CLAIMS

1 A transgenic producer cell line in which the expression of YB1 is reduced compared with a control producer cell line.

2 The transgenic producer cell line of claim 1, wherein the expression of: (i) YB1 and NPM1; (ii) YB1 and NCL; or (iii) YB1, NPM1 and NCL; is reduced compared with a control producer cell line.

3 The transgenic producer cell line of claim 1 or 2, wherein the expression of YB1, NPM1 and/or NCL is reduced using CRISPR genome editing, a double stranded RNA (dsRNA), a small interfering RNA (siRNA), a small hairpin RNA (shRNA),a micro RNA or an antisense RNA.

4 The transgenic producer cell line of claim 3, wherein the expression of YB1, NPM1 and/or NCL is reduced using a shRNA, and preferably:

(a) YB1 expression is reduced using a shRNA comprising the nucleotide sequence SEQ ID NOs: 14 to 18 (Y1 to Y5);
(b) NPM1 expression is reduced using a shRNA comprising the nucleotide sequence SEQ ID NOs: 4 to 8 (NPM-N6 to NPM-N10); and/or
(c) NCL expression is reduced using a shRNA comprising the nucleotide sequence SEQ ID NOs: 9 to 13 (NCL-N1 to NCL-N5).

5 The transgenic producer cell line of claim 3, wherein the expression of YB1, NPM1 and/or NCL is reduced using CRISPR genome editing.

6 The transgenic producer cell line of claim 5, wherein the expression of YB1 is reduced using a gRNA pair selected from SEQ ID NOs: 33 and 34; SEQ ID NOs: 35 and 36; SEQ ID NOs: 37 and 38; and/or SEQ ID NOs: 39 and 40.

7 The transgenic producer cell line of any one of claims 1 to 6, wherein the expression of one or more additional genes and/or proteins listed in Table 2 is modulated compared with a control producer cell line.

8 The transgenic producer cell line of any one of claims 1 to 7, which is a human embryonic kidney 293T cell line.

9 A method for producing an adeno-associated viral (AAV) vector comprising culturing an adeno-associated virus in a producer cell line in which the expression of at least one of YB1, NPM1 and NCL is reduced.

10 The method of claim 9, wherein the expression of: (i) NPM1 and NCL; (ii) YB1 and NPM1; (iii) YB1 and NCL; or (iv) YB1, NPM1 and NCL ; in the producer cell line is reduced.

11 The method of claim 9 or 10, wherein the expression of YB1, NPM1 and/or NCL is reduced using CRISPR genome editing, a double stranded RNA (dsRNA), a small interfering RNA (siRNA), a small hairpin RNA (shRNA),a micro RNA or an antisense RNA.

12 The method of claim 11, wherein the expression of YB1, NPM1 and/or NCL is reduced using a shRNA, and preferably:

(a) YB1 expression is reduced using a shRNA comprising the nucleotide sequence SEQ ID NOs: 14 to 18 (Y1 to Y5);
(b) NPM1 expression is reduced using a shRNA comprising the nucleotide sequence SEQ ID NOs: 4 to 8 (NPM-N6 to NPM-N10); and/or
(c) NCL expression is reduced using a shRNA comprising the nucleotide sequence SEQ ID NOs: 9 to 13(NCL-N1 to NCL-N5).

13 The method of claim 11, wherein the expression of YB1, NPM1 and/or NCL is reduced using CRISPR genome editing.

14 The method of claim 13, wherein the expression of YB1 is reduced using a gRNA pair selected from SEQ ID NOs: 33 and 34; SEQ ID NOs: 35 and 36; SEQ ID NOs: 37 and 38; and/or SEQ ID NOs: 39 and 40.

15 The method of any one of claims 9 to 14, wherein the expression of one or more of the additional genes and/or proteins listed in Table 2 is modulated in the producer cell line.

16 The method of any one of claims 9 to 15, wherein the titre of AAV vector is increased at least 2 fold compared with the titre of AAV vector produced by a control method.

17 The method of any one of claims 9 to 16, wherein the ratio of complete: empty AAV vector is increased by at least 20% compared with the ratio of complete: empty AAV vector produced by a control method.

18 The method of any one of claims 9 to 17, wherein the producer cell line is a human embryonic kidney 293T cell line.

19 The method of any one of claims 9 to 18, wherein the serotype of the AAV vector is AAV2, AAV5 or AAV8.

20 A population of adeno-associated viral (AAV) vectors obtainable from the producer cell line of any one of claims 1 to 8, or by the method of any one of claims 9 to 19, wherein at least 80% of the AAV vectors in the population comprises at least one of YB1, NPM1 and/or NCL.

21 The population of claim 20, wherein the ratio of complete: empty AAV vectors in the population is increased by at least 20% compared the ratio of complete: empty AAV vector in a population produced by a control method.

22 The population of claim 20 or 21, wherein the AAV vectors are AAV2, AAV5 or AAV8 serotype vectors.