CLAIMS

1. A genetically engineered bacterium comprising:

(a) an FNR-responsive promoter, an ANR-responsive promoter or a DNR-responsive promoter that is operably linked to one or more of:

(i) a first gene encoding a non-native anti-inflammation molecule;

(ii) a first gene encoding a non-native gut barrier function enhancer molecule; and

(iii) a gene cassette encoding a biosynthetic pathway, in which the final product of the biosynthetic pathway is selected from the group consisting of an anti-inflammation molecule and a gut barrier function enhancer molecule.

2. A bacterium according to Claim 1, in which the first promoter is an FNR-responsive promoter.

3. A bacterium according to Claim 1 or 2, in which the first gene and/or gene cassette is located on a chromosome in the bacterium.

4. A bacterium according to Claim 1, 2 or 3, in which the first gene and/or gene cassette is located on a plasmid in the bacterium.

5. A bacterium according to any preceding claim, in which the anti-inflammation and/or gut barrier enhancer molecule is selected from a short-chain fatty acid, propionate, butyrate, acetate, IL-10, IL-27, TGF-ß2, TGF-ß1, GLP-2, NAPEs, elafin, and trefoil factor.

6. A bacterium according to any of Claims 1 to 4, in which the anti-inflammation and/or gut barrier enhancer molecule is selected from a scFv, antisense RNA, siRNA, and shRNA directed against a pro-inflammatory molecule selected from TNF-α, IFN-γ, IL-1β, IL-6, IL-8, IL-17, CXCL-8, and CCL2.

7. A bacterium according to any preceding claim, in which the bacterium is a probiotic bacterium.

8. A bacterium according to Claim 7, in which the bacterium is selected from the group consisting of *Bacteroides, Bifidobacterium, Clostridium, Escherichia, Lactobacillus*, and *Lactococcus*.

9. A bacterium according to Claim 8, in which the bacterium is *Escherichia coli* strain Nissle.

10. A bacterium according to any preceding claim, in which the bacterium is an auxotroph in a gene that is complemented when the bacterium is present in a mammalian gut.

11. A bacterium according to Claim 10, in which the mammalian gut is a human gut.

12. A bacterium according to Claim 10 or 11, in which the bacterium is an auxotroph in diaminopimelic acid or an enzyme in the thymine biosynthetic pathway.

13. A bacterium according to any preceding claim, in which the bacterium is further engineered to harbour a second gene coding for a substance toxic to the bacterium, in which the second gene is under the control of a second promoter that is directly or indirectly induced by an environmental factor not naturally present in a mammalian gut.

14. A bacterium according to any preceding claim, in which the bacterium is further engineered to harbour a third gene coding for a substance toxic to the bacterium, in which the third gene is under the control of the first promoter, and in which the expression of the toxic substance is delayed in time as compared to the expression of the anti-inflammation molecule, the gut barrier enhancer molecule, or the gene cassette encoding the biosynthetic pathway.

15. A pharmaceutically acceptable composition comprising a bacterium according to any preceding claim and a pharmaceutically acceptable carrier.

16. A composition according to Claim 15 formulated for oral or rectal administration.

17. Use of a composition according to Claim 15 or 16 in the manufacture of a medicament for treating or preventing an autoimmune disorder.

18. Use of a composition according to Claim 15 or 16 in the manufacture of a medicament for treating an inflammatory bowel disease or a diarrhoeal disease.

19. Use according to Claim 18, in which the autoimmune disorder is selected from the group consisting of acute disseminated encephalomyelitis (ADEM), acute necrotizing hemorrhagic leukoencephalitis, Addison’s disease, agammaglobulinemia, alopecia areata, amyloidosis, ankylosing spondylitis, anti-GBM/anti-TBM nephritis, antiphospholipid syndrome (APS), autoimmune angioedema, autoimmune aplastic anemia, autoimmune

dysautonomia, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune hyperlipidemia, autoimmune immunodeficiency, autoimmune inner ear disease (AIED), autoimmune myocarditis, autoimmune oophoritis, autoimmune pancreatitis, autoimmune retinopathy, autoimmune thrombocytopenic purpura (ATP), autoimmune thyroid disease, autoimmune urticarial, Axonal & neuronal neuropathies, Balo disease, Behcet's disease, Bullous pemphigoid, Cardiomyopathy, Castleman disease, Celiac disease, Chagas disease, Chronic inflammatory demyelinating polyneuropathy (CIDP), Chronic recurrent multifocal ostomyelitis (CRMO), Churg-Strauss syndrome, Cicatricial pemphigoid/benign mucosal pemphigoid, Crohn's disease, Cogan syndrome, Cold agglutinin disease, Congenital heart block, Coxsackie myocarditis, CREST disease, Essential mixed cryoglobulinemia, Demyelinating neuropathies, Dermatitis herpetiformis, Dermatomyositis, Devic's disease (neuromyelitis optica), Discoid lupus, Dressler's syndrome, Endometriosis, Eosinophilic esophagitis, Eosinophilic fasciitis, Erythema nodosum, Experimental allergic encephalomyelitis, Evans syndrome, Fibrosing alveolitis, Giant cell arteritis (temporal arteritis), Giant cell myocarditis, Glomerulonephritis, Goodpasture's syndrome, Granulomatosis with Polyangiitis (GPA), Graves' disease, Guillain-Barre syndrome, Hashimoto's encephalitis, Hashimoto's thyroiditis, Hemolytic anemia, Henoch-Schonlein purpura, Herpes gestationis, Hypogammaglobulinemia, Idiopathic thrombocytopenic purpura (ITP), IgA nephropathy, IgG4-related sclerosing disease, Immunoregulatory lipoproteins, Inclusion body myositis, Interstitial cystitis, Juvenile arthritis, Juvenile idiopathic arthritis, Juvenile myositis, Kawasaki syndrome, Lambert-Eaton syndrome, Leukocytoclastic vasculitis, Lichen planus, Lichen sclerosus, Ligneous conjunctivitis, Linear IgA disease (LAD), Lupus (Systemic Lupus Erythematosus), chronic Lyme disease, Meniere's disease, Microscopic polyangiitis, Mixed connective tissue disease (MCTD), Mooren's ulcer, Mucha-Habermann disease, Multiple sclerosis, Myasthenia gravis, Myositis, Narcolepsy, Neuromyelitis optica (Devic's), Neutropenia, Ocular cicatricial pemphigoid, Optic neuritis, Palindromic rheumatism, PANDAS (Pediatric autoimmune Neuropsychiatric Disorders Associated with Streptococcus), Paraneoplastic cerebellar degeneration, Paroxysmal nocturnal hemoglobinuria (PNH), Parry Romberg syndrome, Parsonnage-Turner syndrome, Pars planitis (peripheral uveitis), Pemphigus, Peripheral neuropathy, Perivenous encephalomyelitis, Pernicious anemia, POEMS syndrome, Polyarteritis nodosa, Type I, II, & III autoimmune polyglandular syndromes, Polymyalgia rheumatic, Polymyositis, Postmyocardial infarction syndrome, Postpericardiotomy syndrome, Progesterone dermatitis, Primary biliary cirrhosis,

Primary sclerosing cholangitis, Psoriasis, Psoriatic arthritis, Idiopathic pulmonary fibrosis, Pyoderma gangrenosum, Pure red cell aplasia, Raynauds phenomenon, reactive arthritis, reflex sympathetic dystrophy, Reiter's syndrome, relapsing polychondritis, restless legs syndrome, retroperitoneal fibrosis, rheumatic fever, rheumatoid arthritis, sarcoidosis, Schmidt syndrome, scleritis, scleroderma, Sjogren's syndrome, sperm & testicular autoimmunity, stiff person syndrome, subacute bacterial endocarditis (SBE), Susac's syndrome, sympathetic ophthalmia, Takayasu's arteritis, temporal arteritis/giant cell arteritis, thrombocytopenic purpura (TTP), Tolosa-Hunt syndrome, transverse myelitis, type 1 diabetes, asthma, ulcerative colitis, undifferentiated connective tissue disease (UCTD), uveitis, vasculitis, vesiculobullous dermatosis, vitiligo, and Wegener's granulomatosis.

20. Use according to Claim 19, in which the autoimmune disorder is selected from the group consisting of type 1 diabetes, lupus, rheumatoid arthritis, ulcerative colitis, juvenile arthritis, psoriasis, psoriatic arthritis, celiac disease, and ankylosing spondylitis.

21. Use according to Claim 18, in which the disease or condition is selected from Crohn's disease, ulcerative colitis, collagenous colitis, lymphocytic colitis, diversion colitis, Behcet's disease, indeterminate colitis, acute watery diarrhoea, cholera, acute bloody diarrhoea, dysentery, persistent diarrhoea, short bowel syndrome, ulcerative proctitis, proctosigmoiditis, left-sided colitis, pancolitis, and fulminant colitis.

22. Use according to Claim 18, in which the inflammatory bowel disease is selected from Crohn's disease and ulcerative colitis.