CFAR Supplement Announcement in HIV/AIDS –FY2014

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

1. The Intersection of HIV Infection and the Human Microbiome

There are a lot of emerging data being generated in the NIH funded Human Microbiome Project and there is a great opportunity to capitalize on these new findings. The microbiome is involved in many aspects of health and disease. It has been shown to play a role in host immunity, and gut homeostasis and has been implicated in several disease including diabetes, colitis, and cancer. There is a great likelihood that it also has a profound effect on HIV pathogenesis including HIV risk, disease progression, host immune responses, therapeutic uptake and pharmacologic efficacy.

Studies should address one of the areas listed:

- Basic studies on the long term impact of HIV infection on the host microbiome
- Identifying the role of the microbiome in establishment and maintenance of HIV latency including epigenetic modifications mediated by the microbiome
- Research on microbial (bacterial, viral, and fungal) mediators that influence the level of inflammation in the HIV infected individual and may impact HIV pathogenesis
- Studies identifying metabolically active microbes that may influence therapeutic outcomes
- Studies on the functional metagenomics of the gastrointestinal (GI) and/or genital mucosa obtained from vaccine trial participants to determine the effect of the microbiome on immune responses

- Research on the role of the existing microbiome, including mimicry of protein immunogens, in shaping host immune responses to HIV-1/SIV vaccine candidates in the GI and genital mucosa
- Characterization of the microbiome and the associated cytokine patterns and inflammatory markers in the genital mucosa that are epidemiologically linked to HIV/SIV transmission and susceptibility

Supplement awards are for one year with maximum funding per application of **$100,000** Direct Costs.

2. PK Interactions Between ARVs and Other Drugs

Pharmacokinetics, pharmacodynamics, and pharmacogenomics are becoming important considerations in HIV treatment, but more research needs to be done before these can be useful in clinical practice. In addition, many HIV patients have co-morbid conditions and take multiple types of drugs. As a consequence, polypharmacy and medication-related problems are emerging as an important challenge facing HIV-positive patients. The drug–drug interactions between antiretroviral drugs and other types of drugs are important in determining the appropriate drug combinations and dosages for these patients. This supplement topic requests studies investigating the pharmacology and potential drug-drug interactions across the spectrum of co-morbid conditions. Supplement requests may incorporate genomics, pharmacogenomics, proteomics, cell biology and metabolomics approaches.

Studies should address one of the areas listed:

- Studies validating analytical methodology used to quantitate plasma, biomatrices (i.e., RBCs, hair, lymph nodes, GALT, and etc.), and intracellular drug concentrations (i.e., macrophages, CD4 cells, dendritic cells, and etc.) in preclinical animal models;
- Studies that develop biomarkers of drug exposure for HIV treatment (e.g., hair assays; drug blood spot assays) to identify and differentiate patients with virologic failure associated with different factors (e.g., poor adherence, special genetic makeups, and drug toxicity);
- Studies that compare interspecies similarities to identify the best alternative model to predict ARV drug-drug interactions in HIV and co-infections, including studies on factors affecting the ARV ADMEs (e.g., anatomical sites, drug class, CYP450s, transporters, pharmacogenomics);
- Studies examine drug-drug interactions of ARVs with new drugs for hepatitis, TB drugs, anti-inflammatory drugs, antineoplastic, and statins, as well as biological drug products for HIV and for co-infection;
- Studies that examine the link between pharmacogenomics and drug interaction studies.

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3. Improve HIV Care Continuum Outcomes

In each of the previous three years, the NIH, through the CFAR program, provided supplements to enhance efforts around the National HIV AIDS Strategy with an emphasis on building collaborations with health departments, identifying community needs, prioritizing research directions, and conducting formative research that targeted the HIV treatment

cascade. Projects were encouraged that focused on factors associated with linkage to HIV care, engagement, and retention -- in part to inform intervention development.

In July 2013, the White House issued an Executive Order focused on the HIV care continuum. Improving HIV care to those infected and reducing new infections remains an urgent priority. The Executive Order highlighted the imperative to increase HIV testing, improve patient linkage to necessary services, and optimize HIV treatment delivery and retention.

This request for supplement applications is expanded to allow eligible CFARs to submit research projects in collaboration with local U.S. health departments and relevant community partners to implement and evaluate interventions to improve outcomes along the HIV care continuum. The project must include an academic and public health department partnership and should reflect local community needs as identified by the science and service partners. Although an expanded existing collaboration may be better positioned based on earlier formative work, a new collaboration could also be responsive to this request.

Studies should address one of the areas listed:

- Studies of pilot interventions to increase the frequency of HIV testing in appropriate populations, timely linkage to care, earlier treatment initiation, better adherence to regimens, improved retention in care, and viral suppression;
- Studies to develop or implement novel interventions for care coordination, particularly those that take a comprehensive approach to co-morbid medical and social service needs. Studies should address local need and may be structured towards all patients or for patients who need specialized approaches for re-engagement and retention in care (e.g., those who have dropped out of care or those not successfully linked to HIV care);
- Studies designed to better understand the interplay and cumulative effect of multi-level factors (e.g., individual, couple, network, social and structural) that may either impede or facilitate all points of the HIV care continuum from testing, repeat testing, through engagement and retention care;
- Studies focused on behaviors after a negative HIV test (e.g., repeat HIV-testing, partner communication, use of other prevention strategies), particularly in difficult to reach and high risk populations such as young men who have sex with men;
- Studies to develop and test interventions to optimize repeat HIV testing, including interventions that reach individuals using technology (e.g., social media, messaging, applications on hand-held devices);
- Implementation science studies designed to evaluate and intervene with providers, clinic or systems-level approaches for HIV care continuum interventions, to promote the adoption, uptake and sustainability of evidence-based interventions in community and clinical settings.

Although interventions are encouraged, they are not required. Some CFARs and their health department partners may still be at the point where additional formative work is needed.

The proposed project should address prevention and treatment among priority subgroups in each city/region who merit additional attention (e.g., tailored to young MSM, recently released prisoners) and different gaps might be addressed by different stakeholders, depending on the factors associated with suboptimal rates of HIV testing, linkage, retention, and treatment outcomes. Participatory research might be helpful to develop and implement innovative

solutions to identify which entities (e.g., testing sites, CBOs, health care settings, mental health treatment centers, health departments) can best fill which gaps in the care continuum.

Supplement awards are for one year with maximum funding per application of **$100,000** Direct Costs.

4. HIV-HCV Co-infection

Hepatitis C virus (HCV) is the fastest rising co-infection in US urban populations among HIV positive individuals. Currently a dramatic increase in chronic HCV infection is being reported in suburban and rural areas of the US among young injection drug users (IDU, 15-22 years of age). How this emerging epidemic contributes to the HIV infection rate among young IDUs is unknown at this time. Despite the significance of the problem, major gaps exist in our basic understanding of the pathogenic interactions between HIV disease and HCV infection.
The purpose of these administrative supplements is to support highly innovative research on the effects of HIV infection on HCV infection with an emphasis on injection drug use in either young or adult IDUs, spread in the MSM population, or hepatocellular carcinoma (HCC) throughout the clinical spectrum of HCV infection and disease.

Studies should address one of the areas listed:

- Impact of substance use (both licit and illicit) injection and non-injection drug use, as well as alcohol use on HCV/ HIV disease processes;
- Host and pathogen mediated mechanisms of HCV latency such as neutralization of host defenses, viral adaptations and development of drug tolerance, and associated targets for potential therapeutic interventions;
- Studies to determine pathogenic or immunological mechanisms involved in HCV, concurrent with an underlying HIV infection;
- Identification of genetic markers, which are informative for diagnosis and therapy;
- Studies aimed at understanding the molecular pathogenesis of HIV/HCV co-infection;
- Cellular mechanisms associated with HIV/HCV co-infection mechanisms of innate immune control (or loss thereof) of latent HCV infection;
- Understanding the humoral immune response and its variability throughout the course of infection;
- Possible Interactions of HCV with race/ethnicity/gender differences;
- Host genetics: impact on chronicity, treatment, or complications;
- Characterization of viral processes of disease sequelae associated with development of hepatocellular carcinoma (at the host cellular level and the viral population level) with an underlying HIV infection;
- Novel assay, bio-imaging/technology, or animal model development that enhance this area of research;
- Translational research or studies with clear translational potential are encouraged.

Supplement awards are for one year with maximum funding per application of **$100,000** Direct Costs.

5. **HIV-TB Co-infection**

TB co-infection remains the leading cause of mortality among those infected with HIV worldwide. Current tools to diagnose, treat and manage the disease in co-infected individuals

are inadequate, particularly for multidrug resistant tuberculosis. Major gaps in our understanding of this disease interfere with our ability to address this public health crisis.

Studies should address one of the areas listed:

- Preclinical studies of new drug combinations to improve treatment outcomes in drug resistant TB or to significantly shorten treatment durations in drug sensitive TB;
- Adjuvant therapies including host-directed/immunomodulatory agents (e.g. modulation of mediated bystander cellular/tissue damage, matrix metalloproteases, superoxide dismutase, and etc.) and efflux pump inhibitors;
- Immunology of resistance to TB infection and/or TB disease.

Use or development of new animal models of co-infection will be allowed.

Supplement awards are for one year with maximum funding per application of **$100,000** Direct Costs.

Eligibility

The grantee institution must not be in the last year of the competitive segment at the time of award. CFARs are encouraged to collaborate with other CFARs. Core and Scientific Working Groups within the CFAR are encouraged to collaborate on their applications, and to collaborate with appropriate individuals not currently involved in AIDS research. Contact Ann Namkung Lee to discuss 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. 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.

Application Instructions

Applications must be submitted before or on **June 2, 2014.** 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 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** and the anticipated contribution of the requested supplement.
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 MS Word PDF
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 letter, if applicable. Otherwise, this letter 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 in the Intersection of HIV Infection and the Human Microbiome, PK Interactions Between ARVs and Other Drugs, Improve HIV Care Continuum Outcomes, HIV-HCV Co-infection, and HIV-TB Co-infection 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 FY2014.

Awards are dependent upon the scientific merit of the applications and funding availability.

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 **June 2, 2014** to the Program Officer listed below. If an application is received after that date, it will be returned to the applicant without review.

Ann Namkung Lee
National Institute of Allergy and Infectious Disease
Telephone: (301) 496-9176
Email: anamkung@niaid.nih.gov

Submit a letter(s) of collaboration endorsing the proposed study from each of the following participants: investigator performing the study and any collaborators, foreign investigator(s) (if applicable), foreign institution (if applicable).

[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. Applicants may submit applications in paper format, although paper applications are strongly discouraged. Do NOT send both an electronic and a paper version of the same administrative supplement.]

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 international collaboration, collaboration with industry, collaboration with early stage or minority investigators, collaboration with other CFAR sites, or collaboration 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 at the international site, 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 (e.g., CDC and USAID), international organizations (e.g., UNAIDS), and NGOs;
13. Evidence that scientific collaborative areas and projects arise from the complementary scientific environment at the CFAR institution(s);

In addition, for applications involving international collaborations:

14. The strength of the international collaboration with scientists from Low-and Middle-Income Country (LMIC) institutions and institutions included in the proposed competitive supplement;
15. The demonstration of continued or of future support for the program from governments, and either institutions or other non-governmental organizations from collaborating countries.

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.

Please contact the CFAR Program Officer if you are considering a project that involves a foreign component.

Schedule for Applications

Announcement Release Date:	***3/28/14***
Application Receipt Date:	***6/02/14***
Review Date:	***6/20/14***
Earliest Anticipated Award (Start) Date:	***6/30/14***

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:

- 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;
- programmatic priorities.

Inquiries

Prospective applicants are strongly encouraged to discuss their applications, including proposed collaborating countries and institutions, 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: (301) 496-9176
Email: anamkung@niaid.nih.gov

For questions concerning a specific scientific area of interest:

- **Intersection of HIV Infection and the Human Microbiome**

  Stacy Carrington-Lawrence, Ph.D.
  Office of AIDS Research
  Telephone: (301) 496-3677
  Email: carringtons@od.nih.gov

- **PK Interactions Between ARVs and Other Drugs**

  Geraldina Dominguez, Ph.D.
  National Cancer Institute
  Telephone: (301) 496-3204
  Email: domingug@mail.nih.gov

- **Improve HIV Care Continuum Outcomes**

  Christopher Gordon, Ph.D.
  National Institute of Mental Health
  Telephone: (301) 443-1613
  Email: cgordon1@mail.nih.gov

- **HIV-HCV Co-infection**

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

- **HIV-TB Co-infection**

  Dan Johnson, M.D.
  National Institute of Allergy and Infectious Diseases
  Telephone: (301) 594-4218
  Email: daniel.johnson@nih.gov

For questions concerning budget and fiscal matters:

Jennifer Schermerhorn
National Institute of Allergy and Infectious Diseases
Telephone: (301) 451-2649
Email: SchermerhornJ@mail.nih.gov