CLAIMS

1. A recombinant lactic acid bacterium (LAB) comprising a first exogenous nucleic acid encoding a fusion protein comprising (a) an N-terminal trefoil factor (TFF) polypeptide and (b) a C-terminal cell adherence polypeptide that comprises a cell-wall anchoring domain.

2. The recombinant LAB of claim 1, wherein said cell adherence polypeptide is selected from the group consisting of: a cell and mucus-binding protein A (CmbA), a mucus binding protein (Mub), a mucus adhesion promoting protein (MapA), and a lactococcal mucin binding protein (MbpL).

3. The recombinant LAB of claim 1 or 2, wherein said cell adherence polypeptide is a CmbA.

4. The recombinant LAB of any one of claims 1 to 3, wherein said CmbA is a *Lactobacillus reuteri* CmbA.

5. The recombinant LAB of claim 2 or 3, wherein said CmbA comprises an amino acid sequence at least 80% identical to SEQ ID NO: 1.

6. The recombinant LAB of any one of claims 1 to 5, wherein said TFF polypeptide is selected from the group consisting of: a TFF1, a TFF2, and a TFF3.

7. The recombinant LAB of any one of claims 1 to 6, wherein said TFF polypeptide comprises an amino acid sequence at least 80% identical to SEQ ID NO: 3.

8. The recombinant LAB of any one of claims 1 to 7, wherein said fusion protein comprises a CmbA and a human TFF3 polypeptide.

9. The recombinant LAB of any one of claims 1 to 8, wherein said fusion protein further comprises a secretion signal peptide.

10. The recombinant LAB of claim 9, wherein said secretion signal peptide is a secretion leader of an unidentified secreted 45-kDa protein (SSusp45).

11. The recombinant LAB of any one of claims 1 to 10, wherein said first exogenous nucleic acid is placed under the control of a promoter selected from the group consisting of: a *thyA* promoter (P*thyA*), an *hllA* promoter (P*hllA*), and a *gapB* promoter (P*gapB*).

12. The recombinant LAB of any one of claims 1 to 11, further comprising a second exogenous nucleic acid encoding at least one therapeutic polypeptide selected from the group consisting of:
    a) a cytokine;
    b) an interleukin (IL);
    c) an antibody or a functional fragment thereof;
    d) an antigen;
    e) a hormone;
    f) a TFF; and
    g) an enzyme or a functional fragment thereof.

13. The recombinant LAB of claim 12, wherein:
    a) said interleukin (IL) is selected from the group consisting of an IL-2, an IL-10, and an IL-18;
    b) said antibody is selected from the group consisting of an anti-TNFα antibody, an antibody to IL-4, an antibody to IL-5, an antibody to IL-13, an antibody to IL-15, and an antibody to immunoglobulin E (IgE);
    c) said antigen is selected from the group consisting of a proinsulin (PINS), a glutamic acid decarboxylase (GAD65), an insulinoma-associated protein 2 (IA-2), an islet-specific glucose-6-phosphatase catalytic subunit-related protein (IGRP), a zinc transporter 8 (ZnT8), a chromogranin A, a (prepro) islet amyloid polypeptide (ppIAPP), a peripherin, a citrullinated glucose-regulated protein (GRP), a tree pollen

allergen, a weed pollen allergen, a grass pollen allergen, a food allergen, a dust-mite allergen, a mold allergen, an animal dander allergen;

d) said hormone selected from the group consisting of a glucagon-like peptide 1 (GLP-1), a glucagon-like peptide 2 (GLP-2), a glucagon, an exendin-4, an epidermal growth factor, and a growth hormone;

e) said TFF is selected from the group consisting of a TFF 1, a TFF2, and a TFF3; and

f) said enzyme is selected from the group consisting of a phenylalanine ammonia lyase (PAL) and an amino acid decarboxylase.

14. The recombinant LAB of claim 13, wherein said at least one therapeutic polypeptide is a PAL.

15. The recombinant LAB of any one of claims 12 to 14, wherein said second exogenous nucleic acid is placed under the control of a *gapB* promoter (P*gapB*).

16. The recombinant LAB of any one of claims 1 to 15, wherein said recombinant LAB is selected from the group consisting of a *Lactobacillus* species (sp.) bacterium, a *Bifidobacterium* sp. bacterium, a *Streptococcus* sp. bacterium, an *Enterococcus* sp. bacterium, and a *Lactococcus* sp. bacterium.

17. The recombinant LAB of any one of claims 1 to 16, wherein said LAB is a *Lactococcus lactis*.

18. The recombinant LAB of any one of claims 1 to 17, wherein said recombinant LAB has at least one feature that is different from a corresponding LAB lacking said first exogenous nucleic acid, wherein said at least one feature is selected from the group of features consisting of:

a) an increased gastro-intestinal (GI) transit time of at least 10%;

b) an increased adherence to intestinal mucosa of at least 10%;

c) an increased *in vitro* mucin-binding capability of at least 20%; and

d) an increased *in vitro* Caco-2 cell-binding capability of at least 10%.

19. The recombinant LAB of claim 18, wherein said recombinant LAB has an increased *in vitro* mucin-binding capability of at least 20% when compared with said corresponding LAB lacking said first exogenous nucleic acid.

20. The recombinant LAB of claim 18 or 19, wherein said recombinant LAB has an increased *in vitro* Caco-2 cell-binding capability of at least 10% when compared with said corresponding LAB lacking said first exogenous nucleic acid.

21. The recombinant LAB of any one of claims 1 to 20, further comprising at least one mutation or insertion that increases trehalose accumulation, wherein said at least one mutation or insertion is selected from the group consisting of:

a) an insertion of a first polycistronic expression cassette comprising, in 5' to 3' order, a *usp45* promoter, a *usp45* gene, an intergenic region that is immediately 5' to a *rpmD* gene, and a nucleic acid encoding an *OtsB* from *Escherichia coli*;
b) an insertion of a second polycistronic expression cassette comprising, in 5' to 3' order, an *hllA* promoter (P*hllA*) and a nucleic acid comprising trehalose transporter genes *llmg_0453* and *llmg_0454*;
c) an inactivated endogenous trehalose 6-phosphate phosphorylase gene (*trePP*), wherein said *trePP* gene is inactivated by gene deletion, so that said recombinant LAB lacks TrePP activity; and
d) an inactivated endogenous cellobiose-specific PTS system IIC component (*ptcC*) gene, wherein said *ptcC* gene is inactivated by insertion of a premature stop codon, so that said recombinant LAB lacks PtcC activity.

22. A pharmaceutical composition comprising said recombinant LAB of any one of claims 1-21, and a pharmaceutically acceptable carrier.

23. The recombinant LAB of any one of claims 1-21, or said pharmaceutical composition of claim 22, for use in the treatment of a disease selected from the group consisting of: an autoimmune disease, an allergy, a metabolic disease, and a gastro-intestinal disease, or

selected from the group consisting of: type-1 diabetes (T1D), celiac disease, inflammatory bowel disease, and phenylketonuria (PKU).

24. Use of said recombinant LAB of any one of claims 1-21, or said pharmaceutical composition of claim 22, in the manufacture of a medicament for the treatment of a disease selected from the group consisting of: an autoimmune disease, an allergy, a metabolic disease, a gastro-intestinal disease, and a nutritional defect, or selected from the group consisting of: type-1 diabetes (T1D), celiac disease, inflammatory bowel disease, and phenylketonuria (PKU).

25. A nucleic acid encoding a fusion protein-comprising a cell-adherence polypeptide and a mucin-binding polypeptide, wherein said cell-adherence polypeptide is selected from the group consisting of: a cell and mucus-binding protein A (CmbA), a mucus binding protein (Mub), a mucus adhesion promoting protein (MapA), and a lactococcal mucin binding protein (MbpL); and wherein said mucin-binding polypeptide is selected from the group consisting of: a trefoil factor (TFF) polypeptide and a MucBP polypeptide.