Administrative Supplements for P30 Cancer Centers Support Grants (CCSG) to Stimulate Research in Immunotherapy and Tumor Microenvironment in HIV/AIDS Cancer Patients at NCI-designated Cancer Centers

Background

Human immunodeficiency virus (HIV)-infected individuals are at increased risk for developing several cancers. Despite the success of combination antiretroviral therapy (cART) in suppressing HIV and improving patients' quality of life, cART does not lead to eradication of the virus. Cellular immunity is central in controlling HIV replication, and the focus now has shifted more to control of viral replication rather than eradication. Several recent studies have demonstrated the safety and feasibility of immunotherapeutic approaches for successful treatment of some cancers in non-HIV infected individuals. Effective strategies include the use of antibodies to check point inhibitory molecules such as PD-1 and antibodies that targets cytotoxic T-lymphocyte associated antigen-4 (CTLA-4) which are regulators of T-cell function. Other reported approaches include the use of chimeric antigen receptor (CAR) T-cells for treatment of adults with relapsed or refractory non-Hodgkin lymphoma patients. The capability of CAR T-cells for long-term engraftment and immune surveillance was recently shown in a large animal preclinical model for HIV/AIDS.

Since HIV adopts numerous strategies to evade immune surveillance, it is of importance to determine if people living with HIV (PLWH) will respond to anticancer immunotherapy modalities in a similar fashion to non-HIV infected individuals in the general population. The ultimate goal to treating cancer is dependent on a safe and effective immunotherapeutic modality concurrently with enhancing a tumor microenvironment that promotes T cell activation and infiltration into premalignant or cancerous tissue. The success rates of first-generation cancer immunotherapies, such as checkpoint inhibitors, genetically engineered T-cells, and new immune activators, have improved remarkably over the past decade resulting in durable, long-term survival, and in some cases cures for a subset of patients with advanced cancers such as melanoma, blood, and lung cancers. However, little is known about how PLWH may respond to immunotherapy; if their tumor microenvironment is more hostile and prevents T-cell activation and infiltration; and if they can achieve similar results as the non-HIV-infected cancer patients.

Purpose and Goals

The National Cancer Institute (NCI) announces an opportunity for supplemental funding to identify and advance immunotherapy translational approaches for HIV/AIDS individuals with cancer. The primary goals will be the discovery and characterization of immunotherapeutic targets, the development of new immunotherapy treatment approaches, and the improved understanding of the immunosuppressive tumor microenvironment, to advance new, more effective immune-based therapeutic regimens for patients with HIV/AIDS-related cancers.

It will be extremely important that the applicant outlines specifically the HIV outcomes for the proposed work. Note that KSHV studies that are proposed should be in the context of HIV (with

HIV outcomes specified) to be aligned at 100%. As such, if the NIH Office of AIDS Research (OAR) does not deem an application as 100% aligned, OCC will be unable to fund it.

To advance new, more effective immune-based therapeutic regimens for patients with HIV/AIDS-related cancers, specific areas of study may include, but are not limited to, the following examples:

- discovery and characterization of immunotherapeutic targets,
- development of new immunotherapy treatment approaches,
- improved understanding of the immunosuppressive tumor microenvironment,
  This FOA is not designed for support of clinical trials.

Eligibility and Budget

- This opportunity is open to all currently NCI-Designated Cancer Centers.
- Only one supplement request per center will be considered.
- To be considered responsive for supplemental funding, centers must articulate a detailed project plan.
- Supplement requests may not exceed $500,000 total costs for 2 years.
- Cancer Centers whose P30 Cancer Center Support Grant will be on an extension at the time the award is made in FY22 are not eligible.
- It is anticipated that awards for this supplement opportunity will be made in September 2022.
- Any proposal that cannot be completed within the 2-year time frame will be viewed as non-responsive.
- Allowable costs include funding for the Project Leader of the study (maximum of 20% effort), who must be a member of the NCI-designated cancer center; funding for required expertise to complete this project; and costs for supplies.
- The purchase of large pieces of equipment through this supplement will not be permitted.

Application Submission Format

Applications must be submitted electronically via eRA Commons to the parent award (P30) using PA-20-272 "Administrative Supplements to Existing Grants and Cooperative Agreements (Parent Admin Supplement)" on or before **May 9, 2022**. Your submission should follow the instructions in the funding opportunity announcement, including the following:

1. **Research Plan** (6 pages) including the following elements

- Make sure to add to the title of the supplement in parenthesis
  Immuno/microenvironment
- Proposed research may include basic, translational, and clinical research on the management of AIDS defining and non-AIDS defining cancers.
- Description of the background, preliminary data (if available), relevant cancer center infrastructure, data sources, and specific aims for the proposed research.

- Inclusion of target diverse population across the spectrum of age, gender, and race is encouraged.
- Leadership of projects by junior or mid-level investigators is encouraged.
- Inclusion of a **statement** of how the proposed project would meet the NIH HIV/AIDS Research Priorities as listed in the NOT-OD-15-137. It should explain which high priority topic or topics will be addressed. General projects focusing, for example, on EBV, HPV, KSHV or other oncogenic viruses or HIV alone are not eligible for support under this supplement award.
- Outline specifically the HIV outcomes for the proposed work. Note that KSHV studies that are proposed should be in the context of HIV (with HIV outcomes specified) to be aligned at 100%. As such, if the NIH Office of AIDS Research (OAR) does not deem an application as 100% aligned, OCC will be unable to fund it.
- Details of the qualifications for the identified lead(s) of the supplement. Note: separate SF424 forms will be needed for biosketches.

2. **Detailed budget and justification** for funding and activities requested using SF424 forms.

In addition, the application must include Project Summary/Abstract and Specific Aims as a part of a submission package. No appendix or attachments are allowed.

For tracking purposes, please notify Nga Nguyen (nga.nguyen@nih.gov) when you submit application (but please do not send the application itself).

Evaluation Criteria
Supplements will be administratively evaluated by NCI staff with appropriate expertise. There will not be a secondary review process.

Awards
Awards will be based on responsiveness to the goals of this announcement and the availability of funds.

Reporting Requirements
As part of the annual progress report of the parent NCI Cancer Center Support Grants include information on what has been accomplished via the administrative supplement during the funding period. A copy of the annual progress report for the administrative supplement should also be sent to Dr. Hasnaa Shafik by email at shafikh@mail.nih.gov.