CFAR ADMINISTRATIVE SUPPLEMENT IN HIV/AIDS ? FY2018

Purpose

The UCSF/Gladstone Center for AIDS Research (CFAR) announces the availability of administrative supplement funding from the NIH CFAR Program for projects related to the following areas of scientific interest:

1. Basic Research on HIV Infection and Persistence
2. Infant Immunity for HIV Vaccine Development
3. Studies to Delineate Sex Differences in the Incidence of Heart, Lung, Blood, and Sleep Comorbidities in People Living with HIV
4. Formative Research on Behavioral Aspects of Novel Biomedical HIV Prevention and Treatment Regimens
5. The Evolving Opioid Epidemic and its HIV Consequences
6. Implementation of Evidence-Based HIV Interventions and Treatments for Health Disparity Populations (in U.S. populations only)

The purpose of this administrative supplement opportunity is to support innovative research from basic science through implementation research 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]).

See additional information below for a description of the types of projects that are being solicited.

Eligibility

Project leaders for all scientific areas of interest are restricted to:

- Early career investigators [2] who have never received an R-series research grant
- Established investigators in non-HIV fields who have never received an NIH research award for HIV/AIDS studies
- Post-doctoral fellows are eligible to apply if they will assume a faculty position by the time the supplement project and funding begins

Mentorship and collaboration with established AIDS investigators is required. CFAR Core and Scientific Working Group leaders are encouraged to collaborate on their applications, and to collaborate with appropriate individuals not currently involved in AIDS research.

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.

Studies involving clinical trials are not allowed (see definition [3]). Contact lauren.sterling@ucsf.edu [4] to check allowability.

**Funding**

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

Awards will be made as supplements to the UCSF/Gladstone CFAR grant.

Each CFAR is limited to submitting a maximum of four total applications; therefore we are conducting an internal competition to determine which applications will go forward for submission to the NIH.

See the full announcement for more information: [2018 CFAR Supplement Announcement Final.pdf](#)

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**Concept Proposal Application Process**

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 partnering foreign institutions in the scientific areas specified and is intended to complement ongoing domestic and international HIV/AIDS research efforts funded or sponsored by the NIH.

To apply for this opportunity, please do the following:

1. Email lauren.sterling@ucsf.edu [6] a non-binding ?email of intent? by Monday, March 26, 2018, noon PDT including:
   A. Proposed Project Director
   B. Application Title
   C. Scientific Area of Interest
   D. Mentor(s) (if applicable) and collaborator names
   E. Indicate whether your proposed project would involve a foreign component and specify the location

2. PLEASE SUBMIT CONCEPT PROPOSALS ELECTRONICALLY IN ONE FILE (MS Word or Adobe PDF) TO lauren.sterling@ucsf.edu [6] BY 5pm PDT, Wednesday, March 28, 2018, including:
   A. Cover letter with title of proposed project (maximum of 81 characters), name and contact information of Project Director, and name(s) and contact information of Mentor(s), if applicable. Please also address the following:
1. Identify your selected Scientific Area of Interest from the six areas listed above.
2. Please note whether you will be proposing an international component and specify the location.
3. Include a table listing the key personnel to participate in the proposed project, including the following information: Names, degrees, institutional affiliations, and roles in project.
4. Include a brief description of how you have addressed the purpose of this opportunity and the eligibility requirements described in the announcement.

B. Specifics Aims Page for proposal (limit one page, Arial 11 font or equivalent). Applicants are strongly encouraged to review the review criteria listed in the full announcement.

C. NIH-formatted Biosketch of Project Director. Please make sure to include past and current Research Support so that we can confirm Project Director eligibility.

D. Brief description of budget by cost category (salaries, benefits, supplies, equipment, travel, other services, subcontracts). Be sure that the aims of the proposal can be achieved with the given budget. Refer to the NIH Grants Policy Statement regarding allowable and unallowable costs. Please note that subcontract indirect costs are allowable and do not count towards the direct cost limit. Contact lauren.sterling@ucsf.edu if you have any budgetary questions.

After selection of the finalists (we anticipate we will notify you on/around April 4th), full proposals (research plan can be in draft form; budget must be final) are due by Friday, April 27, 2018, and research plan must be final by Wednesday, May 9, 2018.

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Additional Information on Scientific Areas of Interest

1. Basic Research on HIV Infection and Persistence

In recent years the balance between basic and translational HIV research has shifted heavily towards the translational side, with increased focus on prevention modalities and curative strategies. While this is a natural progression given the maturity of the field, it is important to maintain a strong basic research foundation to fuel future innovation and discovery. The goal of this topic is to bolster basic research in new and emerging areas of HIV biology and immunology and leverage innovative technologies to address remaining scientific gaps in our understanding of either HIV infection or HIV persistence during long-term ART, including virus-host interactions and both innate and adaptive immune responses.

Supplement requests addressing one or more of the following topics will be of greatest interest:

- Mechanisms and host factors involved in post-fusion intracellular transit, uncoating, and nuclear import of the HIV pre-integration complex
- The role of novel, biologically active host and/or viral RNA species, RNA modifications, or extracellular vesicles in HIV infection or persistence
- Application of innovative single-cell analysis approaches to the study of HIV infection, persistence, or host immune response
- Utilization of innovative technologies for intracellular, intravital, or whole-body imaging to study HIV infection or persistence
• Virologic or immunologic mechanisms or predictive markers associated with spontaneous control of HIV or SIV observed in some individuals after ART interruption
• Novel assays for monitoring HIV persistence and predicting or detecting the earliest stages of viral rebound including the use of oral tissues and fluids

2. Infant Immunity for HIV Vaccine Development

The development of the fetal immune system is an area of great interest especially since new tools have been developed for interrogation before or at birth. It is also important to understand the impact of maternal immunity on the fetus during infection. Information on the fetal exposure to HIV before ARVs are delivered is especially important since the virus targets immune cells. Knowledge of the maternal and fetal response to HIV in utero would be helpful in the development of a vaccine and would inform our understanding of the development of the immune system.

Responsive studies could include, but are not limited to:

• Research on the timing, development and maturation of immune system cells and cytokines, in HIV infected or exposed uninfected infants
• Studies of fetal innate and cellular component development and susceptibility during maternal/placental HIV infection
• In HIV infection, what really passes the placenta? Is the response enhanced or dampened?
• Studies to examine the maternal seeding and evolution of the fetal microbiome in infection/health and the impact on the developing brain
• Monitoring vaccine response or immune status in the oral cavity

3. Studies to Delineate Sex Differences in the Incidence of Heart, Lung, Blood, and Sleep Comorbidities in People Living with HIV

In recent years, sex has become a well-recognized biological variable. In fact, sex is defined as an independent risk factor for the development of a number of heart, lung, blood, and sleep (HLBS) diseases and has been found to play a role not only in disease prevalence but also in disease symptomatology, disease progression, and treatment outcomes. For example, women have a higher prevalence of autoimmune disease, non-obstructive coronary artery disease, and hereditable pulmonary arterial hypertension than men, while males are at a higher risk for developing atrial fibrillation and exhibit a doubled risk of myocardial infarction. In terms of HIV infection, it is well-known that sex differences exist in rates of HIV acquisition, immune responses to infection and protective immune correlates associated with HIV vaccination, and HIV disease progression. To date, very few studies have been conducted to determine sex differences in the incidence of heart, lung, blood, and sleep comorbidities in the context of HIV infection despite overwhelming evidence indicating that people living with HIV (PLWH) are at a much higher risk of developing these comorbidities in general. To inform best treatment practices and reduce disease burden in PLWH, it is of considerable interest to identify and characterize sex differences in the incidence of HLBS comorbidities in the context of HIV infection. Supplement requests addressing one or more of the following HIV-related HLBS comorbidities will be of greatest interest: heart failure and/or coronary artery disease, chronic lung disease (including tobacco use-induced lung disease in PLWH), sleep apnea and other sleep-related disorders, and platelet and endothelial cell dysfunction.

Responsive studies (utilizing existing cohort data and/or pilot, ancillary studies) could include
but are not limited to:

- Investigations into the incidence rates of HLBS comorbidities in the context of HIV infection stratified by sex
- The identification of sex-specific risk factors that increase the likelihood of developing HIV-related HLBS comorbidities
- Investigations into the effects of HLBS comorbid conditions on HIV disease progression (evidenced by CD4+ T cell counts, viral loads, ART failure, progression to AIDS, etc.) in PLWH stratified by sex
- Sickle cell disease

4. Formative Research on Behavioral Aspects of Novel Biomedical HIV Prevention and Treatment Regimens

Although current oral drug regimens for HIV prevention and treatment are highly efficacious, there is significant work to be done to optimize uptake and adherence. To help overcome these barriers, researchers are advancing novel products, long-acting drug regimens and drug delivery systems for HIV prevention and treatment, including long-acting injectable PrEP and ART, sustained-release drug delivery systems, broadly neutralizing monoclonal antibodies, and prime-boost vaccines. Although these methods reduce the burden of daily pill taking, they have other features that may lead to new uptake, adherence, and use challenges. Greater input from end-users and prescribers could lead to the advancement of HIV prevention and treatment technologies that are optimally designed for maximum uptake and adherence and could help prepare the way for any future implementation of long-acting regimens.

Responsive studies could include, but are not limited to:

- Studies to identify product attribute and drug delivery system preferences, and to understand which products and delivery systems are preferred by whom, with which partners, in which contexts
- Studies to understand the trade-offs people are willing (and not willing) to make for their preferred products and delivery systems
- Studies to understand how to optimize or combine existing delivery systems
- Qualitative studies designed to conceptualize novel products and delivery systems not currently in the pipeline that align with end-user preferences and sexual scripts in key populations
- Studies to understand social, contextual and structural influences (e.g., partners, family, sexual and social network, providers, and community) on drug regimen and delivery system preferences
- Studies to investigate patient, provider, and healthcare system delivery factors that may facilitate or impede implementation of HIV prevention and treatment products with non-daily dosing schedules
- Studies to develop behavioral, care, and systems interventions that will facilitate patient use and healthcare delivery of HIV prevention and treatment products with non-daily dosing schedules

5. The Evolving Opioid Epidemic and its HIV Consequences

The opioid epidemic in the US appears dynamic with many different components and considerations. Continuing high rates of opioid overdose death in rural areas have been joined by increased overdose deaths in urban centers among long-term people who inject
drugs (PWID) and non-injection drug users. Synthetic opioids and their widespread availability seem to be fueling these epidemics of overdose and there is some evidence that urban, suburban, and rural opioid epidemics may have increasing areas of overlap and there is potential for newer opioid epidemics to be joined with established HIV epidemics among PWID and users of other drugs. Current trends increase the likelihood that the newer opioid epidemics may see more HIV cases and suggest more attention needs to be given to the needs of long-term drug users living with HIV to reduce the potential consequences of opioid use, including overdose and problems adhering to HIV care. The complexity of the current opioid epidemics may benefit from cross-CFAR collaboration and the inclusion of colleagues from AIDS Centers funded by NIDA (e.g., CDUHR/NYU) and NIMH (e.g., UCSF/CAPS, Yale/CIRA, UCLA/CHIPTS, CAIR/MCW, PMHARC/Penn, HIV Center/Columbia). Multidisciplinary investigator teams working together with clinicians, local community stakeholders, and public health officials are encouraged. The application should include a description of collaborative activities, including any prior relationships with these collaborators.

Projects should be responsive to the opioid epidemic and its recent evolution with particular consideration of preventing HIV and other infectious disease consequences. There is a continuing need to implement evidence-based interventions such as integrated drug/HIV treatment, needle/syringe services, and overdose prevention, particularly outside of urban areas with established opioid-driven HIV epidemics. Prevention of opioid injection in established drug using populations is needed. There needs to be a better understanding of how current opioid use trends may intersect with populations of long-term drug users living with HIV, as well as other risk groups.

Note that projects related to needle exchange and syringe services need to be consistent with US Department of Health & Human Services policy: https://www.aids.gov/pdf/hhs-ssp-guidance.pdf [11]

Responsive studies could include, but are not limited to:

- Addressing knowledge gaps regarding HIV transmission among PWID, including identification of possible transmission networks that connect opioid epidemics in rural areas to established HIV epidemics
- Analysis of phylogenetic HIV transmission networks among PWID exploring spread between rural and historical urban opioid epidemics or how PWID cases may reflect networks that include other risks
- Rapid policy and epidemiology assessments that can inform implementation of evidence-based practices (e.g. PrEP, syringe services)
- Identification of promising approaches for implementing evidence-based infectious disease prevention interventions (e.g., PrEP) in rural or other non-urban areas
- Development of interventions to prevent opioid uptake among long-term drug users living with HIV
- Addressing the impact of pain management practices on the development of opioid use/misuse among PLWH

6. Implementation of Evidence-Based HIV Interventions and Treatments for Health Disparity Populations (in U.S. populations only)

There are a variety of evidence-based interventions and treatments to prevent HIV infection/transmission, and to achieve viral suppression in individuals infected with HIV. However, significant racial/ethnic, socioeconomic, and geographic disparities in new HIV
infections and attainment of viral suppression persist in the US. Health disparity populations in the US still often lack access to culturally appropriate interventions and services, and service providers that serve these populations may lack resources to offer the most efficacious interventions and services. Thus, there is considerable need to conduct research regarding the implementation of evidence-based HIV interventions and treatments for health disparity populations.

The supplement will support pilot and feasibility studies to prepare for implementation science research proposals to understand how to best deliver evidence-based interventions and services for targeted health disparity populations, which include racial/ethnic minorities, socioeconomically disadvantaged populations, underserved rural populations, and sexual and gender minorities. This initiative targets behavioral and health services interventions to prevent HIV infection, increase engagement and retention in HIV care, and increase adherence to ART. The supplement is for U.S. populations only.

Responsive studies could include, but are not limited to:

- Systematic review and evaluation of adapted evidence-based interventions/services tailored to be culturally appropriate, acceptable, or feasible in settings that serve health disparity populations
- Systematic review and evaluation of strategies to increase uptake of evidence-based interventions or treatments such as PrEP or ART by health disparity populations.
- Feasibility study to guide protocol development of comparative effectiveness research that would assess which evidence-based interventions/services in real-world settings are most effective for targeted health disparity populations
- Feasibility study to provide evidence and data to support the design and implementation of optimization research that identifies which elements of multi-component interventions/service models may be most effective or cost-effective in low-resource settings or for particular health disparity populations