UCSF-Gladstone CFAR Supplement Announcement in HIV/AIDS – FY2020

The CFAR Program at the National Institutes of Health (NIH) invites applications from currently funded CFARs that are eligible for administrative supplements. **Each CFAR can submit a maximum of four supplement applications for topics 1-5.**

Purpose and Scientific Areas of Interest

The purpose of this administrative supplement opportunity is to **support innovative research projects, inter-CFAR meetings, and shared instrumentation** that address key gaps in HIV/AIDS and will advance the field. This opportunity should build research capacity and be consistent with the recent NIH HIV/AIDS research priorities (NOT-OD-15-137).

1. Methodology and Data Science of HIV

Researchers are increasingly applying novel analytic tools to large data sets including electronic medical records, pharmacy claims data, biologic, epidemiologic, behavioral, community, geospatial, and even social media data to improve the science and delivery of HIV treatment and prevention. The purpose of this supplement solicitation is to advance methodological and data-analytic approaches to collect, integrate, estimate and/or analyze HIV-related data that contain mental health, psychosocial, neurocognitive, neurologic and/or biologic measures. Responsive applications could also use novel approaches to identify new factors or combination of factors that may lead to the development of innovative HIV-related insights and interventions. Research conducted in either domestic or global settings is allowed.

Examples of potential research topics include, but are not limited to:

- Develop approaches for valid and reliable assessment or estimation of mental health, psychosocial, neurocognitive and neurologic variables in large HIV cohort studies and from Big Data of HIV infected or at-risk populations.
- Develop, adapt, and apply advanced data analytic techniques such as machine learning to discover underlying latent factors in complex neurobehavioral, sociobehavioral, and neurobiological systems related to HIV acquisition, care, and comorbidities that may lead to the identification of new intervention approaches.
- Develop, adapt, and apply state-of-the-art modeling techniques and tools, such as simulation modeling and data visualizations, to evaluate the relative effects of HIV bio-behavioral interventions which include mental health factors as well as structural factors (e.g., gender, power, economics, violence, and stigma and discrimination) on HIV acquisition, engagement in care, and other HIV outcomes.
- Analyze large biological datasets related to HIV transmission phylodynamics, single-cell omics, structure, or imaging, including modeling and machine learning techniques.
- Develop novel approaches to tackling big data science questions by working on common data standards, bringing large data sets together, and ensuring greater access to data.
- Develop novel approaches to study the impact of HIV and behavioral factors on development and progression of HIV-associated comorbidities, coinfections and complications.

Supplement awards are for one year with maximum funding per application of up to **$150,000** Direct Costs, not including third party indirect costs.

2. Increasing the Integration of Substance Abuse Services and HIV Prevention and Care

There is a continuing need for integrating HIV prevention and care with substance use specialty services such as syringe exchange programs and drug treatment. Linkage to these kinds of services from HIV prevention and care settings also is suboptimal. This supplement opportunity would support pilot investigations that test or inform development of interventions that facilitate these service integrations. Research is limited to domestic settings.

Examples of responsive topics include the following:

- Formative research to develop onsite PrEP or ART initiation programs conducted through syringe exchange or drug treatment programs.
- Enhanced substance abuse screening and linkage to services in HIV prevention and care settings.
- Formative research and acceptability testing to develop Telehealth (direct service and consultation models like ECHO) programs that facilitate integration of HIV prevention and care with specialty substance use services, including linkage to care, follow-up medication monitoring, and case management.
- Utilize health records and other electronic clinical databases to develop pilot programs to integrate HIV services and subspecialty substance use services (e.g., medication assisted drug treatment).
- Model service integration programs that incorporate high need activities such as HCV or endocarditis screening and linkage to care which may help increase motivation to participate in HIV care and prevention.
- Quality improvement activities related to existing efforts to integrate substance use and HIV care and prevention.

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3. Impact of Food Insecurity on HIV Prevention and HIV Care

Food insecurity is the limited or uncertain ability to meet the nutritional needs of all household members for an active healthy life due to insufficient resources or the inability to acquire acceptable foods in socially acceptable ways. While food insecurity might be linked to poverty it is not necessarily due to lack of financial resources. Non-financial reasons may include physical limitations and health issues that impact mobility and the capacity to acquire or prepare food, access to stable housing, or caregiver health. Moreover, food insecurity intersects with other social determinants of health so that experiences with food insecurity vary between different groups of people with their own unique obstacles and experiences with food insecurity. Food insecurity can impact health via different mechanisms, which may interact with each other. These mechanisms might involve the effects of poor nutrition on physiology and metabolism, poor mental health and stress, or poor patient health behavior.

This topic invites projects that address how food insecurity impacts people with HIV (PWH) or People at Risk for HIV (PRH). Specific areas of interest include whether and how food insecurity impacts HIV testing and adherence to PrEP by PRH; adherence to antiretroviral therapy by PWH; and the development, exacerbation, and effective management and treatment of comorbidities, coinfections,

and complications (CCCs). Applications focused on specific vulnerable populations such as racial or ethnic minorities, sexual or gender minorities, sex workers, unaccompanied youth, older people, people with disabilities, rural residents, or people living alone should consider how other societal factors, environmental barriers, and/or stigmas intersect with food insecurity. Formative research to inform interventions are allowed. However, projects may not propose testing of an intervention since clinical trials are not allowed through the CFAR mechanism. Research conducted in either domestic or global settings is allowed.

Topics that might be responsive to this topic include, but are not limited to:

- Impact of nutritional inadequacies in PWH with food insecurity on physiological and pathophysiological processes that contribute to CCCs.
- Evaluation of the consequences of food insecurity in PWH on patient engagement in the HIV care continuum and the management of CCCs.
- Impact of food insecurity on PrEP uptake, adherence, or persistence.
- Impact of poor mental health directly related to food insecurity on adherence to PrEP, antiretroviral therapy, or the management of CCCs.
- Formative research to inform interventions for food insecurity in PRH with the primary goal of improving HIV screening and engagement with the HIV prevention continuum.
- Dynamics, mediators, or impact of multiple insecurities (e.g. food, water, housing, etc.) relative to HIV testing, treatment (including CCC treatment), or preventive behaviors and outcomes.
- Formative research to inform interventions for food insecurity in PWH with the primary goal of improving adherence to antiretroviral therapy or improvement in CCCs.

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4. Human Mobility and HIV

This supplement solicitation would encourage formative and pilot research on the impact of human mobility on prevention and treatment outcomes in individuals at risk or living with HIV. Human mobility is broadly defined as human movement, as individuals or groups, in space and time and includes, among others livelihood/work mobility, displacement, household fluidity, rural to urban migrations, and involuntary mobility such as being trafficked for sexual exploitation. The purpose is to advance understanding of how human mobility affects (dis)engagement with the HIV prevention and care cascade and to develop strategies to address these challenges. In the Ending the HIV Epidemic (EHE) initiative, better understanding of these patterns and dynamics could be particularly important as states and counties develop regional HIV epidemic plans. Mobility can disrupt health care, endanger the health of individuals living with illness, and thwart efforts to respond to new HIV outbreaks. Studies could be conducted to improve HIV outcomes in people who are in transition or have recently resettled in new, temporary, or permanent housing. In the US and globally, this includes populations such as those who have relocated due to household fluidity, livelihood mobility, seasonal work opportunities, poverty, homelessness, incarceration, and those who are displaced as refugees, asylees, or internally displaced people due to a variety of socio-political and natural events. Research conducted in either domestic or global settings is allowed. Applications proposing research in prisoners are not allowed.

Examples of potential research topics include, but are not limited to:

- Epidemiological studies to examine/model dynamic patterns of HIV indicators in space and time in mobile populations. (Studies should be conducted with stakeholder input and consideration of the ethical, legal, and social challenges associated with identifying HIV outbreaks among mobile populations).

- Develop strategies to engage in prevention and treatment services for mobile populations who are at risk of HIV acquisition or living with HIV.
- Studies to understand the social and structural determinants of health related to mobility which affect mental health and HIV outcomes.

Supplement awards are for one year with maximum funding per application of up to **$150,000** Direct Costs, not including third party indirect costs.

5. Overcoming Barriers to HIV Reservoir Clearance

Current efforts to eliminate persistent HIV-infected cells are focused on enhancing adaptive immune responses (antibodies, therapeutic vaccination, and engineered bi-specific molecules) to better target the rebound-competent HIV reservoir in the context of ART. However, critical gaps remain in understanding factors that impact the ability of persistently HIV-infected cells in blood and tissues to be recognized and killed, as well as factors that dictate immune-mediated clearance of persistently infected cells. Successful approaches to eliminate persistent HIV reservoirs will require strategies that enhance susceptibility of the diverse pool of persistently infected cells to cell death or immune clearance. Strategies to improve immune effector cell function and maintain their long-term efficacy may also be needed. Research conducted in either domestic or global settings is allowed.

This supplement opportunity will support research related to the following areas:

- Factors that regulate intact or defective HIV transcription, reactivation and antigen expression levels in different persistently infected cell types in blood and tissues, and their impact on susceptibility to immune-mediated elimination.
- Strategies to limit clonal proliferation of latently-infected T cells.
- The roles of defective HIV proviruses in inflammation and immune dysfunction as drivers of HIV reservoir persistence.
- The role of novel, biologically active host and/or viral RNA species, RNA modifications, or other factors in maintaining HIV persistence.
- Factors that enhance long-term immune effector cell function or facilitate reservoir cell death.
- Mechanisms for enhancing immune responses to reactivated HIV for more effective reservoir elimination.
- Application of innovative technologies, such as single-cell analysis approaches and intracellular, intravital, or whole-body imaging, to better understand factors that impact HIV persistence and clearance.
- Studies addressing these issues in pregnant women and children are also encouraged.

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Budget and Funding Information

Funding for supplements will be supported by the CFAR NIH co-funding Institutes. The maximum funding allowed per application is described within each topic above. Funding for administrative supplements to existing CFAR grants will be available for up to one year in FY2020.

Supplemental funds for the scientific research supplements will be provided to the Developmental Core of the CFARs. The inter-CFAR meeting supplement funds will be provided to the Administrative Core and the equipment supplement funds will be provided to the applicable Core.

Eligibility

Project leaders for all scientific areas of interest are restricted to early career investigators who have never received a R01-equivalent, P-series or U-series research grant. Established investigators in non-HIV fields who have never received an NIH research award for HIV/AIDS studies are also eligible. Post-doctoral fellows are eligible to apply if they will assume a faculty position by the time the supplement project and funding begins. Established investigators can be the project leaders for the core equipment and inter-CFAR meeting topics.

Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

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.

Full Application Instructions

Requests submitted in response to this opportunity must use the PHS 398 forms (rev. 1/2018) and include the elements in the request packet as described below. Applicants must submit each application 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 PHS 398 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
- 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 request (with parts 4a and 4b **not exceeding five pages** in total), should include:

a. An introduction that clearly states the **scope of the overall request,** 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 application; 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 activities outlined in the supplement requests 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.

   A statement regarding the expenditure of currently available unobligated grant funds of the parent CFAR grant will be required. The CFAR must include a description of the plans to spend remaining funds in order to demonstrate the need for additional funds.

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. If proposing a study involving vertebrate animals, the CFAR parent grant must already have vertebrate animal approvals in place. All appropriate IRB and IACUC approvals must be in place prior to the initiation of a project. NOTE: Studies involving clinical trials are not allowed. Applications proposing research in prisoners 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.

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 request)

j. NO appendices

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

l. If applicable, please include letters of support or approvals for projects requiring access to data, samples, tissues, cutting edge technologies or etc. Include evidence to support the feasibility of enrollment, including descriptions of prior experiences and yield from research efforts employing similar referral sources and/or strategies for projects involving recruitment of participants.

m. For transitioning post-doctoral fellows, please include a letter from your institution confirming the transition to a faculty position that includes the start date.

Review Considerations

Upon receipt, applications will be reviewed by the CFAR Program Officers 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, and alignment with the NIH HIV/AIDS research priorities 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 scientific applications, unless noted. Reviewers will also examine the appropriateness of the budget, in consideration of the research environment and the supplement request.

1. Evidence that the proposed project will enhance new multidisciplinary collaborations and exert a sustained, powerful influence on HIV/AIDS research;
2. Extent to which the supplement will address scientific gaps and/or development of new strategies which include a variety of scientific disciplines;
3. Adequacy that the strategy, methodology, and analyses are well reasoned and appropriate to accomplish the specific aims;
4. Utilization of existing resources (including CFAR Cores) and/or development of unique and appropriate expertise, technology, and resources at the CFAR institution(s) and other sites, as appropriate;
5. Degree of innovation in project selection and experimental design;
6. Quality and appropriateness of mentorship and collaboration for the research project;
7. Choice of appropriate project PI and co-investigators (e.g., scientific qualifications, commitment, and experience), as well as the collaborations with other institutions, if applicable;
8. Appropriateness of the budget, in consideration of the research environment, for the scientific projects and cores;
9. Feasibility to complete the project within the FY2020 project period (9/1/20-8/31/21).

Reporting

Awarded administrative supplements will be required to submit a progress report to be included in the annual progress report of the parent grant. Progress reports should include a summary of the supplement projects and outcomes.

Award Criteria

The following will be considered in making awards:

- Relevance to NIH HIV/AIDS research priorities;
- Scientific and technical merit of the proposed project as determined by NIH convened internal review panel;
- Funding availability and;
- Program balance.

Inquiries

For questions concerning a specific scientific area of interest, please communicate with the appropriate scientific contact below:

Methodology and Data Science of HIV

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Increasing the Integration of Substance Abuse Services and HIV Prevention and Care

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Impact of Food Insecurity on HIV Prevention and HIV Care

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Human Mobility and HIV

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