

Growing Gene and Cell Therapy (GGACT) Cooperative Project Support Application Instructions

Round Three DEADLINES

Letter of Intent: April 2, 2018

Final applications: June 25, 2018

Notification of support: late August 2018

Please submit LOI's and applications to
maria.suarez@childrens.harvard.edu

For questions regarding these instructions, please contact maria.suarez@childrens.harvard.edu

A. Background: Gene and cell therapies, especially for rare diseases, require complex product-specific development of pre-clinical studies, costly GMP manufacturing, unique laboratory assays for monitoring, and extraordinary regulatory management to initiate, perform, and oversee clinical trials that provide initial assessments of safety and efficacy. Due to the rarity of many serious and life-threatening genetic diseases in the pediatric population, an increasing number of which may be curable using emerging gene and cell therapy approaches, a significant barrier to translation of these innovative therapies and future gene editing approaches is the complex regulatory environment involving biologicals and early phase human studies in children. With the recent successes in curative treatments of several monogenic diseases and emergence of cellular immune therapies in cancer, a key next step in the dissemination of these therapeutic applications is broadening the number of centers participating in foundational pediatric clinical trials utilizing these approaches.

The overall goal of the **Growing Gene and Cell Therapy (GGACT)** cooperative is to support investigators to rapidly translate complex gene and cell therapies to early phase, investigator-initiated clinical trials. The founding collaborative centers (Boston Children's Hospital, Cincinnati Children's Hospital Medical Center, and the University of California Los Angeles) have a history of working together to implement pioneering gene and cell therapy pediatric trials. Their collective experiences have required the development of both expertise and significant infrastructure at each institution that focuses on preclinical models of disease and testing, process development, GMP vector production and cellular manufacturing, protocol development and implementation, trial and data management, and regulatory expertise that is specifically focused on early phase biologics in a manner suitable for transferring to industry for later phase studies.

GGACT is supported by NIH/NCATS U01TR001814.

B. Support Services Available: *(note: while our cooperative can offer support in many ways, we do not offer direct financial project support or financial support for clinical trials).*

- 1) **IND-enabling pre-GMP process development guidance.** The translation from the bench to the clinic requires performing a series of laboratory studies of increasing rigor from proof-of-principle, pre-clinical studies that may support pre-IND discussion with FDA, to formal IND enabling efficacy and toxicology studies. Investigators can be assisted in planning these studies and introduced to the appropriate resources; however, direct support for *in vivo* animal work is not available under this RFA.
- 2) **Pre-GMP vector production and transduction manufacturing process and product development.** Technologies for vector and cell manufacture in support of gene therapy clinical trials require processes, equipment, and facilities that are vastly different from those applicable to research

laboratories. We will provide a collaborative platform to facilitate bench-to-bedside translation of clinical manufacturing of HSC-based gene and cell therapies for pediatric diseases.

- 3) **Trial-supporting assay development/implementation.** Translation of a gene therapy trial proposal to implementation is hampered by lack of support for the development and standardization of trial-supporting assays. We can support trial investigators with assay development.
- 4) **Regulatory pathway planning and assistance.** Experimental gene and cellular therapies are subject to specific regulatory oversights that can present a significant barrier to inexperienced sites. We will provide seasoned regulatory assistance via access to a regulatory affairs professional who is experienced in the nuances of gene therapy regulatory filings.
- 5) **Development of reliance agreements to allow rapid implementation of new protocols via a simplified IRB review process.** The creation of a designated pediatric gene therapy IRB and the use of a single IRB will assure the highest quality gene therapy human research and will improve efficiency of review and minimize regulatory burden.
- 6) **Assistance in clinical trial protocol development, implementation and data management including packaging of data for potential licensing opportunities.**
- 7) **Assistance in clinical trials compliance, monitoring and reporting.**

C. Eligibility and Selection Criteria: Applications will be accepted from faculty members at CTSA institutions that also have established pediatric stem cell transplant programs. Corporate sponsored trials funded by NIH SBIR/STTR mechanisms to be conducted at CTSA institutions are fully eligible. While other corporate-sponsored trials conducted at CTSA institutions are eligible for support, preference will be given to NIH-funded trials, trials supported by patient advocacy groups, or public-private partnerships. Special terms and conditions may apply to corporate-sponsored trials.

Project review, selection, and prioritization will be done based on the following criteria:

- **Significance:** the relevance to rare pediatric diseases (fulfill an unmet clinical need) and impact of the proposed therapy (e.g. is it likely to be an improvement over standard of care?).
- **Rationale/scientific merit:** the project must have a compelling rationale and strong supporting preliminary data including proof of concept studies.
- **Feasibility:** the sponsor/principal investigator's qualifications, commitment, and available resources to support initiation and completion of the project.

D. Process: The initial application will consist of a two-page Letter of Intent (LOI). The LOI will be screened to examine if the proposed research project supports the goals of the cooperative and to verify which support services are requested. The screening process will be performed by the Joint Steering Committee, with final approval by the Executive Committee. Following the initial screening, the committee may request a phone call to discuss the project or provide feedback. An invitation will be sent to selected investigators to submit a full application.

Full applications will undergo reviews by the Translational Technical Steering Committee and the Regulatory Steering Committee, both of which will submit their recommendations to the Joint Steering Committee for final selection.

E. Letter of intent: For project proposals, the LOI consists of the application face page (see page 5) and a two-page description of the research design and methods, support services requested, current grant support (including NIH funding), and whether the project has undergone RAC and FDA review. Please also include any competing and/or complimentary conflict of interest with members of the GGACT cooperative¹.

All LOIs must be submitted to maria.suarez@childrens.harvard.edu. An email confirmation of receipt will be returned to the applicant. **The LOI must be received by 5:00pm ET on Monday, April 2nd, 2018.**

F. Full applications (must be invited following review of LOI): *Invited*, full applications must be submitted in single spaced text, one-half inch margins, and no smaller than an 11-point font. Arial or Helvetica typeface is preferred. The primary applicant's name must appear in the upper right-hand corner of each page. **Proposal text (H. 7. A-C, below) must be limited to five pages (including figures but excluding references).** Standard PHS 398 forms for biosketch, other support, and resources should be used.

Required format: Applications must be submitted electronically as a compiled PDF file to maria.suarez@childrens.harvard.edu

The complete application must be received by 5:00pm ET on Monday, June 25th, 2018.

G. Award Terms

The following terms and conditions apply to projects selected for support by the GGACT cooperative.

Users Steering Committee

A representative from the supported project/trial will be appointed to the Users Steering Committee (USC). The USC will meet on a regular (monthly or quarterly) basis and members will be expected to attend at least 75% of those meetings.

Progress reporting requirements

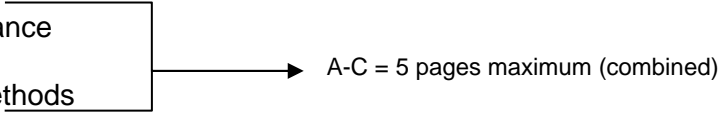
In addition to regular progress updates during USC meetings, the support recipient PI(s) will be required to submit annual reports documenting their progress and accomplishments as well as their future plans for the project.

Publication requirements

Any publications resulting from the project/trial being supported by the GGACT cooperative should make mention of the support in the acknowledgements section.

¹ GGACT Committee Members - BCH: David Williams, Alessandra Biffi, Sung-Yun Pai, Myriam Armant, Colleen Dansereau, Cindy Williams; CCHMC: Laura Weisel, Lilith Reeves, Scott Witting, Jose Cancelas, Dawn Lowe-Gooden, Bill Swaney, James Heubi; UCLA: Don Kohn, Kit Shaw, Sally Shupien, John Adams; NIH NCATS: PJ Brooks

H. Composition of project support proposal: Invited proposals should include:

1. Face page (signed by your institution's Office of Sponsored Programs)
 2. Abstracts (scientific and lay)
 3. Tables of contents
 4. Biosketch(es) (include PI and Co-Investigator; use PHS 398 form)
 5. Other support (PHS 398 form)
 6. Resources (PHS 398 form)
 7. Research Plan
 - A. Background and Significance
 - B. Preliminary Results
 - C. Research Design and Methods
 - D. Project Timeline/Gantt chart
 - E. Literature cited
 8. Cooperative/Contractual Arrangements (*if applicable*)
 9. Statement on any conflict of interest with reviewers (*if applicable*)
 10. Letters of support from collaborators or consultants
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If you have any of the following, even in draft form, please add as appendix (pdf) to help with the review and assessment of project status:

Appendix:

11. Target Product Profile
12. Clinical Trial Protocol
13. Clinical trial budget
14. Informed Consent Document(s)
15. Investigator's Brochure
16. IRB application with reviewer comments OR approval letter
17. IBC application with reviewer comments OR approval letter
18. Other review committees (CTSI, Institutional Scientific Peer Review Committee DSMB, etc.)
19. NIH RAC Appendix M
20. FDA communications (pre-IND application/meeting minutes)
21. Other documents for reviewer consideration

**GGACT Support Application
Face Page**

1. Title of project:

2. Principal Investigator
 - a. Name and Degree(s):
 - b. Position title:
 - c. Institution:
 - d. Department/Division:
 - e. Mailing address:
 - f. Email address:
 - g. Phone number:

3. Co-Investigator
 - a. Name and Degree(s):
 - b. Position title:
 - c. Institution:
 - d. Department/Division:
 - e. Email address:
 - f. Phone number:

4. Support Services requested (check all that apply):
 - IND-enabling pre-GMP process development assistance
 - Pre-GMP vector production and transduction manufacturing process and product development
 - Trial-supporting assay development/implementation
 - Regulatory pathway planning and assistance
 - Development of reliance agreements
 - Assistance in clinical trial protocol development, implementation and data management
 - Assistance in clinical trials compliance, monitoring and reporting

5. Signatures: *The undersigned reviewed this application for GGACT cooperative support and are familiar with the policies, terms, and conditions concerning support and accept the obligation to comply with all such policies, terms, and conditions.*
 - a. Signature of Principal Investigator: _____
 - b. Signature of Co-Investigator: _____
 - c. *Signature of Institutional OSP: _____

**OSP signature required for full applications only*

Principal Investigator (Last, First, Middle):

Scientific Abstract: Using technical language, briefly describe the proposed project in 200 words or less.

Lay Abstract: Using non-technical language, briefly describe the proposed project in 100 words or less.

Principal Investigator/Program Director (Last, First, Middle):

GENE GROWING AND CELL THERAPY Cooperative
Full application

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Biographical Sketch – Principal Investigator (<i>use current PHS 398 form</i>)	
Other Biographical Sketches (<i>PHS 398 form</i>)	
Other Support (<i>PHS 398 form</i>)	
Resources (<i>PHS 398 form</i>)	
Research Plan	
A. Background and Significance..... <i>A-C: not to exceed 5 pages combined</i>	
B. Preliminary Results.....	
C. Research Design and Methods	
D. Project Timeline/Gantt chart	
E. Literature Cited	
Cooperative/Contractual Arrangements (<i>if applicable</i>).....	
Statement on any conflict of interest with reviewers (<i>if applicable</i>).....	
Letters of Support from collaborators/consultants	

Check if Appendix is included

Appendix

Other items (list):

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