

CFAR Supplement Announcement in HIV/AIDS –FY2016

The CFAR Program at the National Institutes of Health (NIH) invites applications from currently funded CFARs that are eligible for administrative supplements.

Purpose

The purpose of this administrative supplement opportunity is two-fold:

1. To support a broad range of highly innovative research projects and pilot studies to address key gaps in our understanding of HIV/AIDS.

and

2. To support early stage investigators who have not yet received an NIH award in HIV/AIDS research as well as established investigators in non-HIV fields who have never received an NIH research award for HIV/AIDS studies. This funding will provide support for the development of preliminary data to support an NIH research project grant application.

Background and Scientific Areas of Interest

CFARs are strongly encouraged to submit projects in collaboration with investigators and disciplines not usually involved in HIV research. Involvement and mentoring of early stage investigators is also strongly encouraged. This opportunity should build research capacity at the CFAR institution or at a partnering foreign institution in the scientific areas specified below and is intended to complement ongoing domestic and international HIV/AIDS research efforts funded or sponsored by the NIH. Supplement proposals should be consistent with the recent [NIH HIV/AIDS research priorities \(NOT-OD-15-137\)](#).

Each eligible CFAR is limited to one application per scientific area of interest below for a maximum of five applications total.

1. Tracking HIV Transmission Phylodynamics: Leveraging Collaborations with Public Health Departments and Others to Research Methods to Analyze Phylogenetic Data in Close to Real-Time.

The goal is to develop strategies to identify HIV transmission networks in close to real-time using phylodynamic tracking and modeling. Current studies are limited to retrospective phylogenetic analysis of archival HIV sequence databases. Retrospective phylogenetic analyses of HIV sequence databases have demonstrated the ability to identify transmission clusters in a given geographic area. However, traditional phylogenetic methods require extensive computational and data analysis resources. Moreover, retrospective studies cannot predict future transmission clustering. Improved monitoring of transmission networks will enable more precise and efficient targeting of testing, prevention, and treatment interventions to key populations that are driving the current epidemic.

The objective of the supplement request is to support interdisciplinary collaborations with groups that maintain HIV sequence databases (e.g., public health departments, CDC or testing labs) to study and optimize approaches for using phylodynamic analyses of HIV sequence databases in close to real-time. This will enable more precise tracking of HIV transmission and

targeting of prevention and treatment efforts. These studies should have a clear description of the public health implication and impact.

Responsive studies could include, but are not limited to the following:

- Optimization of phylogenetic data analysis and mathematical modeling to permit more rapid identification of emerging transmission clusters and to predict the future trajectory of such clusters
- Linkage and collaboration of academic phylogeneticists and bioinformaticians to existing public health databases (e.g. public health departments, Quest, LabCorp, CDC, etc.) to access timely information regarding HIV transmission networks in a defined geographic area
- Proof-of-concept studies leveraging phylodynamic data modeling to target HIV testing, prevention modalities, or drug resistance and adherence monitoring to specific populations or geographic areas and/or to measure the impact of interventions on HIV transmission networks and clusters

Supplement awards are for one year with maximum funding per application of **\$200,000** Direct Costs, not including third party indirect costs.

2. HIV and Host Factor Targets for Structural Research

A complete understanding of HIV pathogenesis and persistence in the host requires more than just the identification of the many host factors that interact with the virus during its replication cycle. Knowledge of how those host factors interact with the virus at the molecular level is necessary in order to potentially exploit such complexes as therapeutic targets. While the identification and validation of these factors can be determined by relatively established screening and infectivity protocols, the biochemical preparation of said factors or their complexes with viral components can be difficult, empirical, time consuming and expensive.

The objective of this supplement is to enable the characterization and preparation of host and/or viral factor complexes for structural analysis. Such targets would already have been identified, but have either not yet been sufficiently characterized or the resources have not been available to do so. A necessary component of this objective is the identification of targets in consultation with a structural biologist with the necessary expertise to guide the development of the target for analysis, since groups with the skills to identify and validate potential targets may lack the knowledge necessary to prepare suitable samples. The goal for a successful project would be for the awardee to have advanced their target of interest at least to the point just shy of actual high resolution data collection. This would typically entail not only structurally tractable samples, but also preliminary low resolution structural data indicating the samples are of sufficient quality. Such low resolution data could include electron microscopy, SAXS, or even preliminary crystallographic data.

Responsive applications are expected to include the following attributes:

- An identified target that would consist of a host factor, a complex of host factors, or a complex of a host factor(s) with a viral component.
- The involvement of this target in the replication cycle of HIV that has been validated by appropriate biological/virological assays.
- The target **must be new** and has not already undergone or be undergoing high resolution structural analysis within the HIV/AIDS research community.

- The identification of a preferred method of high resolution structure determination; although, this may later change as the target characterization progresses.
- Applicants must establish a relationship with a qualified structural biologist for consultation during the funding period and for (eventual) collaboration when the target samples are ready for high resolution analysis. This consultant can be any qualified structural biologist with expertise in state-of-the-art biophysical technologies; although, applicants are encouraged to approach members of the five Centers for HIV/AIDS-Related Structural Biology: [CRNA](#), [CHEETAH](#), [HARC](#), [HIVE](#), or [PCHPI](#).
- Awardees are **very strongly encouraged** to attend the yearly Structural Biology Related to HIV/AIDS meeting on the NIH Campus on June 23 & 24, 2016. Funds requested in the budget to attend this meeting are allowable.

Supplement awards are for one year with a maximum funding per application of **\$200,000** Direct Costs, not including third party indirect costs.

3. Advancing PrEP Delivery

Oral HIV antiretroviral pre-exposure prophylaxis (PrEP) confers a strong preventive benefit to individuals who are at-risk for HIV infection when taken with high adherence. Access to PrEP in young minority populations at greatest risk of HIV infection is a challenge, especially among young MSM (YMSM) who are minors among which the incidence of HIV continues to rise. Furthermore, even when medication is provided, adherence is a particular challenge in these young people, especially among racial and ethnic minority youth. Research is needed to better understand the multi-level factors that may influence effective use and understand the barriers these individuals experience in taking their medication regularly.

Formative research is encouraged to inform better targeting, engagement, and retention of the highest-risk youth populations in PrEP care. Novel approaches designed to identify appropriate individuals for PrEP, especially youth who are minors and may be hidden from common venues of congregation of older youth, and to improve understandings of risk perceptions and decision-making that could improve PrEP uptake. Models for linkage to and retention of individuals in all facets of PrEP care will need to be explored in a variety of potential settings (e.g. school-based clinics, community health centers, juvenile justice, and etc). It is expected that applicants will have ongoing affiliations in such settings. Effective support for consistent high-level adherence is also critical to maximizing the preventive benefits of oral PrEP.

Responsive studies could include, but are not limited to the following:

- Mixed-methods studies to better understand the multi-level factors that may influence selection of PrEP as a prevention option for YMSM
- Studies designed to examine individual and health systems level barriers and facilitators to youth linking to prevention services and initiating PrEP care
- Community level structural interventions such as novel legal/regulatory strategies to improve access and reduce barriers to PrEP for YMSM
- Developmental work to inform communication strategies to promote engagement in PrEP programs and PrEP uptake among YMSM
- Pilot studies on novel approaches to reach high-risk YMSM and link them to PrEP care
- Research to develop and pilot test interventions promoting retention of high-risk YMSM in PrEP care
- Research to develop and pilot test interventions designed to improve and sustain adherence to oral PrEP among YMSM

- Studies designed to characterize rates, patterns, and determinants of PrEP uptake and consistent adherence
- Research examining patterns of PrEP adherence and patterns of risk behavior among YMSM
- Exploratory studies to understand patterns of racial/ethnic disparities in adherence to PrEP among YMSM and identify potential underlying mechanisms that could be targeted to improve adherence rates
- Integration of innovative methods to encourage, promote, normalize, and routinize HIV testing among adolescents with subsequent linkage to adolescent-friendly care facilities for those who test positive or subsequent linkage to appropriate prevention education efforts and services, including PrEP care, for those who test negative

Supplement awards are for one year with maximum funding per application of **\$200,000** Direct Costs, not including third party indirect costs.

4. Rapid HIV Treatment Initiation: Implementation Models, Uptake, and HIV Care Continuum Outcomes

Promising early evidence for implementation of expedited HIV treatment initiation suggests that there may be benefits in rates of treatment initiation, linkage to care, and decreased time to viral suppression. These findings suggest that there may be both treatment and prevention benefit from such programs. However, these types of programs may encounter unique operational challenges, depending upon the setting(s) where they are implemented.

This proposed supplemental topic would encourage CFAR investigators to form partnerships in different types of settings where more rapid HIV treatment initiation could be explored. It is not known what elements of these early programs have contributed to their success, and would be essential for launch in other cities, settings, and countries. More research is needed to understand the impact of such programs on HIV care continuum outcomes.

Responsive studies include, but are not limited to:

- Formative mixed-methods research to inform potential barriers and facilitators to these programs in their potential service settings
- Development and testing of pilot programs, if feasible and appropriate – to provide initial data on HIV care continuum outcomes
- Examination of varying staffing configurations and personnel necessary to provide optimal expedited HIV treatment initiation services
- Multi-level studies (e.g., patients, providers, systems, payors) of factors that influence uptake and successful implementation with fidelity
- Evaluation framework of rapid treatment provision effectiveness

Supplement awards are for one year with maximum funding per application of **\$100,000** Direct Costs, not including third party indirect costs.

5. Drug-Drug Interactions in the Context of Antiretroviral Treatment and HIV Co-Infections and Comorbidities

As HIV-infected individuals are now living much longer, healthier lives thanks to the success of combination antiretroviral therapy (ART), the effects of sustained, life-long antiretroviral therapy, itself, on the health of the individual has become an important question. Since it is

impractical to compare the effects of these drugs in uninfected volunteers to those in HIV-infected individuals over long periods of time, a more tractable scientific question is to look at the effects of sustained ART on comorbidities and coinfections in the HIV-infected population. Much of this work has been ongoing in long-term epidemiologic cohort studies; however, the impact of long-term antiretroviral therapy on the pharmacology and efficacy of drugs used in the treatment of comorbidities and coinfections, as well as the effects of drugs for comorbidities and coinfections on the pharmacology and efficacy of antiretroviral therapy, are poorly understood.

The proposed initiative will support high priority basic or clinical research that focuses on drug-drug interactions between antiretrovirals and drugs used to treat comorbidities (e.g. cancer, diabetes, cardiovascular disease) or coinfections (e.g. TB, HCV) in HIV-positive populations of various ages in domestic and/or international settings with or without co-occurring substance abuse.

Proposed study areas may include, but are not limited to the following:

- Identification of antiretroviral drug interactions with treatments for comorbid conditions including drug dependence, or coinfections
- Pilot studies of the impact of different antiretroviral therapies on clinical outcomes associated with HIV comorbidities or coinfections
- Studies of the pharmacogenomics of antiretrovirals and medications for HIV comorbidities, drug dependence, or coinfections in the context of HIV infection
- Behavioral studies aimed at understanding the impact of combining antiretroviral therapy with treatments for comorbidities or coinfections on adherence and quality of life

Supplement awards are for one year with maximum funding per application of **\$100,000** Direct Costs, not including third party indirect costs.

Eligibility

Project leaders are restricted to early stage investigators (please see [NIH definition of new and early stage investigator](#)) and to established investigators in non-HIV fields who have never received an NIH research award for HIV/AIDS studies. Investigators should be beyond the postdoctoral level to be eligible to apply. Mentorship and collaboration with established AIDS investigators is required.

Studies that are a continuation of previously funded CFAR supplements or funded NIH applications that do not address new specific aims are not eligible for funding under this announcement. Additionally, a proposed supplement application that is linked to a proposed application not yet funded is not eligible for funding under this announcement.

Contact Ann Namkung Lee to discuss eligibility.

Application Instructions

Applications must be submitted before or on **May 23, 2016**. Requests submitted in response to this opportunity must use the PHS 398 forms (rev. 8/2012; available at <http://grants.nih.gov/grants/funding/phs398/phs398.html>) and include the elements in the request packet as described below. Applicants are strongly encouraged to submit applications as an e-mail attachment, in one file, in PDF format; however, the signature of the institutional official must be clearly visible. Font size restrictions apply as designated within the PHS398 instructions

1) **Cover Letter** – Citing this Supplement Announcement, a request for an Administrative Supplement, and the following information:

- CFAR Principal Investigator and Supplement Project Director names
- Parent grant number and title
- The scientific area of interest for this supplement request
- Amount of the requested supplement
- Name and title of the authorized institutional official
- Phone, email, and address information for the PI, the PD and the institutional official

The cover letter must be signed by the authorized organizational representative/institutional official.

2) **PHS 398 Form Page 1** (Face page) (MS Word PDF) – Provide requested information as follows:

- The title of the project (Box 1) should be the title of the parent award and a descriptive title of the supplement application
- The scientific area of interest should be cited under title in Box 2, and the “yes” box should be checked;
- Enter name of CFAR PI and the name of the project director. (Example: Dr. Bill Jones (CFAR PI) and Dr. John Smith (Project Director)).
- The remaining items on the face page should be filled out in accordance with the PHS 398 application instructions.

3) **PHS 398 Form page 2**

Note: The project “summary” is that of the administrative supplement, not the parent grant. All other information requested on Form Page 2 should be provided.

4) A **brief proposal** describing the project (with parts 4a and 4b **not exceeding five pages** in total), should include:

- a. An introduction that clearly states the **scope of the overall project**, the anticipated contribution of the requested supplement, and how the project addresses the NIH HIV/AIDS Research Priorities (NOT-15-137).
- b. The **research project plan** should include the background and rationale for the proposed study; a description of the activities to be undertaken, and roles of key staff; expected outcome of these activities; expected follow-up plan upon completion of the supplement; a description of how the supplement and follow-up plan are expected to achieve this outcome (“value-added”); and plans to monitor and evaluate the ability of the activities to achieve the outcome. Most importantly, applicants must clearly indicate how the proposed research activities are expected to lead to development of the stated goals. Mentorship and collaborations must be explained.
- c. **Budget** for the supplement with a justification that details the items requested, including Facilities and Administrative costs and a justification for all personnel and their role(s) in this project. Note the budget should be appropriate for the work proposed in the supplement request. If funding for travel to a scientific meeting is included, it must be for the early stage investigator and must be for the purpose of presenting data from this supplement award.
- d. **Biographical Sketch** for all new Senior/Key Personnel and for mentors. Use the new biosketch format in [MS Word](#). Please note the personal statement should be related to the CFAR supplement project.
- e. **Human Subjects/Vertebrate Animal documentation** (if applicable). Include a current Human Subjects/Institutional Review Board (IRB) or Vertebrate Animals/Institutional Animal Care and Use Committee (IACUC) approval date, if applicable. Otherwise, this information will be

required at time of funding. All appropriate IRB and IACUC approvals must be in place prior to a supplement award being made. NOTE: Studies involving clinical trials are not allowed.

f. Further NIH-initiated administrative actions and approvals are required for ALL international studies (NOTE: this also includes the [CFAR International Checklist](#) requirement) and any clinical studies deemed above minimal risk or involving vulnerable populations (NOTE: this includes the [CFAR Clinical Research Studies Checklist](#) requirement).

g. **PHS 398 Checklist Form** [MS Word](#) [PDF](#)

i. TYPE OF APPLICATION. Check REVISION box and enter your CFAR grant number;

ii. Applicants must state that all federal citations for PHS grants will be met (e.g., human subjects, animal welfare, data sharing, etc).

h. NO other support. This information will be required for all applications that will be funded. NIH will request complete and up to date “other support” information at an appropriate time after review.

i. NO resource page (unless there are new resources that will be used for this study)

j. NO appendices

Budget and Funding Information

Funding for supplements will be supported by the CFAR NIH co-funding Institutes.

Supplemental funds will be provided to the Developmental Core of the CFARs. Progress reports for supplements should be included in the annual CFAR noncompeting renewal.

The maximum funding allowed per application is described within each scientific area of interest above.

Funding for administrative supplements to existing CFAR grants will be available for one-year in FY2016.

How to Apply

This is a one-time announcement.

Do not send applications to the NIH Center for Scientific Review.

Applications must be signed by the authorized institutional official and submitted on or before **May 23, 2016**. If an application is received after that date, it will be returned to the applicant without review.

Applications should be emailed to:

Ann Namkung Lee
National Institute of Allergy and Infectious Disease
Telephone: (240) 627-3099
Email: anamkung@niaid.nih.gov

Submit a letter(s) of collaboration endorsing the proposed study from all substantial participants.

Applicants are strongly encouraged to submit applications electronically as an e-mail attachment in a single PDF file to the Program Officer; however, the signature of the institutional official must be clearly visible.

Review Considerations

Upon receipt, applications will be reviewed by the CFAR Program Officer for completeness and responsiveness. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to this announcement, the application will be returned without review.

Applications that are complete and responsive to the announcement will be evaluated for scientific and technical merit by an internal NIH review group convened by the NIAID in accordance with standard NIH review procedures.

Review Criteria

The following criteria apply to all applications, unless noted. Each of these criteria will be addressed and considered by the reviewers, weighing them as appropriate for each request. The administrative supplement request does not need to be strong in all categories in order for it to receive a favorable evaluation. Factors to be considered in the evaluation of each application include:

Significance – The effect that a collaborative administrative supplement would have on the development of research in the stated scientific area of interest at the institution(s).

1. Evidence that the proposed project(s) will enhance new multidisciplinary collaborations, which may include collaboration with the local health department, health clinics, community based organizations (CBOs), international site/investigator, industry, early stage or minority investigators, other CFAR sites, or with investigators inside or outside of CFAR who have expertise in the stated scientific area of interest;
2. The extent to which the supplement will address development of new strategies for the field of HIV/AIDS (“value-added” of the supplemental monies);

Approach – The quality of the CFAR scientific project proposed, including planning, management, and training (as appropriate) process.

3. Project design and appropriate Core selection;
4. Utilization of existing resources and/or development of unique and appropriate expertise, technology, and resources at the CFAR institution(s) and other sites, as appropriate;
5. The adequacy of the described plans to monitor the impact of the competitive supplemental award;
6. The quality and appropriateness of mentorship and collaboration;

Innovation - The identification of a unique approach to solve a significant question or gap in the field of HIV/AIDS specifically in the scientific area of interest indicated.

7. The degree of variety/novelty of scientific disciplines that is included in proposed scientific project;
8. The degree of innovation in project selection and experimental design;

Investigator - Choice of appropriate scientists to lead the identification and development of the collaborative administrative supplement project.

9. Choice of appropriate competitive supplement project leader and participating investigators for individual collaborative projects proposed: scientific qualifications, commitment, and experience;
10. The choice of collaborators and mentors available within and outside of the CFAR, as appropriate;

Environment – The likelihood that the proposed project will lead to the development of a new strategy in the scientific area of interest indicated.

11. Availability of appropriate scientific expertise;
12. The potential and intent to collaborate with other institutions and to coordinate program activities with related efforts of other CFARs, NIH programs, other federal agencies, local health departments, health clinics, testing laboratories, CBOs, and international organizations;
13. Evidence that scientific collaborative areas and projects arise from the complementary scientific environment at the CFAR institution(s);

Reviewers will also examine the appropriateness of the budget, in consideration of the research environment, for the scientific projects and cores.

Allowable Costs

Funding may be requested for any category normally funded by a CFAR grant that is required to fulfill the goals of the proposed study, and must be fully justified.

Schedule for Applications

<i>Announcement Release Date:</i>	<i>3/07/16</i>
<i>Application Receipt Date:</i>	<i>5/23/16</i>
<i>Review Date:</i>	<i>6/10/16</i>
<i>Earliest Anticipated Award (Start) Date:</i>	<i>6/30/16</i>

Terms of Award

A formal notification in the form of a Notice of Award (NoA) will be provided to the grantee organization. The NoA signed by the grants management officer is the authorizing document. Once all administrative and programmatic issues have been resolved, the NoA will be generated via email notification from the awarding component to the grantee business official.

Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs.

Reporting

Awarded administrative supplements will be required to submit a progress report to be included in the annual progress report of the parent grant.

Award Criteria

The following will be considered in making awards:

- meeting the NIH HIV/AIDS research priorities;
- quality of the proposed project as determined by the NIH convened internal review panel, and relevance to the ability of the proposed project to lead to scientific advances in the field of HIV;
- funding availability and;
- program balance.

Inquiries

Prospective applicants are encouraged to discuss their applications, including proposed collaborators, with the NIH contacts below.

For questions concerning eligibility of the CFAR to respond to this announcement, and any other administrative issues:

Ann Namkung Lee, M.P.H.
National Institute of Allergy and Infectious Diseases
Telephone: (240) 627-3099
Email: anamkung@niaid.nih.gov

For questions concerning a specific scientific area of interest:

- **Tracking HIV Transmission Phylodynamics: Leveraging Collaborations with Public Health Departments and Others to Research Methods to Analyze Phylogenetic Data in Close to Real-Time.**

Ann Namkung Lee, M.P.H.
National Institute of Allergy and Infectious Diseases
Telephone: (240) 627-3099
Email: anamkung@niaid.nih.gov

- **HIV and Host Factor Targets for Structural Research**

Michael Sakalian, Ph.D.
National Institute of General Medical Sciences
Telephone: (301) 594-0828
Email: michael.sakalian@nih.gov

- **Advancing PrEP Delivery**

Susan Newcomer, Ph.D.
National Institute of Child Health and Human Development
Telephone: (301) 435-6981
Email: newcomes@mail.nih.gov

Denise Russo, Ph.D.
National Institute of Child Health and Human Development
Telephone: (301) 435-6871
Email: drusso1@mail.nih.gov

- **Rapid HIV Treatment Initiation: Implementation Models, Uptake, and HIV Care Continuum Outcomes**

Christopher Gordon, Ph.D.
National Institute of Mental Health
Telephone: (240) 627-3867
Email: cgordon1@mail.nih.gov

- **Drug-Drug Interactions in the Context of Antiretroviral Treatment and HIV Co-Infections and Comorbidities**

Betsy Read-Connole, Ph.D.
National Cancer Institute
Telephone: (240) 276-6226
Email: bconnole@mail.nih.gov

Jag Khalsa, Ph.D.
National Institute on Drug Abuse
Telephone: (301) 443-2159
Email: Jk98p@nih.gov

For questions concerning budget and fiscal matters:

Roberta Wolcott
National Institute of Allergy and Infectious Diseases
Telephone: (240) 669-2964
Email: wolcottr@niaid.nih.gov