~~What Is~~ Claim~~ed I~~s:

Claim 1. A method for increasing the production titer of recombinantly-modified adeno-associated virus (rAAV), wherein said method comprises the steps:

(A) culturing cells that have been transfected with said rAAV in an initial culture medium for an initial period under conditions sufficient to permit the production of rAAV, wherein said cells additionally contain an AAV helper function-providing polynucleotide and a non-AAV helper function-providing polynucleotide;

(B) changing the ionic strength of said culture medium after said initial period by adding K^+ cations and one or more anions selected from the group consisting of $CO_3^=$, HCO_3^-, CH_3COO^-, $SO_4^=$, and NO_3^- to said culture medium, wherein: ~~one or more ions other than Na^+ to said culture medium; and changing the ionic strength of said culture medium after said initial period by adding K^+ cations and one or more anions selected from the group consisting of $CO_3^=$, HCO_3^-, CH3COO$^-$, $SO_4^=$, and NO_3^- to said culture medium;~~

(i) if the anion is $CO_3^=$, the added K^+ cations and $CO_3^=$ anions are added to the culture medium in an amount sufficient to increase the concentrations of K^+ and $CO_3^=$ in the culture medium by from about 40 mM to about 50 mM;

(ii) if the anion is HCO_3^-, said added K^+ cations and HCO_3^- anions are added to the culture medium in an amount sufficient to increase the concentrations of K^+ and HCO_3^- in the culture medium by from about 30 mM to about 50 mM;

(iii) if the anion is CH_3COO^-, the added K^+ cations and CH_3COO^- anions are added to the culture medium in an amount sufficient to increase the concentrations of K^+ and CH_3COO^-, in the culture medium by from about 40 mM to about 70 mM;

(iv) if the anion is $SO_4^=$, the added K^+ cations and $SO_4^=$ anions are added to the culture medium in an amount sufficient to increase the

concentrations of K^+ and $SO_4^=$ in the culture medium by from about 40 mM to about 70 mM, and

(v) if the anion is NO_3^-, the added K^+ cations and NO_3^- anions are added to the culture medium in an amount sufficient to increase the concentrations of K^+ and NO_3^- in the culture medium by from about 50 mM to about 60 mM; and

(C) continuing said culturing of said cells to thereby produce a production titer of ~~with~~ said rAAV that is greater than a titer obtained in the absence of step (B).

~~Claim 2. The method of claim 1, wherein each of said added ion(s) is provided in an amount sufficient to increase the concentration of such ion in said initial culture medium by from about 10 mM to about 80 mM.~~

Claim ~~3~~2. The method of ~~any one of claim 1 or claim 2~~claim 1, wherein the production titer is at least 50% greater than the titer obtained from a similarly conducted cell culturing in the absence of said step (B).

Claim ~~4~~3. The method of ~~any one of claims 1-3~~claim 1, wherein said rAAV comprises a transgene cassette that encodes a protein, or comprises a transcribed nucleic acid, that is therapeutic for a genetic or heritable disease or condition.

Claim ~~5~~4. The method of ~~any one of claims 1-4~~claim 1, wherein said rAAV belongs to the rAAV1, rAAV2, rAAV5, rAAV6, rAAV7, rAAV8, rAAV9 or rAAV10 serotype, or to a hybrid of said serotypes.

Claim ~~6~~5. The method of claim ~~5~~4, wherein said rAAV belongs to the rAAV2, rAAV5, or rAAV9 serotype, or to a hybrid of said serotypes.

~~Claim 7. The method of any one of claims 1-6, wherein said added ions comprise one or more of K^+, Ca^{++}, or Mg^{++}.~~

~~Claim 8. The method of any one of claims 1-7, wherein said added ions comprise one or more of $CO_3^=$, HCO_3^-, HPO_4^-, $PO_4^=$, SCN^-, $SO_4^=$, HSO_4^-, and Cl^-.~~

~~Claim 9. The method of any one of claims 1-7, wherein said added ions comprise one or more of acetate, aspartate, biphthalate, bitartrate, butoxyethoxy acetate, caprylate, citrate, dehydroacetate, diacetate, dihydroxy glycinate, d-saccharate, gluconate, glutamate, glycinate, glycosulfate, hydroxymethane sulfonate, lactate, methionate, oxalate, phenate, phenosulfonate, propionate, propionate, saccharin, salicylate, sarcosinate, sorbate, thioglycolate, and toluene sulfonate.~~

~~Claim 10. The method of any one of claims 1-8, wherein said added ions comprise K^+ and $CO_3^=$.~~

Claim ~~11~~6. The method of ~~any one of claims 1-10~~claim 1, wherein said cells are human embryonic kidney cells.

Claim ~~12~~7. The method of claim ~~11~~6, wherein said human embryonic kidney cells are HEK293 cells.

Claim ~~13~~8. The method of ~~any one of claims 1-10~~claim 1, wherein said cells are baby hamster kidney cells.

Claim ~~14~~9. The method of claim ~~13~~8, wherein said baby hamster kidney cells are BHK21 cells.

Claim ~~15~~10. The method of ~~any one of claims 1-10~~claim 1, wherein said cells are sf9 insect cells.

Claim ~~16~~11. The method of ~~any one of claims 1-15~~claim 1, wherein said initial culture medium is Dulbecco's Modified Eagle's Medium.

Claim ~~17~~12. The method of claim ~~16~~11, wherein said Dulbecco's Modified Eagle's Medium initial culture medium is supplemented with serum.

~~Claim 18. A pharmaceutical composition that comprises:~~

~~(A) a preparation of recombinantly-modified adeno-associated virus (rAAV) produced by the method of any one of claims 1-17, wherein said rAAV comprises a transgene cassette that encodes a protein, or a transcribed~~

~~nucleic acid, that is therapeutic for a genetic or heritable disease or condition, and wherein said pharmaceutical composition contains an effective amount of said rAAV preparation; and~~

~~(B) a pharmaceutically acceptable carrier.~~

~~Claim 19. The preparation of recombinantly-modified adeno-associated virus (rAAV) produced by the method of any one of claims 1-17, wherein the rAAV comprises a transgene cassette that encodes a protein, or a transcribed nucleic acid, or the pharmaceutical composition of claim 18, for use in the treatment of a genetic or heritable disease or condition.~~

Claim 13. The method of claim 1, wherein the ionic strength of said culture medium is changed by the addition of K^+ cations and HCO_3^- anions to said culture medium.

Claim 14. The method of claim 13, wherein the ionic strength of said culture medium is changed to increase the concentrations of K^+ cations and HCO_3^- anions in said culture medium by a concentration of from about 40 mM to about 50 mM by addition of $KHCO_3$.

Claim 15. The method of claim 13, wherein the ionic strength of said culture medium is changed to increase the concentrations of K^+ cations and HCO_3^- anions in said culture medium by a concentration of about 30 mM by addition of $KHCO_3$.

Claim 16. The method of claim 13, wherein the ionic strength of said culture medium is changed by the addition of $KHCO_3$ to said culture medium in an amount sufficient to increase the concentrations of K^+ cations and HCO_3^- anions in said culture medium by a concentration of about 55 mM.

Claim 17. A pharmaceutical composition that comprises:

(A) a preparation of recombinantly-modified adeno-associated virus (rAAV) produced by the method of claim 1, wherein said rAAV comprises a transgene cassette that encodes a protein, or a transcribed nucleic acid, that is therapeutic for a genetic or heritable disease or condition, and wherein

said pharmaceutical composition contains an effective amount of said rAAV preparation; and

(B) a pharmaceutically acceptable carrier

Claim 18. The pharmaceutical composition of claim 17, wherein said culture medium is changed to increase the concentrations of K^+ cations and HCO_3^- anions in said culture medium by a concentration of about 30 mM by addition of $KHCO_3$.

Claim 19. The pharmaceutical composition of claim 17, wherein said culture medium is changed to increase the concentrations of K^+ cations and HCO_3^- anions in said culture medium by a concentration of about 55 mM by addition of $KHCO_3$.