CLAIMS

1. A genetically engineered bacterium comprising an arginine regulon,

in which the bacterium comprises a gene encoding a functional N-acetylglutamate synthetase with reduced arginine feedback inhibition as compared to a wild-type N-acetylglutamate synthetase from the same bacterial subtype under the same conditions, in which expression of the gene encoding arginine feedback resistant N-acetylglutamate synthetase is controlled by a promoter that is induced by exogenous environmental conditions found in a mammalian gut; and

in which the bacterium has been genetically engineered to lack a functional ArgR.

2. A bacterium according to Claim 1, in which the promoter that controls expression of the arginine feedback resistant N-acetylglutamate synthetase is induced under low-oxygen or anaerobic conditions.

3. A bacterium according to Claim 1 or 2, in which each copy of a functional *argR* gene normally present in a corresponding wild-type bacterium has been independently deleted or rendered inactive by one or more nucleotide deletions, insertions or substitutions.

4. A bacterium according to Claim 1, 2 or 3, in which each copy of a functional *argG* gene normally present in a corresponding wild-type bacterium has been independently deleted or rendered inactive by one or more nucleotide deletions, insertions or substitutions.

5. A bacterium according to any of Claims 2 to 4, in which the promoter that is induced under low-oxygen or anaerobic conditions is selected from an FNR, DNR and ANR promoter.

6. A bacterium according to Claim 5, in which the promoter is an FNR promoter.

7. A bacterium according to any preceding claim, in which the arginine feedback resistant N-acetylglutamate synthetase gene has a DNA sequence selected from:

(a) SEQ ID NO: 28,

(b) a DNA sequence that, but for the redundancy of the genetic code, encodes the same polypeptide as encoded by SEQ ID NO: 28, and

(c) a DNA sequence having at least 80% homology to the DNA sequence of (a) or (b).

8. A bacterium according to any preceding claim, in which the gene encoding the arginine feedback resistant N-acetylglutamate synthetase is present on a plasmid in the bacterium.

9. A bacterium according to Claim 8, in which the gene encoding the arginine feedback resistant N-acetylglutamate synthetase is operably linked on the plasmid to a promoter that is induced under low-oxygen or anaerobic conditions.

10. A bacterium according to any of Claims 1 to 7, in which the gene encoding the arginine feedback resistant N-acetylglutamate synthetase is present in the bacterial chromosome.

11. A bacterium according to Claim 10, in which the gene encoding the arginine feedback resistant N-acetylglutamate synthetase is operably linked in the chromosome to a promoter that is induced under low-oxygen or anaerobic conditions.

12. 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.

13. A bacterium according to Claim 12, in which the mammalian gut is a human gut.

14. A bacterium according to Claim 12 or 13, in which the bacterium is a thyA or dapB auxotroph.

15. A bacterium according to any preceding claim, in which the gene sequence encoding the arginine feedback resistant N-acetylglutamate synthetase is present in the bacterial chromosome and is operably linked in the chromosome to a promoter that is induced by low oxygen or anaerobic conditions; and in which the bacterium is a thyA auxotroph.

16. A bacterium according to Claim 15, in which the promoter that is induced by low oxygen or anaerobic conditions is an FNR promoter.

17. A bacterium according to any preceding claim, in which the bacterium is a non-pathogenic bacterium.

18. A bacterium according to Claim 17, in which the bacterium is a probiotic bacterium.

19. A bacterium according to Claim 18, in which the bacterium is selected from the group consisting of *Bacteroides*, *Bifidobacterium*, *Clostridium*, *Escherichia*, *Lactobacillus*, and *Lactococcus*.

20. A bacterium according to Claim 19, in which the bacterium is *Escherichia coli* strain Nissle.

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

22. A pharmaceutically acceptable composition according to Claim 21, in which the composition is formulated for oral or rectal administration.

23. A bacterium according to any of Claims 1 to 20 for use in medicine.

24. Use of a bacterium according to any of Claims 1 to 20 in the preparation of a medicament for the treatment of a hyperammonemia-associated disorder or symptom(s) thereof.

25. Use according to Claim 24, in which the hyperammonemia-associated disorder is a urea cycle disorder.

26. Use according to Claim 25, in which the urea cycle disorder is argininosuccinic aciduria, arginase deficiency, carbamylphosphate synthetase deficiency, citrullinemia, N-acetylglutamate synthetase deficiency, or ornithine transcarbamylase deficiency.

27. Use according to Claim 24, in which the hyperammonemia-associated disorder is a liver disorder; an organic acid disorder; isovaleric aciduria; 3-methylcrotonylglycinuria; methylmalonic acidemia; propionic aciduria; fatty acid oxidation defects; carnitine cycle defects; carnitine deficiency; β-oxidation deficiency; lysinuric protein intolerance; pyrroline-5-carboxylate synthetase deficiency; pyruvate carboxylase deficiency; ornithine aminotransferase deficiency; carbonic anhydrase deficiency; hyperinsulinism-hyperammonemia syndrome; mitochondrial disorders; valproate therapy; asparaginase therapy; total parenteral nutrition; cystoscopy with glycine-containing solutions; post-lung/bone marrow transplantation; portosystemic shunting; urinary tract infections; ureter dilation; multiple myeloma; chemotherapy; infection; neurogenic bladder; or intestinal bacterial overgrowth.

28. Use according to Claim 27, in which the liver disorder is hepatic encephalopathy, acute liver failure, or chronic liver failure.

29. Use according to Claim 28, in which the symptoms of the hyperammonemia-associated disorder are selected from the group consisting of seizures, ataxia, stroke-like lesions, coma, psychosis, vision loss, acute encephalopathy, cerebral edema, as well as vomiting, respiratory alkalosis, and hypothermia.