What is claimed is:

1. A live cell construct comprising,

a scaffold having a top surface and a bottom surface; and

a continuous monolayer of (a) live primary mammary epithelial cells, (b) a mixed population of live primary mammary epithelial cells, mammary myoepithelial cells and mammary progenitor cells, and/or (c) live immortalized mammary epithelial cells on the top surface of the scaffold, the continuous monolayer of (a) live primary mammary epithelial cells, (b) mixed population of live primary mammary epithelial cells mammary myoepithelial cells and mammary progenitor cells, and/or (c) immortalized mammary epithelial cells having an apical surface and a basal surface (e.g., the cells form a polarized and confluent cell monolayer), wherein the construct comprises an apical compartment above and adjacent to the apical surface of the continuous monolayer of the (a) live primary mammary epithelial cells, the (b) mixed population of live primary mammary epithelial cells, mammary myoepithelial cell and mammary progenitor cells, and/or the (c) immortalized mammary epithelial cells and a basal compartment below and adjacent to the bottom surface of the scaffold.

~~2. The live cell construct of claim 1, wherein milk produced by the primary mammary epithelial cells or immortalized mammary epithelial cells is excreted through the apical surface of the cells into the apical compartment.~~

~~3~~2. The live cell construct of claim 1 ~~or claim 2~~, wherein the basal compartment comprises a basal culture medium and the basal culture medium is in contact with the basal surface of the live primary mammary epithelial cells, the mixed population of live primary mammary epithelial cells, mammary myoepithelial cells and mammary progenitor cells, and/or the immortalized mammary epithelial cells~~.~~, preferably

~~4. The live cell construct of claim 3, wherein~~ the basal culture medium comprises a carbon source, a chemical buffering system, one or more essential amino acids, one or more vitamins and/or cofactors, and one or more inorganic salts~~.~~, more preferably

~~5. The live cell construct of claim 3 or claim 4, wherein~~ the basal culture medium is a lactogenic culture medium and further comprises prolactin.

~~6~~3. The live cell construct ~~of any one~~ of claim~~s~~ 1 ~~to~~or ~~5~~claim 2, wherein the scaffold is fabricated as a 2-dimensional surface (e.g., a transwell filter), a 3-dimensional micropatterned surface (e.g., microstructured bioreactor, decellularized tissue), or as a cylindrical structure that can be assembled into bundles (e.g., hollow fiber bioreactor).

~~7~~4. The live cell construct of any one of claims 1 to ~~6~~3, wherein the top surface of the scaffold is coated with one or more extracellular matrix proteins~~.~~, preferably

~~8. The live cell construct of claim 6, wherein~~ the one or more extracellular matrix proteins are collagen, laminin, entactin, tenascin, and/or fibronectin.

~~9~~5. The live cell construct of any one of claims 1 to ~~8~~4, wherein the scaffold comprises a natural polymer, a biocompatible synthetic polymer, a synthetic peptide, and/or a composite derived from any combination thereof~~.~~, preferably

~~10. The live cell construct of claim 9, wherein~~ the natural polymer is collagen, chitosan, cellulose, agarose, alginate, gelatin, elastin, heparan sulfate, chondroitin sulfate, keratan sulfate, and/or hyaluronic acid~~.~~, more preferably

~~11. The live cell construct of claim 9 or claim 10, wherein~~ the biocompatible synthetic polymer may be polysulfone, polyvinylidene fluoride, polyethylene co-vinyl acetate, polyvinyl alcohol, sodium polyacrylate, an acrylate polymer, and/or polyethylene glycol.

~~12~~6. The live cell construct of any one of claims 1 to ~~9~~5, wherein said scaffold is porous.

~~13~~7. The live cell construct of any one of claims 1 to ~~12~~5, wherein the live primary mammary epithelial cells, the mixed population of live primary mammary epithelial cells, mammary myoepithelial cells and mammary progenitor cells, and/or the immortalized mammary epithelial cells are from a mammal~~.~~ and

~~14. The live cell construct of any one of claims 1 to 13,~~ wherein the mammal is a primate (e.g., chimpanzee, orangutan, gorilla, monkey (e.g., Old World, New World), lemur, human), a dog, a cat, a rabbit, a mouse, a rat, a horse, a cow, a goat, a sheep, an ox, a pig, a deer, a

musk deer, a bovid, a whale, a dolphin, a hippopotamus, an elephant, a rhinoceros, a giraffe, a zebra, a lion, a cheetah, a tiger, a panda, a red panda, and an otter~~.~~, preferably

~~15. The live cell construct of any one of claims 1 to 13, wherein~~ the mammal is from an endangered species.

~~16~~8. A method of producing milk in culture, the method comprising culturing the live cell construct of any one of claims 1 to ~~15~~7, thereby producing milk in culture.

~~17~~9. A method of making a live cell construct for producing milk in culture, the method comprising

(a) isolating primary mammary epithelial cells, myoepithelial cells and/or mammary progenitor cells from mammary explants from mammary tissue (e.g., breast, udder, teat tissue), to produce isolated mammary epithelial cells, myoepithelial cells and mammary progenitor cells;

(b) culturing the isolated primary mammary epithelial cells, myoepithelial cells and mammary progenitor cells to produce a mixed population of primary mammary epithelial cells, mammary myoepithelial cells and mammary progenitor cells;

(c) optionally sorting the mixed population of primary mammary epithelial cells, myoepithelial cells, and/or mammary progenitor cells to produce a population of primary mammary epithelial cells;

(~~c~~d) cultivating the mixed population of (b) or (c) on a scaffold, the scaffold having an upper surface and lower surface, to produce a polarized, continuous (i.e., confluent) monolayer of primary mammary epithelial cells, myoepithelial cells and mammary progenitor cells of the mixed population on the upper surface of the scaffold, wherein the polarized, continuous monolayer comprises an apical surface and a basal surface, thereby producing a live cell construct for producing milk in culture, wherein the live cell construct comprises an apical compartment that is adjacent to the apical surface of the monolayer, and wherein the live cell construct comprises a basal compartment that is adjacent to the lower surface of the scaffold.

~~18~~10. The method of claim ~~17~~9, further comprising storing the isolated primary mammary epithelial cells, myoepithelial cells, and/or mammary progenitor cells of (b) prior to cultivating on a scaffold, optionally wherein the storing is in a freezer or in liquid nitrogen.

~~19. A method of making a live cell construct for producing milk in culture, the method comprising:~~

~~a) isolating primary mammary epithelial cells, myoepithelial cells, and/or mammary progenitor cells from mammary explants from mammary tissue (e.g., breast, udder, teat tissue), to produce isolated mammary epithelial cells, myoepithelial cells, and/or mammary progenitor cells;~~

~~(b) culturing the isolated primary mammary epithelial cells, myoepithelial cells, and/or mammary progenitor cells to produce a mixed population of primary mammary epithelial cells, mammary myoepithelial cells and mammary progenitor cells;~~

~~(c) sorting the mixed population of primary mammary epithelial cells, myoepithelial cells, and/or mammary progenitor cells to produce a population of primary mammary epithelial cells; and~~

~~(d) cultivating the population of primary mammary epithelial on a scaffold, the scaffold having an upper surface and lower surface, to produce a polarized, continuous (i.e., confluent) monolayer of primary mammary epithelial cells on the upper surface of the scaffold, wherein the polarized, continuous monolayer comprises an apical surface and a basal surface, thereby producing a live cell construct for producing milk in culture~~

~~20~~11. A method of making a live cell construct for producing milk in culture, the method comprising

(a) culturing immortalized mammary epithelial cells to produce increased numbers of immortalized mammary epithelial cells;

(b) cultivating the immortalized mammary epithelial cells of (a) on a scaffold, the scaffold having an upper surface and lower surface, to produce a polarized, continuous (i.e., confluent) monolayer of immortalized mammary epithelial cells on the upper surface of the scaffold, wherein the polarized, continuous monolayer comprises an apical surface and a basal surface, thereby producing a live cell construct for producing milk in culture, wherein the live cell construct comprises an apical compartment that is adjacent to the apical surface of the monolayer and wherein the live cell construct comprises a basal compartment that is adjacent to the lower surface of the scaffold.

~~21~~12. The method of claim ~~20~~11, wherein prior to culturing immortalized mammary epithelial cells the method comprises:

(i) isolating primary mammary epithelial cells, myoepithelial cells, and/or mammary progenitor cells from mammary explants from mammary tissue (e.g., breast, udder, teat tissue), to produce isolated mammary epithelial cells, myoepithelial cells, and/or mammary progenitor cells;

(ii) culturing the isolated primary mammary epithelial cells, myoepithelial cells, and/or mammary progenitor cells to produce a mixed population of primary mammary epithelial cells, mammary myoepithelial cells and mammary progenitor cells;

(iii) sorting the mixed population of primary mammary epithelial cells, myoepithelial cells, and/or mammary progenitor cells to produce a population of primary mammary epithelial cells; and

(iv) stably transfecting one or more cells of the population of primary mammary epithelial cells of (iii) with one or more nucleic acids encoding hTERT or SV40; or transducing with a small hairpin RNA (shRNA) to p16 Inhibitor of Cyclin-Dependent Kinase 4) (p16(INK4)) and Master Regulator of Cell Cycle Entry and Proliferative Metabolism (c-MYC) to produce immortalized mammary epithelial cells.

~~22~~13. The method ~~of any one~~ of claim~~s~~ ~~20~~12, wherein the immortalized cell line is stably transfected with one or more nucleic acids encoding hTERT or SV40; or transduced with (a) a small hairpin RNA (shRNA) to p16 Inhibitor of Cyclin-Dependent Kinase 4) (p16(INK4)) and (b) Master Regulator of Cell Cycle Entry and Proliferative Metabolism (c-MYC).

~~23~~14. The method of ~~any one of~~ claim~~s~~ ~~19~~12 ~~to~~and claim ~~22~~13, further comprising storing the population of primary mammary epithelial cells or the immortalized mammary epithelial cells prior to cultivating on a scaffold, optionally wherein the storing is in a freezer or in liquid nitrogen.

~~24~~15. The method of any one of claims ~~17~~12 to ~~23~~14, wherein the basal surface of the monolayer is adjacent to the upper surface of the scaffold.

~~25. The method of any one of claims 17 to 24, wherein the live cell construct comprises an apical compartment that is adjacent to the apical surface of the monolayer.~~

~~26. The method of any one of claims 17 to 25, wherein the live cell construct comprises a basal compartment that is adjacent to the lower surface of the scaffold.~~

~~27~~16. The method of any one of claims ~~17~~12 to ~~26~~15, wherein the culturing is carried out at a temperature of about 35°C to about 39°C, optionally about 37°C~~.~~ and/or

~~28. The method of any one of claims 17 to 27, wherein~~ the culturing is carried out at an atmospheric concentration of CO_2 of about 4% to about 6%, optionally about 5%.

~~29~~17. The method of any one of claims ~~17~~12 to ~~28~~16, wherein the culturing of (b) comprises culturing in a culture medium that is exchanged about every day to about every 10 days, optionally about every day to about every 3 days~~.~~ and/or

~~30. The method of any one of claims 19 to 29, wherein~~ the isolating and sorting is via fluorescence-activated cell sorting, magnetic-activated cell sorting, and/or microfluidic cell sorting.

~~31~~18. A method of producing milk in culture comprising,

culturing a live cell construct comprising

(a) a scaffold comprising an upper surface and a lower surface and a continuous (i.e., confluent) polarized monolayer of live primary mammary epithelial cells, a continuous polarized monolayer of a mixed population of live primary mammary epithelial cells, mammary myoepithelial cells and mammary progenitor cells, and/or a continuous polarized monolayer of live immortalized mammary epithelial cells having an apical surface and a basal surface, wherein the continuous polarized monolayer of live primary mammary epithelial cells, the continuous polarized monolayer of the mixed population of live primary mammary epithelial cells, mammary myoepithelial cells and mammary progenitor cells and/or the continuous polarized monolayer of live immortalized mammary epithelial cells are located on the upper surface of scaffold,

(b) a basal compartment and an apical compartment, wherein the lower surface of the scaffold is adjacent to the basal compartment and the apical surface of the monolayer of live primary mammary epithelial cells, the monolayer of the mixed population of live primary mammary epithelial cells, mammary myoepithelial cells and mammary progenitor cells,

and/or the monolayer of live immortalized mammary epithelial cells is adjacent to the apical compartment,

wherein the monolayer of live primary epithelial mammary cells, the live primary epithelial mammary cells of the monolayer of the mixed population of live primary mammary epithelial cells, mammary myoepithelial cells and mammary progenitor cells, or the monolayer of immortalized mammary epithelial cells excretes milk through its apical surface into the apical compartment, thereby producing milk in culture.

~~32~~19. The method of claim ~~31~~18, wherein the basal compartment comprises a basal culture medium and the basal culture medium is in contact with the basal surface of the continuous polarized monolayer of primary mammary epithelial cells, with the basal surface of the continuous polarized the monolayer of the mixed population, or with the basal surface of the continuous polarized monolayer of live immortalized mammary epithelial cells.

~~33~~20. The method of claim ~~31~~18 or claim ~~32~~19, wherein the culturing is carried out at a temperature of about 35°C to about 39°C, optionally about 37°C~~.~~ and/or

~~34. The method of any one of claims 31 to 33, wherein~~ the culturing is carried out at an atmospheric concentration of CO_2 of about 4% to about 6%, optionally about 5%~~.~~ and/or

~~35. The method of any one of claims 31 to 34, wherein~~ the culturing comprises monitoring the concentration of dissolved O_2 and CO_2.

~~36~~21. The method of claim ~~31~~18 to ~~35~~20, further comprising adding prolactin to the basal culture medium, thereby providing a lactogenic culture medium.

~~37~~22. The method of any one of claims ~~31~~18 to ~~36~~21, wherein the culturing comprises monitoring the glucose concentration and/or rate of glucose consumption in the basal culture medium and/or in the lactogenic culture medium.

~~38~~23. The method of claim ~~37~~22, wherein the prolactin is added when the rate of glucose consumption is steady state~~.~~, preferably

~~39. The method of any one of claims 36 to 38, wherein~~ the prolactin is produced by a microbial cell or a human cell expressing a recombinant prolactin (e.g., S179D-prolactin).

~~40~~24. The method of any one of claims ~~31~~18 to ~~39~~23, further comprising collecting the milk from the apical compartment to produce collected milk~~.~~, preferably

~~41. The method of claim 40, wherein~~ the collecting is via a port~~.~~, preferably

~~42. The method of claim 40 or claim 41, wherein~~ the collecting is via gravity or a vacuum, optionally the vacuum is attached to the port.

~~43~~25. The method ~~of any one~~ of claim~~s 40 to 42~~ 24, further comprising freezing the collected milk to produce frozen milk and/or lyophilizing the collected milk to produce lyophilized milk~~.~~ and preferably

~~44. The method of any one of claims 40 to 43,~~ further comprising packaging the collected milk, the frozen milk and/or the lyophilized milk into a container.

~~45~~26. The method ~~of any one~~ of claim~~s~~ ~~40~~25 ~~to~~or claim ~~42~~25, further comprising extracting one or more components from the collected milk~~.~~, preferably

~~46. The method of claim 45, wherein~~ the components from the collected milk are lyophilized or concentrated to produce a lyophilized or a concentrated milk component product~~.~~, more preferably

~~47. The method of claim 46, wherein~~ the components from the collected milk are concentrated by membrane filtration or reverse osmosis, more preferably the components from the collected milk are milk protein, lipid, carbohydrate, vitamin, and mineral contents.

~~48~~27. The method of any one of claims ~~45~~24 to ~~47~~26, wherein the lyophilized or concentrated milk component product is packaged in a container~~.~~, preferably

~~49. The method any one of claims 45 to 48, wherein the components from the collected milk are milk protein, lipid, carbohydrate, vitamin, and mineral contents.~~

~~50. The method of claim 48 or claim 49, wherein~~ the container is sterile~~.~~, more preferably

~~51. The method of any one of claims 48 to 50, wherein~~ the container is vacuum-sealed, even more preferably

~~52. The method of any one of claims 48 to 51, wherein~~ the container is a food grade container~~.~~, more preferably

~~53. The method of any one of claims 48 to 52, wherein~~ the container is a canister, a jar, a bottle, a bag, a box, or a pouch.

~~54~~28. A method of producing a modified primary mammary epithelial cell or an immortalized mammary epithelial cell, wherein the method comprises introducing into the cell:

(a) a polynucleotide encoding a prolactin receptor comprising a modified intracellular signaling domain, optionally wherein the prolactin receptor comprises a truncation wherein position 154 of exon 10 has been spliced to the 3' sequence of exon 11;

(b) a polynucleotide encoding a chimeric prolactin receptor that binds to a ligand, which is capable of activating milk synthesis in the absence of prolactin;

(c) a polynucleotide encoding a constitutively or conditionally active prolactin receptor protein, optionally wherein the polynucleotide encodes a constitutively active human prolactin receptor protein comprising a deletion of amino acids 9 through 187;

(d) a polynucleotide encoding a modified (recombinant) effector of a prolactin protein comprising (i) a JAK2 tyrosine kinase domain fused to a STAT5 tyrosine kinase domain; and/or (ii) a prolactin receptor intracellular domain fused to a JAK2 tyrosine kinase domain;

(e) a loss of function mutation into a circadian related gene *PER2* (period circadian protein homolog 2); and/or

(f) a polynucleotide encoding one or more glucose transporter genes GLUT1 and/or GLUT12, thereby increasing the rate of nutrient uptake at the basal surface of the monolayer.

~~55~~29. The method of claim ~~54~~28, wherein the JAK2 tyrosine kinase domain is fused to the C-terminus of the STAT5 tyrosine kinase domain (e.g., a polynucleotide encoding a JAK2

tyrosine kinase domain is linked to the 3' end of a polynucleotide encoding the STAT5 tyrosine kinase domain).

~~56~~30. The method of claim ~~54~~28 wherein the loss of function mutation comprises an 87-amino acid deletion from position 348 to 434 in *PER2*.

~~57. A composition comprising a biosynthetic milk product produced by a live cell construct according to any one of claims 1-15.~~

~~58. A composition comprising a biosynthetic milk product produced by the method of any one of claims 16-18 or claims 31-54.~~

~~59~~31. A live cell construct comprising lactating primary human mammary epithelial cells (HMECs) forming a continuous monolayer on a plurality of hollow capillary tubes arranged in a parallel array within a tubular cartridge defining an intracapillary (IC) space and an extracapillary (EC) space,

each hollow capillary tube constructed of a semi-permeable membrane defining an internal surface adjacent to the IC space and an external surface adjacent to the EC space,

wherein the external surface of each hollow capillary tube is coated with a mixture of collagen IV and laminin I and the HUMEC monolayer is in contact with the coated surface; and wherein a cell growth medium supplemented with prolactin fills the IC space.

~~60~~32. The live cell construct of claim ~~59~~31, wherein the semi-permeable membrane is fabricated from polyvinylidene difluoride (PVDF) or polysulfone~~.~~, preferably

~~61. The live cell construct of claim 59 or 60, wherein~~ the semi-permeable membrane has a molecular weight cut-off (MWCO) between 5-80 kilodaltons (kDa).

~~62. A composition comprising a biosynthetic human milk product produced by the live cell construct of any one of claims 59-61.~~

~~63~~33. A biosynthetic human milk composition comprising a lipid component, a protein component, and a carbohydrate component, wherein the lipid, protein, and carbohydrate components each consist of human lipids, human proteins or peptides, and human

carbohydrates, and wherein the composition is free of pathogens, cytotoxins, and genetically modified or engineered molecules.

6434. The composition of claim 6333, wherein the composition is not pasteurized. and/or

65. The composition of claim 63 or 64, wherein the lipid component comprises 1-5 % of the composition. and/or

66. The composition of any one of claims 63-65, wherein the protein component comprises 0.5-1 % of the composition. and/or

67. The composition of any one of claims 63-66, wherein the carbohydrate component comprises 6-8 % of the composition.

6835. The composition of any one of claims 6333-67 or claim 34, wherein the lipid component comprises palmitic acid, oleic acid, and one or more bioactive lipid mediators of fatty acids., preferably

69. The composition of claim 68, wherein the one or more bioactive lipid mediators of fatty acids is an anti-inflammatory compound., more preferably

70. The composition of claim 68, wherein the one or more bioactive lipid mediators of fatty acids is selected from the group consisting of epoxyoctadecenoic acid (EpOME); epoxyeicosatrienoic acid (EpETrE); epoxyeicosatetraenoic acid (EpETE); epoxydocosapentaenoic acid (EpDPE); dihydroxyoctadecenoic acid (DiHOME); dihydroxyeicosatrienoic acid (DiHETrE); dihydroxyeicosatetraenoic acid (DiHETE); hydroxyoctadecadienoic acid (HODE); hydroxyeicosatrienoicacid (HETrE); hydroxyeicosatetraenoic acid (HETE); hydroxyoctadecatrienoic acid (HOTrE); hydroxyeicosapentaenoic acid (HEPE); hydro-xydocosahexaenoic acid (HdoHE); and leukotriene.

7136. The composition of any one of claims 6333-7035, wherein the protein component comprises one or more proteins or peptides selected from the group consisting of alpha-lactalbumin, bile salt-activated lipase (BSAL), butyrophilin, casein, fatty acid synthase,

insulin, lactadherin, lactoferrin, lactotransferrin, lysozyme, mucin-1, osteopontin, perilipin-2, serum albumin, and xanthine dehydrogenase/oxidase~~.~~, preferably

~~72. The composition of claim 71, wherein~~ the protein component comprises BSAL, lysozyme, and lactoferrin.

~~73~~37. The composition of any one of claims ~~63~~33-~~72~~36, wherein the carbohydrate component comprises one or more of lactose, 2' fucosyl lactose, myo-inositol, lacto-N-neotetraose (LNnT), 6′-sialyllactose, sialyl-lacto-N-tetraose, lacto-N-fucopentaose (LNFP) I, lacto-N-fucopentaose (LNFP) II, and disialyl-lacto-N-tetraose.

~~74. The composition of any one of claims 63-73, wherein the composition is produced by the live cell construct of any one of claims 59-61.~~

~~75~~38. A method for making a biosynthetic milk product, the method comprising expanding a population of human mammary epithelial cells (HUMECs) in a growth medium on a substrate comprising collagen IV; dislodging the expanded population of HUMECs from the substrate and seeding the dislodged HUMECs into a hollow fiber bioreactor containing capillaries pre-coated with a mixture of collagen IV and laminin I; culturing the HUMECs for a period of time until the HUMECs have reached confluence; and stimulating production of the biosynthetic milk product by contacting the HUMECs with prolactin using a method comprising contacting the cells with 100 ng/ml prolactin for a period of time followed by contacting the cells with 200 ng/ml prolactin for a second period of time.

~~76~~39. The method of claim ~~75~~38, wherein the HUMECs are selected from primary cells, primary immortalized cells, or recombinant cells.

~~77~~40. The method of claim ~~75~~38 or ~~76~~39, further comprising a step of preparing the bioreactor prior to seeding the HUMECs, wherein preparing the bioreactor comprises creating a negative pressure within the bioreactor and applying a 1:1 mixture of collagen IV and laminin I in phosphate buffered saline (PBS) to the hollow fibers~~.~~, preferably

~~78. The method of claim 77, wherein~~ applying the mixture of collagen IV and laminin I is accomplished using a syringe inserted into a port of the bioreactor.