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NOTICE OF ALLOWANCE AND FEE(S) DUE

27500 7590 08/01/2017

PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

EXAMINER
POPA, ILEANA

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 08/01/2017

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/338,200	07/22/2014	Katherine High	074659-0433284	5822

TITLE OF INVENTION: VARIANT AAV AND COMPOSITIONS, METHODS AND USES FOR GENE TRANSFER TO CELLS, ORGANS AND TISSUES

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	11/01/2017

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

27500 7590 08/01/2017
PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/338,200	07/22/2014	Katherine High	074659-0433284	5822

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APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	11/01/2017

EXAMINER	ART UNIT	CLASS-SUBCLASS
POPA, ILEANA	1633	424-093200

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ Applicant certifying micro entity status. See 37 CFR 1.29
  NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27
  NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status.
  NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

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POPA, ILEANA	
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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 14/338,200	Applicant(s) HIGH ET AL.	
	Examiner ILEANA POPA	Art Unit 1633	AIA (First Inventor to File) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the reply filed on 5/22/2017*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *57-61,64-66 and 68-76*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 6/7/2017
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☒ Examiner's Amendment/Comment
6. ☒ Examiner's Statement of Reasons for Allowance
7. ☒ Other *See Continuation Sheet*.

/ILEANA POPA/
Primary Examiner, Art Unit 1633

Continuation of Attachment(s) 7. Other: Attached: annotated claim listing filed on 5/22/2017.

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

DETAILED ACTION

1. The amendments filed on 5/22/2017 have been entered.

Claims 1-56, 62, 63, and 67 have been cancelled. Claims 57, 59, and 66 have been amended. Claims 69-76 are new.

2. The provisional double patenting rejections of claims 1-10, 62, and 63 as being unpatentable over claims 1-7, 9-14, 16, 17, 21, 75, and 76 of copending Application No. 14/360,151 and of claims 1-10 as being unpatentable over claims 1-15 and 17 of copending Application No. 14/394454 are moot because claims 1-10 have been cancelled with the amendment filed on 5/22/2017.

The provisional double patenting rejection of claims 57-61 and 64 as being unpatentable over claims 1-7, 9-14, 16, 17, 21, 75, and 76 of copending Application No. 14/360,151 is withdrawn because the application claims do not recite SEQ ID NO: 5.

The rejection of claims 57-61 and 64 under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, is withdrawn because the recitation of vector genome has been deleted from claim 57.

The rejections of claims 1 and 7-10 under 35 U.S.C. 102(a)(1) as being anticipated by Gao et al. (J. Virol., 2004, 78: 6381-6388) and of claims 1-10 under 35

U.S.C. 102(a)(2) as being anticipated by Gao et al. (PGPUB 2016/0201088) are moot because claims 1-10 have been cancelled with the amendment filed on 5/22/2017.

2. Claim status is as follows:

Claims 1-56, 62, 63, and 67 have been cancelled.

Claims 57-61, 64, and 69-76 are allowable. The restriction requirement set forth in the Office action mailed on 5/12/2016, has been reconsidered in view of the allowability of claims to the elected invention pursuant to MPEP § 821.04(a). **The restriction requirement is hereby withdrawn as to any claim that requires all the limitations of an allowable claim.** Specifically, the restriction requirement of 5/12/2016 is withdrawn. Claims 65, 66, and 68, directed to nonelected inventions are no longer withdrawn from consideration because the claims requires all the limitations of an allowable claim.

In view of the above noted withdrawal of the restriction requirement, applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See In re Ziegler, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claims 57-61, 64-66, and 68-76 are allowable subject to the amendments below.

EXAMINER'S AMENDMENT

3. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in an interview with applicant's representative Robert Bedgood on 7/20/2017.

The claims are amended as follows:

Claim 60 is rewritten as follows:

The recombinant AAV particle of claim 57, wherein the genome of the recombinant AAV particle further comprises at least a portion of an intron.

Claim 61 is rewritten as follows:

The recombinant AAV particle of claim 57, wherein the genome of the recombinant AAV particle further comprises a filler or stuffer polynucleotide sequence.

Claim 65 is rewritten as follows:

A method for producing the recombinant AAV particle of claim 57, comprising culturing a helper cell comprising a recombinant plasmid comprising the genome of the recombinant AAV particle of claim 57.

Claim 66 is rewritten as follows:

A method of treating a subject in need of treatment for hemophilia B comprising administering to said subject a therapeutically effective amount of the pharmaceutical composition of claim 64.

Claim 69 is rewritten as follows:

A recombinant AAV (rAAV) particle comprising a VP1 capsid protein having the amino acid sequence of SEQ ID NO: 5, wherein the genome of said rAAV particle comprises, in 5′ to 3′ order:

(a) a first AAV inverted terminal repeat,

(b) a liver-specific enhancer and promoter,

(c) a polynucleotide sequence encoding a human Factor IX protein operably linked to the liver-specific enhancer and promoter,

(d) a poly-A sequence; and

(e) a second AAV inverted terminal repeat.

Claim 71 is rewritten as follows:

The recombinant AAV particle of claim 69, wherein said liver-specific enhancer and promoter is an ApoE-hAAT enhancer-promoter.

Claim 72 is rewritten as follows:

The recombinant AAV particle of claim 69, wherein said polynucleotide sequence encoding the human Factor IX protein further comprises at least a portion of an intron.

Claim 74 is rewritten as follows:

The recombinant AAV particle of claim 73, wherein said portion of intron I of human Factor IX has a nucleotide length of 0.1 kb to 1.7 kb.

Please add new claims 77-80 as follows:

Claim 77

A method of treating a subject in need of treatment for hemophilia B comprising administering to said subject a therapeutically effective amount of the pharmaceutical composition of claim 76.

Claim 78

The recombinant AAV particle of claim 69, wherein the human Factor IX protein is a variant more active than wild type human Factor IX.

Claim 79

The recombinant AAV particle of claim 78, wherein the human Factor IX protein variant is naturally occurring.

Claim 80

The recombinant AAV particle of claim 69, wherein the human Factor IX protein is a naturally occurring variant that retains activity of human Factor IX.

REASONS FOR ALLOWANCE

4. The following is an examiner's statement of reasons for allowance: the instant claims are free of the prior art of record. Specifically, the prior art of record does not teach the instant SEQ ID NO: 5 nor does the prior art of record render SEQ ID NO: 5 obvious.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher M. Babic can be reached on 571-272-8507. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ILEANA POPA/
Primary Examiner, Art Unit 1633

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	14338200
Filing Date	2014-07-22
First Named Inventor	Katherine High
Art Unit	1632
Examiner Name	POPA, Ileana
Attorney Docket Number	074659-0433284

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6156303	A	2000-12-05	RUSSELL et al.	
	2	6468524	B1	2002-10-22	CHIORINI et al.	
	3					

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20140323956	A1	2014-10-30	MENDELL et al.	
	2	20150273082	A1	2015-10-01	NATHWANI et al.	
	3	20110263027	A1	2011-10-27	GAO et al.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /I.P/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	14338200
Filing Date	2014-07-22
First Named Inventor	Katherine High
Art Unit	1632
Examiner Name	POPA, Ileana
Attorney Docket Number	074659-0433284

	4	20080044386	A1	2008-02-21	JI et al.		
	5	20080220015	A1	2008-09-11	ABINA		
	6	20090317417	A1	2009-12-24	VANDENBERGHE et al.		
	7	20100286242	A1	2010-11-11	BOHN et al.		
	8	20140271550	A1	2014-09-18	THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA		
	9	20160375110	A1	2016-12-29	THE CHILDREN'S HOSPITAL OF PHILADELPHIA		

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2011133933	WO	A2	2011-10-27	UNIVERSITY OF FLORIDA		
	2	2011133890	WO	A1	2011-10-27	UNIV OF MASSACHUSETTS		
	3	2007120542	WO	A2	2007-10-25	UNIV LELAND STANFORD JUNIOR		

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	14338200
Filing Date	2014-07-22
First Named Inventor	Katherine High
Art Unit	1632
Examiner Name	POPA, Ileana
Attorney Docket Number	074659-0433284

	4	2013123503	WO	A1	2013-08-25	THE CHILDRENS HOSPITAL OF PHILADELPHIA		
	5	2004027019	WO	A2	2004-04-01	WARRINGTON et al.		
	6	2013123457	WO	A1	2013-08-22	BIOGEN IDEC MA INC.		
	7	2013/158879	WO	A1	2013-10-24	THE CHILDRENS HOSPITAL OF PHILADELPHIA		

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T5
	1	MARTIN et al., Overexpression of Galgt2 in skeletal muscle prevents injury resulting from eccentric contractions in both mdx and wild-type mice, Am. J. Physiol. Cell Physiol., 2009, 296:C476-88 .	
	2	RODINO-KLAPAC et al., A translational approach for limb vascular delivery of the micro-dystrophin gene without high volume or high pressure for treatment of Duchenne muscular dystrophy, J. Transl. Med., 2007, 5(45):1-11	
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	5	CHIRMULE, N. et al., Humoral Immunity to Adeno-Associated Virus Type 2 Vectors Following Administration to Murine and Nonhuman Primate Muscle, Journal of Virology, 2000, 74(5):2420-2425	

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	9	WRIGHT, J.F. et al., Manufacturing and Characterizing AAV-Based Vectors for Use in Clinical Studies, Gene Therapy, 2008, 15:840-848	
	10	GUO et al., Protein Tolerance to Random Amino Acid Change, PNAS, 2004, 101(25):9205-9210	
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	12	MINGOZZI, F. et al., Overcoming Preexisting Humoral Immunity to AAV Using Capsid Decoys, Science Translational Medicine, 2013, 5(192-196):122-130.	
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	14	SCALLAN et al., Human Immunoglobulin Inhibits Liver Transduction by AAV Vectors at Low AAV2 Neutralizing Titers in SCID Mice, Blood, 2005, 107:1810-1817.	
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Examiner Signature	/ILEANA POPA/	Date Considered	05/31/2017

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CERTIFICATION STATEMENT

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☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Robert M. Bedgood/	Date (YYYY-MM-DD)	2017-05-22
Name/Print	Robert M. Bedgood	Registration Number	43488

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

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Examiner Name	POPA, Ileana
Attorney Docket Number	074659-0433284

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	1	KETTERLING, R.P., et al., The Rates of G:C->C:G Transversions at CpG Dinucleotides in the Human Factgor IX Gene, Am. J. Hum. Genet., 1994, 54:831-835
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REIVINDICACIONES MODIFICADAS

1. Un vector recombinante de AAV que comprende una secuencia de cápside AAV, encapsidando un genoma del vector que comprende una secuencia de polinucleótido heterólogo que codifica la proteína del Factor IX, y donde la secuencia de cápside de AAV comprende una proteína VP1 establecida como SEC ID NO:5.

2. El vector recombinante de AAV de la Reivindicación 1, donde el genoma del vector comprende además un elemento de control de expresión que confiere la transcripción de dicha secuencia de polinucleótido heterólogo que codifica la proteína del Factor IX.

3. El vector recombinante de AAV de la Reivindicación 2, donde el elemento de control de expresión comprende un elemento de control constitutivo o regulable.

4. El vector recombinante de AAV de la Reivindicación 3, donde el elemento de control de expresión comprende un elemento de control de expresión específica de tejido o promotor.

5. El vector recombinante de AAV de cualquiera de las Reivindicaciones 1 a 4, donde una o más de las secuencias de repetición terminal invertida (ITR) flanquean el terminal 5' o 3' de la secuencia de polinucleótido heterólogo que codifica la proteína del Factor IX.

6. El vector recombinante de AAV de cualquiera de las Reivindicaciones 1 a 4, donde el genoma del vector comprende además una secuencia de polinucleótido de relleno o embutidora.

7. El vector recombinante de AAV que comprende una cápside de AAV que encapsida un genoma de vector que comprende una secuencia de polinucleótido heterólogo, donde la cápside de AAV comprende una proteína VP1 que comprende la secuencia de aminoácido de SEC ID NO: 5, donde la secuencia de polinucleótido heterólogo codifica la proteína del Factor IX humano, y donde el genoma del vector comprende además un promotor o potenciador específico de hígado, y las repeticiones terminal invertida AAV flanquean los terminales 5' y 3' de la secuencia de polinucleótido heterólogo.

8. El vector recombinante de AAV de cualquiera de las reivindicaciones 1 a 7, donde la secuencia de polinucleótido heterólogo comprende además al menos una porción de un intrón.

9. El vector recombinante de AAV de la Reivindicación 8, donde el genoma del vector comprende además una secuencia de polinucleótido embutidora o de relleno.

10. Una composición farmacéutica que comprende el vector recombinante de AAV de cualquiera de las Reivindicaciones 1 a 9.

11. La composición farmacéutica de la Reivindicación 10, que comprende además una cápside AAV vacía.

12. El vector recombinante de AAV de la Reivindicación 7, que comprende un potenciador y promotor específico del hígado.

13. El vector recombinante de AAV de las Reivindicaciones 1 o 7, que comprende una secuencia Poli-A que flanquea el término 3' de la secuencia de polinucleótidos heteróloga que codifica para la proteína del Factor IX humano.

14. El vector recombinante de AAV de la Reivindicación 7, donde dichas repeticiones terminal invertida AAV son de AAV2.

15. El vector recombinante de AAV de la Reivindicación 7 o 12, en donde dicho potenciador o promotor específico del hígado es un ApoE-hAAT potenciador y promotor.

16. El vector recombinante de AAV de la Reivindicación 8, donde dicho intrón es la totalidad o una porción del intrón I del Factor IX humano.

17. El vector recombinante de AAV de la Reivindicación 16, donde dicha porción del intrón I del Factor IX humano tiene una longitud de nucleótidos entre 0.1 Kb a 1.7 Kb.

18. El vector recombinante de AAV de las Reivindicaciones 1 o 7, donde dicha secuencia del polinucleótido heterólogo está flanqueada por regiones 5' y 3' no traducidas.

19. El vector recombinante de AAV de las Reivindicaciones 1 o 7, donde la proteína del Factor IX humano es una variante más activa que la variante tipo natural del Factor IX humano.

20. La partícula recombinante de la Reivindicación 19, donde la variante de la proteína del Factor IX se presenta naturalmente.

21. El vector recombinante de AAV de la Reivindicación 1 o 7, en el que la proteína del Factor IX humano es una variante de origen natural que conserva la actividad del Factor IX humano.

LAG\LAG\ID-518664\WPC21563

Señor Director

DIRECCION DE NUEVAS CREACIONES

Superintendencia de Industria y Comercio

E. S. D.

Referencia: Expediente 16018865

Asunto: Solicitud de patente para: *VARIANTE AAV QUE COMPRENDE UNA SECUENCIA QUE CODIFICA PARA LA PROTEÍNA DEL FACTOR IX Y COMPOSICIONES Y MÉTODOS PARA TRANSFERENCIA DE GEN A CÉLULAS, ÓRGANOS Y TEJIDOS*

Solicitante: THE CHILDREN'S HOSPITAL OF PHILADELPHIA

Fecha de solicitud: 27 de enero de 2016

RESPUESTA A PRIMER EXAMEN DE PATENTABILIDAD

ANDRES RINCON USCATEGUI, identificado como aparece al pie de mi firma, en mi condición de apoderado de la sociedad solicitante de la patente de la referencia, doy respuesta al Oficio **10238**, notificado por fijación en lista el 17 de julio de 2017, para lo cual pedí plazo adicional el 10 de octubre de 2017.

I. MODIFICACIONES AL CAPÍTULO REIVINDICATORIO

En respuesta al examen de patentabilidad aporto un Capítulo Reivindicatorio modificado conformado por **21** reivindicaciones en las que se han incluido las siguientes modificaciones:

1. Se eliminaron las Reivindicaciones originales 2 a 7, 13, 14, 20 y 21.

2. En la Reivindicación 1 el fragmento: "*tiene una identidad sustancial a la secuencia de cápside VP1 establecida como SEC ID NO: 1 y tiene una sustitución de aminoácido A, V, P o N en las posiciones 195, 199, 201 o 202, de la secuencia de cápside VP1 establecida como SEC ID NO: 1"* fue sustituido por el fragmento "*la secuencia de cápside de AAV comprende una proteína VP1 establecida como SEC ID NO: 5".*

3. Se adicionaron las Reivindicaciones 12 a 21, las cuales se encuentran soportadas en la descripción de la siguiente manera:

- Reivindicaciones 12 y 15: Párr.170, Párr. 178, Párr. 96.
- Reivindicación 13: Párr. 17 y Párr.83
- Reivindicaciones 14 y 18: Párr. 101 y Párr.53
- Reivindicación 16: Párr. 105
- Reivindicación 17: Párr. 105
- Reivindicaciones 19, 20 y 21: Párr. 72 y Párr. 75.

Estas modificaciones se ajustan al Artículo 34 de la Decisión 486 de 2000, ya que no constituyen una ampliación de la protección que correspondería a la divulgación contenida en la solicitud inicial.

II. EN CUANTO A LA OBJECION DE SUPUESTA FALTA DE CLARIDAD DEL TITULO

Respondiendo a la observación del Examinador sobre la amplitud del título de la presente solicitud, se desea poner de presente que es deseo del solicitante modificarlo como sigue: ***"VARIANTE AAV QUE COMPRENDE UNA SECUENCIA QUE CODIFICA PARA LA PROTEÍNA DEL FACTOR IX Y COMPOSICIONES Y MÉTODOS PARA TRANSFERENCIA DE GEN A CÉLULAS, ÓRGANOS Y TEJIDOS"***. Así, el nuevo título refleja de manera precisa la materia a la que se refiere la invención y, en consecuencia, la objeción formulada a este respecto se ve superada.

III. EN CUANTO A LA SUPUESTA FALTA DE CLARIDAD DE LAS REIVINDICACIONES

1. Con respecto a la objeción del Examinador en contra de la Reivindicación 1, según la cual no es clara porque no define un vector recombinante de AAV con su secuencia, se desea poner de presente que el Solicitante no está de acuerdo con dicha objeción, pues cualquier persona medianamente versada en la materia sabría que hay múltiples secuencias del Factor IX, que adicionalmente ya han sido descritas por el arte previo y por tanto no sería necesario especificarlas por medio de su SEQ ID NO. De esta manera se considera superada esta objeción.

2. Con respecto a la objeción del Examinador en contra de las antiguas Reivindicaciones 1 y 2, según la cual estas no tienen sustento en la descripción porque no hacen referencia a la secuencia de la cápside VP1, se desea poner de presente que el Solicitante está en desacuerdo con el Examinador, sin embargo con el único fin de agilizar el trámite, el solicitante ha eliminado de la antigua Reivindicación 1 el fragmento: "*tiene una identidad sustancial a la secuencia de cápside VP1 establecida como SEC ID NO:1 y tiene una sustitución de aminoácido A, V, P o N en las posiciones 195, 199, 201 o 202, de la secuencia de cápside VP1 establecida como SEC ID NO: 1" y* en cambio ha especificado que "*la secuencia de cápside de AAV comprende una proteína VP1 establecida como SEC ID NO:5".* Adicionalmente, se ha eliminado la antigua Reivindicación 2 del Capítulo reivindicatorio modificado. Teniendo en cuenta las modificaciones anteriormente mencionadas, se debe dar por superada esta objeción.

3. Con respecto a la objeción del Examinador en contra de las antiguas Reivindicaciones 3 a 6, según la cual estas no eran concisas y adicionalmente no tenían sustento en la descripción, se desea poner de presente que tal y como se mencionó en el numeral I del presente memorial, estas Reivindicaciones fueron eliminadas y por tanto cualquier objeción sobre ellas deberá ser retirada.

4. Con respecto a la objeción del Examinador en contra de las antiguas Reivindicaciones 13 y 14, según la cual estas no eran claras y supuestamente carecían de sustento en la descripción, se desea poner de presente que tal y como se mencionó en el numeral I del presente memorial, estas Reivindicaciones fueron eliminadas y por tanto cualquier objeción sobre ellas deberá ser retirada.

5. Con respecto a la objeción del Examinador en contra de las antiguas Reivindicaciones 20 y 21, según la cual supuestamente dichas reivindicaciones reclamaban métodos terapéuticos de tratamiento, se desea poner de presente que aunque el Solicitante difiere de la afirmación del Examinador, con el único animo de agilizar el proceso, el Solicitante ha eliminado las mencionadas reivindicaciones y en tal sentido, cualquier objeción sobre ellas deberá ser retirada.

IV. ESTADO DE LA TÉCNICA

El Examinador determinó 3 documentos como relevantes para realizar el análisis de patentabilidad de la presente patente de invención:

1. D1, referido al documento CO1425304 titulado "*Composición y métodos para una transferencia génica altamente eficiente utilizando variantes de cápsides de aav*" que se relaciona con variantes de AAV que exhiben una eficiencia de transducción incrementada en comparación con serotipos de AAV (por ejemplo, AAV1, AAV2, AAV8, AAV rh74). Tales vectores son útiles para la transducción de una diversidad de tejidos, incluyendo hígado, músculo, cerebro y retina.

2. D2, referido al documento WO2013078400 titulado *"Virus vectors for highly efficient transgene delivery"* que se relaciona con formulaciones de vectores virales y métodos de uso de los mismos para la administración de transgenes o ácidos nucleicos terapéuticos a sujetos humanos. Las formulaciones incluyen un vector y cantidades adecuadas de cápsides vacías, cápsides que contienen un genoma viral o proteínas de cápside viral que están opcionalmente modificadas química o estructuralmente.

3. D3, referido al documento WO2013078316 titulado "*Recombinant adeno-associated virus delivery of alpha-sarcoglycan polynucleotides*" que divulga vectores recombinantes de (rAAV) y métodos de utilización de los mismos en el tratamiento de distrofias musculares de cinturas tipo 2D (LGMD2D).

V. EN CUANTO A LA SUPUESTA FALTA DE NOVEDAD

El Examinador considera que D1 es el arte previo más cercano a la presente invención, sin embargo el Solicitante desea aclarar que D1 solo describe sustituciones de Lys a Arg en las proteínas de cápside de determinado vector AAV, pero D1 no describe una cápside específica de AAV-Rh74 con residuo A en la posición 195, residuo V en la posición 199, residuo 201, y /o residuo N en la posición 202. En consecuencia la Reivindicación 1 modificada cumple el requisito de novedad a la luz del documento D1, así como sus reivindicaciones dependientes.

VI. EN CUANTO A LA SUPUESTA FALTA DE NIVEL INVENTIVO

El Examinador afirma que la reivindicación 7 carece de nivel inventivo a la luz de los documentos D2 y D3, sin embargo el Solicitante desea aclararle al Examinador lo siguiente:

1. El Examinador sostiene que la diferencia entre el vector recombinante de AAV que comprende una secuencia de cápside de AAV modificada definida en la Reivindicación 7, y el vector recombinante de AAV divulgado en el documento D2, consiste en que la secuencia de cápside AAV de la invención comprende adicionalmente una secuencia de cápside VP1 caracterizada según la SEQ ID NO: 5.

2. De acuerdo con el Examinador, el problema técnico que la invención trata de resolver se podría formular así: *¿Cómo modificar el vector recombinante de AAV divulgado en el documento D2 que comprende una secuencia de cápside AAV donde la partícula AAV encapsula un genoma del vector que comprende una secuencia de polinucleótida heteróloga que codifica la proteína del Factor IX, para incrementar los niveles de expresión del transgén del factor humano IX (FIX) a niveles terapéuticos?*

3. Respecto a las afirmaciones del Examinador, el Solicitante desea manifestar su desacuerdo, en primer lugar respecto al problema técnico a resolver, puesto que el Examinador asume que una persona medianamente versada en la materia se vería motivada a modificar la cápside de AAV8 con el fin de alcanzar el vector modificado de la presente invención, sin embargo, no presenta ningún argumento que indique la razón por la cual dicha persona podría partir de la cápside de AAV8 de D2, especialmente teniendo en cuenta que existen otros serotipos, como Rh10, que tienen mayor identidad de secuencia de cápside con Rh74 que AAV8. En tal sentido, cualquier persona con conocimiento medio en el tema se hubiera visto motivada a usar el serotipo con mayor identidad de secuencia en la cápside, como Rh10 y no AAV8 para solucionar el problema técnico planteado. De hecho, el Examinador usa como punto de partida la secuencia con menor identidad respecto a Rh74, como la proteína de cápside de AAV8 en vez de otra secuencia de cápside como Rh10 con mayor identidad de secuencia, lo cual es una evidencia clara de un análisis erróneo en retrospectiva del Examinador.

4. Por otra parte, el Examinador afirma que D3 supuestamente describe la modificación de la secuencia de cápside de AAV del serotipo AAV-8, caracterizada porque presenta un residuo A en la posición de aminoácido 195; un residuo V en la poción de

aminoácido 199; un residuo P en la posición de aminoácido 201, y un residuo N e la posición de aminoácido 202 (Pág. 5, Párr. [0017]–Fig. 1), la cual presenta un 94% de identidad y 100% de cobertura respecto a la SEQ ID NO: 5 reclamada en la solicitud (ver alineamientos). Dicha secuencia de cápside AAV modificada es útil en el desarrollo de un vector viral adenoasociado (AAV) mejorado, que exhibe una eficiencia incrementada de transducción de AAV que transporta transgenes clínicamente importantes en terapia génica (Pág. 4, Párr. [0012] – Pág. 26, Ejemplo 9).

5. Respecto a la afirmación del Examinador sobre D3, el Solicitante desea manifestar su desacuerdo, ya que el Examinador ha afirmado que en D3 la "*secuencia de la cápside de AAV modificada del serotipo AAV-8 está caracterizada porque tiene un residuo A en la posición de aminoácido 195; Un residuo V en la poción de aminoácido 199; un residuo P en la posición de aminoácido 201, y un residuo N es la posición de aminoácido 202*". Sin embargo, la secuencia de la cápside AAV8 en D3 NO es una secuencia de la cápside modificada, en cambio es una secuencia que ocurre en de manera natural. Además, en D3 no se menciona nada con respecto a la importancia de cualquier aminoácido en cualquiera de las posiciones 195, 199, 201 o 202. De esta manera, el hecho que el Examinador se enfoque únicamente en las posiciones es una clara evidencia de un razonamiento en retrospectiva.

6. Por otra parte, las secuencias de la proteína de la cápside de AAV de D2 y D3 son distintas de la SEC ID NUMERO 5 reivindicada. Por ejemplo, la propia alineación del Examinador de la cápside de AAV-8 de D3 frente a la SEQ ID NO: 5 revela más de 44 diferencias en los aminoácidos, cualquiera de los cuales podrían haber sido modificados. De esta manera, no hay indicio que sugiera que D2 o D3 anticipen a realizar las sustituciones particulares en las posiciones específicas de Rh74 para crear la SEQ ID NO: 5.

7. Así mismo, a pesar de la falta de orientación de D2 o D3 en cuanto a las 4 sustituciones de aminoácidos particulares sobre cápside de Rh74 en las posiciones particulares para crear SEC ID NO: 5, el Examinador resaltó los 4 aminoácidos en la alineación de AAV8 frente a SEC ID NO: 5. Aparentemente, el Examinador de alguna manera cree que el experto en la materia habría visto una alineación de secuencia entre la cápside AAV8 y la secuencia de la cápside Rh74 (lo cual, como se mencionó anteriormente no hubiera sido lo más esperado teniendo en cuenta la falta de identidad de las secuencias) y, por cualquier razón y a pesar del hecho de que hay más de 44 diferencias de

aminoácidos, el Examinador afirma que el experto medio en la materia se habría centrado en esos 4 residuos en esas 4 posiciones particulares y de alguna manera de la nada hubiera sabido hacer las 4 sustituciones específicas en las 4 posiciones específicas en la cápside de Rh74. Tal conclusión es simplemente insostenible a la vista de la ausencia de una guía en D2 y D3 que no dice nada sobre la importancia o relevancia de estas 4 posiciones en AAV8, ni cuál sería el efecto de la sustitución de los 4 aminoácidos en Rh74. Esto simplemente muestra que el Examinador está haciendo caso omiso de la falta de orientación de D2 y D3 y, en cambio, está partiendo de la divulgación de la presente aplicación para acercarse al arte previo, lo cual es claramente razonamiento retrospectivo inadmisible.

8. Finalmente, se le recuerda respetuosamente al Examinador que para cualquier persona versada en la materia es claro que el efecto de hacer sustituciones de aminoácidos en las proteínas de la cápside de AAV es impredecible. Así, un experto en la materia no habría sabido cuál es el efecto de hacer las 4 sustituciones en estas posiciones particulares con aminoácidos particulares en la cápside de Rh74. En consecuencia, el experto en la materia habría tenido que realizar experimentos sustanciales de ensayo-error para llegar a SEQ ID NO: 5 basado en D2 y D3, que nuevamente no proporcionan orientación en lo que respecta a la importancia o relevancia y mucho menos el efecto de hacer dichas 4 sustituciones de aminoácidos particulares en las posiciones específicas de Rh74 a crear SEQ ID NO: 5.

Teniendo en cuenta los argumentos y las modificaciones presentadas en el presente memorial, se concluye que los documentos citados como arte previo no anticipan la materia divulgada por la presente invención y tampoco serían suficiente para que una persona versada en la materia llegara al vector recombinante reclamado, y se le solicita respetuosamente al Examinador reconozca que la presente solicitud cumple a cabalidad con los requisitos de novedad y nivel inventivo.

Concesión de solicitudes equivalentes

El mérito investigativo de la presente invención ha sido reconocido por otras oficinas de patentes del mundo, las cuales han otorgado patentes para invenciones

equivalentes. Tal es el caso de la Oficina de Patente de Estados Unidos, las cuales han emitido una notificación de aceptación para la solicitud equivalente No. US 14/338,200.

A este respecto, deseamos poner de presente que si bien cada país es autónomo de conceder o negar una solicitud luego de la realización del estudio de fondo, es claro que el hecho de que la novedad y el nivel inventivo de una invención hayan sido reconocidos por varias oficinas a nivel mundial, es un indicio de la patentabilidad de la misma toda vez que (i) el estudio de novedad y nivel inventivo en todas las Oficinas de Patentes del mundo es realizado por personas con conocimientos técnicos en el área de interés que son consideradas personas idóneas para emitir conceptos sobre la patentabilidad de una invención y que (ii) los resultados de los exámenes de novedad o de patentabilidad efectuados respecto a solicitudes extranjeras pueden ser reconocidos como suficientes para acreditar el cumplimiento de las condiciones de patentabilidad de la invención, tal como se señala en el artículo 46 de la Decisión 486:

> *"Artículo 46.- La oficina nacional competente podrá requerir el informe de expertos o de organismos científicos o tecnológicos que se consideren idóneos, para que emitan opinión sobre la patentabilidad de la invención. Asimismo, cuando lo estime conveniente, podrá requerir informes de otras oficinas de propiedad industrial.*
>
> *De ser necesario, a efectos del examen de patentabilidad y a requerimiento de la oficina nacional competente, el solicitante proporcionará, en un plazo que no excederá de 3 meses, uno o más de los siguientes documentos relativos a una o más de las solicitudes extranjeras referidas total o parcialmente a la misma invención que se examina:*
> *a) copia de la solicitud extranjera;*
> *b) copia de los resultados de exámenes de novedad o de patentabilidad efectuados respecto a esa solicitud extranjera;*
> *(...)*

La oficina nacional competente podrá ***reconocer los resultados de los exámenes referidos en el literal b) como suficientes para acreditar el cumplimiento de las condiciones de patentabilidad de la invención****" (Negrilla fuera del texto).*

VII. PETICIÓN

Puesto que se ha dado respuesta a todas las objeciones formuladas por la Dirección de Nuevas Creaciones, solicito proceder al otorgamiento de la solicitud de patente.

VIII. ANEXOS

1. Capítulo Reivindicatorio modificado conformado por **21** reivindicaciones;
2. Notificación de aceptación de la solicitud estadounidense equivalente.

Señor Director,

ANDRÉS RINCÓN USCÁTEGUI

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