

2017 Alzheimer's Association Grant Awards and Strategic Research Initiatives

— Portfolio Profile

In aggressive pursuit of its vision of a world without Alzheimer's, the Alzheimer's Association made its largest-ever research investment in 2017 with grants of more than \$28 million to over 129 scientific investigations. As the world's leading nonprofit funder of Alzheimer's research, the Association is accelerating the field toward solutions for the global Alzheimer's crisis.

Investments in 2017 include awards to 112 projects funded through the International Research Grant Program, representing proposals ranked highest by a peer-reviewed process in an extremely competitive field of 486 applications that were submitted from 1,005 letters of intent.

Since 1982, the Alzheimer's Association has invested over \$405 million in more than 2,600 scientific investigations. Currently, the Association is investing over \$110 million in nearly 400 best-of-field active projects in 18 countries.

Research Categories

Molecular Pathogenesis and Physiology of Alzheimer's Disease – 54% of the funded projects are exploring the mechanisms that contribute to disease-related processes including the production of beta-amyloid, the mediators of beta-amyloid's toxicity and its adverse effect on cell-to-cell communication, the abnormal chemical alterations of tau, and the functions of related proteins implicated in Alzheimer's disease pathology. These projects may also examine the cellular properties and functions that normally protect and maintain neurons in the brain.

Diagnosis, Assessment and Disease Monitoring – 15% of the projects are investigating brain imaging, biomarkers, and clinical tools that may result in earlier and more accurate diagnoses, timelier interventions, and effective disease monitoring.

Translational Research and Clinical Interventions – 19% of the projects are exploring novel treatment strategies and non-pharmacological interventions.

Epidemiology – 6% of the projects are examining various factors that may contribute to Alzheimer's and other dementias, including blood vessel damage and genetic risk factors.

Care, Support and Health Economics of Alzheimer's Disease – 5% of the projects are studying ways to improve care for people with dementia through new technologies and exploring the values and beliefs of diverse cultures that

impact the use of health services.

Specific Grants Competitions

(Number of grants per competition are indicated in parentheses)

(39) Alzheimer's Association Research Grants (AARG) to fund investigators who are less than 15 years past their doctoral or medical degree, or investigators that are new to the Alzheimer's and related dementias field of research. The purpose of this program is to provide funding for innovative ideas that will develop preliminary or pilot data, to test procedures and to develop hypotheses.

(10) Alzheimer's Association Research Grants to Promote Diversity (AARG-D) similar to the AARG, with focus on 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.

(31) Alzheimer's Association Research Fellowships (AARF) to support exceptional researchers who are engaged in their post-graduate work (i.e. postdoctoral fellows) and before they have their first independent faculty positions (i.e. Assistant Professor) with the goal of bridging the fellow to faculty positions of researchers.

(6) Alzheimer's Association Research Fellowships to Promote Diversity (AARF-D) similar to the AARF, with focus on increasing support to exceptional researchers who are currently underrepresented at academic institutions in Alzheimer's or related dementias research.

(6) Alzheimer's Association Clinical Fellowships (AACSF) to support research training in Alzheimer's and related dementias for clinical fellows who have completed their residency (MD), postdoctoral fellowship (PhD), or both (MD/PhD). For the purpose of this fellowship, clinical research is defined as patient-oriented research conducted with human subjects, or translational research specifically designed to develop treatments or enhance diagnosis of neurological disease.

(3) Alzheimer's Association Clinical Fellowship to Promote Diversity (AACF-D) similar to the AACF, with focus on increasing support to exceptional clinical fellows who are currently underrepresented at academic institutions in clinical research training in Alzheimer's and related dementias.

2017 Alzheimer's Association Grant Awards and Strategic Research Initiatives

— *Portfolio Profile*

Specific Grant Competitions (cont.)

(4) **Zenith Fellows Awards (ZNTH)** to support senior scientists who have made significant contributions to the field of Alzheimer's and related dementia research, and who continue to pursue promising lines of investigation in disease mechanisms, diagnosis, novel treatments, and quality care.

(9) **Alzheimer's Association Sex and Gender in Alzheimer's (SAGA)** research grant awards are to advance understanding of the disproportionate effect of Alzheimer's disease on women. SAGA grants are investigating how gender- and sex-related biology, genetics and lifestyle contribute to Alzheimer's.

(4) **Part the Cloud Translational Research Funding for Alzheimer's Disease (PTC)** awards in partnership with the Part the Cloud initiative to increase research efforts in Phase I and Phase II clinical trials directed towards Alzheimer's disease and other dementias internationally. These awards have been made possible by funding from Part the Cloud, benefiting the Alzheimer's Association.

Peer-Review Evaluation

The Alzheimer's Association Medical and Scientific Relations Division engages a panel of volunteer scientists to evaluate the merits of each proposal anonymously. More than 750 reviewers from 31 countries provided over 1,400 reviews in 2017. The Association's Medical and Scientific Advisory Council (MSAC) evaluates the fairness of these reviews and makes recommendations on each year's awards so that the overall portfolio covers established research areas and moves the field forward in important new directions. The Association estimates that approximately 31 percent of the proposals received in 2017 deserved funding. Twenty-three (23%) percent of projects were supported with available resources.

Research grants awarded by the Alzheimer's Association International Research Grant Program have indirect costs capped at 10%. The Association strictly enforces that at least 90% of the grant goes directly to funding the research itself.

2017 Alzheimer's Association Grant Awards and Strategic Research Initiatives

— Portfolio Profile

Strategic Research Initiatives

The Alzheimer's Association is able to identify and enable special projects with elevated potential for advancing the field. In 2017 the Association supported **17 new and ongoing strategic research initiatives** to advance emerging issues and facilitate global collaboration.

Advance Care Planning in Patients with AD Dementia is a study to develop a greater understanding of advanced care planning (ACP) as it differs by disease stage and race in individuals with dementia. This will be done in conjunction with Alzheimer's Disease Centers across the country.

Alzheimer's Disease Neuroimaging Initiative (ADNI) is to discover, standardize, and validate biomarkers for AD clinical treatment trials. Support has been provided for **ADNI3**, and the **Hippocampal Sub-Region Standardization** to develop methodologies and standardization protocols to measure changes in the volume of hippocampal sub-regions of the brain.

Alzheimer's Prevention Initiative (API) Generation Study to determine whether therapies targeting amyloid may prevent or delay Alzheimer's symptoms in people who are at high genetic risk for developing the disease because they have two copies of the APOE4 gene.

Autosomal Dominant and Late Onset Alzheimer's Disease (DIAN-ADNI) Comparison Study to characterize similarities and differences in biomarkers, memory changes and disease progression in individuals with genetically-based, younger-onset Alzheimer's disease and individuals with the more common sporadic, late-onset Alzheimer's disease.

Dominantly Inherited Alzheimer's Network Trials Unit (DIAN-TU) to test therapeutics on individuals with genetically-based, younger-onset Alzheimer's disease. **DIAN-TU Tau Imaging (Add-On)** to develop and validate tau PET imaging in DIAN participants and investigate how specific treatments may alter the accumulation of abnormal tau in the brain.

DIAN-TU Next Generation (NexGen) to accelerate the testing of new potential Alzheimer's therapies and novel diagnostic approaches in people with genetically-based, younger-onset Alzheimer's disease using innovative trial design and laying the foundation for the next generation of clinical trials in Alzheimer's disease.

Global Alzheimer's Association Interactive Network (GAAIN)™ is a cloud-based, digital network that provides researchers access to a vast repository of shared Alzheimer's research data and the sophisticated analytical tools and computational power needed to analyze it. Support from the Alzheimer's Association will facilitate data sharing through GAAIN for the **Australian Imaging, Biomarkers & Lifestyle Study of Aging (AIBL)**.

Global Brain Health Initiative (GBHI) and the Alzheimer's Association have partnered to offer a pilot fellowship program for GBHI fellows to advance innovative and unique projects that create social change.

Imaging Dementia - Evidence for Amyloid Scanning (IDEAS) Study to determine the clinical value of using brain amyloid PET imaging in diagnosing and managing treatment of individuals age 65 and older with mild cognitive impairment (MCI) or dementia of uncertain cause. The IDEAS Study is led by the Alzheimer's Association and managed by the American College of Radiology (ACR) and the American College of Radiology Imaging Network (ACRIN). **Alzheimer's Neuroimaging and Genetics Initiative (ANGI)** will collect genetic information from IDEAS participants. **The Brain Health Registry (BHR)** is an online registry and database for recruiting and screening volunteers and for monitoring the progression of brain diseases.

Longitudinal Evaluation of Amyloid Risk and Neurodegeneration (LEARN) is a first-of-its-kind natural history study to determine whether the rate of cognitive decline during the development of Alzheimer's is directly related to biological markers, such as beta-amyloid and tau. LEARN is a companion study to the Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) Study.

Preclinical Alzheimer's Disease (AD) Consortium to support a collaboration among four large research studies to identify and examine biomarker changes in the earliest phases of Alzheimer's, before memory loss occurs, with the goal of informing clinical trial design for early phase treatments of Alzheimer's disease.

Quality Control Program for CSF Biomarkers (QC-CSF) to improve the quality of all aspects of cerebrospinal fluid (CSF) biomarker measurements, enabling values to be harmonized worldwide and helping both clinical trials and standard medical practice. QC-CSF is a key initiative of the Alzheimer's Association's Global Biomarker Standardization Consortium (GBSC).

Study of Knowledge and Reactions to Amyloid Testing (SOKRATES) will investigate how learning amyloid imaging status impacts social relationships, and perceptions of stigma and discrimination for those individuals.

Understanding Vascular Contributions to Cognitive Impairment and Alzheimer's Disease (VCID) to further investigate how accumulation of beta-amyloid in the blood vessels of the brain and cellular stress mechanisms are involved in Alzheimer's and related dementias.

2017 Alzheimer's Association Grant Awards and Strategic Research Initiatives

— Portfolio Profile

Emerging Areas of Research for Fiscal Year 2018

Vascular Contributions To Dementia and Amyloid and Tau Lesions in APOE4 Carriers is a multisite research project led by a team at University of Southern California to assess the vascular changes that presage and likely contribute to the onset and progression of Alzheimer's and other dementias in carriers of apolipoprotein E ϵ 4 gene.

Ante-Amyloid Prevention of Alzheimer's Disease Study (A3) is a prevention trial to treat individuals as young as 55 who are at risk for late-onset Alzheimer's. Individuals with very early amyloid deposition in their brain, but cognitively normal will receive biomarker assessments and an experimental anti-amyloid treatment.

DIAN-TU Dose Escalation Study is part of the DIAN-TU Next Generation prevention trial testing therapies and

diagnostic approaches in people with genetically-based, younger-onset Alzheimer's disease. The Dose Escalation Study is an approach to increase the dose of the experimental treatment to maximize its therapeutic benefit.

Japanese Alzheimer's Disease Neuroimaging Initiative (J-ADNI) is to discover, standardize, and validate biomarkers for AD clinical treatment trials. The goal is to track changes over time in biomarkers in MCI and early AD in the population of Japan.

TriBEKa is a multi-national study to develop comprehensive models of Alzheimer's disease focused on starting in midlife. Three leading European dementia research centers in Barcelona, Edinburgh and Karolinska are collaborating to analyze a large collection of normal and Alzheimer's-related imaging data and biological samples in individuals starting at age 40 to model disease onset and progression, as well as identify modifiable and non-modifiable risk factors for Alzheimer's.