Alzheimer's Disease Strategic Fund: *Vascular Contributions to Cognitive Impairment and Dementia - Understanding Mechanisms of Dysfunction (VCID-UMD)*

Program Objective:
The Alzheimer's Association aims to support innovative, high-risk, collaborative team science opportunities that investigate and focus on outstanding questions related to the biological underpinnings of Alzheimer's disease (AD), including the vascular contributions to cognitive impairment and dementia (VCID). This new funding call builds off the last ten years of work to better understand VCID and its contributions to AD/ ADRD pathogenesis by targeting scientific questions on how VCID may intersect with immune, lipid and endolysosomal related functions to contribute to disease. This funding call will be supported through an innovative funding model, the Alzheimer's Disease Strategic Fund, established in 2019 to support studies that advance our understanding of mechanistic and underpinning biology of disease.

Program Overview:
Although Alzheimer's research has made many advances in recent years, there are still significant gaps in understanding how distinct signals and pathways intersect with others to contribute to disease related pathogenesis. Some of these overarching questions focus on understanding of disease causes and contributors; the need for models and other tools (i.e. antibodies) to evaluate disease biology; opportunities to discover and test early and accurate detection and diagnosis procedures; and diverse treatment modalities.

Vascular dysfunction plays a crucial role in Alzheimer's and related disorders, contributing to the disease onset and progression, and may also be an early indicator of disease-specific changes in the brain. Brain infarct, atherosclerosis and cardiovascular diseases such as arteriolosclerosis are often found in brains of individuals with Alzheimer's. This highlights the potential link between vasculature impairment and Alzheimer's disease development.

The *Vascular Contributions to Cognitive Impairment and Dementia - Understanding Mechanisms of Dysfunction (VCID-UMD)* **Grant Program** solicits projects that aim to address some of the key challenges in research today as related to vascular dysfunction biology and contributions to AD/ADRD, including but not limited to:

- Understanding the vascular risk factors associated with AD/ ADRD, including aging or diabetes.
- Explore how vascular dysfunctions alter brain metabolism, and how defects in mechanisms such as alterations in the blood brain barrier (BBB), neurovascular coupling, cerebral blood flow or waste clearance contribute to amyloid aggregation and neuronal loss; and how diverse cell types residing in the vasculature including but not limited to endothelial cells, pericytes, smooth muscle cells, perivascular fibroblasts and/or perivascular immune cells contribute to these mechanisms.
- Investigate vascular-immune crosstalk including but not limited to understanding the roles of parenchymal versus peripheral immune signaling or the innate versus adaptive immune system, and how defects on the vasculature contribute to the disruption of brain immune homeostasis.
- Investigate the intersection between VCID, immune, lipid and endolysosomal function to contribute to AD/ADRD pathogenesis.

- Define the role of APOE contribution to cerebral amyloid angiopathy (CAA) and ARIA that could contribute to AD/ ADRD pathogenesis.
- Developing novel biomarkers and/or drug discovery and development (pre-IND) related to vascular dysfunction to advance understanding of biological implications at early-phases of AD/ ADRD.
- Developing key tools and/or resources, such as imaging, that if developed will benefit a broader range of scientific questions and/or studies related to neurovascular health. Tools and resources developed through this funding would be made broadly available to the scientific field. This could include the development of *Experimental Models of Disease*.

The VCID-UMD Grant Program aims to fund concerted and collaborative efforts that will explore these questions to advance our understanding of disease.

Funding and award period:
The maximum grant amount is $300,000; with anticipated funding ranges to be $150,000 to $300,000 depending on the project scope. Budget spending should be appropriately aligned to the specific aims and proposed milestones of the project. The maximum project duration is 3 years, and there is no minimum timeframe. **No indirect costs will be allowed.** The Association will evaluate projects on progress toward specific milestones; continued disbursement of funds is dependent on demonstrated progress toward key milestones.

Eligibility:
The VCID-UMD Grant Program is open to researchers at academic institutions and other non-profit research institutions. The Principal Investigator of the project must be a full-time faculty member (Assistant Professor, Instructor, Lecturer or higher) or full time paid employee of the organization submitting the proposal. Applications from post-doctoral researchers will not be accepted, however, they can be included on applications as key personnel.

Investigators that have received Alzheimer's Association funding and are currently delinquent in submitting required reports or have awards closed as "Incomplete" are not eligible to apply. For questions about eligibility, please contact the Alzheimer's Association at grantsapp@alz.org.

Note: Alzheimer's Association grants are generally open to scientists and researchers across the globe; however, as a U.S.-based charity, the Alzheimer's Association is subject to, and complies with, U.S. law. As a result, the Alzheimer's Association cannot award, and will not award, grants in violation of applicable U.S. statutes and regulations. This means, among other things, that the Alzheimer's Association cannot, and will not, fund any individual or entity (i) that is subject to U.S. comprehensive or targeted sanctions or if awarding funding would result in a violation of such sanctions, (ii) that is on the U.S. List of Specially Designated Nationals or entities owned or controlled by such persons, or (iii) when doing so is otherwise prohibited by U.S. laws related to combating terrorism.

Submitting a Letter of Intent:
The Letter of Intent (LOI) is a required step in the application process. LOIs must be completed online at https://proposalcentral.com. First-time users must register and complete a Professional Profile to begin the LOI process. No hard copies will be accepted. The LOI is completed through the online interactive system; you will need to complete the required sections and upload any required documents. The main section will have a limit of 10,000 characters, approximately 3 pages, and should include the information below (no figures/graphics or images are allowed):

- Brief project description, including methodology
- Specific aims of the project
- Innovation/novelty of the project
- Project team
- Plan for data management and data sharing

For U.S. entities, the LOI materials will include proof of your organization's not-for-profit status and a W9 signed and dated by the signing official. Non-US entities must provide a W8-BEN-E signed and dated by the signing official. **Your LOI will not be accepted without these documents**. Current awardees of the Alzheimer's Association are eligible, provided their current funded grant does not overlap with this proposal.

Evaluation of LOIs:
Only LOIs that meet program specific guidelines and meet review criteria, including the goals of the VCID-UMD program, will be invited to submit full applications. LOIs will be reviewed by a panel of experts with special attention to:

1. Demonstrable innovation/novelty of the proposed project (especially in the context of the PI/PIs' and team's recent work).
2. Priority will be given to projects that address an important knowledge gap in a way it is not being addressed through other funding mechanisms.
3. Alignment with the research priorities of the RFA.
4. Impact of the project on AD/ ADRD research.
5. Evidence of methodological rigor that addresses the research question(s) being proposed.
6. Priority will be given to studies that leverage and/or identify new opportunities for team science, collaborations and working across disciplines that otherwise could or would not happen.

Feedback is not provided for LOIs that are not invited to submit a full application.

Submitting a Full Application:
For those invited to submit a full application, additional materials will be required. Templates and instructions will be provided after LOI approval.
Full applications will include:
- Executive Summary (1 page)
- Background/Rationale (1 page): should include background and clearly defined hypothesis and/or rationale addressing why the proposed strategy is expected to be fruitful. This should also note the specific aims.
- Work Plan (up to 5 pages): should include goals/specific aims, methods and project plan and should be organized in alignment with the milestones as outlined in the application.
- Project Milestones: workplan should be separated into one-year intervals with specific milestones to be accomplished within that timeframe. Milestones should align with the overall project goals and be designed for easy progress evaluation and for clear determination on whether or not milestones have been met. For each milestone, indicate the relevant Project Aim. (No upload required)
- Principal Investigator(s) and Key Personnel Curriculum Vitae or Biosketch (no more than 5 pages per person); there is no limit on the number of CVs to be included
- Available Resources and Budget Justification (2 pages):

- o Expenses that will not be allowed under this award include: tuition for full degree programs, rent for laboratory/office space, construction or renovation costs, liability insurance, networking and communication fees, and any facilities fees and laboratory/supply costs not directly relevant to the project. If awarded, a full budget of planned expenses will be required. No indirect costs will be allowed. Budget should be broken down in 1-year increments and should align with project milestones.
  - o Include a list of tools/models available (if appropriate, list critical tools and models to be used or needed in the course of the research).
- Data Management and Sharing Plan (3 pages): we recommend using the provided amended NIH template. It is expected that data generated through this funding mechanism will include a robust plan for sharing data and an appropriate included budget to accommodate this plan. Data sharing is a key component of the application and will be considered in the review and evaluation. Information on timelines, feasibility, and the platform(s) and/or mechanisms of sharing should be included. Failure to share data appropriately may prevent investigators from being eligible for future funding. When data sharing may be limited, applicants must explain such limitations at the time of application.
- Recruitment Plan (1 page): Only for projects using human research participants.
- Citations/References (1 page): Use the reference style that is most common in the major journal(s)
- Up to 3 letters of support (no more than 2 pages each) are allowed.
- W9/W8 Documentation

Evaluation of Full Applications

Full Applications will be reviewed by a panel of experts with special attention to:

1. Alignment with the research priorities of the RFA.
2. Demonstrable innovation/novelty of the proposed project (especially in the context of the PI/PIs' and team's recent work); innovation could include scientific areas not well-understood, leveraging unique technologies or model systems to approach vascular-related mechanisms, bridging disciplines to understand the intersectionality of the biological underpinnings.
3. Priority will be given to projects that address an important knowledge gap in a way it is not being addressed through other funding mechanisms; applications should provide context for what is and is not known in the area of research being proposed.
4. Evidence of methodological rigor that addresses the research question(s) being proposed, including the power necessary to sufficiently address the question proposed.
5. Priority will be given to studies that leverage and/or identify new opportunities for team science, collaborations and working across disciplines that otherwise would not happen
6. Quality and Adequacy of Resources and Budget.
7. Potential impact of the project on AD/ADRD research.

Deadlines and Award Timeline:

Key Dates for this program include:
- Letter of Intent Launch……….April 23, 2025 on https://proposalcentral.com
- Letter of Intent Deadline……..May 30, 2025, 5:00pm EDT
- Letter of Intent Notifications… July 8, 2025
- Application Deadline…………. August 12, 2025, 5:00pm EDT
- Application Review…………… August - September

- Award Notifications…………..By October 1, 2025

LOIs will be accepted through May 30. Letters of Intent will not be accepted after this date. **No exceptions will be made**.

All LOIs must be completed online at https://proposalcentral.com. No hard copies or emails will be accepted.

For those invited to submit a full application, the full application must be received by **5:00 PM EDT, August 12, 2025.** Applications will not be accepted after this date. **No exceptions will be made.** No hard copies or emails will be accepted.

Award announcements will be made by October 1, 2025.

For More InformationContact: grantsapp@alz.org

Additional Details
It is the responsibility of the applicant to ensure and verify that:
- The application is submitted by the receipt date/time deadline. Once submitted, you will receive a confirmation email from proposalcentral.com that your application was successfully submitted. If you do not receive a confirmation, click the Proposals tab, and under the "Status" column, make sure it says Submitted and not In Progress, which indicates you have not yet submitted your application.
- The application is complete and accurate before submission. Only a single copy of an application will be accepted. We do not require signatures at the time of submission. The signature page provided is for use should your institution/organization require signatures; we do not override any institutional policies and/or procedures. Please do not submit the signature page with your application.
- Revisions, additional materials, and/or references, manuscripts, appendices, etc., are not allowed and, if attached, will be removed from your application. Up to 3 letters of support (no more than 2 pages each) are allowed. Additional letters will be removed.

Multiple and Overlapping Submissions:
Multiple submissions from one applicant are not permitted. This includes multiple submissions from the same group and/or collaborators.

Allowable costs under this award include:
- Purchase and care of laboratory animals.
- Small pieces of laboratory equipment and laboratory supplies **(purchases over $10,000 require prior approval, even if included in the project proposal budget)**.
- Computer software - if used strictly for data collection and/or analysis.
- Salary for the principal investigator, scientific (including postdoctoral fellows) and technical staff (including modest administrative support).
- Research supplies needed for the proposed studies.
- Support for travel to scientific and professional meetings and additional support for travel expenses necessary to carry out research planned– this may include site visits. A total of $12,500 over a three year period may be requested for travel purposes and is not to exceed $7,000 in any given year.
- Open access publications fees are appropriate and reasonable for the project budget.

Not allowable as direct costs under this award include:

- Computer hardware or standard software (e.g., Microsoft Office).
- Construction or renovation costs.
- Tuition for students or for educational training for trainees or faculty.
- Service contract fees for equipment.
- Construction or renovation costs.
- Tuition.
- Rent for laboratory/office space.
- Visa costs and fees.
- Expenses such as Data Network Recharges and Computing and communication device support services. However, data sharing and/or data storage for imaging, sequencing, and other study data is allowed.
- General liability insurance, such as GAEL.
- Wire and currency exchange fees.
- The Alzheimer's Association <u>Medical and Scientific Advisory Group (MSAG)</u>, the <u>International Research Grant Program (IRGP) Council members</u>, and current employees of the Alzheimer's Association are allowed to be key personnel or collaborators on projects, however they are NOT ALLOWED to receive any salary or compensation. A complete list of MSAG and IRGP Council members can be found on our website <u>alz.org/grants</u>
- No indirect costs are allowed.
- Institutional overheads associated with staff time.
- We reserve the right to decline any charge that is an institutional feed and/or service charge.

<u>Additional Information</u>
Ethical/regulatory approvals and reporting requirements
If awarded for funding, the Alzheimer's Association requires that any necessary ethical and/or regulatory approvals are kept current, and may require specific reporting throughout the lifetime of the award. This includes, but is not limited to, the following:

Human Subject Assurances
Human subject assurances are not required at the time of application. Investigators have up to 90 days after receipt of their award notification to submit these documents. However, the Alzheimer's Association encourages investigators to initiate their certification applications on a schedule that recognizes that approvals at many institutions can take more than 90 days. We will accept only certifications that apply specifically to the funded project and must include the name of the awardee. An award letter will not be issued unless the appropriate certifications are in place and include the name of the awardee within 90 days from award notification. The same applies to animal ethical approvals, if applicable.

Annual Scientific and Financial Reports
Interim Scientific and Financial Reports must be submitted at the end of each reporting period as long as the grant remains active. Final Scientific and Financial Reports must be filed within 90 days of the grant's end date. All reports must be submitted electronically via proposalcentral.com. The Financial Report must be approved and signed by someone with financial authority in the Office of Research and Sponsored Programs at the recipient's institution.

Data Sharing:
The Alzheimer's Association requires the timely release and the sharing of final research data and other research resources generated from Alzheimer's Association funded research studies

be shared and administered in accordance with this policy. Examples included in the "final research data" are the data, samples, physical conditions and other supporting materials created or gathered during the course of the work. The following principles should be followed:

- Make useful datasets and supporting information available to the broader research community every 12 months, at minimum, through an appropriate data-sharing platform and other repositories, noting that not all experimental datasets are useful at early or intermediate stages of generation, exceptions may be made on a case-by-case basis if the AD Strategic Fund agrees that the data are not yet ready to be shared.
- Use a streamlined data access process for the data sharing platform to allow high throughput management of data access request approvals; make novel tools and research reagents (including, but not limited to, research models, cell lines, plasmids, viral vectors, antibodies, code/analysis methods, etc.) available as quickly as possible to academic and industry researchers either directly, or preferably through an appropriate and accessible distribution platform (e.g. Jackson Laboratory, Addgene, and GitHub) with minimal costs and restrictions.
- Whenever possible, avoid use of reagents, tools, samples, or data that cannot be easily shared; pre-approval for use of animal models that cannot be freely shared is required.
- Rapidly bring research findings and results to the research community through presentations at meetings and open-access publication (e.g. preprint servers, open access journals, or making papers available on the investigator's website).

All project reports should include activities related to the sharing of their findings.

Recruitment Efforts for Clinical Studies and/or Studies that involve Human Materials:
Projects involving human participants - whether directly recruiting or using materials from previously conducted studies - must address the appropriate inclusion or exclusion of individuals in the proposed research project.

Financial Responsibility:
Funding is awarded to the institution and/or organization, not to the individual principal investigator. The principal investigator or a first-degree relative cannot be listed as the signing official or financial officer, or have checks sent to their attention if awarded.

Appeals of Scientific Peer Review:
To maintain a fair and rigorous review system, the Alzheimer's Association has a process for appeal of funding decisions. Appeals will not be considered for the letter of intent stage. Regarding applications, an appeal is intended to address extraordinary circumstances. Appropriate reasons for initiating an appeal might include:

- Evidence that a reviewer has an undeclared conflict of interest.
- An egregious error or misunderstanding in the review process.
- Active malfeasance or demonstrable lack of due diligence.

The appeal process is not intended to provide a mechanism for routine protest of failure to receive a grant. It is anticipated that funding through the VCID-UMD Grant Program will be extremely competitive and is limited by availability of funds.

If an applicant believes an extraordinary circumstance has contributed to failure to receive funding, the principal investigator may send a two-page, double-spaced formal letter of appeal

(Word document) to grantsappeals@alz.org. Any supporting documents included must be submitted as a PDF. **Appeals must be submitted within 2 weeks from the date your application outcome notification is sent.** Notification of action on the appeal will be made via email, usually within 90 days of the appeal deadline.

Nondiscrimination and Harassment Statement:
The Alzheimer's Association is committed to providing an environment free from harassment and discrimination. The Alzheimer's Association strictly prohibits harassment and discrimination based on race; creed; color; religion; sex; sexual orientation; national origin; ancestry; age; Veteran status; citizenship status; marital status; physical or mental disabilities; pregnancy, gender identity or expression (including transgender status); genetic information; and any other characteristic protected by federal, state, or local law.