



1000

Reasons for **Hope**

How the first **1,000 Legacy Donors** studied at the VA-BU-CLF Brain Bank are mapping the future of brain trauma research



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We dedicate *1,000 Reasons for Hope* to our **Legacy Donors** – our term for our brain donors. We call them Legacy Donors to honor them and to highlight the legacy they've left through the scientific research chronicled in this report. Everyone involved with the **U.S. Department of Veterans Affairs-Boston University Concussion Legacy Foundation Brain Bank** is forever indebted to our Legacy Donors and their families who trusted us with their loved one. Thanks to their selfless contributions, we have so many reasons for hope.

Executive Summary

In 2007, CLF co-founder **Chris Nowinski** met **Dr. Ann McKee**, one of the world's foremost experts on neurodegenerative disease. Nowinski, a former Harvard football player and WWE professional wrestler who retired due to concussions, had an important question.

Chris Nowinski, PhD, is co-founder and CEO of the Concussion Legacy Foundation and the outreach, recruiting, & education leader for the Boston University CTE Center.



“If CLF works with families to get permission to study the brains of deceased football players, would you be willing to study them and help us understand the degenerative brain disease CTE?”

At the time, only 45 cases of Chronic Traumatic Encephalopathy (CTE) had been published in the literature. Most of the studies concerned boxers and were published over 40 years before, and little was known about the disease.

Dr. McKee said yes, and the rest is history. The VA-BU-CLF Brain Bank, directed by Dr. McKee, was launched in 2008 as a collaboration between three organizations: the Boston VA Healthcare System, Boston University School of Medicine, and the Concussion Legacy Foundation. Over the next 13 years, more than 1,000 amazing families donated their loved one's brain to the research. The work quickly expanded beyond former football players to include all contact sport athletes, military Veterans, victims of interpersonal violence, and most recently, single traumatic brain injuries. The research team has published more than 100 original studies and has redefined our understanding of the long-term effects of head impacts. The work has sparked a global revolution in concussion and brain trauma awareness and changed how we play sports.

Our initial goal was to understand CTE's neuropathology and pathogenesis, clinical presentation, genetics and other risk factors, and biomarkers. With these insights, we could advance CTE prevention, methods of detection during life, and treatment. This report provides a window into what we have learned and celebrates those who made it possible: the generous brain donors and their families, the dedicated scientists and research teams, the diligent outreach teams, the funding organizations and philanthropists.

Even with all we have accomplished so far, what excites us the most is the prospect of what the next 1,000 Legacy Donors will teach us. Researchers for similar diseases published their most important findings only when they surpassed the statistical strength of thousands of donated brains. As you read this report, you will meet our brain donor families, see the game-changing discoveries made by VA-BU-CLF Brain Bank researchers, and learn what the future of research can achieve with your support.

1,000 Reasons for Hope



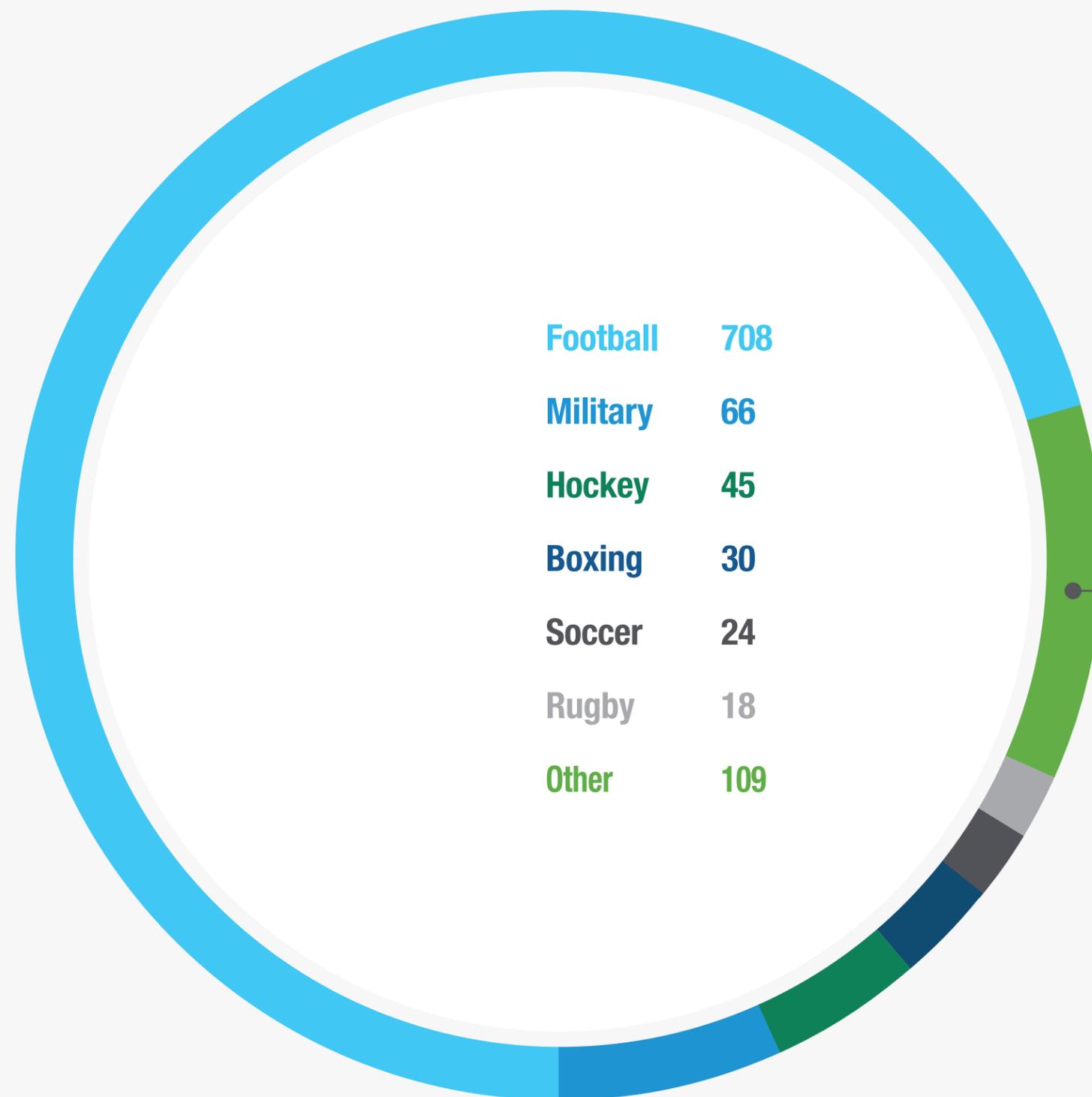
Ann McKee, MD, is the Director of Neuropathology for the Boston VA Healthcare System, the William Fairfield Warren Distinguished Professor of Neurology and Pathology at Boston University, and Director of the BU CTE Center.

Primary Exposure of Donors

Prior to 2005, there were only 45 cases of CTE ever diagnosed in the world's medical literature. 39 were boxers, which is why CTE was first called "Punch Drunk".

The other six cases comprised three victims of abuse, one entertainer, and one amateur soccer player. The world knew almost nothing about CTE, and CLF recognized that the only way to learn about CTE was to recruit at-risk brain donors and learn from them. We thank our VA-BU-CLF Brain Bank Legacy Donors for teaching us that CTE is not just a disease of boxers; a far wider population of athletes are at risk for CTE, as are military Veterans and first responders.

The public's eyes have opened to the scope of populations affected by repetitive brain trauma.



Amateur Wrestling	15
Martial Arts	10
Non-sport TBI	10
Baseball	8
Lacrosse	7
Entertainers	7
First Responders	5
Basketball	4
Domestic Violence	4
Extreme Sports	4
Equestrian	4
Gymnastics	4
Sliding Sports	3
Rodeo	3
Swimming	2
Cycling	2
Ski & Snowboard	2
Field Hockey	2
Volleyball	2
Head Banging	2
Auto Racing	1
Tennis	1
Track & Field	1
Water Polo	1
No Exposure	5

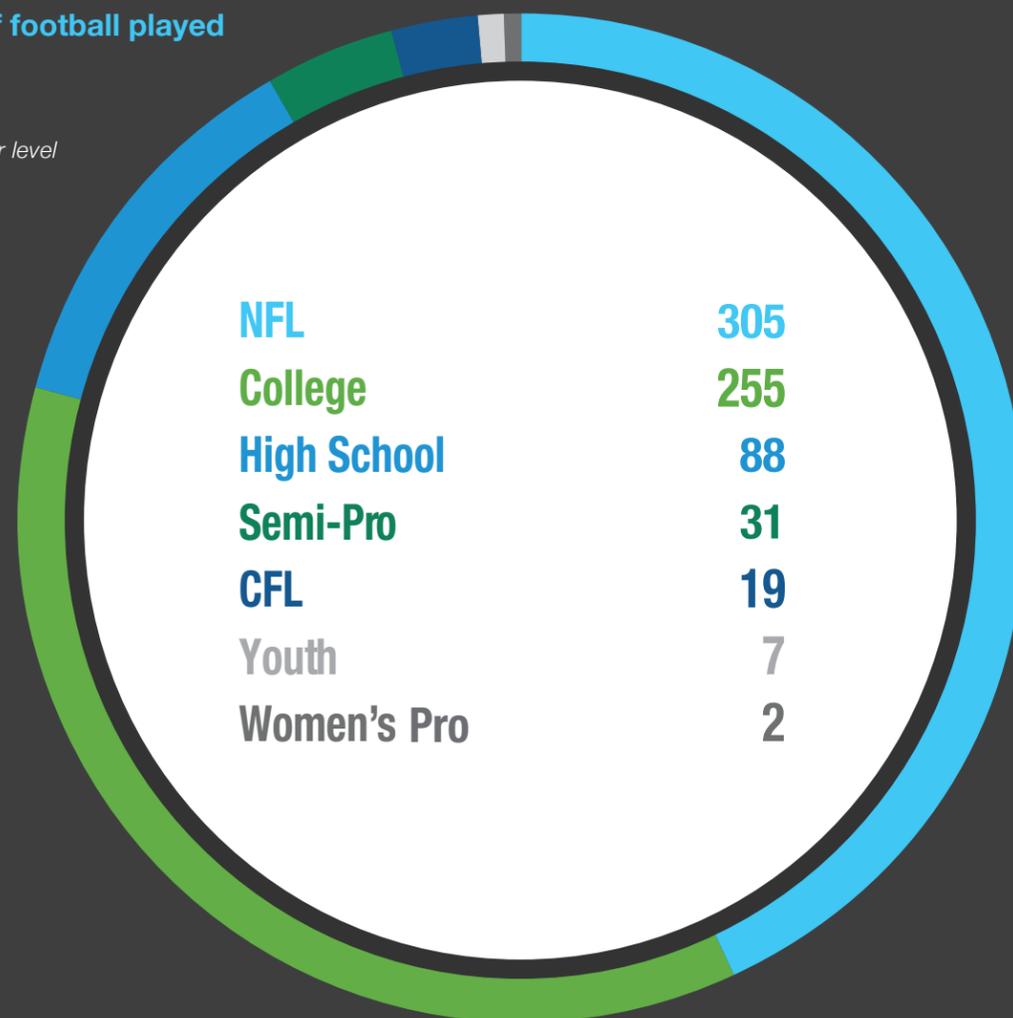
Football Donors and Firsts

The Link Between Football and CTE

More than 70 percent of our Legacy Donors were football players, so we know more about that population than any other. They have taught us that each year of playing football may increase a player's odds of developing CTE by as much as 30 percent. More than 1 in 4 deceased NFL players now become Legacy Donors, which is providing an unprecedented window into the population that played football the longest.

Highest level of football played among donors

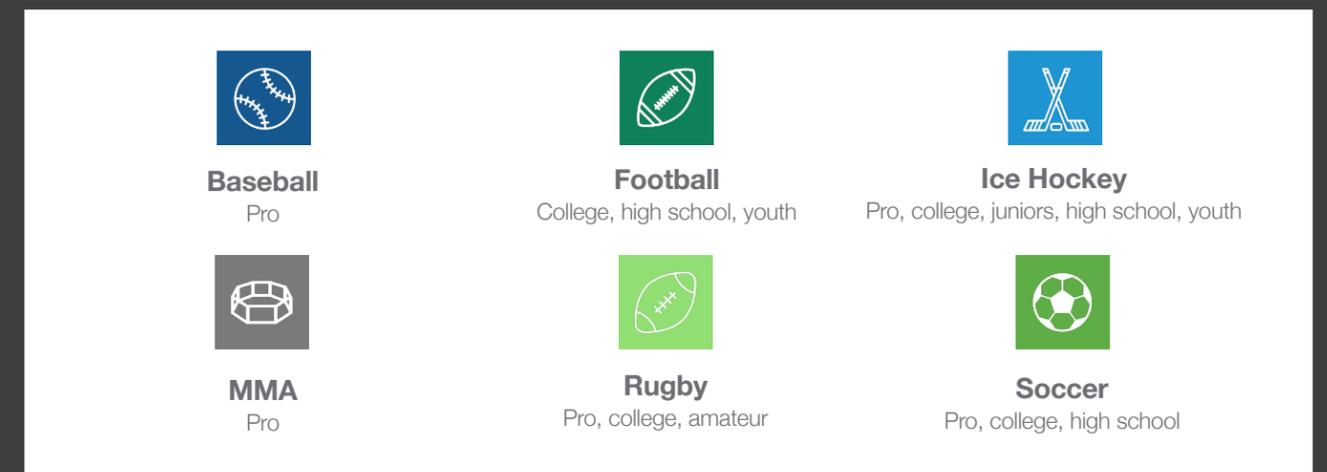
Number of donors per level of football played.



Firsts in CTE Awareness in Sports

By discovering the first cases of CTE in multiple new sports and at the professional, collegiate, and high school levels, our research has moved the CTE conversation beyond boxing and the NFL, and directly inspired safety reforms for children. Below are some of the firsts in CTE we have discovered over the years.

First CTE Cases Identified In:



CTE Discoveries Inspire Sports Reforms

Ice Hockey
In 2009, we diagnosed the first NHL player with CTE. In 2011, USA Hockey **banned checking up to age 13.**



Soccer
In 2014, we diagnosed the first American soccer player with CTE. In 2015, U.S. Soccer **banned heading until age 11.**



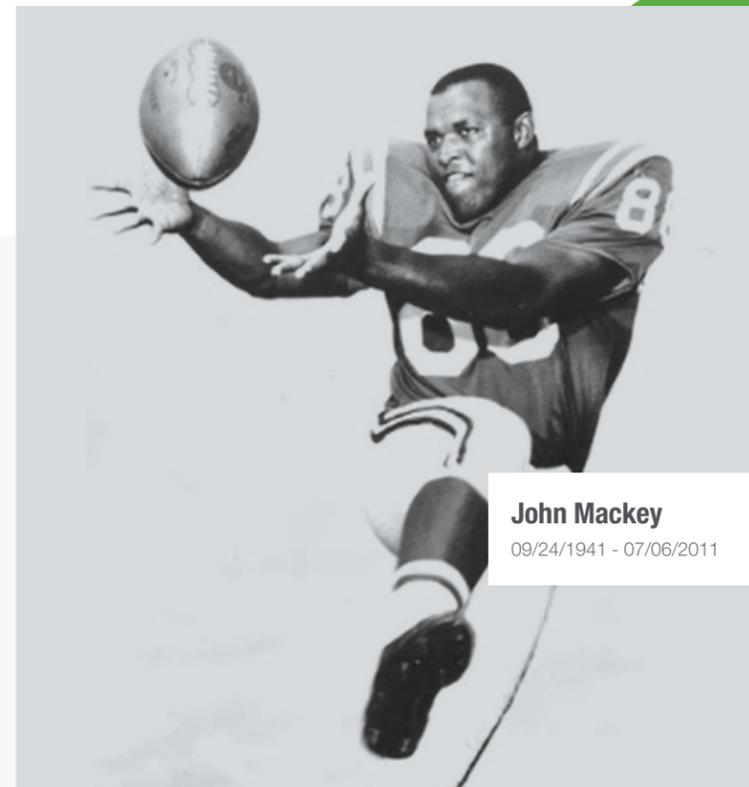
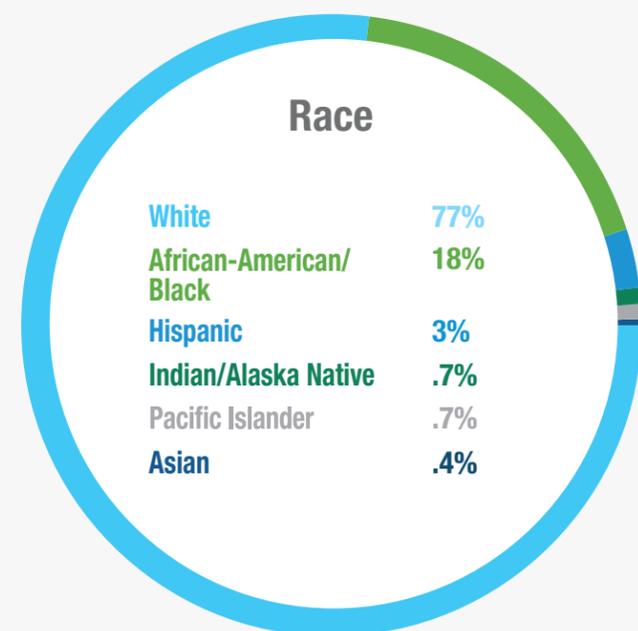
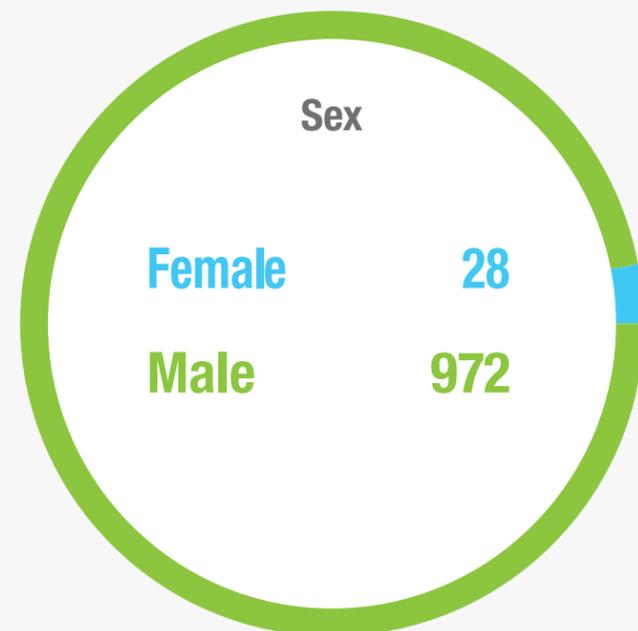
Sex and Race of Donors

It is imperative to understand how brain trauma may differentially impact men and women, as well as individuals of different racial backgrounds.

Recruiting female Legacy Donors has proven difficult, likely due to two main causes. First, most of our donors' primary exposure is American football, which is played almost exclusively by men. Second, Title IX legislation was not passed until 1972, meaning the majority of women who have played organized sports, including contact sports with higher risks of brain trauma, are younger than 70 years old.

The Brain Bank is more diverse when it comes to race, but it is influenced by the history of race relations in America. Collegiate and professional football excluded many Black players from playing football until the late 1960s, which results in the majority of our oldest Legacy Donors who played football being white. Ice hockey, the sport which has produced the second-most Legacy Donors, is not a historically racially diverse sport.

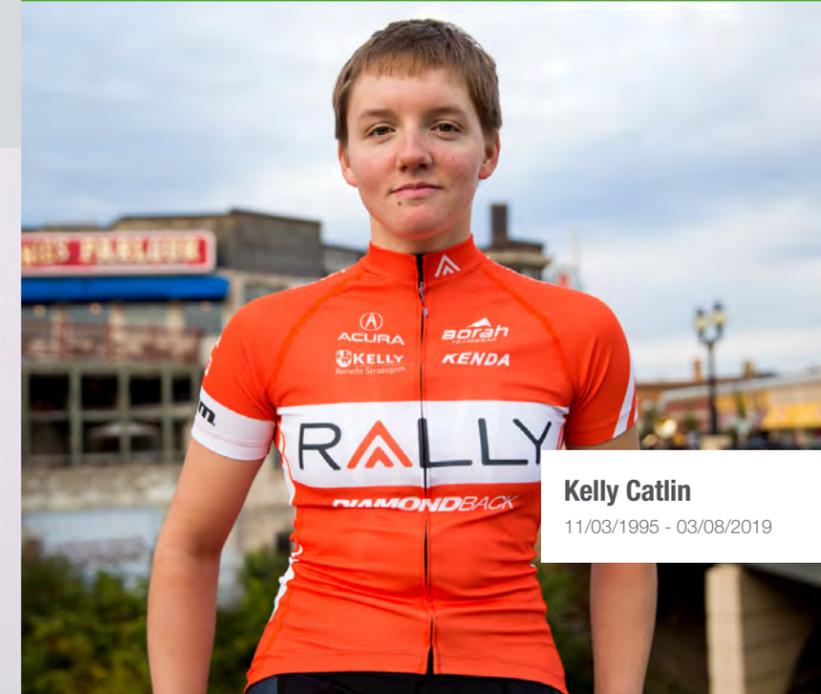
We are actively recruiting more female research participants, athletes, and Veterans from diverse racial backgrounds to ensure our discoveries benefit all.



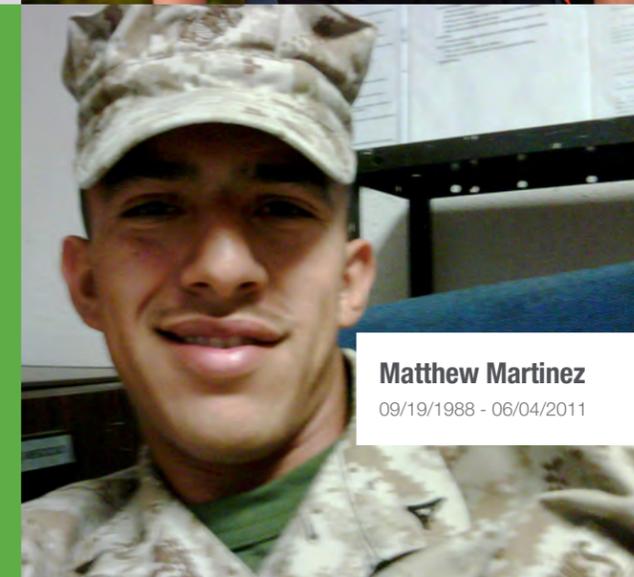
John Mackey
09/24/1941 - 07/06/2011



Rowan Stringer
06/25/1995 - 05/12/2013



Kelly Catlin
11/03/1995 - 03/08/2019



Matthew Martinez
09/19/1988 - 06/04/2011

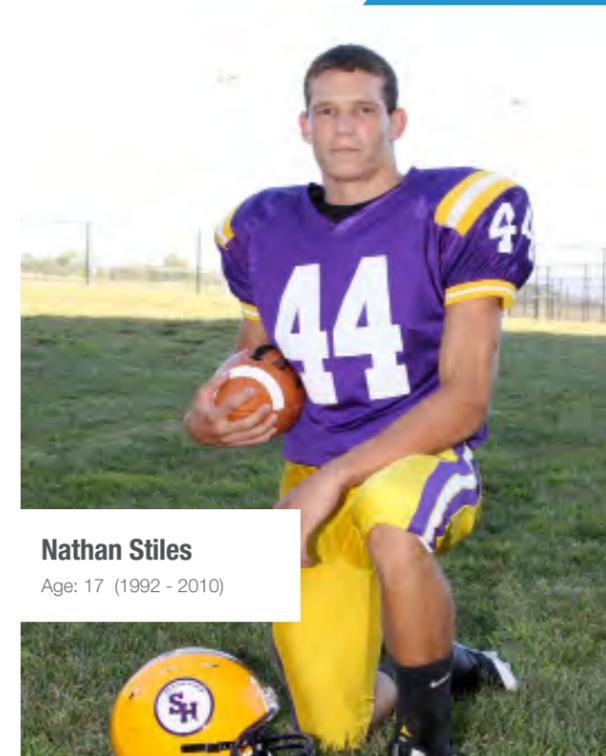
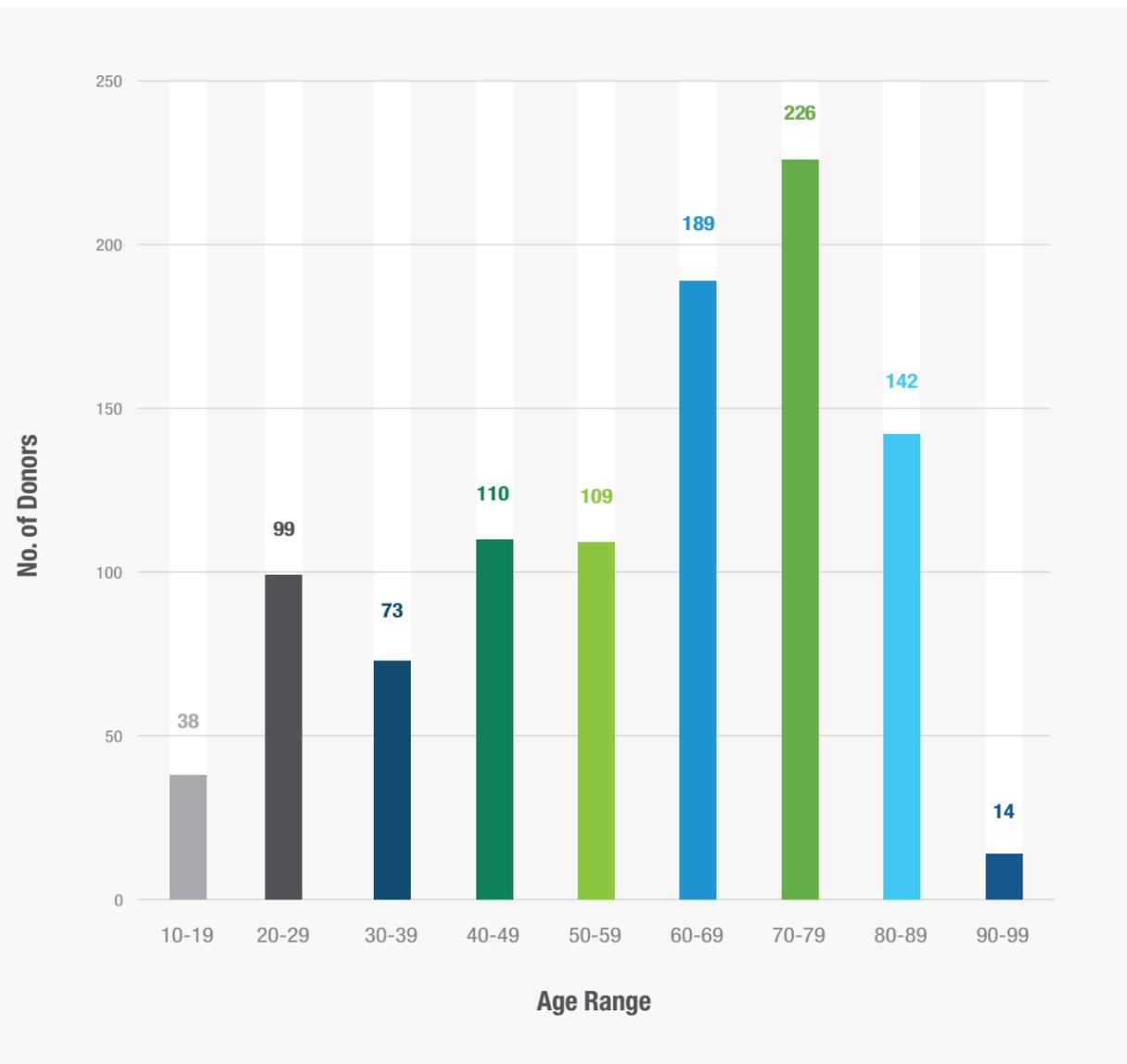
We are actively recruiting more female research participants, athletes, and Veterans from diverse racial backgrounds to ensure our discoveries benefit all.

Decade of Death

The Brain Bank has received tissue from donors who died as young as age 14 and as old as age 98.

The VA-BU-CLF Brain Bank is the only brain bank in the world that has studied CTE from its earliest beginnings to its final stage. With more than 135 donors under age 30, more than half

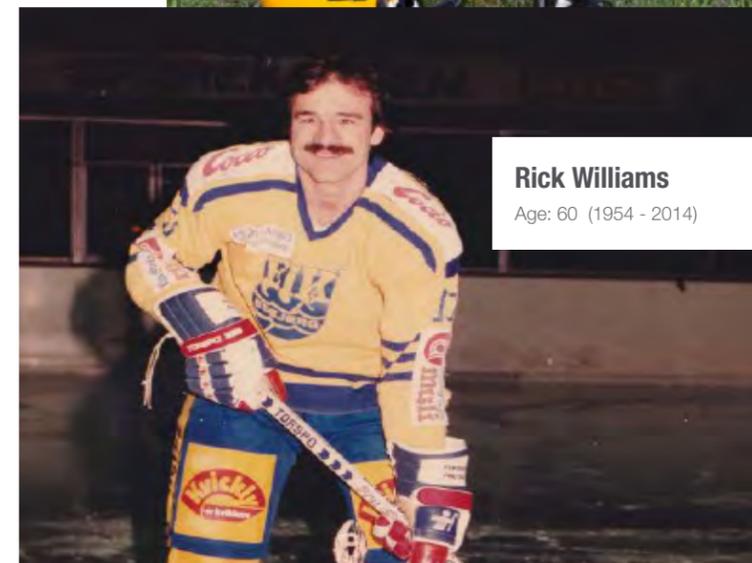
of whom had CTE, this research has provided the world's first window into the earliest stages of CTE, including how and where it begins forming in the brain. The number and diversity of Legacy Donors has enabled the National Institutes of Health (NIH) to produce the first consensus pathologic diagnostic criteria for CTE as well as the first consensus staging system.



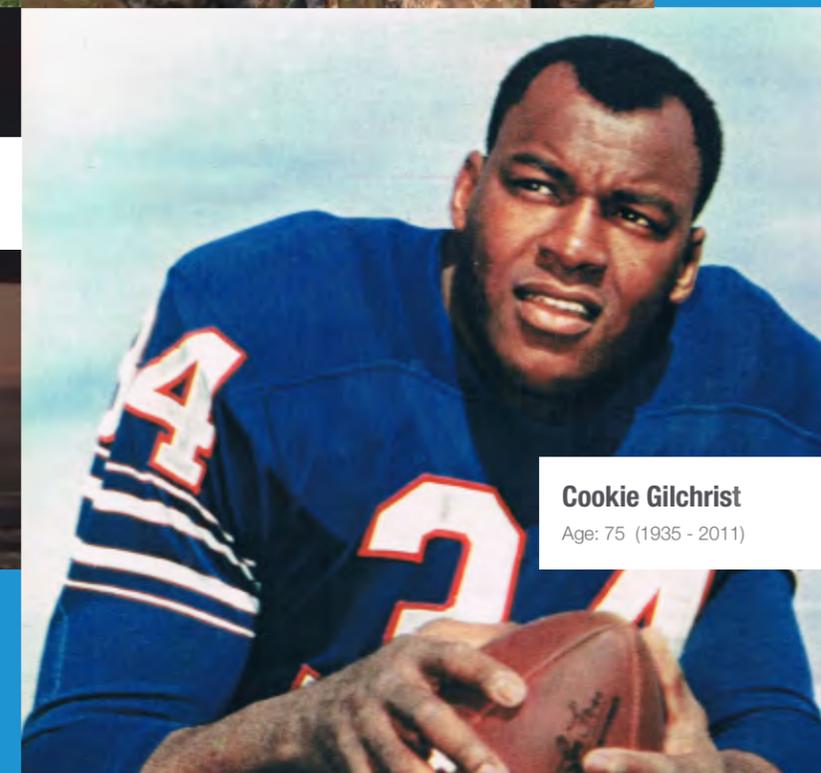
Nathan Stiles
Age: 17 (1992 - 2010)



Kevin Ash
Age: 34 (1982 - 2017)



Rick Williams
Age: 60 (1954 - 2014)



Cookie Gilchrist
Age: 75 (1935 - 2011)

10

Landmark Studies

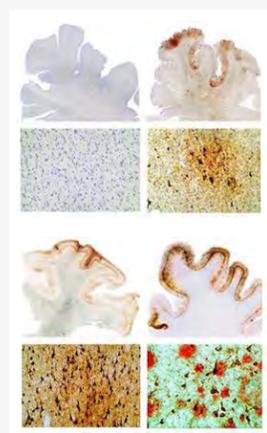
Since 2008, the VA-BU-CLF Brain Bank has published more than 100 game-changing studies. Here, we spotlight 10 breakthrough studies published by Brain Bank researchers since 2009.

2009

Chronic Traumatic Encephalopathy in Athletes: Progressive Tauopathy After Repetitive Head Injury

Journal of Neuropathology & Experimental Neurology

We review 48 cases of neuropathologically verified CTE recorded in the literature and document the detailed findings of CTE in three professional athletes (one football player and two boxers).

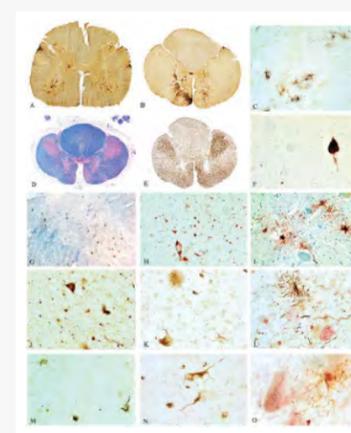


2010

TDP-43 proteinopathy and motor neuron disease in chronic traumatic encephalopathy

Journal of Neuropathology & Experimental Neurology

In some individuals with CTE, the TDP-43 proteinopathy extends to involve the spinal cord and is associated with motor neuron disease. This was the first pathological evidence that repetitive head trauma experienced in collision sports might be associated with the development of a motor neuron disease.

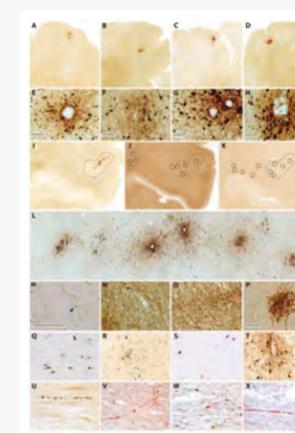


2012

Chronic Traumatic Encephalopathy in Blast-Exposed Military Veterans and a Blast Neurotrauma Mouse Model

Science Translational Medicine

These results identify common pathogenic determinants leading to CTE in blast-exposed military Veterans and head-injured athletes and additionally provide mechanistic evidence linking blast exposure to persistent impairments in neurophysiological function, learning, and memory.

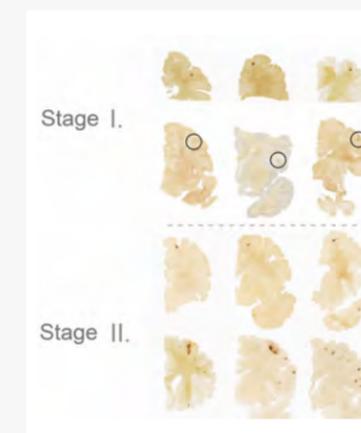


2013

The spectrum of disease in chronic traumatic encephalopathy

Brain

The frequent association of chronic traumatic encephalopathy with other neurodegenerative disorders suggests that repetitive brain trauma and hyperphosphorylated tau protein deposition promote the accumulation of other abnormally aggregated proteins including TAR DNA-binding protein 43, amyloid beta protein and alpha-synuclein.

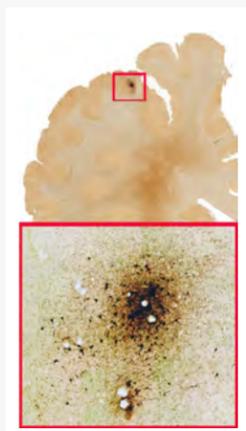


2016

Tau prions from Alzheimer's disease and chronic traumatic encephalopathy patients propagate in cultured cells

Proceedings of the National Academy of Sciences

The progressive nature of neurodegenerative diseases is due to the spread of prions, misfolded infectious proteins, in the brain. This study established that CTE prions are distinct from prions in other tauopathies such as Pick's disease and progressive supranuclear palsy.

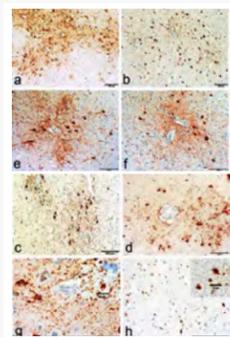


2016

The first NINDS/NIBIB consensus meeting to define neuropathological criteria for the diagnosis of chronic traumatic encephalopathy

Acta Neuropathologica

The first consensus criteria endorsed by the National Institutes of Health for the pathological diagnosis of CTE was made possible by the VA-BU-CLF Brain Bank. In 2015, eminent neuropathologists from around the world, along with observers from the National Institute of Neurological Disorders and Stroke and the National Institute of Biomedical Imaging and Bioengineering, gathered at Boston University School of Medicine to review cases at the Brain Bank.

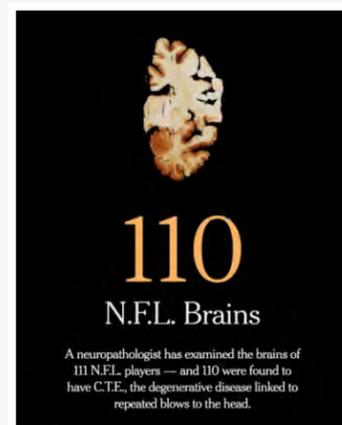


2017

Clinicopathological Evaluation of Chronic Traumatic Encephalopathy in Players of American Football

Journal of the American Medical Association

Among 202 deceased former football players, CTE was neuropathologically diagnosed in 177 players (87%); including 0 of 2 pre-high school, 3 of 14 high school (21%), 48 of 53 college (91%), 9 of 14 semiprofessional (64%), 7 of 8 Canadian Football League (88%), and 110 of 111 National Football League (99%) players.

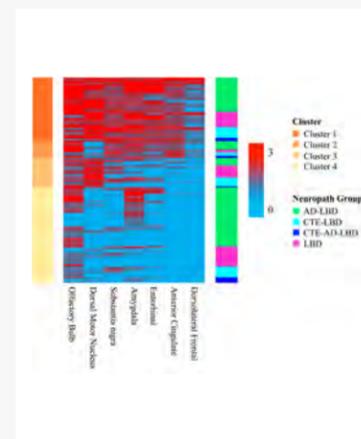


2018

Lewy Body Pathology and Chronic Traumatic Encephalopathy Associated with Contact Sports

Journal of Neuropathology and Experimental Neurology

Contact sports participation may increase risk of developing neocortical Lewy Body Disease, and increased Lewy Body Disease frequency may partially explain extrapyramidal motor symptoms sometimes observed in CTE.

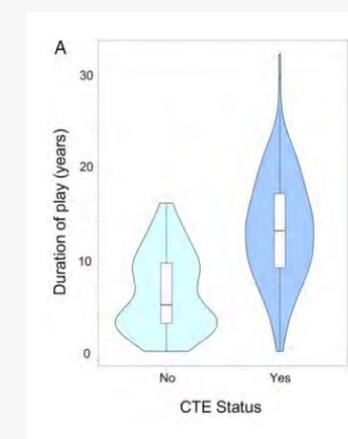


2019

Duration of American Football Play and Chronic Traumatic Encephalopathy

Annals of Neurology

A study of 266 football players, of which 223 had CTE, explored risk factors affecting CTE status and severity. The study revealed that each year of tackle football participation increases the odds of developing CTE by 30 percent and increases the odds of having severe CTE by 14 percent. The findings inspired CLF's award-winning "Tackle Can Wait" campaign.

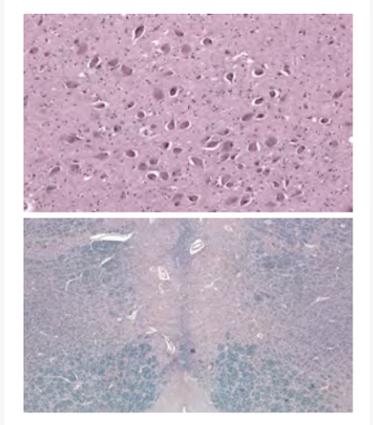


2020

Association of probable REM sleep behavior disorder with pathology and years of contact sports play in chronic traumatic encephalopathy

Acta Neuropathologica

Probable REM Behavior Disorder (pRBD) in CTE is associated with increased years of contact sports participation and may be attributable to Lewy body and brainstem tau pathologies. Athletes with CTE were 32 times more likely than controls to have pRBD.



Family Testimonials

The decision to donate a loved one's brain is often motivated by an interest in helping others. In addition, having watched their loved one suffer, many of our Legacy Donor families want to better understand why their loved one changed.

The results of VA-BU-CLF Brain Bank research can offer insight into their loved one's life, although it doesn't always provide every answer. We asked a few members of CLF's Legacy Family Community to reflect on the decision to donate their loved one's brain for research.



Dwayne Johnson

Son of Rocky Johnson

"I'm very grateful for the insight the Concussion Legacy Foundation has been able to provide me and my family. Losing my dad without warning was a tough kick in the gut, but one of the saving graces of his passing was coming to understand just how healthy his brain was.

As a professional wrestler his entire life, his brain endured a lot. I know he'd be proud knowing the donation of it has impacted brain research and hopefully can shed some light and understanding, not only in science, but also to other families around the world.

Thank you to my good friend, Dr. Chris Nowinski and his brilliant cadre of doctors for their research."



Gail Evans

Widow of James Evans

"I am so very grateful to have donated my husband James' brain. It provided my family and I with final closure, gave us light into a world that had darkened around us, and provided us with understanding and peace. It returned a husband to his wife and a father to his two girls."



Patty Pae

Daughter of Dick Proebstle

"My family is so grateful the Concussion Legacy Foundation was available at the time of my father's death. We have been able to receive answers on the cause of my father's death while also providing a platform to honor him and advocate for others affected by concussions and brain trauma."

Leaving a Legacy

Through programs like **My Legacy** and **Project Enlist**, CLF leads outreach for the **VA-BU-CLF Brain Bank**. My Legacy encourages former athletes and controls to take the #MyLegacyPledge to donate their brain to advance research and raise awareness for brain donation. CLF's Project Enlist is recruiting and conducting outreach to the military and Veteran communities to sign up for research to help solve the invisible wounds of war.

Professional athletes Brandi Chastain, Leonard Marshall, and Elana Meyers Taylor, and decorated military Veteran LT Jason Redman encourage widespread participation in My Legacy and Project Enlist when they share why they pledged to donate their brains.



Brandi Chastain

2x Women's World Cup Champion

"People say, 'Oh, you left a legacy for the next generation.' This would be a more substantial legacy — something that could protect and save some kids, and to enhance and lift up soccer in a way that it hasn't before."

Leonard Marshall

2x Super Bowl Champion

"CTE is no joke and I don't want to see anyone else suffer like me and my friends. This is literally a life-and-death matter, and it's time we start having real, honest conversations about brain trauma in professional and youth sports."

Elana Meyers Taylor

3x Olympic Medalist Bobsledder

"The long-term consequences of brain trauma are a major concern in sports, and I'm doing this for every athlete who will follow in my footsteps."

LT Jason Redman

Retired U.S. Navy SEAL

"I have seen too many good people take their lives after combat and traumatic brain injury. All signs point to CTE but we do not have enough research on combat Veterans' brains. I donated mine to help future Veterans."

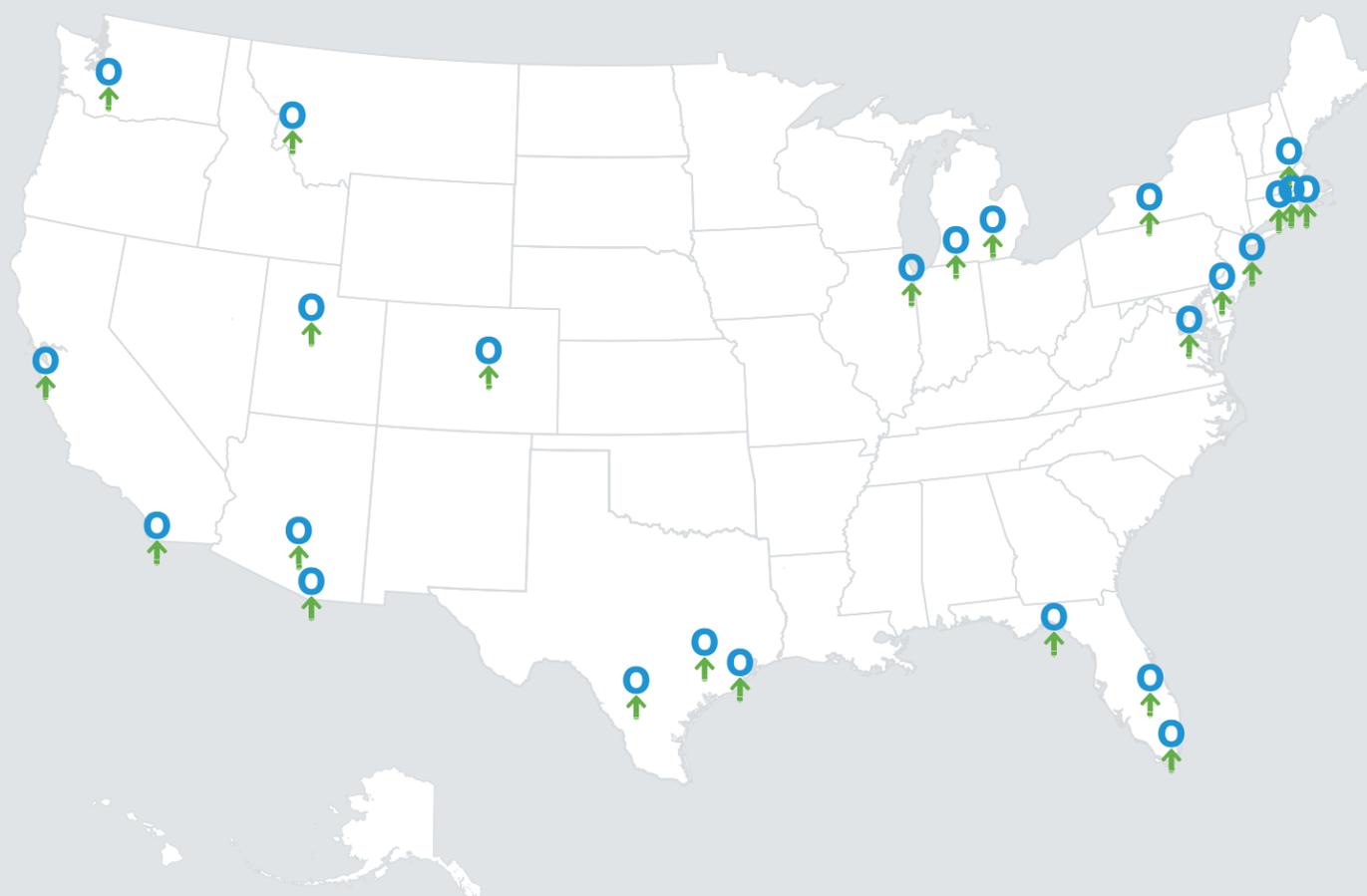
Fostering Global CTE Research

The VA-BU-CLF Brain Bank houses 70 percent of the world's brains diagnosed with CTE.

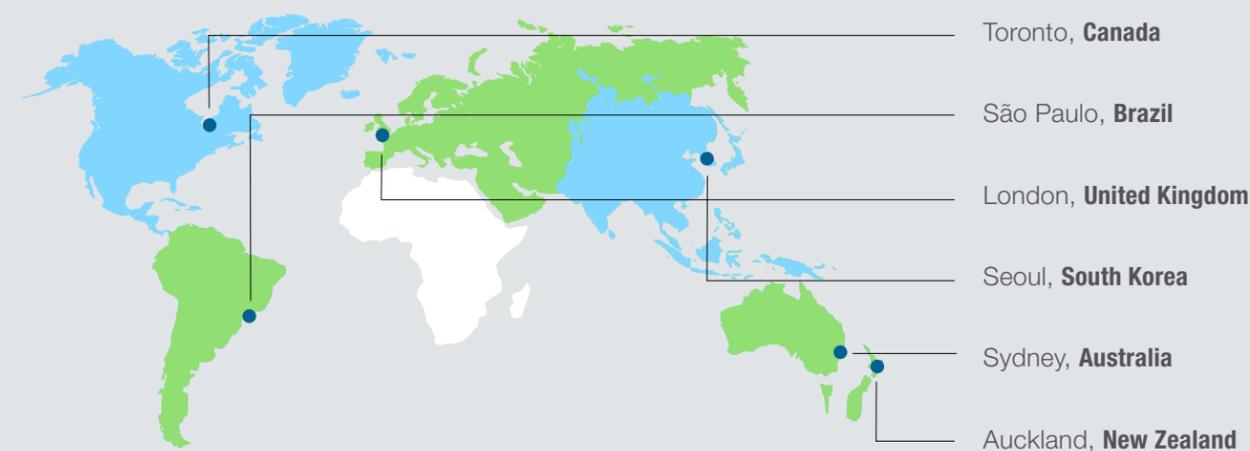
But the best science is propelled by collaboration. From the beginning, we prioritized recruiting more scientists from outside institutions to the fight against CTE. We accomplish that goal by making CTE tissue available to outside researchers with innovative research ideas. We are proud to have shared tissue with 100 outside research groups at 50 institutions around the globe.

We're working towards a world without CTE by making CTE tissue available to outside researchers with innovative research ideas.

Tissue Sharing in the United States



Global Collaborations



Collaborating Institutions

 Centre for Addiction and Mental Health	 University of Cambridge	 University of Auckland
 Seoul National University	 University of Sydney	 University of Sao Paulo



Looking to the Future

Former NFL linebacker Chris Borland (standing, far left), CLF chief impact officer Tyler Maland (standing, center left), CLF CEO Dr. Chris Nowinski (standing, right), and Legacy Family Community members Rebecca Carpenter (kneeling, far left) and Angela Harrison (kneeling, center right) at the filming of the Clio Grand Prize award-winning “Tackle Can Wait” campaign. Both Carpenter and Harrison’s fathers are Legacy Donors who died with CTE. Learn more at [TackleCanWait.com](https://www.tacklecanwait.com).

The Next 1000

Thanks to our unique research foundation at the VA-BU-CLF Brain Bank, we are poised to make tremendous advancements in the fight against CTE and traumatic brain injuries with the next 1,000 Legacy Donors studied.

We have diagnosed more than 70 percent of the world's CTE cases, and the evidence suggests CTE is an environmentally caused disease. But we've also found that clinical outcomes vary significantly among individuals, and part of that variability is caused by genetics. Once we have studied 2,000 brains, we will **finally have the statistical power** to isolate the genes associated with CTE susceptibility and resilience, and unlock new targets for therapies.

We are on the cusp of diagnosing CTE accurately in the living thanks to several key components of the Brain Bank's research. **First, we are working with donor families** to help doctors understand and treat the clinical symptoms of CTE, and we are supporting the development of diagnostic criteria for Traumatic Encephalopathy Syndrome, or TES. **Second, we are working with academic collaborators** and life sciences companies to develop new radioactive ligands that will

bind to CTE tau and allow CTE to be imaged on positron emission topography (PET) scans. **Third, we are identifying the CTE-specific forms of abnormal tau** in our Brain Bank, which we will then be able to identify and measure in blood and cerebrospinal fluid.

To support and accelerate the fight against CTE, CLF is recruiting researchers from around the globe through the Concussion Legacy Foundation Global Brain Bank, which has built brain banking partnerships in Australia, Brazil, and New Zealand, with more to come. **By establishing CTE as a global public health problem**, we will enable our peers around the world to bring their talents to this crucial mission.

Since we have shown that CTE can also be a consequence of military service, **we are investing in understanding CTE and other consequences of traumatic brain injury in our military Veterans.**

We know CTE does not just affect the individual; it also impacts spouses, parents, and children. We launched a formal study investigating the impact of CTE on families so we can build and provide appropriate support to families with CTE in a loved one. Better support will allow **families to stay together longer, live with dignity, protect their finances, and minimize the emotional impact on their children.** We are also intensely studying the relationship between concussions, CTE, and psychiatric symptoms and suicide. Knowing why brain trauma causes these symptoms will enhance prevention efforts to support the mental health of concussion and CTE patients.

As researchers get closer and closer to diagnosing and treating CTE in living people,

we are also advancing CTE prevention. In 2019, we discovered that CTE risk and severity are closely correlated to the number of years of play in male American football players. These findings have **sparked a national discussion on raising the age of first exposure to tackle football** to prevent CTE. We are recruiting research subjects, especially female athletes and military Veterans, so we can advance knowledge that will help these historically understudied populations.

If you would like to be a part of the discoveries and breakthroughs that will be possible with the next 1,000 Legacy Donors, **consider pledging your brain to research or donating to our research efforts** (see page 41). Together, we can create a world without CTE.

As researchers get closer and closer to diagnosing and treating CTE in living people, we are also advancing CTE prevention.



Solving the Invisible



★ PROJECT ★
ENLIST

POWERED IN PART BY WOUNDED WARRIOR PROJECT®

Traumatic brain injury (TBI) due to improvised explosive devices (IED) and other military service-related causes is a significant problem for our active military and Veteran community.

However, the scientific understanding of the relationship between TBI, CTE, and Post-Traumatic Stress Disorder (PTSD) is in its infancy.

The Concussion Legacy Foundation launched Project Enlist, powered in part by Wounded Warrior Project®, to serve as a catalyst for research on TBI, CTE, and PTSD in military Veterans. Brain bank research is an essential step in developing effective treatments for TBI, CTE, and PTSD so we can protect and support the heroes who courageously fight for our nation.

Project Enlist is creating a culture of brain donation within the military community by encouraging service members and Veterans to pledge to donate their brains to the VA-BU-CLF Brain Bank. Through Operation Brain Health, Project Enlist is also providing strategies, tactics, and treatments that can help Veterans feel better today and lower their risk of problems in the future. The next 1,000 Legacy Donors, a larger share of them military Veterans, will get us closer to solving the invisible wounds of war affecting our nation's heroes.



Wounds of War

Nicole Condrey lost her husband, U.S. Navy Special Warfare Veteran Ron Condrey, to suicide in September 2018 after a three-year battle with depression, anger, and impulsiveness. After Ron's death, Nicole received a call from retired Navy SEAL LT Jason Redman, who asked on behalf of CLF if Nicole would consider donating Ron's brain to the VA-BU-CLF Brain Bank as part of Project Enlist. Redman had already pledged his own brain to support Project Enlist. Nicole did not hesitate.

“Ron wanted to give back to Veterans in every way he could, so it was just a clear fit, something that could last.”

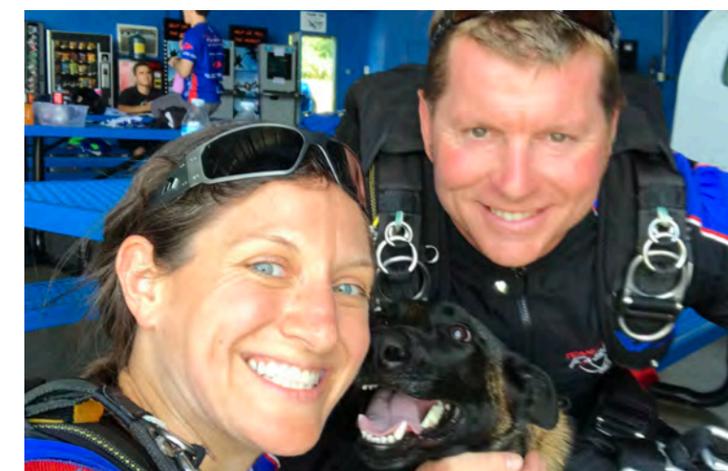
Nicole Condrey

By amplifying stories like Ron Condrey's, CLF hopes to bring the same visibility to the long-term effects of brain trauma in the military as it has the NFL. Because of Project Enlist, when a Veteran passes away, their family is more likely to connect with the VA-BU-CLF Brain Bank and donate, a gesture that will provide answers and help countless other Veterans.

Learn more at ProjectEnlist.org



Ron Condrey 07/15/73 – 09/03/18



Ron Condrey, his widow Nicole and Ron's service dog Via. Nicole now serves on CLF's Veteran Advisory Board.



LT Jason Redman holding his Project Enlist brain donor card.

Researcher Spotlight

VA-BU-CLF Brain Bank

A dedicated and talented team of scientists drive the research at the VA-BU-CLF Brain Bank. We asked some leading members of the research team to share how the next 1,000 Legacy Donors are crucial to advancing the science.



Michael Alosco, PhD

Associate Professor of Neurology, BU School of Medicine

Focus: Diagnosing and Treating CTE in Life

“The next 1,000 Legacy Donors will be instrumental to guide us in the development of clinical tools and methods that will be used to detect CTE in living people. The ability to accurately detect CTE in life will open the doors to research on treatment and bring hope to everyone living with this disease.”



Jonathan Cherry, PhD

Assistant Professor of Pathology and Laboratory Medicine, BU School of Medicine; Research Health Scientist at VA Boston Healthcare

Focus: Mechanism of CTE and Inflammation

“With 1,000 more Legacy Donors we will be able to better identify very subtle, early inflammatory changes that occur after injury and might lead to CTE. As these changes are hard to observe, more donations will increase our resolution and allow for improved study of early inflammatory events. Once we have a better understanding of what these early events are, we can begin to design biomarkers to identify damage during life and therapies to treat disease.”



Dan Daneshvar, MD, PhD

Assistant Professor of Physical Medicine and Rehabilitation, Harvard Medical School

Focus: How Head Impact Exposure Relates to the Pathology of CTE

“With 1,000 more Legacy Donors, we can get better answers about the factors responsible for CTE, which current evidence suggests is related to duration and severity of head impact exposure. Understanding what causes CTE will help inform policy changes to protect the next generation of athletes, while also giving us pathways to work towards a cure.”



Bertrand Huber, MD, PhD

Assistant Professor of Neurology, BU School of Medicine; Director of PTSD Brain Bank, VA Boston Healthcare

Focus: How TBI, CTE, and PTSD Interact

“As a Veteran whose research focus is the neuropathology of CTE, TBI, and Post-Traumatic Stress Disorder (PTSD), I am eager to delve into the uncharted territory of how these disorders interact and overlap, but we need more cases to study. Many service members who have seen combat are fighting two or even three of these disorders simultaneously. I would like nothing more than to give hope to and develop effective treatments for those who have been injured defending our country.”



VA-BU-CLF Brain Bank (Continued)



Ann McKee, MD

Director of Neuropathology for VA Boston Healthcare; William Fairfield Warren Distinguished Professor of Neurology and Pathology, BU School of Medicine; Director, BU CTE Center

Focus: CTE Prevention and Treatment

“Our understanding of CTE is far behind that of other neurodegenerative diseases like Alzheimer’s Disease and ALS. Each case we have the honor to study accelerates the science of CTE. Thanks to our Legacy Donors, incredible team, and growing national and international collaborations, we are now on the cusp of major breakthroughs.”



Jesse Mez, MD, MS

Associate Professor of Neurology, BU School of Medicine

Focus: Genetics of CTE

“With 1,000 more Legacy Donors, including focused efforts on diversity, we’ll have a sufficient number of cases to unlock the genetic mysteries of CTE. A deep dive into the genetics of CTE will yield new insights into how CTE begins and progresses, why some people are more affected than others, and will give us targets for therapies.”



Thor Stein, MD, PhD

Associate Professor of Pathology and Laboratory Medicine, BU School of Medicine

Focus: Comorbid Disease in CTE

“Repetitive head impacts and CTE appear to be risk factors for developing other neurodegenerative diseases. If we can understand why people with CTE are more vulnerable to developing Alzheimer’s Disease, Parkinson’s/Lewy Body Disease, and ALS, we can figure out ways to stop it.”



Yorghos Tripodis, PhD

Associate Professor of Biostatistics, BU School of Public Health

Focus: Quantitative Exposure Analysis

“With 1,000 more Legacy Donors, we will have a sufficient sample size to detect meaningful effects on disease severity. We need more brains, especially from more diverse TBI exposures, sports, and career lengths, so we can have a complete, unbiased picture of the effects of TBI on the brain. With this data, we will learn when CTE risk truly begins in different sports and populations, which could help athletes and parents make more informed choices about participation.”



A photograph of three men in a laboratory setting. They are all wearing white lab coats and safety glasses. The man in the center is wearing a yellow lab coat and blue gloves, and is holding a human brain specimen. The other two men are wearing white lab coats and blue gloves, and are looking at the brain. The background shows laboratory equipment and shelves with containers.

Creating a world without CTE

Dr. Chris Nowinski, Dr. Michael Buckland, and Colin Scotts, the second Australian to play in the NFL, at the launch of the Australian Sports Brain Bank in 2018.

CLF Global Brain Bank

In 2018, CLF launched the Global Brain Bank. CLF partners with existing leading brain banks to enable them to recruit brain donors and study CTE in their country. Global collaborations on research and advocacy are critical for achieving a world without CTE. We asked our partners from the Australian Sports Brain Bank at the University of Sydney, the Brazil Biobank for Aging Studies at the University of São Paulo, and the New Zealand Sports Human Brain Bank at the University of Auckland to share the future of their research.



Michael Buckland, MBBS, PhD, FRCPA

Director, Australian Sports Brain Bank
Focus: CTE in Australian Sports

“By identifying the first cases of CTE in men who have played rugby league and Australian Rules Football, we’ve launched a national conversation on the future of sports in Australia that is already resulting in rule changes in our games. Over the next decade, we look forward to collaborating with our American and global colleagues and contributing to prevention, diagnostic, and treatment efforts. We are particularly focused on developing a blood test for CTE, as well as the relationship between CTE and suicidal behavior.”



Sir Richard Faull, KNZM, FRSNZ, MBChB, PhD, DSc

Director, New Zealand Neurological Foundation Sports Human Brain Bank at the Centre for Brain Research at the University of Auckland
Focus: CTE in New Zealand

“There is so much to be learned about CTE. We are eager to apply the same methods we’ve used to advance knowledge on Huntington’s disease, Alzheimer’s disease, Parkinson’s disease, epilepsy, and Motor Neuron disease to advance the global understanding of CTE.”



Lea T. Grinberg, MD, PhD

John Douglas French Alzheimer’s Foundation Endowed Professor, Memory and Aging Center, UCSF | **Focus:** Postmortem Studies

“Research shows traumatic brain injury increases the risk of developing dementia in later life. The risk seems to go beyond CTE. Postmortem studies will help to clarify what this risk is and, as a consequence, help to mitigate the dementia epidemic.”



Alan Pearce, PhD

Associate Professor in the School of Allied Health at La Trobe University | **Focus:** Identifying Neurophysiological Markers for CTE and Dementia Using Non-Invasive Brain Stimulation

“As CTE is currently only diagnosable post-mortem, a challenge for all of us is to identify markers of CTE in living people. This can then allow us to develop strategies and potential therapeutics to assist those with improvement in their quality of life.”



Adam White, PhD

Assistant Professor, Oxford Brookes University; Executive Director, Concussion Legacy Foundation UK | **Focus:** How CTE Impacts Families

“We need to understand the lived experience of CTE and Post-Concussion Syndrome, including its impact on spouses, children, and even parents. Family structures are diverse, and CTE affects people differently as they age, so we need a significant sample size to learn how to best support families as they support a loved one with CTE.”

From Bench to Bedside and Beyond

Our collaborators have built upon the findings from the VA-BU-CLF Brain Bank to improve clinical care for patients, help families support loved ones with suspected CTE, and prevent future cases of CTE by reforming youth sports.

Ongoing efforts include advancing consensus diagnostic criteria for Traumatic Encephalopathy Syndrome, publishing guidelines for doctors on how to treat patients with suspected CTE, publishing on the impact of CTE on spouses and children and preventing CTE in the next generation of football players by transitioning the youngest and most vulnerable football players from tackle to flag.



Robert Cantu, MD

Co-founder and Medical Director, Concussion Legacy Foundation
Co-founder, VA-BU-CLF Brain Bank

Focus: Helping Patients with Possible CTE

“The discoveries made in the brain bank have inspired the treatment regimens we prescribe to patients who come to our clinic with symptoms that may be due to CTE. My colleague Dr. Andrew Budson and I wrote up our advice in Management of Chronic Traumatic Encephalopathy, and we will continue to update and refine treatment protocols as we learn more.”



Lee Goldstein, MD, PhD

Associate Professor of Psychiatry, Neurology, Radiology, Pathology and Laboratory Medicine, Electrical and Computer Engineering, Biomedical Engineering, BU School of Medicine

Focus: CTE Mechanisms of Disease

“The Brain Bank has been a critical component for our research and discoveries to date. I have no doubt that the Brain Bank, and the families and loved ones who make it possible, will continue to provide motivation as we push forward to develop new diagnostics, treatments, and preventive measures for this devastating disease.”



Chris Nowinski, PhD

Co-founder and CEO, Concussion Legacy Foundation
Co-founder, VA-BU-CLF Brain Bank

Focus: Preventing CTE in Athletes

“The VA-BU-CLF Brain Bank has provided evidence that a football player’s odds of developing CTE increase with each year played, and the younger one starts, the earlier CTE symptoms may develop. This inspired CLF’s Flag Football Under 14 campaign, which encourages parents to wait until high school to enroll their children in tackle football. We believe that simple change might prevent 50 percent of football CTE cases. We are eager to expand this research to other sports, but we need a larger sample size.”



Robert Stern, PhD

Professor of Neurology, Neurosurgery, and Anatomy & Neurobiology, BU School of Medicine

Focus: Diagnosing and Treating CTE in Life

“Our understanding of the clinical presentation and course of CTE has grown through each and every one of the 1,000 Legacy Donors and informed the recently published ‘NINDS Consensus Diagnostic Criteria for Traumatic Encephalopathy Syndrome (TES).’ Moreover, due in large part to our ability to translate what has been learned through the VA-BU-CLF Brain Bank research into clinical studies of new biomarkers (including the possibility of blood tests), we are now getting incredibly close to being able to detect and diagnose CTE during life!”



Behind the Scenes Heroes

The research team is on call 24 hours a day, seven days a week to ensure donated brains are safely and securely transported to the Brain Bank. Their delicate care allows brains to be thoroughly analyzed, creating a legacy of discovery through each family's precious gift of brain donation.

The process most frequently begins with a call to our 24-hour hotline, currently managed by **Madeline Uretsky**. The call is answered on a phone that has been shared by more than 20 research assistants since 2008, each possessing the phone for two weeks at a time, answering urgent calls at all hours of the night. The research assistants work with families to educate them on the brain donation process, get legal documents signed, and hire local medical experts to procure and transport the brain, often by courier.

When the brain then arrives at the Brain Bank, located at the Jamaica Plain VA Medical Center in Boston, Massachusetts, it is handed to neuropathologist **Dr. Victor Alvarez** (see top, page 39) or members of his team. They carefully unpack the brain, photograph it, weigh it, and begin to prepare it for analysis.

From there, a team of histologists take over. The histologists process the brain tissue, embed it into paraffin blocks, and then mount thinly sliced tissue sections onto glass

slides for microscopic study. They brush small amounts of chemicals and antibodies, all by hand, onto the tissue to make target proteins and disease artifacts visible for neuropathologists.

For each case, the neuropathologists review nearly 100 of the histologists' slides, looking for the telltale brown stain of hyperphosphorylated tau protein, as well as other markers of disease like TDP-43, beta-amyloid plaques, hemosiderin-laden macrophages, white-matter disease, Lewy bodies, and more. The neuropathologists then share the diagnosis with families with a written report and phone call.

These are the unsung heroes of the Brain Bank. Their dedication, professionalism, and diligence are imperative to the continued success of this research program. We would like to thank the current and former Brain Bank staff for their contributions over the years. On the next page, you'll find a list of behind-the-scenes superstars on the current Brain Bank staff.



Brain Processing Staff

Amina Burgess
Erin Dixon
Camille Esnault
Stevens Excellent
Lucas Fishbein
Sarah Horowitz
Daniel Kirsch
Robert McCormack
Raymond Nicks
Arsal Shah

24-Hour Brain Donation Hotline Staff

Bobak Abdolmohammadi
Evan Nair
Nicole Saltiel
Arsal Shah
Madeline Uretsky

Histologists

Kerry Cormier
Caroline Kubilus
Anthony Lapiana
Rebecca Mathias



Lisa McHale

CLF's Director of Family Relations

Lisa McHale joined the CLF team in 2010 as the director of legacy family relations. Lisa lost her husband Tom (pictured below), a former NFL player, in 2008 after he died at the age of 45. Lisa donated Tom's brain to the VA-BU-CLF Brain Bank, making him the second brain donor in the brain bank's history. After boldly sharing Tom's CTE diagnosis during a press conference at the 2009 Super Bowl, Lisa asked how else she could help. Brain donor volume was increasing so quickly that CLF co-founder Chris Nowinski asked Lisa to become CLF's first employee so she could provide the dedicated support brain donor families deserve.

Since then, Lisa has supported 1,000 brain donor families through the research process. After a brain arrives at the Brain Bank, Lisa is introduced to the family as their point of contact. Lisa then works with the family to help facilitate the compilation of medical records and schedule

interviews with family members to acquire the donor's sports, military, and brain trauma exposure history, as well as learn all relevant details from their life. Lisa accompanies every family on their call to learn the final diagnosis from the neuropathologist. After the diagnosis, Lisa invites the families to become lifetime members of CLF's Legacy Family Community. Members join quarterly calls with the researchers, create a memorial page on the CLF website, and are invited to biennial Family Huddle conferences with Legacy Families and the CLF, BU, and VA teams to build community and learn how their loved one continues to advance our understanding of the effects of brain trauma.

Lisa is the keystone between our Legacy Donor families, the BU and VA research teams, and CLF. She knows the tragedies of CTE firsthand and has chosen to be a guiding light for the first 1,000 brain donor families as they navigate the loss of a loved one.



Contribute to Hope

We would not have 1,000 Reasons for Hope without the individuals and organizations who support this research through their donations and their advocacy. If you would like to see this research continue to thrive, here are ways you can increase the impact of research at the VA-BU-CLF Brain Bank:

Donate to The Brain Bank

A gift to the Brain Bank directly supports Dr. Ann McKee and her research team so they can meet the growing pace of brain donations and accelerate discoveries and scientific breakthroughs.

Give at bu.edu/cte/financial-support

Donate to CLF

A gift to the Concussion Legacy Foundation helps CLF conduct outreach to families to facilitate brain donation, as well as translate brain bank discoveries into CTE prevention campaigns, education programs, and patient and family support.

Give at ConcussionFoundation.org/Give

Pledge Your Brain

Your support can help advance our understanding of concussion, CTE, and other consequences of head impacts by helping us recruit understudied populations like **women, military Veterans, victims of abuse, and sports** other than football like soccer, ice hockey, and rugby.

You can pledge to donate your brain to the VA-BU-CLF Brain Bank or join our clinical research registry at PledgeMyBrain.org. Veterans can pledge and access Veteran specific support and resources at ProjectEnlist.org.

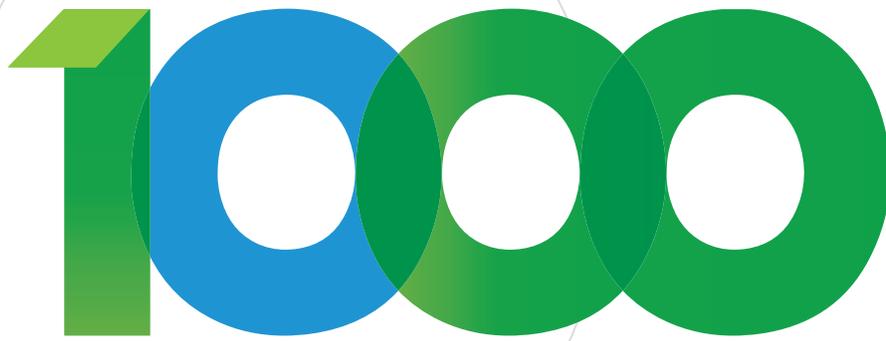


The Concussion Legacy Foundation

VA-BU-CLF Brain Bank discoveries have taught us crucial lessons about brain trauma risk and prevention. To learn more about how we are translating research into our education and advocacy programs like Flag Football Under 14, Team Up Speak Up, and the Media Project, visit ConcussionFoundation.org.

We're Here for You

If you are fighting the effects of concussion, Post-Concussion Syndrome (PCS), or suspected CTE, help is available. We support patients and families through the CLF HelpLine, which provides personalized help to those struggling with the outcomes of brain injury. If you or a loved one are seeking guidance on how to find the right doctor, would benefit from peer support, or have any other specific questions, submit a request to the HelpLine at ConcussionFoundation.org/HelpLine.



Reasons for **Hope**

Learn more at ConcussionFoundation.org

