AIDS AND CANCER SPECIMEN RESOURCE
YOUNG INVESTIGATOR PILOT AWARD

Description:

Funding is made available through the AIDS and Cancer Specimen Resource (ACSR), a U.S. National Cancer Institute (NCI) funded cooperative agreement that supports the collection, preservation and distribution of clinically-annotated biospecimens for multidisciplinary research, bridging laboratory basic science with clinical, behavioral, and epidemiological studies. Since 1994, 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 establishment of relationships and agreements for specimen collection as well as adherence to best practices that assure biospecimen collection and maintenance practices that optimize stability and functionality of different sample types for research purposes over time. The ACSR remains steadfast in building infrastructure for biobanking, encouraging HIV-translational research, expanding services to researchers, and instituting practices to complement innovative new technologies and experimental directions by global HIV investigators.

Purpose:

The ACSR Pilot Award is targeted toward early-stage investigators and faculty who propose innovative ideas for translational, clinical, or behavioral-epidemiological HIV-related research that utilizes ACSR's annotated biospecimens collected from persons living with HIV (PLWH) and controls without HIV from both pre and post-HAART periods. Awards are intended for pilot studies to show feasibility and to generate preliminary data that will support efforts to procure future funding of larger research projects. In addition, researchers with access to other sources of AIDS malignancy tissues are encouraged to apply so as to enhance the repositories of both the ACSR and their programs through sharing of resources.

ACSR holdings include samples and collections that could be used for pilot and feasibility studies that include but are not limited to those that address areas of research that are of interest to the NCI (see bullets C below for examples). Samples are from PLWH 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 controls i.e. samples from persons without HIV (described in bullets A and B). **Special consideration and priority will be given to projects that propose to use samples from the studies in the ACSR special collections (https://acsr1.com/specimens/collections/) described below in bullet A.**

A) Samples and data from Clinical Epidemiological Study Collections:

- *Antiretrovirals in Kaposi Sarcoma (ARKS):* Randomized trial among Uganda adults living with HIV and who have 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, peripheral blood mononuclear cells (PBMCs), whole unstimulated saliva at multiple time points*
- *Uganda AIDS Rural Treatment Outcomes (UARTO):* Prospective cohort study of Ugandan adults living with HIV/AIDS to examine the role of cART on participant outcomes; followed for up to 5 years. *Plasma, buffy coats and unstimulated 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 unstimulated saliva, vaginal fluid, and endo-cervical 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 unstimulated saliva*
- *San Francisco Young Men's Health Study:* Prospective cohort that enrolled men who have sex with men (MSM) living with HIV/AIDS with/without KS from 1998-2003 to examine HIV and HHV8 sero-conversion. Samples also are available for MSM without HIV. *Plasma, pbmc, semen, saliva, whole blood with or w/out DMSO.*

- *Women's Interagency Health Study:* Prospective multisite epidemiologic cohort study of women living with or at increased risk of HIV. *Plasma, pbmc, urine, cervicovaginal lavage (multiple time points)*

B) General Archival Samples include:

- Tissue Micro-arrays (TMAs); list and link to Aperio images https://acsr1.com/specimens/collections/:
  - NHL (primary CNS lymphoma (PCNSL), diffuse large B cell lymphoma (DLBCL), 3 TMAs from 3 autopsies of participants 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)
- Formalin-fixed paraffin-embedded (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 participants with HIV and cancer, primarily NHL or KS
- Limited subsets of control tissues and/or blood products

C) Areas of research that are of interest to the NCI as described in NCI "Notice of Special Interest (NOSI): Use of Biological "High" or "Medium" Priority AIDS Research on Non-AIDS-defining or AIDS-defining Cancers"

- *Etiology, Pathogenesis and Immunology*
  - Studies to determine pathogenic or immune response mechanisms of infectious agents that interact with HIV, mediate tumor initiation and promotion of malignancies;
  - Studies of how aging processes and HIV interact in the development of either non-AIDS-defining (NAD) or AIDS-defining malignancies (AD);
  - Development of animal and/or cell-based models for NAD and AD malignancies with an underlying HIV disease;
  - Studies to determine the cellular epigenome, proteome, glycobiome, and transcriptome of tumors in the context of HIV disease;
  - Studies investigating HIV-associated alteration of the microbiome and its impact on NAD and AD malignancies.

- *Biomarkers, Diagnostics, and Therapeutics*
  - Discovery of reliable molecular and immunological diagnostic and prognostic biomarkers and pathogen markers, useful for early detection, progression, or response to treatment of NAD and AD malignancies;

- *Molecular Epidemiology and Prevention*
  - Determine the relationship of omics data to the natural history of NAD or AD malignancies;
  - Studies to characterize the immunologic, virologic, genetic, and epigenetic differences between those participants on ART who develop pre-neoplastic and neoplastic conditions and those participants who resolve these conditions or do not develop them;
  - Studies to characterize the host genetic susceptibility to NAD and AD malignancies in the context of HIV disease;
  - Assessment of risk factors (e.g., tobacco, infections, diet, and nutrition) that impact cancer in the context of HIV disease, in different geographic locations in domestic and international settings.

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INSTRUCTIONS:

Completed applications are due by 5 pm PDT on April 5, 2021. Applications should be submitted as pdf documents to contact@acsr1.com

1. The award level for this pilot study is up to $40,000 in direct costs, indirect costs (F&A) are not allowed**. A letter from the institutional office of research agreeing to waiver of institutional indirect costs is required. Applications without an institutional letter agreeing to waiver of indirect costs will not be considered.**
2. Institutional review board (IRB) or independent ethics committee (IEC) U.S. National Institutes of Health (NIH) Federal-wide Assurance (FWA) for human subjects approval for non-exempt projects and evidence of IRB or IEC human subjects determination of exempt status is **required**.
3. The funding period is for 12 months (earliest start date May 1, 2021).
4. Progress reports will be due to the ACSR (contact@acsr1.com) within 60 days of the project end date.

Eligibility:
Post-doctoral students, Fellows, Residents, Assistant Professor level early stage investigators faculty, less than or equal to 8 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. U.S. and non-U.S. citizens are eligible to apply. IRB or IEC U.S. federal-wide assurance is required for non-exempt human subjects research and **must be in place at the time of funding**, whereas evidence of IRB or IEC exemption for research defined as exempt per the U.S. NIH criteria is required. Applications without U.S. FWA or IRB/IEC exemption will not be considered.

Criteria for Review/Evaluation of Applications:
Applications that are completed, meet eligibility requirements and which propose to use samples that the ACSR has in its inventory, 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

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All researchers who intend to submit an application are required to send a brief Letter of Intent (LOI) to the ACSR (contact@acsr1.com) by 5 pm PDT on March 15, 2021 before proceeding. The LOI should provide a title, the research question, and description of the samples including diagnosis, types, number and volume of material required. An ACSR PI may be assigned to assist applicants with the proposal process to ensure that the ACSR can support the investigator with their/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 with a maximum 300 words with subheadings for background, aims and objectives, study design and methods including statistical analysis (subheadings not included in total word count); 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, travel to present results at the International Conference on Malignancies in HIV/AIDS (ICMH) or similar conference 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 ICMH meeting or equivalent conference and/or ACSR's annual Meeting of its Scientific Advisors and Executive Committee typically held in May.

The ACSR is funded by a cooperative agreement granted by the National Cancer Institute.