BrightFocus® Foundation | Alzheimer's Disease Research



Powering Progress
Through Bold Science

2026 Alzheimer's Disease Research Projects

Alzheimer's Disease Research

Where Bold Ideas Become Breakthroughs

Alzheimer's Disease Research is currently investing



$33 million in **108** research projects across **14** countries.

Alzheimer's Disease Research, a BrightFocus Foundation program, invests in groundbreaking research and shares vital information about this devastating disease impacting more than 7 million Americans.

We believe that by providing initial funding for highly innovative research and creative ideas, we can spark revolutionary approaches and life-saving breakthroughs for this disease, the seventh-leading cause of death in the United States.

Explore our grants & Alzheimer's resources:

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Your Support Fuels Tomorrow's Life-Changing Discoveries

Alzheimer's disease remains one of the most complex challenges in medicine, with researchers continuing to uncover how age-related changes in the brain along with genetics, health, and lifestyle factors interact over time.

Thanks to your generosity, Alzheimer's Disease Research is advancing bold science that explores these connections from new angles and opens promising paths toward earlier detection, better treatments, risk reduction strategies, and ultimately, a cure.

Each funded project is selected through a rigorous review process conducted by leading experts in the field who serve on our Scientific Review Committee, ensuring support for the most promising science. Together, we are accelerating discovery and moving closer to a future without Alzheimer's disease.
Thank you.

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This portfolio reflects awarded grants as of July 20, 2026. All grants will be awarded pending conclusion of contract negotiations.

Amyloid-Beta

In Alzheimer's disease, amyloid-beta (Aβ) accumulates in the brain, forming toxic plaques that contribute to neurodegeneration, often in conjunction with the tau protein. Advances in technology now allow researchers to measure amyloid plaques in the brain and identify affected brain regions. Two anti-amyloid drugs, lecanemab (Leqembi) and donanemab (Kisunla), were shown to reduce amyloid plaques in clinical trials and are approved by the Food and Drug Administration for Alzheimer's disease.



Linking Plaque Shapes to Amyloid Structures in Alzheimer's Disease

Anllely Fernandez, PhD | Indiana University
Mentor: Ruben Vidal, PhD

Alzheimer's disease is marked by abnormal deposits of Aß and tau proteins in the brain. Using cutting-edge cryo-electron microscopy, researchers aim to study the structures of Aß in different plaque types and brain regions. This research focuses on understanding how these structural variations contribute to disease progression, especially in cases linked to genetic risk factors like *APOE4* (ε4). This work could uncover new diagnostic markers and therapeutic targets, advancing efforts to combat Alzheimer's disease and related disorders.



A New Role for Amyloid Precursor Protein as a Mechanical Linker in Neurons

Ben Goult, PhD | University of Liverpool (UK)

Following their discovery that amyloid precursor protein (APP) is connected to the force-generation machinery in neurons, Dr. Goult's team will test the hypothesis that APP is a force-bearing molecule and under tension in neurons. If this is the case, it would transform the field of Alzheimer's disease by demonstrating a novel role for APP and identifying a new cause of the disease. Researchers predict that this study will validate a new therapeutic approach for treating Alzheimer's by targeting neuronal mechanics to slow the spread.

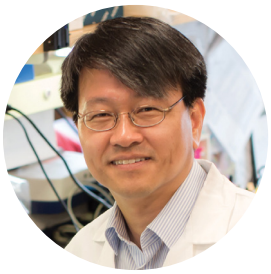
This grant is funded through the Cross Border Grant Program in partnership with Fondation Vaincre Alzheimer.



Exploring the Origin and Composition of a Unique Pathology in Alzheimer's Disease

Cyril Pottier, PhD | Washington University in St. Louis
Co-Principal Investigator: Baayla Boon, MD, PhD, Mayo Clinic Jacksonville

Some people with early-onset Alzheimer's have a rare type of pathology in the brain called "cotton wool plaques" (CWPs), but the cause is still a mystery. This research will explore what makes these plaques unique, what proteins they contain compared to typical Alzheimer's plaques, and whether specific genes are involved. By studying CWPs, the research team hopes to uncover new insights into how Alzheimer's develops and why the disease varies among patients.



Increase of ADAM10 Protein Expression in the Brain as an Alzheimer's Disease Therapeutic

Jaehong Suh, PhD | Massachusetts General Hospital & Harvard Medical School

ADAM10 is an enzyme that prevents the generation of amyloid-beta. Previous studies consistently showed that loss of ADAM10 function increases Alzheimer's risk, suggesting that increasing ADAM10 expression can be a promising therapeutic target. This study will test if brain-selective modulation of ADAM10 expression affects Alzheimer's pathogenesis and will develop an experimental drug that increases ADAM10 expression for Alzheimer's treatment.



Amyloid Precursor Protein (APP) Processing Through a Novel Pathway in Alzheimer's

Justyna Dobrowolska Zakaria, PhD | Northwestern University – Chicago Campus

Although APP, the parent protein of Abeta, was discovered 40 years ago, it wasn't until recently that a new cleavage product of APP was detected in human biofluids, AETA. AETA has been shown to be important in processes that play a role in memory formation, and its levels change in mouse models when prospective Alzheimer's disease (AD) therapies are administered. Researchers will develop a method to measure how quickly AETA is produced and cleared in a healthy older human and then compare this to AETA metabolism in AD.

Biology of Fats & Proteins (*APOE*)

The apolipoprotein E *(APOE)* gene is a risk factor in Alzheimer's disease due to its production of the APOE protein, which metabolizes and transports fats in the body. Scientists are trying to better understand the *APOE4* (ε4) variant, the most prevalent genetic factor associated with late-onset Alzheimer's, whose impact varies by genetic makeup, race, and ethnicity.



The Effects of Peripheral *APOE2* on Alzheimer's Disease Pathology and Pathways

Guojun Bu, PhD | Hong Kong University of Science and Technology (China)

Researchers are working to develop safe and effective therapies to prevent or cure Alzheimer's disease. The *APOE* gene is a strong genetic risk factor, with *APOE2* reducing risk. This project will study the protective effect of *APOE2* using new model systems and advanced technologies to address how *APOE2* in the blood affects brain cognition and Alzheimer's disease pathology. Findings should provide insights on *APOE* targeting for Alzheimer's disease therapy.



Mapping How Cell Compartments Handle Fats in Alzheimer's Disease

Hugo Fernandes, PhD | University of Oxford (UK)
Co-Principal Investigators: Jonathon Nixon-Abell, PhD & Albert Koulman, PhD

Fats (lipids) make up around 60% of the human brain and play an essential role in sustaining brain health. We now know that Alzheimer's disease severely disrupts the cellular pathways responsible for making and organizing these lipids. However, the precise details on how these pathways work, and what goes wrong with them during the disease, are poorly understood. To overcome this knowledge gap, the research team will develop new methods to measure and understand changes in lipids inside brain cell compartments. These findings could result in new therapeutic targets to treat the disease.

Biomarkers

Biomarkers are biological indicators that are detectable through minimally invasive procedures to measure changes associated with Alzheimer's disease. Because Alzheimer's-related brain changes can arise 10-20 years before symptoms appear, researchers are focusing on novel biomarkers that support detection in earlier disease stages. The best hope of stopping Alzheimer's is to identify it as early as possible.



Shining a Light on How Early Tau-Related Brain Changes Affect Memory Loss

Martin J. Dahl, PhD | Max Planck Institute for Human Development (Germany)
Mentor: Ulman Lindenberger, PhD

This project investigates previously understudied brain regions that are the starting point of Alzheimer's-related tau accumulation and how their changes contribute to memory loss. Using innovative brain imaging techniques, blood-based biomarkers, and memory assessments collected over a decade from many participants, this project improves our understanding of the time course of neural changes in later life and their mechanistic role in the earliest stages of Alzheimer's development.



How Biology and Blood Markers Shape Alzheimer's Risk in Diverse Communities

María Carolina Dalmasso, PhD | Studies in Neuroscience and Complex Systems Unit (Argentina)

The goal of this project is to identify shared and population-specific molecular mechanisms in Alzheimer's disease to promote equitable and globally relevant diagnosis. Dr. Dalmasso is studying both shared and population-specific biological markers across diverse and historically underrepresented populations. By integrating genetic, environmental, and blood protein data, the research will support the development of more accurate blood-based diagnostic tools and improve early detection for people worldwide.

This grant is funded through the Cross Border Grant Program in partnership with Alzheimer Forschung Initiative.



Using Protein Signatures to Uncover Alzheimer's Disease Subtypes and Predict Disease Progression

Saima Rathore, PhD | Emory University
Co-Principal Investigators: Nicholas Seyfried, PhD & Allan I. Levey, MD, PhD

Recipient, 2026 Distinguished Investigator Award for Alzheimer's Disease Research

Alzheimer's patients differ greatly in their biology and in how quickly the disease progresses, making treatment and prediction difficult. Dr. Rathore's team has generated large-scale cerebrospinal fluid (CSF) protein data from 1,104 participants and built models that can predict disease onset and progression, showing the power of proteomics to capture this complexity. In this project, they will define CSF-based biological subtypes of Alzheimer's disease and related dementias and test whether blood-based proteins can identify the same subtypes and trajectories, offering a scalable and noninvasive path to diagnosis.



Tracking Early Alzheimer's Disease Over Time Through Spatial Navigation

Vladislava Segen, PhD | German Center for Neurodegenerative Diseases (Germany)
Mentor: Thomas Wolbers, PhD

Alzheimer's disease often damages the brain long before memory problems appear. Current tests and blood markers cannot fully capture these earliest changes. This project uses virtual reality navigation tasks, advanced brain imaging, and spinal fluid tests to study "path integration"—the ability to track one's position while moving—which is disrupted very early in Alzheimer's. By linking these navigation changes to brain and molecular changes, this work aims to develop a sensitive new tool for early detection and monitoring of the disease.



Following the Spread of Iron Through the Brain in Alzheimer's Disease

Louise van der Weerd, PhD | Leiden University Medical Center (the Netherlands)
Co-Principal Investigator: Boyd Kenkhuis, PhD

By tracking iron accumulation across the brain over time, researchers will develop an atlas that visually depicts this process, using brains from hundreds of donors representing different disease stages. Iron accumulation in the brain is a powerful predictor of cognitive decline in Alzheimer's disease, and a pictorial record of the process could form the basis for a standardized staging system for pathological iron accumulation.



Quantifying Cerebrospinal Fluid Flow Dynamics in Alzheimer's Disease Using 4D Flow MRI

Tomas Vikner, PhD | University of Wisconsin-Madison
Mentor: Kevin Johnson, PhD

Alzheimer's disease (AD) is characterized by the accumulation of misfolded proteins in the brain and dysfunctional clearance to cerebrospinal fluid (CSF), suggesting that altered CSF flow dynamics could play a role in the pathophysiology. However, such findings are primarily based on studies in animals. Here, researchers will use a velocity-sensitive brain imaging technique to study CSF flow dynamics in patients with or at risk for AD, aiming to advance our understanding of altered neurofluid dynamics in AD and establish new flow imaging biomarkers of interest in aging and AD.



Clusterin Glycosylation for Early Detection of Alzheimer's Disease

Qi Zhang, PhD | Emory University

Clusterin is recognized as the third major risk factor for Alzheimer's disease, and this research examines how alterations in the sugar structures on the clusterin protein could signal the disease's onset and differ between males and females. By employing cutting-edge mapping techniques, researchers aim to improve early detection and understand the progression of Alzheimer's. Their goal is to spearhead the development of personalized diagnostic tools and treatments that account for individual biological differences.

Cells & Circuits

The human brain has an estimated 100 billion neurons, each with long axons forming connections called synapses with another neuron, creating a circuit for brain signaling. In Alzheimer's disease, neuron death disrupts these circuits, leading to symptoms like memory loss. Scientists are studying the brain's many cells and circuits, looking for ways to preserve neural communications for as long as possible after Alzheimer's disease onset.



Probing the Novel Roles of Neuromodulators in Alzheimer's Disease

Fikri Birey, PhD | Emory University

This project will explore how brain chemicals like serotonin regulate cholesterol balance in nerve cells and how this goes wrong in Alzheimer's disease. Using advanced stem cell models that mimic the human brain, researchers will study how loss of a key Alzheimer's risk gene disrupts this regulation and whether boosting serotonin signaling can restore healthy function. The goal is to uncover new ways to protect brain cells and slow disease progression.



Identifying Brainwide Network Disruptions That Underlie Alzheimer's Disease

Ariel Gilad, PhD | Hebrew University of Jerusalem (Israel)

The main aim of this work is to identify brainwide changes in neural networks that contribute to Alzheimer's disease. Researchers will record brain network activity in mouse models during the completion of cognitive tasks. The team plans to follow these patterns throughout each subject's lifespan to learn how individual traits affect these brain networks in Alzheimer's disease. The work could someday lead to individualized treatments for Alzheimer's disease.



"Cognition in a Dish" to Develop New Alzheimer's Therapies

Matthias Hebisch, PhD | Massachusetts General Hospital & Harvard Medical School
Mentors: Doo Yeon Kim, PhD & Rudolph E. Tanzi, PhD

No current treatment for Alzheimer's disease can stop or reverse the progression of cognitive decline and dementia. Dr. Hebisch's team has built a model of Alzheimer's disease in human brain organoids that shows all classical disease hallmarks, including amyloid plaques, tau tangles, and neuronal death. Now, they will use this model to study the decline of neuronal network coordination as a stand-in for cognition during the progression of Alzheimer's, attempt to block neuronal network degradation by improving cellular energy metabolism, and explore when anti-amyloid therapies might be most beneficial.



Selective Cholinergic Activation Improves Hippocampal Activity

Seonil Kim, PhD | Colorado State University

Changes in brain rhythms (synchronized activity between nerve cells) in the hippocampus have been linked to memory impairments associated with Alzheimer's disease. These alterations in brain rhythms can be detected before people with Alzheimer's disease experience signs of memory loss. For this project, researchers will investigate whether aberrant brain activity and memory loss can be prevented or perhaps reversed in the early stages of Alzheimer's disease.



Targeting Brain Cell Miscommunication to Restore Memory in Alzheimer's Disease

Amira Latif-Hernandez, PhD | Stanford University

The brain's ability to adapt and change, known as synaptic plasticity, requires the expression of specific genes and proteins in different brain cells, neurons, and astrocytes, which is affected in brain disorders like Alzheimer's. To find potential therapeutic strategies to recover synaptic plasticity, enhance cell communication, and improve memory in Alzheimer's, researchers will use advanced techniques in mouse models and lab-grown human cells with Alzheimer's-like pathology. Results will contribute to the development of improved treatments for patients with synaptic plasticity disorders.

Supported by an Innovative Seed Funding Program grant by an anonymous foundation.



Does Alzheimer's Disease Accelerate Brain Aging?

María Llorens-Martín, PhD | Spanish National Research Council (Spain)

The hippocampus, a brain region crucial for learning and memory, generates new neurons throughout life. This process is damaged in Alzheimer's disease, but the cause is unknown. Researchers will use human brains and cutting-edge methodologies to assess the environmental toxicity surrounding new neurons. Study findings will identify novel mechanisms responsible for hippocampal changes in Alzheimer's and generate novel resources for faster, more accurate diagnosis of this condition.



Axons, Synapses, and Myelin: Where Does Alzheimer's Strike First?

Selene Lomoio, PhD | Icahn School of Medicine at Mount Sinai
Co-Principal Investigator: Valentina Fossati, PhD

Alzheimer's disease begins years before symptoms appear, with one of the first signs being a breakdown of the fibers that carry signals between neurons. Researchers still do not know if this damage occurs first in axons, synapses, or myelin, which together control the brain's communication system. To determine this, Dr. Lomoio's team will grow human brain cells in a new platform that recreates how these structures connect and communicate, allowing them to watch early problems as they emerge. By studying genetic variants, they aim to reveal how Alzheimer's disease starts and open paths for prevention and treatment.



Progranulin as a Potential Therapeutic Target for Alzheimer's Disease

Andrew D. Nguyen, PhD | Saint Louis University
Co-Principal Investigator: Susan Farr, PhD

Previous studies suggest that progranulin confers a protective effect on Alzheimer's disease in mouse models and in humans, but several important gaps in knowledge exist. This project aims to determine how progranulin exerts its effects in the central nervous system to enhance memory and to test if pharmacologically increasing progranulin levels can protect against Alzheimer's disease.



Why Alzheimer's Disease Targets Some Cells First: A Clue in the Anterior Hypothalamus

Gowoon Son, PhD | Mayo Clinic Jacksonville
Mentor: Lea Grinberg, MD, PhD

Alzheimer's disease damages some brain cells early while sparing others, but the reasons remain unclear. This project focuses on the hypothalamus, a tiny neuromodulatory subcortical region that regulates sleep, mood, and hormones, functions that are often disrupted in the early stages of Alzheimer's. Using advanced mapping of human brain tissue at the gene expression level, researchers will study how support of human brain cells and the cellular microenvironment shape which neurons survive or degenerate, paving the way for precision treatments that improve daily life beyond memory loss.



Mechanisms of Inhibitory Neuron Vulnerability to Alzheimer's Disease

Emiliano Zamponi, PhD | Columbia University
Mentor: Franck Polleaux, PhD

Inhibitory interneurons, one of the key players in human cognitive processes, are among the first neuronal populations affected by Alzheimer's disease (AD) onset. Dr. Zamponi proposes their elevated energy consumption rates make these interneurons more vulnerable to AD. Using multiple innovative approaches, he will investigate three fundamental aspects underlying inhibitory interneuron vulnerability to AD. He expects to gain new insights into the pathological basis of this devastating neurological condition and contribute to the development of novel therapeutic approaches.

Supported by an Innovative Seed Funding Program grant by an anonymous foundation.

Exposome and Environmental Factors

Genes aren't the only risk factor for Alzheimer's. Research is increasingly pointing to the "exposome," the sum of every environmental exposure a person encounters over a lifetime, from air pollution and neighborhood conditions to diet, stress, and socioeconomic circumstances. Early findings suggest that these factors could be tied to Alzheimer's-related changes in the brain. Because many of these factors are social or environmental rather than genetic, this area of research also highlights why some communities face disproportionate dementia risk and points toward modifiable targets for future prevention efforts.



How Social Conditions and Lifestyle Influence Dementia Biomarkers in Latin America

Claudia Duran-Aniotz, PhD | Adolfo Ibáñez University (Chile)
Co-Principal Investigators: Martin Bruno, PhD; Nilton Custodio, PhD; Agustín Ibáñez, PhD; Hernando Santamaria-Garcia, MD, PhD & Andrea Slachevsky, MD, PhD

Dementia in the Latin American population is strongly shaped by social disparities and lifestyle choices, yet most research comes from other regions, leaving key questions unanswered of their role in dementia biology. This study will use blood dementia biomarkers, a noninvasive tool for detecting brain changes associated with dementia, to investigate how these social and lifestyle factors impact the presentation and characterization of dementia in Latin America. The results will help identify risks we can change and guide fair, culturally relevant strategies for care and prevention.

Genomics: DNA Blueprint for Alzheimer's

Genes carry the instructions that cells use to make proteins, which build and repair tissue. Even slight changes to these instructions can affect the risk of Alzheimer's. While early-onset Alzheimer's is linked to specific gene mutations (10% of cases), the remaining 90% involve genetic risk variants. Researchers are using advanced technologies to study the triggers of Alzheimer's disease, how genes interact with the environment and lifestyle factors to influence risk, and how treatments can be individually tailored.



Visualizing How Alzheimer's Mutations Alter Protein Localization in Human Brain Cells

Shamchal Bakavayev, PhD | National Institute of Neurological Disorders and Stroke

Mentor: Michael Ward, PhD

Alzheimer's disease is caused in part by proteins in the brain moving to the wrong locations due to mutations, which disrupt normal cell function. This project will use a precise genome editing method called prime editing to tag Alzheimer's related proteins and introduce disease-causing mutations in human stem cells. These cells will be differentiated into neuronal and glial cell types, and advanced imaging combined with machine learning algorithms will map where each protein is normally located and how mutations alter their placement, providing a resource to guide future therapies.



PLCG2 Variants and Their Implications in Alzheimer's Disease

Hongjun Fu, PhD | The Ohio State University

PLCG2, an enzyme that is important in cell-to-cell communication, also plays a role in the risk of developing late-onset Alzheimer's disease (AD). The gene that encodes for this enzyme has AD-associated variants—one of which protects against AD, and one of which promotes AD. Researchers aim to identify the role that these two AD-associated PLCG2 variants play in the development and progression of microtubule-associated protein tau aggregates, cell death, and memory loss.



A New Look at Genetics Using Old Data: Alzheimer's Progression

John Hardy, PhD, FRS | University College London (UK)
Co-Principal Investigator: Maryam Shoai, PhD

Most treatments for Alzheimer's disease (AD) are based on research to understand risk factors for developing it. Modification of those factors is then used to see if the speed at which AD progresses can be slowed down. However, there is no evidence that the factors that determine AD risk are the same as those that affect AD progression. To determine what genetic factors are associated with increased disease progression, researchers are "recycling" valuable data from the placebo groups of past clinical trials and bringing together multiple pharmaceutical companies and academic sources.



Determining the Cellular Impacts of ABCA7 Mutations in Alzheimer's Disease

Sarah Heuer, PhD | Brigham and Women's Hospital
Mentor: Tracy Young-Pearse, PhD

Genetics plays a key role in governing Alzheimer's disease risk, with many mutations linked to lipid biology proteins. ABCA7 is a lipid transporter and has several Alzheimer's disease risk mutations, some found exclusively in individuals of African ancestry. However, the effects of these mutations remain unclear due to the historical lack of diverse representation in research studies. Using models of living brain cells derived from humans that harbor these mutations, Dr. Heuer will study how modifying ABCA7 alters proteins, lipids, and cell function, paving the way for inclusive, personalized Alzheimer's disease therapies.



Uncovering How Gene Regulators Protect Neurons Against Alzheimer's

Raffaella Nativio, PhD | Imperial College of Science, Technology, and Medicine (UK)

This study will focus on understanding how epigenetic factors, especially transcriptional repressors, influence gene expression in neurons and contribute to Alzheimer's disease. The research aims to identify how these transcriptional repressors protect neurons from Alzheimer's-related stress, potentially leading to new treatments for enhancing brain resilience against Alzheimer's.



Genetics and Neuroimaging Biomarkers for Neurodegeneration in Latin America

Carolina Ochoa-Rosales, PhD | Adolfo Ibáñez University (Chile)
Co-Principal Investigators: Hieab Adams, PhD & Agustin Ibáñez, PhD

This research seeks to unravel how genetics shapes brain structures and cognition, specifically in the Latin American population. Using novel genetic tools and multiomics approaches, researchers will dive into the biological consequences of the genetic effects and identify unique biomarkers that can guide personalized strategies in Alzheimer's disease and related dementias health care, tailored for Latinos. The outcomes could lead to early detection tools and personalized health interventions to promote better brain health and reduce the risk of neurodegenerative diseases.



Study of a Novel Genetic Risk Factor for Alzheimer's Disease

Giuseppina Tesco, MD, PhD | Tufts University

Dr. Tesco's lab discovered a novel genetic variant associated with late-onset Alzheimer's disease in African American families, called GGA3. Prior research demonstrated that GGA3 plays a critical role in the transport and regulation of BACE1, a key enzyme responsible for amyloid-beta production. The study aims to determine how this genetic variant leads to Alzheimer's. Results may increase understanding of genetic risk factors in the understudied African American population.



Visual System Vulnerability in Dementia: From Detection to Determinants

Keir Yong, PhD | University College London (UK)
Co-Principal Investigators: Andre Altmann, PhD & David M. Cash, PhD

Cortical visual ("brainsight," not eyesight loss) is the earliest sign of dementia for people with posterior cortical atrophy, in whom vulnerability of the brain's visual rather than memory system causes "visual-led Alzheimer's disease." Dr. Yong's team will use a novel brainsight test and brain scans from 35,000 volunteers in a national aging study to improve detection of visual system vulnerability. They will compare genetic risk factors associated with visual system vulnerability and visual-led Alzheimer's disease to determine why Alzheimer's disease may affect people in different ways.



Hidden RNA Alterations by Jumping Genes in Alzheimer's Disease

Yuyun Zhang, PhD | University of California, Los Angeles
Mentor: Xinshu (Grace) Xiao, PhD

This project uncovers a hidden layer of RNA dysregulation driven by transposable elements and links it to genetic risk and pathology in Alzheimer's disease (AD). By integrating large-scale multi-cohort transcriptomics with whole-genome sequencing and AD genome-wide association studies, we introduce teiQTLs as a new class of functional variants linking noncoding genetic risk to RNA processing. This framework opens a new dimension of AD biology and provides a foundation for future biomarker and therapeutic strategies.

Cofunded by Alzheimer's Los Angeles.

Immunity & Inflammation

One theory about Alzheimer's disease is that a breakdown in the brain's immune system plays a role. Microglia, the brain's primary immune cells, normally clear debris and respond to injuries, but in Alzheimer's, they release proinflammatory molecules that worsen the disease. Researchers are investigating the causes of this and how to support cells, including microglia, in fighting Alzheimer's.



Defining Immunometabolic Contributions to Cognitive Impairment in Alzheimer's Disease

Caleb Bailey, PhD | University of Kentucky Research Foundation
Mentor: Linda Van Eldik, PhD

Certain molecules within different brain cells can govern metabolic processes that modulate the progression of Alzheimer's disease and dementia. In this study, Dr. Bailey has identified a molecule, p38MAPK, in a supportive brain cell type, known as astrocytes, that may regulate the neurobiological network involved in cognitive decline in Alzheimer's disease. He will use cutting-edge neuroscience techniques to eliminate production of p38MAPK in such astrocytes to slow disease and dementia progression in a model of Alzheimer's disease.



Understanding Alzheimer's Risk and Immune Health in Heart Disease

Brittany Butts, PhD | Emory University
Co-Principal Investigator: Whitney Wharton, PhD

This study explores how the immune system relates to memory, cognition, and Alzheimer's risk in middle-aged adults with heart conditions. As heart problems surge in the under-65 population, connections to cognitive decline and Alzheimer's remain unclear. Surveys, blood tests, and memory assessments will clarify how factors like high blood pressure affect cognition and Alzheimer's risk. Insights into heart health, immunity, and Alzheimer's can benefit at-risk individuals and shape future treatments.



Targeting the Adaptive Immunity to Prevent Alzheimer's Brain Neurodegeneration

Joshua Emmerson, PhD | Washington University in St. Louis
Mentor: David Holtzman, MD

Neurodegenerative diseases such as Alzheimer's disease involve the buildup of tau proteins and significant brain degeneration. This tau-mediated damage is mainly driven by inflammation in the brain, with recent evidence of infiltrating T-lymphocytes (T-cells) being essential to this process. This project will apply multidisciplinary approaches to determine the candidate signaling pathway(s) responsible for attracting T-cells to the brain in disease and to block T-cell infiltration to prevent subsequent tau-mediated brain degeneration in a genetically modified mouse model.



Understanding the Role of Brain Immune Cells in Protection Against Alzheimer's

Ghazaleh Eskandari-Sedighi, PhD | University of California, Irvine
Mentor: Mathew Blurton-Jones, PhD

Understanding how Alzheimer's disease (AD) develops is challenging due to its complex, multifaceted nature. The heritability of AD is over 60%; so, understanding the disease mechanism can be achieved by exploring these hereditary elements in patients vs. healthy individuals. Some rare hereditary factors can actually be protective against AD. Taking advantage of novel, multi-faceted stem cell models, researchers will study ApoE3 Christchurch as one of these rare, resilient factors, with a specific focus on brain-resident immune cells.



Leveraging How the Brain's Immune Cells Fuel Frontotemporal Dementia

Laura Fumagalli, PhD | Flanders Institute for Biotechnology (Belgium)
Mentor: Renzo Mancuso, PhD

A mutation in the C9orf72 gene is the leading genetic cause of frontotemporal dementia (FTD) and ALS, but its role in brain cell damage remains unclear. The gene is highly active in microglia, the brain's immune cells, which may malfunction due to this mutation. Since unhealthy microglia can worsen brain diseases, researchers will explore how the C9orf72 mutation affects them. Using an innovative model that mimics a brainlike environment, researchers will analyze how the mutation alters microglial activity and function. This research could reveal novel drug targets and diagnostics tools.



Targeting Proinflammatory Molecules Using a Chimeric Receptor to Reduce Inflammation and Tauopathy

Gilbert Gallardo, PhD | Washington University in St. Louis

Brain inflammation has recently been shown to exacerbate Alzheimer's disease pathologies. The research team aims to develop therapeutic strategies that suppress inflammatory molecules regulating brain inflammation, with the goal of combining these strategies with gene therapy that will provide brain specificity and a long-term treatment approach. If successful, this strategy to suppress brain inflammation may have therapeutic value for several neurodegenerative diseases, including Parkinson's and amyotrophic lateral sclerosis (ALS).



Blocking Jumping Genes to Stop Brain Inflammation in Alzheimer's Disease

Joseph Herdy, PhD | Salk Institute for Biological Studies

By generating patient-specific induced neurons (iNs), Dr. Herdy and his team found that there is a small population of inflammatory neurons that could be targeted to treat Alzheimer's disease (AD) instead of using strategies that affect the entire brain. However, how these neurons become inflammatory, and therefore, ways to intervene, are currently unknown. In this project, researchers deeply characterize a promising genetic target driving inflammation and assess if blocking its activity is a candidate for reversing hallmarks of AD.



Understanding the Link Between Alzheimer's Disease Risk Genes and Immune Responses in the Brain

Amanda McQuade, PhD | University of California, San Francisco

Large-scale studies of genetic risk factors for Alzheimer's disease (AD) have revealed that AD-risk genes are highly expressed in immune cells. This suggests that changes in immune function have potential to alter someone's risk of disease onset, representing a novel therapeutic target. To uncover common mechanisms that underlie AD risk, Dr. McQuade will perform a high throughput screen of immune cell function after perturbing AD-risk genes. She will also test the impact of these immune activation states in lab models to determine how blocking or enriching immune activation states alters AD progression.



Cancer-Like Metabolic Changes in Alzheimer's Disease Neurons

Jerome Mertens, PhD | University of California, San Diego

This research focuses on how metabolic changes impact gene expression and protein modifications in Alzheimer's disease (AD). Using neurons from AD patients, researchers identified disruptions in metabolic pathways leading to abnormal gene processing. This study aims to understand how these changes contribute to key AD features, such as tau tangle formation. By understanding upstream metabolic pathways of AD pathology, they aim to identify potential intervention targets to rescue the loss of synaptic function and prevent neuronal cell death.

Supported by an Innovative Seed Funding Program grant by an anonymous foundation.



Exploring Rural Health Disparities in Alzheimer's Disease

Justin Miller, PhD | University of Washington School of Medicine

Emerging evidence shows that older adults living in rural communities are at increased risk for Alzheimer's disease (AD); however, rural communities have been severely underrepresented in AD research, and the contributing factors to these urban-rural disparities are unclear. Dr. Miller's long-term goal is to fully characterize cognitive aging and validate AD-specific biomarkers among rural-dwelling older adults. This project will enrich the biomarker characterization of a rural cohort and facilitate identification of the most viable blood markers for use in rural-dwelling older adults.

Supported by an Innovative Seed Funding Program grant by an anonymous foundation.



Impact of Declined Immunity on Age-Related Inflammation and Dementia

Alon Monsonego, PhD | Ben-Gurion University of the Negev (Israel)
Co-Principal Investigator: Daniel M. Altmann, PhD

In this project, researchers aim to reveal the role of inflammation and blood-brain barrier integrity in Alzheimer's disease pathology. Researchers will carry out a cutting-edge clinical assessment in older adults with and without Alzheimer's using advanced brain imaging, cognitive assessments, and blood-based biomarkers to better understand how inflammation is linked to disease development and progression. The findings could lead to new ways to identify people at risk for Alzheimer's earlier, predict how the disease may progress, and uncover targets for more personalized treatments.



The Role of Immune Cells' Interaction in Alzheimer's Disease Pathology

Emanuela Pasciuto, PhD | Flanders Institute for Biotechnology (Belgium)

Researchers know little about how adaptive immune cells interact with amyloid plaques. MHCII is a microglia-associated Alzheimer's risk gene that mediates interaction with T cells. The relevance of the microglia-T cell interaction in Alzheimer's is unknown. This project will test a T cell-based immunotherapy in Alzheimer's mice lacking MHCII. Study findings will build toward more precise therapies targeting the immune system to protect against the progression of Alzheimer's.



The Astrocyte Cell Surface Proteome in Alzheimer's Disease

Omar Peña-Ramos, PhD | Baylor College of Medicine
Mentor: Hui Zheng, PhD

Cell surface proteins (CSPs) help cells communicate and respond to their environment, making them key drug targets. Researchers performed CSP profiling of mouse astrocytes during amyloid plaque buildup and identified CD44 as a top candidate. They found that when CD44 binds to its ligand OPN, astrocytes trigger lipid accumulation, while mice lacking CD44 show reduced inflammation. By studying CD44 in live mice and cultured astrocytes, the research team aims to uncover its role in Alzheimer's disease and explore its potential as a therapeutic target.



Does Fructose Contribute to Neurodegeneration and Alzheimer's Disease Development?

Justin Perry, PhD | Memorial Sloan Kettering Cancer Center

Fructose may contribute to the onset and progression of Alzheimer's disease (AD), with increased fructose consumption and presence in the brain associated with a higher likelihood of developing AD and worse prognosis, but the how remains unknown. Excitingly, Dr. Perry found that the brain's garbage collector, microglia, consume fructose but at the cost of their garbage collecting duties. His team will explore whether this trade-off is a driver of AD, test whether fructose metabolism is a treatment target, and establish noninvasive imaging of fructose metabolism as a diagnostic and prognostic tool.



Developing a Noninvasive Gene Therapy for Alzheimer's Disease

Dominika Pilat, PhD | Massachusetts General Hospital & Harvard Medical School
Mentors: Ana Griciuc, PhD & Nitin Joshi, PhD

Alzheimer's disease (AD) is the most common neurodegenerative disorder and a leading cause of dementia, yet effective treatments remain unavailable. This project explores a novel strategy targeting CD33, an immune receptor regulating microglial activity. Using a novel humanized CD33 lab model, researchers will deliver siRNA molecules via proprietary nanoparticles designed for microglial uptake and evaluate their CD33 silencing potential. Importantly, they will use an intranasal delivery route to enable direct access of these particles to the brain. This work could advance RNA-based therapies for AD.



Targeting Brain Immune Cells as a Novel Therapeutic in Alzheimer's Disease

Carla Rothlin, PhD | Yale University
Co-Principal Investigator: Sourav Ghosh, PhD

A microglial protein that seems to confer protection against Alzheimer's disease is the focus of this project. Researchers will evaluate each separate function of this protein, AXL, to identify which one is associated with the protective effects. AXL is promising in part because drugs that target it have been being developed for many years, and a natural molecule that activates it has already been identified.



Using Ultrasound to Help the Brain's Defenses in Alzheimer's Disease

Nader Saffari, PhD | University College London (UK)
Co-Principal Investigators: David Attwell, PhD & George Sideris-Lampretsas, PhD

A key factor of Alzheimer's disease is a buildup of a harmful protein, amyloid beta (Aß), in the brain. Current treatments to reduce Aß levels are costly and can cause serious side effects, including brain bleeding. This study explores ultrasound as a safe, noninvasive way to help brain immune cells, called microglia, clear these proteins. Ultrasound activates microglia, restoring their ability to clean the brain, and this promising method could offer a more effective and affordable treatment for Alzheimer's.

Cofunded by Focused Ultrasound Foundation.



Investigating How Immune Cells From the Brain and the Blood Contribute to Alzheimer's Disease

Paula Sanchez-Molina, PhD | University of California, Irvine
Mentor: Mathew Blurton-Jones, PhD

Microglia, the resident immune cells of the brain parenchyma, have been widely associated with Alzheimer's disease. However, the contribution of their peripheral immune cell counterparts to this disease remains underexplored. Increasing evidence of myeloid cell infiltration in the brain of Alzheimer's disease patients compels us to investigate their potential impact on the disease pathogenesis. This project will take advantage of cutting-edge humanized mouse models and spatial technologies to provide important new insights into the role of different human myeloid cell populations in Alzheimer's disease.



Regulation of Microglia Phenotypes in Alzheimer's Disease

Johannes Schlachetzki, MD | University of California, San Diego

Alzheimer's disease is defined by the accumulation of harmful proteins in the brain. Microglia, the immune cells of the brain, play a key role in this process, but the molecular mechanisms that lead to distinct phenotypes are unclear. This study will use advanced techniques to isolate and analyze microglia, revealing how they contribute to the disease and identifying new targets for developing effective treatments.

Supported by an Innovative Seed Funding Program grant by an anonymous foundation.



Monitoring Neural Activity and Neuroinflammation in Alzheimer's Disease

Feng Tian, PhD | Beth Israel Deaconess Medical Center

Neuroinflammation is one key hallmark of Alzheimer's disease (AD) and one of the most attractive directions for novel drug development. However, it is still unclear how neuroinflammation contributes to memory loss and cognitive deficits. Researchers will leverage an advanced brain-machine interface and genetic tools to study the role of neuroinflammation and neural activity changes during AD progression. If successful, this study will offer a strategy to develop disease-modifying treatments for AD by targeting key neuroinflammatory pathways.

This award is made possible by the support of the Luminescence Foundation.



Dysregulated Astrocyte p38, Brain Inflammation & Alzheimer's Pathology

Linda Van Eldik, PhD | University of Kentucky Research Foundation

Astrocytes, the most abundant glial cell type in the brain, become abnormally activated early in Alzheimer's disease (AD) and can lead to detrimental brain inflammation and nerve cell damage. The p38 mitogen-activated protein kinase drives inflammation in microglia, but its role in astrocytes is understudied. This project will use novel mouse models and well-characterized human biospecimens to define the potential linkage between astrocyte p38, neuroinflammation, and AD neuropathologic change, providing new insight into mechanisms by which abnormal astrocyte activation in AD contributes to disease progression.

Supported by an Innovative Seed Funding Program grant by an anonymous foundation.



Understanding the Role of a Suppressed Immune System in Frontotemporal Dementia (FTD)

Rebecca Wallings, DPhil | Indiana University

Dr. Wallings previously published findings that showed that immune cells outside the brain, which carry FTD-associated mutations, have a dampened immune response. A dampened immune response is often associated with immune cell exhaustion (ICE), when immune cells lose the ability to respond to infections and inflammation. Researchers will investigate the downstream effects of ICE on other immune cells and how ICE in the periphery contributes to brain degeneration and inflammation. Findings will inform researchers of the role of immune cell exhaustion in FTD and if this is a potential therapeutic target.



The Role of DYRK1A Kinase in Alzheimer's Disease Microglia Differences

Frances Wiseman, PhD | University College London (UK)
Co-Principal Investigator: Selina Wray, PhD

Down syndrome is a genetic condition caused by an extra copy of chromosome 21 and is associated with an increased risk of developing early-onset dementia caused by Alzheimer's disease. Recent research has demonstrated that the brain's immune response to Alzheimer's disease pathology differs in people with Down syndrome; this may contribute to the development of dementia. Using a new cellular model of Alzheimer's disease, the team will test their hypothesis that the chromosome 21 gene, DYRK1A, may contribute to this process.

Supported by an Innovative Seed Funding Program grant by an anonymous foundation.



Investigating Autoimmune Contributions to Alzheimer's Disease

Jennifer Yokoyama, PhD | University of California, San Francisco
Co-Principal Investigator: Joseph J. Sabatino, MD, PhD

Given that genetic and clinical evidence suggests a link between autoimmune disease and Alzheimer's disease (AD) risk, this study will use advanced sequencing technologies to determine whether people with AD possess self-targeted autoantibodies in their blood or brain that may drive disease. Additionally, researchers will explore whether female sex is associated with an increase of pro-inflammatory proteins or transcripts. This study has the potential to identify a subset of AD patients who possess an immune-mediated form of disease and who may benefit from the development of targeted immunotherapies.

Metabolism & Bioenergetics

The brain consumes 20% of the body's energy and relies on efficient glucose metabolism, which declines with age and in Alzheimer's disease. This metabolic dysregulation impacts brain processing speeds and cognition, and dysfunctional mitochondria (known as the "power plants" of cells) contribute to a neurotoxic environment by releasing reactive oxygen species and other molecules that evoke inflammatory responses in microglia.



Mitochondrial DNA Damage and Microglial Activation in Alzheimer's Disease

Lan Guo, PhD | Wake Forest University School of Medicine

The project aim is to investigate a cause-effect relationship between oxidative damage and subsequent leakage of mitochondrial DNA with the inflammatory microglial response that contributes to Alzheimer's disease pathology. Positive results will reveal a novel mitochondrial pathway of neuroinflammation in Alzheimer's and hold potential for the development of innovative therapies.



Astrocytic NLRX1 Contributes to Multiple Aspects of Alzheimer's Disease

Martin Hsu, PhD | University of North Carolina at Chapel Hill
Mentor: Jenny Ting, PhD

Alzheimer's disease is the leading cause of dementia, marked by memory loss and brain cell dysfunction. Astrocytes, supportive brain cells, influence disease progression. Dr. Hsu's research team is studying the role of NLRX1 in astrocyte mitochondria that regulates metabolism and supports neuronal health. The team's data suggest NLRX1 worsens Alzheimer's by promoting harmful protein buildup and cognitive decline. Removing NLRX1 in astrocytes may boost their protective functions, reduce toxic signals, and support neurons. This work could reveal new therapeutic targets to slow or prevent Alzheimer's disease.



Investigating the Role of Genetic Ancestry and Mitochondrial Dysfunction in Alzheimer's Disease

Austin Reynolds, PhD | University of North Texas Health Science Center at Fort Worth
Co-Principal Investigators: Nicole Phillips, PhD & Robert Clinton Barber, PhD

Mitochondrial function plays a major role in several pathways contributing to Alzheimer's disease (AD) risk, including both amyloid and tau. Genetic ancestry, however, plays a complex role in AD risk, with ancestry on nuclear and mitochondrial genes having contradictory effects. This project will resolve this contradiction and mechanistically link genetic ancestry and mitochondrial function to AD risk by investigating how discordance between mitochondrial and nuclear genetic ancestry contributes to mitochondrial dysfunction and alters AD biomarker profiles in a large, genetically diverse cohort.



Exploring How Signals from the Body Influence Alzheimer's Disease

Haoyue Zhou, PhD | Gladstone Institutes
Mentor: Andrew Yang, PhD

The brain is protected by the blood brain barrier (BBB), which controls what enters from the bloodstream. While often regarded as a rigid shield, Dr. Zhou's previous research showed that plasma can cross the healthy BBB and interact with brain cells. In this project, researchers will identify these proteins under normal conditions and examine how their transport changes in early Alzheimer's disease (AD). This work will reveal how signals from the body support or harm brain function and guide new strategies to slow AD progression by modulating BBB transport of specific plasma proteins.

Microbiome

The human microbiome refers to the trillions of bacteria, viruses, and other microorganisms that inhabit the body, particularly in the gut, but also on the skin, lungs, and other surfaces. These complex ecosystems are essential to health, influencing digestion, immunity, and communication between the body and brain through what's known as the gut-brain axis. Understanding how microbial communities shape brain health may one day reveal novel strategies for preventing or slowing neurodegenerative disease.



Next-Generation Probiotics for Alzheimer's Disease

Laura Cox, PhD | Brigham and Women's Hospital

The gut microbiome changes in aging and may contribute to Alzheimer's disease (AD). Modifying the gut microbiome with beneficial bacteria may slow brain aging and AD; however, current probiotics are not specifically designed to prevent and treat Alzheimer's disease. Dr. Cox's team has discovered novel probiotics that prevent amyloid plaque accumulation, and this project will study how they slow disease processes in AD by regulating inflammation producing beneficial metabolites. These studies will provide critical information which could then be broadly used to prevent and treat AD.



How is Niacin Production in the Gut Associated with Alzheimer's Disease?

Miguel Moutinho, PharmD, PhD | Indiana University

Alzheimer's disease has been correlated with imbalances in gut bacteria; however, the mechanistic link between disease progression and gut dysbiosis has not been fully elucidated. In this project, researchers will test the hypothesis that the synthesis of niacin in the gut is dysregulated in Alzheimer's disease, which leads to a reduced supply of niacin to the brain and exacerbates the disease. They will also assess if increasing niacin synthesis in the gut and supply to the brain can mitigate disease progression, which could pave the way for novel therapeutic strategies.

Oligodendrocyte & Myelin Dysfunction

Oligodendrocytes are specialized brain cells that produce myelin, the insulating layer around nerve fibers that enables fast, efficient communication between neurons. Growing evidence links oligodendrocyte and myelin dysfunction with Alzheimer's disease and related dementias. Studies of oligodendrocyte and myelin dysfunction may reveal novel biomarkers, therapeutic targets, and strategies to preserve white matter integrity and protect brain networks in the face of neurodegenerative disease.



Unraveling the Triggers to Myelin Damage in Alzheimer's Disease

Katerina Akassoglou, PhD | Gladstone Institutes
Co-Principal Investigator: Mark Ellisman, PhD

Myelin damage has emerged as a key player in Alzheimer's disease (AD). However, the triggers of myelin pathology in AD remain largely unknown. Fibrinogen, a blood clotting protein deposited in the AD brain, is a potent inducer of neurotoxic inflammation and inhibitor of myelin repair. Researchers will determine the role of fibrinogen on myelin-forming cells in AD mouse models with state-of-the-art imaging, multiomic technologies, and behavioral analysis of learning and memory, as well as testing pharmacologic treatments promoting remyelination.



Ultrasound Treatment to Replenish Cells Essential for Brain Function

Isabelle Aubert, PhD | Sunnybrook Research Institute (Canada)
Co-Principal Investigator: Laura Vecchio, PhD

Alzheimer's disease affects both white and grey matter. The predominant cells in white matter, oligodendrocytes, produce myelin, which insulates cells to improve communication. White matter deficits can result in cell loss and communication breakdown. In a preclinical model of Alzheimer's disease, researchers have discovered that noninvasive ultrasound waves can generate new oligodendrocytes that may boost myelin production. This project aims to develop this innovative therapy, which has the potential to improve brain function affected by Alzheimer's disease, including learning and memory.

Cofunded by Focused Ultrasound Foundation.



Ultrasound Treatment to Replenish Cells Essential for Brain Function

Yifei Cai, PhD | Shanghai Jiao Tong University (China)

Myelin and axons interact reciprocally to enable fast signal transduction, neuronal plasticity, learning, and memory. Myelin and axonal pathology are involved in Alzheimer's disease (AD); however, the precise mechanisms of myelin-axon disruption remain poorly understood. This project aims to delineate the complex interaction between myelin and axons by using subcellular proteomics at the myelin-axon interface, iPSC modeling, intravital imaging and genetic manipulation, with the ultimate goal to identify molecular targets with therapeutic potential to reverse the myelin-axonal deficit in AD.



How Disrupted Body Clocks Worsen Brain Cell Damage in Alzheimer's Disease

Paula Desplats, PhD | The Ohio State University

The circadian clock, which controls our 24-hour biological cycle, is often disrupted in Alzheimer's patients, causing sleep problems and agitation. New research shows that the health of brain cells called oligodendrocytes and their precursors is connected to the circadian rhythm. These cells are important for nerve function and memory but become dysfunctional in AD patients and animal models. This study will explore how circadian disruptions affect oligodendrocytes and whether restoring normal rhythms can help recover their functions, potentially reducing neuropathology in AD.



Long-Term Changes in Blood Biomarkers Associated with Brain White Matter Injury

Cellas Hayes, PhD | University of Kentucky Research Foundation
Recipient, 2026 Edward H. Koo Postdoctoral Fellowship Award for Alzheimer's Disease Research

White matter hyperintensities (WMH) are spots seen on brain scans that raise the risk for memory loss, stroke, and dementia, but we do not yet know why they form. This study will follow blood markers of myelin, the protective coating of brain, along with Alzheimer's-related proteins over 15 years in African American older adults from the place with the fifth-highest dementia prevalence in the United States: Jackson, Mississippi. Results will show whether these blood markers can predict WMH and point to their biological origins.

Other Misfolded Proteins

Most dementia in people over 80 is of mixed etiology, involving multiple diseases or causes. Misfolded proteins from conditions like amyotrophic lateral sclerosis (ALS), Parkinson's, and vascular dementia interact, worsening cognitive impairment in people with Alzheimer's. Clinically distinguishing between dementias is important for therapies that target specific proteins.



Decoding the Role of an Alzheimer's Causal Gene in Distinct Brain Cell Types

Willem Annaert, PhD | Flemish Institute for Biotechnology (Belgium)

Research has focused on the major causal genes of early-onset familial Alzheimer's disease, PSEN1 and the amyloid precursor protein, ignoring the rare PSEN2 mutations. This project will provide a comprehensive picture with unprecedented insights into the contribution of PSEN2 in Alzheimer's disease pathology. This work could identify novel therapeutic strategies to tackle these rare cases of PSEN2-associated Alzheimer's disease.

Supported by an Innovative Seed Funding Program grant by an anonymous foundation.



Disrupted Nuclear Protein Trafficking in Frontotemporal Dementia

Alyssa Coyne, PhD | Johns Hopkins University School of Medicine

A shared protein factor between frontotemporal dementia and amyotrophic lateral sclerosis is the focus of this project. A variant of this protein is tied to dysfunctional nuclear surveillance in neurons that leads to buildup of another protein, TDP-43, implicated in these two diseases and in Alzheimer's disease. For this work, researchers will follow the steps from failed surveillance to cell injury, highlighting potential therapeutic targets for preventing this injury.



Early Protein Drivers of Alzheimer's Disease

Eleanor Drummond, PhD | University of Sydney (Australia)

This study will explore the pathological role of 10 proteins that researchers believe promote the development of neuropathology in Alzheimer's disease (AD). The team will study the location of each of these proteins in the brains of people with AD, determine if they interact with other major proteins that make up the plaques and the tangles in AD, and determine if these proteins cause cell death. Together, these results will help determine if these proteins of interest are potential new drug targets or biomarkers for AD.



TDP-43 in the Aging Brain: When and Where?

Jack Humphrey, PhD | Icahn School of Medicine at Mount Sinai
Co-Principal Investigator: Kurt Farrell, PhD

Diseases of the aging brain, such as Alzheimer's, are caused by multiple factors, including the proteins amyloid and tau. But recently, an additional protein, TDP-43, has been linked to a faster decline in some patients. Researchers will investigate TDP-43 in a set of autopsied brains from multiple diseases and associate its presence with the presence of amyloid and tau. They will then study which specific brain cells contain changes in TDP-43 levels and what that does to them, which could help to understand how TDP-43 relates to aging and dementia.



Evaluating the Role of the TDP-43 Protein in Alzheimer's Disease Pathogenesis

Mercedes Prudencio, PhD | Mayo Clinic Jacksonville
Co-Principal Investigator: Yongjie Zhang, PhD

TDP-43 proteins abnormally accumulate in up to 70% of brains with Alzheimer's disease and are associated with worse memory and greater volume loss. This proposal will characterize TDP-43 dysfunction in Alzheimer's pathogenesis. Studies will evaluate whether TDP-43 dysfunction heightens Alzheimer's symptoms and pathology and examine the relationship between disease factors and TDP-43. Research outcomes will explore the potential of TDP-43 pathology for therapeutic targeting and biomarker design.

Research Tools & Resources

When embarking on a research project, having the right preliminary information and tools can make or break its success, especially in understudied areas, and taking the first steps requires time and funding. Alzheimer's Disease Research grants support the development of resources used to conduct, translate, and disseminate high-quality dementia research, including shared data and tissue repositories, along with collaborative projects aimed at accelerating new knowledge, disease models, and interventions.



Mapping Brain Resilience in the Oldest-Old: A Multi-Omic Atlas of Cognitive Protection

Vivek Swarup, PhD | University of California, Irvine

Alzheimer's disease is the leading cause of dementia, yet people aged 90 and older show striking differences in how their brains are affected. Some remain sharp despite heavy Alzheimer's changes, while others develop memory loss with little evidence of the disease. This project will use advanced state-of-the art genomics tools to uncover why some of the oldest-old stay resilient, with the goal of identifying new ways to protect brain health as we age and also in disease.



Predicting Therapeutic Interventions for Resilience to Brain Aging

Christina Theodoris, MD, PhD | Gladstone Institutes

Alzheimer's disease (AD) is a disease of the aging brain where cells progress along a degenerative trajectory, leading to devastating effects on quality of life and longevity. Most studies test for interventions that shift cells towards health at that point in time but fall short of testing therapies for their long-term efficacy across extended lifespans. To address this, Dr. Theodoris' team will apply novel artificial intelligence models to map how cells change over human brain aging and enable in silico longitudinal trials to predict treatments that promote an AD-resilient long-term trajectory.

Sex-Based Differences

Women are disproportionately affected by Alzheimer's and account for two-thirds of Alzheimer's-related diagnoses. While their longer life expectancy compared to men was once thought to explain this, recent research has revealed additional sex-based differences in genetics, immunity, hormones, and underlying risk factors such as higher depression rates.



Synergistic Effects of Biological Sex and Sleep Loss in an Alzheimer's Model

Mallar Chakravarty, PhD | Douglas Research Centre (Canada)

Sleep disruptions impact males and females differently in later life and are a known risk factor for Alzheimer's disease. In this project, researchers will use lab models that accumulate Alzheimer's disease pathology and can be used to track how disease processes impact the brain. The goal of this research is to use magnetic resonance imaging, a non-invasive tool with whole brain coverage, to examine changes in structure and function in sleep-deprived brain models. Further, they will examine how the menopause transition in females may further worsen the accumulated risk for Alzheimer's disease.

This grant is funded through the Cross Border Grant Program in partnership with Alzheimer Nederland.



How Ovarian Immune Cells May Shape Alzheimer's Risk

Sarah Ocañas, PhD | Oklahoma Medical Research Foundation
Co-Principal Investigator: Jeffrey Mason, PhD

Women are more likely to develop Alzheimer's disease, but the reasons why are not fully understood. This project explores how immune cells in the aging ovary may send signals to the brain that worsen memory problems and drive disease. By studying ovarian immune aging in Alzheimer's mouse models, researchers aims to discover new ways the body's own immune system may influence brain health and reveal novel targets for protecting women's memory as they age.



Interactions of Pregnancy and Menopause on Alzheimer's Disease Outcomes

Damian Zuloaga, PhD | University at Albany
Co-Principal Investigator: Kristen Zuloaga, PhD

Women are disproportionately affected by Alzheimer's disease (AD) relative to men. Life course factors unique to women, including pregnancy and menopause, likely contribute to female vulnerability, although how these two factors interact to affect AD-related outcomes is unknown. Researchers propose using a mouse model of AD to determine how the combination of pregnancy and menopause impacts cognitive/behavioral functions and AD-associated neuropathology.

Sleep & Circadian Rhythm

Chronic sleep disruption impacts Alzheimer's disease by impairing the brain's ability to clear waste and toxins, including misfolded proteins, and break down and dispose of amyloid-beta plaques present in early Alzheimer's. Changes in sleep patterns often occur in early Alzheimer's. Researchers are investing whether sleep disruption is a symptom of Alzheimer's-related neurodegeneration and can serve as an early warning, or whether it's a contributing factor that can be treated.



The Effect of Alzheimer's Disease on Neurons Across the Sleep/Wake Cycle

Md. Joynal Abedin, PhD | Massachusetts General Hospital & Harvard Medical School
Mentor: Ksenia Kastanenka, PhD

In Alzheimer's disease, the buildup of amyloid beta (Aβ) can result in sleep disturbances. Dr. Abedin and his team are investigating the activity of specific neuronal types in a genetically engineered mouse model of Alzheimer's disease to understand how Aβ affects neuronal activity during the sleep/wake cycle. This research could pave the way for therapeutic development to restore abnormal neuronal activity and potentially lead to a cure for Alzheimer's disease.



Disrupted Sleep Cycles and Alzheimer's Disease Risk

Jingyuan Chen, PhD | Massachusetts General Hospital & Harvard Medical School

Researchers will use cutting-edge imaging to track metabolic changes in the synapses during sleep-wake cycles in people with and without known risk for Alzheimer's disease. In addition, the team will follow how the use of glucose tracks with brain waves associated with Alzheimer's. The work will reveal more of the picture of how Alzheimer's disease and disrupted sleep are linked.



Treating Insomnia in Mild Cognitive Impairment (MCI)

Peter Fried, PhD | Beth Israel Deaconess Medical Center & Harvard Medical School

Many people with MCI experience symptoms of insomnia, which can speed cognitive decline and worsen quality of life. Researchers will test a novel intervention to improve sleep and cognition in persons with MCI that combines noninvasive neuromodulation with transcranial magnetic stimulation with an Internet-delivered cognitive behavioral therapy for insomnia program. If successful, this approach will meet the need for an efficacious, nonpharmacologic, and accessible therapy for people with MCI and insomnia.

Supported by an Innovative Seed Funding Program grant by an anonymous foundation.



A Sleeping Pill for Alzheimer's Disease

Ksenia Kastanenka, PhD | Massachusetts General Hospital & Harvard Medical School

Disruptions in brain activity associated with sleep and memory impairments that Alzheimer's patients experience could hold the key to the development of effective therapeutic strategies. Since Alzheimer's patients suffer from sleep disturbances, the administration of FDA-approved sleeping pills could restore their sleep and slow disease progression. Researchers will administer proven and safe sleeping pills in a mouse model. The results will indicate whether sleeping pills could be effective at slowing Alzheimer's disease.



Repairing the Body Clock to Delay Alzheimer's Disease

Jae-eun Miller, PhD | Columbia University

Breakdown in circadian rhythm is both a risk factor and a symptom of Alzheimer's. This suggests a vicious cycle of circadian disruption driving disease, and disease driving circadian disruption. If we could prevent circadian disruption, we may be able to prevent the disease. To address this, researchers will determine how tauopathy, a key component of Alzheimer's disease, disrupts the function of the master circadian clock. They will also develop an approach to restore circadian rhythm in a disease model and determine if this prevents the disease.



Circadian Rhythm Disruption and Alzheimer's Disease

Ashish Sharma, PhD, MPharm | Washington University in St. Louis
Mentor: Erik Musiek, MD, PhD

This study uses a mouse model of chronic jetlag (CJL) to investigate how disrupted circadian rhythms, common in aging and Alzheimer's disease (AD), impact disease progression. Researchers aim to understand how CJL affects AD markers—amyloid plaques and tau protein accumulation. Investigating the connection between circadian disruption, glial function, and AD-related changes may reveal therapeutic strategies and offer novel approaches to disease prevention.

Supported by an Innovative Seed Funding Program grant by an anonymous foundation.

Tau

Tau, a protein crucial for transporting nutrition and waste in and out of the brain, becomes misshapen and collects in messy tangles in Alzheimer's disease. Unlike amyloid plaques, which can precede symptoms by years, tau tangles signal rapid disease progression. Researchers are studying how misfolded tau and amyloid-beta interact and contribute to Alzheimer's spread in the brain.



Harnessing the Protein CHIP/STUB1 to Reduce Alzheimer's Brain Pathology

Todd J. Cohen, PhD | University of North Carolina at Chapel Hill
Co-Principal Investigators: Nicolas Brown, PhD & Jonathan Schisler, PhD

The research focuses on the role of the protein CHIP/STUB1 in Alzheimer's disease, particularly its ability to prevent the aggregation of tau proteins linked to the disease's progression. By engineering CHIP variants that enhance its chaperone function, the study aims to reduce tau pathology and improve cognitive function in Alzheimer's patients. This innovative approach could lead to new gene therapies for Alzheimer's and other tau-related diseases.

Recipient, Lina Mae Edwards Research Grant; cofunded by Dementia Alliance of North Carolina with Guardian Angel Thrift.



Dorsal Raphe Nucleus: Seam for Earliest Detection of Tau and Symptoms

Heidi Jacobs, PhD | Massachusetts General Hospital & Harvard Medical School

The dorsal raphe nucleus (DRN, Latin:"seam"), a tiny brainstem region providing serotonin, regulates behavior and cognition and is one of the first regions vulnerable to tau. Due to its size, DRN tau has only been investigated at autopsy. Taking advantage of new methods, Dr. Jacobs will examine tau patterns in the DRN, changes in DRN tau, spreading of tau to other brain areas and "seam" DRN tau to cognitive and behavioral changes. The outcomes of this innovative project will inform the field on the earliest brain changes in Alzheimer's disease, improve early detection and design of clinical trials.



Identifying the Mechanisms That Underlie Tau Aggregation and Neurotoxicity

Sarah Kaufman, MD, PhD | University of California, San Francisco
Mentors: Martin Kampmann, PhD & William Seeley, MD

Alzheimer's disease and frontotemporal dementia feature the accumulation of tau protein in neurons that are eventually lost to the disease. The mechanisms underlying tau misfolding and accumulation, and their associated neurotoxicity, are not known. This project employs whole-genome screening techniques to identify the cellular pathways that regulate tau aggregation and toxicity. Study findings will provide critical insight into tau-associated disease mechanisms and identify potential therapeutic targets for these diseases.



A Newly Discovered Version of Toxic Tau as a Therapeutic Target in Alzheimer's Disease

Daniel C. Lee, PhD | University of Kentucky Research Foundation

The potential for citrullinated tau to be especially toxic is the focus of this project. Researchers will assess two therapeutic approaches targeting citrullinated tau, either preventing the citrullination or vaccinating against the citrullinated form. The team will test both potential therapies in animal models of Alzheimer's disease, comparing their effects on disease progression and cognitive decline and opening up a new area of research in Alzheimer's disease.



The Role of JADE1 in Tauopathy

Marcos Schaan Profes, PhD | Icahn School of Medicine at Mount Sinai
Mentor: John Crary, MD, PhD

Tauopathies, such as Alzheimer's disease, result from the toxic aggregation of tau proteins, but the exact process remains unclear. We are investigating JADE1, a protein that specifically binds toxic tau, to determine if it prevents aggregation or promotes clearance via cellular pathways like autophagy. Using advanced cellular models, including one that uses light to control tau behavior, our research aims to uncover how JADE1 works and explore its potential as a target for future treatments.

Translational Research & Clinical Interventions

Translational research aims to move basic science knowledge from the lab or research setting into practical treatments and interventions for Alzheimer's disease. This can include innovations like smartphone-based cognitive tests, promoting brain-healthy activities, and improving lifestyle factors. Clinical trials and studies are essential for testing and advancing new drugs and interventions for people living with Alzheimer's today and those at risk in the future.



Personalized Proteomics to Understand and Predict Alzheimer's Progression

Federica Anastasi, PhD | Barcelonaβeta Brain Research Center (Spain)
Mentors: Marc Suárez-Calvet, MD, PhD & Betty Tijms, PhD

Alzheimer's disease affects people differently, leading to varying rates of memory loss and cognitive decline. While blood tests can help detect early signs of Alzheimer's, there's still much to learn about why these differences occur. This project focuses on identifying new biomarkers to explain why individuals experience Alzheimer's differently and predict who will be most affected. By discovering these markers, researchers aim to develop personalized tools for earlier intervention, improve predictions, and enhance the recruitment of participants for clinical trials.



Neurostimulation to Improve Depression and Memory in Dementia

Davide Cappon, PhD | Tufts Medical Center

This project combines two types of transcranial electrical stimulation, a noninvasive technology that modulates brain network activity to address depressive and memory symptoms in older adults with depression and Alzheimer's dementia. By using cutting-edge technology to study targeted brain circuits and delivering the intervention at home, this study will help develop a scalable, noninvasive intervention with the greatest impact on alleviating depression and Alzheimer's symptoms.



Neuroimaging and Neuropathology of Alzheimer's Disease in Down Syndrome

Jr-Jiun Liou, PhD | University of Pittsburgh
Mentors: Tamer Ibrahim, PhD; Julia Kofler, MD & Elizabeth Head, PhD

Why do individuals with Down syndrome develop Alzheimer's disease decades earlier than the general population? This project will use high-resolution imaging and postmortem brain samples from well-characterized cohorts of adults with Down syndrome and late-onset Alzheimer's disease. By identifying imaging biomarkers and clarifying early disease mechanisms, researchers aim to advance understanding of Alzheimer's in Down syndrome, promote inclusive research, and guide effective interventions to improve diagnostics and treatment strategies.



Home-Based, Noninvasive Brain Stimulation for Mild Alzheimer's Disease

Brad Manor, PhD | Hebrew Rehabilitation Center
Co-Principal Investigator: Alvaro Pascual-Leone, MD, PhD

Memory loss and executive dysfunction are hallmarks of Alzheimer's disease that map onto spatially distinct brain networks. Researchers will deliver two types of transcranial current stimulation (tCS) to provide multisymptom relief for older adults with mild Alzheimer's. With this dual, simultaneous stimulation and assessment of individual therapeutic benefit, this work will support development of tCS interventions with maximal impact on daily life function for this population.



Artificial Intelligence-Guided Drug Discovery for Alzheimer's Disease

Yuanyuan Wei, PhD | University of California, Los Angeles
Mentor: Chao Peng, PhD

In this project, researchers will develop an artificial intelligence (AI)-guided drug discovery platform to identify and validate new therapeutic candidates targeting tau pathology in Alzheimer's disease. Current AI drug design tools were built for conventional proteins and fail to account for the unique repeating fibril structure of Alzheimer's tau. By combining fibril-specific AI prediction and generative design with validation in neurons seeded with actual Alzheimer's patient-derived tau aggregates, this work could accelerate the discovery of drugs that slow or halt Alzheimer's disease by identifying promising compounds far more efficiently than traditional screening.

Cofunded by Alzheimer's Los Angeles.

Vascular Contributions to Dementia

Vascular dementia is the most common condition that co-occurs with Alzheimer's disease, as the brain's neurons rely on a complex vascular system to deliver oxygen and glucose. This system, stretching about 60,000 miles, is protected from the rest of the body by the blood-brain barrier, which prevents harmful substances from entering. Both the brain's circulatory system and protective barrier are important to Alzheimer's research and are key to keeping neurons healthy.



Changes in Cerebral Blood Flow and Dementia

Daniel Bos, MD, PhD | Erasmus University Medical Center Rotterdam (the Netherlands)

Researchers aim to uncover how blood flow in the carotid arteries affects the development of dementia. Over the last several years, the role of vascular disease in the carotid arteries in the development of dementia has been repeatedly emphasized. Researchers believe that biomechanical forces may trigger processes that lead to vascular disease in these vessels, affect brain blood supply, and cause dementia. Through complex computer simulations, researchers will study a large group of people to find links between these biomechanical forces and the risk of dementia.



How Aging and Alzheimer's Affect the Brain's Blood Flow

James Cole, PhD | University College London (UK)

In this project, researchers will model changes in blood flow around the brain across the lifespan and identify how Alzheimer's affects this. Using a statistical model of how the brain's blood flow changes over the lifespan using a brain scanning method called arterial spin labelling, they will determine "normal" brain blood flow for a person's age and sex. Using brain scans collected from large groups of people over time, they will examine how factors such as cardiovascular health, genetics, and ethnicity influence brain aging.

This grant is funded through the Cross Border Grant Program in partnership with Alzheimer Nederland.



The Role of the Brain Vascular-Immune Processes in Alzheimer's

Julie Ottoy, PhD | Sunnybrook Research Institute (Canada)
Mentors: Sandra Black, MD & Maged Goubran, PhD

Damage to the brain's blood vessels can triple Alzheimer's disease risk, and overactive immune cells may further exacerbate this damage. This study examines how vascular-immune responses affect Alzheimer's progression by analyzing brain scans and blood samples from 500+ individuals over time. Outcomes will provide unique insights on key and understudied mechanisms driving Alzheimer's, empowering conversations on personalized biomarkers and treatment strategies targeting the vascular system, brain immune cells, and Alzheimer's.



Identifying the Molecular Connections Between Cardiometabolic Problems and Alzheimer's Disease

Daniel Panyard, PhD | Stanford University
Mentor: Themistocles Assimes, MD

The underlying cause of Alzheimer's disease is unknown, but there is ample evidence that certain cardiovascular problems may increase the risk. The goal of this project is to discover the key proteins and other molecules that connect these cardiovascular risk factors to Alzheimer's disease by using data from some of the largest human studies available. At the completion of this project, we plan to follow up on our findings by testing whether these molecules can be used to improve how we diagnose or treat people with Alzheimer's disease.



Small Vessel Disease Biomarkers to Improve Understanding of Vascular and Alzheimer's Dementia

Leonardo Rivera-Rivera, PhD | University of Wisconsin-Madison

Alzheimer's disease (AD) and cerebral small vessel disease (cSVD) are the most frequent causes of dementia; however, current therapies primarily target AD-related cognitive decline, limiting their effectiveness when both cSVD and AD are present. Due to a gap in available biomarkers, the separation and characterization of cSVD- and AD-related cognitive decline is challenging and incomplete. In this project, Dr. Rivera and his team will evaluate novel imaging markers to study cSVD in individuals with confirmed AD and comorbid cSVD, aiming to advance biomarkers and therapeutic targets for multi-etiology dementia.



Dementia Risk Mitigation in Individuals with Cardiovascular Disease

Myuri Ruthirakuhan, PhD | Sunnybrook Research Institute (Canada)

This project aims to better understand why people with multiple cardiovascular conditions, such as high blood pressure, heart disease, or diabetes, face a higher risk of developing dementia. Researchers will analyze large population datasets and combine blood, imaging, and clinical data to identify biomarkers and biological pathways that link cardiovascular health to cognitive decline. The work will guide the development of targeted therapies to reduce dementia progression and opens new avenues for personalized treatment by linking lipid and metabolic biomarkers to disease mechanisms.



Understanding the Choroid Plexus in Alzheimer's Disease

Monica Santisteban, PhD | Vanderbilt University Medical Center

The renin-angiotensin system may play an important role in Alzheimer's progression. Researchers will look at the choroid plexus, a small tissue within the brain that makes the cerebrospinal fluid, as a novel source contributing to the local brain renin-angiotensin system and cognitive decline in Alzheimer's disease (AD). Since there are likely many more changes happening in the choroid plexus other than the renin-angiotensin system, they will also establish a comprehensive database of the transcriptional changes in the choroid plexus in AD to serve as a tool for future discovery.

Waste-Clearance Mechanisms

In addition to immune-mediated clearance duties of the microglia, cells use self-eating, or autophagy, to remove old or misprocessed proteins and optimize health and function. Abnormalities in the endo-lysosomal pathway, an early feature of Alzheimer's, relate to genetic risk factors. The brain's lymphatic system, which drains fluid and immune cells, may contribute to Alzheimer's pathology if impaired, making it a potential target for therapeutic interventions.



Regulatory Mechanisms Underlying Endosomal Targeting of SORL1

Olav Andersen, PhD | Aarhus University (Denmark)

The SORL1 gene is a major contributing factor for familial Alzheimer's disease, and the sorting of SORL1 in compartments of the endolysosomal network strongly depends on binding of its short tail-domain to trafficking proteins in the cytosol. In this project, researchers will identify novel binding partners and uncover how their interactions with SORL1 are regulated by post-translational modifications. An improved understanding of the biology of SORL1 related to disease mechanisms could potentially open the door for novel therapeutic strategies.

This grant is funded through the Cross Border Grant Program in partnership with Alzheimer Forschung Initiative.



Characterizing Factors That Induce Waste Clearance in Microglia

Anna Podlesny-Drabiniok, PhD | Icahn School of Medicine at Mount Sinai
Co-Principal Investigator: Alison Goate, DPhil

Researchers have identified potential factors that may boost the ability of microglia to dispose of accumulated waste during Alzheimer's. This project aims to validate computational predictions and characterize two factors of human microglia at baseline and with amyloid proteins. Additional investigation will also occur in microglia from people carrying two copies of *APOE4.* Study outcomes will explore potential novel therapeutic strategies aiming to induce waste clearance processes in microglia.



Understanding Tau Seeds: The Role of Protein Clumps on Membranes in Alzheimer's Disease

Sankalp Shukla, PhD | University of California, Berkeley
Mentor: James Hurley, PhD

In Alzheimer's disease, protein clumps build up and spread from one part of the brain to another, damaging the brain. These protein clumps can interact and disrupt the membranes that contain and destroy them, which causes protein clump leakage and spread. This project aims to understand the underlying cause of membrane leakage for therapeutic development to counteract protein clump escape by promoting the repair of damaged membranes.

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