

Description:

Funding is made available through the AIDS and Cancer Specimen Resource (ACSR), an NCI funded cooperative agreement that supports the collection and expert preservation of clinically-annotated biospecimens for multidisciplinary HIV research, bridging laboratory basic science with clinical, behavioral, and epidemiological studies. For the past 24 years the ACSR has provided a foundation for successful translational research reliant on consistent access to high-quality well-annotated biospecimens. It has accomplished this via development of extensive expertise in methods for specimen collection and maintenance including specimen stability and full functionality over time. The ACSR remains steadfast in encouraging HIV-translational research, expanding services to researchers, and instituting practices to complement innovative new experimental directions by global HIV investigators.

Purpose:

The ACSR Pilot Study is targeted toward junior investigators and faculty with innovative ideas for translational, clinical, or behavioral-epidemiological HIV-related research that utilizes ACSR's annotated biospecimens collected from HIV/AIDS patients and controls from both pre and post-HAART periods. Awards are intended for pilot studies to show feasibility and/or to generate preliminary data that will support efforts to procure future funding of larger research projects.

ACSR holdings include samples and collections that could be used for pilot and feasibility studies to address areas of research that are of interest to the NCI (see bullets C, D, and E below for examples). Samples are from HIV-positive patients with and without malignancies, mainly non-Hodgkin lymphoma (NHL) and Kaposi's Sarcoma (KS) although small subsets of other cancers are available, as well as HIV-negative controls (described in bullets A and B).

A) General Archival Samples include:

- TMAs (See website for Aperio images https://acsr.ucsf.edu/?page_id=904):
 - NHL (PCNSL [in development], DLBCL, 3 TMAs from 3 autopsies of patients with NHL)
 - KS (skin, visceral and oral, 4 TMAs from 4 autopsies of disseminated KS, Sub-Saharan Africa KS)
 - Prostate Cancer
 - Anal Cancer ((invasive and in-situ)
 - Hodgkin lymphoma
 - Lung Cancer
 - Breast Cancer (in development)
- FFPE tissue specimens for follow-up examination of TMA findings, tissue DNA/RNA extraction for genomics, molecular markers and methylation studies (limited subsets)
- Archival plasma, PBMCs, serum
- FFPE and/or frozen tissue from multisite autopsies of patients with HIV and cancer, primarily NHL or KS
- Limited subsets of control tissues and/or blood products
- Demographic data; CD4 counts, viral load, and cART also may be available

B) Samples and data from Clinical Epidemiological Study Collections:

- *Antiretrovirals in Kaposi Sarcoma (ARKS)*: Randomized trial among Uganda adults with histologically confirmed KS to evaluate efficacy of protease inhibitor vs non-nucleoside reverse transcriptase inhibitor-based treatment regimens; followed for up to 5 years. *Plasma, PBMCs, whole saliva*

- *Uganda AIDS Rural Treatment Outcomes (UARTO)*: Prospective cohort study of Ugandan adults with HIV/AIDS to examine the role of cART on patient outcomes; followed for up to 5 years. *Plasma, buffy coats and saliva at multiple time points*
- *Epidemiology and Virology of KSHV in Zimbabwe*: Cross-sectional study among women to evaluate prevalence and determinants of KSHV infection and shedding patterns. *Plasma, buffy coats, whole saliva, vaginal fluid and endo- and ecto-cervical swabs*
- *Transmission of KSHV to Children in South Africa*: Cross-sectional study to evaluate the prevalence and determinants of KSHV infection and shedding among children. *Plasma, buffy coats and whole saliva*
- *San Francisco Young Men's Health Study*: Prospective cohort that enrolled HIV+ and HIV- MSM with/without KS from 1998-2003 to examine HIV and HHV8 sero-conversion. *Plasma, pbmc, semen, saliva, whole blood with or w/out DMSO.*
- *Women's Interagency Health Study*: Prospective multisite epidemiologic cohort study of women infected with or at increased risk of infection with HIV. *Plasma, pbmc, urine, cervicovaginal lavage (multiple time points)*

Areas of research that are of interest to the NCI as described in NCI "Provocative Questions in Cancer with an Underlying HIV infection related to AIDS/HIV" and in PAs 15-425 and 15-426

C) Exploration of biomarkers and diagnostics:

- Discovery of reliable molecular and immunological diagnostic and prognostic biomarkers and pathogen markers, useful for early detection, progression, or response to treatment of non-AIDS-defining and AIDS-defining malignancies;
- Discovery and development of novel targets and efficacious new therapeutic agents,
- Studies to understand the pharmacokinetics of targeted therapies for AIDS-defining and non-AIDS defining malignancies in the context of highly active antiretroviral therapy

D) Etiology, Pathogenesis and Immunology:

- Studies to determine pathogenic or immune response mechanisms involved with infectious agents that interact with HIV to mediate tumor initiation and promotion of malignancies;
- Studies aimed at identifying the roles of HIV infection and long-term anti-retroviral therapy on the immune response and pathogenesis of either non-AIDS-defining or AIDS-defining tumors;
- Studies to determine the effects of either HIV-associated immunosuppression, concomitant prolonged exposure, and/or incomplete or failed responses to HAART on the development of either non-AIDS-defining or AIDS-defining malignancies;
- Studies to determine the cellular epigenome, proteome, microbiome and transcriptome of tumors in the context of an HIV infection;
- Studies of how aging and HIV interact in the development of either non-AIDS-defining or AIDS-defining malignancies;
- Studies of the pathogenesis of tumors caused by Kaposi sarcoma associated herpesvirus (KSHV);
- For a given HIV-associated tumor type, studies aimed at understanding similarities and differences in the tumors arising in the context of HIV-infected and uninfected individuals and differences in their pathogenesis and;

E) Molecular Epidemiology and Prevention:

- Studies to integrate omics data into epidemiology studies of either of non-AIDS-defining or AIDS-defining malignancies;
- Studies to characterize the immunologic, virologic, genetic, and epigenetic differences between those patients on HAART who develop pre-neoplastic and neoplastic conditions and those patients who resolve these conditions or do not develop them;
- Studies investigating an HIV-altered microbiome and the impact on non-AIDS-defining and AIDS-defining malignancies;
- Studies involving multiple co-infections, in HIV infected patients to address questions such as: what are the appropriate study designs to understand the etiology of different cancers where multiple infections are reported; what are the effects of "early" antiretroviral therapy on cancer risks, occurrence, progression and outcomes; what is the effect of co-infection on cancer survivors; whether co-infection produces amongst a variable host response, a proliferative response of lymphoid elements to viral antigens and in combination with other factors: genetic, epigenetic, socioeconomic, and/or environmental, which contribute to increased risk of cancer;
- Longitudinal studies on the impact of infections with oncogenic infectious agents on HIV disease progression in aging populations.

INSTRUCTIONS:

Completed applications are due by 5 pm PDT on February 17, 2017. Applications should be submitted as pdf documents to CODCC@acsr.ucsf.edu

1. The award level for this pilot study is up to \$30,000 in direct costs, indirect costs (F&A) are not allowed
2. The number of awards will be determined by the peer review group.
3. The funding period is for 12 months (start date July 1, 2017).
4. Progress reports will be due to the ACSR Central Operations and Data Coordinating Center (CODCC) at six months and within 60 days of the project end date.

Eligibility:

Post-doctoral students, Fellows, Residents, Assistant Professor level junior faculty, less than or equal to 5 years from completion of most recent highest degree at time of funding (not time of application submission) from non-profit U.S. public and private institutes of higher education. Applicants cannot currently hold or previously have been awarded an NIH R01 grant or equivalent funding. Non-U.S. citizens at eligible U.S. institutes are eligible to apply.

Criteria for Review/Evaluation of Applications:

Applications that are completed and meet eligibility requirements will be evaluated for scientific and technical merit by scientific review committee convened by the ACSR in accordance with NIH review criteria: 1. Significance, 2. Approach, 3. Innovation, 4. Environment. Each of these criteria will be addressed and considered in assigning the overall score. Scores will be consistent with NIH scoring, range 1 to 9 where 1-3 is excellent, 4-6 good, 7-9 poor. Scores with an average of 3 or above will not be eligible for funding.

Awarded applicants will be assigned to an ACSR PI/Senior HIV-researcher for guidance as well as regular communication and correspondence to assess milestones and progress toward completion of aims. Funded applications also are required to adhere to all ACSR requirements for use of specimens including IRB approval, Material Transfer Agreement, etc.

Projects MUST be HIV-related, ideally HIV-related malignancies

All researchers who intend to submit an application are required to contact the ACSR Central Operations and Data Coordinating Center CODCC@acsr.ucsf.edu before proceeding. An ACSR PI will be assigned to assist applicants with the proposal process and ensure that the ACSR can assist the investigator with her/his research needs.

Format and Guidelines:

- A. Proposal Length: Maximum 4 page protocol, including Specific Aims and hypotheses, Background, Significance, Innovation, Research Approach, figures and tables, excluding table of contents and bibliography
- B. Format Requirements: Arial font 11 pt. minimum 0.5 inch for all margins; no appendices; include page numbers and table of contents (not part of total page count)
- C. PI Name, Title: Department/Affiliation/Email address/Address/Phone
- D. Project Title: (80 character limit with spaces)
- E. Abstract: Single paragraph only maximum 300 words with subheadings for background, aims and objectives, study design and methods including statistical analysis; not included in the total page count.
- F. Project Narrative: 3 sentences (would like for sharing with non-scientific shareholders); not included in the total page count.
- G. Research Approach/Plan:
 1. Aims and hypotheses:
 2. Background:
 3. Significance to HIV-research and to the applicant's career goals:
 4. Innovation:
 5. Research Approach including study design, laboratory methods, statistical analysis methods, power/sample size justification to address the study aims. Preliminary results or supporting data from the applicant's research or from the published literature.
- H. Bibliography: (Not part of the 4-page limit)
- I. Budget Justification: Justify all costs fully
- J. Budget: Use the NIH PHS 398 form "Page 4: Detailed Budget for Initial Budget Period"
 - a. Allowable costs: investigator salary up to 10% effort; salary for laboratory/research technician; lab reagents and small equipment costs, software for analysis of data, publication costs, required travel to present results at the International Conference on Malignancies and Opportunistic Infections (ICMAOI) and/or ACSR Executive Committee Meeting.

- b. Unallowable costs: computers and capital equipment, administrative costs, indirect costs.
- K. NIH Biosketch for PI and key investigators, Letter of support from Department Chair and/or Supervisor/Mentor
- L. Awarded applicants will be required to submit a Final Progress report and to present their research/results at the annual ICMAOI meeting and/or ACSR Executive Committee Meeting.