Claims

1. An Escherichia coli cell genetically modified to produce at least one bioproduct of the list comprising monosaccharide, phosphorylated monosaccharide, activated monosaccharide, disaccharide, oligosaccharide or glycolipid, said cell comprising an endogenous membrane protein wherein i) the expression of an endogenous membrane protein encoding gene is reduced and/or ii) wherein the endogenous membrane protein encoding gene is mutated, ~~preferably, said mutation results in reduced expression of the membrane protein encoding gene,~~ and wherein said membrane protein is any one of a protein as described in Table 1.
2. Cell according to claim 1 wherein said membrane protein is chosen from the list consisting of: COG groups COG4206, COG2067, COG4771, COG1629, COG4580, COG2885, COG3203, COG4571, COG1538, COG3248, COG0810, COG0457; an outer membrane porin, an outer membrane protease 7, a cobalamin/cobinamide outer membrane transporter, an outer membrane channel, a maltose outer membrane channel, a ferrichrome outer membrane transporter, a Ton complex subunit, a long-chain fatty acid outer membrane channel, a nucleoside-specific channel-forming protein, a ferric enterobactin outer membrane transporter, a putative TonB-dependent outer membrane receptor, an outer membrane protein, a phage receptor.
3. Cell according to any one of claim 1 or 2 wherein said membrane protein is chosen from the list consisting of: OmpA (SEQ ID NO: 2), OmpC (SEQ ID NO: 4), OmpF (SEQ ID NO: 6), OmpT (SEQ ID NO: 8), BtuB (SEQ ID NO: 10), TolC (SEQ ID NO: 12), LamB (SEQ ID NO: 14), FhuA (SEQ ID NO: 16), TonB (SEQ ID NO: 18), FadL (SEQ ID NO: 20), Tsx (SEQ ID NO: 22), FepA (SEQ ID NO: 24), YncD (SEQ ID NO: 26), PhoE (SEQ ID NO: 28), and NfrA (SEQ ID NO: 30), a functional homolog of any one of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, or a membrane protein having at least 70% sequence identity to the full length amino acid sequence of any one of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30.
4. Cell according to any one of claim 1, 2 or 3 wherein said reduced expression of the membrane protein encoding gene and/or mutation of the membrane protein encoding gene confers bacteriophage resistance and wherein said bacteriophage is selected from the bacteriophage families listed in table 2.
5. Cell according to any one of the previous claims, wherein said reduced expression of the membrane protein encoding gene and/or mutation of the membrane protein encoding gene

confers unaffected and/or enhanced i) bioproduct production, ii) productivity, iii) biomass production, and/or iv) cell growth.

6. Cell according to any one of the previous claims, wherein said mutation and/or reduced expression comprises reducing and/or abolishing the bacteriophage binding capacity of said membrane protein.
7. Cell according to any one of the previous claims, wherein said the E. coli cell is transformed with at least one heterologous gene to produce at least any one of a sialic acid pathway or sialylation pathway, or fucosylation pathway or galactosylation pathway or N-acetylglucosamine carbohydrate pathway, preferably the cell is transformed by introduction of a heterologous gene, genetic cassette or set of genes as described in the art.
8. Cell according to any one of the previous claims wherein the mutation and/or reduced expression of the endogenous membrane protein comprises any one or more of:
   i) mutating the transcription unit of the membrane protein encoding gene;
   ii) mutating the endogenous/homologous promoter of the membrane protein encoding gene;
   iii) mutating the ribosome binding site of the membrane protein encoding gene;
   iv) mutating an UTR of the membrane protein encoding gene and/or
   v) mutating the transcription terminator.
9. Cell according to any one of the previous claims wherein the mutation of the membrane protein encoding gene comprises rendering said membrane protein shorter, longer and/or completely knocks out the membrane protein.
10. Cell according to any one of claims 1 to 9 wherein said mutation of the membrane protein encoding gene is an in-frame mutation of the membrane protein encoding gene.
11. Cell according to claim 10, wherein said in-frame mutation is an insertion of at least 2 amino acids into the encoded membrane protein’s amino acid sequence, preferably wherein said mutation comprises an insertion of more than 2 amino acids.
12. Cell according to any one of claims 9 to 11 wherein said mutation occurs in the tolC encoding gene, and wherein said mutation comprises an 11 amino acid duplication of the amino acid sequence VGLSFSLPIYQ (SEQ ID NO: 31).
13. Cell according to any one of the previous claims, wherein at least two of said membrane protein encoding genes are mutated and/or have a reduced expression.
14. Cell according to any one of the preceding claims wherein said bioproduct is an oligosaccharide, preferably said oligosaccharide is selected from the group of fucosyllactoses, sialyllactoses, Lacto-N-tetraoses, difucosyllacto-N-tetraose, sialyl-lacto-N-

tetraoses, lacto-N-fucopentaoses, lewis-type antigens, more preferably selected from the group comprising 2'FL, 3FL, DiFL, Lacto-N-triose, LNT, LNnT, 3'SL, 6'SL, LSTa, LSTb, LSTc, LSTd, DFLNT, lacto-N-fucopentaose I, lacto-N-fucopentaose II, lacto-N-fucopentaose III, lacto-N-fucopentaose V, lacto-N-fucopentaose VI, H1 antigen, $Lewis^a$, $Lewis^b$, sialyl $Lewis^a$, H2 antigen, $Lewis^x$, $Lewis^y$; sialyl-$Lewis^x$.

15. Cell according to any one of the claims 1 to 13, wherein said bioproduct is a disaccharide preferably selected from the group comprising N-acetyllactosamine, lactose; or wherein said bioproduct is a activated monosaccharide preferably selected from the group comprising GDP-fucose, UDP-glucose, UDP-galactose, UDP-N-acetylglucosamine, CMP-sialic acid; or wherein said bioproduct is a monosaccharide preferably selected from the group comprising glucosamine, mannose, xylose, N-acetylmannosamine, N-acetylneuraminic acid, N-glycolylneuraminic acid, sialic acid, N-acetylgalactosamine, galactosamine, fucose, rhamnose, glucuronic acid, gluconic acid, or wherein said bioproduct is a phosphorylated monosaccharide preferably selected from the group comprising glucose-1-phosphate, glucose-6-phosphate, glucose-1,6-bisophosphate, galactose-1-phosphate, fructose-6-phosphate, fructose-1,6-bisphosphate, fructose-1-phosphate, glucosamine-1-phosphate, glucosamine-6-phosphate, N-acetylglucosamine-1-phosphate, mannose-1-phosphate, mannose-6-phosphate or fucose-1-phosphate.
16. A method for conferring bacteriophage resistance in an E. coli cell, said method comprising:
    - providing an E. coli cell genetically modified to produce at least one bioproduct of the list comprising monosaccharide, phosphorylated monosaccharide, activated monosaccharide, disaccharide, oligosaccharide or glycolipid,
    - reducing the expression of and/or mutating a membrane protein encoding gene of said E. coli cell,
    - wherein said membrane protein is any one of a protein as described in Table 1.
17. A method for producing at least one bioproduct of the list comprising monosaccharide, phosphorylated monosaccharide, activated monosaccharide, disaccharide, oligosaccharide or glycolipid with an E. coli cell, said method comprising:
    - providing an E. coli cell genetically modified to produce at least one bioproduct of the list comprising monosaccharide, phosphorylated monosaccharide, activated monosaccharide, disaccharide, oligosaccharide or glycolipid,
    - reducing the expression of and/or mutating a membrane protein encoding gene of said E. coli cell,

- cultivating the cell in a medium under conditions permissive for the production of the desired bioproduct
- preferably separating the bioproduct from the cultivation;

wherein said membrane protein is any one of the proteins as described in Table 1.

18. A method for increasing the production of at least one bioproduct of the list comprising monosaccharide, phosphorylated monosaccharide, activated monosaccharide, disaccharide, oligosaccharide or glycolipid with an E. coli cell as compared to an E. coli cell genetically modified to produce said bioproduct(s), said method comprising:
    - providing an E. coli cell genetically modified to produce at least one bioproduct of the list comprising monosaccharide, phosphorylated monosaccharide, activated monosaccharide, disaccharide, oligosaccharide or glycolipid,
    - reducing the expression of and/or mutating a membrane protein encoding gene of said E. coli cell,
    - cultivating the cell in a medium under conditions permissive for the production of the desired bioproduct
    - preferably separating the bioproduct from the cultivation;

    wherein said membrane protein is any one of the proteins as described in Table 1.
19. Method according to any one of claims 16 to 18 wherein said membrane protein is chosen from the list consisting of: COG groups COG4206, COG2067, COG4771, COG1629, COG4580, COG2885, COG3203, COG4571, COG1538, COG3248, COG0810, COG0457; an outer membrane porin, an outer membrane protease 7, a cobalamin/cobinamide outer membrane transporter, an outer membrane channel, a maltose outer membrane channel, a ferrichrome outer membrane transporter, a Ton complex subunit, a long-chain fatty acid outer membrane channel, a nucleoside-specific channel-forming protein, a ferric enterobactin outer membrane transporter, a putative TonB-dependent outer membrane receptor, an outer membrane protein, a phage receptor.
20. Method according to any one of claims 16 to 19 wherein said membrane protein is chosen from the list consisting of: OmpA (SEQ ID NO: 2), OmpC (SEQ ID NO: 4), OmpF (SEQ ID NO: 6), OmpT (SEQ ID NO: 8), BtuB (SEQ ID NO: 10), TolC (SEQ ID NO: 12), LamB (SEQ ID NO: 14), FhuA (SEQ ID NO: 16), TonB (SEQ ID NO: 18), FadL (SEQ ID NO: 20), Tsx (SEQ ID NO: 22), FepA (SEQ ID NO: 24), YncD (SEQ ID NO: 26), PhoE (SEQ ID NO: 28), and NfrA (SEQ ID NO: 30), a functional homolog of any one of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, or a membrane protein having at least 70% sequence identity to

the full length amino acid sequence of any one of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30.

21. Method according to any one of claims 16 to 20, wherein said modified expression and/or mutation of the membrane protein encoding gene confers bacteriophage resistance and wherein said bacteriophage is selected from the bacteriophage families listed in table 2.
22. Method according to any one of claims 16 to 21, wherein said modified expression and/or mutation of the membrane protein encoding gene confers unaffected and/or enhanced bioproduct production.
23. Method according to any one of claims 16 to 22, wherein said modified expression and/or mutation comprises reducing and/or abolishing the bacteriophage binding capacity of said membrane protein.
24. Method according to any one of the claims 16 to 23, wherein said E. coli cell is genetically modified to produce at least one bioproduct chosen from a fucosylated, sialylated, galactosylated oligosaccharide, N-acetylglucosamine containing oligosaccharide, or sialic acid.
25. Method according to any one of the claims 16 to 24, wherein the modified expression of the endogenous membrane protein encoding gene is a lower or reduced expression, preferably said lower expression comprises any one or more of:
    i) mutating the transcription unit of the membrane protein encoding gene;
    ii) mutating the endogenous/homologous promoter of the membrane protein encoding gene;
    iii) mutating the ribosome binding site of the membrane protein encoding gene;
    iv) mutating an UTR of the membrane protein encoding gene and/or
    v) mutating the transcription terminator
26. Method according to any one of the claims 16 to 25, wherein the mutation of the membrane protein encoding gene comprises rendering said membrane protein shorter, longer or completely knocks out said membrane protein.
27. Method according to any one of claims 16 to 26 wherein said mutation is an in-frame mutation of the membrane protein encoding gene, preferably said in-frame mutation is an insertion of at least 2 amino acids into the encoded membrane protein’s amino acid sequence, more preferably wherein said mutation comprises an insertion of more than 2 amino acids.
28. Method according to any one of claims 16 to 27 wherein said mutation occurs in the tolC gene of Escherichia coli or in a functional homolog of the tolC gene in an E.coli, and wherein said mutation provides resistance against the TLS family of bacteriophages, and wherein said

mutation gives rise to an 11 amino acid duplication of the amino acid sequence VGLSFSLPIYQ (SEQ ID NO: 31)

29. Method according to any one of claims 16 to 28, wherein at least two of said membrane protein encoding genes are mutated and/or have a reduced expression.
30. Method according to any one of claims 16 to 29, wherein said bioproduct is an oligosaccharide, preferably said oligosaccharide is selected from the group of fucosyllactoses, sialyllactoses, Lacto-N-tetraoses, difucosyllacto-N-tetraose, sialyl-lacto-N-tetraoses, lacto-N-fucopentaoses, lewis-type antigens, more preferably, 2'FL, 3FL, DiFL, Lacto-N-triose, LNT, LNnT, 3'SL, 6'SL, LSTa, LSTb, LSTc, LSTd, DFLNT, lacto-N-fucopentaose I, lacto-N-fucopentaose II, lacto-N-fucopentaose III, lacto-N-fucopentaose V, lacto-N-fucopentaose VI, H1 antigen, Lewis^{a}, Lewis^{b}, sialyl Lewis^{a}, H2 antigen, Lewis^{x}, Lewis^{y}; sialyl-Lewis^{x}.
31. Method according to any one of claims 16 to 29, wherein said bioproduct is a disaccharide preferably selected from the group comprising LacNAc, lactose; or wherein said bioproduct is an activated monosaccharide preferably selected from the group comprising GDP-fucose, UDP-glucose, UDP-galactose, UDP-N-acetylglucosamine, CMP-sialic acid; or wherein said bioproduct is a monosaccharide preferably selected from the group comprising glucosamine, mannose, xylose, N-acetylmannosamine, N-acetylneuraminic acid, N-glycolylneuraminic acid, sialic acid, N-acetylgalactosamine, galactosamine, fucose, rhamnose, glucuronic acid, gluconic acid, or wherein said bioproduct is a phosphorylated monosaccharide preferably selected from the group comprising glucose-1-phosphate, glucose-6-phosphate, glucose-1,6-bisophosphate, galactose-1-phosphate, fructose-6-phosphate, fructose-1,6-bisphosphate, fructose-1-phosphate, glucosamine-1-phosphate, glucosamine-6-phosphate, N-acetylglucosamine-1-phosphate, mannose-1-phosphate, mannose-6-phosphate or fucose-1-phosphate.
32. Method for fermentative production of at least one bioproduct of the list comprising monosaccharide, phosphorylated monosaccharide, activated monosaccharide, disaccharide, oligosaccharide or glycolipid using genetically modified cells to produce said bioproduct(s), comprising the steps of:
    - providing a cell as described in any one of the claims 1 to 15;
    - cultivating the cell in a medium under conditions permissive for the production of the desired bioproduct;
    - preferably separating the bioproduct from the cultivation.

33. Method according to any one of the claims 16 to 32, wherein said bioproduct is LNnT, wherein preferably said membrane protein is any one or more of LamB (SEQ ID NO: 14), FhuA (SEQ ID NO: 16), FadL (SEQ ID NO: 20), and NfrA (SEQ ID NO: 30), a functional homolog of any one of SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 20 and SEQ ID NO: 30, or a membrane protein having at least 70% sequence identity to the full length amino acid sequence of any one of SEQ ID NOs 14, 16, 20, 30 and wherein preferably said mutation results in a knock-out phenotype of said gene.
34. Method according to any one of the claims 16 to 32, wherein said bioproduct is sialyllactose, preferably 6'SL, wherein preferably said membrane protein is FhuA (SEQ ID NO: 16), a functional homolog thereof or a membrane protein having at least 70% sequence identity to the full length amino acid sequence of SEQ ID NO: 16 and wherein preferably said mutation and/or reduced expression of the membrane protein encoding gene results in a knock-out phenotype of said gene.
35. Use of a cell as described in any one of the claims 1 to 15.