Wake Forest Alzheimer's Disease Research Center

**Request for Applications for
Development Projects and Pilot Grant Awards**

The Wake Forest Alzheimer's Disease Research Center (WF ADRC) is seeking proposals for projects to stimulate innovative research relevant to Alzheimer's disease (AD) and related disorders (ADRD). The primary goal of this funding is to develop AD research that will lead to publications and extramural research applications, or produce resources useful to the WF ADRC community. Projects can encompass basic, translational, or clinical research. Applications that are aligned with the scientific focus of the WF ADRC and themes for this year's funding cycle are strongly encouraged, but proposals are not confined to these topics. The scientific focus of the WF ADRC is the link between metabolic and vascular diseases and the transitions from normal aging to mild cognitive impairment (MCI), AD, and related disorders. Research that addresses health disparities in AD is also a goal of the WF ADRC.

The themes for this year's funding cycle include:
1) Identification of Cognitive Impairment Risk using Electronic Medical Records & other Health Systems Data
2) Application of Novel Biomarkers or Polygenic Risk Scores to AD Research
3) Relationship of Aging-related Processes (i.e. geroscience processes, physical function) to Risk for ADRD (Use of data from WF ADRC in combination with the WF Pepper Older Americans Independence Center (OAIC), NACC, NCRAD, and/or NIAGADS is encouraged)

This Request for Applications (RFA) will cover two funding tracks: **Development Projects** and **Pilot Grants**. We anticipate funding up to 2 Development Projects and 2 Pilot Grants in this cycle (July 2023 to June 2024).

Development Projects will provide up to $50,000 in funding for the first year, and may be considered for a second year of funding depending on the scope of the project and progress made during the initial year of funding. If applicants anticipate that the project will extend into a second year, they should include the activities in the application. However, current funding approval will only cover one year, so the activities and budget for the first year of the project must be clearly delineated. Approval of a second year funding will be at the discretion of the ADRC Development Project/Pilot Grant Committee if the objectives and milestones are met in the first year and if the additional research proposed continues to align with the goals of the ADRC. Priority for additional funding will be given to projects yielding productive, high-impact research as measured by output of publications and grant applications. Up to 10% of direct costs can be used to support the Principal Investigators' effort. Exceptions may be considered depending on the nature of the project. See section on Budget Guidelines for more details on allowable and non-allowable budget items. Principal Investigators are eligible only once for a Development Project award, unless the additional proposed Developmental Project constitutes a real departure from the investigator's ongoing research.

Pilot Grants will provide up to $20,000 in funding for a one year project period. Up to 10% of direct costs can be used to support the Principal Investigators' effort. See section on Budget Guidelines for more details on allowable and non-allowable budget items. Pilot Grant recipients may apply for Development Projects in the future and the use of Pilot Grant results for Development Project applications is encouraged.

Applicants are strongly encouraged to submit a Letter of Intent (LOI) to the ADRC by 10/24/2022 (see Key Dates). Submission of a LOI will allow the Development Project/Pilot Grant Committee will provide feedback to the applicant on their project and the most appropriate track for their application based on the scope of the research proposed.

Key Dates

Date	Detail
10/24/2022	Letter of Intent Deadline (Strongly encouraged)
12/14/2022, 11:59 pm	Full Application Deadline
3/15/2023	Selection of Development Project Awardees
4/14/2023	Selection of Pilot Grant Awardees
7/1/2023	Anticipated Project Start Date
6/30/2024	Anticipated Project End Date

Criteria
Successful proposals will clearly state:
- Specific focus on Alzheimer's disease or related disorders
- Relevance to the Wake ADRC scientific focus
- Potential for generalizability to AD (*i.e.*, how can the results of this project be used to improve our knowledge of AD)
- Development Projects are required to include a statistical plan and statistician collaborator
- Project plan that will be completed within the project period (For Development Projects, initial funding of one year, but potentially up to two years; one year for Pilot Grants)
- Collaborations with other ADRCs, WF Pepper OAIC, or RCCN Centers are encouraged
- Use and/or production of ADRC resources and Cores are strongly encouraged:
  - Production of resources or methodologies useful for the ADRC
  - Use of existing resources from one or more of the following:
    - Wake Forest ADRC resources (*e.g.*, cognitive data, demographic data, biomarker data, brain imaging data, blood and/or cerebrospinal fluid (CSF)). Descriptions of ADRC resources can be found at the following link: https://school.wakehealth.edu/research/institutes-and-centers/sticht-center/alzheimers-disease-research-center/research-resources
    - Requests for ADRC resources can be submitted via the links on this page: www.wakeshare.org
    - Brain specimens from our affiliated brain bank at the University of Washington http://depts.washington.edu/mbwc/adrc/page/research-resources
    - The National Alzheimer Coordinating Center (NACC), which contains data from clinical evaluations, neuropathology, and magnetic resonance imaging from the 39 past and present Alzheimer's Disease Centers (ADCs) supported by NIA https://www.alz.washington.edu/WEB/researcher_home.html
    - The National Centralized Repository for Alzheimer's Disease and Related Dementias (NCRAD), which is a national resource for clinical information and biological samples, such as DNA, plasma, serum, RNA, CSF, cell lines, and brain tissue from multiple ADCs and AD-related clinical studies https://ncrad.iu.edu/accessing_data.html
- **Due to National Institute of Aging (NIA) guidelines, Development Project applicants may not propose new clinical trials:** analysis of existing clinical trial data or addition of measures to an ongoing trial is permitted; clinical observational studies are also permitted

Eligibility
Applications are welcome from any department at Wake Forest, Atrium Health, or invited institutions. Applications from early-stage investigators are encouraged, provided they will be at their institution for the duration of the funding period. Mid-level and senior faculty members are also encouraged to apply if they do not have substantial prior experience in AD research or if they have a novel approach to AD research. Postdoctoral fellows (with appropriate senior collaborators) are encouraged to apply for Pilot Grants, but will not be considered for Development Projects.

Collaboration
Applicants are encouraged to include at least one investigator from the WF ADRC as a collaborator. Written verification from WF ADRC collaborators stating their willingness to participate in the project must be provided. **Applicants are strongly encouraged to seek input from WF ADRC collaborators as early in the process as possible.** Input into study design should be sought prior to submitting a Letter of Intent. Last-minute requests for proposal review by collaborators (within two weeks of the grant deadline) will receive limited feedback due to time constraints.

Application Procedure
Letter of Intent Deadline: 10/24/2021
Letters of Intent (LOI) should be no more than one page and include a brief abstract including specific aims and study team members for the proposed project. LOIs should be emailed to the WF ADRC Development Project/Pilot Grant Committee Coordinator *(*Sharon Letchworth, PhD (Sharon.Letchworth@wakehealth.edu) by the deadline.

Full Application Deadline: 12/14/2022, 11:59 pm
Application instructions are summarized below.

Format Specifications
- Arial font and no smaller than 11 point
- Margins at least 0.5 inches (sides, top and bottom)
- Single-spaced lines
- Consecutively numbered pages

Submission/Applicant Information
- Project Title
- Submitting Investigator, Co-Investigator(s), and other Key Personnel information
- Suggested Reviewers – cannot be a current or previous mentor or co-author on a publication within the last 2 years

Abstract (300 words max)

Research Plan (6 pages maximum) If Development Project applicants anticipate that the project will extend into a second year, they should include the activities in the application. However, current funding approval will only cover one year, so the activities and budget for the first year of the project must be clearly delineated.
- Specific Aims
- Background and significance – Explain how the project addresses an important problem, how it will improve scientific knowledge, technical capability and/or clinical practice; discuss translational importance and innovation of the project
- Experimental design and methods, including dissemination and implementation
- Investigator(s) – Describe how each member of the team will contribute to the project, including expertise and experience that will be used on this project
- Approach – Describe the overall strategy for this project, including potential problems, alternative strategies and benchmarks for success
- Analysis plan: Statistical approach and power analysis for sample size
- Quarterly milestones and anticipated outcomes with timeline (refer to Appendix I)
- Use of resources as applicable
- Plans for grant applications or manuscripts

References (no page limit)

Information Regarding Human Subjects
Address the following if the project **involves human subjects**.
- Provide a one-page document addressing the Protection of Human Subjects, if applicable
  - Clearly describe risk, protections, benefits and importance of the knowledge to be gained by the revised or new activities as discussed in Part II of NIH competing application instructions
- Clinical Trial Classification (new clinical trials are not allowed under this funding mechanism)
- Inclusion Plans for Women, Minorities, and Children, if applicable
- Targeted Enrollment Table, if applicable (using NIH Targeted Enrollment Table)
- IRB approval is not required for full application submission, but must be in place prior to funding
  - If an award is made:
    - Either an IRB approval letter or an IRB response to a "Determination Whether Research or Similar Activities Require IRB Approval" must be submitted to the ADRC prior to funds being released
    - Human subjects safeguard procedures must be detailed in accordance with the institution's general assurances and HIPAA
    - All key personnel must have current certification of training in the protection of human subjects prior to the start of the grant period
  - **A delay in IRB approval does not alter the project end date**

Information Regarding Live Vertebrates
Address the following if the project **involves vertebrate animals** (1 page max):

- **IACUC Approval Status** (not submitted, pending, approved)
  - IACUC approval is not required for full application submission
  - If an award is made, the grantee must provide verification of IACUC approval or documentation on why the activity does not require IACUC approval prior to the funds being released
  - **A delay in IACUC approval does not alter the project end date**
- **Detailed information on the criteria below:**
  1. Description of Procedures: Provide a concise description of the proposed procedures that involve vertebrate animals in the work outlined in the Research Plan. Identify the species, strains, ages, sex, and total numbers of animals by species, to be used in the proposed work. If dogs or cats are proposed, provide the source of the animals. Identify all project/ performance or collaborating site(s) and describe activities of proposed research with vertebrate animals in those sites.
  2. Justifications: Provide justification that the species are appropriate for the proposed research. Explain why the research goals cannot be accomplished using an alternative model (e.g. computational, human, invertebrate, *in vitro*).
  3. Minimization of Pain and Distress: Describe the interventions including analgesia, anesthesia, sedation, palliative care and humane endpoints to minimize discomfort, distress, pain, and injury.
  4. Euthanasia: State whether the method of euthanasia is consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals. If not, describe the method and provide a scientific justification.

Budget and Justification (budget template plus 1-page justification)
- Complete the budget template form provided, along with a brief justification for the funds requested for this RFA. Please include an explanation of other resources that may be leveraged to support the project. If the proposed research is to be carried out on more than one campus/institution, please include details in the justification
- Sub-awards to other institutions to carry out work on a project are permissible provided the majority of activity occurs within Wake Forest or one of its affiliates

NIH-style biographical sketch for all Key Personnel (new style)

Budget Guidelines
The budget period is for 12 months beginning 7/1/2023 and ending no later than 6/30/2024. Up to $50,000 in direct costs may be requested for Development Projects and up to $20,000 in direct costs may be requested for Pilot Grants.

Grant funds may be budgeted for:
- Limited faculty or other investigator effort (up to 10% direct costs for Development Projects and up to 10% direct costs for Pilot Grants)
- Research support personnel (including undergraduate and graduate students)
- Travel necessary to perform the research
- Small equipment, research supplies and core lab costs (no more than 10% of the total amount)
- Other purposes deemed necessary for the successful execution of the proposed project

Grant funds may **not** be budgeted for:
- Office supplies or communication costs, including printing
- Meals or travel, including to conferences, except as required to collect data
- Professional education or training
- Computers or audiovisual equipment, unless fully justified as a need for the research
- Manuscript preparation and submission
- Indirect costs

Awarded funds must be used to conduct the work proposed. All direct charges to this award must adhere to federal regulations and requirements regarding the use of WF ADRC funds. The Center reserves the right to revoke funding in the event it is determined that funds were not spent in accordance with the approved

protocol. The general criteria for determining allowable direct costs on federally sponsored projects is set forth in 2 CFR Part 200: Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards (The Uniform Guidance).

Review Criteria and Process
ADRC proposals are competitive and peer reviewed. Proposals will be evaluated by internal and external scientists based on NIH review criteria and scoring. Funding decisions will be made based on scientific merit and the project's relevance to WF ADRC goals. Awards for Development Projects will be at the final approval of NIA. Any IACUC and/or IRB protocols must be approved prior to funding of the approved project.

Reviewers will score applications based on:
1. Significance of the problem to be addressed
2. Innovation in the proposed solutions
3. Scientific Approach
4. Strength and breadth of the investigative team
5. Methodological rigor and feasibility with clear milestones
6. A reporting plan regardless of whether the study yields positive or negative results
7. Other elements to be considered in the review include: the likelihood that the investment will lead to publication, external funding, a resource for the WF ADRC, or a licensable innovation, early-career faculty involvement, race/gender inclusiveness of the research team, and inclusion of women, minorities, and older adults as potential participants

Program Expectations
The WF ADRC will work with awardees to: 1) assist with study initiation; 2) convene an initial meeting with the project PI, ADRC administrative personnel, and ADRC leadership to discuss the project and how ADRC resources can be optimized for the study; and 3) provide project oversight throughout the life of the study. If any significant issues arise, the study team will be required to work with the WF ADRC to define an intervention strategy for the study to be successfully completed (or in rare cases, terminated).

Specific Deliverables Include:
- Participation in the study initiation meeting
- Brief updates on progress (see Other Guidelines, below)
- Presentation of progress and results to the ADRC Executive Committee and other ADRC events
- Upon completion of the project:
  - Final report with plans for implementing and disseminating results
  - Potential presentation of findings at Wake Forest ADRC Seminar Series
  - Potential presentation or poster at the ADRC annual External Advisory Committee Meeting
  - Description of how extramural funding will be sought and subsequent notification of any funds obtained and/or related publications or significant collaborations resulting from the project for a minimum of 5 years
  - Participation in review process for future pilot grant cycles

Other Guidelines
1. The ADRC will work closely with funded teams throughout the grant period to monitor progress and provide assistance. Brief interim progress reports are required (typically 2-3 per year for Development Projects and 3-4 per year for Pilot Grants), as well as a final progress report. We expect PIs to report the outcomes achieved due to the pilot award, e.g., subsequent external funding, publications, presentations and patents
2. All publications that are the direct result of this funding must reference the ADRC using the following citation or similar wording: "Research reported in this publication was supported by the Wake Forest Alzheimer's Disease Research Center with funding from the National Institute on Aging under award number P30AG072947." Other sources of support (e.g. CHAAP, Kulynuch, Eagle, and Dickerson funds) must also be cited.
3. Publications must be registered and compliant in PubMed Central
4. Any awardee who leaves their position should contact the ADRC to discuss plans for the project

Grant Administration

The Principal Investigator is responsible for the administration of grant funds.

Contacts

Questions about your proposed research project should be directed to Sharon Letchworth, PhD (Sharon.Letchworth@wakehealth.edu).

Appendix I

Below are examples to show different methods to provide study milestones, outcomes, and timeline. Other formats may be acceptable.

Example 1:

- **Milestone 1 (0-1.5 months):** Milestone 1 Details **Outcome:** Outcome 1 Details
- **Milestone 2 (1.5- 4 months):** Milestone 2 Details **Outcome:** Outcome 2 Details
- **Milestone 3 (4-6 months):** Milestone 3 Details **Outcome**: Outcome 3 Details
- **Milestone 4 (6-12 months):** Milestone 4 Details **Outcome:** Outcome 4 Details
  Milestone 5 (8-12 months): Milestone 5 Details **Outcome:** Outcome 5 Details

Example 2:

Timeline and Milestones

Month	1	2	3	4	5	6	7	8	9	10	11	12
Activity/Aim/Milestone 1	X	X	X	X								
Activity/Aim/Milestone 2	X	X										
Activity/Aim/Milestone 3		X	X	X								
Activity/Aim/Milestone 4					X	X	X	X	X	X		
Activity/Aim/Milestone 5					X							
Activity/Aim/Milestone 6						X	X					
Activity/Aim/Milestone 7								X		X		
Activity/Aim/Milestone 8											X	X

Example 3:

Aim	Milestone	Month 1-3	Month 4-6	Month 7-9	Month 10-12
1	Milestone 1	X	X		
	Milestone 2		X		

Aim 1 Anticipated Outcomes: Detail

Aim	Milestone	Month 1-3	Month 4-6	Month 7-9	Month 10-12
2	Milestone 1		X	X	
	Milestone 2		X		
	Milestone 3			X	

Aim 2 Anticipated Outcomes: Detail

Aim	Milestone	Month 1-3	Month 4-6	Month 7-9	Month 10-12
3	Milestone 1			X	
	Milestone 2			X	X

Aim 3 Anticipated Outcomes: Detail