cell surface in the context of MHC class II molecules. T_H1 cells can activate a number of other immune cells, including macrophages and B cells, thereby promoting more efficient destruction and clearance of intracellular microorganisms. T_H2 cells stimulate the differentiation of B cells and promote the production of antibodies and other effector molecules of the humoral immune response.

SUMMARY ~~OF THE INVENTION~~

[0008] In one aspect, provided herein is a live, recombinant commensal bacterium, wherein the bacterium is engineered to express a non-native protein or peptide, wherein the protein or peptide is associated with a host disease or condition, wherein upon administration of the bacterium to the host resulting in colonization of a native host niche by the bacterium, the host mounts an adaptive immune response to the non-native protein or peptide, wherein the adaptive immune response is a regulatory T-cell (T_{reg}) response or an effector T-cell ($T_{effector}$) response. In some ~~embodiment~~example**s**, the colonization of the native host niche is persistent or transient. In certain ~~embodiment~~example**s**, the native host niche is transiently colonized, and colonization is for 1 day to 60 days. In certain ~~embodiment~~example**s**, the native host niche is transiently colonized, and colonization is for 3.5 days to 60 days. In certain ~~embodiment~~example**s**, the native host niche is transiently colonized, and colonization is for 7 days to 28 days. In some ~~embodiment~~example**s**, colonization is determined by polymerase chain reaction or colony forming assay performed on a sample obtained from the host after 1 day, 3.5 days, 7 days, 14 days, 28 days, or 60 days after administration to the host. In some ~~embodiment~~example**s**, the administration results in interaction of the bacterium with a native immune system partner cell. In certain ~~embodiment~~example**s**, the native immune system partner cell is an antigen-presenting cell. In certain ~~embodiment~~example**s**, the antigen-presenting cell is selected from the group consisting of a dendritic cell, a macrophage, a B-cell, and an intestinal epithelial cell.

[0009] In some ~~embodiment~~example**s**, the native host niche is selected from the group consisting of the gastrointestinal tract, respiratory tract, urogenital tract, and skin. In some ~~embodiment~~example**s**, the non-native protein or peptide is a host protein or peptide. In some ~~embodiment~~example**s**, the bacterium is a Gram-negative bacterium. In certain ~~embodiment~~example**s**, the Gram-negative bacterium is selected from the group consisting of *Bacteroides thetaiotaomicron, Helicobacter hepaticus* and *Parabacteroides sp*. In certain ~~embodiment~~example**s**, the bacterium is a Gram-positive bacterium. In certain ~~embodiment~~example**s**, the Gram-positive bacterium is selected from the group consisting of *Staphylococcus epidermidis, Faecalibacterium sp.* and *Clostridium sp.*

[0010] In some ~~embodiment~~example**s**, the administration is via a route selected from the group consisting of topical, enteral, parenteral and inhalation. In certain ~~embodiment~~example**s**, the

administration route is topical. In some ~~embodiment~~examples, the bacterium is *S. epidermidis*. In certain ~~embodiment~~examples, the administration route is enteral. In some ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides* spp., *Clostridium* spp., *Helicobacter* spp., *Parabacteroides* spp, and *Prevotella* spp. In some ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides thetaiotaomicron, Bacteroides vulgatus* and *Bacteroides finegoldii.*

[0011] In some ~~embodiment~~examples, the adaptive immune response is a T_{reg} response and the bacterium is selected from the group consisting of *Bacteroides* spp., *Helicobacter* spp., *Parabacteroides* spp., *Clostridium* spp., *Staphylococcus* spp., *Lactobacillus* spp., *Fusobacterium* spp., *Enterococcus* spp., *Acenitobacter* spp., *Flavinofractor* spp., *Lachnospiraceae* spp., *Erysipelotrichaceae* spp., *Anaerostipes* spp., *Anaerotruncus* spp., *Coprococcus* spp., *Clostridiales* spp., *Odoribacter* spp., *Collinsella* spp., *Bifidobacterium* spp., *Streptococcus* spp., and *Prevotella* spp. In certain ~~embodiment~~examples, the adaptive immune response is a T_{reg} response and the bacterium is selected from the group consisting of *Clostridium ramosum, Staphylococcus saprophyticus, Bacteroides thetaiotaomicron, Clostridium histolyticum, Lactobacillus rhamnosus, Parabacteroides johnsonii, Fusobacterium nucleatum, Enterococcus faecium, Lactobacillus casei, Acenitobacter lwofii, Bacteroides ovatus, ,Bacteroides vulgatus, Bacteroides uniformis, Bacteroides finegoldii, Clostridium spiroforme, Flavonifractor plautii, Clostridium hathewayi, Lachnospiraceae bacterium, Clostridium bolteae, Erysipelotrichaceae bacterium, Anaerostipes caccae, Anaerotruncus colihominis, Coprococcus comes , Clostridium asparagiforme, Clostridium symbiosum, Clostridium ramosum, Clostridium sp. D5, Clostridium scindens , Lachnospiraceae bacterium , Clostridiales bacterium , Bacteroides intestinalis, Bacteroides caccae, Bacteroides massiliensis, Parabacteroides distasonis, Odoribacter splanchnicus, Collinsella aerofaciens, Acinetobacter lwoffii, Bifidobacterium breve, Bacteroides finegoldii, Bacteroides fragilis, Bacteroides massiliensis, Bacteroides ovatus, Bifidobacterium bifidum, Lactobacillus acidofilus, Lactobacillus casei, Lactobacillus reuteri, Streptococcus thermophilus,* and *Prevotella histicola.* In certain ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides thetaiotaomicron, Bacteroides vulgatus, Bacteroides finegoldii and Helicobacter hepaticus*.

[0012] In some ~~embodiment~~examples, the disease or condition is an autoimmune disorder. In certain ~~embodiment~~examples, the autoimmune disorder is selected from the group consisting of multiple sclerosis, diabetes mellitus Type I, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, celiac disease, Graves' disease, Hashimoto's autoimmune thyroiditis, vitiligo, rheumatic fever, pernicious anemia/atrophic gastritis, alopecia areata,

immune thrombocytopenic purpura, temporal arteritis, ulcerative colitis, Crohn's disease, scleroderma, antiphospholipid syndrome, autoimmune hepatitis type 1, primary biliary cirrhosis, Sjogren's syndrome, Addison's disease, dermatitis herpetiformis, Kawasaki disease, sympathetic ophthalmia, HLA-B27 associated acute anterior uveitis, primary sclerosing cholangitis, discoid lupus erythematosus, polyarteritis nodosa, CREST Syndrome, myasthenia gravis, polymyositis/dermatomyositis, Still's disease, autoimmune hepatitis type 2, Wegener's granulomatosis, mixed Connective tissue disease, microscopic polyangiitis, autoimmune polyglandular syndrome, Felty's syndrome, autoimmune hemolytic anemia, chronic inflammatory demyelinating polyneuropathy, Guillain-Barre Syndrome, Behcet disease, autoimmune neutropenia, bullous pemphigoid, essential mixed cryoglobulinemia, linear morphea, autoimmune polyglandular syndrome 1 (APECED), acquired hemophilia A, Batten disease/neuronal ceroid lipofuscinoses, autoimmune pancreatitis, Hashimoto's encephalopathy, Goodpasture's disease, pemphigus vulgaris, autoimmune disseminated encephalomyelitis, relapsing polychondritis, Takayasu arteritis, Churg-Strauss syndrome, epidermolysis bullosa acquisita, cicatricial pemphigoid, pemphigus foliaceus, autoimmune hypoparathyroidism, autoimmune hypophysitis, autoimmune inner ear disease, autoimmune lymphoproliferative syndrome, autoimmune oophoritis, autoimmune orchitis, autoimmune polyglandular syndrome, Cogan's syndrome, encephalitis lethartica, erythema elevatum diutinum, Evans syndrome, immunodysregulation polyendocrinopathy enteropathy X-linked (IPEX), Issac's syndrome/acquired neuromyotonia, Miller Fisher syndrome, Morvan's syndrome, PANDAS, POEMS syndrome, Rasmussen's encephalitis, stiff-person syndrome, Vogt-Koyanagi-Harada syndrome, neuromyelitis optica, graft vs host disease, and autoimmune uveitis. In certain ~~embodiment~~examples, the autoimmune disorder is selected from the group consisting of multiple sclerosis and diabetes mellitus Type I.

[0013] In some ~~embodiment~~examples, the non-native protein or peptide is selected from the group consisting of ovalbumin, myelin oligodendrocyte glycoprotein, insulin, chromogranin A, hybrid insulin peptides, proteolipid protein, myelin basic protein, villin, epithelial cellular adhesion molecule, collagen alpha-1, aggrecan core protein, 60kDa chaperonin 2, vimentin, alpha-enolase, fibrinogen alpha chain, fibrinogen beta chain, chitinase-3-like protein, 60kDa mitochondrial heat shock protein, matrix metalloproteinase-16, thyroid peroxidase, thyrotropin receptor, thyroglobulin, gluten, TSHR protein, glutamate decarboxylase 2, receptor-type tyrosine-protein phosphatase-like N, glucose-6-phosphatase 2, insulin isoform 2, zinc transporter 8, glutamate decarboxylase 1, GAD65, UniProt:A2RGM0, integrin alpha-Iib, integrin beta-3, EBV DNA polymerase catalytic subunit, 2'3'-cyclic-nucleotide 3' phosphodiesterase, myelin associated

oligodendrocyte basic protein, small nuclear ribonucleoprotein, U1 small nuclear ribonucleoprotein, histone H2B, histone H2A, histone H3.2, beta-2-glycoprotein, histone H4, 60S ribosomal protein L7, TNF-alpha, myeloperoxidase, Cbir1, MS4A12, DNA topoisomerase, CYP2D6, O-phosphoseryl-tRNA selenium transferase, pyruvate dehydrogenase complex, spectrin alpha chain, steroid 21-hydroxylase, acetylcholine receptor, MMP-16, keratin associated proteins. Chondroitin sulfate proteoglycan 4, myeloblastin, U1 small nuclear ribonucleoprotein 70 kDa, blood group Rh(D), blood group Rh(CE), myelin P2 protein, peripheral myelin protein 22, myelin protein P0, S-arrestin, collagen Alpha-1, coagulation factor VIII, collagen alpha-3(IV), desmoglein-3, desmoglein-1, Insulin-2, major DNA-binding protein, tyrosinase, 5,6-dihydroxyindole-2-carboxylic acid oxidase, HLA-A2, aquaporin-4, myelin proteolipid protein, ABC transporter, HLA I B-27 alpha chain, HLA I B-7 alpha chain, and retinol-binding protein 3. In certain ~~embodiment~~examples, the non-native protein or peptide is selected from the group consisting of ovalbumin, myelin oligodendrocyte glycoprotein, insulin, chromogranin A, hybrid insulin peptides, proteolipid protein, myelin basic protein, villin, epithelial cellular adhesion molecule, In some ~~embodiment~~examples, the bacterium is engineered to secrete the expressed protein or peptide. In some ~~embodiment~~examples, the bacterium is engineered to express a fusion protein comprising the protein or peptide and a native bacterial protein or portion thereof. In some ~~embodiment~~examples, the protein or peptide is fused to the N-terminus or the C-terminus of the native bacterial protein or portion thereof. In some ~~embodiment~~examples, the native bacterial protein is selected from the group consisting of sialidase, endonuclease, secreted endoglycosidase, anti-sigma factor, thiol peroxidase, hypothetical protein BT_2621, hypothetical protein BT_3223, peptidase, Icc family phosphohydrolase, exo-poly-alpha-D-galacturonosidase, and hypothetical protein BT_4428. In certain ~~embodiment~~examples, the native bacterial protein is sialidase or anti-sigma factor.

[0014] In some ~~embodiment~~examples, the adaptive immune response is a $T_{effector}$ response and the bacterium is selected from the group consisting of *S. epidermidis*, *Corynebacterium spp.*, *Parabacteroides distasonis, Parabacteroides gordonii, Alistipes senegalensis, Parabacteroides johnsonii, Paraprevotella xylaniphila, Bacteroides dorei, Bacteroides uniformis JCM 5828, Eubacterium limosum, Ruminococcaceae bacterium cv2, Phascolarctobacterium faecium, Fusobacterium ulcerans, Klebsiella pneumoniae , Clostridium bolteae 90B3, Clostridium cf. saccharolyticum K10, Clostridium symbiosum WAL-14673, Clostridium hathewayi 12489931, Ruminococcus obeum A2-162, Ruminococcus gnavus AGR2154, Butyrate-producing bacterium SSC/2, Clostridium sp. ASF356, Coprobacillus sp. D6 cont1.1 , Eubacterium sp. 3_1_31 cont1.1, Erysipelotrichaceae bacterium 21_3 , Subdoligranulum sp. 4_3_54A2FAA, Ruminococcus bromii L2-63, Firmicutes bacterium ASF500, Firmicutes bacterium ASF500, Bacteroides dorei*

5_1_36/D4 supercont2.3, Bifidobacterium animalis subsp. Lactis ATCC 27673, and *Bifidobacterium breve UCC2003*. In certain ~~embodiment~~examples, the bacterium is selected from the group consisting of *S. epidermidis* LM087 and *Corynebacterium spp*.

[0015] In some ~~embodiment~~examples, the disease or condition is a proliferative disorder. In some ~~embodiment~~examples, the proliferative disorder is cancer. In certain ~~embodiment~~examples, the cancer is selected from melanoma, basal cell carcinoma, squamous cell carcinoma, and testicular cancer. In certain ~~embodiment~~examples, the cancer is melanoma.

[0016] In some ~~embodiment~~examples, the non-native protein or peptide is selected from the group consisting of PMEL, TRP2, MART-1, NY-ESO, MAGE-A, and a neoantigen. In certain ~~embodiment~~examples, the non-native protein or peptide is PMEL.

[0017] In some ~~embodiment~~examples, the bacterium is engineered to secrete the expressed protein or peptide. In some ~~embodiment~~examples, the bacterium is engineered to express a fusion protein comprising the protein or peptide and a native bacterial protein or portion thereof. In certain ~~embodiment~~examples, the protein or peptide is fused to the N-terminus or the C-terminus of the native bacterial protein or portion thereof. In some ~~embodiment~~examples, the native bacterial protein is selected from the group consisting of sialidase, endonuclease, secreted endoglycosidase, anti-sigma factor, thiol peroxidase, hypothetical protein BT_2621, hypothetical protein BT_3223, peptidase, Icc family phosphohydrolase, exo-poly-alpha-D-galacturonosidase, and hypothetical protein BT_4428. In certain ~~embodiment~~examples, the native bacterial protein is sialidase or anti-sigma factor.

[0018] In some ~~embodiment~~examples, the bacterium is administered in combination with a high-complexity defined microbial community.

[0019] In some ~~embodiment~~examples, the host is a mammal. In certain ~~embodiment~~examples, the mammal is a human.

[0020] In another aspect, provided herein is a polynucleotide used to engineer the recombinant commensal bacterium as disclosed herein.

[0021] In another aspect, provided herein is a method for generating an antigen-presenting cell displaying an antigen derived from a non-native protein or peptide, comprising: administering the recombinant commensal bacterium as disclosed herein to a subject, wherein the administration results in colonization of the native host niche by the bacterium, internalization of the bacterium by an antigen-presenting cell, and presentation of the antigen by the antigen-presenting cell. In certain ~~embodiment~~examples, the colonization of the native host niche is persistent or transient. In certain ~~embodiment~~examples, the native host niche is transiently colonized, and colonization is for 1 day to 60 days. In certain ~~embodiment~~examples, the native host niche is transiently colonized, and colonization is for 3.5 days to 60 days. In certain ~~embodiment~~examples, the native host niche is

transiently colonized, and colonization is for 7 days to 28 days. In certain ~~embodiment~~examples, colonization is determined by polymerase chain reaction or colony forming assay performed on a sample obtained from the host after 1 day, 3.5 days, 7 days, 14 days, 28 days, or 60 days after administration to the host.

[0022] In some ~~embodiment~~examples, the administration results in interaction of the bacterium with a native immune system partner cell. In some ~~embodiment~~examples, the native immune system partner cell is the antigen-presenting cell. In certain ~~embodiment~~examples, the antigen-presenting cell is selected from the group consisting of a dendritic cell, a macrophage, a B-Cell, and an intestinal epithelial cell. In certain ~~embodiment~~examples, the native host niche is selected from the group consisting of the gastrointestinal tract, respiratory tract, urogenital tract, and skin. In some ~~embodiment~~examples, the presentation is within an MHC II complex. In some ~~embodiment~~examples, the presentation is within an MHC I complex. In some ~~embodiment~~examples, the bacterium is a Gram-negative bacterium. In certain ~~embodiment~~examples, the Gram-negative bacterium is selected from the group consisting of *Bacteroides thetaiotaomicron*, *Helicobacter hepaticus*, *Parabacteroides sp.*, and *Prevotella* spp. In some ~~embodiment~~examples, the bacterium is a Gram-positive bacterium. In certain ~~embodiment~~examples, the Gram-positive bacterium is selected from the group consisting of *Staphylococcus epidermidis, Faecalibacterium sp.* and *Clostridium sp.*

[0023] In some ~~embodiment~~examples, the administration is via a route selected from the group consisting of topical, enteral, parenteral and inhalation. In some ~~embodiment~~examples, the route is topical. In certain ~~embodiment~~examples, the bacterium is *S. epidermidis*. In some ~~embodiment~~examples, the route is enteral. In certain ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides* spp., *Clostridium* spp., *Helicobacter* spp., *Parabacteroides* spp, and *Prevotella* spp. In certain ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides thetaiotaomicron, Bacteroides vulgatus* and *Bacteroides finegoldii*. In some ~~embodiment~~examples, the native bacterial protein is selected from the group consisting of sialidase, endonuclease, secreted endoglycosidase, anti-sigma factor, thiol peroxidase, hypothetical protein BT_2621, hypothetical protein BT_3223, peptidase, Icc family phosphohydrolase, exo-poly-alpha-D-galacturonosidase, and hypothetical protein BT_4428. In certain ~~embodiment~~examples, the native bacterial protein is sialidase or anti-sigma factor. In certain ~~embodiment~~examples, the non-native protein or peptide is melanocyte oligodendrocyte glycoprotein. In certain ~~embodiment~~examples, the disease or condition is multiple sclerosis.

[0024] In another example~~aspect~~, provided herein is a method for generating a T-cell response in a subject, comprising: administering the recombinant commensal bacterium disclosed herein to the subject, wherein the administration results in colonization of a native host niche by the bacterium

and generation of the T-cell response, wherein the T-cell response is to an antigen derived from the non-native protein or peptide. In another aspect, provided herein is use of the recombinant commensal bacterium as disclosed herein in the manufacture of a medicament for generating a T-cell response in a subject, wherein the administration of the medicament results in colonization of a native host niche by the bacterium and generation of the T-cell response, wherein the T-cell response is to an antigen derived from the non-native protein or peptide. In some ~~embodiment~~examples, the colonization of the native host niche is persistent or transient. In certain ~~embodiment~~examples, the native host niche is transiently colonized, and colonization is for 1 day to 60 days. In certain ~~embodiment~~examples, the native host niche is transiently colonized, and colonization is for 3.5 days to 60 days. In certain ~~embodiment~~examples, the native host niche is transiently colonized, and colonization is for 7 days to 28 days.

[0025] In some ~~embodiment~~examples, colonization is determined by polymerase chain reaction or colony forming assay performed on a sample obtained from the host after 1 day, 3.5 days, 7 days, 14 days, 28 days, or 60 days after administration to the host. In some ~~embodiment~~examples, the administration is via a route selected from the group consisting of topical, enteral, parenteral and inhalation. In certain ~~embodiment~~examples, the route is topical. In certain ~~embodiment~~examples, the route is enteral. In some ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides* spp., *Clostridium* spp., *Helicobacter* spp., *Parabacteroides* spp, *Prevotella* spp., and *Staphylococcus epidermidis*. In some ~~embodiment~~examples, the T-cell response is a T_{reg} or a $T_{effector}$ response. In certain ~~embodiment~~examples, the route is enteral and the T-cell response is a T_{reg} response. In some ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides* spp., *Clostridium* spp., *Helicobacter* spp., *Parabacteroides* spp, and *Prevotella* spp. In certain ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides thetaiotaomicron*, *Bacteroides vulgatus*, and *Bacteroides finegoldii*.

[0026] In some ~~embodiment~~examples, the native bacterial protein is selected from the group consisting of sialidase, endonuclease, secreted endoglycosidase, anti-sigma factor, thiol peroxidase, hypothetical protein BT_2621, hypothetical protein BT_3223, peptidase, Icc family phosphohydrolase, exo-poly-alpha-D-galacturonosidase, and hypothetical protein BT_4428. In certain ~~embodiment~~examples, the native bacterial protein is sialidase or anti-sigma factor. In certain ~~embodiment~~examples, the non-native protein or peptide is myelin oligodendrocyte glycoprotein. In certain ~~embodiment~~examples, the disease or condition is multiple sclerosis. In certain ~~embodiment~~examples, the route is topical and the T-cell response is a $T_{effector}$ response. In certain ~~embodiment~~examples, the bacterium is *S. epidermidis*.

[0027] In another example~~aspect~~, provided herein is a method of treating a disease or condition in a subject, comprising: administering the recombinant commensal bacterium disclosed herein to the subject, wherein the administration results in colonization of a native host niche by the bacterium and generation of a T-cell response, wherein the T-cell response is to an antigen derived from the non-native protein or peptide, and wherein the T-cell response treats the disease or condition in the subject. In one aspect, provided herein is use of the recombinant commensal bacterium as disclosed herein in the manufacture of a medicament for treating a disease or condition in a subject, wherein the administration of the medicament results in colonization of a native host niche by the bacterium and generation of a T-cell response, wherein the T-cell response is to an antigen derived from the non-native protein or peptide, and wherein the T-cell response treats the disease or condition in the subject.

[0028] In some ~~embodiment~~examples, the colonization of the native host niche is persistent or transient. In certain ~~embodiment~~examples, the native host niche is transiently colonized, and colonization is for 1 day to 60 days. In certain ~~embodiment~~examples, the native host niche is transiently colonized, and colonization is for 3.5 days to 60 days. In certain ~~embodiment~~examples, the native host niche is transiently colonized, and colonization is for 7 days to 28 days. In certain ~~embodiment~~examples, colonization is determined by polymerase chain reaction or colony forming assay performed on a sample obtained from the host after 1 day, 3.5 days, 7 days, 14 days, 28 days, or 60 days after administration to the host.

[0029] In some ~~embodiment~~examples, the disease or condition is selected from the group consisting of an autoimmune disorder and a proliferative disorder. In some ~~embodiment~~examples, the autoimmune disorder is selected from the group consisting of multiple sclerosis, diabetes mellitus Type I, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, celiac disease, Graves' disease, Hashimoto's autoimmune thyroiditis, vitiligo, rheumatic fever, pernicious anemia/atrophic gastritis, alopecia areata, immune thrombocytopenic purpura, temporal arteritis, ulcerative colitis, Crohn's disease, scleroderma, antiphospholipid syndrome, autoimmune hepatitis type 1, primary biliary cirrhosis, Sjogren's syndrome, Addison's disease, dermatitis herpetiformis, Kawasaki disease, sympathetic ophthalmia, HLA-B27 associated acute anterior uveitis, primary sclerosing cholangitis, discoid lupus erythematosus, polyarteritis nodosa, CREST Syndrome, myasthenia gravis, polymyositis/dermatomyositis, Still's disease, autoimmune hepatitis type 2, Wegener's granulomatosis, mixed Connective tissue disease, microscopic polyangiitis, autoimmune polyglandular syndrome, Felty's syndrome, autoimmune hemolytic anemia, chronic inflammatory demyelinating polyneuropathy, Guillain-Barre Syndrome, Behcet disease, autoimmune neutropenia, bullous pemphigoid, essential mixed cryoglobulinemia, linear morphea, autoimmune polyglandular syndrome 1 (APECED), acquired hemophilia A, Batten disease/neuronal ceroid lipofuscinoses, autoimmune pancreatitis, Hashimoto's encephalopathy, Goodpasture's disease, pemphigus vulgaris, autoimmune disseminated encephalomyelitis, relapsing polychondritis, Takayasu arteritis, Churg-Strauss syndrome, epidermolysis bullosa acquisita, cicatricial pemphigoid, pemphigus foliaceus, autoimmune hypoparathyroidism, autoimmune hypophysitis, autoimmune inner ear disease, autoimmune lymphoproliferative syndrome, autoimmune oophoritis, autoimmune orchitis, autoimmune polyglandular syndrome, Cogan's syndrome, encephalitis lethartica, erythema elevatum diutinum, Evans syndrome, immunodysregulation polyendocrinopathy enteropathy X-linked (IPEX), Issac's syndrome/acquired neuromyotonia, Miller Fisher syndrome, Morvan's syndrome, PANDAS, POEMS syndrome, Rasmussen's encephalitis, stiff-person syndrome,

Vogt-Koyanagi-Harada syndrome, neuromyelitis optica, graft vs host disease, and autoimmune uveitis. In certain ~~embodiment~~examples, the autoimmune disorder is selected from the group consisting of multiple sclerosis, and diabetes mellitus Type I. In some ~~embodiment~~examples, the proliferative disorder is cancer. In certain ~~embodiment~~examples, the cancer is selected from melanoma, basal cell carcinoma, squamous cell carcinoma, and testicular cancer. In certain ~~embodiment~~examples, the cancer is melanoma.

[0030] In some ~~embodiment~~examples, the administration is via a route selected from the group consisting of topical, enteral, parenteral and inhalation. In certain ~~embodiment~~examples, the route is topical. In certain ~~embodiment~~examples, the bacterium is *S. epidermidis.* In some ~~embodiment~~examples, the disease is cancer. In some ~~embodiment~~examples, the cancer is melanoma. In some ~~embodiment~~examples, the non-native protein or peptide is selected from the group consisting of a melanocyte-specific antigen and a testis cancer antigen. In some ~~embodiment~~examples, the melanocyte-specific antigen is selected from the group consisting of PMEL, TRP2 and MART-1. In some ~~embodiment~~examples, the testis cancer antigen is selected from the group consisting of NY-ESO and MAGE-A.

[0031] In some ~~embodiment~~examples, the route is enteral. In some ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides* spp., *Clostridium* spp., *Helicobacter* spp., *Parabacteroides* spp, and *Prevotella* spp. In certain ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides thetaiotaomicron*, *Bacteroides vulgatus*, and *Bacteroides finegoldii.* In some ~~embodiment~~examples, the native bacterial protein is selected from the group consisting of sialidase, endonuclease, secreted endoglycosidase, anti-sigma factor, thiol peroxidase, hypothetical protein BT_2621, hypothetical protein BT_3223, peptidase, Icc family phosphohydrolase, exo-poly-alpha-D-galacturonosidase, and hypothetical protein BT_4428. In certain ~~embodiment~~examples, the native bacterial protein is sialidase or anti-sigma factor.

[0032] In some ~~embodiment~~examples, the autoimmune disorder is selected from the group consisting of multiple sclerosis, diabetes mellitus Type I, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, celiac disease, Graves' disease, Hashimoto's autoimmune thyroiditis, vitiligo, rheumatic fever, pernicious anemia/atrophic gastritis, alopecia areata, immune thrombocytopenic purpura, temporal arteritis, ulcerative colitis, Crohn's disease, scleroderma, antiphospholipid syndrome, autoimmune hepatitis type 1, primary biliary cirrhosis, Sjogren's syndrome, Addison's disease, dermatitis herpetiformis, Kawasaki disease, sympathetic ophthalmia, HLA-B27 associated acute anterior uveitis, primary sclerosing cholangitis, discoid lupus erythematosus, polyarteritis nodosa, CREST Syndrome, myasthenia gravis, polymyositis/dermatomyositis, Still's disease, autoimmune hepatitis type 2, Wegener's granulomatosis, mixed Connective tissue disease, microscopic polyangiitis, autoimmune

polyglandular syndrome, Felty's syndrome, autoimmune hemolytic anemia, chronic inflammatory demyelinating polyneuropathy, Guillain-Barre Syndrome, Behcet disease, autoimmune neutropenia, bullous pemphigoid, essential mixed cryoglobulinemia, linear morphea, autoimmune polyglandular syndrome 1 (APECED), acquired hemophilia A, Batten disease/neuronal ceroid lipofuscinoses, autoimmune pancreatitis, Hashimoto's encephalopathy, Goodpasture's disease, pemphigus vulgaris, autoimmune disseminated encephalomyelitis, relapsing polychondritis, Takayasu arteritis, Churg-Strauss syndrome, epidermolysis bullosa acquisita, cicatricial pemphigoid, pemphigus foliaceus, autoimmune hypoparathyroidism, autoimmune hypophysitis, autoimmune inner ear disease, autoimmune lymphoproliferative syndrome, autoimmune oophoritis, autoimmune orchitis, autoimmune polyglandular syndrome, Cogan's syndrome, encephalitis lethartica, erythema elevatum diutinum, Evans syndrome, immunodysregulation polyendocrinopathy enteropathy X-linked (IPEX), Issac's syndrome/acquired neuromyotonia, Miller Fisher syndrome, Morvan's syndrome, PANDAS, POEMS syndrome, Rasmussen's encephalitis, stiff-person syndrome, Vogt-Koyanagi-Harada syndrome, neuromyelitis optica, graft vs host disease, and autoimmune uveitis. In certain ~~embodiment~~examples, the autoimmune disorder is multiple sclerosis. In some ~~embodiment~~examples, the bacterium is selected from the group consisting of *Bacteroides thetaiotaomicron, Bacteroides vulgatus*, and *Bacteroides finegoldii*. In certain ~~embodiment~~examples, the non-native protein is myelin oligodendrocyte glycoprotein.

[0033] In some ~~embodiment~~examples, the bacterium is administered in combination with a high-complexity defined microbial community.

[0034] In some ~~embodiment~~examples, the host is a mammal. In certain ~~embodiment~~examples, the mammal is a human.

BRIEF DESCRIPTION OF THE DRAWINGS

[0035] FIG. 1 illustrates an exemplary method for generating a regulatory T cell response to an exogenous antigen expressed by a recombinant bacterial strain of the disclosure.

[0036] FIG. 2 shows Western blot data demonstrating expression of OVA antigen peptide by *Bacteroides thetaiotaomicron* engineered to express ovalbumin (OVA) peptide.

[0037] FIG. 3 shows flow cytometry analysis of OVA-specific T cells from the spleen of OTII transgenic mice co-cultured for 4 hours with B16-FLT3L stimulated DCs and OVA+ *B. thetaiotaomicron* or WT *B. thetaiotaomicron* (negative control).