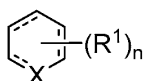


WHAT IS CLAIMED IS:

1. A method of producing recombinant adeno-associated virus (rAAV), the method comprising contacting a host cell with a solution comprising at least one compound of formula (I) or a salt thereof:



(I), wherein:

----- denotes a single bond or a double bond;

n is an integer selected from 1 to 5;

each R^1 is independently, for each occurrence, selected from the group consisting of -OH, C_{1-6} alkyl, C_{1-6} alkyl-OH, C_{1-6} alkyl-O- C_{1-6} alkyl, -O- C_{1-6} alkyl, -C(O)N(R^a)₂, and -C(O)OR^b;

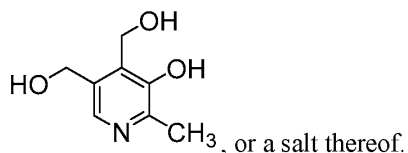
R^a is independently, for each occurrence, hydrogen or C_{1-6} alkyl;

R^b is independently, for each occurrence, hydrogen or C_{1-6} alkyl;

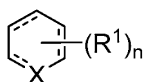
X is CR^cR^d or N;

R^c and R^d are independently, for each occurrence, selected from the group consisting of hydrogen, C_{1-6} alkyl, -OH, and -O- C_{1-6} alkyl, wherein when R^c is hydrogen, R^d is selected from C_{1-6} alkyl, -OH, and -O- C_{1-6} alkyl, and when R^c is selected from C_{1-6} alkyl, -OH, and -O- C_{1-6} alkyl, R^d is hydrogen; and

wherein the at least one compound is not:



2. A method of increasing rAAV titer yield, the method comprising contacting a host cell with a solution comprising at least one compound of formula (I) or a salt thereof:



(I), wherein:

----- denotes a single bond or a double bond;

n is an integer selected from 1 to 5;

each R^1 is independently, for each occurrence, selected from the group consisting of -OH, C_{1-6} alkyl, C_{1-6} alkyl-OH, C_{1-6} alkyl-O- C_{1-6} alkyl, -O- C_{1-6} alkyl, -C(O)N(R^a)₂, and -C(O)OR^b;

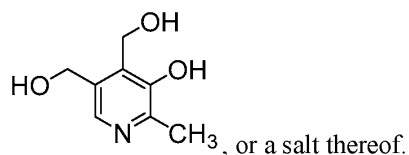
5 R^a is independently, for each occurrence, hydrogen or C_{1-6} alkyl;

R^b is independently, for each occurrence, hydrogen or C_{1-6} alkyl;

X is CR^cR^d or N;

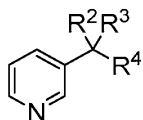
R^c and R^d are independently, for each occurrence, selected from the group consisting of hydrogen, C_{1-6} alkyl, -OH, and -O- C_{1-6} alkyl, wherein when R^c is hydrogen, 10 R^d is selected from C_{1-6} alkyl, -OH, and -O- C_{1-6} alkyl, and when R^c is selected from C_{1-6} alkyl, -OH, and -O- C_{1-6} alkyl, R^d is hydrogen; and

wherein the at least one compound is not:



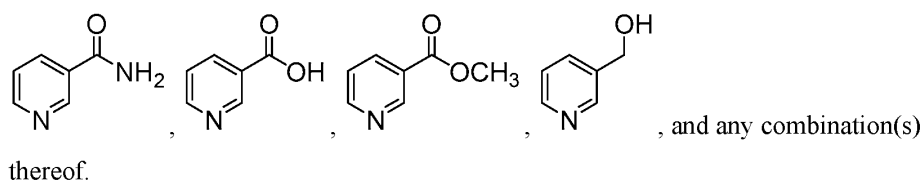
3. The method of claim 1 or 2, wherein X is N.
- 15 4. The method of any one of claims 1-3, wherein n is 1.
5. The method of any one of claims 1-4, wherein each R^1 is independently, for each occurrence, selected from the group consisting of C_{1-6} alkyl-OH, -C(O)N(R^a)₂, and -C(O)OR^b.
6. The method of any one of claims 1-5, wherein each R^1 is independently, for each 20 occurrence, selected from the group consisting of CH₂OH, -C(O)NH₂, -C(O)OH, and -C(O)OCH₃.
7. The method of claim 1 or 2, wherein X is CR^cR^d.
8. The method of any one of claims 1, 2, and 7, wherein R^c is hydrogen and R^d is -OH.
9. The method of any one of claims 1, 2, 3, and 7-8, wherein n is 5.

10. The method of any one of claims 1, 2, 3, 4, and 7-9, wherein R^1 is -OH.
11. The method of claim 1 or 2, wherein the solution comprises at least one compound of formula (I-A) or a salt thereof:

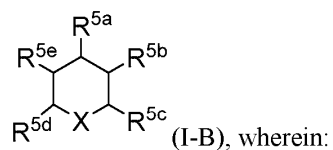


(I-A), wherein:

- 5 R^2 and R^3 are independently, for each occurrence, hydrogen or -OH,
 or R^2 and R^3 can be taken together to form oxo;
 R^4 is selected from the group consisting of hydrogen, -OH, -O-C₁₋₆alkyl, and -
 N(R^e)₂; and
 R^e is independently, for each occurrence, hydrogen or C₁₋₆alkyl.
- 10 12. The method of claim 11, wherein R^2 and R^3 are taken together to form oxo.
13. The method of claim 11 or 12, wherein R^4 is selected from the group consisting of -NH₂, -
 OH, and -OCH₃.
14. The method of claim 11, wherein R^2 and R^3 are both hydrogen.
15. The method of claim 11 or 14, wherein R^4 is -OH.
- 15 16. The method of any one of claims 1, 2, and 11, wherein the solution comprises at least one
 compound selected from the group consisting of:



17. The method of claim 1 or 2, wherein the solution comprises at least one compound of
 20 formula (I-B) or a salt thereof:



X is CR^cR^d; and

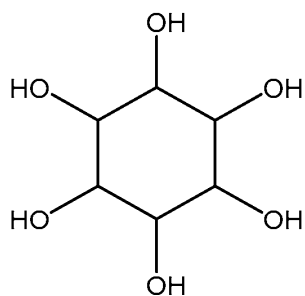
R^{5a}, R^{5b}, R^{5c}, R^{5d}, and R^{5e} are independently, for each occurrence, -OH, -O-C₁₋₆alkyl, C₁₋₆alkyl, C₁₋₆alkyl-OH, and C₁₋₆alkyl-O-C₁₋₆alkyl,

5 wherein R^c and R^d are as defined in claim 1.

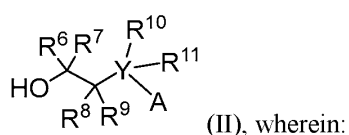
18. The method of claim 17, wherein R^c is hydrogen and R^d is -OH.

19. The method of claim 17 or 18, wherein R^{5a}, R^{5b}, R^{5c}, R^{5d}, and R^{5e} are -OH.

20. The method of any one of claims 17-19, wherein the solution comprises the compound



10 21. A method of producing rAAV, the method comprising contacting a host cell with a solution comprising at least one compound of formula (II) or a salt thereof:



R⁶ and R⁷ are independently, for each occurrence, selected from the group consisting of hydrogen, -OH, -CN, halogen, and C₁₋₆alkyl;

15 R⁸ and R⁹ are independently, for each occurrence, selected from the group consisting of hydrogen, -OH, -CN, halogen, and C₁₋₆alkyl;

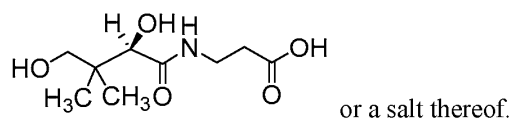
Y is C or N;

R^{10} and R^{11} are independently, for each occurrence, selected from the group consisting of hydrogen, -OH, and C₁₋₆alkyl;

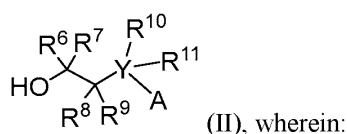
A is selected from the group consisting of hydrogen, C₁₋₆alkyl, and -C(O)N(R^f)₂;
and

5 R^f is independently, for each occurrence, selected from the group consisting of hydrogen, C₁₋₆alkyl, C₁₋₆alkyl-C(O)OH, and C₁₋₆alkyl-OH;

wherein the at least one compound is not:



22. A method of increasing rAAV titer yield, the method comprising contacting a host cell
10 with a solution comprising at least one compound of formula (II) or a salt thereof:



R^6 and R^7 are independently, for each occurrence, selected from the group consisting of hydrogen, -OH, -CN, halogen, and C₁₋₆alkyl;

15 R^8 and R^9 are independently, for each occurrence, selected from the group consisting of hydrogen, -OH, -CN, halogen, and C₁₋₆alkyl;

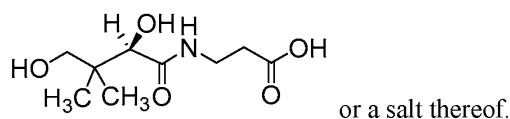
Y is C or N;

R^{10} and R^{11} are independently, for each occurrence, selected from the group consisting of hydrogen, -OH, and C₁₋₆alkyl;

20 A is selected from the group consisting of hydrogen, C₁₋₆alkyl, and -C(O)N(R^f)₂;
and

R^f is independently, for each occurrence, selected from the group consisting of hydrogen, C₁₋₆alkyl, C₁₋₆alkyl-C(O)OH, and C₁₋₆alkyl-OH;

wherein the at least one compound is not:



23. The method of claim 21 or 22, wherein R⁶ and R⁷ are hydrogen.
24. The method of any one of claims 21-23, wherein R⁸ and R⁹ are hydrogen.
25. The method of any one of claims 21-24, wherein Y is N.
- 5 26. The method of any one of claims 21-25, wherein R¹⁰ and R¹¹ are CH₃.
27. The method of any one of claims 21-26, wherein A is CH₃.
28. The method of any one of claims 21-27, wherein the solution comprises the compound
29. A method of producing rAAV or increasing rAAV titer yield, the method comprising

10

contacting a host cell with a solution comprising at least one B vitamin selected from the group consisting of vitamin B₂, vitamin B₇, vitamin B₉, vitamin B₁₂, and any combination(s) thereof.
30. The method of any one of claims 1-29, wherein the final concentration of the at least one compound or B vitamin in the solution is greater than 0.5 mM.
- 15 31. The method of any one of claims 1-29, wherein the final concentration of the at least one compound or B vitamin in the solution is greater than or equal to 0.5 mM.
32. The method of any one of claims 1-29, wherein the final concentration of the at least one compound or B vitamin in the solution is between 0.5 mM and 10 mM.
33. The method of any one of claims 1-29, wherein the final concentration of the at least one

20

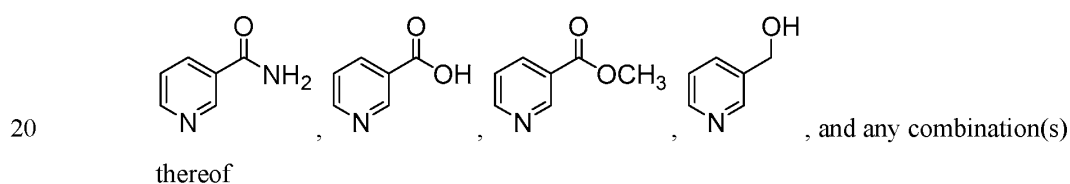
compound or B vitamin in the solution is between 1 mM and 10 mM.
34. The method of any one of claims 1-33, wherein the final concentration of the at least one compound or B vitamin in the solution is sufficient to produce at least 1.2-fold greater

quantities of secreted rAAV compared to that produced by a host cell not contacted with a solution comprising the at least one compound or B vitamin.

35. The method of any one of claims 1-33, wherein the final concentration of the at least one compound in the solution is sufficient to produce at least 1.2-fold greater quantities of total
5 rAAV compared to that produced by a host cell not contacted with a solution comprising the at least one compound or B vitamin.
36. The method of any one of claims 1-33, wherein the final concentration of the at least one compound in the solution is sufficient to produce 1.2 to 2.5-fold greater quantities of secreted rAAV compared to that produced by a host cell not contacted with a solution
10 comprising the at least one compound or B vitamin.
37. The method of any one of claims 1-33, wherein the final concentration of the at least one compound in the solution is sufficient to produce 1.2 to 2.5-fold greater quantities of total rAAV compared to that produced by a host cell not contacted with a solution comprising the at least one compound or B vitamin.
- 15 38. The method of any one of claims 1-37, wherein the host cell is contacted with the solution comprising the at least one compound or B vitamin for at least 2 days.
39. The method of any one of claims 1-38, further comprising the steps of harvesting and purifying the rAAV.
40. The method of any one of claims 1-39, wherein the host cell is a mammalian cell.
- 20 41. The method of claim 40, wherein the host cell is selected from the group consisting of HeLa, HEK293, COS, A549, BHK, and Vero cells.
42. The method of claim 41, wherein the host cell is a HeLa cell.
43. The method of claim 41, wherein the host cell is a HEK293 cell.
44. The method of any one of claims 1-39, wherein the host cell is an insect cell.
- 25 45. The method of claim 44, wherein the host cell is selected from the group consisting of Sf9, Sf-21, Tn-368, and BTI-Tn-5B1-4 (High-Five) cells.

46. The method of any one of claims 1-45, wherein the host cell comprises a heterologous nucleotide sequence flanked by AAV inverted terminal repeats.
47. The method of any one of claims 1-46, wherein the host cell comprises rep and cap genes.
48. The method of any one of claims 1-47, wherein the host cell comprises helper virus genes.
- 5 49. The method of any one of claims 1-48, wherein the host cell comprises i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats, ii) rep and cap genes, and iii) helper virus genes.
50. The method of any one of claims 1-49, wherein the host cell produces at least 1.2-fold greater quantities of secreted rAAV compared to that produced by a host cell not contacted
10 with a solution comprising the at least one compound.
51. The method of any one of claims 1-49, wherein the host cell produces at least 1.2-fold greater quantities of total rAAV compared to that produced by a host cell not contacted with a solution comprising the at least one compound or B vitamin.
52. The method of any one of claims 1-49, wherein the host cell produces 1.2 to 2.5-fold
15 greater quantities of secreted rAAV compared to that produced by a host cell not contacted with a solution comprising the at least one compound or B vitamin.
53. The method of any one of claims 1-49, wherein the host cell produces 1.2 to 2.5-fold greater quantities of total rAAV compared to that produced by a host cell not contacted with a solution comprising the at least one compound or B vitamin.
- 20 54. The method of any one of claims 1-53, wherein the solution comprises cell culture medium.
55. The method of any one of claims 1-53, wherein the solution comprises production medium.
56. The method of any one of claims 1-55 comprising culturing the host cell in a suspension culture.
- 25 57. The method of any one of claims 1-55 comprising culturing the host cell in an adherent culture.

58. The method of any one of claims 1-56 comprising culturing the host cell in a 1L bioreactor.
59. The method of any one of claims 1-56 comprising culturing the host cell in a 2L bioreactor.
60. The method of any one of claims 1-56 comprising culturing the host cell in a 3L bioreactor.
61. The method of any one of claims 1-56 comprising culturing the host cell in a 250L
5 bioreactor.
62. The method of any one of claims 1-56 comprising culturing the host cell in a 500L bioreactor.
63. The method of any one of claims 1-56 comprising culturing the host cell in a 2,000L bioreactor.
- 10 64. A composition comprising a host cell and a compound of formula (I) or a salt thereof.
65. A composition comprising a host cell and a compound of formula (I-A) or a salt thereof.
66. A composition comprising a host cell and a compound of formula (I-B) or a salt thereof.
67. A composition comprising a host cell and a compound of formula (II) or a salt thereof.
68. A composition comprising a host cell and at least one B vitamin selected from the group
15 consisting of vitamin B₂, vitamin B₇, vitamin B₉, and vitamin B₁₂, and any combination(s) thereof.
69. A method of producing recombinant adeno-associated virus (rAAV), the method comprising contacting a host cell with a solution comprising at least one compound selected from the group consisting of:

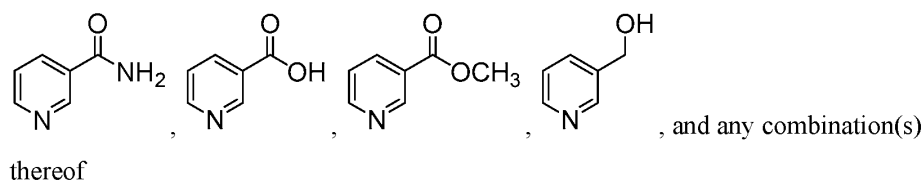


wherein the host cell comprises:

i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,
and

ii) AAV rep and cap genes.

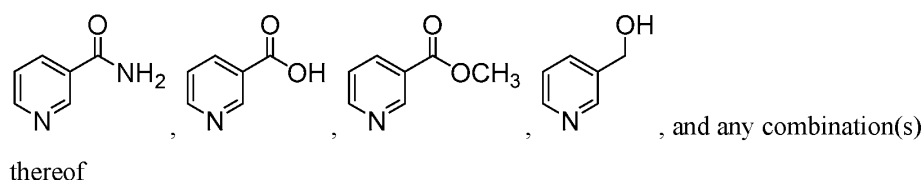
70. A method of increasing rAAV titer yield, the method comprising contacting a host cell
5 with a solution comprising at least one compound selected from the group consisting of:



wherein the host cell comprises:

- i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,
10 and
ii) AAV rep and cap genes.

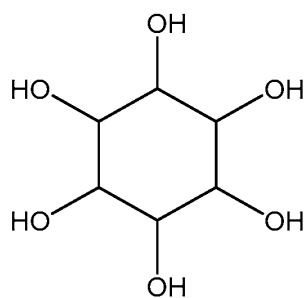
71. A composition comprising a host cell and at least one compound selected from the group
consisting of:



wherein the host cell comprises:

- i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,
and
ii) AAV rep and cap genes.

- 20 72. A method of producing recombinant adeno-associated virus (rAAV), the method
comprising contacting a host cell with a solution comprising



wherein the host cell comprises:

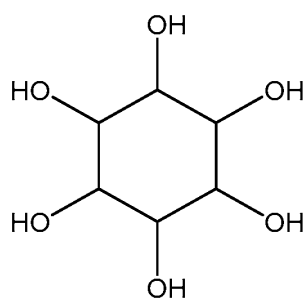
i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,

and

5

ii) AAV rep and cap genes.

73. A method of increasing rAAV titer yield, the method comprising contacting a host cell with a solution comprising



wherein the host cell comprises:

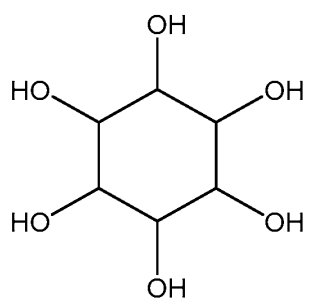
10

i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,

and

ii) AAV rep and cap genes.

74. A composition comprising a host cell and



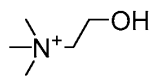
wherein the host cell comprises:

i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,

5 and

ii) AAV rep and cap genes.

75. A method of producing recombinant adeno-associated virus (rAAV), the method comprising contacting a host cell with a solution comprising:



10

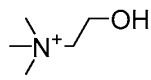
wherein the host cell comprises:

i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,

and

ii) AAV rep and cap genes.

15 76. A method of increasing rAAV titer yield, the method comprising contacting a host cell with a solution comprising:



wherein the host cell comprises:

i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,
and

ii) AAV rep and cap genes.

77. A composition comprising a host cell and



wherein the host cell comprises:

i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,
and

ii) AAV rep and cap genes.

10 78. A method of producing recombinant adeno-associated virus (rAAV), the method comprising contacting a host cell with a solution comprising at least one B vitamin selected from the group consisting of vitamin B₂, vitamin B₇, vitamin B₉, and vitamin B₁₂, and any combination(s) thereof, wherein the host cell comprises:

15 i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,
and

ii) AAV rep and cap genes.

79. A method of increasing rAAV titer yield, the method comprising contacting a host cell with a solution comprising at least one B vitamin selected from the group consisting of vitamin B₂, vitamin B₇, vitamin B₉, and vitamin B₁₂, and any combination(s) thereof,
20 wherein the host cell comprises:

i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,
and

ii) AAV rep and cap genes.

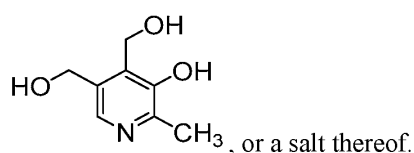
80. The method of any one of claims 69, 70, 72, 73, 75, 76, 78, or 79, wherein the host cell
25 further comprises helper genes.

81. A composition comprising a host cell and at least one B vitamin selected from the group consisting of vitamin B₂, vitamin B₇, vitamin B₉, vitamin B₁₂, and any combination(s) thereof, wherein the host cell comprises:

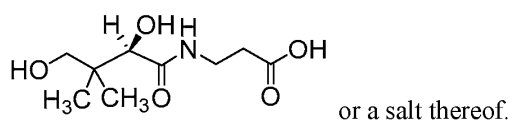
- 5 i) a heterologous nucleotide sequence flanked by AAV inverted terminal repeats,
and
 ii) AAV rep and cap genes.

82. The composition of any one of claims 71, 74, 77, or 81, wherein the host cell further comprises helper genes.

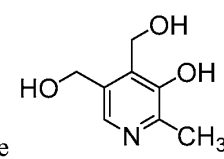
- 10 83. The method of any one of claims 1-20, wherein the solution does not comprise



84. The method of any one of claims 21-28, wherein the solution does not comprise



85. The composition of any one of claims 64-66, 71, or 74, wherein the composition does not

- 15 comprise
- 
- CC1=CN(C(=C1)C(=O)O)C(=C1)CO, or a salt thereof.

86. The composition of claim 67 or 77, wherein the composition does not comprise

