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BIORESOURCE PAPER

AIDS and Cancer Specimen Resource (ACSR)

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The AIDS and Cancer Specimen Resource (ACSR) has four regional biorepositories (RBRs) in the United States and one in South Africa. The ACSR is funded by the National Cancer Institute (NCI) of the National Institutes of Health (United States) to support investigators studying HIV/AIDS and HIV/AIDS-associated malignancies. The ACSR inventory includes more than 450,000 annotated HIV-positive biospecimens from over 10,000 individuals and 100,000 HIV-negative controls from approximately 4,250 individuals, reflecting the pre-highly active antiretroviral therapy (HAART) and post-HAART era of the HIV epidemic, as well as selected geographic regions heavily impacted by this global pandemic.

Keywords: Biobanking; biological samples; HIV; AIDS; AIDS-related malignancies; non-AIDS-related malignancies; Tissue Microarrays

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(1) Bioresource Overview

Project description

The ACSR includes biospecimens from persons with HIV/AIDS who have been diagnosed with a wide spectrum of HIV/AIDS-related diseases and conditions, particularly malignancies. The ACSR's mission is to acquire, store, and equitably distribute these samples and associated clinical data to investigators conducting HIV/AIDS-related research. The current inventory includes several large well-annotated special collections, including domestic and sub-Saharan African HIV-related clinical epidemiology studies, AIDS Malignancy Consortium (AMC) clinical trials, and multisite autopsies. In addition, cancer-specific and multisite autopsy tissue microarrays (TMAs) have been created to support screening studies. Ongoing biospecimen science projects assess the "fit for purpose" of various archival samples, including protein and nucleic acid derivatives, for the evolving needs of HIV/AIDS and the HIV/AIDS malignancy research.

Classification (1)

Human

Species

Human

Classification (2)

Biological samples and clinical data.

Context

Spatial coverage

The ACSR consists of five regional biospecimen repositories (RBRs): four in the USA and one in South Africa. Biospecimens have been collected from patients in the United States, Sub-Saharan Africa (SSA), and Asia.

Description: North America, Sub Saharan Africa, and Asia

Northern boundary: 37.7749° N,

Southern boundary: 33.9249° S,

Eastern boundary: 18.4241° E

Western boundary: 122.4194° W

Temporal coverage

September 1994 to the present with no termination date.

Temporal coverage for accessibility
N/A.

(2) Methods

Steps

- Donor samples and data are obtained from consented individuals through various means including direct recruitment from outpatient clinics and hospitals, donations from AMC clinical trials, and acquisitions from clinical epidemiological studies.
- A customized flexible informatics database and integrated inventory management system (ATLAS) was developed specifically to address the ACSR's needs for Quality Control and Quality Assurance, specimen tracking, and linking specimen-associated clinical, epidemiological and laboratory data.
- Standard Operating Procedures (SOPs) are used to consent, process and store a wide variety of biospecimens. Specimens are distributed to researchers via a formal application process that includes scientific approval by an independent REDP (Review and Evaluation Decision Panel) along with the National Cancer Institute, and the Executive Committee (EC) of the ACSR.
- Fluid samples (e.g. whole blood) or solid samples (e.g. tissue) are collected under a variety of conditions with tissue material typically procured retrospectively for patients with remaining or surplus biopsy/surgical diagnostic samples. Prospective collection of specimens contributes to a growing collection of snap frozen tissue specimens and cell blocks prepared from fine needle aspiration biopsies. Specimens from patients recruited and screened for some clinical trials are donated through an additional consent process.
- Derivatives from fluid and solid samples such as peripheral blood mononuclear cells (PBMCs), plasma, sera, RNA, and DNA are available upon request. The biospecimen inventory can be explored using the ACSR's Inventory Explorer (https://acsr.ucsf.edu/inventory-explorer/).
- A number of annotated cancer-specific and multisite autopsy tissue microarrays (TMAs) constructed using ACSR formalin-fixed paraffin-embedded tumor tissue from patients with HIV and cancers are available for research. TMA inventory (https://acsr.ucsf.edu/specimens/collections/) and digital images (https://acsr.ucsf.edu/wp-content/uploads/2017/09/To-access-the-ACSR-digital-library.pdf) can be viewed on the ACSR home page (https://acsr.ucsf.edu).
- Tissue specimens are validated by ACSR pathologists to confirm tumor content and characterization during acquisition and disbursement. Annotated formalin-fixed paraffin-embedded (FFPE) and fresh frozen tissues stored in LN_2 are available.
- The ACSR website provides instructions for submitting an inquiry or Letter of Intent (LOI) to obtain ACSR samples and data for HIV/AIDS-related research (https://acsr.ucsf.edu/request-specimens). As noted above, LOI approval requires a review of the science and justification for the number and types of samples and is conducted by the ACSR's independent REDP constituted by the U.S. NCI. Use of biospecimens from the SSA RBR requires collaboration with an African investigator, which can be facilitated by the ACSR as needed.

Stabilization/preservation

- Cell-freezing medium (90% Heat Inactivated (HI) Fetal Bovine Sera (FBS) and 10% Dimethyl Sulfoxide (DMSO)
- Formalin Fixation with Paraffin Embedding
- Acid Citrate Dextrose
- Snap freezing with and without OCT

Type of long-term preservation

- Ultra-Low freezers (–70°C) or LN2 MVE (–194°C)
- Formalin Fixed Paraffin Embedded (FFPE) tissue at ambient temperature.

Storage temperature

- –80°C (DNA)
- –190°C to –194°C in LN2 (tissue, serum, plasma, PBMC)
- Ambient Temperature 15°C to 25°C (e.g., FFPE).

Shipping temperature from patient/source to preservation or research use
Varies from ambient temperature (18°C to 25°C), dry ice (–56°C), liquid nitrogen (–190° to –194°C).

Shipping temperature from storage to research use

- Ambient temperature (18°C to 25°C) (none) for FFPE,
- 0 to 4°C (chemical blocks)
- –20°C (wet ice)
- –56°C (dry ice) for frozen tissue and whole blood derivatives stored at –70°C (e.g., PBMCs, sera, and plasma).
- –190°C (Liquid Nitrogen) for snap frozen tissue and whole blood derivatives already stored in LN2.

Quality assurance measures

- ACSR Standard Operating Procedures (SOPs) for technical procedures (e.g., Blood Products Body Fluids Collection, Live Tissue Collection), administration, and management (see https://acsr.ucsf.edu/sop)
- Quality Management Plan (QMP)
- Informatics Quality Management Plan (IQMP)
- Internal ("self") ACSR audits (by RBR) and External Audits

Source of associated data
Level of sample annotation varies widely due to the variety of sources from which samples are/were acquired and when they were acquired. At a minimum, HIV status, date of collection, age at collection, race, sex, ethnicity, specimen diagnosis (tissue) and/or clinical diagnosis (fluids), and organ site, are captured. Additional data may include CD4 count, viral load, and highly active antiretroviral therapy (HAART). Special collections i.e. samples from clinical trials and epidemiological studies are extensively annotated with demographic, behavioral/lifestyle, clinical and outcome data available.

- Medical records and pathology reports. A list of associated data can be found in the Inventory Explorer (https://acsr.ucsf.edu/inventory-explorer).

- Clinical trial data from closed AMC clinical trials.
- Epidemiological studies.

Ethics Statement
Each Regional Biospecimen Repository of the ACSR has local institutional IRB approval. Researchers approved to use specimens must submit an approved IRB from their institution. ACSR specimens are intended to be stored indefinitely. The South African Biorepository has local or national IRB approval.

Constraints
The ACSR inventory has collected material for over 25 years and reflects the research topics, trends, and preservation methods at the time of collection.

(3) Bioresource description

Object name
HIV/AIDS malignancies

Bioresource name
The AIDS and Cancer Specimen Resource (ACSR)

Bioresource location(s)
- George Washington University, 2300 I Street NW, Washington, DC 20052
- University of California San Francisco, 1001 Potrero Ave, San Francisco, CA 94110
- Baylor College of Medicine, One Baylor Plaza, Houston, Texas 77030
- Mayo Clinic, 13400 E. Shea Blvd. Scottsdale, AZ 85259
- Stellenbosch University and National Health Laboratory Service, Tygerberg Hospital, Francie Van Zijl Dr, Parow, Cape Town, 7505, South Africa.

Bioresource contact
CODCC@acsr.ucsf.edu

Bioresource URL
https://acsr.ucsf.edu/

Identifier used
N/A

Bioresource type
HIV, AIDS, and HIV/AIDS malignancy

Type of sampling
Disease based and longitudinal and prospectively collected samples; samples in clinical care (i.e. individuals who are under the care of oncologists); samples under a research protocol; clinical trial samples; retrospective sampling of pathology archives.

Anatomical site
Any.

Disease status of patients/source
- HIV positive;
- HIV positive with malignancy;
- HIV negative with malignancy;
- HIV positive with no malignancy;
- HIV negative with no malignancy.

Clinical characteristics of patients/source
- HIV+ pediatric and adults cases of males and females with or without malignancy from pre- and post-HAART.

Size of the bioresource
- Over 14,787 donors until September 2017
- Acquisition is ongoing

Vital state of patients/source
Alive and deceased.

Clinical diagnosis of patients/source
AIDS defining and Non-AIDS defining malignancies
HIV positive.

Pathology diagnosis
intraepithelial neoplasia
Infectious (e.g. viral)
Lymphoid neoplasm
Myeloid neoplasm
Non-hematopoietic neoplasm
Normal
Reactive process

Control samples
HIV negative without malignancy
HIV negative with malignancy
HIV positive without malignancy

Biospecimen type
Formalin fixed paraffin embedded tissue (FFPE)
Frozen Tissues (~5 mm)
Fine Needle Aspirates cell blocks
Tissue Microarrays
Plasma (0.5 ml aliquots)
Serum (0.5 ml aliquots)
Urine (0.5 ml aliquots)
Saliva
DNA (as requested)
RNA (as requested)

Release date
N/A

Access criteria
The ACSR solicits standard Letters of Intent (LOI) and Feasibility (Short) Form LOIs from investigators throughout the year. LOIs that are completed in accordance with the described requirements (see website (https://acsr.ucsf.edu) will be submitted for scientific review. Confirmation of receipt and submission of an LOI for scientific review is documented via an email that includes an LOI tracking number to be referenced in all future correspondence. Investigators are encouraged to submit an inquiry specifying the type and quantity of biospecimens that they are interested in obtaining from the ACSR – this inquiry can be done from the ACSR website. The RBRs will work with the investigator and the ACSR to

verify the availability of the requested biospecimens and further assist the investigator through the LOI process, which includes assistance in identifying a SSA collaborator for requests of biospecimens from our SSAB. Once the biospecimen type and quantity have been confirmed in the ACSR inventory, the investigator will be directed to submit an LOI. The LOI should succinctly describe the research plan including justification of the number and type of biospecimens requested.

The Feasibility (Short) Form LOI is designed for pilot studies that require a minimal number of biospecimens, e.g., for test development, quality control, and/or to generate preliminary data/research. The Feasibility (Short) Form LOI allows a researcher to request up to 20 biospecimens on a one-time basis for a particular study. (https://acsr.ucsf.edu/wp-content/uploads/2018/03/ACSR_Feasibility_Form-02132018.pdf).

The Standard Form LOI is used for all other requests and requires a more detailed research plan, including a power/sample size and statistical analysis section. The Standard Form LOI is reviewed and scored by members of an independent Research Evaluation and Decision Panel (REDP), which is composed of individuals with the relevant scientific expertise. The review and score are used by the ACSR Executive Committee to make the final decision for the request for biospecimens and associated data. If the ACSR does not have the number and/or types of samples that meet the investigator's research needs, every effort will be made to identify an appropriate resource. For each LOI, an ACSR representative assists with the distribution of biospecimens and/or other inquiries including scientific/technical issues. ((https://acsr.ucsf.edu/wp-content/uploads/2018/03/ACSR-LOI_Standard_Form_02132018.pdf)).

Letters of Support (LOS) to document the ACSR's commitment to work with an investigator to provide the necessary biospecimens required for a proposed research project also can be provided. These letters can be included for a National Institutes of Health (USA) or other grant applications as needed.

IRB approval and completion of a Material/Data Use Agreement (MTA/DUA) must be received by the ACSR before disbursement of any biospecimens. Investigators who fail to complete the MTA/DUA and IRB approval documentation within six months of receiving their letter of approval will have the approval voided, making those biospecimens available to other investigators.

(4) Reuse potential

The ACSR provides high-quality specimens from HIV-infected individuals with or at substantial risk for cancer, with associated clinical data, at no cost to eligible researchers. Requests are handled on an ad hoc basis through an application process described above. There is an expectation that researchers should share data/research findings with the ACSR, addressing the principle of data/information sharing. Researchers should also provide feedback on the quality of the specimens that they received/used in their research, as well as acknowledge the ACSR as the source of the specimens data.
https://acsr.ucsf.edu/request-specimens/

Competing Interests

The authors have no competing interests to declare.

Author Roles

Sylvia Silver	Principal Investigator, Executive Committee, Office of the Chairs, RBR Principal Investigator (GWU), Quality Working Group, and Marketing Working Group
Jeffrey Bethony	Executive Committee, Office of the Chairs, and Science and Technology Working Group
Paige, Bracci	Executive Committee, Office of the Chairs and the Hub for Integrated Informatics and Research Support (HIIRS). Science and Technology Working Group, and Marketing Working Group Chair
Ashokkumar A Patel	Executive Committee, Office of the Chairs, and the Hub for Integrated Informatics and Research Support (HIIRS).
Mostafa Nokta	Executive Committee, Director, AIDS Cancer Clinical Program, National Cancer Institute, NIH, USA
Lisa Rimsza	Executive Committee, RBR Principal Investigator (Mayo), and Science and Technology Working Group Chair
Michael Ittmann	Executive Committee, RBR Principal Investigator (Baylor), and Science and Technology Working Group
Johann Schneider	Executive Committee, RBR Principal Investigator (Stellenbosch), and Science and Technology Working Group
Michael McGrath	Principal Investigator, Executive Committee, Office of the Chairs, RBR Principal Investigator (UCSF), and Science and Technology Working Group

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