

IV. SPECIFIC GRANT COMPETITIONS

i. Novel Pharmacological Strategies to Prevent Alzheimer's Disease

Competition Objectives: The Alzheimer's Association is launching a new initiative to stimulate the development of new pharmacological strategies to prevent or treat Alzheimer's disease. The Association's Request for Applications (RFAs) is aimed at the identification and validation of novel drug targets, the screening and development of drugs for such targets, and the evaluation of drug safety and efficacy, mostly at the preclinical level. 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: A number of drug targets have been identified in Alzheimer's, including proteases that cleave the amyloid precursor protein, aggregation of amyloid- β ($A\beta$) peptides, kinases that phosphorylate tau, tau aggregation, structural and biological properties of apolipoprotein (apo) E that differentiate it from more protective apoE isoforms, and inflammatory mediators. All of these targets are already being pursued in large, highly competitive drug development programs. Indeed, drugs aimed at some of these targets are in advanced clinical trials. However, the long-term efficacy and safety of these drugs will remain unknown for many years to come. Therefore, the Association aims to keep open the pipeline for new drugs with the potential to significantly improve the treatment and prevention of Alzheimer's, either as monotherapy or in combination with drugs that are or soon will be available.

Potential themes: Based on discussions with members of its Medical and Scientific Advisory Council, the Association puts forth several themes that may be particularly worthy of further research. Note that "novel drug target" in the context of this RFA is defined as a drug target that has not yet been published or has not been in the public domain for more than one year and that is clearly different from established drug targets that no longer meet this criterion. Grant proposals could address, but are not limited to, the following areas of study:

1. Discovery of novel drug targets for Alzheimer's. Research projects in this category may focus on hypothesis-driven candidate approaches or use large-scale unbiased systems biology approaches to identify novel drug targets for Alzheimer's disease. Projects may include human subjects, human samples, animal models, samples from such models and/or cell culture models.

2. Validation of novel drug targets. Research projects in this category should aim to validate novel drug targets for Alzheimer's by demonstrating that modulation of the target affects an outcome measure that is clearly relevant to Alzheimer's disease. Projects may include human subjects, human samples, animal models, samples from such models and/or cell culture models.

3. Screening for or development of drugs for novel targets. Research projects in this category may include the development of high-throughput assays, drug screens and medicinal chemistry to synthesize new compounds or modify promising scaffolds.

4. Evaluation of drugs for novel targets. Research projects in this category may focus on the evaluation of drugs at the preclinical or clinical level. Projects may consist of drug trials in well-established experimental models of Alzheimer's disease or of small pilot trials in humans with Alzheimer's, individuals with mild cognitive impairment or cognitively normal elderly individuals. Outcome measures may include clinical, radiological, pathological or biochemical alterations that are relevant to Alzheimer's. Studies focusing on cognitively normal individuals should not be preventive trials per se but should target alterations of physiological processes that have relevance to Alzheimer's and can be tracked (e.g., with biomarkers) whether or not there is an accompanying change in cognition.

5. Evidence-based evaluation of combination therapy. Research projects in this category may evaluate novel combinations of drugs or of drugs and non-pharmacological interventions at the preclinical or clinical level. Although it is unnecessary for both therapeutic components to be novel, their combination must not have been explored before and should be based on a solid rationale (including pertinent preliminary data). See point 4 for details on experimental design.

6. Bench-to-bedside models. Research projects in this category may focus on pioneering translational programs or mechanisms that could facilitate and expedite the path that leads from the identification of novel targets to clinical trials of drugs aimed at the novel targets. Although projects may focus on academic or industrial settings, of particular interest are projects that focus on the academic/industrial interface.

General considerations: Any proposal must have a clear focus on Alzheimer's disease and on a novel drug target as defined above. Any study that uses animal models must clearly and explicitly outline potential methods of translating and relating findings to the human condition in the future. Ultimately, the goal is to translate the research into strategies to delay, halt, reverse or prevent Alzheimer's disease.

Because the principle idea is to encourage studies into new technologies and high-risk ventures and translation of this novel technology to human studies, an interdisciplinary approach might be most fruitful. Therefore, 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 Association anticipates funding 2 awards in this category. Each award is limited to \$400,000 (direct and indirect costs) for two to three years. Requests in any given year may not exceed \$200,000 (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).

Funding cap: The Alzheimer's Association may consider allowing the funding cap to be exceeded for the New Pharmacological Strategies to Prevent Alzheimer's Disease RFAs if the science which the project is based upon calls for increased funds. Applicants requesting a cap increase must submit a written request to the Alzheimer's Association via email to: grantsapp@alz.org no later than three weeks before the submission deadline. The request must include a detailed budget and justification for the cap increase. Approval by the Alzheimer's Association will be required for an application to be submitted with a budget that exceeds the specified funding cap.

Eligibility: Researchers with full-time staff or faculty appointments are encouraged to apply. Applications from post-doctoral candidates will not be accepted.

Deadlines and award dates: Letters of intent must be received by 5:00 PM EASTERN STANDARD TIME, December 1, 2009. 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, January 7, 2010. Scientific and technical review will be conducted from February through May 2010. The second-level review by the Medical and Scientific Advisory Council will be conducted during June 2010. Funding will be awarded by July 2010.

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 unless written permission has been granted by the Alzheimer's Association.

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:

- Purchase and care of laboratory animals
- Small pieces of laboratory equipment and laboratory supplies
- 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 laboratory technicians and administrative support staff whose work is directly related to the funded project)

Costs not allowed under this award include:

- Tuition
- Computer hardware or software for investigators
- Rent for laboratory/office space
- Construction or renovation costs

For more information: E-mail grantsapp@alz.org or call 1.312.335.5747.