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# clear thoughts foundation Impact Report





# Introduction

Clear Thoughts Foundation is a nonprofit organization with a mission to fund breakthrough drugs and novel treatments to eliminate dementia. We are excited to release our first ever impact report, to help better communicate the influence of our mission and funded research on the ever growing problem of dementia.

This report will provide an in-depth look at Clear Thoughts Foundation's:

- CTF Consortium Research
- Collaborative Research Advancements
- Statistical Growth

CTF works to eradicate the growing problem of dementia to individuals and families both nationally and globally. The staggering statistics highlighted below express the magnitude of this problem in the United States alone.



## A Message From Our Founder & President



Hayley D. Jameson

Dear CTF Supporter,

2020 and 2021 were unlike anything we had envisioned. Clear Thoughts Foundation celebrated our 10 year anniversary amongst a pandemic that tragically took over a million lives, spurred countless racial injustices, and divided a nation. While we had all hoped 2021 would bring new hope and a fully-opened society, sadly it remained filled with trials and tribulations beyond measure due to the lingering effects of this horrific national pandemic.

Our hearts broke for those who were not allowed to see their dementia-stricken loved ones due to quarantining restrictions. The isolation and sheer desperation felt by those suffering from dementia and their loved ones during this pandemic increased the need and severity for all of us at CTF to passionately continue our mission to fund the fight against dementia.

I am incredibly proud of the ways in which Clear Thoughts Foundation continued to grow and adapt to our changing society. Over the past two years, CTF has continued upholding our mission through the inaugural launch of the CTF Consortium, which is truly a unique and novel approach to expedite drug and therapeutic discoveries to eliminate dementia. We continued to grow our board and engage with you, our invaluable donors, in new and exciting ways through virtual events and informative research panels. We welcomed our first ever CTF Dementia Awareness Month and look forward to continuing it on an annual basis.

Moving forward, CTF will continue to work relentlessly to engage with you to strive towards our shared vision to see a world free of dementia. Please know that we value each and everyone of you... for YOU are the reason we do what we do. We will not rest until this disease is nothing but an ugly memory and we live in a *world free of dementia*.

Yours in the fight,

Hayley D.

# Our Story to Date

#### CTF Historical Timeline



### Our Vision

To see a world free of dementia.

### Our Mission

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

### Our Research

The CTF Consortium's inaugural grant funding cycle allocated a total of \$150,000 to the collaborative research efforts over a two year period.



# A Story of Hope

Clear Thoughts Foundation (CTF) is a diverse, yet passionate group of individuals who share the common thread of having our lives touched by personal experiences with dementia. Lisa Sevcik, a long time CTF board member, knows the pain caused by this horrific disease through the tragedies of having lost her lost her husband, her mother, her grandmother, her uncle, and her father-in-law to various forms of dementia, including Frontotemporal dementia (FTD), Alzheimer's disease and Parkinson's. Lisa bravely shares her story below and explains why she continues to remain more compelled than ever to fund the fight against dementia.

I became involved with Clear Thoughts Foundation shortly after my husband, Matthew, died at age 50 due to complications from Frontotemporal Dementia (FTD). Our children were 8 and 11 years old when their father retired from practicing medicine in the prime of his career (Matthew was an Interventional Radiologist, a job which he had enjoyed and excelled at, in part because he truly loved helping people). It seemed like overnight our entire lives were sent into a tailspin. I became a single parent, and at the same time added another child to care for: this one six and a half feet tall, with dangerous abilities such as driving a car or running a chainsaw, and no filter on what he said, nor control over his uncharacteristic anger. Over the following five years, as Matthew's physical body aged to that of a geriatric man's, and his cognitive abilities declined to the level of a child, while also becoming mute, and unable



to read or write, let alone feed himself, our entire family suffered from the heartbreak and challenges of caring for our dad/husband/son at home, until we no longer safely could. Along with so many other painful decisions, moving Matthew into a memory care facility was a hard choice to make – both emotionally, and financially. Matthew was the youngest resident the facility had ever taken on, and for the last two years of his life our family schedule included constant visits to the man who had been the rock of our family – now hardly recognizable, and continually slipping away.



One might think that our story is an anomaly, and that someone being afflicted with dementia in their 40's is rare. However, along this path we were on, we met another family nearby with three similarly aged children and a mother in her late 40's suffering from early-onset Alzheimer's. Over the next few years, our two families would meet at a King's Restaurant, where we were given a side room where we could eat and visit with privacy. It was a relief for our children to know that whatever behavior their sick parent might exhibit, there would be no judgement, or embarrassment. Over time I heard about other young families, and also found a support group for early-onset dementia caregivers which met at a library. To this day I still have those friendships forged during the most trying part of my life, although none of our loved ones are still with us. Caregiving is exhausting, and lonely, and frustrating, and unrelenting, and I encourage everyone to seek out help through groups, or personal therapy. Too often, a caregiver will die before their ill loved one passes, because their own needs are neglected. Taking a break from caregiving is not frivolous, it is necessary for one's own precious health.

It was through Matthew's memory care facility that I met Hayley Jameson, one of the founders of Clear Thoughts Foundation. Hayley's father was at the end of his journey, also suffering from FTD, when Matthew moved in. Hayley and her brother, Matt, had promised their dad that they would pursue eradicating dementia diseases so that no other family would have to go through what they experienced – losing a loved one to a fatal, brutal disease which as of now has no treatments or cures. I immediately felt connected to Hayley, Matt, and the other CTF board members, and to our volunteers who selflessly help us spread awareness of our mission, because we have all been personally impacted by dementia. We know how important it is to find a cure or treatment, because with our aging population living longer, the numbers of those afflicted keep multiplying to epidemic proportions. This March, my mother died from Parkinson's after a 7 year battle, and I hear more and more from friends, as we age, that they are now taking care of a loved one with dementia: the seriousness of the diagnosis sinking in like the weight of an anchor. It is easy to feel helpless and hopeless. I know, I have been there.

However, since working with CTF I have felt hope, not despair. Funding research makes sense, as researchers strive to put together the puzzle of how our brains function, and how they fail. Science has made great strides, but time is of the essence. That said: each day brings us closer to a world free from dementia! I will continue to fight for a cure, because I cannot stop caring. Thank you to all our donors, who have joined us in this battle.

~ /isa Sercik

## Funded research: The CTF Consortium

#### **Inaugural Members**



#### Dr. Robert M. Friedlander, MD

Chair, Pitt Walter E. Dandy Professor; Head of Pitt Cerebrovascular Neurosurgery; Director of Pitt Complex Brain Surgery Program; Co-Director of UPMC Neurological Institute



#### Dr. Oscar L. Lopez, MD, FAAN

Pitt Professor of Neurology, Psychiatry, and Clinical and Translational Sciences; Levidow - Pittsburgh Foundation Endowed Chair in Alzheimer's Disease and Related Dementias; Director of Pitt Alzheimer's Disease Research Center; Chief of Pitt Cognitive and Behavioral Neurology Division



Dr. Amantha Thathiah, Ph.D. Pitt Assistant Professor of Neurobiology; Pittsburgh Institute of Neurodegenerative Diseases (PIND)

The CTF Consortium researchers are incredibly grateful for your generous support throughout 2020–2021, allocating \$150,000 to their research collectively. By providing funding to this group, you have helped to pave the way for progress in understanding the pathogenesis of dementia, specifically in most common form Alzheimer's disease, and the development of effective breakthrough drugs and novel treatments.

The CTF Consortium is a catalyst for uniting three highly productive research groups with complementary expertise. Conducting the right experiments at a faster rate through shared knowledge is a transformative approach to advance science and accelerate new treatments to stop the progression of dementia.

Provided in the pages to follow are in-depth reports of the advanced research progression of the CTF Consortium funded by your dollars. A separate section highlighting the collaborative threads can be found on page nine.



**Dr. Robert M. Friedlander** and his team have continued to pursue research to understand the role of melatonin in inhibiting neuroinflammation and slowing dementia in a preclinical mouse model. Research has shown that melatonin levels deplete severely with aging and more so in patients with Alzheimer's Disease (AD). Support from the CTF Consortium led to the establishment of a novel mouse model of age-related neurodegeneration genetically which was engineered not to make melatonin (AANAT-KO).

In vitro tissue culture of neurons from normal (wt) mice and AANAT-KO mice demonstrated that cultured neurons without melatonin have fewer synapses, the connections where neurons communicate to one another, than do neurons from mice that make melatonin.

Dr. Friedlander and his collaborator, Dr. Diane Carlisle, have been working to characterize the mouse model with the help of funding a part of the CTF Consortium. Specifically, they have shown that the AANAT-KO brain had higher levels of protein carbonylation and lipid peroxidation, suggesting that melatonin absence results in increased cerebral oxidative stress.

In the pineal gland, aralkylamine N-acetyltransferase (AANAT) is involved in the conversion of serotonin to melatonin. The knockout mouse lacks this key enzyme to make melatonin. Normal melatonin production was observed when looking at the pineal glands of wt mice, while only background levels of melatonin were seen in the AANAT-KO mice (Figure a). This demonstrated that the team successfully achieved what they set out to accomplish.

The ventricles of the brain are a network of cavities filled with cerebrospinal fluid (CSF). Further studies showed that ventricle volume increased in the AANAT-KO mouse brain compared to wt (Figure b), a clear indication of brain atrophy. Overall, knockout mice have normal sleep patterns (Figure c) suggesting that sleep defects are not contributing to the neurodegeneration in these mice. They will continue to study these mice for one year to fully characterize this mouse model and implement interventions that may block the accelerated aging process.

This new mouse model will be a resource that can be shared to move aging research forward for research scientists globally. Additionally, age-related cognitive decline, dementia, and age-related neurodegenerative disease have common modalities, and the progress made using this new research model of aging will be applicable to many other conditions and diseases with a future goal to identify new strategies for preventing age-related neurodegeneration, including dementia.





**Dr. Oscar L. Lopez** and colleagues recently released a report demonstrating that patients suffering from moderate Alzheimer's Disease (AD) showed improvement in neuropsychological tests of memory, language, and processing speed functions following treatment with plasma exchange (PE). Results from this human clinical trial showed that PE reduced the level of inflammatory biomarkers in blood and was effective in AD patients regardless of CSF Amyloid-beta (Abeta 42). Yet, the underlying mechanism remained unclear. Thus, it has been critical to conduct this research in an AD mouse model that can inform human studies.

Funding through the CTF Consortium has allowed for a longitudinal study testing the impact and efficacy of plasmapheresis treatment in mice as a potential intervention for amyloid plaque deposition.

Preliminary results showed that mice treated early with PE had reduced plaque accumulation, some improved blood vessel function, and increased blood flow in the brain. Improved cerebral perfusion is indicative of reduced inflammation. More importantly, treated mice showed significant slowing of amyloid plaque accumulation over time compared to untreated mice. Dr. Lopez plans to study the efficacy of plasmapheresis treatment in these mice for a total of 18 months and will further examine cognitive and functional improvements, memory, and pathology.



Longitudinal Amyloid Plaque Accumulation Normalized at 6 months old (treatment onset)

The ability to study PE in mice made possible through the CTF Consortium award offers a significant advantage to see how the brain reacts to the treatment in real-time. Imaging studies that measure amyloid deposition and blood flow during plasmapheresis provide key information, which is practically impossible to obtain when applying this technology to humans.

Dr. Lopez is currently working to establish a Plasma Exchange center at the University of Pittsburgh, the first of its kind in the United States, to develop therapeutic strategies that might slow or lessen the impact of this devastating illness.



**Dr. Amantha Thathiah's** research allowed for the development of an innovative model system to study the role of tau aggregation in dementia (optoTAU). Tau is a microtubule-associated protein that aggregates to form neurofibrillary tangles and cause neurodegeneration in the brains of patients with Alzheimer's disease, the leading cause of dementia. Dr. Thathiah's lab attached a photoreceptor to tau and called it optoTAU. Following expression of optoTAU in brain cells, stimulation with blue light induces the aggregation of optoTAU.

This technology is exciting and key for addressing crucial questions regarding the pathological aggregation of tau in Alzheimer's Disease and Frontotemporal Dementia (FTD).

Since there are mutations that cause FTD, Dr. Thathiah expressed normal tau (WT, wild type), tau with the FTD mutation (Pro) in cells. This mutation increases the propensity for tau to aggregate in the brains of patients. Using the optogenetic tau model, Dr. Thathiah showed that the Pro mutation leads to the formation of more tau aggregates than WT tau or tau with a mutation that is less aggregation-prone (ANTI). These studies indicate that the optoTAU system induces the formation of potentially physiologically relevant tau aggregates, thereby mimicking some of the characteristics of tau aggregation observe in patients with dementia.



Dr. Thathiah is also currently investigating whether the optoTAU model could serve as a drug screening platform for candidate inhibitors of tau aggregation and cell death, which ultimately lead to the cognitive impairment observed in Dementia patients. [TA1]

Dr. Thathiah will continue to use the optoTAU model to understand the crosstalk between amyloid plaques and tau. She is developing an optoTAU mouse model and is beginning to test if tau aggregation can be induced in mice using this optogenetic technology. She will create an in vitro system that represents a physiologically relevant model for AD patients to test for inhibitors of tau aggregation.

## CTF Consortium Collaboration

The CTF Consortium supports three unique researchers, all focused on finding drugs and/or treatments to ultimately eliminate dementia. The excitement of this new model, is found within their overlapping entities, that when explored together can accelerate research advancements and double or even triple funding impact. The chart provided below highlights the areas in which collaboration throughout this research has taken place.

#### RESEARCHERS COLLABORATION OUTCOME

Dr. Friedlander & Dr. Thathiah	Developed breakthrough aging mouse model (Alzheimer's disease)	<ul> <li>Uses shared mouse model to test and understand brain aging and melatonin impact on dementia, as well understand the role of G- protein receptors and tau</li> <li>Identified a link between the G- protein coupled receptors and melatonin's prevention of dementia, further exploration needed</li> </ul>
Dr. Friedlander & Dr. Lopez	Clinical application	<ul> <li>Alzheimer's disease mouse model utilized in Plasmapheresis trials to understand the clinical impact– dosage of these treatments for proper prevention of dementia</li> </ul>
Dr. Friedlander, Dr. Lopez, & Dr. Thathiah	Overall shared research findings	• Frequent discussion of project findings provided the development of new potential research avenues to be explored for disease prevention

## CTF Consortium Funding Continued

CTF plans to continue funding the CTF Consortium throughout 2022–2023, building on the strength of the research previously accomplished. The CTF Consortium's next proposed effort is to develop a preclinical model for understanding melatonin signaling, mitochondrial function, and neuronal survival in Alzheimer's disease.

Building on preliminary results from Dr. Thathiah's lab that are distinct from the tau aggregation studies, the CTF Consortium proposes to test the hypothesis that a large family of signaling proteins known as G-protein coupled receptors (GPCR) malfunction with age and predispose the brain to begin to slide into dementia. While this area of exploration is new for the CTF Consortium, the work links with the previous project on melatonin spearheaded by Dr. Friedlander's lab. The linkage is due to the fact that the melatonin receptor belongs to the GPCR family, although a different branch from GPR3. This work proposes two specific aims. The first – based in Dr. Thathiah's lab – is to determine whether GPR3 localizes to mitochondria and is involved in the loss of neurons that occurs during dementia. The second – based in Dr. Friedlander's lab – is to determine whether abnormalities in melatonin signaling are also related to neuronal death.

This collaborative research conducted by both Dr. Thathiah and Dr. Friedlander's labs will have further implications to not only advance Dr. Lopez's clinical research, but also be utilized for application to larger funding grants for preclinical patient trials to further explore the impact of melatonin on dementia.

# Sharing our research...



The annual CTF Connect event was held virtually as the pandemic continued to persist throughout 2021. This educational panel discussion was facilitated by CTF's Chief Scientific Advisor, Dr. Karl Herrup, and featured all three CTF Consortium researchers to share their recent discoveries and advancements. These research updates were shared with many individuals through livestream and video recording.

# CTF Highlights

CTF continued their diligent work of raising funds and awareness through garnering unique media and community features throughout 2020 – 2021. To read, listen, or view these full features, visit CTF's *News and Events* website tab.







April

Jonathan Kersting and Audrey Russo of TechVibe Radio interviewed CTF Founder and President, Hayley Jameson, about how both Clear Thoughts Foundation and HDJ + Associates are managing to push through the unprecedented times of COVID-19.

Dr. Robert Friedlander, Professor and Chairman of Neurosurgery, Neurology and Neurobiology at the University of Pittsburgh, discussed his exciting research with the CTF Consortium on his weekly virtual neurological video cast. Clear Thoughts Foundation Founder and President, Hayley Jameson, was invited to discuss her personal experience with dementia and CTF's mission to fund dementia research.





Pittsburgh Pirates manager, Derek Shelton, generously wore a Clear Thoughts Foundation t-shirt during his pre-game interview in Cincinnati, Ohio. The Pirates announced their campaign to feature varying local non-profit organizations during pre and post game interviews throughout the 2020 season.

While COVID had placed many challenges on in-person events in 2020, CTF quickly adapted and held their annual Roll for a Reason Gala virtually! Guests helped raise a total of \$94,340 for dementia research from the comfort of their own living room with host Pittsburgh WDVE legend, Randy Baumann. There were performance paintings by George Williams and Cody Sabol; musical performances by Chris Jamison, Paul Luc, and Clinton Clegg of the Commonheart; mind bending magic by Lee Terbosic; as well as several other exciting features such as a virtual roulette game, party bags, a raffled trip to Aruba for up to six people, and an online auction! November



#### December



CTF was selected by The Pittsburgh Foundation to be a recipient non-profit organization within their 2020 Wish Book campaign. The Wish Book is a printed soft-cover book that is mailed to The Pittsburgh Foundation's donor community every November/December to fulfill various non-profit "wishes". CTF's very own board member, Lisa Sevcik, was featured on the Wish Book funds request page and CTF was awarded a total of \$5,000 in unrestricted operating funds.



WISH BOOK 2020 Production Biogram

University of Pittsburgh School of Medicine, PITT MED Magazine Spring 2021 edition, featured the work of the CTF Consortium funded by Clear Thoughts Foundation. This feature can be found on pg. 35 of the digital edition posted on CTF's website.





CTF launched its first ever Dementia Awareness Month in May of 2021, partnering with senior living facilities, local restaurants, fitness facilities, corporate sponsors, and more to spread dementia education, research awareness, and hope that one day we will live in a world free of dementia together! This initatitive reached 438 individuals directly in the community and raised a total of \$11,291 dollars for dementia research.

Clear Thoughts Foundation held their annual CTF Connect event, this time in a virtual format. This educational panel discussion was facilitated by CTF's Chief Scientific Advisor, Dr. Karl Herrup, and featured all three CTF Consortium researchers to share on their recent discoveries and advancements. Viewers participated in a short Q&A session following the presentations.





CTF's Chief Scientific Advisor, Dr. Karl Herrup, offered his critical analysis on the FDA's decision to approve new Alzheimer's drug, Aducanumab (please note that the opinions expressed do not necessarily reflect those of CTF). CTF works to keep you informed by providing a variety of gleaned opinions on all news related to dementia research.

CTF proudly earned a 2021 Guidestar Gold Transparency Seal. The GuideStar Seals of Transparency indicates that a nonprofit has provided key information to its GuideStar profile, showing a commitment to transparency to the world. By providing up-to-date information, CTF allows potential donors and funders to stay informed on all gift decisions.





CTF was one of 10 finalists in Clearview Federal Credit Union's 'Tee It Up For Charity' video contest. After two weeks of public online voting, CTF secured 3rd place, winning a total of \$1,250 towards our mission of funding the fight against dementia.



CTF was selected by the glassybaby foundation to receive a \$2,000 grant in support of our mission to fund the fight against dementia. glassybaby is a handblown glass company based in Seattle, WA. September



Chris Mack repped a CTF t-shirt on 93.7 The Fan's morning show, a part of Chris Mack's ChariTees initiative.

This helped to spread the word about CTF's mission and upcoming Roll for a Reason Gala.

#### November



The Pittsburgh Post-Gazette 'SEEN' column captured all the memories, moments, and excitement of CTF's Roll for a Reason Gala, back in person and raising over \$150,000 for dementia research! <text><text><text><text><text><text>

shared on LinkedIn the exciting experience of helping to make our annual annual Roll for a Reason Gala a success - reaching over 1,000 views!

A new volunteer to CTF

## The Stats

### **Research Funding**

The numbers below outline the increase in CTF's allocated research funding from 2019 to the CTF Consortium in 2020 & 2021.



Years



our mission

### **Online Presence**

The numbers below outline the increase in CTF's presence across various social media platforms and website.



## **BIG Impact, BIG Reward**

Helping CTF helps you! You can make a lasting impact on our mission to fund dementia research while receiving several tax benefits – below are a few ways that your partnership can benefit both the continuation of our research as well as yourself!



## **Donor Advised Funds**

A donor-advised fund account is a simple, tax-smart investment solution for charitable giving. You can contribute cash, securities, or appreciated assets throughout the year to CTF, making you eligible for a current year tax deduction on all giving decisions made from this fund. Your charitable gifts to CTF and other non-profit foundations can be managed from this fund account for ease of collective year end annual reporting.

## **Gifts of Stock**



Donating your stock or other securities (bonds, mutual funds, etc.) is an easy way to support our mission while providing you wonderful tax benefits. For example, if your stock has increased in value from the time of your purchase, you can avoid paying the capital gains tax by donating the stock to CTF.

## **Charitable Gift Annuity**

A charitable gift annuity, or CGA, allows you as the donor to make a lump-sum donation to CTF and receive a lifetime income in return. At the time of your donation, you receive a partial tax deduction, and CTF puts up to half of your initial donation towards its mission. You will then receive annual payments per the terms of the annuity agreement for life, with CTF receiving the balance of the invested funds upon passing. A win – win to both help research growth now, while supplying annual income payments to you for the duration of your lifetime!

## RoundUp App

We get there are a lot of awesome causes out there that you are interested in supporting! This option is a small change to make for big changes towards our mission. We are partnered with the RoundUp App, which allows you to "round up" the change from your daily debit or credit card purchases and donate it to CTF directly on a monthly basis. This is a simple way to consistently fund the fight against dementia, just by donating your change! You can download the app for iPhone, Android or create an account on the Web.

For all inquiries or questions in regards to the listed ways above to support Clear Thoughts Foundation, please contact CTF at info@clearthoughtsfoundation.org or 412.407.7170.

## We thank you for your ongoing support of our mission to fund dementia research.

## Acknowledgements

Clear Thoughts Foundation would like to acknowledge several groups of individuals who work tirelessly in support of our mission to fund the fight against dementia. In addition, CTF is grateful to be partnered with the brilliant researchers who are utilizing their scientific expertise to bring us all closer to living in a world free of dementia. Below are those committed to our mission and research:

#### **CTF Founders**

Hayley D. Jameson, Founder & President D. Matthew Jameson, Co-founder & Secretary Sharon Sippel, Co-founder & Board Member Emeritus

*CTF Board Members* Lisa Sevcik, Adam Zaccari, Megan Markley

CTF Chief Scientific Advisor Dr. Karl Herrup

#### **CTF Board Advisors**

Gary Napotnik, Bob Ward, Jim Cook, Justin Shal, Tim Campbell, Kevin Jameson, Jerry Shafran, Melissa Redman, Beth Scott, Julie Allard, Tim Tannert, Nate Joseph

**CTF Executive Director** Cait Fenello

*CTF Consortium Researchers* Dr. Robert Friedlander, Dr. Oscar Lopez, Dr. Amantha Thathiah

#### University of Pittsburgh Personal

Justin Meyer, Lauren Ward, Jodi Fowler

All CTF Supporters, In-kind Donors, and Contributors

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