

RFA Reissuance Request
AIDS and Cancer Specimen Resource

Office of HIV and AIDS Malignancy (OHAM)

Purpose of ACSR RFA

- Facilitate research by basic, translational, and clinical researchers in HIV-associated malignancies by acquiring, storing and equitably distributing tumor tissues and biological fluids
- Support biobanking needs of the AIDS Malignancy Consortium (AMC) domestic and international clinical trials

Proposed programmatic addition:

- Strategically enrich the existing inventory of rare and difficult to obtain specimens through a series of specimen sparing and optimizing initiatives

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- Funds will come from our AIDS budget received through the NIH Office of AIDS Research (OAR). (Concept has been reviewed by the OAR and deemed AIDS-aligned)

Background - HIV Epidemic

- **HIV Epidemic**

- US- 1.2 Million people with HIV (PWH)
- Latin America- 2.1 Million PWH
- Sub-Saharan Africa- 25.6 Million PWH (70% of all PWH)

- **Cancers in People with HIV**

- Prominent manifestation of HIV/AIDS since the beginning of the epidemic
- Combination antiretroviral therapy (cART) led to the decline of cancers most associated with AIDS, however rates of decline have stabilized
- Increase in the incidence of other HIV-associated cancers such as anal cancer, hepatocellular carcinoma, and lung cancer
- Cancer is one of the most, if not the most, frequent cause of death in people with HIV (PWH) in the United States

AIDS and Cancer Specimen Resource (ACSR)

- Established in 1994 to provide high-quality specimens with associated clinical data from PWH with or at substantial risk for cancer to qualified investigators at *little or no cost* to the investigators
- Types of specimens:
 - Formalin-fixed tissues and fresh-frozen tissues
 - PBMCs, plasma, body fluids (e.g., saliva, urine, CSF)
 - HIV-negative control samples; Non-tumor control tissues
 - Tissue micro-arrays (TMAs) with matching DNA/RNA and digital images
- Cancer types: KS, NHL, anal, prostate, lung, cervical (over 700 diff dx)
- Special Collections: clinical trials, prospective cohort studies, longitudinal cohort studies, or epidemiological studies in PWH or at risk for HIV-infection

AIDS and Cancer Specimen Resource (ACSR)

ACSR Regional Biospecimen Repositories (RBRs):

- **George Washington University**
- **University of California San Francisco**
- **Baylor College of Medicine**
- **Stellenbosch University, South Africa**
- **University of Sao Paulo, Brazil**

Biorepository Support for the AIDS Malignancy Consortium (AMC)

- **Domestic Biorepository: George Washington University (2010)**
- **Regional Sub-Saharan Africa Biorepository: Stellenbosch University (2013)**
- **ANCHOR (Anal Cancer HSIL Outcomes Research) Biorepository: University of Arizona, Tucson (2014)**
- **Regional Latin America Biorepository: University of Sao Paulo (2022)**

Regional Biospecimen Repositories (RBRs) Activities

Acquisitions	Patients	Samples
HIV+	277	2,039 ^a
HIV-	240	1,646
ACSR General Inventory (all sites)	Patients	Samples
HIV+	6,219	45,448 ^b
HIV-	3,751	64,181
Sub-Saharan African RBR	314	4,501
Special Collections ^c	Patients	Samples
Antiretrovirals in Kaposi Sarcoma (ARKS)	264	54,532
Uganda AIDS Rural Treatment Outcomes (UARTO)	799	240,287
San Francisco Young Men's Health Study (SFYMHS)	581	82,339
Women's Interagency HIV Study (WIHS)	654	13,234
AMC (Donations to the ACSR)	997	19,942
Zimbabwe KSHV	527	4,236
South Africa KSHV	975	7,328
Rapid Case Ascertainment (RCA)	272	8,096
Multiple Autopsy Collection	57	919
Total	15,927	503,280

a. Specimen types include (but are not limited to) FFPE (62 blocks, 224 unstained slides), frozen tissue (50), plasma (860), and PBMCs (843).

b. 20,629 tumor tissue and 24,819 other sample types. NHL and KS are the most common cancer types (821 and 1076, respectively).

c. Includes saliva, PBMCs, plasma, buffy coat, dried blood spots, and biopsies in RNAlater.

- Acquisitions- strategically focused on obtaining those specimens that are most highly requested tumor types and specimen types
- General inventory- 20,629 tumor tissue; 24,819 other sample types
- NHL (821) and KS (1076) are the most common cancer types
- Special Collections- cohort studies and epidemiological studies with high amounts of annotation, some of the most widely distributed specimens

Regional Biospecimen Repositories (RBRs) Activities

Inquiries		
Interfaces (with investigators)		197
Letters of Intent w/Distributions	LOI	Specimens
Feasibility	25	
Standard	21	
Letters of Support -> LOIs	18	
Distributions	LOI	Specimens
Samples (all types)		20,074
Includes Tumor Microarray Slides		298
includes Tumor Microarray Cores		10,378
Material Shipped	LOI	Specimens
FFPE	14	982
Nucleic acid extractions	13	590
TMA Cores	12	10,378
Plasma	9	6,987
Frozen tissue	6	177
PBMCs	5	960
YIPAs		
Awards		7
Samples distributed thru Oct 2022		587

- 197 investigator interfaces
- 64 LOIs that led to 20,074 specimens distributed
- 10,378 of 20K distributed were TMA cores from 298 slides
- The most requested and fulfilled material included FFPE, nucleic acids and TMA slides
- Young Investigator Pilot Award Program (YIPA)- 7 awards totaling 587 with hundreds more to be distributed

AMC Biorepositories

Biorepositories	
Domestic (Washington, DC) (2010)	
Sub-Sharan Africa (Cape Town) (2013)	
Latin America (Sao Paulo) (2022)	
Protocols	
Active	14
Closed (embargo)	4
Closed (but distributing)	16
Accrual (participants)	
Active	540
Targeted	1,105
Clinical Sites	
Domestic	48
International	10
Investigators supported	
Clinical	250
Laboratory	24
Inventory	
Active AMC (samples banked)	26,776
Donations to ACSR	10,110

ANCHOR Biorepository (2014)

Accrual (participants)	
Screening	10,723
Randomization	4,353
Post-Randomization	4,019
Inventory (samples banked)	
Total	563,098
Processing (by stage)	
Screening	185,701
Randomization	350,078
Post-Randomization	27,319
Clinical Sites	
ANCHOR only	6
ANCHOR and AMC (hybrid)	13

Collection Sparing and Optimizing Initiatives

■ Tissue Microarray (TMA) Program

- Frugal and equitable distribution of rare tissue specimens
- 88 TMAs, 19 developed this cycle
- DNA/RNAs and archived digital images of cancer type appropriate stains

■ Biospecimen Science Program

- Fit for purpose studies; repurposing specimens; optimization and standardization of protocols to produce high quality derivatives from recalcitrant samples
- Standardize and optimize isolation of liquid biopsy analytes from fresh and frozen plasma (with the AMC)
- Dried blood spot program- fit for purpose studies, nucleic acid isolation and optimizing and developing best practices for spotting biofluids

Some Highlights of Scientific Impact of ACSR on HIV Malignancy Research (1)

- **72 manuscripts**
 - 41 represent the use of ACSR specimens and resources;
 - 31 manuscripts reflect AMC clinical trials and correlative science supported by the AMC biorepository activities
- ANCHOR Trial
 - *Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer (Palefsky et al., NEJM, 2022)*

Some Highlights of Scientific Impact of ACSR on HIV Malignancy Research (2)

HIV+ Tumor Molecular Characterization Project (HTMCP)

- *Analysis of Ugandan Cervical Carcinomas Identifies Human Papillomavirus Clade-specific Epigenome and Transcriptome Landscapes* (Gagliardi et al., *Nat Genetics*, 2020)
- *Genetic subgroups inform on pathobiology in adult and pediatric Burkitt lymphoma* (Thomas et al., *Blood*, 2023)

Papers of Note from ACSR Distributions:

- *Insertional activation of STAT3 and LCK by HIV-1 proviruses in T cell lymphomas* (Mellors et al., *Sci Adv.*, 2021)
- *Exosomes derived from HIV-1-infected cells promote growth and progression of cancer via HIV TAR RNA* (Chen et al., *Nat Commun.*, 2018)

Mid-cycle External Evaluation

- Unequivocally a valuable resource for the global HIV-associated malignancy research community
- Has served as a specimen resource to advance scientific understanding in HIV-associated malignancies and HIV for almost three decades
- Provided a vital service in support of biorepository activities for the AMC and for the ANCHOR study embedded with the AMC
- As the research challenges of HIV-associated malignancies have evolved, so too has the ACSR
- ACSR's work continues to be innovative, and their established collaborations address important gaps in the science

Mid-cycle Evaluation Recommendations

- Enhancement of the strategic planning and evaluation process (in progress; development of an External Advisory Board)
- Continued investment in marketing efforts to enhance ACSR visibility and use (ongoing)
- Establishment of a formal ACSR-wide Disaster Recovery Plan (completed)
- Reinvigoration of collaborations and interface with other NCI- and NIH-initiatives
- Continued investments in the support of research in Low- and Middle-income countries (LMICs) (ongoing)

Proposed Budget

	Year 1	Year 2	Year 3	Year 4	Year 5
Office of the Chair	900,000	900,000	900,000	900,000	900,000
Basic RBR support	2,000,000	2,000,000	2,000,000	2,000,000	2,000,000
AMC Repository	1,000,000	2,000,000	2,000,000	2,000,000	2,000,000
Data Management and Coordination Center	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000
Technical Core	400,000	400,000	400,000	400,000	400,000
Independent Procurement	200,000	200,000	200,000	200,000	200,000
Total Cost	5,500,000	6,500,000	6,500,000	6,500,000	6,500,000
Grand Total					31,500,000

Proposed Budget (cont.)

- Proposed moderate increase of \$700,000 for the ACSR in the first year. This increase is meant to address:
 - College of American Pathologists (CAP) Biorepository Accreditation
 - Development of a database management system that better serves the ACSR and is harmonized with the AMC
 - Cost of the science increases for RBRs and AMC Biorepositories
 - NOTE- **\$100,000 decrease** for specimen procurement
- Additional increase of \$1,000,000 in years 2 through 5
 - To cover the fiduciary responsibility of the ANCHOR Biorepository from the AMC Cooperative Agreement to the ACSR Cooperative Agreement as the ANCHOR Trial begins to sunset
- Limited Competition: to maintain the existing ACSR infrastructure, both domestic and international; maintain continuity between the ACSR and AMC Biorepository activities; support transition in leadership of the ACSR

Questions ?



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