Program Name: Cure CF Columbus Research & Development Program (C3RDP) – Pilot & Feasibility Studies Request for Applications (RFA)

Brief Program Overview/Description: Cure CF Columbus (C3) Research Development Program (RDP) supports and promotes groundbreaking research and clinical cystic fibrosis-related activities with individuals located at The Ohio State University and Nationwide Children's Hospital, and subsequently applies this knowledge for the development of new therapeutic strategies to better arm host defense that combat infection.

Mission Statement: Excessive inflammation and recurrent infections are a hallmark of cystic fibrosis pathophysiology. The C3RDP mission is to develop treatments that prevent this pathophysiology. The C3RDP will pursue its mission through investigation of the cellular and molecular mechanisms that underlie inflammation and infection in people with CF.

Our goals for the C3RDP are:

1. To facilitate new collaborations among CF researchers
2. To foster a strong network of CF and non-CF researchers worldwide
3. To expand the C3 RDP community through recruitment of new investigators and trainees/future investigators

The values of diversity, equity and inclusion are integral to the success of the C3 community. The C3RDP commits to fostering diversity in research by recruiting investigators of different scientific disciplines but also of diverse social backgrounds.

Funding Amount: Funding of up to **$125,000** per year per project may be requested (indirect costs are not allowed) for up to a two (2) year period.

Key Dates (Contingent on RDP renewal)

RFA Release date	**October 18, 2023**
Grant Application Deadline	December 11, 2023, at 5 pm EST
Revisions Submitted (if necessary)	Jan 12, 2024, at 5 pm EST
Award Notifications	June 2024
Earliest Project Start Date	July 1, 2024
Award Period	July 1, 2024—June 30, 2025

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C3RDP Pilot and Feasibility Program

C3 is committed to support CF investigators and provide Pilot & Feasibility (P&F) grants to encourage robust cystic fibrosis clinical and basic science research. While our focus area is on the impact of immune dysfunction on infection in CF, topics broadly related to CF are also of interest.

Our goal is to utilize RDP funds to support new or established investigators from diverse basic or clinical science disciplines who plan to apply their expertise to the problems of CF. Investigators should use P&F funding to obtain the preliminary data that is needed to successfully compete for longer-term, more substantial funding from agencies such as the Cystic Fibrosis Foundation, National Institutes of Health (NIH), or other sources.

P&F grant applications must focus on basic and/or translational research questions that: 1) are relevant to the CFF and C3 research missions; and 2) address C3 research priority areas (below). The proposed research must utilize at least two of the three C3 Research Cores (see attached links). The P&F applications will be reviewed, and the applicants may be required to submit a revised P&F application. All P&F applications will be reviewed by the C3 Internal Advisory Board.

Funding

Basic Science P&F Projects: Funding of individual basic science P&F studies cannot extend beyond two years. Year 1 funding (**$125,000** max) will be provided by C3 after completion of the RDP review process. Appointed awardees may apply for a second year. However, second year applications will be reviewed alongside with those submitting new proposals. The second year of funding ($125,000 max) is contingent upon submission and approval of a renewal progress report and the availability of funds. No indirect costs will be provided.

Translational P&F Projects: These projects seek to apply basic scientific knowledge to a clinical problem, acquire basic knowledge from clinical specimens, or examine the feasibility of a therapeutic approach in an appropriate animal model or with appropriate clinical specimens. Translational P&F projects may receive funding for up to two years. Year 1 funding (**$125,000** max) will be provided by C3 after completion of the RDP review process. Appointed awardees may apply for a second year. However, second year applications will be reviewed alongside with those submitting new proposals. Year 2 funding ($125,000 max) is contingent upon submission and approval of a renewal progress report, and the availability of funds. No indirect costs will be provided.

Translational P&F projects may not subject human volunteers to experimental medicines, devices, or techniques; obtain clinical specimens prospectively unless such specimens are collected as a part of routine patient care; or make use of Health Insurance Portability and Accountability Act-protected confidential patient information.

Direct costs may be requested for:

- Salary support
- Research supplies
- Equipment
- Research-related subject costs
- Consultant costs
- Support for multidisciplinary collaborations, including travel
- Travel costs for scientific/technical meeting(s)

Eligibility

The following applicants are eligible for P&F funding:

1. New investigators who have not previously received a CFF research grant
2. Established non-CF investigators who are applying their knowledge and expertise to a CF-related question
3. Established CF investigators who are addressing novel and innovative concepts not currently being pursued by current and past researchers.
4. Applicants must be independent investigators (an individual who is out of fellowship training and whose institution allows them to submit applications for research funding as a Principal Investigator).
5. Studies proposed by new investigators and/or established investigators who have experience in an area related to CF, but are new to CF, should be prioritized. In some cases, this may represent applying techniques, methods, approaches, or theories from other fields to the problems of CF.
6. Studies proposed by established CF investigators who wish to develop and/or test a new approach that is not an extension of their ongoing research and represents a fundamental shift in research effort.

General eligibility criteria:

1. United States residents and applicants outside of the United States are welcome to apply.
2. Applicants cannot hold multiple P&F awards.
3. International applicants and institutions are required to submit additional information in accordance with USA Patriot ACT and the U.S. Department of Treasury Anti-Terrorist Financing Guidelines.
4. Institutional protections including Animal Care and Use, and Institutional Review Board protocols must be in place at the time that the full RDP Grant application is awarded.

Current CF and C3RDP priority areas:

Investigators working in the following areas are particularly encouraged to apply for consideration:

- Developing novel means for repairing and/or replacing the mutant CFTR.
- Evaluating outcomes of inserting a CFTR "superexon" or cDNA into the native locus with particular emphasis on gene regulation, expression, and transcription termination.
- Developing and optimizing the chemistry and formulation of nucleic acid delivery vehicles, both viral and non-viral, that can target disease relevant cells and tissues.
- Characterization of cellular targets for CFTR correction, including airway progenitor cells and other affected epithelial tissues (biliary tract, GI tract, pancreas).
- Characterizing and validating potential targets that regulate CFTR mRNA stability and translation, which includes understanding the pathways and mechanisms that regulate nonsense mediated decay (NMD), premature termination codon (PTC) recognition, splicing, and translation termination.
- Evaluating codon optimization strategies to enhance CFTR protein longevity, stability, and function.
- Understanding of how modulators impact disease pathogenesis across all stages of life as well as the cellular and molecular changes that cannot be reversed by modulators, which may include direct and indirect influences of CFTR modulation on the airway milieu, including resident pathogens, inflammation and inflammatory cell function, mucin structure (tethered and secreted), airway surface liquid (ASL), and mucociliary clearance (MCC), as well as extrapulmonary manifestations.

- Biological mechanisms involved in chronic lung allograft dysfunction (CLAD), rejection and transplant immunology.
- Improved understanding of acquisition, detection, pathogenesis, host-pathogen interactions, and treatment approaches for difficult to treat CF infections (i.e., NTM, MDR Pseudomonas, MRSA, Aspergillus, Burkholderia, Stenotrophomonas). *
- Approaches to understand and treat nutritional deficiencies and CF-related GI complications, including intestinal, pancreatic, and hepatobiliary disease across the lifespan.
- Effects of endocrine system dysfunction in CF, especially projects focused on biological underpinnings of Cystic Fibrosis Related Diabetes (CFRD), CF bone disease, and sexual & reproductive health.

**Projects focused on individual pathogens not listed above or that solely explore basic biology of pathogens that will not have direct applicability to the development of new treatment strategies or improve outcomes for people with CF may be deprioritized for funding.* Infection/microbiology-focused applications should utilize clinically relevant strains and specimens or address host responses to the organism as part of the application.

Letters of Reference:

Letters of Reference for Junior Investigators*: CFF defines "junior investigator" as any individual who has not received a CFF/CFFT Research Grant or NIH equivalent (e.g., R01, R21, R23) as a Principal Investigator AND is within their first five years of their first academic appointment at the level of Assistant Professor or equivalent. Applicant is NOT considered a junior investigator if they meet one or more of the below criteria:

- More than five years after their first academic appointment at the level of Assistant Professor (or equivalent)
- Has received a CFF/CFFT Research Grant or NIH equivalent (e.g., RO1, R21, R23)
- Has been promoted to Associate Professor or higher

Letters of Reference for junior investigators must be submitted by the following individuals:

- The Chair of the Applicant's Department at the Applicant Institution – The letter of reference from the Department Chair should indicate the release of sufficient space and facilities for the work described, as well as guarantee the time commitment of the investigator to the project. If the applicant is currently a fellow, the letter of reference should include confirmation of the pending faculty-level appointment.
- At least two (2) other individuals familiar with the applicant's scientific interests and abilities.

Letters of Reference must be submitted to PulmonaryGrants@NationwideChildrens.org prior to submission of the application.

Abstracts/Relevance

Please provide a statement of no more than 2,000 characters (including spaces) explaining the subject of the research proposal and its relationship to CF. Two different abstracts are required, as follows:

- **Lay Abstract:** This statement will be used to inform the non-scientific departments of CFF and the general public of the nature of this work. Applicants should not include any confidential or proprietary information, including intellectual property, in the lay abstract.
- **Scientific Abstract:** This statement will be used to inform the scientific community.

- **Summary of Relevance to CFF mission:** All applications are reviewed and scored not only on scientific merit but also on relevance to CFF's mission:

The mission of the Cystic Fibrosis Foundation is to cure cystic fibrosis and to provide all people with CF the opportunity to lead long, fulfilling lives by funding research and drug development, partnering with the CF community, and advancing high-quality, specialized care.

Provide a statement of no more than 3,000 characters (including spaces) summarizing the relevance of the proposed research to the health and well-being of CF patients, for a scientific audience who may or may not have a background in the subspecialty of the proposed research.

Budget

- Salaries & Benefits - List the names and positions of all professional and non-professional personnel involved in the project, whether or not salaries are requested. Indicate the percent of effort per week on the project for professional personnel. For each individual, list dollar amounts separately for institutional base salary and fringe benefits. In accordance with National Institutes of Health (NIH) policy, the institutional base salary used to calculate salary requests for of an individual may not exceed the current federal salary cap of $212,000. Fringe benefits may be requested if they are treated consistently by the applicant institution as a direct cost to all sponsors.
- Consultant Costs - Give the name and institutional affiliation of any consultant who has agreed to serve in this capacity. In the budget justification, briefly describe services to be performed, the number of days, rate of compensation, per diem and any other associated costs.
- Major Equipment – List all items of equipment greater than $5,000 requested and the cost of each item. If funds are requested to purchase equipment that is equivalent to items listed under "Facilities Available," justify the duplication. Justify any item of equipment for which the need may not be obvious.
- Travel - Describe the purpose of any travel being requested. Please note: For North American applicants, expenses for travel outside the North American Continent, including travel to Hawaii, Puerto Rico, and other U.S. territories are not allowable expenses without prior written approval from the CFF GCMA Office. Applicants are encouraged to attend the North American CF Conference each year to present their work, therefore Key Personnel on Pilot and Feasibility studies, may charge actual costs to attend the North American CF Conference the grant. All other travel expenses are capped at $1,500 per person per year. Registration fees associated with conferences are in addition to this allowance should be listed under "Other Expenses" category below.
- Consumable Supplies - Itemize supplies e.g., glassware, chemicals, animals, in separate categories and give the estimated cost of each category. If animals are involved, state the number, unit purchase cost, and unit care cost.
- Major Equipment - List all items of equipment greater than $5,000 requested and the cost of each item. If funds are requested to purchase equipment that is equivalent to items listed under "Facilities Available", justify the duplication. Justify any item of equipment for which the need may not be obvious.

- Other Expenses - Itemize other expenses by major categories, such as duplication costs, publication costs, minor equipment (under $5,000), computer charges, conference registration fees, etc.
- Subcontractors Summary – If applicable, detailed budgets and budget justifications for each subcontract must be provided for each year of support.
- Negotiations of subcontracts are between the applicant institution and the subcontractor.
- Indirect Costs – Indirect costs are not allowable for the RDP program.

Full Application

Download the available templates applicable to the project, submit the completed templates, as well as the additional application components as outlined below. All documents must be submitted in PDF format to the corresponding attachment types within this section. Templates available for download include:

- Budget Justification
- Facilities Available
- Biographical Sketch (NIH Format)
- Other Support (NIH Format)
- Research Plan
- Names and Addresses of References

BUDGET JUSTIFICATION

Describe the facilities and equipment available at the applicant's organization that will be used for this project, such as laboratory, clinical, animal, computer, office, etc. Provide any additional information about the environment, including any support services available that will be utilized. Describe their pertinent capabilities, proximity and anticipated extent of use. If facilities or equipment at a consultant's or collaborative site will be used, they should be identified and clearly described. There is no page limit. Use continuation pages, if necessary.

FACILITIES AVAILABLE

Describe the facilities and equipment available at the applicant's organization that will be used for this project, such as laboratory, clinical, animal, computer, office, etc. Provide any additional information about the environment, including any support services available that will be utilized. Describe their pertinent capabilities, proximity and anticipated extent of use. If facilities or equipment at a consultant's or collaborative site will be used, they should be identified and clearly described. There is no page limit. Use continuation pages, if necessary.

BIOGRAPHICAL SKETCHES OF KEY PERSONNEL

Complete and submit an NIH Biographical Sketch for all key project personnel, beginning with the Applicant/Principal Investigator. (CFF defines "key project personnel" as any individual with an advanced degree that will play an instrumental role in the activities of the project.) **Do not exceed five (5) pages per person**. A sample NIH Biographical Sketch is available for download on proposal CENTRAL. (Note: Each Principal Investigator must submit Biosketches for key personnel with their Pilot or Core application)

OTHER SUPPORT

Complete and submit the Other Support form, for all key project personnel, beginning with the Applicant/Principal Investigator. (CFF defines "key project personnel" as any individual with an advanced degree that will play an instrumental role in the activities of the project). There is no page limitation. (Note: Each Principal Investigator must submit Other Support for key personnel with their Pilot or Core Research application.)

RESEARCH PLAN

Page limit: **Six (6) single-sided pages**, not including the Literature Cited. Applications exceeding this page limit will not be reviewed. Type the PI's name in the space available in the header of the document. The template available will track page numbers at the bottom.

- Include sufficient information to permit effective review without reference to previous applications. Information should be presented in a clear and concise manner, while being specific and informative.
- Key figures and legends must be included in the Research Plan and should be of sufficient quality and size to be evaluated by the reviewer.
- If the application is a resubmission of an earlier one, revisions must be clearly indicated by a change in font, bolded or underlined. CFF will not review resubmissions that have not been revised.
    a) Hypothesis and Specific Aims: State concisely and realistically the intent of the proposed research and the hypothesis to be tested. The specific aims should be relevant to the mission of the Cystic Fibrosis Foundation. Do not exceed one page.
    b) Background and Significance: Describe the background. Critically evaluate existing knowledge and specifically identify the gaps that the project is intended to fill. Concisely state the importance and rationale of this research by relating the specific aims to longer-term objectives. This section should also show the potential importance of the proposed work to CF, in particular those areas listed as areas of special interest to CFF. In addition, describe the relationship of the proposed work to your long-term career goals. Preference will be given to applicants who express an interest in a long-term career in CF-related research.
    c) Preliminary Results: If applicable, provide a detailed discussion of any preliminary results.
    d) Experimental Design and Methods: Provide a detailed discussion of the experimental design and methods to be used to accomplish the specific aims. Describe the protocols, including methods for new techniques, and explain potential advantages over existing methodologies. Discuss the data expected to be obtained and the means by which data will be analyzed and interpreted. If clinical samples are included in the research plan, provide details of the methods for patient selection. Discuss potential pitfalls and/or limitations of the proposed procedures and alternative approaches to achieve aims. Point out any procedures, situations or materials that may be hazardous to personnel or patients and the precautions to be exercised. Since Pilot and Feasibility Awards are reviewed by CFF's Research and Research Training Committee, applications that include methodologies requiring sampling of materials from human subjects will only be considered under this mechanism if the sampling method constitutes minimal patient risk (e.g., venipuncture, nasal cell brushing) and patient samples or data are anonymous.

Describe the level of risk and measures taken to assure patient anonymity to the PI and other professional personnel, unless the PI or other professional personnel are care providers. Note: Observational and interventional studies involving human subjects cannot be supported through this program.

e) Consultant Arrangements: If the proposed project includes consultant arrangements and/or collaboration with other individuals outside the applicant's group, describe the working relationships and support this description by letter(s) of intent signed by collaborating individual(s). If clinical material required by this award is to be furnished by other individuals, include a statement from these individuals agreeing to their participation and precautions taken to ensure anonymity of patients.

f) Literature Cited: References should be numbered in the sequence that they appear in the text and listed at the end of the Research Plan. Each citation must include the names of all authors, title, the name of the journal or book, volume number, page number and year of publication (titles are optional).

APPENDICES

Appendices are restricted to the following categories:

- Up to three (3) reprints of the applicant's work relating to the general area of research in the grant proposal may be submitted in PDF format.
- Letters of Support and/or Collaboration: A Letter of Collaboration from Co-PI's, if any, should be submitted and included in the application. Investigators new to CF research are encouraged to consult/collaborate with an established CF investigator/clinician at their own institution or another. The letter from the collaborator/consultant should be explicit as to how the proposed work is relevant to CF and how he/she will assist the investigator new to CF research.
- Certification of IRB approval, or statement indicating a pending approval and anticipated date. Other applicable organization assurances documents such as IACUC and IBC Approval Letters.

Keep in mind that extensive appendix materials may not be reviewed. Please submit only the most relevant documentation.

*Organization Assurances & Certifications

CFF requires, as applicable, that all U.S.-based awardees obtain Institutional Review Board (IRB) approvals for human subject research, Institutional Biosafety Committee (IBC) approval for recombinant or synthetic nucleic acid research, and Institutional Animal Care and Use Committee (IACUC) approval for animal research, (see additional information regarding these approvals below). Copies of these approvals, if available at the time the application is submitted, must be submitted with the application as appendices. CFF will not release payments to awardee institutions until these documents are received and on file with the CFF GCMA Office.

Awardees based outside of the U.S. must comply with the applicable equivalent regulations in their respective countries and provide copies of approvals as soon as they are available. CFF will not release payments until these documents are received and on file with the CFF GCMA Office.

Research Involving Human Subjects: CFF policy pertaining to the protection of individuals as research subjects requires that for each proposal awarded, the awardee institution certify in writing that an Institutional

Review Board (IRB) has reviewed and approved the procedures for the use of human subjects, or human organs, tissues and body fluids, in the proposed research, in accordance with the Department of Health and Human Services policies found at https://www.hhs.gov/ohrp/regulations-and-policy/index.html. In the event the IRB has determined a study is exempt, documentation demonstrating the exempt status must also be submitted to the CFF GCMA Office.

Research Involving Recombinant or Synthetic Nucleic Acid Molecules: All research involving recombinant or synthetic nucleic acid and human gene transfer studies supported by CFF must meet the requirements contained in the document NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (updated April 2019). This publication and announcements of modifications and changes to the NIH Guidelines are available from the Office of Science and Policy, National Institutes of Health, 6705 Rockledge Drive, Ste 750, MSC 7985, Bethesda, MD, 20892-7985 or online at https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf.

Research Involving Animals: Applications submitted to CFF involving the use of animals must meet the guidelines of the National Institutes of Health found at https://grants.nih.gov/grants/olaw/olaw.htm, which require that all proposed studies be reviewed and approved by an Institutional Animal Care and Use Committee (IACUC). In addition, CFF awardee institutions and laboratories must be accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC) and/or have other verifiable assurances that the institution and laboratory meet appropriate standards.

Application Guidelines

1. Application components
   a. The grant application is to be submitted as a single PDF. All application attachments (links) are below and can be found on our website. The pages must be in the following order:
      i. Signed Face Page
      ii. Lay Abstract
      iii. Scientific Abstract
      iv. Summary of Relevance to CFF mission
      v. Scope of Work (SOW) (encompassing a one-year project period)
      vi. Biographic Sketch (NIH Format)
      vii. Other Support (NIH Format)
      viii. Detailed Budget
      ix. Budget Justification
      x. Research Plan: Limited to 6 pages. Describe the aims, preliminary data, approach, and outcomes/alternatives. Indicate how the anticipated results will support the RDP mission and the C3RDP cores to be utilized. Also include a brief description of plans for future funding.
      xi. Name and Addresses of References
   b. NIH formatting must be followed.
   c. Appendices are not allowed.
   d. The scope of the proposed work should be two years, although year two funding is not guaranteed but is contingent upon submission and approval of a renewal progress report.
   e. Application attachments and the descriptions of the C3RDP Cores can be found on our C3 website.
   f. Grant applications must be submitted as a single PDF file due on **December 11, 2023, at 5 pm EST** to PulmonaryGrants@nationwidechildrens.org.

Grant Review Process

1. Review will be conducted by members of the C3 Research Internal Advisory Board.
2. Each reviewer will submit a written review
3. Each grant reviewer will provide 3 scores:
    i. Applicant
    ii. Scientific Merit
    iii. Relevance to the CFF and C3 missions
2. Grants needing clarification or improvement will be returned to the applicant and revisions will be due by **January 12, 2024, at 5 pm EST**. Revisions, if needed, must be submitted via email to PulmonaryGrants@nationwidechildrens.org.
4. Grant awards will be announced in June 2024
5. If accepted, awardees planning on getting specimens through the Translational Core are expected to submit a Specimen Request Form.

Full Application Checklist

Please use provided templates/attachments to complete the full application:

- ☐ Face Page
- ☐ Lay Abstract
- ☐ Scientific Abstract
- ☐ Summary of Relevance to CFF mission
- ☐ Statement of Work (SOW)
- ☐ Biographic Sketch (NIH Format) for key personnel
- ☐ Other Support
- ☐ Detailed Budget
- ☐ Budget Justification
- ☐ Research Plan
- ☐ Letters of Reference (junior investigators only)
- ☐ Name and Address of References (junior investigators only)

Contact Information and Other Resources

Title	Name	Phone #	Email
P&F Program Director	Dan Wozniak	614-247-7629	Daniel.Wozniak@osumc.edu
C3 Administrator	Stephanie Sliemers	614-722-2059	Stephanie.Sliemers@nationwidechildrens.org
Research Operations Manager	Katie Thornton	614-722-4922	Katie.Thornton@nationwidechildrens.org

Please visit our Cure CF Columbus website for more information and resources: http://www.curecfcolumbus.org/

The RDP is administered out of Nationwide Children's Hospital Pulmonary Research Core (PRC). If you have any questions about the application, who to speak to about specimens, or any problems that may arise during the grant period, please contact the PRC at PulmonaryResearchCore@nationwidechildrens.org or Dr. Karen McCoy at Karen.McCoy@nationwidechildrens.org or Dr. Dan Wozniak at Daniel.Wozniak@osumc.edu.