"It is important that individually we work to make a difference, so that collectively we can make an impact."

-Beth Scott, CTF supporter with a loved one battling FTD

CLEAR THOUGHTS FOUNDATION

...funding the fight against dementia

2024-2025

IMPACT REPORT

BRIDGING RESEARCH AND HOPE

JOIN US IN THE FIGHT AGAINST DEMENTIA!

While dementia is complex, we at Clear Thoughts Foundation (CTF) are keeping the pathway to eliminating it simple.

Our Vision

To see a world free of dementia.

Our Mission

To fund the discovery of breakthrough drugs and novel treatments to eliminate dementia.

What is dementia? Dementia is not a disease but a loss of cognitive ability that can be caused by a number of diseases affecting the brain. Cognitive loss worsens over time and interferes with daily life, impacting an individual's ability to remember recent events, find words, make decisions, or complete familiar tasks. *This is NOT a normal part of aging!*

With over 100 different forms of dementia, such as Alzheimer's disease, Frontotemporal dementia (FTD), Lewy body dementia, Vascular dementia, CTF recognizes the need to fund research for viable treatments across all forms.

A note from our Founder & President, *Hayley D. Jameson*

Dear CTF Supporter,

When we founded CTF in 2010, we did so with a clear mission to fund research toward a cure for dementia. We also sought to bring hope to families facing this devastating 'dementia devil,' as we call it.

Your support has allowed us to do just that... fund cutting-edge research, empower innovative scientists, and build meaningful momentum in the field. As an organization proudly rooted in Pittsburgh — a city defined by its bridges — we believe deeply in the power of connection. It is truly an honor to be at the forefront of building the much needed bridges between promising science and life-changing outcomes for families impacted by dementia.

On behalf of CTF, I am proud to share this report, which reflects the progress and connection your support has made possible. Each funded study, each new connection, and each scientific breakthrough brings us closer to our shared vision of seeing a world free of dementia.

We remain unwavering in our mission to eliminate dementia and hope that you will continue to stand with us in this important fight!

Together in the fight,

Hayley D. Jameson

Visit our website at clearthoughtsfoundation.org to learn more about our passionate board!

Bridging the path, in the city of bridges, *towards a world free of dementia.*

CTF is proud to be founded in Pittsburgh, PA, one of the nation's leading, top-tier hubs for dementia research. Our city is at the forefront of developing blood-based biomarkers for early detection, is heavily involved in high-level clinical trials nationally, and supports the ongoing development of translational research leading to preventative treatments.

While dementias' prevalence continues to rise, CTF's impact is strong and continues to combat these statistics each year. Learn more about the staggering statistics of dementia and CTF's impact below!

Dementias' Growing Prevalence

Worldwide

- Every 3 seconds an individual is diagnosed with dementia.
- Over 57 million individuals are currently living with some form of dementia.
- Dementia costs exceed $1.3 trillion dollars annually.
- Dementia is one of the leading causes of disability and dependency among older adults.

Nationwide

- 6 million individuals are living with Alzheimer's disease alone.
- 40% of individuals age 55 and older are expected to develop dementia in their lifetime.
- Funding vs. cost comparison in billions:

Category	*Dementia*	*Cancer*
NIH Research Funding	$3.8B	$8.5B
Direct Medical Cost *Ex: Residential care, hospitalizations, medications, etc.*	$345B	$240B
Total Societal Cost *Ex: Informal care, caregiver burden, legal fees, etc.*	$750B	$500B

A striking reality... despite dementia's greater societal cost, it receives less than half the federal research funding allocated to cancer!

CTF's Impact

Developed the *CTF Consortium*—a collaborative, translational research model bringing together leading physicians and researchers across Pittsburgh.

Supports a research model that accelerates results and maximizes donor investment, generating up to three times the impact of traditional funding models.

Funds the only research initiative in Allegheny County focused exclusively on translational research for all forms of dementia.

Provides critical seed funding to enable under-funded, high-potential research to generate the preliminary data necessary to pursue larger National Institute of Health (NIH) and National Institute of Aging (NIA) grants.

Awarded a total of $700,000 dollars to breakthrough dementia research (CTF Consortium and grant research).

Connects over 18,000 individuals nationwide with online resources and education.

Engages with a community of over 5K annual supporters.

Beth's Story

When Beth Scott looks at her dad, Mark, she doesn't just see a diagnosis — she sees the man who raised her, guided her, and filled her childhood with strength and steady love. Mark was diagnosed with Frontotemporal dementia (FTD), a devastating form of dementia that often strikes early in life. Mark's diagnosis with FTD gradually began altering his personality and behavior, eventually reshaping his career and life with his family in heartbreaking ways.

Today, Mark is still fighting his battle against dementia and Beth, her sister Kelsey, and their mother Patty, continue to walk alongside him — navigating the challenges, advocating for his care, and holding tightly to small moments of connection. Watching her father battle dementia has been painful, but the deepest pain is felt in the moments of disconnections between her own children and her father. This sad and frightening reality has given Beth a firsthand understanding of the urgency behind advancing research for all forms of dementia.

"It takes the people who are impacted by dementia to bring awareness, to raise money, to hopefully and ultimately land on a cure."

For Beth, helping to fund research is hope. It is a way to help build a future where other families won't have to face the same sadness of watching their loved one slip away to the 'dementia devil.' Through supporters like Beth, stories like Mark's become a powerful reminder of why CTF's mission is more important than ever and why accelerating research toward a cure takes all of us. We are grateful to Beth and her family for sharing their story with hopes to inspire others to join the fight!

Beth and her husband, Justin, have been longtime supporters of CTF, with Beth also dedicating several years of service as a valued board advisor.

Visit our website to watch the full story.

With Gratitude

At CTF, we are deeply grateful for every individual who stands with us in the fight against dementia. Your generosity — whether through donations, event participation, or sharing our mission — fuels our cutting-edge research and propels the momentum needed to drive real change. Every gift makes an impact and we do not take your support and trust in our mission lightly. Out of our strong commitment to uphold donor confidentiality, individual gifts will not be acknowledged publicly. However, we are truly thankful to fund the fight with you toward a world free of dementia.

~Clear Thoughts Foundation

CTF Giving Circle

We would like to give special thanks to our giving circle - a community of supporters who choose to honor loved ones and support progress through memorial gifts, personal fundraisers, and planned giving. Each contribution represents more than generosity — it reflects a story, a tribute, and a commitment to accelerating research in the fight against dementia. Whether given in memory, in celebration, or through thoughtful philanthropic planning, these gifts create lasting impact to see a world free of dementia.

Individual Fundraisers

Baird Financial Corporation
Employee Friday Jean Campaign

Stronger Personal Training
Attack on Alzheimer's Workouts

sweb Marketing
PGH Web of Good Social Giveback

Facebook Birthday Fundraisers

Heather Ann
Kevin Craddock

Dementia Awareness Month Fundraisers

Forbes Tavern & Proper Brick Oven
I.C. Light Promotion Giveback

Pure Edge Performance Training
Bootcamp Benefit

R.A.W. Training
Benefit Workout

Thomas Jefferson High School
Student Play w/Dementia Focus

Media Partners

KDKA
North Hills Magazine
WDVE

In-kind Corporate Donors

Lamar Advertising
Seniors Blue Book

Donations Received in Memory Of

Anthony M. DiGioia
Arthur Joseph DiDonato
Carol Bevacqua
Catherine Henke
Charley Bowman
Don 'DJ' Jameson
Doris Yoder
Eileen Flahive
Ethel Dorothy Iskander
Fran Wallace
Jeffrey W. Mertens
Joe Deprimio
Kathy Bann
Kay Frances Fox
Louise Castellucci
Margaret Matus
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Sippel Development
Sippel Steel Fab
The Good Fund
U. S. Steel
UPMC / UPMC Health Plan
Wellington Power

CTF CONSORTIUM RESEARCH

2024-2025

Research Members

Dr. Oscar L. Lopez, MD, FAAN

Pitt Professor of Neurology, Psychiatry, and Clinical and Translational Sciences; Director of Pitt Alzheimer's Disease Research Center; Chief of Pitt Cognitive and Behavioral Neurology Division

Dr. Amantha Thathiah, Ph.D.

Pitt Associate Professor of Neurobiology; Pittsburgh Institute for Neurodegenerative Diseases (PIND)

Dr. Robert M. Friedlander, MD

Following the completion of this research, in December 2025, Dr. Friedlander stepped down as Chair of the Department of Neurological Surgery and is no longer affiliated with UPMC or the University of Pittsburgh.

CTF Consortium Impact

Worldwide, a person is diagnosed with a form of dementia every 3 seconds. By 2050, it is estimated that more than 152 million individuals worldwide will be living with dementia—nearly triple the current number of cases. Addressing this growing global burden requires sustained investment in innovative research aimed at developing effective preventive treatments. As the only research initiative in Pittsburgh focused exclusively on translational research for all forms of dementia, the CTF Consortium leverages complementary expertise to accelerate results and maximize donor investment, generating up to three times the impact of traditional funding models.

Without your support, novel research projects, such as this CTF Consortium work, would fade before their true scientific or clinical impact is known. This narrows the range of ideas being explored across the dementia field, both nationally and worldwide. Your support of the CTF Consortium has provided critical seed funding to bridge this gap, enabling this high-potential research to generate the preliminary data necessary to pursue larger National Institutes of Health (NIH) and National Institute of Aiging (NIA) grants. CTF's continued research progress offers hope to countless families—both those currently supporting a loved one living with dementia and future generations that preventative and viable treatments are on the horizon.

2024-2025 Research

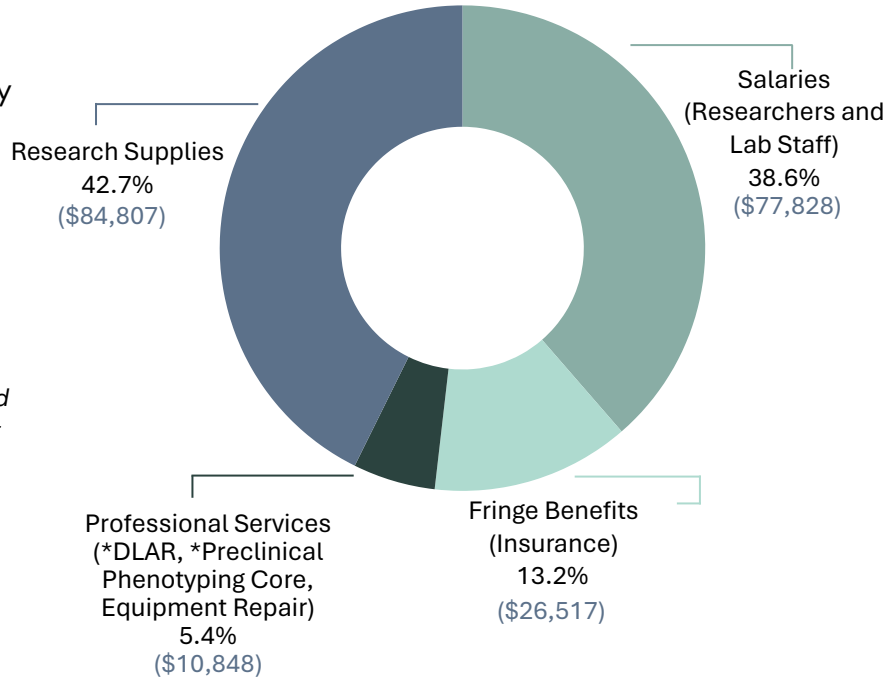
The CTF Consortium researchers are incredibly grateful for your generous support throughout 2024-2025, allowing their research to continue evaluating the efficacy and impact of the commonly used sleep aid, melatonin, as a potential preventive treatment for all forms of dementia. A detailed report of research progress, including distribution of funds, lay summary, and worldwide impact, can be found on the following pages.

Distribution of Funds

CTF allocates a total of $200,000 biannually to support the ongoing research efforts of the CTF Consortium. The provided chart outlines the percentage distribution of how funds were allocated and illustrates how your contribution supported this critical research over the past 24 months.

**Preclinical Phenotyping Core provides optimized and validated lab testing protocols and behavioral testing equipment.*

**Division of Laboratory Animal Resources (DLAR) is dedicated to the ethical and humane care of animals in research.*



Not a scientist? You're not alone! Research reports can feel overwhelming — even we sometimes need to read them twice. That's why we've included a lay summary below from our Chief Scientific Advisor. It breaks down our most recently completed research into clear, easy-to-understand highlights so you can know exactly what your support has made possible!

Lay Research Summary by CTF Chief Scientific Advisor, *Stacey J. Rizzo, PhD*

With the grant money provided by the Clear Thoughts Foundation over 2024-2025, the CTF Consortium researchers investigated the role of melatonin on cognitive function. Melatonin is a hormone that regulates sleep and declines naturally with aging but also has a much greater reduction in individuals with dementia. The CTF Consortium researchers hypothesize that the loss of melatonin activates neuroinflammation in the brain, which may lead to the toxic tau pathology and synapse integrity loss in neurons, contributing to subsequent cognitive decline. For these studies, the research team created a mouse model that cannot make melatonin as a tool to recapitulate the reduction in melatonin observed in aging and dementia.

From this model, they are studying neuroinflammation, cognition, synaptic integrity, and tau pathology as a consequence of loss of melatonin in those mice in comparison to normal aging melatonin-producing mice. At this time, they successfully created the mouse model that does not produce melatonin and have demonstrated increased gene expression in those mice relative to the controls. They also conducted cell culture studies to show that in vitro when the cell culture media is supplemented with melatonin to the neurons that do not produce melatonin, the supplementation rescues the synapse loss, preventing cognitive decline.

The CTF Consortium research team focused its efforts on five key activities: generating resources, measuring tau, neuroinflammatory marker expression, analysis of synapses, and behavioral analysis. By advancing work across these five areas simultaneously, the team accelerated progress on its hypothesis and moved closer to generating the comprehensive data required to pursue NIH funding.

CTF Consortium Research Report *(Provided by the CTF Consortium Researchers)*

Research Strategy

The overall hypothesis of this project was that melatonin activates microglia and causes Tau phosphorylation. These cellular events trigger neuroinflammation causing synaptic pruning and eventually memory deficits. We undertook the testing of this hypothesis in several phases, all of which compared mice that were genetically engineered to prevent melatonin synthesis with the same strain of mice that is competent to make melatonin: 1) quantification of microglial activation; 2) analysis of tau; 3) measuring neuroinflammatory markers; 4) analyzing synapses and neurite length; and 5) behavioral to measure brain function.

Research Activities

Generating the Resources:

The CBA mouse strain is known to have robust melatonin synthesis. In a previous CTF-funded project, we genetically engineered these mice to knock out one of the genes required for melatonin synthesis, AANAT. All downstream experiment can thus compared wild type (WT) CBA mice with AANAT knockout (AANAT-KO) mice that are genetically identical except for the expression of the AANAT gene. These mice are bred internally as heterozygous male to heterozygous female (HETxHET) to guarantee that melatonin is present during embryonic development to ensure that effects seen are related to effects on pregnancy. The mice resulting from this cross result in WT (25%) and AANAT-KO (25%) for experiments and HET (50%) used to breed the next generation. We use these mice for all the experiments described below.

Quantification of Microglial Activation:

We used 1-year old AANAT-KO and WT mice to determine if microglia are activated in the brain when there is a melatonin deficit. To do so, we isolated RNA from the brain, and quantified mRNA transcripts that are specifically expressed in activated microglia. We found increased expression in the transcripts in six different markers, suggesting that microglia are activated. We followed this up with protein analysis. We used to immunoblot to measure IBA-1, which is a marker of all microglia, along with CD68, a marker of activated microglia. We found essentially no difference in the total number of microglia in WT and AANAT-KO brain (no change in average IBA-1 level) but an increase in the average levels of CD68, suggesting that the microglia in the brain are moving into an inflammatory phenotype.

Analysis of Tau:

To continue testing our hypothesis that microglia activation leads to changes in tau pathogenesis, we first optimized detection and assessment of tau pathology in human control and Alzheimer's disease (AD) brain samples. All brain samples were obtained from the Alzheimer's Disease Research Center (ADRC) brain bank at the University of Pittsburgh. Control and AD cases were age- and sex-matched. Tau is a predominantly soluble, monomeric protein under physiological conditions. However, in patients with dementia, tau hyperphosphorylation leads to a decrease in tau solubility and an increase in the accumulation of insoluble pools of tau.

We first extracted Sarkosyl-soluble and insoluble protein fractions from the hippocampus of control and AD patient brains to confirm putative changes in tau solubility in disease. We first determined that total levels of tau are increased in AD and that the increase in tau levels is specifically driven by an increase in insoluble tau (Fig. 1). Next, given the evidence indicating the influence of phosphorylation on changes in tau solubility, we sought to characterize putative changes in tau phosphorylation in human brains using immunoblot analysis of total brain homogenates and immunohistochemistry.

We found that AD brains exhibit elevated levels of tau phosphorylation at the PHF1 site (S396/404), a site used for AD diagnostic purposes (Fig. 2A-B). Additionally, we show that AD brains form characteristic PHF1+ neurofibrillary tangles (NFTs; Fig. 2C). Since melatonin production decreases with age and age is the primary risk factor for AD, we plan to correlate our human data with the mouse data to determine if melatonin deficit exacerbates pathogenic tau changes with age. With this in mind, the Friedlander laboratory has provided the Thathiah laboratory with brain samples from aged WT and AANAT-KO mice for tau analysis.

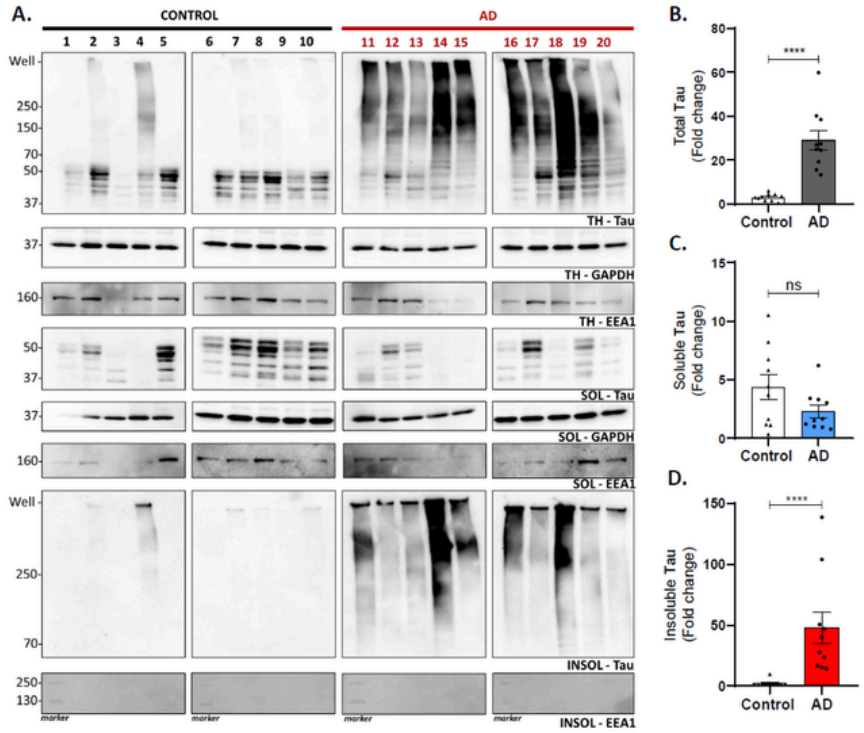


Figure 1. Tau levels are increased in AD dementia brains. Western blot analysis of Tau5 (total tau marker), GAPDH (loading control), and EEA1, a control soluble protein, in total (*top three panels*), soluble (*middle three panels*), and insoluble (*lower two panels*) hippocampal brain homogenates **(A).** Rectangles represent samples run on two separate gels (Gel#1: 1-5;11-15/ Gel#2: 6-10;16-20; a), with an equivalent number of control and AD cases in each gel. Quantification of Western blot results for total tau **(B),** soluble tau **(C),** and insoluble tau **(D)** from control (n=10 cases) and AD (n=10 cases) hippocampal homogenates. Total and soluble protein quantification (fold change) was normalized to GAPDH levels. Total tau levels are elevated in AD cases **(B),** which is due to an increase in insoluble, rather than soluble, tau levels **(C and D).** Mann Whitney test **(B-D).** Data are presented as mean±SEM. ns- not significant; **** p<0.0001. Molecular weight is indicated to the left kDa **(A).**

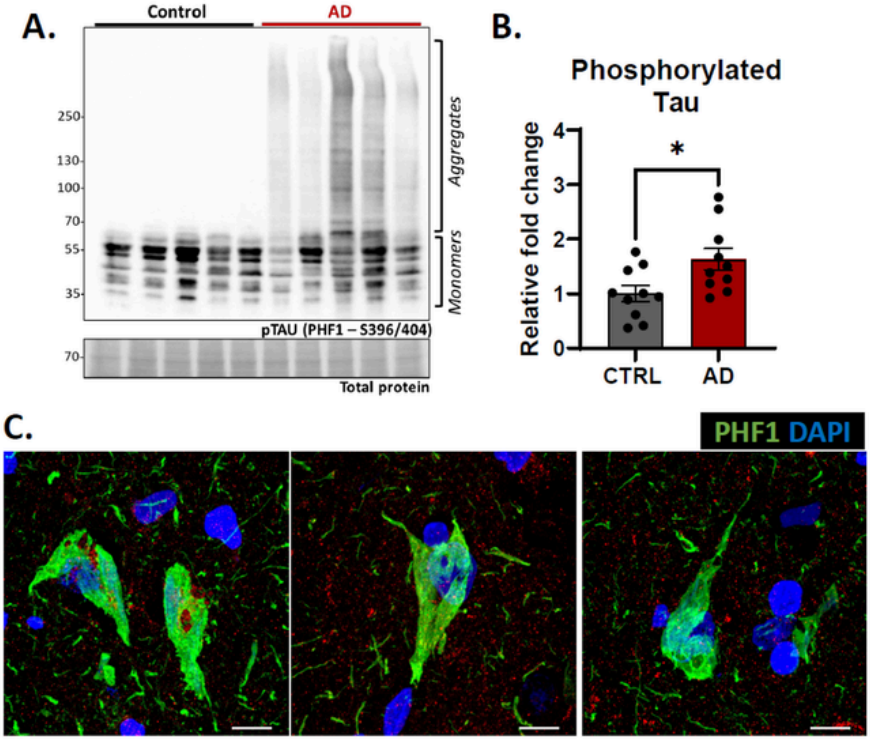


Figure 2. Phosphorylated tau pathology is increased in AD dementia brains. Western blot analysis of PHF1 (ptau marker – S396/404) and total protein load (Ponceau) in hippocampal brain homogenates **(A).** Quantification of Western blot results for ptau **(B)** from control (n=10 cases) and AD (n=10 cases) hippocampal homogenates. Quantification (fold change) was normalized to total protein levels. Mann Whitney test **(B).** Data are presented as mean±SEM. * p<0.05. Molecular weight is indicated to the left kDa **(A).** Representative immunofluorescence analysis of PHF1+ tangles (green) in AD brains. DAPI counterstaining was used to label nuclei (blue). Scale bar is 10um **(C).**

Neuroinflammatory Marker Expression:
Next, we want to determine if melatonin deficit increases neuroinflammation. For this experiment, we looked at expression of five different inflammatory cytokines in aged WT and AANAT-KO brain. We find that in 1-year old mouse brain, gene expression for four of the five neuroinflammatory markers that we measured were increased in AANAT-KO mice as compared with WT mice.

Analyzing Synapses and Neurite Length:
For synapse analysis, we used cultured neurons from WT and AANAT-KO mouse brain in culture and analyzed synapses over time. We found that after 12 passages, there is a slight loss of synapses in AANAT-KO neurons compared with WT. This difference increases with time, and at 30 passages, approximately 40% of the synapses are lost in the melatonin-deficient environment. Importantly, we supplemented melatonin back into the system and found that melatonin supplementation in vitro rescues synapse density.

We are measuring neurite length in brain sections from 2-year old mice. These mice were aged for the entire duration of the funded project and were euthanized for tissue collection in November 2025. Given the length of time that the mice needed to be aged, it was impossible to generate the data before the writing of this report; thus, neurite length measurements in these mice are currently in progress.

Behavioral Analysis:
We have a cohort of mice that was aged for 2-years and tested in a Y-maze using a spontaneous alternation protocol as a fundamental memory test. Mice were tested 3 times over the 2 years to obtain longitudinal data. Analysis of these data has had some unexpected confounding variables. First, we find that at some timepoints, male and female mice behave differently from each other. This was an unexpected finding on which we would like to follow up. Second, while this paradigm is not designed to test motor function, we found that a percentage of mice did not move in the maze as expected, resulting in those mice being excluded from the memory analyses. As a result, some groups had too few mice to analyze, and also at some timepoints, AANAT-KO mice may be over-represented in the category of excluded mice.

We are consulting with Dr. Rizzo, Director of the Pitt Preclinical Phenotyping Core for assistance in understanding these data.

In 2024 and 2025, the laboratories of Dr. Friedlander and Dr. Thathiah submitted two NIH applications for large-scale research projects designed to expand upon the specific aims of the research funded through the CTF Consortium. Details of the NIH applications are outlined below:

2024 NIH Submission
Requested Support: $3 million dollars
Project Title: *Endogenous Melatonin Regulation of Neuronal Mitochondrial Biomass*
Synopsis: This project aims to investigate additional neuronal characterization to understand how the melatonin deficiency affects neurons at a molecular level across a variety of neurodegenerative diseases.

2025 NIH Submission
Requested Support: $3.5 million dollars
Project Title: *Mechanisms of Mitochondrial GPCR MT1 Targeting*
Synopsis: This project aims to develop a deeper understanding of how melatonin 'locks' into the brain as a potential protectant of stressed brain cells. This will help determine targeting of melatonin usage against a variety of neurodegenerative diseases.

Worldwide *impact!*

The research findings of the CTF Consortium have been presented all over the world and shared across a variety of research communities within the dementia field. We are proud to have funded research with worldwide impact, guiding us all closer to a world free of dementia.

2024 Presentations

- International conference on Alzheimer's and Parkinson's Diseases (AD/PD), *Lisbon, Portugal*
- International Society for Molecular Neurodegeneration (ISMND) conference, *Seoul, Korea*
- CTF Connect, *Pittsburgh, PA*
- Tau Global Conference, *Washington, DC*
- Alzheimer's Association International Conference, *Philadelphia, PA*
- University of Pittsburgh Fall Undergraduate Research and Creative Expression Fair, *Pittsburgh, PA*
- Aging Institute 15th Annual Research Day Symposium, University of Pittsburgh, *Pittsburgh, PA*
- Alzheimer's Disease Research Center, Optimizing Scientific Careers in AD Research (OSCAR) Symposium, University of Pittsburgh, *Pittsburgh, PA*

2025 Presentations

- National Conference on Undergraduate Research, *Pittsburgh, PA*
- Postdoctoral Research Symposium, University of Pittsburgh, *Pittsburgh, PA*
- Frederick Honors College Symposium, University of Pittsburgh, *Pittsburgh, PA*
- Alzheimer's Association International Conference, *Toronto, CA/Virtual*
- Society of Neuroscience, *San Diego, CA*
- Aging Institute 16th Annual Research Day, University of Pittsburgh, *Pittsburgh, PA*
- Alzheimer's Disease Research Center, Optimizing Scientific Careers in AD Research (OSCAR) symposium, University of Pittsburgh, Pittsburgh, PA
- Fall Undergraduate Research and Creative Expression Fair, University of Pittsburgh, *Pittsburgh, PA*

CTF CONSORTIUM *–what's next?*

As part of our ongoing commitment towards impact, ensuring the most cutting-edge translational research remains supported, we are excited to share the development and release of an open request for proposal (RFP) for our 2026–2027 CTF Consortium funding cycle and beyond. Only multi-disciplinary collaborative based research proposals, gathering the final preliminary data needed for application to larger National Institute of Health (NIH)/National Institute of Aging (NIA) grant funding will be reviewed through this RFP. All funded research will remain in Pittsburgh as part of CTF's commitment to build the much needed bridges between promising science and life-changing outcomes for families impacted by dementia.

Clear Thoughts Foundation would like to acknowledge our dedicated team, who work tirelessly in support of our mission to fund the fight against dementia.

CTF Founders
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Sharon Sippel

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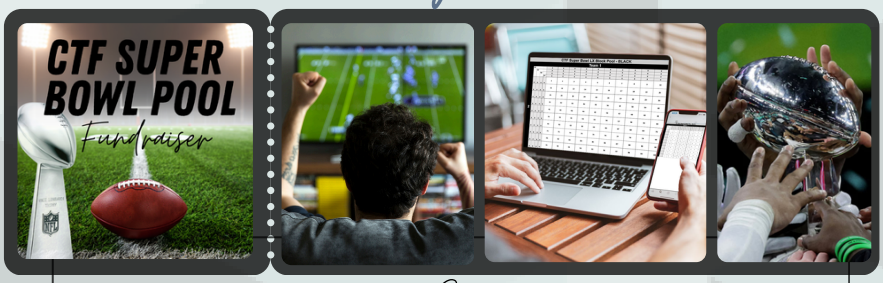
Cait Fenello

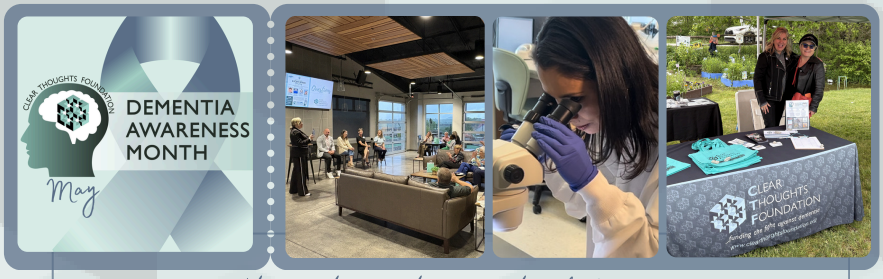
University of Pittsburgh Personnel
Justin Meyer

We thank you for your ongoing support of our vision to see a world free of dementia.

Join us for our *signature* events!



For every Super Bowl



Throughout the month of May

On the first Saturday in November

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