a liquid composition obtained from an *in vitro* culture of mammary epithelial cells, the liquid composition comprising, by weight: about 25% to about 90% water, about 0.1% to about 20% of at least one protein, about 0% to about 60% of at least one fat, about 0% to about 30% of at least one carbohydrate, and about 0.0005% to about 3% of at least one mineral, where the liquid composition is supplemented with a nutritionally beneficial amount of a nutrient. In some ~~embodiments~~examples, the liquid composition is substantially free of at least one of whole cells, at least one of an antibody, and at least one of a bacterial microbe. In some ~~embodiments~~examples, the liquid composition comprises by weight about 0.1% to about 30% lactose. In some ~~embodiments~~examples, the mammary epithelial cells are of human origin. In some ~~embodiments~~examples, the mammary epithelial cells are of bovine origin. In some ~~embodiments~~examples, the bovine cells are dairy cattle cells. In some ~~embodiments~~examples, the mammary epithelial cells are of goat origin. In some ~~embodiments~~examples, the mammary epithelial cells are of camel origin. In some ~~embodiments~~examples, the mammary epithelial cells are of buffalo origin. In some ~~embodiments~~examples, the mammary epithelial cells are of sheep origin. In some ~~embodiments~~examples, the mammary epithelial cells are of whale origin. In some ~~embodiments~~examples, the mammary epithelial cells are of seal origin. In some ~~embodiments~~examples, the mammary epithelial cells are of elephant origin. In some ~~embodiments~~examples, the mammary epithelial cells are of snow leopard origin. In some ~~embodiments~~examples, the liquid composition comprises, by weight, about 40% to about 90% water, about 0.1% to about 15% of at least one protein, about 0% to about 30% of at least one fat, about 0.1% to about 30% of at least one carbohydrate, and about 0.1% to about 3% of at least one mineral. In some ~~embodiments~~examples, the liquid composition comprises, by weight, about 40% to about 90% water, about 3% to about 7% of at least one protein, about 3% to about 8% of at least one fat, about 1% to about 5% of at least one carbohydrate, and about 0.1% to about 1% of at least one mineral. In some ~~embodiments~~examples, the liquid composition comprises, by weight, about 40% to about 90% water, about 1% to about 2% of at least one protein, about 3% to about 5% of at least one fat, about 7% to about 8% of at least one carbohydrate, and about 0.1% to about 1% of at least one mineral. In some ~~embodiments~~examples, the liquid composition further

comprising a nutritionally beneficial amount of at least one of Immunoglobulin IgA, lactoferrin, and a probiotic microbe.

[0007] In some ~~aspects~~examples, the present disclosure provides a food product comprising a composition obtained from an *in vitro* culture of mammary epithelial cells, the composition comprising, by weight about 25% to about 90% water, about 0.1% to about 20% of at least one protein, about 0% to about 60% of at least one fat, about 0% to about 30% of at least one carbohydrate, and about 0.0005% to about 3% of at least one mineral. In some ~~embodiments~~examples, the composition is substantially free of an antibody, substantially free of whole cells, and substantially free of bacterial microbes. In some ~~embodiments~~examples, the food product comprises a cheese. In some ~~embodiments~~examples, the food product comprises a yogurt. In some ~~embodiments~~examples, the food product comprises an infant formula. In some ~~embodiments~~examples, the mammary epithelial cells are of human origin. In some ~~embodiments~~examples, the composition further comprises a nutritionally beneficial amount of at least one of Immunoglobulin IgA, lactoferrin, and a probiotic microbe. In some ~~embodiments~~examples, the composition comprises, by weight about 40% to about 90% water, about 1% to about 2% of at least one protein, about 3% to about 5% of at least one fat, about 7% to about 8% of at least one carbohydrate, and about 0.1% to about 1% of at least one mineral. In some ~~embodiments~~examples, the composition further comprises a nutritionally beneficial amount of at least one of Immunoglobulin IgA, lactoferrin, and a probiotic microbe.

[0008] In some ~~aspects~~examples, the present disclosure provides an engineered cell exhibiting one or more characteristics of a mammary epithelial cell, the engineered cell comprising an attenuated expression mechanism of a target gene or a target transcript as compared to a natural expression mechanism of a corresponding non-engineered cell. In some ~~embodiments~~examples, the attenuated expression mechanism comprises an altered promoter sequence of the target gene. In some ~~embodiments~~examples, the attenuated expression mechanism effects an altered signaling pathway in the engineered cell. In some ~~embodiments~~examples, the attenuated expression mechanism is affected by an endonuclease. In some ~~embodiments~~examples, the target gene or the target transcript regulates production of a monosaccharide, a disaccharide, or an oligosaccharide. In some ~~embodiments~~examples, the disaccharide is lactose. In some ~~embodiments~~examples, the target gene or the target transcript is lactase (LCT). In some ~~embodiments~~examples, the target gene or the target transcript is endogenous to the corresponding non-engineered cell.

[0009] In some ~~aspects~~examples, the present disclosure provides an engineered mammalian cell exhibiting one or more characteristics of a mammary epithelial cell, the engineered cell comprising, in its genome, an exogenous nucleic acid, where the exogenous nucleic acid encodes a hormone or a signaling factor. In some ~~embodiments~~examples, the hormone or the signaling factor is selected from a growth factor, glucocorticoid, insulin, progesterone, prolactin, and estrogen. In some ~~embodiments~~examples, the exogenous nucleic acid is a heterologous nucleic acid.

[0010] In some ~~aspects~~examples, the present disclosure provides an engineered cell exhibiting one or more characteristics of a mammary epithelial cell, the engineered cell comprising at least one exogenous nucleic acid, where the at least one exogenous nucleic acid encodes at least one of a 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 κB (NF-κB), pTHrP, non-phospho β-catenin, p-p65, RELA, CTNNB1, SMAD3, beclomethasone, betamethasone, budesonide, cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, and triamcinolone. In some ~~embodiments~~examples, the exogenous nucleic acid is a heterologous nucleic acid.

[0011] In some ~~aspects~~examples, the present disclosure provides an engineered cell exhibiting one or more characteristics of a mammary epithelial cell, the engineered cell comprising an inducible gene expression system, the inducible expression system including an exogenous nucleic acid, where the inducible gene expression system is configured to express a hormone or a signaling factor.

[0012] In some ~~embodiments~~examples, the inducible gene expression system is configured to inducibly express the hormone or the signaling factor. In some ~~embodiments~~examples, the hormone or the signaling factor is insulin. In some ~~embodiments~~examples, the hormone or the signaling factor is estrogen. In some ~~embodiments~~examples, the hormone or the signaling factor is progesterone. In some ~~embodiments~~examples, the hormone or the signaling factor is prolactin. Provided herein is an engineered cell exhibiting one or more characteristics of a mammary epithelial cell, the engineered cell comprising an altered genome that effects an enhancement in cellular sensitivity to insulin of the engineered cell as compared to a cellular sensitivity to insulin of a corresponding non-engineered cell. In some ~~embodiments~~examples, the altered genome comprises an altered protein tyrosine phosphatase 1B (PTP1B) gene expression mechanism. In some ~~embodiments~~examples, the altered genome comprises an altered protein tyrosine phosphatase receptor type F (PTPRF) gene expression mechanism. In some ~~embodiments~~examples, the altered genome comprises an altered sirtuin 1 (SIRT1) gene expression mechanism. In some ~~embodiments~~examples, the altered SIRT1 gene expression mechanism comprises an altered SIRT1 regulatory pathway that comprises an exogenous inducible promoter. In some ~~embodiments~~examples, the altered SIRT1 gene expression mechanism is configured to overexpress SIRT1.

[0013] In some ~~aspects~~examples, the present disclosure provides a cell culture comprising an effective amount of a reagent, where the reagent is capable of regulating a cellular response to a hormone or a signaling factor of cells in the cell culture. In some ~~embodiments~~examples, the reagent is a small molecule, a small interfering ribonucleotide (siRNA), a peptide, a nucleic acid, or a transcription factor. In some ~~embodiments~~examples, the reagent is capable of enhancing a cellular response to insulin of the cells in the cell culture. In some ~~embodiments~~examples, the reagent is capable of modulating the biological activity of at least one of sirtuin 1 (SIRT1), protein tyrosine phosphatase 1B (PTP1B), and protein tyrosine phosphatase receptor type F (PTPRF) of the cells comprised in the cell culture. In some ~~embodiments~~examples, the reagent is capable of enhancing the biological activity of sirtuin 1 (SIRT1) of the cells in the cell culture. In some ~~embodiments~~examples, the reagent comprises resveratrol.

[0014] In some ~~aspects~~examples, the present disclosure provides a liquid composition comprising, by weight, about 25% to about 90% water, about 0.1% to about 20% of at least one protein, about 0% to about 60% of at least one fat, about 0% to about 30% of at least one carbohydrate, and about 0.0005% to about 3% of at

least one mineral, and a nutritionally beneficial amount of at least one vitamin, where the liquid composition is substantially free of antibodies, substantially free of bacterial microbes, and substantially free of whole cells. In some ~~embodiments~~examples, the liquid composition further comprises a nutritionally beneficial amount of at least one of Immunoglobulin IgA, lactoferrin, and a probiotic microbe.

[0015] In some ~~aspects~~examples, the present disclosure provides a method for generating an engineered cell, the method comprising: (a) providing an adult stem cell or a derivative thereof; and (b) subjecting the adult stem cell or the derivative thereof to conditions sufficient to generate the engineered cell exhibiting one or more characteristics of a cell of a mammary cell lineage. In some ~~embodiments~~examples, the adult stem cell is a non-mammary adult stem cell. In some ~~embodiments~~examples, the adult stem cell (or the non-mammary adult stem cell) is a mesenchymal stem cell. In some ~~embodiments~~examples, the mammary cell lineage is a mammary epithelial cell lineage. In some ~~embodiments~~examples, the mammary epithelial cell lineage is a mammary epithelial luminal cell lineage. In some ~~embodiments~~examples, the mammary epithelial cell lineage is a mammary basal cell lineage. In some ~~embodiments~~examples, the engineered cell is capable of lactation. In some ~~embodiments~~examples, the engineered cell is capable of producing a milk component. In some ~~embodiments~~examples, (b) is performed *in vitro*.

[0016] In some ~~aspects~~examples, the present disclosure provides a method for generating an engineered cell, the method comprising: (a) providing an adult stem cell or a derivative thereof; and (b) subjecting the adult stem cell or the derivative thereof to conditions sufficient to generate the engineered cell capable of lactation. In some ~~embodiments~~examples, the adult stem cell is a non-mammary adult stem cell. In some ~~embodiments~~examples, the adult stem cell (or the non-mammary adult stem cell) is a mesenchymal stem cell. In some ~~embodiments~~examples, the engineered cell is capable of producing a milk component. In some ~~embodiments~~examples, (b) is performed *in vitro*.

[0017] In some ~~embodiments~~examples of the method for generating the engineered cell, (b) comprises: contacting the adult stem cell (or the non-mammary adult stem cell) or the derivative thereof with a heterologous polypeptide including a gene regulating moiety, where the gene regulating moiety is configured to regulate an expression of a target gene, a target transcript, or a target protein of the adult stem cell (or the non-mammary adult stem cell) or the derivative thereof, thereby effecting a modified expression profile of the target gene, the target transcript, or the target protein in the engineered cell as compared to a corresponding non-engineered adult stem cell (or a corresponding non-engineered non-mammary adult stem cell). In some ~~embodiments~~examples, the target gene, the target transcript, or the target protein is associated with production of a milk component. In some ~~embodiments~~examples, the target gene, the target transcript, or the target protein is associated with at least one selected from the group consisting of: CIDEA, XDH, C/EBPβ, 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. In some ~~embodiments~~examples, the target gene, the target transcript, or the target protein is selected from the group consisting of: CIDEA, XDH, C/EBPβ, 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.

[0018] In some ~~embodiments~~examples of the method for generating the engineered cell, the modified expression profile comprises an up-regulated expression of a gene or a transcript that regulates production of a milk protein. In some ~~embodiments~~examples, the modified expression profile comprises a down-regulated expression of a gene or a transcript that regulates production of a milk protein. In some ~~embodiments~~examples, the gene or the transcript regulates production of a milk protein selected from the group consisting of: α S1/S2 casein, β casein, κ casein, α-lactalbumin, lactoferrin, lactoperoxidase, lysozyme, haptocorrin, osteopontin, serum albumin, complement C3, complement C4, and a combination thereof.

[0019] In some ~~embodiments~~examples of the method for generating the engineered cell, the modified expression profile comprises an up-regulated expression of a gene or a transcript that regulates production of a milk carbohydrate. In some ~~embodiments~~examples, the modified expression profile comprises a down-regulated expression of gene or a transcript that regulates production of a milk carbohydrate. In some ~~embodiments~~examples, the gene or the transcript regulates production of 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. In some ~~embodiments~~examples, the gene or the transcript regulating the production of the 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.

[0020] In some ~~embodiments~~examples of the method for generating the engineered cell, the modified expression profile comprises an up-regulated expression of a gene or a transcript that degrades lactose. In some ~~embodiments~~examples, the modified expression profile comprises a down-regulated expression of a gene or a transcript that degrades lactose. In some ~~embodiments~~examples, the gene or the transcript that degrades the lactose is a gene or a transcript selected from the group consisting of: Lac operon, lactase, and glycosidase.

[0021] In some ~~embodiments~~examples of the method for generating the engineered cell, the modified expression profile comprises an up-regulated expression of a gene or a transcript that regulates production of a milk fat. In some ~~embodiments~~examples, the modified expression profile comprises a down-regulated expression of a gene or a transcript that regulates production of a milk fat. In some ~~embodiments~~examples, the gene or the transcript regulating the production of the milk fat is a gene or a transcript selected from the group consisting of: CIDEA, XDH, C/EBPβ, 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.

[0022] In some ~~embodiments~~examples of the method for generating the engineered cell, the modified expression profile comprises an up-regulated expression of a gene or a transcript that regulates production of a milk lipid. In some ~~embodiments~~examples, the modified expression profile comprises a down-regulated expression of a gene or a transcript that regulates production of a milk lipid. In some ~~embodiments~~examples, the gene or the transcript regulates production of 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, dihomo-γ-linoleic acid, arachidonic acid, docosadienoic acid, adrenic acid, asbond acid, tetracosatetraenoic acid, tetracospentaenoic 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. In some ~~embodiments~~examples, the gene or the transcript regulating the production of the milk lipid is a gene or a transcript selected from the group consisting of: CIDEA, XDH, C/EBPβ, 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.

[0023] In some ~~embodiments~~examples of the method for generating the engineered cell, the gene or the transcript regulates a cellular response to a hormone or a signaling factor. In some ~~embodiments~~examples, the gene or the transcript regulating the 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. In some ~~embodiments~~examples, the modified expression profile comprises (1) an up-regulated expression of a first target gene, a first target transcript, or a first target protein, and (2) a down-regulated expression of a second target gene, a second target transcript, or a second target protein. In some ~~embodiments~~examples, the modified expression profile is characteristic of a mammary cell lineage. In some ~~embodiments~~examples, the modified expression profile comprises a modified expression profile 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.

[0024] In some ~~embodiments~~examples of the method for generating the engineered cell, the engineered cell is configured to generate a milk component in response to a hormone or a signaling factor.

[0025] In some ~~embodiments~~examples of the method for generating the engineered cell, the method further comprises contacting the adult stem cell (or the non-mammary adult stem cell) or the derivative thereof with an exogenous polynucleotide, which exogenous polynucleotide (1) includes an inducible promoter sequence and (2) encodes a hormone or a signaling factor. In some ~~embodiments~~examples, the inducible promoter sequence is configured for inducible expression of the hormone or the signaling factor. In some ~~embodiments~~examples, the inducible promoter sequence is configured for activation by a reagent. In some ~~embodiments~~examples, the engineered cell has an altered response to a hormone or a signaling factor as compared to a corresponding non-engineered adult stem cell (or a corresponding non-engineered non-mammary adult stem cell). In some ~~embodiments~~examples, the engineered cell has an enhanced sensitivity to a hormone or a signaling factor as compared to the corresponding non-engineered adult stem cell (or the corresponding non-engineered non-mammary adult stem cell). In some ~~embodiments~~examples, the engineered cell has a diminished sensitivity to a hormone or a signaling factor as compared to the corresponding non-engineered adult stem cell (or the corresponding non-engineered non-mammary adult stem cell).

[0026] In some ~~embodiments~~examples of the method for generating the engineered cell, the hormone or the 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 κB (NF-κB), pTHrP, non-phospho β-catenin, p-p65, RELA, CTNNB1, SMAD3, and a combination thereof. In some ~~embodiments~~examples, the glucocorticoid comprises beclomethasone, betamethasone, budesonide, cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone, or a combination thereof.

[0027] In some ~~embodiments~~examples of the method for generating the engineered cell, where (b) comprises contacting the adult stem cell (or the non-mammary adult stem cell) or the derivative thereof with a

heterologous polypeptide including a gene regulating moiety, the gene regulating moiety is a polynucleotide-guided gene regulating moiety. In some ~~embodiments~~examples, the gene regulating moiety is an endonuclease. In some ~~embodiments~~examples, the endonuclease is a clustered regularly interspaced short palindromic repeats (CRISPR)-associated (Cas) endonuclease. In some ~~embodiments~~examples, the Cas endonuclease is 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.

[0028] In some ~~embodiments~~examples of the method for generating the engineered cell, the mammary cell lineage is a mammary epithelial cell lineage. In some ~~embodiments~~examples, the mammary cell lineage is a mammary alveolar cell lineage. In some ~~embodiments~~examples, the mammary cell lineage is a mammary myoepithelial cell lineage.

[0029] In some ~~embodiments~~examples of the method for generating the engineered cell, (b) further comprises contacting the adult stem cell (or the non-mammary adult stem cell) or the derivative thereof with a heterologous polynucleotide configured to bind at least a portion of the target gene or the target transcript. In some ~~embodiments~~examples, (b) further comprises forming a complex of the gene regulating moiety and the heterologous polynucleotide. In some ~~embodiments~~examples, the complex is a clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated (Cas) protein complex.

[0030] In some ~~embodiments~~examples of the method for generating the engineered cell, (b) comprises contacting the adult stem cell (or the non-mammary adult stem cell) or the derivative thereof with a differentiation medium under conditions sufficient to obtain the engineered cell.

[0031] In some ~~embodiments~~examples of the method for generating the engineered cell, (a) comprises isolating the adult stem cell (or the non-mammary adult stem cell) from a tissue or a bodily secretion of a mammalian subject. In some ~~embodiments~~examples, the tissue or the bodily secretion comprises 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. In some ~~embodiments~~examples, the tissue or the bodily secretion comprises adipose tissue, mammary tissue, umbilical cord, umbilical cord blood, breastmilk, or a combination thereof. In some ~~embodiments~~examples, the subject is a mammal. In some ~~embodiments~~examples, the mammal is 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.

[0032] Certain ~~aspects~~examples of the present disclosure provide a composition comprising the engineered cell produced by the method for generating an engineered cell as described herein.

[0033] In some ~~aspects~~examples, the present disclosure provides a composition comprising an engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) exhibiting a modified expression profile that is different than an expression profile of a corresponding non-engineered cell (or non-engineered adult stem cell, or non-engineered non-mammary adult stem cell), where the engineered cell (or engineered adult stem cell, or 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. In some ~~embodiments~~examples, the cell of the mammary cell lineage is a cell of a mammary epithelial cell lineage. In some ~~embodiments~~examples, the mammary epithelial cell lineage is a mammary epithelial luminal cell lineage. In some ~~embodiments~~examples, the mammary epithelial cell lineage is a mammary basal cell lineage. In some ~~embodiments~~examples, the engineered cell is an engineered cell capable of lactation.

[0034] In some ~~aspects~~examples, the present disclosure provides a composition comprising an engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) exhibiting a modified expression profile that is different than an expression profile of a corresponding non-engineered cell (or non-engineered adult stem cell, or non-engineered non-mammary adult stem cell), where the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) is configured to be differentiated to an engineered cell capable of lactation.

[0035] In some ~~embodiments~~examples of the composition comprising the engineered cell, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) is configured to produce a milk component. In some ~~embodiments~~examples, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) is an engineered mesenchymal stem cell. In some ~~embodiments~~examples, the corresponding non-engineered cell (or non-engineered adult stem cell, or non-engineered non-mammary adult stem cell) is a corresponding non-engineered mesenchymal stem cell. In some ~~embodiments~~examples, the mammary cell lineage is a mammary luminal cell lineage, a mammary epithelial cell lineage, a mammary alveolar cell lineage, or a mammary myoepithelial cell lineage.

[0036] In some ~~embodiments~~examples of the composition comprising the engineered cell, the engineered cell (or engineered adult stem cell, or 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. In some ~~embodiments~~examples, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) comprises a heterologous polypeptide including a gene regulating moiety. In some ~~embodiments~~examples, the gene regulating moiety is a polynucleotide-guided gene regulating moiety. In some ~~embodiments~~examples, the gene regulating moiety is an endonuclease. In some ~~embodiments~~examples, the endonuclease is a clustered regularly interspaced short palindromic repeats (CRISPR)-associated (Cas) endonuclease. In some ~~embodiments~~examples, the Cas endonuclease is 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. In some ~~embodiments~~examples, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) or an ancestor cell thereof has been brought in contact with a heterologous polynucleotide configured to form a complex with the gene regulating moiety.

[0037] In some ~~embodiments~~examples of the composition comprising the engineered cell, the gene regulating moiety is configured to regulate an expression of a target gene, a target transcript, or a target protein of the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell). In some ~~embodiments~~examples, the target gene, the target transcript, or the target protein is associated with production of a milk component. In some ~~embodiments~~examples, the target gene, the target transcript, or the target protein is associated with at least one selected from the group consisting of: CIDEA, XDH, C/EBPβ, 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. In some ~~embodiments~~examples, the target gene, the target transcript, or the target protein is selected from the group consisting of: CIDEA, XDH, C/EBPβ, 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.

[0038] In some ~~embodiments~~examples of the composition comprising the engineered cell, the modified expression profile comprises an up-regulated expression of a gene or a transcript that regulates production of a milk protein. In some ~~embodiments~~examples, the modified expression profile comprises a down-regulated expression of a gene or a transcript that regulates production of a milk protein. In some ~~embodiments~~examples, the gene or the transcript regulating the production of the milk protein selected from the group consisting of:

casein and whey protein. In some ~~embodiments~~examples, the gene or the transcript regulating the production of the milk protein is a gene or a transcript selected from the group consisting of: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, and a combination thereof.

[0039] In some ~~embodiments~~examples of the composition comprising the engineered cell, the modified expression profile comprises an up-regulated expression of a gene or a transcript that regulates production of a milk carbohydrate. In some ~~embodiments~~examples, the modified expression profile comprises a down-regulated expression of a gene or a transcript that regulates production of a milk carbohydrate. In some ~~embodiments~~examples, the gene or the transcript regulates production of 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. In some ~~embodiments~~examples, the gene or the transcript regulating the production of the 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.

[0040] In some ~~embodiments~~examples of the composition comprising the engineered cell, the modified expression profile comprises an up-regulated expression of a gene or a transcript that degrades lactose. In some ~~embodiments~~examples, the modified expression profile comprises a down-regulated expression of a gene or a transcript that degrades lactose. In some ~~embodiments~~examples, the gene or the transcript that degrades lactose is a gene or a transcript selected from the group consisting of: Lac operon, lactase, and glycosidase.

[0041] In some ~~embodiments~~examples of the composition comprising the engineered cell, the modified expression profile comprises an up-regulated expression of a gene or a transcript that regulates production of a milk fat. In some ~~embodiments~~examples, the modified expression profile comprises a down-regulated expression of a gene or a transcript that regulates production of a milk fat. In some ~~embodiments~~examples, the gene or the transcript regulates production of 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, tetracospentaenoic 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. In some

~~embodiments~~examples, the gene or the transcript regulating the production of the milk fat is a gene or a transcript selected from the group consisting of: CIDEA, XDH, C/EBPβ, 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.

[0042] In some ~~embodiments~~examples of the composition comprising the engineered cell, the gene or the transcript regulates a cellular response to a hormone or a signaling factor. In some ~~embodiments~~examples, the gene or the transcript regulating the 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.

[0043] In some ~~embodiments~~examples of the composition comprising the engineered cell, the modified expression profile comprises (i) an up-regulated expression of a first target gene, a first target transcript, or a first target protein, and (ii) a down-regulated expression of a second target gene, a second target transcript, or a second target protein.

[0044] In some ~~embodiments~~examples of the composition comprising the engineered cell, the modified expression profile is indicative of the mammary cell lineage. In some ~~embodiments~~examples, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) exhibits a cellular morphology indicative of the mammary cell lineage. In some ~~embodiments~~examples, the mammary cell lineage is a mammary epithelial cell lineage. In some ~~embodiments~~examples, the mammary cell lineage is a mammary alveolar cell lineage. In some ~~embodiments~~examples, the mammary cell lineage is a mammary myoepithelial cell lineage.

[0045] In some ~~embodiments~~examples of the composition comprising the engineered cell, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) is configured to generate a milk component in response to a hormone or a signaling factor. In some ~~embodiments~~examples, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) comprises an exogenous polynucleotide that (1) includes an inducible promoter sequence and (2) encodes a hormone or a signaling factor. In some ~~embodiments~~examples, the inducible promoter sequence is configured for inducible expression of the hormone or the signaling factor. In some ~~embodiments~~examples, the inducible promoter sequence is configured for activation by a reagent. In some ~~embodiments~~examples, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) has an altered response to a hormone or a signaling factor as compared to a corresponding non-engineered cell (or non-engineered adult stem cell, or non-engineered non-mammary adult stem cell). In some ~~embodiments~~examples, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) has an enhanced sensitivity to a hormone or a signaling factor

as compared to the corresponding non-engineered cell (or non-engineered adult stem cell, or non-engineered non-mammary adult stem cell). In some ~~embodiments~~examples, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) has a diminished sensitivity to a hormone or a signaling factor as compared to the corresponding non-engineered cell (or non-engineered adult stem cell, or non-engineered non-mammary adult stem cell). In some ~~embodiments~~examples, the hormone or the 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 κB (NF-κB), pTHrP, non-phospho β-catenin, p-p65, RELA, CTNNB1, SMAD3, and a combination thereof. In some ~~embodiments~~examples, the glucocorticoid comprises beclomethasone, betamethasone, budesonide, cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone, or a combination thereof.

[0046] In some ~~embodiments~~examples of the composition comprising the engineered cell, the engineered cell (or engineered adult stem cell, or engineered non-mammary adult stem cell) is derived from a non-mammary adult stem cell isolated from a tissue or a bodily secretion of a subject. In some ~~embodiments~~examples, the tissue or the bodily secretion comprises 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. In some ~~embodiments~~examples, the tissue or the bodily secretion comprises adipose tissue, mammary tissue, umbilical cord, umbilical cord blood, breastmilk, or a combination thereof. In some ~~embodiments~~examples, the subject is a mammal. In some ~~embodiments~~examples, the mammal is 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.

[0047] In some ~~aspects~~examples, the present disclosure also provides a method for generating a milk component, the method comprising: (a) providing a reaction vessel including a cell culture, which cell culture comprises an engineered mammary or mammary-like cell derived from an adult stem cell (or a non-mammary adult stem cell); and (b) subjecting the cell culture to conditions sufficient to produce the milk component *in vitro*. In some ~~embodiments~~examples, the cell culture further comprises a culture medium. In some ~~embodiments~~examples, the adult stem cell (or non-mammary adult stem cell) is a mesenchymal stem cell. In some ~~embodiments~~examples, the engineered mammary or mammary-like cell is an engineered milk-producing cell. In some ~~embodiments~~examples, the engineered mammary or mammary-like cell exhibits one or more characteristics of a mammary cell. In some ~~embodiments~~examples, the engineered mammary or mammary-like cell exhibits one or more characteristics of a mammary epithelial cell. In some ~~embodiments~~examples, the engineered mammary or mammary-like cell exhibits one or more characteristics of a mammary myoepithelial cell. In some ~~embodiments~~examples, the cell culture comprises a two-dimensional cell culture including the engineered mammary or mammary-like cell, a three-dimensional cell culture including the engineered mammary or mammary-like cell, or a high-density cell culture including the engineered mammary or mammary-like cell.

[0048] In some ~~embodiments~~examples of the method for generating the milk component, the engineered mammary or mammary-like cell comprises a genome that is different from a genome of a naturally occurring milk-producing cell. In some ~~embodiments~~examples, the engineered mammary or mammary-like cell has been brought in contact with a heterologous polypeptide, which heterologous polypeptide includes a gene regulating moiety. In some ~~embodiments~~examples, the gene regulating moiety is a polynucleotide-guided gene regulating moiety. In some ~~embodiments~~examples, the gene regulating moiety is an endonuclease. In some ~~embodiments~~examples, the endonuclease is a clustered regularly interspaced short palindromic repeats (CRISPR)-associated (Cas) endonuclease. In some ~~embodiments~~examples, the Cas endonuclease is 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.

[0049] In some ~~embodiments~~examples of the method for generating the milk component, (b) comprises using the adult stem cell (or non-mammary adult stem cell) or a derivative thereof to generate the engineered mammary or mammary-like cell or a derivative thereof.

[0050] In some ~~embodiments~~examples of the method for generating the milk component, (b) comprises: contacting the adult stem cell (or non-mammary adult stem cell) or the derivative thereof with a growth medium under conditions sufficient to produce an expanded cell culture.

[0051] In some ~~embodiments~~examples of the method for generating the milk component, (b) comprises: contacting the adult stem cell (or non-mammary adult stem cell) or the derivative thereof with a differentiation medium under conditions sufficient to obtain the engineered mammary or mammary-like cell.

[0052] In some ~~embodiments~~examples of the method for generating the milk component, the method further comprises isolating the adult stem cell (or non-mammary adult stem cell) from a tissue or a bodily secretion of a subject. In some ~~embodiments~~examples, the tissue or the bodily secretion comprises 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. In some ~~embodiments~~examples, the tissue or the bodily secretion comprises adipose tissue, mammary tissue, umbilical cord, umbilical cord blood, breastmilk, or a combination thereof. In some ~~embodiments~~examples, the subject is a mammal. In some ~~embodiments~~examples, the mammal is 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.

[0053] In some ~~embodiments~~examples of the method for generating the milk component, (b) comprises contacting the engineered mammary or mammary-like cell or a derivative thereof with a lactogenic medium

under conditions sufficient to produce the milk component. In some ~~embodiments~~examples, the lactogenic medium comprises a substance capable of activating an expression of a hormone or a signaling factor in the engineered mammary or mammary-like cell or the derivative thereof. In some ~~embodiments~~examples, the lactogenic medium comprises a substance capable of regulating a cellular response to a hormone or a signaling factor of the engineered milk-producing cell or the derivative thereof.

[0054] In some ~~embodiments~~examples of the method for generating the milk component, the milk component comprises whey protein, casein, a lipid, an oligosaccharide, or a combination thereof.

[0055] In some ~~embodiments~~examples of the method for generating the milk component, (b) comprises using the cell culture to generate an aqueous medium comprising one or more particles. In some ~~embodiments~~examples, a particle of the one or more particles comprises a fat surrounded by a layer. In some ~~embodiments~~examples, the layer comprises a milk lipid or fat. In some ~~embodiments~~examples, the layer comprises a milk fat globule membrane (MFGM). In some ~~embodiments~~examples, the milk fat globule membrane (MFGM) comprises a milk fat globule membrane (MFGM) protein. In some ~~embodiments~~examples, the fat comprises a triglyceride. In some ~~embodiments~~examples, the aqueous medium comprises a carbohydrate. In some ~~embodiments~~examples, the carbohydrate comprises a monosaccharide, a disaccharide, an oligosaccharide, or a combination thereof. In some ~~embodiments~~examples, the oligosaccharide comprises from 3 to 20 saccharide units. In some ~~embodiments~~examples, the oligosaccharide comprises a terminal lactose moiety. In some ~~embodiments~~examples, the carbohydrate comprises a plurality of oligosaccharides comprising the oligosaccharide. In some ~~embodiments~~examples, the milk component not comprise lactose. In some ~~embodiments~~examples, the one or more particles are emulsified by the layer and dispersed in the aqueous medium. In some ~~embodiments~~examples, the milk component comprises a fat, a protein, or a carbohydrate, or a combination thereof. In some ~~embodiments~~examples, the protein comprises casein, whey protein, alpha-lactalbumin, lactoferrin, immunoglobulin IgA, lysozyme, and serum albumin, or a combination thereof.

[0056] In some ~~embodiments~~examples of the method for generating the milk component, the method further comprises isolating the milk component from the cell culture.

[0057] In some ~~embodiments~~examples of the method for generating the milk component, the method results in a sterile composition comprising the milk component. In some ~~embodiments~~examples, the sterile composition is free of whole cells.

[0058] Certain ~~aspects~~examples of the present disclosure provides a food composition comprising a milk component, which milk component is produced by a method for generating the milk component as described herein.

[0059] In some ~~aspects~~examples, the present disclosure further provides a food composition comprising a milk component, where the milk component is produced by one or more engineered mammary or mammary-like cells in a culture medium.

[0060] In some ~~aspects~~examples, the present disclosure further provides a food composition comprising a milk component, where the milk component is produced by one or more engineered mammary or mammary-like cells derived from a non-mammary adult stem cell. In some ~~embodiments~~examples, the milk component is produced by the one or more engineered mammary or mammary-like cells in a culture medium.

[0061] In some ~~embodiments~~examples of the food composition, the culture medium comprises one or more particles. In some ~~embodiments~~examples, a particle of the one or more particles comprises a fat surrounded by a layer. In some ~~embodiments~~examples, the layer comprises a milk lipid or fat. In some ~~embodiments~~examples, the layer comprises a milk fat globule membrane (MFGM). In some ~~embodiments~~examples, the milk fat globule membrane (MFGM) comprises a milk fat globule membrane (MFGM) protein. In some ~~embodiments~~examples, the fat of the particle comprises a triglyceride. In some ~~embodiments~~examples, the culture medium comprises a carbohydrate. In some ~~embodiments~~examples, the carbohydrate comprises a monosaccharide, a disaccharide, an oligosaccharide, or a combination thereof. In some ~~embodiments~~examples, the oligosaccharide comprises from 3 to 20 saccharide units. In some ~~embodiments~~examples, the oligosaccharide comprises a terminal lactose moiety. In some ~~embodiments~~examples, the carbohydrate comprises a plurality of oligosaccharides comprising the oligosaccharide. In some ~~embodiments~~examples, the milk component not comprise lactose. In some ~~embodiments~~examples, the one or more particles are emulsified by the layer and dispersed in the culture medium.

[0062] In some ~~embodiments~~examples, the food composition is a dairy composition selected from the group consisting of: milk, yogurt, cheese, cream, and butter. In some ~~embodiments~~examples, the milk is selected from colostrum, mature milk, fore milk, hind milk, and transition milk. In some ~~embodiments~~examples, the milk is formulated for a subject of an age. In some ~~embodiments~~examples, the milk is formulated for a child of an age three-years or younger. In some ~~embodiments~~examples, the milk is formulated for an infant of twelve-month old or younger.

[0063] In some ~~embodiments~~examples of the food composition, the milk component comprises a fat, a protein, a carbohydrate, or a combination thereof. In some ~~embodiments~~examples, the protein comprises casein, whey protein, alpha-lactalbumin, lactoferrin, immunoglobulin IgA, lysozyme, serum albumin, or a combination thereof. In some ~~embodiments~~examples, the carbohydrate comprises a monosaccharide, a disaccharide, an oligosaccharide, or a combination thereof. In some ~~embodiments~~examples, the oligosaccharide comprises from 3 to 20 saccharide units. In some ~~embodiments~~examples, the oligosaccharide comprises a terminal lactose moiety. In some ~~embodiments~~examples, the carbohydrate comprises a plurality of oligosaccharides. In some ~~embodiments~~examples, the carbohydrate does not comprise lactose. In some ~~embodiments~~examples, the fat comprises a triglyceride.

[0064] In some ~~embodiments~~examples, the milk component comprises, by weight, at least (about) 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or 10% protein. In some ~~embodiments~~examples, the milk component comprises, by weight, at most (about) 30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, or 0.5% protein. In some ~~embodiments~~examples, the milk component comprises protein, by weight, in a range of any two of the following values: (about) 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, 25%, 26%, 27%, 28%, 29%, or 30%.

[0065] In some ~~embodiments~~examples, the milk component comprises, by weight, at least (about) 0.01%, 0.05%, 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or 10% carbohydrate. In some ~~embodiments~~examples, the milk component comprises, by weight, at most (about)

30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5%, 0.2%, 0.1%, 0.05%, or 0.01% carbohydrate. In some ~~embodiments~~examples, the milk component comprises carbohydrate, by weight, in a range of any two of the following values: (about) 0.01%, 0.05%, 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, 25%, 26%, 27%, 28%, 29%, or 30%. In some ~~embodiments~~examples, the milk component is substantially free of carbohydrate. In some ~~embodiments~~examples, the milk component does not comprise carbohydrate. In some ~~embodiments~~examples, the milk component comprises, by weight, at least (about) 0.01%, 0.05%, 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or 10% lactose. In some ~~embodiments~~examples, the milk component comprises, by weight, at most (about) 30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5%, 0.2%, 0.1%, 0.05%, or 0.01% lactose. In some ~~embodiments~~examples, the milk component comprises lactose, by weight, in a range of any two of the following values: (about) 0.01%, 0.05%, 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, 25%, 26%, 27%, 28%, 29%, or 30%. In some ~~embodiments~~examples, the milk component is substantially free of lactose. In some ~~embodiments~~examples, the milk component does not comprise lactose.

[0066] In some ~~embodiments~~examples, the milk component comprises, by weight, at least (about) 0.01%, 0.05%, 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or 10% fat. In some ~~embodiments~~examples, the milk component comprises, by weight, at most (about) 60%, 57%, 55%, 53%, 50%, 47%, 45%, 43%, 40%, 37%, 35%, 33%, 30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5%, 0.2%, 0.1%, 0.05%, or 0.01% fat. In some ~~embodiments~~examples, the milk component comprises fat, by weight, in a range of any two of the following values: (about) 0.01%, 0.05%, 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, 25%, 26%, 27%, 28%, 29%, 30%, 33%, 35%, 37%, 40%, 43%, 45%, 47%, 50%, 53%, 55%, 57%, or 60%. In some ~~embodiments~~examples, the milk component is substantially free of fat. In some ~~embodiments~~examples, the milk component does not comprise fat.

[0067] In some ~~embodiments~~examples, the milk component comprises, by weight:

(i) from about 1% to about 20%, from about 2% to about 20%, from about 3% to about 20%, from about 4% to about 20%, from about 5% to about 20%, from about 1% to about 15%, from about 2% to about 15%, from about 3% to about 15%, from about 4% to about 15%, from about 5% to about 15%, from about 1% to about 10%, from about 2% to about 10%, from about 3% to about 10%, from about 4% to about 10%, from about 5% to about 10%, from about 1% to about 9%, from about 2% to about 9%, from about 3% to about 9%, from about 4% to about 9%, from about 5% to about 9%,from about 1% to about 8%, from about 2% to about 8%, from about 3% to about 8%, from about 4% to about 8%, from about 5%

5%, from about 0.5% to about 5%, from about 0.6% to about 5%, from about 0.7% to about 5%, from about 0.8% to about 5%, from about 0.9% to about 5%, from about 1% to about 5% carbohydrate.

[0068] In some ~~embodiments~~examples, the food composition is sterile. In some ~~embodiments~~examples, the food composition is lactose-free. In some ~~embodiments~~examples, the food composition further comprises a mineral. In some ~~embodiments~~examples, the food composition further comprises a vitamin. In some ~~embodiments~~examples, the food composition further comprises an amino acid. In some ~~embodiments~~examples, the food composition further comprises one or more probiotic bacteria. In some ~~embodiments~~examples, the one or more probiotic bacteria comprises one or more strains selected from the group consisting of: *Bifidobacterium*, *Lactobacillus*, *Clostridium*, *Ralstonia*, *Staphylococcus*, *Streptococcus*, and a combination thereof. In some ~~embodiments~~examples, the one or more probiotic bacteria comprises one or more strains selected from the group consisting of: *Pseudomonas*, *Staphylococcus*, *Streptococcus*, *Elizabethkingia*, *Variovorax*, *Bifidobacterium*, *Flavobacterium*, *Lactobacillus*, *Stenotrophomonas*, *Brevundimonas*, *Chryseobacterium*, *Enterobacter*, and a combination thereof. In some ~~embodiments~~examples, the food composition further comprises an antibody. In some ~~embodiments~~examples, the antibody comprises Immunoglobulin IgA. In some ~~embodiments~~examples, the food composition further comprises lactoferrin.

[0069] Another ~~aspect~~example of the present disclosure provides a non-transitory computer readable medium comprising machine executable code that, upon execution by one or more computer processors, implements any of the methods above or elsewhere herein.

[0070] Another ~~aspect~~example of the present disclosure provides a system comprising one or more computer processors and computer memory coupled thereto. The computer memory comprises machine executable code that, upon execution by the one or more computer processors, implements any of the methods above or elsewhere herein.

[0071] Additional ~~aspects~~examples and advantages of the present disclosure will become readily apparent to those skilled in this art from the following detailed description, wherein only illustrative ~~embodiments~~examples of the present disclosure are shown and described. As will be realized, the present disclosure is capable of other and different ~~embodiments~~examples, and its several details are capable of modifications in various obvious respects, all without departing from the disclosure. Accordingly, the drawings and description are to be regarded as illustrative in nature, and not as restrictive.

INCORPORATION BY REFERENCE

[0072] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference. To the extent publications and patents or patent applications incorporated by reference contradict the disclosure contained in the specification, the specification is intended to supersede and/or take precedence over any such contradictory material.

CLAIMS

WHAT IS CLAIMED IS:

1. A method for generating ~~an engineered cell~~a milk component, the method comprising:

~~(~~a) ~~providing~~ providing a reaction vessel including a cell culture, which cell culture comprises an engineered mammary or mammary-like cell derived from a non-mammary adult stem cell ~~or a derivative thereof~~; and

~~(~~b) ~~subjecting~~ subjecting said ~~non-mammary adult stem cell or said derivative thereof~~cell culture 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.~~produce said milk component *in vitro*.

~~3.~~ The method of ~~any one of claims~~claim 1 ~~2~~, wherein ~~(b) is performed *in vitro*.~~

~~4.~~2. ~~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~~comprises whey protein, ~~a carbohydrate~~casein, a lipid, an oligosaccharide, or a combination thereof~~).~~.

3. The method of ~~any one~~claim 1, wherein said engineered mammary or mammary-like cell is an engineered milk-producing cell.

~~5.~~4. The method of ~~claims~~claim 1 ~~4~~, wherein said non-mammary adult stem cell is a mesenchymal stem cell.

5. The method of ~~any one of claims~~claim 1 ~~5, wherein (b) comprises:~~, wherein said engineered mammary or mammary-like cell is derived from said non-mammary adult stem cell at least in part by contacting said non-mammary adult stem cell or ~~said~~ derivative thereof with a heterologous polypeptide including a gene regulating moiety.

6. The method of claim 5, wherein said engineered mammary or mammary-like cell is derived from said non-mammary adult stem cell *in vitro*.

7. The method of claim 5, wherein said gene regulating moiety is ~~configured to regulate~~a

polynucleotide-guided gene regulating moiety.

6.8. The method of claim 5, wherein said gene regulating moiety regulates 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 mammary or mammary-like cell as compared to a corresponding non-engineered non-mammary adult stem cell.

7.9. The method of claim 68, wherein said target gene, said target transcript, or said target protein is associated with production of a milk component (e.g., comprisingselected from the group consisting of a fat, amilk protein, a milk carbohydrate, ora milk fat, a milk lipid, and 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/EBPβ, 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, 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,

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.

13.10. The method of claim 4 or 7The method of claim 8, 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/EBPβ, 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, dihomo-γ-linoleic acid, arachidonic acid, docosadienoic acid, adrenic acid, asbond acid, tetracosatetraenoic acid, tetracospentaenoic 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/EBPβ, 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, 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.~~

~~21.~~11. ~~The method of any one of claims 6-20~~The method of claim 8, wherein said modified expression profile is characteristic of a mammary cell lineage.

~~22.~~12. The method of claim ~~21~~8, wherein said ~~modified expression profile comprises a modified expression profile (e.g., an up-regulated expression, or a down-regulated expression) of a~~target gene, ~~a~~said target transcript, or ~~a~~said target protein is selected from the group consisting of: EpCAM, CD14, CD24, Muc1, CD29, CD49b, CD49f, CD61, Sca1, Prominin, 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.~~13. ~~The method of any one of claims 6-24~~5, wherein said gene regulating moiety is an endonuclease.

~~26.~~14. The method of claim ~~25~~13, 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.

29.15. The method of claim 1, wherein said engineered mammary or mammary-like cell is 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 factorimmortalized cell.

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 κB (NF-κB), 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.

33.16. The method of claim 1, wherein said engineered mammary or mammaryA 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).~~ -like cell is configured to generate said milk component in response to a hormone or a signaling factor.

~~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/EBPβ, 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, 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, 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, tetracospentaenoic 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/EBPβ, 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, dihomo-γ-linoleic acid, arachidonic acid, docosadienoic acid, adrenic acid, asbond acid, tetracosatetraenoic acid, tetracospentaenoic 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/EBPβ, 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 κB (NF-κB), 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.~~17. The method of claim ~~The method of any one of claims 65-74~~1, 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.~~18. The method of ~~any one of claims 65-75~~claim 1, 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.~~19. The method of claim ~~76~~18, wherein said lactogenic medium comprises a substance ~~capable of activating~~that activates an expression of a hormone or a signaling factor in said engineered mammary or mammary-like cell ~~or said derivative thereof~~.

~~78.~~20. The method of claim ~~76 or 77~~18, wherein said lactogenic medium comprises a substance ~~capable of regulating~~that regulates a cellular response to a hormone or a signaling factor of said engineered ~~milk-producing~~mammary or mammary-like 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).~~