resistance or insulin resistance-related complications, such as dyslipidemia and type 2 diabetes mellitus as well as insulin-resistance in endocrine diseases (e.g., obese subjects with type 1 diabetes mellitus, Cushing's disease or lipodystrophy syndromes), cardiovascular disease, ovarian aging, polycystic ovary syndrome, neurodegenerative disorders, such as Alzheimer's disease, multiple sclerosis and dementia, encephalopathy, or others. There is also a need for beneficial GI bacteria that are capable of metabolizing or degrading fructose-lysine to prevent or reduce formation of AGEs.

SUMMARY OF THE INVENTION

In one aspect, the present invention provides a human intestinal isolate bacterium comprising a lysine pathway gene set that allows said bacterium to convert L-lysine into butyric acid and/or butyrate or a salt or ester thereof, and further comprising a fructose-lysine uptake and degradation operon that allows said bacterium to convert fructose-lysine into butyric acid and/or butyrate or a salt or ester thereof, or a strain comprising said lysine pathway gene set and said fructose-lysine uptake and degradation operon and which strain has been derived from said bacterium by mutagenesis, preferably through radiation, UV light, or chemical treatment, wherein

- the lysine pathway gene set comprises genes encoding of the proteins: Lysine 2,3-aminomutase; L-beta-lysine 5,6-aminomutase alpha subunit; L-beta-lysine 5,6-aminomutase beta subunit; 3,5-diaminobexanoate dehydrogenase; 3-keto-5-aminohexanoate cleavage enzyme; 3-aminobutyryl-CoA ammonia-lyase; butyrate-acetoacetate CoA-transferase subunit A; butyrate-acetoacetate CoA-transferase subunit B; acetyl-CoA:acetoacetyl-CoA transferase, and wherein

- the fructose-lysine uptake and degradation operon comprises of the genes encoding the proteins: fructose-lysine kinase; fructosamine deglycase; ABC transporter periplasmic spermidine putrescine-binding protein PotD; spermidine putrescine ABC transporter permease component PotC; spermidine putrescine ABC transporter permease component PotB; and putrescine transport ATP-binding protein PotA.

In another aspect, the present invention provides a human intestinal isolate bacterium deposited as CBS 139326 or a strain comprising said lysine pathway gene set and said fructose-lysine uptake and degradation operon and which strain has been derived from said bacterium by mutagenesis, preferably through radiation, UV light, or chemical treatment.

In yet another aspect, the present invention provides composition comprising a human intestinal isolate bacterium disclosed herein and a physiologically acceptable carrier.

In yet another aspect, the present invention provides a human intestinal isolate bacterium disclosed herein or a composition disclosed herein for use as a medicament.

In yet another aspect, the present invention provides a human intestinal isolate bacterium disclosed herein or a composition disclosed herein for use as a probiotic and/or symbiotic.

In yet another aspect, the present invention provides a human intestinal isolate bacterium disclosed herein or a composition disclosed herein for use in preventing and/or treating conditions or diseases such as cancer (e.g. colorectal cancer), IBD (e.g. Crohn's disease, ulcerative colitis), IBS, obesity, bacterial and viral diarrhoea, constipation, bloating, allergies, urinary tract infections, metabolic diseases, such as metabolic syndrome and insulin resistance or insulin resistance-related complications, such as dyslipidemia and type 2 diabetes mellitus as well as insulin-resistance in endocrine diseases (e.g., obese subjects with type 1 diabetes mellitus, Cushing's disease or lipodystrophy syndromes), cardiovascular disease, ovarian aging, polycystic ovary syndrome, neurodegenerative disorders, such as Alzheimer's disease, multiple sclerosis and dementia, or encephalopathy.

Disclosed is an isolated intestinal bacterial strain, i.e., a human intestinal isolate, comprising a lysine pathway gene set, said bacterium being capable of converting L-lysine into butyric acid and/or butyrate or a derivative thereof, or a strain which has been derived therefrom.

In an example, the lysine pathway gene set comprises one or more of the genes encoding the proteins: Lysine 2,3-aminomutase; L-beta-lysine 5,6-aminomutase alpha subunit; L-beta-lysine 5,6-aminomutase beta subunit; 3,5-diaminobexanoate dehydrogenase; 3-keto-5-aminohexanoate cleavage enzyme; 3-aminobutyryl-CoA ammonia-lyase; butyrate-acetoacetate CoA-transferase subunit A; butyrate-acetoacetate CoA-transferase subunit B; acetyl-CoA:acetoacetyl-CoA transferase.

In an example, the expression of at least one of the genes encoding the proteins: Lysine 2,3-aminomutase; L-beta-lysine 5,6-aminomutase alpha subunit; L-beta-lysine 5,6-aminomutase beta subunit; 3,5-diaminobexanoate dehydrogenase; 3-keto-5-aminohexanoate cleavage enzyme; 3-aminobutyryl-CoA ammonia-lyase; butyrate-acetoacetate CoA-transferase subunit A; butyrate-acetoacetate CoA-transferase subunit B; acetyl-CoA:acetoacetyl-CoA transferase, is upregulated when the bacterium is grown on L-lysine as the sole carbon source as compared to when the bacterium is grown on equimolar amounts of glucose and acetate as sole carbon source.

In an example, at least one of the proteins: Lysine 2,3-aminomutase; L-beta-lysine 5,6-aminomutase alpha subunit; L-beta-lysine 5,6-aminomutase beta subunit; 3,5-diaminobexanoate dehydrogenase; 3-keto-5-aminohexanoate cleavage enzyme; 3-aminobutyryl-CoA ammonia-lyase; butyrate-acetoacetate CoA-transferase subunit A; butyrate-acetoacetate CoA-transferase subunit B; acetyl-CoA:acetoacetyl-CoA transferase, is overexpressed when the bacterium is grown on L-lysine as the sole carbon source as

CLAIMS

1. A human intestinal isolate bacterium comprising a lysine pathway gene set that allows said bacterium to convert L-lysine into butyric acid and/or butyrate or a salt or ester thereof, and further comprising a fructose-lysine uptake and degradation operon that allows said bacterium to convert fructose-lysine into butyric acid and/or butyrate or a salt or ester thereof, or a strain comprising said lysine pathway gene set and said fructose-lysine uptake and degradation operon and which strain has been derived from said bacterium by mutagenesis, preferably through radiation, UV light, or chemical treatment, wherein

- the lysine pathway gene set comprises genes encoding the proteins: Lysine 2,3-aminomutase; L-beta-lysine 5,6-aminomutase alpha subunit; L-beta-lysine 5,6-aminomutase beta subunit; 3,5-diaminobexanoate dehydrogenase; 3-keto-5-aminohexanoate cleavage enzyme; 3-aminobutyryl-CoA ammonia-lyase; butyrate-acetoacetate CoA-transferase subunit A; butyrate-acetoacetate CoA-transferase subunit B; acetyl-CoA:acetoacetyl-CoA transferase, and wherein

- the fructose-lysine uptake and degradation operon comprises the genes encoding the proteins: fructose-lysine kinase; fructosamine deglycase; ABC transporter periplasmic spermidine putrescine-binding protein PotD; spermidine putrescine ABC transporter permease component PotC; spermidine putrescine ABC transporter permease component PotB; and putrescine transport ATP-binding protein PotA.

2. The human intestinal isolate bacterium according to claim 1, wherein the fructose-lysine uptake and degradation operon further comprises the gene encoding the protein fructose-lysine 3-epimerase.

3. The human intestinal isolate bacterium according to any one of the previous claims, wherein the expression of at least one of the genes encoding the proteins: Lysine 2,3-aminomutase; L-beta-lysine 5,6-aminomutase alpha subunit; L-beta-lysine 5,6-aminomutase beta subunit; 3,5-diaminobexanoate dehydrogenase; 3-keto-5-aminohexanoate cleavage enzyme; 3-aminobutyryl-CoA ammonia-lyase; butyrate-acetoacetate CoA-transferase subunit A; butyrate-acetoacetate CoA-transferase subunit B; acetyl-CoA:acetoacetyl-CoA transferase, is upregulated and/or at least one of the proteins: Lysine 2,3-aminomutase; L-beta-lysine 5,6-aminomutase alpha subunit; L-beta-lysine 5,6-aminomutase beta subunit; 3,5-diaminobexanoate dehydrogenase; 3-keto-5-aminohexanoate cleavage enzyme; 3-aminobutyryl-CoA ammonia-lyase; butyrate-acetoacetate CoA-transferase subunit A; butyrate-acetoacetate CoA-transferase subunit B; acetyl-CoA:acetoacetyl-CoA transferase, is overexpressed when the bacterium is grown on L-lysine as the sole carbon source as

compared to when the bacterium is grown on equimolar amounts of glucose and acetate as sole carbon source.

4. The human intestinal isolate bacterium according to any one of the previous claims, wherein the expression of at least one of the genes encoding the proteins: fructose-lysine kinase; fructoselysine 3-epimerase; fructosamine deglycase; ABC transporter periplasmic spermidine putrescine-binding protein PotD; spermidine putrescine ABC transporter permease component PotC; spermidine putrescine ABC transporter permease component PotB; putrescine transport ATP-binding protein PotA, is upregulated and/or at least one of the proteins: fructose-lysine kinase; fructoselysine 3-epimerase; fructosamine deglycase; ABC transporter periplasmic spermidine putrescine-binding protein PotD; spermidine putrescine ABC transporter permease component PotC; spermidine putrescine ABC transporter permease component PotB; putrescine transport ATP-binding protein PotA, is overexpressed when the bacterium is grown on L-lysine as the sole carbon source as compared to when the bacterium is grown on equimolar amounts of glucose and acetate as sole carbon source.

5. The human intestinal isolate bacterium according to any of the preceding claims, which is sensitive to erythromycin, having a minimum inhibitory concentration of erythromycin of less than 20 µg/ml.

6. A human intestinal isolate bacterium deposited as CBS 139326 or a strain comprising said lysine pathway gene set and said fructose-lysine uptake and degradation operon and which strain has been derived from said bacterium by mutagenesis, preferably through radiation, UV light, or chemical treatment.

7. Composition comprising a human intestinal isolate bacterium according to any one of the preceding claims and a physiologically acceptable carrier.

8. Composition according to claim 7, which is a food composition, preferably a dairy product, more preferably a fermented dairy product, preferably a yogurt or a yogurt drink.

9. Composition according to claim 7 or 8, which is a pharmaceutical composition, preferably in solid dosage form, such as a capsule, a tablet, or a powder.

10. Composition according to claim 9, wherein the bacteria belonging to the bacterial strain are present in lyophilized or microencapsulated or other form preserving their activity.

11. A human intestinal isolate bacterium according to any of claims 1-6 or a composition according to any one of claims 7-10 for use as a medicament.

12. A human intestinal isolate bacterium according to any of claims 1-6 or a composition according to any one of claims 7-10 for use as a probiotic and/or symbiotic.

13. A human intestinal isolate bacterium according to any of claims 1-6 or a composition according to any one of claims 7-10 for use in preventing and/or treating conditions or diseases such as cancer (e.g. colorectal cancer), IBD (e.g. Crohn’s disease, ulcerative colitis), IBS, obesity, bacterial and viral diarrhoea, constipation, bloating, allergies, urinary tract infections, metabolic diseases, such as metabolic syndrome and insulin resistance or insulin resistance-related complications, such as dyslipidemia and type 2 diabetes mellitus as well as insulin-resistance in endocrine diseases (e.g., obese subjects with type 1 diabetes mellitus, Cushing's disease or lipodystrophy syndromes), cardiovascular disease, ovarian aging, polycystic ovary syndrome, neurodegenerative disorders, such as Alzheimer’s disease, multiple sclerosis and dementia, or encephalopathy.