Role of Vascular Metabolic Factors in Pathogenesis of Alzheimer’s disease and Related Dementia (VMF)

**Competition Objectives:** The specific aim of the Alzheimer’s Association through the launch of the present Request for Applications (RFAs) is to broaden the conceptual models and areas of explorations regarding potential contributing factors to the pathogenesis of neurodegeneration/Alzheimer’s disease/dementia. This initiative is intended to stimulate new perspectives and encourage further explorations into the contributions or functions of vascular pathologies and associated metabolic dysfunctions in the expression of dementia. The primary interest of the RFAs is to promote the discovery-validation of new knowledge regarding molecular mechanisms [and eventual development] of biomarkers as surrogate markers regarding vascular contributions to Alzheimer’s disease and/or cognitive impairments. The RFA is designed to enable preliminary pilot research or proof-of-principle studies that can provide data for further research support by other funding agencies.

**Background:** There is a growing literature regarding the importance of consequences of micro-vessel pathologies and metabolic dysfunction on neurodegenerative processes. Several research planning efforts by the DHHS/NIH, the Alzheimer’s Association and the American Heart Association/American Stroke Association, have collectively recognized the urgent need to expand current knowledge regarding the precise role or significance of vascular-metabolic factors in the pathogenesis of Alzheimer’s disease and the expression of cognitive impairment in general.

**Potential Themes:** The potential topics of investigation listed here are intended to be illustrative; the applicant is free to propose other areas for investigation provided they are in line with this RFA. The high priority questions for the Alzheimer’s Association are those that would facilitate the conduct or interpretation of next generation of clinical trials. The particular, areas of focus may include but not limited to the discovery and validation of molecular targets and/or mechanisms that intermediary between vascular-metabolic aberrations and neurodegeneration/dementia or cognitive impairments; the discovery and validation of potential therapeutic targets and/or non-invasive biomarkers that could be validated as surrogate markers of disease progression and/or index of key vascular processes related to cognitive and neurologic impairment.

Special attention will be given to applications that focus on **underserved and/or underrepresented** populations disproportionately affected by vascular and metabolic syndromes.

Possible themes may include but are not limited to:

1. **Molecular mechanisms of Vascular Contributions to Alzheimer’s disease & Dementia**
   - Cellular – molecular mechanism of vascular function-dysfunction
   - Animal Model or other models for study of underlying pathogenic mechanisms
   - Basic Biology of Small Vessels in Health and Disease
2. Biomarkers of Vascular Contribution to Alzheimer’s disease & Dementia

- Imaging brain blood–barrier pathologies and/or blood flow/perfusion changes
- Imaging Cerebrovascular lesions and or aggregations of abnormal proteins
- Imaging Cerebrovascular Biomarkers in Humans
- Assay Development for Vascular Dementia Biomarkers

**General considerations:** Proposals must focus on biological mechanisms related vascular physiology with the aim facilitating the discovery-validation of biomarkers. All proposals must clearly outline pathway to be investigated including methods, sample and potential outcomes. The ultimate goal is to advance understanding vascular contributions to the discovery of future therapeutics and diagnostics for Alzheimer’s disease.

The Association strongly encourages submissions from collaborative research teams (e.g., basic scientists and clinical researchers). In addition, while novel and creative ideas are sought, proposals also need to demonstrate feasibility.

The Alzheimer’s Association recognizes the need to increase the number of scientists from underrepresented groups in the research enterprise. Researchers from these groups are encouraged to apply.

**Funding and award period:** The Role of Vascular Metabolic Factors in Pathogenesis of Alzheimer’s disease and Related Dementia awards is limited to $250,000 (direct and indirect costs) for two to three years. Requests in any given year may not exceed $100,000 (direct and indirect costs). Indirect costs are capped at 10 percent (rent for laboratory/office space is expected to be covered by indirect costs paid to the institution).

**Eligibility:** Researchers with full-time staff or faculty appointments (Assistant Professor and above) are encouraged to apply. **Applications from post-doctoral candidates will not be accepted.**

**Please note:** If the applicant institution does not have an Assistant Professor Position, the letter of employment should include sufficient information to allow the Alzheimer’s Association staff to evaluate the eligibility of the applicant.

**Ineligibility:** The Alzheimer's Association will not accept new grant applications from currently funded investigators who are delinquent in submitting required reports and other deliverables on active grants. Investigators that have previous Alzheimer’s Association awards closed as ‘Incomplete’ are not eligible to apply without exception. This policy will be strictly adhered to with no exceptions.
Submission and Review Procedures: The grant submission process will follow a two stage procedure. First, applicants will submit an LOI. These LOIs will be reviewed and a select number of the top rated LOIs will be invited to submit a full grant application. The exact number of full applications invited for full submission will be determined by available funding, with a target of more than 10% rate for full submission. Both LOI and the full submissions will be reviewed based on:

1) Alignment with the research priorities as outlined in the RFA. During the review of both the LOI and application, special attention will be given to applications that focus on underserved and/or underrepresented populations disproportionately affected by vascular and metabolic syndromes.
2) Demonstrable innovation/novelty of the proposed project (especially in the context of the PIs recently funded work).
3) Impact of project on Alzheimer’s disease and related dementia research.
4) Established investigators from other fields new to Alzheimer’s and related dementia research.
5) Evidence of methodological rigor that address the research question(s) being proposed.

Deadlines and award dates: Letters of Intent must be received by 5:00 PM EASTERN STANDARD TIME, March 6, 2015. Letters of Intent will not be accepted after this date. No exceptions will be made.

Applications must be received by 5:00 PM EASTERN STANDARD TIME, May 1, 2015.

Scientific and technical review will be conducted from May through June 2015. The second-level review by the Medical and Scientific Advisory Council will be conducted during June 2015. Funding will be awarded by August 30, 2015.

Applications will be reviewed with special attention to:
- Significance of the question being studied
- Applicant information
- Quality of the work plan
- Quality and adequacy of available resources and budget
- Impact-Risk

Mechanism of award, reporting requirements and allowable costs: The mechanism of the award is the individual research grant. The maximum allowable duration is three years. Annual progress and financial reports are required. Continuation of the grant over the awarded duration is contingent upon the timely receipt of scientific and financial reports.
**Budget:** A budget summary for the proposed research project is required and must be submitted with the application and within the allowable page limits. However, if the application is to be awarded, a more detailed budget will be required and must be approved before the disbursement of funds. Your budget must not exceed the maximum amount of the award ($250,000 for Vascular Metabolic Factors in Pathogenesis of Alzheimer’s disease and Related Dementia awards).

**Allowable costs under this award:**
It is required that most of the funds awarded under this program be used for direct research support. Allowable costs under this award include:
- Computer equipment if used strictly for data collection
- Travel (up to $1,000 per year)
- Salary for the principal investigator, scientific (including post-doctoral fellows) and technical staff (including interviewers, interventionists, data entry staff, technicians, and administrative support staff whose work is directly related to the funded project)
- Manual production/development/website, etc.

**Costs not allowed under this award include:**
- Tuition
- Computer hardware or software for investigators
- Rent for laboratory/office space
- Construction or renovation costs