We claim:

1. A polynucleotide construct comprising, from 5’ to 3’:

(a) a 5’ UTR comprising the sequence of SEQ ID NO: 2;

(b) an mRNA sequence comprising an open reading frame (ORF) encoding a functional human ornithine transcarbamylase (OTC), wherein ORF comprises a codon optimized sequence at least about 95% identical to SEQ ID NO: 1; and

(c) a 3’ UTR comprising the sequence of SEQ ID NO: 3.

2. A polynucleotide construct comprising an mRNA sequence comprising an open reading frame (ORF) encoding a functional human ornithine transcarbamylase (OTC), wherein the mRNA sequence comprises a sequence having no more than five nucleic acids different from SEQ ID NO: 4.

3. The polynucleotide construct of claim 2 comprising, from 5’ to 3’:

(a) a 5’ UTR;

(b) the mRNA sequence comprising the ORF encoding the OTC; and

(c) a 3’ UTR.

4. The polynucleotide construct of claim 3, wherein the 5’ UTR comprises the sequence of SEQ ID NO: 2.

5. The polynucleotide construct of claim 3 or 4, wherein the 3’ UTR comprises the sequence of SEQ ID NO: 3.

6. The polynucleotide construct of any one of claims 1-5, wherein the functional OTC comprises the amino acid sequence of SEQ ID NO:7.

7. The polynucleotide construct of any one of claims 1-6, wherein the OFR sequence comprises SEQ ID NO: 1.

8. The polynucleotide construct of any one of claims 1-7, wherein the mRNA sequence has no more than four, three, two, or one nucleic acids different from SEQ ID NO: 4.

9. The polynucleotide construct of any one of claims 1-8 which comprises the sequence of SEQ ID NO: 4.

10. The polynucleotide construct of any one of claims 1-9 which further comprises a 5' terminal cap.

11. The polynucleotide construct of claim 10, wherein the 5' terminal cap is a Cap1.

12. The polynucleotide construct of any one of claims 1-11 which further comprises a polyA tail.

13. The polynucleotide construct of claim 12, wherein the polyA tail is between 80 and 1000 nucleic acids long.

14. The polynucleotide construct of claim 12, wherein polyA tail is between 100 and 500 nucleic acids long.

15. The polynucleotide construct of any one of claims 1-14, wherein the mRNA comprises at least one chemically modified uridine.

16. The polynucleotide construct of claim 15, wherein at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, or about 100% of the uridines are chemically modified.

17. The polynucleotide construct of claim 15 or 16, wherein the chemically modified uridine is selected from the group consisting of pseudouridine (ψ), N1-methyl pseudouridine (N1-me-ψ), and a combination thereof.

18. A composition comprising:
    (a) a polynucleotide construct of any one of claims 1-17; and
    (b) a delivery agent.

19. The composition of claim 18, wherein the delivery agent comprises a lipid nanoparticle (LNP), a liposome, a polymer, a micelle, a plasmid, a virus, or any combination thereof.

20. The composition of claim 19, wherein the LNP is selected from the group consisting of PEG2000-C-DMA:13-B43:Cholesterol:DSPC, PEG2000-S:13-B43:Cholesterol:DSPC, PEG2000-S:18-B6:Cholesterol:DSPC, and PEG750-C-DLA:18-B6:Cholesterol:DSPC.

21. The composition of claim 19 or 20, wherein the polynucleotide construct is encapsulated in the LNP.

22. The composition of claim 21, wherein the polynucleotide construct is fully encapsulated in the LNP.

23. The composition of claim 22, wherein at least 95% of the polynucleotide construct is encapsulated in the LNP.

24. The composition of any one of claims 18-23 which further comprises a pharmaceutically acceptable carrier.

25. A method for increasing the amount of OTC expression in a cell comprising administering to the cell a composition comprising the polynucleotide construct of any one of claims 1-17 or the composition of any one of claims 18-24.

26. The method of claim 25, wherein the cell is a liver cell.

27. An expression cassette comprising a sequence having at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to SEQ ID NO: 8.

28. The expression cassette of claim 27 which further comprises a promoter.

29. The expression cassette of claim 28, wherein the promoter is a T7 promoter.

30. A plasmid comprising the expression cassette of any one of claims 27-29.

31. A host cell comprising the expression cassette of any one of claims 27-30, or the plasmid of claim 30.

32. Use of the polynucleotide construct of any one of claims 1-17, or the composition of any one of claims 18-24, or the expression cassette of claim any one of claims 27-29, or the plasmid of claim 30, or the host cell of claim 31, for the manufacture of a medicament for the treatment of OTCD in a subject in need thereof.

33. Use of the polynucleotide construct of any one of claims 1-17, or the composition of any one of claims 18-24, or the expression cassette of claim any one of claims 27-29, or the plasmid of claim 30, or the host cell of claim 31, for the manufacture of a medicament for the treatment of or for reducing the risk of hyperammonemia in a subject with OTCD.

34. Use of the polynucleotide construct of any one of claims 1-17, or the composition of any one of claims 18-24, or the expression cassette of any one of claims 27-29, or the plasmid of claim 30, or the host cell of claim 31 in the manufacture of a medicament for *in vivo* delivery of a nucleic acid to a mammalian subject.

35. Use of the polynucleotide construct of any one of claims 1-17, or the composition of any one of claims 18-24, or the expression cassette of any one of claims 27-29, or the plasmid

of claim 30, or the host cell of claim 31 in the manufacture of a medicament for treating a disease or disorder in a mammalian subject in need thereof.

36. The use of claim 35, wherein the disease or disorder is a urea cycle disorder.