

HIV/AGING

Research to Impact Persons Aging with HIV

Request for Applications for the HIV/Aging Pilot Program

I. Basic Information

I.1. Background

This Pilot RFA is a collaboration between the Claude D. Pepper Older Americans Independence Centers (OAICs; aka “Pepper Centers”) and the Centers for AIDS Research (CFARs) and is funded by 1R24AG044325. The OAICs were established to advance research into causes, mechanisms, prevention and treatment of functional decline and disability with aging. For over 20 years, OAIC investigators have developed and validated key measures of function, excelled in recruiting and retaining older research subjects, defined phenotypes and mechanisms of aging and disability, and gathered imaging, biologic sample and clinical data repositories from seniors. The CFARs integrate NIH-funded AIDS research across 20 sites with basic, clinical, and social-behavioral interests. Through these efforts, it has become clear that HIV-infected individuals are developing non-AIDS-defining but HIV-associated co-morbidities at rates much higher than HIV-uninfected populations. Age is the dominant risk factor for these conditions which include cardiovascular disease, neurocognitive decline, metabolic disease, osteoporosis, kidney disease and cancers, and manifestations of these chronic illnesses now account for the majority of morbidity and mortality in those with HIV, not opportunistic infections as previously seen. **The increased burden of disease leads to early multi-morbidity, functional decline and geriatric syndromes (falls, fractures, frailty) in those with HIV.**

A number of “hallmarks” of aging (Figure 1) that collectively define the aging phenotype have been identified. Geroscience is a newly described concept relating these key mechanisms of aging to the development of chronic disease, functional decline and disability limiting healthy years of life. **The focus of this RFA is to use the concept of geroscience, and its interaction with HIV infection, to identify mechanisms that lead to chronic disease and premature multi-morbidity, functional decline and geriatric syndromes (e.g., falls, frailty) in people living and aging with HIV (Figure 2). Only those applications that are focused on the aspects of the biology of aging that contribute to chronic diseases and the hallmarks of aging that drive the aging process within the context of HIV will be considered for funding.**

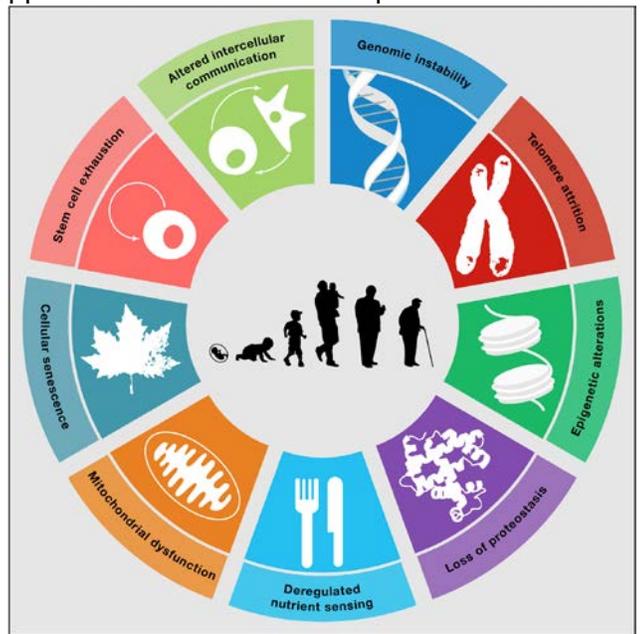


Figure 1. The nine “hallmarks” of aging (from *Cell* 2013 June 153(6): 1194–1217).

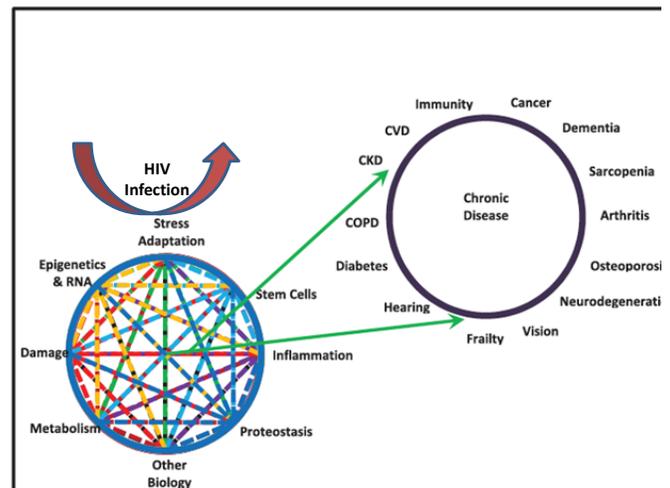


Figure 2: “Pillars” of the Biology of Aging, HIV and Impact Chronic Disease Pathways (adapted from *J Gerontol A Biol Sci Med Sci* 2014 June;69(S1):S1–S3).

I.2. Purpose

The purpose of this R24 program is to promote aging research among the CFAR and other HIV-directed investigators, and engage OAIC and other aging-centered researchers in the field of HIV. In this, the fourth iteration of the R24's pilot program, proposals with an emphasis on the emerging field of Geroscience and its application in HIV will be the focus. Both CFARs and OAICs support pilot grants on their own, and both groups have previously funded a small number of research projects at the interface of HIV and aging, but this RFA is to specifically encourage interactions between OAIC and CFAR investigators and to encourage those investigators to reach out to collaborators in the fields of HIV and aging.

There are a number of unique advantages to this RFA. For example, CFAR sites have significant access to patient samples from older HIV-infected subjects through the CFAR Clinical Cores and CFAR Network of Integrated Clinical Systems (CNICS). OAICs have established large image and bio-specimen repositories in older HIV-uninfected subjects that are available for comparative studies. Coordinated efforts between these two networks have a much greater likelihood of substantially advancing the field than individual projects that lack such integration. Further, led by the National Institute on Aging (NIA), the NIH's Geroscience Network has developed aging-focused projects and staff across the Institutes and Centers (ICs) of the NIH emphasizing the importance of the aging mechanisms in the development of many if not most chronic diseases and providing NIH staff with an understanding of Geroscience in multiple institutes/centers.

I.3. Eligibility and Mentoring

Pilot applications are welcome from any CFAR or OAIC faculty investigator at any rank; post-doctoral fellows are NOT eligible unless they will be a faculty member on July 1, 2017, and can provide a letter from their department chair to this effect. ***Strong preference will be given to early stage investigators (ESI; per the NIH definition), and studies that utilize OAIC- or CFAR-supported specimen repositories and databases (i.e., Pepper Center bio-repositories, repositories at CFAR sites or CNICS). The inclusion of both OAIC and CFAR investigators is MANDATORY.*** If applicants are not able to identify Co-Investigators with HIV or aging/Geroscience expertise at their own institution or within their local CFAR or OAIC network, this should be noted in the online submission form submitted with the Concept Proposal and the funding program will help identify an individual within the OAIC/CFAR network to act as a co-Investigator and develop the full proposal.

I.4. Focus of Projects

Applications submitted for consideration by this RFA should be focused on the emerging field of Geroscience ([J Gerontol A Biol Sci Med Sci 2014;69\(S1\):S1–S3](#) and [Cell 2013;153\(6\): 1194–1217](#) and [J Gerontol A Biol Sci Med Sci 2016; 71 \(11\): 1385-1387](#)) and its application in HIV ([J Acquir Immune Defic Syndr. 2012;60 Suppl 1:S1-18](#); [J Gerontol A Biol Sci Med Sci. 2014;69\(7\):833-42](#)). The intent is that pilot data resulting from studies funded through this RFA will provide “feeder” data for more extensive investigation in high-priority areas via the NIA/multi-institute sponsored FOAs (PAR-15-280-281-282). Only those applications focused on aspects of geroscience that contribute to chronic diseases and functional decline in the context of aging with HIV will be considered for funding. These aspects include:

- Inflammation and other cell-cell signaling
- Senescence
- Mitochondrial dysfunction
- Stem cell exhaustion
- Altered metabolism/nutrient sensing
- Epigenetic modifications and telomere attrition
- Altered proteostasis
- Stress adaptation
- Macromolecular damage (e.g., genomic instability, oxidative damage)

Human participants and/or tissue samples are desired, but animal models that address Geroscience in HIV that have clear translational value are acceptable. Investigative teams with junior faculty will be given preference, but this mechanism is open to faculty investigators at any rank. Pepper Center (OAIC) and CFAR involvement is Mandatory.

I.5. Funding Criteria

It is anticipated that up to two pilot grants will be awarded through this RFA with total funding (including indirect costs) of up to \$50,000 each from this RFA. Additional matching support from the CFAR and/or OAIC is preferred, but not required. Refer to section III.4, page 4 for detailed budgetary considerations.

I.6. Travel Support

Pilot grant awardees are expected, and will be funded, to attend the OAIC Annual Meeting to present their results in a poster session and become “immersed” in aging research opportunities; this two-day meeting in April will include plenary sessions of focused topics in aging research, networking with OAIC Directors and Core Leaders as well as NIA Program personnel, a scientific poster session, and extensive junior faculty activities, such as a mock study section, junior faculty workshops on aging research, and junior/senior faculty match-ups. *Note: funds for travel to the OAIC Annual Meeting will be provided outside the budget for direct grant dollars (i.e. do NOT include travel for this purpose in the grant budget).*

II. Timelines and Contacts

The competition will be administered in a two-phase process: the Concept Proposal phase and the Full Proposal phase. The Concept Proposal phase is open to all eligible candidates. To be eligible to compete in the Full Proposal phase, the applicant must first successfully compete in the Concept Proposal phase.

TIMELINE FOR SUBMISSIONS AND NOTIFICATIONS	
RFA Release.....	November 16 th , 2016
Concept Proposals	January 27 th , 2017
*Full Proposals Due	February 28 th , 2017 (*invited applicants only)
Estimated Award Date.....	March 14 th , 2017

II.1. Electronic Submission of Concepts and Applications

All concept proposals and invited applications must be submitted as *a single electronic (PDF) package* via the UAB CFAR website **by 5:00 pm CST on the deadline dates** listed above. Applications received after the deadline will not be considered *accepted*, even if the website link remains active.

II.2. Questions/Requests for more Information

Questions should be addressed to: Mary Smilie Thielen msmilie@uab.edu or Donna Porter, Ph.D. donnaporter@uabmc.edu.

III. Application Instructions

CONCEPT PROPOSALS

Concept Proposals are due January 27th, 2017

III.1. Concept Proposal Instructions

Concept Proposals will be submitted electronically in one, single Adobe PDF file via the R24 HIV and Aging Submission Form on the CFAR Developmental Core Page (linked [here](#)).

The Concept Proposal should be uploaded using the link above in a single Adobe PDF file, prepared in the order listed below. A cover letter is not required. Only one concept study may be submitted per lead investigator.

1. Two-page concept proposal outlining the hypotheses, specific aims, brief preliminary data (if any), and brief research design. As the criteria for selection in the Concept Proposal phase are primarily based upon the scientific merit, investigator, significance, approach, and innovation, concepts should address these topic areas.
2. Biographical Sketch for the applicant (SF424 (R&R) Format - Download: [MS Word](#)) ****New NIH Biosketch format is Required.**

III.2. Review Process and Criteria

A Scientific Selection Committee (SSC) will review the Concept Proposals. Criteria for selection in the Concept Proposal phase are primarily based upon the scientific merit, investigator, significance, approach, and innovation. For full descriptions of these criteria, see page 5: Review Process and Criteria.

Researchers whose proposals are selected for the full proposal competition phase will be notified by email on or around February 6th, 2016 and will have ~3 weeks to prepare and submit a full proposal.

FULL PROPOSALS

Full proposals are due February 28th, 2017. Only researchers whose proposals were selected from the concept proposal competition phase are invited to submit full proposals.

Successful awardees will be eligible for and encouraged to access OAIC and CFAR Cores for research tools and services. For more information about CFARs and CFAR Core services, see the [NIH CFAR website](#). To access resources from the Claude D. Pepper OAICs, visit the national [website](#).

III.3. Full Application Instructions

Full Proposals will be submitted electronically in one Adobe PDF file via the UAB CFAR website found [here](#). A cover letter is not required or recommended. The full proposal will be on the forms used commonly for NIH grant applications ([PHS 398 forms](#)) and should follow a modified NIH investigator initiated grant application (R21) format (see specifics to include in the order listed below). For applications with human or animal subjects, approvals from the IRB or IACUC at the appropriate institution must be obtained before funds are released. Required letters to accompany the application are listed below.

Reviewers will provide a written critique based in alignment with the goals of this R24, path to subsequent grant applications and research productivity, and the 5 NIH criteria to yield an overall impact score. After the review meeting, written critiques will be provided to the applicants. Pilot Project awardees will be required to provide a 6-month report on progress. A final report will be submitted by the awardees at the end of the funding year cycle. Awardees will be tracked for 2 years to monitor productivity (abstracts, publications, grants), and pilot award grantees will give a poster or slide presentation at the end of the funding period at the OAIC annual meeting.

The Full Proposal should include (in this order in a single Adobe Portable Document Format (PDF) file):

1. Face Page: (Download: [MS Word](#) or [PDF](#)) Include Institutional sign-off and eRA Commons ID.
2. Project Summary Page: (Download: [MS Word](#) or [PDF](#))
3. Detailed budget for 12 month period: (Download: [MS Word](#) or [PDF](#))
4. Complete budget and justification: (Download: [MS Word](#) or [PDF](#))
5. Checklist including institutional indirect (F&A) costs: (Download: [MS Word](#) or [PDF](#))
6. Resources page (Download: [MS Word](#) or [PDF](#))
7. Biographical Sketch for the PI, Co-Investigators and all collaborators (Download: [MS Word](#)) **New NIH Biosketch format is Required.
8. Other Support for the PI (Download: [MS Word](#) or [PDF](#))
9. Research Plan (Maximum 6 pages excluding Specific Aims and References). Use PHS 398 Continuation Format pages (Download: [MS Word](#) or [PDF](#)).
 - a. Specific Aims (suggested length 1 page)
 - b. Significance
 - c. Innovation
 - d. Approach

All research plans will undergo a biostatistical evaluation as part of the review process, therefore applicants are strongly encouraged to consult a biostatistician in the preparation of their application.

10. Description of the Research Environment (suggested length ½ page). Use PHS 398 Continuation Format pages (Download: [MS Word](#) or [PDF](#)).

11. Impact on the field: For studies focused on HIV, describe the impact of the study on the field of aging. For studies focused on aging, describe the impact on the field of HIV (suggested length ½ page or less). Use PHS 398 Continuation Format pages (Download: [MS Word](#) or [PDF](#)).
12. Bibliography and References cited (as needed) Use PHS 398 Continuation Format pages (Download: [MS Word](#) or [PDF](#)).
13. Protection of Human Subjects (if applicable; maximum 1 page). Use PHS 398 Continuation Format pages (Download: [MS Word](#) or [PDF](#)).
14. Vertebrate Animals (if applicable; maximum 1 page). Use PHS 398 Continuation Format pages (Download: [MS Word](#) or [PDF](#)).
15. Letters of Support
 - a. Letters of support from co-investigators and collaborators essential to the proposed project should accompany the application.

Use this link (<https://grants.nih.gov/grants/funding/phs398/phs398.pdf>) for detailed instructions on how to fill out these forms. Bibliography and References Cited sections do not count toward the page limit. No appendices are allowed. Do not submit Targeted/Planned Enrollment Tables. Applications must be in English.

III.4. Budget Development Guidelines and Restrictions

1. Maximum total costs (direct and indirect) are allowed up to \$50,000.
2. Travel to the OAIC Annual conference is provided by this funding mechanism and should not be included in the budget. Budgeting for travel to other conferences to present project research results is allowable and encouraged (travel budget limited to no more than \$2000).
3. Requested support for project collaborators who are NOT at the same institution as the awardee must be listed as consultant costs. If the collaborator cannot accept consultancy fees, a subcontract must be issued to their institution. These costs must be listed in the detailed budget as consortium costs with applicable indirect costs included.
4. **No international components will be allowed through this mechanism.**
5. Costs associated with Institutional Review Board (IRB) review of human research protocols, or Institutional Animal Care and Use Committee (IACUC) review of animal research protocols, are not allowable as direct charges.
6. Awardees who have support from K awards should discuss eligibility issues with their program officers and with institutional officials as eligibility may vary by NIH sponsor for the K award and institutional policies. The staff of this mechanism is not able to determine eligibility for K awardees.
7. All costs must conform to the NIH Grants Policy Statement (GPS) and applicable U.S. Office of Management and Budget OMB circulars for necessity and reasonability, allocability, conformance and consistency, as well as allowability. Please follow the link below to section 7.2 cost principles section of the [NIH Grants Policy Statement](#).

III.5. Review Process and Criteria

Written Reviews:

The evaluation criteria includes:

- Significance – What will be the potential effect of these studies on the concepts or methods that drive the field of research? Does the study address an important problem consistent with the objective to advance our understanding of HIV in the aging population? If the aims are achieved, how will scientific knowledge be advanced?
- Investigator – Are the PI, mentor(s), collaborators, and other researchers well suited to the project? Do the PI and other investigators have appropriate experience and training? If the project is collaborative, do the investigators have complementary and integrated expertise, and are there both OAIC and CFAR researchers involved?

- **Approach** – Are the conceptual framework, design, methods, and statistical analysis plan adequately developed, well integrated and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternatives? Does the study design account appropriately for differences by sex or gender, if applicable?
- **Innovation** – Does the project employ novel concepts, approaches, or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?
- **Environment** – Do the proposed methods take advantage of the unique environment and unique populations where appropriate? Are useful collaborative arrangements between resources in the institution(s) utilized where appropriate and described adequately?

Review Committee:

Applications will be reviewed by the Application Research Committee, consisting of CFAR and OAIC Investigators, with procedures analogous to an NIH Study Section. Each application will have a primary, secondary, and biostatistical reviewer. The reviewers will be asked to summarize the strengths and weaknesses of the proposal based on all of the above criteria. Each project is scored according to the [NIH scoring system](#) using overall impact as the metric for success.

Reviewers will provide a written critique based in alignment with the goals of this funding mechanism, path to subsequent grant applications and research productivity, and the 5 NIH criteria to yield an overall impact score. Each project is scored according to the [NIH scoring system](#) using scientific merit as the metric for success. After the review meeting, written critiques will be provided to the applicants. Those applicants who are selected for funding will be notified immediately.

IV. Award Requirements

IV.1. Pre-Award Requirements

Funding will be awarded via a subcontract from Wake Forest University. All questions regarding the awarding of funding should be directed to the contact listed in the notice of award. Prior to the awarding of funding, the following information should be provided, if applicable:

1. **Human Subjects and Animal Care Approvals:** Animal Care and Institutional Review Board approvals, if applicable, must be obtained prior to **receipt** of an award, but are not required to submit an application. Prior to funding, a copy of all Institutional Biohazard, Animal Care and Institutional Review Board (IRB) approvals must be forwarded to the post-award administrator. Prior to receipt of an award involving human subjects, IRB approval from all participating sites and human subjects training certification for all key personnel will be required.

For more information about human subjects approval, see: <http://www.hhs.gov/ohrp/> and <https://www.niaid.nih.gov/grants-contracts/human-subjects>.

For more information on animal care approvals, see: <http://grants.nih.gov/grants/olaw/olaw.htm> and <https://www.niaid.nih.gov/grants-contracts/research-vertebrate-animals>.

IV.2. Post-Award Requirements

1. Awardees will be required to submit yearly progress reports at 6 months and at the end of the budget period. Awardees will be tracked for 2 years to monitor productivity (abstracts, publications, grants), and pilot award grantees will give a presentation at the end of the funding period at the OAIC annual meeting.
2. Support from this mechanism must be acknowledged in all publications and presentations.
3. If for any reason the awardee is unable to fulfill the requirements or adhere to the policies of the award, at the discretion of the funding mechanism leadership, the award may be revoked.