Wake Forest Alzheimer's Disease Research Center

Request for Applications for Development Projects

The Wake Forest Alzheimer's Disease Research Center (WF ADRC) is seeking proposals for projects to stimulate innovative research relevant to Alzheimer's disease and related disorders (ADRD). The primary goal of this funding is to develop ADRD research that will lead to publications and extramural research applications or produce resources useful to the ADRC community. Projects can encompass basic, translational, or clinical research. **Applications that align with the scientific focus of the WF ADRC and themes for this year's funding cycle and that propose using WF ADRC resources are strongly encouraged, but proposals on other topics will be considered.**

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 ADRD is also a goal of the WF ADRC.

The themes for this year's funding cycle include:

1) Characterization of neuropathological changes in ADRD using WF ADRC human neuropathology tissues and/or data
2) Elucidation of translational non-human primate models of ADRD using WF ADRC non-human primate tissues and/or data
3) Neuroinflammation and/or neuroimmune changes as a basis for ADRD
4) Neuroimaging biomarkers of vascular and metabolic risk factors of ADRD

WF ADRC resources can be requested at www.WakeShare.org. WF ADRC resources can be combined with those of other ADRCs through NACC, NCRAD, and other sources as described in the Use of ADRC Resources section of this RFA.

We anticipate funding up to 2 **Development Projects** in this cycle. Development Projects will provide up to $50,000 in funding for the first year. Projects 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. Since current funding approval will only cover one year, the activities and budget for the first year of the project must be clearly delineated. If applicants anticipate that the project will extend into a second year, they should include the activities in the application. Approval of a second year of 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. 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.

Applicants are required to submit a Letter of Intent (LOI) to the ADRC by 10/11/2024 (see Key Dates). Submission of a LOI will allow the Development Project/Pilot Grant Committee to provide feedback to the applicant. The committee will invite full applications for projects that are closely aligned with the objectives of the WF ADRC.

Key Dates

Date	Detail
10/11/2024	Letter of Intent Deadline
10/31/2024	Invitation to Submit Full Application
12/15/2024, 11:59 pm	Full Application Deadline
2/21/2025	Selection of DP Awardees
3/31/2025	Response to Reviewers Deadline
7/1/2025	NIA Approval & Anticipated Project Start Date
6/30/2026	Anticipated Project Year 1 End Date
6/30/2027	Anticipated Project Year 2 End Date

Criteria

Successful proposals will clearly describe:

- Specific focus on Alzheimer's disease or related disorders
- Relevance to the Wake ADRC scientific focus and/or themes for this year's funding cycle
- Potential for generalizability to ADRD (*i.e.*, how the results will improve knowledge of ADRD)
- Statistical plan and statistician collaborator
- How the project differentiates from other funded projects
- Project plan that will be completed within the project period (for Development Projects, initial funding of one year, but potentially up to two years)
- **Due to National Institute of Aging (NIA) guidelines, 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. https://grants.nih.gov/ct-decision/index.htm

Use of ADRC Resources

- Production of resources or methodologies useful for the ADRC is encouraged
- Use of existing resources from the WF ADRC and additional ADRC sources are strongly encouraged:
    - Wake Forest ADRC resources (*e.g.*, cognitive data, demographic data, biomarker data, brain imaging data, brain tissue, blood, cerebrospinal fluid (CSF), or other tissues). Requests for ADRC resources can be submitted here: www.wakeshare.org
    - The National Alzheimer Coordinating Center (NACC) contains longitudinal data from clinical evaluations, positron emission tomography (PET) imaging, magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) biomarkers, as well as neuropathology and APOE genotyping from the 42 present and past Alzheimer's Disease Research Centers supported by NIA; SCAN and CLARiTI imaging resources can also be requested through NACC: https://www.alz.washington.edu/WEB/researcher_home.html
    - The National Centralized Repository for Alzheimer's Disease and Related Dementias (NCRAD) is a national resource for clinical information and biological samples, such as DNA, plasma, serum, RNA, CSF, cell lines, brain tissue, and blood-based biomarker data from multiple Alzheimer's Disease Research Centers and ADRD-related clinical studies: https://ncrad.iu.edu/accessing_data.html
    - The National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS) houses genomic array and sequence data (GWAS, WES/WGS) from ADRCs: https://www.niagads.org/resources
    - Brain specimens from our affiliated brain bank at the University of Washington: http://depts.washington.edu/mbwc/adrc/page/research-resources
    - Diverse Vascular Contributions to Cognitive Impairment and Dementia (Diverse VCID) can be requested through UC Davis: https://diversevcid.ucdavis.edu/for-researchers
    - Resources from other ADRCs can be requested directly from their websites: https://www.nia.nih.gov/health/clinical-trials-and-studies/alzheimers-disease-research-centers

Eligibility

Applications are welcome from any department at Wake Forest, Atrium Health, Advocate 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 are also encouraged to apply if they do not have substantial prior experience in ADRD research or if they have a novel approach to ADRD research. Postdoctoral fellows will not be considered for Development Projects. We anticipate sponsoring future funding cycles that will be open to postdoctoral fellows.

Collaboration

Applicants are required 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 (email verification will suffice, a formal letter of support is not required). **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 application review by collaborators (within two weeks of the grant deadline) will receive limited feedback due to time constraints. Collaborations with other ADRCs, WF Pepper OAIC, or RCCN Centers are encouraged.

Application Procedure

Letter of Intent (LOI) Deadline: 10/11/2024

One-page LOIs should be emailed to the WF ADRC Development Project/Pilot Grant Committee Leader, Sharon Letchworth, PhD (Sharon.Letchworth@wakehealth.edu) using the following format:

- Project Title
- Study team members/collaborators
- Rationale (1-3 sentences)
- Hypothesis (1-2 sentences)
- Source data and/or sample description (1-2 sentences)
- Methods (4-5 sentences)

Full Application Deadline: 12/15/2024, 11:59 pm

Application instructions are summarized below. A link to the submission form will be sent to researchers that are invited to submit a full application.

Formatting Specifications

- Arial font 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 ADRD reviewers outside of WF with subject matter expertise relevant to the application – cannot be a current or previous mentor or co-author on a publication within the last 2 years

Abstract (300 words max)

Specific Aims & Research Plan (6 pages maximum) If the project is anticipated to extend into a second year, then include those 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 WF ADRC resources as applicable
- Plans for grant applications or manuscripts resulting from the project

References (no page limit)

Information Regarding Human Subjects

Address the following if the project **involves human subjects**. *If the project proposes to use biospecimens or data from ADRC participants and does not involve live human subjects, then the following information is not needed.*

- 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 (blank table will be provided within the link for the application)
- 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 (blank form will be provided within the link for the application), 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 most 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 7/1/2025 and ending no later than 6/30/2026. Up to $50,000 in direct costs may be requested for Development Projects.

Grant funds may be budgeted for:

- Limited faculty or other investigator effort (up to 10% direct costs for PIs and 5% for each Co-I); exceptions may be considered depending on the nature of the project
- Research support personnel (including undergraduate and graduate students)
- Travel necessary to perform the research
- Small equipment (no more than 10% of the total amount), research supplies and core lab costs
- 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. NIA will have final approval of Development Project awards.

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, a licensable innovation, early-career faculty involvement, race/ethnicity/gender inclusiveness of the research team, and inclusion of women, minorities, and older adults as potential participants

Program Expectations

The PI should submit a copy of IRB or IACUC approval letters to the Committee for their records. The WF ADRC will work with awardees to 1) assist with study initiation; 2) convene an initial discussion 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 discussion
- 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 WF ADRC Seminar and/or Full Investigator Meeting
    - 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), 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 if appropriate.
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.

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