[0006] In one aspect, the present disclosure relates to a method of producing an isolated cultured milk product comprising secretory IgA (sIgA) from mammary cells and plasma cells, the method comprising: a. culturing a live cell construct in a bioreactor under conditions which produce the cultured milk product, said live cell construct comprising: i. a three-dimensional scaffold having an exterior surface, an interior surface defining an interior cavity, and a plurality of pores extending from the interior surface to the exterior surface; ii. a matrix material disposed on the exterior surface of the three-dimensional scaffold; iii. a culture medium disposed within the interior cavity and in fluidic contact with the internal surface; iv. a plurality of plasma cells disposed on the matrix material; and v. a confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, and mammary progenitor cells, wherein the polarized mammary cells comprise an apical surface and a basal surface; and vi. said bioreactor comprising an apical compartment that is in fluidic contact with the apical surface of the live mammary cells, is substantially isolated from the interior apical surface of the live mammary cells, is substantially isolated from the interior, b. isolating the cultured milk product secreted into the apical compartment from the apical surface of the live mammary cells and the plasma cell.

[0006a] In another aspect, the present disclosure relates to a live cell construct, comprising: a. a three dimensional scaffold having an exterior surface, an interior surface defining an interior cavity/basal chamber, and a plurality of pores extending from the interior surface to the exterior surface; b. a matrix material disposed on the exterior surface of the three-dimensional scaffold; c. a plurality of plasma cells disposed on the matrix material; and d. an at least 70% confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, and mammary progenitor cells and wherein the live polarized mammary cells comprise an apical surface from which the milk product is secreted and a basal surface; and e. a culture media disposed within the interior cavity/basal chamber and in fluidic contact with the internal surface, wherein the culture medium is substantially isolated from the apical surface of the live mammary cells. Disclosed herein, in certain examples, are methods of producing an isolated cultured milk product from mammary cells, the methods comprising: (a) culturing a cell construct in a bioreactor under conditions which produce the cultured milk product, said cell construct comprising: (i) a three-dimensional scaffold having an exterior surface, an interior surface defining an interior cavity, and a plurality of pores extending from the interior surface to the exterior surface; (ii) a matrix material disposed on the exterior surface of the three-dimensional scaffold; (iii) a culture media disposed within the interior cavity and in fluidic contact with the internal surface; (iv) a plurality of plasma cells disposed on the matrix material; and (v) a confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, and mammary progenitor

cells, wherein the polarized mammary cells comprise an apical surface and a basal surface; and (b) isolating the cultured milk product. In some examples, the monolayer of polarized mammary cells is at least 70% confluent, at least 80% confluent, at least 90% confluent, at least 95% confluent, at least 99% confluent, or 100% confluent. In some examples, at least 70%, at least 80%, at least 90%, at least 95%, at least 99%, or 100% of the mammary cells are polarized in the same orientation. In some examples, the cultured milk product comprises secretory IgA (sIgA). In some examples, the bioreactor comprises an apical compartment that is substantially isolated from the internal cavity of the cell construct. In some examples, the basal surface of the mammary cells is in fluidic contact with the culture media. In some examples, the apical compartment is in fluidic contact with the apical surface of the mammary cells. In some examples, the cultured milk product is secreted from the apical surface of the mammary cells into the apical compartment. In some examples, the culture media substantially does not contact the cultured milk product. In some examples, total cell density of mammary cells within the bioreactor is at least 10^{11}; and alternatively wherein total surface area of mammary cells within the bioreactor is at least 1.5 m^2. In some examples, total cell density of plasma cells in the bioreactor is about 200 to 500 plasma cells per mm^2. In some examples, the culturing is carried out at a temperature of about 27°C to about 39°C. In some examples, the culturing is carried out at an atmospheric concentration of CO^2 of about 4% to about 6%.

[0007] Disclosed herein, in certain examples, are cell constructs, comprising: (a) a three dimensional scaffold having an exterior surface, an interior surface defining an interior cavity/basal chamber, and a plurality of pores extending from the interior surface to the exterior surface; (b) a matrix material disposed on the exterior surface of the three-dimensional scaffold; (c) a culture media disposed within the interior cavity/basal chamber and in fluidic contact with the internal surface; (d) a plurality of plasma cells disposed on the matrix material; and (e) an at least 70% confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, and mammary progenitor cells. In some examples, the polarized mammary

cells comprise an apical surface and a basal surface. In some examples, the basal surface of the mammary cells is in fluidic contact with the culture media. In some examples, at least 70%, at least 80%, at least 90%, at least 95%, at least 99%, or 100% of the mammary cells are polarized in the same orientation. In some examples, the monolayer of polarized mammary cells is at least 70% confluent, at least 80% confluent, at least 90% confluent, at least 95% confluent, at least 99% confluent, or 100% confluent. In some examples, the mammary cells comprise a constitutively active prolactin receptor protein. In some examples, the culture medium comprises prolactin.

[0008] Disclosed herein, in certain aspects, are cultured milk products, comprising: Beta-casein, Alpha-lactalbumin, Kappa-casein, Alpha-S1-casein, Lactoferrin, Lactadherin, Lysozyme, C12:0 (lauric acid), C14:0 (myristic acid), C16:0 (palmitic acid), Lactose, Glucose, 3'-SL, and 6'-SL; wherein the composition does not comprise or is substantially free of persistent organic pollutants (POPs), heavy metals, prescription drugs, recreational drugs, allergens, cells, hormones, or virus; provided that the composition may comprise a human mammary epithelial cell (hMEC) or a plasma cell (PC). In some examples, a cultured milk product disclosed herein further comprises: C18:2n-6 (linoleic acid, LA), C18:3n-3 (alpha-linolenic acid, ALA), Butrophilin, Osteopontin, Mucin-4, Mucin-1, C8:0 (caprylic acid), C10:0 (capric acid), C13:0 (tridecylic acid C16:1 (palmitoleic acid), C20:3n-6 (dihomo-gama-linolenic acid, DGLA), C20:4n-6 (arachadonic acid, AA), C20:5n-3 (eicosopentanoic acid, EPA), C22:6n-3 (docosahexaenoic acid, DHA), C22:1n9 (eruic acid), C24:1 (nervonic acid), LNT, or LNnT. In some examples, a cultured milk product disclosed herein further comprises at least one oxylipin metabolite of a polyunsaturated fatty acid or at least one endocanabinoid. In some examples, the oxylipin metabolite is 9-hydroxyoctadecadienoic acid (9-HODE); 13-hydroxyoctadecadienoic acid (13-HODE); 5,15-dihydroxyeicosatetraenoic acid (5,15-DiHETE); 17,18-dihydroxyeicosatetraenoic acid (17,18-DiHETE); 8,9-Dihydroxyicosatrienoic acid (8,9-DiHETrE); 11,12-Dihydroxyicosatrienoic acid (11,12-DiHETrE); 9,10-dihydroxyoctadecenoic acid (9,10-DiHOME); 12,13-dihydroxyoctadecenoic acid (12,13-DiHOME); 14(15)-epoxyeicosatrienoic acid (14(15)-EpETre); 19(20)-epoxydocosapentanoic acid (19(20)-EpDPE); 17-hydroxydocosahexaenoic acid (17-HDoHE); 5-hydroxyeicosatetraenoic acid (5-HETE); 8-hydroxyeicosatetraenoic acid (8-HETE); 9-hydroxyeicosatetraenoic acid (9-HETE); 11-hydroxyeicosatetraenoic acid (11-HETE); 12-hydroxyeicosatetraenoic acid (12-HETE); 9-hydroxyoctadecatrienoic acid (9-HOTrE); 9-oxo-octadecadienoic acid (9-oxo-ODE); or 13-oxo-octadecadienoic acid (13-oxo-ODE); 17,18-epoxyeicosatetraenoic acid (17(18)-EpETE; 6-Keto-prostaglandin F1alpha (6-keto-PGF1a); or 15(S)-Hydroxyeicosatrienoic acid (15(S)-HETrE). In some examples, the endocannabinoid is anandamide or 2-arachidonoylglycerol (2-AG). In some examples, a cultured milk product disclosed herein further comprises secretory IgA (sIgA). In some examples, the cultured milk product does not comprise or is substantially free of persistent organic pollutants (POPs). In some examples, the cultured milk product does not comprise or is substantially free of polychlorinated

dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), polychlorinated biphenyls (PCBs) and pesticides. In some examples, the cultured milk product does not comprise or is substantially free of DDT. In some examples, the cultured milk product does not comprise or is substantially free of heavy metals. In some examples, the cultured milk product does not comprise or is substantially free of mercury, lead, arsenic, cadmium, nickel, chromium, cobalt, or zinc. In some examples, the cultured milk product does not comprise or is substantially free of pharmaceutical or recreational drugs. In some examples, the cultured milk product does not comprise or is substantially free of chemotherapeutics, antidepressants, or anti-anxiety medications. In some examples, the cultured milk product does not comprise or is substantially free of benzodiazepines. In some examples, the cultured milk product does not comprise or is substantially free of lithium, carbamazepine, chlorpromazine, and clozapine. In some examples, the cultured milk product does not comprise or is substantially free of alcohol, cannabis, opioids, phencyclidine, or cocaine. In some examples, the cultured milk product does not comprise or is substantially free of allergens. In some examples, the cultured milk product does not comprise or is substantially free of ovomucoid, ovalbumin, conalbumin, arachin 6, arachin 3, conarachin, Arah1, and arachin Arah2. In some examples, the cultured milk product does not comprise or is substantially free of human stem cells, human immune cells, or bacterial cells, provided that the cultured milk product comprises one or more human mammary epithelial cells (HMECs) or plasma cells (PCs). In some examples, the cultured milk product does not comprise or is substantially free of myoepithelial cells, myeloid precursor cells, neutrophils, granulocytes, or T cells. In some examples, the cultured milk product does not comprise or is substantially free of Staphylococcus, Acinetobacter, Streptococcus, Pseudomonas, Lactococcus, Enterococcus or Lactobacillus. In some examples, the cultured milk product does not comprise or is substantially free of virus. In some examples, the cultured milk product does not comprise or is substantially free of hepatitis B virus, hepatitis C virus, cytomegalovirus, West Nile virus, human T-cell lymphotrophic virus, and human immunodeficiency virus. In some examples, the cultured milk product does not comprise or is substantially free of hormones. In some examples, the cultured milk product does not comprise or is substantially free of leptin, ghrelin, adiponectin, thyroxine (T4), triiodothyronine (T3) thyroid-stimulating hormone (TSH), epidermal growth factor, beta-endorphin, relaxin, cortisol, or erythropoietin.

[0009] Disclosed herein, in certain aspects, are cultured milk products, comprising: Beta-casein; Alpha-lactalbumin; Kappa-casein; Alpha-S1-casein; Lactoferrin; Butrophilin; Osteopontin; Lactadherin; Lysozyme; Mucin-4; Mucin-1; C8:0 (caprylic acid); C10:0 (capric acid); C12:0 (lauric acid); C13:0 (tridecylic acid); C14:0 (myristic acid); C16:0 (palmitic acid); C16:1 (palmitoleic acid); C18:2n-6 (linoleic acid, LA); C18;3n-3 (alpha-linolenic acid, ALA); C20:3n-6 (dihomo-gama-linolenic acid, DGLA); C20:4n-6 (arachadonic acid, AA); C20:5n-3 (eicosopentanoic acid, EPA); C22:6n-3 (docosahexaenoic acid, DHA); C22:1n9 (eruic acid); C24:1 (nervonic acid); Lactose;

Glucose; 3'-SL; 6'-SL; LNT; LNnT; 9-hydroxyoctadecadienoic acid (9-HODE); 13-hydroxyoctadecadienoic acid (13-HODE); 5,15-dihydroxyeicosatetraenoic acid (5,15-DiHETE); 17,18-dihydroxyeicosatetraenoic acid (17,18-DiHETE); 8,9-Dihydroxyicosatrienoic acid (8,9-DiHETrE); 11,12-Dihydroxyicosatrienoic acid (11,12-DiHETrE); 9,10-dihydroxyoctadecenoic acid (9,10-DiHOME); 12,13-dihydroxyoctadecenoic acid (12,13-DiHOME); 14(15)-epoxyeicosatrienoic acid (14(15)-EpETre); 19(20)-epoxydocosapentanoic acid (19(20)-EpDPE); 17-hydroxydocosahexaenoic acid (17-HDoHE); 5-hydroxyeicosatetraenoic acid (5-HETE); 8-hydroxyeicosatetraenoic acid (8-HETE); 9-hydroxyeicosatetraenoic acid (9-HETE); 11-hydroxyeicosatetraenoic acid (11-HETE); 12-hydroxyeicosatetraenoic acid (12-HETE); 9-hydroxyoctadecatrienoic acid (9-HOTrE); 9-oxo-octadecadienoic acid (9-oxo-ODE); or 13-oxo-octadecadienoic acid (13-oxo-ODE); 17,18-epoxyeicosatetraenoic acid (17(18)-EpETE; 6-Keto-prostaglandin F1alpha (6-keto-PGF1a); or 15(S)-Hydroxyeicosatrienoic acid (15(S)-HETrE); and sIgA; wherein the composition does not comprise or is substantially free of persistent organic pollutants (POPs), heavy metals, prescription drugs, recreational drugs, allergens, cells, hormones, or virus; provided that the composition may comprise human mammary epithelial cells or plasma cells.

[0010] In some examples, a cultured milk product disclosed herein further comprises a preservative, stabilizer, antioxidant, emulsifier, or thickener. In some examples, a cultured milk product disclosed herein further comprises lecithin. In some examples, a cultured milk product disclosed herein further comprises carrageenan. In some examples, a cultured milk product disclosed herein further comprises beta carotene. In some examples, a cultured milk product disclosed herein further comprises vitamin E. In some examples, a cultured milk product disclosed herein further comprises ascorbyl palmitate or ascorbic acid. In some examples, a cultured milk product disclosed herein further comprises lecithin, ascorbyl palmitate and vitamin E. In some examples, a cultured milk product disclosed herein is dehydrated, freeze-dried, or frozen. In some examples, a cultured milk product disclosed herein is food-grade.

[0011] Disclosed herein, in certain aspects, are methods of feeding a subject in need thereof, comprising administering to the subject a cultured milk product disclosed herein. In some examples, the subject is a human. In some examples, the human subject is an infant. In some examples, the human subject is immuno-compromised. In some examples, the human subject has a disease selected from: severe combined immunodeficiency (SCID), HIV/AIDS, a cancer, or an autoimmune disease. In some examples, the human subject has lupus or diabetes (for example, Type I diabetes or Type II diabetes). In some examples, the human subject is an organ or bone marrow transplant recipient. In some examples, the human subject is malnourished. In some examples, the human subject has malabsorption syndrome. In some examples, the human subject has wasting syndrome. In some examples, the human subject is geriatric.

[0012] Disclosed herein, in certain examples, are methods of treating or preventing a microbial infection in a subject in need thereof, comprising administering to the subject a cultured milk product disclosed herein. In some examples, the infection is a bacterial infection, fungal infection or parasitic infection. In some examples, the bacterial infection is an infection of E. coli, Streptococcus pneumoniae, Moraxella catarrhalis, Staphylococcus aureus, Streptococcus pyogenes, Salmonella, Shigella, Campylobacter, Staphylococcus aureus, Helicobacter pylori, C. difficile, or Vibrio cholerae. In some examples, the parasitic infection is an infection of Giardia lamblia, Entamoeba histolytica, Cryptosporidium spp., or Cystoisospora belli. In some examples, the fungal infection is an infection of Aspergillus, Cryptococcus, or Pneumocystis jirovecii. In some examples, the microbial infection is a gastrointestinal infection. In some examples, the gastrointestinal infection is gastroenteritis. In some examples, the microbial infection is Candidiasis.

[0013] In another aspect, the present disclosure provides a method of producing isolated sIgA from mammary cells, the method comprising: a. culturing a live cell construct in a bioreactor under conditions which produce a cultured milk product, said live cell construct comprising: i. a three-dimensional scaffold having an exterior surface, an interior surface defining an interior cavity, and a plurality of pores extending from the interior surface to the exterior surface; ii. a three-dimensional scaffold having an exterior surface, an interior surface defining an interior cavity, and a plurality of pores extending from the interior surface to the exterior surface; iii. a culture media disposed within the interior cavity and in fluidic contact with the internal surface; iv. a plurality of plasma cells disposed on the matrix material; and v. a confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, and mammary progenitor cells, wherein the polarized mammary cells comprise an apical surface and a basal surface; and b. isolating the sIgA from the cultured milk product. Disclosed herein, in certain examples, are methods of producing sIgA from mammary cells, the method comprising: (a) culturing a cell construct in a bioreactor under conditions which produce a cultured milk product, said cell construct comprising: (i) a three-dimensional scaffold having an exterior surface, an interior surface defining an interior cavity, and a plurality of pores extending from the interior surface to the exterior surface; (ii) a matrix material disposed on the exterior surface of the three-dimensional scaffold; (iii) a culture media disposed within the interior cavity and in fluidic contact with the internal surface; (iv) a plurality of plasma cells disposed on the matrix material; and (v) a confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, and mammary progenitor cells, wherein the polarized mammary cells comprise an apical surface and a basal surface; and (b) isolating the sIgA from the cultured milk product. In some examples, the monolayer of polarized mammary cells is at least 70% confluent, at least 80% confluent, at least 90% confluent, at least 95% confluent, at least 99% confluent, or 100% confluent. In some

examples, at least 70%, at least 80%, at least 90%, at least 95%, at least 99%, or 100% of the mammary cells are polarized in the same orientation. In some examples, the cultured milk product comprises secretory IgA (sIgA). In some examples, the bioreactor comprises an apical compartment that is substantially isolated from the internal cavity of the cell construct. In some examples, the basal surface of the mammary cells is in fluidic contact with the culture media. In some examples, the apical compartment is in fluidic contact with the apical surface of the mammary cells. In some examples, the cultured milk product is secreted from the apical surface of the mammary cells into the apical compartment. In some examples, the culture media substantially does not contact the cultured milk product. In some examples, total cell density of mammary cells within the bioreactor is at least 10^{11}; and alternatively wherein total surface area of mammary cells within the bioreactor is at least 1.5 m^2. In some examples, total cell density of plasma cells in the bioreactor is about 200 to 500 plasma

cells per mm^2. In some examples, the culturing is carried out at a temperature of about 27°C to about 39°C. In some examples, the culturing is carried out at an atmospheric concentration of CO^2 of about 4% to about 6%.

[0014] In yet another aspect, the present disclosure provides a pharmaceutical composition, comprising: a. sIgA manufactured by the method as described herein; and b. a pharmaceutically acceptable excipient. Disclosed herein, in certain examples, are pharmaceutical compositions comprising (a) sIgA and (b) a pharmaceutically acceptable excipient; wherein the sIgA is manufactured by a method disclosed herein. In some examples, the pharmaceutically acceptable excipient is a stabilizer, a surfactant, a buffer or tonicity agent. In some examples, the pharmaceutically acceptable excipient is sucrose, trehalose, mannitol, sorbitol, histidine, arginine, glycine, polysorbate 20, polysorbate 80, poloxamer 188, edetic acid/or edetate salts (e.g., EDTA), glutathione, metacresol, phenol, benzyl alcohol, benzalkonium chloride, methionine or cysteine.

[0015] Disclosed herein, in certain examples, are methods of treating or preventing a microbial infection in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising (a) sIgA and (b) a pharmaceutically acceptable excipient; wherein the sIgA is manufactured by a method disclosed herein. In some examples, the pharmaceutically acceptable excipient is a stabilizer, a surfactant, a buffer or tonicity agent. In some examples, the pharmaceutically acceptable excipient is sucrose, trehalose, mannitol, sorbitol, histidine, arginine, glycine, polysorbate 20, polysorbate 80, poloxamer 188, edetic acid/or edetate salts (e.g., EDTA), glutathione, metacresol, phenol, benzyl alcohol, benzalkonium chloride, methionine or cysteine. In some examples, the human subject is an infant. In some examples, the human subject is immuno-compromised. In some examples, the human subject has a disease selected from: severe combined immunodeficiency (SCID), HIV/AIDS, a cancer, or an autoimmune disease. In some examples, the subject has lupus or diabetes (for example, Type I diabetes or Type II diabetes). In some examples, the human subject is an organ or bone marrow transplant recipient. In some examples, the human subject is malnourished. In some examples, the human subject has malabsorption syndrome. In some examples, the human subject has wasting syndrome. In some examples, the human subject is geriatric. In some examples, the human subject has cystic fibrosis, COPD, or non-CF bronchiectasis. In some examples, the infection is a bacterial infection, fungal infection or parasitic infection. In some examples, the bacterial infection is an infection of E. coli, Streptococcus pneumoniae, Moraxella catarrhalis, Staphylococcus aureus, Streptococcus pyogenes, Salmonella, Shigella, Campylobacter, Staphylococcus aureus, Helicobacter pylori, C. difficile, or Vibrio cholerae. In some examples, the parasitic infection is an infection of Giardia lamblia, Entamoeba istolytica, Cryptosporidium spp., or Cystoisospora belli. In some examples, the fungal infection is an infection of Aspergillus, Cryptococcus, or Pneumocystis jirovecii. In some examples, the microbial infection is a gastrointestinal infection. In some examples, the gastrointestinal infection is gastroenteritis. In some examples, the microbial infection is Candidiasis. In some examples, the microbial infection is

a respiratory infection. In some examples, the respiratory infection is pneumonia, bronchitis, Aspergillosis, or

Cryptococcosis. In some examples, the respiratory infection is an infection by B. cepacia, P. aeruginosa S. aureus, Aspergillus, Cryptococcus, or Pneumocystis. In some examples, the composition is formulated for inhalation. In some examples, the composition is a powder. In some examples, the composition is formulation for administration by a nebulizer.

[0016] The present disclosure relates to milk compositions that comprise protein, lipid, and oligosaccharide components and component concentrations that mimic and/or are substantially similar to human breast milk as produced by a lactating female and are produced *in vitro* and/or *ex vivo* from cultured mammary cells.

[0017] Thus, one example of the disclosure relates to milk products comprising specified concentrations or amounts by weight of protein components, lipid components human milk oligosaccharide components and lactose, wherein at least one of the protein components, lipid components, HMOs, and lactose is produced by cultured human mammary epithelial cells.

[0018] In an example, disclosed herein are methods of producing an isolated cultured milk product from mammary cells, the method comprising: (a) culturing a cell construct in a bioreactor under conditions which produce the cultured milk product, said cell construct comprising: (i) a three-dimensional scaffold having an exterior surface, an interior surface defining an interior cavity, and a plurality of pores extending from the interior surface to the exterior surface; (ii) a matrix material disposed on the exterior surface of the three-dimensional scaffold; (iv) a plurality of plasma cells disposed on the matrix material; and (v) a confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, mammary progenitor cells, wherein the polarized mammary cells comprise an apical surface and a basal surface; and (b) isolating the cultured milk product. In some examples, the cultured milk product comprises secretory IgA (sIgA).

[0019] In some examples, the bioreactor comprises an apical compartment that is substantially isolated from the internal cavity of the cell construct. In some examples, the basal surface of the mammary cells is in fluidic contact with the culture media. In some examples, the apical compartment is in fluidic contact with the apical surface of the mammary cells. In some examples, the cultured milk product is secreted from the apical surface of the mammary cells into the apical compartment. In some examples, the culture media substantially does not contact the cultured milk product. In some examples, total cell density of mammary cells within the bioreactor is at least 10^{11}. In some examples, total surface area of mammary cells within the bioreactor is at least 1.5 m^2. In some examples, the matrix material comprises one or more extracellular matrix proteins. In some examples, total cell density of plasma cells in the bioreactor is about 200 to 500 plasma cells per mm^2. In some examples, the culturing is carried

out at a temperature of about 27°C to about 39°C. In some examples, the culturing is carried out at an atmospheric concentration of CO^2 of about 4% to about 6%.

[0020] In certain examples, described herein are cell constructs, comprising: (a) a three dimensional scaffold having an exterior surface, an interior surface defining an interior cavity/basal chamber, and a plurality of pores extending from the interior surface to the exterior surface; (b) a matrix material disposed on the exterior surface of the three-dimensional scaffold; (c) a culture media disposed within the interior cavity/basal chamber and in fluidic contact with the internal surface; and (d) a plurality of plasma cells disposed on the matrix material; and (e) an at least 70% confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, and mammary progenitor cells. In some examples, the polarized mammary cells comprise an apical surface and a basal surface. In some examples, the basal surface of the mammary cells is in fluidic contact with the culture media.

[0021] In some examples, at least 70%, at least 80%, at least 90%, at least 95%, at least 99%, or 100% of the mammary cells are polarized in the same orientation. In some examples, the monolayer of polarized mammary cells is at least 70% confluent, at least 80% confluent, at least 90% confluent, at least 95% confluent, at least 99% confluent, or 100% confluent. In some examples, the mammary cells comprise a constitutively active prolactin receptor protein. In some examples, the 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. In some examples, the culture medium further comprises prolactin. In some examples, the matrix material comprises one or more extracellular matrix proteins. In some examples, the three-dimensional scaffold comprises a natural polymer, a biocompatible synthetic polymer, a synthetic peptide, a composite derived from any of the preceding, or any combination thereof. In some examples, the natural polymer is collagen, chitosan, cellulose, agarose, alginate, gelatin, elastin, heparan sulfate, chondroitin sulfate, keratan sulfate, and/or hyaluronic acid. In some examples, the biocompatible synthetic polymer is polysulfone, polyvinylidene fluoride, polyethylene co-vinyl acetate, polyvinyl alcohol, sodium polyacrylate, an acrylate polymer, and/or polyethylene glycol.

[0022] In certain examples, described herein is a milk product comprising: about 6-14 grams per liter (g/L) protein components; about 18-89 g/L lipid components; about 7-14 g/L human milk oligosaccharides (HMOs); and about 64-77 g/L lactose, wherein at least one of the protein components, lipid components, HMOs, and lactose is produced by cultured human mammary epithelial cells.

[0023] In some examples, the milk product further comprises one or more immunoglobulins. In some examples, the immunoglobulin is secretory IgA.

[0024] In some examples, the protein component comprises about 55-65% dry weight of the milk product. In some examples, the protein component comprises beta-casein, kappa-casein and alpha-casein. In some examples, the beta-casein has a concentration of about 0.5-1.5 g/L, the kappa-casein has a concentration of about 0.5-0.6 g/L, and the alpha-casein has a concentration of about 0.1-0.5 g/L in the milk product. In some examples, the beta-casein, kappa-casein and alpha-casein together comprise about 35-45% dry weight percent of the protein component of the milk product. In some examples, the beta-casein comprises greater than about 50% of total casein content.

[0025] In some examples, the protein component further comprises one or more of alpha-lactalbumin, lysozyme, lactoferrin, haptocorrin, butyrophilin, osteopontin, mucin MC5, mucin BrE3, and lactadherin. In some examples, the protein component further comprises serum albumin. In some examples, the alpha-lactalbumin has a concentration of about 2.7-3.3 g/L in the milk product. In some examples, the lysozyme has a concentration of about 0.2-0.5 g/L in the milk product. In some examples, the lactoferrin has a concentration of about 1.0-2.0 g/L in the milk product. In some examples, the haptocorrin has a concentration of about 0.07-0.7 g/L in the milk product. In some examples, the butyrophilin has a concentration of about 0.03-0.05 g/L in the milk product. In some examples, the osteopontin has a concentration of about 0.05-0.2 g/L in the milk product. In some examples, the mucin MC5 has a concentration of about 0.5-0.6 g/L in the milk product. In some examples, the mucin BrE3 has a concentration of about 0.5-0.7 g/L in the milk product. In some examples, the lactadherin has a concentration of about 0.06-0.07 g/L in the milk product. In some examples, the serum albumin has a concentration of about 0.025-3.5 g/L, or about 0.01-2 g/L, or about 0.15-1 g/L, or about 0.2-0.7 g/L. In some examples, the protein components are of human origin.

[0026] In some examples, the lipid component comprises one or more of saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, cholesterol, phospholipids, plasmalogens and sphingolipids. In some examples, the saturated fatty acids has a concentration of about 5-34 g/L in the milk product. In some examples, the saturated fatty acids comprise palmitic acid, stearic acid, and lauric acid. In some examples, the palmitic acid comprises at least about 50% sn-2 form. In some examples, palmitic acid has a concentration of about 3-18 g/L in the milk product. In some examples, stearic acid has a concentration of about 0.7-5 g/L in the milk product. In some examples, lauric acid has a concentration of about 0.5-5 g/L in the milk product. In some examples, monounsaturated fatty acids have a concentration of about 7-46 g/L in the milk product. In some examples, the monounsaturated fatty acid comprises oleic acid. In some examples, the oleic acid comprises at least about 50% sn-1 form. In some examples, the oleic acid has a concentration of about 7-45 g/L in the milk product. In some examples, polyunsaturated fats have a concentration of about 2-20 g/L in the milk product. In some examples, the polyunsaturated fats comprise one or more of linoleic acid, alpha-linolenic acid,

eicosadienoic acid, arachidonic acid, dihomo-gamma-linolenic acid, and docosahexadienoic acid. In some examples, linoleic acid has a concentration of about 2-19 g/L in the milk product. In some examples, the linoleic acid comprises at least about 50% sn-3 form. In some examples, alpha-linolenic acid has a concentration of about 0.5-0.7 g/L in the milk product. In some examples, eicosadienoic acid has a concentration of about 0.5-0.7 g/L in the milk product. In some examples, arachidonic acid has a concentration of about 0.5-0.7 g/L in the milk product. In some examples, dihomo-gamma-linolenic acid has a concentration of about 0.3-0.5 g/L in the milk product. In some examples, docosahexadienoic acid has a concentration of about 0.02-0.4 g/L in the milk product. In some examples, linoleic acid has a concentration of about 2-19 g/L, alpha-linolenic acid has a concentration of about 0.5-0.7 g/L, eicosadienoic acid has a concentration of about 0.5-0.7 g/L, arachidonic acid has a concentration of about 0.5-0.7 g/L, dihomo-gamma-linolenic acid has a concentration of about 0.3-0.5 g/L, and docosahexadienoic acid has a concentration of about 0.02-0.4 g/L in the milk product. In some examples, the milk product comprises oleic acid, palmitic acid, and linoleic acid, wherein the oleic acid comprises at least about 50% sn-1 form, the palmitic acid comprises at least about 50% sn-2 form, and the linoliec acid comprises at least about 50% sn-3 form. In some examples, the milk product coprises cholesterol having a concentration of about 0.09-0.15 g/L in milk product. In some examples, phospholipids, plasmalogens and sphingolipids together have a concentration of about 0.1-0.4 g/L in the milk product.

[0027] In some examples, the human milk oligosaccharide component comprises one or more neutral oligosaccharides. In some examples, the human milk oligosaccharide component comprises one or more acidic oligosaccharides. In some examples, the human milk oligosaccharide component comprises neutral oligosaccharides and/or acidic oligosaccharides. In some examples, the one or more neutral oligosaccharides comprise TF-LNH (trifucosyllacto-N-hexose), 2'-FL (2'-fucosyllactose), DF- LNHII (difucosyllacto-N-hexaose), LNFP I (lacto-N-fucopentaose I), LNDFHI (lacto-N- difucosylhexaose I), LNT (lacto-N-tetraose), LNnT (lacto-N-neotetraose), DF-L (Difucosyllactose), and 3-FL (3-fucosyllactose).

74. The milk product according to claim 65 or 66, wherein the one or more acidic oligosaccharides comprise 6'-SL (6'-sialyllactose), DS-LNT (disialyllacto-N-tetraose), FS-LNnH I (fucosyl-sialyl-lacto-N-neohexaose I), LST c (sialyl-lacto-N-tetraose c), and 3'-SL (3'- sialyllactose). In some examples, the one or more neutral oligosaccharides comprises TF-LNH (trifucosyllacto-N-hexose), which oligosaccharide has a concentration of about 1-4 g/L in the milk product. In some examples, the one or more neutral oligosaccharides comprises 2'-FL (2'-fucosyllactose), which oligosaccharide has a concentration of about 1-4 g/L in the milk product. In some examples, the one or more neutral oligosaccharides comprises DF-LNHII (difucosyllacto-N-hexaose), which oligosaccharide has a concentration of about 1-4 g/L in the milk product. In some examples, the one or more neutral oligosaccharides comprises LNFP I (lacto-N-fucopentaose I), which

oligosaccharide has a concentration of about 0.5-2 g/L in the milk product. In some examples, the one or more neutral oligosaccharides comprises LNDFHI (lacto-N-difucosylhexaose I), which oligosaccharide has a concentration of about 0.2-2 g/L in the milk product.

80. The milk product according to any of claims 64, 66, 67, or 70-74, wherein the one or more neutral oligosaccharides comprises LNT (lacto-N-tetraose), which oligosaccharide has a concentration of about 0.3-1.5 g/L in the milk product. In some examples, the one or more neutral oligosaccharides comprises LNnT (lacto-N-neotetraose), which oligosaccharide has a concentration of about 0.5-1.5 g/L in the milk product. In some examples, the one or more neutral oligosaccharides comprises DF-L (Difucosyllactose), which oligosaccharide has a concentration of about 0.1-1 g/L in the milk product. In some examples, the one or more neutral oligosaccharides comprises 3-FL (3-fucosyllactose), which oligosaccharide has a concentration of about 0.2-1.5 g/L in the milk product. In some examples, the one or more acidic oligosaccharides comprises 6'-SL (6'-sialyllactose), which oligosaccharide has a concentration of about 0.2-1.2 g/L in the milk product. In some examples, the one or more acidic oligosaccharides comprises DS-LNT (disialyllacto-N-tetraose), which oligosaccharide has a concentration of about 0.05-1 g/L in the milk product. In some examples, the one or more acidic oligosaccharides comprises FS-LNnH I (fucosyl-sialyl-lacto-N-neohexaose I), which oligosaccharide comprises about 0.05-0.7 g/L in the milk product. In some examples, the one or more acidic oligosaccharides comprises LST c (sialyl-lacto-N-tetraose c), which oligosaccharide has a concentration of about 0.05-0.7 g/L in the milk product. In some examples, the one or more acidic oligosaccharides comprises 3'-SL (3'-sialyllactose), which oligosaccharide has a llconcentration of about 0.1-0.3 g/L in the milk product.

[0028] In some examples, the one or more neutral oligosaccharides comprise TF-LNH (trifucosyllacto-N-hexose), 2'-FL (2'-fucosyllactose), DF-LNH II (difucosyllacto-N-hexaose), LNFP I (lacto-N-fucopentaose I), LNDFHI (lacto-N- difucosylhexaose I), LNT (lacto-N-tetraose), LNnT (lacto-N-neotetraose), DF-L (Difucosyllactose), and 3-FL (3-fucosyllactose) and wherein the one or more acidic oligosaccharides comprises 6'-SL (6'-sialyllactose), DS-LNT (disialyllacto-N-tetraose), FS- LNnH I (fucosyl-sialyl-lacto-N-neohexaose I), LST c (sialyl-lacto-N-tetraose c), and 3'-SL (3'-sialyllactose). In some examples, the milk product comprises about 1-4 g/L TF-LNH (trifucosyllacto-N-hexose), about 1-4 g/L 2'-FL (2'-fucosyllactose), about 1-4 g/L DF- LNH II (difucosyllacto-N-hexaose), about 0.5-2 g/L LNFP I (lacto-N-fucopentaose I), about 0.22 g/L LNDFH I (lacto-N-difucosylhexaose I), about 0.3-1.5 g/L LNT (lacto-N-tetraose), about 0.5-1.5 g/L LNnT (lacto-N-neotetraose), about 0.1-1 g/L DF-L (Difucosyllactose), about 0.2-1.5 g/L 3-FL (3-fucosyllactose), about 0.2-1.2 g/L 6'-SL (6'-sialyllactose), about 0.05-1 g/L DS- LNT (disialyllacto-N-tetraose), about 0.05-0.7 g/L FS-LNnH I (fucosyl-sialyl-lacto-N- neohexaose I), about 0.05-0.7 g/L LST c (sialyl-lacto-N-tetraose c), and about 0.1-0.3 g/L 3'-SL (3'-sialyllactose). In some examples, the neutral oligosaccharides content comprises at least about 2-fold, or about 3-fold,

or about 4-fold, or about 5-fold, or about 6- fold, or about 7-fold, or about 8-fold, or about 9-fold, or about 10-fold, or about 11-fold, or about 12-fold, or about 13-fold, or about 14-fold, or about 15-fold more by weight than acidic oligosaccharide content.

[0029] In certain examples, described herein are milk products comprising: about 6-14 grams per liter (g/L) protein components; about 18-89 g/L lipid components; about 7-14 g/L human milk oligosaccharides (HMOs); and about 64-77 g/L lactose, wherein the protein components comprise beta-casein, kappa-casein, and alpha-casein, alpha-lactalbumin, lysozyme, lactoferrin, haptocorrin, butyrophilin, osteopontin, mucin MC5, mucin BrE3, and lactadherin, wherein the lipid components comprise palmitic acid, stearic acid and lauric acid, oleic acid, linoleic acid, alpha-linolenic acid, eicosadienoic acid, arachidonic acid, dihomo-gamma- linolenic acid, docosahexadienoic acid, cholesterol, phospholipids, plasmalogens and sphingolipids, wherein the human milk oligosaccharides comprise TF-LNH (trifucosyllacto-N-hexose), 2'-FL (2'-fucosyllactose), DF-LNHII (difucosyllacto-N-hexaose), LNFP I (lacto-N- fucopentaose I), LNDFHI (lacto-N-difucosylhexaose I), LNT (lacto-N-tetraose), LNnT (lacto- N-neotetraose), DF-L (Difucosyllactose), and 3-FL (3-fucosyllactose), 6'-SL (6'-sialyllactose), DS-LNT (disialyllacto-N-tetraose), FS-LNnH I (fucosyl-sialyl-lacto-N-neohexaose I), LST c (sialyl-lacto-N-tetraose c), and 3'-SL (3'-sialyllactose), and wherein at least one of the protein components, lipid components, HMOs, and lactose is produced by cultured human mammary epithelial cells.

[0030] In some examples, the milk product comprises about 0.5-1.5 g/L beta-casein, about 0.5-0.6 g/L kappa-casein, about 0.1-0.5 g/L alpha-casein, about 2.7-3.3 g/L alpha-lactalbumin, about 0.2-0.5 g/L lysozyme, about 1.0-2.0 g/L lactoferrin, about 0.07-0.7 g/L haptocorrin, about 0.03-0.05 g/L butyrophilin, about 0.05-0.2 g/L osteopontin, about 0.5-0.6 g/L mucin MC5, about 0.5-0.7 g/L mucin BrE3, about 0.06-0.07 g/L lactadherin, about 2-19 g/L linoleic acid, about 0.5-0.7 g/L alpha-linolenic acid, about 0.5-0.7 g/L eicosadienoic acid, about 0.5-0.7 g/L arachidonic acid, about 0.3-0.5 g/L dihomo-gamma-linolenic acid, about 0.02-0.4 g/L docosahexadienoic acid, about 0.09-0.15 g/L cholesterol, about 0.1-0.4 g/L phospholipids, plasmalogens, and sphingolipids combined, about 1-4 g/L TF-LNH (trifucosyllacto-N-hexose), about 1-4 g/L 2'-FL (2'-fucosyllactose), about 1-4 g/L DF-LNHII (difucosyllacto-N-hexaose), about 0.5-2 g/L LNFP I (lacto-N-fucopentaose I), about 0.2-2 g/L LNDFHI (lacto-N- difucosylhexaose I), about 0.3-1.5 g/L LNT (lacto-N-tetraose), about 0.5-1.5 g/L LNnT (lacto-N- neotetraose), about 0.1-1 g/L DF-L (Difucosyllactose), about 0.2-1.5 g/L 3-FL (3- fucosyllactose), about 0.2-1.2 g/L 6'-SL (6'-sialyllactose), about 0.05-1 g/L DS-LNT (disialyllacto-N-tetraose), about 0.05-0.7 g/L FS-LNnH I (fucosyl-sialyl-lacto-N-neohexaose I), about 0.05-0.7 g/L LST c (sialyl-lacto-N-tetraose c), and about 0.1-0.3 g/L 3'-SL (3'- sialyllactose).

[0031] In certain examples, described herein are milk products comprising: about 3-15 percent protein by weight; about 9-92 percent lipid by weight; about 4-15 percent by weight human milk oligosaccharides (HMOs); and about 33-80 percent by weight lactose, wherein at least one of the

protein, lipid, HMOs, and lactose is produced by cultured human mammary epithelial cells. In some examples, the milk product further comprises serum albumin. In some examples, the milk product comprises about 0.025-3.5 g/L, or about 0.01-2 g/L, or about 0.15-1 g/L, or about 0.3-0.7 g/L serum albumin.

[0032] In some examples, the milk product further comprises one or more immunoglobulins. In some examples, the immunoglobulins comprise one or more of IgA, IgG and IgM. In some examples, the IgA comprises one or more of IgA2 (secretory) and IgAl (non-secretory). In some examples, the milk product comprises about 0.2-1.0 g/L secretory IgA. In some examples, the milk product comprises about 0.15-1.6 g/L total IgA. In some examples, the milk product comprises about 0.03-0.3 g/L IgG. In some examples, the milk product comprises about 0.01-0.1 g/L IgM. In some examples, the milk product comprises about 0.2-2 percent by weight immunoglobulins.

[0033] In some examples, the protein components, lipid components, HMOs, and lactose are isolated from cultured mammary epithelial cells. In some examples, the cultured mammary epithelial cells comprise one or more immortalized mammary cell lines. In some examples, the cultured mammary epithelial cells are derived from one or more primary mammary tissue samples. In some examples, the one or more primary mammary tissue samples is derived from a surgical explant of mammary gland tissue. In some examples, the one or more primary mammary tissue samples comprises alveolar and/or luminal tissue or cells collected from the alveolar structure of the mammary gland. In some examples, the one or more primary mammary tissue samples is derived from a needle aspiration of mammary gland tissue. In some examples, the primary mammary tissue further comprises one or more myoepithelial cells. In some examples, the primary mammary tissue further comprises one or more stem cells. In some examples, the primary mammary tissue further comprises one or more immune cells. In some examples, the immune cells comprise B cells. In some examples, the immune cells comprise plasma cells.

[0034] In some examples, the milk product is isolated from cultured mammary epithelial cells from one or more specific persons. In some examples, the milk product isolated from cultured mammary epithelial cells from a specific donor is provided only to that donor or persons authorized by that donor. In some examples, the cultured mammary epithelial cells are co-cultured with one or more plasma cells lines. In some examples, the cultured mammary epithelial cells are co-cultured with one or more myoepithelial cell lines. In some examples, the cultured mammary epithelial cells are co-cultured with one or more stem cell lines.

[0035] In some examples, the milk product comprises at least about 80%, or at least about 85%, or at least about 90%, or at least about 95%, or at least about 97%, or at least about 98%, or at least about 99%, of the overall macromolecular composition of human breast milk. In some examples,

non-protein nitrogen content comprises at least about 10%, or at least about 15%, or at least about 20%, or at least about 25%, or at least about 30% of total nitrogen content.

[0036] In certain examples, described herein are frozen milk products, comprising a milk product described herein that has been frozen. In some examples, the milk product has been lyophilized. In certain examples, described herein is a containerized milk product, comprising a milk product described herein that is packaged into a container. In certain examples, described herein is a containerized frozen milk product, comprising the frozen milk product that is packaged into a container. In certain examples, described herein is a containerized lyophilized milk product, comprising the lyophilized milk product that is packaged into a container.

[0037] In certain examples, described herein are extracted milk products, comprising one or more components extracted from a milk product described herein. In some examples, the one or more components extracted from the collected milk product are lyophilized or concentrated to produce a lyophilized or a concentrated extracted milk product component. In some examples, the one or more components extracted from the collected milk product are concentrated by membrane filtration or reverse osmosis. In some examples, the one or more extracted components from the collected milk product comprise milk protein, lipid, carbohydrate, vitamin, and minerals.

[0038] In certain examples, described herein are containerized extracted milk products, comprising the extracted milk product described herein that is packaged in a container. In some examples, the container is sterile. In some examples, the container is vacuum-sealed. In some examples, the container is a food grade container. In some examples, the container is a canister, a jar, a bottle, a bag, a box, or a pouch.

[0039] In some examples, the milk product comprises about 500-1150 kcal/L available energy content. In some examples, between about 40-55% of the available energy content of the milk product is from lipids. In some examples, the milk product comprises between about 95.8 and 195.2 g/L macromolecular content.

[0040] In certain examples, described herein are methods of treating a patient suffering from an infectious disease, comprising: administering to the patient an effective amount of a milk product comprising: about 6-14 grams per liter (g/L) protein components; about 18-89 g/L lipid components; about 7-14 g/L human milk oligosaccharides (HMOs); and about 64-77 g/L lactose, wherein at least one of the protein components, lipid components, HMOs, and lactose. In some examples, the milk product further comprises one or more immunoglobulins. In some examples, the immunoglobulins comprise one or more of IgA, IgG and IgM. In some examples, the IgA comprises one or more of IgA2 (secretory) and IgAl (non-secretory).

[0041] In some examples, the milk product comprises about 0.2-1.0 g/L secretory IgA. In some examples, milk product comprises about 0.15-1.6 g/L total IgA. In some examples, the milk

product comprises about 0.03-0.3 g/L IgG. In some examples, the milk product comprises about 0.01-0.1 g/L IgM. In some examples, the milk product comprises about 0.2-2 percent by weight immunoglobulins. In some examples, the infectious disease is a gastrointestinal infection. In some examples, the patient is immune compromised.

[0042] In certain examples, described herein are methods of treating an infant suffering from a gastrointestinal infection comprising administering an effective amount of a milk product comprising: about 6-14 grams per liter (g/L) protein components; about 18-89 g/L lipid components; about 7-14 g/L human milk oligosaccharides (HMOs); and about 64-77 g/L lactose, wherein at least one of the protein components, lipid components, HMOs, and lactose. In some examples, the milk product further comprises one or more immunoglobulins. In some examples, the immunoglobulins comprise one or more of IgA, IgG and IgM. In some examples, the IgA comprises one or more of IgA2 (secretory) and IgAl (non-secretory). In some examples, the milk product comprises about 0.2-1.0 g/L secretory IgA. In some examples, the milk product comprises about 0.15-1.6 g/L total IgA. In some examples, the milk product comprises about 0.03-0.3 g/L IgG. In some examples, the milk product comprises about 0.01-0.1 g/L IgM. In some examples, the milk product comprises about 0.2-2 percent by weight immunoglobulins.

[0043] These and other examples of the disclosure are set forth in more detail in the description of the disclosure below.

BRIEF DESCRIPTION OF THE DRAWINGS

[0044] FIG. 1 shows an example of the collection of milk for nutritional use from mammary epithelial cells grown as a confluent monolayer in a compartmentalizing culture apparatus in which either fresh or recycled media is provided to the basal compartment and milk is collected from the apical compartment. TEER, transepithelial electrical resistance.

[0045] FIG. 2 shows an example of polarized absorption of nutrients and secretion of milk across a confluent monolayer of mammary epithelial cells anchored to a scaffold at the basal surface.

[0046] FIG. 3 shows an example micropatterned scaffold that provides increased surface area for the compartmentalized absorption of nutrients and secretion of milk by a confluent monolayer of mammary epithelial cells.

[0047] FIG. 4 shows three examples of a hollow fiber bioreactor depicted as a bundle of capillary tubes (top), which can support mammary epithelial cells lining either the external (top and lower left) or internal (lower right) surface of the capillaries, providing directional and compartmentalized absorption of nutrients and secretion of milk.

[0048] FIG. 5 exemplifies a cross-section of three-dimensional cell construct. The construct is made up of a scaffold having an interior surface defining an interior cavity/basal chamber and an exterior surface. The interior cavity/basal chamber comprises cell culture media. A matrix material sits on

CLAIMS

What is claimed is:

1. A method of producing an isolated cultured milk product comprising secretory IgA (sIgA) from mammary cells and plasma cells, the method comprising:

a. culturing a live cell construct in a bioreactor under conditions which produce the cultured milk product, said live cell construct comprising:

i. a three-dimensional scaffold having an exterior surface, an interior surface defining an interior cavity, and a plurality of pores extending from the interior surface to the exterior surface;

ii. a matrix material disposed on the exterior surface of the three-dimensional scaffold;

iii. a culture medium disposed within the interior cavity and in fluidic contact with the internal surface;

iv. a plurality of plasma cells disposed on the matrix material; and

v. a confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, and mammary progenitor cells, wherein the polarized mammary cells comprise an apical surface and a basal surface; and

vi. said bioreactor comprising an apical compartment that is in fluidic contact with the apical surface of the live mammary cells, is substantially isolated from the interior cavity of the live cell construct, and is substantially free of cell culture medium

b. isolating the cultured milk product secreted into the apical compartment from the apical surface of the live mammary cells and the plasma cell.

2. The method of claim 1, wherein the monolayer of polarized mammary cells is at least 70% confluent, at least 80% confluent, at least 90% confluent, at least 95% confluent, at least 99% confluent, or 100% confluent.

3. The method of claim 1, wherein at least 70%, at least 80%, at least 90%, at least 95%, at least 99%, or 100% of the mammary cells are polarized in the same orientation.

4. The method of claim 1, wherein total cell density of mammary cells within the bioreactor is at least 10^{11}; and alternatively wherein total surface area of mammary cells within the bioreactor is at least 1.5 m^2.

5. The method of claim 1, wherein total cell density of plasma cells in the bioreactor is 200 to 500 plasma cells per mm^2.

6. The method of claim 1, wherein the culturing is carried out at a temperature of 27°C to 39°C.

7. The method of claim 1, wherein the culturing is carried out at an atmospheric concentration of CO^2 of 4% to 6%.

8. A live cell construct, comprising:

    a. a three dimensional scaffold having an exterior surface, an interior surface defining an interior cavity/basal chamber, and a plurality of pores extending from the interior surface to the exterior surface;

    b. a matrix material disposed on the exterior surface of the three-dimensional scaffold;

    c. a plurality of plasma cells disposed on the matrix material; and

    d. an at least 70% confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, and mammary progenitor cells and wherein the live polarized mammary cells comprise an apical surface from which the milk product is secreted and a basal surface; and

    e. a culture media disposed within the interior cavity/basal chamber and in fluidic contact with the internal surface, wherein the culture medium is substantially isolated from the apical surface of the live mammary cells.

9. The live cell construct of claim 8, wherein the basal surface of the mammary cells is in fluidic contact with the culture medium.

10. The live cell construct of claim 8, wherein at least 70%, at least 80%, at least 90%, at least 95%, at least 99%, or 100% of the mammary cells are polarized in the same orientation.

11. The live cell construct of claim 8, wherein the monolayer of polarized mammary cells is at least 70% confluent, at least 80% confluent, at least 90% confluent, at least 95% confluent, at least 99% confluent, or 100% confluent.

12. The live cell construct of claim 8, wherein the mammary cells comprise a constitutively active prolactin receptor protein.

13. The live cell construct of claim 8, wherein the culture medium comprises prolactin.

14. A cultured milk product, comprising: Beta-casein, Alpha-lactalbumin, Kappa-casein, Alpha-S1-casein, Lactoferrin, Lactadherin, Lysozyme, C12:0 (lauric acid), C14:0 (myristic acid), C16:0 (palmitic acid), Lactose, Glucose, 3'-SL, and 6'-SL;

    wherein the cultured milk product does not comprise or is substantially free of persistent organic pollutants (POPs), heavy metals, prescription drugs, recreational drugs, allergens, cells, hormones, or virus;

    provided that the cultured milk product may comprise a human mammary epithelial cell (hMEC) or a plasma cell (PC).

15. The cultured milk product of claim 14, wherein the cultured milk product does not comprise or is substantially free of polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), polychlorinated biphenyls (PCBs) and pesticides.

16. A cultured milk product, comprising: Beta-casein; Alpha-lactalbumin; Kappa-casein; Alpha-S1-casein; Lactoferrin; Butrophilin; Osteopontin; Lactadherin; Lysozyme; Mucin-4; Mucin-1; C8:0 (caprylic acid); C10:0 (capric acid); C12:0 (lauric acid); C13:0 (tridecylic acid); C14:0 (myristic acid); C16:0 (palmitic acid); C16:1 (palmitoleic acid); C18:2n-6 (linoleic acid, LA); C18;3n-3 (alpha-linolenic acid, ALA); C20:3n-6 (dihomo-gama-linolenic acid, DGLA); C20:4n-6 (arachadonic acid, AA); C20:5n-3 (eicosopentanoic acid, EPA); C22:6n-3 (docosahexaenoic acid, DHA); C22:1n9 (eruic acid); C24:1 (nervonic acid); Lactose; Glucose; 3'-SL; 6'-SL; LNT; LNnT; 9-hydroxyoctadecadienoic acid (9-HODE); 13-hydroxyoctadecadienoic acid (13-HODE); 5,15-dihydroxyeicosatetraenoic acid (5,15-DiHETE); 17,18-dihydroxyeicosatetraenoic acid (17,18-DiHETE); 8,9-Dihydroxyicosatrienoic acid (8,9-DiHETrE); 11,12-Dihydroxyicosatrienoic acid (11,12-DiHETrE); 9,10-dihydroxyoctadecenoic acid (9,10-DiHOME); 12,13-dihydroxyoctadecenoic acid (12,13-DiHOME); 14(15)-epoxyeicosatrienoic acid (14(15)-EpETre); 19(20)-epoxydocosapentanoic acid (19(20)-EpDPE); 17-hydroxydocosahexaenoic acid (17-HDoHE); 5-hydroxyeicosatetraenoic acid (5-HETE); 8-hydroxyeicosatetraenoic acid (8-HETE); 9-hydroxyeicosatetraenoic acid (9-HETE); 11-hydroxyeicosatetraenoic acid (11-HETE); 12-hydroxyeicosatetraenoic acid (12-HETE); 9-hydroxyoctadecatrienoic acid (9-HOTrE); 9-oxo-octadecadienoic acid (9-oxo-ODE); or 13-oxo-octadecadienoic acid (13-oxo-ODE); 17,18-epoxyeicosatetraenoic acid (17(18)-EpETE; 6-Keto-prostaglandin F1alpha (6-keto-PGF1a); or 15(S)-Hydroxyeicosatrienoic acid (15(S)-HETrE); and sIgA;

wherein the cultured milk product does not comprise or is substantially free of persistent organic pollutants (POPs), heavy metals, prescription drugs, recreational drugs, allergens, cells, hormones, or virus;

provided that the cultured milk product may comprise human mammary epithelial cells or plasma cells.

17. A method of feeding a human subject in need thereof, comprising administering to the subject a cultured milk product according to claim 16.

18. A method of producing isolated sIgA from mammary cells, the method comprising:

a. culturing a live cell construct in a bioreactor under conditions which produce a cultured milk product, said live cell construct comprising:

i. a three-dimensional scaffold having an exterior surface, an interior surface defining an interior cavity, and a plurality of pores extending from the interior surface to the exterior surface;

ii. a matrix material disposed on the exterior surface of the three-dimensional scaffold;

iii. a culture media disposed within the interior cavity and in fluidic contact with the internal surface;

iv. a plurality of plasma cells disposed on the matrix material; and

v. a confluent monolayer of polarized mammary cells disposed on the plurality of plasma cells, wherein the mammary cells are selected from the group consisting of: mammary epithelial cells, mammary myoepithelial cells, and mammary progenitor cells, wherein the polarized mammary cells comprise an apical surface and a basal surface; and

b. isolating the sIgA from the cultured milk product.

19. A pharmaceutical composition, comprising:

a. sIgA manufactured by the method of claim 18; and

b. a pharmaceutically acceptable excipient.

20. The pharmaceutical composition of claim 19, wherein the pharmaceutically acceptable excipient is a stabilizer, a surfactant, a buffer or tonicity agent.