[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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, the cultured milk product comprises secretory IgA (sIgA). In some ~~embodiment~~examples, the bioreactor comprises an apical compartment that is substantially isolated from the internal cavity of the cell construct. In some ~~embodiment~~examples, the basal surface of the mammary cells is in fluidic contact with the culture media. In some ~~embodiment~~examples, the apical compartment is in fluidic contact with the apical surface of the mammary cells. In some ~~embodiment~~examples, the cultured milk product is secreted from the apical surface of the mammary cells into the apical compartment. In some ~~embodiment~~examples, the culture media substantially does not contact the cultured milk product. In some ~~embodiment~~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 ~~embodiment~~examples, total cell density of plasma cells in the bioreactor is about 200 to 500 plasma cells per mm^2. In some ~~embodiment~~examples, the culturing is carried out at a temperature of about 27°C to about 39°C. In some ~~embodiment~~examples, the culturing is carried out at an atmospheric concentration of CO^2 of about 4% to about 6%.

[0007] Disclosed herein, in certain ~~embodiment~~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 ~~embodiment~~examples, the polarized mammary

cells comprise an apical surface and a basal surface. In some ~~embodiment~~examples, the basal surface of the mammary cells is in fluidic contact with the culture media. In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, the mammary cells comprise a constitutively active prolactin receptor protein. In some ~~embodiment~~examples, the culture medium comprises prolactin.

[0008] Disclosed herein, in certain ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, the endocannabinoid is anandamide or 2-arachidonoylglycerol (2-AG). In some ~~embodiment~~examples, a cultured milk product disclosed herein further comprises secretory IgA (sIgA). In some ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of persistent organic pollutants (POPs). In some ~~embodiment~~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 ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of DDT. In some ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of heavy metals. In some ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of mercury, lead, arsenic, cadmium, nickel, chromium, cobalt, or zinc. In some ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of pharmaceutical or recreational drugs. In some ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of chemotherapeutics, antidepressants, or anti-anxiety medications. In some ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of benzodiazepines. In some ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of lithium, carbamazepine, chlorpromazine, and clozapine. In some ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of alcohol, cannabis, opioids, phencyclidine, or cocaine. In some ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of allergens. In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of Staphylococcus, Acinetobacter, Streptococcus, Pseudomonas, Lactococcus, Enterococcus or Lactobacillus. In some ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of virus. In some ~~embodiment~~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 ~~embodiment~~examples, the cultured milk product does not comprise or is substantially free of hormones. In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, a cultured milk product disclosed herein further comprises a preservative, stabilizer, antioxidant, emulsifier, or thickener. In some ~~embodiment~~examples, a cultured milk product disclosed herein further comprises lecithin. In some ~~embodiment~~examples, a cultured milk product disclosed herein further comprises carrageenan. In some ~~embodiment~~examples, a cultured milk product disclosed herein further comprises beta carotene. In some ~~embodiment~~examples, a cultured milk product disclosed herein further comprises vitamin E. In some ~~embodiment~~examples, a cultured milk product disclosed herein further comprises ascorbyl palmitate or ascorbic acid. In some ~~embodiment~~examples, a cultured milk product disclosed herein further comprises lecithin, ascorbyl palmitate and vitamin E. In some ~~embodiment~~examples, a cultured milk product disclosed herein is dehydrated, freeze-dried, or frozen. In some ~~embodiment~~examples, a cultured milk product disclosed herein is food-grade.

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

[0012] Disclosed herein, in certain ~~embodiment~~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 ~~embodiment~~examples, the infection is a bacterial infection, fungal infection or parasitic infection. In some ~~embodiment~~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 ~~embodiment~~examples, the parasitic infection is an infection of Giardia lamblia, Entamoeba histolytica, Cryptosporidium spp., or Cystoisospora belli. In some ~~embodiment~~examples, the fungal infection is an infection of Aspergillus, Cryptococcus, or Pneumocystis jirovecii. In some ~~embodiment~~examples, the microbial infection is a gastrointestinal infection. In some ~~embodiment~~examples, the gastrointestinal infection is gastroenteritis. In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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

~~embodiment~~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 ~~embodiment~~examples, the cultured milk product comprises secretory IgA (sIgA). In some ~~embodiment~~examples, the bioreactor comprises an apical compartment that is substantially isolated from the internal cavity of the cell construct. In some ~~embodiment~~examples, the basal surface of the mammary cells is in fluidic contact with the culture media. In some ~~embodiment~~examples, the apical compartment is in fluidic contact with the apical surface of the mammary cells. In some ~~embodiment~~examples, the cultured milk product is secreted from the apical surface of the mammary cells into the apical compartment. In some ~~embodiment~~examples, the culture media substantially does not contact the cultured milk product. In some ~~embodiment~~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 ~~embodiment~~examples, total cell density of plasma cells in the bioreactor is about 200 to 500 plasma

cells per mm^2. In some ~~embodiment~~examples, the culturing is carried out at a temperature of about 27°C to about 39°C. In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, the pharmaceutically acceptable excipient is a stabilizer, a surfactant, a buffer or tonicity agent. In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, the pharmaceutically acceptable excipient is a stabilizer, a surfactant, a buffer or tonicity agent. In some ~~embodiment~~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 ~~embodiment~~examples, the human subject is an infant. In some ~~embodiment~~examples, the human subject is immuno-compromised. In some ~~embodiment~~examples, the human subject has a disease selected from: severe combined immunodeficiency (SCID), HIV/AIDS, a cancer, or an autoimmune disease. In some ~~embodiment~~examples, the subject has lupus or diabetes (for example, Type I diabetes or Type II diabetes). In some ~~embodiment~~examples, the human subject is an organ or bone marrow transplant recipient. In some ~~embodiment~~examples, the human subject is malnourished. In some ~~embodiment~~examples, the human subject has malabsorption syndrome. In some ~~embodiment~~examples, the human subject has wasting syndrome. In some ~~embodiment~~examples, the human subject is geriatric. In some ~~embodiment~~examples, the human subject has cystic fibrosis, COPD, or non-CF bronchiectasis. In some ~~embodiment~~examples, the infection is a bacterial infection, fungal infection or parasitic infection. In some ~~embodiment~~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 ~~embodiment~~examples, the parasitic infection is an infection of Giardia lamblia, Entamoeba istolytica, Cryptosporidium spp., or Cystoisospora belli. In some ~~embodiment~~examples, the fungal

infection is an infection of Aspergillus, Cryptococcus, or Pneumocystis jirovecii. In some ~~embodiment~~examples, the microbial infection is a gastrointestinal infection. In some ~~embodiment~~examples, the gastrointestinal infection is gastroenteritis. In some ~~embodiment~~examples, the microbial infection is Candidiasis. In some ~~embodiment~~examples, the microbial infection is a respiratory infection. In some ~~embodiment~~examples, the respiratory infection is pneumonia, bronchitis, Aspergillosis, or

Cryptococcosis. In some ~~embodiment~~examples, the respiratory infection is an infection by B. cepacia, P. aeruginosa S. aureus, Aspergillus, Cryptococcus, or Pneumocystis. In some ~~embodiment~~examples, the composition is formulated for inhalation. In some ~~embodiment~~examples, the composition is a powder. In some ~~embodiment~~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 ~~aspect~~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 ~~embodiment~~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 ~~embodiment~~examples, the cultured milk product comprises secretory IgA (sIgA).

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

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

[0020] In certain ~~embodiment~~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 ~~embodiment~~examples, the polarized mammary cells comprise an apical surface and a basal surface. In some ~~embodiment~~examples, the basal surface of the mammary cells is in fluidic contact with the culture media.

[0021] In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, the mammary cells comprise a constitutively active prolactin receptor protein. In some ~~embodiment~~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 ~~embodiment~~examples, the culture medium further comprises prolactin. In some ~~embodiment~~examples, the matrix material comprises one or more extracellular matrix proteins. In some ~~embodiment~~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 ~~embodiment~~examples, the natural polymer is collagen, chitosan, cellulose, agarose, alginate, gelatin, elastin, heparan sulfate, chondroitin sulfate, keratan sulfate, and/or hyaluronic acid. In some ~~embodiment~~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 ~~aspect~~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 ~~embodiment~~examples, the milk product further comprises one or more immunoglobulins. In some ~~embodiment~~examples, the immunoglobulin is secretory IgA.

[0024] In some ~~embodiment~~examples, the protein component comprises about 55-65% dry weight of the milk product. In some ~~embodiment~~examples, the protein component comprises beta-casein, kappa-casein and alpha-casein. In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, the beta-casein comprises greater than about 50% of total casein content.

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

[0026] In some ~~embodiment~~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 ~~embodiment~~examples, the saturated fatty acids has a concentration of about 5-34 g/L in the milk product. In some ~~embodiment~~examples, the saturated fatty acids comprise palmitic acid, stearic acid, and lauric acid. In some ~~embodiment~~examples, the palmitic acid comprises at least about 50% sn-2 form. In some ~~embodiment~~examples, palmitic acid has a concentration of about 3-18 g/L in the milk product. In some ~~embodiment~~examples, stearic acid has a concentration of about 0.7-5 g/L in the milk product. In some ~~embodiment~~examples, lauric acid has a concentration of about 0.5-5 g/L in the milk product. In some ~~embodiment~~examples, monounsaturated fatty acids have a concentration of about 7-46 g/L in the milk product. In some ~~embodiment~~examples, the monounsaturated fatty acid comprises oleic acid. In some ~~embodiment~~examples, the oleic acid comprises at least about 50% sn-1 form. In some ~~embodiment~~examples, the oleic acid has a concentration of about 7-45 g/L in the milk product. In some ~~embodiment~~examples, polyunsaturated fats have a concentration of about 2-20 g/L in the milk product. In some ~~embodiment~~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 ~~embodiment~~examples, linoleic acid has a concentration of about 2-19 g/L in the milk product. In some ~~embodiment~~examples, the linoleic acid comprises at least about 50% sn-3 form. In some ~~embodiment~~examples, alpha-linolenic acid has a concentration of about 0.5-0.7 g/L in the milk product. In some ~~embodiment~~examples, eicosadienoic acid has a concentration of about 0.5-0.7 g/L in the milk product. In some ~~embodiment~~examples, arachidonic acid has a concentration of about 0.5-0.7 g/L in the milk product. In some ~~embodiment~~examples, dihomo-gamma-linolenic acid has a concentration of about 0.3-0.5 g/L in the milk product. In some ~~embodiment~~examples, docosahexadienoic acid has a concentration of about 0.02-0.4 g/L in the milk product. In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, the milk product coprises cholesterol having a concentration of about 0.09-0.15 g/L in milk product. In some ~~embodiment~~examples, phospholipids, plasmalogens and sphingolipids together have a concentration of about 0.1-0.4 g/L in the milk product.

[0027] In some ~~embodiment~~examples, the human milk oligosaccharide component comprises one or more neutral oligosaccharides. In some ~~embodiment~~examples, the human milk oligosaccharide component comprises one or more acidic oligosaccharides. In some ~~embodiment~~examples, the human milk oligosaccharide component comprises neutral oligosaccharides and/or acidic oligosaccharides. In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~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 ~~aspect~~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 ~~embodiment~~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 ~~aspect~~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 ~~embodiment~~examples, the milk product further comprises serum albumin. In some ~~embodiment~~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 ~~embodiment~~examples, the milk product further comprises one or more immunoglobulins. In some ~~embodiment~~examples, the immunoglobulins comprise one or more of IgA, IgG and IgM. In some ~~embodiment~~examples, the IgA comprises one or more of IgA2 (secretory) and IgA1 (non-secretory). In some ~~embodiment~~examples, the milk product comprises about 0.2-1.0 g/L secretory IgA. In some ~~embodiment~~examples, the milk product comprises about 0.15-1.6 g/L total IgA. In some ~~embodiment~~examples, the milk product comprises about 0.03-0.3 g/L IgG. In some ~~embodiment~~examples, the milk product comprises about 0.01-0.1 g/L IgM. In some ~~embodiment~~examples, the milk product comprises about 0.2-2 percent by weight immunoglobulins.

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

[0034] In some ~~embodiment~~examples, the milk product is isolated from cultured mammary epithelial cells from one or more specific persons. In some ~~embodiment~~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 ~~embodiment~~examples, the cultured mammary epithelial cells are co-cultured with one or more plasma cells lines. In some ~~embodiment~~examples, the cultured mammary epithelial cells are co-cultured with one or more myoepithelial cell lines. In some ~~embodiment~~examples, the cultured mammary epithelial cells are co-cultured with one or more stem cell lines.

[0035] In some ~~embodiment~~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 ~~embodiment~~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 ~~aspect~~examples, described herein are frozen milk products, comprising a milk product described herein that has been frozen. In some ~~embodiment~~examples, the milk product has been lyophilized. In certain ~~aspect~~examples, described herein is a containerized milk product, comprising a milk product described herein that is packaged into a container. In certain ~~aspect~~examples, described herein is a containerized frozen milk product, comprising the frozen milk product that is packaged into a container. In certain ~~aspect~~examples, described herein is a containerized lyophilized milk product, comprising the lyophilized milk product that is packaged into a container.

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

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

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

[0040] In certain ~~aspect~~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 ~~embodiment~~examples, the milk product further comprises one or more immunoglobulins. In some ~~embodiment~~examples, the immunoglobulins comprise one or more of IgA, IgG and IgM. In some ~~embodiment~~examples, the IgA comprises one or more of IgA2 (secretory) and IgAl (non-secretory).

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

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

[0042] In certain ~~aspect~~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 ~~embodiment~~examples, the milk product further comprises one or more immunoglobulins. In some ~~embodiment~~examples, the immunoglobulins comprise one or more of IgA, IgG and IgM. In some ~~embodiment~~examples, the IgA comprises one or more of IgA2 (secretory) and IgAl (non-secretory). In some ~~embodiment~~examples, the milk product comprises about 0.2-1.0 g/L secretory IgA. In some ~~embodiment~~examples, the milk product comprises about 0.15-1.6 g/L total IgA. In some ~~embodiment~~examples, the milk product comprises about 0.03-0.3 g/L IgG. In some ~~embodiment~~examples, the milk product comprises about 0.01-0.1 g/L IgM. In some ~~embodiment~~examples, the milk product comprises about 0.2-2 percent by weight immunoglobulins.

[0043] These and other ~~aspect~~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 the cultured milk product comprises secretory IgA (sIgA).~~

~~5. The method of claim 1, wherein the bioreactor comprises an apical compartment that is substantially isolated from the internal cavity of the cell construct.~~

~~6. The method of claim 1, wherein the basal surface of the mammary cells is in fluidic contact with the culture media.~~

~~7. The method of claim 5, wherein the apical compartment is in fluidic contact with the apical surface of the mammary cells.~~

~~8. The method of claim 7, wherein the cultured milk product is secreted from the apical surface of the mammary cells into the apical compartment.~~

~~9. The method of claim 1, wherein the culture media substantially does not contact the cultured milk product.~~

~~10.~~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.

~~11.~~5. The method of claim 1, wherein total cell density of plasma cells in the bioreactor is ~~about~~ 200 to 500 plasma cells per mm^2.

~~12.~~6. The method of claim 1, wherein the culturing is carried out at a temperature of ~~about~~ 27°C to ~~about~~ 39°C.

~~13.~~7. The method of claim 1, wherein the culturing is carried out at an atmospheric concentration of CO^2 of ~~about~~ 4% to ~~about~~ 6%.

~~14.~~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 culture media disposed within the interior cavity/basal chamber and in fluidic contact with the internal surface;~~

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

~~e.~~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.

~~15. The cell construct of claim 14, wherein the polarized mammary cells comprise an apical surface and a basal surface.~~

~~16.~~9. The live cell construct of claim ~~8~~15, wherein the basal surface of the mammary cells is in fluidic contact with the culture mediuma.

~~17.~~10. The live cell construct of claim ~~8~~14, 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.

~~18.~~11. The live cell construct of claim ~~8~~14, 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.

~~19.~~12. The live cell construct of claim ~~8~~14, wherein the mammary cells comprise a constitutively active prolactin receptor protein.

~~20.~~13. The live cell construct of claim ~~8~~14, wherein the culture medium comprises prolactin.

~~21.~~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).

~~22. The cultured milk product of claim 21, further comprising: 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-~~ 82 -rachidonic~~ 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.~~

~~23. The cultured milk product of claim 21, further comprising at least one oxylipin metabolite of a polyunsaturated fatty acid or at least one endocanabinoid~~ 83 -rachidonic- 83 -oid~~.~~

~~24. The cultured milk product of claim 23, wherein 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).~~

~~25. The cultured milk product of claim 23, wherein the endocannabinoid is anandamide or 2-arachidonoylglycerol (2-AG).~~

~~26. The cultured milk product of claim 21, further comprising secretory IgA (sIgA).~~

~~27. The cultured milk product of claim 21, wherein the cultured milk product does not comprise or is substantially free of persistent organic pollutants (POPs).~~

~~28.~~15. The cultured milk product of claim 14~~27~~, 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.

~~29. The cultured milk product of claim 28, wherein the cultured milk product does not comprise or is substantially free of DDT.~~

~~30. The cultured milk product of claim 21, wherein the cultured milk product does not comprise or is substantially free of heavy metals.~~

~~31. The cultured milk product of claim 30, wherein the cultured milk product does not comprise or is substantially free of mercury, lead, arsenic, cadmium, nickel, chromium, cobalt, or zinc.~~

~~32. The cultured milk product of claim 21, wherein the cultured milk product does not comprise or is substantially free of pharmaceutical or recreational drugs.~~

~~33. The cultured milk product of claim 32, wherein the cultured milk product does not comprise or is substantially free of chemotherapeutics, antidepressants, or anti-anxiety medications.~~

~~34. The cultured milk product of claim 32, wherein the cultured milk product does not comprise or is substantially free of benzodiazepines.~~

~~35. The cultured milk product of claim 32, wherein the cultured milk product does not comprise or is substantially free of lithium, carbamazepine, chlorpromazine, and clozapine~~.

~~36. The cultured milk product of claim 32, wherein the cultured milk product does not comprise or is substantially free of alcohol, cannabis, opioids, phencyclidine, or cocaine.~~

~~37. The cultured milk product of claim 21, wherein the cultured milk product does not comprise or is substantially free of allergens.~~

~~38. The cultured milk product of claim 37, wherein the cultured milk product does not comprise or is substantially free of ovomucoid, ovalbumin, conalbumin, arachin 6, arachin 3, conarachin, Arah1, and arachin Arah2.~~

~~39. The cultured milk product of claim 21, wherein 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).~~

~~40. The cultured milk product of claim 39, wherein the cultured milk product does not comprise or is substantially free of myoepithelial cells, myeloid precursor cells, neutrophils, granulocytes, or T cells.~~

~~41. The cultured milk product of claim 39, wherein the cultured milk product does not comprise or is substantially free of Staphylococcus, Acinetobacter, Streptococcus, Pseudomonas, Lactococcus, Enterococcus or Lactobacillus.~~

~~42. The cultured milk product of claim 21, wherein the cultured milk product does not comprise or is substantially free of virus.~~

~~43. The cultured milk product of claim 42, wherein 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.~~

~~44. The cultured milk product of claim 21, wherein the cultured milk product does not comprise or is substantially free of hormones.~~

~~45. The cultured milk product of claim 44, wherein 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.~~

~~46.~~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~~- 85 -rachidonic 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.

~~47. The cultured milk product of any one of claims 21-46, wherein the cultured milk product further comprises a preservative, stabilizer, antioxidant, emulsifier, or thickener.~~

~~48. The cultured milk product of claim 47, wherein the cultured milk product further comprises lecithin.~~

~~49. The cultured milk product of claim 47, wherein the cultured milk product further comprises carrageenan.~~

~~50. The cultured milk product of claim 47, wherein the cultured milk product further comprises beta-carotene.~~

~~51. The cultured milk product of claim 47, wherein the cultured milk product further comprises vitamin E.~~

~~52. The cultured milk product of claim 47, wherein the cultured milk product further comprises ascorbyl palmitate or ascorbic acid. I~~

~~53. The cultured milk product of claim 47, wherein the cultured milk product further comprises lecithin, ascorbyl palmitate and vitamin E~~

~~54. The cultured milk product of any one of claims 21-53, wherein the cultured milk product is dehydrated, freeze-dried, or frozen.~~

~~55. The cultured milk product of any one of claims 21-54, wherein the cultured milk product is food-grade.~~

~~56.~~17. A method of feeding a human subject in need thereof, comprising administering to the subject a cultured milk product according to ~~any one of~~ claim~~s~~ 16~~21-55~~.

~~57. The method of claim 56, wherein the human subject is an infant.~~

~~58. The method of claim 56, wherein the human subject is immuno-compromised.~~

~~59. The method of claim 58, wherein the human subject has a disease selected from: severe combined immunodeficiency (SCID), HIV/AIDS, a cancer, or an autoimmune disease.~~

~~60. The method of claim 59, wherein the subject has lupus or diabetes (for example, Type I diabetes or Type II diabetes).~~

~~61. The method of claim 58, wherein the human subject is an organ or bone marrow transplant recipient.~~

~~62. The method of claim 56, wherein the human subject is malnourished.~~

~~63. The method of claim 56, wherein the human subject has malabsorption syndrome.~~

~~64. The method of claim 56, wherein the human subject has wasting syndrome.~~

~~65. The method of claim 56, wherein the human subject is geriatric.~~

~~66. A method of treating or preventing a microbial infection in a subject in need thereof, comprising administering to the subject a cultured milk product of claim 26 or 46.~~

~~67. The method of claim 66, wherein the infection is a bacterial infection, fungal infection or parasitic infection.~~

~~68. The method of claim 67, wherein 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.~~

~~69. The method of claim 67, wherein the parasitic infection is an infection of Giardia lamblia, Entamoeba histolytica, Cryptosporidium spp., or Cystoisospora belli.~~

~~70. The method of claim 66, wherein the microbial infection is a gastrointestinal infection.~~

~~71. The method of claim 70, wherein the gastrointestinal infection is gastroenteritis.~~

~~72. The method of claim 66, wherein the microbial infection is Candidiasis.~~

~~73.~~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.

~~74. The method of claim 73, 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.~~

~~75. The method of claim 73, 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.~~

~~76. The method of claim 73, wherein the cultured milk product comprises secretory IgA (sIgA).~~

77. The method of claim 73, wherein the bioreactor comprises an apical compartment that is substantially isolated from the internal cavity of the cell construct.

78. The method of claim 73, wherein the basal surface of the mammary cells is in fluidic contact with the culture media.

79. The method of claim 77, wherein the apical compartment is in fluidic contact with the apical surface of the mammary cells.

80. The method of claim 79, wherein the cultured milk product is secreted from the apical surface of the mammary cells into the apical compartment.

81. The method of claim 73, wherein the culture media substantially does not contact the cultured milk product.

82. The method of claim 73, 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.

83. The method of claim 73, wherein total cell density of plasma cells in the bioreactor is about 200 to 500 plasma cells per mm^2.

84. The method of claim 73, wherein the culturing is carried out at a temperature of about 27°C to about 39°C.

85. The method of claim 73, wherein the culturing is carried out at an atmospheric concentration of CO^2 of about 4% to about 6%.

86. A method 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 according to any one of claims 73-85.

87. The method of claim 86, wherein the human subject is an infant.

88. The method of claim 86, wherein the human subject is immuno-compromised.

89. The method of claim 88, wherein the human subject has a disease selected from: severe combined immunodeficiency (SCID), HIV/AIDS, a cancer, or an autoimmune disease.

90. The method of claim 89, wherein the subject has lupus or diabetes (for example, Type I diabetes or Type II diabetes).

91. The method of claim 88, wherein the human subject is an organ or bone marrow transplant recipient.

~~92. The method of claim 86, wherein the human subject is malnourished.~~

~~93. The method of claim 86, wherein the human subject has malabsorption syndrome.~~

~~94. The method of claim 86, wherein the human subject has wasting syndrome.~~

~~95. The method of claim 86, wherein the human subject is geriatric.~~

~~96. The method of claim 86, wherein the human subject has cystic fibrosis, COPD, or non-CF bronchiectasis.~~

~~97. The method of claim 86, wherein the infection is a bacterial infection, fungal infection or parasitic infection.~~

~~98. The method of claim 96, wherein 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.~~

~~99. The method of claim 96, wherein the parasitic infection is an infection of Giardia lamblia, Entamoeba histolytica, Cryptosporidium spp., or Cystoisospora belli.~~

~~100. The method of claim 86, wherein the microbial infection is a gastrointestinal infection.~~

~~101. The method of claim 99, wherein the gastrointestinal infection is gastroenteritis.~~

~~102. The method of claim 86, wherein the microbial infection is Candidiasis.~~

~~103. The method of claim 86, wherein the microbial infection is a respiratory infection.~~

~~104. The method of claim 103, wherein the respiratory infection is pneumonia, bronchitis, Aspergillosis, or Cryptococcosis.~~

~~105. The method of claim 103, wherein the respiratory infection is an infection by B. cepacia, P. aeruginosa S. aureus, Aspergillus, Cryptococcus, or Pneumocystis.~~

~~106. The method of claim 86 or any one of 103-105, wherein the composition is formulated for inhalation.~~

~~107. The method of claim 106, wherein the composition is a powder.~~

~~108. The method of claim 106, wherein the composition is formulation for administration by a nebulizer.~~

~~109.~~19. A pharmaceutical composition, comprising:

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

b. a pharmaceutically acceptable excipient.

~~110.~~20. The pharmaceutical composition of claim 1~~909~~, wherein the pharmaceutically acceptable excipient is a stabilizer, a surfactant, a buffer or tonicity agent.

~~111. The pharmaceutical composition of claim 109, wherein 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.~~