Purpose:
The purpose of this initiative is to stimulate research in non-AIDS defining cancers (NADCs) among aging individuals with HIV infection via support of pilot projects at NCI-designated Cancer Centers (CC). Findings from this supplement are aimed to expand our knowledge of the impact of aging on the pathogenesis of NADCs. The overarching emphasis of this announcement is to explore the (1) pattern, (2) natural history, and (3) optimization of treatment of NADCs occurring in aging HIV-positive individuals.

Background:
The number of older individuals living with HIV/AIDS has risen dramatically over the last decade. From 2001-2008, the proportion of Americans living with HIV who are ≥ 50 years rose to 31% from 17%, and this is expected to rise to over 50% in 2015. The introduction and widespread use of combination antiretroviral therapy (cART) in the mid-1990s has dramatically improved the health outcomes of HIV+ individuals, leading to decreases in AIDS-defining cancers such as Kaposi’s sarcoma and non-Hodgkin’s lymphoma. However, the longer life expectancy now observed in these individuals has led to the increased incidence of diseases with a longer latency period, such as NADCs. NDACs now account for 50% of all cancers among HIV+ individuals. The incidence and mortality from NADC in HIV+ individuals ≥ 50 years of age have not been extensively studied; however, some studies have shown an increased incidence in liver, bladder, lung, and Hodgkin’s lymphoma.

It has become apparent that individuals living with prolonged HIV infection exhibit many of the clinical characteristics commonly observed in aging, such as multiple co-morbidities, polypharmacy, physical and cognitive impairment, functional decline, alterations in body composition, and increased vulnerability to stressors. Moreover, the clinical picture of HIV in older adults may be complicated by many other risk factors, including infections with oncogenic viruses (e.g., human papillomavirus [HPV], Kaposi-sarcoma associated herpesvirus [KSHV/HHV-8], Epstein-Barr virus [EBV], hepatitis B virus [HBV], and hepatitis C virus [HCV]), obesity, and substance abuse including nicotine, alcohol, marijuana, and prescription drugs. Also, HIV-infected patients on cART often have a degree of immunologic impairment and chronic immune activation, even when their CD4 count is normal. Aging itself is associated with immunologic impairment, and it is unclear how these factors interact in aging HIV-infected patients. As such, improved management of older individuals with HIV will require a much deeper understanding of the interface between aging, HIV, associated co-morbid conditions, and concurrent treatment.

Mechanism and Funds Available:
The NCI may allocate up to $1.6 million dollars per year in total costs depending on funding availability. It is expected that 8 - 9 awards of up to $200,000 total costs per year will be awarded by September 2018 to successful applicants; awards will be for one to two years. Funding will be as a supplement to the parent P30 CCSG, with funds restricted to support of pilot studies in non-AIDS defining cancers among aging, HIV+ patients. The selection of the
pilot projects will be through the established cancer center internal review process. The internal review committee should include members from the cancer center, and ad hoc reviewers with relevant expertise as needed. More than one pilot research project may be selected for funding. All projects must have documentation of approval from the CC’s Protocol Review and Monitoring System and the institutional IRB, as appropriate.

CCs must select pilot projects are that are eligible for high priority AIDS funding according to NOT-OD-15-137. Titles and abstracts of selected pilot projects must be sent to the Office of Cancer Centers (OCC) prior to activation to ensure this requirement has been fulfilled.

Progress of research projects will be monitored by the Office of Cancer Centers. The supplement progress report must be included with the CCSG progress report, and a separate annual report is required on the anniversary date of the award.

Eligibility to Apply and Other Requirements:

All CCs are eligible to apply. Only one application per CC is permitted. A CC may request funding for one - two years. Any proposal that cannot be completed within the 1-2 year time frame will be viewed as non-responsive. Specific areas of study may include, but are not limited to, the following examples:

- Biology of aging and cancer
- Effects of comorbidities (consequences of the aging process and/or the progression of HIV/AIDS)
- Effects of polypharmacy including antiretroviral therapy on treatment of NADCs; Treatment efficacy and tolerance
- Cancer control for early detection, diagnosis, prevention, treatment, prognosis and survivorship

Receipt Date: April 28, 2018

Allowable Costs:

This award is for pilot projects only and does not support the purchase of equipment and salary for project leaders. The general areas in which costs are allowable are as follows: salaries for pilot projects investigators, technicians and reagents.

Application Procedure:

1. Cover letter: signed by the CC Director should accompany each application. Center Director needs to provide the name of the project leader(s) to undertake the project.
2. Format of the Application: SUBMIT your project(s) with your application.
   - Use the standard face page of the PHS 398 including all institutional signatures.
   - Provide 3 -5-page narrative that includes (1) rationale, study design, project time line and methods for each project proposed; and (2) facilities/resources at Cancer Center that will be available to the project.
• Explain how this announcement was made available to the CC investigators; describe
  the review committee membership and review process; number of applications
  submitted and number selected for moving forward.
• If CC received previous NADC/Aging supplements how is that being leveraged in
  the current proposal.
• 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 it will address and how it 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.

3. 3. Overall budget and budget justifications. Clearly detailed costs (Direct and Indirect)
  along with a narrative justifying each requested cost must be provided. If submitting
  more than one project, present separate budget pages per project.
4. 4. Statement assuring compliance with applicable NIH policies e.g., human subjects,
  animal welfare, data sharing, and understanding of the requirements for NIH approvals
  prior to any international study initiation, etc.
5. 5. A biographical sketch for any key personnel.
6. 6. A completed application checklist, please check "REVISION” to grant number. (This
  application is for additional funds to supplement a currently funded grant.)

Where to send the Cover Letter and Application:

Do not send applications to the NIH Center for Scientific Review. The cover letter and the
application (PDF file) can be e-mailed to:

Dr. Hasnaa Shafik at shafikh@mail.nih.gov

If unable to send via email a hard copy can be sent to:

Hasnaa Shafik, MD, PhD
Office of Cancer Centers
National Cancer Institute
National Institutes of Health
9609 Medical Center Drive
Bethesda, MD 20814-9692
Room: 2-W-210

Application Review Process:

The applications will be administratively reviewed for responsiveness to the eligibility criteria
above; relevance of the proposed concept to the CC; and adequacy of the plan, approach and
environment. The review committees will include members from the NCI Office of Cancer
Centers, Office of HIV and AIDS Malignancy (OHAM) and other NCI divisions. Incomplete
and/or non-responsive proposals will be returned without further consideration.

For clarification and /or questions concerning this supplement, contact Hasnaa Shafik MD,
PhD by phone at 240-276-5600 or via email: shafikh@mail.nih.gov