Office of HIV and AIDS Malignancy (OHAM) Re-issuance Request

AIDS and Cancer Specimen Resource
Establishment of the ACSR and Objectives

• The ACSR was established by the NCI in 1994 in response to a BSA Subcommittee assessment of researcher needs in the HIV-associated malignancy field.

• Primary Objective: Meet the specimen needs of clinician and basic researchers in HIV-associated malignancies by **acquiring, storing and equitably distributing tumor tissues and biological fluids from patients with HIV-associated malignancies.**
ACSR Funds

- A portion of NCI’s appropriated funds are restricted for use in HIV-related research. The ACSR is funded using these “AIDS-directed” dollars.
- The NIH Office of AIDS Research (OAR) coordinates the NIH AIDS research program and provides additional oversight and guidance for the use of AIDS restricted funds.
- OAR considers the ACSR a “high priority” project for funding.
Comments on Acquisitions, Curation and Distribution

- HIV-related malignancies encompass a number of rare diseases
- Specimens reflect a wide variety of cancer types
  - Over 20 different diagnosis codes
- Multiple tissue specimen processing types:
  - FFPE, frozen, bloods (PBMC, Plasma, Serum), other bodily fluids (saliva, CVL, urine, CSF), PAP smears
- Multiple time points collected per patient
- Multiple aliquots
- Specimens must be considered in the context of a variety of immunologic and infectious disease states (HIV, KSHV, EBV, HPV). Fortuitous cohort collections with blood specimens that pre-date cancer diagnosis are extremely valuable.
- Tools developed (TMAs, WGA-DNA) to preserve specimen base
Since 2006, 76 different investigators from 50 institutions have received specimens from the ACSR. 125 publications representing 43 institutions (excluding NCI and ACSR institutions); 11 foreign institutions.

ACSR has created 24 Tissue Microarrays. Disbursed 14,751 TMA cores.

African Collections:
- Acquired: 108,672 samples from 2,245 individuals
- Disbursed: 5,827 samples

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• **Kaposi sarcoma**
  - Confirmation of KSHV as the causative agent of KS; Biology of KSHV and its role in tumorigenesis
    *Ex: AIDS (1997); Journal of Virology (1997)*
  - Development of the BCBL-1 primary effusion lymphoma (PEL) cell line. Invaluable research tool with >160 citations in Pubmed.
  - Multi-detection algorithm for seroprevalence of KSHV
    *Journal of Clinical Microbiology* (2006)
  - KSHV in HIV-suppressed and non-suppressed individuals
    *mBio* (Am. Soc. for Micro. on line journal- 2011)
Selected High Impact Research Supported by ACSR

- **Lymphoma**
  - Novel treatment for Burkitt lymphoma
    *Blood* (2005)
  - Impact of HAART on HIV-associated lymphoma incidence and subtypes in South Africa
    *Transfusion and Apheresis Science* (2011)

- **HIV**
  - HIV-1 spread in tissues of HIV+ individuals

- **San Francisco Young Men’s Health Study**
  - “Rescuing” specimens from this study led to advances in KS and KSHV research
Additional Roles of the ACSR and Support of Current and Future Projects

- Serving as AMC Biorepository
- Plays a major role in the HIV+ Tumor Molecular Characterization Project (HTMCP)
- Incoming grant applications for HIV-lymphomas, KS and HPV-related tumors rely on ACSR
- ACSR has written 10 letters of support for investigators submitting grant applications
- A number of funded NCI grants are dependent on the ACSR to achieve research objectives
- At least two, independent, NCI funded clinical trials are relying on the ACSR for curation services for trial specimens
Future High Impact Studies

• A proposed, large clinical trial (over 10,000 screened patients) is planning to use the ACSR as the biorepository for clinical material.

• Activities in Sub-Saharan Africa
  – Capacity building
  – Regional Biospecimen Repository

• NCI’s Provocative Question #12: Cancers caused by novel infectious agents and mechanisms of tumor induction.
  – ACSR specimens may be a very useful source of material to look for novel infectious agents involved in tumorigenesis.
Global HIV-Associated Cancer Burden

- 34 million HIV+ or AIDS pts.
- 70% in resource-limited Sub-Saharan Africa
- High prevalence of oncoviruses that cause HIV-associated malignancies: KSHV, EBV, HPV
- HIV-associated cancers now among the most common tumors in Sub-Saharan Africa
- Lack of adequate pathology; much unknown about types of tumors and epidemiology
- President’s Emergency Plan for AIDS Relief (PEPFAR) rollout
- In future, will become more like the US, with less AIDS-defining but more non-AIDS-defining cancers
ACSR and NCI’s Global Efforts

- OHAM efforts in Sub-Saharan Africa
  - ACSR
  - AIDS Malignancy Clinical Trials Consortium (AMC)
  - D43 Grants: Developing Research Capacity in Africa for Studies on HIV-Associated Malignancies
- The three initiatives were designed to compliment each other
- ACSR PIs assisting with training and capacity building in pathology and in specimen and data curation, and developing expertise in the challenges regarding obtaining and transporting specimens
- Proposed ACSR repository in Africa
Rationale for Continuing to Acquire New Specimens

- HIV epidemic, and the associated malignancies are ever changing within the USA and globally.
  - Increasing incidence of non-AIDS defining tumors, yet each still a rare disease. Inadequate specimens in repository to meet research needs.
- Fresh frozen specimens needed with matching non-tumor germline samples for comprehensive molecular and genomic analysis
- New specimens needed from the developing world, especially Sub-Saharan Africa. Historical specimens non-existent or of little value.
- New samples needed from patients who have been on long term HAART
Proposed Changes to Enhance ACSR

- Restructuring to enhance cooperation and coordination. Single U01, single PI, broadened membership of the Executive Committee.
- Greater central oversight of collection initiatives, participating sites, collaborations, international activities.
- Flexibility to ensure a more rapid response to exceptional opportunities or poor investments.
- Broader expertise to make more effective scientific decisions.
- Facilitate NCI/OHAM Staff’s ability to monitor, and provide guidance and oversight to the ACSR.
Questions?