Request for Proposals (RFP) on improvement of recombinant AAV vector production for human gene therapy for the Accelerating Medicines Partnership® (AMP®) Bespoke Gene Therapy Consortium (BGTC)

A. FNIH RFP NUMBER: 2021-BGTC001	**B. DATE ISSUED:** December 2, 2021	
C. ISSUED BY:	**D. ADDRESS OFFERS TO:**	
FNIH 11400 Rockville Pike Suite 600 Bethesda, MD 20852	**D.1. HARD COPIES (if required):** Electronic Submissions Only	**D.2. ELECTRONIC COPIES:** BGTC@fnih.org
E. FOR INFORMATION REGARDING THIS SOLICITATION CONTACT:		
E.1. NAME: Brad Garrison	**E.2. EMAIL:** bgarrison@fnih.org	
IMPORTANT: **F.** To be considered for award, Offers must be received at the location specified in Block D.2. above by 11:59PM EST February 18, 2022. Offers must be clearly identified with the solicitation number provided in Block A above.		

The Foundation for the National Institutes of Health, a non-profit, 501(c)(3) charitable organization that supports the National Institutes of Health (NIH) in its mission to improve health by forming and facilitating public-private partnerships for biomedical research, is issuing a Request for Proposals (RFP) to support the Accelerating Medicines Partnership® (AMP®) Bespoke Gene Therapy Consortium (BGTC). The BGTC is executed by FNIH as a public-private partnership involving the NIH, the U.S. Food and Drug Administration (FDA), multiple pharmaceutical companies, non-profits and patient advocates and is dedicated to making gene therapy a reality for people with rare genetic diseases affecting populations too small to be viable from the current commercial perspective.

Despite the potential for substantial therapeutic impact, the limited access to bespoke, or tailor-made, gene therapy for such diseases has been recognized by pharmaceutical, academic, NIH and FDA leadership. Ongoing discussions to address this issue have focused on using well-established adeno-associated virus (AAV) vectors as the single delivery technology, and the ability to facilitate and generalize access and processes for the development of bespoke gene therapies. In order to accelerate and advance the scalability, reproducibility, and regulatory ability to deliver individualized, or "bespoke" gene therapies to ultra-rare patient populations, the BGTC will combine a mechanistic and functional understanding of AAV biology with a pilot clinical trial program manufacturing and testing AAV vectors in a more standardized fashion. The BGTC expects to use the research and clinical data to produce an operational playbook that invokes the use of streamlined templates, master regulatory files, and uniform production processes to inform and streamline future gene therapies. This model program provides a tremendous opportunity to impact patients with very rare diseases and offer hope for a pathway toward the commercial viability of these treatments.

Purpose

The overall goal for this RFP is to solicit proposals for assay development and other approaches that will advance efficiency in manufacturing of high-quality and high titer recombinant AAV (rAAV) vectors for gene therapy in humans through greater understanding of the viral life cycle and the molecular steps involved with generation of clinical grade recombinant rAAVvectors. Specifically, the BGTC Steering Committee is interested in applications proposing the development of high-throughput screening (HTS)-compatible assays for individual mechanistic steps in AAV vector production, which could be used in whole genome screens to identify optimization strategies for individual mechanistic steps in AAV vector generation. Applications proposing other approaches to substantially increase efficiency in manufacturing of high-quality and high titer recombinant AAV (rAAV) vectors for gene therapy will also be considered.

Background

Advancing the understanding of AAV biology as related to human gene therapy has been identified as an important pre-competitive area that could benefit from a focused public-private partnership. Many areas of AAV biology, such as viral genome packaging, virion assembly, virion release, cell fusion, intracellular transport, and the regulation of therapeutic gene expression, remain incompletely understood. It is thought that the efficiency in manufacturing of AAV therapies, as well as therapeutic efficacy in patients, could be substantially improved by a better understanding of AAV biology, and optimization of key mechanistic steps. This RFP (2021-BGTC001) is focused on developing methods to interrogate the biology of the host producer cells to increase the efficiency of producing high-quality clinical grade AAV gene therapy vectors. A companion RFP (2021-BGTC002) will focus on interrogating the biology of AAV in target cells to enhance therapeutic gene expression in patients.

Specific Research Objectives

This RFP solicits applications for proposals to substantially increase the efficiency of production of rAAV vectors for human gene therapy. The overarching technical objective for responses to this RFP within the scientific topic areas described below is to develop solutions which improve one or more steps in the recombinant AAV vector generation process. Standardization of the proposed solution or assay is critical, and the responses should outline the planned studies to be conducted to address this requirement. Submissions proposing the development of HTS-compatible assays must be designed such that assay(s) developed can be incorporated into existing NCATS screening capabilities by the conclusion of the term of the award. For further details, see Assay Development & Screening | National Center for Advancing Translational Sciences (nih.gov).

The topic area of investigation targeted by this RFP is improvement of recombinant AAV vector production for human gene therapy, which may include (but is not limited to) assays and other methods for research on and optimization of: AAV genome replication and processing for virion packaging; capsid production and assembly; packaging of viral genome to generate productive viruses; maximizing the ratio of full/empty capsids, transport and release of virus; factors in producer cells that influence the process of high-quality rAAV vectors (i.e. containing intact full-length therapeutic transgenes); and/or other approaches to substantially increase the efficiency of rAAV vector production to manufacture at scale for human gene therapy. HTS-compatible assays for one or more of the mechanistic steps described above are of particular interest. However, applications that propose novel, high impact approaches for improving rAAV vector production will also be considered.

In addition to overall scientific merit and rigor, review criteria will include the following considerations:

- For HTS assays, are they compatible with the NCATS HTS platform?
- For other approaches, is the work likely to result in substantially enhancing the efficiency of production of high-quality and high-titer rAAV vectors for human gene therapy?
- Is the approach scalable and compatible with use in a cGMP facility?
- Is the proposed work likely to result in communicable deliverables within the project period?

Additional funding considerations include:

- Availability of funds
- Current state of knowledge in the field at the time of funding
- Overall BGTC program balance and lack of overlap with other projects

Award Information

I. Funds Available and Anticipated Number of Awards

The number of awards and the amount per award is contingent upon the submission of a sufficient number of meritorious submissions and proper budget justification within the proposal.

II. Award Budget

Proposal budgets are limited to an amount up to $250,000 of direct costs per year for up to two (2) years and need to reflect the actual needs of the development of the proposed assay. Indirect costs (F&A) must be 15% or less. Proper scientific and budget justification will need to be provided for evaluation. The proposal review working group reserves the right to award at a lower amount than requested.

III. Award Project Period

The scope of the proposed assay work should determine the award project period. The request may be for up to two (2) years of funding. The earliest anticipated start date is April 1, 2022.

Eligibility Information

Organizations eligible to apply are:

- Private or public sector
- US-based or international
- Able to comply with the necessary AMP BGTC intellectual property, data sharing, and publication guidelines (AMP BGTC Principles can be found in Appendix 2).

Proposal and Submission Instructions

I. Submission Deliverables

Complete proposals will include:

- Proposal research plan, which should describe the information below, but more details can be provided in the proposal response template (Appendix 1):
  - Background, specific aims, preliminary studies (if applicable), research methods, other relevant supporting documents (optional)
  - For applications proposing HTS assays, address compatibility with NCATS intramural, facility assay criteria (https://ncats.nih.gov/preclinical/drugdev/assay#criteria) For projects not proposing the development of HTS assays, address the applicability and rationale for why the proposed approach would benefit the broader AAV manufacturing field, and how the approach could be used in a cGMP facility.
- Detailed budget that delineates (An example budget table can be found in Appendix 1)
  - Personnel
  - Reagents, materials, equipment, sample acquisition (if necessary)
  - Other requirements for work proposed
- Detailed budget justification
- Proposed project timeline
- Biosketches for the Principal Investigators.

II. Data, Publications and Intellectual Property

All applicants will be expected to comply with the AMP BGTC Principles that have already been established for the partnership. These are available in Appendix 2 and will be attached to any award agreements for those projects selected for funding.

III. Page Limit

Please keep your Research plan responses under 10 pages in length (single spaced, 11-point Arial or Times New Roman font), including figures and legends.
Biosketches for the Principal Investigators should not exceed 3 pages.
Further section length requirements are provided in Appendix 1.

IV. Award Reporting

For those proposals selected for award, the Principal Investigators on the award should expect to submit progress updates for the project every 6 months in a format that will be described in the award agreements.

V. Additional Information Required

Please provide any existing IP or patent information relevant to the assay that may affect its use in the partnership, or the banking of any resulting data funded by this effort in a public controlled access database for use after initial publication of the findings. Further guidance available upon request.

VI. Submission Instructions

Send responses via e-mail to BGTC@fnih.org with "2021-BGTC001 AAV Vector Production Proposal" in the subject line.

Key Dates

Submission Due Date: February 18, 2022, 11:59 PM Eastern Time

Targeted Submission Review Period: February 22, 2022 – March 18, 2022

Potential Oral Presentations from Finalists (*If Needed*): Date TBD
Applicants will be informed after initial review of proposals whether they will need to provide an oral presentation with the ability for Q&A to the BGTC Proposal Review Working Group

Targeted Award Announcement: April 2022
Applicants will be notified by email of the outcome of the RFP.

About the Foundation for the NIH
Established by the United States Congress to support the mission of the NIH – improving health through scientific discovery in the search for cure – the Foundation for the NIH is a leader in identifying and addressing complex scientific and health issues. The Foundation is a non-profit, 501(c)(3) charitable organization that raises private-sector funds for and manages a broad portfolio of unique programs that complement and enhance NIH priorities and activities. For additional information about the Foundation for the NIH, visit www.fnih.org.

Appendix 1

BGTC Recombinant AAV Vector Production RFP Submission Form

Title of Project		
Principal Investigator(s) (submitter) Name: Title: Submitting Organization: Address: e-mail: Tel: ***Co-investigator(s) (add more as needed)*** Name: Title: Submitting Organization: Address: e-mail: Tel:		
Submission Date:		
Time Period of Project:		
Project Total Budget:		
Internal Use Only		
WG Decision, Date:		
Steering Committee Decision, Date: *(if needed)*		
Executive Committee Decision, Date: *(if needed)*		

Section 1: Project Overview *(500 words maximum)*

Describe the assay to be developed, the clinical/scientific need for the assay, and the capability gap being addressed.

1.1 Specific Aims and Objectives

1.2 Project Deliverables/Outputs

1.3 Applicability *- Describe why this project is appropriate for the BGTC RFA, the pre-competitive nature of the project, and how the project is novel.*

- Include a brief description of other efforts known to the applicant to ensure non-duplication.
- Does the work proposed have scientific merit?
- Is the work proposed focused on developing assays or other methods to interrogate the mechanistic steps involved in production of rAAV vectors in order to substantially increase the efficiency of production of rAAV vectors for human gene therapy?
- Does the work proposed add to the work of the Bespoke Gene Therapy Consortium (i.e., is there overlap with other initiatives for the proposed work?)
- Is the work likely to stimulate additional activity leading to progress in understanding the life cycle of AAV? Other?
- Will the proposed work lead to communicable deliverables within the project period?

Section 2: Scientific Design *(2000 words maximum)*

2.1 Background and Supporting Data

- Including Precision, reproducibility, target tissue

2.2 ***Experimental Plan***

- Describe in detail the scientific strategy, design and logistics. Include how the study design will address the project goals and objectives.
- Describe in detail the experiments to be conducted
- Describe the type of data to be analyzed (retrospective and/or prospective)

2.3 ***Analytical Methods***

- Describe in detail analytical methods that will be used.
- Provide a statistical analysis plan.
- If any studies are designed to replicate preliminary data or findings from prior studies, please describe those clearly.

2.4 ***Technologies and Assays***

- Describe the current technologies or assays to be used in the project.
- If project is in Stage 3 or Stage 4, please provide analytical validation data for the assay(s) to be used.

2.5 ***Human/Animal Subjects***

- Will human participants or experimental animals be involved in this Project? If so, how?

Section 3: Data Sharing and Intellectual Property Management Plan *(1000 words maximum)*

Please note: Use of pre-existing IP and sharing of newly generated IP must comply with AMP BGTC Principles in Appendix 2.

3.1 Describe pre-existing intellectual property (IP) that could have a bearing on the project.

3.2 List any relevant existing patents and patent applications held by key participants in the project (include patent number, title, submission date).

3.3 Describe any new IP that may be generated.

3.4 Describe plans for risk management concerning:

- Data Use
- Data security
- Legal compliance

3.5 Describe plans for depositing data in the BGTC Data Portal or a similarly approved public database prior to initial publication.

Please note: Data sharing plans must comply with AMP BGTC Principles in Appendix 2.

Section 4: Timeline, Milestones, Deliverables and Budget *(1000 words maximum)*

4.1 Provide a timeline for deliverables, and an end date for the project.

4.2 Describe the milestones and how will progress on achieving them will be assessed.

- Describe any opportunities for interim feasibility assessment(s) based on Project progress.

4.3 Project Budget

- Please complete the high-level budget table (see next page) *in addition to* attaching a detailed budget justification explaining the need for the costs requested with detailed breakdown of costs. Submission will not be reviewed if both of these items are not included.

Category	% FTE	Year 1	Year 2	Total
Personnel				
List each FTE individually with their percentage				
Supplies				
Equipment				
Subcontracts				
List each individually				
Total Direct Cost				
Overhead (15% of direct costs in lines above)				
Total Project Costs				

4.4 Detail any existing funding relationships.

Section 5: Program Support *(500 words maximum)*

5.1 List key personnel, including names, titles, and role in the Project.

- List collaborators, advisors, and/or hired consultants outside the consortium. Include letters of support for each.

Section 6: Legal Agreements

6.1 Legal Agreements

- List any contracts, memoranda of understanding, grants, data or material transfer agreements that are likely to be necessary to execute the project plan.

Section 7: Provide a brief bio for each investigator in the project *(less than one page each)*

Attachments

Please attach detailed budget and justification.

Appendix 2

Accelerating Medicines Partnership®
Bespoke Gene Therapy Consortium Principles

Publications
This project will operate under a "team science" approach, and publications generated by the Steering Committee will have joint authorship. Specific publication strategies will be developed by the Steering Committee prior to project start, including proposal for lead authors and co-authors. All publications and data resources generated by recipients of BGTC funding must acknowledge BGTC investigators and/or funder(s) and be made publicly accessible within 6 months of publication. Specific publication strategies will be discussed with the BGTC Steering Committee as needed.

Intellectual property (IP)
Given its precompetitive research focus and commitment to making results of that research available as broadly and promptly as possible, it is not expected that BGTC will generate novel IP. BGTC research partners may use pre-existing IP of the other BGTC research partners for work done under the partnership. BGTC research partners agree not to file patent applications on research discoveries made under the partnership, except in the rare instance when a consensus of FNIH and the BGTC agree that it is in the best interests of the partnership and public health to do so. IP developed under NIH awards are subject to applicable Federal law, regulation, and policies.