Advancing Gene Editing Technologies and Tools for Cystic Fibrosis: Postdoctoral Research Award

POLICIES AND GUIDELINES

Published: November 9, 2018
Application Deadline: March 12, 2019
I. ABOUT THE CYSTIC FIBROSIS FOUNDATION
The mission of the Cystic Fibrosis Foundation (CFF) is to cure cystic fibrosis (CF) and to provide all people with the disease the opportunity to lead full, productive lives by funding research and drug development, promoting individualized treatment, and ensuring access to high-quality, specialized care.

To achieve this mission, various types of awards are offered to support meritorious research in CF.

II. BACKGROUND
Cystic Fibrosis is a common, lethal autosomal recessive disorder that affects 70,000 individuals worldwide. Abnormal mucus production in the respiratory tract is the primary cause of morbidity and mortality in CF, but other organs are also affected including the pancreas, sweat gland, intestine, bile duct of the liver, and male reproductive system. CF is caused by dysfunction of a single gene, Cystic Fibrosis transmembrane Conductance Regulator (CFTR), which codes for an ABC transporter protein that functions as a plasma membrane anion channel in epithelial and other cells.

Close to 2,000 variants of CFTR have been identified, however a single mutation, F508del (a 3bp deletion causing absence of phenylalanine 508) is present in ~90% of patients worldwide. The F508del mutation causes instability of CFTR leading to a misfolded protein and defective chloride channel function. Clinical development of small molecule CFTR modulators that reverse the folding defect holds promise for new therapies for the majority of CF patients.

However, there is still an unmet need for patients with CFTR mutations that do not yield sufficient quantities of protein for pharmacological correction. To treat all patients with CF, it will be necessary to correct variants that block protein synthesis (i.e. premature stop codon mutations, splice mutations, insertion/deletion mutations etc.). Gene repair or insertion strategies, as well as overcoming hurdles of poor delivery and cellular penetration, are issues to be addressed.

III. POSTDOCTORAL RESEARCH FELLOWSHIP AWARD OVERVIEW
Postdoctoral research fellowships are offered for support of postdoctoral research training related to CF. The intent of these awards is to enable research training in new research areas and methods to advance the scientific knowledge of the applicant and to collect data to enable their transition into an independent research career.

As an outcome of a CF gene editing workshop held over the summer, the Cystic Fibrosis Foundation announces a Request for Applications (RFA) to identify and support highly meritorious proposals in gene editing that offer potential to repair or circumvent CFTR mutations in individuals with CF. A key concept that emerged from the workshop was that investigators without experience in CF research would be more inclined to become involved if access to CF tools and reagents, as well as CF knowledge, were available. To bring new technologies to the CF field, investigators without experience in CF research are encouraged to apply. Information about CF resources may be found at https://www.hhs.gov/ohrp/regulations-and-policy/index.html. Additional questions may be directed to grants@cff.org.
Note: A summary of results from the CF Gene Editing workshop can be found within the application on proposalCENTRAL as an informational download document in Section #2.

The purpose of this RFA is to and support training of outstanding post-doctoral researchers who are engaged in gene editing that offer potential to repair or circumvent CFTR mutations in individuals with CF.

Proposals will focus on exploring technologies related to gene editing and generating tools for assessing editing. These include, but are not limited to, studies aimed at:

- Creating tools, including animal models, cell lines or organoids, that will be generally applicable and facilitate or accelerate development and assessment of various gene editing strategies
- Developing and optimizing novel gene editing technology platforms and strategies to target the CFTR gene locus.
- Improving our understanding of potential effects of CFTR gene editing on gene and chromatin topology as related to regulation of CFTR expression.
- Developing and applying assays to assess off-target effects and adverse events of CFTR gene editing in vitro and/or in vivo.
- Developing biological endpoints and assays for early in vivo efficacy signals of CFTR gene editing.
- Understanding and developing assays to monitor potential immune responses to gene editing. This may include responses to the delivery vehicle, cargo, or CFTR protein.
- Utilizing CF and/or non-CF animal models to address optimal delivery approaches, appropriate cell targets for long-term correction, dosing, safety, and phenotypic correction of CF pathology.
- Identifying the threshold of CFTR gene editing needed to reach therapeutic relevance.
- Identifying and overcoming barriers for delivery of gene editing cargo into cells relevant to CF.

General Guidelines and Eligibility:

- Awards may be approved for up to a two-year period. Funding for Year 2 is contingent upon submission and approval of a renewal progress report and the availability of funds.
- United States residents and applicants from outside the United States are welcome to apply.
- International applicants and institutions are required to submit additional information in accordance with U.S. anti-terrorism restrictions.
- Postdoctoral applicants engaged in or planning CF-related research are eligible. Preference will be given to recent graduates and those just beginning their research careers.
- Applicants can apply for this fellowship anytime during their postdoctoral period. However, funding levels are based on the year when the award is made, not the year of the applicant’s fellowship.
- Fellowships are awarded on the basis of individual and institutional merit. Awards are not transferable to other individuals or institutions unless previously approved by the CFF Program Director.

Funding Levels:

<table>
<thead>
<tr>
<th>Fellowship Year</th>
<th>Stipend (salary + fringe)</th>
<th>Travel</th>
<th>Research</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-year Fellowship</td>
<td>US$58,850</td>
<td>US$1,250</td>
<td>US$3,000</td>
<td>US$63,100</td>
</tr>
<tr>
<td>Second-year Fellowship</td>
<td>US$61,200</td>
<td>US$1,250</td>
<td>US$3,000</td>
<td>US$65,450</td>
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Note: A third year of support may be available as an option to highly qualified candidates and will be considered after completion of 18 months of CFF-supported training.

IV. RESEARCH AREAS OF INTEREST TO ADVANCING GENE EDITING TECHNOLOGIES AND TOOLS FOR CYSTIC FIBROSIS

Cystic Fibrosis is a common, lethal autosomal recessive disorder that affects 70,000 individuals worldwide. Abnormal mucus production in the respiratory tract is the primary cause of morbidity and mortality in CF, but other organs are also affected including the pancreas, sweat gland, intestine, bile duct of the liver, and male reproductive system. CF is caused by dysfunction of a single gene, Cystic Fibrosis Transmembrane conductance Regulator (CFTR), which codes for an ABC transporter protein that functions as a plasma membrane anion channel in numerous cell types.

Clinical development of small molecule CFTR modulators that reverse the folding defect of the most common CFTR mutation, F508del (a 3bp deletion causing absence of phenylalanine 508), holds promise for new therapies for the majority of CF patients. However, there is still an unmet need for patients with CFTR mutations that do not yield sufficient quantities of protein for pharmacological correction. To treat all patients with cystic fibrosis, it will be necessary to correct variants that block protein synthesis (i.e. premature stop codon mutations, splice mutations, insertion/deletion mutations etc.). Gene repair strategies as well as overcoming hurdles of poor delivery and cellular penetration are issues that need to be addressed. It is anticipated that many applicants with relevant technologies in editing and delivery, for example, will not have a history in CF research, and such applications are strongly encouraged.

Areas of interest with high priority that focus on exploring technologies related to gene editing and generating tools for assessing editing include:

- Creating tools, including animal models, cell lines or organoids, that will be generally applicable and facilitate or accelerate development and assessment of various gene editing strategies
- Developing and optimizing novel gene editing technology platforms and strategies to target the CFTR gene locus.
- Improving our understanding of potential effects of CFTR gene editing on gene and chromatin topology and the effects on regulation of CFTR expression.
- Developing and applying assays to assess off-target effects and adverse events of CFTR gene editing in vitro and/or in vivo.
- Developing biological endpoints and assays for early in vivo efficacy signals of CFTR gene editing.
- Understanding and developing assays to monitor potential immune responses to gene editing. This may include responses to the delivery vehicle, cargo, or CFTR protein.
- Utilizing CF and/or non-CF animal models to address optimal delivery approaches, appropriate cell targets for long-term correction, dosing, safety, and phenotypic correction of CF pathology.
- Identifying the threshold of CFTR gene editing needed to reach therapeutic relevance.
- Identifying and overcoming barriers for delivery of gene editing cargo into cells relevant to CF.
V. REVIEW AND AWARD
All applications will be evaluated by a CFF established ad-hoc review committee. Funding of awards is based on the priority score awarded to each application and the recommendations of the review committee. Funding decisions are based on the relevance of the proposed study to the goals of the RFA and the mission of the Foundation. All awards are subject to compliance with applicable regulations and CFF policies and are contingent upon the availability of CFF funds.

Postdoctoral Fellowship Applications will be evaluated in the following areas:

• Responsiveness to RFA, relevance to one or more of the following priority areas:
  o Editing platform development
  o Animal, cell and/or organoid model development for testing editing
  o Animal model testing
  o Delivery system development or testing
  o Safety/adverse events of editing
  o Immune responses
  o Other

• As well as the below:

<table>
<thead>
<tr>
<th>Applicant</th>
<th>Mentor(s)</th>
<th>Environment</th>
<th>Training &amp; Research Development Plan</th>
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<tr>
<td>• Potential to develop an independent research career related to CF</td>
<td>• Established expertise in gene editing research or related research areas</td>
<td>• Quality (breadth and depth) of faculty in basic and/or clinical sciences related to gene editing and CF at applicant institution</td>
<td>• Feasibility and impact of the proposed plan</td>
</tr>
<tr>
<td>• Research accomplishments</td>
<td>• Commitment of the primary Mentor for the duration of the applicant’s development and research plan</td>
<td>• Quality of institution's CF research and training programs</td>
<td>• Didactic course work required by the applicant (if indicated)</td>
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<td>• Track record of the Mentor training individuals for basic biomedical research</td>
<td>• Demonstrated interaction between basic and clinical investigators</td>
<td>• Scientific and technical merit of the proposed research</td>
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<td>• Institution's commitment and ability to provide opportunities and facilities necessary for research career development</td>
<td>• Ability of the proposed plan to develop research skills of the applicant needed for independence</td>
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<td></td>
<td></td>
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<td>• Relationship to applicant’s career development</td>
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Chief causes for assigning low priority scores to applications during review include the following:

- Unresponsive to RFA
- Insufficient information or documentation
- Inadequate statement of hypothesis, experimental design or methods
- Failure of the applicant to demonstrate awareness of and plans for coping with key problems and pitfalls associated with the proposed research
- Insufficient or improper controls
- Failure of the applicant to describe potential relevance of the proposed study to issues in CF
- Failure of the applicant to document the necessary skills or training to accomplish the goals of the proposal
- Failure of the applicant to meet all of the criteria described in the policy statement for a given award

VI. SUBMISSION INFORMATION & GENERAL TIMELINE

Application Deadline: Tuesday, March 12, 2019 at 5:00 PM (ET)

Submit online through proposalCENTRAL: https://proposalcentral.altum.com/
(Refer to Section VII of these guidelines for specific submission instructions.)

An application will be considered incomplete if it fails to comply with the instructions, or if the submitted material is insufficient to permit adequate review. CFF reviews applications electronically, and only documents submitted online at proposalCENTRAL will be reviewed. Late applications will not be accepted, and the deadline will not be waived.

General Timeline:

<table>
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<tr>
<th>Event</th>
<th>Date</th>
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<tbody>
<tr>
<td>Application Deadline</td>
<td>March 12, 2019</td>
</tr>
<tr>
<td>Review by RFA Review Committee</td>
<td>May 10, 2019</td>
</tr>
<tr>
<td>Notification to Applicants</td>
<td>May 24, 2019</td>
</tr>
<tr>
<td>Earliest Start Date for Awarded Projects</td>
<td>July 1, 2019</td>
</tr>
</tbody>
</table>

VII. FULL APPLICATION GUIDELINES

Applications must be submitted online at proposalCENTRAL: https://proposalcentral.altum.com/

Documents should be typed using:

- Font: Times New Roman 12 or Arial 11
- Margins: No less than a half inch on each side

Note: When all the documents have been uploaded to proposalCENTRAL, the system will compile them into a single PDF file in the correct sequence.

Log-in at proposalCENTRAL: https://proposalcentral.altum.com/.
First-time applicants must register to create a user name and password for proposalCENTRAL and will need to complete a profile online before applying. If you are registered and cannot remember your password, click on the “Forgot Your Username/Password?” link below the “Application Login” fields.

Award opportunities, including this Request for Applications (RFA), are listed on the opening screen, but you must be logged in first to see them.

Select the gray tab labeled “Grant Opportunities” found in the upper right-hand side of the page. Click on the light blue “Filter by Grant Maker” button to the left and scroll down to locate Cystic Fibrosis Foundation in the list.

Locate the listing for the “Advancing Gene Editing Technologies and Tools for CF: Postdoctoral Fellowship Award” program. Click on the “Apply Now” button in the column on the far right to open the application form.

Applicants may stop at any point but must click the “Save” button before exiting in order to save their work. When logging in to continue, click on the blue tab, “Proposals”, and then the “Edit” button.

The following sections are listed in the navigation menu to the left of the application screen. Click on each section and follow the directions.

1. **Title Page**: Enter the title of your project, and indicate whether the Principal Investigator (PI) is an investigator new to CF.

2. **Download Templates & Instructions**: Download the available templates applicable to the project, fill them out and upload them when completed in Section #10. Templates available include: Applicant Instructions for Letters of Reference (for reference purposes only), CF Gene Editing Workshop Summary (for reference purposes only), Biographical Sketches for Key Personnel, Mentor’s Results of Past and Current CFF/CFFT Support, Other Support, Facilities Available, Budget Detail, Budget Justification, Research Plan, Training Plan, Names and Addresses of References, and International Institution Form.

3. **Enable Other User to Access this Proposal**: Complete this section online if you wish to designate access to another individual, such as an assistant who has registered on proposalCENTRAL. Enter the email address of the individual and in the “Permissions” column, use the pulldown menu to select the type of access you wish to give. Please note that only delegates who are granted “Administrator” rights can submit applications on behalf of the applicant. Check the “Auto Notify” box and then “Save”.

4. **Applicant/PI**: If a profile was completed upon registration, the fields in this section will already be populated with the information entered in your Professional Profile. If you need to make any changes, click the “Edit Professional Profile” button and follow the instructions. If a profile was not completed, enter the required information and click “Save”.

**Advancing Gene Editing for CF: Postdoctoral Fellowship Policies and Guidelines**

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5. **Institution & Contacts:** If a profile was completed upon registration, the Principal Investigator’s (PI) institution will be preloaded as Lead Institution. If a profile was not completed, enter the required information and click “Save”. Be sure to use the full legal name of the institution.

6. **Letters of Support/Reference:** Letters of Support and Reference are weighted heavily in the review. At least four (4) Letters of Support/Reference are required as follows:
   - **The Mentor(s) for this award** – A Letter of Support from the current Mentor(s) should clearly identify the merits of the applicant and must include a description of training the applicant will receive while working under the Mentor’s direction (i.e. seminars, new techniques, professional development, etc.). Any CF-related training should be highlighted.
   - **Additional referees** – Letters of Reference from at least three (3) other individuals familiar with the applicant’s scientific interests and abilities (with no more than two [2] from the same institution) should attest to the candidate's academic qualifications, motivation, and research potential.

Enter the email addresses of the individuals who will be asked to submit Letters of Support/Reference for the applicant. Automated emails (with instructions) will be sent to each Referee through the proposalCENTRAL website. **The letters must be uploaded by the referees prior to submitting the application, preferably one (1) week before the application deadline.** Additionally, applicants must complete the “Names and Addresses of References” template and upload it in Section #10.

**Note:** Detailed Instructions on how to invite referees to submit the letters of reference are also available in a downloadable document found in Section #2. Letters uploaded to proposalCENTRAL should not be password protected or otherwise encrypted. **Such encryption will cause errors in assembling a single-print PDF of the application.** The applicant should inform the individuals writing letters to not include password protection on their documents.

7. **Abstracts/Relevance/Keywords:** In the space provided online for abstracts, 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 and RFA:**
All applications are reviewed and scored not only on scientific merit but also on relevance to CFF’s mission.
   - **Mission:**
     The mission of the Cystic Fibrosis Foundation is to cure cystic fibrosis and to provide all people with the disease the opportunity to lead full, productive lives by funding research and drug development, promoting
individualized treatment, and ensuring access to high-quality, specialized care.

RFA Objectives:
The objectives of the Advancing Gene Editing Technologies and Tools for Cystic Fibrosis RFA are to develop, optimize and apply gene editing technologies to the CFTR locus and generate tools to assess editing efficiency, functional outcome, and potential off-target effects.

Provide a statement of no more than 2,000 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.

Responsiveness to this RFA: From the lists of options provided in this section, select all applicable areas of interest for the proposed project. A minimum of one (1) option must be selected per category. Click each area you want to select, the “Add (+) icon”, until you have all applicable keywords selected on the list to the right. If selecting Other, please indicate the area of interest of the proposal.

Budget Summary: Fill in the start and end date for each year of support requested. The total requested salary and benefits must not exceed US$58,850 for Year 1 and US$61,200 for Year 2. The total budget requested cannot exceed US$63,100 for Year 1 and US$65,450 for Year 2. Note: The Budget Detail and Budget Justification templates downloaded in Section #2 need to be completed and uploaded in Section #10 for each year of the award and for each subcontract (if applicable). The amounts included in this uploaded Budget Detail must match the amounts entered in the Budget Summary online.

Organization Assurances: Select the type of assurances that are applicable to the project and provide all required information (i.e. IRB, IACUC, and/or IBC/rDNA approval letter and status at the time of submitting the application). Refer to section VII.10.J. ORGANIZATION ASSURANCES & CERTIFICATIONS below in these guidelines for details.

Research Plan & Supporting Documents: In this section, upload the completed templates downloaded in Section #2 above in PDF format. Fill out the fields describing the attachment, select the attachment type from the pulldown menu, enter a description for the attachment in the corresponding field, choose the file to be uploaded, and drag and drop it as indicated in the online form. Click “Upload and Continue”. Do this for each attachment.

A. BIOGRAPHICAL SKETCHES FOR KEY PERSONNEL (template available for download)
Complete and upload an NIH Biographical Sketch for all key project personnel, beginning with the Applicant/Principal Investigator (fellow) and the Mentor(s). (CFF defines “key personnel” as any individual with an advanced degree that will play an instrumental role in the accomplishment of the research project.) Do not exceed five (5) pages per person.
B. MENTOR’S RESULTS OF PAST AND CURRENT CFF/CFFT SUPPORT (template available for download)
Mentors are requested to identify the results of past and current Cystic Fibrosis Foundation and/or Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) support (e.g., subsequent funding from other sources, journal articles, and invited presentations) and the CFF/CFFT grant/award from which they resulted for the past three to five years. Please note that the following information must be included with each research project identified:
- CFF/CFFT Award #
- Principal Investigator (PI)
- CFF/CFFT Project Title
- Applicant’s Title on Project
- Project Start/End Dates
- Total CFF/CFFT Award Amount
- Results of Support

C. OTHER SUPPORT (template available for download)
Complete and upload an “Other Support” form for all key project personnel, beginning with the Applicant/Principal Investigator (fellow) and the Mentor(s). There is no page limitation. Information on other support assists CFF in the identification and resolution of potential sources of overlap. Scientific and budgetary overlap should be minimized. Commitment of an individual’s effort greater than 100 percent, is not permitted.

D. FACILITIES AVAILABLE (template available for download)
Describe the facilities and equipment available at the applicant’s institution 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.

E. BUDGET DETAIL AND BUDGET JUSTIFICATION (templates available for download)
Fill out the Budget Detail and Budget Justification templates for each and all years of support requested. In the space provided on the templates, indicate the year as well as start and end dates for the proposed budget period. (Be sure the amounts entered in the Budget Detail(s) match the amounts in the online budget summary in Section #8).
- **Budget Detail – Direct Costs Only**
  Personnel - List the name and title of the applicant. Indicate the percent effort on the project. The total requested salary and benefits must not exceed **US$58,850** for Year 1 and **US$61,200** for Year 2. List dollar amounts separately for institutional base salary and fringe benefits. In accordance with National Institutes of Health (NIH) policy, salary requests may not use an institutional base salary above the current federal salary cap of US$189,600. Fringe benefits may be requested if they are treated consistently by the applicant institution as a direct cost to all funding agencies and foundations.
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.

Travel - Describe the purpose of any CF relevant travel. Please note: 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 Grants and Contracts Office. Travel expenses may not exceed US$1,250 per person per year. Registration fees associated with conferences are in addition to this allowance should be listed under “Other Expenses”. Applicants are encouraged to attend the North American Cystic Fibrosis Conference (NACFC) and submit an abstract on their work each year of the award.

Other Expenses - Itemize other expenses by major categories, such as duplication costs, publication costs, computer charges, etc. Tuition costs may be requested for personnel supported through this study but may not exceed US$10,000 per person per year.

• Budget Detail – Indirect Costs
  Indirect costs are not allowable on Postdoctoral Research Fellowship Awards.

• Budget Justification
  Describe costs listed in the Budget Detail. Use major categories, such as Personnel, Supplies, etc. Justify all items.

F. RESEARCH PLAN (template available for download)
• 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 uploaded as Appendices, they will NOT be reviewed.
• Type the applicant's name in the space available in the header of the document. The template available will track page numbers at the bottom.
• Page limit: Seven (7) single-sided pages, not including the Literature Cited. Applications exceeding this page limit will not be reviewed. 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.

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: Briefly 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 responsiveness of the proposed work to the RFA objectives. 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. As new investigators to CF are encouraged to apply, CF-specific preliminary data is not necessary.

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 difficulties and/or limitations of the proposed procedures and alternative approaches to achieve aims. Point out any procedures, situation or materials that may be hazardous to personnel or patients and the precautions to be exercised.

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

G. **TRAINING PLAN (template available for download)**
The applicant, in conjunction with the Mentor(s), should develop a training plan that outlines skills and techniques that will be learned during this fellowship period as well as any CF-specific training that will be available to the applicant. This plan should also address the applicant’s long-term career goals and include training and professional development activities that will facilitate the applicant’s transition to the next phase of their career. Do not exceed four (4) pages.

H. **NAMES AND ADDRESSES OF REFERENCES (template available for download)**
List the names, titles, and contact information of the individuals who have been asked to submit Letters of Support/Reference on the applicant’s behalf via Section #6 in proposalCENTRAL. A PDF copy of the completed form should be uploaded.

I. **VERIFICATION OF APPLICANT INSTITUTION’S TAX STATUS (upload as PDF documents)**
The CFF Grants and Contracts Office must have a copy of the applicant institution’s current W-9 and 501(c)3 letter, or other documentation verifying its Federal tax status and will not issue Award Letters to Awardees if these documents are not received and on file.
- Applicants from for-profit organizations must submit a copy of the applicant institution’s W-9 and IRS documentation verifying the organization’s Federal tax status. Awards are not issued prior to having these documents on file with the CFF Grants and Contracts Office.
• Non-U.S. applicants must provide a copy of the W-8BEN-E form (required). In addition, a tax equivalency letter should be uploaded, if available. If a tax equivalency letter is not available, applicants must upload a letter stating this documentation is not available.

J. ORGANIZATION ASSURANCES & CERTIFICATIONS (upload under Appendices template type)
CFF requires, as applicable, that all U.S.-based awardees obtain Institutional Review Board (IRB) approvals for human subject research, Institutional Animal Care and Use Committee (IACUC) approval for animal research, and Institutional Biosafety Committee (IBC) approval for recombinant DNA research (see additional information regarding these approvals below). Copies of these approvals, if available at the time the application is submitted, must be uploaded with the application as appendices. CFF will not release payments to awardee institutions until these documents are received and on file with the CFF Grants and Contracts 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 Grants and Contracts 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 Grants and Contracts 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 2016). 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 http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines.

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.
K. INTERNATIONAL INSTITUTION FORM (template available for download, if applicable)
Applicants whose institution is not a United States based-entity must complete the International Institution Form. Upload a PDF version of the completed and signed form, together with the following documents*:
• A copy of the institution’s most recent Mission Statement.
• A copy of the institution’s tax status documentation or equivalent, or a letter stating it is not available.
• A brief description of other sources of support, such as official awards, private endowments, and commercial activities, received by the institution.
• A copy of the institution’s Standard Operating Procedure(s) or relevant policy to ensure that funds provided are neither distributed to terrorists or their support networks, nor are funds used for activities that support terrorism or terrorist organizations.
• For-profit institutions must submit a complete list of key employees, members of the governing board, and/or other senior management.

Applicants who have provided these documents within the past three (3) years are not required to resubmit them. However, if any of the above documents have been updated since they were previously submitted, please upload any updated documents. The CFF Grants and Contracts Office will contact applicants if documents are outdated or missing.

*Applicants must provide English translations for all non-English documents, including material provided in support of the Research Plan.

L. APPENDICES (upload materials as PDF documents)
Appendices are restricted to the following two (2) categories:
• Certification of organization assurances (i.e. IRB, IACUC and IBC approvals), if applicable.
• Up to three (3) reprints of the applicant’s work relating to the general area of research in the proposal may be uploaded in PDF format.

11. PI Data Sheet: Fill in the required fields, save and exit.

12. Print Face Pages: Follow the prompts on the screen to generate and print a Face Page. The Face Page will be populated automatically with data entered in the online application (applicant’s name, institution, title of application, etc.). The Face Page must be signed by the Principal Investigator and Authorized Institutional Official and uploaded in Section #10. Co-Principal Investigators, if any, are not expected to sign the Face Page. Note: CFF will not submit applications for committee review if it does not have the Face Page on file signed by the Principal Investigator and Authorized Institutional Official.

13. Validate: Upon completing the application, click on the “Validate” button on the main screen. Attend to any omissions/errors as prompted onscreen, and then click “Validate” again.

14. Submit: Click on the blue button with white lettering. CFF will not receive your application unless the “Submit” button is clicked.
**Confirmation:** Applicants will receive an e-mail confirmation from proposalCENTRAL (not from CFF) that the Application was successfully submitted. This e-mail will be your only acknowledgement. If you do not receive this confirmation, please contact proposalCENTRAL immediately to ensure that your submission was submitted and processed.

For technical support with the online application:

proposalCENTRAL at pcsupport@altum.com or 800-875-2562 on weekdays, 8:00 a.m. to 5:00 p.m. (Eastern)

For program/content information:

CFF Grants and Contracts at grants@cff.org or 301-841-2614
VIII. SUBMISSION INFORMATION & GENERAL TIMELINE

Application Deadline: Tuesday, March 12, 2019 at 5:00 PM (ET)

Applications must be submitted at proposalCENTRAL: https://proposalcentral.altum.com/

Face Page which includes:

☐ Signatures
  o Principal Investigator (Co-PI’s are not required to sign)
  o The Official authorized to sign on behalf of the Awardee Institution

☐ Applicant/PI information (online)

☐ Complete Institution and PI Contact Information, including correct mailing address (online)

☐ Organization Assurances (check those that apply online/complete the required information)
  o Human Subjects Certification
  o Recombinant DNA/Biosafety Information
  o Research Involving Animals information

Research Plan, Supporting Documents and Appendices:

☐ Abstracts ~ Summary of Relevance ~ Responsiveness - (complete online)

☐ Biographical Sketches for Key Personnel - (upload)

☐ Mentors Results of Past and Current CFF/CFFT Support - (upload)

☐ Other Support (NIH Format) - (upload)

☐ Facilities Available - (upload)

☐ Budget Detail for each year - (upload)

☐ Budget Justification for each year - (upload)

☐ Research Plan - (upload)
  o Hypothesis and Specific Aims
  o Background and Significance
  o Preliminary Results
  o Experimental Design and Methods
  o Literature Cited (not included in Research Plan page limitation)

☐ Training Plan – (upload)

☐ Names and Addresses of References - (upload)

☐ Verification of Applicant Institution’s Tax Status - (upload)
  o W-9 (U.S. applicants) or W-8BEN-E (non-U.S. applicants)
  o Federal (IRS) tax status letter (U.S.-based applicants) or equivalent tax status letter, or letter indicating it is not available (non-U.S.-based applicants)

☐ International Institution Form (non-U.S.-based entities only - upload, if applicable)
  o Institution’s most recent Mission Statement
  o Applicant institution’s tax status documentation or equivalent, or a letter stating it is not available
  o Description of other sources of support, such as official awards, private endowments, and commercial activities, received by institution
  o Institution’s Standard Operating Procedure(s) or relevant policy to ensure that funds provided are neither distributed to terrorists or their support networks nor used for activities that support terrorism or terrorist organizations
For-profit institutions must submit a complete list of key employees, members of the governing board, and/or other senior management.

☐ Appendices (upload, if applicable)
  o Certification of organization assurances (i.e. IRB, IACUC and IBC approvals), if applicable
  o Up to three (3) reprints of the applicant’s work relating to the general area of research in the proposal