Claims

1. An isolated genetically engineered bacteria or yeast cell, wherein the cell has been transformed by at least one polynucleotide molecule;

the at least one polynucleotide molecule comprising lipoic acid pathway genes which encode an octanoyltransferase, a lipoyl synthase, a protein substrate that is lipoylated, a lipoamidase and an S-adenosylmethionine synthase, operably linked to at least one promoter,

wherein the lipoic acid pathway genes are heterologous and said genetically engineered bacteria or yeast cell is capable of increased production of free lipoic acid compared to a non-transformed cell.

2. The isolated genetically engineered bacteria or yeast cell of claim 1, wherein the protein substrate that is lipoylated is selected from a group comprising Gcv3p (H protein of the glycine cleavage system), Lat1p and Kgd2p.

3. The isolated genetically engineered bacteria or yeast cell of claim 1 or 2, wherein the S-adenosylmethionine synthase is from a cell selected from a group comprising Kluyveromyces, Candida, Pichia, Yarrowia, Debaryomyces, Saccharomyces spp., and *Schizosaccharomyces pombe*.

4. The isolated genetically engineered bacteria or yeast cell of any one of claims 1 to 3, wherein the lipoic acid pathway genes comprise *LIP2* (octanoyltransferase), *LIP5* (lipoyl synthase), *GCV3* (H protein of the glycine cleavage system), *LPA* (lipoamidase), and one or both of *SAM1* and *SAM2*.

5. The isolated genetically engineered bacteria or yeast cell of any one of claims 1 to 4, wherein the lipoic acid pathway genes are expressed in mitochondria.

6. The isolated genetically engineered bacteria or yeast of claim 5, wherein the lipoic acid pathway genes are expressed in the mitochondria by virtue of a mitochondrial targeting peptide (MTP).

7. The isolated genetically engineered bacteria or yeast of claim 6, wherein the lipoamidase is LPA, the S-adenosylmethionine synthase is Sam1 and/or Sam2, and the mitochondrial targeting peptide (MTP) for LPA, Sam1 and/or Sam2 is from yeast cytochrome c oxidase subunit IV (COX4).

8. The isolated genetically engineered yeast of any one of claims 1 to 7, wherein the yeast is selected from a group comprising Kluyveromyces, Candida, Pichia, Yarrowia, Debaryomyces, Saccharomyces spp., and *Schizosaccharomyces pombe*.

9. The isolated genetically engineered bacteria or yeast of any one of claims 1 to 8, wherein said at least one promoter is a constitutive promoter.

10. The isolated genetically engineered bacteria or yeast of any one of claims 1 to 9, wherein said lipoic acid pathway genes are expressed from one or more plasmids.

11. The isolated genetically engineered bacteria or yeast of any one of claims 1 to 10, wherein at least one of said lipoic acid pathway genes is integrated into the bacteria or yeast genome.

12. The isolated genetically engineered bacteria or yeast of any one of claims 1 to 11, wherein the lipoamidase is from *Enterococcus faecalis* (EfLPA).

13. The isolated genetically engineered bacteria or yeast of any one of claims 4 to 12, wherein the *LIP2, LIP5, GCV3, LPA,* and one or both of *SAM1* and *SAM2* genes respectively encode an amino acid sequence comprising SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9 and/or SEQ ID NO: 11.

14. The isolated genetically engineered bacteria or yeast of any one of claims 4 to 13, wherein the *LIP2, LIP5, GCV3, LPA,* and one or both of *SAM1* and *SAM2* genes respectively comprises a polynucleotide sequence having at least 70% sequence identity, at least 80% sequence identity, at least 90% sequence identity or 100% sequence identity to SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 and/or SEQ ID NO: 12.

15. A recombinant expression vector comprising one or more heterologous lipoic acid pathway genes defined in any one of claims 1 to 14*,* operably linked to a promoter, wherein an expressed protein from said pathway genes is located to the mitochondria.

16. The recombinant vector of claim 15, wherein said promoter is a constitutive promoter.

17. A method of producing free lipoic acid in a genetically engineered cell, comprising the steps:

a) culturing a plurality of genetically engineered cells of any one of claims 1 to 14 in medium under conditions for lipoic acid biosynthesis, and

b) supplementing the medium with cysteine,

wherein said genetically engineered cell is capable of increased production of free lipoic acid compared to a non-transformed cell.

18. The method of claim 17, wherein the medium is supplemented with cysteine at a concentration of at least 0.05 mg/ml, at least 0.1 mg/ml, at least 0.2 mg/ml, at least 0.5 mg/ml or in the range from 0.05 mg/ml to 0.7 mg/ml, preferably in the range 0.1 mg/ml to 0.4 mg/ml.

19. The method of claim 17 or 18, further comprising isolating said free lipoic acid.

20. The method of any one of claims 17 to 19, wherein the engineered cell is a yeast cell.

21. The method of claim 20, wherein the engineered cell is *Saccharomyces cerevisiae.*