



## RESEARCH GRANTS PROGRAM ANNOUNCEMENT FISCAL YEAR 2009 (JULY 2008 – JUNE 2009)

Also available in PDF format on the Alzheimer's Association Web site at  
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<b>I. BACKGROUND: ASSOCIATION MISSION AND SCIENTIFIC AGENDA.....</b>	<b>2</b>
<b>II. AREAS OF FOCUS FOR THE 2009 RESEARCH GRANTS PROGRAM</b>	
i. Research in Diverse Populations: Closing the Gap.....	3
ii. Social and Behavioral Focus: Evaluating Interventions and Translating Knowledge into Practice .....	6
iii. Biological Focus: Causes, Early Detection, Treatment, Models, Prevention and Risk Factors.....	8
<b>III. RESEARCH GRANTS PROGRAM</b>	
i. Program Summary and Key Dates .....	13
ii. Scientific Categories of Proposals .....	14
iii. Eligibility, Ineligibility and Nondiscrimination Statement .....	15
iv. Application Procedures.....	16
v. Multiple and Overlapping Submissions.....	17
vi. Review Procedures .....	17
vii. Appeals of Scientific Peer Review .....	18
viii. Animal and Human Subject Assurances.....	18
ix. Contact Information .....	18
<b>IV. SPECIFIC GRANT COMPETITIONS</b>	
i. New Investigator Research Grant (NIRG) .....	19
ii. Investigator-Initiated Research Grant (IIRG) .....	21
iii. The Senator Mark Hatfield Award for Clinical Research in Alzheimer's Disease.....	23
iv. The Zenith Fellows Award Program .....	25
v. Everyday Technologies for Alzheimer Care (ETAC) Grants .....	27
vi. New Investigator Research Grant to Promote Diversity (NIRGD).....	31
vii. Mentored New Investigator Research Grant to Promote Diversity (MNIRGD).....	34
viii. Molecular Imaging in Alzheimer's Disease Grant .....	38
ix. Conference Grants Program.....	43

*The purpose of the Research Grants Program Announcement is to help applicants understand the context and history of the Alzheimer's Association research grant program and to publicize high-priority areas of focus for the current fiscal year. However, applicants should not consider areas of focus restrictive—projects exploring other topics are actively encouraged, even if they fall outside the areas discussed below.*

## **I. BACKGROUND: ASSOCIATION MISSION AND SCIENTIFIC AGENDA**

The Alzheimer's Association was founded in 1980 by a small group of family members caring for loved ones with Alzheimer's disease. These individuals were united in disappointment with the quality of information available to them and in dissatisfaction with the lack of medical and social awareness of this devastating condition. Two years after its founding, the fledgling organization funded its first research grant, awarding a total of about \$80,000 to a handful of investigators. Since then, the Association has grown into the largest private funder of Alzheimer research, awarding over \$26 million during the 2008 grants cycle (21 percent funding level) to bring the cumulative total of Association-funded research to more than \$250 million.

The Association supplements its own funding efforts with public policy initiatives directed toward increasing Alzheimer research funding to the U.S. National Institutes of Health to \$1 billion annually. The Association also works tirelessly to support and educate its constituents by providing high-quality information in non-specialist language about its grants program and general issues in Alzheimer research, prevention, treatment and care.

The Association's grants program has served historically as an incubator for novel ideas, complementing the programs of the National Institute on Aging and the other National Institutes of Health. As our funding initiative has grown and matured, grant categories have expanded to support researchers at every stage in their careers. Funded projects now explore the broadest possible spectrum of biological approaches to understanding, preventing and treating Alzheimer's; social and behavioral strategies for ameliorating the effects of the disease on individuals and their family and professional caregivers; clinical studies; and adaptive technologies.

Surveys conducted on behalf of the Association continue to affirm that research support is the highest priority of our constituents and the general public. In response to this overwhelming sentiment, the Association's National Board mandates research as an ongoing major emphasis. For the 2009 grants cycle, our areas of focus include historically underserved populations, as well as the growing number of specific cultural and ethnic groups, and their aging members, in this rapidly diversifying society.

Expanding our emphasis in these directions affirms the Association's long support of research and emphasizes the following goal and objective in the Association's 2006-2008 Strategic Plan:

**Goal 1: Advancing Research:** Together we will accelerate the progress in Alzheimer research.

**Objective 2:** Increase the Association's research funding for basic science, prevention and care, with special attention to diverse ethnic populations.

In addition, there are three overarching objectives embedded in all programs of the Association, as well as the Strategic Plan:

1. Support and extend the ability of people with Alzheimer's disease to function independently through safe and effective interventions, using pharmacological, behavioral and other approaches.
2. Find the cause(s) of Alzheimer's disease, from its biological underpinnings to the impact of cultural, behavioral, social and environmental factors on disease progression.
3. Prevent Alzheimer's disease through improved methods of detection, early intervention and the discovery of risk factors, including the interactions of molecular, genetic, environmental and cultural variables.

The thrust of the Association's research program can be summed up in three words: quality of life. All of the Association's research efforts are aimed at some aspect of improving the quality of life of people with the disease, their families and care providers through social and behavioral research, studies to improve diagnosis or design new treatments, research to elucidate the cause of the disease(s) and ultimately, studies and programs to eradicate Alzheimer's disease.

## **II. AREAS OF FOCUS FOR THE 2009 RESEARCH GRANTS PROGRAM**

Areas of focus are high-priority research arenas in which the Association actively seeks proposals. The areas are defined broadly and the examples cited are not intended to preclude or constrain other investigator-initiated projects or proposals. Potential applicants are strongly encouraged to submit proposals in their own areas of interest or formulate questions different from those presented in this announcement. Investigator-initiated research projects are the core of the Association's scientific program.

### **i. Research in Diverse Populations: Closing the Gap**

Results of the 2000 census confirm that the overall population of the United States is rapidly becoming more diverse. However, the language and techniques often used to characterize diverse populations fail to reflect the true richness of origin, culture, and genetic variation represented in our society. This failure is well illustrated by the following excerpt: "Today, discussion of cultural diversity—ethnicity—most often identifies four major U.S. ethnic subgroups: African Americans (Blacks), Asian Americans and Pacific Islanders (or Pan Asian populations), American Indians and Alaska Natives, and Hispanics (or Latinos). Indeed, the term 'Asian Americans' represents more than 50 distinct linguistic groups. African Americans include persons who trace their roots to Africa, who were born in Africa, or who were born in the Caribbean Islands. Hispanics count more than 25 different countries of national origin. American Indians and Alaska Natives encompass over 500 federally recognized tribes and groups, with at least 30 different languages." (From *The Fourth Report of the Advisory Panel on Alzheimer's Disease, 1992: A Report to the U.S. Congress and the U.S. Department of Health and Human Services*; NIH Publication 03-3520.)

As the general population reflects a richer ethnic mix, subpopulations of older adults and those at risk for Alzheimer's disease are also growing more diverse. These

extraordinarily rapid demographic changes are forcing organizations to re-evaluate whether they have sufficient knowledge of all groups within their potential clientele to deliver programs and services effectively. The Alzheimer's Association has concluded that there are significant information and data deficits about ethnic and cultural groups in most major research areas in Alzheimer's disease, including screening and neuropsychological testing instruments; diagnostic procedures; recruitment and retention in research protocols and clinical trials; clinical and neuropathological correlative studies; caregiving and family studies; basic laboratory investigations; genetics projects; development of new models of long-term care and management of these services; epidemiological and health services research; and the economics of care.

Our understanding of Alzheimer's disease is limited by the characteristics of the people who have traditionally been included in investigations. There is a need for basic sociological and anthropological data about Alzheimer's disease, families, and caregiving in specific cultural and regional contexts to provide a working platform for effective service, education and program delivery.

To fill these gaps in knowledge, projects must address the following issues:

**Socioeconomic status:** Does high or low socioeconomic status have the same meaning in diverse populations? How can services for people with Alzheimer's disease and their families be developed most effectively to reach the poor or minority-group members who reside in majority communities? What is more important in specific diverse groups—information or funds to purchase help and services? What is the best method to convey information to specific diverse groups?

**Values and beliefs:** How do values and beliefs shape receptivity to and perceptions about community-based and institutional services for Alzheimer's disease? How do values, beliefs, and perceptions vary among groups? How do the beliefs about Alzheimer's disease and normal aging encourage or prevent use of services? How must services and programs respond to be effective?

**Role of the family and community:** In specific diverse groups, how does the role of family differ in the long-term care of older members with dementia? How does the decision-making process differ in these groups? Is it necessary to understand family dynamics before planning interventions and services?

**Geographical and regional variation:** How do these factors affect the development and provision of services and programs? How do they interact with socioeconomic status and minority group membership in majority locales?

**Interactions among factors:** How do socioeconomic status, values and beliefs, the role of the family, and geographical and regional differences interact to influence care and service delivery to people with Alzheimer's disease and their families?

Incidence, prevalence and risk factors—key facts about the epidemiology of Alzheimer's disease—remain unknown in many defined ethnic and cultural groups.

To better quantify the public health implications of Alzheimer's and support the development of necessary programs and services, reliable and valid data on the distribution of the disease in the U.S. population must be obtained.

Acquiring meaningful epidemiological data for diverse groups will require the ability to accurately detect and monitor Alzheimer's disease in the target population. In most cases, adequate tools for detection and monitoring do not exist. These instrumentation deficits inhibit epidemiological investigations and limit the conduct of behavioral, social and clinical studies.

The following points outline some of the tools, instruments and strategies needed to address these deficiencies. Although very large population studies fall outside the funding scope of the Alzheimer's Association, smaller, well-designed studies can effectively address a number of the information and instrument gaps that must be filled. This list is not exhaustive but is intended to highlight the types of research needed:

**Screening and assessment instruments** that are valid and reliable for specific age, gender, cultural, language, and ethnic groups, as well as for different levels of education and literacy, are needed as soon as possible. Expansion of epidemiological, behavioral, social and clinical research is hampered by the lack of these instruments.

**Test norms standardized for age and gender for specific ethnic groups** are also needed urgently. These norms must take into account language, education level, and literacy as well as educational equivalency between cultures and countries of origin. Norms derived from majority group data are often applied to minority groups and can result in misleading interpretations. This misapplication is especially serious for people with little or no formal education.

In research on Alzheimer's disease—especially in clinical drug trials—identification, recruitment, enrollment and retention of members of diverse cultural groups have lagged. Minority group members have been underrepresented in much of the research in Alzheimer's disease. The published literature on barriers to enrollment and retention has been largely descriptive and anecdotal. It is time to initiate a program of hypothesis-driven research to determine the efficacy of specific methods to enlist and retain ethnic minority and cultural group members in Alzheimer's disease research. Some of the issues of interest include:

**Cross validation:** Programs that are successful in the recruitment, enrollment, and retention of cultural group members must be cross-validated with other cultural groups and in different geographic areas to determine their broad-based usefulness in research.

**Contacts:** The differences in the effectiveness of recruitment approaches, and the mechanisms underlying these differences, must be explored. For example, under what circumstances are individual or local community-rooted approaches more effective than large mass media or marketing approaches? How do specific, clearly defined cultural groups differ from one another in the acceptability of various approaches and methods of contact?

***Culturally competent investigators or investigators who are members of the cultural group:*** What difference does the cultural identity of the investigator make in successful identification, recruitment, enrollment and retention of specific cultural group members? Does it enhance long-term successful retention to have investigators who are of the same cultural group as the people to be recruited? Or, is it adequate that the investigator be culturally competent? And what, precisely, does it mean to be culturally competent for the purposes of Alzheimer research?

***Community barriers:*** What are the real and perceived barriers to participation in Alzheimer's disease research in specific cultural groups? How can these barriers be overcome?

## ii. **Social and Behavioral Focus: Evaluating Interventions and Translating Knowledge into Practice**

Social and behavioral research has the potential to increase our understanding of the effects of Alzheimer's disease and other dementias on individuals with the disease, their families and other caregivers. At the same time, it can increase our knowledge about interventions that improve care practices, health, functional and emotional outcomes and quality of life, as well as prevent or reduce symptoms for millions of individuals and their families. Three key components are necessary to effectively meet the challenge of social and behavioral research—(1) formulate important, novel and testable questions; (2) apply rigorous methodology to determine what works, for whom and why; and (3) get information out to the people who need it most.

Studies must bridge the gap between what has been demonstrated empirically and daily care practices for people with Alzheimer's disease. Often, lack of knowledge about what constitutes a successful intervention hinders the transfer of the technique to everyday care settings. The research world is fragmented and disseminates its findings in ways that are not easily or routinely available to various audiences. Finding ways to meet this challenge and getting the information out to those who need it is essential.

It is important to consider the influence of socioeconomic status, cultural and ethnic diversity, health/lifestyle practices, stigma and family attitudes about seeking care, availability of services and regional variation when proposing research about social and behavioral issues. Alzheimer's disease is heterogeneous, and the people with Alzheimer's disease are also heterogeneous. These factors must be considered in hypothesis construction, planning and design of research projects.

In addition, earlier detection and diagnosis are increasing the number of individuals identified with early-stage dementia. The characteristics and care needs of diagnosed individuals and their families in early, middle and late stages of Alzheimer's disease differ greatly. Social and behavioral research proposals should consider these differences in the design of proposed studies and the translation of findings from research to practice.

A wide range of questions in the social and behavioral arenas is ready for research. The answers to these questions, if broadly applied, would improve the quality of daily life for people with Alzheimer's disease and their families. Six research domains, with the first five as identified by Pearlin et al. (2001), are outlined below to provide a conceptual framework for these questions. The broad questions under each domain are provided as examples to facilitate the development of more specific research questions. Each investigator is encouraged to tailor his or her question to specific populations.

**(1.) Person with Dementia:** Over time, we have been able to gain an understanding of the experience of the person with dementia. This can be attributed to such things as people in the early stages speaking and writing about their experiences and the development of individualized approaches to care. Whenever possible, studies should be designed to elicit the experiences of individuals with dementia.

- How can the experience of the person with dementia be characterized throughout the disease course to provide insight into areas such as decision-making capacity, quality of life and advance planning?
- How can the perspective of the person early in the disease process help shape decisions and care?
- Do personal or social factors influence the experience of the person with dementia in important and measurable ways?

**(2.) Physical and social environment:** Environmental design for persons with dementia is a multi-dimensional construct that purports to satisfy the need for autonomy, dignity, safety, comfort and community as well as enhance one's mobility, cognition and memory. We need to gain a better understanding of the specific dimensions of the environment, as well as their interaction, and how they produce desired outcomes.

- What characteristics of one's physical and social environment contribute to an individual's quality of life? How do these characteristics change through the course of illness?
- What are the components of a supportive environment in the home or residential care setting for someone with cognitive impairment? How do these components change through the course of illness?

**(3.) Family and household:** The family of a person with dementia plays a critical role in providing care and navigating the health and long-term care systems. Although caregiving has been studied intensively, there is still no explanation for the differences and inequalities of its impact on the family.

- What unique problems are encountered by families of persons with various types of dementia (e.g., early-onset dementia), and what interventions, services and policies are needed to mitigate those problems? How are these problems affected by the characteristics (e.g., socioeconomic status, culture and ethnicity, region of the country) of the families?
- What interventions can improve communication among family caregivers, persons with dementia and their health and long-term care providers and have a positive effect on care and outcomes?
- What effect do family attitudes about dementia have on the self-image and functioning of persons with dementia?

**(4.) Identification and evaluation of services and interventions:** Researchers and service providers together must identify and evaluate the broad range of factors that can affect programmatic interventions.

- What care service interventions or programs are most likely to have positive effects for people with Alzheimer's disease or their families in the community?
- What characteristics of programs and services render them most acceptable to people with the illness and their families?
- What are the most effective strategies to motivate physicians and other health care providers to improve the quality of care they provide to people with dementia in clinical and long-term care settings?
- How can we effectively sustain improved practices subsequent to training programs received by residential care staff?

**(5.) Health policy:** Research can guide the adoption of policies that reshape systems of support in the home, community and health and long-term care settings. Researchers and policy makers together must ensure that public and private policies respond to the unique needs of those with dementia.

- What techniques should be used to determine consumer preferences for and satisfaction with their health and long-term care when the consumers have dementia?
- What techniques should publicly funded programs use to identify and properly care for people with dementia, including those with multiple chronic conditions?

**(6.) Maintaining cognitive function:** Growing evidence suggests that lifestyle factors and behaviors interact with biological functions in maintaining cognitive function. It is important to find ways to effectively share information about prevention and about the potential benefits of changing behaviors.

- What strategies are effective for getting the science of prevention out to the general public?
- How can we measure and evaluate public response to (or acceptance of) prevention information?
- How can we measure and evaluate people's use of the information to change important behaviors? What help do people need to support important lifestyle changes?
- How can the effect of these strategies be measured in relation to cognitive decline?

iii. **Biological Focus: Causes, Early Detection, Treatment, Models, Prevention and Risk Factors**

Although there have been vast advances in Alzheimer research, the field still faces a great number of serious impediments to progress in translating basic science discoveries into effective treatments and evidence-based clinical practices for dementia. Some of the many challenges that remain for investigators to address include:

***Cause(s) of the Disease: How and why do specific sets of neurons in select brain structures become dysfunctional? Why do some neurons and not others die? What initiates these processes? What is the key step in the cascade of***

***events leading to cell death? How do genetic factors interact with other factors to influence these processes?***

The primary neuropathological events in Alzheimer's disease involve abnormal expression and processing of proteins. Advances in molecular biology have provided the tools needed to begin to unravel the mechanisms of synthesis, trafficking, and accumulation of these proteins in the brain. Research in this area has begun to produce promising leads about the role of these proteins in neural function, dysfunction, and cell death and to suggest strategies to correct this molecular mischief. Although these insights into the neurobiology of the disease have generated a number of ideas, the precise etiology of the disease is still not known. While there are many theories on possible mechanisms of neural dysfunction and/or cell death, critical questions remain unanswered.

None of these theories has been validated by crucial experiments designed to demonstrate the functional relationship(s) between characteristic molecular aberrations and the clinical manifestations of the disease. One of the most difficult challenges for the field is to link the perspectives of investigators inhabiting two totally different worlds: those who view Alzheimer's disease only through the prism of molecular/neuropathological events and those who know it only through its behavioral and clinical manifestations.

The precise relationships between the clinical symptomatology and the neuropathology of the disease are not well defined. There is a critical need to understand not only the presumptive causal links between the neurobiology and clinical course of the disease but also the mechanisms for the heterogeneity of presentation, which may vary widely and may influence differential diagnosis and differences in adverse events/responses to treatments.

***Early and Accurate Detection and Diagnosis: What are the most sensitive, specific and cost-effective diagnostic procedures? What are the most sensitive, specific and cost-effective procedures for assessing change through the course of the disease?***

Several converging lines of evidence suggest that the neurodegenerative processes associated with dementia begin several years before the first clinical features can be detected with current instruments. The precise duration of the preclinical period and the details of the early molecular events are not known. This uncertainty about symptom-free early stages of the disease stems from the lack of well-validated tools or technologies for detection.

Although clinical information can be gleaned from longitudinal studies, even these data are usually obtained in the middle to later stages of the disease when some of the cognitive and behavioral signs appear. As a result, there is little or no information on manifestations of the disease during its earliest preclinical stages or the very earliest behaviors of individuals at risk. These gaps result from the lack of appropriate technologies for noninvasive observation and early detection of the disease. Finding sensitive and specific markers will become even more important as pressure increases to develop very early treatments. If these early interventions have the potential for harmful side effects, it is crucial that they be targeted appropriately. Thus, there is an urgent need to find accurate biological markers of the disease,

including improved imaging techniques and more sensitive cognitive and behavioral assessment instruments.

Any effective biomarker must not only detect a fundamental biological process in the disease, but should also be validated in an adequately powered study with neuropathologically confirmed cases. The ideal marker should have sensitivity greater than 80 percent for detecting disease and specificity also greater than 80 percent for distinguishing Alzheimer's from other dementias. Testing for the marker should be reliable, reproducible, non-invasive, simple to perform and inexpensive. In addition, a putative biomarker should have confirmation by at least two independent studies conducted by qualified investigators. Currently, none of the putative biochemical markers have been validated in adequately powered investigations.

Well-tested biological markers for Alzheimer's disease are not the only critical need—it is also important for investigators to explore the observational and subjective perspective that family members, care providers and people with the illness can provide about the very earliest events. The observations of family members, nurses, social workers and other care providers have already provided some important insights about early cognitive and behavioral events.

***Treatment: What are the most effective and safe pharmacological treatment strategies, behavioral management techniques, and combinations of therapies? This focus area includes testing of complementary and alternative medicine approaches and health services research.***

Research on interventions is poised for a revolution. The timing of the revolution is open to speculation—it may take two years, it may take ten—but it will happen. Dramatic advances in understanding the neurobiology of Alzheimer's—including elucidation of many genetic and molecular mechanisms involved in the disease—have provided many promising leads for drug development. It is now generally agreed that the most critical neurobiological events underlying the behavioral problems and clinical manifestations of the disease concern dysfunctions in nerve cell signal transduction, loss of synapses, and premature cell death. The primary scientific dispute revolves around theories concerning the precise cause or source of these destructive processes. Currently, the field of Alzheimer therapy has a rich array of promising leads as therapeutic targets. If such potential treatments, using a variety of approaches, could be validated by well-powered clinical trials, they will have a profound effect on the disease. The eventual utility/efficacy of any intervention can only be evaluated through clinical trials, which are expensive.

Until recently, strategies for developing interventions focused primarily on symptomatic treatments for middle and late stages of the disease. It is anticipated that as new therapeutic targets are discovered, it will be possible to improve the quality of signal transduction and the ability of nerve cells to communicate. As even more is learned about the neurobiology of Alzheimer's disease, there will be greater reliance on techniques to design specific molecules aimed at correcting a particular cellular dysfunction. Some important therapeutic approaches should involve the discovery of interventions aimed at preventing premature cell death and restoring or prolonging the function of surviving damaged nerve cells.

Until effective pharmacological treatments are discovered, family and facility-based care providers must rely on a variety of behavioral and social interventions to assist in managing symptoms and maintaining the highest quality of life for people with Alzheimer's disease. The development and testing of new social and behavioral interventions, in the appropriate cultural context, is a priority and is discussed under "Social and Behavioral Research."

***Models of the Disease: Inadequate disease models and modeling systems is a major handicap for developing effective disease-modifying agents and other interventions.***

While considerable advances have been made in the development of animal models—especially transgenic mice carrying human genes for key Alzheimer proteins and variant forms of genes shown to be involved in dementia—these models have serious potential limitations. One serious limitation is that the design of these models is predicated on the assumption—yet to be validated—that development of amyloid plaques and neurofibrillary tangles is directly related to the cognitive and behavioral changes associated with Alzheimer's disease.

Current modeling systems may prove adequate if the presumed relationship between hallmark Alzheimer pathologies and clinical manifestations holds. If the strategy of reducing brain amyloid burden through various interventions under development, in fact, improves symptoms of the disease, this improvement will be accepted as confirmation that brain amyloid pathology is involved in causing clinical symptoms.

Another potential limitation, however, is that the relationship between hallmark brain pathologies and symptoms—if it exists—may not be linear. The human brain epitomizes a complex physiological system in which dynamically integrated systems create emergent properties. It is very likely that the relationships between the clinical/behavioral symptoms of Alzheimer's and molecular changes in the brain are nonlinear and thus may be much more complex than the relationship modeled in current transgenic systems. As a result, other modeling approaches, such as complex systems modeling, might become useful adjuncts to the transgenic models.

***Prevention: What are the prospects and strategies for prevention?***

One of the most important priorities is research on strategies to prevent Alzheimer's. The importance of prevention is rooted in the severe effects of the disease on individuals and their families, the very large number of persons with the illness and the anticipated growth of these numbers with the aging of the population in the United States and other developed countries. Developing effective preventive strategies will bring significant benefit in reducing the economic and social cost, preserving the productivity of family caregivers and lessening the impact on the health care system. The most convincing argument, however, is the humanitarian one—effective prevention can spare future generations from one of the most feared infirmities associated with advancing age.

Research into basic disease mechanisms can have immense benefit for development of strategies for disease prevention, but there is not always a tight link between understanding the mechanisms of a disease and preventing it. Highly successful

prevention efforts have been designed and conducted under circumstances in which disease mechanisms were understood poorly, or not at all.

***Risk Factors: What are the characteristics, either genetic or acquired, that increase the risk of Alzheimer's disease or offer protection against or delay the onset? How do the risk factors vary among specific diverse populations? Are any risk factors modifiable?***

Epidemiological studies reveal growing evidence that most cases of Alzheimer's disease likely involve a combination of genetic and environmental risk factors. Identifying and validating these risk factors remains one of the most critical scientific challenges. In recent years, several putative risk factors have been identified; however, the only risk factors so far validated for late-onset disease are age, family history and one susceptibility gene.

The potential link between cerebral blood vessel disease and Alzheimer's is one promising area of research. Vascular disease in the aged appears to have strong implications for neurodegeneration leading to dementia. Preliminary studies indicate that a broad spectrum of cerebrovascular lesions could lead to a decline in cognitive function. In addition, recent epidemiological studies have begun to implicate vascular conditions outside the central nervous system—such as heart disease and high blood pressure—as important risk factors for dementia. There is some evidence that nearly 80 percent of individuals with Alzheimer's disease also have cardiovascular disease at autopsy. The broader implications of such findings support the hypothesis that systemic vascular factors are risk factors for developing Alzheimer's disease. This risk encompasses different forms of cardiovascular disease, including coronary artery disease, carotid atherosclerosis, history of hypertension or high cholesterol, Type II diabetes and stroke or transient ischemic attacks.

The e4 allele of the apolipoprotein E gene (APOE-e4)—which has been associated with increased risk of cardiovascular disease—is the best-validated susceptibility gene to date, with more widespread effects than any other genetic factor implicated in the late-onset, sporadic form of Alzheimer's. The mechanism(s) by which APOE-e4 exerts its influence in Alzheimer's disease is unknown, but several hypotheses involving molecular events in brain pathology and physiological actions on the cardiovascular system have been proposed.

### III. RESEARCH GRANTS PROGRAM

#### i. Program Summary and Key Dates: Fiscal Year 2009

Grant Competition	New Investigator Research Grant (NIRG)	Investigator-Initiated Research Grant (IIRG)	Senator Mark Hatfield Award for Clinical Research	Zenith Fellows Award	Everyday Technologies for Alzheimer Care Grant (ETAC)	New Investigator Research Grant to Promote Diversity (NIRGD)	Mentored New Investigator Research Grant to Promote Diversity (MNIRGD)	Molecular Imaging in Alzheimer's Disease Grant (MIAD)
Letter of Intent:	<b>Open Receipt Date: September 26, 2008</b> <b>Deadline Date: December 1, 2008, 5:00 PM EST</b>							
Application Deadline Date:	<b>January 8, 2009, 5:00 PM EST</b>							
Review Process:	<b>February–May 2009</b>							
Award Announcement:	<b>July 2009</b>							
Number of Awards:	Anticipate funding 30	Anticipate funding 55	Anticipate funding 1	Anticipate funding 5	Anticipate funding 4	Anticipate funding up to 5 NIRGD & MNIRGD awards combined		Anticipate funding 3
Request per year (in any given year) may not exceed:	\$60,000	\$100,000	\$112,500	\$250,000	\$90,000	\$60,000	\$60,000	\$200,000
Maximum per award:	\$100,000	\$240,000	\$225,000	\$450,000	\$200,000	\$100,000	\$150,000	\$400,000
Maximum number of years:	2	3	3	3	3	2	3	2-3

Scientists from underrepresented groups are encouraged to apply

The funding level for fiscal year 2008 was 21 percent of submitted applications.

Each of the grant competitions, except the ETAC Research Grant and Zenith Fellows Award, shares the preceding areas of focus for fiscal year 2009 covered in Section II. Section IV of this program announcement provides complete details about each individual competition, including objectives, funding and award period, eligibility, receipt and award dates, mechanism of award, reporting requirements and allowable costs.

Procedures and processes common to all of the grant competitions are discussed here.

## ii. Scientific Categories of Proposals

Each proposal must be submitted to a specific grant competition. In addition, all applicants in every competition are asked to classify their proposals according to four broad categories of scientific inquiry: (1) social and behavioral research, (2) clinical investigations, (3) basic biology and (4) adaptive technology. During second-level review, these categories help the Alzheimer’s Association Medical and Scientific Advisory Council ensure a balanced, well-distributed award portfolio.

Topics that would fall into the four cross-competition categories might include, but are not limited to:

**1.) Social and behavioral research** (relevant to the NIRG, IIRG, ETAC, Hatfield, NIRGD and MNIRGD competitions): research in diverse populations; assessment of novel approaches to care and support of diagnosed individuals and caregivers; special needs of early-stage and early-onset individuals; analysis of the impact of the physical and social environment; evaluation of services and interventions; quality of life; ethical issues; and health policy.

**2.) Clinical investigations** (relevant to all competitions): projects in which the majority of data is derived directly from studies involving active participation of human subjects. Examples include pilot studies of new therapies; neuropsychological testing; drug administration; biomarker collection; imaging technology; and risk factors including genetics, cardiovascular issues, diabetes and metabolic factors and lifestyle issues. *In vitro* projects conducted in human samples should be categorized as basic biology rather than clinical work.

**3.) Basic biology** (relevant to NIRG, IIRG, Zenith, NIRGD, MNIRGD and MIAD competitions): these are bench science projects involving *in vitro* or animal work pertaining to the causes of dementia; early and accurate detection and diagnosis; animal models; treatments; and prevention. Please note that *in vitro* work involving human samples falls into this category.

**4.) Adaptive technology** (relevant to NIRG, IIRG, ETAC, Hatfield, NIRGD and MNIRGD competitions): research focusing on the use of emerging technologies and their clinical and social implications, including mobile computing, high-bandwidth sensing, “smart” environments, robotics, imaging, face recognition, natural language processing and behavioral monitoring for early detection.

**Please note** that there are a few cases in which certain scientific categories do not apply to specific grant competitions. Applicability of categories to competitions is summarized in the table below.

Scientific Category	NIRG	IIRG	Zenith	ETAC	Hatfield	NIRGD	MNIRGD	MIAD
Social/behavioral	X	X		X	X	X	X	
Clinical	X	X	X	X	X	X	X	X
Basic biology	X	X	X			X	X	X
Adaptive technology	X	X		X	X	X	X	

### iii. Eligibility, Ineligibility and Nondiscrimination Statement

To avoid disqualification, investigators are encouraged to carefully consider these eligibility and ineligibility requirements before applying.

#### ***Eligibility***

In general, public, private, domestic and foreign research laboratories, medical centers, hospitals and universities are eligible to apply, with the exception of state and federal government-appropriated laboratories and for-profit organizations, which are prohibited from serving as the applicant institution. However, state and federal government scientists can participate as collaborating scientists with research teams from other eligible applicant institutions. During the LOI or the Application stage, you may be asked to provide proof of your organization's not-for-profit status.

#### ***Ineligibility***

This section describes general exclusion criteria. Specific requirements and additional exclusions to eligibility are noted in some detailed competition descriptions.

**1.) Overlapping funding** of more than one Alzheimer's Association grant is **not allowed**. Investigators who are receiving an **active Association grant** may apply for another award in the last year of their grant **if that last year concludes by June 30<sup>th</sup>** before the start of the new funding year on July 1.

**2.) Investigators delinquent in reporting:** The Alzheimer's Association will not accept new grant applications from currently funded investigators who are delinquent in submitting interim/final scientific reports or interim/final financial reports on active grants. **This policy will be strictly adhered to with no exceptions.**

**3.) Current and past holders of a Zenith Fellows Award** will not be considered for another award in the Zenith competition.

**4.) Members of the Association's Medical and Scientific Advisory Council** are ineligible to compete for any research grant.

**5.) Postdoctoral fellows are not eligible to apply for any Alzheimer's Association grant**, except in one special case. Applications for a New Investigator Research Grant (NIRG), New Investigator Research Grant to Promote Diversity (NIRGD) and Mentored New Investigator Research Grant to Promote Diversity (MNIRGD) will be accepted from postdocs who can provide a letter indicating they will have a full-time faculty position, such as an assistant professorship, by the application deadline. The letter of employment must be on hiring institution letterhead and must indicate that the position will be activated by the grant award date. If the anticipated position is not activated by the award date for any reason, any offer of funding will be withdrawn.

**6.) Checks are awarded to the institution, not to the individual principal investigator.** The signing official and the financial officer cannot be the principal investigator.

### ***Nondiscrimination statement***

The Alzheimer's Association values diversity and seeks applicants from diverse backgrounds. The Alzheimer's Association does not discriminate on the basis of race, sex, sexual orientation, religion, color, nationality or ethnic origin, age, disability, or status as a Vietnam Era Veteran or disabled veteran, in the administration of educational policies, programs or activities.

### **iv. Application Procedures**

#### ***Submitting a letter of intent (LOI) on-line via proposal CENTRAL***

The first step in applying to the Alzheimer's Association for any research grant is to submit a Letter of Intent (LOI) through the *proposalCENTRAL* on-line application system at <http://proposalcentral.altum.com>. First-time users **must** register and fill out a Professional Profile in *proposalCENTRAL* to begin the application process. **In addition, you must register to become a reviewer (if you have not done so already) to be able to submit your LOI. It is required that you review at least one grant proposal within your area of expertise, outside of the grant competition to which you are applying.**

**The LOI and completed application must be submitted by a single principal investigator (PI).** Additionally, a PI cannot submit an LOI that had been approved or rejected during a previous grant cycle. All LOIs must be approved or rejected in the current grant cycle. Hard copies of the LOI will not be accepted. The purpose of the LOI is to ensure that all applicants are eligible for the competition they are applying to and to assist Association staff in planning for peer reviews. **LOIs will not be accepted after the deadline date. No exceptions will be made.**

*The LOI must include:*

- Name of the principal investigator
- Contact information for the principal investigator (**complete** mailing address, telephone number, fax number and email address)
- Institution(s) involved in the research proposal
- Title of the investigation
- Area of focus of the submission, such as diverse populations, social and behavioral or biological, as outlined in Section ii
- Grant competition for which you are applying (Investigator-Initiated Research Grant, New Investigator Research Grant, Zenith Fellows Award, Hatfield Award, Everyday Technologies for Alzheimer Care Grant, New Investigator Research Grant to Promote Diversity, Mentored New Investigator Research Grant to Promote Diversity or Molecular Imaging in Alzheimer's Disease Grant)
- Brief rationale for the proposal

#### ***On-line application via proposalCENTRAL***

Once the on-line LOI is approved, an e-mail notification will be sent granting access to the on-line application at *proposalCENTRAL*. **The online system must be used to submit a grant application** – hard copies of the application will not be accepted.

**The PI who submits the LOI must be the same PI who submits the application.**

LOIs submitted on behalf of other applicants will result in a rejected application. Once the applicant enters the application system, on-screen instructions will be provided to complete the application process. The application does not need to be completed in one session; a partially completed application can be saved and completed at any time before the deadline.

**(Important Note: It is imperative that you proofread your application before submission; you will not be allowed to make any changes to the application after the deadline).**

It is the responsibility of the applicant to ensure and to verify that:

(1) The application is received by the receipt date/time deadline  
(2) The application is complete and correct before submission. Only a single copy of an application will be accepted. **Signatures are not required at the time of submission.**

**(3) Revisions, additional materials, letters of collaboration and/or reference, manuscripts, appendices, etc., are not allowed and if attached, will be removed from your application. Additionally, we are no longer accepting the above under a separate email.**

#### **v. Multiple and Overlapping Submissions**

If separate proposals are submitted to different grant competitions, each proposal submitted must address **a distinctly different topic**. Only one proposal will be funded if scores for multiple submissions fall within the funding range of different grant competitions.

**Applicants cannot submit two proposals in the same grant competition—even if the proposals cover distinctly different topics.**

Applicants may revise and resubmit an application that was previously submitted for an earlier grant cycle; however, an LOI is required each year. A current LOI corresponding to the application year must accompany each application. **Revisions of previous submissions will be treated as new applications. Efforts will be made to provide some continuity in reviews.**

Overlapping funding of more than one Alzheimer's Association grant is not allowed. Investigators who are receiving an **active** Association grant may apply for another award in the last year of their grant **if** that last year concludes by June 30<sup>th</sup> before the start of the new funding year, which begins on July 1.

#### **vi. Review Procedures**

All proposals are subject to a two-stage peer-review process carried out with an on-line system. In the first stage, applications are reviewed and rated by three to four peer scientists with expertise in the proposed area of research. The second stage includes further review and discussion of the scores and comments resulting from the initial review process. This second review is carried out by the Medical and Scientific Advisory Council of the Alzheimer's Association to ensure fairness and equity in the initial review procedures and to make funding recommendations to the Association.

Members of this Council are internationally recognized experts with distinguished careers in Alzheimer's and related dementias.

This two-stage process is central to our award decisions and is designed to ensure both scientific rigor and fairness to all submitted applications.

#### **vii. Appeals of Scientific Peer Review**

To maintain a fair and rigorous review system, the Alzheimer's Association has established a process for appeal of funding decisions. 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. Disparities in peer reviewers' enthusiasm for a proposal and the scores they assign are nearly always considered part of the normal variation in human judgment. The reality is that the Alzheimer's Association research grants program is extremely competitive and is limited by availability of funds. In recent grant cycles, 15 to 21 percent of proposals have been awarded grants, although about twice that number fall into the "fundable" category based on overall score.

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 to [grantsappeals@alz.org](mailto:grantsappeals@alz.org). Appeals must be submitted by July 24, 2009, 5:00pm EST to be considered. Notification of action on the appeal will be made via email usually within 30 days of the appeal deadline.

#### **viii. Animal and Human Subject Assurances**

Animal welfare and human subject certifications 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 the fact that IRB/IACUC approval at many institutions can take more than 90 days.** The Association accepts only certifications that apply specifically to the funded project. An award letter will not be issued unless the appropriate certifications are in place within the 90-day window.

#### **ix. Contact Information**

This program announcement is posted on the Web site of the Alzheimer's Association at [www.alz.org/2009grantsprogram](http://www.alz.org/2009grantsprogram). For additional information, contact [grantsapp@alz.org](mailto:grantsapp@alz.org) or call (312) 335-5747 or (312) 335-5889.

## IV. SPECIFIC GRANT COMPETITIONS

### i. New Investigator Research Grant (NIRG)

**Competition objectives:** The competition, formerly known as the Pilot Research Grant Program, has become the New Investigator Research Grant Program. This change is designed to reinforce the historical emphasis of this competition—to fund investigators who are no more than 10 years past their doctoral degree. The purpose of this program is to provide new investigators with funding that will allow them to develop preliminary or pilot data, to test procedures and to develop hypotheses. The intent is to support early-career development that will lay the groundwork for future research grant applications to the National Institutes of Health, National Science Foundation and other funding agencies and groups, including future proposals to the Alzheimer's Association. All applications submitted to the New Investigator Research Grant program must target defined areas of focus for fiscal year 2009 to be considered responsive to the program announcement (see Section II, pages 3–12).

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

**Funding and award period:** The Association anticipates funding 30 awards under this competition. Each total award is limited to \$100,000 (direct and indirect costs) for up to two years. Requests in any given year may not exceed \$60,000 (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:** Eligibility to apply for this grant competition is restricted to investigators who have less than 10 years of research experience after receipt of their terminal degree. The 10-year period applies to the date of submission of the grant application. Adjustments for career interruptions can be made. These would include, but are not limited to, family leave, military service, and major illness or injury. It is the responsibility of the applicant to point out and document such interruptions.

In general, **postdoctoral fellows are not eligible to apply for any Alzheimer's Association grant** except for applications to the NIRG, NIRGD and MNIRGD). Applications will be accepted from postdocs who can provide a letter indicating they will have a full-time faculty position, such as an assistant professorship, by the application deadline. A letter of employment must accompany the LOI, must be printed on the hiring institution's letterhead and must indicate that the position will be activated by the grant award date. If the anticipated position is not activated by the award date for any reason, any offer of funding will be withdrawn.

**Deadlines and award dates:** Letters of intent must be received by **5:00 PM EASTERN STANDARD TIME, December 1, 2008**. 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 8, 2009**. Scientific and technical review will be conducted from February through May 2009. The second-level review by the Medical and Scientific Advisory Council will be conducted during June 2009. Funding will be awarded by July 2009.

***Mechanism of Award, Reporting Requirements and Allowable Costs:*** The mechanism of the award is the individual research grant. The maximum allowable duration is two 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 (\$100,000 for NIRG).**

**Allowable costs under this award:**

- It is required that most of the funds awarded under this program be used for direct research support.

**Other allowable costs include:**

- Purchase and care of laboratory animals
- Small pieces of laboratory equipment and laboratory supplies
- Computer software if used strictly for data collection
- Salary for the principal investigator, scientific (including postdoctoral fellows) and technical staff (including laboratory technicians and modest secretarial support)
- Support for travel to scientific and professional meetings not to exceed \$1,000 per year

**Costs not allowed under this award include:**

- Computer hardware or standard software (e.g. Microsoft Office).
- Construction or renovation costs.
- Tuition
- Rent for laboratory/office space

***For more information:*** Contact [grantsapp@alz.org](mailto:grantsapp@alz.org) or call (312) 335-5747.

## ii. Investigator-Initiated Research Grant (IIRG)

**Competition objectives:** The Investigator-Initiated Research Grant (IIRG) forms the backbone of the Alzheimer's Association grant program. To be considered responsive, the research grant application must address a question or questions relevant to the 2009 areas of focus (see Section II, pages 3-12) or a compelling issue in Alzheimer research pertinent to the applicant's special interest or expertise.

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 55 awards under the IIRG program. Each total award is limited to \$240,000 (direct and indirect costs) for up to three years. Requests in any given year may not exceed \$100,000 (direct and indirect). 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 are encouraged to apply. **IIRG 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, 2008**. 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 8, 2009.** Scientific and technical review will be conducted from February through May 2009.

The second-level review by the Medical and Scientific Advisory Council will be conducted during June 2009. Funding will be awarded by July 2009.

**Mechanism of award and reporting requirements:** The mechanism of award is the individual research grant. The maximum duration of award is three years. Annual progress and financial reports are required. Continuation of the grant over the awarded duration is contingent upon the timely submission of interim 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 prior to the disbursement of funds. **Your budget must not exceed the maximum amount of the award (\$240,000 for IIRG).**

### **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 software if used strictly for data collection
- Salary for the principal investigator, scientific (including post-doctoral fellows) and technical staff (including laboratory technicians and administrative support related directly to the funded project)
- Travel to scientific and professional meetings, not to exceed \$1,000 per year

**Costs not allowed under this award include:**

- Tuition
- Computer hardware or standard software (e.g., Microsoft Office) for investigators
- Rent for laboratory/office space
- Construction or renovation costs

**For more information:** Contact [grantsapp@alz.org](mailto:grantsapp@alz.org) or call (312) 335-5747.

### **iii. The Senator Mark Hatfield Award for Clinical Research in Alzheimer's Disease**

**Competition objectives:** When Senator Mark Hatfield announced his retirement from the United States Senate in 1996, the Alzheimer's Association established the Hatfield Award for Clinical Research to honor his long commitment to Alzheimer's disease research, especially clinical investigations. In 1996 and 1997, the Association selected a recipient of the Hatfield Award from among those investigators who had submitted an application in response to another Association program announcement. In 1998, it was decided to announce the program and seek applications specifically for the Hatfield Award. To be considered responsive to the program announcement, the research grant application must focus on a clinical question or questions in interventions for Alzheimer's disease.

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:** We anticipate funding one award under this program. The total award is limited to \$225,000 (direct and indirect costs) for up to three years. Requests in any given year may not exceed \$112,500 (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:** The Hatfield Award is aimed at those investigators whose goal is to establish research careers focused on clinical issues in Alzheimer's disease.

**Deadlines and award dates:** **Letters of intent must be received by 5:00 PM EASTERN STANDARD TIME, December 1, 2008.** 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 8, 2009.** Scientific and technical review will be conducted from February through May 2009.

The second-level review by the Medical and Scientific Advisory Council will be conducted during June 2009. Funding will be awarded by July 2009.

**Mechanism of award, reporting requirements and allowable costs:** The mechanism of award is the individual research grant. The maximum duration of the award 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 progress 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 prior to the disbursement of funds. **Your budget must not exceed the maximum amount of the award (\$225,000 for Hatfield).**

**Allowable costs under this award:**

- It is required that most of the funds awarded under this program be used for direct research support.

**Other allowable costs include:**

- Purchase and care of laboratory animals
- Small pieces of laboratory equipment and laboratory supplies
- computer software if used strictly for data collection
- Salary for the principal investigator, scientific (including postdoctoral fellows) and technical staff (including laboratory technicians and modest secretarial support)
- Support for travel to scientific and professional meetings, not to exceed \$1,000 per year

**Costs not allowed under this award include:**

- Computer hardware or standard software (e.g. Microsoft Office)
- Construction or renovation costs
- Rent for laboratory/office space
- Tuition

***For more information:*** Contact [grantsapp@alz.org](mailto:grantsapp@alz.org) or call (312) 335-5747.

#### iv. The Zenith Fellows Award Program

**Competition objectives:** The Zenith Fellows award was initiated in 1991 to provide a vehicle for research support for donors with a substantial personal commitment to the advancement of Alzheimer's disease research. The awards are made possible by the generosity of a group of individuals and organizations (Zenith Fellows) that have each committed \$1 million to the Alzheimer's Association for support of the program.

The objective of the 2009 Zenith Fellows Awards competition is to provide major support for investigators who have:

- 1) contributed significantly to the field of Alzheimer's disease research or
- 2) made significant contributions to other areas of science and are now beginning to focus more directly on problems related to Alzheimer's disease and
- 3) are likely to make substantial contributions in the future.

The proposed research must be "on the cutting edge" of basic science or biomedical research and thus may not conform to current conventional scientific wisdom or may challenge the prevailing orthodoxy. The proposed research should address fundamental problems related to early detection, etiology, pathogenesis, treatment, and prevention of Alzheimer's disease.

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:** We anticipate funding five awards under this competition. Each award is limited to \$450,000 (direct and indirect costs) for three years. Requests in any given year may not exceed \$250,000 (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:** Only established independent investigators are eligible as evidenced by:

- 1) academic appointment;
- 2) major, peer-reviewed, external multi-year grant support on which the applicant is the principal investigator (PI);
- 3) independent laboratory operation;
- 4) quality and independence of publication record.

Only applicants who have already contributed significantly to the field of Alzheimer's disease research or have the clear likelihood of making significant contributions will be seriously considered. **Previous recipients of Zenith Awards, Medical and Scientific Advisory Council members and members of the National Board of the Alzheimer's Association are ineligible to apply.**

**Deadlines and award dates:** Letters of intent must be received by **5:00 PM EASTERN STANDARD TIME, December 1, 2008**. Letters of intent will not be accepted after the receipt date. No exceptions will be made.

**Applications must be received by 5:00 PM EASTERN STANDARD TIME, January 8, 2009.** Scientific and technical review will be conducted from February through May 2009. The second-level review by the Medical and Scientific Advisory Council will be conducted in June 2009. Funding will be awarded by July 2009.

***Mechanism of award, reporting requirements and allowable costs:*** The mechanism of award is the regular research grant. The maximum duration of award is three years—there is no program for competing continuation applications (3-year) funding as was the case in the early years of the Zenith program. Annual progress and financial reports are required. Continuation of the grant over the awarded duration is contingent upon receipt of scientific progress and financial status 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 prior to the disbursement of funds. **Your budget must not exceed the maximum amount of the award (\$450,000 for Zenith).**

**Allowable costs under this award:**

- It is required that most of the funds awarded under this program be used for direct research support.

**Other allowable costs include:**

- Purchase and care of laboratory animals
- Small pieces of laboratory equipment and laboratory supplies
- Computer software if used strictly for data collection
- Salary for the principal investigator, scientific (including postdoctoral fellows) and technical staff (including laboratory technicians and modest secretarial support)
- Support for travel to scientific and professional meetings, not to exceed \$1,000 per year

**Costs not allowed under this award include:**

- Computer hardware or standard software (e.g., Microsoft Office)
- Construction or renovation costs
- Tuition
- Rent for laboratory/office space

***For more information:*** Contact [grantsapp@alz.org](mailto:grantsapp@alz.org) or call (312) 335-5747.

## v. Everyday Technologies for Alzheimer Care (ETAC) Grants

Everyday Technologies for Alzheimer Care is a cooperative research funding initiative sponsored by the Alzheimer's Association and Intel Corporation. ETAC seeks proposals on personalized diagnostics, preventive tools and interventions for adults coping with the spectrum of cognitive aging and neurodegenerative disease, particularly Alzheimer's disease. We are interested in new groundbreaking studies on emerging information and communication technologies (ICTs) as well as their clinical and social implications. Strongest consideration will be given to novel innovative ideas rather than more evolutionary incremental research. Originality of the study is more important than extensive evidence for why it is a logical next step in a research program. ETAC is designed to support exploratory multidisciplinary research that would not typically be funded by national health and science granting foundations. Minor iterations in testing plans or populations will not be considered for funding. Collaboration between social science/medical/public health and computer science/engineering researchers is valued. Mobile computing, high bandwidth sensing, robotics, imaging, face recognition, natural language processing, statistical modeling and a host of other technology advances allow unprecedented opportunities to study disease progression and therapeutic strategies in the context of everyday life. ETAC supports research that integrates such emerging technology capabilities with leading directions in behavioral science and biomedical research. *Grants that merely create Internet-based versions of existing services or paper tools will not be considered. Submissions must be original ideas, not continuations of previously funded ETAC projects.* Please see links provided below for examples of studies that have been funded by ETAC.

The following list of research topics is not exhaustive; we invite researcher-initiated proposals in any of these or other topic areas.

1. Behavioral assessment for early detection: What kinds of behavioral data can be captured through everyday devices for the early detection of Alzheimer's? Are there key speech/conversational features that today's or tomorrow's cell phones could help to analyze for early detection? Are there gait and other movement patterns that home camera systems could capture to provide early warnings of potential cognitive conditions? How might different forms of dementia be differentiated by the analysis of such video and audio data? How can data from sensors, imaging and traditional clinical measures be triangulated to enhance assessment?
2. Prevention: How can technologies foster the cognitive resilience and reserve that may protect against dementia? How can innovative systems provide the cognitive, social and physical engagement (throughout the lifespan) that may prevent or delay Alzheimer's disease and related disorders? How can such systems motivate lifestyle changes and help people manage health conditions to limit vulnerability to dementia?
3. Safety monitoring and support for caregivers: How can new technologies augment and improve upon existing safety monitoring systems? What acoustic and visual cues can be relied upon to help identify and triage patients' needs? For example, how can advances in high bandwidth sensing and statistical inferencing help detect and prevent falls?
4. Supporting independent function in daily life: Early-stage products based on wireless sensor networks have been developed to support activities of

daily living—how can additional processing capabilities improve upon these systems? What analytic tools could identify changes in individuals' typical patterns and provide customized assistance?

5. Social support through face or audio recognition: How might speech, face and voice recognition technologies provide diagnosed individuals with real-time, just-in-time feedback, reminders and support for their social interactions? Can these technologies help someone with memory loss to keep track of past conversations, topics and social encounters in a way that does not require great effort or technological expertise? How can mobile technologies (for example, phones, hearing aids, and watches) serve as social assistants?
6. Detecting moments and patterns of lucidity: Given the sometimes weekly, daily or even hourly variability of function of many people with Alzheimer's, how can we identify the optimal times for a patient to conduct complex household tasks like bill paying or self-medication? How can technologies help to find opportune moments for interacting with someone with Alzheimer's?
7. Privacy and security concerns of Alzheimer's families: What privacy and security concerns do families and patients with Alzheimer's have regarding home monitoring? How do these concerns differ according to generational, regional, cultural, gender and other differences? How can technology help people negotiate the sharing of health-related information?

ETAC applicants are strongly encouraged to consider partnerships with chapters of the Alzheimer's Association when it is advantageous to the goals of the project.

#### **Past Awarded ETAC Proposals:**

2008 Awards:

[http://www.alz.org/professionals\\_and\\_researchers\\_2008\\_research\\_grants.asp](http://www.alz.org/professionals_and_researchers_2008_research_grants.asp)

2007 Awards:

[http://www.alz.org/professionals\\_and\\_researchers\\_2007\\_research\\_grants.asp](http://www.alz.org/professionals_and_researchers_2007_research_grants.asp)

2006 Awards:

[http://www.alz.org/professionals\\_and\\_researchers\\_2006\\_research\\_grants.asp](http://www.alz.org/professionals_and_researchers_2006_research_grants.asp)

2005 Awards:

[http://www.alz.org/professionals\\_and\\_researchers\\_2005\\_research\\_grants.asp](http://www.alz.org/professionals_and_researchers_2005_research_grants.asp)

2004 Awards:

[http://www.alz.org/professionals\\_and\\_researchers\\_2004\\_research\\_grants.asp](http://www.alz.org/professionals_and_researchers_2004_research_grants.asp)

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.

#### **Background research from Intel Corporation**

The following paper from Intel Corporation presents preliminary findings of Intel's Proactive Health research. The authors report on identified needs of cognitively impaired individuals and their caregivers that may be addressed through home computing technologies.

##### **Ubiquitous Computing for Cognitive Decline: Findings from Intel's Proactive Health Research**

[http://www.alz.org/national/documents/Intel\\_UbiquitousComputing.pdf](http://www.alz.org/national/documents/Intel_UbiquitousComputing.pdf)

**Funding and award period:** The Association anticipates funding 4 awards under this program. Each total award is limited to \$200,000 (direct and indirect costs) for up to three years. Requests in any given year may not exceed \$90,000 (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 are encouraged to apply. **ETAC applications from post-doctoral candidates will not be accepted.**

**Ineligibility:** The Alzheimer's Association will not accept new research grant applications from currently funded Alzheimer's disease investigators who are delinquent in submitting interim/final scientific or interim/final financial reports on active grants. **This policy will be strictly adhered to with no exceptions.**

**Deadlines and award dates:** Letters of intent (LOIs) must be received by **5:00 PM EASTERN STANDARD TIME, December 1, 2008**. LOIs will not be accepted after this date. No exceptions will be made.

**Applications must be received by 5:00 PM EASTERN STANDARD TIME, January 8, 2009.** Scientific and technical review will be conducted from February through May 2009.

The second-level review by the ETAC Review Board and Medical and Scientific Advisory Council will be conducted during June 2009. Funding will be awarded by July 2009.

**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 prior to the disbursement of funds. **Your budget must not exceed the maximum amount of the award (\$200,000 for ETAC).**

**Allowable costs under this award:**

- It is required that most of the funds awarded under this program be used for direct research support.

**Other allowable costs include:**

- Small pieces of laboratory equipment and laboratory supplies
- Salary for the principal investigator, scientific (including postdoctoral fellows) and technical staff (including laboratory technicians and administrative support related directly to the funded project)
- Purchase and care of laboratory animals
- Purchase of a computer

- Support for travel to scientific and professional meetings, not to exceed \$1,000 per year

**Costs not allowed under this award include:**

- Tuition
- Rent for laboratory/office space
- Construction or renovation costs

**Multiple and Overlapping Submissions:** If separate proposals are submitted to different grant competitions, each proposal submitted must be distinctly different. Only one proposal will be funded if scores for multiple submissions fall within funding range of different grant categories.

Applicants **cannot** submit two proposals in the ETAC grant competition—even if the proposals are distinctly different.

**Active ETAC or Consortium Funding Recipients:** Overlapping funding of more than one Alzheimer's Association grant is not allowed. Investigators who have an active Alzheimer's Association or Intel grant may apply for another award that is clearly new work rather than an extension of their current grant. The new research proposal can be proposed in the last year of their grant if that last year concludes by the time the new funding year begins on July 1.

Current holders of awards for support of research related to the project described in the ETAC LOI (whether these awards arise from federal or private sources, but especially if awards arise from other Alzheimer's Association or Intel program resources) are obliged to provide sufficient detail (e.g., budgetary detail, specific aims) so that it is clear that the LOI represents novel research. An LOI for work that might be viewed as an extension of an existing line of (funded) research should clearly but briefly distinguish goals and progress for the current funding period from goals proposed in the LOI for the next period. The responsibility lies with the applicant to include rationale to dispel any notion of "double dipping" or "re-dipping." As with most grantmaking programs, ETAC recognizes that scientific overlap may occur across funded grants; as is also usually the case, budgetary overlap is not permitted. Coincidentally awarded grants must be negotiated in good faith according to this principle. ETAC program staff are available to assist PIs at the LOI stage to avoid the possibility of administrative disqualification at the full proposal review stage.

**For more information:** Contact [grantsapp@alz.org](mailto:grantsapp@alz.org) or call (312) 335-5747.

## vi. New Investigator Research Grant to Promote Diversity (NIRGD)

**Competition objectives:** The New Investigator Research Grant to Promote Diversity in Alzheimer's research is a two-year award to investigators who are currently underrepresented at academic institutions in Alzheimer's or related dementias research.

The objective of this award is to increase the number of highly trained investigators from diverse backgrounds whose basic, clinical and social/behavioral research interests are grounded in the advanced methods and experimental approaches needed to solve problems related to Alzheimer's and related dementias in general and in health disparities populations. The Alzheimer's Association recognizes the need to increase the number of underrepresented scientists participating in biomedical and behavioral research. The Association anticipates that by providing these research opportunities, the number of underrepresented scientists entering and remaining in biomedical research careers in Alzheimer's disease will increase.

The purpose of this program is to provide underrepresented new investigators with funding that will allow them to develop preliminary or pilot data, to test procedures, and to develop hypotheses. The intent is to support early-career development that will lay the groundwork for future research grant applications to the National Institutes of Health, National Science Foundation and other funding agencies and groups, including future proposals to the Alzheimer's Association. All applications submitted to the New Investigator Research Grant to Promote Diversity program must target defined areas of focus outlined in the 2009 Program Announcement (see pages 3-12).

### **GENERAL REQUIREMENTS FOR NIRGD**

**Funding and award period:** The Association anticipates funding up to five NIRGD/MNIRGD awards total under this competition. Each NIRGD award is limited to \$100,000 (direct and indirect costs) for up to two years. Requests in any given year may not exceed \$60,000 (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:** Eligibility to apply for this grant competition is restricted to investigators who have less than 10 years of research experience after receipt of their terminal degree. **For the purpose of this announcement, eligible applicants are faculty members who have been determined by the grantee institution to be underrepresented on faculty in biomedical and behavioral research on a national or institutional basis, such as individuals from racial and ethnic minority groups and individuals with disabilities. Nationally underrepresented groups in biomedical research careers include but are not limited to African Americans, Hispanic Americans, American Indians/Alaska Natives, Native Hawaiians and Pacific Islanders.**

**Young investigators currently funded through other mentored awards (federal or other) are ineligible to apply for this award.**

The 10-year period applies to the date of submission of the grant application. Adjustments for career interruptions can be made. These would include, but are not limited to, family leave, military service and major illness or injury. It is the responsibility of the applicant to point out and document such interruptions. In general, **postdoctoral fellows are not eligible to apply for an NIRGD grant**. The only exception is the special case in which an applicant can provide a letter indicating they will have a full-time faculty position, such as an assistant professorship, by the application deadline. The letter of employment must be on hiring institution letterhead and must indicate that the position will be activated by the grant award date. If the anticipated position is not activated by the award date for any reason, any offer of funding will be withdrawn.

***Deadlines and award dates:*** Letters of intent must be received by **5:00 PM EASTERN STANDARD TIME, December 1, 2008**. 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 8, 2009**. Scientific and technical review will be conducted from February through May 2009.

The second-level review by the Medical and Scientific Advisory Council will be conducted during June 2009. Funding will be awarded by July 2009.

***Mechanism of award, reporting requirements and allowable costs:*** The mechanism of the award is the individual research grant. The maximum allowable duration is two 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.**

**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 related directly 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

***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 prior to the disbursement of funds. **Your budget must not exceed the maximum amount of the award (\$100,000 for NIRGD).**

***For more information:*** Contact [grantsapp@alz.org](mailto:grantsapp@alz.org) or call (312) 335-5747.

## **vii. Mentored New Investigator Research Grant to Promote Diversity (MNIRGD)**

**Competition objectives:** The Mentored New Investigator Research Grant to Promote Diversity is a three-year award intended to be a research-based and mentoring investment in the process of closing the health disparities gap between diverse and non-diverse investigator populations. The Alzheimer's Association feels strongly that the mentoring and involvement of diverse researchers in independently funded Alzheimer's research is a pressing need. The MNIRGD is intended to enhance the capacity of diverse and non-diverse scientists to conduct basic, clinical and social/behavioral research.

### **The MNIRGD competition has the following general requirements:**

- foster mentoring relationships between experienced researchers and those not previously funded or considered new investigators (under 10 years post degree);
- increase the diversity presence of scientists conducting research on Alzheimer's and related dementias;
- enhance the research skills and scientific visibility of junior faculty from diverse backgrounds;
- support mentoring relationships that will establish enduring research careers of diverse researchers.

The purpose of this competition is to provide underrepresented new investigators with mentored funding that will allow them to develop preliminary or pilot data, to test procedures, and to develop hypotheses. The intent is to support early-career development through mentorship that will lay the groundwork for future research grant applications to the National Institutes of Health, National Science Foundation and other funding agencies and groups, including future proposals to the Alzheimer's Association. All applications submitted to the Mentored New Investigator Research Grant to Promote Diversity program must target defined areas of focus for fiscal year 2009 (see Section II, pages 3-12) to be considered responsive to the program announcement.

### **Mentor's Statement Required for MNIRGD**

The mentor should be experienced in conducting Alzheimer's and related dementia research and in mentoring investigators. The application must include a statement from the selected mentor that includes information on his/her research qualifications and experience as a research supervisor. The application must also include information to describe the mentor's research support relevant to the applicant's research plan and the nature and extent of supervision and training that he/she will provide during the period of the award. The primary mentor must agree to provide annual evaluations of the applicant's progress for the duration of the award, as required for the yearly progress report.

Mentoring relationships may include early-career researchers and/or fostering the recruitment of mid-career scientists into Alzheimer's and related dementia research. The applicant and proposed mentor must specify a mechanism for assuring effective mentoring. The application should contain a plan for and an evaluation strategy of the mentoring process for enhancing diversity in the professional research

workforce. Specific benchmarks are outlined below and considered by the Alzheimer's Association as critical for the development of early-career investigators. A successful mentorship plan should include some of these benchmarks but should not be limited to these alone.

**MENTOR'S STATEMENT WILL BE LIMITED TO ONE PAGE.**

**REQUIRED MNIRGD Benchmarks:**

- Attendance at an Association-sponsored luncheon for mentors and new investigators at the Association's International Conference on Alzheimer's Disease (ICAD)
- Acceptance of an abstract at ICAD
- Mandatory documentation of hours spent on face-to-face mentoring
- Citation of specific exercises of mentorship such as supervision of manuscript writing and submission, grant writing and submission
- Specific instances of the facilitation of networking, introductions to colleagues and/or inclusion in discussions at scientific meetings
- Submission of a proposal to an Alzheimer's Association grant program or submission of a grant proposal to the NIH or NSF
- Submission of an application to the NIA's Summer Institute (*suggested but not required*)

**GENERAL REQUIREMENTS FOR MNIRGD**

**Funding and award period:** The Alzheimer's Association anticipates funding up to five NIRGD/MNIRGD awards total under this competition. Each MNIRGD award is limited to \$170,000. A total of \$150,000 will be awarded for costs related to the proposed research for up to **three** years (direct and indirect costs). Requests in any given year may not exceed \$60,000 (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). The Principal Investigator must commit to a 50 percent effort toward the proposed project over the three-year funding period.

The remaining funds, \$10,000 to the applicant and \$10,000 to the primary mentor, will be awarded upon successful completion of the three-year program. These additional funds are to be applied to sustaining ongoing research in the Alzheimer's field and will be awarded through the applicant's and mentor's institutions. Successful completion of the program includes, but is not limited to, reaching all of demonstrable benchmarks listed above.

**Eligibility:** Eligibility for this grant competition is restricted to investigators who have less than 10 years of research experience after receipt of their terminal degree. **Eligible applicants are faculty members who have been determined by the grantee institution to be underrepresented on faculty in biomedical and behavioral research on a national or institutional basis, such as individuals from racial and ethnic groups and individuals with disabilities. Nationally underrepresented groups in biomedical research careers include but are not limited to African Americans, Hispanic Americans, American Indians/Alaska Natives, Native Hawaiians and Pacific Islanders.**

**Young investigators currently funded through other mentored awards (federal or other) are ineligible to apply for this award.**

The 10-year period applies to the date of submission of the grant application. Adjustments for career interruptions can be made. These would include, but are not limited to, family leave, military service and major illness or injury. It is the responsibility of the applicant to point out and document such interruptions. In general, **postdoctoral fellows are not eligible to apply for an MNIRGD grant.** The only exception is the special case in which an applicant can provide a letter indicating they will have a full-time faculty position, such as an assistant professorship, by the application deadline. The letter of employment must be on hiring institution letterhead and must indicate that the position will be activated by the grant award date. If the anticipated position is not activated by the award date for any reason, any offer of funding will be withdrawn.

***Deadlines and award dates:* Letters of intent must be received by 5:00 PM EASTERN STANDARD TIME, December 1, 2008.** 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 8, 2009.** Scientific and technical review will be conducted from February through May 2009.

The second-level review by the Medical and Scientific Advisory Council will be conducted during June 2009. Funding will be awarded by July 2009.

***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 as well as a mentor's report outlining progress toward meeting MNIRGD benchmarks.**

**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 related directly 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

***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 prior to the disbursement of funds. **Your budget must not exceed the maximum amount of the award (\$150,000 for MNIRGD).**

***For more information:*** Contact [grantsapp@alz.org](mailto:grantsapp@alz.org) or call (312) 335-5747.

## **viii. Molecular Imaging in Alzheimer's Disease Grant**

### **Purpose**

The Alzheimer's Association is launching a new initiative to stimulate further research and development of new approaches to image molecular changes associated with early neurodegenerative processes in living humans, animal models and cells. The Association's Request for Applications (RFAs) is aimed at supporting new high-risk exploratory approaches to stimulate new directions of research in molecular imaging. 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**

Tremendous advances have been made in the field of radiological imaging in patients with Alzheimer's disease. MRI, functional MRI, PET, and SPECT are all showing great promise as diagnostic tools. Nevertheless, the best value for imaging will come from an ability to detect more subtle changes preceding the onset of clinical symptoms.

The best way to detect those at risk for developing AD is to have good imaging or biological markers. Existing markers are not yet fully validated, and some of the markers under investigation are markers of clinical rather than biological phenotype. For example, there is currently no obvious way to measure loss of synapses or dendrites, metabolic changes, alteration in membrane potentials or integrity, protein expression or structural changes at the nanoscale. Finding a way to measure any, or even one, of these parameters represents a huge scientific challenge. The Association's goal for this RFA is to lay some groundwork, stimulate research and promote novel approaches.

### **Potential Themes**

Based on a "think tank" discussion, the Association puts forth several themes that may be particularly worthy of further research. Grant proposals could address, but are not limited to, the following areas of study:

#### **1. Blood-brain barrier (BBB) carriers.**

Currently, one of the major limitations to brain imaging is finding tracer molecules that easily pass the BBB. This is a complex problem because tracer molecules are often conjugated to carrier molecules that bind targets of interest. Conjugates are often poor candidates for brain penetration. There are ways to temporarily open the BBB, such as using focused ultrasound, or osmotic agents, but these methodologies are not perfect.

#### **2. BBB as an early pathogenic mechanism; endothelial integrity, repair, and function.**

Breaches in the BBB can lead to infiltration of immune and other cells and molecules that may trigger inflammatory or adverse reactions in the brain. Measuring BBB integrity is technically challenging, but being able to image when the BBB is not working optimally could yield some useful information. Vascular dementia is well studied and some vascular change occurs in AD, but exactly how the vascular system contributes to AD pathology is not clear. What fraction of endothelial cell repair in brain vessels is carried out by local

cells, for example? And how do different sized blood vessels in the brain correlate with areas that are most pathologically susceptible? There are also varying degrees of inflammation in the brain in people with AD, which may be related to blood vessel pathology and BBB compromise. Amyloid has also been shown to be toxic to endothelial cells, which adds another level of complexity. And it is unclear how endothelial cell function and properties change with age. All these factors may impact blood vessel function. While there are ways to study blood vessels—pulse transit time is used to measure elasticity, for example—the methodologies are relatively unsophisticated. More refined measurement may reveal some relevant relationships.

At a finer scale, transporters in the vessels are key for keeping the brain sated with nutrients, minerals, etc. Are these transporters compromised, and would it be possible to find ways to image transporter function?

### **3. Algorithm for composite analysis of ADNI data.**

The Alzheimer Disease Neuroimaging Initiative (ADNI) is collecting a vast amount of longitudinal data, such as blood and CSF biomarkers, MRI, CSF A $\beta$  and tau, PIB PET, and the data will be open source. However, a composite analysis is needed that takes all the data into account and can come up with sensitive and reliable measures that predict progression to MCI or AD.

### **4. Markers of early diagnosis.**

To find out exactly how the disease begins to manifest, it is imperative to look at the very earliest changes that occur in the brain. One approach would be to look at presymptomatic people with autosomal dominant familial Alzheimer's disease. However, findings from that group may not be relevant to people with sporadic Alzheimer's. An alternative approach would be to look at groups that are at higher risk for developing the disease, such as those with a family history of sporadic AD, cardiovascular disease, ApoE4 genotype, or diabetes. Obtaining longitudinal imaging and biomarker data on those groups prior to the emergence of mild cognitive impairment may help to detect the earliest pathogenic changes. There is a need to push the envelope technologically and use these at-risk groups as a basis for improving current imaging modalities, rather than just repeating other ongoing population studies.

### **5. Agents to measure soluble beta-amyloid (A $\beta$ ) assemblies and other molecules of interest.**

Agents that measure A $\beta$  typically do not detect soluble forms of A $\beta$  or do not distinguish between fibrillar and oligomeric soluble forms of the peptide. Finding a compound that fulfills this requirement is a major challenge because agents that do bind soluble forms are likely to bind insoluble A $\beta$  as well. Since most of the A $\beta$  in the brain resides in the insoluble plaques, it is not clear how soluble and insoluble amyloid can be distinguished. It may be possible to develop compounds with the right affinity and kinetics, or to develop compounds that can serve as a scaffold upon which the signal can be amplified further, much like a pro-drug. The pro-drug approach might also work to image other molecules of interest in AD pathology, such as the beta- and gamma-secretases and kinases that phosphorylate tau.

**6. Non-invasive evaluation of brain membrane potential.**

There are indications that amyloid toxicity may lead to an imbalance in neural network activity and in the flow of ions across the cell membrane. Calcium influx may be particularly toxic to the cell, but technically this may be difficult to measure. Measuring changes in the ratio of intra- and extracellular sodium and potassium may be more tractable. In fact, recent advances in whole body imaging, namely increases in the power of the magnetic field, has allowed these measurements, albeit not at very high resolution. Nevertheless, the technique may reveal patterns of functional neuronal alterations in the AD brain. Other technical hurdles are worth exploring, such as the need for high levels of replacement ions such as rubidium and lithium.

**7. Proteomic, lipidomic, and other metabolomic approaches to broadly profile molecular changes in the brain.**

MR spectroscopy and related approaches could be combined in potentially powerful ways with analyses of postmortem tissues or blood/CSF sampling.

**8. Neural responses to functional challenges.**

There is currently no equivalent to a “stress test” for AD, though there is evidence that people with mild cognitive impairment exhibit differences in fMRI signals during memory tasks. Does the brain respond differently when faced with additional challenges? One possibility is to find ways to objectively measure changes during psychological challenges that might highlight differences between early or presymptomatic patients and controls using conventional and new imaging approaches described above.

**9. Cellular energetics.**

Alzheimer’s disease has been linked to mitochondrial dysfunction and increased oxidative stress in the cells of the brain but it is not clear if changes to the energetics of the cell contribute to the disease. It is also not clear how cellular energetics can be measured. There is a need to find ways of probing cellular metabolism and energetics to explore their relation to disease.

**General considerations**

Any proposal must have a human connection. Proposals that simply study animal models will not be looked on favorably. Any study that uses animal models must clearly and explicitly demonstrate potential methods of translating and relating findings to the human condition. Ultimately, the goal is to translate the research into strategies to block the earliest presymptomatic processes leading to AD.

Because the principle idea is to encourage studies into new technologies and high-risk ventures and translation of this novel technology to human studies, a multidisciplinary 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.

## **GENERAL REQUIREMENTS**

**Funding and award period:** The Association anticipates funding up to 3 Molecular Imaging awards. 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).

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

**Deadlines and award dates:** Letters of intent (LOIs) must be received by **5:00 PM EASTERN STANDARD TIME, December 1, 2008**. LOIs will not be accepted after this date. No exceptions will be made.

Once the LOI is approved by the Alzheimer's Association, **applications must be received by 5:00 PM EASTERN STANDARD TIME, January 8, 2009**. Scientific and technical review will be conducted from February through May 2009.

The second-level review by the Medical and Scientific Advisory Council will be conducted during June 2009. Funding will be awarded by July 2009.

**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.**

### **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 related directly 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

***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 prior to the disbursement of funds. **Your budget must not exceed the maximum amount of the award (\$400,000 for Molecular Imaging).**

***For more information:*** Contact [grantsapp@alz.org](mailto:grantsapp@alz.org) or call (312) 335-5747.

## ix. Conference Grants Program

**Mission and Background:** The Alzheimer's Association has a long history of supporting scientific conferences that advance research on Alzheimer's disease. One of the principal goals of the Association from its inception has been to increase public awareness and to facilitate the exchange of information through the scientific and clinical communities. The support of conferences, workshops and meetings has been a key vehicle in achieving this goal.

The range of acceptable topics is as broad as the entire arena of Alzheimer's disease research and includes, but is not limited to:

- Patient care and outcomes
- Family and social support
- Care settings
- Etiology and pathophysiology
- Risk factors and epidemiology
- Diagnosis
- Management, treatment and clinical trials of new therapies
- Prevention

Population and patient diversity must be key considerations in the development of all conference proposals. Conferences, workshops and meetings that break new scientific ground, bring together investigators around not-yet-explored questions or assemble scientists from disciplines/specialties/perspectives who do not usually interact are of particular funding interest.

**Objectives:** The objectives for conference support are to:

- Facilitate and speed the exchange of information relevant to Alzheimer's disease
- Convene experts to address emerging issues in Alzheimer's disease research
- Offer opportunities for new investigators and graduate students to participate in scientific meetings
- Facilitate the creation of networks among investigators in related areas
- Increase visibility of the research interests and programs of the Alzheimer's Association.

The Alzheimer's Association places a high priority on requests for conference support that (1) provide support for trainees, post-doctoral fellows, junior investigators or scientists, especially those from less developed countries, who could not attend otherwise, (2) provide an opportunity, where possible, for the conference organizer to work through a local chapter of the Alzheimer's Association and (3) address the issues of population and patient diversity in relationship to the other scientific foci of the conference.

Requests for support for other aspects of a conference or other participants will be considered.

***Application Procedures:***

***The Alzheimer's Association will not accept applications from commercial conference entities.***

***Submission dates:*** Requests for conference support may be submitted at any time. It is recommended that requests be submitted at least three months before the conference.

***Budget and allowable costs:*** Awards are based on available funds. At this time, support requests must be limited to no more than \$10,000 per conference. Most awarded conference support requests have been in the range of \$2000 to \$5000.

***Application format:*** The request for conference support is to be submitted in a letter format over the signature of the senior organizer and the relevant business official. The letter is not to exceed four pages and should include:

- Title, location and date of the conference.
- List of the scientific organizers and their affiliations.
- 200-word abstract.
- List of the major participants (who are committed as of the date of submission) and titles of their sessions or presentations.
- Funding requested: total and purpose.
- Benefit: In three to four sentences, clearly state how funding this conference would advance the research mission of the Alzheimer's Association.
- Other sponsors: List other fiscal sponsors (corporate, foundation, government, other voluntary health organizations, academic institutions, private donors, etc.).
- Advertising plans: How is the conference being advertised? What are the target audiences?
- Include brochures, programs, or pamphlets describing the conference.

***Review of conference support request:*** All conference support requests are reviewed and evaluated by the Medical and Scientific Advisory Council (MSAC), either during a regularly scheduled telephone conference call or during a face-to-face meeting. The MSAC will receive all materials on the conference support request before the conference call or meeting during which the review of the request is scheduled.

***Notifications of applicants:*** Applicants will be notified of the acceptance of their request for funding or of the inability to provide support for the meeting. No information will be provided to the applicant regarding the discussions or deliberations of the MSAC on the support request.

***Reporting requirements:*** For funded conference requests, final scientific and fiscal reports are required within 90 days of the completion of the conference. Copies of final brochures, pamphlets, and programs describing the meeting must be submitted, as well as the budget detailing the use of the awarded funds. Final scientific and fiscal reports must be submitted over the signature of the scientific organizer and the relevant business official.

***Acknowledgement of contribution of the Alzheimer's Association:*** All conference materials must acknowledge the support of the Alzheimer's Association.

**Submission procedures:** Conference support requests and final reports of funded projects may be submitted by e-mail to [Rachel.Souris@alz.org](mailto:Rachel.Souris@alz.org) or mailed to:

Rachel Souris  
Alzheimer's Association  
225 North Michigan Avenue, Fl. 1700  
Chicago, Illinois 60601-7633

**For more information:** Contact [Rachel.Souris@alz.org](mailto:Rachel.Souris@alz.org) or call (312) 335-5807.