



Alzheimer's Association Leveraging Model & Data Resources to Advance Alzheimer's and Dementia Discovery Program (ALZ Discovery Grant Program)

Background:

In recent decades, research has focused on developing and characterizing genetically engineered rodent models of Early Onset Alzheimer's disease (EOAD). These models have provided key insights into genes implicated in human Alzheimer's and how they lead to some neuropathological abnormalities observed in Alzheimer's disease (AD) with a focus on beta amyloid (A β) and tau. While current models have provided critical information on biological mechanisms underlying A β and tau pathology, a number of confounds impact the translatability for some scientific questions and discovery.

There is a critical need to generate multiple new animal models of Alzheimer's, particularly focused on Late Onset Alzheimer's Disease (LOAD). Therefore, in 2015 the National Institute on Aging (NIA) Alzheimer's Research Summit made a recommendation to develop and characterize novel animal models of Alzheimer's disease that would facilitate the development of novel Alzheimer's therapies, using genetics and systems biology to inform animal model development and subsequent non-clinical drug testing.

To address this need, in 2016, the National Institute of Aging (NIA) established the Model Organism Development and Evaluation for Late-onset Alzheimer's Disease (MODEL-AD) centers to directly address the field's need. MODEL-AD is a collaboration among Indiana University (IU), University of California, Irvine (UCI), The Jackson Laboratory (JAX), University of Pittsburgh (Pitt), and Sage Bionetworks. The main goals of MODEL-AD are to identify novel combinations of genetic variants and develop new models for LOAD, including humanized A β and tau models that recapitulate key hallmarks of the human disease, develop robust preclinical testing pipelines, and identify and test novel therapeutic agents. For more information on MODEL-AD: www.model-ad.org. Similarly, other funding organizations have made investments to develop and make available other model systems for AD and related dementia (ADRD).

As these models are developed and characterized, there is an opportunity to leverage and utilize the resources generated and made available to the scientific community. MODEL-AD aims for open access data and all data are publicly available via the NIA-funded AD Knowledge Portal (<https://adknowledgeportal.synapse.org/>). The [AD Knowledge Portal](#), is an NIH designated, FAIR data repository and knowledgebase hosting and providing access to data from humans, animal models and cell based models, analytical and experimental tools for research on AD, related dementias and brain aging. More information on the AD Knowledge portal and related resources are detailed below (under *ALZ Discovery Program Data Sharing expectations*). In addition, data generated from these models have potential to address questions in a new and important way.

Program Objective:

The Alzheimer's Association has recognized the opportunity to leverage the tremendous resources being developed and advanced throughout the field, including those developed by

MODEL-AD centers. The ALZ Discovery Program will aim to fund projects that leverage and utilize data sets such as those now available through the MODEL-AD AD Knowledge Portal or MODEL-AD and related animal models available through The Jackson Laboratory for new research proposals. Although Alzheimer’s research has significantly advanced in recent years, the field still faces challenges in the ability to translate basic science discoveries into effective treatments and evidence-based clinical practices for dementia care. **Preference will be given to projects that are collaborative and multidisciplinary.**

Animal models: Animal models eligible for consideration in applications for the ALZ Discovery Program are those indicated below, which includes models from MODEL-AD and other funding bodies (with confirmation that these are available). A full list of the MODEL-AD mouse models can be found at <https://www.model-ad.org/resources/>

For animal model studies, applicants must outline the study design and data reporting plans explaining how they are in compliance with the general [ARRIVE guidelines for rigorous animal research](#) and the best practices guidelines for AD preclinical efficacy studies (if applicable).

The Jackson Laboratory will make the following mouse models eligible for this funding program available from live colonies to facilitate projects funded by this RFA. However, if your project would benefit from another model system to answer your scientific question, this can be considered with clear scientific rationale. Please note, the creation of new models is not a fit within this funding program. In addition, there may be additional models newly developed and /or available during the timeline of this funding call. Please re-check the options noted on our website and/or reach out to grantsapp@alz.org to inquire about a potential model not listed that you would like to use and/or leverage for your application. As of October 1, models confirmed to be available to research teams include:

MODEL-AD mouse models relevant to late-onset AD

JAX Stock number	Common Name	Familial(fAD) vs LOAD vs TAU	Transgenic vs knock-in
31050	hAbeta-loxP-KI	LOAD	KI
33013	hAbeta KI	LOAD	KI
27894	APOE4	LOAD	KI
30670	LOAD2 = Abeta/APOE4/Trem2	LOAD	KI
37778	LOAD3 = Abeta/APOE4/MAPT(H1.0)	LOAD	KI
36243	Abca7 ^{A1527G} on LOAD 2	LOAD	KI
34454	Plcg2 ^{M28L} on LOAD 2	LOAD	KI
36242	Mthfr ^{677C>T} on LOAD 2	LOAD	KI
33781	Trem2*R47H ^{HSS}	LOAD	KI
37497	hTREM2*R47H	LOAD	KI
35794	MAPT(H1.0*N279K)-GR	TAU	KI
37420	MAPT(H1.0*P301L)-GR	TAU	KI

35398	MAPT(H1.0)-GR	TAU	KI
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In addition, the following mouse models have recently been developed, or are under development at the Jackson Laboratory, and are expected to be available to researchers by the time of the award notifications.

JAX Stock number	Common Name	Familial(fAD) vs LOAD vs TAU	Transgenic vs knock-in
34711	APP ^{SAA} Swedish/Arctic/Austrian	EOAD	KI
37784	APP ^{SAA} /MAPT ^{N279K} / APOE4	EOAD	KI
37453	APP ^{SDI} Swedish/Dutch/Iowa	EOAD	KI
37454	APP ^{SFL} Swedish/Florida/London	EOAD	KI
36682	APOE3-Christchurch	LOAD	KI
36681	APOE4-Christchurch	LOAD	KI
36679	APOE3-Jacksonville	LOAD	KI
37777	APOE4-->APOE3 inducible	LOAD	KI
37776	APOE3-->APOE4 inducible	LOAD	KI
37779	APOE3-->APOE2 inducible	LOAD	KI
37773	Apoe cre-dependent GFP	Reporter	KI
33731	Spp1-tdT	Reporter	KI
33563	Sall1-GFP	Reporter	KI
33562	Grn-mOrange	Reporter	KI
33732	Ms4A7-tdT	Reporter	KI
37775	Lcn2-tdT	Reporter	KI

We encourage investigators to explore the data of these models that are available through the AD Knowledge Portal and Agora and explore the data resources available in the MODEL-AD Explorer.

- The [AD Knowledge Portal](#), is an NIA-supported FAIR data repository and knowledgebase hosting and providing access to data from humans, animal models and cell based models, analytical and experimental tools for research on AD, related dementias and brain aging.
- The portal-linked open source platform [Agora](#) features over 600 candidate targets for AD along with the supporting evidence and druggability information, and allows researchers to explore whether their gene(s) of interest is associated with AD based on various, curated, systems biology meta-analyses.
- The [Model AD Explorer](#) open source platform is also linked to the AD Knowledge Portal

and provides summaries of phenotypic data for available mouse models including the LOAD mouse models developed by the MODEL-AD consortium. The platform allows researchers to explore the molecular homology between individual mouse models and the human disease.

Funding and award period:

The maximum grant amount is \$250,000, with anticipated funding ranges to be \$100,000 to \$250,000 depending on the project scope and resources utilized (experimental or experimental/computational projects). Projects using entirely public downloadable data from AD Knowledge Portal (computational projects) and no other resources (for example: animals, brain tissue, organs) are limited to \$100,000. Budget spending should be appropriately aligned to the specific aims and proposed milestones of the project. The maximum project duration is 3 years for projects utilizing live animals and up to 2 years for projects not using live animals. There is no minimum timeframe. Indirect costs are restricted to no more than 10% of the total budget and are inclusive of the maximum grant amount noted.

Eligibility:

- In general, public, private, domestic and foreign research laboratories, medical centers, hospitals and universities, for-profit organizations are eligible to apply. State and federal government-appropriated laboratories in the U.S. and abroad and are not eligible to serve as the primary applicant institution. However, state and federal government scientists can participate as collaborating scientists with research teams from other eligible applicant institutions.
- For the Letter of Intent (LOI), you will be required to upload proof of your organization's not-for-profit status. *An IRS Letter of Determination is not accepted* and you **must** submit either of the following:
 - W-9 that is signed and dated by the signing official for US entities
 - W-8 or W-8-BEN that is signed and dated by the signing official for international entities.
 - Each must include the EIN, TIN or VAT number.
- Small for-profit agencies must submit documentation of net assets and annual earnings for consideration during the letter of intent process, in addition to a W9 or W8
- For non-profit organizations (non-academic), additional documentation may be required to confirm your organization has segregation of duties between transaction execution and transaction recording.
- **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.**
- Full time postdoctoral fellows THAT ARE ABLE TO SERVE AS PI ON FUNDING APPLICATIONS AND/OR THOSE WITH AN ADMINISTRATIVE PI, Assistant and Associate Professors are eligible to apply.

Ineligibility

- **Overlapping funding** of more than one Alzheimer's Association grant **is not allowed**. Investigators who currently have an active Association grant may apply for another award in the last year of their grant if that last year concludes by June 30th before the start of the new funding year on July 1.
 - There are some exceptions so please contact grantsapp@alz.org if you have questions regarding your eligibility.
- Investigators that have received Alzheimer's Association funding and are currently

delinquent in submitting required reports or have awards closed as “Incomplete” are not eligible to apply. For questions about eligibility, please contact the Alzheimer’s Association at grantsapp@alz.org.

- **Current members of the Association's Medical and Scientific Advisory Group (MSAG) and the International Research Grant Program (IRGP) Council** are ineligible to:
 - Compete as a primary applicant or co-investigator for any research grant
 - To receive any financial benefit from an application. These individuals may be listed as key personnel/collaborators to an application and will be recused from participating in their peer-review.

Submitting a Letter of Intent:

The Letter of Intent (LOI) is a required step in the application process. LOIs must be completed online at <https://proposalcentral.com>. First-time users must register and complete a Professional Profile to begin the LOI process. No hard copies will be accepted. The LOI is completed through the online interactive system; you will need to complete the required sections and upload all required documents. The main section will have a limit of 5,000 characters (approximately 1-to 1.5 pages), and should include the information below (no figures/graphics or images are allowed):

- Specific aims of the project
- Data set and/ or Models to be used
- Timeline

For U.S. entities, the LOI materials will include a W9 signed and dated by the signing official. Non-US entities must provide a W8-BEN-E signed and dated by the signing official. In addition, small for-profits must include documentation of net assets and annual earnings for consideration.

Your LOI will not be accepted without these documents.

Evaluation of LOIs:

All LOIs will be evaluated prior to invitation for a full proposal. Only LOIs that meet program specific guidelines and review criteria will be invited to submit full applications. LOIs will be reviewed by a panel of experts with special attention to:

1. Demonstrable innovation/novelty of the proposed project (especially in the context of the PI/PIs and team recent work)
2. Alignment with the research priorities of the RFA
3. Utilization of available MODEL-AD resources
4. Impact of project on AD and ADRD research

Feedback is not provided at the LOI stage.

Submitting a Full Application:

For those invited to submit a full application, additional materials will be required. Templates and instructions will be provided after LOI approval.

Full applications will include:

- Background/ Rationale (1 page): should include background and clearly defined hypothesis and/or rationale addressing why strategy is expected to be fruitful. This should also note the specific aims.
- Work Plan (up to 5 pages): should include goals/specific aims, methods and project plan

- and should be organized in alignment with the milestones as outlined in the application.
- Principal Investigator(s) and Key Personnel Curriculum Vitae or Biosketch (no more than 5 pages per person); there is no limit on the number of CVs to be included
 - Available Resources and Budget Justification (2 pages):
 - Expenses that will not be allowed under this award include: Computer hardware or standard software (e.g. Microsoft Office, mouse monitor, computer parts), laboratory equipment such as freezers, ultracentrifuges, RT-PCR, microscopy/imaging equipment, service contract fees of equipment, construction or renovation costs, tuition, rent for laboratory/office space, expenses such as Data Network Recharges and Computing and communication device support services, general liability insurances, such as GAEL, wire and currency exchange fees. If awarded, a full budget of planned expenses will be required.
 - A list of tools/models available (if appropriate, list critical tools and models to be used or needed in the course of the research); budget should be broken down in 1 year increments and align with project milestones.
 - **Data sharing plan (1 page):** it is expected that data generated through this funding mechanism will include a robust plan for data sharing as well as appropriate included budget to accommodate this plan. Data sharing is a key component of the application and will be considered during review and evaluation. Information on timelines, feasibility, and the platform(s) and/or mechanisms of sharing should be included. Failure to share data appropriately may prevent investigators from being eligible for future funding. Data should be shared through AD Knowledge Portal and/or Agora and/or AlzPED (as applicable, for details see section *Data Sharing Expectations for ALZ Discovery Program*).
 - Citations/References (1 page): Use the reference style that is most common in the major journal(s)
 - W9/W8 Documentation

Deadlines and Award Timeline:

Key Dates for this program include:

- Letter of Intent Launch.....October 18, 2022 on proposalcentral.com
- Letter of Intent Deadline.....November 18, 2022 at 5:00 pm Eastern Time (No Exceptions)
- Letter of Intent Notifications.....Week of December 19, 2022
- Application Deadline.....January 30, 2023 at 5:00 pm Eastern Time (No Exceptions)
- Application Review.....Throughout January to June 2023
- Award Notifications.....By June 30, 2023

Letters of intent will be accepted through 5:00 PM EST November 18, 2022. Letters of Intent will not be accepted after this date. **No exceptions will be made.**

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

For those invited to submit a full application, the full application must be received by 5:00 PM EST, January 30, 2023. Applications will not be accepted after this date. **No exceptions will be made.** No hard copies or emails will be accepted.

Award announcements will be made by June 30, 2023. For more information: Contact grantsapp@alz.org

Review Process Overview

All proposals are subject to a multi-stage peer-review process carried out through an online system. In the first stage, applications are reviewed and rated by a minimum of three peer scientists with expertise in the proposed area of research. Applicants may include recommended reviewers and also have the option to exclude specific reviewers from evaluating their application if a conflict of interest exists. Conflicts of interest include (but are not limited to):

1. The Applicant trained with/or by the reviewer.
2. The Reviewer published with the Applicant in the last four (4) years.
3. The Reviewer has been a co-investigator on a grant application or award with the Applicant in the last four (4) years.
4. Reviewer has a conceptual difference of opinion with the Applicant that will prevent a fair review.
5. Reviewer will receive financial benefit from the Applicant receiving an award.

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 International Research Grant Program (IRGP) Council and invited review committee members, Research Steering Committee, to ensure fairness and equity in the initial review procedures and to make funding recommendations to the Association. Final recommendations from the IRGP Council are shared with the Medical and Scientific Advisory Group (MSAG) and with the Alzheimer's Association for final approval. This multi-stage process is central to our award decisions and is designed to ensure both scientific rigor and fairness in the review of all submitted applications.

Additional Details

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

The application is submitted by the receipt date/time deadline. Once submitted, you will receive a confirmation email from proposalcentral.com that your application was successfully submitted. If you do not receive a confirmation, click the Proposals tab and under the "Status" column, make sure it says Submitted and not In Progress, which indicates you have not yet submitted your application.

The application is complete and accurate before submission. Only a single copy of an application will be accepted. We do not require signatures at the time of submission. The signature page provided is for use should your institution/organization require signatures; we do not override any institutional policies and/or procedures. Please do not submit the signature page with your application.

Revisions, additional materials, and/or reference, manuscripts, appendices, etc., are not allowed and, if attached, will be removed from your application. Letters of support are also not allowed with this program and will be removed prior to review.

Multiple and Overlapping Submissions:

Multiple submissions from one applicant is not permitted. This includes multiple submissions from the same group and/or collaborators.

Allowable costs under this award include:

- It is required that most of the funds awarded under this program be used for direct research support. No more than 10% of the total direct costs may be included as indirect

costs; this is inclusive of indirect costs for the implementing institution as well as to any subcontracts.

- Costs of animals and related animal housing costs.
- Small pieces of laboratory equipment and laboratory supplies (**purchases over \$10,000 require prior approval, even if included in the project proposal budget**).
- Computer software if used strictly for data collection and/or analysis.
- Salary for the principal investigator, scientific (including postdoctoral fellows) and technical staff (including modest administrative support).
- Research supplies needed for the proposed studies.
- Support for travel to scientific and professional meetings not to exceed \$4,000 in any given year; additional support for travel expenses necessary to carry out research planned not to exceed \$2,000 in any given year. Total travel cost should not exceed \$6,000 for the duration of the award.
- Travel must include attendance, at least once, to the annual “Principle and Techniques for Improving Preclinical Translation in Alzheimer’s disease Workshop” and, at least, once to the Alzheimer’s Association International Conference (AAIC).
- Open access publications fees are appropriate and reasonable for the project budget.
- Costs related to sharing data and any outputs from the funded study

Not allowable as direct costs under this award include:

- Computer hardware or standard software (e.g., Microsoft Office, mouse monitor, computer parts)
- Construction or renovation costs.
- Laboratory equipment such as freezers, ultracentrifuges, RT-PCR, Microscopy/imaging equipment
- Service contract fees of equipment
- Tuition.
- GAEL insurance
- Rent for laboratory/office space.
- Expenses such as Data Network Recharges and Computing and communication device support services
- Wire and currency exchange fees
- Salary and/or compensation for Alzheimer’s Association staff or for current members of the Alzheimer’s Association Medical and Scientific Advisory Group (MSAG), International Research Grant Program (IRGP) Council.

Additional Information:

Ethical/regulatory approvals and reporting requirements

If awarded for funding, the Alzheimer’s Association require that any necessary ethical and/or regulatory approvals are kept current, and may require specific reporting throughout the lifetime of the award. Ethical assurances are not required at the time of application. Investigators have up to 90 days after receipt of their award notification to submit these documents. The Alzheimer’s Association encourages investigators to initiate their certification applications on a schedule that recognizes that rDNA certification, IRB/IACUC approval at many institutions can take more than 90 days. The Association accepts only certifications that apply specifically to the funded project and must include the name of the awardee.

NOTE: AN AWARD LETTER WILL NOT BE ISSUED UNLESS THE APPROPRIATE CERTIFICATIONS ARE IN PLACE AND INCLUDE THE NAME OF THE AWARDEE WITHIN 90 DAYS FROM AWARD NOTIFICATION.

Annual Scientific and Financial Reports

Interim Scientific and Financial Reports must be submitted at the end of each reporting period as long as the grant remains active. Final Scientific and Financial Reports must be filed within 90 days of the grant's end date. All reports must be submitted electronically via proposalcentral.com. The Financial Report must be approved and signed by someone with financial authority in the Office of Research and Sponsored Programs at the recipient's institution. In addition, awardees will be required to document the specific models, datasets used and how the data is shared back with the scientific community. Timely sharing is expected of awardees.

Data Sharing Expectations for ALZ Discovery Program

The ALZ Discovery Grant Program expects and requires timely sharing, based on the following principles:

- In keeping with with Alzheimer's Association and NIA/NIH goal to enable and promote open science practices and FAIR ([Findable, Accessible, Interoperable, and Reusable](#)) data practices, and the goal to enhance transparent reporting and increase research rigor and reproducibility, awardees must make all data, analytical methods, network models, and research tools available to the broad scientific community via the NIA-supported AD Knowledge Portal, or through other designated data repositories, and/or open-source/open-access platforms such as AlzPED.
- All findings, including both negative and positive findings, are expected to be incorporated in NIA funded public data base [AlzPED Portal](#) no later than 12 months after funding completion or at the time of first manuscript publication, whichever comes first. Published studies will be incorporated in AlzPED as a curated record; unpublished studies will be incorporated in AlzPED as a citable pre-print.
- All the data generated from the RFA should be available to the broader research community no later than 12 months after the completion of the funding of the project, through the AD Knowledge Portal and/or Agora and/or AlzPED (as applicable). Exceptions may be made on a case-by-case basis if the Alzheimer's Association agrees that the data are not yet ready to be shared.
 - The [AD Knowledge Portal](#), is an NIA-supported FAIR data repository and knowledgebase hosting and providing access to data from humans, animal models and cell based models, analytical and experimental tools for research on AD, related dementias and brain aging.
 - The portal-linked open source platform [Agora](#) features over 600 candidate targets for AD along with the supporting evidence and druggability information, and allows researchers to explore whether their gene(s) of interest is associated with AD based on various, curated, systems biology meta-analyses.
 - The [Model AD Explorer](#) open source platform is also linked to the AD Knowledge Portal and provides summaries of phenotypic data for available mouse models including the LOAD mouse models developed by the MODEL-AD consortium. The platform allows researchers to explore the molecular homology between individual mouse models and the human disease.
 - [AlzPED](#) is an NIA-supported, publicly available, data resource that aims to increase the transparency, reproducibility and translatability of preclinical efficacy studies of candidate therapeutics for Alzheimer's disease
- Whenever possible, avoid use of reagents, tools, samples, or data that cannot be easily shared;
- Rapidly bring research findings and results to the research community through presentations at meetings and open-access publication (e.g. preprint servers, open

- access journals, or making papers available on the investigator's website).
- The research team's clear commitment to sharing in a timely manner will be part of both application and project evaluation throughout the project duration.

Financial Responsibility

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

Appeals of Scientific Peer Review

To maintain a fair and rigorous review system, the Alzheimer's Association have a process for appeal of funding decisions. Appeals will not be considered for the letter of intent stage.

Regarding applications, an appeal is intended to address extraordinary circumstances. Appropriate reasons for initiating an appeal might include:

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

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

If an applicant believes an extraordinary circumstance has contributed to failure to receive funding, the principal investigator may send a two-page, double-spaced formal letter of appeal (Word document) to grantsappeals@alz.org. Any supporting documents included must be submitted as a PDF. **Appeals must be submitted within 2 weeks from the date your application outcome notification is sent.** Notification of action on the appeal will be made via email, usually within 90 days of the appeal deadline.

Nondiscrimination and Harassment Statement

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

This program announcement is posted on the website of the Alzheimer's Association at alz.org/grants. For additional information, please send all inquiries to grantsapp@alz.org